Alkaline salts of sodium and potassium: from C–X reduction to C–H functionalization and beyond

Thesis by

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In Partial Fulfillment of the Requirements for the degree of

Doctor of Philosophy

CALIFORNIA INSTITUTE OF TECHNOLOGY

Pasadena, California

2017

(Defended Sept 26, 2016)

ACKNOWLEDGEMENTS

I would like to first acknowledge and thank my advisor Prof. Bob Grubbs and the rest of my committee: Profs. Sarah Reisman, Theodor Agapie, Brian Stoltz, and Scott Virgil for their assistance and guidance.

There are a number of members of the group with whom I have had the pleasure of working and whom I would like to especially acknowledge here. First, I want to thank Dr. Alexey Fedorov for inviting me to join his ongoing project related to lignin valorization and for acting as my mentor for my first two months in the lab. His seminal work on the C–O cleavage chemistry was highly inspiring and very impressive to me. I am very glad to call him my good friend and colleague ever since our first meeting nearly 4 years ago during a soccer game on the south field of Caltech. Next, I would like to acknowledge Kerry Betz, whom I initially met as a sophomore at Caltech, and whom I would have the pleasure of mentoring during my time at Caltech. I've had the great privilege of seeing her grow as both an individual and a scientist throughout our four years of working together and I am extremely proud of her accomplishments, which are substantial, and am grateful for her many contributions. Another undergraduate, Andrew Romine, joined our team a few years later and likewise deserves praise for his important contributions, great efforts, and excellent work ethic. My interactions and experiences with Kerry and Andrew have been among the most pleasant, meaningful, and satisfying at Caletch and I cannot overstate their quality; I am so grateful to have been a stewerd of their very bright careers. I would like to acknoweldge Nicholas Swisher for assistance with the reductive cleavage of aryl alkyl ethers and Dr. Mike Haibach who had kindly offered his expertise in the latter stages of the silyl ether synthesis work.

I have been extremely fortunate to have worked with many collaborators, most substantially with Prof. Brian Stoltz. In particular, I have worked closely with his excellent postdoctoral fellow Dr. Wen-Bo "Boger" Liu on many aspects of the science described in this thesis, and also with two visiting students at the time: Kazuma Oda and Betül Kitir. Most recently, I have worked closely with his talented graduate student, David Schuman, who is further investigating and expanding the work introduced and described in this thesis; he is also playing a key role in mechanistic investigations. As a result of these collaboration, we have also begun working with Prof. Nasri Nesnas (Florida Tech) and his graduate student Mozhgan Navidi, so I am likewise thankful to them for their contributions thus far. I have been very fortunate to collaborate with Prof. Ken Houk (UCLA) and his postdoctoral students Drs. Yong Liang and Yun-Fang Yang, and Prof. Dick Zare (Stanford) and his postdoctoral student Dr. Monon Banerjee in combined efforts toward the elucidation of the mechanism of our discovered reactions. Most recently, we have also initiated a collaboration with Prof. Gang Wu (Queen's University at Kingston) and his student Jiahui Shen to use their unique alkali metal NMR methods to gain further insight into the reaction mechanism and the structures of intermediates. Moreover, I've been extremely fortunate to have worked with British Petroleum for a number of years and in that regard I would like to in particular thank Drs. John Shabaker, George Huff, Eric Doskocil, Renan Cariou, Mike Salata, Drew Braden, and Glenn Sunley for their support of my projects and their helpful scientific guidance.

My work at Caltech would not have been possible without the gracious financial support of many organizations including the Resnick Sustainability Institute at Caltech, Bristol–Myers Squibb (BMS), Dow Chemical, British Petroleum (BP), the National Science and Engineering Research Council of Canada (NSERC), and the National Science Foundation CCHF. I would like to express my deep gratitude to these organizations for their faith in me personally as well as in my ideas and

abilities. I would like to also make a special acknoweldgement to Dr. Neil Fromer and to all of the members, staff, and fellows of the Resnick Sustainability Institute at Caltech for creating a wonderful working and learning environment during my time at Caltech, well beyond my fellowship activities and responsibilities. Great thanks are in order especially to Heidi Rusina for being an exceptional creative force for the institute in digital media and beyond, having also directed our documentary film *Element 19* (brought to life by the creative teams of M.Samuels Media and Oshin Studio with Sandy Gilfillan of Altered Tastes creating the film's original score). I am very grateful to call her my good friend and colleague. I thank also Stephanie Yanchiski, Director of the FLoW program at Caltech, for her friendship and guidance to me personally, but also for providing a venue for scientist-entrepreneurs at Caltech and beyond to hone their talents.

I would like to emphatically acknowledge a number of organizations, institutions, and individuals for awards and recognitions including Caltech, the Resnick Sustainability Institute of Caltech (Lynda and Stewart Resnick and the Resnick family), the Demetriades family, NSERC, BMS, Sigma–Aldrich Corporation, Milliken Chemical, the Resnick Institute, Dow Chemical, and Springer–Nature.

I am grateful to Drs. Farnaz Bakhshi and Oliver Losón at the Caltech Office of Technology Transfer and Corporate Partnerships for guidance and assistance with provisional patents and patent strategy and to Dr. Thomas Dekleva (BakerHostetler) for generating our patent documents and helping to build our intellectual property portfolio from my very first year at Caltech.

From the technical staff at Caltech I particulary wish to thank Dr. David Vander Velde (NMR), Naseem Torian and Dr. Mona Shahgoli (HRMS), and Dr. Nathan Dalleska (ICP-MS and GC-TCD). I also wish to thank Agnes Tong for being an engaging and overall excellent option coordinator.

Finally, I want to thank my mom and dad, to whom I owe everything, for being my greatest supporters and strongest advocates, and for always believing in me and loving me. I lovingly and gratefully dedicate this thesis to you.

ABSTRACT

The discovery and contemplations of Gilbert N. Lewis (1875–1946) regarding the concept of electron pair acceptors has led to an improved fundamental understanding of molecular interactions. Lewis's recognition that acidic character can exist in substances not containing hydrogen (i.e., Brønsted acids) led to the classification of a new group of reagents and catalysts for organic synthesis: Lewis acids. Over the last half-century, the application of these reagents and catalysts has in turn led to the discovery of a plethora of new chemical reactions, enabling previously unknown transformations. It has also been appreciated that electron pair donors (i.e., Lewis bases) are characterized by analogous and opposite behavior. Perhaps most intriguing is that in certain cases Lewis bases are capable of modifying simultaneously the electrophilic and nucleophilic character of the substance to which they are coordinated. It is also known that neutral tetravalent silicon can act as a Lewis acid for a variety of nucleophiles (i.e., Lewis bases) generating pentavalent Si species; these adducts are observed to have enhanced electrophilicity at Si and enhanced electron density at the ligands bound to silicon. In the case of organosilanes wherein at least one of the groups on silicon is a hydrogen (i.e., a hydrosilane), the reaction with Lewis bases can lead to pentavalent adducts with weakened Si–H bonds wherein the H has enhanced hydridic character. This property has been exploited by researchers in a number of ways, perhaps most prevalently in the development of hydrosilanes as mild reducing agents for the reduction of carbonyl compounds or for the mechanistically-related carbonyl hydrosilylation reaction.

This thesis details the discovery and development of fundamentally new chemical reactivity of silanes enabled by their interaction with basic salts of certain alkali metals (and includes some, but certainly not all of the work that I have performed in this area). First, it was found that specific combinations of hydrosilanes with basic alkali metal salts – in particular KO*t*-Bu – under certain

conditions form exceptionally powerful reductive couples capable of selectively cleaving strong aromatic C–O and C–S bonds with exceptional effectiveness and novel selectivity. Second, I found that certain modifications and elaborations of this chemical system lead to dramatic changes in the operative reaction manifold: from C–X bond cleavage to E–Si bond formation. I determined that this concept of activating hydrosilanes with alkaline salts of the alkali metals can be harnessed for the mild and efficient construction of a wide array of E–Si bond classes by catalytic cross-dehydrogenative coupling. Surprisingly, these challenging chemistries all occur in the absence of transition metal species, providing new horizons and opportunities for investigating Earth-abundant elements as catalysts and reagents for a host of applications.

PUBLISHED CONTENT AND CONTRIBUTIONS

Toutov, A. A.; Betz, K. N.; Haibach, M. C.; Romine, A. M.; Grubbs, R. H. Sodium hydroxide–catalyzed dehydrocoupling of alcohols with hydrosilanes. *Organic Letters* **2016**. *accepted*

A.A.T. conceived of the project, performed experiments, analysed data, and co-wrote the manuscript.

Toutov, A. A.; Liu, W.-B.; Stoltz, B. M.; Grubbs, R. H. Potassium *tert*-butoxide–catalyzed dehydrogenative cross-coupling of heteroarenes with hydrosilanes. *Organic Syntheses* **2016**, *93*, 263. doi: 10.15227/orgsyn.093.0263.

A.A.T. conceived of the project, performed experiments, analysed data, and co-wrote the manuscript.

Toutov, A. A.; Liu, W.-B.; Betz, K. N.; Stoltz, B. M.; Grubbs, R. H. Catalytic C–H bond silylation of aromatic heterocycles. *Nature Protocols* **2015**, *10*, 1897. doi: 10.1038/nprot.2015.118.

A.A.T. conceived of the project, performed experiments, analysed data, and co-wrote the manuscript.

Toutov, A. A.; Liu, W.-B.; Betz, K. N.; Fedorov, A.; Stoltz, B. M.; Grubbs, R. H. Silylation of C–H bonds in aromatic heterocycles by an Earth-abundant metal catalyst. *Nature* **2015**, *518*, 80. doi:10.1038/nature14126.

A.A.T. conceived of the project, performed experiments, analysed data, and co-wrote the manuscript.

Fedorov, A.; Toutov, A. A.; Swisher, N. A.; Grubbs. R. H. Lewis-base silane activation: from reductive cleavage of aryl ethers to selective *ortho*-silylation. *Chemical Science* **2013**, *4*, 1640. doi: 10.1039/C3SC22256J.

A.A.T. optimized the reaction, developed analytics, performed experiments, and co-wrote the manuscript.

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Chapter 1

REDUCTIVE CLEAVAGE OF C–X BONDS BY THE KOSI METHOD

Abstract.

Inspired by the need for new selective aromatic C–O and C–S bond cleavage methods, we have discovered that in the absence of exogenous transition metal species, stoichiometric mixtures of potassium alkoxide bases and organosilanes form potent regioselective reductive systems for the cleavage of diaryl and aryl alkyl ethers in lignin model compounds to the corresponding phenolic and aromatic compounds. This potassium (*K*) alkoxide (*O*)/hydrosilane (*Si*)-based (*KOSi*) system is likewise amenable to the hydrodesulfurization (HDS) of thiophenols, thioethers, and sulfur-containing heterocycles, which are naturally occurring sulfur impurities found in fossil fuel streams. Application of this method to the HDS of diesel fuel itself provides remarkable sulfur reduction activity.

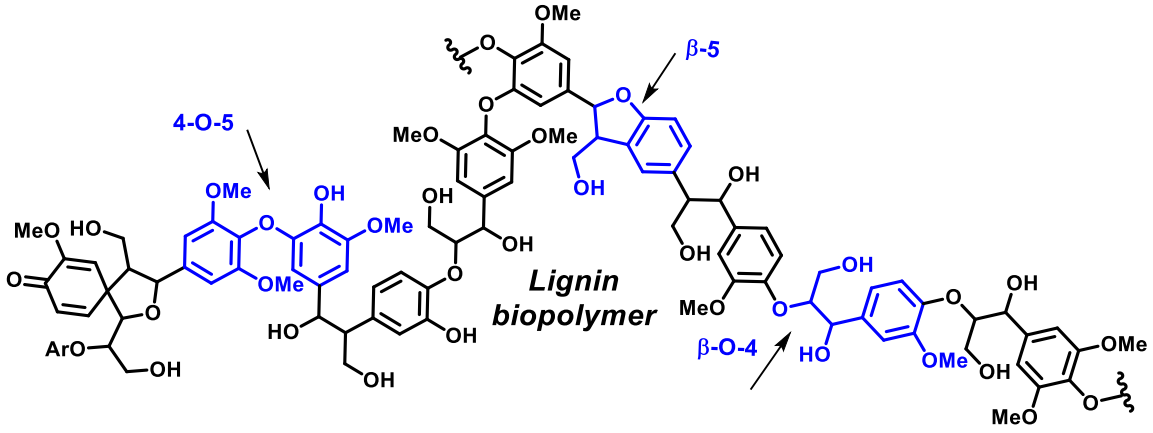
Introduction.

Methods for the cleavage of C–O and C–S bonds are valuable techniques, which are employed routinely in a variety of applications. Although a number of catalytic and stoichiometric methods for the title transformation exist, strategies for the efficient and selective reductive cleavage of such C–X bonds in aromatic systems remains particularly challenging and new methods are desired. Furthermore, the importance of aromatic C–O and C–S bond cleavage extends beyond the realm of chemical synthesis, constituting the key chemical challenge in reductive strategies aimed at the valorization of biomass, the liquefaction of coal, and the desulfurization of petroleum streams, which are all important large scale industrial processes.

Reductive aryl C–O bond cleavage.

There is a healthy surge in interest for efficient manufacturing of fuels and bulk chemicals from renewable bioresources due to the decline of fossil fuel reserves globally.[1] Thus, the natural biopolymer lignin has emerged as an important target for biomass conversion because of its complex structure which, if valorization would be possible, represents a source of fine chemicals as well as fuels through complete deoxygenation **(Figure 1.1**).[2]

Figure 1.1. Examples of C–O bonds present in the lignin biopolymer showing key disconnections (blue).

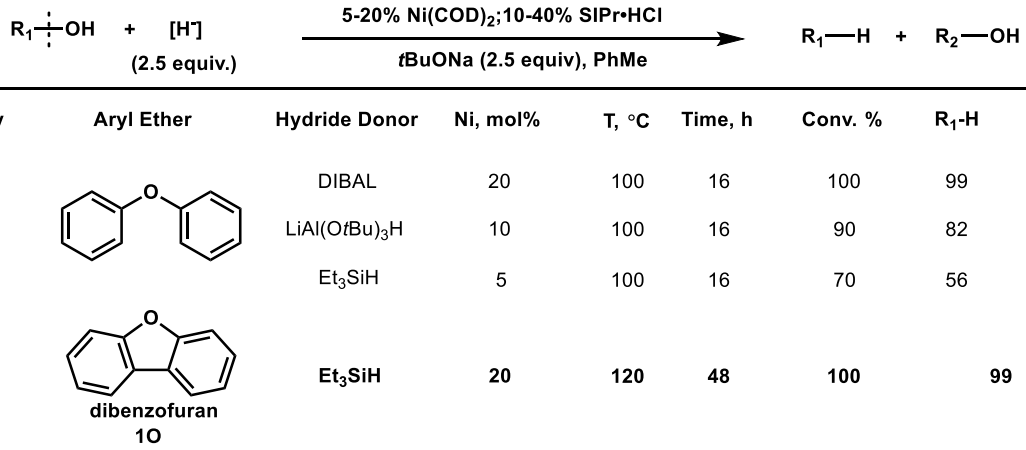


However, technologies for lignin decomposition do not currently allow for sufficiently cost-effective, practicable, and selective valorization.[3] In particular, a major challenge is the cleavage of the strong aromatic C–O bonds which represent the key strategic disconnection points of the highly oxygenated biopolymer.[4] Some inspiration for the cleavage of the aromatic C–O bonds found in lignin has been found in the utilization of aryl alkyl ethers as electrophiles in cross-coupling reactions with Ni catalysts.[5]

This has led Martin to employ *in situ* prepared phosphine-ligated Ni species to cleave the aryl–oxygen bond in aryl alkyl ethers of relevance to lignin using tertiary silanes as the stoichiometric reductant;[6] a similar approach was also reported by Chatani.[7] Employing instead *N*-heterocyclic

carbenes as supporting ligands allowed Hartwig to develop a Ni-catalyzed, homogeneous C–O bond cleavage system using different reductants including dihydrogen, albeit with Ni loadings as high as 20 mol %, which is a significant limitation on scale (**Figure 1.2**).[8,9,10] Interestingly, Hartwig demonstrated that in the case of dibenzofuran (**1O**) and a number of other aryl ethers, even the mild Et_3SiH is a competent reducing agent (entry 4).

Figure 1.2. Hartwig's Ni-catalyzed hydrogenolysis of aryl ethers with various reductants including the mild triethylsilane (bolded).



Entry	Aryl Ether	Hydride Donor	Ni, mol%	T, °C	Time, h	Conv. %	R_1-H	R_2-OH
1		DIBAL	20	100	16	100	99	99
2		$LiAl(OtBu)_3H$	10	100	16	90	82	86
3		Et_3SiH	5	100	16	70	56	70
4	**dibenzofuran 1O**	**Et_3SiH**	**20**	**120**	**48**	**100**	**99**	

SiPr•HCl = 1,3-Bis(2,6-diisopropylphenyl)imidazolinium chloride. DIBAL = diisobutylalumium hydride. COD = 1,5-cyclooctadiene.

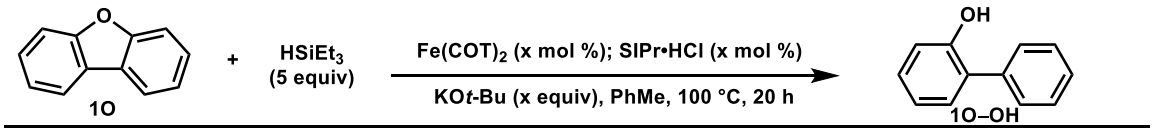
The issue of impracticable catalyst loadings was remedied by the same group by employing a heterogeneous Ni catalyst.[11] It is interesting to note that in the supplementary information accompanying the first Hartwig paper,[8] the authors report the use of a superstoichiometric quantity of NaO*t*-Bu as the base for deprotonating the NHC and that the excess base was necessary, but its role was not known. The use of Pd nanoparticles in aqueous solution has also been investigated.[12] Most recently, Stahl and co-workers have recently demonstrated the efficient oxidative cleavage of not only lignin model compounds but of lignin itself, providing the highest yields of monomeric aromatic fragments from the biopolymer reported to date.[13]

We were thus interested in developing a reductive C–O bond cleavage method which overcomes certain limitations of previous approaches, in particular the use of high loadings of expensive and/or sophisticated transition metal complexes. It was at this point that my talented colleague and friend Dr. Alexey Fedorov began to investigate the use of iron catalysts for lignin decomposition and made an intriguing serendipitous discovery.

Control reactions lead to discovery

Dr. Fedorov initially decided to investigate the use of a homogeneous iron complex and hydrosilanes as the stoichiometric reductant in the reductive cleavage of dibenzofuran (**1O**).

Figure 1.3. Dr. Alexey Fedorov's investigations into the reductive cleavage of the aryl C–O bond in dibenzofuran (1O) using hydrosilanes.



Entry	$Fe(COT)_2$	SIPr•HCl	KO*t*-Bu	Yield
1	5 mol%	10 mol%	2 equiv	98%
2	5 mol%	10 mol%	–	–
3	5 mol%	–	2 equiv	98%
4	**–**	**–**	**2 equiv**	**34%**

SiPr•HCl = 1,3-Bis(2,6-diisopropylphenyl)imidazolinium chloride. COT = cyclooctatetraene.

This would be essentially analogous to the homogeneous system reported by Hartwig,[8] but would replace Ni with Fe in the hopes of obtaining a more active system and thus lowering the loadings of metal – a significant limitation of that particular system. Thus, combining $Fe(COT)_2$ (5 mol %) with the NHC ligand SIPr•HCl (10 mol %), 5 equivalents of Et_3SiH (as the stoichiometric reductant) and 2 equivalents of KO*t*-Bu (as the strong base to deprotonate the NHC) in toluene at 100 ˚C, Dr.

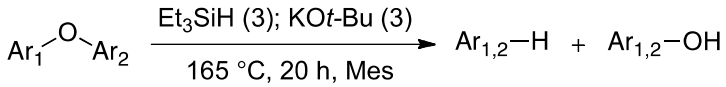
Fedorov observed a high-yielding C–O bond cleavage of dibenzofuran (**1O**) to produce the resulting biphenyl-2-ol **1O–OH** (**Figure 1.3**, entry 1).

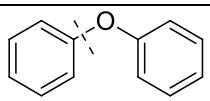
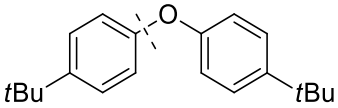
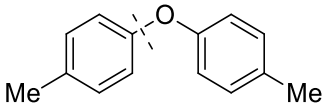
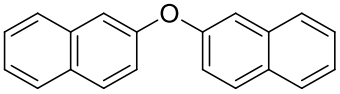
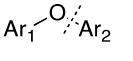
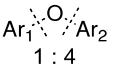
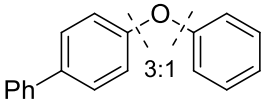
Thus, Dr. Fedorov had discovered an efficient Fe-catalyzed analogue to Hartwig's nickel system. However, the use of an iron catalyst for aryl C–O bond cleavage was unprecedented, making this immediate success somewhat even more interesting. As a result, Dr. Fedorov began to perform control experiments to better understand the role of each component of the system. It was found that repeating the reaction without the KO*t*-Bu led to no conversion of the starting material (entry 2), but attempting the chemistry with base but without the NHC led again to high-yielding C–O bond cleavage the (entry 3). This was intriguing since the role of the base was initially believed to be necessary for deprotonating the NHC. This led Dr. Fedorov to perform what would be the crucial experiment: repeating the reaction in the absence of both NHC and iron catalyst. This reaction provided, unexpectedly, the desired C–O bond cleavage product **1O–OH** simply by the action of KO*t*-Bu and Et_3SiH alone in 34% yield (entry 4, bolded). I would later find in my own explorations that closer investigation and optimization exercises for this reaction would lead to other unanticipated discoveries and will therefore be discussed in the next chapter. Nevertheless, I undertook the optimization of this C–O cleavage reaction and found that by increasing the temperature to 165 ˚C and employing 3 equivalents each of KO*t*-Bu and Et_3SiH in mesitylene as the solvent, the yield of **1O–OH** could be increased to 85% (entry 5). Careful ICP-MS analyses of the reagents and reaction mixtures ruled out catalysis with transition metals (See **Experimental and analytics** section, **Table 1.2**).[14]

Investigation of the scope of aryl ether C–O bond cleavage

This transition metal–free C–O bond cleavage protocol could be applied to a variety of symmetrical diaryl ether connections having differing steric and electronic factors with typically good combined yields (**Figure 1.4**).

Figure 1.4. Transition metal–free reductive cleavage of diaryl ethers.[a]



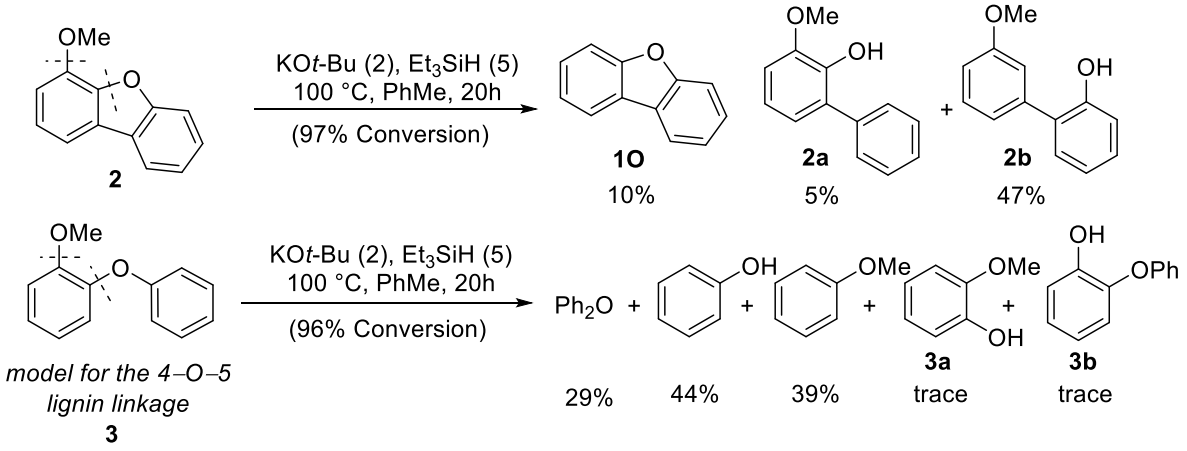
Entry	Diaryl Ether	Conv. (%)	Ar_1-H Ar_2-H	Ar_1-OH Ar_2-OH
1		96	64	65
2		100	76	98
3		100	52	84
4[b]		100	50	88
5[c]	 Ar_1 = phenyl Ar_2 = 1-naphthyl	100	— 70	91 —
6[d]	 1 : 4 Ar_1 = 2-naphthyl Ar_2 = 1-naphthyl	100	57	58 15
7[d]	 3:1 Ar_1 = 4-Ph-Ph Ar_2 = Ph	100	41 19	21 65

[a]GC yields and conversions are reported using tridecane as a standard. [b]Trace amount of 1,2,3,4-tetrahydronaphthalene detected. [c]100 °C for 20 h in toluene with 2 equiv. each of Et_3SiH and KO*t*-Bu. [d]Run at 75 °C for 40h in toluene. Mes = mesitylene (solvent).

It was found that unsymmetrical diaryl ethers were cleaved regioselectively (**Figure 1.4**, entries 5–7). For example, in the case of 1-naphthyl phenyl ether (entry 5), bond cleavage occurred regiospecifically at the naphthyl C–O bond to furnish naphthalene and phenol in 70 and 91% yield respectively, with no 1-naphthol or benzene detected. With the unsymmetrical dinaphthyl ether

(entry 6), C–O bond reduction occurred regioselectively to provide 2-naphthol and 1-naphthol in good combined yield with approximately a 4:1 ratio of the two isomers, respectively. The unsymmetrical para-phenyl substituted diphenyl ether (entry 7) reacts with good overall yield and with moderate regioselectivity for reduction of the slightly more electron rich C–O bond indicating the apparent influence of electronic effects in site-selectivity of C–O bond cleavage. This factor becomes determining for the selectivity of cleavage of 4-*O*-5 lignin models that contain strong methoxy donors adjacent to the C–O bond being broken (**Figure 1.5**).

Figure 1.5. Cleavage of unsymmetrical aryl ethers containing methoxy donors.

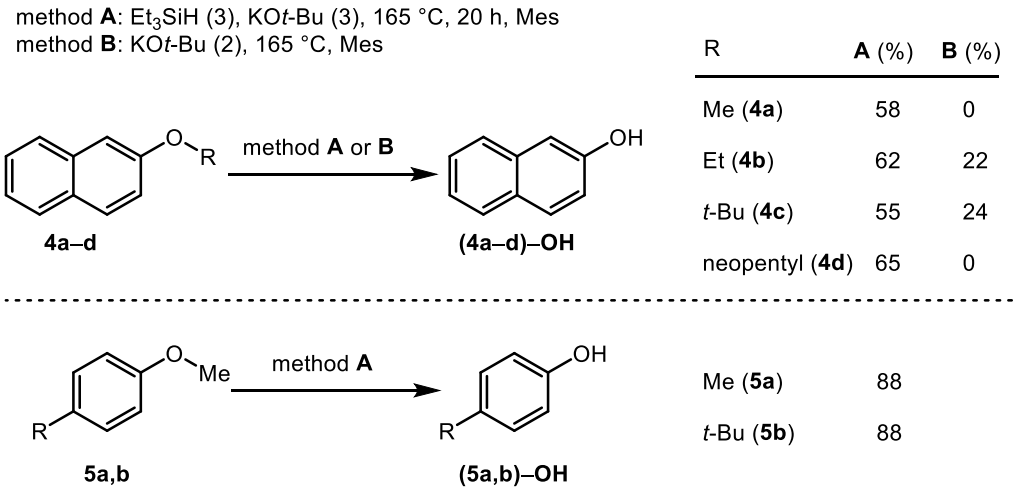


It is also noteworthy to point out that such selectivity is complementary to that reported by Hartwig for Ni catalyzed reduction with dihydrogen wherein unsymmetrical diaryl ethers were preferentially cleaved at the side of the more electron-deficient aryl ring.[8,11]

Nicholas Swisher had also found that this reaction, under the optimized conditions, could also be applied to a variety of aryl-alkyl ethers with good success. This result is potentially useful both in the context of lignin valorization but also in the removal of protecting groups in organic synthesis applications (**Figure 1.6**).

It became especially apparent in the investigation of aryl-alkyl cleavage that the reaction showed an essential insensitivity to the steric environment about the C–O bond, which is generally counterintuitive. For example, in **Figure 1.6**, aryl-alkyl ethers having R = methyl, or R = *t*-butyl (i.e.,

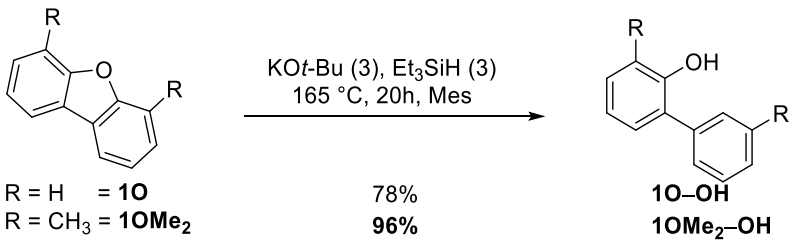
Figure 1.6. Transition metal–free reductive cleavage of aryl-alkyl ethers.



Mes = mesitylene (solvent).

comparing **4a** with **4c**) are cleaved with the same yield. The yields of C–O cleavage in **5a** and **5b** are higher due to the lack of aromatic reduction in benzene derivatives compared to naphthalenes (wherein partial aromatic reduction is observed). Interestingly, the selectivity for isolated alkyl aryl-alkyl C–O bond scission that we observe with our system contrasts with that observed in Ni-[6-8] and even borane-catalyzed C–O cleavage reactions where exclusive aryl C–O reduction occurs.[15]

Scheme 1.1. Comparison of the reductive cleavage of dibenzofuran (1O) and its 4,6-dimethyl analogue (1OMe$_2$).

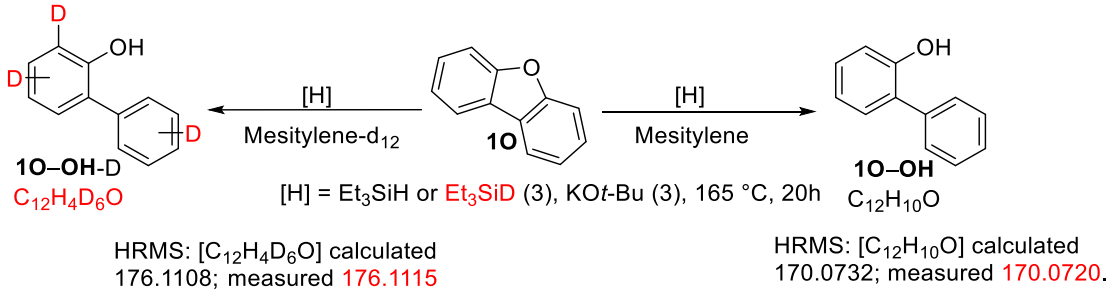


An additional example demonstrating the steric insensitivity of the method is the reaction of 4,6-dimethyldibenzofuran (**1OMe$_2$**), which undergoes C–O bond cleavage in markedly higher yield than does dibenzofuran (**1O**) itself (**Scheme 1.1**).

Preliminary mechanistic investigations

Throughout this process, the very unusual nature of this reaction led us to actively contemplate its mechanism. Although the underlying manifolds of this reaction are still unknown and are under investigation, a suite of interesting mechanistic experiments were performed. First, Dr. Fedorov had found that a mixture of KO*t*-Bu, Et_3SiH, and dibenzofuran in toluene was EPR active (See **Experimental and analytics** section, **Figure 1.17**) and that essentially the same signal was observed without dibenzofuran added. This suggested the presence of open-shell species and potentially hinted at the presence of productive single-electron pathways of some sort, but this signal was certainly not proof of such. Second, we had wanted to performed a deuteration study in order to gain additional insights into the mechanism and in particular to probe the potential pathway for H atom delivery to the final product.

Scheme 1.2. Reductive cleavage of dibenzofuran in the presence of deuterium sources.



However, we were surprised to find that subjecting dibenzofuran (**1**) to the standard reactions conditions, but now using Et_3SiD led to essentially zero deuterium incorporation into the product **1O–OH** (**Scheme 1.2**).

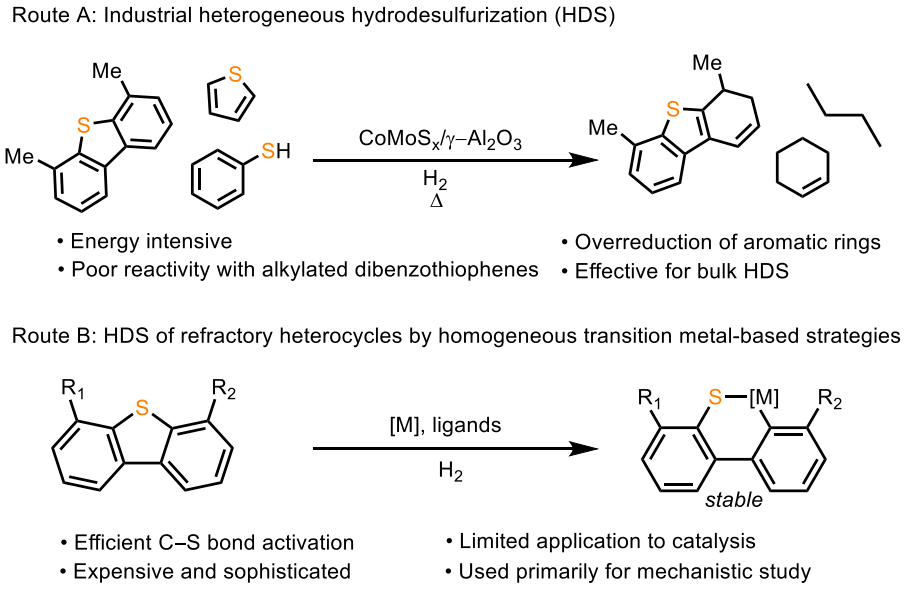
In agreement with this observation, identical base peaks in high-resolution MS spectra of biphenyl-2-ol (**1O–OH**) prepared either from Et_3SiH or Et_3SiD in Mes-d_{12} indicate that rapid H/D exchange with the solvent occurs under the reaction conditions. Interestingly, as proton, carbon, and HSQC spectra of deuterated dibenzofuran (**1O–OH-D**) suggest (See **Experimental and analytics** section, **Figures 1.17–1.22**), while all of the protons undergo partial H/D exchange, only for the *ortho*-OH position does this process reach completion.

Reductive aryl C–S bond cleavage.

Crude petroleum streams contain naturally-occurring organosulfur impurities, with quantities varying depending on the geographical source of the feedstock.[16,17,18,19] These organosulfur species poison the precious metals in the catalytic converters of automobiles and generate harmful sulfur dioxides when combusted.[16,17,18] Hydrodesulfurization (HDS), the industrial process by which sulfur impurities are removed from petroleum fractions, is currently performed by treating petroleum with H_2 at high pressures and temperatures (i.e., 150–2250 psi and 400 °C) over heterogeneous catalysts such as cobalt-doped molybdenum sulfide supported on alumina (i.e., $CoMoS_x/\gamma\text{-}Al_2O_3$; **Figure 1.7,** Route A).[18,19] However, certain aromatic sulfur heterocycles, such as the alkylated dibenzothiopenes, are not efficiently removed.[16,17,18,19,20] Homogeneous strategies based on well-defined molecular transition metal complexes have been extensively investigated to specifically target the removal of these refractory S-heterocycles and have in some cases generated interesting data.[21,22,23,24,25,26,27,28,29,30,31] However, the formation of stable transition metal metal-sulfide

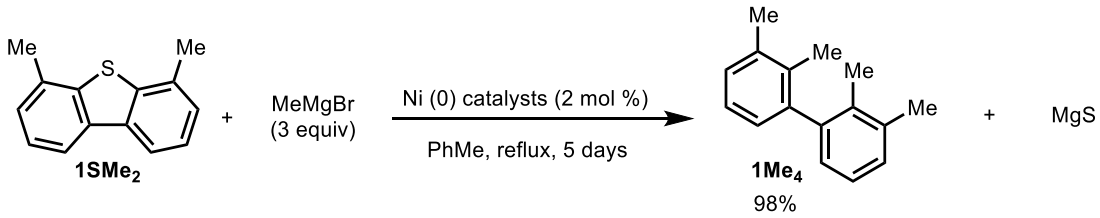
complexes upon C–S bond activation by the metal center (**Figure 1.7**, route B) have largely prevented catalytic turnover, thus precluding industrial implementation. An example of homogeneous transition metal–catalyzed HDS of 4,6-dimethyldibenzothiophene (4,6-Me_2DBT, **1SMe$_2$**) has been reported; however, the chemistry requires superstoichiometric alkyl Grignard

Figure 1.7. Methods for the hydrodesulfurization (HDS) of sulfur-containing aromatics and heteroaromatics.



reagents – to enable catalyst turnover – in combination with expensive, air-sensitive Ni catalysts (**Scheme 1.3**).[30]

Scheme 1.3. Ni-catalyzed HDS of 4,6-Me_2DBT (1SMe$_2$).

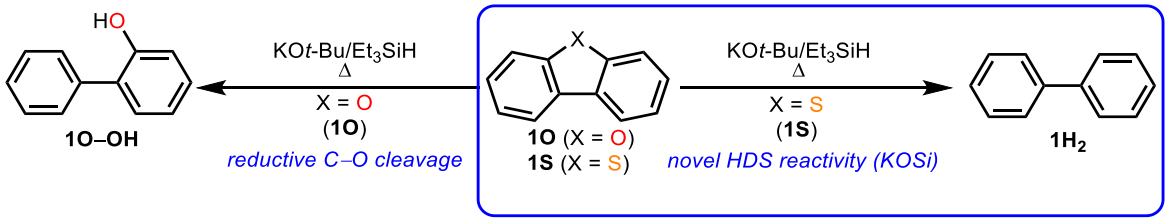


These issues pose a formidable challenge for the development of new HDS methods. In addition, as HDS method development remains restricted by fundamental scientific and technological

limitations, increasingly strict governmental regulations require limiting the sulfur content in diesel fuel and gasoline to unprecedentedly low levels in the coming years: in the US: typically <15 and <30 ppm, respectively.[16,17,18] Taken together, these issues render the development of new powerful HDS methods an urgent and primary global concern.[16,17,18,19,31]

Discovery of HDS of dibenzothiophenes

Scheme 1.4. Discovery of HDS of dibenzothiophene by the *KOSi* method.

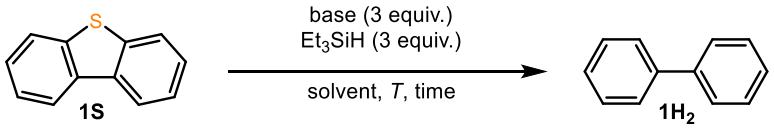


As was discussed previously, we had recently observed the cleavage of aryl C–O bonds in lignin models in the absence of transition metals using hydrosilanes.[14] In the case of dibenzofuran (**1O**; **Scheme 1.4**, X = O), use of the potassium (*K*) alkoxide (*O*)/hydrosilane (*Si*)-based (*KOSi*) in hydrocarbon solvent at elevated temperatures (>100 °C) led to successful C–O bond cleavage producing biphenyl-2-ol (**1O–OH**) in good yield. We thus became interested in extending this method to sulfur heterocycles of relevance in oil and gas refining applications.

We had anticipated initially that applying these same conditions to dibenzothiophene (**1S**; **Scheme 1.4**, X = S) would result in the formation of a biphenyl-2-thiol; however, rather than obtaining the single C–S bond cleavage product, a complete desulfurization of the heterocycle affording biphenyl (**1H$_2$**) in good yield was observed. Moreover, no reduction of aromatic rings was detected. Optimization studies demonstrated that, similarly to the C–O cleavage chemistry,[14] the HDS chemistry was most successful with superstoichiometric base and hydrosilane, in hydrocarbon solvent, and at elevated temperatures (**Table 1.1**). The reaction appears to require a strong inorganic

base (**Table 1.1**, entries 4–10) and does not occur with potassium hydroxide (entry 3) or with organic bases (entries 11–13). A potassium base appears to be vital for HDS to occur and the reaction does not proceed with lithium- or sodium alkoxide bases (entries 1 & 2). KO*t*-Bu proved to be the optimal basic activator for the HDS (entry 7) while KOMe (entry 5) and KOEt (entry 6) afforded the product in significantly lower yield. It appeared then that the effectiveness of the *KOSi* system correlates

Table 1.1. Optimization of the *KOSi* HDS of dibeozthiophene.[a]



entry	base	[Si]–H	solvent	*T* (°C)	time (h)	yield $1H_2$[a]
1	LiO*t*-Bu	Et_3SiH	Mesitylene	100	72	–
2	NaO*t*-Bu	Et_3SiH	Mesitylene	100	72	–
3	KOH	Et_3SiH	Mesitylene	100	72	–
4	KH	Et_3SiH	Mesitylene	100	40	12%
5	KOMe	Et_3SiH	Mesitylene	100	40	21%
6	KOEt	Et_3SiH	Mesitylene	100	40	29%
7	KO*t*-Bu	Et_3SiH	Mesitylene	100	40	46%
8	KO*t*-Bu	Et_3SiH	Mesitylene	120	40	66%
9	KO*t*-Bu	Et_3SiH	Mesitylene	165	40	83%
10	KO*t*-Bu	Et_3SiH	Mesitylene	200	40	90%
11	Pyridine	Et_3SiH	Mesitylene	165	72	–
12	DBU	Et_3SiH	Mesitylene	165	72	–
13	NEt_3	Et_3SiH	Mesitylene	165	72	–
14	KO*t*-Bu	Et_2SiH_2	Mesitylene	165	40	13%
15	KO*t*-Bu	$EtMe_2SiH$	Mesitylene	165	40	26%
16	KO*t*-Bu	Et_4Si	Mesitylene	165	72	–
17	KO*t*-Bu	Et_3SiH	THF	165	40	22%
18	KO*t*-Bu	Et_3SiH	Benzene	100	40	47%
19	KO*t*-Bu	Et_3SiH	MeCy	165	40	81%
20	KO*t*-Bu	Et_3SiH	1,4-dioxane	165	40	30%
21	KO*t*-Bu	Et_3SiH	Toluene	120	40	49%
22	KO*t*-Bu	Et_3SiH	*t*-BuOH	120	40	–
23	KO*t*-Bu	Et_3SiH	Diglyme	165	40	–
24	KO*t*-Bu	Et_3SiH	DMF	100	40	–
25	KO*t*-Bu	Et_3SiH	DMA	100	40	–
26	KO*t*-Bu	Et_3SiH	Diisopropyl carbinol	165	40	–

[a]Yields determined by GC-FID analysis using tridecane as a standard. MeCy = methyl cyclohexane. DMA = *N*,*N*-dimethylacetamide.

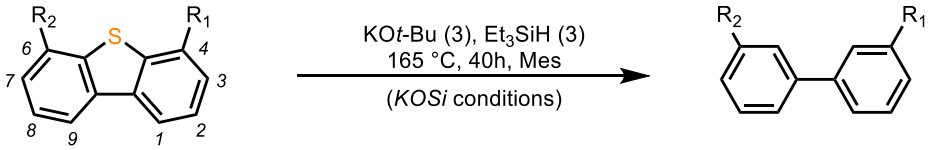
with the basicity of the alkoxide; however, consideration of solubility of the base in the reaction medium cannot be discounted as a contributing factor. The yield of biphenyl (**1H$_2$**) increases with increasing temperature (entries 7→10). Considerations of energy input led us to run the HDS reactions at 165 °C; however, increasing the temperature to 200 °C further improves the yield of **1H$_2$** (entry 10). With respect to the hydrosilane, triethylsilane (Et_3SiH) demonstrated the highest HDS activity; a dihydrosilane, Et_2SiH_2, performed poorly compared to Et_3SiH (entry 14). The light and low-boiling $EtMe_2SiH$ was also less effective (entry 15).

KOSi HDS of higher dibenzothiophenes and non-heterocyclic organosulfur species

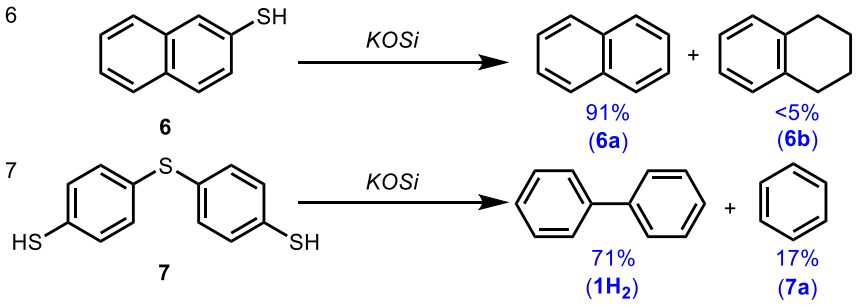
With optimized conditions for the HDS of **1S** established, we proceeded to investigate the scope of aromatic organosulfur species amenable to this protocol. The oxidized analogue of **1S**, dibenzothiophene sulfone (**1S–SO$_2$**), was also desulfurized in good yield under the reaction conditions (**Figure 1.8**, entry 2).

It is well appreciated that dibenzothiophene and especially its oxidized analogue are relatively non-problematic for known HDS methods, so we proceeded to investigate the reactivity of more refractory sulfur species which have proven to be particularly resistant to currently employed HDS technologies.[16,17,18,19,20,32,33,34,35] In this regard, 4-methyl- and 4,6-dimethyl dibenzothiophenes (**1SMe** and **1SMe$_2$**) were subjected to *KOSi* conditions and also succumbed to desulfurization, leading to the corresponding biphenyls **1Me** and **1Me$_2$** in high yields (entries 3 & 4). Based on the nearly identical product hydrocarbon yields obtained with the various dibenzothiophene starting materials, it became apparent that the steric hindrance around the sulfur atom in the heterocycle had essentially no effect on the efficiency of desulfurization. To further probe this unanticipated property of our *KOSi* system, we selected the very bulky 4,6-diethyldibenzothiophene (**1SEt$_2$**). Remarkably,

Figure 1.8. *KOSi* HDS of organosulphur aromatics.



Entry	Dibenzothiophene Derivative	Yield Hydrocarbon
1	R_1=R_2=H (DBT) (**1S**)	82% (**1H$_2$**)
2	R_1=R_2=H; SO_2 (DBT-SO_2) (**1S–SO$_2$**)	87% (**1H$_2$**)
3	R_1=Me; R_2=H (4-MeDBT) (**1SMe**)	83% (**1Me**)
4	R_1=R_2=Me (4,6-Me_2DBT) (**1SMe$_2$**)	83% (**1Me$_2$**)
5	R_1=R_2=Et (4,6-Et_2DBT) (**1SEt$_2$**)	87% (**1Et$_2$**)
Non-heterocyclic organosulphur species		



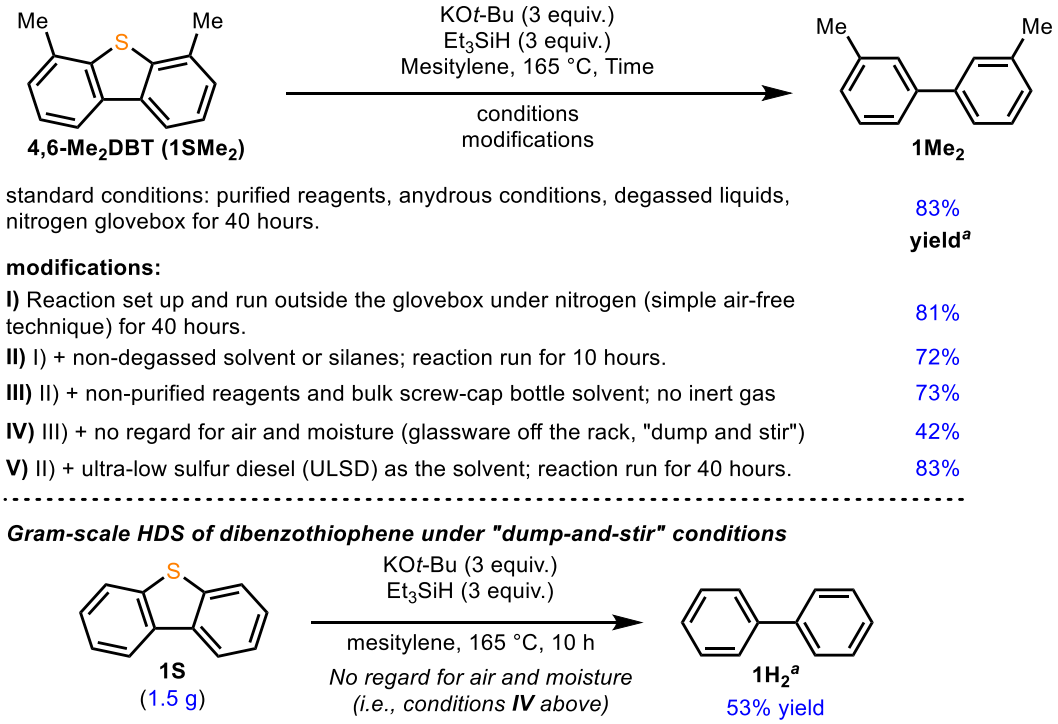
it too underwent desulfurization to the corresponding hydrocarbon **1Et2** (entry 5), again with an efficiency similar to that of unsubstituted dibenzothiophene.

These data suggest that the *KOSi* system is virtually insensitive to the presence of alkyl functionalities at the 4- and 6- positions of dibenzothiophene. This property is beneficial since competing HDS strategies are typically highly sensitive to steric factors.[16,17,18,19,21,25,26] Non-heterocyclic S-containing aromatics containing C–S bonds that are relevant to oil refining,[16,17,18,36] such as naphthalene thiol **6** and thioether **7**, were efficiently desulfurized (**Figure 1.8**, entries 6 & 7). In the case of the latter, using merely 0.75 equivalents each of KO*t*-Bu and Et_3SiH per aryl C–S bond provided an intriguing formal reductive desulfurative coupling of two aromatic rings to give biphenyl (**1H2**) and benzene (**7a**) as the major and minor product respectively.[37]

Robustness and practicability of the KOSi method

Practical considerations of the *KOSi* method will have an important impact on the likelihood of its eventual implementation in industry. Fortunately, a brief robustness evaluation demonstrates that the reaction is tolerant of conditions that attempt to model a general operating environment in a refinery

Figure 1.9. Robustness evaluation of the KOSi HDS of 4,6-dimethyldibenzothiophene (1SMe$_2$) and gram-scale HDS of dibenzothiophene (1S).



[a]Yields are by GC-FID analysis using tridecane as a standard.

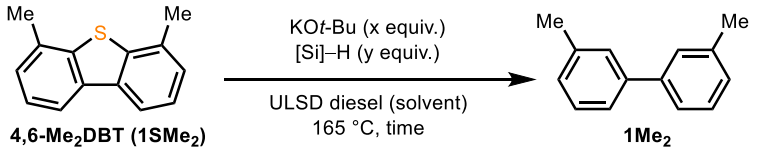
setting (**Figure 1.9**). The robustness investigation conducted in the context of the *KOSi* HDS of 4,6-Me$_2$DBT (**1SMe$_2$**) shows that the reaction tolerates impurities such as those that would be found in bulk, unpurified solvents and reagents and that it can be performed under air (**Figure 1.9**, **I**–**III**). A 10-hour reaction time leads to slightly lower conversion. The reaction shows some sensitivity to water, as would be expected given the sensitivity of KO*t*-Bu to moisture. Although impacting the

yield (**IV**), the reaction proceeds in the presence of ambient moisture both on the surface of the glassware as well as in the solvent and reagents. The reaction also proceeds well in ultra-low sulfur diesel (ULSD) as the solvent (see **V**). The scalability of the reaction was evaluated using dibenzothiophene (**1S**) due to its much lower cost and greater ease of synthesis compared to **1SMe$_2$**. The reaction scales well with gram quantities of **1S** to give the hydrocarbon product (**1H$_2$**) in 53% yield after 10 h at 165 °C.

*Optimization of the KOSi HDS of 4,6-Me2DBT (**1SMe$_2$**)*

Having determined that the *KOSi* HDS of 4,6-Me$_2$DBT (**1SMe$_2$**) proceeds well in ULSD (see **Figure 1.9**, **V**) we proceeded to investigate the effect of silane and base loading as well as reaction time using ULSD as an industrially-relevant model solvent.

Figure 1.10. *KOSi* HDS of 4,6-dimethyldibenzothiophene (1SMe$_2$) under varying conditions.



4,6-Me$_2$DBT (1SMe$_2$) → 1Me$_2$

entry	KO*t*-Bu (equiv.)	[Si]–H (equiv.)	time (h)	yield 1Me$_2$[a]
1	3	Et_3SiH (3)	40	83%
2	2	Et_3SiH (2)	40	65%
3	1	Et_3SiH (1)	40	25%
4	3	Et_3SiH (3)	10	79%
5	3	Et_3SiH (3)	5	42%
6	3	PMHS (3)	40	49%

[a]Yields are by GC-FID analysis using tridecane as a standard.

Decreasing the number of equivalents each of base and silane from 3 (**Figure 1.10**, entry 1 (standard conditions)) to 2 (entry 2) to 1 (entry 3) shows a step-wise decrease of the yield. With 3 equivalents each of KO*t*-Bu and Et_3SiH, the reaction time can be lowered to 10 hours with a slight drop in the yield (entry 4) as was shown in the case of mesitylene as the solvent (see **Figure 1.9**, **II**). Further lowering reaction time to 5 hours results in a large corresponding decrease in yield (**Figure 1.10**,

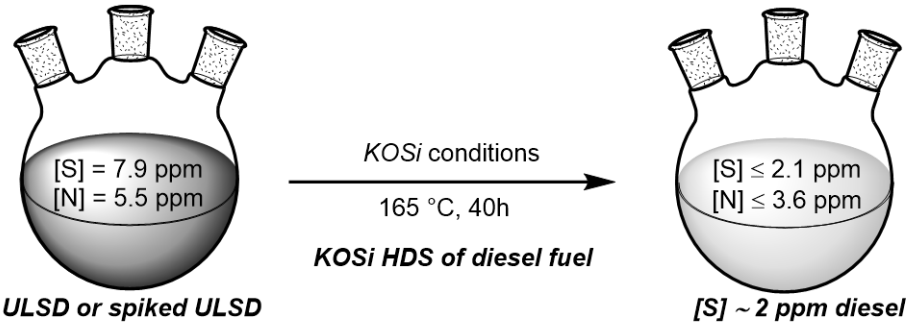
entry 5). Et_3SiH could be replaced by polymethylhydrosiloxane (PMHS) – an inexpensive, non-toxic, air- and water stable polymeric hydrosiloxane which is a byproduct of the silicone industry – though with decreased yield (entry 6).[38] In this latter case, despite the non-negligible decrease in yield, the fact that the *KOSi* reaction proceeds in the presence of such a simple, inexpensive, and abundantly available Si–H source is very surprising since PMHS is generally employed for facile reductions, most often of carbonyl derivatives. Most importantly, *KOSi* with PMHS is a vital proof of principle for future improvements toward eventual implementation.

KOSi HDS of ULSD and spiked ULSD

Having established that *KOSi* is effective in the desulfurization of a variety of aromatic sulfur species relevant to the HDS of gas oil, we were intrigued to investigate the HDS of a true petroleum fraction. We therefore proceeded to apply our *KOSi* technique to the HDS of ultra-low sulfur diesel (ULSD) itself.[16,17] Subjecting this fuel to our reductive method resulted in a solution wherein the sulfur content was further reduced beyond the already low levels using varying concentrations of the *KOSi* reagents under standard conditions (**Figure 1.11**, entries 3–7). The nitrogen concentration was likewise reduced, which could potentially be interesting for future hydrodenitrogenation (HDN) investigations.[19] As expected, the control experiments (entries 1 and 2) showed no significant sulfur reduction, although a slight increase in the nitrogen concentration was observed in these controls, which is attributed to partial evaporation of the diesel fuel during the reaction. To simulate the desulfurization of a sulfur-rich fuel stream, the ULSD was spiked with 4,6-Me_2DBT (**1SMe$_2$**) to give a 10,000 ppm concentration of the sulfur heterocycle in diesel. This mixture was also efficiently desulfurized to furnish ULSD with a remarkably low sulfur content of 2.4 ppm (entry 8). While the method would need to be adapted to a continuous flow system (and other engineering challenges

resolved) for use in a refinery setting, these data clearly establish *KOSi* as a powerful novel HDS polishing strategy, which is capable of lowering the sulfur levels in liquid fuel streams to remarkably low levels under practical conditions.

Figure 1.11. *KOSi* HDS of ultra-low sulfur diesel (ULSD).



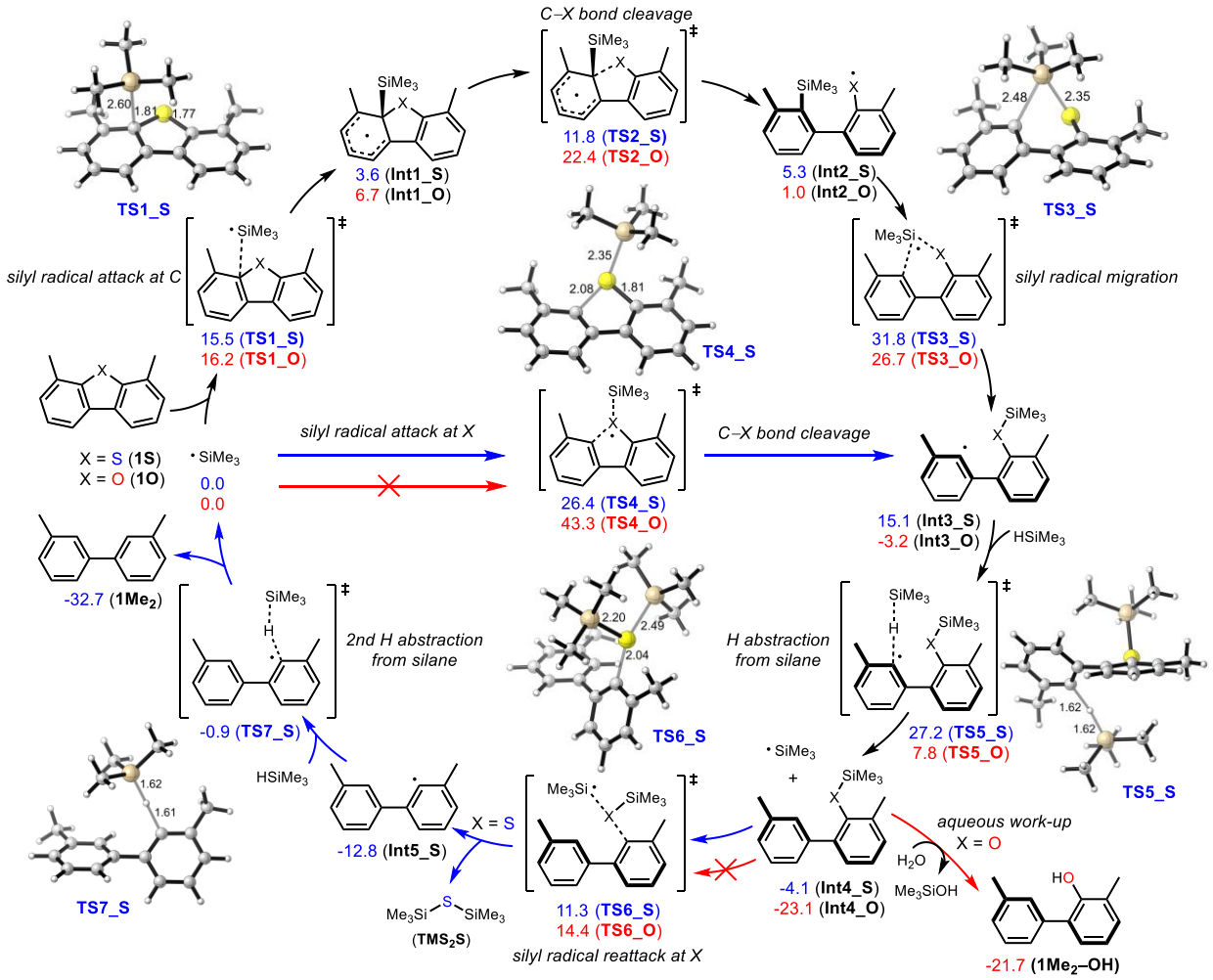
Entry	[KOt-Bu] in Diesel (M)	[Et_3SiH] in Diesel (M)	[N] (ppm)	[S] (ppm)
Control reactions:				
1	1.0	–	4.3	6.2
2	–	1.0	8.3	7.6
HDS of true diesel fuel by the KOSi technique:				
3	2.0	2.0	3.4	1.9
4	1.0	1.0	2.2	1.1
5	0.5	0.5	1.9	2.0
6	0.3	0.3	1.8	1.6
7	0.1	0.1	3.6	2.1
*HDS of ULSD spiked with 4,6-Me_2DBT (**3**) to give an initial sulfur content of [S] ~ 10,000 ppm:*				
8	0.5	0.5	0.4	2.4

DFT studies of aryl C–O bond cleavage and HDS by KOSi

A combined DFT mechanistic study regarding the *KOSi* C–O bond cleavage reaction and the HDS was investigated by Prof. Ken Houk and his co-workers at UCLA. The reaction cycles for both the C–O bond cleavage of **1OMe$_2$** and the *KOSi* HDS of **1SMe$_2$** are shown in **Figure 1.12**. The presence

of open-shell species in a related system and the observed H/D exchange in deuterated solvent (**Scheme 1.2**)[14] led us to begin our computational study with trimethylsilyl radical.

Figure 1.12. Proposed mechanism for hydrodesulfurization (HDS) of dibenzothiophenes and hydrogenative cleavage of diarylethers by *KOSi*.



Attack of the silyl radical at the carbon of the C–X bond in 4,6-dimethyldibenzothiophene (**1SMe$_2$**) or the dibenzofuran analogue (**1OMe$_2$**) gives the silyl radical adduct (**Int1_X**; X = S, O) proceeding through **TS1**. In each case, subsequent homolytic C–X bond cleavage occurs to give **Int2_X**, and subsequent silyl radical migration from C to X through **TS3** forms the aryl radical **Int3_X**.[39,40]

Figure 1.13. Free energy profile for *KOSi* HDS of 4,6-dimethyldibenzothiophene (1SMe$_2$).

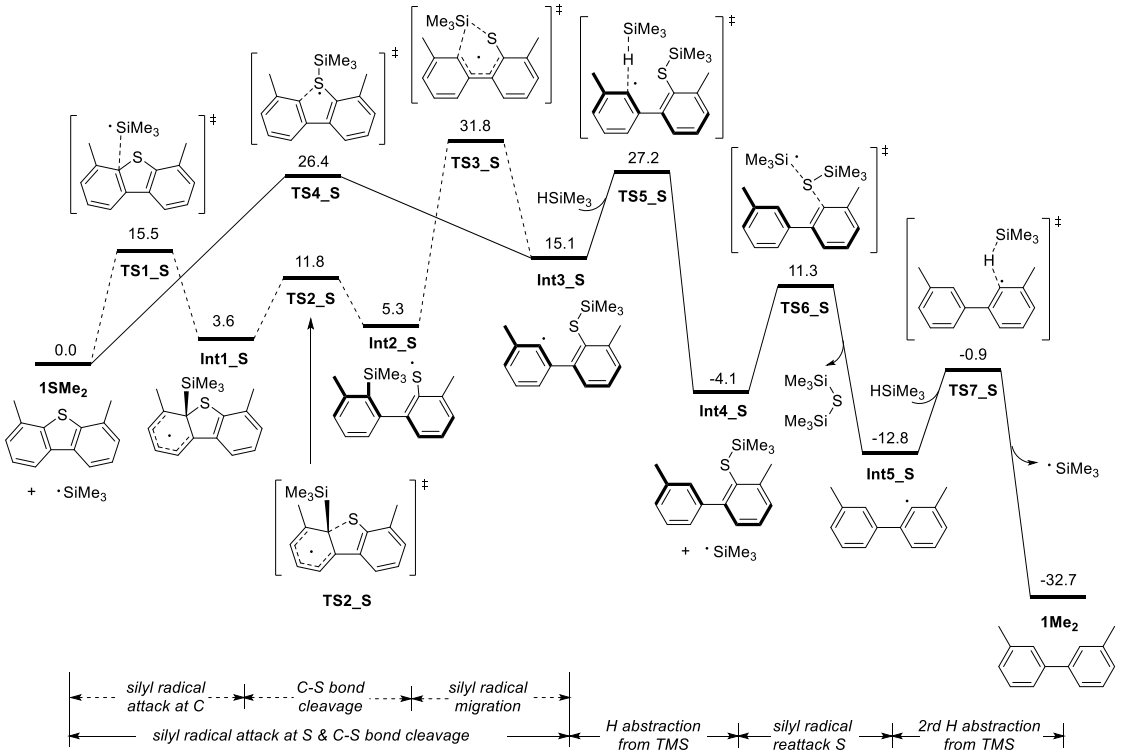
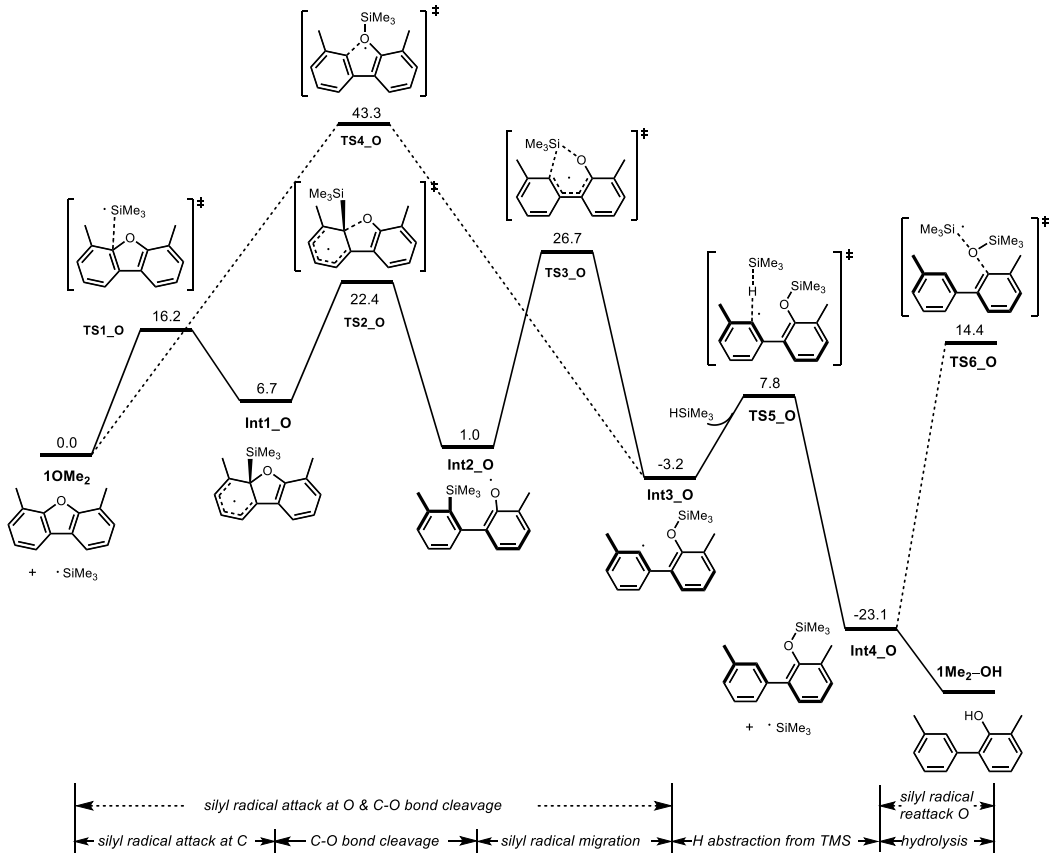


Figure 1.14. Free energy profile for *KOSi* HDS of 4,6-dimethyldibenzofuran (1OMe$_2$).

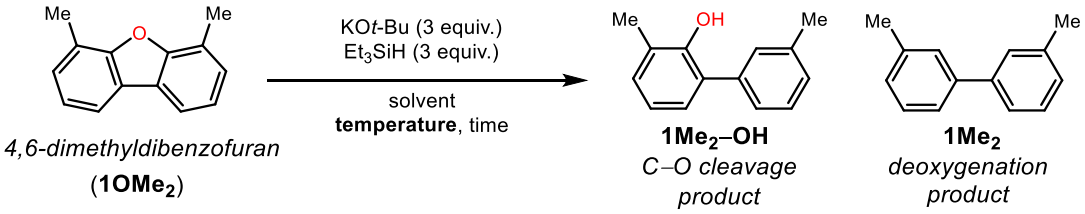


An alternative pathway to this carbon radical species involves silyl radical attack at the X atom followed by C–X bond cleavage, proceeding through **TS4_S** as shown in the center of the scheme; interestingly, this pathway is not accessible for 4,6-dimethyldibenzofuran **1OMe$_2$** because **TS4_O** is very high in energy at 43.3 kcal mol^{-1}. Subsequently, the aryl radical **Int3_X** abstracts a hydrogen atom from Me_3SiH through **TS5** to afford silylated biaryl-2-thiol **Int4_X**. For X = O, silyl ether **Int4_O** is believed to represent the reaction endpoint, and it is hydrolysed upon aqueous work-up to generate the experimentally observed 4,6-dimethylbiphenyl-2-ol (**1Me$_2$–OH**).[17] In the case of the silylated biphenyl-2-thiol **Int4_S**, a second attack of a silyl radical at the S atom forms disilathiane (**TMS)$_2$S** and biaryl radical **Int5_S**. We note that the formation of $Et_3Si–S–SiEt_3$ in the desulfurization of thioformamides and related carbonyl species using silanes and stoichiometric transition metal species under photoirradiation is precedented.[41] Finally, the biaryl radical can abstract hydrogen from Me_3SiH through **TS7_S** to form the experimentally observed 4,6-dimethylbiphenyl **1Me$_2$** and regenerate the trimethylsilyl radical. Thus, for substrate 4,6-Me_2DBT (**1SMe$_2$**), silyl radical attack either at the heteroatom S (both in **1SMe$_2$** and in the intermediate **Int4_S**, leading to desulfurization) or at C2 are both favorable pathways. In contrast, for 4,6-dimethyldibenzofuran **1OMe$_2$**, silyl radical attack at oxygen is unfavorable for both the substrate (cf. **TS4_O**) and the intermediate biaryl silyl ether **Int4_O** (cf. **TS6_O**). These significant differences in energetics become especially clear in comparing **Figure 1.13** and **Figure 1.14**, which show the energy profiles for both pathways. Thus, the silyl radical preferentially attacks the aryl group of the substrate and generates **Int4_O** as the reaction endpoint (which upon aqueous quench affords biaryl-2-ol **1Me$_2$–OH**), instead of proceeding to the deoxygenated product **1Me$_2$.**

However, the deoxygenation pathway can indeed be accessed at higher temperatures, as evidenced by the observation of a small amount of **1Me$_2$** when the reaction is conducted at 200 °C,

demonstrating the appropriateness and predictive capability of the proposed mechanistic model and additionally providing an intriguing proof of concept for further studies into the hydrodeoxygenation (HDO) of aromatic oxygenates by *KOSi* (**Figure 1.15**).

Figure 1.15. Observed deoxygenation of 4,6-dimethyldibenzofuran (1OMe$_2$) at elevated temperatures.



entry	solvent	temperature (°C)	time (h)	yield 1Me$_2$–OH[a]	yield 1Me$_2$[a]
1	toluene	100	20	78%	–
2	mesitylene	165	20	96%	–
3	mesitylene	200	60	93%	7%

[a]Yields are by GC-FID analysis with tridecane as a standard.

For both **1SMe$_2$** and **1OMe$_2$,** whether the silyl radical adds to the heteroatom or to C2 of the heterocycle, the attack occurs from above the plane defined by the molecule as can be seen in the computed transition states **TS1_S** and **TS4_S**. This provides a rationale for the insensitivity of the reaction to steric congestion at C4 and C6. Finally, two key transition states were located (**TS1_S_Et** and **TS4_S_Et**; see Appendix Table 1) for the attack of triethylsilyl radical at C2 and S of 4,6-dimethyldibenzothiophene (**1SMe$_2$**). The computed activation free energies are 17.2 and 26.1 kcal mol^{-1}, which are close to those using trimethylsilyl radical (15.5 and 26.4 kcal mol^{-1}) as seen in **Figures 1.12–1.14**. This indicates that trimethylsilane is a suitable model for investigating the experimental system computationally.

This mechanistic profile is in good agreement with experimental findings and rationalizes the different reaction pathway of the O- and S-dibenzoheterocycles, the absence of H_2S during the

reaction due to the formation of an Si–S–Si species, the retention of unsaturation in benzene rings,[42] and the unique insensitivity of *KOSi* HDS to the steric bulk around the heteroatom.

Conclusion.

We have discovered an unanticipated and novel protocol for the reduction of recalcitrant aryl ether C−O bonds. Remarkably, this challenging transformation occurs by action of simple, commercially available reagents that operate in the absence of exogenous transition-metal species. This (*K*) alkoxide (*O*)/hydrosilane (*Si*)-based (*KOSi*) method was found to be regioselective, easily tunable, and is not accompanied by hydrogenation of aromatic rings in appreciable amounts and was applied to the valorization of lignin model compounds. This chemistry led me to consider investigating *KOSi* as a potential aryl C−S bond reduction method. Applying the *KOSi* system to sulfur dibenzoheterocycles leads, unexpectedly, to complete desulfurization rather than single C−S bond cleavage. The *KOSi* system desulfurizes refractory 4,6-dialkylated dibenzothiophenes and lowers the sulfur content of ULSD and sour diesel fuel streams to unprecedentedly low levels (i.e., [S] ~ 2 ppm). DFT investigations reveal previously unknown HDS reactivity manifolds, successfully rationalize the unique features of the chemistry, and provide valuable insights facilitating future developments. *KOSi* is currently being investigated in an industrial refining setting as an HDS polishing technology.

Experimental and analytics.

General information

All reactions were carried out in dry glassware under an argon atmosphere using standard Schlenk line techniques or in a Vacuum Atmospheres Glovebox under a nitrogen atmosphere unless specified otherwise. Mesitylene (puriss., ≥99.0% (GC)) was degassed by three freeze-pump-thaw cycles prior to use. All other solvents were purified by passage through solvent purification columns and further degassed with argon.[43] NMR solvents for air-sensitive experiments were dried over CaH_2 and vacuum transferred or distilled into a dry Schlenk flask and subsequently degassed with argon. Triethylsilane (99%) and deuterotriethylsilane (97 atom % D) were purchased from Sigma–Aldrich and degassed by three freeze-pump-thaw cycles prior to use and other commercially available liquid reagents were treated analogously. Di-4-(methyl)phenyl ether, 1-naphthol, 2-naphthol, 4-tert-butylanisole, 4-methylanisole, 1,3-diphenoxybenzene, 2-methoxynaphthalene, and 1.0M tetrabutylammonium fluoride THF solution were purchased from Sigma-Aldrich and used as received. Sublimed grade KO*t*-Bu (99.99%) was purchased from Sigma-Aldrich and subjected to vacuum sublimation (30 mTorr, 160 °C) prior to use. 4-(Methoxy)dibenzofuran,[44] di-4-(tert-butyl)phenyl ether,[8] naphthyl ethers,[45] 4-(phenyl)phenyl phenyl ether,[8] 2-ethoxynaphthalene,[45] 2-neopentyloxynaphthalene,[45] 2-tert-butyloxynaphthalene[46] were synthesized according to the literature procedures. Standard NMR spectroscopy experiments were conducted on a Varian Mercury (1H, 300 MHz) spectrometer, a Varian Inova 400 MHz spectrometer, a Varian 500 MHz spectrometer equipped with an AutoX probe, or a Varian 600 MHz spectrometer equipped with a Triax Probe. Chemical shifts are reported in ppm downfield from Me_4Si by using the residual solvent peak as an internal standard. Spectra were analyzed and processed using MestReNova Ver. 7.[47] GC-FID analyses were obtained on an Agilent 6890N gas chromatograph equipped with a HP-5 (5%-

phenyl)-methylpolysiloxane capillary column (Agilent). GC-MS analyses were obtained on an Agilent 6850 gas chromatograph equipped with a HP-5 (5%-phenyl)-methylpolysiloxane capillary column (Agilent). High-resolution mass spectra (EI and FAB) were acquired by the California Institute of Technology Mass Spectrometry Facility. EPR spectra were recorded on a Bruker EMS spectrometer. Sulfur-containing organics were purchased from Aldrich and were purified by distillation or recrystallization. Ultra-low sulfur diesel (ULSD) was obtained from the Harlem terminal in Chicago, which receives its diesel predominantly from the Whiting refinery where it would have been hydrotreated. The ULSD did not contain any additives or biodiesel. The sulfur concentration of the ULSD was 7.9 ppm and the nitrogen concentration was 5.5 ppm. The ULSD was used as received. Yields are generally determined by GC-FID analysis (using tridecane as a standard) unless otherwise stated.

ICP-MS Analysis

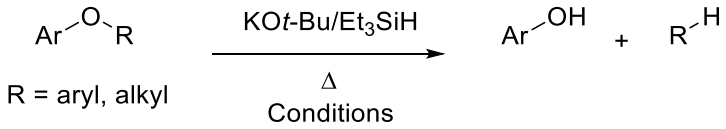
ICP-MS analysis was conducted using the California Institute of Technology MS facility with 100 mg samples of dibenzofuran, triethylsilane, mesitylene and potassium *tert*-butoxide, which were added to 50 mL DigiTUBE digestion tubes (SCP Science) followed by addition of 3.0 mL of Plasma Pure nitric acid (SCP Science) to each digestion tube and heating to 75 $^{\circ}$C for 36 hours. After digestion, each sample was diluted using Nanopure/Milli Q water to 50 mL and sample analysis performed on an HP 4500 ICP-MS spectrometer. Semiquantitative analysis was performed using a 10 ppm solution of lithium, yttrium, cerium, and thallium for calibration. Each sample was analyzed twice and the average measurements are given in **Table 1.2**.

Table 1.2. ICP-MS microanalysis of trace metal content in the reagents, solvent, and reaction mixture.

	Reagent (unit: ppm)

Element	Dibenzofuran (**1O**)	KO*t*-Bu	Et_3SiH	Mesitylene	Reaction Mixture
Fe	0.15	4.92	0.67	0.11	5.80
Ru	0.00	0.07	0.00	0.01	3.13
Os	0.01	0.01	0.01	0.00	0.20
Co	0.00	0.01	0.00	0.00	0.26
Rh	0.00	0.00	0.00	0.00	1.07
Ir	0.00	0.01	0.00	0.09	0.40
Ni	0.12	0.06	0.06	0.38	0.79
Pd	0.00	0.04	0.00	0.01	0.88
Pt	0.00	0.07	0.00	0.01	1.74
Cu	0.03	10.42	0.04	0.09	7.59

General Procedure for KOSi C–O bond cleavage



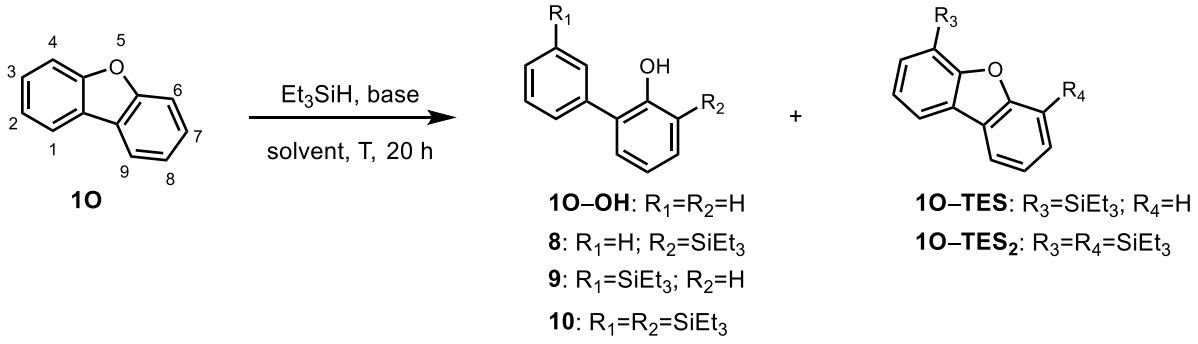
In a glovebox, a 4 mL screw cap vial was loaded with the corresponding substrate (0.1 mmol, 1 equiv.), base (0.5–5 equiv.) and a magnetic stirring bar, followed by syringe addition of the solvent (1 mL) and triethylsilane (1–5 equiv.). The reaction vial was sealed with a Teflon-lined screw cap and heated at a given temperature and time inside the glovebox. After cooling to room temperature, dark red to black reaction mixture was diluted with diethyl ether (3 mL) and carefully quenched with 1 ml of 1 N aqueous HCl. Tridecane (internal standard for GC) was added, the organic layer was separated and the aqueous layer was extracted with ether (3 mL) until TLC controls show no UV-active compounds present in the extracts. The combined organic layers were passed through a short pad of Celite and subjected to GC/FID, GC/MS and ^{1}H NMR analyses. Unless stated otherwise, and in the case of preparative experiments, only products with the overall yield exceeding 2% were isolated and characterized.

In the case of naphthyl alkyl ethers, a different workup procedure was used. After cooling, the reaction was diluted with dichloromethane (5 mL) and carefully quenched with 2 mL of 1 N aqueous HCl. Tridecane was added, and the mixture was transferred to a separatory funnel. The organic phase was separated, and the aqueous layer was extracted with dichloromethane (3 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and filtered. For all reactions, the products were identified using GC/MS and GC-FID and NMR by comparison with the authentic samples. Trace soluble side products observed in naphthyl alkyl ether reductions included naphthalene, 1,2,3,4-tetrahydronaphthalene, and 5,6,7,8-tetrahydro-2-naphthol.

Optimization details for KOSi C–O bond cleavage

Full optimization details for the reductive C–O cleavage of dibenzofuran **1O** by the *KOSi* method are summarized in **Table 1.3**. The general procedure was followed.

Table 1.3. Reaction optimization for the KOSi C-O bond cleavage in dibenzofuran (1O).



Entry	Et_3SiH (equiv)	Base (equiv.)	Solvent	T (°C)	Conv (%)	**1O–OH**	**1O-TES**	**1O–TES_2**	**8**	**9**	**10**
1	0	KO*t*-Bu (2)	Toluene	100	0	—	—	—	—	—	—
2	5	None	Toluene	100	0	—	—	—	—	—	—
3[a]	5	KO*t*-Bu (2)	Toluene	100	70	34	28	4	—	—	—
4[b]	5	KO*t*-Bu (2)	Toluene	100	98	38	16	10	21	2	7
5	4	KO*t*-Bu (2)	Toluene	100	100	41	17	15	12	1	9
6	3	KO*t*-Bu (2)	Toluene	100	96	42	20	9	13	1	4

7	2	KO*t*-Bu (2)	Toluene	100	87	34	30	10	6	1	3
8	1	KO*t*-Bu (2)	Toluene	100	56	19	29	1	2	—	1
9	5	KO*t*-Bu (0.5)	Toluene	100	89	12	48	20	9	—	1
10	2	KO*t*-Bu (0.5)	Toluene	100	66	9	43	8	2	—	—
11	5	KO*t*-Bu (5)	Toluene	100	97	63	10	1	22	—	2
12	5	KH (1)	Dioxane	100	49	1	43	5	—	—	—
13	5	KO*t*-Bu (2)	Dioxane	100	70	25	28	10	4	1	1
14[c]	—	KO*t*-Bu (2)	Et_3SiH	100	99	26	13	25	11	1	21
15	5	KO*t*-Bu (2)	Toluene	80	98	29	18	26	9	—	7
16	3	KO*t*-Bu (3)	Mesitylene	165	100	85	3	—	5	2	—
17	2	KO*t*-Bu (2)	Mesitylene	165	100	62	8	1	12	1	—
18	3	KOt-Bu (2)	Mesitylene	165	97	52	17	5	16	1	2
19	1	KO*t*-Bu (1)	Mesitylene	165	57	30	21	—	—	—	—
20	3	KO*t*-Bu (0.5)	Mesitylene	165	85	29	35	15	4	—	2
21	5	KO*t*-Bu (5)	Mesitylene	165	100	77	3	0	3	8	—
22	3	KH (3)	Mesitylene	165	100	66	3	0	5	11	—
23	3	KOEt (3)	Mesitylene	165	95	77	10	0	6	1	—
24	3	KOEt (3)	Toluene	100	40	19	19	2	—	—	—
25	3	KOMe (3)	Mesitylene	165	64	31	27	2	3	1	—
26	3	NaO*t*-Bu (3)	Mesitylene	165	0	—	—	—	—	—	—
27	3	LiO*t*-Bu (3)	Mesitylene	165	0	—	—	—	—	—	—
28	3	NaOEt (3)	Mesitylene	165	0	—	—	—	—	—	—
29	5	CsOR[d] (2)	Toluene	100	89	75	3	11	—	—	—
30	3	KO*t*-Bu (3)	Benzene	85	96	37	20	13	12	—	9
31	5	KO*t*-Bu (2)	DMF	100	0	—	—	—	—	—	—
32	5	KO*t*-Bu (2)	DMA	100	0	—	—	—	—	—	—
33	5	KO*t*-Bu (2)	Diglyme	100	0	—	—	—	—	—	—
34	5	KO*t*-Bu (2)	*t*-BuOH	100	0	—	—	—	—	—	—
35	5	KO*t*-Bu (2)	Diisopropyl carbinol	100	0	—	—	—	—	—	—

[a]Yields were reproducible within ±2% when performed in another laboratory at the Center for Catalysis and Chemical Synthesis (California Institute of Technology) and are by GC analysis. [b]Reaction performed in 0.05M solution. [c]Reaction performed in neat Et_3SiH. [d]R = 2-ethylhexyl.

Optimization details for KOSi C–O bond cleavage

The *KOSi* C–O bond cleavage of **1O** was performed in the presence of a variety of additives to evaluate their effect on the reaction outcome (**Table 1.4**). The general procedure was followed.

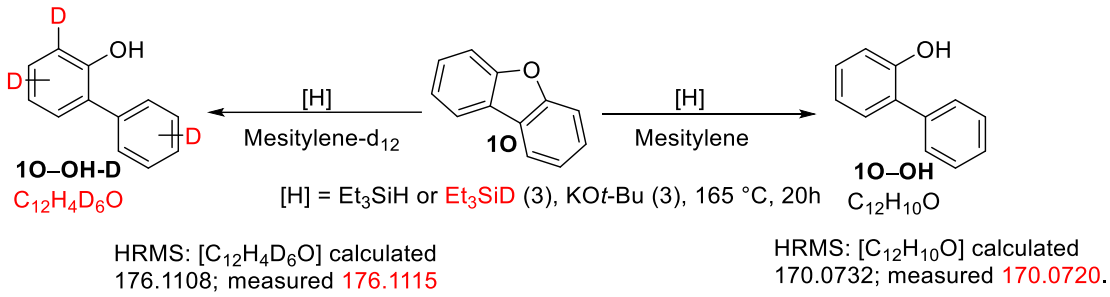
Table 1.4. Influence of additives on the KOSi C−O bond cleavage of 1O.[a,c]

Entry	Et_3SiH (equiv.)	Base (equiv.)	Additive (equiv.)	Solvent	T (^oC)	Conv. (%)

1	5	KO*t*-Bu (2)	1,10-phen[b] (2)	Toluene	100	5
2	5	KO*t*-Bu (2)	18-crown-6 (2.5)	Toluene	100	0
3	3	—	KBH_4 (3)	Mesitylene	165	0
4	3	—	KCN (3)	Mesitylene	165	0
5	3	—	DIBAL (3)	Mesitylene	165	0
6	3	—	$LiAlH_4$ (3)	Mesitylene	165	0
7	3	—	Bu_3SnH (3)	Mesitylene	165	0
8	5	—	Me_4NF (2)	Toluene	100	0
9	5	—	TBAF (2)	Toluene	100	0
10	—	KO*t*-Bu (2)	KH (2)	Dioxane	100	0

[a]General Procedure was followed (100 °C, 20 hours); [b]1,10-phen = 1,10-phenanthroline. [c]Conversion by GC. DIBAL = diisobutylaluminum hydride. TBAF = tetrabutylammonium bromide.

*Preparative scale cleavage of dibenzofuran (**1O**) and deuteration experiments*



The reaction was conducted according to the General Procedure by heating dibenzofuran (**1O**, 250 mg, 1.49 mmol, 1 equiv.), KO*t*-Bu (500 mg, 4.46 mmol, 3 equiv.) and Et_3SiH (713 µl, 4.46 mmol, 3 equiv.) in 4.4 mL of mesitylene for 20 hours at 165 °C. After dilution with diethyl ether (5 mL), the organic phase was first washed with water (1 mL), and then with 2.5 N KOH solution (3 x 20 mL). The basic aqueous fractions were collected and washed through once with CH_2Cl_2 (25 ml) to remove any undesired organics. The resulting basic aqueous fractions were then acidified with concentrated HCl until a pH of 1 and then subsequently extracted with CH_2Cl_2 (3 x 25 mL). The organic fractions were collected and concentrated under reduced pressure to give pale yellow crystals. Purification by chromatography on silica gel with hexanes/ethyl acetate (gradient elution:

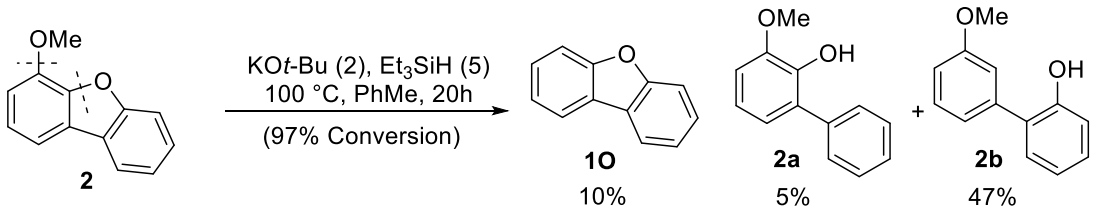
0% to 5% ethyl acetate) afforded biphenyl-2-ol (**1O–OH**, 198 mg, 1.16 mmol, 79 %) as a colorless solid. ^{1}H and ^{13}C NMR spectral assignments of **1O–OH** were consistent with those of the authentic sample.

The identical procedure applied to the reductive cleavage of dibenzofuran but now with Et_3SiD gave undeuterated biphenyl-2-ol **1O–OH** with 76% isolated yield. HRMS: [$C_{12}H_{10}O$] calculated 170.0732; measured 170.0720.

Repeating the aforementioned experiment with Et_3SiH and Mes-d_{12} gave deuterated biphenyl-2-ol **1O–OH-D** in 73% isolated yield. HRMS: [$C_{12}H_4D_6O$] calculated 176.1108; measured 176.1115; FWHM ~ 4 Da.

The identical procedure applied to the reductive cleavage of dibenzofuran but now with Et_3SiD and Mes-d_{12} gave deuterated biphenyl-2-ol **1O–OH-D** with 79% isolated yield. HRMS: [$C_{12}H_4D_6O$] calculated 176.1108; measured 176.1108; FWHM ~ 4 Da.

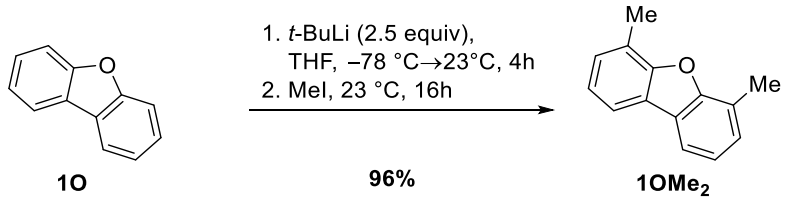
*Cleavage of 4-methoxydibenzofuran (**2**)*



The reaction was conducted according to the General Procedure by heating 4-MeO-dibenzofuran (**2**, 89 mg, 0.5 mmol, 1 equiv.), KO*t*-Bu (112 mg, 1 mmol, 2 equiv.), and Et_3SiH (401 μl, 2.5 mmol, 5 equiv.) in 2 ml of toluene for 20 hours at 100 ^{o}C. After aqueous work up, the crude reaction mixture was purified by chromatography on silica using hexanes and hexanes-ether to recover unconsumed starting material **2** (3 mg, 0.015 mmol, 3%) and isolate dibenzofuran (**1O**, 8.4 mg, 0.05 mmol, 10%;

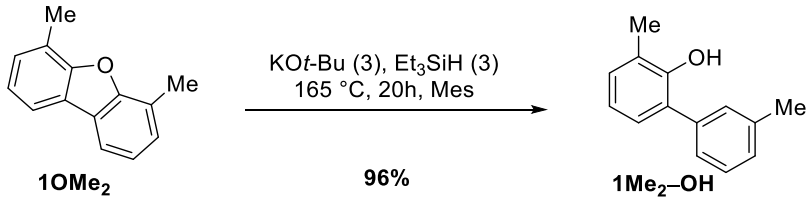
since fractions of **1O** contained small amounts of starting **2**, quantification was done by ^{1}H NMR with CH_2Br_2 as an internal standard), 1,1′-biphenyl-2-ol (**2a**, 4.3 mg, 0.025 mmol, 5%), 2-(3'-methoxyphenyl)phenol (**2b**, 47 mg, 0.235 mmol, 47%). Note: only compounds with the yield exceeding 2% were characterized. ^{1}H and ^{13}C NMR spectral assignments of **2a**[48] and **2b**[49] were consistent with literature reports.

Synthesis and cleavage of 4,6-dimethyldibenzofuran



To a solution of dibenzofuran (2.00 g, 11.9 mmol, 1 equiv.) and tetramethylethylenediamine (11.1 mL, 29.7 mmol, 2.5 equiv.) in diethyl ether (50 ml) *t*-butyllithium (17.5 mL of 1.7 M solution in pentane, 29.8 mmol, 2.5 equiv.) was slowly added at −78 °C under argon. The mixture was allowed to reach ambient temperature and stirring was continued for 4 h prior to addition of methyl iodide (3.7 mL, 60 mmol, 5 equiv.). The resulting mixture was stirred at ambient temperature for another 16 h. After quenching the reaction with the saturated ammonium chloride solution (40 mL) and extraction with diethyl ether (3x30 mL), the combined organic layers were dried over anhydrous sodium sulfate, filtered and the filtrate concentrated in vacuo. Crude reaction mixture was purified by chromatography on silica (hexanes) and product obtained was recrystallized from methanol to afford 4,6-dimethyldibenzofuran **1OMe$_2$** (480 mg, 2.45 mmol, 21%) as a colorless solid. Data for (**1OMe$_2$**): 1H-NMR (300 MHz, CDCl3): δ 7.75

(dd, *J* = 1.0, 6.0 Hz, 2Har), 7.24-7.20 (m, 4Har), 2.61 (s, 6H, 2CH3). 13C NMR (75 MHz, CDCl3): δ 155.07, 128.00, 124.17, 122.60, 122.02, 118.2, 15.41. HRMS: [$C_{14}H_{12}O$] calculated 196.0888; measured 196.0884.



1OMe$_2$ **1Me$_2$–OH**

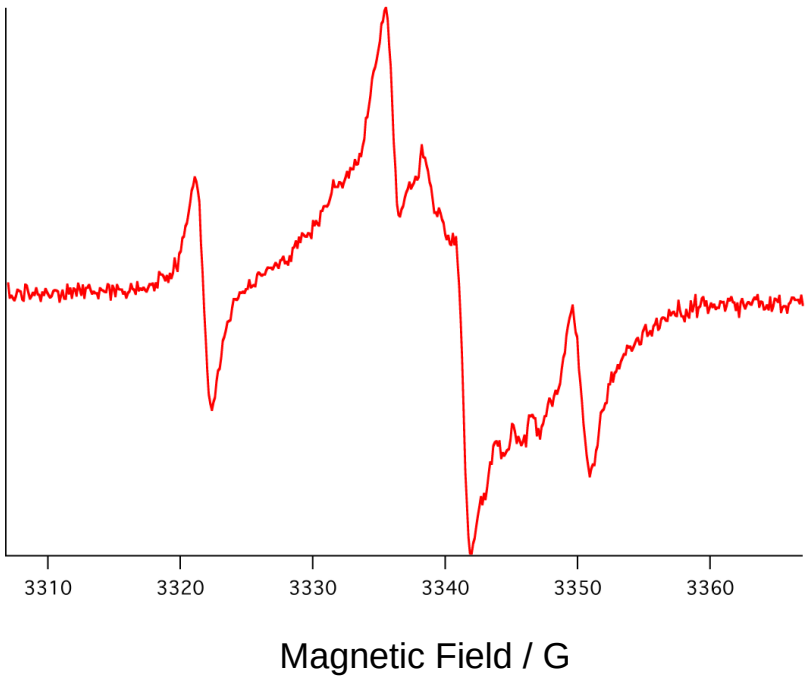
The reaction was conducted according to the General Procedure by heating 4,6-dimethyldibenzofuran (**1OMe$_2$**, 98 mg, 0.5 mmol, 1 equiv.), KO*t*-Bu (112 mg, 1 mmol, 2 equiv.) and Et_3SiH (401 μl, 2.5 mmol, 5 equiv.) in 2 ml of toluene for 20 hours at 100 ^oC. After aqueous work up, the crude reaction mixture was purified by chromatography on silica using hexanes-ether 4:1 to obtain 96 mg of product **1Me$_2$–OH** as a yellow oil. Data for (**1Me$_2$–OH**): ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.35 (t, *J* = 7.5 Hz, 1H$_{ar}$), 7.25-7.22 (m, 2H$_{ar}$), 7.20-7.18 (m, 1H$_{ar}$), 7.11 (d-like, *J* = 10 Hz, 1H$_{ar}$), 7.05 (d-like, *J* = 7.5 Hz, 1H$_{ar}$), 6.87 (t, *J* = 7.5 Hz 1H$_{ar}$), 5.31 (s, 1H, OH), 2.39 (s, 3H, CH_3), 2.30 (s, 3H, CH_3). ^{13}C-NMR (126 MHz, $CDCl_3$): δ 150.68, 139.26, 137.36, 130.51, 129.93, 129.39, 128.73, 127.83, 127.76, 126.20, 124.70, 120.25, 21.60, 16.33. HRMS: [$C_{14}H_{14}O$] calculated 198.1045, measured 198.1046.

EPR Spectrum

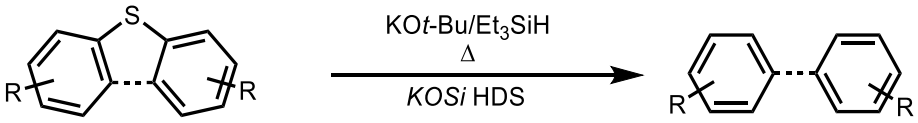
Dibenzofuran (**1O**, 16.8 mg, 0.1 mmol, 1 equiv.), KO*t*-Bu (22.5 mg, 0.2 mmol, 2 equiv.) and Et_3SiH (80 μl, 0.5 mmol, 5 equiv.) were heated in 0.4 ml of toluene for 1 hour at 100 ^oC inside the glovebox. After this time, the reaction mixture was diluted with 0.8 ml of toluene and filtered into an EPR tube. The spectrum was recorded within 20 min after filtration. In a control experiment recorded without

dibenzofuran, the same signal was observed albeit with lower intensity. The spectrum is given in **Figure 1.17**.

Figure 1.17. EPR spectrum of dibenzofuran (1O), Et_3SiH and KO*t*-Bu reaction mixture in toluene. The same signal is observed without dibenzofuran added.



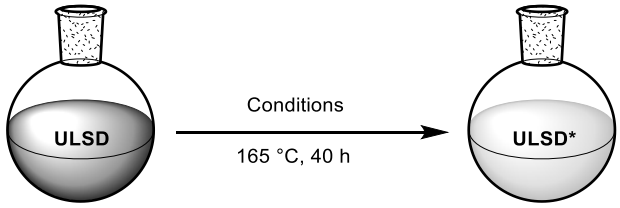
General Procedure for KOSi HDS of S-containing organics



In a nitrogen-filled glovebox, the S-containing substrate (0.5 mmol, 1 equiv.), KO*t*-Bu (168.3 mg, 1.5 mmol, 3 equiv.), and mesitylene (solvent, 5.0 mL) were added to a 20 mL scintillation vial equipped with a magnetic stirring bar. Hydrosilane (1.5 mmol, 3 equiv.) was added, the vial was sealed tightly, and the mixture was stirred for 40 h. The vial was then removed from the glovebox,

allowed to cool to room temperature, and the contents were filtered. The yield of the corresponding hydrocarbon was determined by GC-FID analysis of the crude mixture using tridecane as a standard.

General Procedure for KOSi HDS of diesel fuel



In a nitrogen-filled glovebox, KO*t*-Bu and Et_3SiH (in a 1:1 molar ratio; with varying absolute quantities) were added to a 20 mL scintillation vial equipped with a magnetic stirring bar. ULSD (5 mL) was added, the vial was sealed tightly, and the mixture was stirred for 40 h at 165 °C. The vial was then removed from the glovebox, allowed to cool to ambient temperature, and the mixture was filtered and analyzed. The quantity of sulfur and nitrogen remaining in the mixture was determined using a PAC MultiTek Elemental Analyzer.

For the spiked ULSD containing [S] ~ 10,000 ppm: In a nitrogen-filled glovebox, to a 10 mL volumetric flask is added 4,6-dimethyldibenzothiophene (**1SMe2**, 661.4 mg, 3.12 mmol), and the flask is filled to the meniscus with ULSD to give a ULSD solution with the sulfur concentration increased by 10,000 ppm. Once this solution is completely homogeneous (i.e., **1SMe2** is completely dissolved), 5.0 mL of this solution are transferred into a 20 mL scintillation vial. To this are added KO*t*-Bu (280.5 mg, 2.5 mmol), Et_3SiH (399.3 μL, 2.5 mmol), and a magnetic stirring bar. The vial is capped and the mixture is stirred for 40 h at 165 °C. The general post-reaction procedure for sulfur content analysis is followed.

Analysis of sulfur and nitrogen content

Sulfur levels above 50 ppm were determined using a PAC MultiTek Elemental Analyzer with horizontal boat inlet followed by ASTM D-5453 with UV detection. The limit of detection for sulfur is ~5 ppm-w.

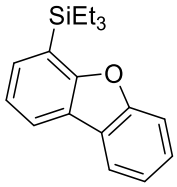
Sulfur levels below 10 ppm were determined using a PAC MultiTek Elemental Analyzer with vertical injection followed by ASTM D-5453 with UV detection. The limit of detection for sulfur is ~0.2 ppm-w but the limit of quantitation may be ~0.5 ppm-w.

ASTM D-5453 is the Standard Test Method for Determination of Total Sulfur in Light Hydrocarbons, Spark Ignition Engine Fuel, Diesel Engine Fuel, and Engine Oil by Ultraviolet Fluorescence.

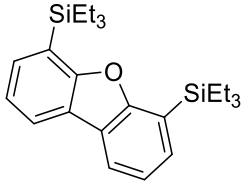
General information regarding computational investigations of the KOSi method

All calculations were carried out with Gaussian 09. Geometry optimizations were performed with the B3LYP method. The 6-31G(d) basis set was used on all atoms. The vibrational frequencies were computed at the same level to evaluate the zero-point vibrational energies (ZPVE) and thermal corrections at 298 K, which also verified that the stationary points are minima or saddle points. Single-point energies and solvent effects were computed at the M06-2X/6-311+G(d,p) level of theory using the gas-phase optimized structures. Solvation energies (solvent = mesitylene) were calculated by a self-consistent reaction field (SCRF) using the CPCM model. Computed structures are illustrated using CYLview. Trimethylsilane was used as a computational model for the experimentally used triethylsilane in order to facilitate the calculations.

Characterization

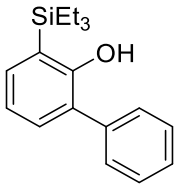


4-(Triethylsilyl)dibenzofuran (1O–TES). Data for (**1O–TES**): Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99-7.96 (m, $2H_{ar}$), 7.59 (d-like, J = 10 Hz, $1H_{ar}$), 7.54 (dd, J = 2, 5 Hz, $1H_{ar}$), 7.48-7.44 (m, $1H_{ar}$), 7.37-7.33 (m, $2H_{ar}$), 1.03 (m, 15H, $3CH_2CH_3$). ^{13}C-NMR (126 MHz, $CDCl_3$): δ 161.30, 156.05, 133.57, 126.92, 122.52, 122.48, 121.58, 120.68, 111.75, 7.63, 3.59. HRMS: [$C_{18}H_{22}OSi$] calculated 282.1440; measured 282.1444.



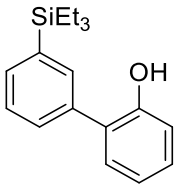
4,6-bis(triethylsilyl)dibenzofuran (1O–TES$_2$). To a solution of dibenzofuran (2.00 g, 11.9 mmol, 1 equiv.) and tetramethylethylenediamine (11.1 mL, 29.7 mmol, 2.5 equiv.) in tetrahydrofuran (50 ml) *t*-butyllithium (17.5 mL of 1.7 M solution in pentane, 29.8 mmol, 2.5 equiv.) was slowly added at -78 ^{o}C under argon. The mixture was allowed to reach ambient temperature and stirring was continued for 4 h prior to addition of chlorotriethylsilane (10.1 mL, 60 mmol, 5 equiv.). The resulting mixture was stirred at ambient temperature for another 16 h. After quenching the reaction with the saturated ammonium chloride solution (40 mL) and extraction with diethyl ether (3x30 mL), the combined organic layers were dried over anhydrous sodium sulfate, filtered, and the filtrate concentrated in vacuo. Crude reaction mixture was purified by chromatography on silica (hexanes) and product obtained was recrystallized from a mixture of methanol and isopropanol (1:1) to afford 4,6-bis(triethylsilyl)dibenzofuran (1.28 g, 2.45 mmol, 28%) as colorless needles. Data for (**1O–TES$_2$**): Colorless needles. M.p. = 59−61 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (dd, J = 3, 9 Hz,

$2H_{ar}$), 7.54 (dd, *J* = 3, 9 Hz, $2H_{ar}$), 7.33 (t, *J* = 9 Hz, $2H_{ar}$), 1.07-0.95 (m, 30H, $6CH_2CH_3$). ^{13}C NMR (126 MHz, $CDCl_3$): δ 160.90, 133.48, 122.87, 122.34, 121.57, 120.03, 7.66, 3.52. HRMS: [$C_{24}H_{36}OSi_2$] calculated 396.2305; measured 396.2321.



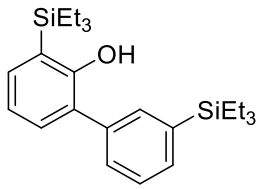
3-(triethylsilyl)biphenyl-2-ol (8). The title compound was prepared via cleavage of **1O–TES**

Data for (**8**): White solid. M.p. = 44-46 ^oC ^1H NMR (300 MHz, $CDCl_3$): δ 7.52-7.40 (m, $5H_{ar}$), 7.36 (dd, *J* = 3, 9 Hz, $1H_{ar}$), 7.23 (dd, *J* = 3, 6 Hz, $1H_{ar}$), 6.98 (t, *J* = 9 Hz, $1H_{ar}$), 5.41 (s, 1H, OH), 1.02-0.96 (m, 9H, CH_3), 0.91-0.83 (m, 6H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.25, 137.51, 135.97, 131.30, 129.58, 129.39, 128.01, 127.17, 123.04, 120.40, 7.79, 3.69. HRMS: [$C_{18}H_{24}OSi$] calculated 284.1596; measured 284.1583.



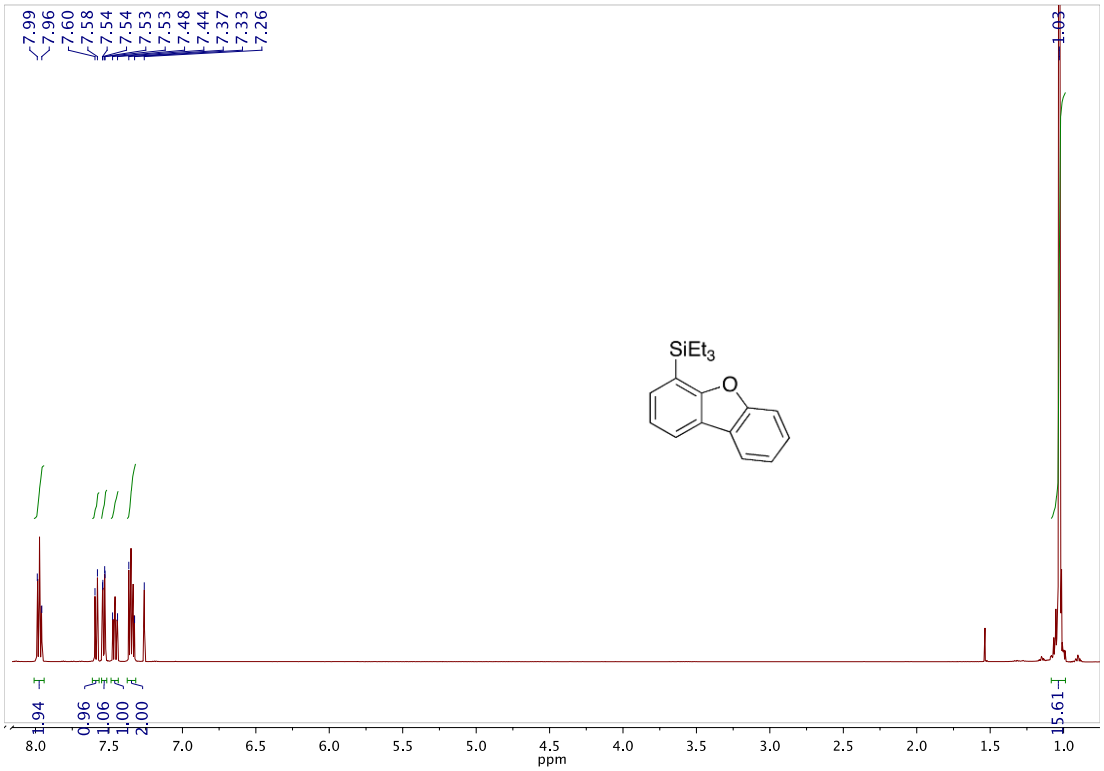
(3'-triethylsilyl)biphenyl-2-ol (9). The title compound was prepared via cleavage of **1O–TES**

Data for (**9**): Colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ 7.57-7.56 (m, $1H_{ar}$), 7.54-7.52 (m, $1H_{ar}$), 7.49-7.44 (m, $2H_{ar}$), 7.28-7.24 (m, $2H_{ar}$), 7.02-6.99 (m, $2H_{ar}$), 5.24 (s, 1H, OH), 0.98 (t, *J* = 10 Hz, 9H, CH_3), 0.82 (q, *J* = 15 Hz, 6H, CH_2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 152.44, 139.07, 136.12, 134.71, 133.76, 130.23, 129.36, 129.08, 128.53, 128.44, 120.80, 115.72, 7.43, 3.31. HRMS: [$C_{18}H_{24}OSi$] calculated 284.1596; measured 284.1585.

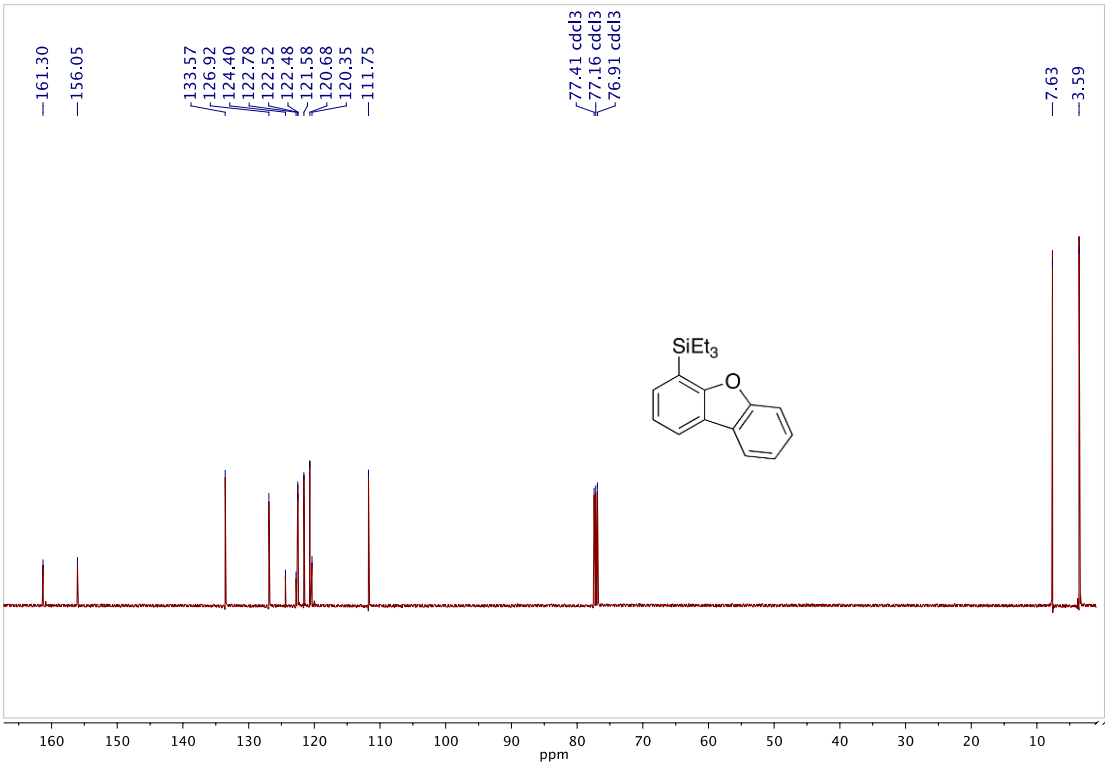


3,3'-bis(triethylsilyl)biphenyl-2-ol (10). The title compound was prepared according to General Procedure by heating **1O–TES$_2$** (840 mg, 5.0 mmol, 1 equiv.) with KO*t*-Bu (1.12 g, 10 mmol, 2 equiv.) and Et_3SiH (4.0 ml, 25 mmol, 5 equiv.) in 20 ml of toluene for 20 hours at 100 ºC. After acidic aqueous work up, the crude reaction mixture was purified by chromatography on silica using hexanes and hexanes-ether (10:1) to give, among other isolated products, 20 mg (0.05 mmol, 1%) of **10**. Data for (**10**): oily solid ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.53-7.44 (m, $2H_{ar}$), 7.46-7.44 (m, $2H_{ar}$), 7.36 (dd, *J* = 1.5, 7.5 Hz, $1H_{ar}$), 7.23 (dd, *J* = 1.5, 7.5 Hz, $1H_{ar}$), 6.98 (t, *J* = 7 Hz, $1H_{ar}$), 5.42 (s, 1H, OH), 1.01-0.96 (m, 18H, $6CH_3$) 0.91-0.77 (m, 15H, $6CH_2$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.37, 139.45, 136.61, 135.87, 135.09, 133.86, 131.38, 129.57, 128.71, 127.55, 122.97, 120.36, 7.80, 7.57, 3.69, 3.46. HRMS: [$C_{24}H_{38}OSi_2$] calculated 398.2461; measured 396.2470.

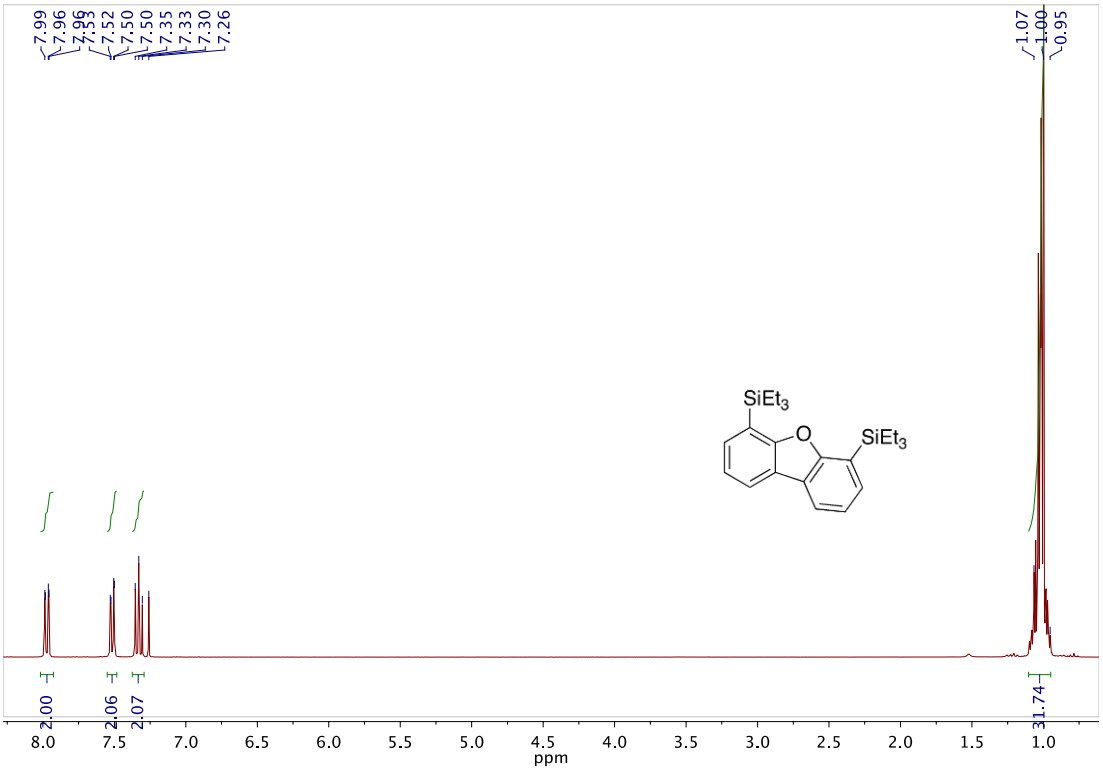
NMR Spectra



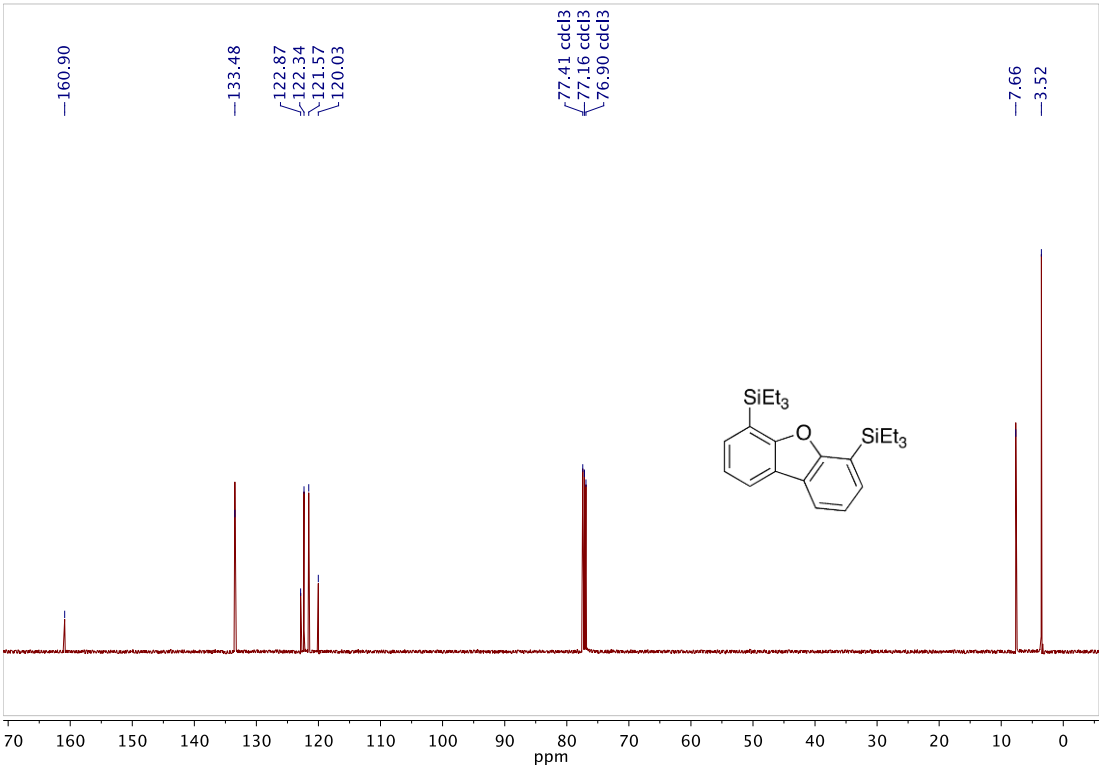
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4-(triethylsilyl)dibenzofuran (**1O–TES**)



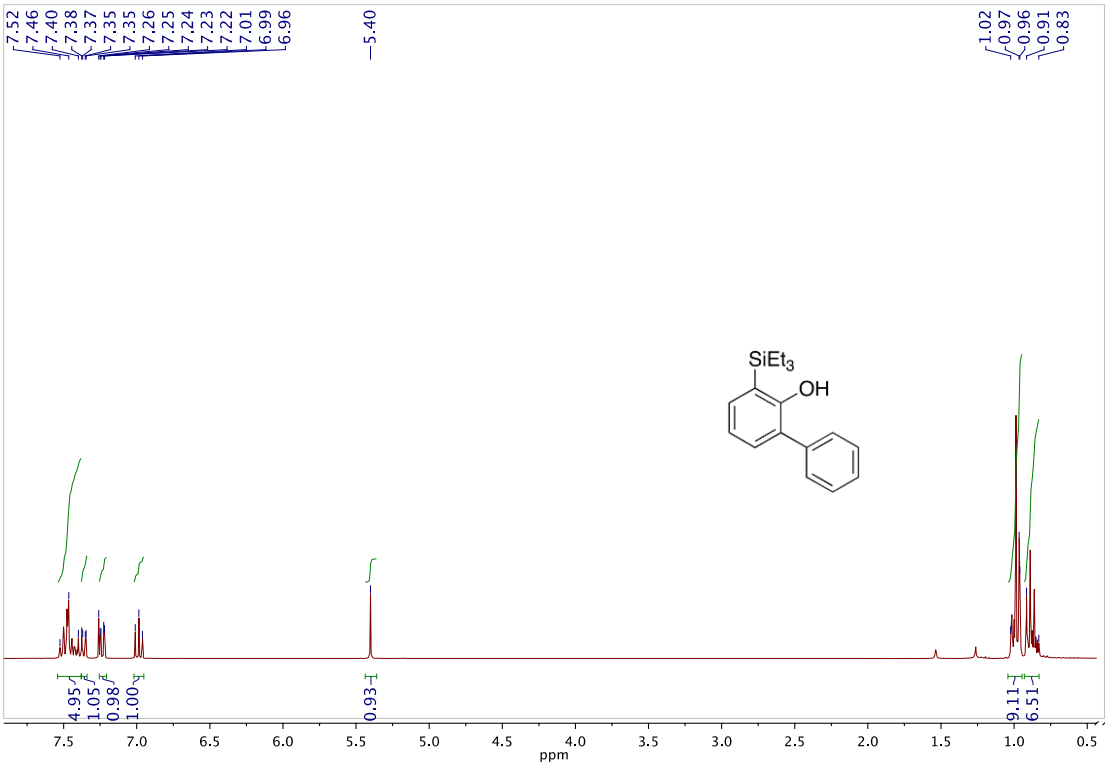
^{13}C NMR (126 MHz, $CDCl_3$) spectrum of 4-(triethylsilyl)dibenzofuran (**1O–TES**)



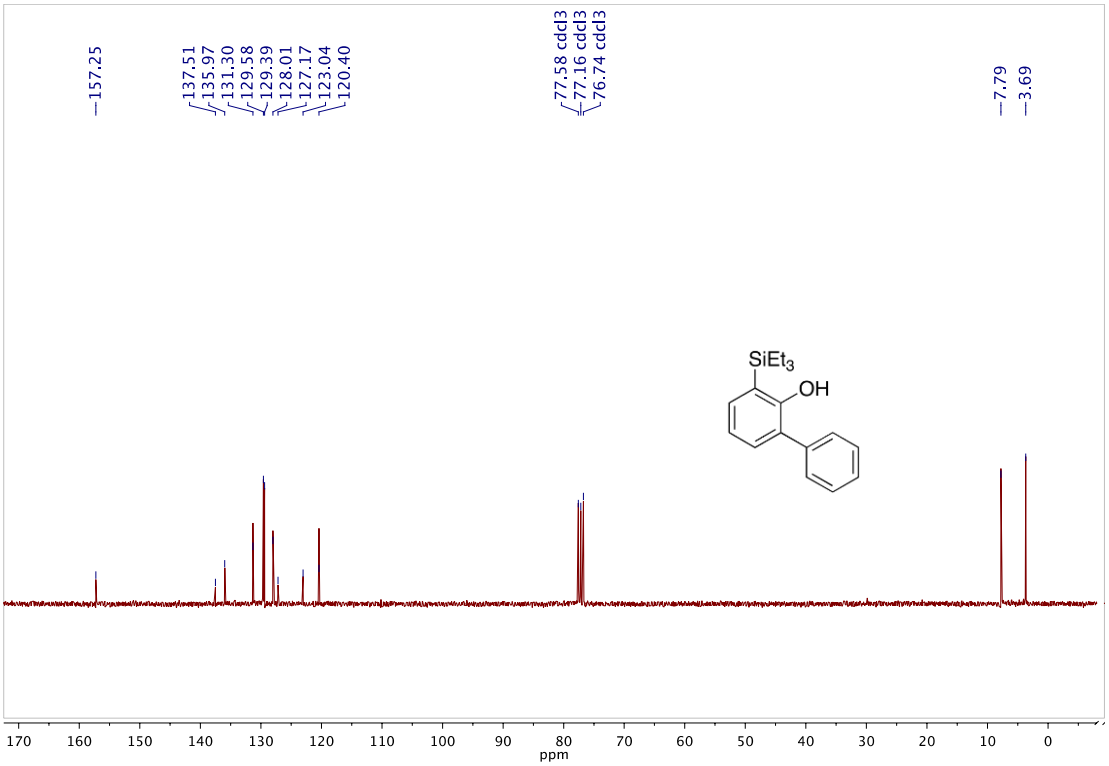
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 4,6-bis(triethylsilyl)dibenzofuran (**1O–TES$_2$**)



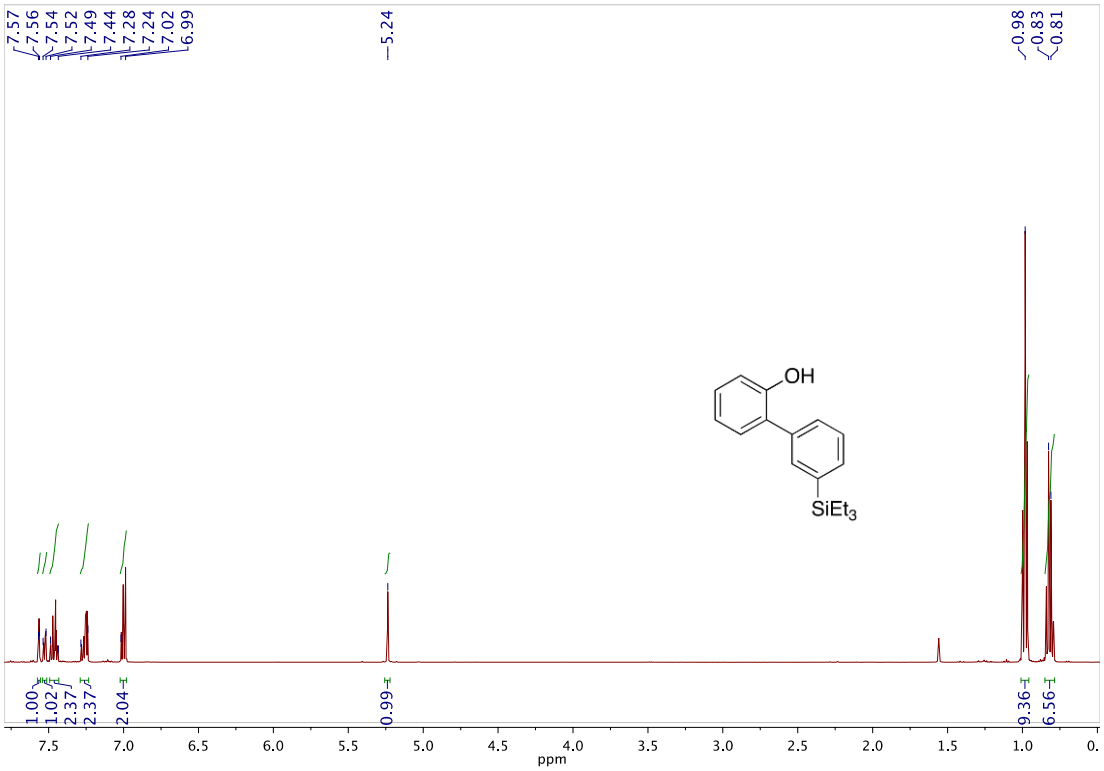
^{13}C NMR (126 MHz, $CDCl_3$) spectrum of 4,6-bis(triethylsilyl)dibenzofuran (**1O–TES$_2$**)



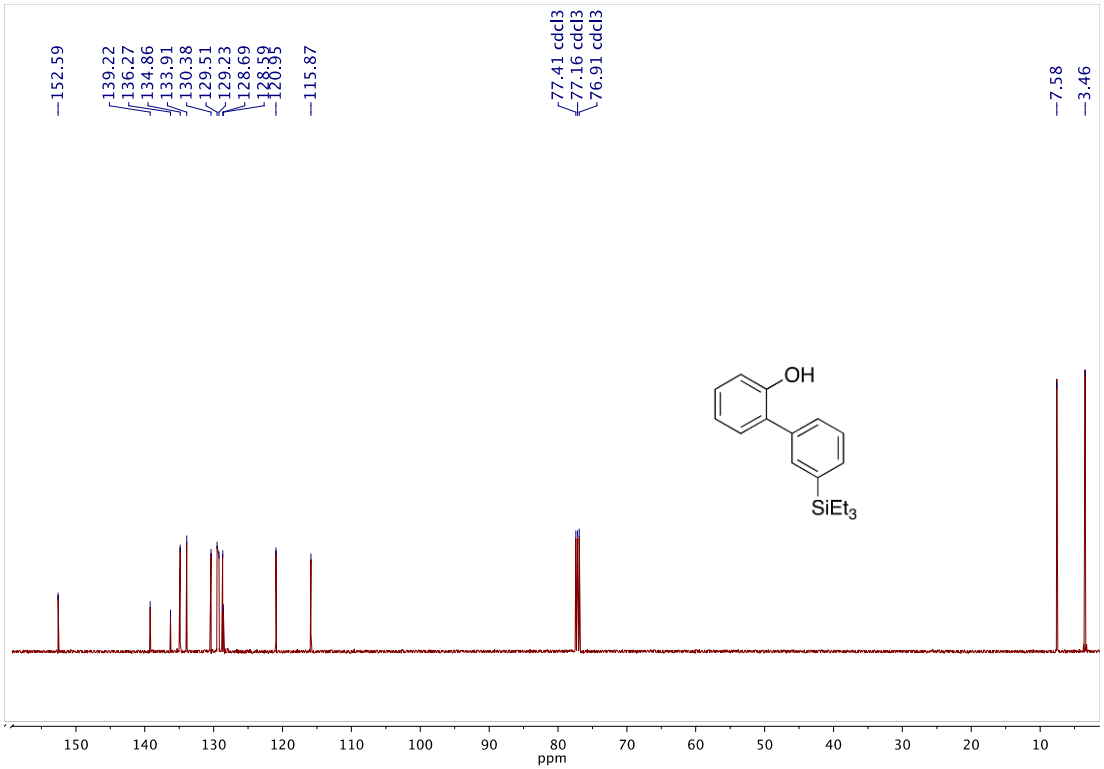
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 3-(triethylsilyl)biphenyl-2-ol (**8**)



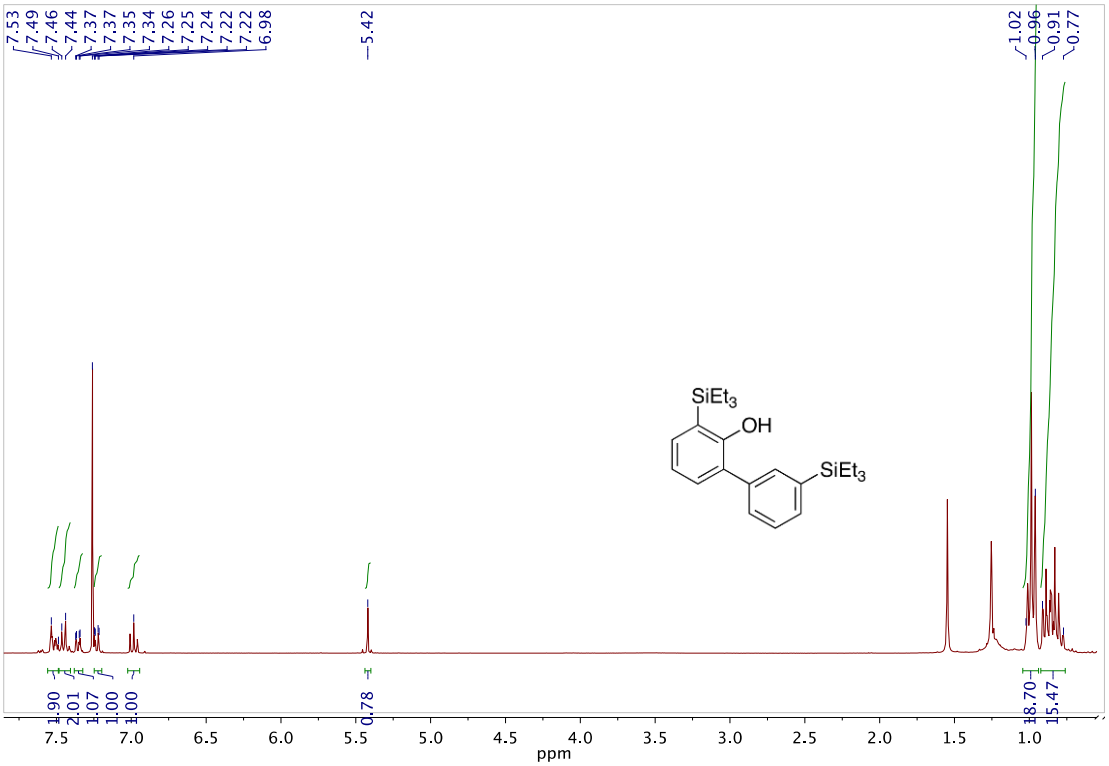
^{13}C NMR (75.4 MHz, $CDCl_3$) spectrum of 3-(triethylsilyl)biphenyl-2-ol (**8**)



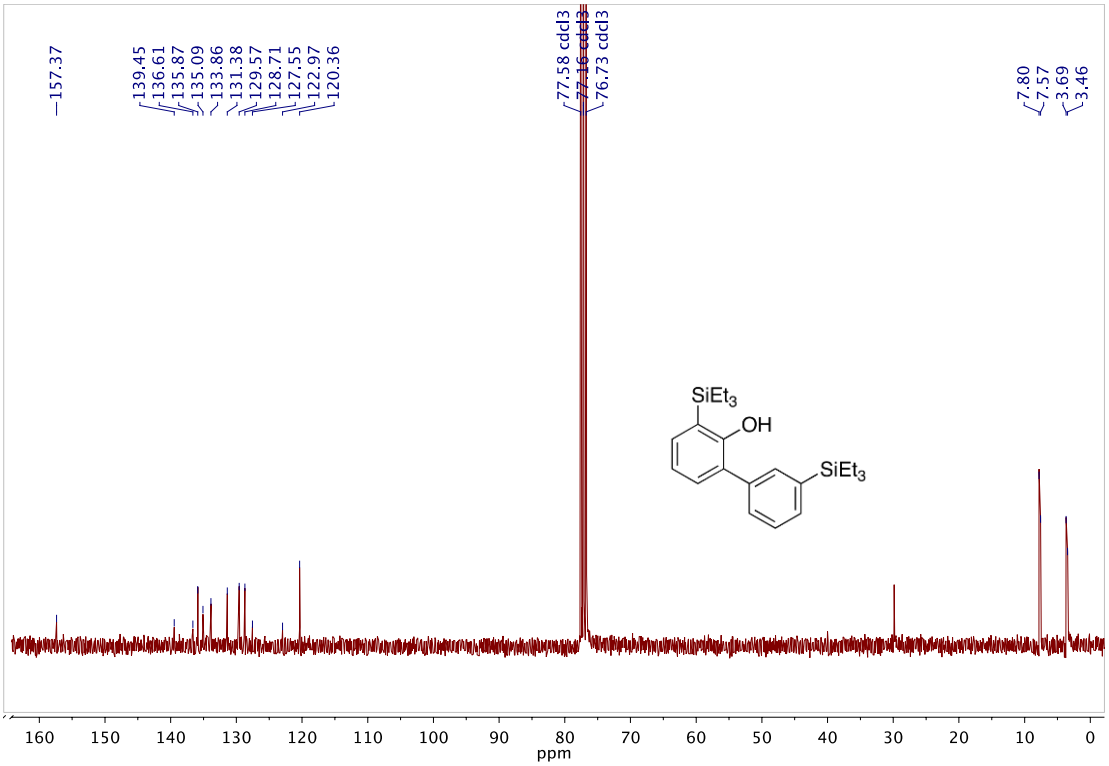
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of (3'-triethylsilyl)biphenyl-2-ol (**9**)



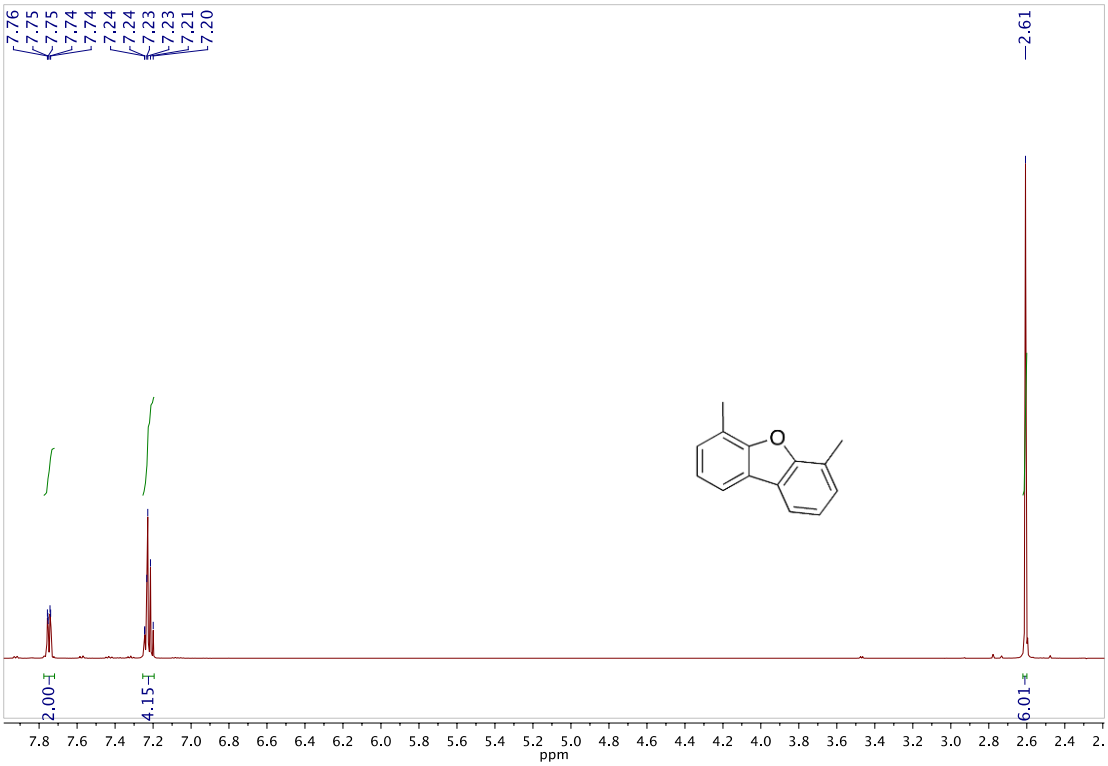
^{13}C NMR (126 MHz, $CDCl_3$) spectrum of (3'-triethylsilyl)biphenyl-2-ol (**9**)



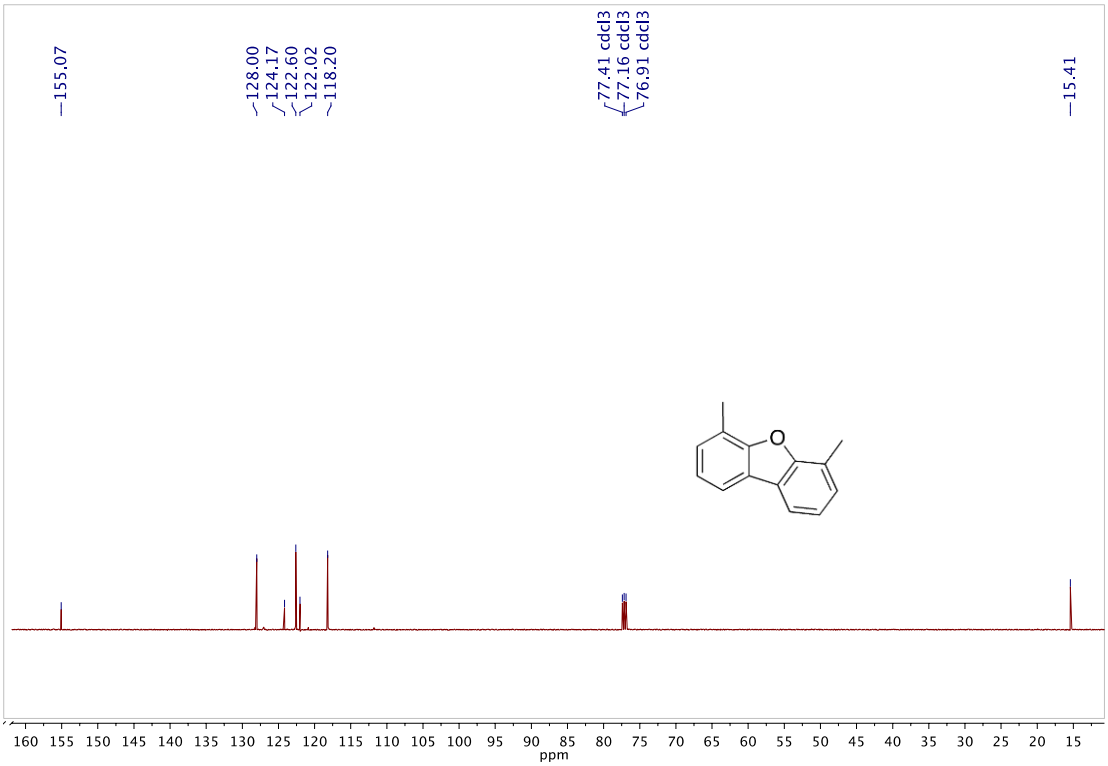
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 3,3'-bis(triethylsilyl)biphenyl-2-ol (**10**)



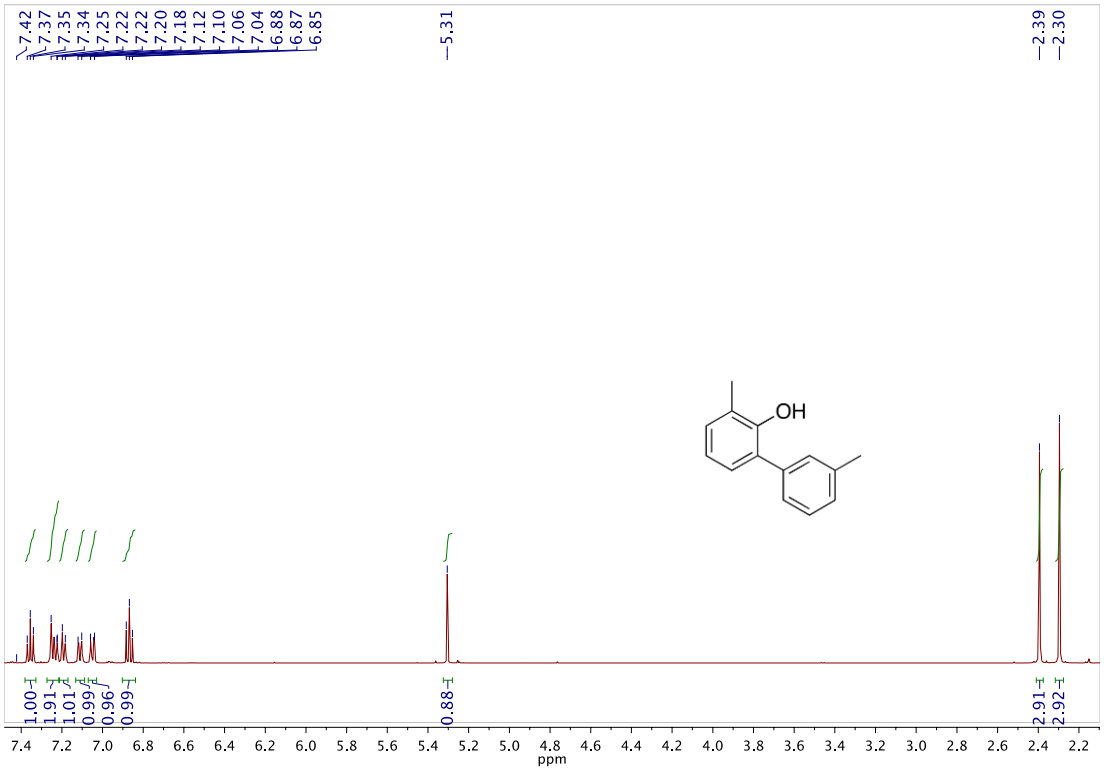
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of 3,3'-bis(triethylsilyl)biphenyl-2-ol (**10**)



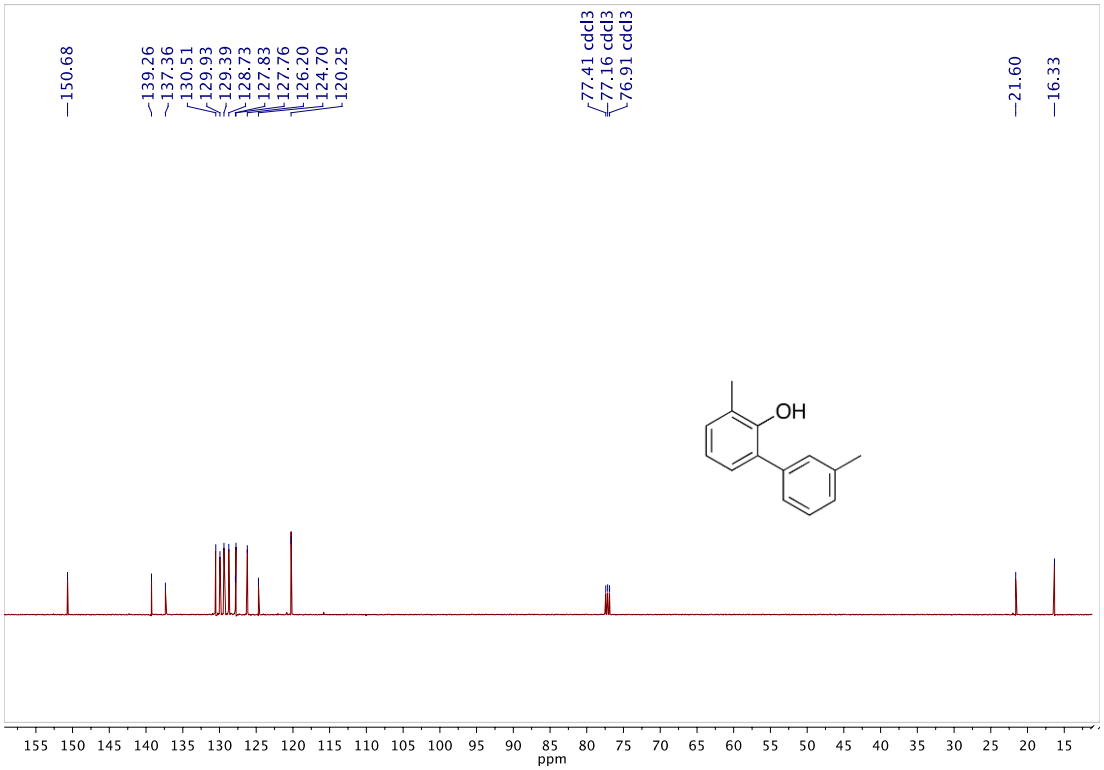
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 4,6-(dimethyl)dibenzofuran (**1OMe$_2$**)



^{13}C NMR (75 MHz, $CDCl_3$) spectrum of 4,6-(dimethyl)dibenzofuran (**1OMe$_2$**)



^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3,3'-dimethylbiphenyl-2-ol (**1Me$_2$–OH**)



^{13}C NMR (126 MHz, $CDCl_3$) spectrum of 3,3'-dimethylbiphenyl-2-ol (**1Me$_2$–OH**)

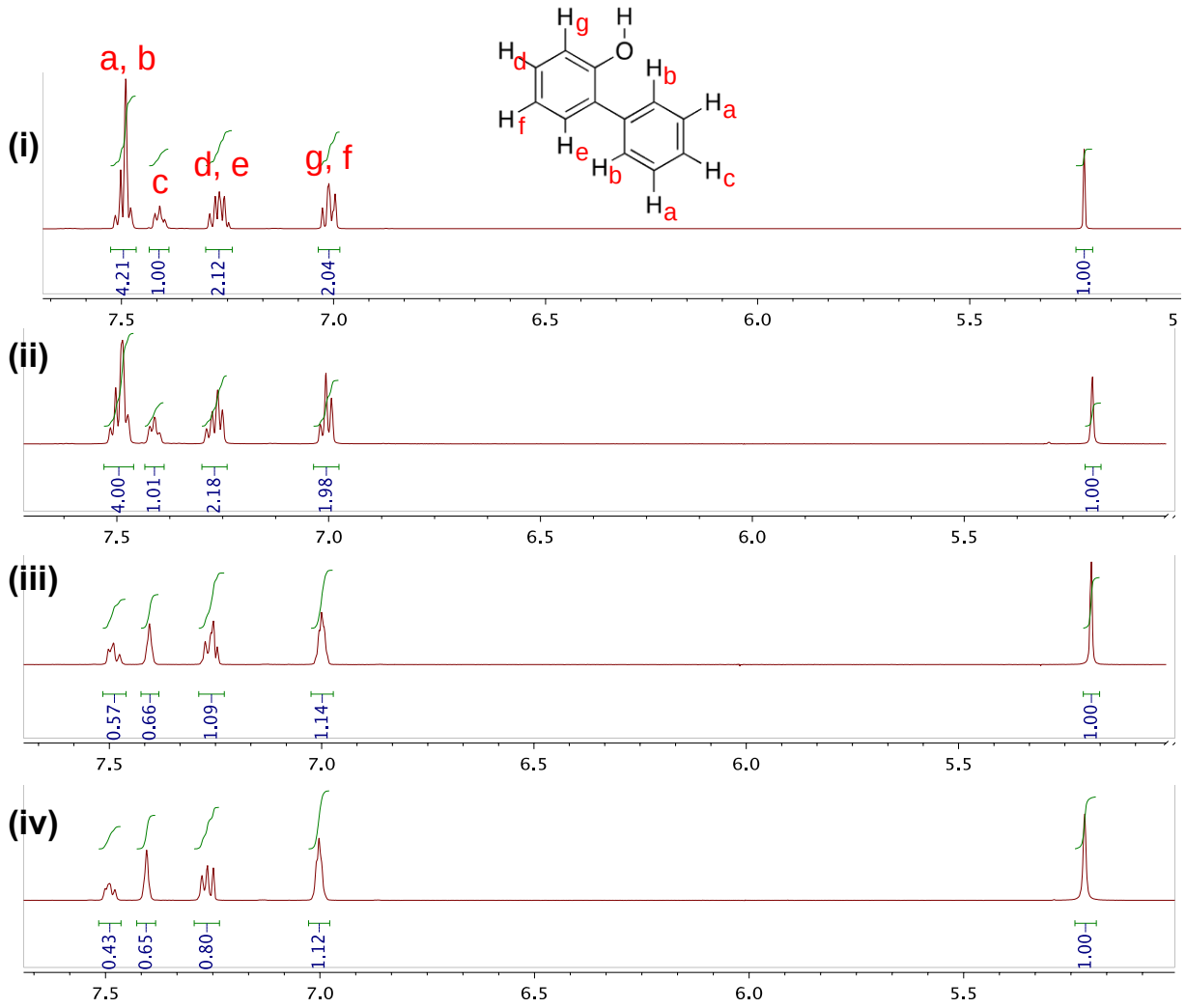


Figure 1.17. ^{1}H NMR (600 MHz, $CDCl_3$) single-scan overlaid spectra for quantitative comparison of a commercial sample of biphenyl-2-ol (**1O–OH**) (**i**) with those obtained from dibenzofuran and Et_3SiH in mesitylene (**ii**); with Et_3SiH in mesitylene-d_{12} (**iii**); with Et_3SiD in mesitylene-d_{12} (**iv**).

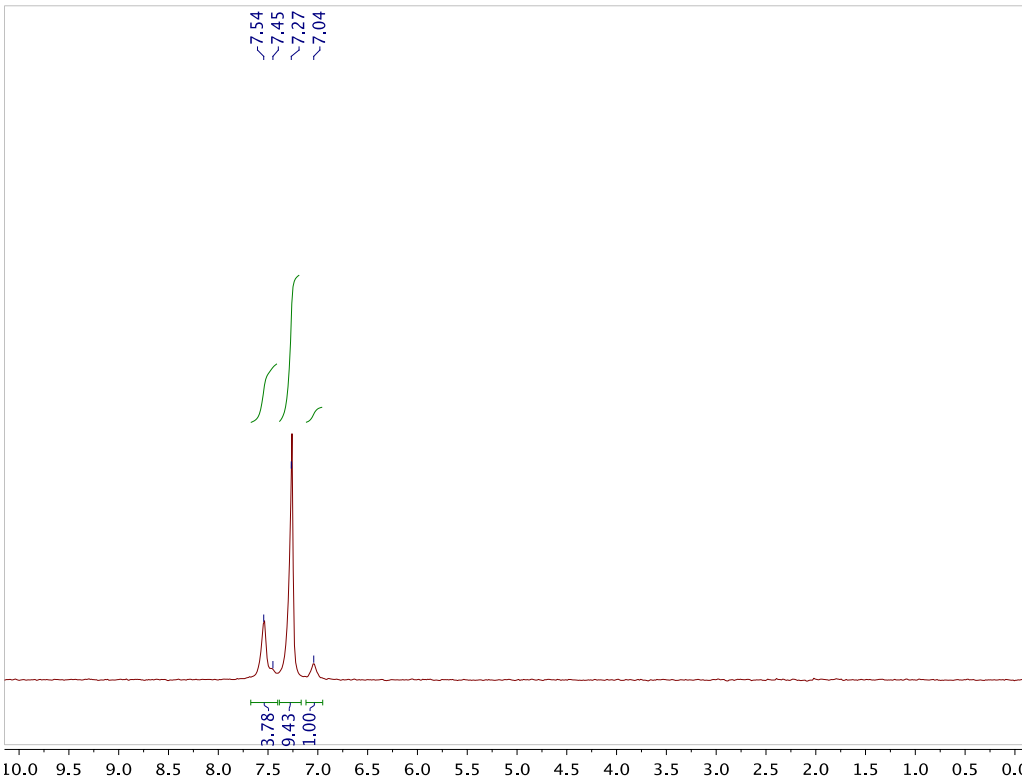


Figure 1.18. ^{2}D NMR (61.4 MHz, $CHCl_3$) spectrum of partially deuterated biphenyl-2-ol (**1O–OH-D**) prepared from Et_3SiD in Mes-D_{12}. A drop of deuterated $CDCl_3$ was added for signal locking purposes.

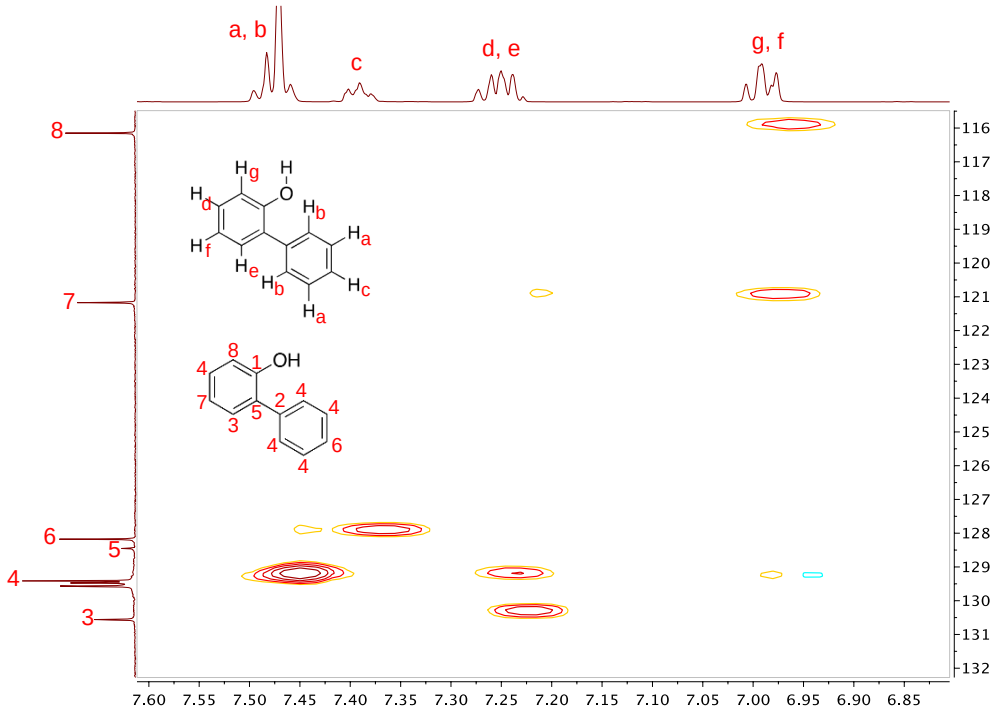


Figure 1.19. HSCQ ($CDCl_3$) spectrum of a commercial sample of biphenyl-2-ol (**1O-OH**)

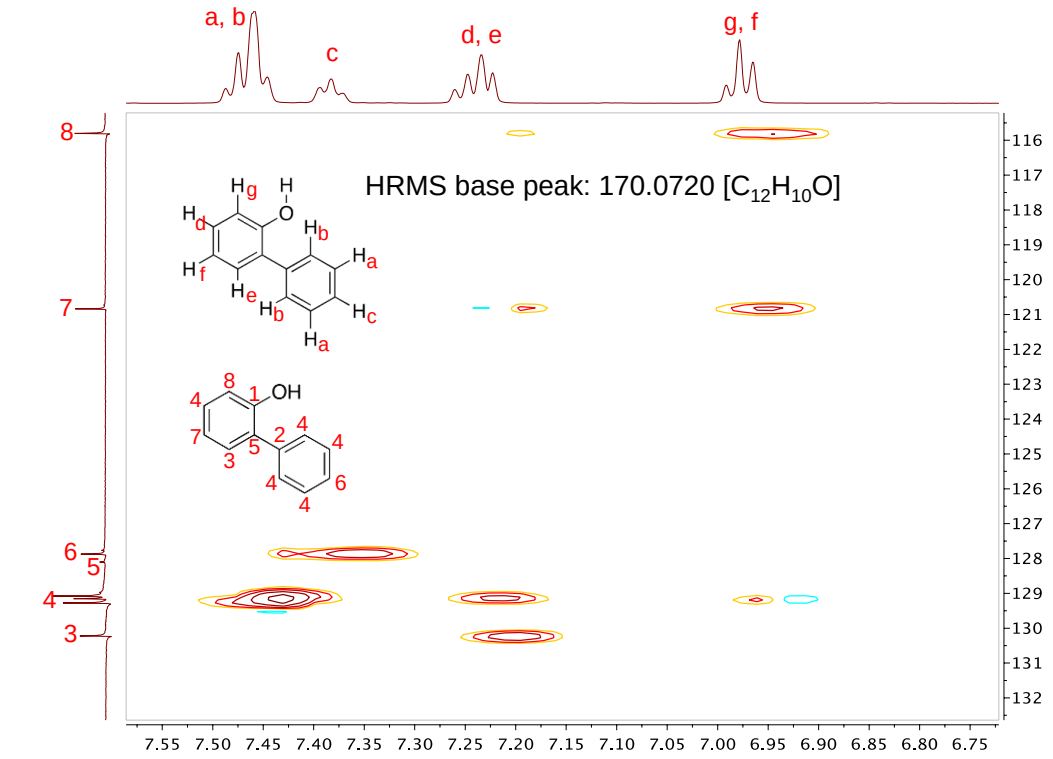


Figure 1.20. HSCQ ($CDCl_3$) spectrum of biphenyl-2-ol prepared from Et_3SiD in Mes

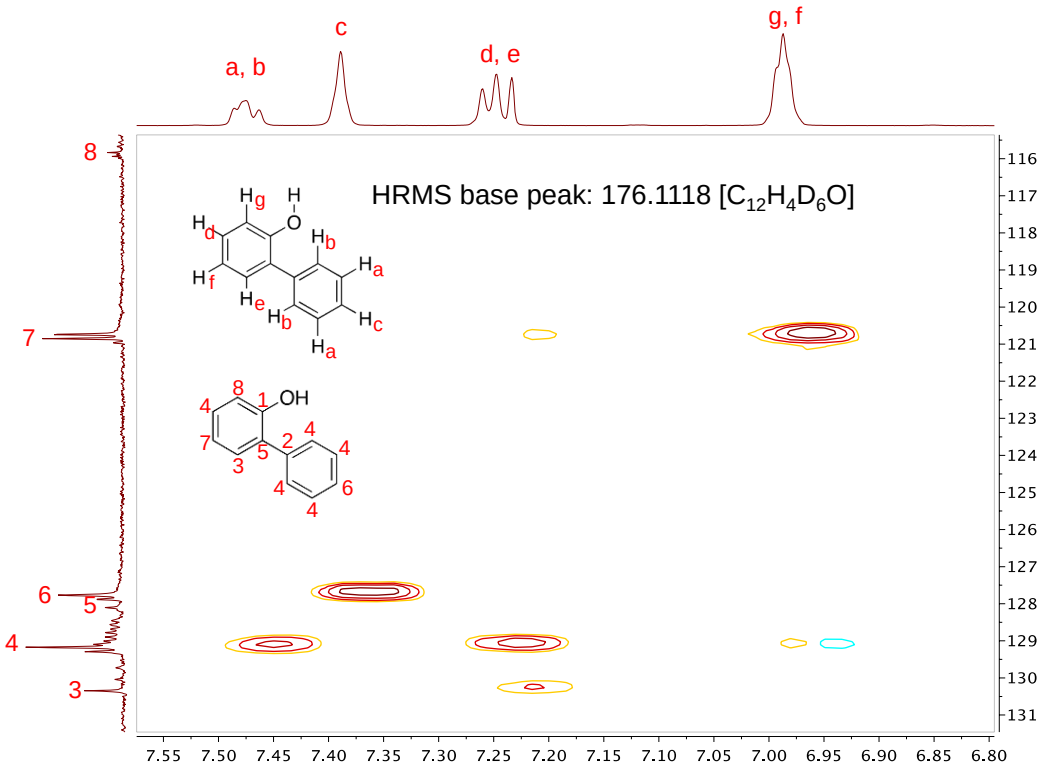


Figure 1.21. HSCQ ($CDCl_3$) spectrum of biphenyl-2-ol prepared from Et_3SiH in Mes-D_{12}

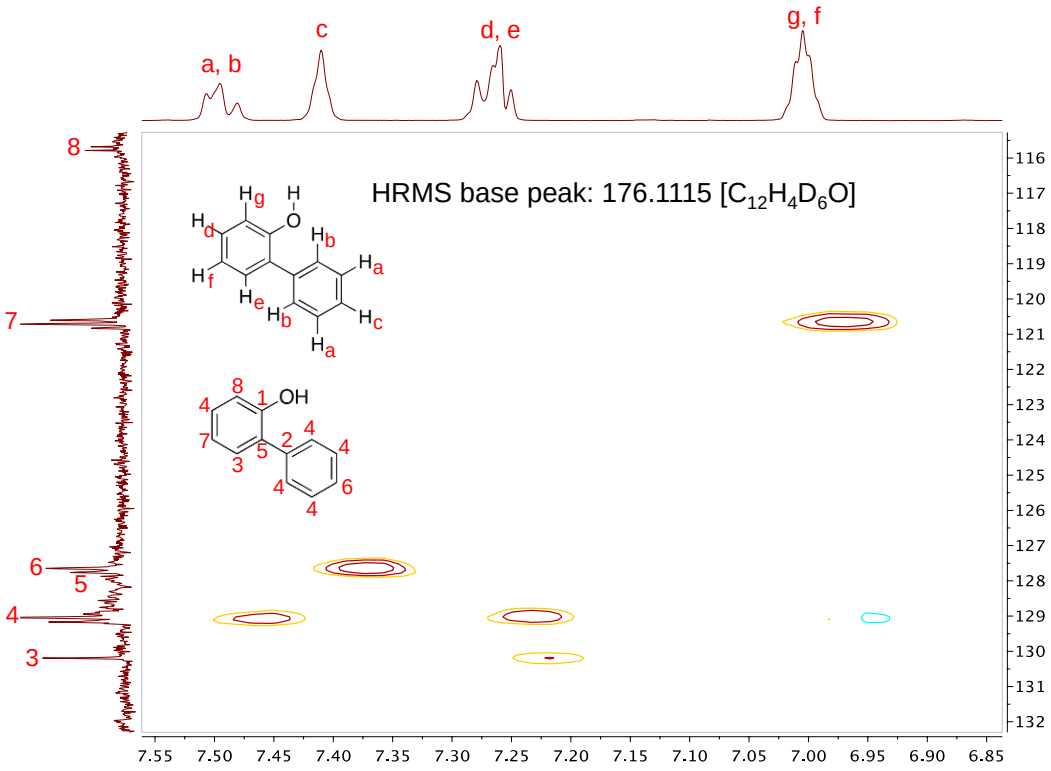


Figure 1.22. HSCQ ($CDCl_3$) spectrum of biphenyl-2-ol prepared from Et_3SiD in Mes-D_{12}

Acknowledgements.

I am grateful to Dr. Alexey Fedorov who initially combined KO*t*-Bu and Et_3SiH together toward the reduction of aromatic C–X bonds in the absence of transition metal species. Nicholas Swisher is acknowledged for applying the conditions that I had optimized to the cleavage of aryl alkyl ethers. I am also grateful to Drs. Yong Liang and Yun-Fang Yang and Prof. Ken Houk at UCLA for their computational mechanistic insights into the mechanism of the hydrodesulfurization (HDS) and C–O bond cleavage chemistry by this new *KOSi* method.

Chapter 2

POTASSIUM *TERT*-BUTOXIDE–CATALYZED CROSS-DEHYDROGENATIVE C–H BOND SILYLATION OF HETEROARENES

Abstract.

During optimization investigations of the reductive C–O bond cleavage of dibenzofuran using mixtures of KO*t*-Bu and hydrosilanes (Chapter 1), I performed careful analysis which revealed the presence of unanticipated byproducts containing C–Si bonds (e.g., 4-triethylsilyldibenzofuran (**1O–TES**)). Given this proof-of-principle reactivity, we were – through extensive optimization and investigation – able to develop an unprecedented cross-dehydrogenative C–Si bond construction method. The protocol enables the direct silylation of unfunctionalized aromatic heterocycles into their corresponding silyl derivatives using catalytic quantities of KO*t*-Bu and with hydrosilanes as the silicon source.

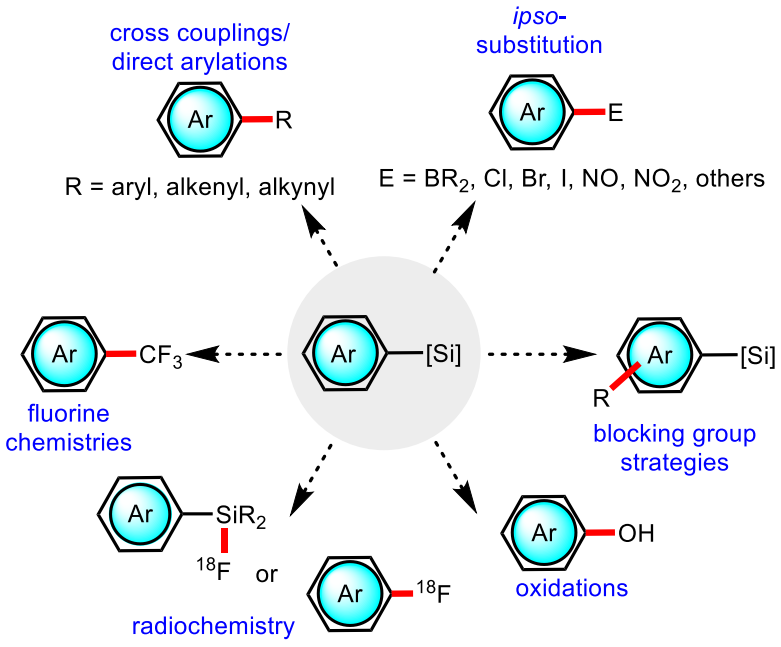
Introduction.

The catalytic transformation of C–H bonds into a variety of useful functional groups has the potential to greatly improve the power, diversity, and efficiency of chemical syntheses. Particularly attractive is the concept of catalytic cross-dehydrogenative C–H functionalization, wherein neither coupling partner is prefunctionalized. This powerful but relatively rarely encountered synthetic strategy can further streamline synthesis, lower cost, and limit waste. However, accomplishing such challenging transformations often necessitates the use of stoichiometric additives, demanding reaction conditions, complex ligands, and especially, expensive and sophisticated precious metal catalysts based on Pd, Pt, Rh, Ir, and others. These factors can limit the utility and accessibility of such powerful C–H functionalization methods, particularly for preparative scale syntheses. Thus, the development of fundamentally new and efficient methods for the conversion of C–H bonds is a primary and fundamental concern in modern chemical synthesis.

Heteroarylsilanes: synthesis and utility.

Enabled by their useful physico-chemical properties, molecules containing carbon–silicon (C–Si) bonds have found widespread application in various fields of study. For example aryl- and heteroarylsilanes are of emerging interest in drug discovery,[50,51] nuclear medicine,[52] polymer chemistry,[53,54] and even organic electronics and photonics applications.[55] In addition, C–Si containing molecules are highly useful synthetic intermediates for the preparation of complex molecules[56] (e.g., crop protection agents, human medicines, natural products, cosmetics and fragrances) due to the high abundance and low cost of silicon[54] as well as the superior stability and lower toxicity of organosilicon compounds compared to the more commonly employed boron and tin reagents respectively (**Figure 2.1**).[54,57]

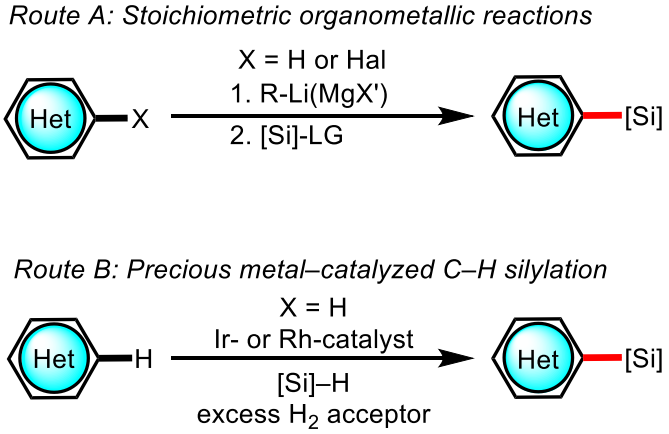
Figure 2.1. Synthetic applications of aryl- and heteroarylsilanes.



Despite the favorable features of C–Si-containing small molecules, the lack of mild, general methods for their preparation remains a significant barrier to their widespread use.[58] Consequently, the use of organosilicon-based chemistries in academic- and industrial organic synthesis has been somewhat

limited. For example, the preparation of aryl- and heteroarylsilanes, which are used in medicinal chemistry as versatile chemical building blocks[54,56,57] as well as biologically-active carbon bioisosteres,[50,51] are generally prepared by stoichiometric reactions between organometallic species with silicon electrophiles such as halosilanes (**Figure 2.2**, Route A). [59,60]

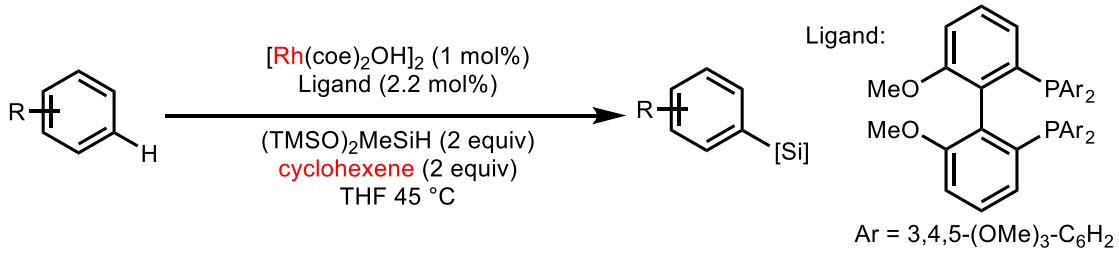
Figure 2.2. Strategies for the synthesis of aryl- and heteroarylsilanes.



This classical method necessitates the use of pyrophoric materials in stoichiometric quantities, which is intolerant of many functional groups[54,60] and requires starting material prefunctionalization,[57,58] or the use of directing-groups.[59] In fact, due to these limitations, incorporation of a silicon functionality into a complex molecule, such as a lead pharmaceutical compound, normally requires *de novo* synthesis.[50,51] Careful temperature control and/or cryogenic conditions are often required to obtain reproducible yields.[61] In addition, this process generates considerable solvent, water, and inorganic salt waste, which can be costly and cumbersome on large scale. Catalytic methods are beginning to emerge, but most variants require prefunctionalized coupling partners (i.e., aryl halides),[62] specialized Si species,[63] and/or directing groups.[64] An attractive solution would be the direct catalytic conversion of C–H to C–Si bonds. Toward this end, Ir and Rh catalysts have shown promise in certain applications (**Figure 2.2**, Route B).[65,66,67,68]

However, unlike the powerful C–H borylation chemistry of (hetero)aromatics that is becoming a mainstay in both academic and industrial sciences,[57b,69] the corresponding catalytic C–H silylation is not yet widely applicable and suffers from limitations in scope as well as poor availability and high cost of catalysts and ligands. Thus, the development of new tools and general broad protocols for (hetero)aromatic C–H bond silylation would be of significant value to the synthetic community.

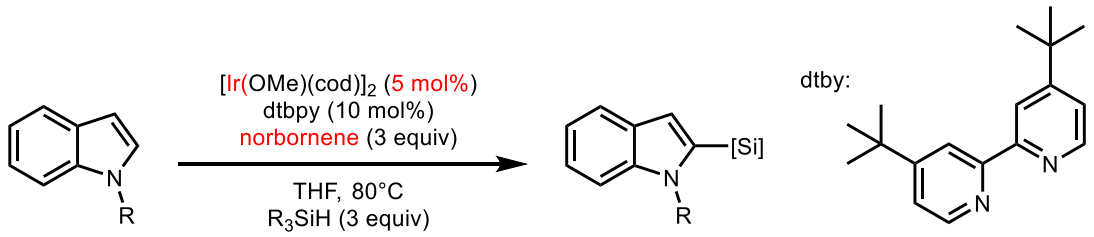
Scheme 2.1. Rh–catalyzed C–H silylation of arenes.



Prior to our work in the area, very few reports detailing the direct catalytic silylation of arenes with hydrosilanes have appeared. The chemistry requires the use of non-commercially available catalysts based on either Pt under harsh conditions (i.e. 200 °C),[70] or most recently Ir,[65,68] or Rh (**Scheme 2.1**) with the use of excess sacrificial hydrogen acceptors and an expensive biphenylphosphine ligand, though under milder conditions.[66,67]

The direct silylation of aromatic heterocycles is generally more challenging, but has been investigated employing high loadings of an iridium catalyst for the direct silylation of indoles and other electron rich heteroarenes (**Scheme 2.2**).[68] Although these are important silylation methods, the use of catalysts based on precious metals and the requirement of excess hydrogen acceptors, elaborate ligands, and demanding reaction conditions can be a considerable limitation, especially when large scale syntheses are desired.

Scheme 2.2. Ir–catalyzed C–H silylation of electron rich heteroarenes.

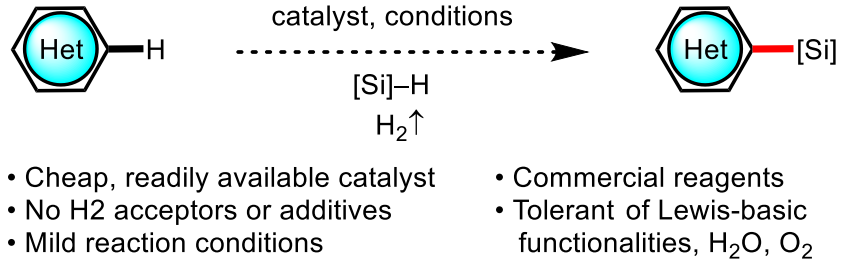


Indeed, reactions on preparative scale were not reported in any publications describing these catalytic methods. Moreover, substrates containing Lewis-basic functionalities such as pyridines and amines are notably absent in these reports, likely limiting the use of these methods in medicinal chemistry and other biomedical applications where such functionalities are commonly encountered.

Very recently, an Ir-catalyzed system with improved tolerance toward heteroarenes has been disclosed; however, issues of demanding reaction conditions, H_2O and O_2 intolerance, unproven scalability, use of sacrificial additives, and poor availability and high cost of catalyst remain important considerations, which limit the method's general accessibility.[65] Clearly, the direct C–H silylation of aromatics and especially heteroaromatics represents a challenging and unsolved problem in organic synthesis.

The development of a general synthetic method to construct heterocyclic C–Si bonds from C–H precursors under mild conditions and with high regiocontrol using a readily-available catalyst would constitute an important advance in the broader field of C–H functionalization (**Figure 2.3**). If the catalyst and overall process would additionally prove tolerant of Lewis-basic nitrogen functionalities, sulfur moieties, H_2O and O_2, this strategy would represent a new and potentially powerful tool for medicinal chemistry overcoming the limitations that plagued previous methods (i.e., catalyst availability, catalyst and ligand cost, use of stoichiometric additives, deactivation by basic heteroatoms). From a personal perspective, these gaps in the state-of-the-art of chemical synthesis presented an exciting scientific challenge and one which I was keen to actively investigate.

Figure 2.3. Idealized strategy for the catalytic C–H silylation of aromatic heterocycles.

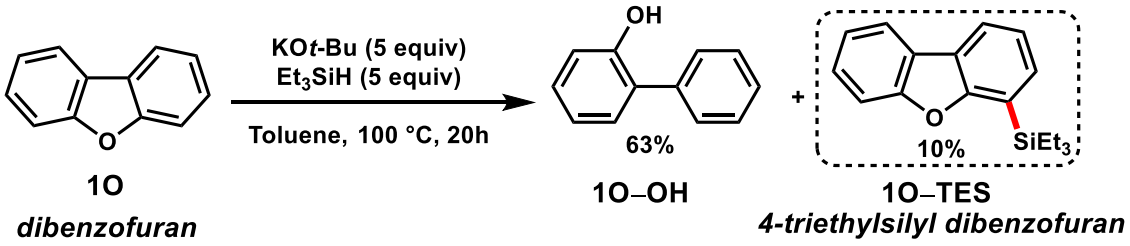


KO*t*-Bu–catalyzed cross-dehydrogenative C–H silylation of heteroarenes.

From C–O cleavage to C–H silylation

During our investigations and optimization of the reductive cleavage of aryl ethers using the potassium (*K*) alkoxide (*O*)/hydrosilane (*Si*)-based (*KOSi*) method (Chapter 1), and after careful analysis and investigation, I observed unanticipated products being formed in the reaction.[14]

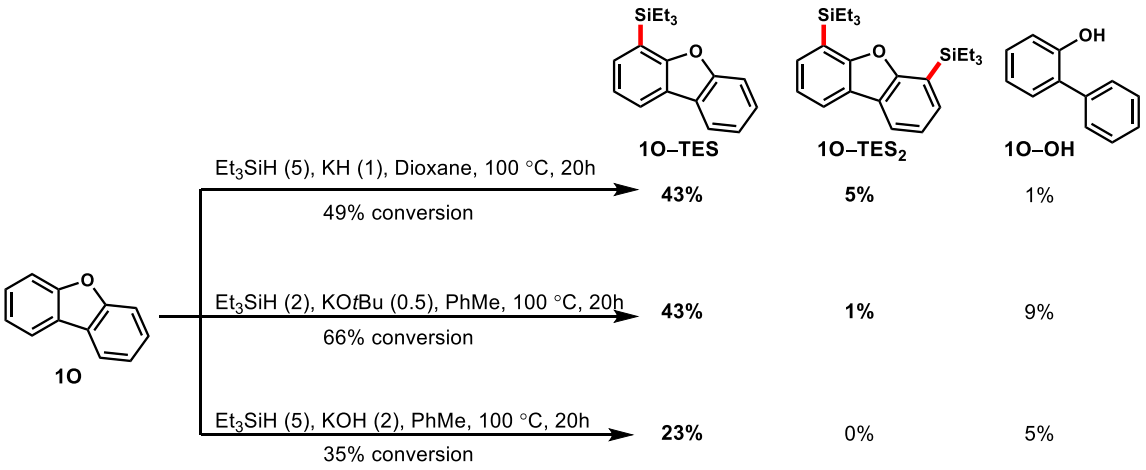
Scheme 2.3. First observation of KO*t*-Bu-mediated C–H silylation of an aromatic heterocycle.



With dibenzofuran **1O** as the substrate (**Scheme 2.3**), I observed 4-triethylsilyl dibenzofuran **1O–TES** as a minor byproduct. Formally, this product must arise from the cross-dehydrogenative silylation of dibenzofuran and triethylsilane, which was initially intended to be a reductant. Although our interests at the time involved optimizing the yield of the C–O cleavage reaction, I also began to at this point contemplate whether the C–H silylation manifold could be promoted. Indeed, a very preliminary investigation uncovered that by simple modifications of the reaction

conditions, the C–O silylation chemistry could be essentially thwarted in favor of the silylation pathway, albeit in low yield and still under relatively forcing conditions (**Figure 2.4**).

Figure. 2.4. Initial preoptimization of the C–H silylation of dibenzofuran (1O).

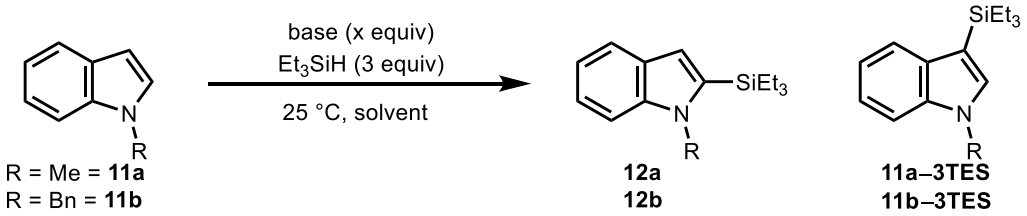


Optimization of the C–H silylation using 1-methylindole

With this encouraging data in hand and considering prior reports of Lewis-base activation of hydrosilanes,[71,72] I questioned whether these unanticipated silylation byproducts could be pointing to a more general reaction manifold. I therefore chose to test this C–H silylation reaction on the indole scaffold due to the general utility of indole frameworks in medicinally relevant substances.[73] An optimization exercise was conducted using 1-methylindoles **11a** and **11b** (**Table 2.1**).[74]

It was determined during this study that good catalysts for the C–H silylation reaction are categorized by the combination of a bulky basic anion and a potassium cation: KO*t*-Bu proved to be ideal catalyst and operated under neat conditions or in THF and MeO*t*-Bu (entry 18, 20 and 22), but KHMDS (entry 21) and KOTMS (entry 24) were also effective. The complete lack of reactivity with LiO*t*-Bu and NaO*t*-Bu (entries 1 and 2) as well as the precipitous drop in reactivity when 18-crown-6 is added to KO*t*-Bu (entry 23) lend support to the crucial, albeit unknown, role

Table 2.1. Optimization of the KO*t*-Bu–catalyzed C-H silylation reaction.



entry[a]	R	base	solvent	x	*t* (h)	C2:C3[b]	C2 (%)[b]
1	Me	LiO*t*-Bu	THF	100	16	–	0
2	Me	NaO*t*-Bu	THF	100	16	–	0
3	Me	NaOEt	THF	100	16	–	0
4	Me	NaOAc	THF	100	16	–	0
5	Me	KOMe	THF	100	16	–	<5
6	Me	KOEt	THF	100	16	–	14
7	Me	KO*t*-Bu	THF	100	16	>20:1	67
8	Me	KHMDS	THF	100	16	>20:1	44
9	Me	KOAc	THF	100	16	–	0
10	Me	KH	THF	100	72	–	0
11	Me	KOH	THF	100	16	–	0
12	Me	Cs_2CO_3	THF	100	16	–	0
13	Me	DABCO	THF	100	16	–	0
14	Me	TBAF	THF	100	16	–	0
15	Me	CsF	THF	100	16	–	0
16	Me	KF	THF	100	16	–	0
17[c]	Me	KO*t*-Bu	THF	20	60	4:1	98
18[c]	Me	KO*t*-Bu	MeO*t*-Bu	20	60	>20:1	89
19[c]	Me	KO*t*-Bu	DME	20	60	3.4:1	95
20[c]	**Me**	**KO*t*-Bu**	**neat**	**20**	**48**	**>20:1**	**88**
21[d]	Me	KHMDS	THF	20	72	17:1	75
22[c,e]	**Bn**	**KO*t*-Bu**	**THF**	**20**	**61**	**>20:1**	**90**
23[c,e,f]	Bn	KO*t*-Bu	THF	20	96	>20:1	22

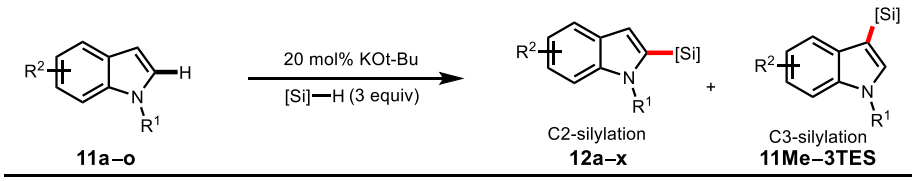
[a]Reactions performed with 0.2 mmol of **11a** or **11b** and 0.6 mmol of Et_3SiH in 0.2 mL of solvent. [b]Determined by GC analysis using an internal standard. [c]At 45 °C. [d]At 35 °C. C2:C3 and yield determined by ^1H NMR analysis. [f]With 50 mol % of 18-crown-6.

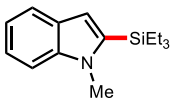
of the potassium cation. Conversion roughly correlates with basicity in stoichiometric reactions (i.e., O*t*-Bu > OEt > OMe; Entries 5–7). No product was observed in the absence of catalyst, or when KH, KOH, KOAc and Cs_2CO_3 were employed (Entries 9–12). The organic base DABCO and common fluoride-based activators for silicon – TBAF, CsF, and KF – were also investigated and failed to convert the starting material (Entries 13–16). Control experiments and micro-analyses to rule out the presence of transition metal residues in the reagents, catalyst, and reaction mixtures were carefully conducted and the results argued against any unanticipated transition metal catalysis (see **Experimental and analytics** section of this chapter).

Indole scope of the KOt-Bu–catalyzed C–H silylation

An evaluation of the scope of the KO*t*-Bu–catalyzed demonstrated that a variety of indoles with Me, Et, Bn, Ph and the readily cleavable MOM and SEM groups on nitrogen all leads to regioselective C2 silylation in moderate to good yields (**Figure 2.5**, **12a**–**f**). We then explored the influence of substituents at various positions of the indole nucleus and found that Me, OMe, OBn, CH_2OMe and Ph are all compatible, giving the desired products **12g**–**n** in 48–83% yield. Several hydrosilanes were examined and the silylation products (**12o**–**x**) were obtained in good yield. In general, the selectivities were excellent for silylation at the C2 position. For the reactions leading to **12g** and **12i,** silylation on the benzylic methyl group was observed with THF as solvent for the reaction leading to **12k**, silylation at C6 was observed as a byproduct in THF. Although solvent-free conditions often led to improved regioselectivity and yield, these byproducts provided a proof-of-concept for the silylation of sp^3 C–H bonds and also the C–H bonds of simple arenes by our method. This would prove to be a valuable extension and will be discussed later in

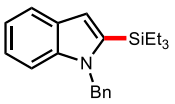
Figure 2.5. Evaluation of the scope of KO*t*-Bu–catalyzed indole C–H silylation.[a]





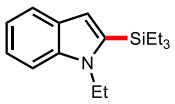
12a

neat, 45 °C
C2:C3 > 20:1
78% yield



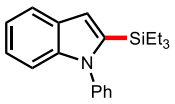
12b

THF, 45 °C
C2:C3 > 20:1
82% yield



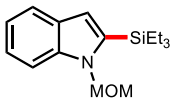
12c

neat, 60 °C
C2:C3 > 20:1
71% yield



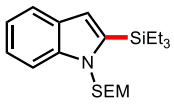
12d

neat, 60 °C
C2:C3 > 20:1
45% yield



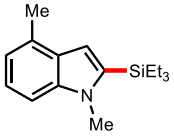
12e

neat, 60 °C
C2:C3 = 10:1
55% yield



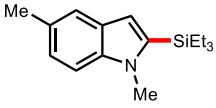
12f

neat, 60 °C
C2:C3 = 14:1
67% yield



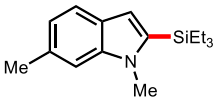
12g

neat, 45 °C
C2:C3 > 20:1
69% yield



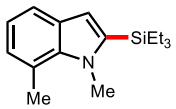
12h

THF, 25 °C
C2:C3 > 20:1
68% yield



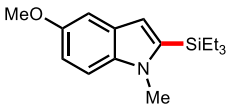
12i

neat, 45 °C
C2:C3 > 20:1
83% yield



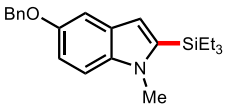
12j

neat, 45 °C
C2:C3 > 20:1
61% yield



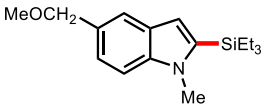
12k

THF, 25 °C
C2:C3 > 20:1
64% yield



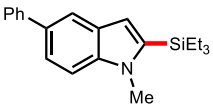
12l

THF, 25 °C
C2:C3 > 20:1
68% yield



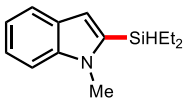
12m

neat, 45 °C
C2:C3 > 20:1
48% yield



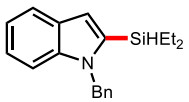
12n

THF, 45 °C
C2:C3 > 20:1
48% yield



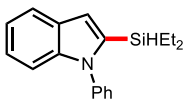
12o

THF, 45 °C
C2:C3 > 20:1
68% yield



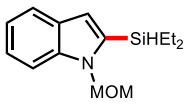
12p

neat, 60 °C
C2:C3 > 20:1
78% yield



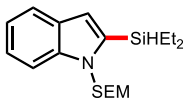
12q

MeOt-Bu, 55 °C
C2:C3 > 20:1
55% yield



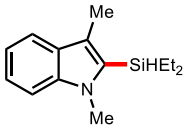
12r

neat, 60 °C
C2:C3 = 14:1
66% yield



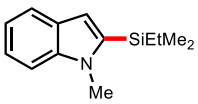
12s

neat, 60 °C
C2:C3 > 20:1
64% yield



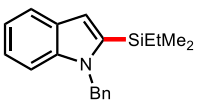
12t

THF, 65 °C
65% yield



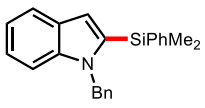
12u

MeOt-Bu, 45 °C
C2:C3 > 20:1
54% yield



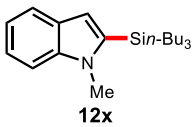
12v

THF, 45 °C
C2:C3 > 20:1
60% yield



12w

THF, 45 °C
C2:C3 > 20:1
58% yield



12x

THF, 35 °C
C2:C3 > 20:1
75% yield

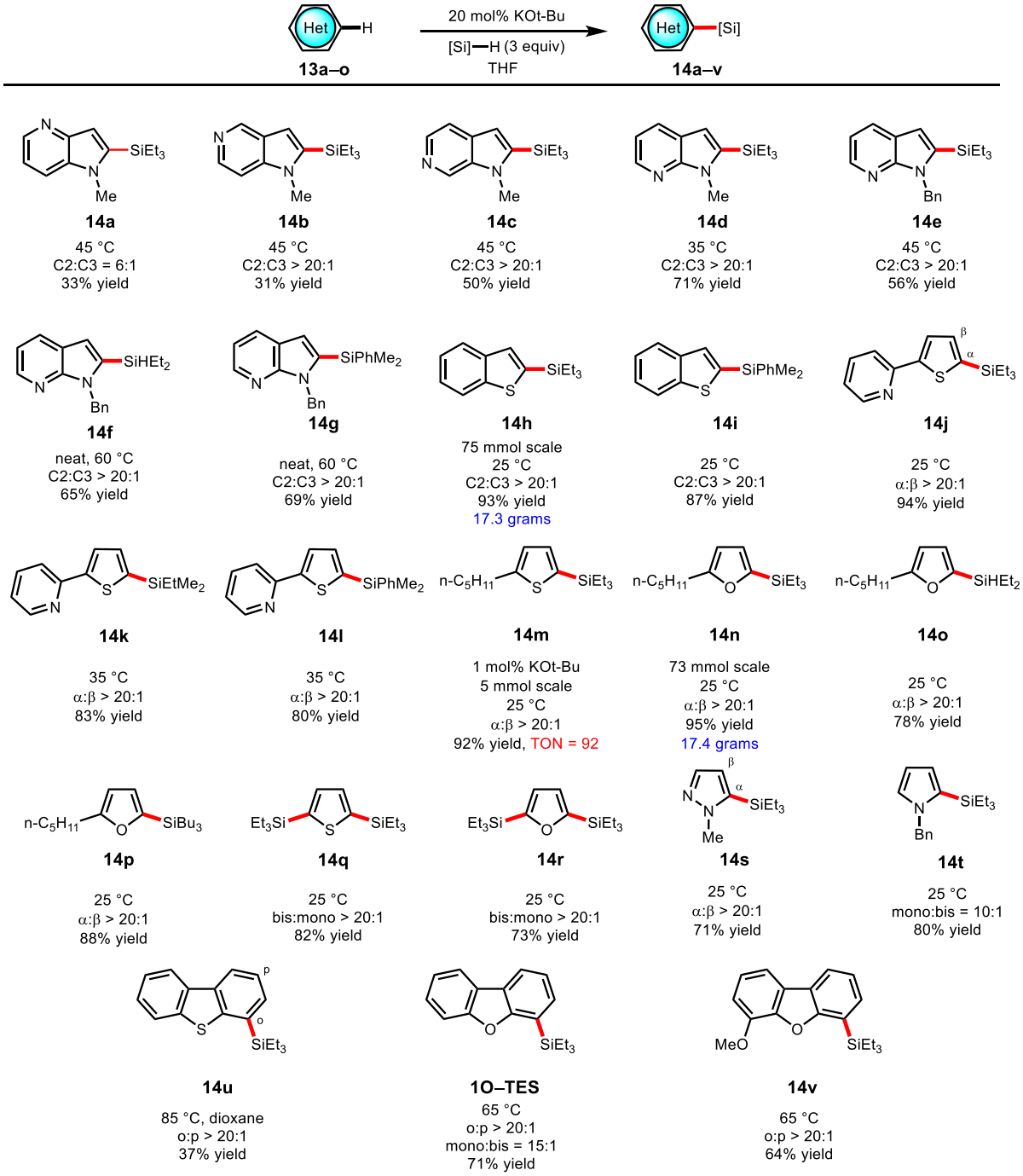
[a][Si]–H = Et_3SiH, Et_2SiH_2, $EtMe_2SiH$, $PhMe_2SiH$, and n-Bu_3SiH. MOM, methoxylmethyl; SEM, 2-[(trimethylsilyl)ethoxy]methyl

this chapter. The use of 1,3-dimethyl indole as a substrate allowed us to evaluate the steric considerations for silylation at the C2 position. Indeed, attempting the silylation with Et_3SiH and $PhMe_2SiH$ were sluggish; however, the use of the smaller Et_2SiH_2 enabled the silylation to occur in moderate yield and also provided a product (**12t**) which still contained a valuable Si–H bond. In this reaction, bisindolyldiethylsilane was also isolated as a byproduct, clearly arising from a silylation of the silylated product with another molecule of starting indole. Gratifyingly, this new silylation method does not require the addition of hydrogen acceptors, initiators, or other additives. The reaction can be conveniently performed under optionally solvent-free conditions (without any appreciable exotherms observed) and the process has moderate tolerance to ambient conditions (air and moisture).

KOt-Bu–catalyzed C–H silylation of N-, O-, and S-heterocycles

One of the important questions, which warranted substantial investigation at this point, was whether this method was amenable to the direct silylation of other heterocyclic nuclei and in particular whether the method would tolerate Lewis-basic functionalities. These had been issues that plagued known state-of-the-art systems at the time of our investigations and had limited the utility of C−H silylation methods in general. Gratifyingly, a wide variety of privileged nitrogen-containing heteroaromatics such as indoles (see **Figure 2.5, 12a–x)**, pyrazole (**Figure 2.6**, **14s**), and even the challenging and pharmaceutically valuable 4,5,6- and 7-azaindoles[73,75] (**Figure 2.6**, **14a–14g**) undergo smooth and regioselective C2 silylation yielding more than 30 new silylated N-heterocyclic building blocks. A diverse range of oxygen-, and sulfur-containing heteroaromatics such as benzothiophene, thiophene, furan, and dibenzofuran are regioselectively silylated, demonstrating the method's useful substrate scope (**Figure 2.6**, **14h**, **14i**, **14m–v**).

Figure 2.6. KO*t*-Bu–catalyzed C–H silylation of N, O, and S-containing heteroarenes.[a]

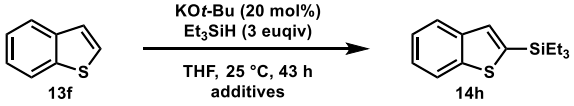


[a][Si]–H = Et_3SiH, Et_2SiH_2, $EtMe_2SiH$, $PhMe_2SiH$, and *n*-Bu_3SiH. TON = turnover number. NB: the numbering convention for the compounds gives products as **14a–v**, but starting materials as only **13a–o**. This is because in many cases, the same starting material is silylated with different hydrosilanes leading to different products. For example, products **14e, 14f,** and **14g** arise from the same starting material designated alphabetically as **13e**.

Unprecedented C–H silylations of pyridine-containing heteroaromatics such as pyridylthiophenes, which would be expected to deactivate precious metal catalysts (yielding **14k**, and **14l)** highlights a benefit of catalysis by an alkali-metal species over precious metal complexes. In general, the reaction proved to be selective for electron neutral and electron-rich heterocycles; those possessing electron withdrawing groups (e.g., nitrile, nitro, triflate) are

Table 2.2. Robustness evaluation for the KO*t*-Bu–catalyzed C–H silylation of benzothiophene (13f).

√ > 70%
– > 35%
× < 35%



entry	additive (1.0 equiv)	yield (%)	additive remaining (%)	entry	additive (1.0 equiv)	yield (%)	additive remaining (%)
1	–	99	–	14	PhOH	0 ×	91 √
2	C_6H_{13} C_6H_{13}	95 √	95 √	15	BnOTES	60 –	89 √
3	C_4H_9 C_4H_9	67 √	97 √	16	Ph Ph O	0 ×	91 √
4	C_3H_7 C_3H_7	83 √	99 √	17	$PhCO_2Me$	0 ×	84 √
5	PhF	95 √	N.D.	18	Ph OMe OMe	82 √	50 –
6	PhCl	74 √	100 √	19	$PhNO_2$	0 ×	98 √
7	PhBr	0 ×	100 √	20	PhCN	0 ×	81 √
8	PhI	0 ×	86 √	21	O	60 –	100 √
9	$PhCF_3$	90 √	N.D.	22	N OBn	40 –	100 √
10	$PhNMe_2$	80 √	79 √	23	N	71 √	N.D.
11	*n*-Bu_3N	38 –	100 √	24	N N	47 –	100 √
12	O NH	19 ×	N.D.	25	N H	0 ×	99 √
13	BnOH	31 ×	0 ×	26	PPh_3	48 –	97 √

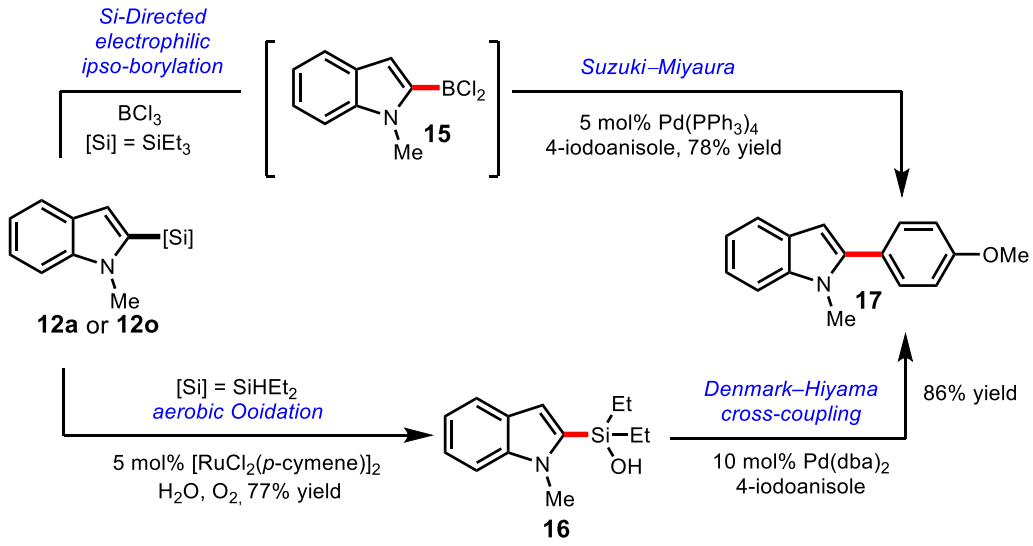
unreactive and starting material is quantitatively recovered. This remains an important limitation of the method that will need to be resolved. To further probe the functional group tolerance of the method, a comprehensive robustness evaluation was performed (**Table 2.2**).[76] The results showed that carbonyl groups in general are not tolerated, but are compatible if protected as the corresponding acetal (entry 18). Ar–Br (entry 7), Ar–I (entry 8), Ar–NO_2 (entry 19), and Ar–CN (entry 20) also shut down the reaction. However, Ar–F (entry 5), Ar–Cl (entry 6), Ar–CF_3 (entry 9), epoxide (entry 21), N-alkyl aziridine (entry 22), *cis*- and *trans*-olefins (entries 2 and 3 respectively), alkyne (entry 4), pyridine (entry 23), tertiary amine (entry 11), and even phosphine (entry 26) moieties are all compatible with the silylation chemistry. Hydrosilylation of olefins and acetylenes was not detected (entries 2–4). Even free OH (entry 13) and NH (entry 12) groups are tolerated to some extent, apparently due to a fortuitous, albeit somewhat unusual, silylative protection of the heteroatom *in situ*.[72] This heteroatom silylation will be discussed in Chapter 4.

Synthetic applications of the KOt-Bu–catalyzed C–H silylation of heteroarenes

Part of our motivation for these extensive investigations into developing a powerful and useful new heteroaryl silylation method derived from our realization of the value of the products that such a reaction would generate. Indeed, heteroarylsilane derivatives are known to undergo a variety of powerful synthetic transformations.[56,57b,58b,59,66,67,77] Although it was not within the scope of our work at the time to exhaustively investigate their reactivity, we had nonetheless intended to remind ourselves of their downstream value through a few representative examples. For example, we first sought to take advantage of the cross-coupling reactivity enabled by the aryl- and heteroaryl C−Si bond by two different methods and using two different starting materials, both accessible by our silylation chemistry. First, Dr. Wen-Bo Liu found that it was possible to engage the 2-triethylsilyl-

1-methylindole (**12a**) in a C2 Si-directed Suzuki–Miyaura cross-coupling by the method of Snieckus.[78] This reaction is thought to proceed through an initial electrophilic desilylative *ipso*-borylation with a BX_3 species (in this case BCl_3) to yield the corresponding borylated indole (**15**) (**Scheme 2.4**).

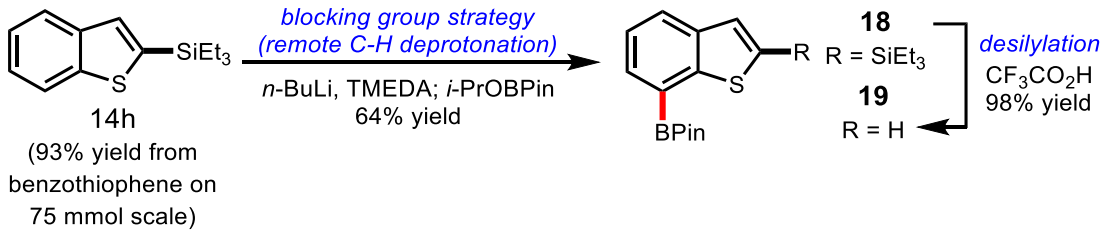
Scheme 2.4. Arylation chemistries of 2-silyl-1-methylindoles.



This electrophilic functionalization is regiospecific for borylation at the C2 position, provides what is in my opinion a striking demonstration of the ability of a C–Si bond to completely override the innate reactivity of an indole, enabling electrophilic functionalization at C2 over the Friedel–Crafts active C3 position. This material is directly subjected to standard Suzuki–Miyaura conditions to furnish arylated indole **17** in one pot in 78% yield. Next, and cognizant of the powerful Denmark–Hiyama cross-coupling[79] protocol, we wished to demonstrate a palladium-catalyzed cross-coupling protocol directly from our silylated heteraorylsilane. Thus, 2-diethylsilyl-1-methylindole was readily advanced to the corresponding heteroarylsilanol **16**,[80] providing the necessary Si–OH functionality for the corresponding cross-coupling chemistry. **16** underwent successful Pd-catalyzed cross-coupling to furnish 2-arylated indole **17** in 86% yield.

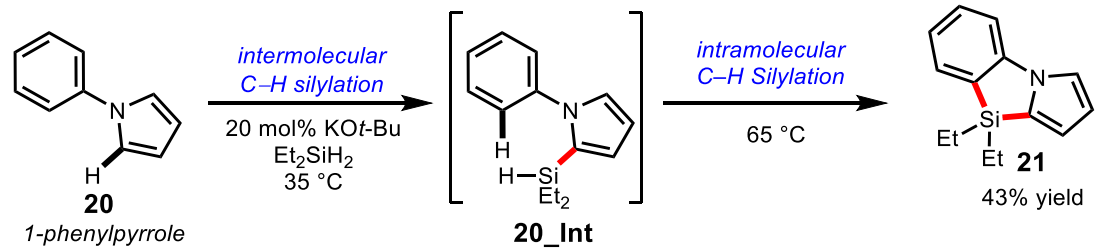
Having demonstrated the ability of the C–Si bond to enable arylation reactions under different conditions via C−Si bond cleavage, we were next intrigued to investigate a yet more common application of the C−Si bond: protecting group chemistry. Cognizant that our silylation chemistry provides access to indoles (and other heteroarenes) functionalized at the most acidic position (i.e., *ortho* to the heteroatom), it became clear to me that we could use the C–Si bond to block well-established functionalization methods that would typically engage the C2−H bond and perhaps enable remote and unexpected functionalizations. It is known, for example, that benzothiophene undergoes ready lithiation at C2 when treated with organilithium bases such as *n*-BuLi. It is further known that even 2-trimethylsilylbenzothiophene lithiates at C2, presumably because the Si center of the TMS group is simply not sufficiently sterically shielded to be protected from nucleophilic attack by *n*-BuLi. We therefore chose to investigate the lithiation chemistry of 2-triethtysilylbenzothiophene (**14h**) – a product which bears a more sterically encumbered Si center and that is accessed in excellent yield and on large scale by our silylation method. Thus, treatment of **14h** with *n*-BuLi at room temperature followed by treatment with isopropoxypinacolborane (*i*-PrOBPin) as the electrophile led to an unusual direct C7 functionalization of benzothiophene to give boronate ester **18** (**Scheme 2.5**). This heterocyclic nucleus now contains orthogonally activatable C−Si and C−B bonds – both installed without the use of precious metal reactions – which should enable sequential and controlled diversification at C2 and C7. As a trivial exercise, we chose to demonstrate the deprotection of the 2-triethylsilyl group to furnish the C7-borylated building block **19** as the final product via this unusual strategy employing silicon as a blocking group enabling remote lithiation.[81]

Scheme 2.5. Remote functionalization strategies: 2-silyl moieties as blocking groups.



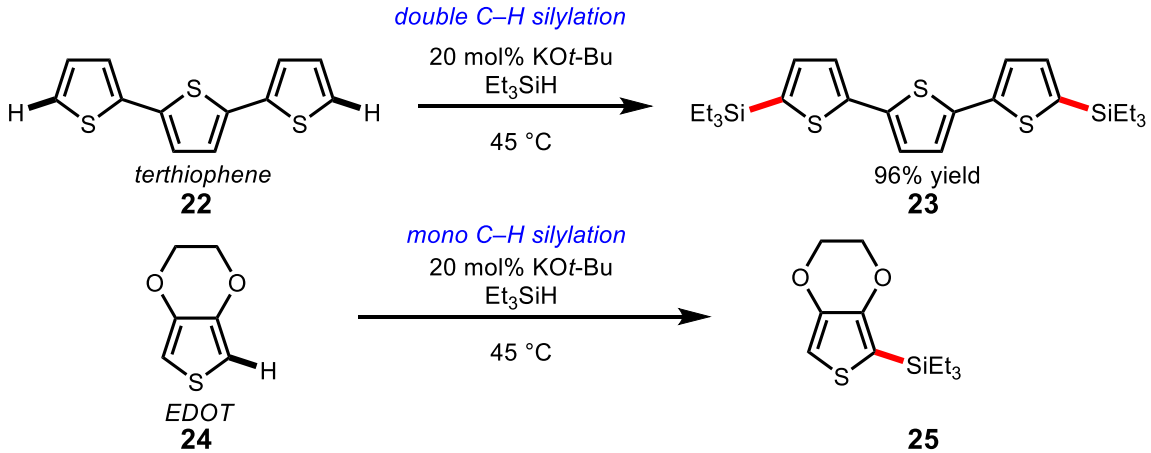
Organosilicon has been extensively investigated in the development of advanced materials due to silicon's unique physical and chemical properties.[53,55] To demonstrate the utility of our method for

Scheme 2.6. Inter/intra-molecular C–H silylation in the synthesis of an azasilacycle.



possible materials science applications, we prepared sila-heterocycle **21** in one step directly from the corresponding commercially available unfunctionalized heteroarene (**Scheme 2.6**). This unanticipated product must derive from an initial intermolecular C2 silylation of commercially-available 1-phenylpyrrole (**20**) with diethylsilane to furnish silylated pyrrole **20_Int** containing a

Scheme 2.7. Direct silylation of thiophenes relevant to materials science applications.



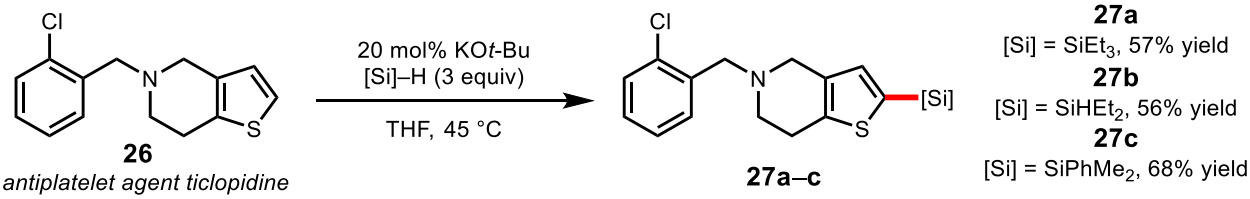
EDOT = 3,4-ethylenedioxythiophene.

remaining Si–H bond. This intermediate then presumably undergoes intramolecular silylation on the aromatic ring, forming the 5-membered azasilacycle and furnishing the final product.[82,83] A high-yielding bis-silylation of thiophene oligomer **22** furnishes bis-silylated **23**, the starting material for a known entirely transition metal-free catalytic route to block copolymers.[53] Finally, the mono-selective silylation of the EDOT monomer (**24**) provides a potential strategy for the modification of polythiophene-derived materials (**Scheme 2.7**, **25**).[83]

Late-stage silylation of pharmaceutically-relevant substances

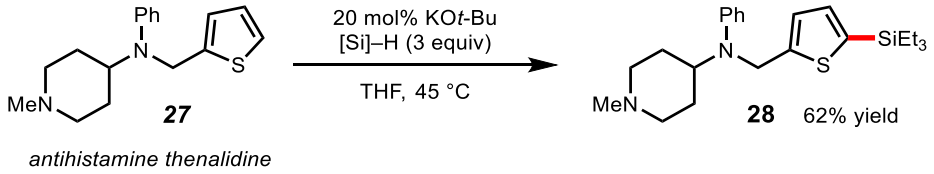
Sila-drug analogues have garnered much attention from medicinal chemists as they can offer improved stability, solubility, and pharmacokinetic properties compared to the parent all-carbon parent compounds.[50,51] Moreover, the installed organosilicon functionality can serve as a synthetic handle for subsequent elaboration, facilitating library synthesis and SAR studies. As a result, organosilicon-containing small molecules are an emerging field of interest in pharmaceutical science, and the direct silylation of lead compounds would thus represent a new and potentially powerful tool in drug discovery.[50,51] To evaluate our method for such late stage C–H functionalization applications, we subjected the antiplatelet drug ticlopidine (**26**) to our catalytic silylation conditions. The reaction proceeded smoothly in the case of all of the silanes that were tested to provide 3 new sila derivatives of the API (**27a–c**) in 56–68% yield (**Scheme 2.8**).

Scheme 2.8. Late-stage direct silylation of ticlopidine.



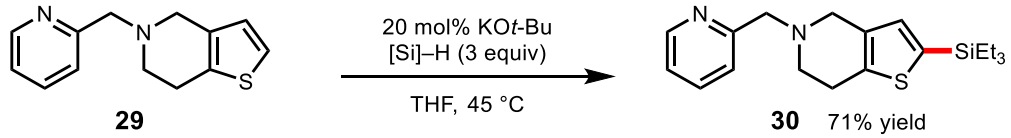
Next, we subjected another API, the antihistamine thenalidine, to the same conditions using triethylsilane as the silicon source and again the reaction proceeded well to give the product drug derivative **28** in 62% yield (**Scheme 2.9**). The piperidines, aniline, benzylic C–H bonds, and aryl chloride moieties were all tolerated without any observed side reactions. In order to further

Scheme 2.9. Direct KO*t*-Bu–catalyzed C–H silylation of thenalidine.



demonstrate the unique tolerance of this silylation method to Lewis-basic functionalities, which was at the time of this work a substantial limitation in the C−H silylation field, a pyridine-containing analogue of ticlopidine (**29**) was preparaed and subjected to the standard KO*t*-Bu−catalyzed silylation conditions (**Scheme 2.10**).

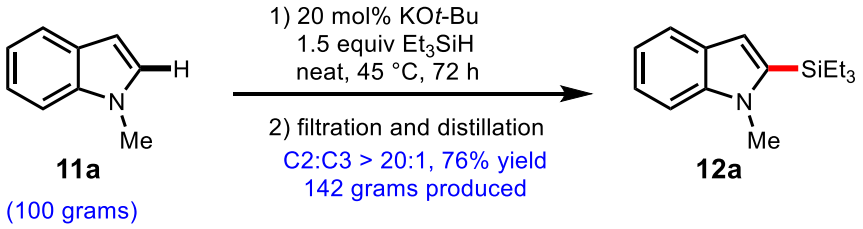
Scheme 2.10. Silylation of a pyridine-containing ticlopidine derivative: demonstration of tolerance to basic N-heterocycles.



This aza analogue too underwent successful functionalization demonstrating compatibility of our method with pyridine-containing complex molecules of potential pharmaceutical significance. In all cases, the C−H silylation occurred regiospecifically at the position *ortho* to the sulfur atom at the thiophene nucleus; only product and starting material were present in the reaction mixtures. Finally, we were of course interested the concept of scalability of our silylation protocol, especially since the competing dehydrogenative C–H silylation methods published in the literature still to this point do not report reactions on typically larger than a few millimoles scale. Should this KO*t*-Bu−catalyzed silylation scale well then it would represent another advantage of employing this method over

alternative protocols. Thus, we decided to perform the silylation on 100 grams of 1-methylindole (**11a**) and a lower loading (i.e., 1.5 equivalents) of Et_3SiH. To keep the volume low and to ensure that the reaction could be performed conveniently using standard laboratory glassware, the reaction was further performed in the absence of solvent. The standard 20 mol % of KO*t*-Bu catalyst was used (**Scheme 2.11**).

Scheme 2.11. 100-gram scale silylation of 1-methylindole (11a).

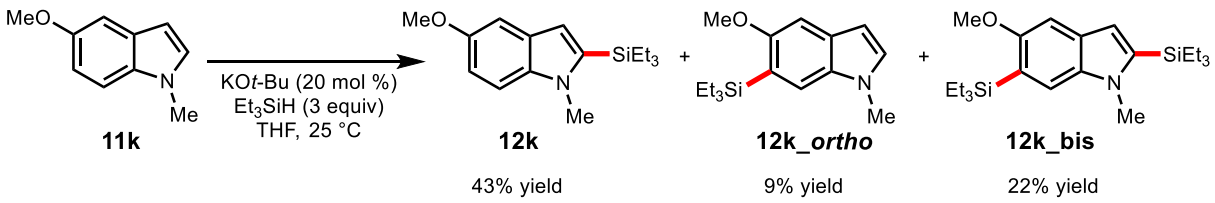


The entire contents of this reaction comfortably occupies about 40% of a 500 mL flask reaction. This mixture is stirred at 45 ˚C for 72 h after which point the dark purple solution is simply filtered and the crude pale yellow material is subjected to a distillation under vacuum to afford 142 grams of the product (**12a**) as a thermally- and hydrolytically robust pale yellow or clear liquid.

Extension to non-heterocyclic silylation

During the course of our investigations regarding the silylation of substituted and functionalized indoles, we observed some unanticipated behavior in the case of methoxy-substituted indoles. Specifically, in the case of 5-methoxy-1-methylindole (**11k**) we found that we were obtaining silylated products with the C−Si bond being formed at the C6 position *ortho* to the oxygen

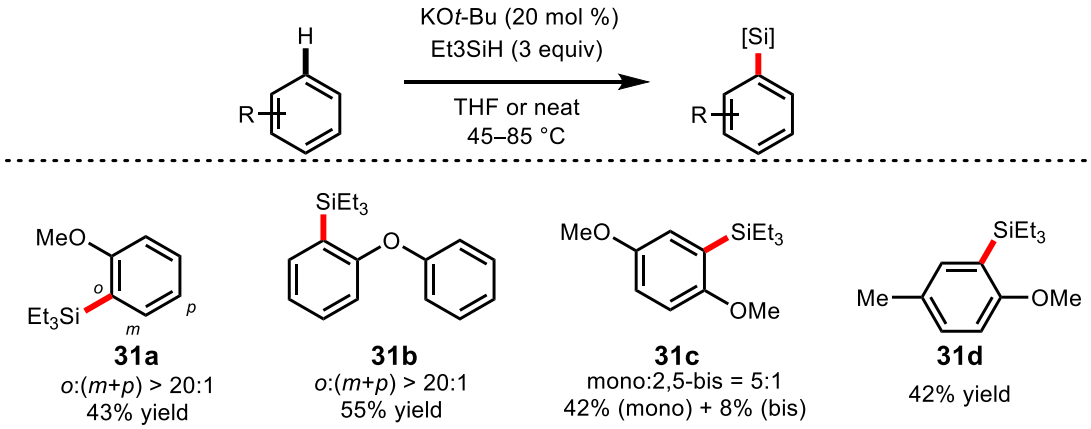
Scheme 2.12. Discovery of oxygen directed silylation on the benzenoid ring of indole 11k.



(**Scheme 2.12, 12k_*ortho*** and **12k_bis**). This result intrigued us since the utility of such a direct silylation method of aromatic oxygenates could be substantial. Indeed, simple aromatics such as oxygenated arenes are common moieties in natural and unnatural bioactive complex molecules and drug targets and are core frameworks in ligands for metal-catalyzed transformations.[84]

Using anisole as a model substrate and in the absence of solvent, *ortho*-selective C–H functionalization was achieved furnishing the silylated product with excellent regioselectivity (**Figure 2.7**, **31a**). Promising reactivity was observed for a number of oxygen-substituted arenes **31a**–**d**. Despite the modest yields to date, this appears to be, to the best of our knowledge, only the second report of catalytic *ortho* C–H silylation of aromatic oxygenates and the first such catalytic reaction operating in the absence of transition metal species.[85]

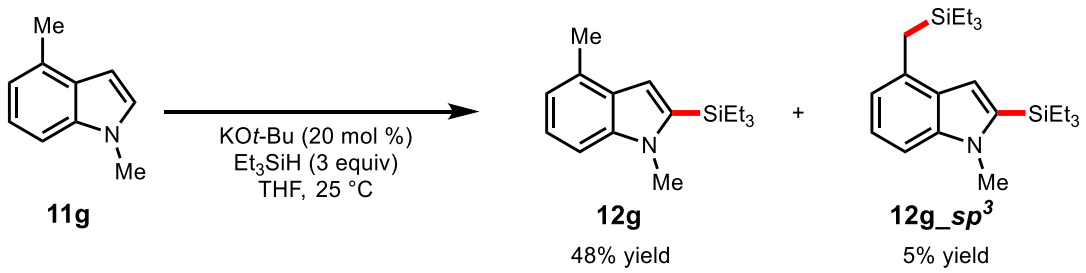
Figure 2.7. Direct KO*t*-Bu–catalyzed C–H silylation of aromatic oxygenates.



Interestingly, compared to the corresponding scandium-catalyzed method which requires large excesses of arene (>10 equiv.) under harsh conditions (i.e., benzene, 120 °C),[85] the use of KO*t*-Bu allows for silylation at lower temperatures, with economical reagent ratios, improved regioselectivity and allows the use of various hydrosilanes as coupling partners. The products of

the KO*t*-Bu-catalyzed *ortho* C–H silylation of aromatic oxygenates are versatile building blocks of potential use as aryne precursors,[86] cross-coupling partners,[77] and as masked phenols.[87] Interestingly, our explorations of the silylation of methyl-substituted indoles revealed another surprising form of reactivity: the silylation of benzylic C−H bonds. In particular, subjecting 4-methyl-1-methylindole (**11g**) to our standard silylation conditions furnishes the 2-silylated species (**12g**) as predicted, but also generates the bis-silylated **12g_*sp*^{3}** in 5% yield, having the methyl group on the benzene nucleus silylated. As with the oxygenates, this again led us to contemplate whether a more general reaction manifold could be developed.

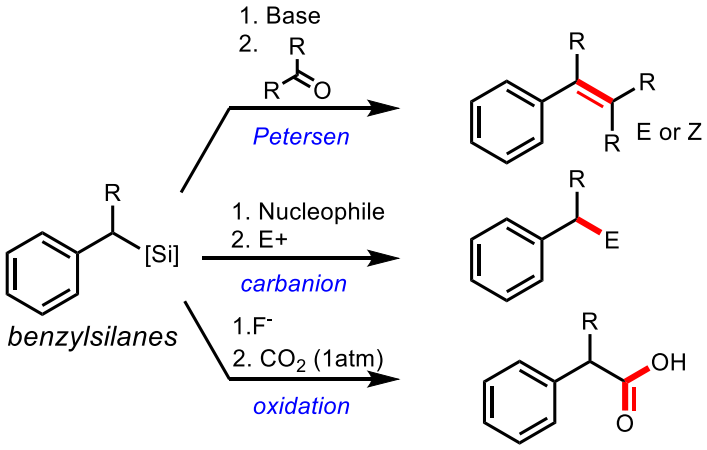
Scheme 2.13. Discovery of C–H silylation of the aromatic methyl group on indole 11g.



Such a method could again be of significant value since C(sp^3)–Si fragments have been employed in various powerful reaction classes such as the Peterson olefination yielding styrene derivatives,[88] electrophilic substitution reactions,[89] and various oxidation manifolds such as carboxylation (**Figure 2.8**).[90] However, selective and mild synthesis of the starting organosilanes remains challenging and is primarily accomplished by hydrosilylation,[91] or by stoichiometric organometallic reactions.[92] These processes can be circuitous and are often limited in scope. Due to challenging synthesis, complex C(sp^3)–Si fragments have had relatively poor visibility in the medicinal chemistry- and total synthesis literature despite their high synthetic utility and mild activation. Moreover, only two examples of catalytic intermolecular C(sp^3)–H silylation with hydrosilanes have been reported in the literature, both occurring at benzylic C–H bonds and

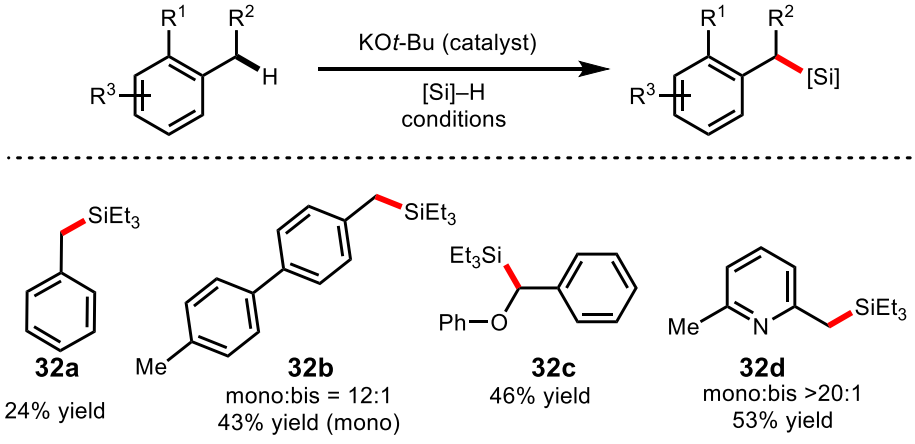
requiring precious-metal catalysis, high temperatures, large excesses of reagents, and directing groups[93]or irradiation.[94]

Figure 2.8. Synthetic aplications of benzylsilanes.



Furthermore, the direct catalytic intermolecular silylation of other C(sp^3)–H bond classes has not been reported – testament to the difficulty of the title transformation. Our goal will be the development of a general catalytic platform for C(sp^3)–H bond silylation in order to unlock the true utility of and by making these fragments more readily accessible.

Figure 2.9. Direct KO*t*-Bu–catalyzed C–H silylation of aromatic methyl groups.



Thus, the reaction of toluene under standard C–H silylation conditions provided benzyltriethylsilane **32a** in modest yield and with excellent selectivity for reaction at the methyl group over the aromatic ring (**Figure 2.9**). A number of methyl-substituted arenes and heteroarenes were tested and all were shown to be amenable to C(sp^3)–H silylation giving the corresponding benzyltriethylsilyl products in modest yields (**32a**–**c**), with **32c** containing a Si-substituted chiral center. Even the electron poor heteroarene 2,6-lutidine undergoes selective desymmetrizing mono-silylation in moderate yield, providing our first observation of silylation in an electron deficient system **32d**.

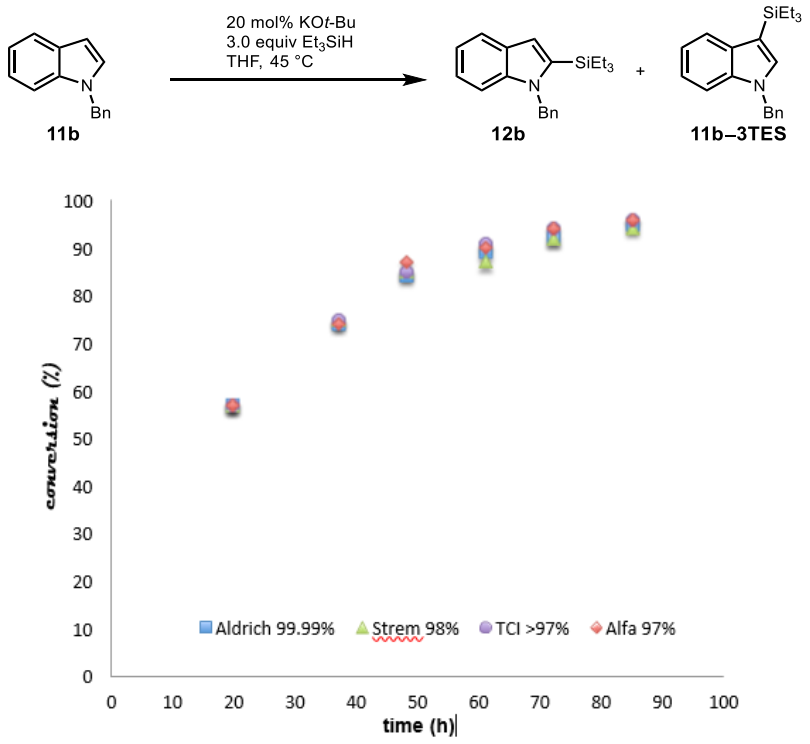
Preliminary mechanistic studies.

Control experiments and microanalyses

Throughout the process of developing this chemistry, it became apparent that our insight into the mechanism of this reaction was highly limited. Most likely, this chemistry appeared to represent a new form of reactivity and operates by manifolds that remain largely unknown. Because of these fundamental considerations, and because knowledge of mechanism would enable rational improvement and development, we were constantly contemplating how to best extract at least some mechanistic information from this system. As a first point, we wished to convince the scientific community, and equally importantly ourselves, that this chemistry was not proceeding as a result of some adventitious impurity in the reagents, on the glassware, or otherwise present in the mixture. In particular, we were weary of the hypothetical possibility of catalysis by adventitious transition metal residues. In order to investigate these possibilities and provide as substantial scientific rigor as possible, we undertook a number of control experiments and micro-analyses.[74] First, Dr. Wen-Bo Liu performed control reactions with commercially available KO*t*-Bu (Aldrich, sublimed grade,

99.99%, trace metal basis), re-sublimed KO*t*-Bu, and freshly-prepared KO*t*-Bu were performed in parallel. No difference in yield or selectivity was observed in the silylation reaction of these catalyst materials with 1-methylindole. Next, Control reaction with KO*t*-Bu of different grade purchased from different vendors were performed in parallel under standard conditions using 1-benzylindole as the starting material (**Figure 2.10**). Materials tested were as follows: KO*t*-Bu (Aldrich, sublimed

Figure 2.10. Investigating the influence of KO*t*-Bu purchased from different vendors in the C–H silylation reaction.



grade, 99.99% trace metal basis), b) KOt-Bu (Strem, 98%), c) KOt-Bu (TCI, >97%), and d) KOt-Bu (Alfa-Aesar, 97%). The reactions were monitored by UHPLC-LCMS and gain, no appreciable differences in conversion and selectivity in these four reactions was observed.

With these results clearly indicating that the form and manufacture of the KO*t*-Bu in general were not contributing to the catalysis, we next wished to confirm the absence of any transition metal residues that could be present in the reaction mixtures and potentially contributing to the catalysis.

To achieve this, careful ICP-MS analyses of the reagents, solvents, and reaction mixtures were conducted (**Table 2.3**).

Table 2.3. Results of the ICP-MS trace metal analysis.

ICPMS Trace Metal Analysis – Agilent 7900 (quantities in ppb)[a]								
Element	**KO*t*-Bu Strem (98%)**	**KO*t*-Bu TCI (>97%)**	**KO*t*-Bu Alpha (97%)**	**KO*t*-Bu Aldrich (99.99%)**	**THF**	**$HSiEt_3$**	**1-Bn-indole**	**Rxn Mixture**
Ti	0.360	0.051	0.138	0.464	LOD	2.073	9.408	31.082
Mn	1.343	1.168	1.338	1.525	LOD	0.177	88.191	LOD
Fe	12.285	10.171	13.080	14.036	1.691	9.531	86.191	LOD
Co	0.005	LOD	0.006	0.008	0.001	0.006	0.416	LOD
Ni	0.064	LOD	0.232	1.418	0.011	LOD	16.540	19.826
Cu	0.134	0.211	1.126	0.366	LOD	0.520	17.936	3.092
Zr	0.038	LOD	LOD	0.633	LOD	0.031	LOD	8.889
Mo	2.005	1.650	1.744	2.243	LOD	LOD	LOD	LOD
Ru	0.002	0.002	0.001	0.008	LOD	0.004	0.146	LOD
Rh	LOD	LOD	LOD	0.001	LOD	LOD	LOD	LOD
Pd	0.014	0.006	0.029	0.116	0.002	0.004	0.070	0.593
Ag	0.001	LOD	0.290	0.015	LOD	0.004	0.055	0.013
Os	0.001	LOD	LOD	0.001	LOD	LOD	0.007	0.016
Ir	0.001	0.001	0.002	0.026	LOD	0.001	0.047	0.041
Pt	0.009	0.004	0.002	0.010	LOD	0.001	LOD	LOD
Au	0.017	0.013	0.013	0.023	0.108	0.024	0.738	1.582

[a]LOD = Limit of detection. These values fall below the detection limit of the instrument.

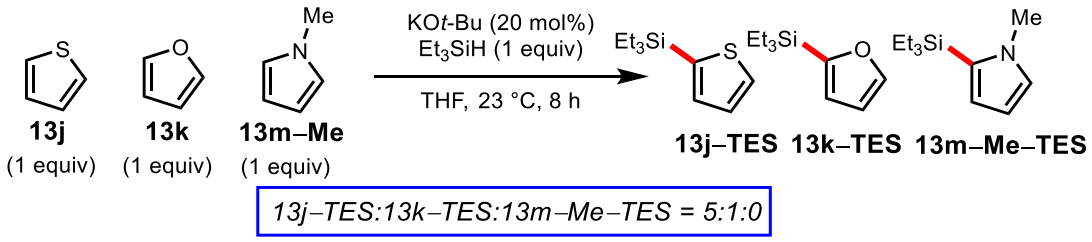
These ICP-MS measurement data appear to suggest that although some transition metals are present in varying quantities in the reagents and reaction mixtures – as would be anticipated – the quantities of metals which are known to promote direct C–H silylation reactions similar to ours are either very low (i.e., Ir), or are functionally absent (i.e., Rh, Pt) in the reaction mixtures. Although this certainly does not conclusively and unambiguously exclude the participation of trace quantities of transition

metal residues in the silylation chemistry – indeed, this is essentially impossible to exclude – it provides further support against such a possibility.

Competition experiments

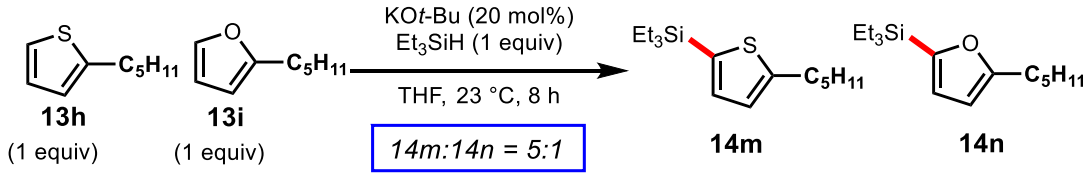
We wondered next whether we could probe the relative rates of the various heterocycles undergoing silylation by our method to attempt to gain further insight into the reactivity. To investigate the relative reactivities of nitrogen-, oxygen-, and sulfur-containing aromatic heterocycles by KO*t*-Bu-catalyzed C–H silylation, two internal competition experiments were conducted using one equivalent of Et_3SiH and one equivalent of each heteroarene (**Scheme 2.13**). Reactions were run to partial consumption of Et_3SiH and relative quantities of silylated heteroarene were determined by ^1H NMR analysis. Results demonstrated that for 5-membered heteroarenes, the relative rate of reactivity trends as: thiophene **13j** > furan **13k** >1-methylpyrrole **13m–Me.** This

Scheme 2.13. Competition experiments of 5-membered heteroarenes.



trend is corroborated in the competition between substituted thiophene **13h** and furan **13i**, as shown in **Scheme 2.14**.

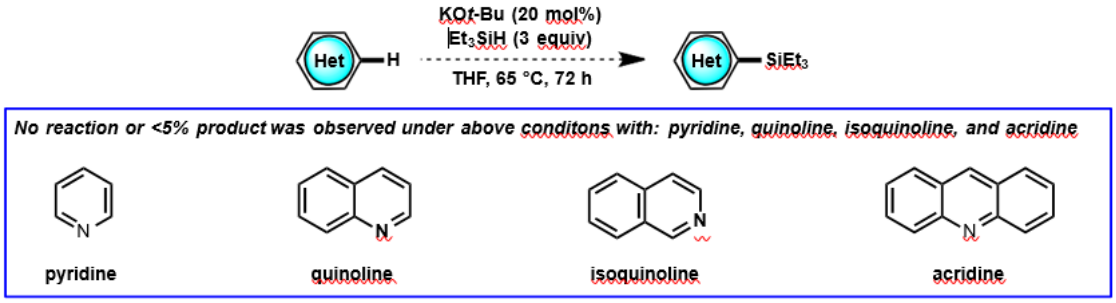
Scheme 2.14. Competition experiment to confirm relative silylation rates of furan and thiophene.



A potential single-electron process?

As the development of this reaction proceeded, we began to contemplate the possibility of a radical process being operative in the KO*t*-Bu catalyzed C–H silylation due to the general reactivity, selectivity, and other trends observed. As a first test of this notion, we chose to evaluate the reactivity of the pyridine nucleus under our silylation conditions. Pyridine derivatives would be expected to react readily if a conventional silyl radical addition process was operational. However, a variety of pyridine substrates were examined and were found to be essentially unreactive under the KO*t*-Bu–catalyzed C–H silylation conditions (**Figure 2.11**).

Figure 2.11. Investigation of C–H silylation in electron deficient heteroarenes.

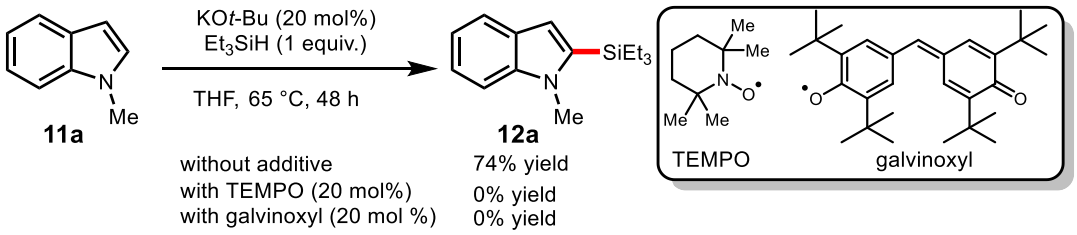


This observation argues against the likelihood of an elementary Minisci-type mechanism and suggests that the reaction is proceeding by an alternative and presently unidentified pathway.

To further probe the possibility of a radical process, we performed the reaction in the presence of the radical traps TEMPO and galvinoxyl. In both cases, the addition of the radical trap in a 1:1 molar ratio to catalyst (i.e., 20 mol %) thwarted the silylation reactivity and starting material was recovered (**Figure 2.12**).

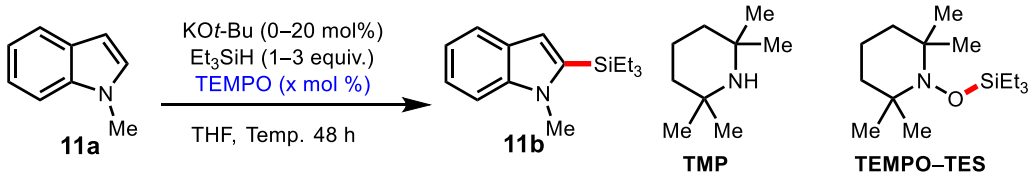
Subsequently, we conducted three control experiments in an attempt to probe the role of TEMPO (**Table 2.4**). Interestingly, a trace amount of triethylsilyl protected adduct (**TEMPO–TES**) was observed at 23 °C with 1 equivalent of TEMPO (entry 5), presumably arising from the radical

Figure 2.12. Impact of radical scavengers.



combination of a silyl radical and TEMPO itself. **TEMPO−TES** becomes the major component of the mixture when the temperature is raised to 65 °C, lending support to the involvement of silyl radical species in the silylation reaction. In contrast, this **TEMPO−TES** adduct is not observed in the absence of KO*t*-Bu, indicating that the catalyst is critical to generate the silyl radical. Although

Table 2.4. Observation of a TEMPO–$SiEt_3$ (TEMPO–TES) adduct.



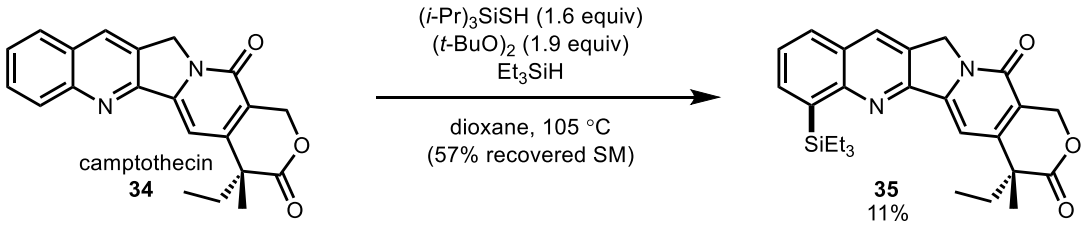
entry	11a	TEMPO (mol %)	KO*t*-Bu (mol %)	Et_3SiH (equiv)	Temp (°C)	11b (%)	TMP	TEMPO–TES
1	–	–	100	1	23	ND[a]	ND	ND
2	–	100	–	1	65	ND	ND	ND
3	1	20	20	3	23	ND	ND	ND
4	1	20	20	3	65	ND	ND	ND
5	–	100	20	1	23	ND	trace[b]	trace
6	–	100	20	1	65	ND	minor[b]	major

[a]ND = Not detected; [b]Determined by GC-MS analysis.

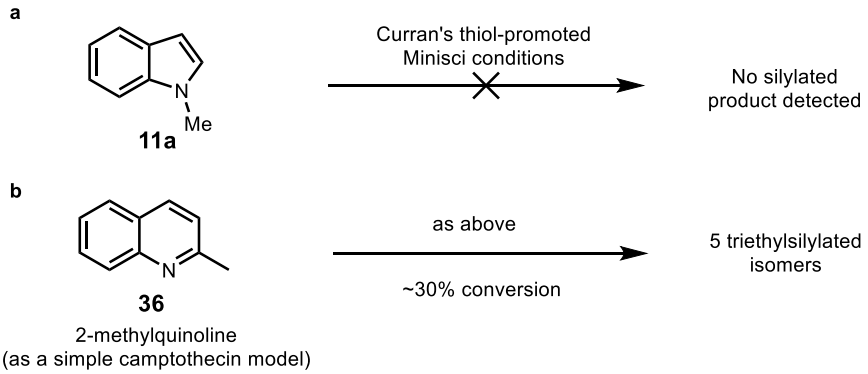
we are unsure as to the mechanism of formation of the putative silyl radical, we considered that if such radical species were formed in appreciable amounts, then the reaction couldproceed by an elementary addition of a silyl radical to a heterocycle (i.e., sila-Minisci reaction). A rare example of this reactivity is demonstrated by Curran in his preparation of silyl camptothecin derivatives (e.g., **35**) starting from camptothecin (**34**) itself (**Scheme 2.15**). To probe this hypothesis, we subjected 1-methylindole **11a** to a mixture of reagents under conditions that are reported by the

Curran group[95] to generate discrete putative silyl radicals (see Scheme **2.15** for Curran's conditions, and **Scheme 2.16a** for the result of indole **11a** under these conditions). Interestingly, no silylated product of any kind was detected in this reaction (**Scheme 2.16**).

Scheme. 2.15. Curran's sila–Minisci reaction.



Scheme 2.16. Application of Curran's sila-Minisci conditions to model substrates.



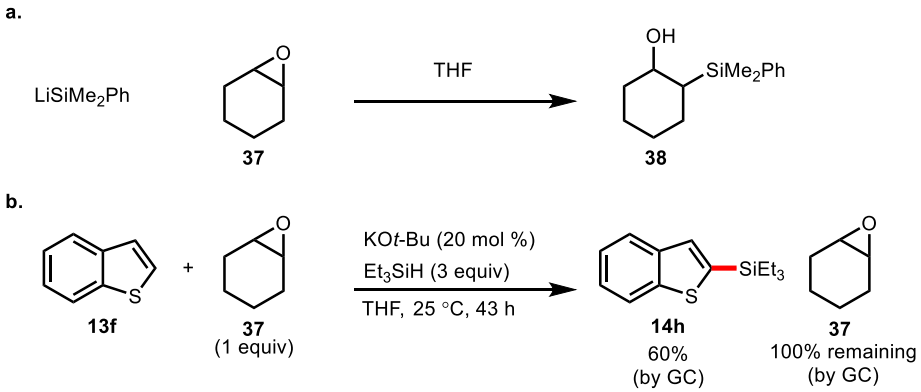
Conversely, we confirmed that the Curran's conditions do silylate electron poor heterocycles (such as 2-methyl quinoline, **36**, **Scheme 2.16b**), but our method fails in the case of these substrates (see also **Figure 2.11**).

Exploring the potential of an anionic pathway

To investigate the possibility of a potential polar mechanism (i.e., formation of silyl anions), our KO*t*-Bu–catalyzed reaction with benzothiophene **13f** as a substrate was conducted in the presence of cyclohexene oxide (**37**) as an additive. Since epoxides, including cyclohexene oxide, are known to undergo nucleophilic ring opening by silyl anions (**Scheme 2.17a**), this control reaction could

serve as a probe for the formation of discrete anionic silicon species.[96] However, under our conditions, the epoxide is quantitatively recovered after the reaction, and the desired silylation product **14h** was obtained in moderate yield (**Scheme 2.17b**), providing some evidence against the formation of significant quantities of long-lived and discrete silyl anions in solution.

Scheme. 2.17. Control reactions exploring a potential anionic mechanism.



Taken together, the results of control reactions with radical traps (**Figure 2.12**) and the observation of **TEMPO-TES** (**Table 2.4**), we propose that silyl radical species appear to be involved and may be playing an important role in this catalytic C–H silylation reaction. However, based on the results from **Figure 2.11** and **Scheme 2.16a**, an elementary radical generation/addition mechanism (i.e., sila-Minisci reaction) is likely not operative. Although an anionic pathway can by no means be discounted, the survival of the epoxide additive (**Scheme 2.17b**) provides some support against a standard silyl anion pathway. These preliminary studies point to a previously unreported (hetero)aromatic C–H functionalization mechanism. Efforts to elucidate the mechanism in collaboration with our group by experimental and computational methods are underway both at Caltech (David Schuman, Wen-Bo Liu (Stoltz group)), as well as at UCLA (Yong Liang, Yun-Fang Yang (Houk group)), Stanford (Monon Banerjee (Zare group)) and Florida Institute of Technology (Prof. Nasri Nesnas). Ongoing collaborative work with these groups is generating a substantial amount of very interesting data, substantially improving our understanding of this KO*t*-Bu–

catalyzed C–H silylation reaction. However, the data produced through these extensive and ongoing studies continue to raise new and interesting questions and cannot at this point conclude whether the reaction proceeds via a polar mechanism or a radical one; testament to the novel and unusual nature of this process.

Conclusion.

An sp^2 and sp^3 cross-dehydrogenative C–H silylation reaction using the inexpensive, commercially available, and bench stable KO*t*-Bu is discovered. The transformation has been applied to an array of privileged heteroaromatic scaffolds and to a number of carbocylic aromatic moieties. Potential for late stage functionalization has been demonstrated by the direct silylation of active pharmaceutical ingredients. The most poorly understood aspect of this chemistry, however, is the mechanism (which appears to be substantially different from all known C−H silylation reactions reported previously). The eventual elucidation of the mechanism of this reaction will indeed be a significant achievement and will provide important new insights into the operative manifolds of this reaction, hopefully enabling a powerful rational effort toward improving this protocol and developing the next generation of C−H bond functionalization methods (as well as other chemistries) using catalysts based on abundant metals.

Experimental and analytics.

General information

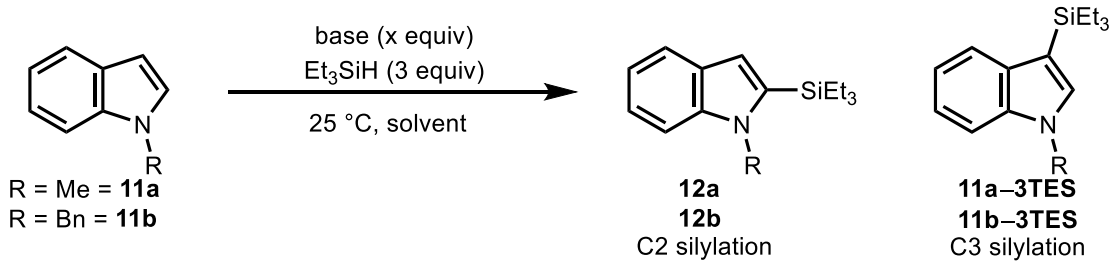
Unless otherwise stated, reactions were performed in oven-dried brand-new Fisherbrand scintillation vials in a nitrogen filled glove box or in flamed-dried Schlenk flasks under argon connected on a Schlenk line using dry, degassed solvents and brand-new stirring bars. Solvents were dried by passage through an activated alumina column under argon.[43] Reaction progress was monitored by thin-layer chromatography (TLC), UHPLC-LCMS or GC-FID analyses. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, phosphomolybdic acid, or $KMnO_4$ staining. Silicycle SiliaFlash P60 Academic Silica gel (particle size 40–63 nm) was used for flash chromatography. ^{1}H NMR spectra were recorded on Varian Inova 500 MHz and 600 MHz spectrometers in $CDCl_3$ or C_6D_6 and are reported relative to residual solvent peak at δ 7.26 ppm or δ 7.16 ppm respectively. ^{13}C NMR spectra were recorded on a Varian Inova 500 MHz spectrometer (125 MHz) in $CDCl_3$ or C_6D_6 and are reported relative to residual solvent peak at δ 77.16 ppm or δ 128.06 ppm respectively. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septet, m = multiplet, br s = broad singlet, br d = broad doublet, app = apparent. Data for ^{13}C NMR are reported in terms of chemical shifts (δ ppm). IR spectra were obtained on a Perkin Elmer Spectrum BXII spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm–1). UHPLC-LCMS analyses were obtained on an Agilent 1290 ultra high performance liquid chromatography/mass spectrometry equipped with an Agilent EclipsePlus C18 RRHD 1.8 µM column. GC-FID analyses were obtained on an Agilent 6890N gas chromatograph equipped with a HP-5 (5%-phenyl)-methylpolysiloxane capillary column (Agilent). GC-MS analyses were obtained

on an Agilent 6850 gas chromatograph equipped with a HP-5 (5%-phenyl)-methylpolysiloxane capillary column (Agilent). High resolution mass spectra (HRMS) were obtained on an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed ionization mode (MM: ESI-APCI+), or were acquired from the California Institute of Technology Mass Spectrometry Facility. ICP-MS analysis was conducted at the California Institute of Technology Mass Spectrometry Facility. Al_2O_3 was purchased from Aldrich and activated by storing in a 200 °C oven for one week and then heating in a round bottom flask at 200 °C under vacuum (60 millitorr). Silanes were purchased from Aldrich and distilled before use. KO*t*-Bu was purchased from Aldrich (sublimed grade, 99.99% trace metals basis) and used directly. Heteroaromatic substrates were purchased from Aldrich, TCI, or Acros, or synthesized according to literature procedures.[97]

Procedure for ICP-MS analysis

500 mg samples each of KO*t*-Bu from four different vendors (Strem, Aldrich, TCI, Alfa- Aesar), 1-benzylindole, Et_3SiH, THF, and a standard reaction mixture (0.5 mmol scale mixture, prepared following the general procedure with 103.5 mg of 1-Bn-indole, 11.2 mg of KO*t*-Bu from Aldrich, 173.5 mg of Et_3SiH in 0.5 mL of THF and stirred in the glovebox for 72 h.) were analyzed. Each sample was added to a 50 mL DigiTUBE digestion tube (SCP Science) followed by addition of 3.0 mL of Plasma Pure nitric acid (SCP Science) and heating to 75 ^{o}C for 36 hours. After digestion, each sample was diluted using Milli Q water to 50 mL and sample analysis was performed on an Agilent 7900 ICP-MS spectrometer.

Procedure for reaction optimization



Procedure for reaction condition optimization: In a nitrogen-filled glovebox, base and indole **11a** or **11b** (0.2 mmol, 1 equiv) were added to a 2 dram scintillation vial equipped with a magnetic stirring bar. Next, Et_3SiH (97 µL, 0.6 mmol, 3 equiv, filtered through a short pad of activated alumina before use) and solvent (0.2 mL, unless the reaction was run neat) were added. The vial was sealed and the mixture was stirred at the indicated temperature for the indicated time. Then the vial was removed from the glovebox, diluted with diethyl ether (1 mL) and concentrated under reduced pressure. The regioselectivity (C2 silylation product to C3 silylation product: C2:C3) and yield were determined by ^1H NMR or GC analysis of the crude mixture using an internal standard. Data were presented in **Table 2.1** and were subsequently discussed.

Procedure for control experiments

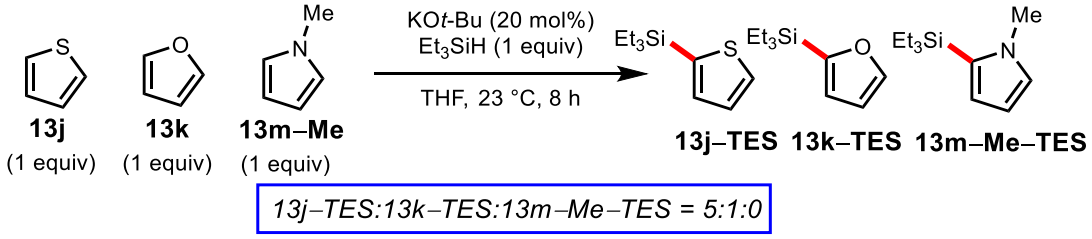
Careful control experiments were conducted to rule out the presence of adventitious impurities that could be influencing the reaction outcome.

Control reactions were performed with commercially available KO*t*-Bu, re-sublimed KO*t*-Bu, and freshly-prepared KO*t*-Bu. The reactions were performed in parallel (THF, 45 °C, 1-methylindole, 20 mol% KO*t*-Bu, 0.2 mmol scale): a) KO*t*-Bu (Aldrich, sublimed grade, 99.99%, trace metal basis) was used as received; b) KO*t*-Bu (Aldrich, sublimed grade, 99.99% trace metal basis) was used after re-sublimation by heating the material under vacuum; and c) KO*t*-Bu, freshly prepared by reaction

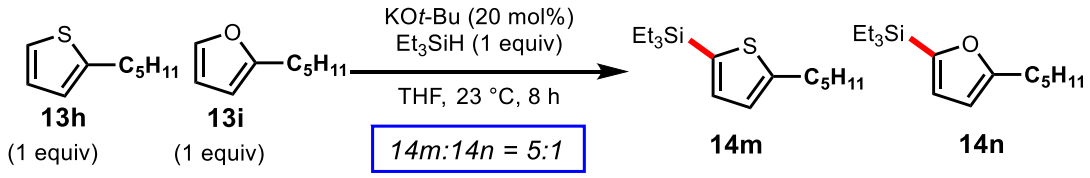
of potassium metal with anhydrous *t*-BuOH followed by evaporation of the *t*-BuOH and sublimation of the solid, was used. No appreciable differences in conversion and selectivity in these reactions were observed.

Control reaction with KOt-Bu of different grade purchased from different vendors were also performed in parallel (THF, 45 °C, 1-benzylindole, 20 mol% KO*t*- Bu, 0.2 mmol scale): a) KO*t*-Bu (Aldrich, sublimed grade, 99.99% trace metal basis), b) KO*t*-Bu (Strem, 98%), c) KO*t*-Bu (TCI, >97%), and d) KO*t*-Bu (Alfa-Aesar, 97%). The reactions were monitored by UHPLC-LCMS and no appreciable differences in conversion and selectivity in these four reactions was observed. Data were presented in Figure 2.10.

Procedure for competition experiments

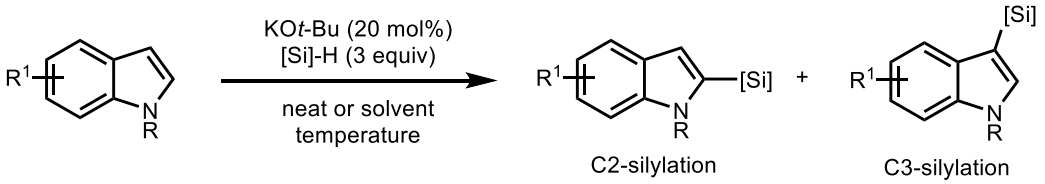


In a nitrogen-filled glove box, KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), thiophene **13j** (42.1 mg, 0.5 mmol, 1 equiv), furan **13k** (34.0 mg, 0.5 mmol, 1 equiv) and 1-methylpyrrole **13m–Me** (40.5 mg, 0.5 mmol, 1 equiv) were added to a 2 dram scintillation vial equipped with a magnetic stirring bar. THF (0.3 mL) and Et_3SiH (81 µL, 0.5 mmol, 1 equiv – *filtered through a short pad of activated alumina before use*) were then added. The vial was sealed and stirred at 23 °C for approximately 8 hours. The vial was removed from the glove box, diluted with diethyl ether (2 mL) and concentrated under reduced pressure. Analysis of the crude reaction mixture by 1H NMR revealed that the ratio of **13j–TES:13k–TES:13m–Me–TES** was 5:1:0.



In a nitrogen-filled glove box, KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2-pentylthiophene **13h** (77.0 mg, 0.5 mmol, 1 equiv), and 2-pentylfuran **13i** (69.1 mg, 0.5 mmol, 1 equiv) were added to a 2 dram scintillation vial equipped with a magnetic stirring bar. THF (0.3 mL) and Et_3SiH (81 µL, 0.5 mmol, 1 equiv – *filtered through a short pad of activated alumina before use*) were then added. The vial was sealed and stirred at 23 °C for approximately 8 hours. The vial was removed from the glove box, diluted with diethyl ether (2 mL), and concentrated under reduced pressure. Analysis of the crude reaction mixture by 1H NMR revealed that the ratio of **14m**:**14n** was 5:1.

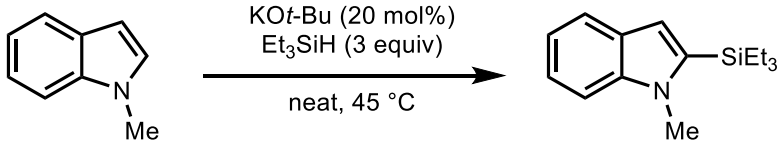
General procedure for KOt-Bu–catalyzed silylation of heteroaromatics



In a nitrogen-filled glove box, KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%) and indole (0.5 mmol, 1 equiv) were added to a 2 dram scintillation vial equipped with a magnetic stirring bar, [*solvent was added if indicated, see individual reaction details*], followed by silane (1.5 mmol, 3 equiv, filtered through a short pad of activated alumina before use). Then the vial was sealed and the mixture was stirred at the indicated temperature for the indicated time. The vial was removed from the glove box, the reaction mixture was diluted with diethyl ether (2 mL) and concentrated under reduced pressure. The regioselectivity (C2 silylation product to C3 silylation product: C2:C3) was determined by ^{1}H NMR or GC analysis of the crude mixture. The residue was purified by silica

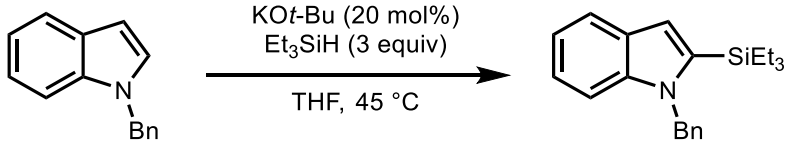
gel flash chromatography to give the desired product.

Characterization



12a

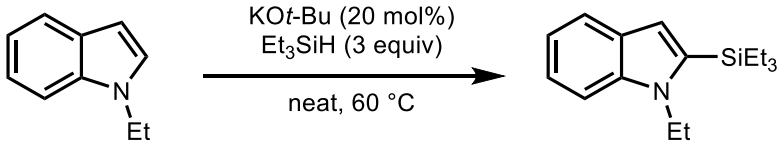
1-Methyl-2-(triethylsilyl)-1H-indole 12a: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-methylindole (65.5 mg, 0.5 mmol, 1 equiv), and Et_3SiH (243 µL, 1.5 mmol, 3 equiv) at 45 °C for 96 h. C2:C3 >20:1. The desired product **12a** (95.6 mg, 78% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (gradient elution, 2→3% CH_2Cl_2 in hexanes). R_f = 0.4 (10% CH_2Cl_2 in hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.70 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.40 (dq, *J* = 8.3, 1.0 Hz, 1H), 7.30 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.16 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 6.81 (d, *J* = 1.1 Hz, 1H), 3.90 (s, 3H), 1.13 – 1.05 (m, 9H), 1.03 – 0.95 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.4, 138.3, 128.7, 122.0, 120.7, 119.1, 113.1, 109.1, 33.1, 7.7, 4.2. IR (Neat Film, NaCl) 2953, 2909, 2874, 1492, 1464, 1415, 1372, 1356, 1299, 1233, 1166, 1101, 1069, 1007, 973, 797 cm^{-1}; HRMS (ESI+) calc'd for $C_{15}H_{24}NSi$ [M+H]+: 246.1673, found 246.1674.



