A Novel, General Method for the Construction of C–Si Bonds by an Earth-Abundant Metal Catalyst

Thesis by

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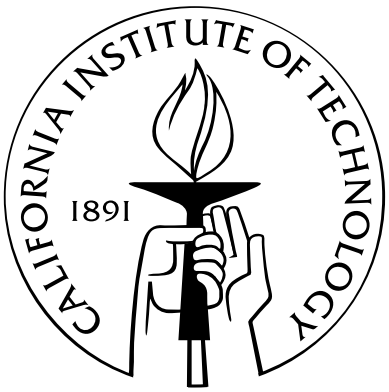

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Abstract

Compounds containing carbon–silicon (C–Si) bonds are of great interest in numerous fields, including but not limited to synthetic chemistry, organic electronics, pharmaceutical chemistry, nuclear medicine, and complex molecule synthesis. Compounds that contain C–Si bonds display useful physicochemical properties, and the C–Si bond can readily be converted into other desirable functional groups. Current methods for the creation of C–Si bonds are somewhat limited, requiring either stoichiometric pyrophoric organometallic species or highly expensive, fine-tuned precious-metal catalysts; both methods have significant limitations in terms of applicability and scope. A novel and general catalytic approach to C–Si bond construction avoiding such limitations has been developed. Herein is disclosed a new method of cross-dehydrogenative heteroaromatic C–H functionalization catalyzed by certain Earth-abundant alkali metal species that is able to access all hybridizations of carbon: sp^3, sp^2, and sp –hybridized carbons are all silylated in good yield under different conditions; prior to the discovery of this method, no known chemistry for C–Si bond construction was capable of accessing all hybridizations of carbon. Aromatic compounds, including heterocycles and oxygen-substituted arenes; benzylic sp^3-hybridized carbons; and terminal alkynes, are directly silylated by potassium and sodium bases using hydrosilanes as the Si source, furnishing the silylated product in a single step. The overall catalysis is highly efficient: it proceeds under mild conditions, in the absence of hydrogen acceptors or other additives, and liberates dihydrogen as the sole byproduct; no competing hydrosilylation is observed. The scope of the method is broad, enabling the direct silylation of aromatic and aliphatic substrates in the presence of a wide array of valuable functional groups. Substrate classes such as nitrogen heterocycles that are challenging to activate with known transition metal catalysis strategies are functionalized in good yields by this Earth-abundant metal catalysis. Facile scalability, low cost, and excellent scope make this an attractive method for either large scale synthesis of versatile building blocks or late-stage functionalization of advanced intermediates and lead compounds. Turn-over numbers (TONs) of nearly 100 are achieved, demonstrating the remarkably high, albeit unanticipated efficiency and activity of the catalysis. The derived products readily engage in versatile transformations enabling new synthetic strategies for molecular diversification, and are useful in their own right in pharmaceutical and materials science applications.

Contents

Acknowledgements **iii**

Abstract **iv**

I Review of C–H Silylation 1

1 Si-containing Organic Molecules 2

1.1 Relevance 2

1.2 Previous Synthetic Methods 2

2 Synthetic Methods for the Conversion of C–H Bonds to C–Si Bonds 4

2.1 Stoichiometric Organometallic Reactions 4

2.2 Recently Emerging Catalytic Methods 4

II Development of C–H Functionalization of Aromatic Heterocycles 6

3 C–H Silylation of Heterocycles 7

3.1 Importance of Heteroarylsilanes 7

3.2 Proposal Outline 7

4 The Genesis of a New Method 8

4.1 Origins 8

4.2 Development and Optimization 9

4.2.1 Reaction Optimization 9

4.2.2 Control Experiments and Trace Metal Analysis 9

4.2.3 Competition Experiments and Evaluation of Functional Group Compatibility 12

4.3 Evaluation of the Scope 13

4.4 Catalyst Variations 15

4.5 Interesting Applications 15

5 Mechanistic Investigations **18**

5.1 Competition Experiments with Thiophene, Furan and Pyrrole. 18

5.2 Reactions with Electron-Deficient Heteroarenes. 19

5.3 Support for a Radical Mechanism 19

5.4 Possible Mechanism 21

5.5 Interesting (and Confusing) Observations 22

6 Summary of Heterocyclic Silylation **24**

III Extension to Non-Heterocyclic Systems **25**

7 Direct Silylation of C(sp^3)–H Bonds **26**

7.1 Background 26

7.2 Discovery 26

7.3 Evaluation of the Scope 27

8 Silylation of C(sp^2)–H Bonds **29**

8.1 Background 29

8.2 Discovery 29

8.3 Evaluation of the Scope 30

8.4 Unanticipated Expansion of the Silane Scope 31

8.5 Non-aromatic C(sp^2)–H Systems 31

9 Silylation of C(*sp*)–H Bonds **32**

9.1 Background 32

9.1.1 Previous Approaches to Silylation of Terminal Acetylenes 32

9.1.2 Synthetic Utility 33

9.2 Discovery 33

9.3 Optimization 33

9.3.1 Initial Studies 34

9.3.2 Catalyst Screen 35

9.3.3 Influence of Reaction Time 36

9.3.4 Mechanistic Investigations 37

9.4 Silane Scope Investigation 39

9.5 Evaluation of the Substrate Scope 41

9.5.1 Extension using the "Default" Conditions 41

9.5.2 Discovery of a New Catalyst 44

9.5.3 Establishing a Complete Substrate Scope 45

9.6 Reevaluation of the Silane Scope 48

9.6.1 Versatile Silicon Partners 48

9.6.2 Different Catalysts for Different Silanes 49

9.7 Application to Pharmaceuticals 51

9.8 Summary of Alkyne Silylation 52

IV Conclusions **54**

10 Discussion and Conclusions **55**

Bibliography **56**

A Experimental **62**

A.1 General Information 62

A.2 Experimental Information for Heterocyclic, Benzylic, and O-directed Silylations 63

1. General procedure for KO*t*-Bu–catalyzed silylation and characterization data SI-4

2. Multi-gram scale syntheses of **2a**, **4h**, and **4n** SI-42

3. One-pot Si-directed *ipso*-substitution / Suzuki-Miyaura cross-coupling SI-44

4. Synthesis of a heteroarylsilanol and application in Denmark-Hiyama cross-coupling SI-45

5. Direct C7 lithiation-borylation by a Si-blocking group strategy SI-46

6. Synthesis of a sila-heterocycle by inter-/intramolecular double C–H silylation SI-48

7. C–H silylation of terthiophene and EDOT SI-48

8. Late stage silylation of active pharmaceutical ingredients (APIs) SI-50

9. Oxygen-directed C(sp^2)–H silylation of anisole derivatives SI-54

10. Direct C(sp^3)–H silylation reactions SI-56

A.3 GC-FID Spectra of the Robustness Screen SI-59

A.4 NMR Spectra of C(sp^2)–H and C(sp^3)–H Silylated Compounds SI-72

A.5 Experimental Information for Acetylenic Silylations SI-208

1. General procedure for MOH-catalyzed silylation and characterization data SI-208

2. Multi-gram scale synthesis of **4s** SI-233

3. Synthesis of *mono*- and *bis*-silylated diynes SI-234

4. Synthesis of symmetric and unsymmetric diethynylsilanes SI-237

5. Late-stage silylation of pharmaceuticals SI-239

A.6 NMR Spectra of C(*sp*)–H Silylated Compounds SI-241

List of Figures

Figure 1.1.1. Synthetic applications of arylsilanes 2

Scheme 1.2.1. Previous approaches to heteroarylsilanes 3

Scheme 2.1.1. Stoichiometric organometallic methods for creating C–Si bonds 4

Scheme 2.2.1. Catalytic methods for C–Si bond construction 5

Scheme 4.1.1. Investigations of silylated byproducts from reductive cleavage of aryl ethers 8

Chart 4.2.1. Reaction results with KO*t*-Bu purchased from different vendors 11

Figure 4.3.1. Scope of the KO*t*-Bu–catalyzed silylation of indoles 13

Figure 4.3.2. KO*t*-Bu–catalyzed silylation of nitrogen-, oxygen-, and sulfur-containing heteroarenes .. 14

Scheme 4.5.1. Applications of KO*t*-Bu–catalyzed heterocyclic silylation 16

Figure 4.5.2. Late-stage chemoselective modification of pharmaceuticals 17

Scheme 5.1.1. Competition experiments with thiophene, furan, and pyrrole 18

Figure 5.2.1. Examples of unreactive pyridine derivatives 19

Scheme 5.3.1. Control reactions with radical traps for heterocyclic silylation 19

Scheme 5.3.2. Control reactions under sila-Minisci reaction conditions 20

Scheme 5.3.3. Control experiments with cyclohexene oxide 21

Scheme 5.4.2. KO*t*-Bu–catalyzed C–H silylation of 1-methylindole: a potential mechanism 22

Scheme 7.1.1 Synthetic utility of benzylsilanes 26

Scheme 7.2.1 Discovery of benzylic silylation 27

Figure 7.3.1. Silylation of benzylic positions - unoptimized results 27

Scheme 7.3.2. Silylation of benzyl phenyl ether 27

Scheme 8.2.1 Discovery of oxygen-directed silylation 29

Figure 8.3.1 Silylation of non-heterocyclic sp^2 positions - unoptimized results 30

Scheme 8.3.2 Silylation of 4-methoxytoluene 30

Figure 8.4.1. Expansion of silane scope 31

Scheme 8.5.1. Silylation of 1-dodecene 31

Scheme 9.1.1. Zinc-catalyzed silylation of terminal acetylenes 32

Scheme 9.1.2. Synthesis of tetrasubstituted olefins from silylated alkynes 33

Scheme 9.2.1. Silylation product and byproduct of cyclohexylpropyne 33

Chart 9.3.1. Time profile of acetylene silylation reaction 37

Scheme 9.3.1. Addition of radical traps to alkyne silylation 38

Scheme 9.3.2. Addition of cation chelators to alkyne silylation 38

Figure 9.4.1. Initial silane scope for the acetylene silylation reaction 40

Scheme 9.4.2. Byproducts with different silanes 41

Figure 9.5.1. Initial substrate scope 42

Scheme 9.5.2. Silylation attempt of N-pentynylphthalimide 42

Scheme 9.5.3. Double propargylic silylation of 4-octyne 42

Scheme 9.5.4. Synthesis of diethynylsilanes 48

Scheme 9.7.1. Silylation of pargyline 51

Scheme 9.7.2. Silylation of ethynyl ticlopidine 51

Figure 9.7.3. NaOH silylation of mestranol 51

Scheme 9.7.4 Successful silylation of mestranol 52

Scheme 9.7.5 Dimethylsilylpyridine as a directing group 52

Scheme 11.1. C–Si as a functional handle 55

List of Tables

Table 4.2.1. Condition optimization of direct C–H silylation of indoles 10

Table 4.2.2. ICP-MS Trace metal analysis 11

Table 4.2.3. Examination of the compatibility of various functional groups and heterocycles 12

Table 5.3.1. Control experimental results with TEMPO 20

Table 9.3.1. Initial optimization studies of direct C–H silylation of alkynes 34

Table 9.3.2. Optimization of thecatalyst in acetylene silylation 35

Table 9.3.3. Reaction time profile 37

Table 9.3.4. ICP-MS Trace metal analysis 39

Table 9.4.1. Temperature and solvent effects with a selection of silanes 40

Table 9.5.1. Comparison of KOH and NaOH 44

Table 9.5.2. Silylation of aliphatic alkynes 45

Table 9.5.3. Silylation of substituted phenylacetylenes 46

Table 9.5.4. Silylation of heteroatom- and organometallic-containing acetylenes 46

Table 9.5.5. *Mono*- and *bis*-silylation of diynes 47

Table 9.3.1. Final silane scope 50

Part I

Review of C–H Silylation

Chapter 1

Si-containing Organic Molecules

1.1 Relevance

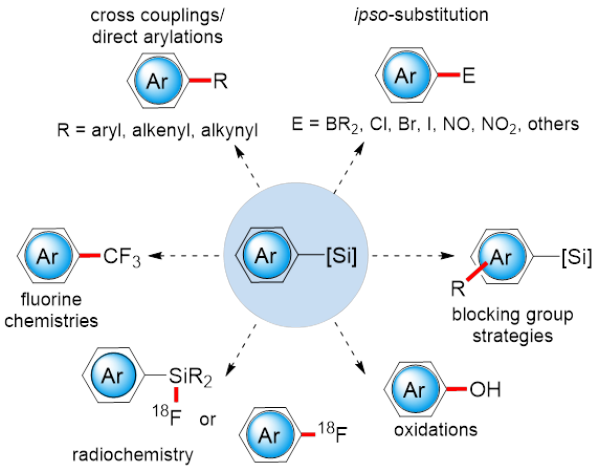
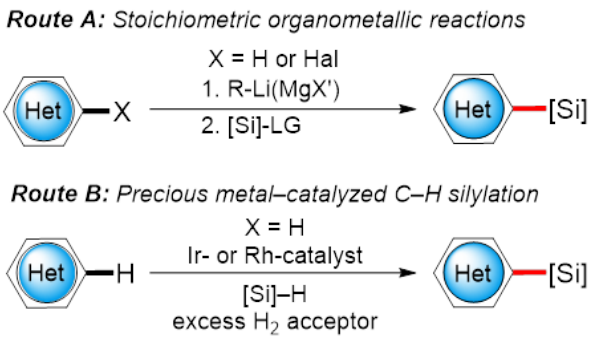


Figure 1.1.1 Synthetic applications of arylsilanes.

Enabled by their useful physico-chemical properties, molecules containing carbonsilicon (C–Si) bonds have found widespread application in various fields of study. For example, aryl- and heteroarylsilanes are of emerging interest in drug discovery,[1] nuclear medicine,[2] polymer chemistry and complex molecule synthesis,[3][4][5] and even organic electronics and photonics applications[6]. In addition, C–Si containing molecules are highly useful synthetic intermediates for the preparation of complex molecules[7] (e.g., crop protection agents, human medicines, natural products, cosmetics and fragrances) due to the high abundance and low cost of silicon[8] as well as the superior stability and lower toxicity of organosilicon compounds compared to the more commonly employed boron and tin reagents respectively (Figure 1.1.1).[8]

1.2 Previous Synthetic Methods

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. 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[7][8][9][10] as well as biologically-active carbon bioisosteres,[11] are generally prepared by stoichiometric reactions between organometallic species with silicon electrophiles (Scheme 1.2.1, Route A).



Scheme 1.2.1 Previous approaches to heteroarylsilanes.

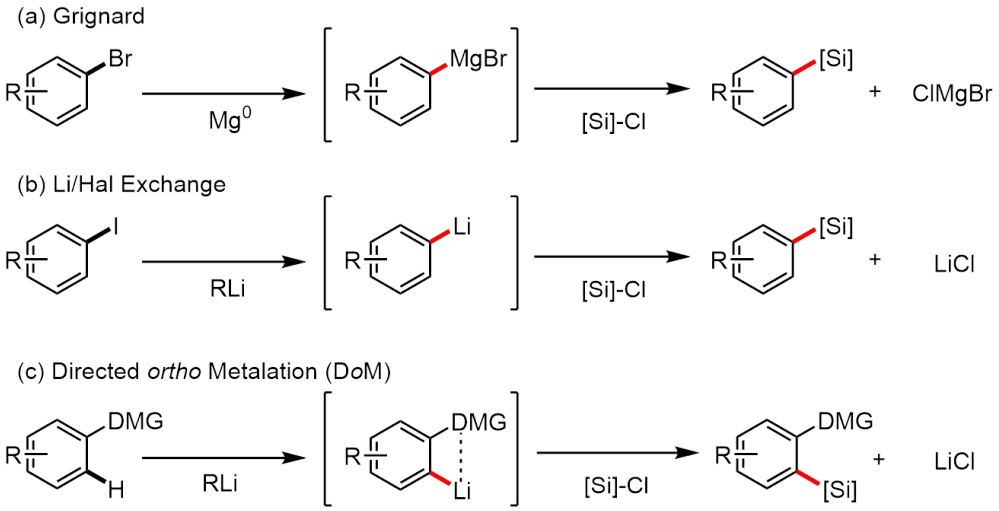
This classical method necessitates the use of pyrophoric materials in stoichiometric quantities, which is intolerant of many functional groups[7][9][12][13][14][15] and requires starting material prefunctionalization, or the use of directing groups.[12][15] In fact, due to these limitations, incorporation of a silicon functionality into a complex molecule, such as a lead pharmaceutical compound, normally requires *de novo* synthesis.[11] Careful temperature control and/or cryogenic conditions are often required to obtain reproducible yields. 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), specialized Si species, and/or directing groups. An ideal solution would be the direct catalytic conversion of C–H to C–Si bonds. Toward this end, Ir and Rh catalysts have shown some promise in certain applications (Scheme 1.2.1, Route B). However, unlike the powerful C–H borylation chemistry of (hetero)aromatics that is becoming a mainstay in both academic and industrial sciences,[10] 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.

Chapter 2

Synthetic Methods for the Conversion of C–H Bonds to C–Si Bonds

2.1 Stoichiometric Organometallic Reactions

Several different methods based on the use of stoichiometric organometallics are currently used for construction of C–Si bonds (Scheme 2.1.1). These methods are widely utilized because they are reliable, general, and highly selective. However, all these methods require prefunctionalization of the starting material and employ silyl chlorides; they use pyrophoric materials, which are difficult to use on large scale, are sensitive to and destructive of many functional groups, and produce stoichiometric amounts of waste.

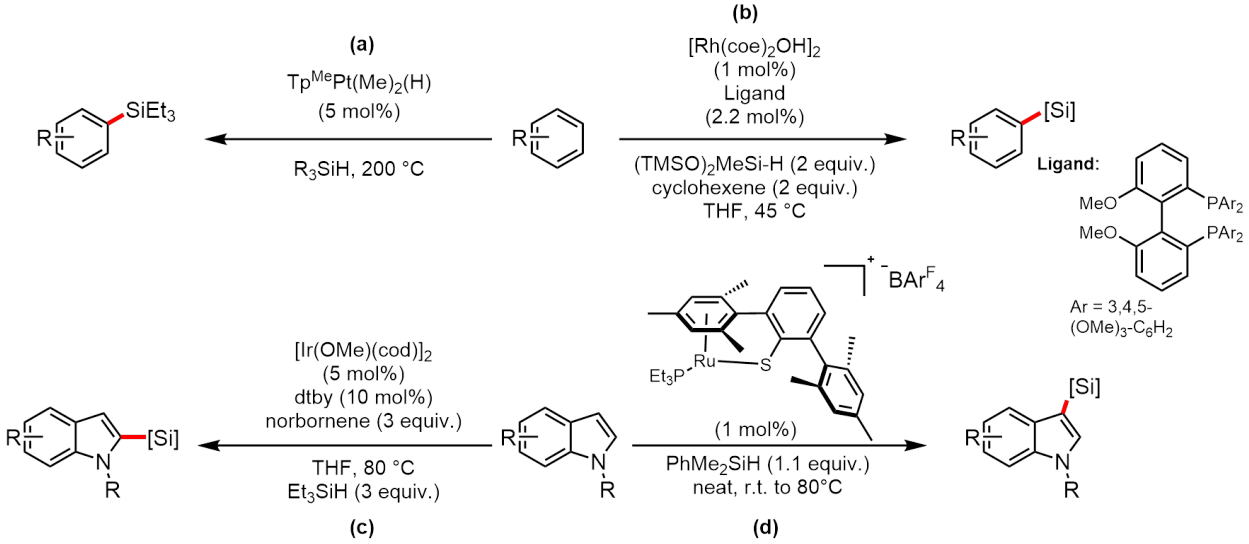


Scheme 2.1.1. Stoichiometric organometallic methods for creating C–Si bonds.

2.2 Recently Emerging Catalytic Methods

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) (Scheme 2.2.1a), or most recently Ir,[16][17] or Rh (Scheme 2.2.1b) with the use of excess sacrificial hydrogen acceptors and an expensive biphenylphosphine ligand, though under milder conditions.[18][19] The direct silylation of aromatic heterocycles is more challenging, but has been investigated by employing high loadings of an iridium catalyst for the direct C2-silylation of indoles and other electron rich heteroarenes (Figure 2.2.1d).[17]



Scheme 2.2.1. Catalytic methods for C–Si bond construction.

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. 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 (Scheme 2.2.1c), however, the problems of harsh conditions, H_2O and O_2 intolerance, unproven scalability, use of sacrificial additives, and poor availability and high cost of catalyst remain prevalent in this report, which limits the method's general accessibility.[16] Clearly, the direct C–H silylation of aromatics and especially heteroaromatics represents an attractive and unsolved problem in organic synthesis.

Part II

Development of C–H Functionalization of Aromatic Heterocycles

Chapter 3

C–H Silylation of Heterocycles

3.1 Importance of Heteroarylsilanes

Heteroarylsilanes are important motifs in medicinal chemistry and drug discovery,[1][2] advanced materials and polymer synthesis,[6][20] and various biomedical applications.[2][21] In addition, they are emerging as one of the most versatile heteroaryl metal species for complex molecule synthesis owing to the high natural abundance and low toxicity of silicon.[3][4][5]

The results described in this part (Part II) are published in *Nature*.[22]

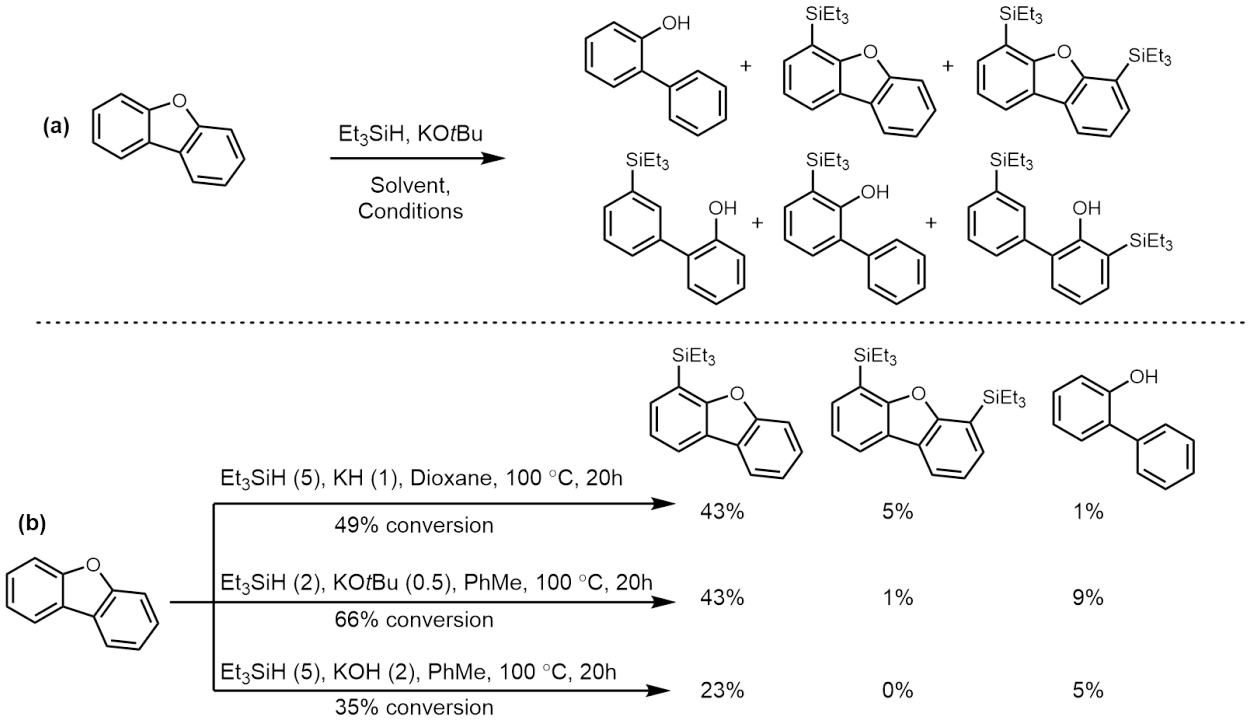
3.2 Proposal Outline

Due to the aforementioned limitations of current methods for the construction of C–Si bonds, the development of a general catalytic method for heteroaromatic C–Si bond formation remains a considerable challenge in the broader field of C–H functionalization. The goals of this project, which began shortly before January 2013 when I joined this project, were to develop this general method and apply it to the silylation of heterocycles. An eventual goal would be to expand this method to other aromatic and non-aromatic scaffolds with the aim of developing the first general catalytic procedure for C–Si bond construction.

Chapter 4

The Genesis of a New Method

4.1 Origins



Scheme 4.1.1. Investigation of silylated byproducts from reductive cleavage of aryl ethers.

A recent report, written by researchers in the Grubbs group shortly before I joined the lab, described the reductive cleavage of C–O bonds in aryl ethers using stoichiometric quantities of alkali metal alkoxides to activate hydrosilanes at elevated temperatures.[23] When dibenzofuran was used as the substrate for reductive cleavage, a small amount of byproducts displaying *ortho*-C–H silylation was observed (Scheme 4.1.1a). This led us to consider whether the unanticipated silylated heterocycle could be pointing to a more general reaction manifold, and if this reaction could be optimized to favor the silylation product (Scheme 4.1.1b).

4.2 Development and Optimization

We chose to test this unusual C–H silylation reaction on the indole scaffold, using 1-methylindole as a model substrate, due to the general utility of indole frameworks in medicinally relevant substances.NIH4h An extensive optimization exercise was conducted, described in this section.

4.2.1 Reaction Optimization

An extensive optimization exercise eventually revealed that KO*t*-Bu could be employed in sub-stoichiometric quantities and proved to be the ideal catalyst for the process furnishing synthetically useful C2-silylated indole in good yield under mild conditions with > 20:1 regioselectivity (Table 4.2.1).

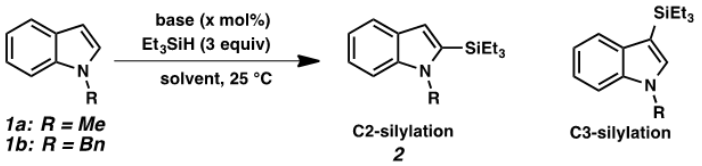
Procedure for reaction condition optimization: In a nitrogen-filled glovebox, base and *N*-Methylindole (0.2 mmol, 1 equiv) were added to a 2 dram scintillation vial equipped with a magnetic stirring bar. Next, Et_3SiH (97 μL, 0.6 mmol, 3 equiv, filtered through a short pad of activated alumina before 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. The vial was then 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 ^{1}H NMR or GC analysis of the crude mixture using an internal standard.

The results from Table 4.2.1 reveal that good catalysts for the CH 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 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 Cs2CO3 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). Headspace GC-TCD analysis of successful silylation reactions indicated the formation of H_2.

4.2.2 Control Experiments and Trace Metal Analysis

Careful experiments were conducted in order to rule out catalysis by adventitious transition metal impurities in the reaction mixture [see below (1) – (3)].

Table 4.2.1. Condition Optimization of Direct C–H Silylation of Indoles.



entry[a]	R	base	solvent	base loading	*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
24[c,e]	Bn	KOTMS	THF	20	72	>20:1	79

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

(1) Control reactions with commercially available KO*t*-Bu, re-sublimed KO*t*-Bu, and freshly-prepared KO*t*-Bu. Three reactions were performed in parallel (THF, 45 C, 1-methylindole, 20 mol% KOt-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.

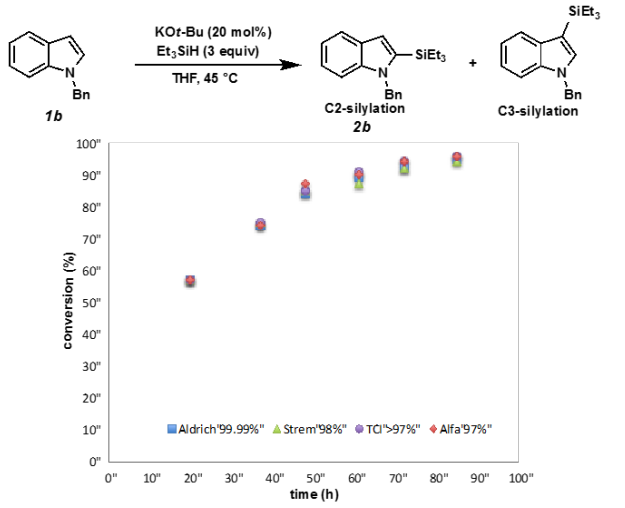


Chart 4.2.1 Reaction results with KO*t*-Bu purchased from different vendors.

(2) Control reaction with KO*t*-Bu of different grade purchased from different vendors. Four reactions were 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 (Scheme 4.2.1).

(3) ICP-MS trace metal analysis of all the reaction components. To provide further support against involvement of adventitious trace metal species in the C–H activation catalysis, inductively coupled plasma mass spectrometry was performed on samples of KO*t*-Bu from different vendors, 1-benzylindole starting material, THF, Et_3SiH and a standard reaction mixture that was run under optimal conditions in the glove box ("Rxn Mixture in Table 4.2.2). 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). Microgram per liter (ppb) quantities of metal contaminants are given in Table 4.2.2.

Table 4.2.2. ICP-MS Trace Metal Analysis.

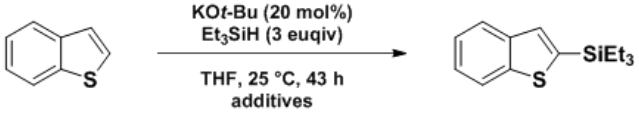
ICPMS Trace Metal Analysis – Agilent 7900 (quantities in ppb)								
Element	**KO*t*-Bu Strem (98%)**	**KO*t*-Bu TCI (>97%)**	**KO*t*-Bu Alpha (97%)**	**KO*t*-Bu Aldrich (99.99%)**	**THF**	**$HSiEt_3$**	**1-Bn-indole**	**Rxn Mixture**
Ti	0.360	0.051	0.138	0.464	LOD	2.073	9.408	31.082
Mn	1.343	1.168	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

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 ° 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. LOD indicates that the analyte concentration is below the instrument's Lowest Limit of Detection. Values in ppb (microgram per liter).

4.2.3 Competition Experiments and Evaluation of Functional Group Compatibility

Table 4.2.3. Examination of the compatibility of various functional groups and heterocycles.[a]

√ > 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	O Ph Ph	0 ×	91 √
4	C_3H_7 C_3H_7	83 √	99 √	17	$PhCO_2Me$	0 ×	84 √
5	PhF	95 √	N.D.	18	OMe Ph 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	OBn N	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 √

[a] The reaction was performed with 0.5 mmol of benzothiophene and 0.5 mmol of additive under the general procedure. 0.5 mmol of tridecane was added as an internal standard at the start of the reaction. Yield of product, remaining amounts of the benzothiophene and additive were determined by GC-FID analyses. [b] Control reaction without the addition of additive. [c] Not determined (overlapped with solvent peak due to the low boiling point). [d] Triethyl silyl protected morpholine was formed and confirmed by GCMS analysis. [e] BnOTES was formed. [f] Acetal partially hydrolyzed to PhCHO.

To further probe the functional group tolerance of the method, a comprehensive robustness evaluation was performed (Table 4.2.3).[24] 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.[25]

4.3 Evaluation of the Scope

A variety of indoles with Me, Et, Bn, Ph and the readily cleavable MOM and SEM groups on nitrogen leads to regioselective C2 silylation in moderate to good yields (Figure 4.3.1, **2a**–**2f**). 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 **2g**–**2n** in 48–83% yield. Several hydrosilanes were examined and the silylation products (**2o**–**2x**) were obtained in good yield.

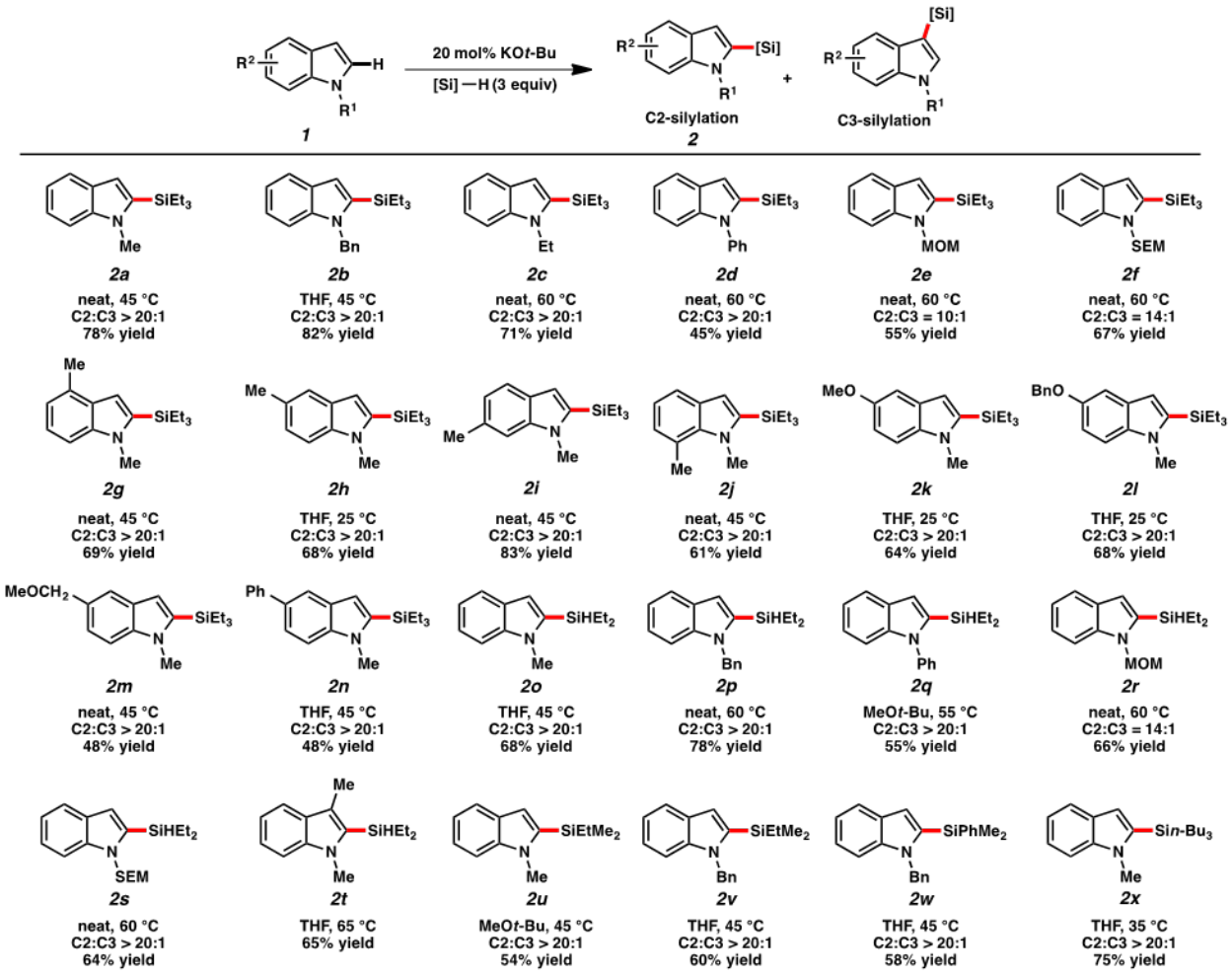


Figure 4.3.1. Scope of the KO*t*-Bu–catalyzed silylation of indoles. For the reactions of **2g** and **2i**, silylation on the benzylic methyl group was observed with THF as solvent; solvent-free conditions often led to improved regioselectivity and yield. For the reaction of **2k**, silylation at C6 was observed as a byproduct in THF. The reactions of 1,3-dimethyl indole with Et_3SiH and $PhMe_2SiH$ were sluggish probably due to steric congestion at C2. For the reaction of **2o**, bisindolyldiethylsilane was isolated as a byproduct. See Appendix (Experimental Data) for details. [Si]–H = Et_3SiH, Et_2SiH_2, $EtMe_2SiH$, $PhMe_2SiH$, and n-Bu_3SiH. MOM, methoxylmethyl; SEM, 2-[(trimethylsilyl)ethoxy]methyl.

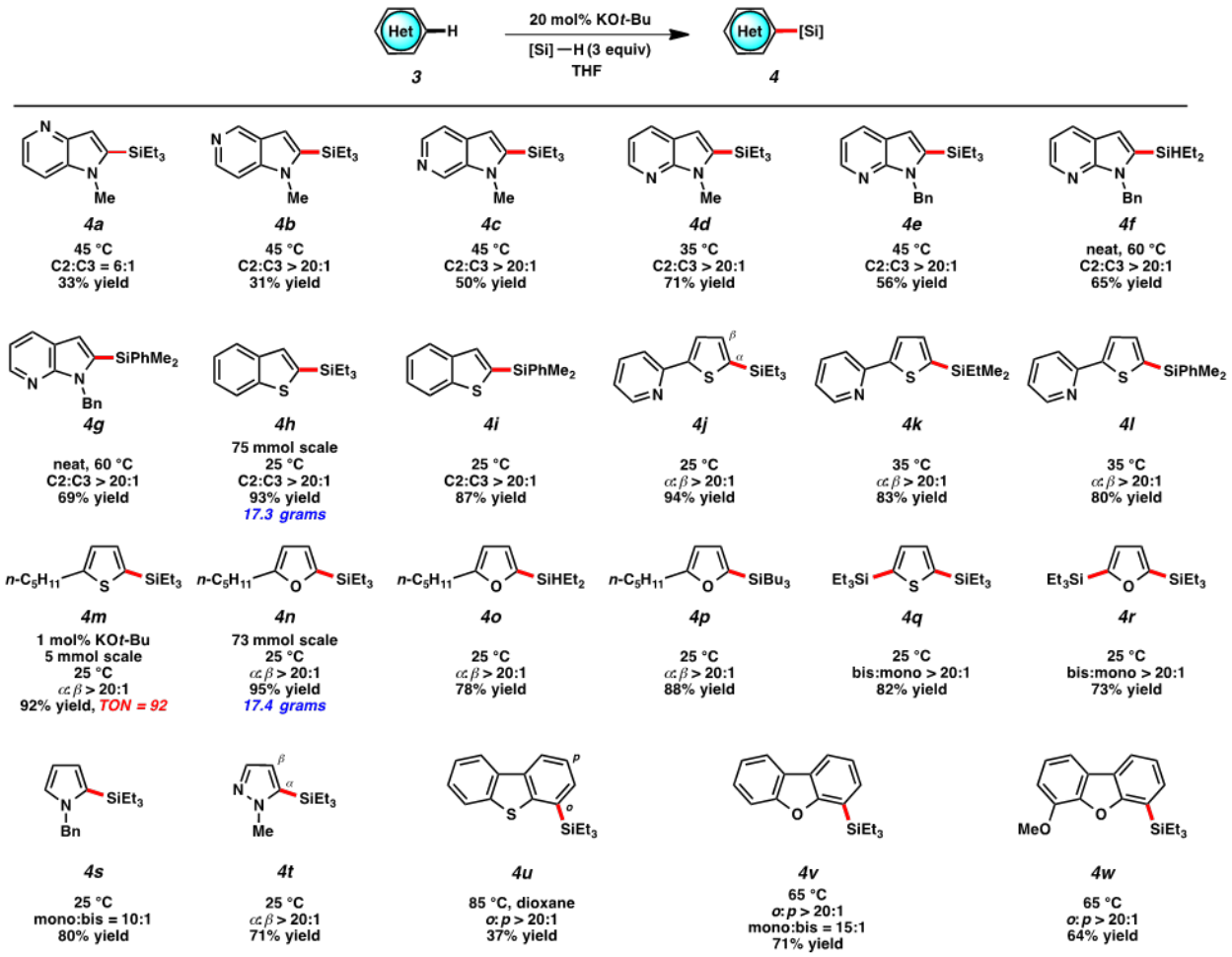


Figure 4.3.2. KO*t*-Bu–catalyzed silylation of nitrogen-, oxygen-, and sulfur-containing heteroarenes. Multi-gram scale syntheses were presented for **4h** and **4n**. Catalyst loadings can be reduced to 1 mol% with a TON of 92 (**4m**). For **4j**, with 3.5 mol% KO*t*-Bu, TON = 23; for **4n**, with 1.5 mol% KO*t*-Bu, TON = 61. Bisfuranyldiethylsilane was isolated as a byproduct in the reaction of **4o**. Unsubstituted thiophene and furan favored 2,5-bis-silyation (**4q** and **4r**). See Appendix (Experimental Data) for details. [Si]–H = Et_3SiH, Et_2SiH_2, $EtMe_2SiH$, $PhMe_2SiH$, and n-Bu_3SiH. TON = turnover number.

A diverse range of N-, O-, and S-containing heteroaromatics, including pyridine-containing scaffolds (Figure 4.3.2, **4a**–**4g**, **4j**–**4l**),[26] undergo the reaction with high regioselectivity. Reactions at decreased catalyst loadings (1–3.5 mol%, **4j**, **4m** and **4n**) and on large scale (**4h** and **4n**) demonstrate the robustness and preparative scale utility of the process.

This method is able to access a wide variety of privileged nitrogen-containing heteroaromatics such as indoles, pyrazole, and even the challenging and pharmaceutically valuable azaindoles, of which every single azaindole isomer was successfully silylated. A diverse range of oxygen-, and sulfur-containing heteroaromatics such as benzothiophene, thiophene, furan, and dibenzofuran are regioselectively silylated, demonstrating the useful substrate scope of the chemistry. In general, the reaction proved to be selective for electron neutral and electron-rich heterocycles; those possessing electron withdrawing groups are unreactive (and starting material is quantitatively recovered). Unprecedented C–H silylations of pyridine-containing heteroaromatics such as pyridylthiophene, which would be expected to deactivate precious metal catalysts, highlight a benefit of catalysis by an alkali-metal species over precious-metal complexes. Silylation proceeds with excellent regioselectivity in these systems, yielding more than 30 new silylated heterocyclic building blocks.

4.4 Catalyst Variations

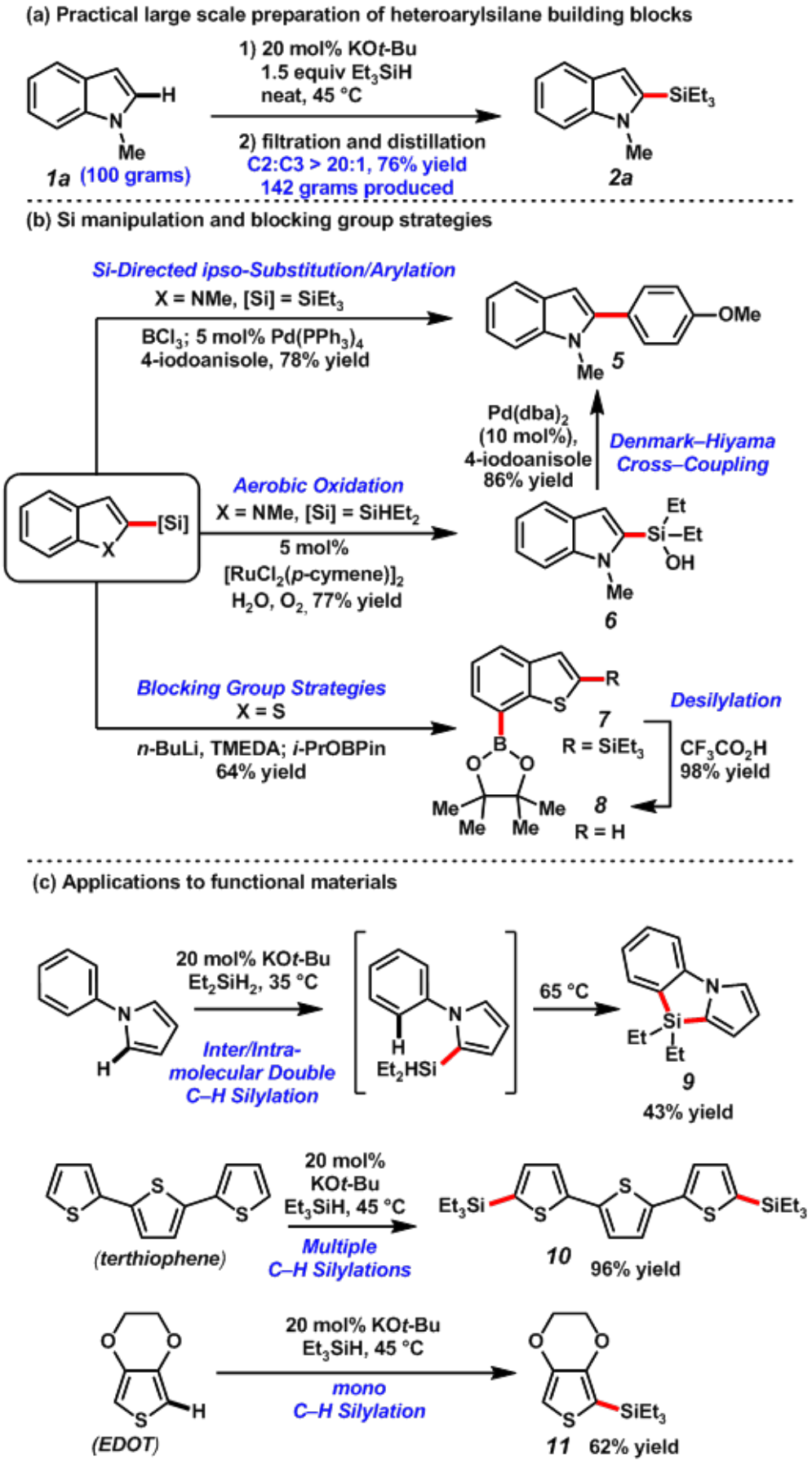
During the optimization of the heterocyclic substrates, numerous bases were tested as catalysts for the silylation of heterocycles; however, KOH was not part of the catalytic screen (and had only showed poor performance in the "stoichiometric" base screen). Returning to the catalyst screen, we found that, in the case of *N*-methylindole (the heterocycles test substrate), KOH was remarkably effective in catalyzing its silylation; although slower, KOH had greatly improved selectivity compared to KO*t*-Bu in the silylation of *N*-methylindole. With KO*t*-Bu, we observed a > 20:1 C2:C3 silylation preference; however, KOH gave a selectivity of approximately 103:1 C2:C3–silylated product. Using KOH, monosilylation of both the unsubstituted thiophene and furan has been achieved, when before, KO*t*-Bu only produced the *bis*-silylated product. Further tests are underway for the implementation of KOH as a catalyst in the context of numerous other heterocyclic systems.

4.5 Interesting Applications

The reaction scaled without loss of catalyst activity to greater than 100 grams of starting material under procedurally convenient conditions (Scheme 4.5.1a).[27] Filtration and distillation were sufficient to isolate the product, providing an industrially attractive chromatography-free protocol for large scale preparations.

Heteroarylsilane derivatives are known to undergo a variety of powerful synthetic transformations; a number of representative examples are demonstrated (Scheme 4.5.1b). For example, C2 Si-directed Suzuki–Miyaura cross-coupling by the method of Snieckus,[28] or Denmark–Hiyama cross-coupling[4] via heteroarylsilanol **6**,[25] both produce the 2-arylated indole **5**. An unusual direct C7 functionalization of benzothiophene to give boronate esters **7** and **8** was achieved by employing a blocking group strategy from silylated precursor **4h**.[29]

Organosilicon has been extensively investigated in the development of advanced materials due to silicon's unique physical and chemical properties.[6][30] To demonstrate the utility of our method for possible materials science applications, we prepared sila-heterocycle **9** in one step directly from the commercially available unfunctionalized heteroarene by an unprecedented inter-/intramolecular double C–H silylation (Scheme 4.5.1c).[20][31][32] A high-yielding bis-silylation of thiophene oligomer **10** furnishes the starting material for a known entirely transition metal-free catalytic route to block copolymers.[30] Finally, the mono-selective silylation of the EDOT monomer provides a potential strategy for the modification of polythiophene-derived materials (Scheme 4.5.1c, **11**).



Scheme 4.5.1. **a**, Preparation of 142 grams of C2-silylated indole building block **2a**. **b**, Application of heteroarosilanes in cross-coupling and a formal C–H borylation at C7 of benzothiophene. **c**, Synthesis of precursors to advanced materials and polymers. [Si] = Et_3Si, EDOT = 3,4-ethylenedioxythiophene.

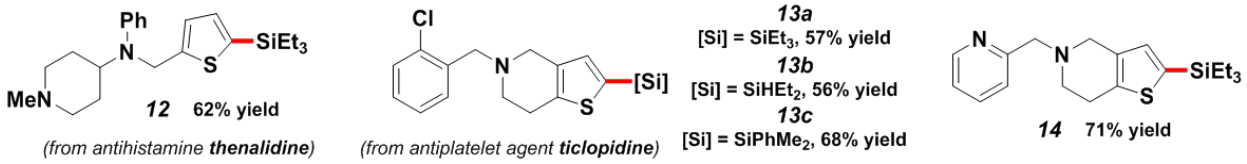


Figure 4.5.2. Late-stage chemoselective modification of pharmaceuticals.

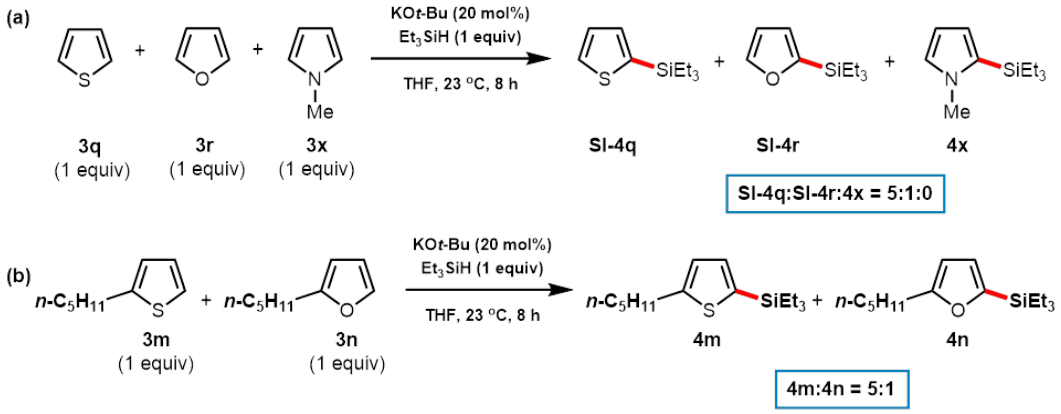
Sila-drug analogues have garnered much attention from medicinal chemists as they can offer improved stability, solubility and pharmacokinetic properties compared to the parent all-carbon compounds.[33] Moreover, the installed organosilicon moiety can serve as a functional group handle for subsequent elaboration, facilitating library synthesis and SAR studies.[34] 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 be a new and potentially powerful tool in drug discovery.[33][34][35][36] To evaluate our method for such late stage C–H functionalization applications, we subjected the antihistamine thenalidine and the antiplatelet drug ticlopidine to our catalytic silylation conditions. The reactions proceeded smoothly in the case of both active pharmaceutical ingredients yielding the Si-containing target compounds **12** and **13a–c** in 56–68% yield with excellent chemo- and regioselectivity (Figure 4.5.2).

The piperidines, aniline, benzylic C–H bonds, and aryl chloride moieties were all tolerated without any observed side reactions. Other methods of C–H silylation (either stoichiometric or catalytic) would not be able to access these molecules in the C2 position; lithiation would be directed by the aryl chloride moiety in the case of silylation of ticlopidine, and the basic nitrogen functionalities would deactivate most precious metal catalysts. Silylation of aza analogue **14** also proceeded well, demonstrating compatibility of our method with pyridine-containing complex molecules of potential pharmaceutical significance.

Chapter 5

Mechanistic Investigations

5.1 Competition Experiments with Thiophene, Furan and Pyrrole.



Scheme 5.1.1. Procedures for competition experiments: For reaction (a): In a nitrogen-filled glove box, KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), thiophene **3q** (42.1 mg, 0.5 mmol, 1 equiv), furan **3r** (34.0 mg, 0.5 mmol, 1 equiv) and 1-methylpyrrole **3x** (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 L, 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 ^{1}H NMR revealed that the ratio of **SI-4q:SI-4r:4x** was 5:1:0. For reaction (b): In a nitrogen-filled glove box, KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2-pentylthiophene **3m** (77.0 mg, 0.5 mmol, 1 equiv), and 2-pentylfuran **3n** (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 ^{1}H NMR revealed that the ratio of **4m:4n** was 5:1.

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 1). Reactions were run to partial consumption of Et_3SiH and relative quantities of silylated heteroarene were determined by ^{1}H NMR analysis. An internal competition experiment demonstrated that for 5-membered heteroarenes, the relative rate of reactivity

trends as: thiophene **3q** > furan **3r** > 1-methylpyrrole **3x** (Scheme 5.1.1). This trend is corroborated in the competition between substituted thiophene **3m** and furan **3n**.

An elementary silyl radical generation-substitution mechanism appears to be unlikely due to poor reactivity with electron-deficient heteroarenes.[22][37][38][39] Moreover, the rate of silylation trends as thiophene > furan > 1-methylpyrrole as observed in an internal (Figure Scheme 5.1.1), which provides complementary reactivity to known heteroaromatic functionalization manifolds such as electrophilic substitution and Minisci-type reactions. These observations point to an underlying mechanism that is distinct from known aromatic and heteroaromatic C–H functionalization reactions.

5.2 Reactions with Electron-Deficient Heteroarenes.

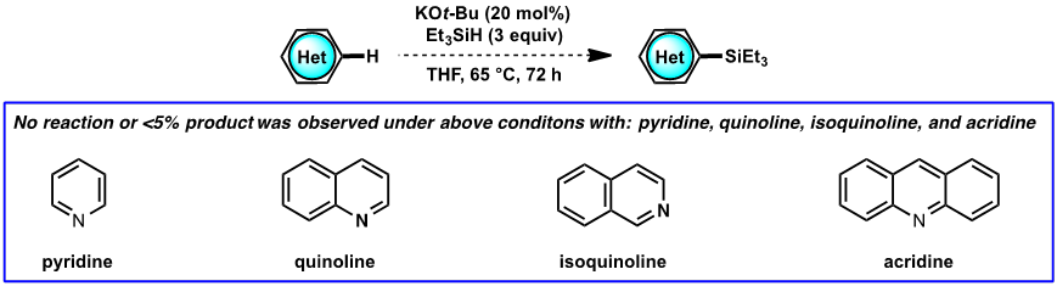
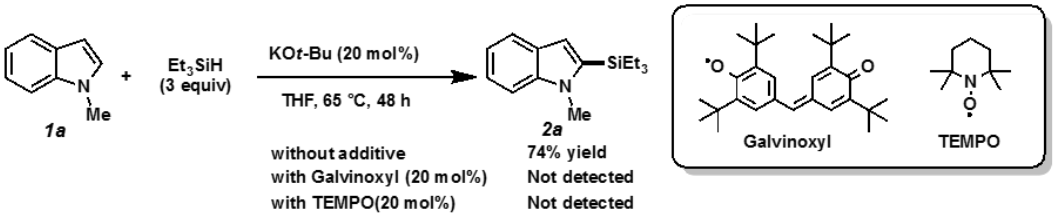


Figure 5.2.1. Examples of unreactive pyridine derivatives.

Pyridine derivatives would be expected to react readily if a conventional silyl radical addition process was operational. However, the above substrates were unreactive under the KO*t*-Bucatalyzed C–H silylation conditions. 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.

5.3 Support for a Radical Mechanism

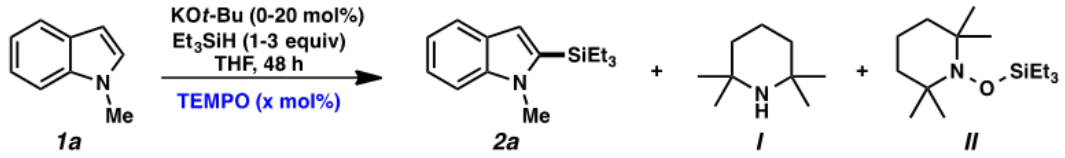
A number of experiments were conducted to gain insight into the reaction mechanism. As a first investigation, we decided to probe whether the silylation reaction was polar or radical in nature. We began by performing our reaction in the presence of the radical traps TEMPO and galvinoxyl. Both additives thwarted the C–H silylation (Scheme 5.3.1).



Scheme 5.3.1. Control reactions with radical traps.

Subsequently, we conducted three control experiments in an attempt to probe the role of TEMPO (Table 5.3.1). A trace amount of triethylsilyl-protected product II was observed at 23° C with 1 equivalent of TEMPO (entry 5), presumably arising from the radical combination of a silyl radical and TEMPO itself. Product II 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 protected compound II is not observed in the absence of KO*t*-Bu, indicating that the catalyst is critical to generate the silyl radical (entry 2).

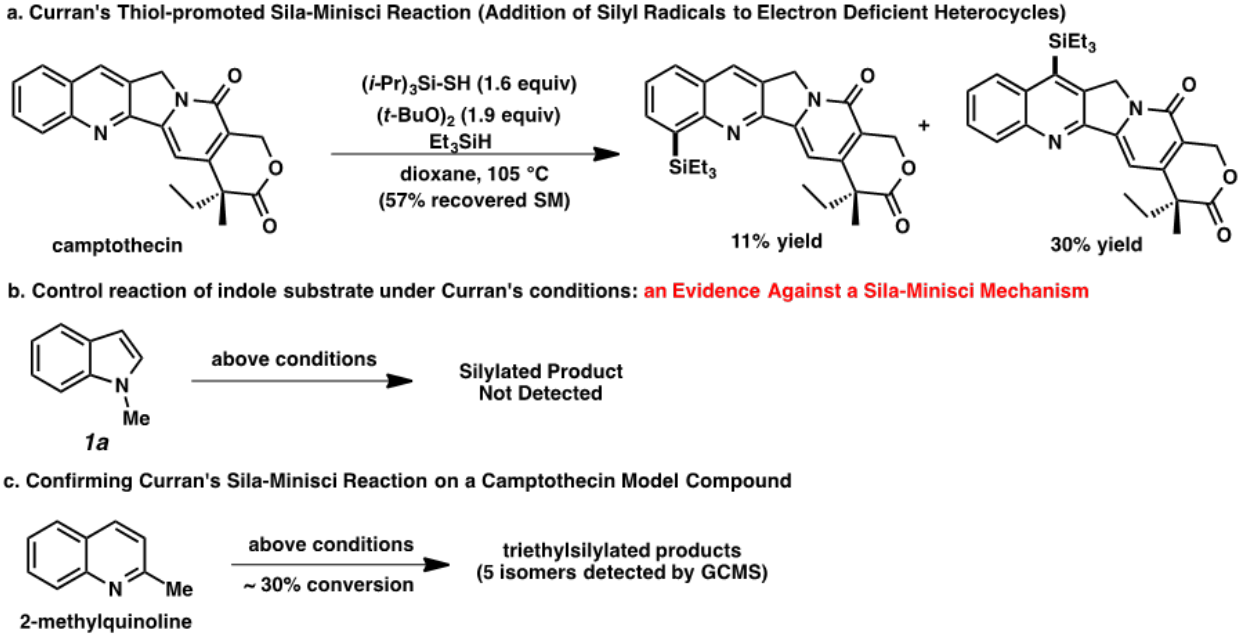
Table 5.3.1. Control experimental results with TEMPO.



entry	*1a*	TEMPO (mol%)	KO*t*-Bu (mol%)	$HSiEt_3$ (equiv)	Temp (°C)	*2a* (%)	*I*	*II*
1	–	100	–	1	23	ND[a]	ND[a]	ND[a]
2	–	100	–	1	65	ND[a]	ND[a]	ND[a]
3	1	20	20	3	23	ND[a]	ND[a]	ND[a]
4	1	20	20	3	65	ND[a]	ND[a]	ND[a]
5	–	100	20	1	23	ND[a]	trace[b]	trace[b]
6	–	100	20	1	65	ND[a]	minor[b]	major[b]

[a] Not detected; [b] Determined by GCMS analysis.

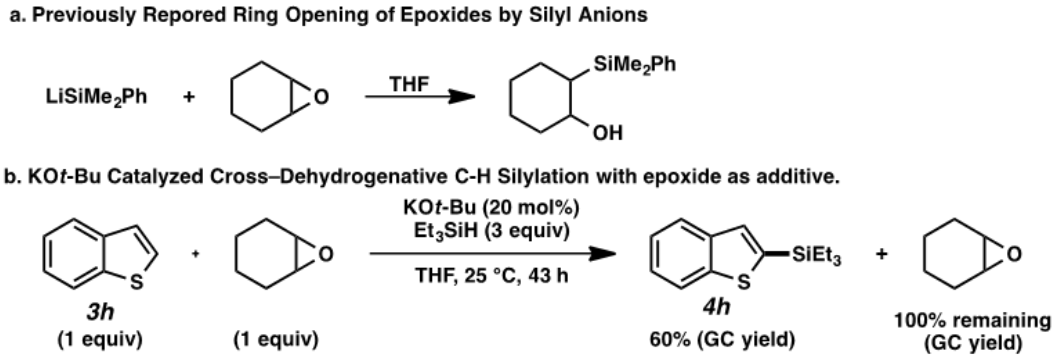
Although we are unsure as to the mechanism of formation of the putative silyl radical, we considered that if such radical species were formed in appreciable amounts, then the reaction could proceed by an elementary addition of a silyl radical to a heterocycle (i.e., sila-Minisci reaction). To probe this hypothesis, we subjected



Scheme 5.3.2. Control experiments under sila-Minisci reaction conditions.

1-methylindole to a mixture of reagents under conditions that are reported by the Curran group to generate discrete silyl radicals (see Scheme 5.3.2a for Curran's conditions,[40] and Scheme 5.3.2b for the result of 1-methylindole under these conditions). Interestingly, no silylated product of any kind was detected in this reaction (Scheme 5.3.2). Conversely, we confirmed that the Currans conditions do silylate with electron poor heterocycles (such as 2-methyl quinoline, Scheme 5.3.2c), but our method fails in the case of these substrates.

To provide further evidence against a polar mechanism (i.e., formation of silyl anions), our KO*t*-Bu–catalyzed reaction with benzothiophene **3h** as a substrate was conducted in the presence of cyclohexene oxide as an additive (epoxides, including cyclohexene oxide, are known to undergo nucleophilic ring opening by silyl anions, Scheme 5.3.3a).[41] However, under our conditions, the epoxide is quantitatively recovered after the reaction, and the desired silylation product **4h** was obtained in moderate yield (Scheme 5.3.3b.), providing evidence against the formation of discrete silyl anions.

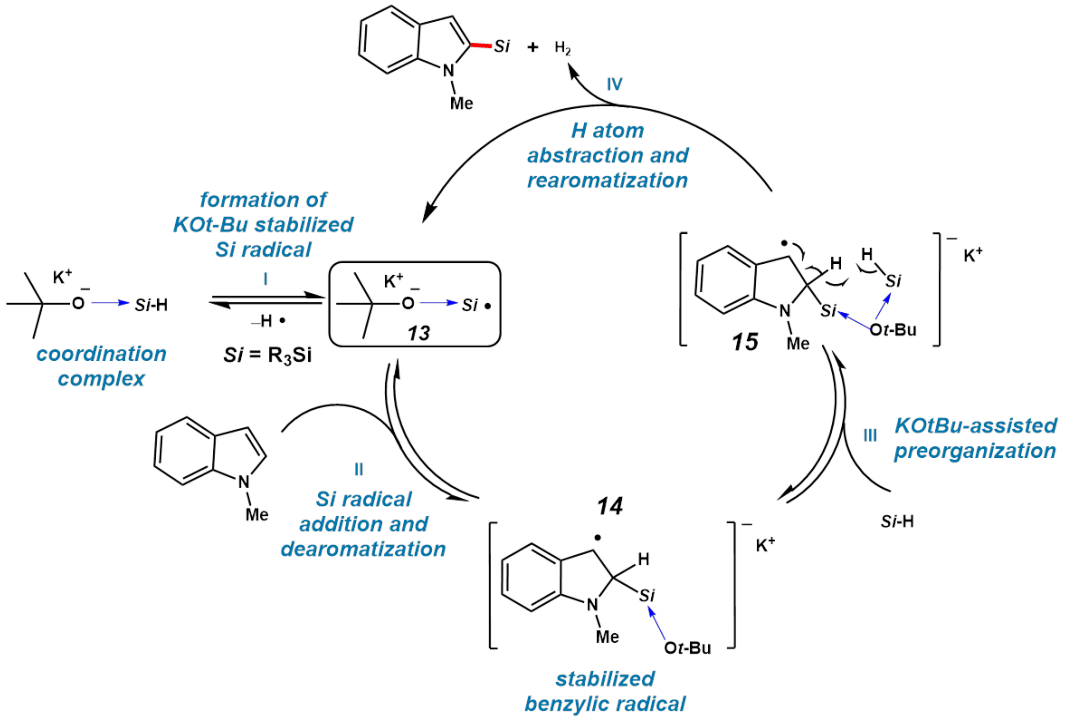


Scheme 5.3.3. Control experiments with cyclohexene oxide.

In summary, based on the results of control reactions with radical traps (Scheme 5.3.3) and the observation of TEMPO-$SiEt_3$ ***II*** (Table 5.3.1), 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, an elementary radical generation/addition mechanism (i.e., sila-Minisci reaction) is likely not operative. The survival of the epoxide additive (Scheme 5.3.3) is inconsistent with the silyl anion pathway. Taken together, these preliminary studies point to a previously unreported (hetero)aromatic CH functionalization mechanism. Efforts to elucidate the mechanism by experimental and computational methods are underway.

5.4 Possible Mechanism

One potential mechanistic manifold based on these initial observations is outlined in Scheme 5.4.2. We hypothesize that there is likely an initial interaction between KO*t*-Bu and hydrosilane wherein the formation of an alkoxide-stabilized silicon-centered radical **13** is formed. This radical then adds to the heterocycle leading to dearomatization of the latter; a benzylic radical is formed, likely further stabilized by coordination from KO*t*-Bu.



Scheme 5.4.2. KOt-Bu-catalyzed C-H silylation of 1-methylindole: a potential mechanism.

In the next step, KO*t*-Bu could facilitate a preorganization of the heterocycle-silane complex with a second molecule of hydrosilane **15**. At this stage, the entering hydrosilane donates a hydrogen radical to homolytically cleave the indole C2–H bond, which restores aromaticity to the heterocycle generating the desired C2-silylated product. This step also produces an equivalent of alkoxide-stabilized silyl radical **13** for the next round of catalysis as well as an equivalent of H_2 (which is observed by GC-headspace analysis of the reaction mixtures). The excellent C2 selectivity obtained in this transformation could be potentially attributed to a difference in stability of radical intermediates: the C3 benzyl-stabilized radical which is formed upon silyl addition to C2 **14** is likely of lower energy than the corresponding C2 radical formed by C3 attack of silicon. This difference in energies has been supported by preliminary DFT calculations.

The mechanism presented in Scheme 5.1.2 is only one of a many possibilities in what seems to be a very intriguing mechanistic picture. We are excited to be collaborating with Prof. Kendall Houk and his group at UCLA to complement our ongoing experimental studies with their unique computational insights.

5.5 Interesting (and Confusing) Observations

Interestingly, the potassium countercation proved vital as the use of Na or Li bases failed to promote the silylation reaction.1 The addition of a stoichiometric quantity of 18-crown-6 relative to KO*t*-Bu led to a precipitous drop in catalyst activity, which further corroborated the crucial, albeit presently unknown role of K^+.1 Control experiments and micro-analyses to rule out the presence of transition metal residues in the reagents, catalyst and reaction mixtures were carefully conducted.1 (Paper refs)

Recent investigations have also revealed a 10 hour time delay associated with the start of the reaction. No product formation is observed for the first 10 hours; however, after this time has passed, the reaction is nearly complete in approximately 5 hours. This delay period appears to fluctuate, possibly due to variations in the quantity of adventitious O_2 and possibly H_2O in the system. This behavior can be characteristic of radicals; however, a "traditional" radical mechanism is unlikely to be involved due to the selectivities of this reaction compared to other radical additions.

Chapter 6

Summary of Heterocyclic Silylation

This first contribution to the field of catalytic cross-dehydrogenative functionalizations came in the form of a mild and efficient direct C($sp2$)–H silylation of electron rich aromatic heterocycles with hydrosilanes using catalytic quantities of potassium *tert*-butoxide alone. The reaction proceeded often at ambient temperature, without additives, with turnover numbers (TONs) up to 100, and showed good robustness, scalability, and scope of hydrosilane and heteroarene.

We have presented a conceptually novel strategy for the functionalization of C-H bonds in organic molecules all by a single, readily available catalyst: KOt-Bu. This catalytic cross-dehydrogenative silylation with hydrosilanes enables the preparation of useful Si-containing heteroaromatic molecules under mild conditions in the absence of hydrogen acceptors, additives and directing groups. The starting materials can be complex drug-like structures with a high density of sensitive functional groups, or bulk chemicals such as simple arenes and olefins, which lack functional groups and directing groups. The products are potentially useful in their own right as sila-drug analogues for medicinal chemistry and various other applications; they are also emerging as among the most powerful and versatile synthetic building blocks due to their excellent stability and tunable reactivity. The surprising catalyst, KOt-Bu, is bench-stable, inexpensive, and commercially available on very large scale.

Moreover, it appears likely that the KOt-Bu catalyzed direct cross-dehydrogenative C–H silylation will be complementary to the wide array of C–H functionalization methods reported in the literature. There are many existing strategies for linking the KOt-Bu-catalyzed C–H silylation to oxidation, arylation, substitution, and directing group chemistries for the rapid and systematic generation of chemical diversity. This chemistry has the possibility to be of great utility in a range of yet unanticipated applications across numerous disciplines.

Part III

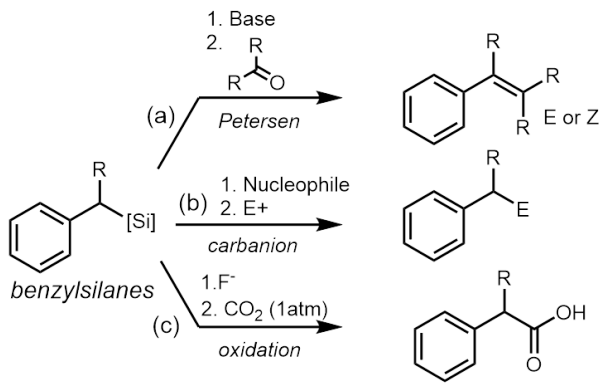
Extension to Non-Heterocyclic Systems

Chapter 7

Direct Silylation of C(sp^3)–H Bonds

7.1 Background

C(sp^3)–Si fragments have been employed in various powerful reaction classes such as the Peterson olefination yielding styrene derivatives, electrophilic substitutions, and various oxidation manifolds such as carboxylation (Scheme 7.1.1abc, respectively).[8][42] However, selective and mild synthesis of the starting organosilanes remains challenging and is primarily accomplished by hydrosilylation or by stoichiometric organometallic reactions. 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 or irradiation.[43]



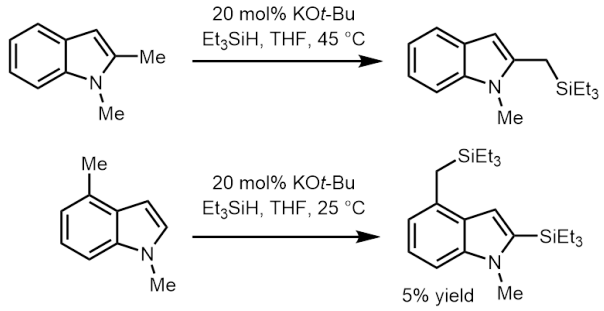
Scheme 7.1.1 Synthetic utility of benzylsilanes.

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. The development of a general catalytic platform for C(sp^3)–H bond silylation is one of our goals, in order to unlock the true utility of alkyl-, allyl-, and benzylsilanes by making these fragments synthetically accessible.

7.2 Discovery

During the initial investigation into heterocycles, several reactions generated byproducts that were immediately interesting, since they involved silylation at positions remote to the heterocycle.

The possibility of benzylic C(sp^3)–H silylation was discovered during the silylations of 1,2- and 1,4-dimethylindole. When 1,4-dimethylindole was subjected to the reaction conditions, the desired C2-silylated product was isolated but a small amount of byproduct with benzylic silylation on the C4 methyl was also isolated (Scheme 7.2.1). Similarly, for 1,2-dimethylindole, silylation on the C2 methyl was observed; no ring silylation was observed in this case.



Scheme 7.2.1 Discovery of benzylic silylation in small amounts in the cases of 1,2- and 1,4-dimethylindole.

When toluene was used as a solvent during earlier optimization of the heterocycles cases, some amount of silylated toluene was observed by GCMS at elevated temperatures. Until this point, we never followed up on this minor result. However, the observation of benzylic silylation in methyl-substituted indoles lent further promise for a general benzylic silylation method.

7.3 Evaluation of the Scope

The silylation method that was initially applied to heterocycles was then extended to access silylation at benzylic positions. Several examples of benzylic silylation are shown in Figure 7.3.1.

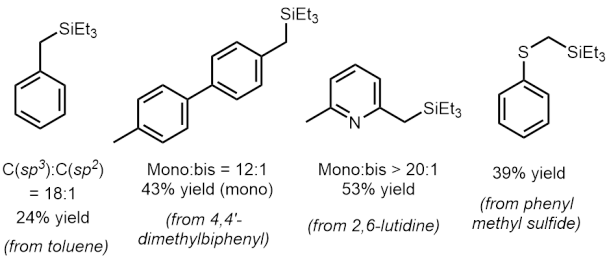
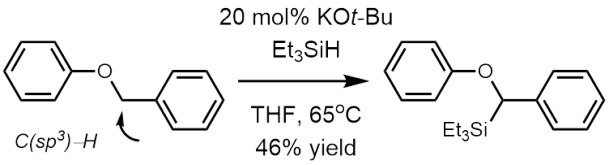


Figure 7.3.1 Silylation of benzylic positions is possible. Currently, these results are unoptimized. The yield of silylated toluene is low due to its propensity to evaporate under highvac.