12b

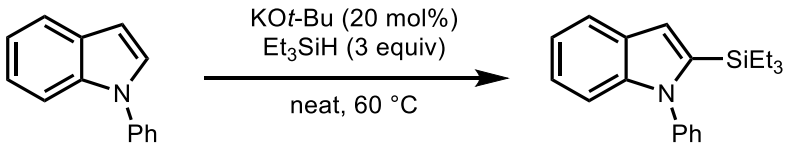
1-Benzyl-2-(triethylsilyl)-1*H*-indole 12b: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-benzylindole (103.5 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 40 h. C2:C3 > 20:1.

The desired product **12b** (132.2 mg, 82% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (10% CH_2Cl_2 in hexanes). R_f = 0.3 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 – 7.77 (m, 1H), 7.38 – 7.29 (m, 3H), 7.26 – 7.19 (m, 3H), 7.02 (ddd, *J* = 6.9, 2.2, 1.0 Hz, 2H), 6.97 (s, 1H), 5.59 (s, 2H), 1.08 – 1.04 (m, 9H), 0.94 – 0.89 (m, 6H); ^{13}C NMR (125 MHz, CDCl3) δ 140.2, 138.5, 138.3, 129.1, 128.7, 127.3, 125.9, 122.3, 120.7, 119.5, 114.1, 110.2, 50.2, 7.5, 4.0. IR (Neat Film, NaCl) 3060, 3029, 2954, 2909, 2875, 1606, 1495, 1466, 1452, 1416, 1377, 1353, 1333, 1300, 1238, 1196, 1164, 1115, 1096, 1014, 798, 734 cm–1; HRMS (ESI+) calc'd for $C_{21}H_{28}NSi$ $[M+H]^+$: 322.1986, found 322.1985.



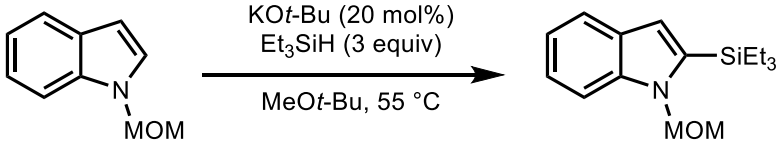
12c

1-Ethyl-2-(triethylsilyl)-1*H*-indole 12c: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-ethylindole (72.5 mg, 0.5 mmol, 1 equiv), and Et_3SiH (243 µL, 1.5 mmol, 3 equiv) at 60 °C for 84 h. C2:C3 > 20:1. The desired product **12c** (92.4 mg, 71% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (5% CH_2Cl_2 in hexanes). R_f = 0.4 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, CDCl3) δ 7.67 (dt, *J* = 7.9, 0.9 Hz, 1H), 7.40 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.25 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.13 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H), 6.75 (d, *J* = 1.0 Hz, 1H), 4.31 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H), 1.08 – 1.04 (m, 9H), 0.99 – 0.92 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0, 137.4, 129.1, 121.7, 120.7, 119.0, 113.0, 109.4, 41.5, 15.5, 7.5, 4.0. IR (Neat Film, NaCl) 2953, 2909, 2874, 1491, 1466, 1416, 1378, 1347, 1335, 1299, 1218, 1165, 1090, 1069, 1012, 956, 900, 820, 787, 773, 750, 733 cm_{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{16}H_{26}NSi$ $[M+H]^+$: 260.1829, found 260.1829.



12d

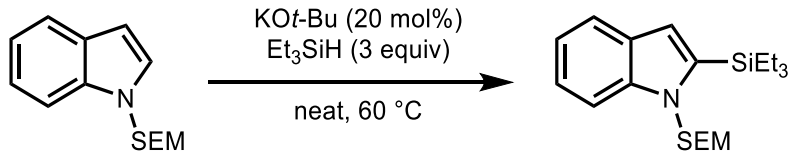
1-Phenyl-2-(triethylsilyl)-1*H*-indole 12d: The general procedure was followed. The reaction was performed with KO*t*-Bu (7.4 mg, 0.07 mmol, 20 mol%), *N*-phenylindole (63.2 mg, 0.33 mmol, 1 equiv), and Et_3SiH (160 µL, 1.0 mmol, 3 equiv) at 60 °C for 84 h. C2:C3 > 20:1. The desired product **12d** (45.6 mg, 45% yield) was obtained as a white solid after purification by silica gel flash chromatography (3% CH_2Cl_2 in hexanes). R*f* = 0.5 (10% CH_2Cl_2 in hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 1H), 7.58 – 7.47 (m, 3H), 7.44 – 7.36 (m, 2H), 7.21 – 7.12 (m, 2H), 7.12 – 7.05 (m, 1H), 6.93 (d, *J* = 0.9 Hz, 1H), 0.92 (t, *J* = 7.9 Hz, 9H), 0.68 – 0.55 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.6, 140.8, 139.1, 129.2, 128.8, 128.7, 128.3, 122.4, 120.5, 119.8, 114.9, 110.5, 7.5, 4.0. IR (Neat Film, NaCl) 3058, 2952, 2909, 2873, 1597, 1498, 1465, 1428, 1362, 1297, 1237, 1214, 1122, 1071, 1012, 976, 922, 820, 793, 736 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{20}H_{26}NSi$ $[M+H]^+$: 308.1829, found 308.1824.



12e

1-(Methoxymethyl)-2-(triethylsilyl)-1*H*-indole 12e: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-methoxymethylindole (80.5 mg, 0.5 mmol, 1 equiv) and Et_3SiH (243 µL, 1.5 mmol, 3 equiv) at 60 °C for 84 h. C2:C3 = 10:1. The desired product **12e** (75.1 mg, 55% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (3% EtOAc in hexanes). R_f

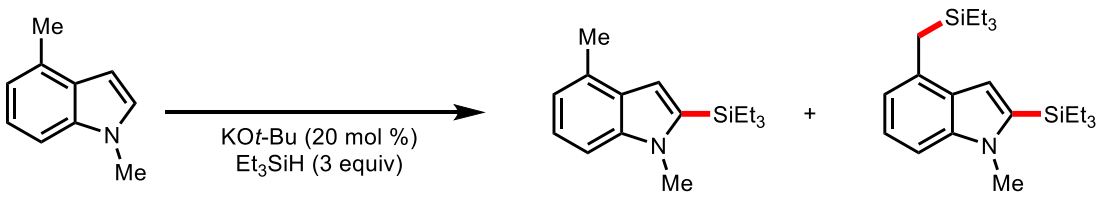
= 0.3 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.53 (dq, *J* = 8.3, 0.9 Hz, 1H), 7.28 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.17 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H), 6.86 (d, *J* = 0.9 Hz, 1H), 5.55 (s, 2H), 3.30 (s, 3H), 1.10 – 1.01 (m, 9H), 1.01 – 0.92 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.7, 138.3, 129.2, 122.6, 120.8, 120.0, 115.6, 109.8, 76.8, 55.6, 7.5, 4.1. IR (Neat Film, NaCl) 2952, 2908, 2874, 1495, 1466, 1416, 1393, 1344, 1311, 1299, 1224, 1166, 1126, 1104, 1091, 1045, 1004, 961, 913, 797, 762, 735 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{16}H_{26}NOSi$ $[M+H]^+$: 276.1778, found 276.1769.



12f

2-(Triethylsilyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-indole 12f: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-(2-trimethylsilyl-ethoxymethyl)-1*H*-indole (123.5 mg, 0.5 mmol, 1 equiv) and Et_3SiH (243 µL, 1.5 mmol, 3 equiv) at 60 °C for 84 h. C2:C3 > 20:1. The desired product **12f** (121.4 mg, 67% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (15% CH_2Cl_2 in hexanes). R*f* = 0.2 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.50 (dq, *J* = 8.3, 0.9 Hz, 1H), 7.24 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.12 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H), 6.80 (d, *J* = 0.9 Hz, 1H), 5.54 (s, 2H), 3.54 – 3.48 (m, 2H), 1.04 – 0.98 (m, 9H), 0.96 – 0.90 (m, 8H), -0.02 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.5, 138.1, 129.1, 122.4, 120.7, 119.9, 115.3, 109.8, 75.2, 65.6, 18.1, 7.6, 4.0, -1.3. IR (Neat Film, NaCl) 2952, 2875, 1495, 1466, 1443, 1417, 1378, 1343, 1312, 1299, 1249, 1167, 1081, 1003, 972, 939, 894, 859, 836, 796, 760, 749, 734 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for

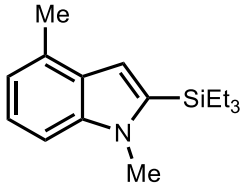
$C_{20}H_{36}NOSi_2$ $[M+H]^+$: 362.2330, found 362.2340.



11g **12g** **12g_*sp*^{3}**

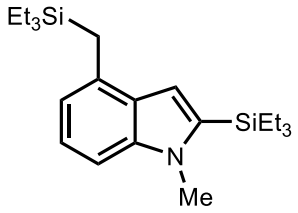
conditions A: THF, 25 °C, 120 h:	48%	5%
conditions B: neat, 45 °C, 84 h:	69%	–

The general procedure was followed. *For condition A*: The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1,4-dimethylindole (72.5 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 120 h. C2:C3 > 20:1. The desired mono-silylation product **12g** (61.8 mg, 48% yield) and bis-silylation **12g_*sp*^{3}** (9.7 mg, 5% yield) were obtained after purification by silica gel flash chromatography (gradient elution, 2→3% CH_2Cl_2 in hexanes). *For condition B*: The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1,4-dimethylindole (72.5 mg, 0.5 mmol, 1 equiv) and Et_3SiH (243 μL, 1.5 mmol, 3 equiv) at 45 °C for 84 h. C2:C3 > 20:1. Only mono silylation product **12g** (89.7 mg, 69% yield) was formed and obtained after purification by silica gel flash chromatography (3% CH_2Cl_2 in hexanes).

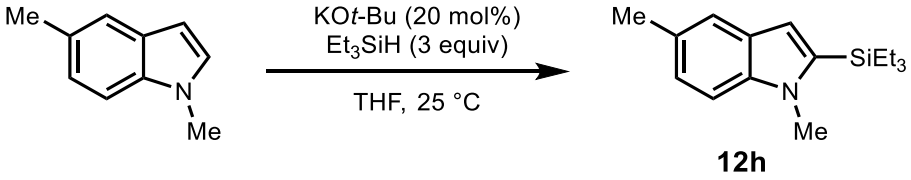


1,4-Dimethyl-2-(triethylsilyl)-1*H*-indole 12g: Colorless oil; R_f = 0.4 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 – 7.14 (m, 2H), 6.91 (dt, *J* = 6.7, 1.0 Hz, 1H), 6.75 (d, *J* = 0.9 Hz, 1H), 3.85 (s, 3H), 2.60 (s, 3H), 1.07 – 1.00 (m, 9H), 0.98 – 0.92 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 137.6, 130.2, 128.6, 122.2, 119.4, 111.5, 106.8, 33.2, 18.8, 7.7, 4.3. IR (Neat Film, NaCl) 2953, 2910, 2874, 1586, 1502, 1454, 1415, 1366, 1323, 1280, 1238, 1160, 1140, 1077, 1004,

953, 765, 752, 735 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{16}H_{26}NSi$ $[M+H]^+$: 260.1829, found 260.1823.



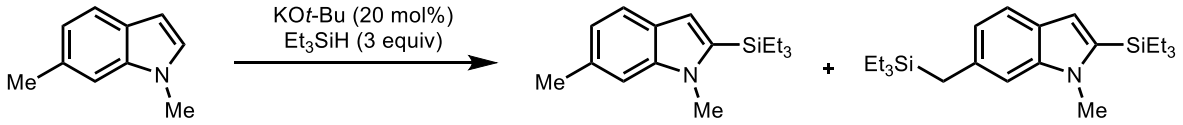
1-Methyl-2-(triethylsilyl)-4-((triethylsilyl)methyl)-1*H*-indole 12g_*sp*^{3}: Colorless oil; R*f* = 0.4 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, C_6D_6) δ 7.28 (dd, *J* = 8.2, 7.1 Hz, 1H), 6.98 (d, *J* = 8.3 Hz, 1H), 6.97 – 6.94 (m, 2H), 3.31 (s, 3H), 2.50 (s, 2H), 1.01 (t, *J* = 7.8 Hz, 9H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.83 (q, *J* = 7.8 Hz, 6H), 0.58 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 141.1, 136.0, 133.3, 122.8, 118.9, 113.0, 105.8, 32.9, 19.2, 7.7, 4.5, 4.1. IR (Neat Film, NaCl) 2952, 2909, 2874, 1579, 1498, 1454, 1443, 1414, 1359, 1322, 1285, 1237, 1151, 1070, 1008, 980, 774, 734 cm^1; HRMS (EI+) calc'd for $C_{22}H_{39}NSi_2$ $[M•]^+$: 373.2621, found 373.2624.



12h

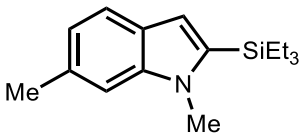
1,5-Dimethyl-2-(triethylsilyl)-1*H*-indole 12h: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 5-methyl-1-methylindole (72.5 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 96 h. C2:C3 > 20:1. The desired product **12h** (88.7 mg, 68% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (10% CH_2Cl_2 in hexanes). R_f = 0.3 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (s, 1H), 7.25 – 7.19 (m, 1H), 7.05 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.63 (d, *J* = 0.8 Hz, 1H), 3.81 (s, 3H), 2.45 (s, 3H), 1.03 – 0.97 (m, 9H), 0.93 – 0.86 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.8, 138.3, 128.9, 128.3, 123.6, 120.2, 112.4, 108.8, 33.1, 21.5,

7.7, 4.1. IR (Neat Film, NaCl) 2952, 2909, 2873, 1505, 1456, 1358, 1321, 1236, 1181, 1104, 1069, 1003, 833, 788, 736 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{26}NSi$ $[M+H]^+$: 260.1826, found 260.1827.



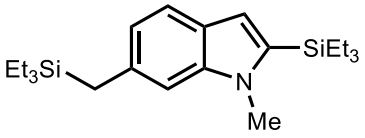
	12i	12i_sp^3
conditions A: THF, 25 °C, 120 h:	54%	3%
conditions B: neat, 45 °C, 84 h:	83%	–

The general procedure was followed. *For condition A*: The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 6-methyl-1-methylindole (72.5 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 120 h. C2:C3 > 20:1. The desired mono silylation product **12i** (69.5 mg, 54% yield) and bis-silylation **12i_*sp*^{3}** (5.2 mg, 3% yield) were obtained after purification by silica gel flash chromatography (gradient elution, 2→3% CH_2Cl_2 in hexanes). *For condition B*: The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 6-methyl-1-methylindole (72.5 mg, 0.5 mmol, 1 equiv) and Et_3SiH (243 μL, 1.5 mmol, 3 equiv) at 45 °C for 84 h. C2:C3 > 20:1. Only mono silylation product **12i** (108.1 mg, 83% yield) was formed and obtained after purification by silica gel flash chromatography (3% CH_2Cl_2 in hexanes).

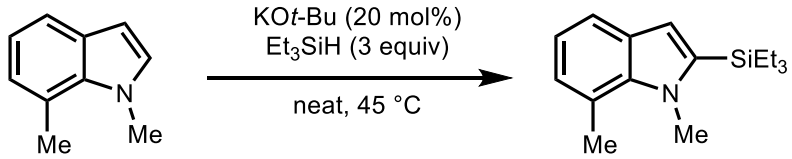


1,6-Dimethyl-2-(triethylsilyl)-1*H*-indole 12i: Colorless oil; R*f* = 0.4 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.0 Hz, 1H), 7.18 (s, 1H), 6.98 (ddd, *J* = 8.0, 1.4, 0.7 Hz, 1H), 6.73 (d, *J* = 0.9 Hz, 1H), 3.85 (s, 3H), 2.57 (s, 3H), 1.08 – 1.03 (m, 9H), 0.98 – 0.92 (m, 6H); ^{13}C NMR (125 MHz, CDCl3) δ 140.9, 137.6, 131.8, 126.7, 121.0, 120.3, 113.0, 109.1, 33.0, 22.0, 7.6, 4.2. IR (Neat Film, NaCl) 2953, 2910, 2874, 1617, 1480, 1451, 1413, 1376, 1360, 1333, 1296, 1233, 1065, 1003, 941, 808, 781, 736 cm^{-1}; HRMS (ESI+) calc'd for

$C_{16}H_{26}NSi$ $[M+H]^+$: 260.1826, found 260.1823.



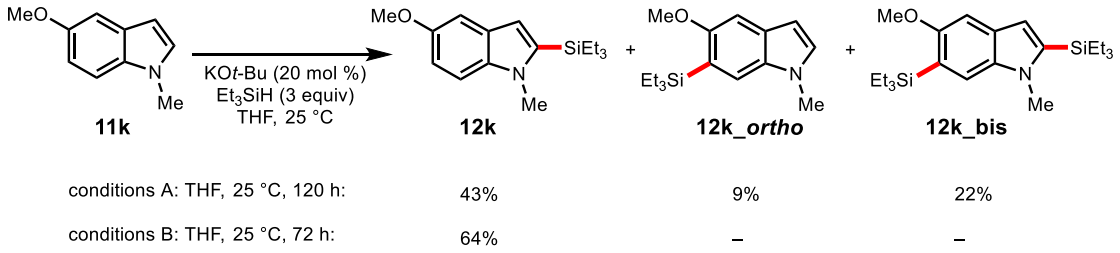
1-Methyl-2-(triethylsilyl)-6-((triethylsilyl)methyl)-1*H*-indole 12i_*sp*^{3}: Colorless oil; R*f* = 0.4 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, C_6D_6) δ 7.64 (dd, *J* = 7.9, 0.8 Hz, 1H), 6.99 – 6.93 (m, 2H), 6.81 (d, *J* = 0.9 Hz, 1H), 3.41 (s, 3H), 2.31 (s, 2H), 1.02 – 0.93 (m, 18H), 0.79 (q, *J* = 7.7 Hz, 6H), 0.58 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ141.9, 136.3, 134.6, 126.7, 121.2, 120.9, 114.0, 108.3, 32.7, 22.4, 7.8, 7.7, 4.5, 3.7. IR (Neat Film, NaCl) 2952, 2909, 2874, 1615, 1568, 1479, 1463, 1414, 1361, 1336, 1319, 1299, 1234, 1195, 1157, 1090, 1065, 1009, 948, 842, 817, 787, 771, 736 cm^{-1}; HRMS (EI+) calc'd for $C_{22}H_{39}NSi_2$ $[M^{\bullet}]^+$: 373.2621, found 373.2609.



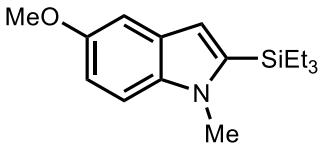
12j

1,7-Dimethyl-2-(triethylsilyl)-1*H*-indole 12j: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 7-methyl-1-methylindole (72.5 mg, 0.5 mmol, 1 equiv) and Et_3SiH (243 μL, 1.5 mmol, 3 equiv) at 45 °C for 84 h. C2:C3 > 20:1. The desired product **12j** (78.9 mg, 61% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (3% CH_2Cl_2 in hexanes). R_f = 0.4 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.7 Hz, 1H), 6.94 – 6.87 (m, 2H), 6.66 (s, 1H), 4.11 (s, 3H), 2.80 (s, 3H), 1.03 – 0.97 (m, 9H), 0.92 – 0.85 (m, 6H); 13C NMR (125 MHz, $CDCl_3$) δ 139.2, 139.1, 129.7, 125.0, 121.0, 119.4, 119.0, 113.6, 36.8, 20.6, 7.7, 4.2. IR (Neat Film, NaCl) 2953, 2909, 2873, 1503, 1459, 1415, 1396, 1377, 1358, 1340, 1315, 1304, 1238, 1156, 1113, 1086, 1063, 1004,

861, 798, 742 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{26}NSi$ $[M+H]^+$: 260.1826, found 260.1828.

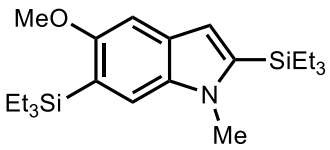


The general procedure was followed. *For condition A*: The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-methyl-5-methoxyindole (80.7 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 120 h. C2:C3 > 20:1. The C2-silylation product **12k** (58.7 mg, 43% yield), C6-silylation product **12k_*ortho*** (12.5 mg, 9% yield), and bis-silylation product **12k_bis** (42.9 mg, 22% yield), were obtained after purification by silica gel flash chromatography (gradient elution, 5→10→25% CH_2Cl_2 in hexanes). *For condition B*: The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-methyl-5-methoxyindole (80.5 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 72 h. C2:C3 > 20:1. The desired product **12k** (87.6 mg, 64% yield) was obtained after purification by silica gel flash chromatography (gradient elution, 5→10→25% CH_2Cl_2 in hexanes) and a minor amount (<5%) of byproducts were observed.

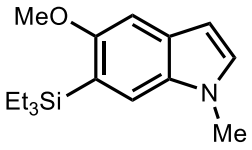


5-Methoxy-1-methyl-2-(triethylsilyl)-1*H*-indole 12k: White solid; R_f = 0.2 (33% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (s, 1H), 7.07 (d, *J* = 2.4 Hz, 1H), 6.89 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.63 (d, *J* = 0.8 Hz, 1H), 3.85 (s, 3H), 3.81 (s, 3H), 1.03 – 0.96 (m, 9H), 0.93 – 0.86 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.0, 139.0, 135.9, 128.8, 112.6, 112.3, 109.8,

102.0, 56.1, 33.2, 7.7, 4.1. IR (Neat Film, NaCl) 2950, 2909, 2872, 1503, 1450, 1413, 1334, 1237, 1208, 1173, 1147, 1102, 1072, 1027, 997, 843, 801, 735, 716 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{26}NOSi$ $[M+H]^+$: 276.1778, found 276.1776.

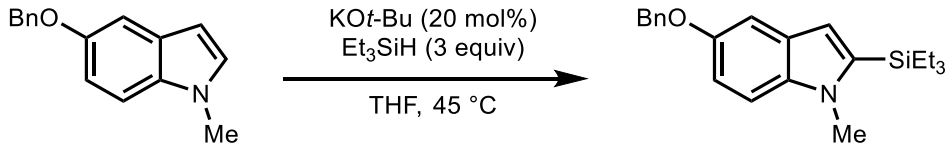


5-Methoxy-1-methyl-2,6-bis(triethylsilyl)-1*H*-indole 12k_bis: White solid, R_f = 0.6 (33% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (s, 1H), 7.01 (s, 1H), 6.64 (d, *J*= 0.8 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 1.06 – 0.97 (m, 18H), 0.95 – 0.86 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 138.9, 136.1, 130.1, 120.8, 116.3, 112.2, 99.7, 55.5, 33.2, 7.9, 7.7, 4.3, 4.1. IR (Neat Film, NaCl) 2952, 2874, 2908, 1608, 1556, 1475, 1454, 1407, 1363, 1337, 1236, 1205, 1172, 1144, 1123, 1072, 1004, 971, 837 cm^{-1}; HRMS (ESI+) calc'd for $C_{22}H_{40}NOSi_2$ $[M+H]^+$: 390.2643, found 390.2632.



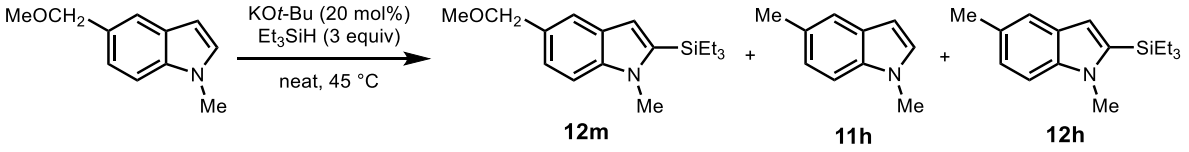
5-Methoxy-1-methyl-6-(triethylsilyl)-1*H*-indole 12k_*ortho*: Colorless oil; R_f = 0.4 (33% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (s, 1H), 7.01 (s, 1H), 7.00 (d, *J* = 3.0 Hz, 1H), 6.38 (dd, *J* = 3.0, 0.8 Hz, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 1.00 – 0.94 (m, 9H), 0.91 – 0.83 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 132.5, 130.1, 129.3, 120.2, 116.5, 100.4, 100.3, 55.5, 33.0, 7.9, 4.1. IR (Neat Film, NaCl) 2950, 2908, 2873, 1612, 1554, 1505, 1471,

1414, 1310, 1268, 1231, 1190, 1148, 1123, 1059, 1017, 984, 831 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{26}NOSi$ $[M+H]^+$: 276.1778, found 276.1765.



12l

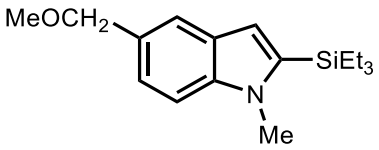
5-(Benzyloxy)-1-methyl-2-(triethylsilyl)-1*H*-indole 12l: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*- methyl-5-benzyloxyindole (118.5 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 64 h. C2:C3 > 20:1. The desired product **12l** (119.4 mg, 68% yield) was obtained as a yellow solid after purification by silica gel flash chromatography (25% CH_2Cl_2 in hexanes). R_f = 0.4 (5% EtOAc in hexanes). ^1H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.0 Hz, 2H), 7.41 – 7.36 (m, 2H), 7.35 – 7.29 (m, 1H), 7.22 (d, *J* = 8.9 Hz, 1H), 7.14 (d, *J* = 2.4 Hz, 1H), 6.97 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.62 (d, *J* = 0.8 Hz, 1H), 5.11 (s, 2H), 3.81 (s, 3H), 1.04 – 0.96 (m, 9H), 0.96 – 0.84 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.3, 139.1, 138.1, 136.2, 129.0, 128.6, 127.8, 127.6, 113.4, 112.5, 109.8, 104.0, 71.3, 33.2, 7.6, 4.2. IR (Neat Film, NaCl) 2951, 2908, 2872, 1492, 1452, 1422, 1336, 1288, 1237, 1192, 1150, 1102, 1075, 1018, 840, 812, 751, 735 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{22}H_{30}NOSi$ $[M+H]^+$: 352.2091, found 352.2093.



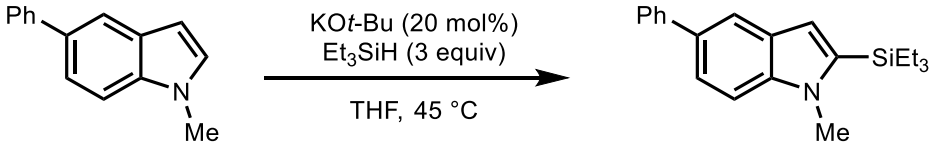
12m **11h** **12h**

The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 5-(methoxymethyl)-*N*-methylindole (87.5 mg, 0.5 mmol, 1 equiv) and Et_3SiH (243 µL, 1.5 mmol, 3 equiv) at 45 °C for 84 h. C2:C3 > 20:1. The desired product **12m** (69.3

mg, 48% yield), byproducts **11h** (2.5 mg, 2% yield) and **12h** (11.3 mg, 9% yield) were obtained after purification by silica gel flash chromatography (gradient elution, 25→50% CH_2Cl_2 in hexanes).



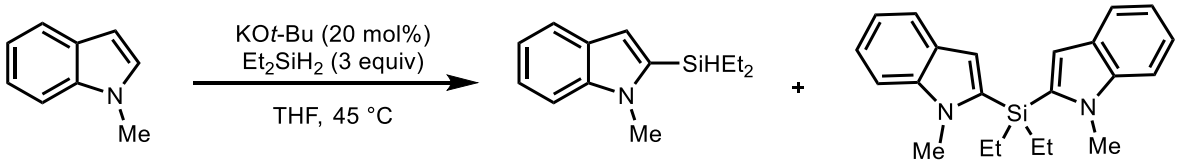
5-(Methoxymethyl)-1-methyl-2-(triethylsilyl)-1*H*-indole12m: Colorless oil, R_f = 0.4 (50% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 0.8 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 6.73 (d, *J* = 0.8 Hz, 1H), 4.59 (s, 2H), 3.85 (s, 3H), 3.38 (s, 3H), 1.06 – 0.99 (m, 9H), 0.96 – 0.90 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.0, 138.9, 128.8, 128.5, 122.6, 120.5, 113.0, 109.1, 75.6, 57.6, 33.2, 7.6, 4.1. IR (Neat Film, NaCl) 2952, 2873, 2817, 1504, 1455, 1415, 1357, 1324, 1297, 1236, 1188, 1153, 1137, 1094, 1069, 1004, 971, 878, 840, 798, 783, 726 cm^{-1}; HRMS (ESI+) calc'd for $C_{17}H_{28}NOSi$ $[M+H]^+$: 290.1935, found 290.1948.



12n

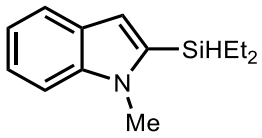
1-Methyl-5-phenyl-2-(triethylsilyl)-1*H*-indole 12n: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 5-phenyl-*N*- methylindole (103.5 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 108 h. C2:C3 > 20:1. The desired product **12n** (77.8 mg, 48% yield) was obtained as a white solid after purification by silica gel flash chromatography (gradient elution, 5→10% CH_2Cl_2 in hexanes). R_f = 0.3 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (s,

1H), 7.72 (d, *J* = 7.6 Hz, 2H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.44 (d, *J* = 8.5 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 1H), 6.85 (s, 1H), 3.91 (s, 3H), 1.09 (t, *J* = 7.8 Hz, 9H), 1.03 – 0.95 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.9, 140.0, 139.3, 132.8, 129.2, 128.7, 127.5, 126.3, 122.0, 119.2, 113.5, 109.4, 33.2, 7.6, 4.2. IR (Neat Film, NaCl) 2950, 2908, 2873, 1600, 1485, 1455, 1361, 1325, 1301, 1214, 1162, 1074, 1004, 1086, 887, 820, 807, 787, 759, 733 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{21}H_{28}NSi$ $[M+H]^+$: 322.1986, found 322.1984.



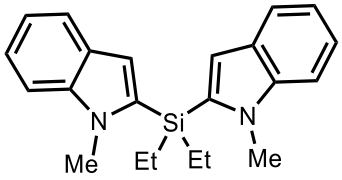
12o **12o_dim**

The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-methylindole **1a** (65.5 mg, 0.5 mmol, 1 equiv), Et_2SiH_2 (194 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 72 h. C2:C3 > 20:1. The silylation product **12o** (73.4 mg, 68% yield) and a minor bisindolyl silane byproduct **12o_dim** were obtained after purification by silica gel flash chromatography (gradient elution, 1→2→5% CH_2Cl_2 in hexanes).

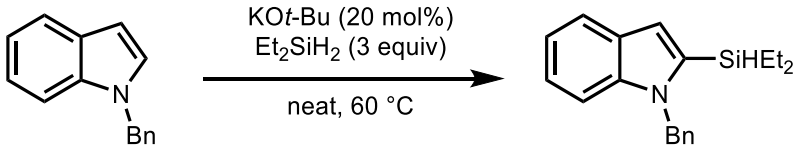


2-(Diethylsilyl)-1-methyl-1*H*-indole 12o: Colorless oil; R_f = 0.4 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.37 (dt, *J* = 8.3, 1.1 Hz, 1H), 7.28 – 7.25 (m, 1H), 7.16 – 7.09 (m, 1H), 6.79 (d, *J* = 0.9 Hz, 1H), 4.50 – 4.43 (m, 1H), 3.88 (s, 3H), 1.14 – 1.06 (m, 6H), 1.00 – 0.93 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 136.6, 128.6, 122.2, 120.8, 119.3, 112.8, 109.3, 32.8, 8.4, 3.7. IR (Neat Film, NaCl) 2954, 2908, 2872, 2110, 1492, 1464, 1412, 1371, 1357, 1327, 1301, 1233, 1166, 1101, 1071, 1009, 974,

987, 815, 785 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{13}H_{20}NSi$ $[M+H]^+$: 218.1360, found 218.1354.



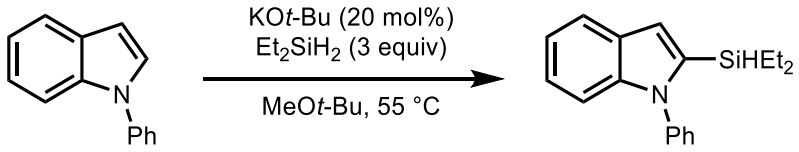
Diethylbis(1-methyl-1*H*-indol-2-yl)silane 12o_dim: Colorless oil; R_f = 0.2 (10% CH_2Cl_2 in hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.68 (dt, *J* = 7.9, 1.0 Hz, 2H), 7.31 (dt, *J* = 8.3, 1.0 Hz, 2H), 7.25 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 2H), 7.13 (ddd, *J* = 7.9, 6.9, 1.1 Hz, 2H), 6.92 (d, *J* = 0.9 Hz, 2H), 3.57 (s, 6H), 1.31 (q, *J* = 8.4 Hz, 4H), 1.07 (t, *J* = 7.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.7, 136.5, 128.7, 122.5, 120.9, 119.4, 113.8, 109.4, 32.7, 7.5, 4.5. IR (Neat Film, NaCl) 2955, 2874, 1492, 1463, 1414, 1355, 1327, 1299, 1233, 1166, 1101, 1072, 1008, 799, 751 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{22}H_{27}N_2Si$ $[M+H]^+$: 347.1938, found 347.1934.



12p

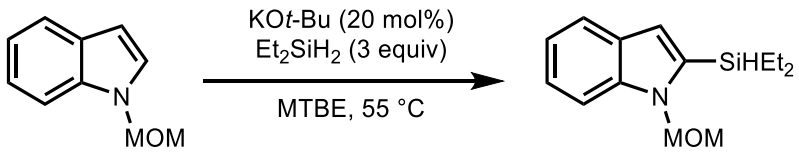
1-Benzyl-2-(diethylsilyl)-1*H*-indole 12p: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-benzyl indole (103.5 mg, 0.5 mmol, 1 equiv) and Et_2SiH_2 (194 µL, 1.5 mmol, 3 equiv) at 60 °C for 72 h. C2:C3 > 20:1. The desired product **12p** (114.1 mg, 78% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (5% CH_2Cl_2 in hexanes). R_f = 0.5 (25% CH_2Cl_2 in hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.75 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.36 – 7.26 (m, 4H), 7.26 – 7.15 (m, 2H), 7.07 – 7.01 (m, 2H), 6.94 (d, *J* = 0.9 Hz, 1H), 5.56 (s, 2H), 4.44 (p, *J* = 3.3 Hz, 1H), 1.12 – 1.03 (m, 6H), 0.94 – 0.79 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.1, 138.5, 136.7, 129.0, 128.7,

127.4, 126.1, 122.5, 120.8, 119.6, 113.7, 110.1, 49.8, 8.3, 3.6. IR (Neat Film, NaCl) 2954, 2873, 2114, 1605, 1494, 1466, 1450, 1413, 1353, 1334, 1301, 1233, 1198, 1164, 1116, 1095, 972, 815 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{19}H_{24}NSi$ $[M+H]^+$: 294.1673, found 294.1668.



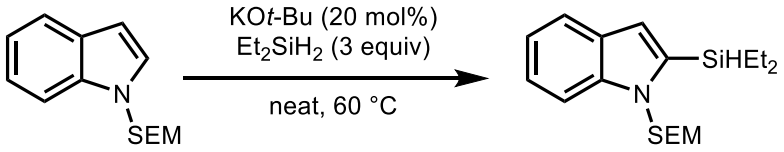
12q

2-(Diethylsilyl)-1-phenyl-1*H*-indole 12q: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-phenyl indole (96.5 mg, 0.5 mmol, 1 equiv), Et_2SiH_2 (194 µL, 1.5 mmol, 3 equiv), and 0.5 mL of MeO*t*-Bu at 55 °C for 96 h. C2:C3 > 20:1 The desired product **12q** (76.9 mg, 55% yield) was obtained as a yellow oil after purification by silica gel flash chromatography (10% CH_2Cl_2 in hexanes). R_f = 0.6 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 – 7.74 (m, 1H), 7.60 – 7.55 (m, 2H), 7.53 – 7.47 (m, 3H), 7.30 – 7.17 (m, 3H), 7.03 (d, *J* = 0.9 Hz, 1H), 4.30 (p, *J* = 3.3 Hz, 1H), 1.02 – 0.98 (m, 6H), 0.79 – 0.63 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.1, 140.3, 137.1, 129.4, 128.8, 128.1, 128.0, 122.8, 120.7, 120.1, 115.1, 110.5, 8.2, 3.4. IR (Neat Film, NaCl) 3058, 2953, 2872, 2117, 1597, 1498, 1466, 1433, 1415, 1363, 1300, 1215, 1202, 1146, 1121, 1072, 1013, 978, 921, 902, 823, 759, 748, 737 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{18}H_{22}NSi$ $[M+H]^+$: 280.1516, found 280.1515.



12r

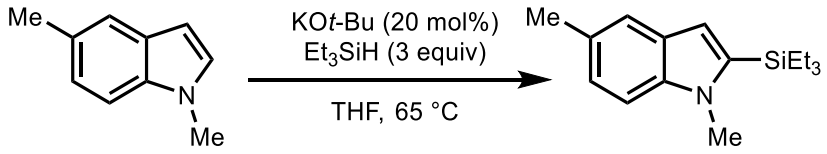
2-(Diethylsilyl)-1-(methoxymethyl)-1*H*-indole 12r: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1- methoxymethylindole (80.5 mg, 0.5 mmol, 1 equiv) and Et_2SiH_2 (193 µL, 1.5 mmol, 3 equiv) at 60 °C for 96 h. C2:C3 > 20:1. The desired product **12r** (81.0 mg, 66% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (3% EtOAc in hexanes). R_f = 0.3 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.54 (ddd, *J* = 8.3, 2.0, 0.9 Hz, 1H), 7.29 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.18 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H), 6.88 (d, *J* = 0.9 Hz, 1H), 5.60 (s, 2H), 4.49 (p, *J* = 3.3 Hz, 1H), 3.29 (s, 3H), 1.14 – 1.08 (m, 6H), 1.03 – 0.94 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.4, 136.6, 129.2, 122.8, 120.9, 120.2, 115.1, 109.9, 76.6, 55.6, 8.3, 3.8. IR (Neat Film, NaCl) 2954, 2874, 2819, 2115, 1496, 1467, 1443, 1413, 1393, 1360, 1344, 1314, 1300, 1282, 1226, 1190, 1166, 1127, 1102, 1091, 1047, 1009, 974, 914, 896, 818, 749, 736 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{14}H_{22}NOSi$ $[M+H]^+$: 248.1465, found 248.1459.



12s

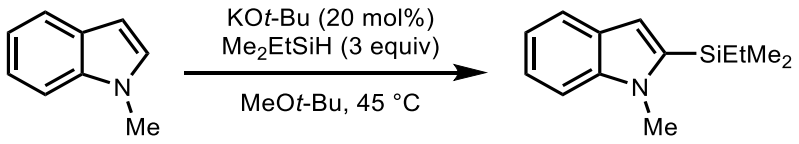
2-(Diethylsilyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-indole 12s: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-(2-trimethylsilyl-ethoxymethyl)-1*H*-indole (123.5 mg, 0.5 mmol, 1 equiv) and Et_2SiH_2 (194 µL, 1.5 mmol, 3 equiv) at 60 °C for 84 h. C2:C3 > 20:1. The desired product **2s** (106.7 mg, 64% yield) was obtained after purification by silica gel flash chromatography (14% CH_2Cl_2 in hexanes) as a colorless oil. R_f = 0.2 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (dt, *J* =

7.9, 1.0 Hz, 1H), 7.53 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.27 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.15 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H), 6.84 (d, *J* = 0.8 Hz, 1H), 5.61 (s, 2H), 4.48 (p, *J* = 3.3 Hz, 1H), 3.55 – 3.48 (m, 2H), 1.14 – 1.04 (m, 6H), 1.03 – 0.88 (m, 6H), -0.02 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 136.5, 129.1, 122.7, 120.8, 120.1, 114.7, 110.1, 75.0, 65.6, 18.0, 8.4, 3.7, -1.3. IR (Neat Film, NaCl) 2953, 2874, 2116, 1496, 1466, 1443, 1413, 1379, 1343, 1318, 1300, 1249, 1219, 1165, 1081, 1010, 974, 922, 895, 859, 835, 748, 735 cm^{-1}; HRMS (MM: ESI- APCI+) calc'd for $C_{18}H_{32}NOSi_2$ $[M+H]^+$: 334.2017, found 334.2028.



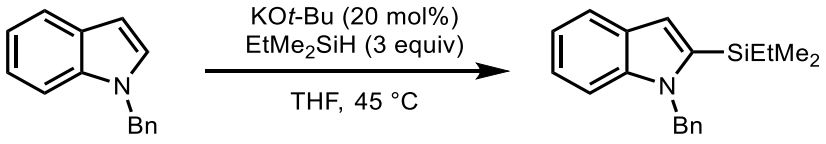
12t

2-(Diethylsilyl)-1,3-dimethyl-1*H*-indole 12t: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1,3-dimethyl-1*H*- indole (72.6 mg, 0.5 mmol, 1 equiv), Et_2SiH_2 (193 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 65 °C for 120 h. The desired product **12t** (84.2 mg, 65% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). R_f = 0.6 (100% hexanes); ^{1}H NMR (500 MHz, C_6D_6) δ 7.67 (d, *J* = 7.9 Hz, 1H), 7.30 (dd, *J* = 8.3, 6.9 Hz, 1H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.10 (d, *J* = 8.2 Hz, 1H), 4.59 (p, *J* = 3.7 Hz, 1H), 3.31 (s, 3H), 2.46 (s, 3H), 0.98 (t, *J* = 7.8 Hz, 6H), 0.77 (qd, *J* = 7.9, 3.9 Hz, 4H); ^{13}C NMR (125 MHz, C_6D_6) δ 140.6, 131.5, 129.8, 122.7, 122.3, 119.4, 119.0, 109.4, 32.4, 10.9, 8.8, 4.7. IR (Neat Film, NaCl) 2952, 2871, 2125, 1509, 1460, 1351, 1317, 1237, 1167, 1138, 1011, 975, 839, 803, 737 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{21}NSi$ $[M^{\bullet+}]$: 231.1443, found 231.1446.



12u

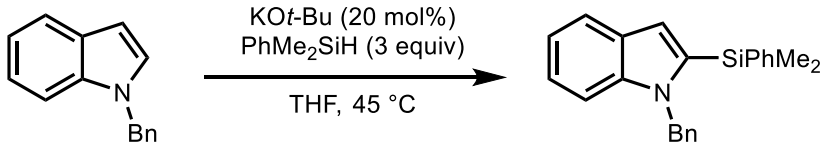
2-(Ethyldimethylsilyl)-1-methyl-1*H*-indole 12u: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-methylindole (66.8 mg, 0.5 mmol, 1 equiv), $EtMe_2SiH$ (197 µL, 1.5 mmol, 3 equiv) and 0.5 mL of MeO*t*-Bu at 45 °C for 120 h. C2:C3 > 20:1. The desired product **12u** (58.5 mg, 54% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (3% CH_2Cl_2 in hexanes). R_f = 0.4 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.37 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.28 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 7.14 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 6.77 (d, *J* = 0.9 Hz, 1H), 3.89 (s, 3H), 1.11 – 1.02 (m, 3H), 0.95 – 0.90 (m, 2H), 0.43 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.3, 140.2, 128.5, 122.1, 120.7, 119.2, 112.0, 109.1, 33.1, 7.8, 7.6, - 2.6. IR (Neat Film, NaCl) 2954, 2908, 2873, 1492, 1464, 1418, 1356, 1326, 1300, 1249, 1233, 1166, 1131, 1101, 1071, 1007, 958, 897, 821 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{13}H_{20}NSi$ $[M+H]^+$: 218.1360, found 218.1353.



12v

1-Benzyl-2-(ethyldimethylsilyl)-1*H*-indole 12v: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-benzylindole (102.5 mg, 0.5 mmol, 1 equiv), $EtMe_2SiH$ (197 µL, 1.5 mmol, 3 equiv) and 0.5 mL of THF at 45 °C for 96 h. C2:C3 > 20:1. The desired product **12v** (87.9 mg, 60% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (10% CH_2Cl_2 in hexanes). R_f = 0.3 (10%

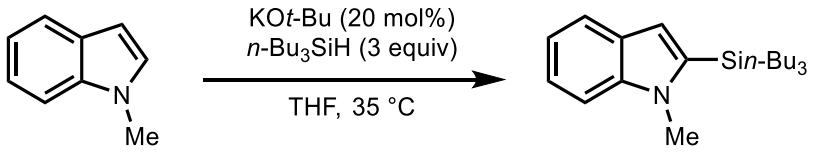
CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.69 (m, 1H), 7.34 – 7.23 (m, 3H), 7.23 – 7.11 (m, 3H), 6.96 (ddd, *J* = 6.8, 2.2, 1.2 Hz, 2H), 6.88 (s, 1H), 5.54 (s, 2H), 1.00 (t, *J* = 7.9 Hz, 3H), 0.79 (q, *J* = 7.8 Hz, 2H), 0.32 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.5, 140.1, 138.4, 128.9, 128.7, 127.3, 125.9, 122.4, 120.8, 119.6, 112.9, 110.1, 50.1, 7.8, 7.5, -2.6. IR (Neat Film, NaCl) 3060, 3028, 2954, 2910, 2873, 1605, 1495, 1466, 1450, 1377, 1353, 1334, 1300, 1249, 1196, 1164, 1115, 1096, 1014, 958, 823, 780, 725 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{19}H_{24}NSi$ $[M+H]^+$: 294.1673, found 294.1669.



12w

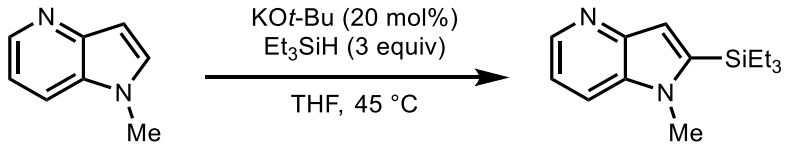
1-Benzyl-2-(dimethyl(phenyl)silyl)-1*H*-indole 12w: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1- benzylindole **1b** (103.5 mg, 0.5 mmol, 1 equiv), $PhMe_2SiH$ (230 µL, 1.5 mmol, 3 equiv) and 0.5 mL of THF at 45 °C for 96 h. C2:C3 > 20:1. A mixture of starting material and product **12w** (*174.5 mg of mixture, contains 133.9 mg of **12w**, 78% yield, calculated based on ^{1}H NMR*) was obtained after purification by silica gel flash chromatography (2% EtOAc in hexanes). *Analytically pure compound **12w** was obtained as a white solid after subsequent purification by Preparative HPLC (3% EtOAc in hexanes).* R_f = 0.4 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 1H), 7.51 – 7.48 (m, 2H), 7.40 – 7.35 (m, 1H), 7.34 – 7.29 (m, 2H), 7.21 – 7.16 (m, 3H), 7.14 – 7.08 (m, 3H), 6.90 (d, *J* = 0.7 Hz, 1H), 6.78 – 6.75 (m, 2H), 5.25 (s, 2H), 0.50 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.4, 139.4, 138.3, 137.5, 134.2, 129.6, 128.9, 128.6, 128.1, 127.2, 125.9, 122.6, 121.0, 119.6, 114.1, 110.2, 50.0, -1.7. IR (Neat Film, NaCl) 3064, 3027,

2956, 1605, 1587, 1494, 1466, 1450, 1427, 1353, 1335, 1301, 1250, 1197, 1164, 1116, 1106, 1096, 1014, 905, 822 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{23}H_{24}NSi$ $[M+H]^+$: 342.1673, found 342.1676.



12x

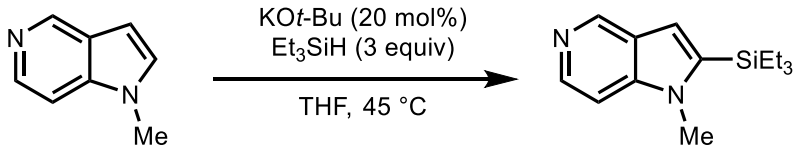
1-Methyl-2-(tributylsilyl)-1*H*-indole 12x: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-methylindole (65.6 mg, 0.5 mmol, 1 equiv), *n*-Bu_3SiH (385 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 35 °C for 65 h. C2:C3 > 20:1. The desired product **12x** (123.5 mg, 75% yield) was obtained as a white solid after purification by silica gel flash chromatography (100% hexanes). R_f = 0.5 (100% hexanes). ^1H NMR (500 MHz, $CDCl_3$) δ 7.61 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.37 – 7.30 (m, 1H), 7.22 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 7.08 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 6.69 (d, *J* = 0.9 Hz, 1H), 3.84 (s, 3H), 1.38 – 1.27 (m, 12H), 0.94 – 0.86 (m, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 139.0, 128.6, 121.7, 120.5, 118.9, 112.7, 108.9, 32.9, 26.6, 26.1, 13.6, 12.7; IR (Neat Film, NaCl) 2955, 2922, 2871, 2855, 1492, 1464, 1411, 1375, 1356, 1325, 1298, 1232, 1196, 1166, 1102, 1070, 897, 885, 799, 788, 749, 732 cm^{-1}; HRMS (EI+) calc'd for $C_{21}H_{35}NSi$ $[M^{\bullet+}]$: 329.2539, found 329.2523



14a

1-Methyl-2-(triethylsilyl)-1*H*-pyrrolo[3,2-*b*]pyridine 14a: The general procedure was followed. The reaction was performed with KO*t*-Bu (4.5 mg, 0.04 mmol, 20 mol%), 1- methyl-4-azaindole (26.4 mg, 0.2 mmol, 1 equiv), Et_3SiH (98 µL, 0.6 mmol, 3 equiv) and 0.2 mL of THF

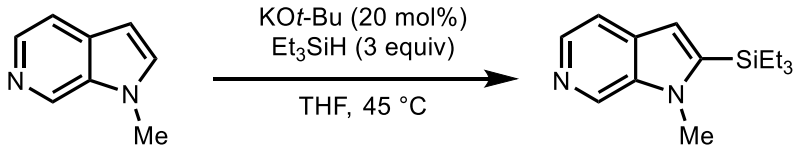
at 45 °C for 96 h. C2:C3 = 6:1. *A mixture of C2- and C3-silylation products* (16.2 mg, 33% yield) was obtained after purification by silica gel flash chromatography (50% EtOAc in hexanes). *Analytically pure C2-silylation* ***14a*** *was obtained as a colorless oil after subsequent purification by Preparative TLC (50% EtOAc in hexanes).* R_f = 0.1 (33% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (dd, *J* = 4.6, 1.4 Hz, 1H), 7.60 (dt, *J* = 8.3, 1.2 Hz, 1H), 7.09 (dd, *J* = 8.3, 4.6 Hz, 1H), 6.90 (d, *J* = 0.9 Hz, 1H), 3.83 (s, 3H), 1.03 – 0.97 (m, 9H), 0.96 – 0.89 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.0, 143.0, 142.7, 133.0, 116.4, 116.1, 113.8, 33.1, 7.6, 4.0. IR (Neat Film, NaCl) 2953, 2909, 2874, 1596, 1557, 1455, 1434, 1413, 1355, 1317, 1288, 1237, 1134, 1064, 1004, 800 cm^{-1}; HRMS (ESI+) calc'd for $C_{14}H_{23}N_2Si$ $[M+H]^+$: 247.1625, found 247.1621.



14b

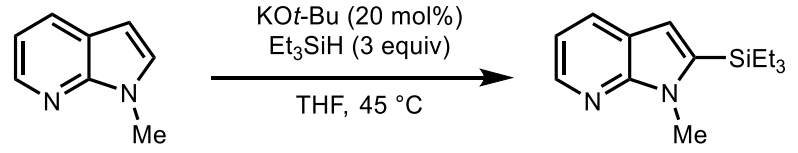
1-Methyl-2-(triethylsilyl)-1*H*-pyrrolo[3,2-*c*]pyridine 14b: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-methyl-5-azaindole **(**66.0 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 120 h. C2:C3 > 20:1. The desired product **14b** (37.9 mg, 31% yield) was obtained as a yellow oil after purification by silica gel flash chromatography (100% EtOAc). R_f = 0.2 (100% EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (d, *J* = 1.1 Hz, 1H), 8.28 (d, *J* = 5.9 Hz, 1H), 7.24 – 7.18 (m, 1H), 6.80 (d, *J* = 0.9 Hz, 1H), 3.82 (s, 3H), 1.02 – 0.96 (m, 9H), 0.94 – 0.87 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.7, 143.6, 140.8, 140.4, 125.7, 112.9, 104.5, 32.9, 7.6, 4.0. IR (Neat Film, NaCl) 2953, 2909, 2874, 1597, 1563, 1485, 1463, 1435, 1415,

1368, 1334, 1310, 1291, 1219, 1184, 1123, 1069, 1004, 900, 809 cm^{-1}; HRMS (ESI+) calc'd for $C_{14}H_{23}N_2Si$ $[M+H]^+$: 247.1625, found 247.1626.



14c

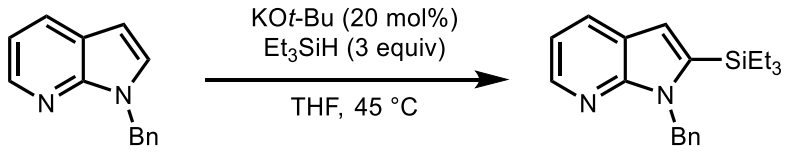
1-Methyl-2-(triethylsilyl)-1*H*-pyrrolo[2,3-*c*]pyridine 14c: The general procedure was followed. The reaction was performed with KO*t*-Bu (5.8 mg, 0.52 mmol, 20 mol%), 1- methyl-6-azaindole (35.0 mg, 0.26 mmol, 1 equiv), Et_3SiH (126 µL, 0.78 mmol, 3 equiv), and 0.3 mL of THF at 45 °C for 94 h. C2:C3 > 20:1. The desired product **14c** (32.9 mg, 50% yield) was obtained as a yellow oil after purification by silica gel flash chromatography (gradient elution, 2.5→5% MeOH in CH_2Cl_2). R_f = 0.3 (5% MeOH in CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.20 (d, *J* = 5.5 Hz, 1H), 7.47 (dd, *J* = 5.5, 1.1 Hz, 1H), 6.68 (d, *J* = 0.8 Hz, 1H), 3.93 (s, 3H), 1.03 – 0.97 (m, 9H), 0.95 –0.89 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 138.1, 137.2, 133.0, 132.6, 114.7, 112.0, 33.3, 7.5, 3.9. IR (Neat Film, NaCl) 2952, 2909, 2874, 1594, 1559, 1496, 1475, 1457, 1415, 1358, 1333, 1315, 1286, 1241, 1167, 1120, 1070, 1004, 817, 808 cm^{-1}; HRMS (ESI+) calc'd for $C_{14}H_{23}N_2Si$ $[M+H]^+$: 247.1625, found 247.1620.



14d

1-Methyl-2-(triethylsilyl)-1*H*-pyrrolo[2,3-*b*]pyridine 14d: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*- methyl-7-azaindole (66 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF

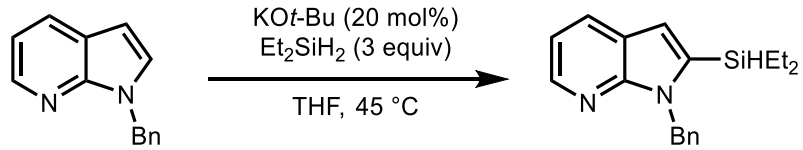
at 35 °C for 63 h. C2:C3 > 20:1. The desired product **14d** (87.1 mg, 71% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (gradient elution, 0→10% EtOAc in hexanes). R_f = 0.3 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (dd, *J* = 4.7, 1.6 Hz, 1H), 7.87 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.02 (dd, *J* = 7.8, 4.7 Hz, 1H), 6.67 (s, 1H), 3.95 (s, 3H), 1.04 – 0.97 (m, 9H), 0.96 – 0.88 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.0, 143.2, 139.2, 128.3, 120.7, 115.3, 111.0, 31.4, 7.6, 3.9. IR (Neat Film, NaCl) 3052, 2953, 2910, 2874, 1590, 1570, 1489, 1444, 1403, 1302, 1286, 1226, 1162, 1134, 1107, 1066, 1004, 906, 804, 772, 739 cm^{-1}; HRMS (FAB+) calc'd for $C_{14}H_{23}N_2Si$ $[M+H]^+$: 247.1631, found 247.1637.



14e

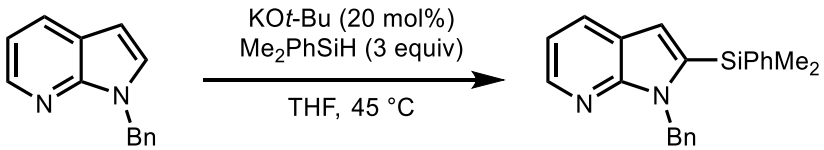
1-Methyl-2-(triethylsilyl)-1*H*-pyrrolo[2,3-*b*]pyridine 14e: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*- benzyl-7-azaindole (104.0 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 144 h. C2:C3 > 20:1. The desired product **14e** (89.4 mg, 56% yield) was obtained as a colorless oil purification by silica gel flash chromatography (gradient elution, 2.5→5% EtOAc in hexanes). R_f = 0.3 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (dd, *J* = 4.7, 1.6 Hz, 1H), 7.94 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.25 – 7.16 (m, 3H), 7.07 (dd, *J* = 7.8, 4.6 Hz, 1H), 6.87 – 6.85 (m, 2H), 6.79 (s, 1H), 5.69 (s, 2H), 0.91 – 0.83 (m, 9H), 0.74 – 0.69 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.2, 143.7, 139.04, 138.96, 128.6, 128.4, 127.0, 125.9, 120.5, 115.7, 112.2, 47.8, 7.4, 3.7. IR (Neat Film, NaCl) 2954, 2874, 1589, 1570, 1495, 1452,

1439, 1422, 1378, 1357, 1309, 1239, 1157, 1103, 1004, 909, 803, 777 cm^{-1}; HRMS (MM: ESI- APCI+) calc'd for $C_{20}H_{27}N_2Si$ $[M+H]^+$: 323.1938, found 323.1947.



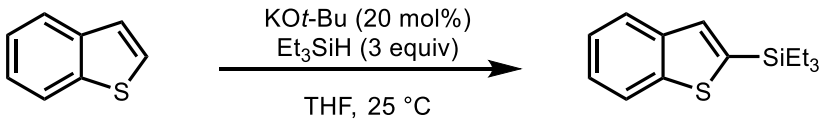
14f

1-Benzyl-2-(diethylsilyl)-1*H*-pyrrolo[2,3-*b*]pyridine 14f: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1- benzyl-7-azaindole (104.5 mg, 0.5 mmol, 1 equiv) and Et_2SiH_2 (194 µL, 1.5 mmol, 3 equiv) at 60 °C for 84 h. C2:C3 > 20:1. The desired product **14f** (96.2 mg, 65% yield) was obtained as a yellow oil after purification by silica gel flash chromatography (3% EtOAc in hexanes). R_f = 0.4 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (dd, *J* = 4.7, 1.6 Hz, 1H), 7.95 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.30 – 7.16 (m, 3H), 7.09 (dd, *J* = 7.8, 4.6 Hz, 1H), 7.01 – 6.99 (m, 2H), 6.80 (s, 1H), 5.71 (s, 2H), 4.32 (p, *J* = 3.3 Hz, 1H), 0.95 (t, *J* = 7.9 Hz, 6H), 0.78 – 0.63 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9, 143.8, 138.9, 137.4, 128.6, 128.5, 127.2, 126.6, 120.5, 115.8, 111.7, 47.6, 8.1, 3.4. IR (Neat Film, NaCl) 2955, 2873, 2120, 1590, 1568, 1495, 1453, 1439, 1422, 1358, 1300, 1235, 1156, 1100, 1009, 973, 910, 808 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{18}H_{23}N_2Si$ $[M+H]^+$: 295.1625, found 295.16.



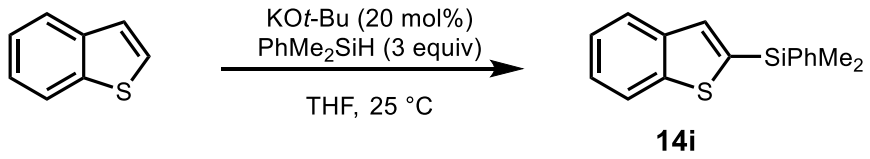
14g

1-Benzyl-2-(dimethyl(phenyl)silyl)-1H-pyrrolo[2,3-b]pyridine 14g: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-benzyl-7-azaindole (103.9 mg, 0.5 mmol, 1 equiv) and $PhMe_2SiH$ (230 µL, 1.5 mmol, 3 equiv) at 60 °C for 96 h. C2:C3 > 20:1. The desired product **14g** (118.0 mg, 69% yield) was obtained as a yellow oil after purification by silica gel flash chromatography (3% EtOAc in hexanes). R*f* = 0.4 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (dd, *J* = 4.7, 1.6 Hz, 1H), 7.97 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.49 – 7.45 (m, 2H), 7.41 – 7.38 (m, 1H), 7.37 – 7.32 (m, 2H), 7.20 – 7.13 (m, 3H), 7.08 (dd, *J* = 7.8, 4.6 Hz, 1H), 6.84 (s, 1H), 6.77 – 6.68 (m, 2H), 5.46 (s, 2H), 0.42 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.3, 144.0, 140.0, 138.8, 136.9, 134.2, 129.7, 128.8, 128.5, 128.1, 127.0, 126.1, 120.4, 115.9, 112.2, 47.6, -2.0. IR (Neat Film, NaCl) 3050, 3027, 2956, 1589, 1569, 1495, 1439, 1427, 1359, 1309, 1250, 1156, 1107, 1029, 987, 910, 822 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{22}H_{23}N_2Si$ $[M+H]^+$: 343.1625, found 343.1635.



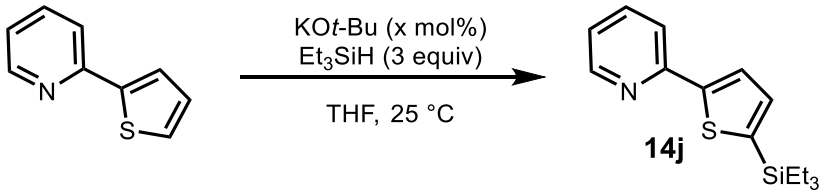
14h

Benzo[*b*]thiophen-2-yltriethylsilane 14h: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), benzo[*b*]thiophene (67.0 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 60 h. The desired product **14h** (120.3, 97% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). R_f = 0.6 (100% hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (m, 1H), 7.87 – 7.81 (m, 1H), 7.49 (m, 1H), 7.41 – 7.29 (m, 2H), 1.07 – 1.03 (m, 9H), 0.96 – 0.85 (m, 6H).



14i

Benzo[*b*]thiophen-2-yldimethyl(phenyl)silane 14i: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), benzo[*b*]thiophene (67.0 mg, 0.5 mmol, 1 equiv), $PhMe_2SiH$ (230 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 60 h. The desired product **14i** (116.6 mg, 87% yield) was obtained as colorless oil after purification by silica gel flash chromatography (100% hexanes). R_f = 0.5 (100% hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.87 (m, 1H), 7.87 – 7.79 (m, 1H), 7.68 – 7.59 (m, 2H), 7.51 (d, *J* = 0.8 Hz, 1H), 7.46 – 7.39 (m, 3H), 7.38 – 7.31 (m, 2H), 0.69 (s, 6H).

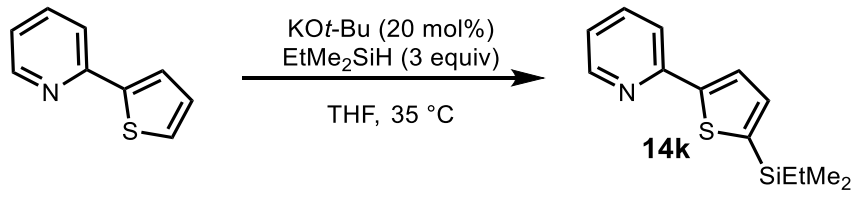


14j

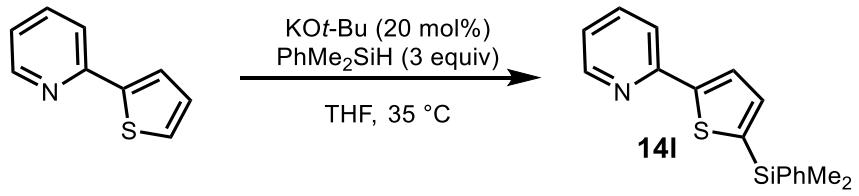
Condition A: 0.5 mmol, 20 mol% KO*t*-Bu, 35 h	94%
Condition B: 5 mmol, 3.5 mol% KO*t*-Bu, 96 h	82%

2-(5-(Triethylsilyl)thiophen-2-yl)pyridine 14j: The general procedure was followed. *Condition A*: The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2 (thiophen-2-yl)pyridine (80.5 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 35 h. The desired product **14j** (129.3 mg, 94% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (5% EtOAc in hexanes). *Condition B*: The reaction was performed with KO*t*-Bu (19.6 mg, 0.18 mmol, 3.5 mol%), 2-(thiophen-2-yl)pyridine (0.81 g, 5 mmol, 1 equiv), Et_3SiH (2.43 mL, 15 mmol, 3 equiv), and 3.0 mL of THF at 25 °C for 96 h. The desired product **14j** (1.13 g, 82% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (5% EtOAc in hexanes). R_f =

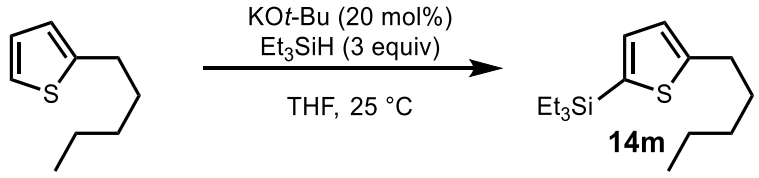
0.3 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 4.7 Hz, 1H), 7.61 (dt, *J* = 3.9, 1.7 Hz, 3H), 7.23 (d, *J* = 3.3 Hz, 1H), 7.08 (q, *J* = 4.8 Hz, 1H), 1.01 (t, *J* = 7.9 Hz, 9H), 0.82 (q, *J* = 7.9 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.8, 149.8, 149.6, 139.7, 136.6, 135.6, 125.7, 121.8, 119.0, 7.4, 4.5; IR (Neat Film, NaCl) 3054, 3001, 2953, 2909, 2874, 1585, 1563, 1528, 1517, 1464, 1436, 1422, 1377, 1315, 1290, 1238 ,1207, 1151, 1077, 1066, 1047, 1007, 990, 962, 807, 774, 737 cm^{-1}; HRMS (FAB+) calc'd for $C_{15}H_{22}NSSi$ $[M+H]^+$: 276.1242, found 276.1239.



2-(5-(Ethyldimethylsilyl)thiophen-2-yl)pyridine 14k: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2- (thiophen-2-yl)pyridine (80.5 mg, 0.5 mmol, 1 equiv), $EtMe_2SiH$ (198 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 35 °C for 48 h. The desired product **14k** (107.4 mg, 87% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (10% Et_2O in hexanes). R_f = 0.4 (10% Et_2O in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (ddd, *J* = 4.9, 1.8, 1.1 Hz, 1H), 7.72 – 7.63 (m, 2H), 7.62 (d, *J* = 3.5 Hz, 1H), 7.24 (d, *J* = 3.5 Hz, 1H), 7.13 (ddd, *J* = 6.7, 4.9, 2.0 Hz, 1H), 1.05 – 0.96 (m, 3H), 0.78 (qd, *J* = 7.8, 0.8 Hz, 2H), 0.32 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.7, 149.7, 149.6, 141.9, 136.6, 135.0, 125.6, 121.7, 118.9, 8.3, 7.2, -2.5; IR (Neat Film, NaCl) 3054, 3001, 2953, 2909, 2874, 1585, 1563, 1528, 1517, 1464, 1436, 1422, 1315, 1290, 1248, 1207, 1151, 1077, 1066, 1047, 1007, 990, 964, 836, 812, 774, 752, 737, 712 cm^{-1}; HRMS (FAB+) calc'd for $C_{13}H_{18}NSSi$ $[(M+H)^+–H_2]$: 248.0929, found 248.0935.

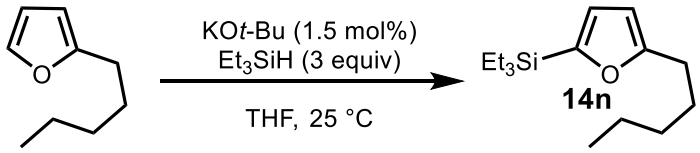


2-(5-(Dimethyl(phenyl)silyl)thiophen-2-yl)pyridine 14l: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2 (thiophen-2-yl)pyridine (80.5 mg, 0.5 mmol, 1 equiv), $PhMe_2SiH$ (230 µL, 1.5 mmol, 3 equiv), and 1.0 mL of THF at 35 °C for 48 h. The desired product **14l** (118.1 mg, 80% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (10% Et_2O in hexanes). R_f = 0.3 (10% Et_2O in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 – 8.54 (m, 1H), 7.72 – 7.56 (m, 5H), 7.43 – 7.33 (m, 3H), 7.26 (m, 1H), 7.14 (m, 1H), 0.63 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.4, 150.3, 149.5, 140.6, 137.3, 136.6, 136.0, 133.8, 129.3, 127.8, 125.6, 121.8, 118.9, –1.6; IR (Neat Film, NaCl) 3067, 2955, 1586, 1563, 1527, 1463, 1423, 1316, 1290, 1249, 1207, 1151, 1112, 1077, 1005, 989, 963, 807, 773, 731 cm^{-1}; HRMS (FAB+) calc'd for $C_{17}H_{18}NSSi$ $[M+H]^+$: 296.0929, found 296.0938.

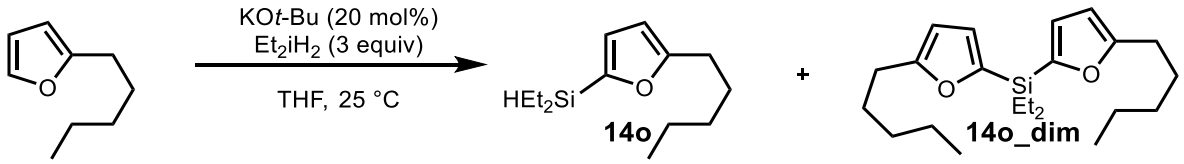


Triethyl(5-pentylthiophen-2-yl)silane 14m: The general procedure was followed. *Condition A*: The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2-pentylthiophene (77.0 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 48 h. The desired product **14m** (130.0 mg, 96% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). *Condition B:* The reaction was performed with KO*t*-Bu (5.6 mg, 0.05 mmol, 1 mol%), 2-pentylthiophene (770.4 mg, 5.0 mmol,

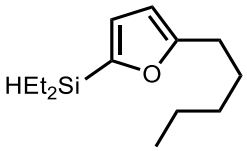
1 equiv), Et_3SiH (2.43 mL, 15 mmol, 3 equiv), and 3.0 mL of THF at 25 °C for 96 h. The desired product **14m** (1.23g, 92% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). R_f = 0.6 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (dd, *J* = 3.3, 1.5 Hz, 1H), 6.91 (dt, *J* = 3.3, 1.0 Hz, 1H), 2.90 (td, *J* = 7.7, 1.2 Hz, 2H), 1.81 – 1.71 (m, 2H), 1.48 – 1.36 (m, 4H), 1.06 (t, *J* = 7.8 Hz, 9H), 0.99 – 0.94 (m, 3H), 0.84 (qd, *J* = 7.8, 1.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.6, 134.7, 134.1, 125.5, 31.7, 31.6, 30.2, 22.6, 14.1, 7.5, 4.7; IR (Neat Film, NaCl) 3054, 2955, 2934, 2874, 1750, 1528, 1456, 1438, 1413, 1378, 1339, 1235, 1213, 1058, 1011, 988, 799, 736 cm^{-1}; HRMS (FAB+) calc'd for $C_{15}H_{27}SSi$ $[(M+H)–H_2]^+$: 267.1603, found 267.1609.



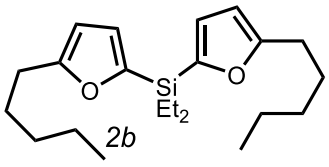
Triethyl(5-pentylfuran-2-yl)silane 14n: The general procedure was followed. The reaction was performed with KO*t*-Bu (8.4 mg, 0.075 mmol, 1.5 mol%), 2-pentylfuran (691 mg, 5.0 mmol, 1 equiv), Et_3SiH (2.43 mL, 15 mmol, 3 equiv), and 3 mL of THF at 25 °C for 96 h. The desired product **14n** (1.15 g, 91% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). R_f = 0.6 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.53 (d, *J* = 3.0 Hz, 1H), 5.96 (dt, *J* = 3.0, 0. Hz, 1H), 2.67 – 2.60 (m, 2H), 1.64 (dq, *J* = 9.4, 7.4 Hz, 2H), 1.36 – 1.28 (m, 4H), 1.05 – 0.95 (m, 9H), 0.92 – 0.85 (m, 3H), 0.74 (qd, *J* = 7.8, 0.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.2, 156.2, 121.5, 104.6, 31.6, 28.3, 27.9, 22.6, 14.1, 7.5, 3.6; IR (Neat Film, NaCl) 3108, 2954, 2933, 2874, 1807, 1721, 1588, 1493, 1459, 1414, 1378, 1340, 1237, 1186, 1173, 1118, 1084, 1011, 962, 923, 782, 736, 724 cm^{-1}; HRMS (FAB+) calc'd for $C_{15}H_{27}OSi$ $[(M+H)–H_2]^+$: 251.1831, found 251.1821.



The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2-pentylfuran (69.1 mg, 0.5 mmol, 1 equiv), Et_2SiH_2 (195 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 76 h. The desired product **14o** (87.4 mg, 78% yield) and silicon-tethered product **14o_dim** (12.4 mg, 8% yield) were obtained after purification by silica gel flash chromatography (100% hexanes).

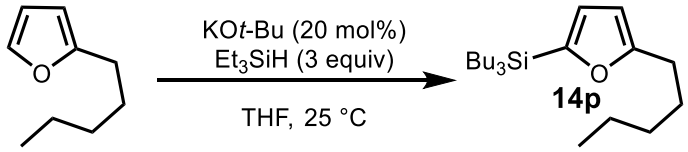


Diethyl(5-pentylfuran-2-yl)silane 14o: Colorless oil, R_f = 0.6 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.63 (d, *J* = 3.1 Hz, 1H), 6.00 (dt, *J* = 3.1, 0.9 Hz, 1H), 4.21 (p, *J* = 3.2 Hz, 1H), 2.75 – 2.64 (m, 2H), 1.73 – 1.62 (m, 2H), 1.38 – 1.32 (m, 4H), 1.11 – 1.04 (m, 6H), 0.95 – 0.90 (m, 3H), 0.88 – 0.81 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 153.7, 122.7, 105.0, 31.6, 28.4, 27.9, 22.6, 14.1, 8.1, 3.2; IR (Neat Film, NaCl) 2955, 2931, 2873, 2120, 1588, 1493, 1461, 1233, 1082, 1010, 974, 925, 798, 715 cm^{-1}; HRMS (FAB+) calc'd for $C_{13}H_{23}OSi$ [(M+H)–H_2]$^+$: 223.1518, found 223.1519.

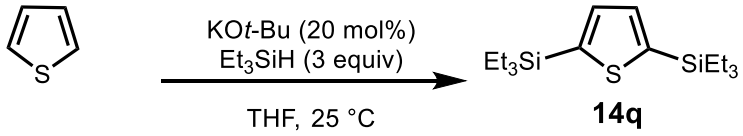


Diethylbis(5-pentylfuran-2-yl)silane 14o_dim: Colorless oil, R_f = 0.7 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.62 (d, *J* = 3.1 Hz, 2H), 5.98 (dt, *J* = 3.1, 0.9 Hz, 2H), 2.69 – 2.61 (m, 4H), 1.70 – 1.59 (m, 4H), 1.36 – 1.30 (m, 8H), 1.08 – 1.01 (m, 6H), 1.01 – 0.93 (m, 4H), 0.93 –

0.81 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5, 153.7, 122.8, 104.8, 31.4, 28.2, 27.7, 22.4, 13.9, 7.2, 4.2; IR (Neat Film, NaCl) 2955, 2928, 2873, 2859, 1587, 1493, 1461, 1378, 1233, 1187, 1122, 1010, 961, 925, 783, 726 cm^{-1}; HRMS (EI+) calc'd for $C_{22}H_{36}O_2Si$ [$M^{\bullet+}$]: 360.2485, found 360.2468.

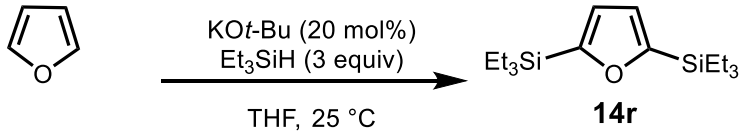


Tributyl(5-pentylfuran-2-yl)silane 14p: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2-pentylfuran (69.1 mg, 0.5 mmol, 1 equiv), *n*-Bu_3SiH (386 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 108 h. The desired product **14p** (137.8 mg, 82% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). R_f = 0.71 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.50 (d, *J* = 3.0 Hz, 1H), 5.95 (d, *J* = 3.0, 1H), 2.67 – 2.60 (m, 2H), 1.69 – 1.59 (m, 2H), 1.39 – 1.24 (m, 16H), 0.94 – 0.83 (m, 12H), 0.79 – 0.69 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0, 156.8, 121.3, 104.7, 31.6, 28.3, 28.0, 26.7, 26.2, 22.6, 14.1, 13.9, 12.3; IR (Neat Film, NaCl) 3107, 2956, 2923, 2871, 2857, 2099, 1677, 1588, 1493, 1464, 1410, 1376, 1341, 1296, 1271, 1217, 1187, 1175, 1082, 1050, 1010, 961, 925, 885, 781, 759, 732 cm^{-1}; HRMS (EI+) calc'd for $C_{21}H_{40}OSi$ [$M^{\bullet+}$]: 336.2848, found 336.2859.



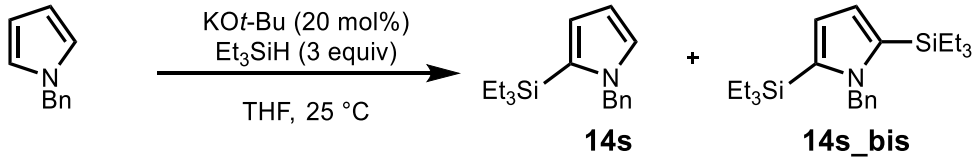
2,5-Bis(triethylsilyl)thiophene 14q: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), thiophene (42.1 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 72 h. The desired product

14q (134.2 mg, 86% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). R_f = 0.6 (100% hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (s, 2H), 1.02 – 0.99 (m, 18H), 0.83 – 0.79 (m, 12H).



14r

2,5-Bis(triethylsilyl)furan 14r: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), furan (34.0 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 48 h. The desired product **14r** (106.6 mg, 72% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). R_f = 0.7 (100% hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.66 (s, 2H), 1.09 – 0.95 (m, 18H), 0.86 – 0.70 (m, 12H).

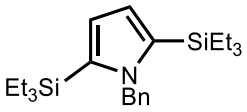


14s **14s_bis**

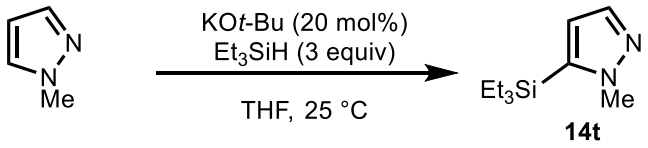
The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-benzyl-1*H*-pyrrole (78.5 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 108 h. The desired product **14s** (100.3 mg, 74% yield) and bis-silylation product **14s_bis** (9.6 mg, 5%) were obtained after purification by silica gel flash chromatography (100% hexanes).

1-Benzyl-2-(triethylsilyl)-1*H*-pyrrole 14s: Colorless oil, R_f = 0.3 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 2H), 7.32 – 7.25 (m, 1H), 7.04 – 6.98 (m, 2H), 6.86 (dd, *J* =

2.4, 1.5 Hz, 1H), 6.51 (dd, *J* = 3.5, 1.5 Hz, 1H), 6.30 (dd, *J* = 3.4, 2.4 Hz, 1H), 5.22 (s, 2H), 0.95 (t, *J* = 7.8 Hz, 9H), 0.73 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.2, 129.9, 128.7, 127.5, 126.62, 126.56, 120.9, 108.9, 53.5, 7.6, 4.2; IR (Neat Film, NaCl) 3088, 3064, 3029, 2952, 2908, 2873, 1516, 1506, 1495, 1454, 1418, 1353, 1329, 1288, 1237, 1175, 1112, 1080, 1008, 969, 760 cm^{-1}; HRMS (EI+) calc'd for $C_{17}H_{25}NSi$ [$M^{\bullet+}$]: 271.1756, found 271.1755.



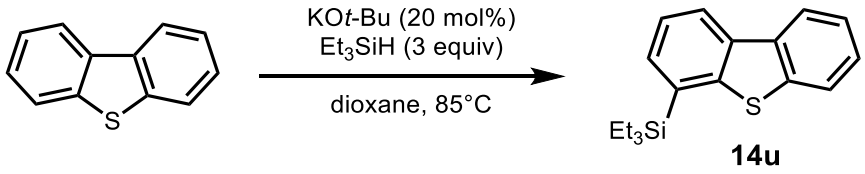
1-Benzyl-2,5-bis(triethylsilyl)-1*H*-pyrrole 14s_bis: Colorless oil, R_f = 0.4 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.21 (m, 2H), 7.21 – 7.15 (m, 1H), 6.72 (dq, *J* = 7.1, 1.0 Hz, 2H), 6.52 (s, 2H), 5.28 (s, 2H), 0.85 – 0.82 (m, 18H), 0.63 – 0.52 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.4, 135.6, 128.2, 126.9, 125.5, 121.2, 53.3, 7.4, 3.9; IR (Neat Film, NaCl) 3027, 2952, 2909, 2874, 1605, 1498, 1485, 1454, 1416, 1377, 1343, 1277, 1237, 1161, 1075, 1002, 912, 775, 764, 731 cm^{-1}; HRMS (EI+) calc'd for $C_{23}H_{39}NSi_2$ [$M^{\bullet+}$]: 385.2621, found 385.2638.



14t

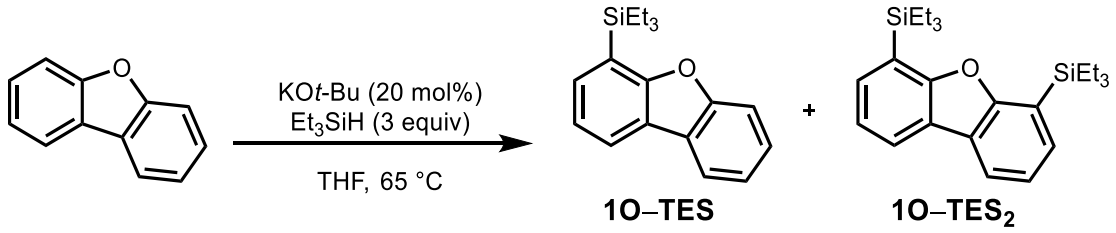
1-Methyl-5-(triethylsilyl)-1*H*-pyrazole 14t: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-methyl-1*H* pyrazole (41.1 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF \ at 25 °C for 120 h. The desired product **14t** (72.6 mg, 74% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (1:1 Et_2O:hexanes). R_f = 0.3 (1:1

Et_2O:hexanes). ^1H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 1.9 Hz, 1H), 6.37 (d, *J* = 1.8 Hz, 1H), 3.95 (s, 3H), 0.96 (m, 9H), 0.83 (m, 6H).



14u

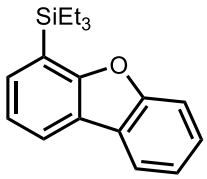
Dibenzo[*b,d*]thiophen-4-yltriethylsilane 14u: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), dibenzothiophene (92 mg, 0.5 mmol, 1.0 equiv), Et_3SiH (243 µL, 1.5 mmol, 3.0 equiv), and 3 mL of dioxane at 85 °C for 72 h. The desired product **14u** (55.4 mg, 38% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). R_f = 0.7 (100% hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (m, 2H), 7.86 (m, 1H), 7.58 (m, 1H), 7.45 (m, 3H), 1.10 – 0.93 (m, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.6, 139.3, 135.4, 134.7, 133.7, 131.5, 126.5, 124.2, 123.7, 122.4, 122.2, 121.4, 7.4, 3.2. IR (Neat Film, NaCl) 3060, 2953, 2908, 2873, 1450, 1440, 1415, 1366, 1283, 1250, 1238, 1098, 1080, 1042, 1019, 1003, 972, 812, 749, 733 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{22}SSi$ [$M^{\bullet+}$]: 298.1212, found 298.1214.



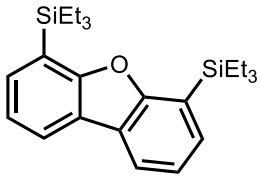
1O–TES **$1O–TES_2$**

The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), dibenzo[*b*,*d*]furan (84.1 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 65 °C for 65 h. Desired product **1O–TES** (100.2 mg, 71% yield)

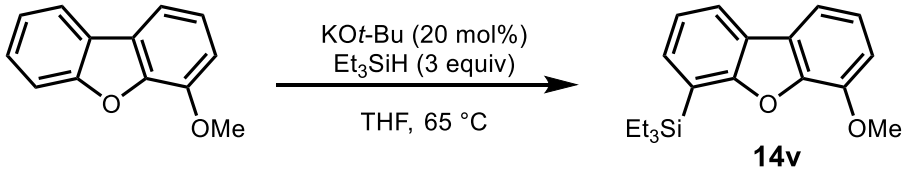
and bis-silylated product **1O–TES$_2$** (6.9 mg, 4% yield) were obtained after purification by silica gel flash chromatography (100% hexanes).



Dibenzo[*b,d*]furan-4-yltriethylsilane 1O–TES: Colourless oil, R_f = 0.6 (100% hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 – 7.94 (m, 2H), 7.61 – 7.50 (m, 2H), 7.46 (td, *J* = 7.7, 1.4 Hz, 1H), 7.34 (td, *J* = 7.6, 4.4 Hz, 2H), 1.02 (m, 15H).



4,6-Bis(triethylsilyl)dibenzo[b,d]furan 1O–TES$_2$: White solid, R_f = 0.7 (100% hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.6, 1.4 Hz, 2H),7.54 (dd, *J* = 7.1, 1.4 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 1.12 – 0.96 (m, 30H).

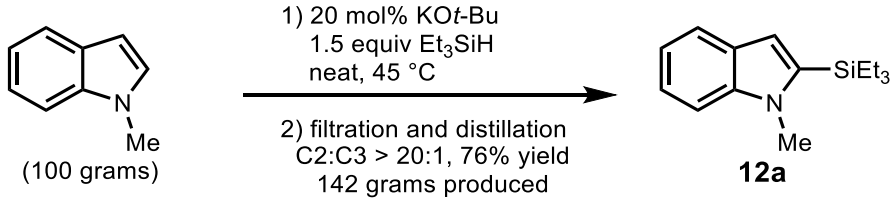


14v

Triethyl(6-methoxydibenzo[*b,d*]furan-4-yl)silane 14w: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 4 methoxydibenzo[*b,d*]furan (99.0 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 65 °C for 65 h. The desired product **14v** (99.9 mg, 64% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). R_f = 0.3 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.53 (ddd, *J* =

15.4, 7.4, 1.2 Hz, 2H), 7.37 – 7.30 (m, 1H), 7.24 (t, *J* = 7.8 Hz, 1H), 6.99 (dd, *J* = 8.0, 1.0 Hz, 1H), 4.09 (s, 3H), 1.08 – 0.95 (m, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 145.7, 145.3, 133.4, 126.1, 123.0, 122.8, 122.3, 121.5, 120.4, 112.9, 111.0, 56.9, 7.4, 3.5; IR (Neat Film, NaCl) 3052, 2952, 2925, 2873, 2852, 2361, 1627, 1596, 1576, 1497, 1483, 1456, 1432, 1387, 1322, 1308, 1270, 1220, 1180, 1168, 1147, 1125, 1038, 1006, 854, 836, 767, 752, 729 cm^{-1}; HRMS (EI+) calc'd for $C_{19}H_{24}O_2Si$ [$M^{\bullet+}$]: 312.1546, found 312.1555.

Multi-gram scale syntheses

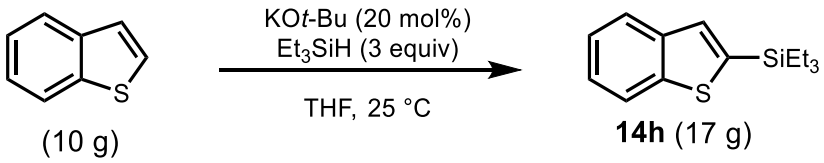


A 500 mL oven-dried Schlenk flask equipped with a stir bar and stoppered with a rubber septum was evacuated and refilled once with argon. KO*t*-Bu (18.8 grams, 167.9 mmols, 20 mol%) was weighed out on the bench and added to the flask under a strong flow of argon. The charged flask was then evacuated and refilled with argon. 1-Methylindole (95% purity, AKSci, undistilled, yellow oil; 95.1 mL, 762.4 mmol, 1.0 equiv) and Et_3SiH (182.6 mL, 1142 mmol, 1.5 equiv), which were previously degassed, were added through the septum by syringe. The mixture was then cooled to –78 °C (dry ice/acetone) and evacuated/backfilled with argon for three cycles. The cooling bath was removed and the flask was allowed to warm to room temperature under a positive pressure of argon. The flask was then transferred to a heating mantle set at 45 °C and stirred for 72 hours. The flask with the resultant deep red-purple solution was removed from heating and allowed to cool to room temperature, diluted with anhydrous Et_2O (50 mL), and filtered to remove solid residue. After the solvent was removed *in vacuo*, a stirbar was added

and the transparent deep amber solution was stirred under high vacuum (100 mmHg) for several hours to remove remaining volatiles. The mixture was then subjected to distillation under vacuum. A thermometer installed at the distillation head measured the temperature of the vapor being distilled.

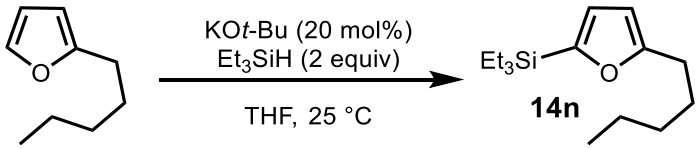
a) Heating bath to 120 °C, vacuum stabilizes at 300 mmHg as the solution boils. Forerun comes off as pale yellow oil. Thermometer reads 65–80 °C.
b) Vacuum stabilizes at 180 mmHg. Boiling continues vigorously.
c) As dripping rate in the forerun decreases (ca. one drop every three seconds), increase temperature. Remaining 1-methylindole comes over at 140 °C bath temp and 100 mmHg as a pale yellow oil. Thermometer reads 80–85 °C.
d) Increase temperature to 160 °C, vacuum at 100 mmHg to distil over the desired 2-triethylsilyl-1-methylindole (pale yellow oil). Thermometer reads 110–120 °C.

The desired product **12a** is obtained as a pale yellow oil (141.88 g, 76% yield).



(10 g) **14h** (17 g)

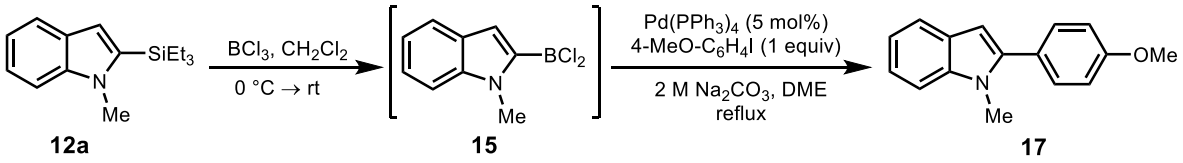
In a nitrogen-filled glove box, KO*t*-Bu (1.7 g, 15 mmol, 20 mol%), benzo[*b*]thiophene (10.1 g, 75 mmol, 1 equiv), Et_3SiH (23.3 mL, 146 mmol, 2 equiv), and 75 mL of THF were added to a 250 mL media jar equipped with a magnetic stir bar and sealed with a polypropylene cap. The reaction mixture was stirred at 25 °C for 60 h. The jar was then removed from the glovebox, opened carefully (*caution: gas released!*), and diluted with anhydrous Et_2O (30 mL). The reaction was filtered, the solvent was removed *in vacuo* and the residual volatiles were removed under high vacuum *(30 mmHg, 23 °C).* The desired product **14h** (17.3 g, 93% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes).



(10 g) (17 g)

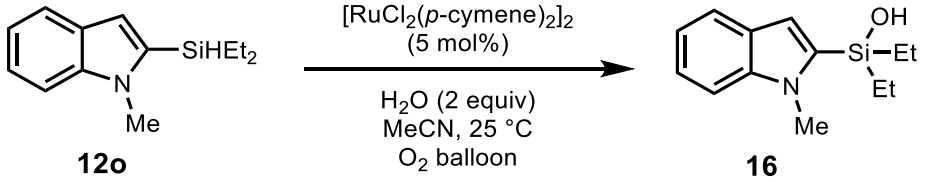
Followed the same procedure as for the multi-gram scale synthesis of **4h**: The reaction was performed with KO*t*-Bu (1.6 g, 14.6 mmol, 20 mol%), 2-pentylfuran **3n** (10.1 g, 73 mmol, 1 equiv), Et_3SiH (23.3 mL, 146 mmol, 2 equiv), and 73 mL of THF at 25 °C for 72 h. The desired product **4n** (17.4 g, 95% yield) was obtained as a colorless oil after filtration, removal of volatiles under high vacuum (30 mmHg, 23 °C) and purification by silica gel flash chromatography (100% hexanes).

Applications of silylated heteroarenes



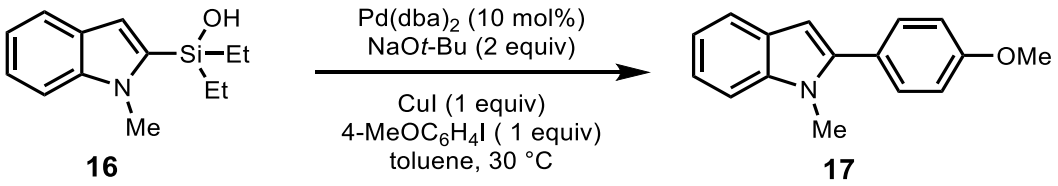
A solution of BCl_3 (1.0 M, 0.48 mL, 0.48 mmol) in CH_2Cl_2 was added by syringe under N_2 to a stirred solution of indolesilane **12a** (98.2 mg, 0.4 mmol) in CH_2Cl_2 (4 mL) at 0 °C. The mixture was stirred at room temperature for 3 h, after which time the solvent was removed *in vacuo*. After the residue was dried under high vacuum for 20 min, 4-iodoanisole (94.0 mg, 0.4 mmol), Pd$(PPh_3)_4$ (23.2 mg, 5 mol%), DME (4 mL, degassed) and 2M Na_2CO_3 aqueous solution (1 mL, degassed) were added and the mixture was stirred under reflux for 5 h. Then the reaction mixture was cooled to room temperature and water (20 mL) was added. The mixture was extracted with Et_2O (3 x 30 mL), the combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated. The desired 2-(4-methoxyphenyl)-1-methyl-1*H*- indole **17** (71.9 mg, 76%

yield) was obtained as a white solid after purification by silica gel flash chromatography (gradient elution, 10→33% CH_2Cl_2 in hexanes). R_f = 0.4 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.7 Hz, 1H), 7.49 – 7.39 (m, 2H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.24 (dt, *J* = 8.2, 1.2 Hz, 1H), 7.14 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.05 – 6.96 (m, 2H), 6.51 (br s, 1H), 3.88 (s, 3H), 3.73 (s, 3H).

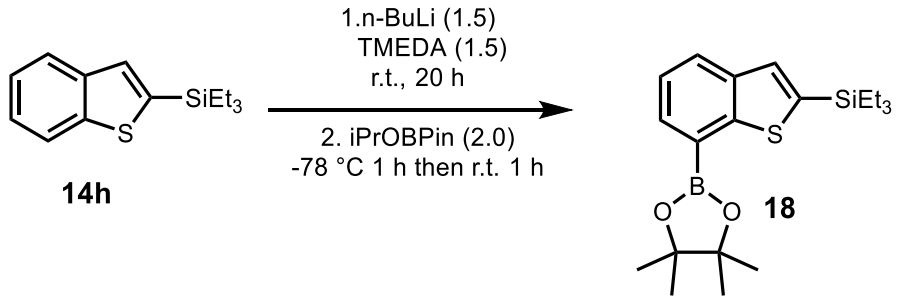


12o **16**

Diethyl(1-methyl-1*H*-indol-2-yl)silanol 16: Compound **12o** (44.5 mg, 0.2 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (6.3 mg, 0.01 mmol) were added to a 5 mL flask equipped with a stirring bar. The flask was sealed with a septum and placed under high vacuum for 5 min before being connected with an O_2 balloon and back-filled with O_2, then acetonitrile (1 mL) and H_2O (7.4 µL, 0.4 mmol) were added by syringe through the septum. The reaction mixture was stirred for 12 h at room temperature. The solvent was evaporated and the product **16** (36.0 mg, 77% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (gradient elution, 10→20% EtOAc in hexanes). R_f = 0.2 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.37 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.28 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.13 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 6.80 (d, *J* = 0.9 Hz, 1H), 3.93 (s, 3H), 2.12 (br s, 1H), 1.12 – 1.05 (m, 6H), 1.02 – 0.95 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.4, 138.1, 128.4, 122.6, 121.1, 119.4, 112.7, 109.4, 33.1, 7.1, 6.7. IR (Neat Film, NaCl) 3315, 2956, 2876, 1493, 1463, 1413, 1357, 1328, 1300, 1234, 1166, 1102, 1075, 1007, 960, 897, 839, 798, 751, 732 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{13}H_{20}NOSi$ $[M+H]^+$: 234.1309, found 234.1305.

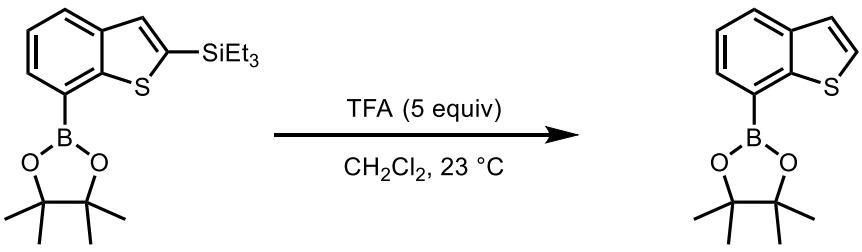


2-(4-Methoxyphenyl)-1-methyl-1*H*-indole 17: In a nitrogen-filled glovebox, a 2 dram vial equipped with a stir bar was charged with NaO*t*-Bu (26.8 mg, 0.28 mmol) and CuI (26.6 mg, 0.14 mmol), 4-iodoanisole (33.0 mg, 0.14 mmol), $Pd(dba)_2$ (8.2 mg, 0.014 mmol, 10 mol%) and 0.2 mL of toluene. The mixture was sealed with a cap and stirred for 10 min. Then this mixture was transferred by syringe to another 2 dram vial containing silanol **16** (33.1 mg, 0.14 mmol). The vial was washed with toluene (2 x 0.4 mL) and that rinse was added to the reaction mixture. After the reaction was stirred at 30 °C for 4 h, the starting material was completely converted (monitored by TLC). The desired product **17** (28.1 mg, 84% yield) was obtained as a white solid after purification by silica gel flash chromatography (gradient elution, 10→50% CH_2Cl_2 in hexanes).



Triethyl(7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzo[b]thiophen-2-yl)silane 18: To a flame-dried, round bottom flask charged with a stir bar, capped with a septum and under a steady stream of argon was added benzo[*b*]thiophen-2-yltriethylsilane **14h** (992 mg, 4.0 mmol, 1 equiv), pentane (5.0 mL) and TMEDA (0.703g, 0.907 mL, 1.5 equiv) at 23 °C. *n*-Butyllithium (1.6 M in hexanes, 3.78 mL, 1.5 equiv) was added dropwise such that the internal temperature remained between 22 and 25 °C (*a thermocouple was inserted through*

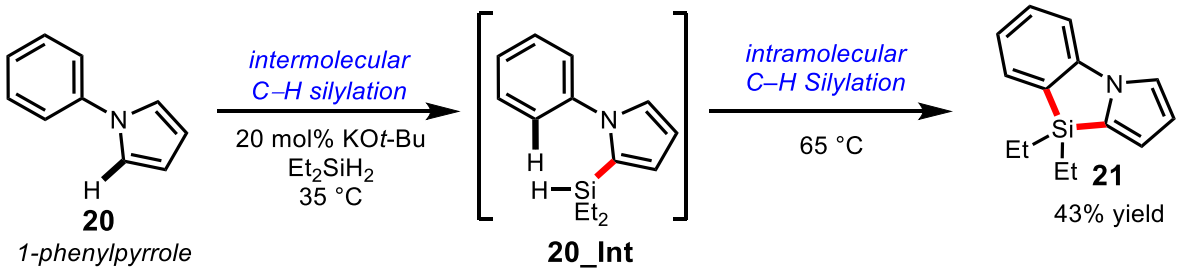
the septum directly into the solution for internal monitoring of the temperature). The resultant dark brown solution was allowed to stir at 22 °C for 20 h. The solution was then cooled to –78 °C (dry ice/acetone) and *i*-PrOBPin (1.52 g, 1.64 mL, 8.06 mmol, 2.0 equiv) was added as a 1 M solution in THF (8.06 mL) dropwise such that the temperature was kept below –75 °C (*careful temperature control is crucial for reproducibility*). The resulting solution was allowed to stir for 1 h at –78 °C after which time the cooling bath was removed. The solution was allowed to naturally warm to 23 °C and stirred at that temperature for an additional hour. The resulting turbid yellow reaction mixture was carefully quenched with NH_4Cl (5 mL). The mixture was extracted with Et_2O (3 x 10 mL), the combined organic fractions were washed with brine, dried over $MgSO_4$, filtered, and the solvent was evaporated to give a viscous brown liquid. The desired product **18** (926 mg, 64% yield) was obtained as a colorless solid after purification by silica gel flash chromatography (gradient elution 0→3% EtOAc in hexanes). R_f = 0.2 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.80 (dd, *J* = 7.0, 1.3 Hz, 1H), 7.48 (s, 1H), 7.35 (dd, *J* = 7.9, 7.0 Hz, 1H), 1.42 (s, 12H), 1.10 – 1.00 (m, 9H), 0.89 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.7, 140.8, 139.8, 132.0, 131.4, 126.4, 123.4, 84.3, 25.1, 7.6, 4.4. IR (Neat Film, NaCl) 2955, 2937, 1375, 1367, 1359, 1134, 1059, 854, 735 cm^{-1}; HRMS (EI+) calc'd for $C_{20}H_{31}BSSiO_2$ [$M^{\bullet+}$]: 374.1907, found 374.1907.



18 **19**

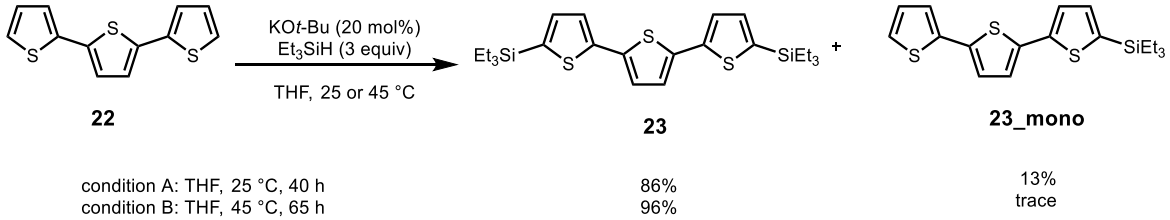
2-(Benzo[*b*]thiophen-7-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 19: To a vial charged with a magnetic stirbar and triethyl(7- (4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-

yl)benzo[b]thiophen-2-yl)silane **18** (300 mg, 0.80 mmol) was added CH_2Cl_2 (0.3 mL) and trifluoroacetic acid (306 µL, 4.0 mmol, 5.0 equiv) at room temperature. The reaction was allowed to stir for 3 hours, after which time the mixture was quenched with water (0.5 mL), extracted with Et_2O (3 x 5 mL) and the combined organic fractions were washed with brine (5 mL). The solvents were removed to give **19** (203.8 mg, 98%) as a white solid without further purification. R_f = 0.4 (3% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.83 (dd, *J* = 7.1, 1.3 Hz, 1H), 7.48 (d, *J* = 5.5 Hz, 1H), 7.38 (dd, *J* = 7.9, 7.0 Hz, 1H), 7.34 (d, *J* = 5.5 Hz, 1H), 1.41 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.8, 139.4, 132.0, 127.5, 126.7, 123.7, 123.4, 84.4, 25.1. IR (Neat Film, NaCl) 2977, 1564, 1504, 1461, 1372, 1330, 1300, 1267, 1199, 1165, 1135, 1097, 1038, 969, 851, 829, 801, 714, 672 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{17}BSO_2$ [$M^{\bullet+}$]: 260.1042, found 260.1039.

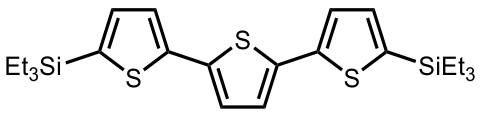


9,9-Diethyl-9*H*-benzo[d]pyrrolo[1,2-*a*][1,3]azasilole 21: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1- phenyl-1*H*-pyrrole (72.0 mg, 0.5 mmol, 1 equiv), Et_2SiH_2 (97 µL, 0.75 mmol, 1.5 equiv), and 0.5 mL of THF at 35 °C for 72 h and then at 65 °C for 72 h. The desired product **21** (48.8 mg, 43% yield) was obtained as colorless needles after purification by silica gel flash chromatography (100% hexanes). R_f = 0.6 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (ddd, *J* = 7.1, 1.4, 0.6 Hz, 1H), 7.46 – 7.33 (m, 2H), 7.31 (dt, *J* = 7.9, 0.7 Hz, 1H), 7.09 (td, *J* = 7.2, 1.0 Hz, 1H), 6.52 (dd, *J* = 3.3, 1.0 Hz, 1H), 6.41 (dd, *J* = 3.3, 2.6 Hz, 1H), 1.05 – 0.96 (m, 6H), 0.96 – 0.79 (m,

4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 134.1, 130.8, 129.4, 128.5, 123.9, 117.5, 117.1, 113.3, 111.6, 7.5, 4.4; IR (Neat Film, NaCl) 2958, 2921, 2873, 2849, 1658, 1598, 1462, 1471, 1451, 1377, 1332, 1260, 1086, 1017, 799, 755, 717 cm^{-1}; HRMS (FAB+) calc'd for $C_{14}H_{18}NSi$ $[M+H]^+$: 228.1208, found 228.1206.

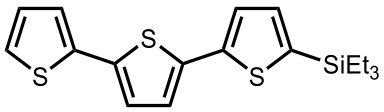


The general procedure was followed. *For condition A*: The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2,2':5',2''-terthiophene (124 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 40 h. Products **23** (204.7 mg, 86% yield) and **23_mono** (23.5 mg, 13% yield) were obtained after purification by silica gel flash chromatography (100% hexanes). *For condition B:* The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2,2':5',2''- terthiophene (124 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 65 h. Product **23** (228.6 mg, 96% yield) was obtained after purification by silica gel flash chromatography (100% hexanes); **23_mono** was observed as a trace product by ^{1}H NMR and GC-MS, but was not isolated.

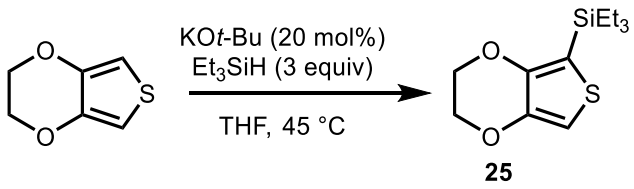


5,5''-Bis(triethylsilyl)-2,2':5',2''-terthiophene 23: Yellow oil, R_f = 0.5 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 3.5 Hz, 2H), 7.14 (d, *J* = 3.5 Hz, 2H), 7.10 (s, 2H), 1.03 (m, 18H), 0.82 (m, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.4, 136.7, 136.5, 135.7, 124.9, 124.5, 7.2, 4.4; IR (Neat Film, NaCl) 3057, 2953, 2934, 2908, 2874, 1750, 1455, 1428, 1417,

1377, 1303, 1236, 1212, 1198, 1068, 988, 1009, 911, 892, 792, 736, 723 cm^{-1}; HRMS (EI+) calc'd for $C_{24}H_{36}S_3Si_2$ [$M^{\bullet+}$]: 476.1518, found 476.1534.



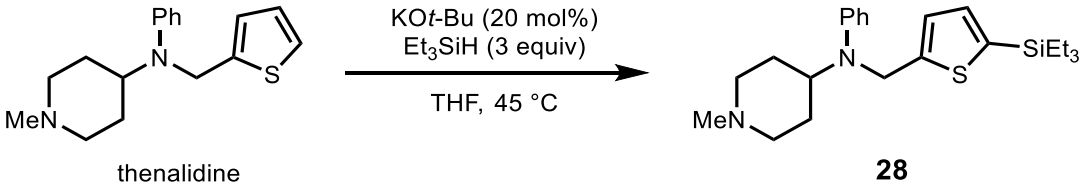
[2,2':5',2''-Terthiophen]-5-yltriethylsilane 23_mono: Yellow oil, R_f = 0.4 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 3.4 Hz, 1H), 7.21 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.17 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.14 (dd, *J* = 3.4, 1.6 Hz, 1H), 7.09 (q, *J* = 3.7 Hz, 2H), 7.02 (dd, *J* = 5.1, 3.6 Hz, 1H), 1.07 – 0.98 (m, 9H), 0.82 (qd, *J* = 7.8, 0.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.3, 137.5, 136.8, 136.6, 136.4, 135.6, 128.0, 125.0, 124.6, 124.5, 124.5, 123.8, 7.5, 4.6; IR (Neat Film, NaCl) 3068, 2953, 2873, 1458, 1425, 1377, 1235, 1195, 1069, 1011, 989, 913, 865, 836, 793, 737 cm^{-1}; HRMS (FAB+) calc'd for $C_{18}H_{23}S_3Si$ [M+H]$^+$: 363.0731, found 363.0742.



25

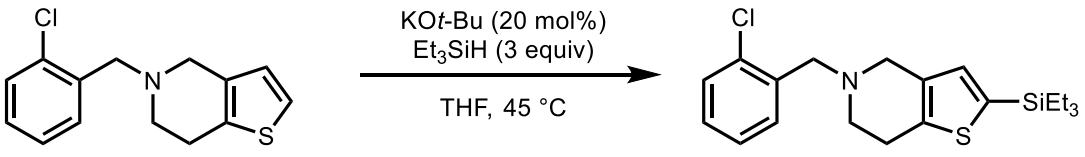
(2,3-Dihydrothieno[3,4-b][1,4]dioxin-5-yl)triethylsilane 25: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), EDOT (2,3-dihydrothieno[3,4-b][1,4]dioxine, 71.1 mg, 0.5 mmol), Et_3SiH (240 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 72 h. The desired product **25** (79.3 mg, 62% yield) was obtained after purification by silica gel flash chromatography (gradient elution, 0→5% EtOAc in hexanes) as a cloudy yellow oil. R_f = 0.3 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.56 (s, 2H), 4.17 (s, 4H), 0.98 (td, *J* = 7.8, 0.8 Hz, 9H), 0.84 – 0.74 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.5, 142.5, 108.7, 105.0, 64.5, 64.5, 7.4, 3.9; IR (Neat Film NaCl) 2952, 2873, 1468, 1440,

1422, 1361, 1244, 1181, 1151, 1072, 1042, 1009, 899, 721 cm^{-1}; HRMS (EI+) calc'd for $C_{12}H_{21}O_2SSi$ $[M+H]^+$: 257.1032, found 257.1064.



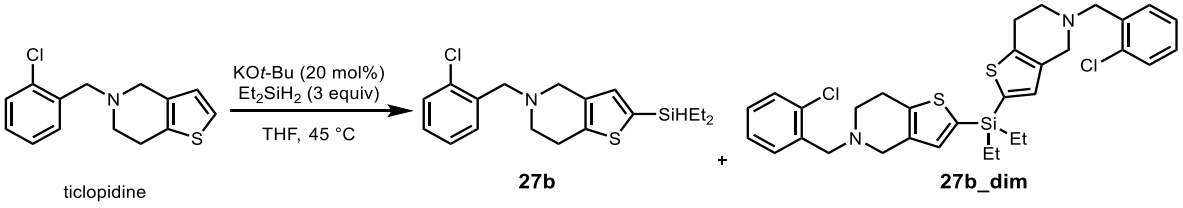
thenalidine **28**

1-Methyl-*N*-phenyl-*N*-((5-(triethylsilyl)thiophen-2-yl)methyl)piperidin-4-amine 28: The general procedure was followed. The reaction was performed with KO*t*-Bu (2.2 mg, 0.02 mmol, 20 mol%), thenalidine (28.2 mg, 0.1 mmol, 1 equiv), Et_3SiH (48 µL, 0.3 mmol, 3 equiv), and 0.1 mL of THF at 45 °C for 72 h. The desired product **28** (24.9 mg, 62% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (hexanes:EtOAc:Et_3N = 100:100:1). R_f = 0.2 (hexanes:EtOAc:Et_3N = 20:20:1); ^1H NMR (50 MHz, $CDCl_3$) δ 7.24 – 7.17 (m, 2H), 7.05 (d, *J* = 3.4 Hz, 1H), 6.97 (d, *J* = 3.3 Hz, 1H), 6.82 (dt, *J* = 7.8, 1.0 Hz, 2H), 6.72 (tt, *J* = 7.2, 1.0 Hz, 1H), 4.62 (s, 2H), 3.70 (tt, *J* = 11.6, 4.0 Hz, 1H), 2.96 – 2.92 (m, 2H), 2.30 (s, 3H), 2.07 (td, *J* = 11.9, 2.5 Hz, 2H), 1.93 – 1.85 (m, 2H), 1.85 – 1.73 (m, 2H), 0.97 (t, *J* = 7.9 Hz, 9H), 0.76 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.0, 149.0, 135.2, 134.7, 129.3, 125.3, 117.3, 113.8, 55.8, 55.6, 46.4, 46.0, 29.6, 7.5, 4.6. IR (Neat Film, NaCl) 2951, 2873, 2780, 2734, 1597, 1574, 1503, 1459, 1377, 1352, 1278, 1237, 1207, 1131, 1068, 1008, 987, 850, 802, 745 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{23}H_{37}N_2SSi$ $[M+H]^+$: 401.2441, found 401.2460.

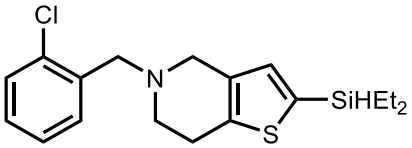


ticlopidine **27a**

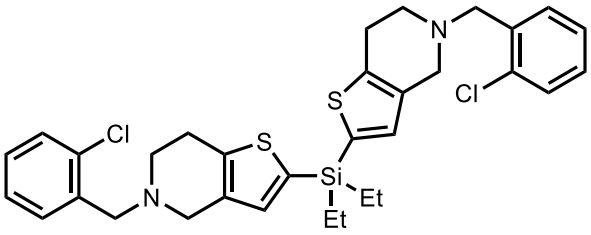
5-(2-Chlorobenzyl)-2-(triethylsilyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine 27a: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), ticlopidine (132.5 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 48 h. The desired product **27a** (107.7 mg, 57% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (gradient elution, 5→10% Et_2O in hexanes). R_f = 0.4 (10% Et_2O in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.37 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.25 (td, *J* = 7.4, 1.5 Hz, 1H), 7.20 (td, *J* = 7.6, 1.9 Hz, 1H), 6.86 (s, 1H), 3.84 (s, 2H), 3.67 (d, *J* = 1.6 Hz, 2H), 2.94 (t, *J* = 5.9 Hz, 2H), 2.87 (t, *J* = 5.4 Hz, 2H), 1.02 – 0.98 (m, 9H), 0.80 – 0.74 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.2, 136.5, 135.6, 134.4, 134.0, 133.2, 130.8, 129.6, 128.3, 126.8, 58.7, 53.3, 51.0, 26.1, 7.5, 4.6. IR (Neat Film, NaCl) 2952, 2908, 2873, 2805, 2763, 1462, 1443, 1413, 1375, 1360, 1347, 1303, 1289, 1234, 1169, 1125, 1106, 1047, 1032, 1018, 991, 907, 835, 752 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{20}H_{29}ClNSSi$ $[M+H]^+$: 378.1473, found 378.1480.



The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), ticlopidine (134.5 mg, 0.5 mmol, 1 equiv), Et_2SiH_2 (194 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 108 h. Products **27b** (97.9 mg, 56% yield) and **27b_dim** (27.3 mg, 18% yield) were obtained after purification by silica gel flash chromatography (gradient elution, 5→50% Et_2O in hexanes).

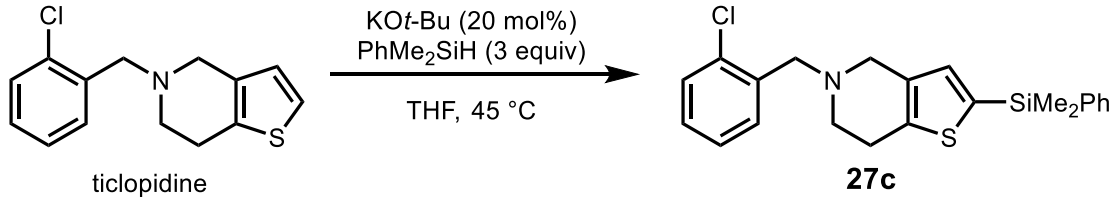


5-(2-Chlorobenzyl)-2-(diethylsilyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine 27b: Colorless oil, R_f = 0.4 (10% Et_2O in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.38 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.26 (td, *J* = 7.4, 1.5 Hz, 1H), 7.21 (td, *J* = 7.6, 1.9 Hz, 1H), 6.93 (s, 1H), 4.30 (p, *J* = 3.2 Hz, 1H), 3.84 (s, 2H), 3.67 (t, *J* = 1.7 Hz, 2H), 2.96 – 2.94 (m, 2H), 2.88 – 2.85 (m, 2H), 1.05 (t, *J* = 7.8 Hz, 6H), 0.83 (qd, , *J* = 7.5, 3.3 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.0, 136.4, 135.9, 134.4, 134.2, 131.3, 130.8, 129.6, 128.3, 126.8, 58.6, 53.2, 50.9, 26.1, 8.1, 4.5. IR (Neat Film, NaCl) 2953, 2909, 2872, 2805, 2112, 1456, 1447, 1361, 1348, 1303, 1290, 1231, 1169, 1125, 1106, 1048, 1033, 1009, 992, 907, 810, 752 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{18}H_{25}ClNSSi$ $[M+H]^+$: 350.1160, found 350.1155.

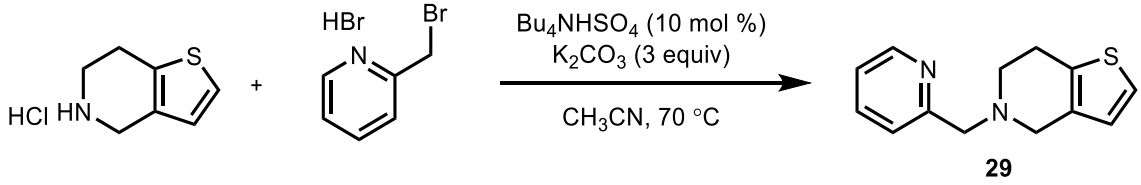


Bis(5-(2-chlorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl)diethylsilane 27b_dim: Colorless oil, R_f = 0.3 (50% Et_2O in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55(dd, *J* = 7.6, 1.8 Hz, 2H), 7.37 (dd, *J* = 7.8, 1.5 Hz, 2H), 7.25 (td, *J* = 7.4, 1.5 Hz, 2H), 7.20 (td, *J* = 7.6, 1.9 Hz, 2H), 6.92 (s, 2H), 3.83 (s, 4H), 3.65 (t, *J* = 3.3 Hz, 4H), 2.94 (t, *J* = 5.4 Hz, 4H), 2.86 (t, *J* = 5.6 Hz, 4H), 1.09 – 0.95 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 136.4, 135.8, 134.53, 134.45, 132.4, 130.9, 129.6, 128.3, 126.8, 58.7, 53.2, 50.9, 26.1, 7.5, 6.5. IR (Neat Film, NaCl) 3059, 2953, 2913, 2868, 2806, 1471, 1453, 1446, 1361, 1289, 1125, 1105, 1033,

989, 907, 839, 805, 753 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{32}H_{37}Cl_2N_2S_2Si$ $[M+H]^+$: 611.1539, found 611.1523.

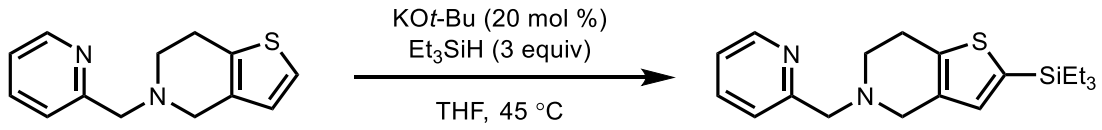


5-(2-Chlorobenzyl)-2-(dimethyl(phenyl)silyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine 27c: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), ticlopidine (134.5 mg, 0.5 mmol, 1 equiv), $PhMe_2SiH$ (230 µL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 108 h. Product **27c** (135.4 mg, 68% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (3% Et_2O in hexanes). R_f = 0.3 (10% Et_2O in hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 – 7.52 (m, 3H), 7.39 – 7.34 (m, 4H), 7.25 – 7.18 (m, 2H), 6.87 (s, 1H), 3.82 (s, 2H), 3.64 (t, *J* = 1.7 Hz, 2H), 2.95 – 2.92 (m, 2H), 2.88 – 2.84 (m, 2H), 0.56 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.1, 138.2, 136.4, 135.9, 135.2, 134.4, 134.1, 133.9, 130.8, 129.6, 129.4, 128.3, 128.0, 126.8, 58.6, 53.2, 50.9, 26.1, -1.1. IR (Neat Film, NaCl) 3067, 2953, 2918, 2806, 2764, 1652, 1471, 1446, 1427, 1361, 1248, 1169, 1109, 1033, 990, 907, 832, 810, 777, 753 cm^{-1}; HRMS (MM: ESI-APCI+) calc'd for $C_{22}H_{25}ClNSSi$ $[M+H]^+$: 398.1160, found 398.1152.



5-(Pyridin-2-ylmethyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine SM-14: To a flame-dried 50 mL Schlenk flask was added 4,5,6,7-tetrahydrothieno[3,2-c]pyridine HCl salt (1.0 g, 5.7

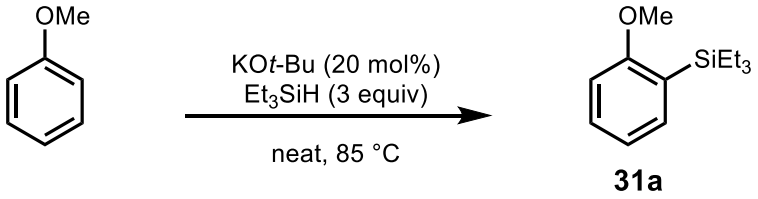
mmol), 2-(bromomethyl)pyridine HBr salt (2.18 g, 8.6 mmol, 1.5 equiv), Bu_4NHSO_4 (0.20 g, 0.6 mmol, 10 mol%), K_2CO_3 (3.94 g, 28.5 mmol, 5 equiv), and 10 mL of acetonitrile. The flask was purged with argon and the reaction was stirred at 70 °C for 18 h. The desired product **29** (346.5 mg, 26% yield) was obtained after purification by silica gel flash chromatography (gradient elution, 50→100% Et_2O in hexanes) as a yellow oil. R_f = 0.1 (50% Et_2O in hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H), 7.67 (td, J = 7.6, 1.8 Hz, 1H), 7.51 (dt, J = 7.9, 1.0 Hz, 1H), 7.19 (ddd, J = 7.5, 4.8, 1.2 Hz, 1H), 7.07 (dt, J = 5.1, 0.7 Hz, 1H), 6.70 (d, J = 5.1 Hz, 1H), 3.89 (s, 2H), 3.64 (t, J = 1.7 Hz, 2H), 2.96 – 2.83 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.79, 149.20, 136.52, 133.78, 133.36, 125.22, 123.13, 122.63, 122.13, 63.82, 53.22, 50.89, 25.50; IR (Neat Film, NaCl) 3403, 3062, 2918, 2813, 1648, 1588, 1569, 1473, 1431, 1356, 1320, 1236, 1167, 1109, 1053, 1015, 993, 905, 840, 809, 761 cm^{-1}; HRMS (EI+) calc'd for $C_{13}H_{13}SN_2$ $[(M+H)-H_2]^+$: 229.0799, found 229.0806.



29 **30**

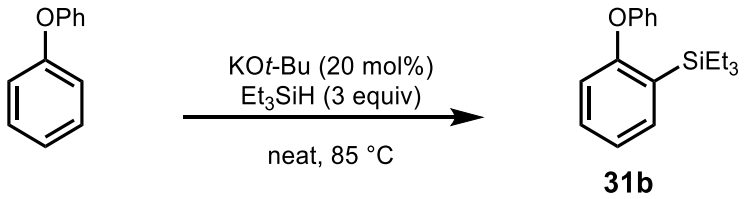
5-(Pyridin-2-ylmethyl)-2-(triethylsilyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine 30: The general procedure was followed. The reaction was performed with KO*t*-Bu (4.5 mg, 0.04 mmol, 20 mol%), 5-(pyridin-2-ylmethyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine **29** (46.1 mg, 0.2 mmol), Et_3SiH (96 μL, 0.6 mmol, 3 equiv), and 0.2 mL of THF at 45 °C for 72 h. The desired product **30** (49.1 mg, 71% yield) was obtained after purification by silica gel flash chromatography (gradient elution, 75→100% Et_2O in hexanes) as a colourless oil. R_f = 0.5 (75% Et_2O in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.66

(td, *J* = 7.7, 1.8 Hz, 1H), 7.50 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.17 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 6.83 (s, 1H), 3.87 (s, 2H), 3.64 (t, *J* = 1.6 Hz, 2H), 2.94 (tt, *J* = 5.3, 1.5 Hz, 2H), 2.86 (dd, *J* = 5.9, 5.0 Hz, 2H), 0.97 (t, *J* = 7.9 Hz, 9H), 0.74 (qd, *J* = 7.7, 0.8 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 149.1, 138.9, 136.5, 135.3, 133.8, 133.0, 123.1, 122.1, 63.9, 53.2, 50.9, 25.8, 7.4, 4.4; IR (Neat Film, NaCl) 3048, 2951, 2873, 2806, 1588, 1569, 1448, 1430, 1361, 1289, 1235, 1169, 1114, 1031, 1005, 992, 908, 835, 757, 735, 718 cm^{-1}; HRMS (EI+) calc'd for $C_{19}H_{29}N_2SSi$ $[M+H]^+$: 345.1821, found 345.1835.



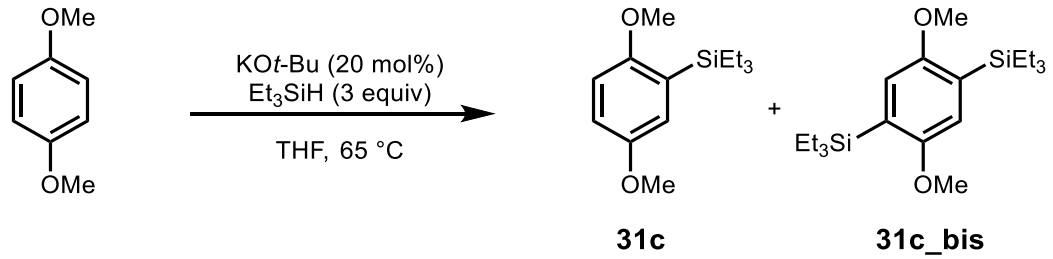
31a

Triethyl(2-methoxyphenyl)silane 31a: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), anisole (54.0 mg, 0.5 mmol, 1 equiv), and Et_3SiH (243 µL, 1.5 mmol, 3 equiv) without any added solvent at 85 °C for 72 h. *ortho*:(*meta* + *para)* > 20:1. The GC yield of desired product **31a** is 65%. The analytically pure product (47.7 mg, 43% yield) was obtained as a colorless oil after evaporation of starting material and volatiles under vacuum (60 mmHg, 23 °C). *Note: compound **31a** is volatile and can be removed under vacuum.* R_f = 0.3 (10% Et_2O in hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.30 (m, 2H), 6.97 (m, 1H), 6.87 – 6.81 (m, 1H), 3.80 (s, 3H), 1.05 – 0.90 (m, 9H), 0.91 – 0.77 (m, 6H).



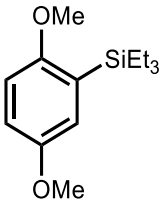
31b

Triethyl(2-phenoxyphenyl)silane 31b: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), oxydibenzene (85.0 mg, 0.5 mmol), and Et_3SiH (240 µL, 1.5 mmol, 3 equiv) without solvent at 85 °C for 120 h. The desired product **31b** (84.5 mg, 55% yield) was obtained after purification by silica gel flash chromatography (100% hexanes) as a colorless oil. R_f = 0.4 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 – 7.46 (m, 1H), 7.38 – 7.25 (m, 3H), 7.10 (t, *J* = 7.4 Hz, 2H), 7.00 (d, *J* = 7.9 Hz, 2H), 6.81 (d, *J* = 8.1 Hz, 1H), 0.97 (t, *J* = 7.9 Hz, 9H), 0.85 (q, *J* = 7.9 Hz, 6H).



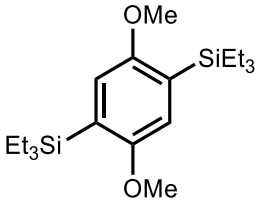
31c **31c_bis**

The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1,4-dimethoxybenzene (69.1 mg, 0.5 mmol), and Et_3SiH (240 µL, 1.5 mmol, 3 equiv), in 0.5 mL of THF at 65 °C for 72 h. The desired product **31c** (53.1 mg, 42% yield) and bis-silylated byproduct **31c_bsis** (16.1 mg, 8% yield) were obtained after purification by silica gel flash chromatography (100% hexanes).

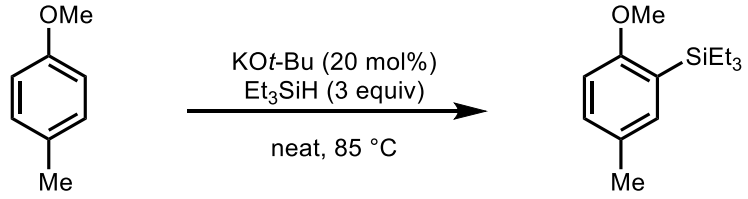


(2,5-Dimethoxyphenyl)triethylsilane 31c: Colorless oil, R_f = 0.5 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.93 (d, *J* = 3.1 Hz, 1H), 6.85 (dd, *J* = 8.8, 3.1 Hz, 1H), 6.76 (d, *J* = 8.8 Hz, 1H), 3.80 (s, 3H), 3.74 (s, 3H), 0.99 – 0.91 (m, 9H), 0.85 – 0.74 (m, 6H); ^{13}C NMR (126 MHz,

$CDCl_3$) δ 158.8, 153.3, 126.7, 122.2, 122.3, 114.1, 55.7, 55.5, 7.6, 3.7; IR (Neat Film, NaCl) 2952, 2873, 1580, 1478, 1463, 1398, 1272, 1220, 1177, 1050, 1026, 872, 800, 769, 732 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{24}O_2Si$ [$M^{+\bullet}$]: 252.1546, found 252.1540.



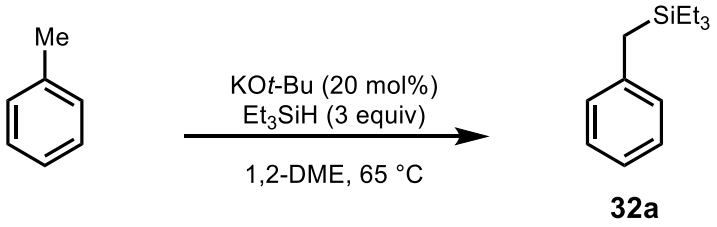
(2,5-Dimethoxy-1,4-phenylene)bis(triethylsilane) 31c_bis: White solid, R_f = 0.8 (100% hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 6.81 (s, 2H), 3.75 (s, 6H), 0.95 (td, *J* = 7.9, 0.9 Hz, 9H), 0.85 – 0.77 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.5, 127.1, 116.9, 55.6, 7.7, 3.8; IR (Neat Film, NaCl) 2948, 2870, 1459, 1418, 1345, 1262, 1203, 1107, 1045, 999, 868, 727, 700 cm^{-1}; HRMS (EI+) calc'd for $C_{20}H_{38}Si_2O_2$ [$M^{+\bullet}$]: 366.2410, found 366.2415.



31d

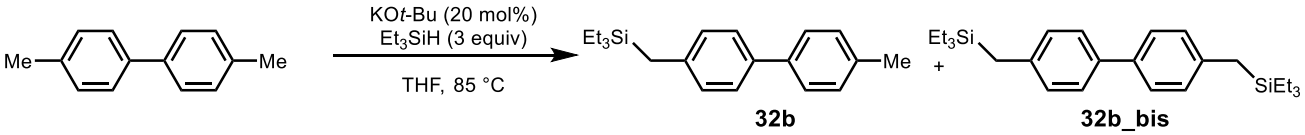
Triethyl(2-methoxy-5-methylphenyl)silane 31d: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-methoxy-4-methylbenzene (61.0 mg, 0.5 mmol), and Et_3SiH (240 µL, 1.5 mmol, 3 equiv) at 85 °C for 120 h. The desired product **31d** (38.5 mg, 32% yield) was obtained after purification by silica gel flash chromatography (100% hexanes) as a colorless oil. R_f = 0.4 (100% hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.17 – 7.08 (m, 2H), 6.74 (dt, *J* = 8.7, 1.3 Hz, 1H), 3.76 (s, 3H), 2.30 (s, 3H), 0.97 – 0.92 (m, 9H), 0.85 – 0.79 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.7, 136.7, 130.9,

129.2, 125.0, 109.5, 55.2, 20.8, 7.8, 3.7; IR (Neat Film, NaCl) 2951, 2873, 1595, 1480, 1464, 1385, 1238, 1175, 1147, 1081, 1034, 1004, 876, 806, 708 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{24}OSi$ [$M^{+\bullet}$]: 236.1596, found 236.1598.



32a

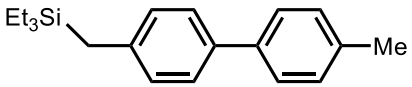
Benzyltriethylsilane 32a: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), toluene (46 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 µL, 1.5 mmol, 3 equiv) and DME (0.5 mL) at 65 °C for 108 h. $C(sp^3)$:$C(sp^2)$ = 18:1. The GC yield of desired product **32a** is 53%. The analytically pure product (25.0 mg, 24% yield) was obtained as a colorless oil after evaporation of starting material and volatiles under vacuum (60 mmHg, 23 °C). *Note: compound **18a** is volatile and readily removed under vacuum.* R_f = 0.8 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (m, 2H), 7.09 – 7.05 (m, 1H), 7.05 – 7.02 (m, 2H), 2.12 (s, 2H), 0.96 – 0.91 (t, 9H), 0.53 (q, *J* = 7.9 Hz, 6H).



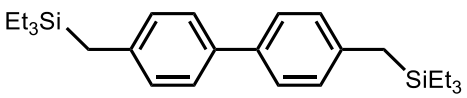
32b **32b_bis**

Triethyl((4'-methyl-[1,1'-biphenyl]-4-yl)methyl)silane 32b: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 23 mol%), 4,4'-dimethyl-1,1'-biphenyl (80.0 mg, 0.44 mmol), Et_3SiH (240 µL, 1.5 mmol, 3.4 equiv), and 0.5 mL of THF at 85 °C for 96 h. The ratio of mono-silylation product to bis-silylation product is 16:1. A mixture of desired product **32b** and starting material 4,4'-dimethyl-1,1'-biphenyl (*69.7 mg of mixture, contains 56.6 mg of **32b**, 43% yield, calculated based on ^{1}H NMR*) was obtained after

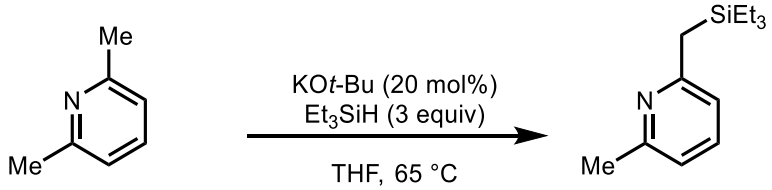
purification by silica gel flash chromatography (100% hexanes). *A small fraction of analytically pure compound **32b_bis** was obtained as a colorless oil after subsequent purification by silica gel flash chromatography.* R_f = 0.5 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 – 7.47 (m, 2H), 7.46 – 7.42 (m, 2H), 7.25 – 7.21 (m, 2H), 7.11 – 7.04 (m, 2H), 2.39 (s, 3H), 2.14 (s, 2H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.54 (q, *J* = 8.0 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.7, 138.5, 136.7, 136.5, 129.6, 128.6, 126.8, 126.7, 21.4, 21.2, 7.5, 3.1; IR (Neat Film, NaCl) 3022, 2951, 2909, 2873, 1610, 1497, 1455, 1416, 1238, 1209, 1153, 1005, 845, 806, 773, 729 cm^{-1}; HRMS (EI+) calc'd for $C_{20}H_{28}Si$ [$M^{+\bullet}$]: 296.1960, found 296.1954.



2-Methyl-6-((triethylsilyl)methyl)pyridine 32b: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2,6-lutidine (53.5 mg, 0.5 mmol), Et_3SiH (240 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 65 °C for 120 h. The desired product **32b** (58.6 mg, 53% yield) was obtained after purification by silica gel flash chromatography (gradient elution, 5%→10% EtOAc in hexanes) as a colorless oil. *Note: compound **18c** is volatile and is readily removed under vacuum.* R_f = 0.3 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (t, *J* = 7.6 Hz, 1H), 6.90 – 6.73 (m, 2H), 2.47 (s, 3H), 2.32 (s, 2H), 0.98 – 0.83 (m, 9H), 0.58 – 0.48 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.8, 157.4, 135.9, 119.0, 118.4, 25.4, 24.5, 7.2, 3.3; IR (Neat Film, NaCl) 3060, 2951, 2874, 1587, 1575, 1450, 1414, 1372, 1269, 1238, 1145, 1078, 1016, 919, 796, 748, 726 cm^{-1}; HRMS (EI+) calc'd for $C_{13}H_{24}NSi$ [M+H]$^+$: 222.1678, found 222.1666.



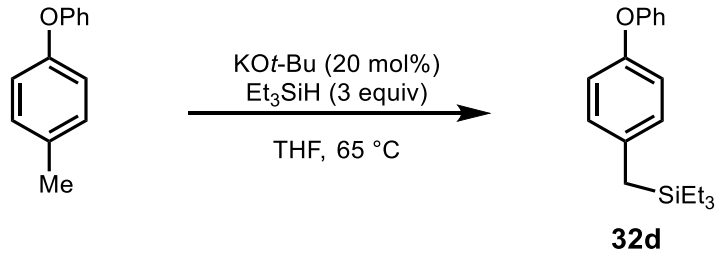
Triethyl(phenoxy(phenyl)methyl)silane 32b_bis: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), (benzyloxy)benzene (92.0 mg, 0.5 mmol), Et_3SiH (240 μL, 1.5 mmol, 3 equiv), and 0.25 mL of THF at 65 °C for 120 h. The desired product **32b_bis** (68.4 mg, 46% yield) was obtained after purification by silica gel flash chromatography (100% hexanes) as a colorless oil. R_f = 0.3 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.37 (m, 4H), 7.38 – 7.28 (m, 4H), 7.30 – 7.20 (m, 2H), 5.80 (s, 1H), 0.92 (t, *J* = 7.9 Hz, 9H), 0.66 – 0.55 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.3, 128.1, 128.1, 126.9, 126.9, 126.4, 126.3, 6.7, 4.9; IR (Neat Film, NaCl) 3063, 3026, 2954, 2875, 1598, 1492, 1454, 1413, 1302, 1239, 1188, 1090, 1065, 1006, 974, 833, 740, 700 cm^{-1}; HRMS (EI+) calc'd for $C_{19}H_{25}OSi$ $[(M+H)-H_2]^+$: 297.1675, found 297.1668.



32c

2-Methyl-6-((triethylsilyl)methyl)pyridine 32c: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2,6-lutidine (53.5 mg, 0.5 mmol), Et_3SiH (240 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 65 °C for 120 h. The desired product **32c** (58.6 mg, 53% yield) was obtained after purification by silica gel flash chromatography (gradient elution, 5%→10% EtOAc in hexanes) as a colorless oil. *Note: compound **32c** is volatile and is readily removed under vacuum.* R_f = 0.3 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (t, *J* = 7.6 Hz, 1H), 6.9 – 6.73 (m, 2H), 2.47 (s, 3H), 2.32 (s, 2H), 0.98 – 0.83 (m, 9H), 0.58 – 0.48 (m, 6H); ^{13} NMR (126 MHz, $CDCl_3$) δ 160.8, 157.4, 135.9, 119.0, 118.4, 25.4, 24.5, 7.2, 3.3; I (Neat Film, NaCl) 3060, 2951, 2874, 1587, 1575, 1450, 1414,

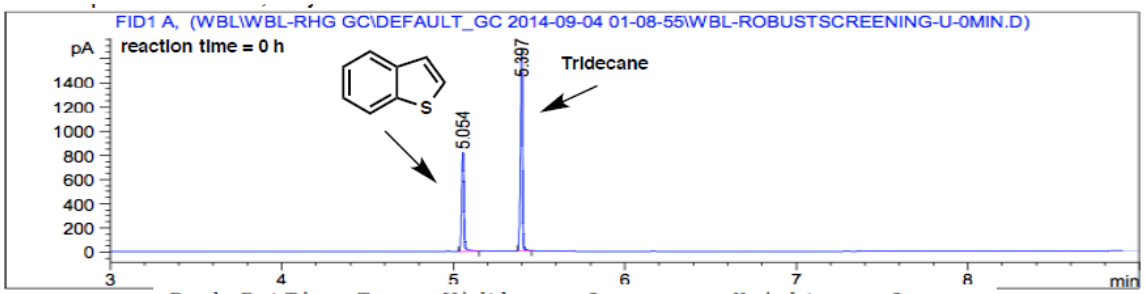
1372, 1269, 1238, 1145 1078, 1016, 919, 796, 748, 726 cm^{-1}; HRMS (EI+) calc'd for $C_{13}H_{24}NSi$ $[M+H]^+$ 222.1678, found 222.1666.



32d

Triethyl(phenoxy(phenyl)methyl)silane 32d: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), (benzyloxy)benzene (92.0 mg, 0.5 mmol), Et_3SiH (240 µL, 1.5 mmol, 3 equiv), and 0.25 mL of THF at 65 °C for 120 h. The desired product **32d** (68.4 mg, 46% yield) was obtained after purification by silica gel flash chromatography (100% hexanes) as a colorless oil. R_f = 0.3 (100% hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.37 (m, 4H), 7.38 – 7.28 (m, 4H), 7.30 – 7.20 (m, 2H), 5.80 (s, 1H), 0.92 (t, *J* = 7.9 Hz, 9H), 0.66 – 0.55 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.3, 128.1, 128.1, 126.9, 126.9, 126.4, 126.3, 6.7, 4.9; IR (Neat Film, NaCl) 3063, 3026, 2954, 2875, 1598, 1492, 1454, 1413, 1302, 1239, 1188, 1090, 1065, 1006, 974, 833, 740, 700 cm^{-1}; HRMS (EI+) calc'd for $C_{19}H_{25}OSi$ $[(M+H)-H_2]^+$: 297.1675, found 297.1668.

GC–FID spectra from the robustness investigation (Wen-Bo Liu)



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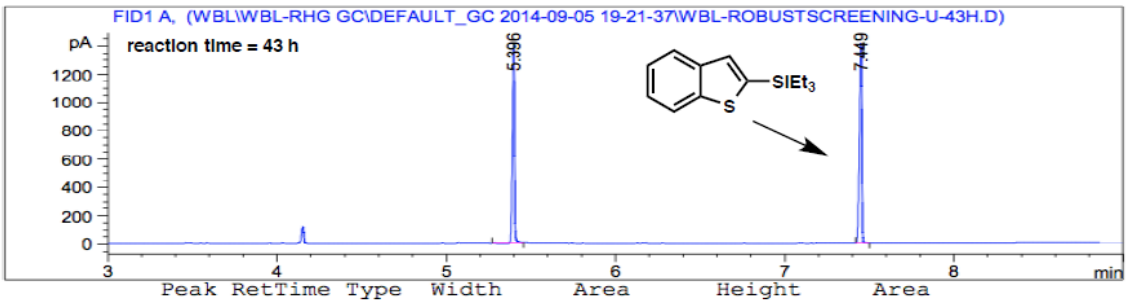

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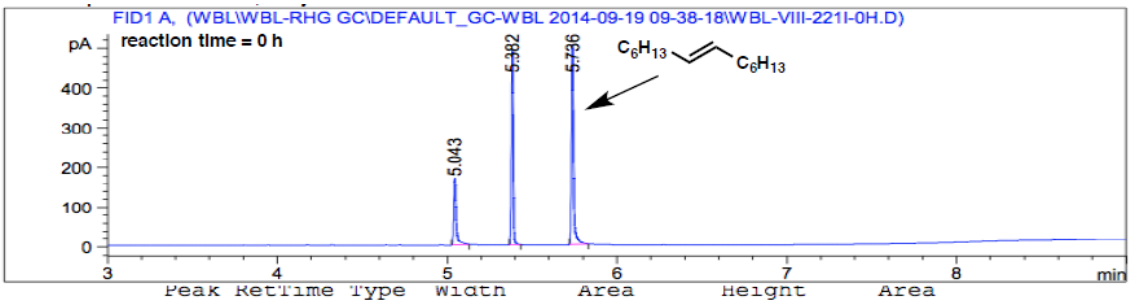

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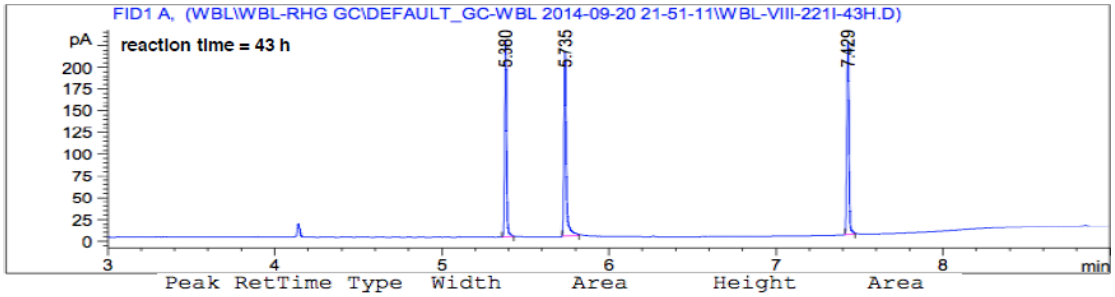

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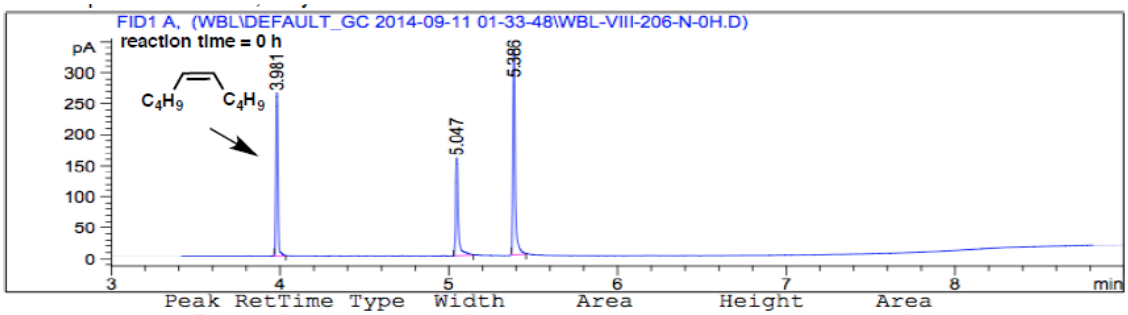

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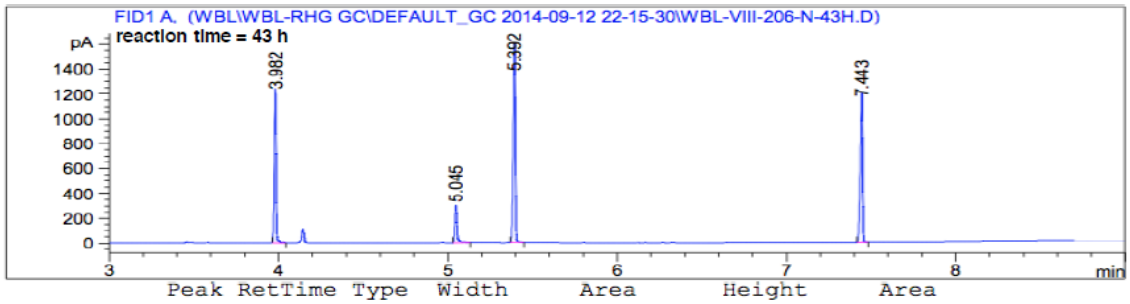

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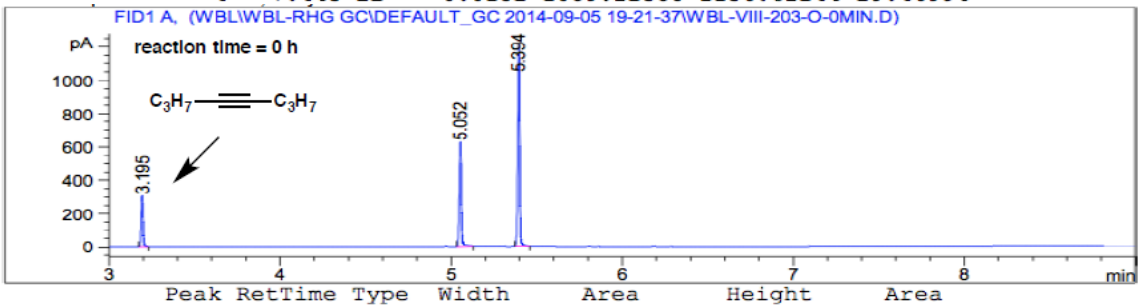

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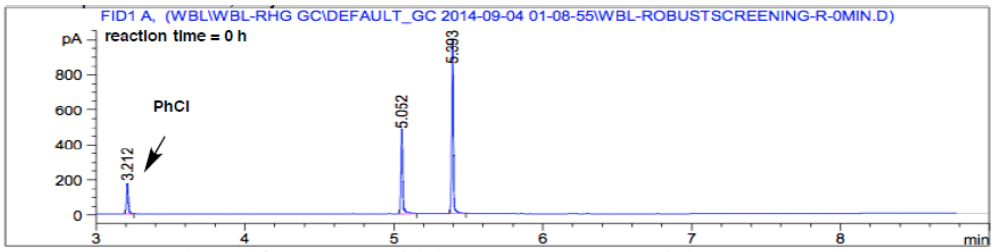

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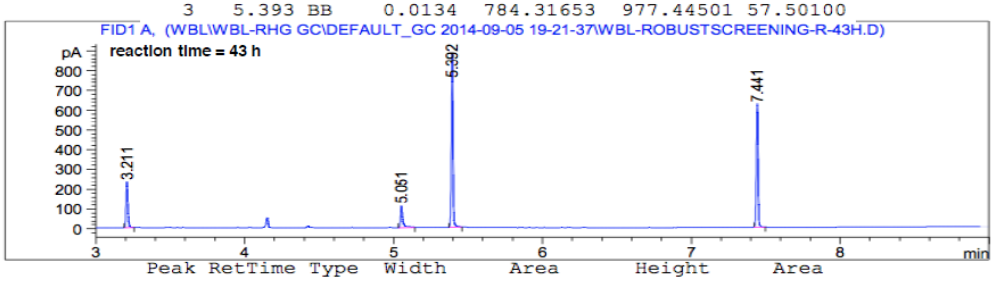

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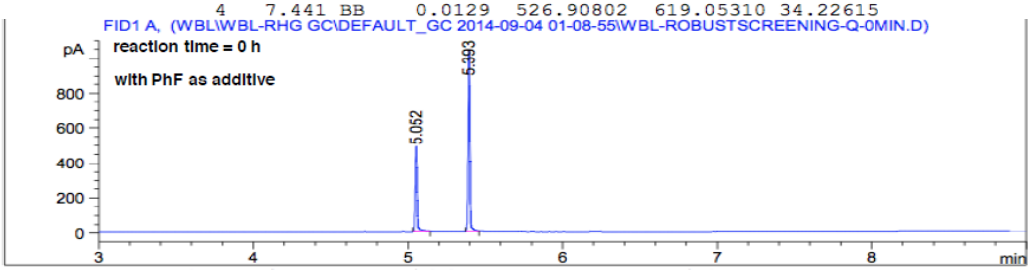

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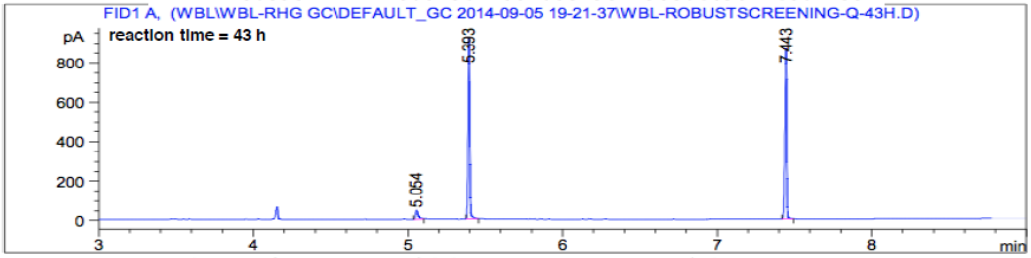
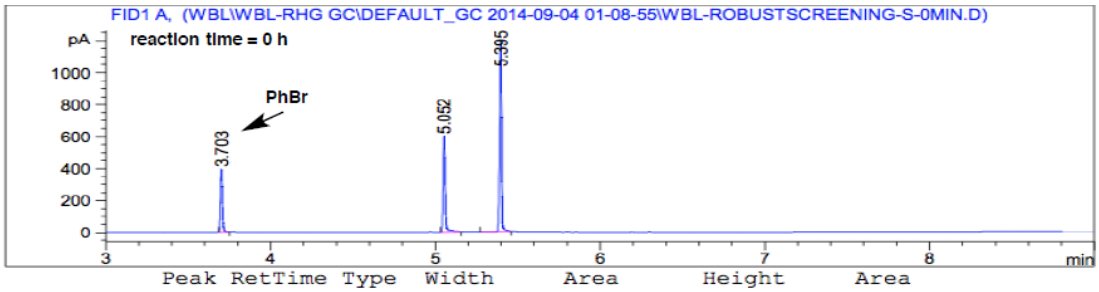
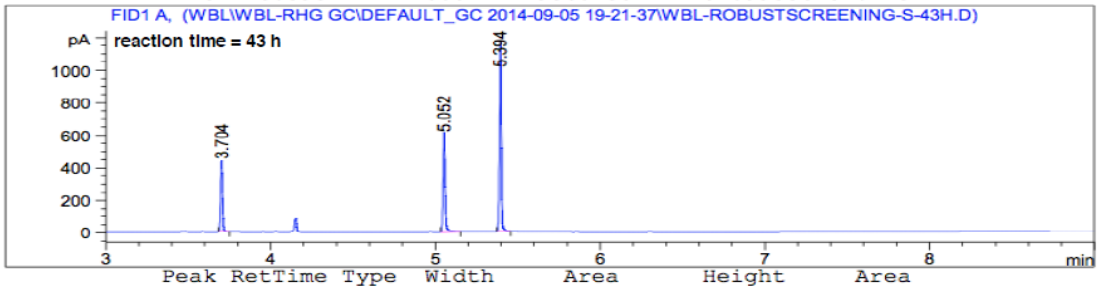
1	5.052	BB	0.0134	432.28278	483.75388	34.88006
2	5.393	BB	0.0136	807.05798	983.66907	65.11994



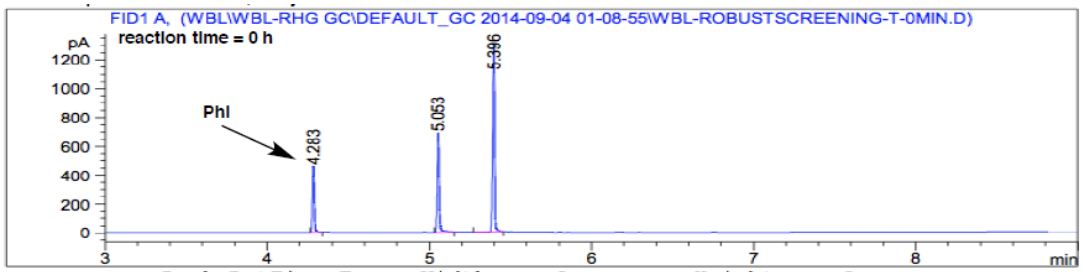
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.054	BB	0.0185	60.12766	48.45945	3.97540
2	5.393	BB	0.0136	724.24512	882.39813	47.88423
3	7.443	BB	0.0138	728.11908	866.32690	48.14036



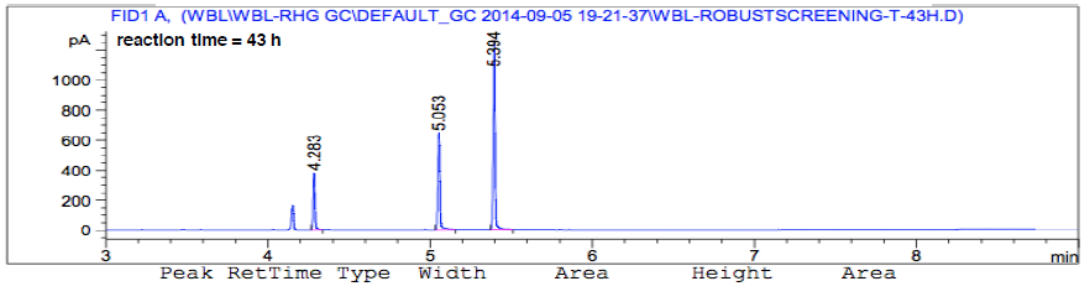
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.703	BB	0.0137	321.18744	384.43445	17.70586
2	5.052	BB	0.0146	536.59937	587.90198	29.58071
3	5.395	BB	0.0124	956.23077	1187.99536	52.71342



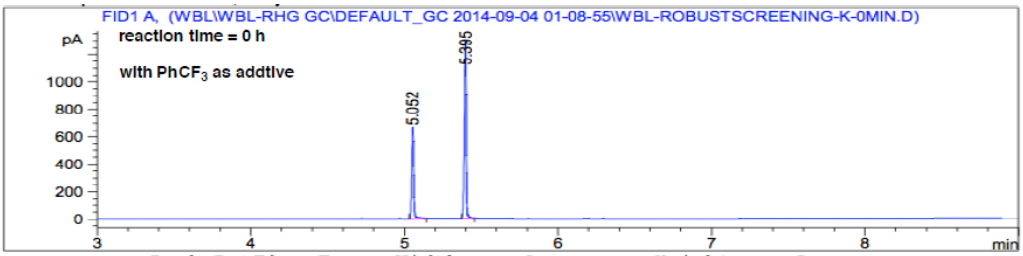
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.704	BB	0.0137	354.46970	425.76340	19.23968
2	5.052	BB	0.0134	533.08838	597.62415	28.93462
3	5.394	BB	0.0136	954.83105	1163.62964	51.82570



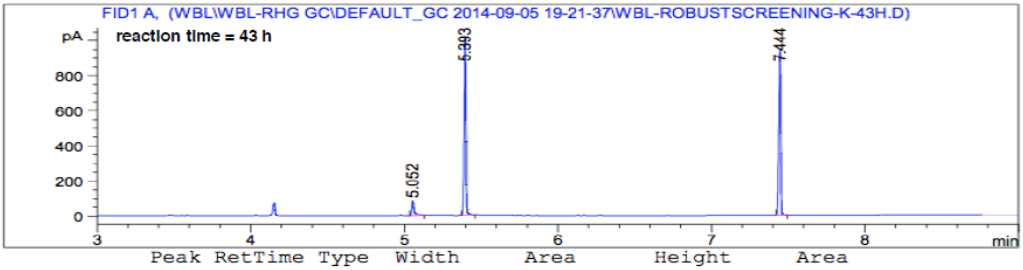
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.283	BB	0.0138	372.08484	444.89694	18.28708
2	5.053	BB	0.0145	604.12518	671.07733	29.69130
3	5.396	BB	0.0127	1058.47729	1274.90295	52.02162



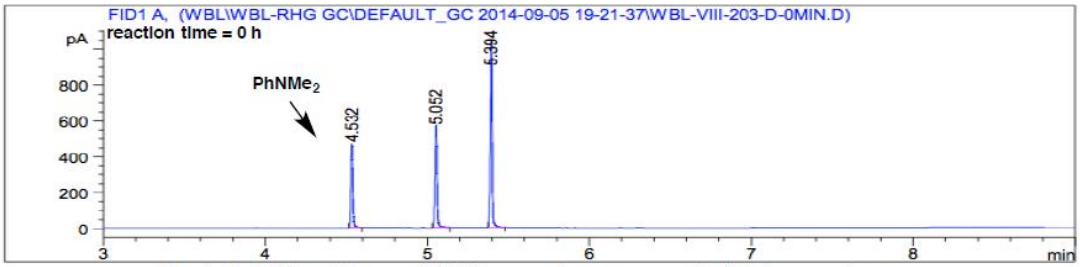
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.283	BB	0.0126	305.44244	372.80069	16.14080
2	5.053	BB	0.0146	577.15674	635.40320	30.49928
3	5.394	BB	0.0135	1009.76276	1238.18677	53.35992



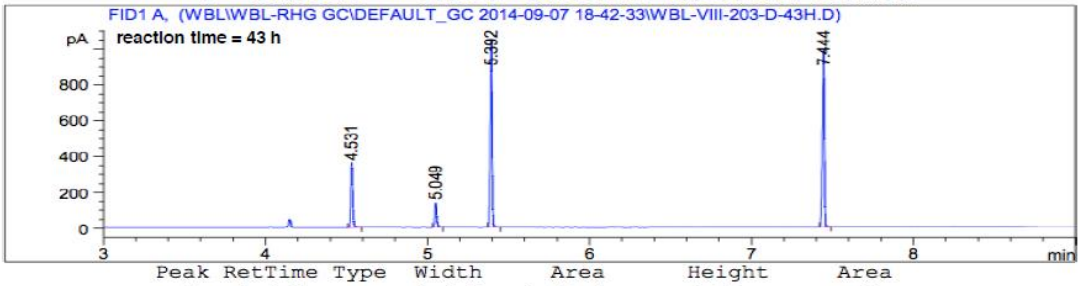
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.052	BB	0.0135	588.29590	655.02374	35.17884
2	5.395	BB	0.0130	1084.00464	1270.07581	64.82116



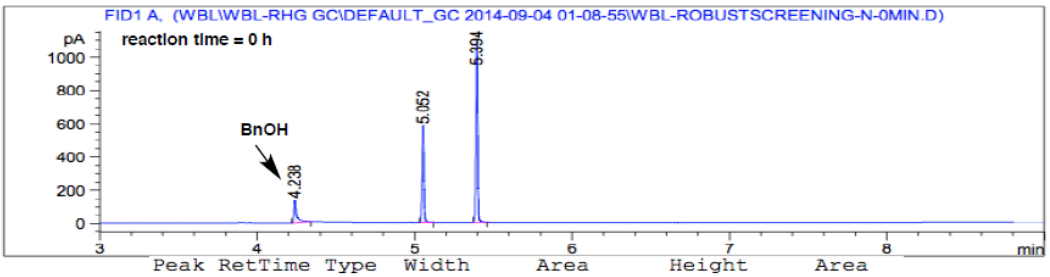
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.052	BB	0.0160	88.95304	79.72253	5.24940
2	5.393	BB	0.0138	804.46118	955.82367	47.47379
3	7.444	BB	0.0139	801.12335	939.42273	47.27681



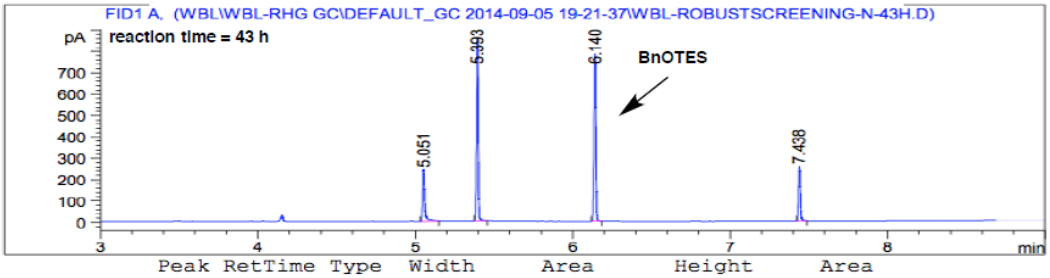
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.532	BB	0.0137	377.70926	454.98398	21.89827
2	5.052	BB	0.0145	499.47571	553.67822	28.95787
3	5.394	BB	0.0126	847.65112	1034.31641	49.14387



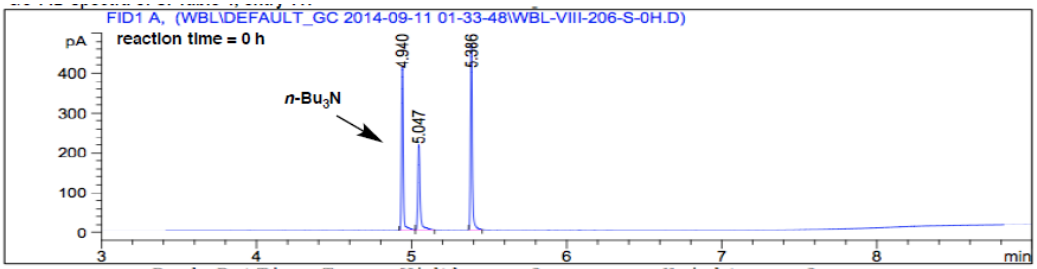
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.531	BB	0.0138	297.83487	354.08572	14.02392
2	5.049	BB	0.0146	121.14701	133.53572	5.70436
3	5.392	BB	0.0127	842.06940	1013.86646	39.64987
4	7.444	BB	0.0142	862.71204	989.58295	40.62185



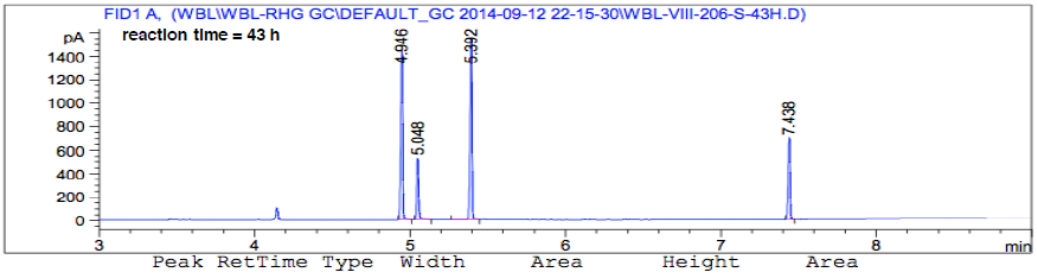
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.238	BB	0.0190	164.34883	127.53644	10.89584
2	5.052	BB	0.0130	489.51434	571.82513	32.45335
3	5.394	BB	0.0132	854.50006	1081.55774	56.65081



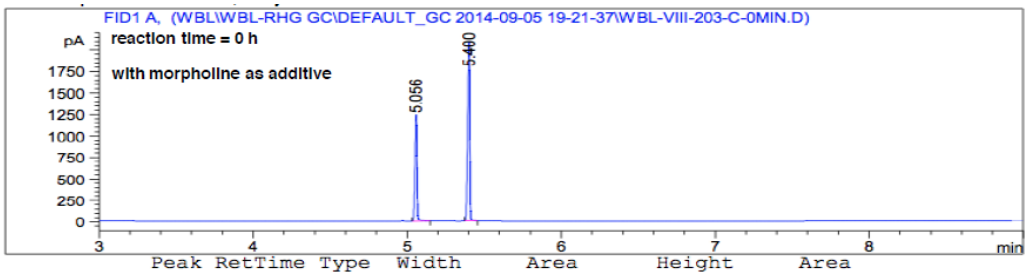
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.051	BB	0.0157	237.87219	237.71118	14.04074
2	5.393	BB	0.0130	629.44916	818.91058	37.15411
3	6.140	BB	0.0137	623.10913	746.75342	36.77988
4	7.438	BB	0.0124	203.72693	254.05693	12.02527



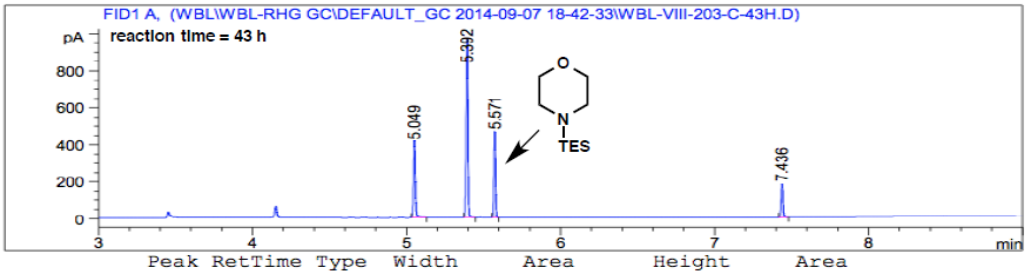
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.940	BV	0.0137	330.20572	398.56238	35.52488
2	5.047	VB	0.0164	219.53682	207.19090	23.61867
3	5.386	BB	0.0127	379.76306	457.34445	40.85646



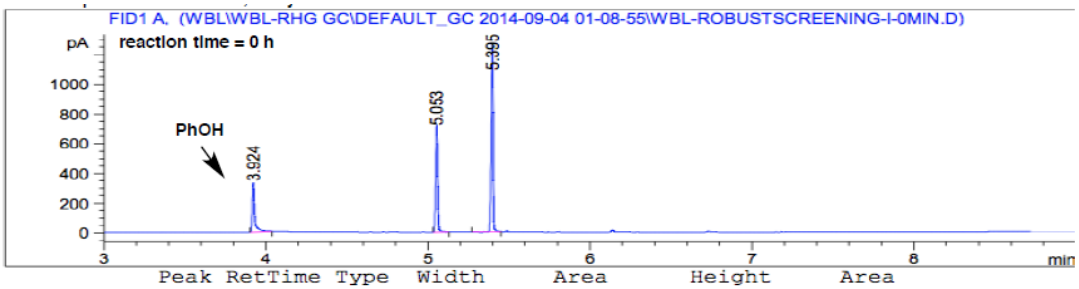
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.946	BB	0.0141	1203.80591	1394.00037	33.46110
2	5.048	BB	0.0145	471.45068	522.15521	13.10449
3	5.392	BB	0.0132	1334.67249	1523.16736	37.09868
4	7.438	BB	0.0129	587.69885	689.41693	16.33573



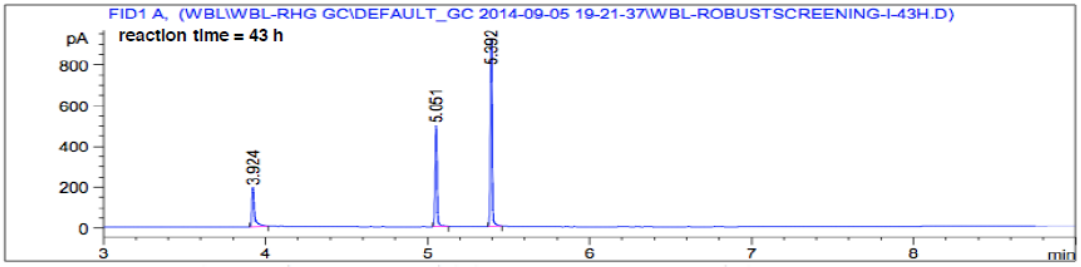
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.056	BB	0.0146	1114.04028	1226.71338	36.92116
2	5.400	BB	0.0154	1903.30896	1953.58960	63.07884



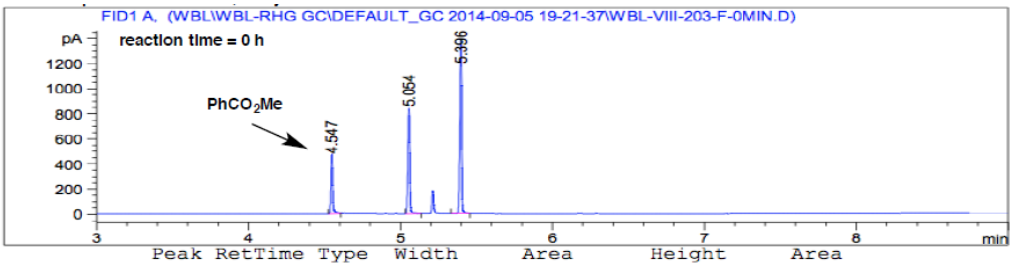
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.049	BB	0.0143	359.11511	406.27972	21.90699
2	5.392	BB	0.0126	783.82477	952.01721	47.81542
3	5.571	BB	0.0116	338.93201	457.76031	20.67577
4	7.436	BB	0.0144	157.39992	176.92252	9.60182



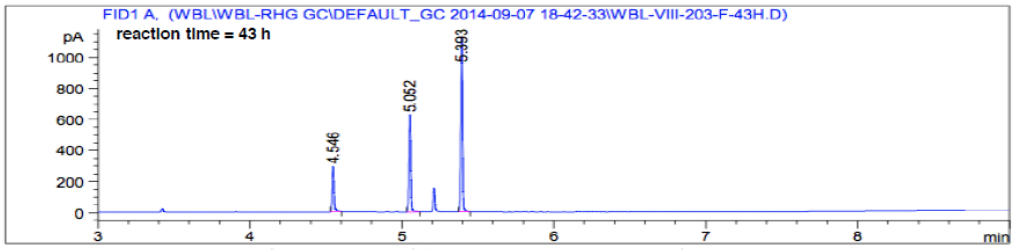
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.924	BB	0.0167	347.61041	318.65836	17.61199
2	5.053	BB	0.0141	596.71674	691.87122	30.23318
3	5.395	BB	0.0129	1029.38770	1215.88281	52.15483



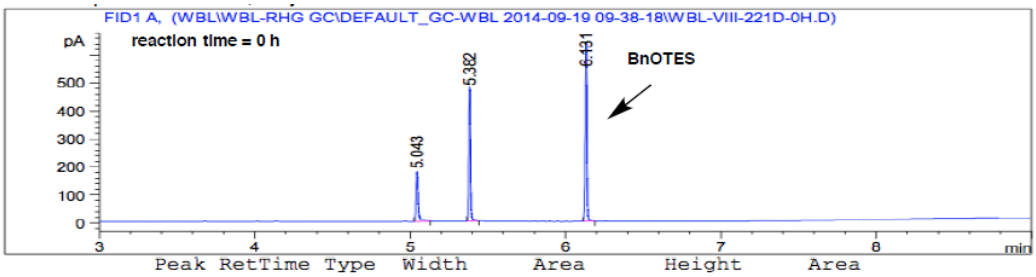
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.924	BB	0.0177	219.71886	186.97559	16.18693
2	5.051	BB	0.0130	419.85248	489.05118	30.93100
3	5.392	BB	0.0124	717.81268	889.42621	52.88206



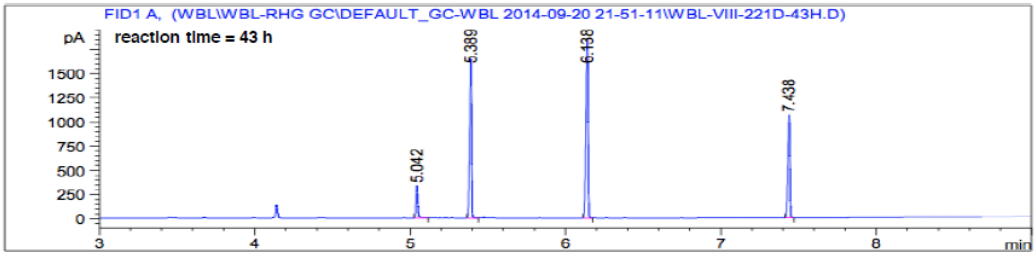
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.547	BB	0.0138	379.91116	454.35962	16.80495
2	5.054	BB	0.0140	708.21655	824.81445	31.32717
3	5.396	BB	0.0144	1172.58264	1309.76538	51.86788



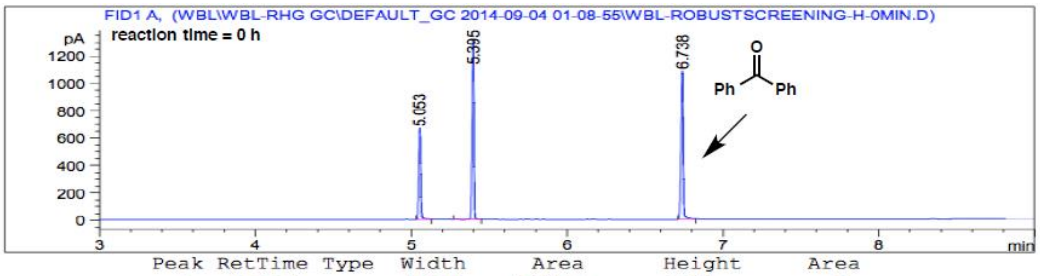
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.546	BB	0.0128	239.78859	286.69708	14.65431
2	5.052	BB	0.0127	514.46545	616.55530	31.44076
3	5.393	BB	0.0137	882.04706	1057.42419	53.90494



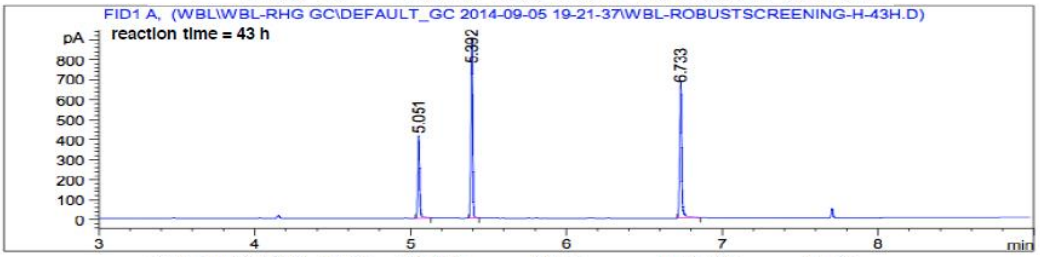
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.043	BB	0.0157	177.43666	176.76627	17.25147
2	5.382	BB	0.0117	350.31625	472.30042	34.05988
3	6.131	BB	0.0132	500.77747	634.92981	48.68864



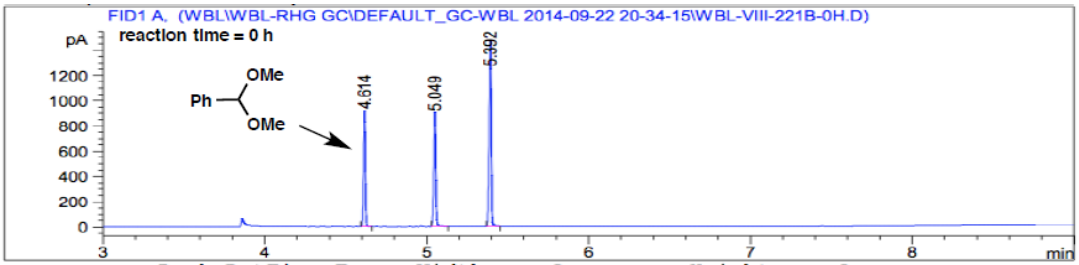
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.042	BB	0.0130	285.85907	334.54684	6.61147
2	5.389	BB	0.0130	1359.89429	1584.62854	31.45222
3	6.138	BB	0.0152	1734.73511	1799.69421	40.12170
4	7.438	BB	0.0144	943.19476	1057.01978	21.81461



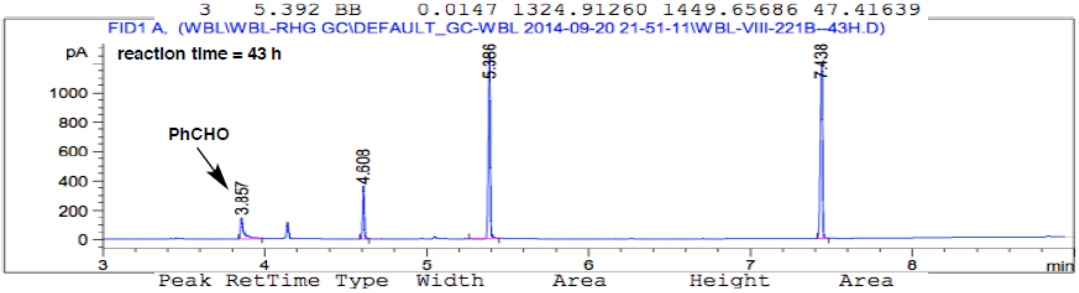
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.053	BB	0.0144	581.33722	653.60175	22.02989
2	5.395	BB	0.0123	1024.88892	1285.39587	38.83837
3	6.738	BB	0.0152	1032.63074	1078.53052	39.13174



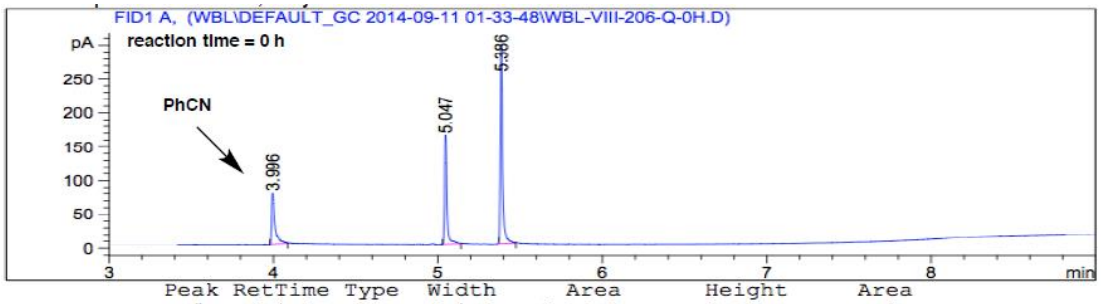
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.051	BB	0.0144	362.96750	408.90005	20.54536
2	5.392	BB	0.0123	701.74109	884.47821	39.72125
3	6.733	BB	0.0153	643.90259	665.52136	36.44737
4	10.496	BB	0.0239	58.05304	35.86992	3.28603



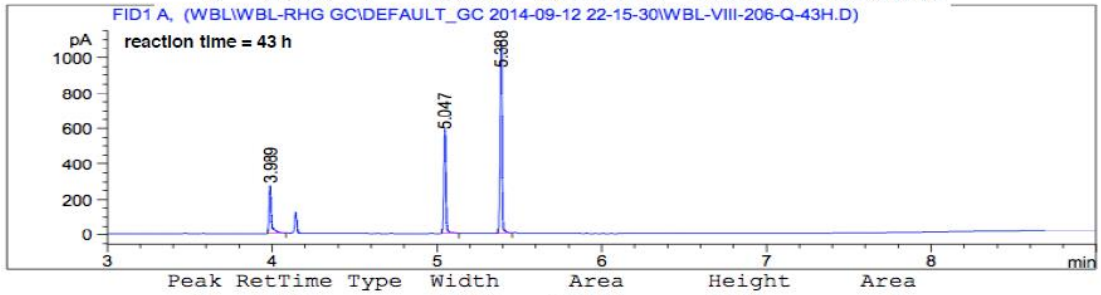
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.614	BB	0.0131	700.10925	902.38428	25.05573
2	5.049	BB	0.0131	769.18634	887.87695	27.52788
3	5.392	BB	0.0147	1324.91260	1449.65686	47.41639



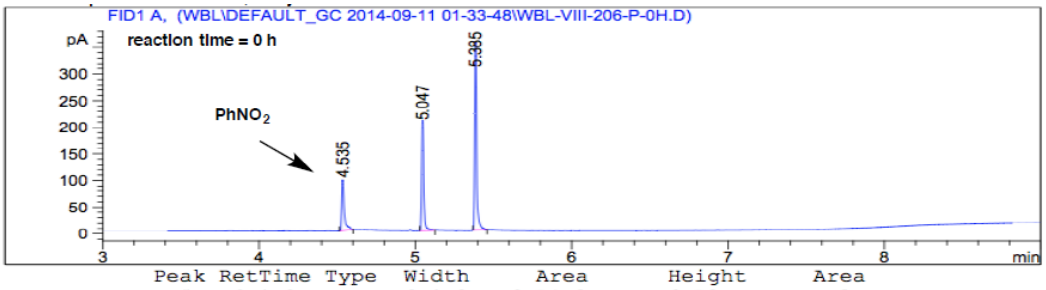
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.857	BB	0.0214	205.34763	137.73538	7.82671
2	4.608	BB	0.0129	268.36557	350.84610	10.22861
3	5.386	BB	0.0127	1024.33691	1225.97473	39.04203
4	7.438	BB	0.0151	1125.62695	1178.64563	42.90265



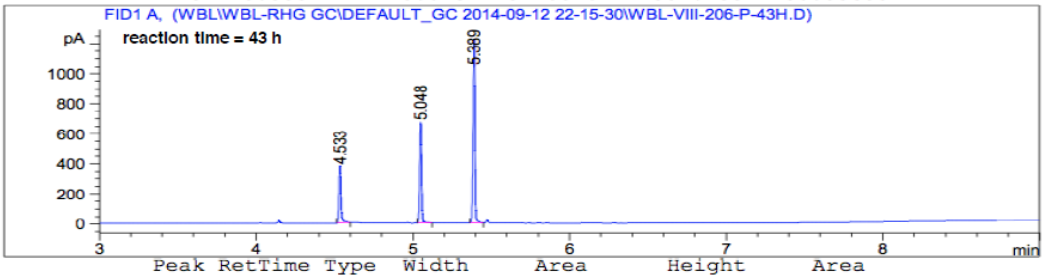
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.996	BB	0.0203	104.37083	74.60351	19.55841
2	5.047	BB	0.0158	161.13466	159.39436	30.19557
3	5.386	BB	0.0149	268.13120	286.23087	50.24602



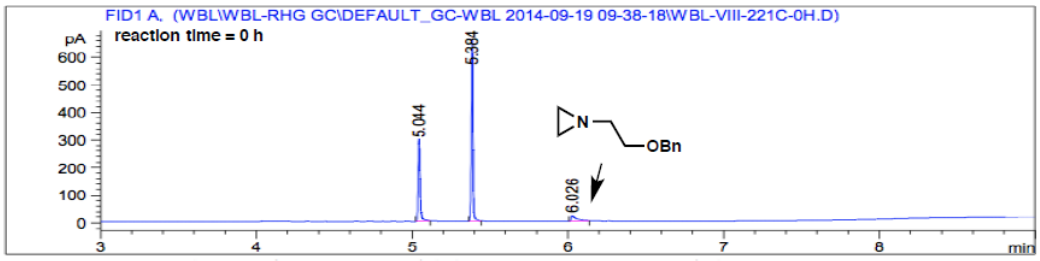
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.989	BB	0.0154	283.01514	267.23007	16.80506
2	5.047	BB	0.0144	506.30051	569.71454	30.06345
3	5.388	BV	0.0137	894.79102	1078.10925	53.13149



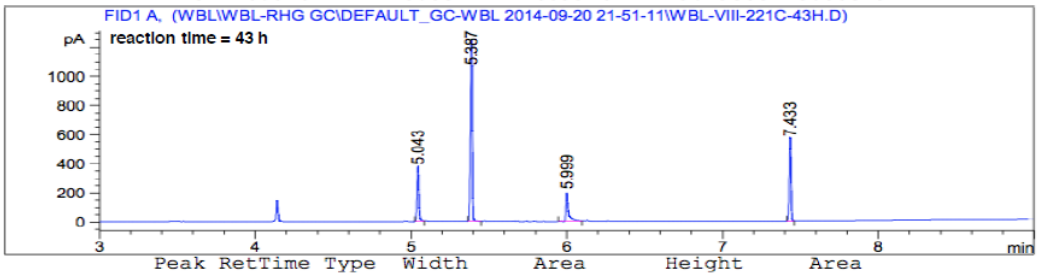
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.535	BB	0.0177	111.61236	94.77935	18.16164
2	5.047	BB	0.0150	190.39711	201.12346	30.98156
3	5.385	BB	0.0134	312.54041	351.13321	50.85680



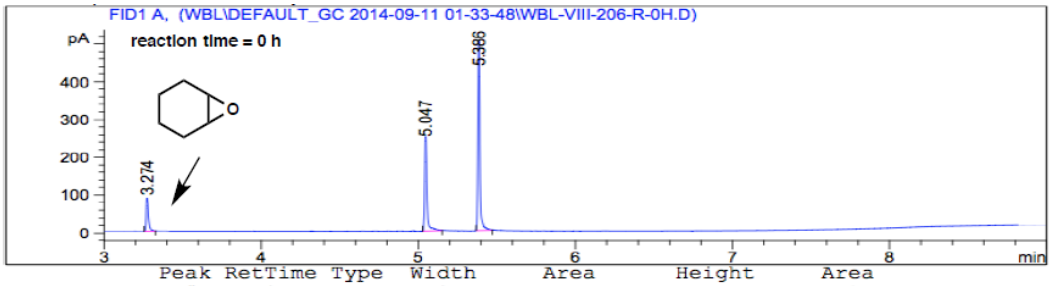
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.533	BB	0.0150	347.16339	367.95538	18.21877
2	5.048	BB	0.0130	570.93298	664.53088	29.96196
3	5.389	BV	0.0141	987.42975	1141.82764	51.81927



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.044	BB	0.0144	259.58676	290.56866	32.05666
2	5.384	BB	0.0130	503.19037	649.27142	62.13955
3	6.026	BB	0.0314	46.99762	19.29555	5.80379



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.043	BB	0.0129	312.46866	367.83182	15.38465
2	5.387	BB	0.0140	1016.13641	1183.95178	50.03032
3	5.999	BB	0.0168	232.78250	197.34129	11.46124
4	7.433	BB	0.0138	469.65353	557.11810	23.12378



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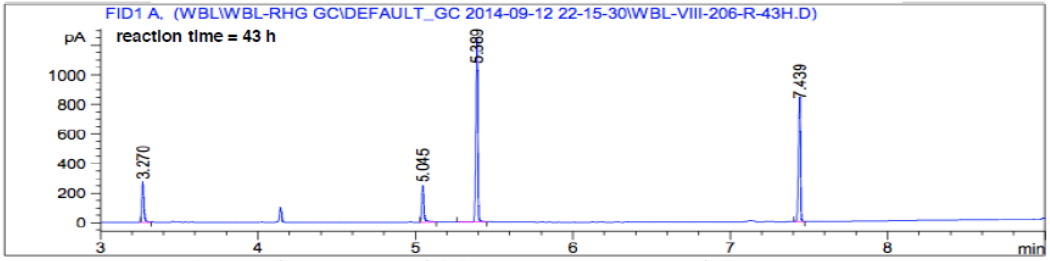
1	3.274	BB	0.0155	84.74000	86.20313	11.10321
2	5.047	BB	0.0159	247.62512	242.42696	32.44551
3	5.386	BB	0.0143	430.83789	489.86090	56.45128



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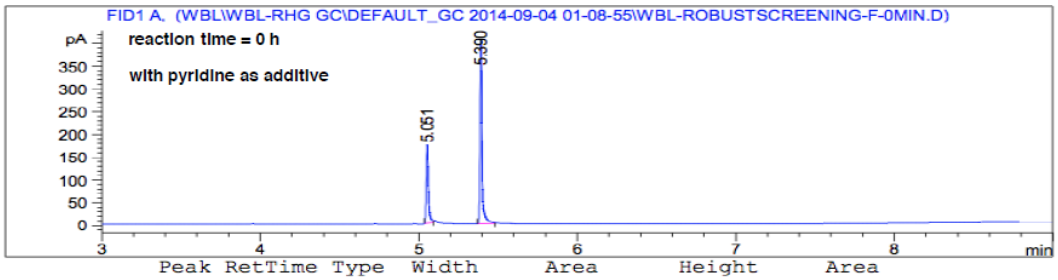
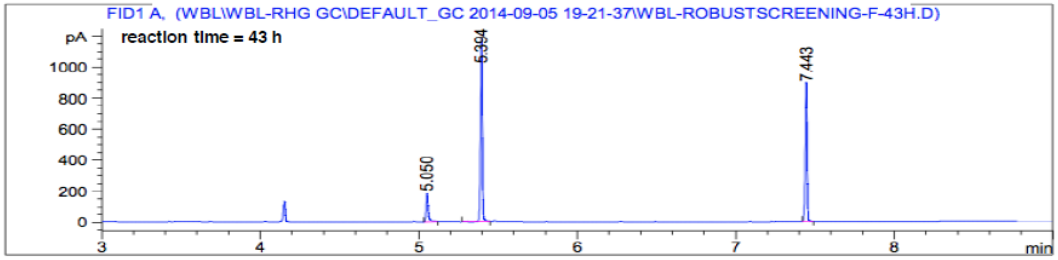
1	3.270	BB	0.0145	237.99971	264.70377	10.68970
2	5.045	BB	0.0140	228.91533	242.20050	10.28168
3	5.389	BB	0.0141	1037.04797	1199.63281	46.57877
4	7.439	BB	0.0144	722.47601	810.45892	32.44985



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.051	BB	0.0138	156.20609	168.59203	31.01447
2	5.390	BB	0.0143	347.44943	394.23758	68.98553



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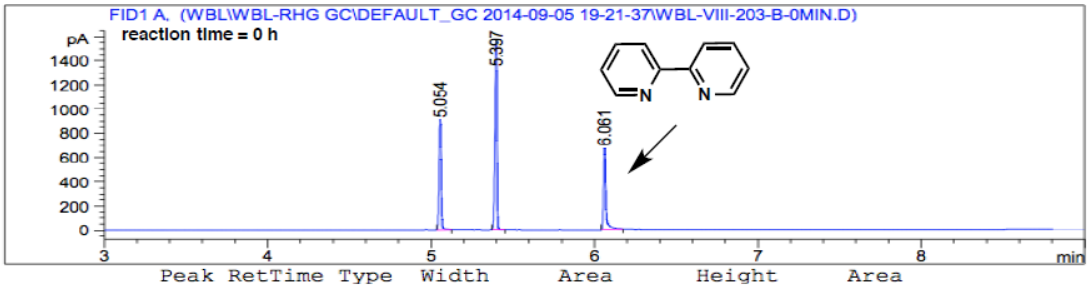
1	5.050	BB	0.0150	166.53435	176.15463	8.89926
2	5.394	BB	0.0135	951.68530	1171.16174	50.85614
3	7.443	BB	0.0140	753.10858	882.47650	40.24460



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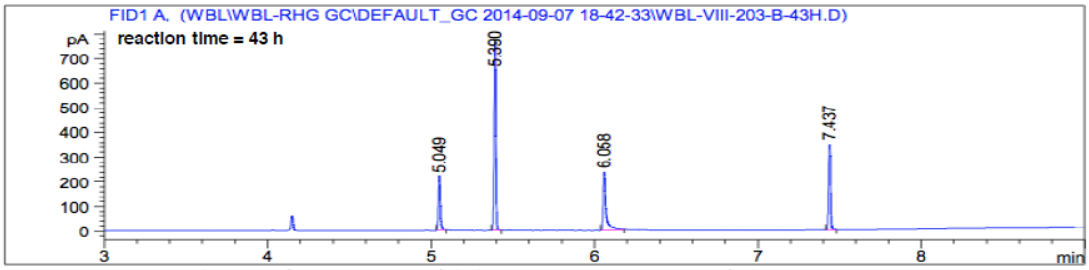
1	5.054	BB	0.0142	784.29218	899.93848	28.42038
2	5.397	BB	0.0137	1296.84875	1561.22388	46.99389
3	6.061	BB	0.0159	678.47058	665.00964	24.58573



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1	5.049	BB	0.0130	186.29955	217.96092	14.19997
2	5.390	BB	0.0126	550.36261	746.06616	41.94928
3	6.058	BB	0.0183	287.27814	233.70592	21.89667
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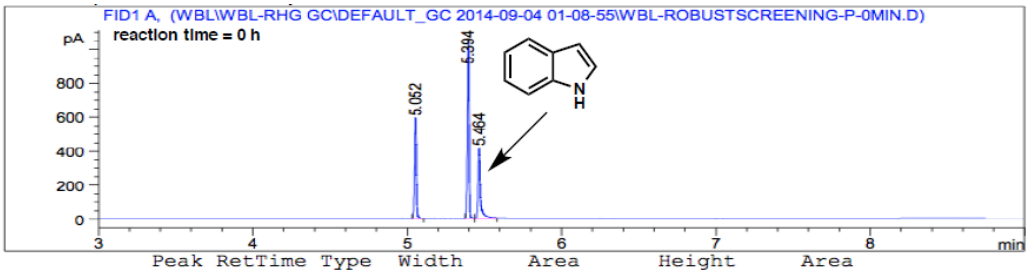

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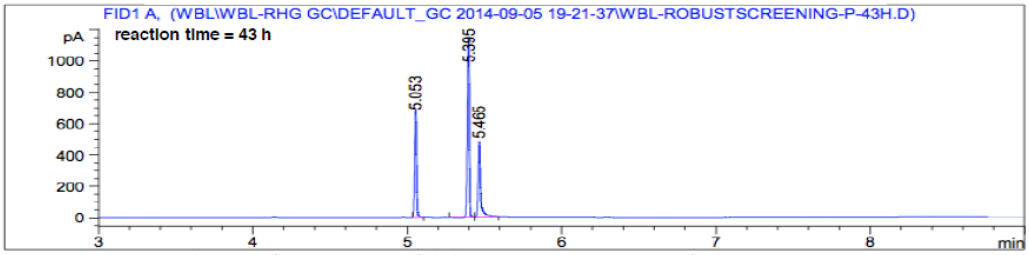
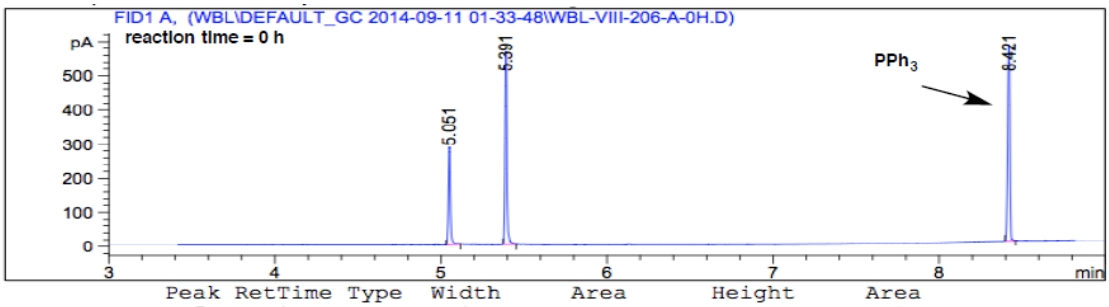
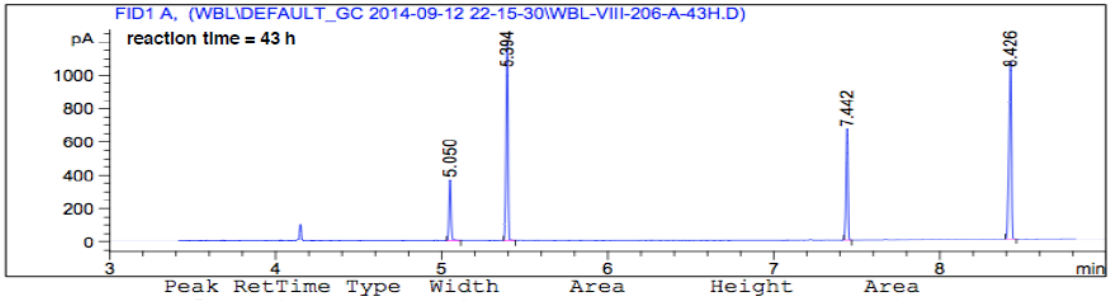


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.053	BB	0.0140	566.89130	664.10944	27.16086
2	5.395	BV	0.0144	991.34656	1110.61658	47.49734
3	5.465	VB	0.0170	528.92432	473.68710	25.34179



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.051	BB	0.0144	250.97217	282.10843	20.80203
2	5.391	BB	0.0122	436.13669	555.49304	36.14953
3	8.421	BB	0.0146	519.37061	570.63788	43.04844



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1	5.050	BB	0.0139	308.54736	363.27356	10.49166
2	5.394	BB	0.0125	970.49554	1192.30505	33.00015
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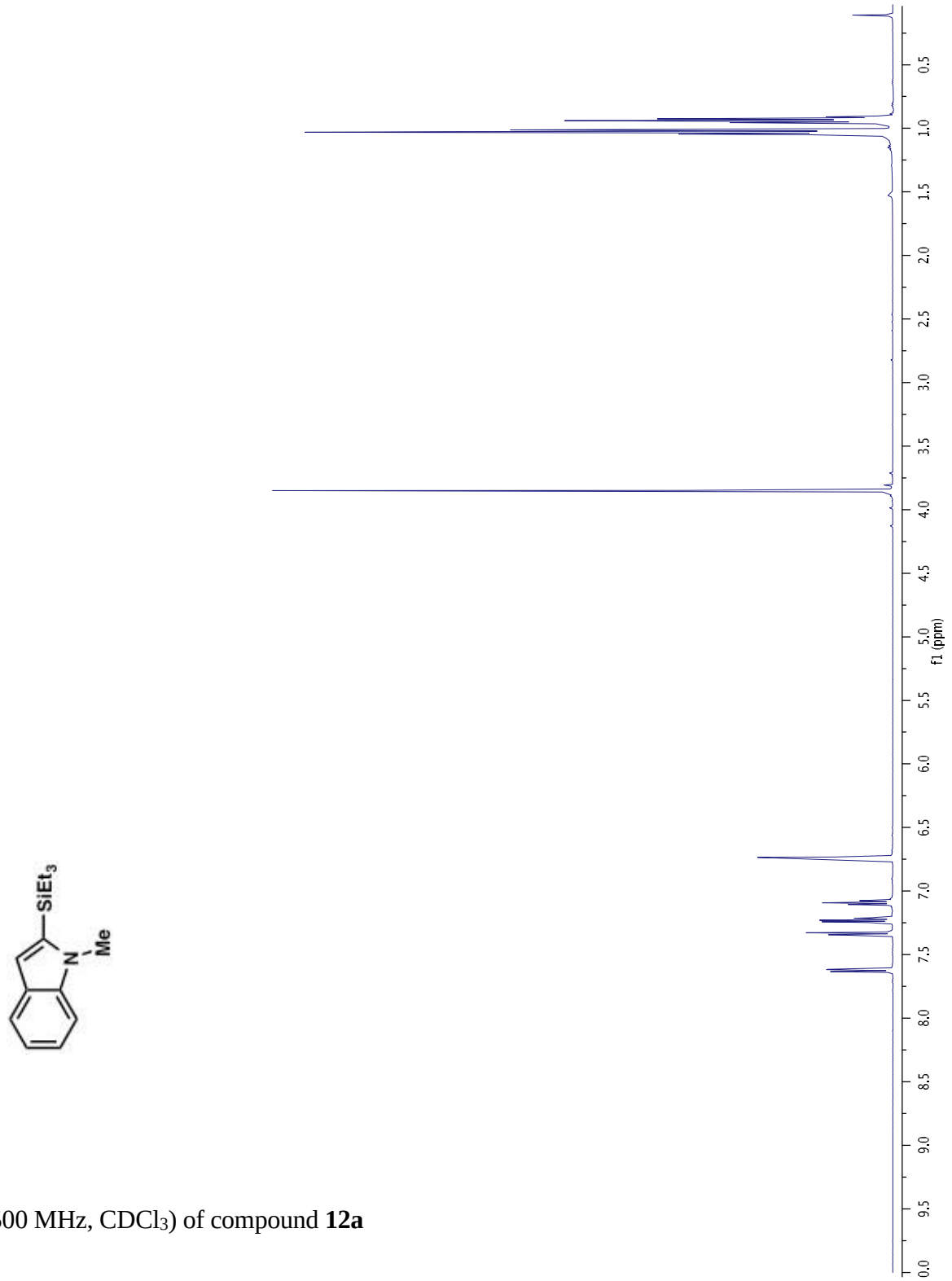
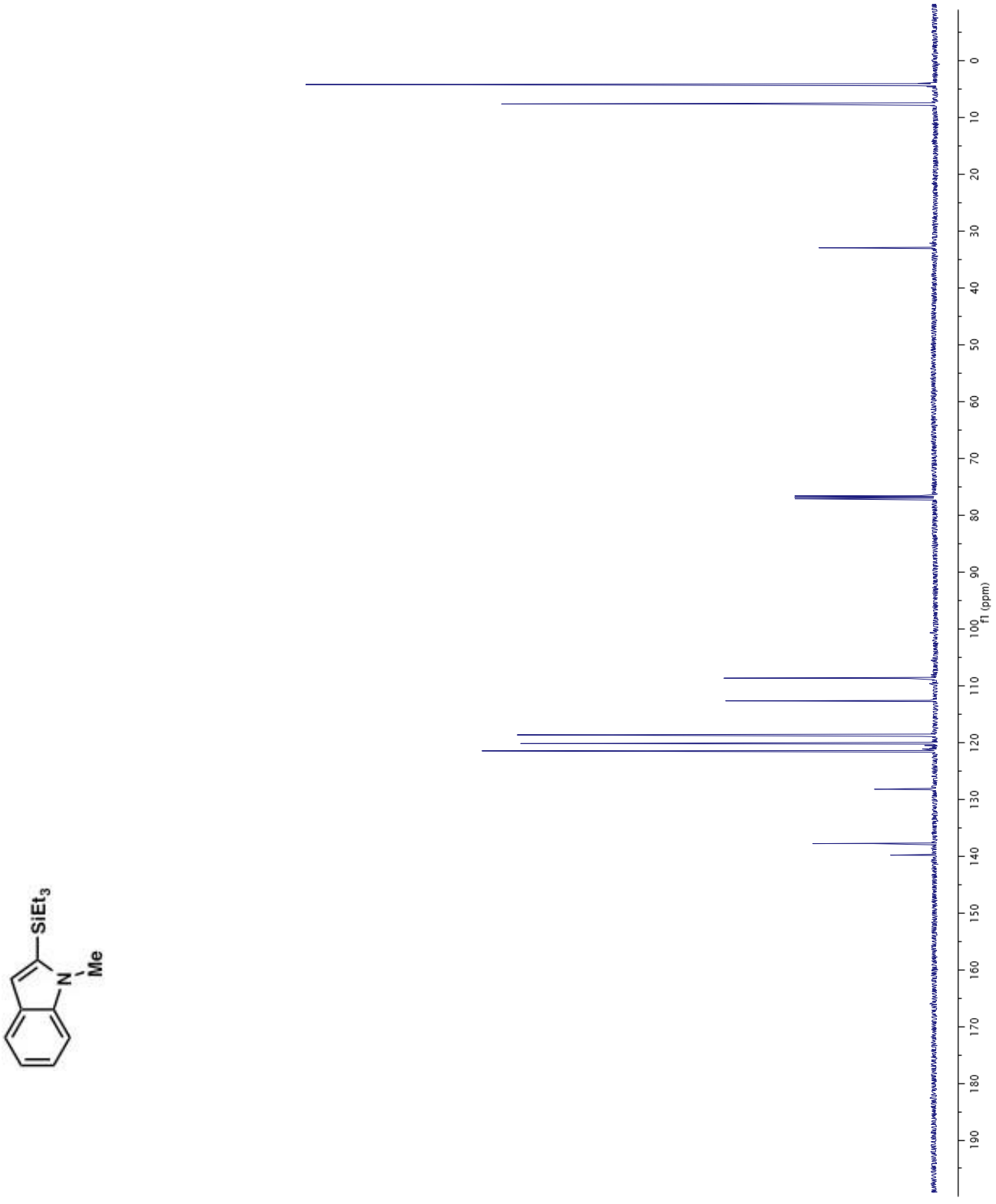
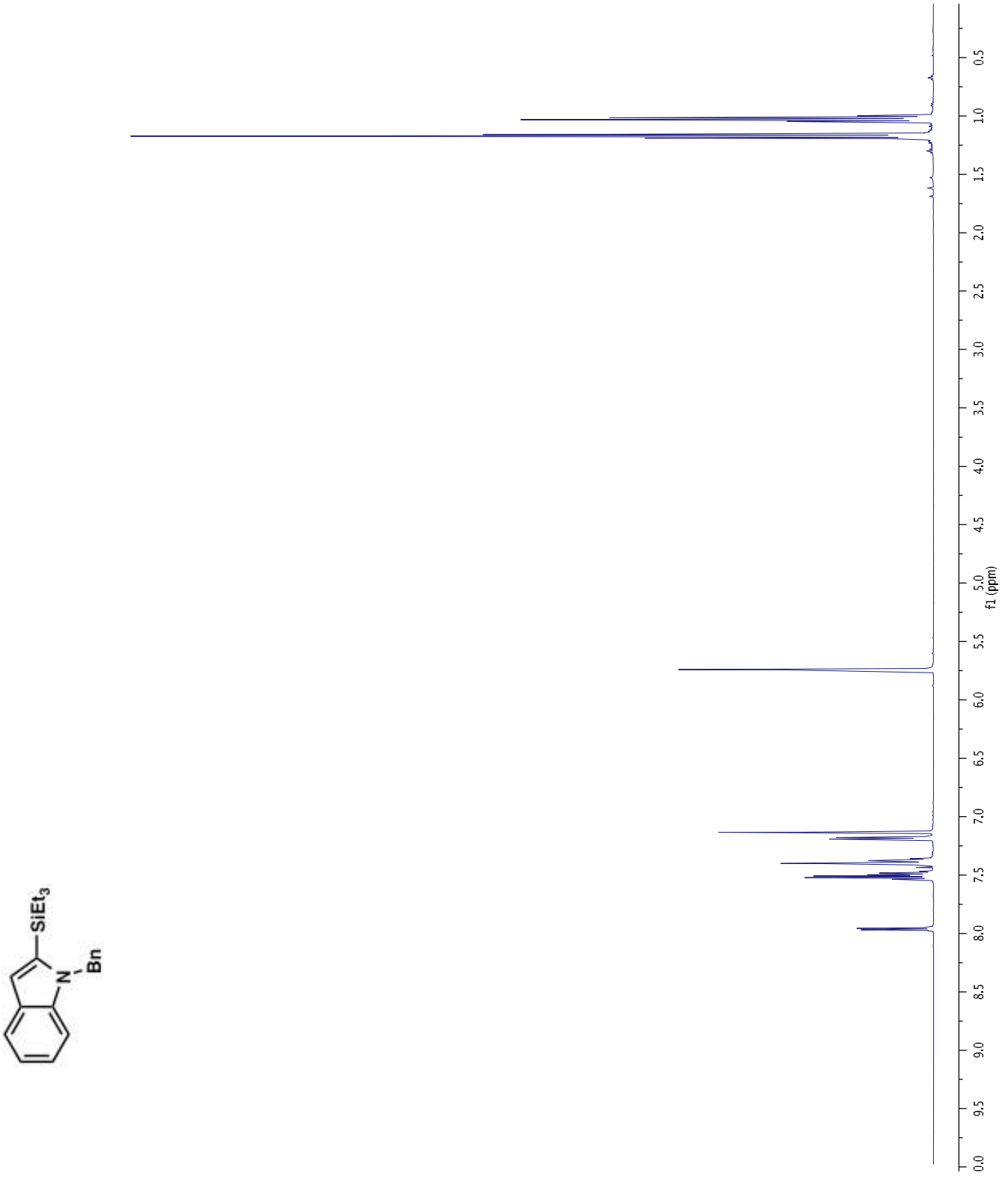
4	8.426	BB	0.0168	1126.76465	1028.11218	38.31383



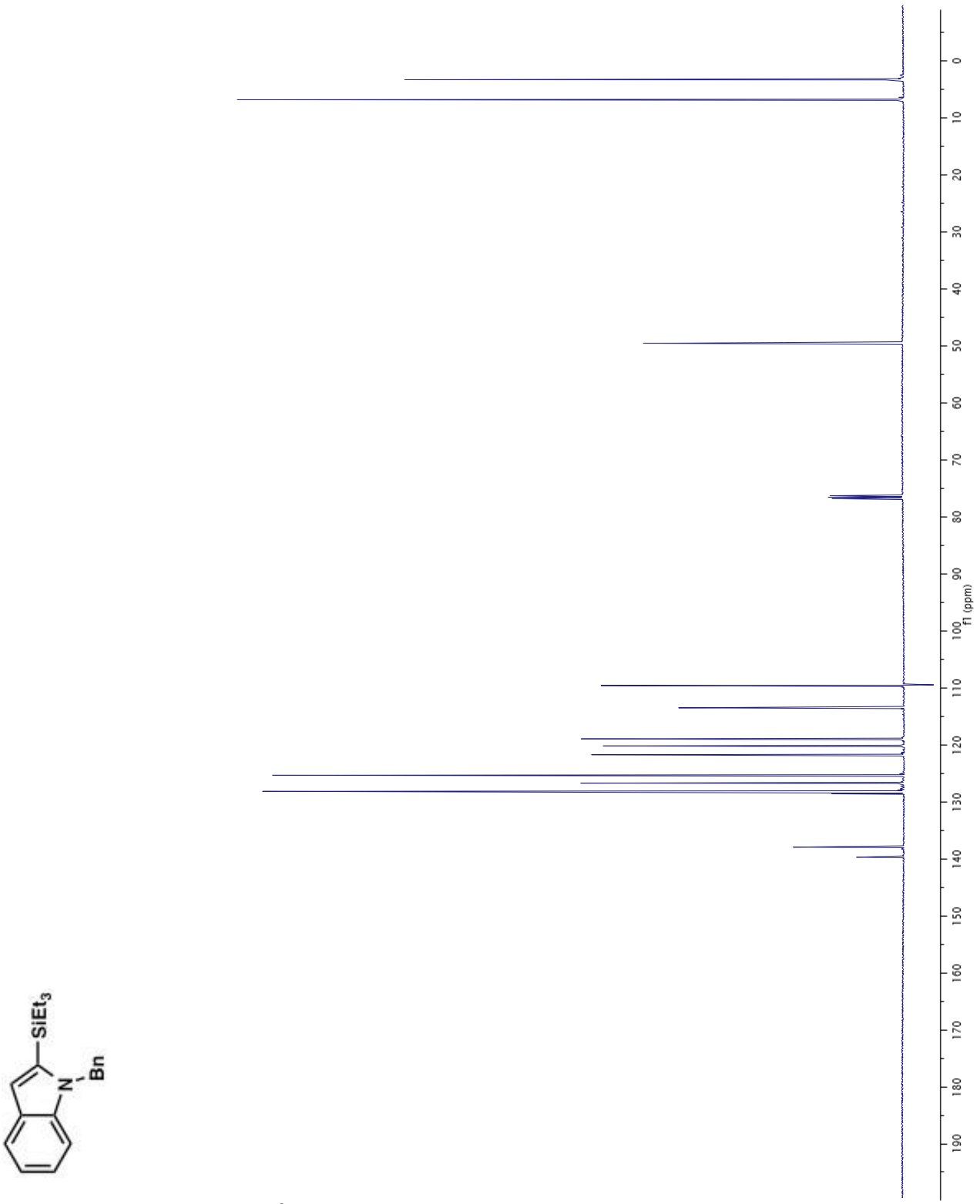
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12a**



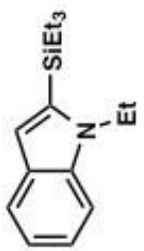
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12a**



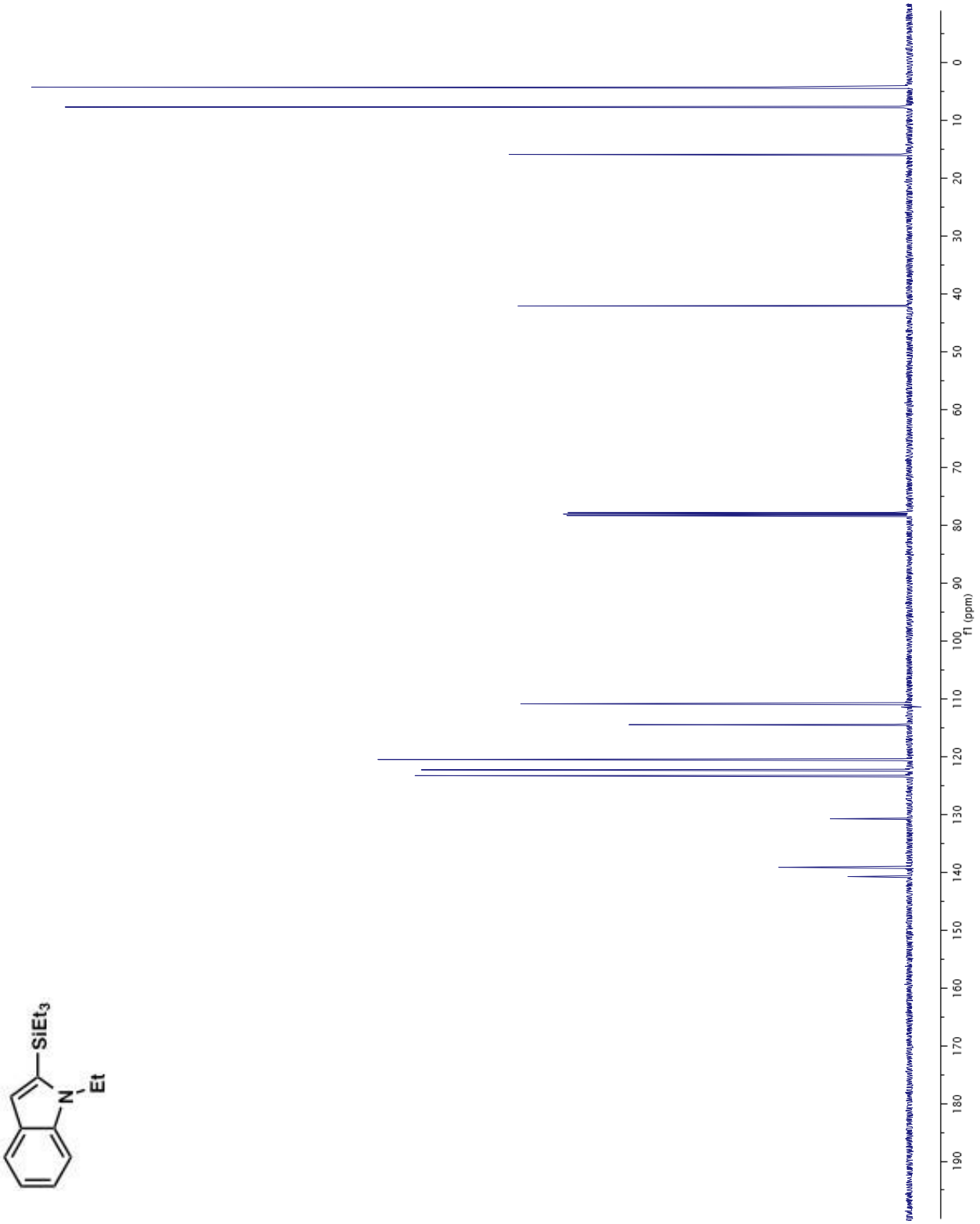
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12b**



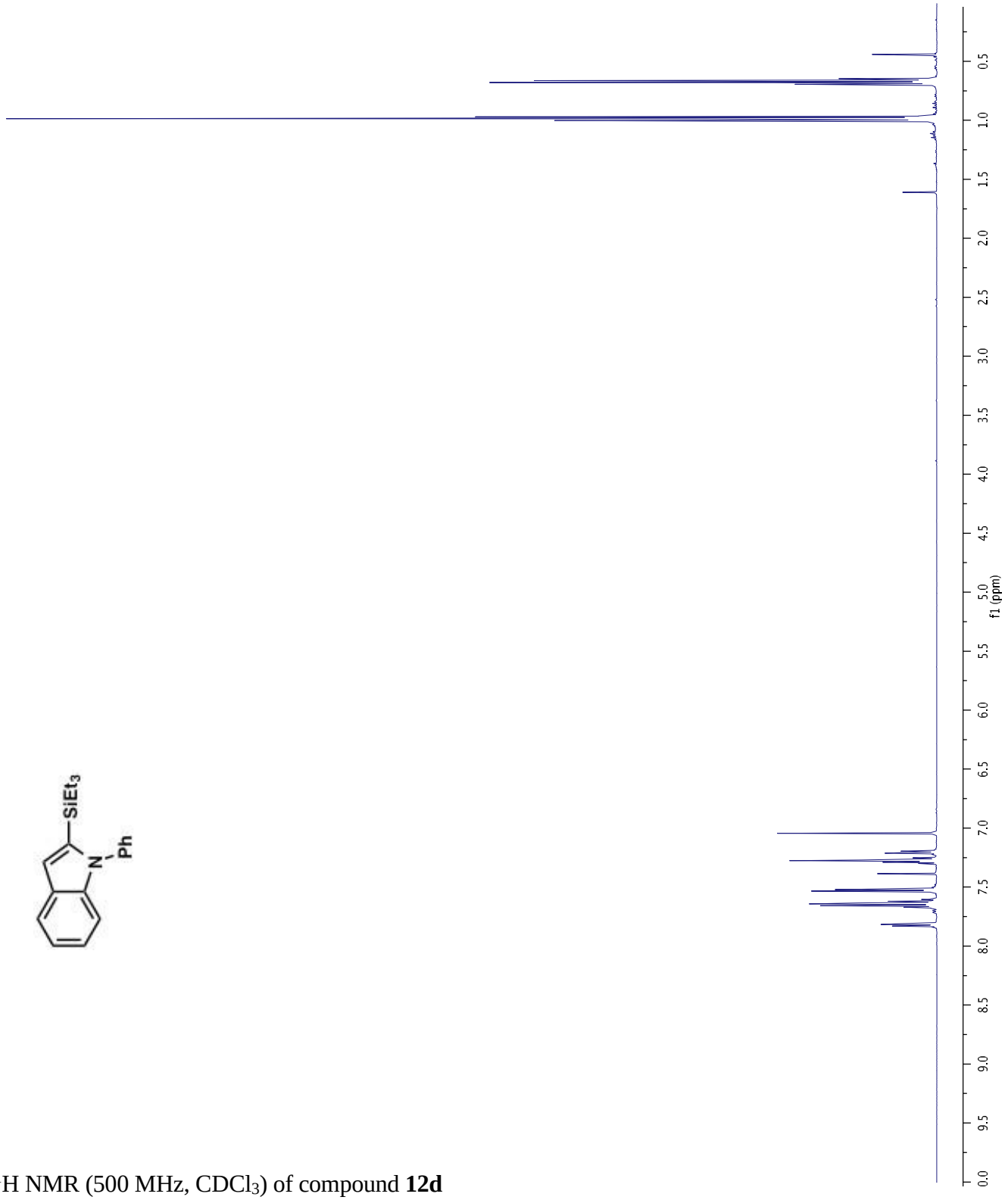
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12b**



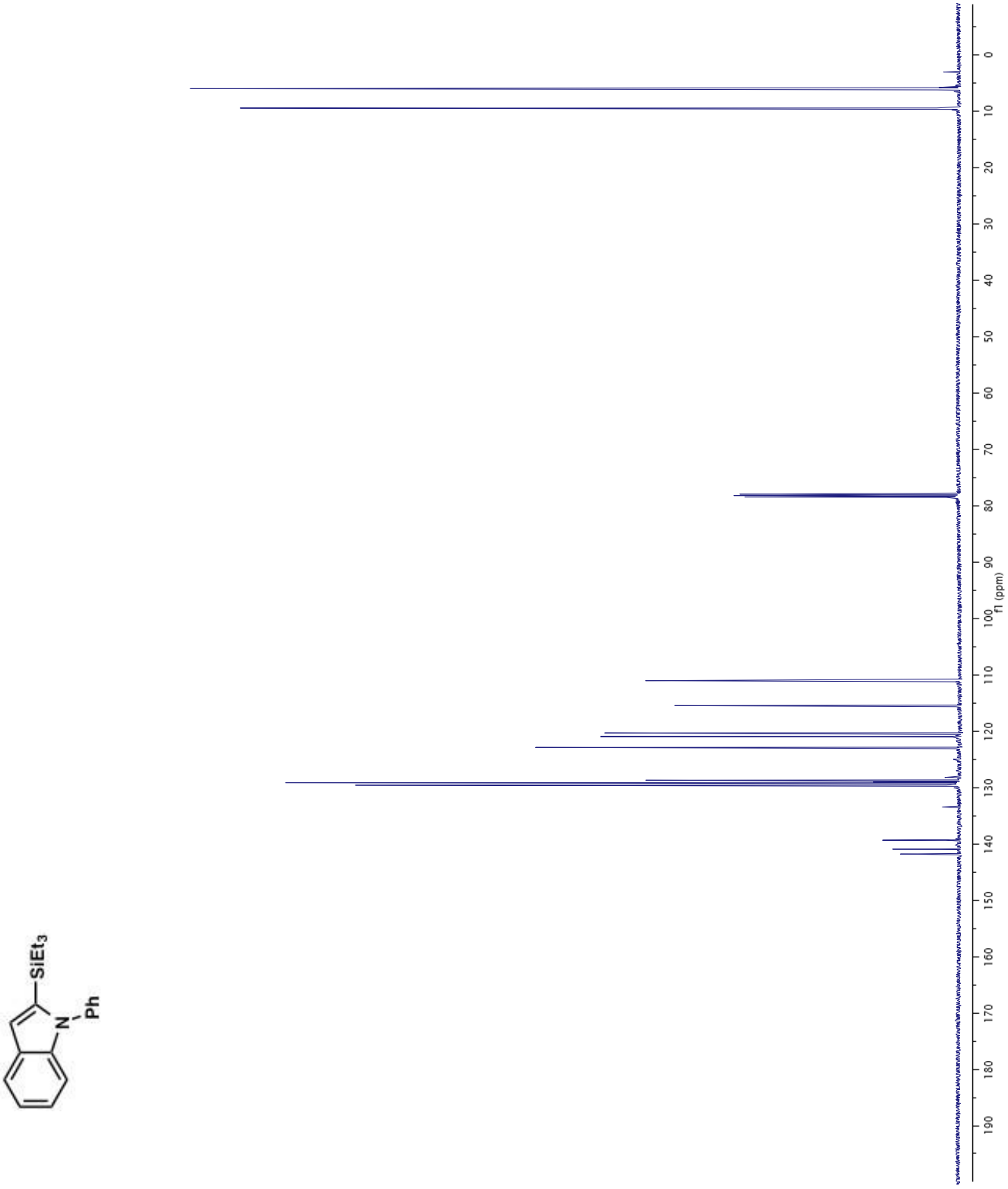
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12c**



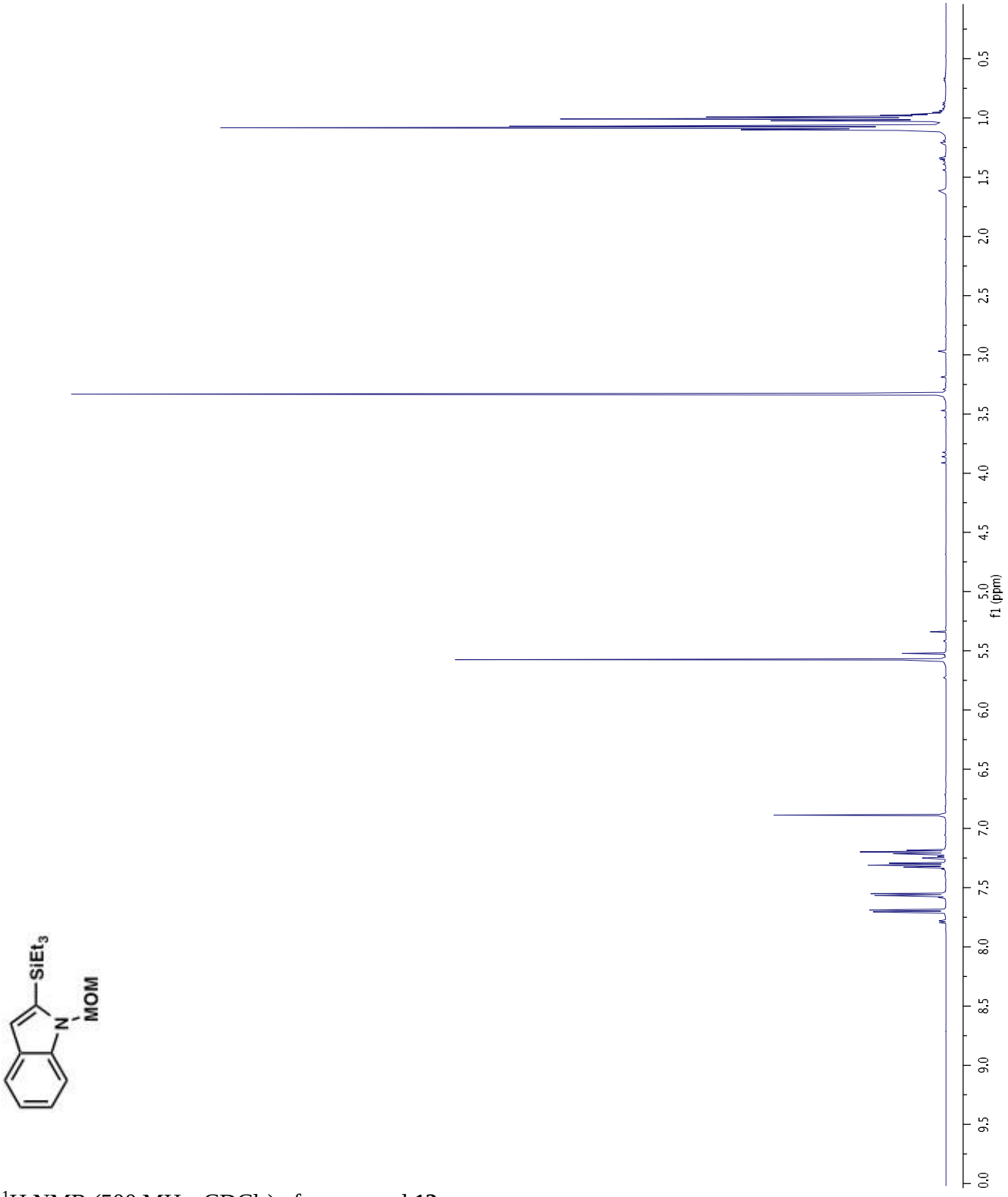
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12c**



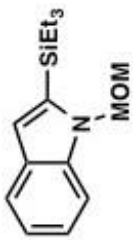
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12d**

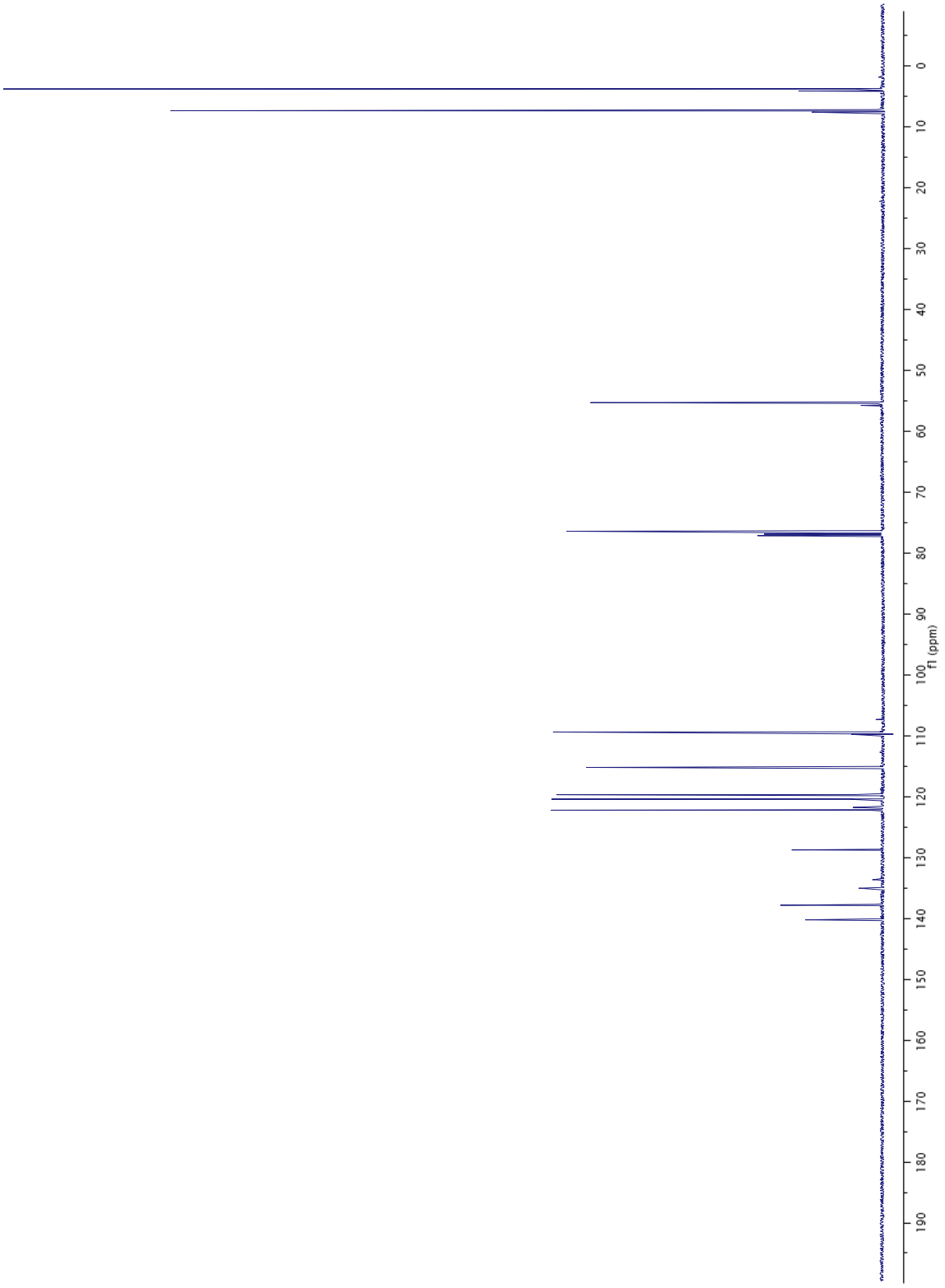


^{13}C NMR (125 MHz, $CDCl_3$) of compound **12d**

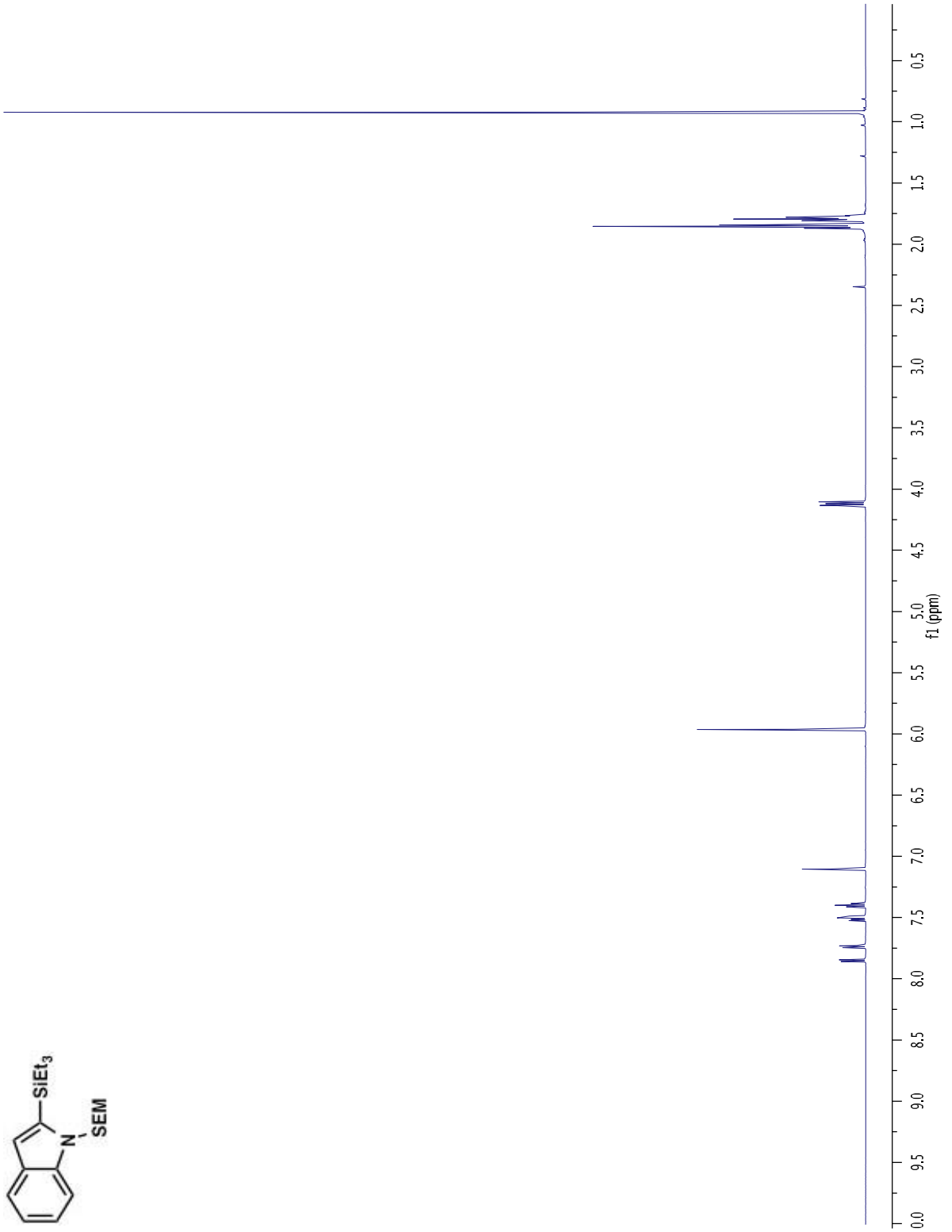


^{1}H NMR (500 MHz, $CDCl_3$) of compound **12e**

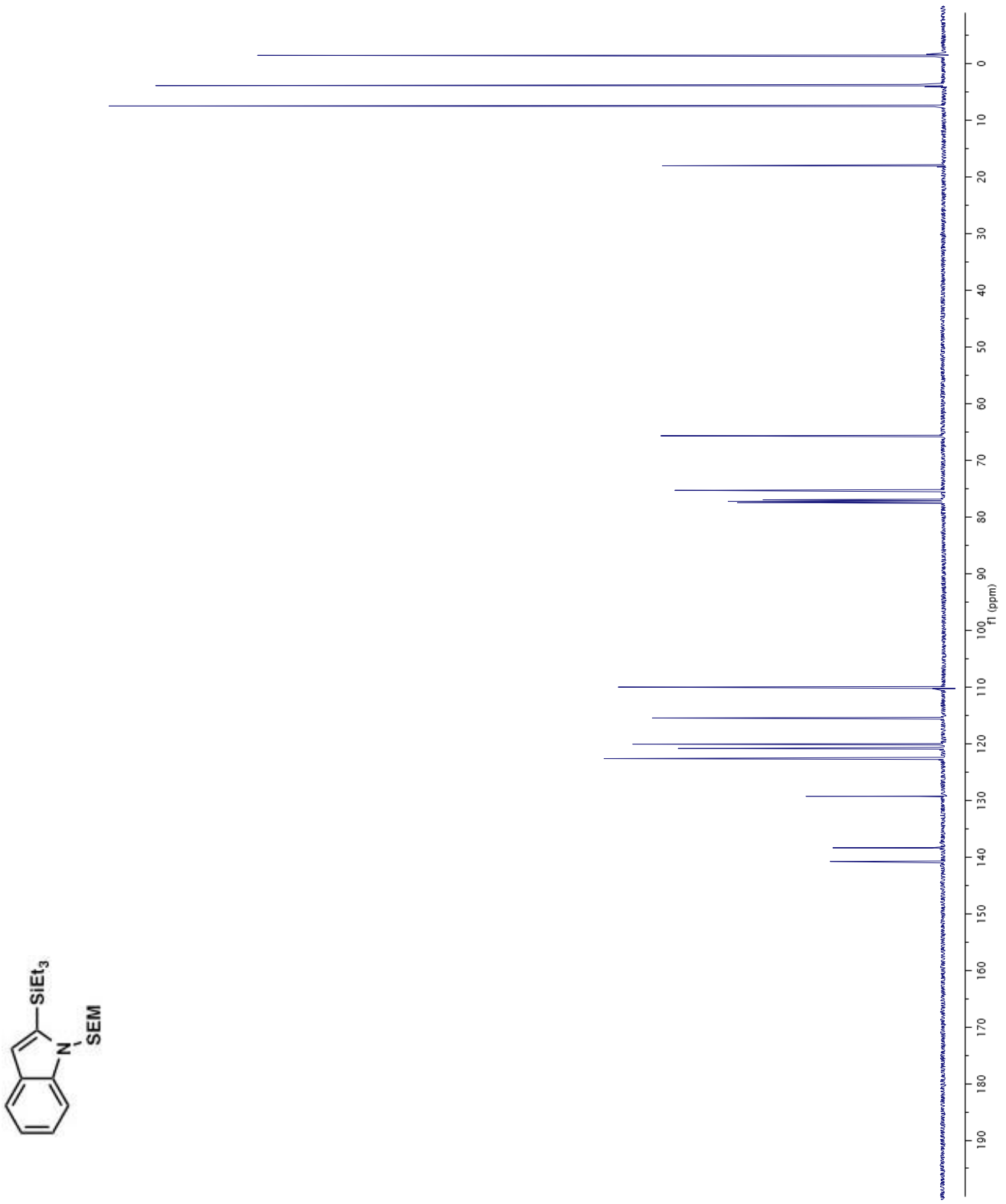




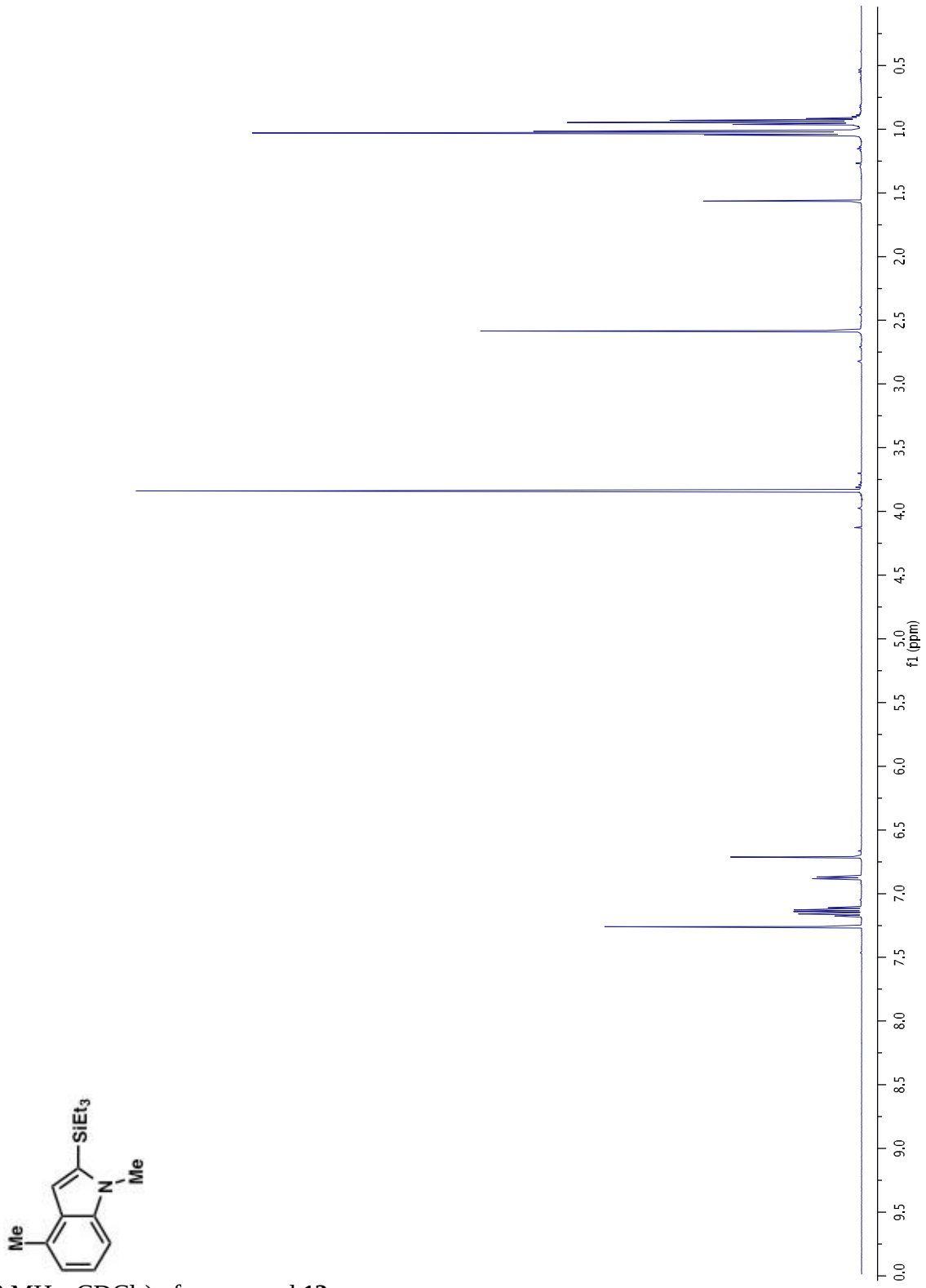
^{13}C NMR (500 MHz, $CDCl_3$) of compound **12e**



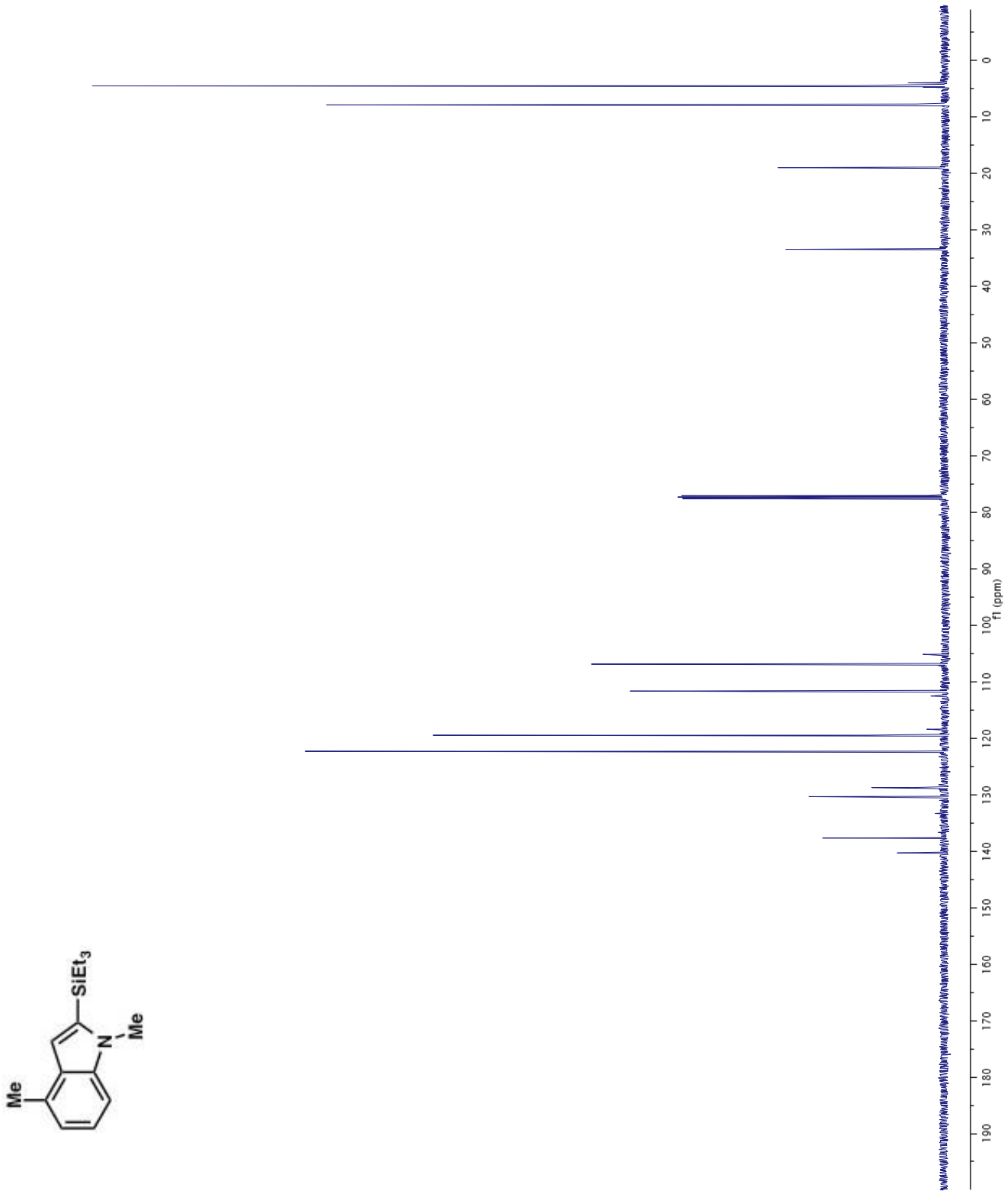
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12f**



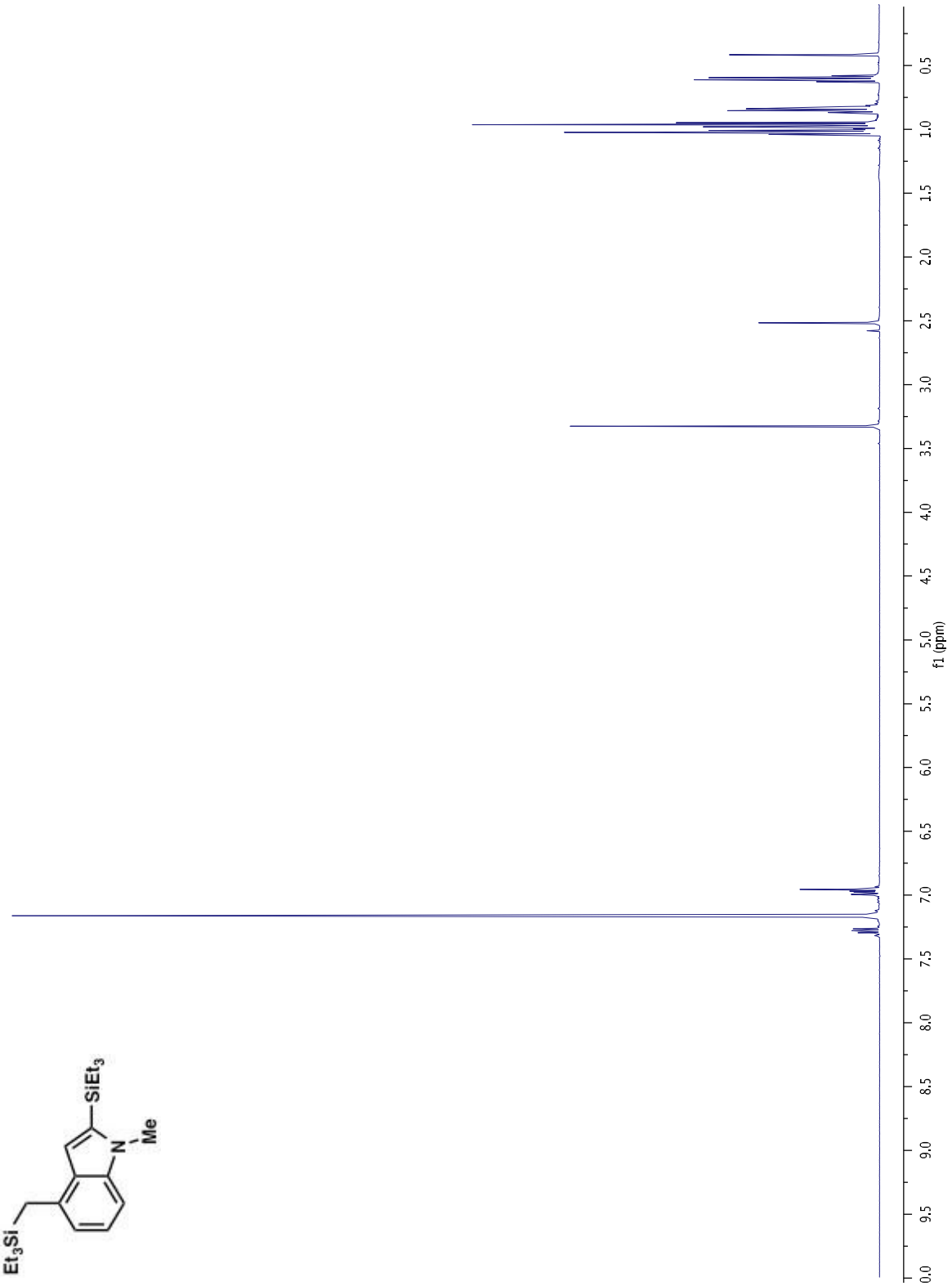
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12f**



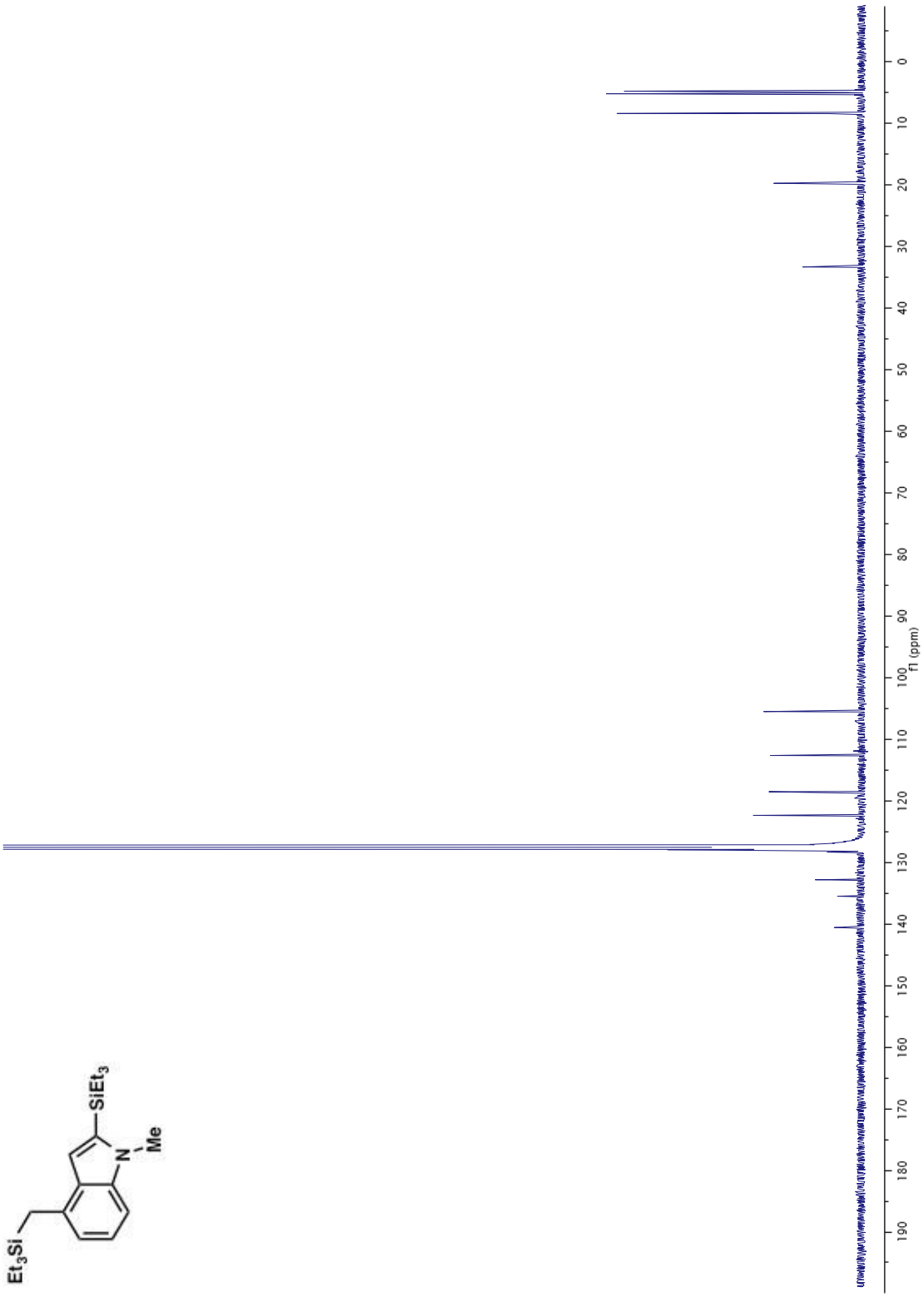
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12g**



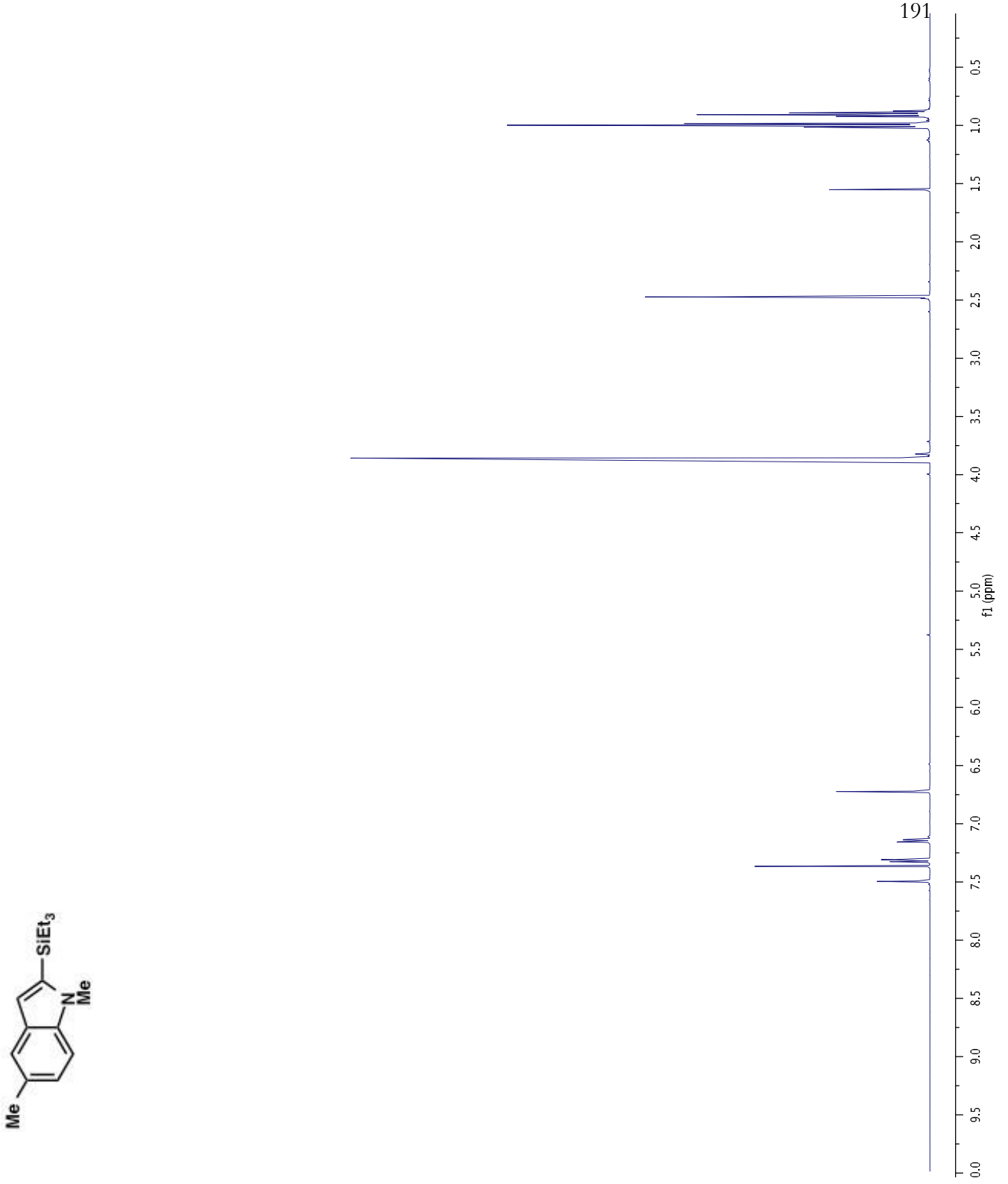
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12g**