Silylation of toluene proves the basic, unsubstituted case for this reaction, since it is the simplest benzylic substrate. However, isolation of the product is challenging due to its high volatility. Interestingly, silylation of 4,4'-dimethylbiphenyl proceeds in decent yield only when 40 mol% KOt-Bu is used, as opposed to 20 mol%, but is still selective for monosilylation. The silylation of 2,6-lutidine provides an example of silylation of an electron-deficient system, as the pyridine ring in 2,6-lutidine is electron-withdrawing. Certainly, the yields will need to be optimized; however, these three results point to the possibility of a very broad substrate scope for this benzylic silylation reaction.



Scheme 7.3.2 Silylation of benzyl phenyl ether is selective for the benzylic carbon, as opposed to the oxygen-directed site on the phenyl ring.

Also of note is the sp^3 silylation of benzyl phenyl ether (Scheme 7.3.2). As will be discussed in Chapter 8, there are two possible sites for silylation to occur – the benzylic position, as shown in this case, and the O–directed site on the phenyl ring. However, this reaction is completely selective for the sp^3–silylated product.

The sp^3 substrate scope is currently being extended; my immediate efforts were on extension to non-aromatic systems, as seen in the case of *sp* silylation. However, the addition of these four substrates shows that this KO*t*-Bu–catalyzed method can indeed be developed into a general method and will have great potential applicability to silylation of benzylic carbons.

Chapter 8

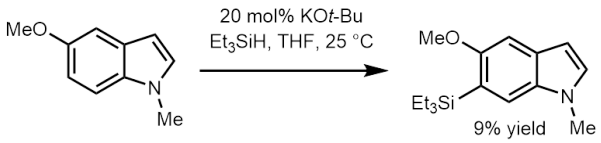
Silylation of C(sp^2)–H Bonds

8.1 Background

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. The direct catalytic C-H functionalization of simple electron-rich arenes would constitute a powerful and broadly applicable method. C-H silylated products of aromatic oxygenates are versatile building blocks of potential use as aryne precursors, cross-coupling partners, and as masked phenols.

8.2 Discovery

This silylation method was extended to non-heterocyclic sp^2 carbons in a similar way as for the sp^3 substrates (section 7.2). While investigating the substrate scope for the heterocycles, during the silylation of 5-methoxyindole, along with the desired C2-silylated product a byproduct involving silylation *ortho* to the methoxy group was observed (Scheme 8.2.1).



Scheme 8.2.1 Discovery of oxygen-directed silylation in small amounts in the case of 5-methoxyindole. Silylation is observed *ortho*- to the oxygen substituent (methoxy) on the phenyl ring.

We then investigated the performance of other methoxy-containing molecules and compounds with oxygen-substituted phenyl rings in this reaction, since, as with the benzylic case, this result pointed to a promising new direction for expansion of the scope of the KO*t*-Bu–catalyzed silylation reaction.

8.3 Evaluation of the Scope

A preliminary substrate scope for the oxygen-directed silylation of phenyl rings has been determined (Figure 8.3.1); as stated before, my main efforts have been directed towards development of the *sp*-silylation method. However, the addition of this number of substrates indicates that this reaction will be a general method for silylation of oxygen-substituted phenyl moieties.

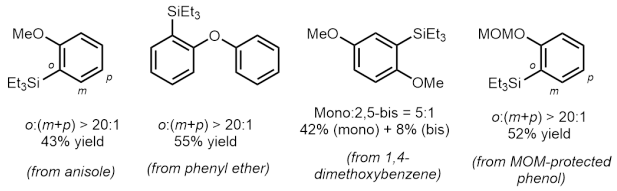
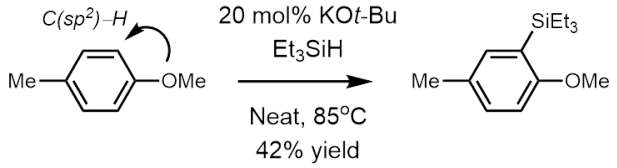


Figure 8.3.1 Silylation of non-heterocyclic sp^2 positions is possible. Currently, these results are unoptimized. As with the case with toluene, the yield of silylated anisole is low due to its propensity to evaporate under highvac.



Scheme 8.3.2 In the case of 4-methoxytoluene, sp^2-silylation is achieved by reaction without solvent.

Anisole is the most basic example of an oxygen-substituted phenyl ring, aside from phenol. In this preliminary extension, only protected oxygens were chosen for silylation, since the interaction of the base with the unprotected O–H was a complication that we did not want to yet investigate. Silylation of anisole proceeds with good yield in excellent regioselectivity. The silylation of diphenyl ether shows selectivity for the monosilylated product over the possible *bis*-silylated product. In the case of 1,4-dimethoxybenzene, both the *mono*- and the *bis*-silylated isomers were observed; presumably, higher temperatures and base loadings could be used to select for the 2,5-*bis*-silylated product. Silylation of MOM-protected phenol also proceeds in good yield.

4-Methoxytoluene has two possible sites for silylation: benzylic silylation on the methyl group is a possibility, as is *ortho*-silylation directed by the methoxy group. Earlier, the oxygen-directed silylation procedure was found to work neat (without solvent), which is advantageous for material cost, environmental impact, reaction volume, and ease of isolation of the product. The benzylic silylation, however, requires solvent. When reacted in THF, 4-methoxytoluene produces a mixture of the two silylated products; however, when this reaction is performed neat, only the *ortho* silylation product is produced (Scheme 8.3.2).

Currently, high temperatures are needed for both the oxygen-directed sp^2 silylation as well as the benzylic sp^3 silylation procedures. Further optimization of these reactions is ongoing; lower temperatures and larger substrate scopes are necessary for both cases. Despite the modest yields to date, this appears to be, to the best of my knowledge, only the second report of catalytic *ortho* 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),42a 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.

8.4 Unanticipated Expansion of the Silane Scope

After the silane scope was completed for the heterocycles, di-*tert*-butylsilane and diisopropylsilylpyridine were acquired – they were not part of the original heterocycle investigations. Due to their synthetic utility,[44][45][46][47] I investigated their behaviors with heterocycles and the other aromatic substrates.

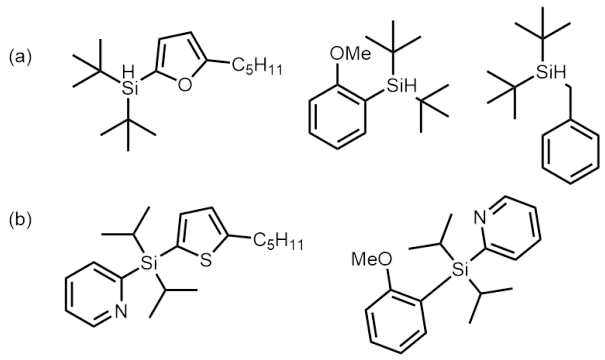
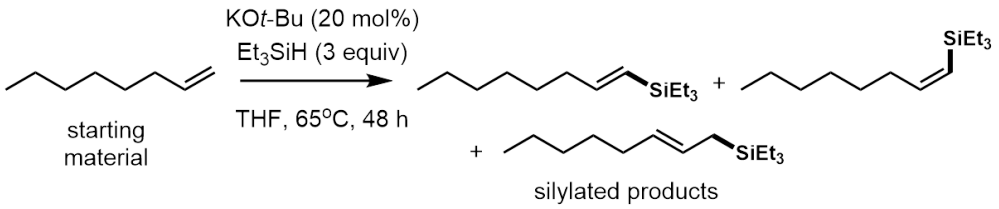


Figure 8.4.1. (a) Silylation with di-*tert*-butylsilane: 2-pentylfuran – unsuccessful; anisole – successful; toluene – successful. (b) Silylation with diisopropylsilylpyridine: 2-pentylthiophene – successful; anisole – unsuccessful.

Di-*tert*-butylpyridylsilane successfully silylated both anisole and toluene; however, it did not display great efficacy when silylating 2-pentylfuran (Figure 8.4.1a). Diisopropylsilylpyridine successfully silylated 2-pentylthiophene; however, it was not very effective when silylating anisole, presumably due to steric hindrance (Figure 8.4.1b). These results will be further optimized and are a preliminary investigation into the performance of these silanes in different substrate classes.

8.5 Non-aromatic C(sp^2)–H Systems



Scheme 8.5.1. Silylation of 1-dodecene produces both isomers of silylated olefin product as well as an isomerized alkene.

Initial tests pointed to the possibility of silylation of olefins using this method. A reaction with KO*t*-Bu and 1-dodecene showed both the E and Z silylated isomers as well as a silylated product with olefin migration (Scheme 8.5.1). This system has not been investigated yet (as of May 2015 I have begun optimization investigations) but the success of 1-dodecene in this system shows promise for the functionalization of olefins using this procedure.

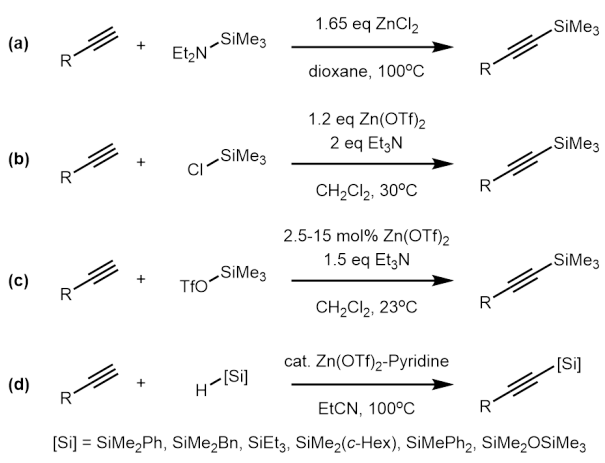
Chapter 9

Silylation of C(*sp*)–H Bonds

9.1 Background

9.1.1 Previous Approaches to Silylation of Terminal Acetylenes

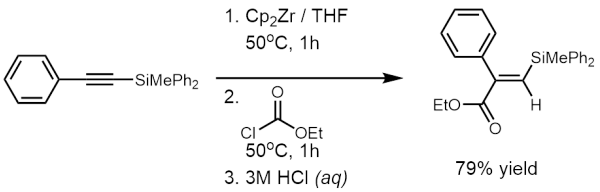
A number of methods for the synthesis of ethynylsilanes have been developed,[48] most of which rely on the interception of metal acetylide intermediates with silicon electrophiles.[9][14][49][50] However, these approaches have the expected limitations in functional group compatibility and overall scope expected from stoichiometric deprotonation reactions with strong bases. Transition-metal-mediated alkyne silylations using activated silicon coupling partners such as [Si–Cl][51][52] and [Si–N][53] as well as catalytic approaches using [Si–OTf][54] have been developed, improving the scope of the alkyne partner (Scheme 9.1.1).[54][55][56][57]



Scheme 9.1.1 Zinc-catalyzed silylation of terminal acetylenes. (a) Ref [53]. (b) Ref [56]. (c) Ref [54]. (d) Ref [57].

Only a few recent approaches have been able to incorporate convenient and inexpensive hydrosilanes as the silicon source at high temperatures while still maintaining a synthetically valuable substrate scope and high yields. However, these reactions often employ expensive and sensitive transition-metal salts such as Ir,[58] Au,[55] Ru,[59] require high temperatures (i.e. 80–120° C), non-commercially available silicon sources and stoichiometric additives for high conversion. In addition, undersired hydrosilylation chemistries can become competitive with certain substrates and catalysts. Moreover, most catalytic systems developed so far have relied on transition-metal salts containing highly Lewis-acidic metal centers, which appears to have limited the alkyne scope to substrates not containing strongly Lewis-basic functionalities such as nitrogen heterocycles. For these reasons, the development of a general method for C(*sp*)-Si bond formation remains an important problem in the broader field of C-H functionalization catalysis.

9.1.2 Synthetic Utility

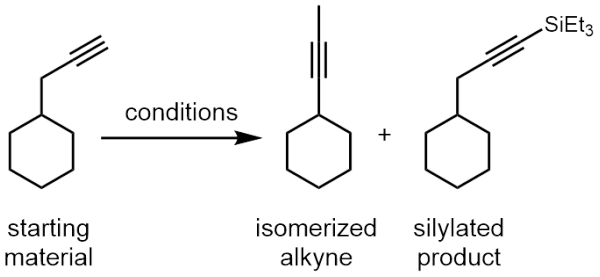


Scheme 9.1.2 Synthesis of tetrasubstituted olefins from silylated alkynes. Method: Ref [57].

Silylated acetylenes are valuable building blocks, having been employed in the construction of electronically and geometrically interesting materials, [60][61] as precursors in metathesis reactions,[62] as readily activated alkynyl nucleophiles and cross-coupling partners,[63] and as versatile intermediates in the synthesis of a variety of natural products and other complex molecules.[64] They can be easily transformed into useful tetrasubstituted olefins (Scheme 9.1.2)

9.2 Discovery

After the initial development of silylation of aromatics and heterocycles, we became intrigued whether our Earth-abundant alkali metal catalysis strategy could be applied to cross-dehydrogenative couplings employing other C–H bond classes, especially those in non-aromatic systems. In this regard, we became interested in the direct catalytic silylation of terminal acetylenes with hydrosilanes to directly yield synthetically useful ethynylsilanes. The first non-aromatic system investigated was an acetylene: 3-cyclohexyl-1-propyne, which when tested in non-optimized silylation conditions, showed conversion of the starting material into the silylated product as well as an isomerized alkyne (Scheme 9.2.1).



Scheme 9.2.1 Silylation product and byproduct of cyclohexylpropyne.

Although the yield was not ideal (79%, with 20 mol % KO*t*-Bu and 3 eq. Et_3SiH at 85° C in THF for 2 days), the remaining mass balance being attributed to undesired isomerized alkyne byproduct, this reaction was the proof of concept that non-aromatic systems were amenable to silylation using the KO*t*-Bu–catalyzed reaction developed for heterocycles. Once the proof of concept was established, I began optimization of this reaction for the silylation of alkynes with an alkali metal catalyst.

9.3 Optimization

Before investigations on this system began, I anticipated a (relatively) simple optimization procedure, expecting similar results to the heterocycles optimization. However, this turned out to not be the case – the optimization and eventual extension to substrates proved to be a very complicated, interesting process that was not at all straightforward.

Table 9.3.1. Initial Optimization Studies.

(A) Solvent	Product (%)	Isomer (%)
Neat	21.7	60.1
THF	93.6	0.8
Dioxane	88.1	0.0
DME	99.6	0.0
MTBE	30.0	53.4
Toluene	26.7	58.9
CyMe	15.1	66.1
Pentane	12.5	74.1
Mesitylene	25.9	55.8
DCM	0.0	0.0
Et_2O	23.1	61.0
Benzene	25.8	54.3
2-MeTHF	48.4	50.9

(B) Temp (°C)	Product (%)	Isomer (%)
25	7.0	63.1
55	59.0	29.7
85	98.7	0.0

(C) Eq. Silane	Product (%)	Isomer (%)
1.0	70.8	21.1
1.5	92.1	6.4
2.0	92.8	5.7
2.5	96.5	2.3
3.0	98.0	1.0
3.5	98.7	1.0
4.0	97.0	2.4

Optimization of conditions for the silylation of 3-cyclohexyl-1-propyne with triethylsilane and 20 mol% KO*t*-Bu catalyst. **(a)** Solvent optimization revealed that DME and THF were the highest yielding, while DME and Dioxane had the lowest amount of isomerization. The neat reaction produced a significant amount of isomer. Reaction time: 3 days. **(b)** Temperature optimization obtained quantitative yield of the product, but required forcing conditions. This optimization was done in DME; reaction time: 2 days. **(c)** Between 2.5 and 3.5 equivalents of silane gave approximately equal product yield. Reaction time: 2 days.

I used 3-cyclohexyl-1-propyne as a test substrate for all of the optimizations, since it had shown promise in its initial, unoptimized reaction. The silylated product was isolated by evaporation of the starting material and isomerized byproduct to yield the pure silylated product, which was used to obtain an Rf value for the GC-FID, so that subsequent optimizations could be analyzed quickly using the GC-FID.

9.3.1 Initial Studies

The first optimization study investigated the ideal solvent for the reaction, attempting to use a solvent effect to reduce the isomerization. Previously, in the case of the heterocycles, coordinating solvents improved performance, but the reaction also worked at slightly elevated temperature in neat conditions. Evaluation of the solvent took place with 20 mol % KO*t*-Bu and 3 equivalents of triethylsilane at 85° C; reactions were run for 3 days. Subsequent GC-FID analysis of these reactions revealed that 1,2-dimethoxyethane (DME) and tetrahydrofuran (THF) were the best solvents for this reaction (Table 9.3.1a). Dioxane, DME, and THF showed very little of the isomerized starting material; all other solvents had significant alkyne isomerization.

Temperature effects have been consistenly found to be very important in the silylation reactions, as seen in the heterocycle studies. A temperature optimization study showed that the silylation of cyclohexylpropyne with triethylsilane proceeded well at 85° C; lower temperatures saw greater amounts of the starting material isomer (Table 9.3.1b). Although almost quantitative yield was achieved at 85° C, this temperature is considered high enough to be "forcing conditions" and did pose problems for the extension to different substrates.

Changing the equivalents of the silane affected conversion as was expected; higher amounts of silane relative to substrate promoted formation of the product compared to the starting material isomer (Table 9.3.1c). However, at large excesses of silane, the product yield decreased; this is consistent with a phenomenon we observed in the heterocycles case, where higher silane loadings promote a de-silylation, supporting the hypothesis that this silylation reaction is reversible.

9.3.2 Catalyst Screen

I began a (what I thought was) routine test for base types in the acetylene silylation reaction. Expecting similar results to the heterocycles case, in which potassium *tert*-butoxide and KHMDS (potassium hexamethyl disilazide) were the best performing bases, and all other bases performed poorly, I tested all the bases that had been in the heterocycles base test. The results of this test, however, were not what were expected – instead of a small number of bases working well, with KO*t*-Bu outperforming all the others, a large number of bases worked in a study with a reaction time of 3 days (Table 9.3.2a).

What was surprising was that, unlike in the case of the heteroaromatic silylation, the potassium ion was not essential for silylation to occur. The sodium analogues of several bases showed medium to excellent conversion; however, in every case, they had slightly more of the isomer than the corresponding potassium bases. What was also surprising was that KH and KOH worked – previously, our studies in the heterocyclic cases showed that a large, bulky organic base and a potassium counterion promoted silylation the most. However, since KOH displayed remarkable silylation, the alkyne silylation evidently did not need a bulky organic base. Indeed, many smaller organic bases worked better than their bulkier counterparts - compare KOMe, with 98.3% yield, and KOEt, with 99.3% yield, to KO*t*-Bu with 97.9% yield. A third interesting result from this test was that TMAF (tetramethyl ammonium fluoride) was adept at acetylene silylation, as it does not have a potassium ion, is a nucleophile, and also contains fluoride, which typically bonds tightly to silicon and would be expected to shut down reactivity.

Table 9.3.2. Optimization of the base in acetylene silylation.

(A) Base	Product (%)	Isomer (%)
KO^{t}Bu	97.9	0.0
KH	98.9	0.0
KHMDS	98.6	0.2
NaO^{t}Bu	50.9	39.8
LiO^{t}Bu	0.2	4.7
DABCO	0.1	0.0
NaOEt	81.5	0.6
KOEt	99.3	0.1
NaOAc	0.2	0.0
KOAc	0.1	0.0
KOMe	98.3	0.6
Cs_2CO_3	0.0	0.0
NaOMe	94.8	2.6
KO^{t}Amylate	99.8	0.1
KOH	93.5	0.1
K_2CO_3	0.3	0.0
TMAF	97.9	0.9
KF	0.1	0.0

(B) Base	Product (%)	Isomer (%)
KO^{t}Bu	88.7	9.1
KH	87.0	10.9
KHMDS	95.9	3.4
NaO^{t}Bu	46.1	51.5
LiO^{t}Bu	0.3	0.0
NaOEt	90.7	0.5
KOEt	95.9	1.7
KOMe	95.5	4.2
NaOMe	83.2	0.4
KO^{t}Amylate	91.2	5.8
KOH	95.3	2.9
TMAF	99.3	0.6

(C) Base (mol %)	Product (%)	Isomer (%)
40	89.4	0.0
20	99.3	0.0
10	99.8	0.0
5	98.9	0.9
1	97.4	2.4

Reaction done on 3-cyclohexyl-1-propyne with 3 eq. triethylsilane at 85° C in DME. (a) Numerous bases worked in this reaction – neither a potassium counterion nor a bulky organic base was necessary for silylation to occur. Study done in THF with 20 mol% base loading; reaction time: 3 days. (b) A shorter base study revealed numerous bases that are adept at alkyne silylation (and one non-base). Study done in THF with 10 mol% base loading; reaction time: 1 days. (c) Base loading study with KO*t*-Bu. Base loading can be reduced to 1 mol% without loss in yield.

From this base test, I selected the best performing bases (and the lithium and sodium analogues of several bases) to do a shorter, more competitive base screen. In this study, I used 10 mol% base (instead of 20 mol%, which was used in the previous base study) and reacted them for 1 day instead of 3 in order to determine which base was the most adept at silylation under more competitive conditions (Table 9.3.2b). The results of this test were again surprising - even under these more strenuous conditions, most of the bases I tested displayed yields in the 90% range. Since so many bases work, this enables high tunability of this reaction. The base used can be tuned for each substrate in order to maximize silylation and minimize damage to the rest of the molecule, which I would use later during the substrate investigation. Surprisingly, KOH outperformed the traditionally-used KO*t*-Bu; TMAF displayed quantitative conversion. TMAF could be used in the silylation of substrates that are base-sensitive. This led me to try TBAF, a commonly-used reagent in many labs; although silylation was successful with TBAF, I had to set this reaction up outside of the glovebox (since TBAF contains some amount of water impurities) and limitations with the physical set-up prevented me from obtaining an accurate yield. Due to time constraints, I have not currently fully investigated the performance of TBAF and TMAF in this reaction, focusing instead on the performance of bases in this silylation reaction.

I also investigated the base loadings that performed in this reaction (Table 9.3.2c). Low base loadings were achievable using KO*t*-Bu, and decreasing the base loading to 1 mol% did not greatly affect the reaction. Slightly more of the isomerized starting material was observed in the cases with extremely low base loadings. From these studies, KOH at a loading of 10 mol% was used as the default catalyst system.

9.3.3 Influence of Reaction Time

Continuing my optimization studies, I decided to obtain a profile of the reaction mixture at different times. I set up parallel reactions and quenched them at appropriate times to obtain the percent yield and isomerization at different times throughout the reaction (Table 9.3.3). These results looked particularly interesting when graphed (Chart 9.3.1).

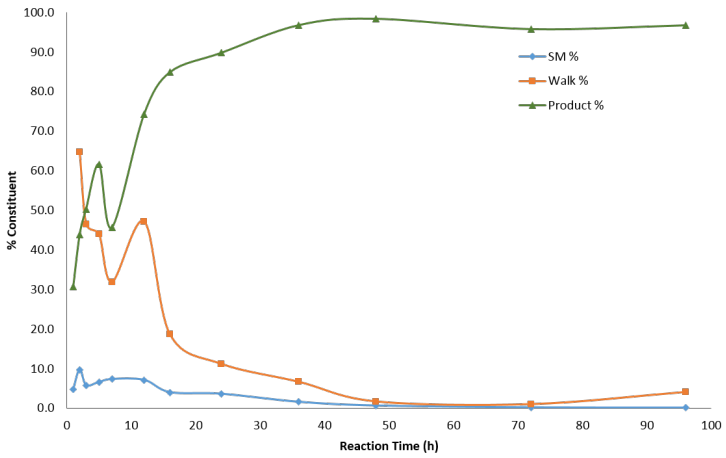
From this data and the chart, one can observe several important features about this reaction. Firstly, at a reaction time of 1 hour, there is already 30% yield of the product; however, there is 60% conversion to the alkyne isomerization byproduct. This indicates several things. Firstly, unlike in the case of the heterocycles, there is no delay in the start of this reaction. We have recently found that there is a ten hour delay in the start of product formation in the case of heteroaromatic substrates; after this delay, the reaction is complete in several hours. Evidently, there is no such delay in the silylation of acetylene substrates. Secondly, one can see that the silylation reaction and the alkyne isomerization are competing processes - once the alkyne is isomerized, it cannot silylate (we have observed no silylation and isomerization product, i.e., silylation of the terminal alkyne C–H and then subsequent alkyne isomerization).

Table 9.3.3. Reaction time profile.

Time (h)	Product (%)	Isomer (%)
1	30.6	64.6
2	43.8	46.5
3	50.3	43.9
5	61.6	31.8
7	45.6	47.1
12	74.3	18.6
16	84.9	11.2
24	89.8	6.6
36	96.8	1.7
48	98.3	1.0
72	95.7	4.1
96	96.7	3.2

Time study done with KOH at 85° C. Maximum yield occurs at approximately 48 hours. The 7 hour point has been replicated and remains an unusual point in the study.

Chart 9.3.1. Time profile of acetylenic silylation reaction.



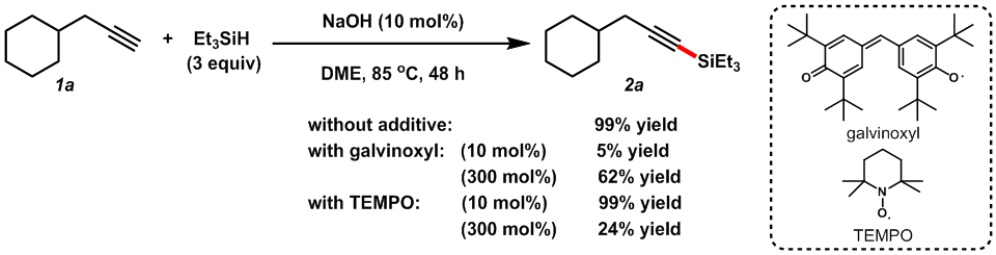
At 1h, one sees already 30% yield of the product; however, alkyne isomerization yield is 65%. The isomer ("walk") is initally the main product but then is slowly converted into the silylation product. Maximum yield occurs at 48h and then decreases as the silylation process is thought to be reversible.

The isomerization reaction is faster than the silylation reaction by a small amount, resulting in more of the isomerized product forming initially. However, as the reaction time increases, one observes the isomerized product decreasing – the isomerization reaction is reversible under these conditions – and the silylated product increasing. Since the amount of starting material throughout the reaction is less than 10% for the entire reaction, one can infer that as soon as the isomerized starting material converts back to the terminal acetylene, it is silylated. This points to the swiftness of the silylation reaction. Presumably, if one could eliminate the alkyne isomerization pathway, the silylation reaction would be complete in several hours. One also observes that at longer reaction times, the amount of silylated product decreases, again pointing to the reversibility of the silylation reaction.

9.3.4 Mechanistic Investigations

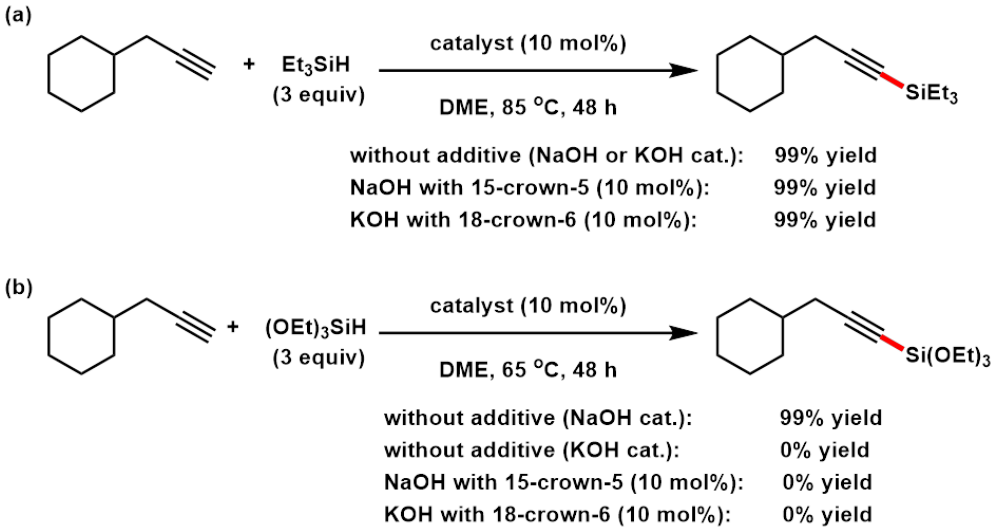
During the course of this investigation, I made some brief investigations into the mechanism of the alkyne silylation reaction. In the case of the heterocyclic silylation, described in Part II, preliminary mechanistic investigations pointed to the involvement of radical species, since the addition of radical traps inhibited the reaction. Also observed was the necessity of the potassium ion, since the addition of 18-crown-6, a potassium chelator, also shut down the observed reactivity.

Repeating these same experiments for the alkynes yielded very different results. The addition of the radical traps TEMPO and Galvinoxyl did not inhibit silylation (Scheme 9.3.1); some effects are observed from the addition of these molecules, but if radicals played a critical role in the alkyne silylation reaction, then addition of these radical traps would likely shut down reactivity almost completely.



Scheme 9.3.1. Addition of radical traps.

Two investigations of the cation were performed: (1) KOH and 18-crown-6, and (2) NaOH and 15-crown-5, which chelates the sodium ion effectively. Neither reaction was affected by the addition of the cation chelator, displaying the same quantitative conversion obtained without the addition of the cation chelator (Scheme 9.3.2). Note: see later sections for discussion of the different catalysts and silanes.



Scheme 9.3.2. Addition of cation chelators.

However, silylation with triethylsilane proceeds in equal yield using KOH or NaOH as the catalyst. Therefore, we decided to investigate how 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 potassium and sodium chelating agents shut down reactivity completely, indicating that the sodium ion is indeed necessary for the silylation of alkynes with triethoxysilane (Scheme 2b). The difference in behavior between these two silanes shows the non-innocence of the cation in this reaction. It appears that formal sequestration of the alkali metal cation from the system shuts down productive silylation and rather induces an unexpected disproportionation of the silane, as only $(OEt)_4Si$ (tetraethoxysilicate) is found in reactions with the cation chelators.

These two results point to the involvement of a different mechanism than that at play in the heterocycles case. Indeed, an acetylene moiety is much different from a heterocycle, and the terminal C–H affected by the silylation reaction is much more acidic in the case of the alkynes than in the heterocycles. Certainly, this mechanism must be further investigated and compared to the mechanism of the heterocyclic silylation.

A trace-metals analysis was also performed in order to make sure that no adventitious transition-metal catalysis was at play. The results show that the levels of transition metals in the reaction mixture are too small for any adventitious transition-metal catalysis to be significant (Table 9.3.4).

Table 9.3.4. Trace Metals Analysis.

	Values in ng/g (ppb) Unless Otherwise Stated*					
Element	NaOH	KOH	3-cyclohexyl-1-propyne	1,2-dimethoxyethane	$PhMe_2SiH$	Reaction Mixture
Ti	LOD	0.767*	0.324*	0.206*	0.545*	0.059*
Co	–	–	18.543	–	–	–
Cu	–	–	10.440	0.069*	3.048	0.116
Zn	–	0.682*	25.908*	1.787*	0.063*	0.320
Zr	–	–	–	–	0.232*	–
Mo	LOD	–	–	–	1.118*	–
Ru	LOD	21.248	1.576	–	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	–	–	–	–	–
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	–	–	0.115	–	1.729	1.383

Trace metals detection found very little adventitious catalytic species. * = ppm.

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.

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° C for 36 hours. After digestion, each sample was diluted using Milli Q water to 50 mL and subjected 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 instruments Lowest Limit of Detection. Values in ppb unless otherwise stated.

9.4 Silane Scope Investigation

One of the advantages of this catalytic silylation method is that it can be done with many different silanes. Although my main optimization for these acetylenes was done with triethylsilane, I also investigated the

performance of different silanes in this reaction. My initial investigation into the silane scope is discussed here; later, this selection would be substatially expanded.

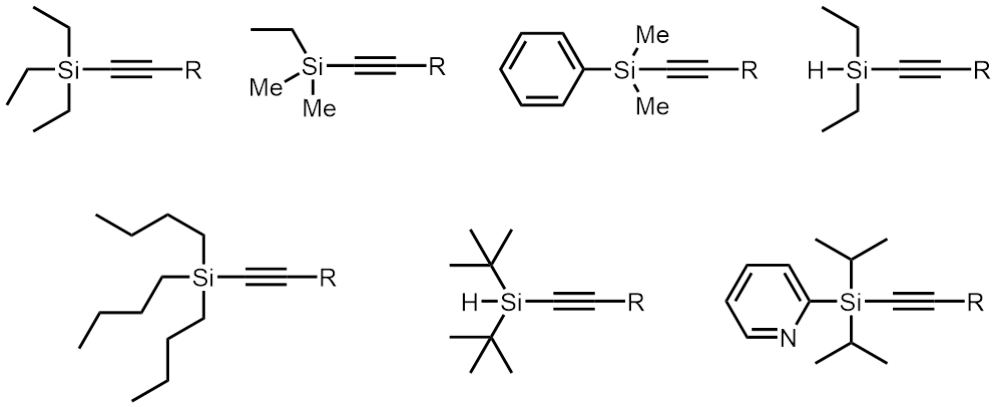


Figure 9.4.1. Successful silylation of 3-cyclohexyl-1-propyne (denoted as R) was initially accomplished with eight different silanes. From left to right, the silanes used were: (top row) triethylsilane (Et_3SiH), ethyldimethylsilane ($EtMe_2SiH$), phenyldimethylsilane ($PhMe_2SiH$), diethylsilane (Et_2SiH_2); (bottom row) tributylsilane ($^nBu_3SiH$), di-*tert*-butylsilane ($^tBu_2SiH_2$), and diisopropylsilylpyridine ($^iPr_2$(pyr)SiH). These tests were done in THF at 85° C.

I found that seven different silanes showed promise in this reaction (Figure 9.4.1). Several of these silanes are of considerable interest – di-*tert*-butylsilane is useful since its extra hydrogen can be exchanged with a fluorine, which can then undergo exchange with the radioactive ^{18}F for use as a radiolabeled drug molecule in positron emission tomography (PET) imaging. The wide array of silanes that work with acetylenic substrates is encouraging and will enable further tunable elaboration off of these installed silyl groups. Also, this enables tunability of the silane to the substrate - substrates that have sterically hindered environments around the acetylene can be silylated with smaller silanes, such as diethylsilane or ethyldimethylsilane; regioselectivity can also be achieved with substrates that have two alkyne moieties, since if one alkyne is sterically hindered, one could possibly selectively silylate the other using a large, hindered silane like tributylsilane.

Another interesting silane that worked in this reaction was diisopropylsilylpyridine, referred to as the Gevorgyan silane.(REF) This is the first catalytic approach to silylation using this silane, which is an incredibly synthetically useful silane for its ability to act as a directing group.

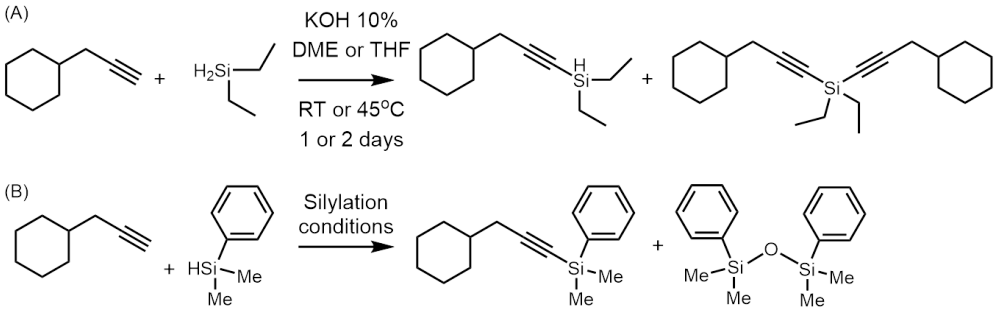
Table 9.4.1. Temperature and solvent effects with a selection of silanes.

Silane	Temperature (°C) (THF)	Temperature (°C) (DME)
Et_3SiH	85	85
Et_2SiH_2	RT	-
$PhMe_2SiH$	45	RT
$EtMe_2SiH$	65	45

The four studied silanes show strong dependencies on temperature and solvent. Diethylsilane showed no product in any reaction in DME. RT = room temperature.

Different silanes display different behaviors in this reaction, and so I studied the effects of temperature on the performance of several silanes in this reaction. Having seen less-than-optimal performance of triethylsilane and the more "delicate" silanes (diethylsilane, phenyldimethylsilane, and ethyldimethylsilane) at the higher temperature of 85° C, I studied each silane's performance at room temperature, 45° C, and 65° C and compared these tests to the 85° C reaction. I did two studies of temperature effects, one in THF and one in DME, to see the role that solvent plays in the reactions with different silanes. The results are summarized in Table 9.4.1.

This temperature and solvent study with different silanes showed remarkable differences in the reaction's behavior at different conditions. Triethylsilane required high (forcing) temperatures in both tested solvents; diethylsilane showed considerable performance in THF at ambient temperature, but switching the solvent to DME resulted in no product formation. In DME, the "tethered" product was favored (Scheme 9.4.2a).



Scheme 9.4.2. (A) Formation of tethered product with diethylsilane. (B) Formation of disiloxane with phenyldimethylsilane.

For the other delicate silanes, however, excellent conversion was achieved in DME at lower temperatures than those required in THF for the same conversion. Phenyldimethylsilane was also found to produce some amount of an oxidized disiloxane byproduct (Scheme 9.4.2b); the analogous disiloxanes were found with several other silanes. Higher temperatures, as well as higher base loadings, promote formation of the disiloxane. These temperature studies later proved very useful when extending the substrate scope. All other silanes that worked but that were not tested at lower temperatures showed excellent conversion at 85° C; these were later optimized to lower temperatures (discussed in Section 9.6).

9.5 Evaluation of the Substrate Scope

9.5.1 Extension using the "Default" Conditions

The default reaction conditions of 10% KO*t*-Bu, 3 eq. Et_3SiH, 1M in DME, at 85° C were used to perform an initial investigation of a number of substrates, shown in Figure 9.4.1.

This initial extension afforded disappointing results. Out of the eighteen substrates investigated, only six worked: only cyclohexylpropyne (Figure 9.5.1a), 4-ethynyltoluene (Figure 9.5.1h), 4-fluoro-1-ethynylbenzene (Figure 9.5.1i), 4-ethynylanisole (Figure 9.5.1l), 4-ethynyl-(*N*,*N*)-dimethylaniline (Figure 9.5.1m), and ethynylferrocene (Figure 9.5.1p) produced the silylated product. Surprisingly, 4-octyne (Figure 9.5.1o) also produced a silylated product, discussed later. These reactions were analyzed using GC-MS to look for the silylated product mass peaks.

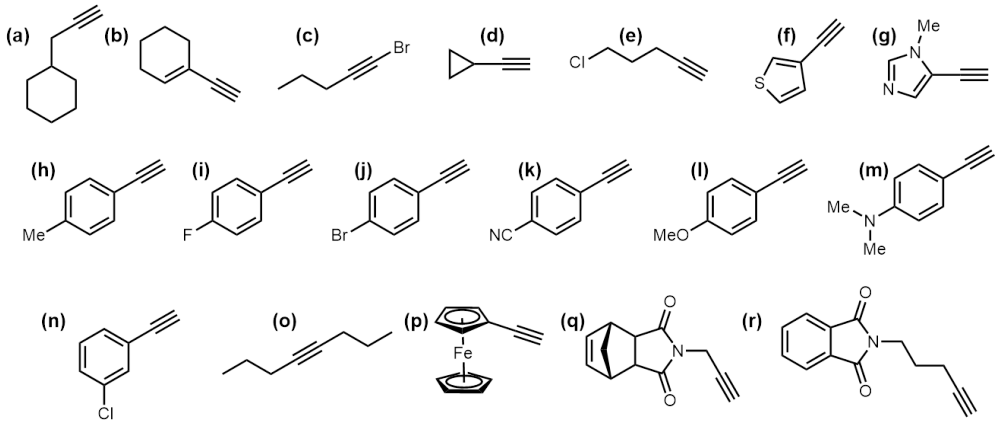
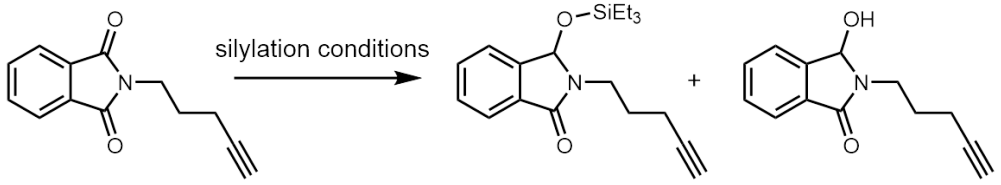


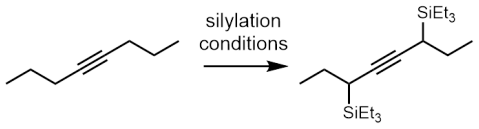
Figure 9.5.1. A number of different substrates were tested in the reaction conditions set out from the optimization (10% KOH, 3 eq. Et_3SiH, 1M in DME, 85° C). These molecules are: (top row) cyclohexylpropyne, ethynylcyclohexene, 2-bromopentyne, cyclopropylacetylene, 5-chloropentyne, 3-ethynylthiophene, 5-ethynyl-1-methylimidazole; (middle row) 4-ethynyltoluene, 4-fluoro-1-ethynylbenzene, 4-bromo-1-ethynylbenzene, 4-ethynylbenzonitrile, 4-ethynylanisole, 4-ethynyl-(N,N)-dimethylaniline; (bottom row) 3-chloro-1-ethynylbenzene, 4-octyne, ethynylferrocene, N-propynylnorbornimide, and N-pentynylphthalimide.

I also briefly studied the performance of TMAF and TBAF in silylation of several substrates. Surprisingly, 5-chloropentyne showed excellent conversion to the silylated product using TMAF (but not TBAF); N-pentynylphthalimide also showed a peak in the GC-MS that matched the silylated product mass when reacted with TBAF or KO*t*-Bu (but not TMAF); unfortunately, column chromatography and subsequent mass analysis proved that this was the reduced product (Scheme 9.5.2).



Scheme 9.5.2. Subjecting N-pentynylphthalimide to silylation conditions (20 mol% catalyst loading, 3 equiv. Et_3SiH, 1 M in DME, at 85° C) using either TBAF or KO*t*-Bu as the catalyst resulted in reduction of one of the carbonyl groups and subsequent TES protection. A small amount of the deprotected alcohol was also isolated.

The reduction of the N-pentynylphthalimide carbonyl is aided by the aromatic ring's resonance with the carbonyls. The delocalized electron density in the five-membered ring promotes reduction of the carbonyl over silylation of the alkyne. In the case of the norbornyl imide, no reduction of the carbonyl is observed, consistent with the hypothesis that this resonance with the aromatic ring is responsible for the reduction. However, no silylation is observed, which is consistent with the heterocyclic robustness screen, which showed that carbonyl groups are not tolerated by this chemistry.



Scheme 9.5.3. Double propargylic slylation of 4-octyne.

Returning to the problem of the initial substrate screen, I hypothesized that the forcing conditions required by the triethylsilane were conflicting with the substrates, which might prefer lower temperatures. An attempt at silylating these molecules at 45° C in DME successfully silylated cyclopropylacetylene and obtained trace silylation of ethynylcyclohexene and 3-ethynylthiophene. Ethynylferrocene showed lower conversion.

Surprisingly, 4-octyne also displayed silylation at this lowered temperature, and showed a peak with a mass that indicated *bis*-silylation. Intrigued by the apparent double silylation of 4-octyne, which has no acetylenic hydrogens, I isolated the silylated compound. NMR identification of the product revealed two propargylic silylations (Scheme 9.5.3). This points to a new direction in which to expand this project – propargylic silylation of internal alkynes. This would be a complementary reaction to the benzylic silylation system, which accesses sp^3-hybridized carbons, but on non-aromatic systems. Presumably, at lower silane loadings, one could promote monosilylation; in cases where only one propargylic position is accessible, monosilylation could also be achieved. Currently, there are few (if any) methods capable of selectively accessing propargylic positions – this silylation procedure could be the first method capable of doing so. However, due to time constraints, I have not further investigated this reaction behavior, and instead directed my attentions to silylation of terminal alkynes.

Returning to the problem of extending silylation to other substrates, I hypothesized that the temperature preferences of the substrates and the silane (triethylsilane) were conflicting. Triethylsilane poorly silylates at lower temperatures; however, in previous cases (such as in the heteroaromatic molecules), I observed that higher temperatures promote the desilylation process of this reversible reaction, and that substrates tend to prefer lower temperatures.

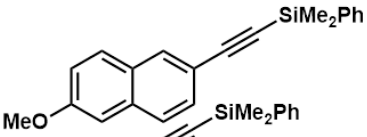
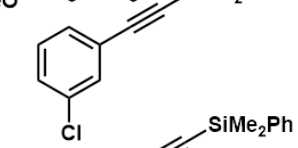
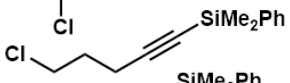
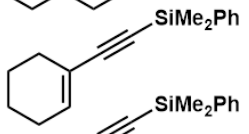
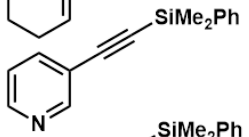
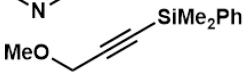
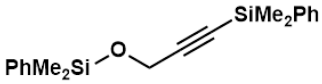
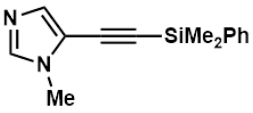
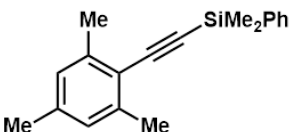
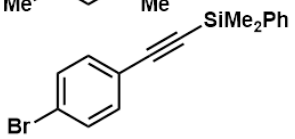
Considering this problem led me to reconsider my silane–temperature studies. Specifically, phenyl-dimethylsilane showed considerable silylation of cyclohexylpropyne at room temperature in DME. When one considers the synthetic utility of different silanes, one could argue that triethylsilane is the *least* synthetically useful silane – for example, di-*tert*-butylsilane is useful for fluoride labeling, diisopropylsilylpyridine is useful for directed activations, diethylsilane is useful for aerobic oxidation and subsequent Denmark–Hiyama cross-coupling, and oxidation reactions of silanes proceed swiftly using phenyldimethylsilanes. Therefore, I began to consider switching my "default" silane from triethylsilane to phenyldimethylsilane. In the case of the heterocyclic silylation, we used triethylsilane as our "default" silane because it frequently silylated at low temperatures and was not very sterically hindered. Triethylsilane was used to silylate every substrate in the case of the heterocyles, and then it was demonstrated that other silanes worked on a selection of those substrates. In the case of the acetylene silylation, phenyldimethylsilane could be the "default" silane in place of triethylsilane. New substrates could be tested at the optimized conditions using phenyldimethylsilane at room temperature in DME.

This was indeed the case, and preliminary tests showed a remarkable scope with phenyldimethylsilane at varying temperatures. I was immediately able to isolate several molecules using 10 mol % KOH, 3 equivalents of $PhMe_2SiH$ at 1 M concentration in dimethoxyethane (DME) at various temperatures and reaction times. However, many of the most challenging (and valuable) substrates, such as ethynylpyridine and 4-bromo-1-ethynylbenzene, continued to be low-yielding with production of undesirable byproducts. In order to optimize the reaction to favor silylation of these more difficult but very valuable substrates, I returned to my optimization tables to try to find a solution.

9.5.2 Discovery of a New Catalyst

While I was conducting these silylation reactions expanding the substrate scope of the reaction, I also made an addition to my optimization table. In optimization tables, it is important to investigate any trends and make sure that every major aspect of the system is considered. Specifically for this unique "potassium-catalyzed" silylation method, it is important to show that the sodium and lithium analogues of the catalyst are less reactive. In my base screen, I showed that KO*t*-Bu was a better catalyst than NaO*t*-Bu and LiO*t*-Bu. I also demonstrated several other sodium and lithium analogues of potassium bases; however, my base optimization showed that KOH was the best catalyst, and I did not have entries investigating other hydroxide bases.

Table 9.5.1. Comparison of KOH and NaOH.

Product	Yield (KOH)	Yield (NaOH)
	12 %	85 %
	38 %	90 %
	0 %	79 %
	60 %	85 %
	7 %	77 %
	0 %	60 %
	51 %	88 %
	19 %	82 %
	75 %	86 %
	0 %	52 %

Silylation reactions were performed with 3 equivalents $PhMe_2SiH$, 10% catalyst, 1 molar in DME. In all cases, NaOH resulted in improved yields. In the case of propargyl alcohol, low selectivity for bis-silylated product over mono-silylated (not isolated): with KOH selectivity is 1:1.3 mono:bis; with NaOH this selectivity is 1:6.

For the sake of completeness, and not really expecting any significant results, I decided to add NaOH to my base screen. To my surprise, after one day, quantitative yield had been achieved (Et_3SiH - 3eq., NaOH - 0.1eq., DME, 85° C for 1 day). This was in stark contrast to the heterocycles cases where the potassium ion was necessary for catalysis to occur: in the acetylene case, NaOH was actually the best-performing catalyst.

With the discovery of this new catalyst, I decided to retry my substrate scope using NaOH instead of KOH. The results were surprising - using NaOH as the silylation catalyst improved yields in every case studied (Table 9.5.1). In some cases, yield was improved only marginally (ethynylferrocene, 3-ethynylthiophene) but in other cases, such as for 3-chloro-1-ethynylbenzene, the yield was drastically improved from 38.2% to 90%.

Using NaOH also improved the performance of reactions with more challenging acetylene substrates. Silylation of ethynylpyridine immediately improved upon replacement of KO*t*-Bu with NaOH (for some reason, KOH only produced trace product) to yield 77.3% yield in a remarkably clean reaction. I was also able to isolate silylated 4-bromo-1-ethynylbenzene,

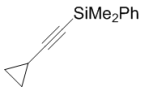
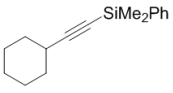
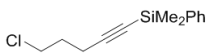
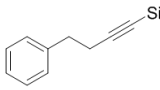
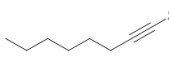
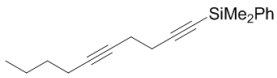
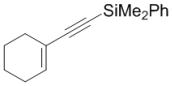
which had only produced in trace amounts up to that point. Several other substrates produced little or no conversion with KOH, but had moderate to excellent yields using NaOH.

9.5.3 Establishing a Complete Substrate Scope

With the optimal catalyst now determined, I started silylating, isolating, and characterizing all the molecules in my projected substrate scope (Tables 9.5.2, 9.5.3, 9.5.4, and 9.5.5).

The basic isolation procedure was to subject the material to vacuum (60 mTorr) at 80° C to remove as much of the unreacted silane as possible. In lower molecular weight substrates (such as cyclopropylacetylene, chloropentyne, cyclohexylacetylene, methyl propargyl ether, and methyl propargyl amine), isolation proceeded either without this heating and high vacuum step, or with a much shorter heating time in order to avoid losing the silylated material. In many cases, this heating and higvac step also removed unreacted starting material. The phenyldimethylsilane was easily removed under highvac at heat (85° C); unfortunately, the boiling point of the disiloxane is too high to remove via highvac, so a column is necessary to remove thie impurity. This impurity occurs in almost all the reactions with phenyldimethylsilane (and the equivalent disiloxanes of the other silanes were visible in trace amounts in certain cases as well). For characterization, it was necessary to run columns to remove the disiloxane; however, most reactions after heating and highvac for an hour were 90% pure with only the disiloxane as an impurity. This could be advantageous for synthetic usage of this reaction; in many cases, disiloxane can be an acceptable impurity and column chromatography of the silylated alkyne might not be necessary. This procedural convenience and high purity lends promise to telescoping protocols. In the case of very nonpolar substrates, it was very difficult to separate the silylated compound and this disiloxane; in particular, cyclohexylacetylene and 4-bromo-1-ethynylbenzene were isolated as 85:15 and 90:10 mixtures with the disiloxane, respectively.

Table 9.5.2. Silylation of aliphatic alkynes.

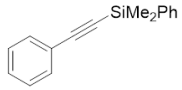
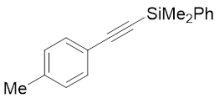
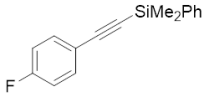
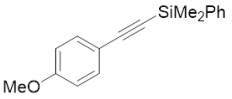
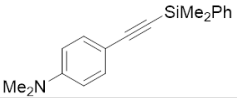
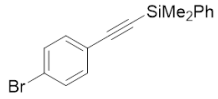
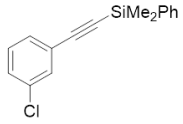
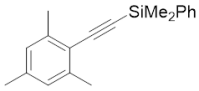
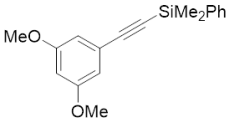
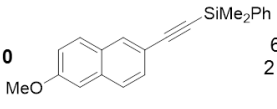
Entry	Product	Conditions	Isolation	Yield	Entry	Product	Conditions	Isolation	Yield
1		25°C 2 days	column 100% hexanes Rf = 0.38	70.0%	5		25°C 2 days	column 100% hexanes Rf = 0.53	80.3%
2		45°C 2 days	column 100% hexanes Rf = 0.31	78.8%	6		45°C 2 days	highvac at 80°C	98.3%
3		25°C 2 days	column 100% hexanes Rf = 0.53	82.7%					
4		45°C 2 days	highvac at 80°C	97.8%	7		45°C 2 days	column 100% hexanes Rf = 0.50	85.4%

Silylation of aliphatic alkynes proceeds at ambient to mild temperatures and in good yield. (1) Direct functionalization of a cyclopropyl-containing alkyne, which can be susceptible to ring-opening by transition metals as well as radical- and electrophile-induced chemistries,[65] demonstrates the unique benefit of catalysis by NaOH over strategies based on transition-metal catalysis and stoichiometric deprotonation with strong bases. (2) Chloro groups are tolerated in the reaction, although this substrate did not work with either KOH or KO*t*-Bu. (3) Unfunctionalized acetylenes proceed in good yield. (4) Internal alkynes are not modified by this procedure when there is another alkyne present - silylation occurs preferentially on terminal acetylenes. (5) Cyclohexylacetylene was difficult to purify from the disiloxane byproduct. (6) The alkyne is not isomerized even in substrates that have a longer tether between the alkyne and a stabilizing group. (7) Vinylic functionalities are tolerated and are not modified in the alkyne silylation reaction.

Going through the substrate tables, one can see that the substrate scope of this reaction is very large. It can access both aliphatic and aromatic acetylenes; internal alkynes are preserved, and no isomerization of the

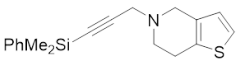
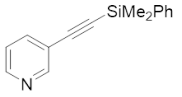
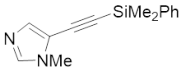
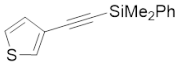
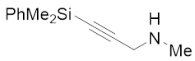
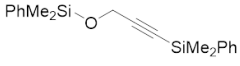
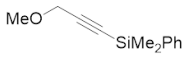
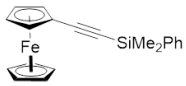
acetylene is observed. Strained rings such as cyclopropyl rings are not affected by this reaction. Halogens such as chloro, bromo, and fluoro groups are tolerated. Vinyl groups are not affected by this reaction; substituents in all positions of the benzene ring are tolerated in the case of substituted phenylacetylenes.

Table 9.5.3. Silylation of substituted phenylacetylenes.

Entry	Product	Conditions	Isolation	Yield
1		65°C 2 days	column 100% hexanes Rf = 0.38	89.4%
2		65°C 2 days	highvac at 80°C	92.2%
3		65°C 2 days	column 100% hexanes Rf = 0.49	88.0%
4		65°C 2 days	column 100% hexanes → 5% EtOAc Rf = 0.27	91.3%
5		65°C 2 days	highvac at 80°C	99.8%
6		65°C 2 days	column 100% hexanes Rf = 0.54	51.6%
7		45°C 2 days	column 100% hexanes Rf = 0.42	90.0%
8		25°C 1 day	highvac at 80°C	85.6%
9		65°C 2 days	highvac at 80°C	94.9%
10		65°C 2 days	highvac at 80°C	85.2%

Silylation of substituted phenylacetylenes proceeds readily at 65° C with 10 % NaOH catalyst and 3eq. of phenyldimethylsilane relative to substrate, 1 molar in DME. Substitutions at all positions of the ring are tolerated. Both electron-withdrawing and electron-donating substituents are compatible with the silylation reaction. Entry 10: an ethynylnaphthalene was successfully silylated without hydrogenation of the ring. Reactions were done on a 0.5 mmol scale.

Table 9.5.4. Silylation of heteroatom-containing and organometallic acetylenes.

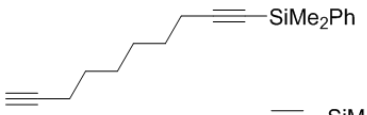
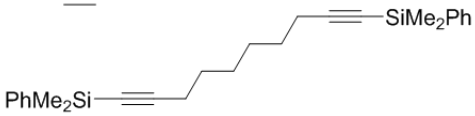
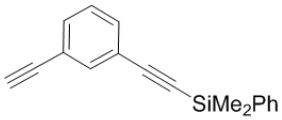
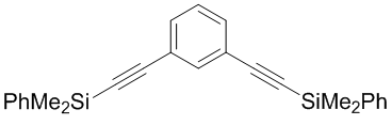
Entry	Product	Conditions	Isolation	Yield
1		65°C 2 days	column 10% EtOAc Rf = 0.40	77.3%
2		65°C 2 days	column 20% EtOAc Rf = 0.31	77.4%
3		45°C 2 days	column 100% EtOAc Rf = 0.45	82.1%
4		65°C 2 days	column 100% hexanes Rf = 0.39	93.4%
5		45°C 2 days	column 100% EtOAc Rf = 0.32	80.4%
6		45°C 1 day	highvac at 80°C	88.0%
7		45°C 2 days	column 1:1 DCM:hexanes Rf = 0.38	59.7%
8		45°C 2 days	highvac at 80°C	98.8%

(1) Silylation of a propynyl-protected basic amine with different regio- and chemoselectivities proceeded in good yield and selectivity. (2) Silylation of ethynylpyridine was successful, highlighting the ability of this reaction to work on pyridine-containing substrates. (3) 4-Ethynyl-N-methylimidazole is an accepted substrate in this reaction. The Lewis-basic nitrogen functionalities on this molecule and in Entry 1 demonstrate the substrate compatibility of this reaction, since other methods are incapable of accessing molecules containing Lewis-basic nitrogen groups. (4) 3-Ethynylthiophene demonstrates silylation, showing that heterocycles are tolerated in this reaction. (5) Propargylic amines and acidic N–H bonds are tolerated in this reaction, and presumably there is *in-situ* protection of the amine with a –$SiMe_2Ph$ group with deprotection upon workup. (6) Of particular note is the double silylation of propargylic alcohol. In this case, the installed O–Si bond during the *in-situ* protection step is preserved. (7) The low yield from the silylation of methyl propargyl ether is due to the product's volatility. Conversion is complete by GC-FID analysis. (8) Silylation of the organometallic-containing alkyne ethynylferrocene proceeds in excellent yield.

Sterically congested systems are silylated with remarkable ease, as evidenced by ethynylmesitylene (Table 9.5.3, entry 8). Silylation of several substituted phenylacetylenes proceeds in quantitative yield, and on substrates that other methods have difficulty accessing, such as the dimethylaniline (Table 9.5.3, entry 5) and the methoxynaphthalene (Table 9.5.3, entry 10). Also silylated is ethynylpyridine (Table 9.5.4, entry 2), which is particularly exciting for a variety of applications. Firstly, other methods of terminal acetylene

functionalization frequently cannot cope with pyridine rings, which have a nitrogen that can easily coordinate to transition metal complexes. Secondly, pyridine is a very electron-withdrawing group, and so the alkyne in this case is considerably more electron poor than the other aromatic systems silylated. This substrate shows that this method is capable of accessing both electron-poor and electron-rich alkynes.

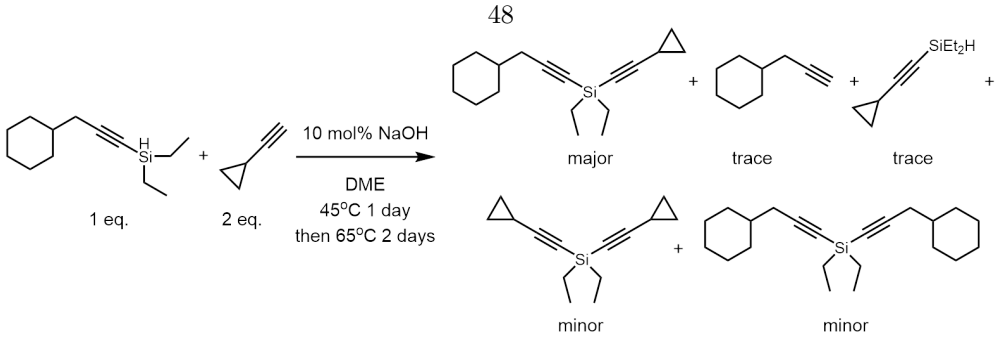
Table 9.5.5. ***Mono-*** **and** ***bis-*** **selection in diynes.**

Entry	Product	Conditions	Isolation	Yield
1		45°C 1 day	column 100% hexanes Rf = 0.48	94.0%
2		65°C 2 days	column 100% hexanes Rf = 0.43	94.8%
3		45°C 2 days	column 100% hexanes → 3% EtOAc Rf = 0.27	76.2%
4		65°C 2 days	column 100% hexanes → 3% EtOAc Rf = 0.26	87.9%

Both the *mono*-selective and *bis*-selective silylation products can be achieved in this reaction. In the case of 1,9-decadiyne (Entries 1 and 2), 20 mol% KOH is used with 3 equivalents of silane for each product. NaOH proved to be too swift of a catalyst to properly select for the *mono*-selective product: *bis*-silylated product was formed as quickly as the desired *mono*-silylated product. In the case of 1,3-diethynylbenzene (Entries 3 and 4), 20 mol% NaOH is used with 3 equivalents of silane to obtain each product. The ability to de-symmetrize molecules using this reaction is a very powerful synthetic tool.

Another remarkable and extremely advantageous feature of this silylation reaction is that in the case of diynes, both the *mono*- and *bis*-silylated products can be formed. In fact, by using slightly different reaction conditions, I was able to select for each of these products (Table 9.5.5), demonstrating a remarkable and facile way to desymmetrize diynes.

Diethylsilane was used to tether two different alkynes together (Scheme 9.5.4). A three-component, one-pot reaction involving two different alkynes and a dihydrosilane provides unsymmetrical diethynylsilanes. These scaffolds are challenging to prepare by alternate methods and are useful in a number of applications such as the rapid assembly of polysubstituted siloles, which can then be extended to polysiloles or silole-heterocycle co-polymers.[66] I was successful in reacting silylated cyclohexylpropyne with cyclopropylacetylene to produce the cyclohexylpropyne–diethylsilyl–cyclopropylacetylene product in 78.1% yield; altough several other products were formed in this reaction (identified by GCMS), I was able to increase the selectivity by reacting first at 45° C for 1 day then raising the temperature to 65° C. The one day reacting at 45° C is necessary for optimal product distribution – reacting at 65° C without this lower temperature start results in lowered selectivity. The lower molecular weight products are removed under highvac, and then the product can be separated from the cyclohexylpropyne tethered byproduct via column chromatography. Diethynylsilanes are useful synthetic products, since they can be rapidly converted into siloles, which are silicon-containing hybridized rings that are used in conducting polymers.



Scheme 9.5.4. Synthesis of diethynylsilanes. The tethering reaction between diethylsilylated cyclohexylpropyne and cyclopropylacetylene creates many products. Subjecting a silylated compound results in some amount of desilylation, as evidenced by the formation of cyclohexylpropyne and the tethered cyclohexylpropyne silane product.

9.6 Reevaluation of the Silane Scope

9.6.1 Versatile Silicon Partners

After the discovery of NaOH as an excellent catalyst, I returned to the silane scope. I hoped that by redoing the silane scope with NaOH, I could increase the yields (as seen in the case of several substrates) and even access different silanes that did not work with KOH.

This was indeed the case for a number of silanes. I extended the silane scope to include thirteen different silanes and optimized the conditions and catalysts for each silane (Table 9.6.1). Notable are the silanes with considerable steric bulk (like triisopropylsilane) – these did not work in the heteroaromatic silylation reactions, most likely due to steric hindrance. Triethoxysilane is particularly interesting for materials research and further transformations of the silicon group; benzyldimethylsilane is commonly referred to as a "safety catch" silane, since the benzyl can selectively be oxidized to an OH which can then be carried through via known methods to valuable products. Entries 11 and 12 consist of silylation with pyridylsilanes, which are a versatile multifunctional group for organic synthesis, and can be used as valuable directing groups. This work is the first catalytic installation of pyridylsilanes on any type of carbon. Entry 13 shows the first catalytic installation of a disilane, which features a weak Si–Si bond. Traditional transition metal catalysis breaks this Si–Si bond, as did KOH; surprisingly, NaOH did not decompose the silane, and instead afforded the silylated alkyne in excellent yield. Silicon chain tethers are interesting as materials and for their electronic properties; installing a disilane is a proof of concept for the catalytic attachment of long silicon chains using this method.

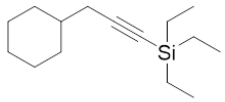
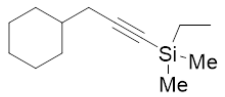
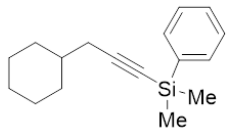
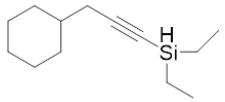
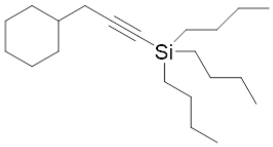
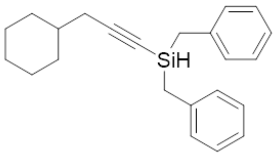
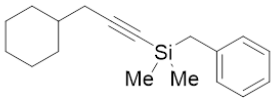
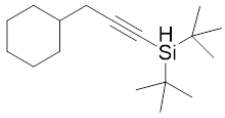
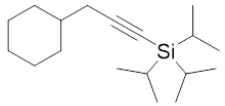
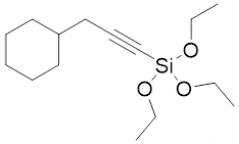
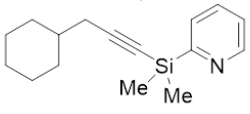
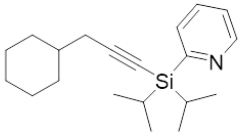
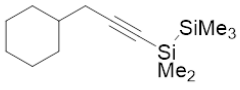
Purification of the cyclohexylpropyne with Bn_3SiH was incredibly difficult. The yield reported is after two columns, a recrystallization, and then a third column. This silane is also a special case since it appears that silylation occurs on a rearranged form of the silane, making Bn_2SiH_2 the effective silane. Rearrangement of sterically-hindered silanes has been observed before in the heterocycles case but not completely investigated. The low yield and not currently investigated rearrangement of the silane makes it likely that this result will not be reported in a publication, and instead investigated further in the future.

9.6.2 Different Catalysts for Different Silanes

Of particular note in the silane scope table is the fact that NaOH is not the optimal catalyst for every silane. In fact, using NaOH can drastically decrease the yield of the product in several cases, as seen in Table 9.6.1, but other silanes require KOH and are unreactive with NaOH. However, the reverse is also true – some substrates and silanes exhibit no productive silylation when using KOH, and product is only seen when using NaOH. For example, benzyldimethylsilane, triethoxysilane, and pentamethyldisilane all had no conversion of the starting material using KOH. In fact, KOH split up the disilane along the Si–Si bond, while NaOH produced no such decomposition. Clearly, the potassium metal species plays a very important role in the silylation of acetylenes, but is not exactly the same as for the heterocycles!

This observation further increases the complexity of this new reaction - the conditions are far more tunable and nuanced than I originally thought. The reasons for this are not known at the present, and further mechanistic studies are needed to investigate these bewildering behaviors. From a purely scientific perspective, the fact that potassium and sodium could have such enormous effects on the reaction is an entirely unexplored concept. They have always been believed to be similar, interchangeable bystander cations. In the future of chemistry, concepts like these suggest that it is possible to develop ultra-powerful new catalysts for important chemistries by varying the abundant metal cation – similar to how platinum and palladium behave differently, it seems entirely possible that sodium and potassium could be as vastly different.

Table 9.6.1. Final Silane Scope.

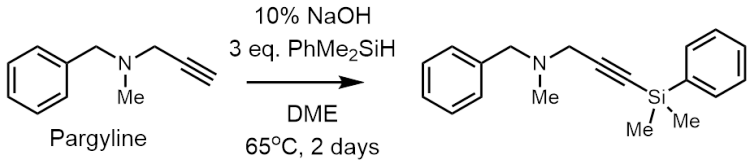
Entry	Product	Silane	Conditions	Yield (KOH)	Yield (NaOH)
1		Et_3SiH	DME 85°C 2 days	**94.6**	93.0
2		$EtMe_2SiH$	DME 45°C 1 day	**91.3**	14.1
3		$PhMe_2SiH$	DME 25°C 2 days	88.6	**92.5**
4		Et_2SiH_2	THF 25°C 1 day	**70.6**	46.2
5		$^{n}Bu_3SiH$	DME 65°C 2 days	**73.1**	21.5
6		Bn_3SiH	DME 45°C 2 days	**34.0**	0.0
7		$BnMe_2SiH$	DME 45°C 2 days	0.0	**75.3**
8		$^{t}Bu_2SiH_2$	DME 65°C 2 days	86.6	**90.9**
9		$^{i}Pr_3SiH$	DME 85°C 2 days	**68.6**	0.0
10		$(EtO)_3SiH$	DME 65°C 2 days	0.0	68.3
11		$Me_2(Pyr)SiH$	DME 65°C 2 days	50.6	**77.6**
12		$^{i}Pr_2(Pyr)SiH$	DME 65°C 2 days	**78.1**	0.0
13		$Me_3Si\text{-}Me_2SiH$	DME 25°C 2 days	**0**	95.0

Successful silylation of 3-cyclohexyl-1-propyne was accomplished with twelve different silanes. Conditions are outlined for each silane. Changing the catalyst sometimes has drastic effects on the performance of the reaction.

9.7 Application to Pharmaceuticals

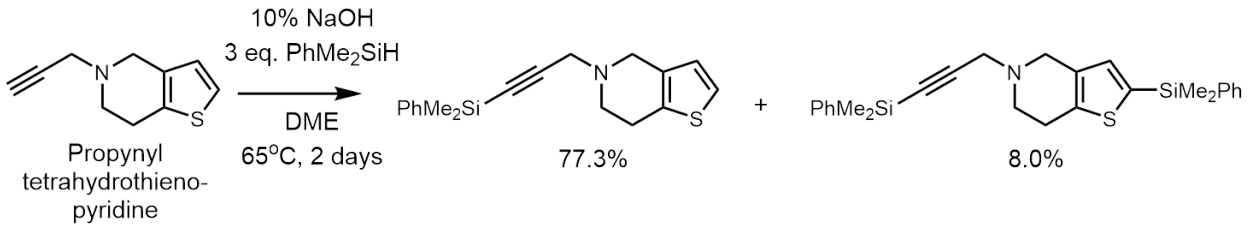
In order to demonstrate the applicability of this method to late-stage modification of pharmaceutical products, I subjected several interesting acetylene-containing molecules to the silylation reaction.

Pargyline is an irreversible non-selective monoamine oxidase inhibitor (MAOI) that was used as an antihypertensive drug. It is no longer used in pharmaceuticals today but still presents a biologically active molecule for silylation. Pargyline contains a benzylic amine and readily underwent silylation with NaOH as the catalyst (Scheme 9.7.1) in high yield (95.7%).



Scheme 9.7.1. Silylation of pargyline proceeds in high yield.

Inspired by the pharmaceutical molecules in the heterocycles case, an ethynyl ticlopidine analogue was synthesized. This molecule was readily silylated but produced a small amount of *bis*-silylated product was isolated (Scheme 9.7.2). The silylation reaction selects primarily for the alkyne position but has some silylation of the heterocycle (also seen for 3-ethynylthiophene, in which two *bis*-silylated isomers were found in very small yield). This is interesting because NaOH was used as the catalyst, which does not silylate heterocycles as evidenced by the fact that no reaction occurs with thiophene using NaOH.



Scheme 9.7.2. Silylation of ethynyl ticlopidine analogue produces both *mono*- and *bis*-silylated products.

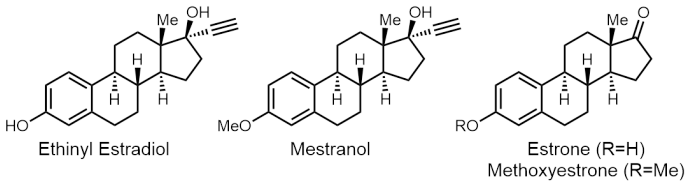
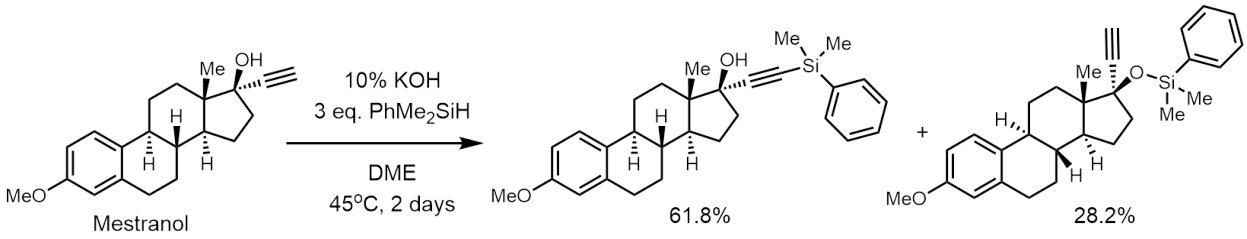


Figure 9.7.3. Silylation with NaOH of both ethinyl estradiol and mestranol produces estrone and the methoxy analogue of estrone, respectively.

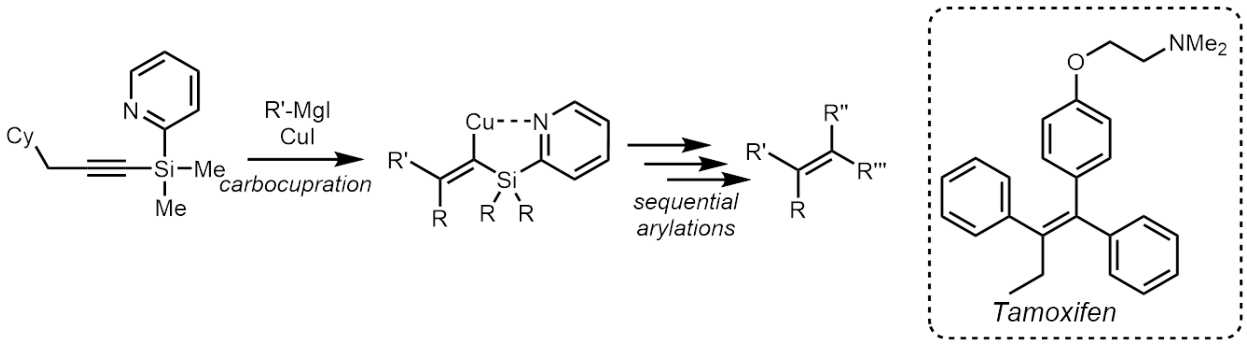
Several estrogen-like compounds are also of current pharmaceutical use. Mestranol and ethinyl estradiol are estrogen compounds that have been used in birth control pills. Mestranol is the biologically inactive pre-drug to ethinyl estradiol, where deprotection of the phenol takes place in the liver. When ethinyl estradiol and mestranol were subjected to the silylation reaction under NaOH-catalyzed conditions, estrone and the corresponding methoxy estrone were the sole products, respectively (Figure 9.7.3). Presumably, the NaOH deprotonates the tertiary OH; the carbonyl is then formed, breaking the C–C bond to the acetylene moiety.



Scheme 9.7.4. Silylation of mestranol produces the alkyne-silylated product as well as an O-protected mestranol analogue.

However, when KOH was used as the catalyst in the silylation of mestranol, two silylated products were formed (Scheme 9.7.4). One product has protection of the tertiary OH; the other product is the desired silylation on the acetylene. This region of the molecule is incredibly sterically congested; *bis*-silylation (as observed in the case of propargyl alcohol) presumably does not occur due to steric hindrance. This silylation reaction is a remarkable example of catalytic silylation of a pharmaceutical molecule in a region of the molecule that is sterically congested. The success of this silylation method in the silylation of pharmaceutical molecules lends promise to late stage C–H silylation for pharmaceutical applications.[67]

Another potential use of this silylation reaction is for the rapid construction of biologically interesting molecules. Since pyridylsilanes work as silicon partners in this reaction, they can be installed to act as valuable directing groups in order to install organometallic reagents onto the alkyne, resulting in tetrasubstituted olefins (Scheme 9.7.5).



Scheme 9.7.5. Using dimethylsilylpyridine to silylate an acetylene-containing molecule is synthetically valuable, since this installed pyridine can act as a directing group for metallation of the alkyne. An example of a biologically relevant tetrasubstituted olefin is Tamoxifen, an estrogen suppressor used for hormone therapy after cancer treatment.

9.8 Summary of Alkyne Silylation

A novel cross-dehydrogenative C–H functionalization employing readily available and inexpensive Earth-abundant metal catalysts is disclosed. The method allows for the direct coupling of C(*sp*)–H bonds and silane Si–H bonds to make acetylinic C–Si bonds in a single step. The overall catalysis is highly efficient: it proceeds under mild conditions, in the absence of hydrogen acceptors or other additives, and liberates dihydrogen as the sole byproduct - no competing hydrosilylation is observed. The scope of the method is broad, enabling the direct silylation of aromatic and aliphatic acetylenes in the presence of a wide array of valuable functional groups. The method proceeds in the presence of electron rich and electron deficient aromatic heterocycles, π-conjugated systems, various heteroatoms, alkyl- and aryl halides, and organometallic scaffolds. Substrate classes such as nitrogen heterocycles that are challenging to activate with known transition metal

catalysis strategies are functionalized in good yields. Facile scalability, low cost, and excellent scope make this an attractive method for either large scale synthesis of versatile building blocks or late-stage functionalization of advanced intermediates and lead compounds. TONs of nearly 100 are achieved demonstrating the remarkably high, albeit unanticipated efficiency and activity of the catalysis.

The details of the underlying mechanistic manifold are not well understood at this point; however, preliminary studies suggest that the mechanism of this C(*sp*)-H silylation is different from that of the KO*t*-Bu-catalyzed C-H silylation of heteroarenes.[Xref Nature 4a]. In contrast to the heteroarene silylation, neither radical trapping additives (i.e., TEMPO) nor the addition of a cation chelant molecule (in this case 15-crown-5) hampered alkyne silylation reaction.

Although a deprotonative functionalization could hypothetically be possible, such reactions have generally required very strong alkyl (e.g., *n*-BuLi) or amide (e.g., $NaNH_2$) bases, electrophilic silicon sources (e.g., Si–Cl), and are not catalytic.[14][49][50] Thus, our empirical observations do not seem to agree well with previously proposed mechanisms for alkyne silylation suggesting that a new C(*sp*)–H bond functionalization mechanism may be operative.

In conclusion, I have developed a novel, procedurally-convenient, and mild C(*sp*)–H bond functionalization methodology enabling ready access to valuable and versatile organosilane building blocks. The remarkably powerful, albeit surprising, Earth-abundant metal hydroxide-catalyzed cross-dehydrogenative silylation is compatible with twelve different hydrosilanes, many of which have been unreported in C–H silylation catalysis, including synthetically versatile pyridylsilanes, greatly increasing the scope and utility relative to previous methods. The scope of the acetylene fragment is broad, and the coupling occurs in high yield and with exceptional selectivity in the presence of aryl- and alkyl halides, ethers, amines, olefins, enynes, diynes, organometallics, strained rings, pyridines, acidic hydrogens, and electron-rich aromatic heterocycles making this method attractive for materials science, pharmaceuticals, and natural product synthesis applications. Overall, the facile scalability, low catalyst cost, simple purification, consistently good yields, and high robustness makes this a promising C–H functionalization method for the preparation of versatile silicon-containing chemical building blocks.

Part IV

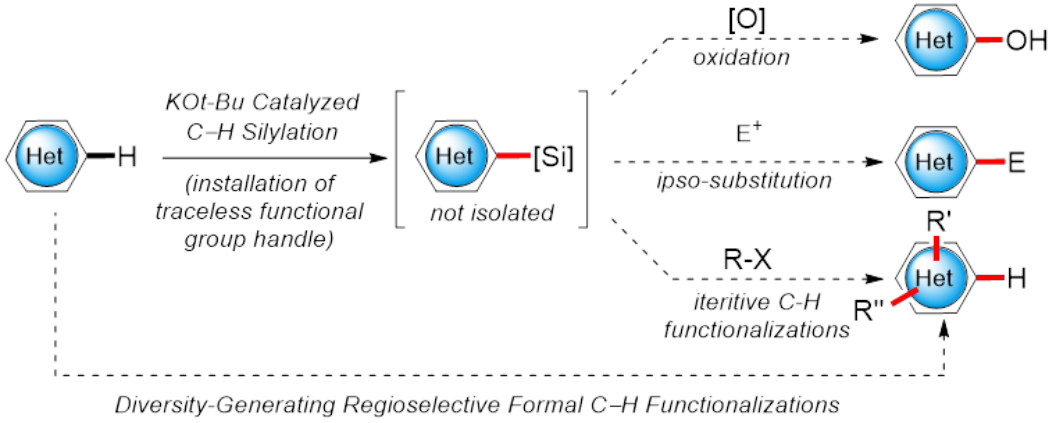
Conclusions

Chapter 10

Discussion and Conclusions

The herein described Earth-abundant-metal–catalyzed C–H functionalization appears to be a remarkably general method for the direct silylation of numerous *sp*, sp^2, and sp^3 C-H bonds. The reaction proceeds in the absence of precious metal precatalysts, complex ligand systems, sacrificial olefin H_2 acceptors, other additives, and (optionally) solvent.

The catalytic system is tolerant of O_2, moisture, amines and even phosphines, and produces only H_2 as the byproduct. The silylated products themselves tend to be thermally and hydrolytically robust,[14][15][22] which makes them particularly useful as versatile chemical building blocks. Moreover, the C–Si bond can be transformed under mild conditions into an array of useful functionalities;[7][14] and the organosilicon byproducts are generally non-toxic.[7][14][15][68] These are attractive properties, especially when compared to the corresponding organoboronic acids or esters (hydrolytic instability),[9][10] organostannanes (toxicity),[14][15][36][69][70] and organolithium or magnesium reagents (reactivity).[12][7][14][15][25][27][28][71][72][73][74][75] Owing to the simplicity of the reaction mixtures, high procedural convenience, and excellent tolerance of the reaction to ambient conditions and various heteroatoms, it is expected that this Earth-abundant-metal–catalyzed C-H silylation should lend itself well to one-pot and tandem reactions such as oxidation, directed electrophilic substitutions, and iterative C-H functionalization chemistries (Scheme 11.1).



Scheme 11.1. Transformation of an *in situ* installed Si functional group handle: formal regiocontrolled C-H functionalizations.

Bibliography

[1] Showell, G. A. and Mills, J. S. Chemistry challenges in lead optimization: silicon isosteres in drug discovery. *Drug Discov. Today* **8,** 551–556 (2003).

[2] Franz, A. K. and Wilson, S. O. Organosilicon molecules with medicinal applications. *J. Med. Chem.* **56,** 388–405 (2013).

[3] Ball, L. T., Lloyd-Jones, G. C. and Russell, C. A. Gold-catalyzed direct arylation. *Science* **337,** 1644–1648 (2012).

[4] Denmark, S. E. and Baird, J. D. Palladium-catalyzed cross-coupling reactions of silanolates: a paradigm shift in silicon-based cross-coupling reactions. *Chem. Eur. J.* **12,** 4954–4963 (2006).

[5] Langkopf, E. and Schinzer, D. Uses of silicon-containing compounds in the synthesis of natural products. *Chem. Rev.* **95,** 13751408 (1995).

[6] Zhang, F., Wu, D., Xu, Y. and Feng, X. Thiophene-based conjugated oligomers for organic solar cells. *J. Mater. Chem.* **21,** 1759017600 (2011).

[7] Weber, W. P. *In Silicon reagents for Organic Synthesis*; Springer Verlag: Berlin, 1983; Vol. 14, p 114–128.

[8] Brook, M. *Silicon in Organic, Organometallic, and Polymer Chemistry*, Wiley: New York, 2000, p 569.

[9] Fleming, I. *Science of Synthesis*; Thieme: Stuttgart, 2002; Vol. 4, p 685.

[10] Hartwig, J. F. Borylation and Silylation of CH Bonds: A Platform for Diverse C–H Bond Functionalizations. *Acc. Chem. Res.*, **45,** 864–873 (2012).

[11] a) Showell, G. A.; Mills, J. S. Chemistry challenges in lead optimization: silicon isosteres in drug discovery. *Drug Discov. Today* **8,** 551–556 (2003). b) Franz, A. K.; Wilson, S. O. Organosilicon molecules with medicinal applications. J. *Med. Chem.*, **56,** 388–405 (2013).

[12] Whisler, M. C.; MacNeil, S.; Snieckus, V.; Beak, P. Beyond thermodynamic acidity: A perspective on the complex-induced proximity effect (CIPE) in deprotonation reactions. *Angew. Chem. Int. Ed.*, **43,** 2206–2225 (2004).

[13] Wang, Y.; Watson, M. D. Transition-metal-free synthesis of alternating thiophene-perfluoroarene copolymers. *J. Am. Chem. Soc.*, **128,** 2536–2537 (2006).

[14] Colvin, E. *Silicon in Organic Synthesis*; Butterworth: New York, 1981; p 125.

[15] Snieckus, V. Directed Ortho Metalation. Tertiary Amide and O–Carbamate Directors in Synthetic Strategies for Polysubstituted Aromatics. *Chem. Rev.*, **90,** 879–933 (1990).

[16] Cheng, C.; Hartwig, F. Iridium-Catalyzed Silylation of Aryl CH Bonds. *J. Am. Chem. Soc.*, **137,** 592–595 (2015).

[17] Lu, B.; Falck, J. R. Efficient iridium-catalyzed C–H functionalization/silylation of heteroarenes. *Angew. Chem. Int. Ed.* **47,** 7508–7510 (2008).

[18] Cheng, C.; Hartwig, J. F. Rhodium-catalyzed intermolecular C–H silylation of arenes with high steric regiocontrol. *Science* **343,** 853–857 (2014).

[19] Cheng, C.; Hartwig, F. Mechanism of the Rhodium-Catalyzed Silylation of Arene C–H Bonds. *J. Am. Chem. Soc.* **136,** 12064–12072 (2014).

[20] Tamao, K., Uchida, M., Izumizawa, T., Furukawa, K. and Yamaguchi, S. Silole derivatives as efficient electron transporting materials. *J. Am. Chem. Soc.* **118,** 11974–11975 (1996).

[21] Ting, R., Adam, M. J., Ruth, T. J. and Perrin, D. M. Arylfluoroborates and alkylfluorosilicates as potential PET imaging agents: high-yielding aqueous biomolecular 18F-labeling. *J. Am. Chem. Soc.* **127,** 13094–13095 (2005).

[22] 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*, **518,** 80–84 (2015) (DOI 10.1038/nature14126).

[23] Fedorov, A., Toutov, A. A., Swisher, N. A. and Grubbs, R. H. Lewis-base silane activation: from reductive cleavage of aryl ethers to selective ortho-silylation. *Chem. Sci.*, **4,** 16401645 (2013).

[24] Collins, K. D. and Glorius, F. A robustness screen for the rapid assessment of chemical reactions. *Nature Chem.*, **5,** 597–601 (2013).

[25] Lee, M., Ko, S. and Chang, S. Highly selective and practical hydrolytic oxidation of organosilanes to silanols catalyzed by a ruthenium complex. *J. Am. Chem. Soc.*, **122,** 12011–12012 (2000).

[26] Song, J. J. et al. Organometallic methods for the synthesis and functionalization of azaindoles. *Chem. Soc. Rev.,* **36,** 1120–1132 (2007).

[27] Li, C.-J. and Trost, B. M. Green chemistry for chemical synthesis. *Proc. Natl Acad. Sci. USA*, **105,** 13197–13202 (2008).

[28] Zhao, Z. and Snieckus, V. Directed ortho metalation-based methodology. Halo-, nitroso-, and boro-induced ipso-desilylation. Link to an in situ Suzuki reaction. *Org. Lett.*, **7,** 2523–2526 (2005).

[29] Hansen, M. M. et al. Lithiated benzothiophenes and benzofurans require 2-silyl protection to avoid anion migration. *Synlett*, **8,** 1351–1354 (2004).

[30] Wang, Y. and Watson, M. D. Transition-metal-free synthesis of alternating thiophene-perfluoroarene copolymers. *J. Am. Chem. Soc.*, **128,** 2536–2537 (2006).

[31] Seregin, I. V. and Gevorgyan, V. Direct transition metal-catalyzed functionalization of heteroaromatic compounds. *Chem. Soc. Rev.*, **36,** 1173–1193 (2007).

[32] Kuznetsov, A., Onishi, Y., Inamoto, Y. and Gevorgyan, Y. Fused heteroaromatic dihydrosiloles: synthesis and double-fold modification. *Org. Lett.* **15,** 2498–2501 (2013).

[33] Showell, G. A.; Mills, J. S. Chemistry challenges in lead optimization: silicon isosteres in drug discovery. *Drug Discov. Today*, **8,** 551–556 (2003).

[34] Franz, A. K.; Wilson, S. O. Organosilicon molecules with medicinal applications. *J. Med. Chem.*, **56,** 388–405 (2013).

[35] Langkopf, E.; Schinzer, D. Uses of silicon-containing compounds in the synthesis of natural products. *Chem. Rev.*, **95,** 1375–1408 (1995).

[36] de Sa Alves, F. R.; Barreiro, E. J.; M, Fraga; C. Alberto From Nature to Drug Discovery: The Indole Scaffold as a 'Privileged Structure'. *Mini Reviews in Medicinal Chemistry*, **9,** 782–793 (2009).

[37] Studer, A.; Curran, D. P. Organocatalysis and C–H Activation Meet Radical- and Electron-Transfer Reactions. *Angew. Chem. Int. Ed.*, **50,** 5018–5022 (2011).

[38] Sun, C.-L.; Li, H.; Yu, D.-G.; Yu, M.; Zhou, X.; Lu, X.-Y.; Huang, K.; Zheng, S.-F.; Li, B.-J.; Shi, Z.-J. An efficient organocatalytic method for constructing biaryls through aromatic CH activation. *Nature. Chem.*, **2,** 1044–1049 (2010).

[39] Duncton, M. A. J. Minisci reactions: Versatile CH-functionalizations for medicinal chemists. *Med. Chem. Commun.*, **2,** 1135–1161 (2011).

[40] Du, W.; Kaskar, B.; Blumbergs, P.; Subramanian, P. K.; Curran, D. P. *Bioorg. Med. Chem.*, **11,** 451 (2003).

[41] Gilman, H.; Aoki, D.; Wittenberg, D. *J. Am. Chem. Soc.*, **81,** 1107 (1959).

[42] Sore, H. F.; Galloway, W. R. J. D.; Spring, D. R. Palladium-catalysed cross-coupling of organosilicon reagents. *Chem. Soc. Rev.*, **41,** 1845–1866 (2012).

[43] Sakakura, T.; Tokunaga, Y.; Sodeyama, T; Tanaka, M. Catalytic C–H activation. Silylation of arenes with hydrosilane or disilane by $RhCl(CO)(PMe_3)_2$ under irradiation. *Chem. Lett.*, **16,** 2375–2378 (1987).

[44] Chernyak, N.; Dudnik, A. S.; Huang, C.; Gevorgyan, V. PyDipSi: A General and Easily Modifiable/Traceless Si-Tethered Directing Group for CH Acyloxylation of Arenes. *J. Am. Chem. Soc.*, **132,** 8270–8272 (2010).

[45] Ghavtadze, N.; Melkonyan, F. N; Gulevich, A. V.; Huang, C.; Gevorgyan, V. Conversion of 1-alkenes into 1,4-diols through an auxiliary mediated formal homoallylic CH oxidation. *Nature Chem.*, **6,** 122–125 (2014).

[46] Huang, C.; Chernyak, N.; Dudnik, A. S.; Gevorgyan, V. The Pyridyldiisopropylsilyl Group: A Masked Functionality and Directing Group for Monoselective ortho-Acyloxylation and ortho-Halogenation Reactions of Arenes. *Adv. Synth. Catal.*, **353,** 1285–1305 (2011).

[47] Gulevich, A. V.; Melkonyan, F. S.; Sarkar, D.; Gevorgyan, V. Double-Fold CH Oxygenation of Arenes Using PyrDipSi: a General and Efficient Traceless/Modifiable Silicon-Tethered Directing Group. *J. Am. Chem. Soc.*, **134,** 5528–5531 (2012).

[48] (a) Voronkov, M. G.; Ushakova, N. I.; Tsykhanskaya, I. I.; Pukhnarevich, V. B. *J. Organomet. Chem.*, **264,** 39–48 (1984). (b) Liu, H. Q.; Harrod, J. F. *Can. J. Chem.*, **68,** 1100–1105 (1990). (c) Takaki, K.; Kurioka, M.; Kamata, T.; Takehira, K.; Makioka, Y.; Fujiwara, Y. *J. Org. Chem.*, **63,** 9265–9269 (1998). (d) Itoh, M.; Kobayashi, M.; Ishikawa, J. *Organometallics*, **16,** 3068–3070 (1997). (e) Tsuchimoto, T.; Fujii, M.; Iketani, Y.; Sekine, M. *Adv. Synth. Catal.*, **354,** 2959–2964 (2012).

[49] Fleming, I.; Dunogus, J.; Smithers, R. *Org. React.*, **37,** 57 (1989).

[50] Eaborn, C. J. *Organomet. Chem.*, **100,** 43–57 (1975).

[51] Yamaguchi, M.; Hayashi, A.; Minami, T. *J. Org. Chem.*, **56,** 4091–4092 (1991).

[52] (a) Sugita, H.; Hatanaka, Y.; Hiyama, T. *Tetrahedron Lett.*, **36,** 2769–2772 (1995). (b) Sugita, H.; Hatanaka, Y.; Hiyama, T. *Synlett*, 637–639 (1996).

[53] Andreev, A. A.; Konshin, V. V.; Komarov, N. V.; Rubin, M.; Brouwer, C.; Gevorgyan, V. Direct Electrophilic Silylation of Terminal Alkynes. *Org. Lett.*, **6,** 421–424 (2004).

[54] Rahaim, R. J. Jr.,Shaw, J. T., *J. Org. Chem.*, **73(7),** 2912–2915 (2008).

[55] Yamaguchi, K.; Wang, Y.; Oishi, T.; Kuroda, Y.; Mizuno, N. *Angew. Chem. Int. Ed.*, **52,** 5627–5630 (2013).

[56] Jiang, H.; Zhu, S. *Tet. Lett.*, **46,** 517–519 (2005).

[57] Tsuchimoto, T., Fujii, M., Iketani, Y., Sekine, M. *Adv. Synth. Catal.* **354,** 2959–2964 (2012).

[58] Fuchikami, T.; Shimizu, R. *Tet. Lett.*, **41,** 907–910 (2000).

[59] Dudziec, B.; Marciniec, B. *Organometallics*, **27,** 5598–5604 (2008).

[60] (a) Hein, S. J.; Arslan, H.; Keresztes, I.; Dichtel, W. R. *Org. Lett.*, **16,** 4416–4419 (2014). (b) R. Gleiter, D. B. Werz, Chem. Rev. **110,** 44474488 (2010). (c) Phillips, A. J.; Keaton, K. A. *J. Am. Chem. Soc.*,, **128,** 408–409 (2006).

[61] (a) Marsden, J. A.; Miller, J. J.; Shirtcliff, L. D.; Haley, M. M. *J. Am. Chem. Soc.*, **127,** 24642476 (2005). (b) Matsuda, T.; Kadowaki, S.; Goya, T.; Murakami, M. *Org. Lett.*,, **9,** 133–136 (2007).

[62] (a) Wang, J.; Gurevich, Y.; Botoshansky, M.; Eisen, M. S. *J. Am. Chem. Soc.*, **128,** 9350–9351 (2006). (b) Kim, M.; Park, S.; Maifeld, S. V.; Lee, D. *J. Am. Chem. Soc.*, **126,** 10242–10243 (2004). (c) Baba, T.; Kato, A.; Takahashi, H.; Toriyama, F.; Handa, H. Ono, Y.; Sugisawa, H. *J. Catal.*, **176,** 488–494 (1998).

[63] (a) Lukevics, E.; Rubina, K.; bele, E.; Fleisher, M; Arsenyan, P.; Grnberga, S.; Popelis, J. *J. Organomet. Chem.*, **634,** 69–73 (2001). (b) Severin, R., Reimer, J.; Doye, S. *J. Org. Chem.*, **75,** 3518–3521 (2010). (c) Sakai, N.; Komatsu, R.; Uchida, N.; Ikeda, R.; Konakahara, T. *Org. Lett.*, **12,** 1300–1303 (2010). d) Aikawa, K.; Hioki, Y.; Mikami, K. *Org. Lett.*, **12,** 5716–5719 (2010). (e) Trost, B. M.; Rudd, M. T.; Costa, M. G.; Lee, P. I.; Pomerantz, A. E. *Org. Lett.*, **6,** 4235–4238 (2004). (f) Brand, J. P.; Gonzlez, D. F.; Nicolai, S.; Waser, *J. Chem. Commun.*, **47,** 102–115 (2011).

[64] (a) Chinchilla, R.; Njera, C. *Chem. Soc. Rev.*, **40,** 5084–5121 (2011). (b) Shi Shun, A. L. K; Tykwinski, R. R. *Angew. Chem. Int. Ed.*, **45,** 1034–1057 (2006). (c) Langkopf, E.; Schinzer, D. *Chem. Rev.*, **95,** 1375–1408 (1995). (d) Denmark, S. E.; Yang, S.-M. *J. Am. Chem. Soc.*, **126,** 12432–12440 (2004). (e) Trost, B. M.; Frederiksen, M. U.; Pappilon, J. P. N.; Harrington, P. E.; Shin, S.; Shireman, B. T. *J. Am. Chem. Soc.*, **127,** 3666–3667 (2005). (f) Mujahidin, D.; Doye, S. *Eur. J. Org. Chem.*, 2689–2693 (2005). (g) O'Neil, G. W.; Phillips, A. G. *J. Am. Chem. Soc.*, **128,** 5340–5341 (2006).

[65] Wong, H. N. C.; Hon, M.; Tse, C.; Yip, Y.; Tanko, J.; Hudlicky, T. *Chem. Rev.*, **89,** 165–198 (1989).

[66] Cheng, Y.-J.; Shang, S.-J.; Hsu, C.-S. *Chem. Rev.*, **109 (11),** pp 5868–5923 (2009).

[67] (a) Franz, A. K.; Wilson, O. S. *J. Med. Chem.*, **56,** 388–405 (2013). (b) Showell, G. A.; Mills, J. S. *Drug Discov. Today*, **8,** 551–556 (2003).

[68] (a) Hiyama, T. *Metal-Catalysed Cross-Coupling Reactions,* Wiley-VCH, Weinheim, 421–453 (1998). (b) Tsuji, J. *Palladium Reagents and Catalysts,* John Wiley and Sons, Chichester, 338–351 (2004). (c) Denmark, S. E. The Interplay of Invention, Discovery, Development, and Application in Organic Synthetic Methodology: A Case Study. *J. Org. Chem.*, **74,** 2915–2927 (2009).

[69] (a) McNeill, E.; Barder, T. E.; Buchwald, S. L. Palladium-Catalyzed Silylation of Aryl Chlorides with Hexamethyldisilane. *Org. Lett.*, **9,** 3785–3788 (2007). (b) Ishiyama, T.; Sato, K.; Nishio, Y.; Saiki, T.; Miyaura, N. Regioselective aromatic C–H silylation of five-membered heteroarenes with fluorodisilanes catalyzed by iridium(I) complexes. *Chem. Commun.*, 5065–5067 (2005).

[70] Song, J. J. et al. Organometallic methods for the synthesis and functionalization of azaindoles. *Chem. Soc. Rev.*, **36,** 1120–1132 (2007).

[71] a) Studer, A.; Curran, D. P. Organocatalysis and C–H Activation Meet Radical- and Electron-Transfer Reactions. *Angew. Chem. Int. Ed.*, **50,** 5018–5022 (2011). b) Sun, C.-L.; Li, H.; Yu, D.-G.; Yu, M.; Zhou, X.; Lu, X.-Y.; Huang, K.; Zheng, S.-F.; Li, B.-J.; Shi, Z.-J. An efficient organocatalytic method for constructing biaryls through aromatic CH activation. *Nature. Chem.*, **2,** 1044–1049 (2010).

[72] a) Bronner, S. M.; Mackey, J. L.; Houk, K. N.; Garg, N. K. Steric Effects Compete with Aryne Distortion To Control Regioselectivities of Nucleophilic Additions to Silylarynes. *J. Am. Chem. Soc.*, **134,** 13966–13969 (2012). b) Tadross, P.; Stoltz, B. M. A Comprehensive History of Arynes in Natural Product Total Synthesis. *Chem. Rev.* **112,** 3550–3577 (2012). c) Wenk, H. H.; Winkler, M.; Sander, W. One Century of Aryne Chemistry. *Angew. Chem. Int. Ed.*, **42,** 502–528 (2003). d) Bronner, S. M.;

Goetz, A. E.; Garg, N. K. Understanding and Modulating Indolyne Regioselectivities. *Synlett*, 2599–2604 (2011). e) Bronner, S. M.; Goetz, A. E.; Garg, N. K. Overturning Indolyne Regioselectivities and Synthesis of Indolactam V. *J. Am. Chem. Soc.*, **133,** 3832–3835 (2011).

[73] Ball, L. T.; Lloyd-Jones, G. C.; Russell, C. A. Gold-catalyzed direct arylation. *Science*, **337,** 1644–1648 (2012).

[74] Nakao, Y.; Hiyama, T. Silicon-based cross-coupling reaction: an environmentally benign version. *Chem. Soc. Rev.*, **40,** 4893–4901 (2011).

[75] *Science of Synthesis (Houben-Weyl)*; Fleming, I., Ed.; Georg Thieme Verlag: Stuttgart, Germany, 2002; Vol. 4, Chapter. 4.4.

[76] Pangborn, A. M.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics*, **15,** 1518 (1996).

[77] (a) Kong, A.; Han, X.; Lu, X. *Org. Lett.*, **8,** 1339 (2006). (b) Islam, S.; Larrosa, I. *Chem. - Eur. J.*, **19,** 15093 (2013). (c) Huestis, M. P.; Fagnou, K. *Org. Lett.*, **11,** 1357 (2009). (d) Mahadevan, I.; Rasmussen, M. *Tetrahedron*, **49,** 7337 (1993).

Appendix A

Experimental

A.1 General Information

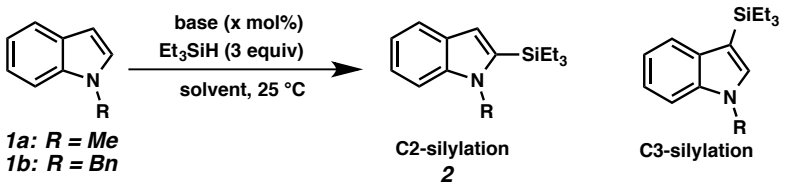
Unless otherwise stated, reactions were performed in oven-dried brand-new Fisherbrand scintillation vials in a nitrogen filled glove box or in flamed-dried Schlenk flasks under argon connected on a Schlenk line using dry, degassed solvents and brand-new stirring bars. Solvents were dried by passage through an activated alumina column under argon.[**?**] 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 KMnO4 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 C6D6 and are reported relative to residual solvent peak at 7.26 ppm or 7.16 ppm respectively. ^{1}3C 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 ^{1}3C NMR are reported in terms of chemical shifts (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 mmHg). 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.[7]7

Part I. Reaction optimizations, control experiments and trace metal analysis.

1. Reaction optimization.

Procedure for reaction condition optimization: In a nitrogen-filled glovebox, base and indole **1** (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 ^{1}H NMR or GC analysis of the crude mixture using an internal standard.

Table 1. Condition optimization of direct C–H silylation of indoles.



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
24 [c,e]	Bn	KOTMS	THF	20	72	>20:1	79

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

The results from Table 1 reveal 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 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). Headspace GC-TCD analysis of successful silylation reactions indicated the formation of H_2.

2. Control experiments and trace metal analysis.

Careful experiments were conducted in order to rule out catalysis by adventitious transition metal impurities in the reaction mixture [see below (1) – (3)].

*(1) Control reactions with commercially available KO*t*-Bu, re-sublimed KO*t*-Bu, and freshly-prepared KO*t*-Bu.* Three 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.

(2) Control reaction with KOt-Bu of different grade purchased from different vendors. Four reactions were 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 (Figure 1).

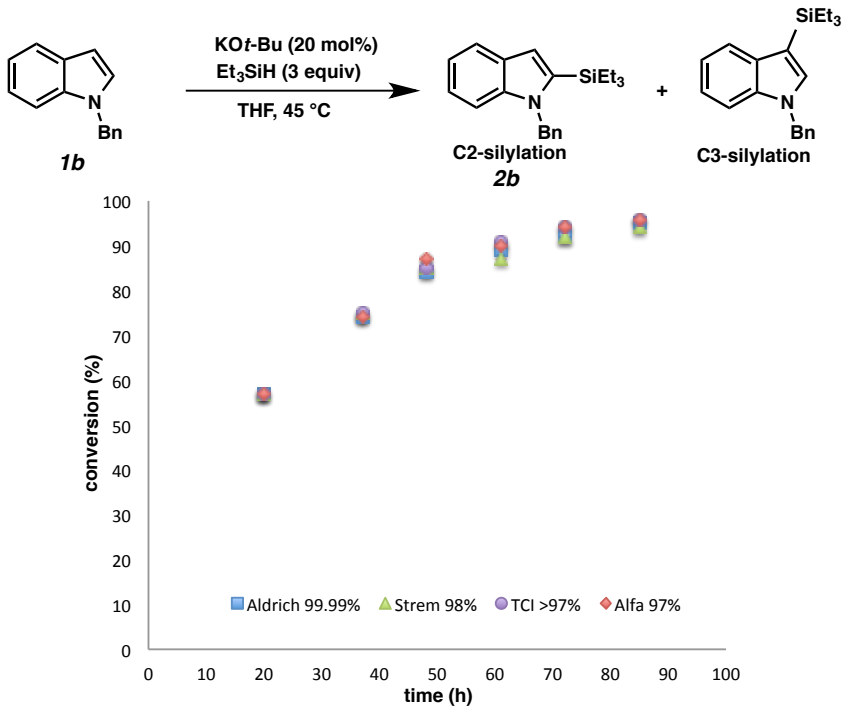


Figure 1. The results of with KO*t*-Bu purchased from different vendors

(3) ICP-MS trace metal analysis of all the reaction components. To provide further support against involvement of adventitious trace metal species in the C–H activation

catalysis, inductively coupled plasma mass spectrometry was performed on samples of KO*t*-Bu from different vendors, 1-benzylindole starting material, THF, Et_3SiH and a standard reaction mixture that was run under optimal conditions in the glove box ("Rxn Mixture" in Table 2). 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). Microgram per liter (ppb) quantities of metal contaminants are given in Table 2.

Table 2. ICP-MS trace metal 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 ^oC 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. LOD indicates that the analyte concentration is below the instrument's *Lowest Limit of Detection*. Values in ppb (*microgram per liter*).

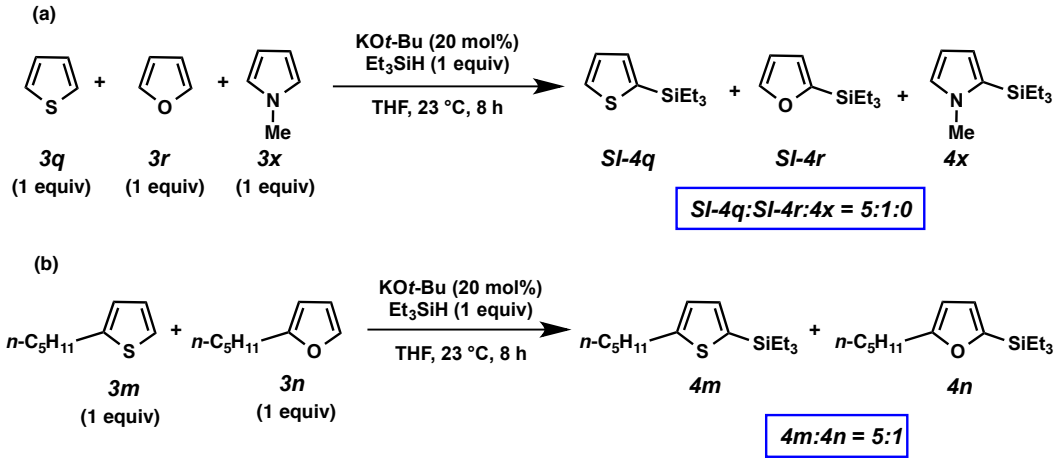
ICPMS Trace Metal Analysis – Agilent 7900 (quantities in ppb)								
Element	**KO*t*-Bu Strem (98%)**	**KO*t*-Bu TCI (>97%)**	**KO*t*-Bu Alpha (97%)**	**KO*t*-Bu Aldrich (99.99%)**	**THF**	**$HSiEt_3$**	**1-Bn-indole**	**Rxn Mixture**
Ti	0.360	0.051	0.138	0.464	LOD	2.073	9.408	31.082
Mn	1.343	1.168	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

Part II. Competition experiments and evaluation of functional group compatibility.

1. Competition experiments with thiophene, furan and pyrrole.

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 1). 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 **3q** > furan **3r** > 1-methylpyrrole **3x** (Scheme 1a). This trend is corroborated in the competition between substituted thiophene **3m** and furan **3n**, as shown in Scheme 1b.

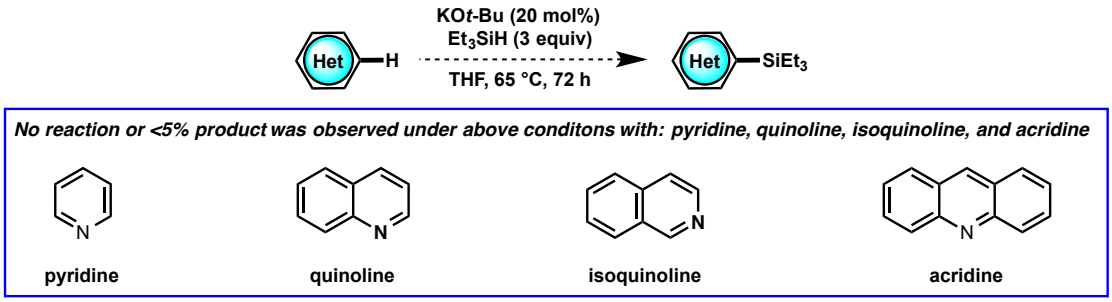


Scheme 1. Competition experiments

Procedures for competition experiments as shown in Figure 1: *For reaction (a)*: In a nitrogen-filled glove box, KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), thiophene **3q** (42.1 mg, 0.5 mmol, 1 equiv), furan **3r** (34.0 mg, 0.5 mmol, 1 equiv) and 1-methylpyrrole **3x**

(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 ^{1}H NMR revealed that the ratio of **SI-4q**:**SI-4r**:**4x** was 5:1:0. *For reaction (b):* In a nitrogen-filled glove box, KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2-pentylthiophene **3m** (77.0 mg, 0.5 mmol, 1 equiv), and 2-pentylfuran **3n** (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 ^{1}H NMR revealed that the ratio of **4m**:**4n** was 5:1.

2. Reactions with electron-deficient heteroarenes.

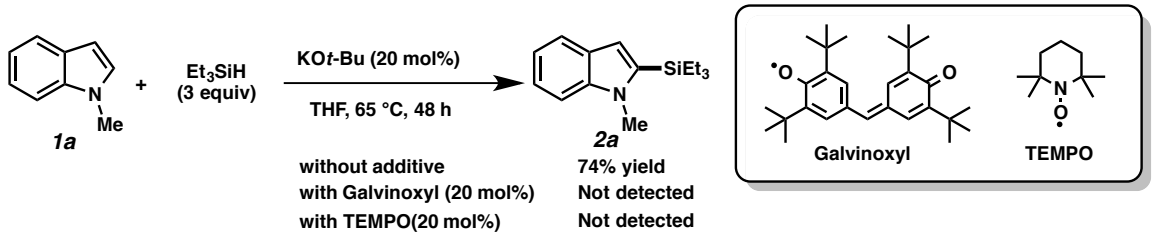


Scheme 2. Examples of unreactive pyridine derivatives

Pyridine derivatives would be expected to react readily if a conventional silyl radical addition process was operational. However, the above substrates were unreactive under the KO*t*-Bu–catalyzed C–H silylation conditions. 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.

3. Investigation into the radical nature of the KO*t*-Bu–catalyzed C–H silylation.

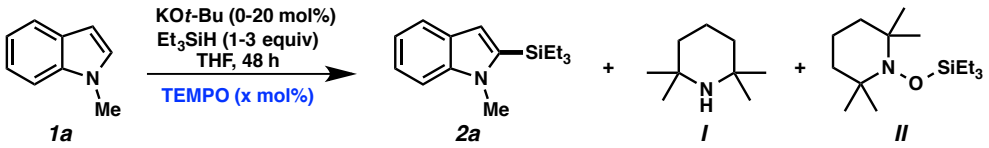
A number of experiments were conducted to gain insight into the reaction mechanism. As a first investigation, we decided to probe whether the silylation reaction was polar or radical in nature. We began by performing our reaction in the presence of the radical traps TEMPO and galvinoxyl. Both additives thwarted the C–H silylation (Scheme 3).



Scheme 3. Control reactions with radical traps

Subsequently, we conducted three control experiments in an attempt to probe the role of TEMPO (Table 3). A trace amount of triethylsilyl protected product **II** was observed at 23 °C with 1 equivalent of TEMPO (entry 5), presumably arising from the radical combination of a silyl radical and TEMPO itself. Product **II** 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 protected compound **II** is not observed in the absence of KO*t*-Bu, indicating that the catalyst is critical to generate the silyl radical (entry 2).

Table 3. Control experimental results with TEMPO.

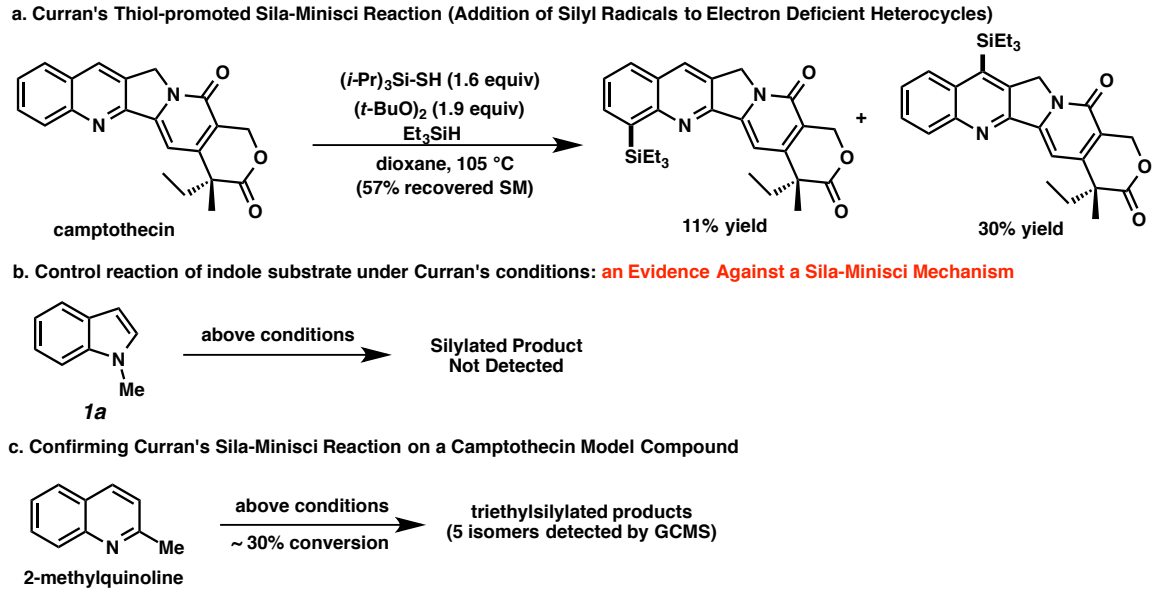


entry	*1a*	TEMPO (mol%)	KO*t*-Bu (mol%)	$HSiEt_3$ (equiv)	Temp (°C)	*2a* (%)	*I*	*II*
1	–	100	–	1	23	ND[a]	ND[a]	ND[a]
2	–	100	–	1	65	ND[a]	ND[a]	ND[a]
3	1	20	20	3	23	ND[a]	ND[a]	ND[a]
4	1	20	20	3	65	ND[a]	ND[a]	ND[a]
5	–	100	20	1	23	ND[a]	trace[b]	trace[b]
6	–	100	20	1	65	ND[a]	minor[b]	major[b]

[a] Not detected; [b] Determined by GCMS analysis.

Although 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

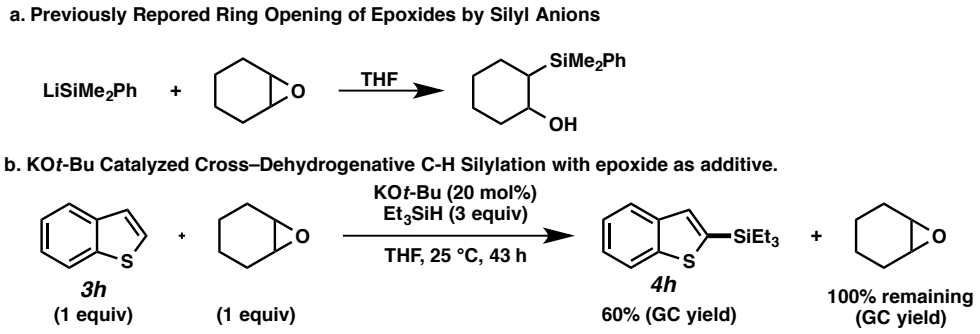
reaction could proceed by an elementary addition of a silyl radical to a heterocycle (i.e., sila-Minisci reaction). To probe this hypothesis, we subjected 1-methylindole **1a** to a mixture of reagents under conditions that are reported by the Curran group[3] to generate discrete silyl radicals (*see Scheme 4a for Curran's conditions, and Scheme 4b for the result of indole **1a** under these conditions*). Interestingly, no silylated product of any kind was detected in this reaction (Scheme 4b). Conversely, we confirmed that the Curran's conditions do silylate with electron poor heterocycles (such as 2-methyl quinoline, Scheme 4c), but our method fails in the case of these substrates (*vide supra*, Supplementary Information Part 12).



Scheme 4. Control experiments under sila-Minisci reaction conditions

To provide further evidence against a polar mechanism (i.e., formation of silyl anions), our KO*t*-Bu–catalyzed reaction with benzothiophene **3h** as a substrate was conducted in the presence of cyclohexene oxide as an additive (epoxides, including cyclohexene oxide, are known to undergo nucleophilic ring opening by silyl anions, Scheme 5a).[4] However, under our conditions, the epoxide is quantitatively recovered after the reaction, and the desired silylation product **4h** was obtained in moderate yield (Scheme 5b), providing evidence against the formation of discrete silyl anions.

(3) Du, W.; Kaskar, B.; Blumbergs, P.; Subramanian, P. K.; Curran, D. P. *Bioorg. Med. Chem.* **2003**, *11*, 451.
(4) Gilman, H.; Aoki, D.; Wittenberg, D. *J. Am. Chem. Soc*. **1959**, *81*, 1107.



Scheme 5. Control experiments with cyclohexene oxide

In summary, based on the results of control reactions with radical traps (Scheme 3) and the observation of TEMPO-$SiEt_3$ **II** (Table 3), 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 Scheme 2 and Scheme 4, an elementary radical generation/addition mechanism (i.e., sila-Minisci reaction) is likely not operative. The survival of the epoxide additive (Scheme 5) is inconsistent with the silyl anion pathway. Taken together, these preliminary studies point to a previously unreported (hetero)aromatic C–H functionalization mechanism. Efforts to elucidate the mechanism by experimental and computational methods are underway.

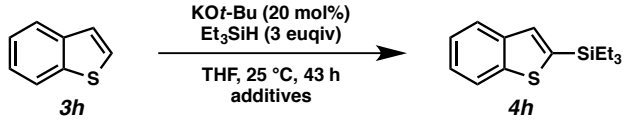
4. Evaluation of functional group compatibility.

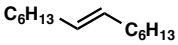
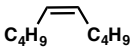
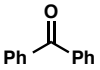
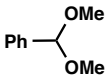
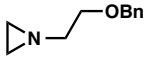
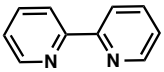
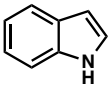
In order to provide a comprehensive treatment of functional group tolerance for the silylation reaction, a "robustness screen" as per the method of Glorius has been performed (Table 4).[5] Certain generalizations can be made from the results. For example, carbonyl groups shut down the reaction (entries 16, 17). Nevertheless, protection as an acetal, such as benzaldehyde dimethyl acetal is well tolerated (entry 18). Aryl-X groups where X = Br, I, CN, NO_2 likewise thwart the reactivity (entries 7, 8, 19 and 20). Intriguingly, these functional groups remain intact in most cases. However, alkene, alkyne, Ar-F, Ar-Cl, Ar-CF_3, tertiary amine, pyridine, and phosphine moieties are compatible (entries 2–6, 9, 11, 23–26). No obvious hydrosilylation or reduction of alkene and alkyne occurs. Even free OH and NH groups are tolerated to some extent

(5) Collins, K. D.; Glorius, F. *Nature Chem*. **2013**, *5*, 597.

presumably due to a fortuitous silylative protection of the heteroatom *in situ*, which was confirmed by using BnOTES as an additive (entries 12, 13, and 15).

Table 4. Examining of the functional groups and heterocycles compatibility.[a]



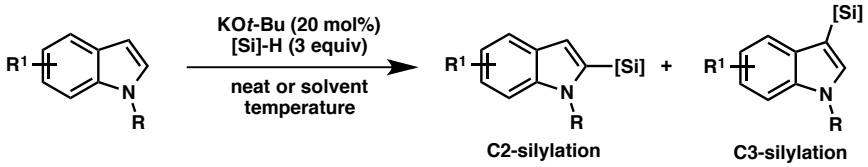
entry	additive (1.0 equiv)	*4h* yield (%)	*3h* remaining (%)	additive remaining (%)	entry	additive (1.0 equiv)	*4h* yield (%)	*3h* remaining (%)	additive remaining (%)
1[b]	_	99	0	_	14	PhOH	0	63	91
2		95	0	95	15	BnOTES	60	37	89
3		67	31	97	16		0	83	91
4		83	26	99	17	$PhCO_2Me$	0	87	84
5	PhF	95	5	N.D.[c]	18		82	0	50[f]
6	PhCl	74	25	100	19	$PhNO_2$	0	86	98
7	PhBr	0	89	100	20	PhCN	0	85	81
8	PhI	0	91	86	21		60	35	100
9	$PhCF_3$	90	10	N.D.[c]	22		40	53	100
10	$PhNMe_2$	80	20	79	23		71	28	N.D.[c]
11	*n*-Bu_3N	38	55	100	24		47	50	100
12		19	73	N.D.[c,d]	25		0	92	99
13	BnOH	31	60	0[e]	26	PPh_3	48	50	97

[a] The reaction was performed with 0.5 mmol of **3h** and 0.5 mmol of additive under the general procedure. 0.5 mmol of tridecane was added as an internal standard at the start of the reaction. Yield of product, remaining amounts of **3h** and additive were determined by GC-FID analyses. [b] Control reaction without the addition of additive. [c] Not determined (overlapped with solvent peak due to the low boiling point). [d] Triethyl silyl protected morpholine was formed and confirmed by GCMS analysis. [e] BnOTES was formed. [f] Acetal partially hydrolyzed to PhCHO.

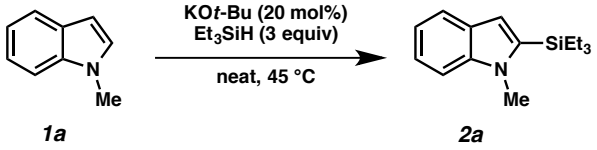
Moreover, epoxide and aziridine are tolerated as well and nucleophilic ring opening of these additives was not observed (entries 21, 22). In conclusion, these results demonstrate that a wide array of versatile organic functionalities is tolerated in the KO*t*-Bu–catalyzed silylation reaction. This is encouraging for the application of the current method to alkaloid natural product synthesis and pharmaceutical science applications either at an early stage or for advanced intermediate functionalization.

Part III. Experimental and analytics.

1. General procedure for KO*t*-Bu–catalyzed silylation and characterization data.

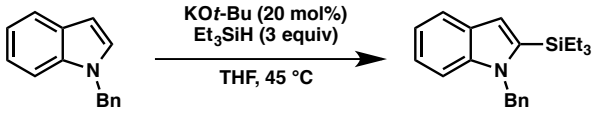


In a nitrogen-filled glove box, KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%) and indole (0.5 mmol, 1 equiv) were added to a 2 dram scintillation vial equipped with a magnetic stirring bar, [*solvent was added if indicated, see the details below*], followed by silane (1.5 mmol, 3 equiv, *filtered through a short 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.



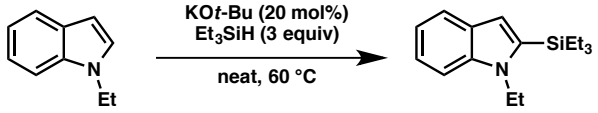
1-Methyl-2-(triethylsilyl)-1*H*-indole 2a: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-methylindole **1a** (65.5 mg, 0.5 mmol, 1 equiv) and Et_3SiH (243 μL, 1.5 mmol, 3 equiv) at 45 °C for 96 h. C2:C3 > 20:1. The desired product **2a** (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); ^{1}H 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.



1b *2b*

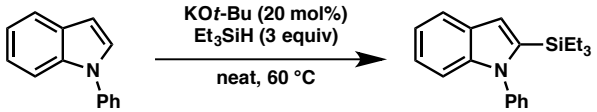
1-Benzyl-2-(triethylsilyl)-1*H*-indole 2b: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-benzylindole **1b** (103.5 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 40 h. C2:C3 > 20:1. The desired product **2b** (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, $CDCl_3$) 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.



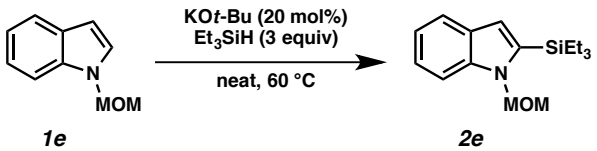
1c *2c*

1-Ethyl-2-(triethylsilyl)-1*H*-indole 2c: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-ethylindole **1c** (72.5 mg, 0.5 mmol, 1 equiv), and Et_3SiH (243 μL, 1.5 mmol, 3 equiv) at 60 °C for 84 h.

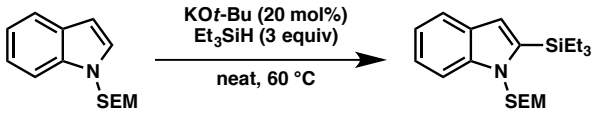
C2:C3 > 20:1. The desired product **2c** (92.4 mg, 71% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (5% CH_2Cl_2 in hexanes). R_f = 0.4 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (dt, *J* = 7.9, 0.9 Hz, 1H), 7.40 (dt, *J* = 8.2, 0.9 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.



1-Phenyl-2-(triethylsilyl)-1*H*-indole 2d: The general procedure was followed. The reaction was performed with KO*t*-Bu (7.4 mg, 0.07 mmol, 20 mol%), *N*-phenylindole **1d** (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 **2d** (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); ^{1}H 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.

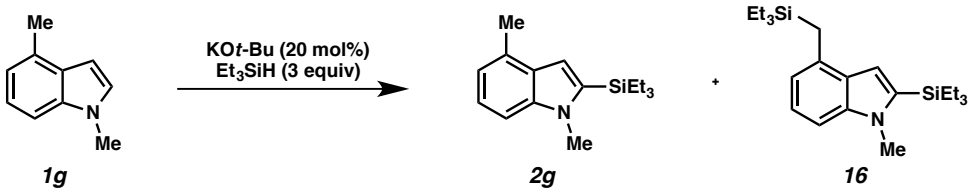


1-(Methoxymethyl)-2-(triethylsilyl)-1*H*-indole 2e: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-methoxymethylindole **1e** (80.5 mg, 0.5 mmol, 1 equiv) and Et_3SiH (243 μL, 1.5 mmol, 3 equiv) at 60 °C for 84 h. C2:C3 = 10:1. The desired product **2e** (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.



1f *2f*

2-(Triethylsilyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-indole 2f: 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 **1f** (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 **2f** (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.



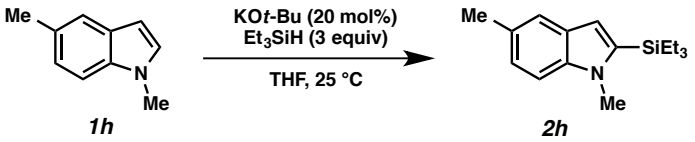
condition A: THF, 25 °C, 120 h:	48%	5%
condition B: neat, 45 °C, 84 h:	69%	–

The general procedure was followed. *For condition A*: The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 4-methyl-*N*-methylindole **1g** (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 **2g** (61.8 mg, 48% yield) and bis-silylation **16** (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%), 4-methyl-*N*-methylindole **1g** (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 **2g** (89.7 mg, 69% yield) was formed and obtained after purification by silica gel flash chromatography (3% CH_2Cl_2 in hexanes).

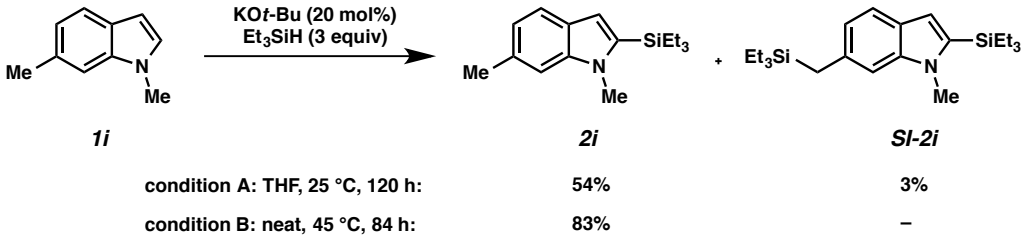
1,4-Dimethyl-2-(triethylsilyl)-1*H*-indole 2g: Colorless oil; R_f = 0.4 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 – 7.14 (m, 2H), 6.91 (dt, *J* = 6.7, 1.0 Hz, 1H), 6.75 (d, *J* = 0.9 Hz, 1H), 3.85 (s, 3H), 2.60 (s, 3H), 1.07 – 1.00 (m, 9H), 0.98 – 0.92 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) 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 16: 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 $C_{22}H_{39}NSi_2$ [$M^{\bullet+}$]: 373.2621, found 373.2624.



1,5-Dimethyl-2-(triethylsilyl)-1*H*-indole 2h: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 5-methyl-*N*-methylindole **1h** (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 **2h** (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); ^1H 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.

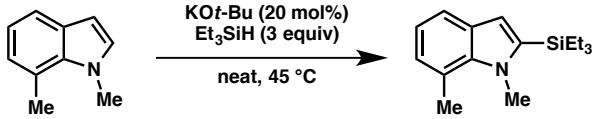


The general procedure was followed. *For condition A*: The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 6-methyl-*N*-methylindole **1i** (72.5 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 120 h. C2:C3 > 20:1. The desired mono silylation product **2i** (69.5 mg, 54% yield) and bis-silylation **SI-2i** (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-*N*-methylindole **1i** (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 **2i** (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 2i: 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, $CDCl_3$) 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.

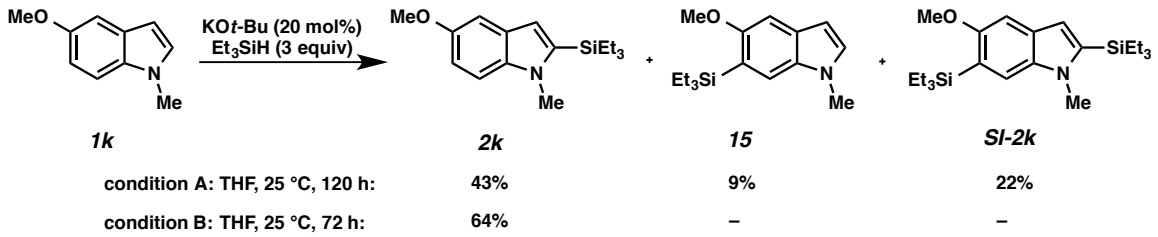
1-Methyl-2-(triethylsilyl)-6-((triethylsilyl)methyl)-1*H*-indole SI-2i: Colorless oil; R_f = 0.4 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, C_6D_6) δ 7.64 (dd, *J* = 7.9, 0.8 Hz, 1H), 6.99 – 6.93 (m, 2H), 6.81 (d, *J* = 0.9 Hz, 1H), 3.41 (s, 3H), 2.31 (s, 2H), 1.02 – 0.93 (m, 18H), 0.79 (q, *J* = 7.7 Hz, 6H), 0.58 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 141.9, 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.



1j *2j*

1,7-Dimethyl-2-(triethylsilyl)-1*H*-indole 2j: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 7-methyl-*N*-methylindole **1j** (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 **2j** (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); ^{13}C 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.



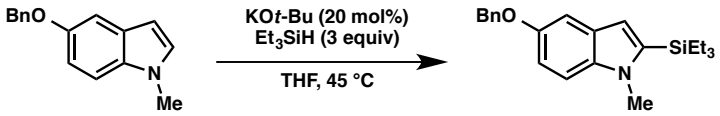
The general procedure was followed. *For condition A*: The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-methyl-5-methoxyindole **1k** (80.7 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 120 h. C2:C3 > 20:1. The C2-silylation product **2k** (58.7 mg, 43% yield), C6-silylation product **15** (12.5 mg, 9% yield), and bis-silylation product **SI-2k** (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 **1k** (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 **2k** (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 2k: White solid; R_f = 0.2 (33% CH_2Cl_2 in hexanes); ^1H 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 SI-2k: White solid, R_f = 0.6 (33% CH_2Cl_2 in hexanes); ^1H 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

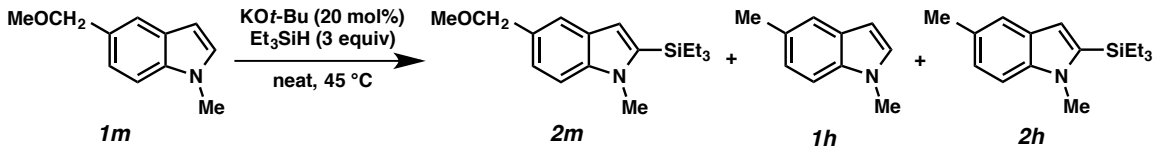
NMR (125 MHz, $CDCl_3$) δ 159.1, 138.9, 136.1, 130.1, 120.8, 116.3, 112.2, 99.7, 55.5, 33.2, 7.9, 7.7, 4.3, 4.1. IR (Neat Film, NaCl) 2952, 2874, 2908, 1608, 1556, 1475, 1454, 1407, 1363, 1337, 1236, 1205, 1172, 1144, 1123, 1072, 1004, 971, 837 cm^{-1}; HRMS (ESI+) calc'd for $C_{22}H_{40}NOSi_2$ $[M+H]^+$: 390.2643, found 390.2632.

5-Methoxy-1-methyl-6-(triethylsilyl)-1*H*-indole 15: Colorless oil; R_f = 0.4 (33% CH_2Cl_2 in hexanes); ^1H 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.



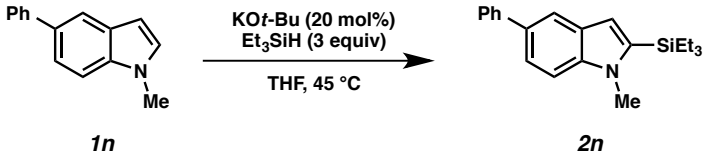
1l *2l*

5-(Benzyloxy)-1-methyl-2-(triethylsilyl)-1*H*-indole 2l: 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 **1l** (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 **2l** (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.



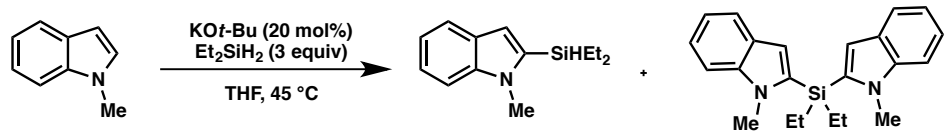
The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 5-(methoxymethyl)-*N*-methylindole **1m** (87.5 mg, 0.5 mmol, 1 equiv) and Et_3SiH (243 μL, 1.5 mmol, 3 equiv) at 45 °C for 84 h. C2:C3 > 20:1. The desired product **2m** (69.3 mg, 48% yield), byproducts **1h** (2.5 mg, 2% yield) and **2h** (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*-indole 2m: 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.



1-Methyl-5-phenyl-2-(triethylsilyl)-1*H*-indole 2n: 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 **1n** (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 **2n** (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.

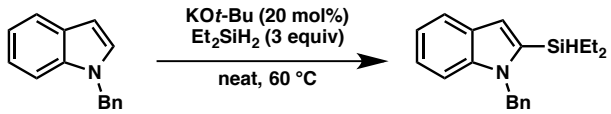


1a ***2o*** ***SI-2o***

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 **2o** (73.4 mg, 68% yield) and a minor bisindolyl silane byproduct **SI-2o** were obtained after purification by silica gel flash chromatography (gradient elution, 1→2→5% CH_2Cl_2 in hexanes).

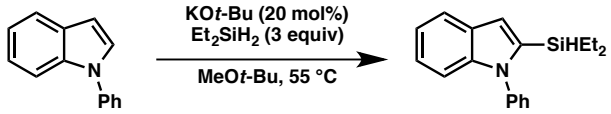
2-(Diethylsilyl)-1-methyl-1*H*-indole 2o: Colorless oil; R_f = 0.4 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.37 (dt, *J* = 8.3, 1.1 Hz, 1H), 7.28 – 7.25 (m, 1H), 7.16 – 7.09 (m, 1H), 6.79 (d, *J* = 0.9 Hz, 1H), 4.50 – 4.43 (m, 1H), 3.88 (s, 3H), 1.14 – 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 SI-2o: Colorless oil; R_f = 0.2 (10% CH_2Cl_2 in hexanes); ^{1}H 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.



1b *2p*

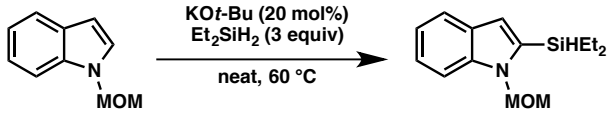
1-Benzyl-2-(diethylsilyl)-1*H*-indole 2p: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-benzyl indole **1b** (103.5 mg, 0.5 mmol, 1 equiv) and Et_2SiH_2 (194 μL, 1.5 mmol, 3 equiv) at 60 °C for 72 h. C2:C3 > 20:1. The desired product **2p** (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); ^{1}H 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.



1d *2q*

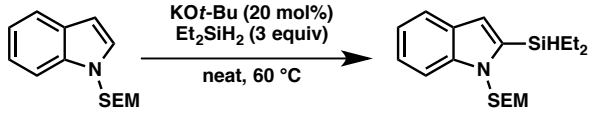
2-(Diethylsilyl)-1-phenyl-1*H*-indole 2q: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-phenyl indole **1d** (96.5 mg, 0.5 mmol, 1 equiv), Et_2SiH_2 (194 μL, 1.5 mmol, 3 equiv), and 0.5 mL of MeO*t*-Bu at 55 °C for 96 h. C2:C3 > 20:1. The desired product **2q** (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.



1e *2r*

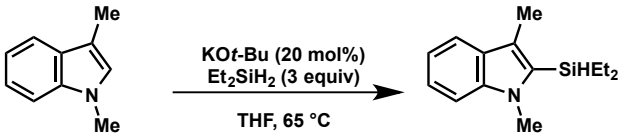
2-(Diethylsilyl)-1-(methoxymethyl)-1*H*-indole 2r: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-methoxymethylindole **1e** (80.5 mg, 0.5 mmol, 1 equiv) and Et_2SiH_2 (193 μL, 1.5 mmol, 3 equiv) at 60 °C for 96 h. C2:C3 > 20:1. The desired product **2r** (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.



1f *2s*

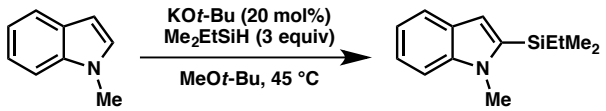
2-(Diethylsilyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-indole 2s: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-(2-trimethylsilyl-ethoxymethyl)-1*H*-indole **1f** (123.5 mg, 0.5 mmol, 1 equiv) and Et_2SiH_2 (194 μL, 1.5 mmol, 3 equiv) 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.



1t *2t*

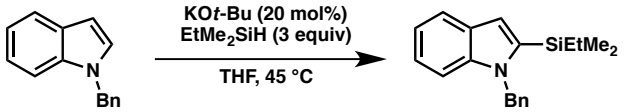
2-(Diethylsilyl)-1,3-dimethyl-1*H*-indole 2t: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1,3-dimethyl-1*H*-indole **1t** (72.6 mg, 0.5 mmol, 1 equiv), Et_2SiH_2 (193 µL , 1.5 mmol, 3 equiv), and 0.5 mL of THF at 65 °C for 120 h. The desired product **2t** (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.



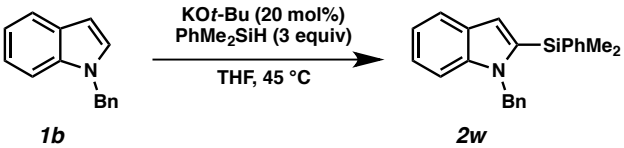
1a *2u*

2-(Ethyldimethylsilyl)-1-methyl-1*H*-indole 2u: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-methylindole **1a** (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 **2u** (58.5

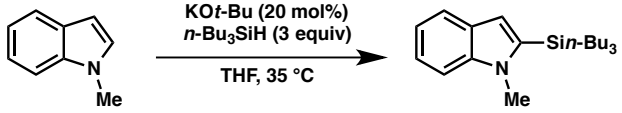
mg, 54% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (3% CH_2Cl_2 in hexanes). R_f = 0.4 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.37 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.28 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 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.



1-Benzyl-2-(ethyldimethylsilyl)-1*H*-indole 2v: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-benzylindole **1b** (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 **2v** (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.

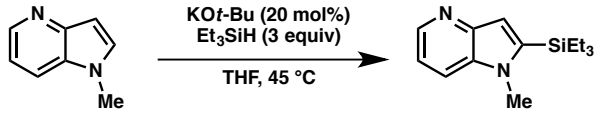


1-Benzyl-2-(dimethyl(phenyl)silyl)-1*H*-indole 2w: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-benzylindole **1b** (103.5 mg, 0.5 mmol, 1 equiv), $PhMe_2SiH$ (230 μL, 1.5 mmol, 3 equiv) and 0.5 mL of THF at 45 °C for 96 h. C2:C3 > 20:1. A mixture of starting material **1b** and product **2w** (*174.5 mg of mixture, contains 133.9 mg of **2w**, 78% yield, calculated based on ^1H NMR*) was obtained after purification by silica gel flash chromatography (2% EtOAc in hexanes). *Analytically pure compound **2w** 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.



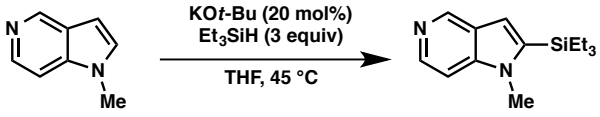
1-Methyl-2-(tributylsilyl)-1*H*-indole 2x: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-methylindole **1a** (65.6 mg, 0.5 mmol, 1 equiv), *n*-Bu_3SiH (385 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 35 °C for 65 h. C2:C3 > 20:1. The desired product **2x** (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). ^{1}H 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



3a ***4a***

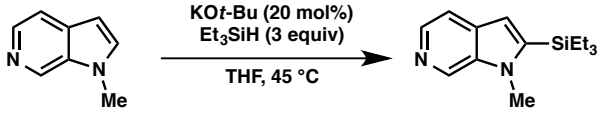
1-Methyl-2-(triethylsilyl)-1*H*-pyrrolo[3,2-*b*]pyridine 4a: The general procedure was followed. The reaction was performed with KO*t*-Bu (4.5 mg, 0.04 mmol, 20 mol%), *N*-methyl-4-azaindole **3a** (26.4 mg, 0.2 mmol, 1 equiv), Et_3SiH (98 μL, 0.6 mmol, 3 equiv) and 0.2 mL of THF at 45 °C for 96 h. C2:C3 = 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 **4a** 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.



3b ***4b***

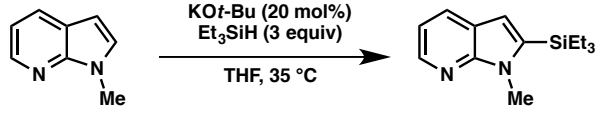
1-Methyl-2-(triethylsilyl)-1*H*-pyrrolo[3,2-*c*]pyridine 4b: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-methyl-5-azaindole **3b** (66.0 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 120 h. C2:C3 > 20:1. The desired product **4b** (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.



3c *4c*

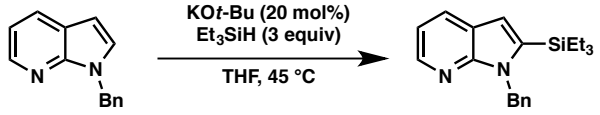
1-Methyl-2-(triethylsilyl)-1*H*-pyrrolo[2,3-*c*]pyridine 4c: The general procedure was followed. The reaction was performed with KO*t*-Bu (5.8 mg, 0.52 mmol, 20 mol%), *N*-methyl-6-azaindole **3c** (35.0 mg, 0.26 mmol, 1 equiv), Et_3SiH (126 μL, 0.78 mmol, 3 equiv), and 0.3 mL of THF at 45 °C for 94 h. C2:C3 > 20:1. The desired product **4c** (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); ^{1}H 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.



3d *4d*

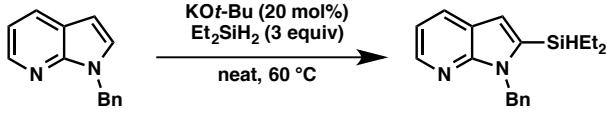
1-Methyl-2-(triethylsilyl)-1*H*-pyrrolo[2,3-*b*]pyridine 4d: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-methyl-7-azaindole **3d** (66 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 35 °C for 63 h. C2:C3 > 20:1. The desired product **4d** (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.



3e ***4e***

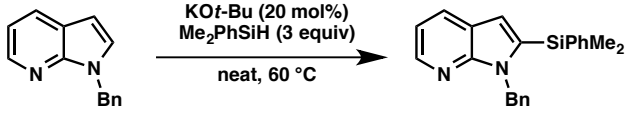
1-Methyl-2-(triethylsilyl)-1*H*-pyrrolo[2,3-*b*]pyridine 4e: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-benzyl-7-azaindole **3e** (104.0 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 144 h. C2:C3 > 20:1. The desired product **4e** (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); ^1H 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.