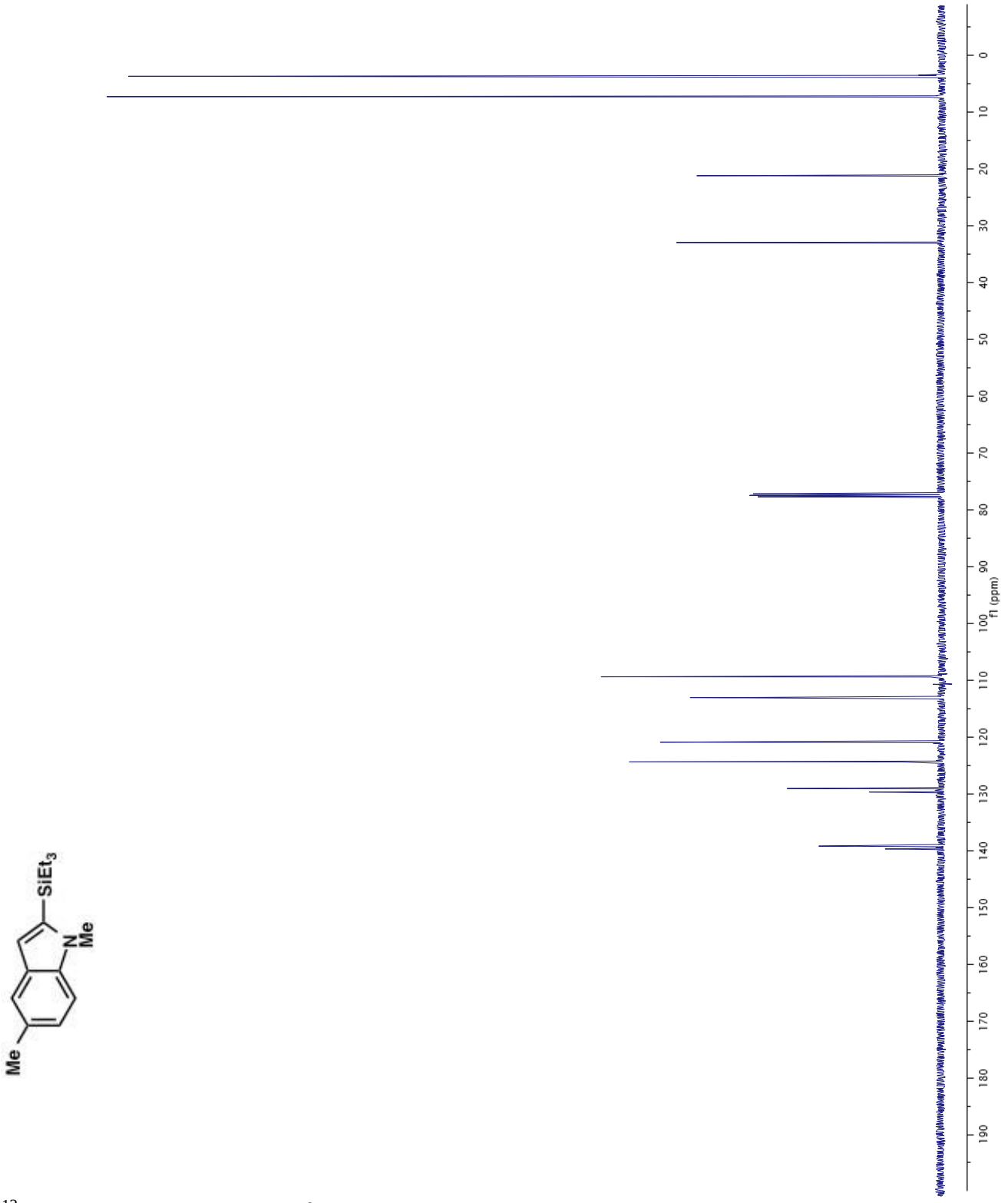
^{1}H NMR (500 MHz, C_6D_6) of compound **12g_*sp*^{3}**



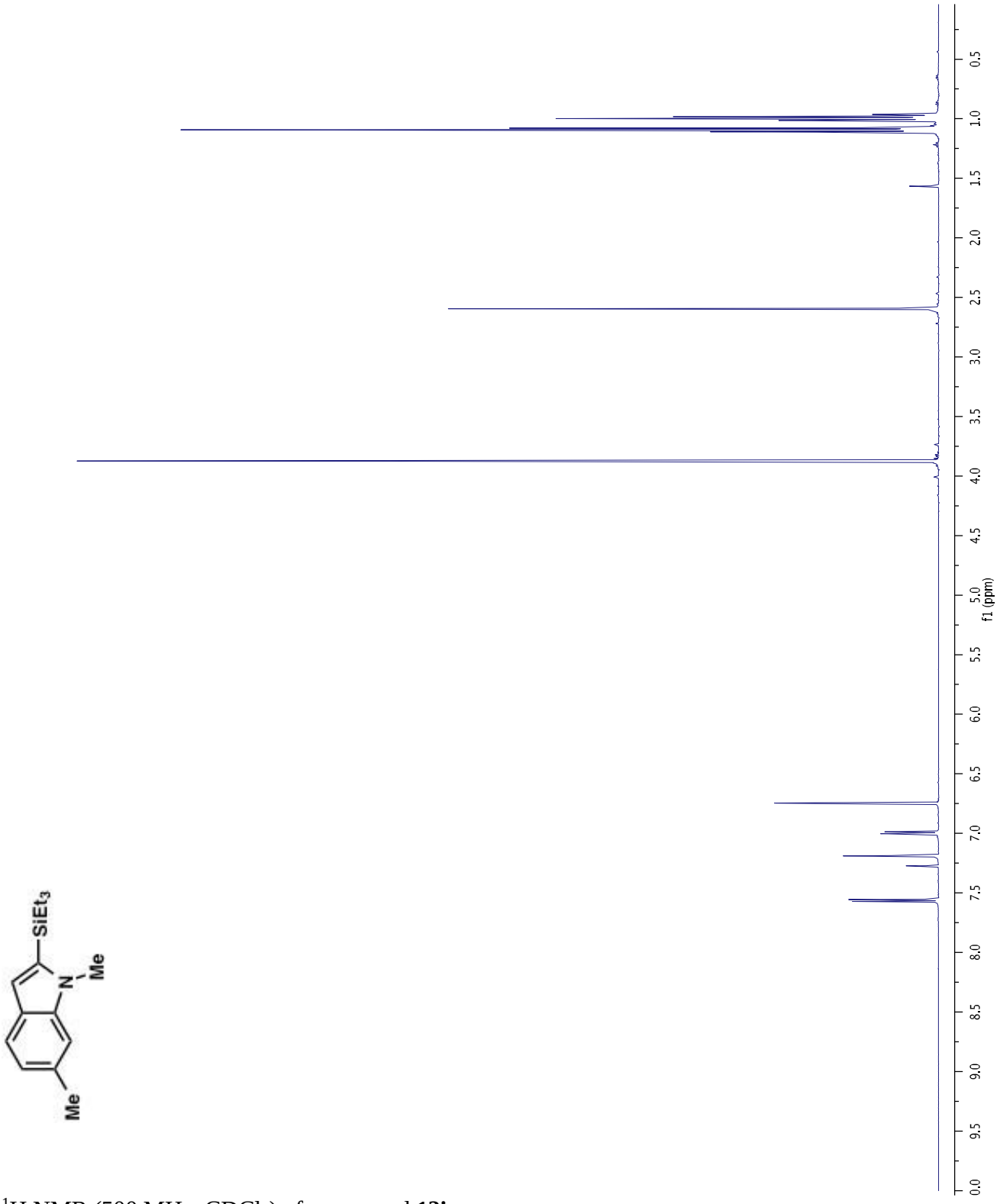
^{13}C NMR (125 MHz, C_6D_6) of compound **12g_*sp*^{3}**



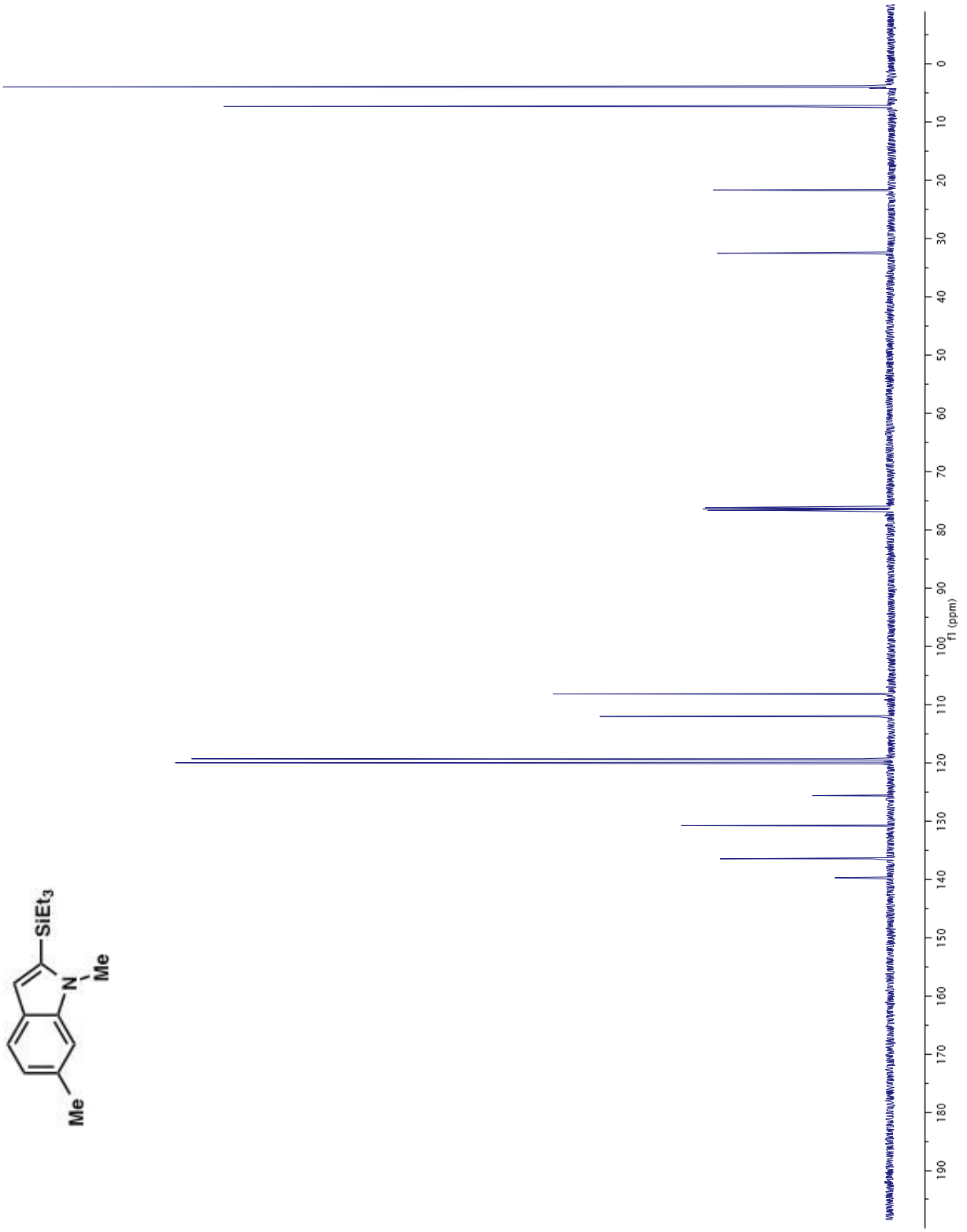
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12h**



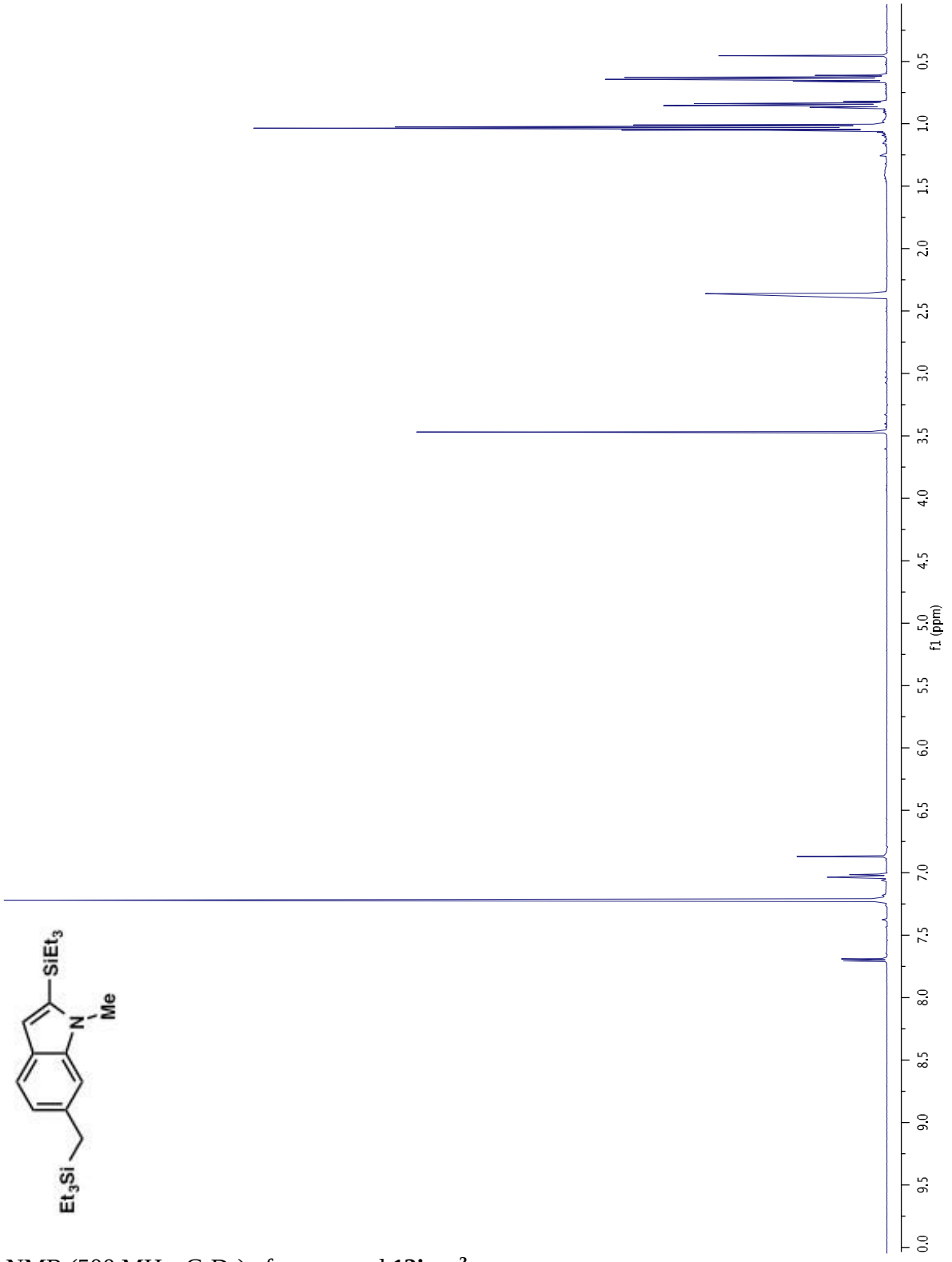
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12h**



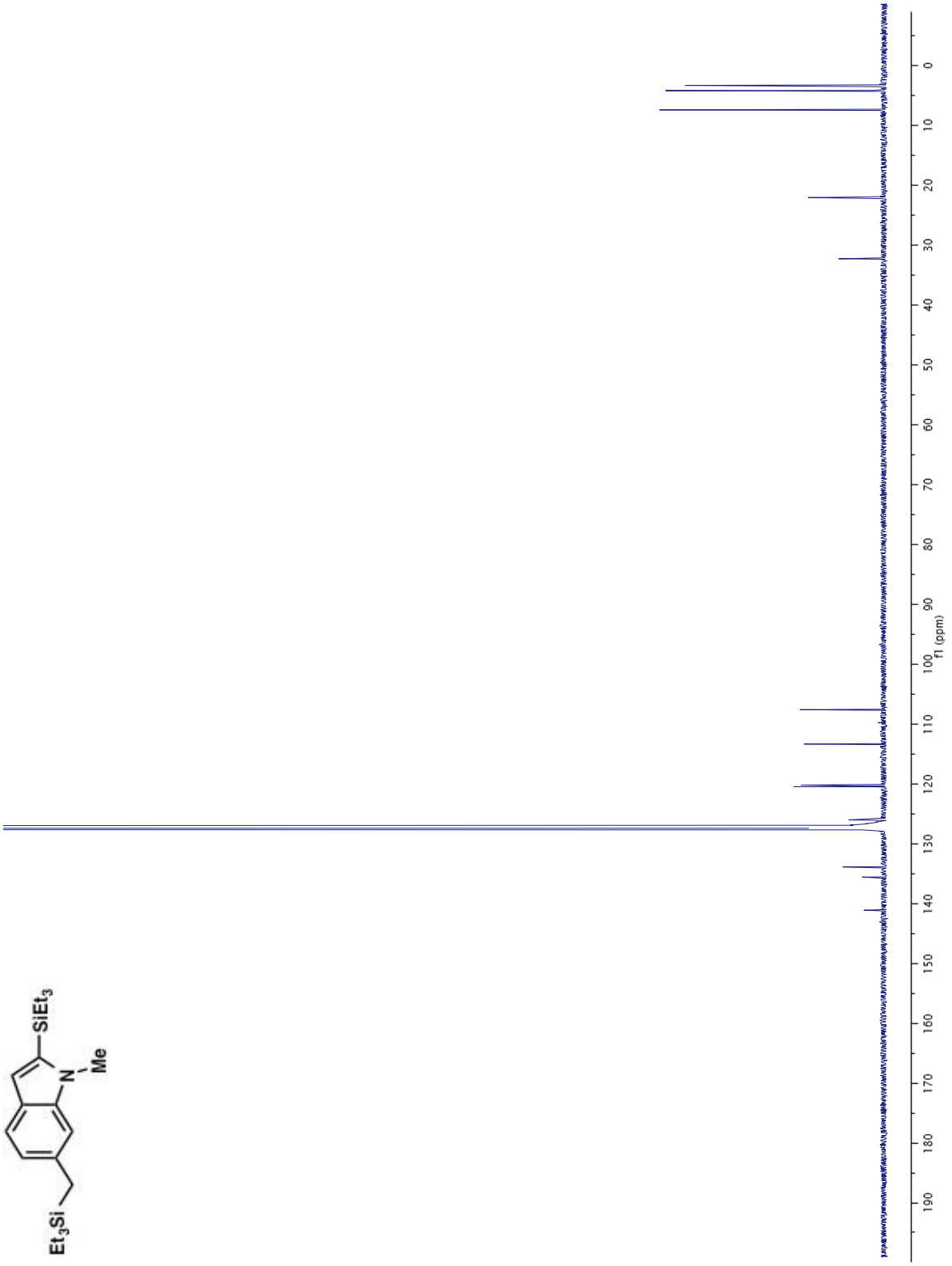
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12i**



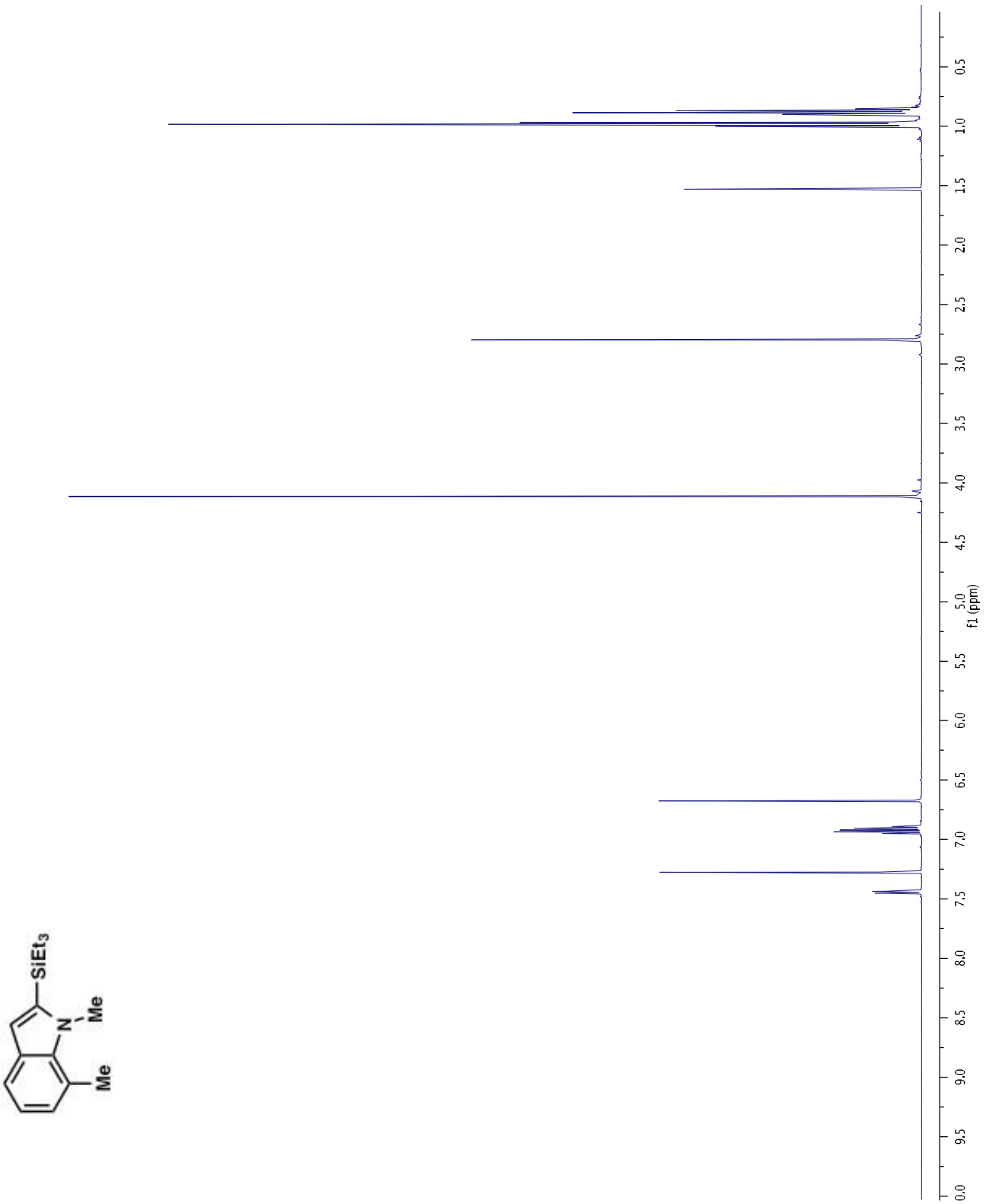
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12i**



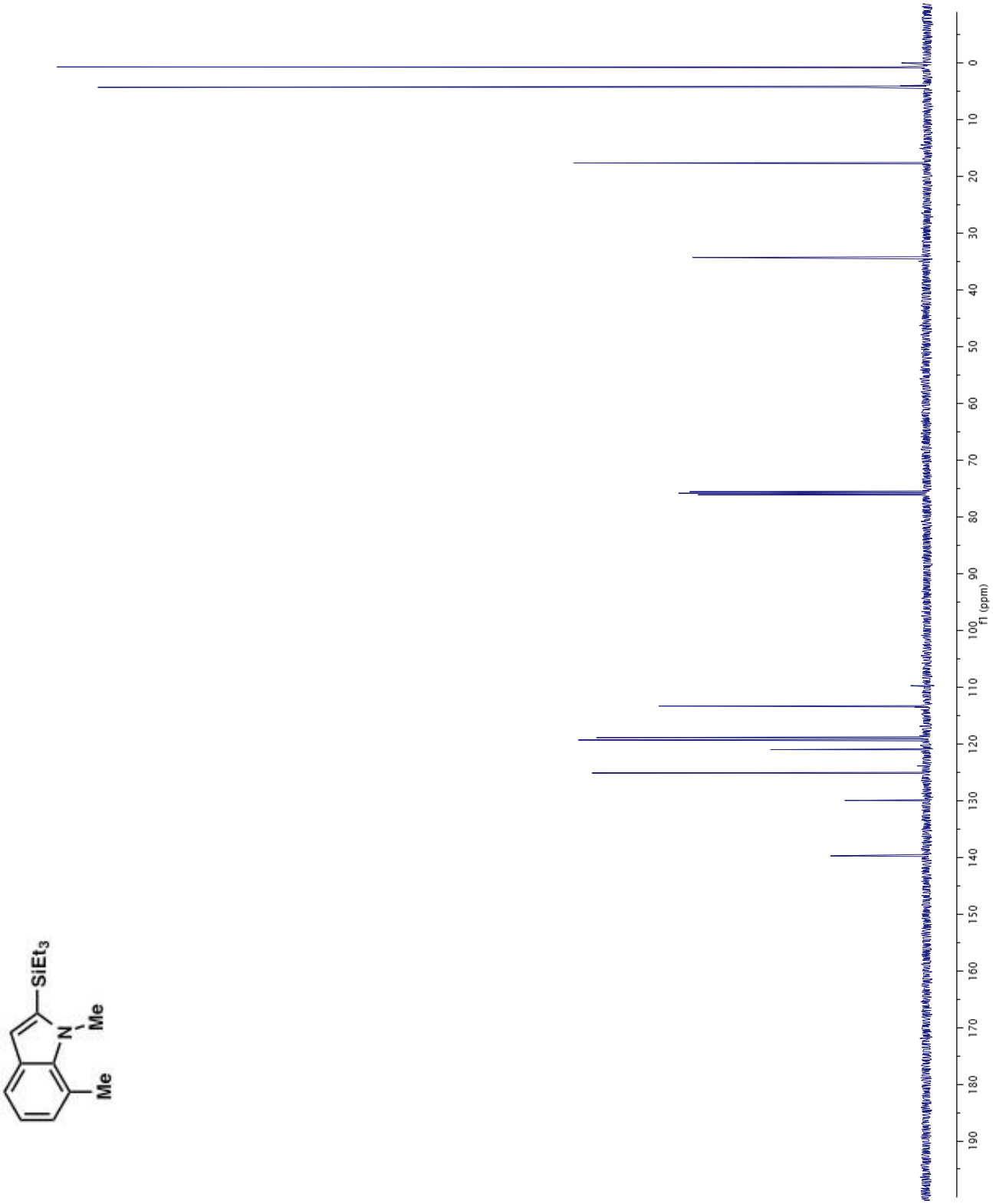
^{1}H NMR (500 MHz, C_6D_6) of compound **12i_*sp*^{3}**



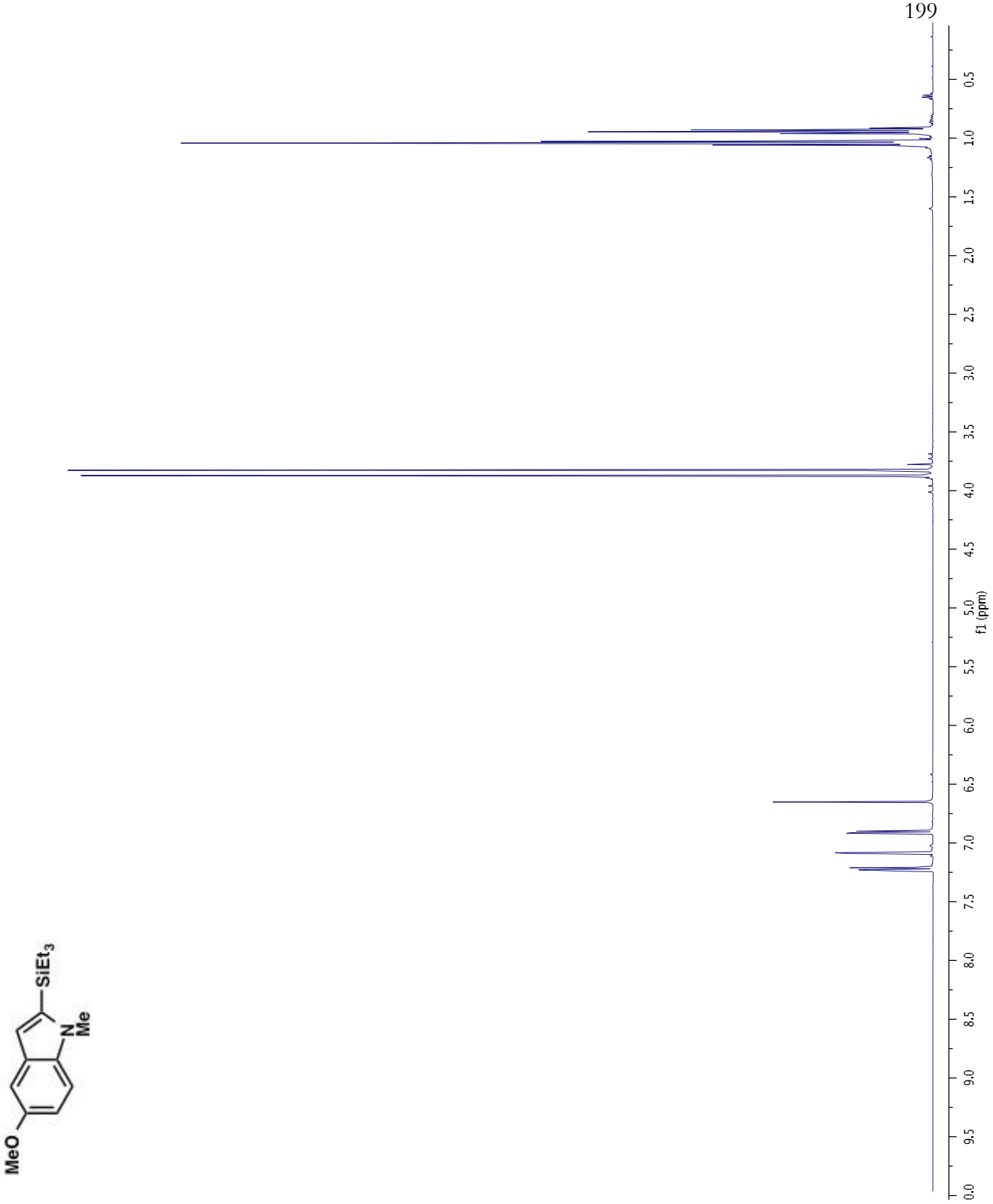
^{13}C NMR (125 MHz, C_6D_6) of compound **12i_*sp*^{3}**



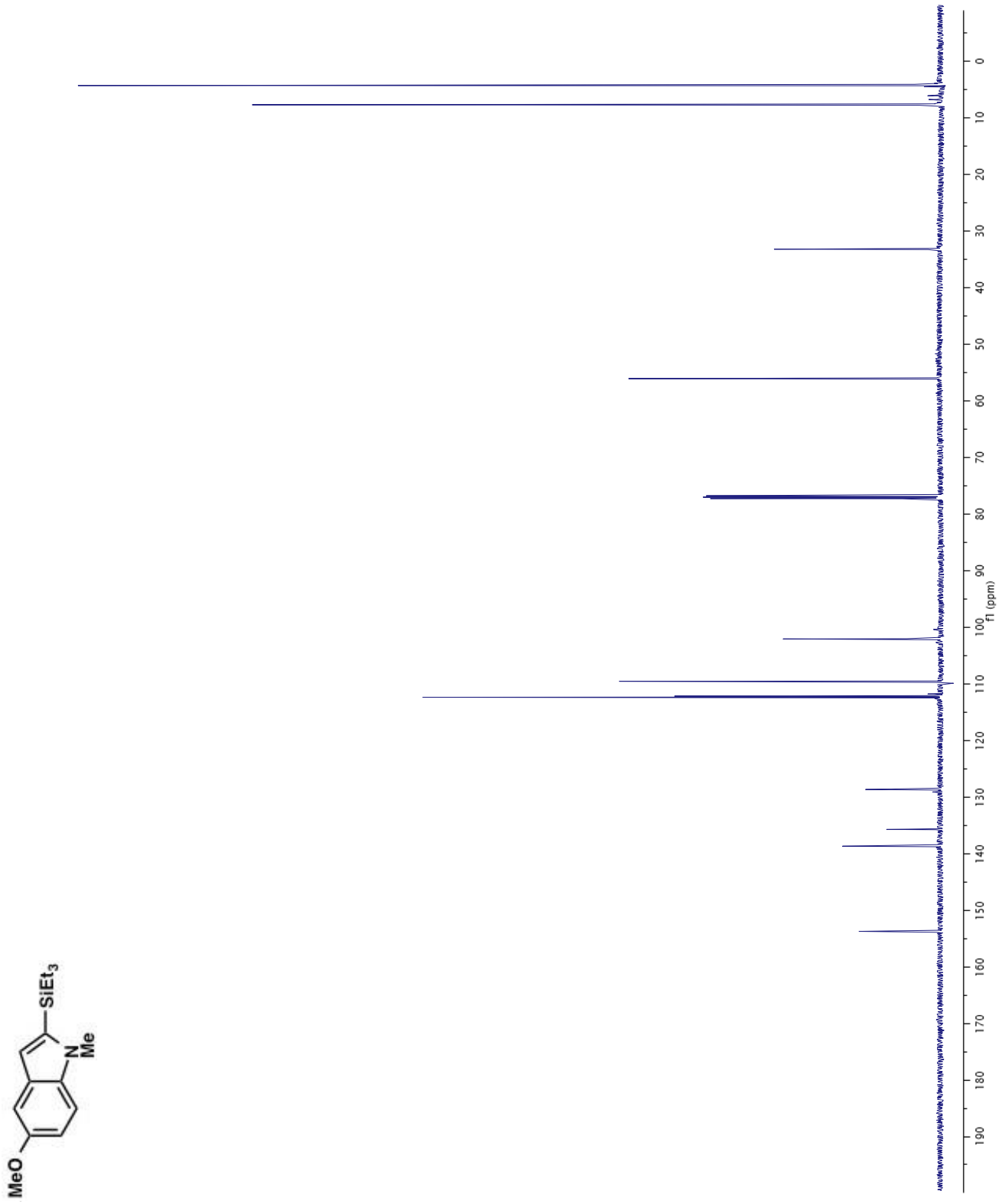
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12j**



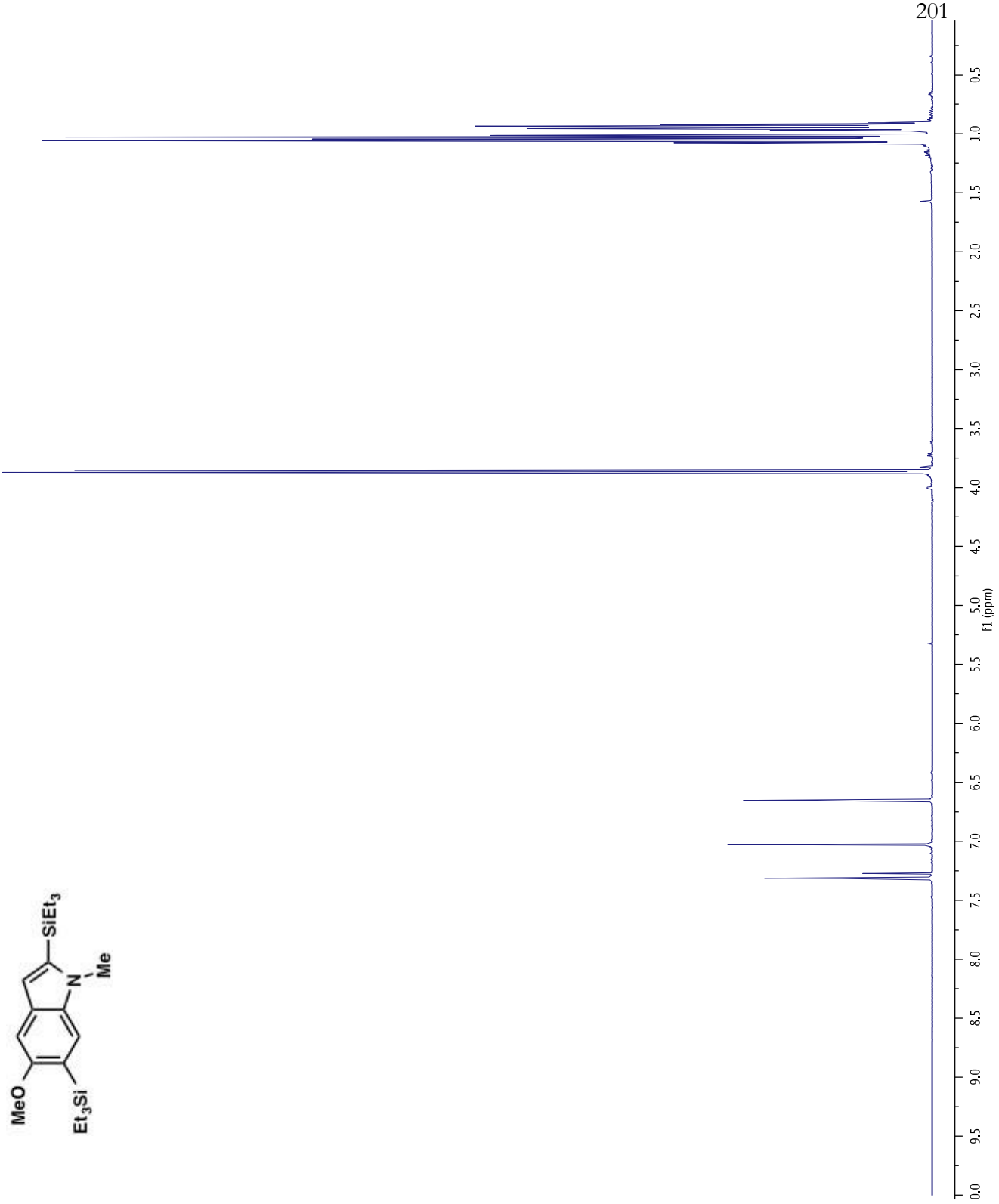
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12j**



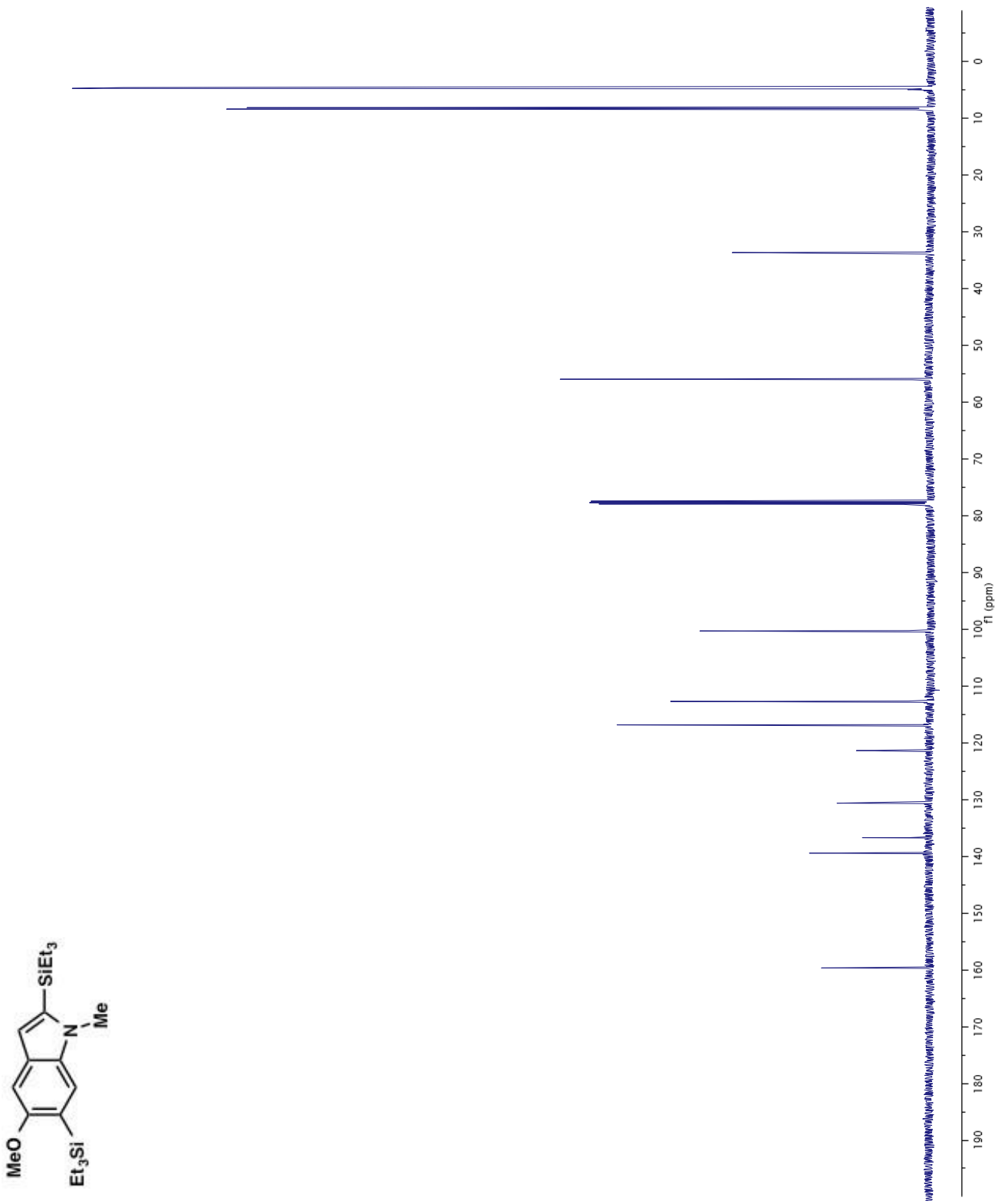
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12k**



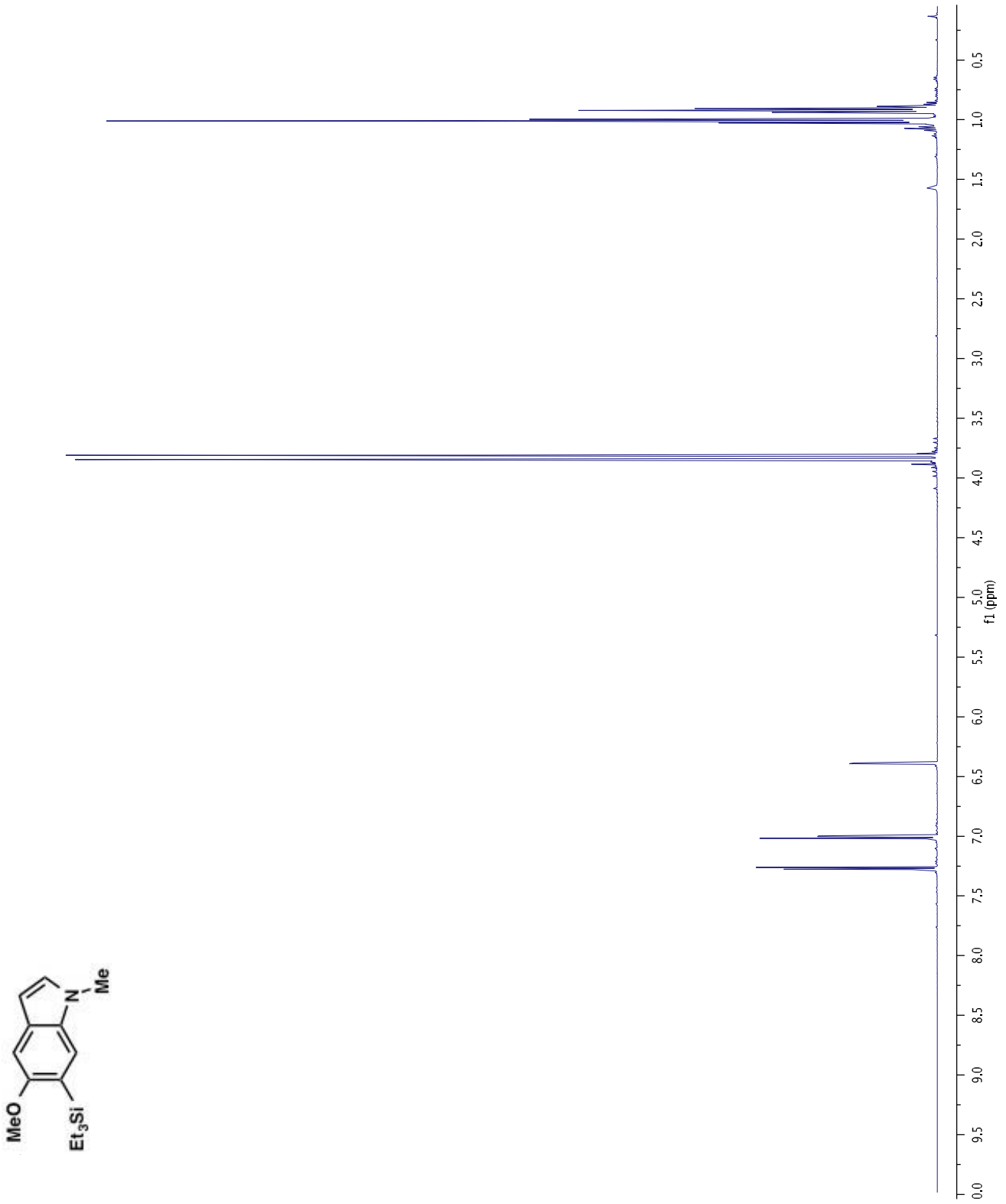
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12k**



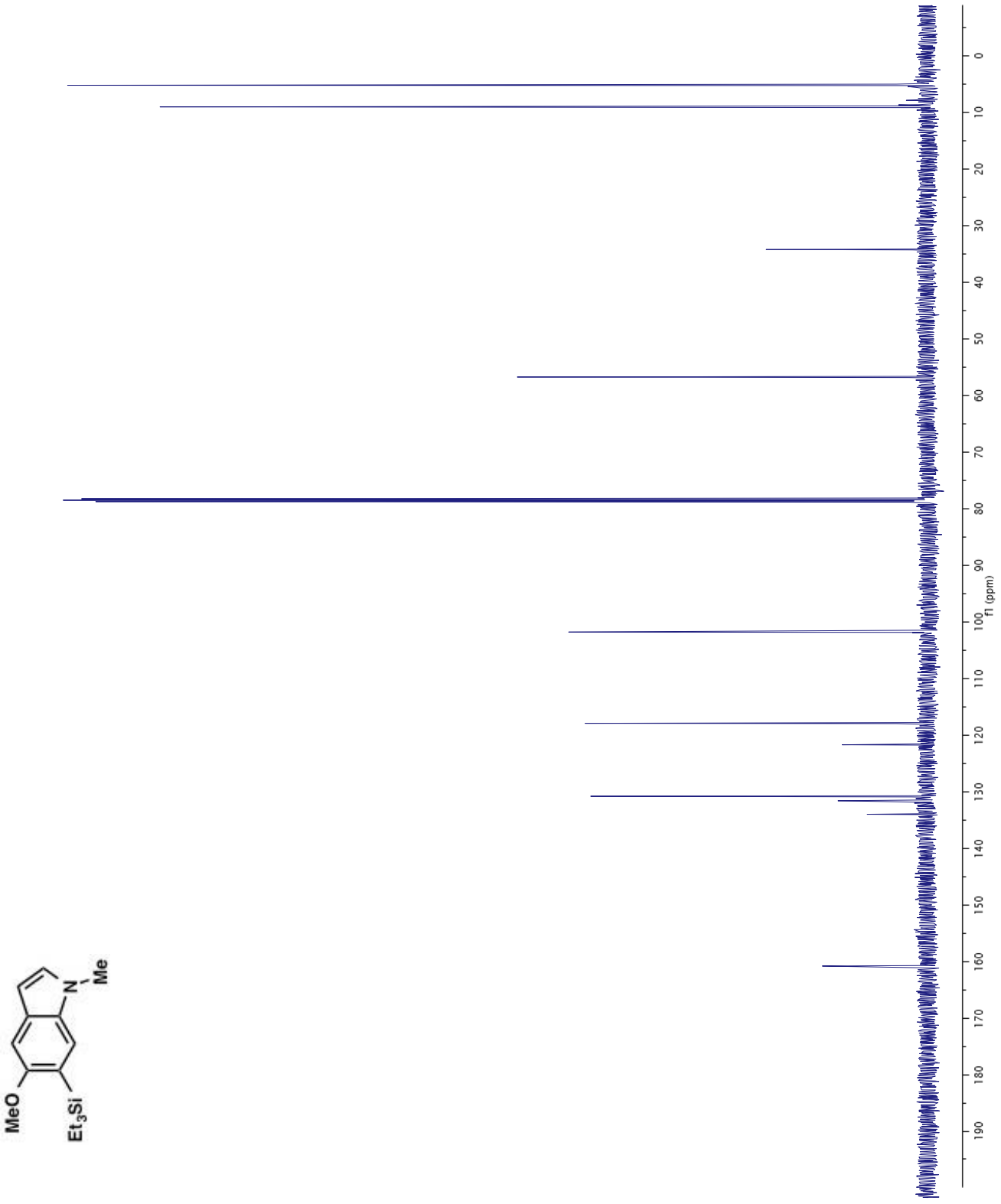
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12k_bis**



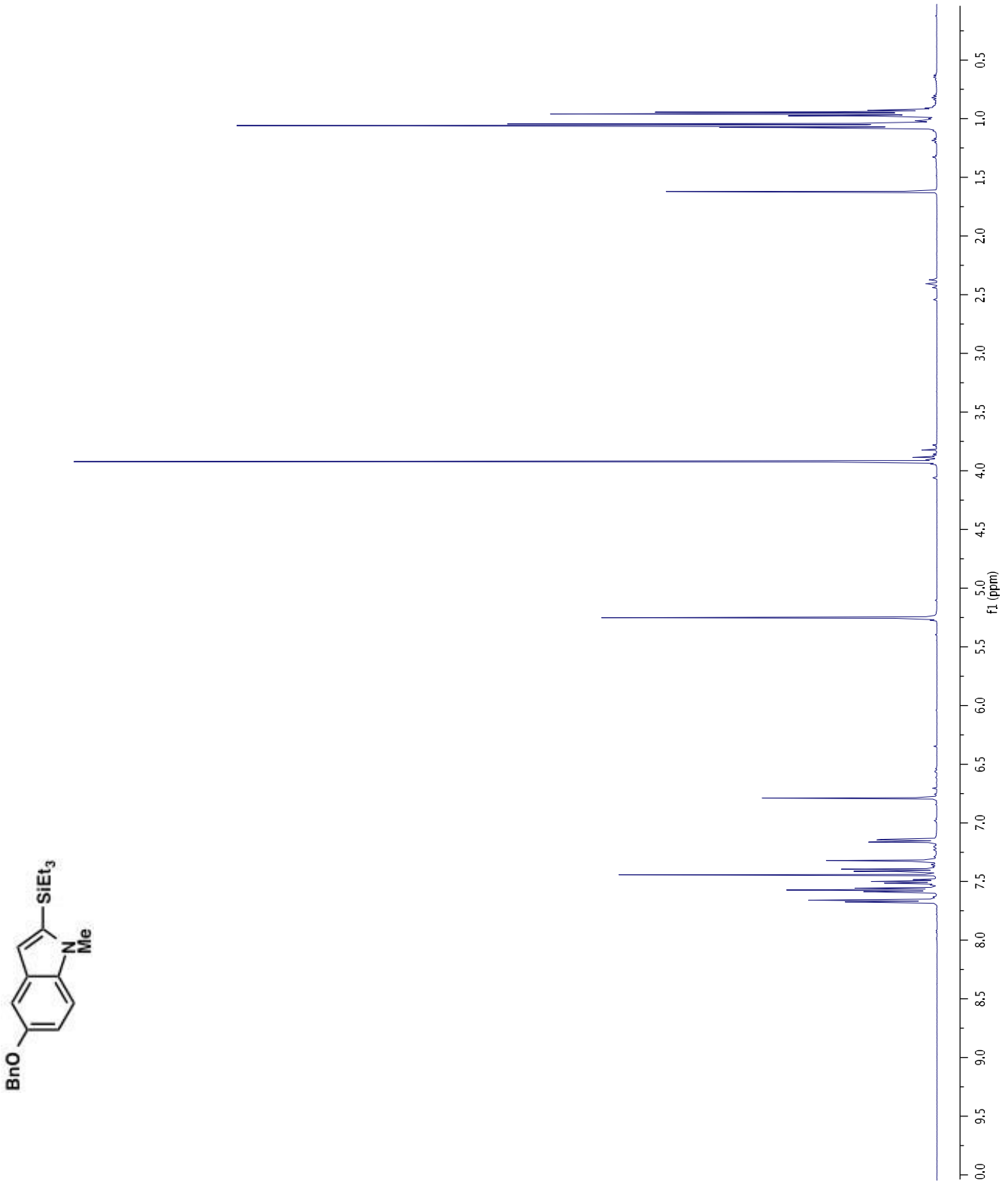
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12k_bis**



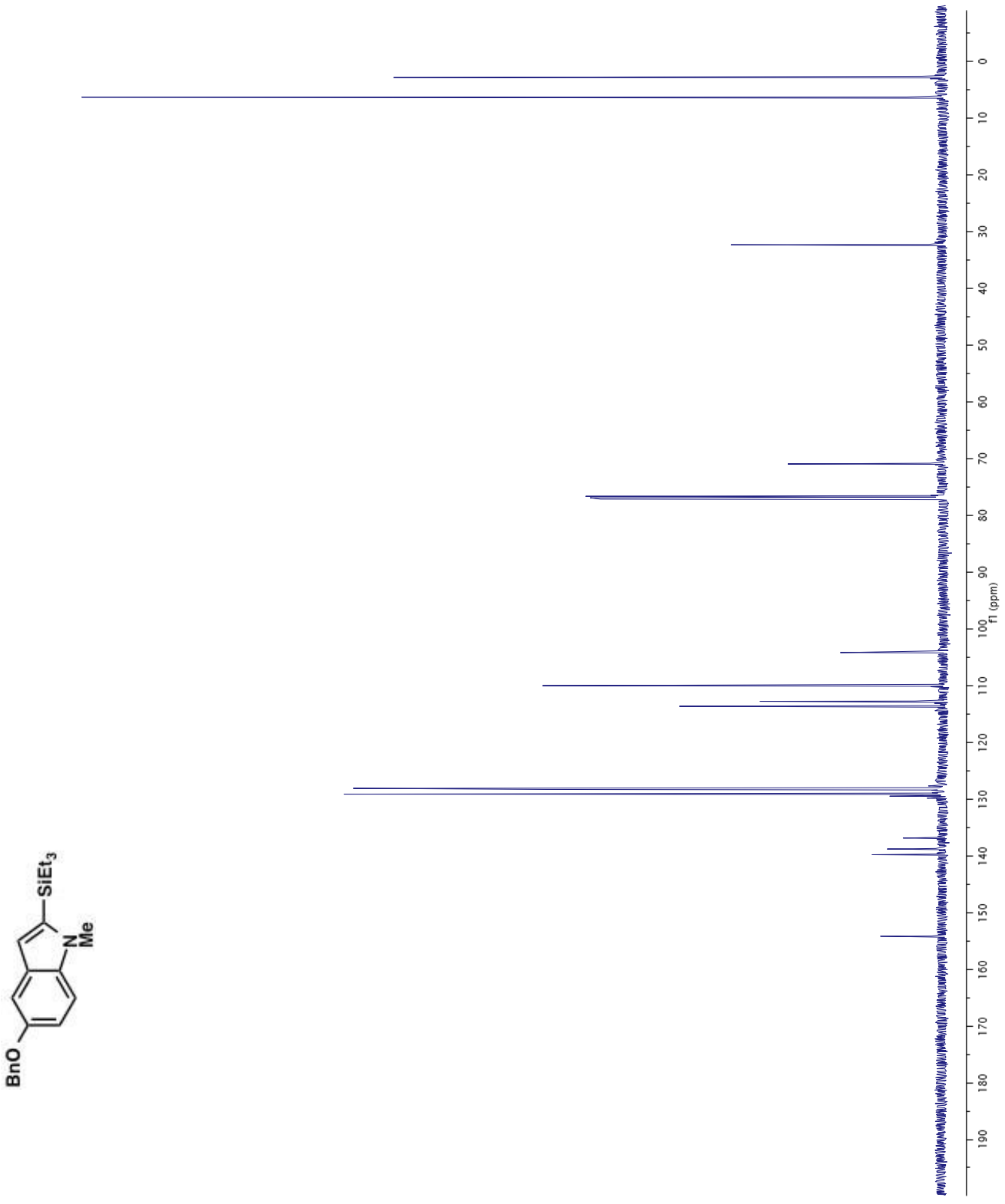
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12k_*ortho***



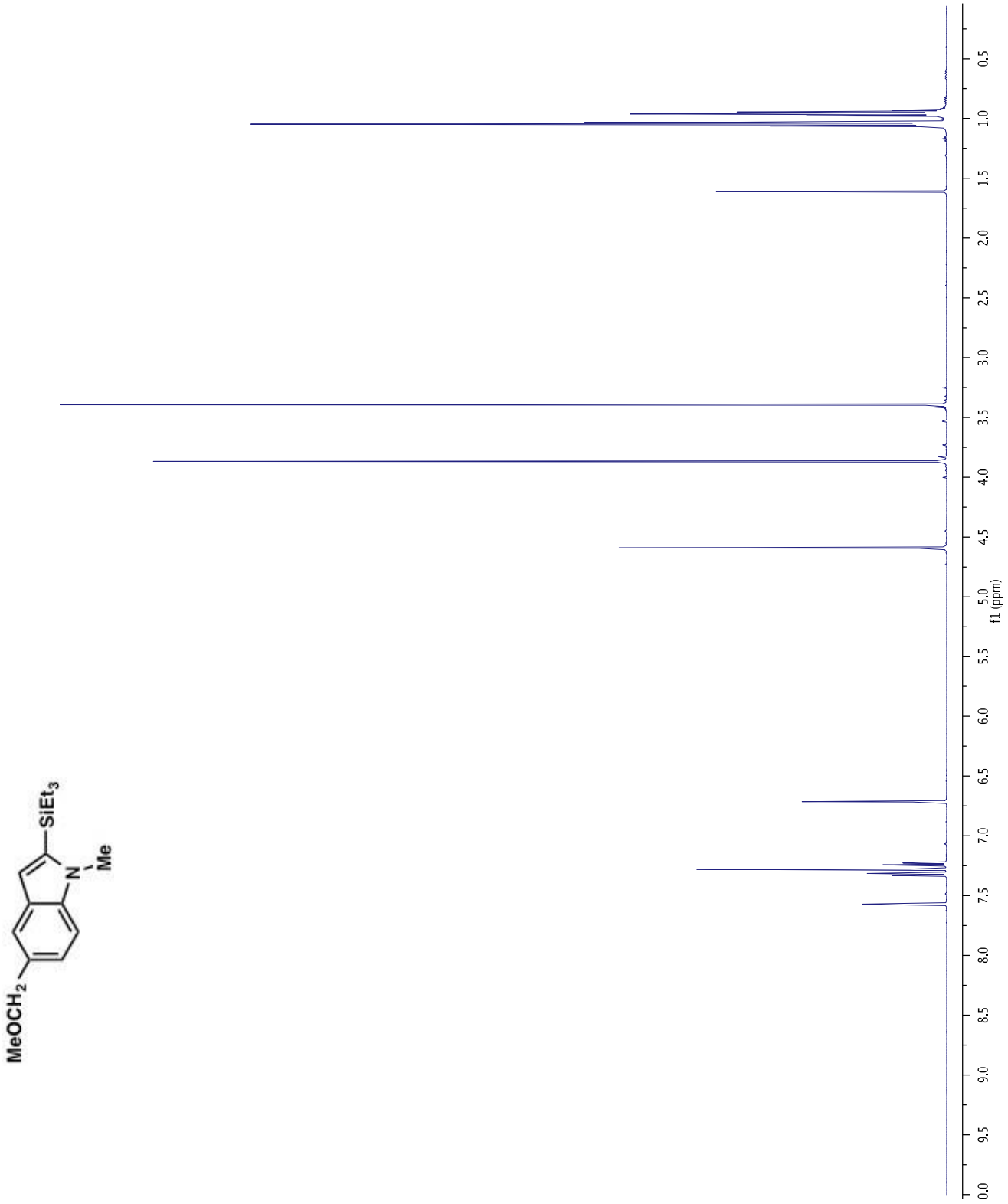
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12k_*ortho***



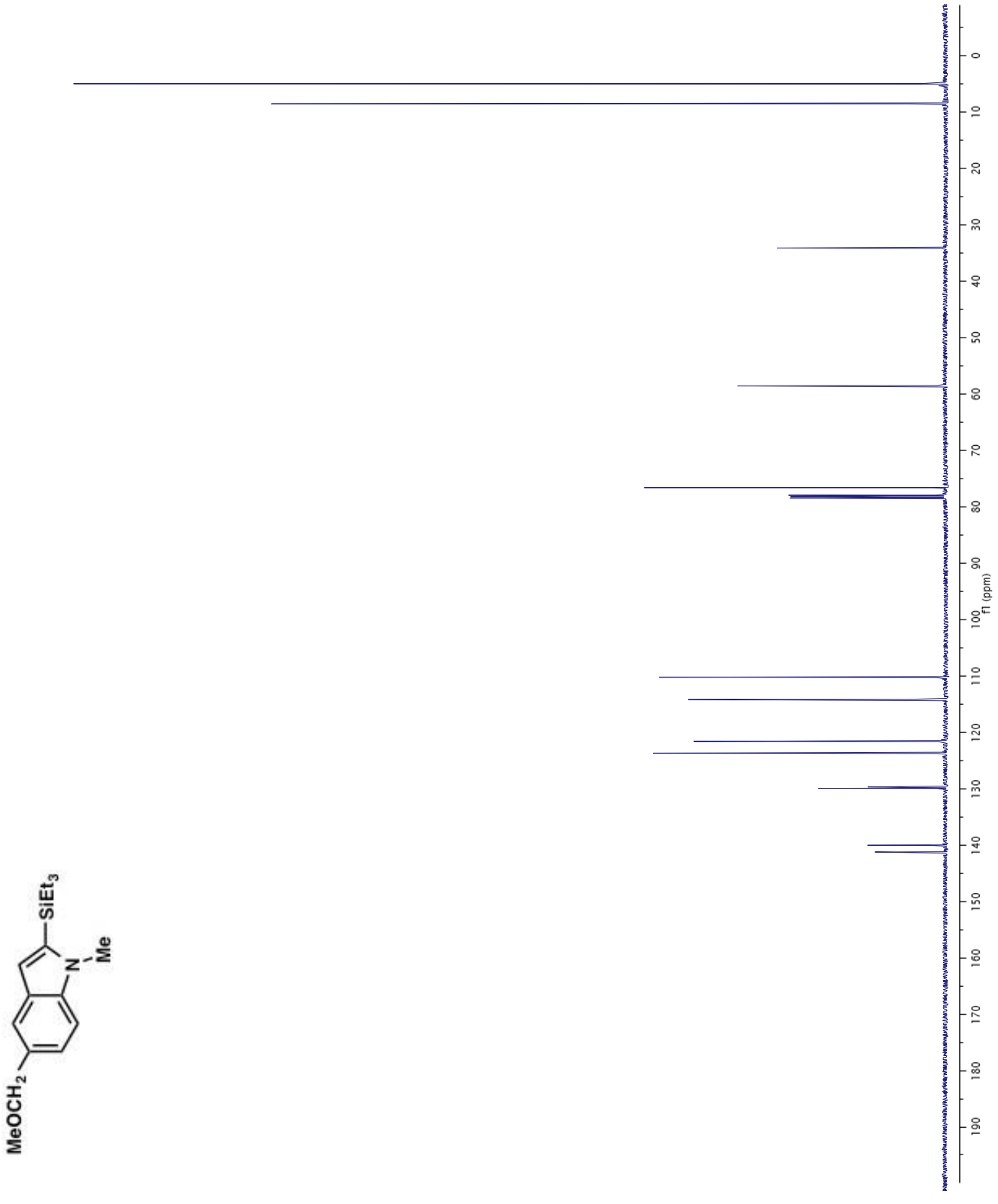
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12l**



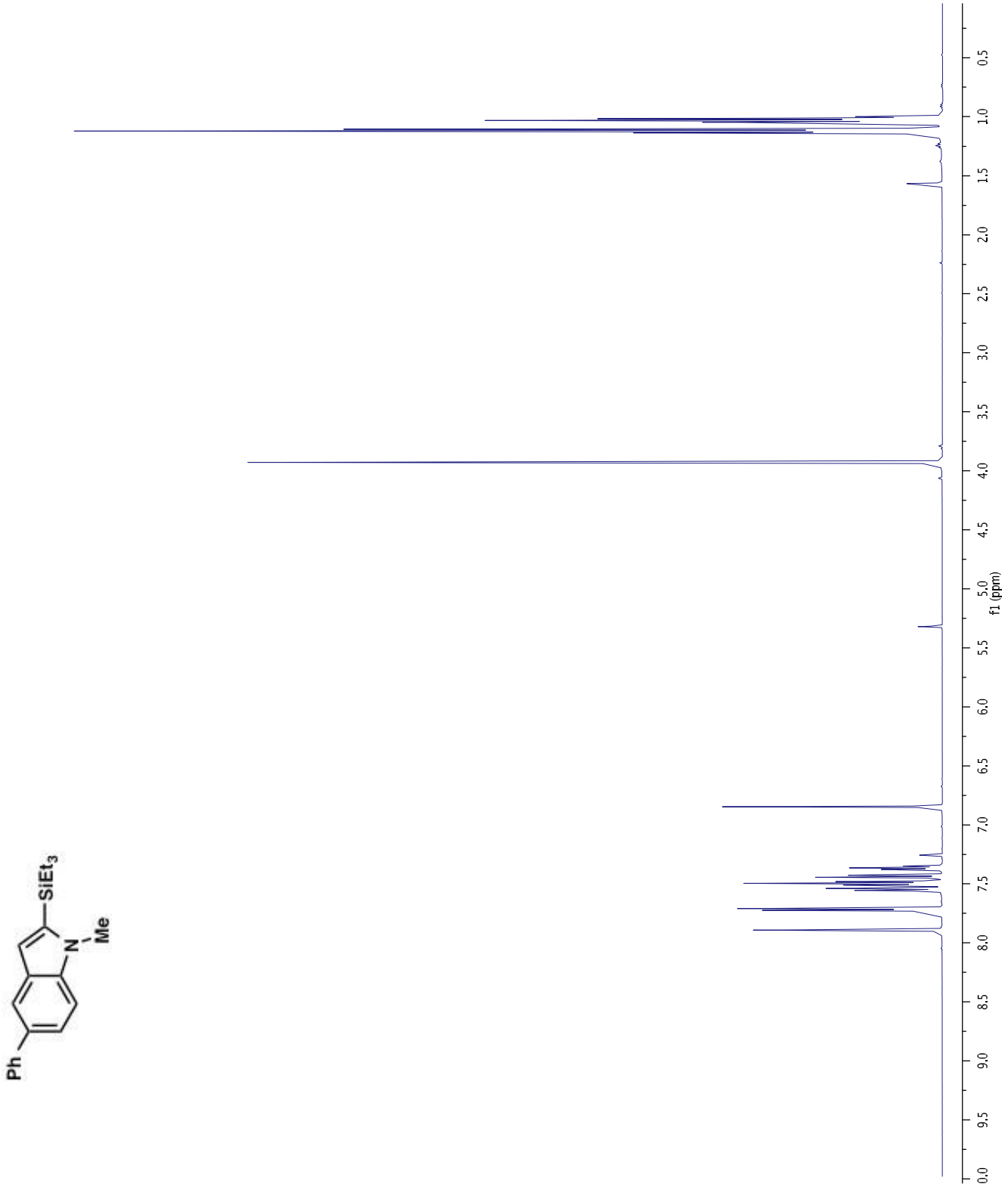
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12l**



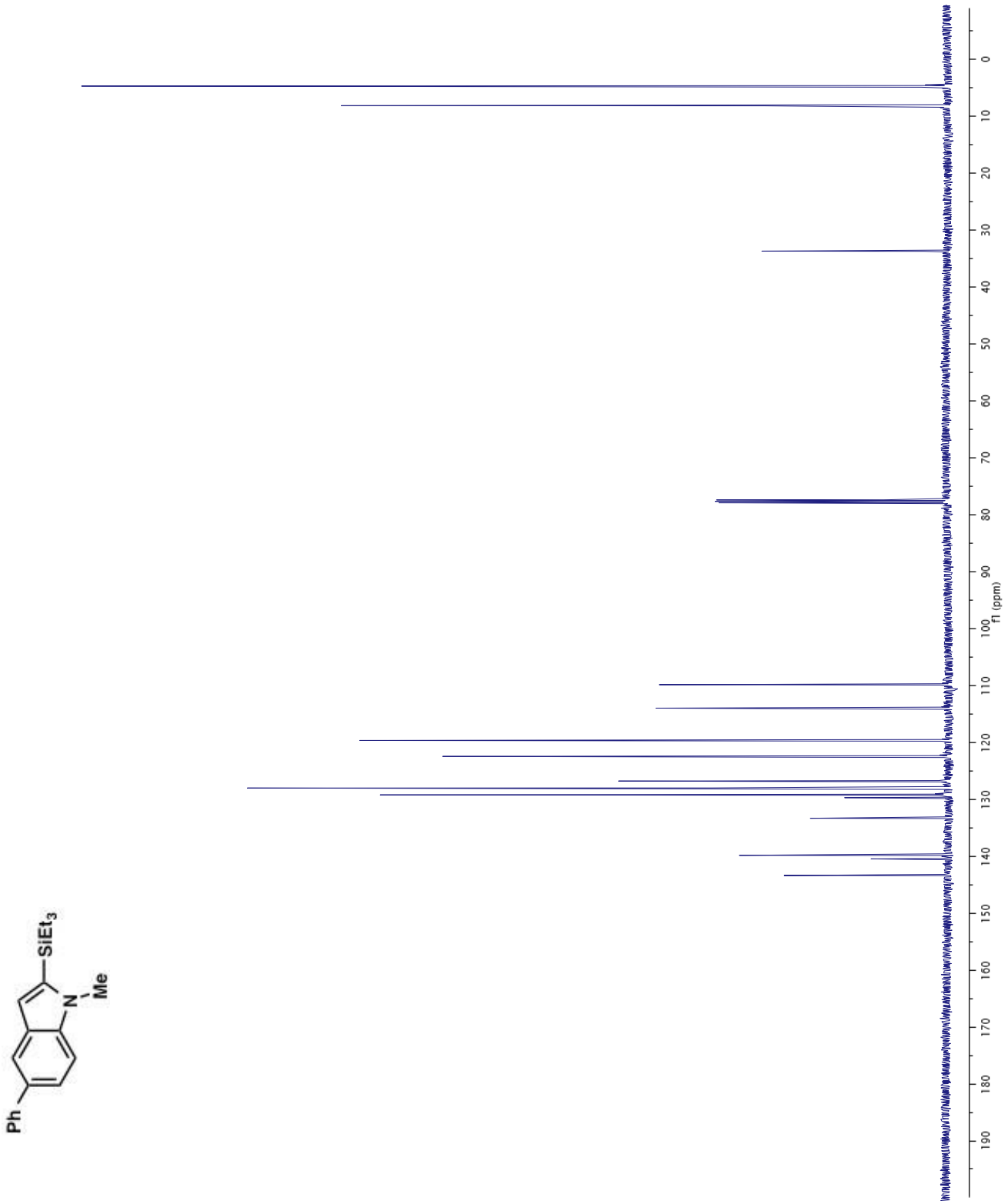
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12m**



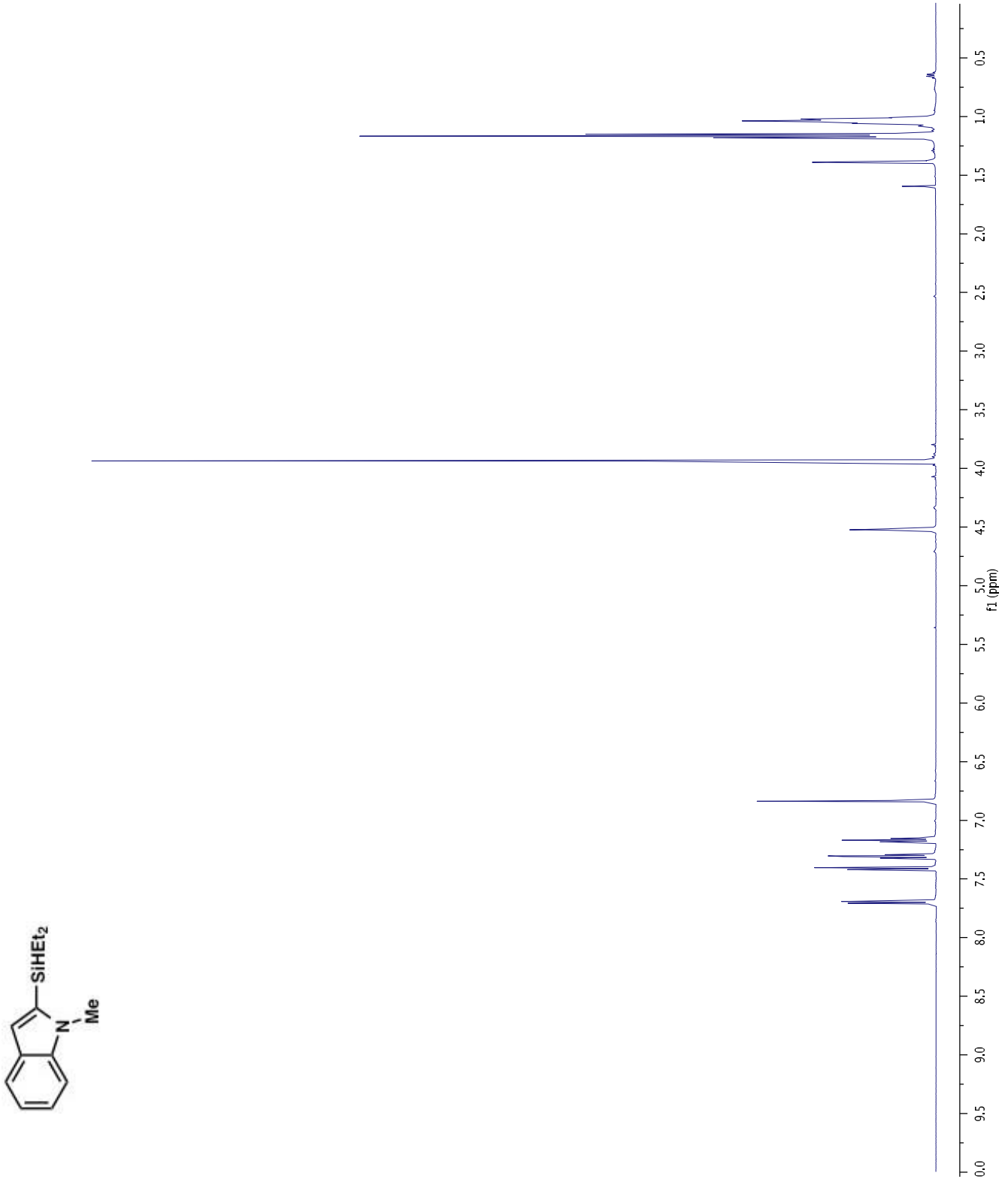
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12m**



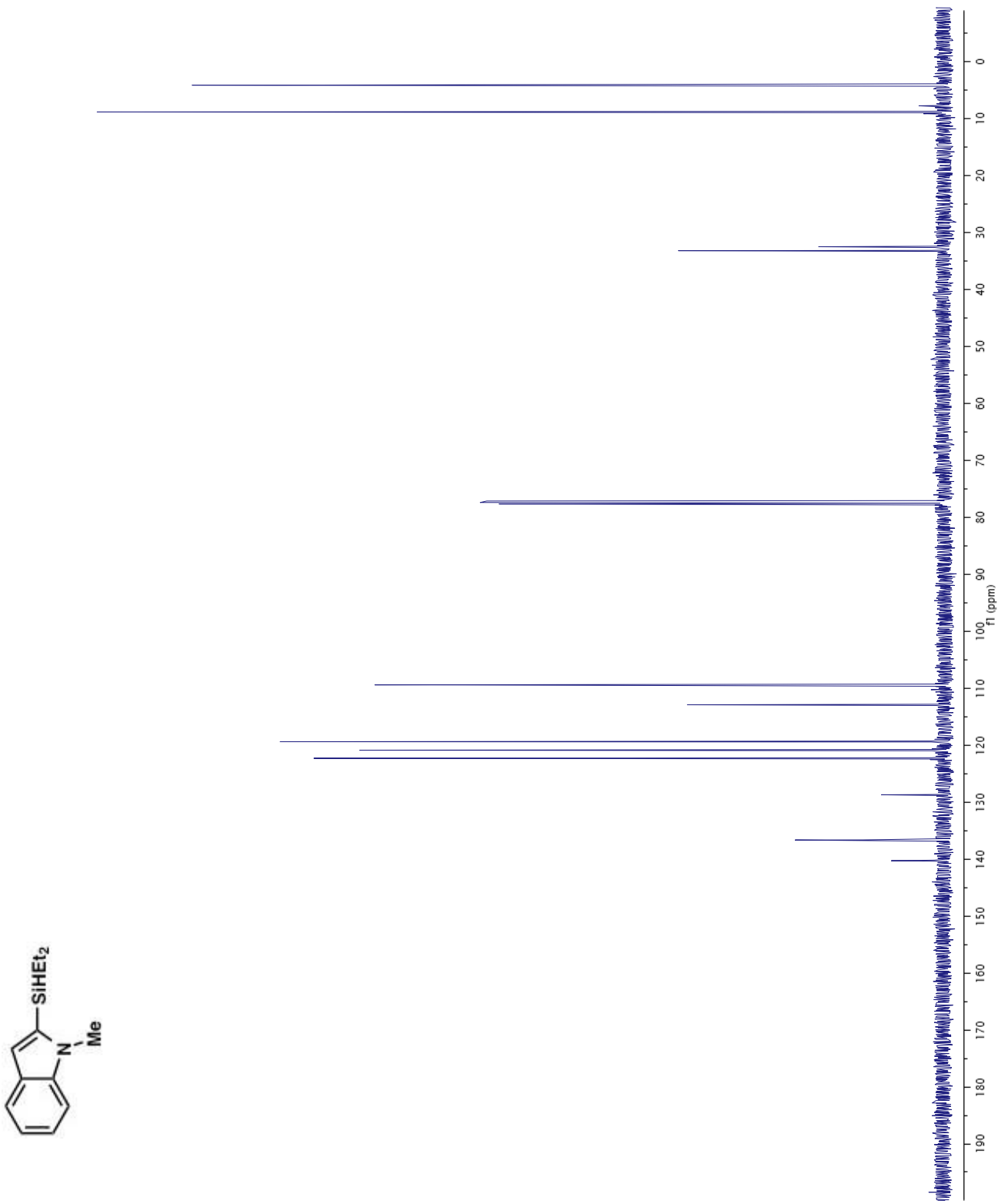
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12n**



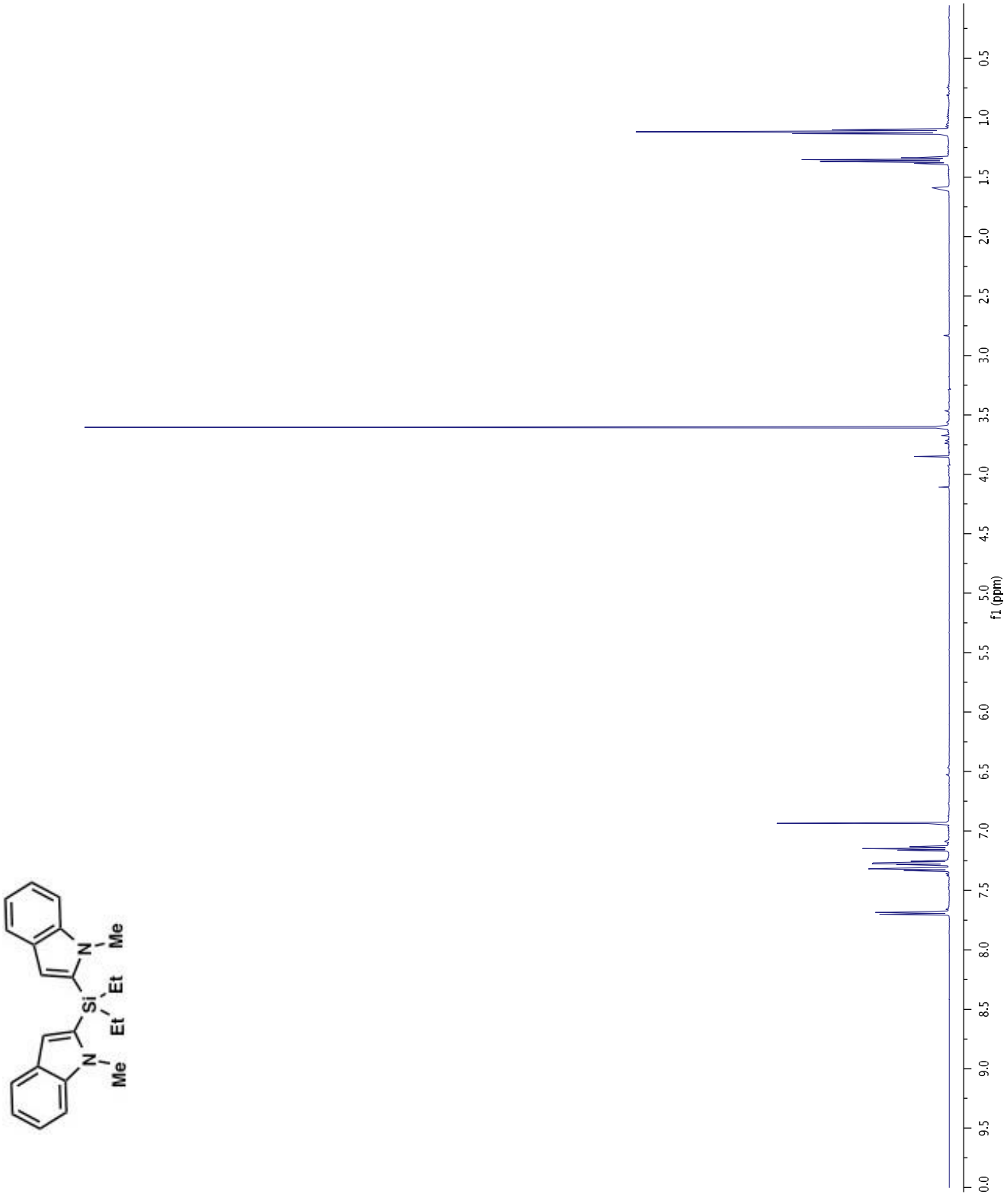
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12n**



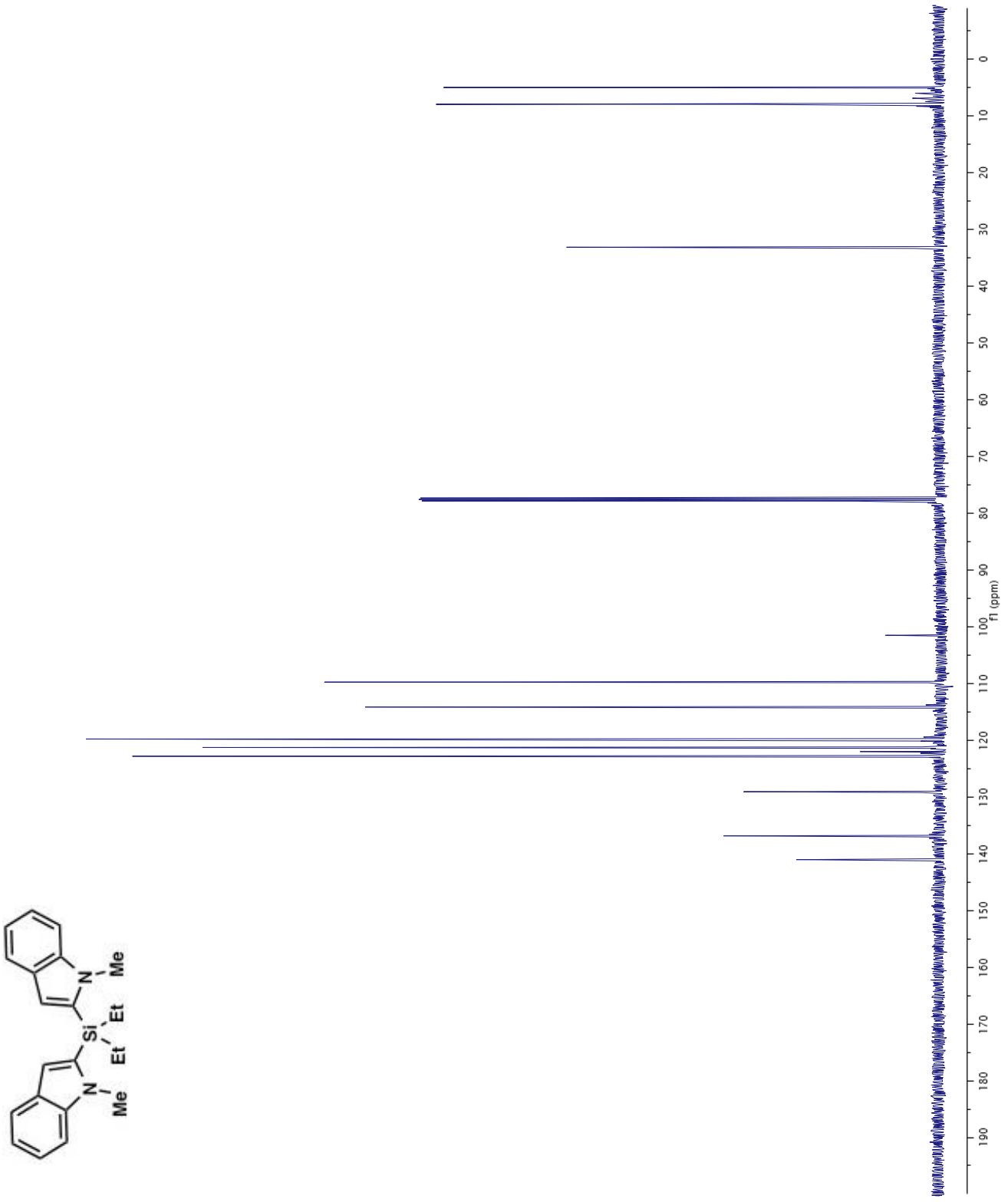
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12o**



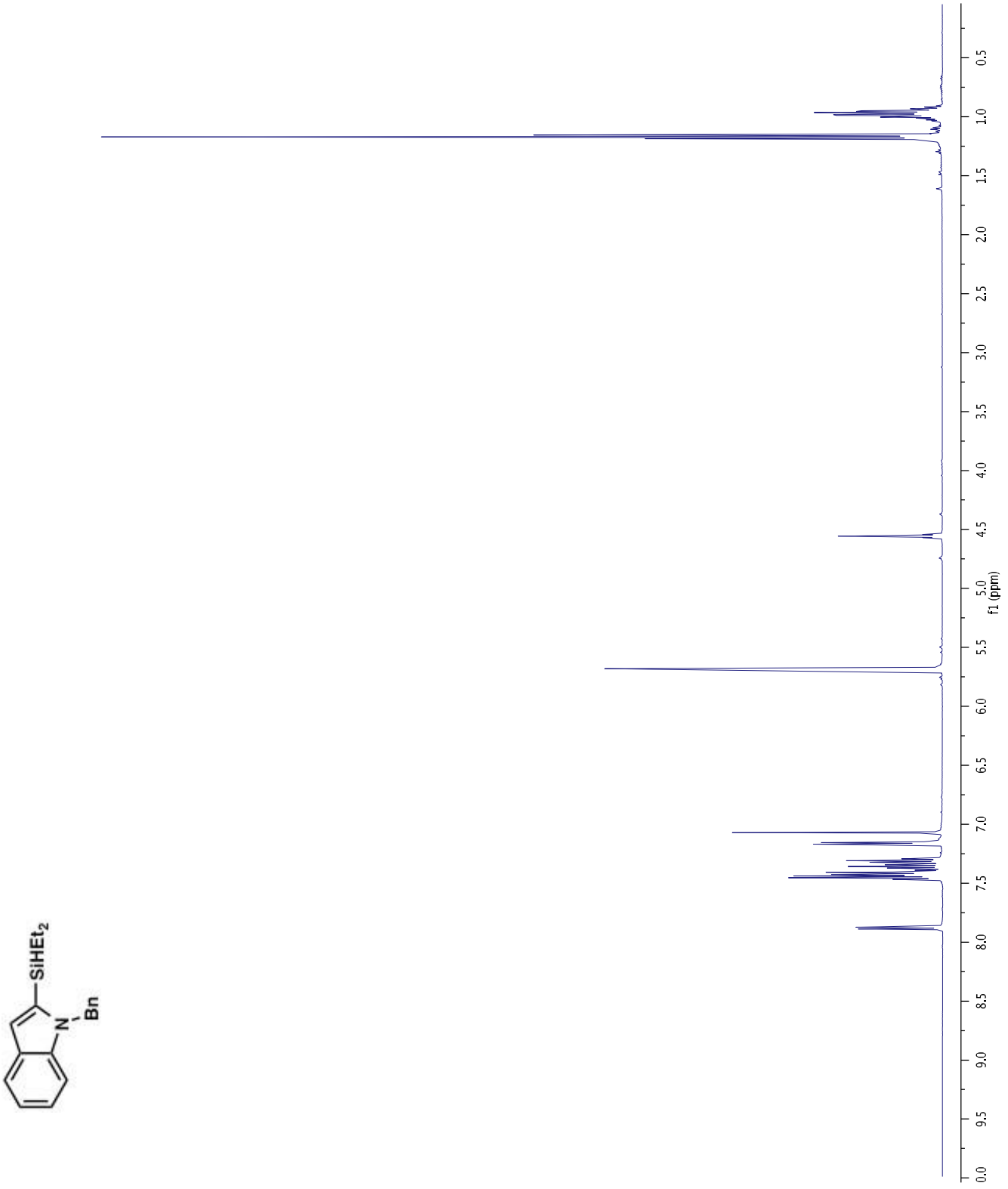
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12o**



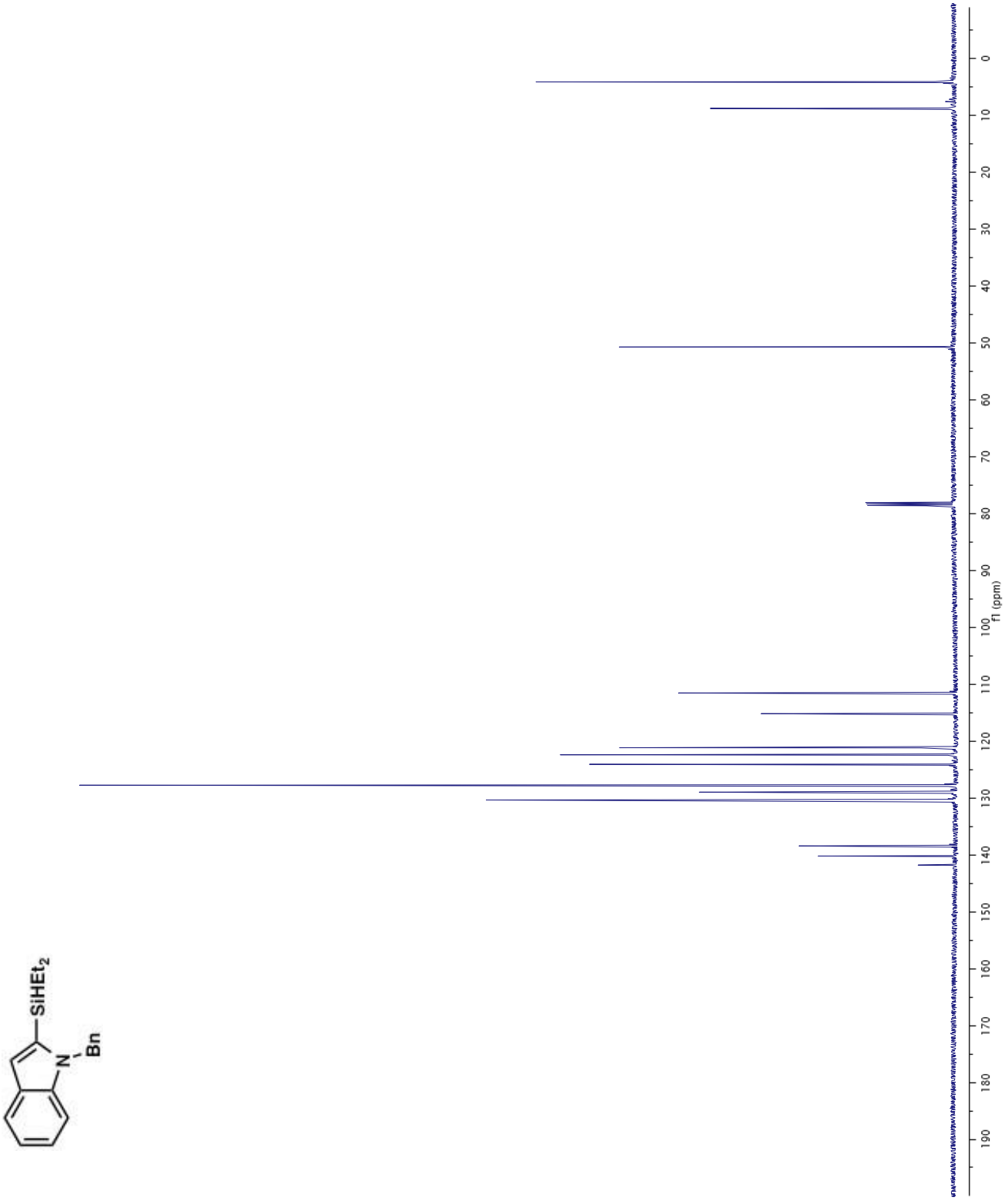
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12o_dim**



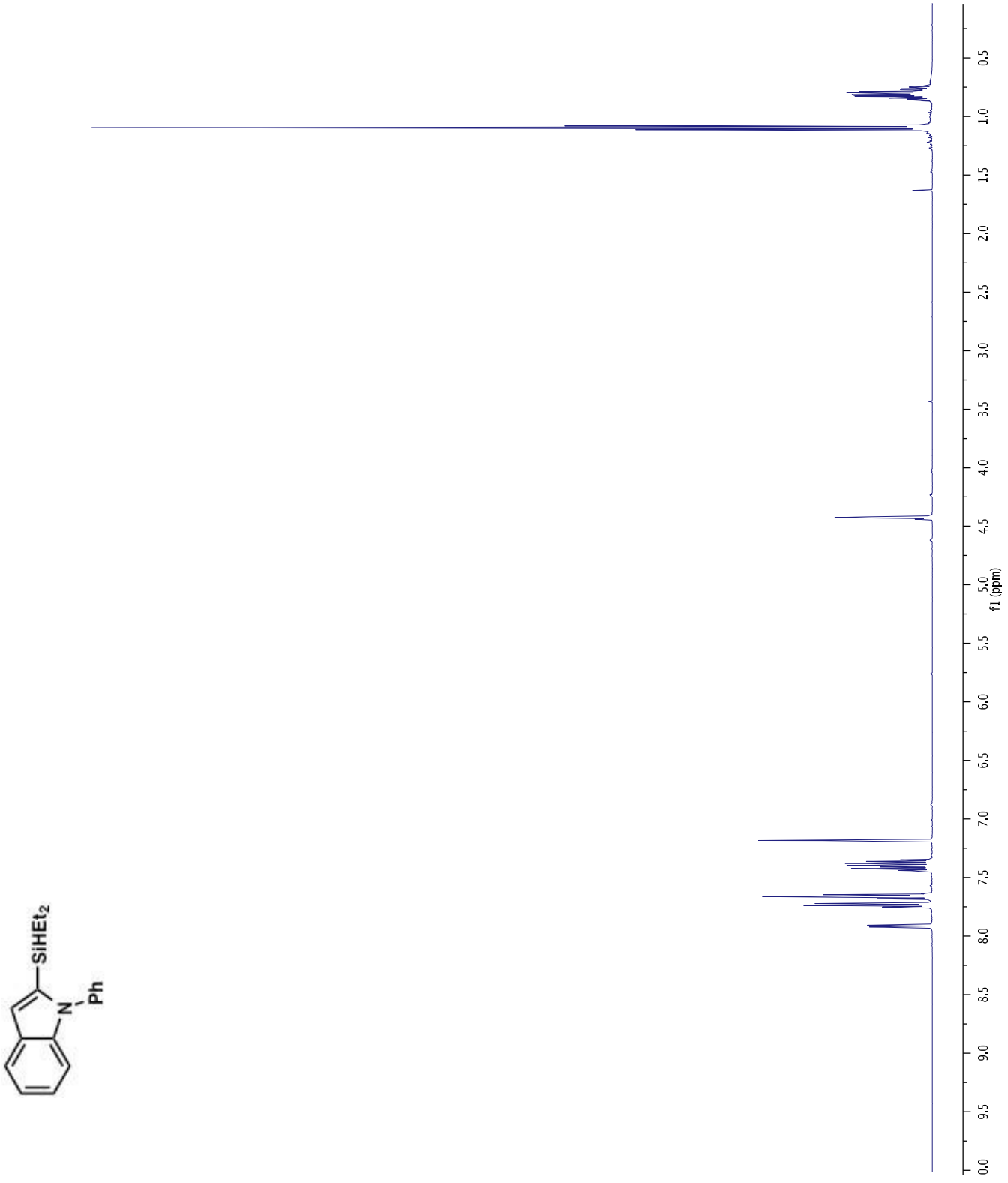
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12o_dim**



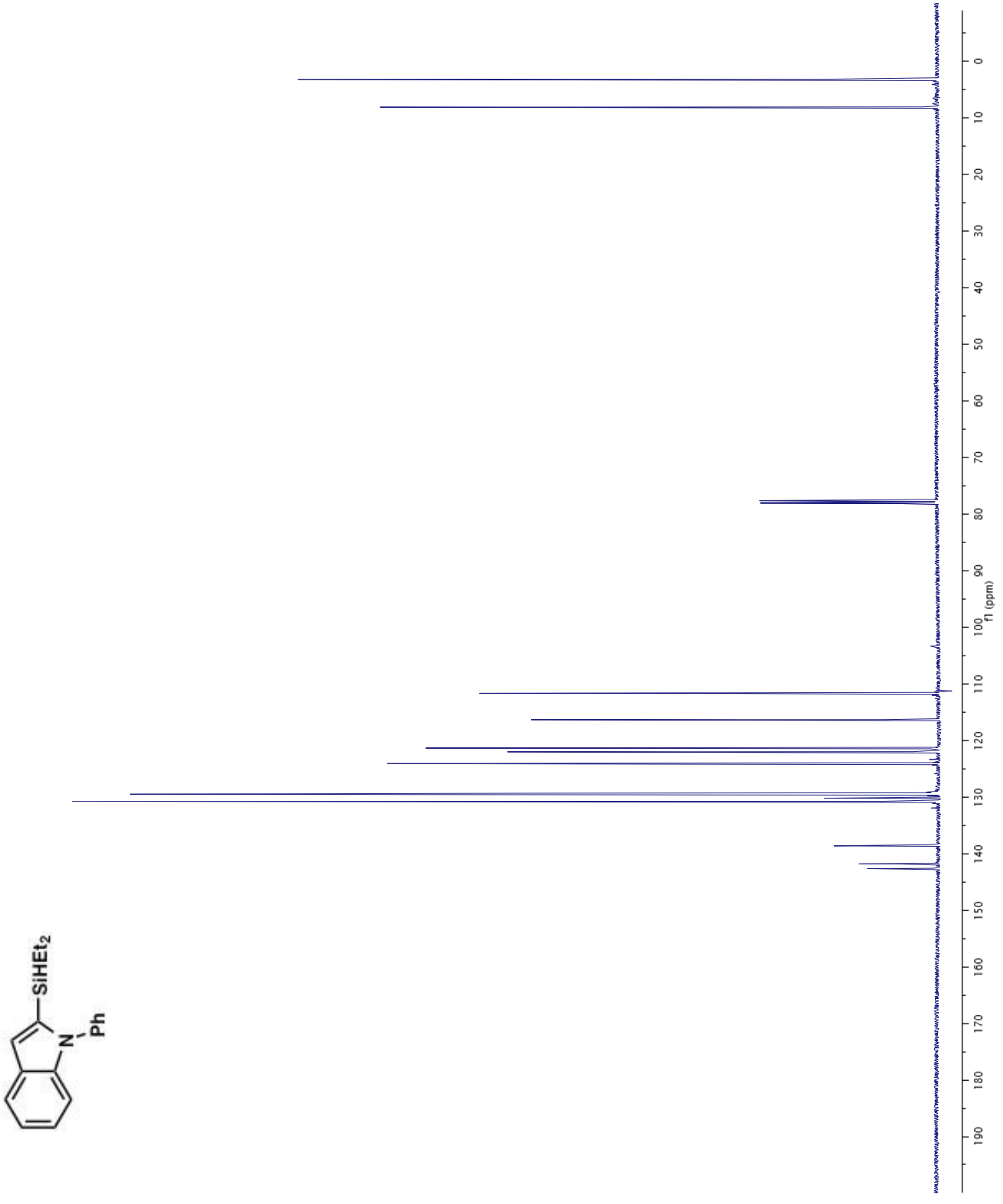
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12p**



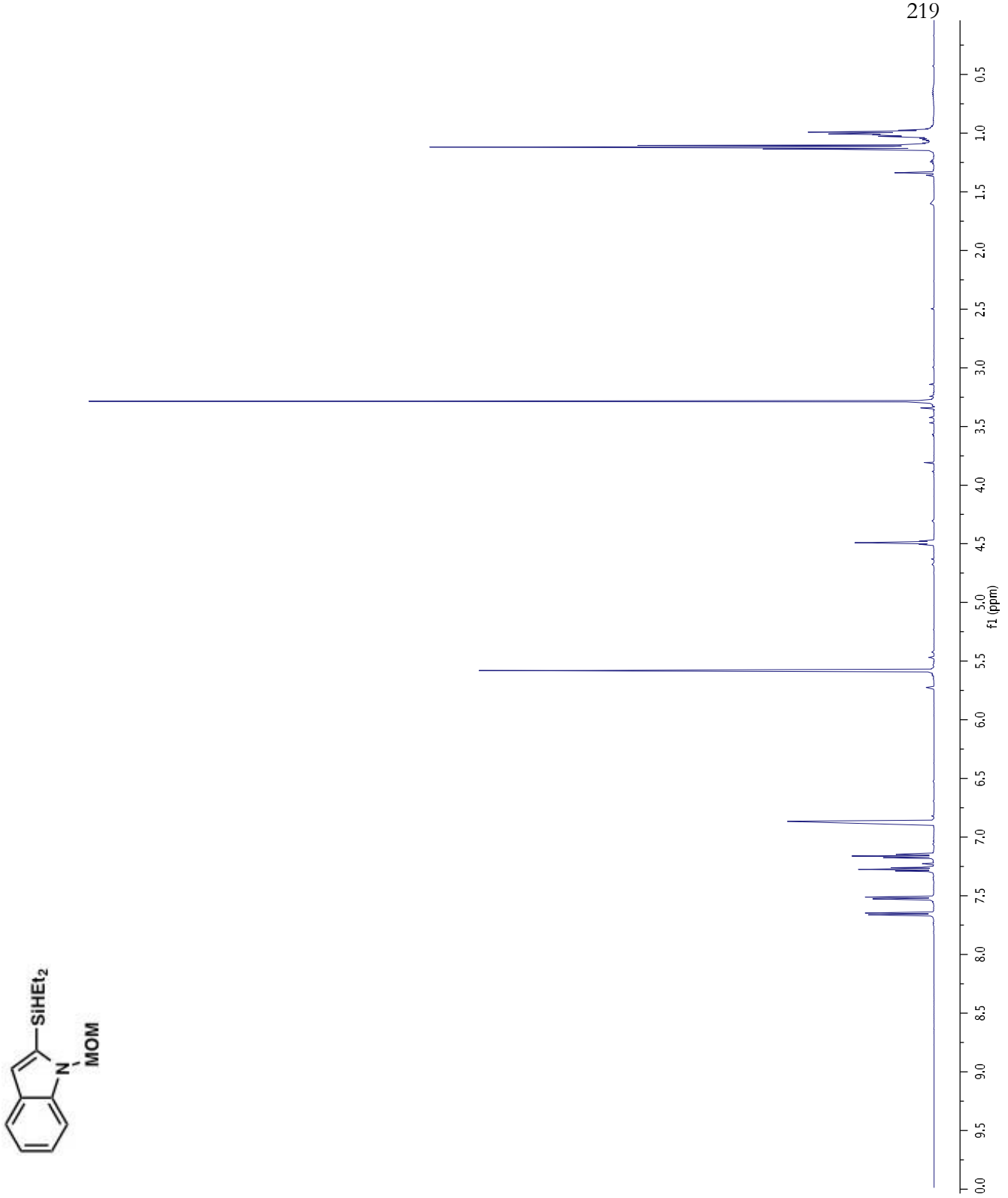
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12p**



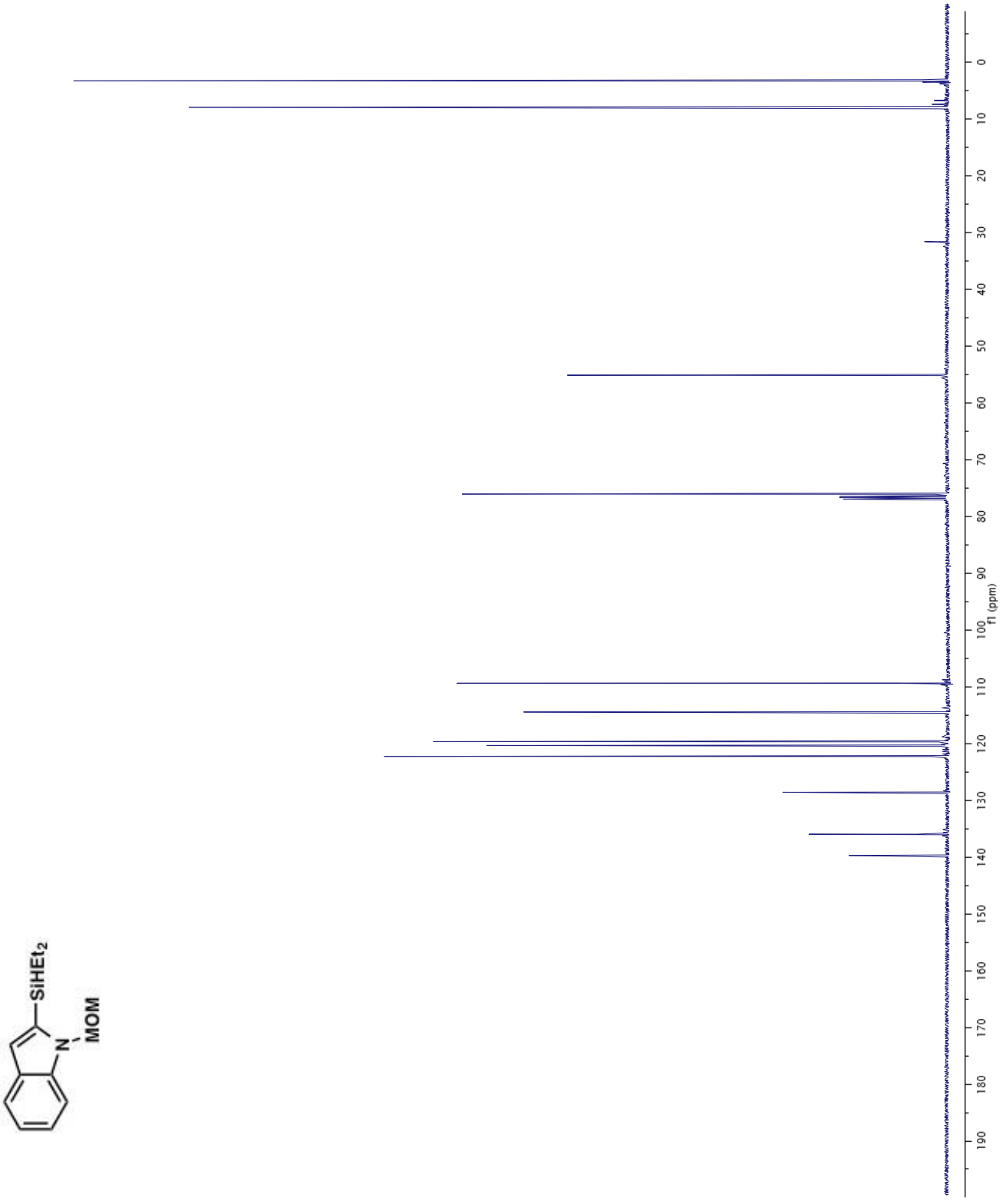
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12q**



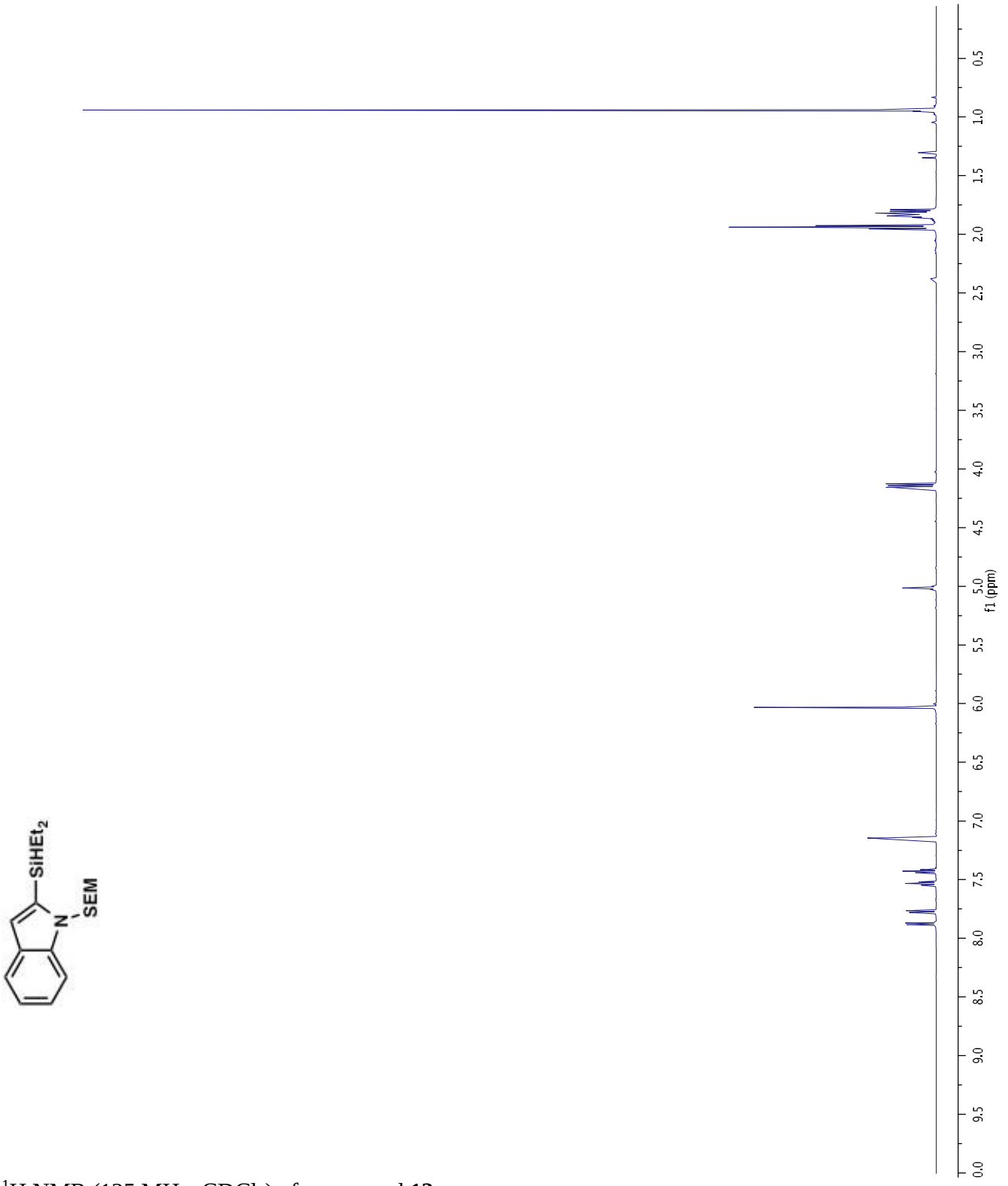
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12q**



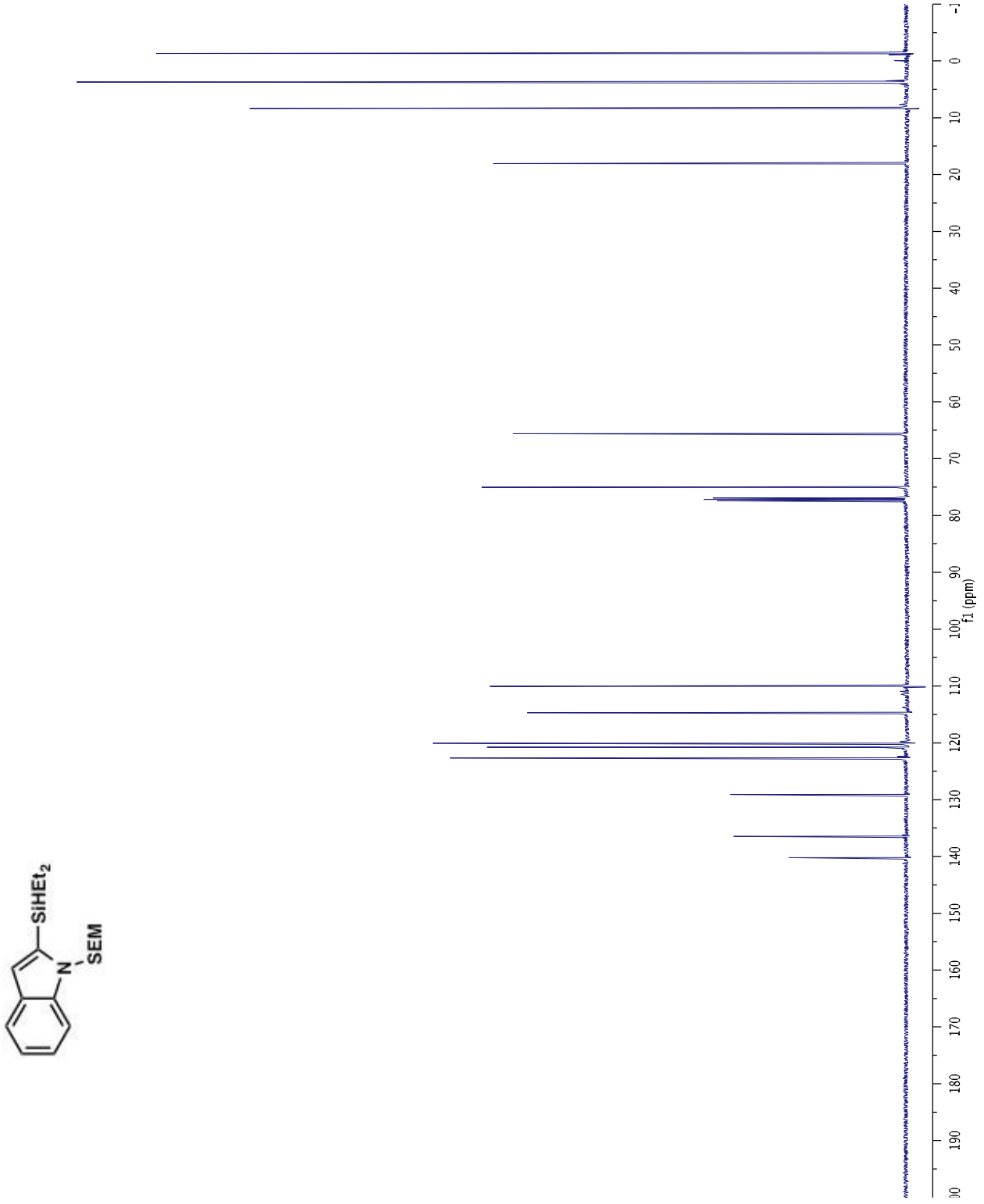
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12r**



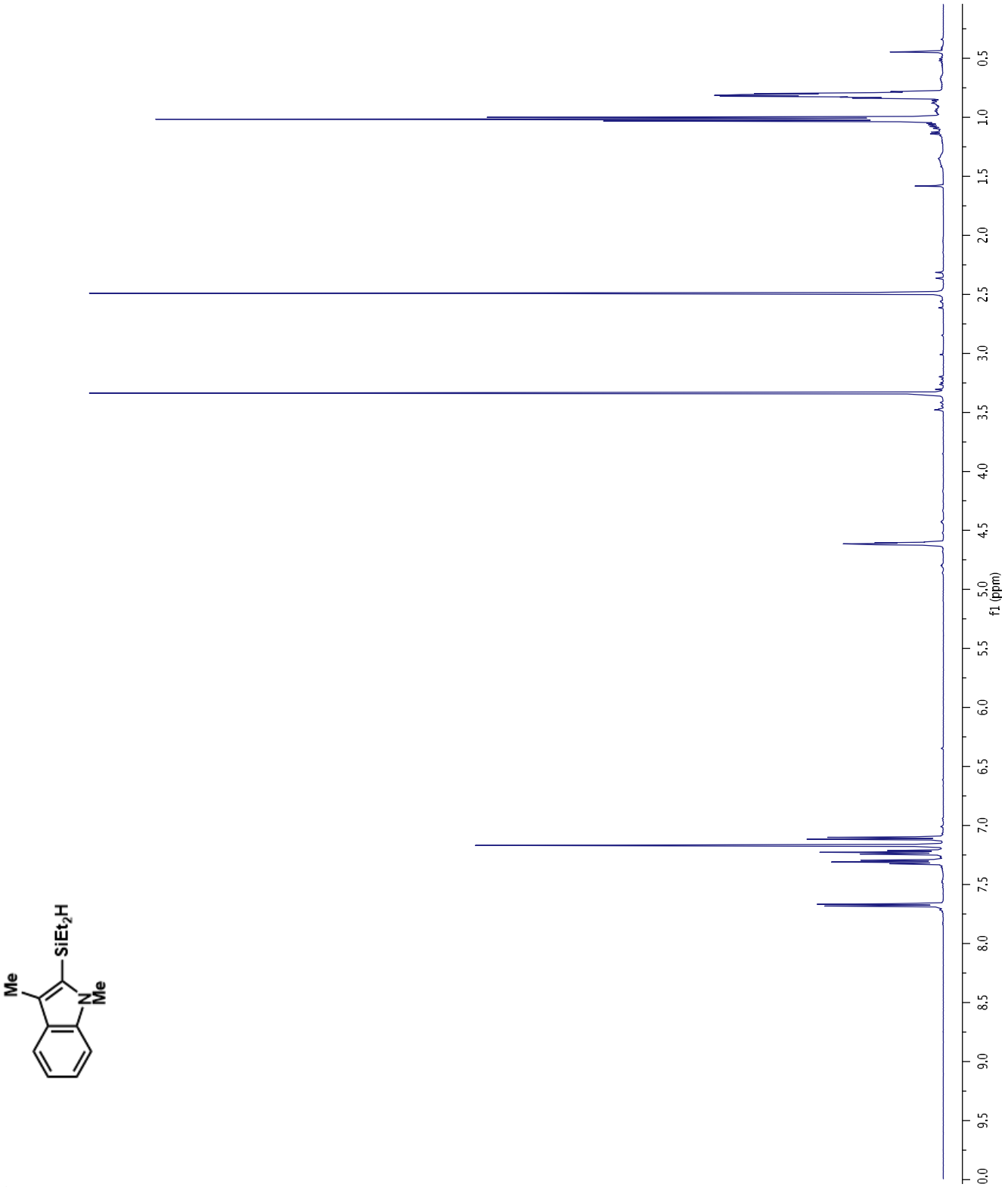
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12r**



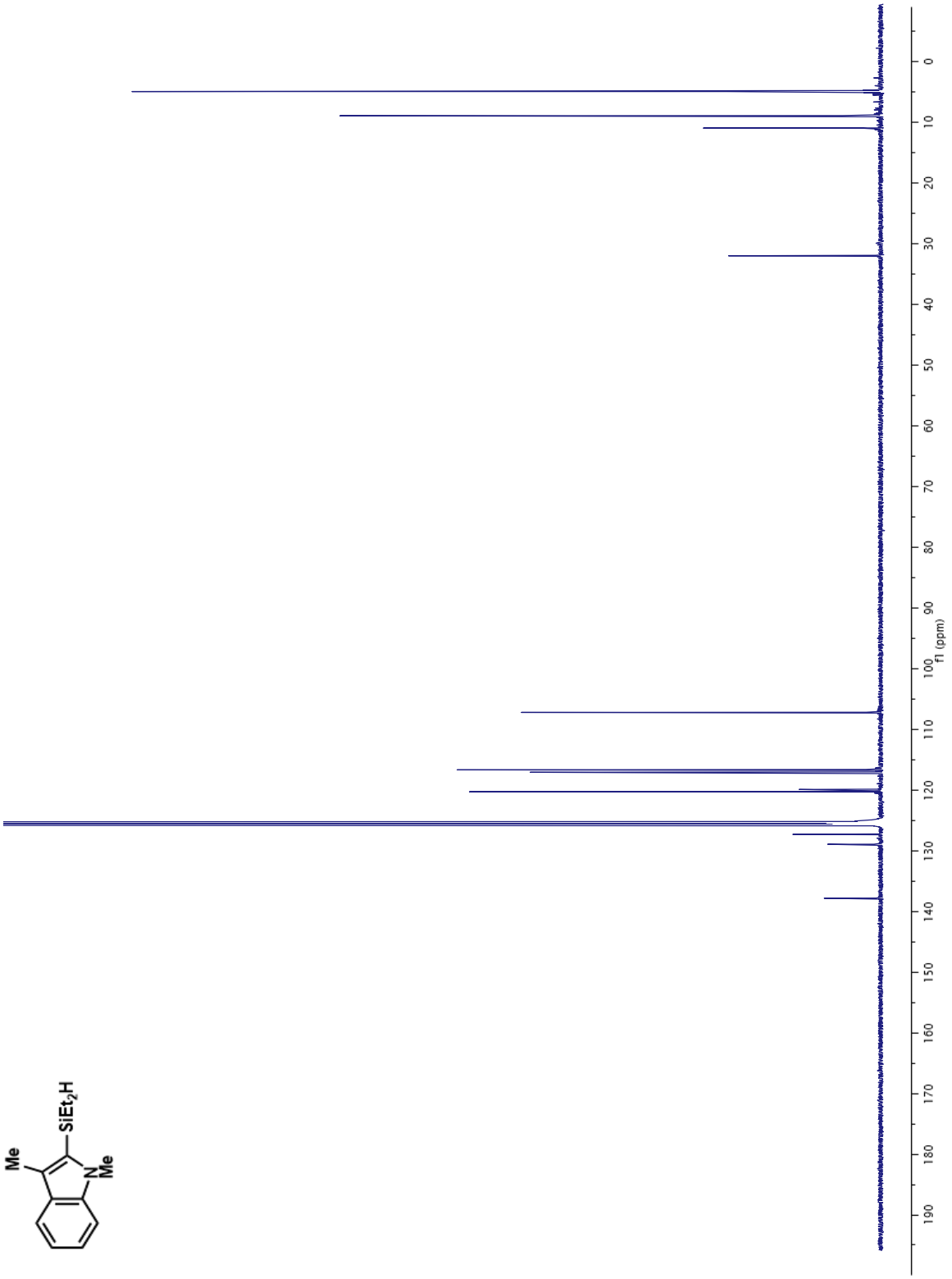
^{1}H NMR (125 MHz, $CDCl_3$) of compound **12s**



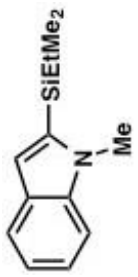
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12s**

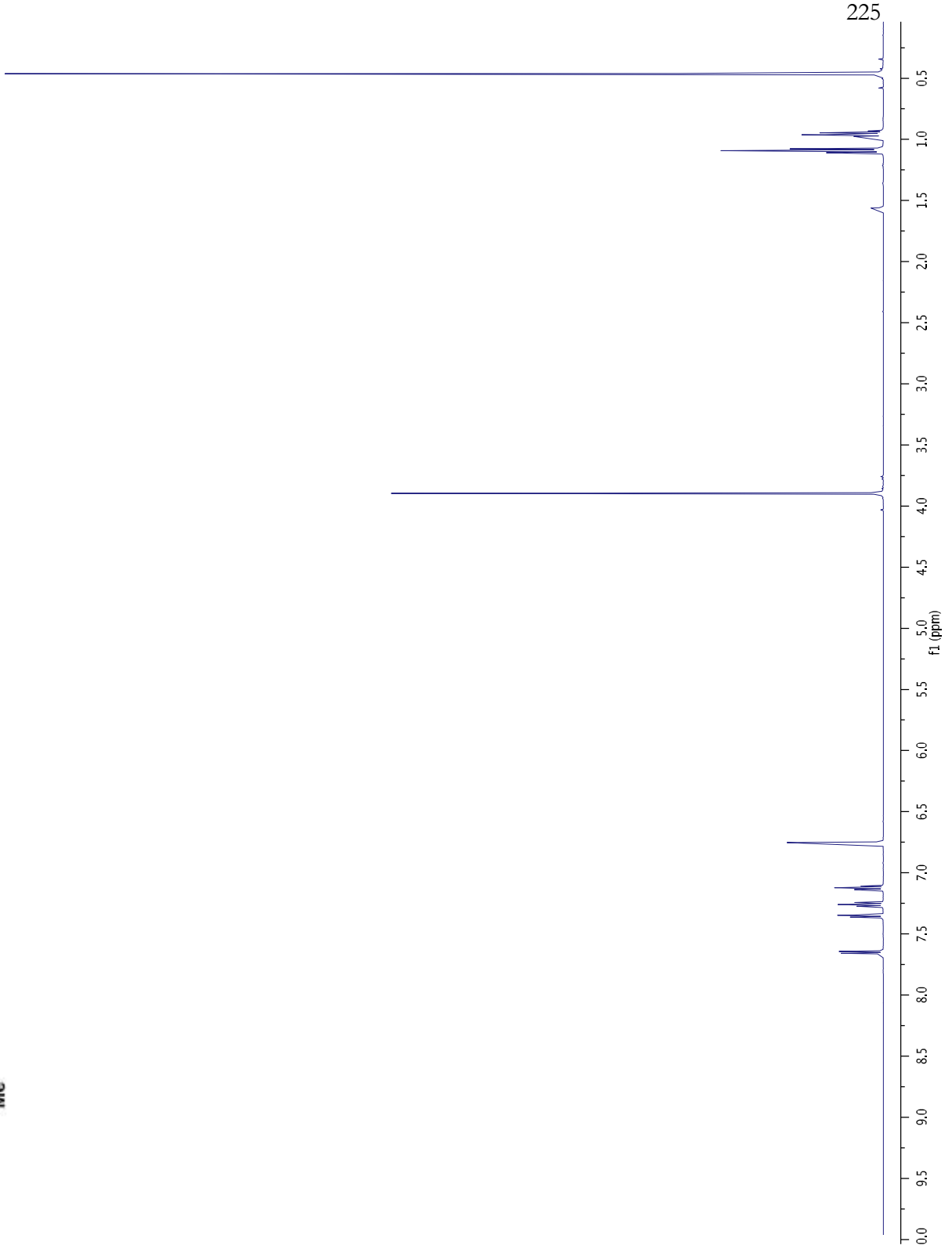


^{1}H NMR (500 MHz, C_6D_6) of compound **12t**

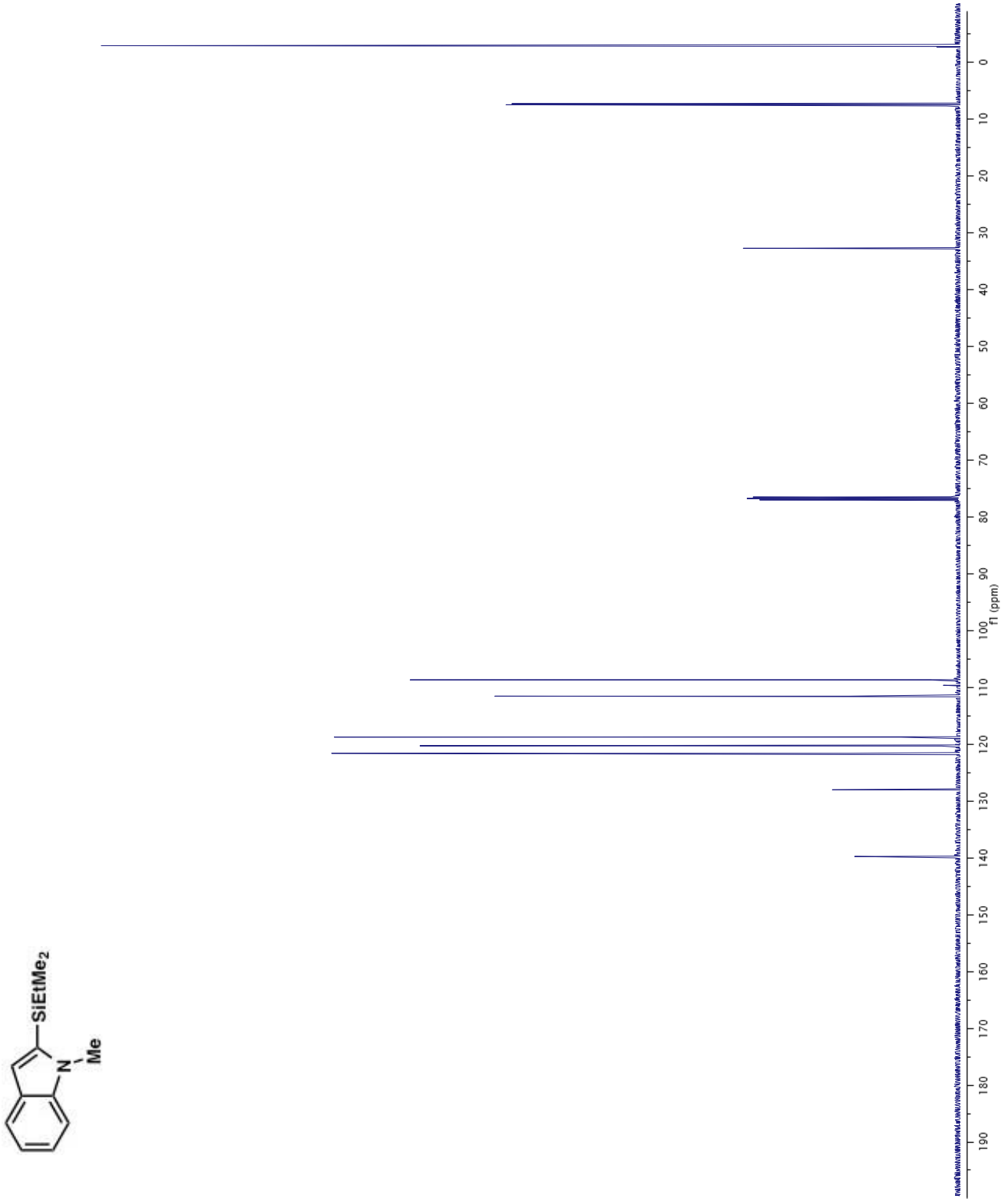


^{13}C NMR (125 MHz, C_6D_6) of compound **12t**

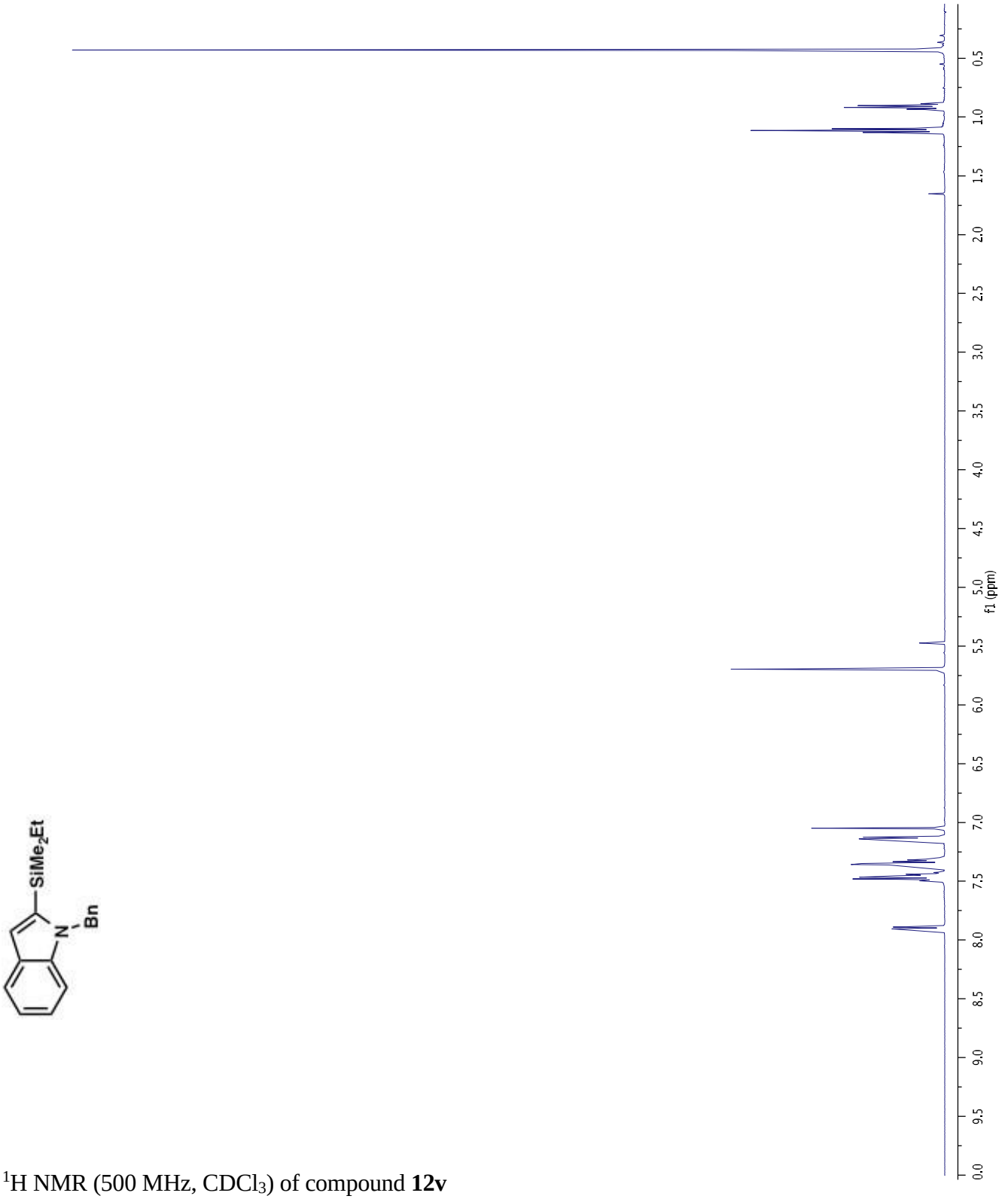




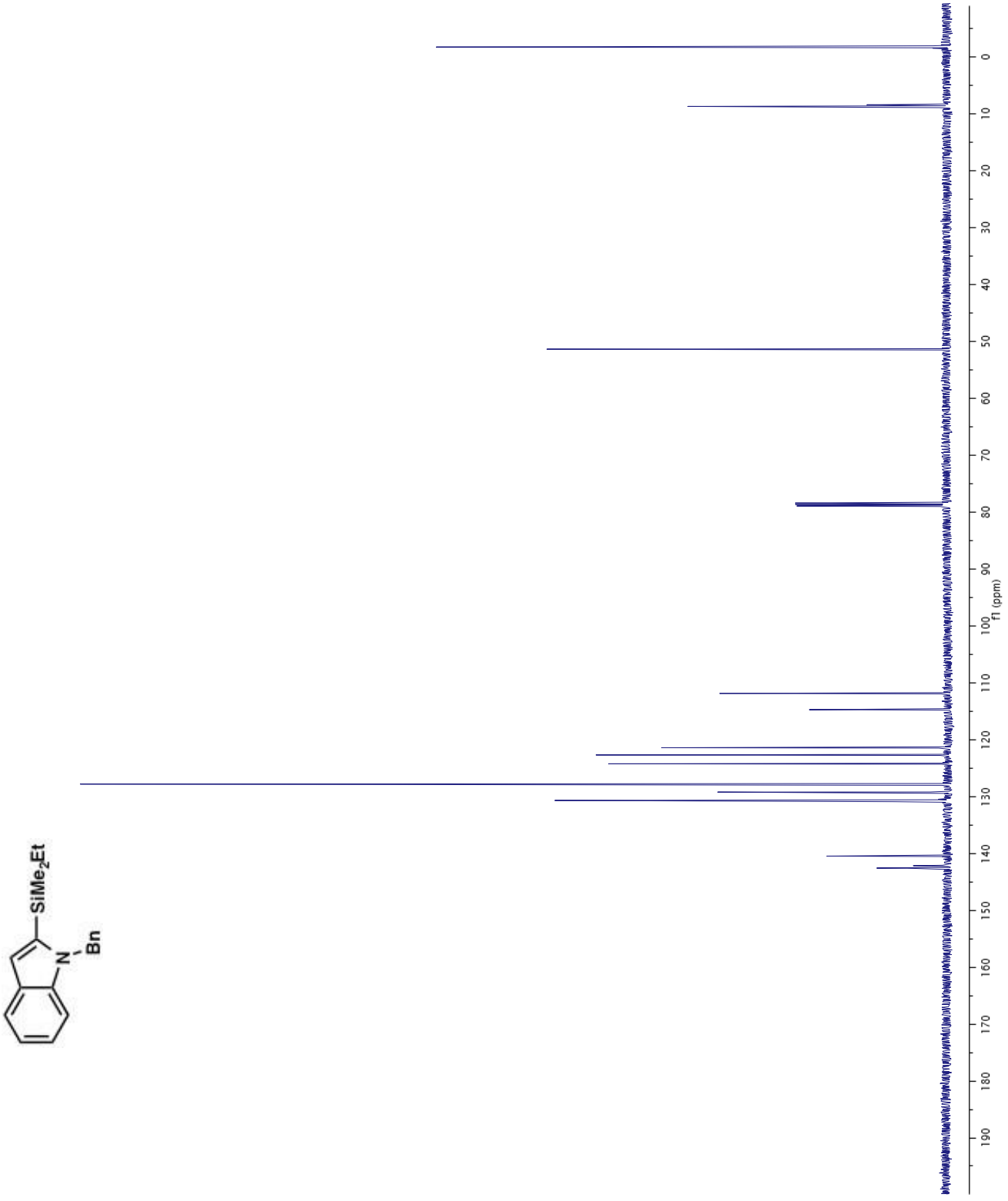
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12u**



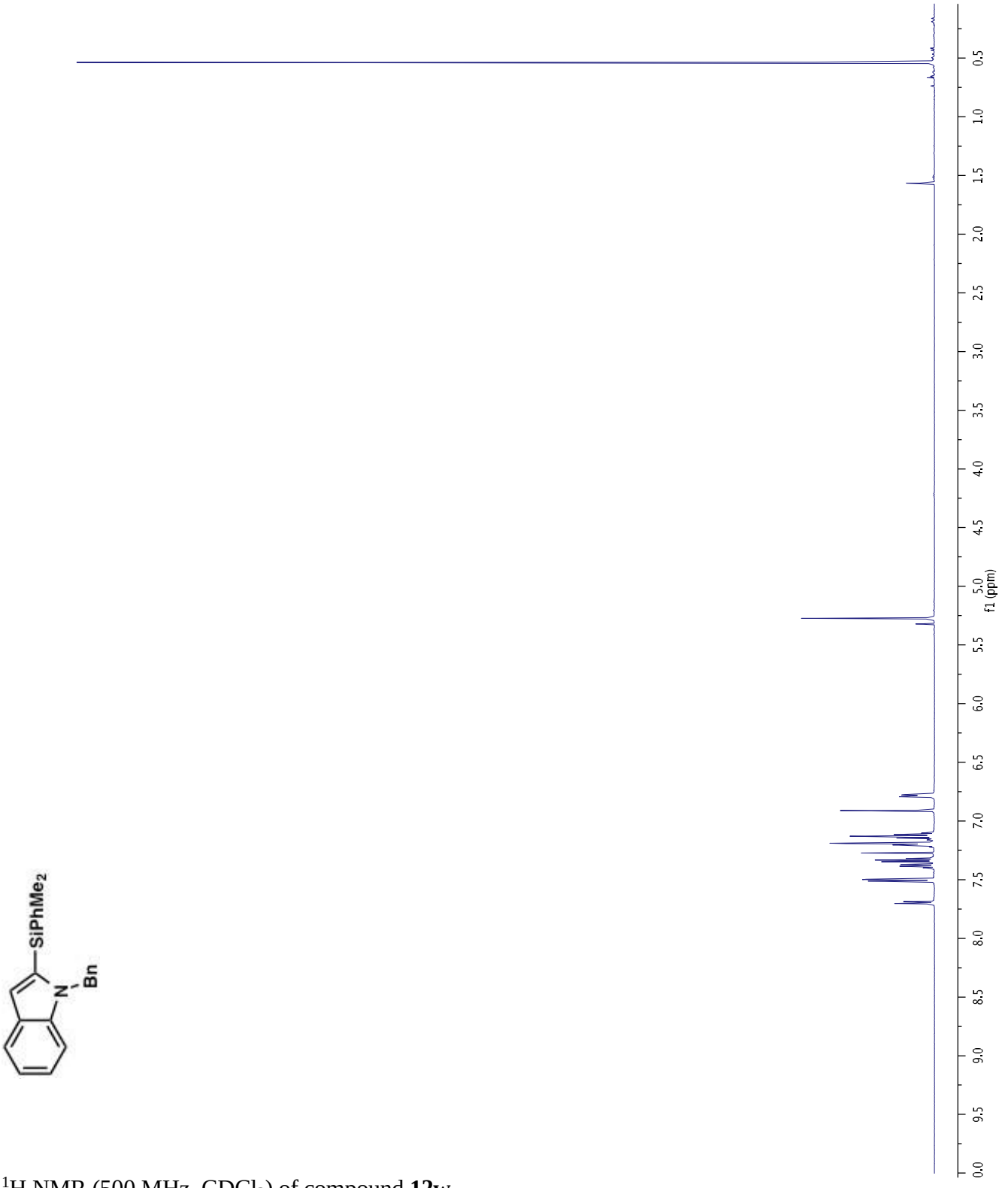
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12u**



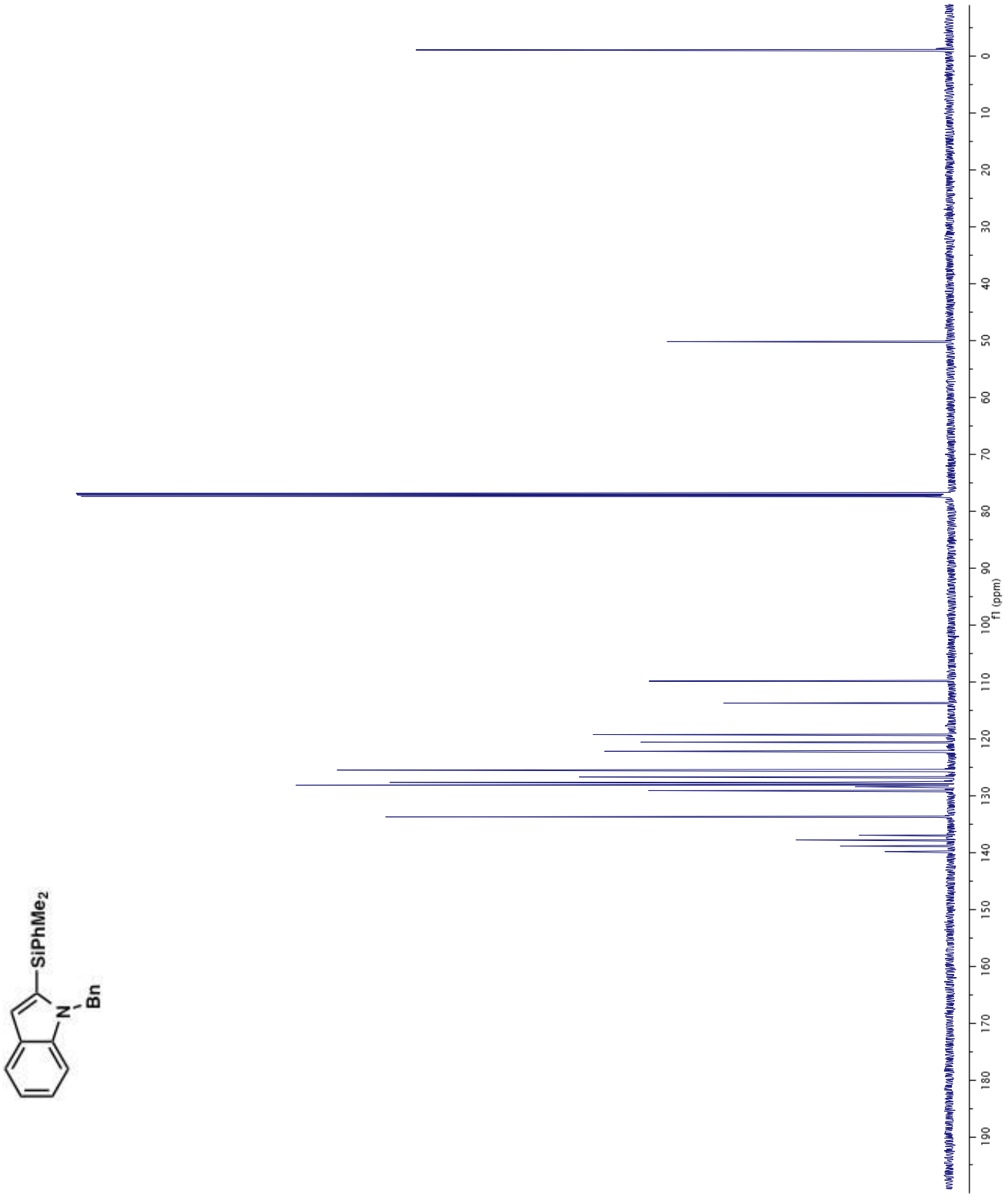
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12v**



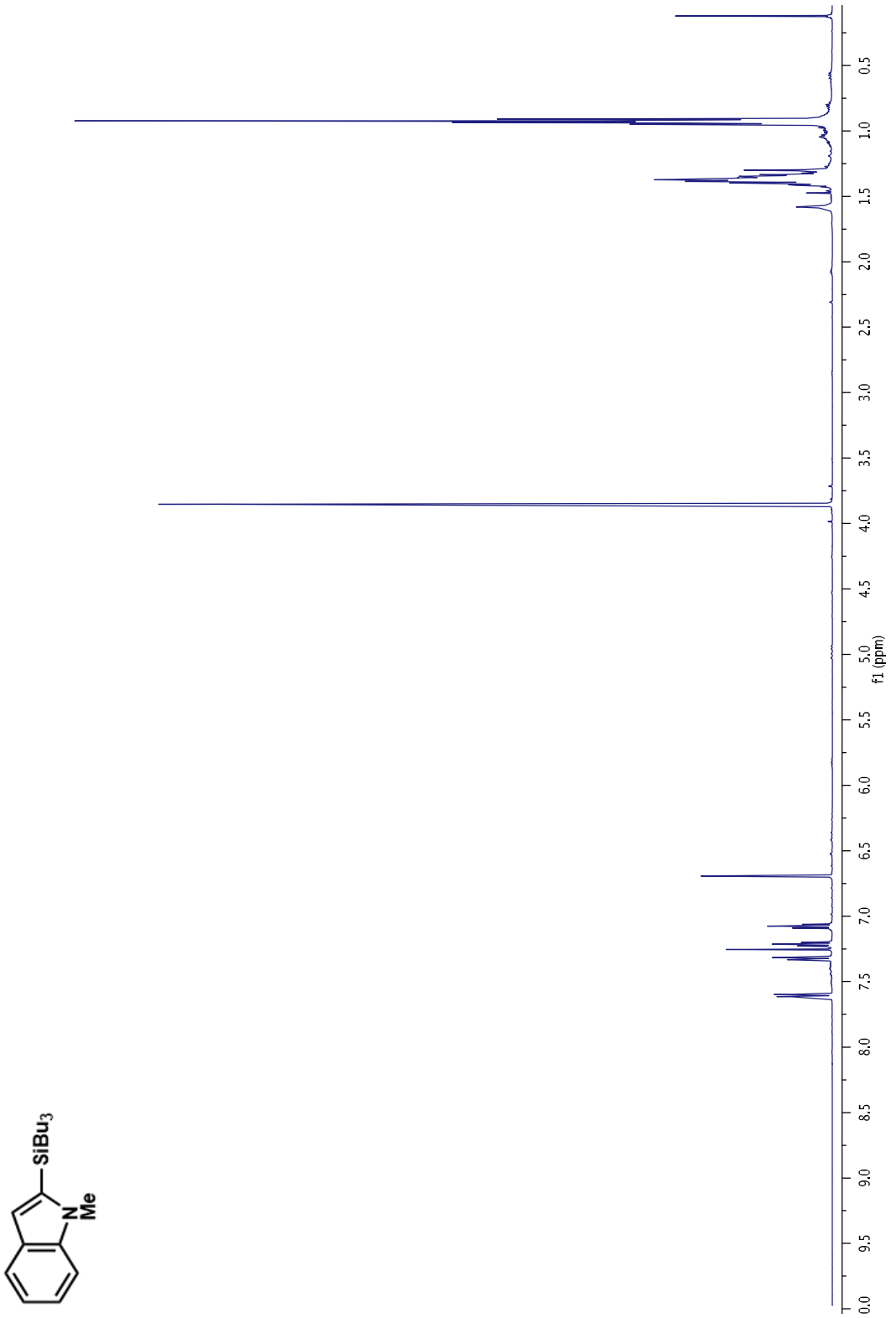
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12v**



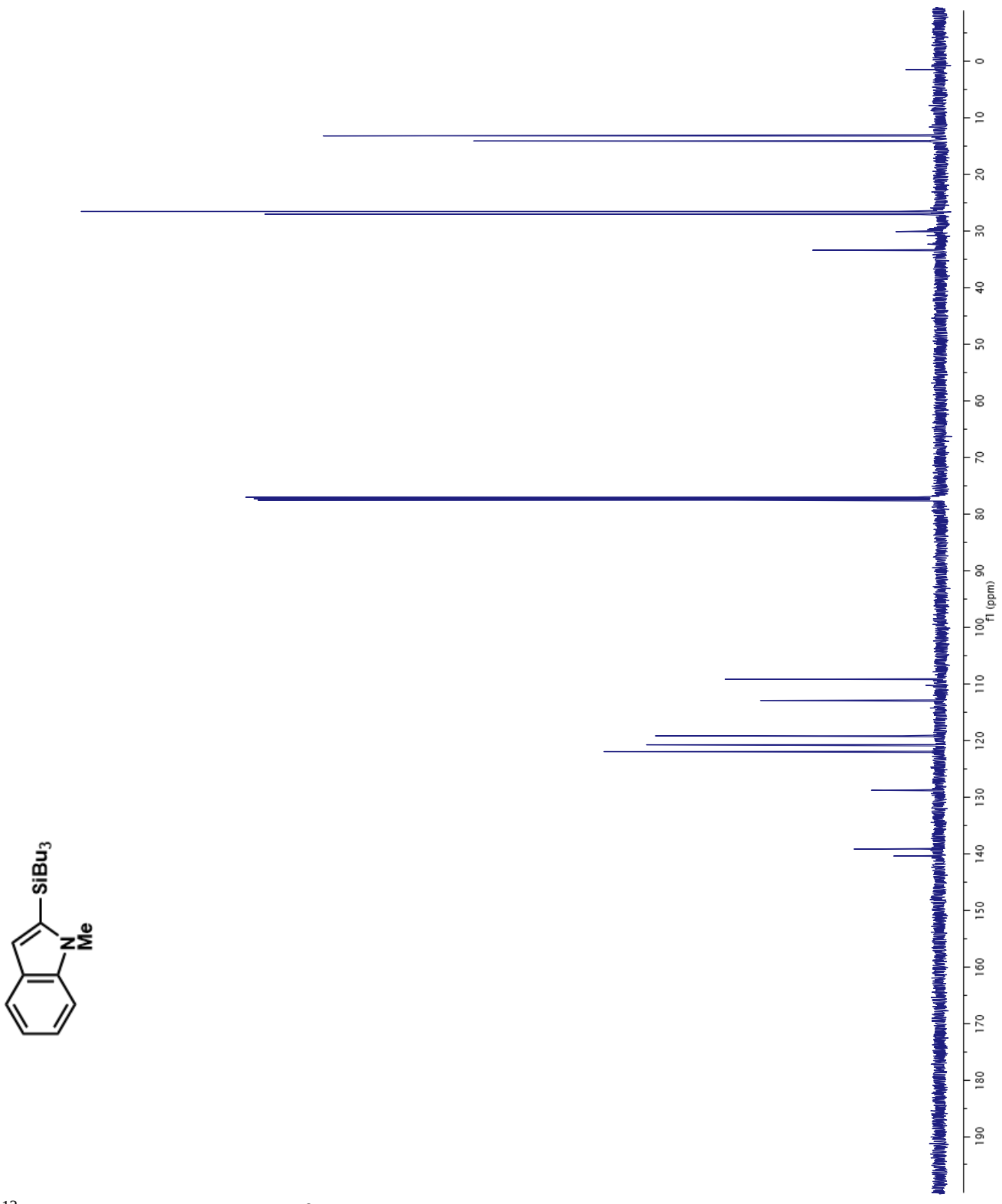
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12w**



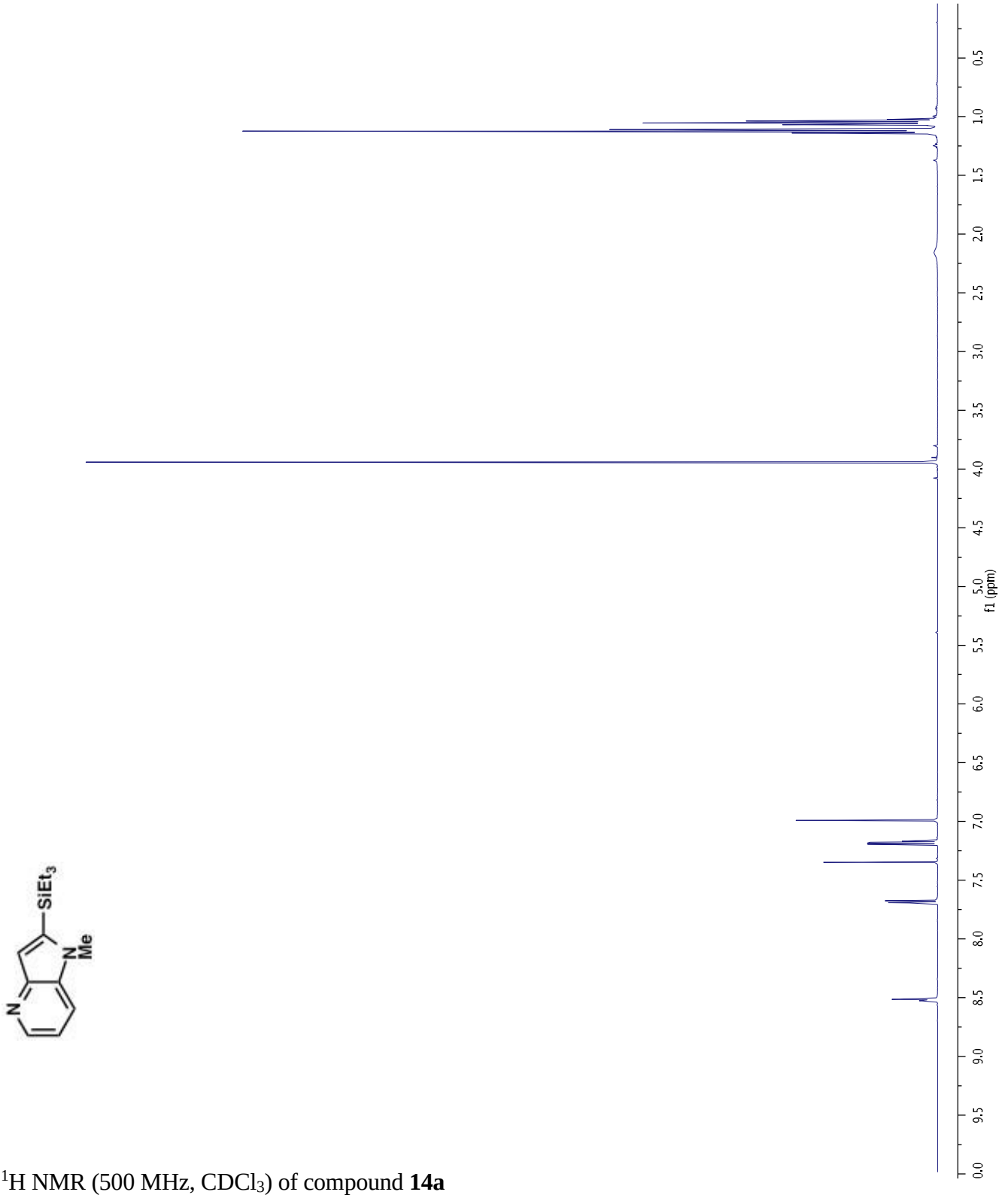
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12w**



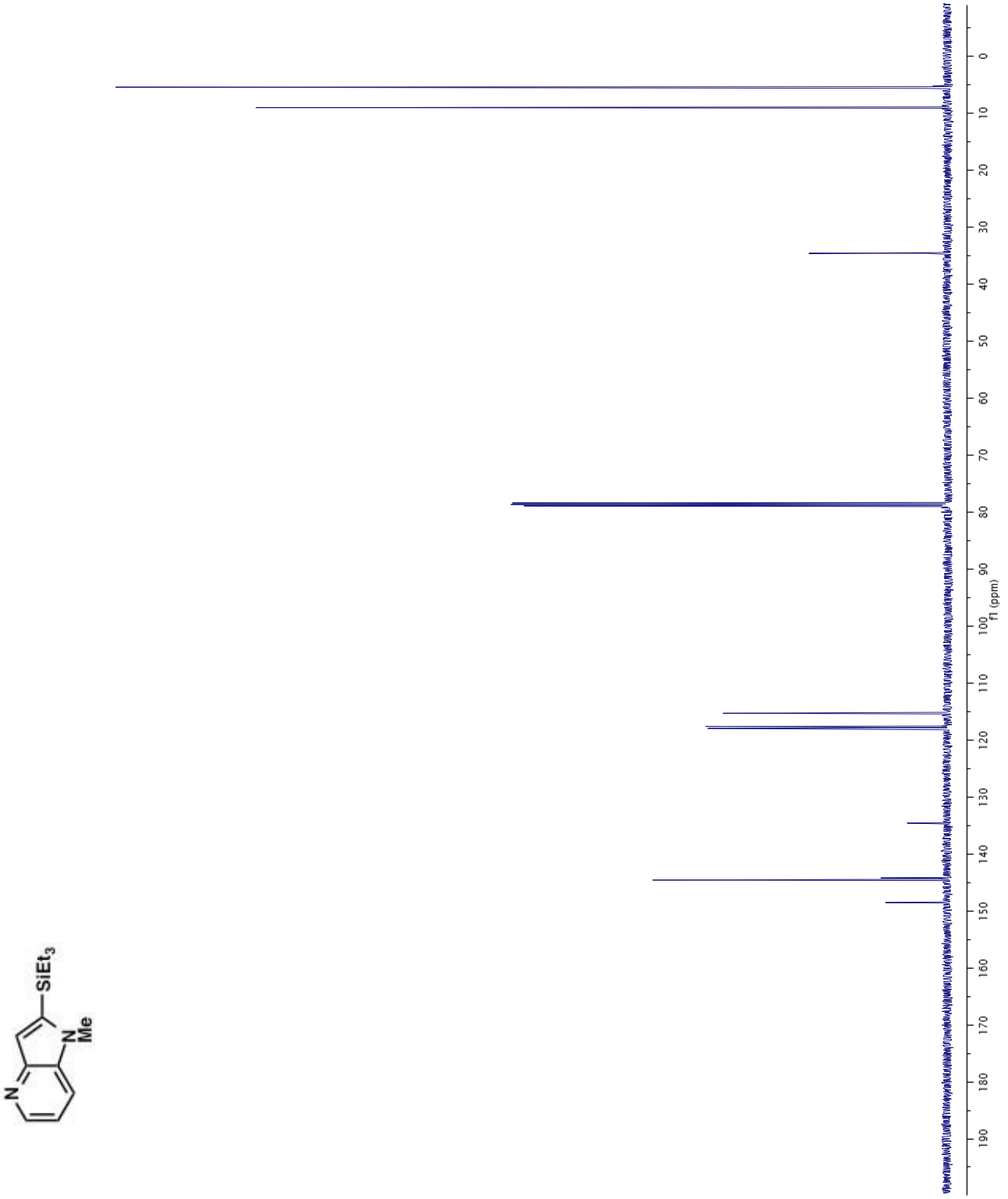
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12x**



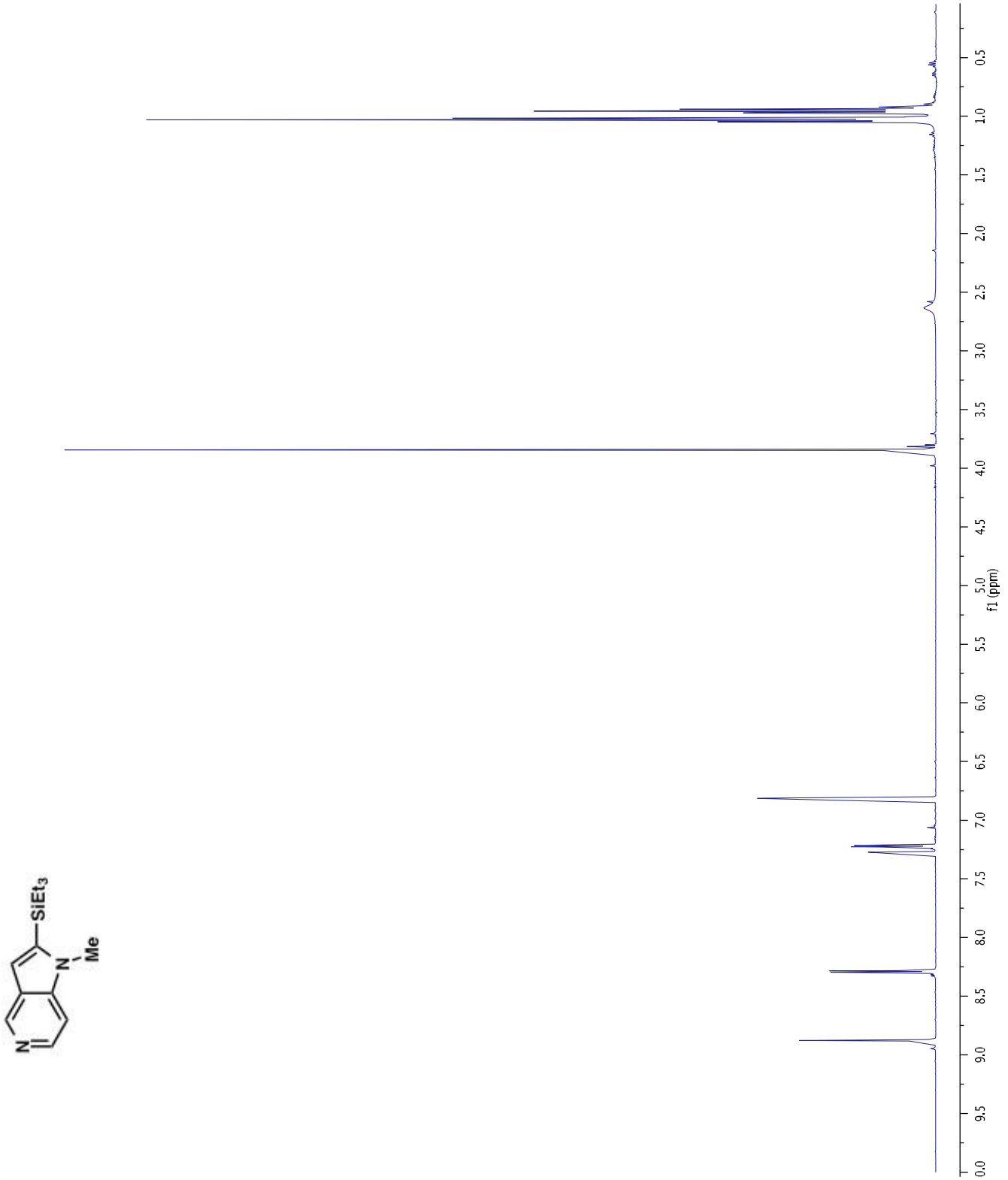
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12x**



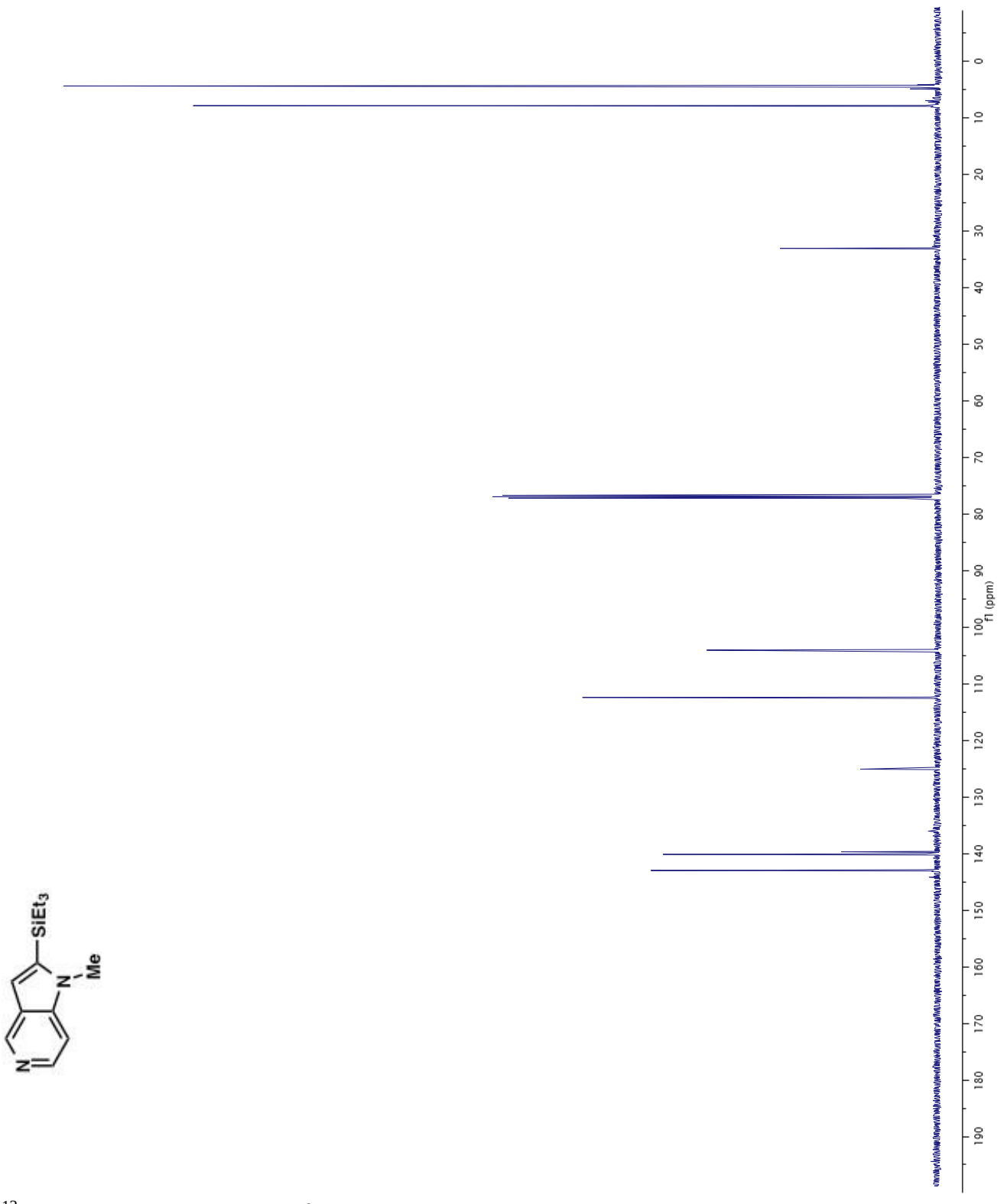
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14a**



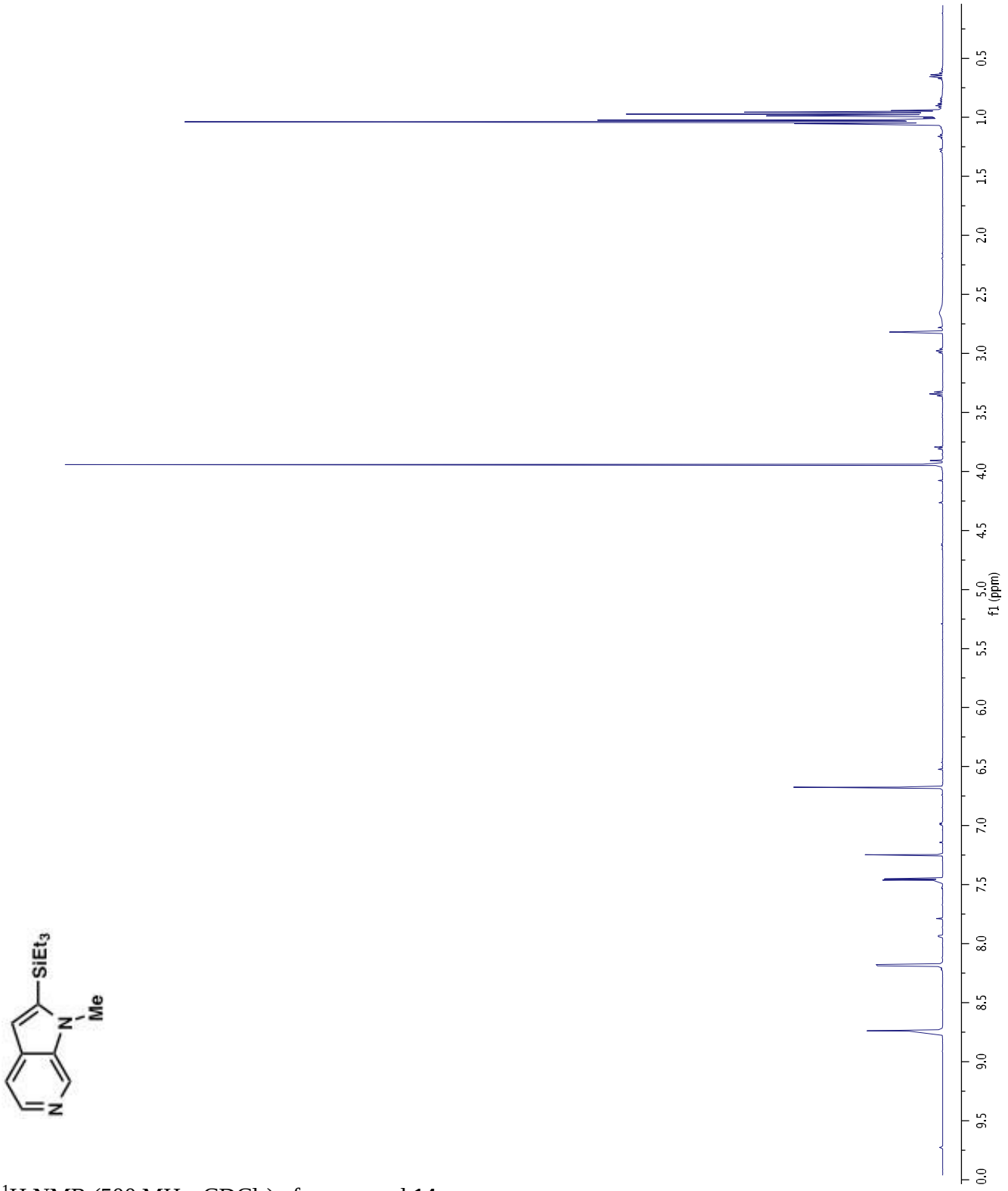
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14a**



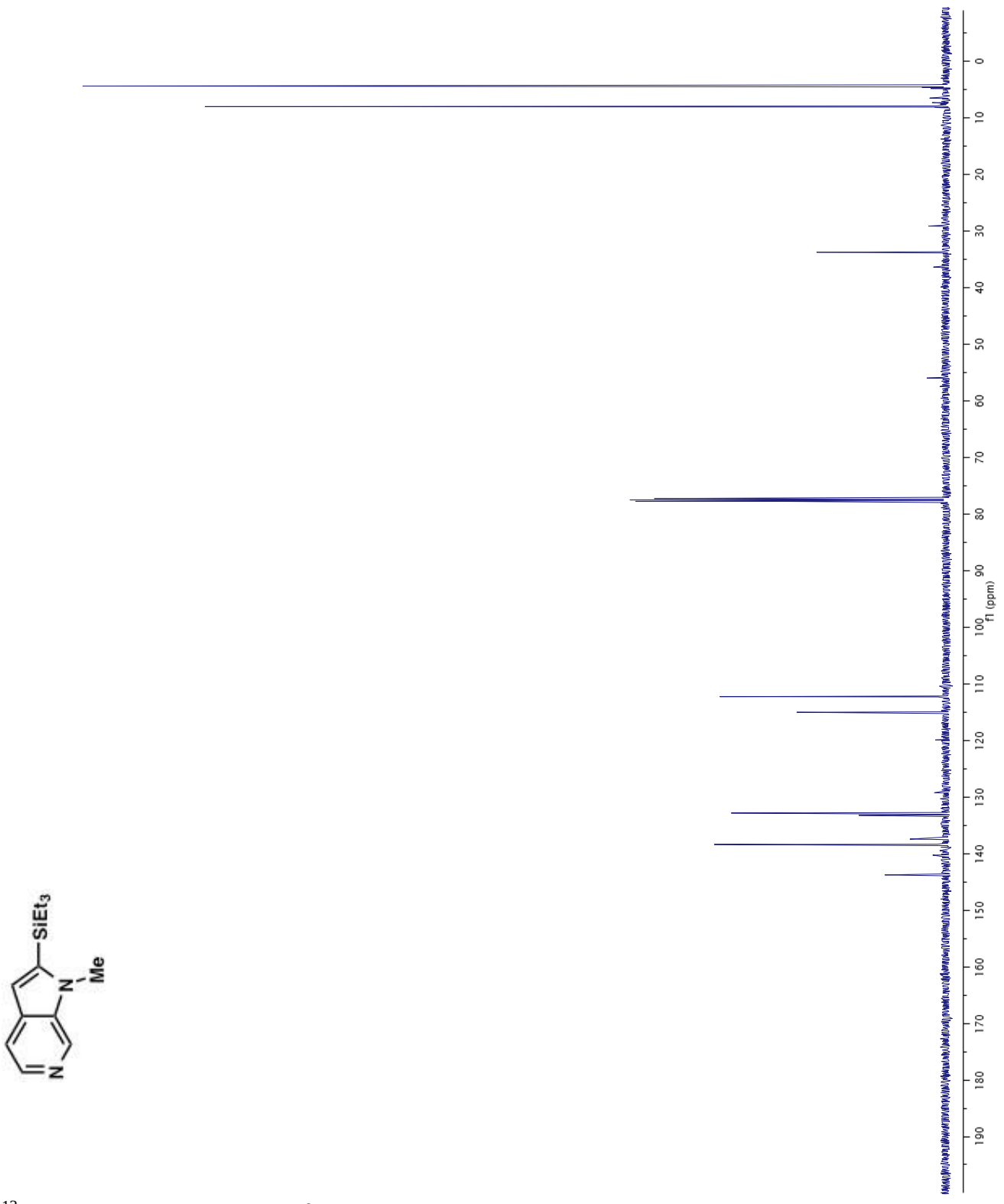
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14b**



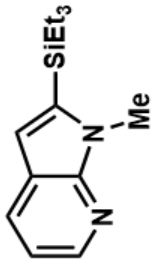
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14b**

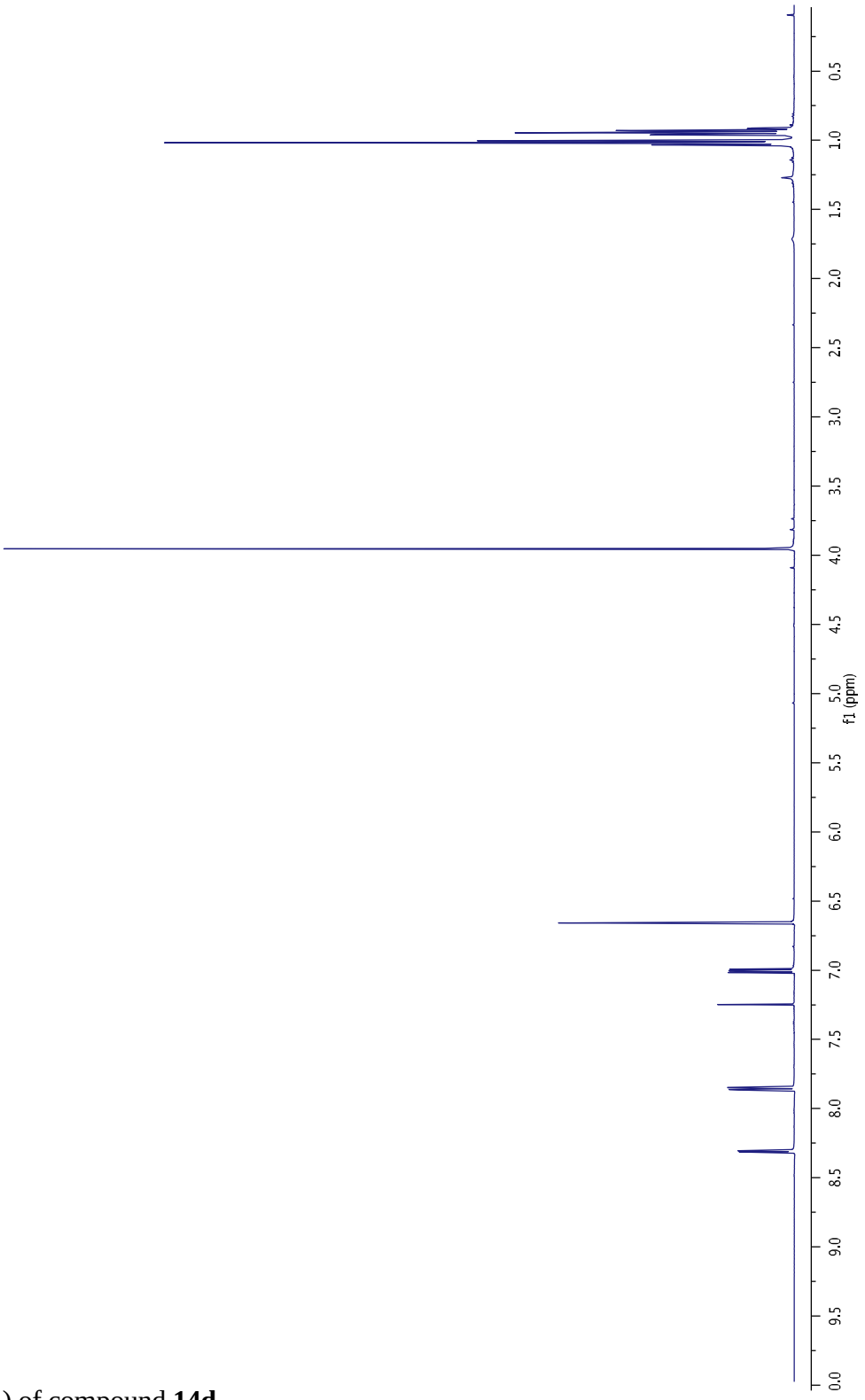


^{1}H NMR (500 MHz, $CDCl_3$) of compound **14c**

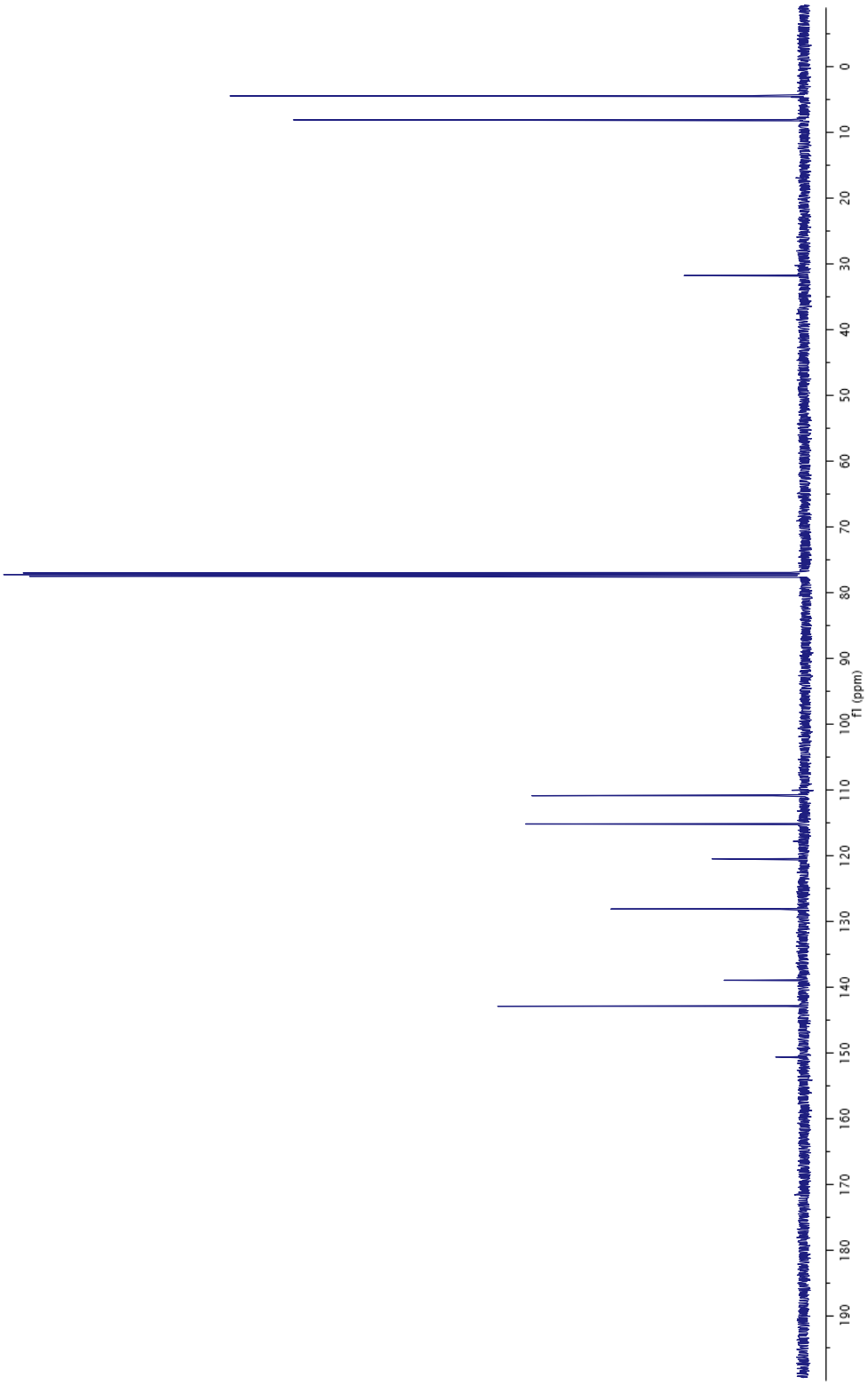


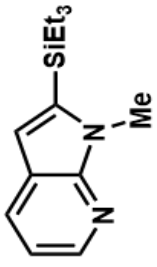
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14c**



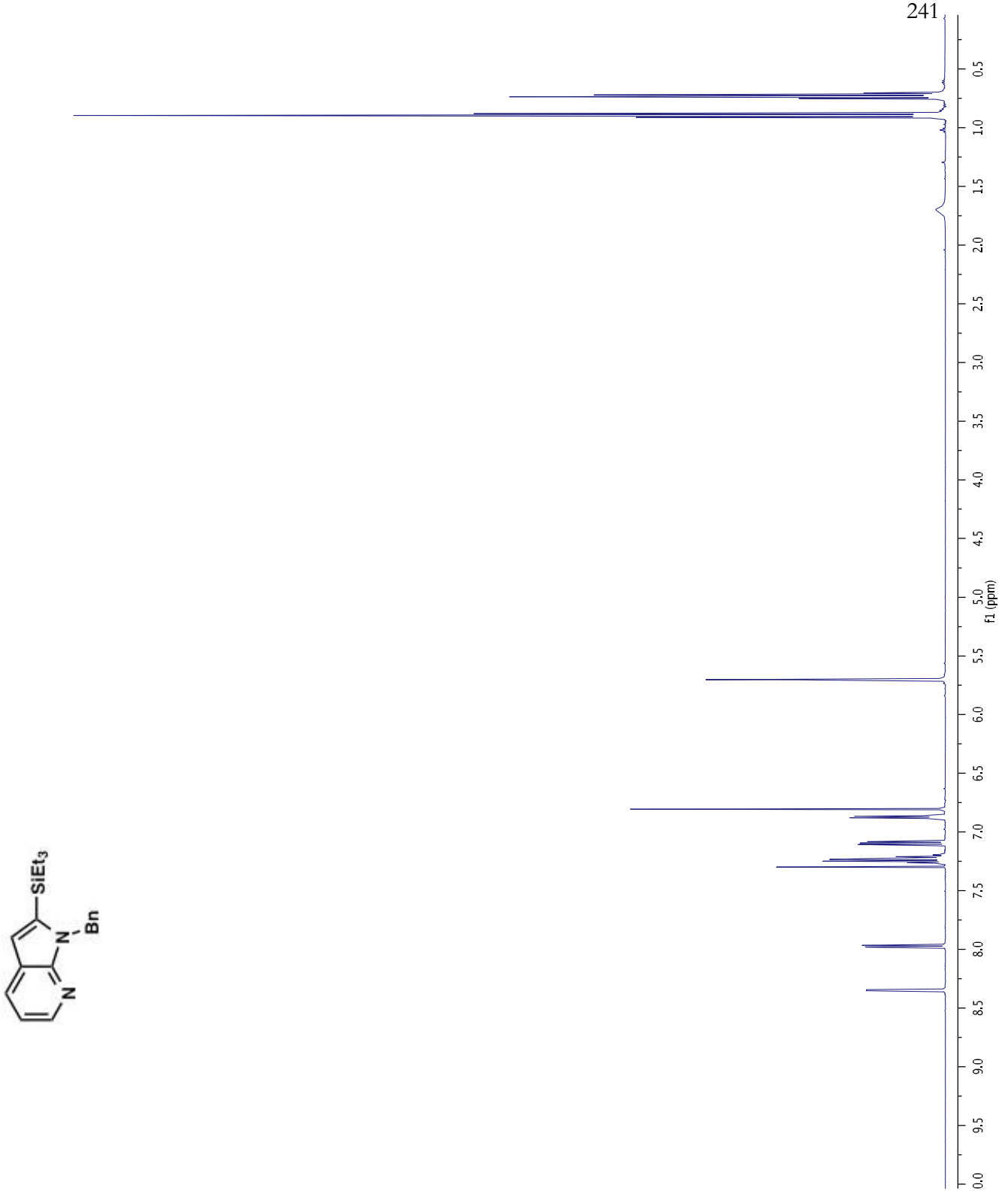


^{1}H NMR (500 MHz, $CDCl_3$) of compound **14d**

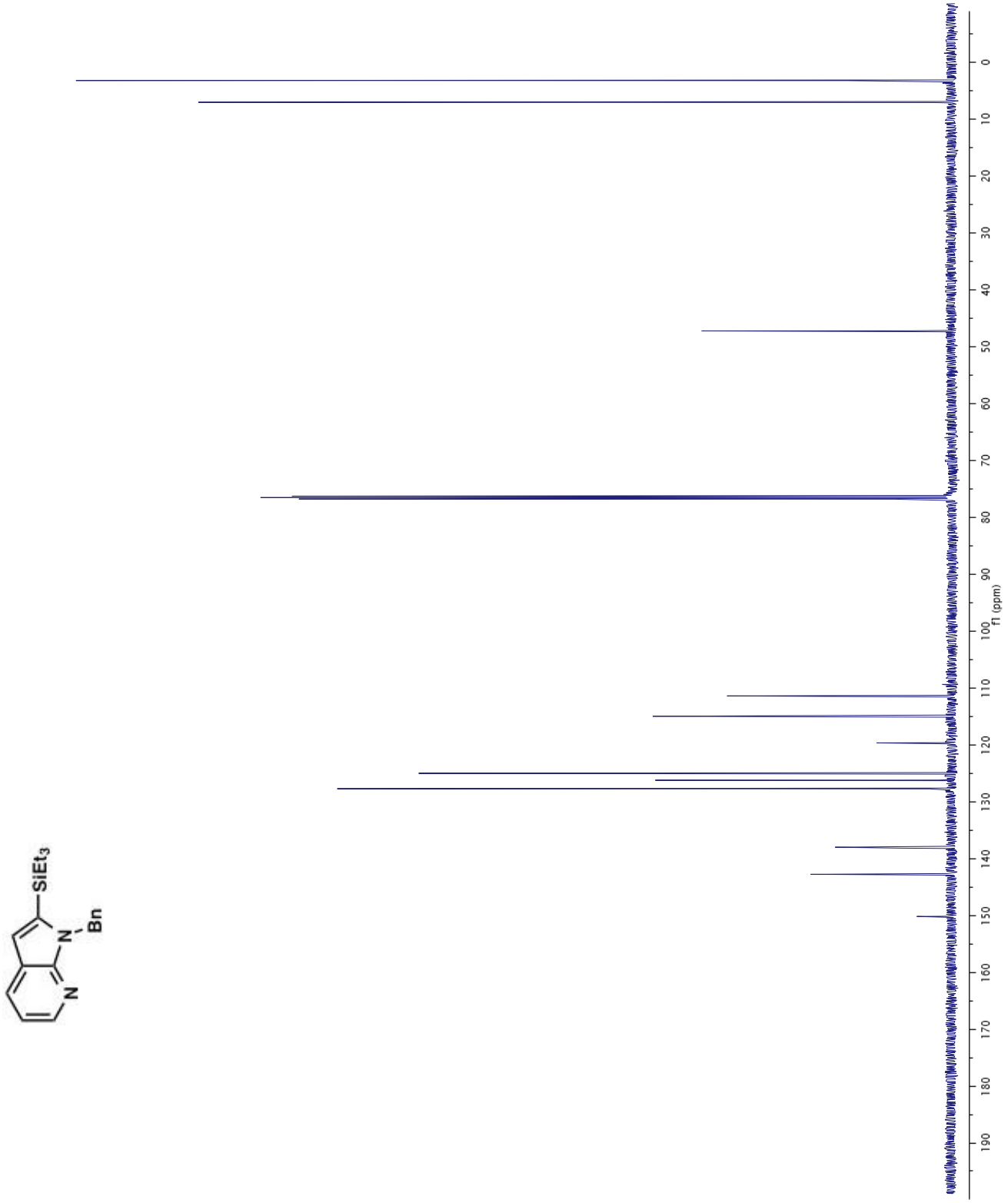




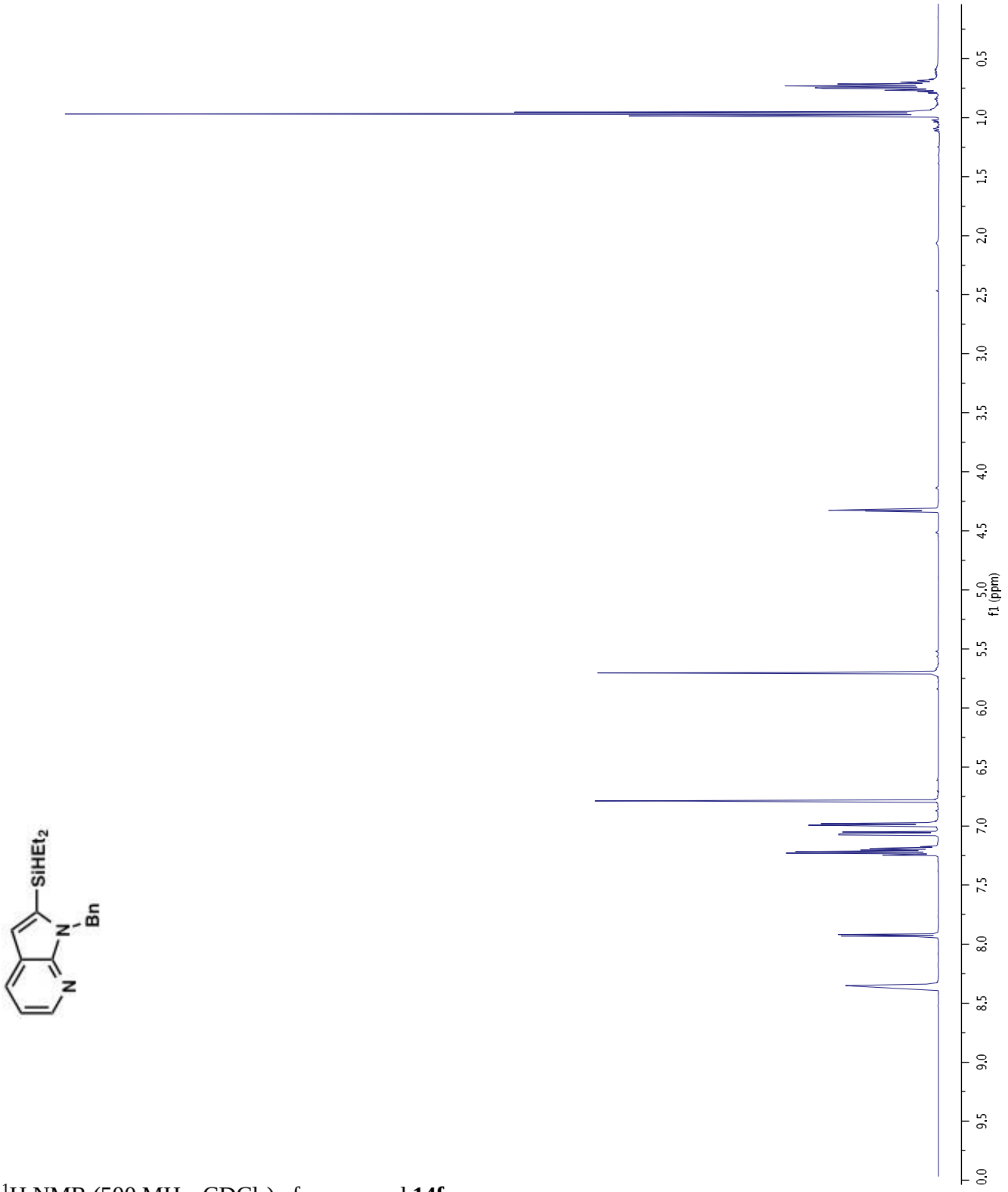
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14d**



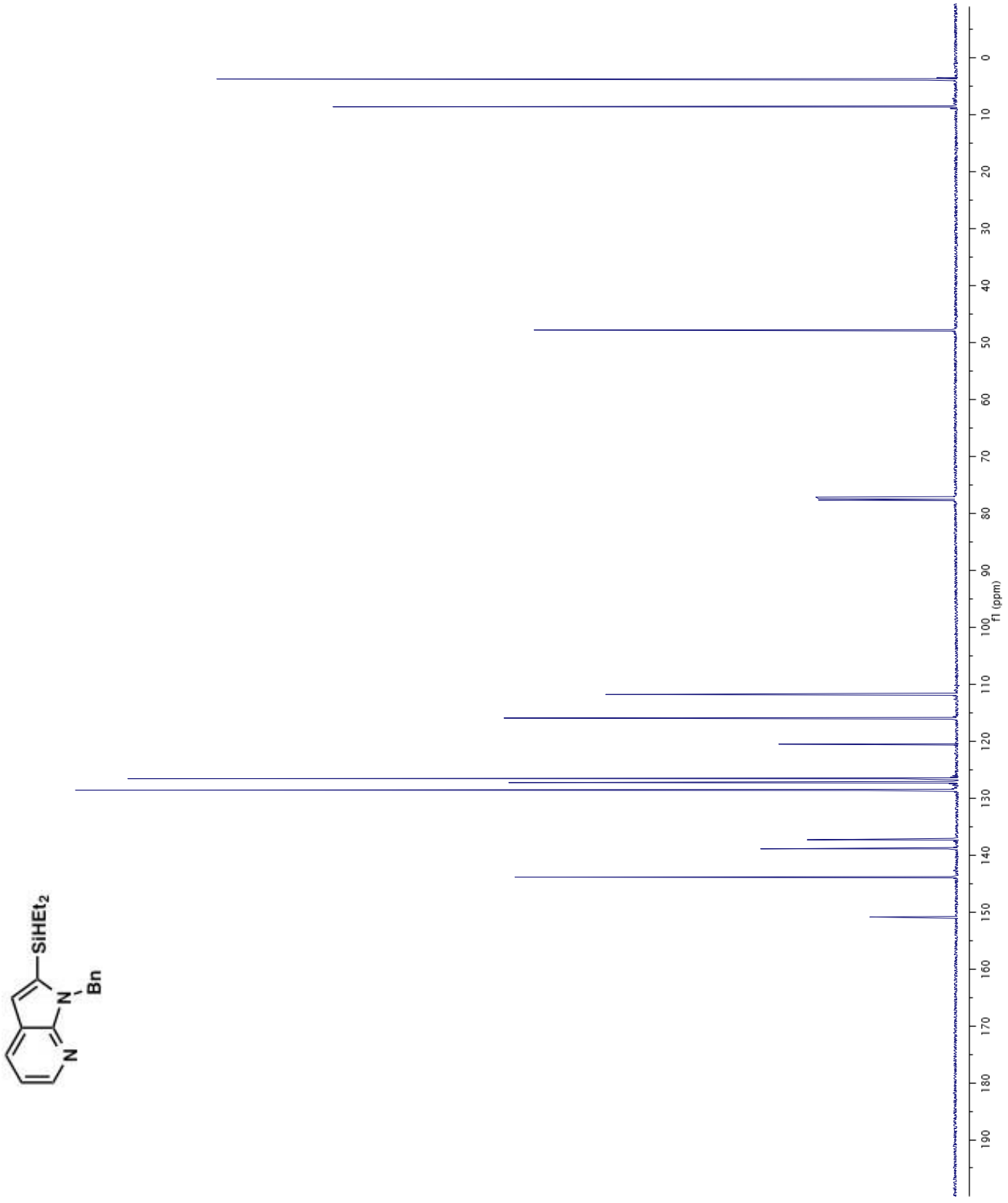
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14e**



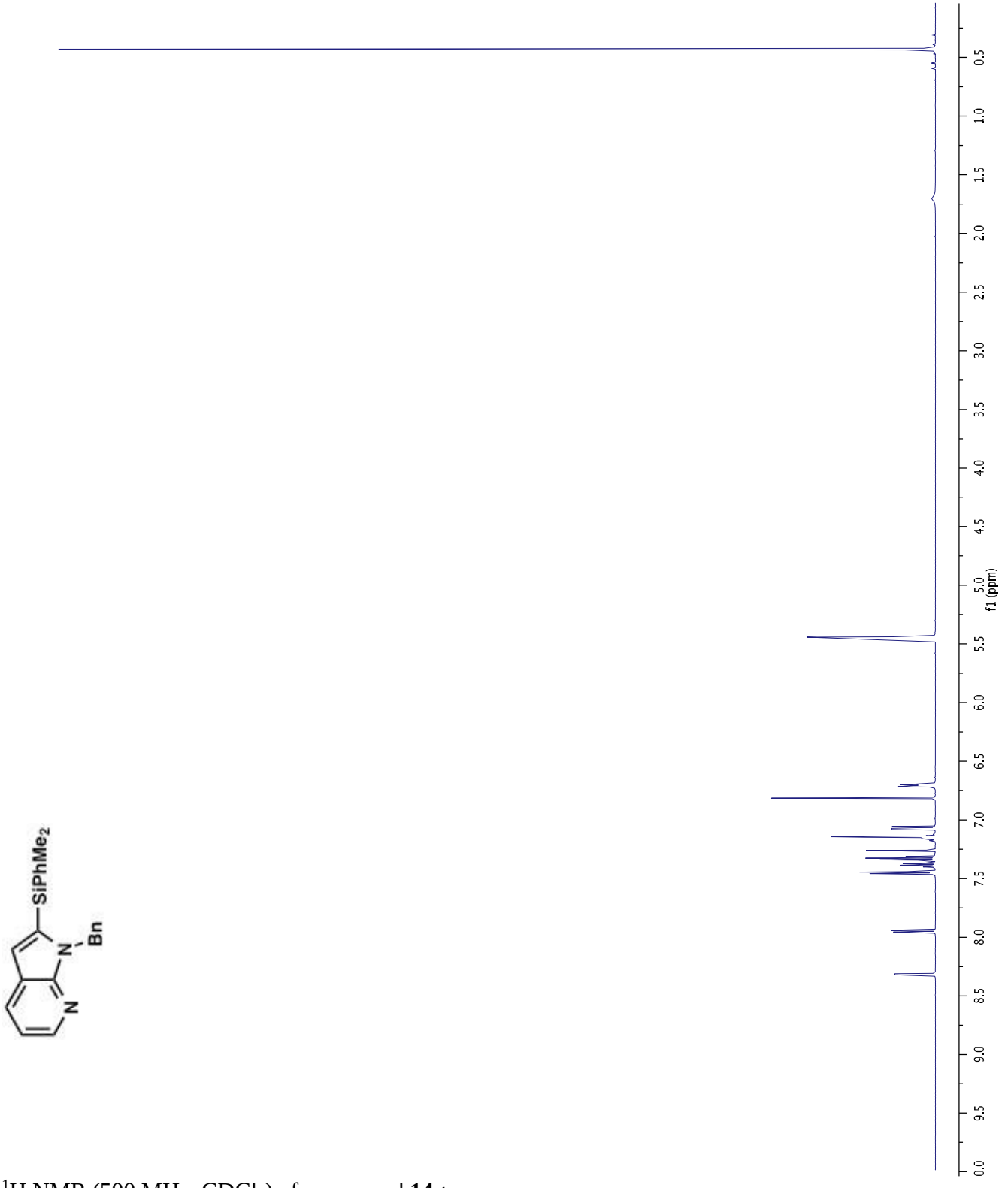
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14e**



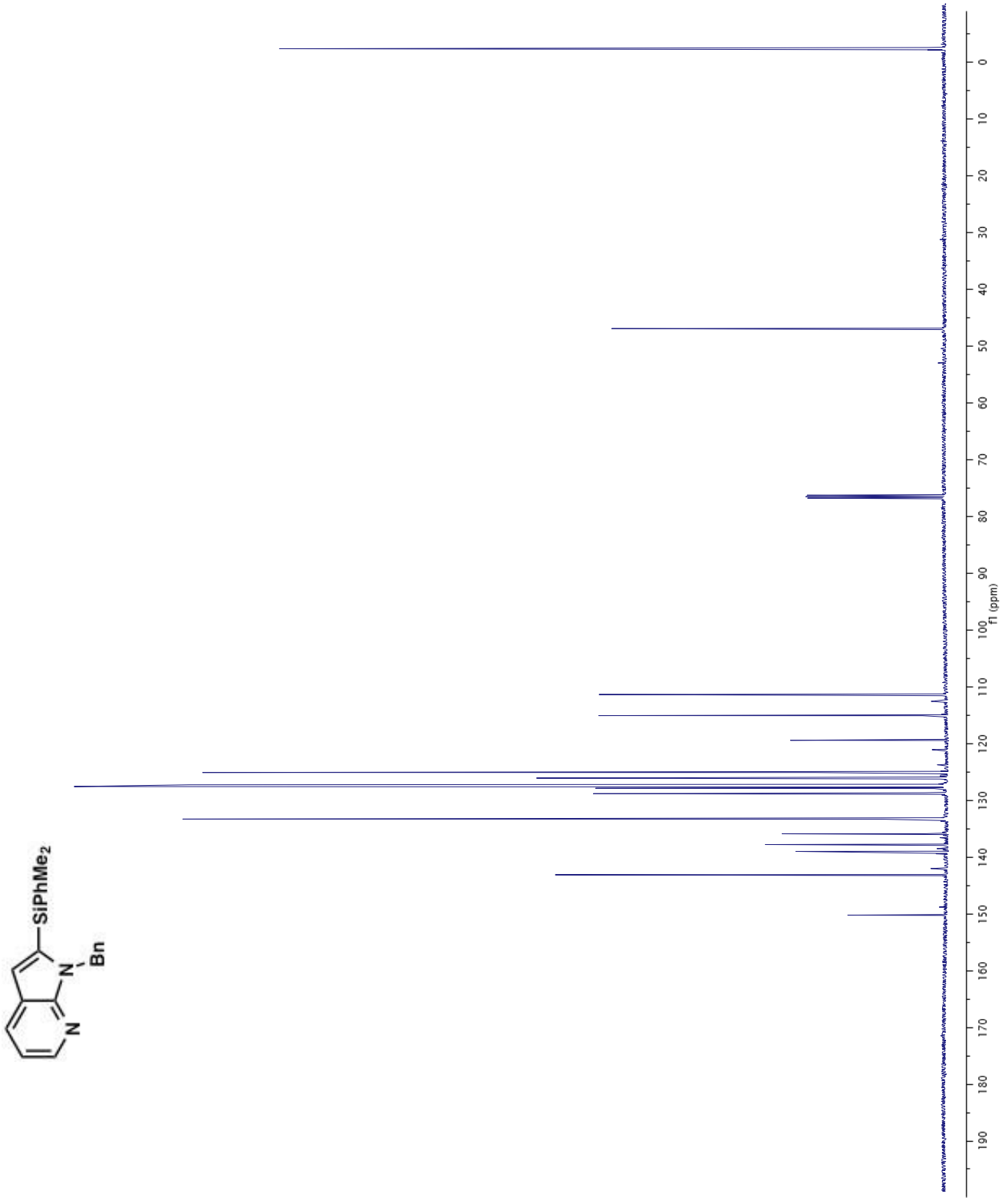
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14f**



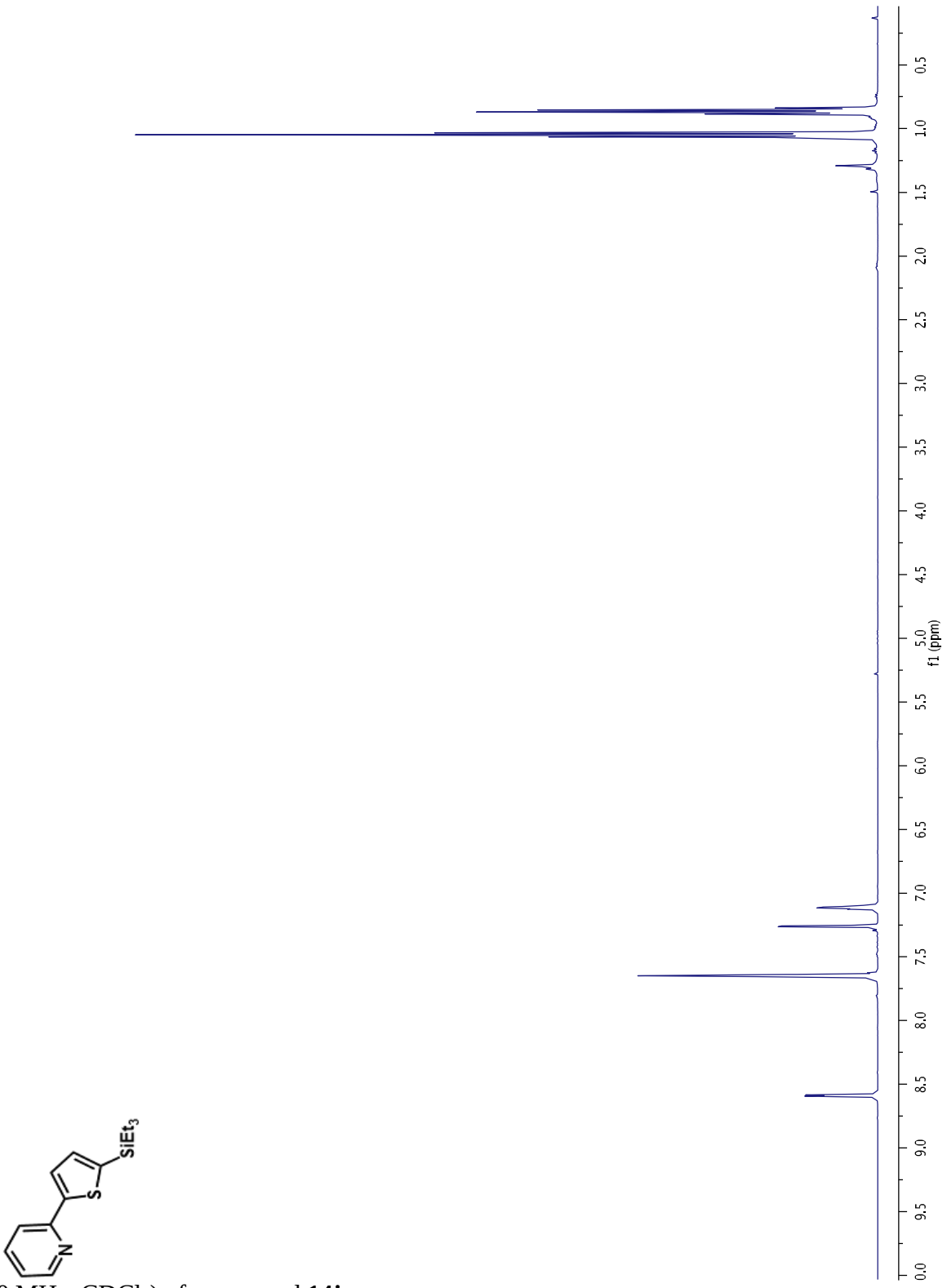
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14f**



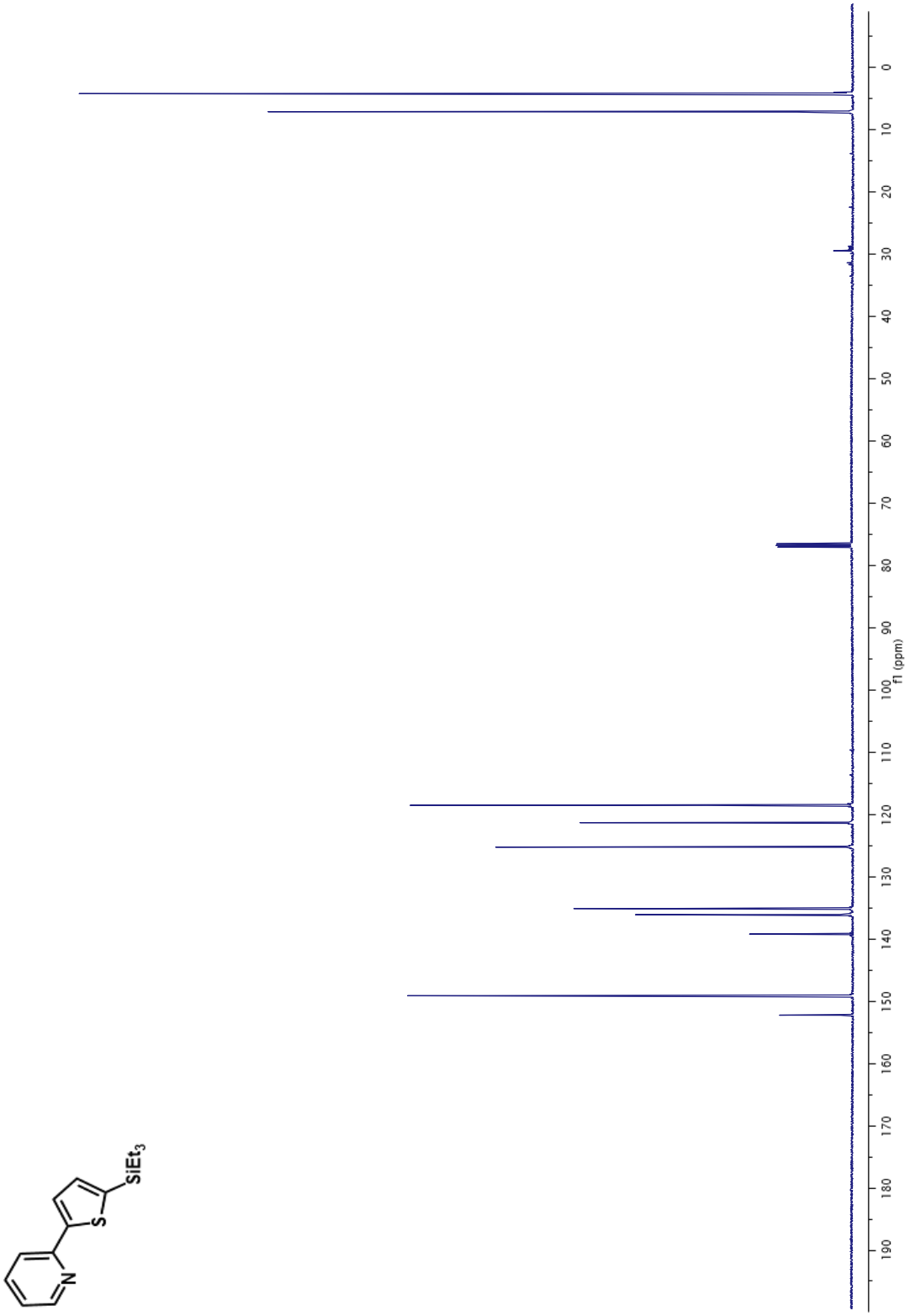
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14g**



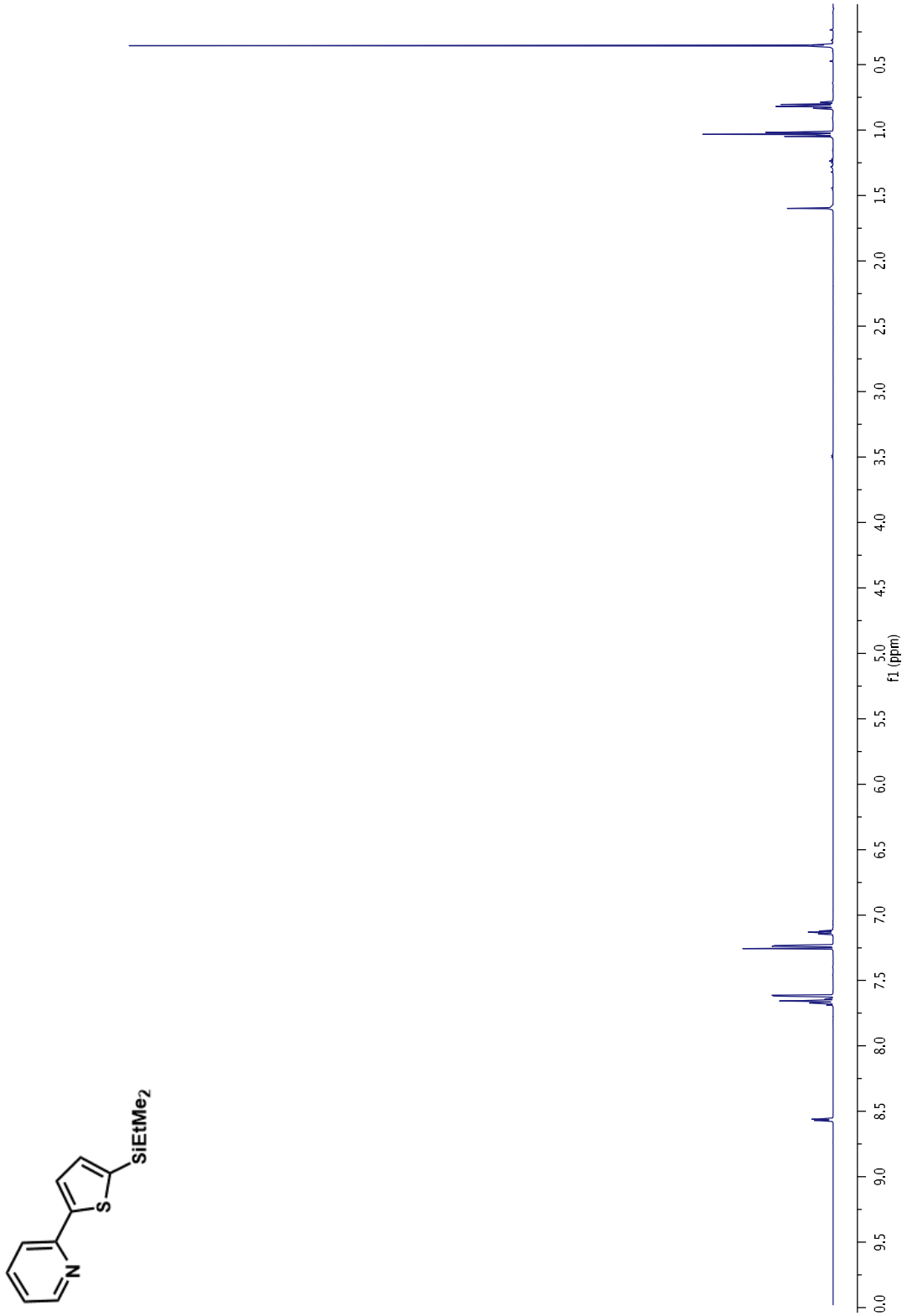
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14g**



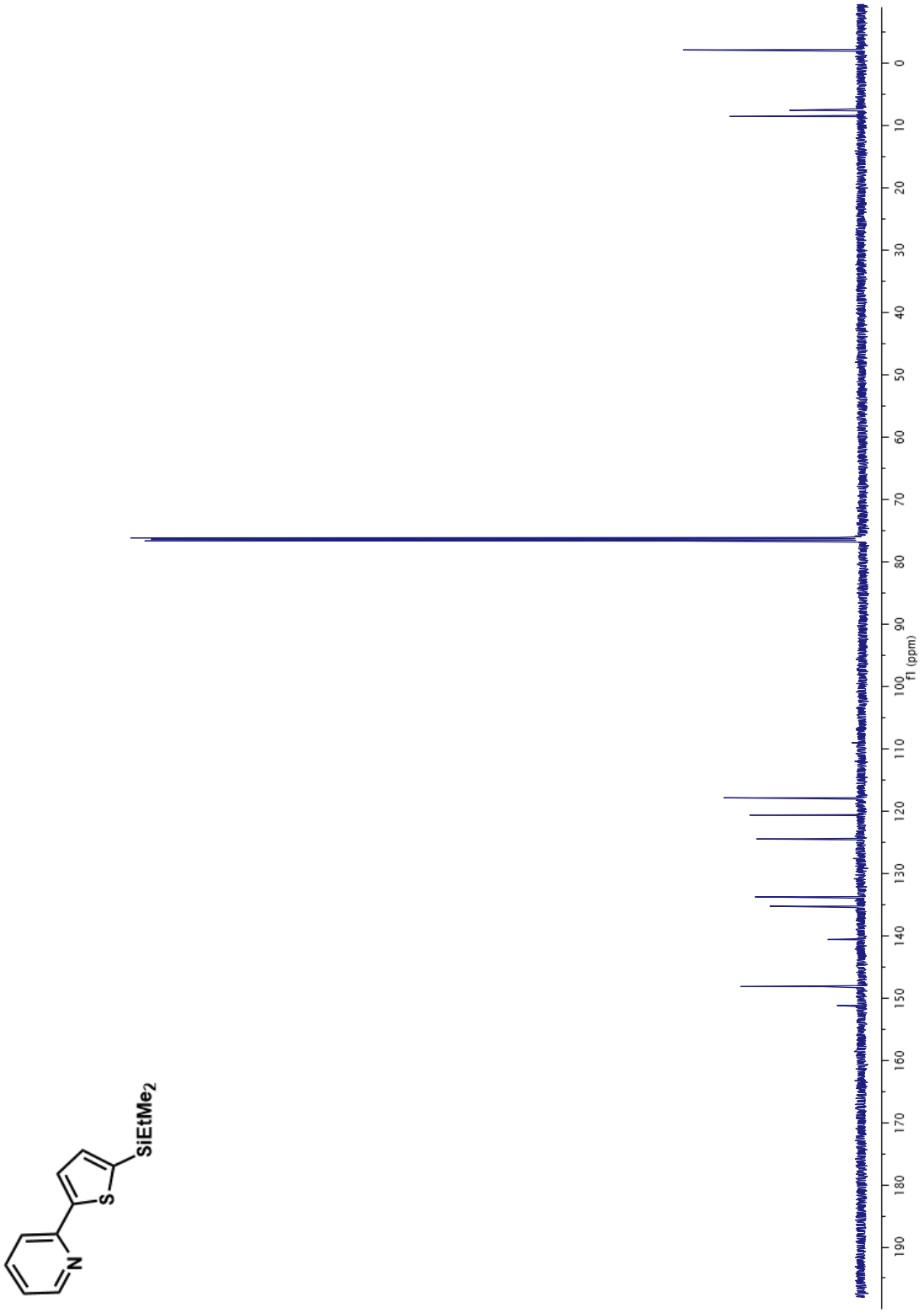
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14j**



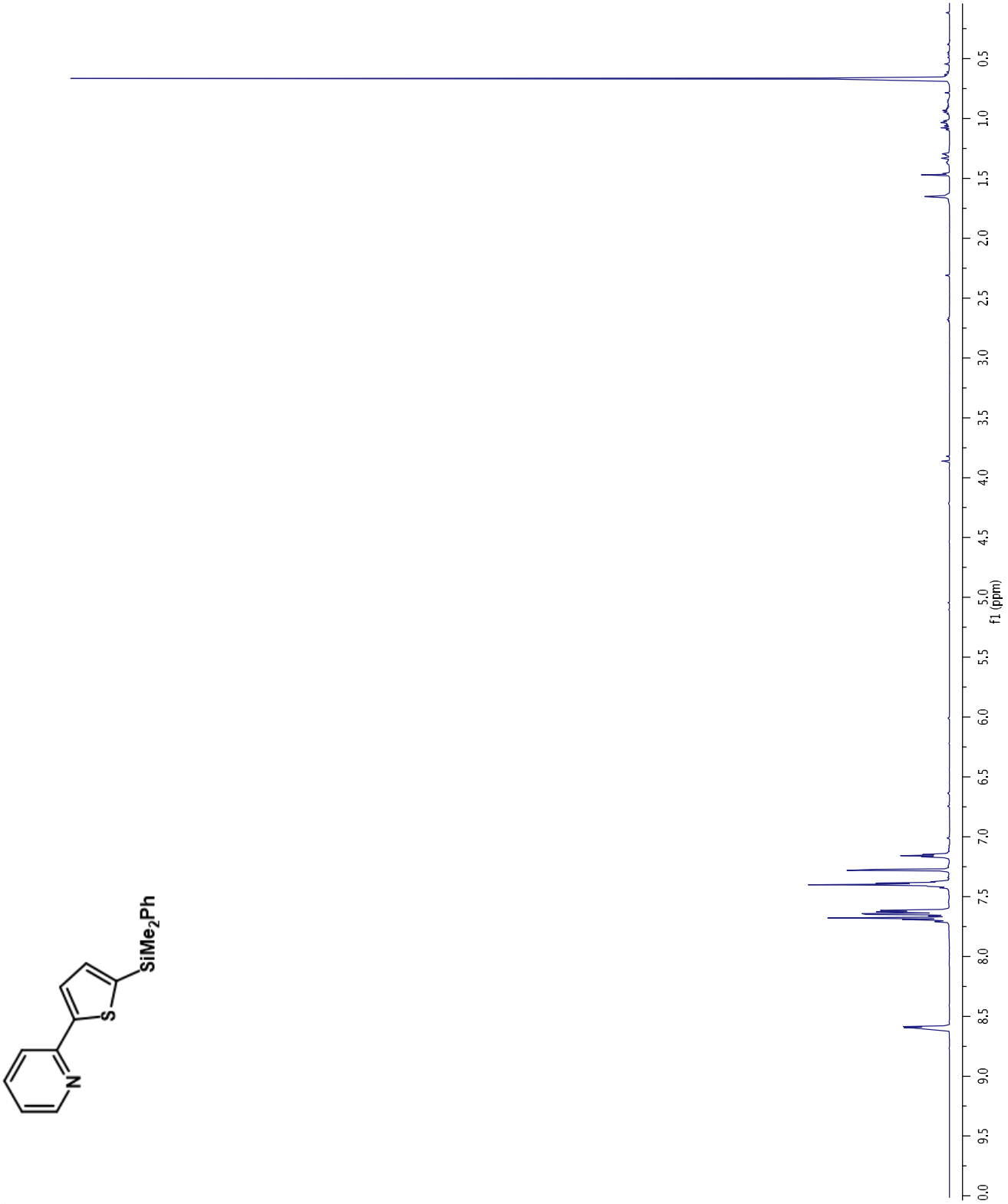
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14j**



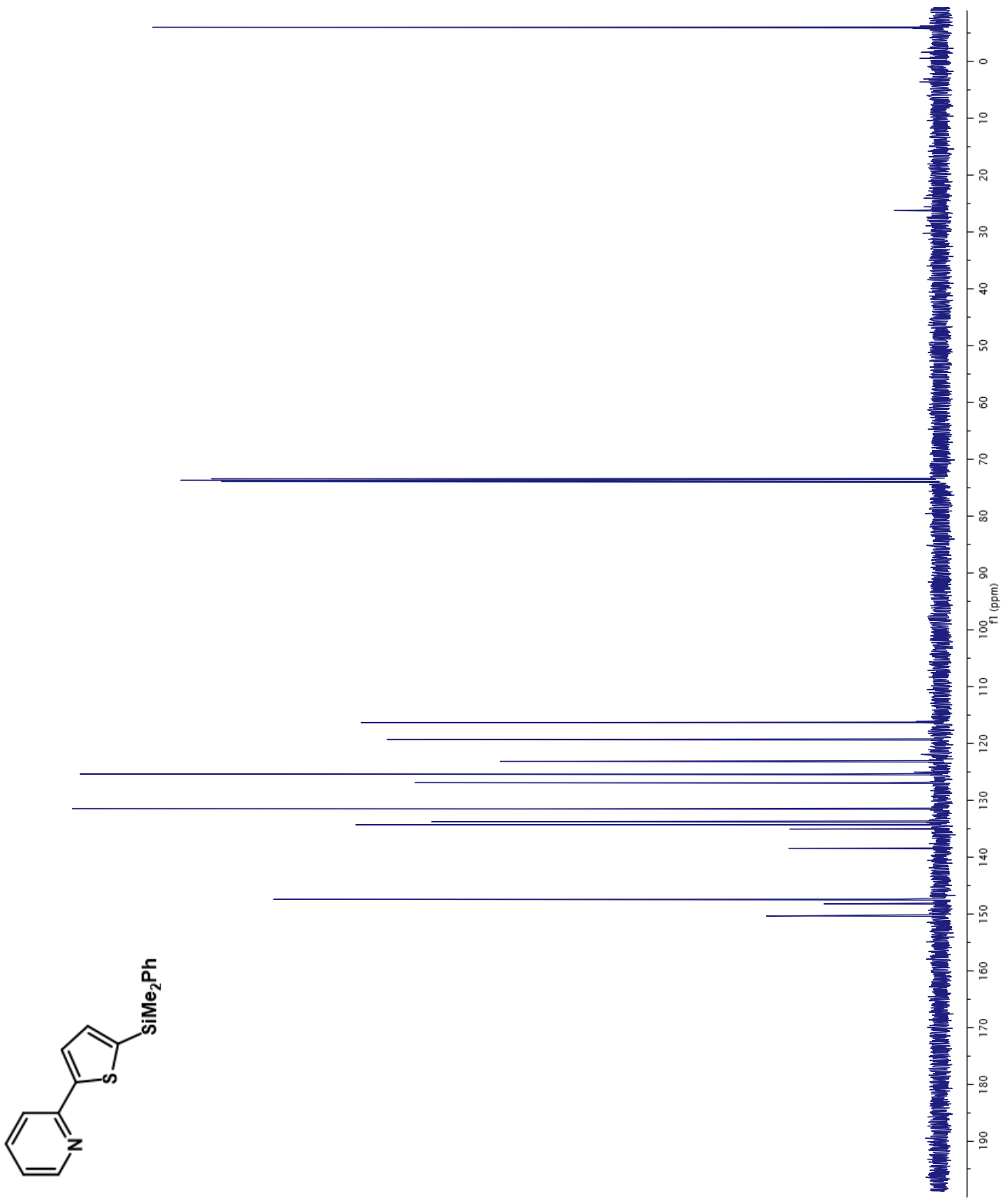
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14k**



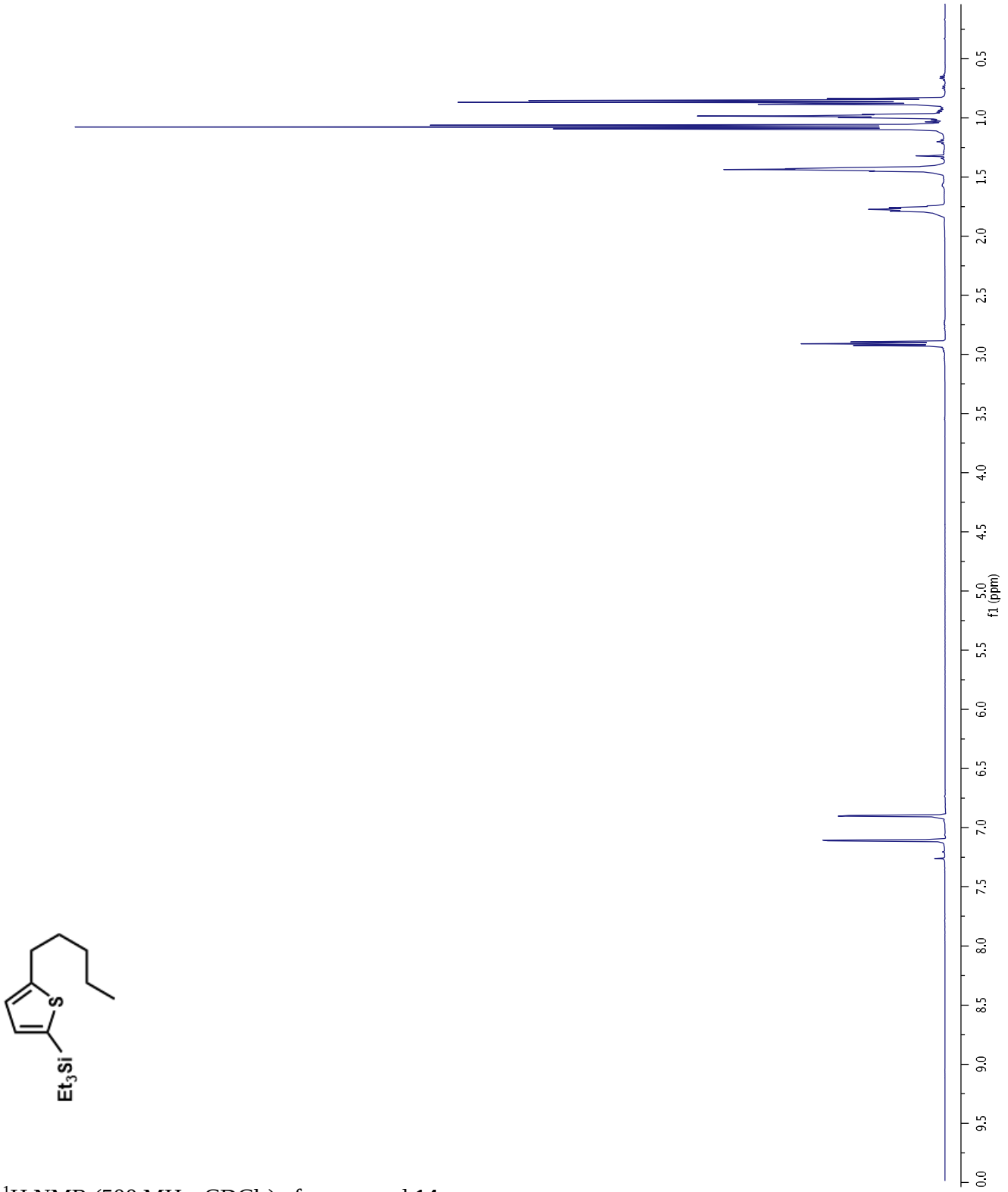
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14k**



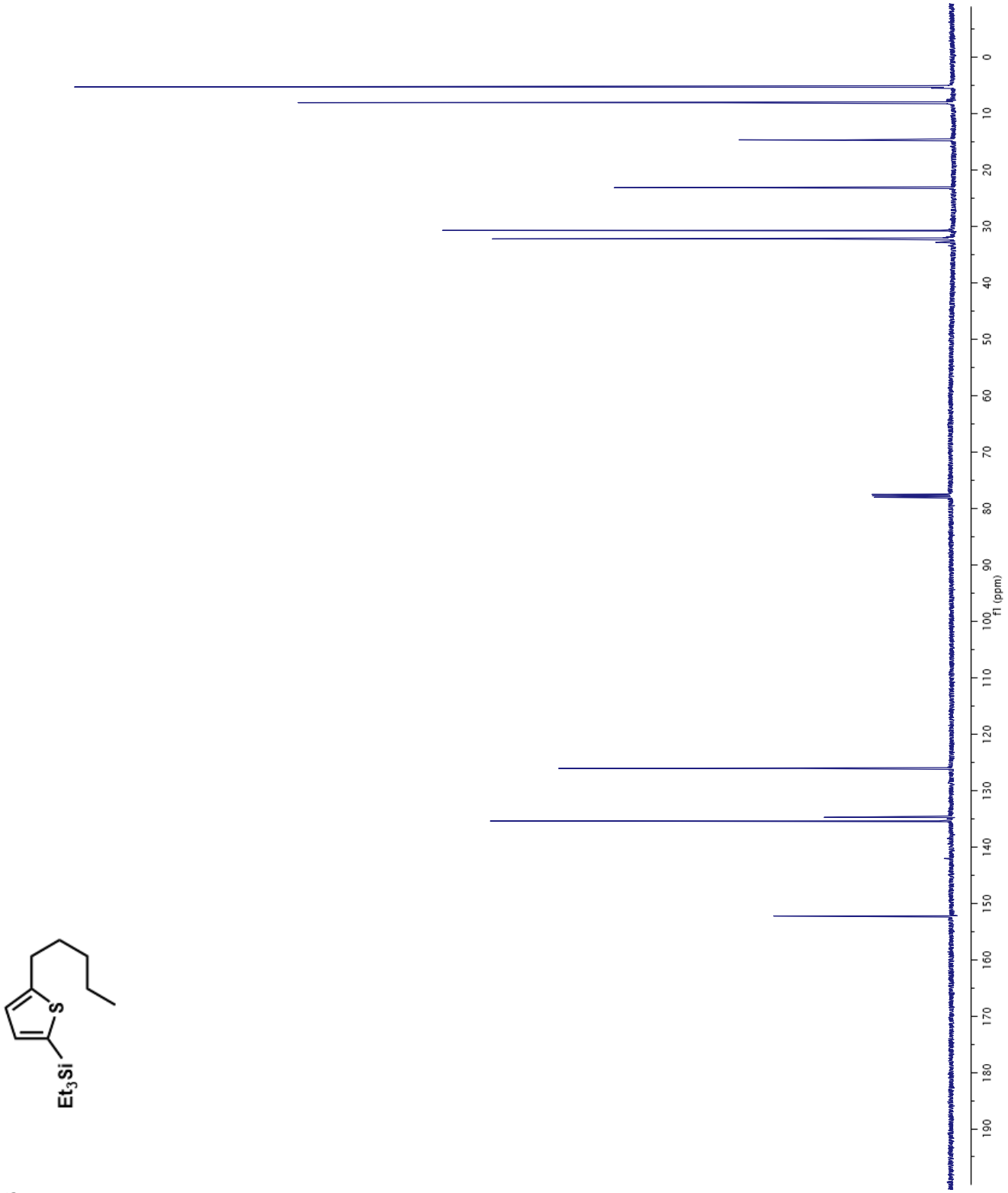
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14l**



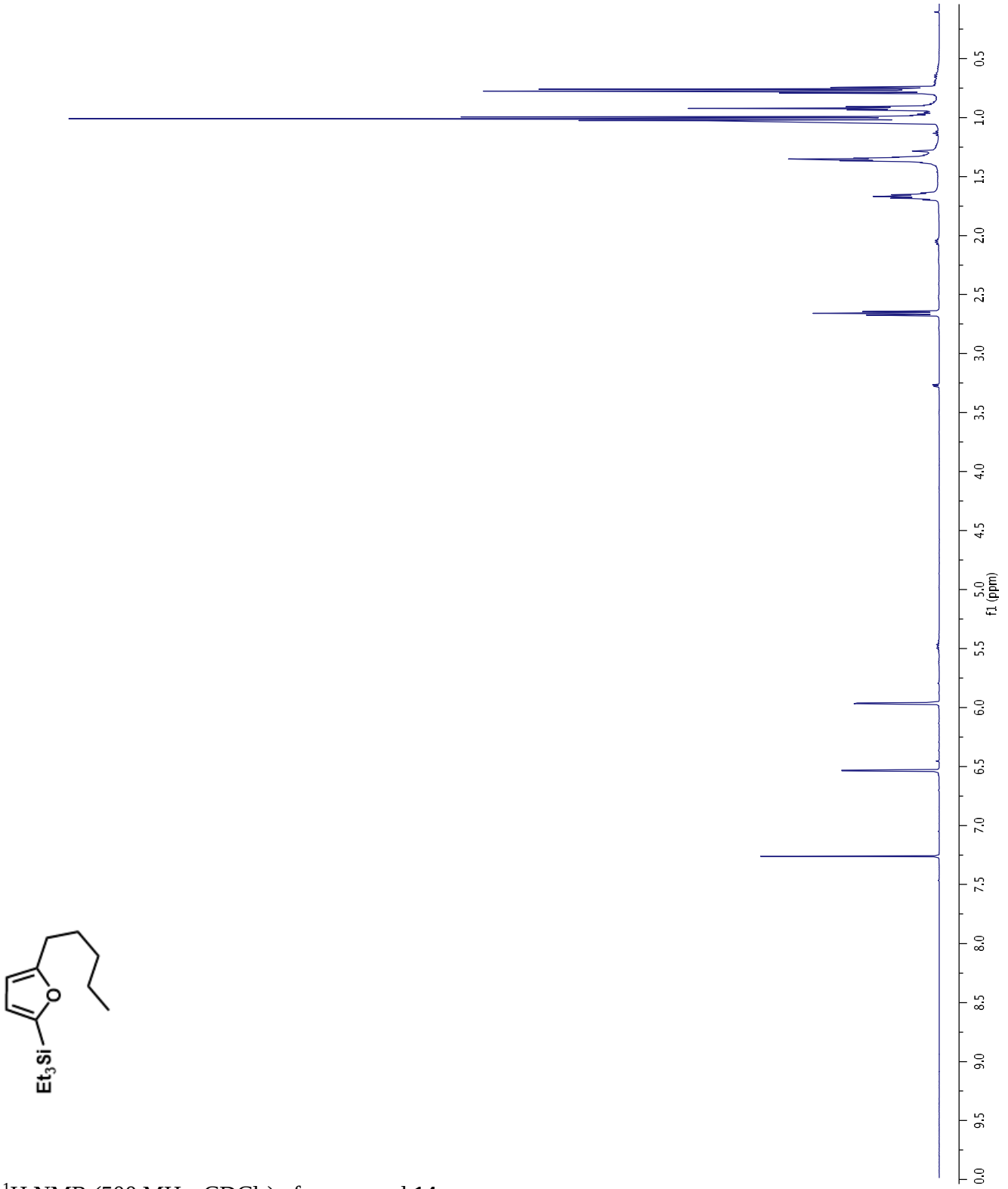
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14l**



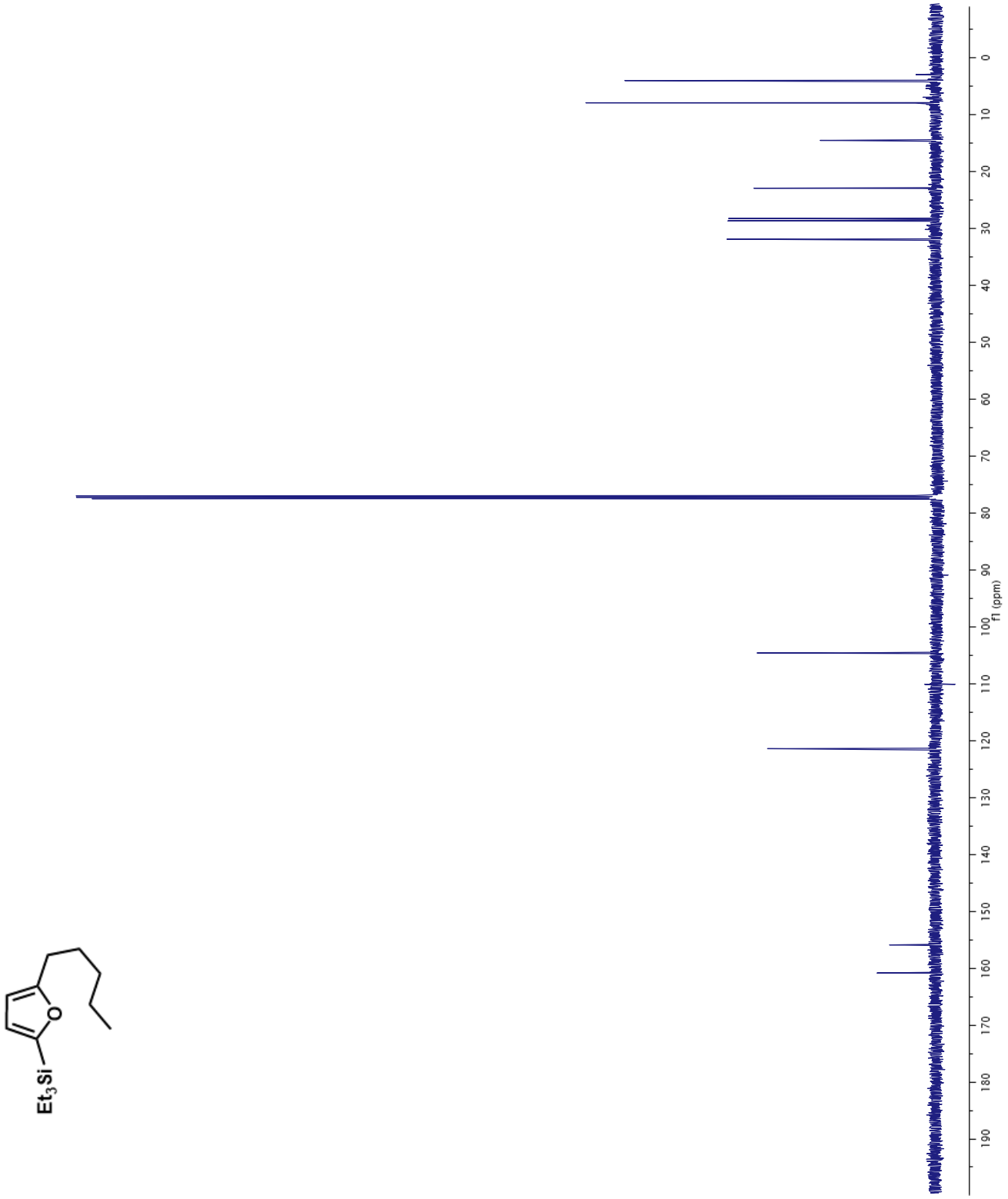
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14m**



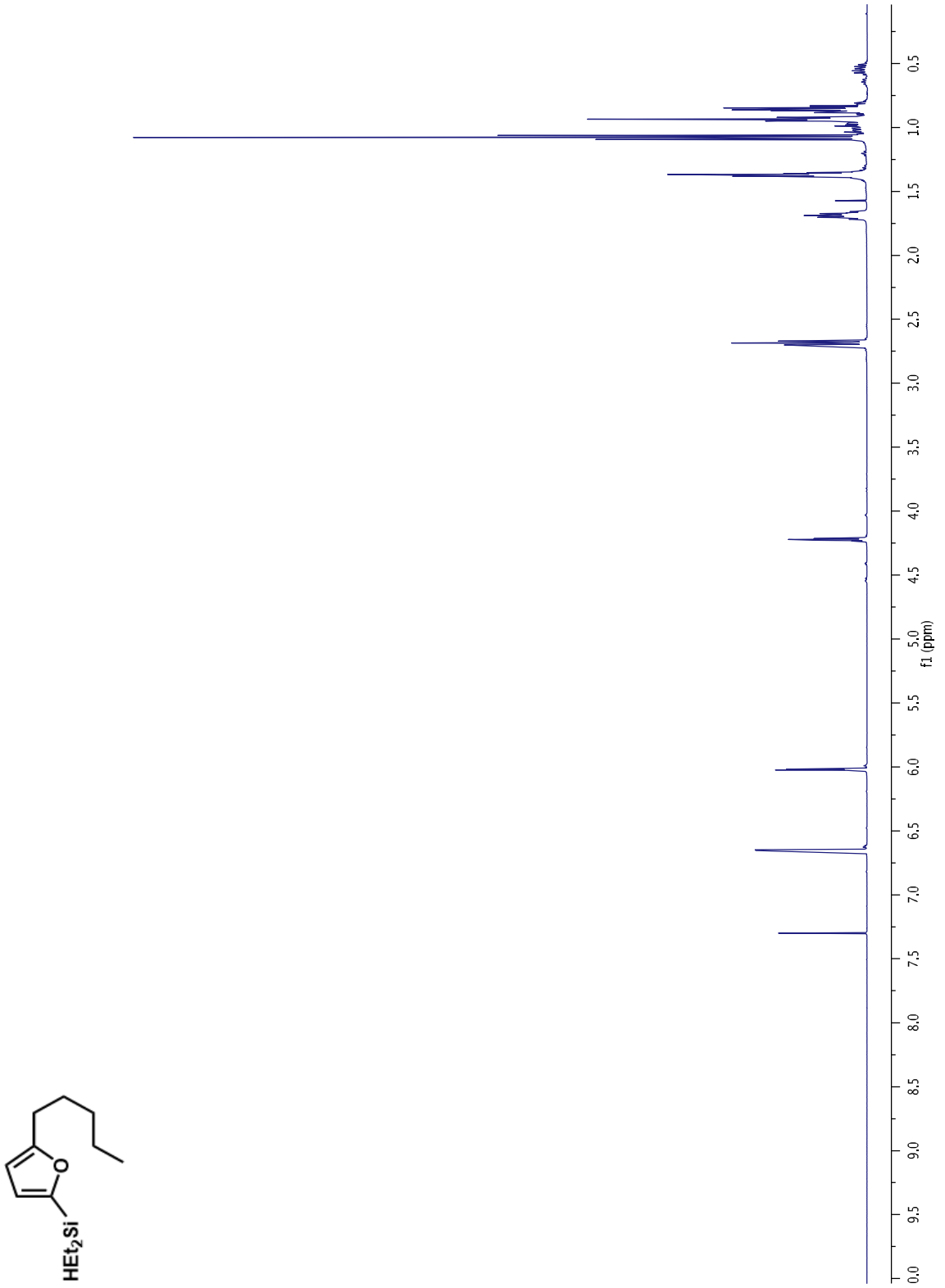
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14m**



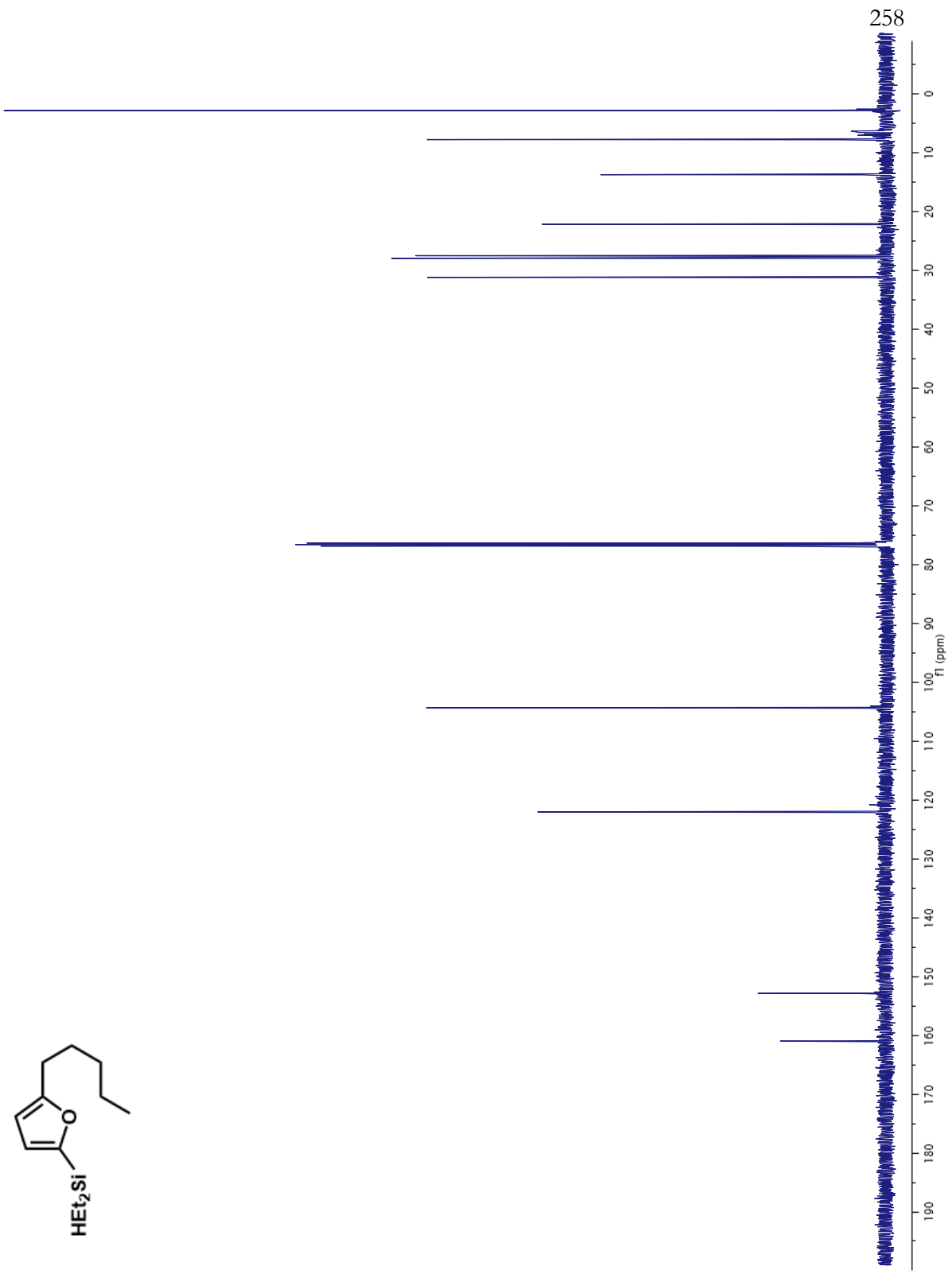
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14n**



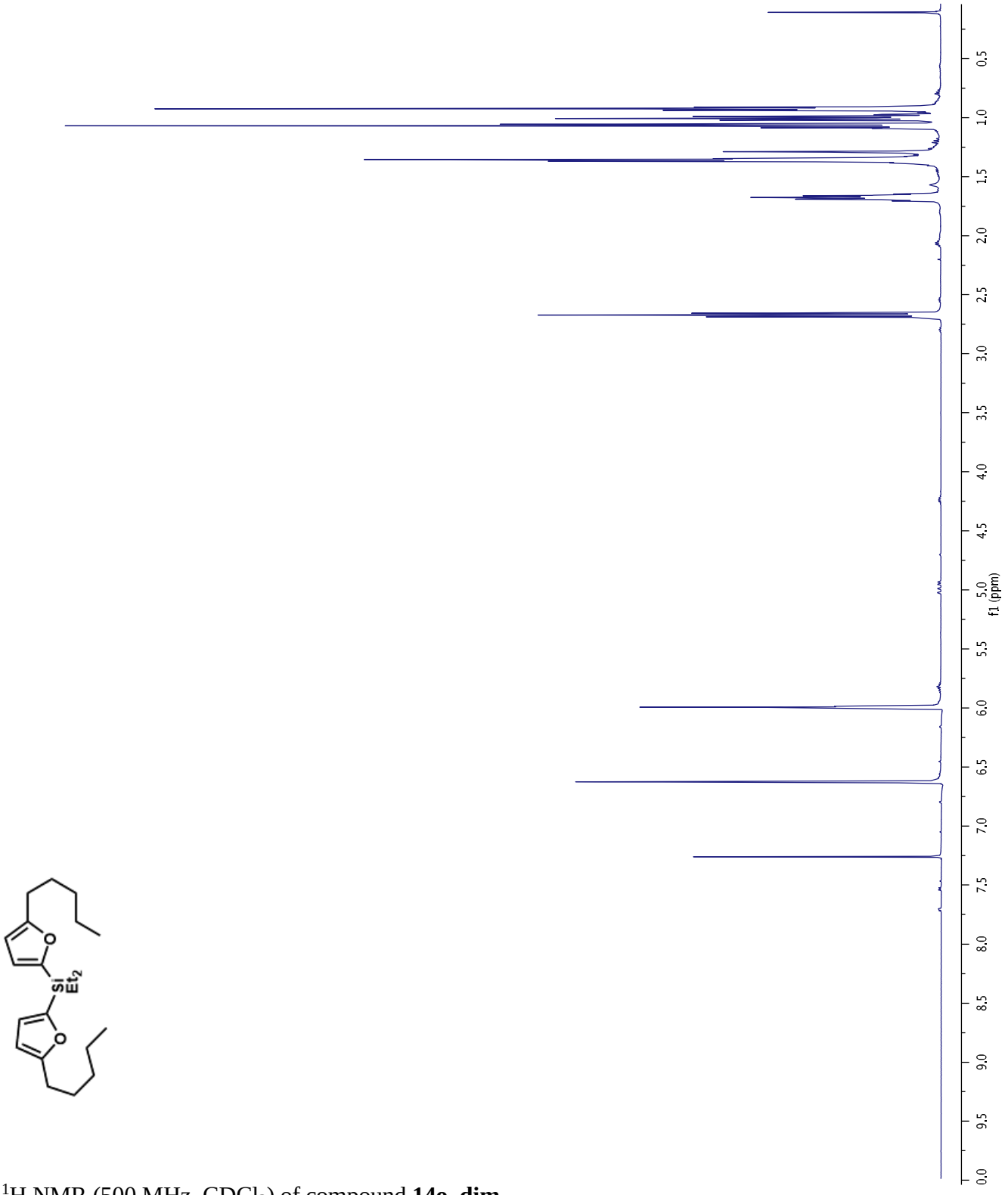
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14n**



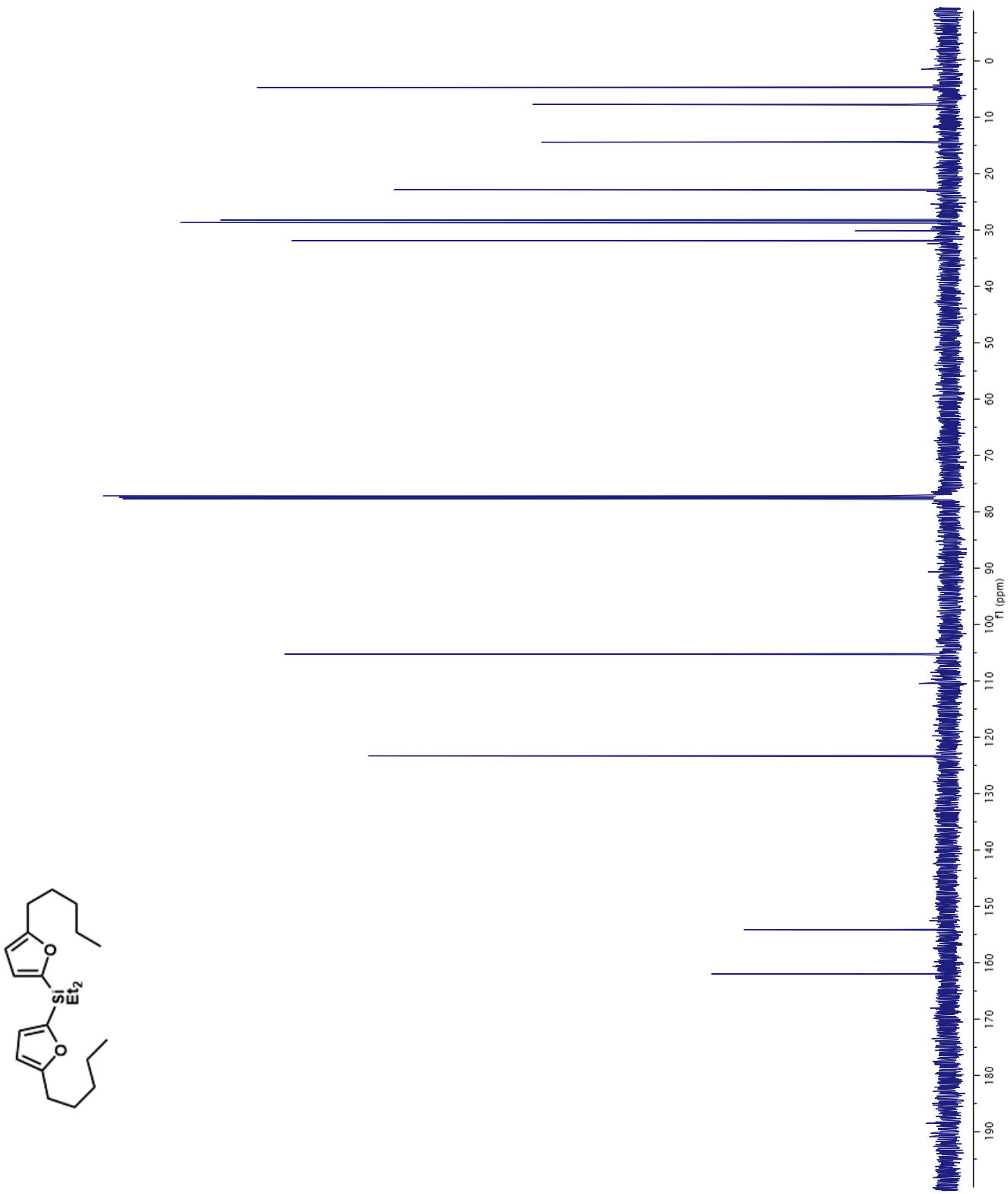
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14o**



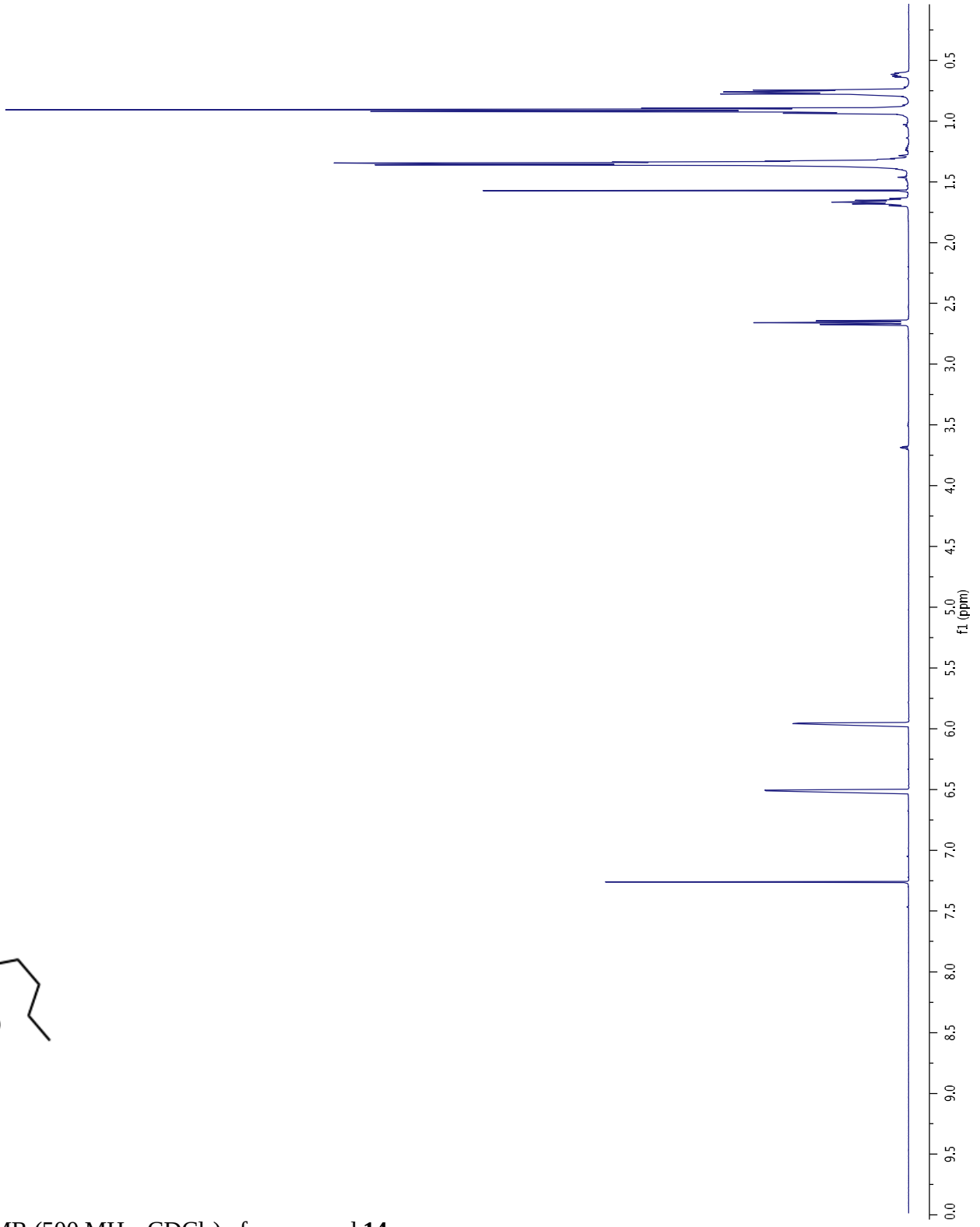
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14o**