3e ***4f***

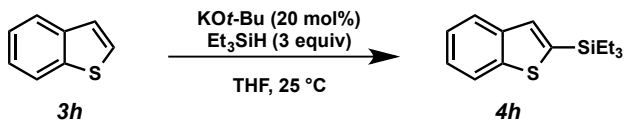
1-Benzyl-2-(diethylsilyl)-1*H*-pyrrolo[2,3-*b*]pyridine 4f: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-benzyl-7-azaindole **3e** (104.5 mg, 0.5 mmol, 1 equiv) and Et_2SiH_2 (194 μL, 1.5 mmol, 3 equiv) at 60 °C for 84 h. C2:C3 > 20:1. The desired product **4f** (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 295.1636.



3e ***4g***

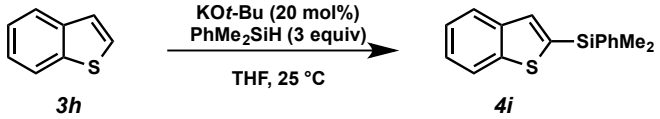
1-Benzyl-2-(dimethyl(phenyl)silyl)-1*H*-pyrrolo[2,3-*b*]pyridine 4g: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), *N*-benzyl-7-azaindole **3e** (103.9 mg, 0.5 mmol, 1 equiv) and $PhMe_2SiH$ (230 μL, 1.5 mmol, 3 equiv) at 60 °C for 96 h. C2:C3 > 20:1. The desired product **4g** (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.



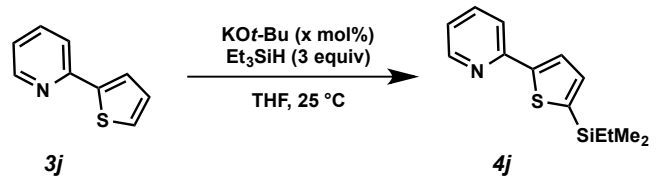
3h ***4h***

Benzo[*b*]thiophen-2-yltriethylsilane 4h: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), benzo[*b*]thiophene

3h (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 **4h** (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); this compound is known.[6] ^{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).



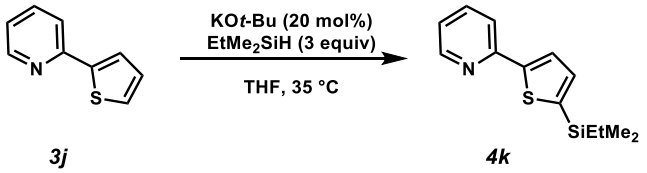
Benzo[*b*]thiophen-2-yldimethyl(phenyl)silane 4i: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), benzo[*b*]thiophene **3h** (67.0 mg, 0.5 mmol, 1 equiv), $PhMe_2SiH$ (230 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 60 h. The desired product **4i** (116.6 mg, 87% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). R_f = 0.5 (100% hexanes); this compound is known.[3] ^{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).



2-(5-(Triethylsilyl)thiophen-2-yl)pyridine 4j: 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 **3j** (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 **4j** (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 **3j** (0.81 g, 5 mmol, 1 equiv),

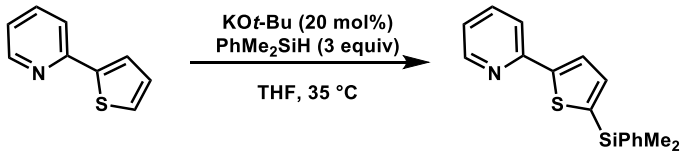
(6) Lu, B.; Falck, J. R. *Angew. Chem. Int. Ed.* **2008**, *47*, 7508

Et_3SiH (2.43 mL, 15 mmol, 3 equiv), and 3.0 mL of THF at 25 °C for 96 h. The desired product **4j** (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.



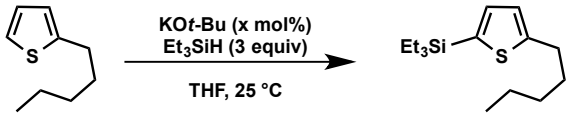
3j *4k*

2-(5-(Ethyldimethylsilyl)thiophen-2-yl)pyridine 4k: 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 **3j** (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 **4k** (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.



3j *4l*

2-(5-(Dimethyl(phenyl)silyl)thiophen-2-yl)pyridine 4l: 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 **3j** (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 **4l** (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.

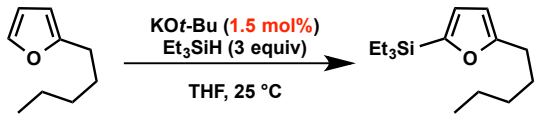


3m *4m*

condition A: 0.5 mmol, 20 mol% KO*t*-Bu, 48 h 96%
condition B: 5 mmol, 1 mol% KO*t*-Bu, 96 h 92%

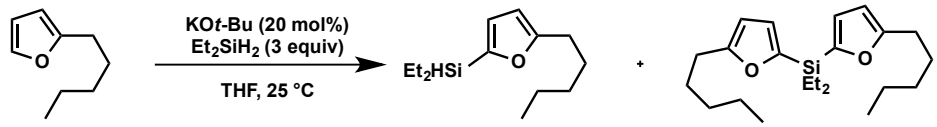
Triethyl(5-pentylthiophen-2-yl)silane 4m: The general procedure was followed. *Condition A*: The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2-pentylthiophene **3m** (77.0 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 48 h. The desired product **4m** (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 **3m** (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 **4m** (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.



3n *4n*

Triethyl(5-pentylfuran-2-yl)silane 4n: The general procedure was followed. The reaction was performed with KO*t*-Bu (8.4 mg, 0.075 mmol, 1.5 mol%), 2-pentylfuran **3n** (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 **4n** (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, 0.9 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.

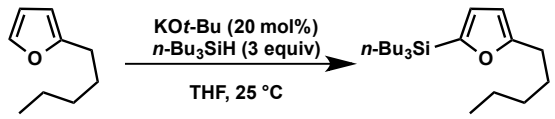


3n *4o* *SI-4o*

The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2-pentylfuran **3n** (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 **4o** (87.4 mg, 78% yield) and silicon-tethered product **SI-4o** (12.4 mg, 8% yield) were obtained after purification by silica gel flash chromatography (100% hexanes).

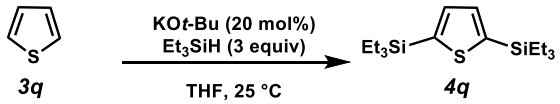
Diethyl(5-pentylfuran-2-yl)silane 4o: Colorless oil, R_f = 0.6 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.63 (d, *J* = 3.1 Hz, 1H), 6.00 (dt, *J* = 3.1, 0.9 Hz, 1H), 4.21 (p, *J* = 3.2 Hz, 1H), 2.75 – 2.64 (m, 2H), 1.73 – 1.62 (m, 2H), 1.38 – 1.32 (m, 4H), 1.11 – 1.04 (m, 6H), 0.95 – 0.90 (m, 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 SI-4o: 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.

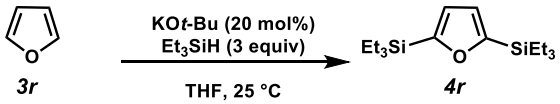


3n ***4p***

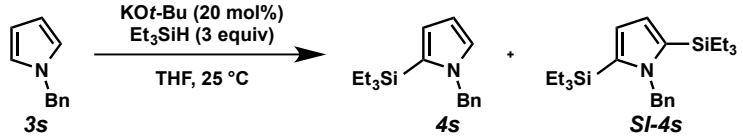
Tributyl(5-pentylfuran-2-yl)silane 4p: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 2-pentylfuran **3n** (69.1 mg, 0.5 mmol, 1 equiv), *n*-Bu_3SiH (386 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 108 h. The desired product **4p** (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 4q: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), thiophene **3q** (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 **4q** (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); this compound is known.[3] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (s, 2H), 1.02 – 0.99 (m, 18H), 0.83 – 0.79 (m, 12H).



2,5-Bis(triethylsilyl)furan 4r: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), furan **3r** (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 **4r** (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); this compound is known.[3] ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.66 (s, 2H), 1.09 – 0.95 (m, 18H), 0.86 – 0.70 (m, 12H).

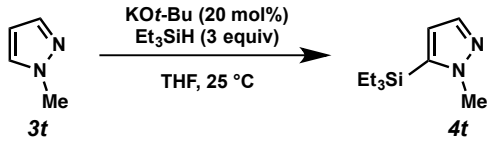


The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-benzyl-1*H*-pyrrole **3s** (78.5 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 108 h. The desired product **4s** (100.3 mg, 74% yield) and bis-silylation product **SI-4s** (9.6 mg, 5%) were obtained after purification by silica gel flash chromatography (100% hexanes).

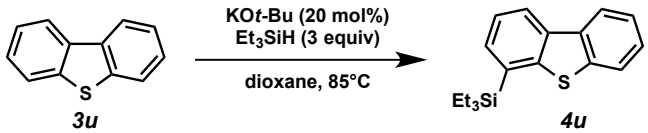
1-Benzyl-2-(triethylsilyl)-1*H*-pyrrole 4s: Colorless oil, R_f = 0.3 (100% hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 2H), 7.32 – 7.25 (m, 1H), 7.04 – 6.98 (m, 2H), 6.86 (dd, *J* = 2.4, 1.5 Hz, 1H), 6.51 (dd, *J* = 3.5, 1.5 Hz, 1H), 6.30 (dd, *J* = 3.4, 2.4 Hz,

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 SI-4s: 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.



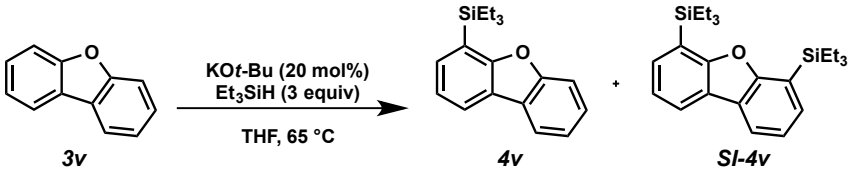
1-Methyl-5-(triethylsilyl)-1*H*-pyrazole 4t: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-methyl-1*H*-pyrazole **3t** (41.1 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 25 °C for 120 h. The desired product **4t** (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); this compound is known.[7] ^{1}H 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).



Dibenzo[*b,d*]thiophen-4-yltriethylsilane 4u: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), dibenzothiophene

(7) Despotopoulou, C.; Klier, L.; Knochel, P *Org. Lett.* **2009**, *11*, 3326

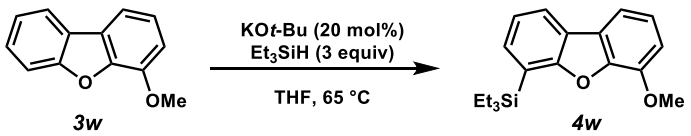
3u (92 mg, 0.5 mmol, 1.0 equiv), Et_3SiH (243 μL, 1.5 mmol, 3.0 equiv), and 3 mL of dioxane at 85 °C for 72 h. The desired product **4u** (55.4 mg, 38% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes). R_f = 0.7 (100% hexanes); ^{1}H NMR (500 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.



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 **3v** (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 **4v** (100.2 mg, 71% yield) and bis-silylated product **SI-4v** (6.9 mg, 4% yield) were obtained after purification by silica gel flash chromatography (100% hexanes).

Dibenzo[*b,d*]furan-4-yltriethylsilane 4v: Colourless oil, R_f = 0.6 (100% hexanes); This compound is known.[8] ^{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 SI-4v: White solid, R_f = 0.7 (100% hexanes); This compound is known.[5] ^{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).



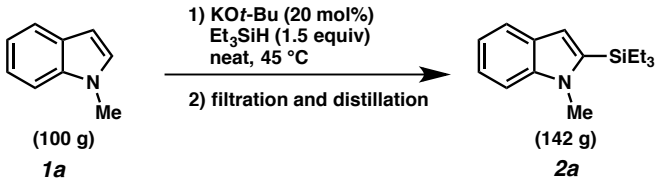
Triethyl(6-methoxydibenzo[*b,d*]furan-4-yl)silane 4w: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 4-

(8) Fedorov, A.; Toutov, A. A.; Swisher, N. A.; Grubbs, R. H. *Chem. Sci.* **2013**, *4*, 1640.

methoxydibenzo[*b*,*d*]furan **3w** (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 **4w** (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.

2. Multi-gram scale syntheses of 2a, 4h and 4n.

2.1. Procedure for the multi-gram scale synthesis of 2a.



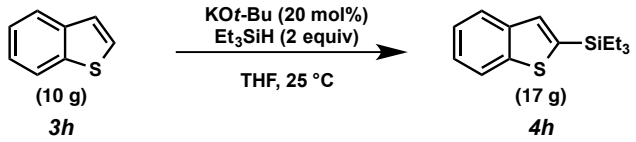
A 500 mL oven-dried Schlenk flask equipped with a stir bar and stoppered with a rubber septum was evacuated and refilled once with argon. KO*t*-Bu (18.8 grams, 167.9 mmols, 20 mol%) was weighed out on the bench and added to the flask under a strong flow of argon. The charged flask was then evacuated 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 millitorr) 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 millitorr as the solution boils. Forerun comes off as pale yellow oil. Thermometer reads 65–80 °C.
b) Vacuum stabilizes at 180 millirtorr. 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 millitorr as a pale yellow oil. Thermometer reads 80–85 °C.
d) Increase temperature to 160 °C, vacuum at 100 millitorr to distil over the desired 2-triethylsilyl-1-methylindole (pale yellow oil). Thermometer reads 110–120 °C.

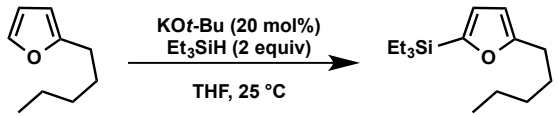
The desired product **2a** is obtained as a pale yellow oil (141.88 g, 76% yield).

2.2. Procedure for the multi-gram scale synthesis of 4h.



In a nitrogen-filled glove box, KO*t*-Bu (1.7 g, 15 mmol, 20 mol%), benzo[*b*]thiophene **3h** (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 millitorr, 23 °C)*. The desired product **4h** (17.3 g, 93% yield) was obtained as a colorless oil after purification by silica gel flash chromatography (100% hexanes).

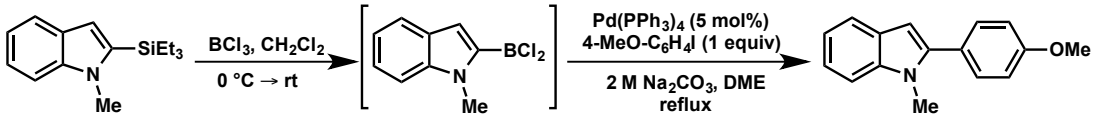
2.3. Procedure for the multi-gram scale synthesis of 4n.



(10 g) ***3n*** (17 g) ***4n***

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 millitorr, 23 °C) and purification by silica gel flash chromatography (100% hexanes).

3. One-pot Si-directed *ipso*–substitution/Suzuki–Miyaura cross-coupling.



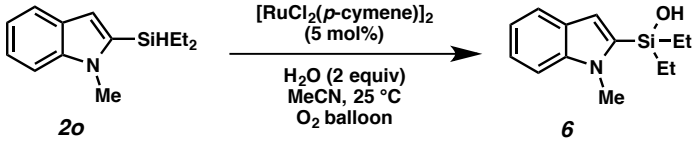
2a ***5***

Followed a modified known procedure:[9] 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 **2a** (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 **5** (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). This compound is known.[10] 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,

(9) Zhao, Z.; Snieckus, V. *Org. Lett*. **2005**, *7*, 2523.
(10) Denmark, S. E.; Baird, J. D. *Org. Lett*. **2004** , *6*, 3649.

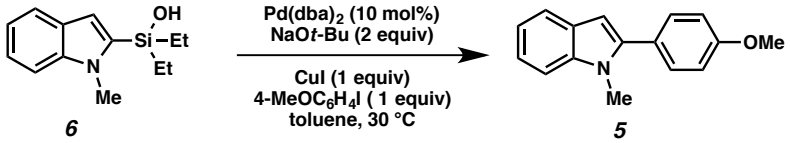
1.2 Hz, 1H), 7.14 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.05 – 6.96 (m, 2H), 6.51 (br s, 1H), 3.88 (s, 3H), 3.73 (s, 3H).

4. Synthesis of a heteroarylsilanol and application in Denmark–Hiyama cross-coupling.



2o *6*

Diethyl(1-methyl-1*H*-indol-2-yl)silanol 6: Followed a modified known procedure.[11] Compound **2o** (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 **6** (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.



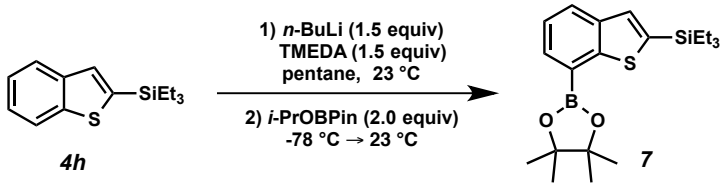
6 *5*

2-(4-Methoxyphenyl)-1-methyl-1*H*-indole 5: Followed a modified known procedure.[10] In a nitrogen-filled glovebox, a 2 dram vial equipped with a stir bar was charged with

(8) Lee, M.; Ko, S.; Chang, S. *J. Am. Chem. Soc*. **2000**, *122*, 12011.

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 **6** (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 **5** (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).

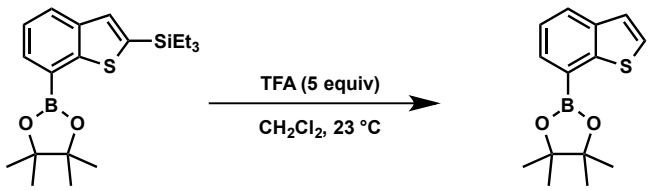
5. Direct C7 lithiation-borylation by a Si-blocking group strategy.



Triethyl(7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzo[b]thiophen-2-yl)silane 7: Followed a modified known procedure.[12] 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 **4h** (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

(9) Hansen, M.; Clayton, M.; Godfrey, A.; Grutsch, Jr. J.; Keast, S.; Kohlman, D.; McSpadden, A.; Pedersen, S.; Ward, J.; Xu, Y.-C. *Synlett*, **2004**, *8*, 1351

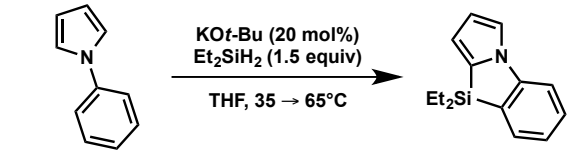
with NH_4Cl (5 mL). The mixture was extracted with Et_2O (3 x 10 mL), the combined organic fractions were washed with brine, dried over $MgSO_4$, filtered, and the solvent was evaporated to give a viscous brown liquid. The desired product **7** (926 mg, 64% yield) was obtained as a colorless solid after 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.



7 *8*

2-(Benzo[*b*]thiophen-7-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 8: Followed a modified known procedure.[9] 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 **7** (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 **8** (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.

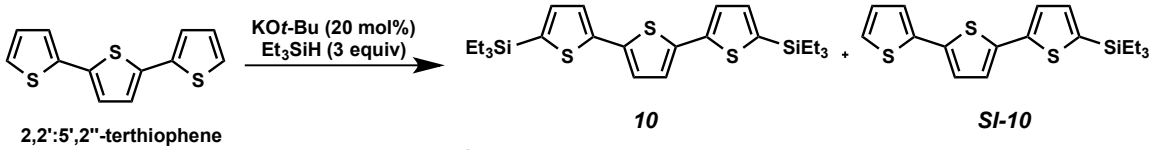
6. Synthesis of a sila-heterocycle by inter-/intramolecular double C–H silylation.



1-phenyl-1*H*-pyrrole — ***9***

9,9-Diethyl-9*H*-benzo[d]pyrrolo[1,2-*a*][1,3]azasilole 9: 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 **9** (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.

7. C–H silylation of terthiophene and EDOT.



2,2':5',2''-terthiophene — ***10*** — ***SI-10***

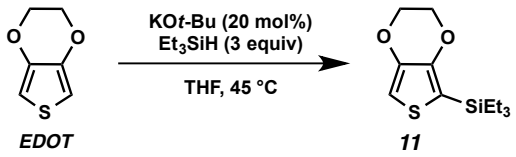
condition A: THF, 25 °C, 40 h — 86% — 13%
condition B: THF, 45 °C, 65 h — 96% — trace

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 **10** (204.7 mg, 86% yield) and **SI-10** (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 **10** (228.6 mg, 96% yield) was obtained after purification by silica gel flash chromatography (100% hexanes); **SI-10** 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 10: 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 SI-10: 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.

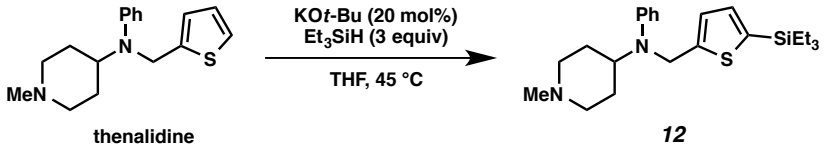


EDOT *11*

(2,3-Dihydrothieno[3,4-b][1,4]dioxin-5-yl)triethylsilane 11: 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 **11** (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,

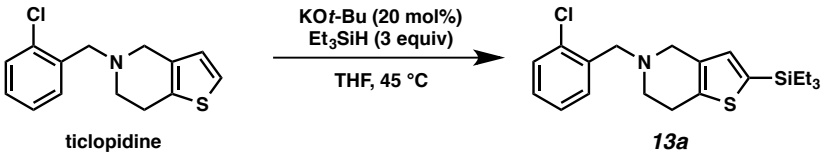
1042, 1009, 899, 721 cm^{-1}; HRMS (EI+) calc'd for $C_{12}H_{21}O_2SSi$ $[M+H]^+$: 257.1032, found 257.1064.

8. Late stage silylation of active pharmaceutical ingredients (APIs).



thenalidine **12**

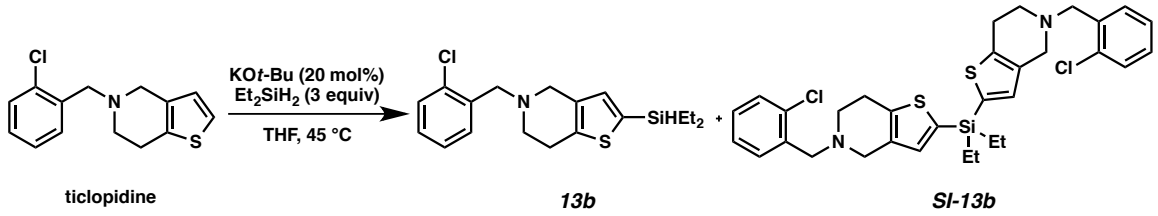
1-Methyl-*N*-phenyl-*N*-((5-(triethylsilyl)thiophen-2-yl)methyl)piperidin-4-amine 12: The general procedure was followed. The reaction was performed with KO*t*-Bu (2.2 mg, 0.02 mmol, 20 mol%), thenalidine (28.2 mg, 0.1 mmol, 1 equiv), Et_3SiH (48 μL, 0.3 mmol, 3 equiv), and 0.1 mL of THF at 45 °C for 72 h. The desired product **12** (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 (500 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 **13a**

5-(2-Chlorobenzyl)-2-(triethylsilyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine 13a: 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 **13a** (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); ^1H 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.

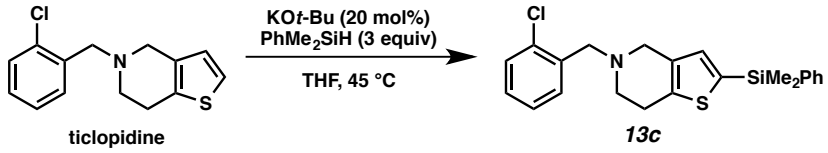


The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), ticlopidine (134.5 mg, 0.5 mmol, 1 equiv), Et_2SiH_2 (194 μL, 1.5 mmol, 3 equiv), and 0.5 mL of THF at 45 °C for 108 h. Products **13b** (97.9 mg, 56% yield) and **SI-13b** (27.3 mg, 18% yield) 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 13b: Colorless oil, R_f = 0.4 (10% Et_2O in hexanes); ^1H 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.

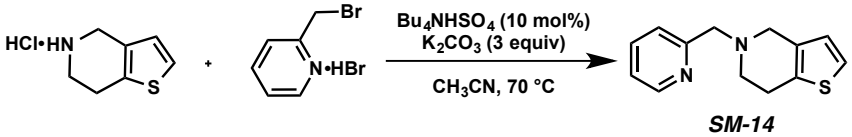
Bis(5-(2-chlorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl)diethylsilane SI-13b: Colorless oil, R_f = 0.3 (50% Et_2O in hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.55

(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.



ticlopidine *13c*

5-(2-Chlorobenzyl)-2-(dimethyl(phenyl)silyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine 13c: 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 **13c** (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); ^{1}H 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.

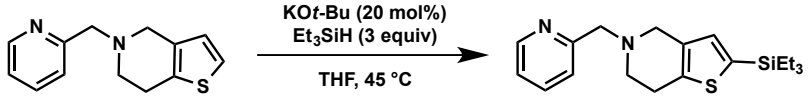


SM-14

5-(Pyridin-2-ylmethyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine SM-14: Followed a modified known procedure.[13] To a flame-dried 50 mL Schlenk flask was added 4,5,6,7-

(13) Pan, X.; Huang, R.; Zhang, J.; Ding, L.; Li, W.; Zhang, Q.; Liu, F. *Tetrahedron Lett* **2012**, *53*, 5364.

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 **SM-14** (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). ^1H 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.

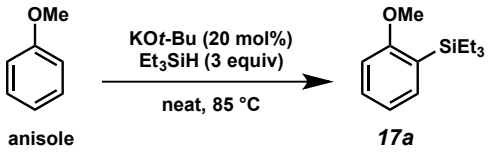


SM-14 ***14***

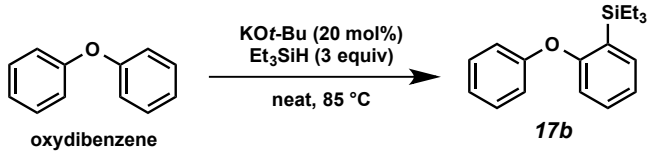
5-(Pyridin-2-ylmethyl)-2-(triethylsilyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine 14: The general procedure was followed. The reaction was performed with KO*t*-Bu (4.5 mg, 0.04 mmol, 20 mol%), 5-(pyridin-2-ylmethyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine **SM-14** (46.1 mg, 0.2 mmol), Et_3SiH (96 μL, 0.6 mmol, 3 equiv), and 0.2 mL of THF at 45 °C for 72 h. The desired product **14** (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); ^1H 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.

9. Oxygen-directed C(sp^2)–H silylation of anisole derivatives.

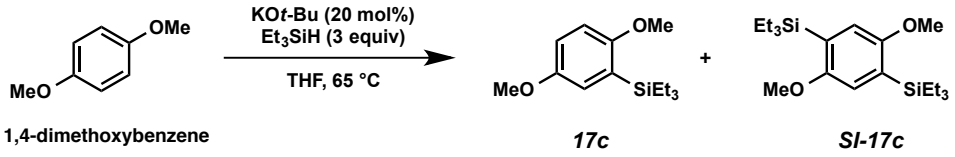


Triethyl(2-methoxyphenyl)silane 17a: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), anisole (54.0 mg, 0.5 mmol, 1 equiv), and Et_3SiH (243 μL, 1.5 mmol, 3 equiv) without any added solvent at 85 °C for 72 h. *ortho*:(*meta* + *para)* > 20:1. The GC yield of desired product **17a** 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 millitorr, 23 °C). *Note: compound **17a** is volatile and can be removed under vacuum.* This compound is known.[14] R_f = 0.3 (10% Et_2O in hexanes). ^1H 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).



Triethyl(2-phenoxyphenyl)silane 17b: 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 **17b** (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); ^1H 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). This compound is known.[8]

(14) Yamanoi, Y.; Nishihara, H. *J. Org. Chem.* **2008**, *73*, 6671.

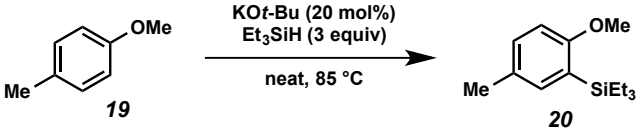


1,4-dimethoxybenzene — ***17c*** — ***SI-17c***

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 **17c** (53.1 mg, 42% yield) and bis-silylated byproduct **SI-17c** (16.1 mg, 8% yield) were obtained after purification by silica gel flash chromatography (100% hexanes).

(2,5-Dimethoxyphenyl)triethylsilane 17c: 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) SI-17c: White solid, R_f = 0.8 (100% hexanes); ^{1}H 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.

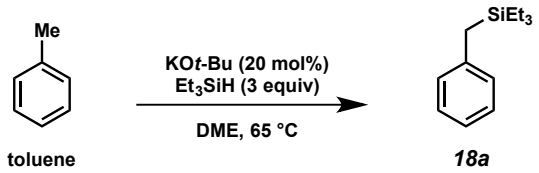


19 — ***20***

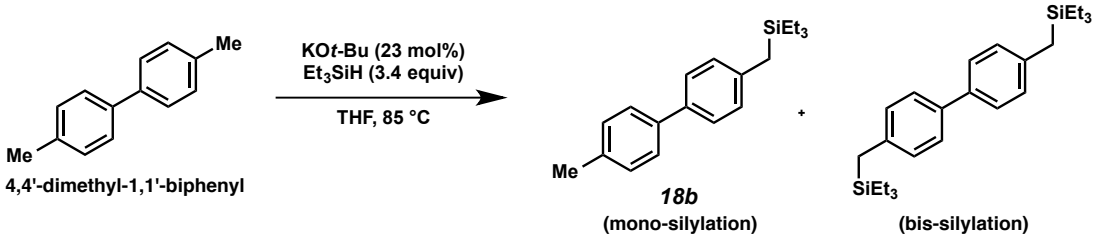
Triethyl(2-methoxy-5-methylphenyl)silane 20: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), 1-methoxy-4-methylbenzene **19** (61.0 mg, 0.5 mmol), and Et_3SiH (240 μL, 1.5 mmol, 3 equiv) at 85 °C for 120 h. The desired product **20** (38.5 mg, 32% yield) was obtained after purification by silica gel flash chromatography (100% hexanes) as a colorless oil. R_f = 0.4 (100% hexanes); ^{1}H 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.

10. Direct C(sp^3)–H silylation reactions.



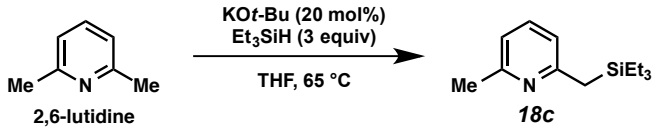
Benzyltriethylsilane 18a: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%), toluene (46 mg, 0.5 mmol, 1 equiv), Et_3SiH (243 μL, 1.5 mmol, 3 equiv) and DME (0.5 mL) at 65 °C for 108 h. C(sp^3):C(sp^2) = 18:1. The GC yield of desired product **18a** 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 millitorr, 23 °C). *Note: compound **18a** is volatile and readily removed under vacuum.* This compound is known.[15] 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).



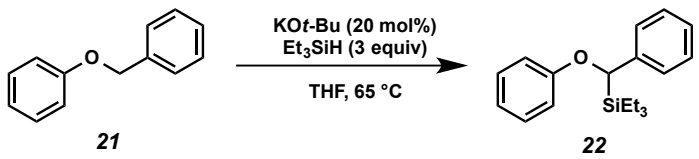
Triethyl((4'-methyl-[1,1'-biphenyl]-4-yl)methyl)silane 18b: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 23 mol%), 4,4'-dimethyl-1,1'-biphenyl (80.0 mg, 0.44 mmol), Et_3SiH (240 μL, 1.5 mmol, 3.4 equiv), and 0.5 mL of THF at 85 °C for 96 h. The ratio of mono-silylation product to bis-silylation product is 16:1. A mixture of desired product **18b** and starting material 4,4'-dimethyl-1,1'-biphenyl (*69.7 mg of mixture, contains 56.6 mg of **18b**, 43% yield, calculated based*

(15) Huckins, J. R.; Rychnovsky, S. D. *J. Org. Chem.* **2003**, *68*, 10135.

on ^1H NMR) was obtained after purification by silica gel flash chromatography (100% hexanes). *A small fraction of analytically pure compound **18b** 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 18c: 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 **18c** (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.

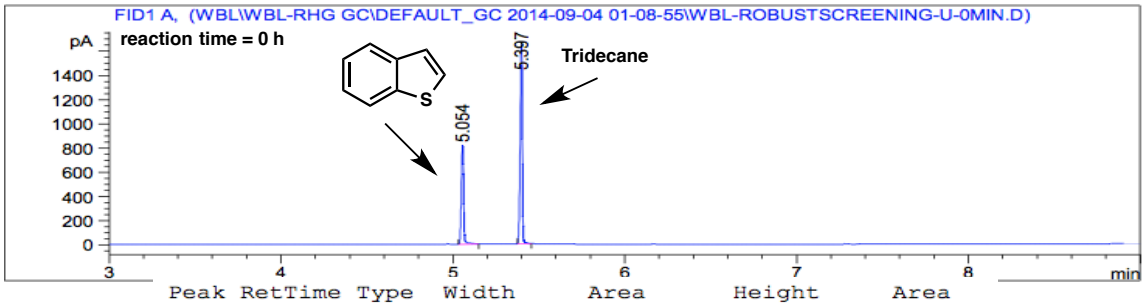


Triethyl(phenoxy(phenyl)methyl)silane 22: The general procedure was followed. The reaction was performed with KO*t*-Bu (11.2 mg, 0.1 mmol, 20 mol%),

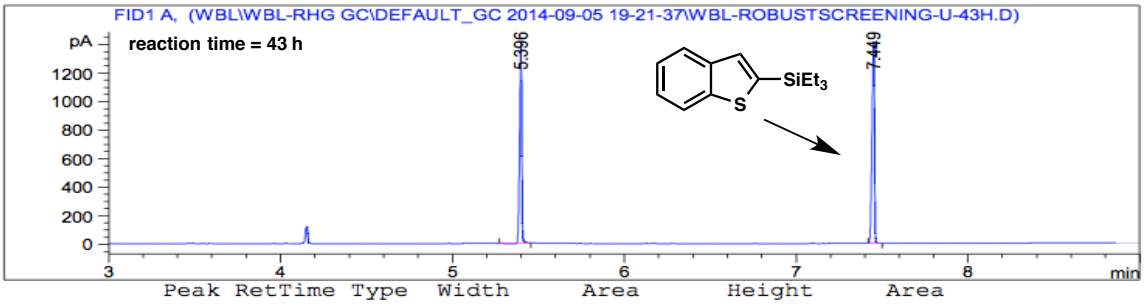
(benzyloxy)benzene **21** (92.0 mg, 0.5 mmol), Et_3SiH (240 μL, 1.5 mmol, 3 equiv), and 0.25 mL of THF at 65 °C for 120 h. The desired product **22** (68.4 mg, 46% yield) was obtained after purification by silica gel flash chromatography (100% hexanes) as a colorless oil. R_f = 0.3 (100% hexanes); ^{1}H 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.

Part IV. GC-FID spectra of the robustness screen.

GC-FID spectra of SI-Table 4, entry 1:

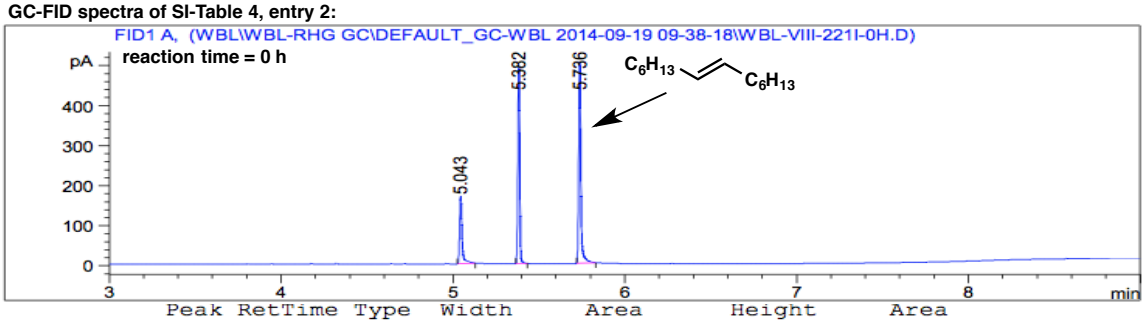


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.054	BB	0.0149	757.81213	813.08362	35.50033
2	5.397	BB	0.0137	1376.85034	1656.54895	64.49967

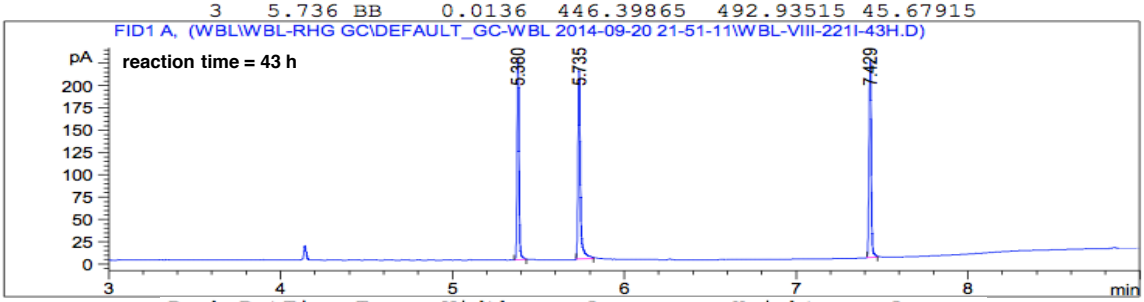


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.396	BB	0.0139	1193.07715	1403.63696	46.17764
2	7.449	BB	0.0161	1390.59131	1344.55493	53.82236

GC-FID spectra of SI-Table 4, entry 2:

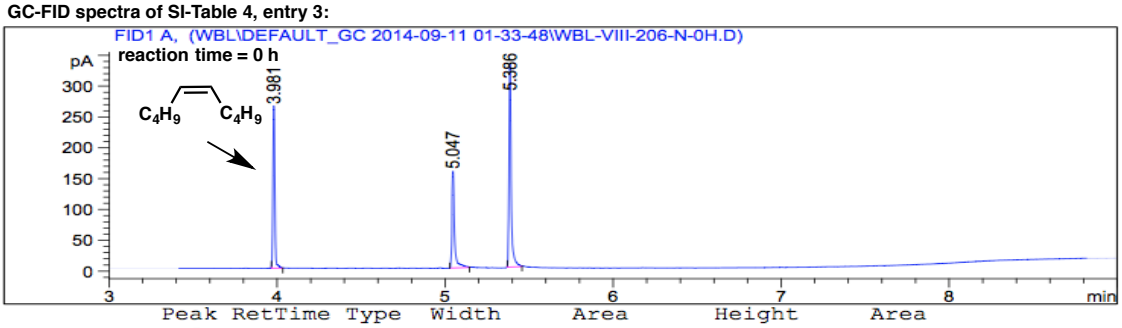


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.043	BB	0.0159	167.35704	164.46207	17.12534
2	5.382	BB	0.0118	363.49246	483.96515	37.19551
3	5.736	BB	0.0136	446.39865	492.93515	45.67915

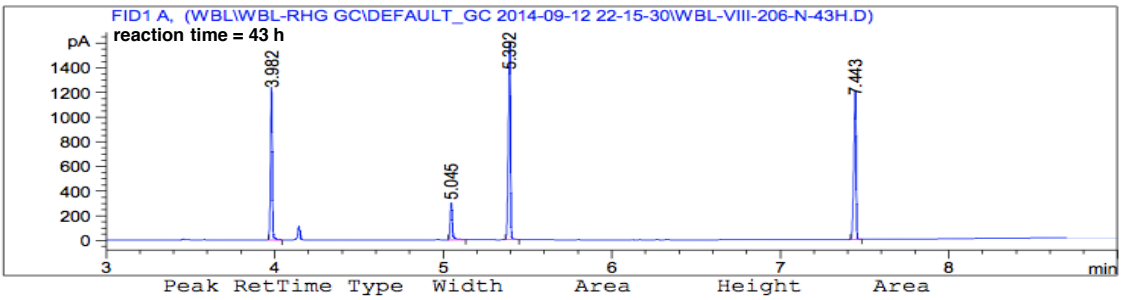


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.380	BB	0.0132	172.35509	218.78630	30.70791
2	5.735	BB	0.0142	200.51813	209.03979	35.72563
3	7.429	BB	0.0142	188.39932	215.53876	33.56646

GC-FID spectra of SI-Table 4, entry 3:

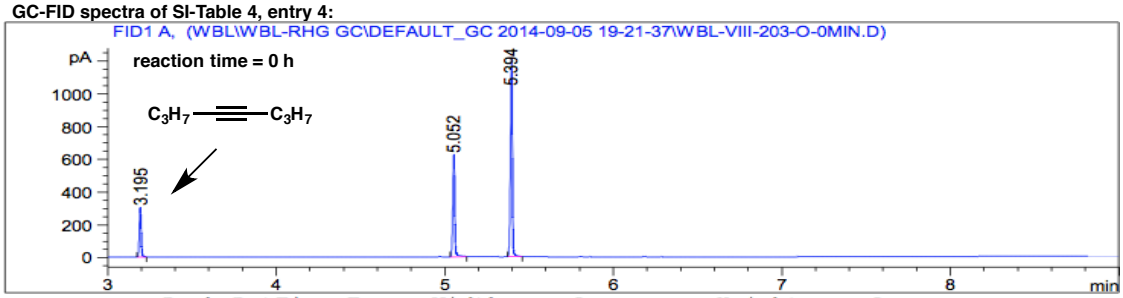


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.981	BB	0.0121	203.23712	259.37045	30.86568
2	5.047	BB	0.0163	163.03261	154.42287	24.75981
3	5.386	BB	0.0147	292.18683	317.25317	44.37450

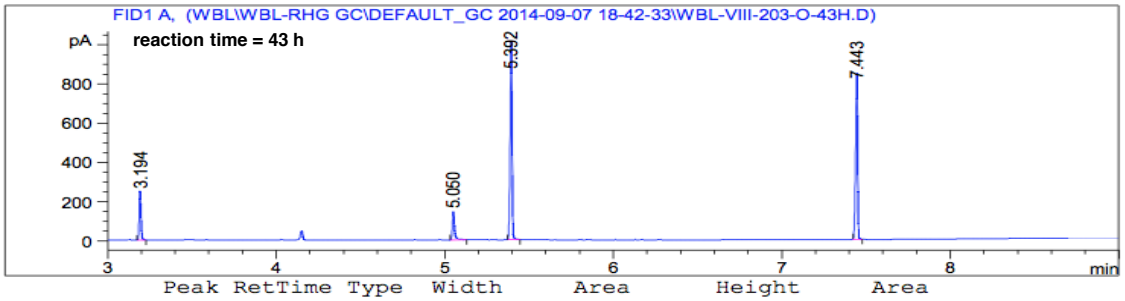


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.982	BB	0.0121	940.36487	1207.33105	25.44243
2	5.045	BB	0.0137	269.47769	293.51743	7.29096
3	5.392	BB	0.0134	1396.98389	1564.41138	37.79667
4	7.443	BB	0.0152	1089.22388	1136.62244	29.46994

GC-FID spectra of SI-Table 4, entry 4:

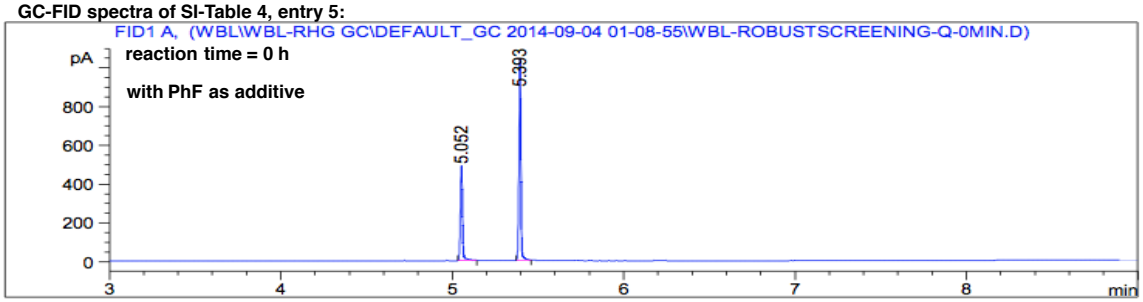


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.195	BB	0.0133	233.26434	293.04001	13.60265
2	5.052	BB	0.0130	527.93085	613.78699	30.78591

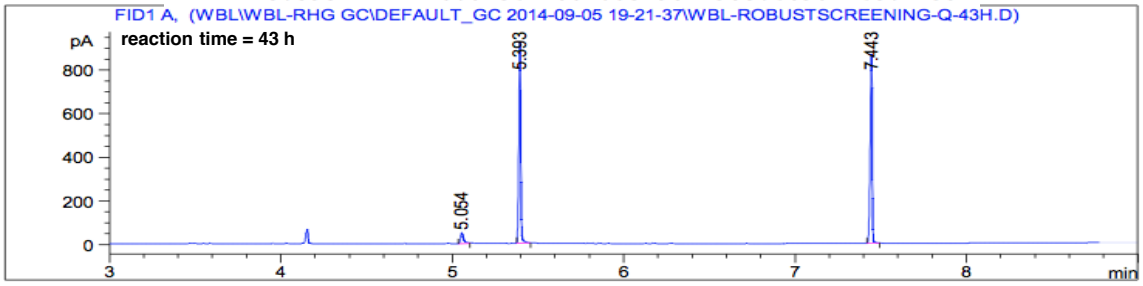


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.194	BB	0.0133	194.81905	244.24142	10.56992
2	5.050	BB	0.0152	135.15347	140.84714	7.33276
3	5.392	BB	0.0126	807.20825	980.40820	43.79512
4	7.443	BB	0.0143	705.96582	803.04401	38.30221

GC-FID spectra of SI-Table 4, entry 5:

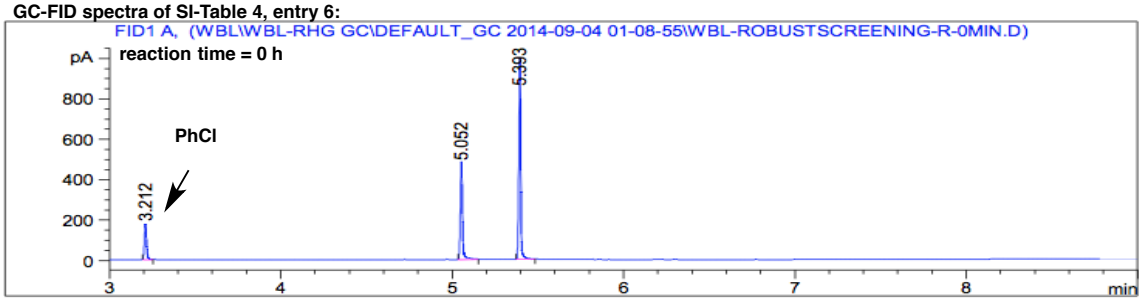


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.052	BB	0.0134	432.28278	483.75388	34.88006
2	5.393	BB	0.0136	807.05798	983.66907	65.11994

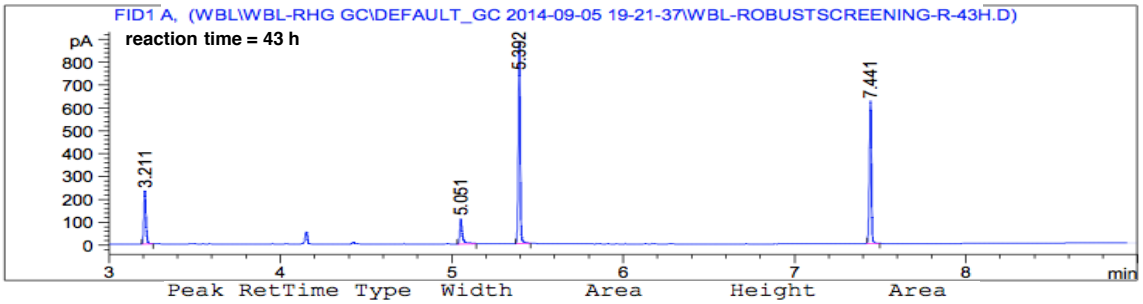


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.054	BB	0.0185	60.12766	48.45945	3.97540
2	5.393	BB	0.0136	724.24512	882.39813	47.88423
3	7.443	BB	0.0138	728.11908	866.32690	48.14036

GC-FID spectra of SI-Table 4, entry 6:

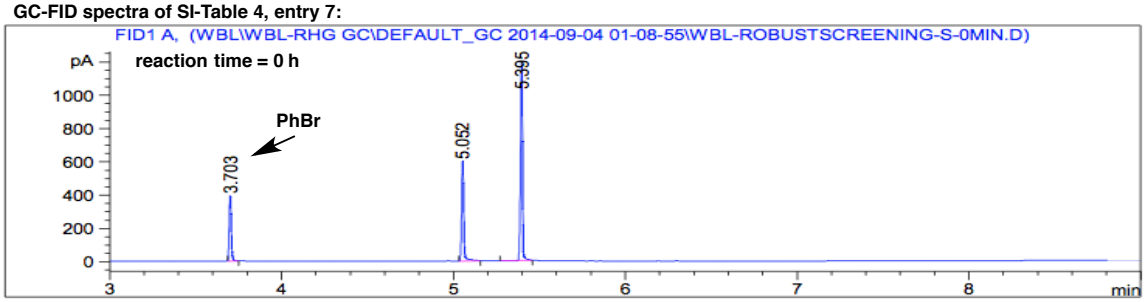


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.212	BB	0.0133	154.23224	173.96222	11.30731
2	5.052	BB	0.0135	425.45627	473.00186	31.19169
3	5.393	BB	0.0134	784.31653	977.44501	57.50100

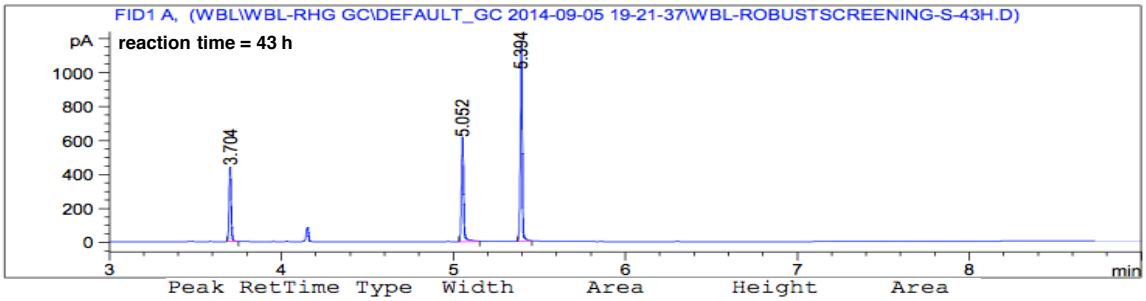


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.211	BB	0.0145	205.19017	229.02733	13.32845
2	5.051	BB	0.0175	123.75800	107.26932	8.03890
3	5.392	BB	0.0124	683.63361	851.12238	44.40650
4	7.441	BB	0.0129	526.90802	619.05310	34.22615

GC-FID spectra of SI-Table 4, entry 7:

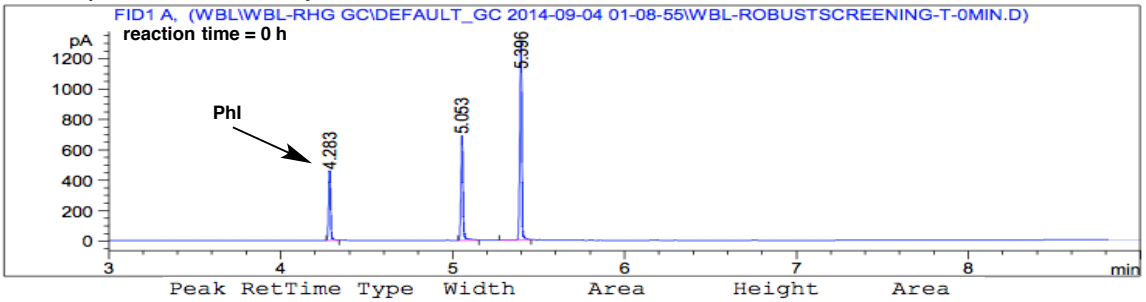


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.703	BB	0.0137	321.18744	384.43445	17.70586
2	5.052	BB	0.0146	536.59937	587.90198	29.58071
3	5.395	BB	0.0124	956.23077	1187.99536	52.71342

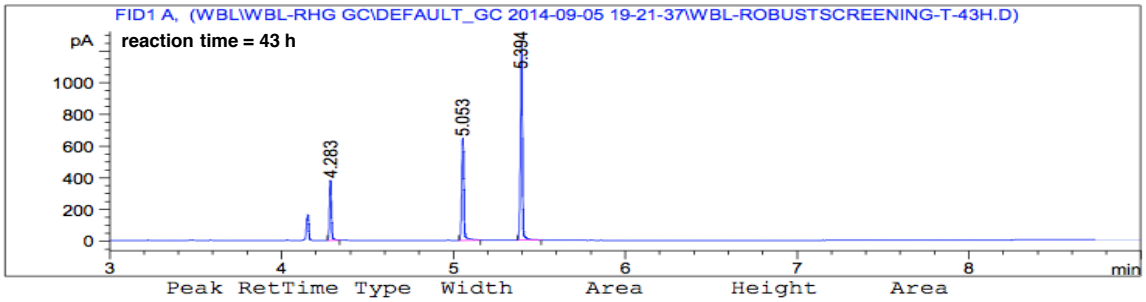


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.704	BB	0.0137	354.46970	425.76340	19.23968
2	5.052	BB	0.0134	533.08838	597.62415	28.93462
3	5.394	BB	0.0136	954.83105	1163.62964	51.82570

GC-FID spectra of SI-Table 4, entry 8:

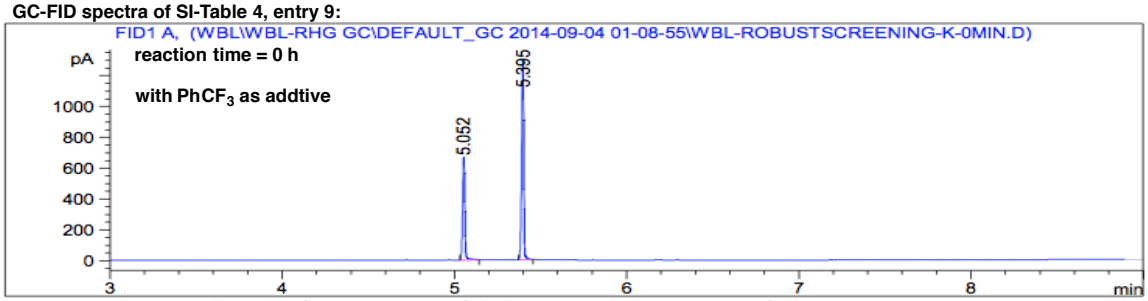


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.283	BB	0.0138	372.08484	444.89694	18.28708
2	5.053	BB	0.0145	604.12518	671.07733	29.69130
3	5.396	BB	0.0127	1058.47729	1274.90295	52.02162

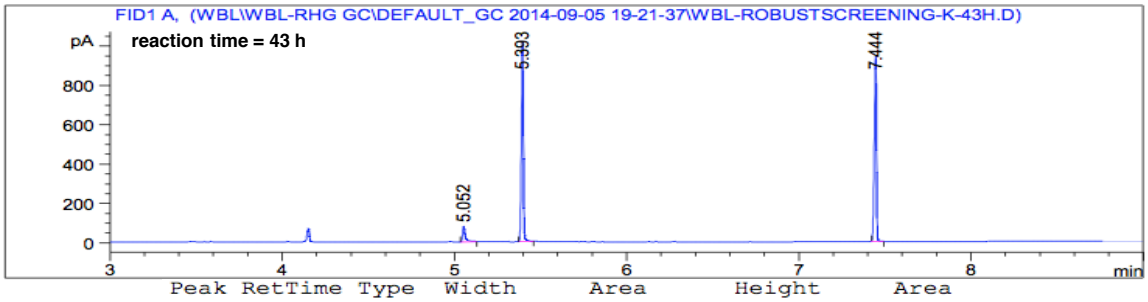


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.283	BB	0.0126	305.44244	372.80069	16.14080
2	5.053	BB	0.0146	577.15674	635.40320	30.49928
3	5.394	BB	0.0135	1009.76276	1238.18677	53.35992

GC-FID spectra of SI-Table 4, entry 9:

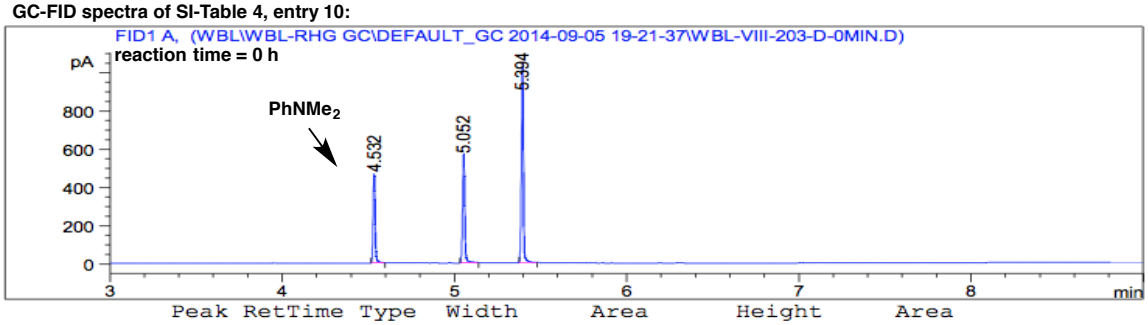


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.052	BB	0.0135	588.29590	655.02374	35.17884
2	5.395	BB	0.0130	1084.00464	1270.07581	64.82116

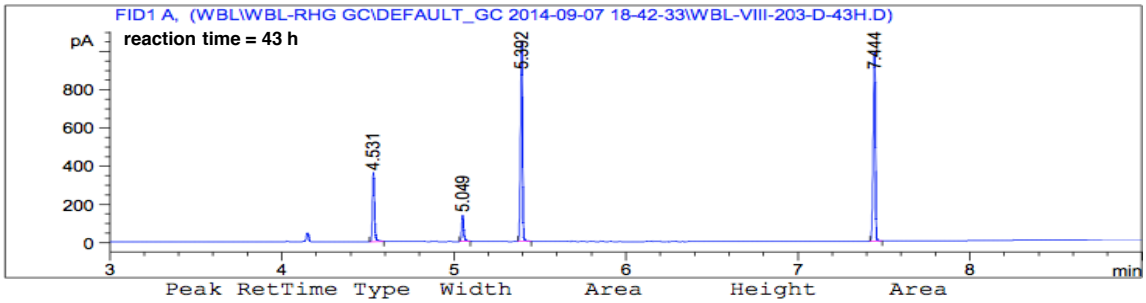


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.052	BB	0.0160	88.95304	79.72253	5.24940
2	5.393	BB	0.0138	804.46118	955.82367	47.47379
3	7.444	BB	0.0139	801.12335	939.42273	47.27681

GC-FID spectra of SI-Table 4, entry 10:

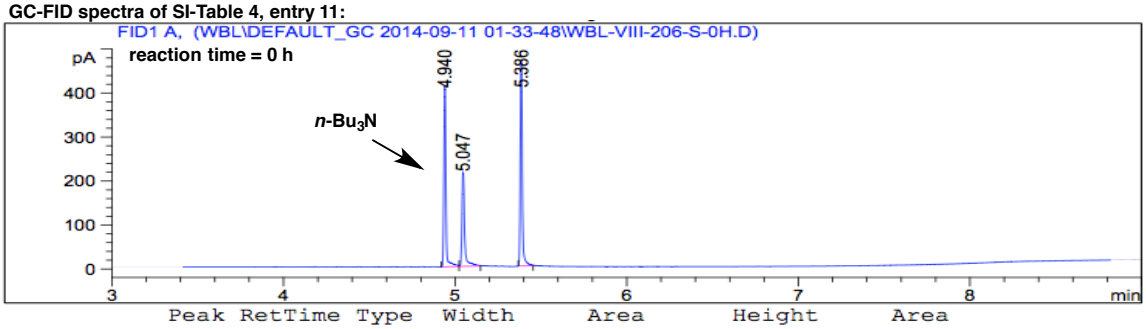


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.532	BB	0.0137	377.70926	454.98398	21.89827
2	5.052	BB	0.0145	499.47571	553.67822	28.95787
3	5.394	BB	0.0126	847.65112	1034.31641	49.14387

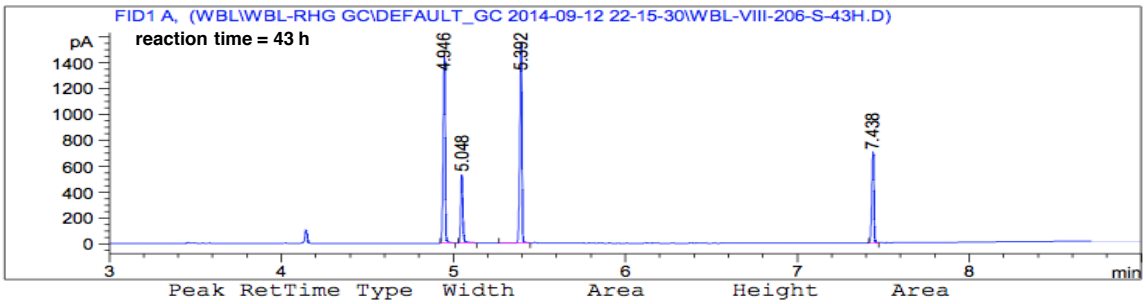


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.531	BB	0.0138	297.83487	354.08572	14.02392
2	5.049	BB	0.0146	121.14701	133.53572	5.70436
3	5.392	BB	0.0127	842.06940	1013.86646	39.64987
4	7.444	BB	0.0142	862.71204	989.58295	40.62185

GC-FID spectra of SI-Table 4, entry 11:

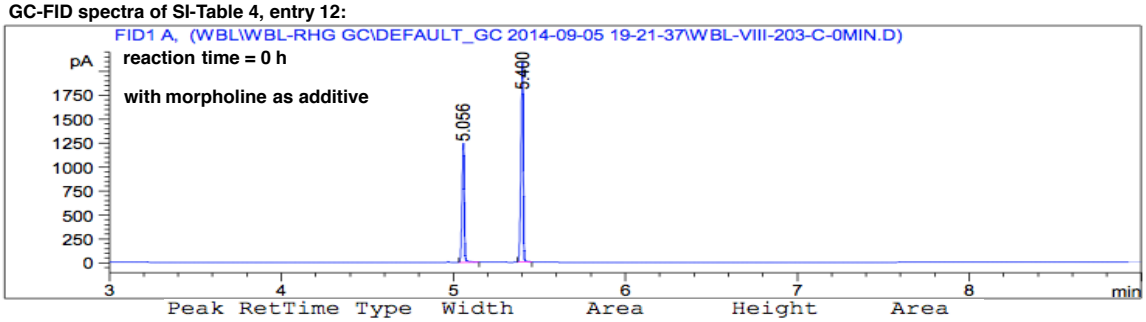


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.940	BV	0.0137	330.20572	398.56238	35.52488
2	5.047	VB	0.0164	219.53682	207.19090	23.61867
3	5.386	BB	0.0127	379.76306	457.34445	40.85646

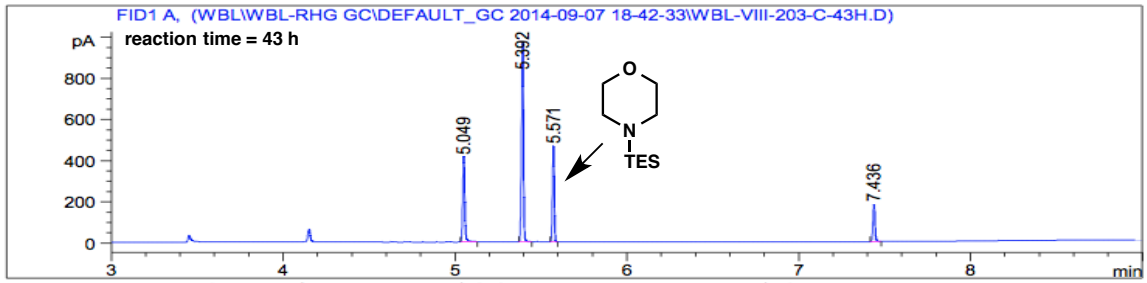


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.946	BB	0.0141	1203.80591	1394.00037	33.46110
2	5.048	BB	0.0145	471.45068	522.15521	13.10449
3	5.392	BB	0.0132	1334.67249	1523.16736	37.09868
4	7.438	BB	0.0129	587.69885	689.41693	16.33573

GC-FID spectra of SI-Table 4, entry 12:

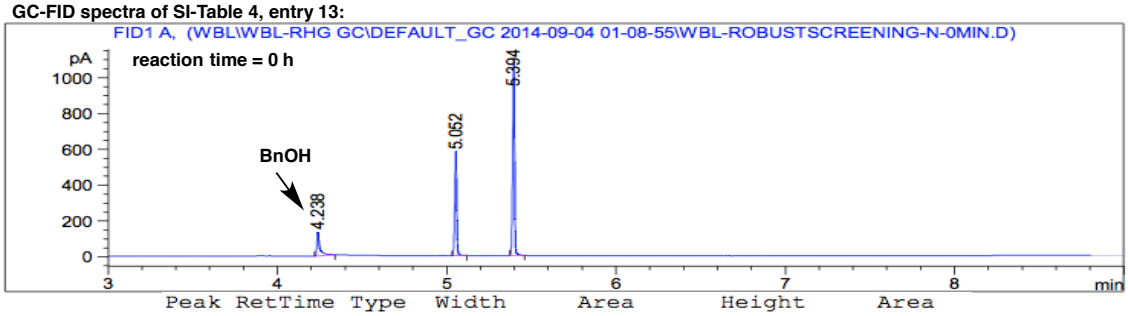


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.056	BB	0.0146	1114.04028	1226.71338	36.92116
2	5.400	BB	0.0154	1903.30896	1953.58960	63.07884

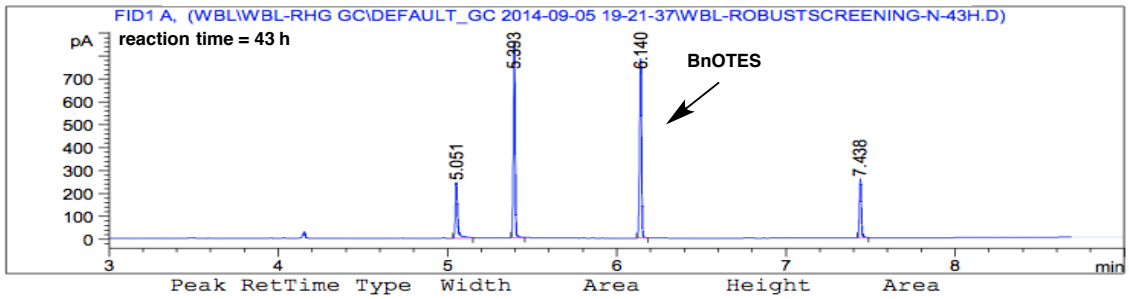


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.049	BB	0.0143	359.11511	406.27972	21.90699
2	5.392	BB	0.0126	783.82477	952.01721	47.81542
3	5.571	BB	0.0116	338.93201	457.76031	20.67577
4	7.436	BB	0.0144	157.39992	176.92252	9.60182

GC-FID spectra of SI-Table 4, entry 13:

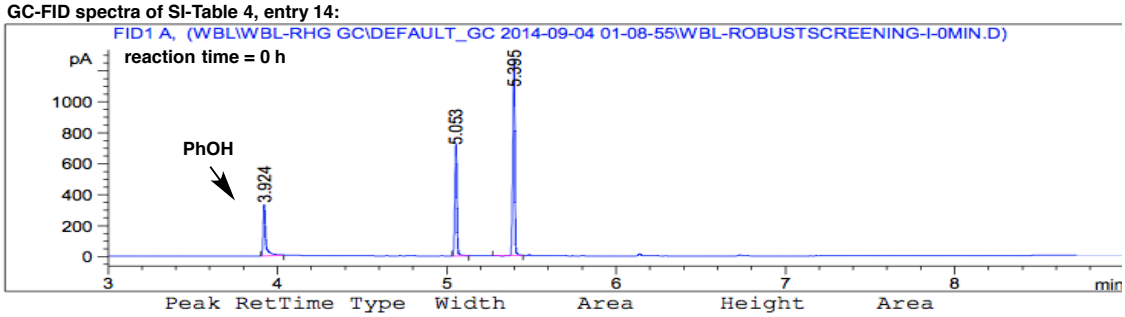


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.238	BB	0.0190	164.34883	127.53644	10.89584
2	5.052	BB	0.0130	489.51434	571.82513	32.45335
3	5.394	BB	0.0132	854.50006	1081.55774	56.65081

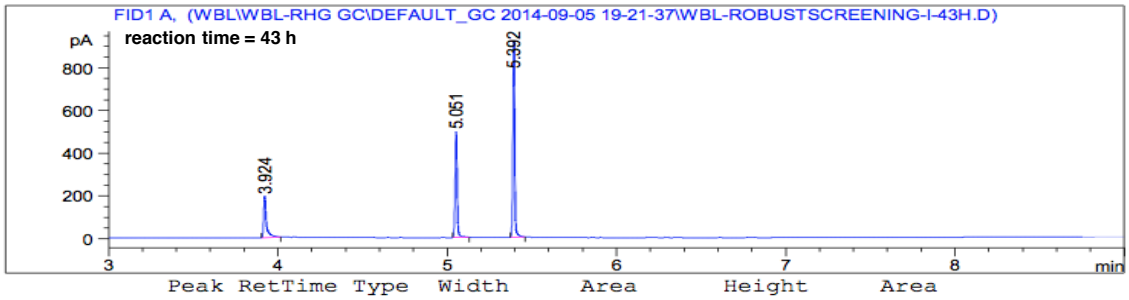


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.051	BB	0.0157	237.87219	237.71118	14.04074
2	5.393	BB	0.0130	629.44916	818.91058	37.15411
3	6.140	BB	0.0137	623.10913	746.75342	36.77988
4	7.438	BB	0.0124	203.72693	254.05693	12.02527

GC-FID spectra of SI-Table 4, entry 14:

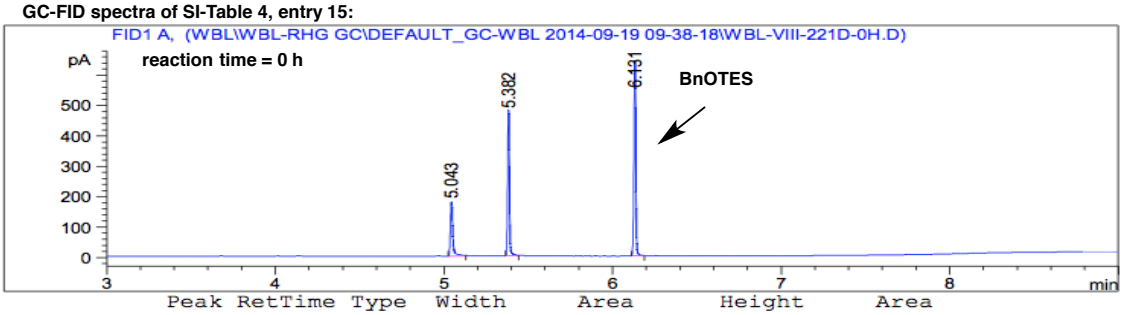


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.924	BB	0.0167	347.61041	318.65836	17.61199
2	5.053	BB	0.0141	596.71674	691.87122	30.23318
3	5.395	BB	0.0129	1029.38770	1215.88281	52.15483

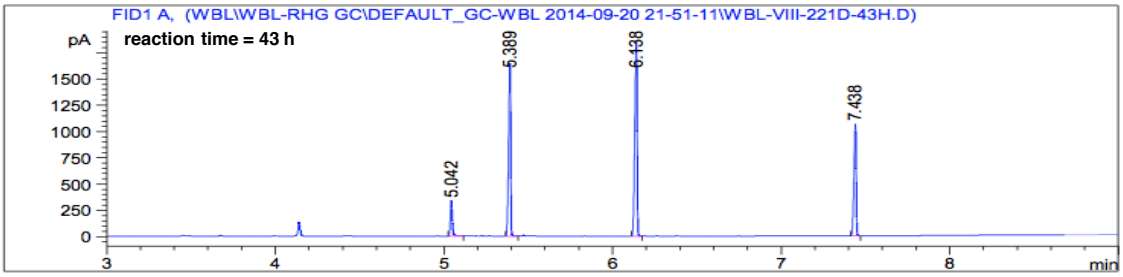


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.924	BB	0.0177	219.71886	186.97559	16.18693
2	5.051	BB	0.0130	419.85248	489.05118	30.93100
3	5.392	BB	0.0124	717.81268	889.42621	52.88206

GC-FID spectra of SI-Table 4, entry 15:

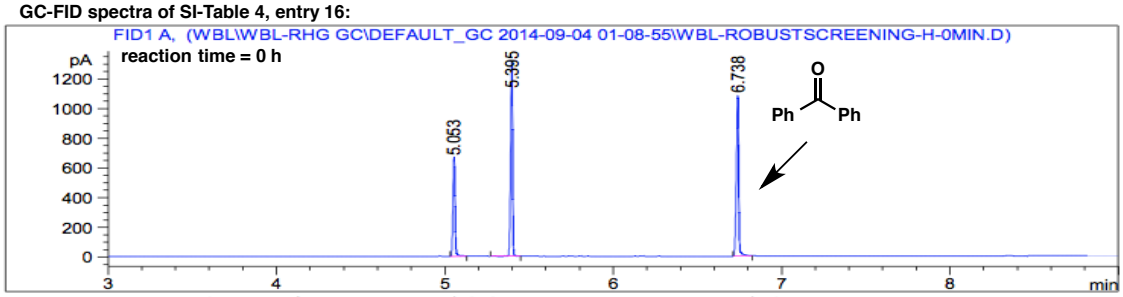


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.043	BB	0.0157	177.43666	176.76627	17.25147
2	5.382	BB	0.0117	350.31625	472.30042	34.05988
3	6.131	BB	0.0132	500.77747	634.92981	48.68864