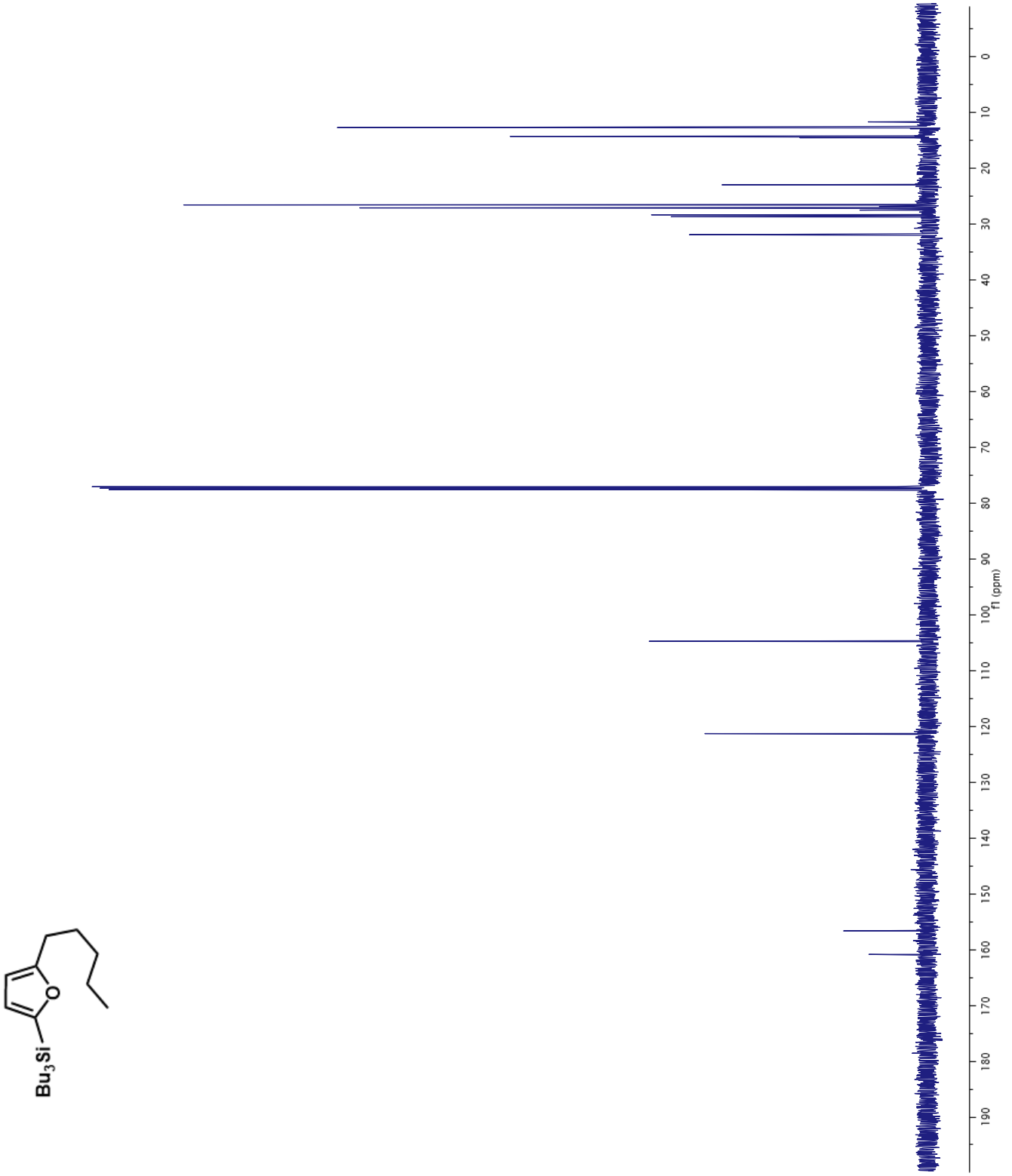
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14o_dim**



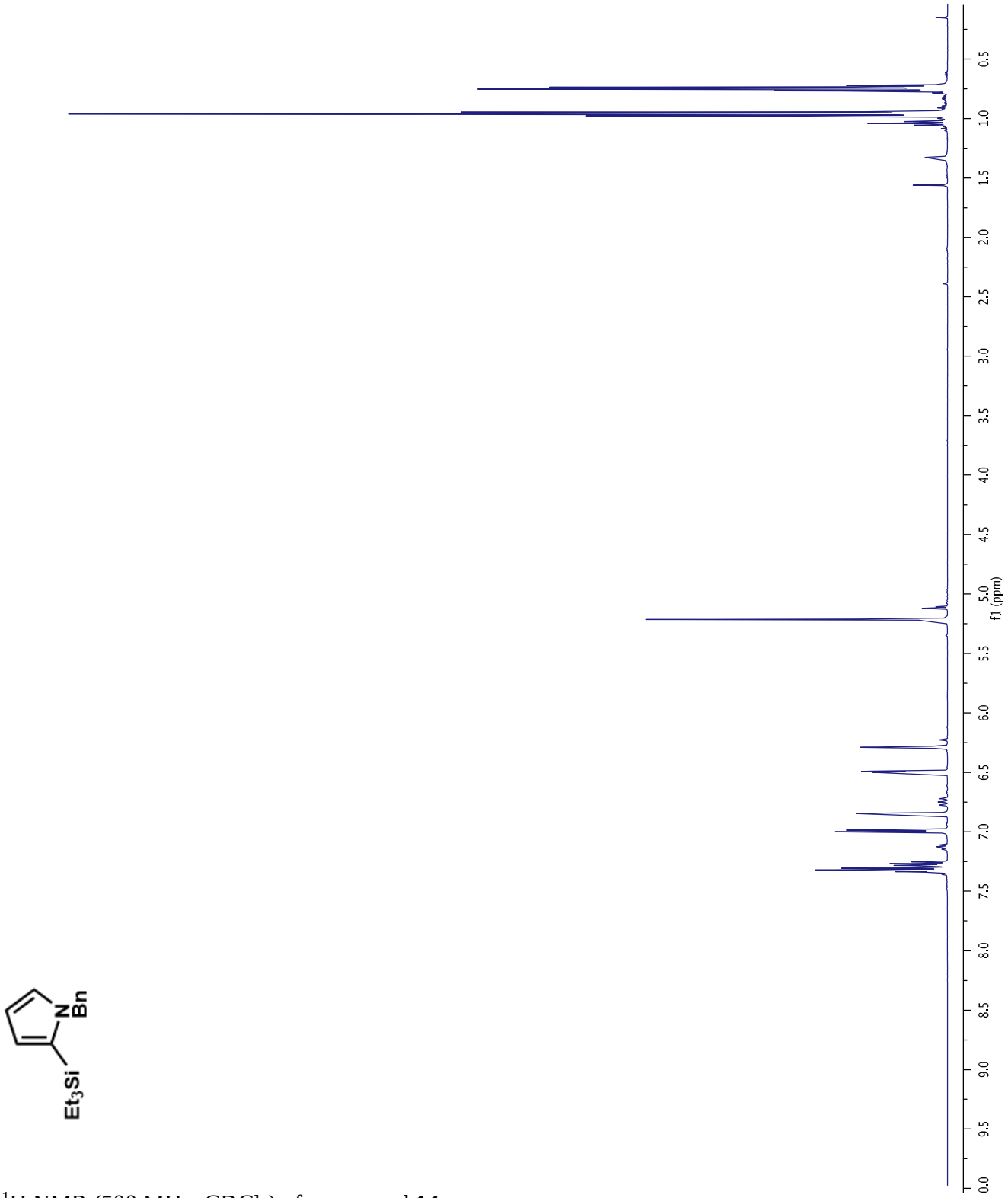
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14o_dim**



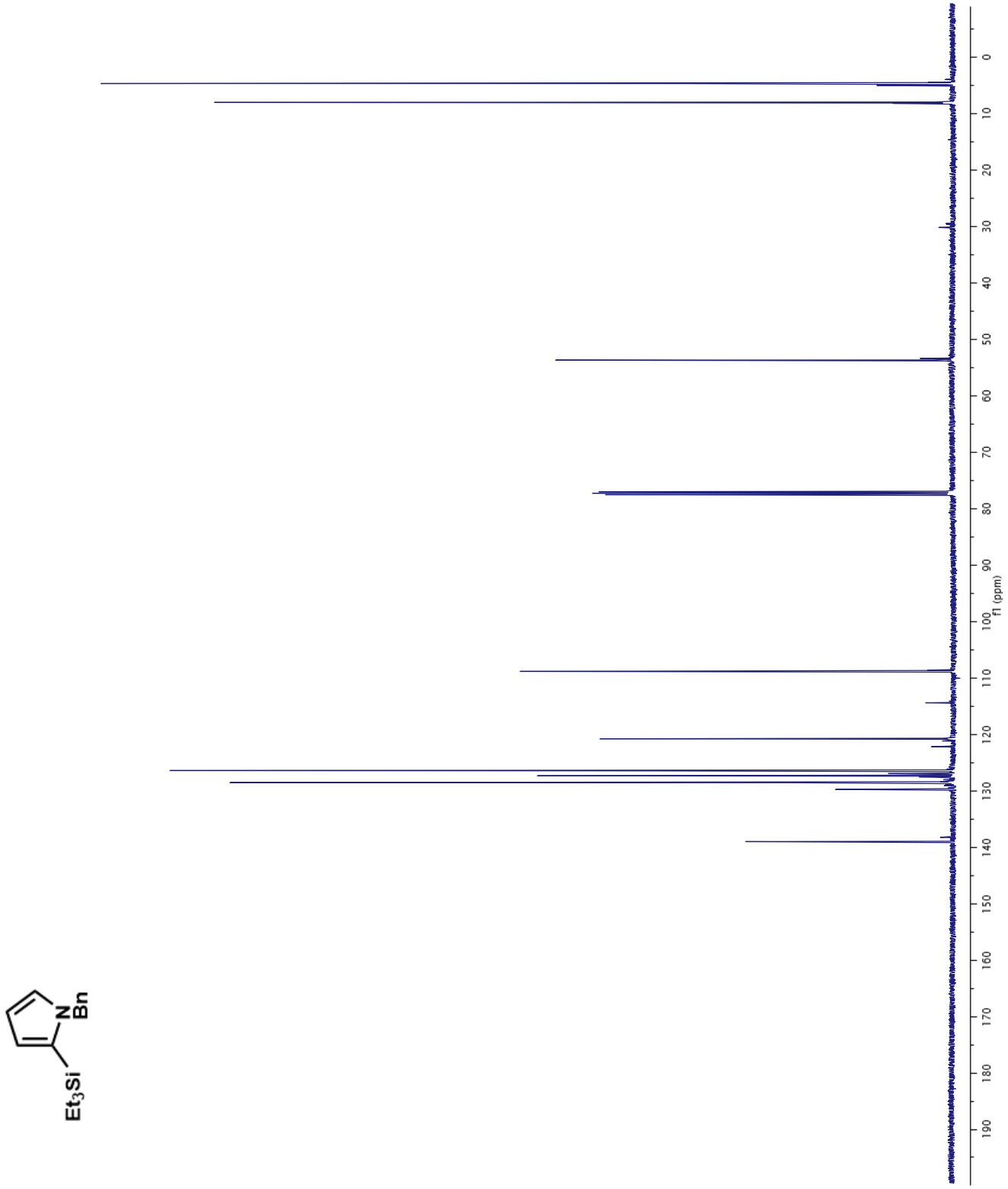
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14p**



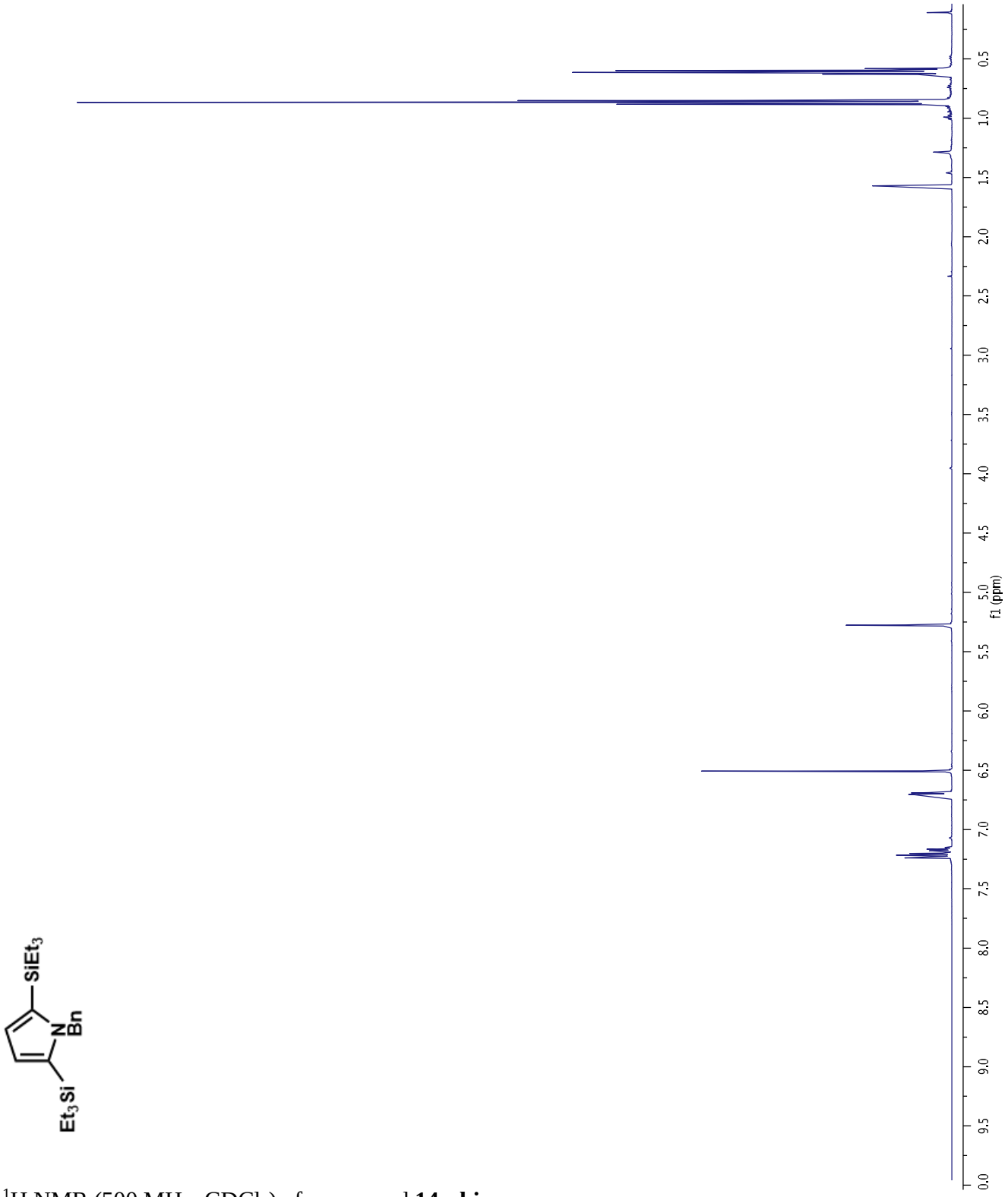
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14p**



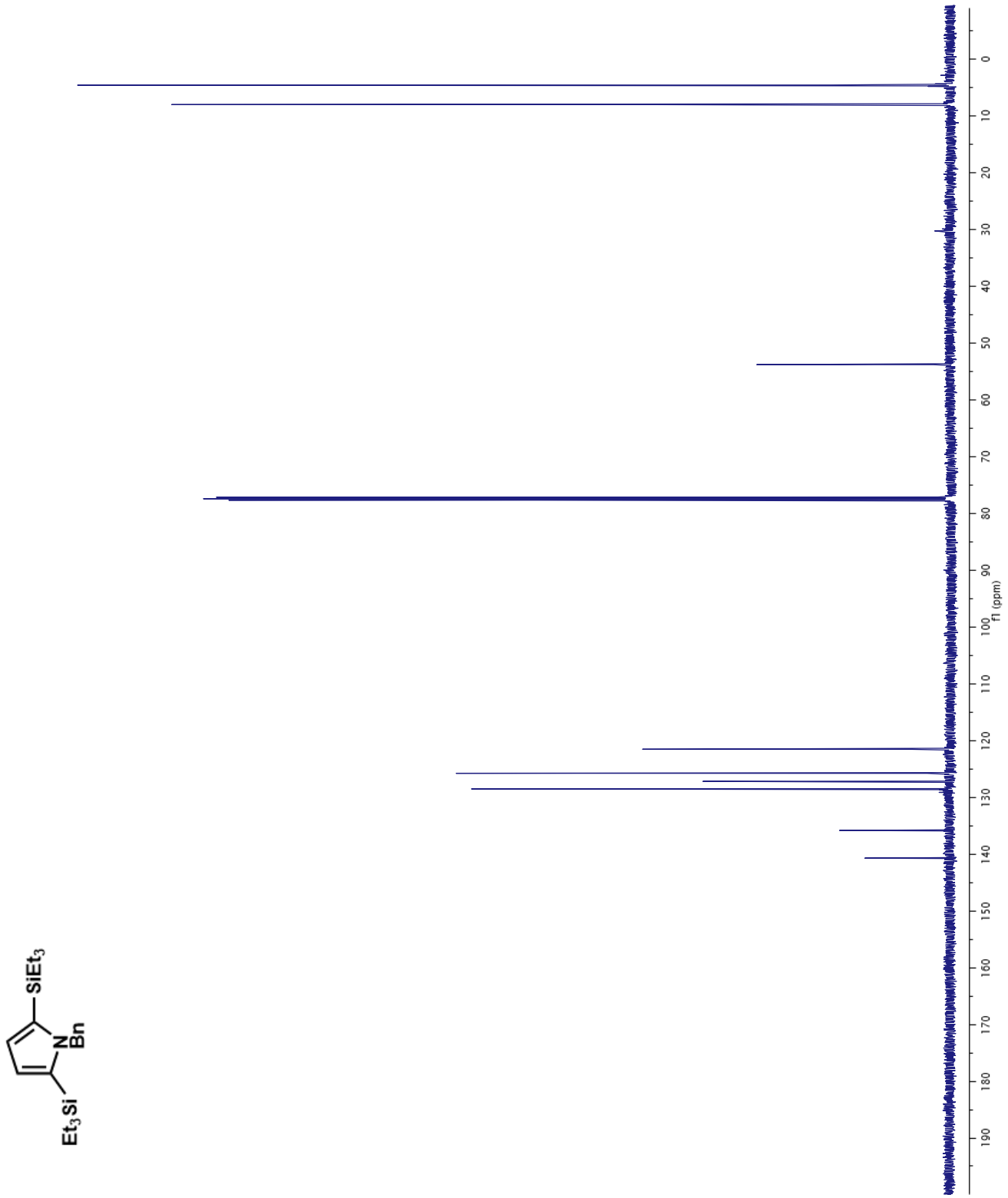
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14s**



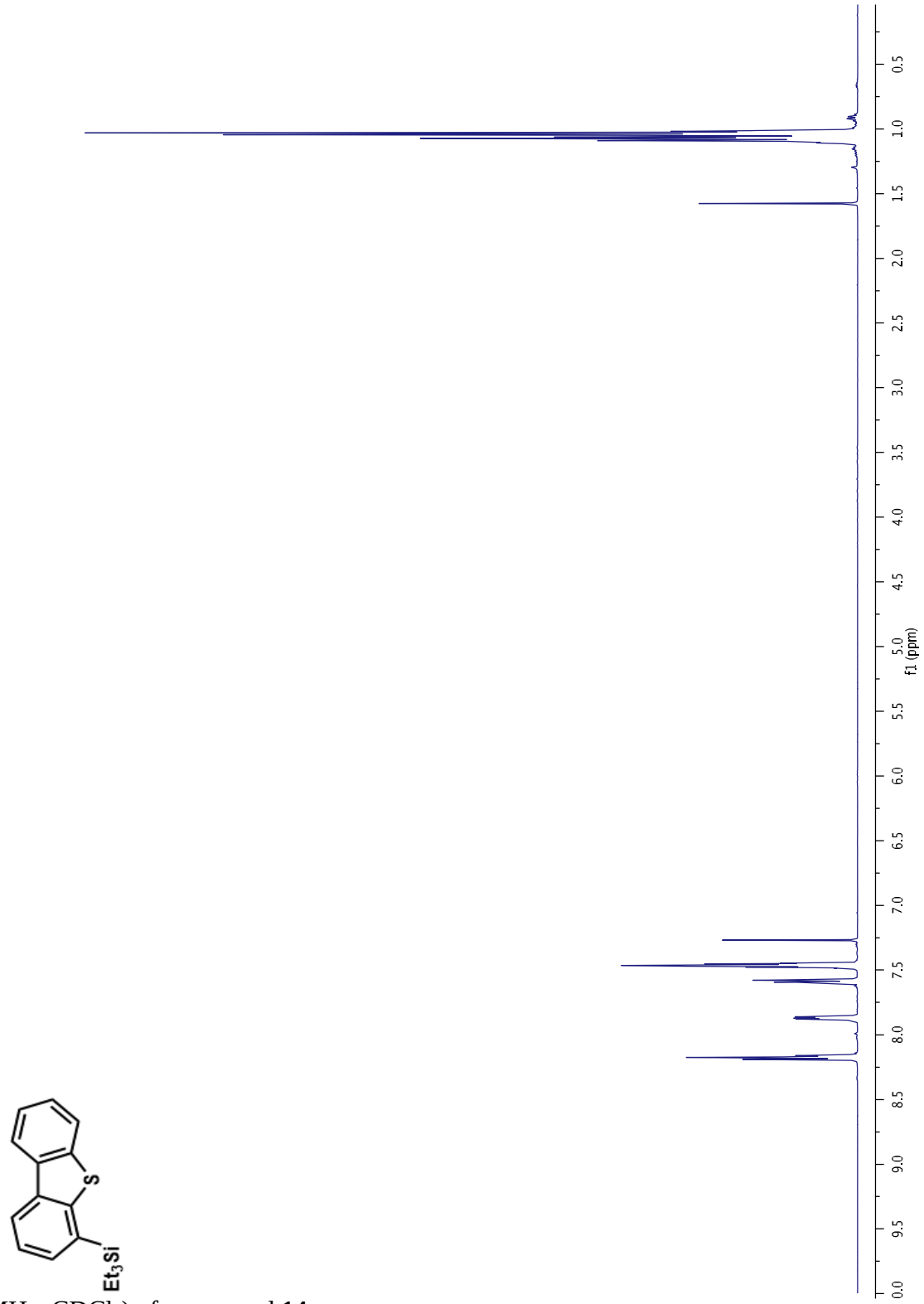
^{3}C NMR (125 MHz, $CDCl_3$) of compound **14s**



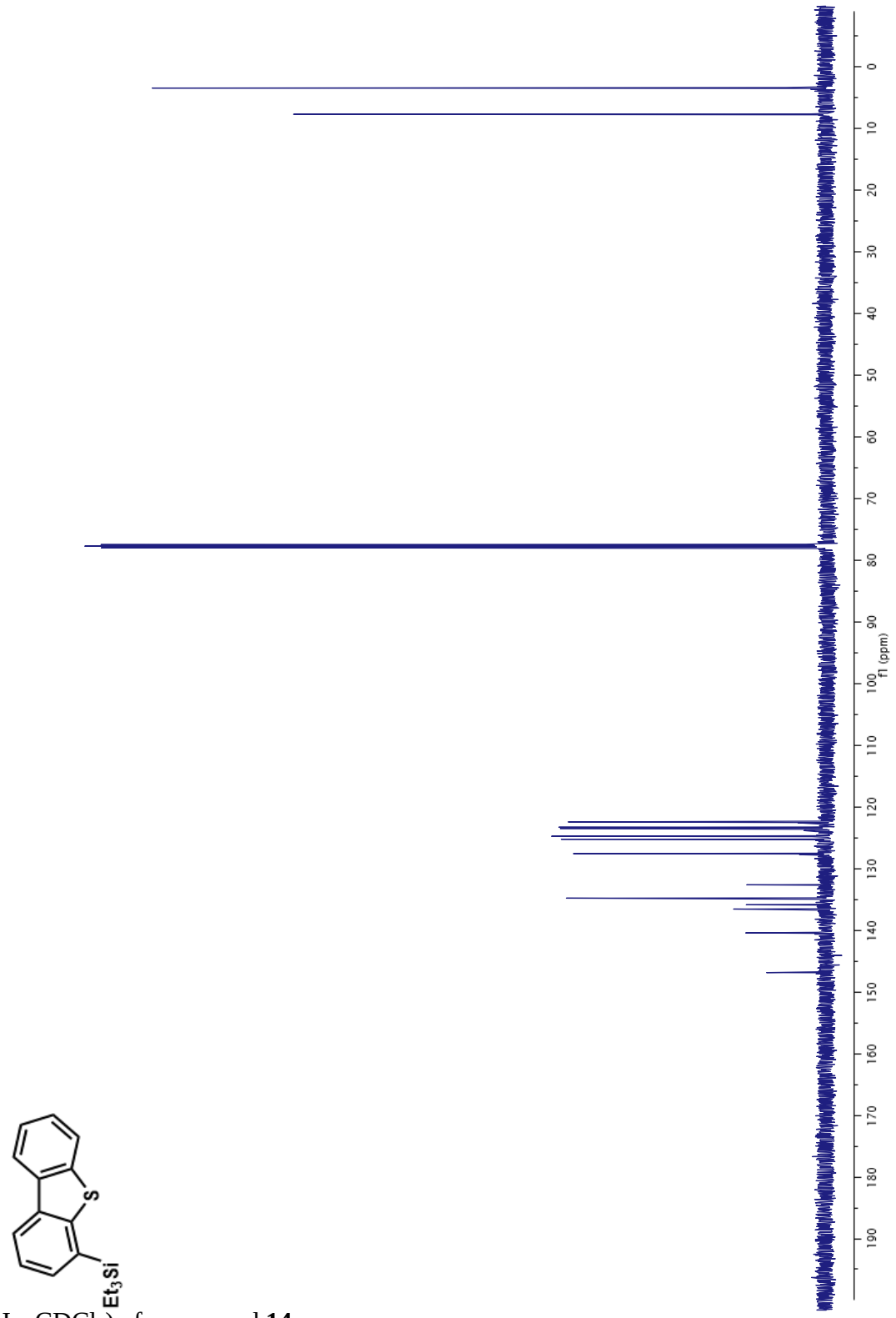
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14s_bis**



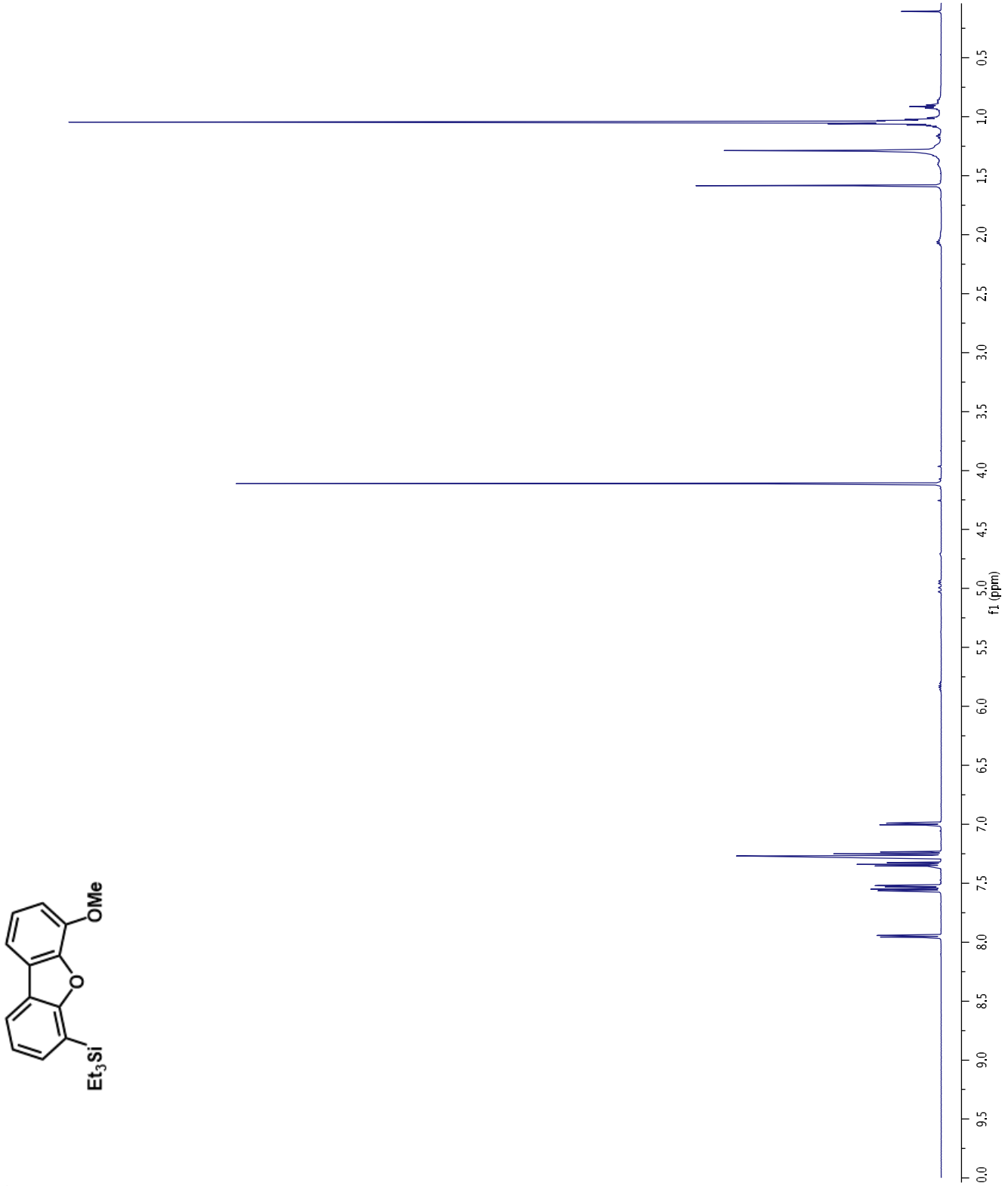
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14s_bis**



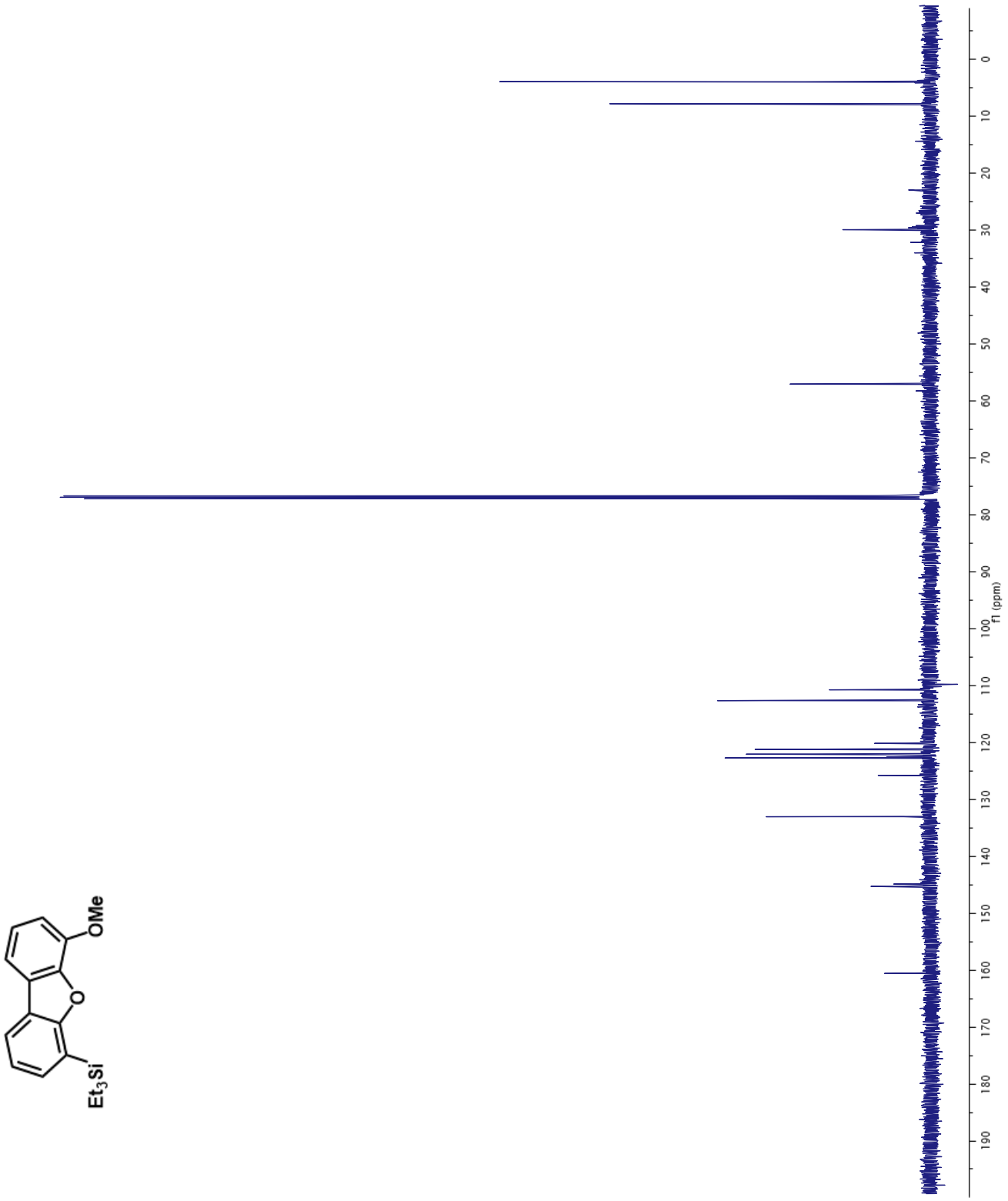
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14u**



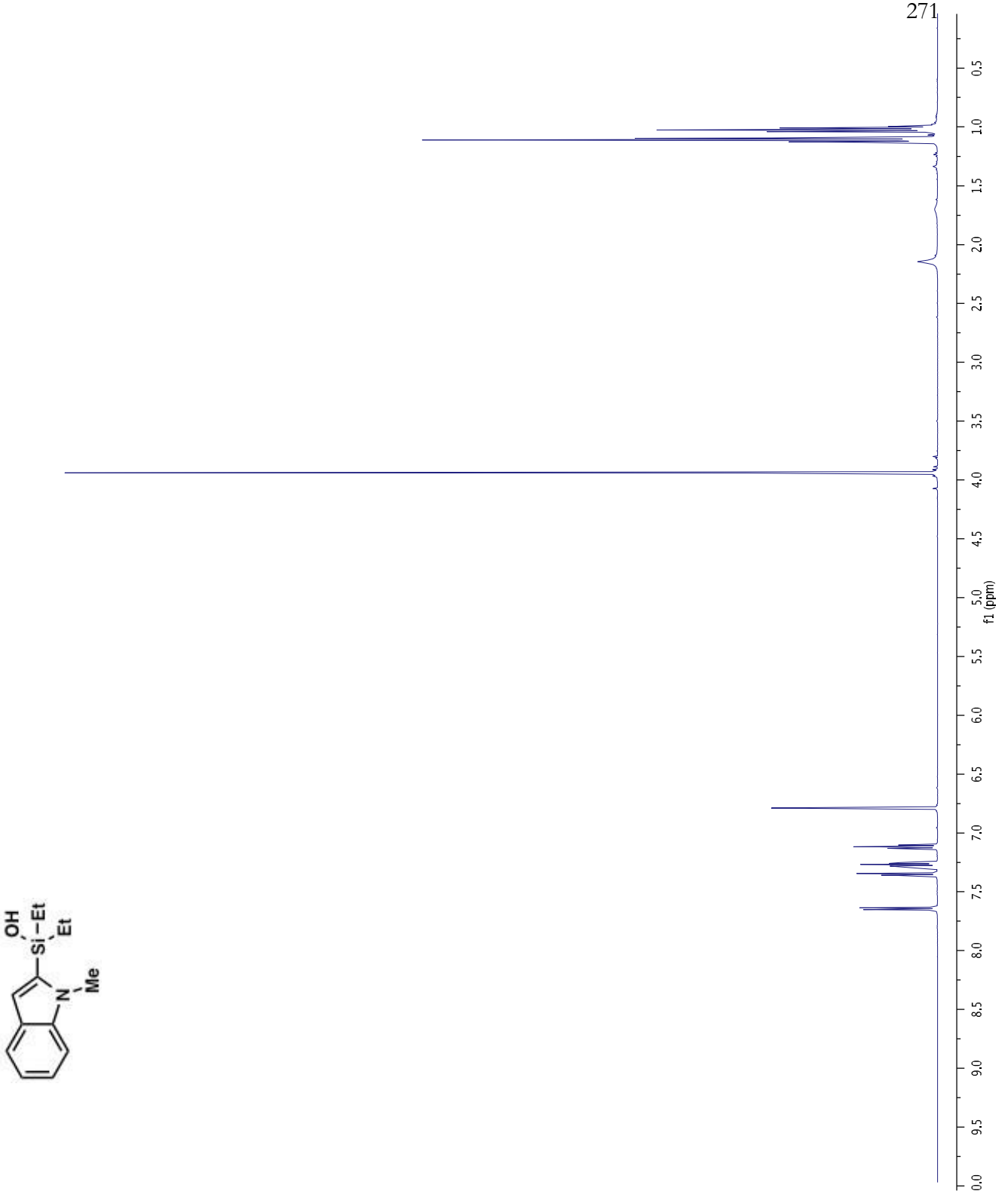
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14u**



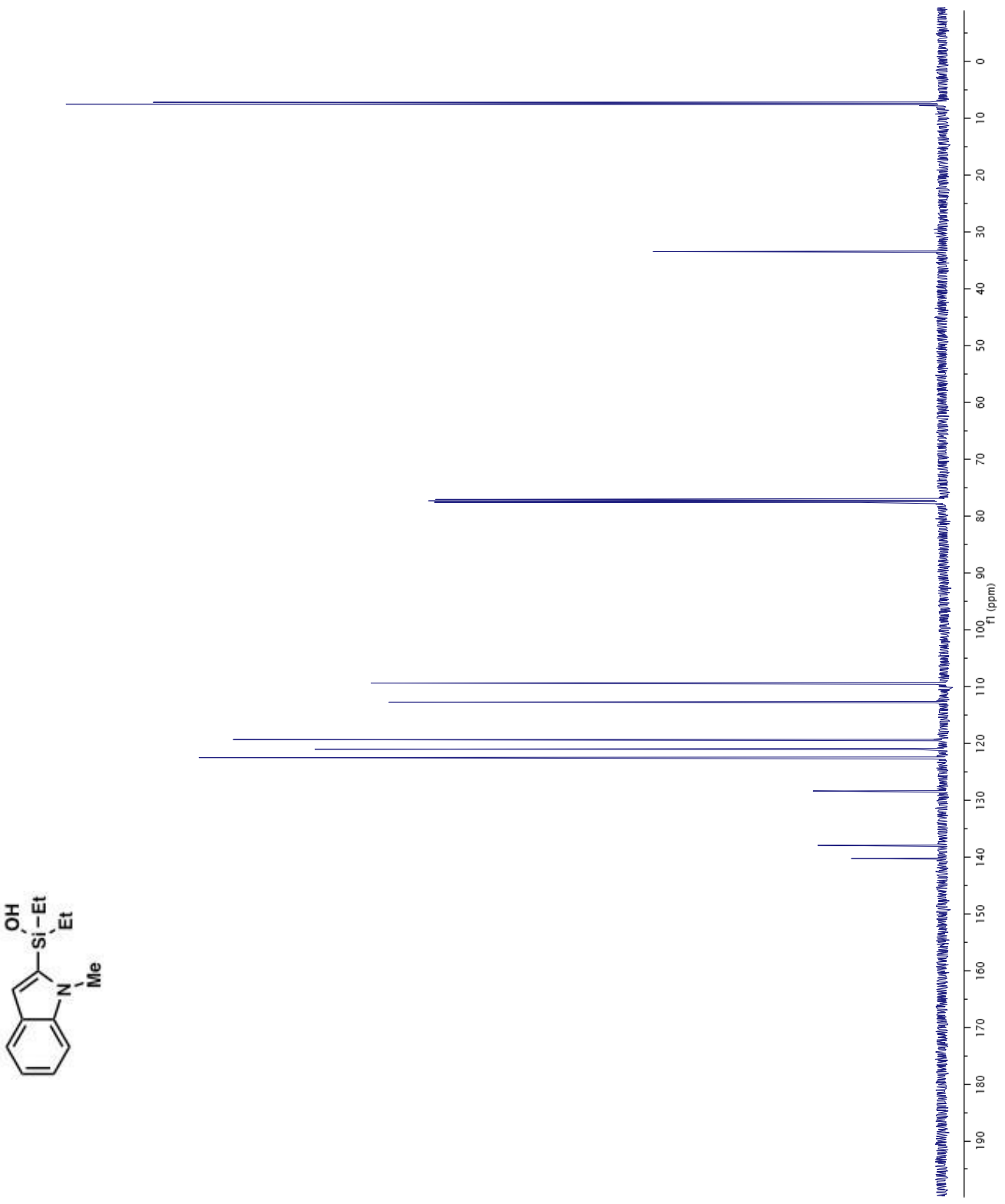
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14v**



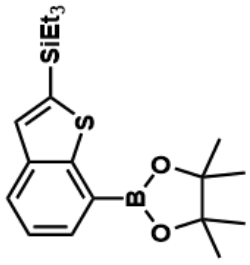
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14v**

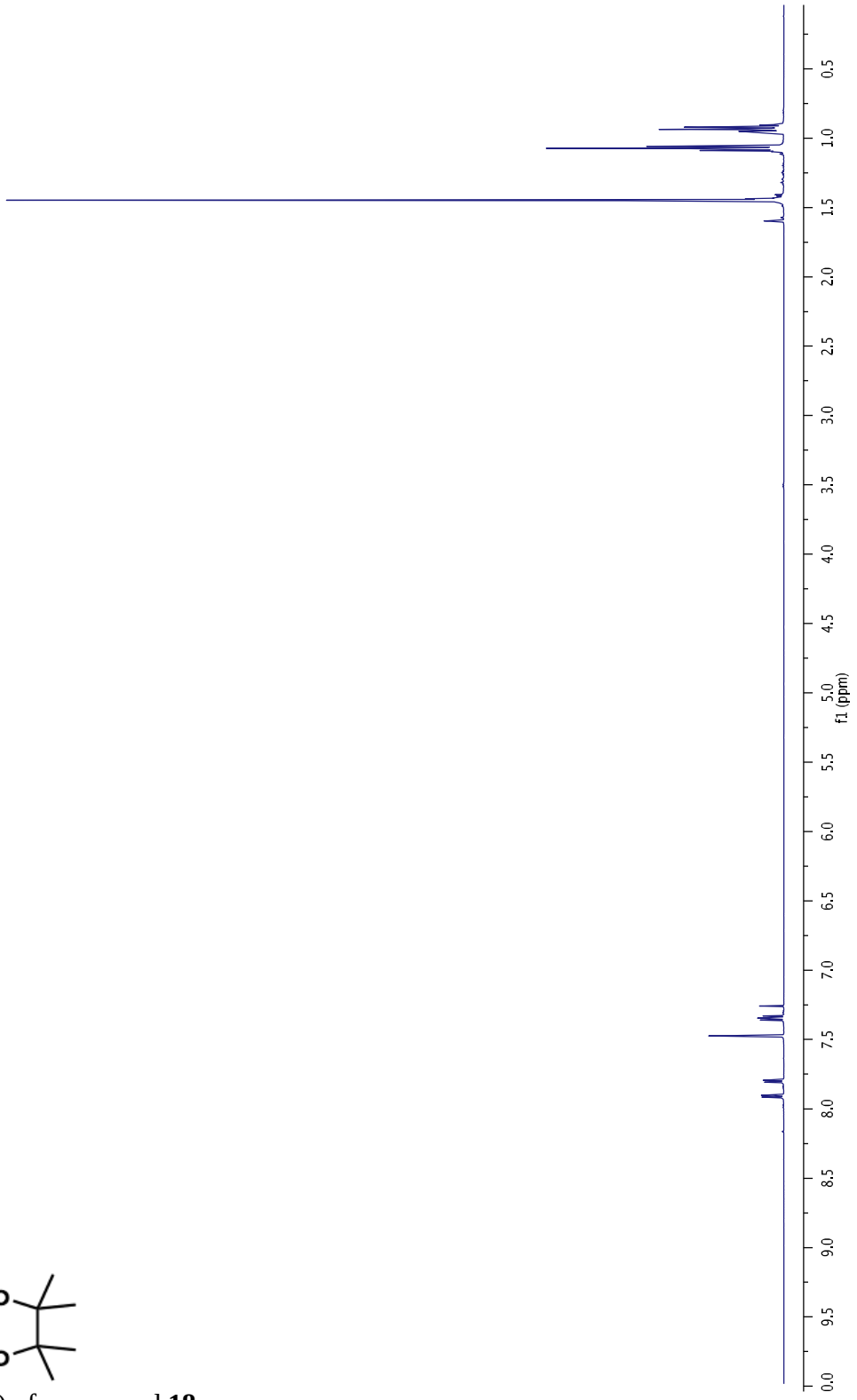


^{1}H NMR (500 MHz, $CDCl_3$) of compound **16**

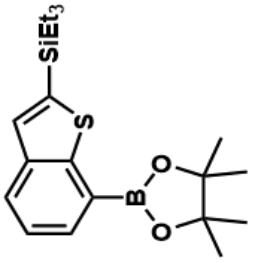


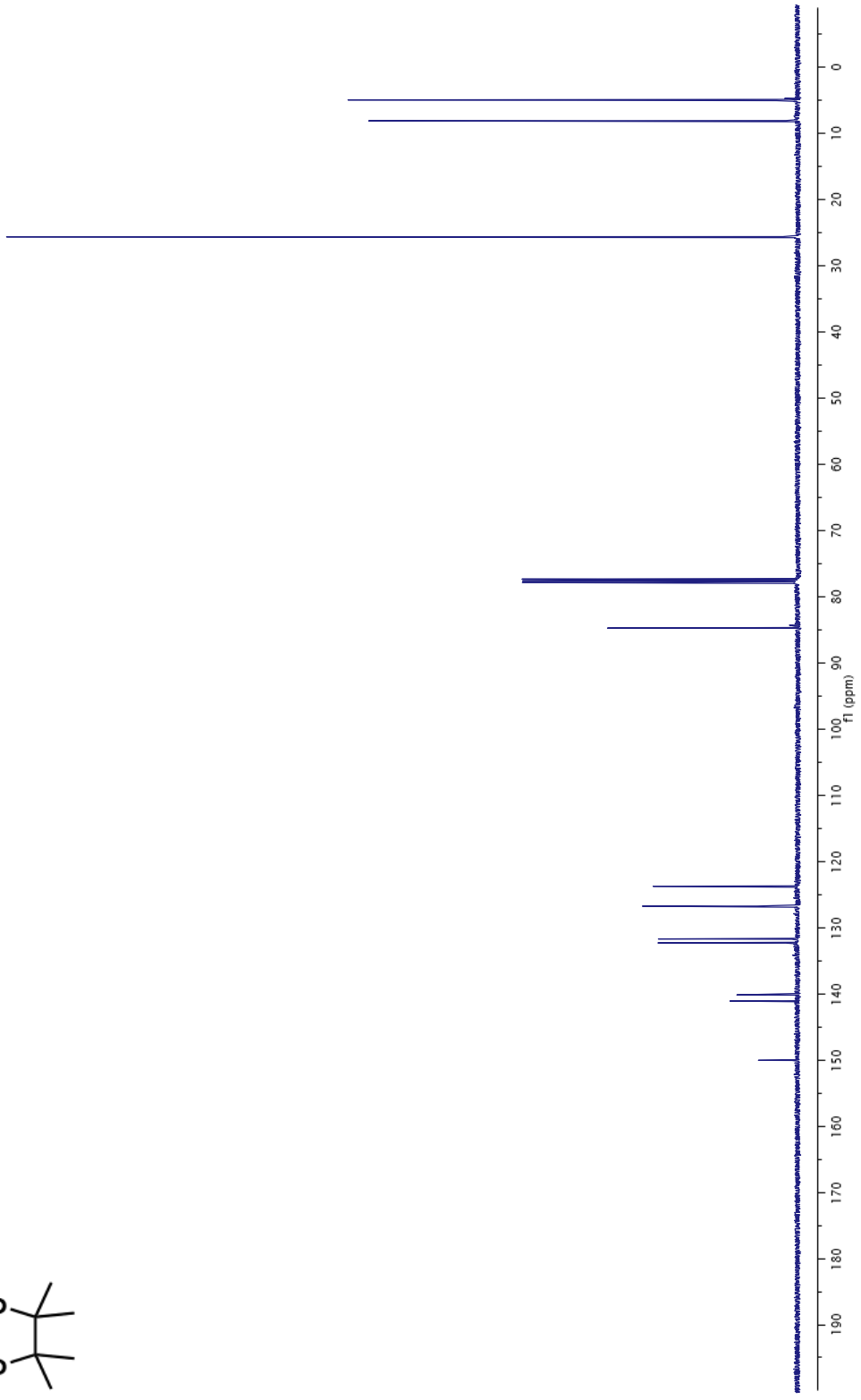
^{13}C NMR (125 MHz, $CDCl_3$) of compound **16**



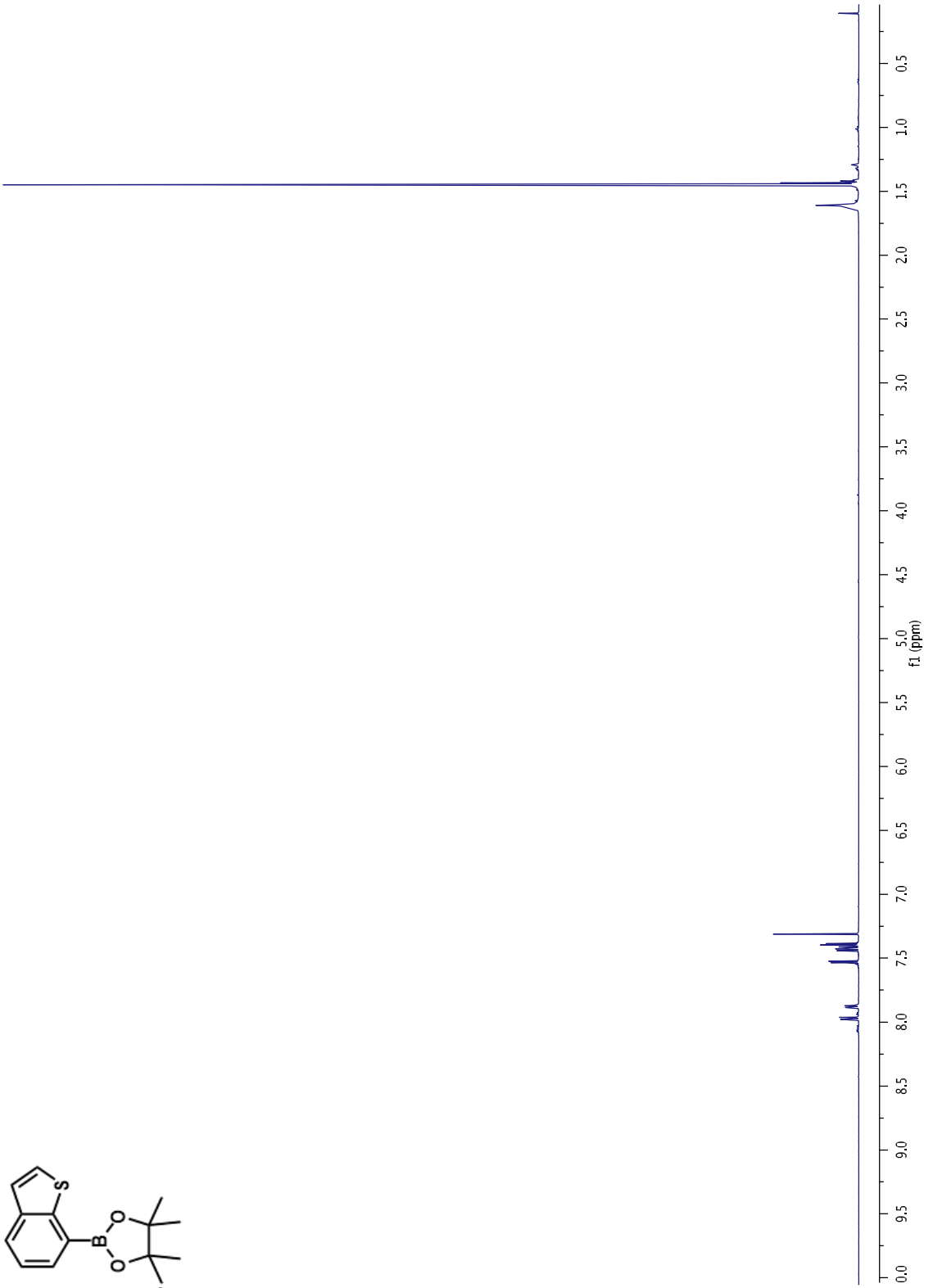


^{1}H NMR (500 MHz, $CDCl_3$) of compound **18**

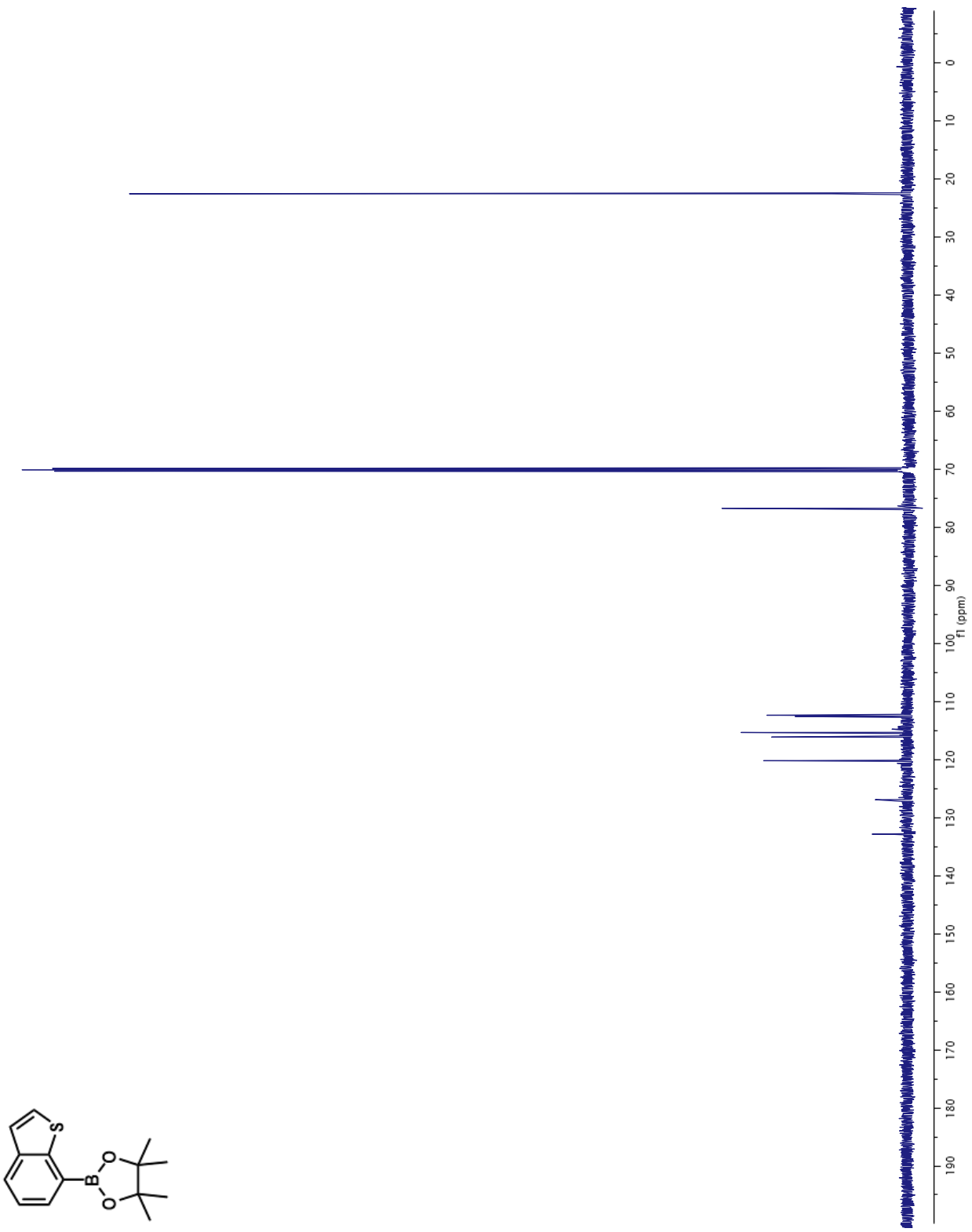




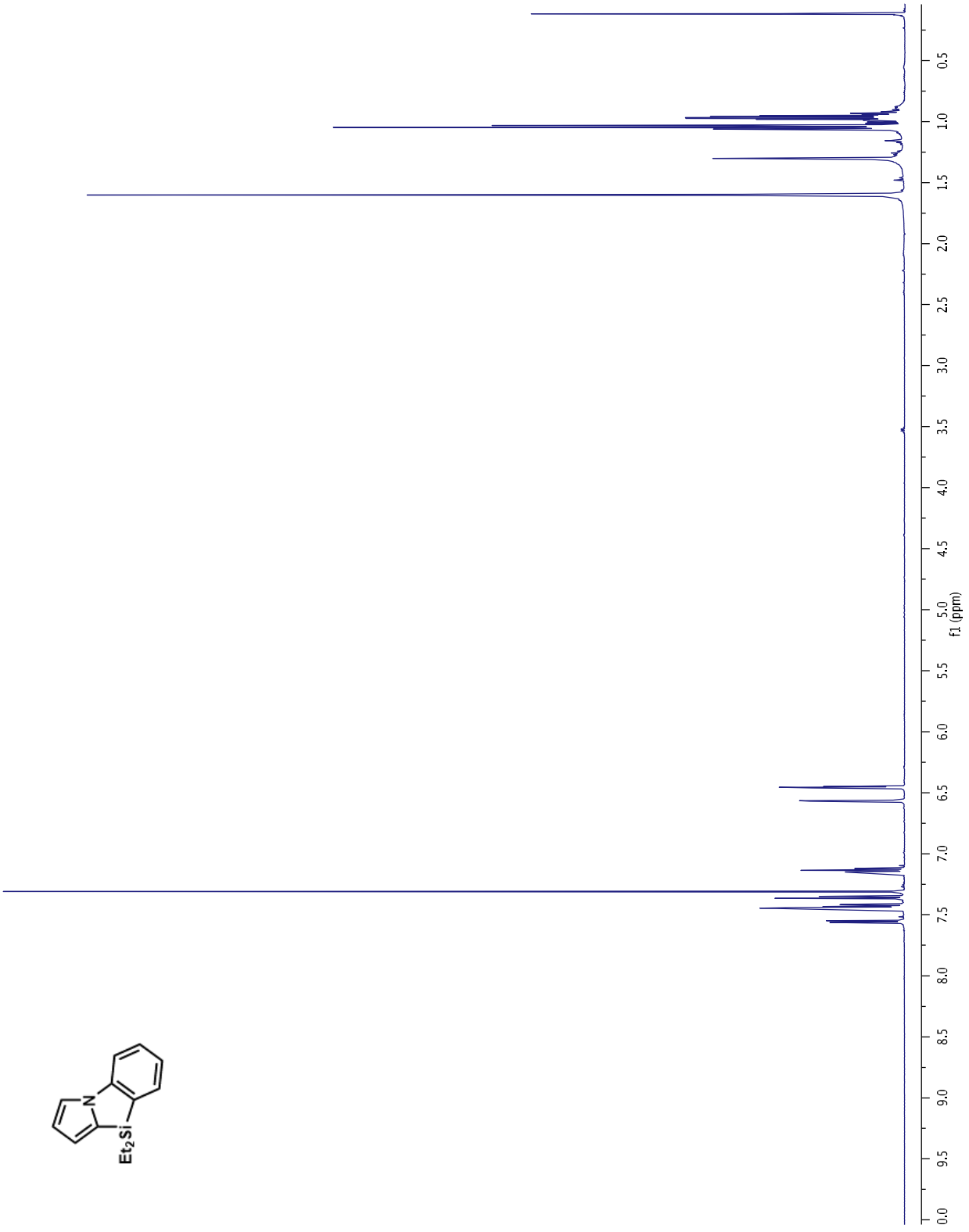
^{13}C NMR (125 MHz, $CDCl_3$) of compound **18**



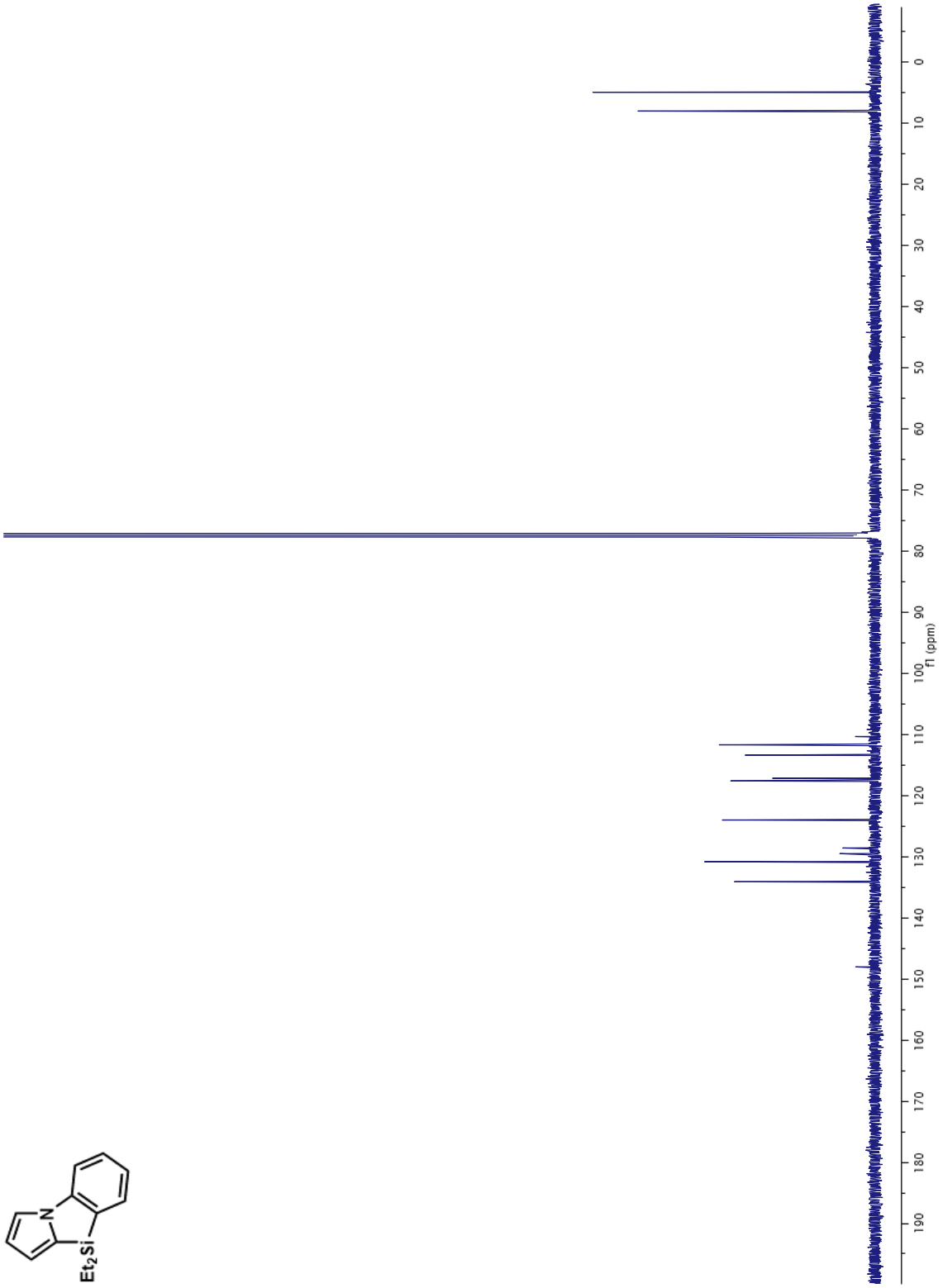
^{1}H NMR (500 MHz, $CDCl_3$) of compound **19**



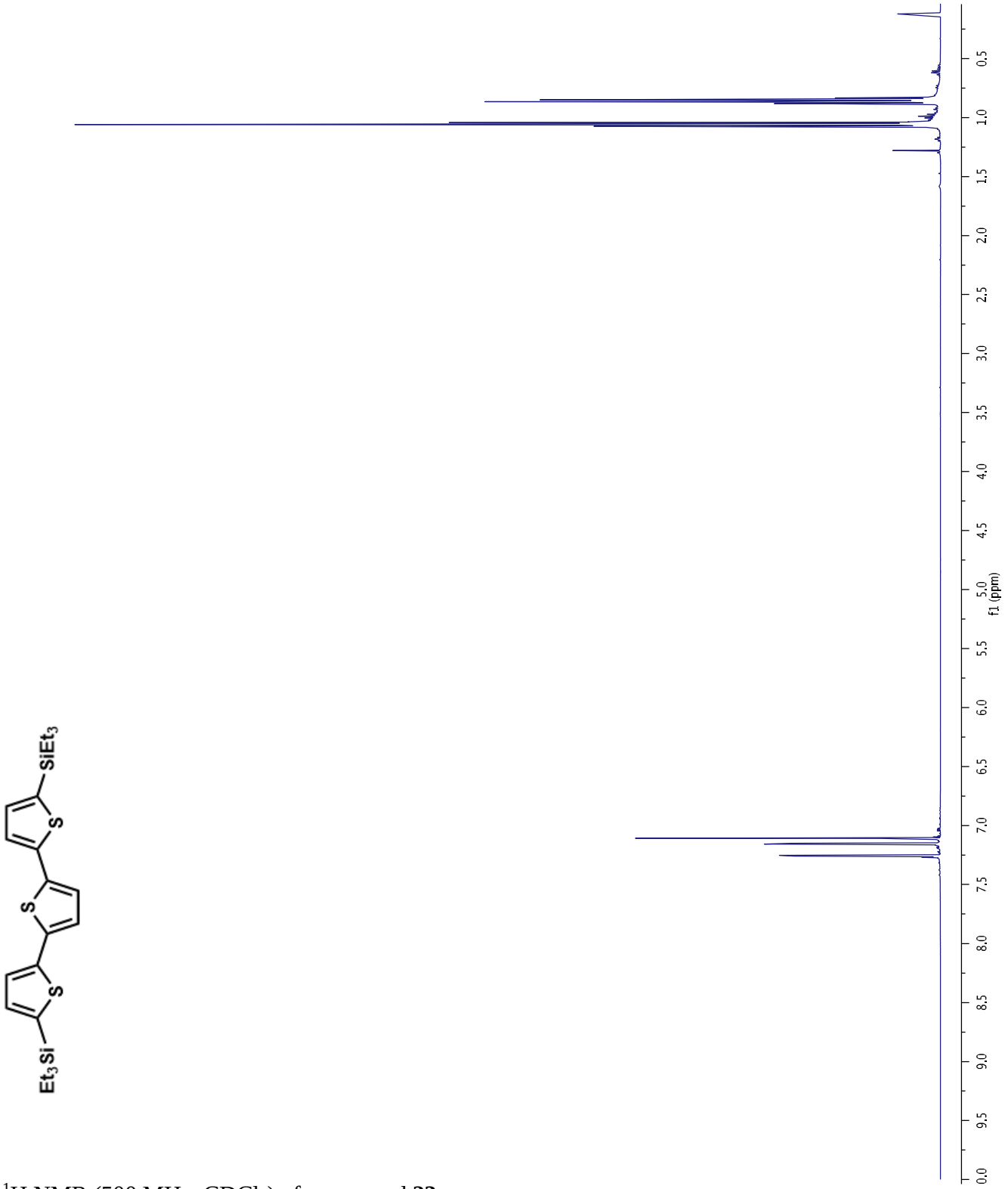
^{13}C NMR (125 MHz, $CDCl_3$) of compound **19**



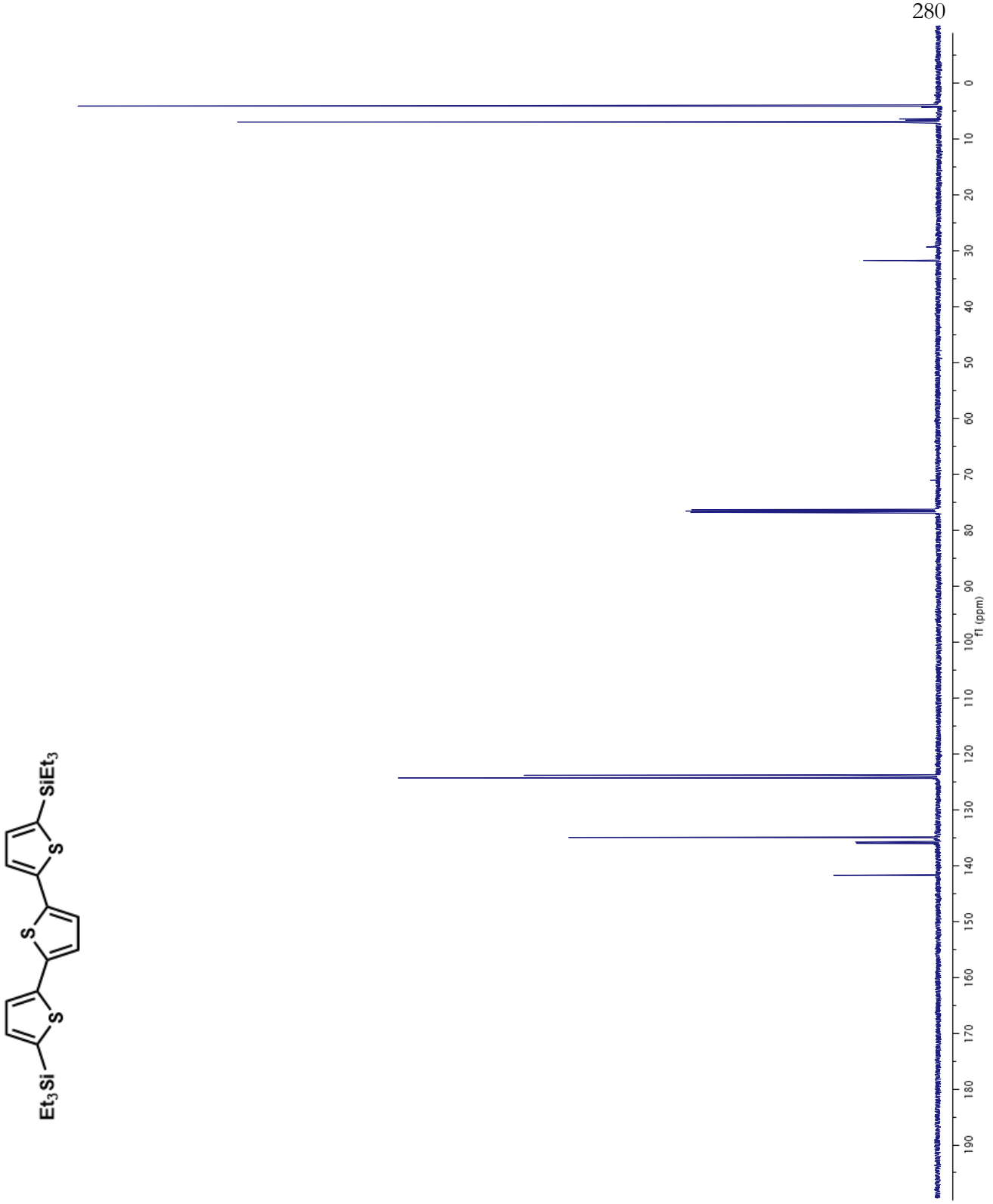
^{1}H NMR (500 MHz, $CDCl_3$) of compound **21**



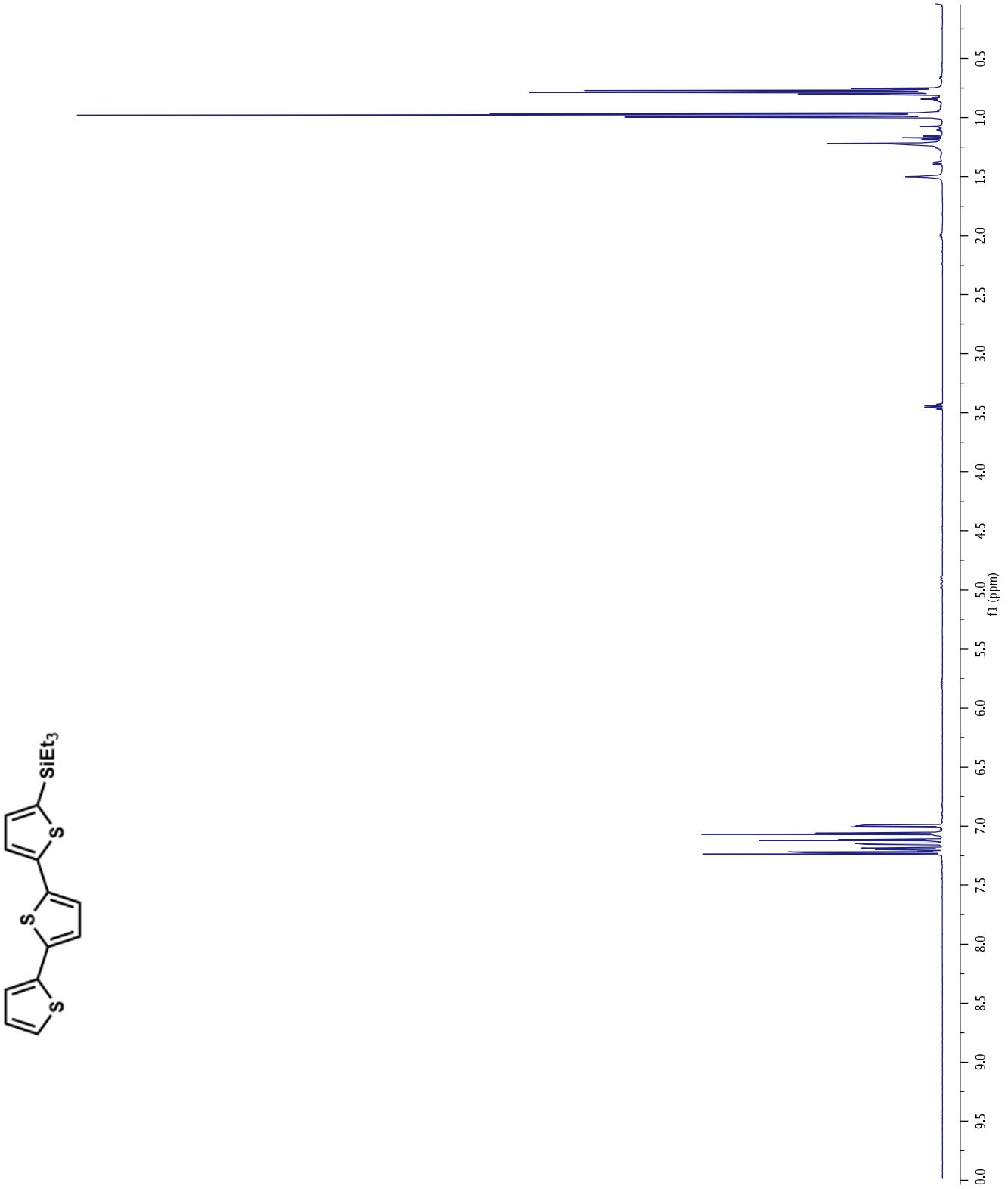
^{13}C NMR (125 MHz, $CDCl_3$) of compound **21**



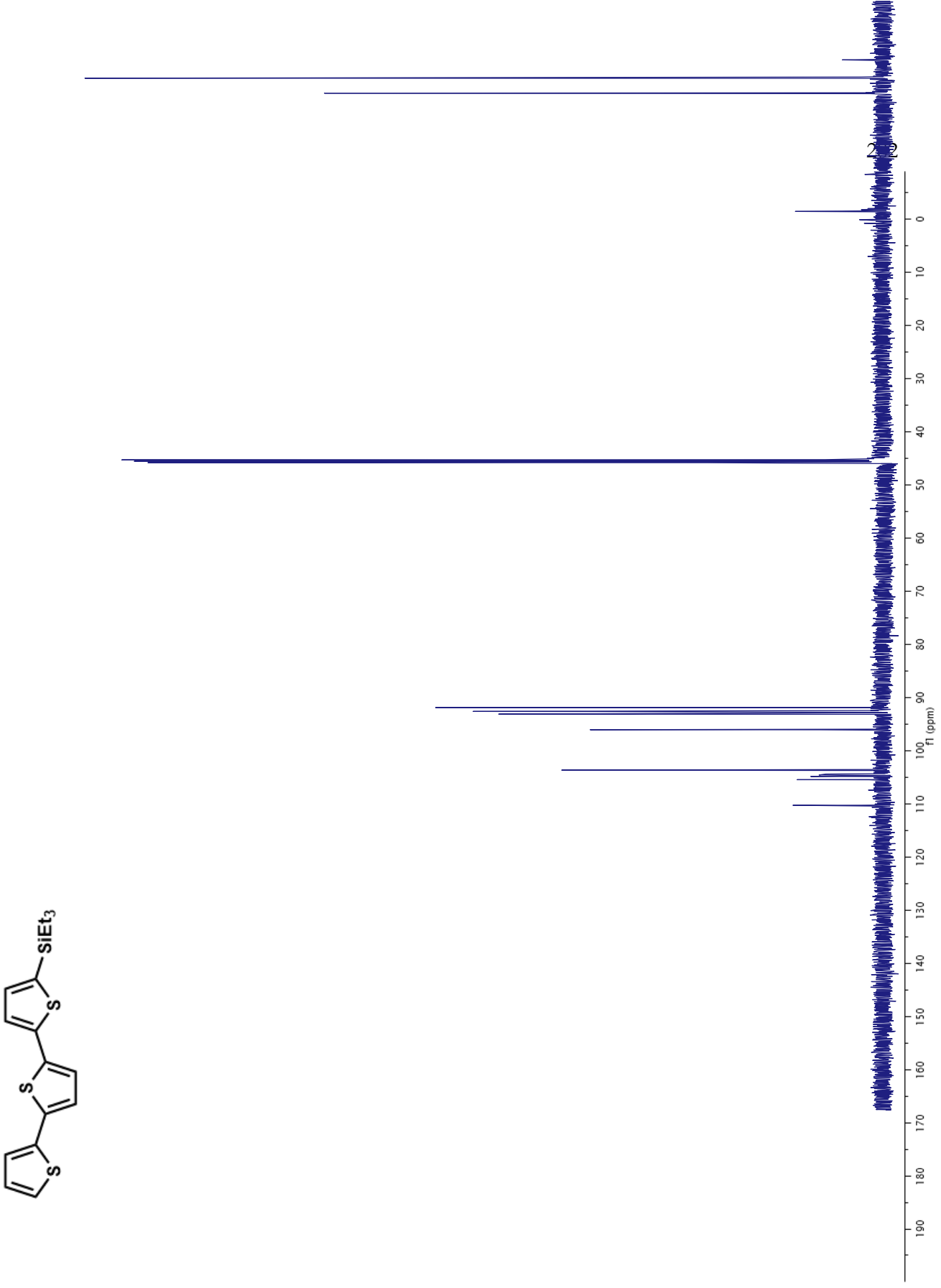
^{1}H NMR (500 MHz, $CDCl_3$) of compound **23**



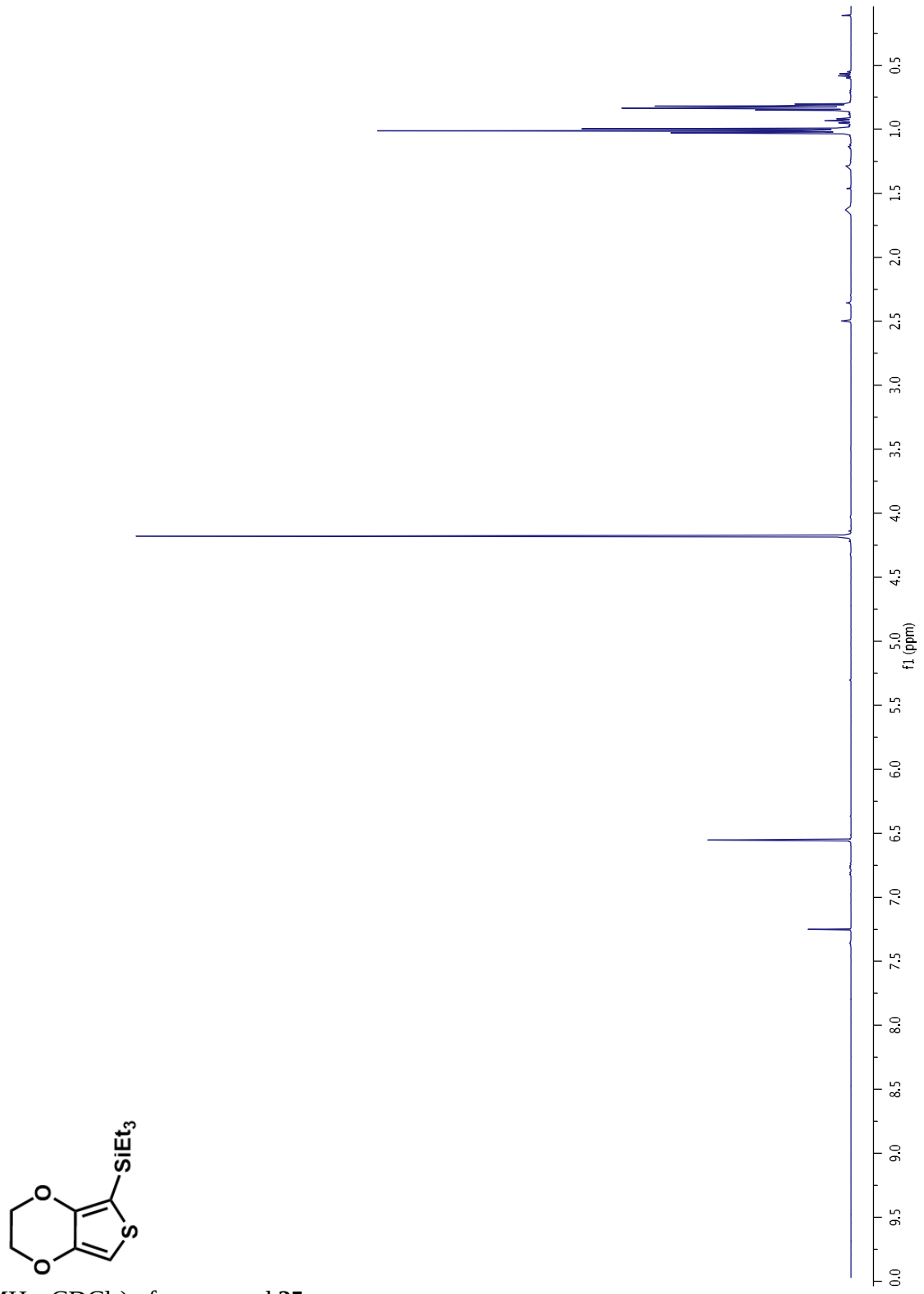
^{13}C NMR (125 MHz, $CDCl_3$) of compound **23**



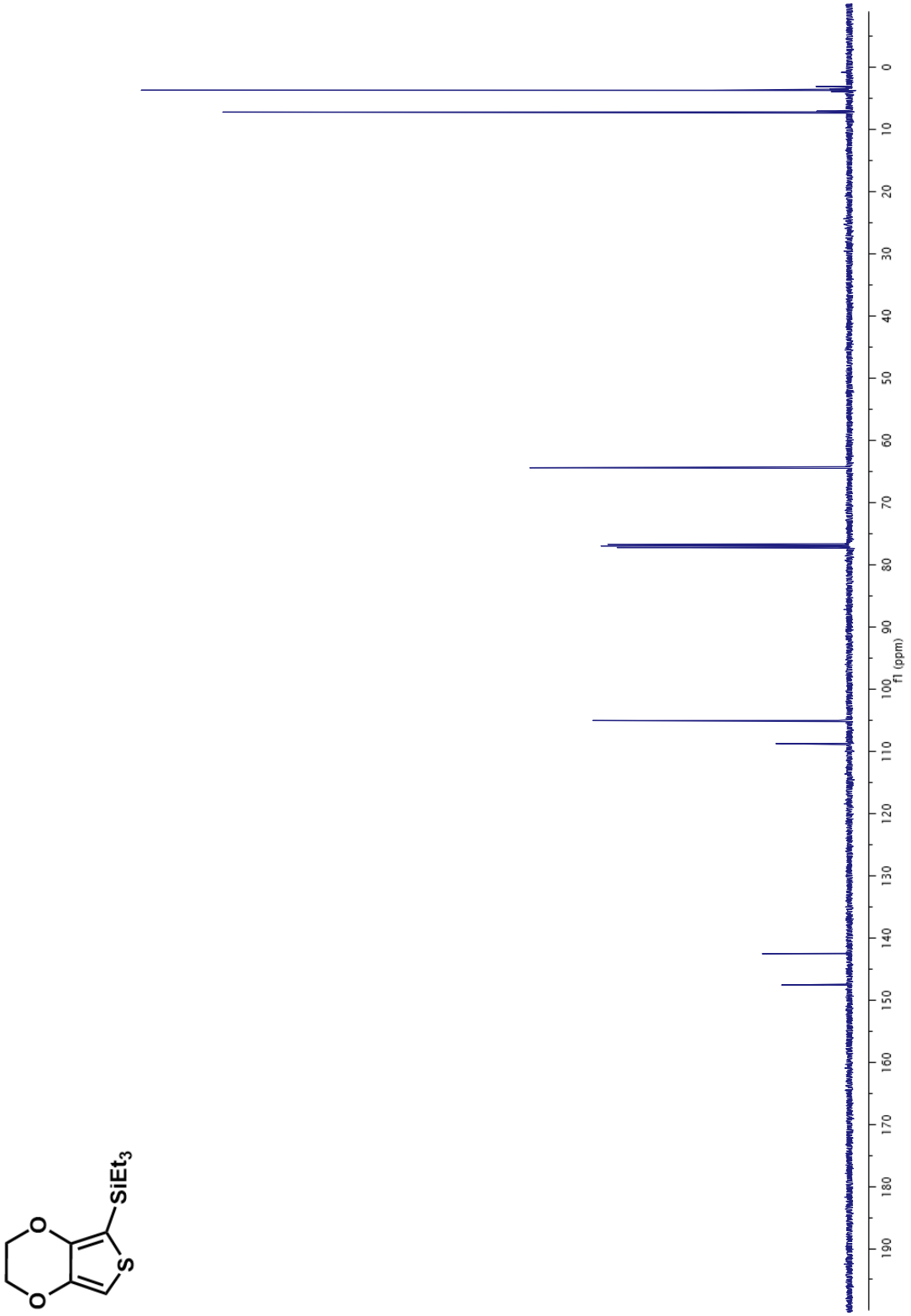
^{1}H NMR (500 MHz, $CDCl_3$) of compound **23_mono**



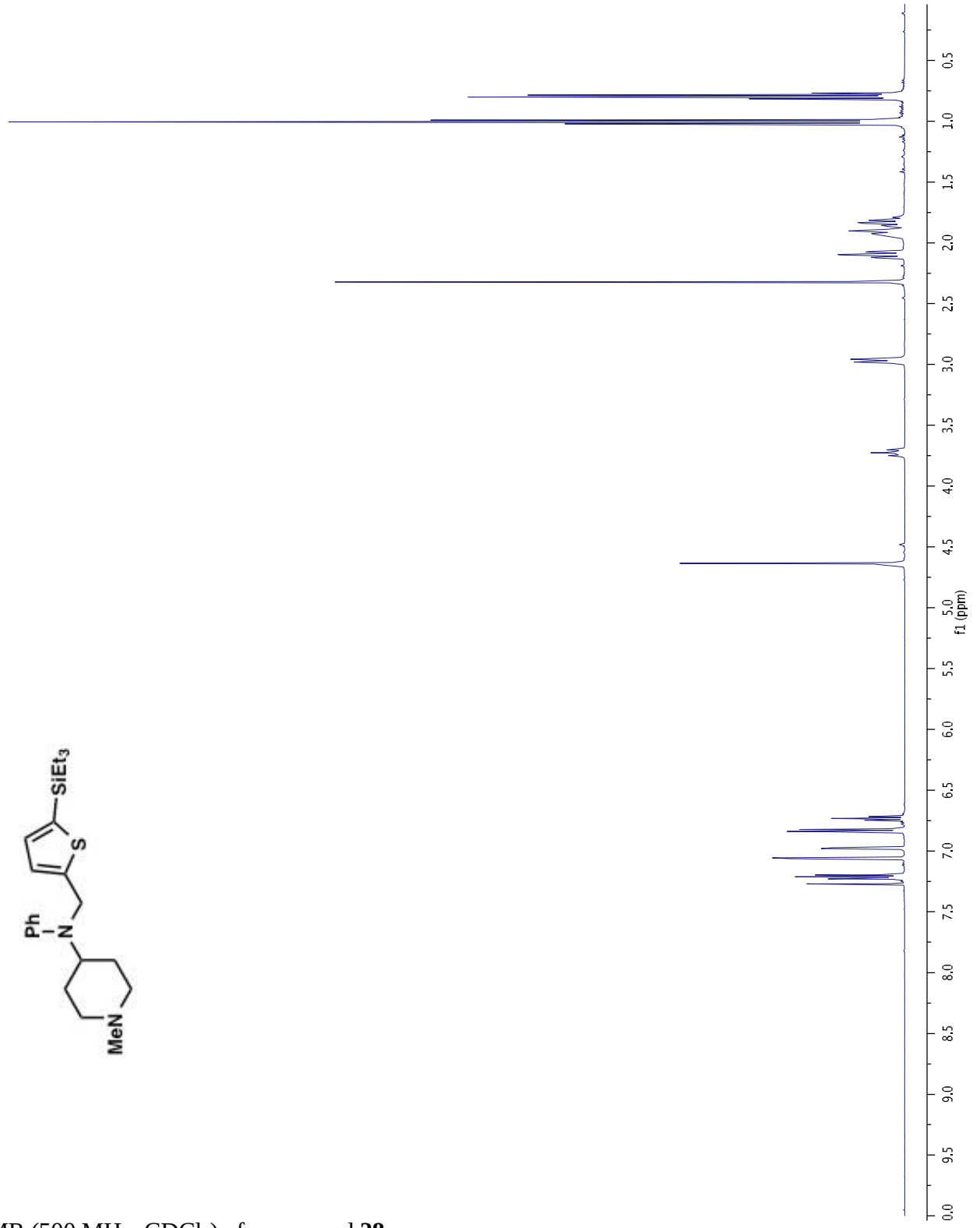
^{13}C NMR (125 MHz, $CDCl_3$) of compound **23_mono**



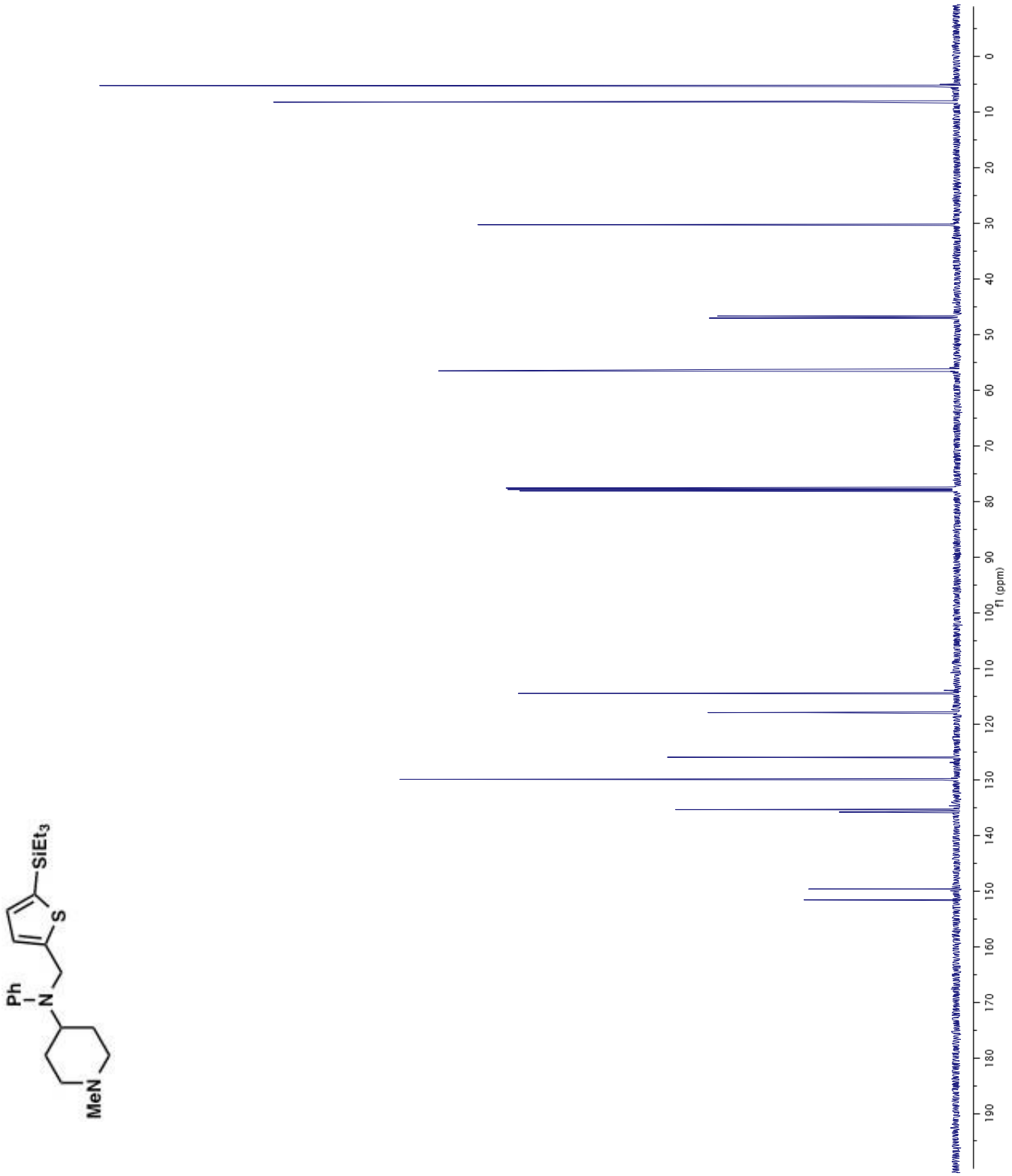
^{1}H NMR (500 MHz, $CDCl_3$) of compound **25**



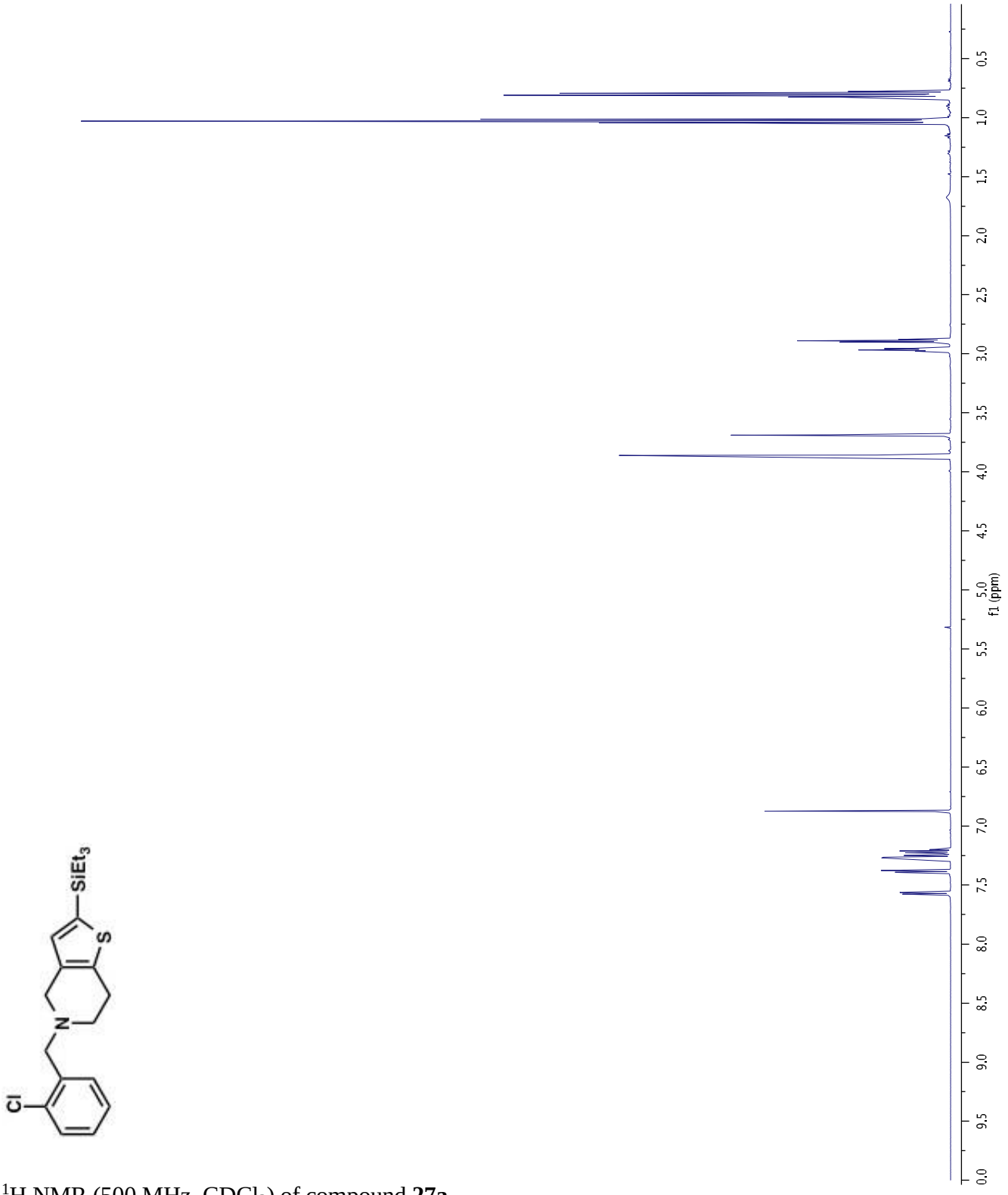
^{13}C NMR (125 MHz, $CDCl_3$) of compound **25**



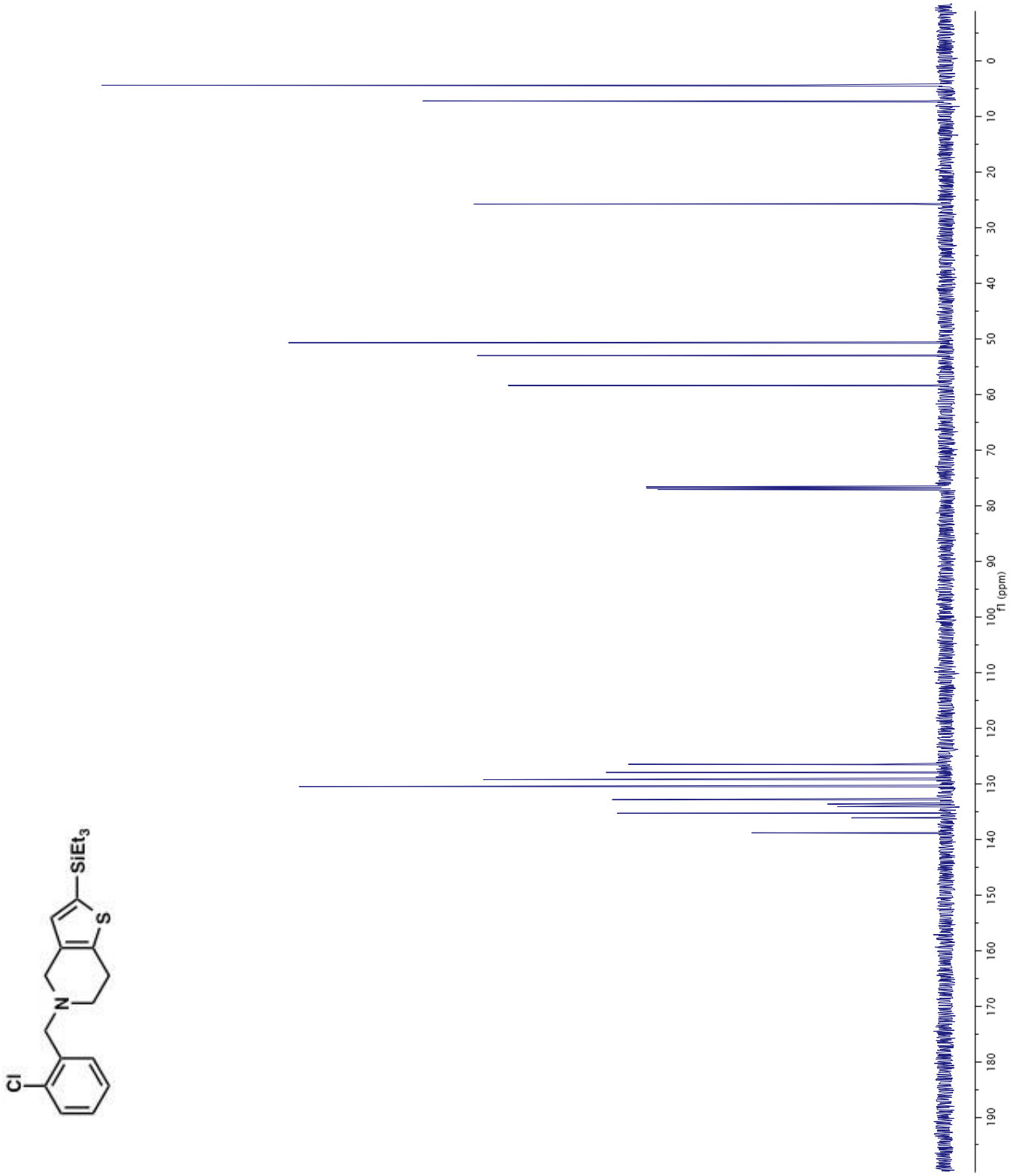
^{1}H NMR (500 MHz, $CDCl_3$) of compound **28**



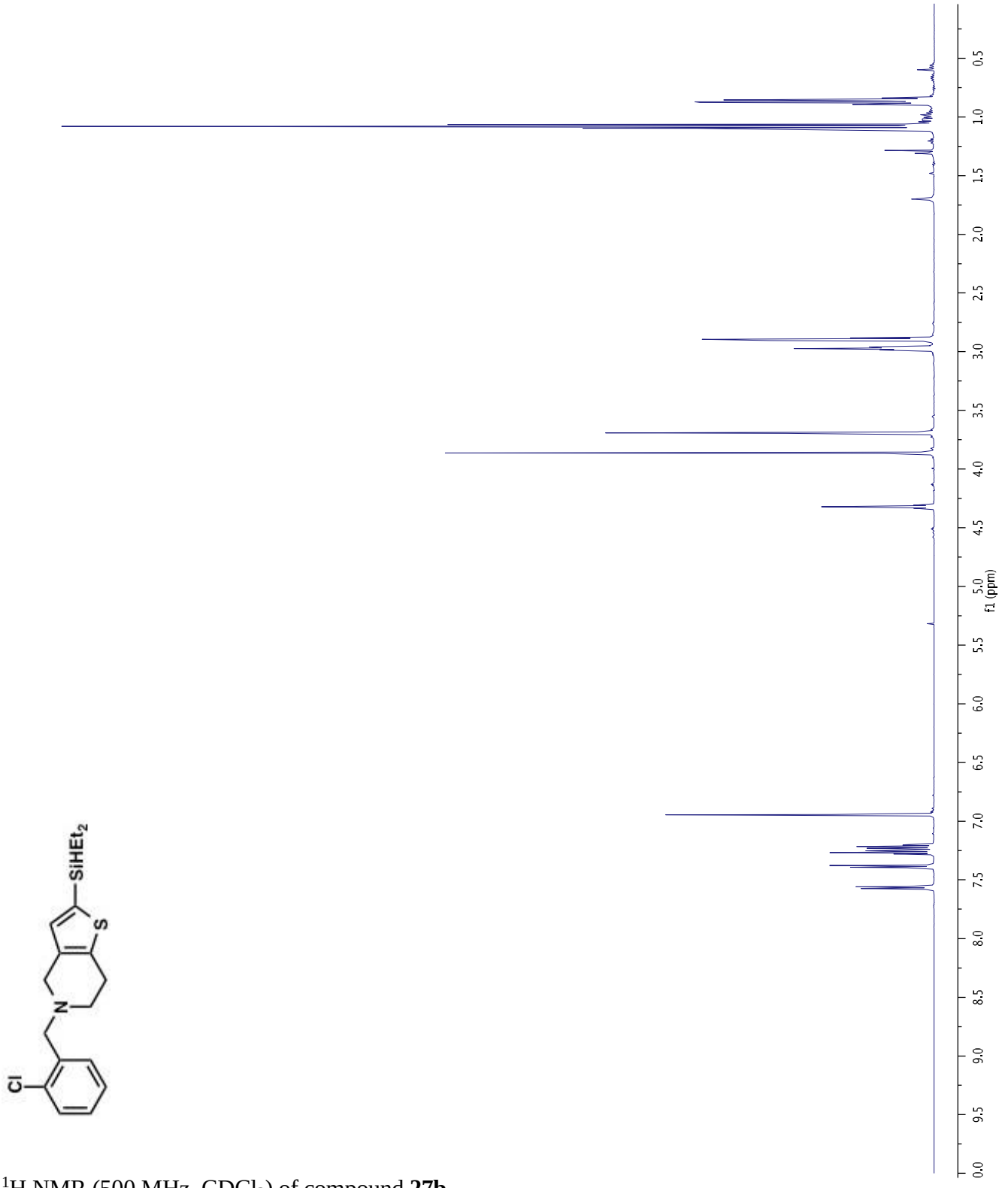
^{13}C NMR (125 MHz, $CDCl_3$) of compound **28**



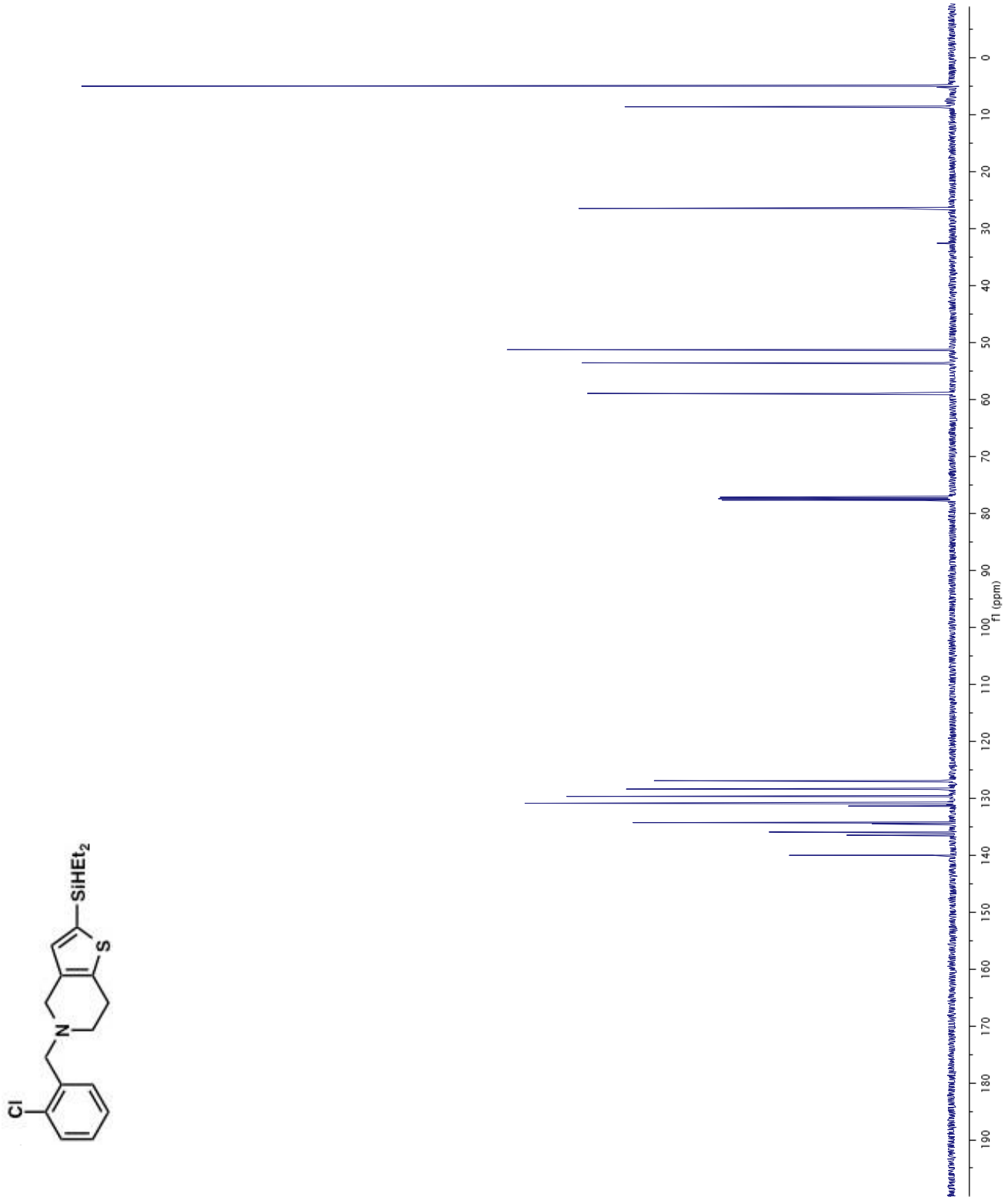
^{1}H NMR (500 MHz, $CDCl_3$) of compound **27a**



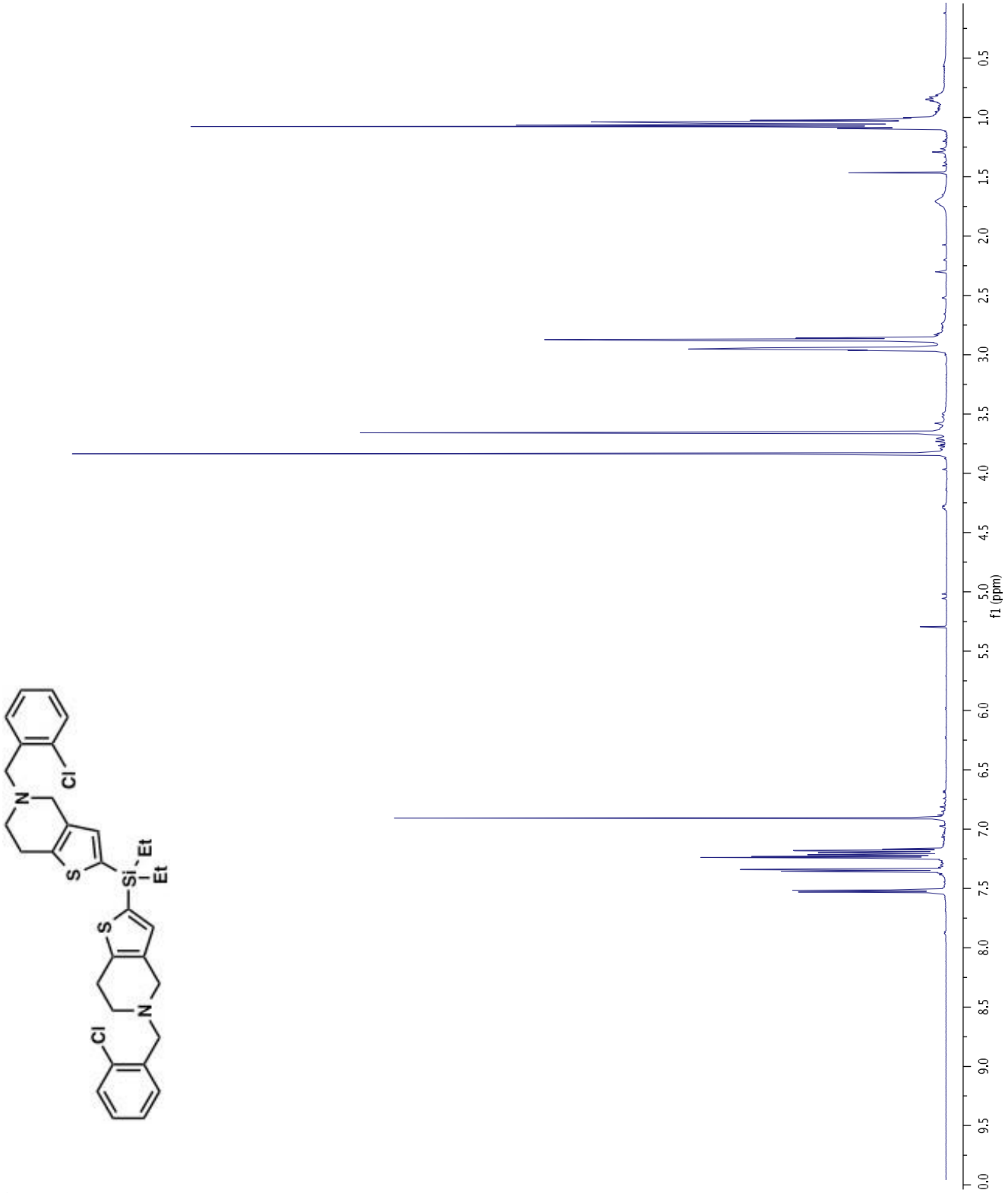
^{13}C NMR (125 MHz, $CDCl_3$) of compound **27a**



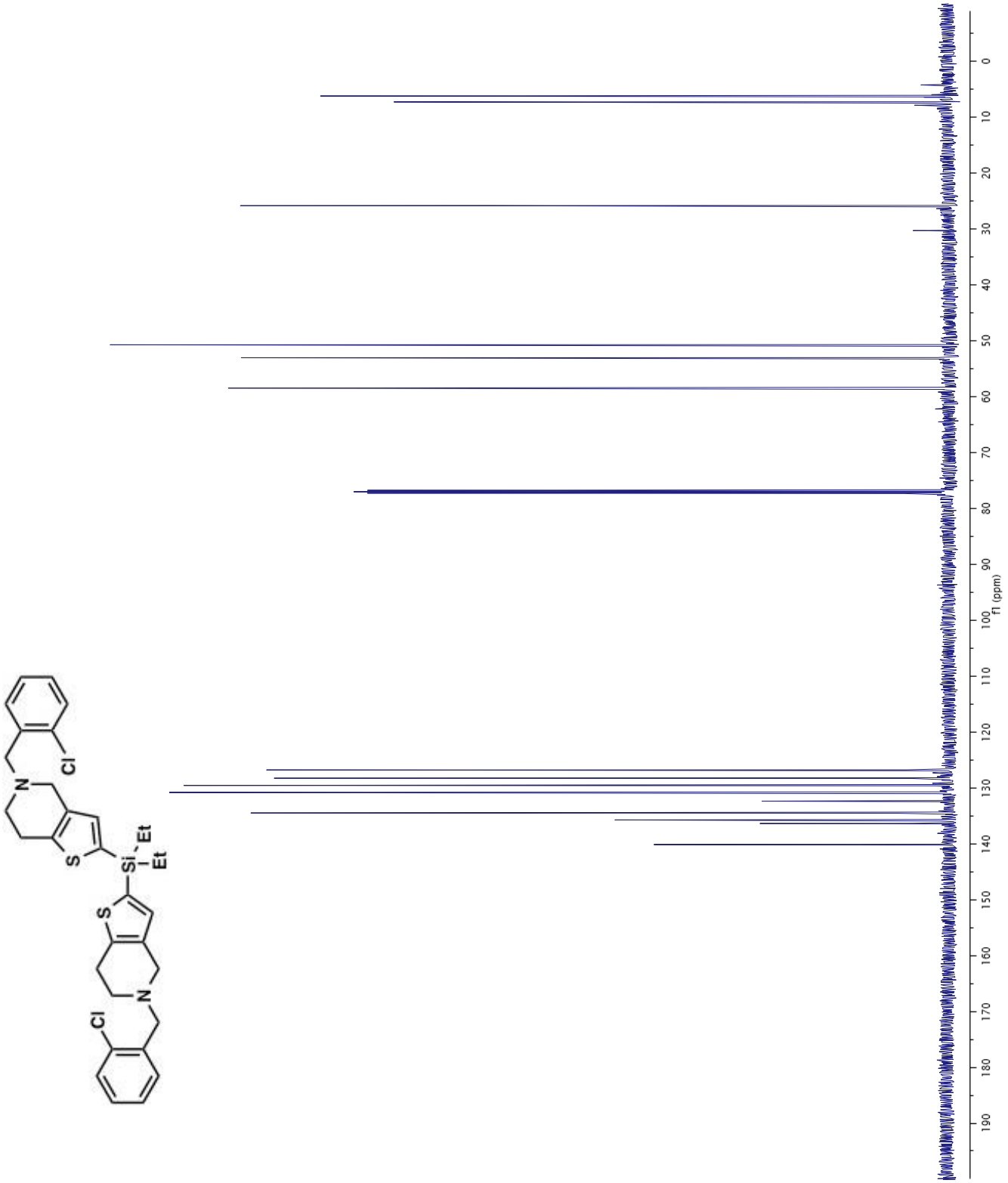
^{1}H NMR (500 MHz, $CDCl_3$) of compound **27b**



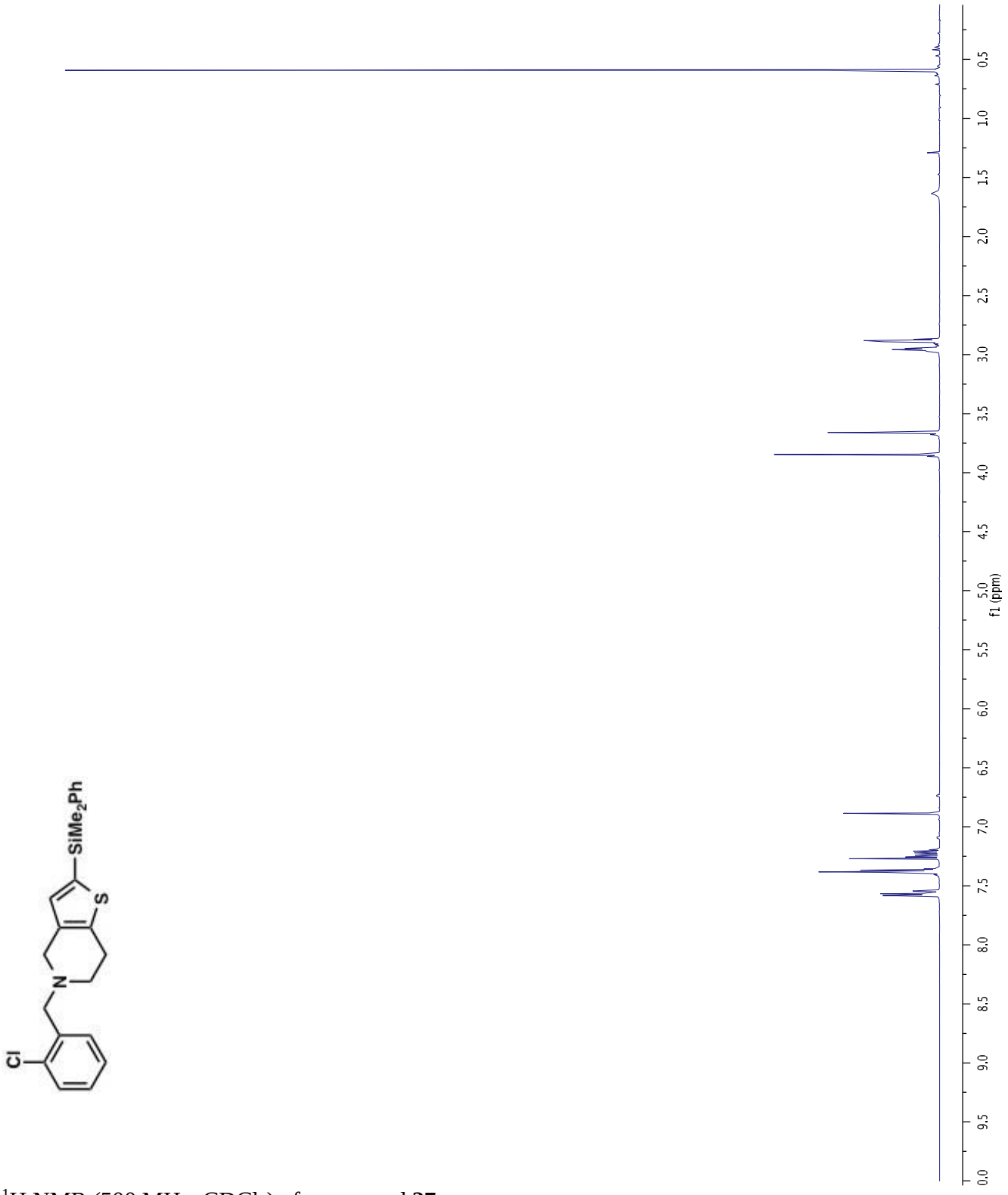
^{13}C NMR (125 MHz, $CDCl_3$) of compound **27b**



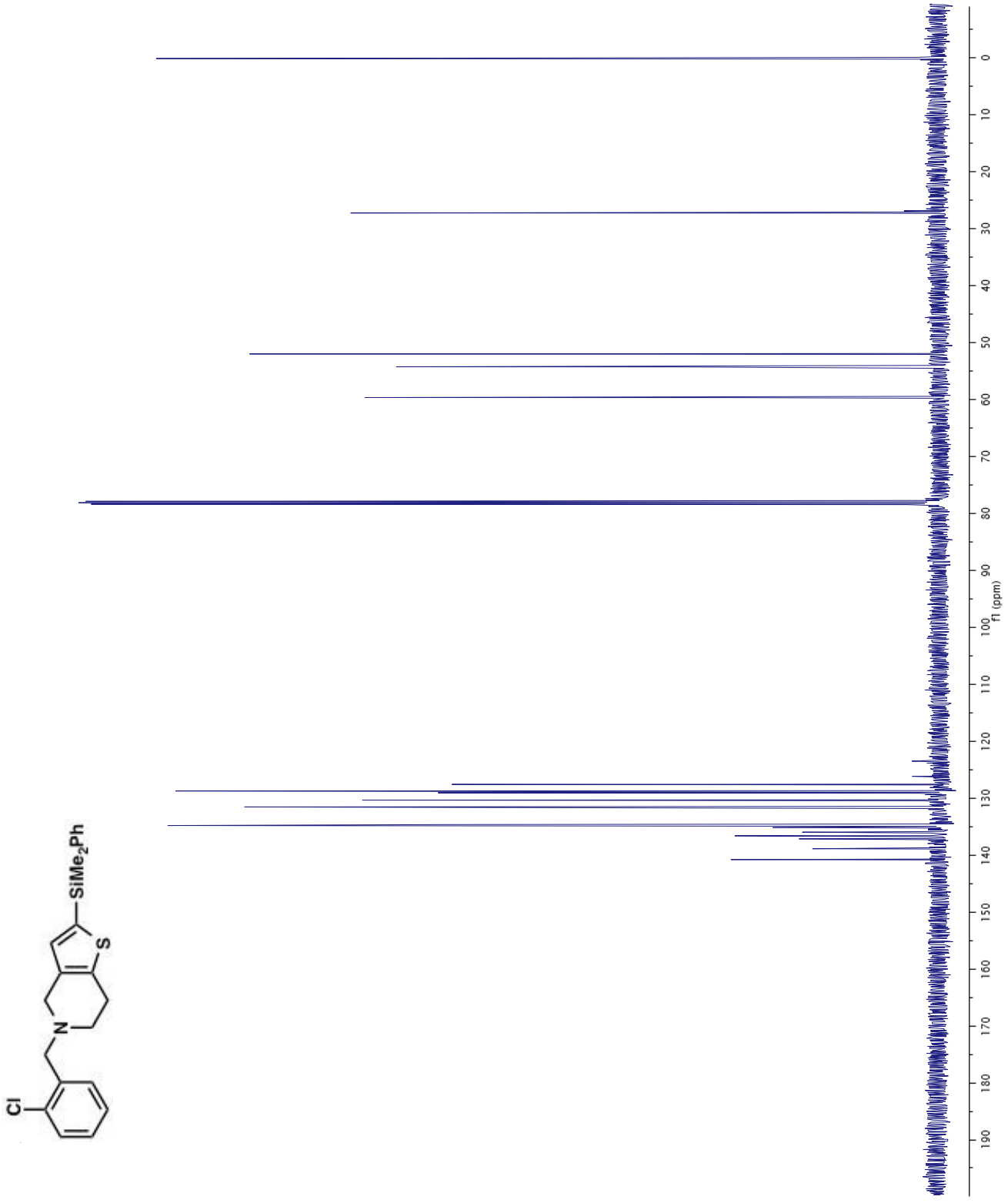
^{1}H NMR (500 MHz, $CDCl_3$) of compound **27b_dim**



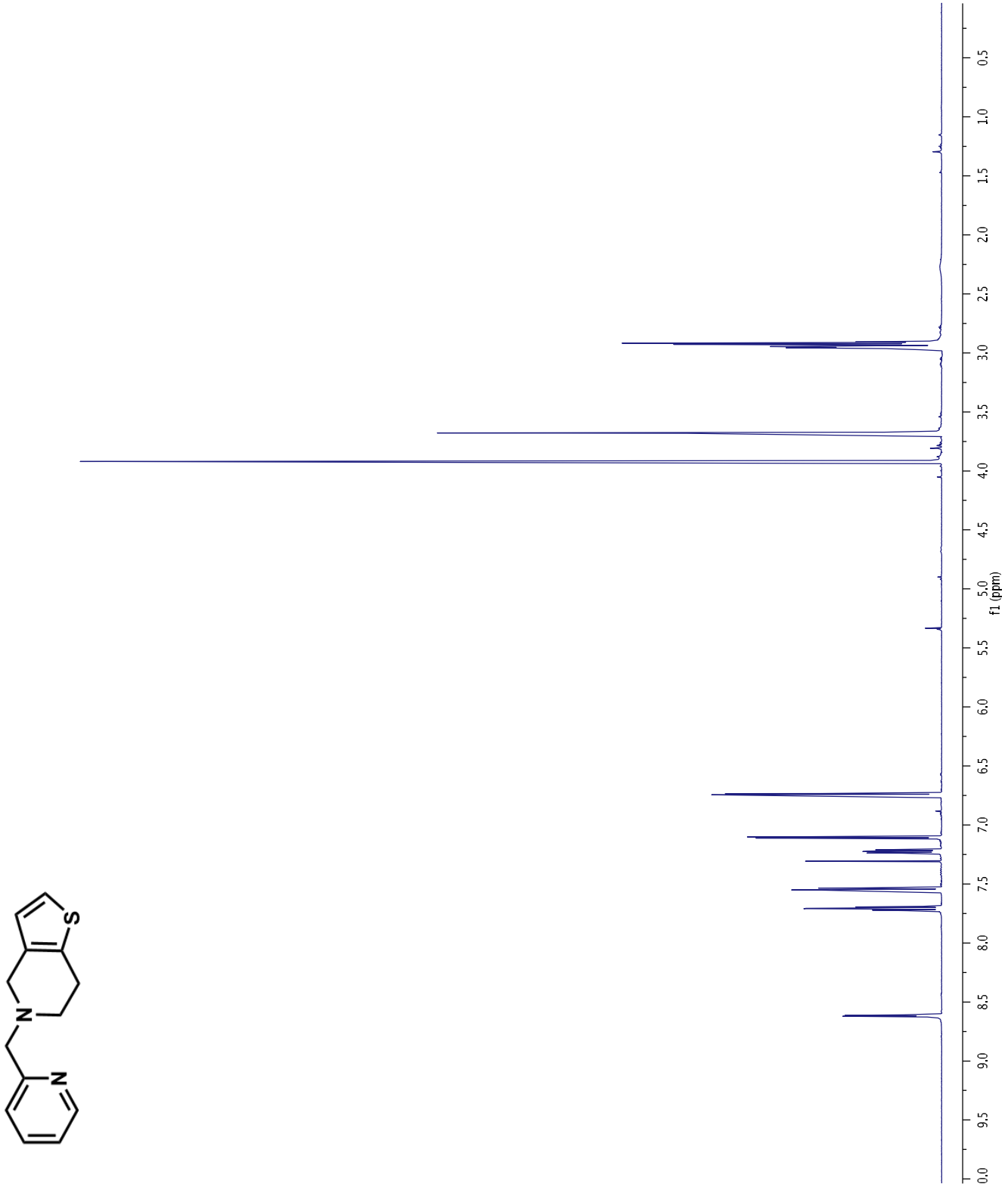
^{13}C NMR (125 MHz, $CDCl_3$) of compound **27b_dim**



^{1}H NMR (500 MHz, $CDCl_3$) of compound **27c**



^{13}C NMR (125 MHz, $CDCl_3$) of compound **27c**



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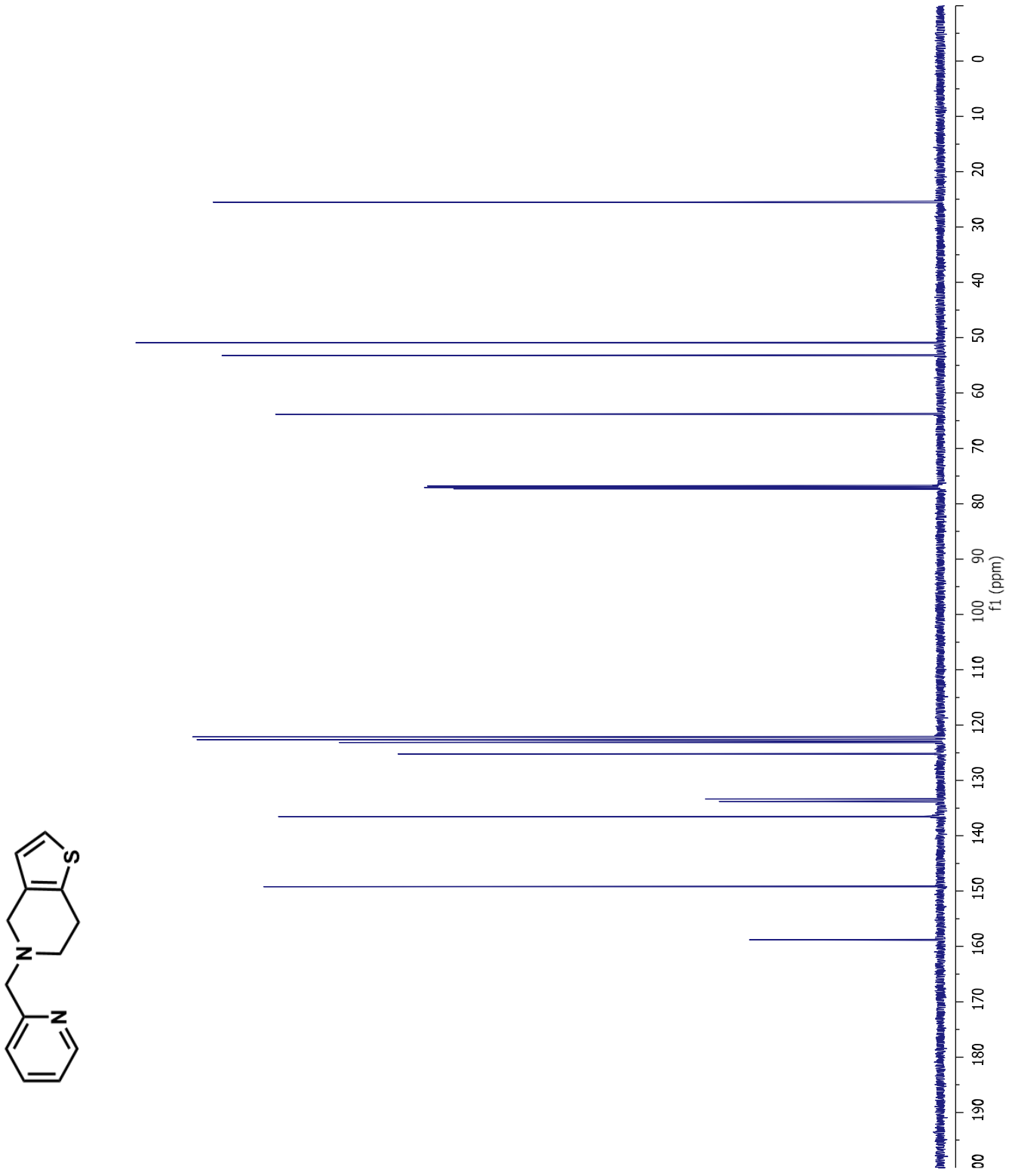

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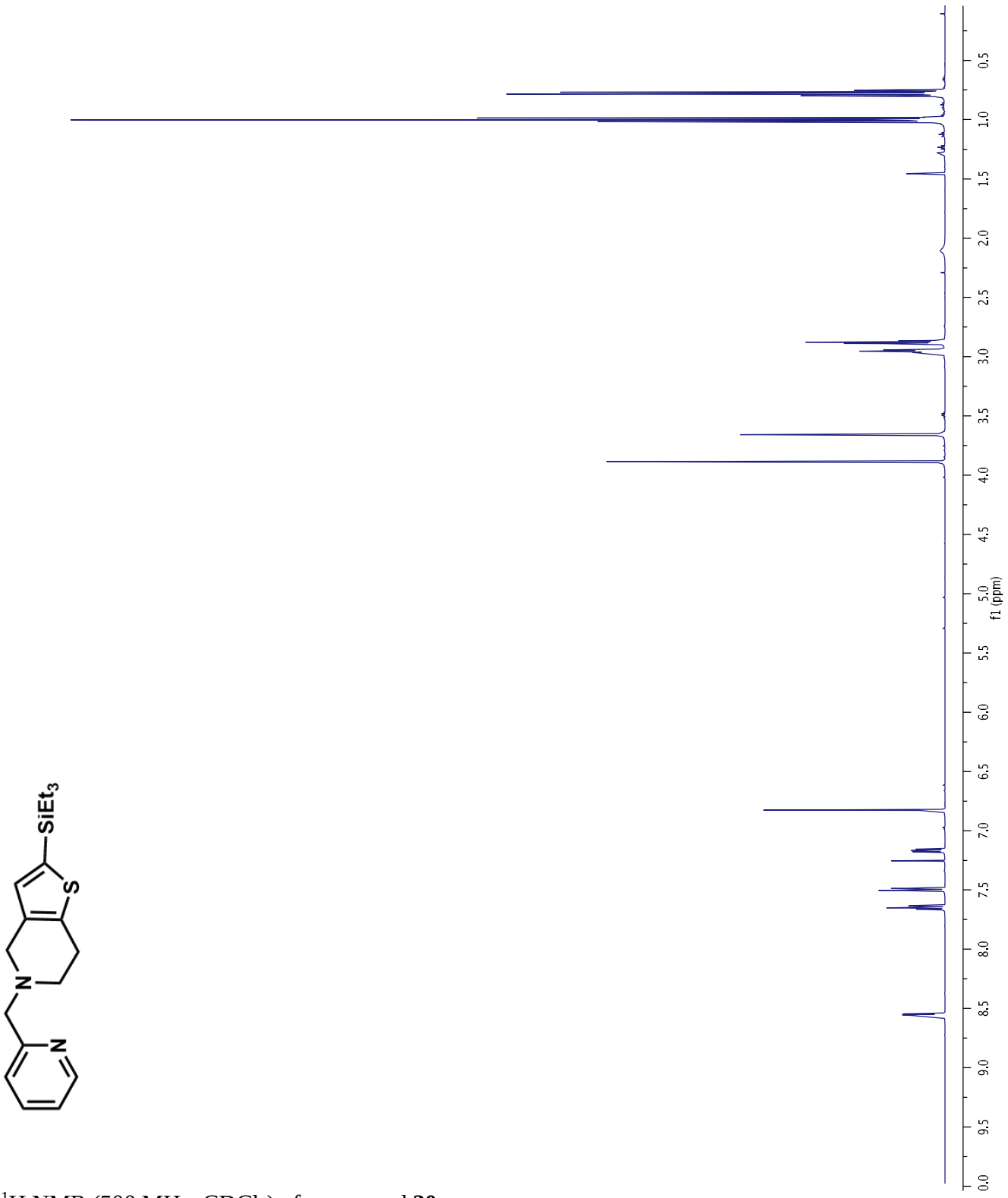

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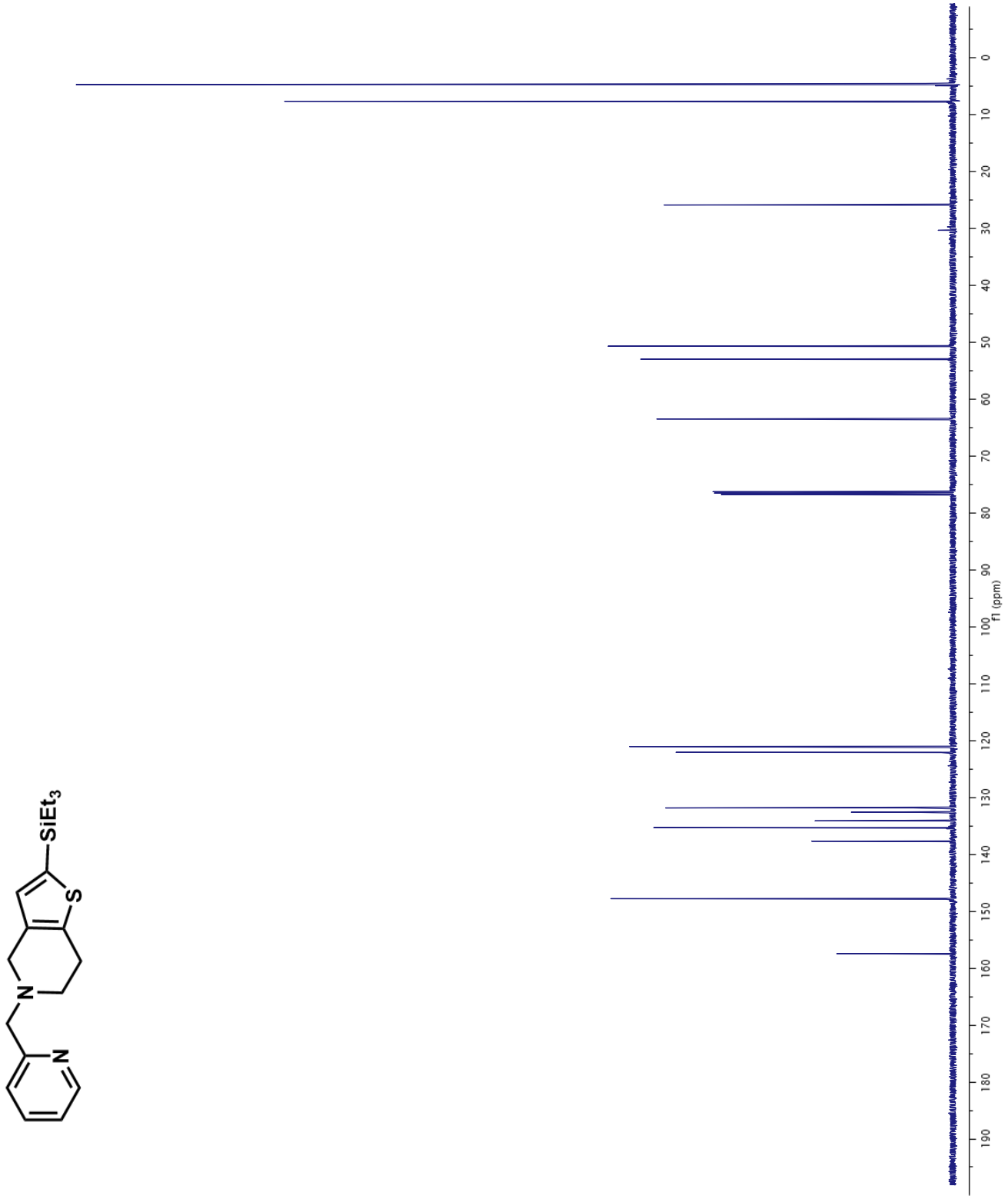

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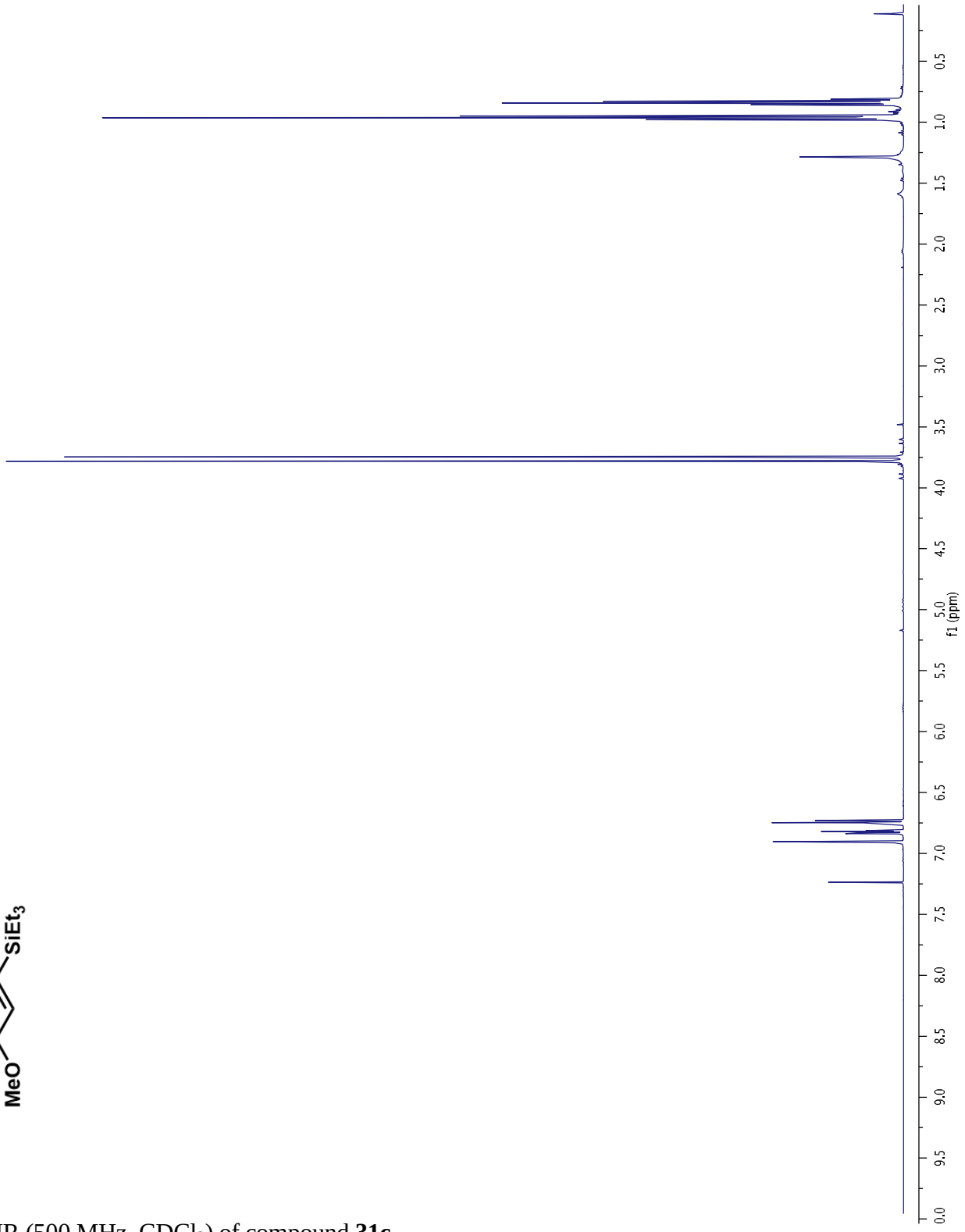

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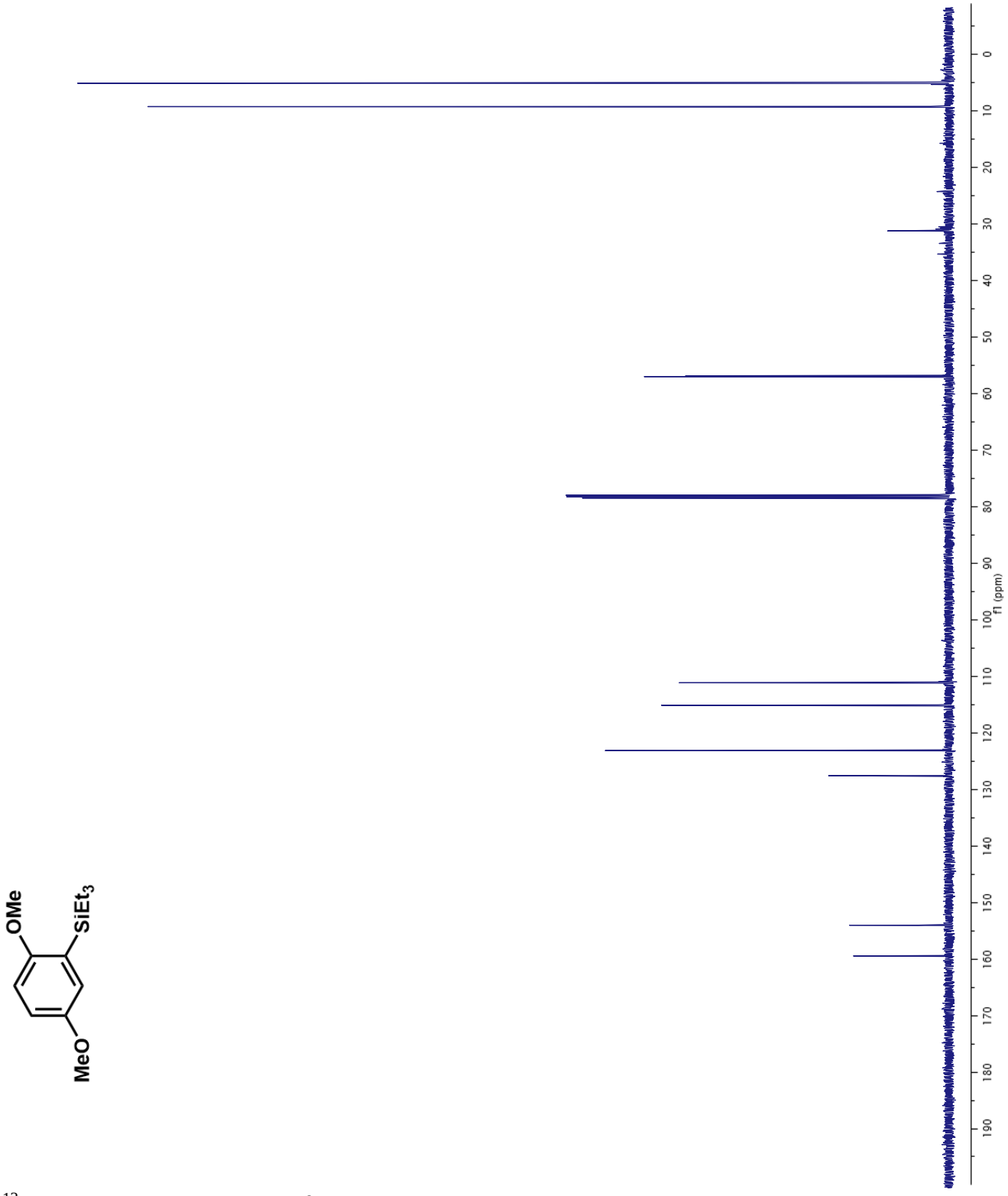
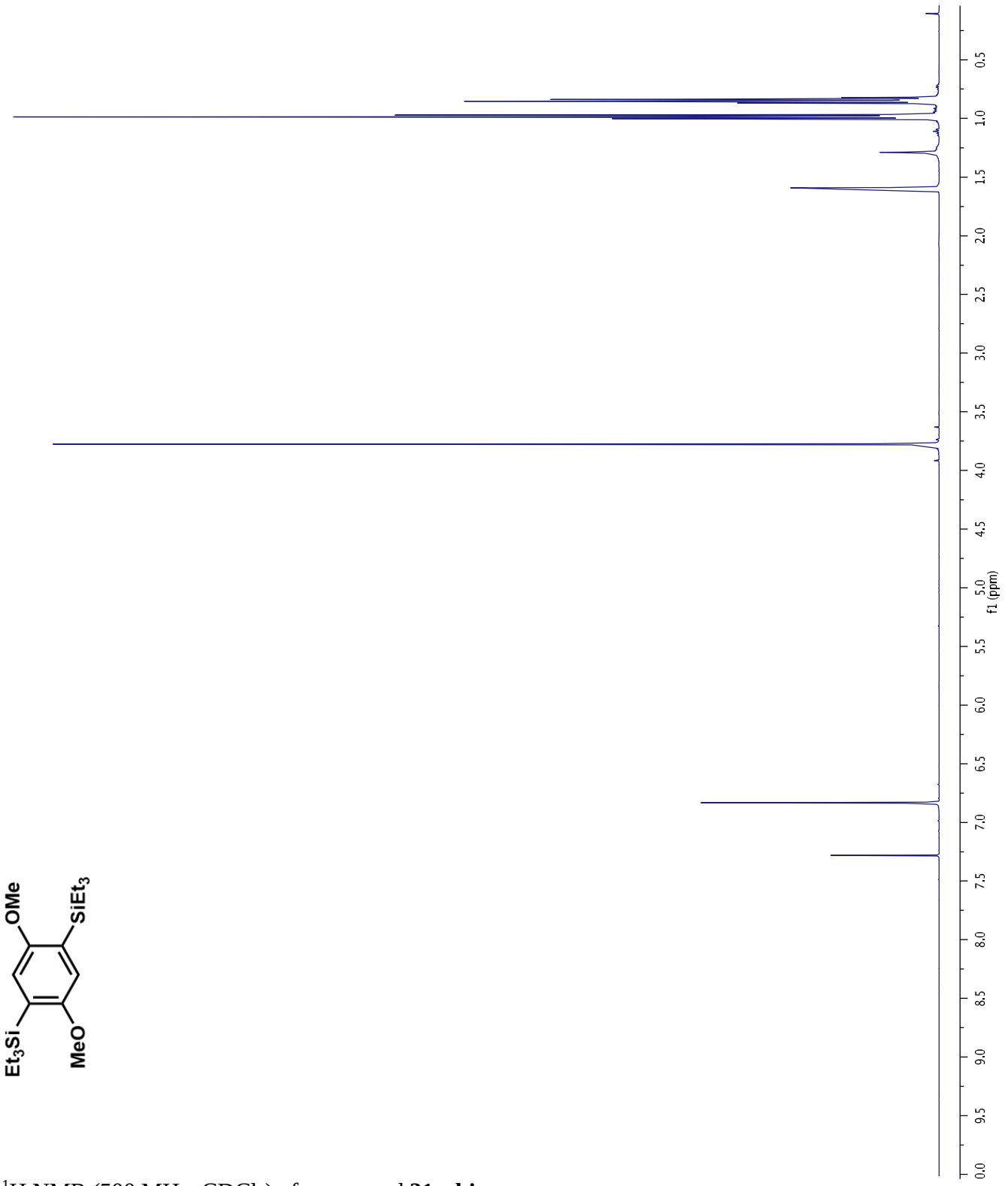
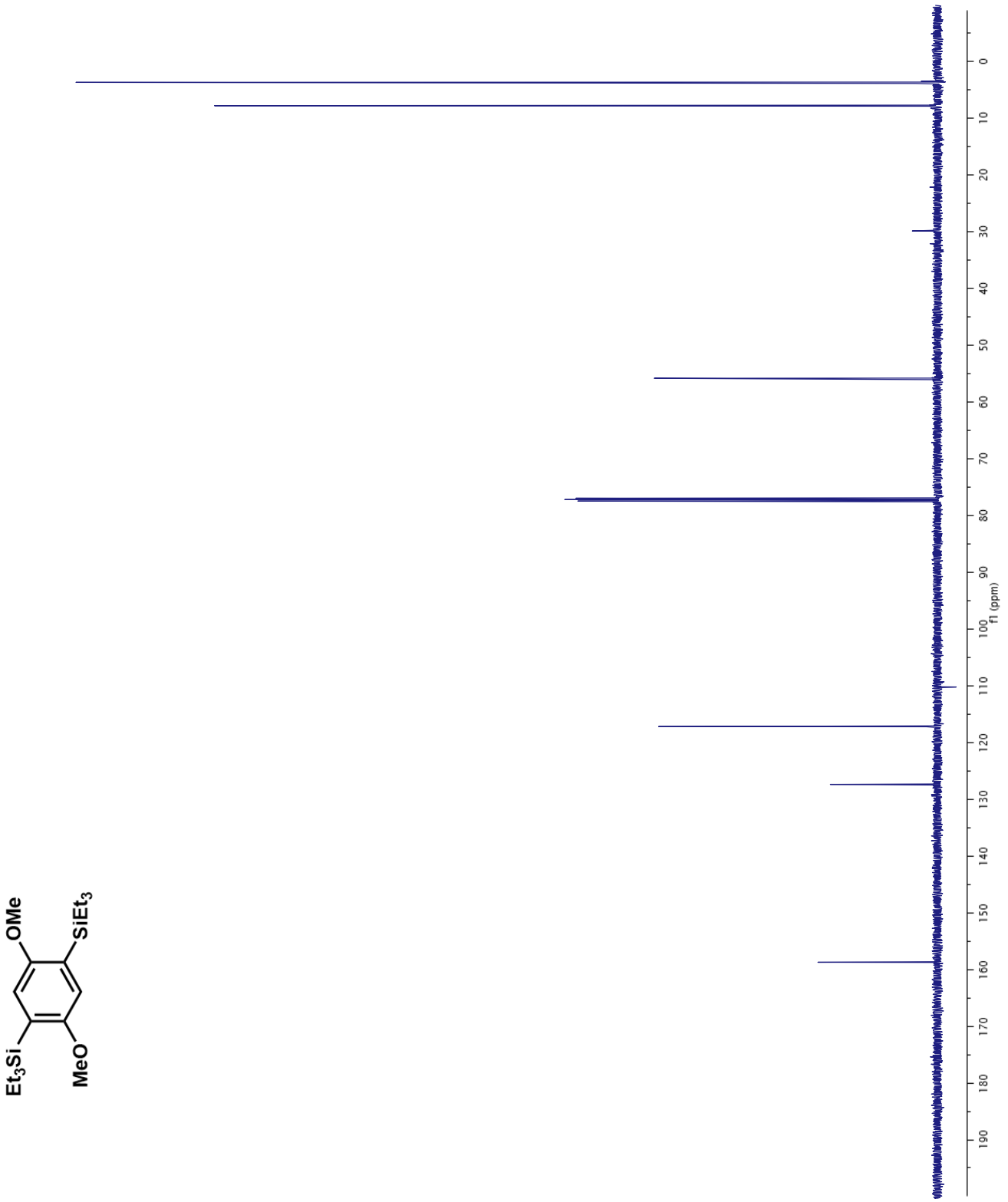


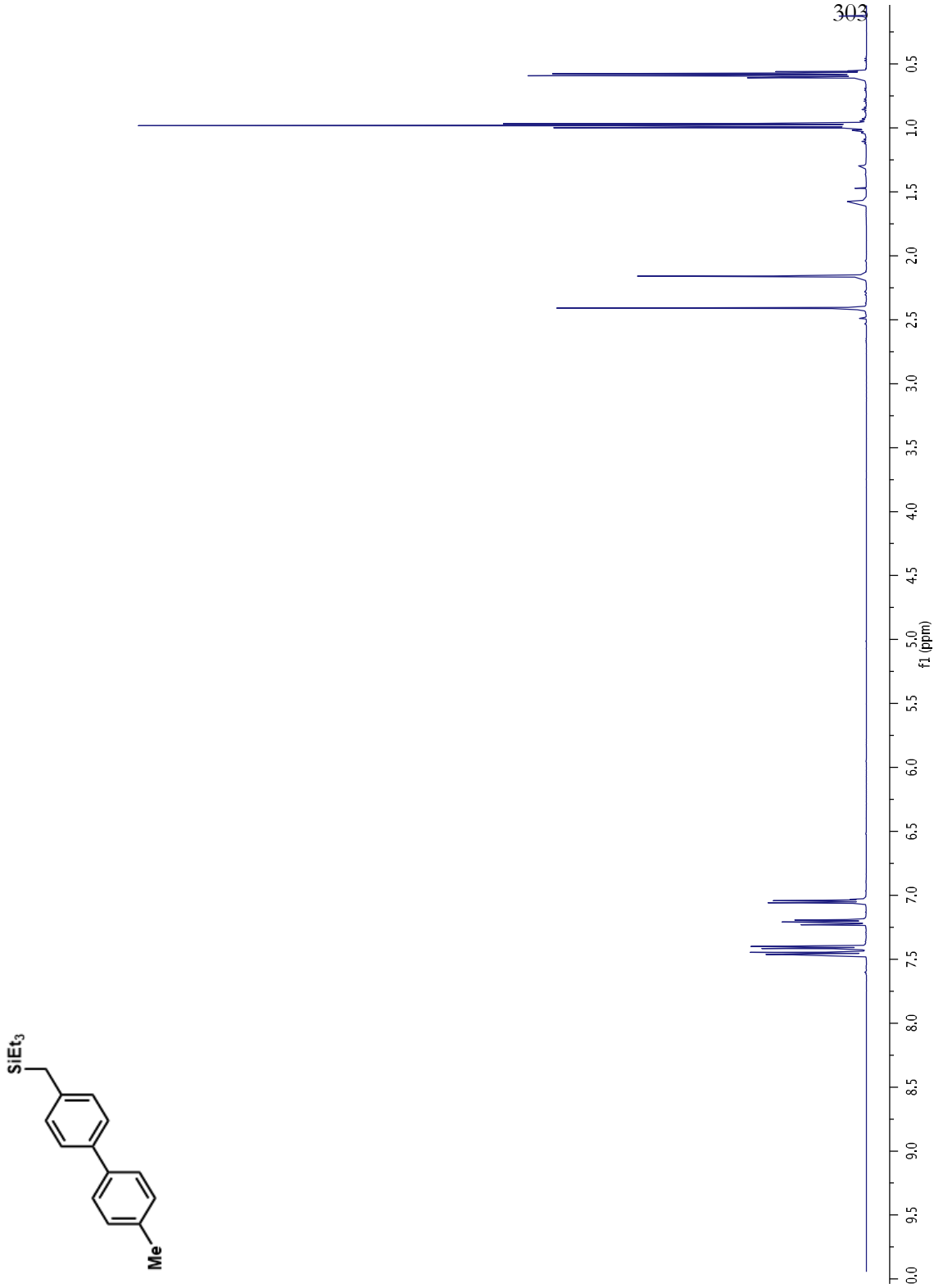
^{13}C NMR (125 MHz, $CDCl_3$) of compound **31c**



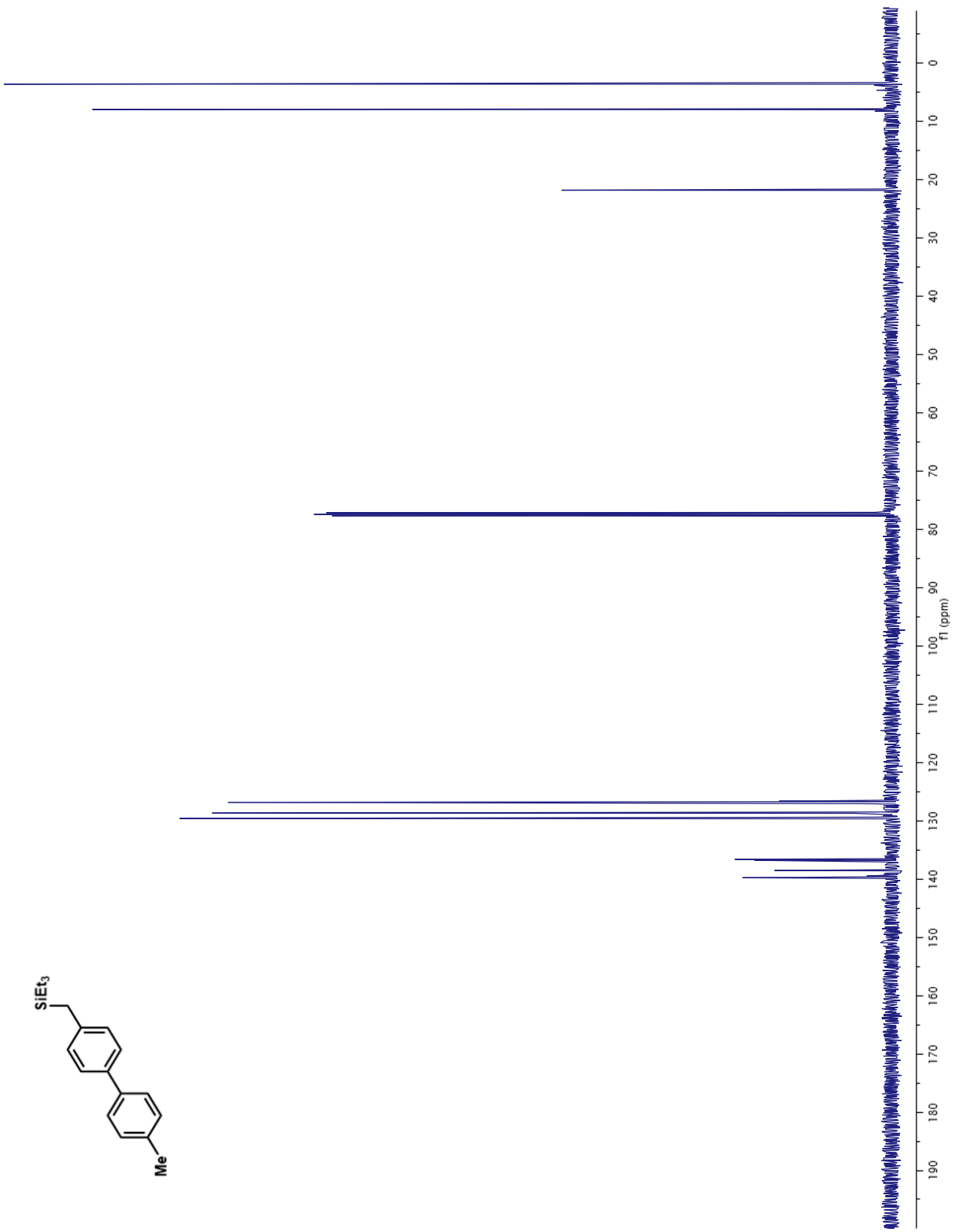
^{1}H NMR (500 MHz, $CDCl_3$) of compound **31c_bis**



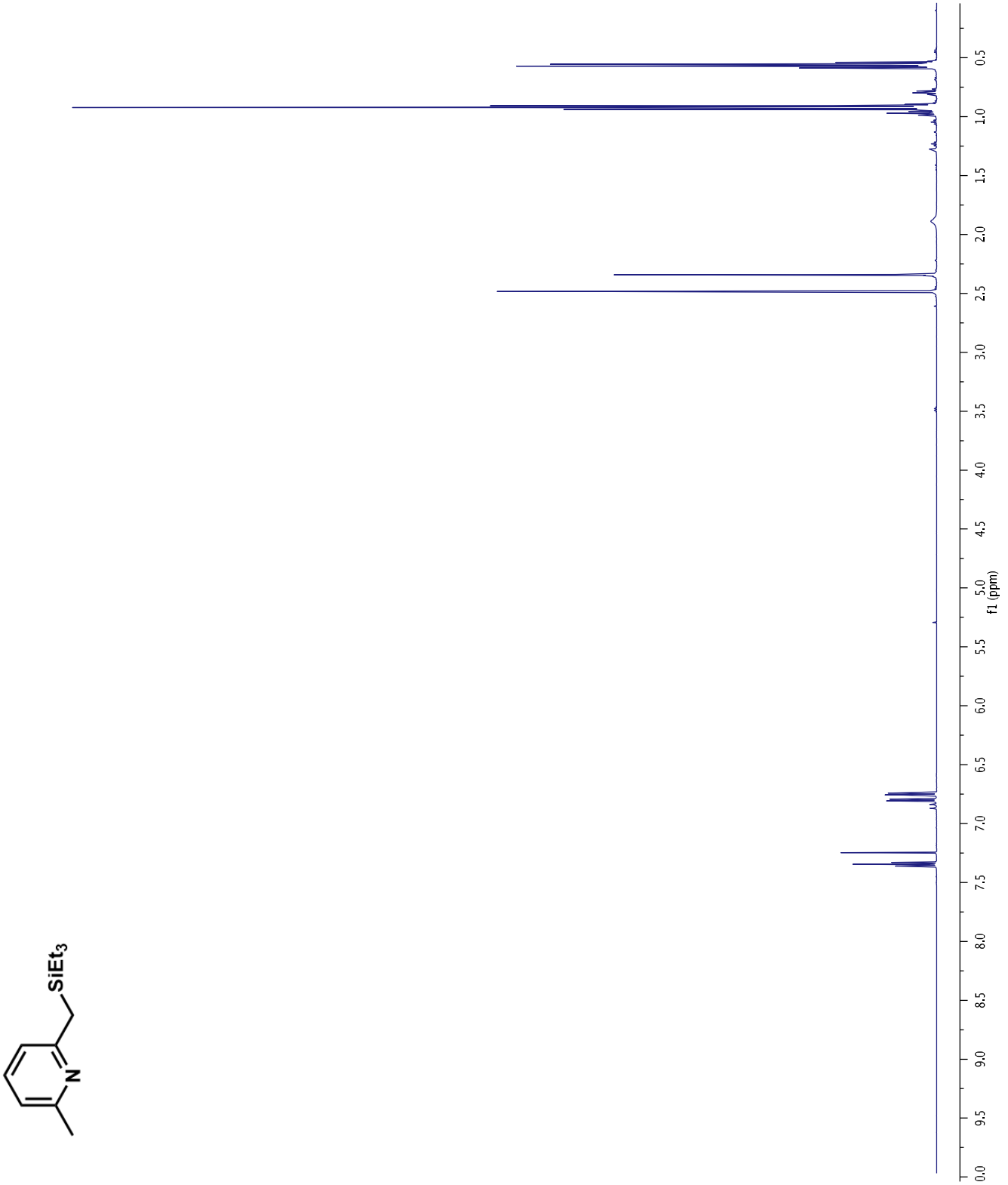
^{13}C NMR (125 MHz, $CDCl_3$) of compound **31c_bis**



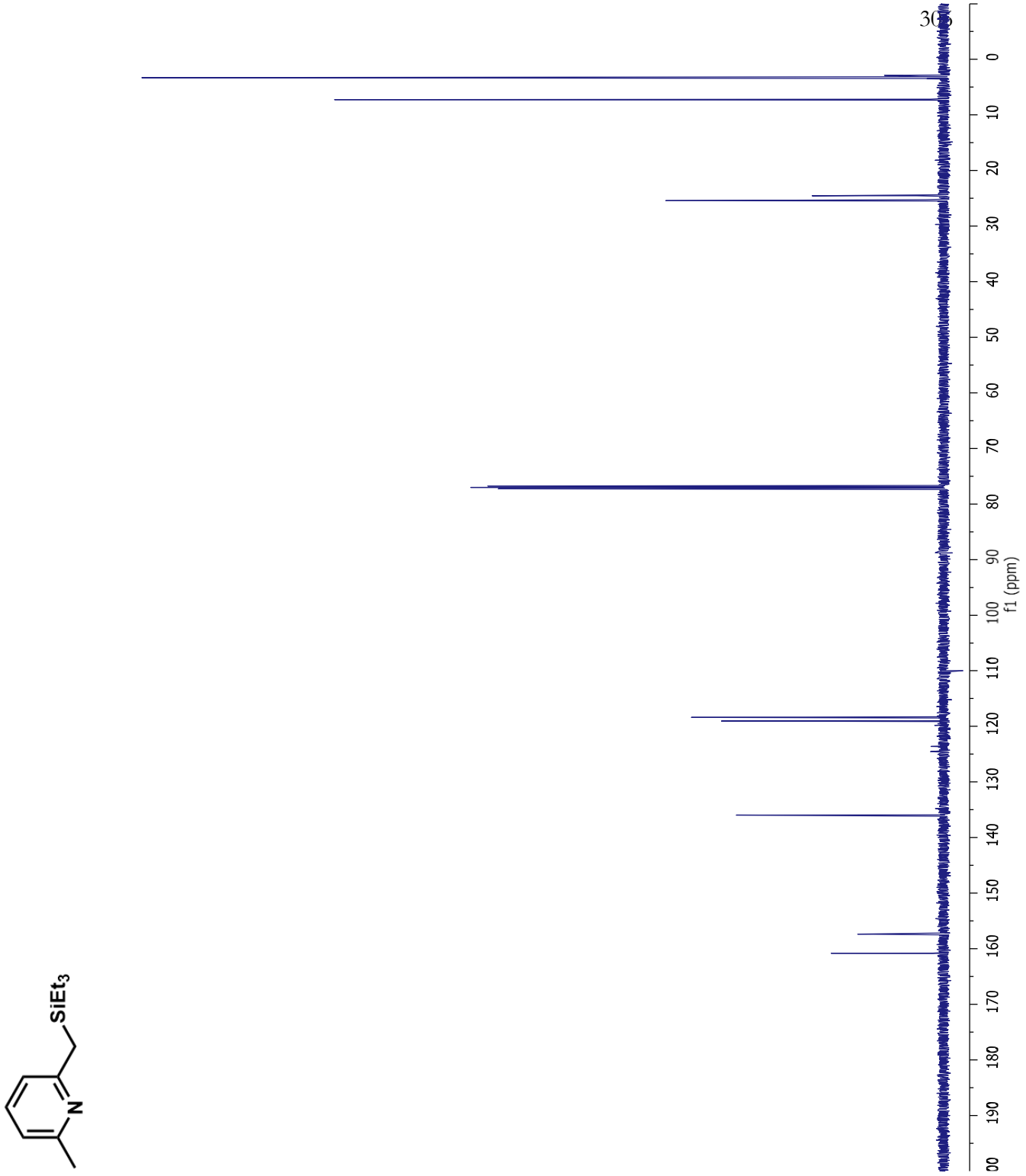
^{1}H NMR (500 MHz, $CDCl_3$) of compound **32b**



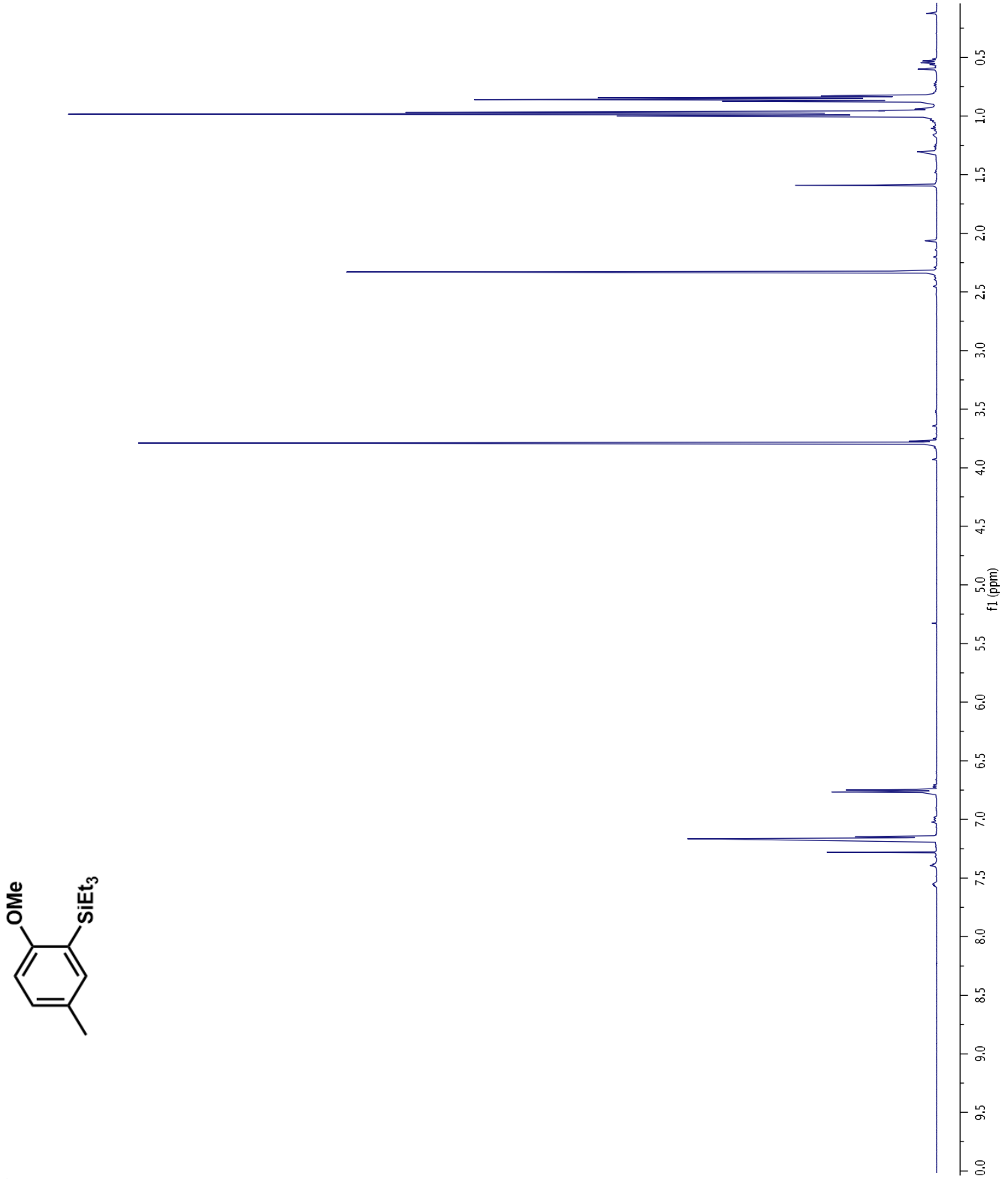
^{13}C NMR (125 MHz, $CDCl_3$) of compound **32b**



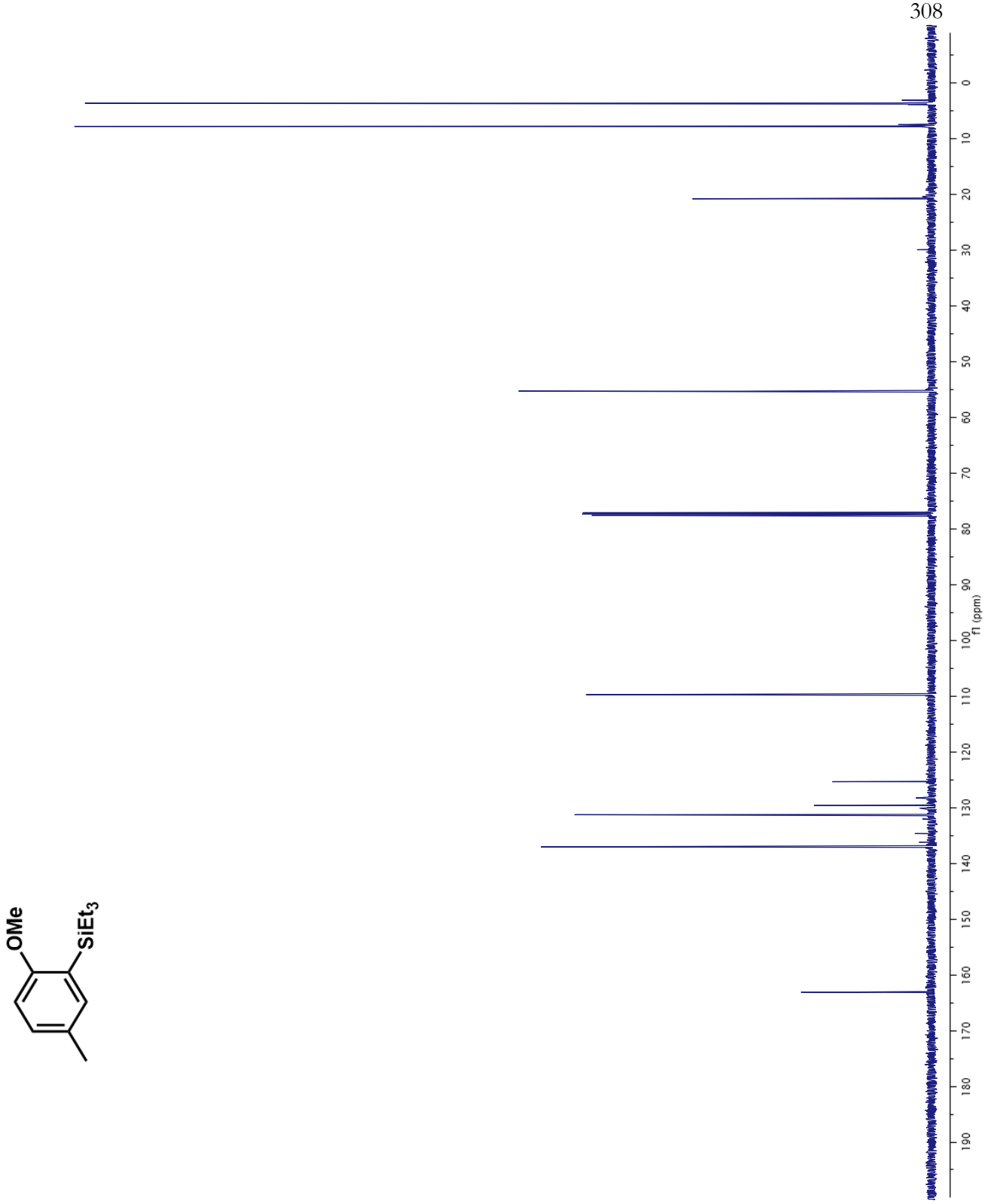
^{1}H NMR (500 MHz, $CDCl_3$) of compound **32d**



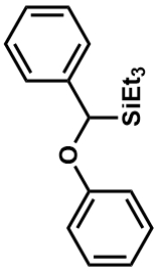
^{13}C NMR (125 MHz, $CDCl_3$) of compound **32d**

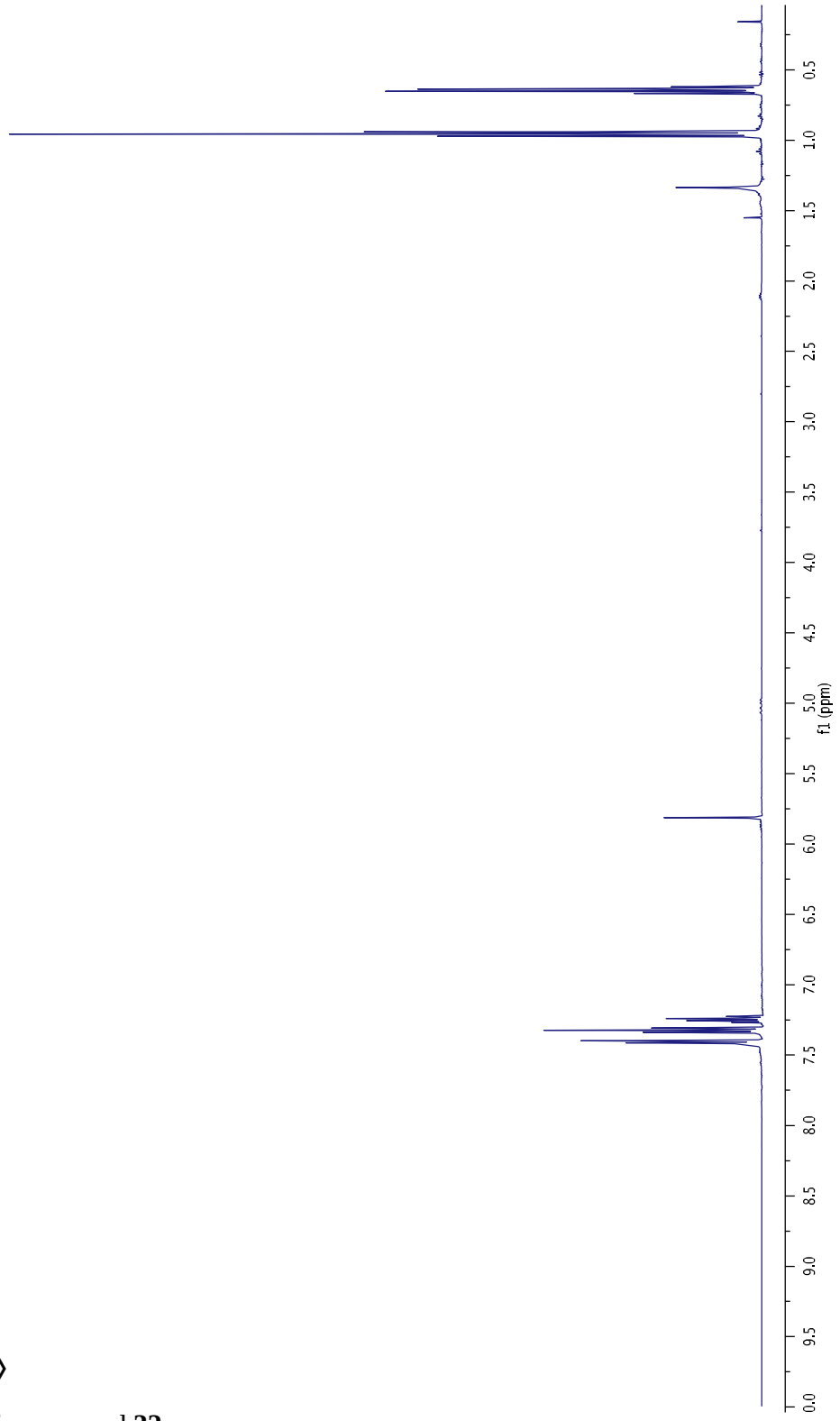


^{1}H NMR (500 MHz, $CDCl_3$) of compound **31d**

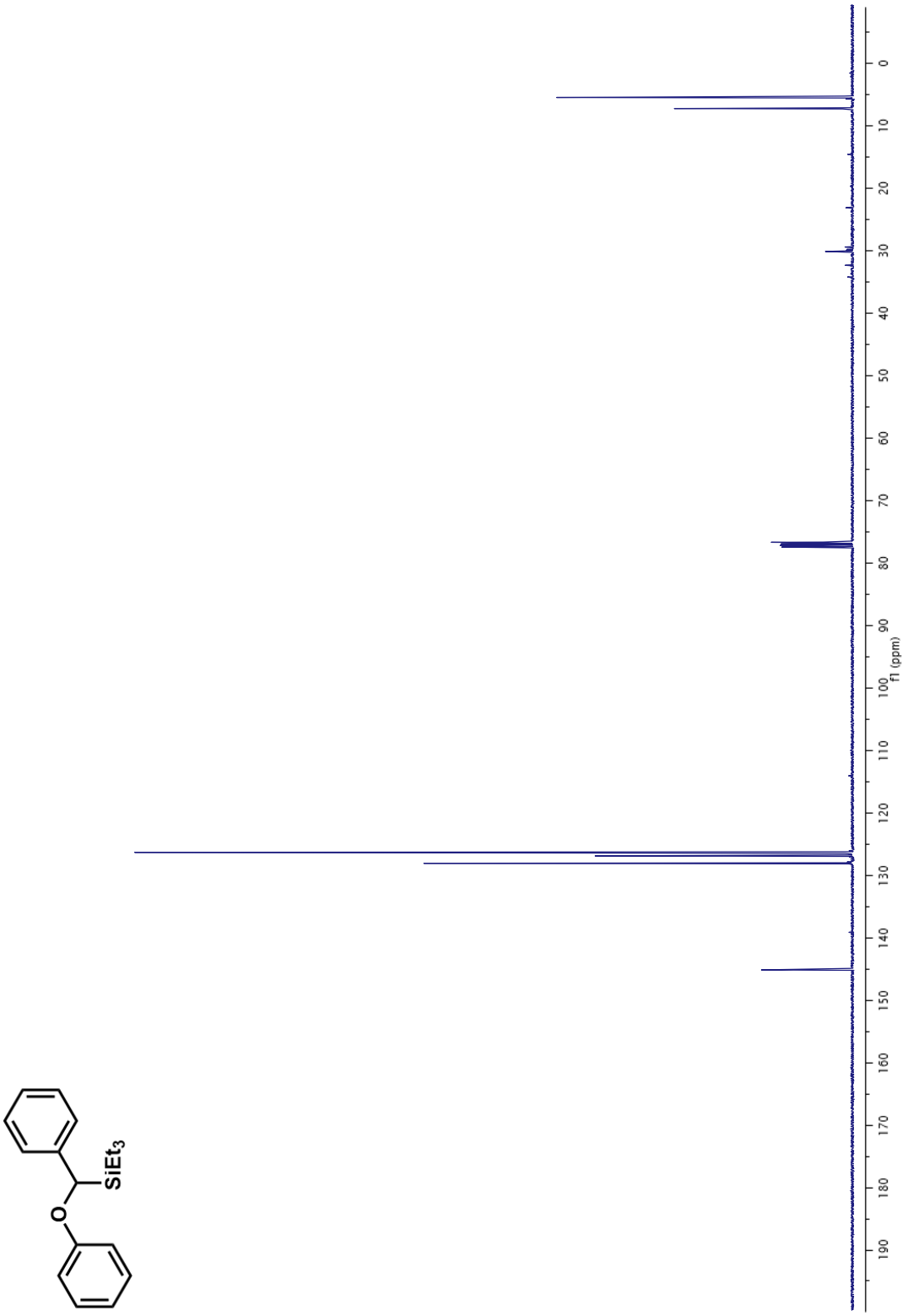


^{13}C NMR (125 MHz, $CDCl_3$) of compound **31d**





^{1}H NMR (500 MHz, $CDCl_3$) of compound **32c**



^{13}C NMR (125 MHz, $CDCl_3$) of compound **32c**

Acknowledgements.

I am again here grateful to Dr. Alexey Fedorov for his seminal work on the C–O bond cleavage reaction and the use of KO*t*-Bu and hydrosilanes toward this aim, which inspired me to look in greater detail at the use of alkali metal species in chemical reactions. This in turn led me to observe the hydrodesulfurization (HDS) chemistry (Chapter 1) as well as the cross-dehydrogenative silylation (the focus of this chapter). I would like to here express how proud and thankful I am of Kerry Betz, who joined this project as a sophomore and made very valuable contributions. Her excellent work on this project with me led her to become the recipient of two prestigious Caltech awards: the 2015 Library Friends' Thesis Prize and the George W. and Bernice E. Green Memorial Award. I am grateful to Dr. Wen-Bo "Boger" Liu and to Prof. Brian Stoltz for working with me in the expansion of the initial KO*t*-Bu-catalyzed C–H silylation concept and again contributing substantially to many aspects of the chemistry. I would like to thank Dr. Scott Virgil for his assistance with analytical equipment, especially for use of the glovebox and analytical machinery in the Caltech Center for Catalysis and Chemical Synthesis (Caltech 3CS) as well as for invaluable discussion. I am also grateful to Drs. Yong Liang and Yun-Fang Yang and Prof. Ken Houk at UCLA for their computational mechanistic insights. I wish to thank Dr. Monon Banerjee and Prof. Richard N. Zare (Stanford) for conducting investigations into the mechanism of the C–H silylation by DESI-MS. I would like to thank Dr. Nasri Nesnas (Florida Tech) for his work on mechanistic aspects of this reaction both currently at Florida Tech and during his two sabbaticals at Caltech with Prof. Brian Stoltz.

Chapter 3

ALKALI METAL HYDROXIDE–CATALYZED CROSS-DEHYDROGENATIVE C(*sp*)–H BOND SILYLATION

Abstract.

We have found that NaOH and KOH are excellent catalysts for mild and convenient cross-dehydrogenative C(*sp*)–H bond silylation with hydrosilanes. This alkali metal hydroxide–catalyzed cross-dehydrogenative method avoids the limitations of competing strategies and successfully couples alkynes and hydrosilanes on multi-gram scale, with high yield and chemoselectivity, and with excellent scope. The method is highly chemo- and regioselective, gives access to organosilanes previously inaccessible by catalysis, and enables a wealth of new alkyne-based chemistries. Interestingly, KO*t*-Bu, which has been essentially necessary to enable our earlier chemistries (Chapters 1 and 2), generally does not promote this C(*sp*)–H bond silylation.

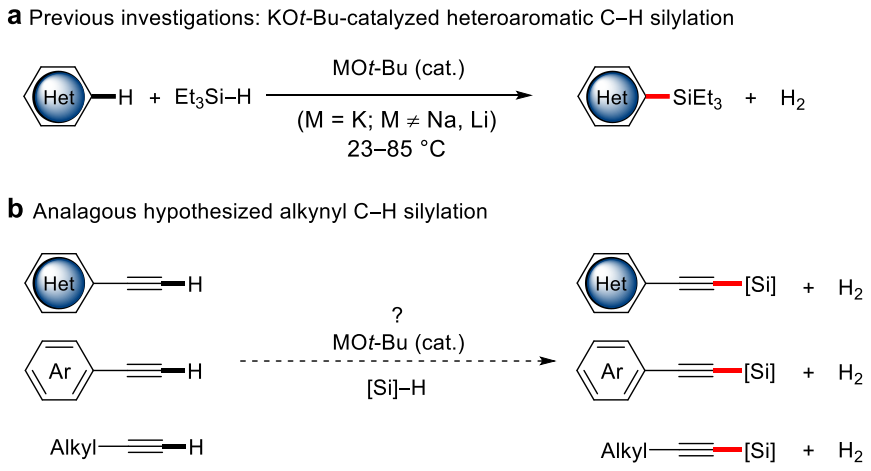
Introduction.

Building on our results in aromatic and heteroaromatic C−H bond silylation, and desiring to extend our alkali metal catalysis concept, we became interested in whether KO*t*-Bu could promote the silylation of C−H bond classes other than those of (hetero)arenes. Simultaneously, this would allow us to investigate the effect of C−H bond acidity and other factors on the reactivity. We thus became interested in exploring the direct, cross-dehydrogenative silylation of terminal alkynes at the C(*sp*)−H bond. Despite the importance and prevalence of alkynylsilanes and despite the myriad of catalytic and stoichiometric methods which have been developed for their synthesis, the interception of acetylides with chlorosilanes remains the most reliable and broadly applied method. Given the mild and convenient conditions of our KO*t*-Bu catalyzed process, we saw an opportunity to potentially provide a valuable new approach to making C(*sp*)−Si bonds.

Alkynylsilanes: synthesis and utility.

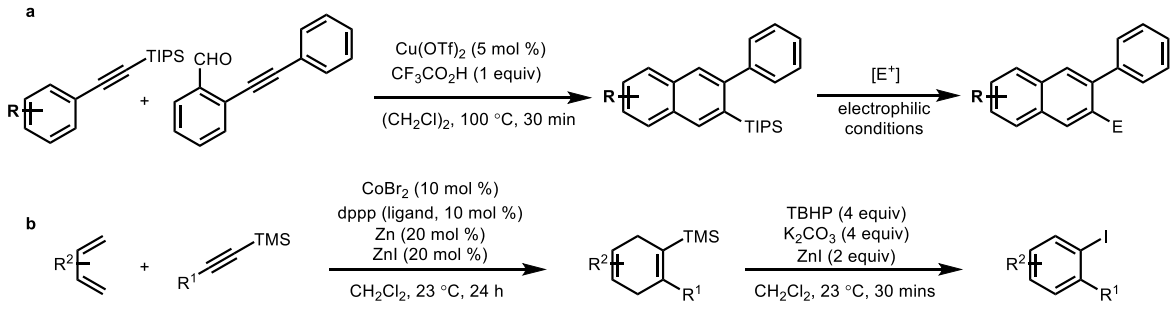
The catalytic transformation of C–H bonds into a variety of useful functional groups has revolutionized chemical synthesis.[98,99] However, the necessity of precious metal catalysts or stoichiometric organometallic species for these transformations remain fundamental and longstanding limitations.[100,101] With the aim of developing a suite of new methods for powerful, sustainable, and cost-effective chemical synthesis, I had been engaged in invstigating and applying Earth-abundant alkali metal salts for catalytic cross-dehydrogenative C–H bond functionalization reactions and bond reduction processes.[102,103,104] Up to this point, I had found that mixtures of hydrosilanes with KO*t*-Bu in the presence of aromatic heterocycles lead to either C−X bond reduction or C−H silylation depending on the conditions employed.[14,74,105] With respect to chemical synthesis applications, the discovery that KO*t*-Bu was a remarkably useful catalyst for the cross-dehydrognative silylation of aromatic heterocycles demonstrated the ability of oxygen-centered Lewis bases to activate hydrosilanes and C–H bonds in a mild and convenient fashion.[74,105]

Figure 3.1. Hypothesized KO*t*-Bu–catalyzed C–H silylation of terminal alkynes.



Building upon this concept, I sought to evaluate alkali metal salts as catalysts for other C–H bond functionalization reactions, thus aiming to broaden our initial developments as much as possible. I thus became interested in catalytic C–Si bond construction for the preparation of terminal alkynylsilanes and wondered wether the KO*t*-Bu catalysis could enable this transformation (**Figure 3.1**). These important building blocks are used in the construction of electronically- and topologically-relevant materials,[106] employed as substrates in metathesis reactions[107] and cycloadditions,[108] and used as precursors to heterocycles[109] and polycyclic aromatic frameworks.[110] Moreover, alkynylsilane nucleophiles and cross-coupling partners react under mild conditions[111,112] and therefore are commonly used as versatile intermediates en route to complex molecules.[113,114] Recently, terminal alkynes wherein the C(*sp*)–H bond has been replaced with a bulky di-*tert*-butylsilyl group have been proposed to be precursors to novel radiofluorinated positron emission tomography (i.e., [^{18}F]PET) probes with among the highest in vivo stability for biomedical imaging applications.[115] Implementation of our method for PET will be discussed in Chapter 5. With respect to organic synthesis, a number of clever methods have been developed employing alkynylsilanes as substrates; these are far too numerous to list – though instructive examples will be provided, as appropriate, throughout the chapter. However, to provide just one intriguing concept, alkynylsilanes have been used as partners in cycloaddition reactions,

Scheme 3.1. Examples of cyclization chemistries using alkynylsilanes.

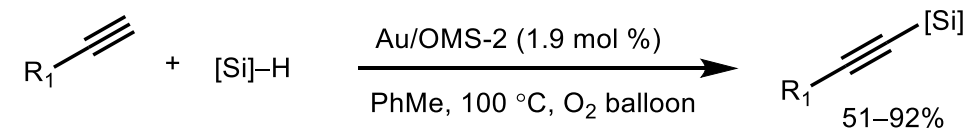


leading to functionalized aromatics with sometimes unusual substitution patterns (**Scheme 3.1**). For example, aryl alkynylsilanes with a bulky silyl group (i.e., TIPS) undergo a copper triflate–catalyzed cycloaddition with diarylalkynes to generate polycyclic aromatics with a remaining aryl C–Si bond available for downstream functionalization (**Scheme 3.1a**). Alternatively, simple alkynylsilanes undergo highly regioselective cobalt-catalyzed Diels–Alder reactions with substituted dienes to generate cyclic vinyl silanes. The reaction can be stopped at this stage, or the products can undergo oxidative aromatization leading to polysubstituted aryl iodides in one pot (**Scheme 3.1b**).

Strategies for the synthesis of alkynylsilanes have employed strong bases [58a,59,116,117] or have relied on stoichiometric[118,119,120] or catalytic transition metal species including Pt,[121] Zn,[122,123] Au,[124] and Ir,[125,126] and typically use various pre-activated organosilicon coupling partners such as [Si–Cl],[58a,59,119,120] [Si–I],[116,126] [Si–NR_2],[120] [Si–Si],[117] and [Si–OTf][123] at temperatures in excess of 80 °C in the majority of cases. An NHC/NaH-catalyzed C(*sp*)–H silylation protocol has also recently been disclosed; however, it necessitates the use of the expensive and sensitive Ruppert-Prakash reagent, CF_3SiMe_3, as the silicon source.[127] Inexpensive, and convenient hydrosilanes have been investigated for C(*sp*)–H silylation;[117,118,121,122,124,125,126] however, these particular silicon sources have introduced new challenges: the requisite in situ Si–H bond activation has thus far necessitated additional exogenous bases,[122,124,127] sacrificial hydrogen acceptors[126] or oxidants,[121,125] and elevated temperatures (i.e., 80–120 °C).[117,118,124,125] Moreover, undesired hydrosilylation of the alkyne can be competitive,[121,124,126] further complicating catalyst and reaction design. These factors have led to significant limitations in scope and practical utility and in many cases only a handful of simple, unfunctionalized substrates are demonstrated.[116,117,121,125] Moreover, most catalytic systems developed to date have relied on transition-metal complexes containing highly

electrophilic metal centers, which appears to have limited the alkyne scope to substrates lacking Lewis-basic functionalities. Consequently, substrates containing nitrogen heterocycles and aliphatic amines are notably absent in all prior reports of catalytic silylation of terminal alkynes with hydrosilanes. For example, the most recent catalytic method involves the use of gold supported on a molecular sieve catalyst to drive the dehydrocoupling of alkynes and hydrosilanes with good yield.[124] In general, moderate scope of alkyne and silane is demonstrated; however, this Au-catalyzed method is one of the only catalytic methods known that tolerates the useful yet capricious $(OEt)_3SiH$ (**Scheme 3.2**). Nevertheless, the chemistry proceeds under rather elevated temperatures (i.e., 100 ˚C) and requires the use of molecular oxygen as the stoichiometric oxidant. Silylation of complex substrates is not demonstrated.

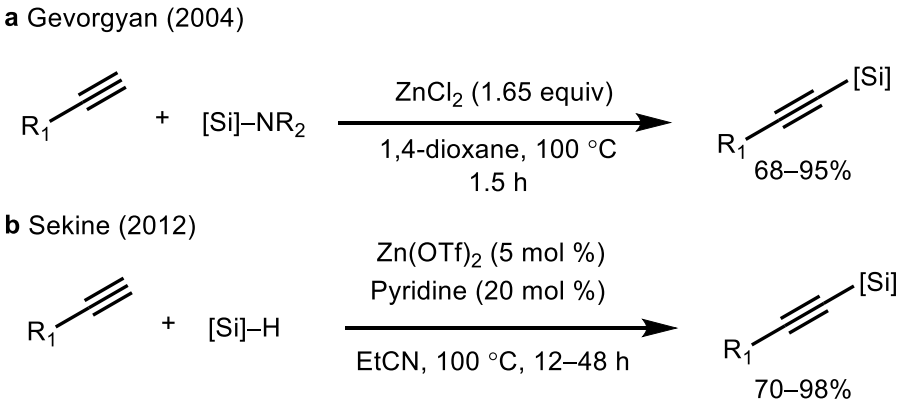
Scheme 3.2. Yamaguchi's Au-catalyzed C–H silylation of terminal alkynes.



Methods employing abundant transition metals have also been reported, primarily employing zinc (II) species. In particular, Gevorgyan observed that with stoichiometric $ZnCl_2$ alone, terminal alkynes efficiently couple with silylamines to provide the electrophilic silylation product in good yields (**Scheme 3.3a**).[120] This protocol was shown to be scalable to 100 mmol of starting alkyne and enjoys a relatively broad scope of alkyne, though has important limitations in the scope of hydrosilane. Nearly a decade later, Sekine found that a catalytic Zn (II) salt, when combined with a Lewis base such as pyridine, promotes the catalytic electrophilic silylation of terminal alkynes

with good scope of both silane and alkyne (**Scheme 3.3b**).[123] Complex substrates, however, are not demonstrated and the chemistry requires elevated temperatures to operate. Substrates containing Lewis-basic nitrogens such as aliphatic amines, heterocycles, and others are not reported, presumably because these moieties deactivate the highly electrophilic catalyst.

Scheme 3.3. Electrophilic silylation: Zn-mediated silylation of terminal alkynes using silylamines and Zn-catalyzed dehydrocoupling of alkynes and hydrosilanes.



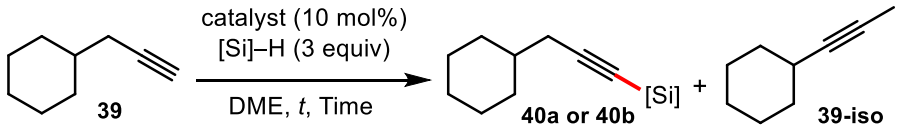
These methods, though useful in their own rights, demonstrate well the limitations in the methods that currently exist for the synthesis of alkynylsilanes (as was previously mentioned): the incompatibility of transition metal catalysts with Lewis basic substrates (due to the electrophilic nature of the reaction), the demanding conditions required, the relatively limited silane scope, all of which results in limited utility. Therefore, despite the increased acidity of C(*sp*)–H bonds compared to other C–H bond classes, a mild and general catalytic method for cross-dehydrogenative C(*sp*)–Si bond formation remains elusive.

Alkali metal salt−catalyzed cross-dehydrogenative C(*sp*)−H silylation.

Discovery and optimization

We chose to begin our investigations with with the silylation of simple and unbiased alkyne-containing hydrocarbon **39** using Et_3SiH under our previously reported conditions for the KO*t*-Bu-catalyzed C(sp^2)–H silylation of heteroarenes[14,74] and gratifyingly observed alkynylsilane **40a** in good yield, though along with 9% of undesired alkyne migration product **39-iso** (**Table 3.1**, entry 1). It is worth mentioning at this point that although coincidentally successful for the silylation of **39**, KO*t*-Bu would prove to be a surprisingly *poor* catalyst for the desired alkyne silylation reaction in general; this unexpected phenomenon will be discussed later.

Table 3.1. Discovery of alkali metal hydroxides as C(*sp*)–H functionalization catalysts.[a]



Entry	Catalyst	[Si]–H	*t* (°C)	Time (h)	Yield 40	Yield 39-iso
1	KO*t*-Bu	Et_3SiH	85	24	**40a (89%)**	**9%**
2	NaO*t*-Bu	Et_3SiH	85	24	**40a (46%)**	**52%**
3	LiO*t*-Bu	Et_3SiH	85	24	**40a (<1%)**	–
4	DABCO	Et_3SiH	85	48	–	–
5	Pyridine	Et_3SiH	85	48	**40a (1%)**	–
6	Et_3N	Et_3SiH	85	48	**40a (4%)**	–
7	KOH	Et_3SiH	85	24	**40a (95%)**	**3%**
8	KOH	$PhMe_2Si–H$	25	48	**40b (89%)**	–
9	NaOH	$PhMe_2Si–H$	25	48	**40b (93%)**	–
10	LiOH	$PhMe_2Si–H$	25	48	–	–

[a]Reactions were conducted on 0.5 mmol scale with 0.5 mL of solvent at the prescribed temperature. Entries 1–6, 8, and 10: yields are by GC-FID analysis using tridecane as an internal standard. Entries 7, 9: yields are of analytically pure isolated materials. The reaction does not proceed in the absence of catalyst. DME = 1,2-dimethoxyethane; DABCO = diazabicyclo[2.2.2]octane.

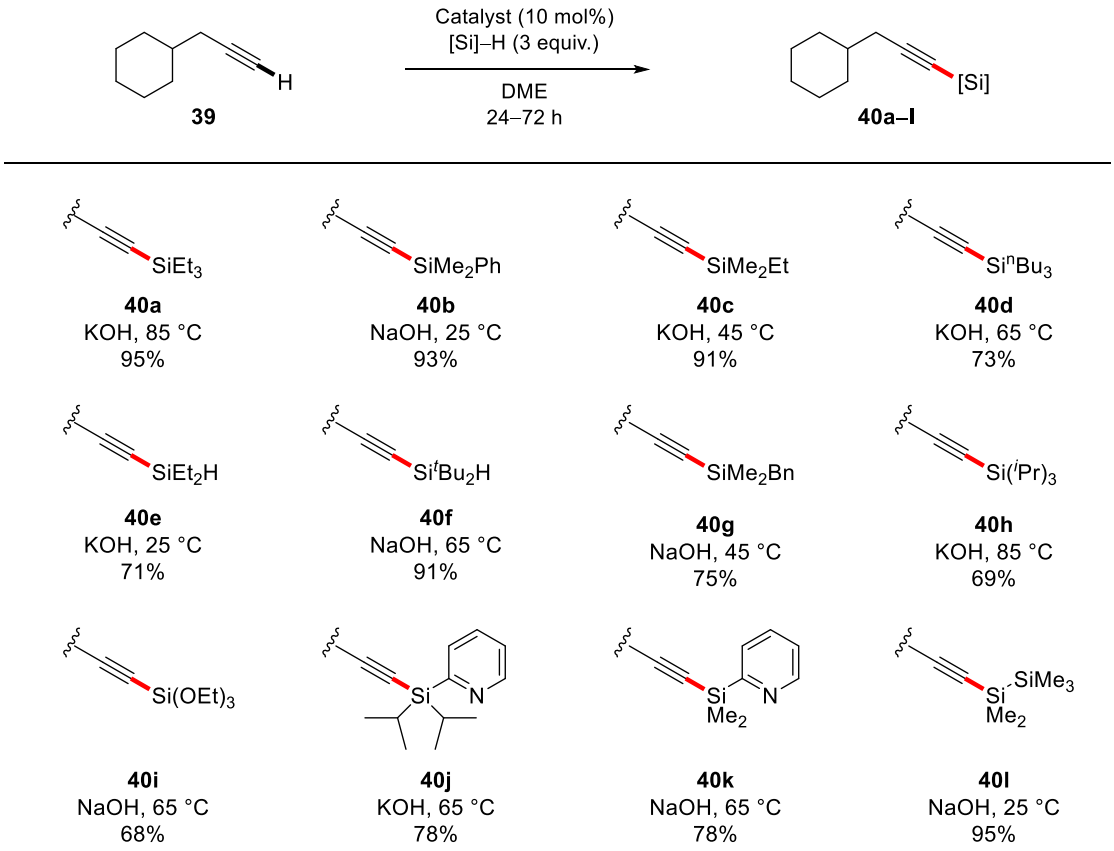
NaO*t*-Bu (entry 2) and LiO*t*-Bu (entry 3) show poor reactivity, and common organic bases (entries 4–6) also give poor results. A significant and unexpected finding was that KOH was superior to KO*t*-Bu at 10 mol% catalyst loading (entry 7), generating decreased quantities (3%) of the

undesired **39-iso**. Moving from Et_3SiH to $PhMe_2SiH$ permits the reaction to occur at ambient temperature while still maintaining high yields (entry 8). At this point it became clear that in sharp contrast to our previously reported heteroarene C(sp^2)–H silylation protocol wherein the catalysis was essentially limited to KO*t*-Bu,[14,74] KOH and NaOH emerged as the ideal catalysts for the C(*sp*)–H silylation affording **40b** in 89% and 93% yield respectively (entries 8 & 9) and without alkyne isomerization. By contrast, LiOH (entry 10) does not catalyze the reaction. Analyses to rule out catalysis by adventitious transition metal residues were carefully conducted and the generation of H_2 during the reaction was confirmed independently by both GC and NMR analyses (see **Experimental and analytics** section of this chapter).

Scope of the coupling partners

We next proceeded to evaluate the scope of the hydrosilane partner and found that a substantial array of hydrosilanes could be employed in the catalysis (**Figure 3.2**). Alkyl- and phenyl-substituted hydrosilanes of varying steric demand readily undergo coupling providing alkynylsilanes **40a**–**d** in high yields**.** More elaborate hydrosilanes, many of which contained sensitive functionalities that were not compatible with previously reported stoichiometric- and catalytic alkyne silylation strategies, could be readily employed in the alkali metal hydroxide-catalyzed C–H silylation. This enabled the facile preparation of alkynylsilanes containing synthetically versatile hydride- (**40e** and **40f**), benzyldimethyl- (**40g**), triisopropyl- (**40h**), triethoxy- (**40i**), and even 2-dialkylpyridyl (**40j** and **40k**; the latter discussed in **Scheme 3.6** and **Scheme 3.7**) substituents on silicon in good yield. The bulky di-*tert*-butylsilane could also be introduced for the first time by catalytic C–H silylation yielding **40f** in excellent yield, providing

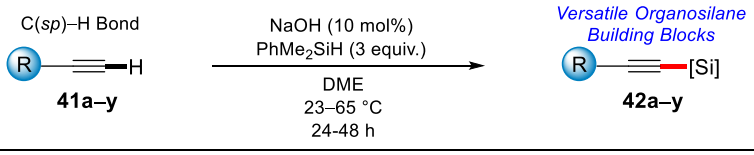
Figure 3.2. Evaluation of the hydrosilane scope.[a]

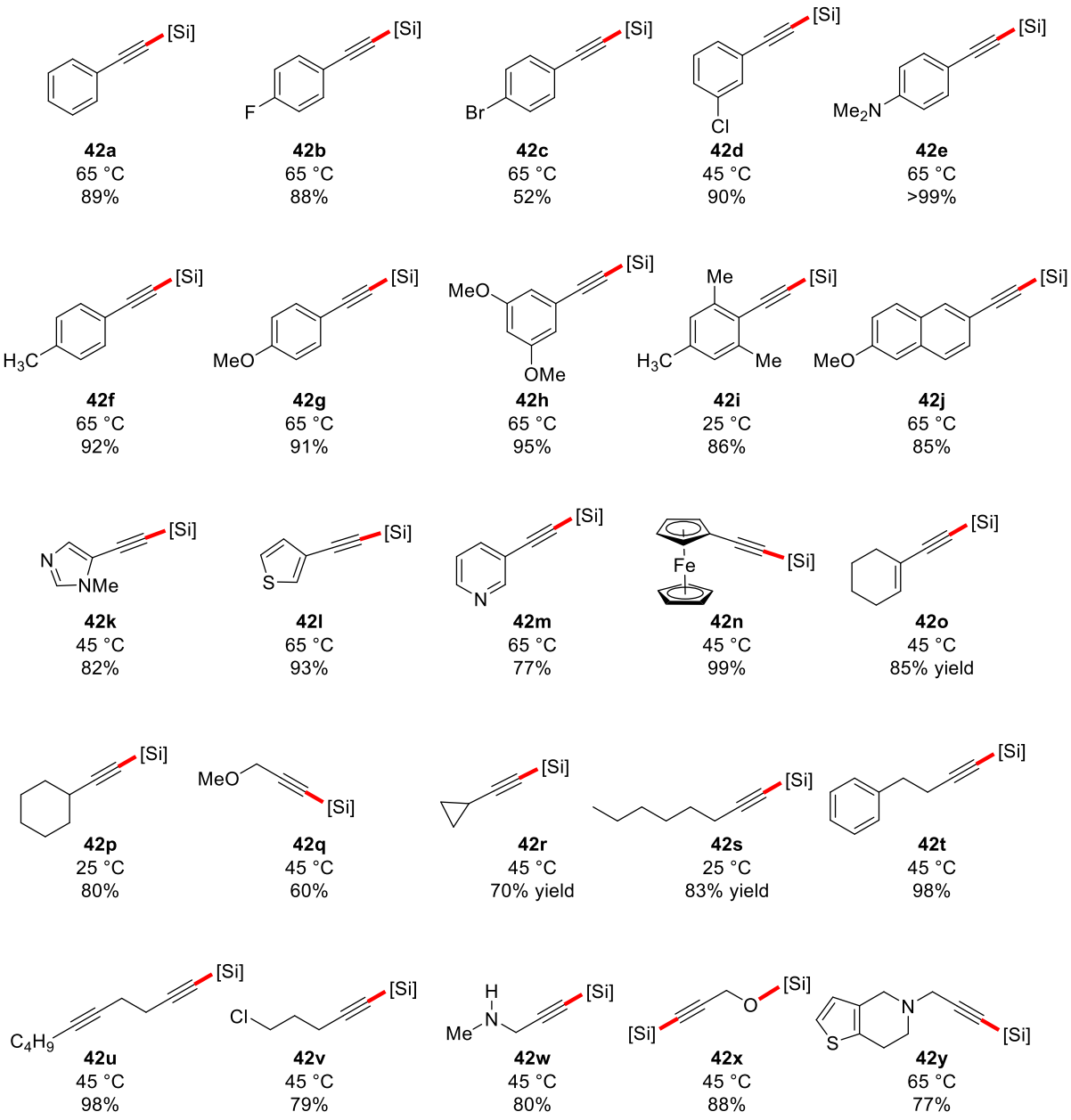


[a]Reactions were conducted on 0.5 mmol scale with 0.5 mL of solvent at the prescribed temperature. Reactions are run for 48 h except for examples **40c** and **40e,** which are run for 24 h.

a point of entry into novel alkynylsilyl [^{18}F]PET probes.[115] Polysilanes are a widely studied class of organosilicon materials containing $(R_2Si)_n$ units giving them distinctive optical and electronic properties.[128,129] However, the presence of highly labile Si–Si bonds that are often cleaved under transition metal catalysis or in the presence of certain nucleophiles or acids severely limits the methods that can be used for their installation onto organic molecules or surfaces. Using $(CH_3)_5Si_2$–H as a polysilane model compound and subjecting it to our cross-dehydrogenative silylation conditions using NaOH (10 mol%) as the catalyst at ambient temperature gave **2l** in 95%

Figure 3.3. Scope of the alkyne partner.[a]





[a]Reactions were conducted on 0.5 mmol scale with 0.5 mL of solvent at the prescribed temperature. Reactions are run for either 24 or 48 h, except for examples **42c** and **42l**, which are run for 96 h and 72 h respectively. Yields are of analytically pure isolated materials. Selectivities determined by NMR and GC. [Si] = $PhMe_2Si$.

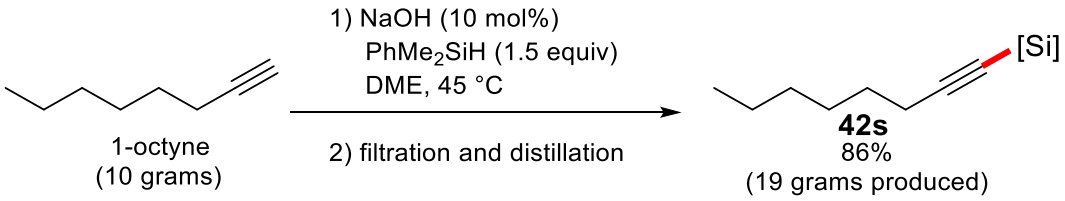
yield, providing a new synthetic strategy for the construction of advanced polysilane materials. To the best of our knowledge, this is the broadest scope of hydrosilanes reported to date for any single catalytic C–H silylation system.

We next proceeded to explore the scope of the alkyne coupling partner (**Figure 3.3**). Gratifyingly, a large variety of alkynylsilanes could be prepared from the corresponding terminal alkynes, including those bearing electron-rich and electron-deficient aryl (**42a–j**), heteroaryl (**42k–m**), ferrocenyl (**42n**), and alkyl (**42o–y**) groups. Substrates containing sensitive functional groups such as aryl halides (**42b–d**), an alkyl chloride (**42v**), and a cyclopropane (**42r**) are tolerated without any undesired side reactions. Molecules bearing acidic functionalities such as propargylamines and propargyl alcohols also react well, providing **42w** and bis-silylated **42x**[72] respectively in high yields. Unprecedented catalytic cross-dehydrogenative silylation of N-heterocyclic systems, such as those substrates containing an imidazole and a pyridine, are also successful affording the corresponding silylated building blocks **42k** and **42m** without any observed Minisci-type reactivity. Substrates containing C–H bonds that are susceptible to our KO*t*-Bu-catalyzed silylation,[74] or those that could be engaged under a variety of other C–H functionalization chemistries, react specifically at the terminal alkyne C–H bond. Thus, alkynylsilane products bearing toluene (**42f**), anisole (**42g**), thiophene (**42l** and **42y**), propargyl ether (**42q)**, and phenethyl (**42**) moieties could be readily accessed. In particular, electron-rich systems are especially excellent substrates and undergo the desired C(*sp*)–H silylation to furnish alkynylsilanes containing aniline (**42e**), dimethoxy benzene (**42h**), and ferrocene (**42n**) fragments without any products derived from electrophilic silylation observed.

Synthetic applications of the alkali metal hydroxide–catalyzed C–H silylation

As in our investigations of heterocycles silylation, we sought to ensure that our method could perform well on larger scales, something that is so rarely investigated in reports detailing new C–H silylation methods in any context. In this regard, and having established a scope of reactivity, we exmplored the scalability of the hydroxide-catalyzed C(*sp*)–H silylation reaction and determined that the protocol scales well without loss of catalyst activity as demonstrated by the practical multi-gram synthesis of **42s** employing 1.5 molar equivalents of the hydrosilane (**Scheme 3.4**).

Scheme 3.4. Multi-gram scale cross-dehydrogenative silylation of a simple terminal alkyne.

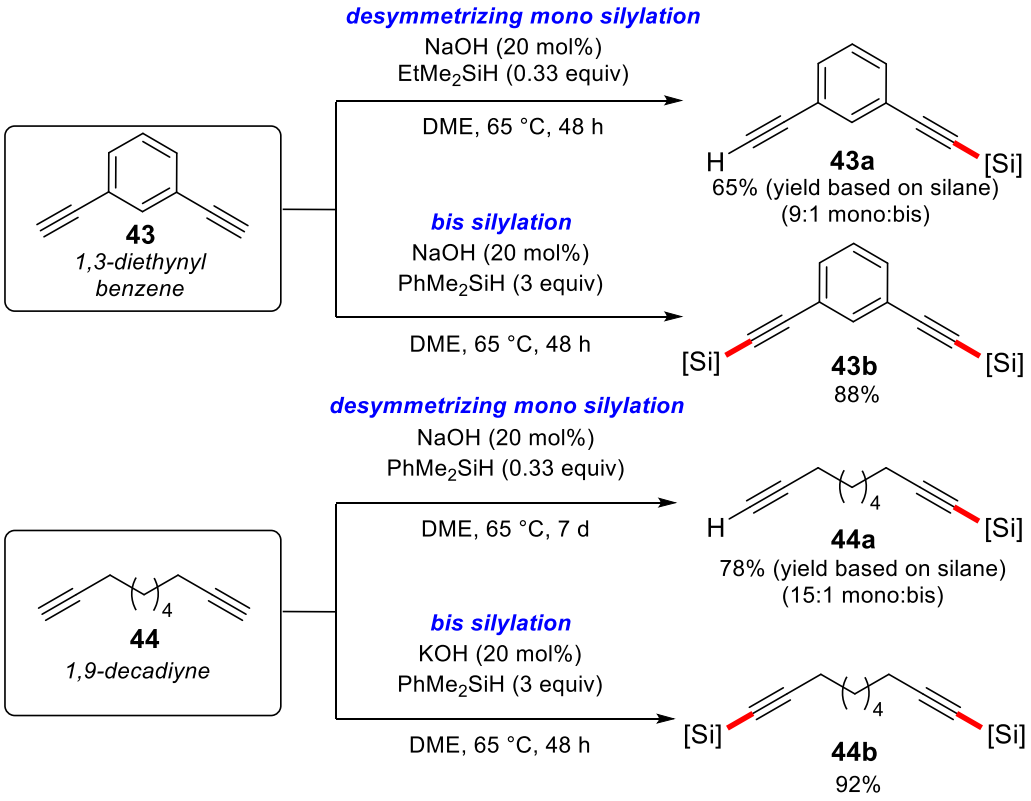


With all of this encouraging data in hand, we became interested in developing new synthetic methods, which could be uniquely enabled by the practical convenience, mildness, and scope of hydroxide-catalyzed silylation in the context of organic synthesis, drug discovery, and materials science.

For example, it was found that symmetrical aliphatic or aromatic diynes undergo bis-functionalization resulting in the exhaustively silylated dialkyne fragments **43b** and **44b** (**Scheme 3.5**). These same diynes undergo catalytic mono-silylation to yield valuable desymmetrized building blocks **43a** and **44a** by using an excess of substrate.

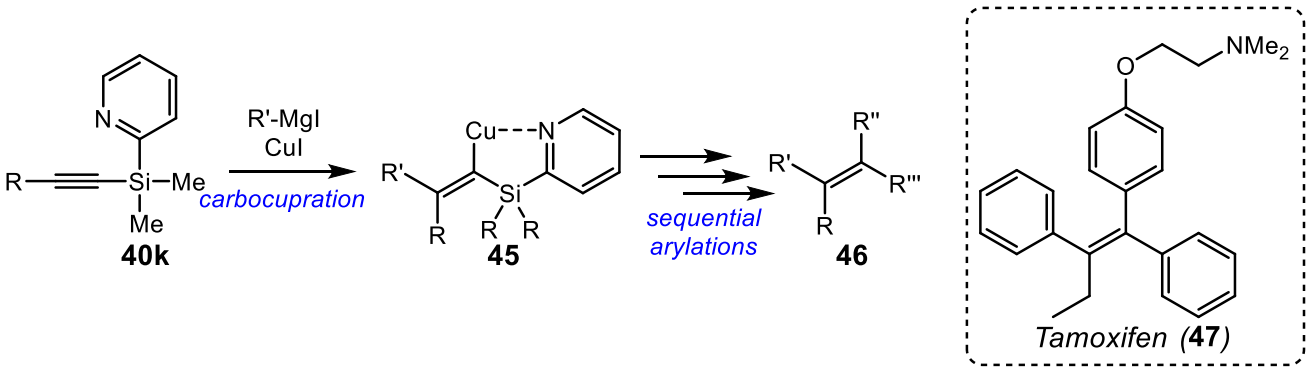
Yoshida and Itami[130] have exploited alkynylsilylpyridines as powerful directing groups to enable a variety of metal-catalyzed reactions of terminal alkynes. For example, it was shown that by

Scheme 3.5. Mono- or bis-functionalization of symmetrical diynes.



installing a 2-dimethylsilylpyridyl (2-Me_2SiPy) group onto a simple alkyne, this transforms the alkyne into a starting material (**40k**) for a carbocupration reaction leading to **45**. This intermediate

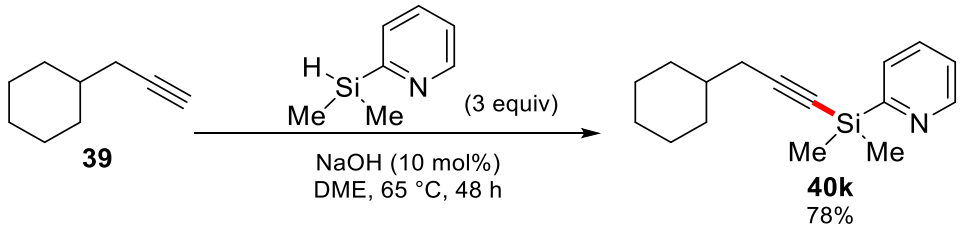
Scheme 3.6. Application of alkynylsilylpyridines.



has a vinyl copper functionality, which is available for a subsequent arylation. Finally, the C–Si bond itself can participate in cross-coupling chemistries, enabling the introduction of a final aryl

moiety. The authors demonstrated this sequential arylation strategy in the synthesis of the API tamoxifen (**Scheme 3.6**). However, the 2-Me_2SiPy directing group must be installed by addition of the acetylide to the silane.[130] In other words, no catalytic method exists for its introduction. This restricts the kinds of functionalities which can be present on the strating alkyne and limits the value of the downstream chemistry. As a result, we sought to further demonstrate the utility of our cross-dehydrogenative silylation methodology by attempting to install the versatile 2-dimethylsilylpyridine group through C–H bond functionalization. Gratifyingy, catalytic silylation of **39** with NaOH occurred smoothly to provide **40k** in 78% yield (**Scheme 3.7**).

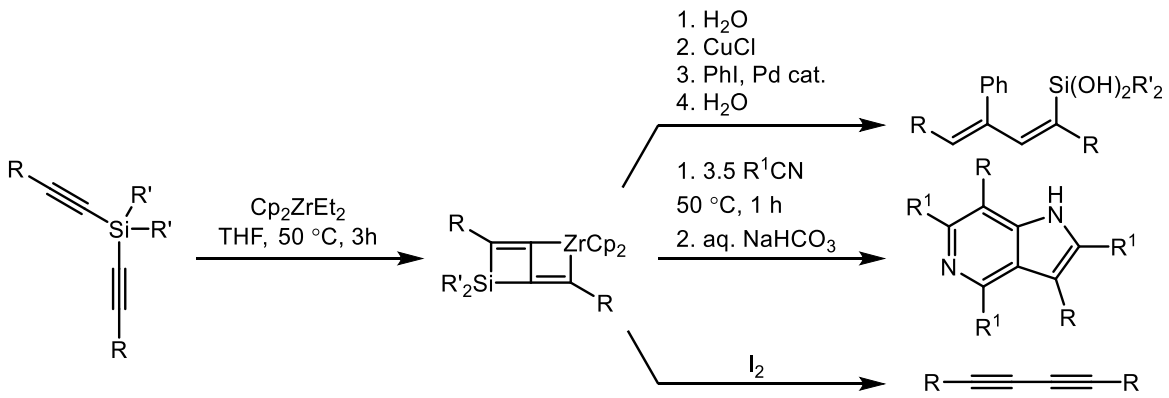
Scheme 3.7. First catalytic installation of the 2-Me_2SiPy moiety onto a carbon atom.



Si-tethered diynes have a rich history in organometallic chemistry and organic synthesis.[131,132] Indeed, they can be readily advanced to substituted arenes, enones, dienes, and aromatic N-heterocycles as well as siloles, polysiloles or silole-heterocycle co-polymers, through well-established synthetic sequences (**Scheme 3.8**).[110,133,134,135,136]

The broad reactivity profile of these organosilyl building blocks is owed to the presence of Si–C and C≡C moieties in close proximity within the molecule. However, synthesis can be challenging and even in the case of symmetrical Si-tethered diynes, a general method for their construction continues to be elusive due to issues of functional group tolerance and robustness inherent to current methods.[137,138] Moreover, no stoichiometric or catalytic methodology for the direct preparation of unsymmetrical variants has been reported. In order to evaluate our alkali-metal

Scheme 3.8. Applications of Si-tethered diynes in the synthesis of complex molecules.

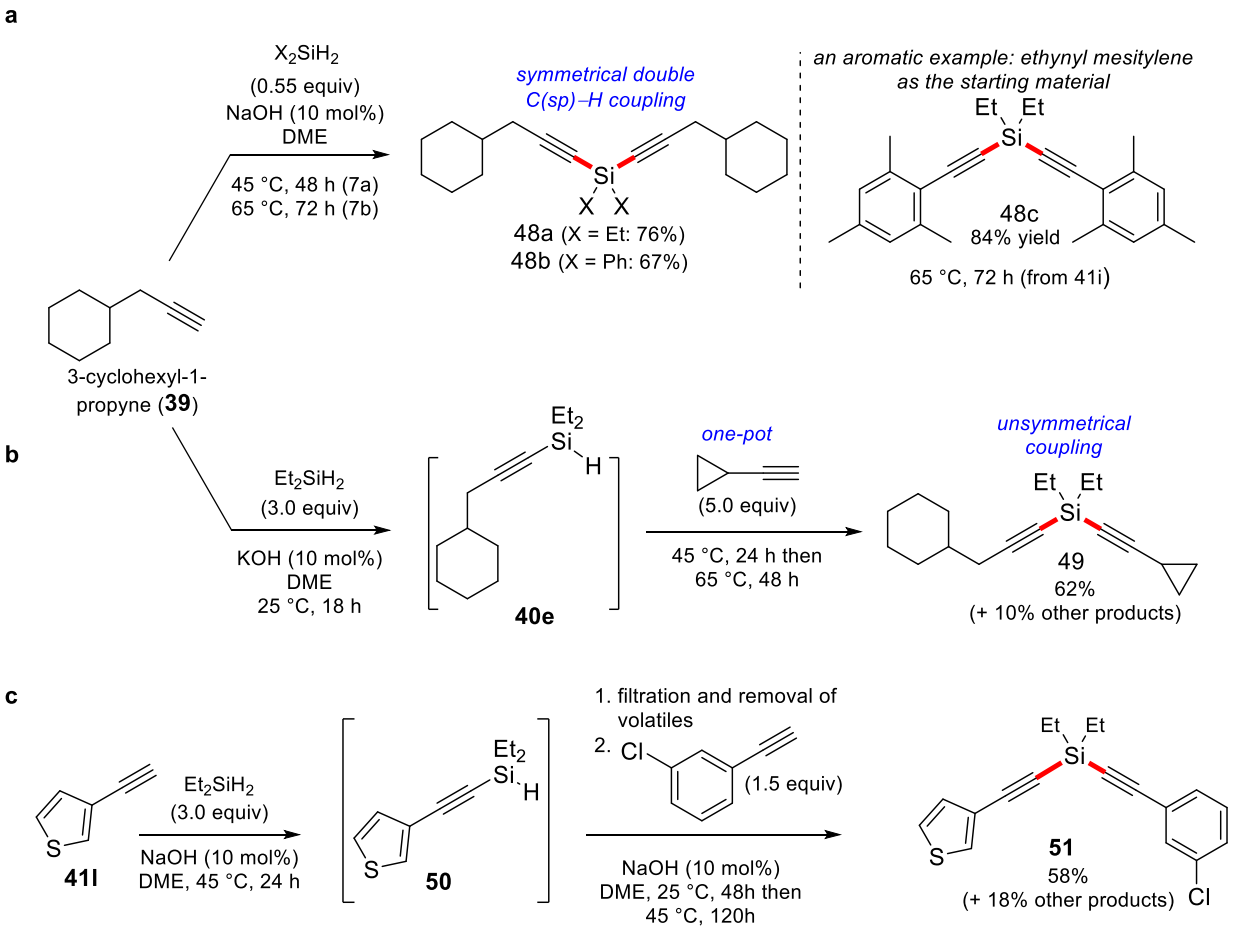


hydroxide–catalyzed silylation methodology for the synthesis of Si-tethered diynes, we treated alkyl- and aryl-substituted dihydrosilanes with **39** (or **41i**, in the case of **48c**) and obtained the desired symmetrical **48a–c** respectively in good yields by double cross-dehydrogenative C(*sp*)–H silylation (**Figure 3.4a**).

At this point, we became interested in whether unsymmetrical variants could be accessed. Treating an alkyne with a dihydrosilane gives rise to the alkynylhydrosilane, which can then be combined with a second alkyne to furnish the unsymmetrical Si-tethered diyne. This methodology proved to be effective for alkynes with both aliphatic and aromatic or heteroaromatic substituents (conducted under somewhat different conditions), generating **49** (**Figure 3.4b**) and **51** respectively (**Figure 3.4c**).

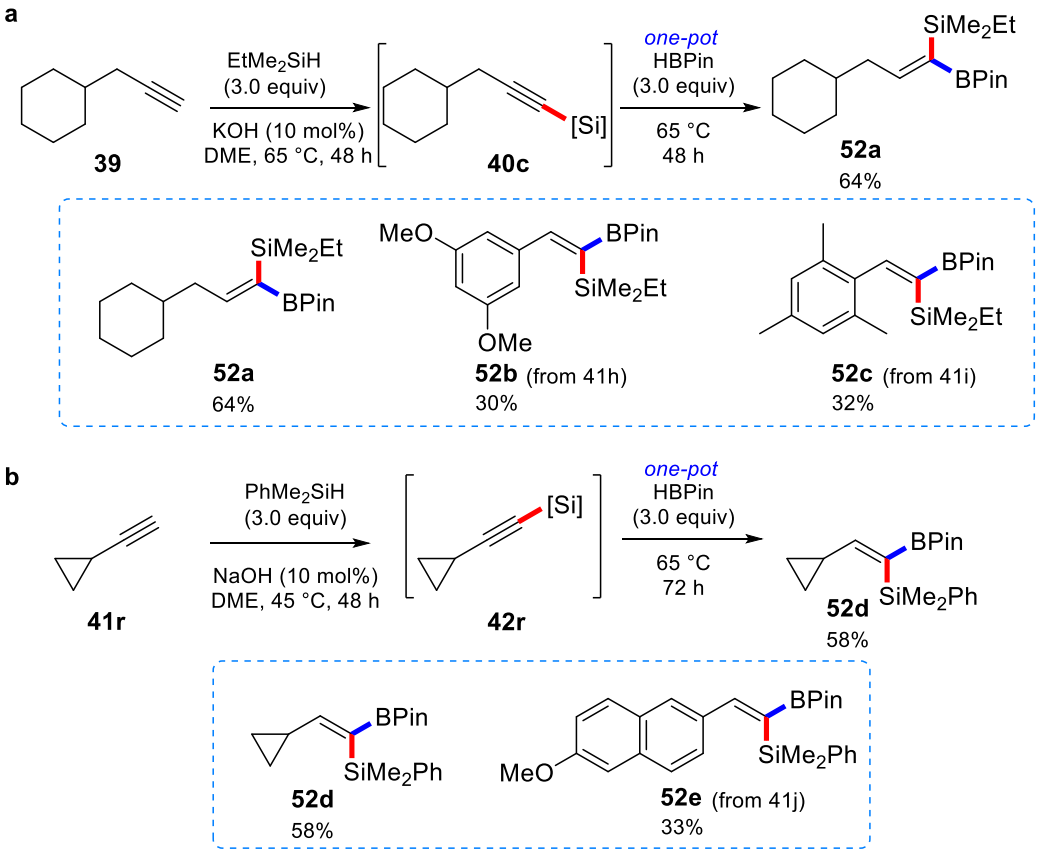
Silicon- and boron-containing difunctionalized olefins are valuable synthetic building blocks that take part in catalytic C–C bond formation processes such as the Hiyama and Suzuki–Miyaura reactions as well as many others, enabling rapid generation of molecular diversity.[139,140,141] Employing our alkali metal hydroxide–catalyzed silylation followed by simple treatment of the

Figure 3.4. Synthesis of Si-tethered diynes.



intermediate alkynylsilane with a borane (i.e., HBPin)[142,143] leads to a one-pot catalytic geminal di-functionalization of terminal alkynes (**Figure 3.5**). This method furnishes tri-substituted olefins **52a–e** containing both a vinyl C–Si and C–B bond as a single olefin isomer from inexpensive, commercially available materials. Combinations of both alkyl- and aryl-substituted silanes and alkynes are amenable to this reaction, though the use of KOH (**Figure 3.5a**) or NaOH (**Figure 3.5b**) is favoured as the catalyst depending on the substrate/silane combination employed. As mentioned, the reason for this is not understood at this point. This strategy appears to be the first

Figure 3.5. Catalytic one-pot *geminal* silylboration of terminal alkynes.

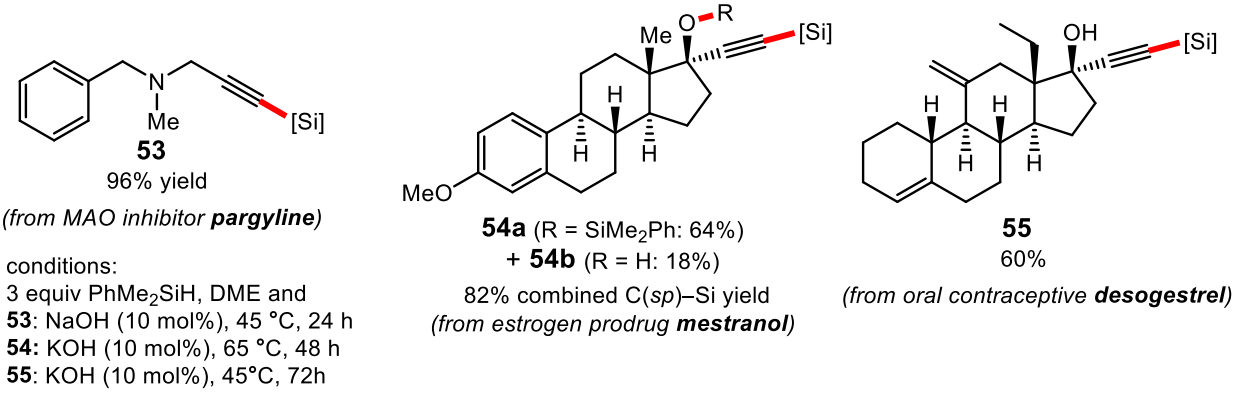


catalytic one-pot synthesis of gem-silaboryl olefins directly from terminal alkynes and constitutes a convenient and practical method for the synthesis of this unique and useful class of molecules.

Late-stage silylation of pharmaceutically-relevant substances

Sila-drug analogues are garnering increased attention from medicinal chemists, which in some cases demonstrate improved pharmacokinetic properties relative to the corresponding all-carbon compound.[51,105] Moreover, the installed organosilicon functionality can serve as either a functional group handle for subsequent elaboration or an easily-removable protecting group, enabling reliable late-stage functionalizations[50] at other sites on the molecule using chemistries that would otherwise be incompatible with alkynyl C–H bonds. To evaluate our method for such late-stage C–H

Figure 3.6. Late-stage C(*sp*)–H silylation of APIs.



functionalization applications, we subjected the monoamine oxidase (MAO) inhibitor pargyline, the estrogen prodrug mestranol, and third-generation oral contraceptive desogestrel to the catalytic silylation conditions, successfully providing novel sila-drug analogues **53**, **54**, and **55** respectively (**Figure 3.6**). In the case of mestranol, bis-silylated **54b** containing a silyl ether functionality is isolated as the main product in 64% yield, whereas for desogestrel less than 5% of an O–Si bond formation product is observed.

Preliminary mechanistic studies.

ICP-MS analysis

To provide further support against involvement of adventitious trace metal species in the cross-dehydrogenative C(*sp*)–H silylation catalysis, inductively coupled plasma mass spectrometry (ICP-MS) was performed on samples of NaOH, KOH, 3-cyclohexyl-1-propyne starting material, 1,2-dimethoxyethane (DME) solvent, $PhMe_2SiH$, and a standard reaction mixture that was run under optimized conditions in the glove box. The results from quantitative analysis revealed that most metal contaminants were present below the instrument's lowest limit of detection.

Microgram per liter (ppb) quantities of metal contaminants are given in **Table 3.2**. As with the ICP-MS analyses that were performed in the context of the C−X bond cleavage reaction (Chapter 1) and heteroarene C−H bond silylation (Chapter 2), these microanalysis results support (but certainly cannot alone confirm) that adventitious impurities such as transition metal salts are in some way contributing to the catalysis.

Table 3.2. Results of ICP-MS trace metal analysis.

	Values in ng/g unless otherwise stated[a]*					
Element	**NaOH**	**KOH**	**3-cyclohexyl-1-propyne (39)**	**1,2-DME**	**$PhMe_2SiH$**	**Reaction Mixture**
Ti	LOD	0.767*	0.324*	0.206*	0.545*	0.059*
Co	LOD	LOD	18.543	LOD	LOD	LOD
Cu	LOD	LOD	10.440	0.069*	3.048	0.116
Zn	LOD	0.682*	25.908*	1.787*	0.063*	0.320
Zr	LOD	LOD	LOD	LOD	0.232*	LOD
Mo	LOD	LOD	LOD	LOD	1.118*	LOD
Ru	LOD	21.248	1.576	LOD	41.188	18.692
Rh	LOD	0.165	LOD	LOD	0.908	LOD
Pd	LOD	1.834	0.612	7.950	7.339	0.612
Ag	LOD	LOD	LOD	LOD	LOD	LOD
Re	LOD	0.156	LOD	0.700	5.835	0.311
Os	LOD	LOD	LOD	LOD	LOD	LOD
Ir	LOD	0.063*	7.776*	0.253*	2.429*	0.604
Pt	LOD	0.406	0.135	0.813	1.490	0.271
Au	LOD	LOD	0.115	LOD	1.729	1.383

[a]LOD = Limit of detection (these values fall below the detection limit of the instrument). *ppm

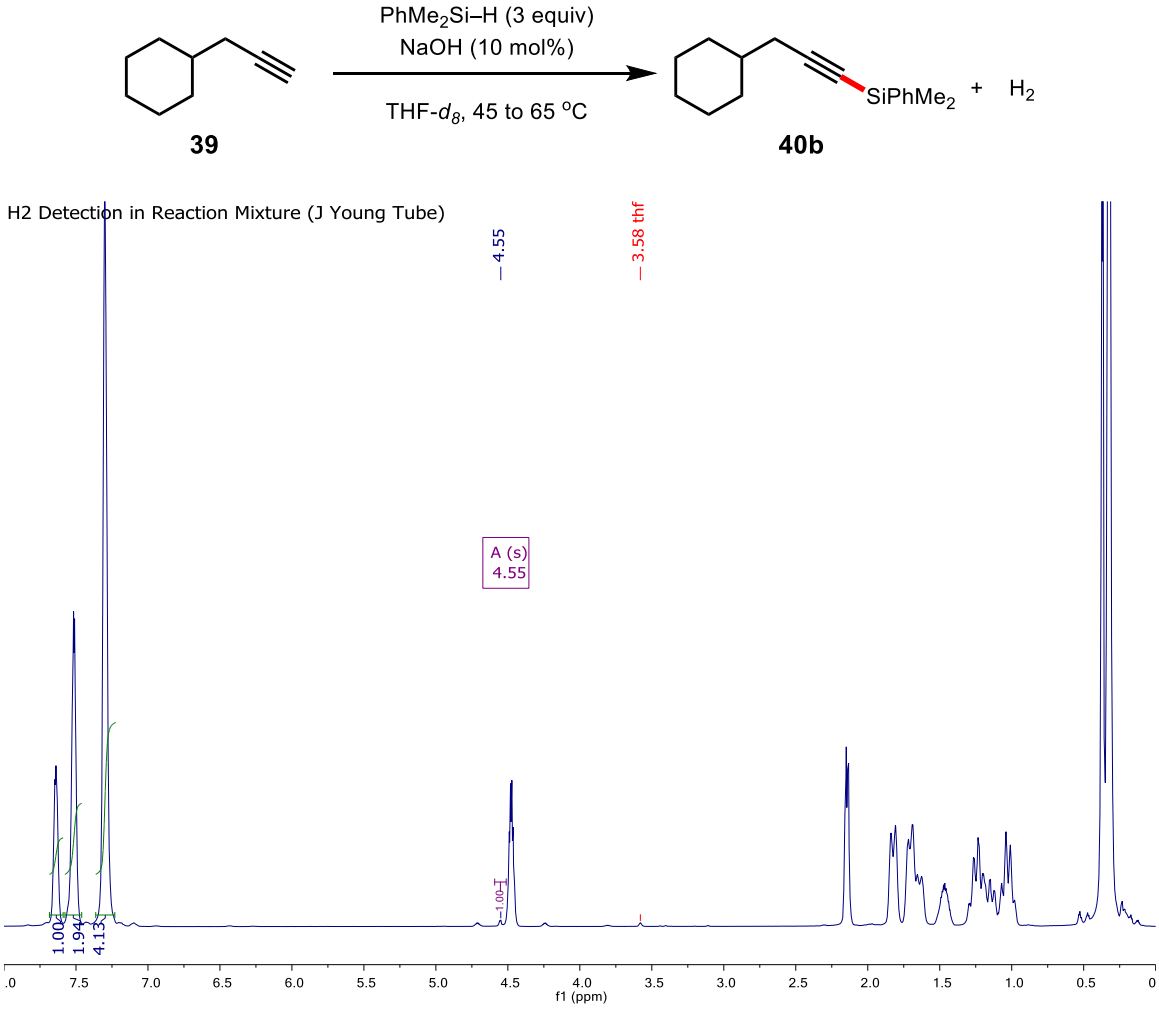
Confirmation of H_2 production

The evolution of hydrogen gas during the alkyne silylation reaction was confirmed by ^{1}H NMR and headspace GC-TCD analysis. This was done to establish the cross-dehydrogenative nature of the reaction.

^{1}H NMR was performed by David Schuman by conducting a standard silylation reaction in a J-Young tube and heating to 65 °C for 48 h, after which time the crude ^{1}H NMR indicated the

presence of H_2 (**Figure 3.7**; THF-d_8, 400 MHz, δ 4.55 ppm, s). To further confirm the presence of H_2, the J-Young tube containing the reaction mixture was fitted with a septum and the headspace was transferred with a needle and syringe to freshly degassed $CDCl_3$ in a dry NMR tube with a septum cap. ^1H NMR clearly showed the presence of H_2 in the headspace (**Figure 3.8**; $CDCl_3$, 500 MHz, δ 4.62 ppm, s).

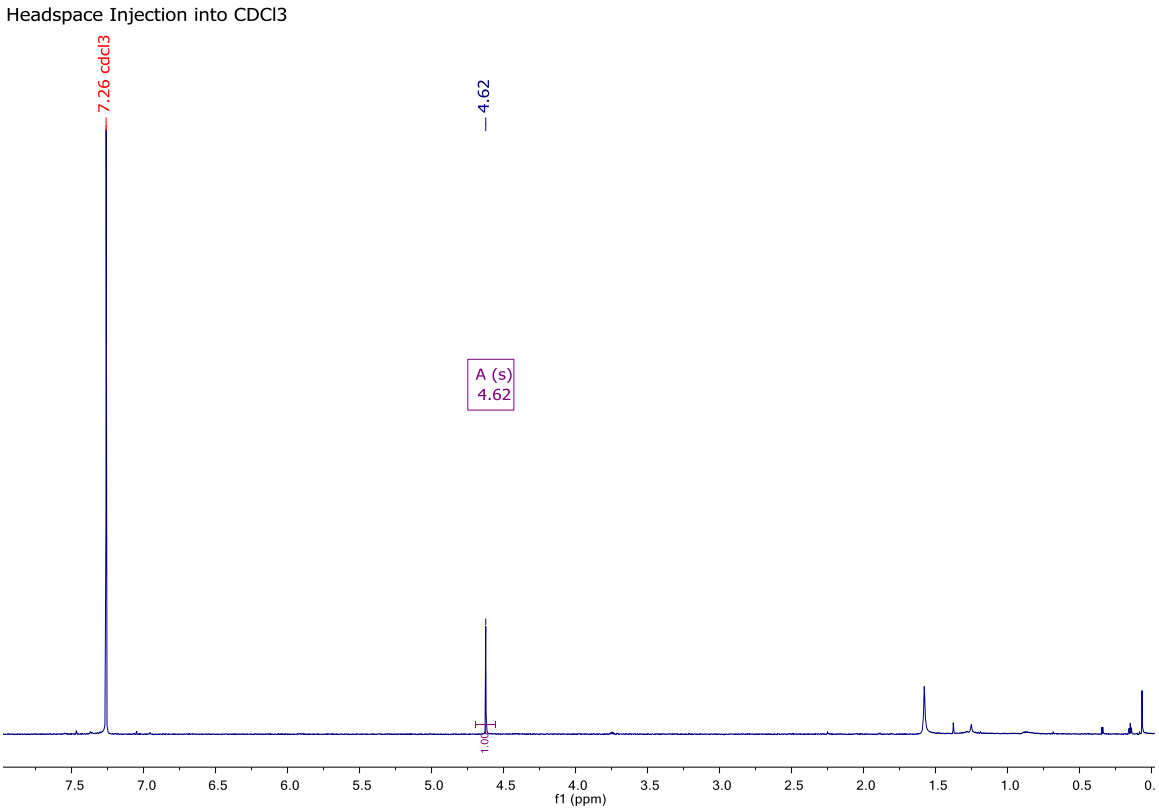
Figure 3.7. Detection of H_2 by ^1H NMR analysis of an NMR-scale reaction in a J-Young tube.



The presence of hydrogen was also analyzed by gas chromatography (GC) with thermal conductivity detection (TCD). Hydrogen eluted at approximately 1.8 minutes under these

conditions (see chromatogram of injected pure H_2 reference standard, **Figure 3.9**). This was done by performing a standard reaction in a vial, but sealing it with a septumed cap such that the headspace could be sampled with an air-tight syringe. The reaction was heated to 45 °C for 24 h. Injection of the reaction headspace showed a single signal at 1.8 min (**Figure 3.10**), which overlays very well with the H_2 reference stardard), strongly corroborating the presence of H_2.

Figure 3.8 Detection of H_2 by ^{1}H NMR analysis via injection of reaction headspace into an NMR tube.



Note: raised temperatures were necessary for the experiment conducted in the J Young tube compared to standard preparatory scale reactions in vials due to the lack of stirring in such a setup.

Figure 3.9. GC-TCD chromatogram of a pure sample of H_2 as a reference standard.

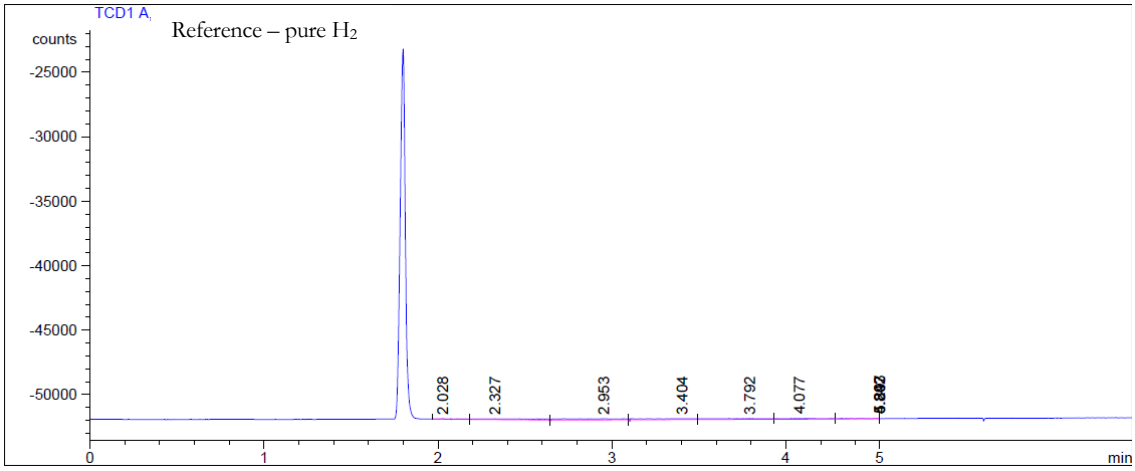
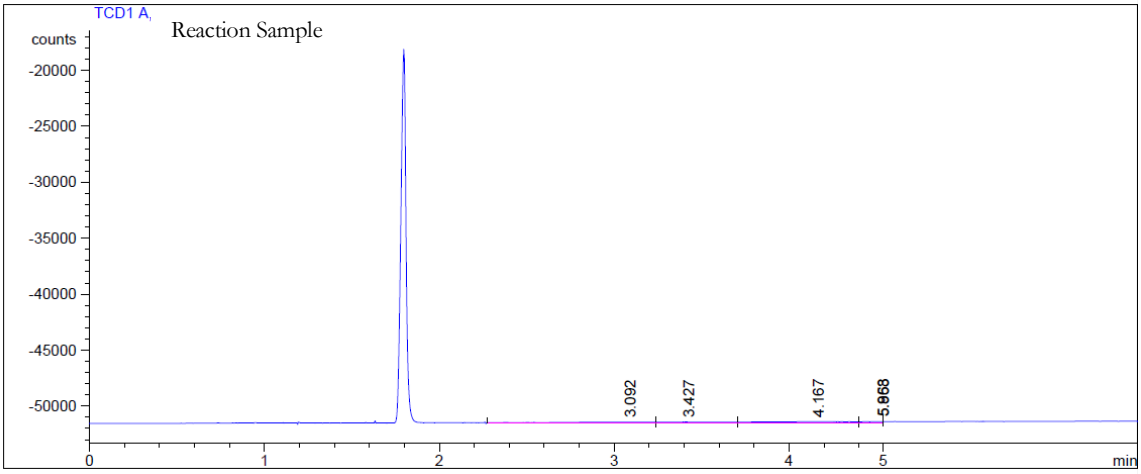


Figure 3.10. GC-TCD chromatogram of the headspace of a reaction mixture (see Figure 3.7 for reaction details) clearly showing the presence of H_2.



Mechanistic considerations

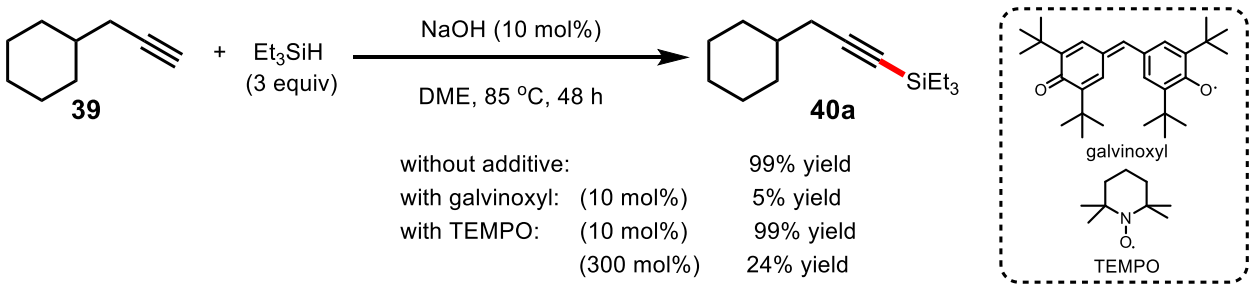
A number of mechanisms for the C(*sp*)–H silylation reaction occurring under various conditions with different catalyst systems have been proposed;[57a,59,116,117,119–123] however, the underlying mechanistic details of the alkali metal hydroxide–catalyzed silylation are not well understood at this point. Preliminary studies and empirical results suggest that the mechanism is distinct from previously disclosed cross-dehydrogenative C–H silylation reactions in general, including the

recently reported KO*t*-Bu-catalyzed C(sp^2)–H silylation of heteroarenes.[14,51,74] This is based primarily on three considerations: 1) that these reactions are not inhibited by Lewis basic functionalities such as pyridines and amines (see substrate scope, **Figure 3.3**), which provides evidence against an electrophilic mechanism proceeding via a silylium ion and 2) the results from radical trapping and countercation chelation studies, and 3) surprisingly, we found empirically that there was a significant difference in terms of product yield based on the hydroxide salt employed (i.e., KOH vs. NaOH) and that employing KO*t*-Bu as the catalyst results in a precipitous drop in reactivity for nearly all cases evaluated.

As a first investigation, we decided to probe whether the silylation reaction was polar or radical in nature. We began by performing our reaction in the presence of the radical traps TEMPO and galvinoxyl. Neither additive completely thwarted the alkyne C–H silylation: TEMPO did not inhibit the reaction at 10% loading but lowered the silylation yield at 300% loading; the addition of 10 mol% galvinoxyl almost completely inhibited the reaction (**Scheme 3.9**). Although these stable radical reagents could decrease the yield of the ethynylsilane **40a**, these data certainly cannot conclude whether the reaction is anionic in nature or whether it proceeds via single electron species. One can only conclude that galvinoxyl and TEMPO do inhibit the reaction and that the former is a more effective inhibitor.

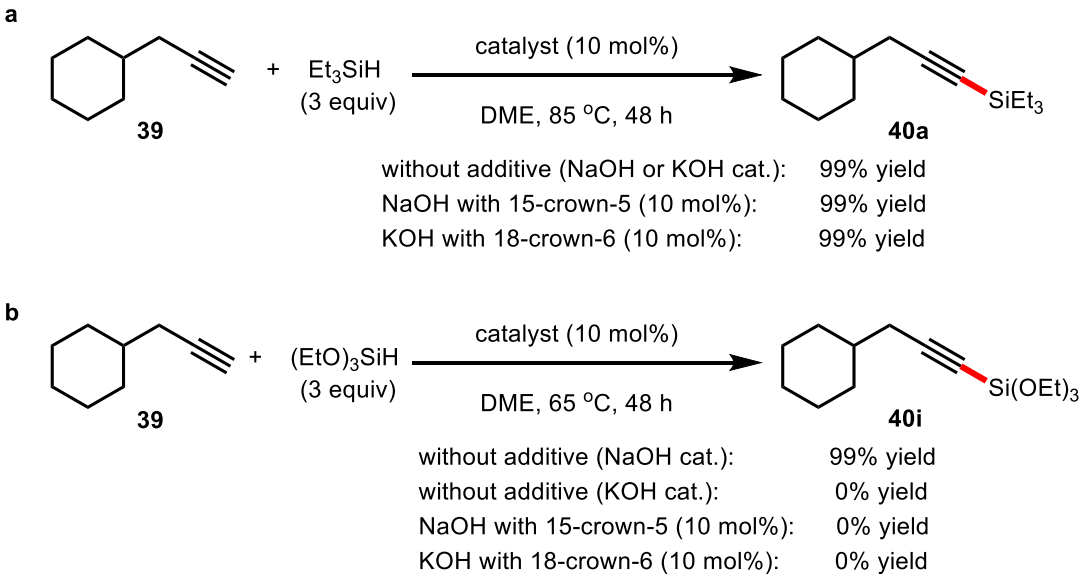
We also studied the effect of potassium and sodium chelating agents in the silylation reaction to investigate the importance of the cation in the catalysis. When 18-crown-6 and 15-crown-5 were added to reactions using KOH and NaOH as the catalysts respectively, quantitative silylation was still observed when using triethylsilane as the silicon partner, suggesting either that ineffective

Scheme 3.9. Impact of radical trap additives on the reaction outcome.



chelation of the metal ion had occurred or that the cation was not necessary to the reactivity in this particular case (**Figure 3.11a**).

Figure 3.11. Impact of crown ether additives on the reaction outcome.[a]



[a]Yields are by GC analysis and are corroborated by NMR analysis.

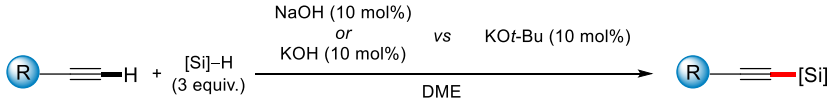
However, the reaction with Et_3SiH intrinsically proceeds equally well using KOH or NaOH as the catalyst, thus it may not be an ideal silane for such a control experiment. Therefore, we proceeded to interrogate whether potassium and sodium chelating agents affect silylation using a silicon partner that does not perform equally well with KOH and NaOH. Triethoxysilane was chosen as the test silane, since it only displays product formation using NaOH as the catalyst. In this case,

the addition of the chelating agent shut down reactivity, suggesting that the sodium ion is indeed necessary for the silylation of alkynes with triethoxysilane (**Figure 3.11b**). The only product when crown ethers are added is $(EtO)_4Si$, which indicates that sequestration of the alkali metal cation from the system shuts down the productive C–H silylation pathway and induces disproportionation of the silane. These counterion chelation studies clearly demonstrate that the cation does seem to have some sort of role in the reaction (and subsequent studies which will be discussed in the following paragraphs will corroborate this fact), though its exact role remains unclear.

Comparison of NaOH, KOH, and KOt-Bu catalysts

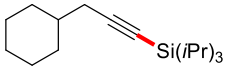
Throughout my entire thesis work, it became apparently clear that the identity of the counterion played a significant role in C−X cleavage (Chapter 1)[14] and heterocycle silylation (Chapter 2) reactions.[74] In these cases, a potassium alkoxide (preferably KO*t*-Bu) was crucial for reactivity, whereas sodium- and lithium alkoxides were unreactive. In this alkyne silylation reaction, the importance of the counterion was not nearly as clear; however, the observation that sodium- or potassium hydroxide was preferred depending on the substrate/silane combination seems unusual and suggests an important counterion effect. To probe this in a meaningful and systematic fashion, we have directly compared several catalysts: KO*t*-Bu, which is an adept silylation catalyst in our recently reported cross-dehydrogenative C–H silylation of aromatic heterocycles,[14,74,105] and KOH and NaOH, which both show excellent performance as catalysts for the silylation of C(*sp*)–H bonds in this report for a number of substrates. The results of these comparisons are shown in **Table 3.3** and **Table 3.4**. In order to compare the performance of the MOH (i.e., where M=Na, K) catalysts

Table 3.3. Comparison of KO*t*-Bu vs MOH (M = K, Na) as catalysts for the C(*sp*)–H silylation under identical conditions.[a]



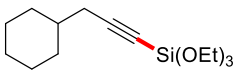
40g

NaOH	KO*t*-Bu
45 °C	45 °C
75% yield	0% yield



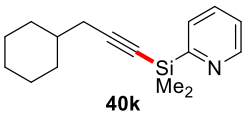
40h

KOH	KO*t*-Bu
85 °C	85 °C
69% yield	0% yield



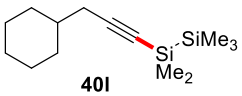
40i

NaOH	KO*t*-Bu
65 °C	65 °C
68% yield	0% yield



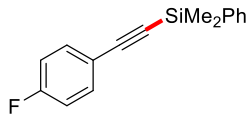
40k

NaOH	KO*t*-Bu
65 °C	65 °C
78% yield	0% yield



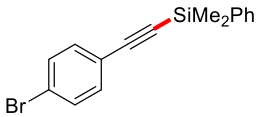
40l

NaOH	KO*t*-Bu
25 °C	25 °C
95% yield	0% yield



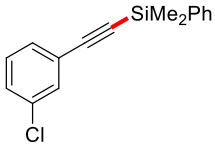
42b

NaOH	KO*t*-Bu
65 °C	65 °C
88% yield	< 5% yield



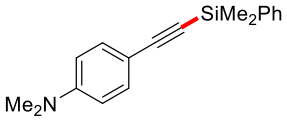
42c

NaOH	KO*t*-Bu
65 °C	65 °C
52% yield	0% yield



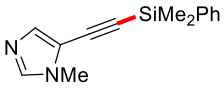
42d

NaOH	KO*t*-Bu
45 °C	45 °C
90% yield	< 5% yield



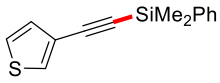
42e

NaOH	KO*t*-Bu
65 °C	65 °C
>99% yield	< 5% yield



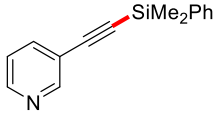
42k

NaOH	KO*t*-Bu
45 °C	45 °C
82% yield	< 5% yield



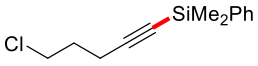
42l

NaOH	KO*t*-Bu
65 °C	65 °C
93% yield	< 5% yield



42m

NaOH	KO*t*-Bu
65 °C	65 °C
77% yield	0% yield



42v

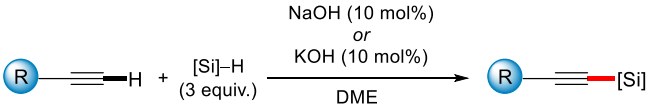
NaOH	KO*t*-Bu
45 °C	45 °C
79% yield	0% yield

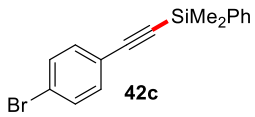
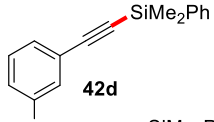
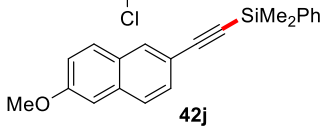
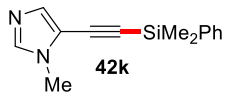
[a]A direct comparison of NaOH and KOH under identical conditions reveals that the two catalysts cannot be used interchangeably, providing empirical evidence for the importance of Na^+ and K^+ countercations. R = $PhMe_2Si$ (**54a**); R = H (**54b**). Reaction conditions are equivalent to those given in Figures 3 and 4 for each particular hydrosilane and alkyne. Reactions were conducted on 0.5 mmol scale with 0.5 mL of solvent unless otherwise stated and at the prescribed temperature. Yields are of analytically pure isolated materials. DME = 1,2-dimethoxyethane.

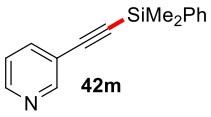
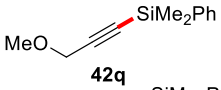
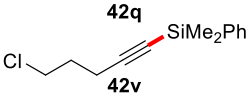
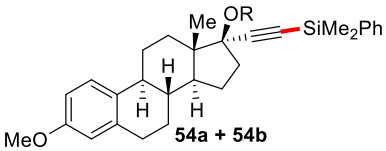
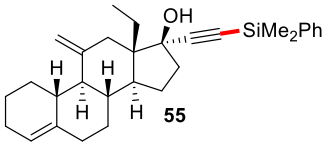
with the KO*t*-Bu catalyst used in the case of the heterocyclic silylation, several alkyne substrates and silanes were subjected to the reaction using KO*t*-Bu as a catalyst under identical conditions. The results are summarized in **Table 3.3.**

In the reaction of cyclohexylpropyne with triethylsilane, KO*t*-Bu successfully produced the silylated alkyne **40a** in moderate yield; however (and as alluded to in the main text), this result would turn out to be largely coincidental since in virtually all other investigated cases, KO*t*-Bu failed to convert the starting material or produced only trace product. These data were unanticipated and it appears that the acetylinic silylation described in this report and the heterocyclic silylation described previously[14,74,105] require different catalysts and might proceed via a distinct mechanism.

Table 3.4. Comparison of NaOH and KOH as catalysts for the C(*sp*)–H silylation under identical conditions.[a]



Entry	Product	Yield KOH	Yield NaOH
1	[Si] = $SiEtMe_2$ (**40c**)	91%	14%
2	= $Si(n\text{-}Bu)_3$ (**40d**)	73%	22%
3	= $Si(i\text{-}Pr)_3$ (**40h**)	68%	0%
4	= $Si(i\text{-}Pr)_2Py$ (**40j**)	78%	0%
5	= $Si(OEt)_3$ (**40i**)	0%	68%
6	= $SiMe_2$–$SiMe_3$ (**40l**)	0%	95%
7	 **42c**	<5%	52%
8	 **42d**	38%	90%
9	 **42j**	12%	85%
10	 **42k**	19%	82%

Entry	Product	Yield KOH	Yield NaOH
11	 **42m**	7%	77%
12	 **42q**	0%	60%
13	 **42v**	0%	79%
14	 **54a + 54b**	82%	0%
15	 **55**	60%	0%

[a]A direct comparison of NaOH and KOH under identical conditions reveals that the two catalysts cannot be used interchangeably, providing empirical evidence for the importance of Na^+ and K^+ countercations. R = $PhMe_2Si$ (**54a**); R = H (**54b**). Reaction conditions are equivalent to those given in Figures 3 and 4 for each particular hydrosilane and alkyne. Reactions were conducted on 0.5 mmol scale with 0.5 mL of solvent unless otherwise stated and at the prescribed temperature. Yields are of analytically pure isolated materials. DME = 1,2-dimethoxyethane.

Next, NaOH and KOH catalysts were directly compared in the reaction of a number of alkyne substrates and with different silanes (**Table 3.4**). Clearly there is a marked difference in the reaction performance in these cases; however, there is no immediately discernable trend (i.e., basicity, aggregation states, or solubilities) that explains the differece in the performance of the two catalysts. The differences between NaOH and KOH are most pronounced when using different silanes (entries 1–6); however, most substrates studied performed better using NaOH, rather than KOH, except for the notable cases of mestranol and desogestrel, which displayed no silylation when using NaOH.

Conclusion.

Abundantly available and inexpensive NaOH and KOH are found to be remarkably useful catalysts for the direct construction of C(*sp*)–Si bonds, further corroborating the potential of alkali metal salts in catalytic C–H bond functionalization reactions. These catalysts are shown to enable an efficient, mild, and powerful cross-dehydrogenative C(*sp*)–H bond silylation methodology having an unprecedented scope in both the hydrosilane and the alkyne. These investigations have also led to the discovery of a method for the synthesis of unsymmetrical Si-tethered alkyne building blocks, and a one-pot *gem*-silaboration of alkynes among other novel protocols. The late stage C(*sp*)–H silylation of three pharmaceutically relevant substances further demonstrates the potential utility of the method in complex molecule settings. Elucidation of the mechanism of this reaction as well as its application to a variety of systems including [^{18}F]PET radiopharmaceutical synthesis are currently underway. This latter aspect will be discussed in Chapter 5.

Experimental and analytics.

General information

Unless otherwise stated, reactions were performed in oven-dried brand-new Fisherbrand scintillation vials in a nitrogen filled glove box or in flame-dried Schlenk flasks under argon connected on a Schlenk line using dry, degassed solvents and brand-new stirring bars. Solvents were dried by passage through an activated alumina column under argon.[43] Reaction progress was monitored by thin-layer chromatography (TLC) or GC-FID analyses. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, phosphomolybdic acid, or $KMnO_4$ staining. Silicycle SiliaFlash P60 Academic Silica gel (particle size 40–63 nm) was used for flash chromatography. ^{1}H NMR spectra were recorded on a Varian Inova 500 MHz in $CDCl_3$ or THF-d_8 and are reported relative to residual solvent peak at δ 7.26 ppm or δ 3.58 ppm respectively. ^{13}C NMR spectra were recorded on a Varian Inova 500 MHz spectrometer (126 MHz) in $CDCl_3$ or THF-d_8 and are reported relative to residual solvent peak at δ 77.16 ppm or δ 67.21 ppm respectively. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septet, m = multiplet, br s = broad singlet, br d = broad doublet, app = apparent. Data for ^{13}C NMR are reported in terms of chemical shifts (δ ppm). IR spectra were obtained on a Perkin Elmer Spectrum BXII spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). GC-FID analyses were obtained on an Agilent 6890N gas chromatograph equipped with a HP-5 (5%-phenyl)-methylpolysiloxane capillary column (Agilent). GC-MS analyses were obtained on an Agilent 6850 gas chromatograph equipped with a HP-5 (5%-phenyl)-

methylpolysiloxane capillary column (Agilent). High resolution mass spectra (HRMS) were acquired from the California Institute of Technology Mass Spectrometry Facility. ICP-MS analysis was conducted at the California Institute of Technology Mass Spectrometry Facility.

Silanes were purchased from Aldrich and distilled before use. KO*t*-Bu was purchased from Aldrich (sublimed grade, 99.99% trace metals basis) and used directly. KOH was purchased from Aldrich (semiconductor grade, pellets, 99.99% trace metals basis) and was pulverized (mortar and pestle) and heated (150 °C) under vacuum for 24 h prior to use. NaOH was purchased from Aldrich (semiconductor grade, pellets, 99.99% trace metals basis) and was pulverized (mortar and pestle) and heated (150 °C) under vacuum prior to use. Alkyne substrates were purchased from Aldrich, TCI, or Acros and used as received.

Procedure for ICP-MS analysis

Inductively coupled plasma mass spectrometry (ICP-MS) was performed on samples of NaOH, KOH, 3-cyclohexyl-1-propyne starting material (**39**), 1,2-dimethoxyethane (1,2-DME) solvent, $PhMe_2SiH$, and a standard reaction mixture that was run under optimized conditions in the glove box. The results from quantitative analysis revealed that most metal contaminants were present below the instrument's lowest limit of detection (i.e., in ppt range or lower). 1000 mg samples each of NaOH (99.99% Aldrich), 3-cyclohexyl-1-propyne, $PhMe_2SiH$, 1,2-dimethoxyethane, and a standard reaction mixture (0.5 mmol scale mixture, prepared following the general procedure with 61.1 mg of 3-cyclohexyl-1-propyne, 2 mg of NaOH, 204.4 mg of $PhMe_2SiH$ in 0.5 mL of 1,2-dimethoxyethane (DME) and stirred in the glovebox for 48 h) were analyzed (**Table 3.2**).

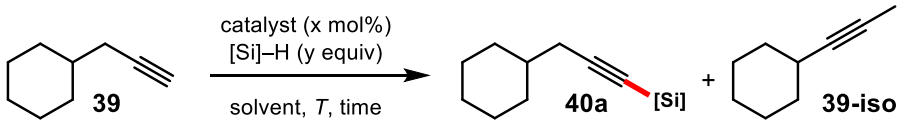
Each sample was added to a 50 mL DigiTUBE digestion tube (SCP Science) followed by addition of 3.0 mL of Plasma Pure nitric acid (SCP Science) and heating to 75 ^{o}C for 36 hours. After

digestion, each sample was diluted using Milli Q water to 50 mL and subjected to trace metal analysis. Trace metal concentrations were determined by Inductively Coupled Plasma Mass Spectrometry using an Agilent 8800. The sample introduction system consisted of a micromist nebulizer, scott type spray chamber and fixed injector quartz torch. A guard electrode was used and the plasma was operated at 1500 W. Elements were determined in single-quad mode with either no gas or helium (kinetic energy discrimination mode) in the collision cell. 33 elements were calibrated using external standard solutions ranging from 1 to 100 ppb (micrograms/L). Detection limits of trace elements of concern were below the 1 ppb standard. In addition Quick Scan data in helium mode data were calibrated semiquantitatively. LOD indicates that the analyte concentration is below the instrument's *Lowest Limit of Detection*. Values are in ppb unless otherwise stated.

Full optimization details for the alkali metal hydroxide−catalyzed C(sp)−H silylation

Procedure for reaction condition optimization: In a nitrogen-filled glovebox, catalyst and alkyne **39** (0.1 mmol, 1 equiv) were added to a 2 dram scintillation vial equipped with a magnetic stirring bar. Next, hydrosilane and solvent (0.1 mL) were added. The vial was sealed and the mixture was stirred at the indicated temperature for the indicated time. The vial was then removed from the glovebox, diluted with diethyl ether (1 mL), and concentrated under reduced pressure. The yield was determined by ^{1}H NMR or GC analysis of the crude mixture using an internal standard. The results from **Table 3.5** reveal that there is a high degree of tunability in the reaction conditions for the C(*sp*)–H silylation reaction. THF, dioxane, and DME all proved to be suitable solvents, with low amounts of the isomerized starting material produced (entries 2, 3, 4 respectively).

Table 3.5. Full optimization details of the C(*sp*)–H bond silylation of unbiased model terminal alkyne 39.



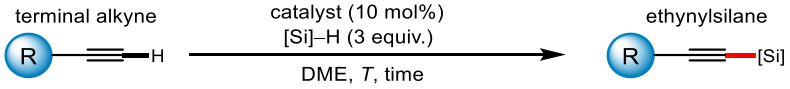
entry	catalyst	[Si]–H	solvent	*T* (°C)	time (h)	yield 40a[a]	yield 39-iso[a]
1	KO*t*-Bu (20 mol%)	Et_3SiH	–	85	72	**22%**	**60%**
2	KO*t*-Bu (20 mol%)	Et_3SiH	THF	85	72	**94%**	**1%**
3	KO*t*-Bu (20 mol%)	Et_3SiH	1,4-dioxane	85	72	**88%**	–
4	KO*t*-Bu (20 mol%)	Et_3SiH	DME	85	72	**>99%**	–
5	KO*t*-Bu (20 mol%)	Et_3SiH	MTBE	85	72	**30%**	**53%**
6	KO*t*-Bu (20 mol%)	Et_3SiH	toluene	85	72	**27%**	**59%**
7	KO*t*-Bu (20 mol%)	Et_3SiH	CyMe	85	72	**15%**	**66%**
8	KO*t*-Bu (20 mol%)	Et_3SiH	Pentane	85	72	**13%**	**74%**
9	KO*t*-Bu (20 mol%)	Et_3SiH	Mesitylene	85	72	**26%**	**56%**
10	KO*t*-Bu (20 mol%)	Et_3SiH	DCM	85	72	–	–
11	KO*t*-Bu (20 mol%)	Et_3SiH	Et_2O	85	72	**23%**	**61%**
12	KO*t*-Bu (20 mol%)	Et_3SiH	2-Me-THF	85	72	**48%**	**51%**
13	KO*t*-Bu (40 mol%)	Et_3SiH	DME	85	48	**89%**	–
14	KO*t*-Bu (20 mol%)	Et_3SiH	DME	85	48	**99%**	–
15	KO*t*-Bu (10 mol%)	Et_3SiH	DME	85	48	**>99%**	–
16	KO*t*-Bu (5 mol%)	Et_3SiH	DME	85	48	**99%**	**<1%**
17	KO*t*-Bu (1 mol%)	Et_3SiH	DME	85	48	**97%**	**2%**
18	KO*t*-Bu (10 mol%)	Et_3SiH	DME	25	48	**7%**	**63%**
19	KO*t*-Bu (10 mol%)	Et_3SiH	DME	55	48	**59%**	**30%**

entry	catalyst	[Si]–H	solvent	*T* (°C)	time (h)	yield 40a[a]	yield 39-iso[a]
20	KH (20 mol%)	Et_3SiH	DME	85	72	**99%**	–
21	KHMDS (20 mol%)	Et_3SiH	DME	85	72	**99%**	**<1%**
22	NaO*t*-Bu (20 mol%)	Et_3SiH	DME	85	72	**51%**	**40%**
23	LiO*t*-Bu (20 mol%)	Et_3SiH	DME	85	72	**<1%**	**5%**
24	DABCO (20 mol%)	Et_3SiH	DME	85	72	**<1%**	–
25	NaOEt (20 mol%)	Et_3SiH	DME	85	72	**82%**	**<1%**
26	KOEt (20 mol%)	Et_3SiH	DME	85	72	**99%**	**<1%**
27	NaOAc (20 mol%)	Et_3SiH	DME	85	72	**<1%**	–
28	KOAc (20 mol%)	Et_3SiH	DME	85	72	**<1%**	–
29	KOMe (20 mol%)	Et_3SiH	DME	85	72	**98%**	**<1%**
30	NaOMe (20 mol%)	Et_3SiH	DME	85	72	**95%**	**3%**
31	KO*t*-Amyl (20 mol%)	Et_3SiH	DME	85	72	**>99%**	**<1%**
32	KOH (20 mol%)	Et_3SiH	DME	85	72	**94%**	**<1%**
33	K_2CO_3 (20 mol%)	Et_3SiH	DME	85	72	**<1%**	–
34	Cs_2CO_3 (20 mol%)	Et_3SiH	DME	85	72	–	–
35	KF (20 mol%)	Et_3SiH	DME	85	72	**<1%**	–
36	KO*t*-Bu (10 mol%)	Et_3SiH	DME	85	24	**89%**	**9%**
37	KH (10 mol%)	Et_3SiH	DME	85	24	**87%**	**11%**
38	NaO*t*-Bu (10 mol%)	Et_3SiH	DME	85	24	**46%**	**2%**
39	LiO*t*-Bu (10 mol%)	Et_3SiH	DME	85	24	**<1%**	–
40	KOEt (10 mol%)	Et_3SiH	DME	85	24	**96%**	**2%**
41	NaOEt (10 mol%)	Et_3SiH	DME	85	24	**91%**	**<1%**
42	KOMe (10 mol%)	Et_3SiH	DME	85	24	**96%**	**4%**
43	NaOMe (10 mol%)	Et_3SiH	DME	85	24	**83%**	**<1%**
44	KO*t*-Amyl (10 mol%)	Et_3SiH	DME	85	24	**91%**	**6%**
45	KOH (10 mol%)	Et_3SiH	DME	85	24	**95%**	**3%**
46	NaOH (10 mol%)	Et_3SiH	DME	85	24	**98%**	–
47	LiOH (10 mol%)	Et_3SiH	DME	85	24	**3%**	–
48	Et_3N (10 mol%)	Et_3SiH	DME	85	48	**4%**	–
49	Pyridine(10 mol%)	Et_3SiH	DME	85	48	**1%**	–
50	KOH (10 mol%)	Et_3SiH (1.0 eq)	DME	85	48	**71%**	**21%**
51	KOH (10 mol%)	Et_3SiH (1.5 eq)	DME	85	48	**92%**	**6%**
52	KOH (10 mol%)	Et_3SiH (2.0 eq)	DME	85	48	**93%**	**6%**
53	KOH (10 mol%)	Et_3SiH (2.5 eq)	DME	85	48	**97%**	**2%**
54	KOH (10 mol%)	Et_3SiH (3.0 eq)	DME	85	48	**98%**	**1%**
55	KOH (10 mol%)	Et_3SiH (3.5 eq)	DME	85	48	**99%**	**1%**
56	KOH (10 mol%)	Et_3SiH (4.0 eq)	DME	85	48	**97%**	**2%**

[a]Yields determined by GC analysis of the crude reaction mixture using an internal standard.

Low loadings of catalyst were achieved with KO*t*-Bu, down to 1 mol%, without significant loss of yield (entries 15–17). High temperatures (85 °C) proved necessary for silylation with triethylsilane (entries 15, 18, 19); as seen in the silane screen in the text, the reaction proceeded at lower temperatures when employing various other silanes. The extensive base screen (entries 20–35) with longer reaction times (72 h) showed that there are a number of good catalysts for the C–H silylation reaction. A refined base screen with lower catalyst loading (entries 36–49) revealed that there were still several catalysts that performed with surprisingly high efficiency, but NaOH proved to be the most convenient and high-performing catalyst. No product was observed in the absence of catalyst, or when LiO*t*-Bu, NaOAc, KOAc, DABCO, K_2CO_3, Cs_2CO_3, or KF were employed (entries 39, 27, 28, 24, 33, 34, 35 respectively).

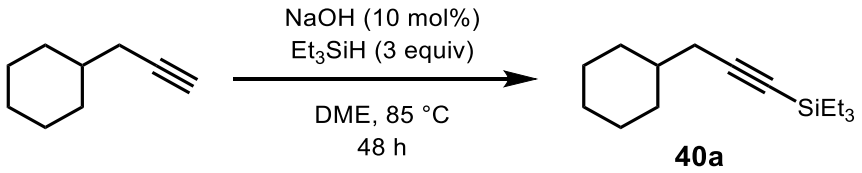
General procedure for alkali-metal hydroxide–catalyzed silylation of heteroaromatics



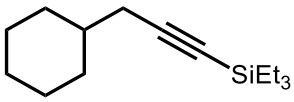
In a nitrogen-filled glove box, catalyst (0.05 mmol, 10 mol%) and alkyne (0.5 mmol, 1 equiv) were added to a 2 dram scintillation vial equipped with a magnetic stirring bar, followed by solvent (0.5 mL) and silane (1.5 mmol, 3 equiv). The vial was then sealed and the mixture was stirred at the indicated temperature for the indicated time. The vial was then removed from the glove box; the reaction mixture was diluted with diethyl ether (2 mL), filtered through a short pad of silica gel, and concentrated under reduced pressure. Volatiles were removed under high vacuum with heating as indicated and the resultant material was purified by silica gel flash chromatography if necessary to give the desired C(*sp*)–Si product.

The reaction can likewise be comfortably performed outside of the glovebox using simple air-free technique and non-degassed solvents under a nitrogen or argon atmosphere on both small and large (i.e., see **Scheme 3.4, multi-gram scale synthesis of **42s**) scales. However, in the case of small scale preparations especially, particular care must be given to ensure that weighing of the hygroscopic catalysts in air is rapid such that moisture does not enter the system. If rigorous exclusion of moisture is not achieved, the presence of oxidized silanes is sometimes observed (i.e., silanols, siloxanes, only in the case of certain silanes), but this does not generally appear to impact the product yield.*

Characterization

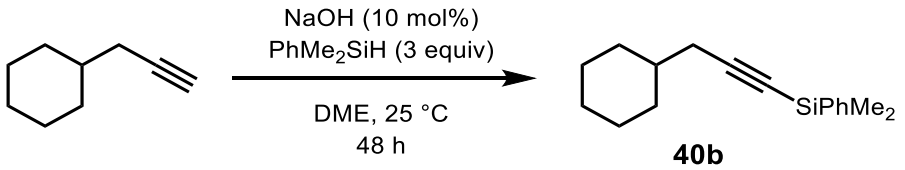


40a

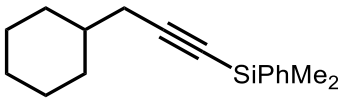


(3-Cyclohexylprop-1-yn-1-yl)triethylsilane 40a: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), Et_3SiH (174 mg, 240 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 85 °C for 48 h. The desired product **40a** (111.9 mg, 95% yield) was obtained as a colorless oil in analytical purity after removal of volatiles under high vacuum (45 mtorr, 2 hours). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.13 (d, *J* = 6.6 Hz, 2H), 1.84 – 1.76 (m, 2H), 1.75 – 1.68 (m, 2H), 1.65 (dtt, *J* = 12.9, 3.4, 1.5 Hz, 1H), 1.47 (dddd, *J* = 14.8, 6.8, 4.7, 3.4 Hz, 1H),

1.24 (tdd, *J* = 15.9, 9.4, 3.4 Hz, 2H), 1.19 – 1.07 (m, 2H), 1.07 – 1.01 (m, 1H), 0.98 (t, *J* = 7.9 Hz, 9H), 0.57 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 107.73, 82.39, 37.54, 32.72, 27.86, 26.47, 26.32, 7.65, 4.75. IR (Neat Film NaCl) 3422, 2925, 2172, 1645, 1449, 1018, 802, 724 cm^{-1}; HRMS (EI+) calc'd for $C_{15}H_{27}Si$ [(M+H)–H_2]: 235.1882, found 235.1881.

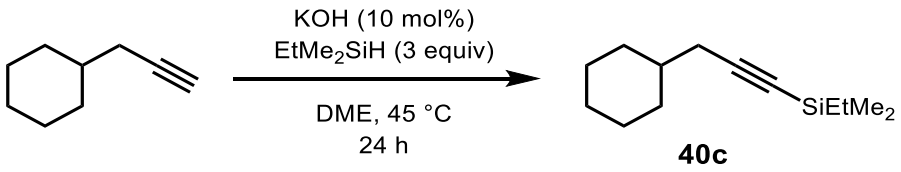


40b

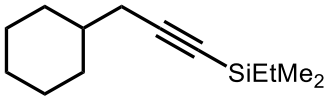


(3-Cyclohexylprop-1-yn-1-yl)dimethyl(phenyl)silane 40b: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 25 °C for 48 h. The desired product **40b** (113.6 mg, 89% yield) was obtained as a colorless oil after removal of volatiles by heating to 85°C at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.67 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 – 7.63 (m, 2H), 7.40 – 7.34 (m, 3H), 2.19 (d, *J* = 6.6 Hz, 2H), 1.87 – 1.80 (m, 2H), 1.74 (dt, *J* = 12.8, 3.3 Hz, 2H), 1.67 (dddd, *J* = 11.3, 5.2, 3.3, 1.6 Hz, 1H), 1.52 (ddtd, *J* = 14.9, 11.5, 6.7, 3.5 Hz, 1H), 1.27 (dddd, *J* = 15.9, 12.6, 9.5, 3.3 Hz, 2H), 1.15 (qt, *J* = 12.7, 3.3 Hz, 1H), 1.08 – 0.98 (m, 2H), 0.41 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.93, 133.81, 129.33, 127.91, 108.67, 83.19, 37.42, 32.81, 27.94, 26.42, 26.29, –0.38. IR (Neat Film NaCl) 3420, 2924, 2852, 2173, 1646, 1448, 1427, 1322, 1248,

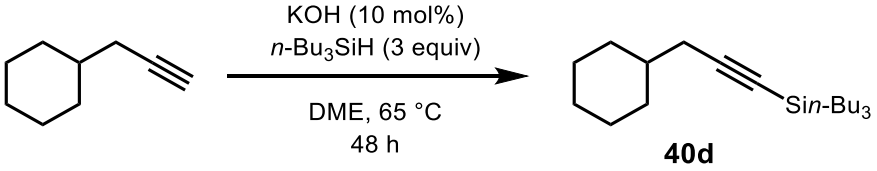
1115, 1071, 1027, 815, 730 cm^{-1}; HRMS (EI+) calc'd for $C_{17}H_{25}Si$ [M+H]: 257.1726, found 257.1720.



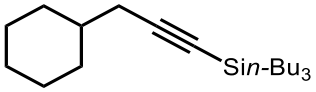
40c



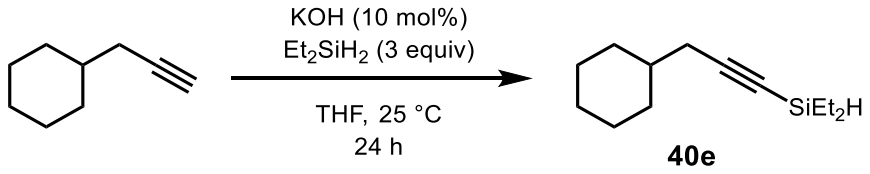
(3-Cyclohexylprop-1-yn-1-yl)(ethyl)dimethylsilane 40c: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), $EtMe_2SiH$ (132 mg, 198 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 24 h. The desired product **40c** (95.1 mg, 91% yield) was obtained as a colorless oil in analytical purity after removal of volatiles under high vacuum (45 mtorr, 2 hours). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.12 (d, *J* = 6.6 Hz, 2H), 1.86 – 1.76 (m, 2H), 1.77 – 1.69 (m, 2H), 1.66 (dtd, *J* = 12.6, 3.3, 1.6 Hz, 1H), 1.53 – 1.40 (m, 1H), 1.32 – 1.19 (m, 2H), 1.20 – 1.07 (m, 2H), 1.06 – 0.94 (m, 4H), 0.57 (q, *J* = 7.9 Hz, 2H), 0.12 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 107.01, 84.30, 37.46, 32.76, 27.84, 26.45, 26.30, 8.47, 7.50, –1.85. IR (Neat Film NaCl) 3422, 2922, 2103, 1646, 1558, 1260, 1027, 720 cm^{-1}; HRMS (EI+) calc'd for $C_{13}H_{23}Si$ [(M+H)–H_2]: 207.1569, found 207.1562.

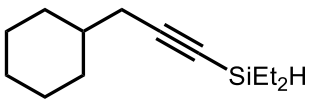


40d



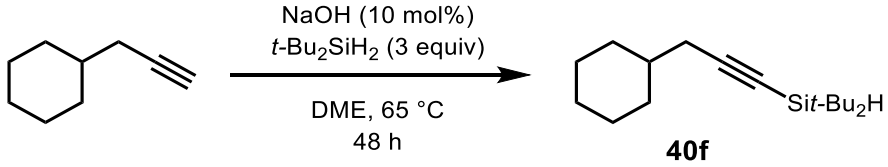
Tributyl(3-cyclohexylprop-1-yn-1-yl)silane 40d: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), *n*-Bu_3SiH (301 mg, 386 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **40d** (117.2 mg, 73% yield) was obtained as a colorless oil by silica gel flash chromatography (100% hexanes). R_f = 0.78 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.18 (d, *J* = 6.5 Hz, 2H), 1.85 (dddd, *J* = 12.3, 6.2, 3.1, 1.8 Hz, 2H), 1.77 (ddd, *J* = 14.0, 4.5, 2.3 Hz, 2H), 1.70 (dddt, *J* = 12.8, 5.1, 3.3, 1.5 Hz, 1H), 1.52 (dddt, *J* = 14.5, 7.9, 6.6, 3.2 Hz, 1H), 1.43 – 1.36 (m, 12H), 1.29 (qt, *J* = 12.6, 3.3 Hz, 2H), 1.18 (qt, *J* = 12.7, 3.3 Hz, 1H), 1.11 – 1.02 (m, 2H), 0.97 – 0.91 (m, 9H), 0.67 – 0.59 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 107.65, 83.25, 37.57, 32.72, 27.88, 26.64, 26.46, 26.39, 26.32, 13.98, 13.45. IR (Neat Film NaCl) 2955, 2922, 2854, 2172, 1449, 1376, 1191, 1080, 1029, 886, 758, 708 cm^{-1}; HRMS (EI+) calc'd for $C_{21}H_{40}Si$ [M+·]: 320.2899, found 320.2905.

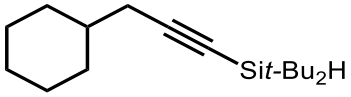




(3-Cyclohexylprop-1-yn-1-yl)diethylsilane 40e: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg,

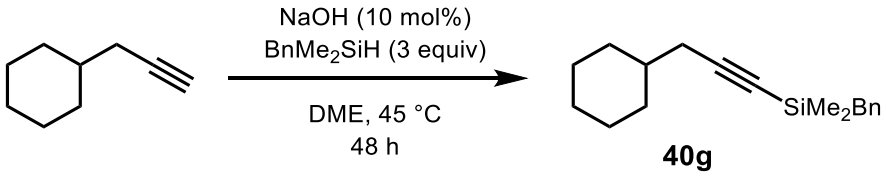
0.5 mmol, 1.0 equiv), Et_2SiH_2 (132 mg, 194 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of tetrahydrofuran (THF) at 25 °C for 24 h. The desired product **40e** (73.6 mg, 71% yield) was obtained in as a colorless oil after removal of volatiles under high vacuum at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.77 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.92 (pt, *J* = 3.2, 1.2 Hz, 1H), 2.15 (dd, *J* = 6.7, 1.2 Hz, 2H), 1.85 – 1.78 (m, 2H), 1.72 (ddd, *J* = 13.9, 4.5, 2.2 Hz, 2H), 1.66 (dddt, *J* = 12.7, 5.1, 3.3, 1.5 Hz, 1H), 1.49 (ddtd, *J* = 14.9, 11.5, 6.8, 3.5 Hz, 1H), 1.31 – 1.20 (m, 2H), 1.15 (tt, *J* = 12.6, 3.2 Hz, 1H), 1.07 – 0.95 (m, 8H), 0.70 – 0.64 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 109.00, 80.24, 37.39, 32.76, 27.91, 26.41, 26.28, 8.09, 4.23. IR (Neat Film NaCl) 3422, 2957, 2174, 2120, 1646, 1558, 1457, 1260, 1055, 804 cm^{-1}; HRMS (EI+) calc'd for $C_{13}H_{23}Si$ [(M+H)-H_2]: 207.1569, found 207.1562.



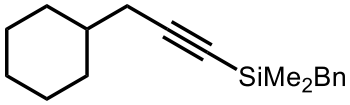


Di-tert-butyl(3-cyclohexylprop-1-yn-1-yl)silane 40f: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), *t*-Bu_2SiH_2 (216 mg, 297 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **40f** (120.3 mg, 91% yield) was obtained as a colorless oil after removal of volatiles under high vacuum at 45 mtorr for 30 minutes

and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.88 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.57 (t, J = 1.2 Hz, 1H), 2.17 (dd, J = 6.5, 1.2 Hz, 2H), 1.84 – 1.78 (m, 2H), 1.76 – 1.70 (m, 2H), 1.66 (dddt, J = 12.8, 5.1, 3.3, 1.5 Hz, 1H), 1.50 (dddt, J = 14.5, 7.8, 6.5, 3.1 Hz, 1H), 1.26 (qt, J = 12.7, 3.4 Hz, 3H), 1.19 – 1.09 (m, 2H), 1.06 (s, 18H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 108.94, 79.54, 37.51, 32.75, 28.28, 27.88, 26.44, 26.29, 18.63. IR (Neat Film NaCl) 2958, 2927, 2855, 2173, 2111, 1469, 1449, 1363, 1028, 1012, 810, 793, 617 cm^{-1}; HRMS (EI+) calc'd for $C_{17}H_{31}Si$ [(M+H)-H_2]: 263.2195, found 263.2206.

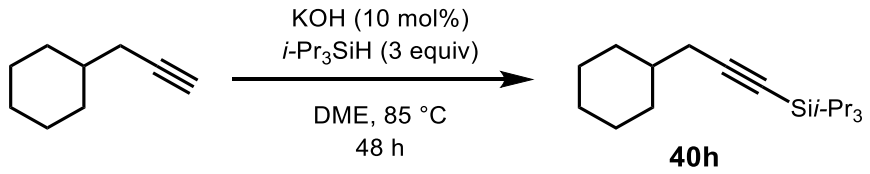


40g

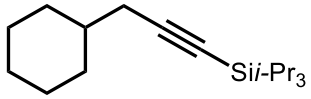


Benzyl(3-cyclohexylprop-1-yn-1-yl)dimethylsilane 40g: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), $BnMe_2SiH$ (150 mg, 238 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **40g** (101.9 mg, 75% yield) was obtained as a colorless oil by silica gel flash chromatography (100% hexanes). R_f = 0.51 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.21 (m, 2H), 7.12 – 7.08 (m, 3H), 2.20 (s, 2H), 2.14 (d, *J* = 6.8 Hz, 2H), 1.81 (ddd, *J* = 13.3, 3.5, 1.5 Hz, 2H), 1.75 (dt, *J* = 12.7, 3.2 Hz, 2H), 1.69 (dddd, *J* = 11.3, 5.3, 3.4, 1.7 Hz, 1H), 1.49 (tdt, *J* = 11.4, 6.7, 3.3 Hz, 1H), 1.28 (qt, *J* = 12.6, 3.3 Hz, 2H), 1.16 (qt, *J* = 12.7, 3.3 Hz, 1H), 1.06 – 0.94 (m, 2H), 0.13 (s, 6H); ^{13}C NMR (126 MHz,

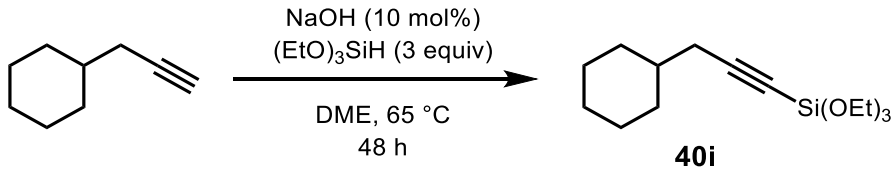
$CDCl_3$) δ 139.44, 128.51, 128.19, 124.32, 108.08, 83.69, 37.38, 32.77, 27.86, 26.71, 26.41, 26.29, –1.69. IR (Neat Film NaCl) 3081, 3060, 3024, 2999, 2922, 2851, 2664, 2173, 1936, 1600, 1493, 1449, 1422, 1408, 1368, 1322, 1249, 1207, 1155, 1056, 1029, 947, 839, 761, 697 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{26}Si$ [M+•]: 270.1804, found 270.1810.



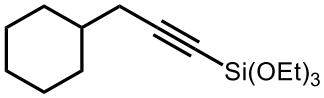
40h



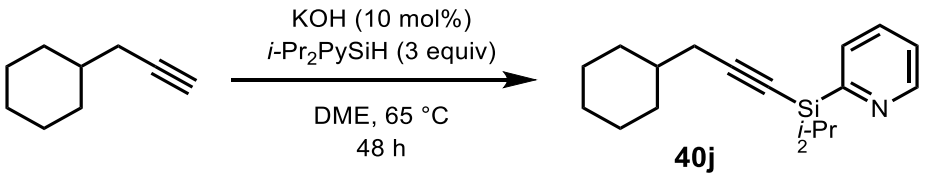
(3-Cyclohexylprop-1-yn-1-yl)triisopropylsilane 40h: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), *i*-Pr_3SiH (238 mg, 307 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 85 °C for 48 h. The desired product **40h** (95.6 mg, 69% yield) was obtained as a colorless oil by silica gel flash chromatography (100% hexanes). R_f = 0.79 (100% hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 2.16 (d, *J* = 6.4 Hz, 2H), 1.84 – 1.77 (m, 2H), 1.73 (dt, *J* = 12.8, 3.4 Hz, 2H), 1.66 (dtd, *J* = 12.7, 3.3, 1.6 Hz, 1H), 1.48 (ddtd, *J* = 14.6, 11.2, 6.5, 3.4 Hz, 1H), 1.25 (qt, *J* = 12.6, 3.4 Hz, 2H), 1.15 (tt, *J* = 12.6, 3.3 Hz, 1H), 1.10 – 0.99 (m, 23H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 108.17, 80.94, 37.64, 32.71, 27.87, 26.49, 26.33, 18.80, 11.48. IR (Neat Film NaCl) 2924, 2864, 2170, 2463, 1449, 1264, 1025, 995, 883, 743, 676, 633 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{33}Si$ [(M+H)-H_2]: 277.2352, found 277.2349.



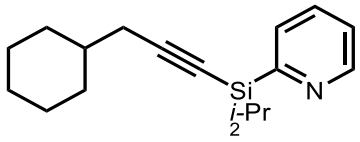
40i



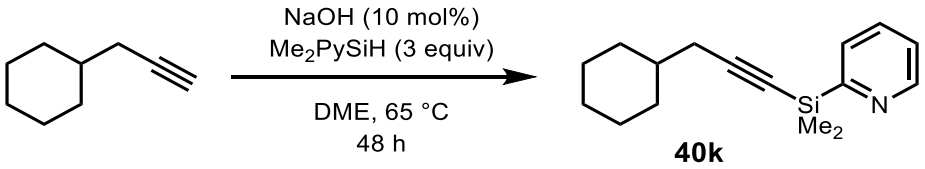
(3-Cyclohexylprop-1-yn-1-yl)triethoxysilane 40i: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), $(EtO)_3SiH$ (246 mg, 277 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **40i** (97.1 mg, 68% yield) was obtained as a colorless oil by silica gel flash chromatography (5% Et_2O in hexanes). R_f = 0.41 (5% Et_2O in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (q, *J* = 7.0 Hz, 6H), 2.16 (d, *J* = 6.6 Hz, 2H), 1.84 – 1.78 (m, 2H), 1.72 (dp, *J* = 12.6, 3.7 Hz, 2H), 1.66 (dddt, *J* = 12.8, 5.1, 3.3, 1.5 Hz, 1H), 1.52 (ddtd, *J* = 14.9, 11.5, 6.8, 3.5 Hz, 1H), 1.26 (t, *J* = 7.0 Hz, 9H), 1.24 – 1.19 (m, 2H), 1.13 (qt, *J* = 12.7, 3.3 Hz, 1H), 1.02 (qd, *J* = 12.7, 3.5 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 106.50, 76.85, 59.02, 37.10, 32.74, 27.55, 26.33, 26.20, 18.18. IR (Neat Film NaCl) 2974, 2925, 2852, 2182, 1449, 1390, 1168, 1101, 1079, 1036, 964, 790, 721 cm^{-1}; HRMS (EI+) calc'd for $C_{15}H_{29}O_3Si$ [M+H]: 285.1886, found 285.1889.

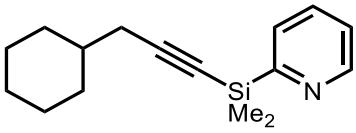


40j

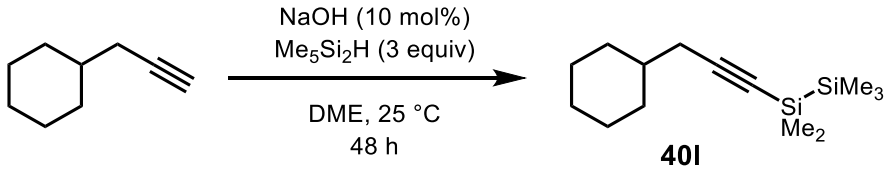


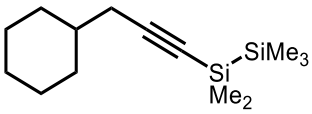
2-((3-Cyclohexylprop-1-yn-1-yl)diisopropylsilyl)pyridine 40j: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), *i*-Pr_2(Pyr)SiH (290 mg, 322 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **40j** (122.5 mg, 78% yield) was obtained as a colorless oil by silica gel flash chromatography (10% EtOAc in hexanes). R_f = 0.47 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, THF-d_8) δ 8.65 (ddd, *J* = 4.8, 1.7, 1.1 Hz, 1H), 7.76 (dt, *J* = 7.5, 1.3 Hz, 1H), 7.59 (td, *J* = 7.6, 1.8 Hz, 1H), 7.19 (ddd, *J* = 7.7, 4.8, 1.4 Hz, 1H), 2.26 (d, *J* = 6.4 Hz, 2H), 1.95 – 1.84 (m, 2H), 1.78 – 1.73 (m, 2H), 1.67 (dtt, J = 13.0, 3.4, 1.6 Hz, 1H), 1.55 (ddtd, *J* = 14.9, 11.4, 6.6, 3.5 Hz, 1H), 1.37 – 1.26 (m, 4H), 1.21 – 1.16 (m, 1H), 1.16 – 1.11 (m, 2H), 1.09 (d, *J* = 7.4 Hz, 6H), 0.99 (d, *J* = 7.3 Hz, 6H); ^{13}C NMR (126 MHz, THF-d_8) δ 164.80, 150.76, 134.42, 132.12, 123.73, 110.50, 80.33, 38.63, 33.66, 28.41, 27.38, 27.23, 18.46, 18.40, 12.71. IR (Neat Film NaCl) 2924, 2862, 2170, 1573, 1462, 1449, 1417, 1136, 1081, 1028, 995, 882, 747, 723 cm^{-1}; HRMS (EI+) calc'd for $C_{20}H_{32}NSi$ [M+H]: 314.2304, found 314.2311.



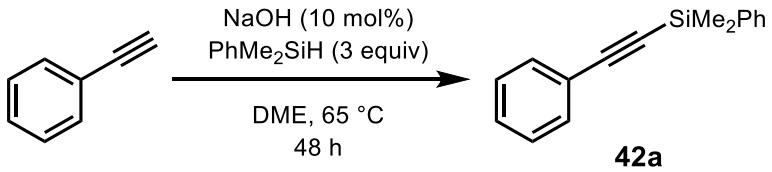


2-((3-Cyclohexylprop-1-yn-1-yl)dimethylsilyl)pyridine 40k: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), Me_2(Py)SiH (206 mg, 225 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **40k** (99.9 mg, 78% yield) was obtained as a colorless oil by silica gel flash chromatography (10% EtOAc in hexanes). R_f = 0.42 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, THF-d_8) δ 8.65 (ddd, *J* = 4.8, 1.8, 1.1 Hz, 1H), 7.74 (dt, *J* = 7.5, 1.2 Hz, 1H), 7.59 (td, *J* = 7.6, 1.8 Hz, 1H), 7.18 (ddd, *J* = 7.7, 4.8, 1.4 Hz, 1H), 2.19 (d, *J* = 6.6 Hz, 2H), 1.88 – 1.81 (m, 2H), 1.73 – 1.70 (m, 2H), 1.66 (dddd, *J* = 12.7, 5.1, 3.2, 1.5 Hz, 1H), 1.50 (dddt, *J* = 14.7, 7.9, 6.7, 3.2 Hz, 1H), 1.28 (tdd, *J* = 16.0, 9.4, 3.4 Hz, 2H), 1.17 (qt, *J* = 12.7, 3.3 Hz, 1H), 1.05 (qd, *J* = 12.8, 3.4 Hz, 2H), 0.36 (s, 6H); ^{13}C NMR (126 MHz, THF-d_8) δ 166.55, 150.96, 134.69, 130.13, 123.84, 109.23, 83.58, 38.47, 33.68, 28.42, 27.34, 27.22, –1.00. IR (Neat Film NaCl) 3423, 2924, 2852, 2175, 1646, 1449, 1255, 1044, 832, 797, 676 cm^{-1}; HRMS (EI+) calc'd for $C_{16}H_{24}NSi$ [M+H]: 258.1678, found 258.1672.

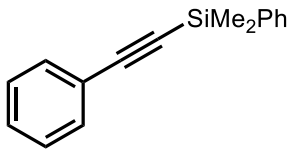




1-(3-Cyclohexylprop-1-yn-1-yl)-1,1,2,2,2-pentamethyldisilane 40l: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), Me_5Si_2H (246 mg, 277 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 25 °C for 48 h. The desired product **40l** (120.0 mg, 95% yield) was obtained in analytical purity as a cloudy, colorless oil after removal of volatiles at 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, THF-d_8) δ 2.11 (d, J = 6.5 Hz, 2H), 1.81 (dddd, J = 13.1, 6.1, 3.1, 1.9 Hz, 2H), 1.73 – 1.69 (m, 2H), 1.65 (dddt, J = 12.7, 5.1, 3.2, 1.5 Hz, 1H), 1.44 (dddt, J = 14.6, 8.0, 6.7, 3.2 Hz, 1H), 1.33 – 1.21 (m, 2H), 1.15 (qt, J = 12.7, 3.2 Hz, 1H), 1.03 (qd, J = 12.8, 3.5 Hz, 2H), 0.15 (s, 6H), 0.11 (s, 9H); ^{13}C NMR (126 MHz, THF-d_8) δ 109.11, 84.06, 38.62, 33.61, 28.52, 27.37, 27.22, –2.25, –2.35. IR (Neat Film NaCl) 2923, 2852, 2168, 1449, 1259, 1244, 1077, 1027, 871, 833, 799, 765, 725, 691, 667 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{28}Si_2$ [M+•]: 252.1730, found 252.1737.

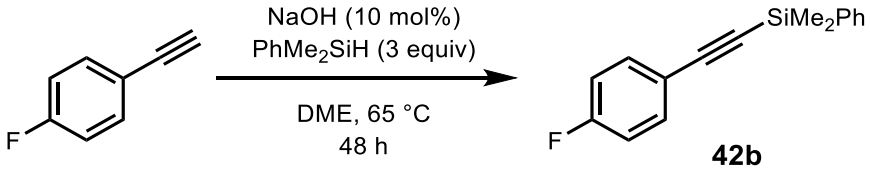


42a

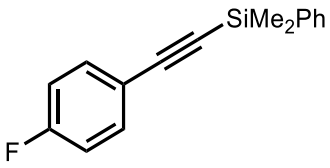


Dimethyl(phenyl)(phenylethynyl)silane 42a: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), ethynylbenzene (52 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane

(DME) at 65 °C for 48 h. The desired product **42a** (105.7 mg, 89% yield) was obtained as a colorless oil after removal of volatiles by heating to 85°C at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.38 (100% hexanes); ^{1}H NMR (500 MHz, THF-d_8) δ 7.71 – 7.65 (m, 2H), 7.49 – 7.44 (m, 2H), 7.38 – 7.28 (m, 6H), 0.46 (s, 6H). ^{13}C NMR (126 MHz, THF-d_8) δ 137.86, 134.66, 132.88, 130.35, 129.75, 129.28, 128.79, 124.15, 107.86, 92.55, –0.50. IR (Neat Film NaCl) 3068, 3051, 2959, 2899, 2158, 1592, 1488, 1442, 1428, 1278, 1250, 1219, 1118, 1068, 1026, 846, 807, 780, 731, 690 cm^{-1}; HRMS (EI+) calc'd for $C_{16}H_{17}Si$ [M+H]: 237.1100, found 237.1101.

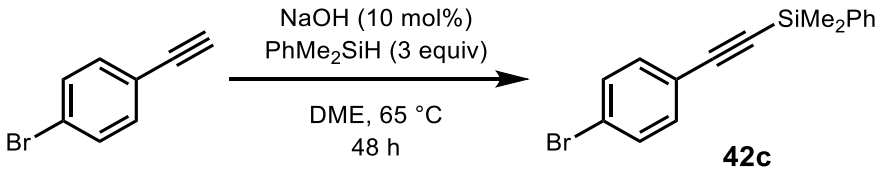


42b

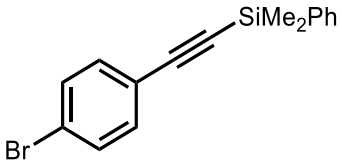


((4-Fluorophenyl)ethynyl)dimethyl(phenyl)silane 42b: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 1-ethynyl-4-fluorobenzene (60 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **42b** (111.9 mg, 88% yield) was obtained as a colorless oil after solvent removal at 85°C at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.49 (100% hexanes); ^{1}H NMR (500 MHz, THF-d_8) δ 7.68 – 7.65 (m, 2H), 7.53 – 7.48 (m, 2H), 7.34 (dd, *J* =

4.9, 1.9 Hz, 3H), 7.08 (t, *J* = 8.8 Hz, 2H), 0.46 (s, 6H); ^{13}C NMR (126 MHz, THF-d_8) δ 163.94 (d, J = 249.1 Hz), 137.74, 135.10 (d, J = 8.5 Hz), 134.65, 130.38, 128.80, 120.42 (d, J = 3.8 Hz), 116.50 (d, J = 21.7 Hz), 106.67, 92.42, -0.57. IR (Neat Film NaCl) 3420, 3069, 2961, 2160, 1653, 1600, 1505, 1428, 1251, 1233, 1155, 1117, 1092, 857, 835, 816, 781, 731, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{16}H_{16}FSi$ [M+H]: 255.1005, found 255.1000.

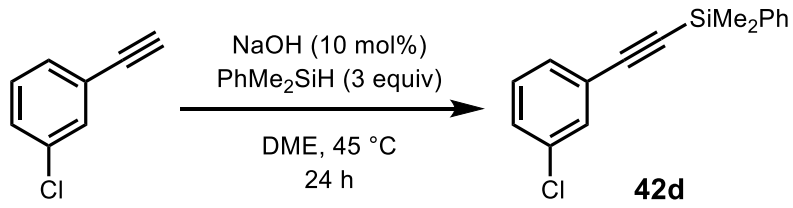


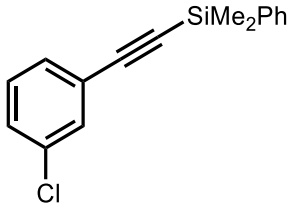
42c



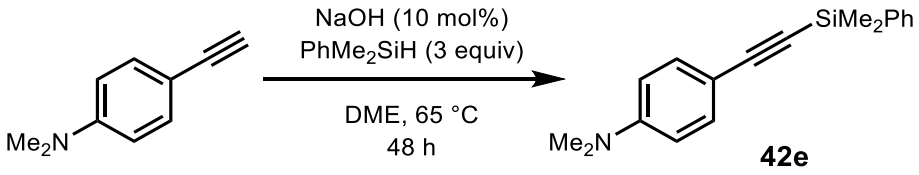
((4-Bromophenyl)ethynyl)dimethyl(phenyl)silane 42c: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 1-bromo-4-ethynylbenzene (90 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **42c** (81.3 mg, 52% yield) was obtained as colorless crystals after solvent removal at 85°C at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.54 (100% hexanes); ^{1}H NMR (500 MHz, THF-d_8) δ 7.69 – 7.63 (m, 2H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 2H), 7.36 – 7.30 (m, 3H), 0.46 (s, 6H); ^{13}C NMR (126 MHz, THF-d_8) δ 137.55, 134.65, 134.53, 132.66, 130.44, 128.83, 123.94, 123.19, 106.51, 94.19, –0.66. IR (Neat Film NaCl)

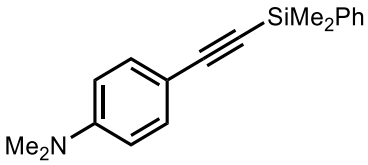
3068, 2958, 2159, 1653, 1540, 1484, 1473, 1457, 1427, 1249, 1214, 1114, 1071, 1010, 846, 830, 780, 730, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{16}H_{16}Si^{18}Br$ [M+H]: 317.0184, found 317.0180.



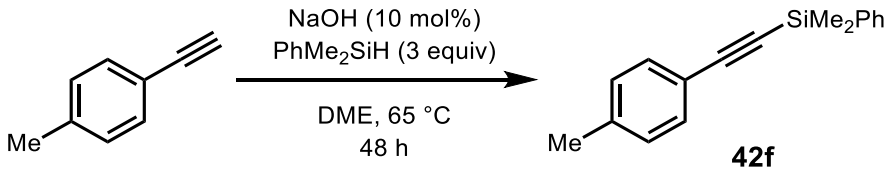


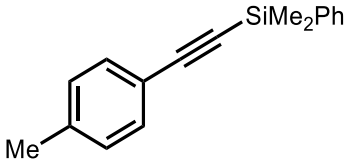
((3-Chlorophenyl)ethynyl)dimethyl(phenyl)silane 42d: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 1-chloro-3-ethynylbenzene (68 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 24 h. The desired product **42d** (121.6 mg, 90% yield) was obtained as a colorless oil after solvent removal at 85°C at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.42 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.66 (m, 2H), 7.49 (ddd, *J* = 2.1, 1.5, 0.5 Hz, 1H), 7.40 (dd, *J* = 5.0, 1.9 Hz, 3H), 7.38 (dt, *J* = 7.6, 1.4 Hz, 1H), 7.31 (ddd, *J* = 8.1, 2.1, 1.2 Hz, 1H), 7.24 (ddd, *J* = 8.0, 7.6, 0.5 Hz, 1H), 0.51 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.75, 134.21, 133.86, 132.05, 130.29, 129.70, 129.61, 129.12, 128.10, 124.77, 105.13, 93.82, –0.79. IR (Neat Film NaCl) 3420, 2163, 1684, 1647, 1559, 1521, 1507, 1457, 1249, 1117, 1091, 884, 781, 681 cm^{-1}; HRMS (EI+) calc'd for $C_{16}H_{16}ClSi$ [M+H]: 271.0710, found 271.0710.



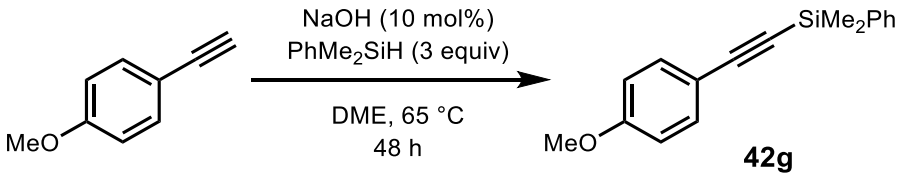


4-((Dimethyl(phenyl)silyl)ethynyl)-N,N-dimethylaniline 42e: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 4-ethynyl-N,N-dimethylaniline (73 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **42e** (139.4 mg, 100% yield) was obtained in analytical purity as colourless crystals after removal of volatiles at 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 – 7.68 (m, 2H), 7.41 – 7.36 (m, 5H), 6.61 (d, J = 8.9 Hz, 2H), 2.98 (s, 6H), 0.48 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.46, 137.88, 133.93, 133.38, 129.36, 127.94, 111.69, 109.78, 108.49, 89.19, 40.32, -0.39. IR (Neat Film NaCl) 3067, 2957, 2147, 1682, 1607, 1519, 1487, 1427, 1360, 1248, 1186, 1115, 945, 850, 817, 779, 730, 699, 653 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{21}NSi$ [M+•]: 279.1443, found 279.1445.

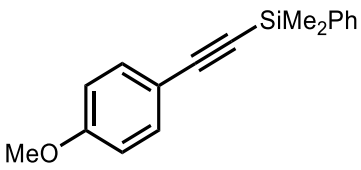




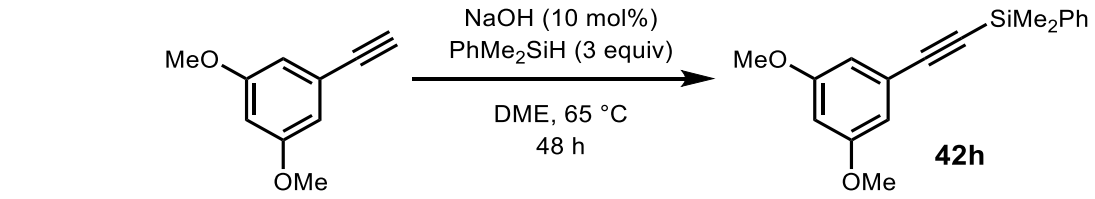
Dimethyl(phenyl)(*p*-tolylethynyl)silane 42f: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 1-ethynyl-4-methylbenzene (58 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **42f** (115.5 mg, 92% yield) was obtained in analytical purity as a pale yellow oil after removal of volatiles at 85°C at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.46 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (ddt, *J* = 6.0, 2.4, 1.1 Hz, 2H), 7.41 (ddq, *J* = 5.8, 3.0, 0.9 Hz, 5H), 7.16 – 7.10 (m, 2H), 2.37 (s, 3H), 0.51 (d, *J* = 1.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.02, 137.33, 133.90, 132.10, 129.52, 129.12, 128.02, 120.00, 107.18, 91.28, 21.69, –0.59. IR (Neat Film NaCl) 3420, 3068, 3049, 2959, 2920, 2156, 1507, 1428, 1408, 1249, 1223, 1117, 1020, 851, 816, 780, 731, 700, 656 cm^{-1}; HRMS (EI+) calc'd for $C_{17}H_{19}Si$ [M+H]: 251.1256, found 251.1257.

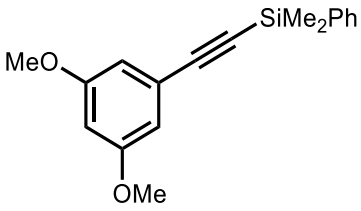


42g



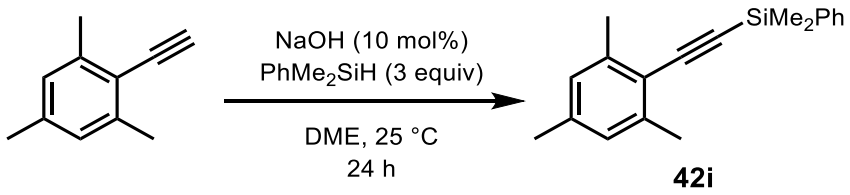
((4-Methoxyphenyl)ethynyl)dimethyl(phenyl)silane 42g: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 1-ethynyl-4-methoxybenzene (66 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **42g** (121.6 mg, 91% yield) was obtained as a yellow oil after removal of volatiles at 85°C at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (100% hexanes → 5% EtOAc in hexanes). R_f = 0.27 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 6.5, 3.0 Hz, 2H), 7.46 (d, *J* = 8.9 Hz, 2H), 7.43 – 7.38 (m, 3H), 6.84 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H), 0.51 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.02, 137.42, 133.89, 133.73, 129.50, 128.01, 115.20, 113.96, 107.03, 90.47, 55.42, -0.56. IR (Neat Film NaCl) 3068, 2959, 2154, 1605, 1507, 1441, 1293, 1249, 1171, 1116, 1032, 853, 832, 812, 779, 755, 731, 699 cm^{-1}; HRMS (EI+) calc'd for $C_{17}H_{18}OSi$ [M+•]: 266.1127, found 266.1135.



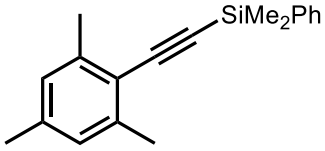


((3,5-Dimethoxyphenyl)ethynyl)dimethyl(phenyl)silane 42h: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 1-ethynyl-3,5-dimethoxybenzene (81 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0

equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **42h** (140.6 mg, 95% yield) was obtained in analytical purity as a light yellow oil after removal of volatiles at 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (ddd, *J* = 5.5, 2.7, 1.2 Hz, 2H), 7.41 (dd, *J* = 4.6, 2.1 Hz, 3H), 6.67 (d, *J* = 2.3 Hz, 2H), 6.47 (t, *J* = 2.3 Hz, 1H), 3.79 (s, 6H), 0.52 (d, *J* = 1.5 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.56, 137.05, 133.90, 129.61, 128.05, 124.29, 109.87, 106.78, 102.53, 91.75, 55.57, –0.68. IR (Neat Film NaCl) 3421, 3069, 3001, 2959, 2837, 2160, 1596, 1456, 1419, 1348, 1298, 1250, 1205, 1155, 1116, 1064, 979, 964, 817, 753, 732, 681 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{21}O_2Si$ [M+H]: 297.1311, found 297.1309.

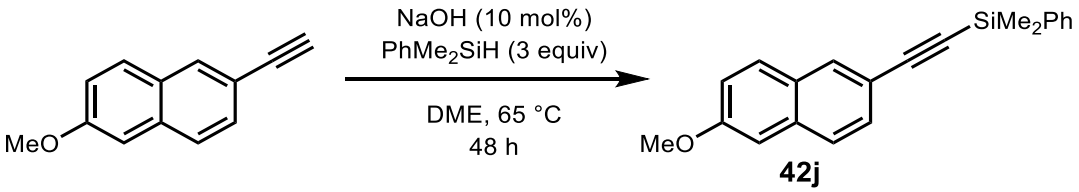


42i

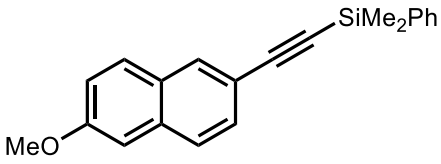


(Mesitylethynyl)dimethyl(phenyl)silane 42i: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 2-ethynyl-1,3,5-trimethylbenzene (72 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 25 °C for 24 h. The desired product **42i** (119.1 mg, 86% yield) was obtained in analytical purity as a colorless oil after removal of volatiles at 85 °C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (ddt, *J* = 4.5, 3.2, 0.8 Hz, 3H), 7.40 (dd, *J* = 2.5, 0.8 Hz, 2H), 6.88 – 6.86 (m, 2H), 2.42 (s, 6H), 2.29 (s, 3H), 0.52 (t, *J* = 0.7 Hz, 6H); ^{13}C NMR (126

MHz, $CDCl_3$) δ 140.86, 138.23, 137.66, 133.89, 129.45, 127.99, 127.67, 119.94, 104.95, 99.66, 21.51, 21.15, –0.34. IR (Neat Film NaCl) 3440, 3068, 2959, 2146, 1646, 1610, 1474, 1428, 1224, 1117, 841, 825, 779, 753, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{19}H_{23}Si$ [M+H]: 279.1569, found 279.1561.

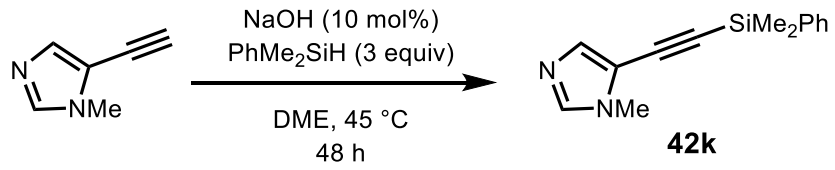


42j

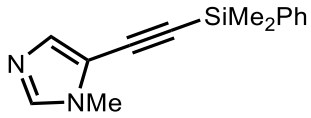


((6-Methoxynaphthalen-2-yl)ethynyl)dimethyl(phenyl)silane 42j: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 2-ethynyl-6-methoxynaphthalene (91 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **42j** (134.8 mg, 85% yield) was obtained in as a colorless oil after removal of volatiles at 85°C at 45 mtorr for 30 minutes and subsequent purification by alumina flash chromatography (gradient 2.5% Et_2O in hexanes → 10% Et_2O in hexanes). R_f = 0.36 (5% Et_2O in hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 1.5, 0.7 Hz, 1H), 7.78 – 7.72 (m, 2H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 1H), 7.53 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.46 – 7.40 (m, 3H), 7.17 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.11 (d, *J* = 2.6 Hz, 1H), 3.93 (s, 3H), 0.56 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.57, 137.30, 134.48, 133.93, 132.17, 129.56, 129.34, 128.44, 128.05, 126.85, 122.76, 119.59, 117.93, 107.50,

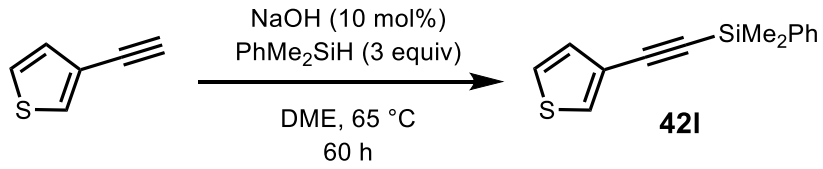
105.91, 91.68, 55.50, –0.57. IR (Neat Film NaCl) 3422, 2959, 2152, 1631, 1601, 1499, 1481, 1461, 1390, 1267, 1232, 1161, 1117, 1031, 937, 890, 814, 780, 731, 703, 656 cm^{-1}; HRMS (EI+) calc'd for $C_{21}H_{20}OSi$ [M+•]: 316.1284, found 316.1296.

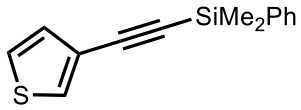


42k

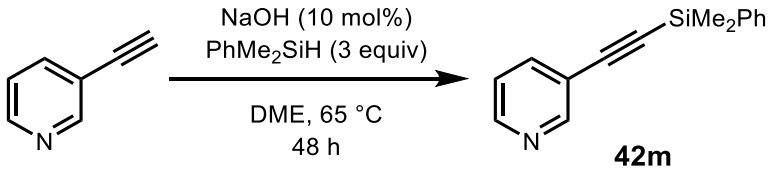


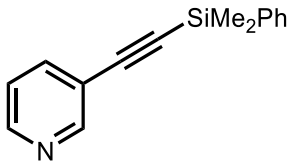
5-((Dimethyl(phenyl)silyl)ethynyl)-1-methyl-1*H*-imidazole 42k: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 5-ethynyl-1-methyl-1*H*-imidazole (53 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **42k** (98.7 mg, 82% yield) was obtained as a colorless oil after removal of volatiles at 85°C at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (100% EtOAc). R_f = 0.45 (100% EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 – 7.65 (m, 2H), 7.40 (m, 4H), 7.31 (d, *J* = 1.0 Hz, 1H), 3.68 – 3.65 (m, 3H), 0.52 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.37, 136.49, 135.29, 133.74, 129.73, 128.09, 116.28, 100.60, 94.11, 32.11, –0.85. IR (Neat Film NaCl) 3417, 2960, 2157, 1646, 1533, 1489, 1428, 1274, 1250, 1227, 1116, 924, 823, 782, 732, 702, 661 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{17}N_2Si$ [M+H]: 241.1161, found 241.1169.



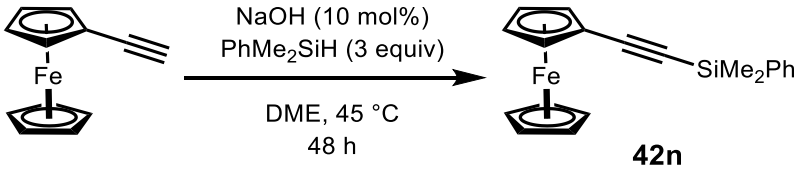


Dimethyl(phenyl)(thiophen-3-ylethynyl)silane 42l: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 3-ethynylthiophene (54 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 60 h. The desired product **42l** (113.2 mg, 93% yield) was obtained as a colorless oil after removal of volatiles at 85°C at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.39 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 – 7.68 (m, 2H), 7.53 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.43 – 7.39 (m, 3H), 7.27 – 7.24 (m, 1H), 7.17 (dd, *J* = 5.0, 1.2 Hz, 1H), 0.51 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.08, 133.88, 130.26, 130.11, 129.59, 128.04, 125.36, 122.32, 101.67, 91.93, –0.68. IR (Neat Film NaCl) 3107, 3068, 2959, 2152, 1427, 1356, 1249, 1163, 1116, 944, 870, 781, 753, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{14}SSi$ [M+•]: 242.0586, found 242.0576.

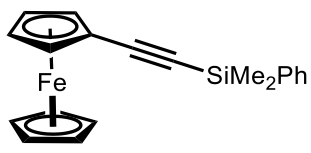




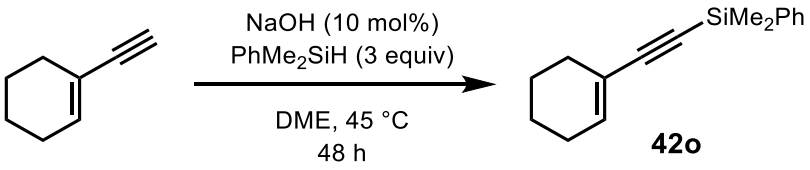
3-((Dimethyl(phenyl)silyl)ethynyl)pyridine 42m: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 3-ethynylpyridine (52 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **42m** (91.8 mg, 77% yield) was obtained as a colorless oil after removal of volatiles at 85°C at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.31 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (dd, *J* = 2.1, 0.9 Hz, 1H), 8.54 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.77 (ddd, *J* = 7.9, 2.1, 1.7 Hz, 1H), 7.71 – 7.67 (m, 2H), 7.42 (dd, *J* = 4.9, 1.9 Hz, 3H), 7.24 (ddd, *J* = 7.9, 4.9, 0.9 Hz, 1H), 0.54 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.82, 149.02, 139.01, 136.49, 133.81, 129.74, 128.11, 123.00, 120.21, 103.14, 96.34, –0.88. IR (Neat Film NaCl) 3420, 3069, 3048, 3025, 2960, 2161, 1559, 1474, 1406, 1250, 1184, 1119, 1022, 847, 781, 754, 703, 670 cm^{-1}; HRMS (EI+) calc'd for $C_{15}H_{16}NSi$ [M+H]: 238.1052, found 238.1049.

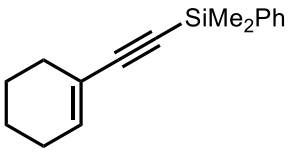


42n



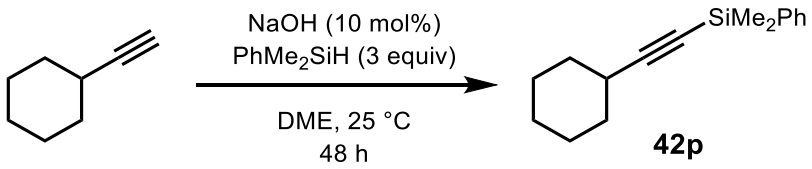
((Dimethyl(phenyl)silyl)ethynyl)ferrocene 42n: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), ethynylferrocene (105 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **42n** (170.1 mg, 99% yield) was obtained in analytical purity as an orange crystalline solid after removal of volatiles at 85°C at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (gradient 100% hexanes → 5% EtOAc in hexanes). R_f = 0.45 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, J = 6.1, 3.1 Hz, 2H), 7.43 – 7.37 (m, 3H), 4.49 (t, J = 1.7 Hz, 2H), 4.22 (s, 5H), 4.22 – 4.20 (m, 2H)., 0.47 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.71, 133.89, 129.44, 127.98, 106.30, 88.52, 72.02, 70.26, 69.00, 64.64, –0.40. IR (Neat Film NaCl) 2958, 2147, 1428, 1248, 1106, 1024, 1001, 925, 819, 779, 753, 730, 699 cm^{-1}; HRMS (EI+) calc'd for $C_{20}H_{20}FeSi$ [M+•]: 344.0684, found 344.0696.

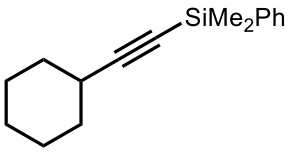




(Cyclohex-1-en-1-ylethynyl)dimethyl(phenyl)silane 42o: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 1-ethynylcyclohex-1-ene (53 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **42o** (102.7 mg, 85% yield)

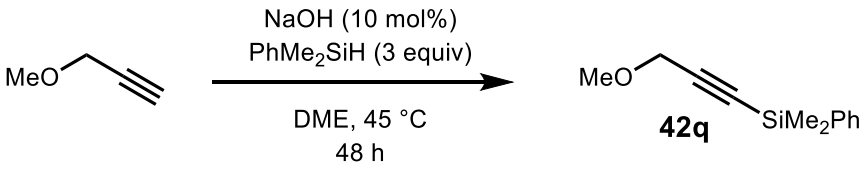
was obtained as a colorless oil after removal of volatiles at 85°C at 45 mtorr for 15 minutes and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.50 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 – 7.63 (m, 2H), 7.39 – 7.36 (m, 3H), 6.24 (tt, *J* = 3.9, 1.8 Hz, 1H), 2.17 (tdd, *J* = 6.0, 2.7, 1.8 Hz, 2H), 2.11 (tdd, *J* = 6.4, 4.6, 2.5 Hz, 2H), 1.68 – 1.55 (m, 4H), 0.43 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.59, 136.90, 133.84, 129.40, 127.94, 120.82, 109.17, 88.79, 29.14, 25.81, 22.33, 21.54, –0.51. IR (Neat Film NaCl) 3422, 2937, 2145, 1647, 1428, 1249, 1116, 863, 819, 779, 730, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{16}H_{21}Si$ [M+H]: 241.1413, found 241.1402.

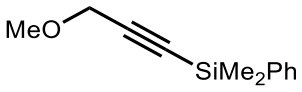




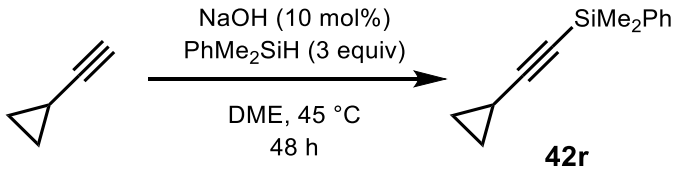
(Cyclohexylethynyl)dimethyl(phenyl)silane 42p: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), ethynylcyclohexane (54 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 25 °C for 48 h. The desired product **42p** (97.4 mg, 80% yield) was obtained as a colorless oil after removal of volatiles at 85°C at 45 mtorr for 15 minutes and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.53 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (ddd, *J* = 5.4, 2.4, 1.7 Hz, 2H), 7.37 (ddq, *J* = 4.0, 1.9, 0.8 Hz, 3H), 2.47 (tt, *J* = 9.0, 3.8 Hz, 1H), 1.89 – 1.79 (m, 2H), 1.73 (ddd, *J* = 9.8, 6.2, 3.1 Hz,

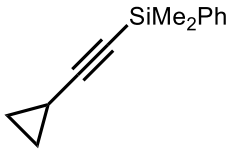
2H), 1.52 (td, *J* = 9.7, 9.2, 3.8 Hz, 3H), 1.38 – 1.26 (m, 3H), 0.40 (d, J = 1.0 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.82, 133.13, 129.29, 127.89, 113.93, 81.74, 32.70, 30.23, 26.00, 24.93, -0.30. IR (Neat Film NaCl) 2931, 2854, 2173, 1448, 1427, 1248, 1116, 1076, 843, 834, 816, 779, 729, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{16}H_{21}Si$ [(M+H)-H_2]: 241.1413, found 241.1419.



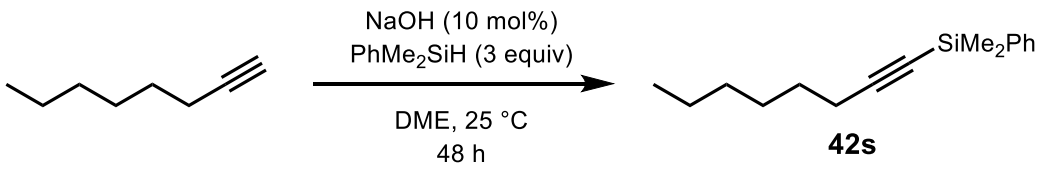


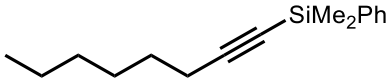
(3-Methoxyprop-1-yn-1-yl)dimethyl(phenyl)silane 42q: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 3-methoxyprop-1-yne (35 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **42q** (61.0 mg, 60% yield) was obtained as a colorless oil after removal of volatiles at 85°C at 45 mtorr for 15 minutes (careful heating is necessary, as the product is volatile under these conditions) and subsequent purification by silica gel flash chromatography (1:1 DCM:hexanes). R_f = 0.38 (1:1 DCM:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 – 7.62 (m, 2H), 7.41 – 7.36 (m, 3H), 4.16 (s, 2H), 3.41 (s, 3H), 0.45 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.63, 133.66, 129.49, 127.90, 103.05, 89.53, 60.48, 57.67, –0.97. IR (Neat Film NaCl) 3423, 2925, 2173, 1640, 1428, 1353, 1250, 1186, 1103, 1007, 990, 903, 838, 817, 781, 731, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{12}H_{16}OSi$ [M+•]: 204.0971, found 204.0977.



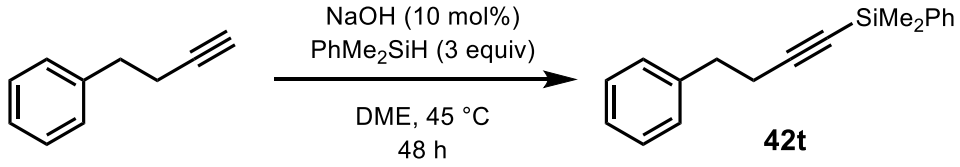


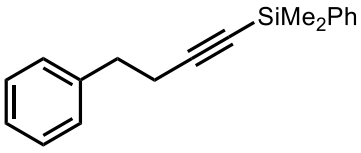
(Cyclopropylethynyl)dimethyl(phenyl)silane 42r: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), ethynylcyclopropane (33 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **42r** (70.1 mg, 70% yield) was obtained as a colorless oil after removal of volatiles at 85°C at 45 mtorr for 30 minutes (careful heating is necessary, as this product is volatile under these conditions) and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.38 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.61 (m, 2H), 7.39 – 7.36 (m, 3H), 1.40 – 1.30 (m, 1H), 0.87 – 0.75 (m, 4H), 0.40 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.77, 133.79, 129.36, 127.92, 112.40, 77.65, 8.97, 0.70, –0.45. IR (Neat Film NaCl) 3423, 3068, 2960, 2172, 2158, 1646, 1428, 1348, 1249, 1114, 1028, 839, 779, 730, 659 cm^{-1}; HRMS (EI+) calc'd for $C_{13}H_{16}Si$ [M+•]: 200.1021, found 200.1031.





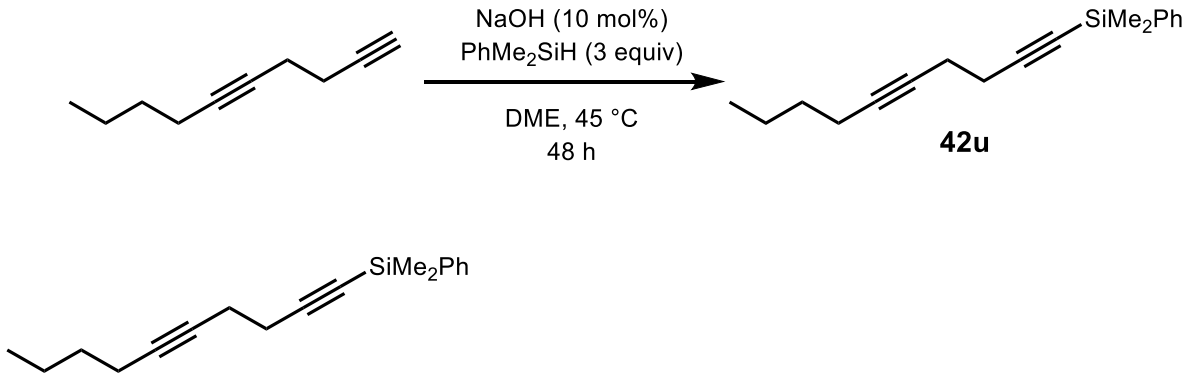
Dimethyl(oct-1-yn-1-yl)(phenyl)silane 42s: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), oct-1-yne (55 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 25 °C for 48 h. The desired product **42s** (101.0 mg, 83% yield) was as a colorless oil after removal of volatiles at 85°C at 45 mtorr for 15 minutes and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.53 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 – 7.62 (m, 2H), 7.40 – 7.35 (m, 3H), 2.28 (t, J = 7.1 Hz, 2H), 1.59 – 1.53 (m, 2H), 1.47 – 1.39 (m, 2H), 1.35 – 1.27 (m, 4H), 0.91 (t, J = 6.9 Hz, 3H), 0.40 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.86, 133.80, 129.35, 127.92, 109.85, 82.31, 31.43, 28.68, 28.64, 22.69, 20.12, 14.19, –0.44. IR (Neat Film NaCl) 3422, 3069, 2957, 2931, 2858, 2174, 1647, 1428, 1248, 1115, 836, 815, 779, 729, 699 cm^{-1}; HRMS (EI+) calc'd for $C_{16}H_{23}Si$ [M+H]: 245.1726, found 245.1727.





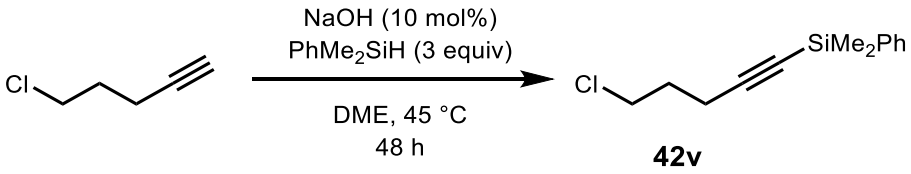
Dimethyl(phenyl)(4-phenylbut-1-yn-1-yl)silane 42t: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), but-3-yn-1-ylbenzene (65 mg,

0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **42t** (130.0 mg, 98% yield) was obtained in analytical purity as a pale yellow oil after removal of volatiles at 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.59 (m, 2H), 7.42 – 7.37 (m, 3H), 7.31 (dd, J = 8.0, 6.8 Hz, 2H), 7.28 – 7.23 (m, 3H), 2.90 (t, *J* = 7.5 Hz, 2H), 2.60 (t, *J* = 7.5 Hz, 2H), 0.42 (d, *J* = 0.6 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.63, 137.56, 133.80, 129.39, 128.68, 128.47, 127.93, 126.43, 108.62, 83.39, 35.10, 22.38, –0.56. IR (Neat Film NaCl) 3423, 3086, 3067, 3027, 2959, 2174, 1647, 1602, 1495, 1453, 1427, 1248, 1114, 1077, 1042, 869, 811, 779, 729, 696, 661 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{19}Si$ [(M+H)-H_2]: 263.1256, found 263.1258.

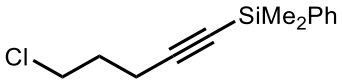


Deca-1,5-diyn-1-yldimethyl(phenyl)silane 42u: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), deca-1,5-diyne (67 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **42u** (131.3 mg, 98% yield) was obtained in analytical purity as a colorless oil after removal of volatiles at 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 – 7.64 (m, 2H), 7.38 (dd, *J* = 5.0, 1.9 Hz, 3H), 2.49 (ddd, *J* = 7.7, 6.1, 1.7 Hz, 2H), 2.46 – 2.39 (m, 2H), 2.18 (tt, *J* = 7.0, 2.3 Hz, 2H), 1.52 – 1.39 (m,

4H), 0.92 (t, J = 7.2 Hz, 3H), 0.42 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.56, 133.81, 129.40, 127.92, 107.79, 83.33, 81.59, 78.33, 31.20, 22.05, 20.79, 19.16, 18.54, 13.77, –0.54. IR (Neat Film NaCl) 2958, 2932, 2872, 2177, 1465, 1428, 1336, 1249, 1115, 1042, 870, 837, 816, 780, 754, 731, 700, 662 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{23}Si$ [(M+H)-H_2]: 267.1569, found 267.1565.

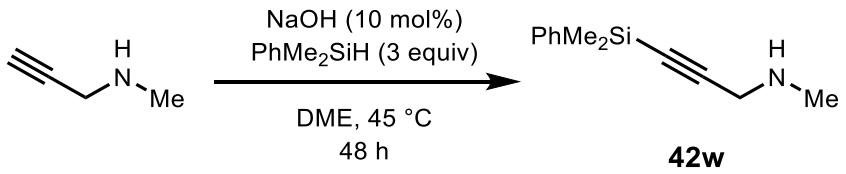


42v

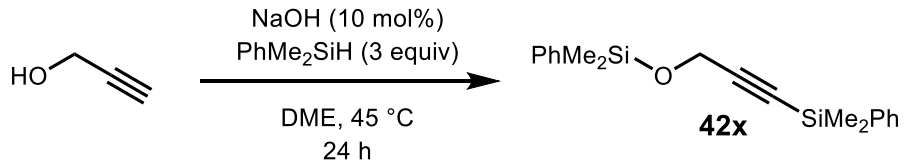


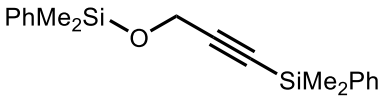
(5-Chloropent-1-yn-1-yl)dimethyl(phenyl)silane 42v: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 5-chloropent-1-yne (51 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **42v** (93.3 mg, 79% yield) was obtained as a colorless oil after removal of volatiles at 85°C at 45 mtorr for 15 minutes (careful heating is necessary, as this product is volatile under these conditions) and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.31 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 – 7.60 (m, 2H), 7.38 (dd, J = 4.9, 1.9 Hz, 3H), 3.67 (t, J = 6.4 Hz, 2H), 2.49 (t, J = 6.8 Hz, 2H), 2.01 (p, J = 6.6 Hz, 2H), 0.41 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.46, 133.75, 129.48, 127.99, 107.20, 83.81, 43.77, 31.40, 17.57, –0.56. IR (Neat Film NaCl) 3420,

3069, 2960, 2928, 2174, 1646, 1428, 1249, 1114, 1041, 837, 816, 780, 731, 701, 665 cm^{-1}; HRMS (EI+) calc'd for $C_{13}H_{16}ClSi$ [(M+H)-H_2]: 235.0710, found 235.0713.

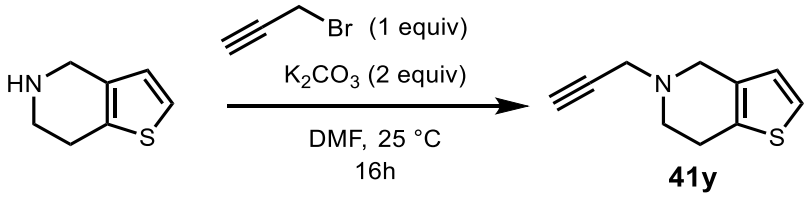


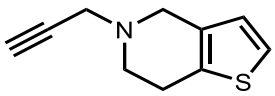
3-(Dimethyl(phenyl)silyl)-*N*-methylprop-2-yn-1-amine 42w: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), *N*-methylprop-2-yn-1-amine (69 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **42w** (81.8 mg, 80% yield) was obtained as a colorless oil after removal of volatiles at 85°C at 45 mtorr for 15 minutes (careful heating is necessary, as the product is volatile under these conditions) and subsequent purification by silica gel flash chromatography (100% EtOAc). R_f = 0.32 (100% EtOAc); ^{1}H NMR (500 MHz, THF-d_8) δ 7.63 – 7.59 (m, 2H), 7.33 – 7.29 (m, 3H), 3.36 (s, 2H), 2.39 (s, 3H), 0.36 (s, 6H); ^{13}C NMR (126 MHz, THF-d_8) δ 138.26, 134.58, 130.18, 128.67, 108.45, 85.45, 41.75, 35.64, –0.33. IR (Neat Film NaCl) 3416, 3068, 2957, 2165, 1725, 1651, 1427, 1250, 1116, 1044, 836, 817, 730, 699 cm^{-1}; HRMS (EI+) calc'd for $C_{12}H_{18}NSi$ [M+H]: 204.1208, found 204.1214.



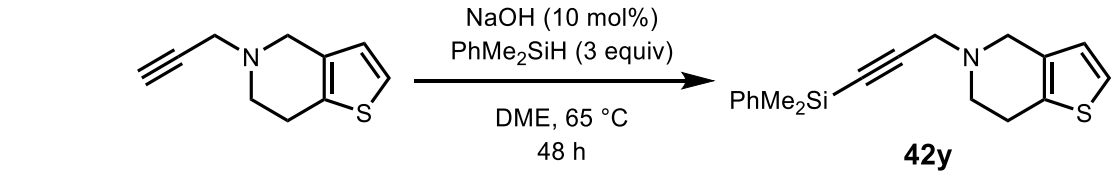


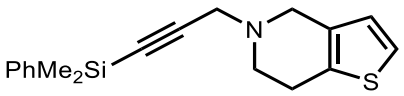
(3-((Dimethyl(phenyl)silyl)oxy)prop-1-yn-1-yl)dimethyl(phenyl)silane 42x: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), prop-2-yn-1-ol (28 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 24 h. The desired product **42x** (142.9 mg, 88% yield) was obtained in analytical purity as a colorless oil after removal of volatiles at 85°C at 45 mtorr for 30 minutes (careful heating is necessary, as the product is volatile under these conditions). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (ddt, *J* = 6.4, 1.8, 0.9 Hz, 4H), 7.44 – 7.36 (m, 6H), 4.35 (s, 2H), 0.48 (s, 6H), 0.43 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.08, 136.80, 133.82, 133.73, 129.93, 129.57, 128.01, 127.98, 105.77, 88.23, 52.27, –0.93, –1.36. IR (Neat Film NaCl) 3069, 3049, 2959, 2177, 1428, 1363, 1250, 1117, 1085, 1043, 1004, 817, 782, 731, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{19}H_{23}OSi_2$ [(M+H)–H_2]: 323.1288, found 323.1297.





5-(Prop-2-yn-1-yl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine 41y: To a mixture of tetrahydrothieno[3,2-*c*]pyridine hydrochloride (1.40 g, 10 mmol, 1 equiv) and K_2CO_3 (2.76 g, 20 mmol, 2 equiv) in DMF (30 ml), was added 1-propyne-3-bromide (1.18 g, 10 mmol, 1 equiv) and the mixture was stirred at room temperature for 16 h. The mixture was filtered and solvent was removed under reduced pressure to give a brown oil. This oil was diluted with 20 mL of diethyl ether and washed with 20 mL of water, then 20 mL brine, then dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (10:1 hexanes:Et_2O) yielding the product **41y** as a yellow liquid (1.27 g, 72% yield). R_f = 0.35 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (dt, *J* = 5.1, 0.7 Hz, 1H), 6.73 (d, *J* = 5.1 Hz, 1H), 3.69 (t, *J* = 1.7 Hz, 2H), 3.53 (d, *J* = 2.4 Hz, 2H), 2.95 – 2.91 (m, 2H), 2.91 – 2.88 (m, 2H), 2.29 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.55, 132.89, 125.19, 122.83, 78.78, 73.39, 51.50, 49.70, 46.37, 25.57. IR (Neat Film NaCl) 3937, 3626, 3390, 3289, 3103, 3065, 2910, 2816, 2101, 2651, 1614, 1565, 1461, 1428, 1405, 1328, 1275, 1219, 1191, 1166, 1130, 1109, 1079, 1051, 1017, 983, 902, 835, 789, 703 cm^{-1}; HRMS (EI+) calc'd for $C_{10}H_{12}NS$ [M+H]: 178.0690, found 178.0689.

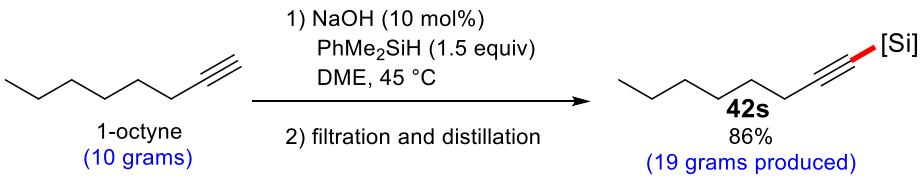




5-(3-(Dimethyl(phenyl)silyl)prop-2-yn-1-yl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine 42y:

The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 5-(prop-2-yn-1-yl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine (89 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **42y** (120.4 mg, 77% yield) was obtained as a yellow oil after removal of volatiles at 85 °C at 45 mtorr for 15 minutes and subsequent purification by silica gel flash chromatography (10% EtOAc in hexanes). R_f = 0.40 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 – 7.61 (m, 2H), 7.43 – 7.34 (m, 3H), 7.09 (dd, *J* = 5.1, 0.8 Hz, 1H), 6.75 (d, *J* = 5.1 Hz, 1H), 3.72 (t, *J* = 1.6 Hz, 2H), 3.61 (d, *J* = 0.7 Hz, 2H), 2.99 – 2.88 (m, 4H), 0.43 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.12, 133.78, 133.16, 133.06, 129.54, 128.00, 125.36, 122.92, 102.74, 88.35, 51.69, 49.89, 47.60, 25.69, –0.60. IR (Neat Film NaCl) 3067, 2957, 2906, 2814, 2163, 1427, 1327, 1249, 1166, 1115, 1034, 1016, 975, 836, 817, 780, 731, 699 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{20}NSSi$ [(M+H)-H_2]: 310.1086, found 310.1087.

*Multi-gram scale synthesis of **42s**.*



Dimethyl(oct-1-yn-1-yl)(phenyl)silane 42s: A 500 mL oven-dried Schlenk flask equipped with a stir bar and stoppered with a rubber septum was evacuated and refilled once with argon. NaOH (364 mg, 9.1 mmols, 10 mol%) was weighed out on the bench and added to the flask under a strong flow of argon. The charged flask was then evacuated and heated under vacuum for 2 minutes with

a heat gun, then refilled with argon. 1,2-dimethoxyethane (DME) (90 mL), 1-octyne (13.4 mL, 90.7 mmol, 1.0 equiv) and $PhMe_2SiH$ (20.9 mL, 136.1 mmol, 1.5 equiv) were added through the septum by syringe. The flask was then heated with a heating mantle set at 45 °C and stirred for 60 hours. The flask with the resultant cloudy brown-tan solution was removed from heating and allowed to cool to room temperature, diluted with anhydrous Et_2O (50 mL), and filtered through a short pad of silica to remove solid residue. After the solvent was removed *in vacuo*, a stirbar was added and the transparent deep amber solution was stirred under high vacuum (100 millitorr) for several hours to remove remaining volatiles. The mixture was then subjected to distillation under vacuum:

a) Heating bath to 80 °C, vacuum stabilizes at 200 millitorr as a small amount of droplets condense into the forerun. Forerun comes off as a colorless liquid. Thermometer reads 22 °C.

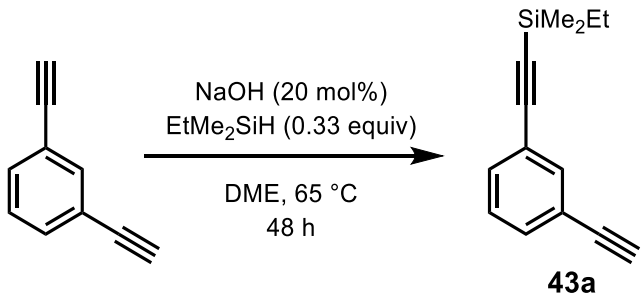
b) Vacuum stays at 200 millitorr. Heating bath set to 85 °C as the last of the remaining silane boils off.

c) Heating bath temperature increased to 125 °C. The solution starts to boil slowly. Thermometer reads 60 °C. Vacuum stays at 200 millitorr.

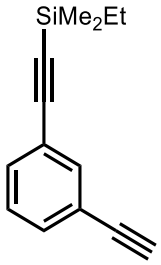
d) Increase temperature to 130 °C, vacuum at 200 millitorr to distill over the desired dimethyl(oct-1-yn-1-yl)(phenyl)silane (colorless oil). Thermometer reads 85 °C. The desired product **42s** is obtained as a colorless oil (19.0 g, 86% yield).

Optimization and synthesis of mono- and bis-silylated diynes.

For the monosilylation of 1,3-diethynylbenzene, yield is based on silane. $EtMe_2SiH$ was chosen as the silane in this case (instead of $PhMe_2SiH$) due to improved reactivity in this particular case.

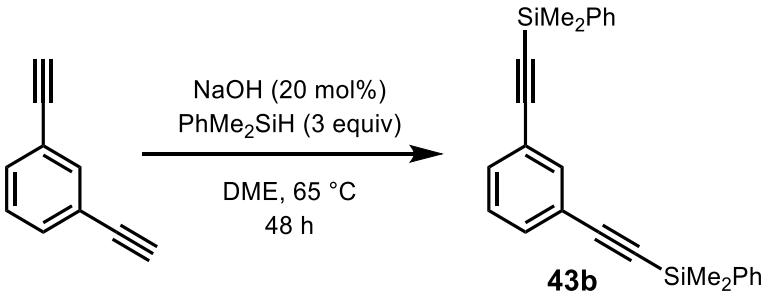


43a

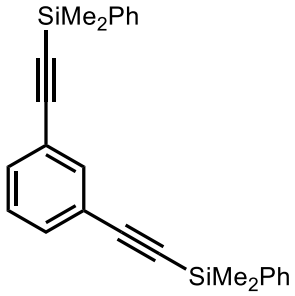


Ethyl((3-ethynylphenyl)ethynyl)dimethylsilane 43a: The general procedure was followed. The reaction was performed with NaOH (4.0 mg, 0.1 mmol, 20 mol%), 1,3-diethynylbenzene (189 mg, 1.5 mmol, 3.0 equiv), $EtMe_2SiH$ (44 mg, 66 μL, 0.5 mmol, 1.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **43a** (68.9 mg, 65% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). The bis-silylated product **43b** was also obtained in 4% yield. R_f = 0.33 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (t, J = 1.7 Hz, 1H), 7.43 (ddd, J = 7.8, 6.2, 1.4 Hz, 2H), 7.26 (t, J = 7.8 Hz, 1H), 3.07 (s, 1H), 1.04 (t, J = 7.9 Hz, 3H), 0.67 (q, J = 7.9 Hz, 2H), 0.21 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.66, 132.32, 132.11, 128.43, 123.66, 122.44, 104.41, 94.44, 82.85, 77.87, 8.16, 7.49, -2.15. IR (Neat Film NaCl) 3300, 3063, 2956, 2914, 2874, 2152, 2111, 1593, 1569,

1474, 1407, 1249, 1152, 1014, 960, 943, 925, 839, 821, 794, 780, 701, 685 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{17}Si$ [M+H]: 213.1100, found 213.1089.



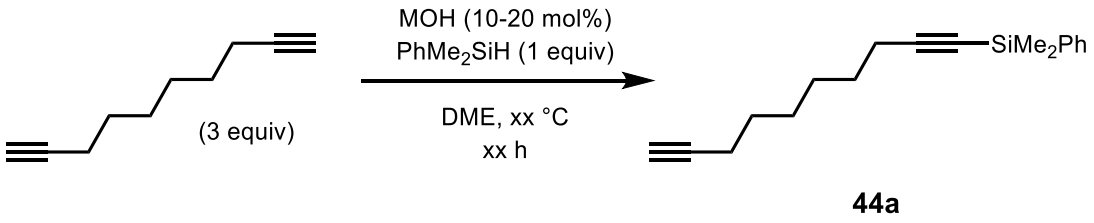
43b



1,3-bis((dimethyl(phenyl)silyl)ethynyl)benzene 43b: The general procedure was followed. The reaction was performed with NaOH (4.0 mg, 0.1 mmol, 20 mol%), 1,3-diethynylbenzene (63 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **43b** (173.5 mg, 88% yield) was obtained as a light yellow oil after removal of volatiles at 85 °C at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (100% hexanes → 3% EtOAc in hexanes). R_f = 0.26 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 – 7.70 (m, 4H), 7.69 (t, *J* = 1.7 Hz, 1H), 7.47 (dd, *J* = 7.8, 1.7 Hz, 2H), 7.44 – 7.41 (m, 6H), 7.28 (ddd, *J* = 8.0, 7.4, 0.5 Hz, 1H), 0.53 (s, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.88, 135.69, 133.86, 132.23, 129.64, 128.40, 128.08, 123.33, 105.73, 93.08, –0.74. IR (Neat Film NaCl) 3068, 2959, 2153, 1589, 1474,

1428, 1405, 1249, 1164, 1118, 944, 838, 816, 780, 753, 730, 702, 685 cm^{-1}; HRMS (EI+) calc'd for $C_{26}H_{27}Si_2$ [M+H]: 395.1651, found 395.1659.

Optimization of 1,9-decadiyne monosilylation



44a

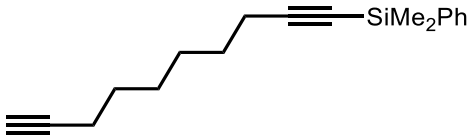
In all reactions, yield is based on silane, and uses 3 equivalents of 1,9-decadiyne and 1 equivalent of $PhMe_2SiH$. Longer reaction times (>1 week) resulted in almost quantitative yield for the *mono*-silylated 1,9-decadiyne when using 0.1 equiv of KOH at either 45 °C or 65 °C. At the higher temperature, yields were slightly higher; for both temperatures, the selectivities were similar, at approximately 20:1 *mono:bis*, for any reaction time measured. Moderately higher yields (>80%) were achieved with similar selectivity (20:1 *mono:bis*) with 0.2 eq NaOH at 65 °C for shorter reaction times (5–9 days). Using higher equivalents of KOH resulted in a drastic decrease in yield compared to either NaOH or 0.1 equiv KOH. In these cases, yields were below 40%, although no bis-silylation was observed.

Table 3.6. Optimization of 1,9-decadiyne *mono*-silylation.

Conditions	Time (days)	Yield *Mono* (%)[1]	Yield *Bis* (%)[1]	*Mono*:*bis*[1]	Isolated Yield (*mono*, %)	Isolated Yield (*bis*, %)
0.1 equiv **NaOH**, 45 °C	2	18.6	0.2	119.4	-	-
	5	38.2	0.5	70.5	-	-
	7	47.6	0.9	51.3	-	-
	9	54.2	1.4	39.5	-	-
	12	61.2	1.9	32.4	-	-
	14	64.6	2.2	29.1	-	-
	16	64.3	1.8	35.6	-	-
0.1 equiv **NaOH**, 65 °C	2	24.1	0.0	-	-	-
	5	43.2	0.8	57.4	-	-
	7	50.6	1.0	49.9	-	-
	9	56.6	1.4	39.2	-	-
	12	61.1	1.9	32.6	-	-
	14	65.5	2.1	31.9	-	-
	16	64.8	2.0	32.6	-	-

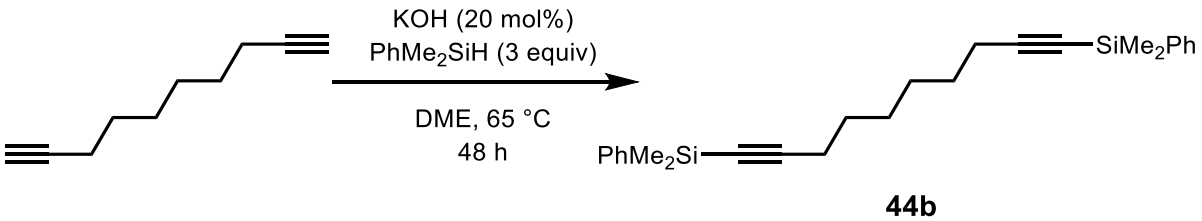
Conditions	Time (days)	Yield *Mono* (%)[1]	Yield *Bis* (%)[1]	*Mono*:*bis*[1]	Isolated Yield (*mono*, %)	Isolated Yield (*bis*, %)
0.1 equiv **KOH**, 45 °C	**2**	**59.6**	**1.7**	**35.9**	**46**	**1**
	5	**78.2**	**3.2**	**24.5**	**60**	**0**
	7	**82.8**	**4.0**	**20.5**	**65**	**2**
	9	86.2	4.3	20.2	-	-
	12	88.7	4.8	18.5	-	-
	14	90.0	5.0	17.9	-	-
	16	90.6	4.6	19.8	-	-
0.1 equiv **KOH**, 65 °C	**2**	**75.3**	**3.5**	**21.3**	**63**	**1**
	5	**84.1**	**4.2**	**19.8**	**68**	**4**
	7	**82.5**	**4.2**	**19.6**	**71**	**4**
	9	79.2	4.0	20.0	-	-
	12	85.6	4.3	20.1	-	-
	14	92.6	5.1	18.3	-	-
	16	97.1	5.3	18.4	-	-
0.2 equiv **NaOH**, 45 °C	1	23.8	0.0	-	-	-
	2	39.4	0.0	-	-	-
	5	54.8	1.2	45.0	-	-
	7	58.7	1.5	38.2	-	-
	9	61.1	1.9	33.0	-	-
0.2 equiv **NaOH**, 65 °C	**1**	**52.5**	**1.1**	**46.1**	**32**	**0**
	2	**68.7**	**2.1**	**33.4**	**57**	**2**
	5	**84.7**	**3.9**	**21.7**	**66**	**5**
	7	**87.1**	**4.8**	**18.3**	**73**	**5**
	9	88.9	5.2	17.2	-	-
0.2 equiv **KOH**, 45 °C	1	16.3	0.0	-	-	-
	2	24.9	0.0	-	-	-
	5	32.8	0.0	-	-	-
	7	35.0	0.0	-	-	-
	9	35.6	0.5	66.1	-	-
0.2 equiv **KOH**, 65 °C	1	28.1	0.0	-	-	-
	2	26.8	0.0	-	-	-
	5	27.3	0.0	-	-	-
	7	30.5	0.0	-	-	-
	9	34.2	0.0	-	-	-

[1]Yields and selectivities determined by GC-FID. Several experiments were also isolated via column chromatography as shown in the table (1:30 CH_2Cl_2:hexanes). The difference between GC-FID and the isolated yields are due to volatility of the *mono*-silylated product under high vacuum. Mono = **44a**, bis = **44b**

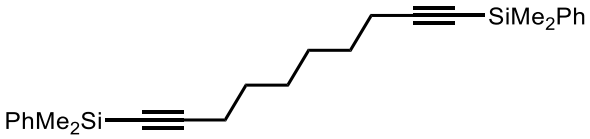


Deca-1,9-diyn-1-yldimethyl(phenyl)silane 44a: The general procedure was followed. The reaction was performed with either KOH or NaOH (10–20 mol%), deca-1,9-diyne (201 mg, 1.5 mmol, 3.0 equiv), $PhMe_2SiH$ (68 mg, 77 μL, 0.5 mmol, 1.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at either 45 °C or 65 °C for the specified amount of time. The desired product **44a** (see yield in **Table 3.6**) was obtained as a colorless oil after purification by silica gel flash chromatography (gradient 1:30 dichloromethane : hexanes → 1:10 dichloromethane : hexanes). R_f = 0.31 (10% dichloromethane in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 – 7.61 (m, 2H), 7.40 – 7.35 (m, 3H), 2.29 (t, *J* = 7.1 Hz, 2H), 2.20 (td, *J* = 7.1, 2.6 Hz, 2H), 1.96 (t, *J* = 2.6 Hz, 1H), 1.57 (dtd, *J* = 9.6, 7.1, 4.5 Hz, 4H), 1.47 – 1.42 (m, 4H), 0.40 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.79, 133.78, 129.37, 127.93, 109.55, 84.74, 82.51, 68.34, 28.51, 28.45, 28.39, 28.31, 20.04, 18.48, –0.46. IR (Neat Film NaCl) 3420, 3306, 3068, 2936, 2859, 2173, 2117, 1646, 1457, 1428, 1325, 1248, 1114, 1026, 836, 816, 754, 731, 700, 661 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{23}Si$ [(M+H)-H_2]: 267.1569, found 267.1556.

Bis-silylation of 1,9-decadiyne

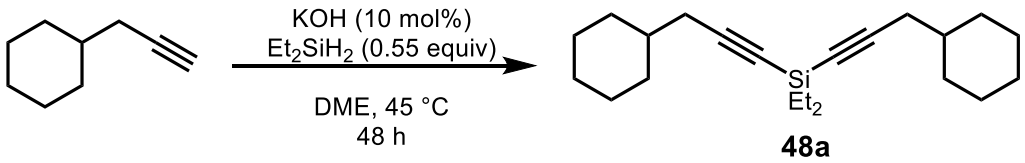


44b

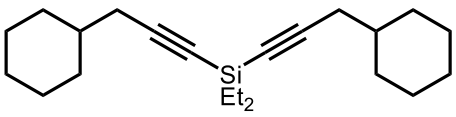


1,10-Bis(dimethyl(phenyl)silyl)deca-1,9-diyne 44b: The general procedure was followed. The reaction was performed with KOH (5.6 mg, 0.1 mmol, 20 mol%), deca-1,9-diyne (67 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **44b** (189.3 mg, 93% yield) was obtained as a colorless oil after removal of volatiles at 85 °C at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (gradient 1:30 dichloromethane : hexanes → 1:10 dichloromethane : hexanes). R_f = 0.28 (10% dichloromethane in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (ddt, *J* = 5.4, 3.0, 1.4 Hz, 4H), 7.38 (ddt, *J* = 4.4, 2.2, 1.1 Hz, 6H), 2.30 (td, *J* = 7.2, 1.1 Hz, 4H), 1.59 (t, *J* = 6.8 Hz, 4H), 1.49 – 1.42 (m, 4H), 0.43 – 0.40 (s, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.79, 133.78, 129.37, 127.93, 109.58, 82.49, 28.53, 28.38, 20.04, –0.45. IR (Neat Film NaCl) 3423, 3068, 2937, 2858, 2173, 1647, 1428, 1248, 1114, 836, 815, 753, 730, 699, 661 cm^{-1}; HRMS (EI+) calc'd for $C_{26}H_{33}Si_2$ [(M+H)-H_2]: 401.2121, found 401.2120.

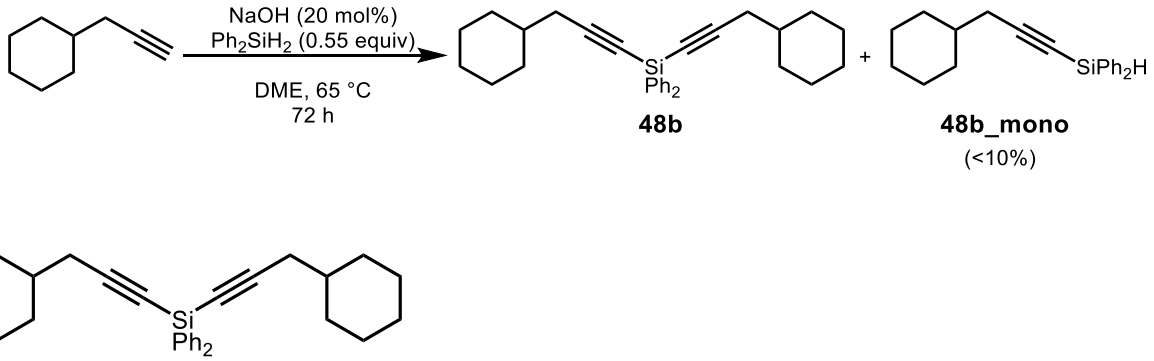
Synthesis of symmetric and unsymmetric diethynylsilanes



48a

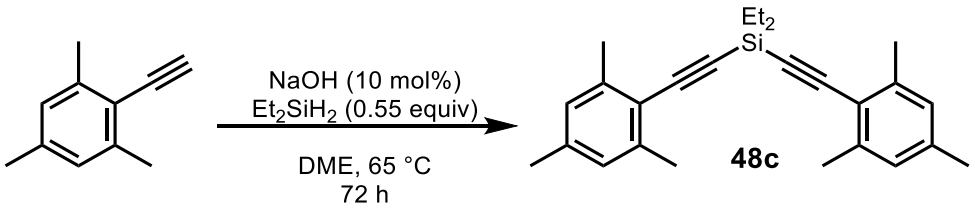


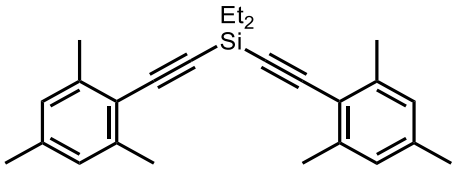
Bis(3-cyclohexylprop-1-yn-1-yl)diethylsilane 48a: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), Et_2SiH_2 (24 mg, 36 μL, 0.275 mmol, 0.55 equiv), and 0.5 mL of tetrahydrofuran (THF) at 45 °C for 48 h. The desired product **48a** (62.5 mg, 76% yield) was obtained as a colorless oil after removal of volatiles under high vacuum at 45 mtorr for 30 minutes and subsequent purification by silica gel flash chromatography (100% hexanes). R_f = 0.51 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.15 (d, *J* = 6.6 Hz, 4H), 1.81 (ddd, *J* = 13.6, 4.0, 1.8 Hz, 4H), 1.72 (dt, *J* = 12.7, 3.2 Hz, 4H), 1.65 (dddt, *J* = 12.7, 5.1, 3.3, 1.5 Hz, 2H), 1.49 (dddt, *J* = 14.6, 8.0, 6.7, 3.2 Hz, 2H), 1.25 (qt, *J* = 12.7, 3.4 Hz, 4H), 1.15 (tt, *J* = 12.6, 3.2 Hz, 4H), 1.05 (t, *J* = 7.8 Hz, 6H), 1.03 – 0.98 (m, 2H), 0.67 (q, *J* = 7.8 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 108.03, 80.73, 37.36, 32.76, 27.95, 26.43, 26.29, 7.47, 7.02. IR (Neat Film NaCl) 2923, 2873, 2852, 2175, 1448, 1031, 725, 688 cm^{-1}; HRMS (EI+) calc'd for $C_{22}H_{37}Si$ [M+H]: 329.2665, found 329.2661.



Bis(3-cyclohexylprop-1-yn-1-yl)diphenylsilane 48b: The general procedure was followed. The reaction was performed with NaOH (4.0 mg, 0.1 mmol, 20 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), Ph_2SiH_2 (51 mg, 51 μL, 0.275 mmol, 0.55 equiv), and 0.5 mL of 1,2-

dimethoxyethane (DME) at 65 °C for 72 h. The desired product **48b** (71.5 mg, 67% yield) was obtained as a colorless oil via silica gel flash chromatography (gradient 100% hexanes → 2.5% Et_2O in hexanes); less than 10% of the monoalkynylhydrosilane (**48b_mono**) was observed by GC-MS. R_f = 0.21 (2.5% Et_2O in hexanes); ^{1}H NMR (500 MHz, THF-d_8) δ 7.72 – 7.67 (m, 4H), 7.38 – 7.28 (m, 6H), 2.25 (d, J = 6.6 Hz, 4H), 1.86 (dd, J = 13.9, 1.8 Hz, 4H), 1.72 (ddt, J = 9.2, 7.1, 3.5 Hz, 4H), 1.65 (dtd, J = 11.1, 3.4, 1.8 Hz, 2H), 1.55 (dddd, J = 14.5, 11.4, 6.6, 3.2 Hz, 2H), 1.28 (qt, J = 12.6, 3.3 Hz, 4H), 1.18 (tt, J = 12.6, 3.3 Hz, 2H), 1.08 (qd, J = 12.1, 3.3 Hz, 4H); ^{13}C NMR (126 MHz, THF-d_8) δ 135.60, 135.58, 130.64, 128.68, 110.99, 80.68, 38.43, 33.68, 28.47, 27.32, 27.21. IR (Neat Film NaCl) 2922, 2850, 2175, 1448, 1429, 1115, 1034, 740, 710, 697 cm^{-1}; HRMS (EI+) calc'd for $C_{30}H_{37}Si$ [M+H]: 425.2665, found 425.2663.





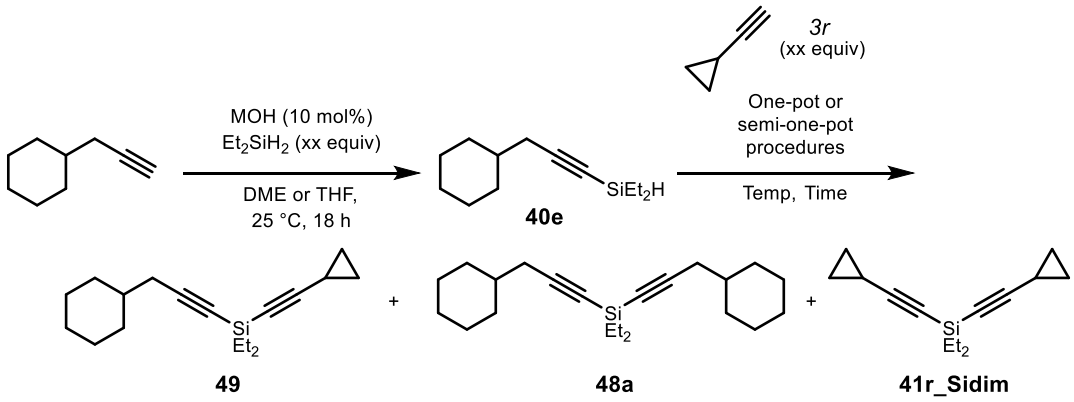
Diethylbis(mesitylethynyl)silane 48c: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 2-ethynyl-1,3,5-trimethylbenzene (72 mg, 0.5 mmol, 1.0 equiv), Et_2SiH_2 (24 mg, 36 μL, 0.275 mmol, 0.55 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 72 h. The desired product **48c** (78.3 mg, 84% yield) was obtained as a colorless oil via silica gel flash chromatography (2.5% Et_2O in hexanes). R_f = 0.38

(2.5% Et_2O in hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 6.86 (dd, J = 1.4, 0.7 Hz, 4H), 2.43 (t, J = 0.6 Hz, 12H), 2.28 (s, 6H), 1.19 (t, J = 7.8 Hz, 6H), 0.92 – 0.84 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.97, 138.26, 127.63, 119.95, 104.37, 97.04, 21.52, 21.10, 7.61, 7.05. IR (Neat Film NaCl) 2955, 2915, 2873, 2147, 1609, 1558, 1506, 1473, 1457, 1436, 1224, 1147, 1008, 967, 851, 810, 726, 679 cm^{-1}; HRMS (EI+) calc'd for $C_{26}H_{33}Si$ [M+H]: 373.2352, found 373.2351.

Optimization of unsymmetrical tethered diyne synthesis

Scheme 3.9 describes the synthetic strategy and product distribution for the synthesis of unsymmetrical diyne **49**. **Table 3.7** details the practical considerations, product distribution, and other factors that were observed during our optimization efforts in the development of a protocol for the synthesis of Si-tethered diynes. A protocol for obtaining the product in moderate yield (i.e., with the desired selectivity) is presented. Products are readily separated by conventional silica gel column chromatography.

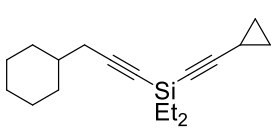
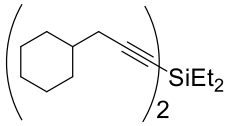
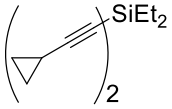
Scheme 3.9. Synthesis and optimization of unsymmetrical diynes 49.



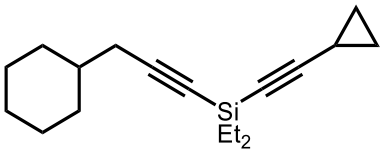
The conditions given in **Table 3.7**, entry 3 proved to be the most appropriate for the synthesis of unsymmetrical Si-tethered diyne **49**. For entry 3, KOH, which generally catalyzes the dehydrocoupling to a lesser rate than NaOH, was used along with an excess of diethylsilane in

order to minimize production of **48a** in the first step. For the second step, an excess (5.0 equivalents) of cyclopropylacetylene (**41r**) were added in a one-pot protocol. This reaction setup had the highest yield of the desired unsymmetrical dialkynylsilane **49** (62% isolated yield) along with minimal production of **48a** (4% isolated yield). An excess of **41r_Sidim** was also isolated (0.65 mmol), as expected, and could be readily separated from the desired product by standard silica gel chromatography. A two-step process involving isolation of **40e** provides the product in comparable yield.

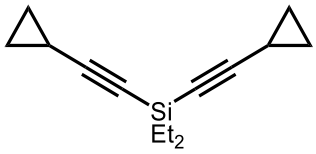
Table 3.7. Study of reaction conditions for unsymmetrical tethered diynes.[a]

Entry	Reaction Conditions *Reactions done on a 0.5 mmol scale.*	 **Yield 49** GC-FID; (Isolated)	 **Yield 48a** GC-FID; (Isolated)	 **41r_Sidim** GC-FID; (Isolated)
1	*"Semi-one-pot":* 1. **39**, KOH (10 mol%), Et_2SiH_2 (3.0 equiv) THF, 25 °C, 18 h 2. filtration, removal of volatiles 3. **41r** (1.2 equiv), NaOH (10 mol%) DME, 45 °C, 24 h then 65 °C, 48 h	**52%** (30%)	**18%** (14%)	**23%** (7%) *this product is volatile and is removed easily on high-vacuum*
2	*One-pot:* 1. **39**, NaOH (10 mol%), Et_2SiH_2 (1.5 equiv) DME, 25 °C, 18 h 2. **41r** (1.2 equiv) 45 °C, 24 h then 65 °C, 48 h	**53%** (51%)	**21%** (13%)	**25%** (14%)
3	*Excess of second alkyne:* 1. **39**, KOH (10 mol%), Et_2SiH_2 (3.0 equiv) DME, 25 °C, 18 h 2. **41r** (5.0 equiv) 45 °C, 24 h then 65 °C, 48 h	**66%** (62%)	**8%** (4%)	**0.82 mmol** (0.65 mmol) *due to excess **41r**, a large amount of* **41r_Sidim** *is produced.*

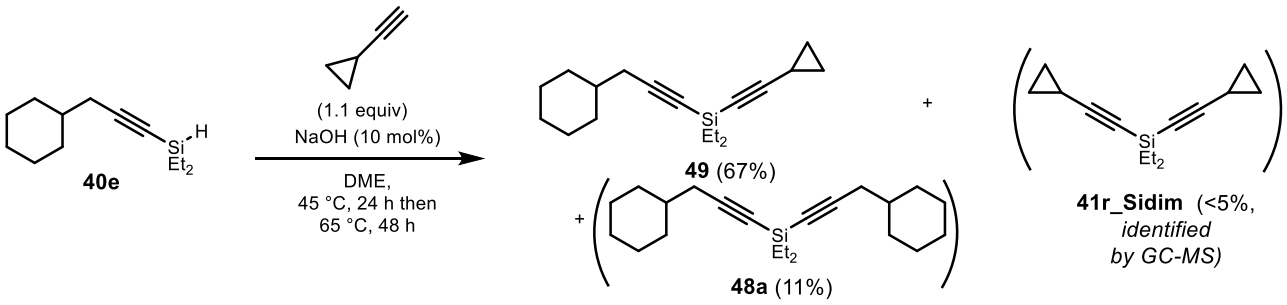
[a]Yields and selectivities determined by GC-FID; isolated yields are shown in parentheses. The difference between GC-FID and the isolated yields are due to volatility of the products under high vacuum.



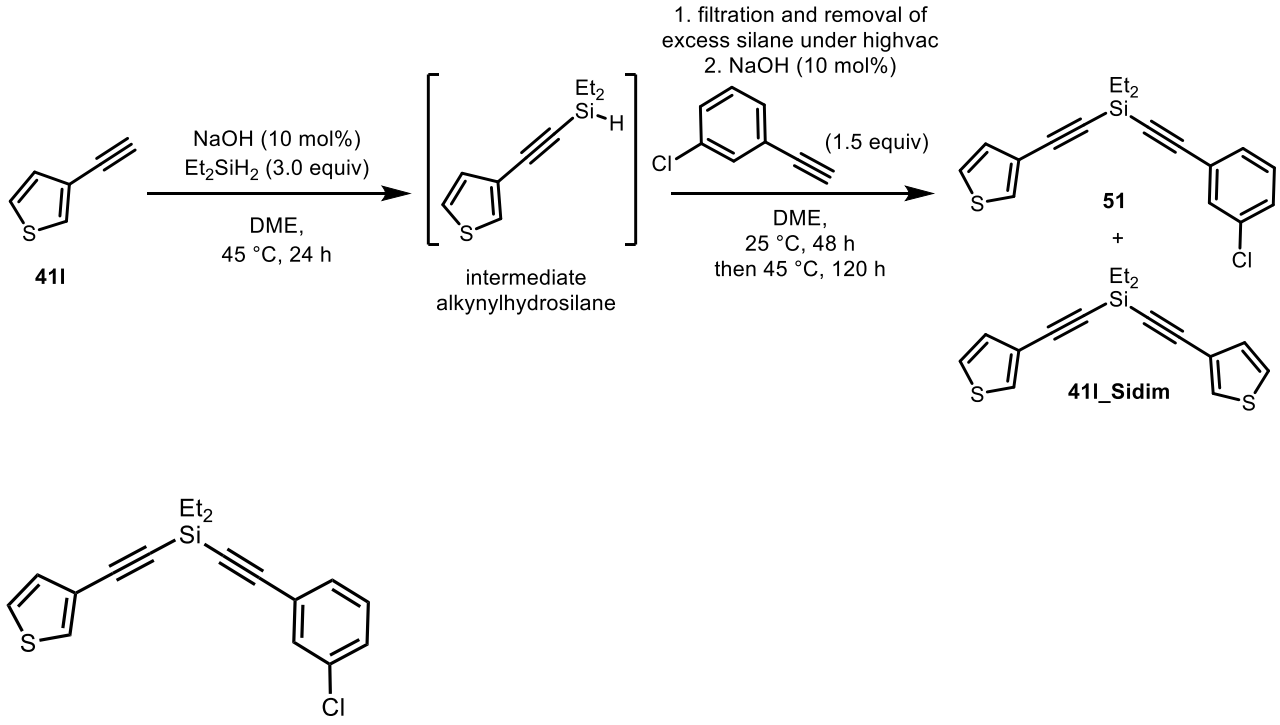
(3-Cyclohexylprop-1-yn-1-yl)(cyclopropylethynyl)diethylsilane 49: *The procedure written is for the one-pot reaction using excess of the second alkyne (entry 3 in* ***Table 3.7****).* The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), Et_2SiH_2 (132 mg, 194 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 25 °C for 18 h, after which cyclopropylacetylene (165 mg, 2.5 mmol, 5.0 equiv) was added. The reaction was stirred at 45 °C for 24 h then 65 °C for 48 h. The desired product **49** (84.4 mg, 62% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). Also isolated was <5% yield of the homocoupled 3-cyclohexyl-1-propyne product **48a** and the expected homocoupled cyclopropylacetylene **41r_Sidim** (see below). R_f = 0.34 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.14 (d, *J* = 6.6 Hz, 2H), 1.83 – 1.77 (m, 2H), 1.71 (dt, *J* = 12.7, 3.2 Hz, 2H), 1.65 (dddt, *J* = 12.8, 5.1, 3.3, 1.5 Hz, 1H), 1.48 (ddtd, *J* = 15.0, 11.6, 6.8, 3.6 Hz, 1H), 1.33 – 1.28 (m, 1H), 1.28 – 1.19 (m, 2H), 1.13 (qt, *J* = 12.8, 3.3 Hz, 1H), 1.03 (t, *J* = 7.9 Hz, 6H), 1.01 – 0.95 (m, 2H), 0.81 – 0.73 (m, 4H), 0.65 (q, *J* = 7.9 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 111.83, 108.11, 80.57, 75.08, 37.34, 32.76, 27.94, 26.41, 26.27, 8.98, 7.43, 6.98, 0.73. IR (Neat Film NaCl) 3422, 3094, 3012, 2955, 1923, 2852, 2174, 2105, 1641, 1449, 1424, 1376, 1348, 1322, 1275, 1232, 1130, 1073, 1052, 1028, 979, 891, 873, 828, 779, 725, 688, 642 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{29}Si$ [M+H]: 273.2039, found 273.2025.



Bis(cyclopropylethynyl)diethylsilane 41r_Sidim: Also isolated from the column was **41r_Sidim** (140.7 mg, 0.65 mmol = 65% yield from excess cyclopropylacetylene added) as a colourless oil. R_f = 0.21 (100% hexanes); ^{1}H NMR (500 MHz, Benzene-d_6) δ 1.33 – 1.25 (m, 2H), 1.00 (t, J = 7.9 Hz, 6H), 0.79 – 0.72 (m, 8H), 0.62 (q, J = 7.5 Hz, 4H); ^{13}C NMR (126 MHz, Benzene-d_6) δ 111.86, 74.96, 8.94, 7.37, 6.93, 0.71. IR (Neat Film NaCl) 3094, 3012, 2957, 2916, 2875, 2162, 1461, 1378, 1348, 1233, 1131, 1052, 1009, 828, 780, 725 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{20}Si$ [M+•]: 216.1334, found 216.1337.

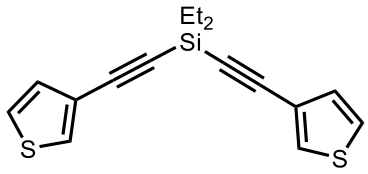


(3-Cyclohexylprop-1-yn-1-yl)(cyclopropylethynyl)diethylsilane 49: This product can also be achieved in comparable yield (91.3 mg, 67% yield) in a 2-step process by first obtaining the silylated cyclohexylpropyne **40e** and then following the general procedure, combining the pre-silylated product **40e** (104 mg, 0.5 mmol) with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclopropylacetylene (36 mg, 0.55 mmol, 1.1 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 24 h, then 65 °C for 48 h.



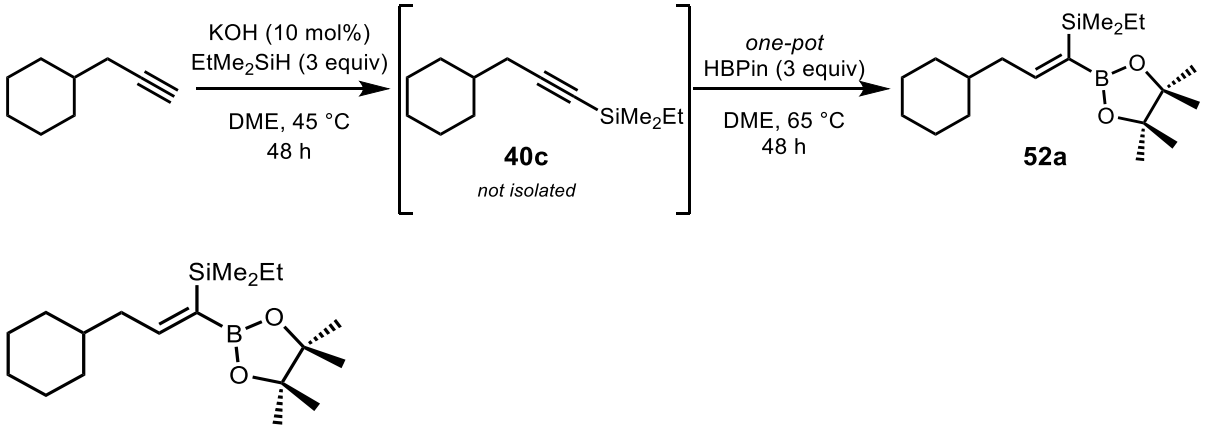
((3-Chlorophenyl)ethynyl)diethyl(thiophen-3-ylethynyl)silane 51: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 3-ethynylthiophene (54 mg, 0.5 mmol, 1.0 equiv), Et_2SiH_2 (132 mg, 195 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 24 h. The remaining silane and solvent were removed from the reaction mixture under high vacuum after removal of NaOH via filtration through a pad of silica, yielding the crude intermediate diethyl(thiophen-3-ylethynyl)silane. The intermediate alkynylhydrosilane was then resubjected to the reaction conditions to accomplish the second silylation without further isolation in a semi-one-pot procedure. The second step was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 3-chloroethynylbenzene (102 mg, 0.75 mmol, 1.5 equiv), and 0.5 mL of DME at 25 °C for 48 h, then 45 °C for 120 h. The desired product **51** (95.4 mg, 58% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). R_f = 0.28 (100% hexanes); ^{1}H NMR (500 MHz, Benzene-d_6) δ

7.38 (t, J = 1.9 Hz, 1H), 7.14 (dd, J = 3.0, 1.2 Hz, 1H), 7.08 (dt, J = 7.7, 1.3 Hz, 1H), 6.95 (dd, J = 5.0, 1.2 Hz, 1H), 6.87 (ddd, J = 8.1, 2.2, 1.0 Hz, 1H), 6.54 – 6.52 (m, 2H), 1.25 (t, J = 7.9 Hz, 6H), 0.91 (q, J = 7.9 Hz, 4H); ^{13}C NMR (126 MHz, Benzene-d_6) δ 134.42, 132.32, 130.80, 130.41, 130.27, 129.69, 129.28, 125.57, 124.85, 122.36, 105.66, 102.67, 91.04, 88.77, 7.69, 6.96. IR (Neat Film NaCl) 2957, 2932, 2874, 2154, 1591, 1559, 1473, 1406, 1357, 1232, 1162, 1091, 1007, 968, 884, 870, 782, 734, 681 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{18}SSiCl$ [M+H]: 329.0587, found 329.0580.



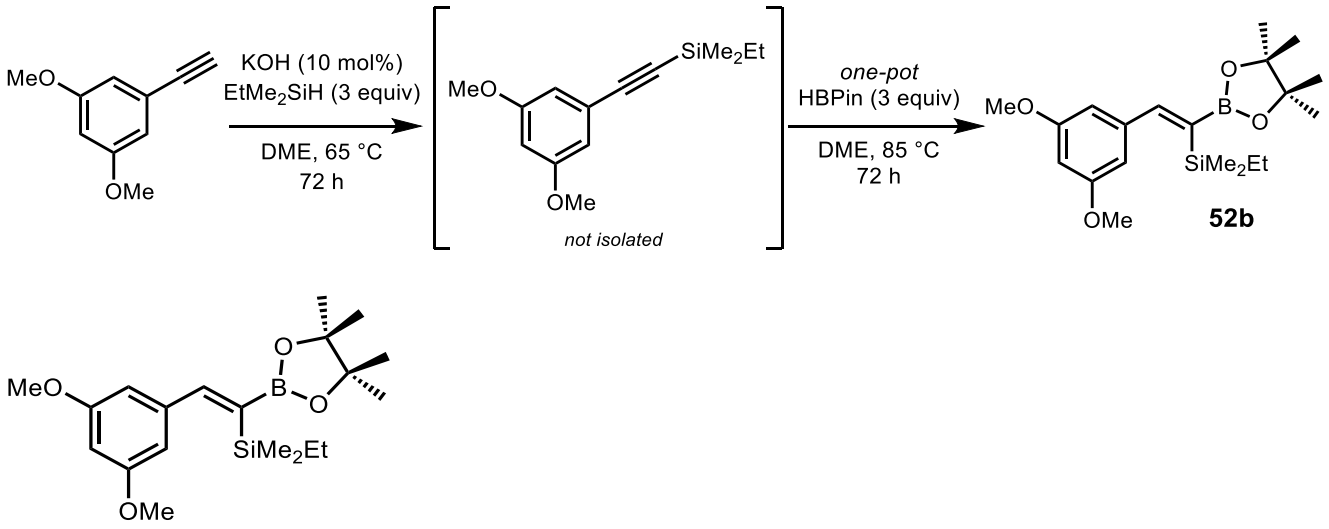
Diethylbis(thiophen-3-ylethynyl)silane 41l_Sidim: Also isolated from the column was **41l_Sidim** (13.7 mg, 18% yield) as a light yellow oil. R_f = 0.20 (100% hexanes); ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.11 (dd, J = 3.0, 1.2 Hz, 2H), 6.93 (dd, J = 5.0, 1.2 Hz, 2H), 6.54 (dd, J = 5.0, 3.0 Hz, 2H), 1.27 (t, J = 7.9 Hz, 6H), 0.93 (q, J = 7.9 Hz, 4H); ^{13}C NMR (126 MHz, Benzene-d_6) δ 130.65, 130.31, 125.44, 122.52, 102.44, 89.18, 7.73, 7.08. IR (Neat Film NaCl) 3108, 2957, 2930, 2874, 2153, 1559, 1457, 1357, 1223, 1162, 1102, 1008, 944, 870, 812, 782, 736, 627 cm^{-1}; HRMS (EI+) calc'd for $C_{16}H_{17}S_2Si$ [M+H]: 301.0541, found 301.0547.

Geminal silaboration of alkynes: one-pot synthesis of vinyl dimetallics



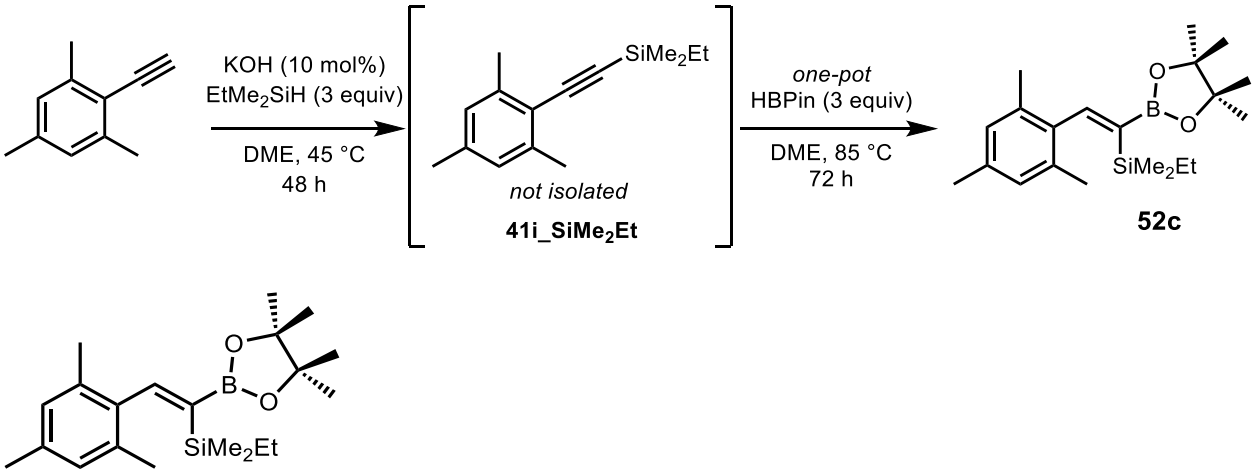
(Z)-(3-cyclohexyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-en-1-yl) (ethyl)dimethylsilane 52a: The general procedure was followed for the silylation portion of the reaction. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv), $EtMe_2SiH$ (132 mg, 198 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h to yield the intermediate **2c**. HBPin (192 mg, 218 μL, 1.5 mmol, 3.0 equiv) was then added and the reaction mixture was stirred for a further 48 h at 65 °C. The desired product **52a** (107.6 mg, 64% yield) was obtained as a colorless oil by silica gel flash chromatography (2.5% EtOAc in hexanes). Note: product is somewhat unstable on silica gel, possibly contributing to the lower isolated yield. R_f = 0.24 (2.5% EtOAc in hexanes); ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.57 (t, J = 7.2 Hz, 1H), 2.23 (t, J = 7.0 Hz, 2H), 1.72 (ddd, J = 14.7, 5.0, 2.6 Hz, 2H), 1.67 – 1.51 (m, 4H), 1.34 (dddq, J = 14.6, 11.0, 7.0, 3.5 Hz, 1H), 1.14 (td, J = 7.9, 0.7 Hz, 3H), 1.09 (d, J = 0.6 Hz, 12H), 1.08 – 1.04 (m, 2H), 0.93 (q, J = 8.0 Hz, 2H), 0.89 – 0.84 (m, 2H), 0.42 (d, J = 0.6 Hz, 6H); ^{13}C NMR (126 MHz, Benzene-d_6) δ 163.13, 82.76, 43.20, 38.62, 33.68, 26.94, 26.79, 26.72, 24.93, 9.42, 8.15, -0.51. IR (Neat Film NaCl) 2976, 2923, 2852, 1581, 1448, 1370, 1326, 1292, 1270, 1245, 1213, 1146, 1109, 1006, 981,

962, 856, 835, 817, 777, 696 cm^{-1}; HRMS (EI+) calc'd for $C_{19}H_{36}BSiO_2$ [(M+H)-H_2]: 335.2578, found 335.2577. Olefin geometry was confirmed by 2D-NOESY.



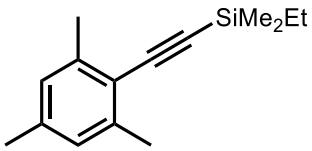
(Z)-(2-(3,5-dimethoxyphenyl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl) (ethyl)dimethylsilane 52b: The general procedure was followed for the silylation portion of the reaction. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), 1-ethynyl-3,5-dimethoxybenzene (81 mg, 0.5 mmol, 1.0 equiv), $EtMe_2SiH$ (132 mg, 198 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 72 h to yield the silylated alkyne intermediate. HBPin (192 mg, 218 μL, 1.5 mmol, 3.0 equiv) was then added and the reaction mixture was stirred for a further 72 h at 85 °C. The desired product **52b** (56.5 mg, 30% yield) was obtained as a colorless oil by silica gel flash chromatography (10% EtOAc in hexanes). Note: product is somewhat unstable on silica gel, possibly contributing to the lower isolated yield. R_f = 0.49 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, Benzene-d_6) δ 8.59 (s, 1H), 6.60 (dt, J = 2.3, 0.6 Hz, 2H), 6.52 (t, J = 2.3 Hz, 1H), 3.30 (s, 6H), 1.12 (s, 12H), 1.06 (t, J = 7.6 Hz, 3H), 0.89 (q, J = 7.8 Hz, 2H), 0.30 (s, 6H); ^{13}C NMR (126 MHz, Benzene-d_6) δ 161.03, 159.67, 144.06, 106.46,

100.75, 83.21, 54.86, 24.94, 9.40, 8.11, -0.93. IR (Neat Film NaCl) 2976, 2953, 2873, 1592, 1569, 1458, 1422, 1370, 1316, 1270, 1246, 1204, 1154, 1066, 1009, 960, 855, 832, 780, 691, 673 cm^{-1}; HRMS (EI+) calc'd for $C_{20}H_{34}BSiO_4$ [M+H]: 377.2320, found 377.2318. Olefin geometry was confirmed by 2D-NOESY.

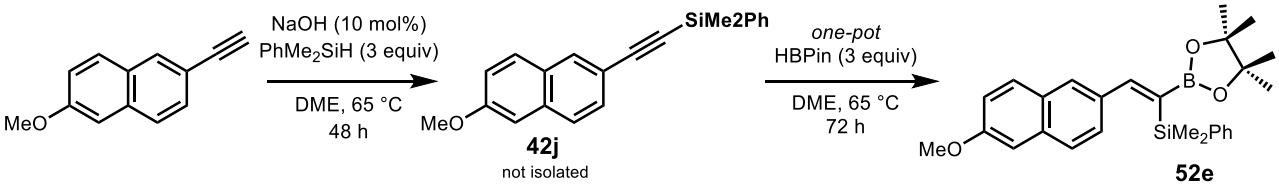


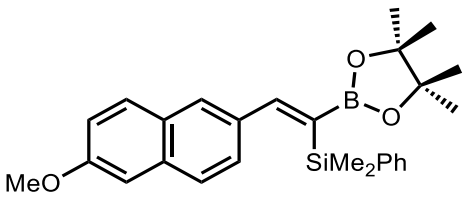
(Z)-ethyl(2-mesityl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)dimethyl silane 52c: The general procedure was followed for the silylation portion of the reaction. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), 2-ethynyl-1,3,5-trimethylbenzene (72 mg, 0.5 mmol, 1.0 equiv), $EtMe_2SiH$ (132 mg, 198 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h to yield the intermediate **41i_SiMe2Et**. HBPin (192 mg, 218 μL, 1.5 mmol, 3.0 equiv) was then added and the reaction mixture was stirred for a further 72 h at 85 °C. The desired product **52c** (57.3 mg, 32% yield) was obtained as a yellow gel by silica gel flash chromatography (2.5% EtOAc in hexanes). Note: product is somewhat unstable on silica gel, possibly contributing to the lower isolated yield. R_f = 0.25 (2.5% EtOAc in hexanes); ^{1}H NMR (500 MHz, Benzene-d_6) δ 8.36 (s, 1H), 6.73 (d, J = 1.3 Hz, 2H), 2.21 (s, 6H), 2.13 (s, 3H), 1.11 (s, 12H), 1.03 (t, J = 7.9 Hz, 3H), 0.77 (q, J = 7.9 Hz, 2H), 0.07 (s, 6H); ^{13}C NMR (126 MHz, Benzene-

d$_6$) δ 159.59, 138.85, 136.10, 134.38, 128.16, 83.07, 24.91, 21.16, 20.71, 8.44, 8.10, -2.33. IR (Neat Film NaCl) 2976, 2950, 2872, 1612, 1579, 1478, 1461, 1370, 1317, 1270, 1244, 1145, 1008, 960, 860, 849, 837, 822, 811, 777, 690 cm^{-1}; HRMS (EI+) calc'd for $C_{21}H_{35}BSiO_2$ [M+•]: 358.2499, found 358.2495. Olefin geometry was confirmed by 2D-NOESY.

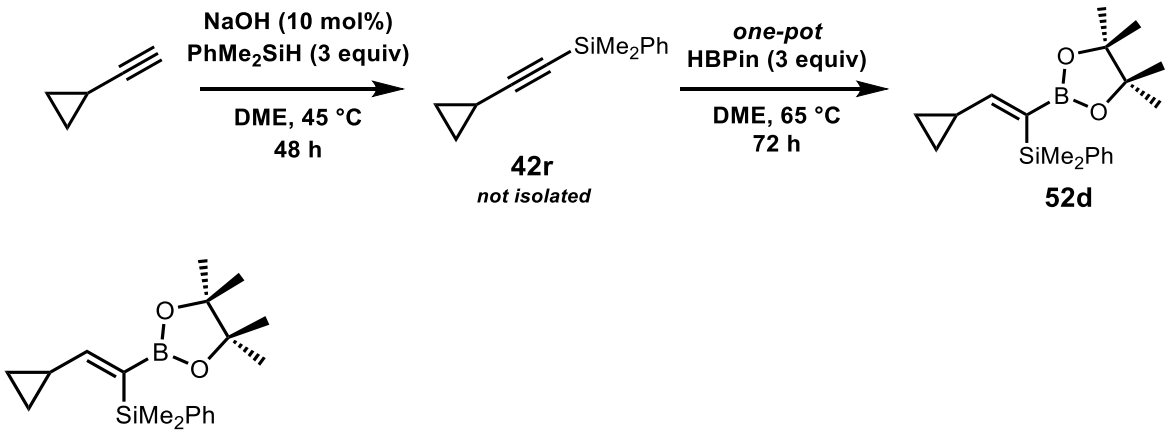


ethyl(mesitylethynyl)dimethylsilane 41i_SiMe$_2$Et: Also isolated from the column was **41i_SiMe$_2$Et** (50.7 mg, 44% yield) as a colourless oil. R_f = 0.63 (2.5% EtOAc in hexanes); ^{1}H NMR (500 MHz, Benzene-*d*$_6$) δ 6.67 (d, J = 0.6 Hz, 2H), 2.47 (s, 6H), 2.05 (s, 3H), 1.13 (t, J = 7.9 Hz, 3H), 0.69 (q, J = 7.9 Hz, 2H), 0.26 (s, 6H); ^{13}C NMR (126 MHz, Benzene-*d*$_6$) δ 140.71, 137.96, 128.01, 120.75, 104.46, 101.00, 21.35, 21.24, 8.70, 7.81, -1.76. IR (Neat Film NaCl) 2956, 2914, 2874, 2147, 1610, 1476, 1413, 1376, 1249, 1224, 1013, 960, 832, 779, 729, 699, 617 cm^{-1}; HRMS (EI+) calc'd for $C_{15}H_{22}Si$ [M+•]: 230.1491, found 230.1495.



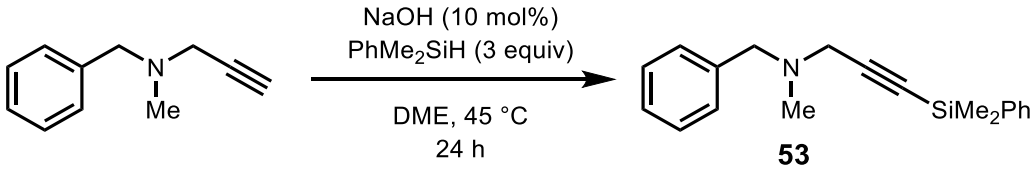


(Z)-(2-(6-methoxynaphthalen-2-yl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) vinyl)dimethyl(phenyl)silane 52e: The general procedure was followed for the silylation portion of the reaction. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 2-ethynyl-6-methoxynaphthalene (91 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h to yield the intermediate **42j**. HBPin (192 mg, 218 μL, 1.5 mmol, 3.0 equiv) was then added and the reaction mixture was stirred for a further 72 h at 65 °C. The desired product **52e** (73.4 mg, 33% yield) was obtained as a colorless gel by silica gel flash chromatography (gradient 2.5% EtOAc in hexanes → 10% EtOAc in hexanes). Note: product is somewhat unstable on silica gel, possibly contributing to the lower isolated yield. Also isolated was the silylated intermediate **42j** (13.5 mg, 4% yield). R_f = 0.49 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, Benzene-d_6) δ 8.76 (d, J = 1.0 Hz, 1H), 7.81 (dd, J = 8.0, 1.4 Hz, 2H), 7.63 (d, J = 1.4 Hz, 1H), 7.41 – 7.33 (m, 3H), 7.26 (tt, J = 7.8, 1.3 Hz, 2H), 7.19 (tt, J = 7.5, 1.5 Hz, 1H), 7.09 (dd, J = 8.9, 2.5 Hz, 1H), 6.80 (d, J = 2.5 Hz, 1H), 3.33 (s, 3H), 1.12 (s, 12H), 0.47 (s, 6H); ^{13}C NMR (126 MHz, Benzene-d_6) δ 160.46, 158.55, 141.64, 136.58, 134.79, 134.45, 130.16, 128.84, 128.82, 128.54, 127.44, 126.53, 119.45, 106.01, 83.31, 54.76, 24.93, 0.18. IR (Neat Film NaCl) 3049, 2976, 1630, 1604, 1563, 1499, 1481, 1462, 1427, 1410, 1370, 1392, 1315, 1265, 1220,1166, 1110, 1032, 987, 851, 816, 733, 702 cm^{-1}; HRMS (EI+) calc'd for $C_{27}H_{33}BSiO_3$ [M+•]: 444.2292, found 444.2304. Olefin geometry was confirmed by 2D-NOESY.

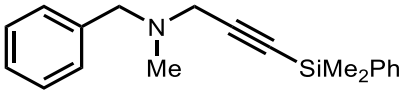


(Z)-(2-cyclopropyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)dimethyl (phenyl)silane 52d: The general procedure was followed for the silylation portion of the reaction. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclopropylacetylene (33 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h to yield the intermediate **42r**. HBPin (192 mg, 218 μL, 1.5 mmol, 3.0 equiv) was then added and the reaction mixture was stirred for a further 72 h at 65 °C. The desired product **52d** (94.6 mg, 58% yield) was obtained as a colorless oil by silica gel flash chromatography (2.5% EtOAc in hexanes). Note: product is somewhat unstable on silica gel, possibly contributing to the lower isolated yield. R_f = 0.38 (2.5% EtOAc in hexanes); ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.77 – 7.72 (m, 2H), 7.29 – 7.22 (m, 3H), 6.83 (d, J = 10.5 Hz, 1H), 1.58 – 1.48 (m, 1H), 1.07 (s, 12H), 0.69 (s, 6H), 0.41 – 0.36 (m, 2H), 0.27 (dt, J = 6.9, 4.2 Hz, 2H); ^{13}C NMR (126 MHz, Benzene-d_6) δ 169.81, 141.35, 134.42, 128.81, 128.02, 82.75, 24.91, 17.52, 8.87, 0.56, -1.52. IR (Neat Film NaCl) 3068, 2977, 1580, 1443, 1427, 1370, 1333, 1309, 1293, 1270,1246, 1145, 1110, 1048, 944, 849, 836, 816, 775, 730, 700, 671 cm^{-1}; HRMS (EI+) calc'd for $C_{19}H_{29}BSiO_2$ [M+•]: 328.2030, found 328.2037. Olefin geometry was confirmed by 2D-NOESY.

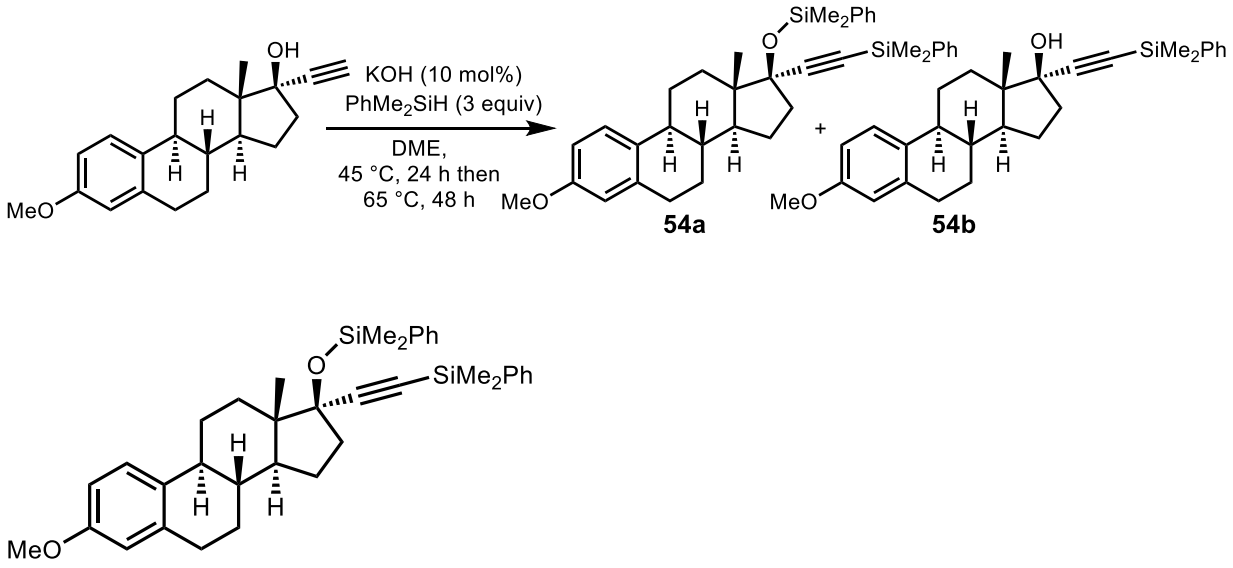
Late-stage silylation of APIs



53

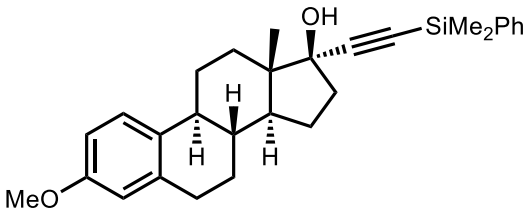


N-benzyl-3-(dimethyl(phenyl)silyl)-N-methylprop-2-yn-1-amine 53: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), Pargyline (N-benzyl-N-methylprop-2-yn-1-amine) (80 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 24 h. The desired product **53** (140.4 mg, 96% yield) was obtained in analytical purity as a pale yellow oil after removal of volatiles at 85 °C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (dq, *J* = 6.8, 3.4, 2.7 Hz, 2H), 7.40 (dt, *J* = 4.3, 2.1 Hz, 3H), 7.35 – 7.31 (m, 4H), 7.30 – 7.26 (m, 1H), 3.60 (d, *J* = 3.0 Hz, 2H), 3.38 (d, *J* = 3.1 Hz, 2H), 2.38 (d, *J* = 3.2 Hz, 3H), 0.47 (d, *J* = 3.4 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.47, 137.34, 133.82, 129.54, 129.39, 128.45, 128.01, 127.35, 102.95, 88.41, 60.17, 46.08, 42.09, –0.49. IR (Neat Film NaCl) 3067, 3026, 2958, 2793, 2162, 1494, 1453, 1428, 1366, 1249, 1115, 1026, 980, 837, 817, 780, 732, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{19}H_{24}NSi$ [M+H]: 294.1678, found 294.1689.



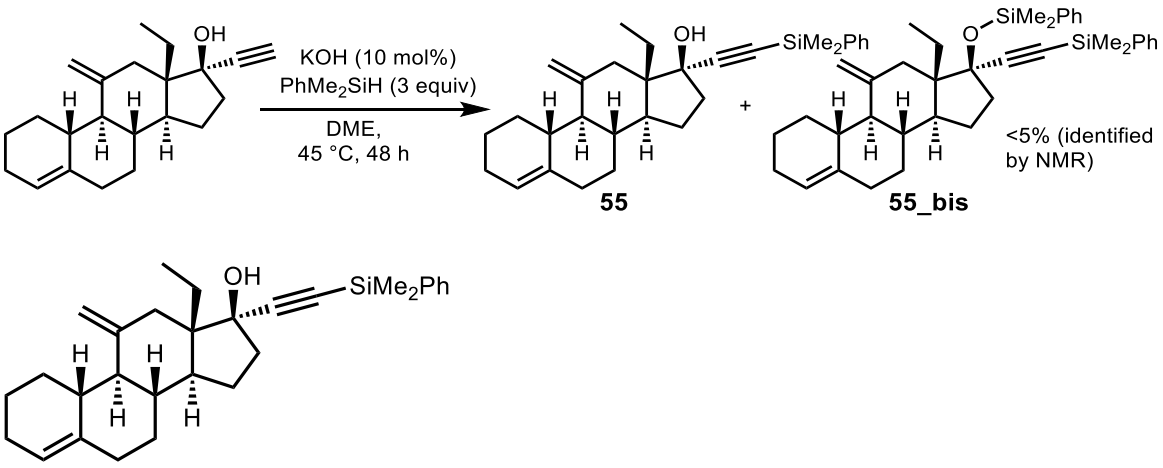
(((8R,9S,13S,14S,17S)-17-((dimethyl(phenyl)silyl)ethynyl)-3-methoxy-13-methyl-7,8, 9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-17-yl)oxy)dimethyl (phenyl)silane 54a: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), mestranol ((8R,9S,13S,14S,17R)-17-ethynyl-3-methoxy-13-methyl- 7,8,9,11,12,13,14,15,16,17- decahydro -6H-cyclopenta[a]phenan-thren-17-ol) (155 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 24 h then 65 °C for 48 h. The product **54a** (185.5 mg, 64% yield) was obtained as a colorless oil by silica gel flash chromatography (1% → 5% EtOAc in hexanes). R_f = 0.50 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, THF-d_8) δ 7.59 (ddd, *J* = 7.6, 3.6, 2.1 Hz, 4H), 7.34 – 7.26 (m, 6H), 7.16 (d, *J* = 8.6 Hz, 1H), 6.63 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.57 (d, *J* = 2.7 Hz, 1H), 3.70 (s, 3H), 2.87 – 2.79 (m, 2H), 2.36 (dq, *J* = 13.4, 3.9 Hz, 1H), 2.30 (ddd, *J* = 13.3, 9.2, 5.3 Hz, 1H), 2.16 (ddd, *J* = 14.6, 7.7, 2.8 Hz, 1H), 2.02 (dtd, *J* = 26.4, 12.8, 4.1 Hz, 2H), 1.88 (ddt, *J* = 12.7, 5.6, 2.5 Hz, 1H), 1.83 – 1.74 (m, 3H), 1.51 – 1.37 (m, 3H), 1.35 – 1.26 (m, 1H), 0.93 (s, 3H), 0.44 (d, *J* = 8.0 Hz, 6H), 0.34 (s, 6H); ^{13}C NMR (126 MHz, THF-d_8) δ

158.89, 140.79, 138.43, 137.86, 134.65, 134.38, 133.10, 130.31, 129.97, 128.73, 128.44, 127.12, 114.47, 112.89, 112.38, 90.45, 82.69, 68.10, 55.34, 49.87, 49.47, 45.17, 41.66, 40.97, 34.18, 30.86, 28.64, 27.69, 24.00, 1.41, 1.36, -0.63, -0.65. IR (Neat Film NaCl) 3417, 3068, 3048, 2946, 2869, 2234, 2160, 2081, 1610, 1575, 1500, 1465, 1427, 1279, 1252, 1136, 1117, 1088, 1045, 929, 886, 818, 783, 730, 699, 642 cm^{-1}; HRMS (EI+) calc'd for $C_{37}H_{47}O_2Si_2$ [M+H]: 579.3115, found 579.3109.



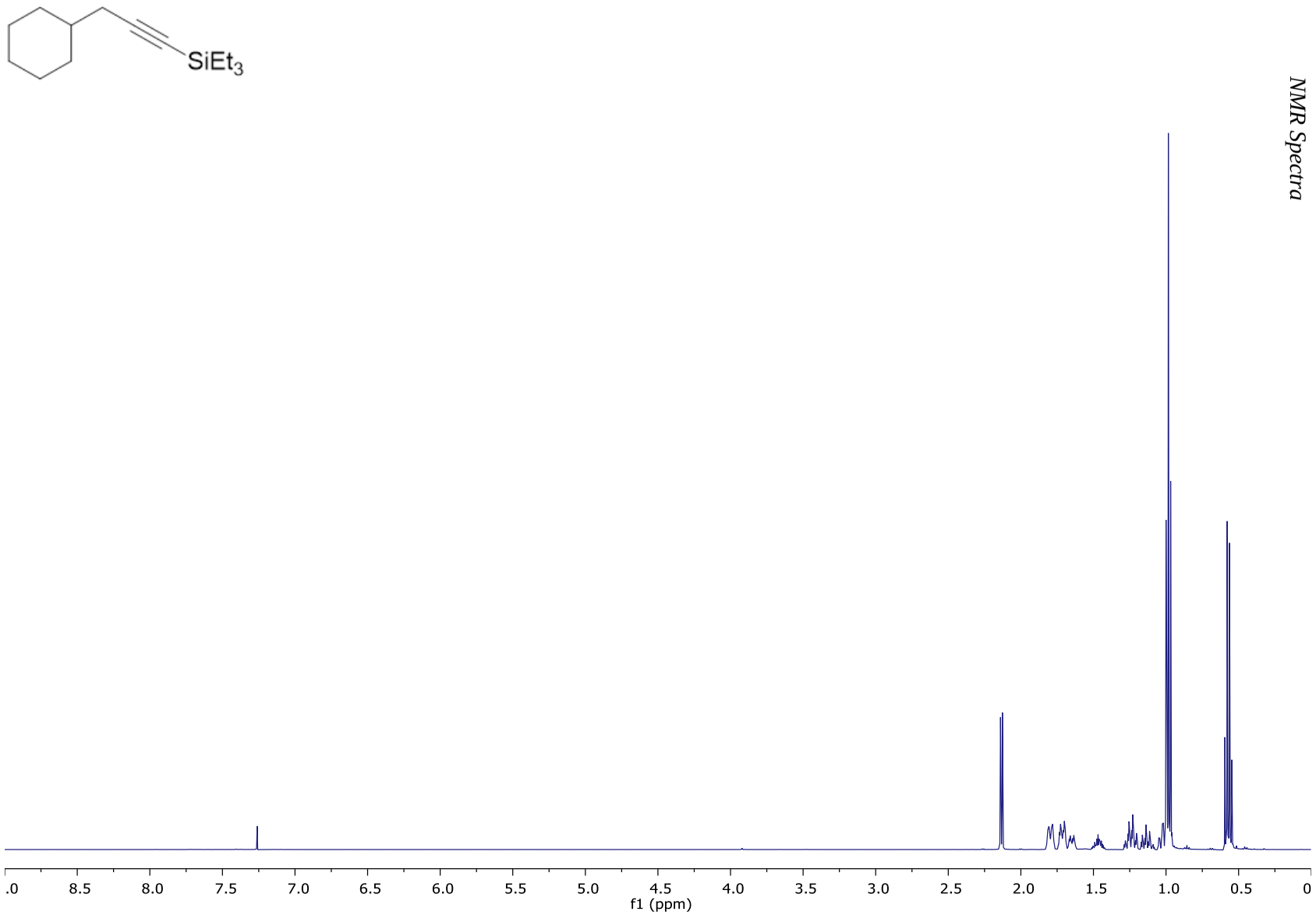
(8R,9S,13S,14S,17S)-17-((dimethyl(phenyl)silyl)ethynyl)-3-methoxy-13-methyl-7,8,9, 11,12,13,14,15,16,17- decahydro- 6H- cyclopenta[a]phenanthren- 17- ol 54b: The desired product **54b** (40.0 mg, 18% yield) was also obtained from this reaction as a white solid foam by silica gel flash chromatography (1% → 5% EtOAc in hexanes) in a 9:1 mixture with **54a**. R_f = 0.39 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, THF-d_8) δ 7.61 – 7.56 (m, 2H), 7.35 – 7.30 (m, 3H), 7.13 (dd, *J* = 8.7, 1.1 Hz, 1H), 6.62 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.58 – 6.53 (m, 1H), 3.69 (s, 3H), 2.85 – 2.77 (m, 2H), 2.27 (dtd, *J* = 13.5, 4.2, 2.7 Hz, 1H), 2.11 (td, *J* = 11.2, 4.3 Hz, 1H), 1.91 – 1.84 (m, 4H), 1.66 – 1.61 (m, 1H), 1.57 – 1.47 (m, 1H), 1.46 – 1.38 (m, 2H), 1.36 – 1.30 (m, 1H), 1.17 – 1.09 (m, 2H), 0.80 (d, *J* = 0.7 Hz, 3H), 0.34 (d, *J* = 0.7 Hz, 6H); ^{13}C NMR (126 MHz, THF-d_8) δ 158.91, 140.86, 138.41, 134.21, 132.93, 130.04, 128.59, 127.30, 114.46, 112.45, 91.05, 82.88, 68.10, 55.37, 49.98, 49.46, 45.21, 40.94, 40.81, 34.18, 30.90, 28.64, 27.77, 24.00, 14.21, 1.64, 1.45. IR (Neat Film NaCl) 3421, 2932, 2869, 1609, 1500, 1464, 1427, 1979, 1253, 1138,

1117, 1099, 1035, 888, 829, 783, 742, 699 cm^{-1}; HRMS (EI+) calc'd for $C_{29}H_{37}O_2Si$ [M+H]: 445.2563, found 445.2575.

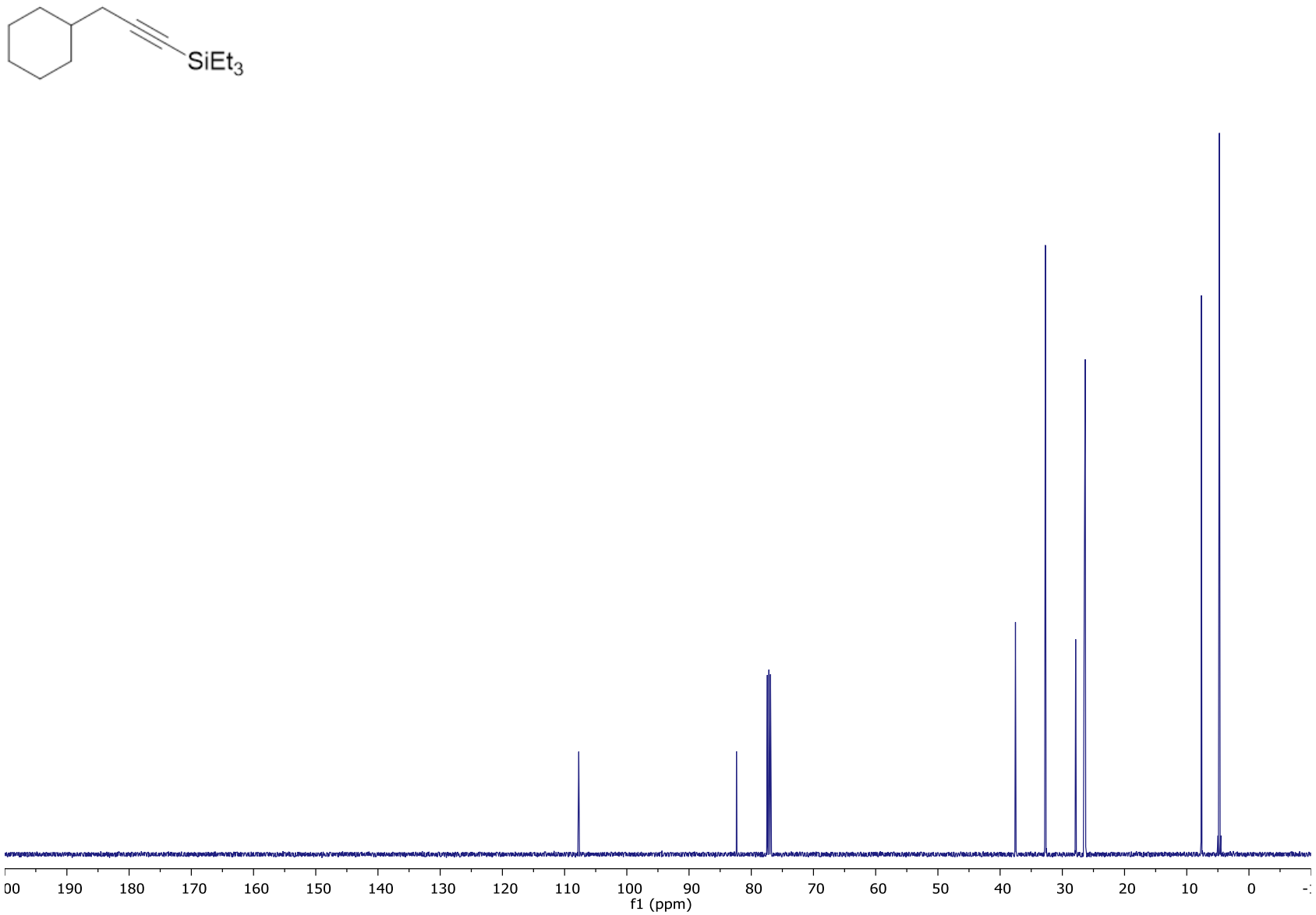


(8S,9S,10R,13S,14S,17S)-17-((dimethyl(phenyl)silyl)ethynyl)-13-ethyl-11-methylene-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-ol 55: The general procedure was followed. The reaction was performed with KOH (1.1 mg, 0.02 mmol, 10 mol%), desogestrel ((8S,9S,10R,13S,14S,17R)-13-ethyl-17-ethynyl-11-methylene-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phen-anthren-17-ol) (62 mg, 0.2 mmol, 1.0 equiv), $PhMe_2SiH$ (82 mg, 92 μL, 0.6 mmol, 3.0 equiv), and 0.2 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The product **55** (53.4 mg, 60% yield) was obtained as a colorless solid by silica gel flash chromatography (2.5% Et_2O in hexanes). Also observed were what appear to be <5% of the *bis*-silylated product **55-bis** and <5% of the *mono*-O-silylated desogestrel. R_f = 0.28 (2.5% Et_2O in hexanes); ^1H NMR (500 MHz, THF-d_8) δ 7.63 – 7.54 (m, 2H), 7.33 – 7.28 (m, 3H), 5.44 (dt, J = 4.2, 2.4 Hz, 1H), 4.99 (s, 1H), 4.76 (s, 1H), 2.67 (d, J = 12.4 Hz, 1H), 2.24 (q, J = 7.7, 7.1 Hz, 2H), 2.17 (ddt, J = 13.8, 7.0, 3.8 Hz, 2H), 2.13 – 2.01 (m, 2H), 1.96 – 1.90 (m, 3H), 1.88 – 1.77 (m, 1H), 1.67 – 1.54 (m, 2H), 1.49 – 1.37 (m, 4H), 1.35 – 1.28

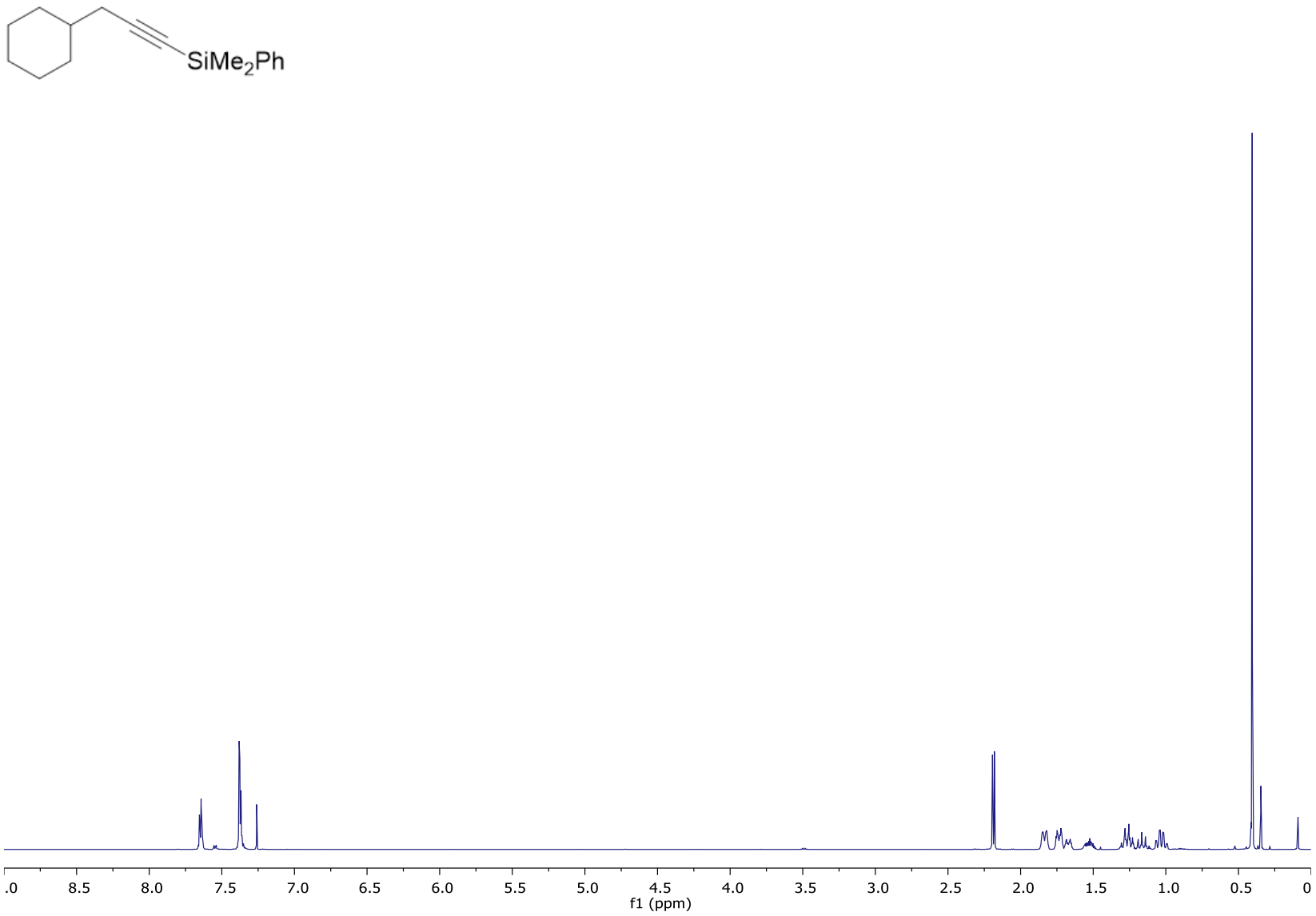
(m, 4H), 1.01 (t, J = 7.3 Hz, 3H), 0.93-0.86 (m, 1H), 0.38 (d, J = 6.0 Hz, 6H); ^{13}C NMR (126 MHz, THF-d_8) δ 149.06, 140.69, 134.18, 130.11, 128.67, 122.17, 109.00, 91.27, 83.94, 56.19, 52.97, 52.25, 43.92, 41.63, 41.58, 37.63, 36.62, 32.98, 30.34, 26.70, 25.99, 23.13, 22.98, 21.40, 9.99, 1.60, 1.16. IR (Neat Film NaCl) 3543, 3164, 3000, 2926, 2854, 2293, 2253, 1636, 1506, 1455, 1374, 1249, 1118, 1038, 917, 829, 784, 741, 700 cm^{-1}; HRMS (EI+) calc'd for $C_{30}H_{41}OSi$ [M+H]: 445.2927, found 445.2931.



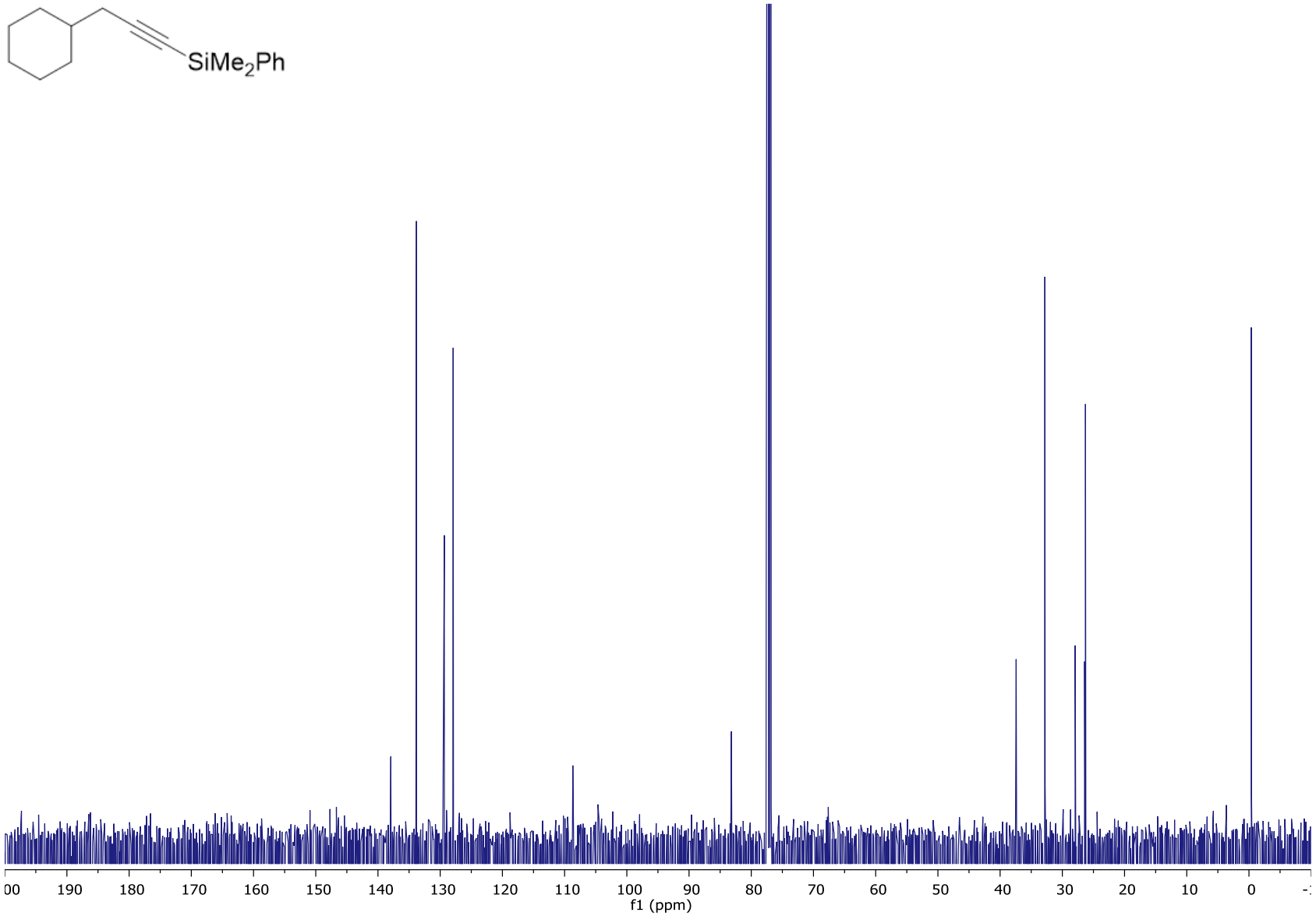
^{1}H NMR (500 MHz, $CDCl_3$) of compound **40a**.



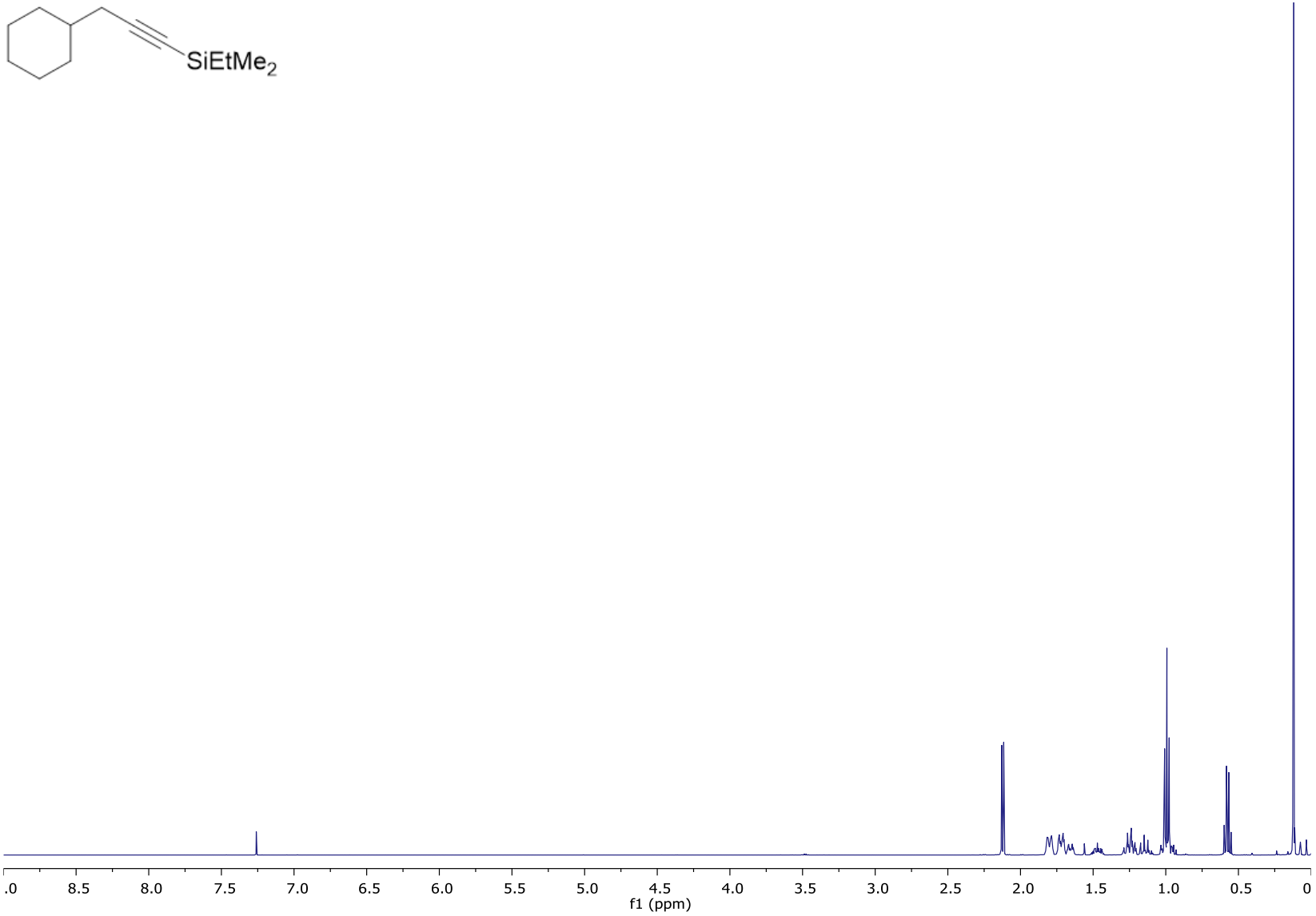
^{13}C NMR (126 MHz, $CDCl_3$) of compound **40a.**



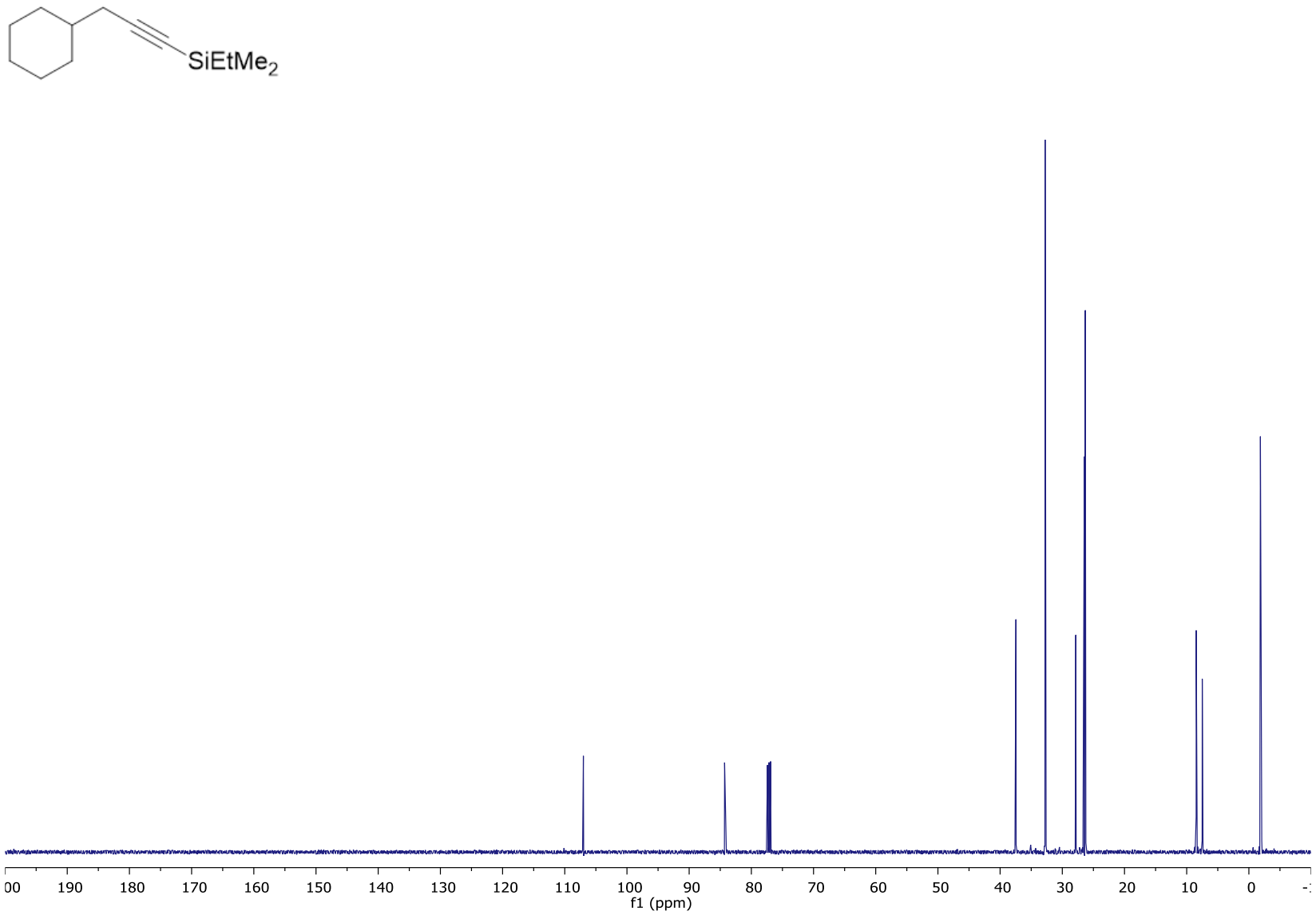
^{1}H NMR (500 MHz, $CDCl_3$) of compound **40b.**



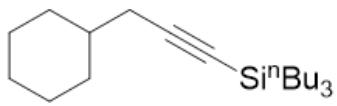
^{13}C NMR (126 MHz, $CDCl_3$) of compound **40b.**

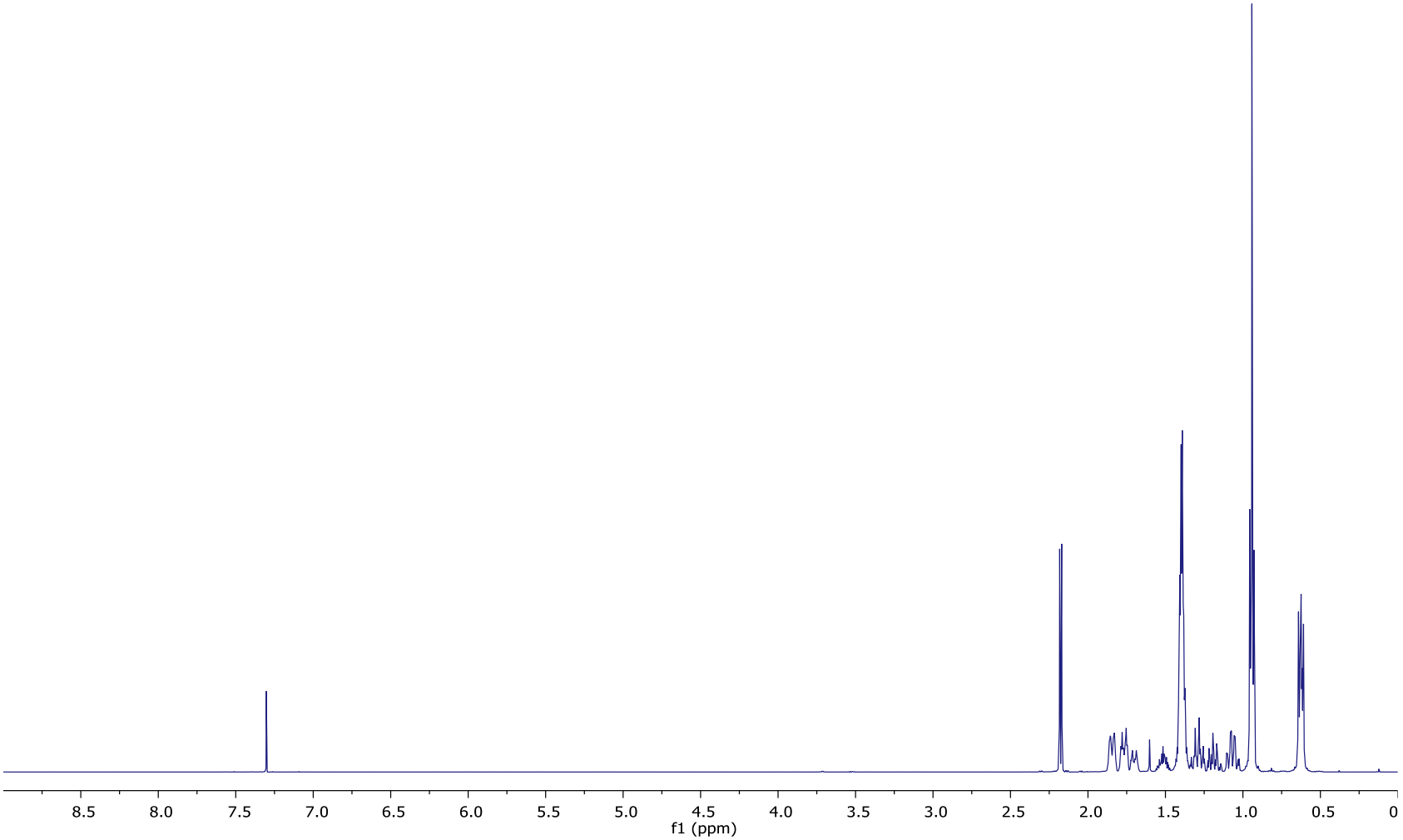


^{1}H NMR (500 MHz, $CDCl_3$) of compound **40c.**

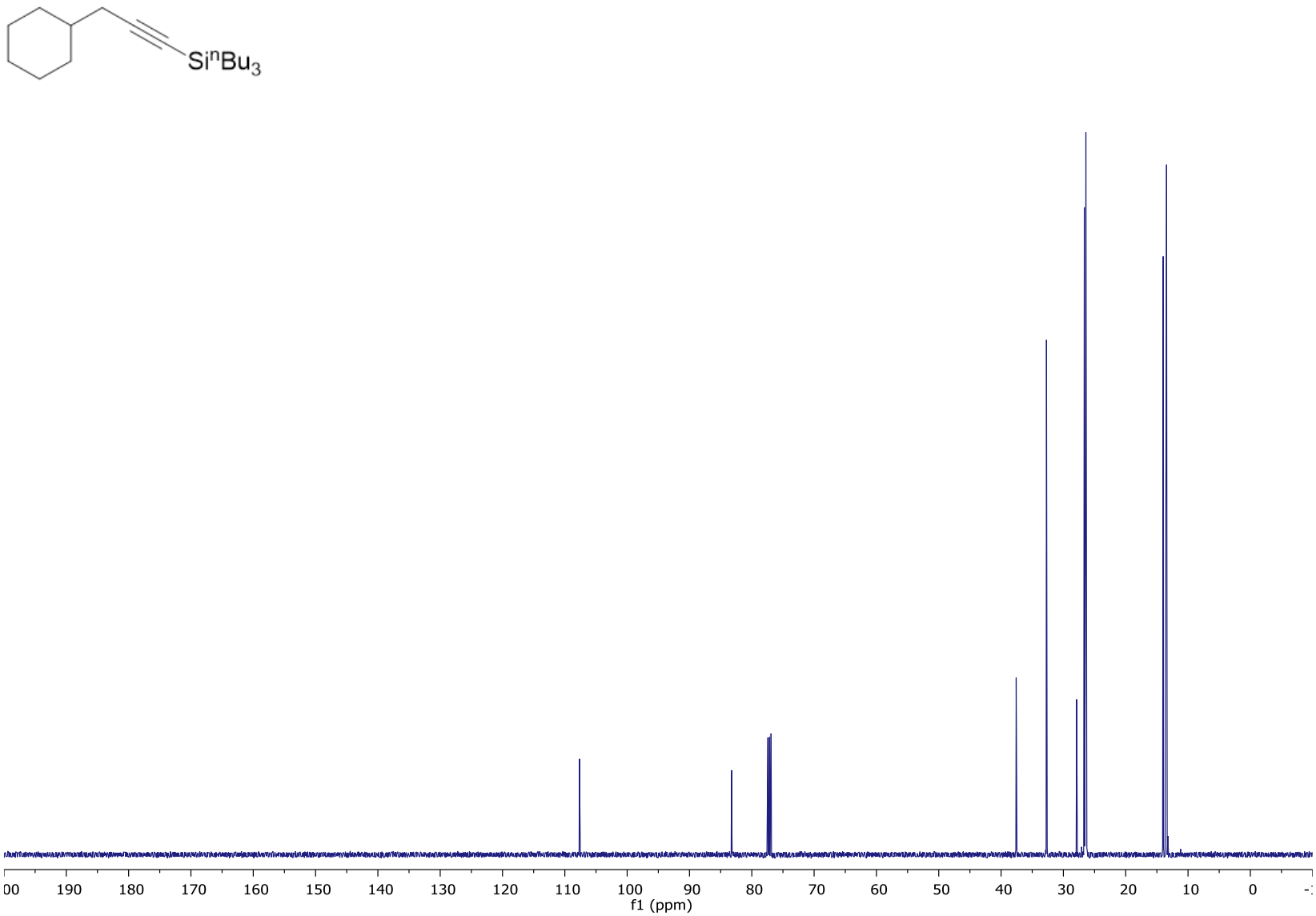


^{13}C NMR (126 MHz, $CDCl_3$) of compound **40c.**

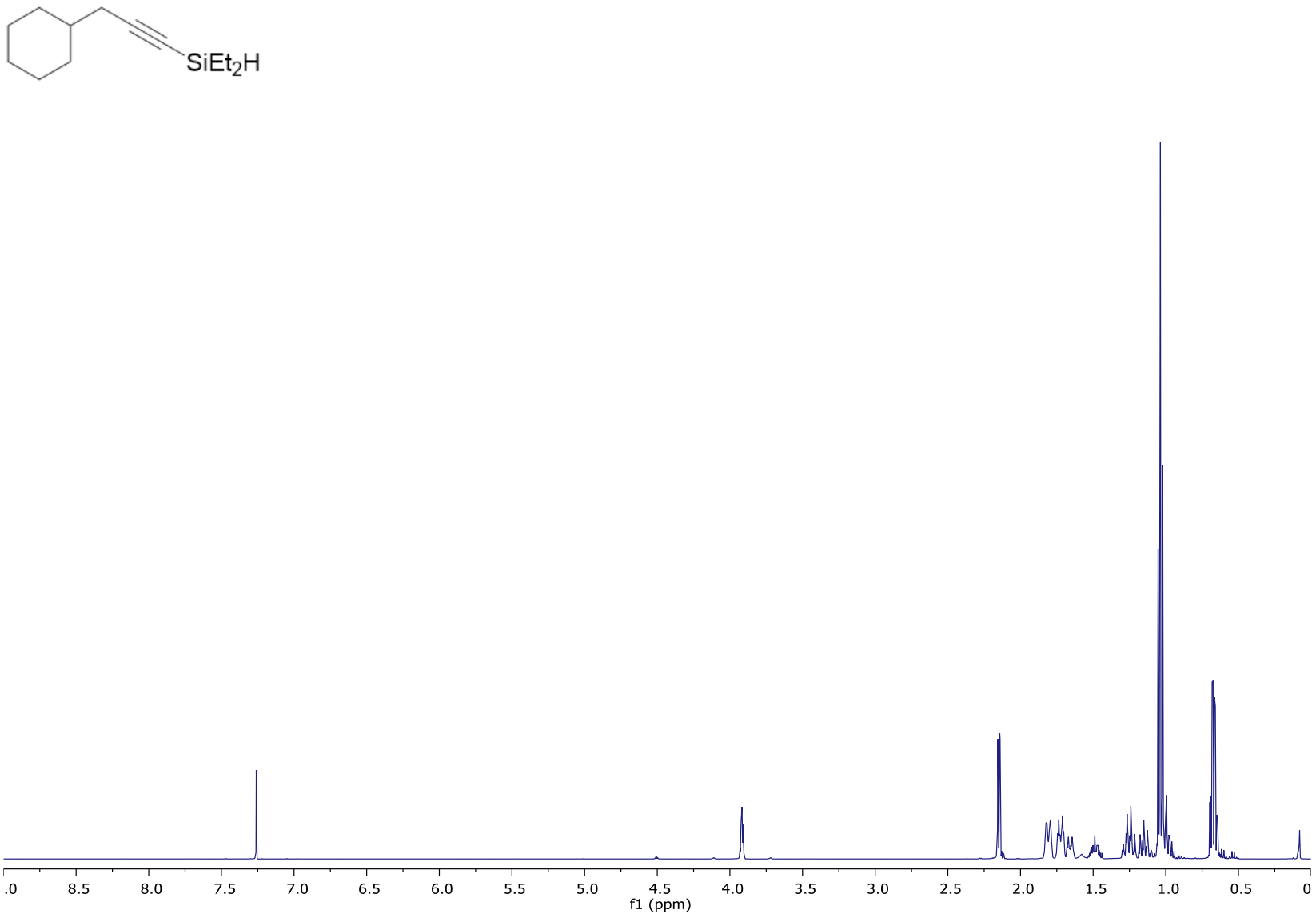




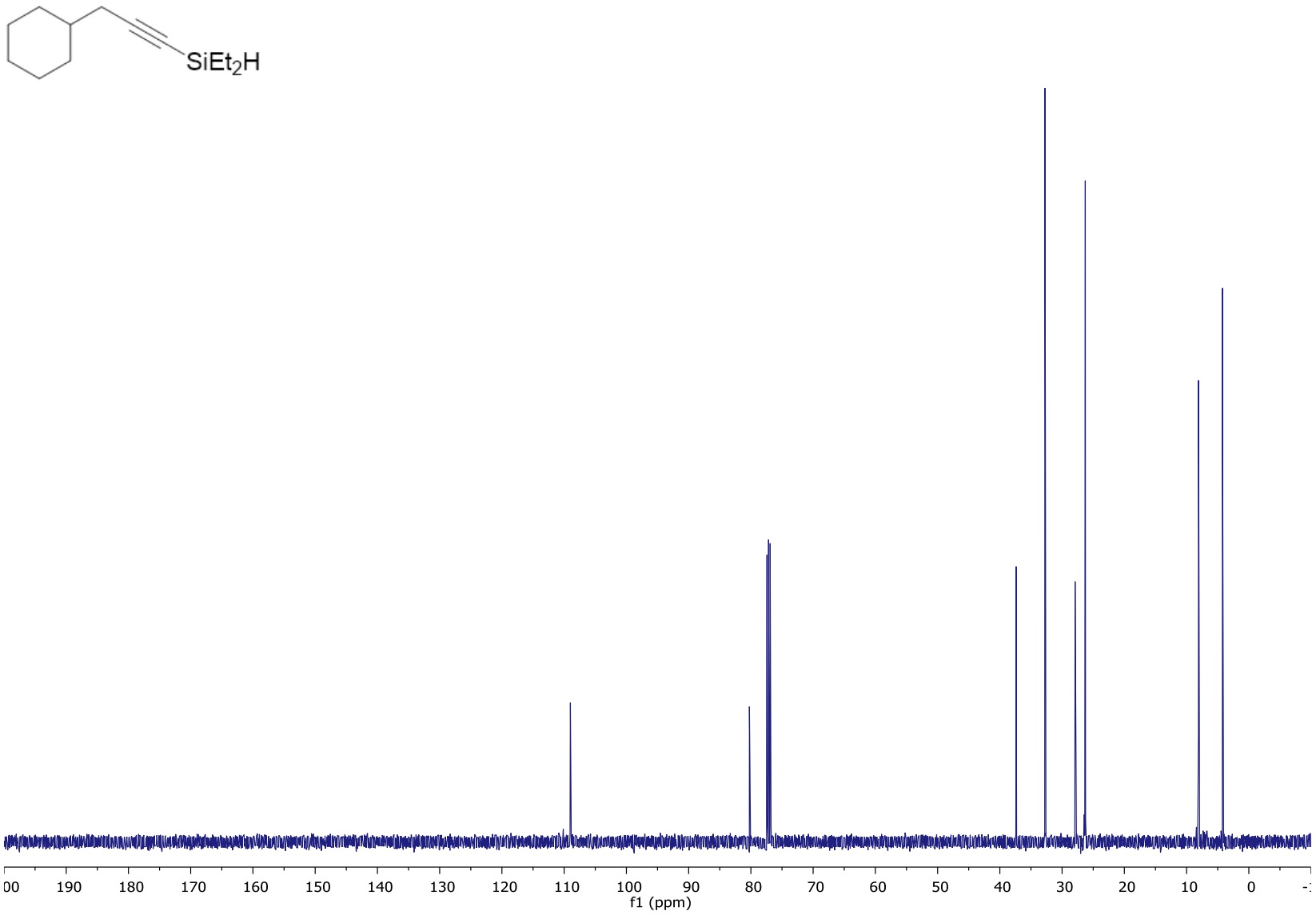
^{1}H NMR (500 MHz, $CDCl_3$) of compound **40d.**



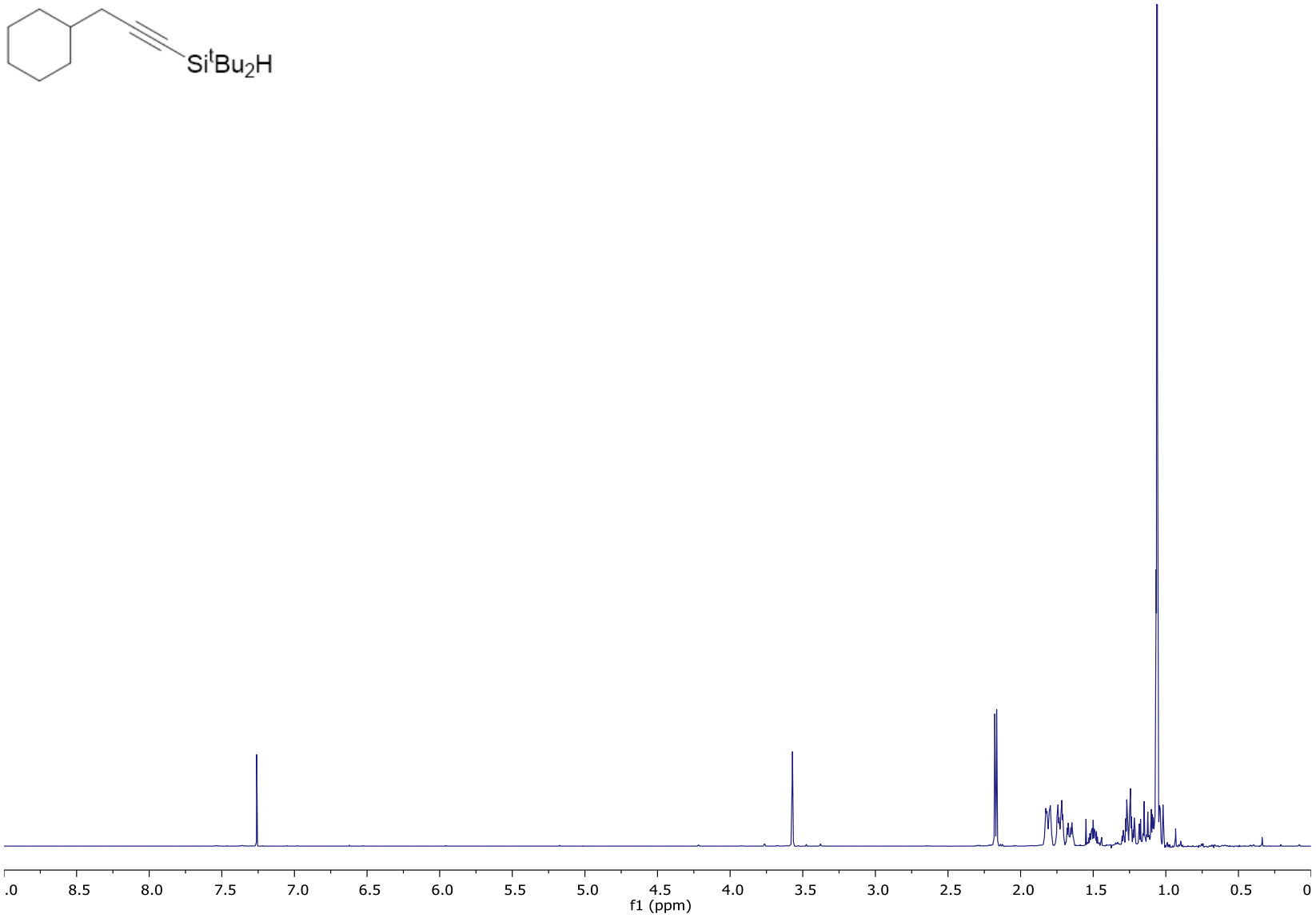
^{13}C NMR (126 MHz, $CDCl_3$) of compound **40d.**



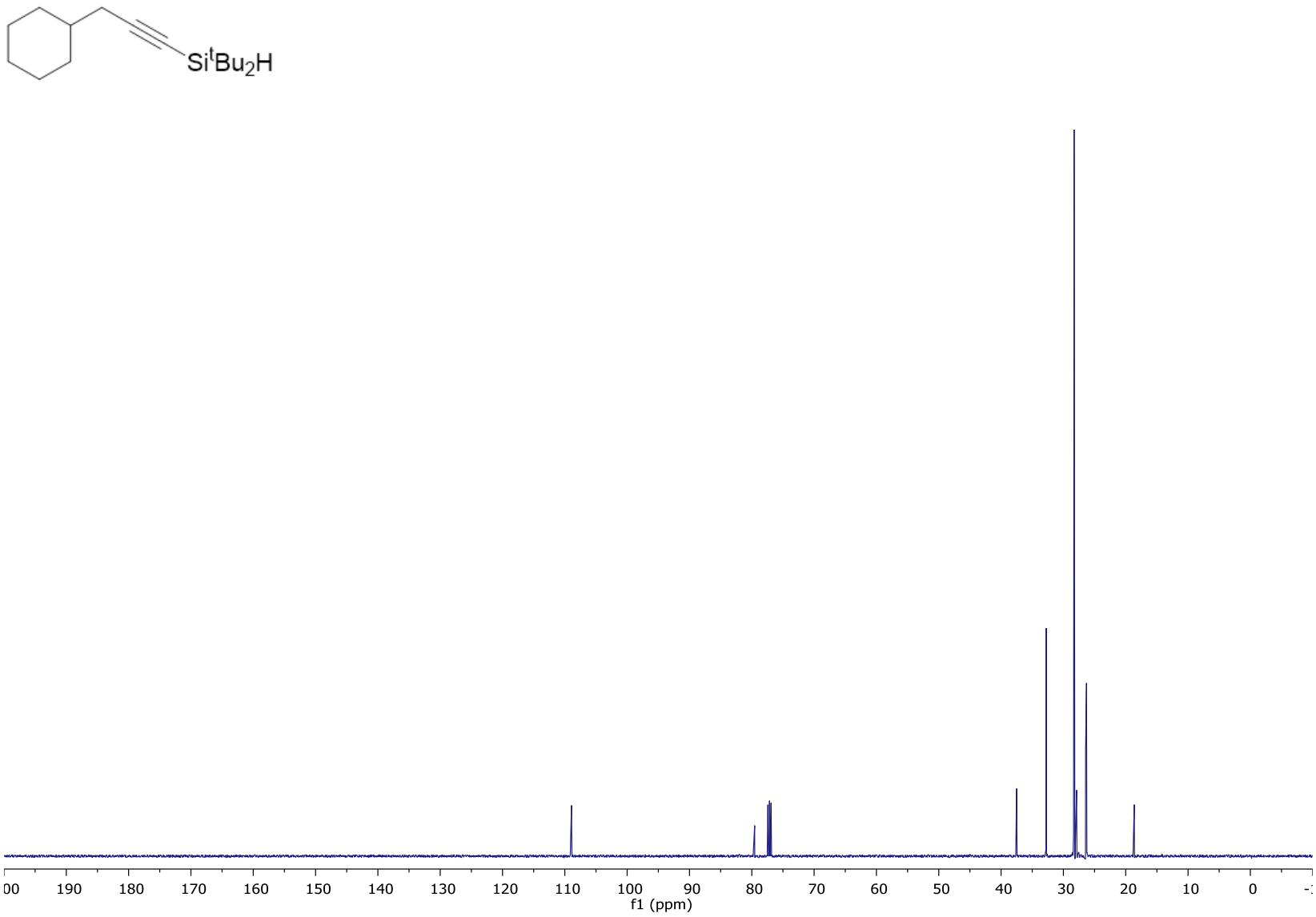
^{1}H NMR (500 MHz, $CDCl_3$) of compound **40e.**



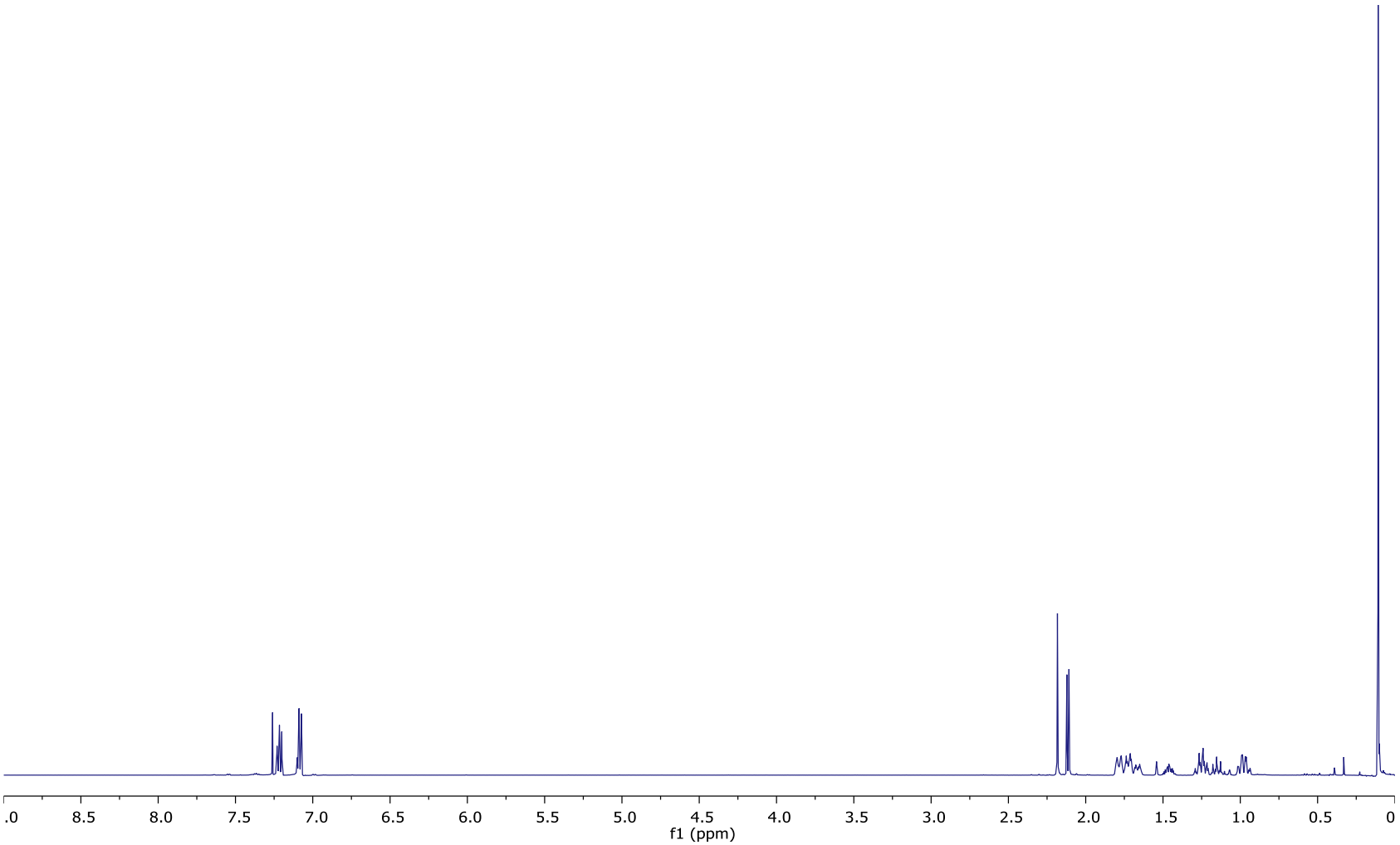
^{13}C NMR (126 MHz, $CDCl_3$) of compound **40e.**



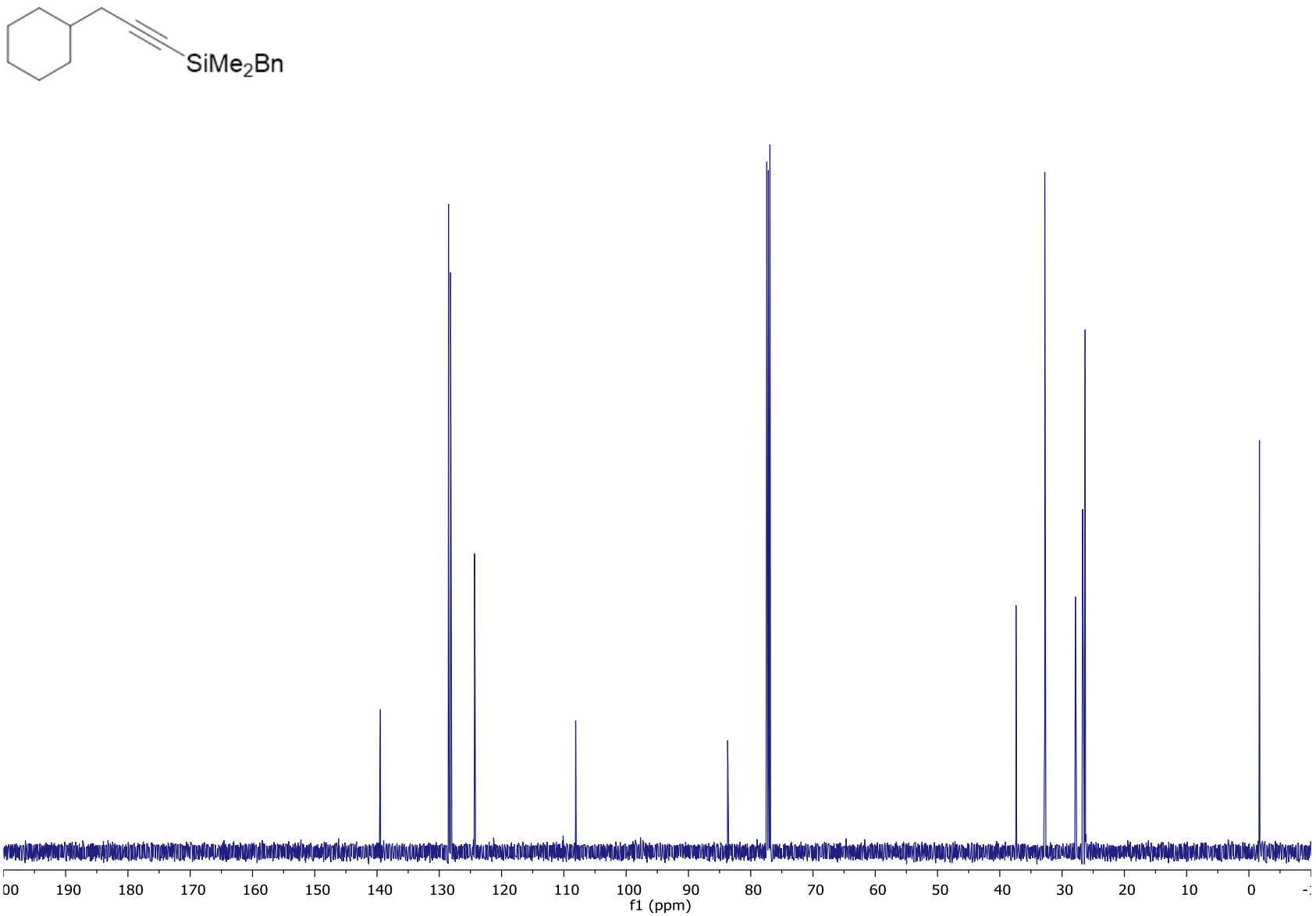
^{1}H NMR (500 MHz, $CDCl_3$) of compound **40f.**



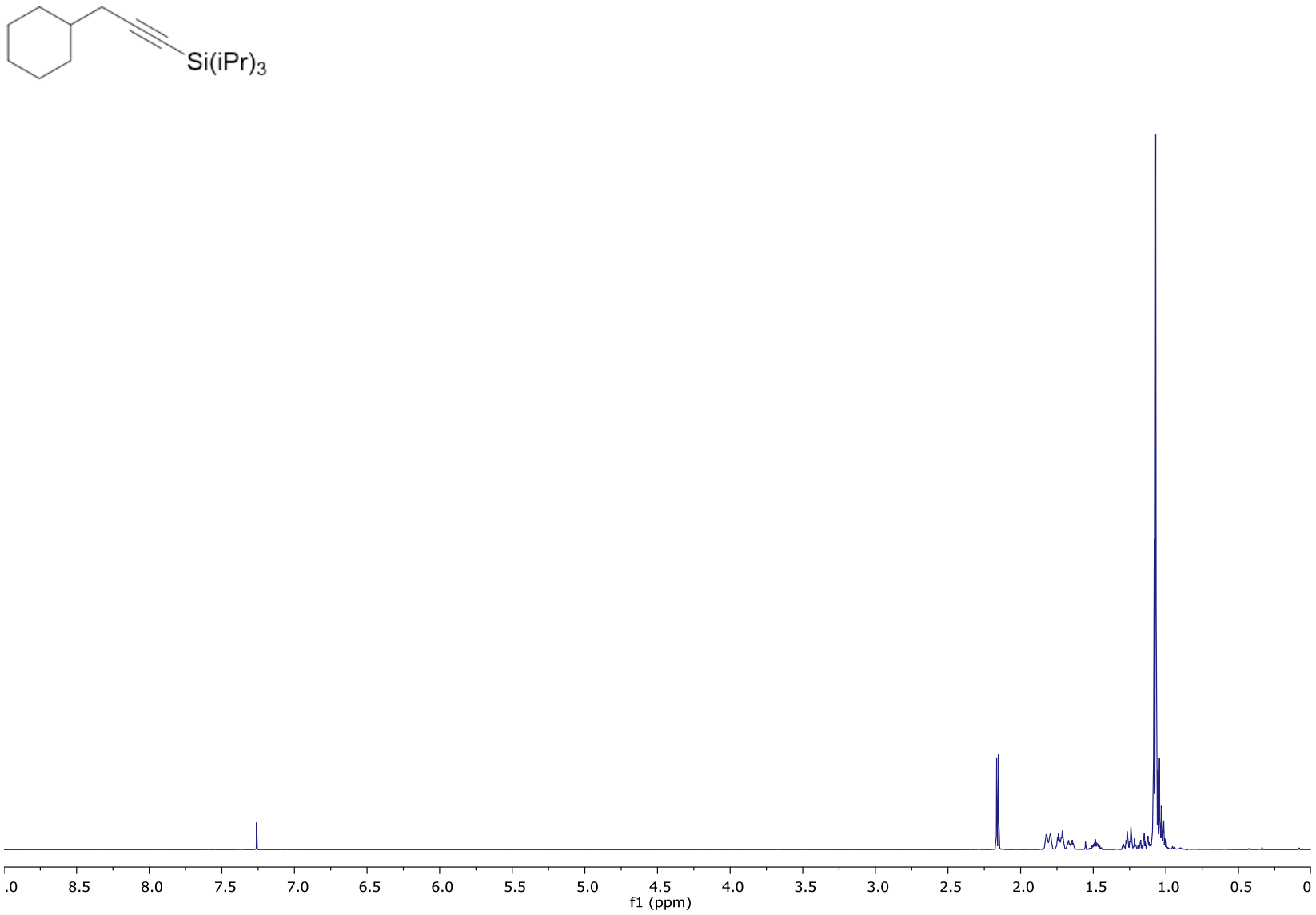
^{13}C NMR (126 MHz, $CDCl_3$) of compound **40f.**



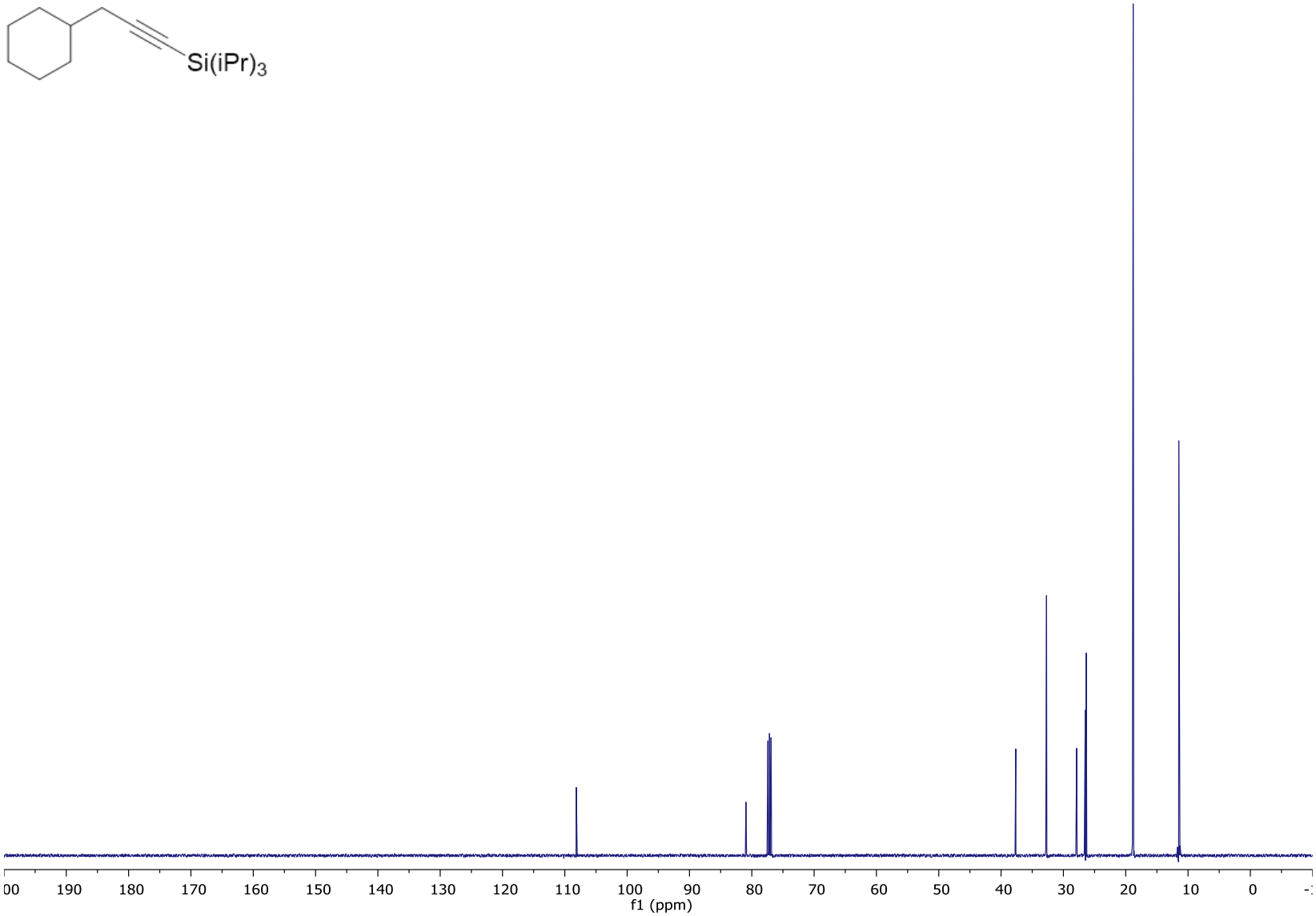
^{1}H NMR (500 MHz, $CDCl_3$) of compound **40g.**



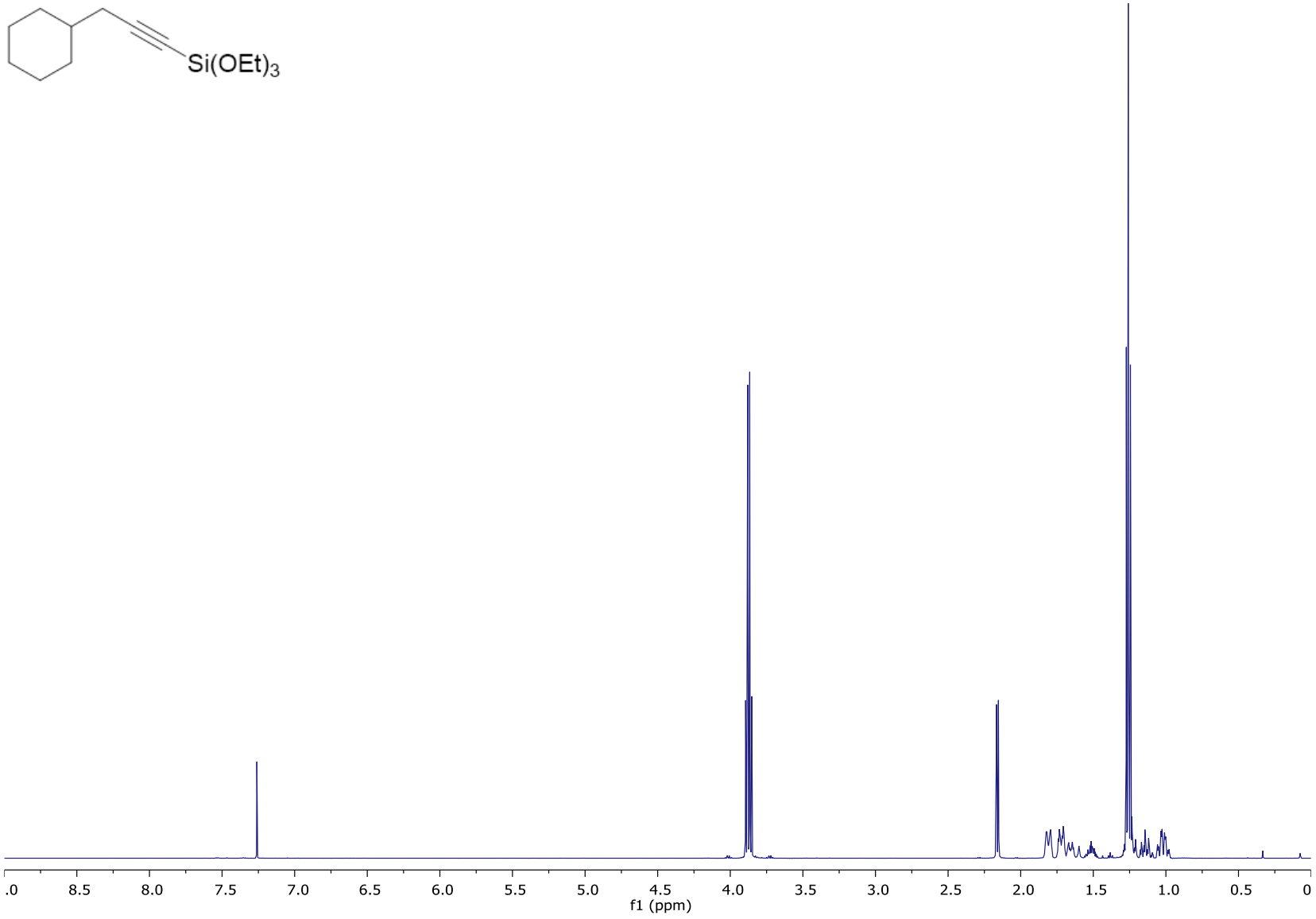
^{13}C NMR (126 MHz, $CDCl_3$) of compound **40g.**



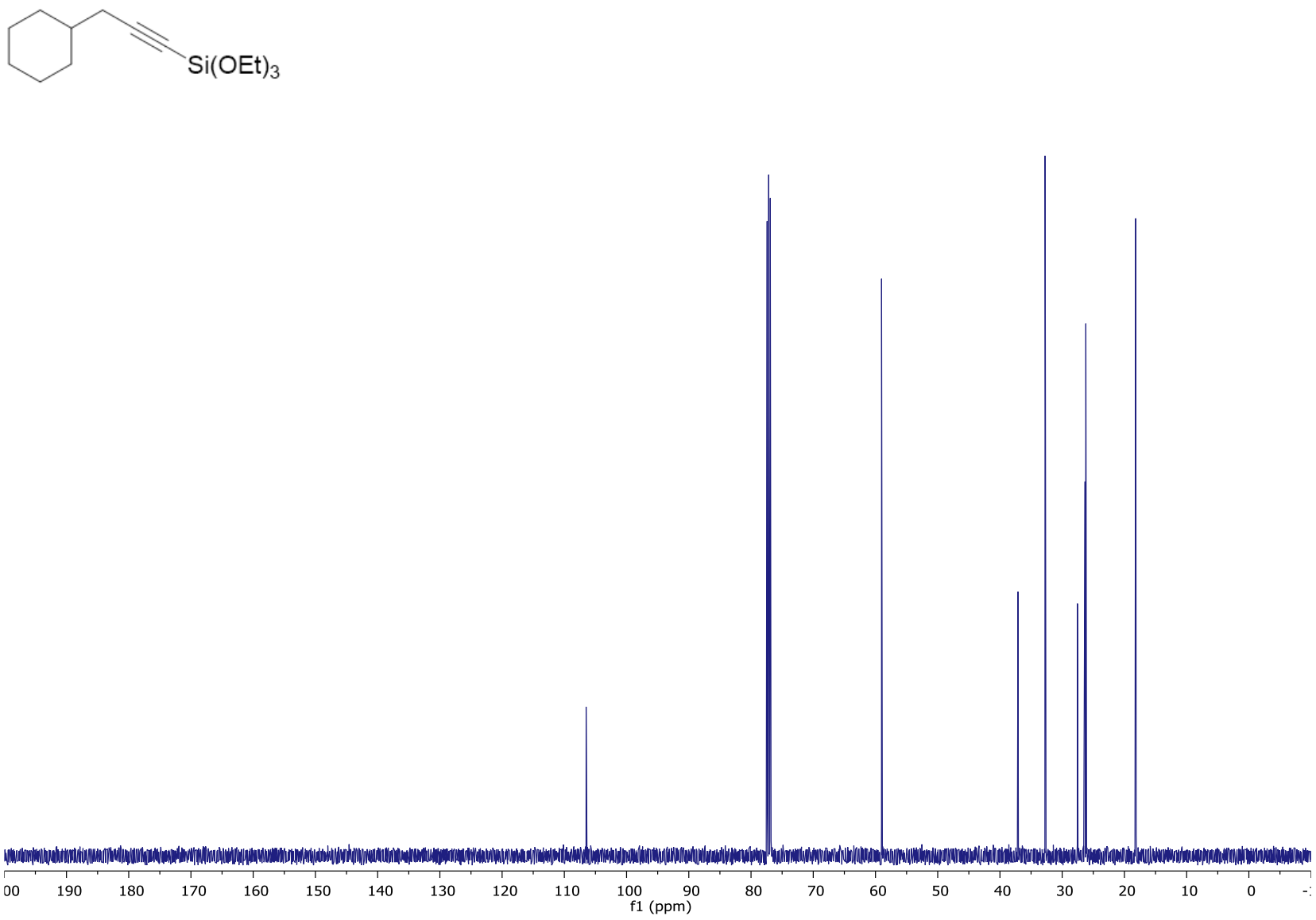
^{1}H NMR (500 MHz, $CDCl_3$) of compound **40h.**



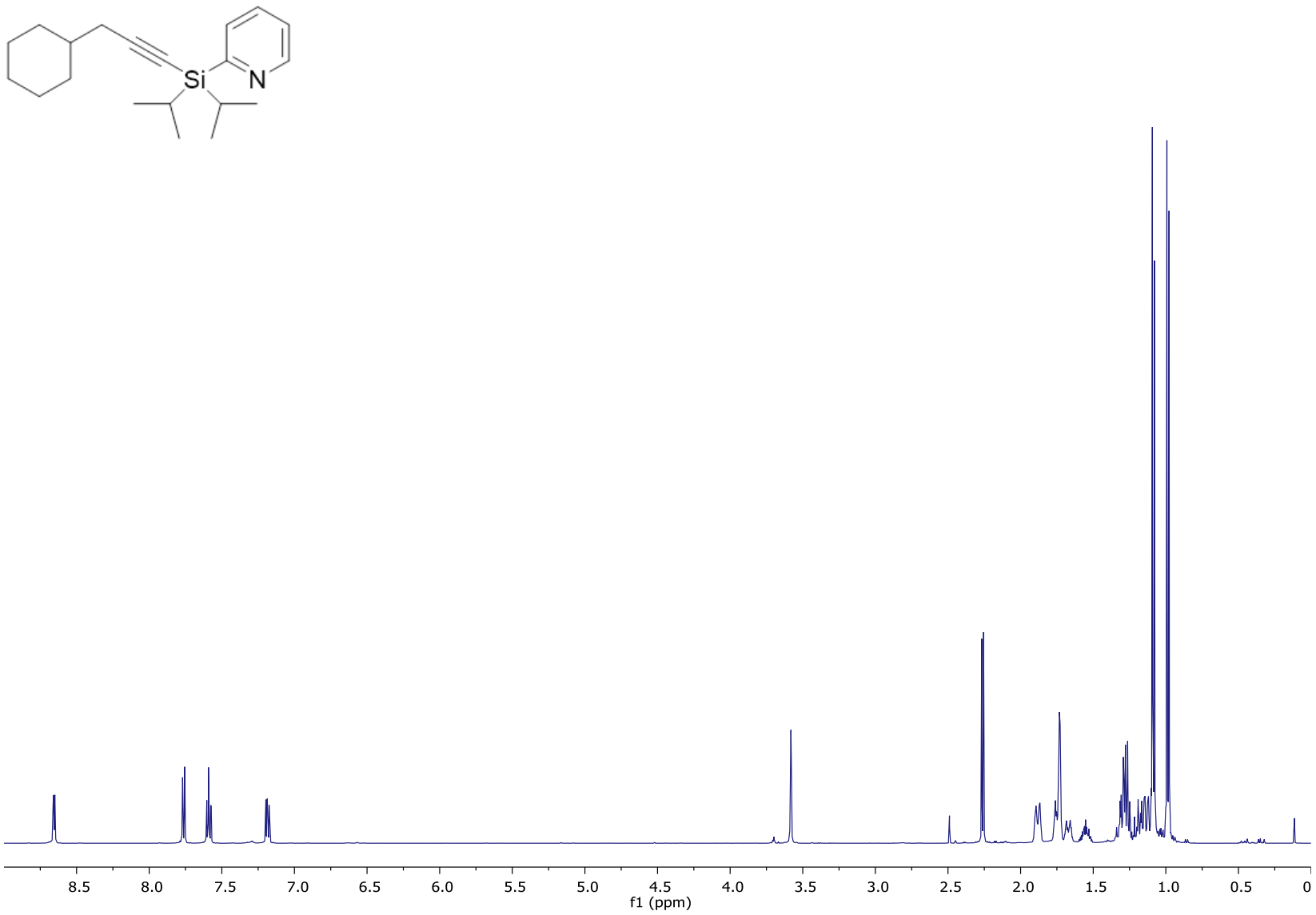
^{13}C NMR (126 MHz, $CDCl_3$) of compound **40h.**



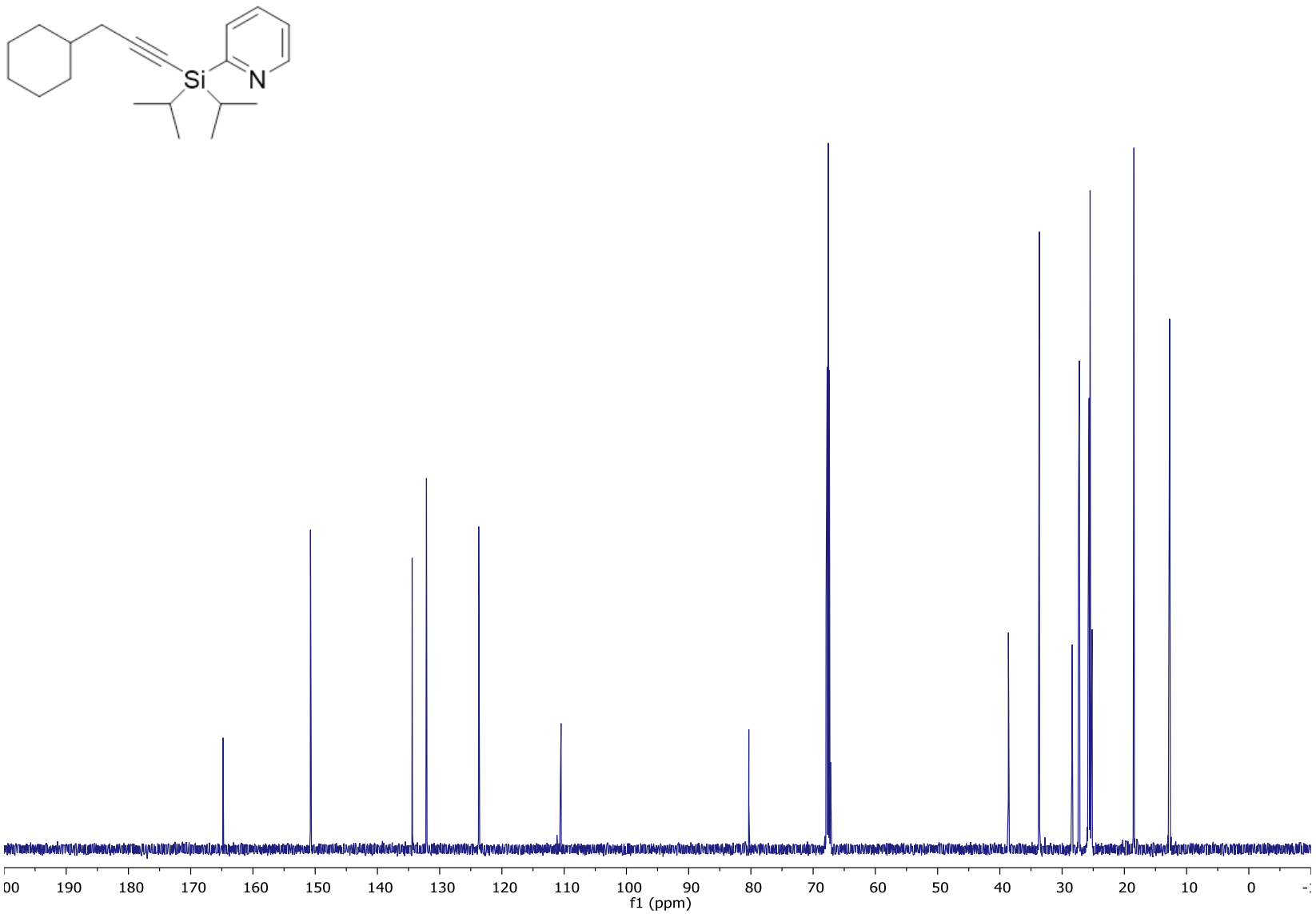
^{1}H NMR (500 MHz, $CDCl_3$) of compound **40i.**



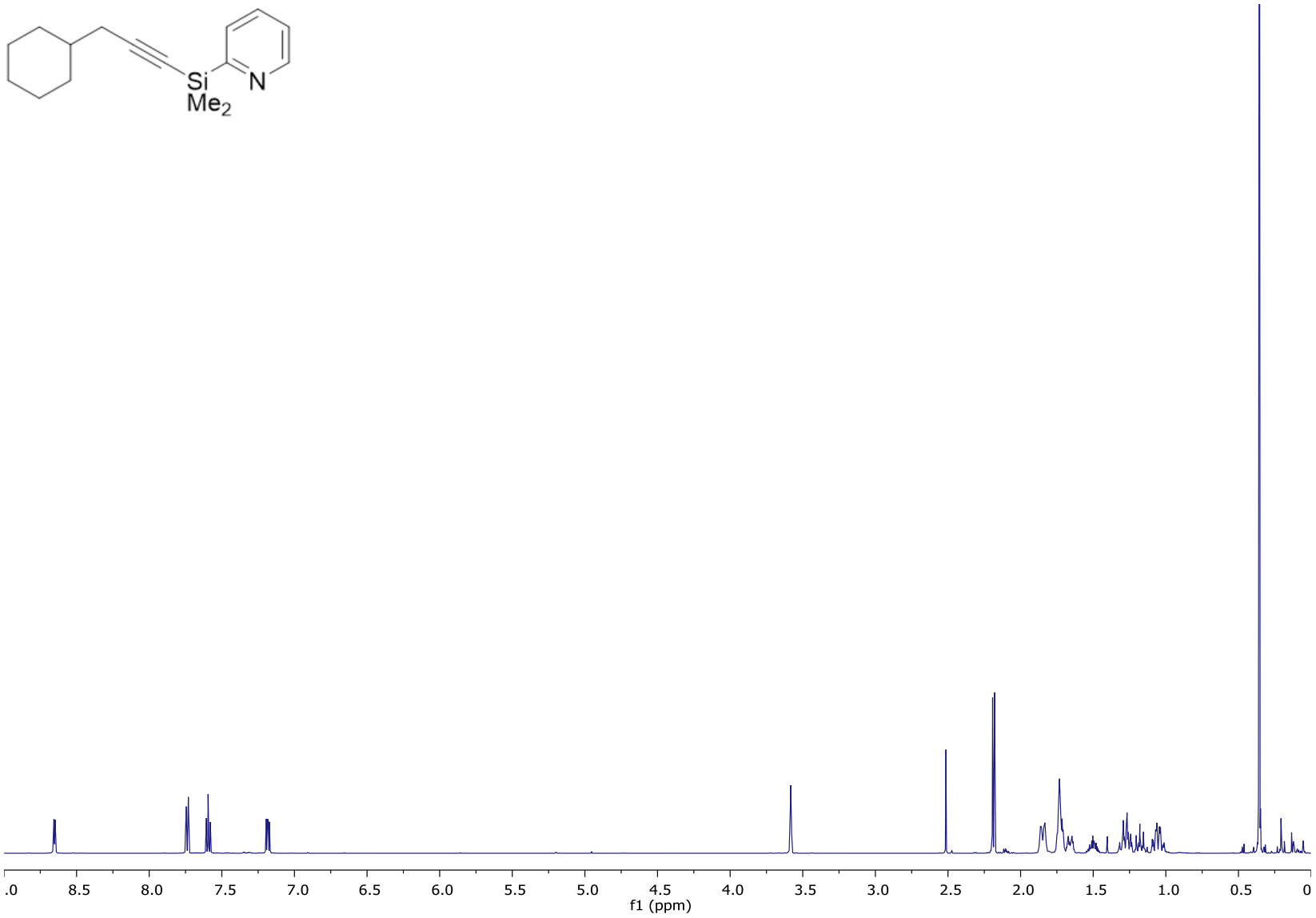
^{13}C NMR (126 MHz, $CDCl_3$) of compound **40i.**



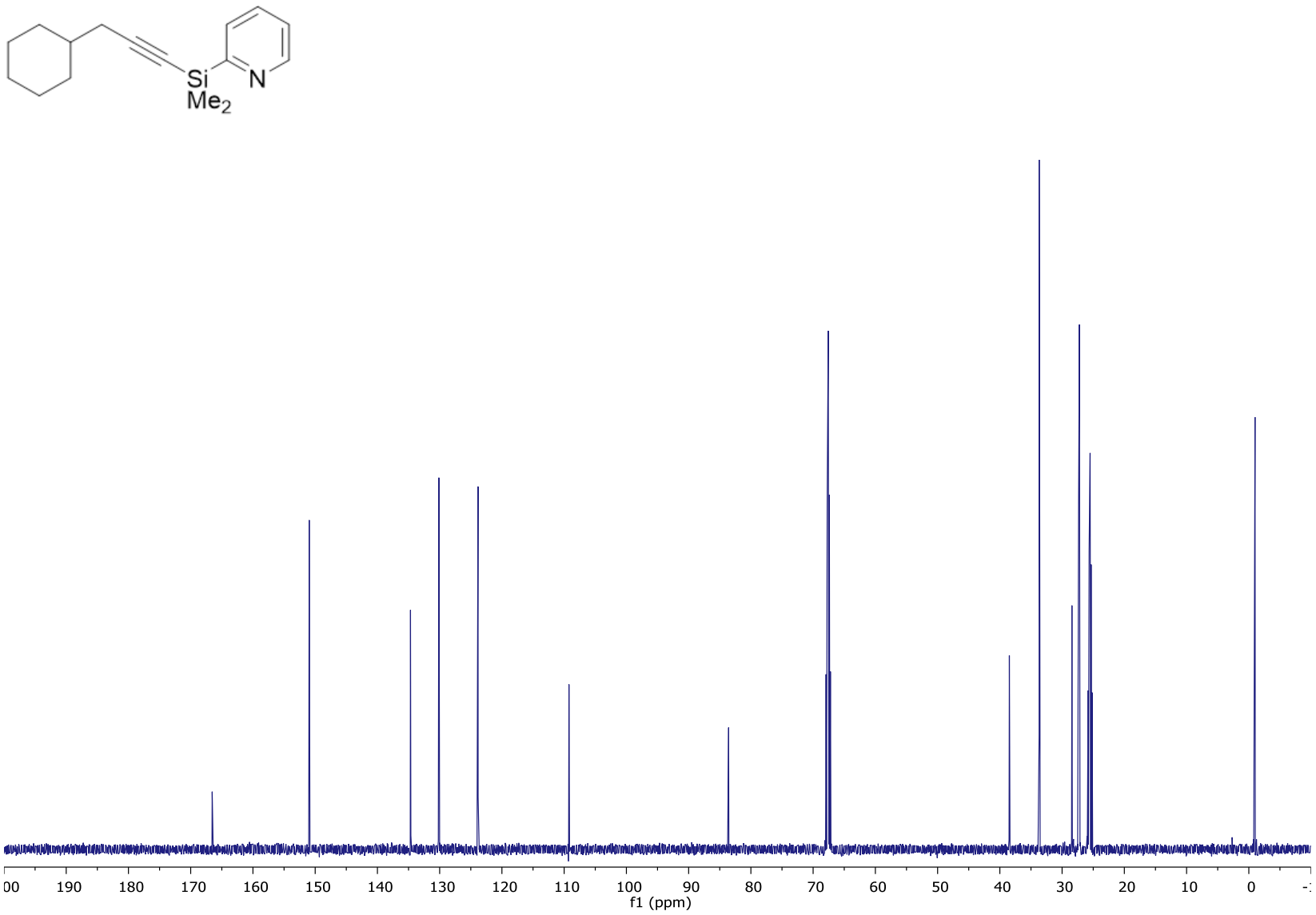
^{1}H NMR (500 MHz, THF-d_8) of compound **40j.**



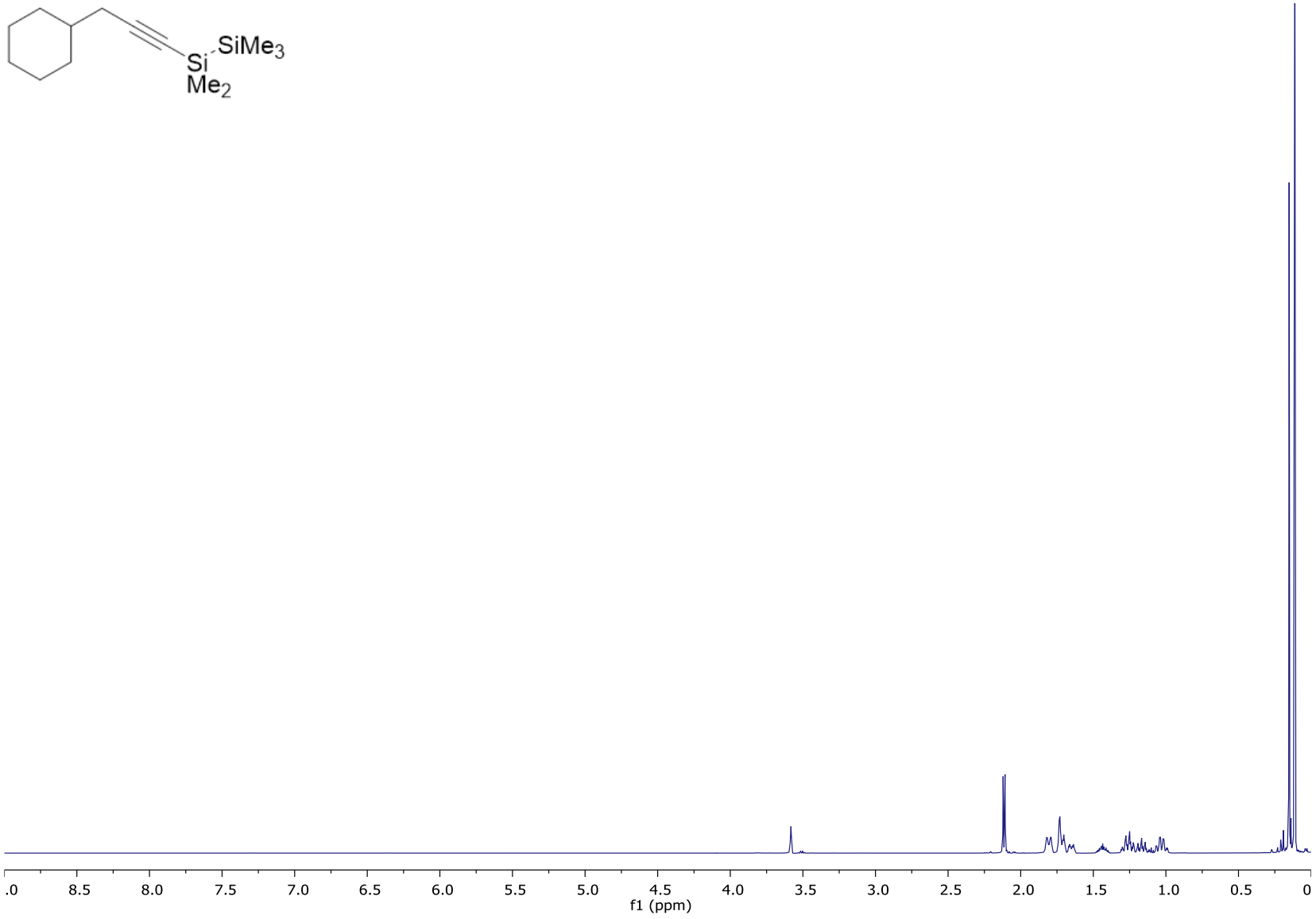
^{13}C NMR (126 MHz, THF-d_8) of compound **40j.**



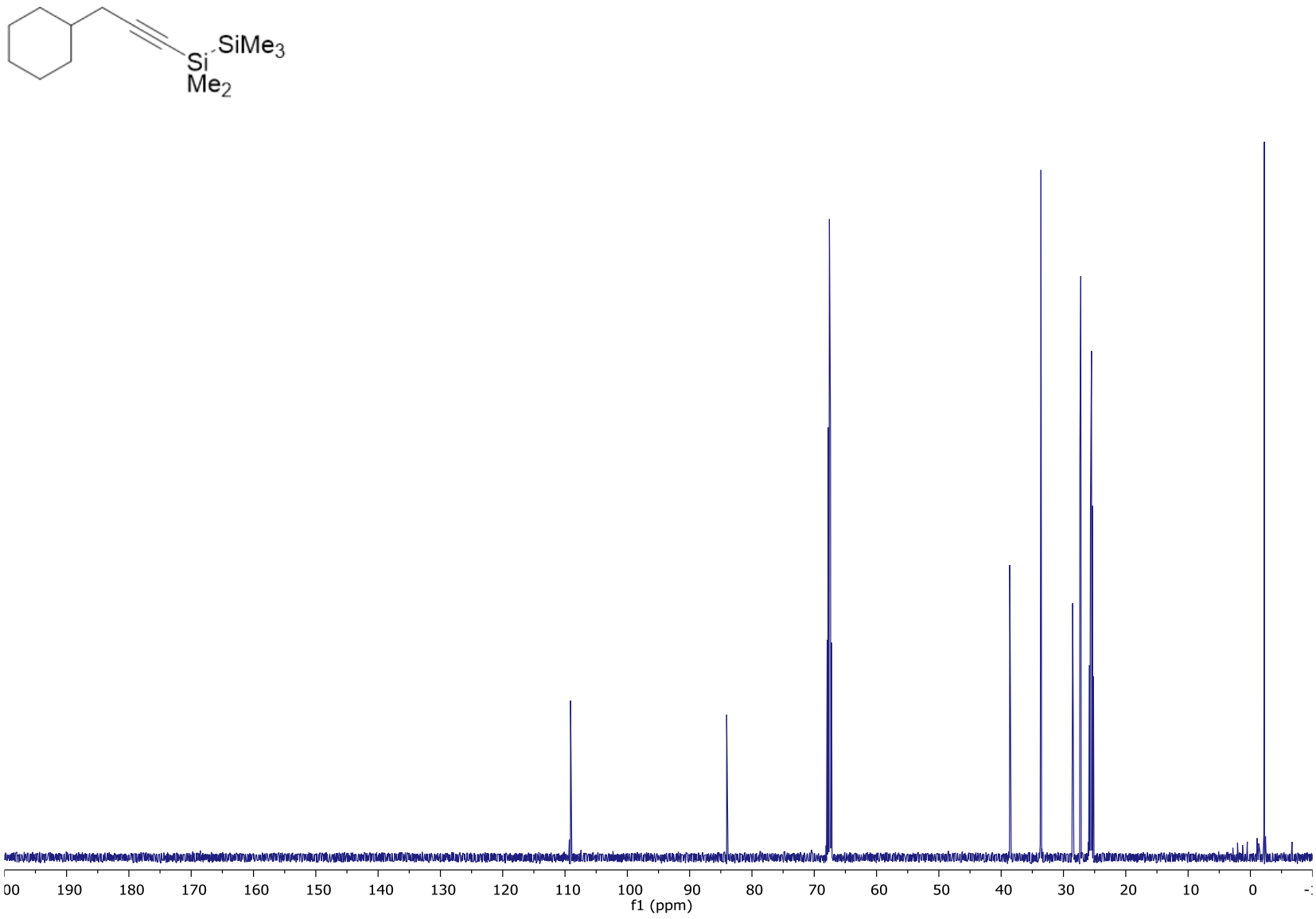
^{1}H NMR (500 MHz, THF-d_8) of compound **40k.**



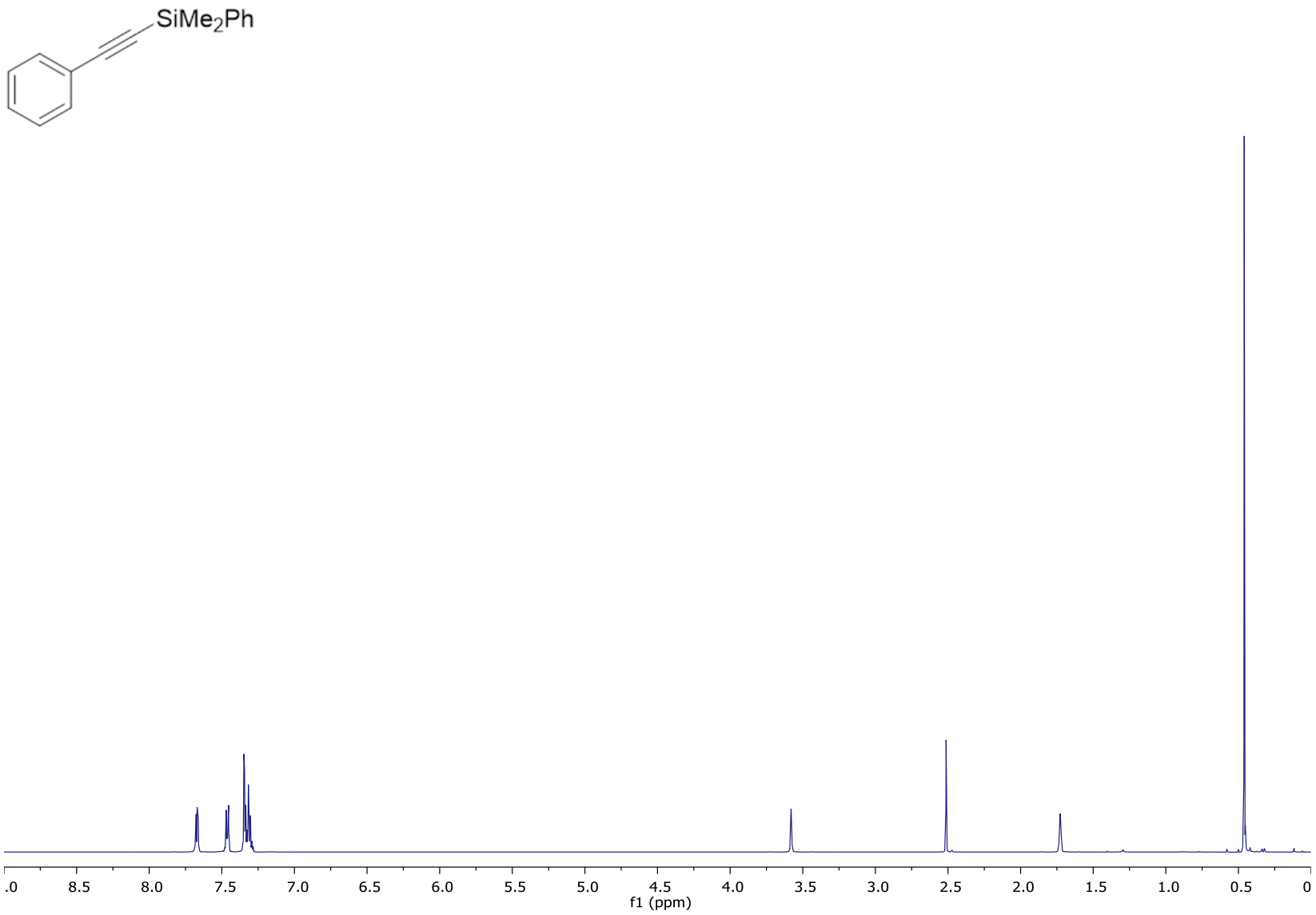
^{13}C NMR (126 MHz, THF-d_8) of compound **40k.**



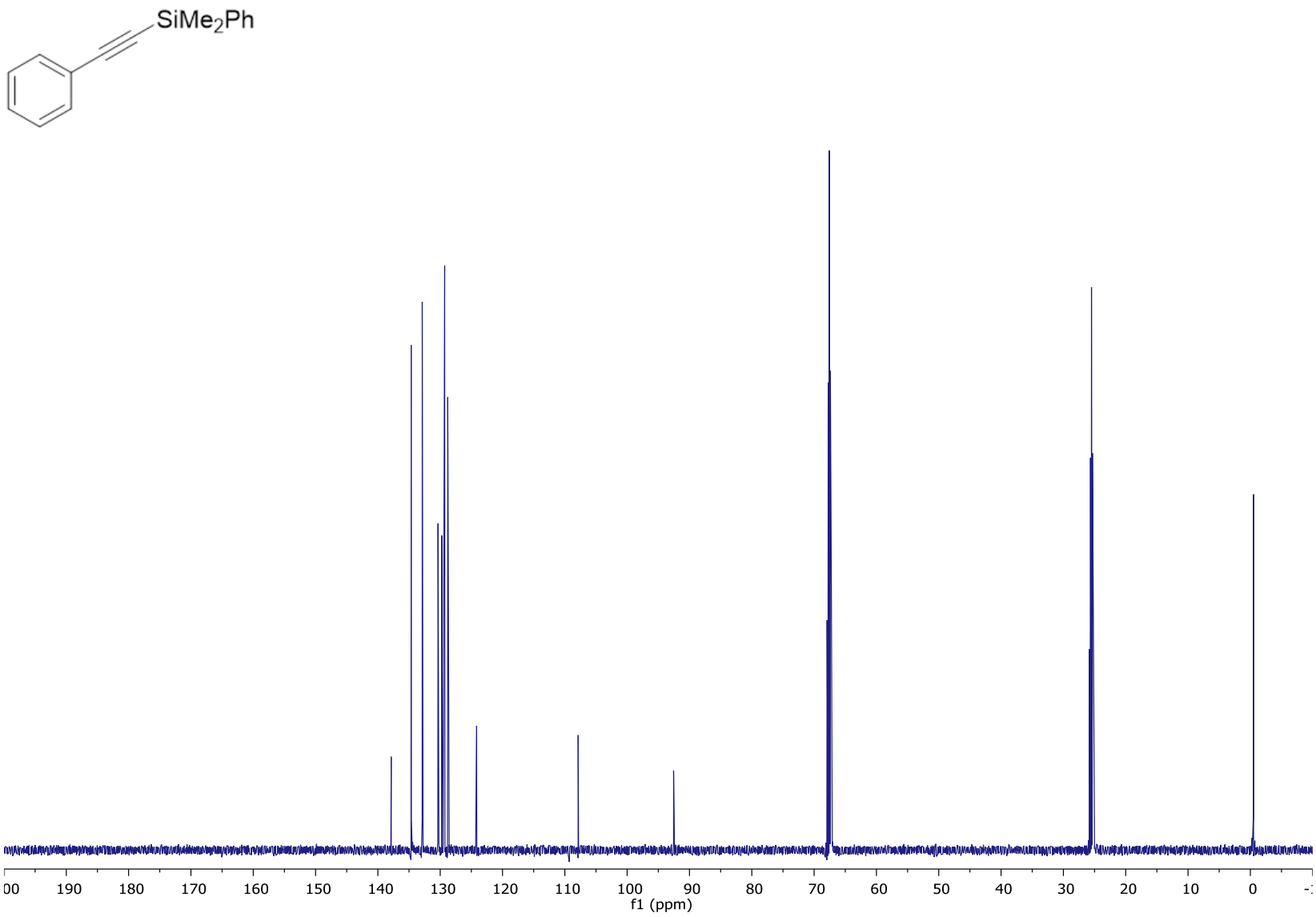
^{1}H NMR (500 MHz, THF-d_8) of compound **401.**