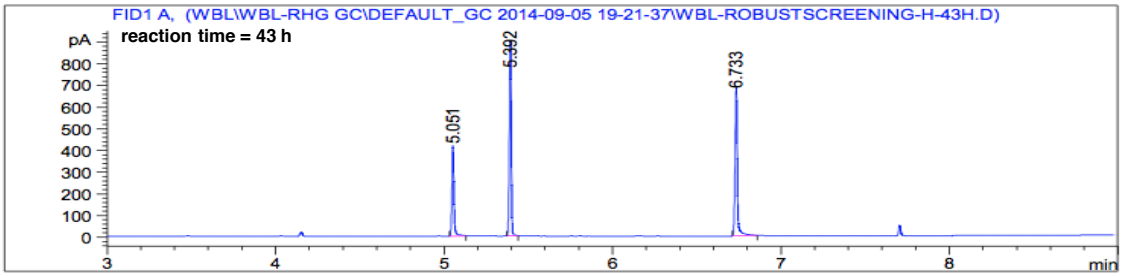


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.042	BB	0.0130	285.85907	334.54684	6.61147
2	5.389	BB	0.0130	1359.89429	1584.62854	31.45222
3	6.138	BB	0.0152	1734.73511	1799.69421	40.12170
4	7.438	BB	0.0144	943.19476	1057.01978	21.81461

GC-FID spectra of SI-Table 4, entry 16:

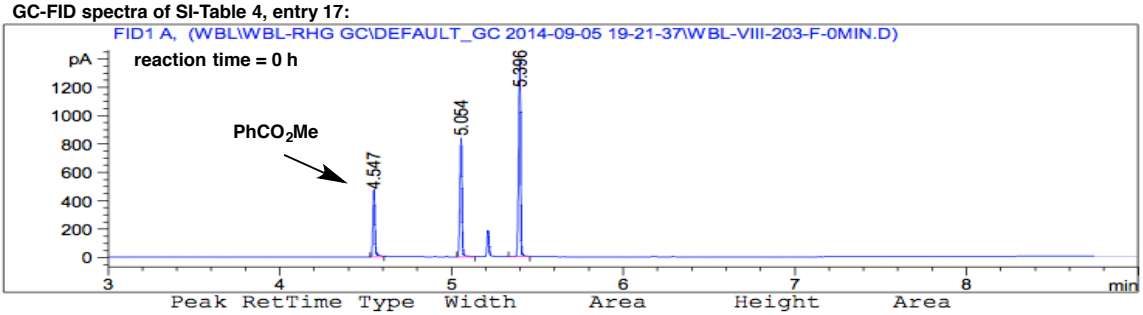


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.053	BB	0.0144	581.33722	653.60175	22.02989
2	5.395	BB	0.0123	1024.88892	1285.39587	38.83837
3	6.738	BB	0.0152	1032.63074	1078.53052	39.13174

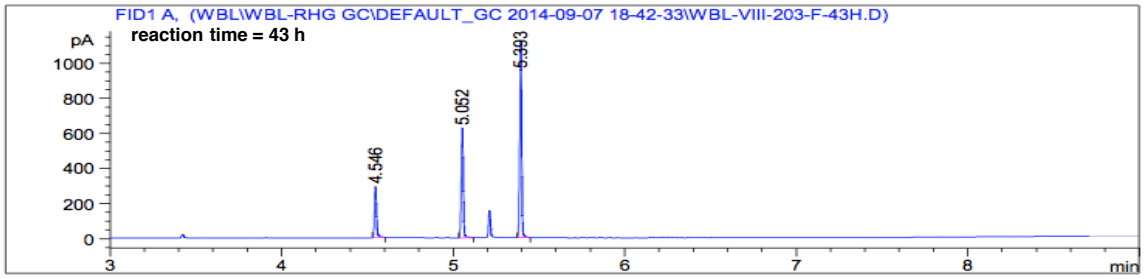


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.051	BB	0.0144	362.96750	408.90005	20.54536
2	5.392	BB	0.0123	701.74109	884.47821	39.72125
3	6.733	BB	0.0153	643.90259	665.52136	36.44737
4	10.496	BB	0.0239	58.05304	35.86992	3.28603

GC-FID spectra of SI-Table 4, entry 17:

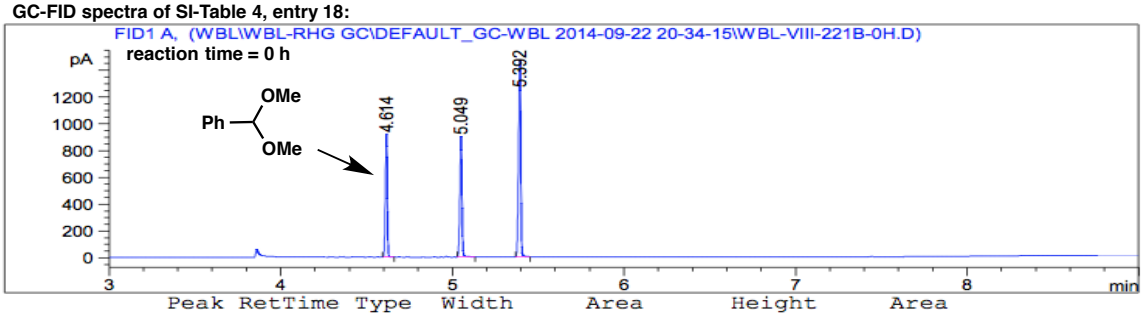


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.547	BB	0.0138	379.91116	454.35962	16.80495
2	5.054	BB	0.0140	708.21655	824.81445	31.32717
3	5.396	BB	0.0144	1172.58264	1309.76538	51.86788

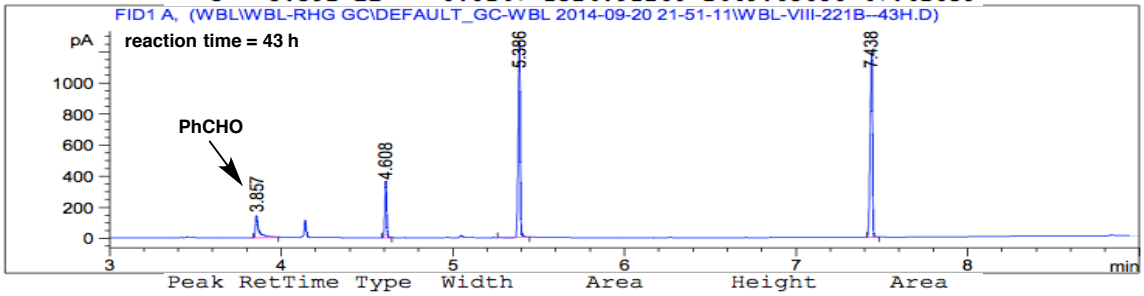


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.546	BB	0.0128	239.78859	286.69708	14.65431
2	5.052	BB	0.0127	514.46545	616.55530	31.44076
3	5.393	BB	0.0137	882.04706	1057.42419	53.90494

GC-FID spectra of SI-Table 4, entry 18:

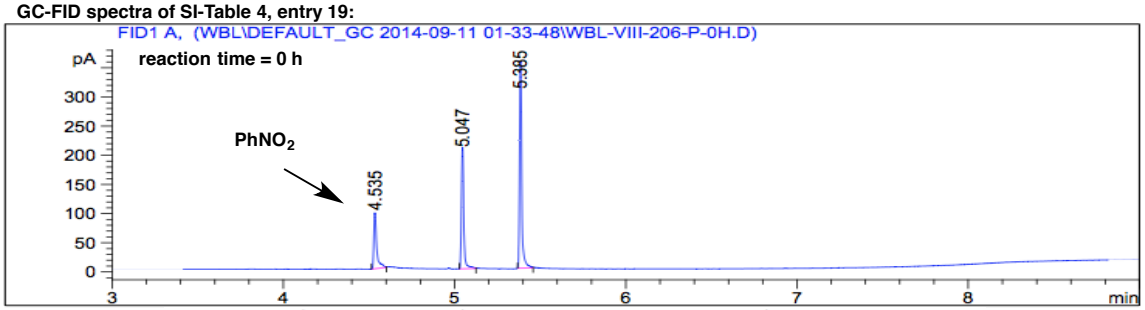


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.614	BB	0.0131	700.10925	902.38428	25.05573
2	5.049	BB	0.0131	769.18634	887.87695	27.52788
3	5.392	BB	0.0147	1324.91260	1449.65686	47.41639

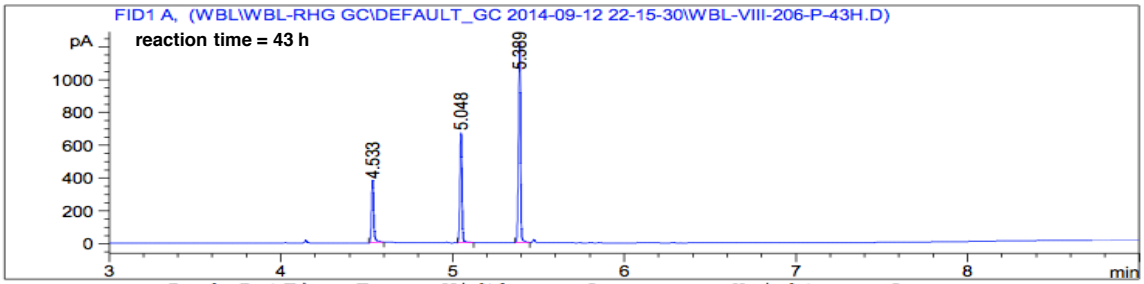


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.857	BB	0.0214	205.34763	137.73538	7.82671
2	4.608	BB	0.0129	268.36557	350.84610	10.22861
3	5.386	BB	0.0127	1024.33691	1225.97473	39.04203
4	7.438	BB	0.0151	1125.62695	1178.64563	42.90265

GC-FID spectra of SI-Table 4, entry 19:

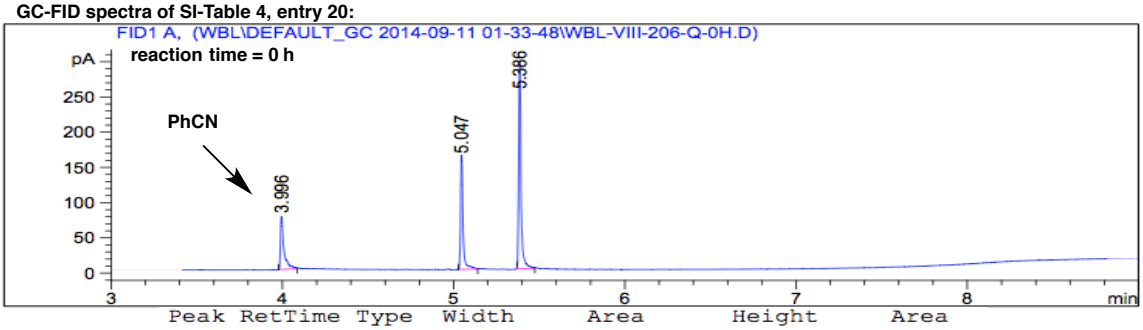


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.535	BB	0.0177	111.61236	94.77935	18.16164
2	5.047	BB	0.0150	190.39711	201.12346	30.98156
3	5.385	BB	0.0134	312.54041	351.13321	50.85680

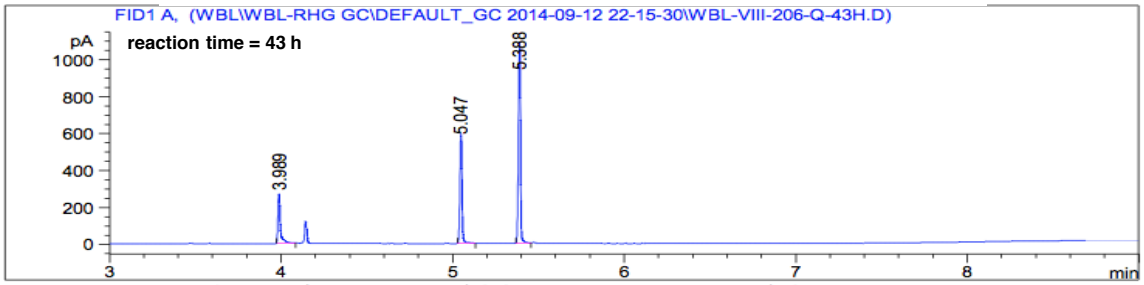


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	4.533	BB	0.0150	347.16339	367.95538	18.21877
2	5.048	BB	0.0130	570.93298	664.53088	29.96196
3	5.389	BV	0.0141	987.42975	1141.82764	51.81927

GC-FID spectra of SI-Table 4, entry 20:

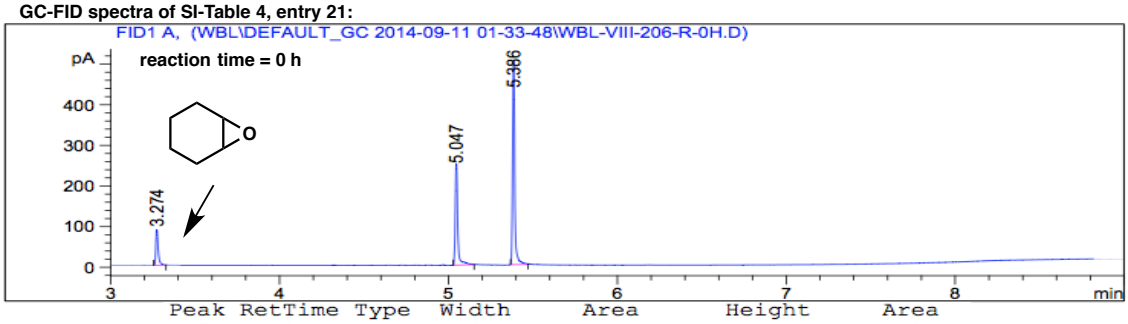


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.996	BB	0.0203	104.37083	74.60351	19.55841
2	5.047	BB	0.0158	161.13466	159.39436	30.19557
3	5.386	BB	0.0149	268.13120	286.23087	50.24602

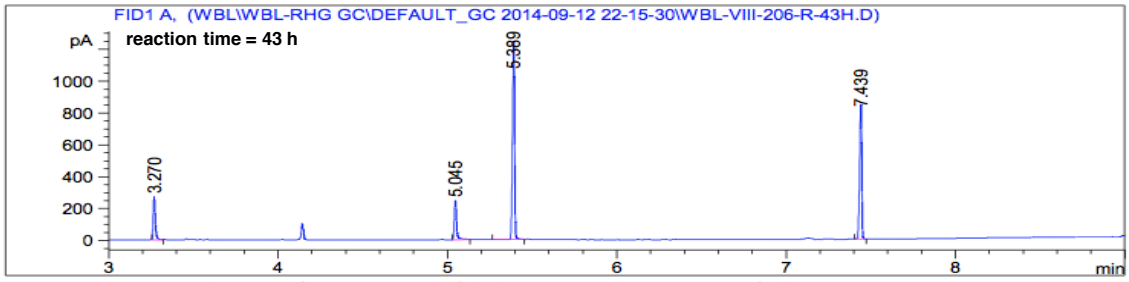


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.989	BB	0.0154	283.01514	267.23007	16.80506
2	5.047	BB	0.0144	506.30051	569.71454	30.06345
3	5.388	BV	0.0137	894.79102	1078.10925	53.13149

GC-FID spectra of SI-Table 4, entry 21:

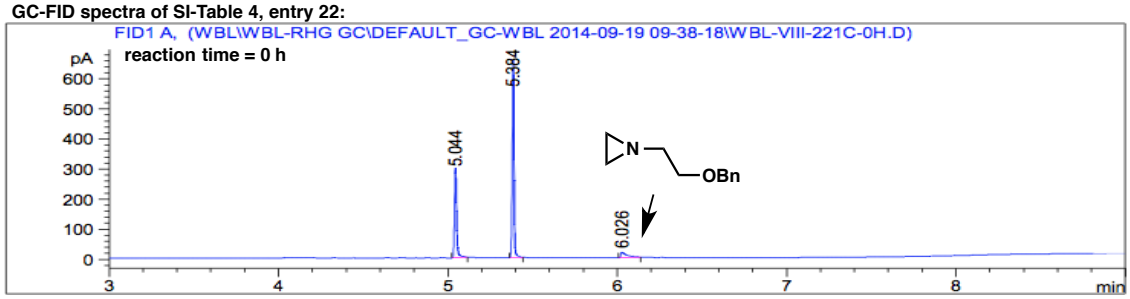


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.274	BB	0.0155	84.74000	86.20313	11.10321
2	5.047	BB	0.0159	247.62512	242.42696	32.44551
3	5.386	BB	0.0143	430.83789	489.86090	56.45128

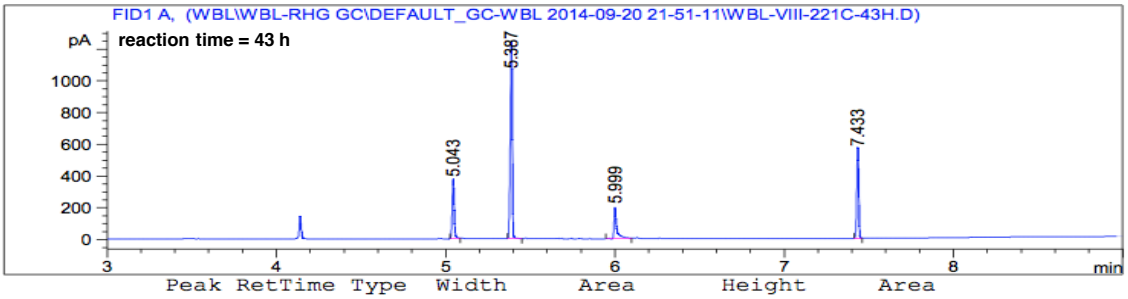


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	3.270	BB	0.0145	237.99971	264.70377	10.68970
2	5.045	BB	0.0140	228.91533	242.20050	10.28168
3	5.389	BB	0.0141	1037.04797	1199.63281	46.57877
4	7.439	BB	0.0144	722.47601	810.45892	32.44985

GC-FID spectra of SI-Table 4, entry 22:

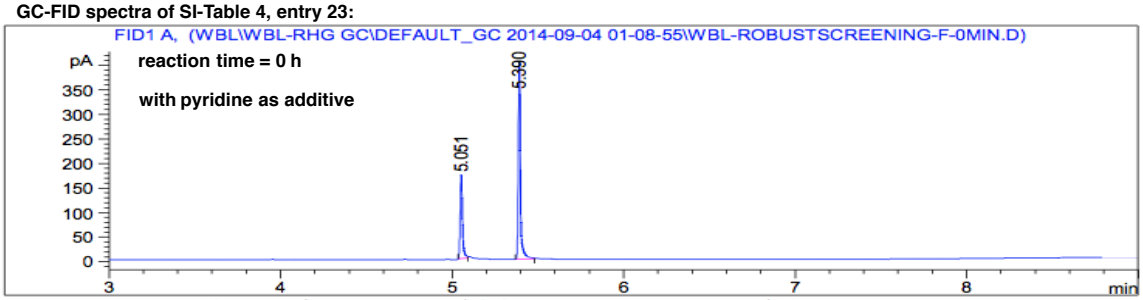


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.044	BB	0.0144	259.58676	290.56866	32.05666
2	5.384	BB	0.0130	503.19037	649.27142	62.13955
3	6.026	BB	0.0314	46.99762	19.29555	5.80379

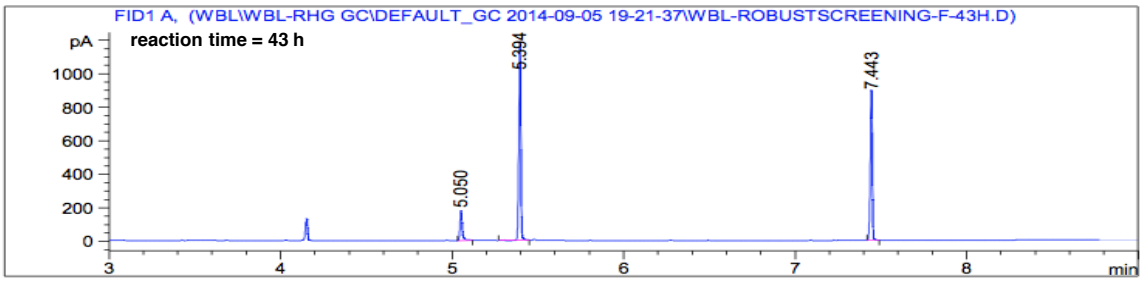


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.043	BB	0.0129	312.46866	367.83182	15.38465
2	5.387	BB	0.0140	1016.13641	1183.95178	50.03032
3	5.999	BB	0.0168	232.78250	197.34129	11.46124
4	7.433	BB	0.0138	469.65353	557.11810	23.12378

GC-FID spectra of SI-Table 4, entry 23:

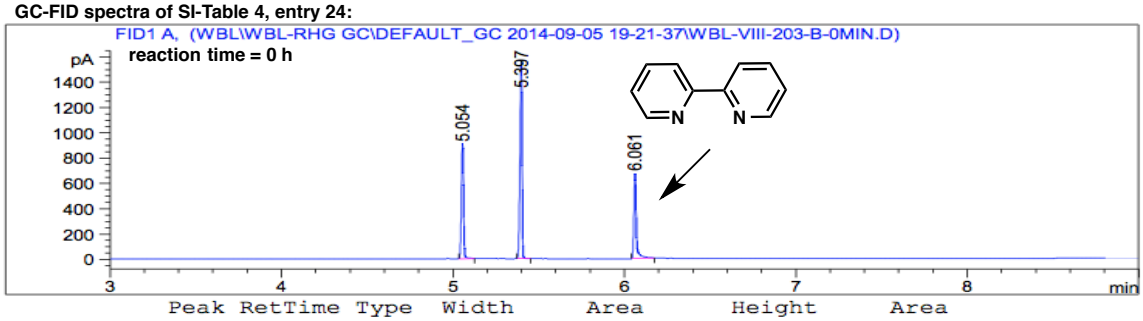


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.051	BB	0.0138	156.20609	168.59203	31.01447
2	5.390	BB	0.0143	347.44943	394.23758	68.98553

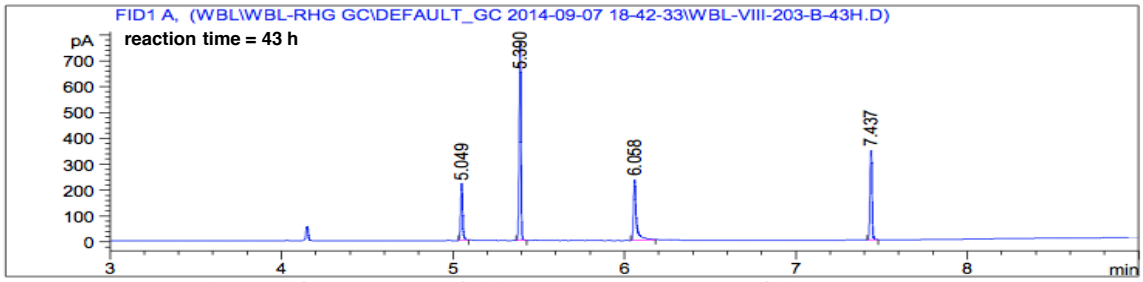


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.050	BB	0.0150	166.53435	176.15463	8.89926
2	5.394	BB	0.0135	951.68530	1171.16174	50.85614
3	7.443	BB	0.0140	753.10858	882.47650	40.24460

GC-FID spectra of SI-Table 4, entry 24:

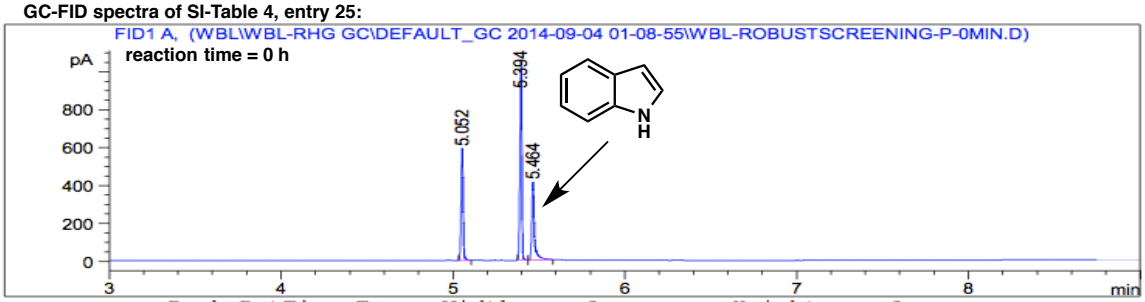


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.054	BB	0.0142	784.29218	899.93848	28.42038
2	5.397	BB	0.0137	1296.84875	1561.22388	46.99389
3	6.061	BB	0.0159	678.47058	665.00964	24.58573

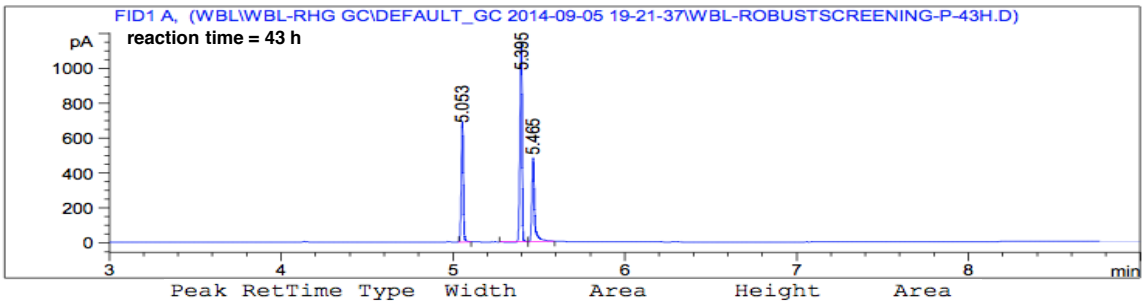


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.049	BB	0.0130	186.29955	217.96092	14.19997
2	5.390	BB	0.0126	550.36261	746.06616	41.94928
3	6.058	BB	0.0183	287.27814	233.70592	21.89667
4	7.437	BB	0.0137	288.03137	347.25116	21.95408

GC-FID spectra of SI-Table 4, entry 25:

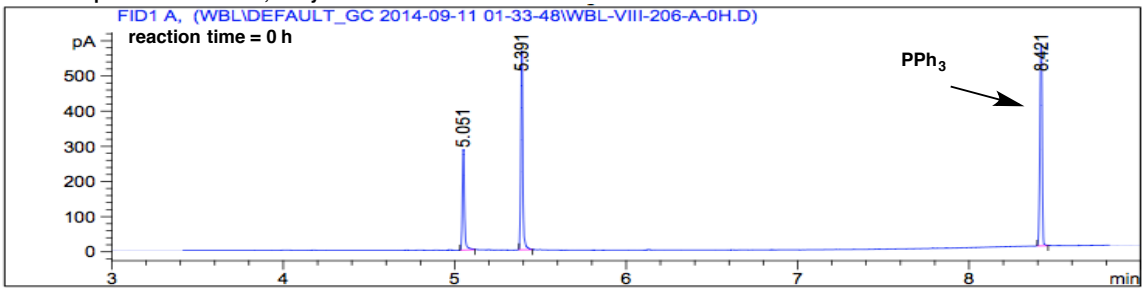


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.052	BB	0.0126	480.47305	581.80505	27.64849
2	5.394	BV	0.0122	819.30896	1037.32178	47.14657
3	5.464	VB	0.0167	438.00916	403.49310	25.20494

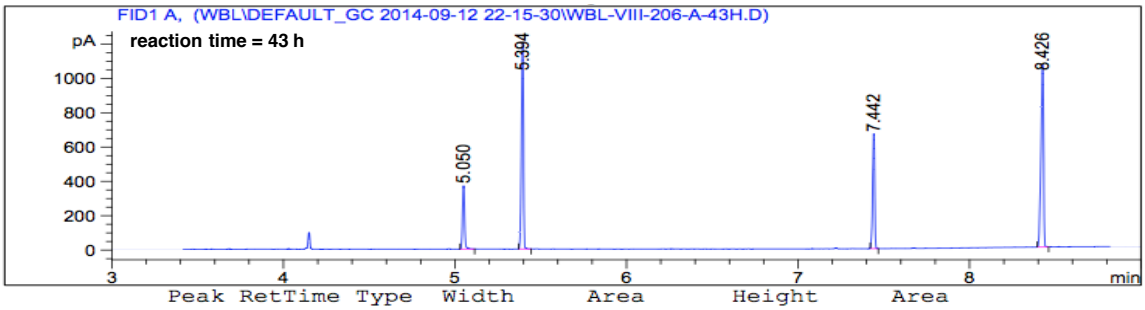


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.053	BB	0.0140	566.89130	664.10944	27.16086
2	5.395	BV	0.0144	991.34656	1110.61658	47.49734
3	5.465	VB	0.0170	528.92432	473.68710	25.34179

GC-FID spectra of SI-Table 4, entry 26:

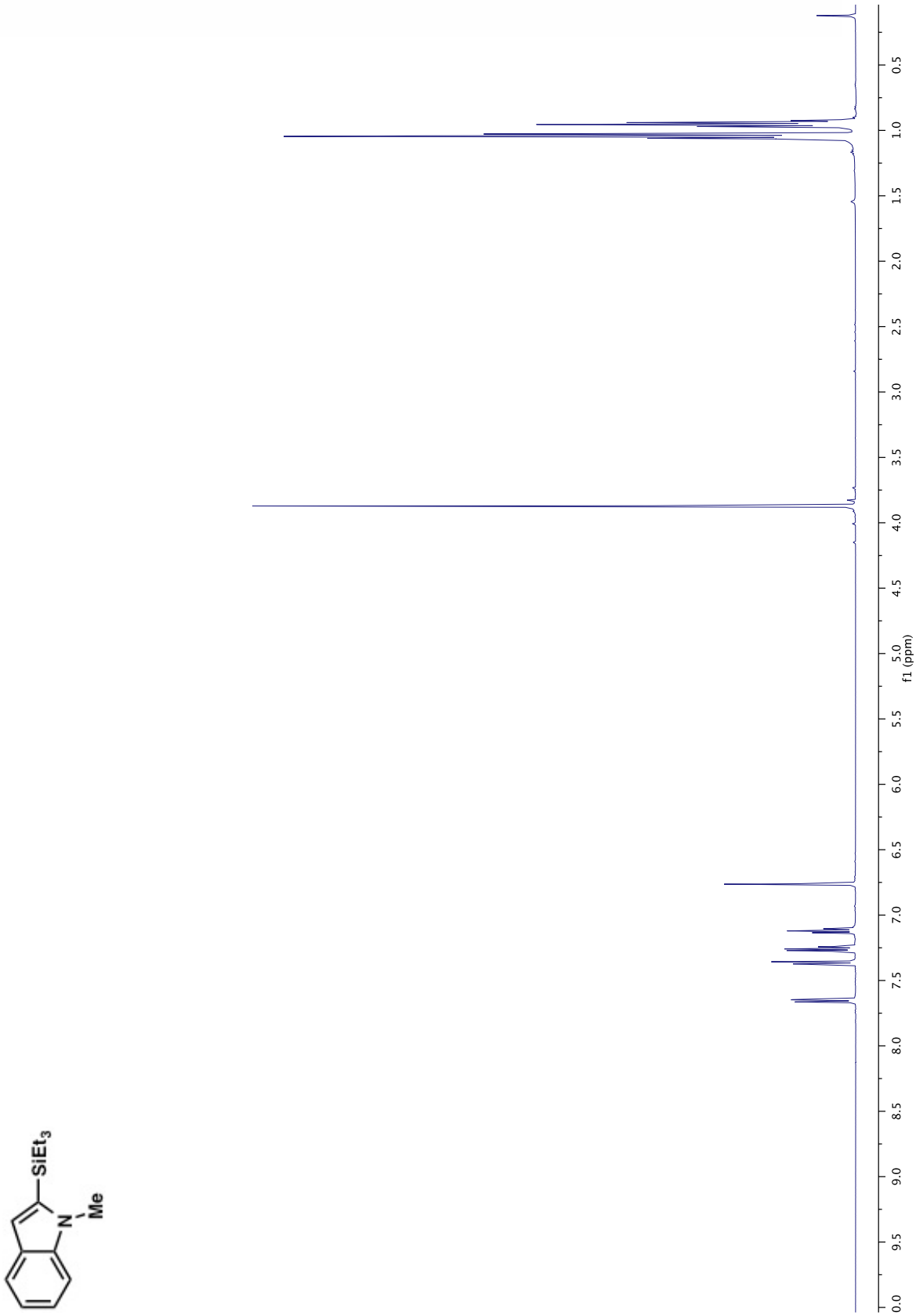


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.051	BB	0.0144	250.97217	282.10843	20.80203
2	5.391	BB	0.0122	436.13669	555.49304	36.14953
3	8.421	BB	0.0146	519.37061	570.63788	43.04844

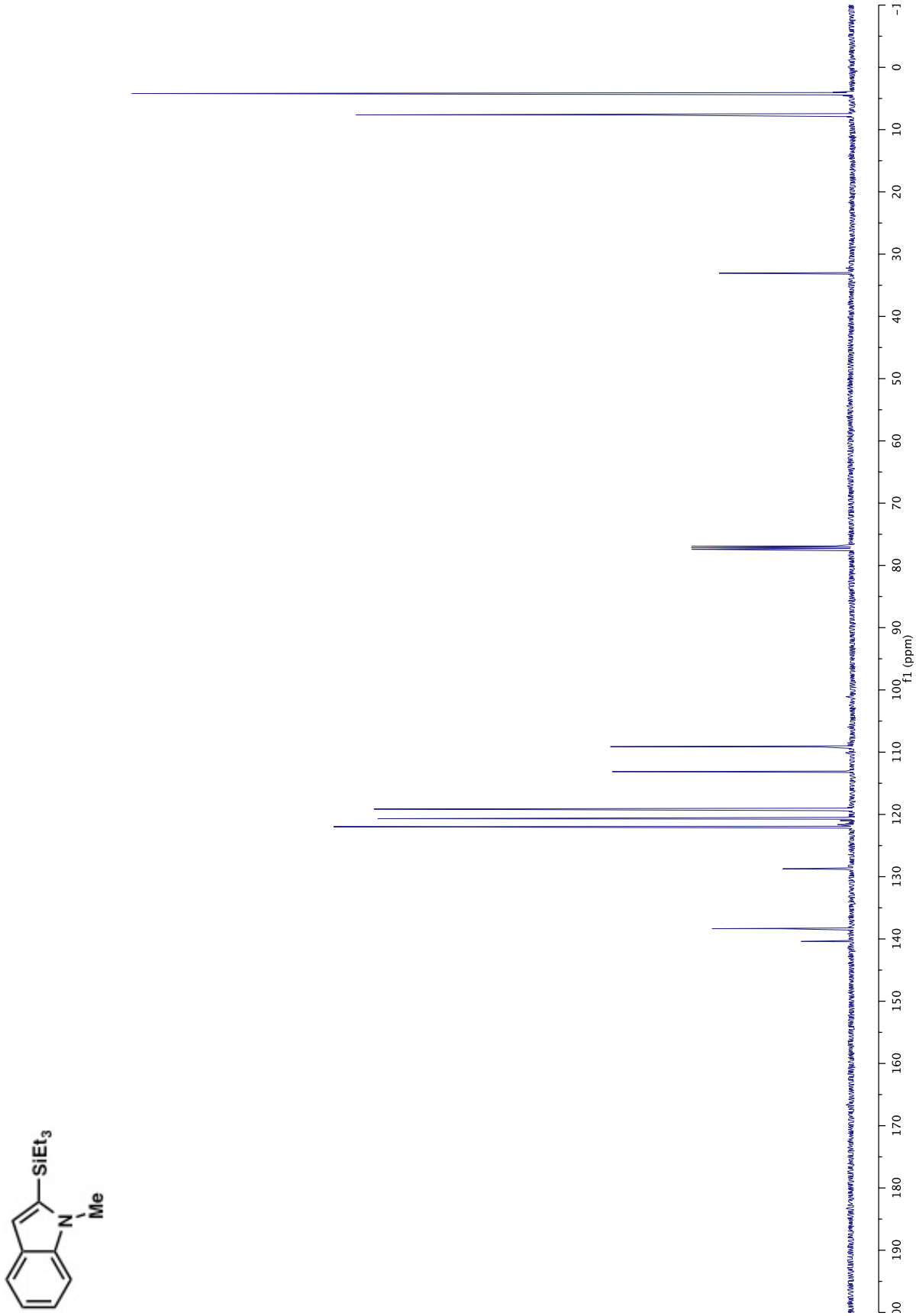


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.050	BB	0.0139	308.54736	363.27356	10.49166
2	5.394	BB	0.0125	970.49554	1192.30505	33.00015
3	7.442	BB	0.0125	535.07501	656.23175	18.19437
4	8.426	BB	0.0168	1126.76465	1028.11218	38.31383

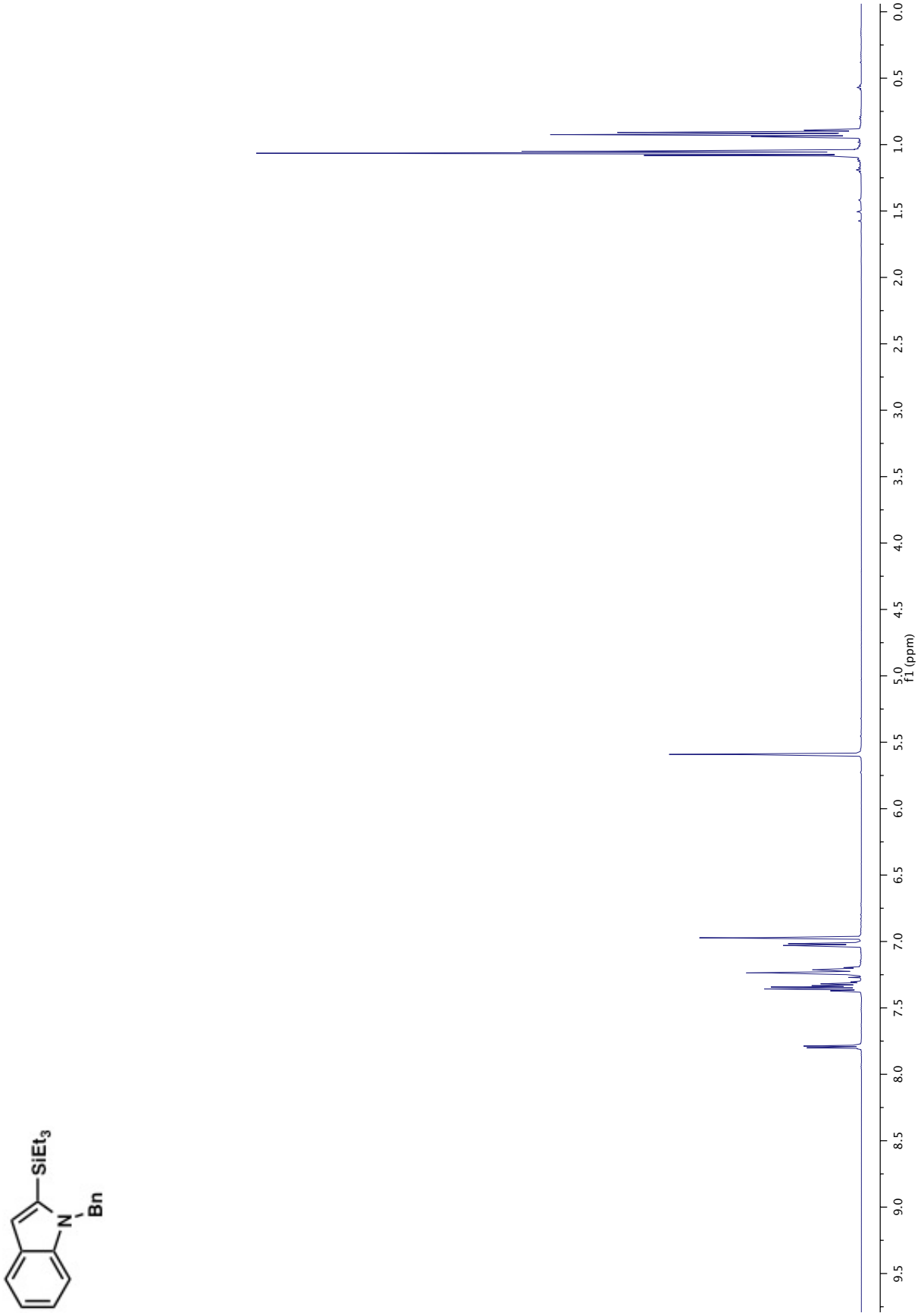
3 ^{1}H NMR and ^{13}C NMR Spectra of New Compounds



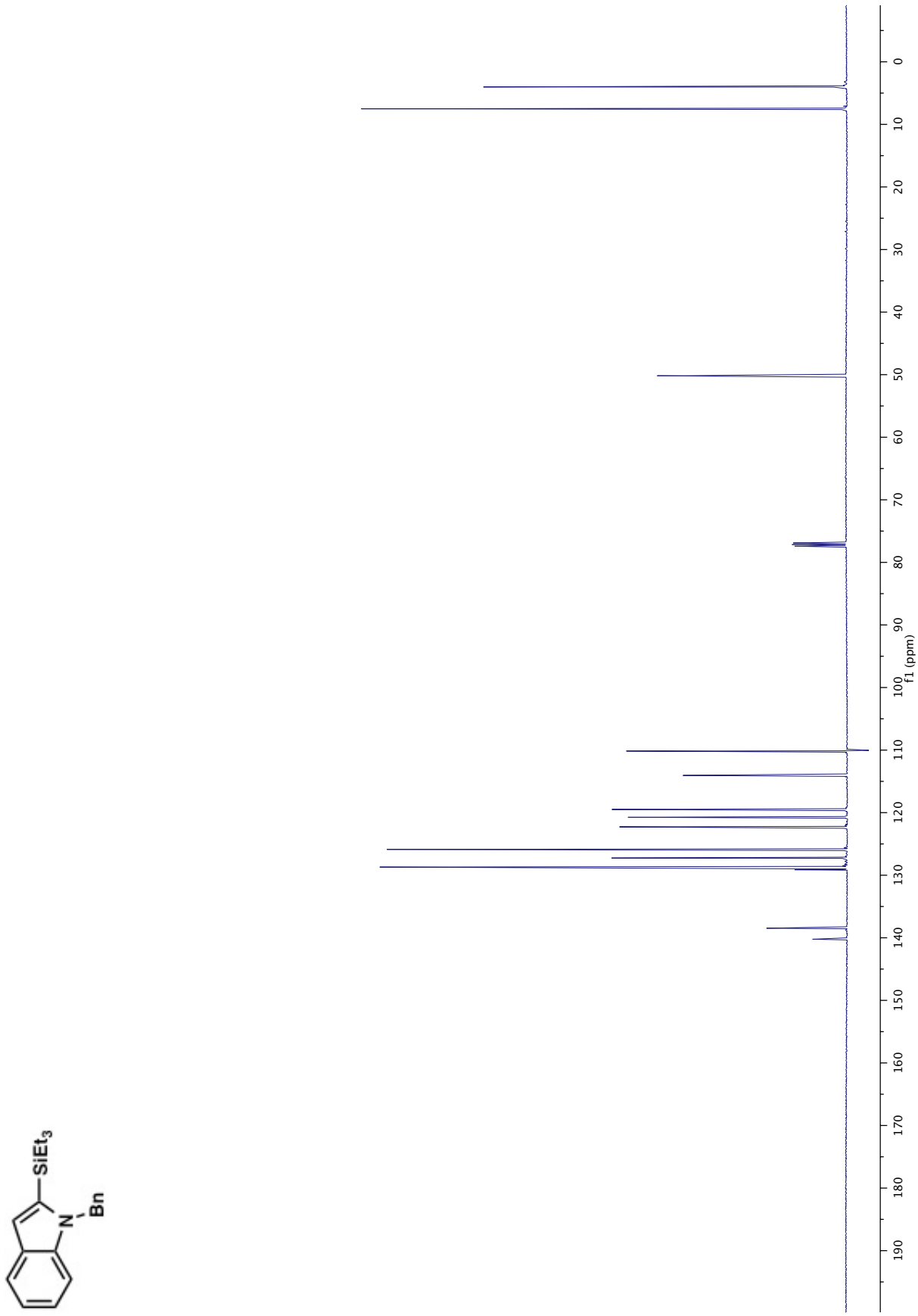
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2a**.



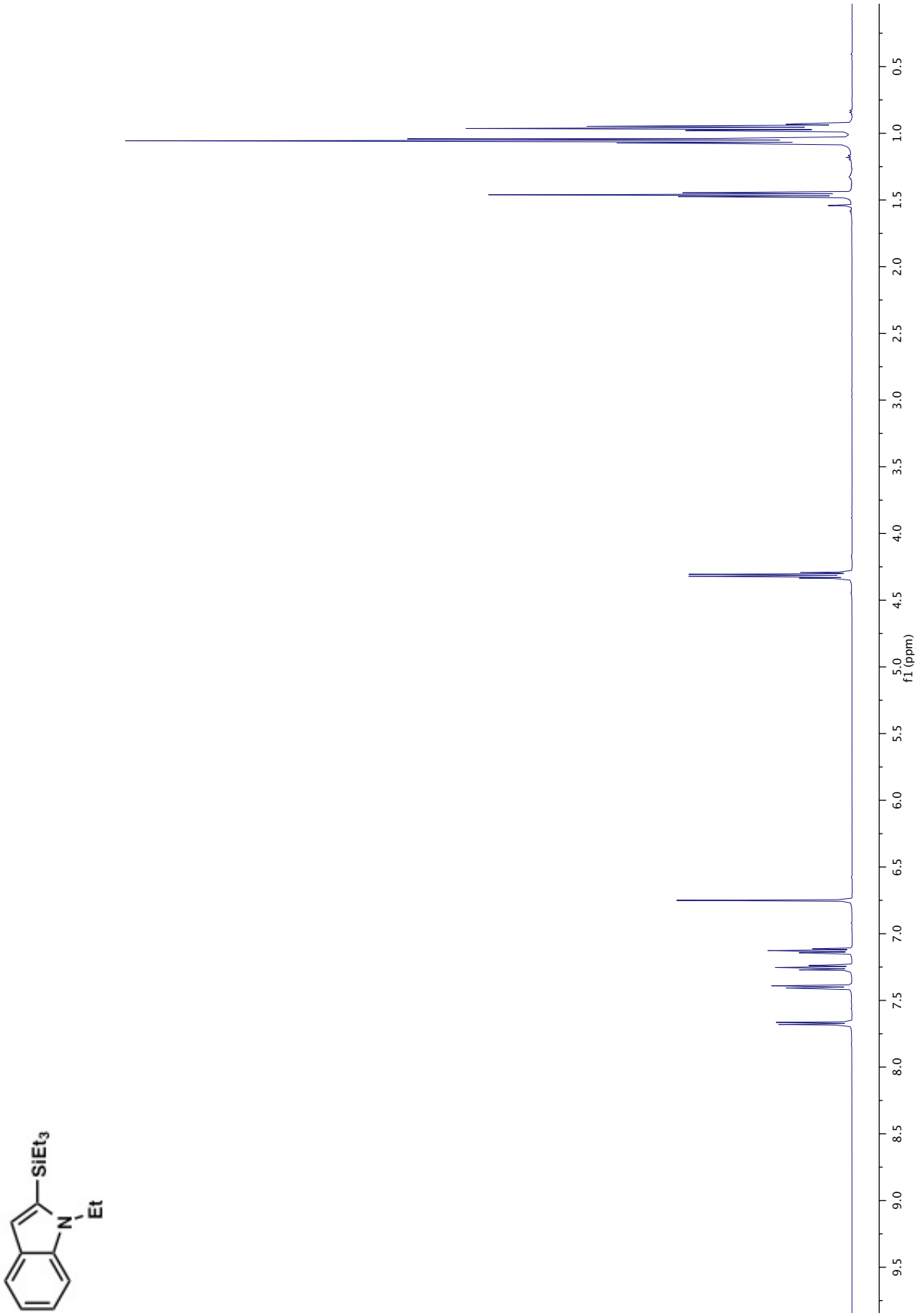
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2a.**



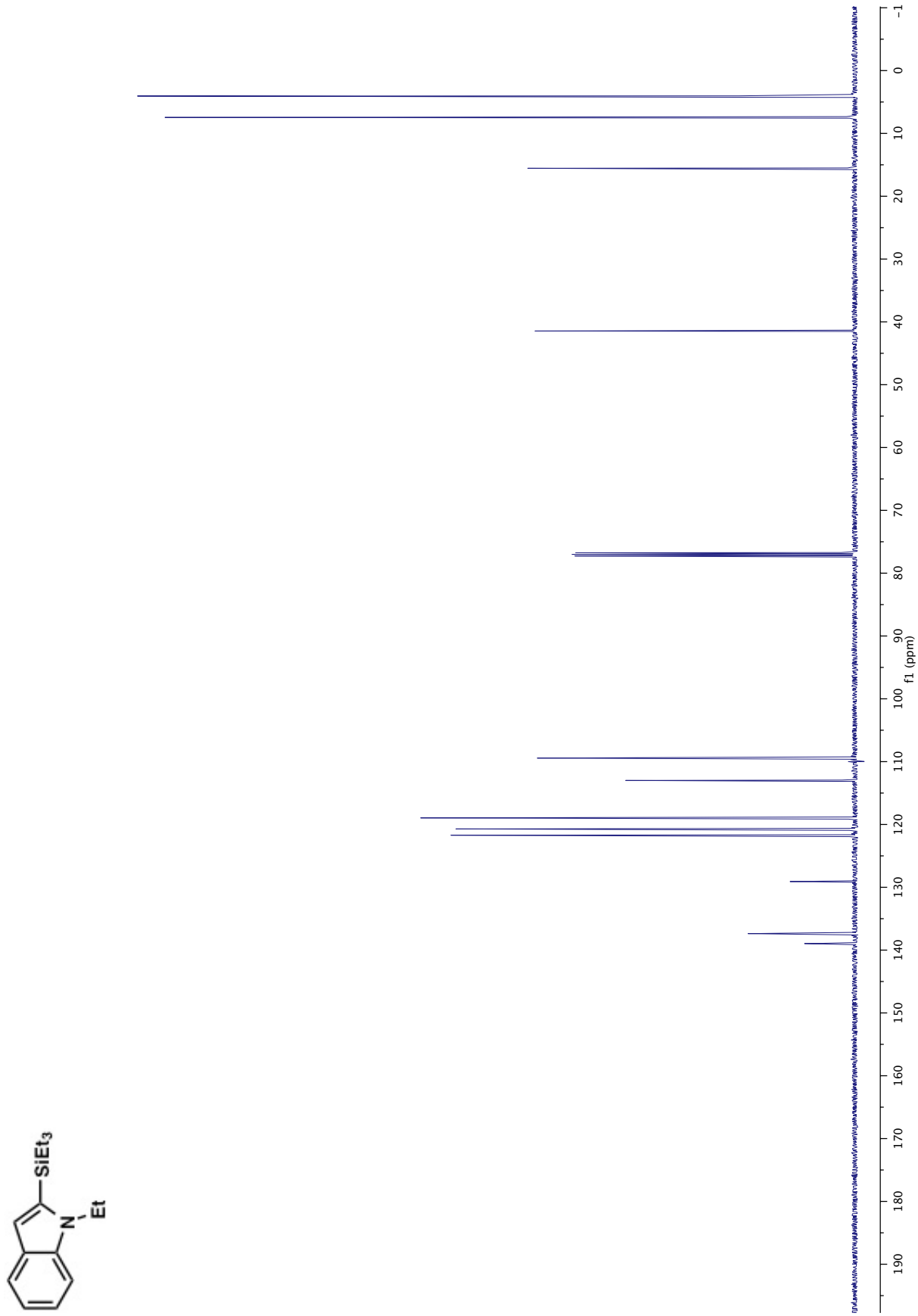
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2b**.



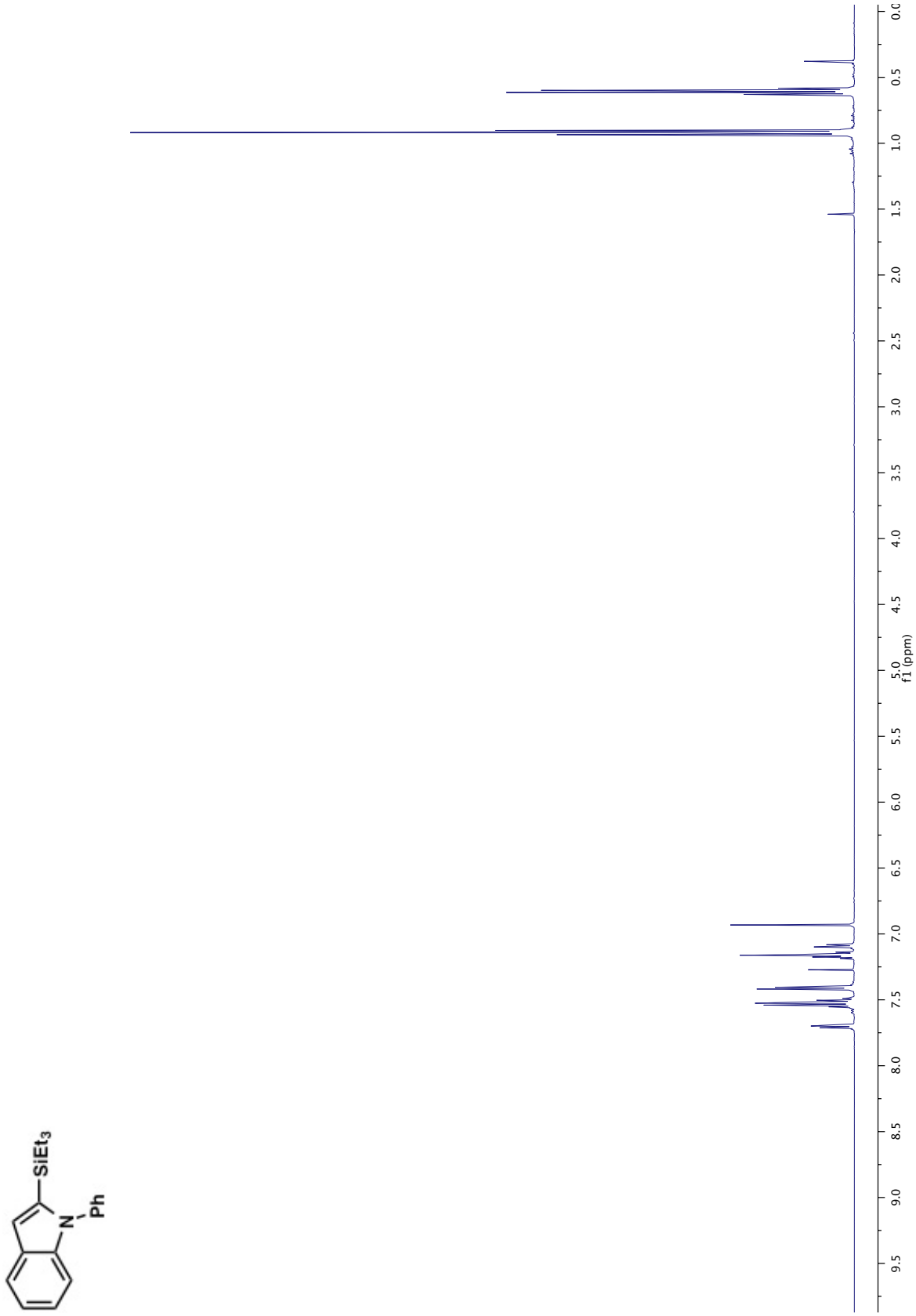
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2b**.



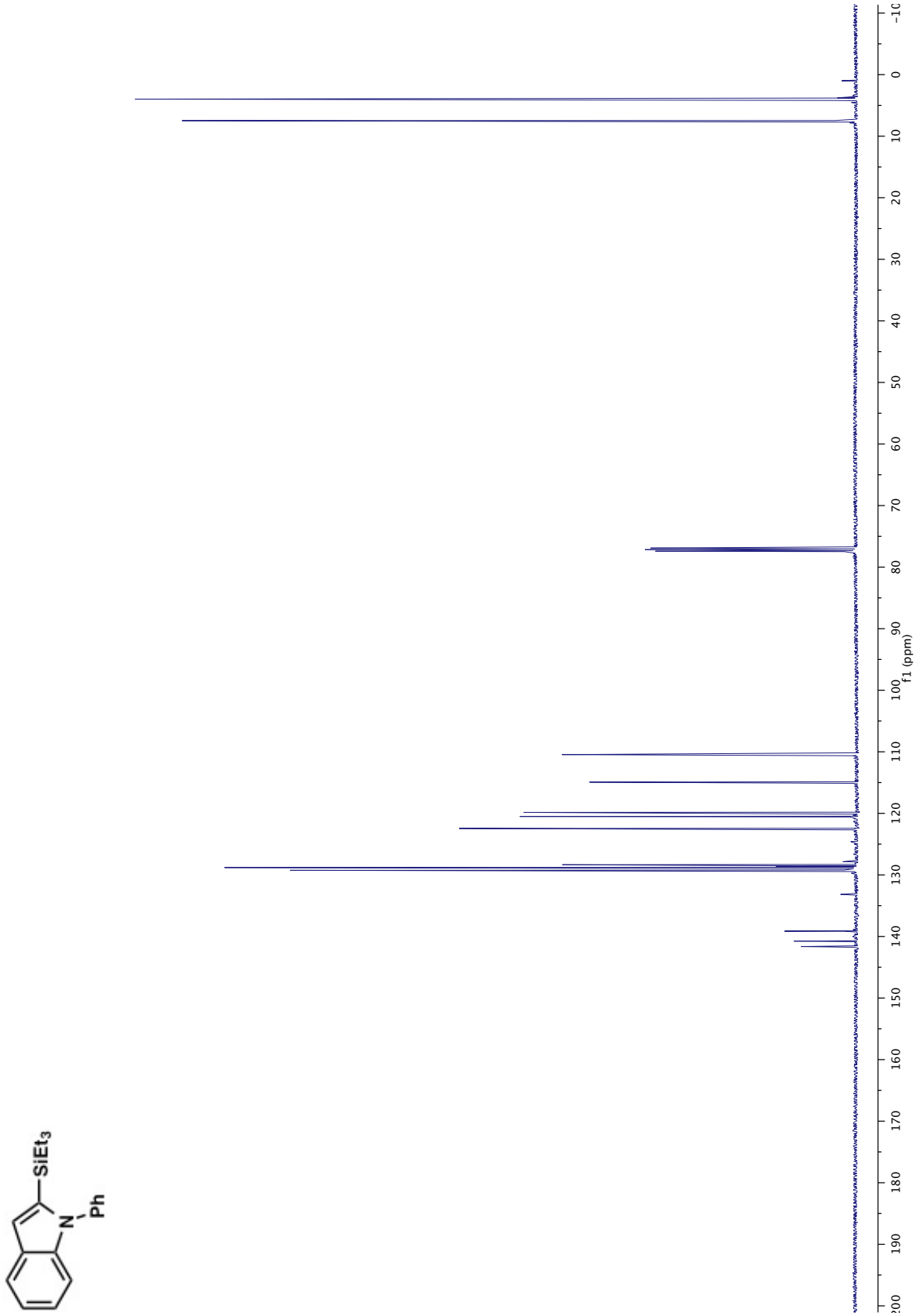
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2c**.



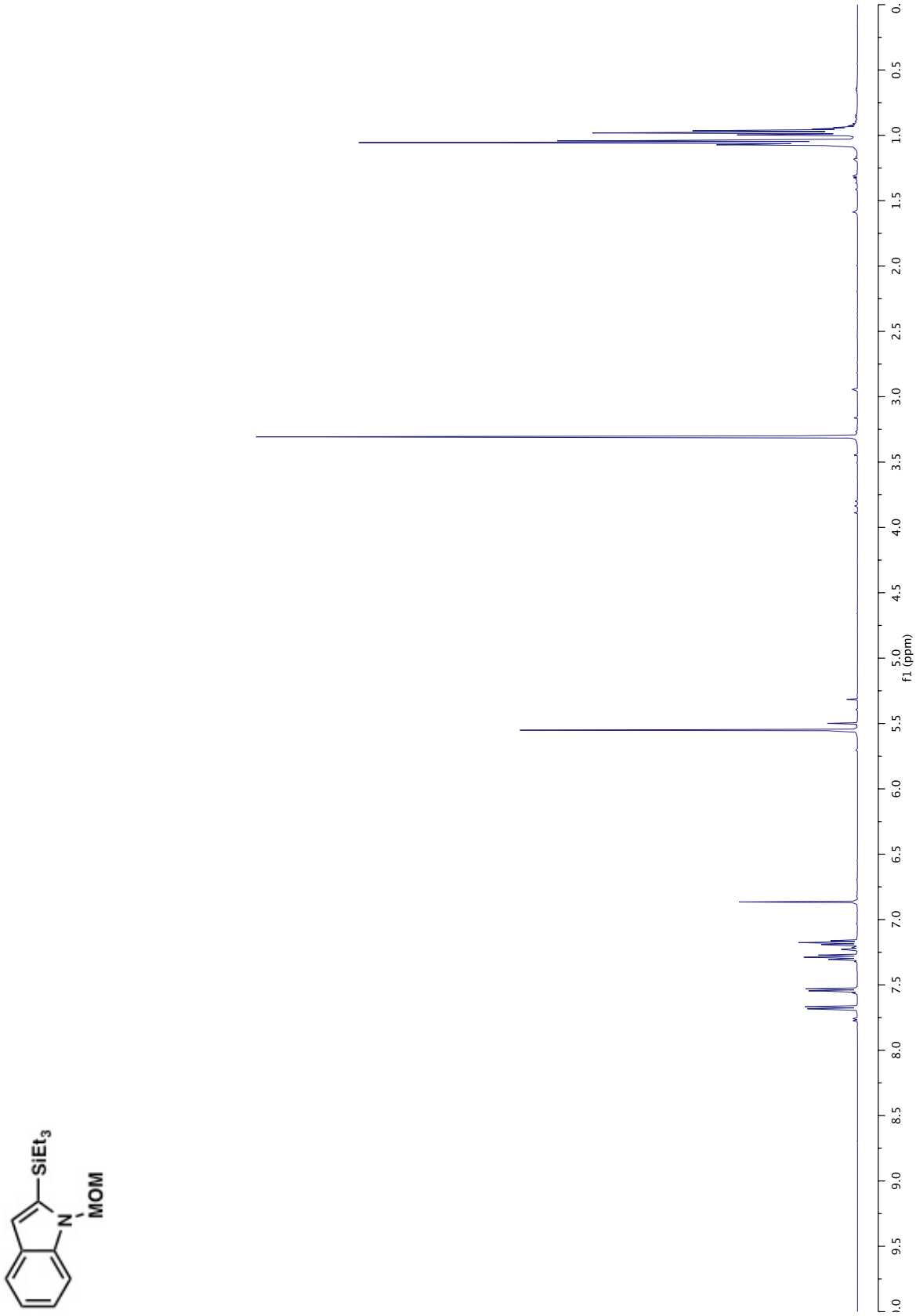
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2c**.



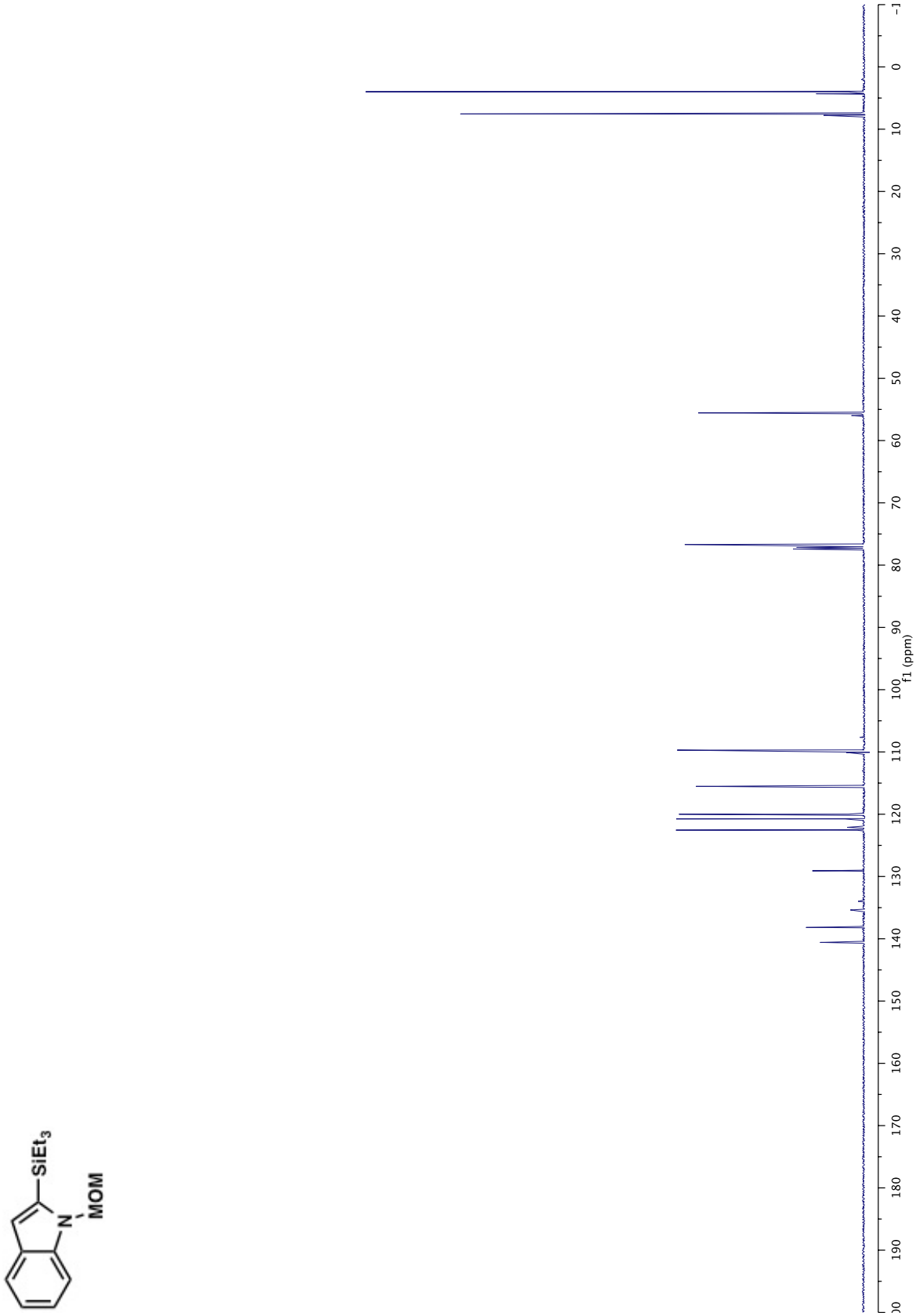
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2d**.



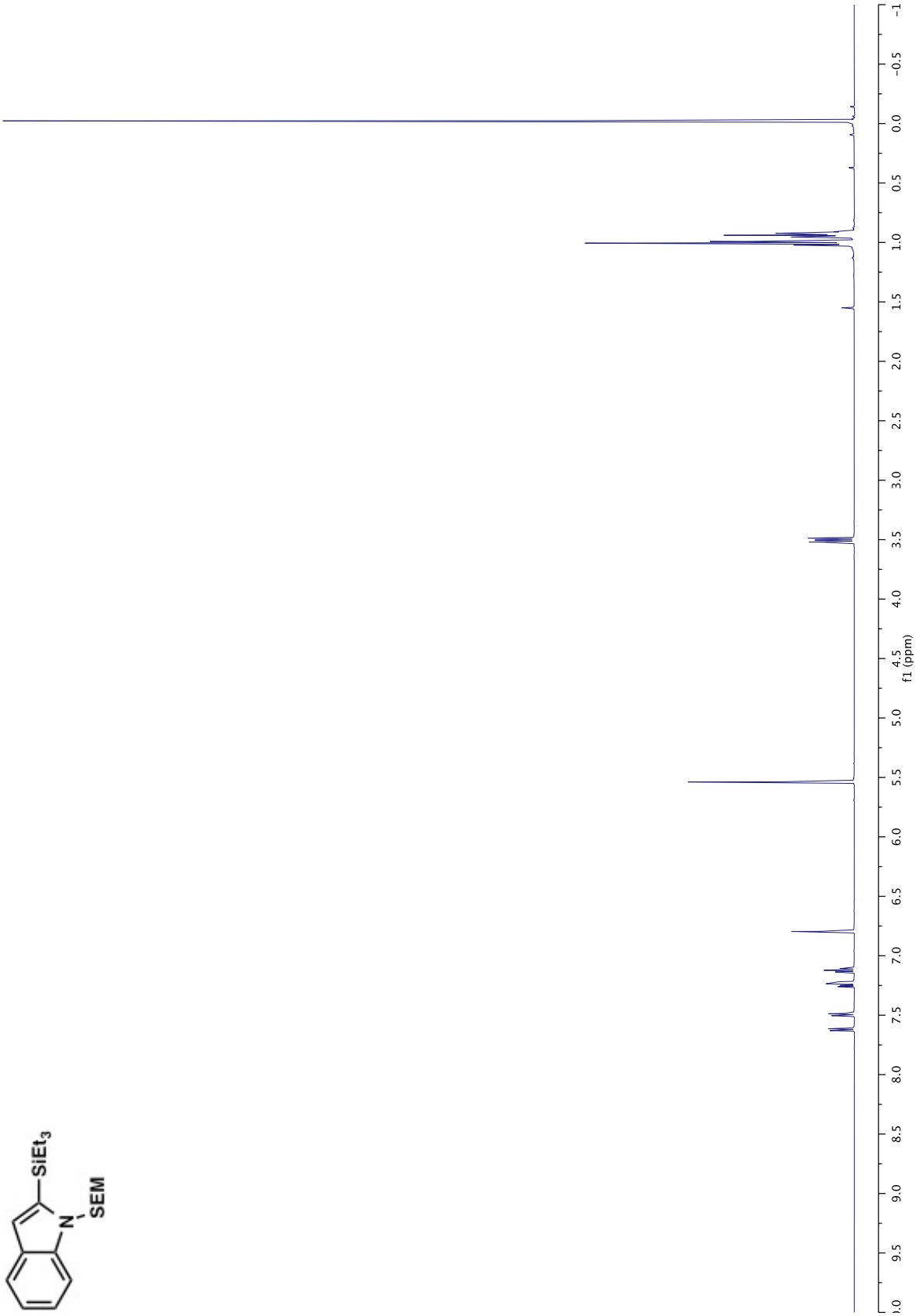
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2d**.



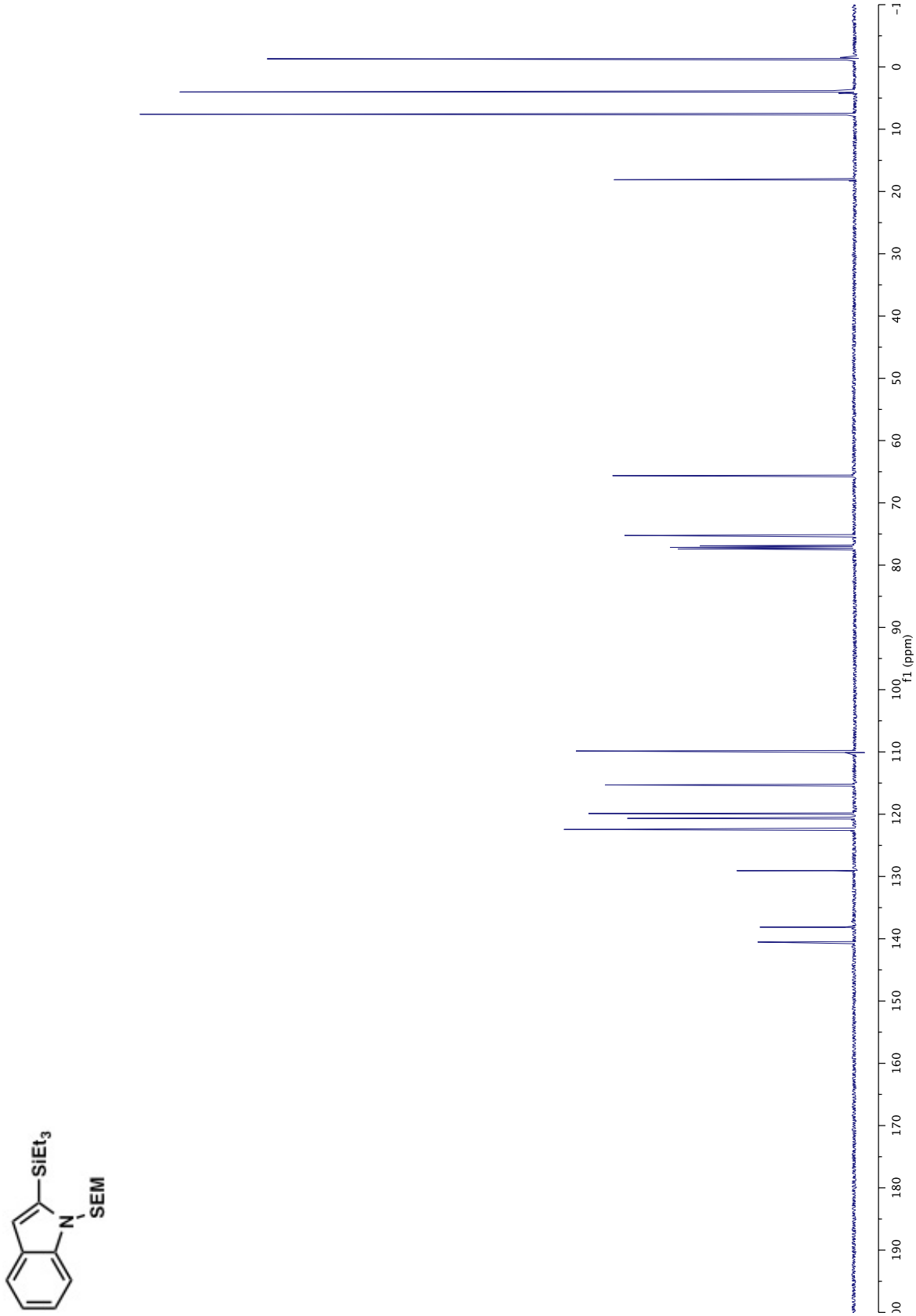
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2e**.