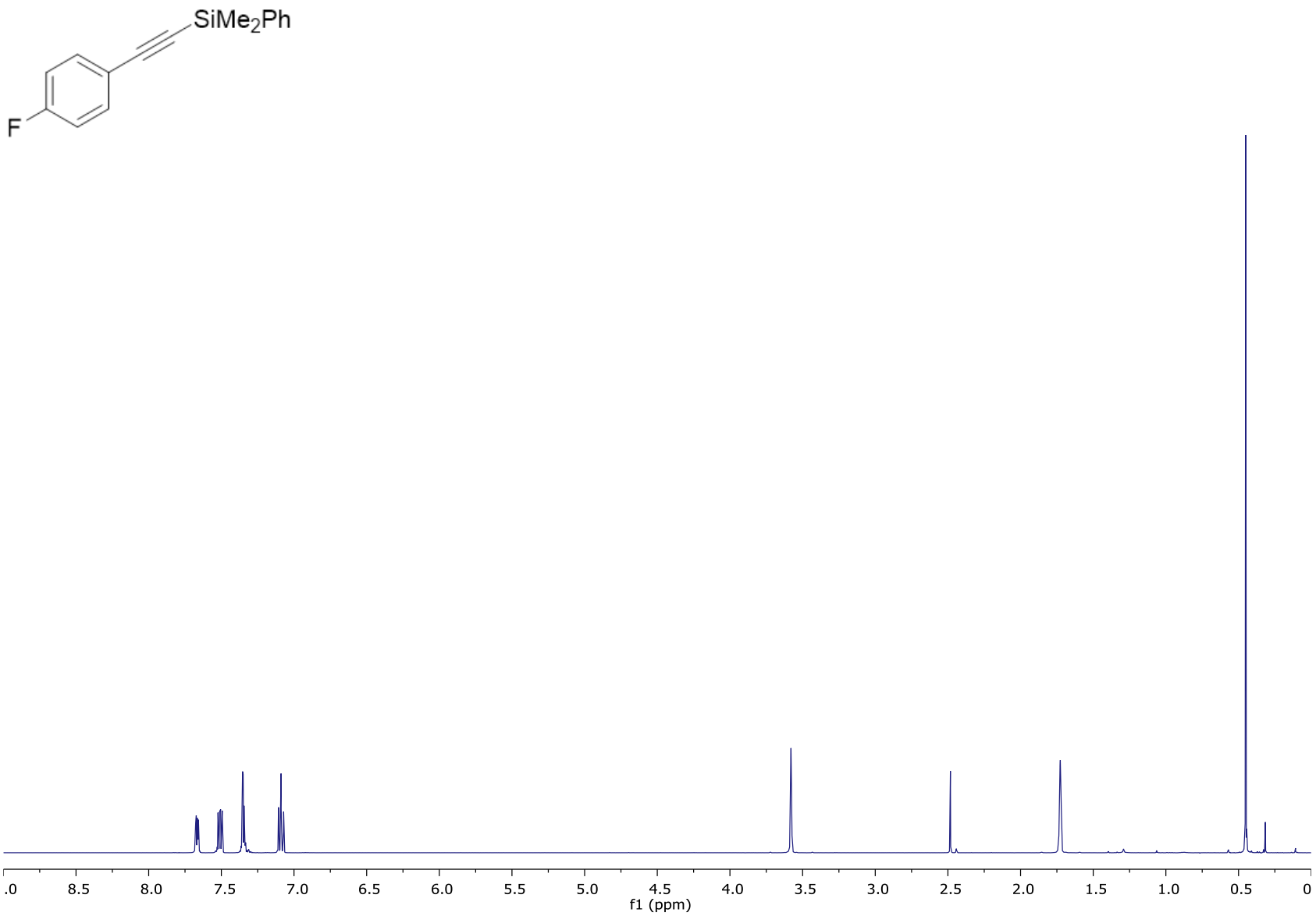
^{13}C NMR (126 MHz, THF-d_8) of compound **401.**



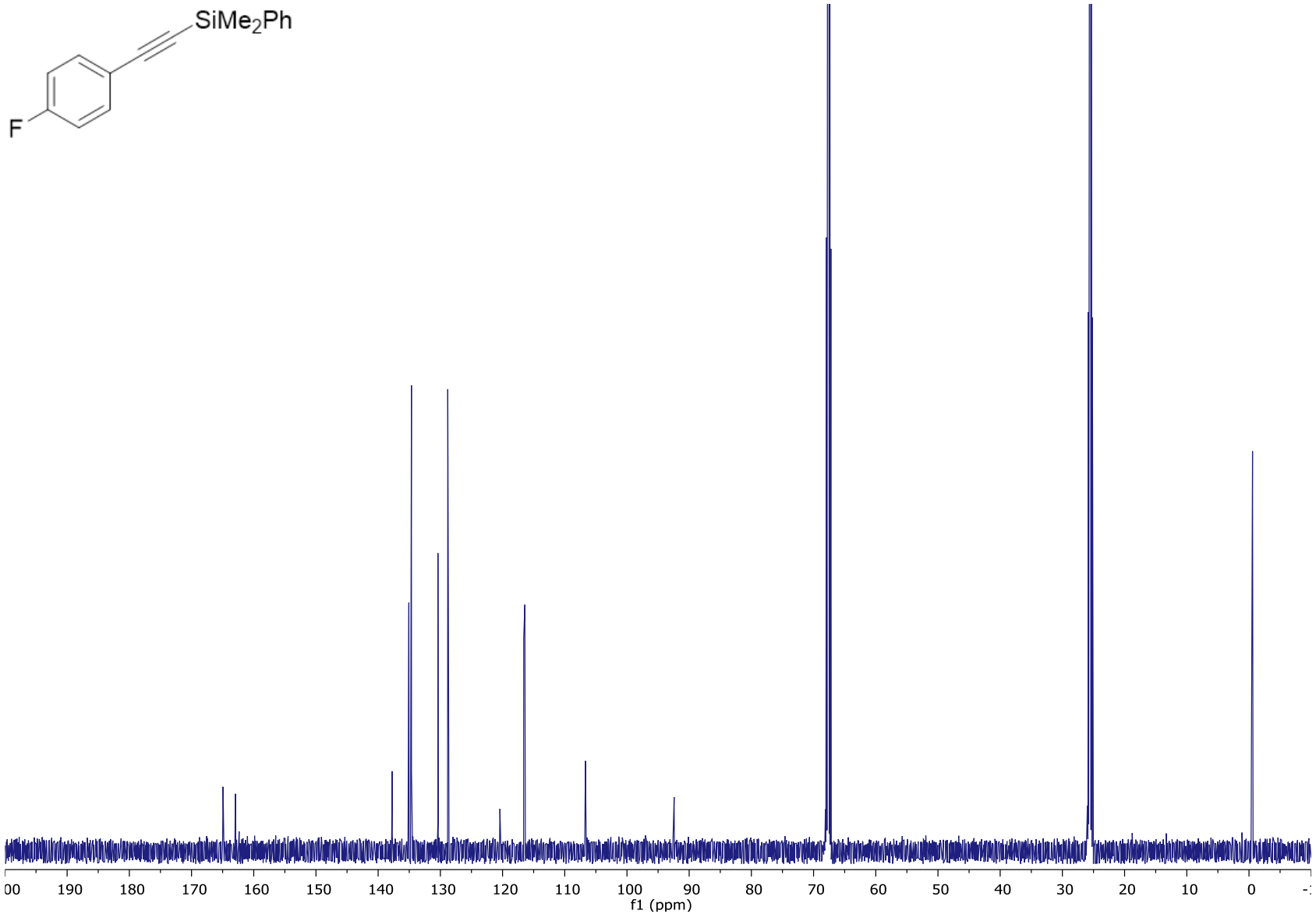
^{1}H NMR (500 MHz, THF-d_8) of compound **42a.**



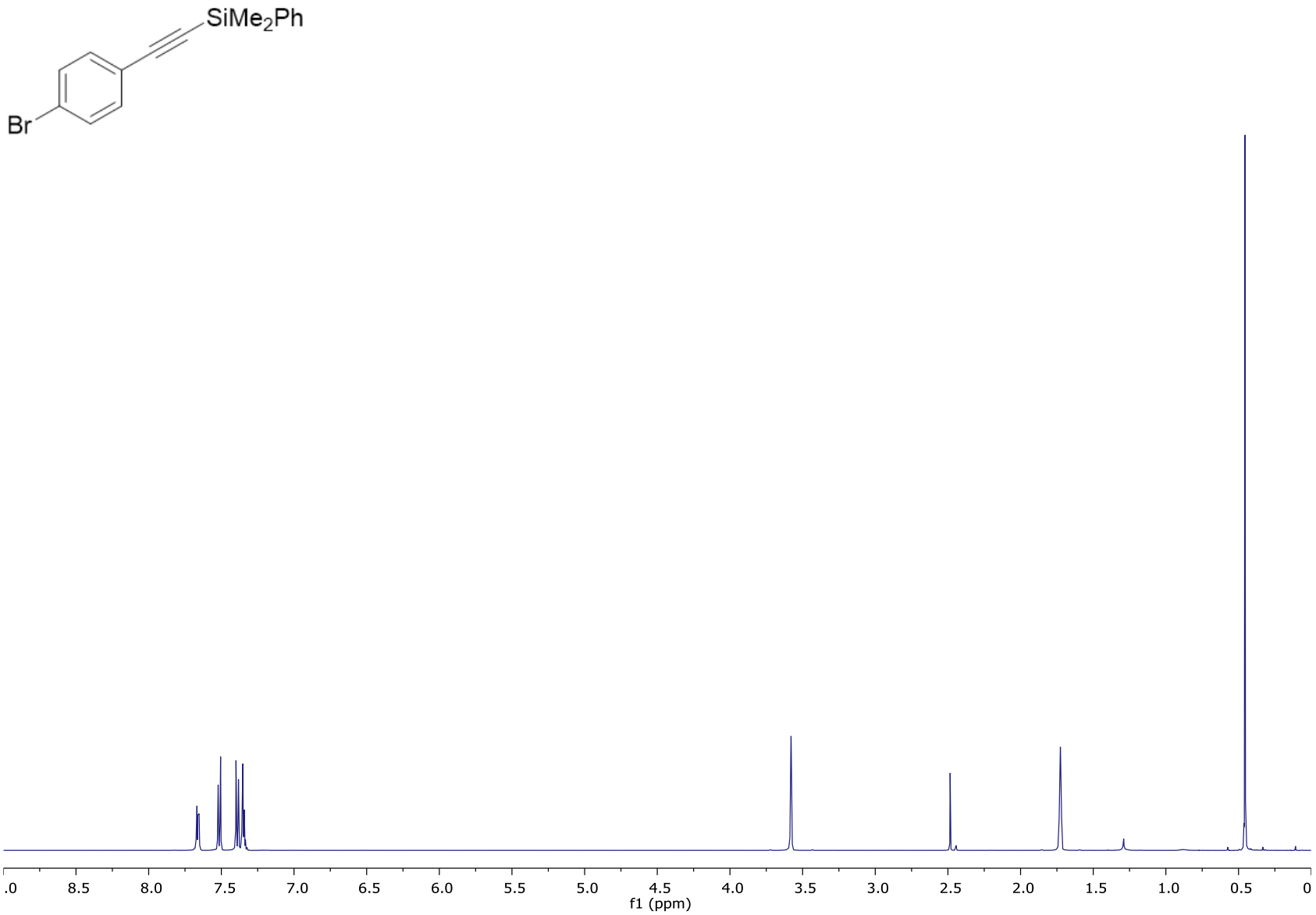
^{13}C NMR (126 MHz, THF-d_8) of compound **42a.**



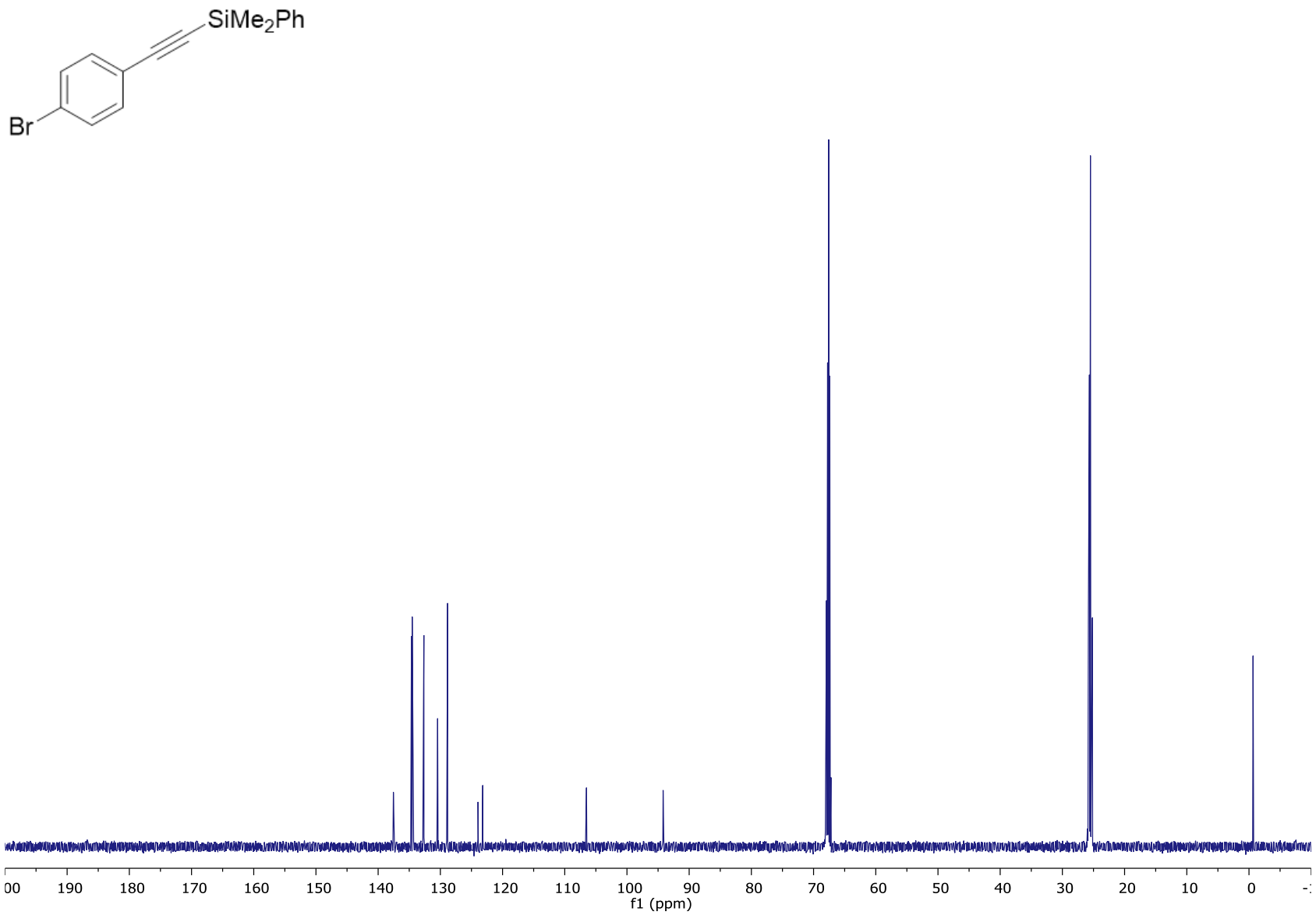
^{1}H NMR (500 MHz, THF-d_8) of compound **42b.**



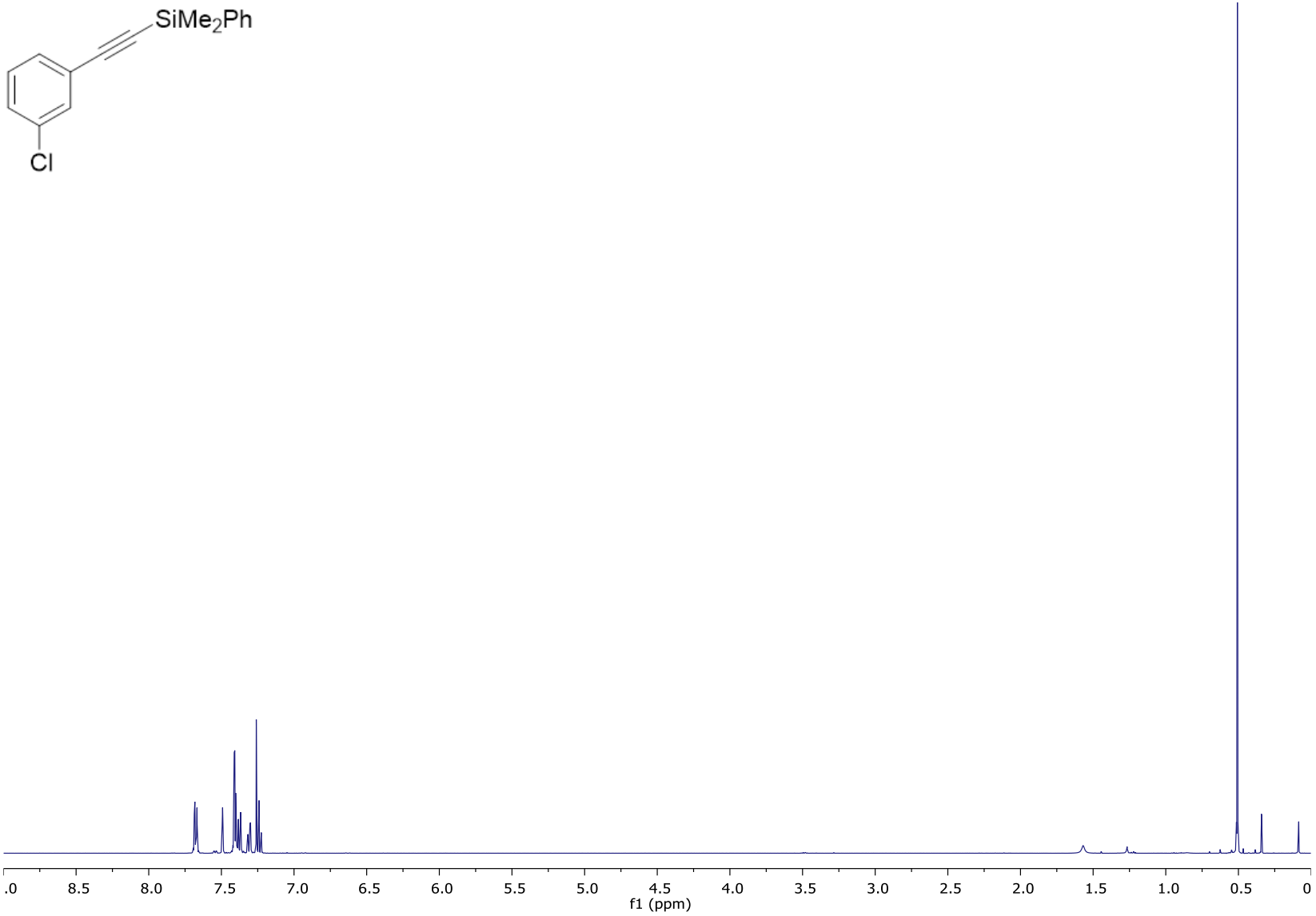
^{13}C NMR (126 MHz, THF-d_8) of compound **42b.**



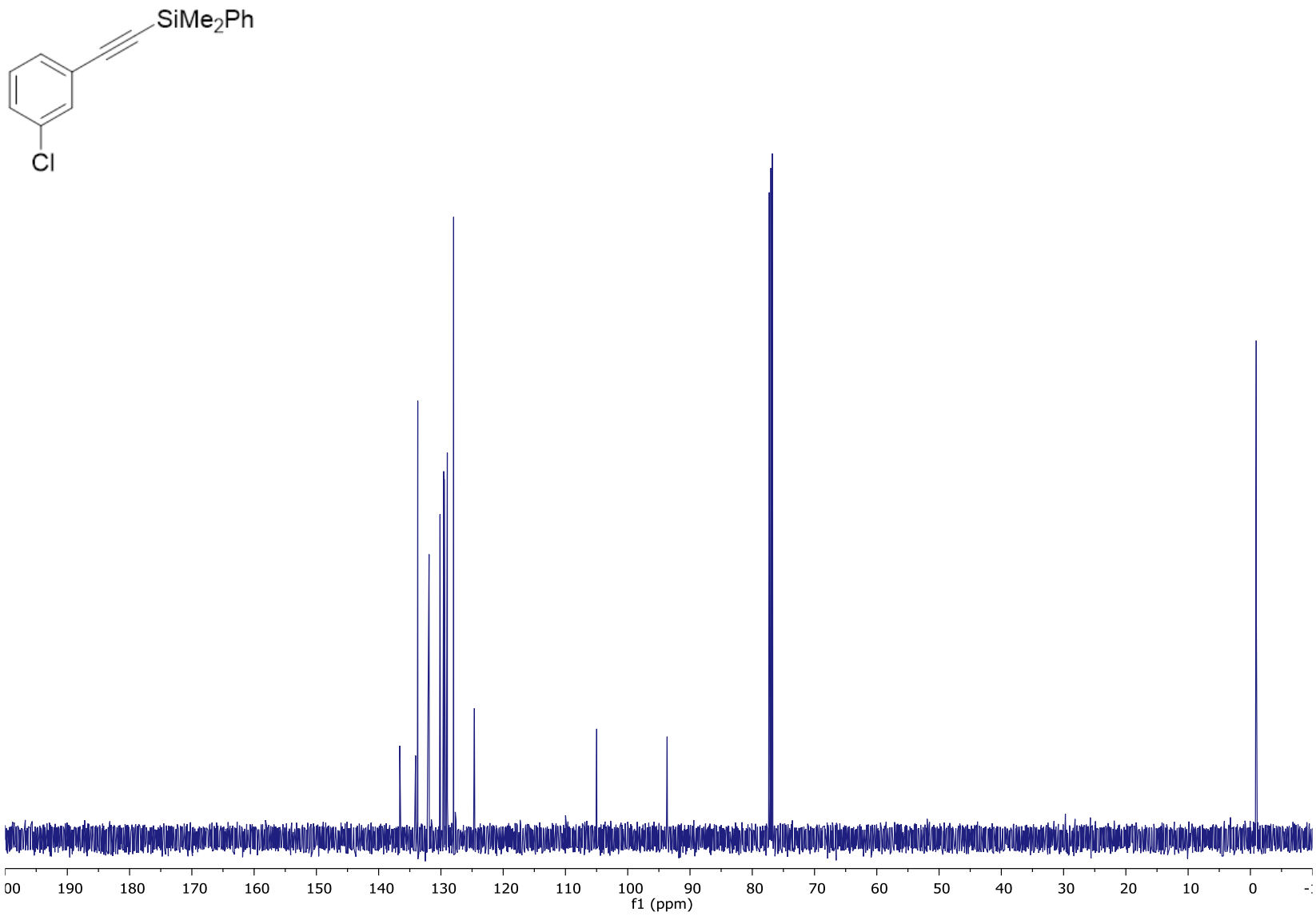
^{1}H NMR (500 MHz, THF-d_8) of compound **42c.**



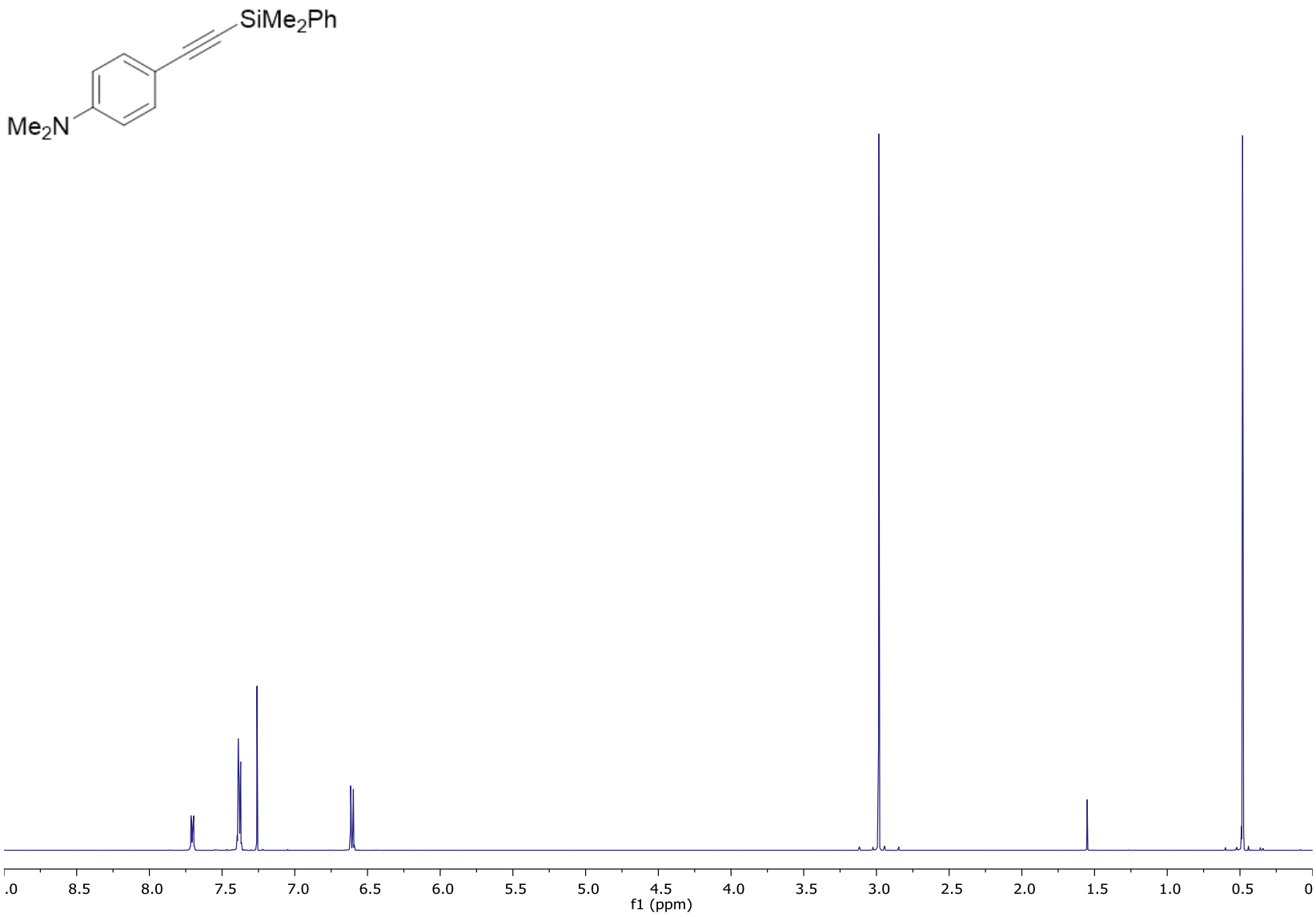
^{13}C NMR (126 MHz, THF-d_8) of compound **42c.**



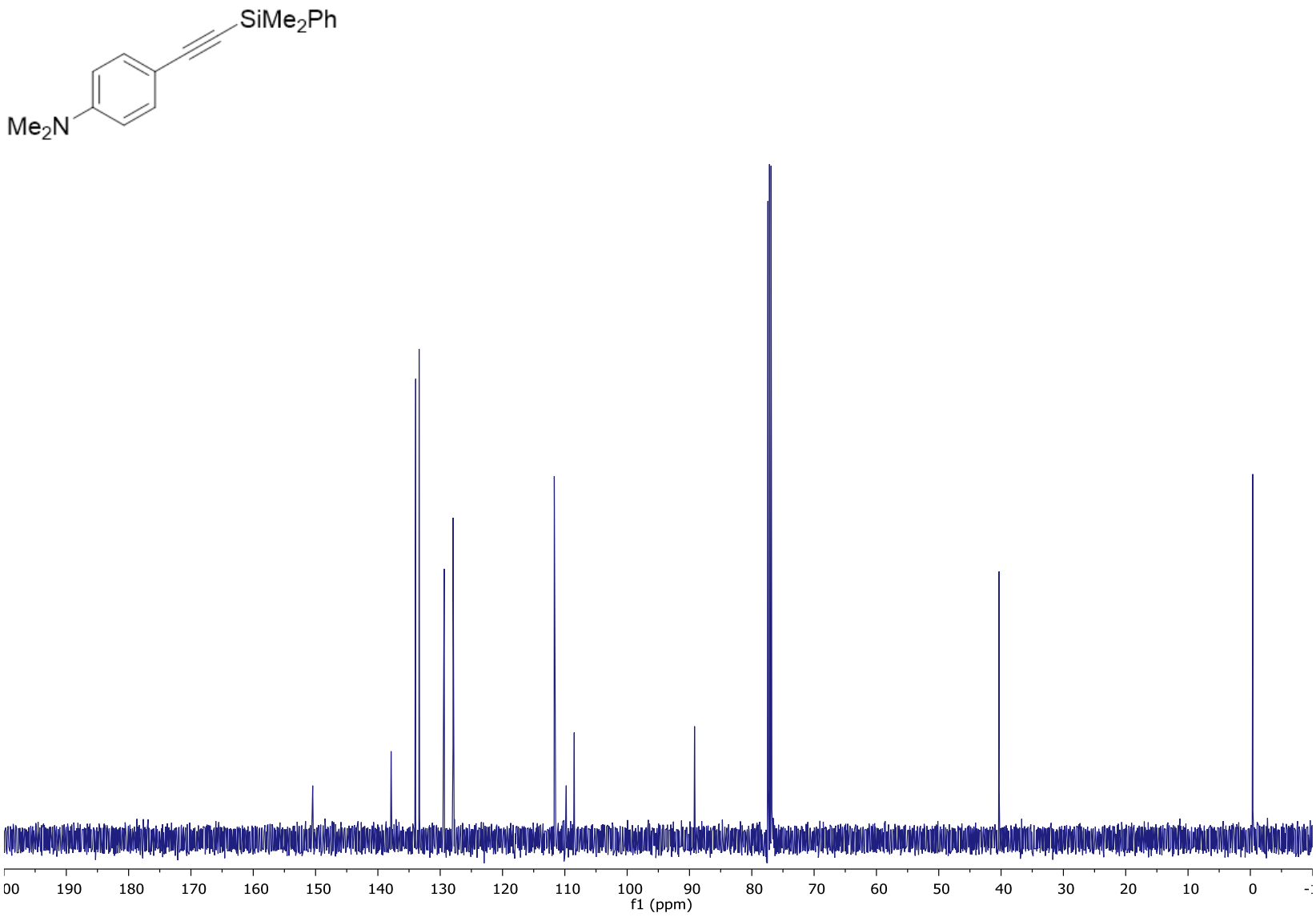
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42d.**



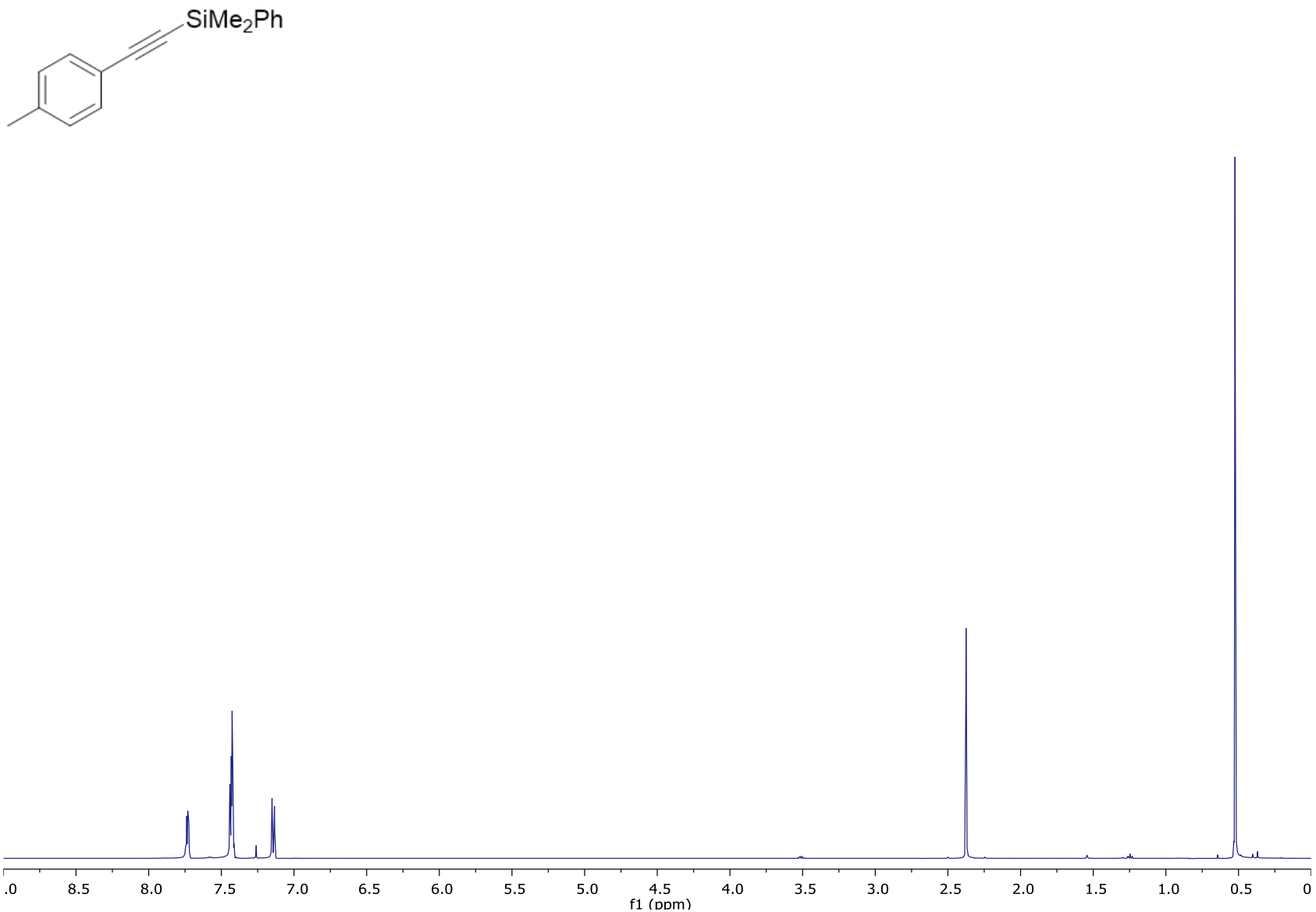
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42d.**



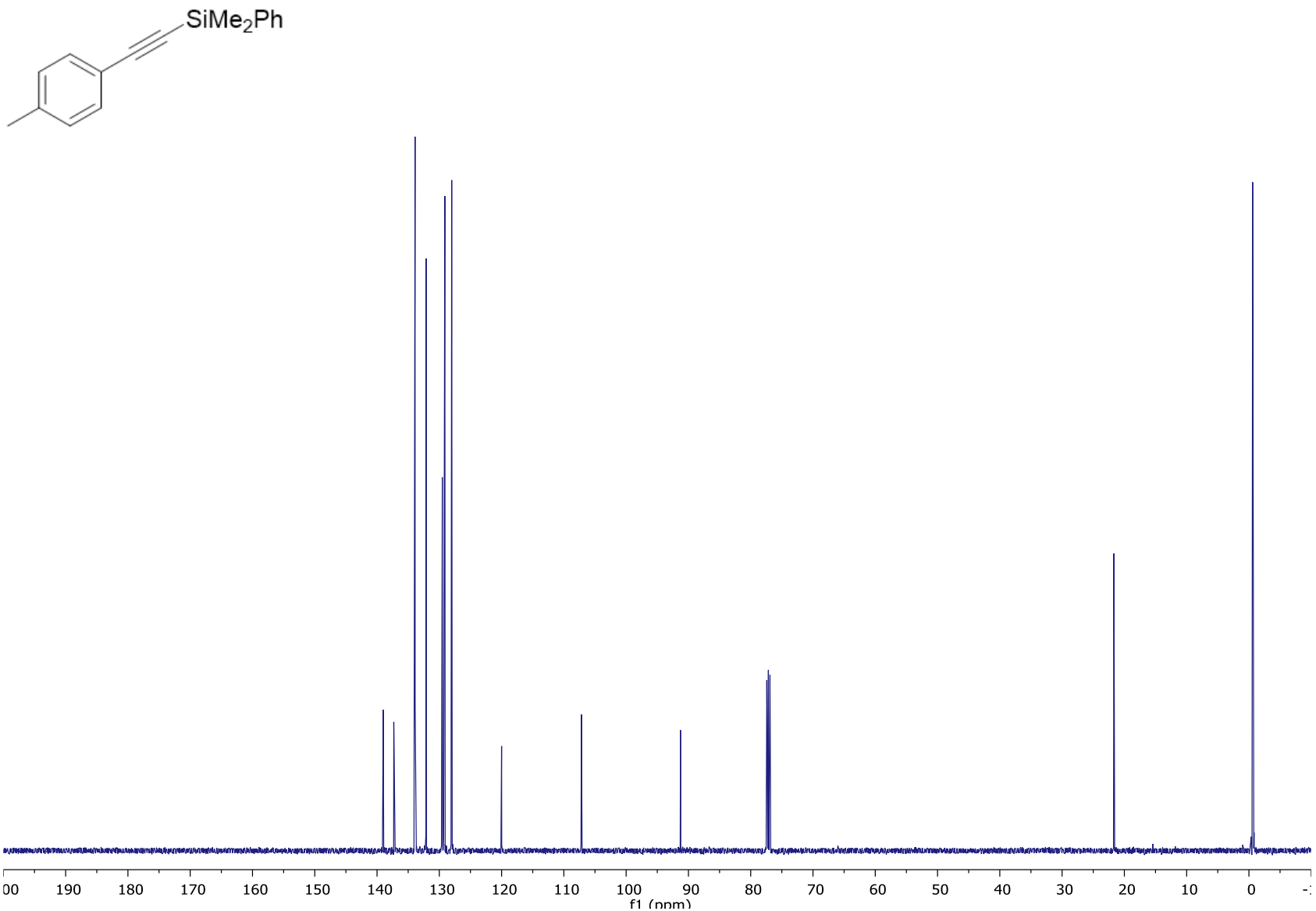
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42e.**



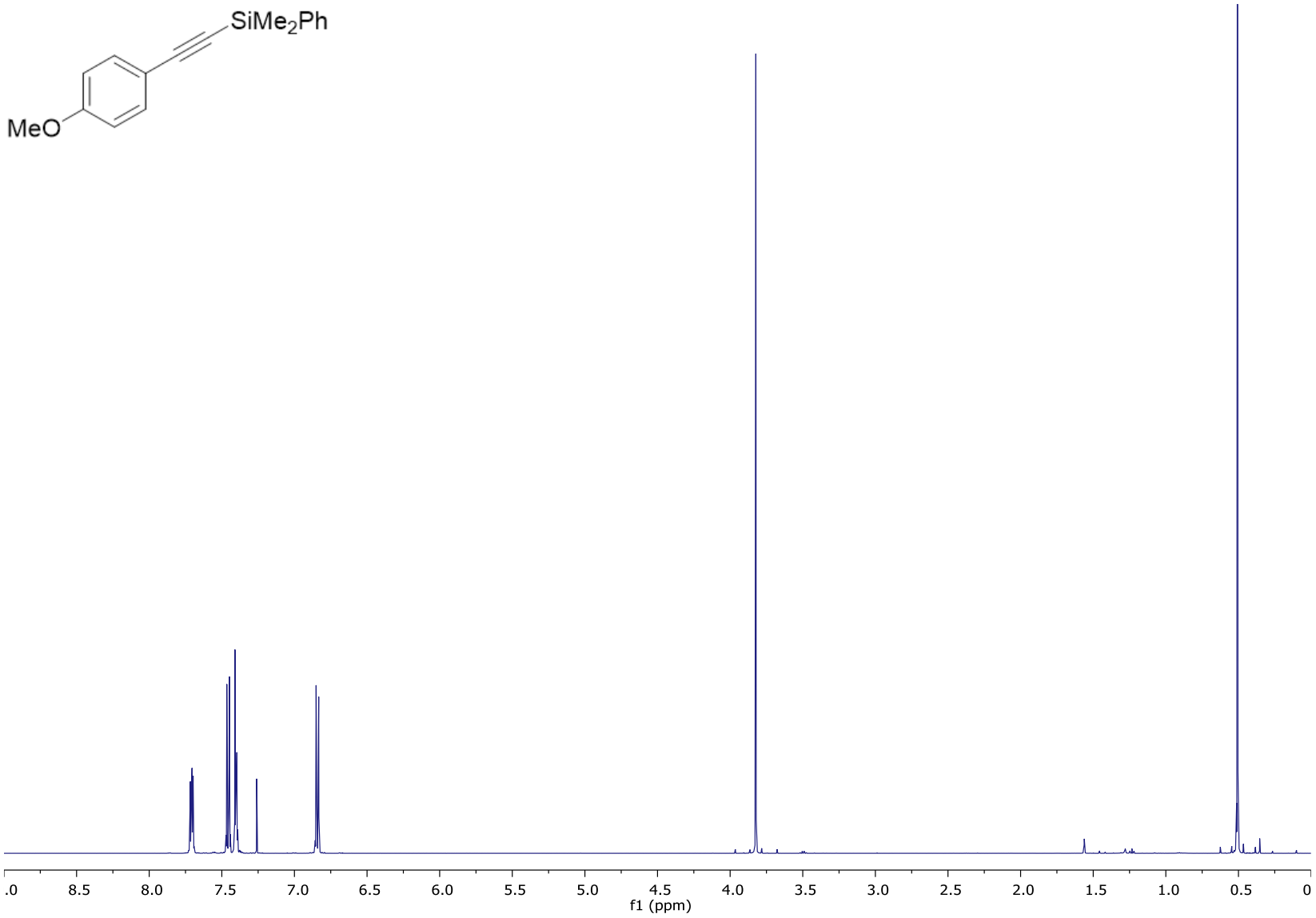
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42e.**



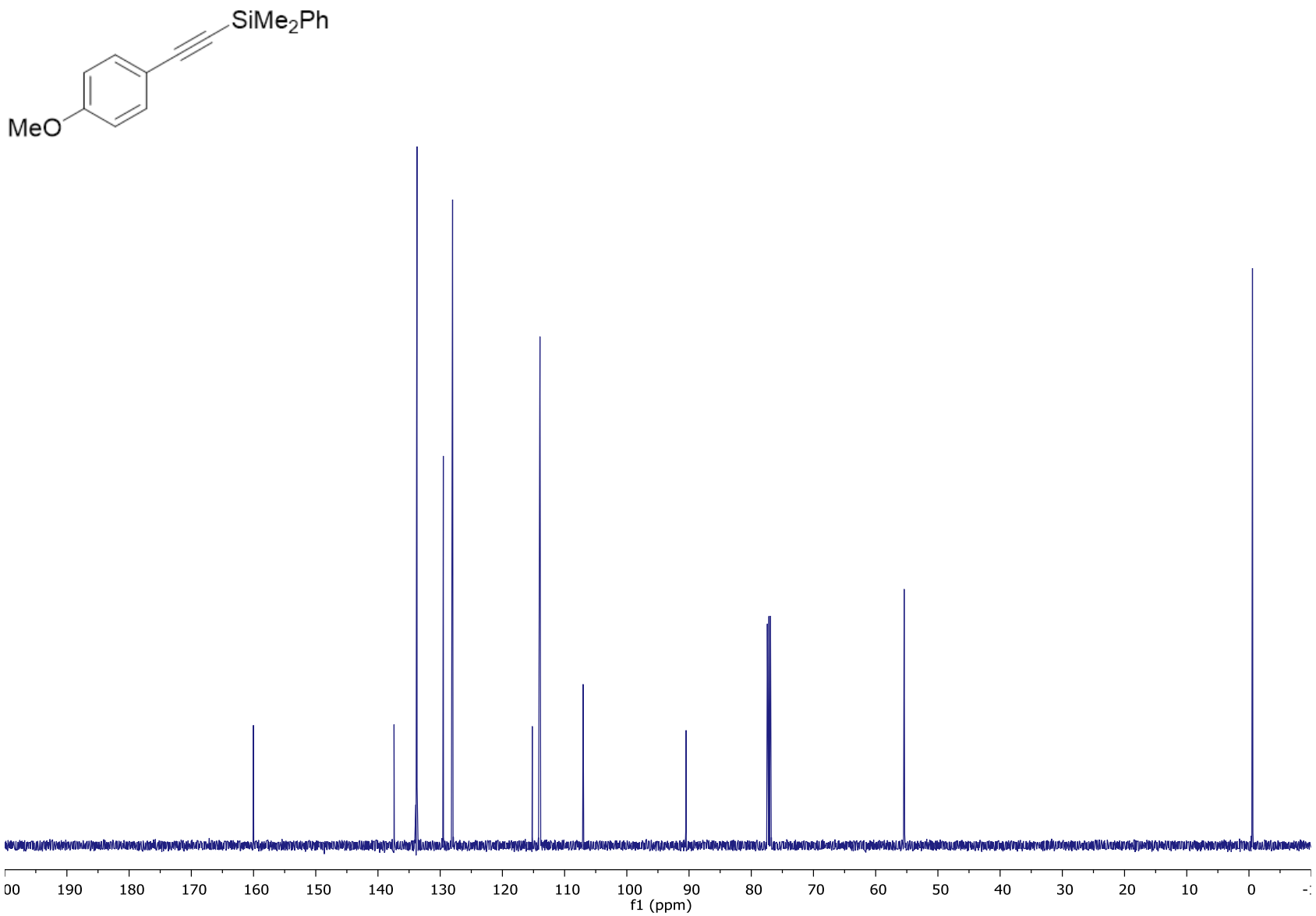
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42f.**



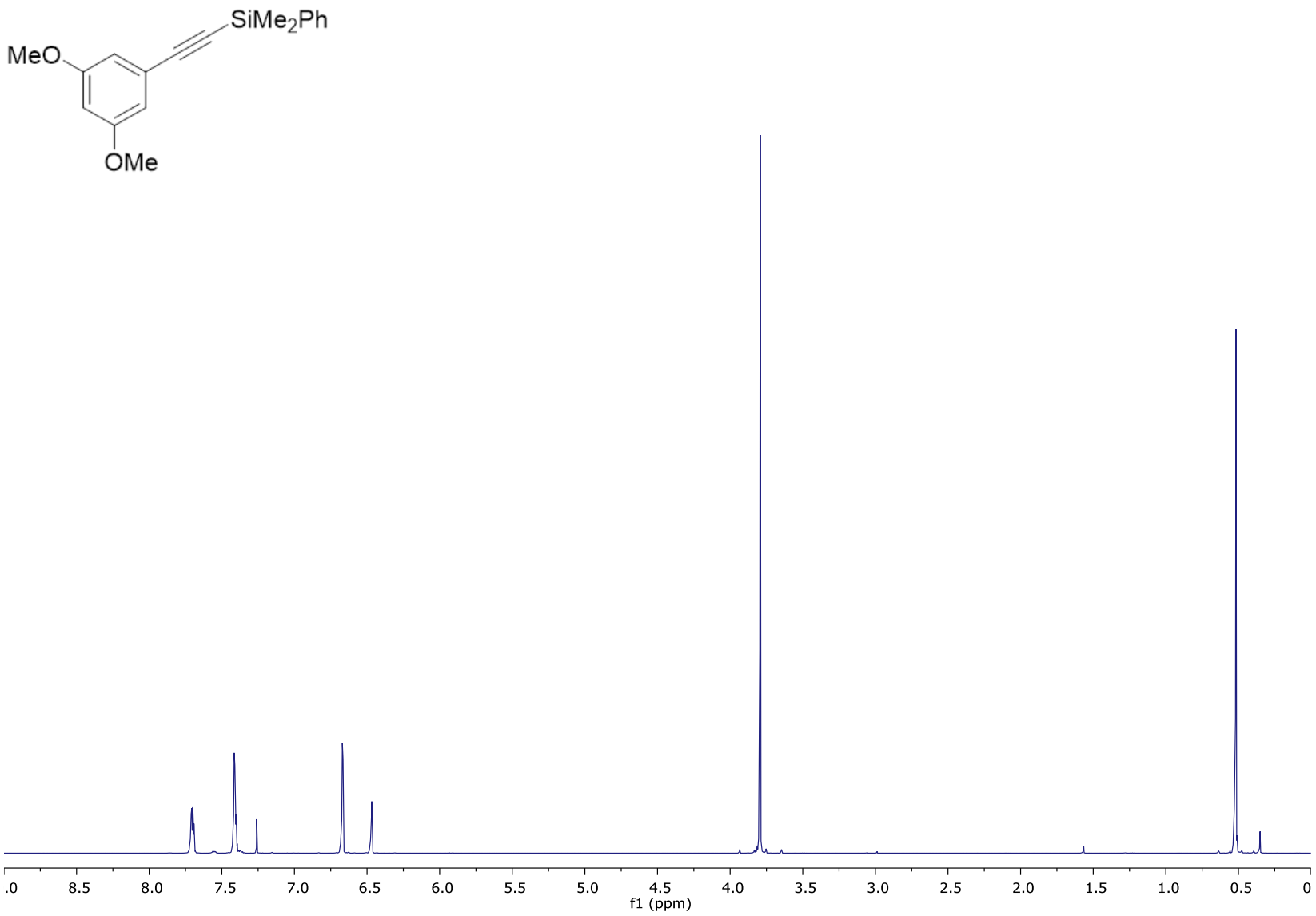
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42f.**



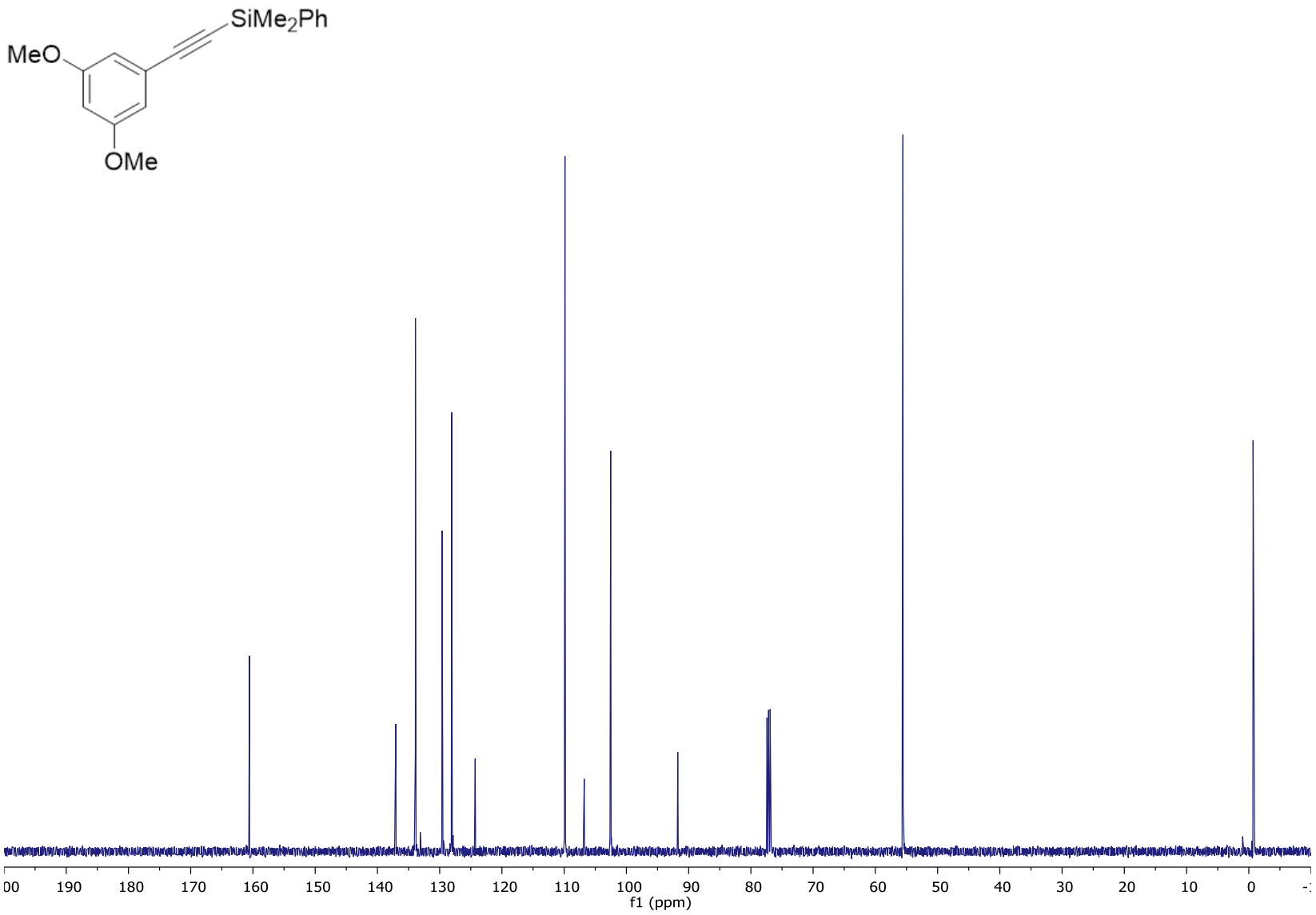
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42g.**



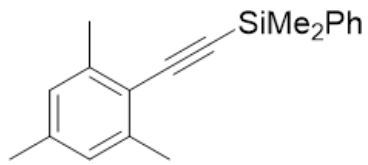
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42g.**

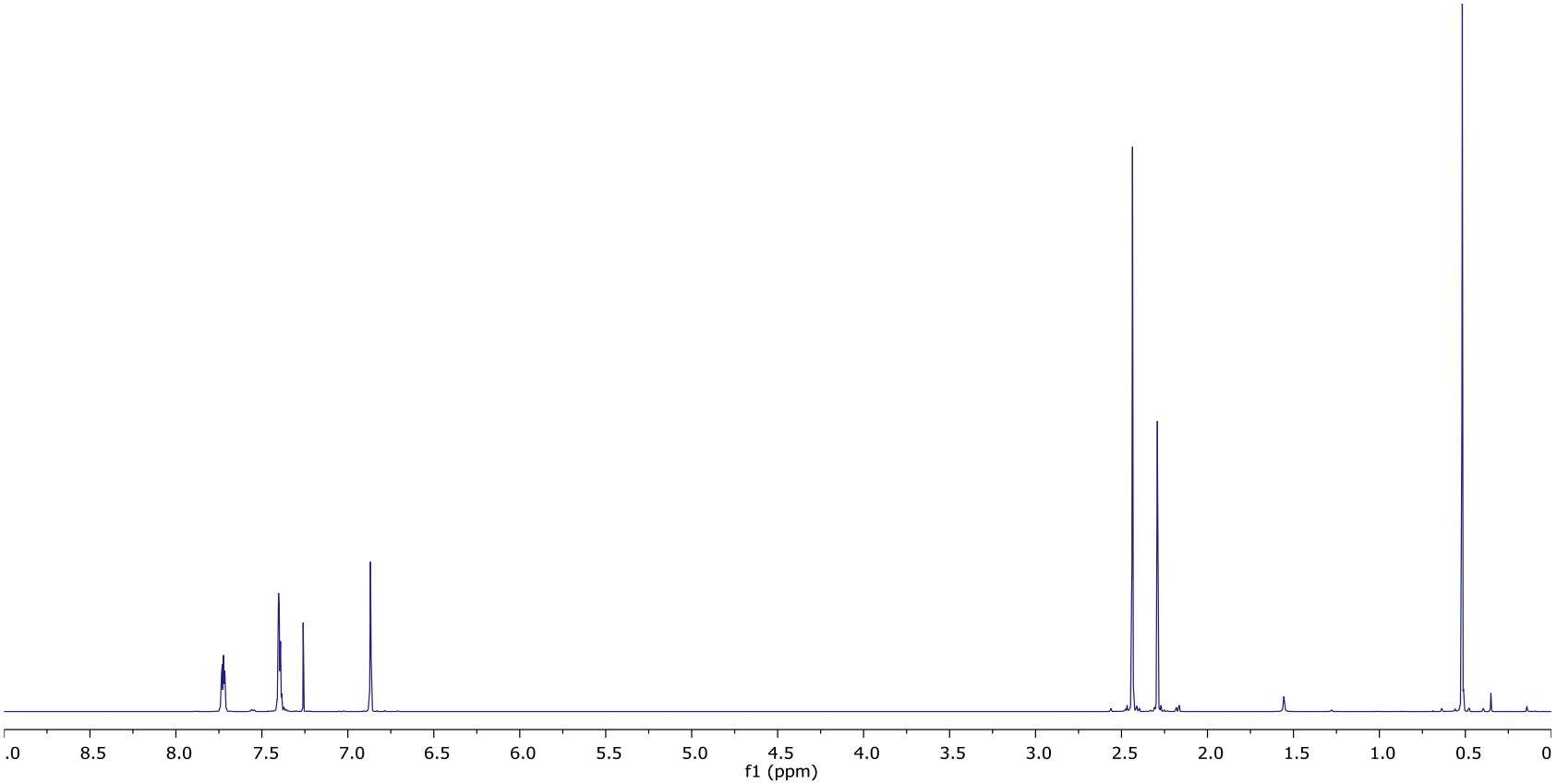


^{1}H NMR (500 MHz, $CDCl_3$) of compound **42h.**

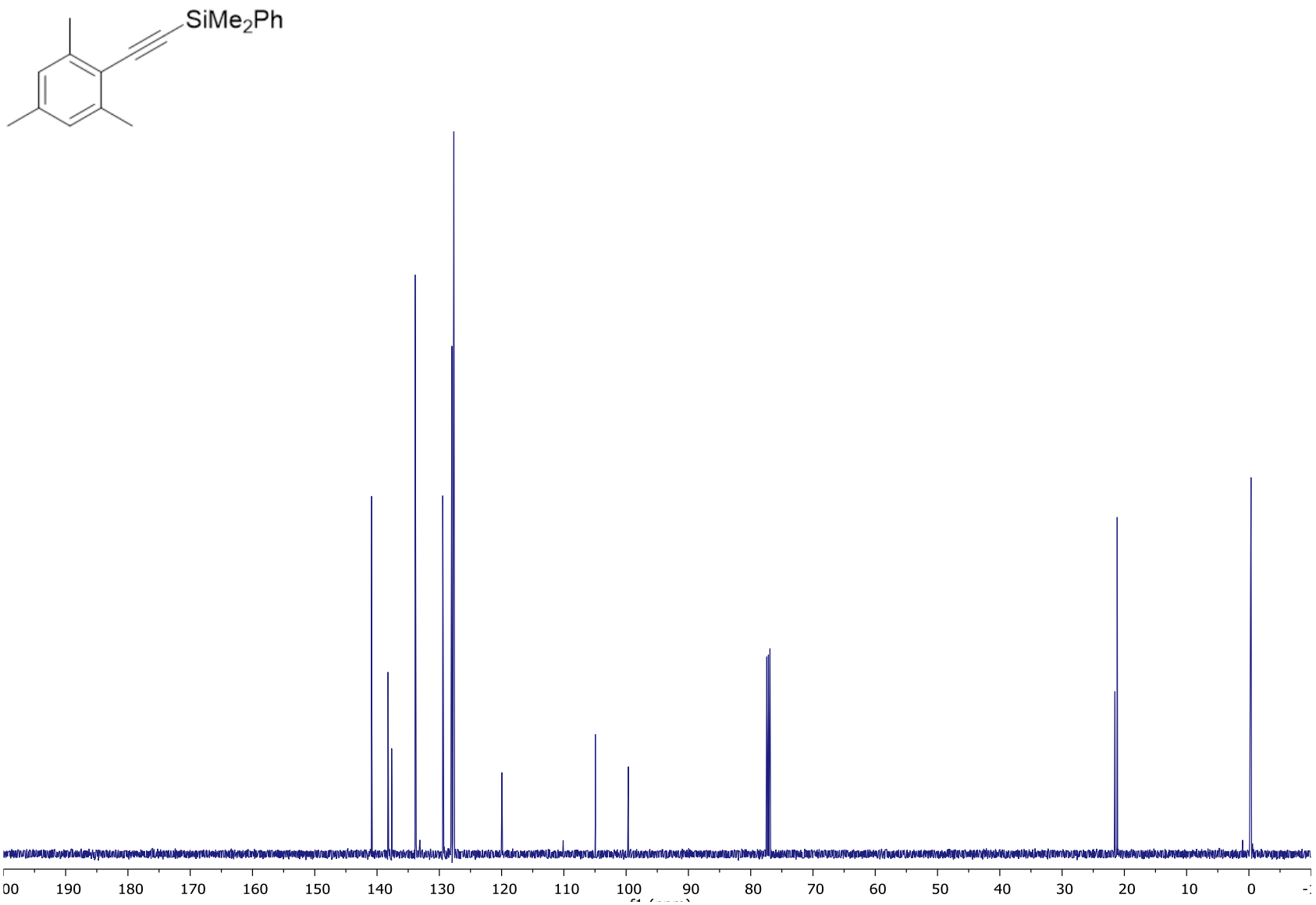


^{13}C NMR (126 MHz, $CDCl_3$) of compound **42h.**

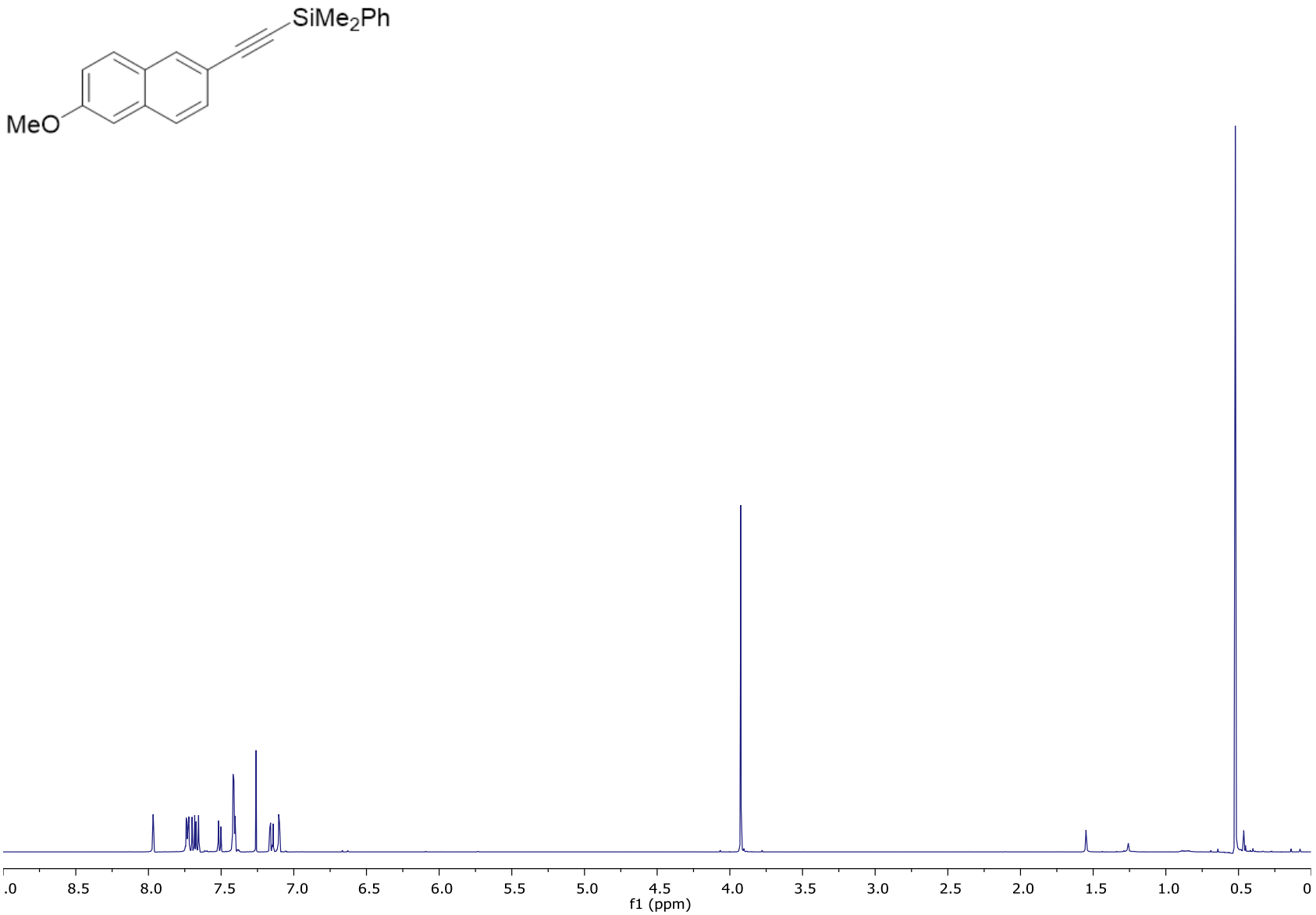




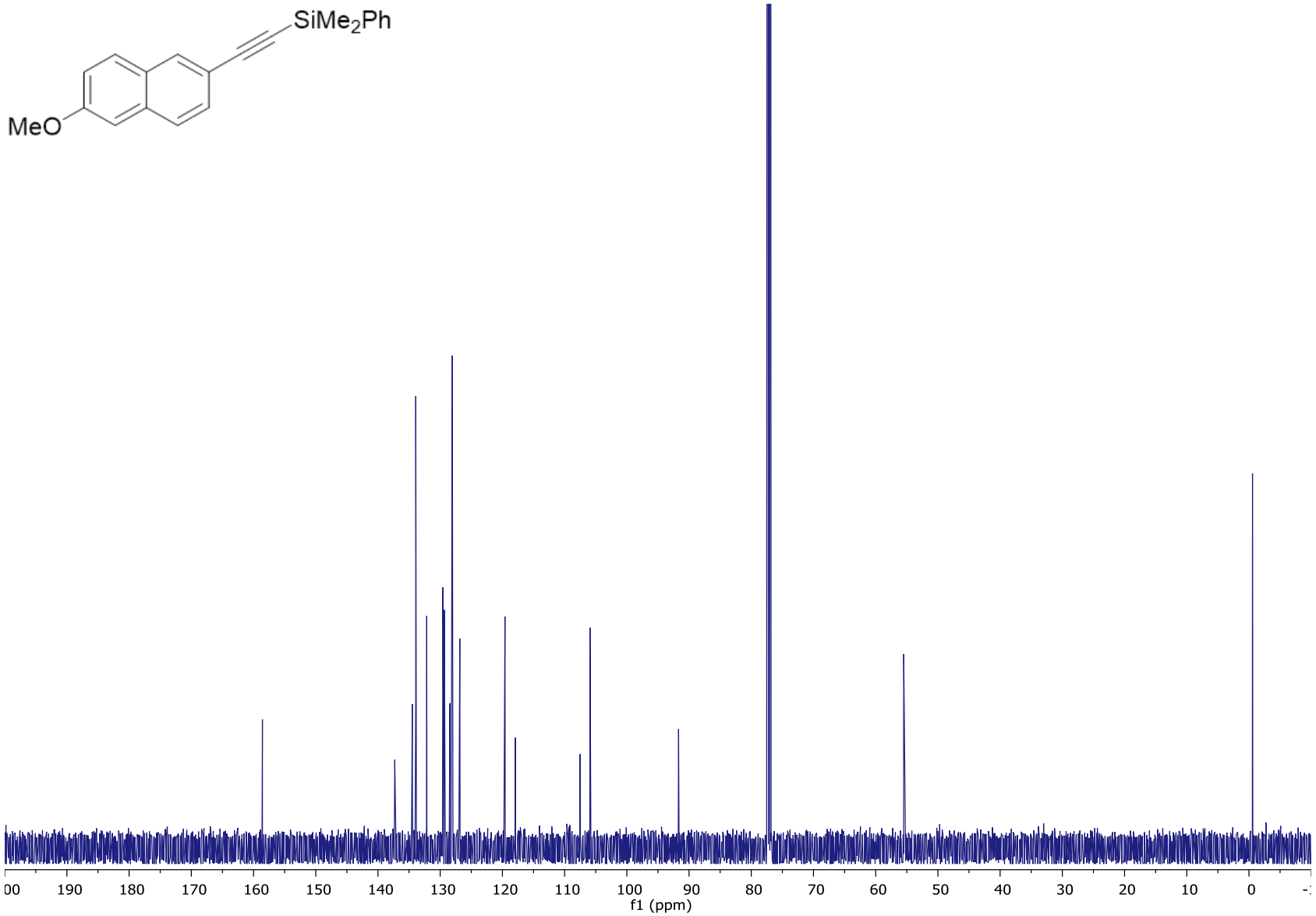
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42i.**



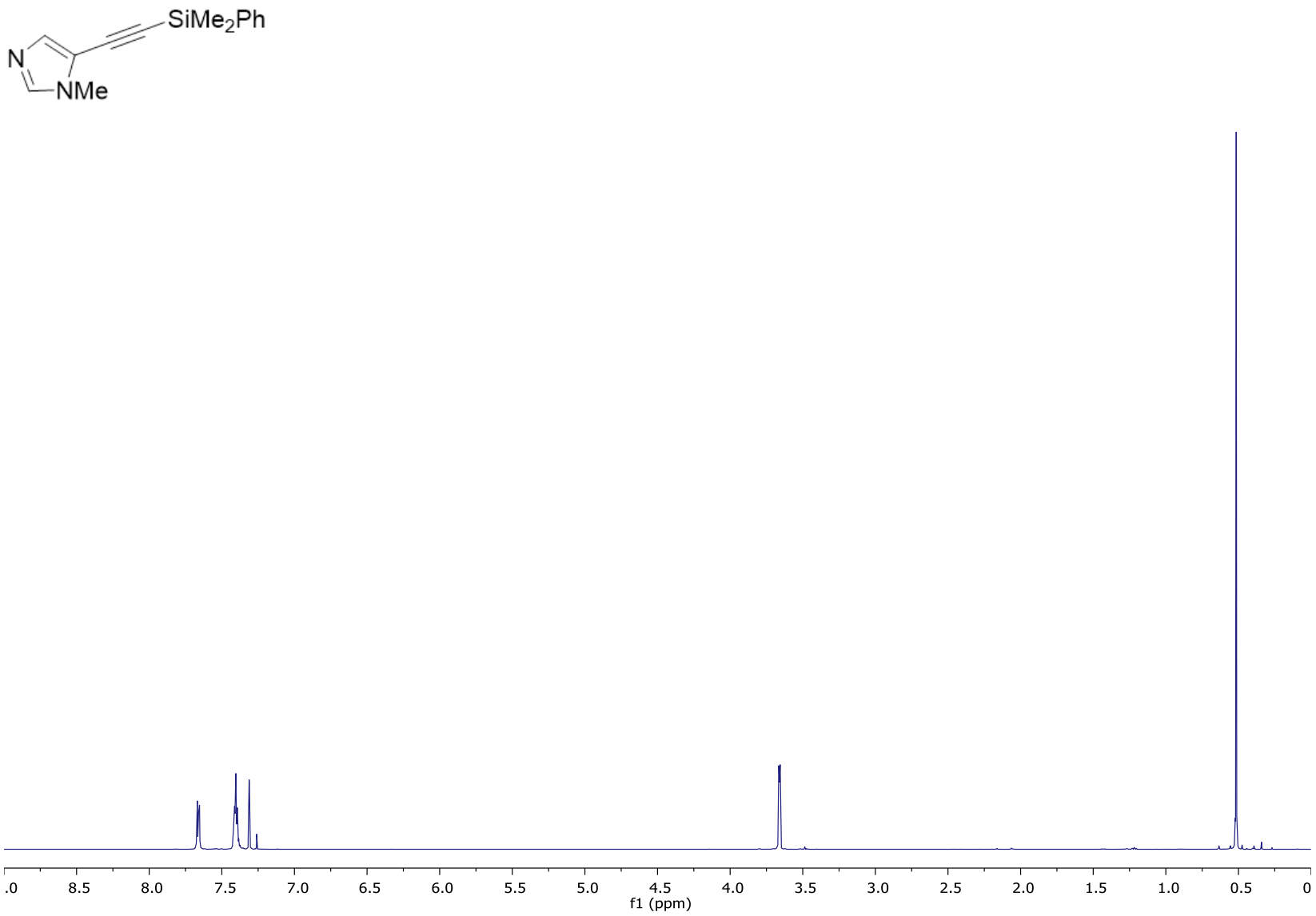
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42i.**



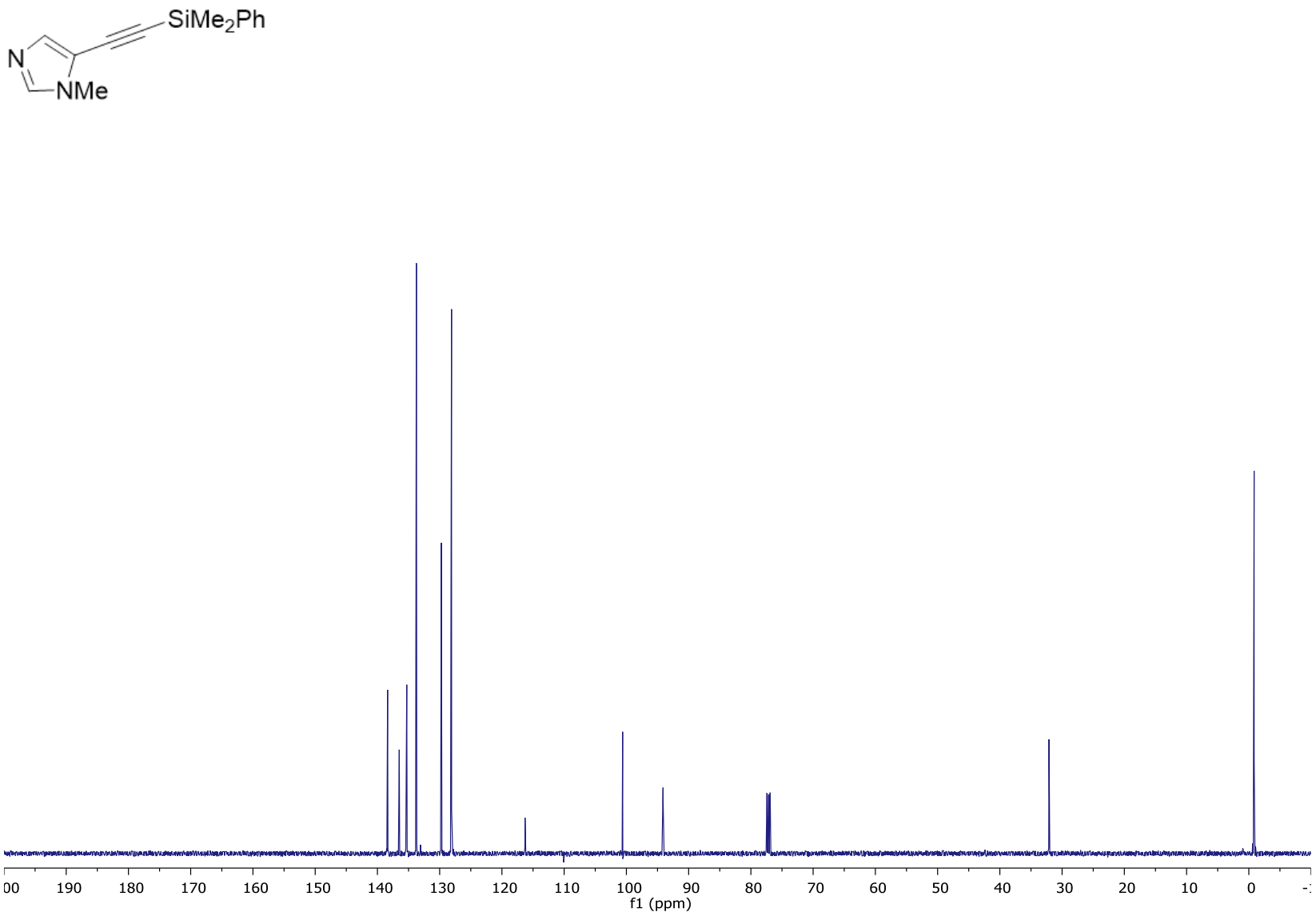
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42j.**



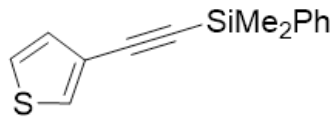
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42j.**

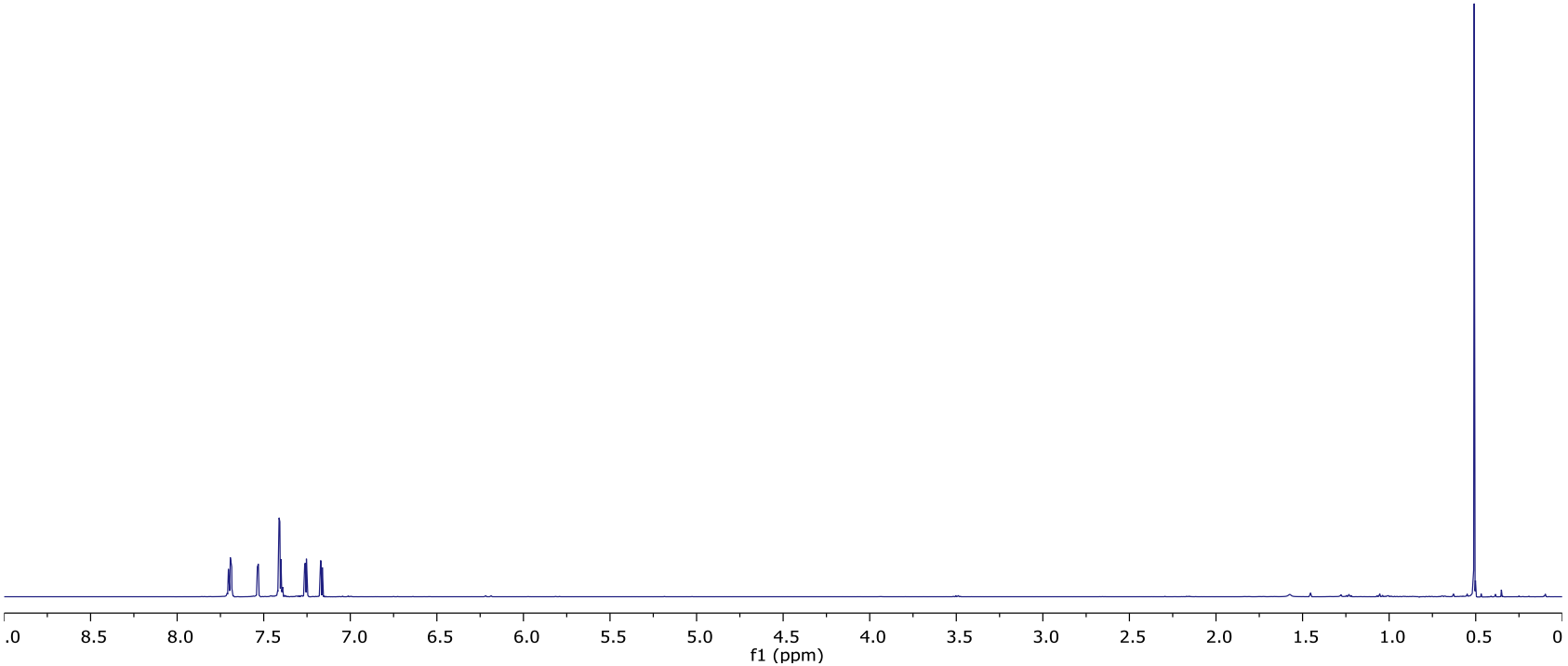


^{1}H NMR (500 MHz, $CDCl_3$) of compound **42k.**

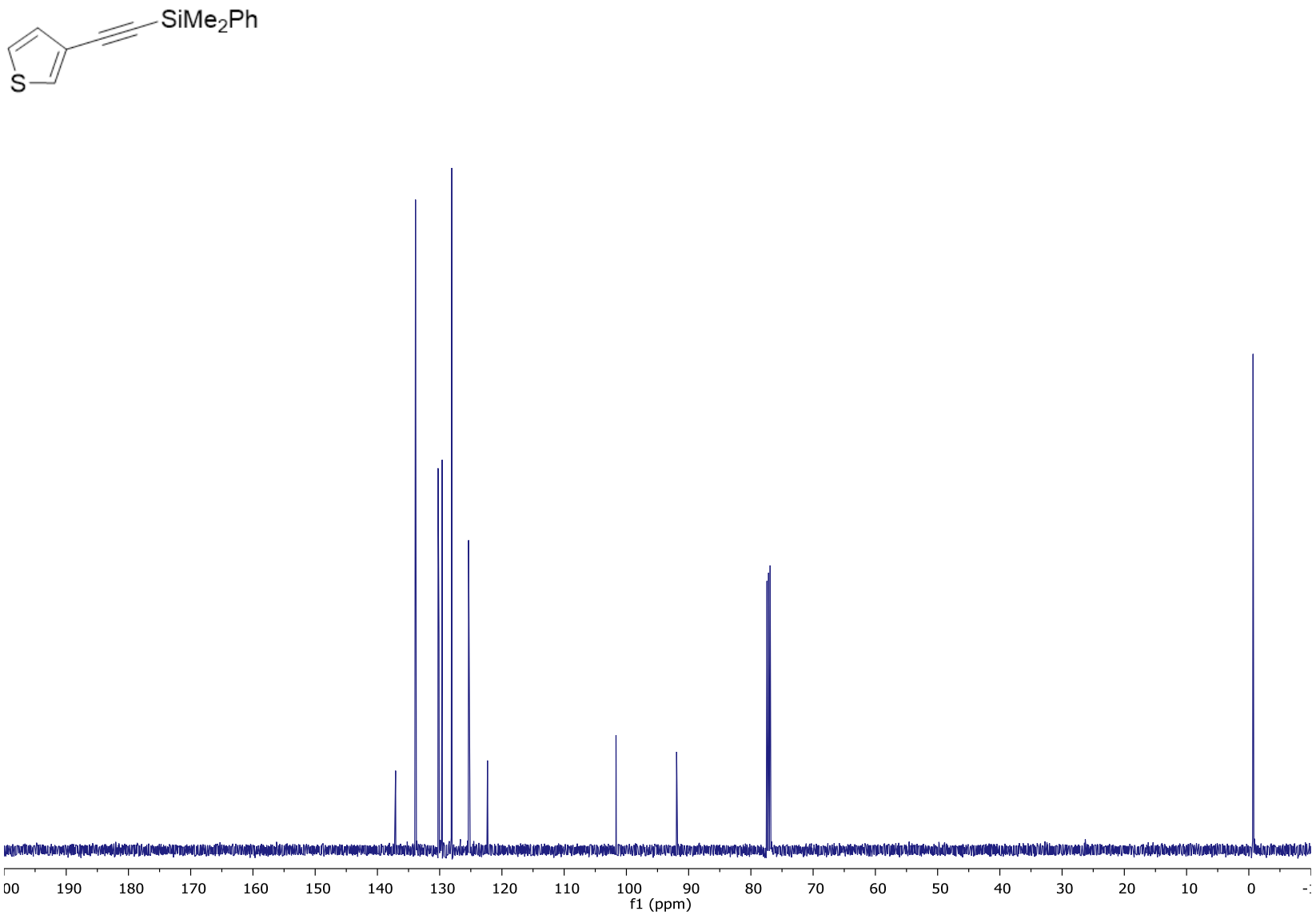


^{13}C NMR (126 MHz, $CDCl_3$) of compound **42k.**

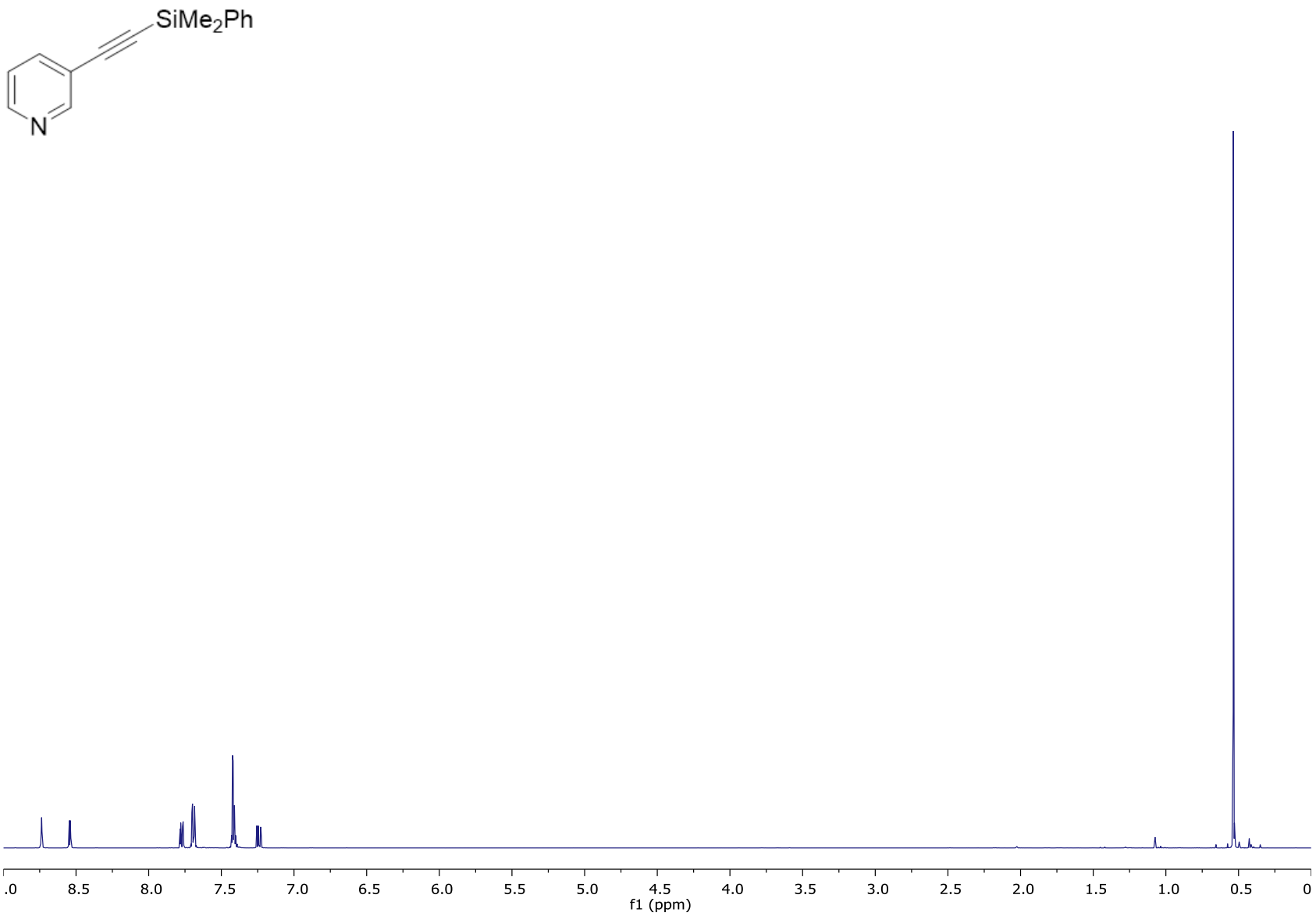




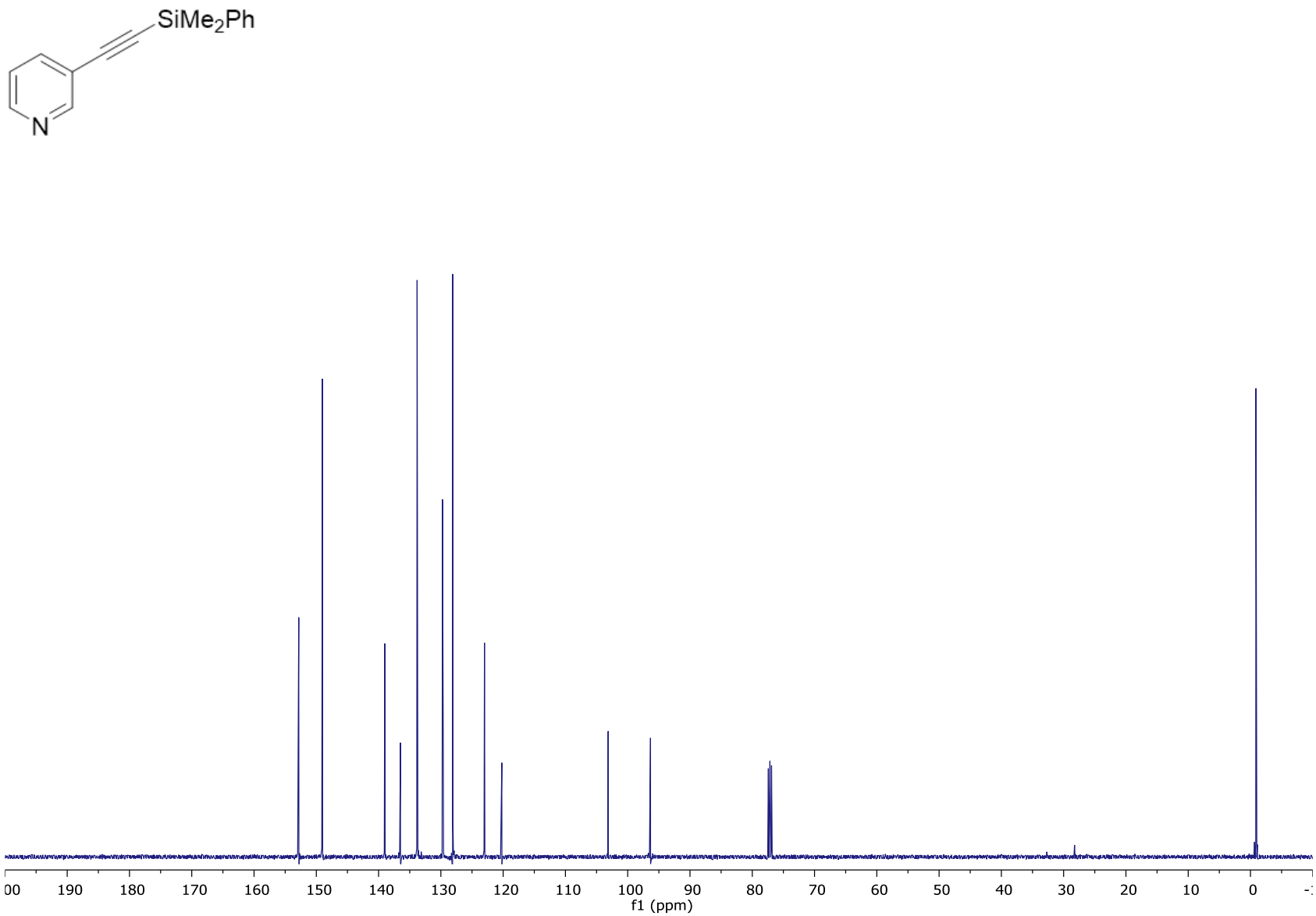
^{1}H NMR (500 MHz, $CDCl_3$) of compound **421.**



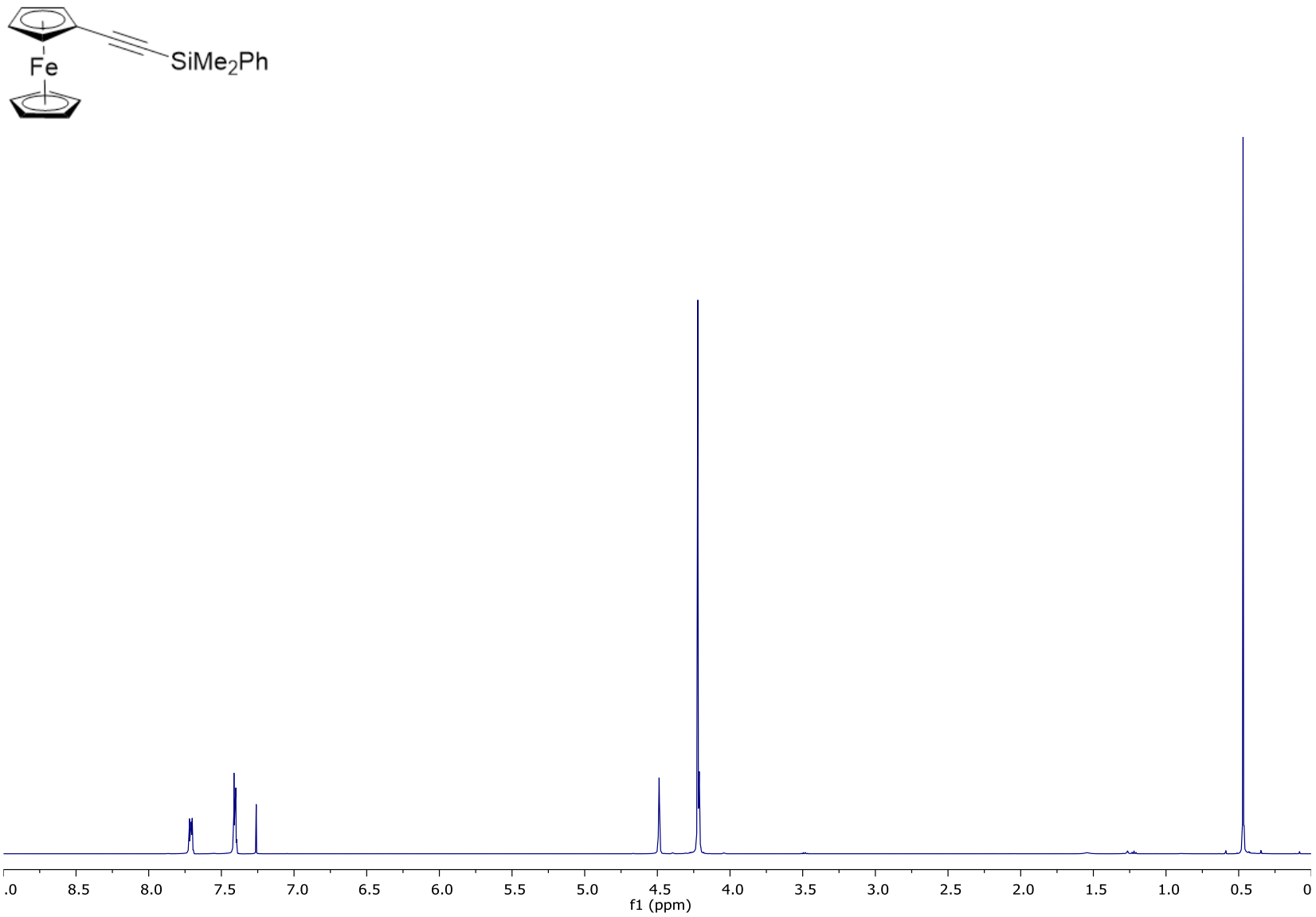
^{13}C NMR (126 MHz, $CDCl_3$) of compound **421.**



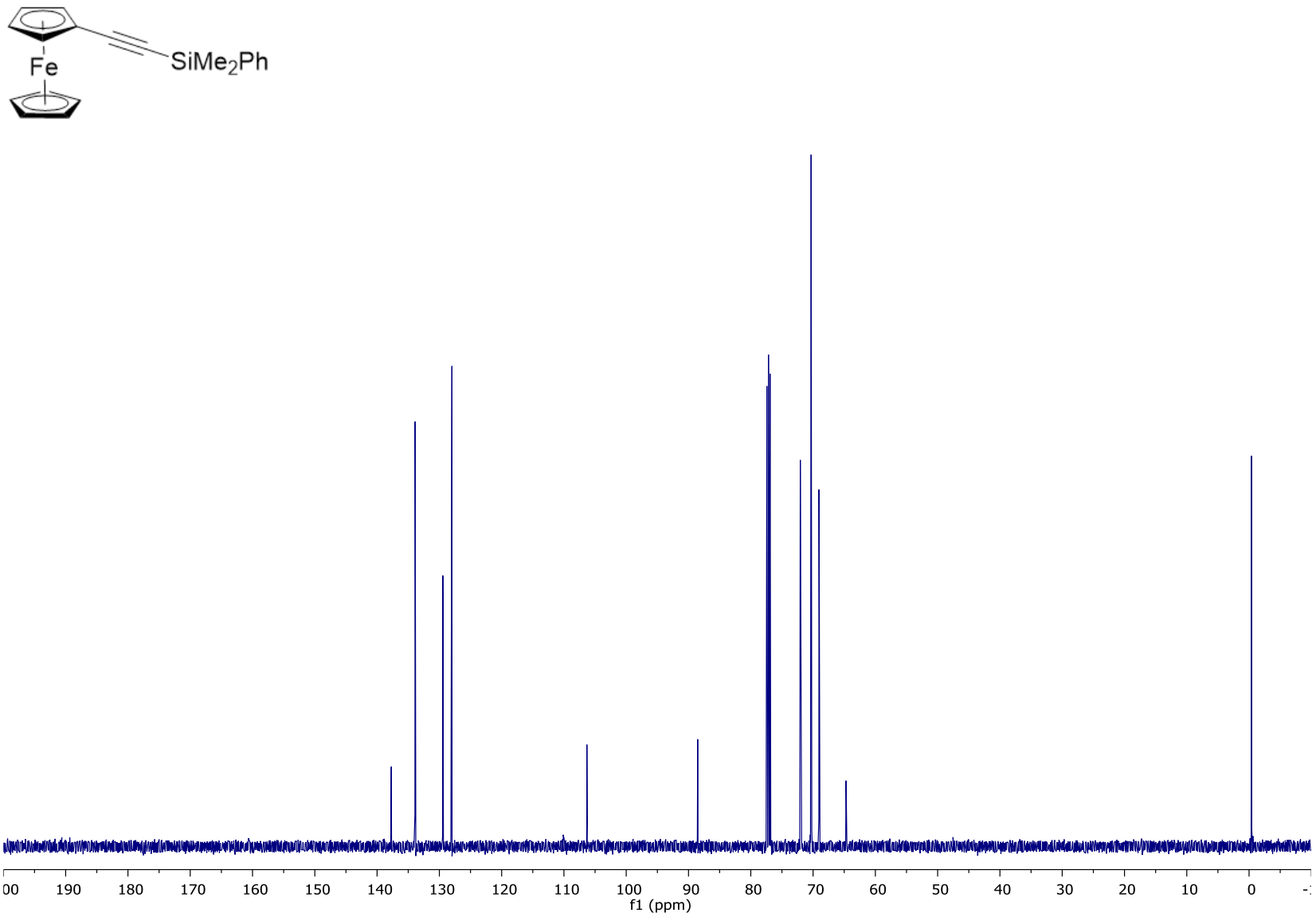
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42m.**



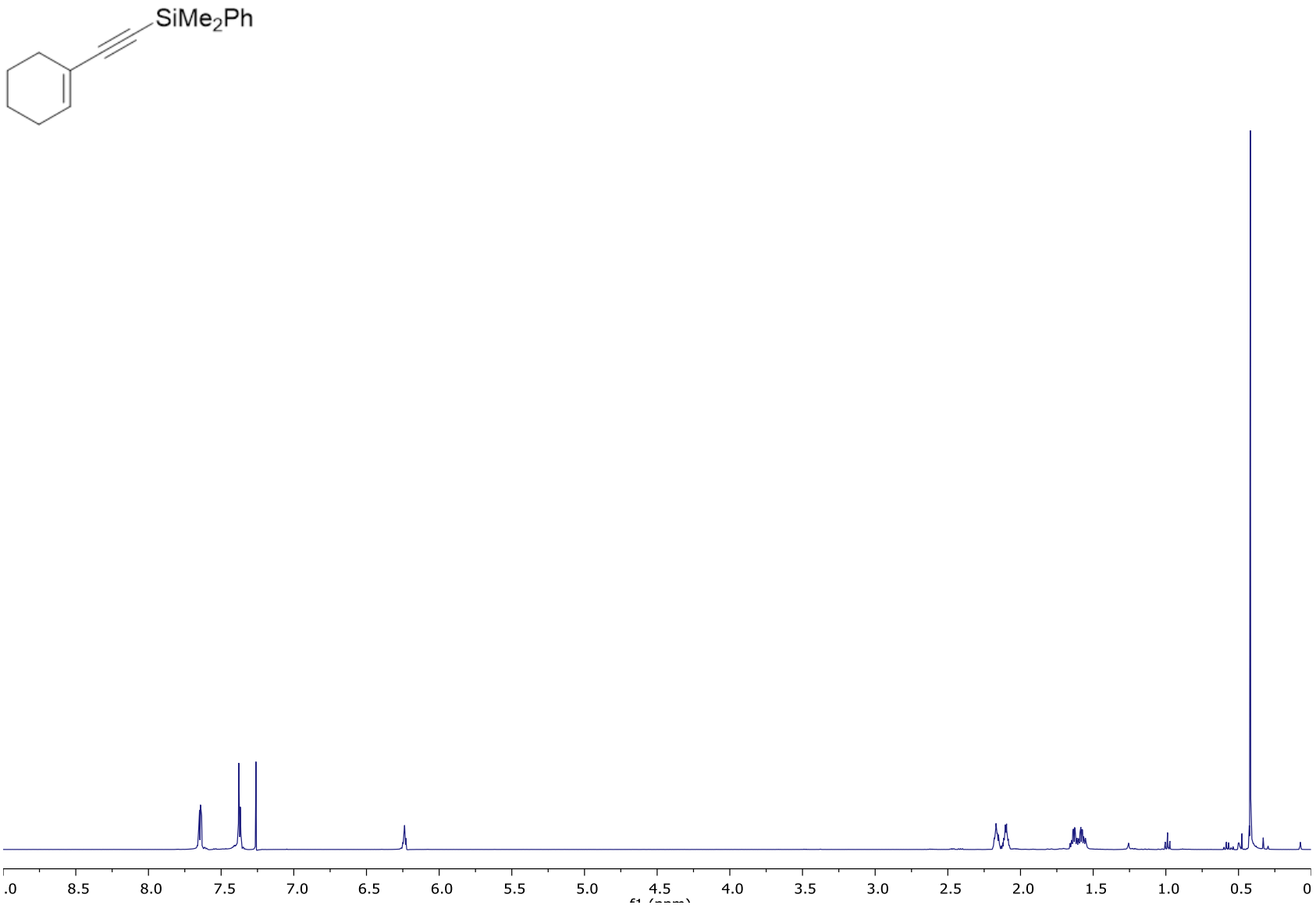
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42m.**



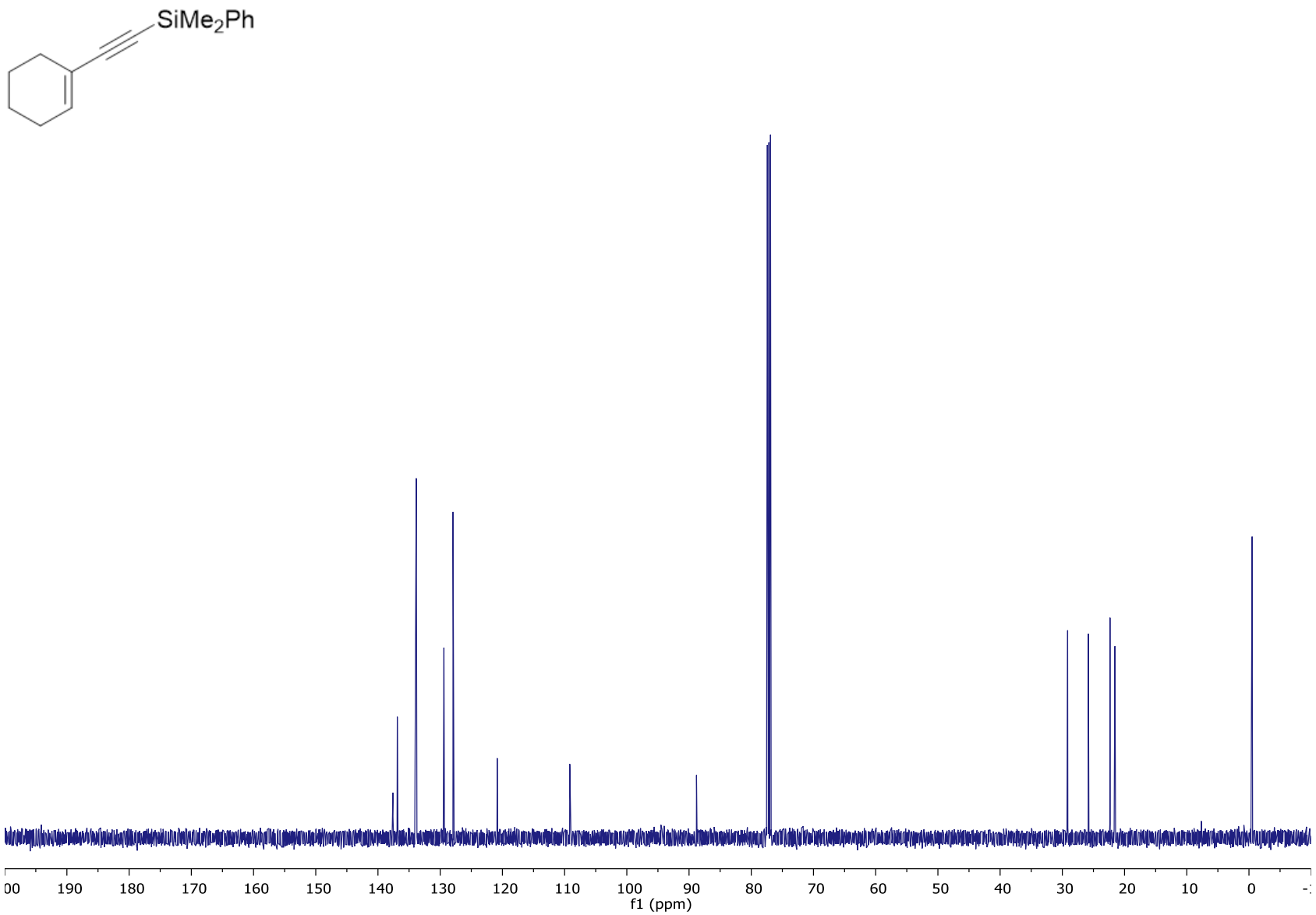
^{1}H NMR (500 MHz, $CDCl_3$ of compound **42n.**



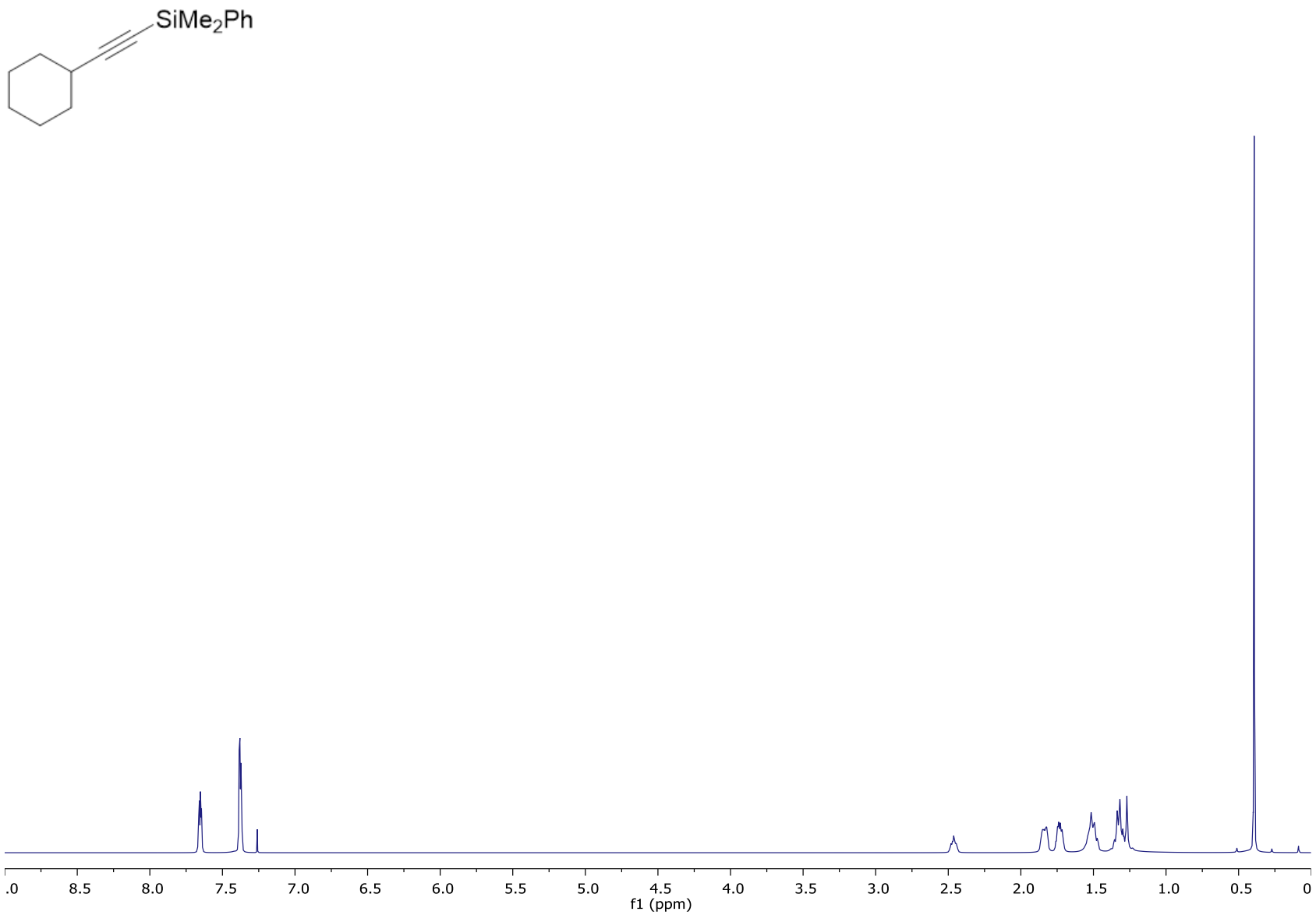
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42n.**



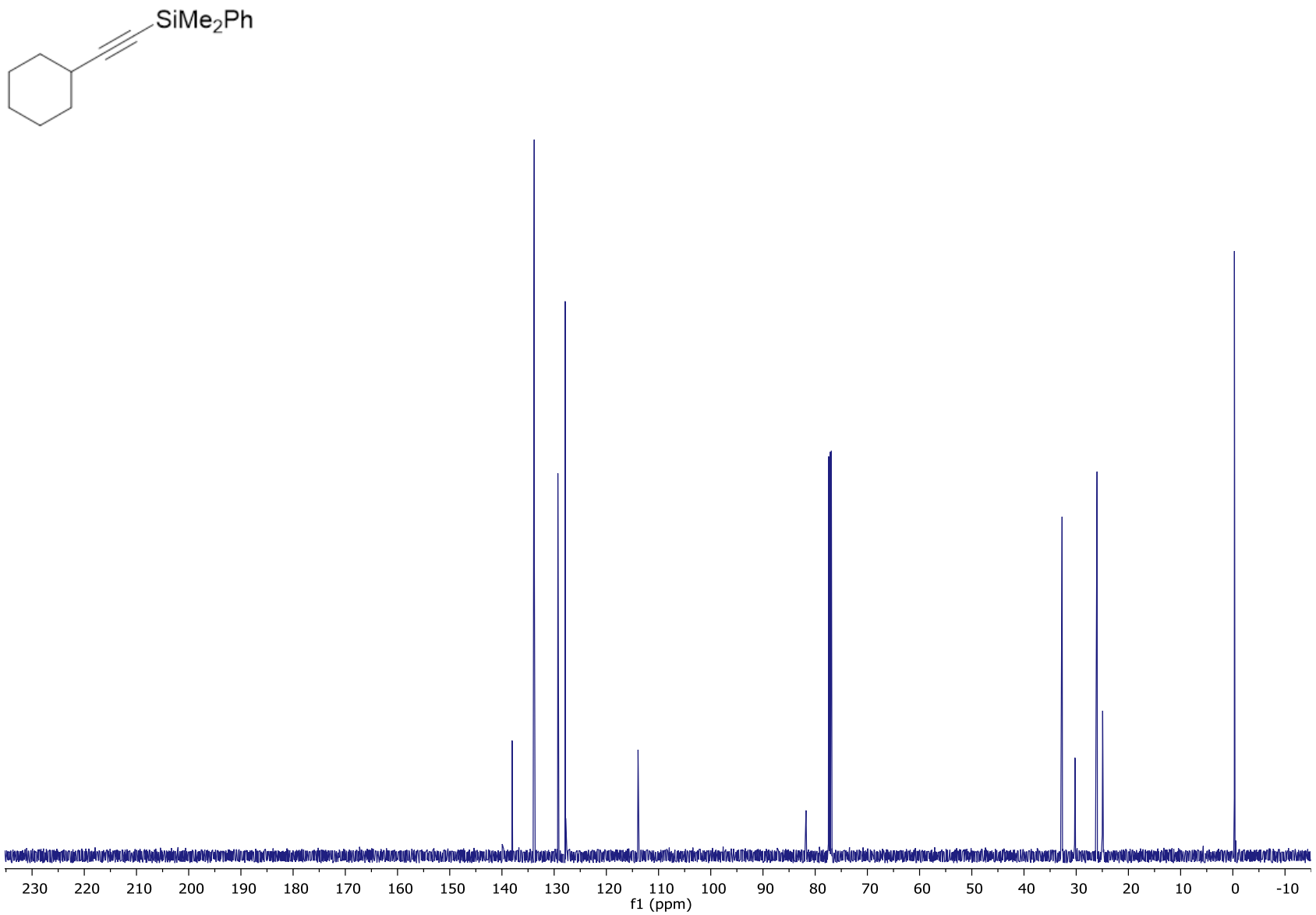
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42o.**



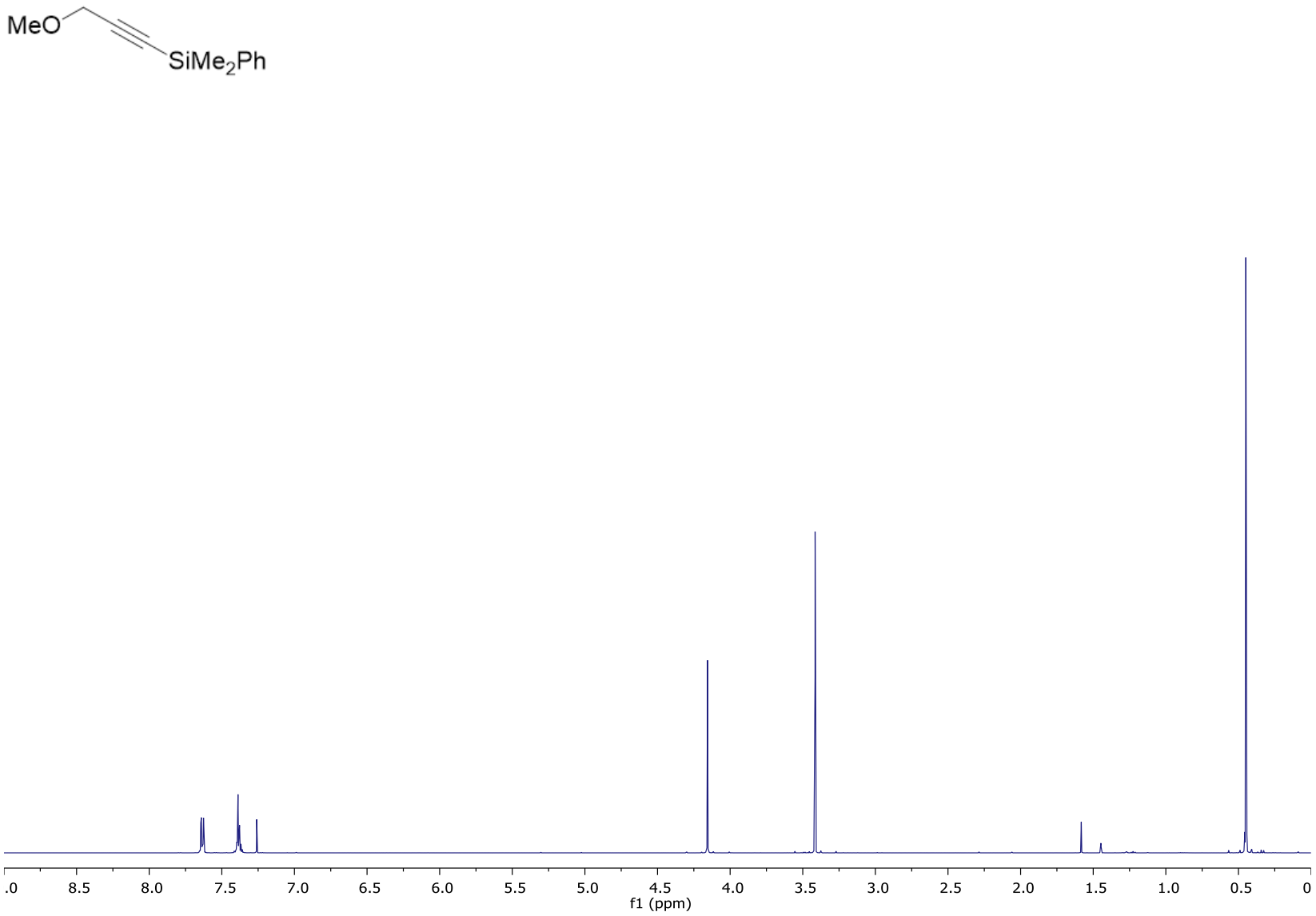
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42o.**



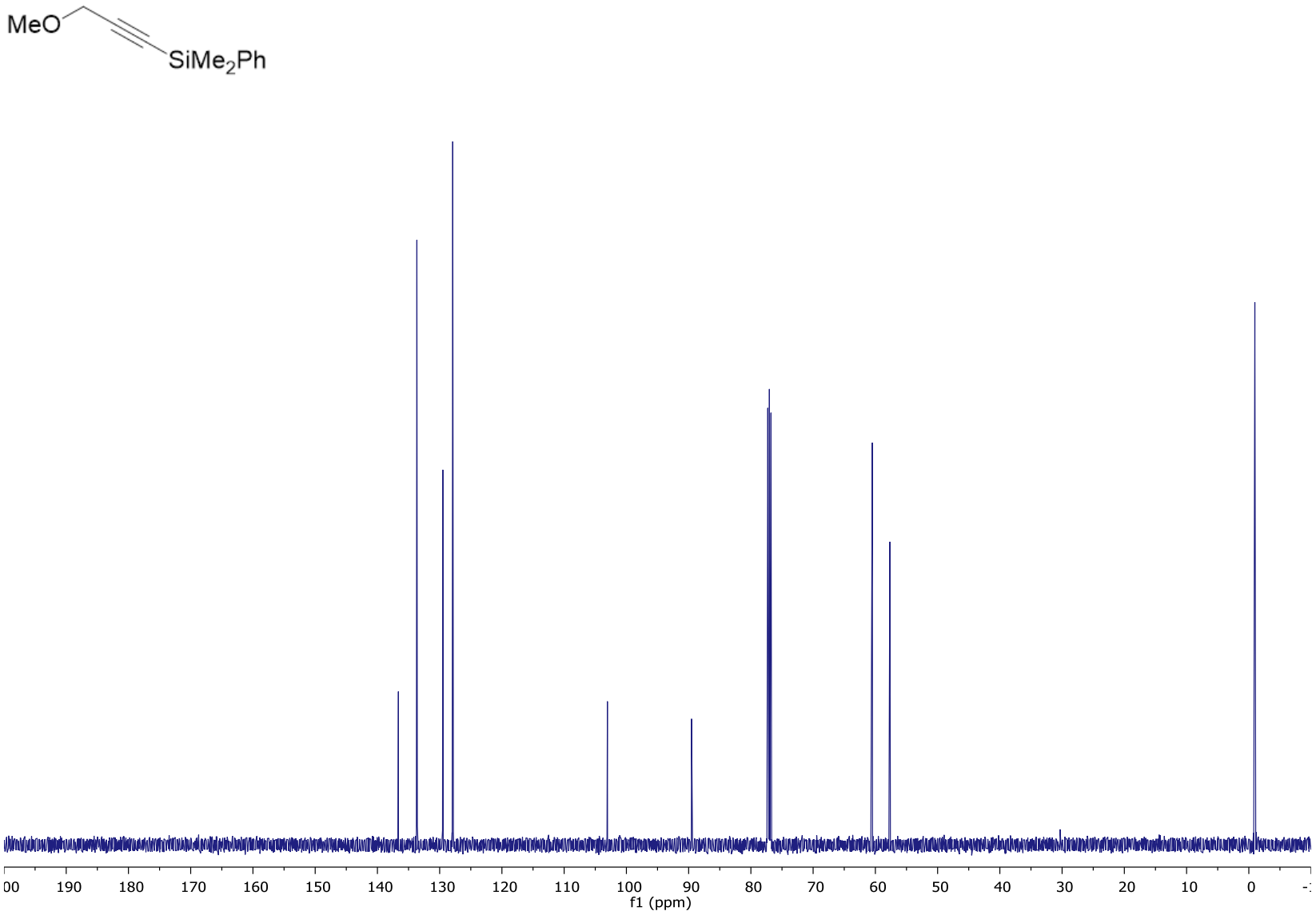
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42p.**



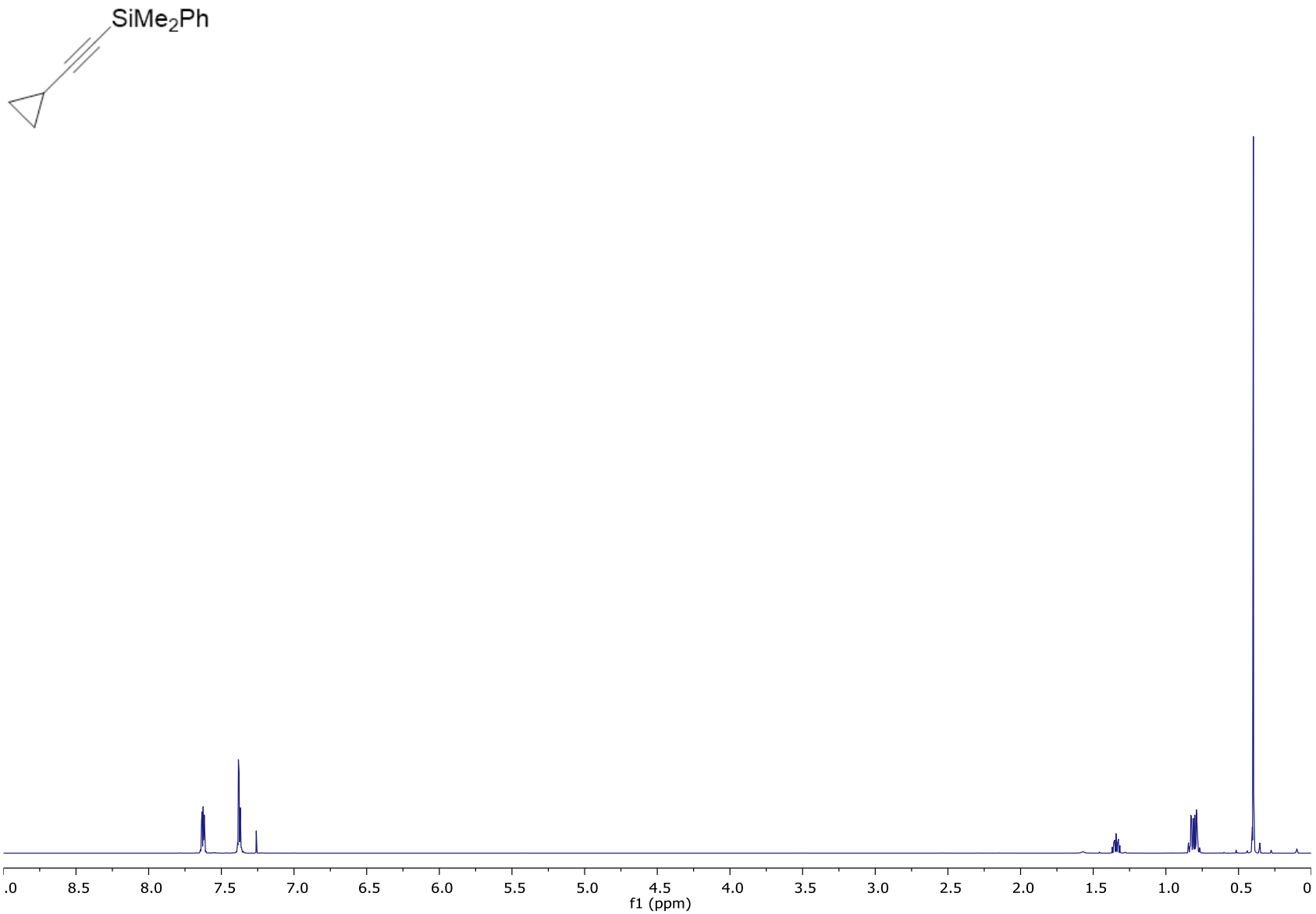
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42p.**



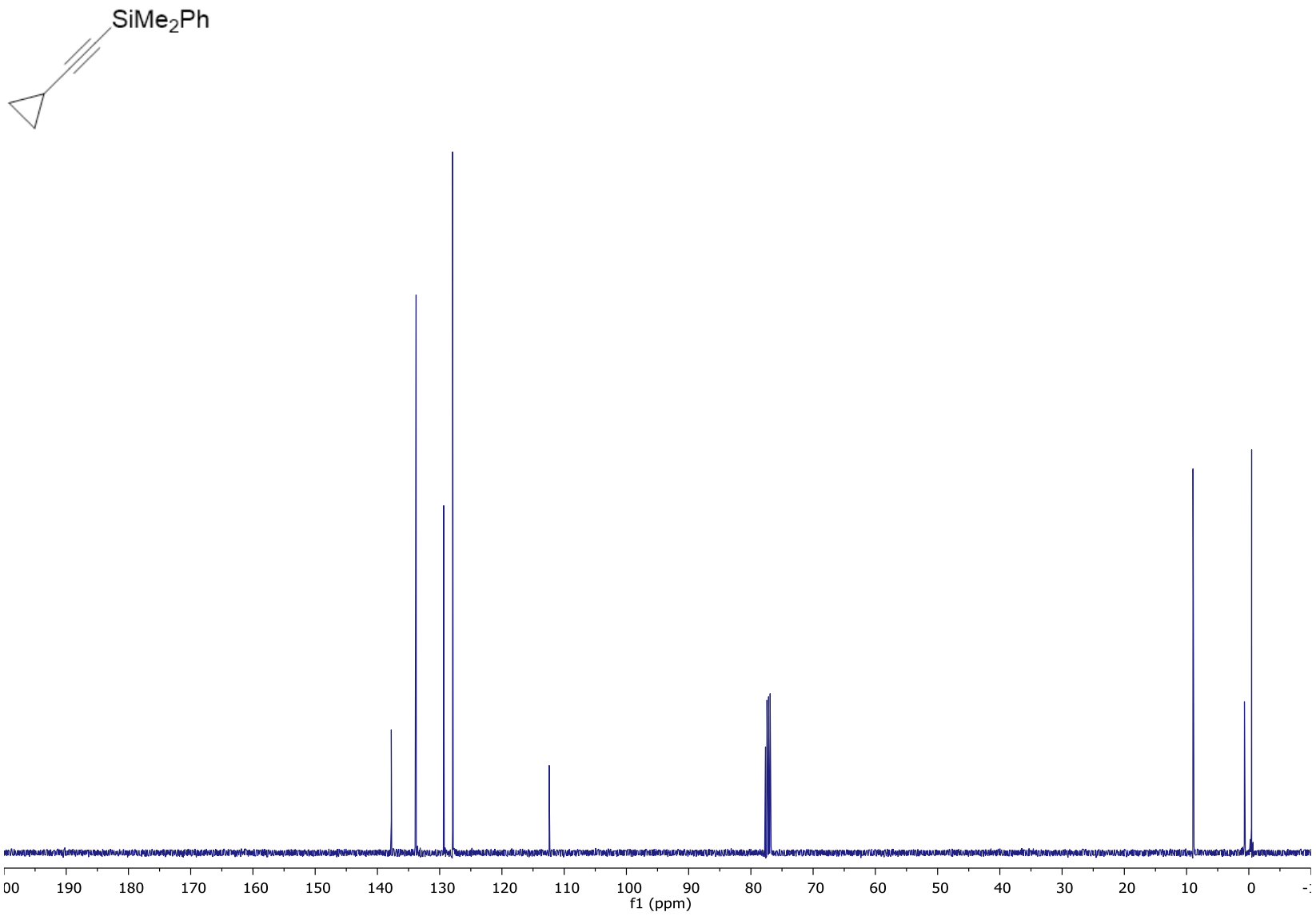
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42q.**



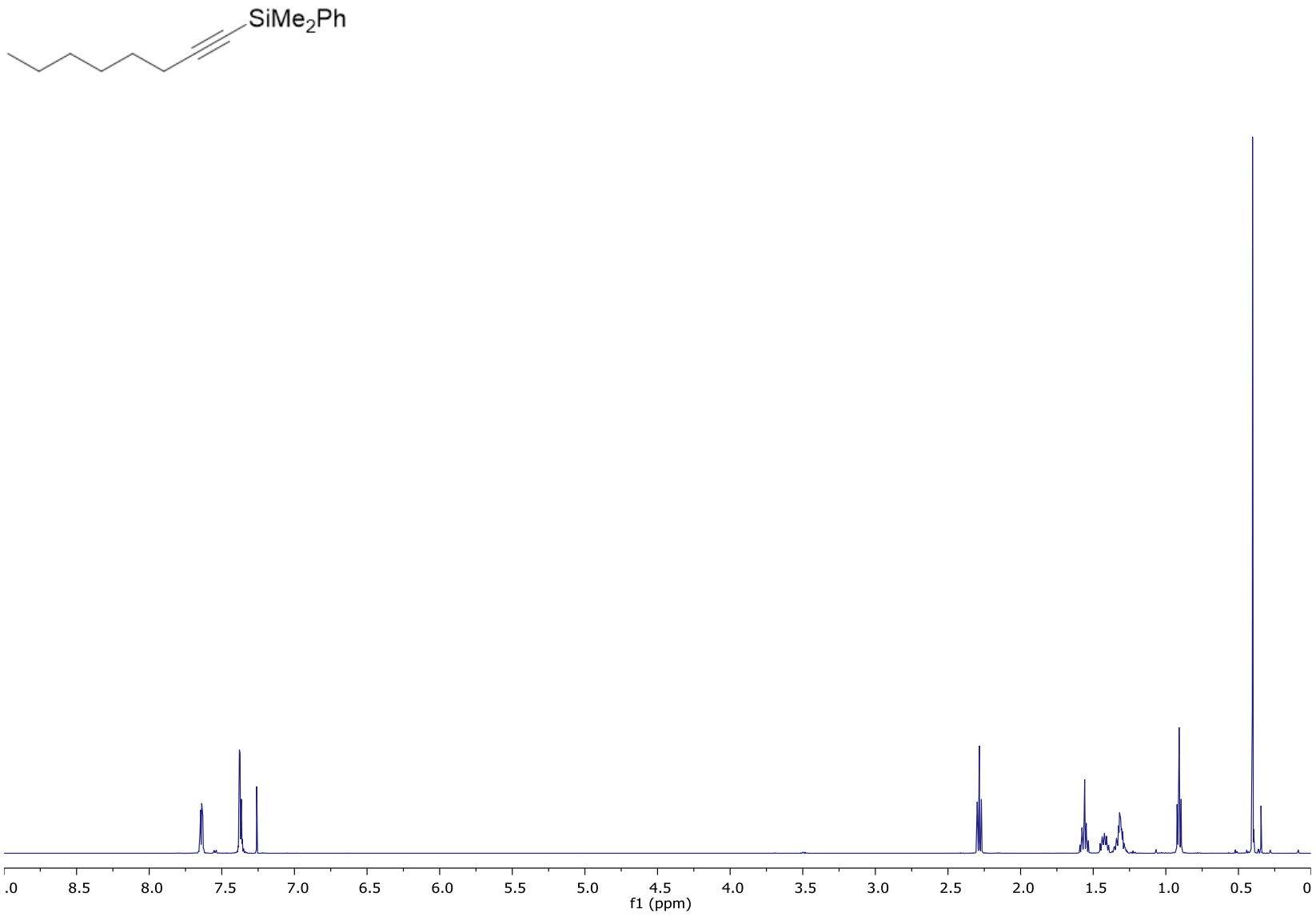
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42q.**



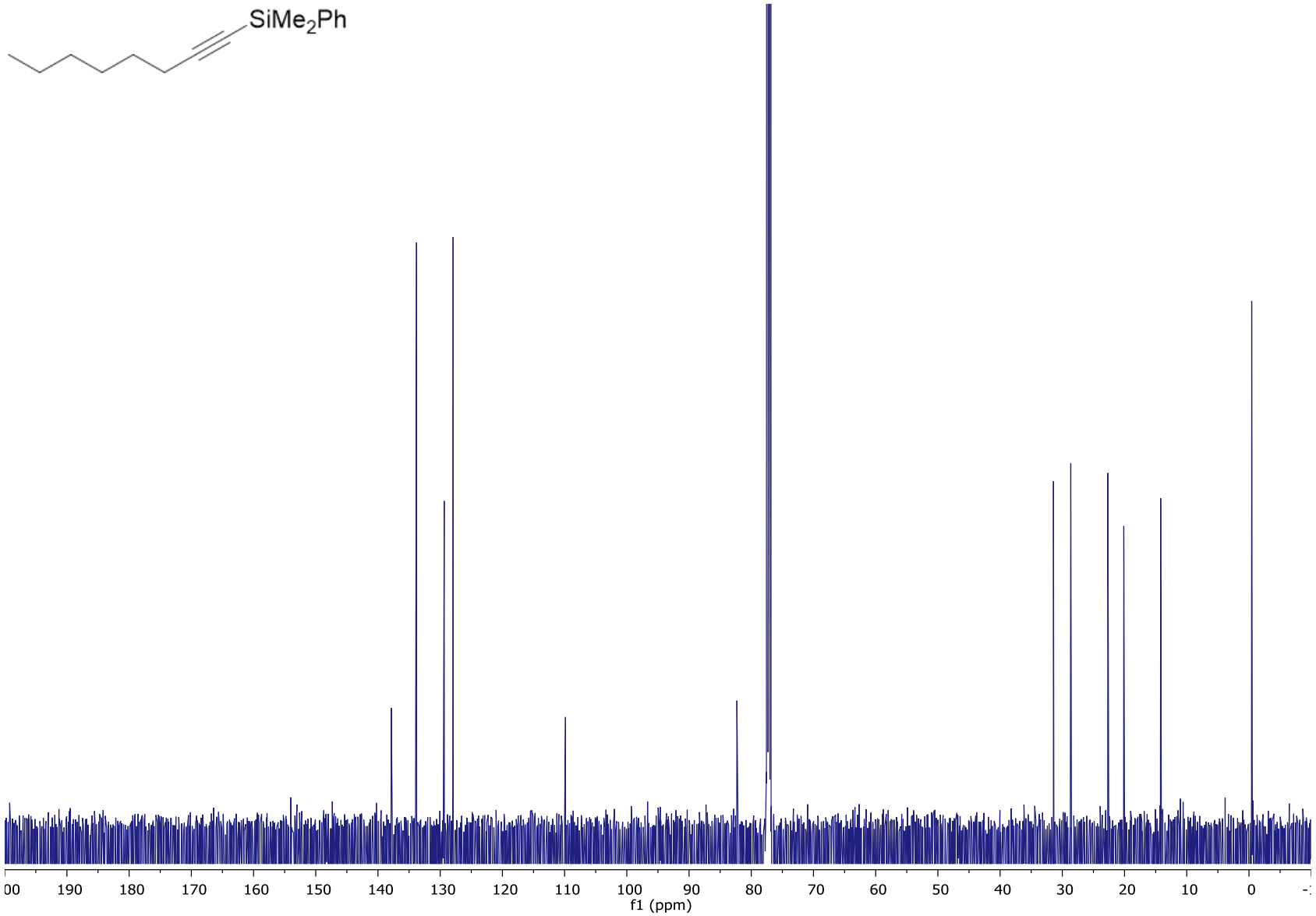
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42r.**



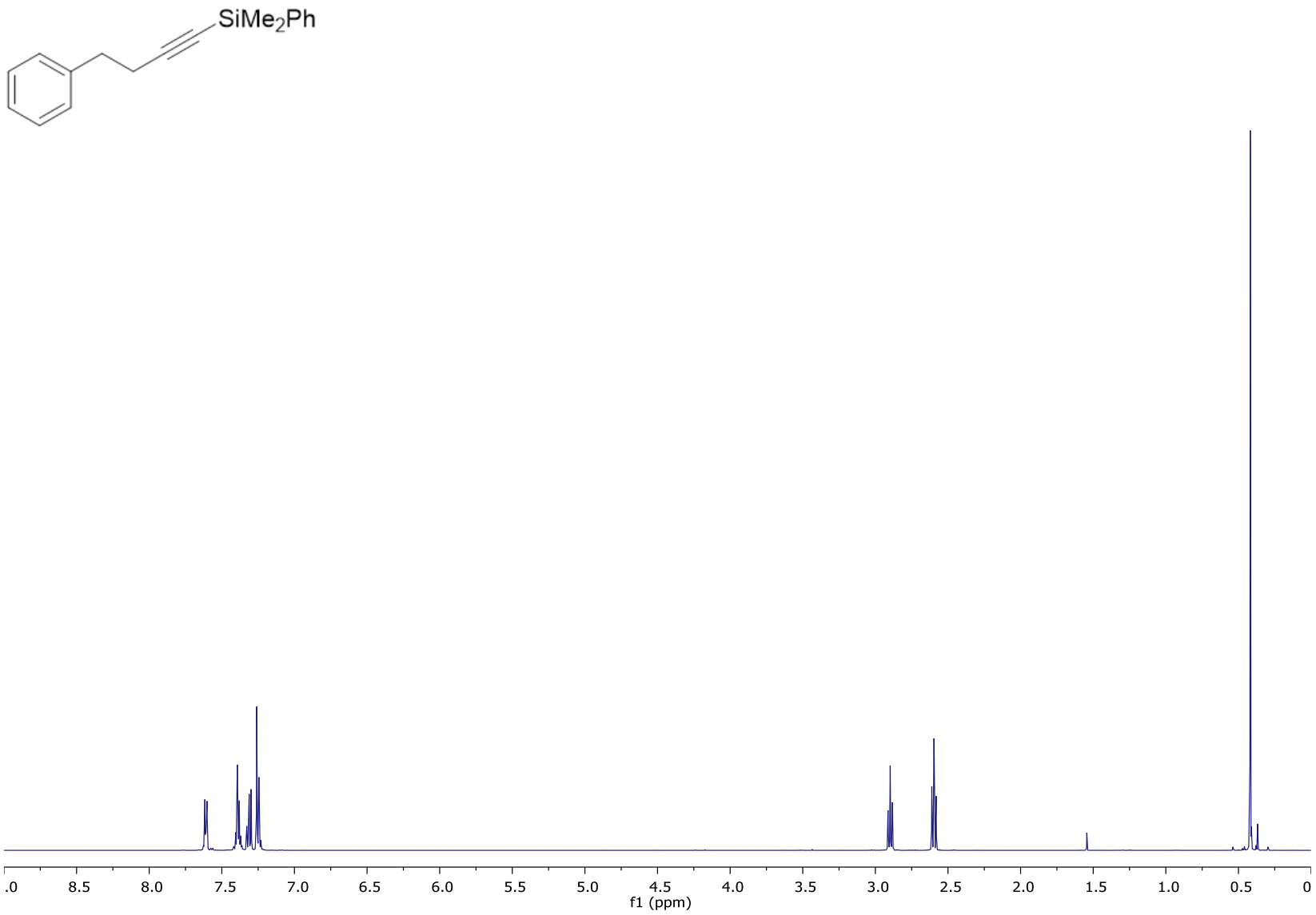
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42r.**



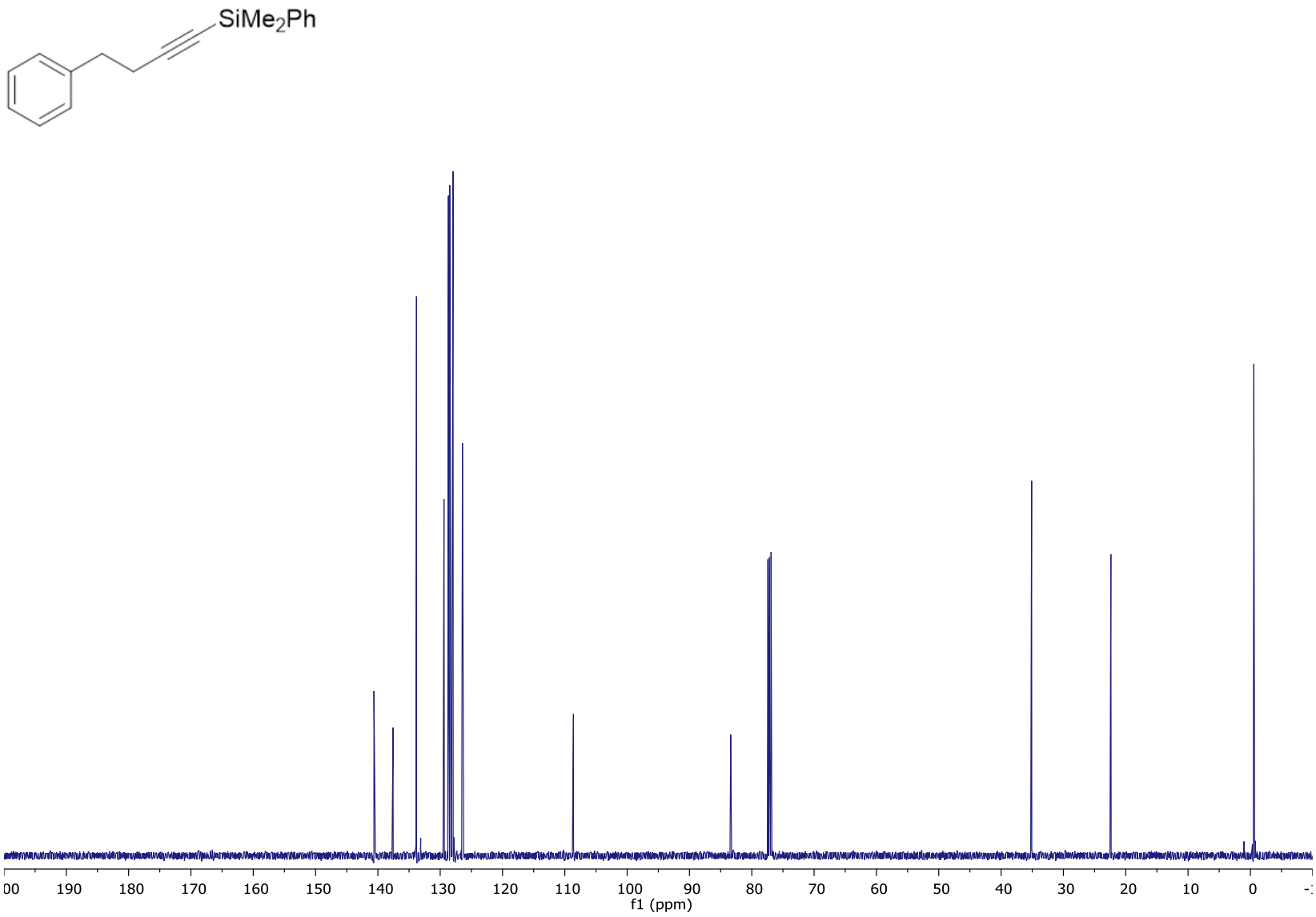
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42s.**



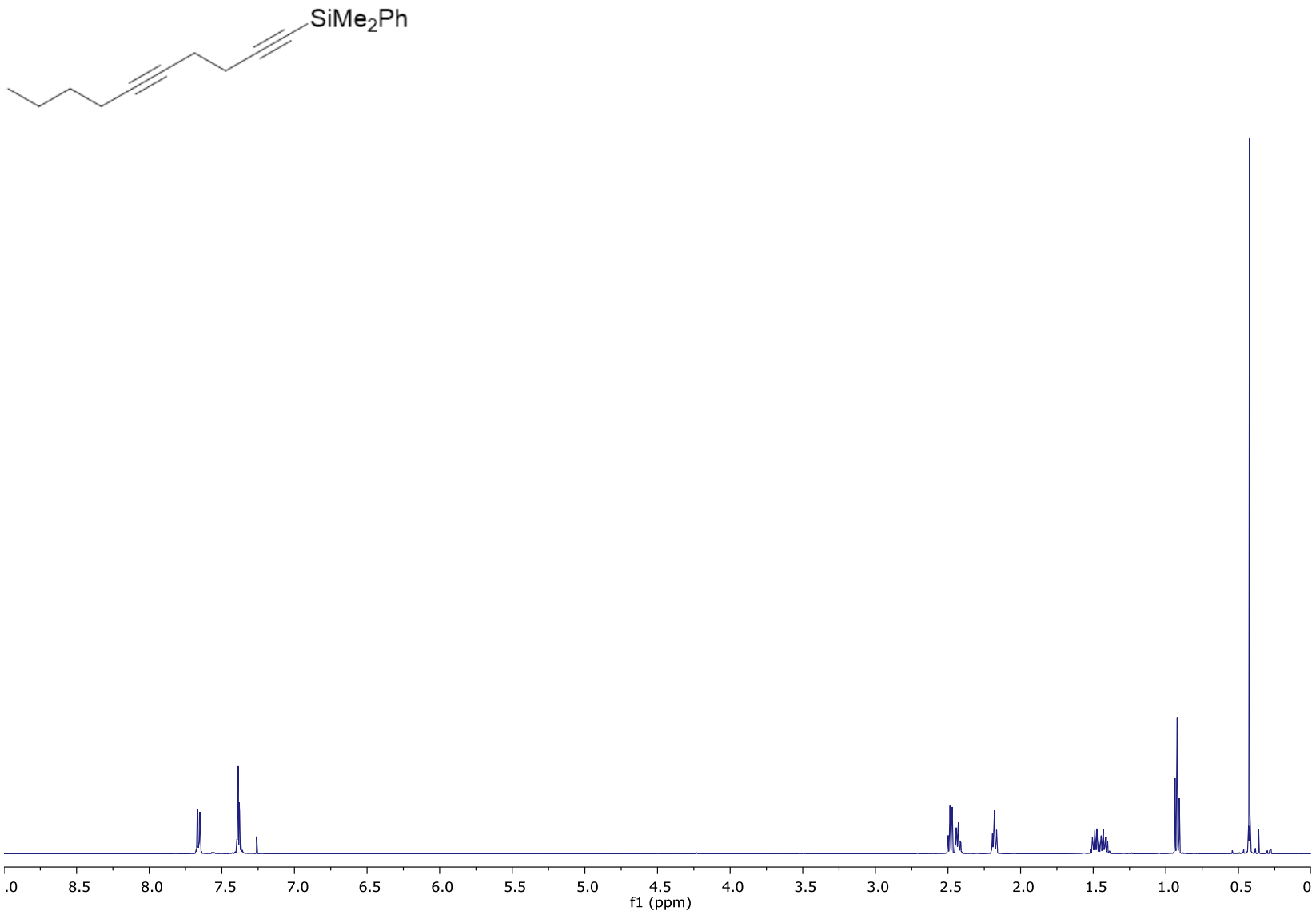
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42s.**



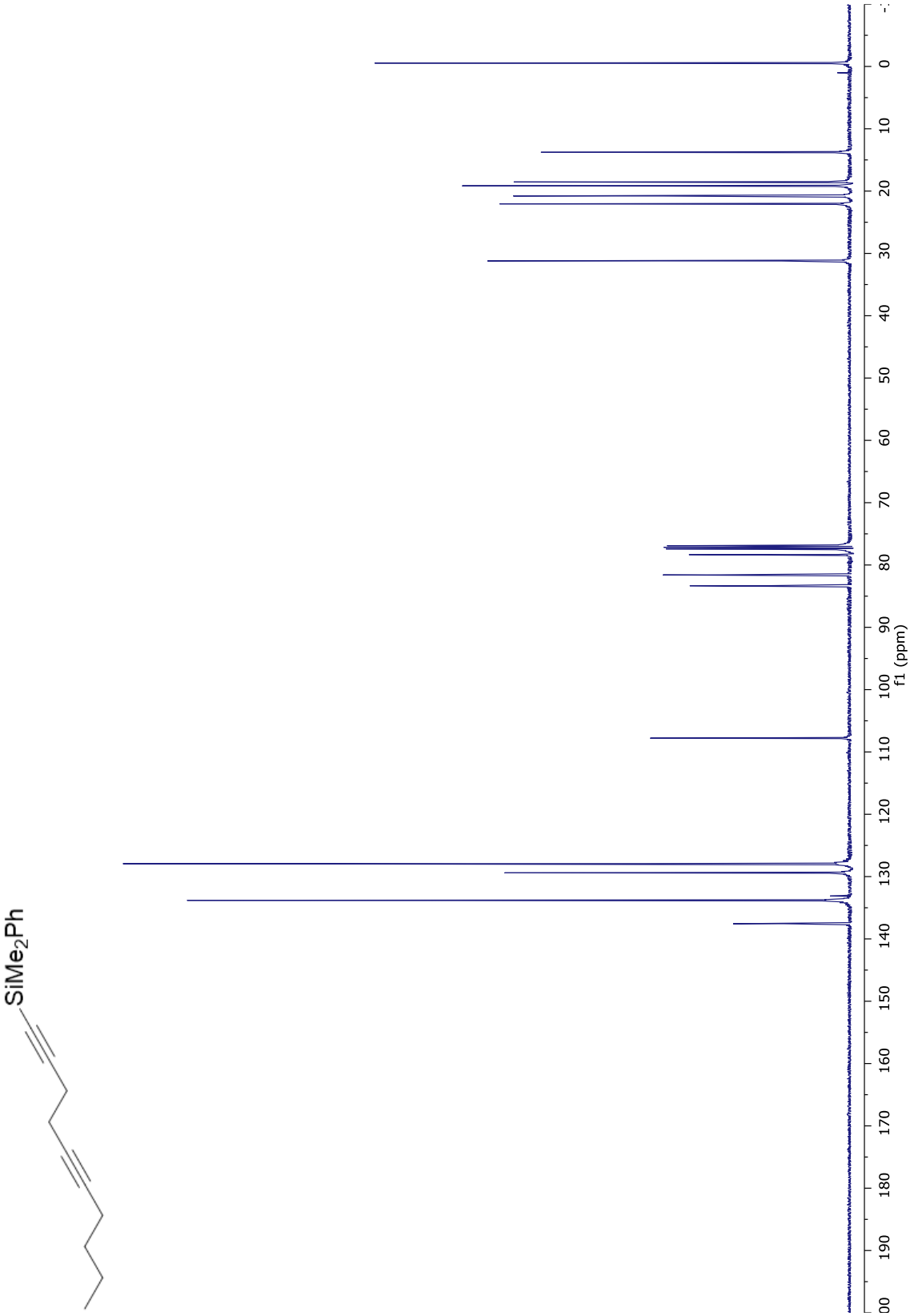
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42t.**



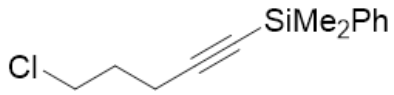
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42t.**

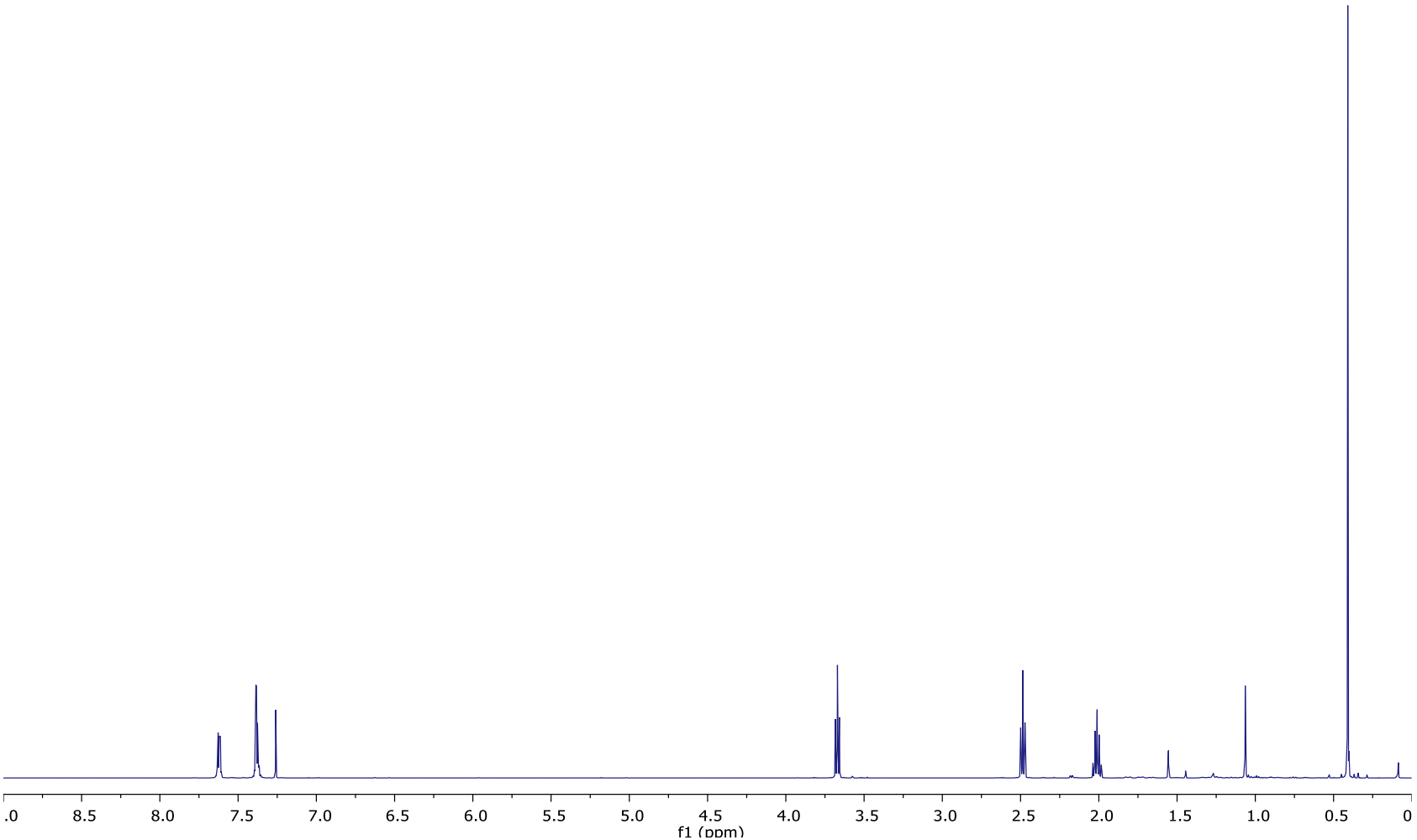


^{1}H NMR (500 MHz, $CDCl_3$) of compound **42u.**

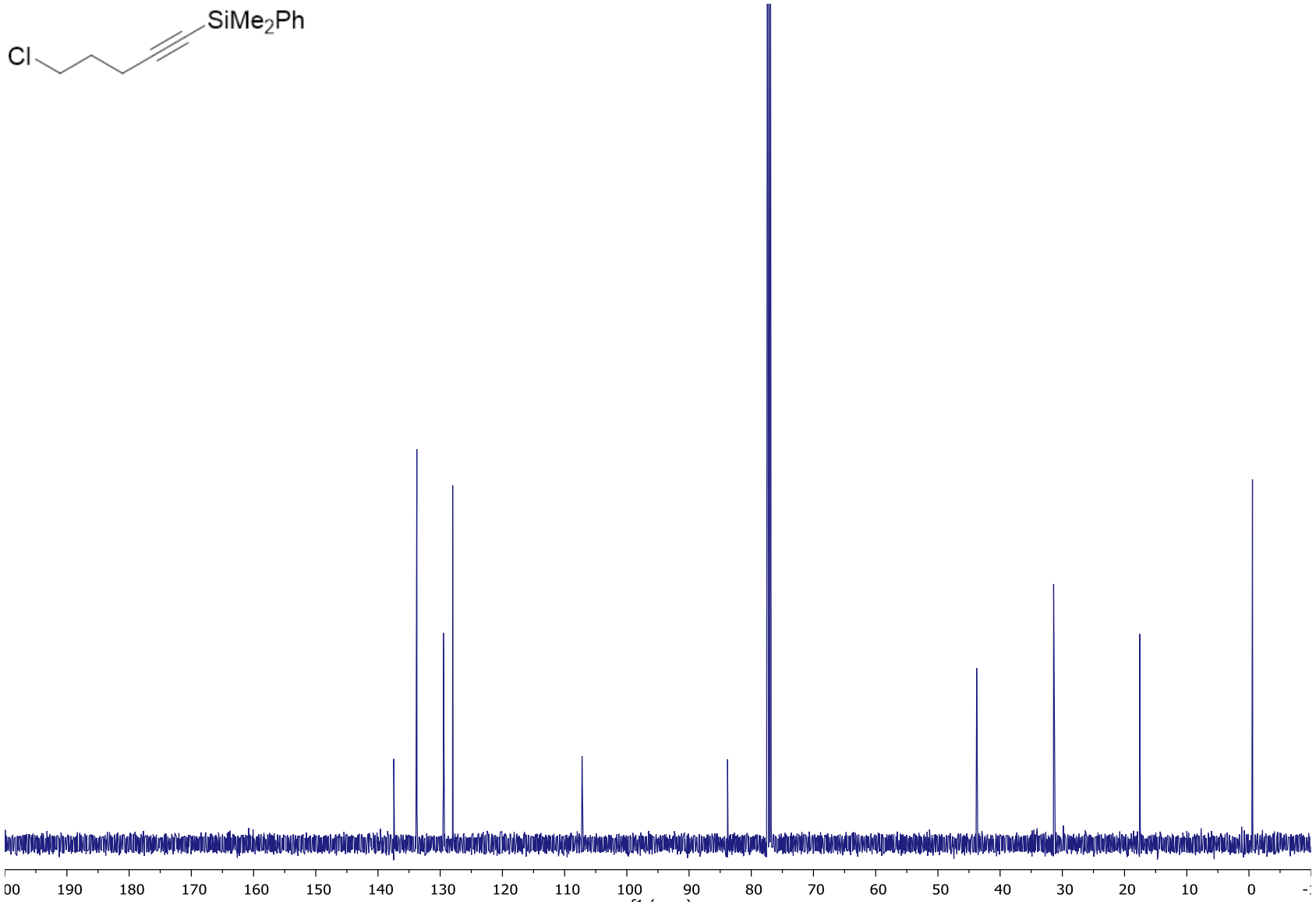


^{13}C NMR (126 MHz, $CDCl_3$) of compound **42u.**

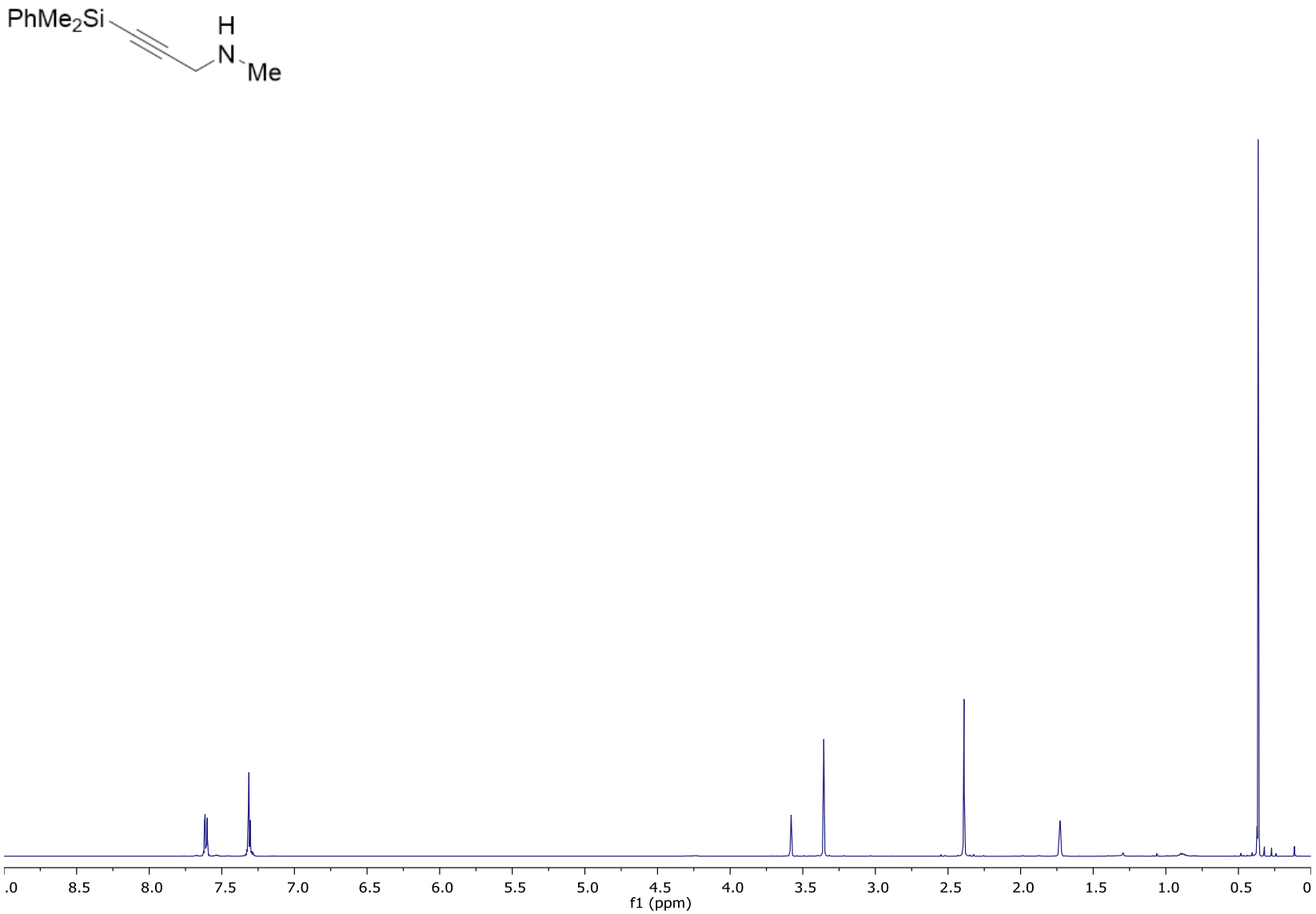




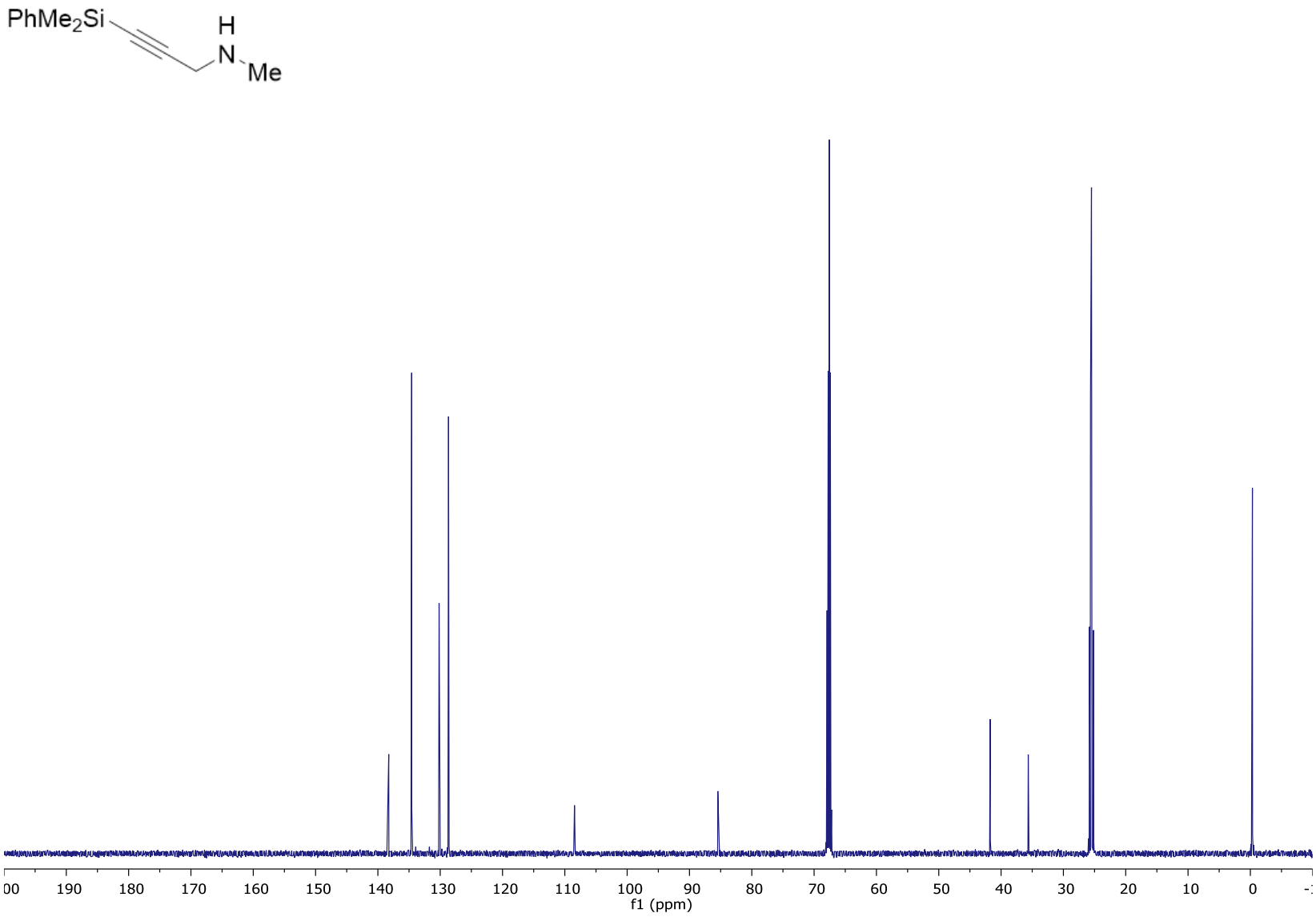
^{1}H NMR (500 MHz, $CDCl_3$) of compound **42v.**



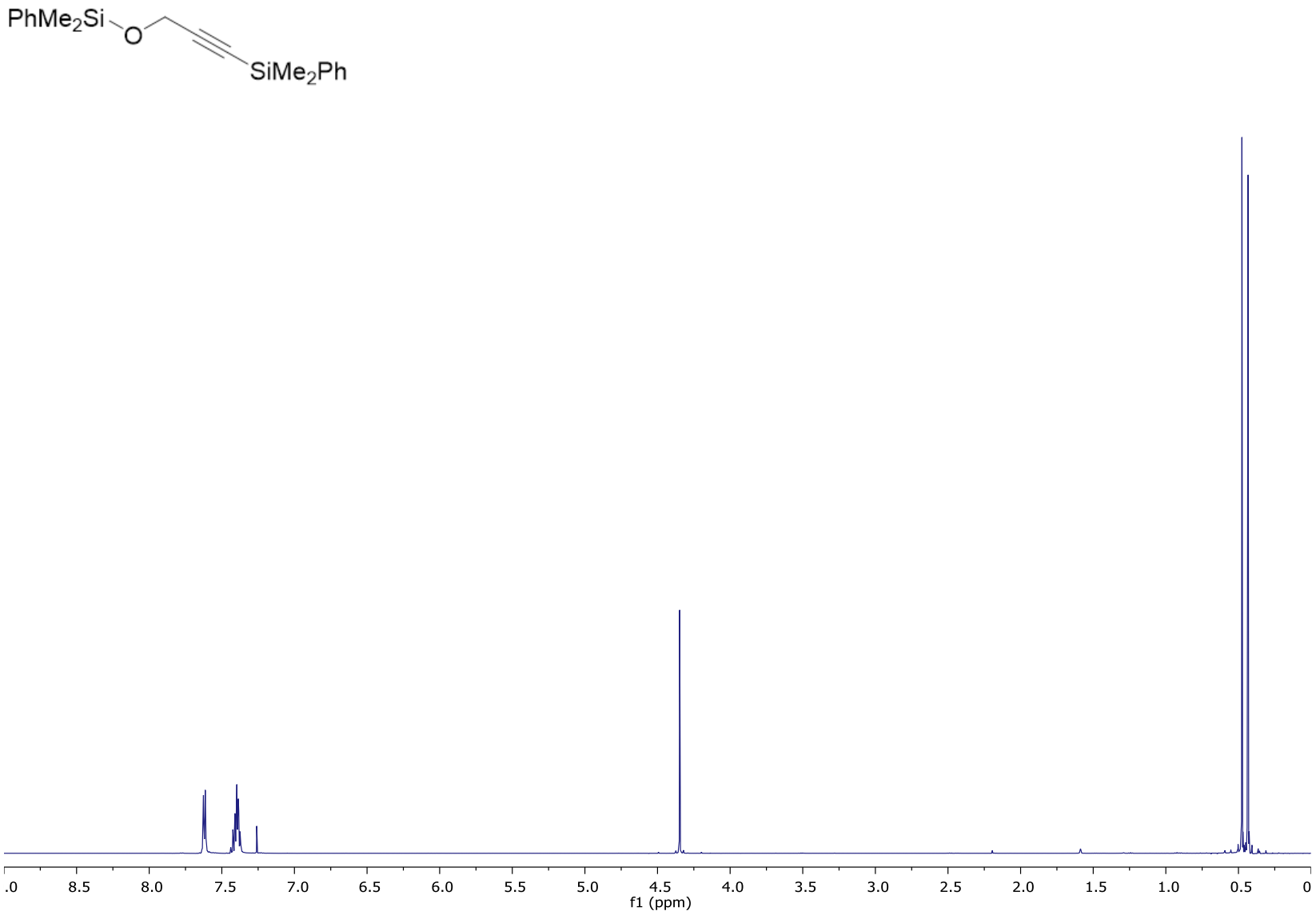
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42v.**



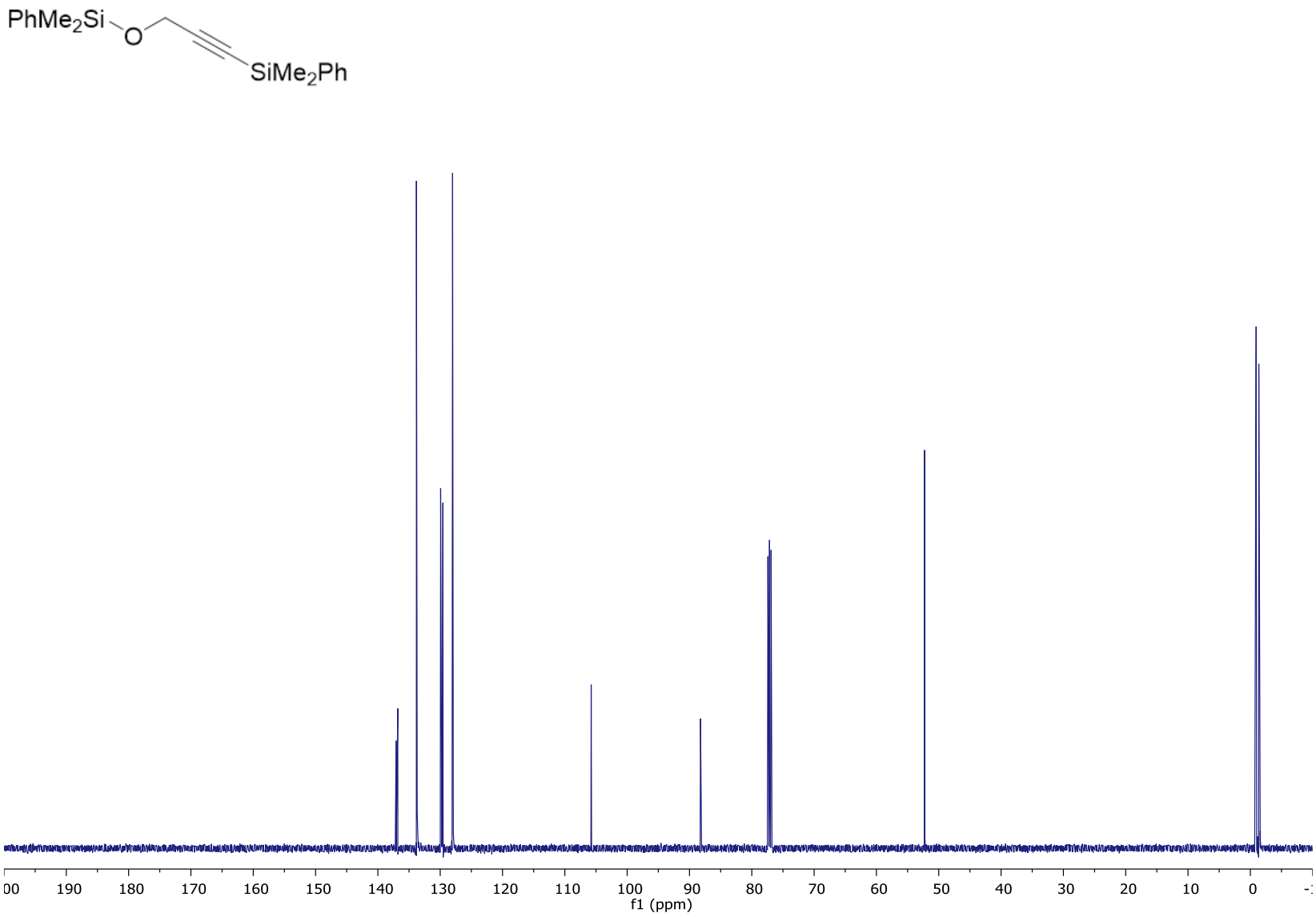
^{1}H NMR (500 MHz, THF-d_8) of compound **42w.**



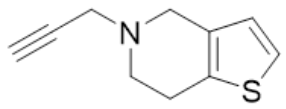
^{13}C NMR (126 MHz, THF-d_8) of compound **42w.**

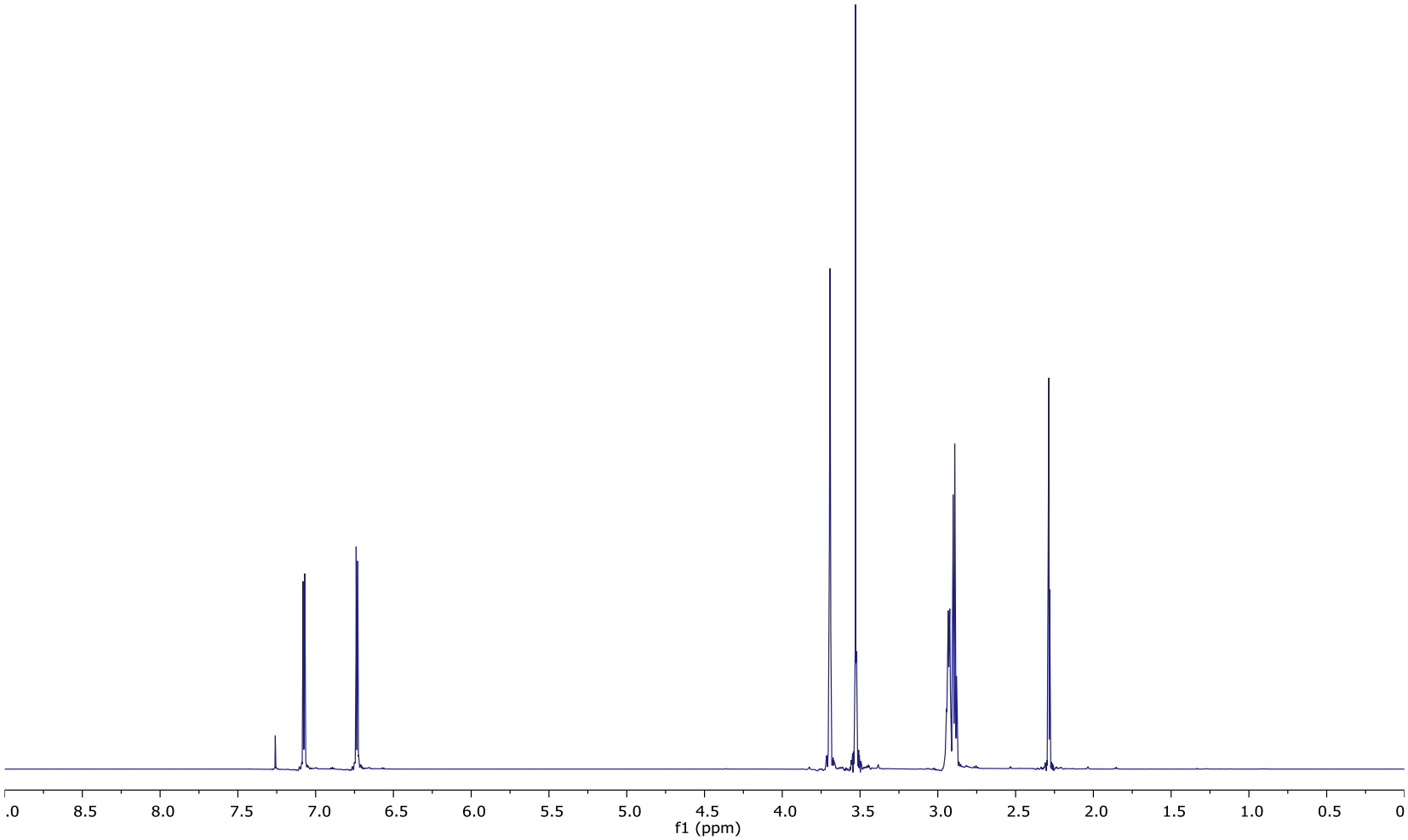


^{1}H NMR (500 MHz, $CDCl_3$) of compound **42x.**

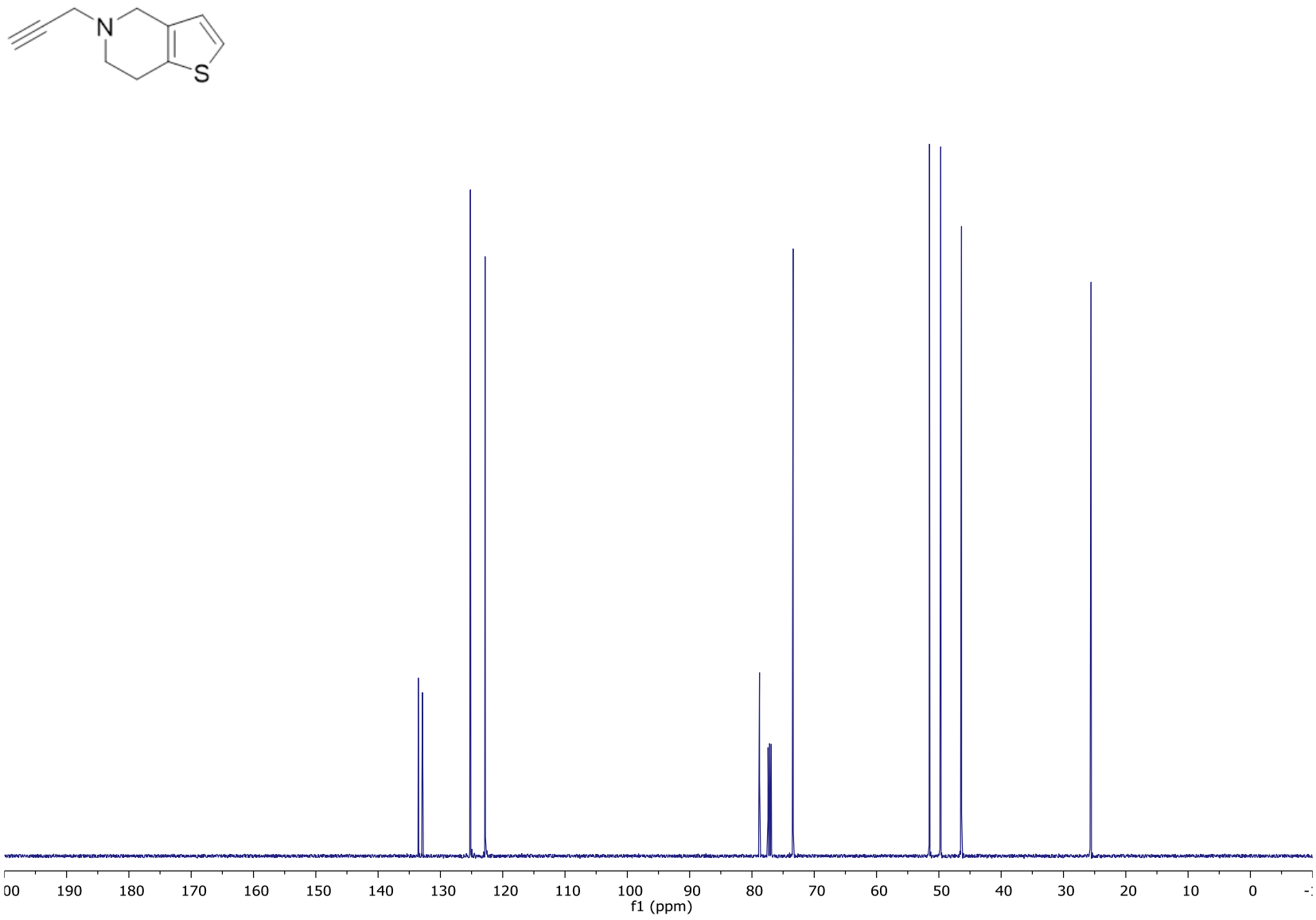


^{13}C NMR (126 MHz, $CDCl_3$) of compound **42x.**

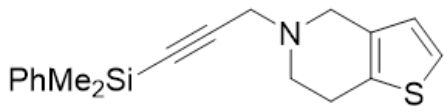


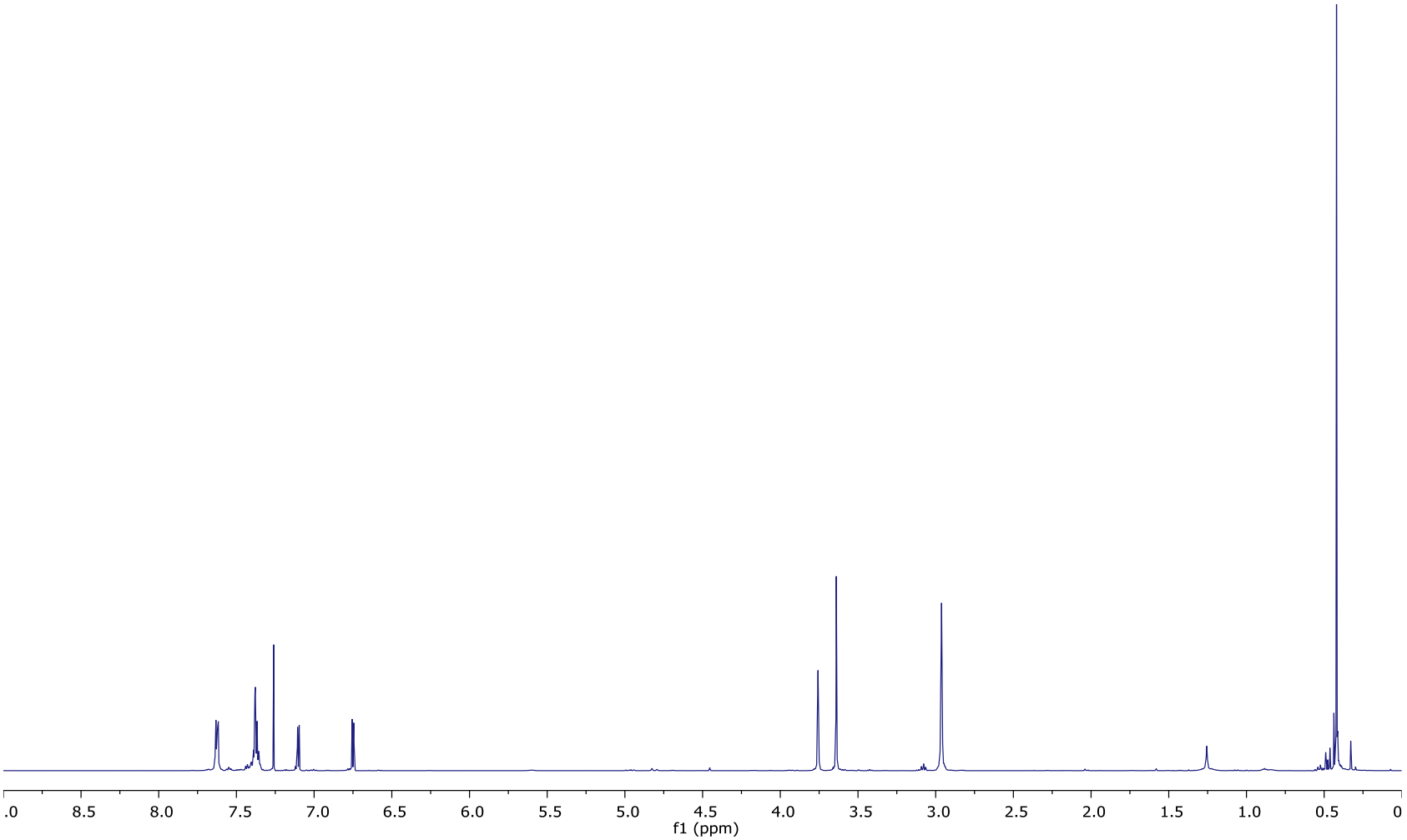


^{1}H NMR (500 MHz, $CDCl_3$) of compound **41y.**

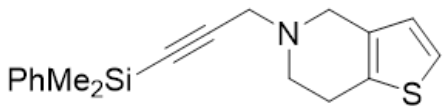


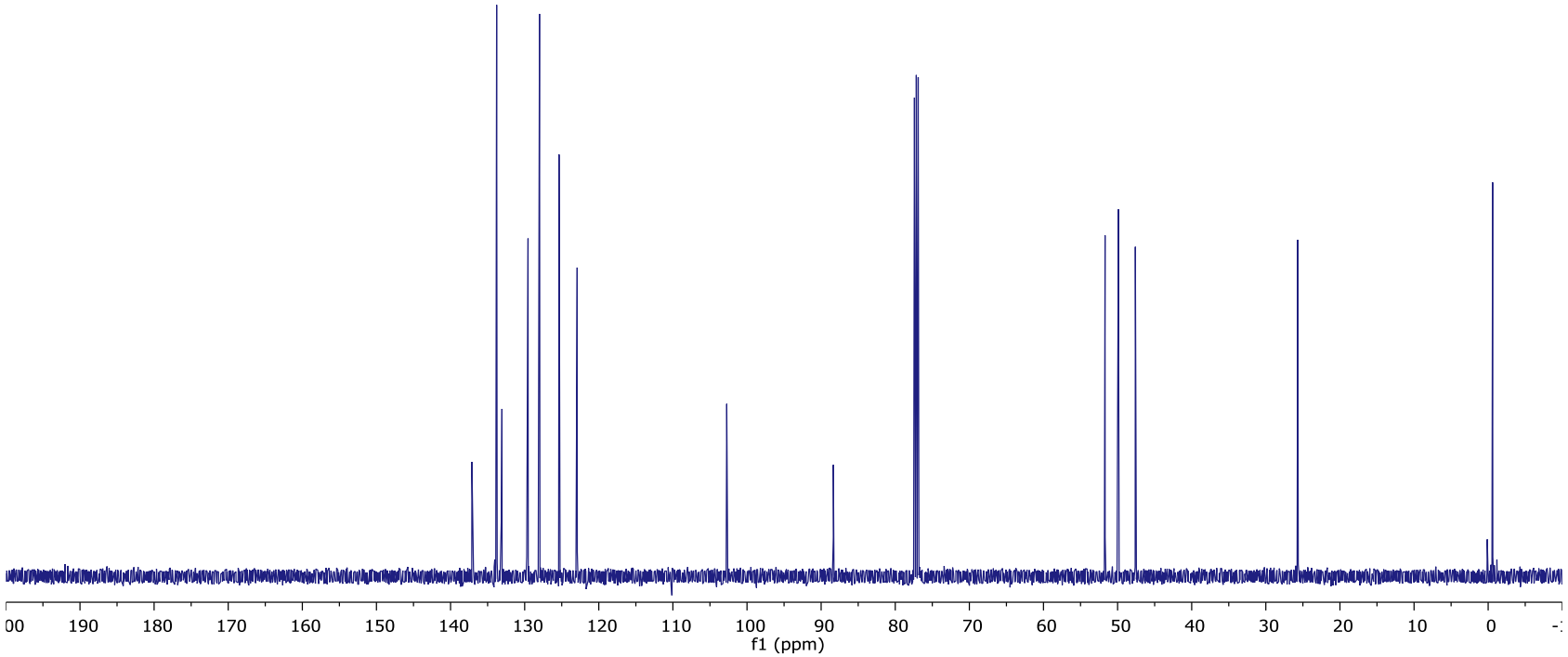
^{13}C NMR (126 MHz, $CDCl_3$) of compound **41y.**



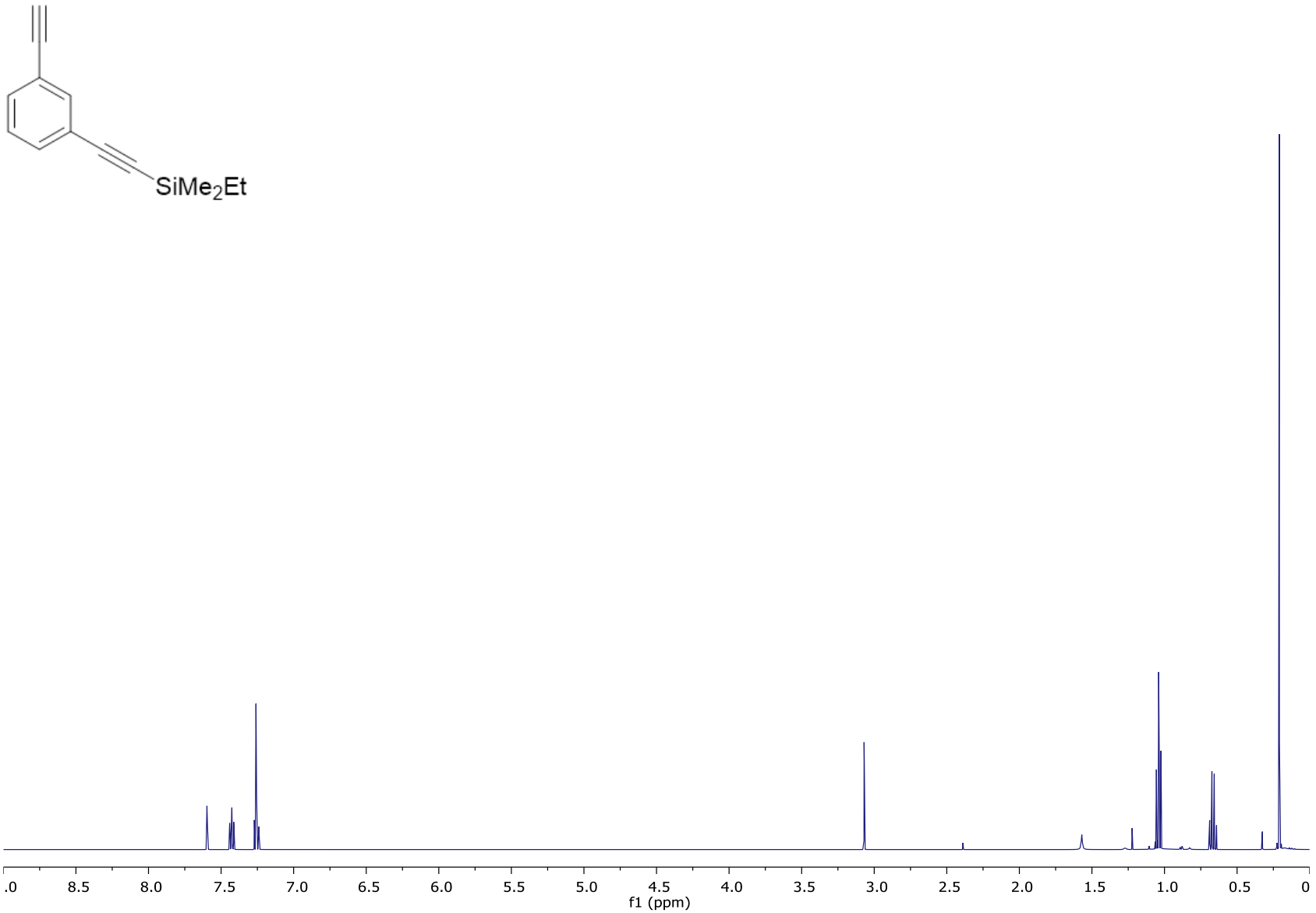


^{1}H NMR (500 MHz, $CDCl_3$) of compound **42y.**

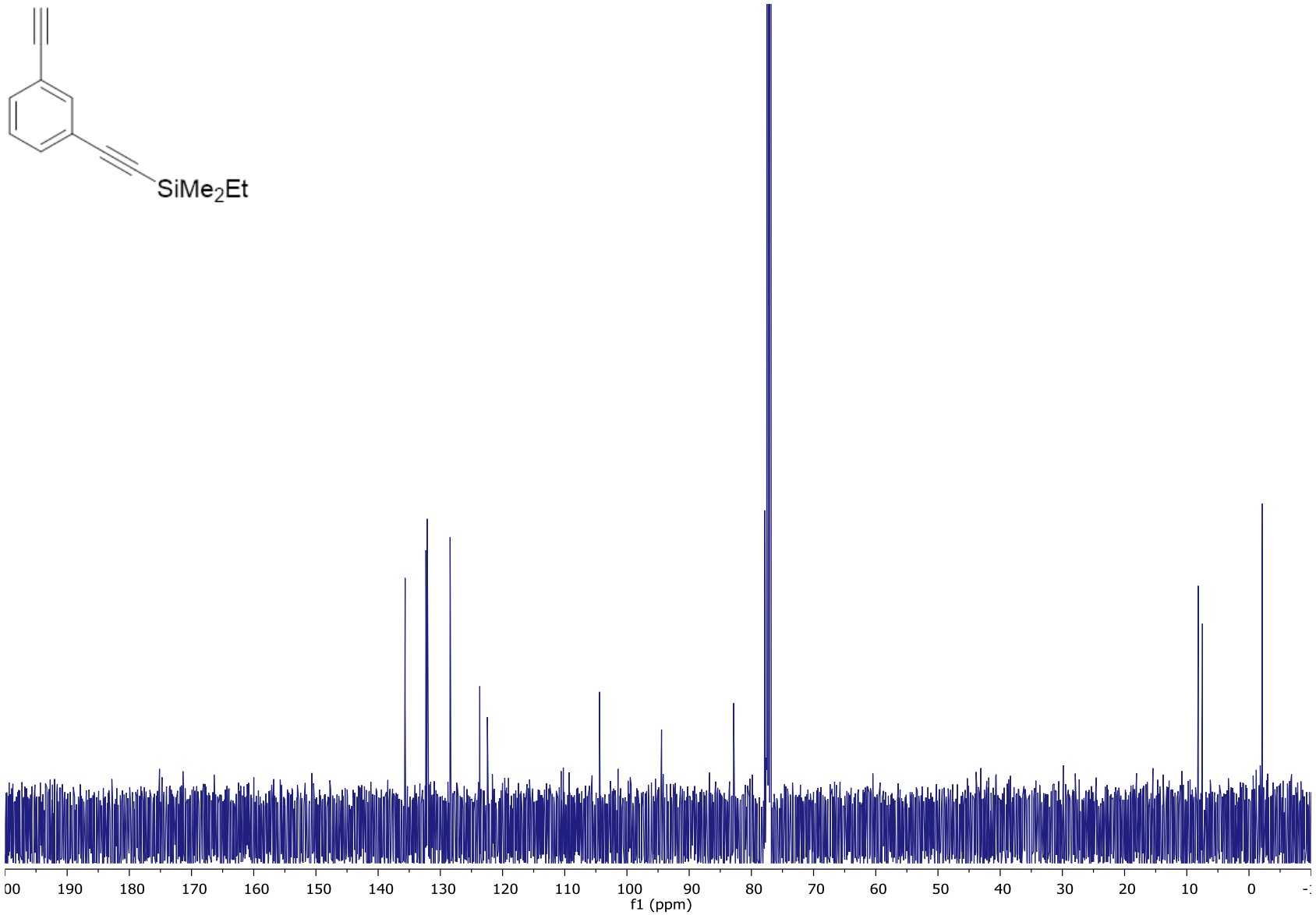




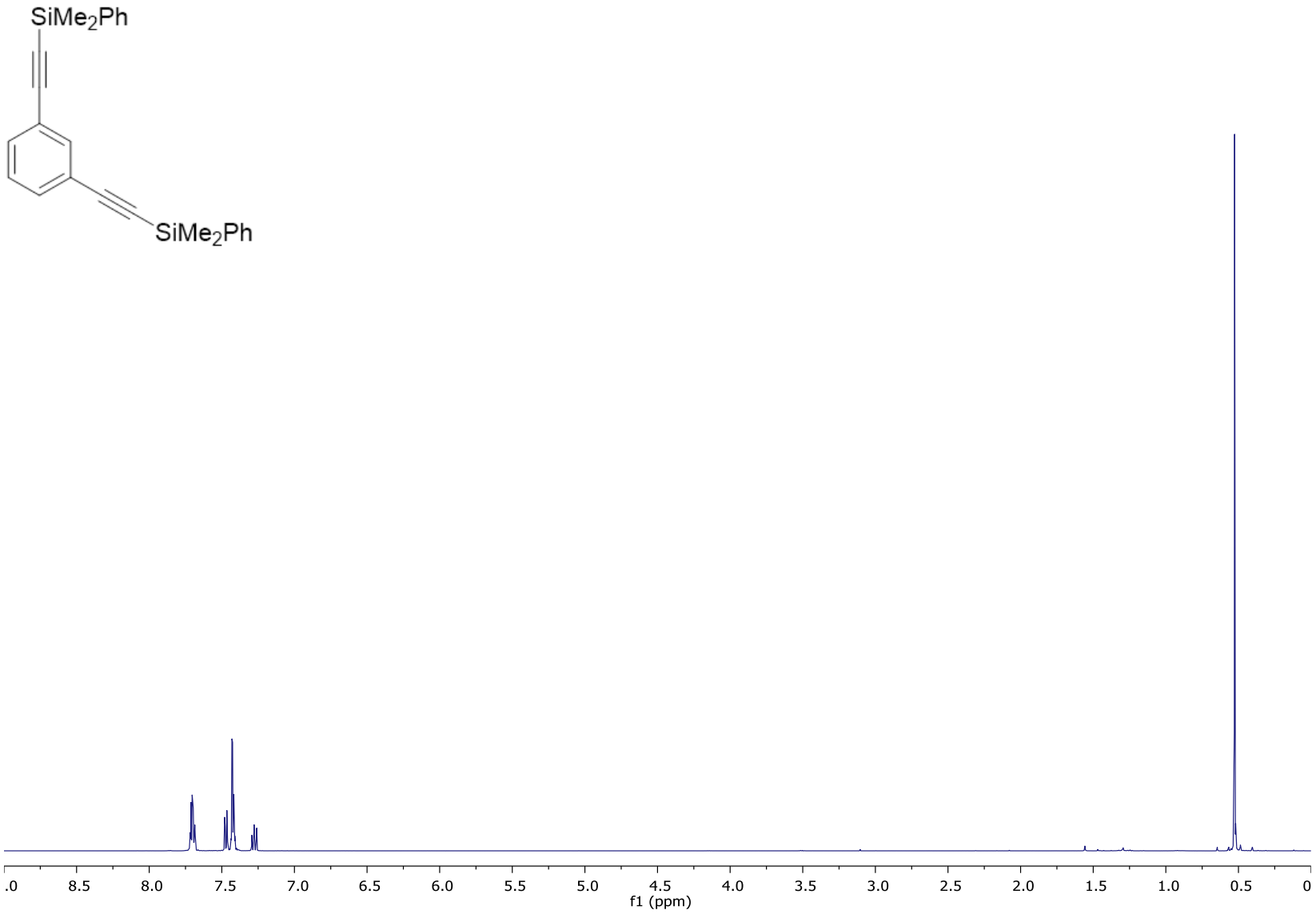
^{13}C NMR (126 MHz, $CDCl_3$) of compound **42y.**



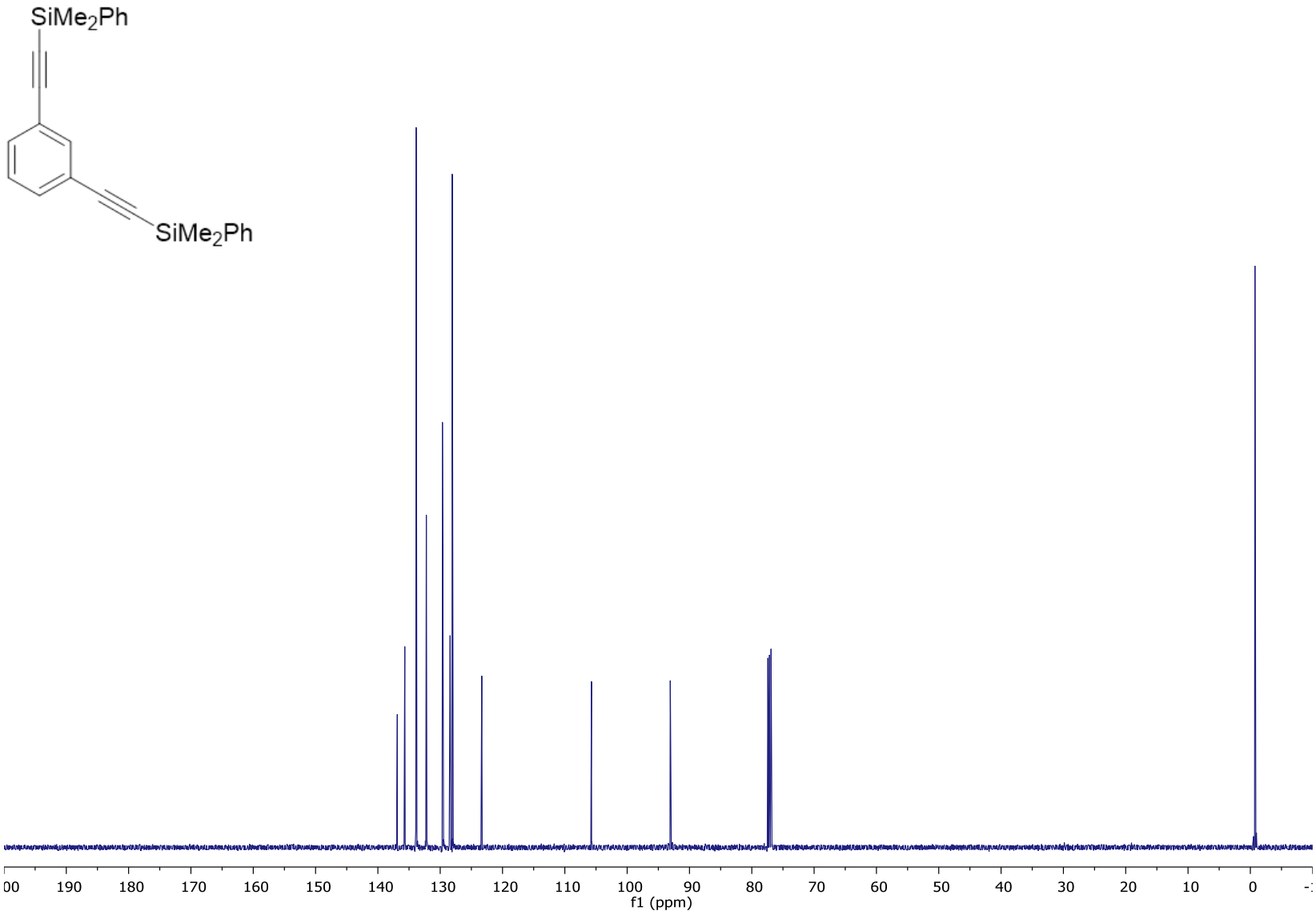
^{1}H NMR (500 MHz, $CDCl_3$) of compound **43a.**



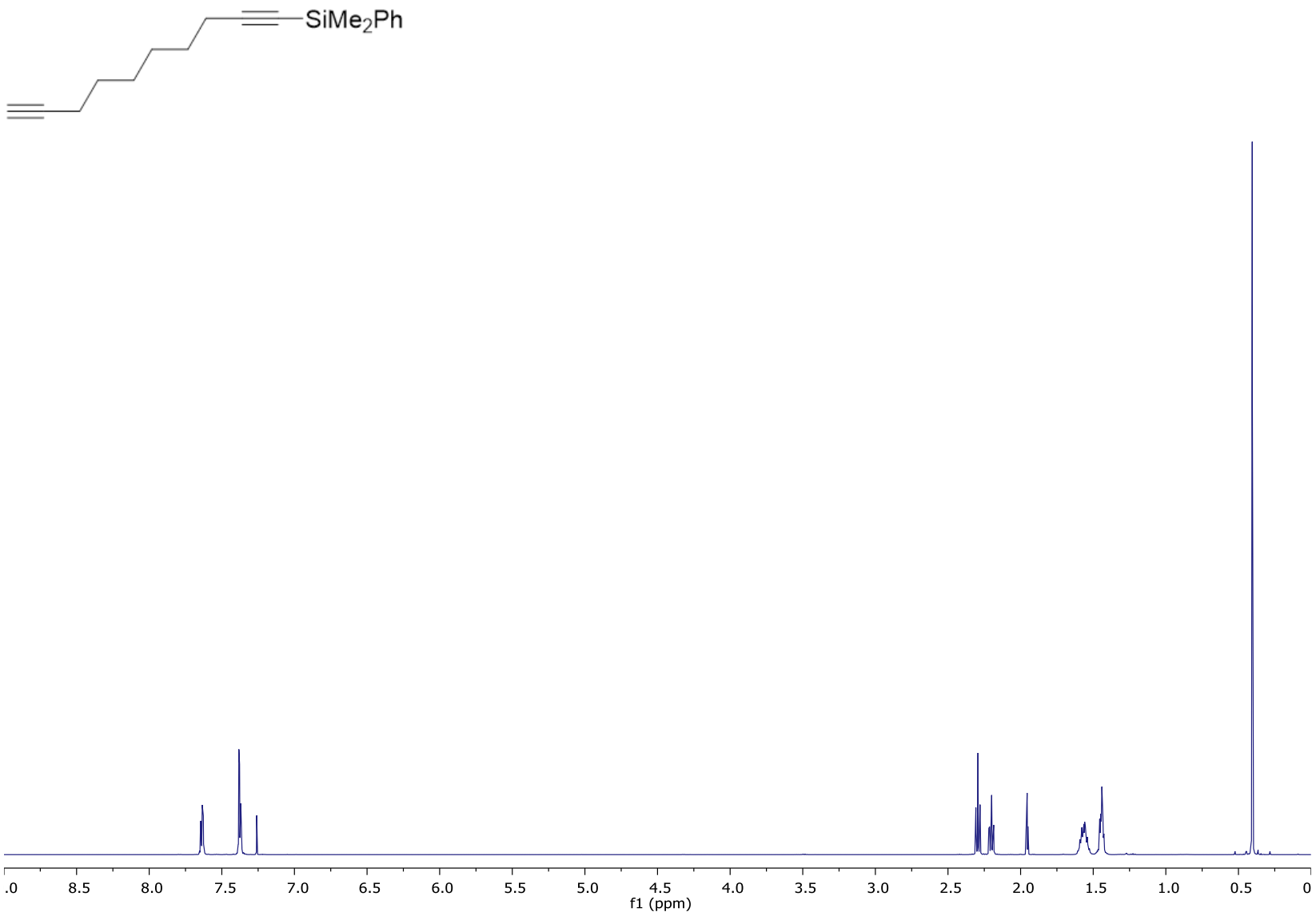
^{13}C NMR (126 MHz, $CDCl_3$) of compound **43a.**



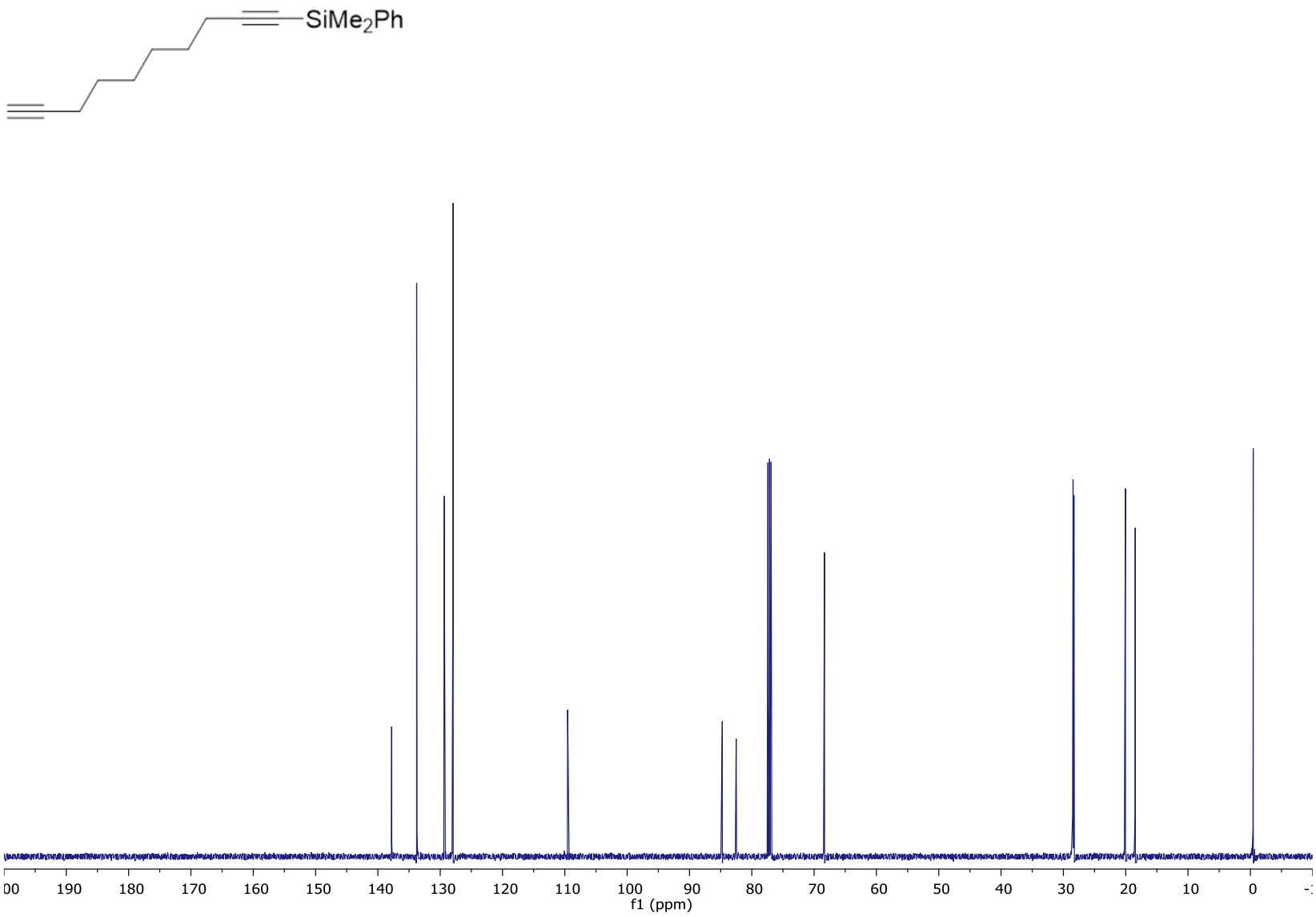
^{1}H NMR (500 MHz, $CDCl_3$) of compound **43b.**



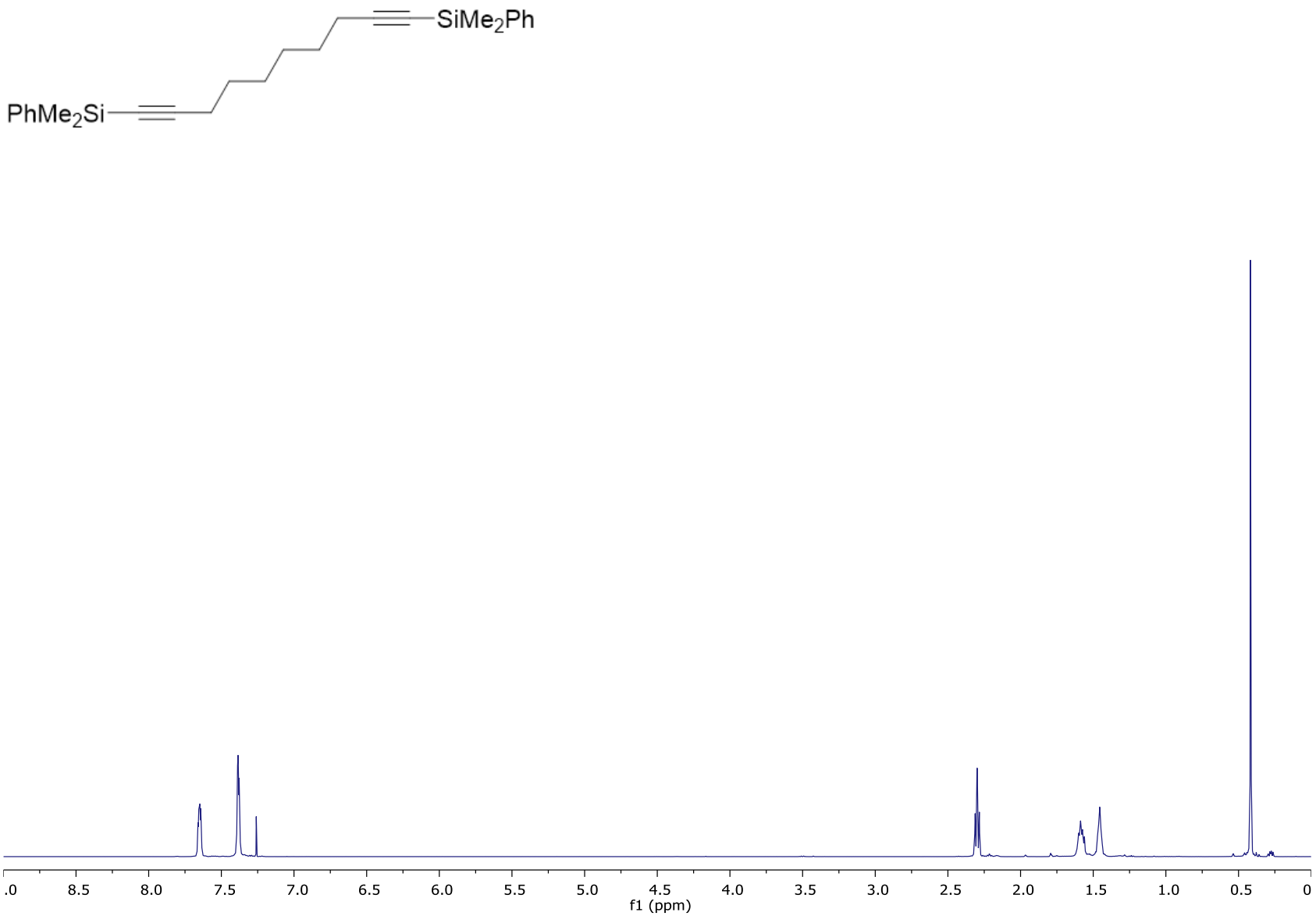
^{13}C NMR (126 MHz, $CDCl_3$) of compound **43b.**



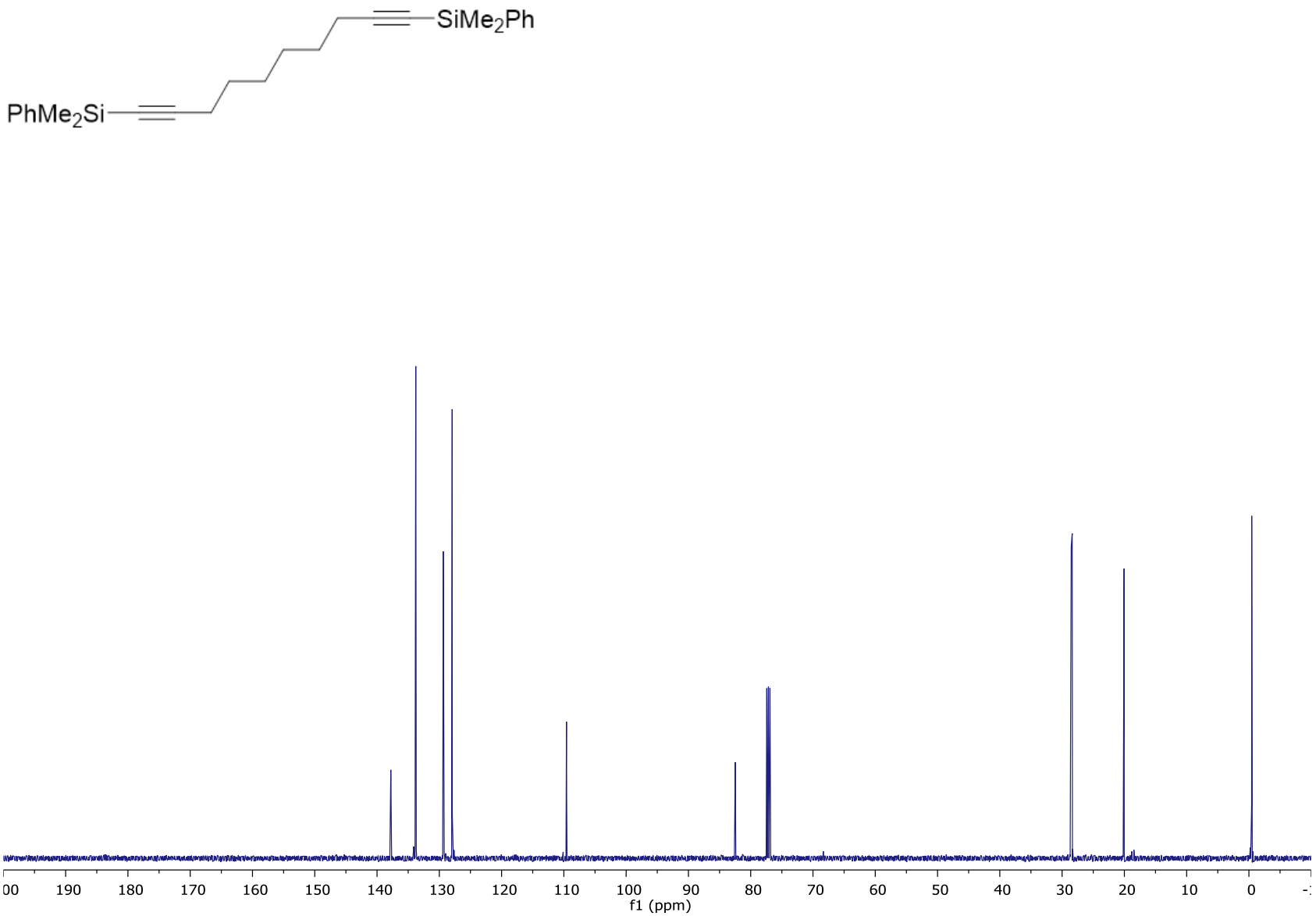
^{1}H NMR (500 MHz, $CDCl_3$) of compound **44a.**



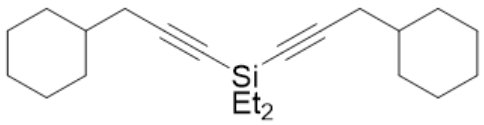
^{13}C NMR (126 MHz, $CDCl_3$) of compound 44**a.**

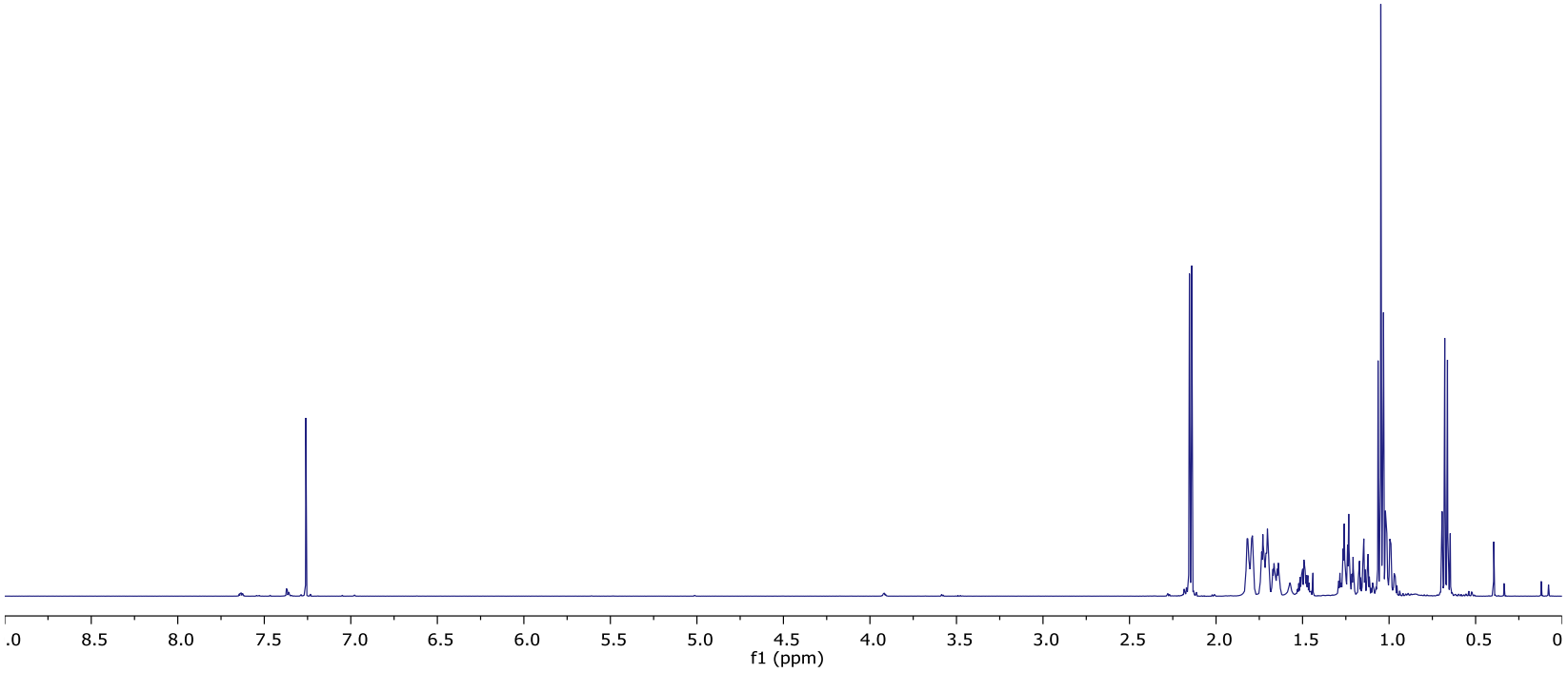


^{1}H NMR (500 MHz, $CDCl_3$) of compound **44b.**

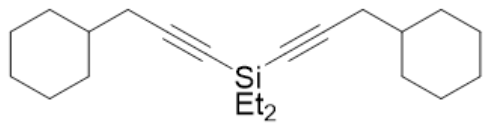


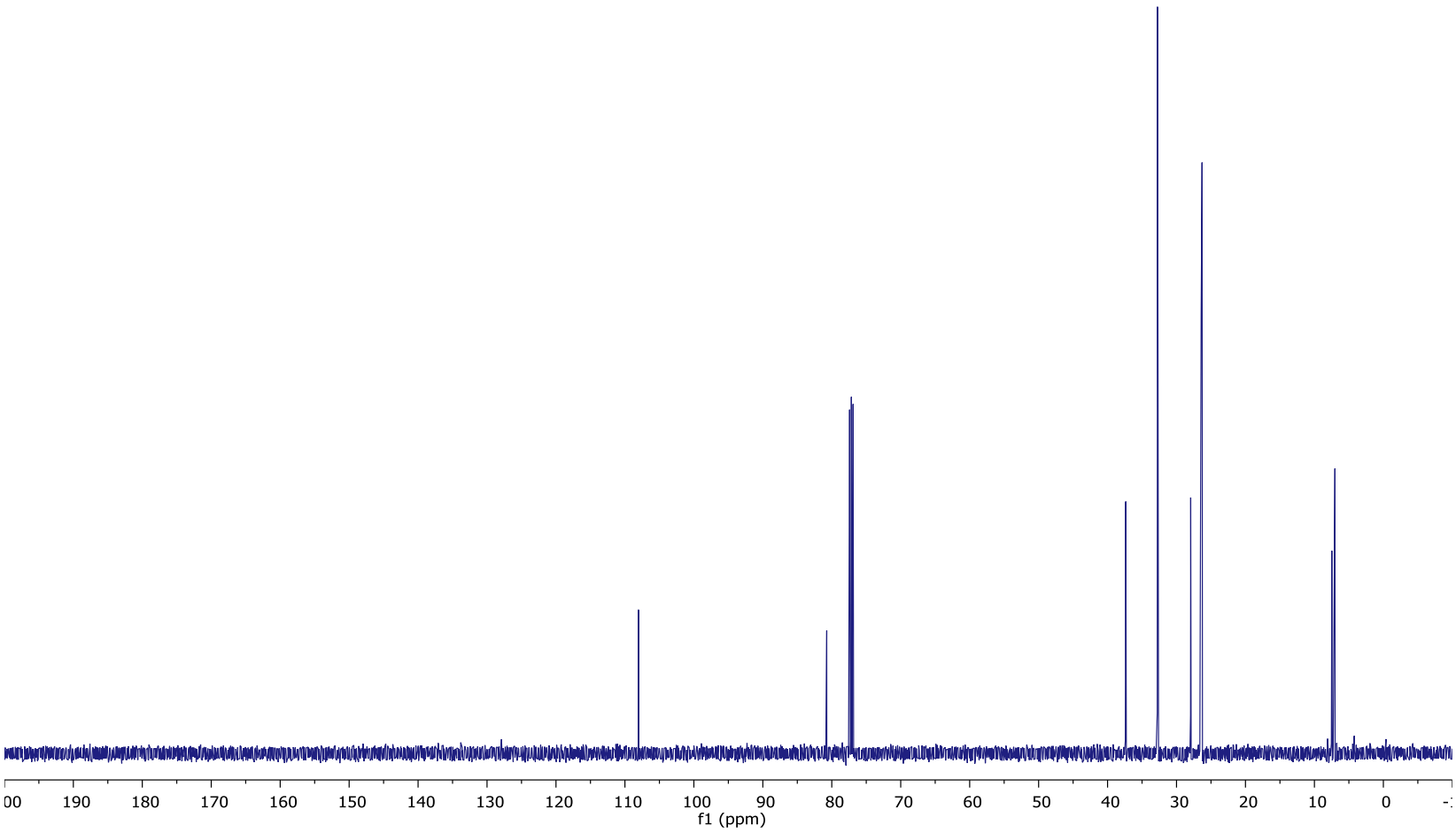
^{13}C NMR (126 MHz, $CDCl_3$) of compound **6b.**



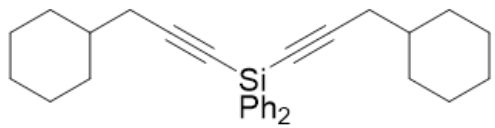


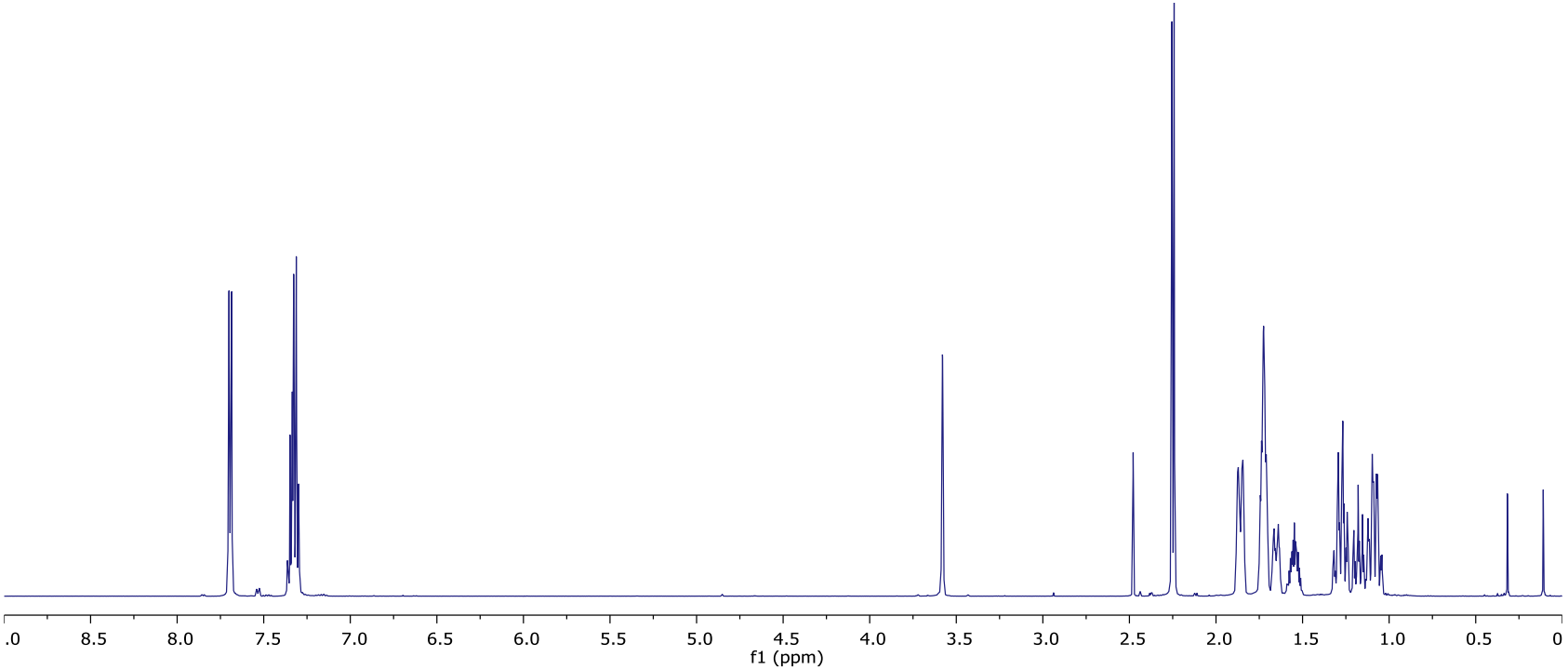
^{1}H NMR (500 MHz, $CDCl_3$) of compound **48a.**



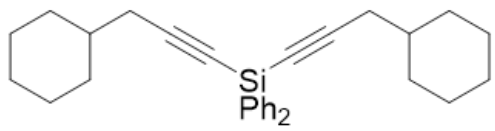


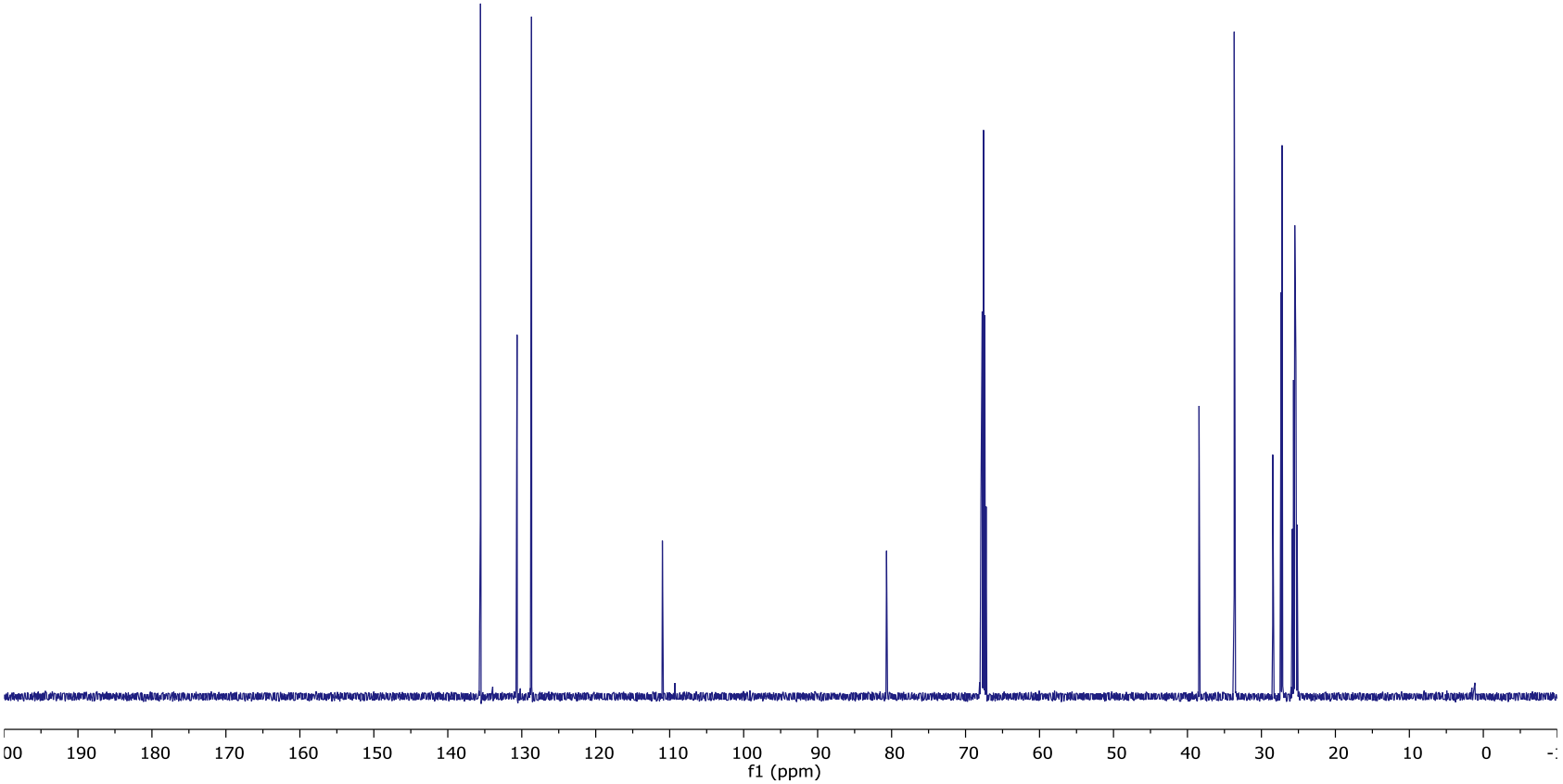
^{13}C NMR (126 MHz, $CDCl_3$) of compound **48a.**



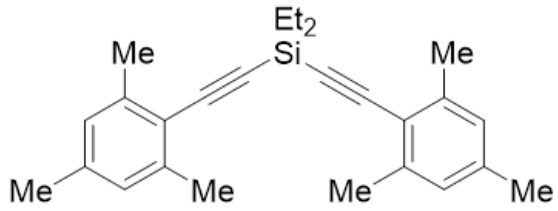


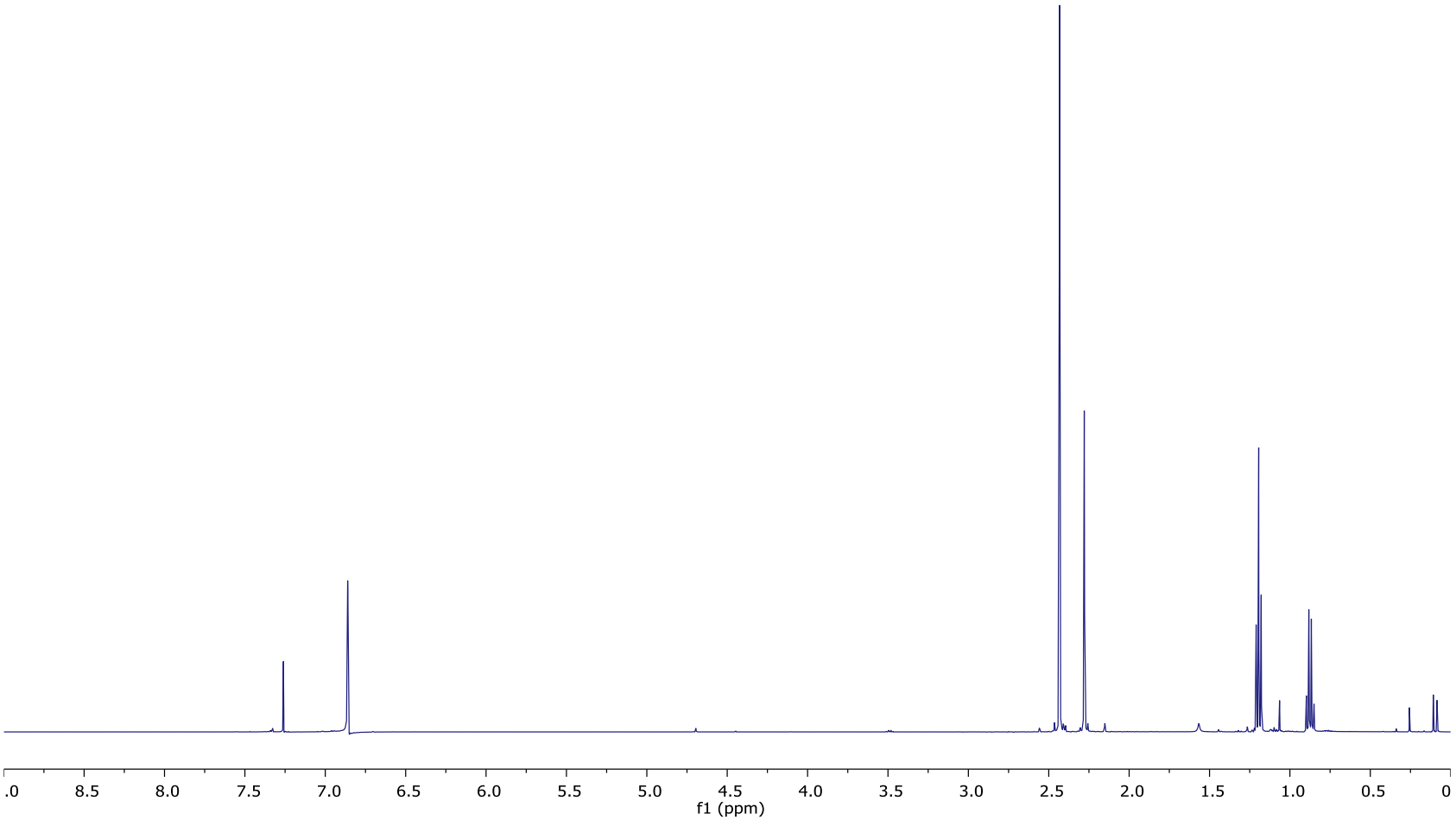
^{1}H NMR (500 MHz, THF-*d*$_{8}$) of compound **48b.**



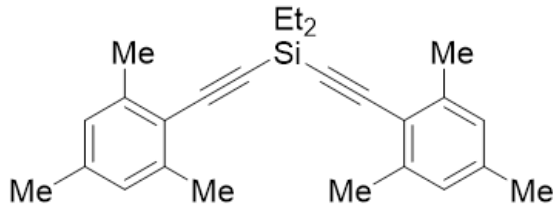


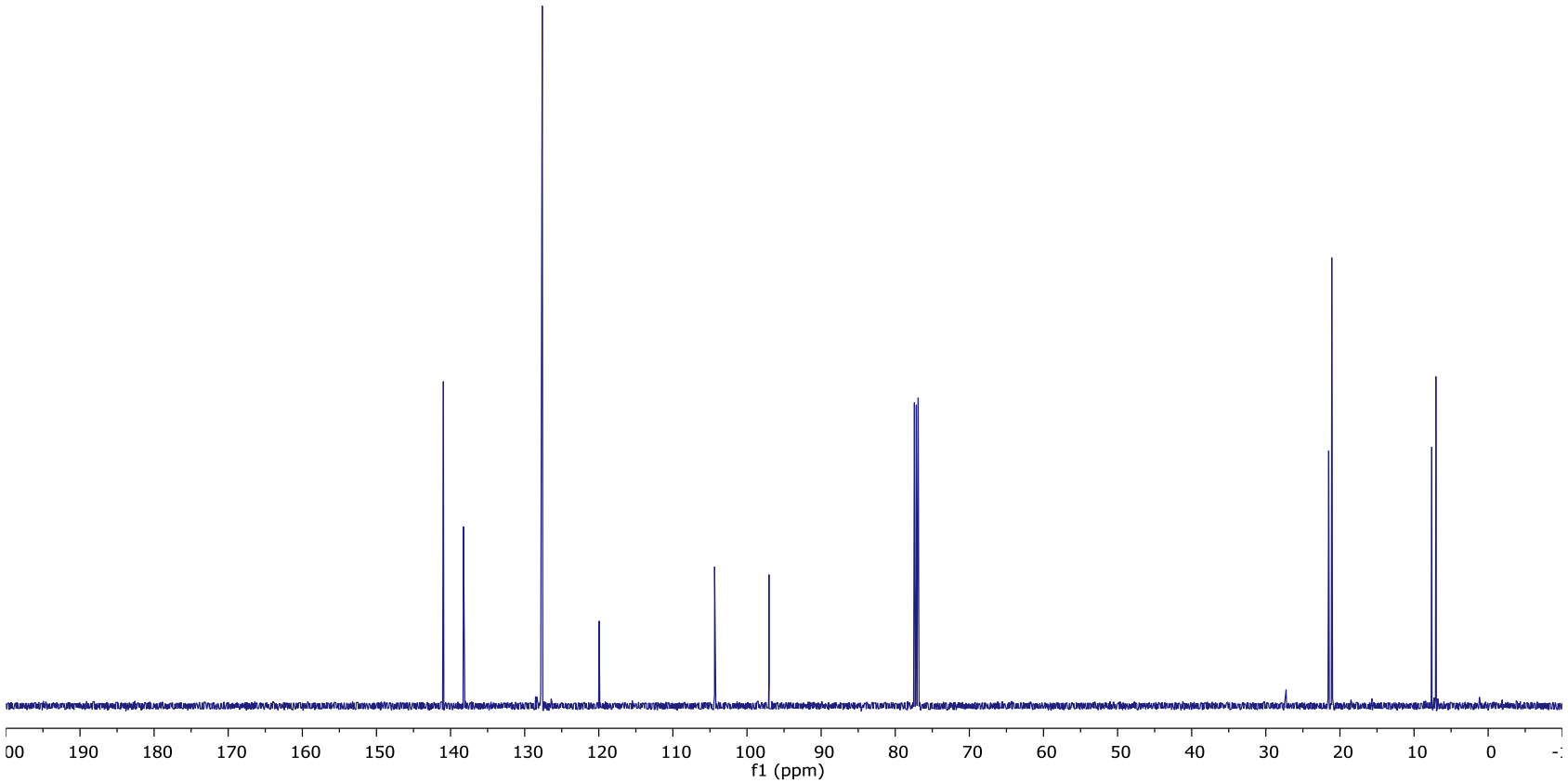
^{13}C NMR (126 MHz, THF-d_8) of compound **48b.**



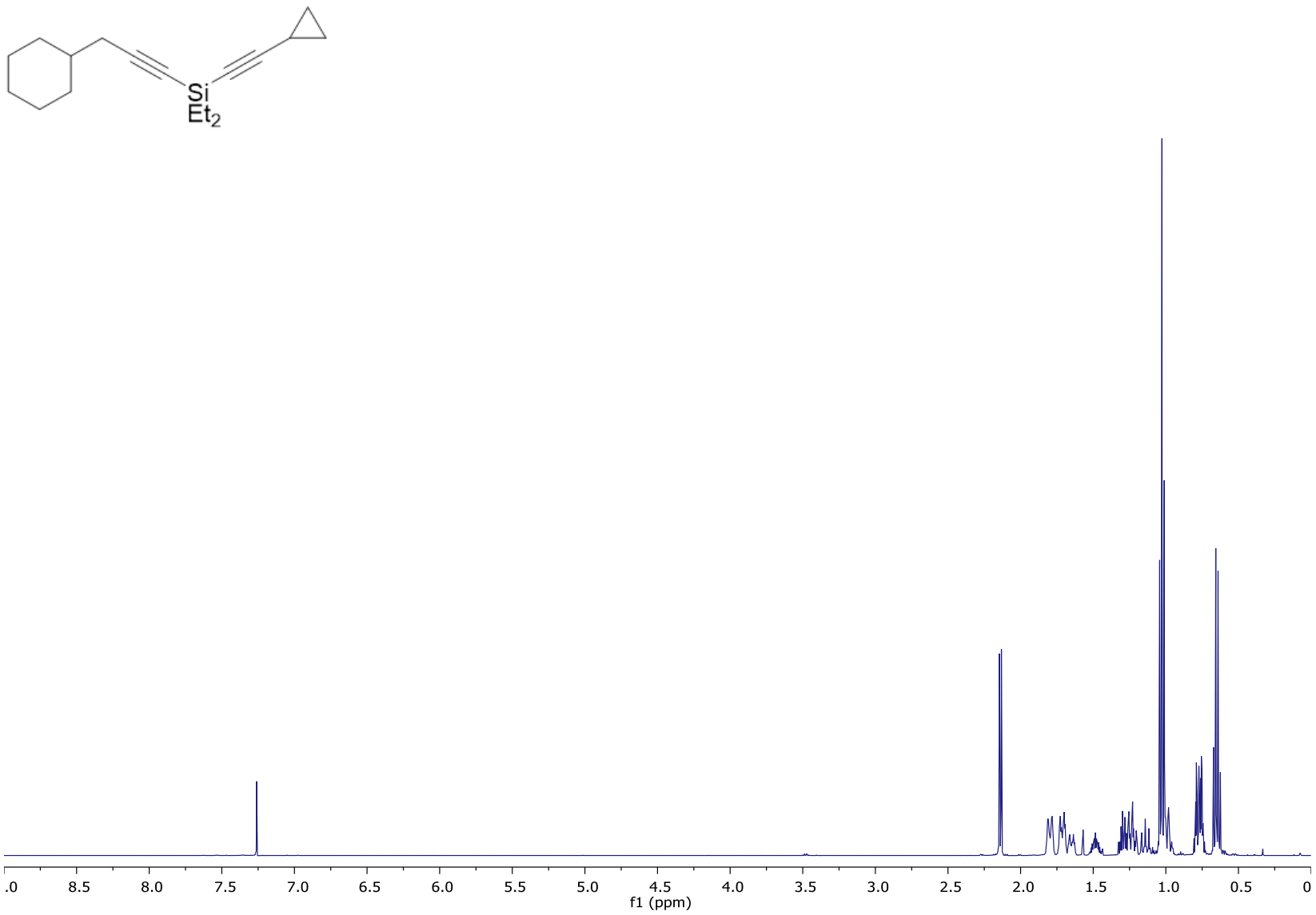


^{1}H NMR (500 MHz, $CDCl_3$) of compound **48c.**

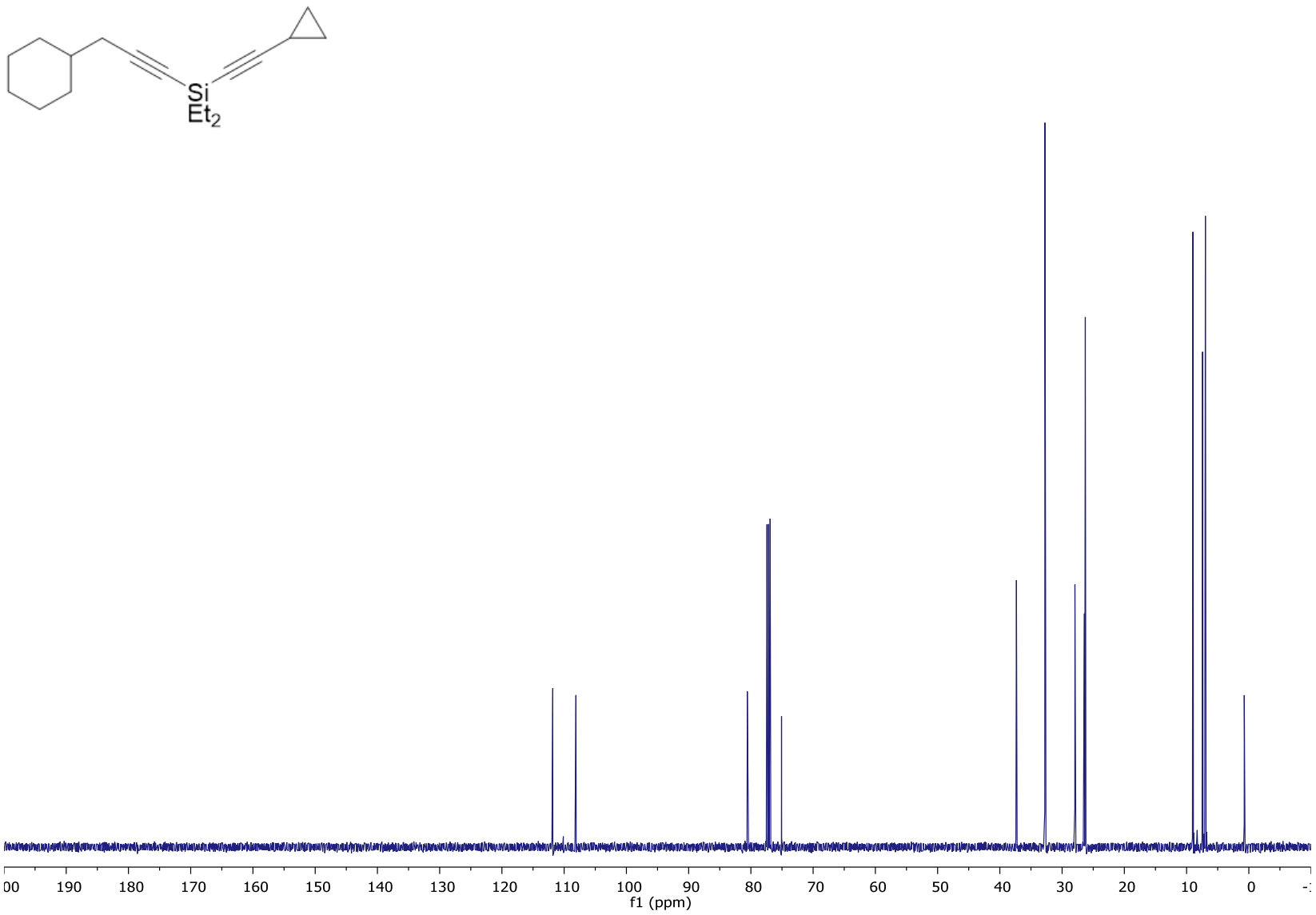




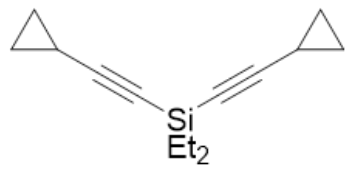
^{13}C NMR (126 MHz, $CDCl_3$) of compound **48c.**