^{13}C NMR (125 MHz, $CDCl_3$) of compound **2e**.

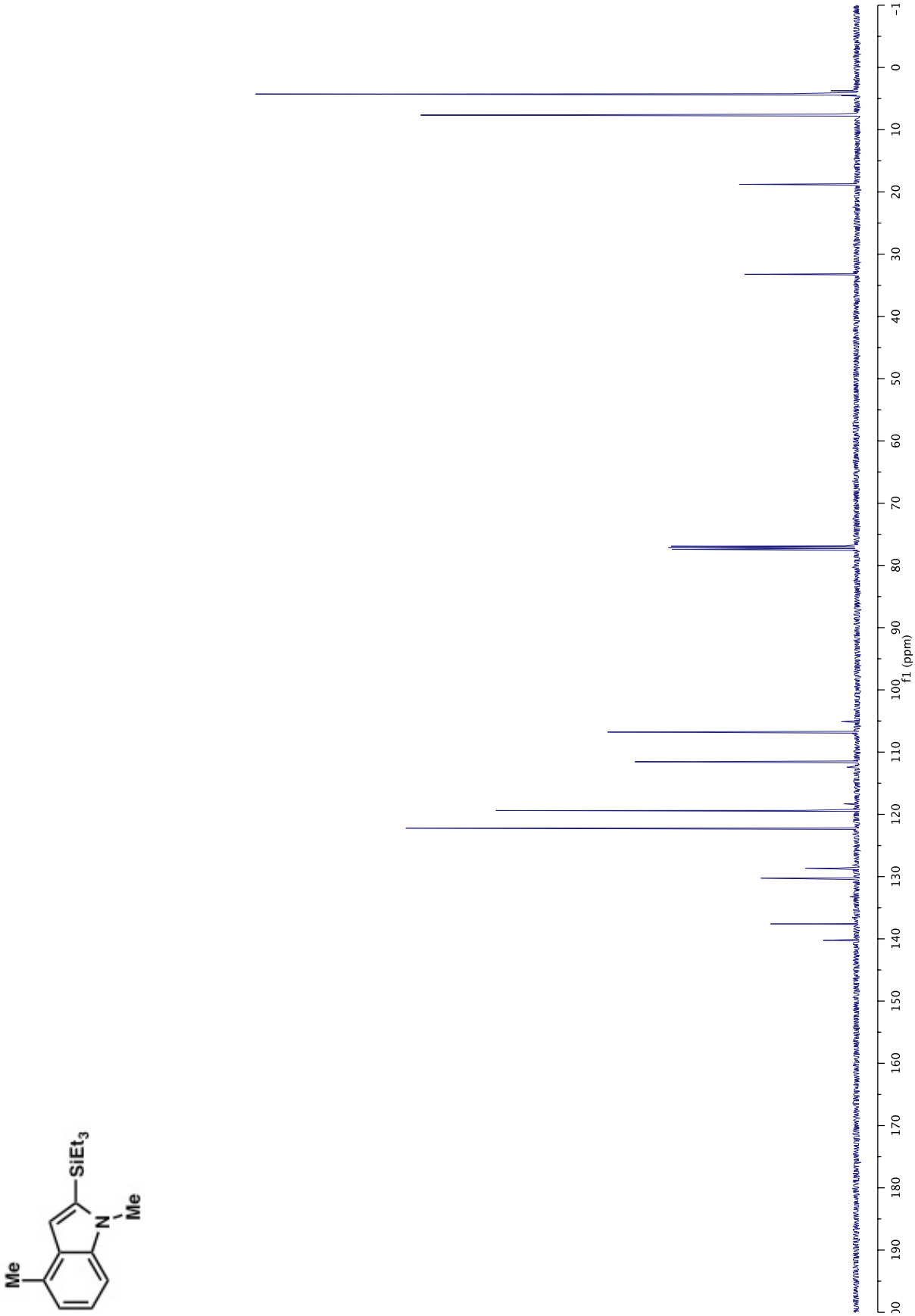


^{1}H NMR (500 MHz, $CDCl_3$) of compound **2f**.

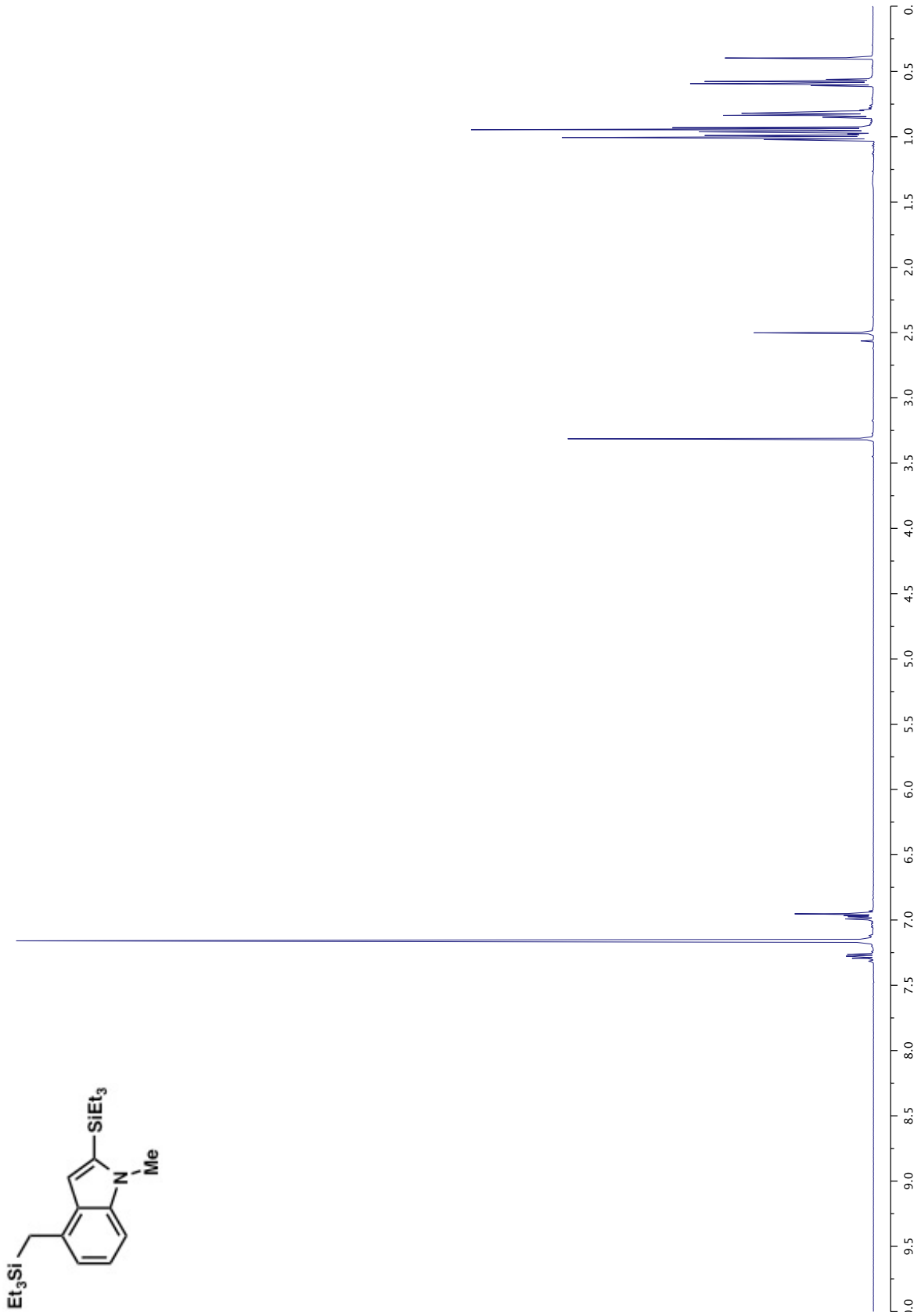


^{13}C NMR (125 MHz, $CDCl_3$) of compound **2f**.

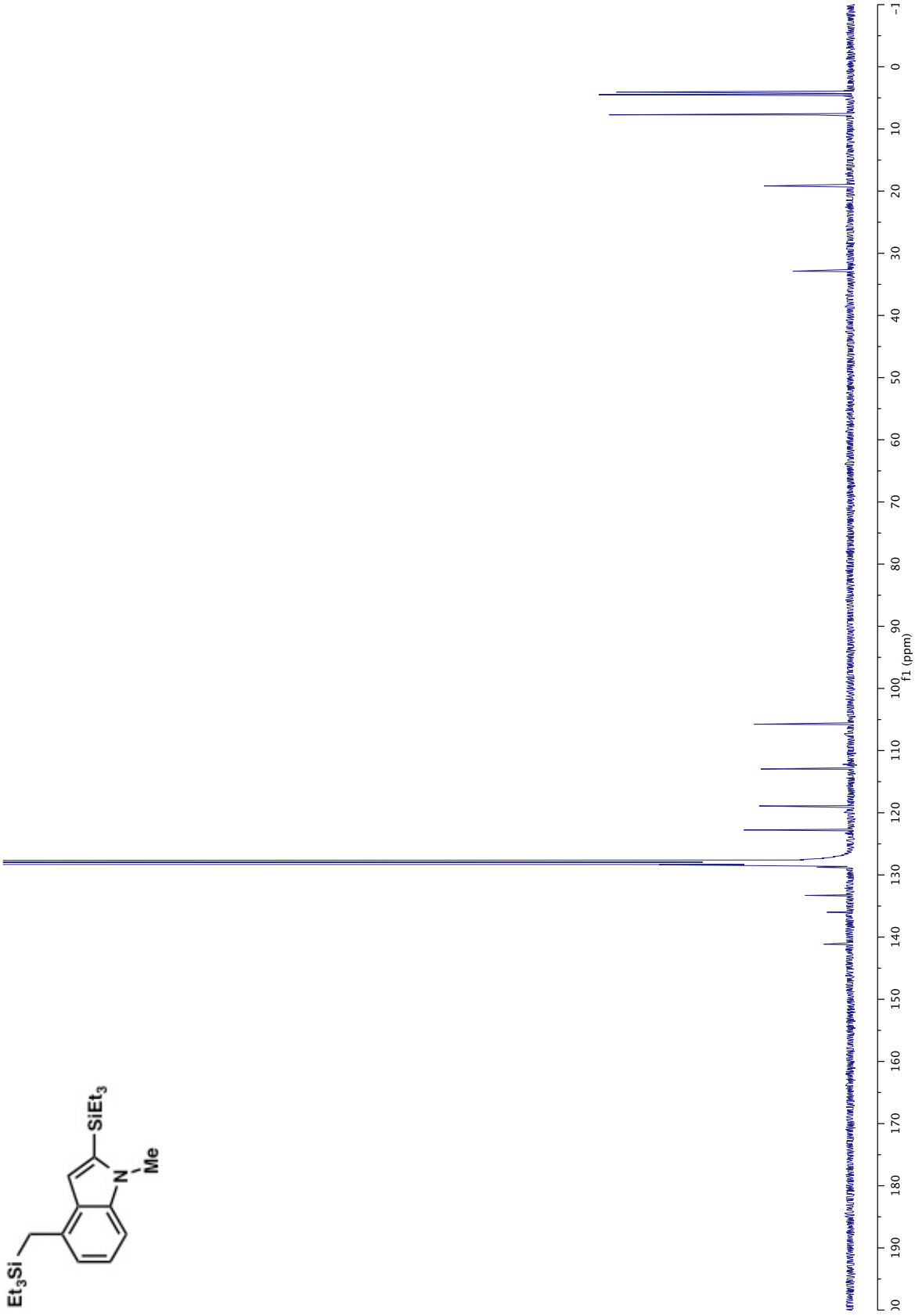
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2g**.



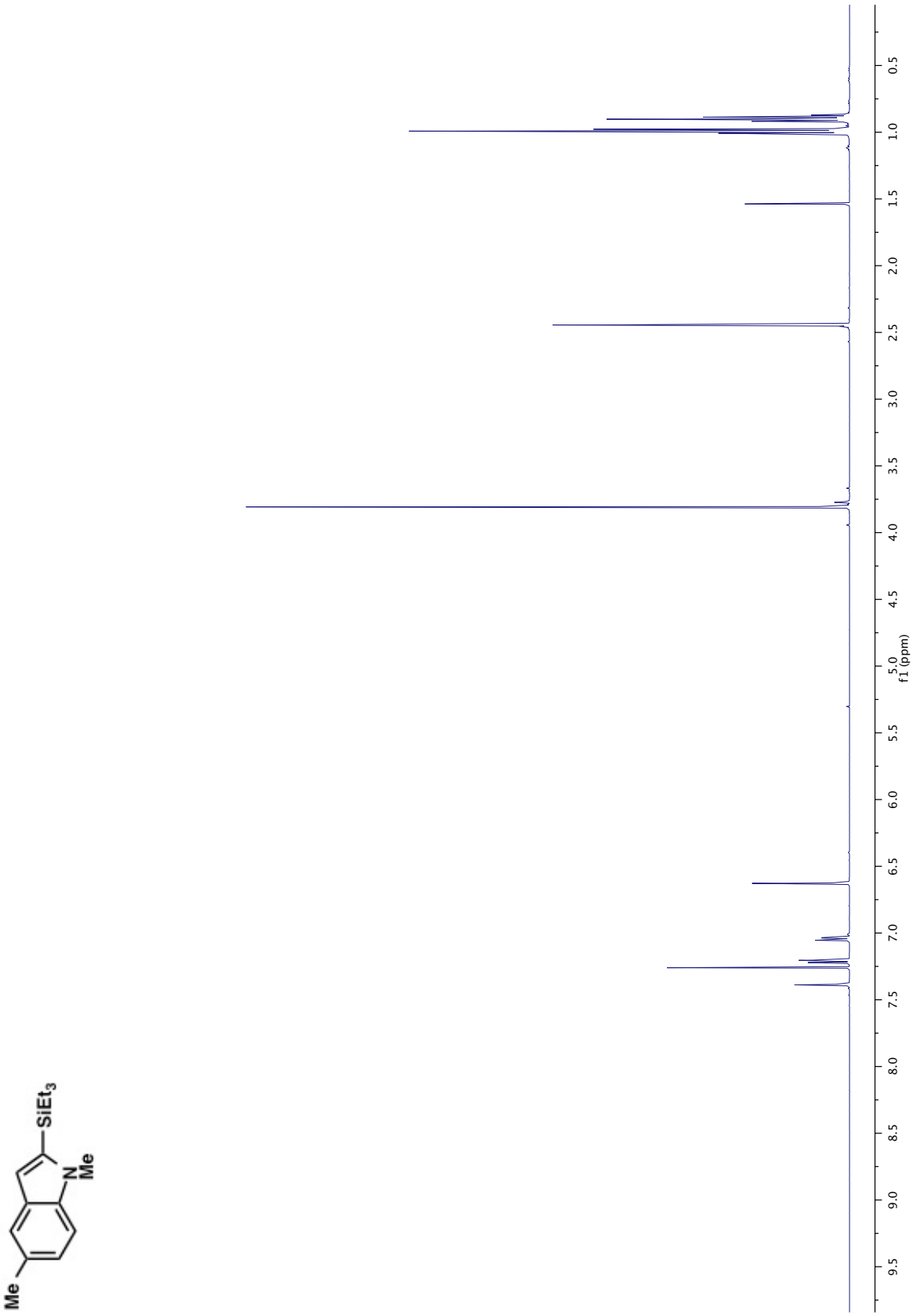
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2g**.



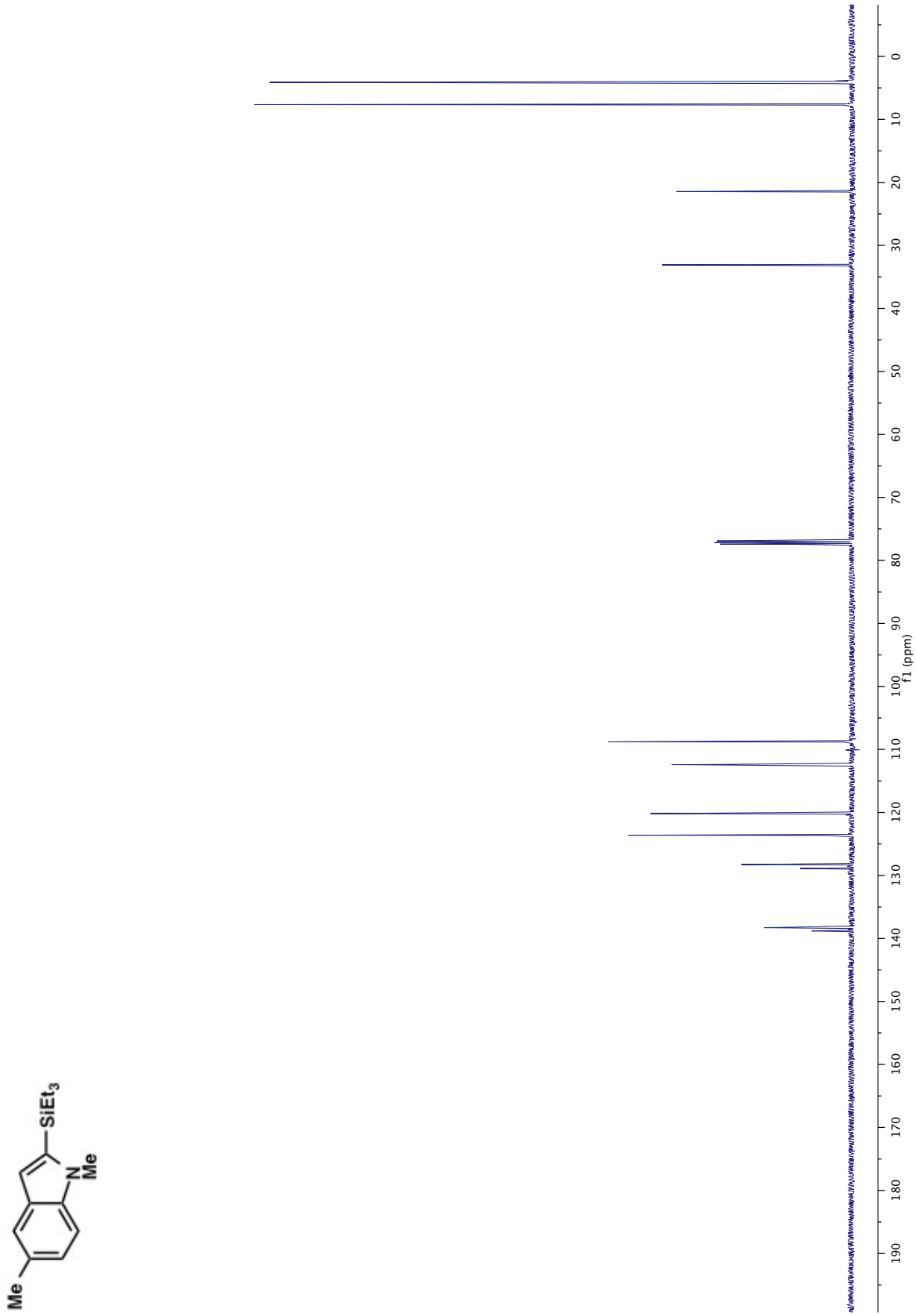
^{1}H NMR (500 MHz, C_6D_6) of compound **16**.



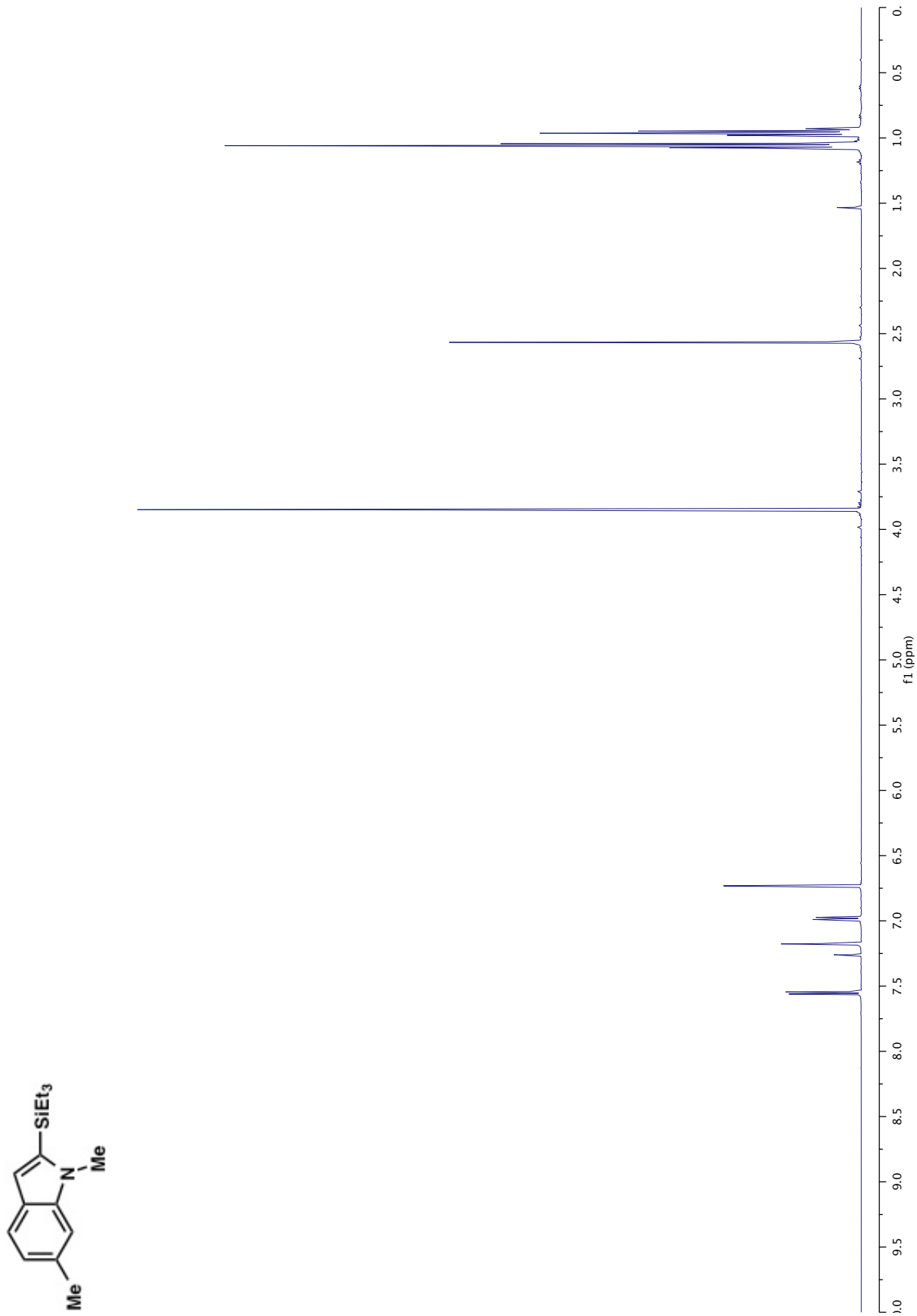
^{13}C NMR (125 MHz, C_6D_6) of compound **16**.



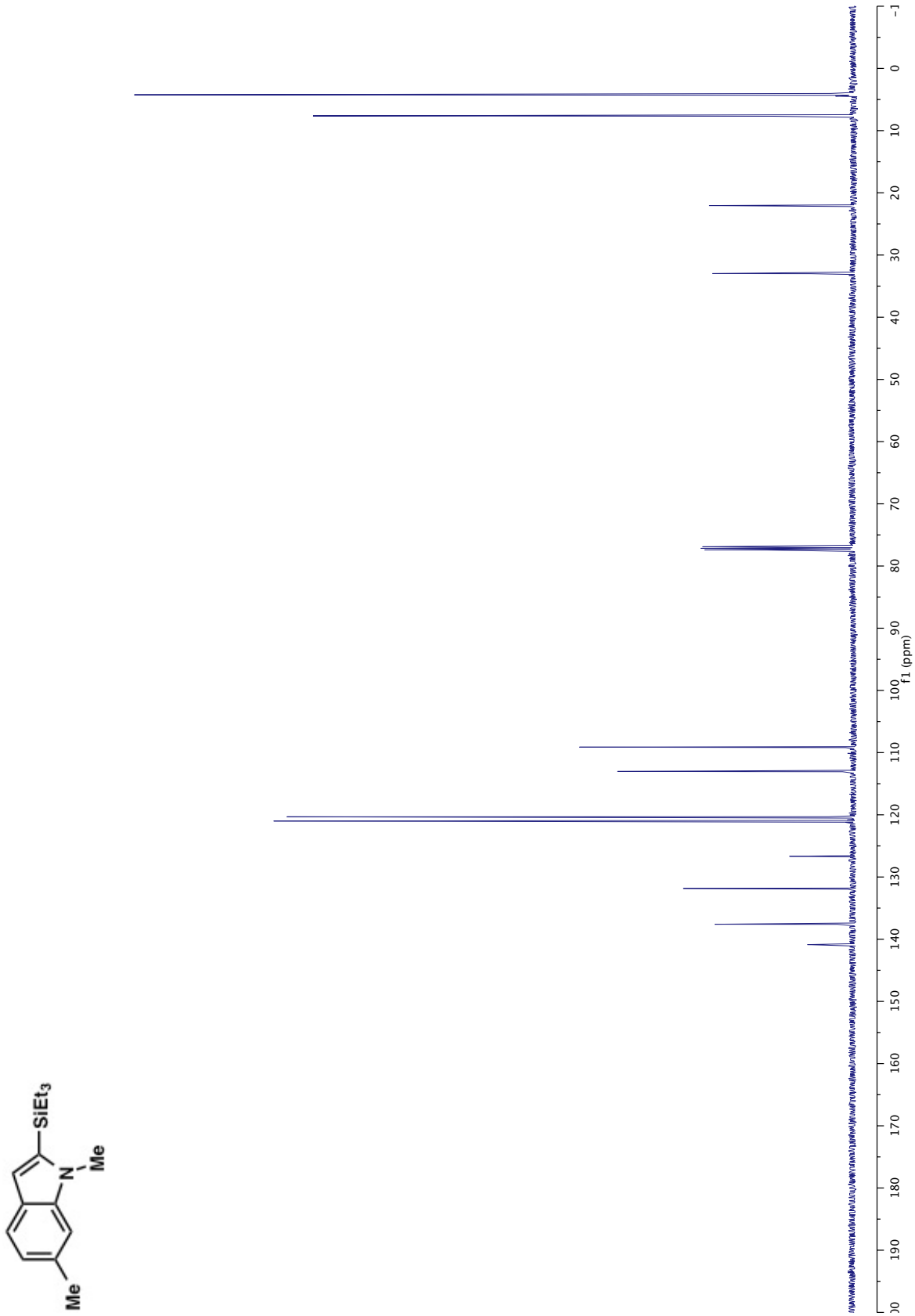
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2h**.



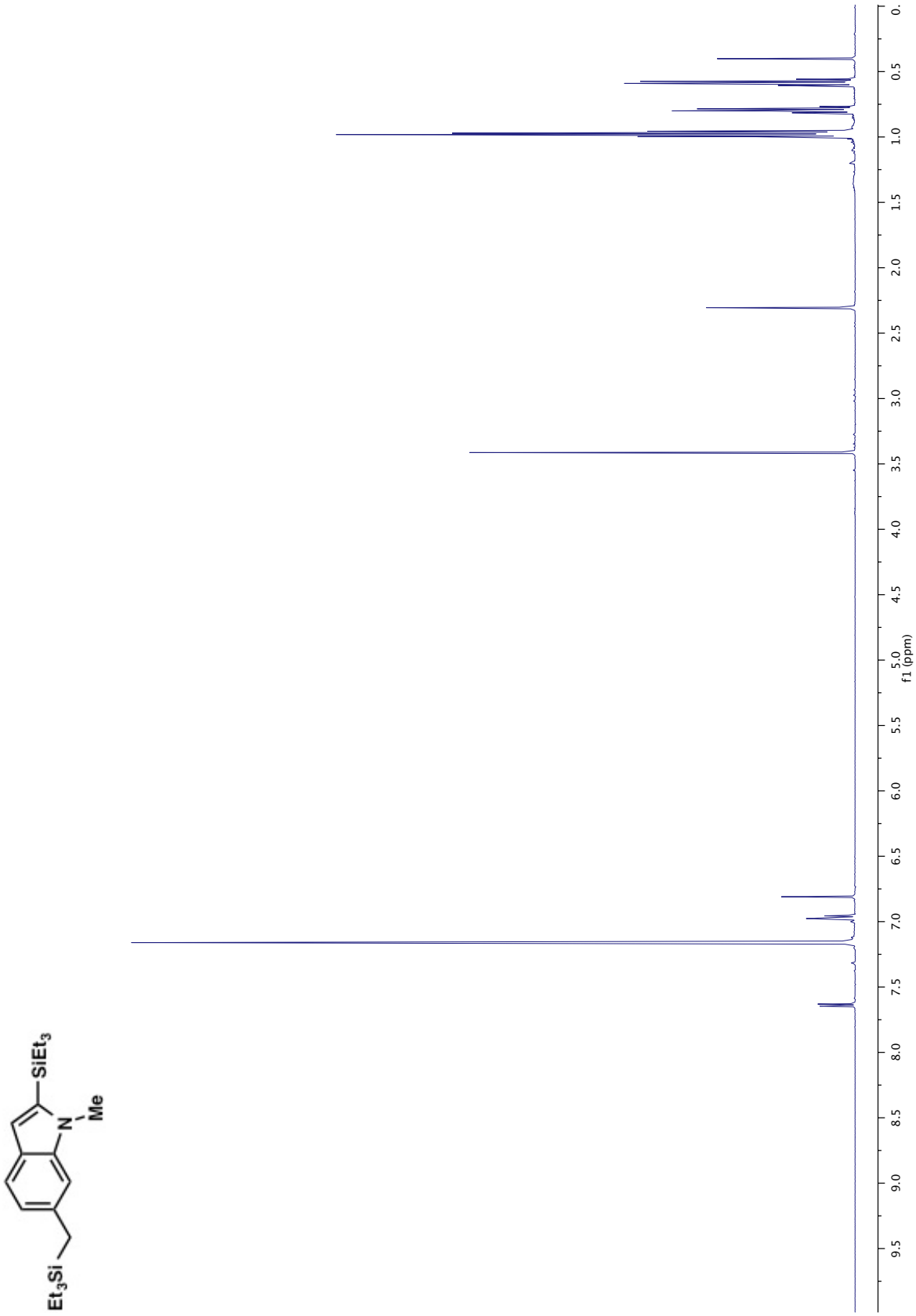
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2h**.



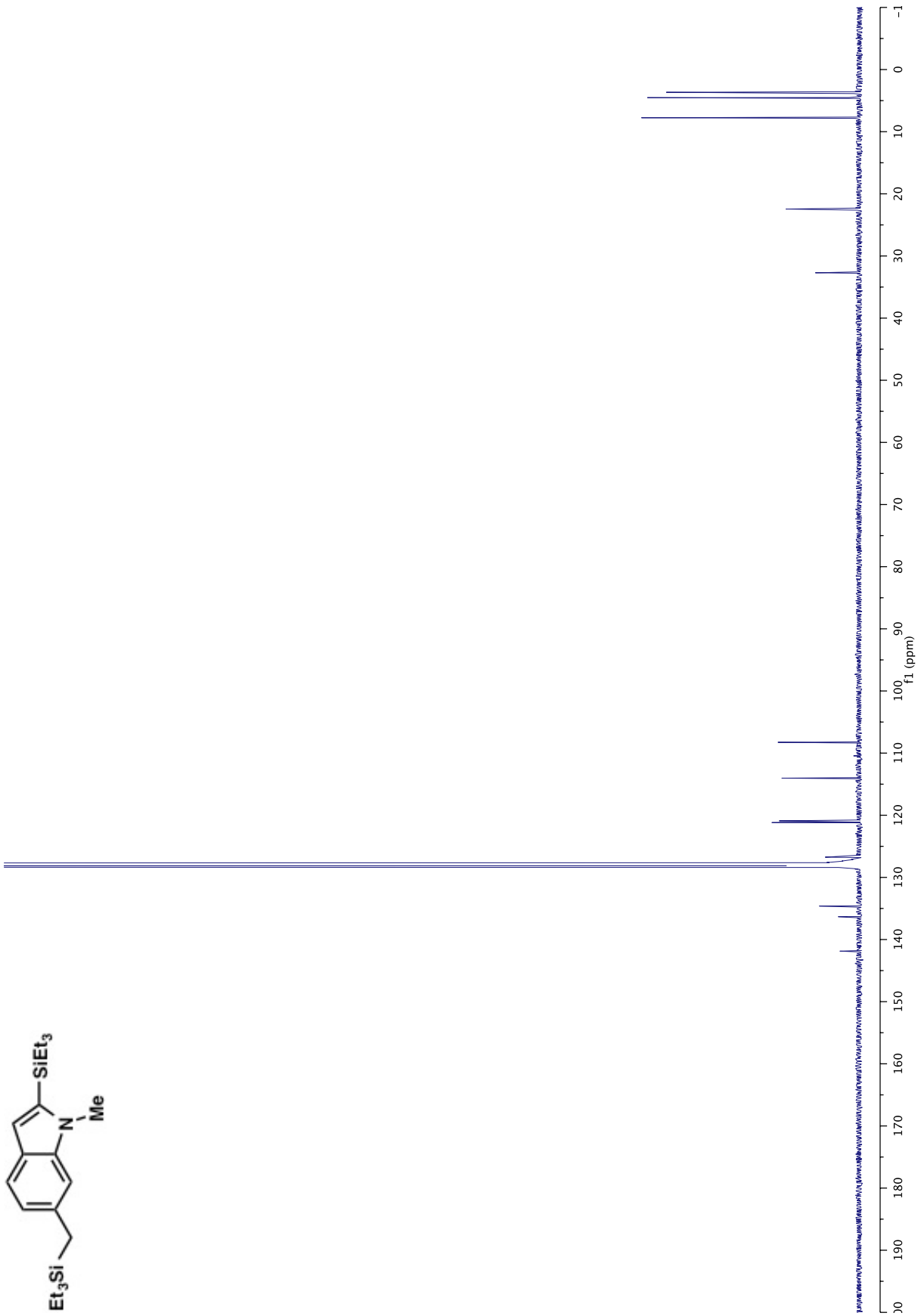
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2i**.



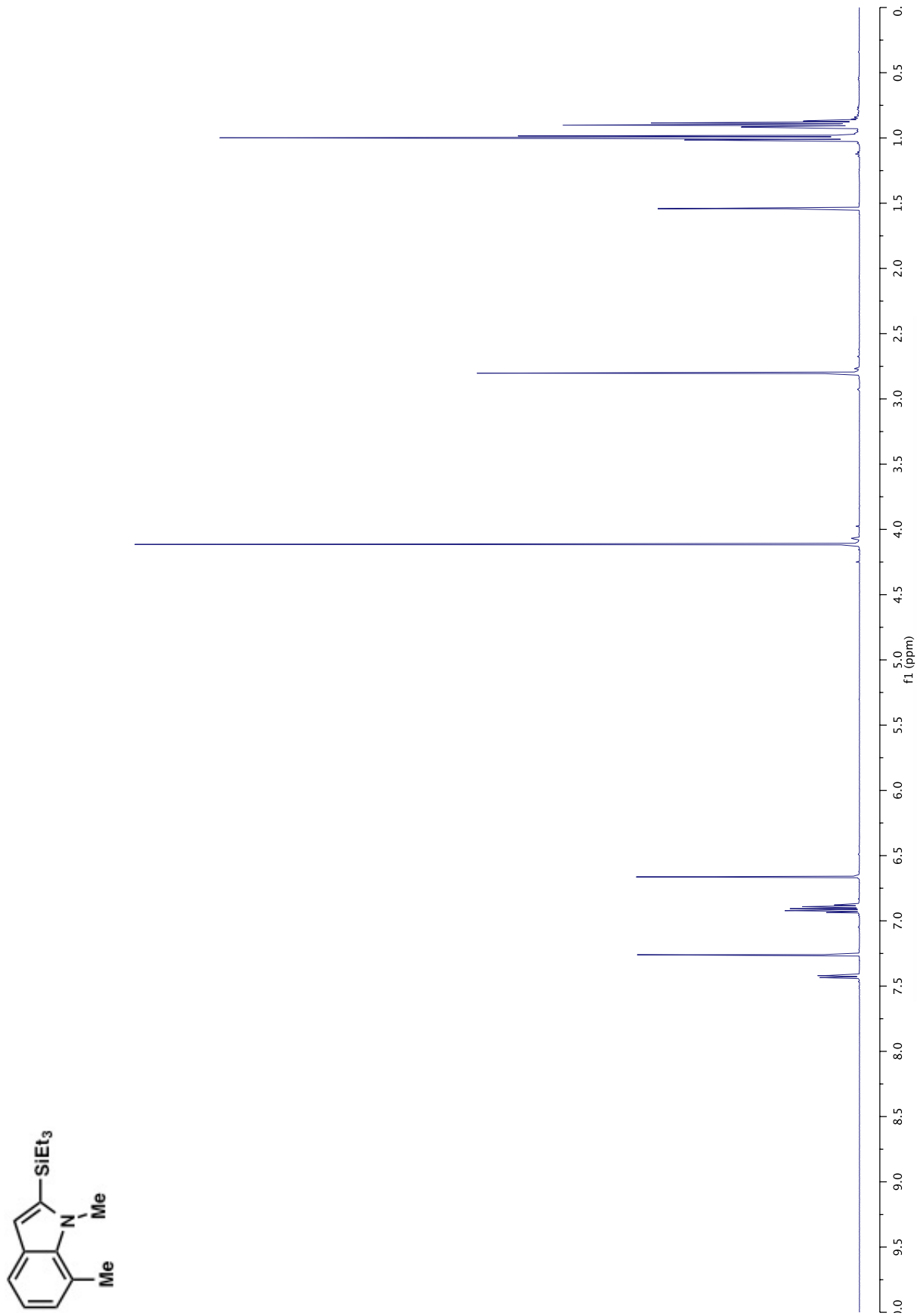
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2i**.



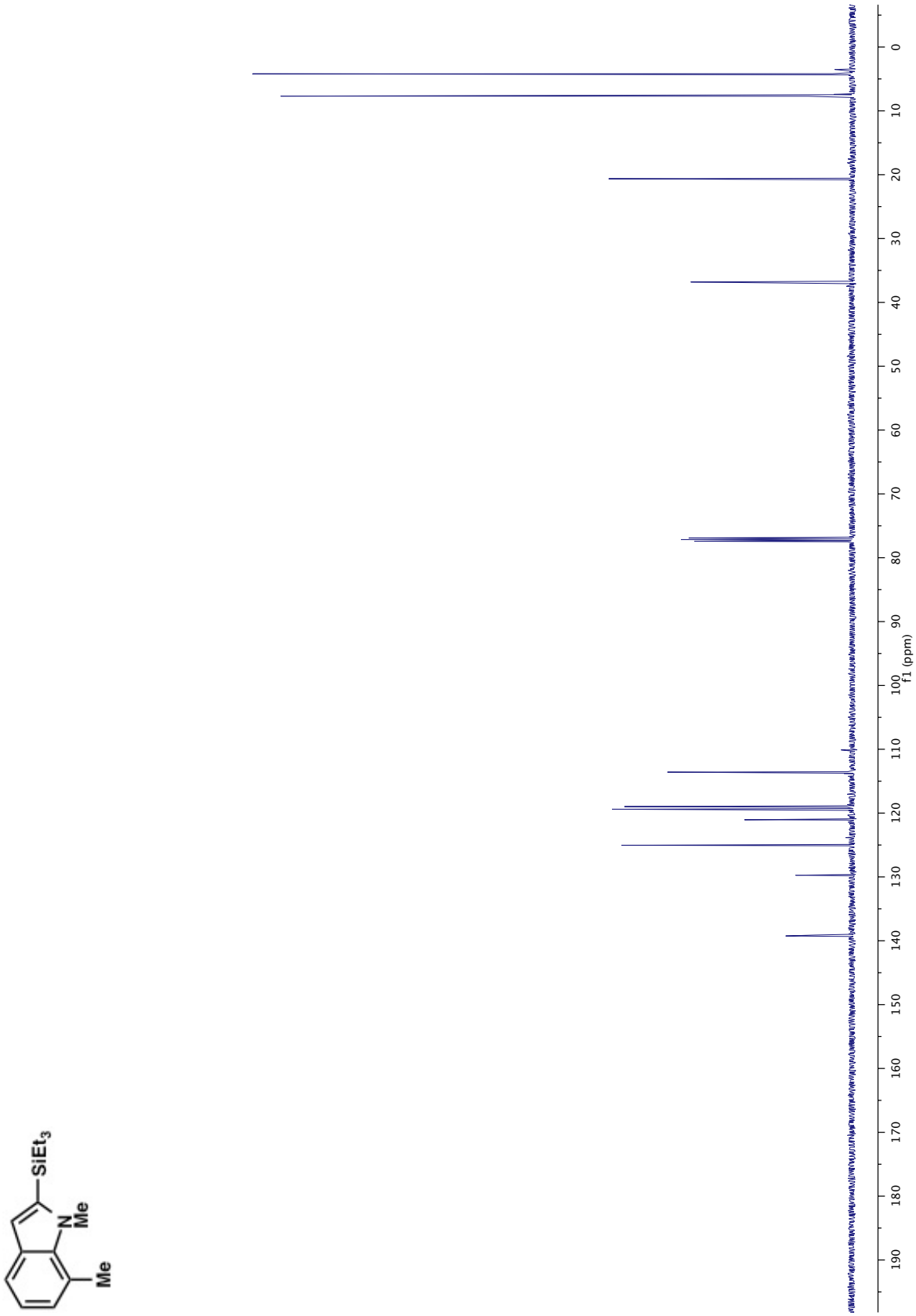
^{1}H NMR (500 MHz, C_6D_6) of compound **SI-2i.**



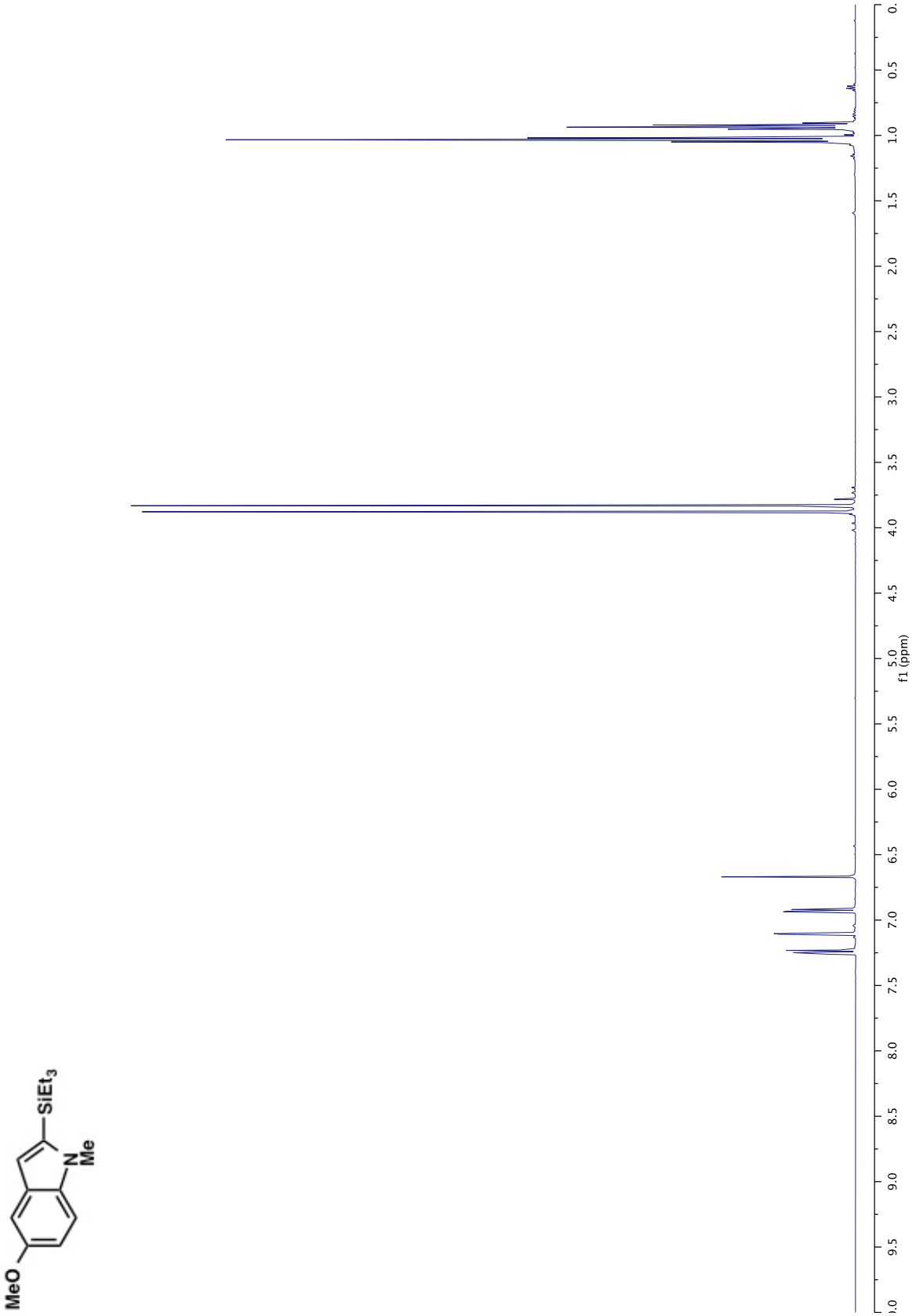
^{13}C NMR (125 MHz, C_6D_6) of compound **SI-2i**.



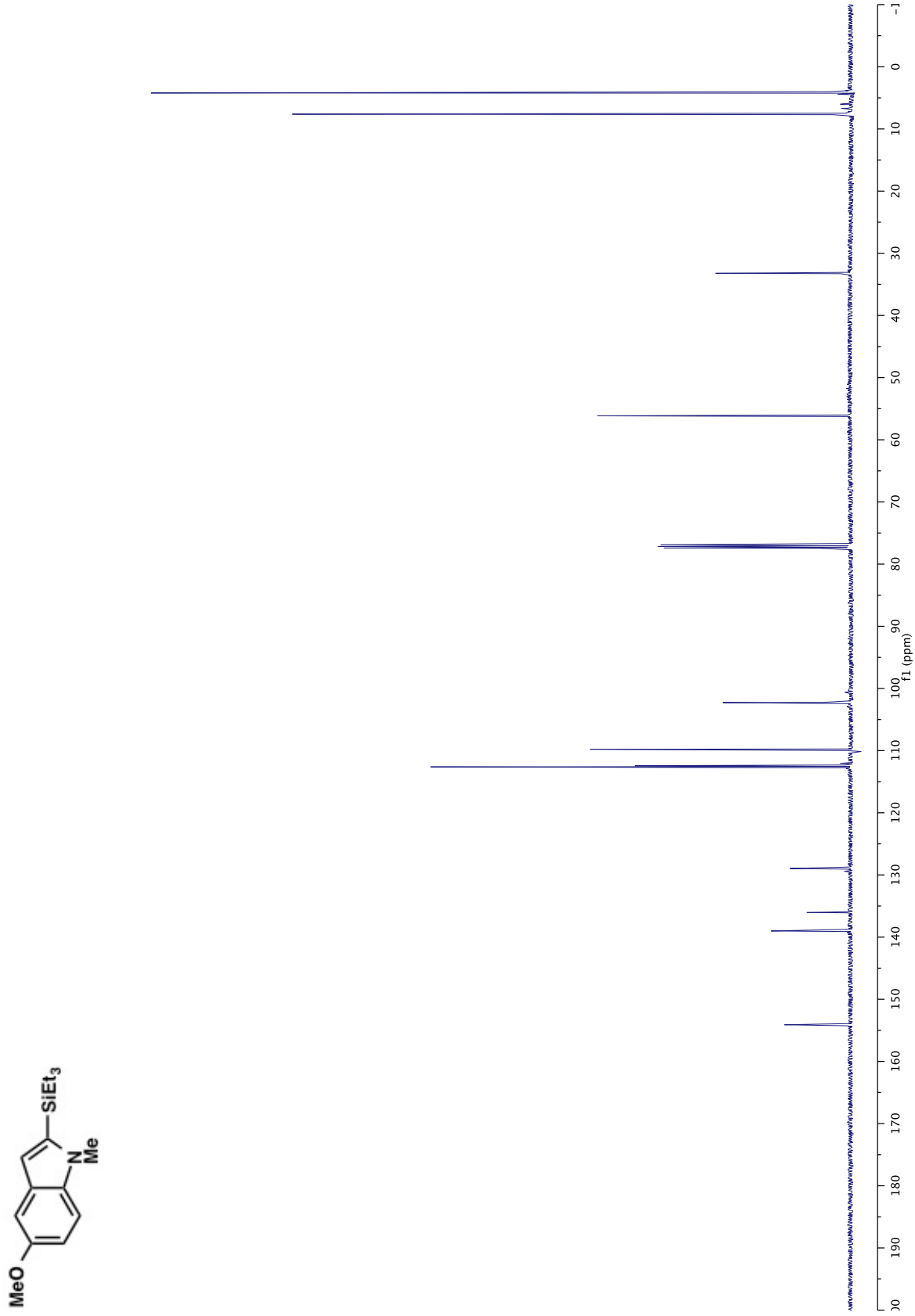
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2j**.



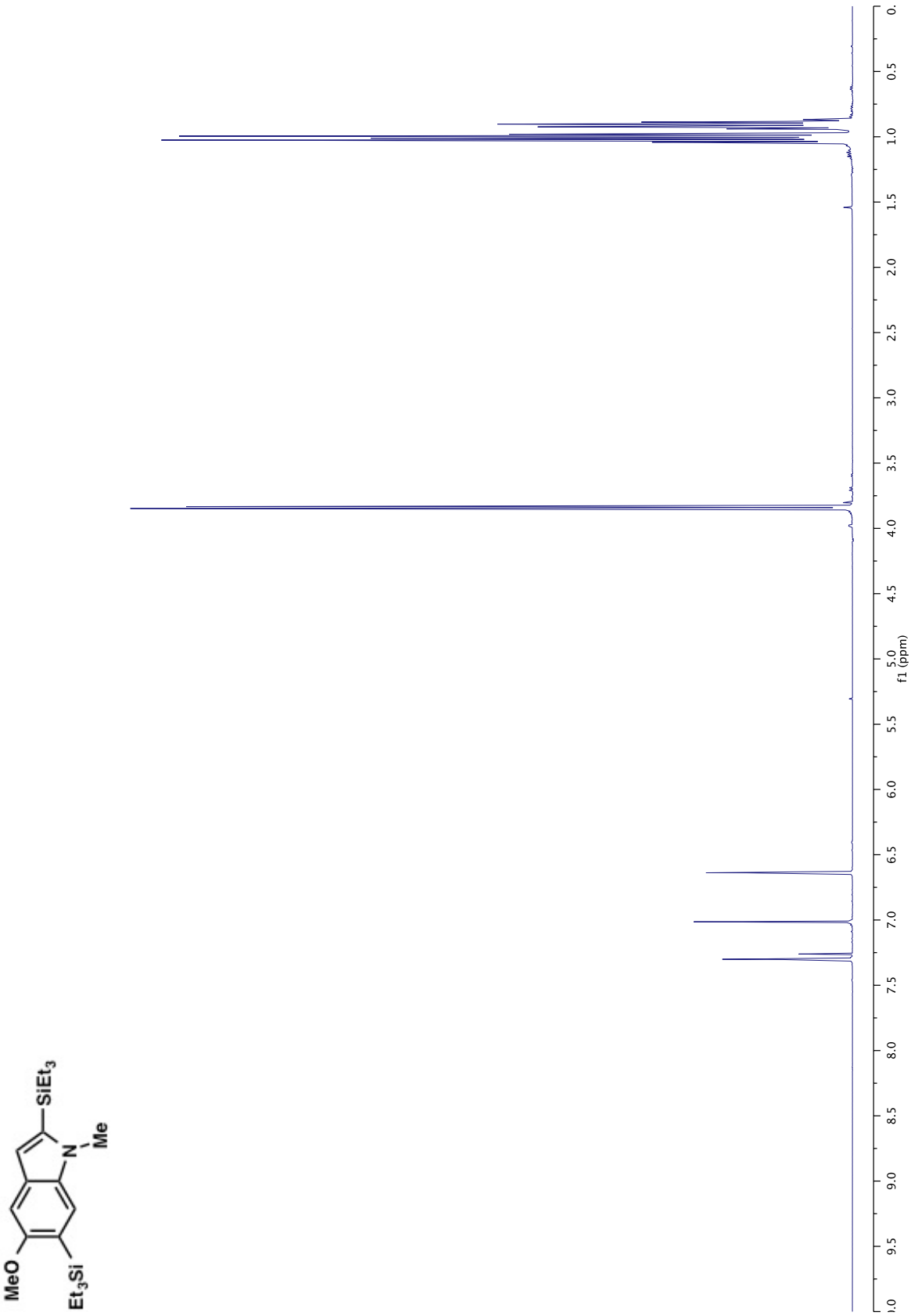
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2j**.



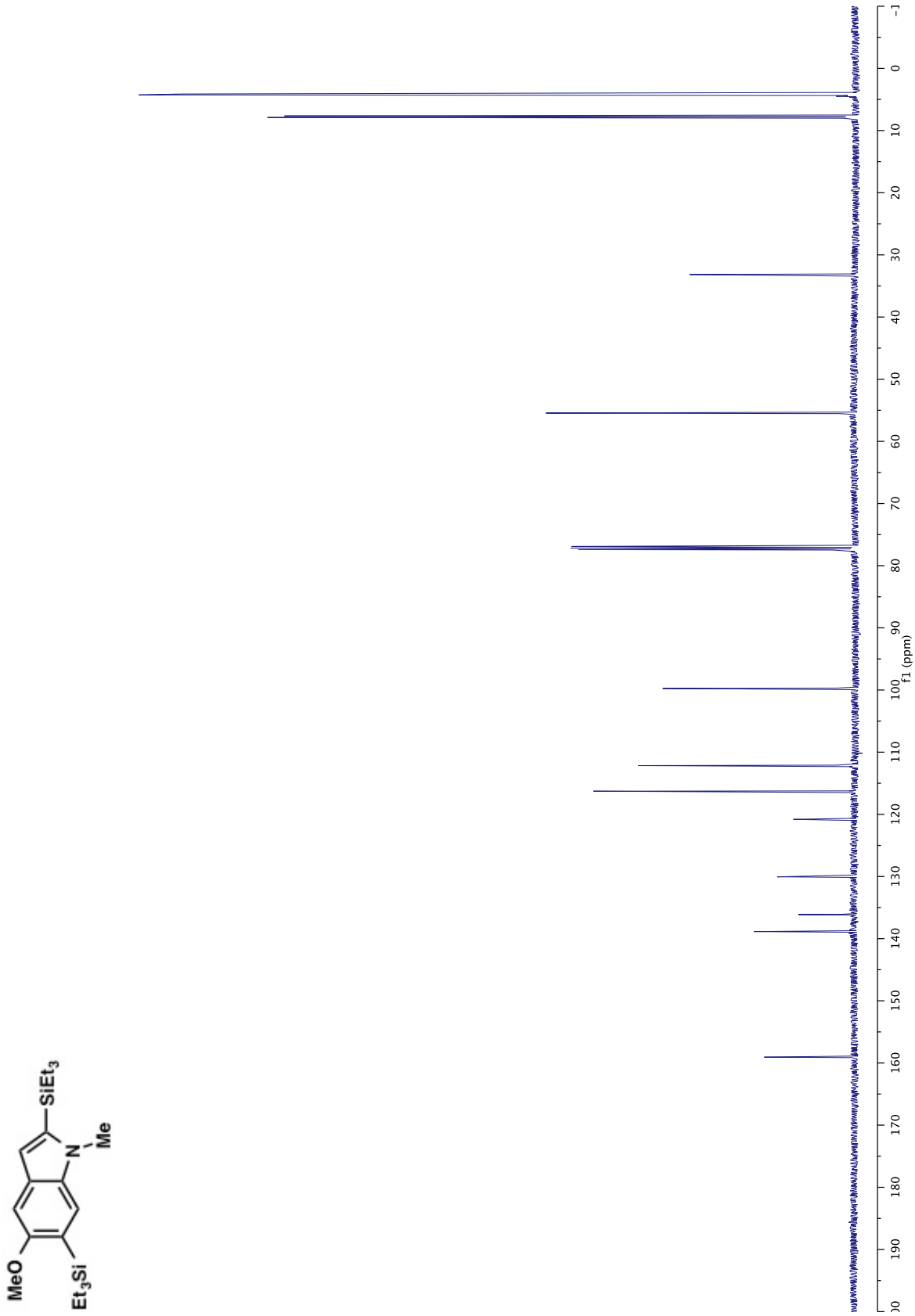
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2k**.



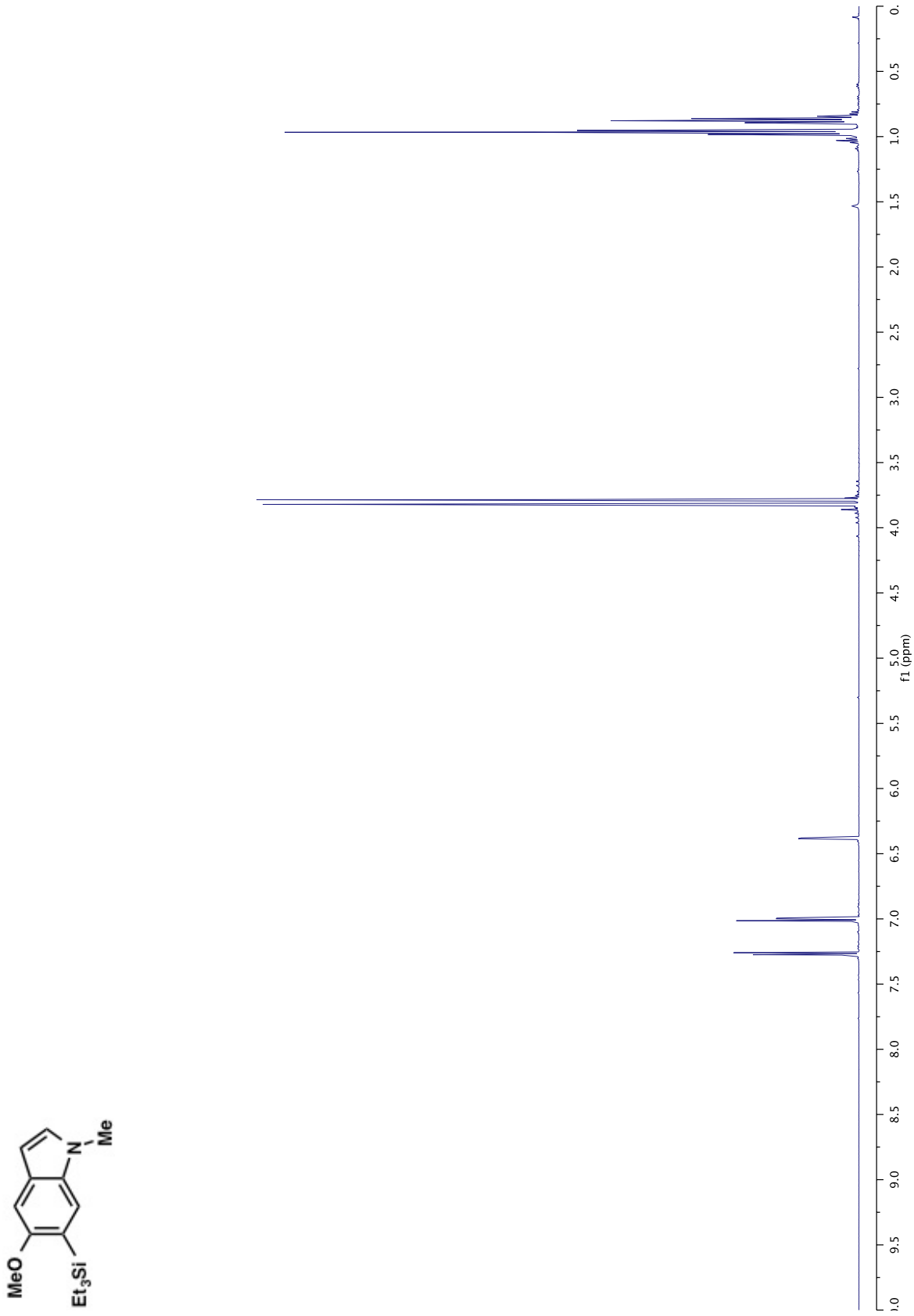
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2k**.



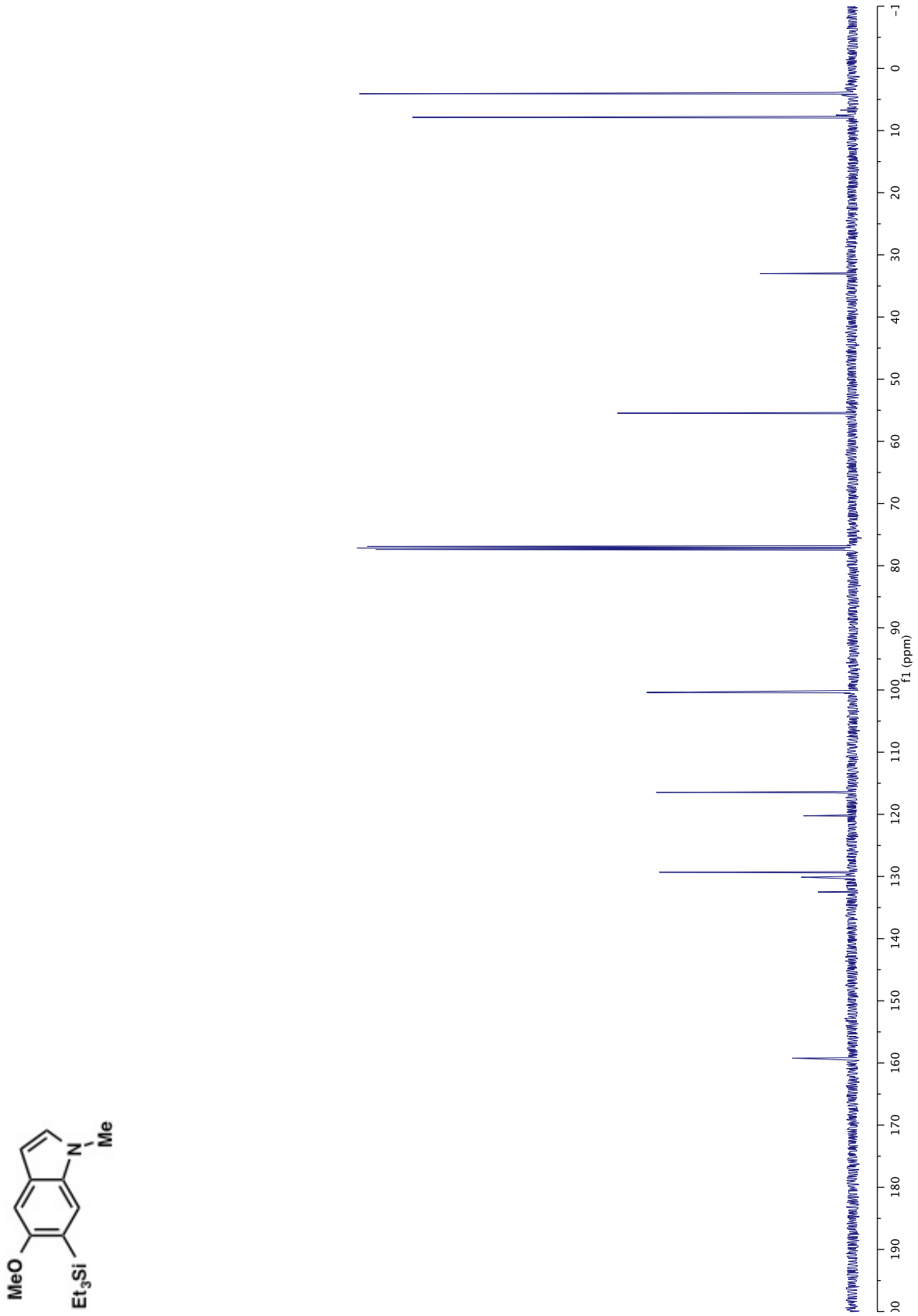
^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-2k**.



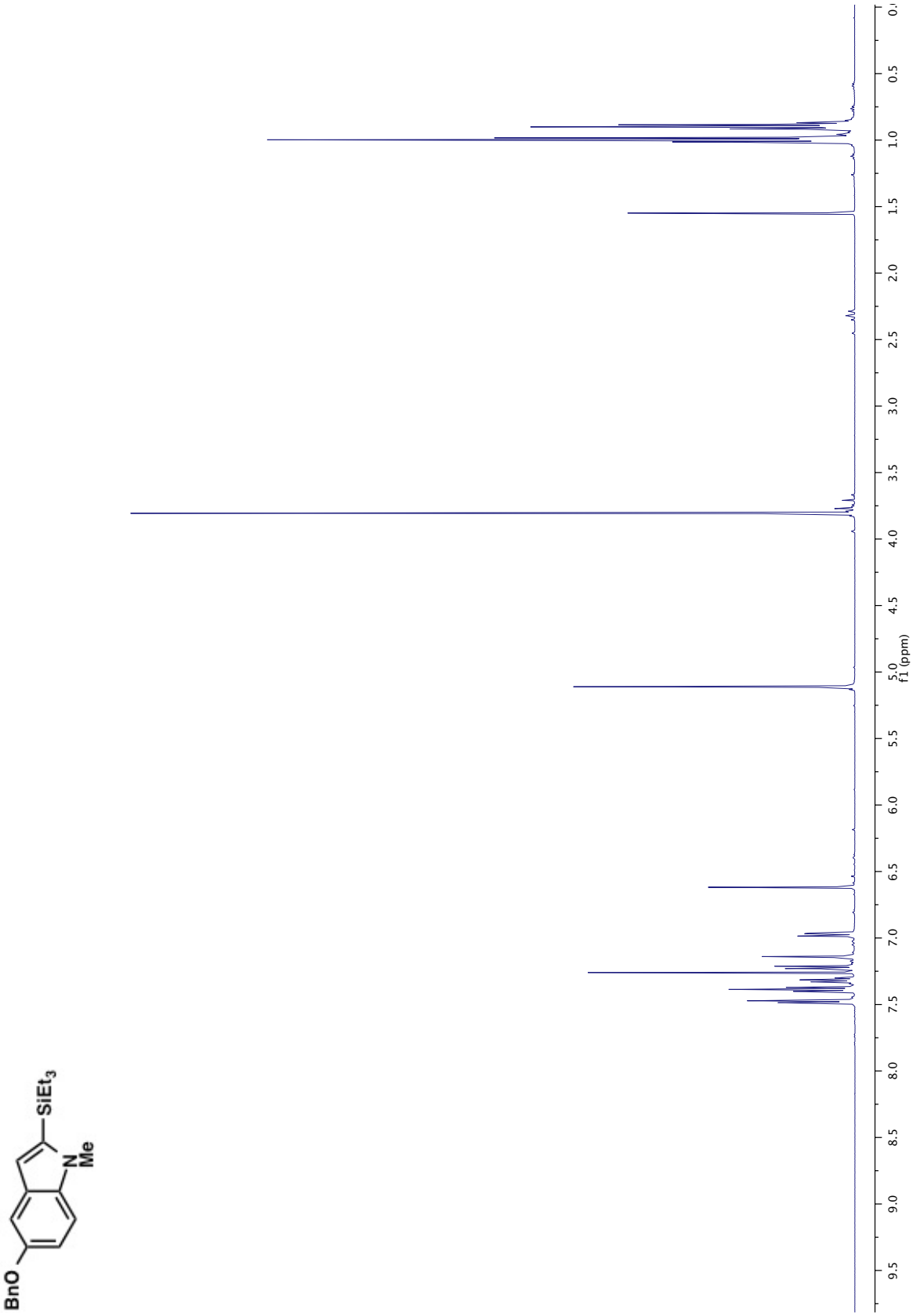
^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-2k**.



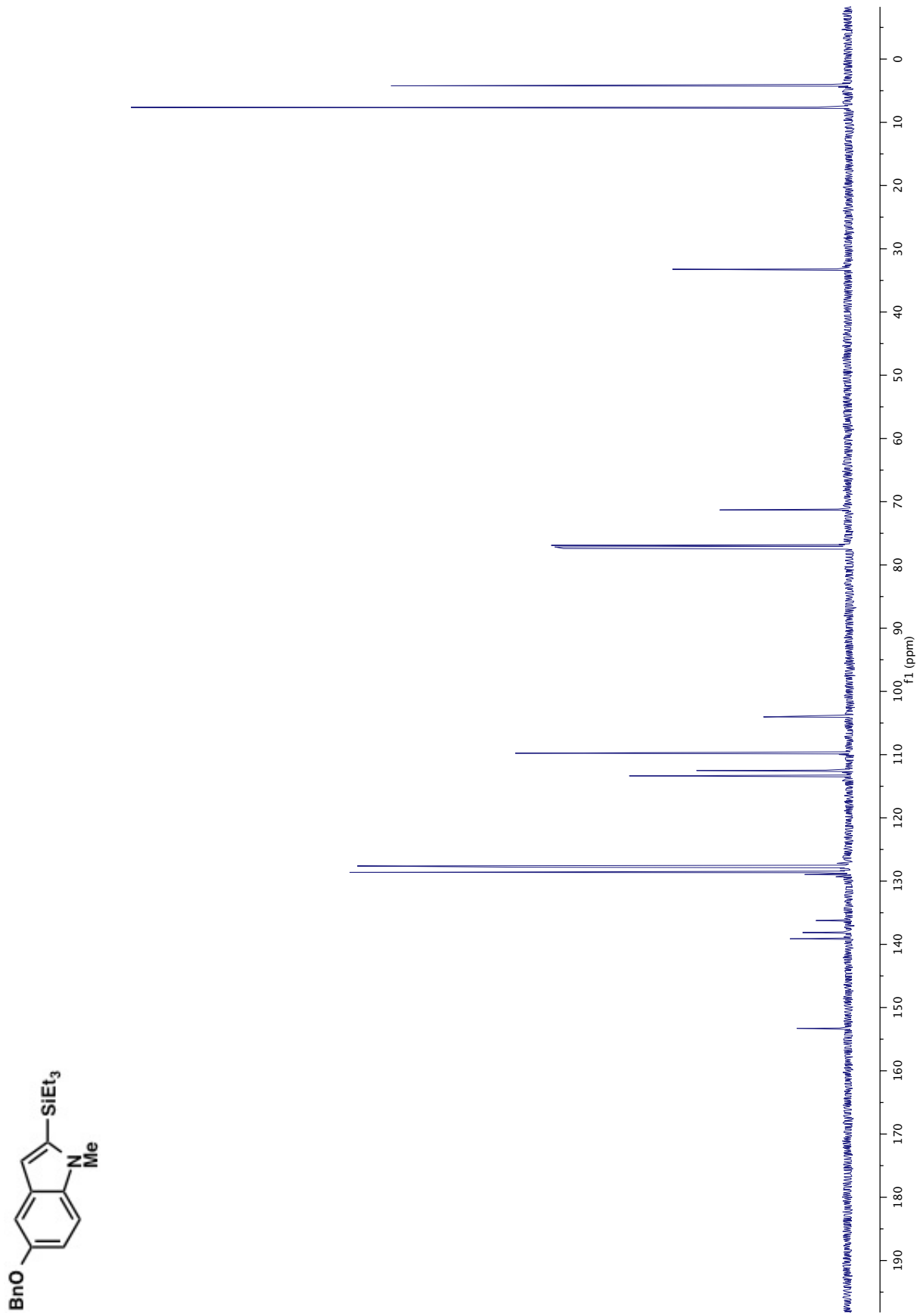
^{1}H NMR (500 MHz, $CDCl_3$) of compound **15**.