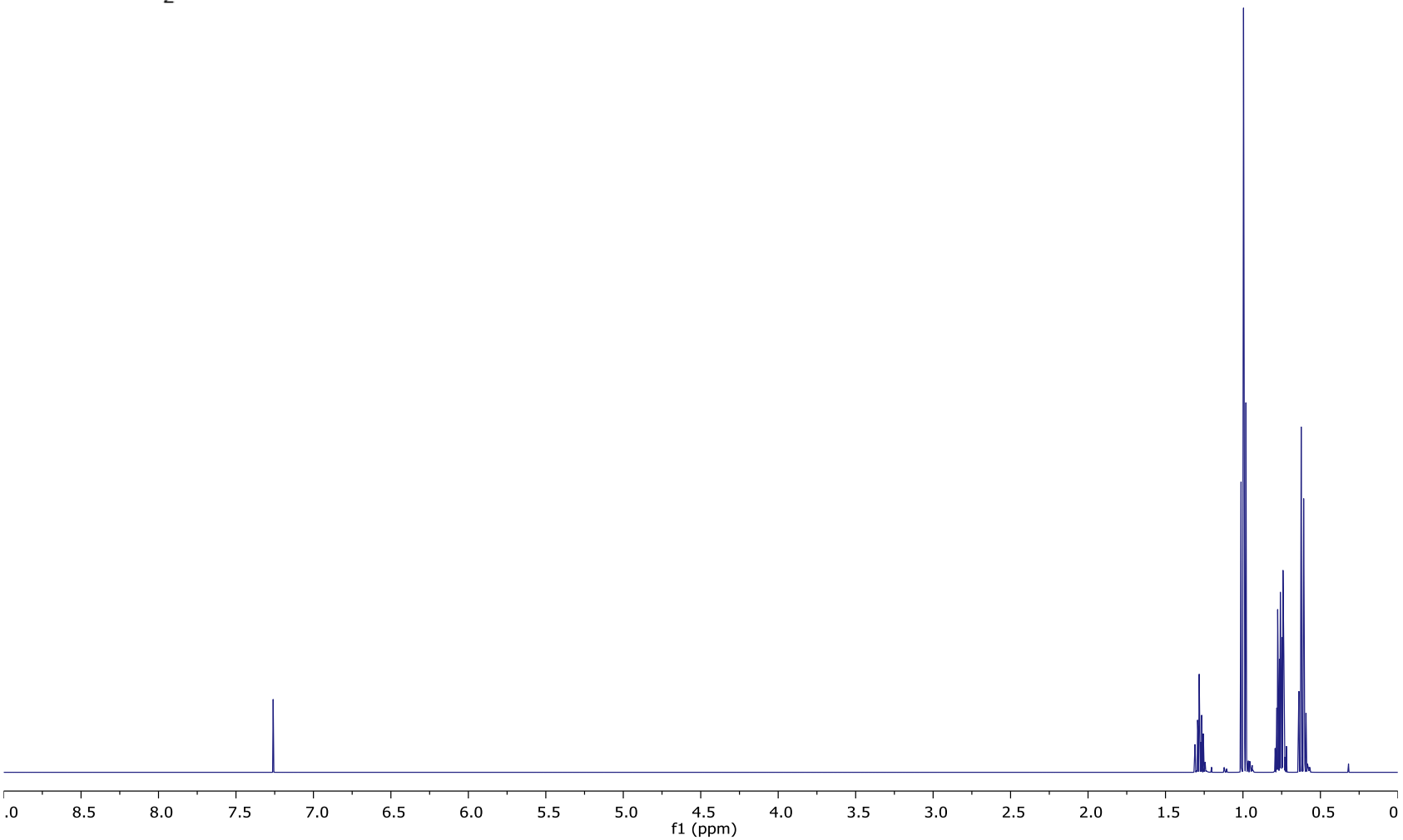


^{1}H NMR (500 MHz, $CDCl_3$) of compound **49.**

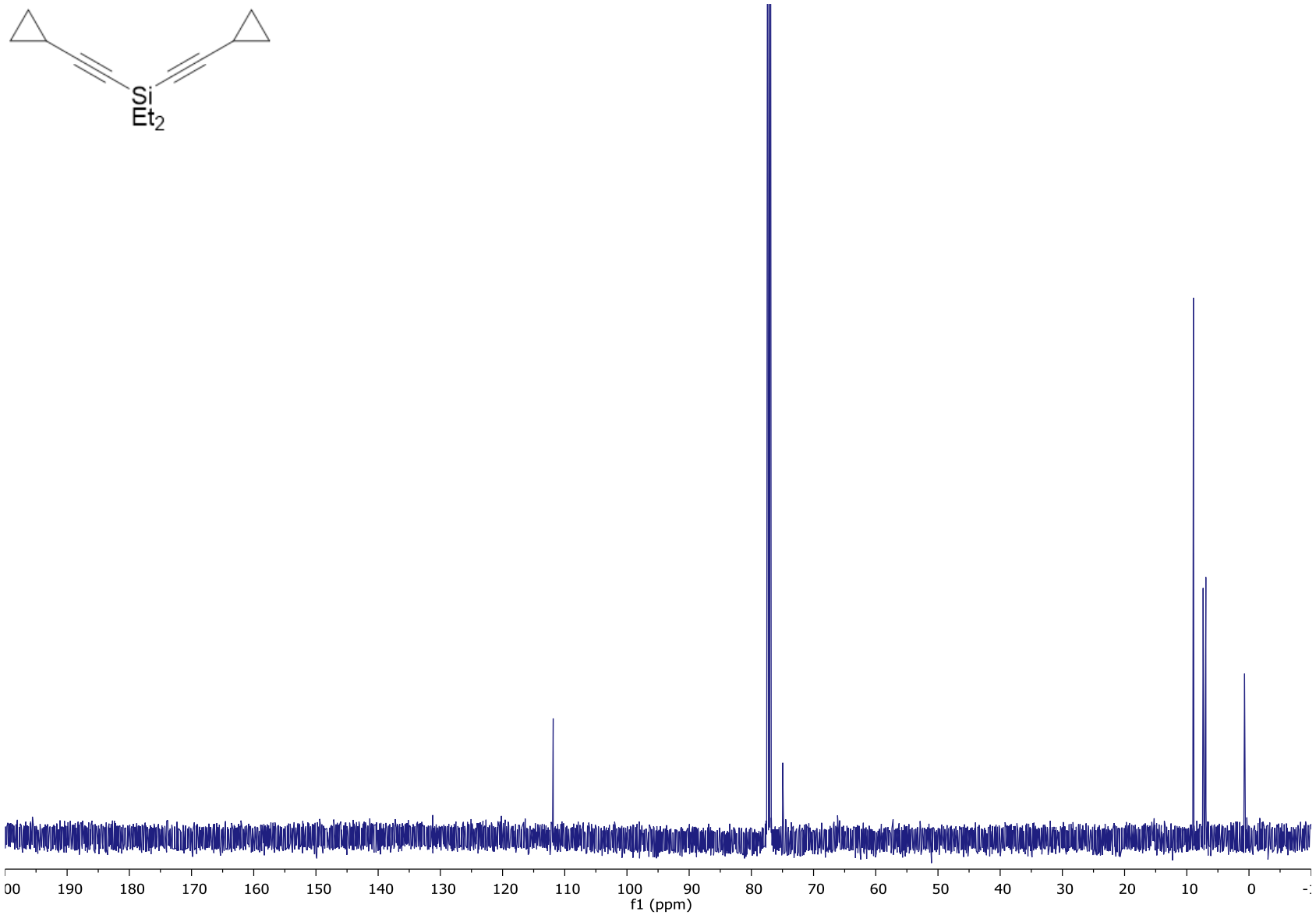


^{13}C NMR (126 MHz, $CDCl_3$) of compound **49.**

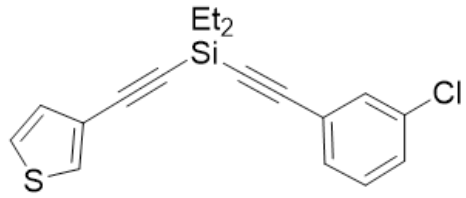


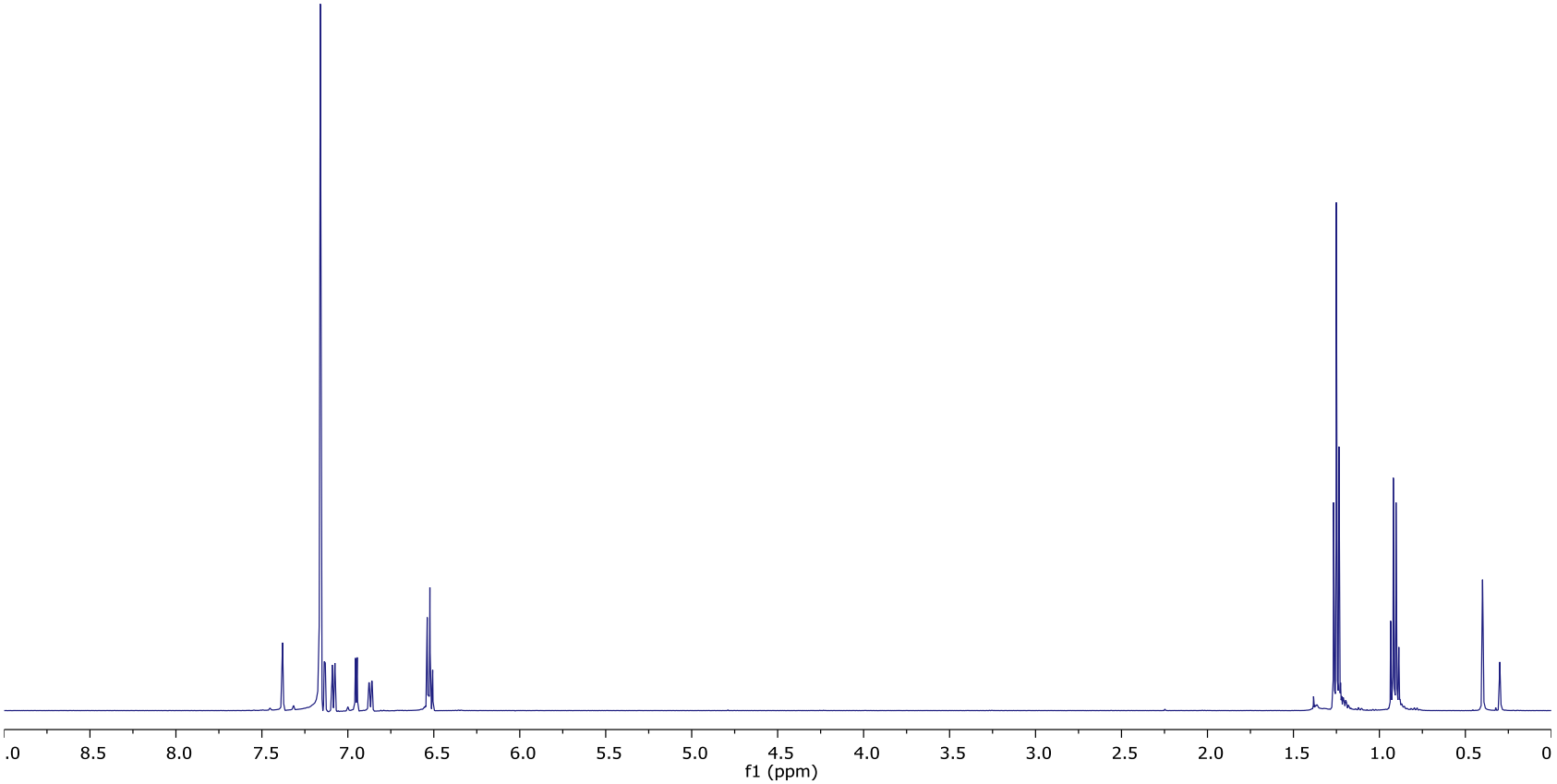


^{1}H NMR (500 MHz, $CDCl_3$) of compound **41r_Sidim.**

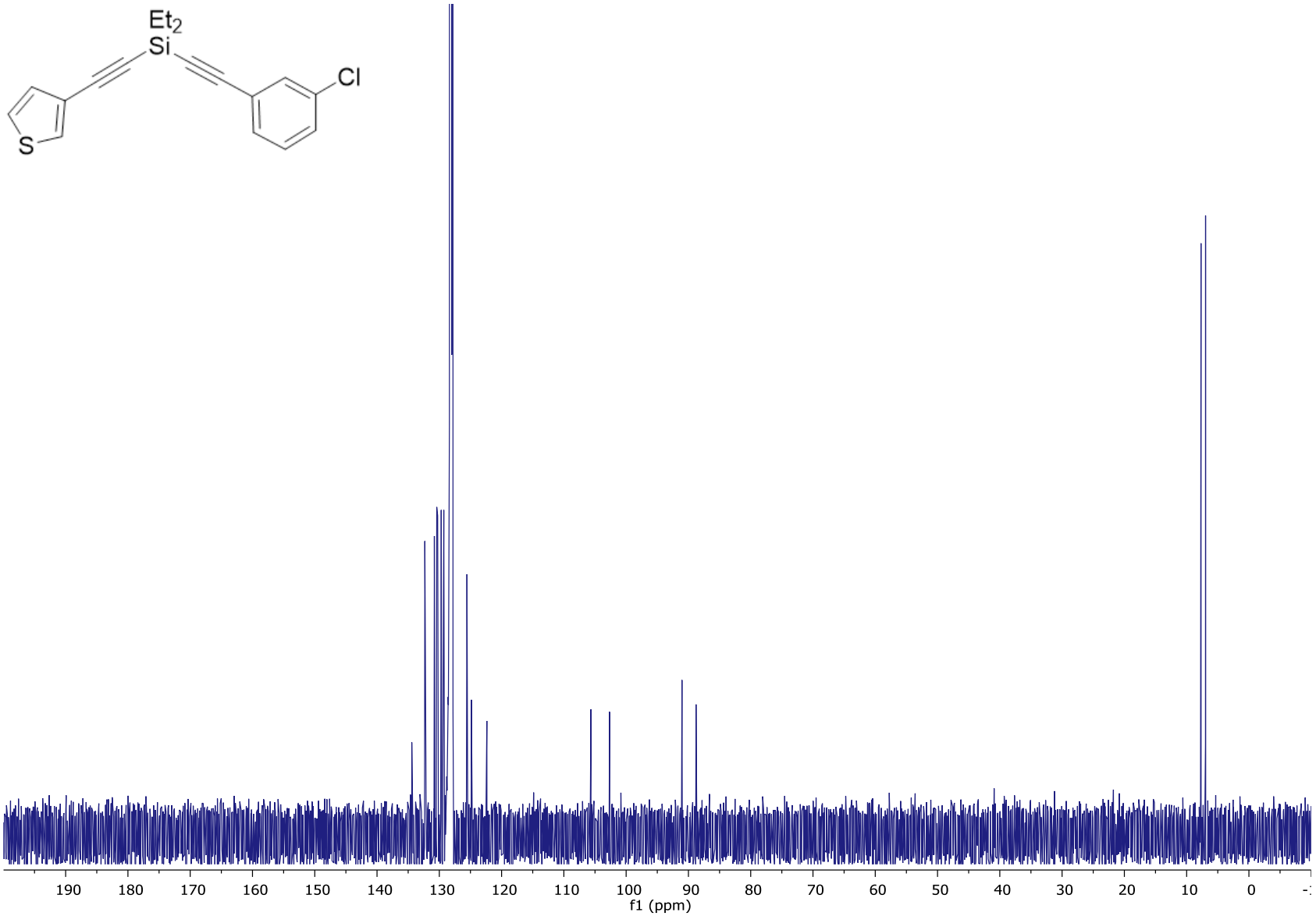


^{13}C NMR (126 MHz, $CDCl_3$) of compound **41r_Sidim.**

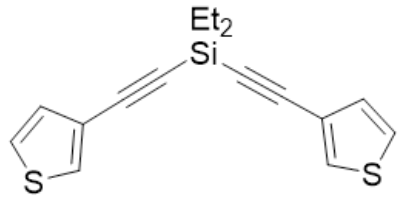


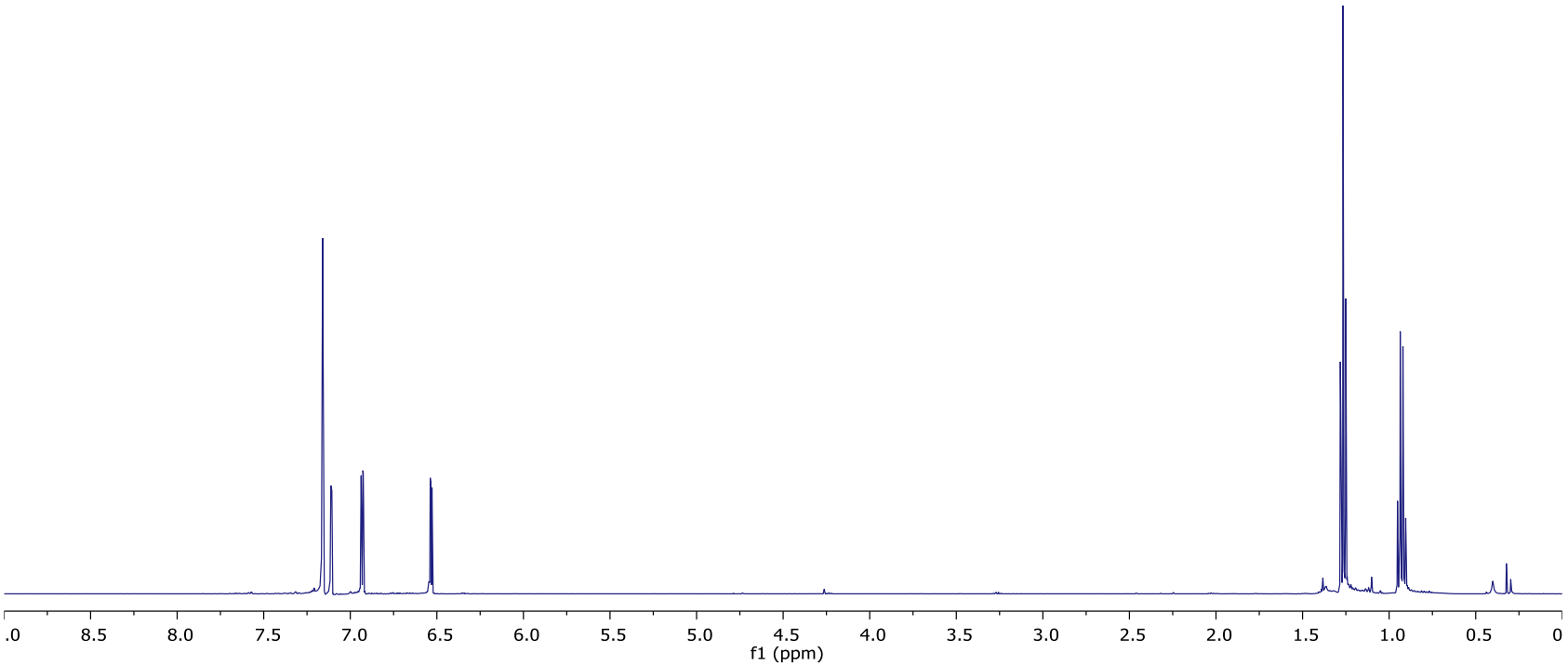


^{1}H NMR (500 MHz, C_6D_6) of compound **51.**

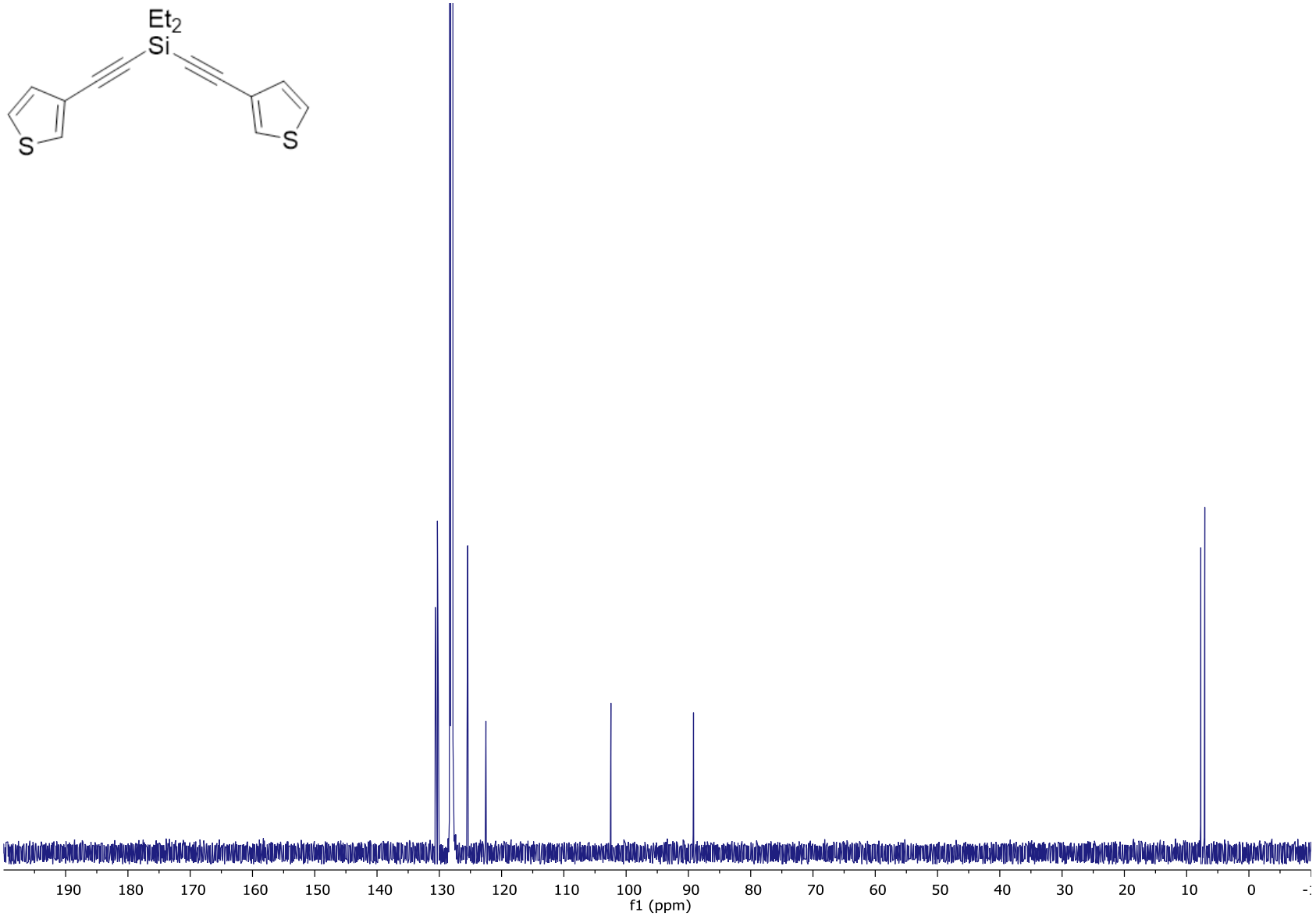


^{13}C NMR (126 MHz, C_6D_6) of compound **51.**

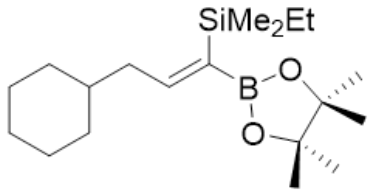


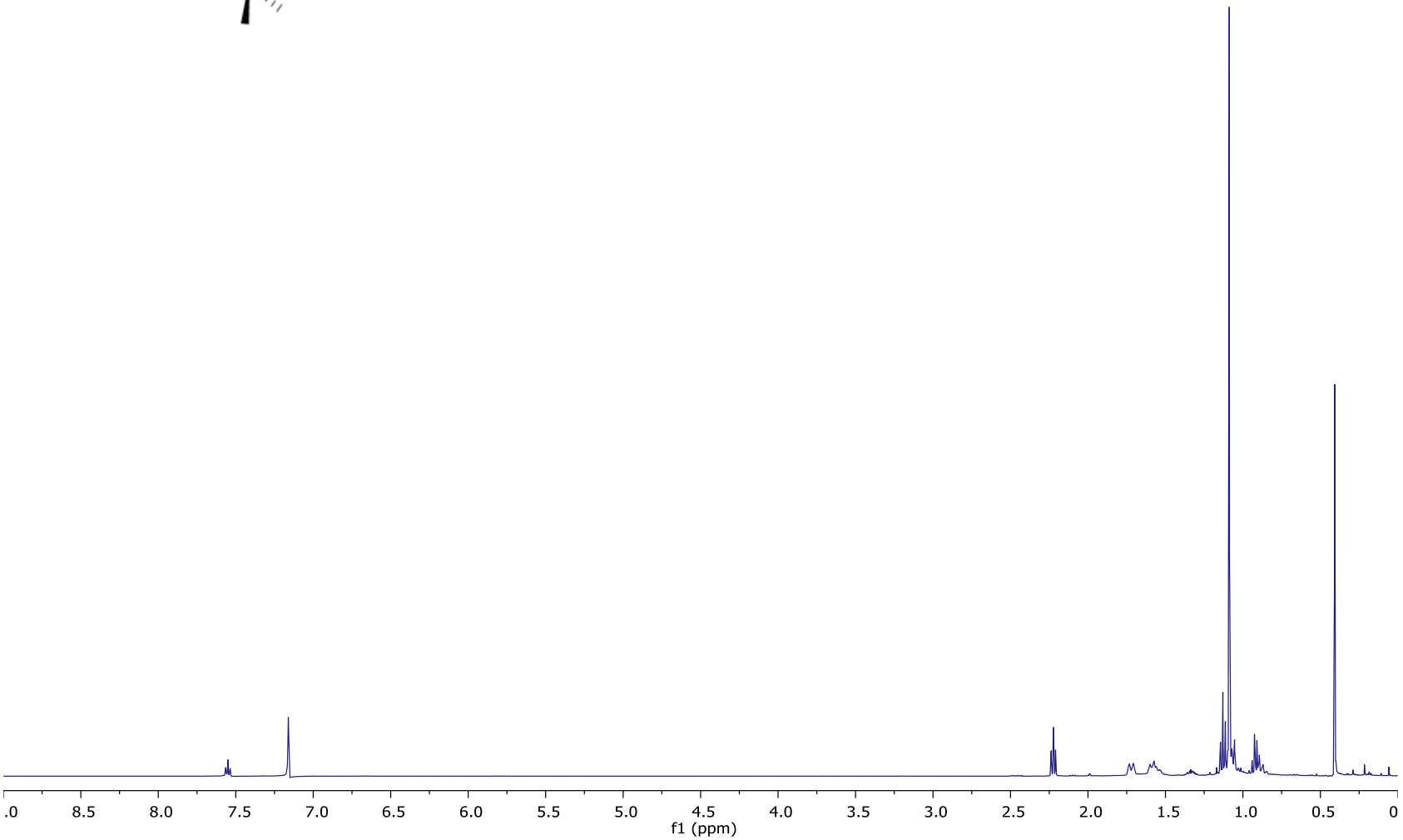


^{1}H NMR (500 MHz, C_6D_6) of compound **411_Sidim.**

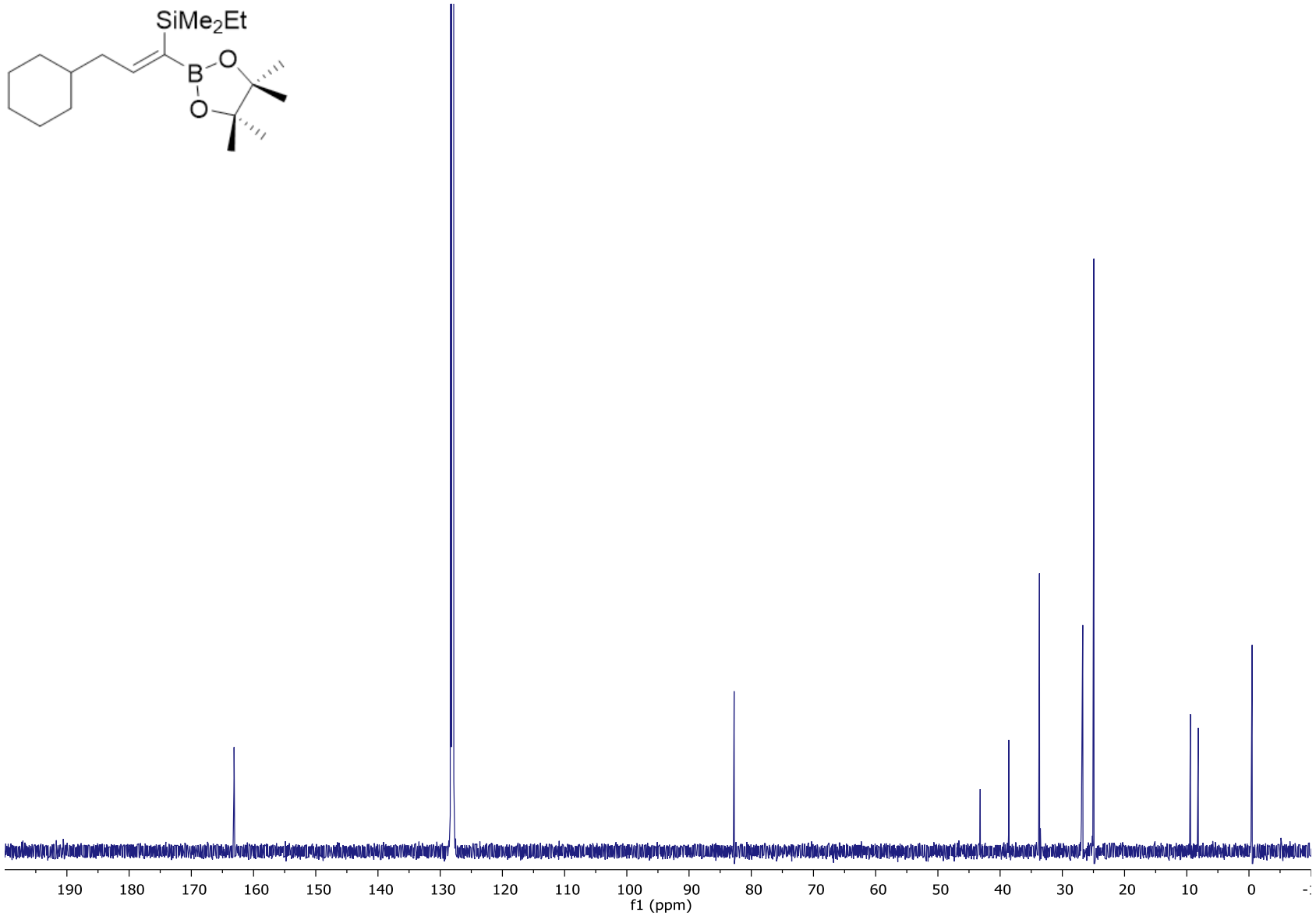


^{13}C NMR (126 MHz, C_6D_6) of compound **411_Sidim.**

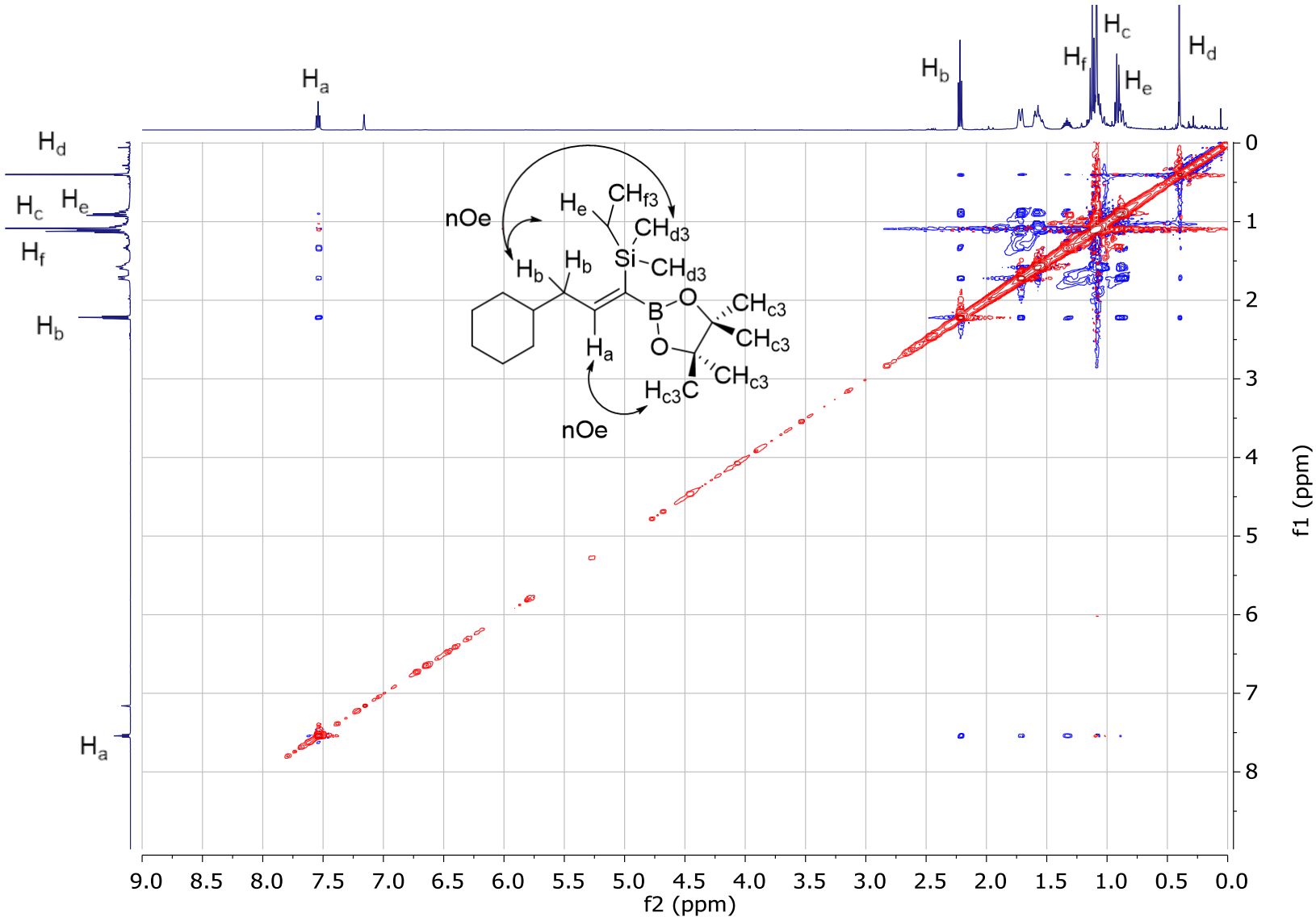




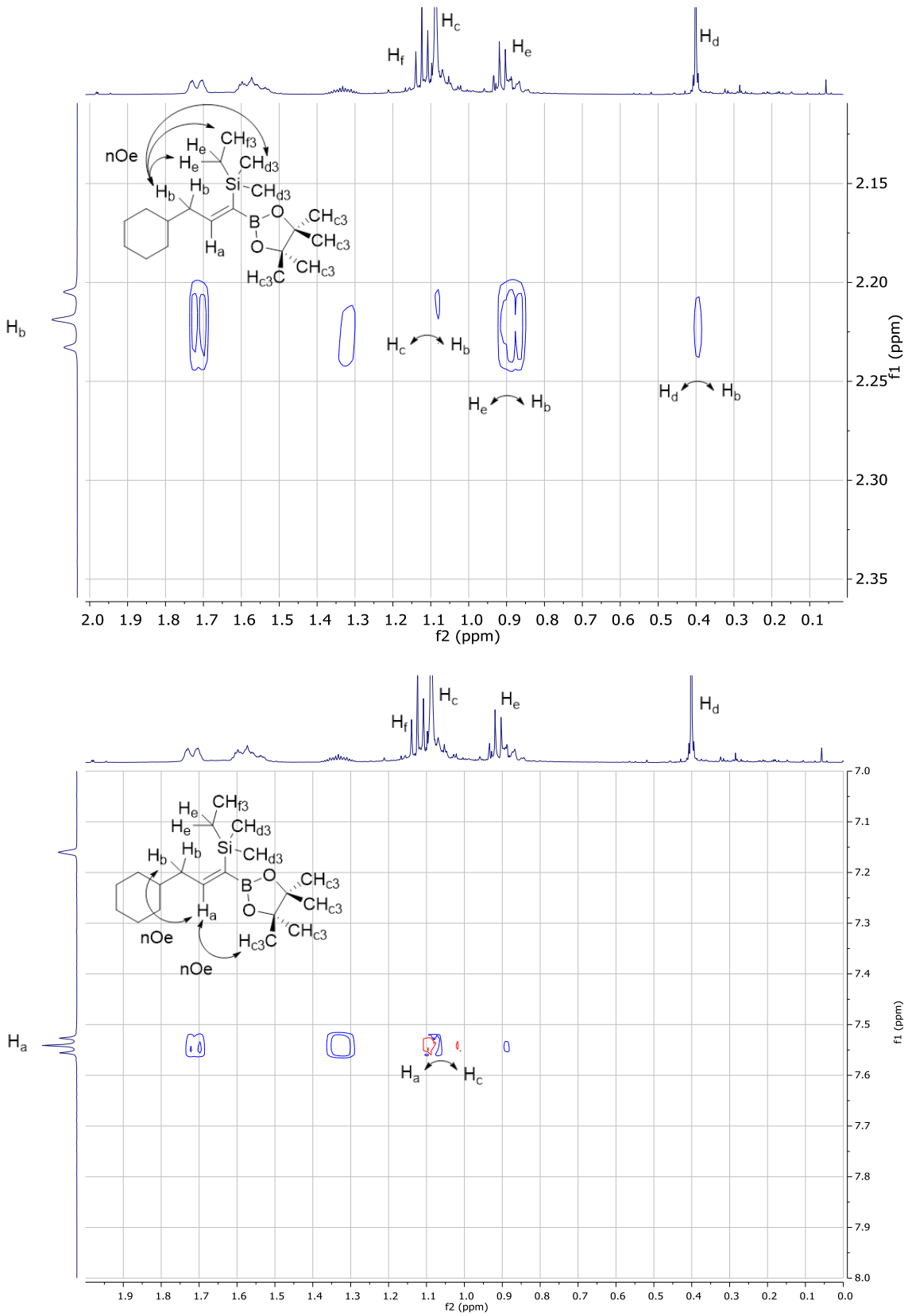
^{1}H NMR (500 MHz, C_6D_6) of compound **52a.**



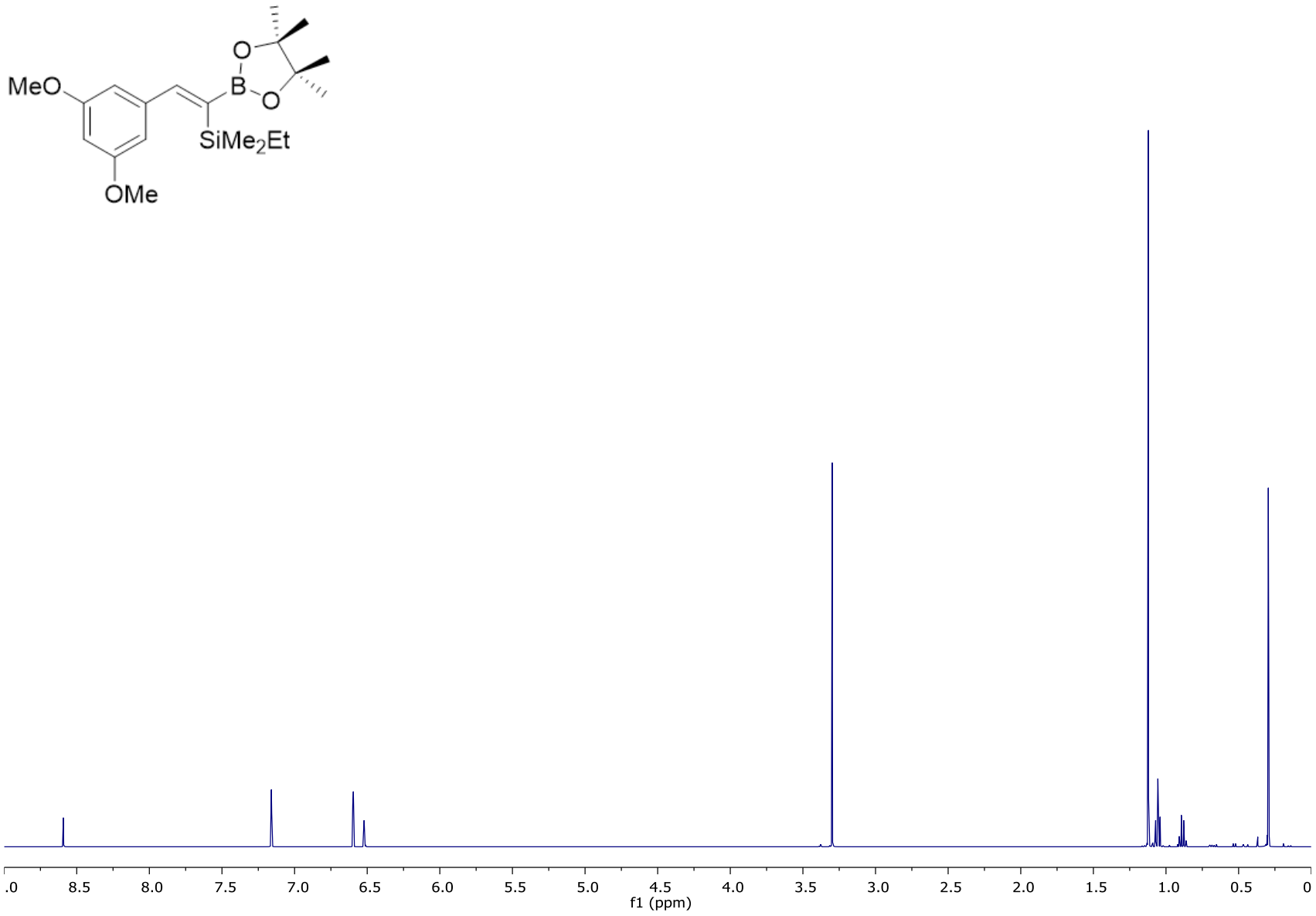
^{13}C NMR (126 MHz, C_6D_6) of compound **52a.**



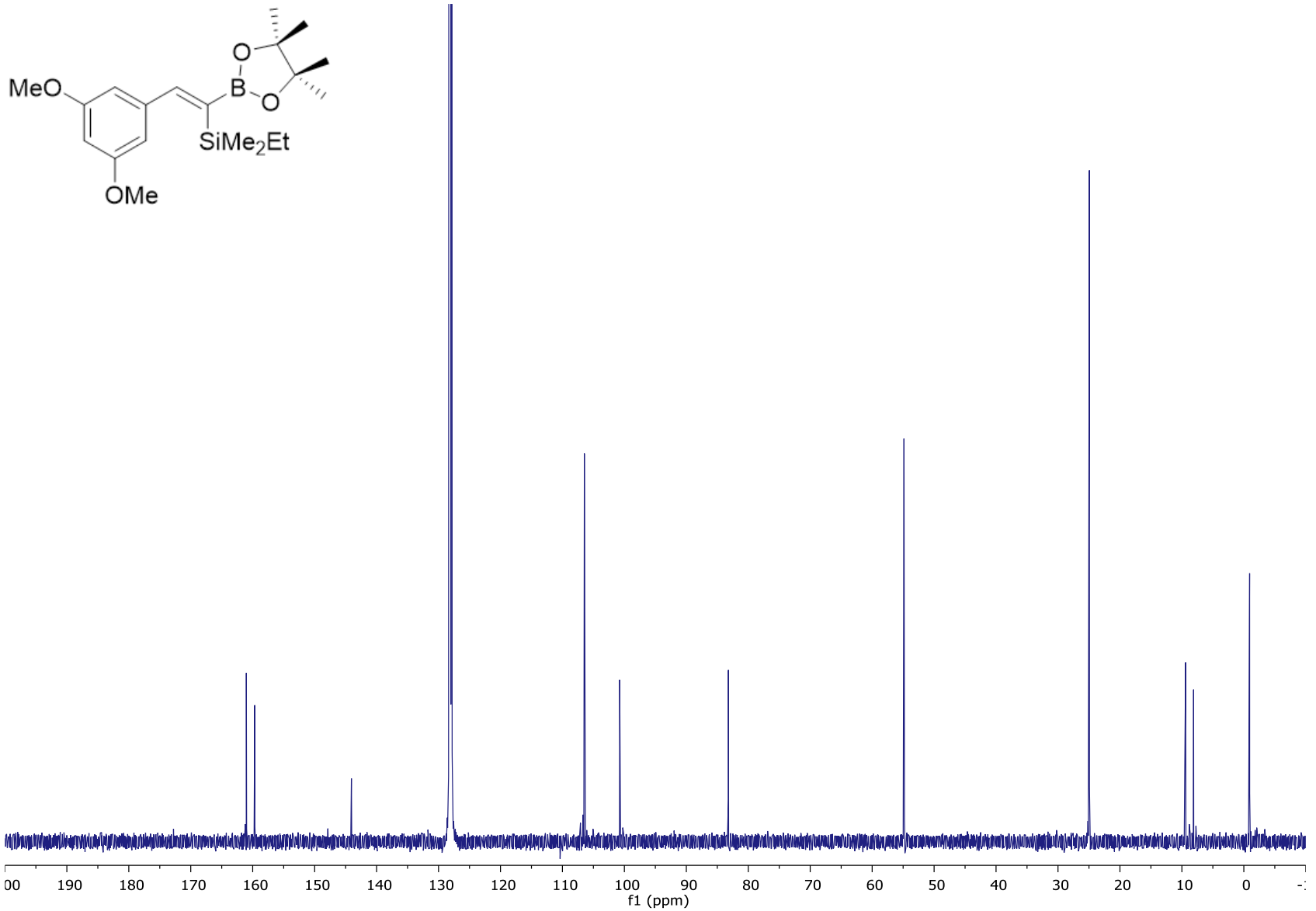
NOESY (500 MHz, C_6D_6) of compound **52a.**



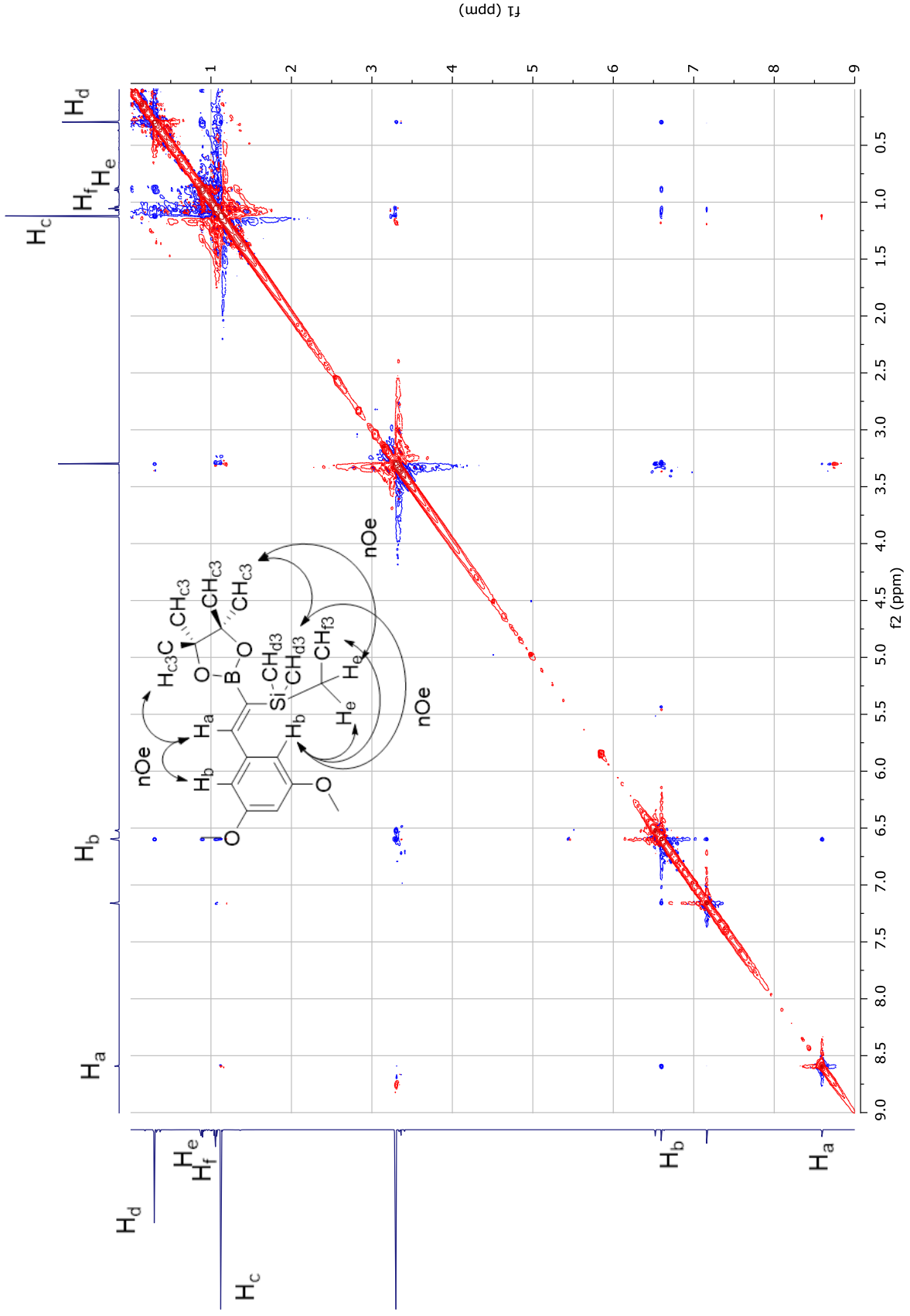
NOESY (500 MHz, C_6D_6) of compound **52a.**



^{1}H NMR (500 MHz, C_6D_6) of compound **52b.**



^{13}C NMR (126 MHz, C_6D_6) of compound **52b.**



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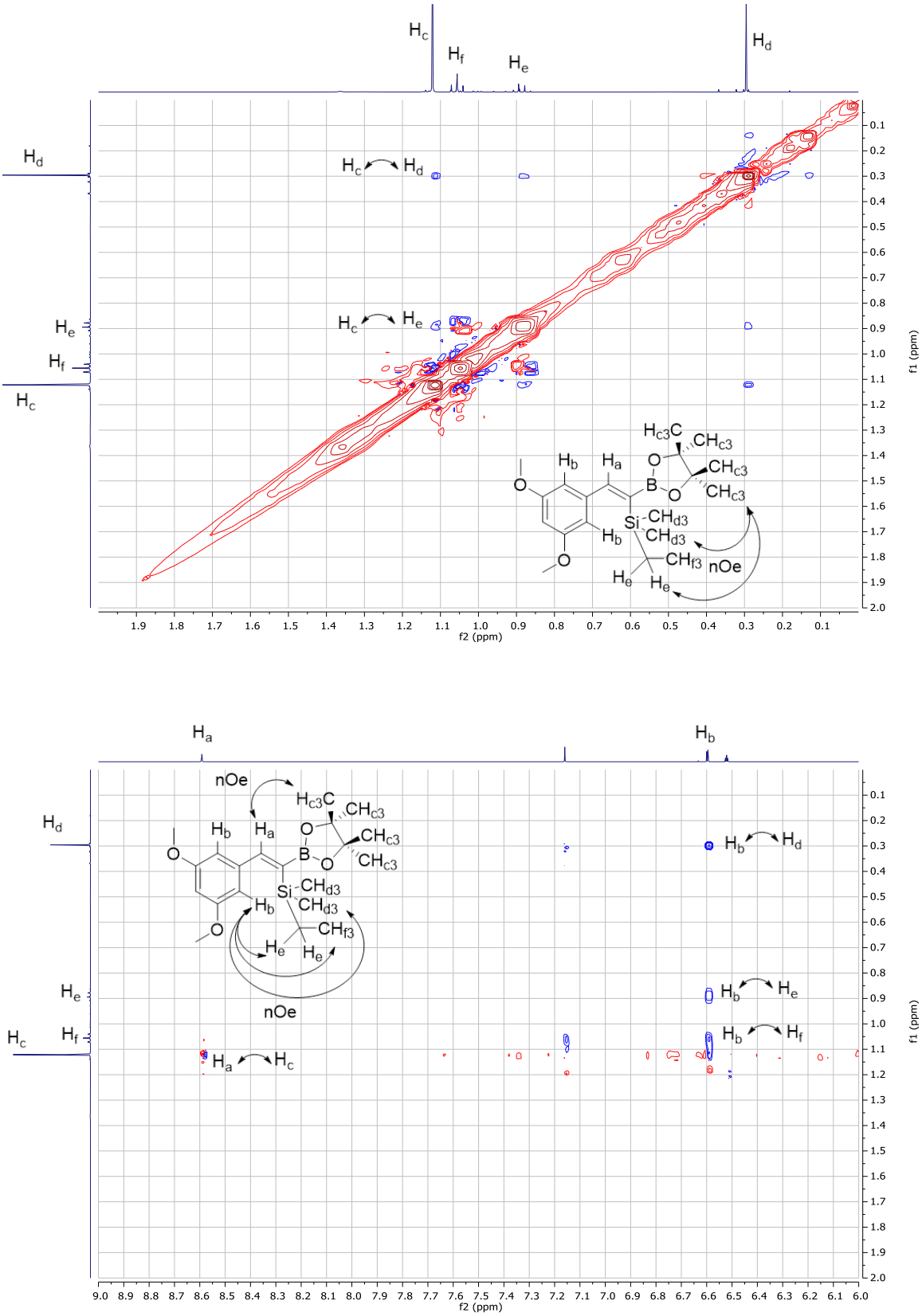
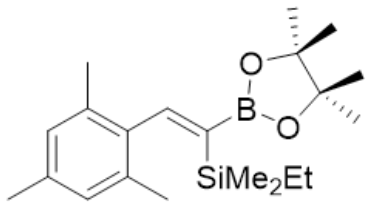
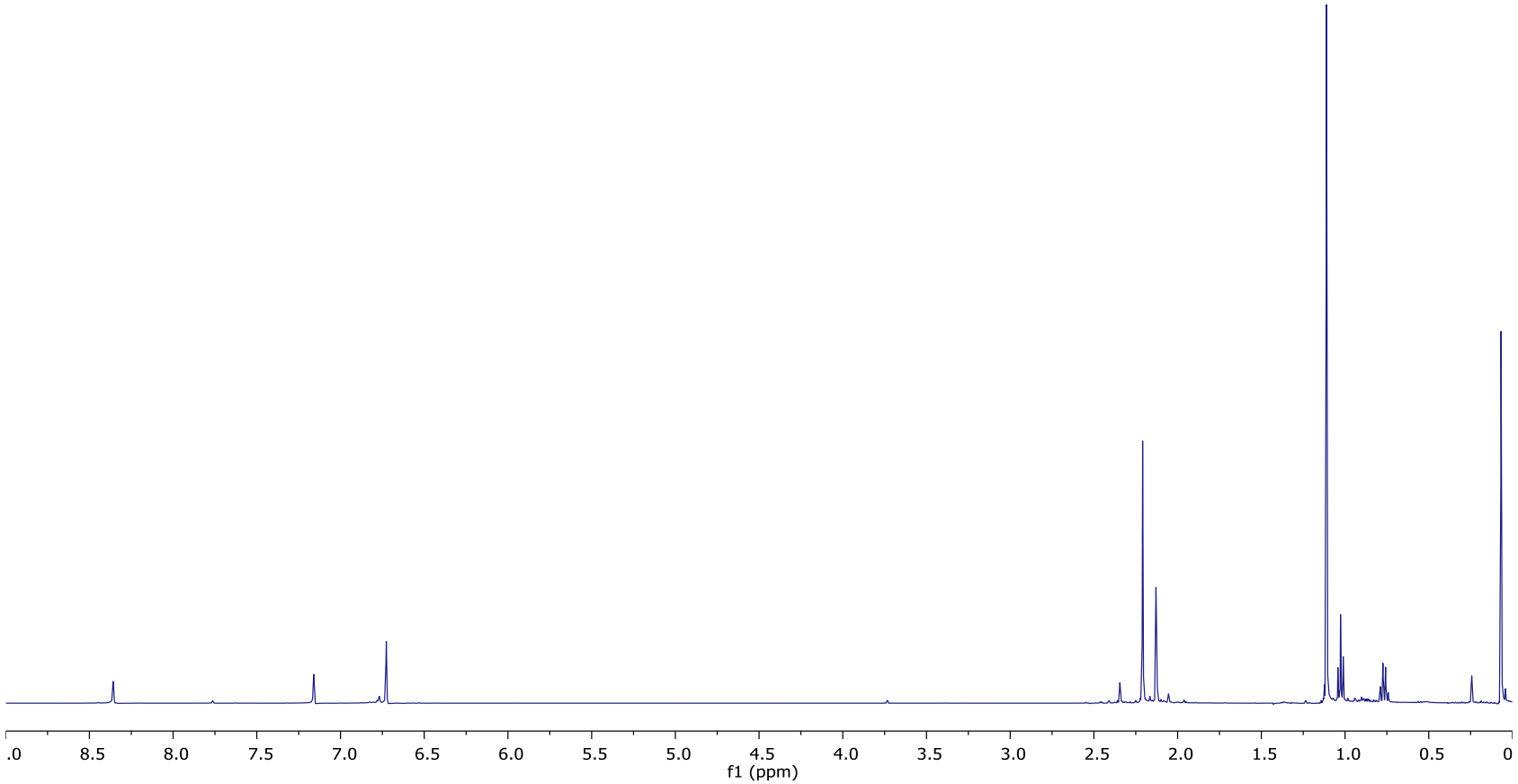


NOESY (500 MHz, C_6D_6) of compound **52b.**





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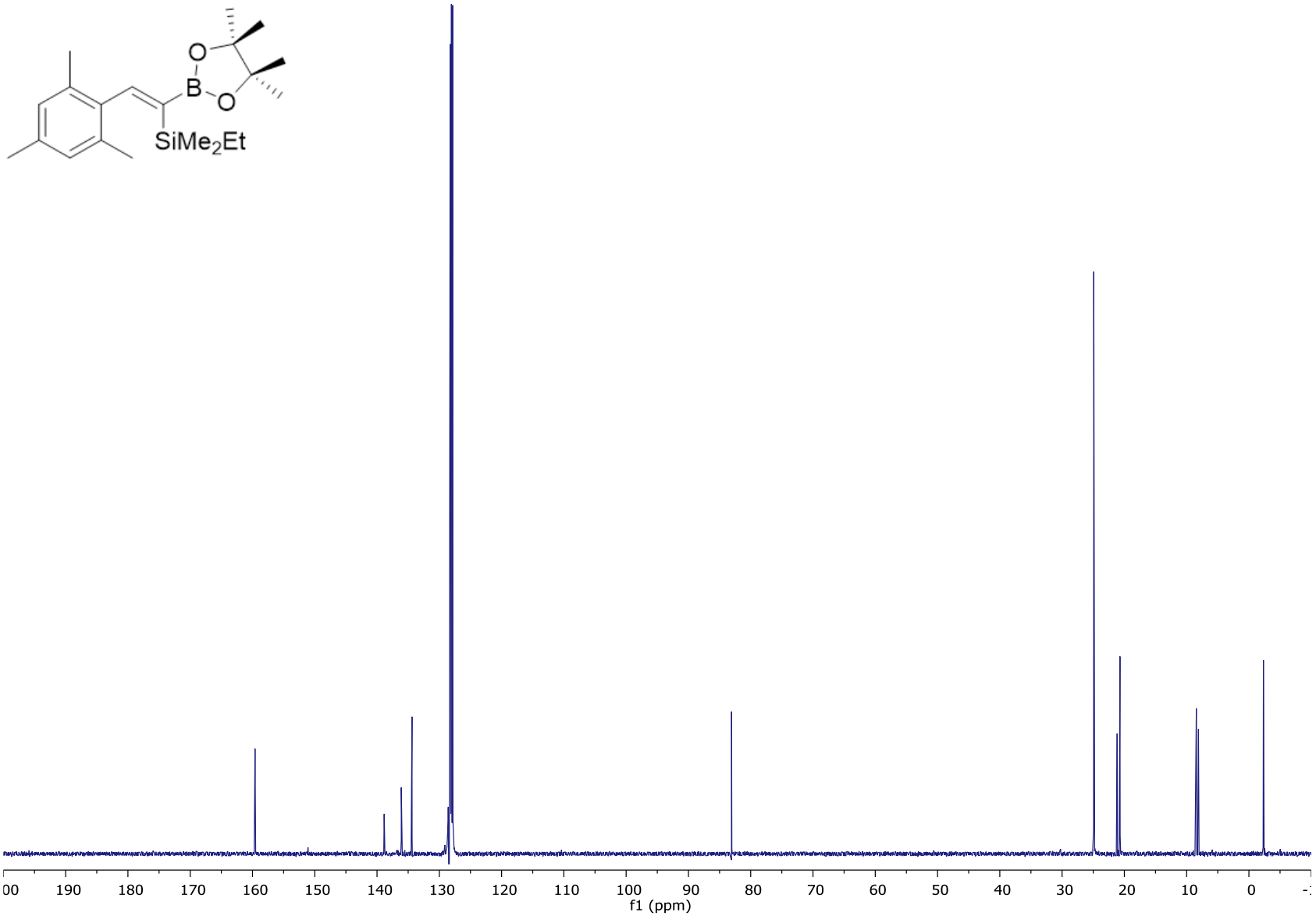

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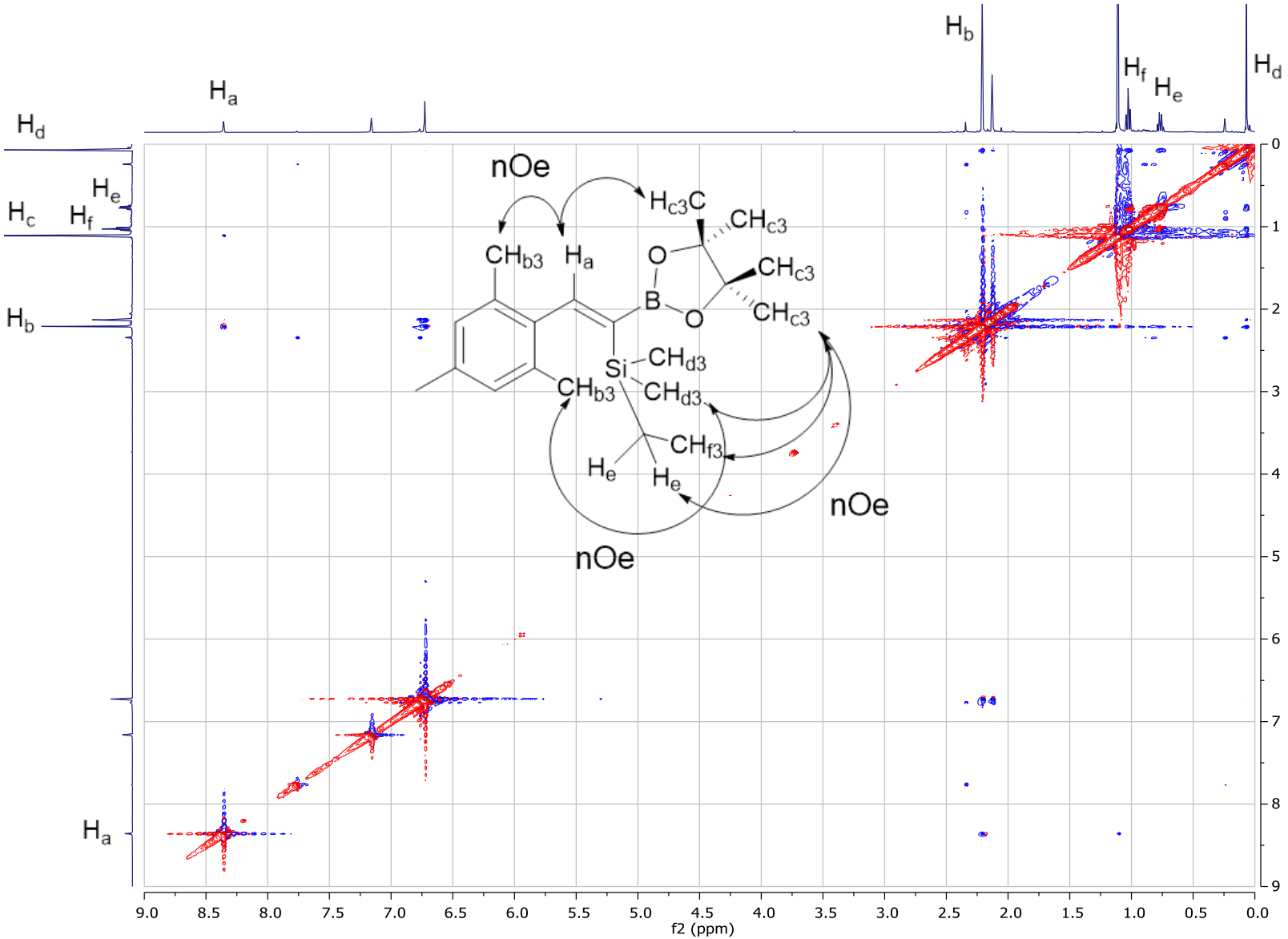
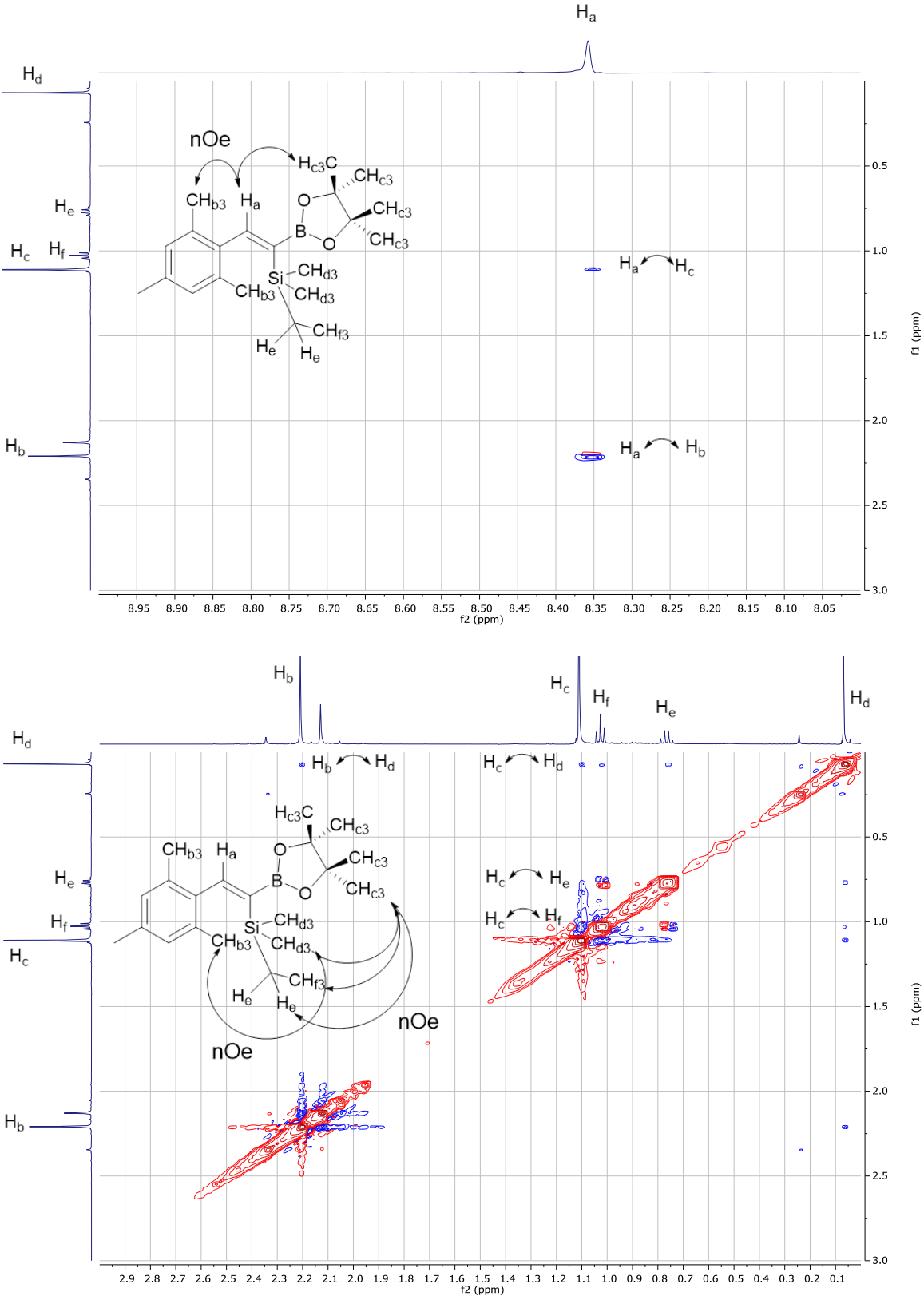
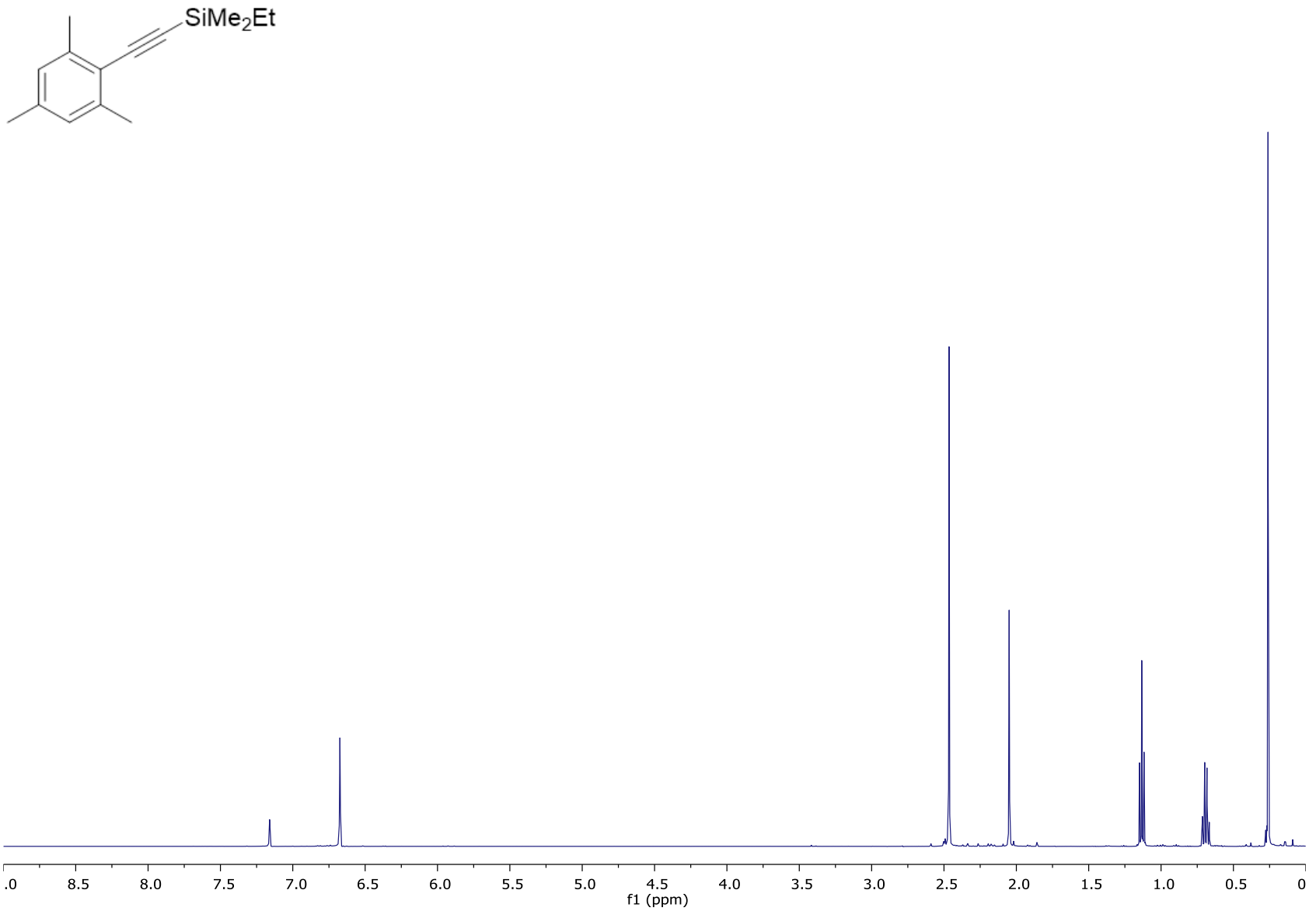


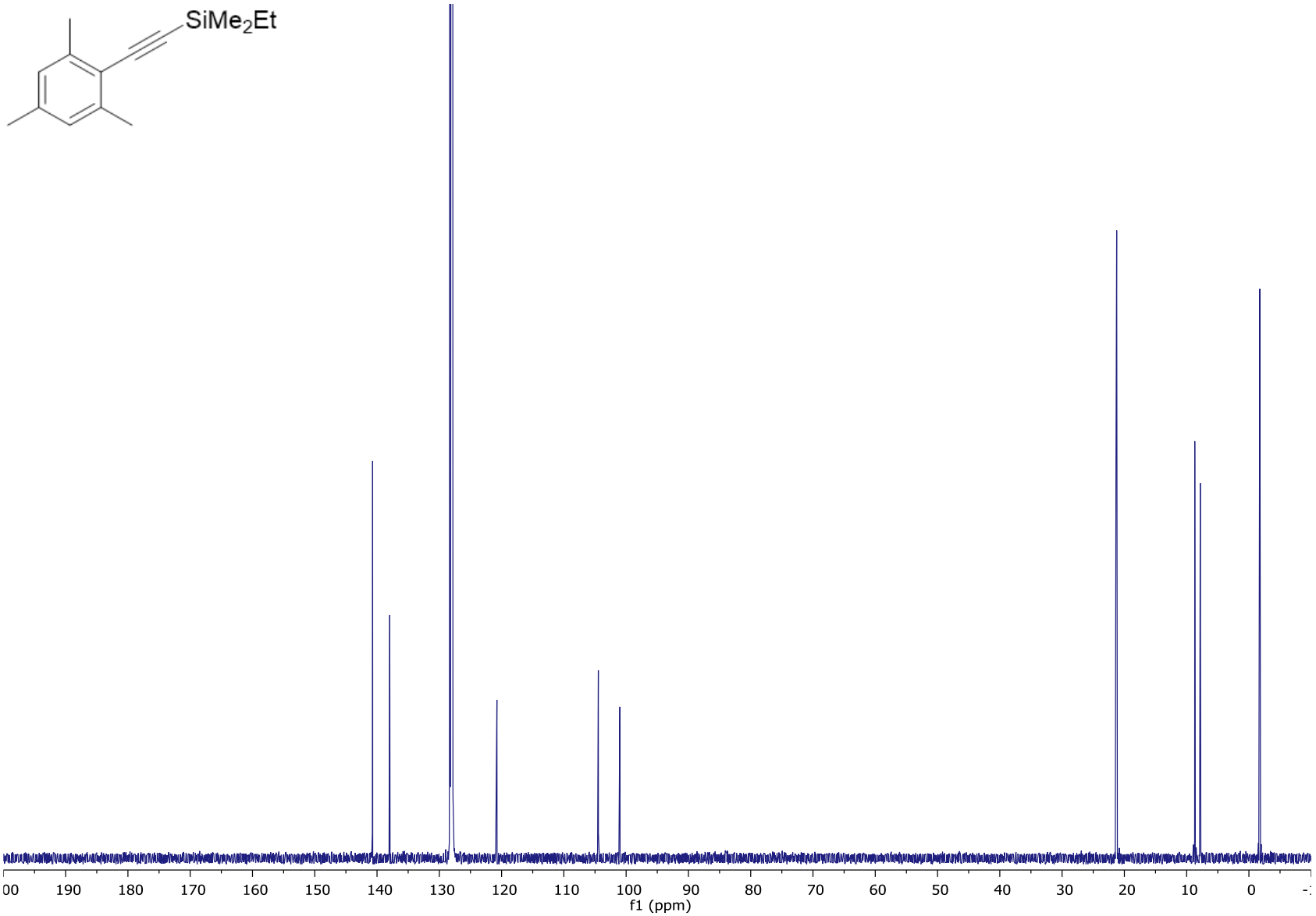
NOESY (500 MHz, C_6D_6) of compound **52c.**



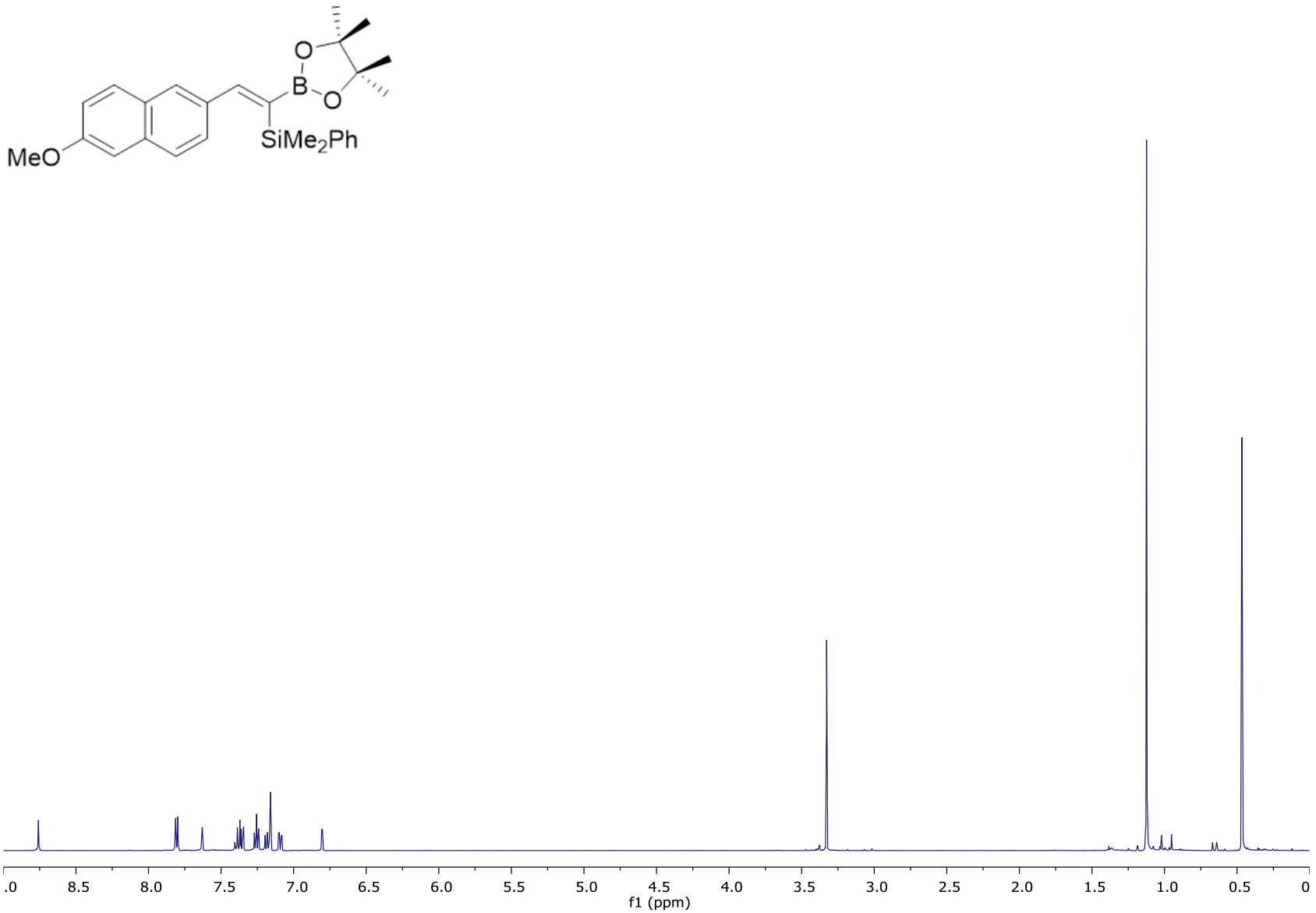
NOESY (500 MHz, C_6D_6) of compound **52c.**



^{1}H NMR (500 MHz, C_6D_6) of compound **41i_SiMe$_2$Et.**



^{13}C NMR (126 MHz, C_6D_6) of compound **41i_SiMe$_2$Et.**



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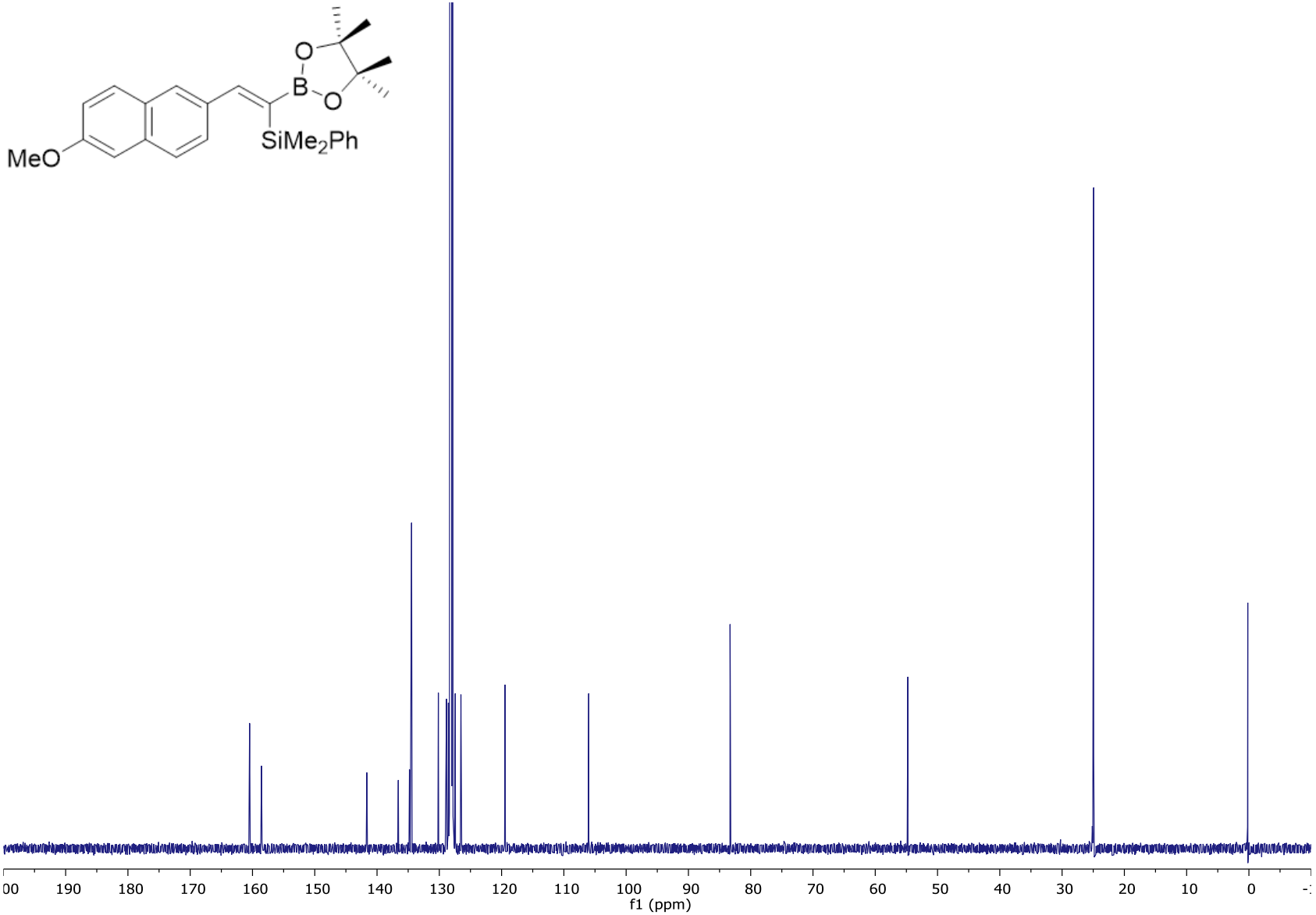

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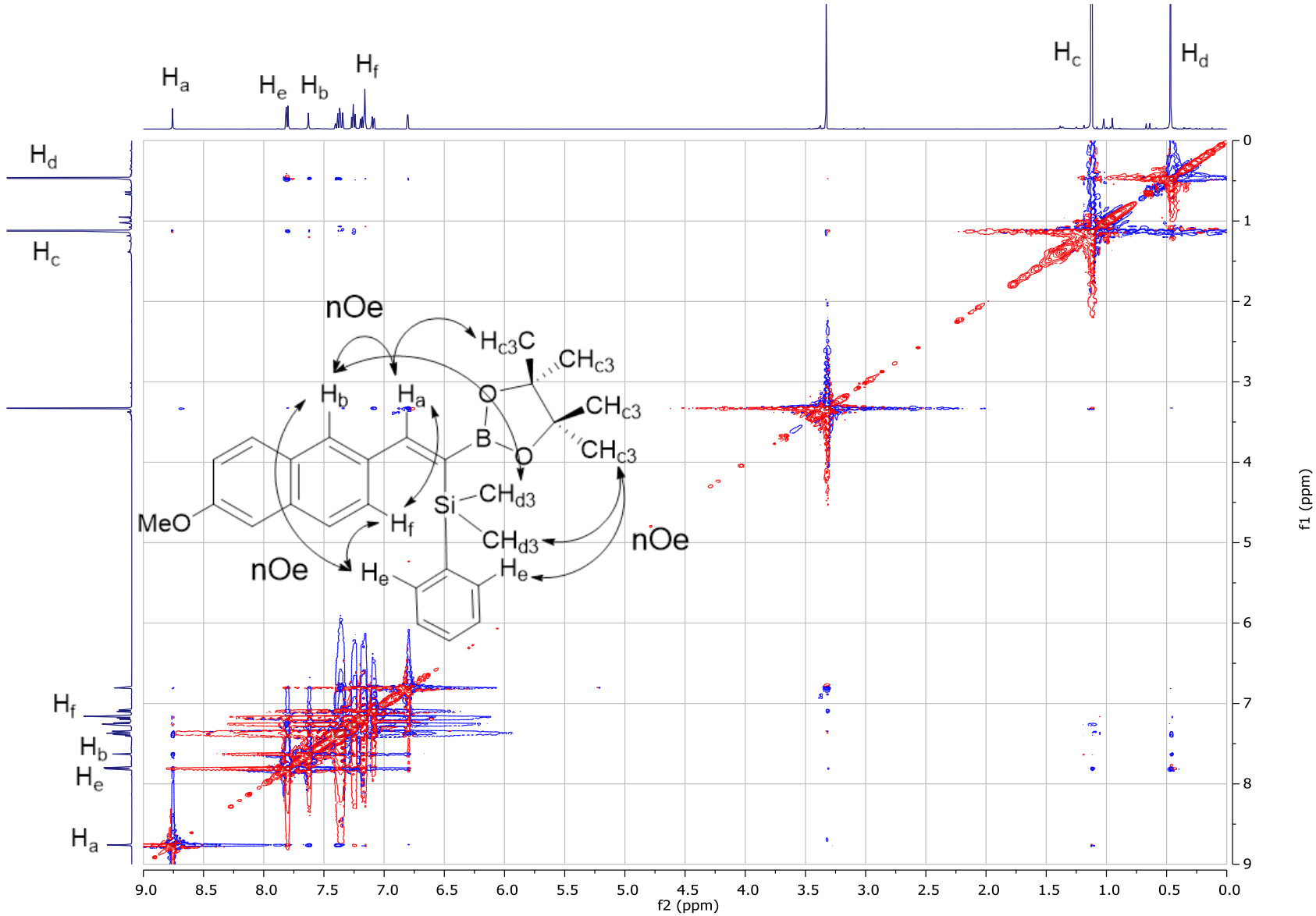

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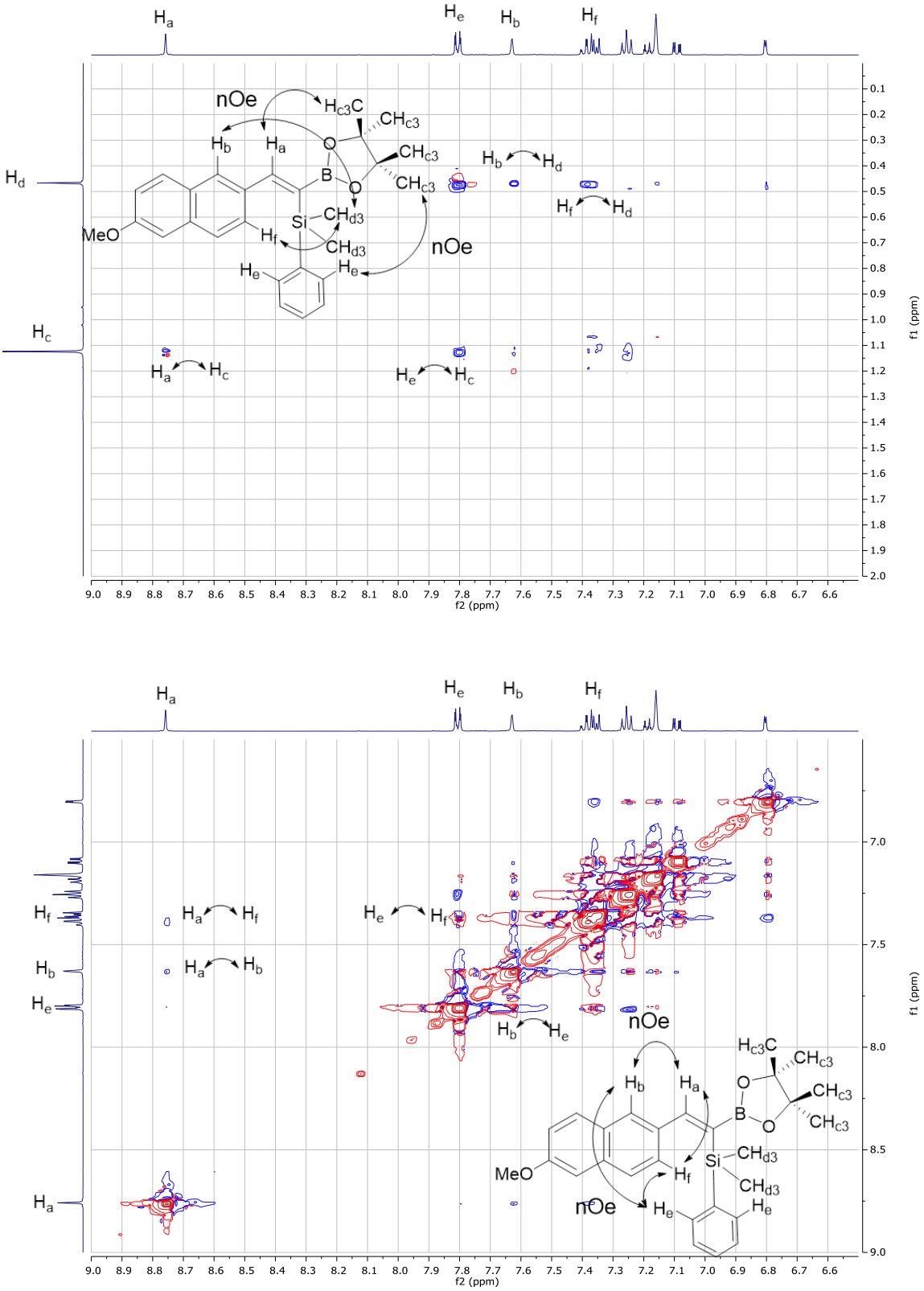

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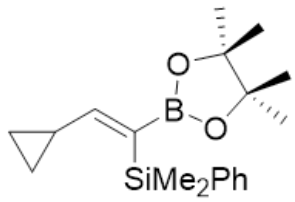
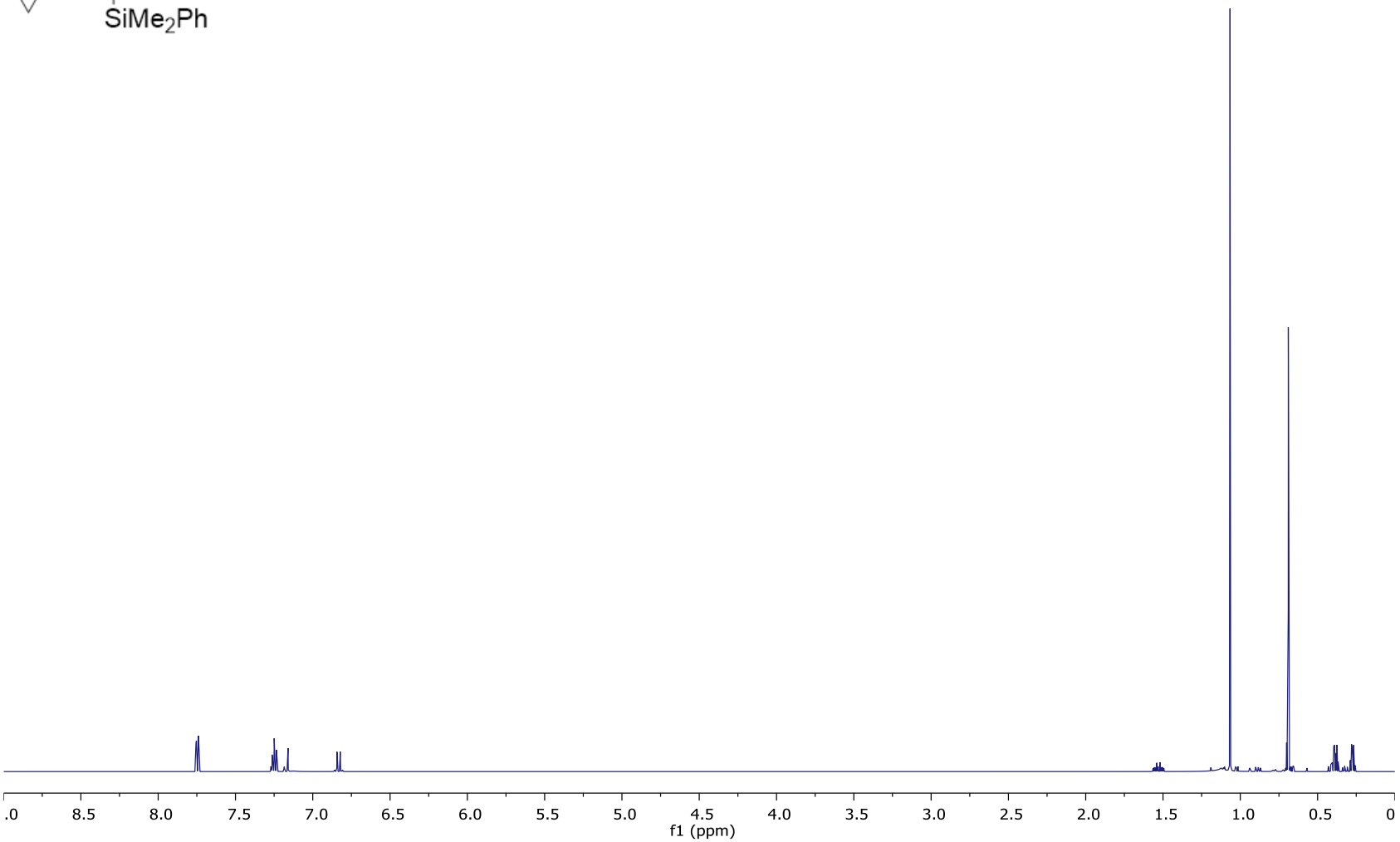
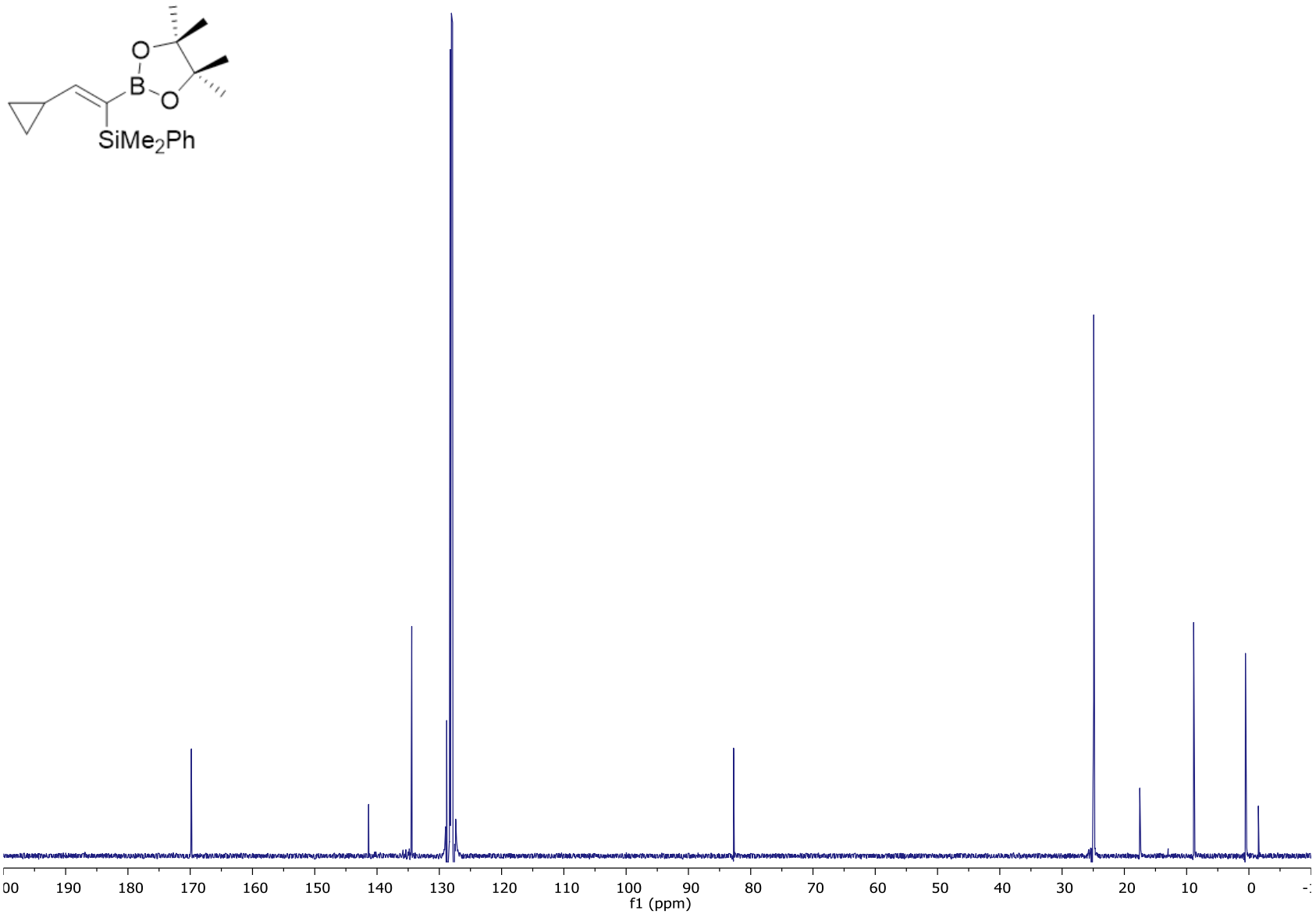




^{1}H NMR (500 MHz, C_6D_6) of compound **52d.**



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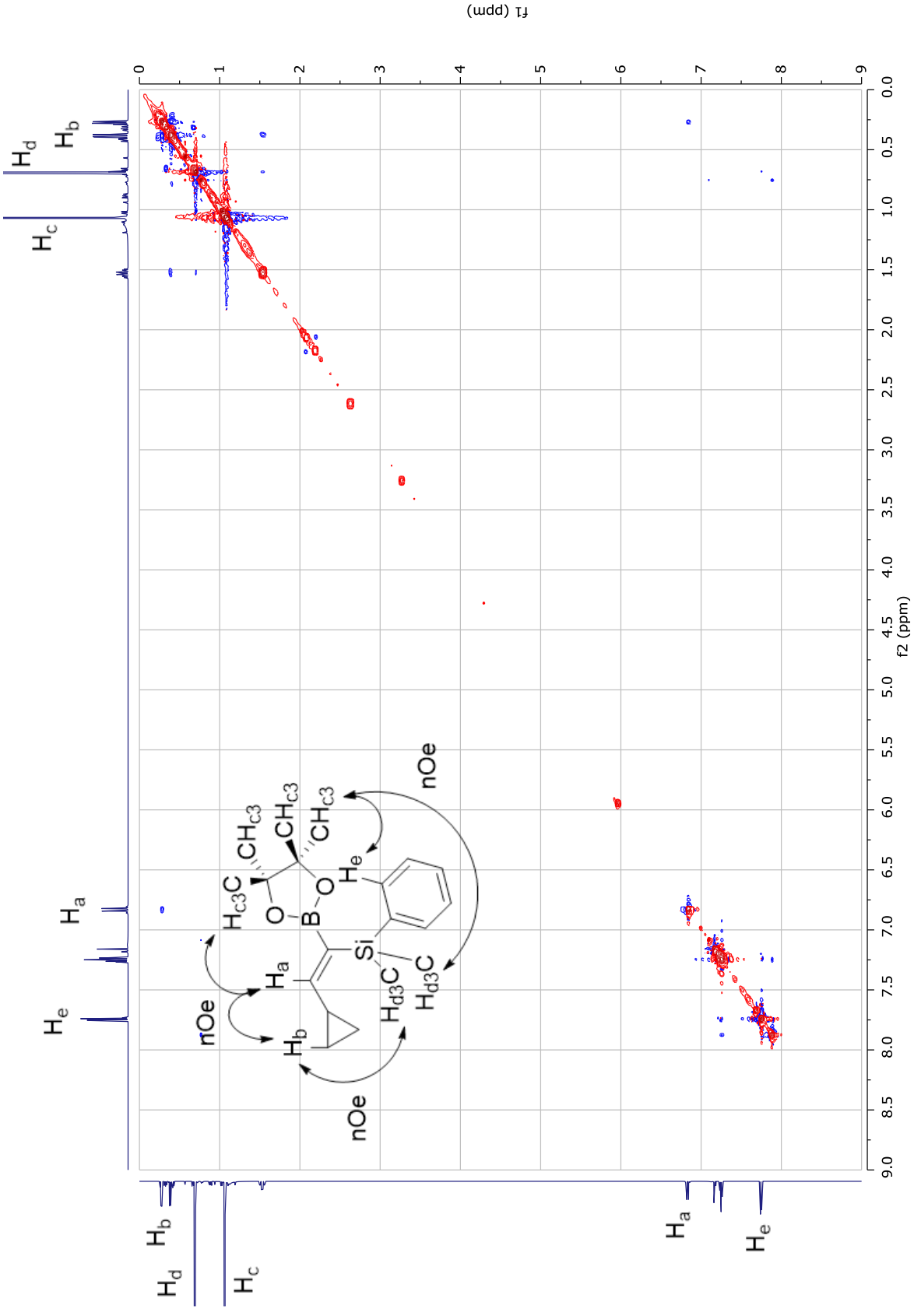
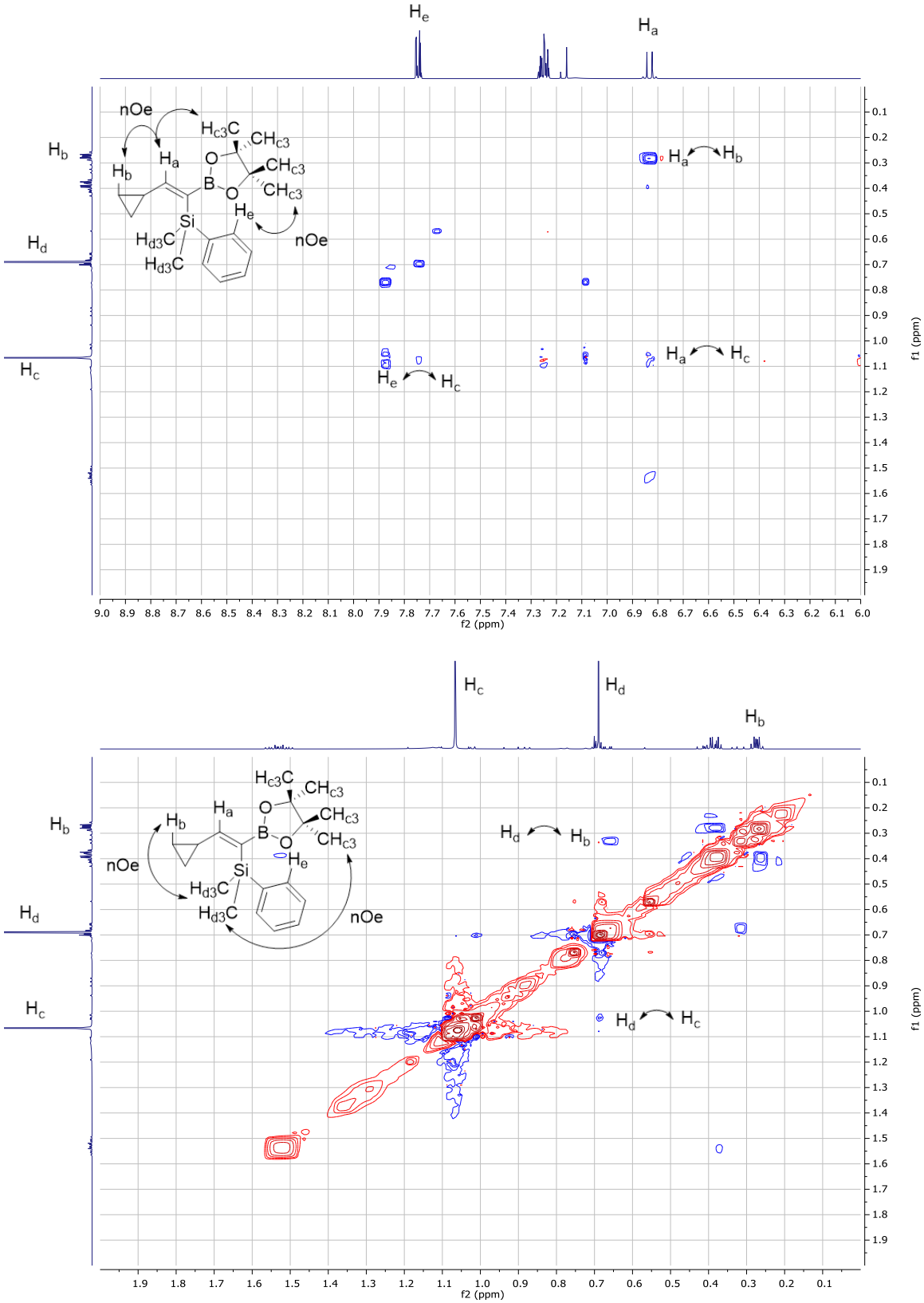


NOESY (500 MHz, C_6D_6) of compound **52d.**



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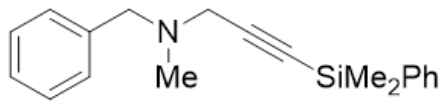
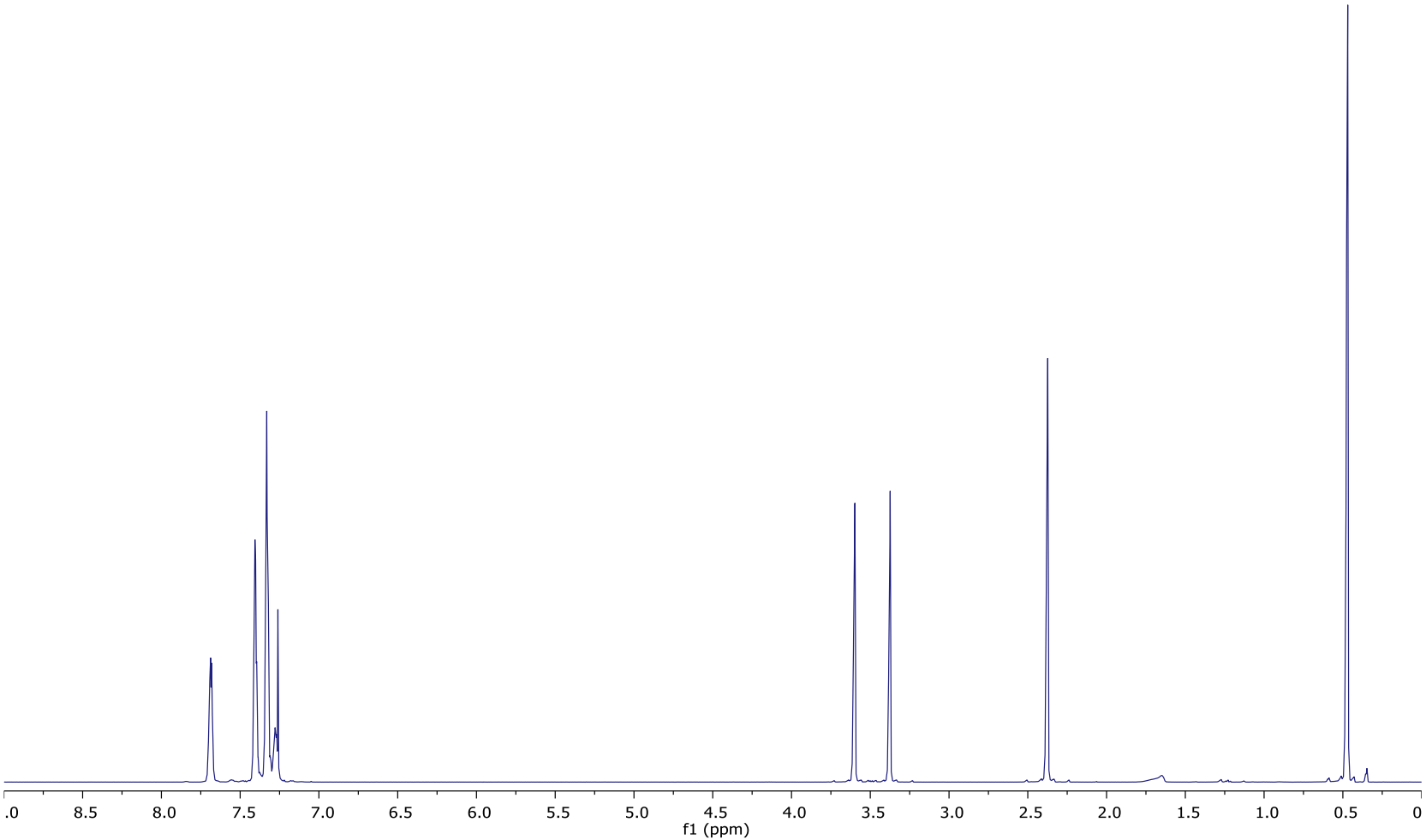
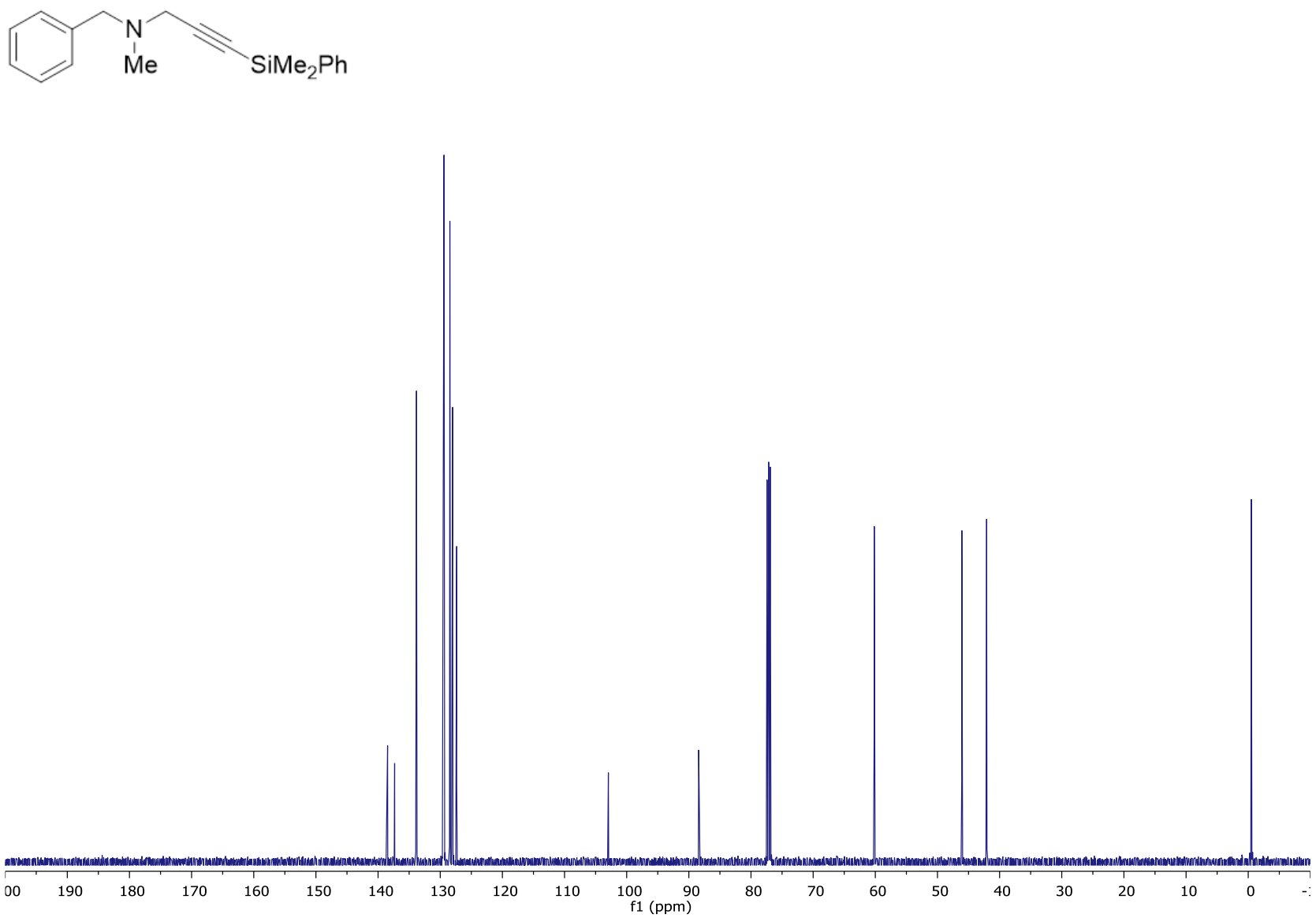
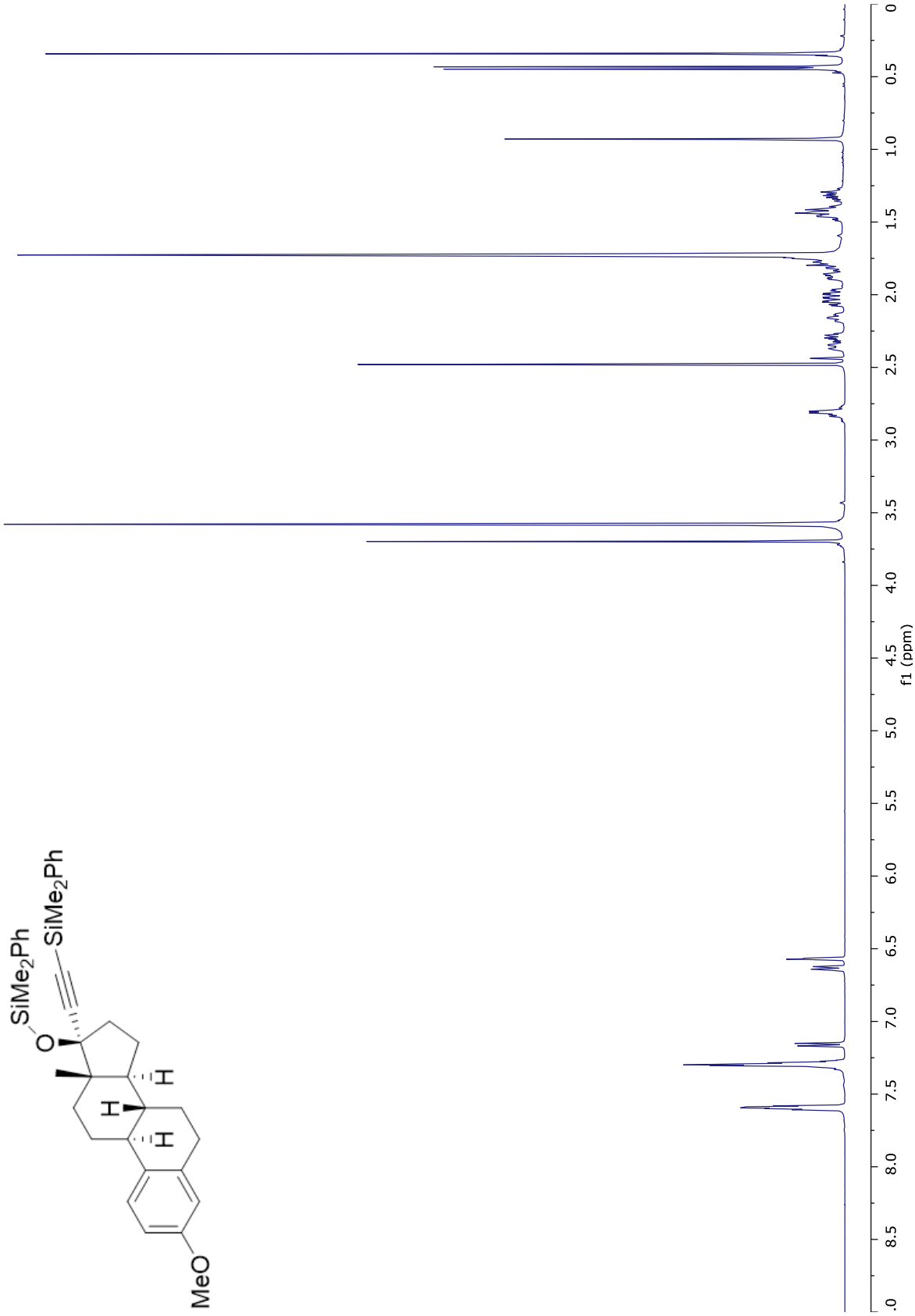




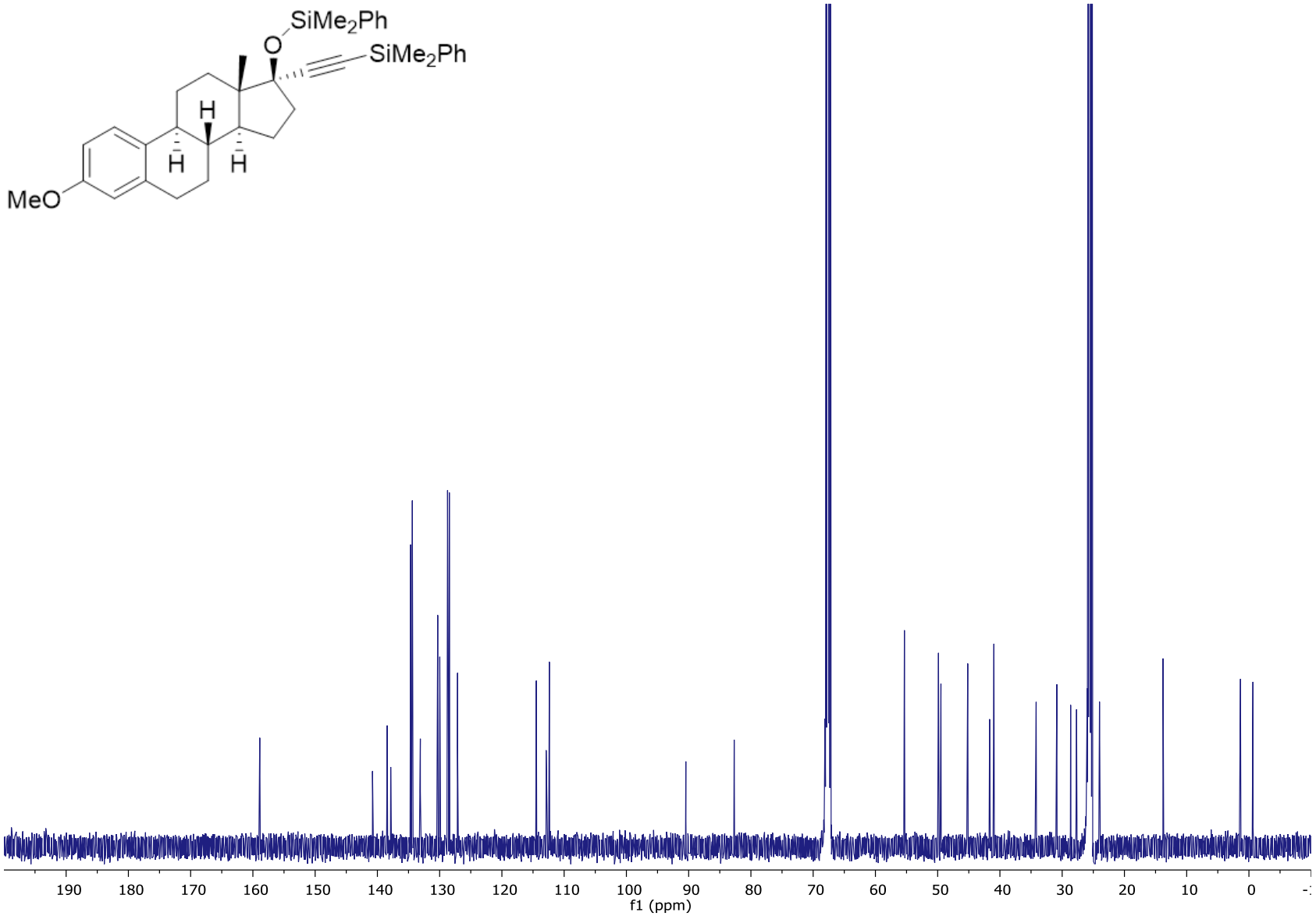
^{1}H NMR (500 MHz, $CDCl_3$) of compound **53.**



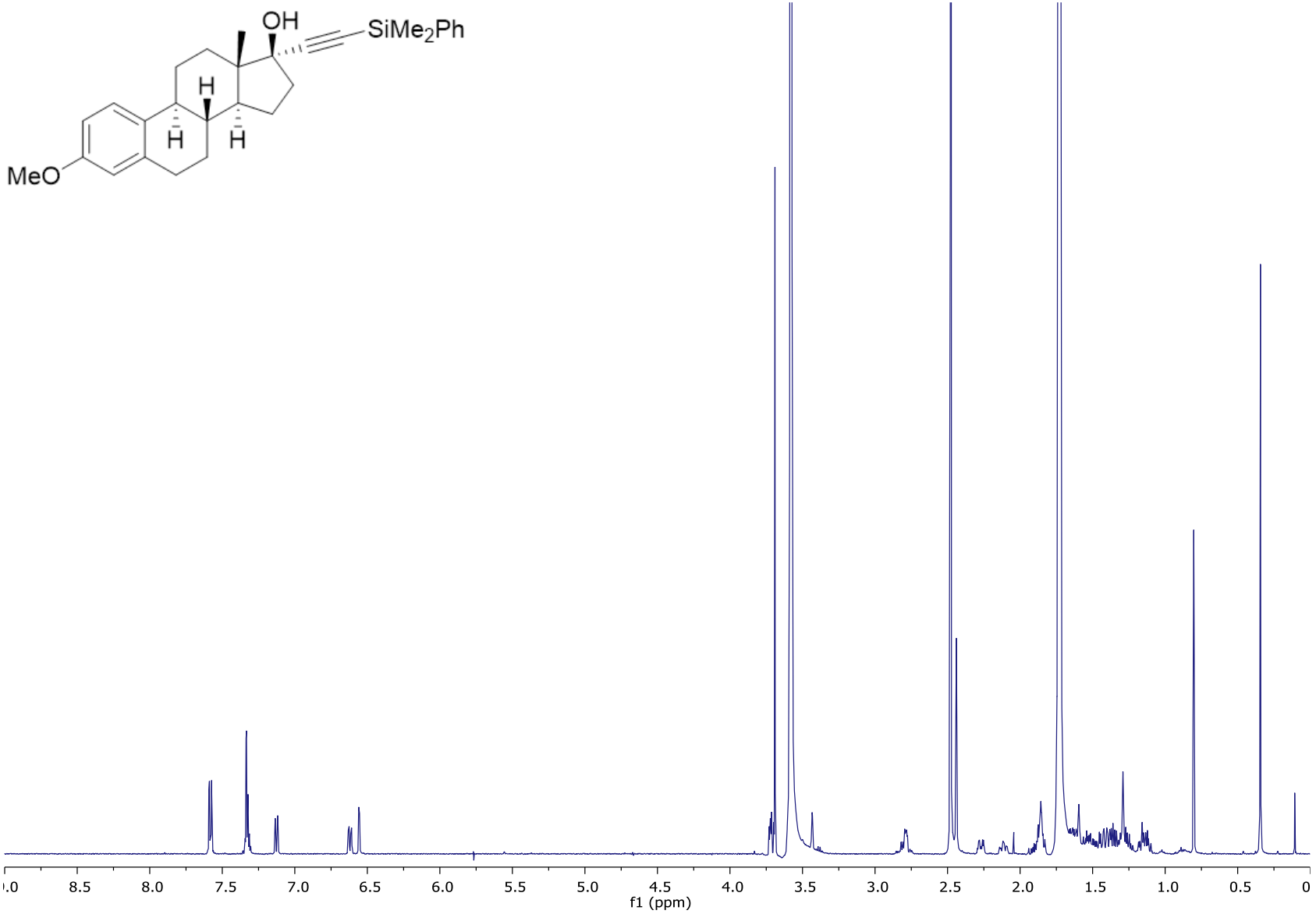
^{13}C NMR (126 MHz, $CDCl_3$) of compound **53.**



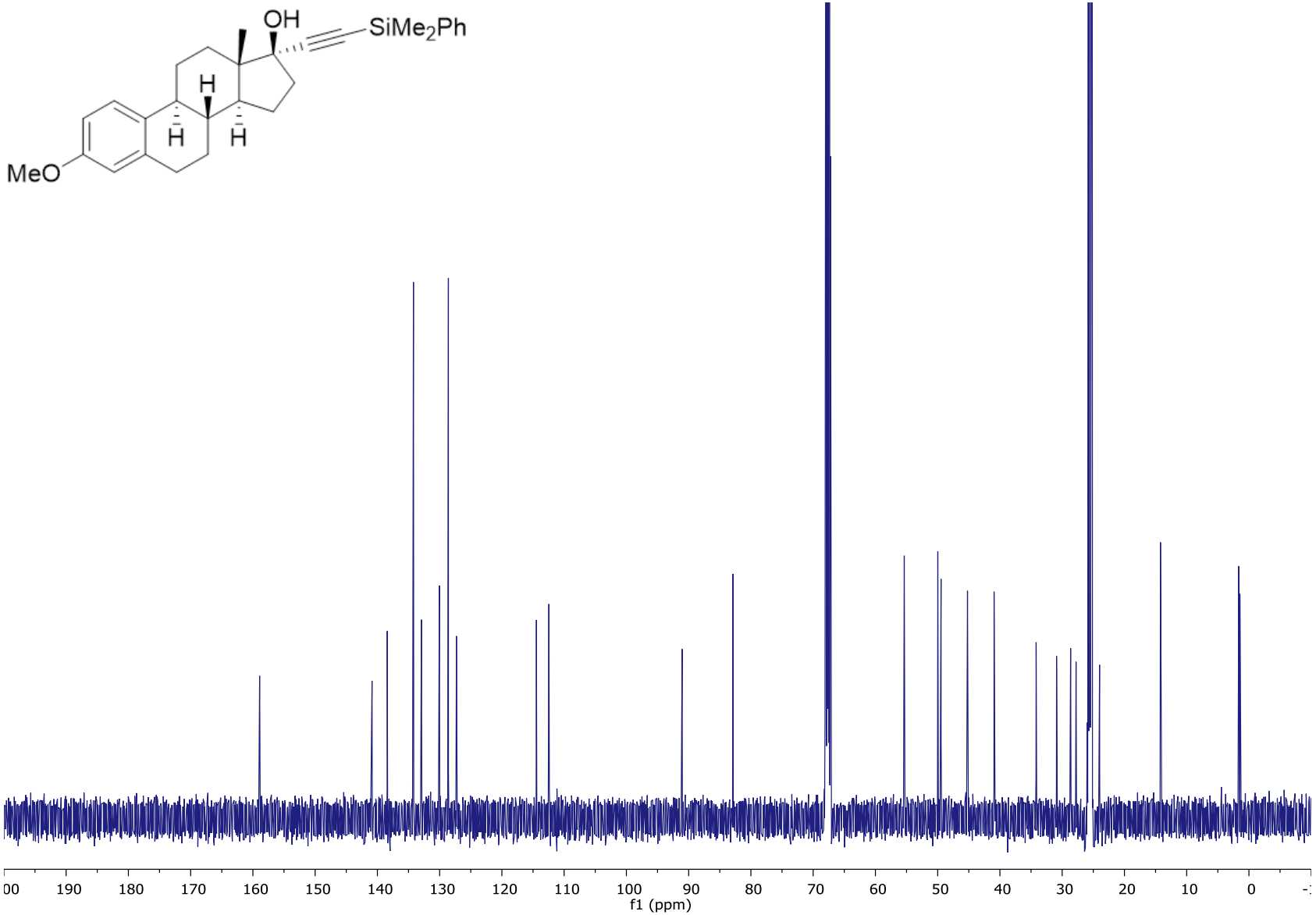
^{1}H NMR (500 MHz, THF-d_8) of compound **54a.**



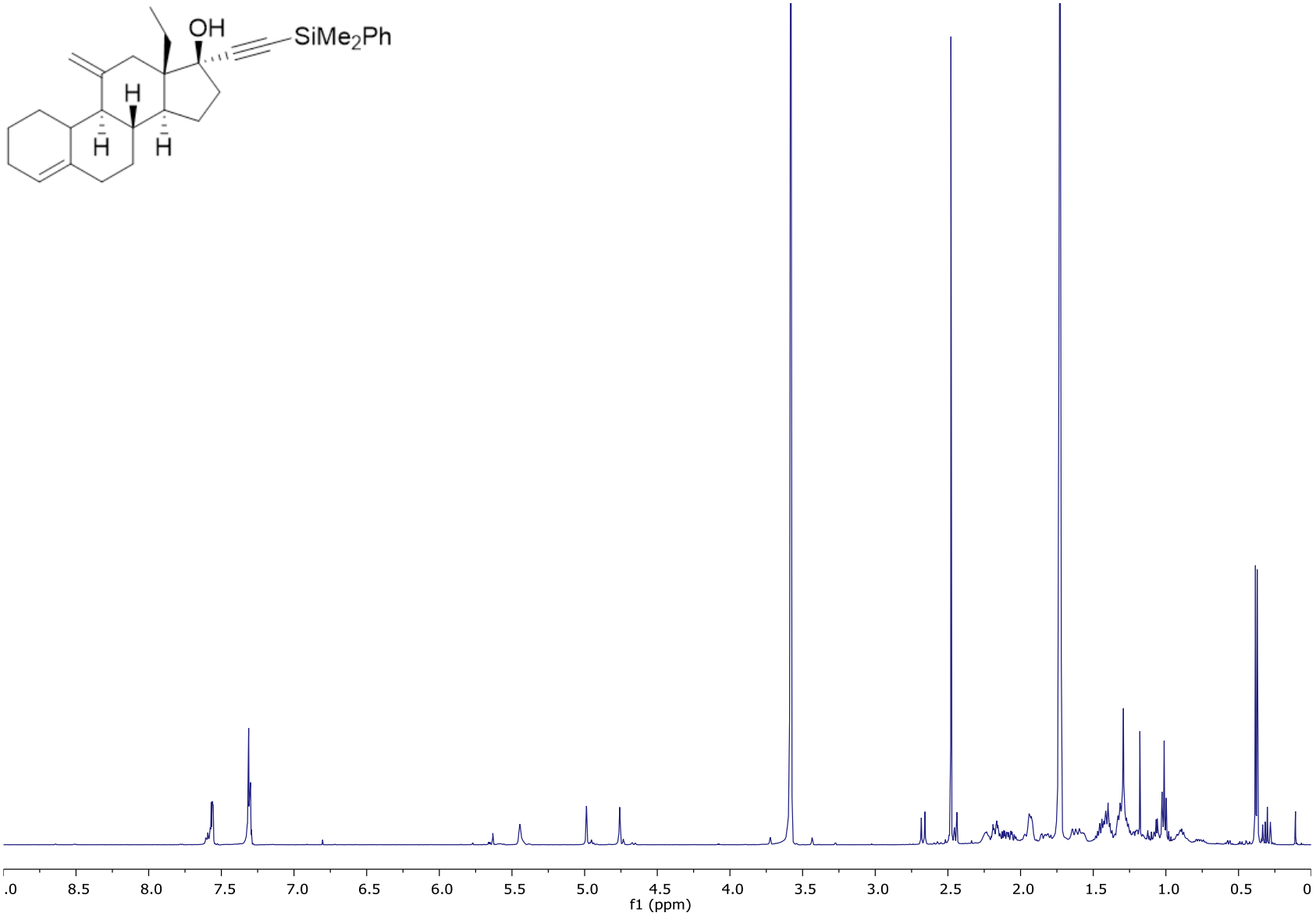
^{13}C NMR (126 MHz, THF-d_8) of compound **54a.**



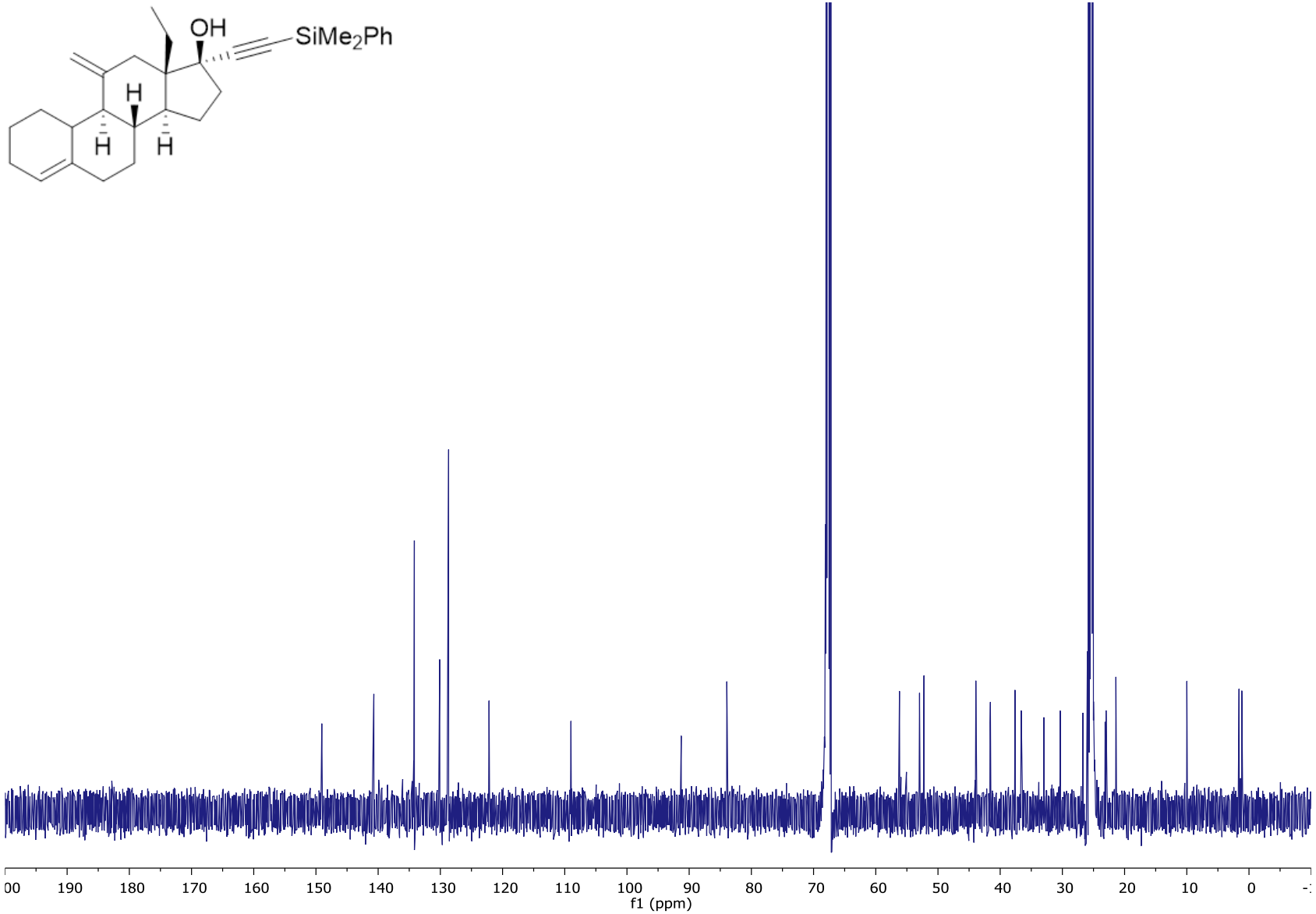
^{1}H NMR (500 MHz, THF-d_8) of compound **54b.**



^{13}C NMR (126 MHz, THF-d_8) of compound **54b.**



^{1}H NMR (500 MHz, THF-d_8) of compound **55.**



^{13}C NMR (126 MHz, THF-d_8) of compound **55.**

Acknowledgements.

I am grateful especially to Kerry Betz who did significant work in the alkali metal hydroxide–catalyzed C(*sp*)–H silylation, assisting me greatly in moving this project forward. During this time, she significantly improved her experimental abilities and demonstrated independence, making very important contributions along the way. I'm extremely proud of her and grateful to her for assisting me in better understanding the scope and limitations of this chemistry. I'm also grateful to David Schuman and Dr. Wen-Bo "Boger" Liu for their experimental assistance and in the writing and editing of the manuscript corresponding to this work. David Schuman also performed the NMR H_2 detection experiments.

Chapter 4

CATALYTIC CROSS-DEHYDROGENATIVE SILYLATION OF ALCOHOLS

Abstract.

We have found a practical, convenient, and general cross-dehydrogenative O–Si bond construction protocol enabled by NaOH-catalyzed coupling of alcohols with hydrosilanes. The reaction is practically convenient and has a broad substrate scope. The chemistry is powerful and selective enough to enable, for example, the silylene protection of even a di-tertiary 1,2- and 1,4-diol in high yield. Due to its convenience, practical utility, and broad scope, this NaOH-catalyzed dehydrocoupling method is expected to be accessible to chemists and non-chemists alike for the synthesis of silyl ethers across the chemical and biological sciences.

Introduction.

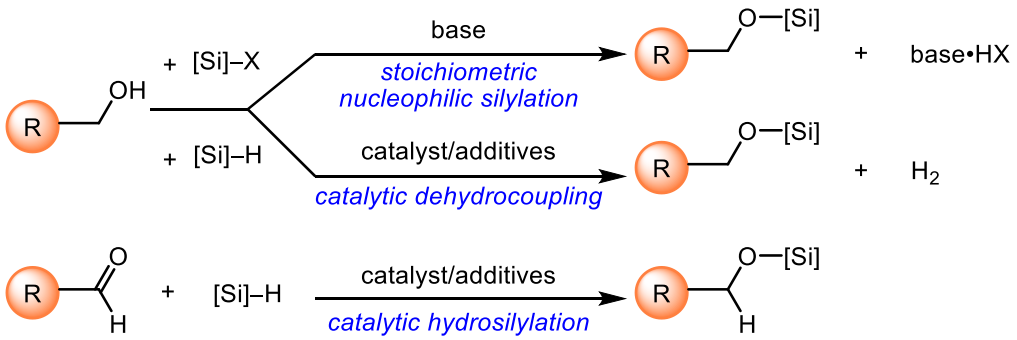
Cross-dehydrogenative bond functionalization reactions (i.e., coupling reactions wherein neither coupling partner has been prefunctionalized and the stoichiometric byproduct is H_2) are valuable from the perspective of atom- and step-economy and in the context of waste minimization and streamlining syntheses. However, they are intrinsically challenging from the perspective of reactivity and selectivity, making practically valuable catalytic and even stoichiometric systems difficult to develop. As a result, cross-dehydrogenative protocols are not commonly encountered. To this point, we had discovered and developed methods for C(sp^2)–H and C(sp^3)–H (Chapter 2) as well as C(sp)–H (Chapter 3) bond silylation reactions enabled by catalysts based on alkaline salts of the alkali metals sodium and potassium. Specifically, the direct C–H silylation of aromatic heterocycles with hydrosilanes catalyzed by potassium *tert*-butoxide (KO*t*-Bu) (Chapter 2) and the NaOH- and KOH–catalyzed dehydrocoupling of alkynes with hydrosilanes (Chapter 3) were significant observations and could be developed into remarkable synthetic methods. Interestingly, it was during these investigations that we had observed that substrates containing free hydroxy groups were adventitiously silylated under the reaction conditions employed for the C–H silylation. These interesting proofs of concept led me to consider our alkali-metal catalysis concept for the construction of the O–Si bond by dehydrogenative coupling of alcohols and hydrosilanes.

Silyl ethers: synthesis and utility.

The O–Si bond is an important and commonly encountered bond class in the chemical sciences; its value extends well beyond its importance in protecting group chemistries.[144] Indeed, it is implicated as a traceless directing group in organic synthesis,[145] it is encountered in a number of important functional material classes,[146] and the silyl ether functionality has also been implicated in improving the pharmacokinetic properties of pharmaceutically relevant molecules and enhancing drug efficacy.[50,51,147]

Through many decades of synthetic and mechanistic work, a large number of catalytic methods for the construction of O–Si bonds have been developed. In particular, the direct silylation of alcohols by transition metal catalysis,[148] Brønsted and Lewis acids/bases,[149] and catalytic hydrosilylation of carbonyl compounds[150] have been the most commonly employed protocols (**Figure 4.1**).

Figure 4.1. Strategies for the synthesis of silyl ethers.



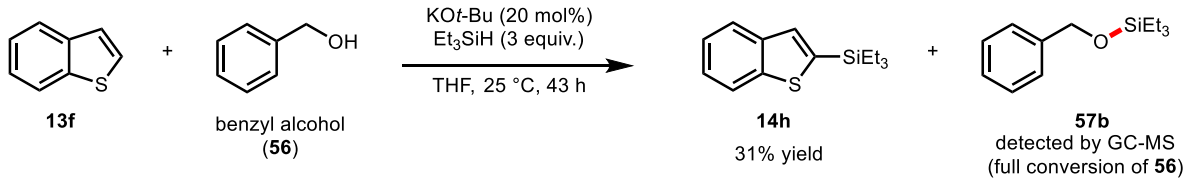
However, despite these decades of work, the most straightforward and generally applied method for the construction of the O–Si bond is the treatment of alcohols with moisture-sensitive chlorosilanes in the presence of nucleophilic catalysts and a base to scavenge the HCl generated.[57a,58a,59,151]

Unfortunately, this classical method can be unsuitable with acid-sensitive substrates and for certain especially challenging silylations such as the silylene protection of 1,2-diols (especially in the cases of hindered systems). In these cases, the use of specialized substrate/silane combinations and particularly reactive systems[152] or toxic electrophilic silicon reagents[153] is necessary. As a result, the development of an effective and convenient O–Si bond construction methodology, which circumvents the production of stoichiometric salt byproducts and avoids the use of toxic or moisture-sensitive electrophilic silicon sources and simultaneously improves the scope in comparison to previous methods, would be of interest and significant practical value to chemists working in a variety of fields. The utility of such a hypothetical method prompted me to investigate this concept further in the context of our developed alkali metal based catalysis.

Observation of silyl ethers in previous investigations

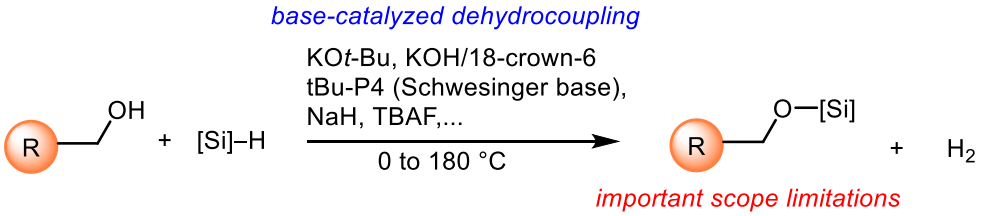
During our prior studies of catalytic C–H silylation using Earth-abundant alkali metal bases, we had observed the fortuitous formation of silyl ethers in certain substrates and contexts. Particulary, during our studies into the direct C–H silylation of aromatic heterocycles with hydrosilanes catalyzed by potassium *tert*-butoxide (KO*t*-Bu) (Chapter 2), a robustness evaluation revealed that an additive compound containing an –OH group (i.e., benzyl alcohol, **56**) was adventitiously silylated under the standard reaction conditions giving silyl ether **57b** (**Scheme 4.1**).

Scheme 4.1. First observation of silyl ether synthesis by dehydrocoupling during robustness evaluation of KO*t*-Bu–catalyzed C–H silylation of heteroarenes (Chapter 2).



This was not entirely unanticipated since base-catalyzed methods for the formation of O–Si bonds by dehydrocoupling with hydrosilanes have been previously explored.[72,154,155,156,157,158] However, base-catalyzed systems reported thus far often use highly basic activators,[72,154,155,] tend to require the use of additives such as crown-ethers to obtain suitable reactivity, [72,158,159,160] and can require unacceptably high temperatures (i.e., >150 °C). From a practical utility perspective, these reports have shown only moderate functional group tolerance with respect to both the alcohol and hydrosilane partner, rendering them generally unsuitable for complex molecule applications.[72,195,161] Fluoride salts have also been shown to catalyze the dehydrocoupling; however, reactions can be energy intensive (i.e., temperatures between 0 °C and 180 °C), require highly polar solvents (e.g., NMP) and are also generally reported with modest substrate scope (**Scheme 4.2**).[149c–e,158]

Scheme 4.2. Previous base-catalyzed and base-mediated strategies in the synthesis of silyl ethers by dehydrocoupling of alcohols with hydrosilanes.



Nevertheless, an efficient base-catalyzed (and ideally fluoride-free) strategy would be attractive, potentially representing a convenient, low-cost, transition metal-free strategy for silyl ether synthesis.

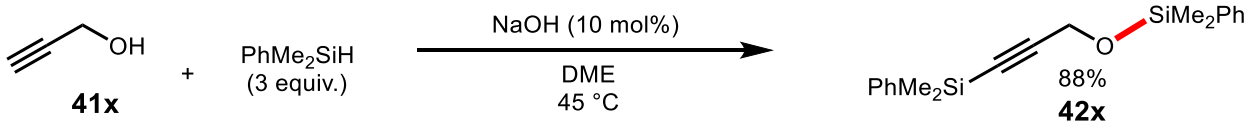
Conversely, the Lewis-acid tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) has also been shown to be a catalyst for the dehydrogenative silylation of alcohols with hydrosilanes.[149b] This method proceeds under mild conditions and has a useful functional group tolerance. However, the presence of Lewis-basic nitrogen functionalities dramatically lowers the reactivity or leads to complete catalyst

deactivation. Moreover, cyclic ethers such as THF derivatives are ring-opened in the course of the reaction except in rare special cases. These issues and others limit the utility of Lewis-acid–catalyzed methods, especially in alkaloid natural product synthesis and the derivatization and manipulation of pharmaceutical targets.

NaOH–catalyzed dehydrocoupling of alcohols and hydrosilanes.

A key discovery in the context of silyl ether formation was made during investigations into the NaOH- and KOH–catalyzed dehydrocoupling of alkynes with hydrosilanes (Chapter 3, **Figure 3.3**). Specifically, while exploring the scope of the C–H silylation reaction using NaOH as the catalyst, we had also observed silyl ether formation in the case of hydroxyl-containing substrates (**Scheme 4.3**).

Scheme 4.3. Discovery of NaOH–catalyzed dehydrosilylation of an alcohol with a hydrosilane.



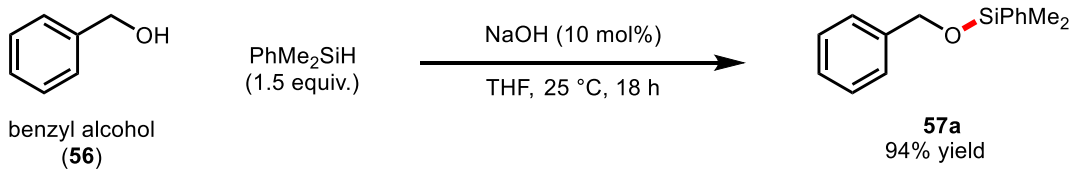
As discussed, base-catalyzed methods for silyl ether synthesis have been known for many years, but have required rather forcing conditions or have been limited in scope. In contrast, this reaction was occurring under the catalytic action of NaOH alone under convenient conditions. Nevertheless, these initial proof of concept observations suggested that a cross-dehydrogenative O–Si bond coupling reaction that employs a mild and inexpensive catalyst, operates under mild conditions in the absence of costly additives, and shows superior functional group tolerance to prior strategies. We surmised that a sterically unencumbered, mildly basic alkali metal–based catalyst like NaOH would

potentially circumvent the issues encountered with prior O–Si bond formation strategies, such as improving tolerance to acid- and nucleophile-sensitive functionalities in the alcohol substrate and greatly broadening the scope of the hydrosilane. If successful, this would potentially lead to a convenient cross-dehydrogenative O–Si bond construction method suitable for application across the chemical sciences including natural product total synthesis, medicinal chemistry, and materials science. Thus, inspired by the work of others and encouraged by our earlier results in silylation catalysis, we became engaged in evaluating the effectiveness of NaOH as a catalyst for silyl ether formation from alcohols and hydrosilanes.

Evaluation of the hydrosilane scope

Unfunctionalized benzyl alcohol was chosen as the model substrate along with $PhMe_2SiH$ as the model hydrosilane to evaluate the reactivity. Gratifyingly, the reaction proceeded in THF as the solvent with 10 mol % NaOH as the catalyst to afford 94% yield of the desired benzyl silyl ether **57a** at ambient temperature (**Figure 4.2**). We determined, given the success of this very simple catalytic system, that an optimization exercise was not required prior to proceeding to the exploration of silane and substrate scope.

Figure 4.2. NaOH–catalyzed dehydrosilylation of benzyl alcohol with $PhMe_2SiH$.



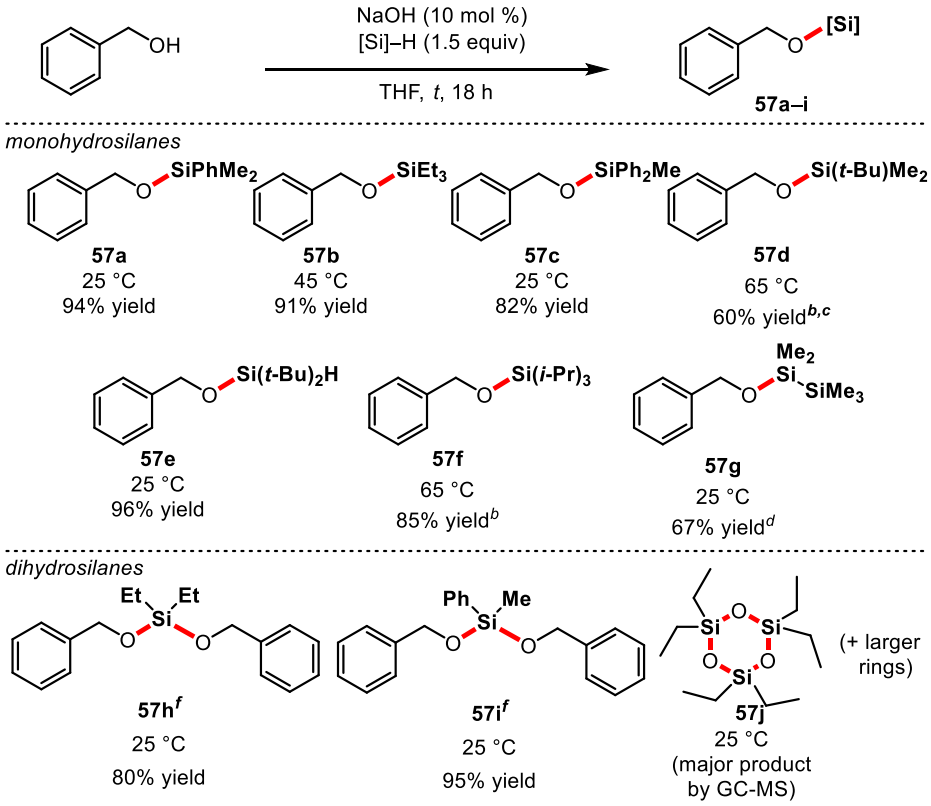
Again, although we were aware at the outset of these studies that many methods existed for synthesizing silyl ethers, this particular result represented perhaps the most convenient and straightforward synthetic method for the construction of O–Si bonds to date. Although these

reactions are practically performed under conditions strictly excluding moisture, the dehydrosilylation reaction can be performed without regard for air and moisture with an identical 94% yield. In these cases, however, siloxane $(PhMe_2Si)_2O$ is generated as a byproduct, likely arising from the double silylation of adventitious H_2O.

We were aware that a general method for making silyl ethers would have to be amenable to a very large variety of hydrosilane partners, providing the opportunity for tuning the steric and electronic environment about the O–Si bond in the product. It would thus be insufficient if only $PhMe_2SiH$ was a competent hydrosilane, for example. With these considerations in mind, we next proceeded to evaluate the scope of the hydrosilane. Fortunately, we observed that a wide array of hydrosilanes were amenable to the NaOH-catalyzed reaction (**Figure 4.3**). Monohydrosilanes with small- and medium-sized substituents including alkyl (**57b)** and aryl (**57a** and **57c**) moieties gave the corresponding silyl ethers in high yields. The larger TBDMS and TIPS groups could also be introduced yielding **57d** and **57f** respectively; however, that the use of DMF as a co-solvent was necessary to obtain good yields in these cases.[162] These results were encouraging, demonstrating that products containing silyl functions that are typically employed in protecting group chemistry and other applications could also be introduced by our NaOH–catalyzed dehydrocoupling method. The use of the bulky dihydrosilane di-*tert*-butyl silane led to efficient mono-silylation generating **57e** in high yield; however, the use of less sterically hindered dihydrosilanes led exclusively to Si-tethered species **57h** and **57i** at ambient temperature. The cross-dehydrogenative O–Si coupling tolerates even highly sensitive disilanes such as $H–Si_2(CH_3)_5$ leading to product **57g** and could thus be useful for appending polysilanes onto small molecules and potentially surfaces for materials science applications.[128,129] Thus, it becomes clear that this NaOH–catalyzed protocol not only successfully

introduces hydrosilanes that are typically installed by other methods, but also enables the introduction of other species such as H–$Si_2(CH_3)_5$, which cannot be installed by other methods due

Figure 4.3. Evaluation of the hydrosilane scope.[a,e]



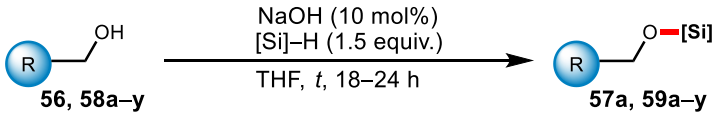
[a]Reactions performed with 0.5 mmol of starting material and 0.5 mL of THF at the prescribed temperature. [b]A 1:1 mixture of DMF:THF was used as the solvent. [c]3.0 equiv. of hydrosilane and 20 mol % NaOH. [d]The reaction is conducted for 24 h. [e]Yield of isolated material after purification. [f] Yield based on a theoretical maximum of 0.25 mmol of Si-tethered product.

to the extremely sensitive Si–Si bond in this substrate. Indeed, employing KOH or KO*t*-Bu with this silane leads to its decomposition and results in no productive silylation occurring. Finally, the reaction of diethylsilane with water under NaOH catalysis results in the formation of cyclic siloxanes, with trisiloxane **57j** being the major product (by GC-MS analysis). Such cyclic siloxane products are precursors to valuable polysiloxanes.[163]

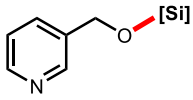
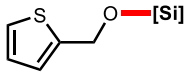
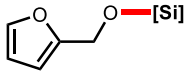
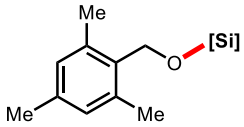
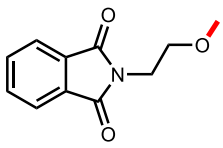
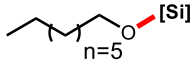
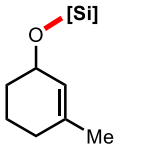
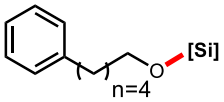
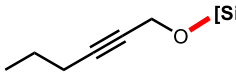
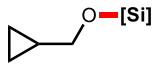
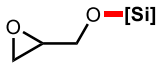
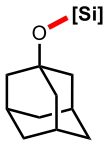
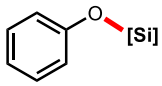
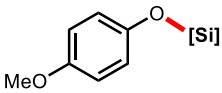
Evaluation of the alcohol scope

Having determined that the method enables the cross-dehydrogenative silyl ether formation to occur with a wide range of hydrosilanes, we next proceeded to explore the scope of the alcohol substrate.

Table 4.1. Investigation of the scope of the alcohol partner.[a]



56, 58a–y → **57a, 59a–y**

Entry	Silylated Product	T (°C)	Yield
1	R = H	25	**57a (94%)**
2	R = 4-F	25	**59a (79%)**
3	R = 4-Br	65	**59b (91%)**
4	R = 4–NO_2	65	**59c (71%)**
5	R = 4-CO_2Me[f]	65	**59d (84%)**[b]
6	R = 4-OMe	25	**59e (87%)**
7		25	**59f (97%)**
8		25	**59g (96%)**
9		45	**59h (87%)**
10		65	**59i (92%)**[b]
11		65	**59j (62%)**
12		25	**59k (84%)**
13		45	**59l (92%)**[b]
14		45	**59m (98%)**
15		45	**59n (86%)**
16		65	**59o (70%)**
17		25	**59p (72%)**
18		65	**59q (96%)**
19		65	**59r (89%)**[c]
20		65	**59s (82%)**

[a]Reactions performed with 0.5 mmol of starting material and 0.5 mL of THF at the prescribed temperature. [b]2:3 DMF:THF used as the solvent. [c]3.0 equiv. hydrosilane, 20 mol % NaOH, DME [1.0M] solvent. [Si]= $PhMe_2SiH$. Yields are of isolated material after purification.

Once again, we were pleased to observe that a wide variety of hydroxyl-containing small molecules proved to be excellent substrates in this reaction (**Table 4.1**). The NaOH-catalyzed cross-dehydrogenative coupling is amenable to substrates containing aromatic (Table 1, entries 1–11, 14, 19, and 20) as well as aliphatic (entries 12, 13, 15–18) moieties. The reaction proceeds well in the presence of arenes bearing halides (entries 2 and 3), nitro- (entry 4), ether (entry 6), and alkyl (entry 10) functionalities leading to the corresponding silyl ethers in generally high yields.

Electron rich aromatic heterocycles (entries 8 and 9) are likewise excellent substrates for the dehydrocoupling providing the corresponding silyl ethers in high yield. A 2° allylic alcohol (entry 13) and a 1° propargylic alcohol (entry 15) also react well, with no reduction or hydrosilylation detected. Cyclopropanes are also tolerated (entry 16). Functionalities that deactivate organic and organometallic Lewis-acid catalysts such as pyridines (entry 7) and those that are acid- and nucleophile sensitive such as an epoxide (entry 17) are silylated in 97% and 72% yield respectively. The 3° alcohol 1-adamantol (entry 18) also undergoes dehydrosilylation affording the silyl ether product in excellent yield. We were surprised to find that functionalities such as an aromatic methyl ester (entry 5)[164] and a phthalimide (entry 11),[165] which are known to readily undergo hydrosilylation or direct reduction in the presence of mixtures comprising Lewis bases and hydrosilanes, react well under the reaction conditions with little (5–7%) hydrosilylation detected only in the latter case. Phenols are likewise silylated readily (entries 19 and 20). Although the broad scope observed in this transformation is valuable in its own right, it is especially encouraging that substrates that are challenging to silylate under competing systems are by this method silylated cleanly and with good yields.

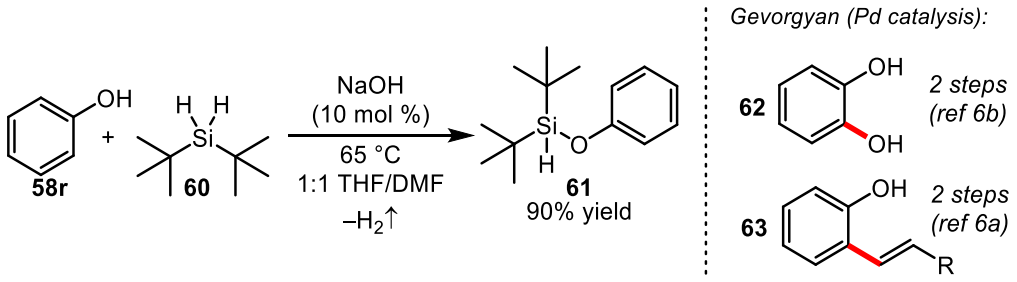
A number of mechanistic pathways for Lewis-base activation of silanes in the context of related dehydogenative couplings have been proposed.[166,167] Most recently Oestreich and co-workers

investigated the mechanism of a related dehydrogenative silyl ether synthesis using a KO*t*-Bu-based system.[15c] In that insightful study, the authors propose the formation of a key pentacoordinate potassium silicate by interaction of KO*t*-Bu with the hydrosilane. An analogous activation mode is likely to also be occurring in the title system.

Synthetic applications of the NaOH-catalyzed dehydrogenative silyl ether synthesis

With a scope of substrates established, we turned to employ our NaOH-catalyzed method to the synthesis of silyl ethers that could be used in directing group chemistry and cross-coupling reactions. For example, the reaction of phenol (**58r**) with the bulky and commercially available di-*tert*-butylsilane **60** with 10 mol % NaOH furnishes the corresponding di-*tert*-buylhydrosilyl ether **61** in high yield and without undesirable double activation of the Si–H bond (**Figure 4.4**). Gevorgyan has reported that silane **61** is elaborated by palladium-catalyzed C–H functionalization reactions

Figure 4.4. Applications to directing group chemistry.[a,b]



[a]Reaction performed with 0.5 mmol of starting material and 0.5 mL of THF. [b]Yield of isolated material after purification.

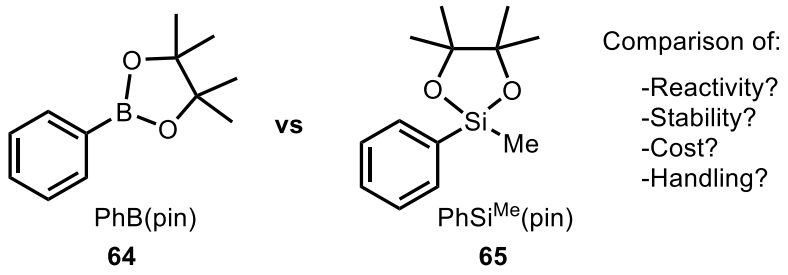
such as *ortho*-oxidation to generate catechols (**Figure 4.4**, **61**→**62**)[145b] and *ortho*-alkenylation to access α-hydroxy styrenes (**61**→**63**) via the corresponding silanol.[145a]

Given the importance of heteroatom-substituted arylsilanes in C–C and C–X bond-forming reactions,[57a,58a,59,166c,168] we sought to employ the catalytic O–Si bond construction method for the

expedient and cost-efficient synthesis of novel cross-coupling reagents. [57a,58a,59 168] Toward this aim, we aimed to construct the silicon analogue of the aryl boronic acid pinacol ester PhB(pin): PhSi^{Me}(pin) (**Scheme 4.5**; compare **64** and **65**) where Me is chosen as a non-transferrable group, and evaluate its suitability as an aryl transfer reagent. This would be beneficial given the increased abundance and lower cost of silicon relative[58b,69a,168,] and the potential for improved stability or overall utility of the silicon reagent.[54,168]

However, one-step preparation of the proposed silicon-based aryl transfer reagent **65** would involve a silylene protection of a 1,2-diol, which has proven challenging, especially in the case of sterically hindered diols such as pinacol even using standard electrophilic silicon sources (i.e., [Si]–Cl).[152,153,160,169,170] This is normally due to either poor cyclization reactivity, uncontrollable oligomerization, or rearrangements, all of which are known to occur.[152,153,160] As a result, and to the best of our knowledge, this cyclic siloxane compound has only been prepared by two strategies:

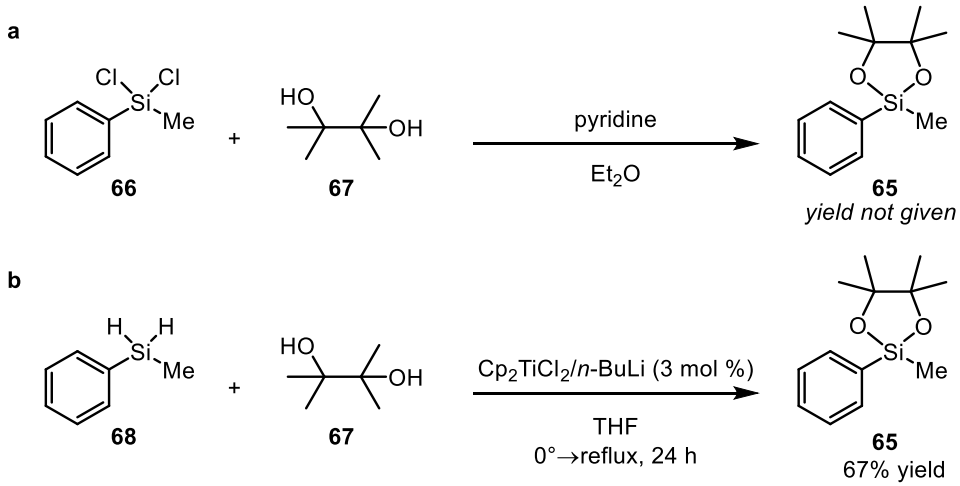
Figure 4.5. Contemplative comparison between PhB(pin), the common synthetic reagent, and a newly hypothesized silicon analogue: PhSi^{Me}(pin).



refluxing pinacol **67** in THF for 24 h with a) the dichlorosilane **66** in the presence of stoichiometric pyridine (**Figure 4.6a**), the yield was not reported[169] or b) the dihydrosilane **68** in the presence of a catalytic quantity of Cp_2TiCl_2/*n*-BuLi providing the product in 67% yield. (**Figure 4.6b**).[170] In both cases, the product was not fully characterized. In the latter case, though a serviceable yield is obtained, the harshness of the conditions and reagents employed limits the variety of substitution on

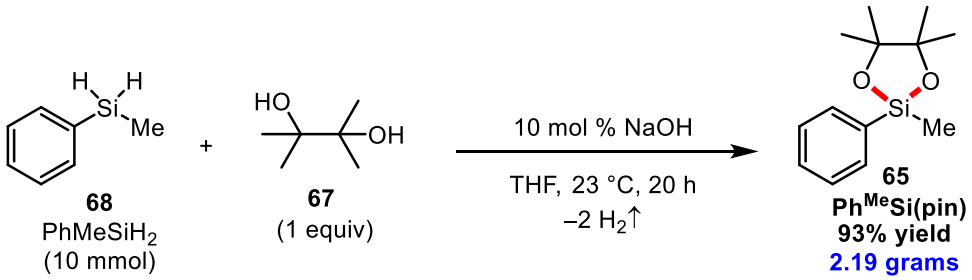
the aryl ring that would be tolerated if functionalized variants beyond phenyl would be desired. The conditions would additionally be potentially inconvenient to employ, lowering utility and preventing rapid adoption of the method.

Figure 4.6. Previous strategies toward PhSi^{Me}(pin).



We therefore saw an opportunity here to explore the suitability of our method for the silylene protection of challenging diols and simultaneously evaluate its ability to construct valuable molecules that could potentially have new and interesting downstream reactivity profiles.

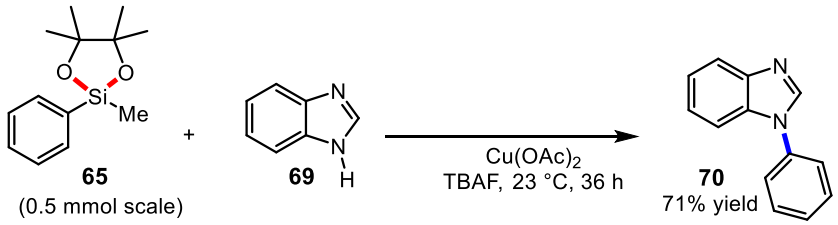
Scheme 4.4. Gram scale synthesis of PhSi^{Me}(pin) by a NaOH–catalyzed silylene protection strategy



Toward this end, combining the commercially available $PhMeSiH_2$ **68** with the di-tertiary 1,2-diol pinacol **67** in a 1:1 stoichiometry resulted in the immediate and vigorous evolution of hydrogen upon addition of the NaOH catalyst.

Remarkably, the reaction is complete in 20 hours at ambient temperature, giving a high yield (2.19 grams, 93% yield) of the corresponding colourless liquid PhSi^{Me}(pin) **65** (**Scheme 4.4**, **68**→**65**) after purification by distillation. No oligomers, polymers, or uncyclized products were detected. This is a marked improvement on previous strategies. With this compound in hand, its ability to transfer the phenyl moiety bound to silicon in a Hiyama-type cross-coupling reaction could finally be investigated.[168,171] To test this, the PhSi^{Me}(pin) reagent was treated with benzimidazole (**69**), $Cu(OAc)_2$, and TBAF and the mixture was stirred at ambient temperature for 36 h to provide the desired *N*-arylation product **70** in 71% yield (**Scheme 4.5**).[65,172]

Scheme 4.5. A new aryl transfer reagent: N-arylation of benzimidazole with PhSi^{Me}(pin).[a]



[a]Cu-mediated reaction performed on 0.5 mmol scale. Yields are of isolated material after purification.

Conclusion.

During our investigation into the C(sp^2)–H silylation of heteroarenes and the C(sp)–H silylation of terminal alkynes, we observed that hydroxyl-containing substrates underwent silylation not only at the C–H bond, but also on the hydroxyl group, forming a silyl ether. The work in this chapter detailed our progress in extending this proof of principle reaction into a mild and general cross dehydrogenative O–Si bond construction protocol using simple NaOH as the catalyst. The reaction is convenient to perform under simple conditions using THF (or in some cases 1,2-DME) as the solvent and has been demonstrated on 10 mmol scale. Certain challenging substrate/silane combinations benefit from the use of THF/DMF mixtures to obtain high yields and/or to provide reactivity in a suitable timeframe. The scope of the hydrosilane and alcohol partners is excellent, allowing for the preparation of silyl ethers – many of which include sensitive functionalities on silicon or on the substrate – that are inaccessible by prior methods. The products are useful as protected alcohols for a variety of applications and the method itself is potentially valuable in its own right for the construction of O–Si-containing materials, silyl ether derivatives of pharmaceutical substances, or lead compounds containing –OH functionalities. A convenient and high-yielding catalytic silylene protection of pinacol is shown, generating the distillable liquid $Ph^{Me}Si(pin)$ in a single step. This new organosilicon reagent is able to transfer its phenyl substituent in a Cu-mediated *N*-arylation reaction, potentially providing new opportunities and strategies for Si-based cross-coupling chemistry and other transformations.

Experimental and analytics.

General information

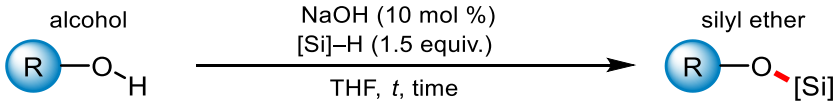
Unless otherwise stated, reactions were performed in oven-dried brand-new Fisherbrand scintillation vials flushed with argon or in flame-dried Schlenk flasks under argon connected on a Schlenk line using dry, degassed solvents and brand-new stirring bars. Solvents were dried by passage through an activated alumina column under argon.[43] Reaction progress was monitored by thin-layer chromatography (TLC), GC-MS, or GC-FID analyses. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, phosphomolybdic acid, or $KMnO_4$ staining. Silicycle SiliaFlash P60 Academic Silica gel (particle size 40–63 nm) was used for flash chromatography. ^{1}H NMR spectra were recorded on a Varian Inova 500 MHz spectrometer in $CDCl_3$, THF-d_8, or Benzene-d_6 and are reported relative to residual solvent peak at δ 7.26 ppm, δ 3.58 ppm, or δ 7.16 ppm respectively. ^{13}C NMR spectra were recorded on a Varian Inova 500 MHz spectrometer (126 MHz) in $CDCl_3$, THF-d_8, or Benzene-d_6 and are reported relative to residual solvent peak at δ 77.16 ppm, δ 67.21 ppm, or δ 128.06 ppm respectively. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septet, m = multiplet, br s = broad singlet, br d = broad doublet, app = apparent. Data for ^{13}C NMR are reported in terms of chemical shifts (δ ppm). IR spectra were obtained on a Perkin Elmer Spectrum BXII spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). GC-FID analyses were obtained on an Agilent 6890N gas chromatograph equipped with a HP-5 (5%-phenyl)-methylpolysiloxane capillary column (Agilent). GC-MS analyses were obtained on an Agilent 6850 gas chromatograph equipped with a

HP-5 (5%-phenyl)-methylpolysiloxane capillary column (Agilent). High resolution mass spectra (HRMS) were acquired from the California Institute of Technology Mass Spectrometry Facility. Silanes were purchased from Aldrich and distilled before use. NaOH was purchased from Aldrich (semiconductor grade, pellets, 99.99% trace metals basis) and was pulverized (mortar and pestle) and heated (150 °C) under vacuum prior to use. Powdered and vacuum-dried (as above) ACS grade ≥97% NaOH from Aldrich gives identical results. Alcohol and phenol substrates were purchased from Aldrich, TCI, or Acros.

General observations

THF and DME proved to be suitable solvents. The addition of DMF to reaction mixtures as a co-solvent enabled the silylation to occur in challenging cases; several substrates failed to silylate without the addition of DMF. See characterization data for a comprehensive view of all substrates that required addition of DMF. No product was observed in the absence of catalyst.

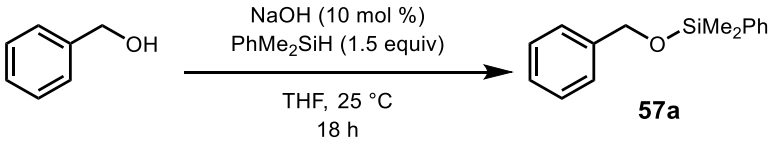
General procedure for NaOH–catalyzed dehydrocoupling of alcohols and hydrosilanes



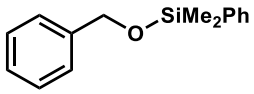
To a hot, oven-dried 2 dram scintillation vial equipped with a magnetic stirring bar, NaOH (0.05 mmol, 10 mol %) was added and the vial was purged with argon until cool. Alcohol (0.5 mmol, 1 equiv) was then added under a steady stream of argon, followed by solvent (0.5 mL) and silane (0.75 mmol, 1.5 equiv). The vial was then sealed and the mixture was stirred at the indicated temperature for the indicated time. After the reaction was complete, the reaction mixture was diluted with diethyl ether (2 mL), filtered through a short pad of silica gel, and concentrated under reduced pressure.

Volatiles were removed under high vacuum and the resultant material was purified by silica gel flash chromatography, if necessary, to give the desired silyl ether product.

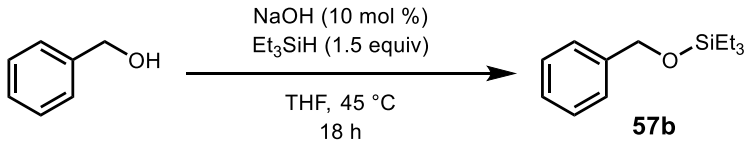
Characterization



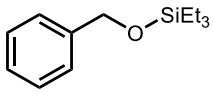
57a



(Benzyloxy)dimethyl(phenyl)silane 57a: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), benzyl alcohol (54 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 25 °C for 18 h. The desired product **57a** (113.9 mg, 94% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.53 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.66 (m, 2H), 7.48 – 7.42 (m, 3H), 7.40 – 7.35 (m, 4H), 7.30 (dddd, J = 6.7, 6.2, 3.1, 1.7 Hz, 1H), 4.77 (s, 2H), 0.49 (s, 6H). This compound has been previously characterized.[173]

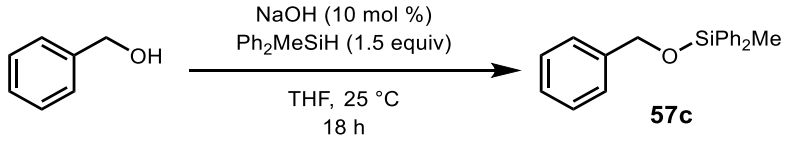


57b

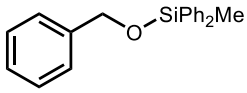


(Benzyloxy)triethylsilane 57b: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), benzyl alcohol (54 mg, 0.5 mmol, 1.0 equiv), Et_3SiH (87 mg, 120 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 45 °C for 18 h. The

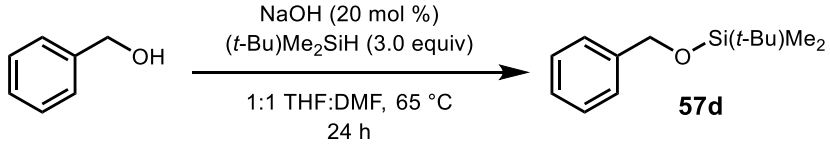
desired product **57b** (101.2 mg, 91% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.27 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.31 (m, 4H), 7.27 – 7.23 (m, 1H), 4.75 (s, 2H), 1.00 (t, J = 8.0 Hz, 9H), 0.67 (q, J = 7.9 Hz, 6H). This compound has been previously characterized.[174]



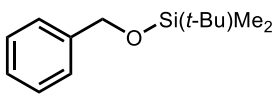
57c



(Benzyloxy)(methyl)diphenylsilane 57c: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), benzyl alcohol (54 mg, 0.5 mmol, 1.0 equiv), Ph_2MeSiH (149 mg, 150 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 25 °C for 18 h. The desired product **57c** (129.4 mg, 85% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.50 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (p, J = 7.7, 7.0 Hz, 3H), 7.69 – 7.58 (m, 2H), 7.54 – 7.37 (m, 10H), 4.90 (dt, J = 13.7, 3.0 Hz, 2H), 0.77 (dt, J = 14.1, 2.9 Hz, 3H). This compound has been previously characterized.[175]

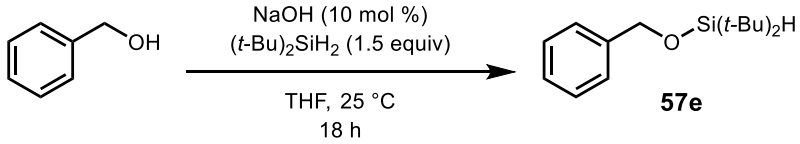


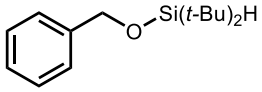
57d



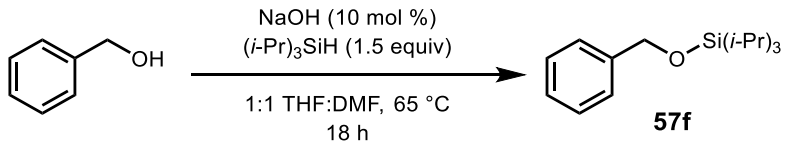
(Benzyloxy)(tert-butyl)dimethylsilane 57d: The general procedure was followed. The reaction was performed with NaOH (4.0 mg, 0.1 mmol, 20 mol %), benzyl alcohol (54 mg, 0.5 mmol, 1.0

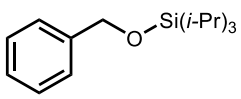
equiv), (*t*-Bu)Me_2SiH (87 mg, 124 μL, 1.5 mmol, 3.0 equiv), 0.25 mL dimethylformamide (DMF) and 0.25 mL of tetrahydrofuran (THF) at 65 °C for 24 h. The desired product **57d** (66.2 mg, 60% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.42 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, J = 4.6 Hz, 4H), 7.28 – 7.24 (m, 1H), 4.78 (d, J = 0.6 Hz, 2H), 0.98 (s, 9H), 0.14 (s, 6H). This compound has been previously characterized.[176]



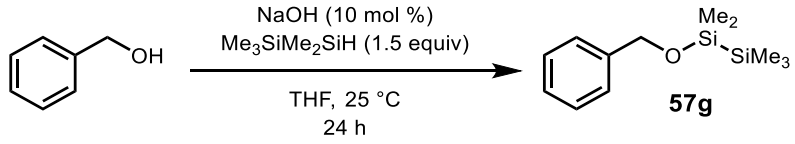


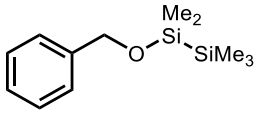
(Benzyloxy)di-*tert*-butylsilane 57e: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), benzyl alcohol (54 mg, 0.5 mmol, 1.0 equiv), (*t*-Bu)$_2SiH_2$ (108 mg, 148 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 25 °C for 18 h. The desired product **57e** (120.2 mg, 96% yield) was obtained as a colorless oil after removal of volatiles under high vacuum (45 mtorr) for 2 hours. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.34 (m, 4H), 7.29 – 7.25 (m, 1H), 4.88 (d, J = 0.7 Hz, 2H), 4.12 (s, 1H), 1.05 (s, 18H). This compound has been previously characterized.[177]



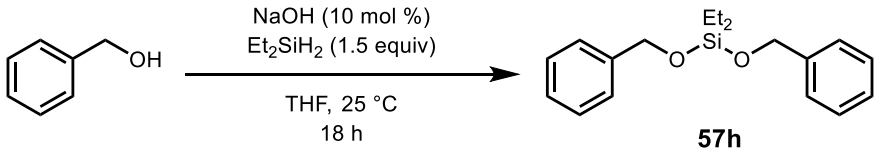


(Benzyloxy)triisopropylsilane 57f: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), benzyl alcohol (54 mg, 0.5 mmol, 1.0 equiv), (*i*-Pr)$_3$SiH (119 mg, 154 μL, 0.75 mmol, 1.5 equiv), 0.25 mL dimethylformamide (DMF), and 0.25 mL of tetrahydrofuran (THF) at 65 °C for 18 h. The desired product **57f** (112.4 mg, 85% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.52 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 4H), 7.27 – 7.23 (m, 1H), 4.87 (d, J = 1.5 Hz, 2H), 1.26 – 1.17 (m, 3H), 1.15 – 1.11 (m, 18H). This compound has been previously characterized.[178]

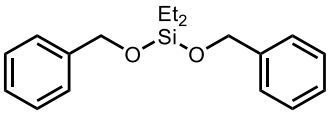




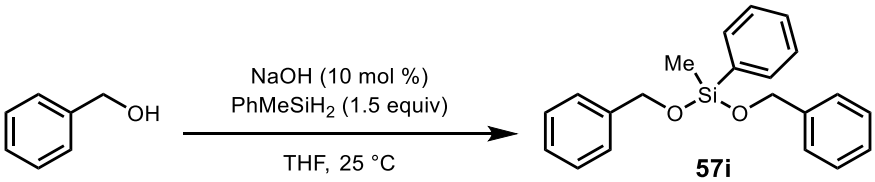
1-(Benzyloxy)-1,1,2,2,2-pentamethyldisilane 57g: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), benzyl alcohol (54 mg, 0.5 mmol, 1.0 equiv), Me_5Si_2H (99 mg, 137 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 25 °C for 24 h. Concentration of the reaction mixture and purification of the resulting residue via Kugelrohr distillation (120 mTorr, 60 °C) gave 79.9 mg (67% yield) of **57g** as a colorless oil. ^{1}H NMR (500 MHz, THF-d_8) δ 7.31 – 7.24 (m, 4H), 7.21 – 7.15 (m, 1H), 4.68 (q, J = 0.7 Hz, 2H), 0.23 (s, 6H), 0.10 (s, 9H); ^{13}C NMR (126 MHz, THF-d_8) δ 142.61, 128.96, 127.71, 127.01, 66.02, -0.52, -1.79. IR (Neat Film NaCl) 3363, 3088, 3065, 3030, 2952, 2893, 1595, 1495, 1453, 1376, 1259, 1246, 1207, 1091, 1067, 1026, 835, 803, 766, 729, 695, 655, 617 cm^{-1}; HRMS (EI+) calc'd for $C_{12}H_{23}OSi_2$ [M+H]: 239.1288, found 239.1295.



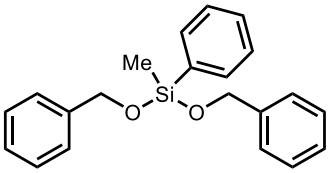
57h



Bis(benzyloxy)diethylsilane 57h: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), benzyl alcohol (108 mg, 1.0 mmol, 1.0 equiv), Et_2SiH_2 (49 mg, 71 μL, 0.55 mmol, 0.55 equiv), and 1.0 mL of tetrahydrofuran (THF) at 25 °C for 18 h. The desired product **57h** (120.8 mg, 80% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f =0.43 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, J = 4.4 Hz, 8H), 7.31 – 7.26 (m, 2H), 4.82 (s, 4H), 1.05 (t, J = 7.9 Hz, 6H), 0.76 (q, J = 8.0 Hz, 4H). This compound has been previously characterized.[179]

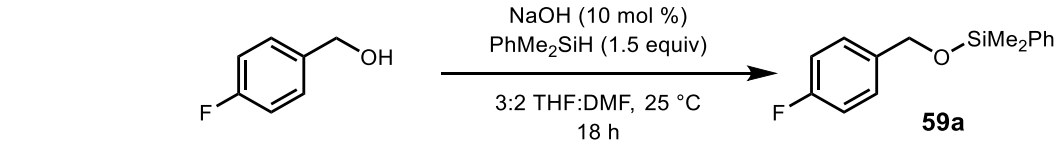


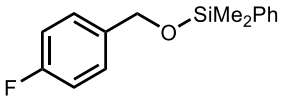
57i



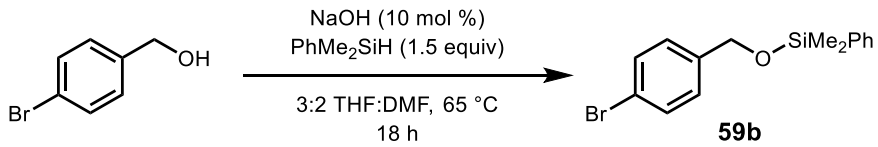
Bis(benzyloxy)(methyl)(phenyl)silane 57i: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), benzyl alcohol (108 mg, 1.0 mmol, 1.0 equiv), $MePhSiH_2$ (67 mg, 76 μL, 0.55 mmol, 0.55 equiv), and 1.0 mL of tetrahydrofuran (THF) at 25 °C for 18 h. The desired product **57i** (158.8 mg, 95% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.44 (5% EtOAc in hexanes); ^{1}H NMR

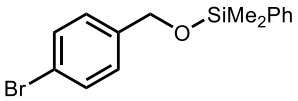
(500 MHz, $CDCl_3$) δ 7.76 (dd, J = 7.9, 1.5 Hz, 2H), 7.49 – 7.43 (m, 3H), 7.39 – 7.37 (m, 8H), 7.33 – 7.28 (m, 2H), 4.91 – 4.82 (m, 4H), 0.50 (s, 3H). This compound has been previously characterized.[180]



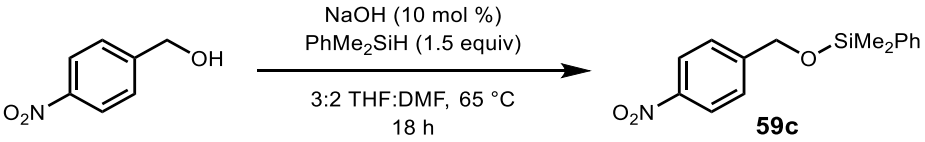


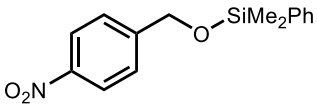
((4-Fluorobenzyl)oxy)dimethyl(phenyl)silane 59a: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), 4-fluorobenzyl alcohol (63 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), 0.2 mL dimethylformamide (DMF) and 0.3 mL of tetrahydrofuran (THF) at 25 °C for 18 h. The desired product **59a** (146.0 mg, 79% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.48 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 – 7.59 (m, 2H), 7.46 – 7.37 (m, 3H), 7.31 – 7.25 (m, 2H), 7.06 – 6.97 (m, 2H), 4.67 (q, J = 0.8 Hz, 2H), 0.45 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.14 (d, J = 244.4 Hz), 137.50, 136.53 (d, J = 2.9 Hz), 133.64, 129.90 , 128.37 (d, J = 8.3 Hz), 128.06, 115.19 (d, J = 21.1 Hz), 64.48, -1.60. IR (Neat Film NaCl) 3440, 3070, 3050, 3022, 2958, 2866, 1605, 1509, 1463, 1427, 1417, 1375, 1294, 1253, 1221, 1155, 1117, 1082, 1014, 826, 789, 741, 700, 645 cm^{-1}; HRMS (EI+) calc'd for $C_{15}H_{16}OSiF$ [(M+H)-H_2]: 259.0955, found 259.0951.





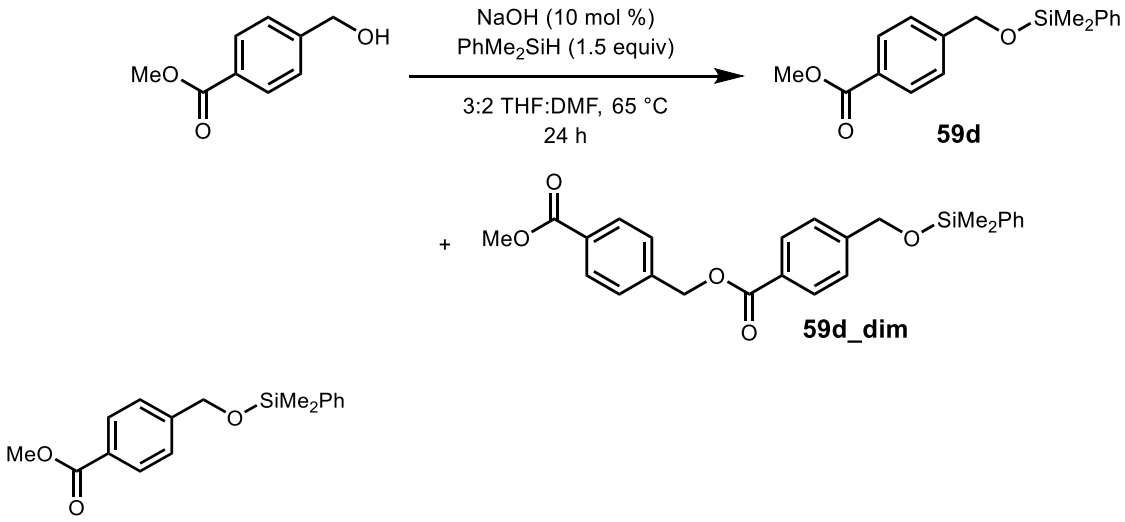
((4-Bromobenzyl)oxy)dimethyl(phenyl)silane 59b: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), 4-bromobenzyl alcohol (94 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), 0.2 mL dimethylformamide (DMF) and 0.3 mL of tetrahydrofuran (THF) at 65 °C for 24 h. The desired product **59b** (146.2 mg, 91% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.48 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (dd, J = 7.7, 1.8 Hz, 2H), 7.47 – 7.34 (m, 5H), 7.19 (dt, J = 8.7, 0.7 Hz, 2H), 4.66 (d, J = 0.8 Hz, 2H), 0.44 (s, 6H). This compound has been previously characterized.[181]



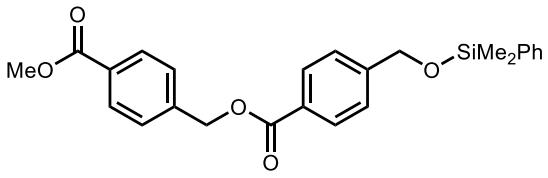


Dimethyl((4-nitrobenzyl)oxy)(phenyl)silane 59c: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), 4-nitrobenzyl alcohol (77 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), 0.2 mL dimethylformamide (DMF) and 0.3 mL of tetrahydrofuran (THF) at 65 °C for 18 h. The desired product **59c** (102.2 mg, 71% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.38 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 – 8.15 (m, 2H), 7.60 (dd, J = 7.8, 1.7 Hz, 2H), 7.47 (dt, J = 8.8, 0.8 Hz, 2H), 7.44 – 7.38 (m, 3H), 4.79 (t, J = 0.8 Hz, 2H), 0.47 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.51, 147.18, 136.92, 133.59,

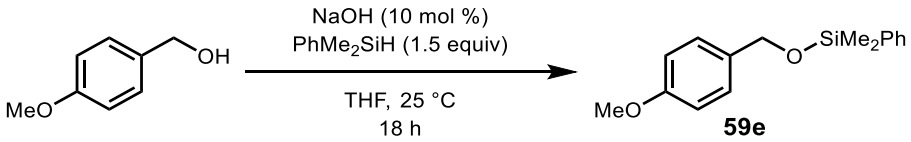
130.13, 128.18, 126.77, 123.68, 64.03, -1.73. IR (Neat Film NaCl) 3423, 2958, 1641, 1608, 1519, 1527, 1253, 1117, 1094, 856, 830, 786, 735, 700 cm^{-1}; HRMS (EI+) calc'd for $C_{15}H_{18}SiO_3N$ [M+H]: 288.1056, found 288.1058.

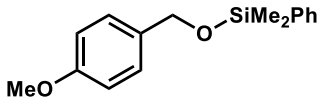


Methyl 4-(((dimethyl(phenyl)silyl)oxy)methyl)benzoate 59d: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), methyl 4-(hydroxymethyl)benzoate (83 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), 0.2 mL dimethylformamide (DMF) and 0.3 mL of tetrahydrofuran (THF) at 65 °C for 24 h. The desired product **59d** (100.6 mg, 67% yield) was obtained as a colorless oil by silica gel flash chromatography (gradient 15% EtOAc to 30% EtOAc in hexanes). R_f = 0.62 (15% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 8.3 Hz, 2H), 7.63 – 7.60 (m, 2H), 7.45 – 7.36 (m, 5H), 4.76 (d, J = 0.8 Hz, 2H), 3.92 (s, 3H), 0.46 (s, 6H). This compound has been previously characterized.[182]

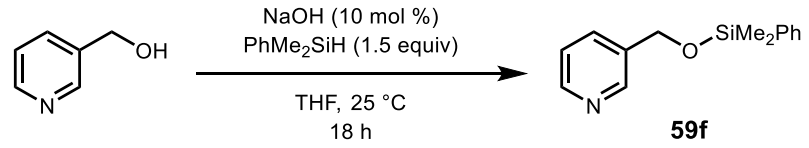


4-(Methoxycarbonyl)benzyl 4-(((dimethyl(phenyl)silyl)oxy)methyl)benzoate 59d_dim: Also isolated from the column was **59d_dim** (36.9 mg, 34% silylation yield / 17% yield based on methyl 4-(hydroxymethyl)benzoate stoichiometry) as a colorless solid. R_f = 0.43 (15% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 – 8.03 (m, 4H), 7.62 – 7.58 (m, 2H), 7.51 (dt, J = 8.6, 0.7 Hz, 2H), 7.43 – 7.37 (m, 5H), 5.42 (s, 2H), 4.76 (d, J = 0.8 Hz, 2H), 3.93 (s, 3H), 0.44 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.88, 166.31, 146.62, 141.30, 137.26, 133.61, 130.02, 129.97, 129.90, 128.63, 128.09, 127.72, 126.27, 65.94, 64.53, 52.32, -1.64.

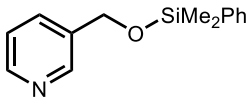




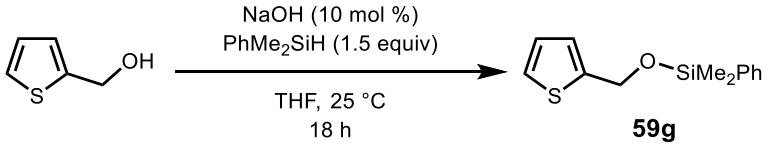
((4-Methoxybenzyl)oxy)dimethyl(phenyl)silane 59e: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), 4-methoxybenzyl alcohol (69 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 25 °C for 18 h. The desired product **59e** (117.9 mg, 87% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.29 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (dd, J = 7.5, 2.0 Hz, 2H), 7.44 – 7.37 (m, 3H), 7.25 – 7.20 (m, 2H), 6.87 (d, J = 8.6 Hz, 2H), 4.64 (d, J = 0.6 Hz, 2H), 3.81 (s, 3H), 0.42 (s, 6H). This compound has been previously characterized.[154]



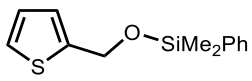
59f



3-(((Dimethyl(phenyl)silyl)oxy)methyl)pyridinesilane 59f: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), pyridin-3-ylmethanol (55 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 25 °C for 18 h. The desired product **59f** (118.1 mg, 97% yield) was obtained as a colorless oil by removal of volatiles at 80 °C at 60mTorr. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (dt, J = 2.3, 0.8 Hz, 1H), 8.49 (dd, J = 4.8, 1.6 Hz, 1H), 7.65 (dtd, J = 7.8, 1.7, 0.9 Hz, 1H), 7.61 – 7.57 (m, 2H), 7.43 – 7.37 (m, 3H), 7.26 (ddd, J = 7.9, 4.8, 0.9 Hz, 1H), 4.70 (dt, J = 0.6 Hz, 2H), 0.44 (s, 6H). This compound has been previously characterized.[183]

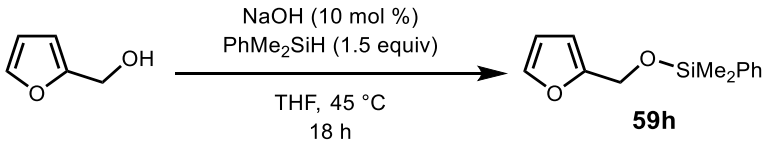


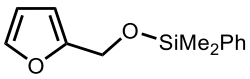
59g



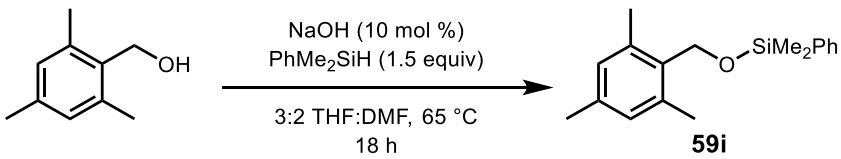
Dimethyl(phenyl)(thiophen-2-ylmethoxy)silane 59g: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), thiophen-2-ylmethanol (57 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 25 °C for 18 h. The desired product **59g** (119.2 mg, 96% yield) was obtained as a colorless oil by removal of volatiles at 80 °C at 60mTorr. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 – 7.63 (m, 2H), 7.47 – 7.43 (m, 3H), 7.26 (dd, J = 5.0, 1.3 Hz, 1H), 6.97 (dd, J = 5.0, 3.4 Hz,

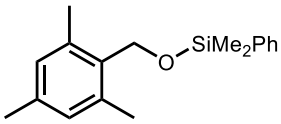
1H), 6.94 – 6.91 (m, 1H), 4.87 (d, J = 0.8 Hz, 2H), 0.47 (s, 6H). This compound has been previously characterized.[184]





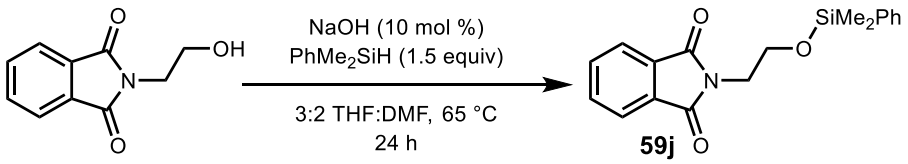
(Furan-2-ylmethoxy)dimethyl(phenyl)silane 59h: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), furfuryl alcohol (49 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 45 °C for 18 h. The desired product **59h** (101.1 mg, 87% yield) was obtained as a colorless oil by removal of volatiles at 80 °C at 60mTorr. ^1H NMR (500 MHz, $CDCl_3$) δ 7.62 (ddd, J = 7.5, 2.4, 1.3 Hz, 2H), 7.46 – 7.33 (m, 4H), 6.32 (dt, J = 3.4, 1.8 Hz, 1H), 6.21 (t, J = 2.5 Hz, 1H), 4.62 (d, J = 2.0 Hz, 2H), 0.39 – 0.35 (m, 6H). This compound has been previously characterized. [184]

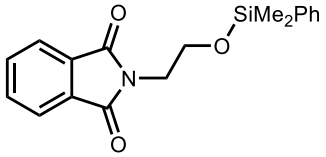




Dimethyl(phenyl)((2,4,6-trimethylbenzyl)oxy)silane 59i: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), mesitylmethanol (75 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), 0.2 mL dimethylformamide (DMF) and 0.3 mL of tetrahydrofuran (THF) at 65 °C for 18 h. Concentration of the reaction mixture and purification of the resulting residue via Kugelrohr distillation (100 mTorr,

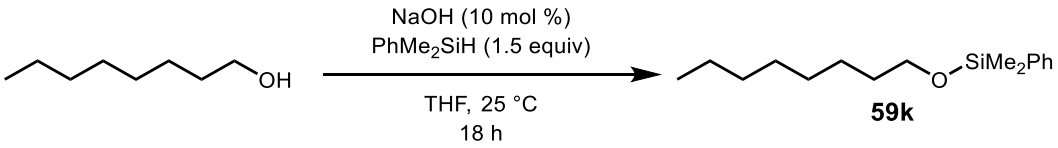
210 °C) gave 118.7 mg (84% yield) of **59i** as a colorless oil. (Note: the purified material obtained by Kugelrohr distillation was accompanied by ca. 5% unidentified by-products; however, further purification by chromatography was precluded by the instability of **59i** on SiO_2 as well as its decomposition under prolonged heating). ^{1}H NMR (500 MHz, THF-d_8) δ 7.59 – 7.55 (m, 2H), 7.36 – 7.30 (m, 3H), 6.79 – 6.73 (m, 2H), 4.66 (s, 2H), 2.24 (t, J = 0.6 Hz, 6H), 2.20 (s, 3H), 0.35 (s, 6H); ^{13}C NMR (126 MHz, THF-d_8) δ 139.02, 137.93, 137.61, 134.72, 134.46, 130.42, 129.65, 128.68, 59.98, 21.23, 19.79, -1.48. IR (Neat Film NaCl) 3421, 3069, 3048, 3008, 2957, 2918, 1614, 1583, 1427, 1373, 1253, 1147, 1118, 1046, 848, 829, 784, 740, 699, 644 cm^{-1}; HRMS (EI+) calc'd for $C_{16}H_{16}FSi$ [(M+H)-H_2]: 283.1518, found 283.1526.

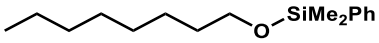




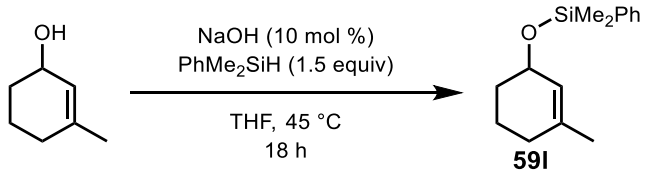
2-(2-((Dimethyl(phenyl)silyl)oxy)ethyl)isoindoline-1,3-dione 59j: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), 2-(2-hydroxyethyl)isoindoline-1,3-dione (96 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), 0.2 mL dimethylformamide (DMF) and 0.3 mL of tetrahydrofuran (THF) at 65 °C for 24 h. The desired product **59j** (101.6 mg, 62% yield) was obtained as a colorless oil by silica gel flash chromatography (20% EtOAc in hexanes). R_f = 0.45 (20% EtOAc in hexanes); ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.52 – 7.50 (m, 1H), 7.50 (dd, J = 2.4, 0.6 Hz, 1H), 7.43 (dd, J = 5.4, 3.0 Hz, 2H), 7.16 – 7.15 (m, 1H), 7.15 – 7.14 (m, 1H), 7.14 (d, J = 2.3 Hz, 1H), 6.87 (ddd, J = 5.5, 3.0,

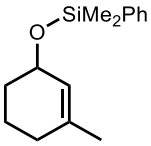
0.5 Hz, 2H), 3.74 – 3.67 (m, 2H), 3.68 – 3.62 (m, 2H), 0.26 (s, 6H); ^{13}C NMR (126 MHz, Benzene-d_6) δ 167.96, 137.77, 133.81, 133.39, 132.66, 129.84, 128.13, 122.95, 60.16, 40.23, -1.81. IR (Neat Film NaCl) 2956, 1773, 1713, 1615, 1467, 1427, 1392, 1362, 1319, 1252, 1189, 1116, 1022, 929, 859, 829, 788, 718, 700 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{20}O_3SiN$ [M+H]: 326.1213, found 326.1223.



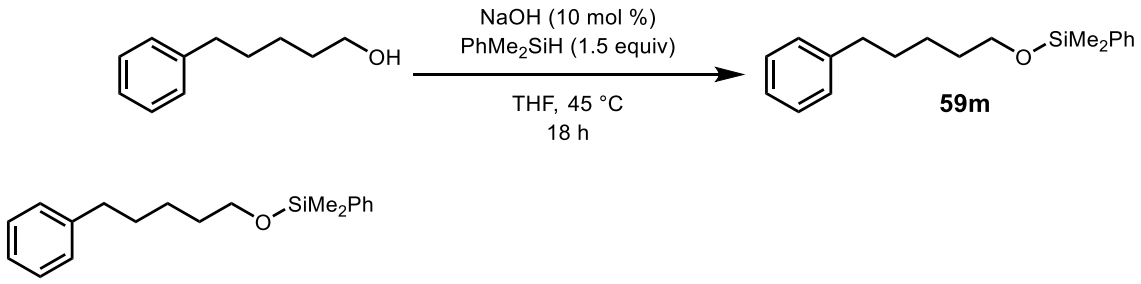


Dimethyl(octyloxy)(phenyl)silane 59k: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), 1-octanol (65 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 25 °C for 18 h. The desired product **59k** (111.1 mg, 84% yield) was obtained as a colorless oil by silica gel flash chromatography (100% hexanes). R_f = 0.49 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.58 (m, 2H), 7.41 (dd, J = 5.0, 1.9 Hz, 3H), 3.62 (t, J = 6.7 Hz, 2H), 1.60 – 1.51 (m, 2H), 1.32 – 1.24 (m, 10H), 0.97 – 0.85 (m, 3H), 0.41 (s, 6H). This compound has been previously characterized.[185]



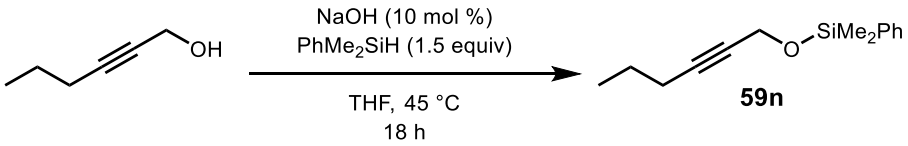


Dimethyl((3-methylcyclohex-2-en-1-yl)oxy)(phenyl)silane 59l: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), 3-methylcyclohex-2-en-1-ol (56 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 45 °C for 48 h. The desired product **59l** (113.4 mg, 92% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.43 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.56 (m, 2H), 7.38 (dd, J = 5.0, 1.9 Hz, 3H), 5.34 (dd, J = 3.1, 1.6 Hz, 1H), 4.20 (dt, J = 5.0, 1.6 Hz, 1H), 1.99 – 1.69 (m, 4H), 1.64 (tt, J = 1.6, 0.9 Hz, 3H), 1.55 – 1.42 (m, 2H), 0.40 (d, J = 1.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.64, 137.78, 133.69, 129.59, 127.89, 125.14, 67.41, 32.13, 30.08, 23.80, 19.83, -0.80, -0.91. IR (Neat Film NaCl) 3423, 3069, 2935, 2862, 1645, 1427, 1251, 1116, 1074, 1024, 992, 894, 880, 828, 786, 738, 700 cm^{-1}; HRMS (EI+) calc'd for $C_{15}H_{21}OSi$ [(M+H)-H_2]: 245.1362, found 245.1368.

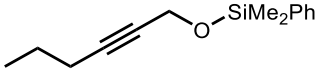


Dimethyl(phenyl)((5-phenylpentyl)oxy)silane 59m: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), 5-phenylpentan-1-ol (82 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 45 °C for 18 h. The desired product **59m** (146.3 mg, 98% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.46 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (ddq, J = 6.2, 1.9, 0.9 Hz, 2H), 7.46 – 7.41

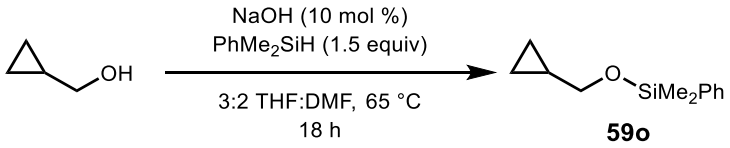
(m, 3H), 7.32 (tt, J = 7.5, 0.9 Hz, 2H), 7.22 (ddt, J = 9.9, 7.3, 1.3 Hz, 3H), 3.65 (td, J = 6.7, 1.1 Hz, 2H), 2.67 – 2.63 (m, 2H), 1.74 – 1.58 (m, 4H), 1.47 – 1.38 (m, 2H), 0.44 (t, J = 1.0 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.79, 138.10, 133.58, 129.66, 128.51, 128.34, 127.93, 125.71, 63.15, 36.04, 32.57, 31.41, 25.59, -1.65. IR (Neat Film NaCl) 3385, 3067, 3025, 2933, 2857, 1603, 1495, 1452, 1427, 1341, 1254, 1119, 1055, 831, 791, 726, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{19}H_{27}OSi$ [M+H]: 299.1831, found 299.1840.



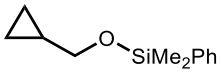
59n



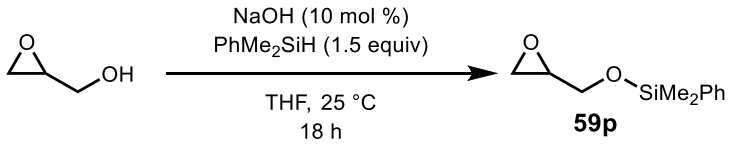
(Hex-2-yn-1-yloxy)dimethyl(phenyl)silane 59n: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), hex-2-yn-1-ol (49 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of 1 tetrahydrofuran (THF) at 45 °C for 18 h. The desired product **59n** (99.9 mg, 86% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.43 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 77.62 – 7.59 (m, 2H), 7.42 – 7.36 (m, 3H), 4.27 (t, J = 2.2 Hz, 2H), 2.16 (tt, J = 7.1, 2.2 Hz, 2H), 1.51 (h, J = 7.3 Hz, 2H), 0.97 (t, J = 7.3 Hz, 3H), 0.45 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.36, 133.71, 129.84, 127.97, 85.99, 78.37, 51.93, 22.11, 20.92, 13.66, -1.46. *Note: this product decomposes slowly in $CDCl_3$.* IR (Neat Film NaCl) 3420, 2956, 1646, 1254, 1118, 1067, 1026, 830, 789, 726, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{19}OSi$ [M+H]: 231.1205, found 231.1207.



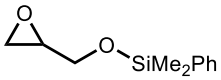
59o



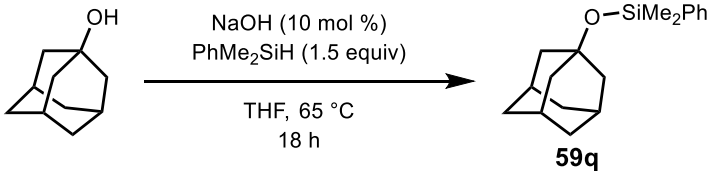
(Cyclopropylmethoxy)dimethyl(phenyl)silane 59o: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), cyclopropanemethanol (36 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), 0.2 mL dimethylformamide (DMF) and 0.3 mL of tetrahydrofuran (THF) at 65 °C for 18 h. Concentration of the reaction mixture and purification of the resulting residue via Kugelrohr distillation (120 mTorr, 65 °C) gave 65.4 mg (63% yield) of **59o** as a colorless oil. *Note: product is volatile under high vacuum.* (Note: the purified material obtained by Kugelrohr distillation was accompanied by ca. 5% unidentified by-products; however, further purification by chromatography was precluded by the instability of **59o** on SiO_2). ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.63 – 7.58 (m, 2H), 7.27 – 7.19 (m, 3H), 3.40 (d, J = 6.4 Hz, 2H), 0.95 (ttt, J = 8.0, 6.4, 4.9 Hz, 1H), 0.34 (s, 6H), 0.32 – 0.28 (m, 2H), 0.12 – 0.05 (m, 2H); ^{13}C NMR (126 MHz, Benzene-d_6) δ 138.63, 133.92, 129.80, 128.15, 67.54, 13.68, 3.23, -1.38. IR (Neat Film NaCl) 3070, 3006, 2958, 2862, 1470, 1427, 1403, 1251, 1177, 1116, 1073, 851, 826, 785, 740, 699 cm^{-1}; HRMS (EI+) calc'd for $C_{12}H_{18}OSi$ [M+•]: 206.1127, found 206.1148.



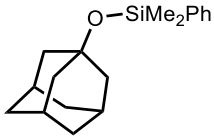
59p



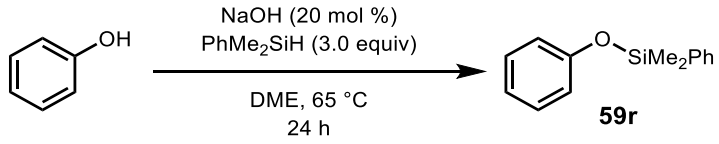
Dimethyl(oxiran-2-ylmethoxy)(phenyl)silane 59p: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), glycidol (37 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 25 °C for 18 h. The desired product **59p** (74.8 mg, 72% yield) was obtained as a colorless oil by silica gel flash chromatography (10% EtOAc in hexanes). R_f = 0.60 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.63 – 7.53 (m, 2H), 7.22 (dd, J = 5.5, 1.8 Hz, 3H), 3.58 (dd, J = 11.9, 2.9 Hz, 1H), 3.33 (dd, J = 11.9, 5.3 Hz, 1H), 2.78 (ddt, J = 5.4, 3.9, 2.7 Hz, 1H), 2.24 (dd, J = 5.3, 4.0 Hz, 1H), 2.16 (dd, J = 5.3, 2.6 Hz, 1H), 0.33 (s, 6H). This compound has been previously characterized. [154]

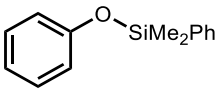


59q

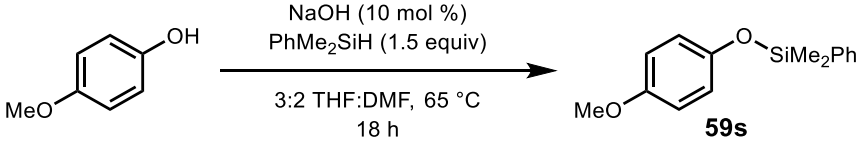


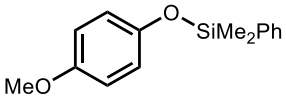
(((3s,5s,7s)-Adamantan-1-yl)oxy)dimethyl(phenyl)silane 59q: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), 1-adamantol (76 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of tetrahydrofuran (THF) at 65 °C for 18 h. The desired product **59q** (66.2 mg, 60% yield) was obtained as a colorless oil by removal of volatiles at 80 °C at 60 mTorr. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 – 7.62 (m, 2H), 7.40 – 7.38 (m, 3H), 2.13 – 2.08 (m, 3H), 1.80 (dt, J = 3.3, 0.8 Hz, 6H), 1.64 – 1.55 (m, 6H), 0.43 (s, 6H). This compound has been previously characterized.[186]





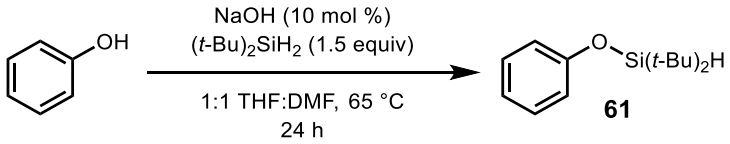
Dimethyl(phenoxy)(phenyl)silane 59r: The general procedure was followed. The reaction was performed with NaOH (4.0 mg, 0.1 mmol, 20 mol %), phenol (47 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), and 0.5 mL of dimethoxyethane (DME) at 65 °C for 24 h. The desired product **59r** (101.6 mg, 89% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.42 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.71 (m, 2H), 7.52 – 7.47 (m, 3H), 7.31 – 7.24 (m, 2H), 7.05 – 7.00 (m, 1H), 6.93 – 6.88 (m, 2H), 0.61 (s, 6H). This compound has been previously characterized.[149d]

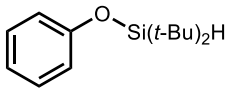




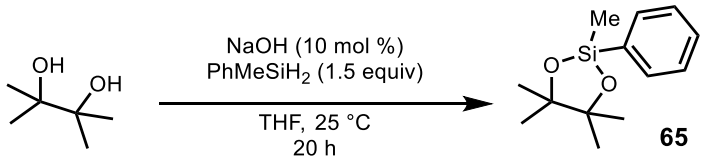
(4-Methoxyphenoxy)dimethyl(phenyl)silane 59s: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), 4-methoxyphenol (62 mg, 0.5 mmol, 1.0 equiv), $PhMe_2SiH$ (102 mg, 115 μL, 0.75 mmol, 1.5 equiv), 0.2 mL dimethylformamide (DMF) and 0.3 mL of tetrahydrofuran (THF) at 65 °C for 18 h. The desired product **59s** (106.0 mg, 82% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.45 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (dd, J = 7.8, 1.7 Hz, 2H), 7.45 – 7.36 (m, 3H), 6.74 (s, 4H), 3.74 (s, 3H), 0.50 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$)

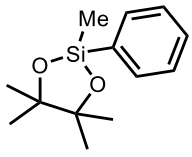
δ 154.32, 148.85, 137.40, 133.61, 130.00, 128.06, 120.73, 114.57, 55.70, -1.11. IR (Neat Film NaCl) 3420, 2958, 2833,1638, 1505, 1465, 1441, 1427, 1253, 1233, 1118, 1037, 911, 831,787, 729, 700 cm^{-1}; HRMS (EI+) calc'd for $C_{15}H_{18}O_2Si$ [M+•]: 258.1076, found 258.1083.





Di-*tert*-butyl(phenoxy)silane 61: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol %), phenol (47 mg, 0.5 mmol, 1.0 equiv), $(t\text{-Bu})_2SiH_2$ (108 mg, 148 μL, 0.75 mmol, 1.5 equiv), 0.25 mL dimethylformamide (DMF) and 0.25 mL of tetrahydrofuran (THF) at 65 °C for 24 h. The desired product **61** (106.5 mg, 90% yield) was obtained as a colorless oil by silica gel flash chromatography (5% EtOAc in hexanes). R_f = 0.77 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.21 (m, 3H), 6.95 – 6.93 (m, 2H), 4.44 (s, 1H), 1.07 (s, 18H). This compound has been previously characterized.[145a]

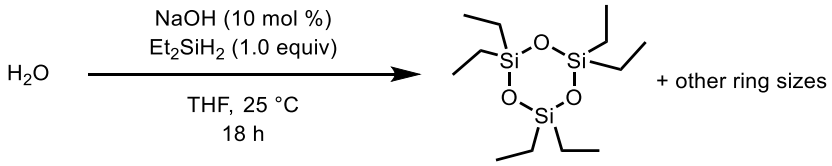




2,4,4,5,5-Pentamethyl-2-phenyl-1,3,2-dioxasilolane 65: The general procedure was followed. The reaction was performed with pinacol (1.18 g, 10.0 mmol, 1.0 equiv), $MePhSiH_2$ (1.83 g, 2.06 mL, 15.0 mmol, 1.5 equiv), and 10.0 mL of tetrahydrofuran (THF), then NaOH (40.0 mg, 1.0 mmol, 10

mol %) was added and the mixture was stirred at 25 °C for 20 h. *Note: vigorous evolution of hydrogen occurs upon addition of NaOH.* Concentration of the reaction mixture and purification of the resulting residue via Kugelrohr distillation (150 mTorr, 120 °C) gave 2.19 g (93% yield) of **65** as a colorless oil. *Note: product is volatile under high vacuum*. ^{1}H NMR (500 MHz, Benzene-d_6) δ 7.77 – 7.71 (m, 2H), 7.20 – 7.17 (m, 3H), 1.22 (s, 6H), 1.16 (s, 6H), 0.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.58, 134.03, 130.42, 128.21, 81.80, 26.03, -0.35. IR (Neat Film NaCl) 3441, 3071, 2980, 1643, 1464, 1428, 1366, 1260, 1161, 1121, 1026, 793, 736, 699 cm^{-1}; HRMS (EI+) calc'd for $C_{13}H_{20}O_2Si$ [M+•]: 236.1233, found 236.1237.

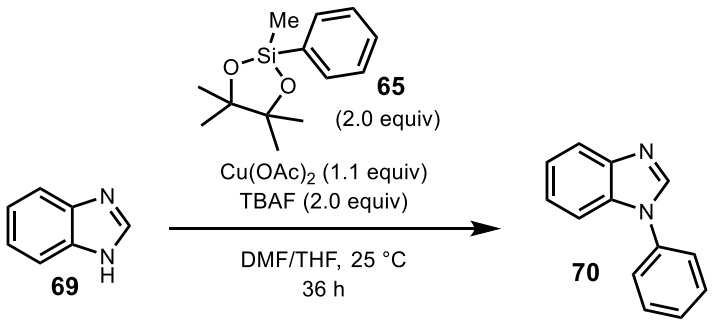
2. Synthesis of 2,2,4,4,6,6-Hexaethyl-1,3,5,2,4,6-trioxatrisilinane 2j.



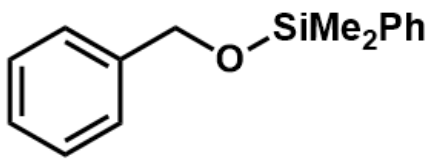
major (GC-MS)
57j

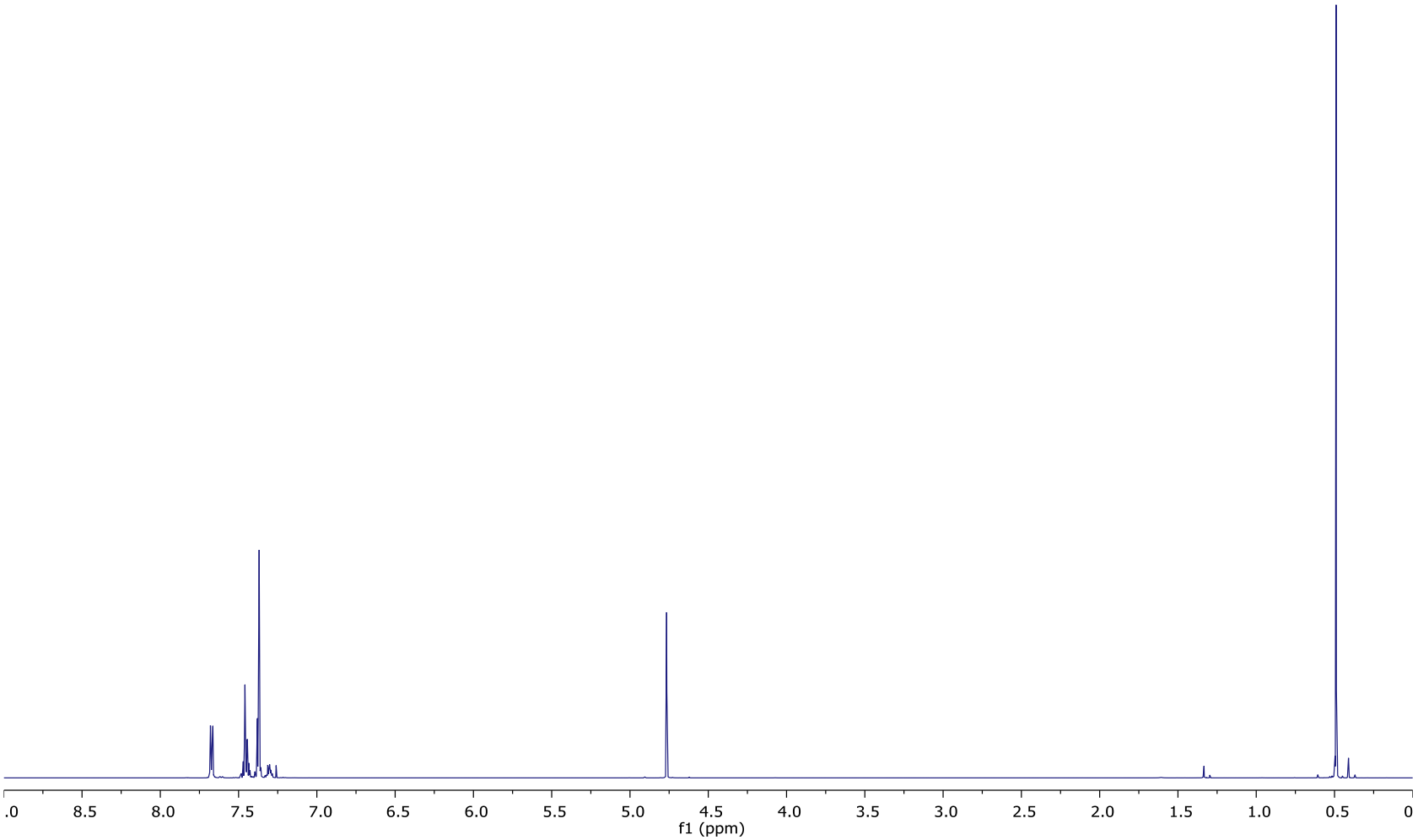
2,2,4,4,6,6-Hexaethyl-1,3,5,2,4,6-trioxatrisilinane 57j: To a solution of diethylsilane (0.5 mL, 3.85 mmol, 1.0 equiv) in THF (2.0mL) was added NaOH (15.4 mg, 0.39 mmol, 10 mol %) and H_2O (1.0 mL, 55 mmol, 15 equiv). The vial was then sealed and the mixture was stirred at 25 C for 24 h. The reaction mixture was diluted with 2 mL Et_2O and analyzed by GC-MS, in which 2,2,4,4,6,6-hexaethyl-1,3,5,2,4,6-trioxatrisilinane was the major product observed (mass = 306.2). Several other larger ring sizes were observed in smaller amounts.

3. Procedure for cross-coupling using 2,4,4,5,5-Pentamethyl-2-phenyl-1,3,2-dioxasilolane 13.

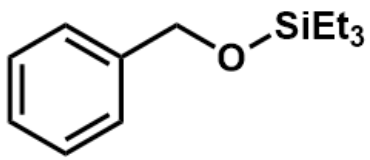


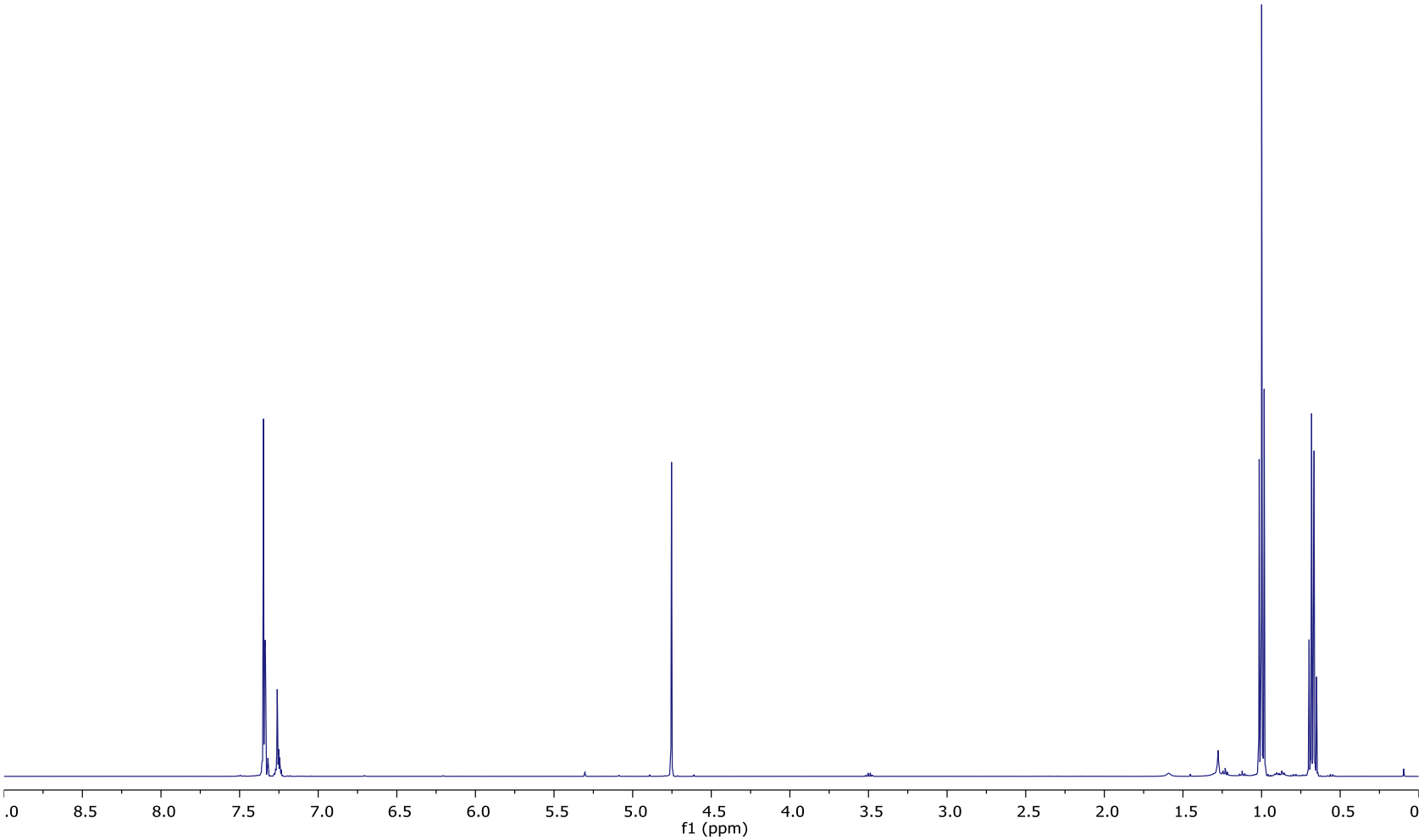
1-phenyl-1H-benzo[d]imidazole 70: To a mixture of the $PhSi^{Me}$(pin) reagent **65** (freshly prepared, 71.0 mg, 0.3 mmol, 2.0 equiv), benzimidazole **69** (17.6 mg, 0.15 mmol, 1.0 equiv) and $Cu(OAc)_2$ (30.0 mg, 0.165 mmol, 1.1 equiv) in DMF (1.5 mL) is added TBAF (0.3 mL, 1.0M solution in THF) dropwise at 25 °C. The mixture is allowed to stir for 36 h at 25° C, after which $NaHCO_3$ saturated solution (2.0 mL) is carefully added and then the mixture is partitioned between EtOAc and hexanes (5.0 mL each). The aqueous layer is extracted with a 1:1 EtOAc:hexanes mixture (2x15 mL) and then the combined organic layers are washed with H_2O (2x10 mL) and brine (1x10 mL), then dried over $MgSO_4$. The mixture is then filtered, the solvent is removed, and the resulting residue is purified via silica gel flash chromatography (gradient 20% EtOAc in hexanes to 70% EtOAC in hexanes) to yield **70** as a colorless solid (21.2 mg, 71% yield). R_f = 0.25 (20% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.93 – 7.84 (m, 1H), 7.65 – 7.42 (m, 6H), 7.39 – 7.31 (m, 2H). This compound has been previously characterized.[65a]



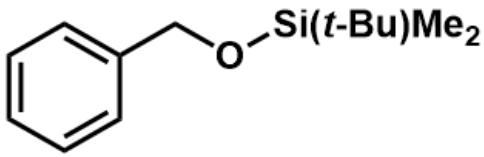


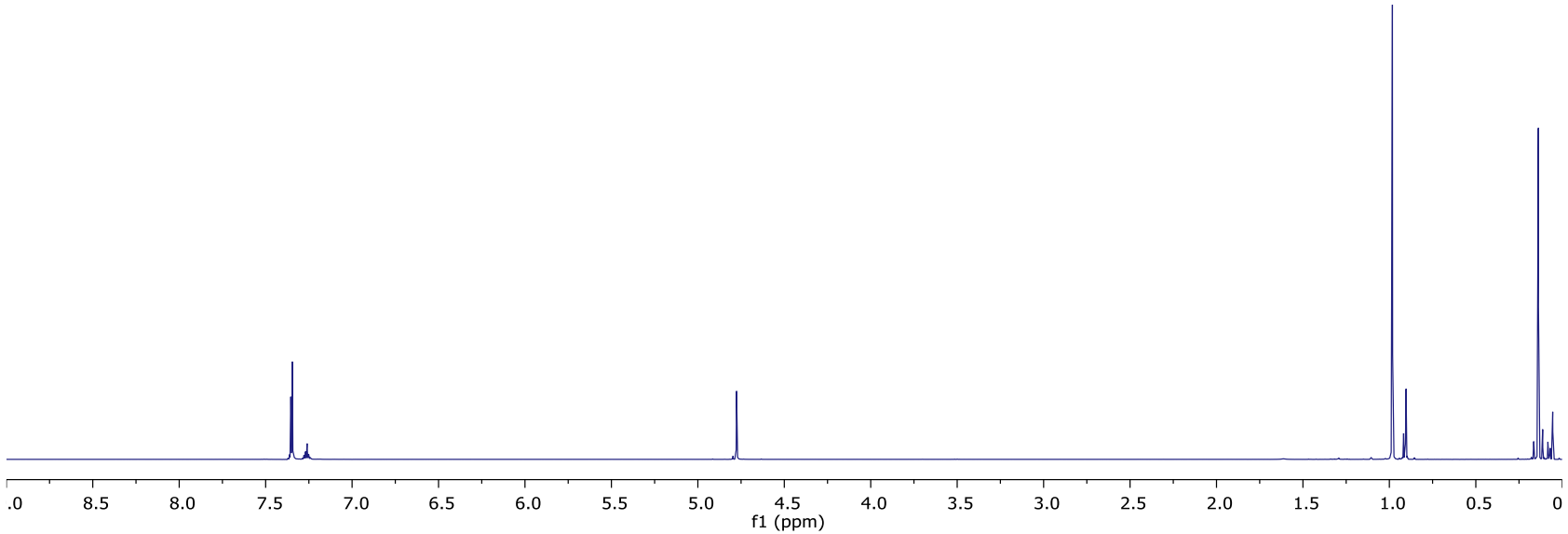
^{1}H NMR (500 MHz, $CDCl_3$) of compound **57a**.



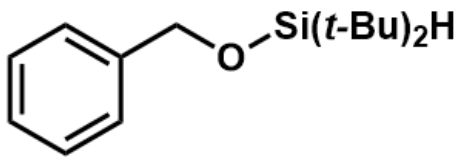


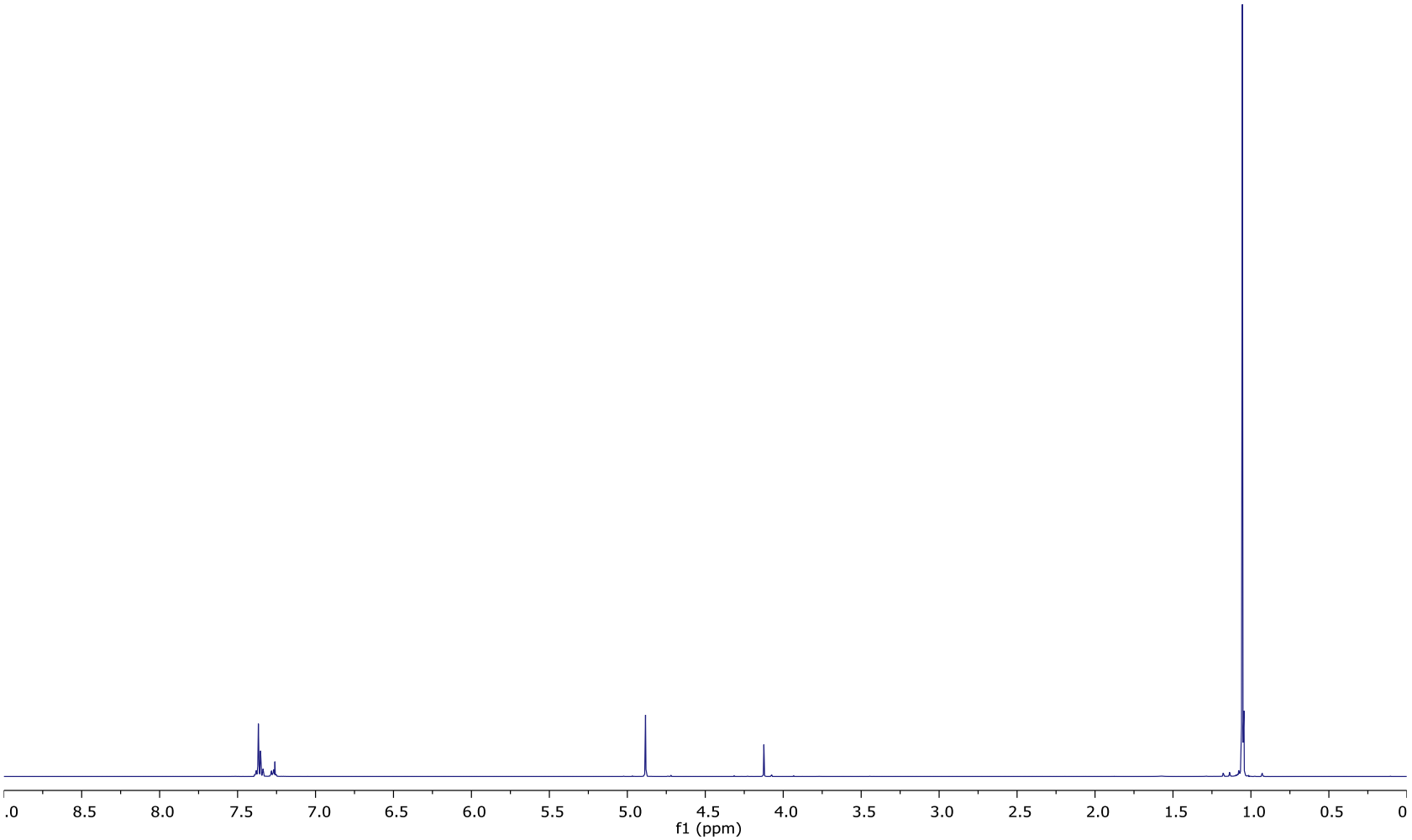
^{1}H NMR (500 MHz, $CDCl_3$) of compound **57b**.



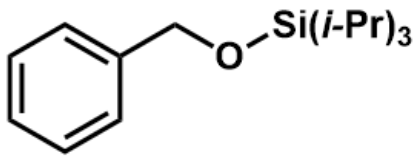


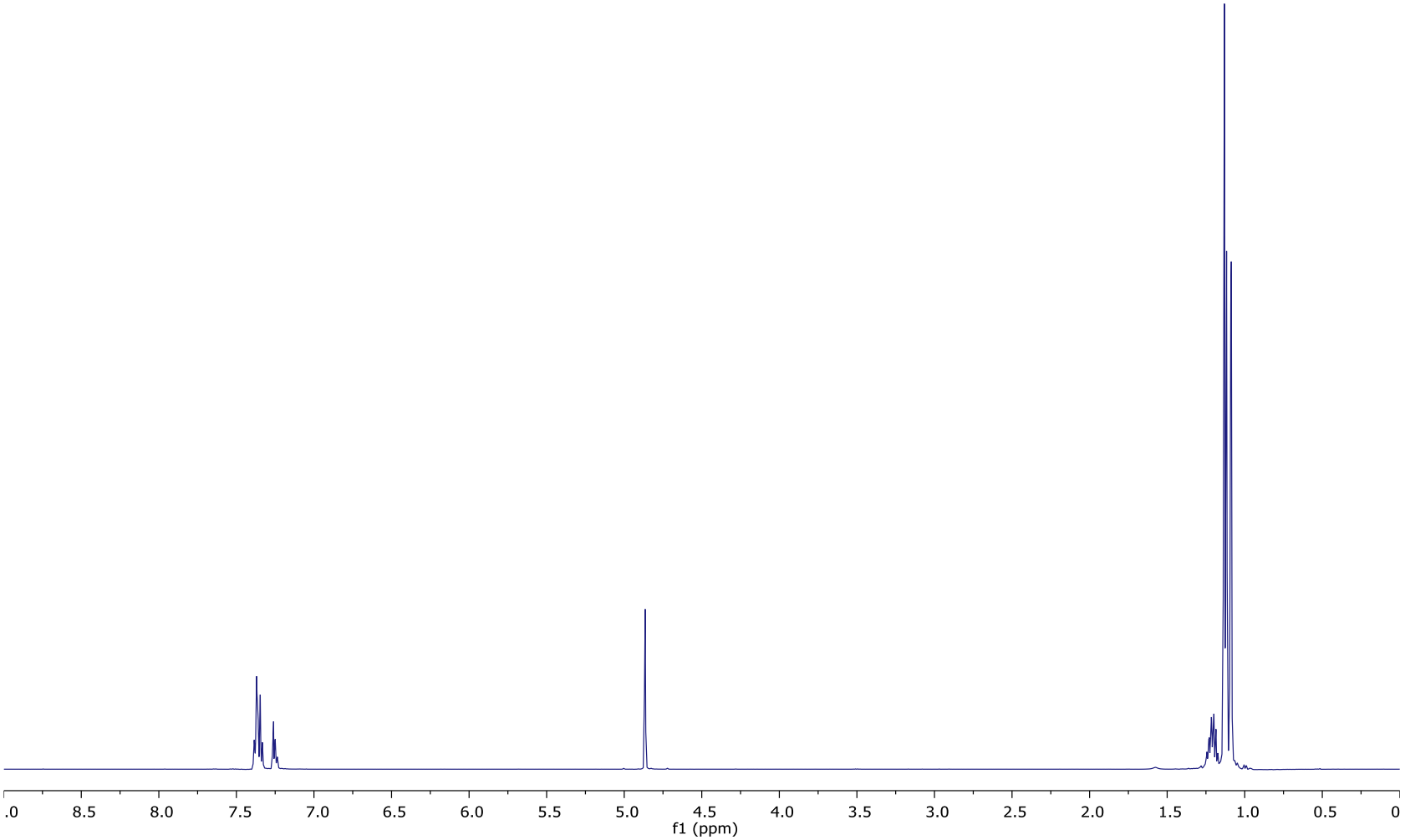
^{1}H NMR (500 MHz, $CDCl_3$) of compound **57d**.



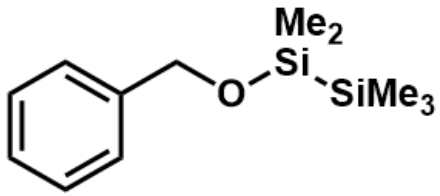


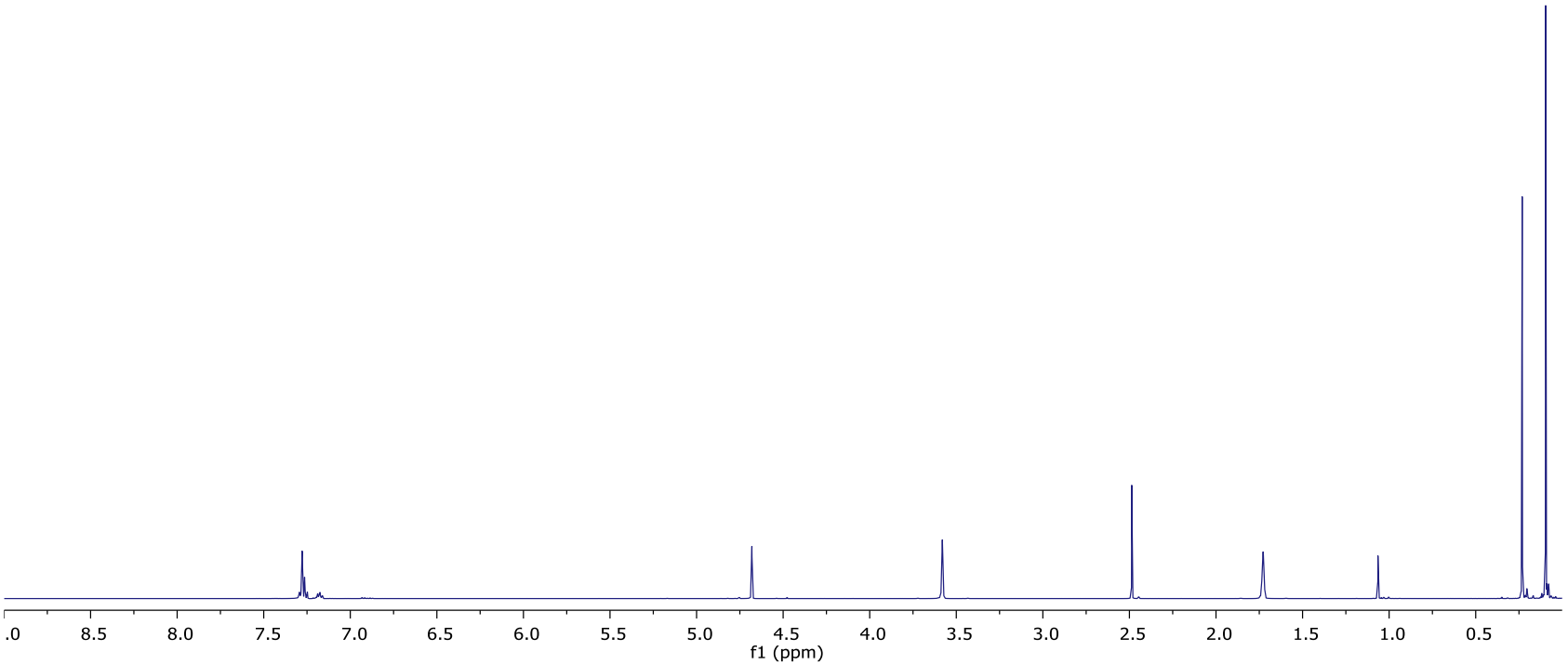
^{1}H NMR (500 MHz, $CDCl_3$) of compound **57e**.



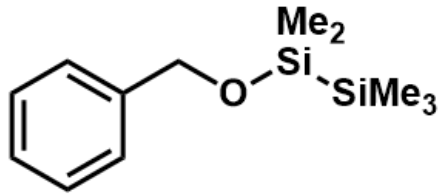


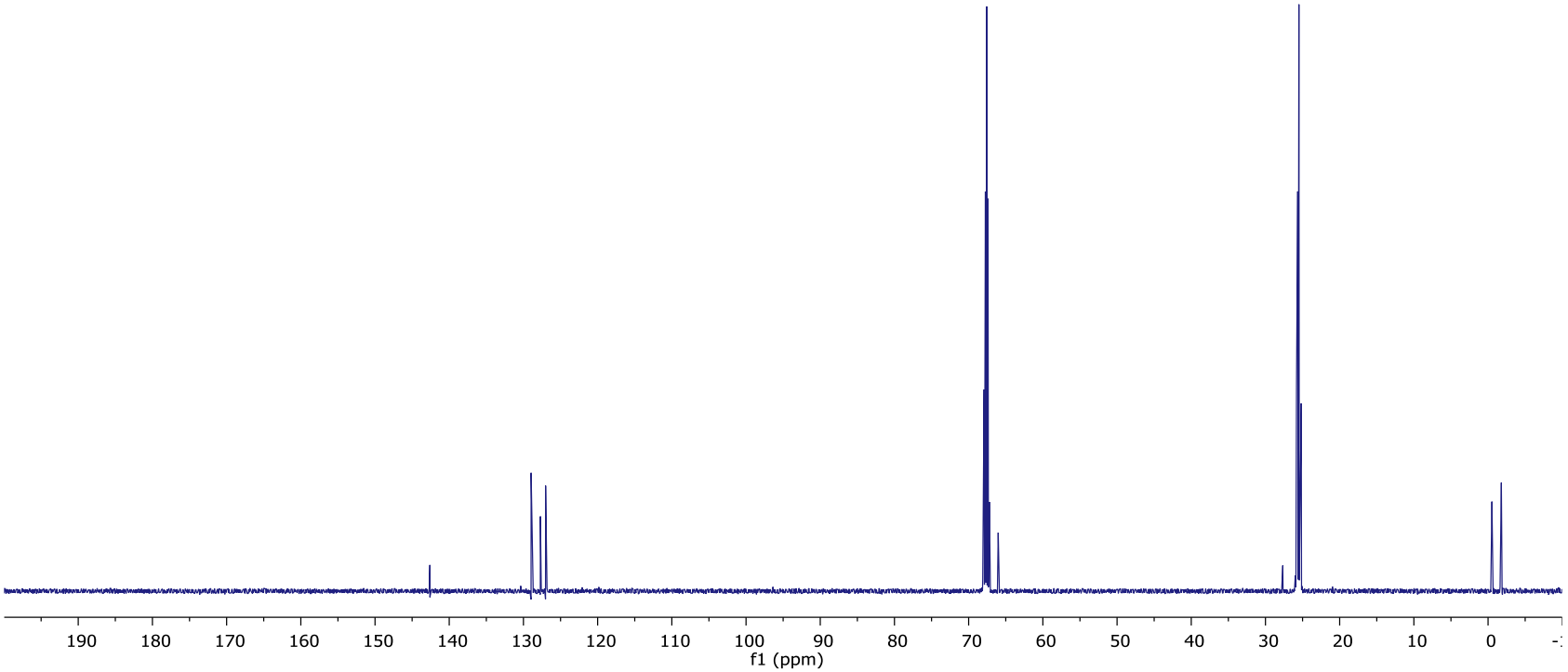
^{1}H NMR (500 MHz, $CDCl_3$) of compound **57f**.



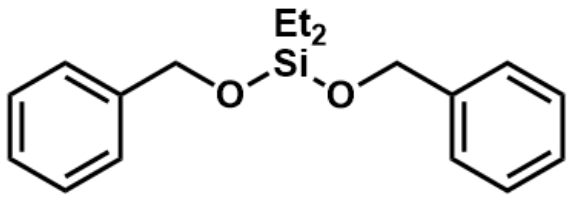


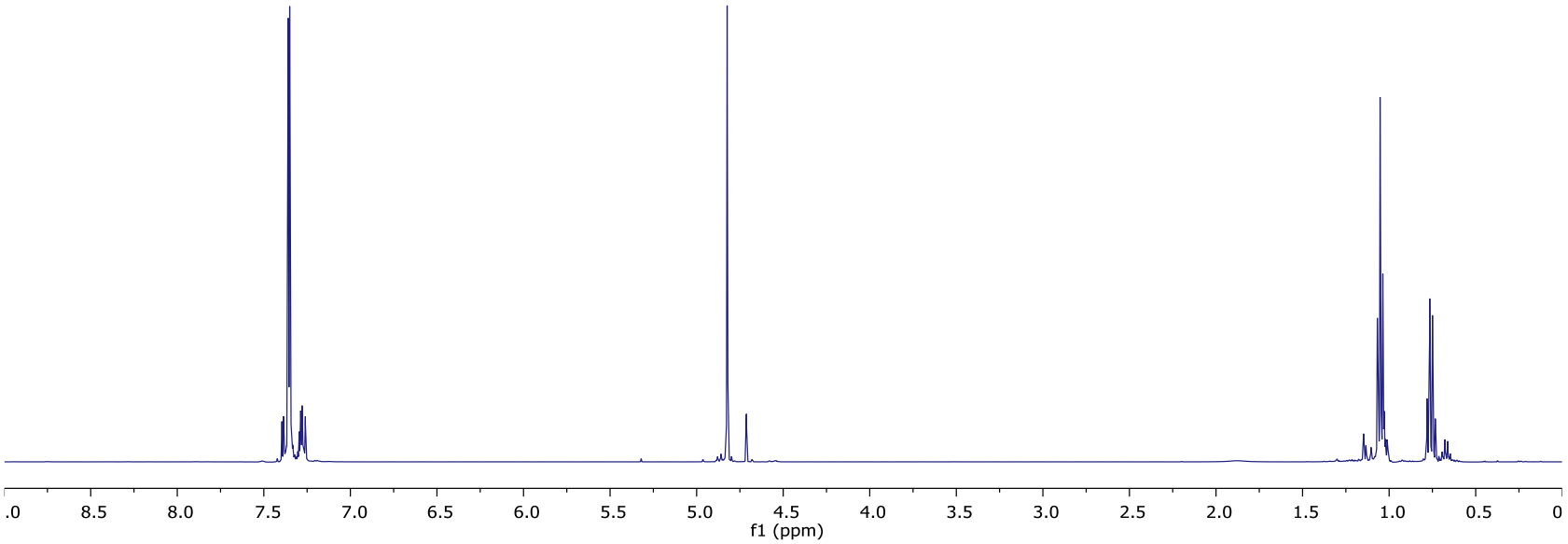
^{1}H NMR (500 MHz, THF-d_8) of compound **57g**.



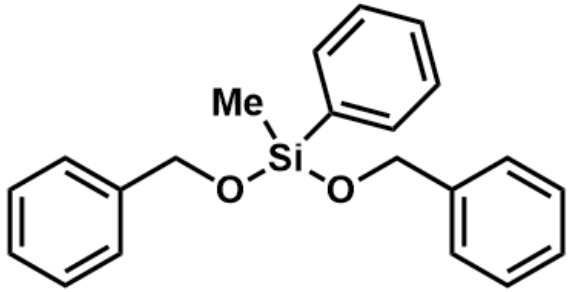


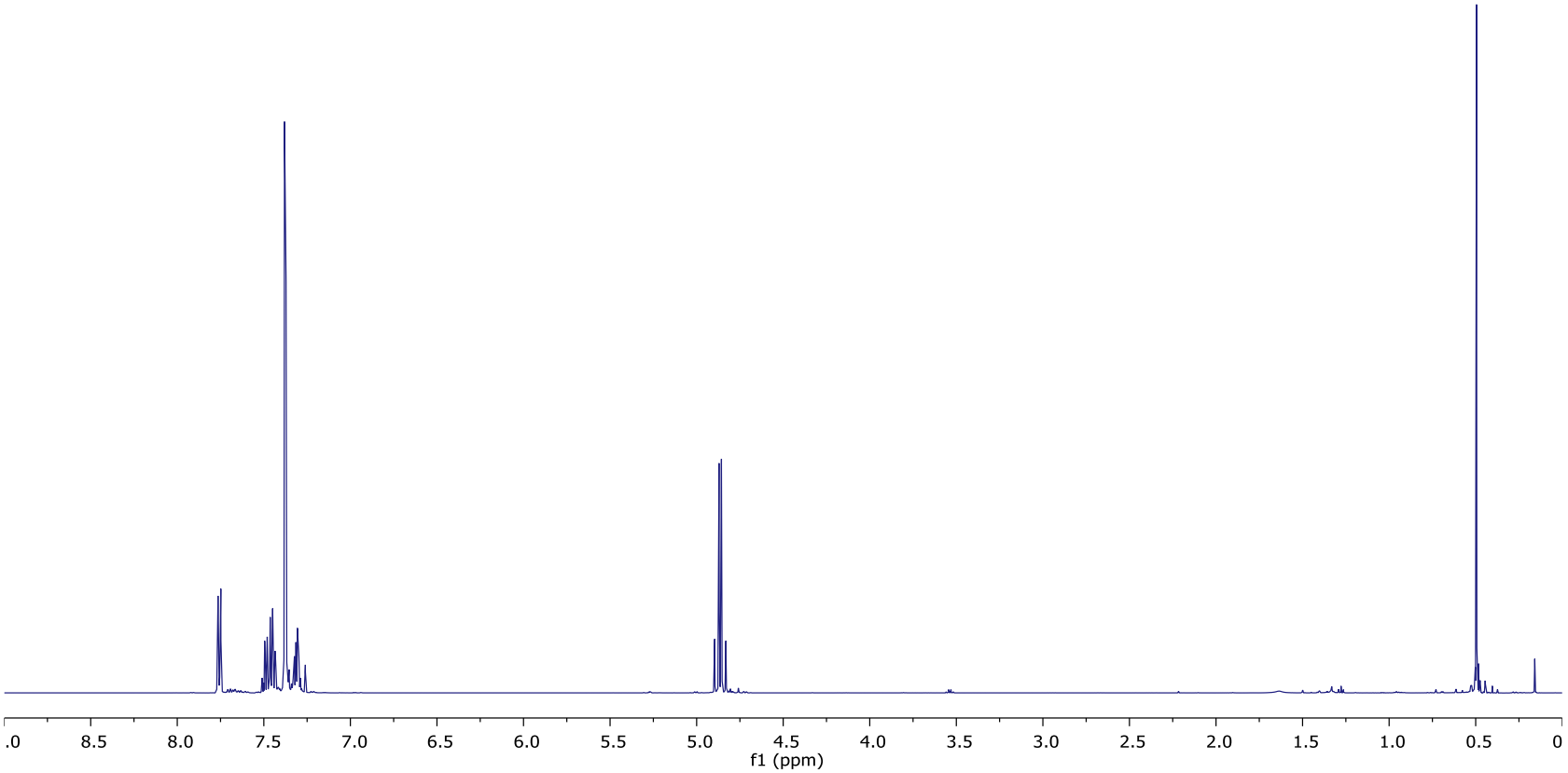
^{13}C NMR (126 MHz, THF-d_8) of compound **57g.**



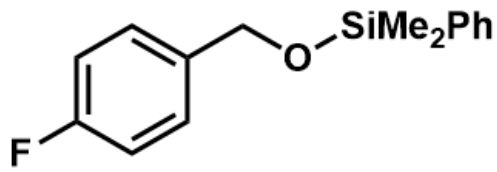


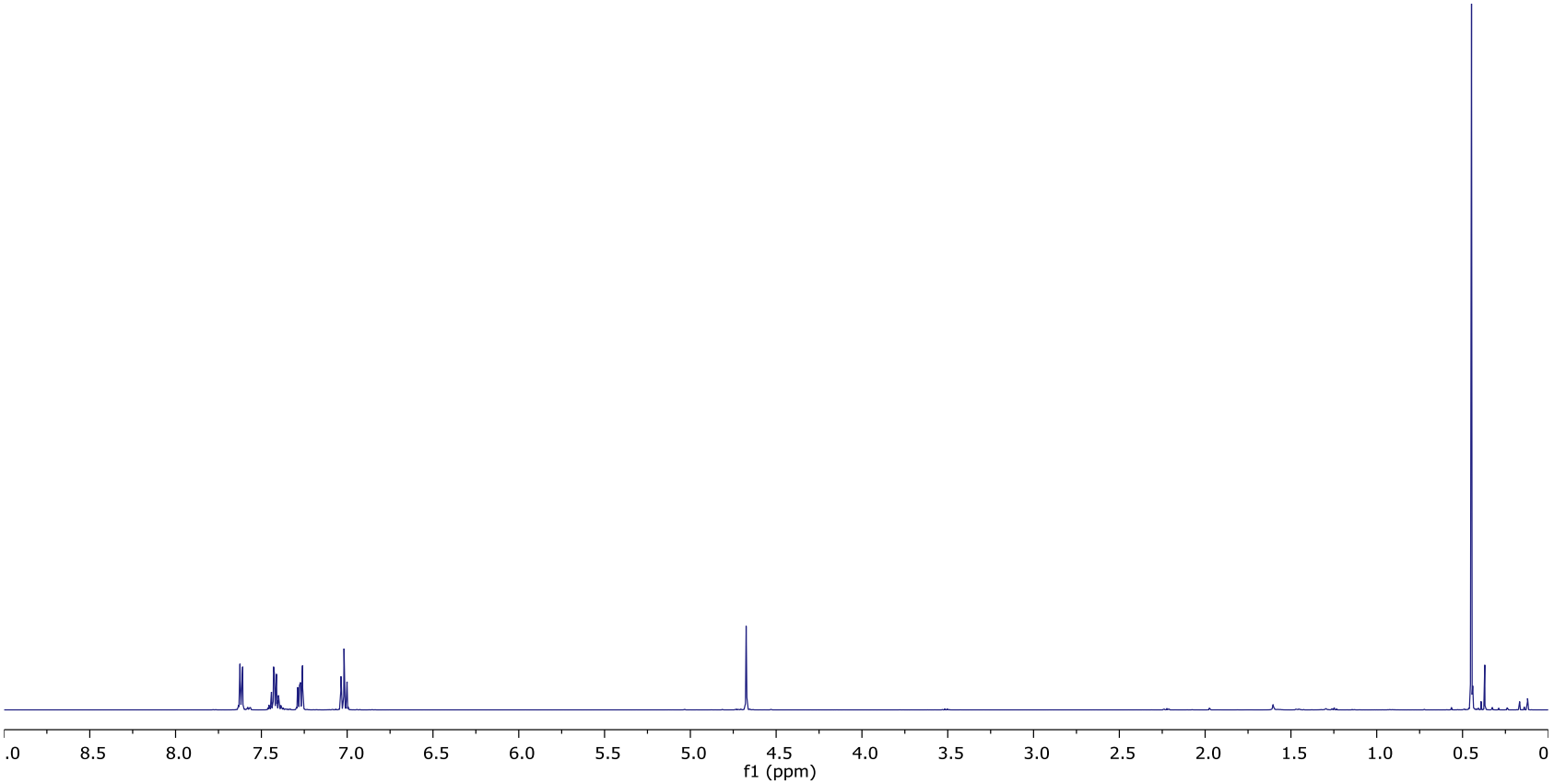
^{1}H NMR (500 MHz, $CDCl_3$) of compound **57h**.



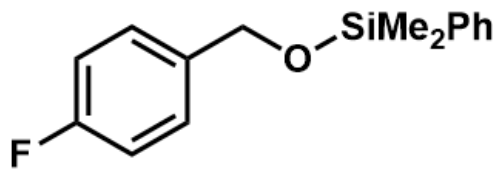


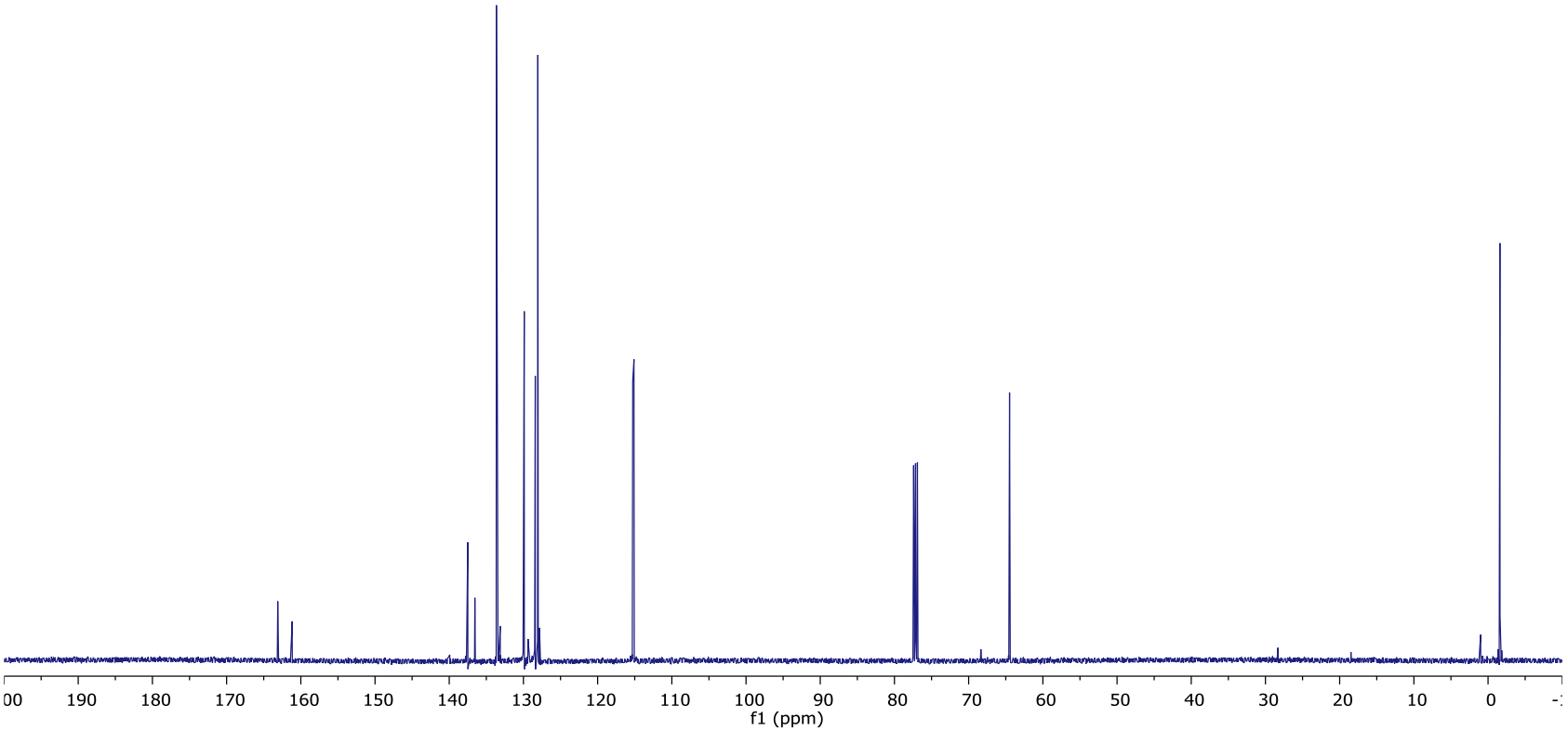
^{1}H NMR (500 MHz, $CDCl_3$) of compound **57i**.



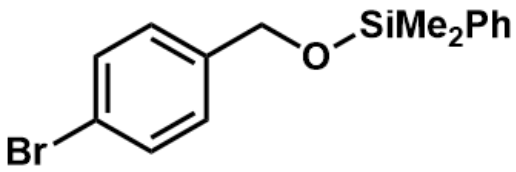


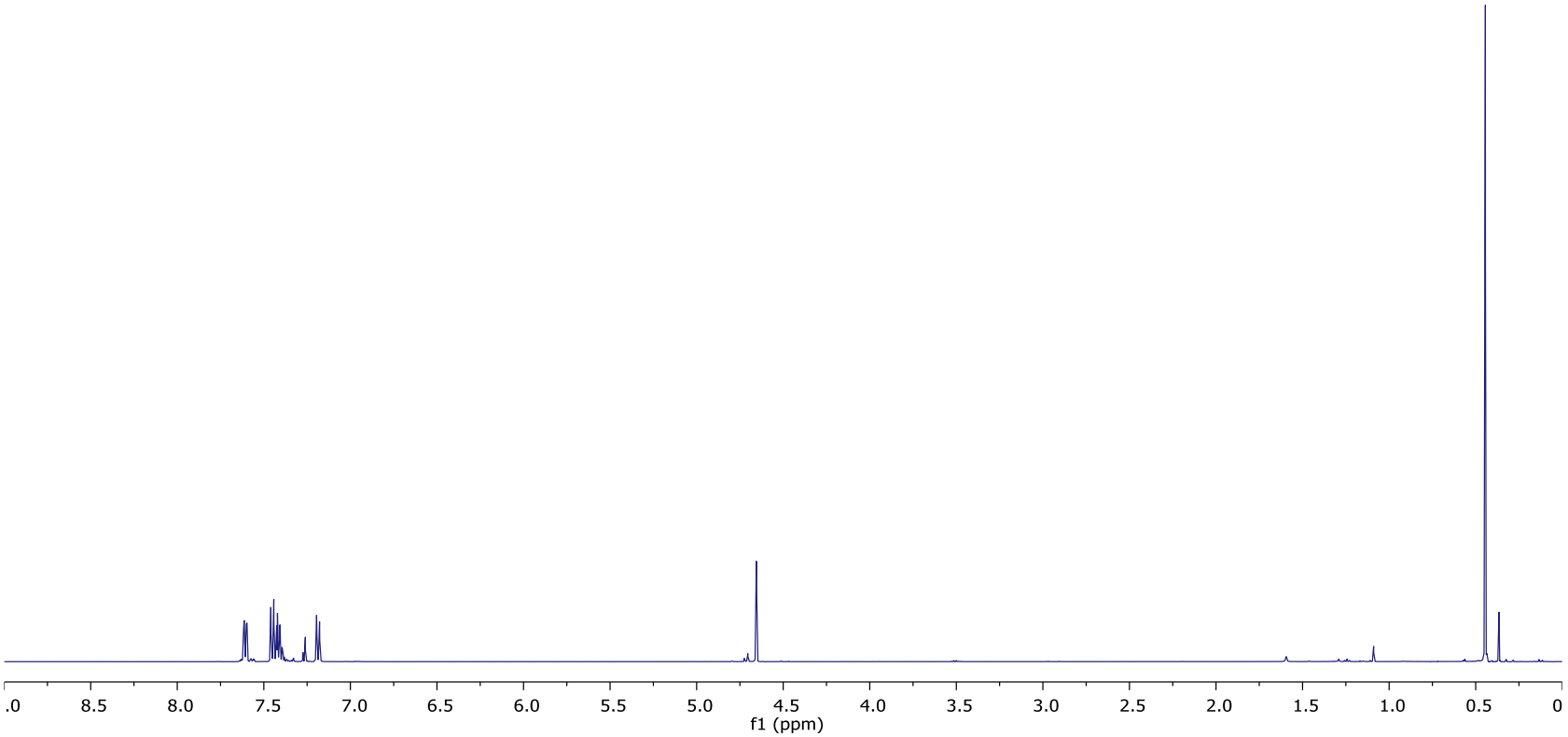
^{1}H NMR (500 MHz, $CDCl_3$) of compound **59a**.



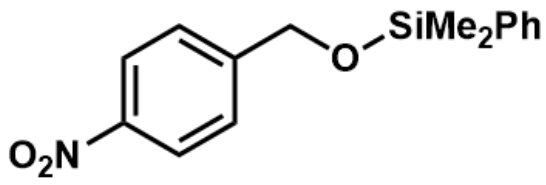


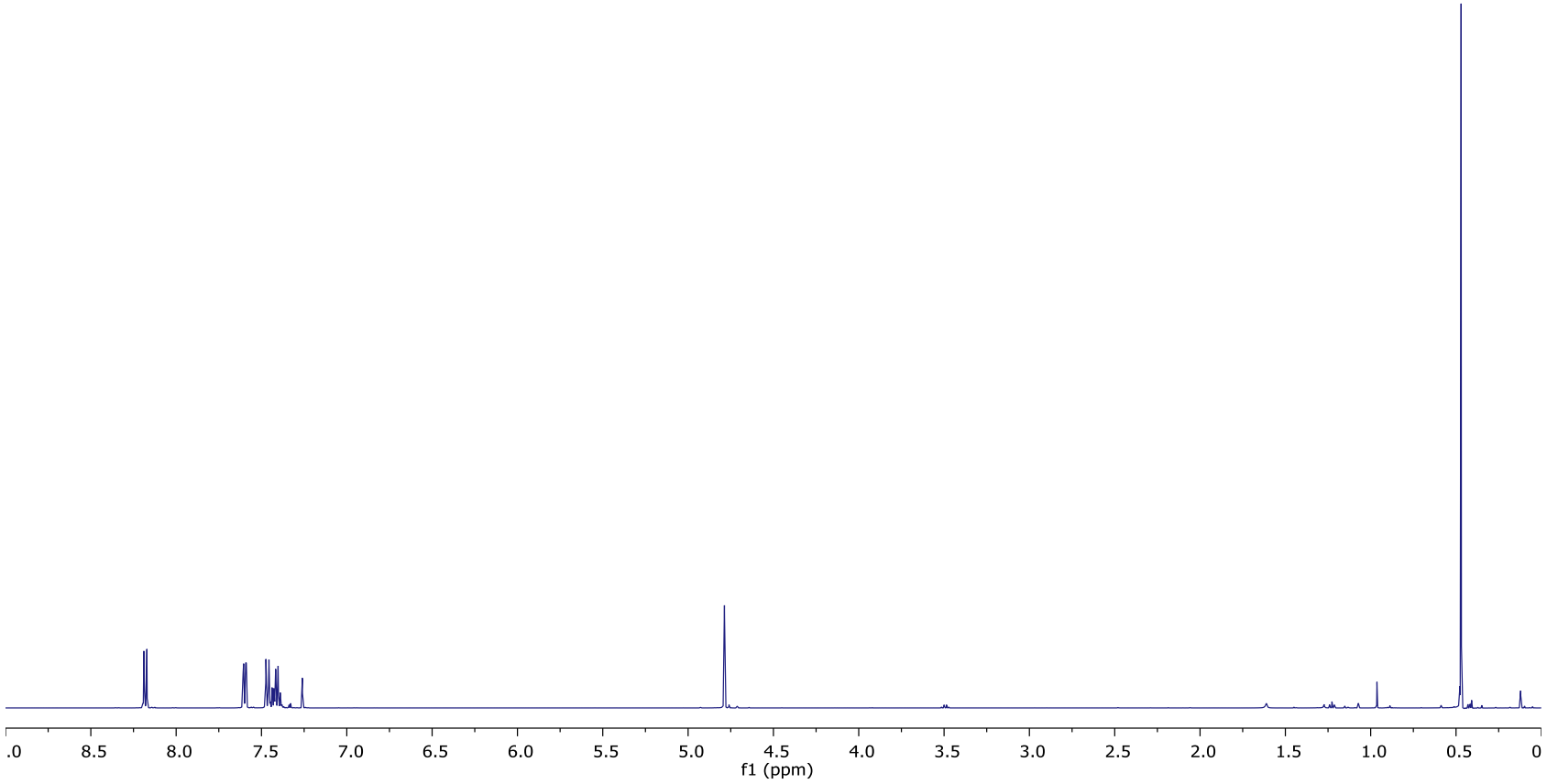
^{13}C NMR (126 MHz, $CDCl_3$) of compound **59a**.