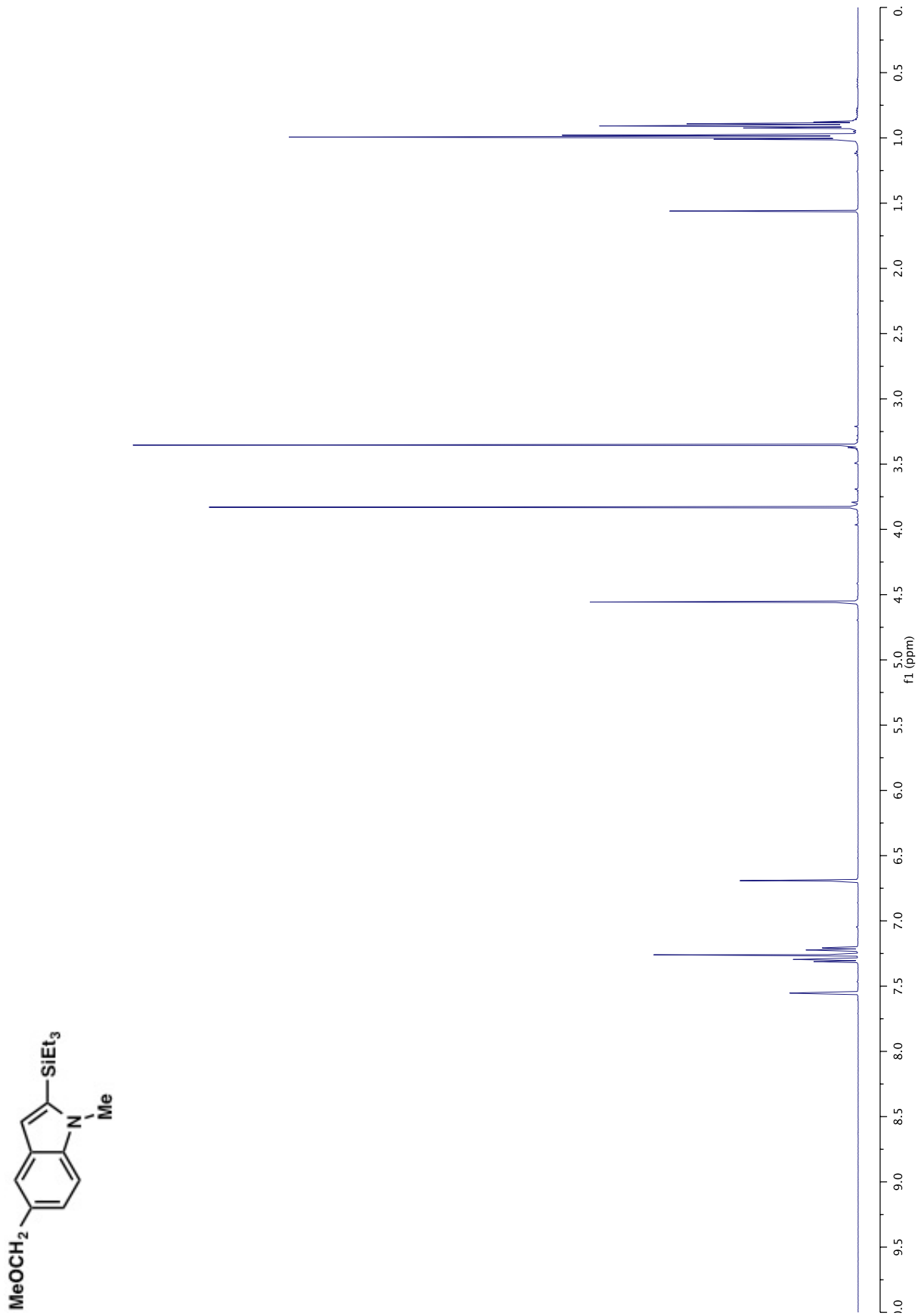
^{13}C NMR (125 MHz, $CDCl_3$) of compound **15**.



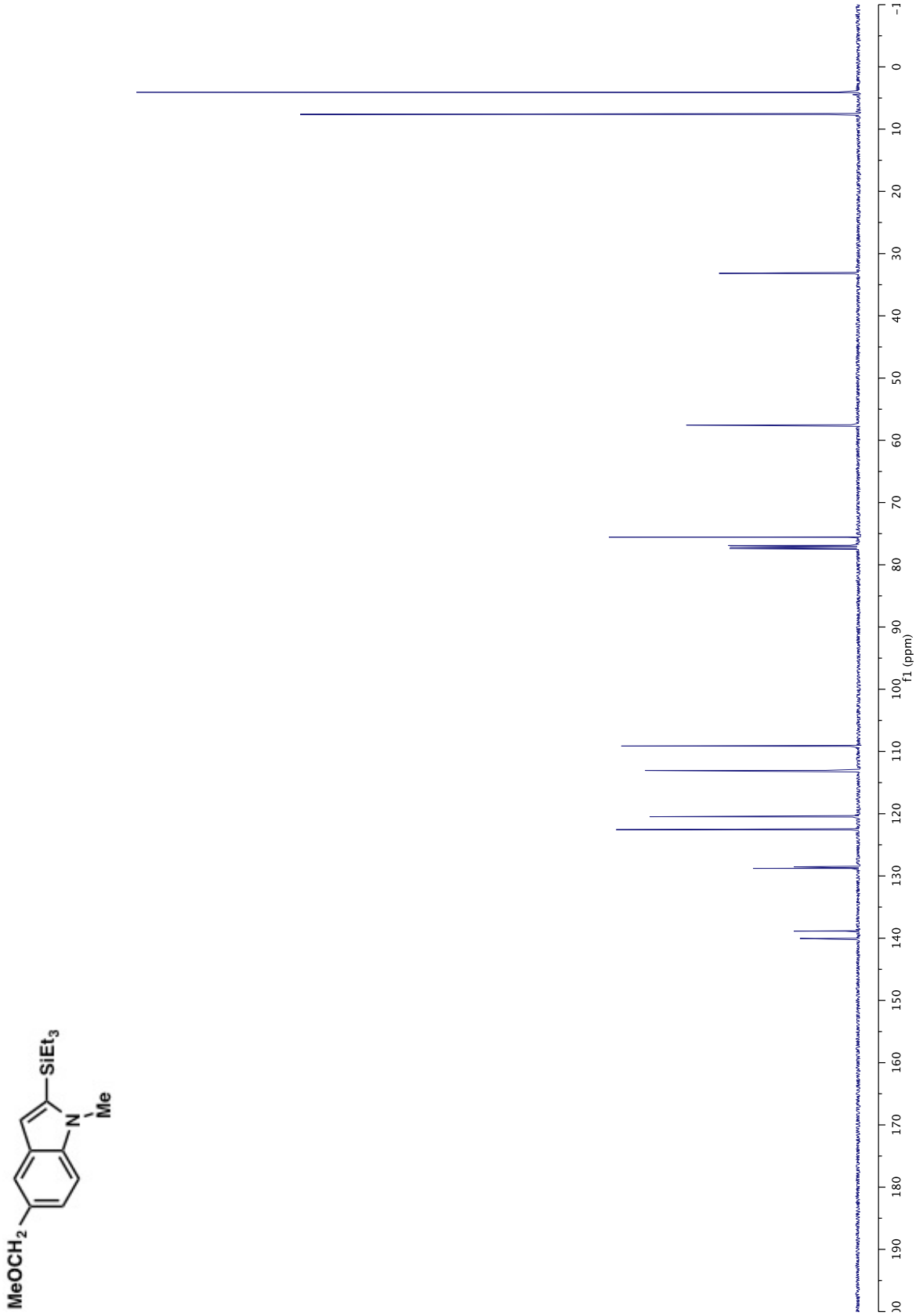
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2l**.



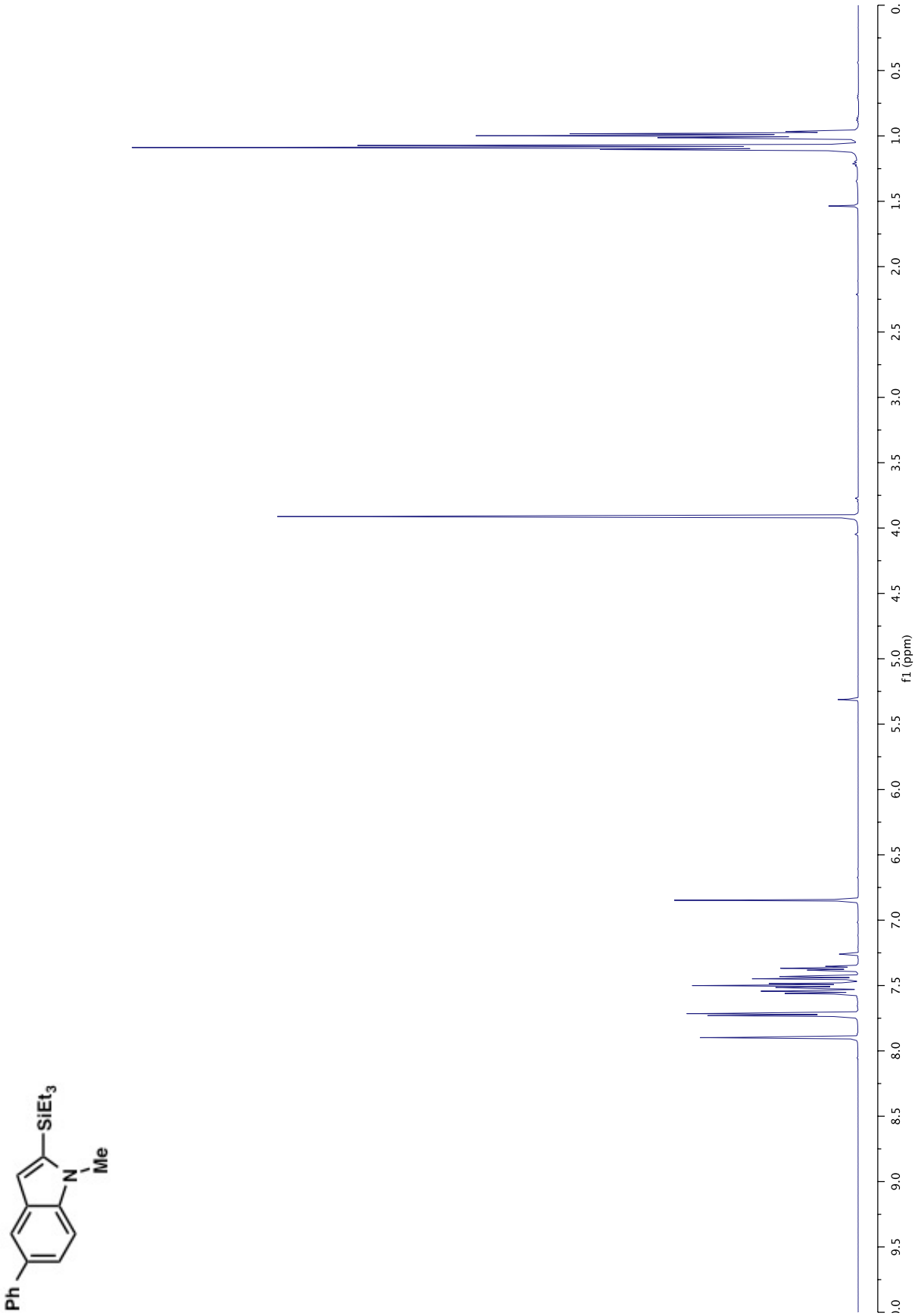
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2l**.



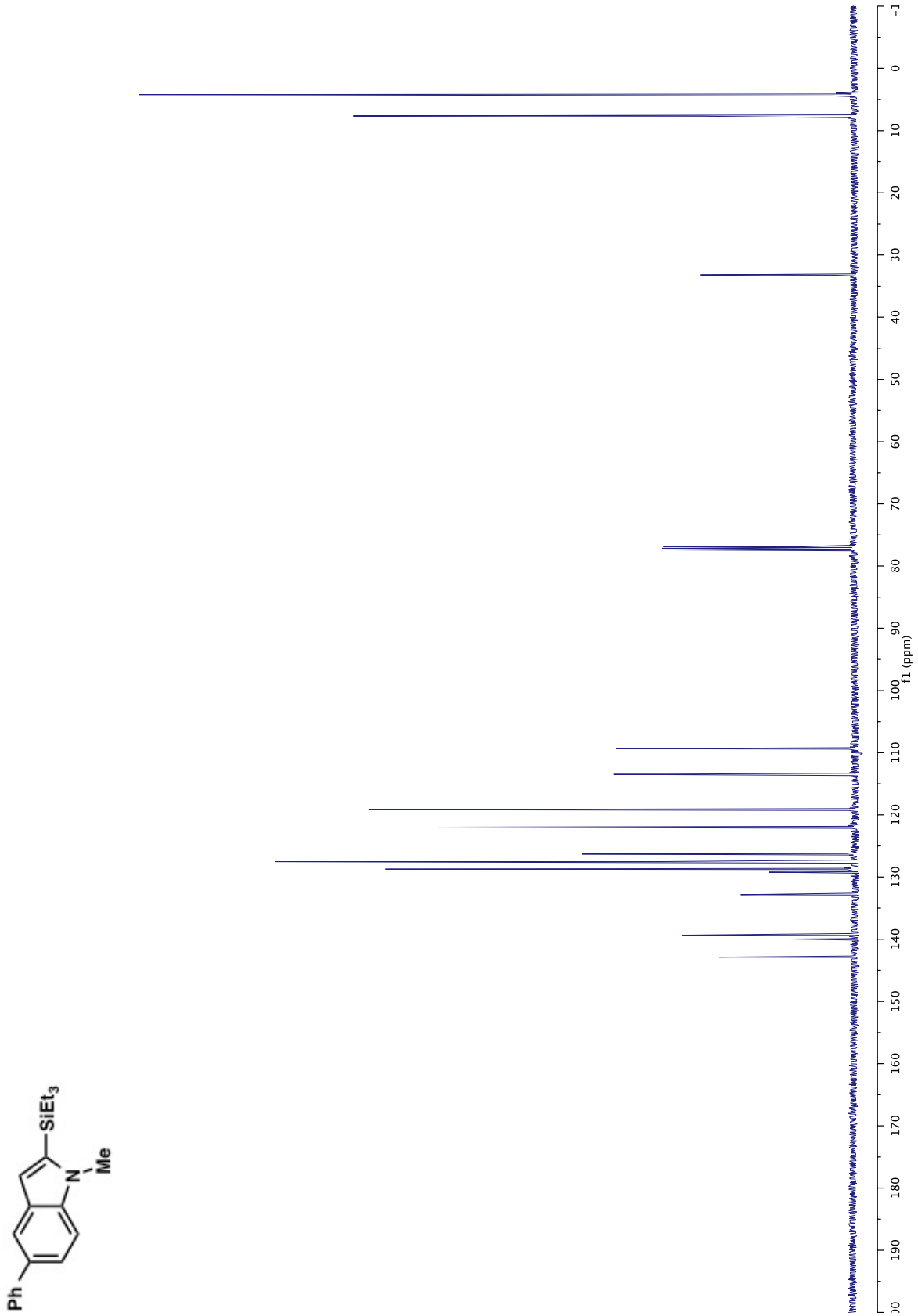
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2m**.



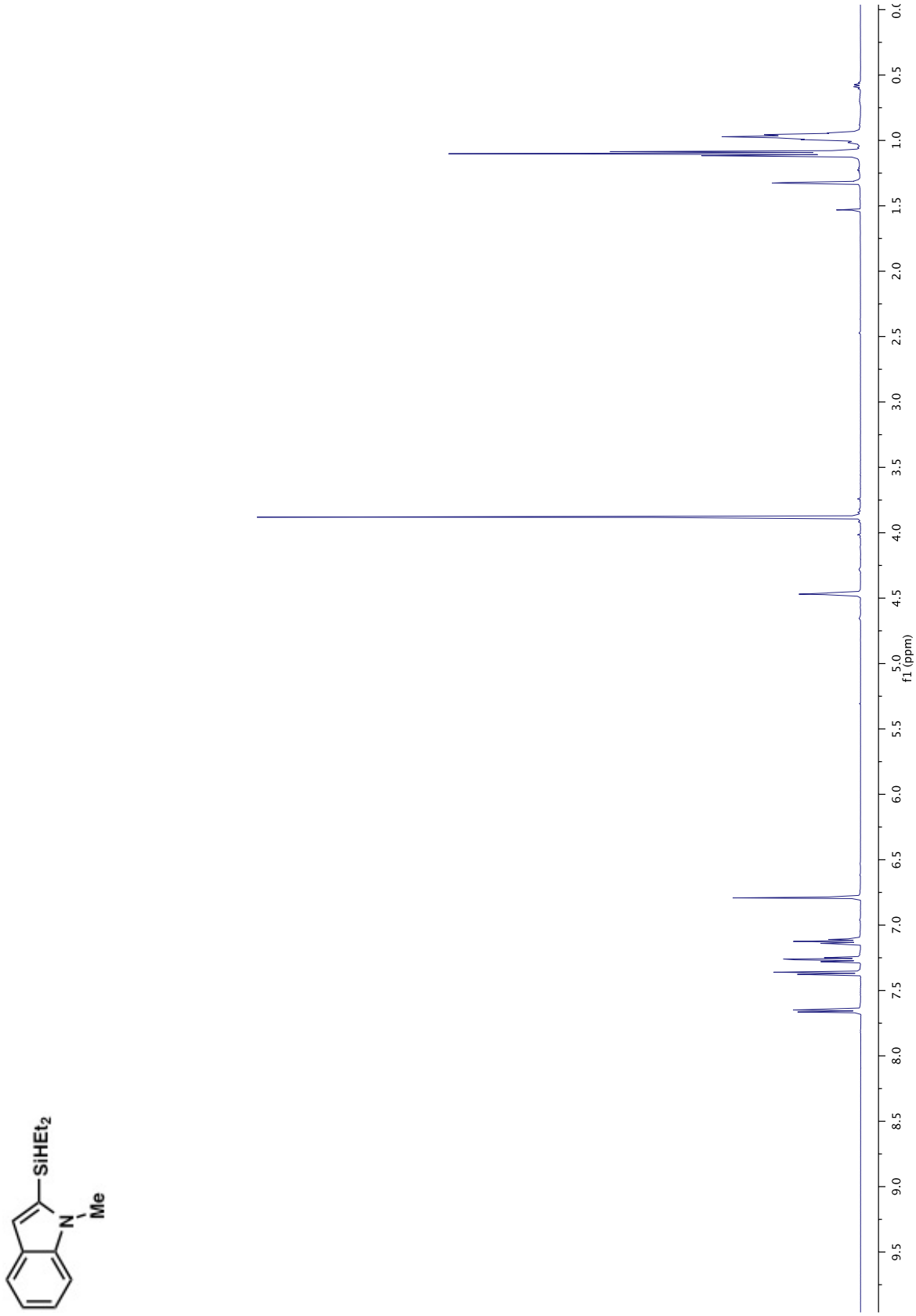
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2m**.



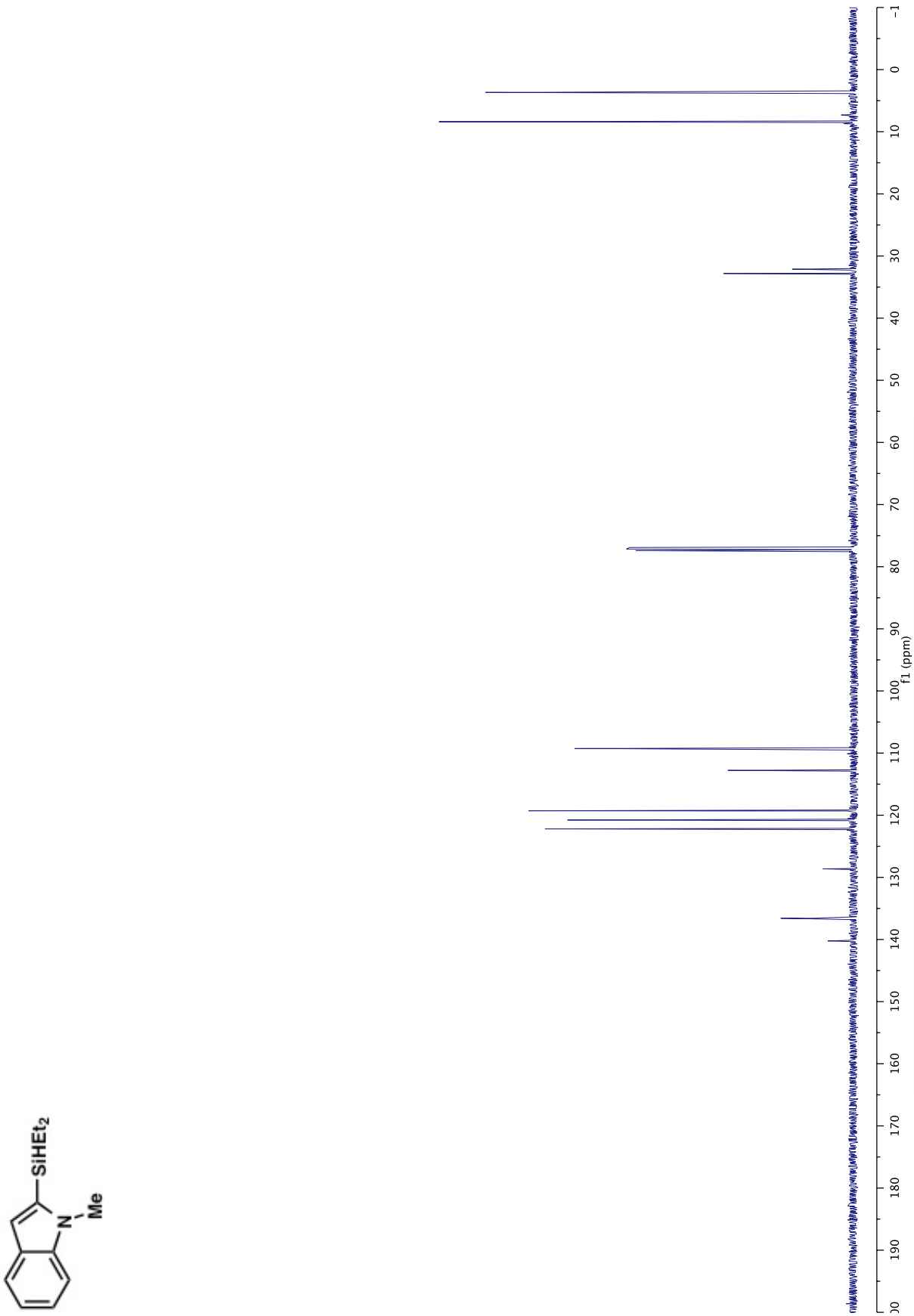
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2n**.



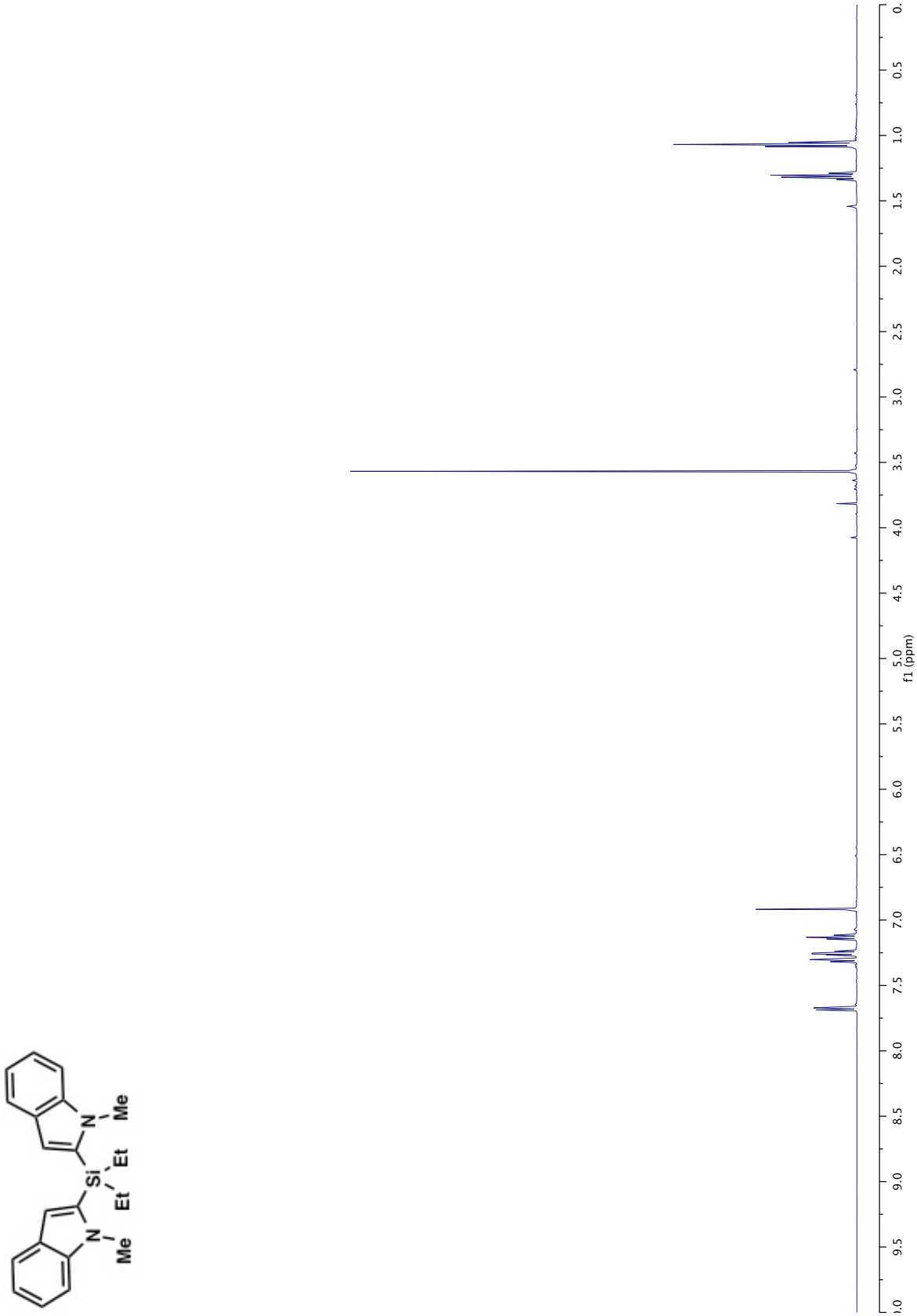
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2n**.



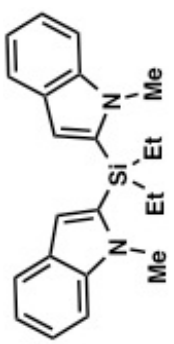
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2o**.

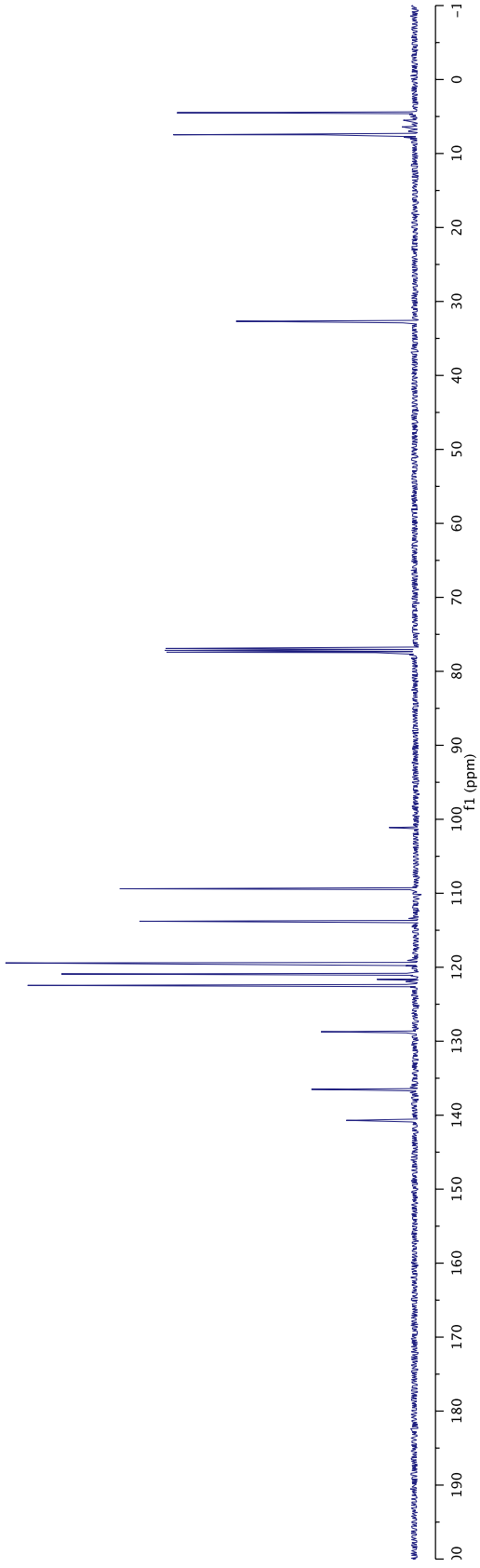


^{13}C NMR (125 MHz, $CDCl_3$) of compound **2o**.

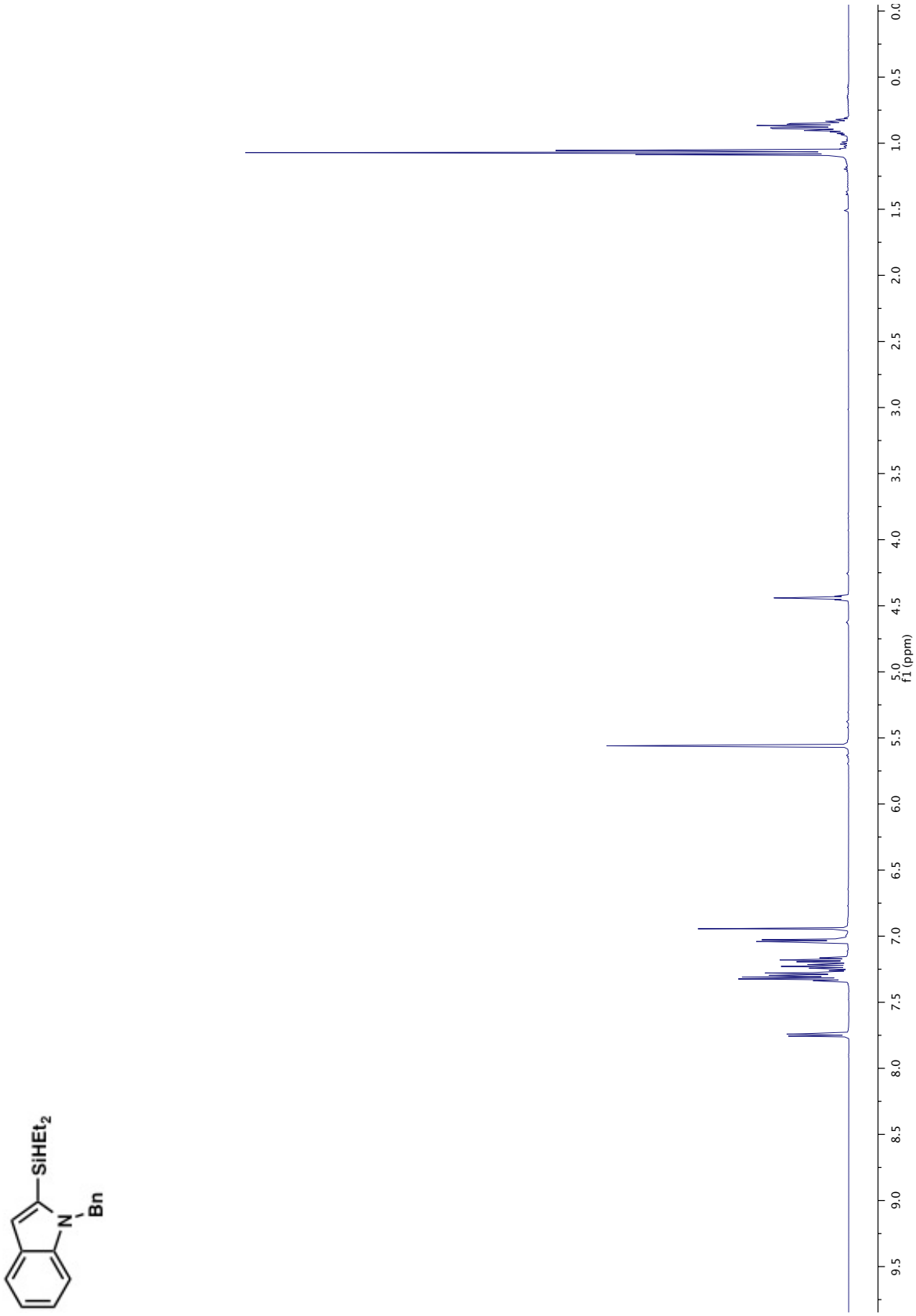


^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-2o**.

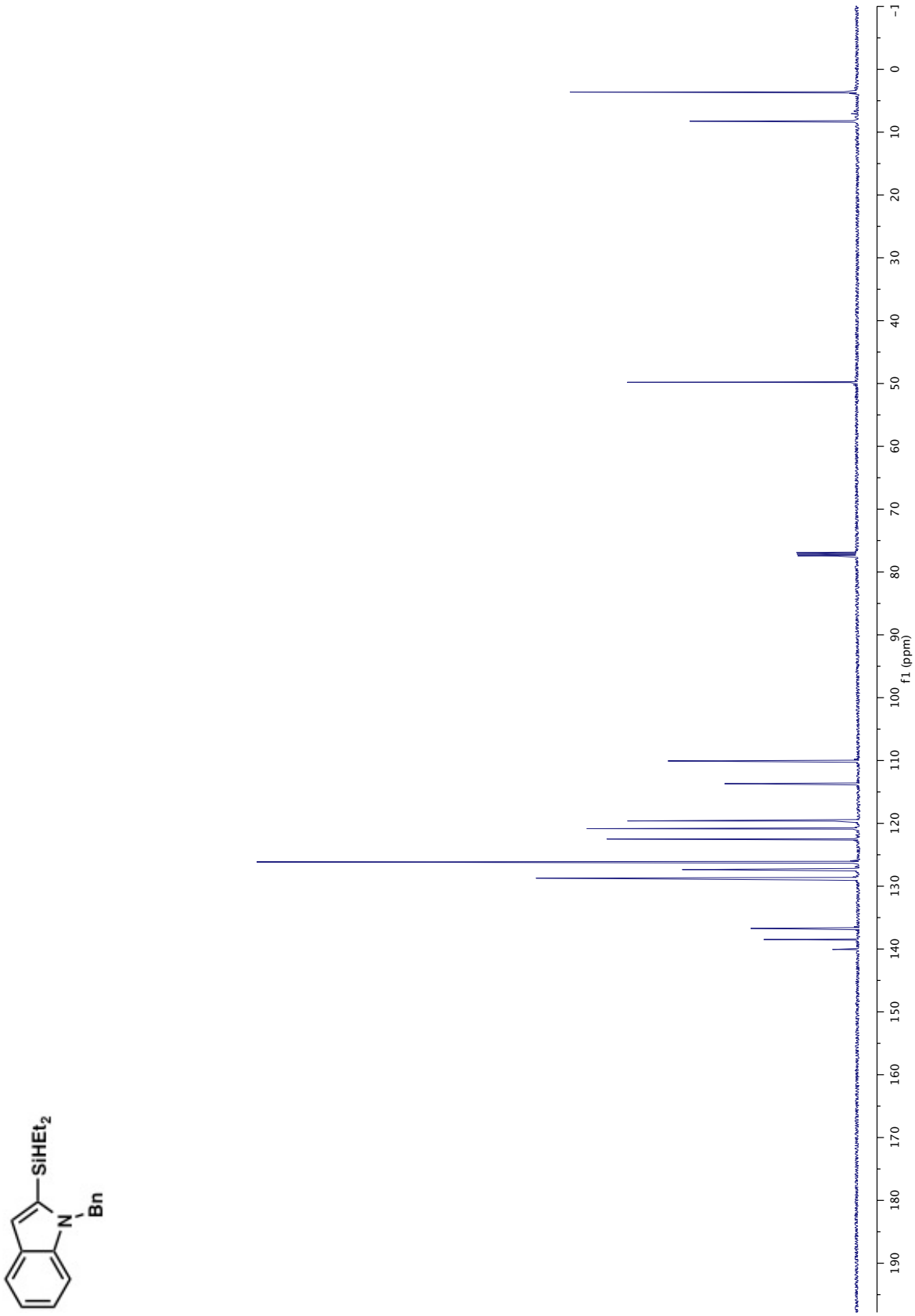




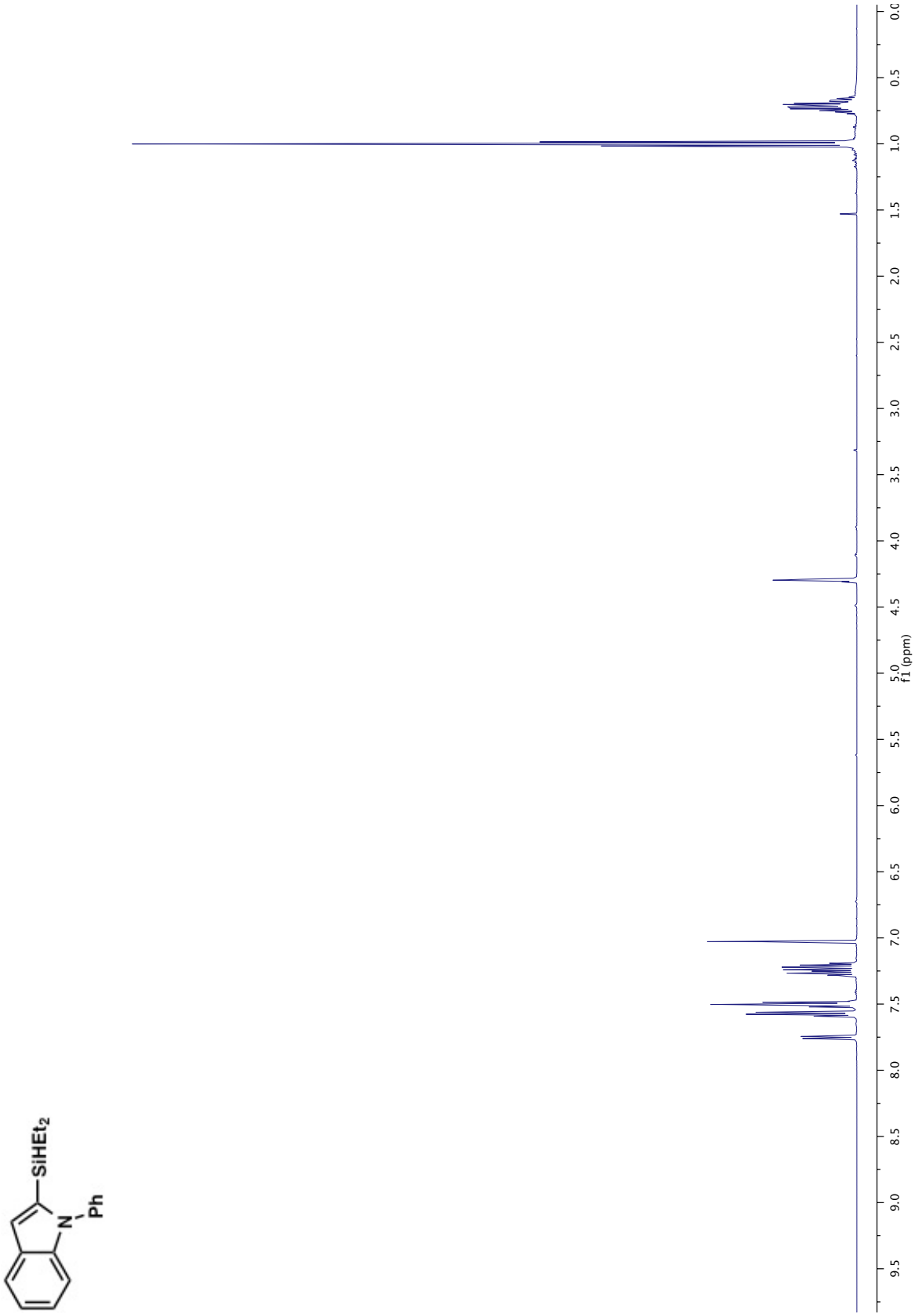
^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-2o**.



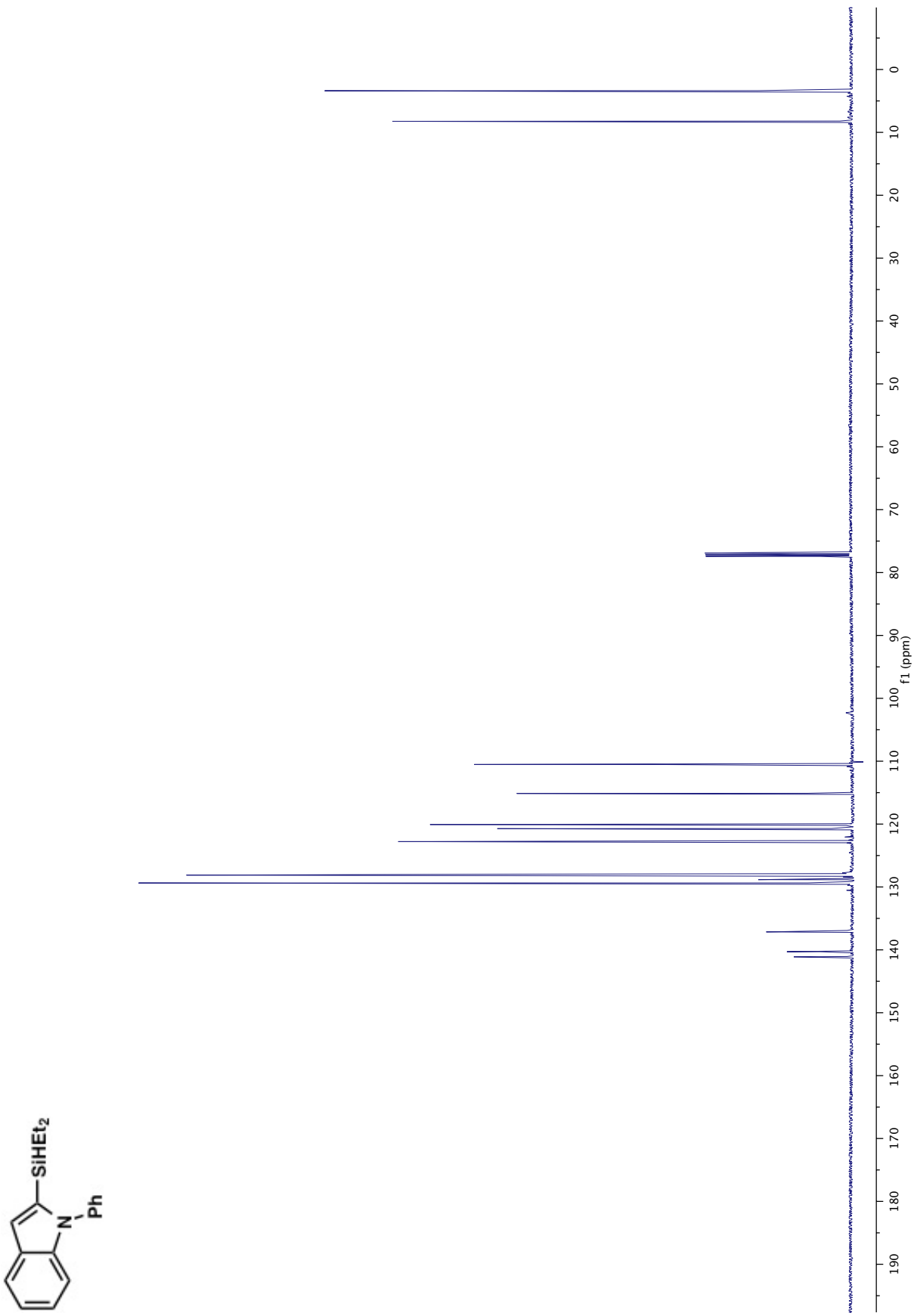
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2p**.



^{13}C NMR (125 MHz, $CDCl_3$) of compound **2p**.

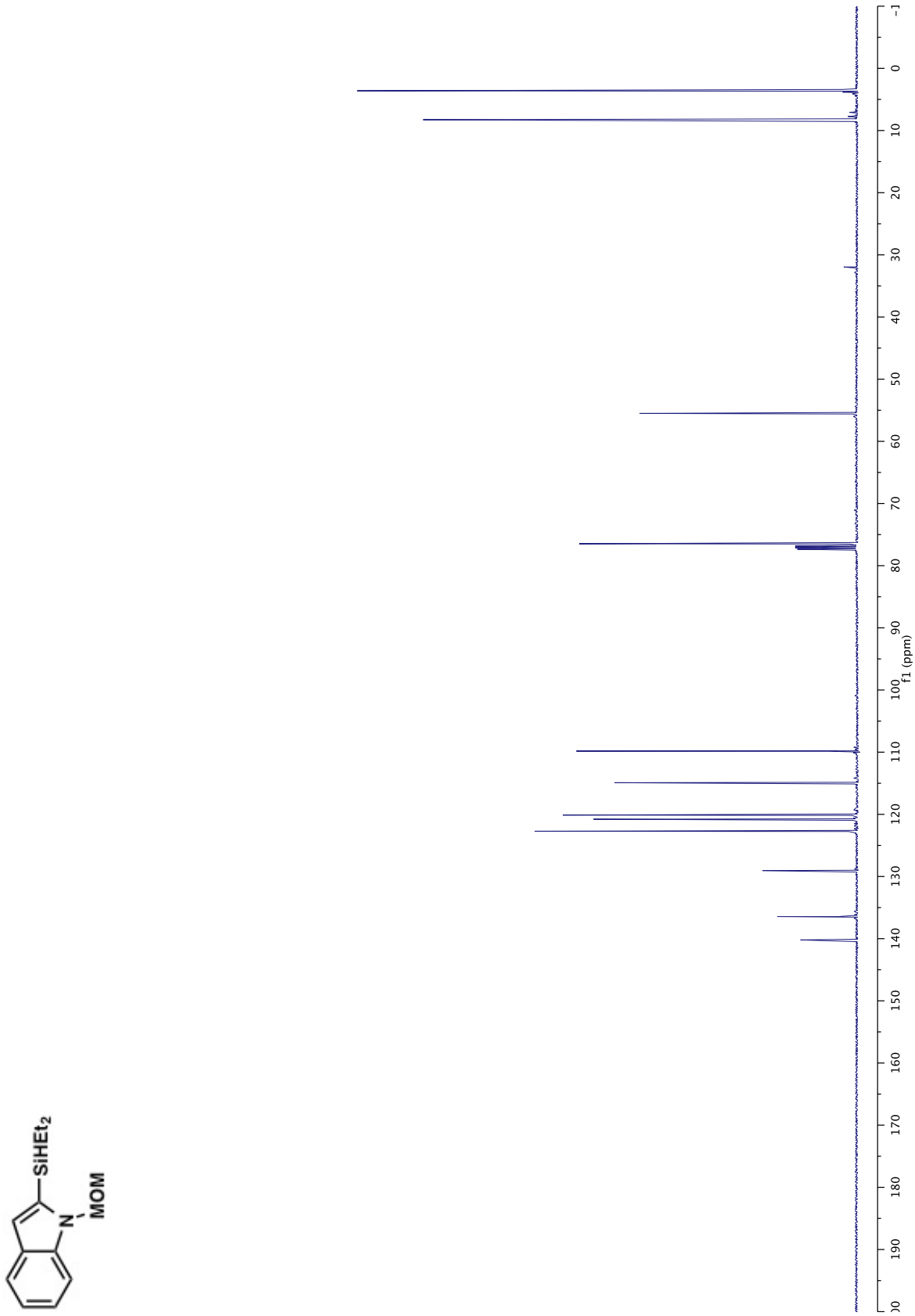


^{1}H NMR (500 MHz, $CDCl_3$) of compound **2q**.

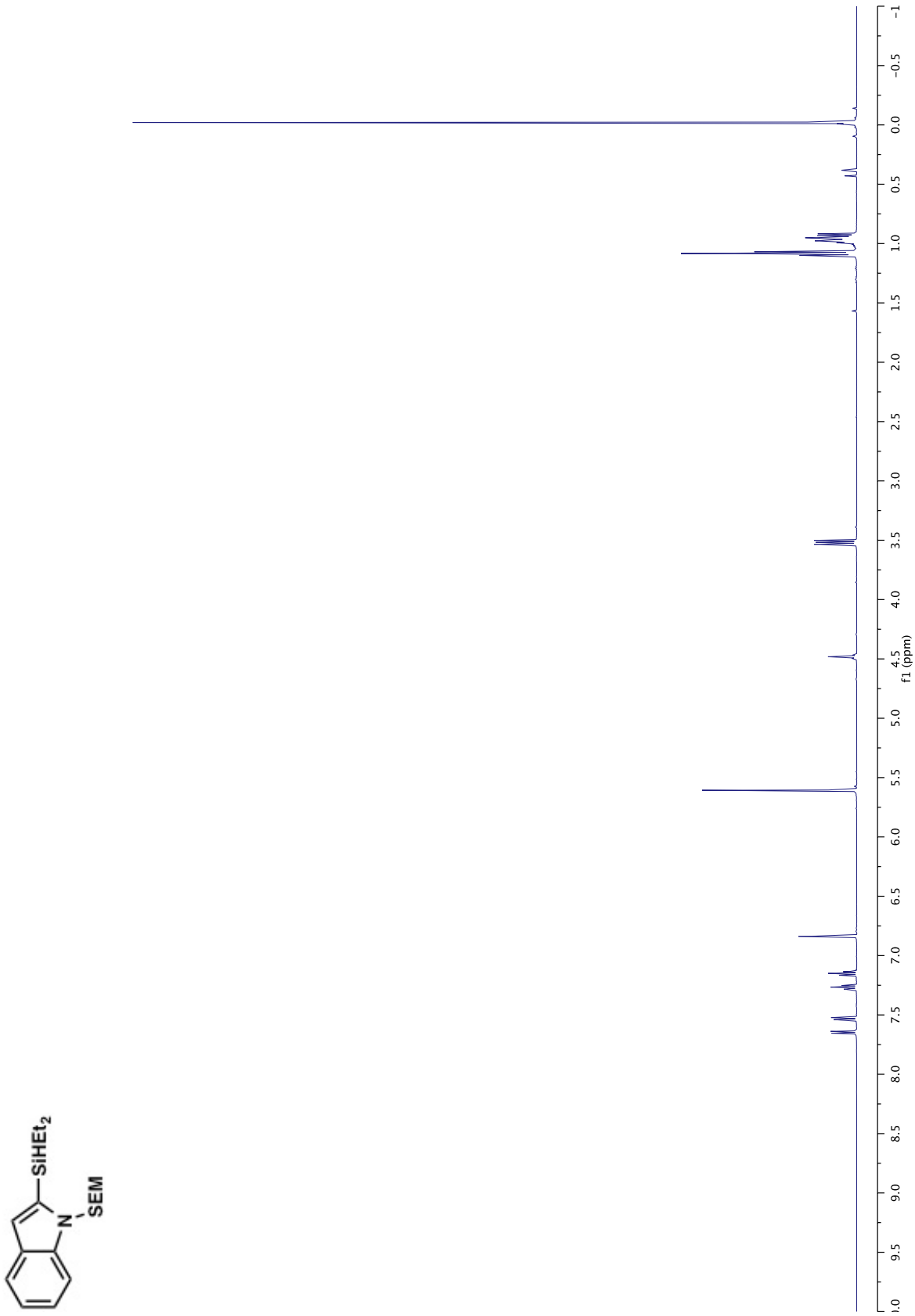


^{13}C NMR (125 MHz, $CDCl_3$) of compound **2q**.

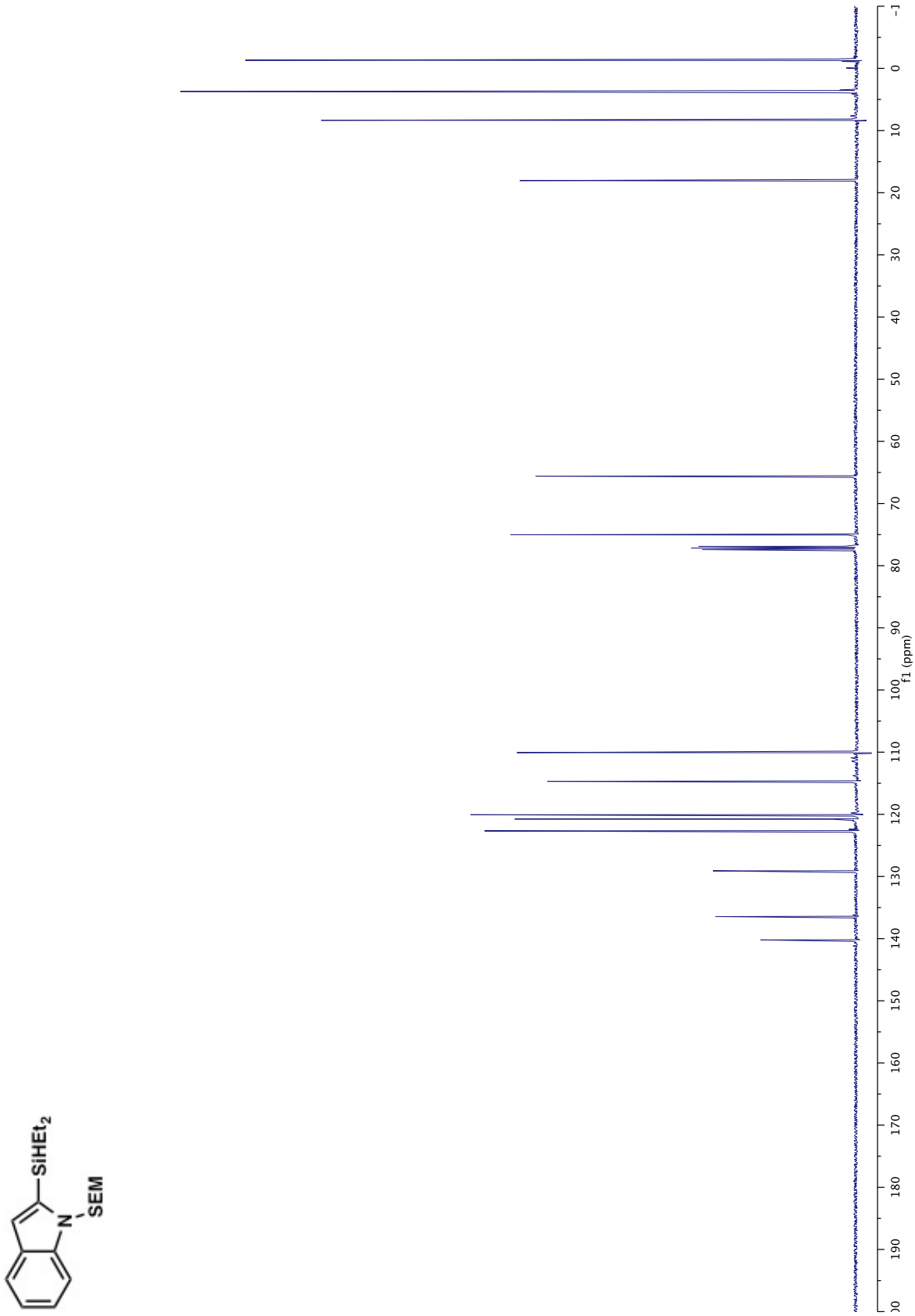
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2r**.



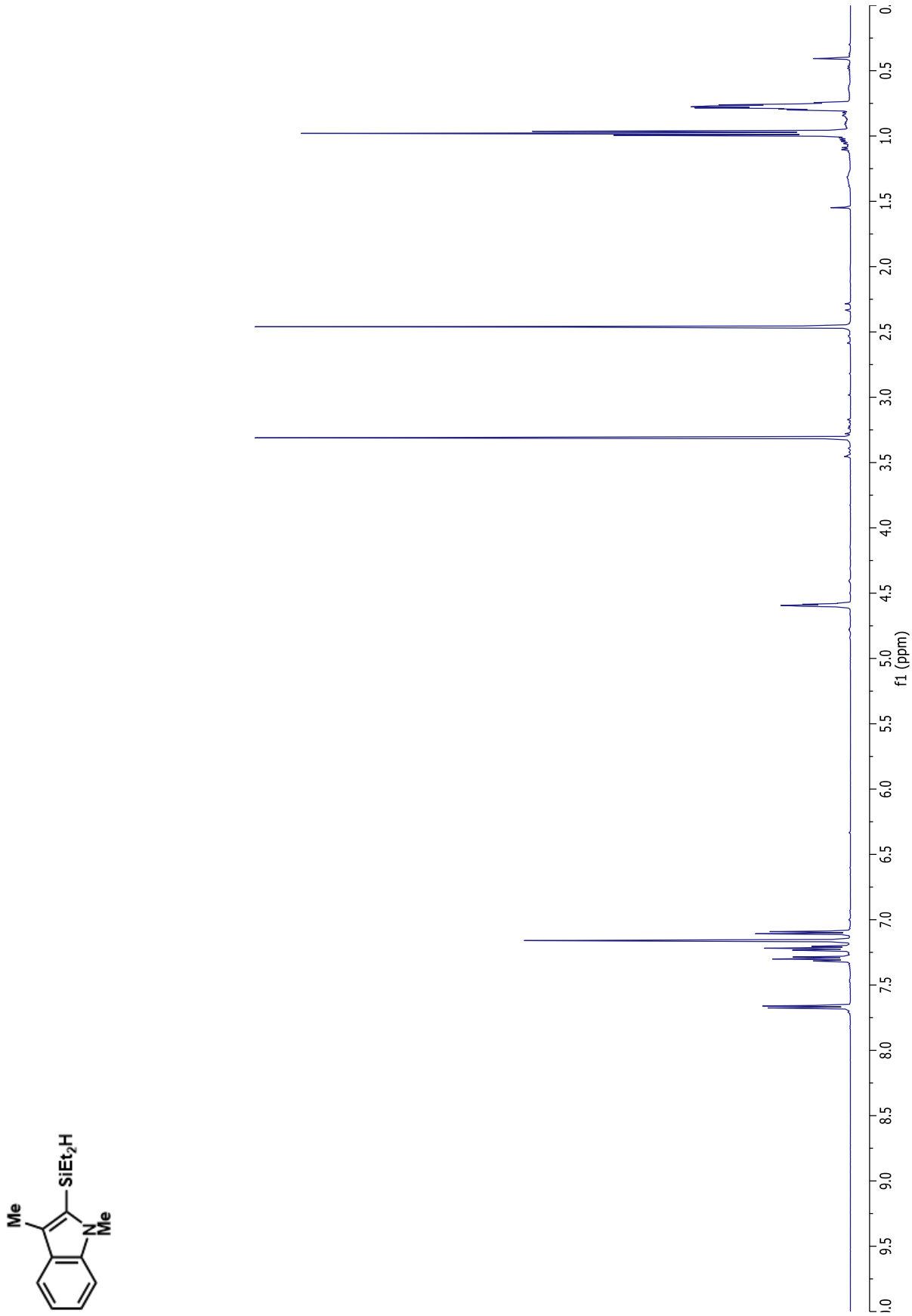
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2r**.



^{1}H NMR (500 MHz, $CDCl_3$) of compound **2s**.

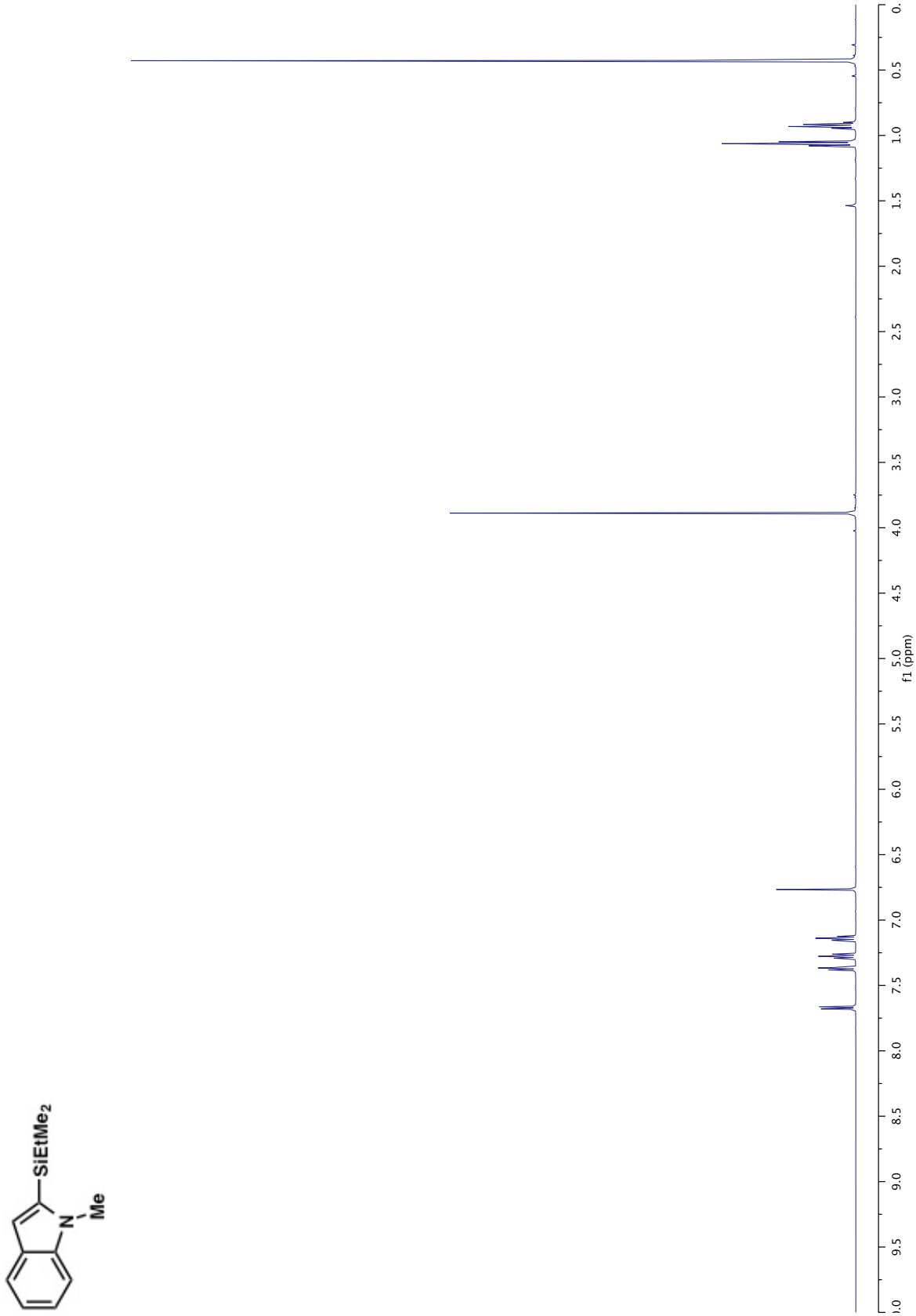


^{13}C NMR (125 MHz, $CDCl_3$) of compound **2s**.

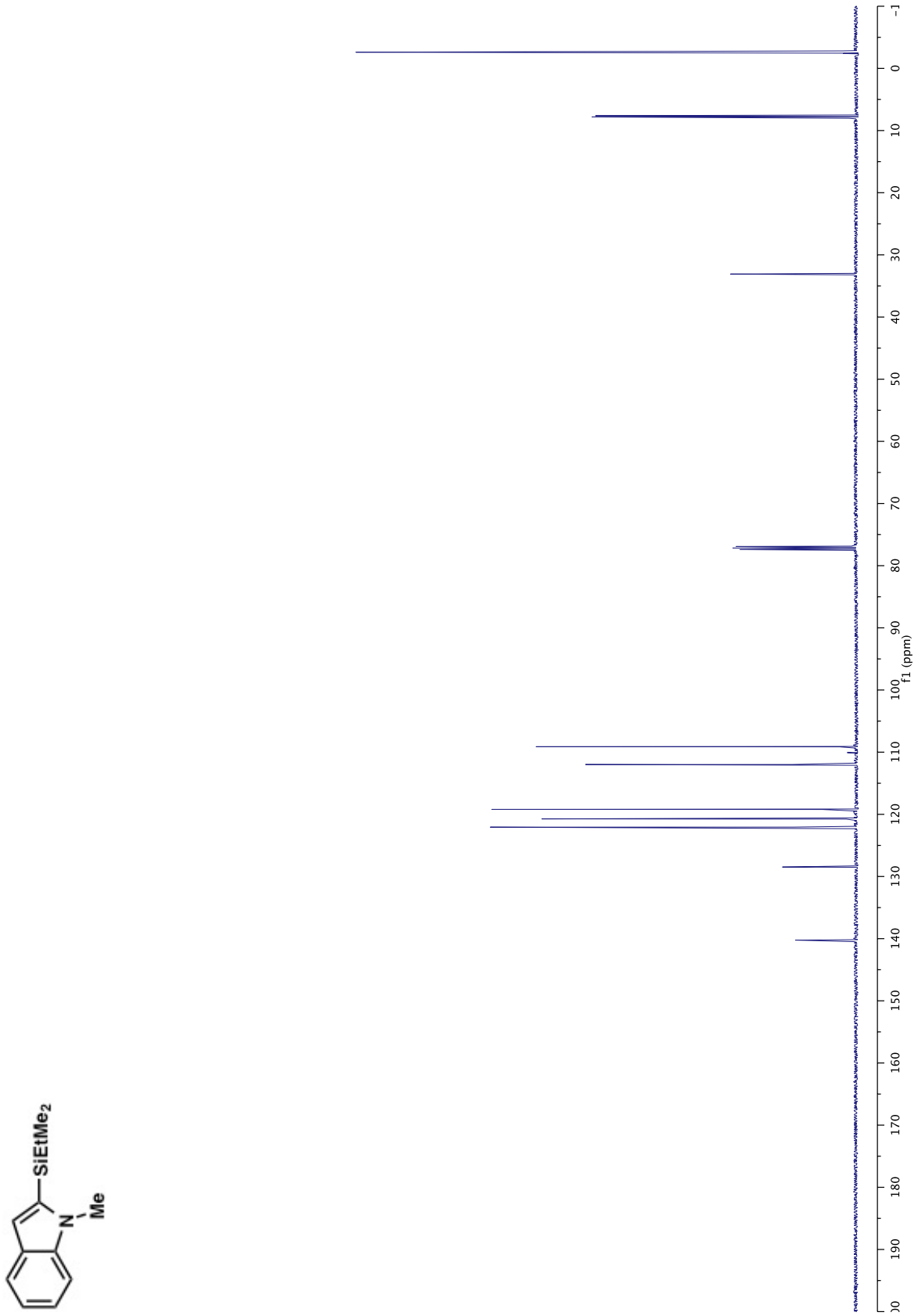


^{1}H NMR (500 MHz, C_6D_6) of compound **2t**.

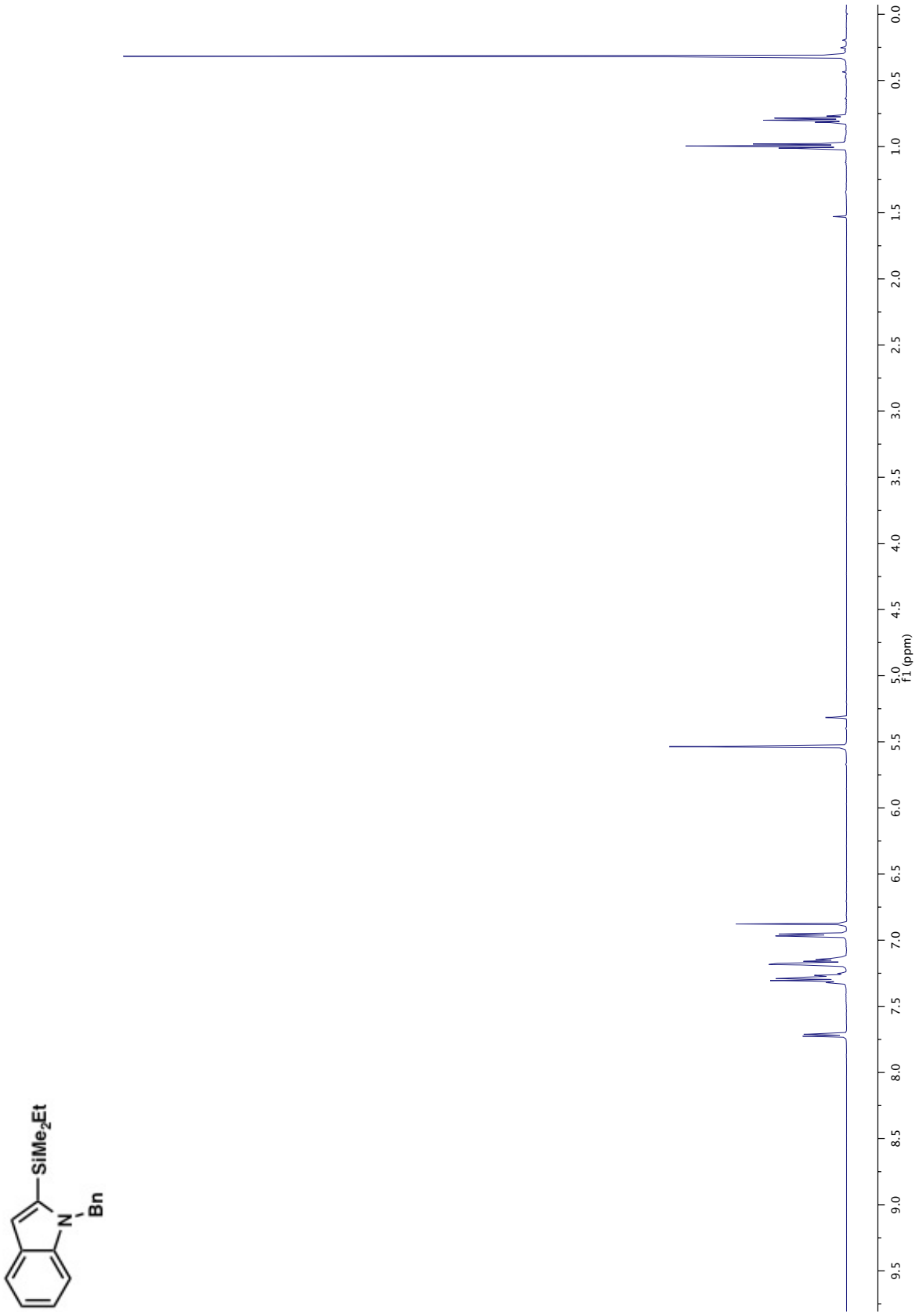
^{13}C NMR (125 MHz, C_6D_6) of compound **2t**.



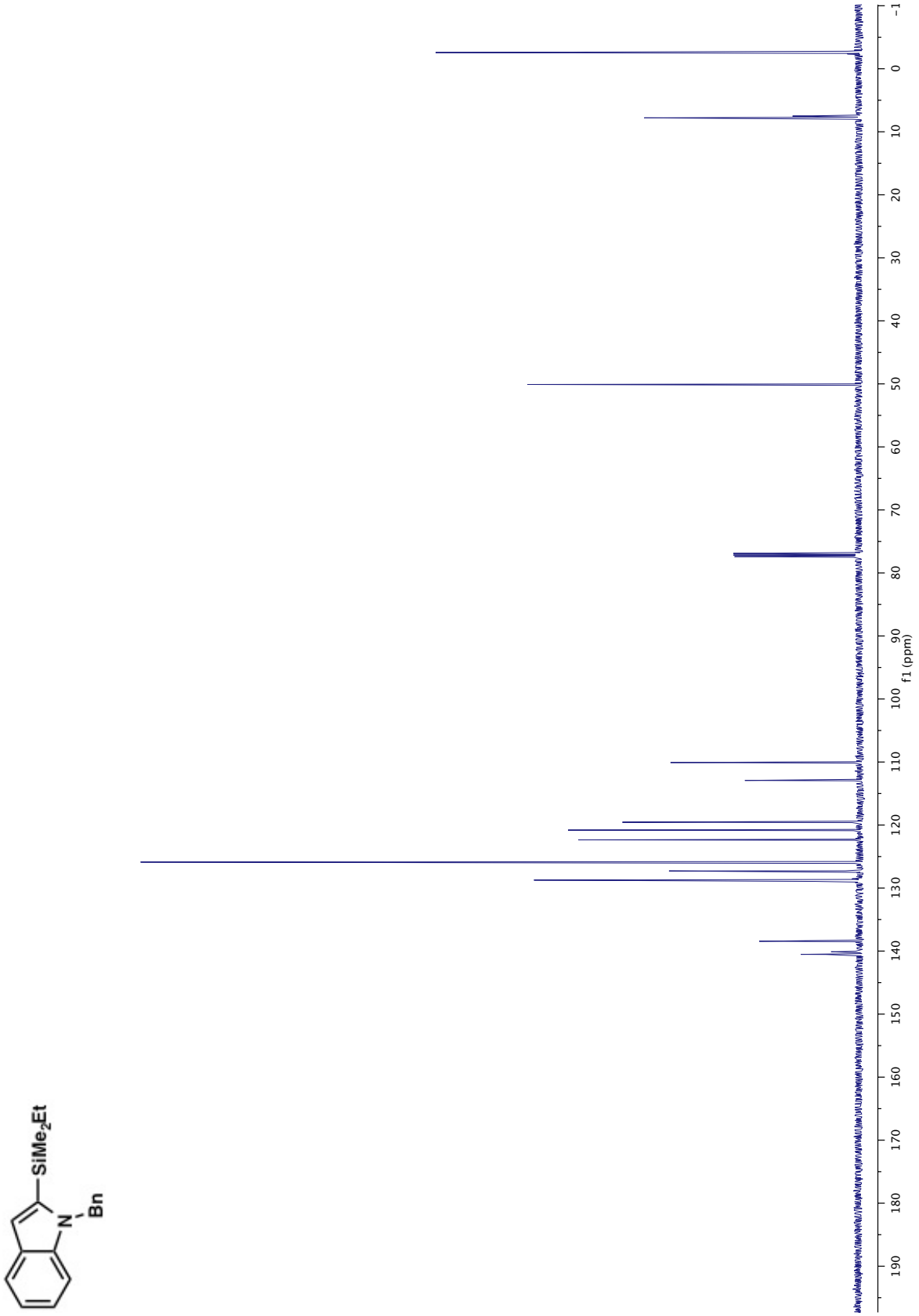
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2u**.