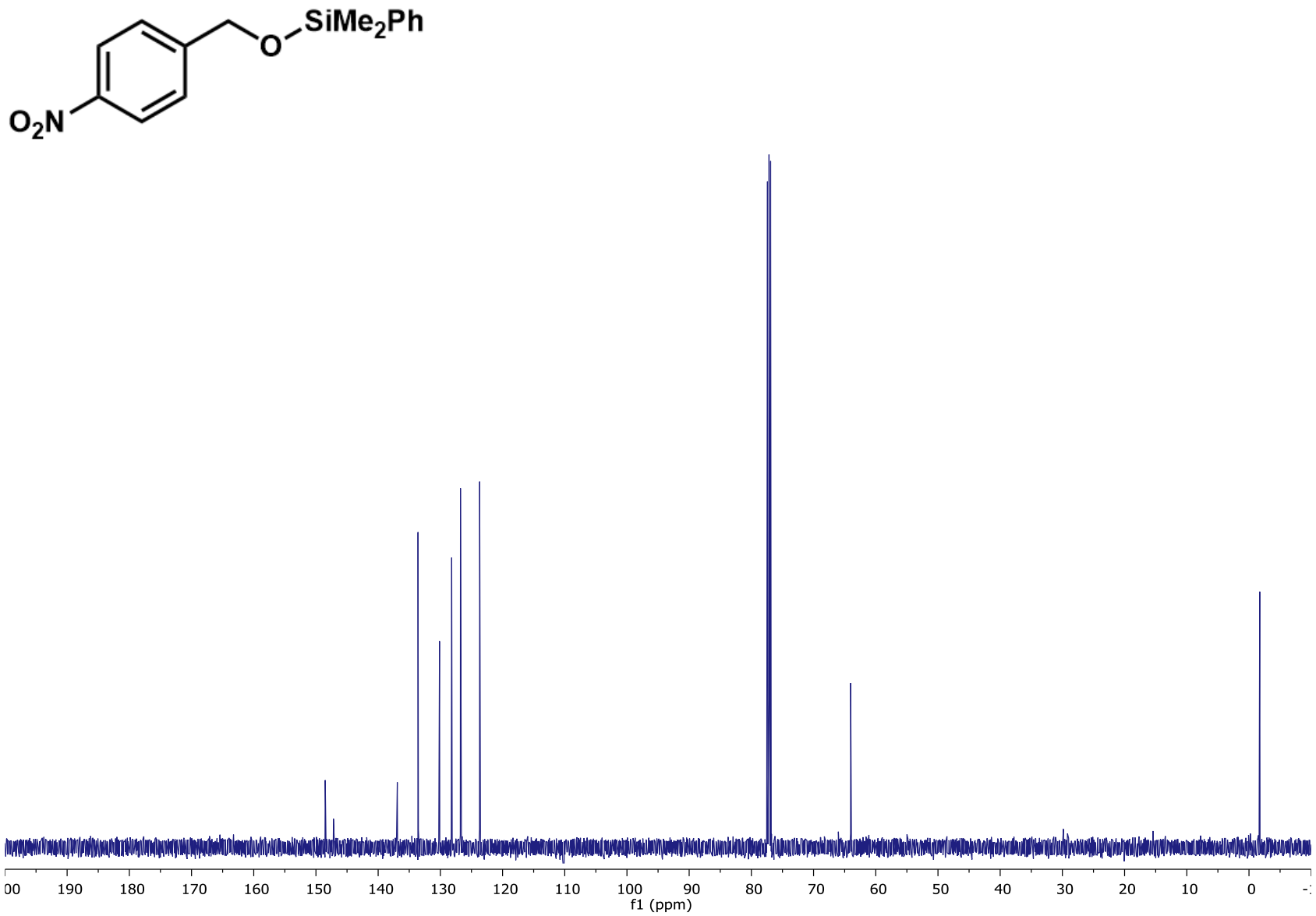


^{1}H NMR (500 MHz, $CDCl_3$) of compound **59b.**

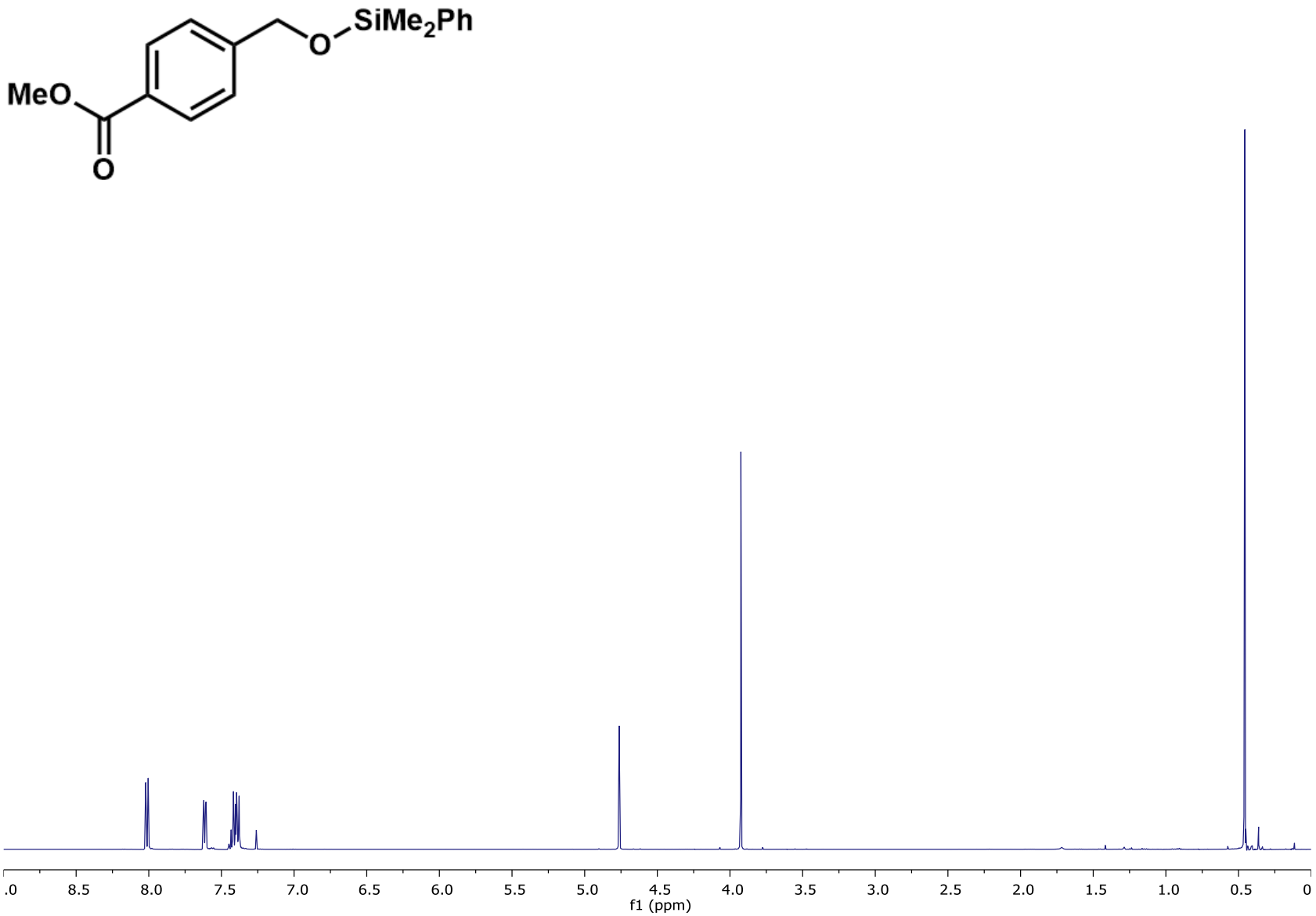




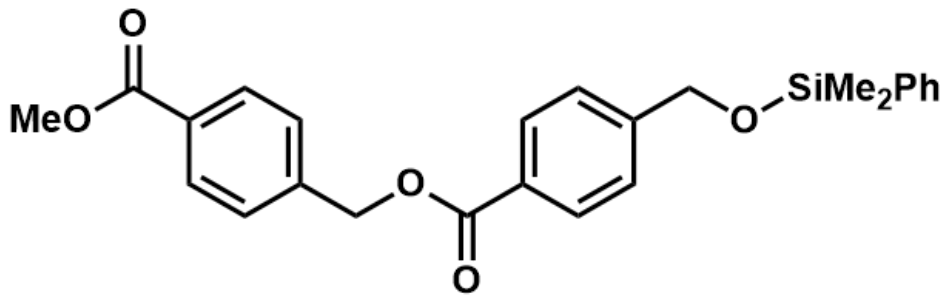
^{1}H NMR (500 MHz, $CDCl_3$) of compound **59c.**

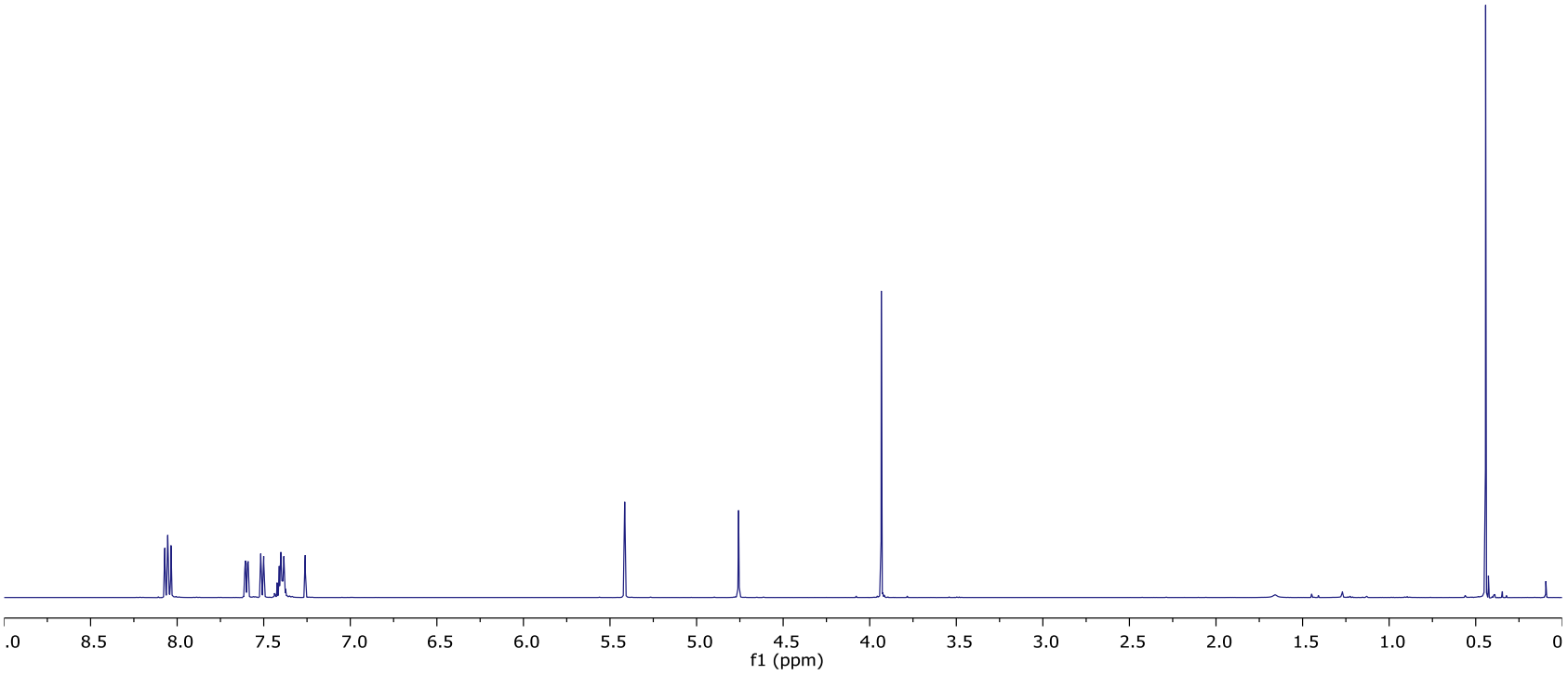


^{13}C NMR (126 MHz, $CDCl_3$) of compound **59c.**

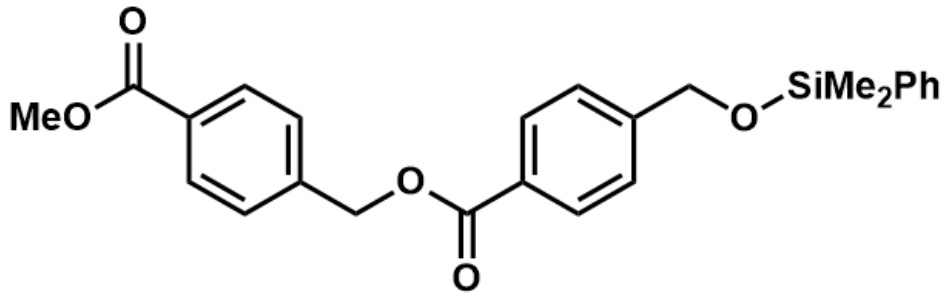


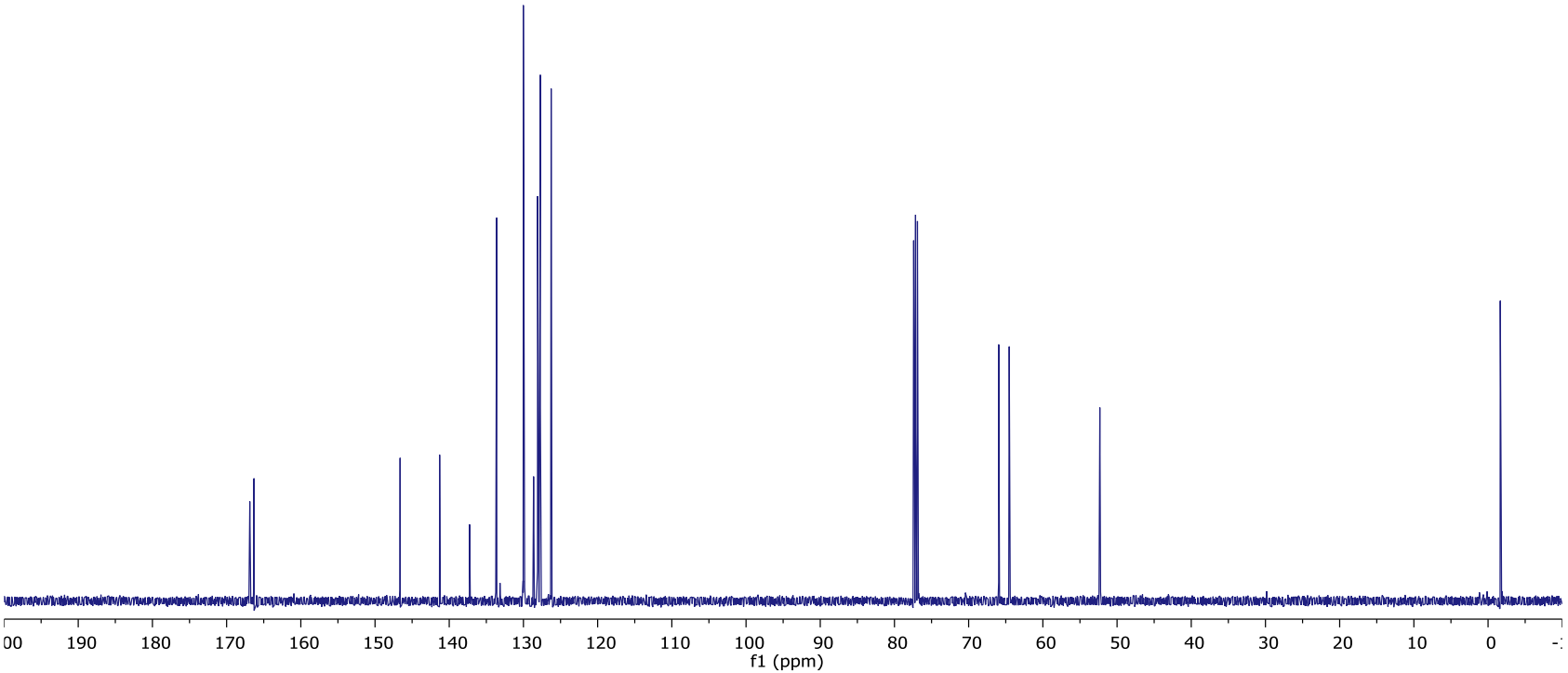
^{1}H NMR (500 MHz, $CDCl_3$) of compound **59d.**



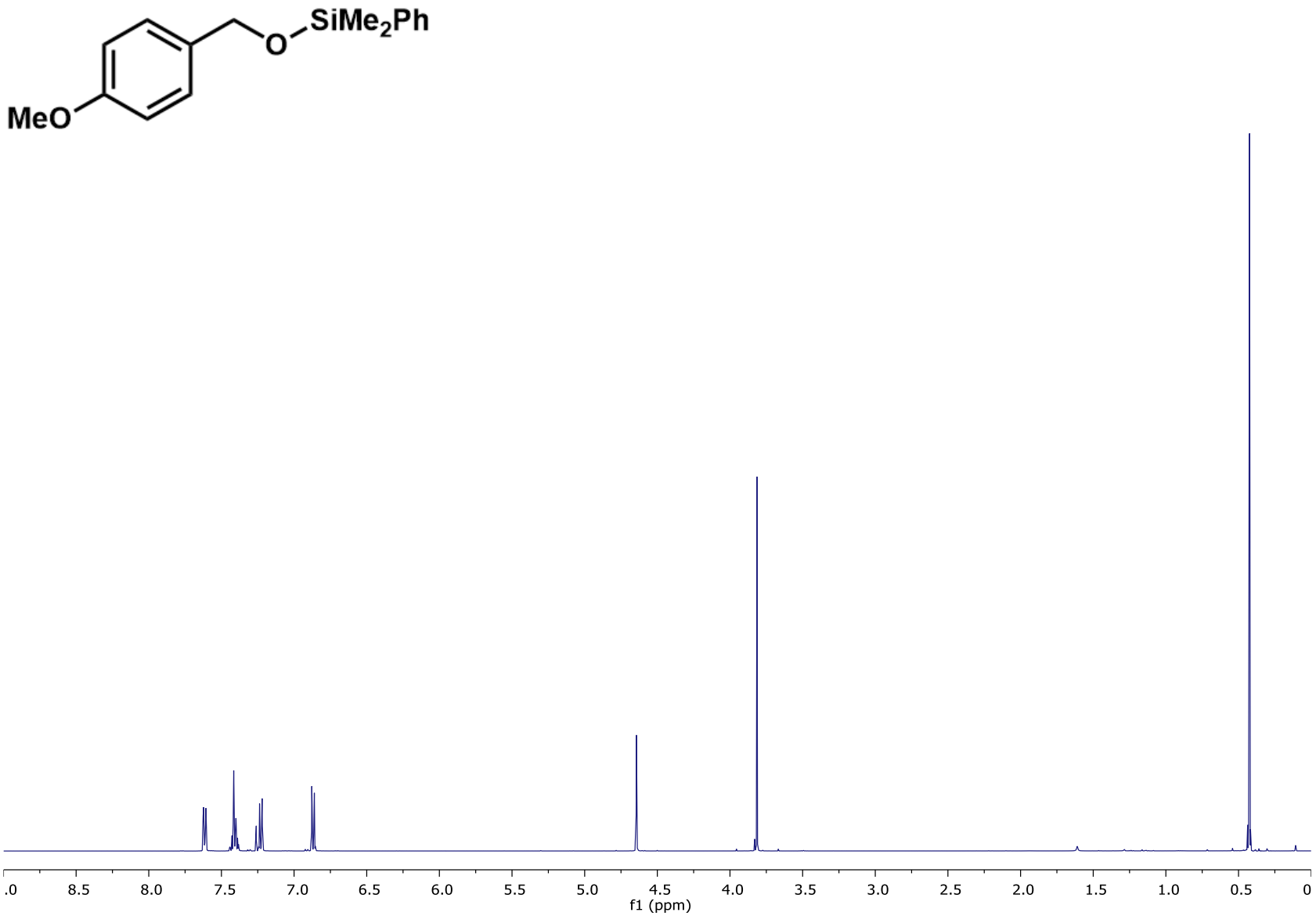


^{1}H NMR (500 MHz, $CDCl_3$) of compound **59d_dim.**

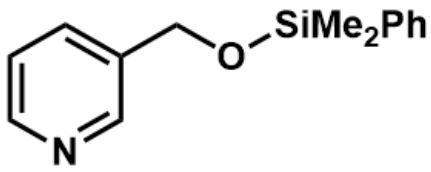


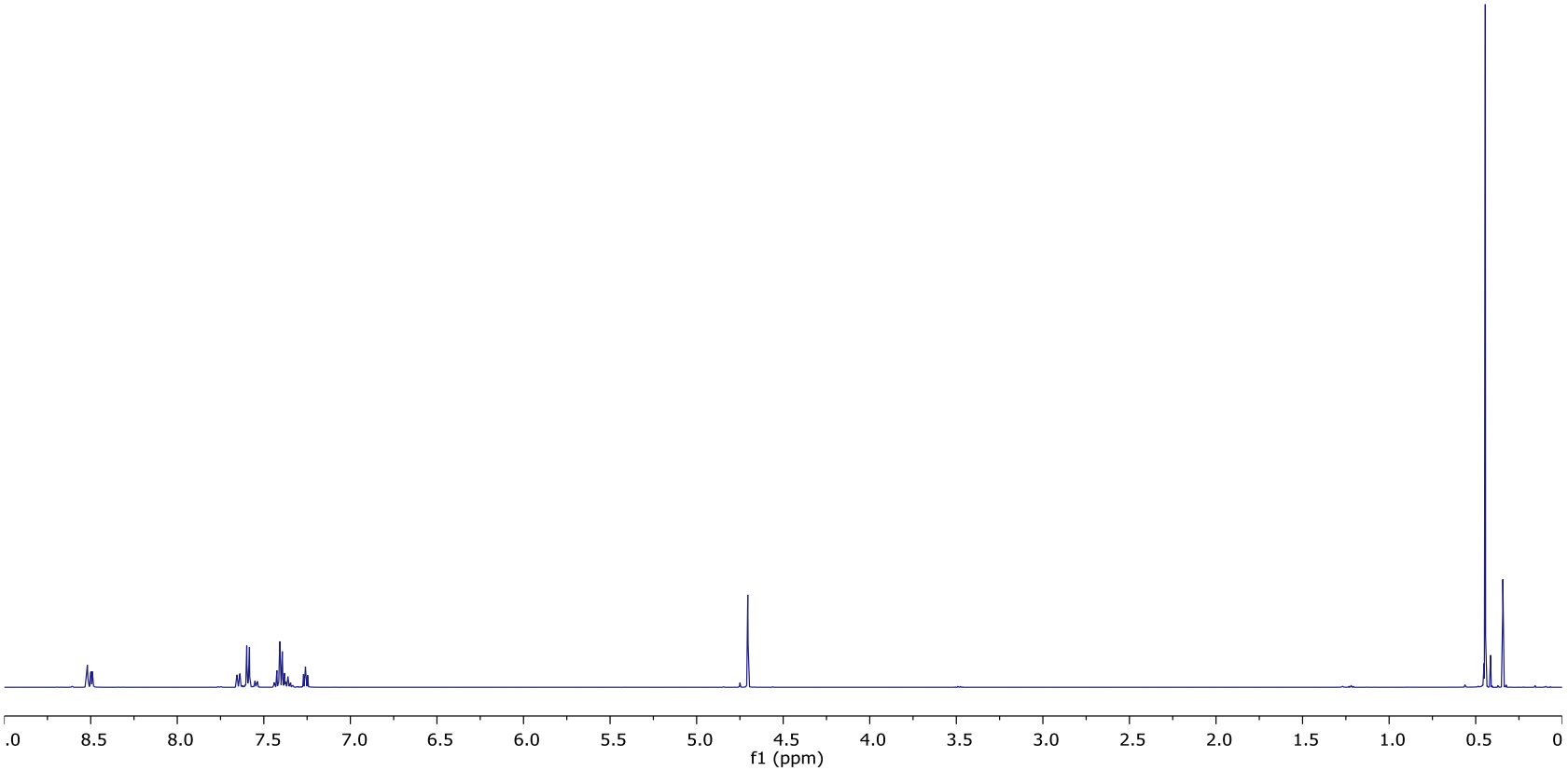


^{13}C NMR (126 MHz, $CDCl_3$) of compound **59d_dim.**

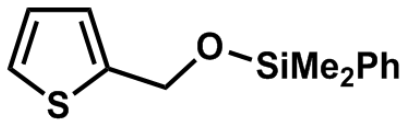


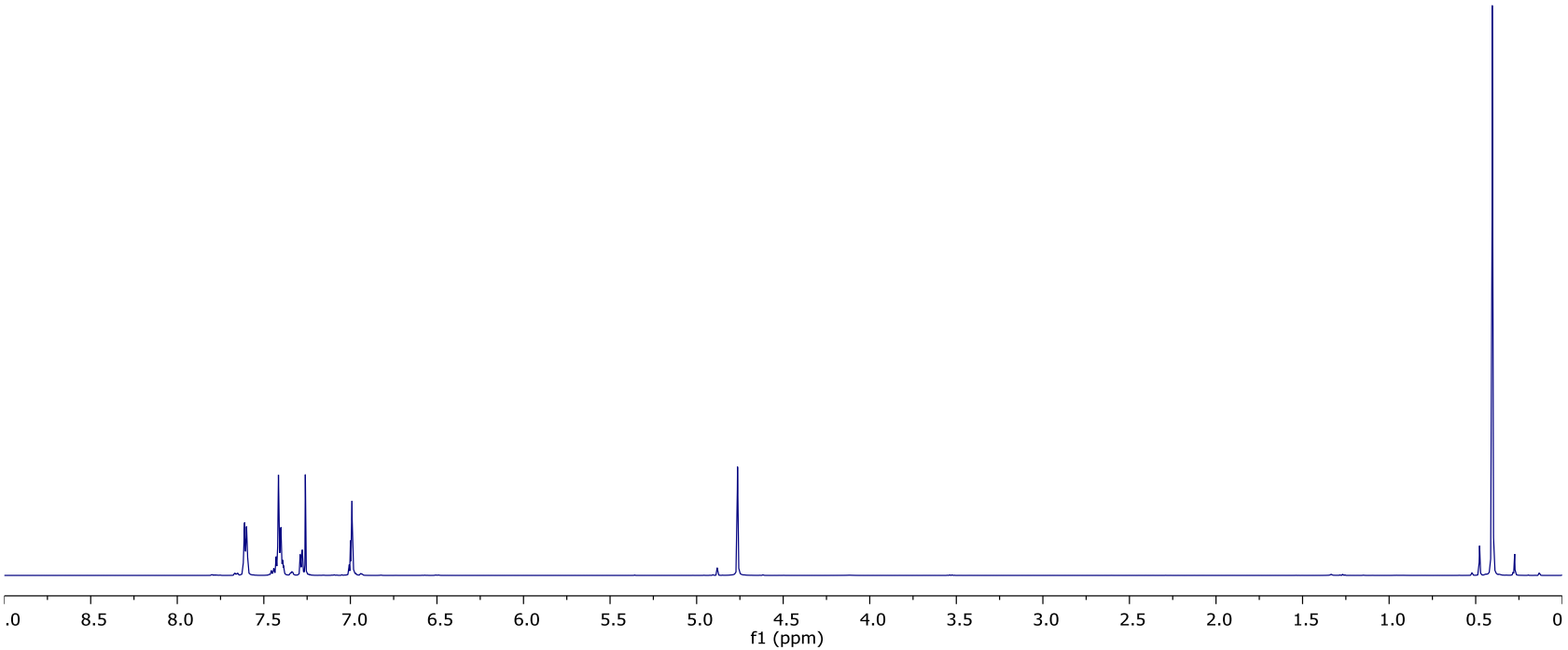
^{1}H NMR (500 MHz, $CDCl_3$) of compound **59e.**



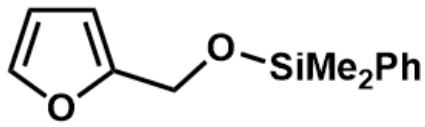


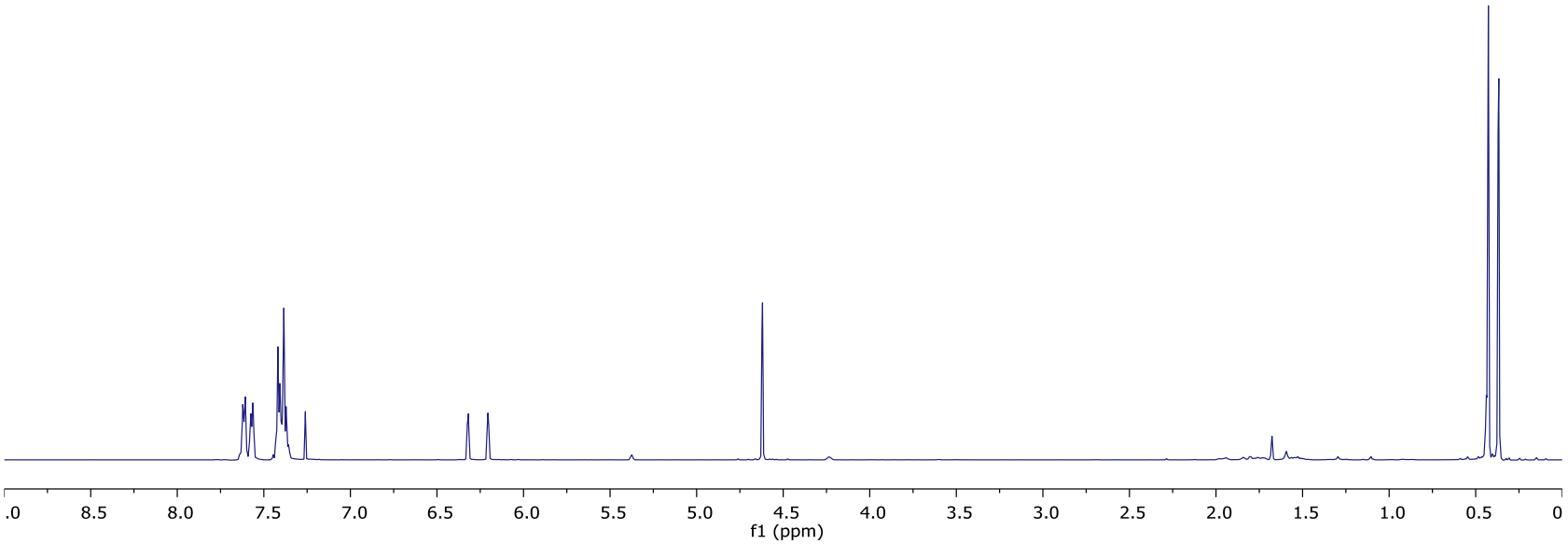
^{1}H NMR (500 MHz, $CDCl_3$) of compound **59f.**



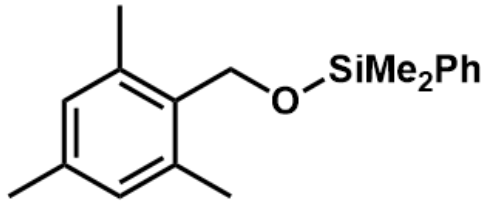


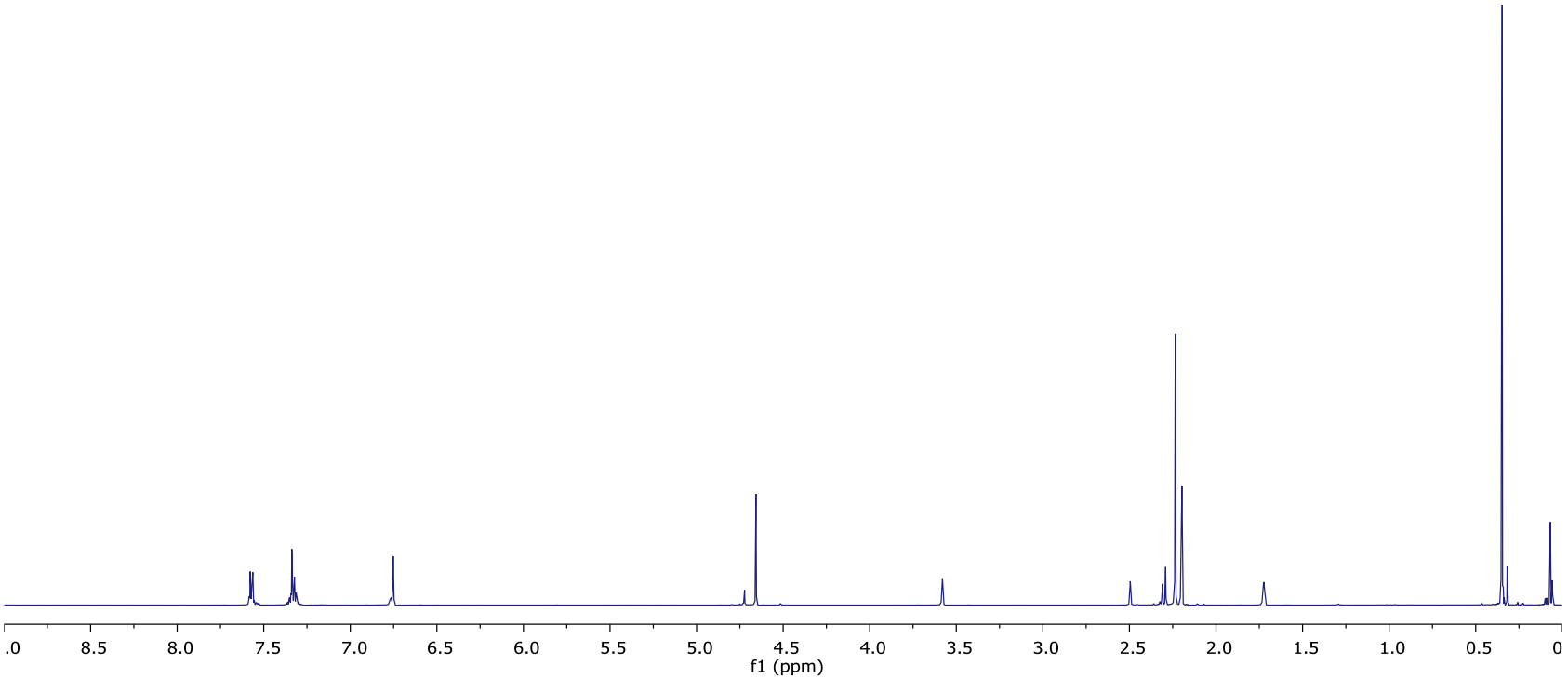
^{1}H NMR (500 MHz, $CDCl_3$) of compound **59g.**



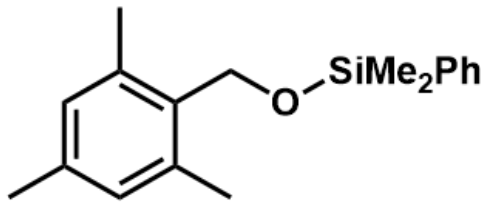


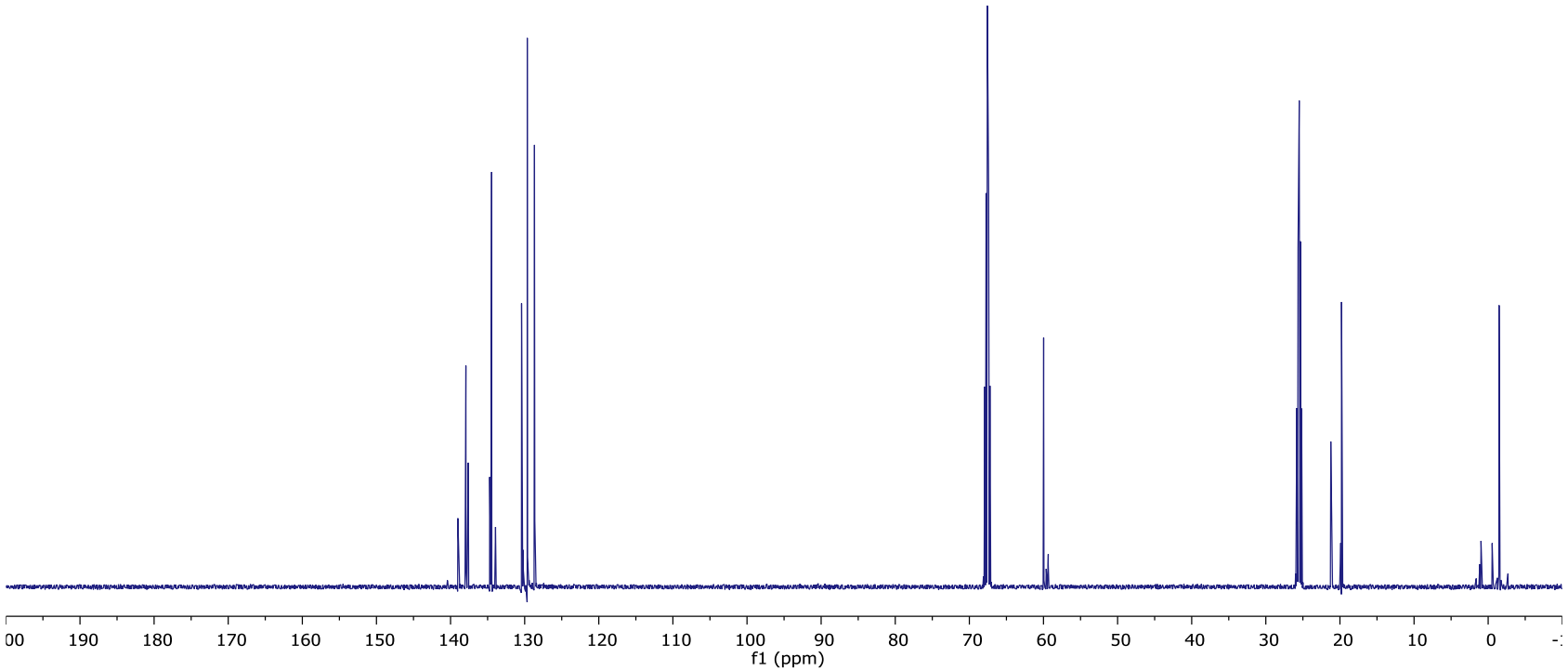
^{1}H NMR (500 MHz, $CDCl_3$) of compound **59h.**



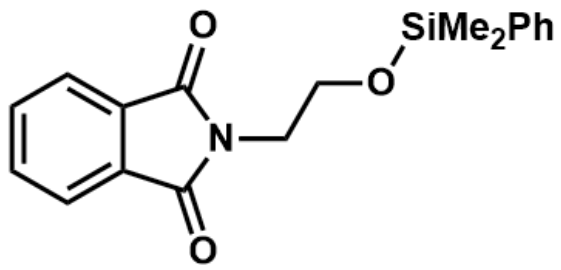


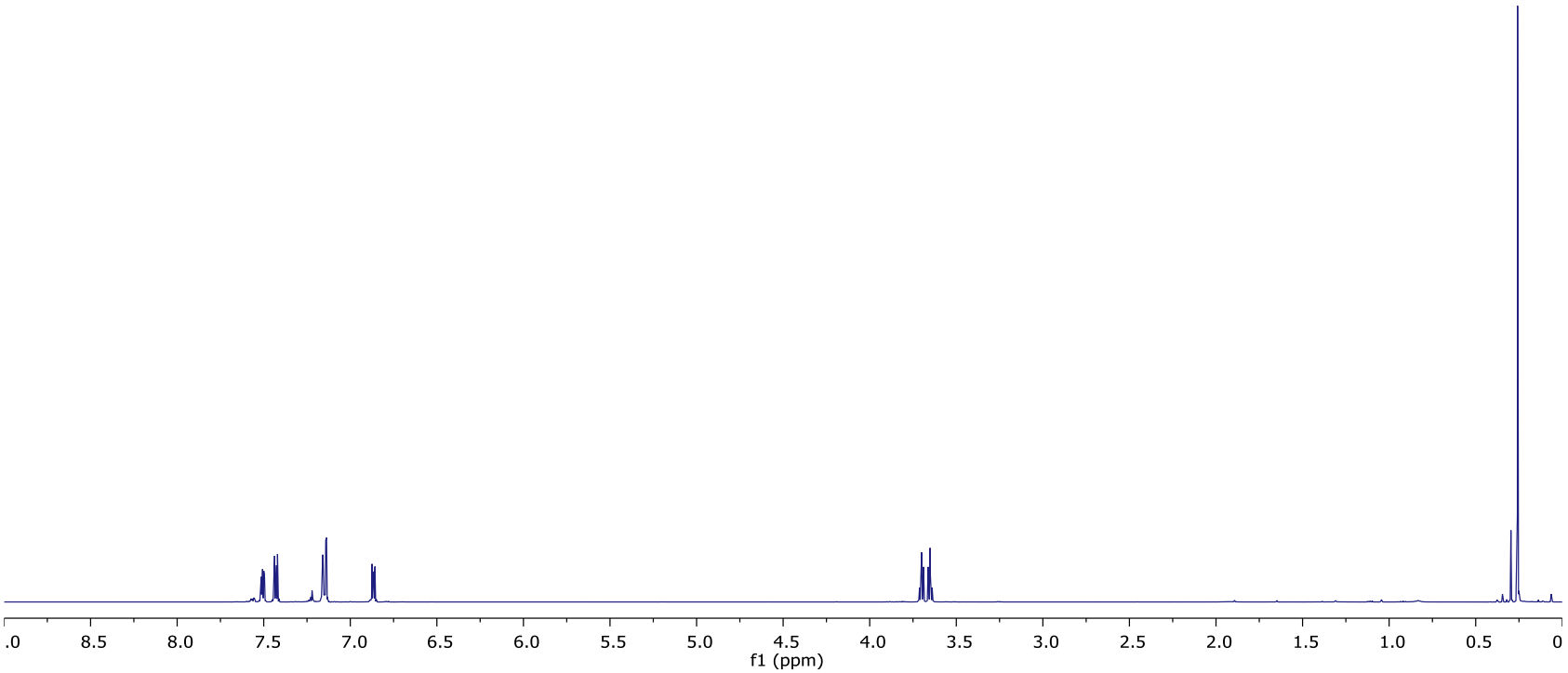
^{1}H NMR (500 MHz, THF-d_8) of compound **59i.**



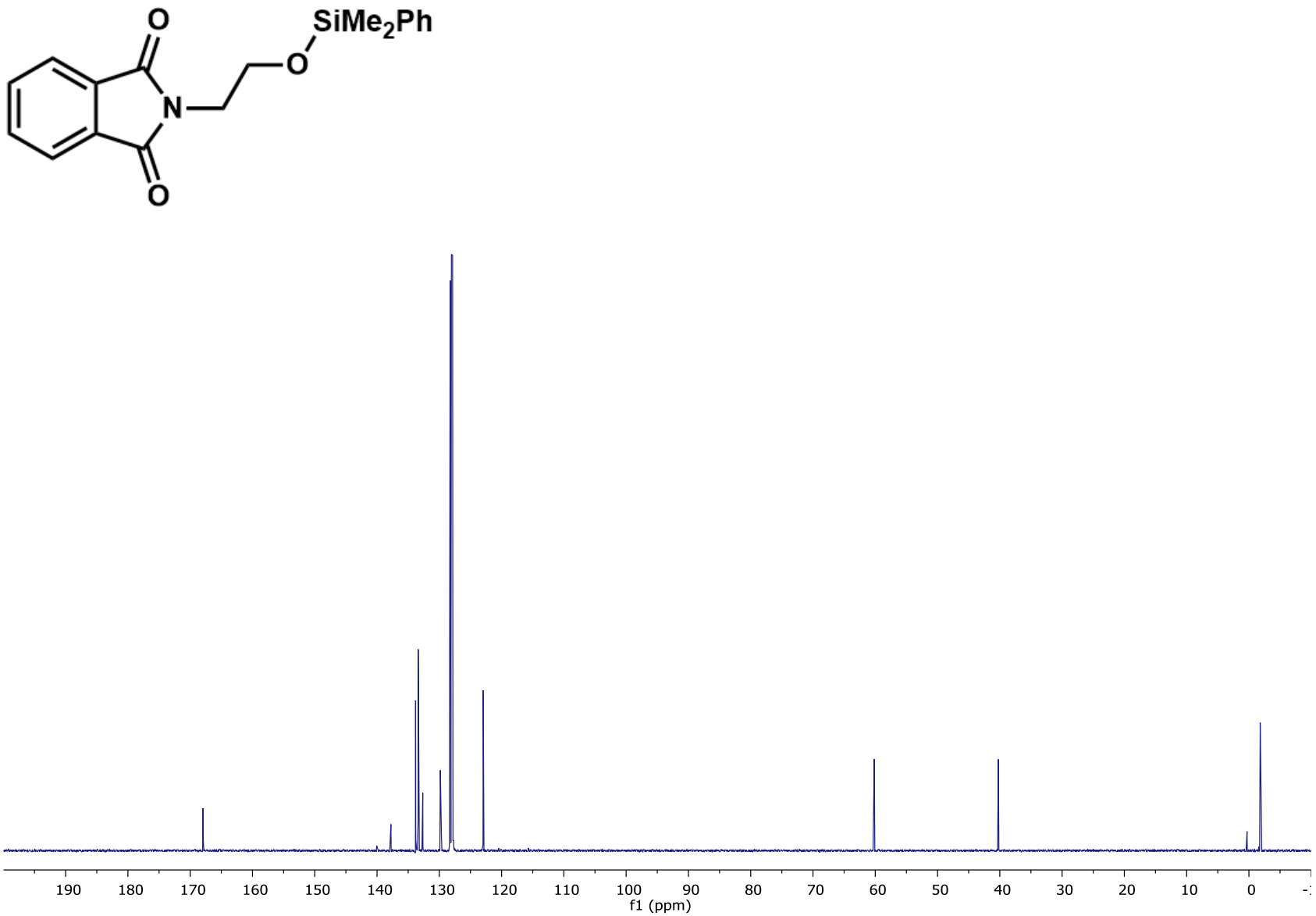


^{13}C NMR (126 MHz, THF-d_8) of compound **59i.**

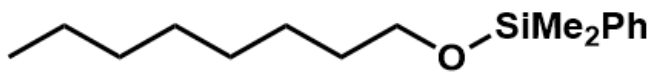


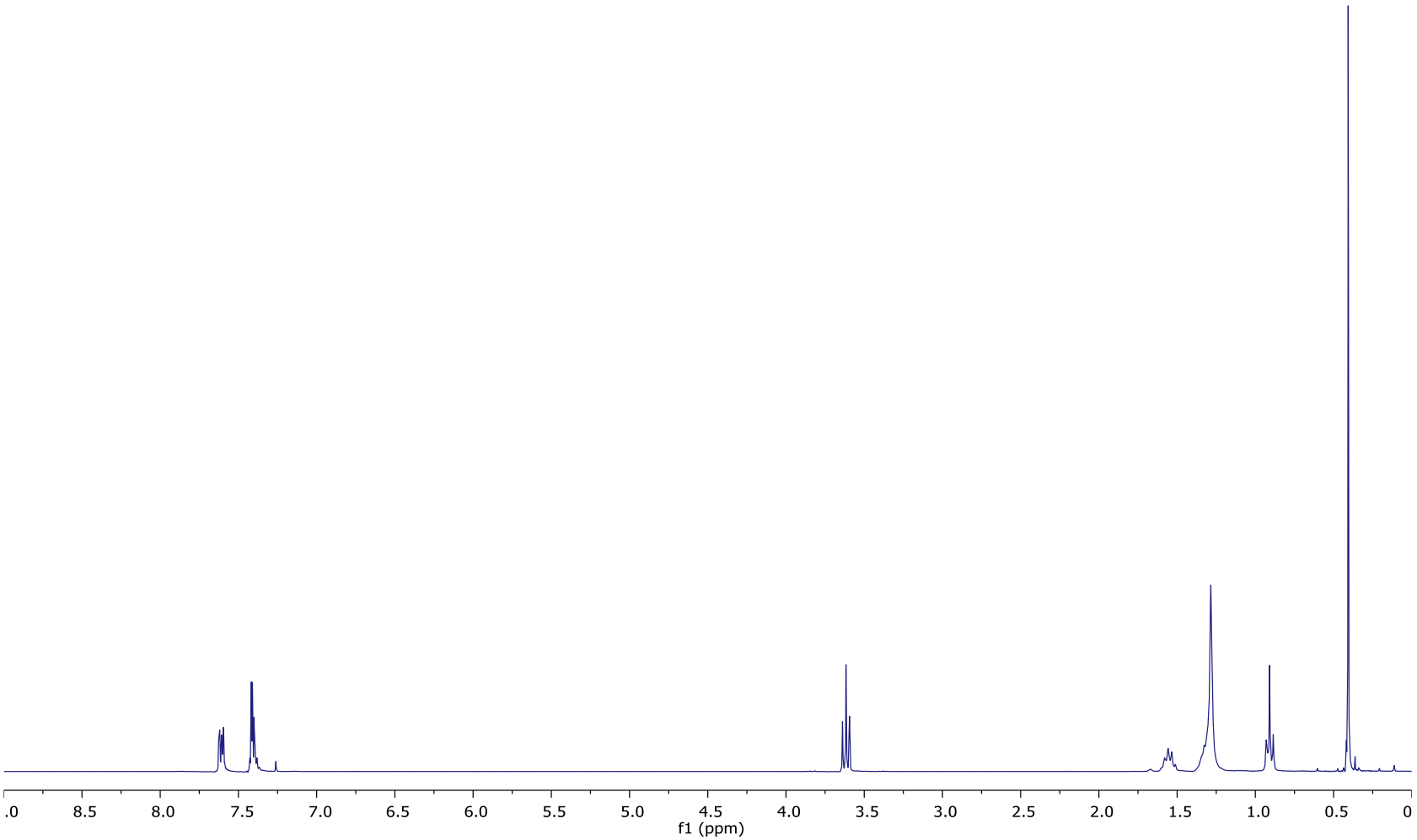


^{1}H NMR (500 MHz, Benzene-d_6) of compound **59j.**

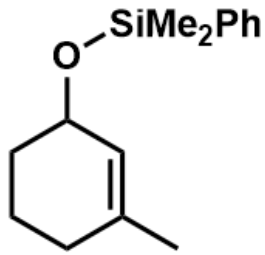


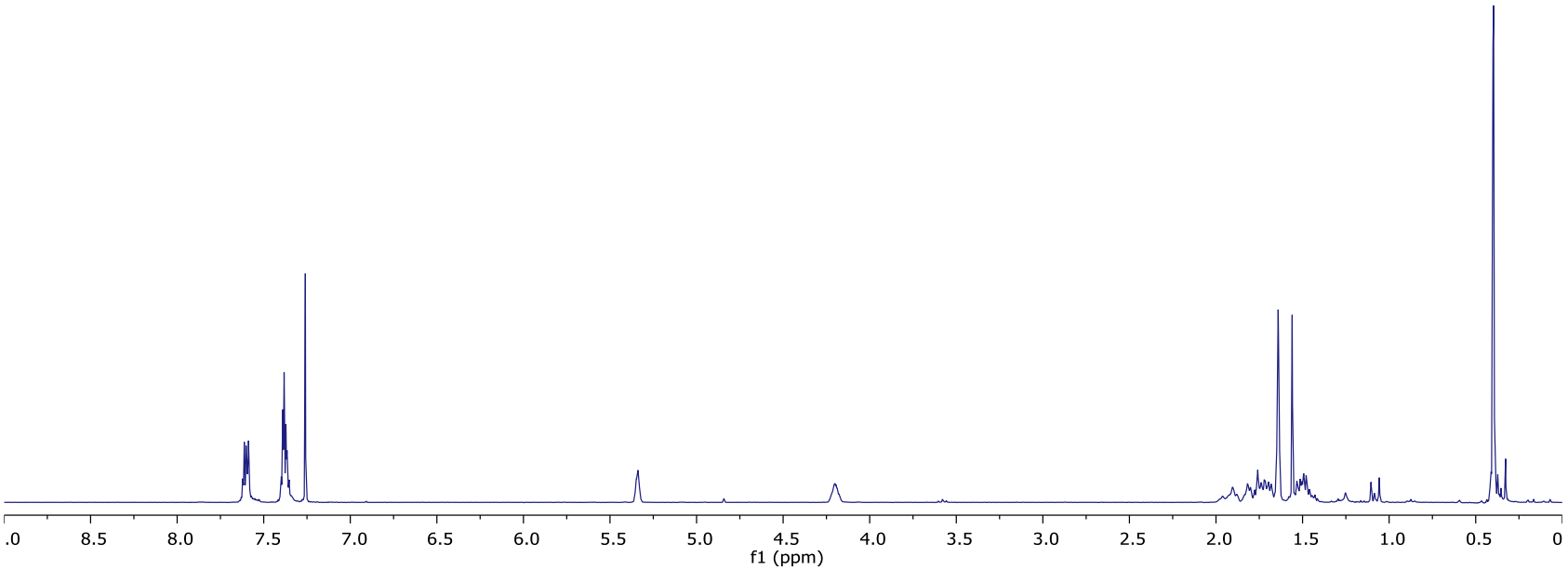
^{13}C NMR (126 MHz, Benzene-d_6) of compound **59j.**



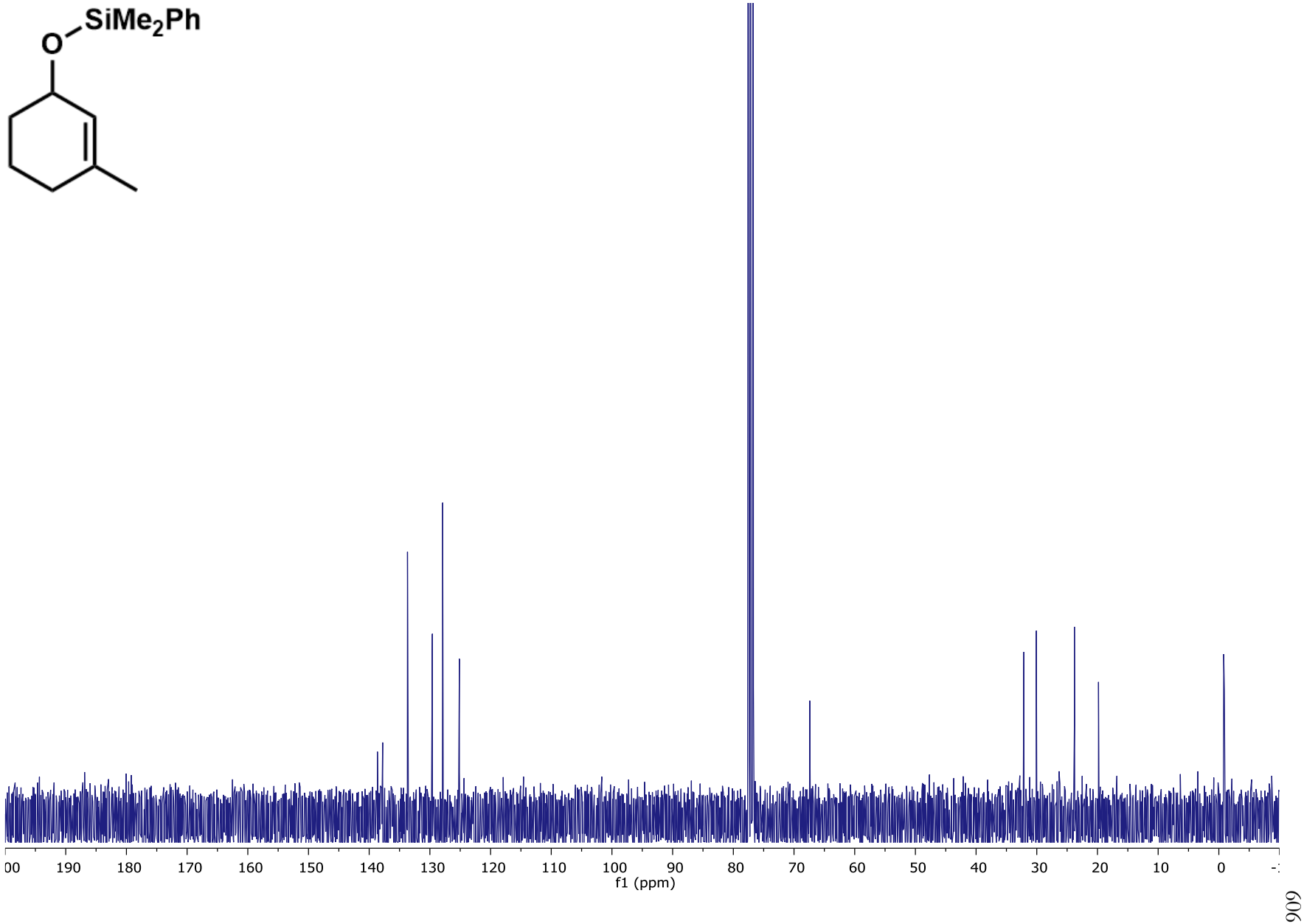


^{1}H NMR (500 MHz, $CDCl_3$) of compound **59k.**

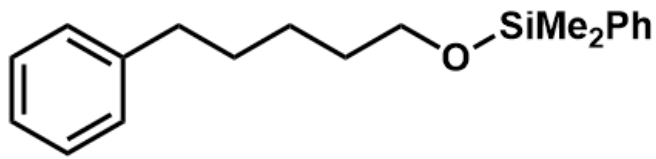


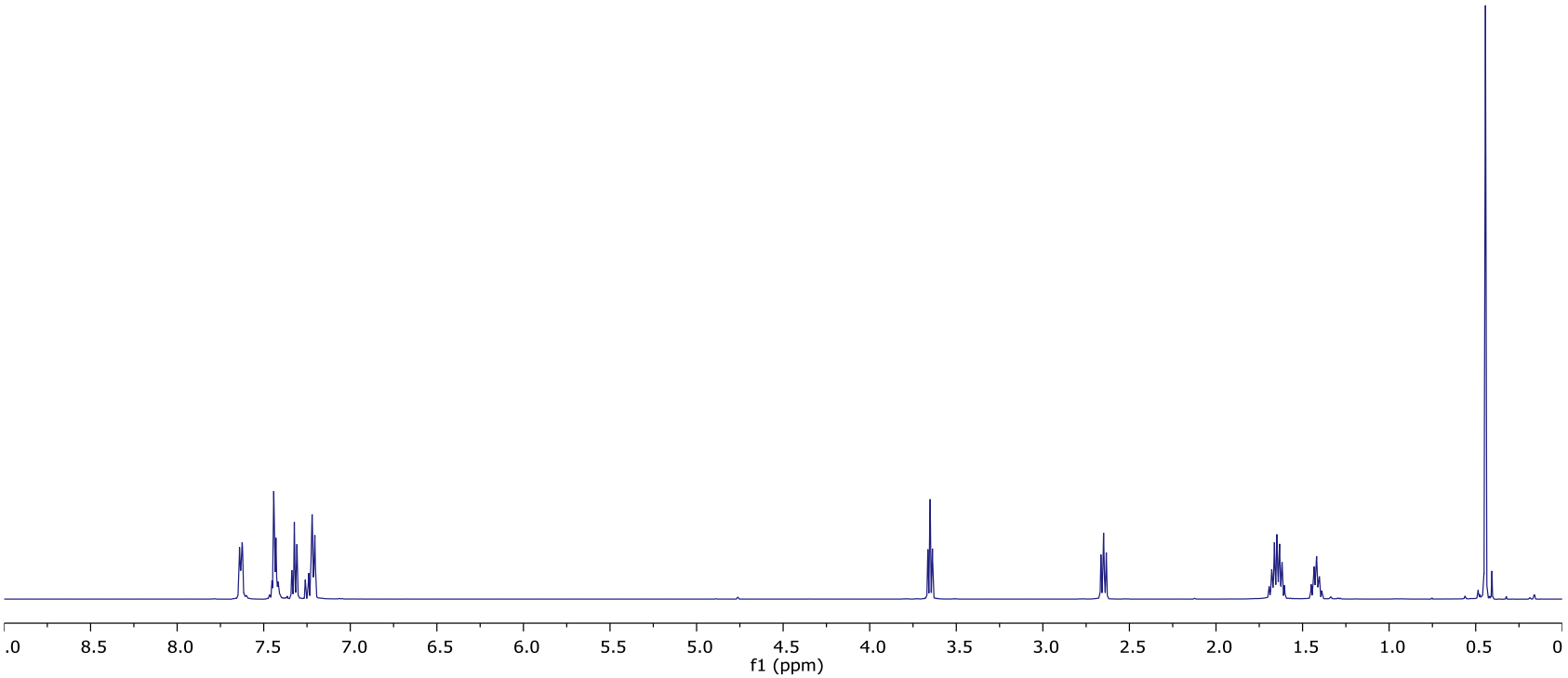


^{1}H NMR (500 MHz, $CDCl_3$) of compound **59l.**

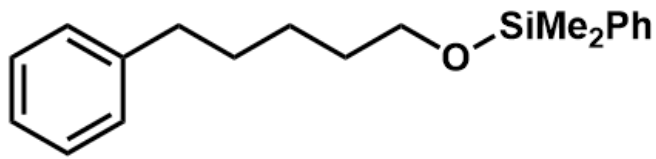


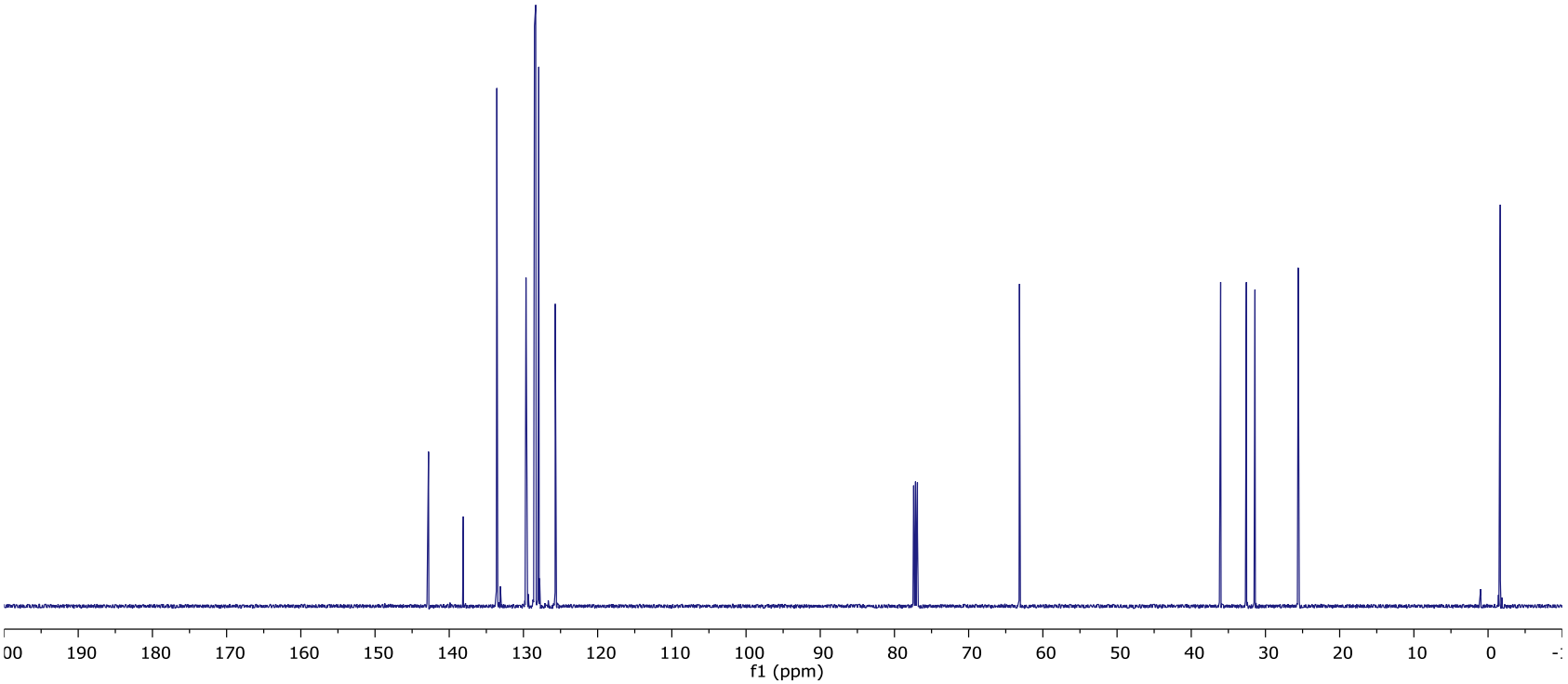
^{13}C NMR (126 MHz, $CDCl_3$) of compound **59l.**



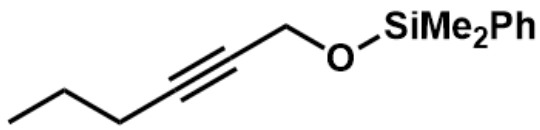


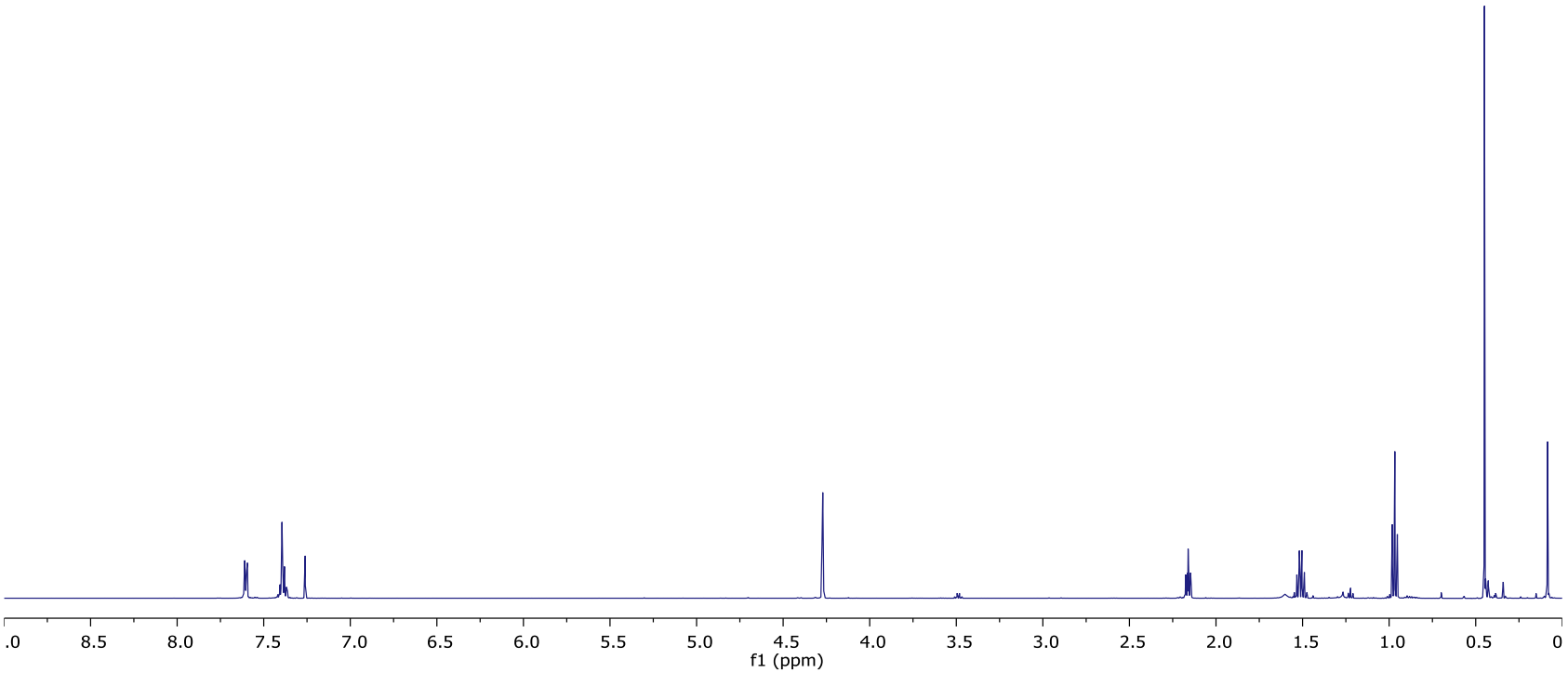
^{1}H NMR (500 MHz, $CDCl_3$) of compound **59m.**



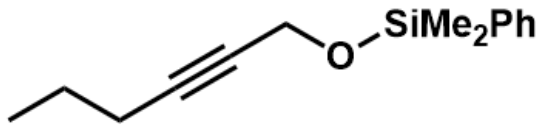


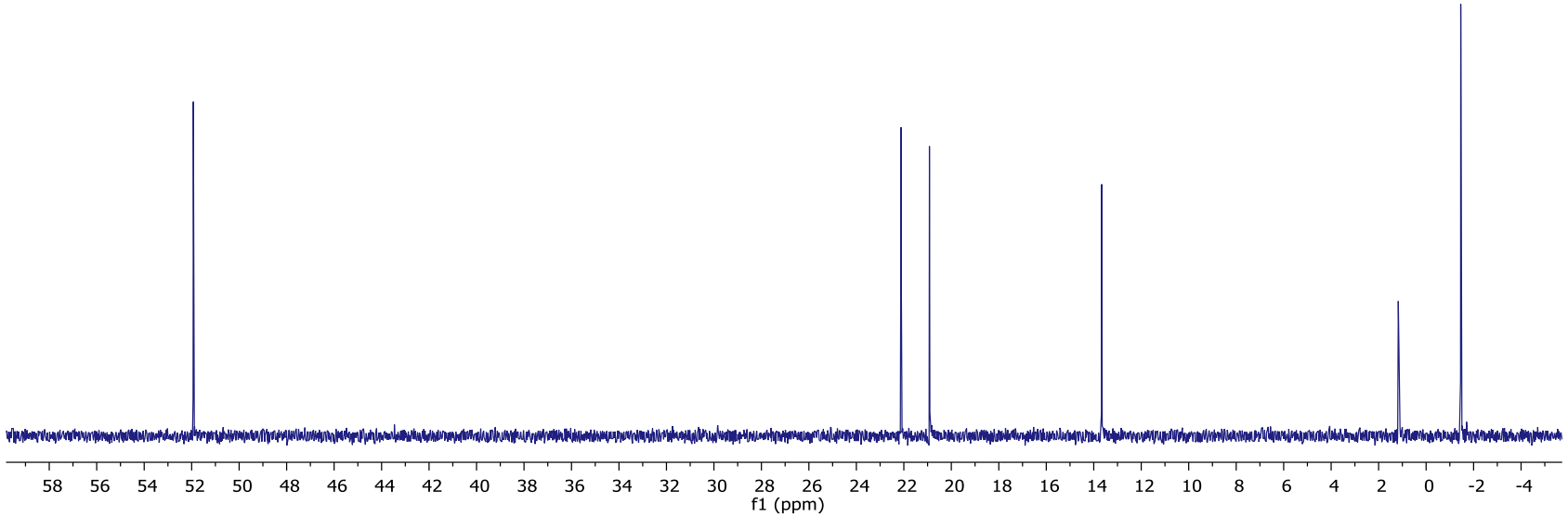
^{13}C NMR (126 MHz, $CDCl_3$) of compound **59m.**



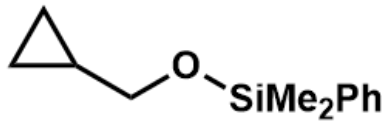


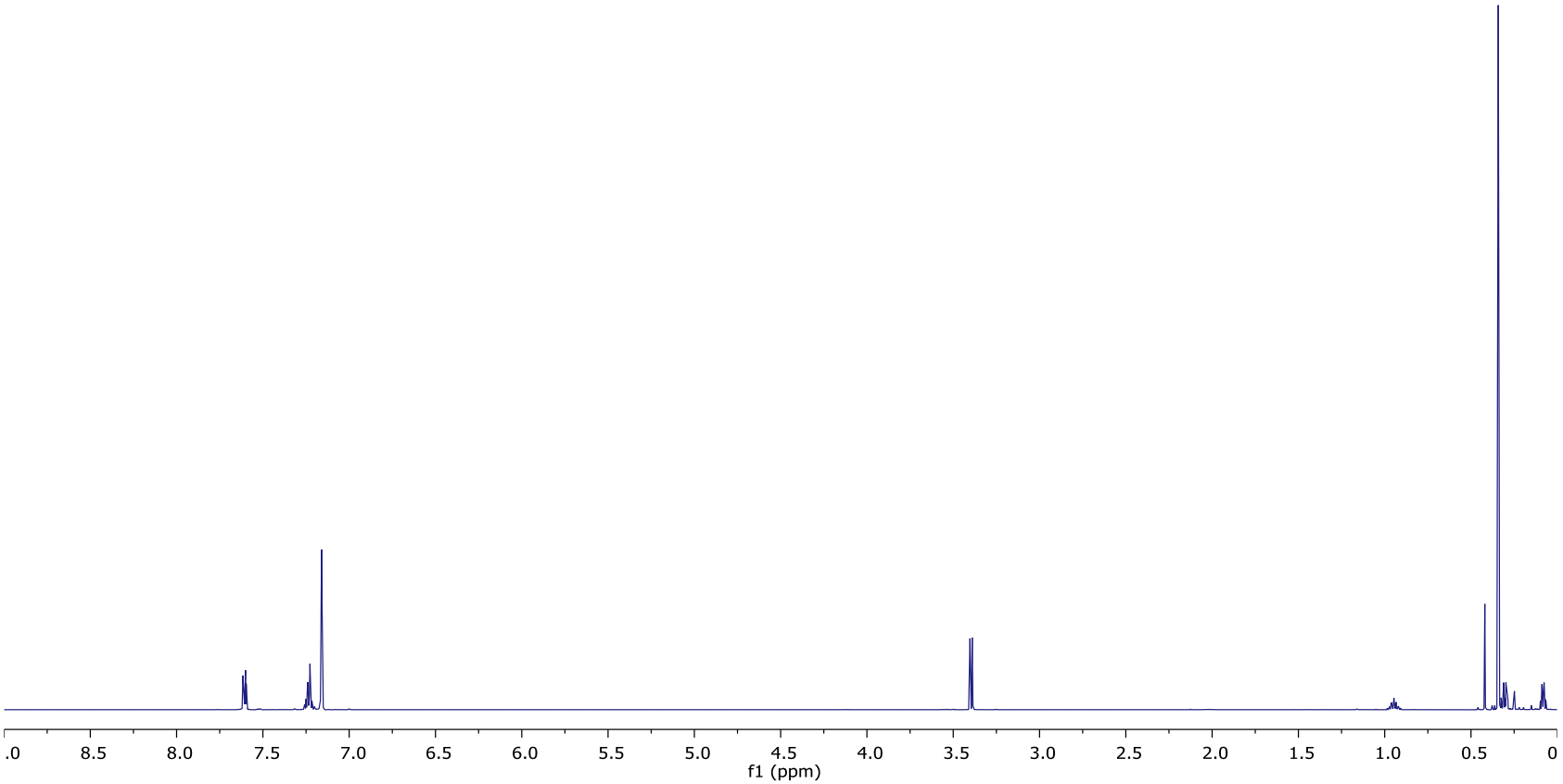
^{1}H NMR (500 MHz, $CDCl_3$) of compound **59n.**



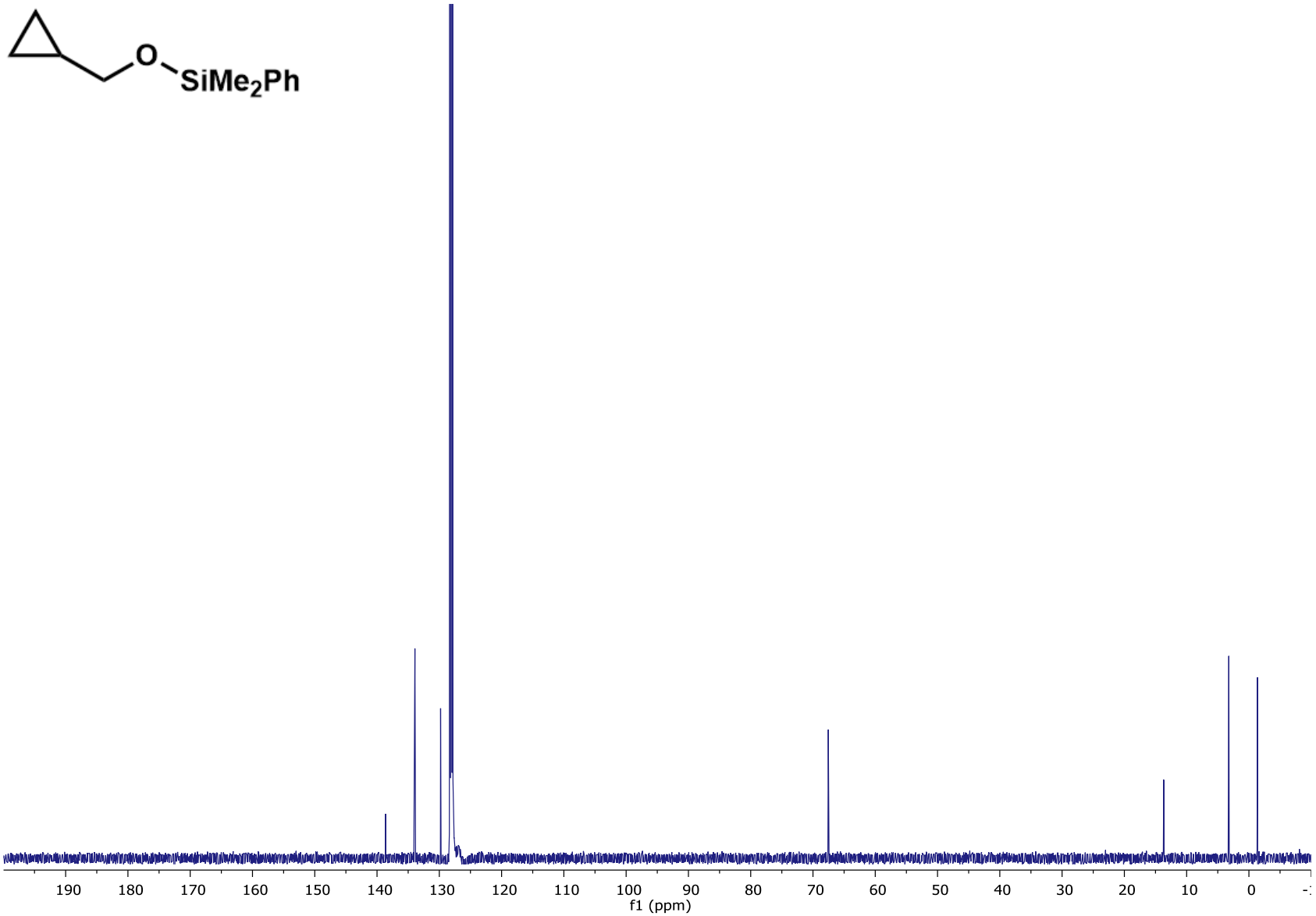


^{13}C NMR (126 MHz, $CDCl_3$) of compound **59n.**

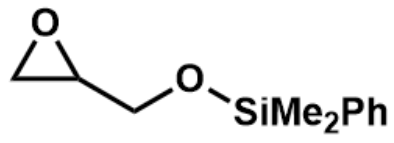


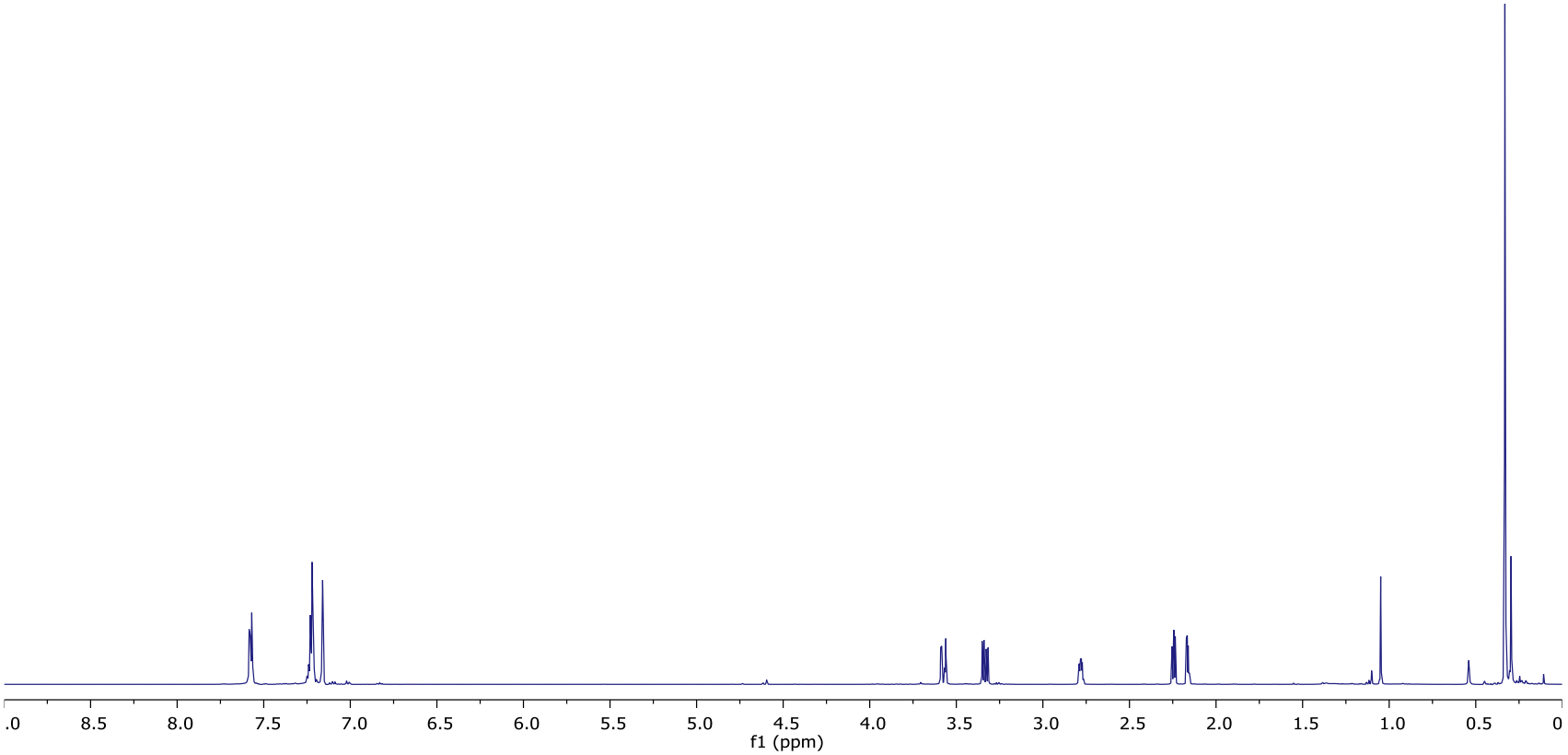


^{1}H NMR (500 MHz, Benzene-d_6) of compound **59o.**

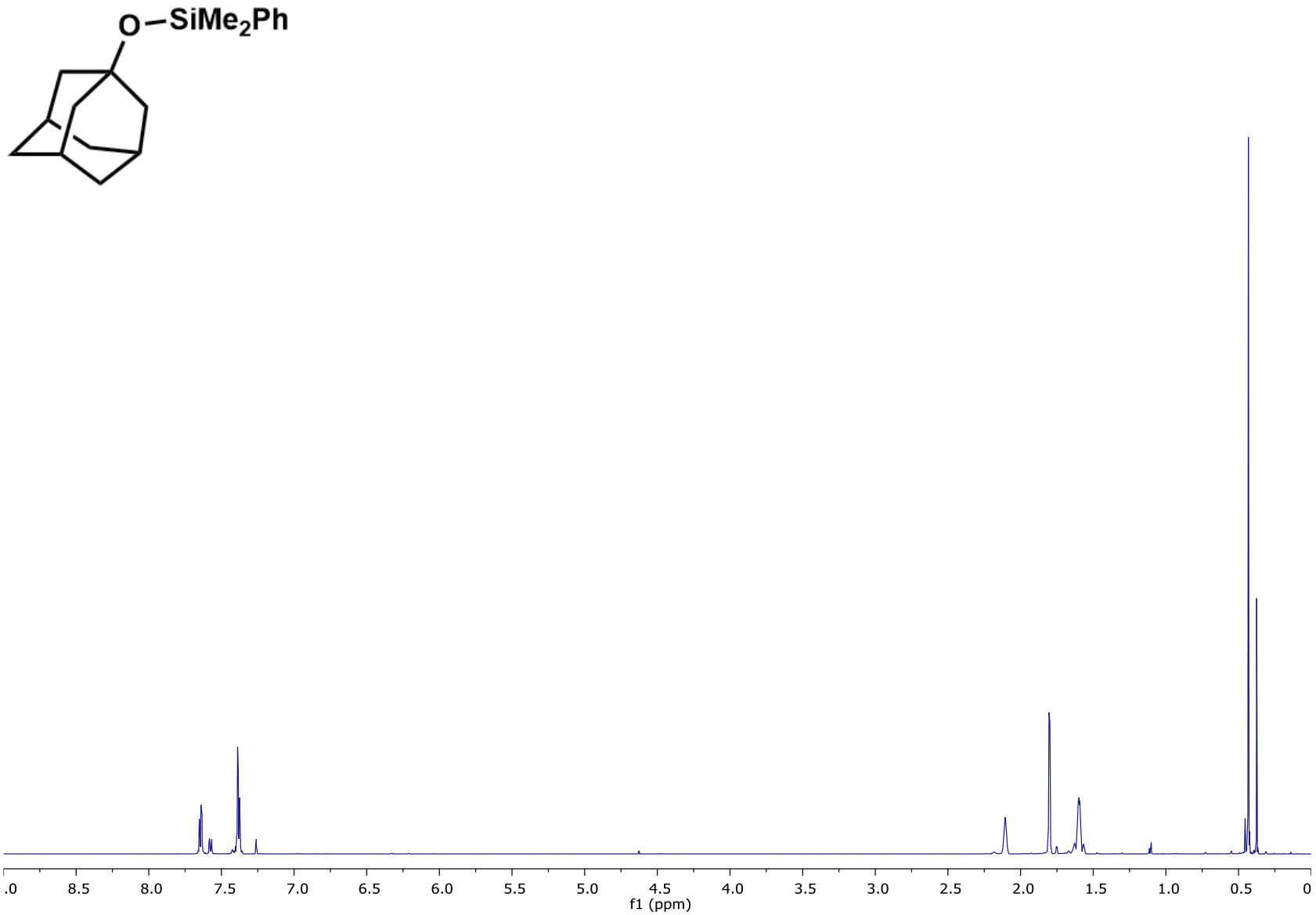


^{13}C NMR (126 MHz, Benzene-d_6) of compound **59o.**

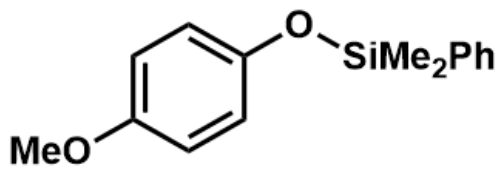


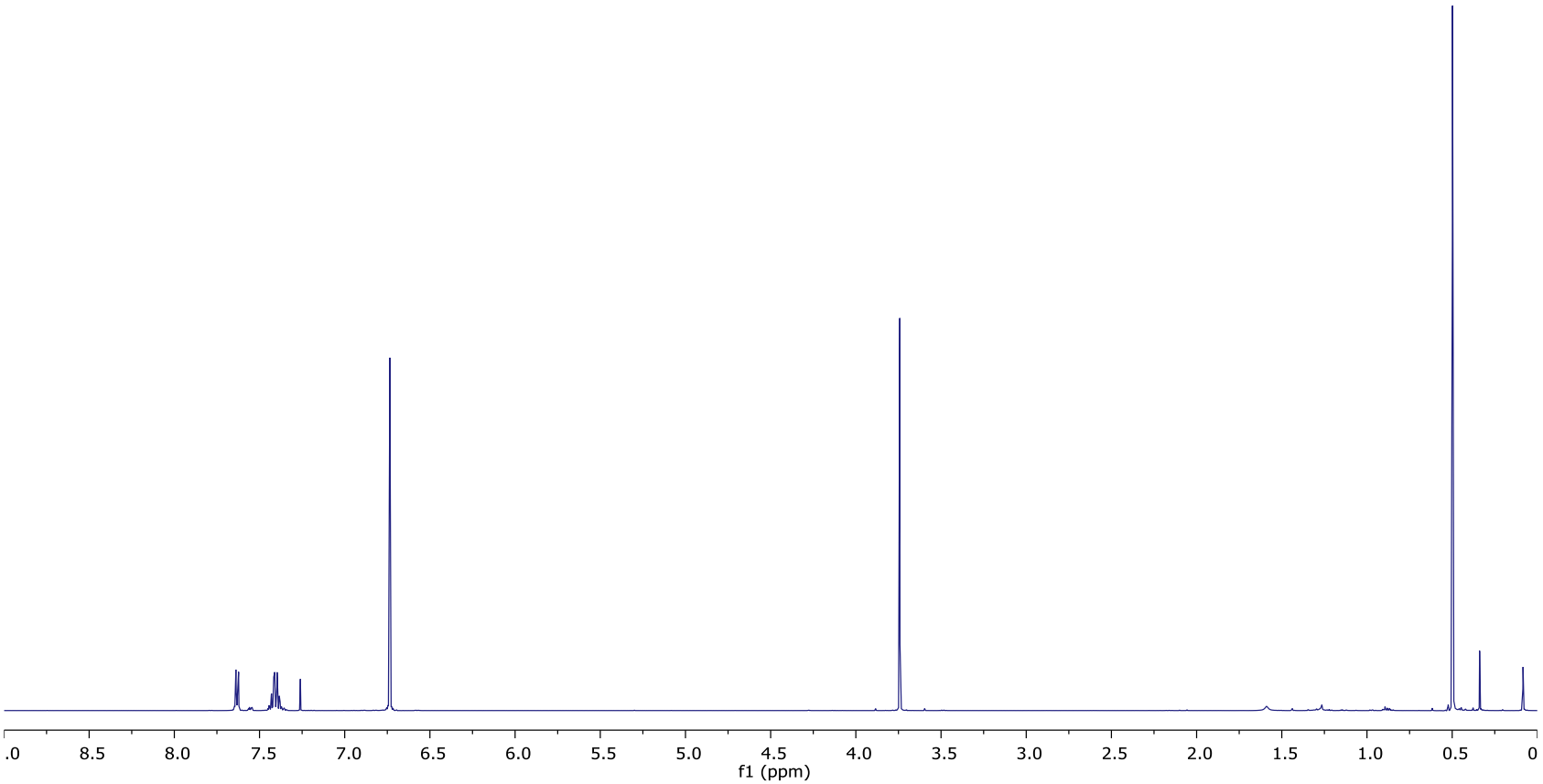


^{1}H NMR (500 MHz, Benzene-d_6) of compound **59p.**

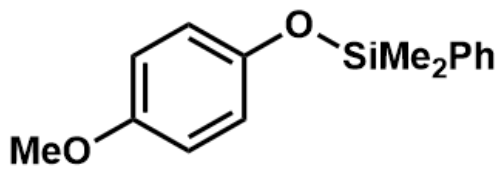


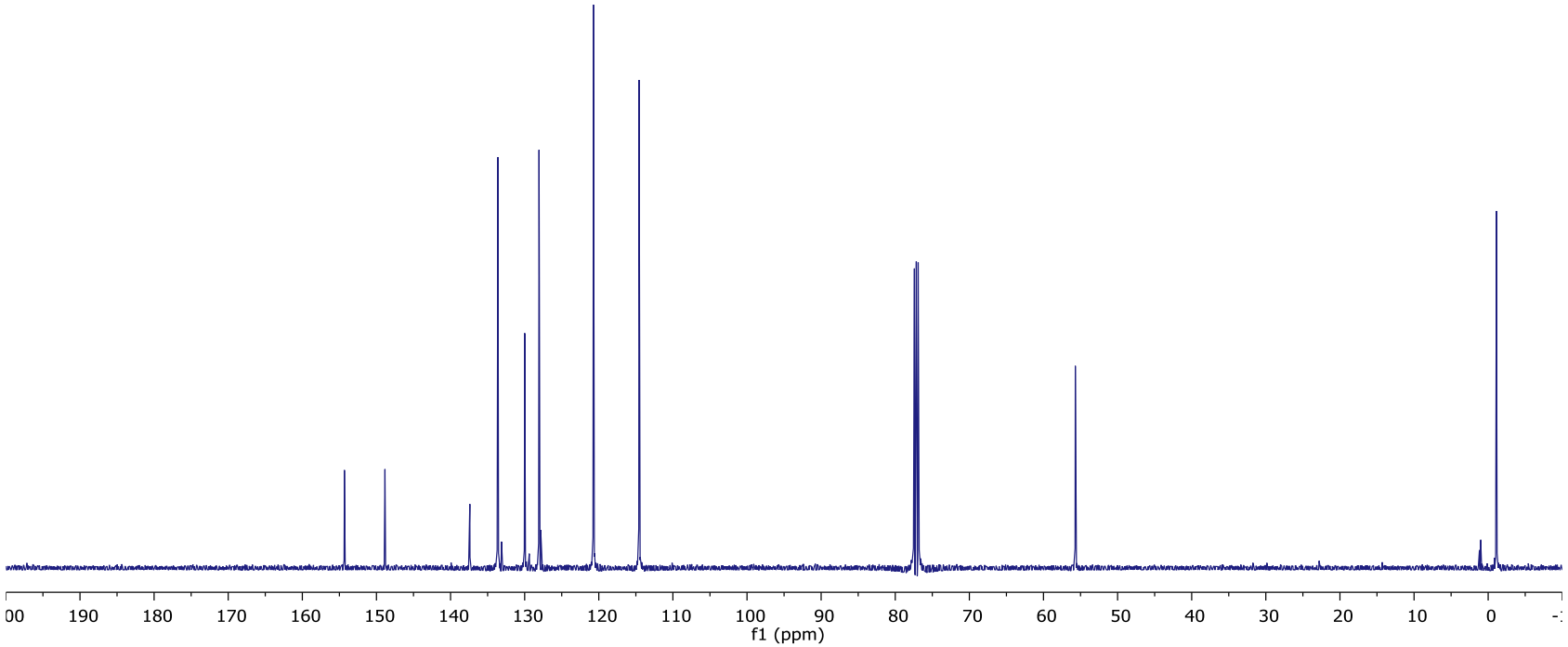
^{1}H NMR (500 MHz, $CDCl_3$) of compound **59q.**



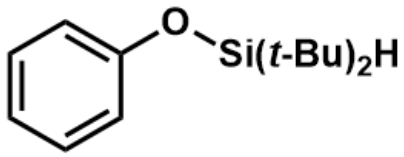


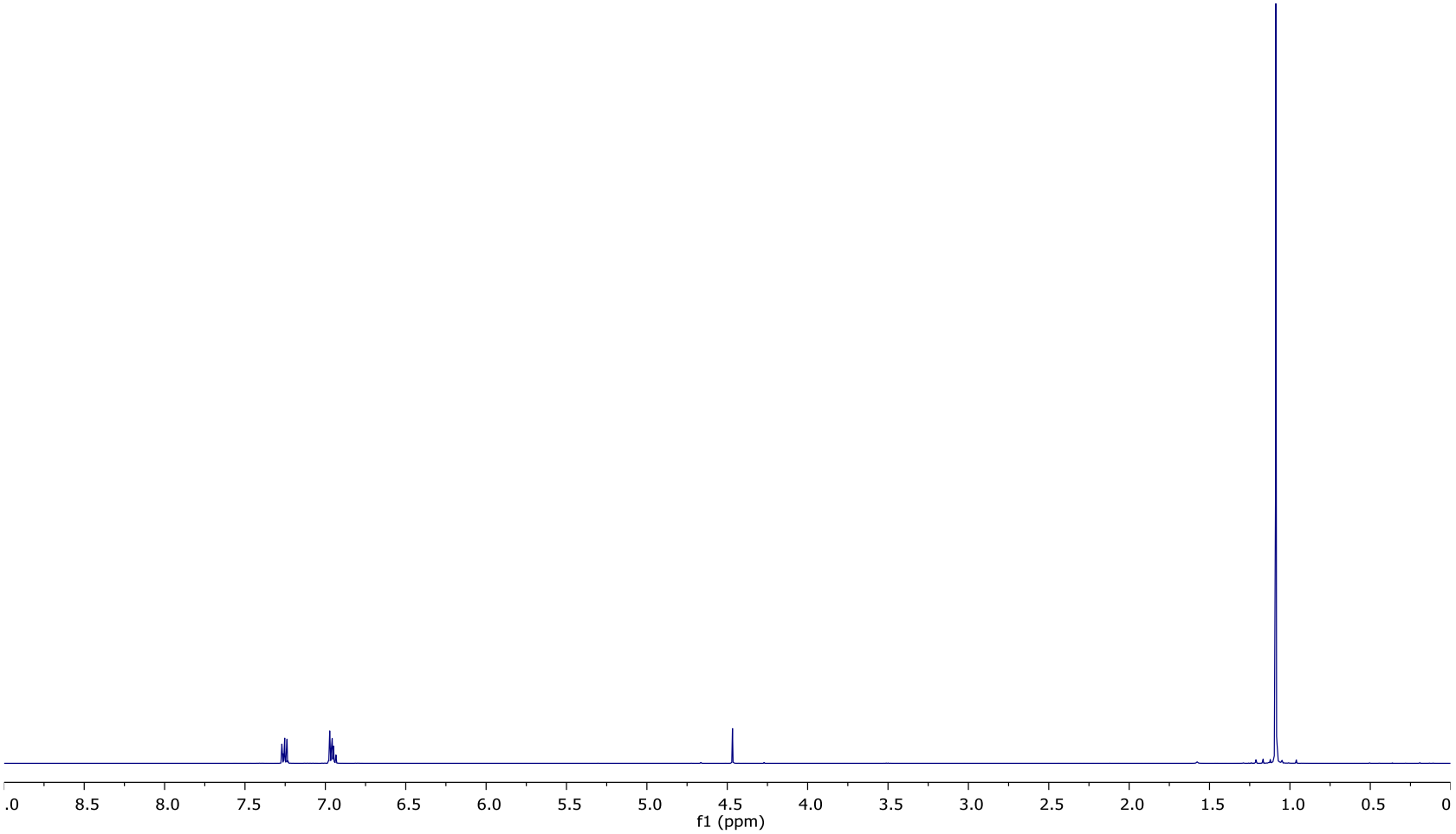
^{1}H NMR (500 MHz, $CDCl_3$) of compound **59s.**



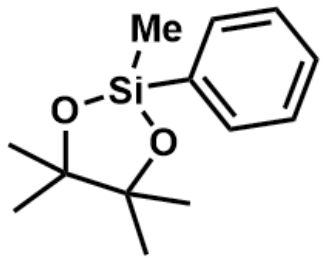


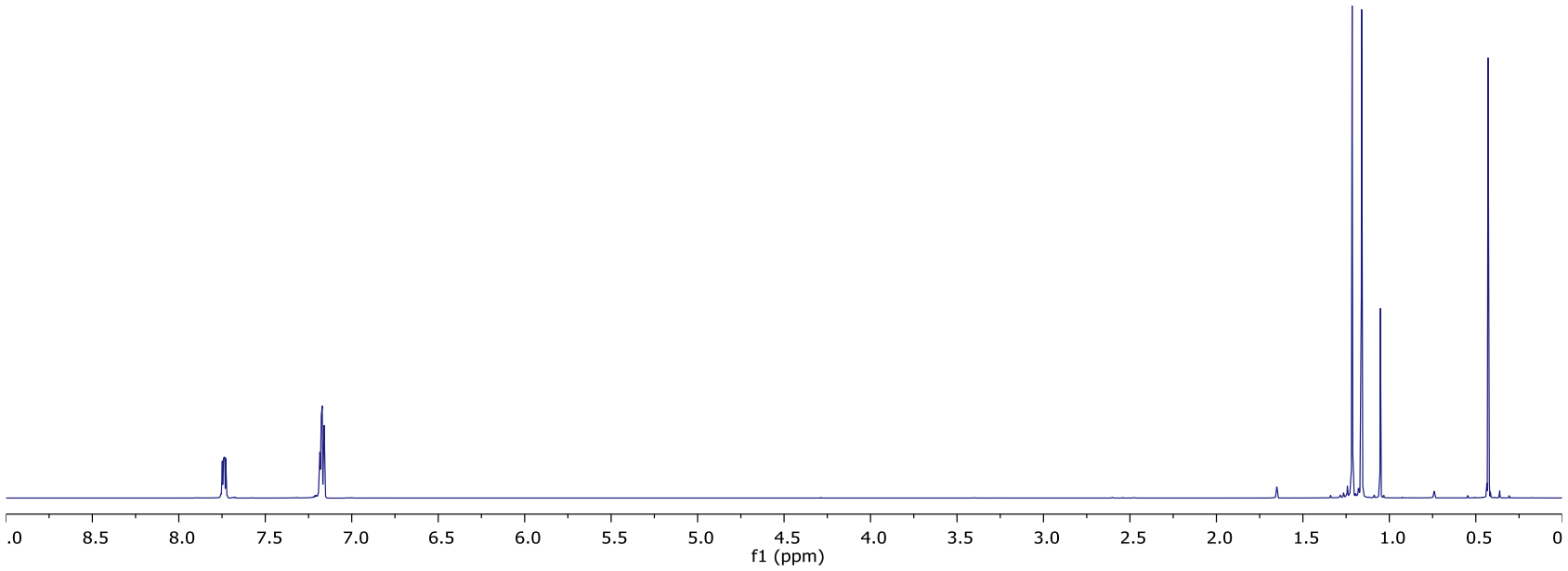
^{13}C NMR (126 MHz, $CDCl_3$) of compound **59s.**



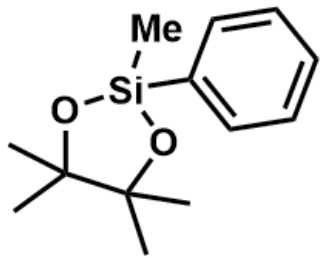


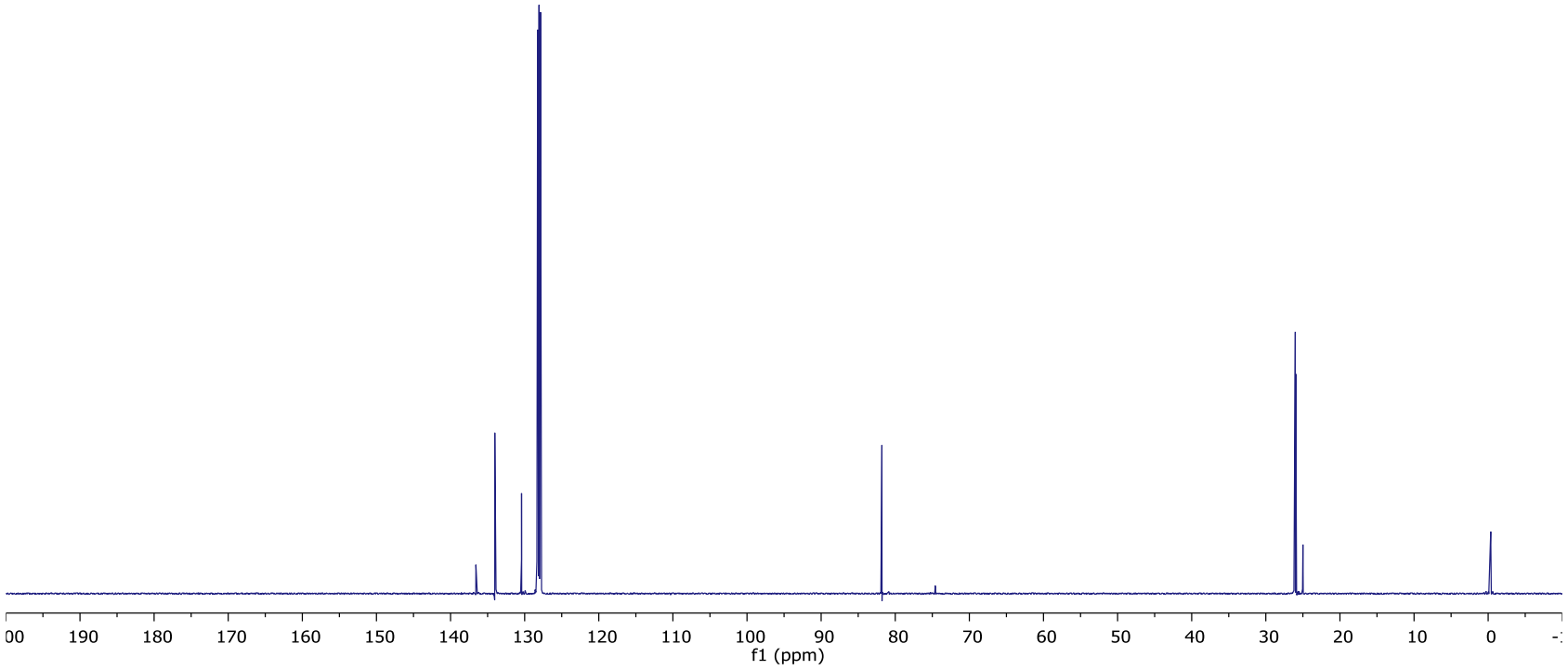
^{1}H NMR (500 MHz, $CDCl_3$) of compound **61.**





^{1}H NMR (500 MHz, Benzene-d_6) of compound **65.**





^{13}C NMR (126 MHz, Benzene-d_6) of compound **65.**

Acknowledgements.

I am grateful to Kerry Betz who worked extensively with me in the development of the NaOH–catalyzed O–Si bond formation. Andrew Romine also made important contributions and worked with Kerry and I in our efforts to develop a useful silyl ether bond synthesis method which would have broad value in the chemical sciences. I’m also grateful to Dr. Michael Haibach for his assistance with expanding the scope of this reaction.

Chapter 5

NOVEL [^{18}F]SIFA PROBES FOR POSITRON EMISSION TOMOGRAPHY (PET) IMAGING APPLICATIONS

Abstract.

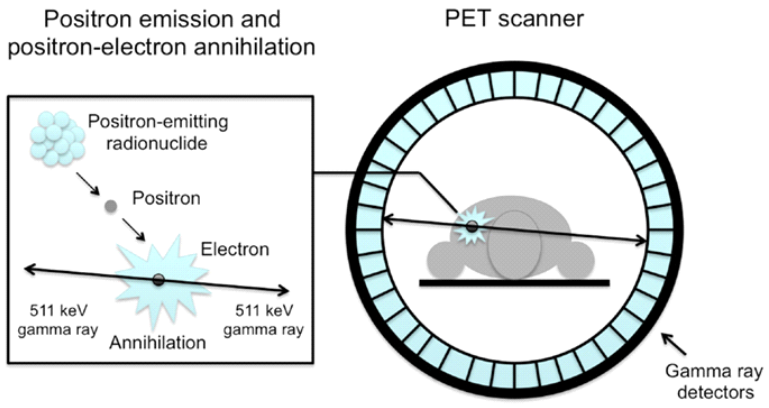
Enabled by our cross-dehydrogenative silylation methods, and in collaboration with our colleagues at UCLA, we have developed a series of novel [^{18}F]SiFAs based on heteroaromatic- and alkynylorganosilanes wherein a silicon atom on the molecule acts as an efficient acceptor for radiofluoridation. The synthesis of the precursor molecules is made possible for the first time by our KO*t*-Bu–catalyzed C–H silylation methodology, enabling the installation of the key di-*tert*-butylflurosilyl functionality. The subsequent radiofluoridation occurs at the UCLA Crump Institute for Molecular Imaging. Our colleagues at UCLA, Dr. Christopher Waldmann and Prof. Jennifer Murphy, have found that these new SiFA scaffolds undergo rapid and efficient radiofluoridation under clinically-relevant aqueous conditions and are stable under physiological conditions. Dr. Waldmann has moreover developed a new methodology for radiosynthesis made possible by our novel [^{19}F]SiFA precursors. The overall process is rapid, robust, and avoids HPLC purification and radiosynthesis machinery. The advantages to this method, when taken together, give hope for the potential development of a kit-like strategy for the synthesis and use of [^{18}F]PET radiopharmaceuticals for pre-clinical and clinical applications.

Introduction.

Generally, biological and medical imaging has been driven by anatomy-based imaging, such as magnetic resonance imaging (MRI) and computed tomography (CT).[187] Nuclear medicine as a field, by contrast, has focused on studying molecular events in living subjects through the use of technologies that can localize radiotracers, which are chemical systems (often small molecules) containing a radioactive isotope of an element.[187,188]

With the recent advances in molecular/cell biology that have led to target discovery, it is now possible to design specific radiotracers to image events non-invasively in small animals and humans with positron emission tomography (PET).[189] PET images high-energy gamma-rays that are emitted from inside the subject (**Figure 5.1**).

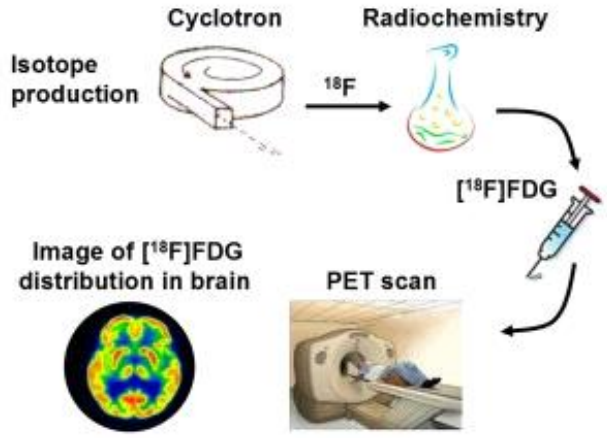
Figure 5.1. Simplified theoretical definition of PET imaging.



Biologically-relevant molecules can be labelled with an isotope that emits a positron from its nucleus. The positron eventually collides with a nearby electron and they annihilate to produce energy in the form of two 511 keV gamma-rays, which are emitted in directions approximately 180 degrees apart. Frequently used positron-emitting isotopes include ^{15}O, ^{13}N, ^{11}C, and ^{18}F. PET radiopharmacies exist throughout the world and are capable of providing commonly used PET tracers on a daily basis. For example, ^{18}F is produced in a cyclotron, typically in a $^{18}O(p,n)^{18}F$

reaction to generate [^{18}F]fluoride.[189] This is then used to label biomolecules and create labelled radiotracers. A labelled radiotracer can then be injected into the subject of interest and PET allows for imaging of its distribution *in vivo* (**Figure 5.2**).

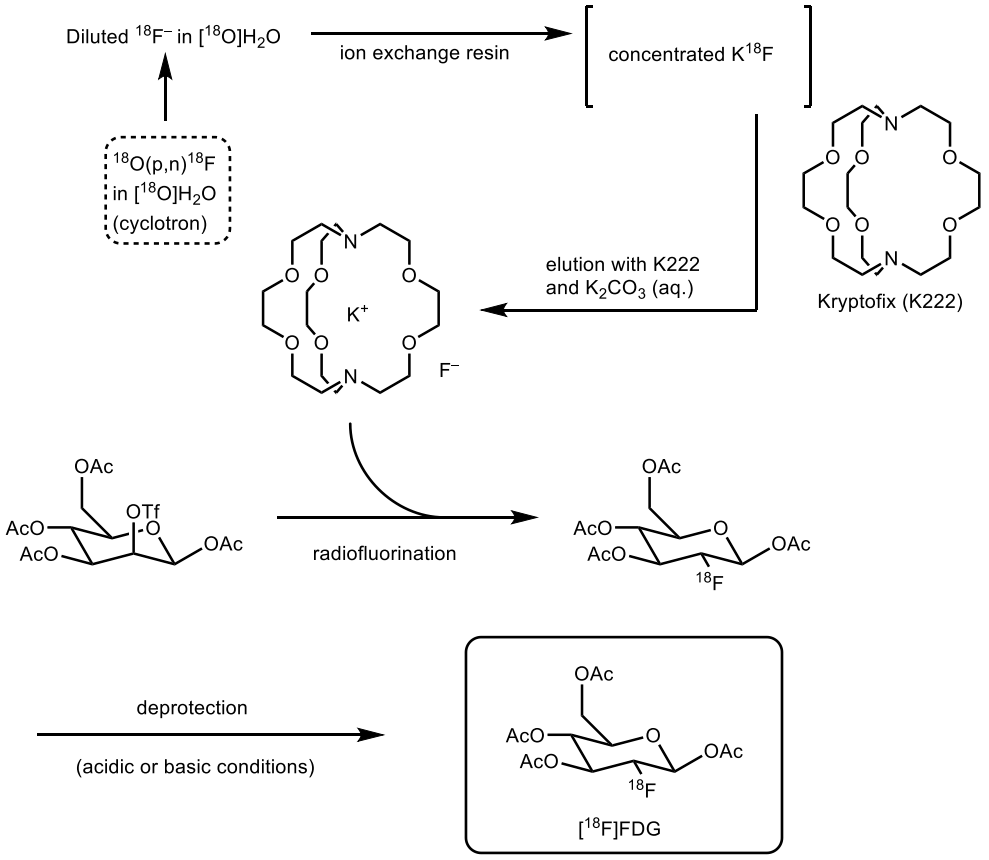
Figure 5.2. Clinical applications of PET imaging: from cyclotron to image reconstruction.



The most commonly used radiotracer, 2-deoxy-2-[^{18}F]fluoroglucose ([^{18}F]FDG), is produced by a triflate displacement using [^{18}F]F^- (**Figure 5.3**).[190]

Many of the positron-emitting isotopes that are used in PET have relatively short half-lives (e.g., 109.8 minutes for ^{18}F) so the chemistry employed for incorporation of the isotope into the parent molecule and its subsequent introduction into the subject must take place rapidly. The advent and recent applications of PET, especially when combined with magnetic resonance imaging (MRI) and computed tomography (CT), have had a remarkable impact on healthcare as a whole and on improved patient outcomes un particular by facilitating early detection, improving diagnostic confidence, and enabling detailed presurgical planning.[191]

Figure 5.3. Radiosynthesis of [^{18}F]FDG.



[^{18}F]PET

PET using fluorine-18 has the potential to become the foremost nuclear imaging methodology for clinical diagnostic medicine as well as for research applications due to the radionuclide's low radiation profile, the high imaging sensitivity, and the potentially extremely high selectivity of the [^{18}F]PET radiopharmaceuticals for targeting specific diseases and processes.[187–191] However, despite the favorable properties of [^{18}F]PET in whole body imaging and identification of target structures, this imaging modality exhibits important limitations. Indeed, although the instrumentation for [^{18}F]PET is reasonably well established, the method continues to comprise only a small percentage of all clinical imaging activities in healthcare. Interestingly, it is limitations in fundamental chemical

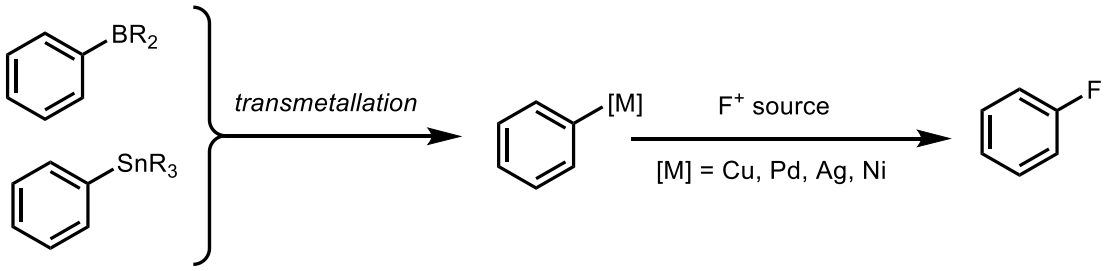
synthesis that are one of the primary impedances in the widespread use of [^{18}F]PET as a general and widely-applied medical diagnostic imaging modality.

Limitations in fluorination chemistry

Radiofluorination has in the past been typically accomplished by electrophilic fluorination using [^{18}F]F_2; this continues to be a practiced method.[192] However, the improved convenience of handling aqueous fluoride over fluorine gas has led nucleophilic fluorination reactions (i.e., fluoridation) to become the often preferred strategy.[193] However, historically, certain radiotracers could only be prepared using electrophilic methods because of limitations in the chemistry of [^{18}F]-fluoride. As such, chemical synthesis stands as one of the foremost limitations in the development of new [^{18}F]PET methods which are clinically relevant, resulting in [^{18}F]PET remaining somewhat limited in scope within the preclinical and clinical arenas. With respect to chemical synthesis activities in the development of new [^{18}F]PET, the specific goal is the necessity to install an ^{18}F atom onto a small molecule or biomolecule to generate the desired radiochemical probe. This may at first be somewhat surprising given the number of efficient and selective synthetic methods for fluorination with ^{19}F, especially those developed in recent years, which have been made available to the scientific community.[194] However, it is well appreciated by researchers and workers in the [^{18}F]PET field that the fluorination methodologies which have been developed for the installation of ^{19}F onto an organic small molecule or a biomolecule are often not amenable to ^{18}F. Indeed, and as mentioned, typical fluorination strategies often employ electrophilic fluorine sources, require lengthy reaction times and subsequent time-consuming chromatographic purification, and rarely can be performed under aqueous conditions. For example, modern fluorination methods developed by Hartwig, Sanford, Ritter, Gouverneur, and others employing aryl organometallic precursors or using transition metal

catalysis have enabled the formation of C–^{19}F bonds in arenes under mild conditions (**Scheme 5.1**).[195,196]

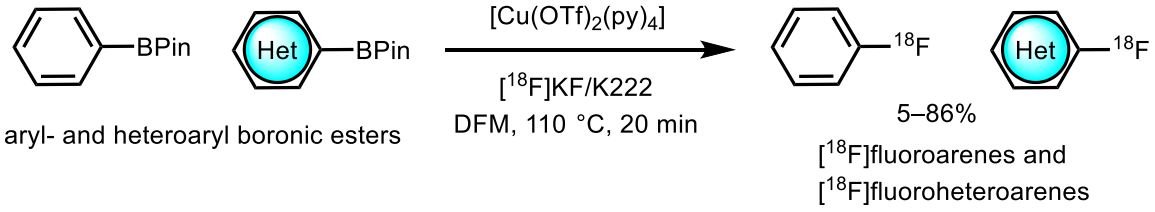
Scheme 5.1. Modern strategies for the synthesis of fluoroarenes using transition metal mediated transformations



Though these methods are efficient and powerful fluorination strategies, perhaps most limiting in these reports with respect to applications in [^{18}F]PET is the necessity to use electrophilic fluorine sources (and often the requirement for anhydrous reaction conditions). This is problematic because the ^{18}F obtained from a cyclotron in a clinical setting is delivered in the form of aqueous [^{18}F]-fluoride, making these electrophilic fluorination methods highly limited given the current state of the art and requirements in clinical [^{18}F]PET technologies. Moreover, ^{18}F has a half-life of only 109.8 minutes and for a variety of the aforementioned methods the fluorination chemistry is simply not rapid enough to enable sufficient imaging time following synthesis. This issue of slow fluorination is exacerbated by the necessity to subsequently perform HPLC purification on the newly synthesized [^{18}F]PET probe, which requires yet additional time. It is clear, then, that a) the methodologies for the installation of ^{18}F onto an organic molecule or biomolecule must occur by a fast, convenient, and highly efficient fluorination and b) typical radiofluorination methods simply do not satisfy these criteria. As a result, there is a healthy surge in research and development – beyond FDG (**Figure 5.3**) – in the burgeoning field of nucleophilic fluorination for PET applications.[197] Indeed, a number

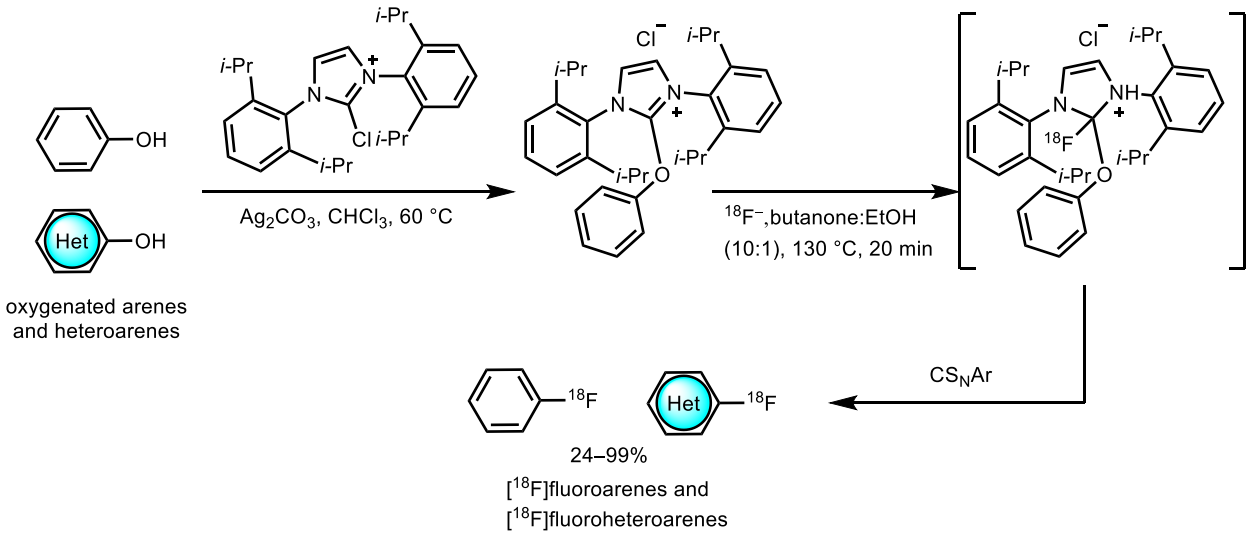
of methods which employ [^{18}F]fluoride and which proceed in reasonable timeframes have been developed for the synthesis of molecules containing ^{18}F. For example, most recently, Gouverneur and Ritter have made significant contributions to this field. Gouverneur has reported on the copper–mediated nucleophilic ^{18}F fluorination of aryl- and heteroaryl boronic acids.[198] The chemistry tolerates a wide array of functionalities on the (hetero)arene and, importantly, the fluorination proceeds rapidly using [^{18}F]F$^-$ (**Scheme 5.2**).

Scheme 5.2. Gouverneur's copper-mediated ^{18}F fluorination of aryl- and heteroaryl boronic acids.



Ritter has also recently reported on an unusual strategy toward ^{18}F-substituted arenes from the corresponding oxygenates proceeding via a concerted nucleophilic aromatic substitution (CS_NAr)

Scheme 5.3. Ritter's ^{18}F fluorination of aryl- and heteroaryl boronic acids through a concerted nucleophilic aromatic substitution (CS_NAr) mechanism



mechanism employing imidazolium reagents (**Scheme 5.3**).[199] This chemistry too demonstrates an excellent scope and convenient deoxygenative fluorination conditions. Given the prevalence of oxygenates in pharmaceutically relevant molecules and other small molecules, this method could be used to readily develop libraries of [^{18}F]fluoro(hetero)arenes.

These methods are truly important advances in the field. However, in the context of practical implementation, these strategies necessitate HPLC purification, which can be costly and time-consuming, as well as multi-step synthetic protocols requiring specialized personnel and the use of organic solvents (which in the context of clinical applications can be problematic), creating potentially additional practical challenges. Moreover, these methods have thus far not been demonstrated for the general and direct radiofluorination of macro- or biomolecules. Indeed, such radiofluorinations are generally challenging either due to functional group incompatibilities, the requirement for prefunctionalization (for example, C–H borylation or oxidation, which is often challenging in its own right), and/or issues of site-selectivity.

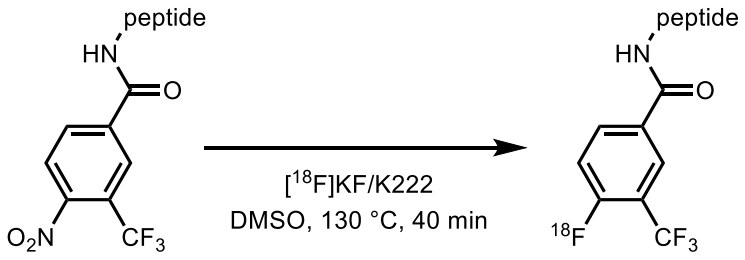
Prosthetic groups for the radiolabeling of biomolecules with ^{18}F

Bioactive molecules have substantial potential value as imaging agents because of their target specificity. However, peptides, proteins, and oligonucleotides are typically not particularly tolerant to the reaction conditions employed in radiofluorination reactions. This is true even for those state-of-the-art methods that have been developed specifically for PET radiochemistry applications, some of which were discussed earlier. However, methods have been developed for both the direct and indirect radiolabeling of these molecules.

These methods employ nucleophilic fluoride and have the potential to be performed under practically relevant conditions. Specifically, direct methods are those in which the nucleophilic fluoride is

reacted directly with the molecule/biomolecule, which may have been previously modified to facilitate radiolabeling. Only subsequent purification is required to obtain the final product. For example, Chen has reported a direct labeling strategy using [18F]fluoride by displacing an aromatic nitro group in an arene which is activated toward nucleophilic substitution by an ortho trifluoromethyl group (**Scheme 5.4**).[200] This method was successfully applied to the radiolabeling of monomeric and dimeric cyclic RGD peptides as well as other peptides. However, a number of issues exist in addition to the challenging synthesis of the precursors. First, separation of the nitro-containing peptide precursors from radiolabeled products proved challenging. Second, the reaction conditions utilized high temperatures and basic conditions that would not be tolerated by most biomolecules.

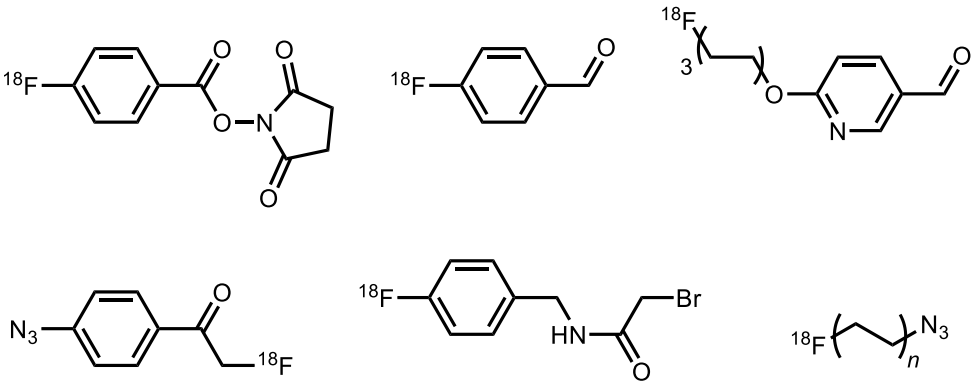
Scheme 5.4. Chen's S_NAr strategy for the radifluorination of biomolecules



Indirect methods, in contrast, are based on the concept of prosthetic groups – pre-synthesized small molecules having a targeted radiolabeling site – followed by their subsequent bioconjugation to a molecular entity that has a functionality with which the prosthetic group can react (e.g., an azide-alkyne cycloaddition reaction or other rapid and robust methods). Typically, ^{18}F-labeled prosthetic groups are prepared in one to three synthetic steps and require subsequent purification processes to remove fluorination reagents, unreacted starting material, and other byproducts.[201] Of course, one substantial limitation is again the relatively short half-life of ^{18}F; this offers a considerable challenge when designing a radiosynthesis that includes several synthetic and purification steps. Despite the half-life limitations, numerous prosthetic groups have been developed for conjugation with

biomolecules or small molecules using nucleophilic chemistries and typically multi-step procedures (**Figure 5.4.**)[202]

Figure 5.4. Common ^{18}F-labeled prosthetic groups.



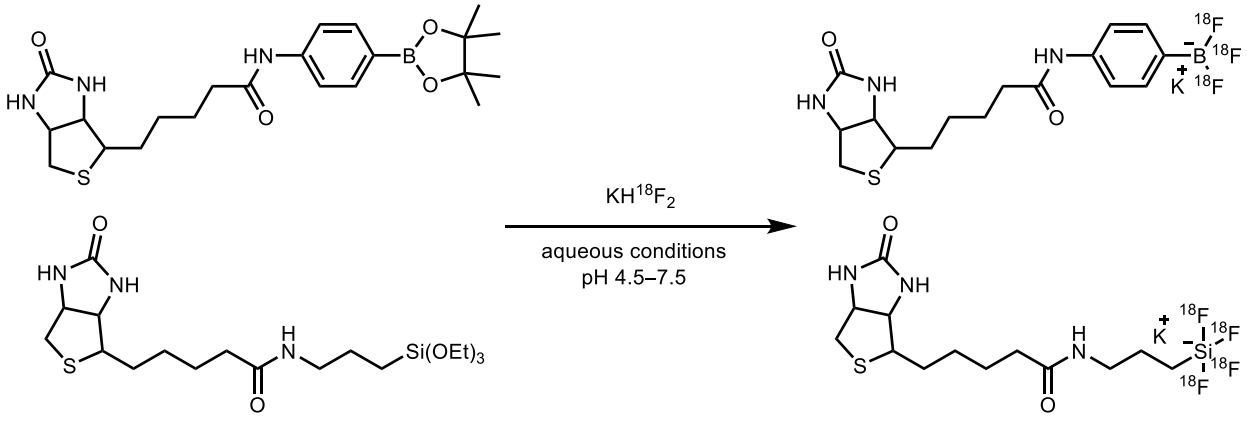
These syntheses typically aim to construct a small molecule prosthetic group with either an aryl- or an alkyl C–^{18}F bond. Again, the substantial limitations introduced by the necessity of multi-step syntheses and purifications are a primary factor in limiting the immediate application of these prosthetic groups in pre-clinical and clinical applications. Also restrictive, however, is the sophistication of the chemistry, requiring trained personel and specialized chemical equipment for synthesis.[203] These kinds of conditions are rarely found, for example, in a hospital setting. Therefore, in addition to the challenges discussed thus far, an additionally important consideration is the ability to generate the active PET radiopharmaceutical substance without using specialized equipment (save the cyclotron), or special chemical techniques and trained chemists. This would allow nurses and doctors to perform the necessary steps toward creating the radiolabeled substance.

Tetrafluoroborates and tetrafluorosilicates

Typically, fluorination methodologies dealing with the functionalization of small molecules and biomolecules, and this is certainly the case in [^{18}F]PET radiosynthesis, focus on the formation of C–^{18}F bonds. However, as previously discussed, these methods suffer from a number of intrinsic

limitations including unsuitably long fluorination and purification times, the necessity to use electrophilic sources of ^{18}F or, conversely, the necessity to use highly activated [^{18}F]fluoride prepared via a radiosynthesizier, among a variety of other issues. An alternative strategy involves introduction of the [^{18}F] by other means, specifically by forming a bond between ^{18}F and a non-carbon atom. For example, Perrin has demonstrated that arylpinacolboranes and alkylltrialkoxysilanes are potentially valuable moieties for PET imaging applications (**Scheme 5.5**).[204] These functionalities undergo radiofluoridation in a single, rapid, and high-yielding step at pH 4-7 providing the corresponding arylfluoroborates (B–F bonds) and alkylfluorosilicates (Si–F bonds) in an aqueous, bimolecular ^{18}F labeling. In a particular application, the silicon and boron moieties were bioconjugated to unmodified biotin, and analysis was performed. Interestingly, the authors of that work found that the aryltrifluoroborate is appreciably more stable than the alkyltetrafluorosilicate moiety in physiologically relevant media, suggesting that the latter may not be valuable, except in special cases, for PET applications.

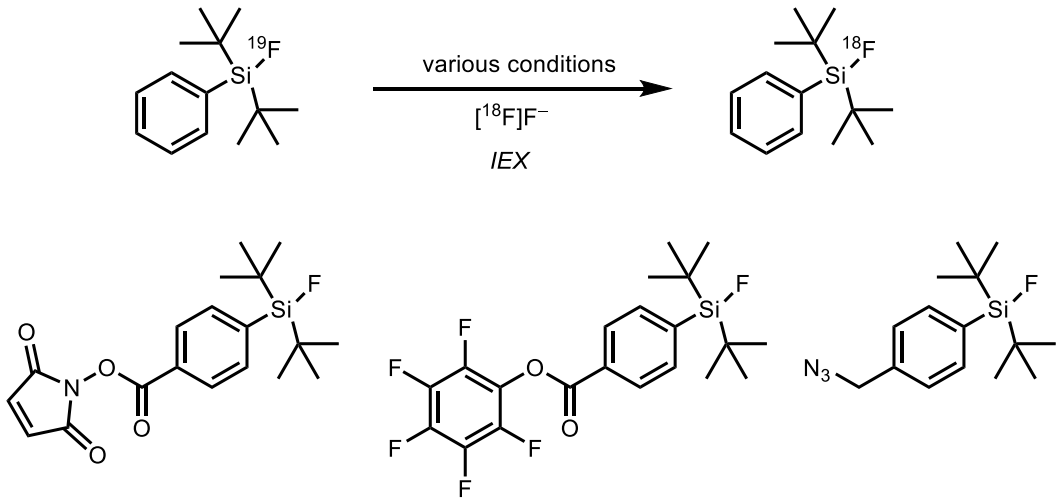
Scheme 5.5. Perrin's tetrafluorborates and tetrafluorosilicates for PET applications.



Silicon fluoride acceptors (SiFAs) as prosthetic groups.

As has been discussed, the introduction of ^{18}F under aqueous conditions has been made possible by both direct and indirect C–F bond formation methodologies. The use of electrophilic Si and B moieties bearing alkoxy leaving groups has provided new avenues for the introduction of radiofluoride under mild conditions. Thus, the concept of organosilicon-based moieties for the introduction of radiofluoride (i.e., silicon fluoride acceptors (SiFAs)) has been, in particular, an area of intense interest.[197,205] With such moieties, the radionuclide is introduced by a nucleophilic displacement reaction at silicon forming the necessary Si–^{18}F bond. Seminal developments by Perrin (**Scheme 5.3**) and others has demonstrated the value of this strategy from the perspective of rapid, aqueous radiolabeling of organic molecules for PET applications, solving a variety of limitations inherent to other radifluoridation strategies.[197,201–205] It was realized subsequently that nucleophilic radiofluoridation of an organic molecule already containing a Si–^{19}F bond would result in an isotopic exchange. This strategy would enable an initial fluorine-containing molecule to be synthesized and for radiofluronation to occur at a late stage, substantially enabling the concept of prosthetic groups for PET applications. Indeed, the concept of [^{19}F]/[^{18}F] isotopic exchange (IEX) reaction has now been actively studied (**Figure 5.5**).[197,205,206] The advantages to this method are numerous: 1) the initial installation of the Si–F bond can be done without consideration of rapidity or aqueous conditions since at this stage only "cold" fluorine (i.e., ^{19}F) sources are used, 2) the IEX reaction is often facile and can occur under aqueous conditions, allowing the introduction of the radionuclide in a rapid and clinically-relevant fashion, and 3) the product and starting material are identical from a constitutional point of view making HPLC purification a moot issue, further streamlining the radiosynthesis process.[197,205,206] These SiFAs have been used as prosthetic groups for subsequent bioconjugation for the development of new radiotracers. Here, however, it was found that a number

Figure 5.5. Silicon fluoride acceptors (SiFAs) and their synthesis by [^{19}F]/[^{18}F] isotopic exchange (IEX) reaction.

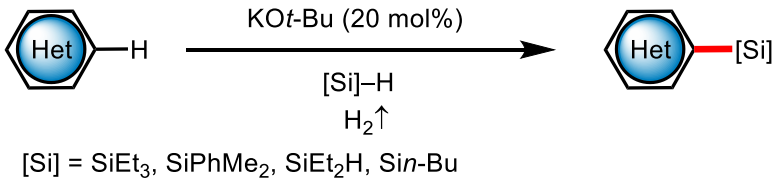


of issues with SiFAs existed. First, the Si–F bond, though thermodynamically stable, is kinetically unstable under physiological (i.e., aqueous) conditions. Second, in order for the Si–F bond to be protected from nucleophilic attack by water, the Si atom must be flanked by very bulky di-*tert*-butyl groups, making that part of the molecule extremely lipophilic. This is problematic given that lipophilic molecules often suffer from the hepatic first pass effect, severely lowering bioavailability and tremendously minimizing the SiFA's diagnostic value. Thus, in order for fluorosilicon functionalities to represent a meaningful alternative to classical [^{18}F]PET synthesis strategies and perhaps to show advantages over the fluoroboron strategy, the aforementioned issues of polarity and stability would have to be solved.

The first heterocyclic SiFAs.

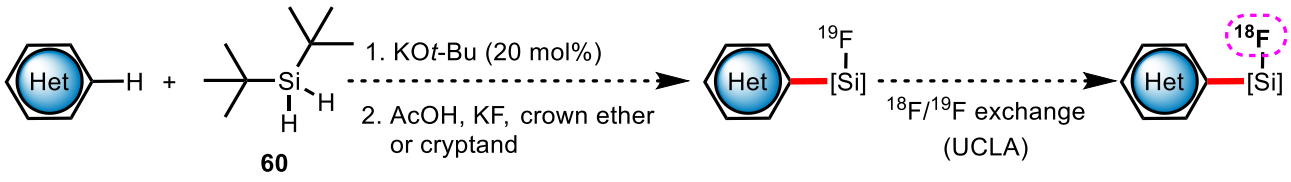
In Chapter 2 was discussed the discovery of KO*t*-Bu–catalyzed C–H silylation of heteoarenes (**Scheme 5.6**).[74,105] Reflecting on this chemistry, we made a number of realizations that could have relevance to the synthesis of [^{18}F]PET molecules. First, we realized that alkyl-substituted silanes

Scheme 5.6. KO*t*-Bu–catalyzed dehydrosilylation of heteroarenes with several hydrosilanes.



were excellent coupling partners in our silylation chemistry. Second, we understood that dihydrosilanes were also competent in the silylation chemistry, which allowed for the synthesis of silylated heterocycles with a remaining Si–H bond (though some bis coupling did occur in certain cases with unhindered substrates). Given these considerations, we made the connection that installation of a bulky di-*tert*-butylsilyl group could potentially be accomplished by our method, employing the commercially available *t*-Bu_2SiH_2 as the hydrosilane coupling partner. If this silylation were successful, it would furnish the corresponding hydrosilylheterocycle. Fortunately, the conversion of an Si–H to an Si–F is possible using robust methods and so this would enable a two-step synthesis of a precursors which could be potentially converted to the corresponding [^{18}F]PET molecules by IEX chemistry (**Scheme 5.7**).[207] This IEX chemistry could be performed by our close colleagues at the Crump Institute for Molecular Imaging at UCLA, Dr. Christopher Waldmann and Prof. Jennifer Murphy.

Scheme 5.7. Proposed synthesis of novel heterocyclic SiFAs.

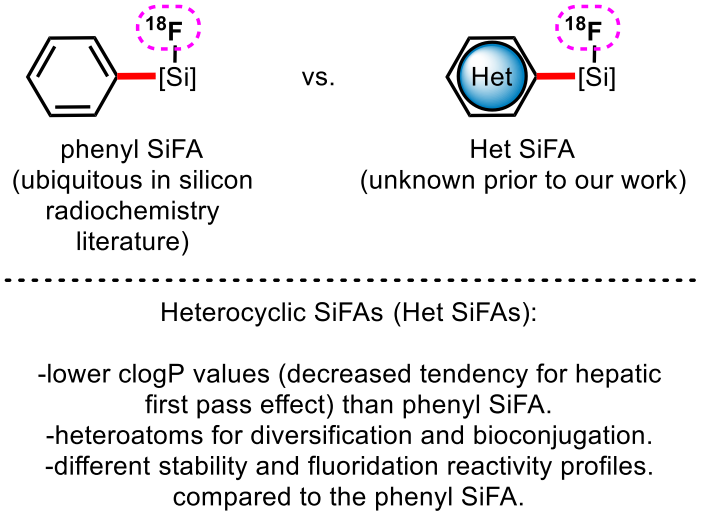


Heterocylcic SiFAs: potential advantages over the current state-of-the-art in Si radiochemistry

Heterocyclic SiFAs had not been prepared when we had first contemplated this work, presumably due to challenges in heterocyclic chemistry compounded by the bulkiness of *t*-Bu_2SiClH, which is

the typical reagent for installation of the *t*-Bu_2SiH group. However, if the silylation could be made possible by our method, then it would provide the first opportunity to study heterocyclic SiFAs and compare them to the phenyl SiFA, which is standard aromatic SiFA fragment in silicon radiochemistry. The benefits could be substantial. First, the increased polarity of heterocycles compared to simple arenes decreases the tendency of the small molecule to be subjected to the hepatic first pass effect, which leads to metabolism and destruction of the SiFA. This is an issues that is commonly encountered in the silicon radiochemistry literature due to the requirement for the bulky (and lipophilic) *tert*-butyl groups on silicon for stability. The presence of heteroatom functional group handles inherent to heteroarenes could allow for diversification such as quaternerization of a nitrogen leading to decreased clogP values or bionconjugation to a peptide or antibody. Moreover, due to differences in the steric and electronic parameters of heterocycles compared to a simple benzene ring, there could be potentially improved radiochemical labeling efficiency and stability, which are longstanding challenges in the silicon radiochemistry field (**Figure 5.6**).[194,197,205,206]

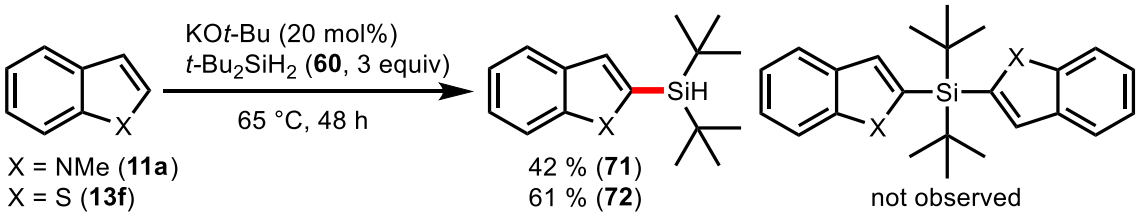
Figure 5.6. Comparison of the hypothesized heterocyclic SiFAs against the standard phenyl SiFA.



KOt-Bu–catalyzed C–H silylation: an enabling method for installation of the t-Bu$_2$SiH group

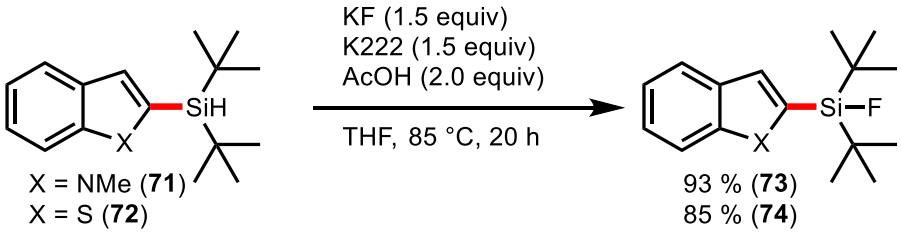
We chose to begin our synthetic investigations using two of our well-performing model compounds discussed in Chapter 2: 1-methylindole (**11a**) and benzothiophene (**13f**). Subjecting these substrates to the standard dehydrogenative heterocycle silylation conditions,[74,105] but employing *t*-Bu$_2$SiH$_2$ as the silane coupling partner, afforded the corresponding silylated products **71** and **72** in modest yields and with no undesired tethering through silicon observed (as anticipated, due most likely to steric congestion) (**Scheme 5.8**).

Scheme 5.8. KO*t*-Bu–catalyzed C–H silylation of 1-methylindole (11a) and benzothiophene (13f) with *t*-Bu$_2$SiH$_2$.



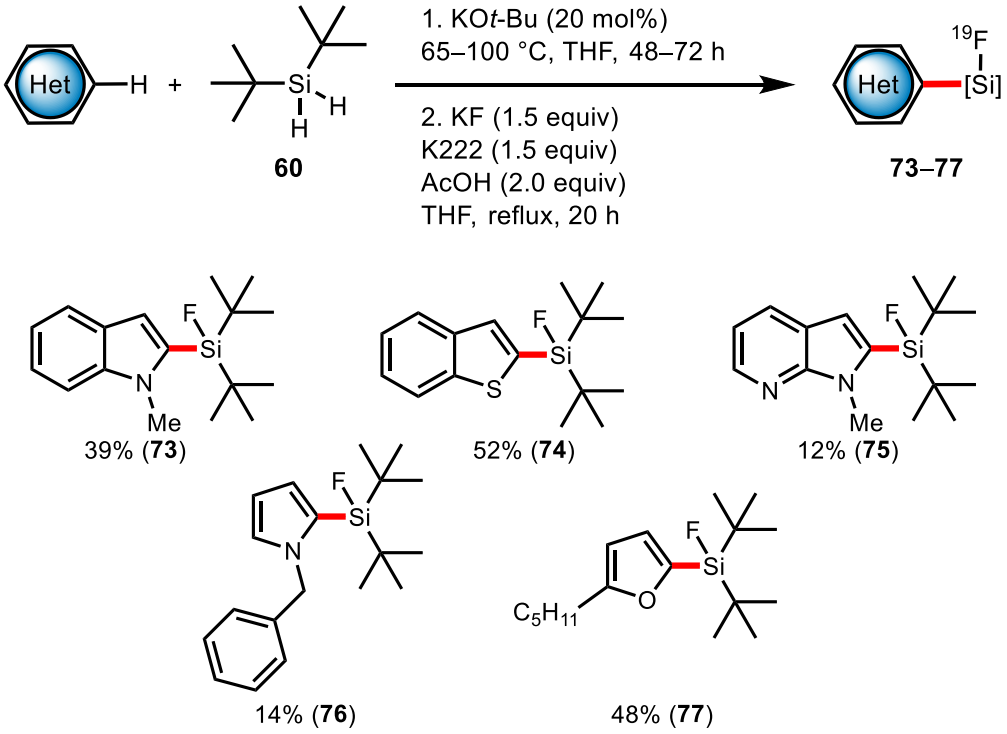
With the silylated products in hand, we proceeded to evaluate the subsequent fluoridation chemistry in order to complete the synthesis of the desired [^{18}F]HetSiFA precursors. For this we chose to employ the method of Klar[207] for transforming an Si–H bond into an Si–F bond by treating the hydrosilane with KF/K222 cryptand (K222 = 4,7,13,16,21,24-Hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane) in THF/AcOH. This strategy was successful, furnishing [^{19}F]HetSiFAs **73** and **74** (**Scheme 5.9**).

Scheme 5.9. SiFA synthesis: fluoridation of heteroarylhydrosilanes under nucleophilic conditions



Having demonstrated the proof-of-principle for unprecedented dehydrosilylation with *t*-Bu_2SiH_2 and subsequent fluoridation of furnishing **73** and **74** from simple heteroarenes 1-methylindole (**11a**) and benzothiophene (**13f**), we proceeded to prepare a number of other heterocyclic [^{18}F]SiFA precursors starting from a diverse group of unfunctionalized heteroarenes (**Figure 5.7**). These reactions were likewise successful, giving rise to [^{19}F]HetSiFAs **73–77** in just 2 steps from the C–H heteroarene.

Figure 5.7. [^{18}F]HetSiFA precursors prepared by the two-step silylation/fluoridation method.[a]



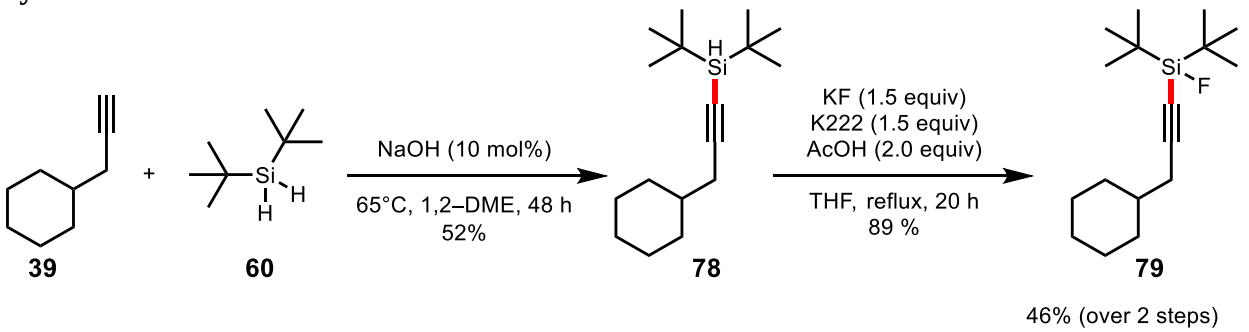
[a]Yields given over two steps (silylation then fluorination; from the C–H heterocycles)

The first acetylinic SiFAs.

In Chapter 3 was discussed the discovery of hydroxide–catalyzed C–H silylation of terminal alkynes. In that particular dehydrocoupling reaction, the scope of both alkyne and hydrosilane was essentially unprecedented, providing an excellent basis for silylation of a wide array of alkynes with challenging

hydrosilanes. Once we had established the scope, we contemplated the broad utility of the products, many of which are discussed in Chapter 3. Among the many applications that were established, there was one in particular that was not discussed in Chapter 3: application of C(*sp*)–Si bonds in PET. Specifically, Ametamey has previously disclosed experimental and computational investigations of organofluorosilanes as model compounds for ^{18}F-labeled silicon-based PET tracers and their hydrolytic stability.[208] In his most recent work, the authors tested the hydrolytic stability of the Si–F bond in a wide variety of known and hypothesized SiFAs and determined that the acetylinic SiFA is predicted to have among the highest hydrolytic stability with respect to the Si–F bond.[209] However, such acetylinic SiFA functionalities have not been reported experimentally and so we saw an opportunity to employ our methods in the synthesis of these moieties, which would finally enable experimental investigations of their reactivity and stability. Toward this end, we employed simple unbiased alkyne (**39**, Chapter 3) and subjected it to the hydroxide–catalyzed dehydrosilylation conditions using *t*-Bu_2SiH_2 as the silane coupling partner and successfully obtained **78** in 52% yield. Subsequent fluoridation by the conditions of Klar[207] was successful and high yielding (as was also the case for the heteroarylsilanes; see **Scheme 5.9**) providing the desired SiFA **79** (**Scheme 5.10**).

Scheme 5.10. Synthesis of the first acetylinic SiFA by hydroxide–catalyzed silylation followed by fluoridation.



Radiosynthesis by IEX, evaluation of hydrolytic stability, and animal studies.

All radiosynthesis, hydrolytic stability testing, and advanced studies employing the synthesized heteroaryl- and acetylinic SiFAs were performed in their entirety by Dr. Christopher Waldman (Prof. Murphy Lab, UCLA). An extensive amount of data has been generated, demonstrating the promise of heterocyclic and acetylnic SiFAs for PET biomedical imaging applications; however, these data will not be presented or discussed in this thesis.

Conclusion.

The KO*t*-Bu–catalyzed dehydrogenative silylation chemistry described in Chapter 2 has been applied successfully to the synthesis of an entirely novel suite of heterocyclic SiFA molecules (i.e., [^{19}F]HetSiFAs). Some of these moieties have been radiolabeled and their stabilities have been evaluated by Dr. Christopher Waldmann at the Crump Center for Molecular Imaging at UCLA. The hydroxide–catalyzed dehydrocoupling chemistry was employed in the synthesis of the first acetylinic SiFA molecule. Efforts toward applying these scaffolds in a variety of biomedical imaging applications are underway.

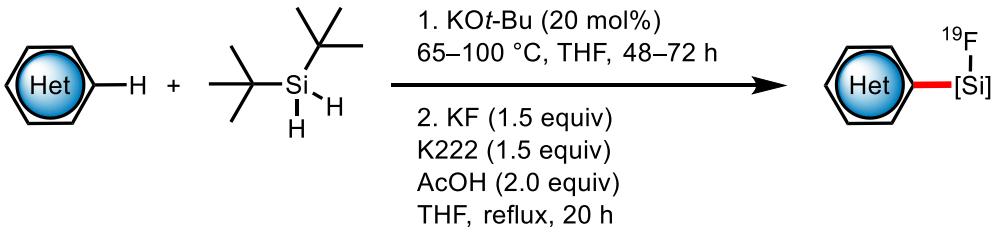
Experimental and analytics.

General information

Unless otherwise stated, reactions were performed in oven-dried brand-new Fisherbrand scintillation vials in a nitrogen filled glove box or in flamed-dried Schlenk flasks under argon connected on a Schlenk line using dry, degassed solvents and brand-new stirring bars. Solvents were dried by passage through an activated alumina column under argon.[43] Reaction progress was monitored by thin-layer chromatography (TLC), UHPLC-LCMS or GC-FID analyses. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, phosphomolybdic acid, or $KMnO_4$ staining. Silicycle SiliaFlash P60 Academic Silica gel (particle size 40–63 nm) was used for flash chromatography. ^{1}H NMR spectra were recorded on Varian Inova 500 MHz and 600 MHz spectrometers in $CDCl_3$ or C_6D_6 and are reported relative to residual solvent peak at δ 7.26 ppm or δ 7.16 ppm respectively. 13C NMR spectra were recorded on a Varian Inova 500 MHz spectrometer (125 MHz) in $CDCl_3$ or C_6D_6 and are reported relative to residual solvent peak at δ 77.16 ppm or δ 128.06 ppm respectively. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septet, m = multiplet, br s = broad singlet, br d = broad doublet, app = apparent. Data for 13C NMR are reported in terms of chemical shifts (δ ppm). IR spectra were obtained on a Perkin Elmer Spectrum BXII spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm–1). UHPLC-LCMS analyses were obtained on an Agilent 1290 ultra high performance liquid chromatography/mass spectrometry equipped with an Agilent EclipsePlus C18 RRHD 1.8 µM column. GC-FID analyses were obtained on an Agilent 6890N gas chromatograph equipped with a HP-5 (5%-phenyl)-methylpolysiloxane capillary column (Agilent). GC-MS analyses were obtained

on an Agilent 6850 gas chromatograph equipped with a HP-5 (5%-phenyl)-methylpolysiloxane capillary column (Agilent). High resolution mass spectra (HRMS) were obtained on an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed ionization mode (MM: ESI-APCI+), or were acquired from the California Institute of Technology Mass Spectrometry Facility. ICP-MS analysis was conducted at the California Institute of Technology Mass Spectrometry Facility. Al_2O_3 was purchased from Aldrich and activated by storing in a 200 °C oven for one week and then heating in a round bottom flask at 200 °C under vacuum (60 millitorr). Silanes were purchased from Aldrich and distilled before use. KO*t*-Bu was purchased from Aldrich (sublimed grade, 99.99% trace metals basis) and used directly. Substrates were purchased from Aldrich, TCI, or Acros.

General procedure for synthesis of [^{19}F]HetSiFAs



Silylation (step 1):

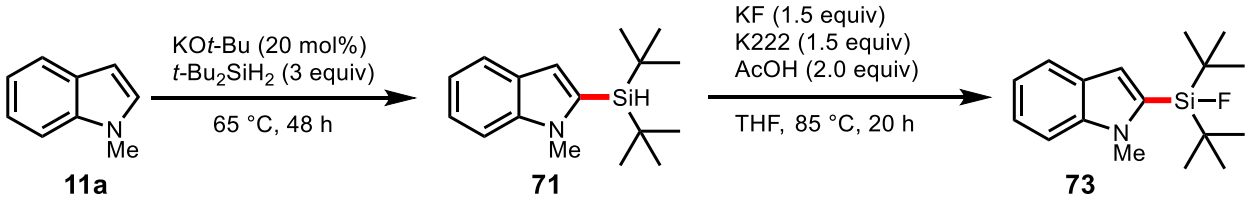
In a nitrogen-filled glove box, KO*t*-Bu (20 mol%) and heteroarene (1 equiv) were added to a scintillation vial equipped with a magnetic stirring bar. THF (solvent, 1.0 M relative to heteroarene) is added, followed by di-*tert*-butylsilane (3 equiv). Then the vial was sealed and the mixture was stirred at the indicated temperature for the indicated time. The vial was removed from the glove box, the reaction mixture was diluted with diethyl ether and concentrated under reduced pressure. The residue was purified by silica gel flash chromatography to give the desired product or was simply filtered and subjected to fluoridation reaction conditions in a telescope protocol (yields of

the final SiFA molecule were comparable for both procedures).

Fluoridation (step 2):

The method of Klar was employed.[207] A round bottom flask containing di-*tert*-butylsilylated heteroarene (1 equiv), potassium fluoride (1.5 equiv) and K222 cryptand (1.5 equiv) and a magnetic stirring bar was evacuated and then refilled with argon. To the flask, THF (solvent, 0.2 M relative to hydrosilylated heteroarene) and acetic acid (2.0 equiv) were added, and the reaction mixture was stirred at reflux overnight. Progress of the reaction was monitored by GC and TLC. Once the reaction is complete (as determined by GC and TLC), the reaction mixture is diluted with DCM, filtered through a short pad of celite, and concentrated in vacuo. The residue is purified by silica gel flash chromatography to give the desired product.

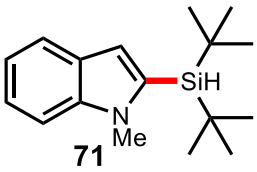
Characterization



The general silylation procedure was followed with isolation of the hydrosilane product. The reaction was performed with KO*t*-Bu (89.6 mg, 0.8 mmol, 20 mol%), 1-methylindole (**11a**, 262.3 mg, 4.0 mmol), and di-*tert*-butylsilane (2.40 mL, 12 mmol, 3 equiv), in 4.0 mL of THF at 65 °C for 72 h. The desired product **71** (459.0 mg, 42% yield) was obtained after purification by silica gel flash chromatography (100% hexanes).

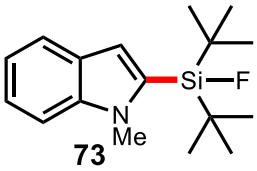
The general fluoridation procedure was followed. The reaction was performed with di-*tert*-butylsilylated indole **71** (136.6 mg, 0.5 mmol, 1 equiv), potassium fluoride (43.6 mg, 1.5 equiv, 0.75 mmol), and K222 cryptand (282.4 mg, 1.5 equiv, 0.75 mmol). To the flask, THF (2.5 mL) and

acetic acid (57 µL, 2.0 equiv, 1.0 mmol) were added, and the reaction mixture was stirred at reflux overnight. The residue is purified by silica gel flash chromatography (100% hexanes) to give the desired product **73** (135.5 mg, 93% yield) (i.e., 39% yield over 2 steps from 1-methylindole).



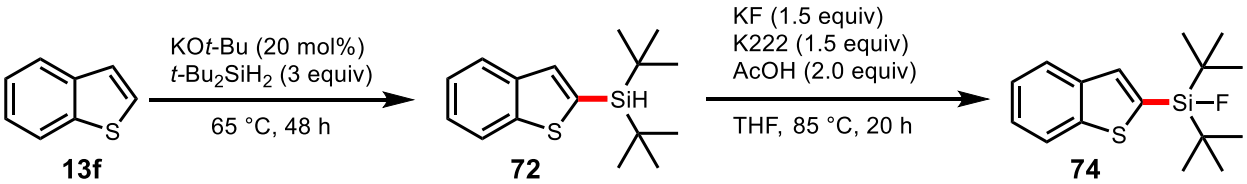
71

2-(di-tert-butylsilyl)-1-methyl-1H-indole 71: characterization pending.



73

2-(di-tert-butylfluorosilyl)-1-methyl-1H-indole 73: characterization pending.

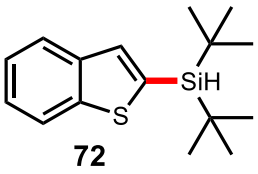


13f **72** **74**

The general silylation procedure was followed with isolation of the hydrosilane product. The reaction was performed with KO*t*-Bu (89.6 mg, 0.8 mmol, 20 mol%), benzothiophene (**13f**, 536.8 mg, 4.0 mmol), and di-*tert*-butylsilane (2.40 mL, 12 mmol, 3 equiv), in 4.0 mL of THF at 65 °C for 72 h. The desired product **72** (53.1 mg, 61% yield) was obtained after purification by silica gel flash chromatography (100% hexanes).

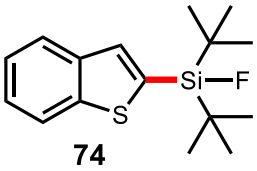
The general fluoridation procedure was followed. The reaction was performed with di-*tert*-butylsilylated benzothiophene **72** (136.6 mg, 0.5 mmol, 1 equiv), potassium fluoride (43.6 mg, 1.5 equiv, 0.75 mmol), and K222 cryptand (282.4 mg, 1.5 equiv, 0.75 mmol). To the flask, THF (2.5 mL) and acetic acid (57 µL, 2.0 equiv, 1.0 mmol) were added, and the reaction mixture was stirred

at reflux overnight. The residue is purified by silica gel flash chromatography (100% hexanes) to give the desired product **74** (125.1 mg, 85% yield) (i.e., 52% yield over 2 steps from benzothiophene).



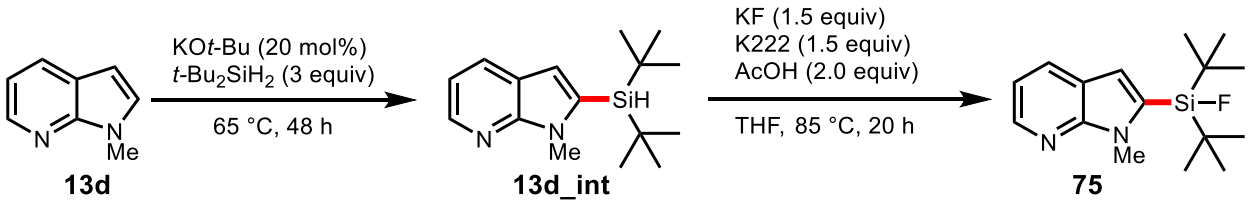
72

benzo[b]thiophen-2-yldi-tert-butylsilane 72: characterization pending.



74

benzo[b]thiophen-2-yldi-tert-butylfluorosilane 74: characterization pending.

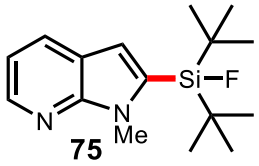


13d **13d_int** **75**

The general silylation procedure was followed without isolation of the hydrosilane product. The reaction was performed with KO*t*-Bu (89.6 mg, 0.8 mmol, 20 mol%), 1-methyl-7-azaindole (**13d**, 528.3 mg, 4.0 mmol), and di-*tert*-butylsilane (2.40 mL, 12 mmol, 3 equiv), in 4.0 mL of THF at 65 °C for 72 h. The crude reside containing **13d_int** was carried through to the fluoridation step.

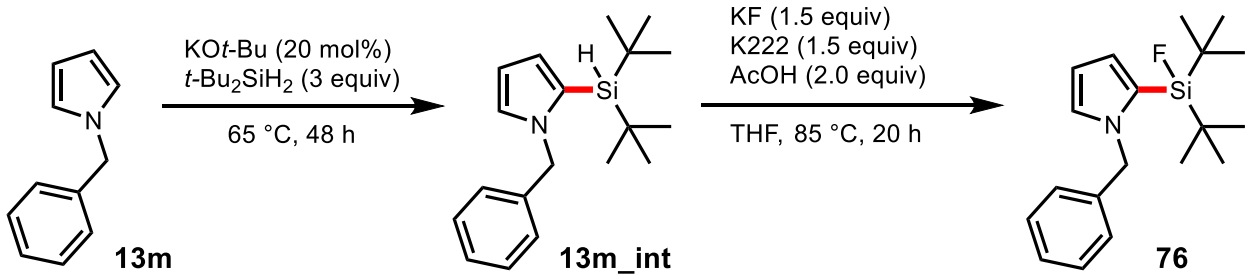
The general fluoridation procedure was followed. The reaction was performed with di-*tert*-butylsilylated 1-methyl-7-azaindole **13d_int** (136.6 mg, 0.5 mmol, 1 equiv), potassium fluoride (43.6 mg, 1.5 equiv, 0.75 mmol), and K222 cryptand (282.4 mg, 1.5 equiv, 0.75 mmol). To the flask, THF (2.5 mL) and acetic acid (57 µL, 2.0 equiv, 1.0 mmol) were added, and the reaction mixture was stirred at reflux overnight. The residue is purified by silica gel flash chromatography

(gradient elution: 100% hexanes → 10% EtOAc in hexanes) to give the desired product **75** in 14% overall yield (i.e., 163.6 mg, 2 steps from 1-methyl-7-azaindole).



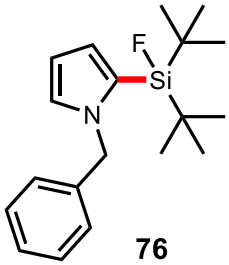
75

2-(di-tert-butylfluorosilyl)-1-methyl-1H-pyrrolo[2,3-b]pyridine 75: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.28 (dd, *J* = 4.6, 1.6 Hz, 1H), 7.88 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.00 (dd, *J* = 7.8, 4.6 Hz, 1H), 6.82 (s, 1H), 4.00 (d, *J* = 2.5 Hz, 4H), 3.58 (dp, *J* = 2.2, 1.0 Hz, 6H), 1.73 (ddp, *J* = 3.1, 2.1, 1.0 Hz, 8H), 1.23 – 1.09 (m, 24H). HRMS (FAB+) calc'd for $C_{16}H_{26}N_2FSi$ [M+H]: 293.1853, found 293.1849.



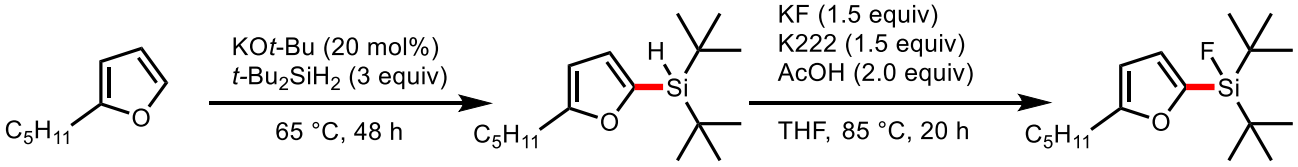
The general silylation procedure was followed without isolation of the hydrosilane product. The reaction was performed with KO*t*-Bu (89.6 mg, 0.8 mmol, 20 mol%), 1-benzylpyrrole (**13m**, 314.4, 4.0 mmol), and di-*tert*-butylsilane (2.40 mL, 12 mmol, 3 equiv), in 4.0 mL of THF at 65 °C for 72 h. The crude reside containing **13m_int** was carried through to the fluoridation step. The general fluoridation procedure was followed. The reaction was performed with di-*tert*-butylsilylated 1-benzylpyrrole **13m_int** (136.6 mg, 0.5 mmol, 1 equiv), potassium fluoride (43.6 mg, 1.5 equiv, 0.75 mmol), and K222 cryptand (282.4 mg, 1.5 equiv, 0.75 mmol). To the flask, THF (2.5 mL) and acetic acid (57 µL, 2.0 equiv, 1.0 mmol) were added, and the reaction mixture was stirred at reflux overnight. The residue is purified by silica gel flash chromatography (gradient elution: 100%

hexanes → 5% CH_2Cl_2 in hexanes) to give the desired product **76** in 17% yield (i.e., 215.9 mg, 2 steps from 1-benzylpyrrole).



76

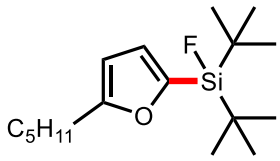
1-benzyl-2-(di-tert-butylfluorosilyl)-1H-pyrrole 76: full characterization pending. HRMS (FAB+) calc'd for $C_{19}H_{29}NFSi$ [M+H]: 318.2062, found 318.2053.



13i **13i_int** **77**

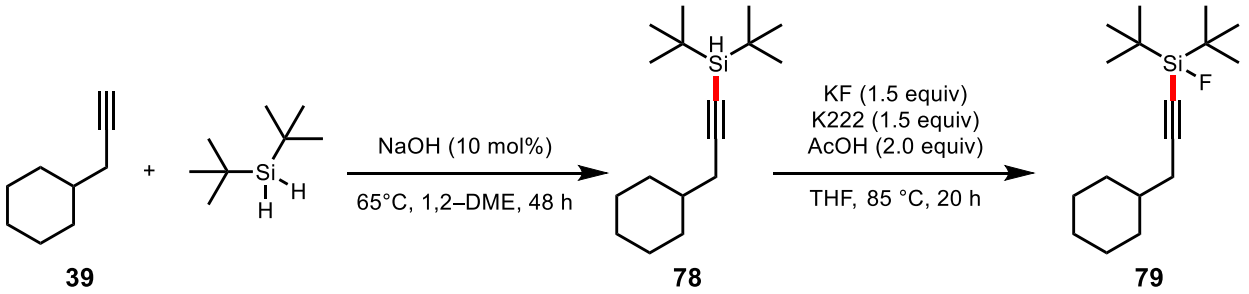
The general silylation procedure was followed without isolation of the hydrosilane product. The reaction was performed with KO*t*-Bu (89.6 mg, 0.8 mmol, 20 mol%), 2-pentylfuran (**13i**, 552.8 mg, 4.0 mmol), and di-*tert*-butylsilane (2.40 mL, 12 mmol, 3 equiv), in 4.0 mL of THF at 65 °C for 72 h. The crude reside containing **13i_int** was carried through to the fluoridation step.

The general fluoridation procedure was followed. The reaction was performed with di-*tert*-butylsilylated 2-pentylfuran **13i_int** (136.6 mg, 0.5 mmol, 1 equiv), potassium fluoride (43.6 mg, 1.5 equiv, 0.75 mmol), and K222 cryptand (282.4 mg, 1.5 equiv, 0.75 mmol). To the flask, THF (2.5 mL) and acetic acid (57 µL, 2.0 equiv, 1.0 mmol) were added, and the reaction mixture was stirred at reflux overnight. The residue is purified by silica gel flash chromatography (gradient elution: 100% hexanes → 5% EtOAc in hexanes) to give the desired product **77** in 48% yield (i.e., 573.1 mg, 2 steps from 2-pentylfuran).



77

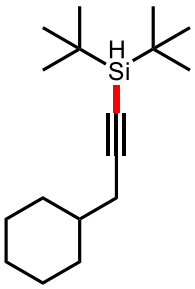
di-tert-butylfluoro(5-pentylfuran-2-yl)silane 77: characterization pending.



39 **78** **79**

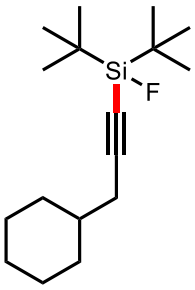
In a nitrogen-filled glove box, NaOH (0.2 mmol, 10 mol%) and 3-cyclohexyl-1-propyn (**39**, 2 mmol, 1 equiv) were added to a scintillation vial equipped with a magnetic stirring bar, followed by solvent (0.5 mL) and di-*tert*-butylsilane (240 µL, 1.5 mmol, 3 equiv), in 2.0 mL of 1,2-DME at 65 °C for 48 h. The desired product **78** (272.7 mg, 52% yield) was obtained after purification by silica gel flash chromatography (100% hexanes).

The general fluoridation procedure was followed. The reaction was performed with di-*tert*-butylsilylated 3-cyclohexyl-1-propyne **78** (264.5 mg, 1.0 mmol, 1 equiv), potassium fluoride (87.2 mg, 1.5 equiv, 1.5 mmol) and K222 cryptand (564.8 mg, 1.5 equiv, 1.5 mmol). To the flask, THF (5 mL) and acetic acid (114 µL, 2.0 equiv, 2.0 mmol) were added, and the reaction mixture was stirred at reflux overnight. The residue is purified by silica gel flash chromatography (100% hexanes) to give the desired product **79** (251.2 mg, 89% yield) (i.e., 46% yield over 2 steps from 3-cyclohexyl-1-propyne).



78

di-tert-butyl(3-cyclohexylprop-1-yn-1-yl)silane 78: ^{1}H NMR (500 MHz, Benzene-d_6) δ 3.95 (s, 1H), 1.89 (dd, J = 6.5, 2.3 Hz, 2H), 1.69 – 1.60 (m, 2H), 1.60 – 1.53 (m, 2H), 1.53 – 1.44 (m, 1H), 1.31 – 1.20 (m, 1H), 1.17 – 1.16 (s, 18H),1.12 – 0.95 (m, 3H), 0.95 – 0.79 (m, 2H).

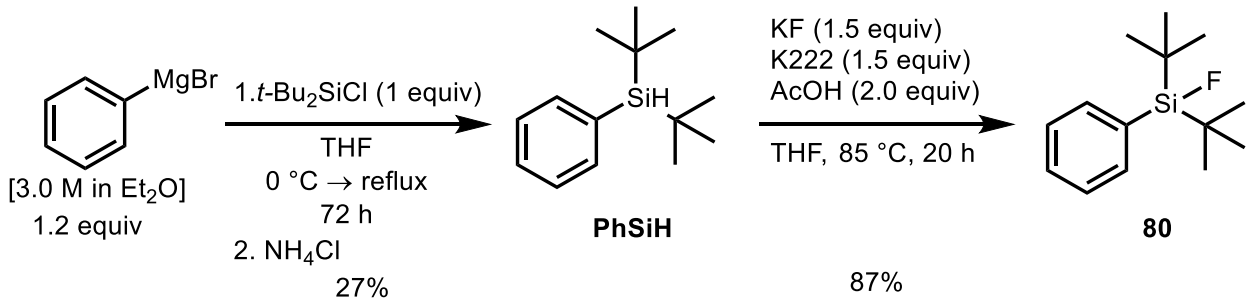


79

di-tert-butyl(3-cyclohexylprop-1-yn-1-yl)fluorosilane 79: ^{1}H NMR (500 MHz, Benzene-d_6) δ 1.89 (dd, J = 6.5, 2.3 Hz, 2H), 1.69 – 1.60 (m, 2H), 1.60 – 1.53 (m, 2H), 1.53 – 1.44 (m, 1H), 1.31 – 1.20 (m, 1H), 1.17 – 1.16 (s, 18H),1.12 – 0.95 (m, 3H), 0.95 – 0.79 (m, 2H).

Preparation of phenyl SiFA

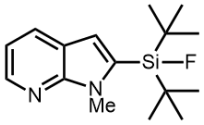
The typical aromatic SiFA comprising of a simple benzene ring functionalized with the *t*-Bu$_2$SiF group was synthesized in order to provide a comparison of the radiochemistry of our heteroaromatic SiFAs with the current state-of-the-art. As mentioned, these comparative studies are not presented in this thesis, but the molecule was prepared and utilized at UCLA for such studies.

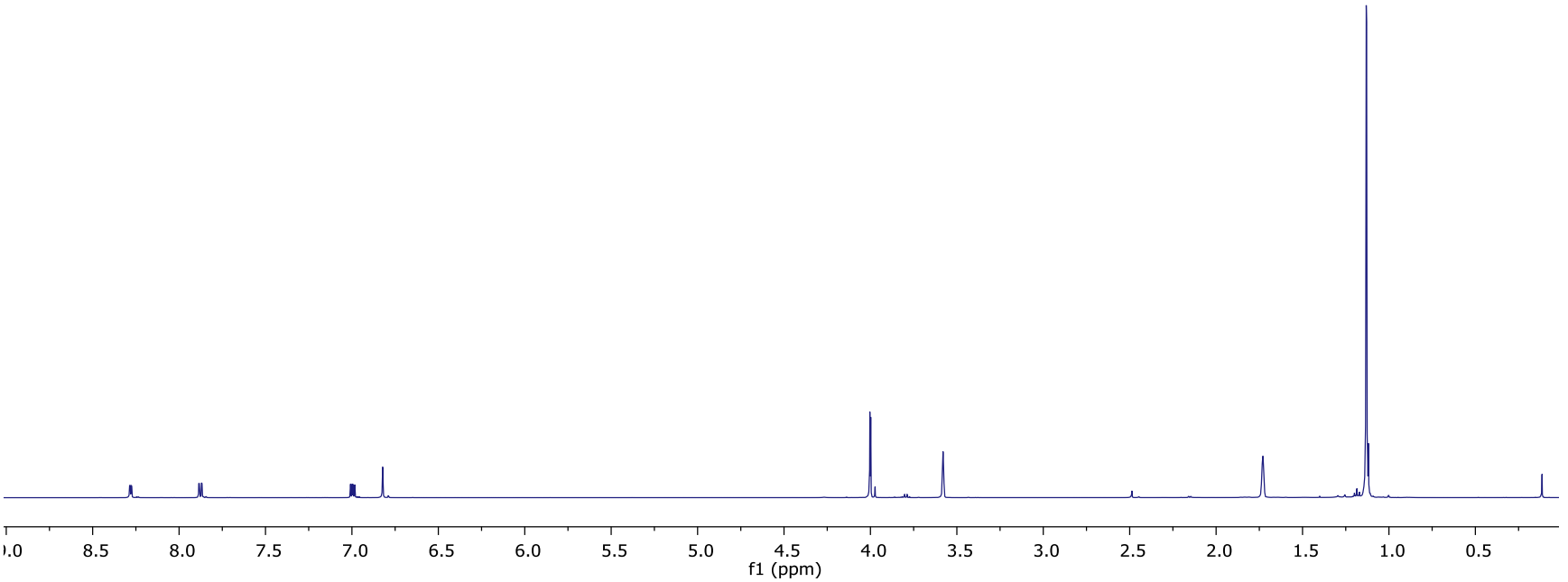


A flame-dried 50 mL 2-neck roundbottom flask is equipped with a reflux condenser (chilled with cold water circulation), a stirring bar, and having the second neck fitted with a rubber septum. To this flask, through the septum, is added di-*tert*-butylchlorosilane (5.1 mL, 25.0 mmol) and THF (10 mL) both via needle. The flask and its contents are cooled to 0 °C by means of an ice bath. To this is added dropwise PhMgBr (3.0 M solution in Et_2O; 10 mL, 30 mmol, 1.2 equiv) over a period of 10 minutes. Once the addition is complete, the cooling bath is removed and the rubber septum is replaced with a lightly greased glass stopper, which is fitted snugly with the aid of a green clamp. The contents are heated to reflux by means of an oil bath set to 90 °C. Reflux occurs at a steady drip rate for 72 hours after which time the heat is removed and the flask and its contents are allowed to cool to ambient temperature. The reaction mixture is then carefully quenched with saturated NH_4Cl (10 mL) and diluted with Et_2O. The organic layer is washed with H_2O once (10 mL). The combined aqueous fractions are extracted with Et_2O (3 x 20 mL) and washed with brine (1 x 10 mL). The combined organic fractions were collected and concentrated in vacuo. This material, **PhSiH**, was filtered through a short plug of silica (100% hexanes) and carried through to the fluoridation without isolation.

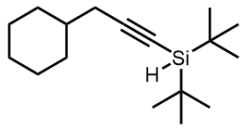
The general fluoridation procedure was followed. The reaction was performed with **PhSiH** (220.2 mg, 1.0 mmol, 1 equiv), potassium fluoride (87.2 mg, 1.5 equiv, 1.5 mmol), and K222 cryptand (564.8 mg, 1.5 equiv, 1.5 mmol). To the flask, THF (5 mL) and acetic acid (114 µL, 2.0 equiv, 2.0

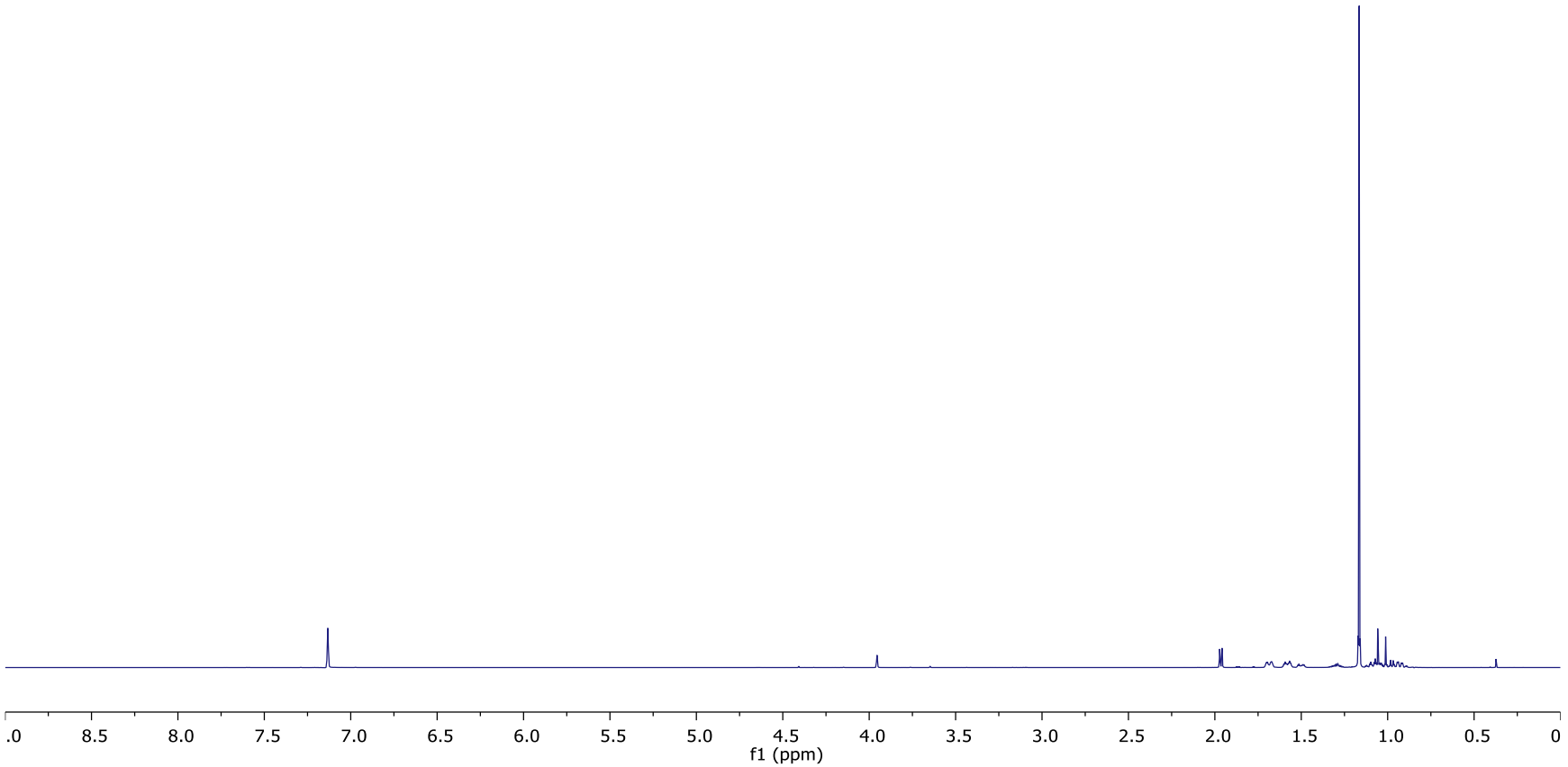
mmol) were added, and the reaction mixture was stirred at reflux overnight. The residue is purified by silica gel flash chromatography (100% hexanes) to give the desired product **80** (207.20 mg, 87% yield) (i.e., 23% yield over 2 steps from phenyl magnesium bromide).



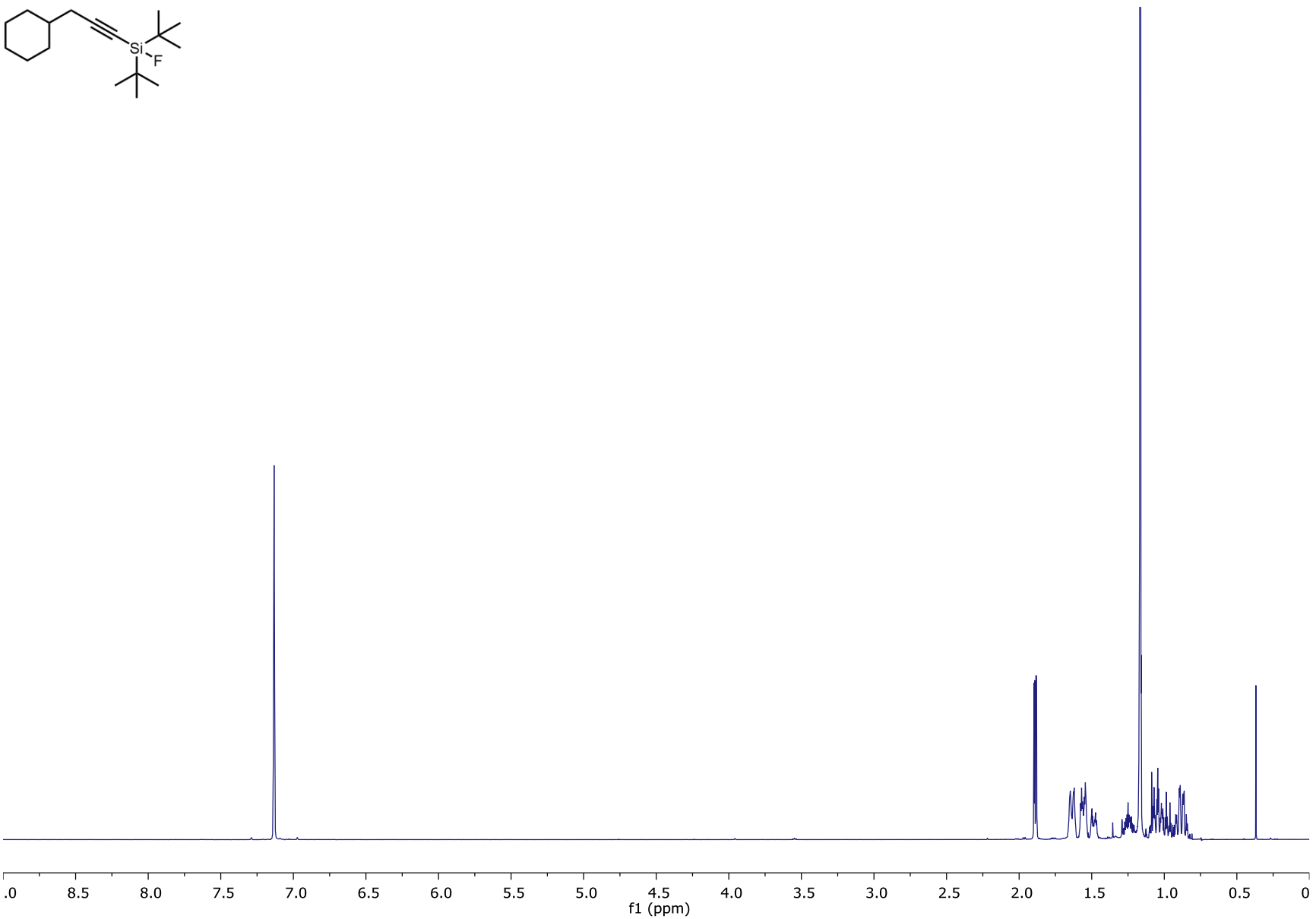


^{1}H NMR (500 MHz, THF-d_8) of compound **75**

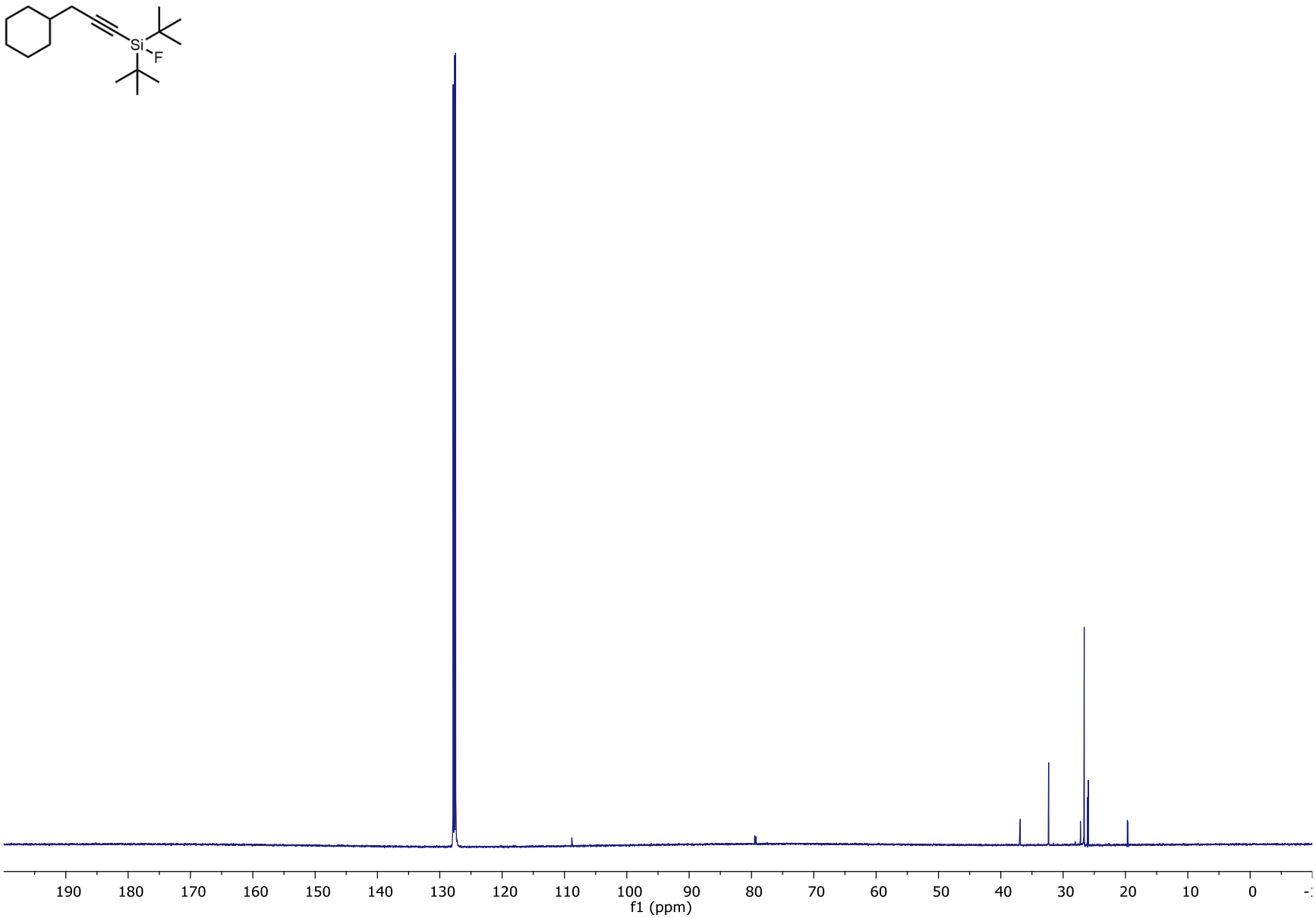




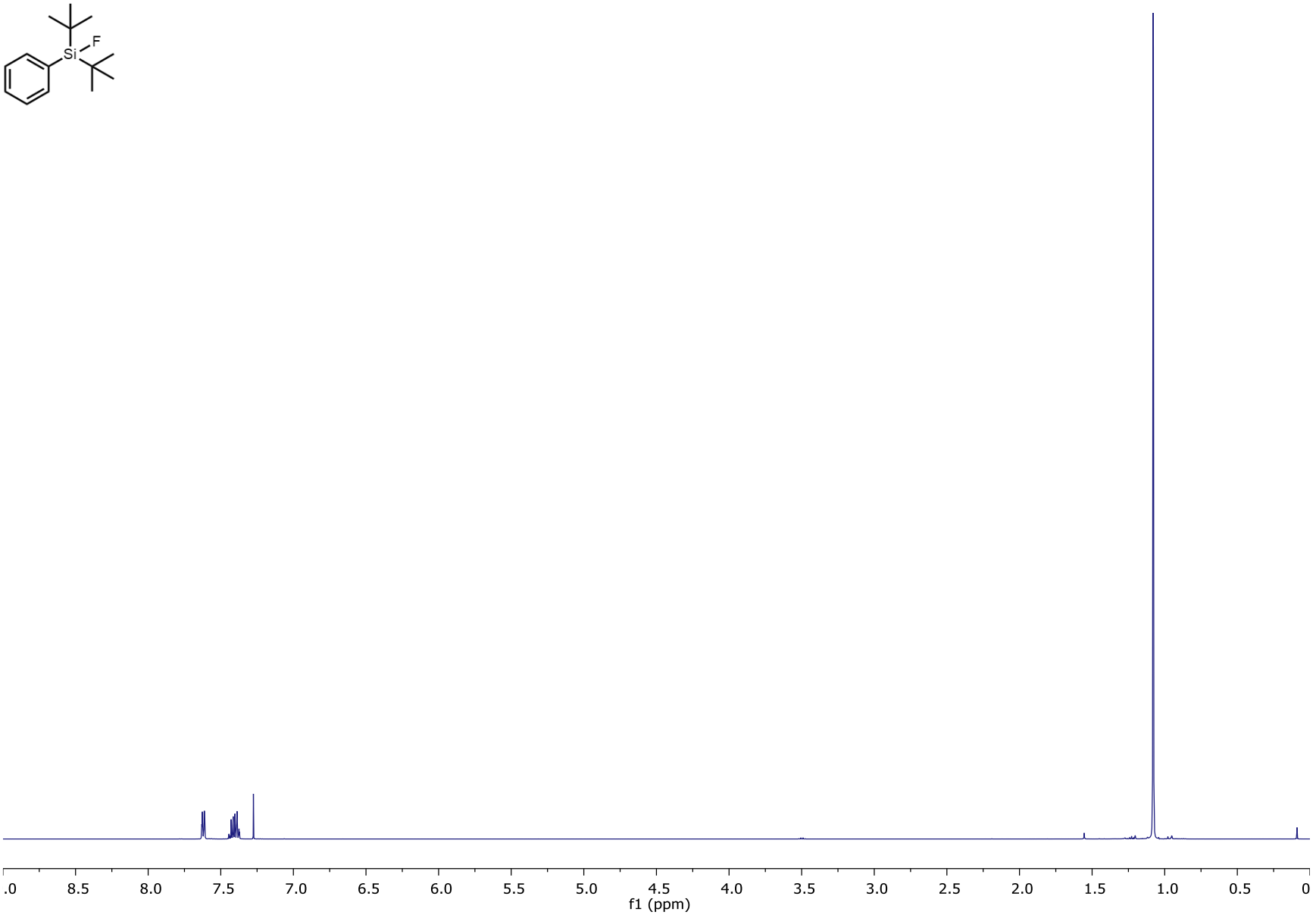
^{1}H NMR (500 MHz, C_6D_6) of compound **78**.



^{1}H NMR (500 MHz, C_6D_6) of compound **79**.



^{13}C NMR (126 MHz, C_6D_6) of compound **79**.



^{1}H NMR (500 MHz, $CDCl_3$) of compound **80**.

Acknowledgements.

I am grateful to Dr. Christopher Waldmann and Prof. Jennifer Murphy at UCLA who were responsible for all radiosynthesis, kinetics, and stability studies (which were not discussed in this thesis). I am also thankful to Andrew Romine who contributed greatly to the synthesis of fluorine-19 heterocyclic- and alkynyl SiFAs – precursors to the [^{18}F]SiFAs. I am grateful to Kazuma Oda, Kerry Betz, and Prof. Brian Stoltz for experimental assistance.

Appendix

COMPUTATIONAL DETAILS

In Chapter 1 were discussed the DFT studies related to the mechanism of the *KOSi* C–O bond cleavage and *KOSi* HDS. Below are given the general details of the computations performed as well as the tabulated energies, enthalpies, and free energies of calculated structures.

General information

All the calculations were carried out with Gaussian 09.[210] Geometry optimizations were performed with the B3LYP method.[211] The 6-31G(d) basis set[212] was used on all atoms. The vibrational frequencies were computed at the same level to evaluate the zero-point vibrational energies (ZPVE) and thermal corrections at 298 K, which also verified that the stationary points are minima or saddle points. Single-point energies and solvent effects were computed at the M06-2X[213]/6-311+G(d,p) level of theory using the gas-phase optimized structures. Solvation energies (solvent = mesitylene) were calculated by a self-consistent reaction field (SCRF) using the CPCM[214] model. Computed structures are illustrated using CYLview.[215] Trimethylsilane was used as a computational model for the experimentally used triethylsilane in order to facilitate the calculations. We located two key transition states (**TS1_S_Et** and **TS4_S_Et**; for details, see Supplementary Table 1) for the triethylsilyl radical attack at C2 and at S in 4,6-dimethyldibenzothiophene (**3**). The computed activation free energies are 17.2 and 26.1 kcal/mol, which are close to those using trimethylsilyl radical (15.5 and 26.4 kcal/mol, Figure 5 of the text). This indicates that the trimethylsilane model is suitable for investigating the experimental system.

Energies, enthalpies, and free energies of calculated structures

The raw computational data obtained from the density functional theory calculations are given in **Appendix Table 1**. Included in the table are the electronic energies, enthalpies, and free energies of calculated structures. This is followed by the Cartesian coordinates of the structures.

Appendix Table 1. Electronic energies, enthalpies, and free energies of the structures calculated at the M06-2X/6-311+G(d,p) (CPCM^{mesitylene})//B3LYP/ 6-31G(d).

Structures	ZPVE	TCE	TCH	TCG	*E*sol	*H*sol (*E*sol + TCH)	*G*sol (*E*sol + TCG)	Imaginary Frequency (cm^{-1})	□*G*sol (kcal/mol)
·SiMe$_3$	0.110424	0.117885	0.118829	0.079221	-409.158357	-409.039528	-409.079136	—	—
3	0.217085	0.229713	0.230657	0.178435	-938.839221	-938.608564	-938.660786	—	0.0
Int1_S	0.328288	0.349215	0.350159	0.279833	-1348.014038	-1347.663879	-1347.734205	—	3.6
Int2_S	0.330154	0.351135	0.352080	0.280549	-1348.012083	-1347.660003	-1347.731534	—	5.3
Int3_S	0.328484	0.350246	0.351190	0.276754	-1347.992661	-1347.641471	-1347.715907	—	15.1
Int4_S	0.341170	0.363113	0.364057	0.289086	-1348.674759	-1348.310702	-1348.385673	—	-4.1
Int5_S	0.224008	0.236741	0.237686	0.181958	-541.146777	-540.909091	-540.964819	—	-12.8
3a	0.237022	0.249704	0.250648	0.196045	-541.831749	-541.581101	-541.635704	—	-32.7
TS1_S	0.327127	0.348360	0.349304	0.276936	-1347.992210	-1347.642906	-1347.715274	-337.565	15.5
TS2_S	0.328544	0.348977	0.349922	0.280571	-1348.001678	-1347.651756	-1347.721107	-120.53	11.8
TS3_S	0.328904	0.349338	0.350282	0.280941	-1347.970110	-1347.619828	-1347.689169	-202.426	31.8
TS4_S	0.327483	0.348823	0.349767	0.276719	-1347.974625	-1347.624858	-1347.697906	-246.532	26.4
TS5_S	0.445642	0.476409	0.477353	0.381812	-1757.796673	-1757.319320	-1757.414861	-837.468	27.2
TS6_S	0.451190	0.482019	0.482964	0.386782	-1757.827069	-1757.344105	-1757.440287	-270.192	11.3
TS7_S	0.341541	0.363019	0.363963	0.288859	-950.953069	-950.589106	-950.664210	-837.588	-0.9
3O	0.220027	0.232261	0.233205	0.181464	-615.861082	-615.627877	-615.679618	—	0.0
Int1_O	0.331020	0.351420	0.352365	0.283120	-1025.031234	-1024.678869	-1024.748114	—	6.7
Int2_O	0.331018	0.352039	0.352984	0.281176	-1025.038304	-1024.685320	-1024.757128	—	1.0
Int3_O	0.330414	0.351891	0.352836	0.278016	-1025.041895	-1024.689059	-1024.763879	—	-3.2
Int4_O	0.343489	0.364900	0.365844	0.292144	-1025.726940	-1025.361096	-1025.434796	—	-23.1
TS1_O	0.330084	0.350780	0.351724	0.280156	-1025.013163	-1024.661439	-1024.733007	-339.657	16.2
TS2_O	0.330092	0.350194	0.351138	0.282888	-1025.005890	-1024.654752	-1024.723002	-254.07	22.4
TS3_O	0.330244	0.350341	0.351285	0.282306	-1024.998477	-1024.647192	-1024.716171	-183.413	26.7
TS4_O	0.327728	0.348515	0.349459	0.278658	-1024.968347	-1024.618888	-1024.689689	-642.444	43.3
TS5_O	0.447660	0.478053	0.478997	0.384030	-1434.848709	-1434.369712	-1434.464679	-703.013	7.8
TS6_O	0.452636	0.482724	0.483668	0.391004	-1434.845160	-1434.361492	-1434.454156	-765.371	14.4
·SiEt$_3$	0.197772	0.209068	0.210012	0.159653	-527.056709	-526.846697	-526.897056	—	—
TS1_S_Et	0.414615	0.439549	0.440493	0.359844	-1465.890237	-1465.449744	-1465.530393	-346.000	17.2
TS4_S_Et	0.414891	0.440035	0.440980	0.358859	-1465.875045	-1465.434065	-1465.516186	-253.873	26.1

ZPVE = zero-point vibrational energy; **TCE** = thermal correction to energy; **TCH** = thermal correction to enthalpy; **TCG** = thermal correction to Gibbs free energy.

Cartesian coordinates of the structures

·SiMe$_3$

C	-1.49714500	-1.00812600	0.17717800
H	-1.53736900	-1.03536900	1.27530500
H	-2.43737100	-0.57371600	-0.18009200
H	-1.44989200	-2.04255300	-0.18063800
C	1.62202200	-0.79170400	0.17728500
H	1.71810200	-1.82273000	-0.18070000
H	2.49328300	-0.23151500	-0.17964300
H	1.66493800	-0.81329300	1.27540400
C	-0.12509400	1.80036800	0.17698200
H	0.72180800	2.39776300	-0.17838200
H	-1.04393200	2.27608900	-0.18319200
H	-0.13134200	1.84923400	1.27520600
Si	0.00022000	-0.00051000	-0.42371000

3

C	-2.97746000	1.81226100	-0.00023600
C	-3.48455200	0.50418600	-0.00036300
C	-2.64305200	-0.61029200	-0.00010000
C	-1.26237000	-0.35835800	0.00029000
C	-0.72749700	0.94797200	0.00033900
C	-1.60737000	2.04098800	0.00014200
H	-3.66610600	2.65259800	-0.00044400
H	-4.56063600	0.34765400	-0.00072700
H	-1.21915200	3.05583000	0.00025100
C	1.26236900	-0.35835800	0.00029200
C	2.64305100	-0.61029200	-0.00009700
C	3.48455200	0.50418600	-0.00035400
C	2.97745900	1.81226100	-0.00022800
C	1.60736900	2.04098800	0.00014500
C	0.72749700	0.94797200	0.00033900
H	4.56063600	0.34765400	-0.00070900
H	3.66610500	2.65259900	-0.00043000
H	1.21915100	3.05583000	0.00025100
C	3.18249300	-2.01804800	-0.00033000
H	2.84273500	-2.57644200	0.88174100
H	2.84225600	-2.57628400	-0.88231700
H	4.27648300	-2.02246700	-0.00060300
C	-3.18249300	-2.01804900	-0.00031300
H	-2.84216100	-2.57633800	-0.88222900
H	-2.84283000	-2.57639000	0.88183000
H	-4.27648300	-2.02246800	-0.00070100
S	0.00000100	-1.59914200	0.00043300

Int1_S

C	-3.59767600	1.51757900	0.76158400
C	-4.01236400	0.29963700	0.20897100
C	-3.10416700	-0.57865300	-0.39649300
C	-1.75852300	-0.18992800	-0.42212000
C	-1.31609600	1.03906400	0.12316200
C	-2.25981600	1.89366400	0.71953100
H	-4.32869000	2.17155000	1.22909000
H	-5.06274800	0.02135100	0.24907600
H	-1.94070700	2.83760100	1.15294300
C	0.85308400	0.02587200	-0.46211400
C	2.02590800	0.29530000	-1.36429300
C	2.60806900	1.53555200	-1.30819100
C	2.04170100	2.61994200	-0.57906500
C	0.75953700	2.49173100	-0.03416300
C	0.09822700	1.27148300	-0.07130900

H	3.51097700	1.71447800	-1.88899400
H	2.54860900	3.57963600	-0.56287800
H	0.23974100	3.37424200	0.33174100
C	2.54241300	-0.78263500	-2.27546000
H	2.76659400	-1.71693300	-1.74680800
H	1.79192500	-1.03101600	-3.03941600
H	3.45154000	-0.45732800	-2.79099800
C	-3.55113200	-1.88631200	-0.99980200
H	-3.32187000	-1.93097000	-2.07265100
H	-3.04124600	-2.73794700	-0.53099600
H	-4.62943600	-2.02920200	-0.88087100
S	-0.45656000	-1.14493700	-1.16070400
Si	1.49225300	-0.84670000	1.21293300
C	2.78085700	0.26091300	2.04465400
H	2.36648000	1.23812400	2.31165900
H	3.13216000	-0.21888900	2.96718700
H	3.65043500	0.43108900	1.40198200
C	2.28362400	-2.52709800	0.83527300
H	2.45371900	-3.05952800	1.78002300
H	1.63869000	-3.15778700	0.21429300
H	3.25496000	-2.42917600	0.33881300
C	0.04838600	-1.10636500	2.40690200
H	-0.43119000	-0.16456900	2.69077400
H	-0.72034500	-1.76491200	1.99132300
H	0.43162700	-1.57550300	3.32251000

Int2_S

C	-2.38919300	-1.07039500	2.07870600
C	-3.47541000	-0.92908700	1.20949500
C	-3.37324600	-0.17938800	0.04061200
C	-2.11894600	0.44541700	-0.27988200
C	-1.00797900	0.29217200	0.61873500
C	-1.17023700	-0.45838800	1.78489100
H	-2.49922200	-1.64856300	2.99242900
H	-4.42103100	-1.40713000	1.45183800
H	-0.33669400	-0.54658800	2.47547000
C	1.51642500	0.32577000	0.15122400
C	2.70757500	1.10317200	0.19565100
C	2.64819100	2.48001700	0.44563100
C	1.43507100	3.12839800	0.64925600
C	0.26299900	2.38474800	0.64309700
C	0.29499100	0.99948600	0.41701900
H	3.57444100	3.04922600	0.47932000
H	1.40572700	4.19935100	0.83185700
H	-0.69024500	2.86623600	0.84029900
C	4.08988000	0.51400200	-0.01162800
H	4.20976600	-0.46050600	0.47077900
H	4.32238600	0.38263100	-1.07455700
H	4.85121100	1.18061000	0.40616300
C	-4.57040300	-0.05171400	-0.86660700
H	-4.81416600	0.99793500	-1.05972800
H	-4.38120200	-0.50809000	-1.84437500
H	-5.44324300	-0.53963400	-0.42185000
Si	1.58809500	-1.53604500	-0.34000600
C	2.11737700	-2.58935900	1.14989200
H	2.22090500	-3.64102800	0.85406400
H	3.07597500	-2.26981400	1.57448400
H	1.37067300	-2.54468800	1.95128800
C	2.80520400	-1.82797900	-1.77516800
H	2.69160900	-1.07256200	-2.56194900
H	3.85668100	-1.84800000	-1.47707500
H	2.57448400	-2.80121900	-2.22622700
C	-0.04619300	-2.22687900	-1.00989200

H	-0.44552400	-1.60663700	-1.81974000
H	0.16417100	-3.21880700	-1.43124600
H	-0.82862300	-2.34601400	-0.25724900
S	-1.94050300	1.32799800	-1.75250700

Int3_S

C	-1.85901300	3.35259800	0.38838000
C	-2.82894000	2.51356400	-0.15256200
C	-2.50343700	1.23149900	-0.61224800
C	-1.16592100	0.78825900	-0.50057300
C	-0.16382400	1.63977800	0.02991200
C	-0.54098900	2.92119600	0.46692800
H	-2.12572900	4.35047200	0.72617100
H	-3.85678600	2.85730000	-0.23701200
H	0.22201200	3.59681300	0.83997400
C	1.84762000	0.37059900	-0.78862500
C	3.16489600	-0.05000600	-0.80627100
C	3.98867900	0.48485800	0.20129300
C	3.47001300	1.37355300	1.14685800
C	2.12960500	1.75404800	1.11117300
C	1.26684500	1.24614400	0.11392000
H	5.03755500	0.19589600	0.24464800
H	4.11605000	1.76352000	1.92894200
H	1.74145500	2.41994700	1.87771200
C	3.69530600	-1.00043300	-1.85581400
H	2.98226000	-1.80733900	-2.05379800
H	3.86569400	-0.48173900	-2.80781300
H	4.64628300	-1.44520300	-1.54426200
C	-3.58761000	0.38346300	-1.23708400
H	-3.33833000	0.11596900	-2.26985300
H	-3.73596500	-0.55802200	-0.69916300
H	-4.53897500	0.92475100	-1.24331500
S	-0.74751300	-0.85356400	-1.14147700
Si	-0.82961700	-2.16359500	0.61931100
C	0.44501500	-1.68085300	1.92186100
H	0.25052200	-0.68279700	2.32752300
H	0.40956700	-2.39516700	2.75507800
H	1.45921800	-1.67897700	1.51107200
C	-0.43575500	-3.86215300	-0.10870000
H	-1.16296900	-4.15224800	-0.87501000
H	0.56095000	-3.88159600	-0.56320800
H	-0.45777500	-4.62495000	0.67972700
C	-2.55243800	-2.15117600	1.39687300
H	-2.55827300	-2.77264500	2.30186300
H	-2.85184300	-1.13865900	1.68929400
H	-3.31039500	-2.54760700	0.71277100

Int4_S

C	-1.02044200	3.55095000	0.66167300
C	-2.12373700	3.04488400	-0.01944800
C	-2.10011700	1.76871900	-0.59505600
C	-0.93021000	0.98276100	-0.46618300
C	0.21629500	1.50685700	0.17998500
C	0.13904100	2.79001600	0.74910500
H	-1.05653900	4.54401300	1.10170200
H	-3.02355000	3.64751700	-0.11555700
H	1.01978500	3.19436000	1.23944100
C	2.20679100	0.35391600	-0.86541500
C	3.47131100	-0.23861300	-0.78865100
C	4.07045900	-0.37741700	0.47071600
C	3.41800300	0.07002000	1.61843000
C	2.15838700	0.66167900	1.52456600
C	1.52910600	0.80187300	0.27832100

H	5.05533100	-0.83270800	0.54942400
H	3.89339000	-0.03756000	2.59012900
H	1.65269900	1.00899200	2.42161800
C	4.16489800	-0.73567400	-2.03653200
H	3.92064700	-1.78815300	-2.23394000
H	3.86119400	-0.16291100	-2.91904700
H	5.25441200	-0.66668300	-1.94543400
C	-3.31590300	1.28927300	-1.35436000
H	-3.06256600	1.03151100	-2.38840800
H	-3.75241000	0.39009000	-0.90917900
H	-4.08546300	2.06755200	-1.37240100
S	-0.91809500	-0.67551300	-1.20280600
Si	-1.53689900	-2.01732000	0.41187900
C	-0.31096700	-2.02757700	1.84622500
H	-0.26817800	-1.05508600	2.34721700
H	-0.61940000	-2.77421400	2.59015500
H	0.70171000	-2.27358600	1.51212400
C	-1.56620100	-3.70241900	-0.44374700
H	-2.27234300	-3.71906000	-1.28110600
H	-0.57693600	-3.97197500	-0.82969100
H	-1.87084700	-4.48075000	0.26722400
C	-3.25311700	-1.58165200	1.07687200
H	-3.50725500	-2.24694000	1.91243100
H	-3.29315800	-0.55247900	1.45072200
H	-4.02678000	-1.69692000	0.31012200
H	1.74078000	0.48012000	-1.83796500

Int5_S

C	2.88875100	-1.57054000	-0.38836900
C	3.57223000	-0.37455700	-0.15288200
C	2.86778400	0.80881900	0.13801900
C	1.49462900	0.67500700	0.16678300
C	0.74129600	-0.46847500	-0.04130100
C	1.49732800	-1.62521000	-0.33790900
H	3.45045600	-2.47098400	-0.62203900
H	4.65948900	-0.34950100	-0.19614600
H	0.98667100	-2.56082400	-0.55000900
C	-1.44956500	0.72716400	-0.18897100
C	-2.84343500	0.78229300	-0.12721000
C	-3.54507800	-0.39644400	0.16496700
C	-2.85981700	-1.58753900	0.39723000
C	-1.46719500	-1.62588800	0.33730500
C	-0.74006000	-0.46497900	0.03625000
H	-4.63178400	-0.37813900	0.21207300
H	-3.41298600	-2.49320500	0.63266900
H	-0.94710900	-2.55548300	0.54827200
C	-3.58079200	2.08160800	-0.35825200
H	-2.92423700	2.84256800	-0.79168200
H	-4.43213400	1.94484900	-1.03530000
H	-3.97907300	2.48588600	0.58166700
C	3.56906500	2.12259700	0.39692600
H	3.29940800	2.87174600	-0.35694700
H	3.29307400	2.53428600	1.37440300
H	4.65616600	1.99787100	0.37535900
H	-0.88878800	1.62778000	-0.42783800

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C	2.82011100	-1.55389400	-0.60951100
C	3.54302600	-0.40970800	-0.27562200
C	2.88292300	0.74157200	0.17549600
C	1.48889000	0.71335200	0.27550900
C	0.74059500	-0.42850600	-0.05697300
C	1.43015700	-1.56720200	-0.50202600

H	3.34136700	-2.43812300	-0.96759400
H	4.62717500	-0.40743100	-0.36564600
H	0.87321700	-2.45324500	-0.79314000
C	-1.49046900	0.70732700	-0.29150100
C	-2.88520600	0.73489100	-0.19299000
C	-3.54450500	-0.41428600	0.26292600
C	-2.81995800	-1.55287500	0.61416700
C	-1.42988900	-1.56323300	0.51476200
C	-0.74110000	-0.42813700	0.05803100
H	-4.62954700	-0.41655800	0.34034100
H	-3.34143800	-2.43694300	0.97230200
H	-0.87204900	-2.44605500	0.81384800
C	-3.66143700	1.98025000	-0.55633800
H	-3.10553700	2.60827600	-1.26031900
H	-4.62638100	1.73317400	-1.01252800
H	-3.87070800	2.59182100	0.33168700
C	3.66434500	1.97345200	0.57239800
H	3.02039200	2.85720100	0.62496300
H	4.13209400	1.84889000	1.55805200
H	4.46926400	2.18393100	-0.14113100
H	-0.97216600	1.58270900	-0.67575300
H	0.96942500	1.59434000	0.64495200

TS1_S

C	-3.59760800	1.23249600	1.16972600
C	-4.00215500	0.13995100	0.39040600
C	-3.11107600	-0.52564200	-0.45793700
C	-1.79264800	-0.05010600	-0.49243500
C	-1.35918400	1.04889700	0.28452500
C	-2.28648200	1.69092600	1.12215600
H	-4.31798000	1.72289000	1.81872800
H	-5.03270800	-0.20310500	0.44103900
H	-1.97785100	2.53687500	1.73040600
C	0.71212500	0.38216900	-0.74086900
C	1.94771200	0.72725300	-1.39047000
C	2.60554900	1.85751400	-0.93433400
C	2.04310800	2.71265800	0.03898500
C	0.75261000	2.48699300	0.50865300
C	0.03760300	1.36861200	0.06738400
H	3.57489200	2.10603400	-1.36097500
H	2.59465200	3.58951300	0.36510300
H	0.27960300	3.20661600	1.17219000
C	2.51514400	-0.14863300	-2.47328000
H	2.67880000	-1.17632400	-2.12080200
H	1.82922600	-0.21481200	-3.32874300
H	3.47110400	0.24035900	-2.83677800
C	-3.54384000	-1.69434200	-1.30668000
H	-3.42148700	-1.47885200	-2.37643000
H	-2.94475300	-2.58881700	-1.09192700
H	-4.59526800	-1.94199600	-1.13298800
S	-0.50117100	-0.71950900	-1.50492900
Si	1.57831000	-1.24065400	1.09535000
C	3.03085500	-0.40271500	1.98606200
H	2.72811900	0.55284700	2.42641800
H	3.41243000	-1.04290500	2.79389800
H	3.85856500	-0.20236300	1.29734000
C	2.14204500	-2.90220100	0.35726700
H	2.37452300	-3.61896000	1.15777900
H	1.35957100	-3.34536200	-0.26830300
H	3.04349600	-2.79027300	-0.25585300
C	0.14716000	-1.53497100	2.30787100
H	-0.21589600	-0.59718500	2.74060700
H	-0.70019500	-2.02536100	1.81752500

H	0.47806100	-2.18068500	3.13354900

TS2_S

C	-3.46131900	1.26775500	1.19404200
C	-3.91691000	0.28475900	0.30847600
C	-3.05385300	-0.37493400	-0.57111500
C	-1.68664000	-0.02301800	-0.54923800
C	-1.21739400	0.97533800	0.34266600
C	-2.11630900	1.61686000	1.20683900
H	-4.15804400	1.75133100	1.87294300
H	-4.97160000	0.01895500	0.30096500
H	-1.75078800	2.37052600	1.89954300
C	1.07975500	0.25614300	-0.26648400
C	2.30596300	0.67351400	-0.92396800
C	2.68009000	2.00815100	-0.89126900
C	1.88973100	2.98726100	-0.26551200
C	0.63860100	2.64250900	0.24030000
C	0.19730400	1.31900100	0.19112800
H	3.61731400	2.30184800	-1.35879700
H	2.22171000	4.02132800	-0.24588600
H	-0.03908200	3.41647500	0.59007500
C	3.18988800	-0.32639000	-1.62694300
H	3.72577000	-0.97898300	-0.92648000
H	2.60286000	-0.97550500	-2.28749700
H	3.94198000	0.18596300	-2.23491100
C	-3.57114600	-1.42500700	-1.52162100
H	-3.41922000	-1.12823900	-2.56723900
H	-3.04285800	-2.37726300	-1.38739400
H	-4.64127000	-1.59995000	-1.37179900
S	-0.50277800	-0.77662700	-1.62361000
Si	1.28736200	-1.27220700	0.94847100
C	2.71590200	-0.75072500	2.08749600
H	2.48199900	0.18469200	2.60931000
H	2.89532000	-1.52017600	2.84904700
H	3.65415400	-0.59765700	1.54296300
C	1.72553900	-2.91420300	0.11404100
H	1.84177100	-3.67425000	0.89804700
H	0.92522500	-3.24191900	-0.55581700
H	2.65860300	-2.88863100	-0.45560000
C	-0.22400000	-1.56616400	2.04327700
H	-0.51607400	-0.67806800	2.61121900
H	-1.09654600	-1.90688600	1.47940000
H	0.03895000	-2.35174400	2.76436500

TS3_S

C	-3.27815100	1.94889100	0.77753400
C	-3.79810900	0.85709200	0.08010100
C	-2.96123200	-0.06072300	-0.56110600
C	-1.56694700	0.15212600	-0.50226600
C	-1.02590500	1.27936400	0.16037800
C	-1.90631400	2.15780800	0.81573000
H	-3.94680400	2.63576200	1.28917000
H	-4.87368100	0.70304900	0.04193400
H	-1.50808900	3.00468600	1.36596800
C	1.30559800	0.48689500	-0.24873500
C	2.64519700	0.70997000	-0.59980700
C	3.13787300	2.01286200	-0.45423800
C	2.31363900	3.05346900	-0.01485600
C	0.96809900	2.82123600	0.23759300
C	0.42746700	1.52691300	0.08669200
H	4.17786000	2.21630900	-0.70219800
H	2.71730400	4.05745700	0.08463400
H	0.32076600	3.65365200	0.49708300

C	3.54863900	-0.38165500	-1.12488500
H	3.77213400	-1.13744800	-0.36246500
H	3.08530600	-0.90112900	-1.97156000
H	4.50188900	0.03384300	-1.46624400
C	-3.55648500	-1.24000600	-1.29272200
H	-3.26681900	-1.24765500	-2.35007900
H	-3.21618200	-2.19148200	-0.86736900
H	-4.64946900	-1.21475300	-1.24110800
S	-0.46039000	-1.02651300	-1.26782900
Si	0.69381200	-1.73605800	0.65184800
C	1.84893000	-1.14370200	2.05942000
H	1.41448100	-0.29152200	2.59224200
H	1.94477200	-1.97472100	2.77347100
H	2.84862900	-0.85577600	1.72648100
C	1.52254700	-3.22517400	-0.18079700
H	0.76978700	-3.87187300	-0.64448400
H	2.23999100	-2.94124900	-0.95589000
H	2.06286500	-3.81221400	0.57226100
C	-0.83991400	-2.28119700	1.63503400
H	-1.42231900	-1.42142300	1.98374200
H	-1.50231600	-2.91243300	1.03380400
H	-0.52683100	-2.84707500	2.52159000

TS4_S

C	-0.17722000	3.86743100	0.27592600
C	-1.35033300	3.34523300	-0.26725100
C	-1.46793900	1.99110000	-0.61288000
C	-0.36321500	1.15526800	-0.36579600
C	0.85843700	1.68841200	0.11245100
C	0.93085800	3.04572600	0.44707900
H	-0.11837600	4.92265000	0.52839000
H	-2.19613600	4.00317600	-0.45216200
H	1.86495700	3.45973300	0.81552000
C	1.72758200	-0.47400400	-0.44536600
C	2.64795500	-1.51876000	-0.50405000
C	3.91330400	-1.26322200	0.04320300
C	4.21440100	-0.03235000	0.64218000
C	3.26036800	0.97966000	0.70758300
C	1.98680700	0.75374900	0.15870900
H	4.67822100	-2.03646600	-0.00497900
H	5.20303300	0.13039800	1.06306300
H	3.50510100	1.92776400	1.18027000
C	2.31440600	-2.84642900	-1.14320900
H	1.50470200	-3.35529800	-0.60431600
H	1.97761000	-2.71792400	-2.17861800
H	3.18281100	-3.51298400	-1.14855100
C	-2.74290900	1.51950100	-1.27103900
H	-2.54226000	0.76483000	-2.03817700
H	-3.44421400	1.07780800	-0.55394800
H	-3.25739900	2.36251200	-1.74409500
S	-0.32976300	-0.62162900	-0.72674400
Si	-2.15841700	-1.47983500	0.48319500
C	-2.54064700	-0.41304700	1.99963200
H	-3.01305100	0.53871600	1.73753600
H	-3.21717600	-0.95039000	2.67739700
H	-1.62254600	-0.18698400	2.55280600
C	-1.36797300	-3.11206400	1.02761800
H	-1.06590300	-3.71833600	0.16505300
H	-0.47911100	-2.93960600	1.64394200
H	-2.07902100	-3.70695500	1.61512400
C	-3.72008000	-1.91075500	-0.51237300
H	-4.38664200	-2.54042000	0.09339900
H	-4.28616500	-1.02991500	-0.82838600

H	-3.45719900	-2.48124500	-1.41060100

TS5_S

C	0.73134500	2.21884300	-3.03567800
C	1.38878000	2.88866400	-2.00765900
C	1.50853900	2.32478600	-0.73136400
C	0.95207100	1.04491200	-0.49463100
C	0.25096700	0.36993200	-1.52322400
C	0.16484500	0.97375600	-2.78954100
H	0.64665400	2.67324000	-4.01931700
H	1.81693700	3.87139400	-2.18956500
H	-0.37730100	0.45626700	-3.57569700
C	-1.37022800	-1.22505900	-0.39304000
C	-2.01786400	-2.44749800	-0.24691600
C	-1.66330600	-3.47054300	-1.14159800
C	-0.71448700	-3.24730300	-2.14091600
C	-0.09269000	-2.00521300	-2.25468200
C	-0.40595700	-0.96154000	-1.36026200
H	-2.14106200	-4.44501800	-1.05495300
H	-0.45581100	-4.04642000	-2.83068400
H	0.65686000	-1.83893100	-3.02550800
C	-3.06375200	-2.67599100	0.82211000
H	-2.67460700	-2.43953500	1.81881700
H	-3.94523700	-2.04247100	0.66104400
H	-3.40116200	-3.71751500	0.82834400
C	2.20878700	3.11522200	0.34984700
H	1.54690600	3.29682500	1.20369900
H	3.08374100	2.58793200	0.74188400
H	2.54035300	4.08317900	-0.03928200
S	1.08708200	0.34166800	1.17131900
Si	2.86979000	-0.92868900	1.13873300
C	2.61531700	-2.49673600	0.12212200
H	2.50168100	-2.27781500	-0.94387500
H	3.48159800	-3.16121100	0.24076900
H	1.71967900	-3.03834200	0.44270700
C	3.08973200	-1.36972400	2.96408700
H	3.25575400	-0.47806300	3.57828500
H	2.21163300	-1.89330200	3.35846800
H	3.95568000	-2.03180500	3.09027700
C	4.38164700	0.00351600	0.48948600
H	5.23820200	-0.67906000	0.41570300
H	4.20230800	0.41867000	-0.50840400
H	4.66516200	0.82597200	1.15493200
Si	-2.97005300	1.22965500	0.95887700
H	-2.07114000	0.02829600	0.34791700
C	-4.56543400	1.31645800	-0.06433300
H	-5.12173800	0.37237500	-0.02811200
H	-5.23103700	2.10747900	0.30499600
H	-4.34612500	1.53177400	-1.11656300
C	-2.03150800	2.87073800	0.84851400
H	-1.12563700	2.84253700	1.46412100
H	-1.72864200	3.09471100	-0.18007500
H	-2.65471900	3.70133500	1.20555500
C	-3.35604800	0.82229200	2.77036500
H	-3.89702000	-0.12598700	2.86633300
H	-2.43261500	0.74070800	3.35517700
H	-3.97345100	1.60550900	3.22924300

TS6_S

C	-3.38298100	-2.76124100	-1.10054600
C	-2.18111700	-3.45815100	-1.20794500
C	-0.95387900	-2.83253100	-0.94383700
C	-0.96840000	-1.48095000	-0.56272200

C	-2.16330000	-0.74670500	-0.47718000
C	-3.37331800	-1.41837100	-0.73886300
H	-4.32466000	-3.26187700	-1.31022800
H	-2.18832200	-4.50698100	-1.49773100
H	-4.30576200	-0.86321100	-0.67522300
C	-1.60657200	1.68716700	-0.87943000
C	-1.73212500	3.04749500	-0.58204700
C	-2.52293500	3.42390800	0.51317600
C	-3.17050700	2.45981400	1.28320700
C	-3.03851000	1.10535600	0.97056300
C	-2.24472600	0.70002000	-0.11265300
H	-2.63502700	4.47809600	0.75790600
H	-3.78533300	2.76235000	2.12724100
H	-3.54716600	0.35559700	1.57088800
C	-1.01827200	4.09071000	-1.41154100
H	-0.73859100	3.69836200	-2.39477400
H	-1.64299600	4.97762300	-1.56727500
H	-0.09635000	4.42869900	-0.91916500
C	0.32312500	-3.63464400	-1.06575600
H	1.00581500	-3.19476900	-1.80061200
H	0.87107200	-3.67347100	-0.11751700
H	0.10369000	-4.66231800	-1.37331500
S	0.84304600	-0.57805700	-0.28114400
Si	0.99786600	-0.64215600	1.91517300
C	-0.27415900	-1.86524500	2.58648200
H	-0.14903600	-2.86612400	2.16074800
H	-0.15223800	-1.94382300	3.67495200
H	-1.29902000	-1.54205300	2.38281100
C	0.68135100	1.07282900	2.64024400
H	1.41397600	1.80412900	2.28310000
H	-0.31590800	1.43711100	2.37250500
H	0.74928900	1.03824000	3.73585200
C	2.72849200	-1.23424400	2.40479000
H	2.78193200	-1.34448700	3.49619100
H	2.96250600	-2.20645800	1.95756100
H	3.51111000	-0.52916900	2.10651500
Si	2.94096500	0.61630000	-0.90033800
H	-1.00869500	1.38200800	-1.73299900
C	2.40748500	1.21313300	-2.61793600
H	1.60728600	1.95835700	-2.54661100
H	3.24974500	1.67313700	-3.15136700
H	2.03697400	0.38274800	-3.22962400
C	4.36858900	-0.62310700	-1.08912900
H	4.74337700	-0.96788900	-0.11930000
H	4.04497900	-1.50446100	-1.65394300
H	5.20885400	-0.16769800	-1.63155400
C	3.51388400	2.11661700	0.12413900
H	2.69708500	2.83156200	0.27411500
H	3.89044400	1.82288400	1.11030900
H	4.32583900	2.64363900	-0.39694300

TS7_S

C	-2.42998800	-3.13635900	-0.08255500
C	-3.29366600	-2.10057300	0.28169500
C	-2.80504700	-0.80417500	0.50831400
C	-1.43365800	-0.61228800	0.36531800
C	-0.53323600	-1.61506500	0.00915300
C	-1.06402800	-2.90216400	-0.21612100
H	-2.82548500	-4.13457300	-0.25148700
H	-4.35871400	-2.29661700	0.39283000
H	-0.39253600	-3.72045600	-0.46514200
C	1.58889600	-0.56783800	0.84616300
C	2.96596000	-0.32920400	0.78136500

C	3.69525500	-0.91157000	-0.26450000
C	3.05712500	-1.70847700	-1.21501100
C	1.68417900	-1.93788900	-1.13667500
C	0.92779100	-1.36638200	-0.10196400
H	4.76812300	-0.74392700	-0.33011900
H	3.63309800	-2.15204000	-2.02330300
H	1.19016000	-2.54479000	-1.89025700
C	3.65113800	0.54230300	1.80981800
H	3.06719300	0.60554000	2.73387000
H	4.64483600	0.15687500	2.06417300
H	3.78893300	1.56669800	1.43813100
C	-3.73626100	0.32301000	0.89623900
H	-3.45250000	0.76112400	1.86056900
H	-3.71553900	1.13198500	0.15665900
H	-4.76942300	-0.02931800	0.97878200
Si	-0.48930000	2.37894200	-0.38226100
H	1.01091700	-0.14925700	1.66630400
C	0.33298800	3.29711800	1.05852900
H	1.21852900	2.76186500	1.41895200
H	0.65249200	4.30183600	0.75234400
H	-0.35554900	3.41209400	1.90384500
C	-2.02023800	3.33554100	-0.96870200
H	-2.54216000	2.80050700	-1.77075100
H	-2.73500000	3.49902400	-0.15404800
H	-1.73539100	4.32060200	-1.36119500
C	0.71623700	2.14942200	-1.82352000
H	1.59674700	1.57418800	-1.51859900
H	0.23977100	1.61230100	-2.65179500
H	1.05844300	3.11891100	-2.20881200
H	-0.95743900	0.90978100	0.12543400

3O

C	3.05368800	-1.55897200	-0.00017200
C	3.38965900	-0.19444300	-0.00027800
C	2.42031400	0.81472200	-0.00008100
C	1.10143300	0.36270700	0.00018300
C	0.72623800	-0.99206700	0.00022200
C	1.72464100	-1.97377100	0.00007100
H	3.84851300	-2.29959200	-0.00032600
H	4.43821600	0.09355600	-0.00058000
H	1.47036600	-3.02992000	0.00011600
C	-1.10143300	0.36270700	0.00017900
C	-2.42031400	0.81472100	-0.00002500
C	-3.38965900	-0.19444300	-0.00018100
C	-3.05368800	-1.55897200	-0.00013300
C	-1.72464100	-1.97377100	0.00005900
C	-0.72623800	-0.99206700	0.00021100
H	-4.43821600	0.09355600	-0.00036000
H	-3.84851300	-2.29959200	-0.00024200
H	-1.47036600	-3.02992000	0.00009400
O	0.00000000	1.19304200	0.00028200
C	-2.75490500	2.28364100	-0.00014800
H	-2.33853000	2.78793200	0.88029500
H	-2.33764200	2.78788900	-0.88019800
H	-3.83809900	2.43706700	-0.00067900
C	2.75490400	2.28364100	-0.00000300
H	2.33463700	2.78868600	-0.87813900
H	2.34154100	2.78713200	0.88234000
H	3.83809100	2.43707100	-0.00399500

Int1_O

C	3.68741500	1.23270500	-0.72560600
C	3.89932700	0.03496000	-0.02594200

C	2.84913000	-0.68130900	0.56653500
C	1.57782000	-0.12874100	0.40930400
C	1.33015400	1.07234100	-0.28873000
C	2.40786400	1.76720500	-0.85771600
H	4.53570300	1.74871200	-1.16658900
H	4.90987900	-0.35687200	0.06358800
H	2.24633800	2.69784600	-1.39456700
C	-0.69499100	0.09901600	0.42820100
C	-1.74432100	0.39887100	1.45576400
C	-2.45152300	1.56282400	1.28890500
C	-2.07733600	2.56850900	0.34564600
C	-0.83894300	2.48889300	-0.30709900
C	-0.07924100	1.33805200	-0.16032700
H	-3.29389000	1.76191700	1.94889700
H	-2.68423900	3.46409600	0.25439500
H	-0.43378500	3.35803600	-0.82004500
C	-1.99775700	-0.56999000	2.57362300
H	-2.24680800	-1.57568900	2.21289500
H	-1.09823100	-0.68181700	3.19284000
H	-2.81456500	-0.22246700	3.21423600
C	3.05605100	-1.96115100	1.33450600
H	2.69957400	-1.86827900	2.36771700
H	2.50080800	-2.79376800	0.88490100
H	4.11531800	-2.23427700	1.36279700
Si	-1.44206500	-1.03615200	-1.03304900
C	-2.91430300	-0.16899500	-1.83802000
H	-2.63256500	0.80524400	-2.24973100
H	-3.30343700	-0.78371900	-2.65973900
H	-3.72833000	-0.00660700	-1.12432700
C	-1.98632700	-2.70781400	-0.32607600
H	-2.19181000	-3.40514400	-1.14845400
H	-1.20369500	-3.15219400	0.29824900
H	-2.90010800	-2.63129500	0.27312500
C	-0.08894200	-1.32863700	-2.32288900
H	0.23999000	-0.39591000	-2.79186000
H	0.79286800	-1.81489100	-1.89270700
H	-0.47719300	-1.98262500	-3.11445300
O	0.44407800	-0.69057500	0.93138000

Int2_O

C	-3.26026300	1.11079100	1.46875900
C	-3.92464100	0.32291200	0.50785800
C	-3.24117700	-0.21438000	-0.56349000
C	-1.80155200	0.03323400	-0.69921500
C	-1.13090600	0.85634600	0.31990700
C	-1.88735800	1.37824900	1.36093400
H	-3.82003200	1.51766500	2.30657900
H	-4.99078800	0.13697000	0.61582400
H	-1.40172500	1.99383100	2.11348000
C	1.36372600	0.32283900	-0.03317400
C	2.62358700	0.85764000	-0.41727600
C	2.80461300	2.24294000	-0.53015900
C	1.76434700	3.13222700	-0.28657800
C	0.50867800	2.62921600	0.02546500
C	0.29012700	1.24276900	0.12647500
H	3.78188100	2.62446700	-0.81717200
H	1.92382700	4.20442000	-0.36527200
H	-0.33145100	3.30605100	0.15256100
C	3.80834400	-0.00993300	-0.79985200
H	3.96396000	-0.85893100	-0.13265100
H	3.67502800	-0.41638300	-1.81050600
H	4.73179400	0.57781600	-0.80628100
C	-3.90374000	-1.05524000	-1.61505300

H	-3.75840200	-0.62041800	-2.61054800
H	-3.45682600	-2.05581900	-1.65481100
H	-4.97646800	-1.15636000	-1.42548800
Si	1.23908200	-1.54016900	0.43381500
C	2.45403200	-1.86484200	1.86903900
H	2.43481700	-2.93274300	2.12271000
H	3.49670300	-1.59074900	1.68711800
H	2.12433300	-1.31535700	2.75986100
C	1.59360600	-2.66317200	-1.04924000
H	0.88846200	-2.43359700	-1.85590100
H	2.60814600	-2.56246200	-1.44624500
H	1.45066200	-3.71369200	-0.76569700
C	-0.41026900	-2.11354600	1.17965100
H	-1.19739700	-2.25853700	0.43630800
H	-0.22091900	-3.08798000	1.64972300
H	-0.79156000	-1.44696800	1.95983600
O	-1.17351500	-0.44964500	-1.67139200

Int3_O

C	1.79829900	-3.32925500	0.03742600
C	2.79447100	-2.43895000	-0.36049100
C	2.51205300	-1.08865200	-0.58773400
C	1.19184000	-0.63360100	-0.40228700
C	0.16247600	-1.52610700	-0.03327800
C	0.49371900	-2.87218900	0.19071900
H	2.03354900	-4.37662600	0.20439900
H	3.81259300	-2.79321700	-0.50500200
H	-0.29768800	-3.56707100	0.45698100
C	-1.88378600	-0.26335500	-0.81056600
C	-3.20344300	0.14348600	-0.80755700
C	-3.97894300	-0.34692800	0.26022400
C	-3.41266600	-1.17912900	1.22901900
C	-2.07025700	-1.54987800	1.15773100
C	-1.25156000	-1.09015800	0.10135100
H	-5.02983900	-0.07062700	0.32580800
H	-4.02545000	-1.54149300	2.05014200
H	-1.63891500	-2.18896500	1.92460400
C	-3.77765600	1.06031600	-1.86324500
H	-4.87164900	1.06947500	-1.82453300
H	-3.47133600	0.75077200	-2.86789500
H	-3.42953900	2.09148700	-1.72202600
C	3.59455900	-0.13581600	-1.03197600
H	3.86606800	0.57554300	-0.24145400
H	3.27290900	0.45676200	-1.89508200
H	4.50208300	-0.68276100	-1.30584300
Si	0.96714000	2.00594100	0.43274900
C	1.68863200	1.45701000	2.08647100
H	1.07952900	0.66901500	2.54388500
H	1.71842900	2.30172500	2.78595000
H	2.70934800	1.07103500	1.98745200
C	2.03662100	3.31924900	-0.39402200
H	1.64450600	3.56861700	-1.38716300
H	3.07340800	2.98918200	-0.52010200
H	2.04793900	4.24275700	0.19828800
C	-0.76898200	2.69306800	0.66987800
H	-1.23094700	2.93219000	-0.29486400
H	-0.73612800	3.61676600	1.26204400
H	-1.42382500	1.98227600	1.18353000
O	0.91284000	0.68816300	-0.63344600

Int4_O

C	-1.90792700	-3.28107300	-0.09176300
C	-2.89348700	-2.39096500	0.33096700

C	-2.60013500	-1.04569600	0.57399000
C	-1.27882800	-0.59630600	0.37997500
C	-0.25501000	-1.49053900	-0.00494700
C	-0.60180800	-2.82973000	-0.24946000
H	-2.15192300	-4.32390800	-0.27428500
H	-3.91231600	-2.74058500	0.48203100
H	0.18254500	-3.52488000	-0.53560000
C	1.82403500	-0.36801000	0.88101700
C	3.18226200	-0.04056600	0.79872800
C	3.89980100	-0.43786000	-0.33761900
C	3.26910400	-1.14338200	-1.36172200
C	1.91580100	-1.46549500	-1.26442200
C	1.17067000	-1.08031900	-0.13777300
H	4.95737700	-0.19592000	-0.41713500
H	3.83464900	-1.44657900	-2.23924500
H	1.42727700	-2.01154300	-2.06690300
C	3.85443100	0.73924200	1.90644100
H	3.78100300	1.82159800	1.73403400
H	3.39163100	0.53525600	2.87775500
H	4.91942500	0.49417300	1.98009200
C	-3.67402200	-0.09635100	1.04608300
H	-3.32713200	0.50835600	1.89057700
H	-3.97950200	0.60433100	0.25960600
H	-4.56561900	-0.64904700	1.35849300
Si	-0.84787600	2.05081600	-0.41052600
C	-0.50901000	1.48022900	-2.17305900
H	-1.29488100	0.80583000	-2.53325400
H	-0.47956900	2.34395500	-2.84926200
H	0.44713500	0.95338500	-2.25342100
C	0.55917300	3.08763100	0.28443800
H	0.36929200	3.35481300	1.33074100
H	1.50812100	2.54325900	0.24294000
H	0.67536900	4.02055900	-0.28086700
C	-2.44023200	3.06454500	-0.36500700
H	-2.28998100	4.02542100	-0.87398000
H	-3.27264400	2.55621100	-0.86447500
H	-2.74830100	3.28031500	0.66450600
H	1.25981400	-0.07664000	1.76196500
O	-0.99380100	0.72226000	0.63223000

3a-OH

C	2.63829900	-1.81693700	0.68308000
C	3.44156100	-0.71793900	0.38505400
C	2.88205300	0.48240300	-0.06078600
C	1.48423500	0.56289400	-0.20425400
C	0.64636300	-0.53255400	0.08991000
C	1.25774700	-1.71549800	0.53402200
H	3.08381500	-2.74220100	1.03664500
H	4.52103200	-0.78337300	0.50039800
H	0.62355900	-2.56127900	0.78385100
C	-1.59333500	0.60543000	0.39138700
C	-2.98727700	0.62916200	0.28255400
C	-3.63284700	-0.46125500	-0.31498600
C	-2.89604600	-1.54756700	-0.78470500
C	-1.50762200	-1.56027200	-0.66378100
C	-0.83276700	-0.48062100	-0.07094700
H	-4.71599900	-0.45524200	-0.41665400
H	-3.40444000	-2.38439800	-1.25709800
H	-0.93737100	-2.39944500	-1.05231300
C	-3.78114300	1.79587700	0.82579500
H	-3.19155200	2.71867300	0.81978400
H	-4.68959200	1.97055700	0.23884500
H	-4.09538500	1.61690000	1.86304800

C	3.74940900	1.67537000	-0.39375000
H	3.66220500	1.97454600	-1.44909500
H	3.50308200	2.55413100	0.21988000
H	4.80427200	1.44819000	-0.21676000
H	-1.08485200	1.44875700	0.84730300
O	0.89111100	1.71562300	-0.65396100
H	1.58055500	2.35824700	-0.87770100

TS1_O

C	-3.67729600	0.97199700	1.02464000
C	-3.88102300	-0.06362600	0.09824500
C	-2.84669100	-0.56312400	-0.70400300
C	-1.60433300	0.04099600	-0.51516200
C	-1.36157500	1.07783400	0.40682300
C	-2.42321900	1.55505000	1.18824800
H	-4.51531100	1.32190100	1.62106800
H	-4.87338200	-0.49603800	-0.00545100
H	-2.27117600	2.35759900	1.90454500
C	0.57871000	0.45741200	-0.66236400
C	1.75245800	0.76465700	-1.42175400
C	2.51911300	1.81597700	-0.94120700
C	2.10227600	2.63164300	0.13745500
C	0.84114600	2.46632500	0.71056900
C	0.03335300	1.42382800	0.25359900
H	3.46141800	2.04130600	-1.43590200
H	2.74445200	3.44282000	0.46779000
H	0.47213200	3.17326000	1.44910100
C	2.12796100	-0.05436100	-2.62432500
H	2.27989700	-1.11049100	-2.36497400
H	1.33169100	-0.03158900	-3.37863700
H	3.04748300	0.32158300	-3.08311500
C	-3.04403700	-1.66467900	-1.71299700
H	-2.78211000	-1.33081200	-2.72440500
H	-2.40717600	-2.53011100	-1.49221200
H	-4.08478100	-2.00210100	-1.72442800
Si	1.43547200	-1.35631100	0.91137500
C	2.97177400	-0.67428100	1.79114200
H	2.73629700	0.24063200	2.34461100
H	3.36875100	-1.40980900	2.50459000
H	3.76719300	-0.43411300	1.07768500
C	1.87603600	-2.95967900	-0.01609900
H	2.14229200	-3.75614900	0.69343300
H	1.03233800	-3.31792500	-0.61626300
H	2.73036500	-2.81840300	-0.68769700
C	0.06268400	-1.71150100	2.17508100
H	-0.25306000	-0.79910400	2.69153200
H	-0.82275300	-2.14368500	1.69668200
H	0.41551900	-2.42319900	2.93496800
O	-0.47258800	-0.29925200	-1.21994100

TS2_O

C	-3.58938900	1.21867500	0.83040600
C	-3.85442800	0.15185900	-0.05121000
C	-2.84924100	-0.50703900	-0.75175500
C	-1.51734500	-0.05605800	-0.55730000
C	-1.24089700	1.01729600	0.34036400
C	-2.28812900	1.65820300	1.02125100
H	-4.40980600	1.69071600	1.36311000
H	-4.88326700	-0.17464200	-0.18949800
H	-2.07502000	2.47583100	1.70536900
C	0.97983200	0.26877700	-0.25897700
C	2.13653500	0.66369800	-1.03811700
C	2.59054000	1.96713200	-0.92928200

C	1.92364900	2.93851000	-0.15046100
C	0.69322600	2.63907700	0.41941200
C	0.16356100	1.34932100	0.28011000
H	3.50181200	2.24717700	-1.45355200
H	2.33040500	3.94318600	-0.07997500
H	0.08677900	3.42312400	0.86488500
C	2.87478600	-0.33514000	-1.89405600
H	3.45068000	-1.05551600	-1.29872000
H	2.17536400	-0.91010700	-2.51046300
H	3.57885600	0.17582400	-2.55836000
C	-3.12298900	-1.63960600	-1.70585000
H	-2.81536800	-1.38327300	-2.72721000
H	-2.55807500	-2.53846900	-1.42915500
H	-4.18767200	-1.89306500	-1.72247400
Si	1.19504700	-1.33811500	0.83677500
C	2.77367100	-1.01736400	1.84099900
H	2.67325400	-0.11714700	2.45876400
H	2.97468500	-1.86084500	2.51355800
H	3.65513200	-0.88359600	1.20397300
C	1.38558000	-2.93210700	-0.16455500
H	1.37290800	-3.78819700	0.52251900
H	0.55488000	-3.04490900	-0.86677500
H	2.32076200	-2.97954400	-0.73036000
C	-0.22497400	-1.55128600	2.06519400
H	-0.39089300	-0.65520000	2.67129800
H	-1.17256400	-1.80862400	1.58326500
H	0.03781000	-2.37036600	2.74781000
O	-0.49440700	-0.59530400	-1.19498600

TS3_O

C	3.34514800	-1.94283300	0.40201000
C	3.77278300	-0.74329000	-0.18129100
C	2.86889500	0.23542100	-0.59391200
C	1.49341200	-0.02813900	-0.42300400
C	1.04084800	-1.24814700	0.12865100
C	1.98858300	-2.19614800	0.54993800
H	4.07507100	-2.67811700	0.72800500
H	4.83673900	-0.56187500	-0.31659200
H	1.66175500	-3.13335800	0.99077200
C	-1.26301700	-0.37160500	-0.19597700
C	-2.58388900	-0.55911100	-0.64259900
C	-3.12824300	-1.83513400	-0.46244900
C	-2.35928200	-2.88821000	0.04899800
C	-1.01254700	-2.70733000	0.32463800
C	-0.41091200	-1.44475200	0.12694400
H	-4.16692900	-2.00662900	-0.73613600
H	-2.80908400	-3.86914200	0.17681100
H	-0.40426900	-3.55512000	0.62379600
C	-3.40706800	0.52104300	-1.30319800
H	-4.47130100	0.26601400	-1.28573900
H	-3.28136900	1.49560100	-0.82748700
H	-3.10998300	0.63618900	-2.35364000
C	3.32102400	1.52688100	-1.22723600
H	2.85161700	1.67473800	-2.20661100
H	3.04850500	2.39595400	-0.61594200
H	4.40726200	1.53542900	-1.36049100
Si	-0.60414400	1.61446700	0.50337100
C	-2.09094200	1.53479400	1.75608300
H	-1.92695000	0.73465800	2.48692000
H	-2.10561200	2.49028000	2.29956400
H	-3.07603600	1.38310400	1.30814900
C	-0.97212900	3.09821100	-0.61726100
H	-0.05181600	3.66552700	-0.79601000

H	-1.34171500	2.78038600	-1.59801900
H	-1.71475600	3.77147500	-0.17473000
C	0.76935700	1.92369300	1.78199400
H	0.42761200	2.65762700	2.52125200
H	1.02026200	1.00784900	2.33051400
H	1.69202400	2.29541300	1.32535300
O	0.58310800	0.89492500	-0.80011400

TS4_O

C	3.07637800	-2.26445500	0.21778000
C	3.45129800	-1.07641300	-0.42864500
C	2.49100600	-0.09446400	-0.76450800
C	1.18857500	-0.41591300	-0.44350600
C	0.74417500	-1.64402300	0.11555000
C	1.74531500	-2.56456200	0.49275900
H	3.84583000	-2.98799300	0.47614200
H	4.48996100	-0.90779500	-0.69916400
H	1.47540200	-3.51242900	0.94976900
C	-1.14961000	-0.54384700	-0.66725500
C	-2.48528200	-0.17838300	-0.84137600
C	-3.40725800	-1.11610900	-0.37231600
C	-3.00451400	-2.26106300	0.37428500
C	-1.66833900	-2.52803600	0.62099400
C	-0.68343600	-1.66559200	0.09186400
H	-4.45593200	-0.99695300	-0.63718100
H	-3.76759200	-2.93311100	0.75722300
H	-1.37895100	-3.38882000	1.22020500
C	-2.91995000	1.04319900	-1.61736700
H	-3.94262700	0.91837300	-1.98711200
H	-2.26299800	1.21859900	-2.47688800
H	-2.91172700	1.95636300	-1.00675600
C	2.89140100	1.18528300	-1.45994500
H	3.19473300	1.97045200	-0.75482100
H	2.07383900	1.58276900	-2.06931400
H	3.74627300	1.00449900	-2.11955000
Si	-0.03360900	1.83123800	0.72346500
C	1.48483100	1.73481600	1.82638700
H	1.58719600	0.73929600	2.26942000
H	1.35239600	2.45453300	2.64576500
H	2.42160100	1.97567300	1.31894200
C	-0.11484600	3.42466800	-0.26827600
H	-0.94865500	3.41702600	-0.97784000
H	0.80789800	3.59081300	-0.83424600
H	-0.25541800	4.28238500	0.40182800
C	-1.55802400	1.53367500	1.77650100
H	-2.50041500	1.67258500	1.24266200
H	-1.53451800	2.24076000	2.61681700
H	-1.55776300	0.51934900	2.18766400
O	0.06270800	0.51670100	-0.57120700

TS5_O

C	1.58488800	-1.63845700	3.09616000
C	2.33591900	-2.16793100	2.04761400
C	2.22809900	-1.65954500	0.74909500
C	1.33290200	-0.59684700	0.51203500
C	0.54268300	-0.06816900	1.55327100
C	0.69751900	-0.59637200	2.84410100
H	1.68226700	-2.04388200	4.09940800
H	3.02392900	-2.98961600	2.23373900
H	0.09039900	-0.18854000	3.64781600
C	-1.51376300	0.94472100	0.46862000
C	-2.45411000	1.95021300	0.27030500
C	-2.27737200	3.13983500	0.99668300

C	-1.20677500	3.28404200	1.88167800
C	-0.29018800	2.24766900	2.05375000
C	-0.42904400	1.04310900	1.33382700
H	-2.98728600	3.95510600	0.86775200
H	-1.08720600	4.20940100	2.43922800
H	0.54619500	2.36346000	2.73973400
C	-3.61485700	1.78550900	-0.68588400
H	-3.26490000	1.60963300	-1.71024600
H	-4.24309600	0.93104500	-0.40891700
H	-4.24785900	2.67870600	-0.69704300
C	3.05672800	-2.22696300	-0.37736900
H	2.44357900	-2.43869600	-1.25969500
H	3.84074100	-1.52854800	-0.69829700
H	3.54972700	-3.15343200	-0.06676200
Si	1.94637400	1.22336700	-1.50577700
C	0.61231600	2.42780400	-2.05979200
H	0.09145100	2.87959400	-1.21011400
H	1.05123900	3.23432100	-2.66126700
H	-0.13704700	1.92181000	-2.67958800
C	2.85286000	0.57086900	-3.02557700
H	3.66154100	-0.11808400	-2.75845900
H	2.16520500	0.03426900	-3.69014600
H	3.29231700	1.39470400	-3.60194800
C	3.14093900	2.03893200	-0.29640000
H	3.66273000	2.87277900	-0.78233600
H	2.61129200	2.44046200	0.57459500
H	3.90076800	1.33770300	0.06731300
Si	-2.20542800	-2.00320000	-0.71576600
H	-1.85908300	-0.52877700	-0.16553500
C	-4.09176400	-2.17052900	-0.85440900
H	-4.51249900	-1.44703300	-1.56228600
H	-4.37182500	-3.17367800	-1.20178000
H	-4.57766600	-2.01095600	0.11552300
C	-1.53790400	-3.28113200	0.51114200
H	-0.45416300	-3.18642600	0.63707500
H	-1.99705200	-3.15636300	1.49866100
H	-1.75272600	-4.30269800	0.17074700
C	-1.39374800	-2.19772000	-2.41620000
H	-1.81923100	-1.49341700	-3.14103500
H	-0.31872600	-1.99787800	-2.34982000
H	-1.53201200	-3.21068200	-2.81572300
O	1.21547400	-0.11885400	-0.76811300

TS6_O

C	-0.15600100	3.96133900	-1.02754400
C	-1.44658100	3.56125900	-0.67717600
C	-1.69513600	2.28099600	-0.16770200
C	-0.60046900	1.42209600	-0.00408600
C	0.71012000	1.78345700	-0.34868100
C	0.90885800	3.08142400	-0.85542500
H	0.01785600	4.95598000	-1.42853900
H	-2.27707700	4.25587200	-0.78792100
H	1.91862100	3.39123300	-1.11409400
C	2.14380600	-0.25328400	-0.83959900
C	3.31336100	-1.00693100	-0.67207100
C	4.27504800	-0.55484800	0.23980400
C	4.07190800	0.62375600	0.95820000
C	2.90667200	1.36633900	0.77367500
C	1.91845400	0.93111000	-0.12527200
H	5.19044100	-1.12514700	0.38126200
H	4.82735200	0.96788200	1.66008500
H	2.75239800	2.28812900	1.32801500
C	3.52274300	-2.28710400	-1.44877300

H	3.10889400	-2.21557700	-2.46063600
H	4.58631700	-2.53284300	-1.53582000
H	3.03098200	-3.13710400	-0.95695600
C	-3.10055000	1.88208800	0.21991200
H	-3.48831800	1.08337100	-0.42199600
H	-3.14793000	1.51373700	1.25091000
H	-3.78071000	2.73559600	0.13609500
Si	-0.84911400	-0.83562800	1.81433600
C	-0.36744500	0.58642300	2.95864100
H	-1.09325300	1.40617900	2.94770300
H	-0.31199100	0.20557400	3.98797000
H	0.61207500	1.00357500	2.70592100
C	0.48405400	-2.16535600	1.94249000
H	0.23116500	-3.07735300	1.39276300
H	1.44396600	-1.79753400	1.56578800
H	0.62133900	-2.43868300	2.99810500
C	-2.51048800	-1.51247000	2.41726200
H	-2.47282400	-1.64700500	3.50751100
H	-3.33307200	-0.82228700	2.19970600
H	-2.76343400	-2.48003300	1.97254100
Si	-1.62876400	-1.51835800	-1.16332600
H	1.40251000	-0.58268800	-1.56094600
C	-1.45306300	-0.38136400	-2.67010500
H	-0.41934000	-0.07109800	-2.85616600
H	-1.80623500	-0.90931400	-3.56592900
H	-2.04765600	0.53255800	-2.56686300
C	-3.47765000	-1.95909400	-1.02151100
H	-3.64466500	-2.78838500	-0.32578000
H	-4.08704400	-1.11466100	-0.68140700
H	-3.86464600	-2.26548400	-2.00444800
C	-0.66674200	-3.12169500	-1.55556300
H	0.41633900	-2.95958400	-1.56474500
H	-0.87934200	-3.90535800	-0.81980800
H	-0.95162800	-3.50700900	-2.54647300
O	-0.97327500	-0.17944800	0.18389500

·$SiEt_3$

Si	0.00040300	0.00271400	-0.31495700
C	0.43328900	-1.76024900	0.29044500
H	1.44504600	-2.00458700	-0.05940500
H	0.49722900	-1.73113600	1.39036100
C	-1.73913500	0.50802500	0.30070900
H	-1.73412400	0.45355800	1.40141500
H	-2.45513500	-0.25565100	-0.03109300
C	1.31325200	1.25348400	0.29597300
H	1.01901100	2.25555300	-0.04336600
C	-0.54500100	-2.86515200	-0.14341700
H	-0.23606300	-3.84709000	0.23600200
H	-1.55874900	-2.67698200	0.22906900
H	-0.60649200	-2.93823300	-1.23558800
C	-2.22064100	1.89816600	-0.14831400
H	-3.22171100	2.12156000	0.24098000
H	-1.55066100	2.69170200	0.20284300
H	-2.26802800	1.97037700	-1.24115700
C	2.75783300	0.96223700	-0.14485500
H	2.84995300	0.96001700	-1.23731800
H	3.45530900	1.71511300	0.24293800
H	3.10158900	-0.01486700	0.21415900
H	1.25960300	1.28360500	1.39631200

TS1_S_Et

C	3.92312500	-1.04344000	1.24972600
C	4.27174000	0.03855500	0.43008200

C	3.37136600	0.57802900	-0.49472300
C	2.10134800	-0.01220700	-0.56362200
C	1.72370700	-1.10198300	0.25447100
C	2.65952600	-1.61687700	1.16768000
H	4.64892900	-1.43507900	1.95710900
H	5.26531700	0.47313300	0.50878200
H	2.39425000	-2.45496700	1.80642500
C	-0.34669500	-0.67817700	-0.90524600
C	-1.47560300	-1.20363500	-1.63586600
C	-2.03335300	-2.38398300	-1.17579800
C	-1.46115500	-3.12508200	-0.11699700
C	-0.24219800	-2.73331300	0.43030600
C	0.37566700	-1.56078800	-0.01446800
H	-2.92360000	-2.76822300	-1.66945400
H	-1.93426900	-4.04599500	0.21046900
H	0.25983600	-3.37057300	1.15403900
C	-2.03001900	-0.46751500	-2.82415500
H	-2.30649900	0.56520800	-2.57437700
H	-1.28727200	-0.40789600	-3.63162600
H	-2.91783500	-0.96936000	-3.22072100
C	3.74646500	1.73389100	-1.38735400
H	3.68678300	1.45586900	-2.44795200
H	3.07052600	2.58691900	-1.24366000
H	4.76690200	2.07376800	-1.18690500
S	0.81488200	0.48144500	-1.67619300
Si	-1.49604800	0.93538500	0.74766800
C	-2.57729200	-0.06687700	1.96793800
H	-2.00982300	-0.94673300	2.29566300
H	-2.69344000	0.56168900	2.86558400
C	-2.61363500	2.20934100	-0.14758400
H	-3.19093600	2.70800400	0.64867800
H	-3.35905700	1.67552200	-0.75163000
C	-0.15884600	1.89494700	1.72891200
H	0.64532600	2.18793100	1.04260200
C	-3.96577900	-0.49783800	1.46615800
H	-4.51742900	-1.04247400	2.24304100
H	-4.57808800	0.36458900	1.17765700
H	-3.88794900	-1.15620300	0.59547600
C	-1.90515400	3.27374600	-1.00150300
H	-2.62160600	3.98813100	-1.42652100
H	-1.18292900	3.84807100	-0.40984000
H	-1.35227800	2.82466900	-1.83377500
C	0.43528300	1.19570000	2.96291500
H	0.97038900	0.28108800	2.68972800
H	1.14948600	1.84821100	3.48087400
H	-0.34137500	0.92348000	3.68696100
H	-0.63778700	2.83771700	2.03987000

TS4_S_Et

C	0.87163600	4.02501200	0.16815700
C	-0.35958100	3.72589300	-0.41372400
C	-0.71386000	2.41407800	-0.76350900
C	0.20787800	1.39033400	-0.47778300
C	1.49454100	1.69249300	0.03094500
C	1.80513900	3.01451300	0.37000900
H	1.11598300	5.05245200	0.42379400
H	-1.06185300	4.52791700	-0.62833700
H	2.78921500	3.25230500	0.76330100
C	1.98002600	-0.58357700	-0.54589100
C	2.71295700	-1.76670900	-0.62282600
C	3.99253300	-1.74357100	-0.04811400
C	4.48681000	-0.59703200	0.58768400
C	3.71944500	0.56282200	0.66048100

C	2.43705300	0.57033800	0.08717000
H	4.61654100	-2.63371100	-0.10781900
H	5.47984500	-0.61534200	1.02871900
H	4.11485400	1.44576000	1.15682700
C	2.18311100	-2.99664600	-1.32296700
H	1.27725900	-3.37788900	-0.83520300
H	1.91746700	-2.77725300	-2.36379400
H	2.92529500	-3.80131600	-1.32387900
C	-2.03033100	2.18131500	-1.46599900
H	-1.95594500	1.37460500	-2.20193400
H	-2.83081000	1.91433600	-0.76755600
H	-2.34692400	3.09241300	-1.98465400
S	-0.08215100	-0.36219800	-0.83324300
Si	-2.01888600	-0.92925100	0.40039500
C	-2.08144200	-0.04406400	2.08858300
H	-2.56020400	-0.75623000	2.77908800
H	-1.05084900	0.06678200	2.45016600
C	-1.58343900	-2.76494000	0.67963100
H	-1.31285400	-3.21362800	-0.28696300
H	-2.51416300	-3.26795800	0.98358900
C	-3.71433600	-0.89157900	-0.48633200
H	-4.41975000	-1.41312400	0.18060500
H	-4.08146200	0.13865100	-0.55833700
C	-3.73701000	-1.55047200	-1.87628600
H	-3.42558900	-2.60061800	-1.83145400
H	-4.74212500	-1.52650600	-2.31481100
H	-3.06057100	-1.03937200	-2.57108100
C	-0.48114700	-3.05190000	1.71425700
H	-0.76013000	-2.68609200	2.70908100
H	-0.29030300	-4.12841000	1.80560600
H	0.46481200	-2.57051800	1.44314000
C	-2.80927400	1.30815600	2.16842000
H	-3.84374100	1.23432800	1.81288100
H	-2.84715600	1.67361100	3.20201100
H	-2.30229400	2.07270200	1.57192800

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