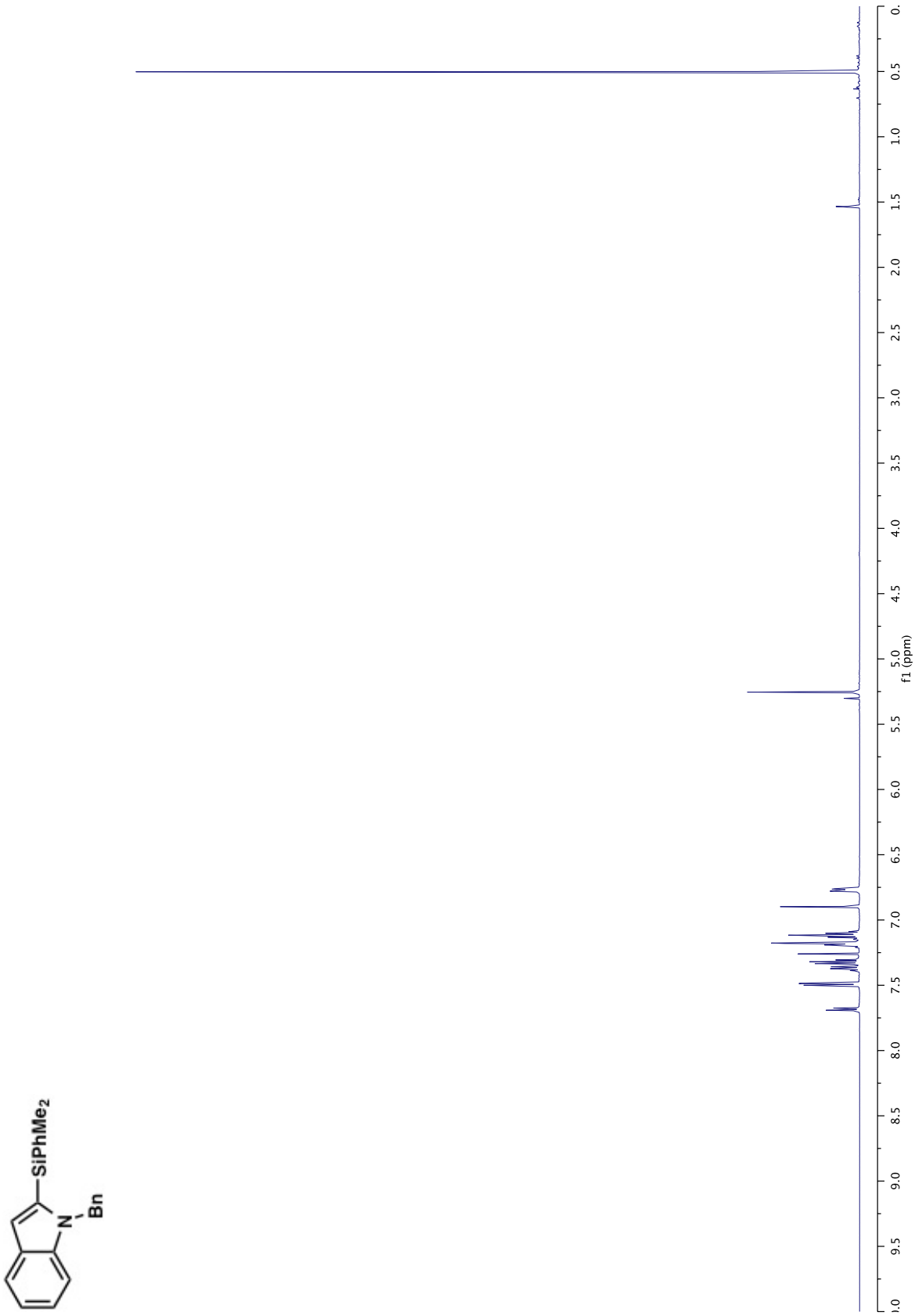
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2u**.



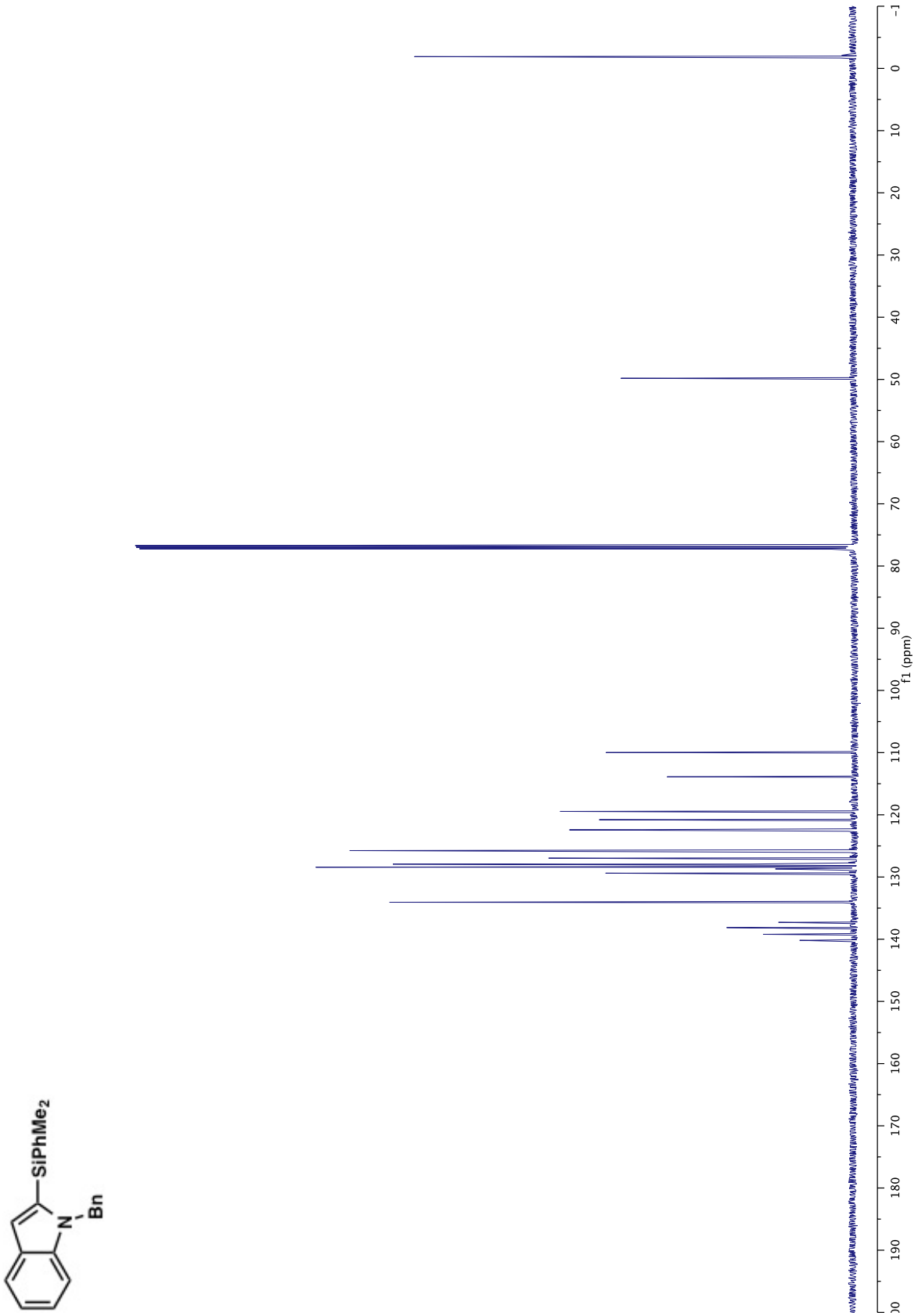
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2v**.



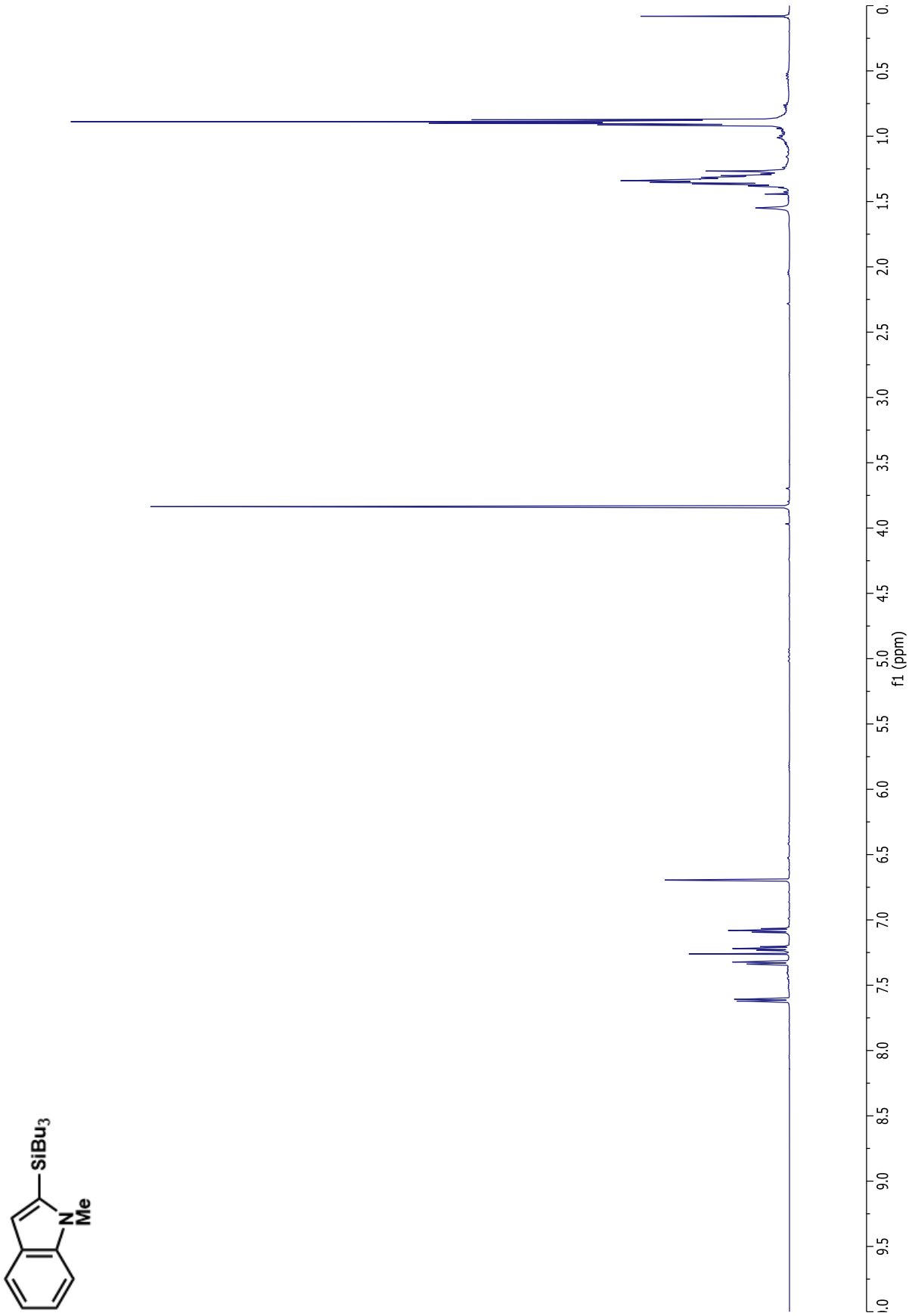
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2v**.



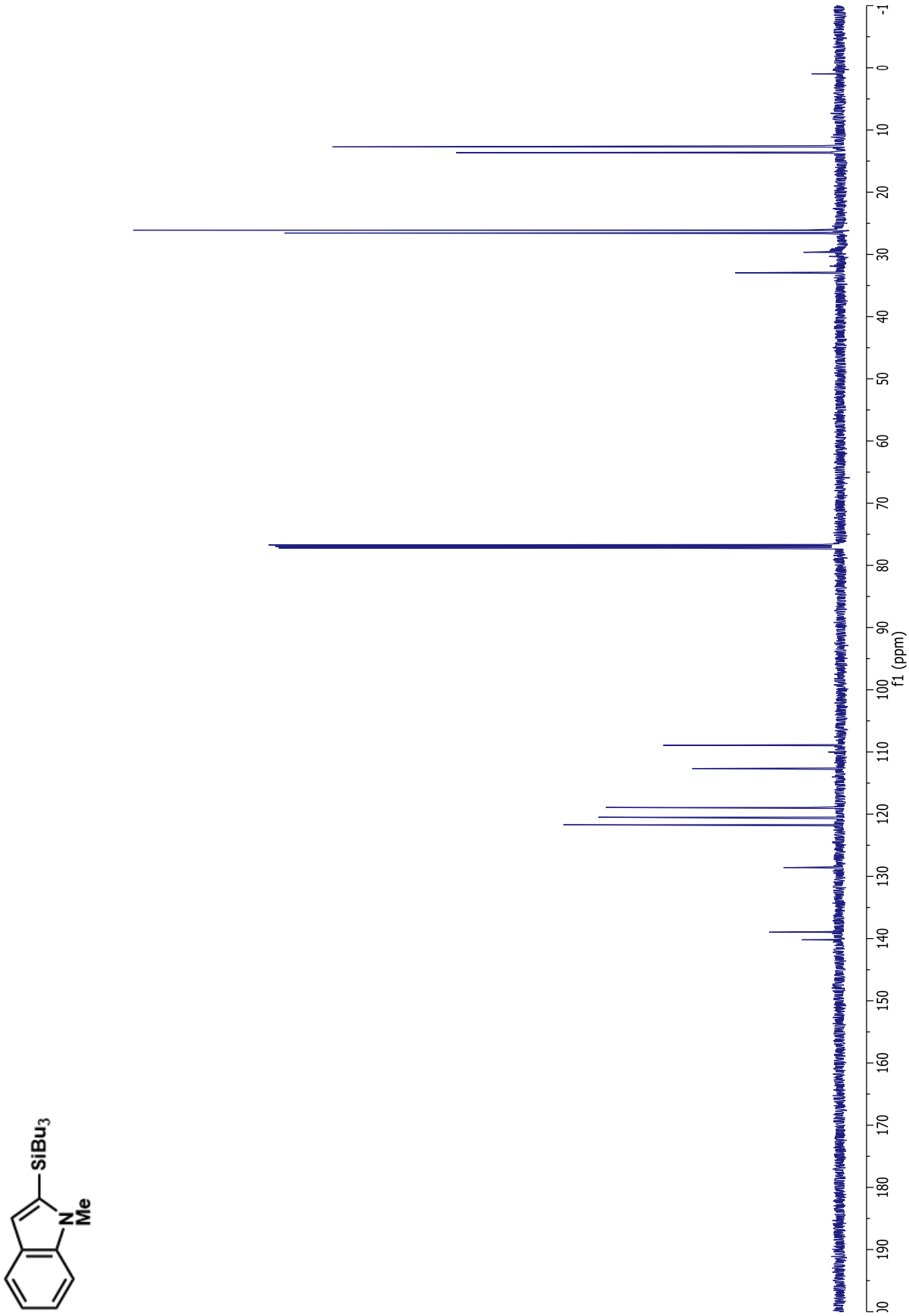
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2w**.



^{13}C NMR (125 MHz, $CDCl_3$) of compound **2w**.

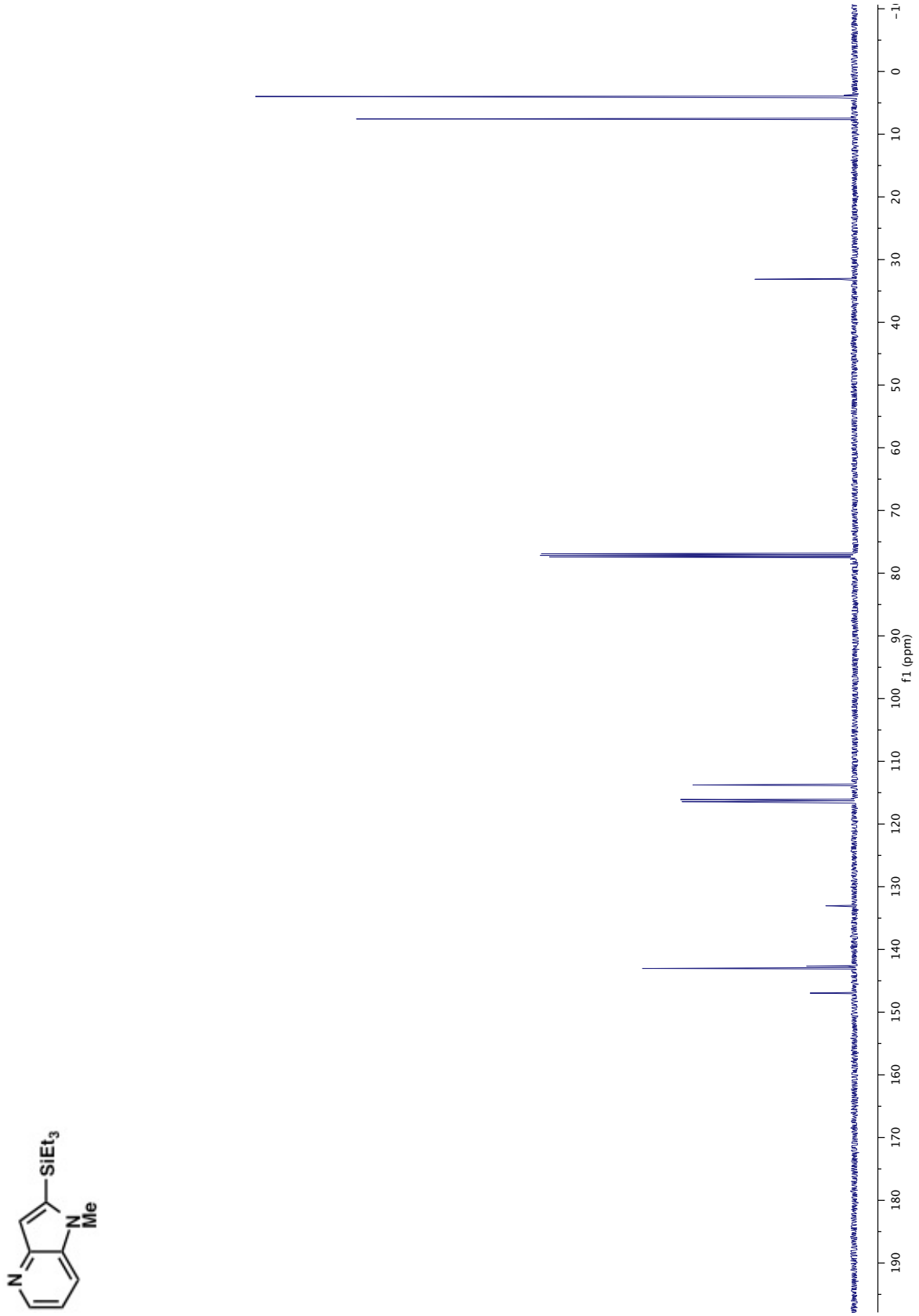


^{1}H NMR (500 MHz, $CDCl_3$) of compound **2x**.

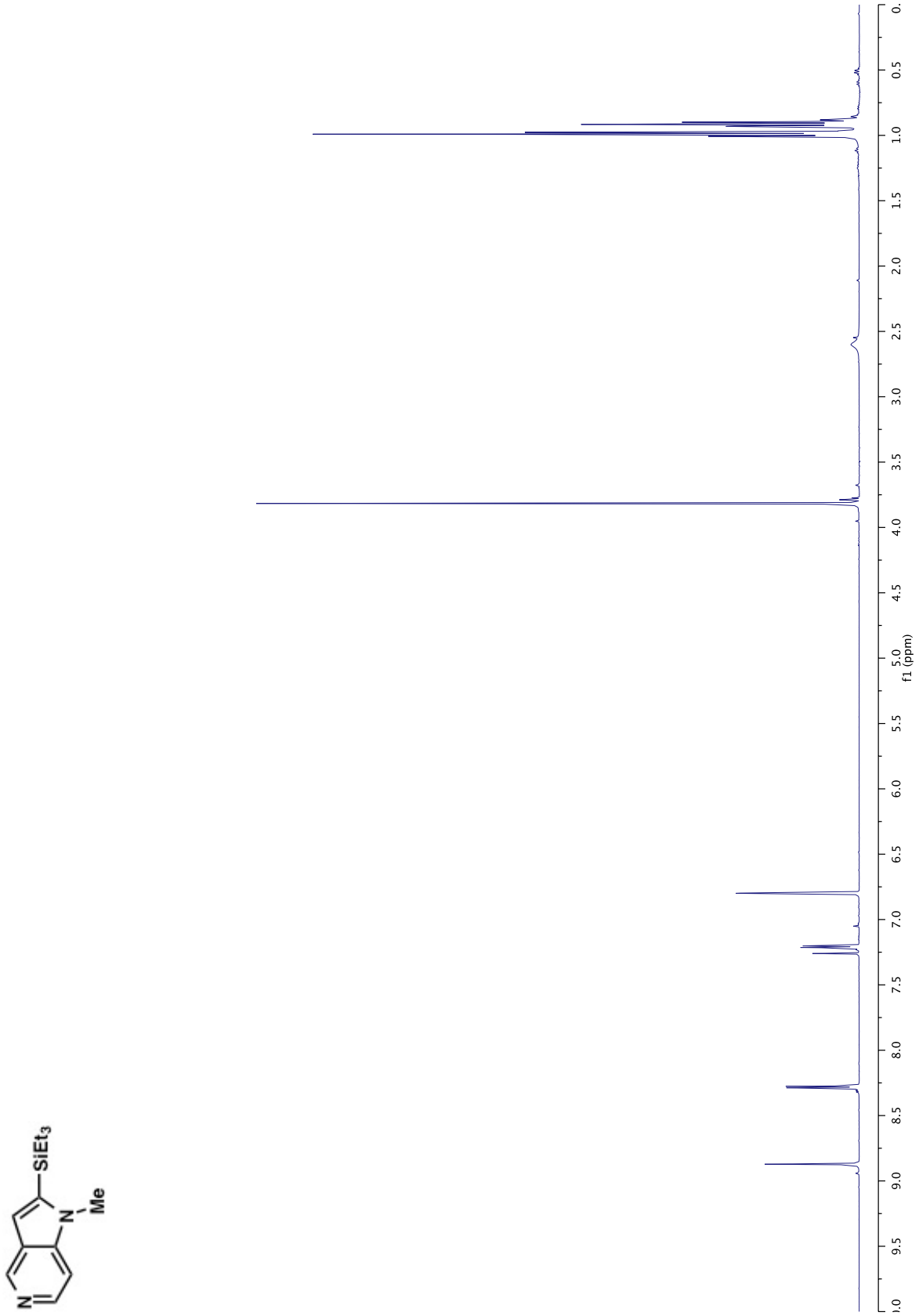


^{13}C NMR (125 MHz, $CDCl_3$) of compound **2x**.

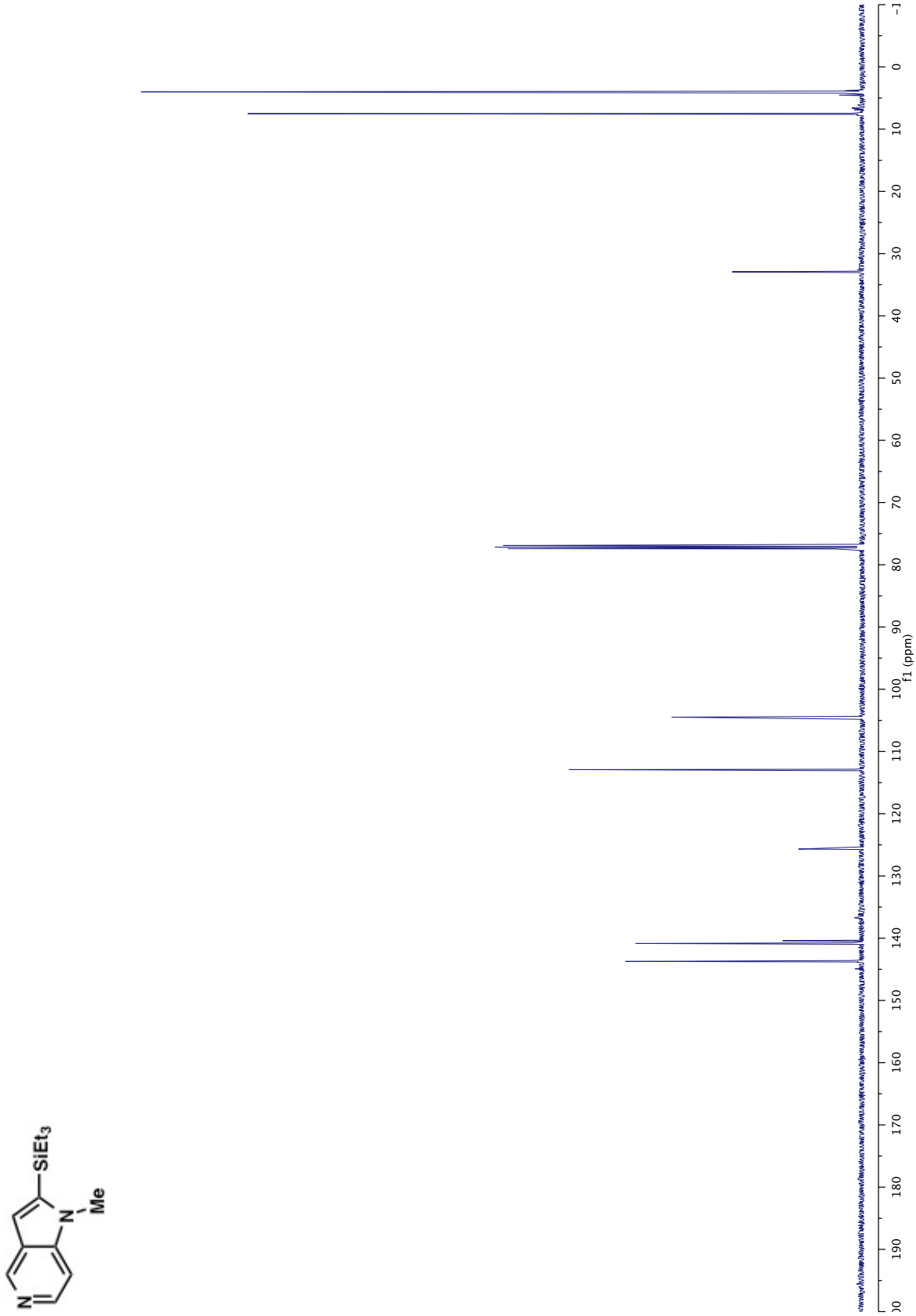
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4a.**



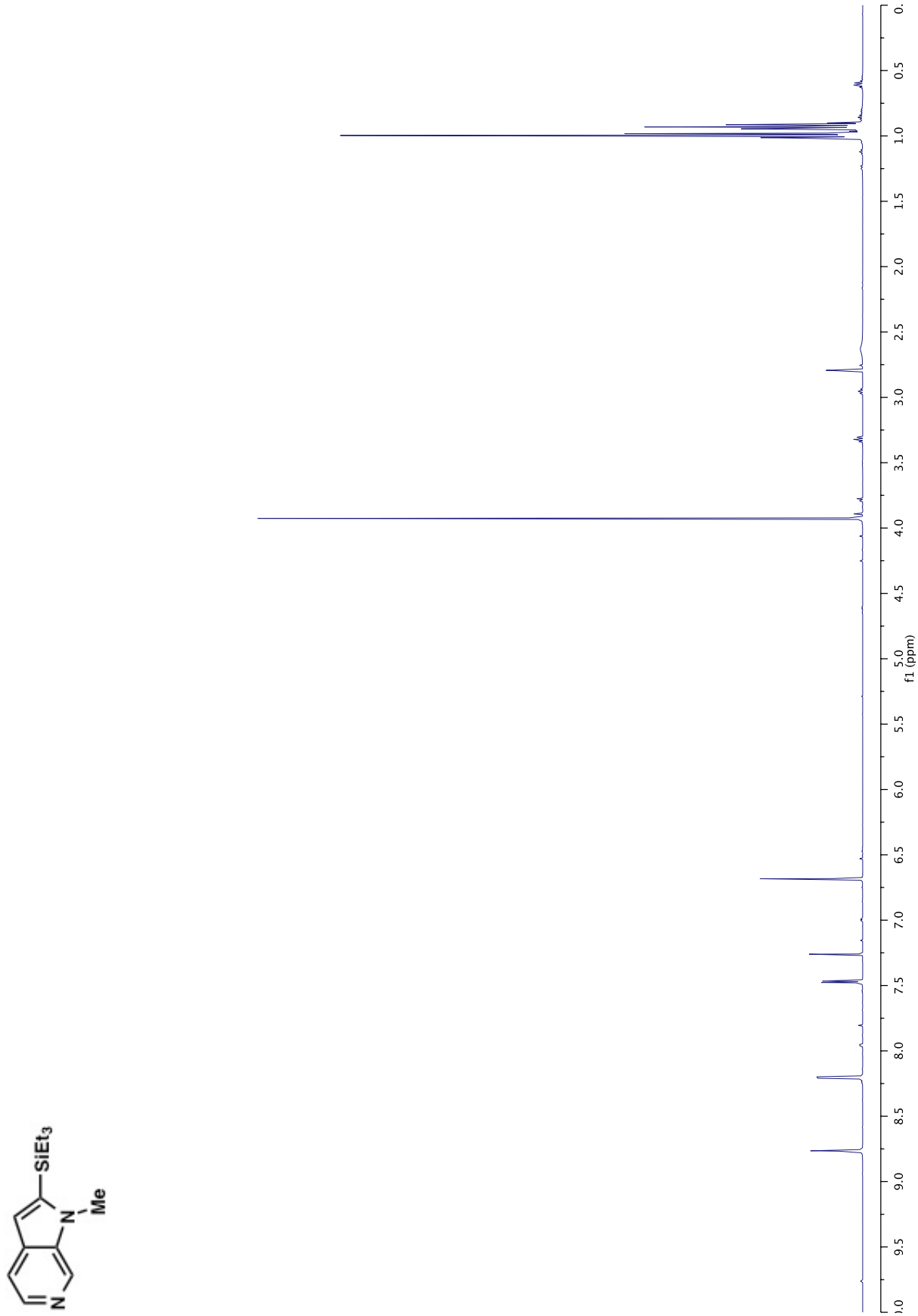
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4a**.



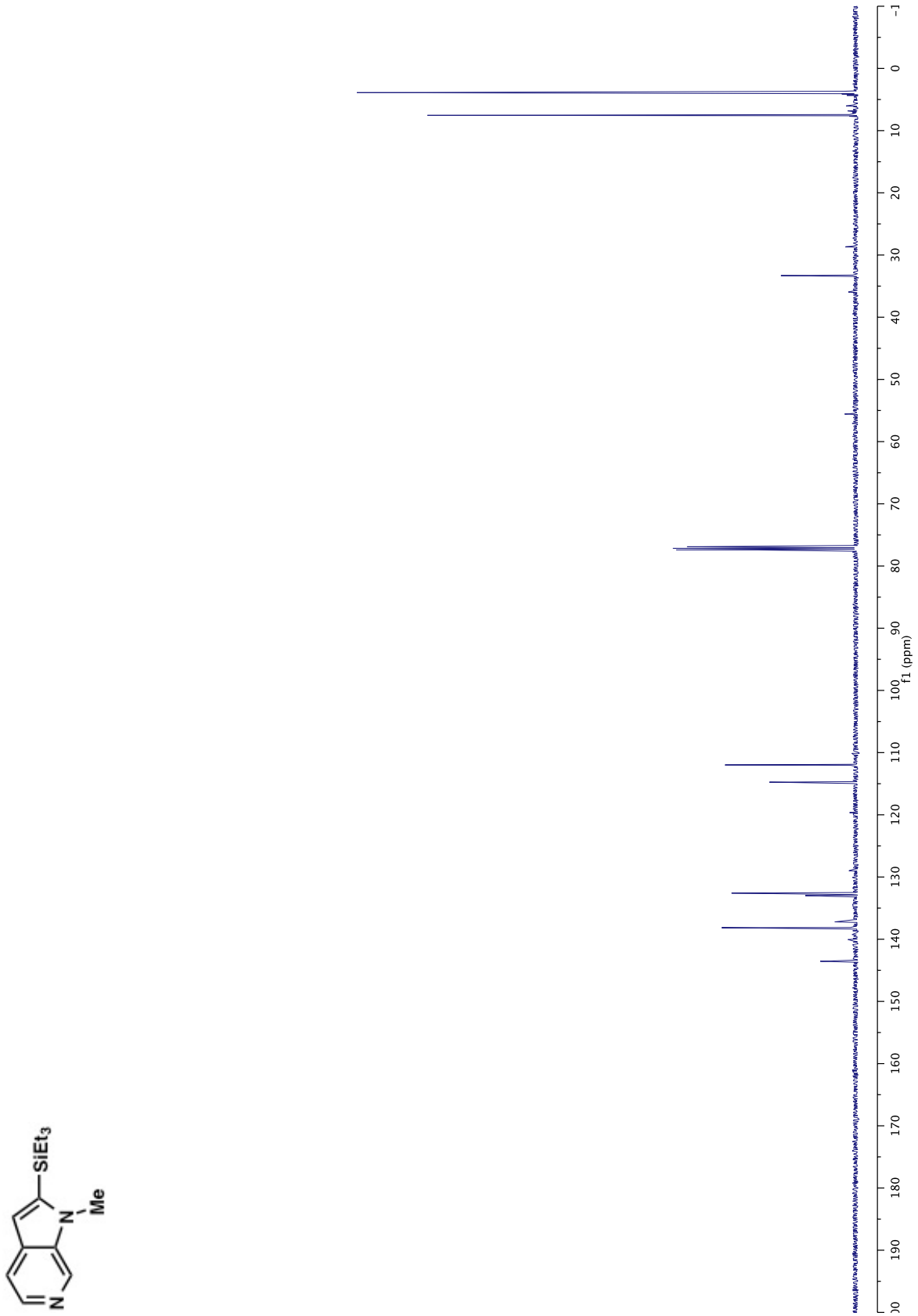
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4b.**



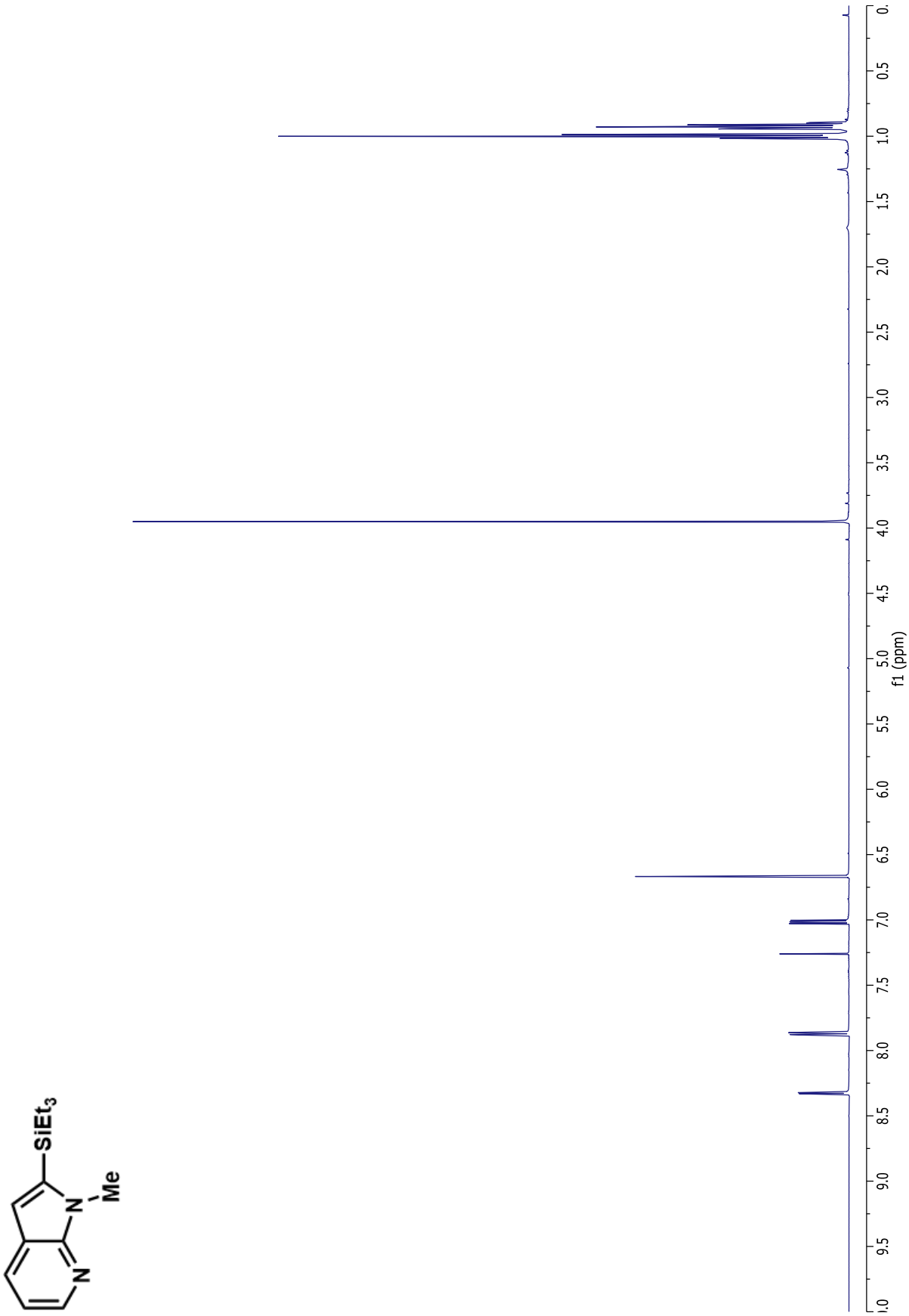
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4b.**



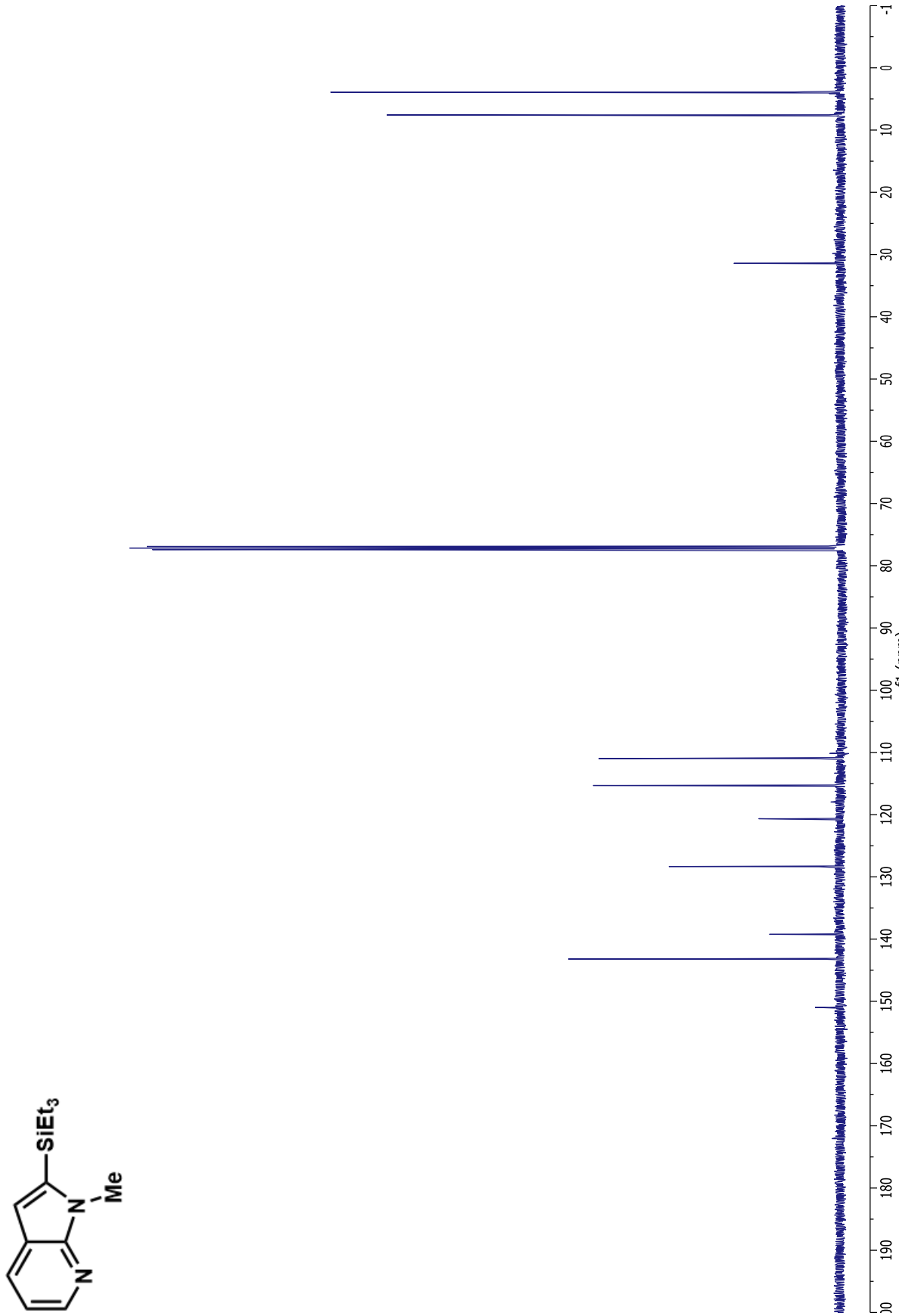
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4c**.



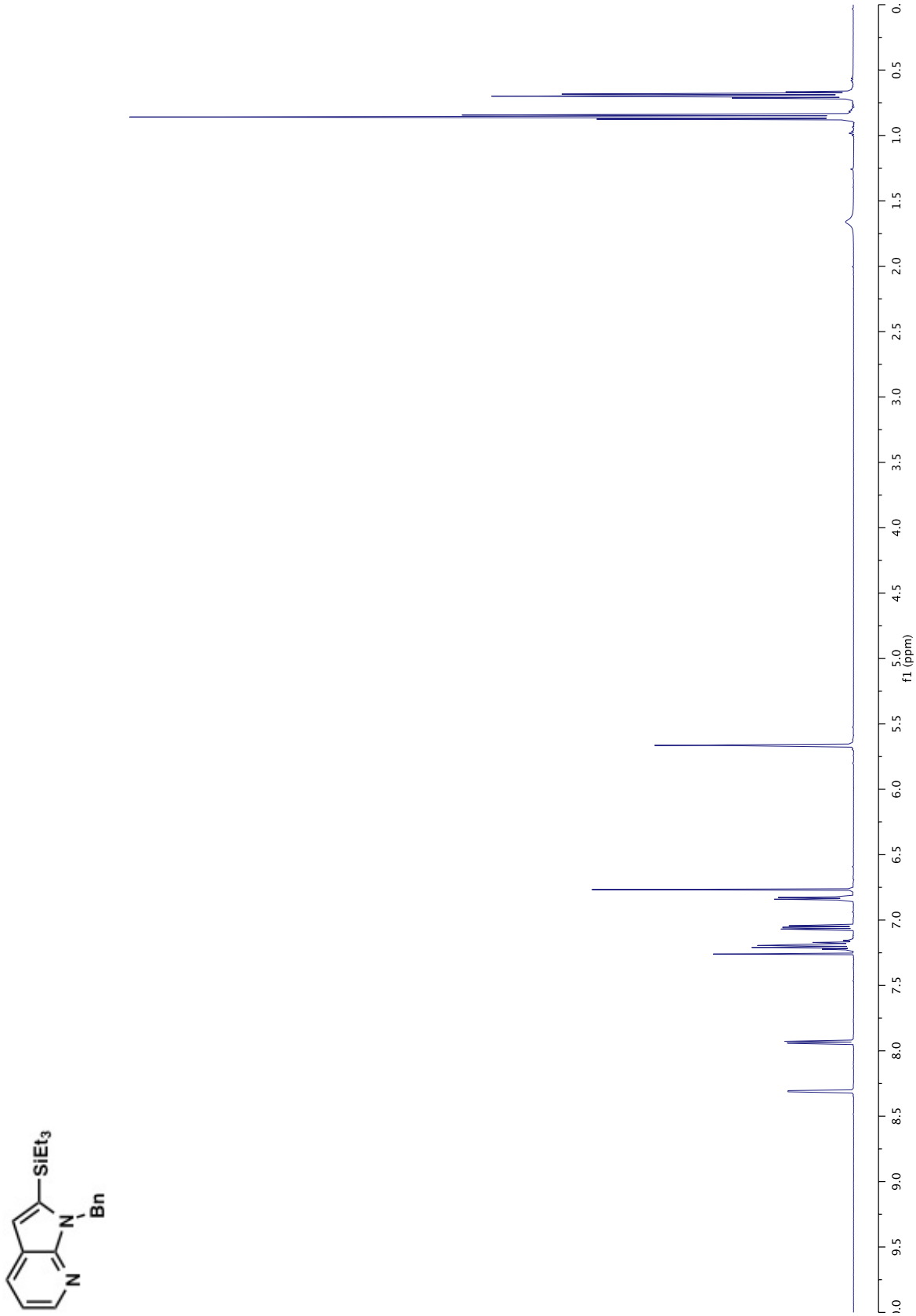
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4c**.



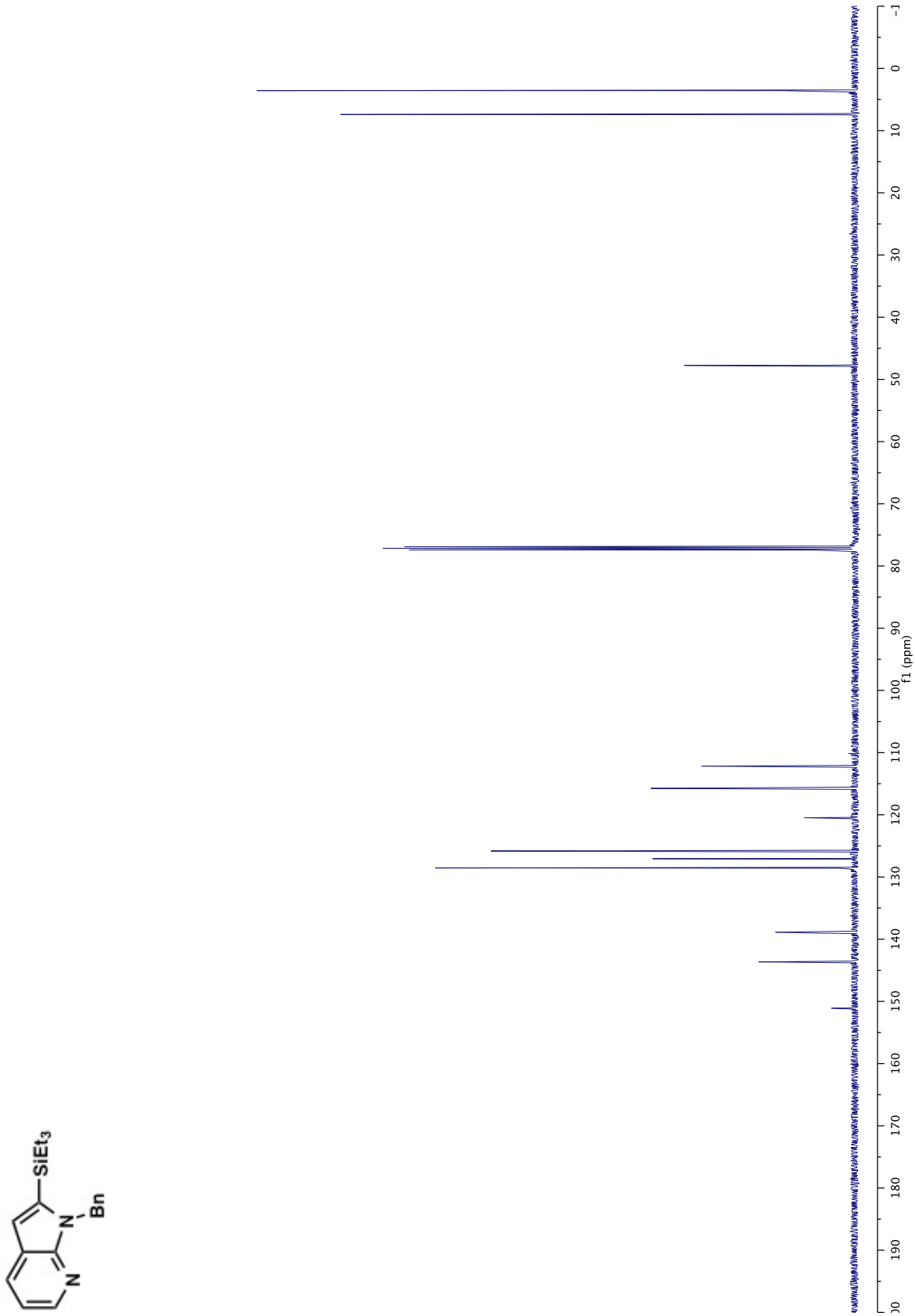
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4d**.



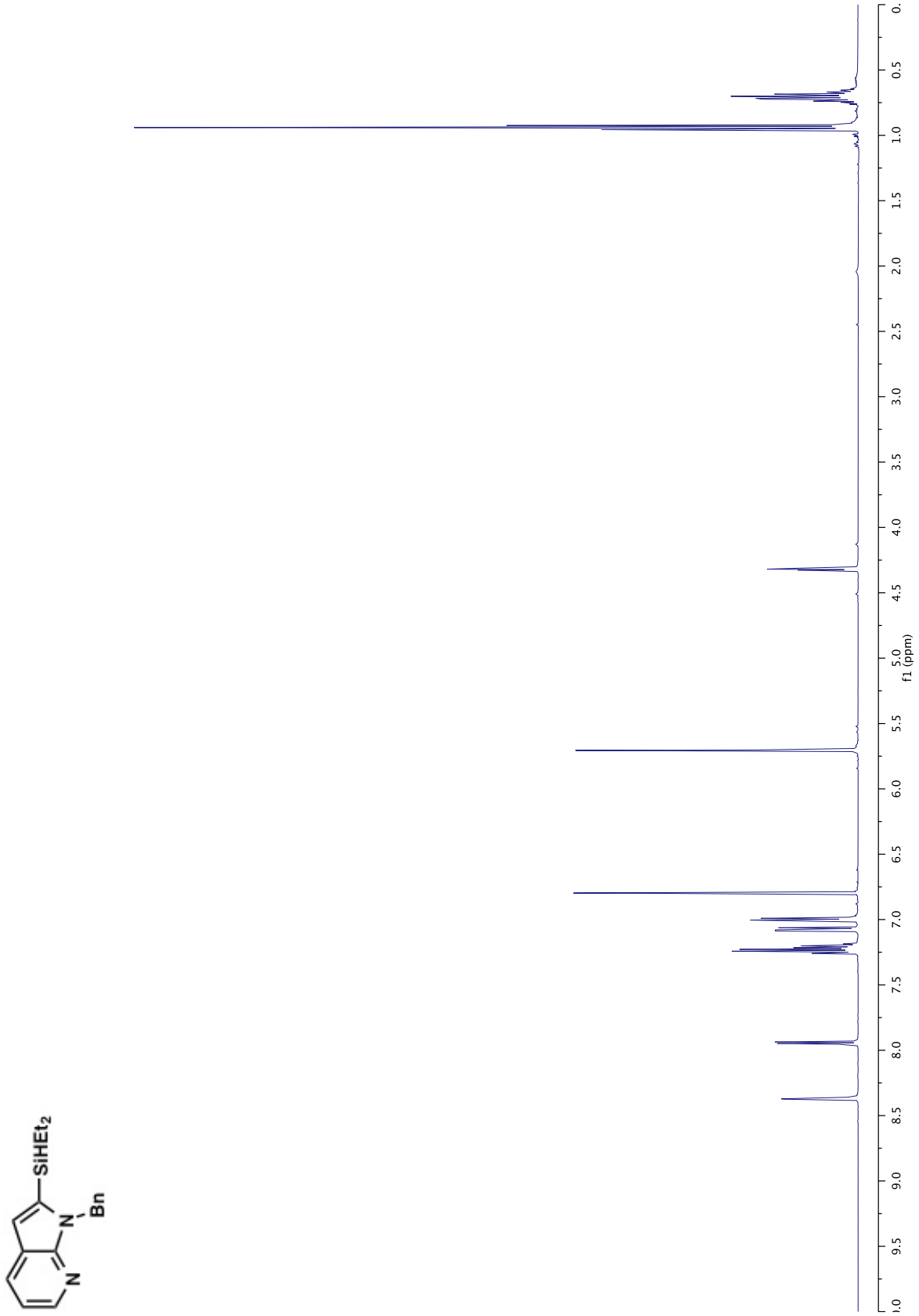
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4d**.



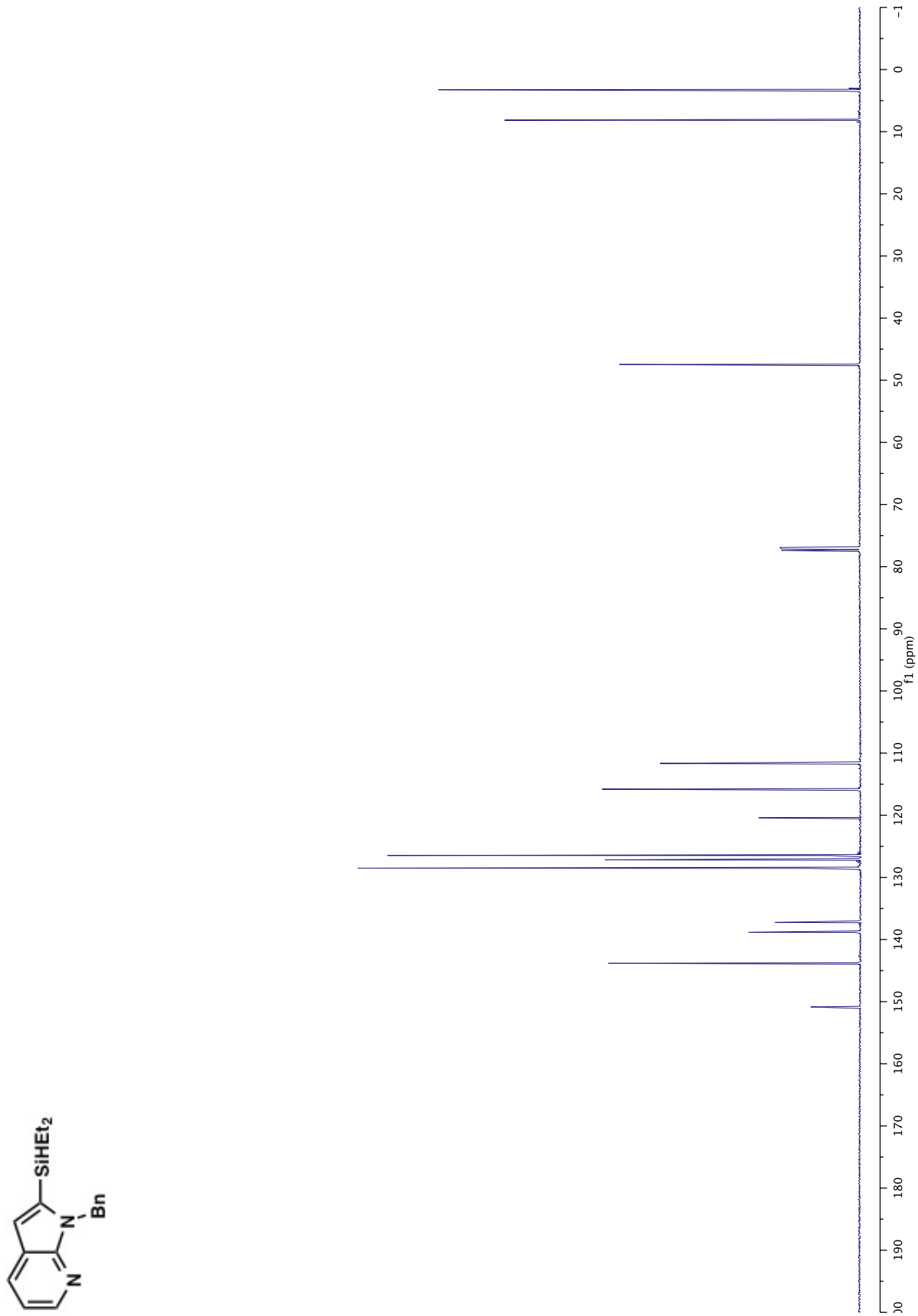
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4e**.



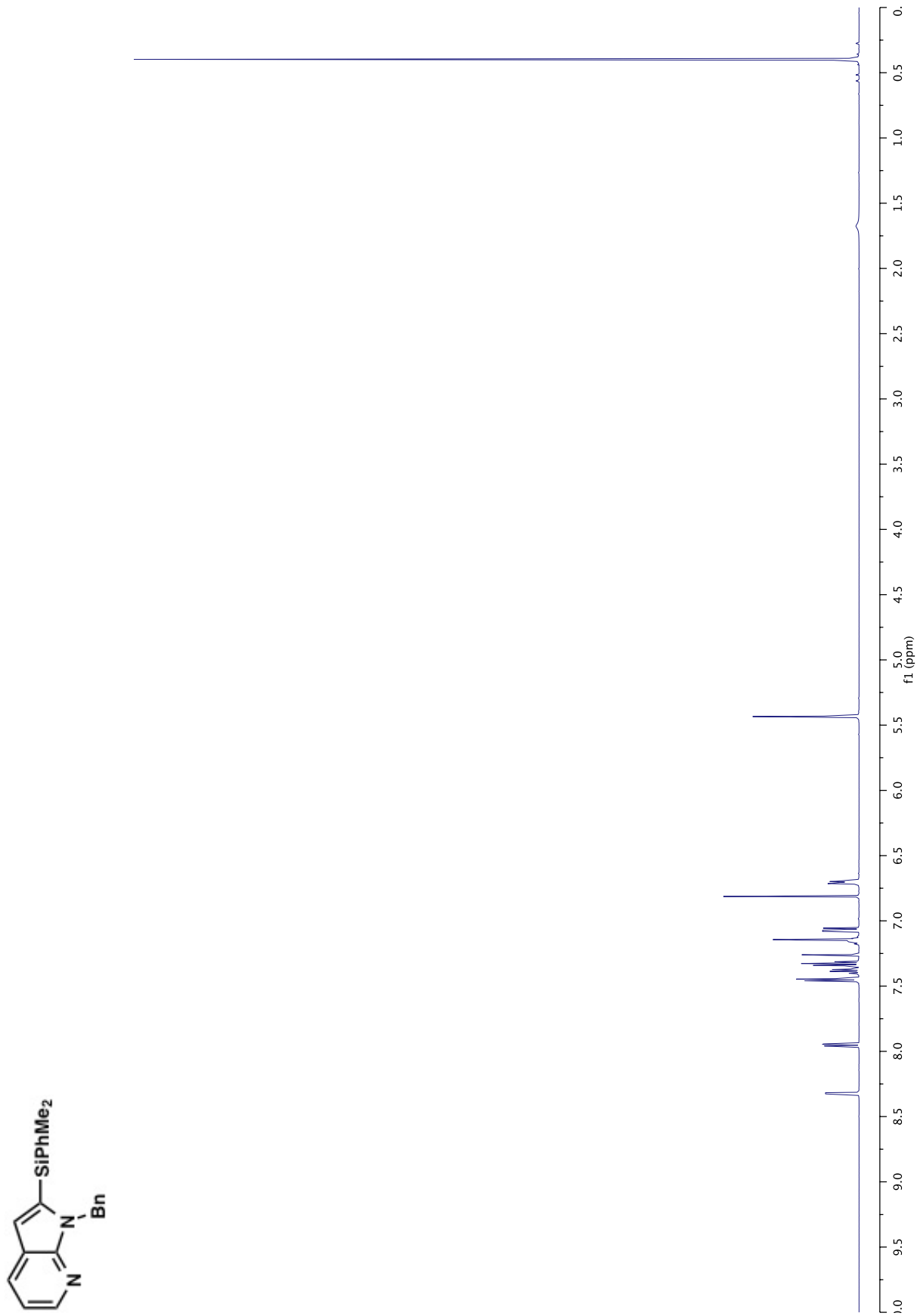
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4e.**



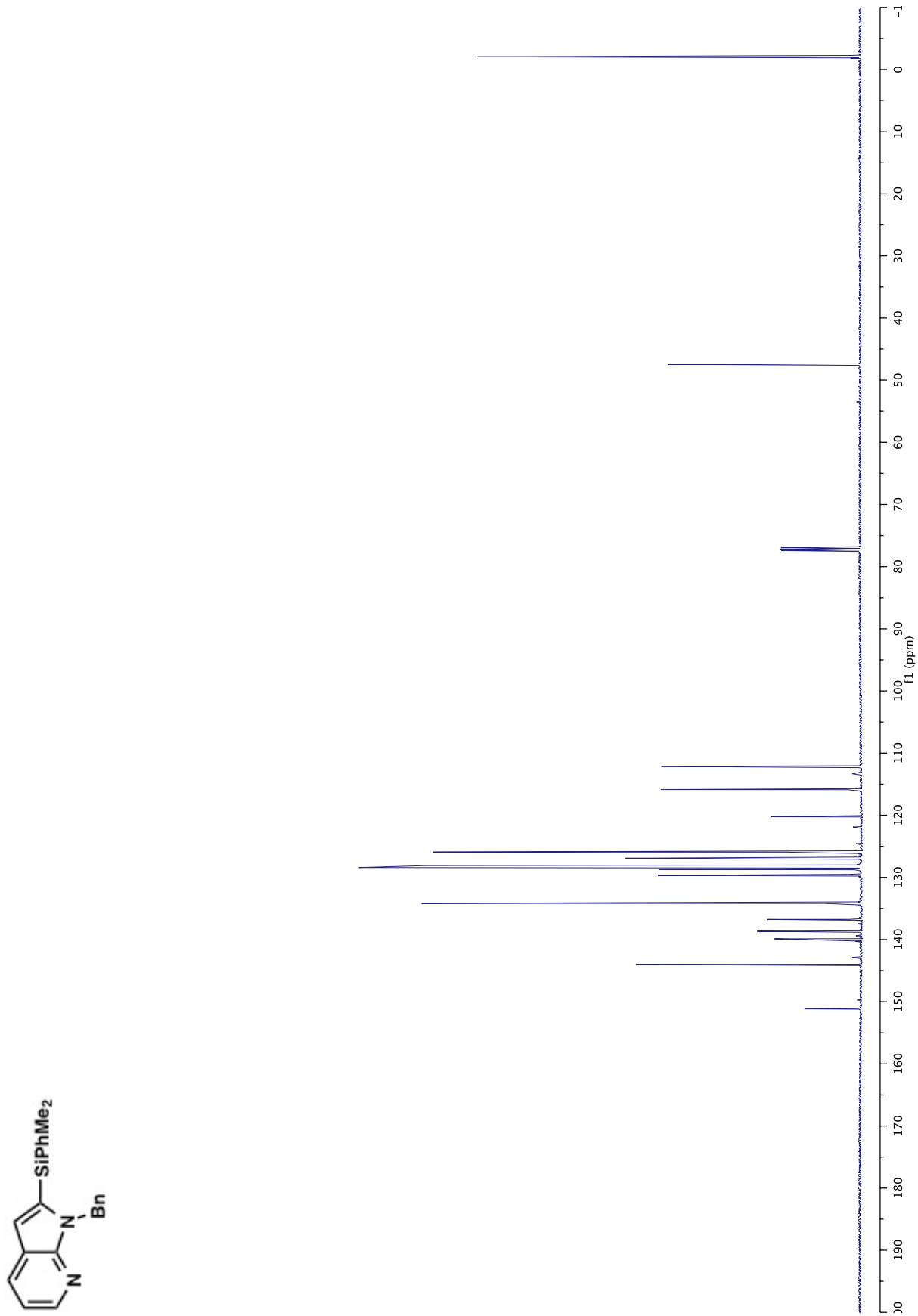
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4f**.



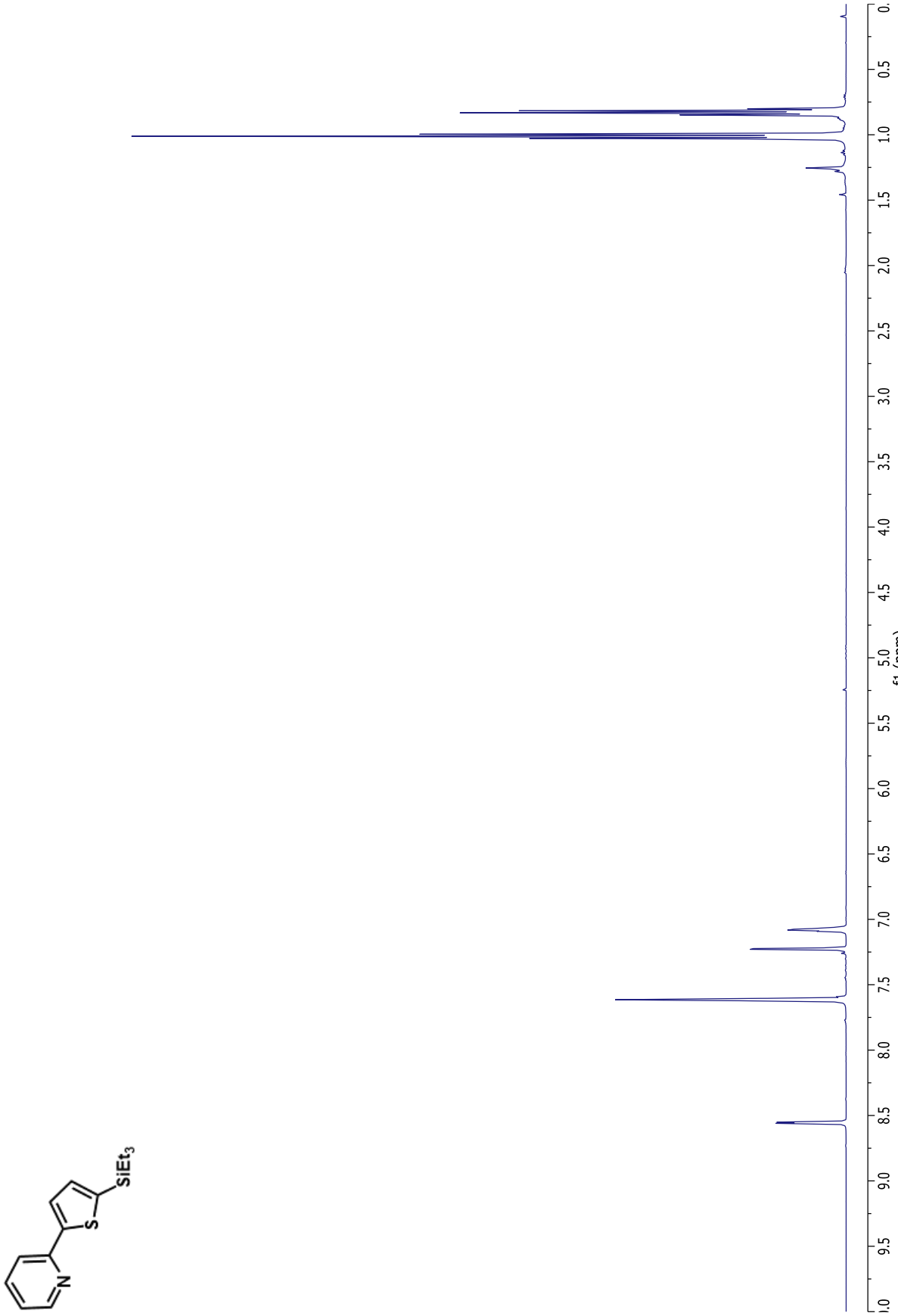
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4f**.



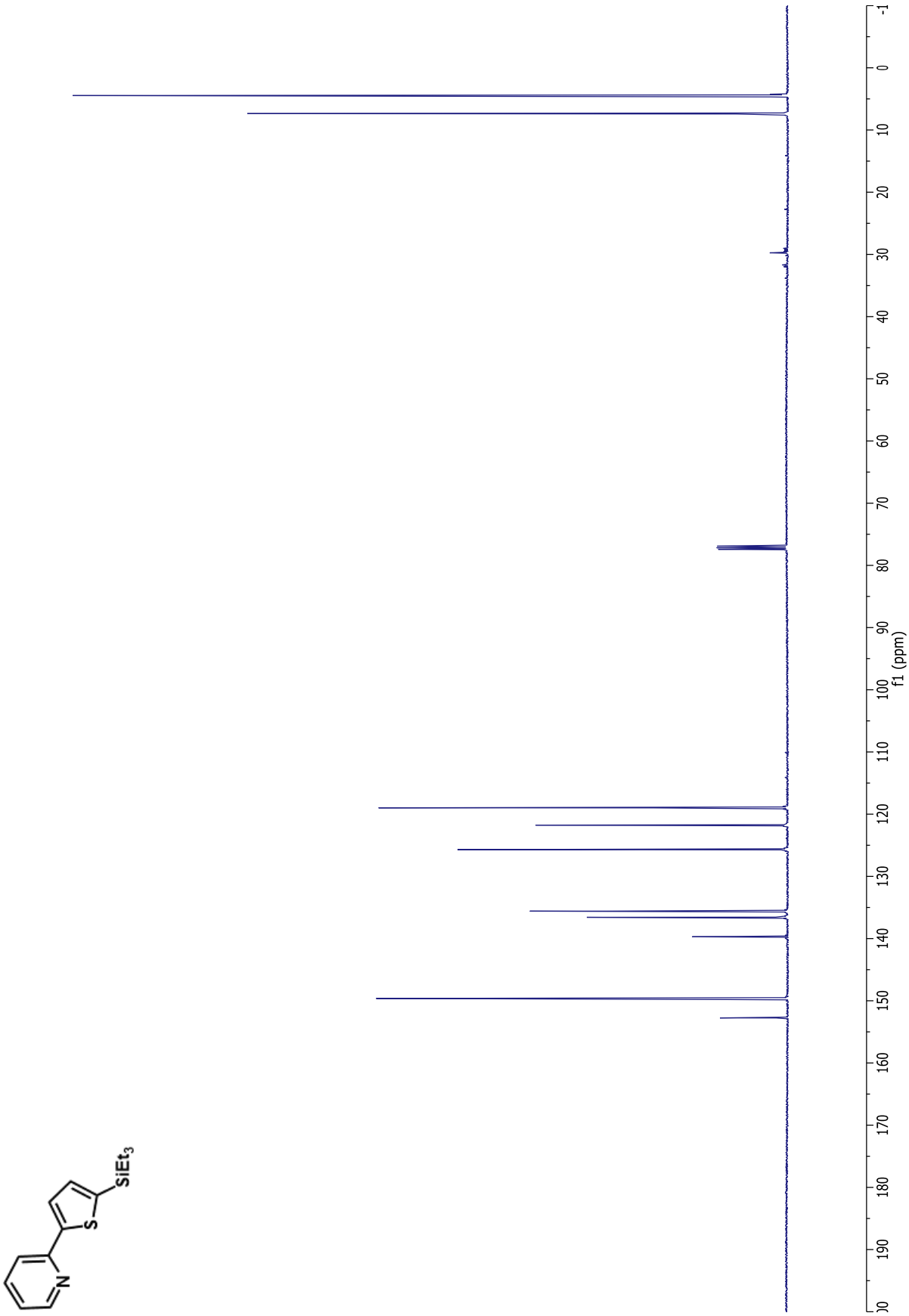
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4g**.



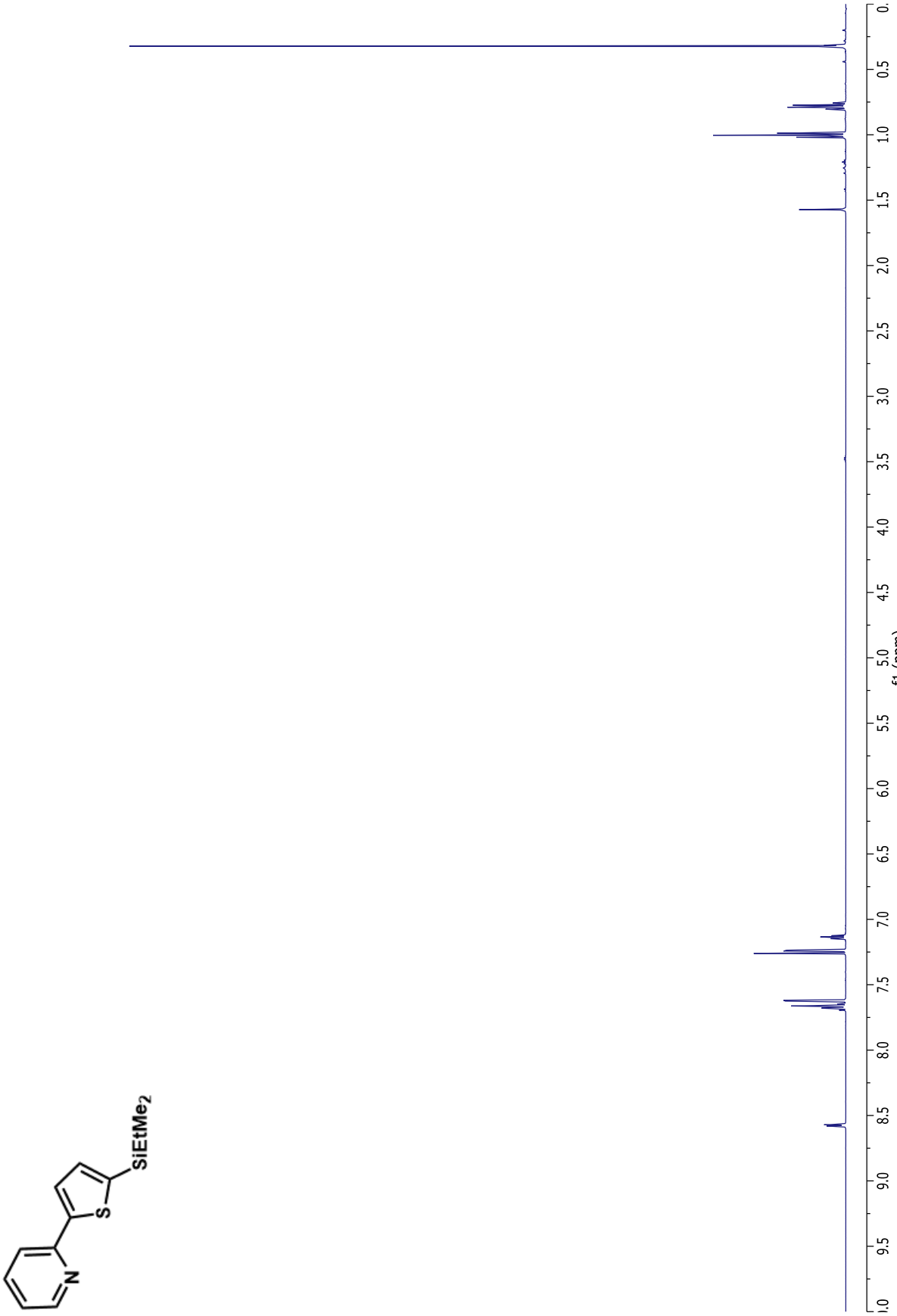
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4g**.



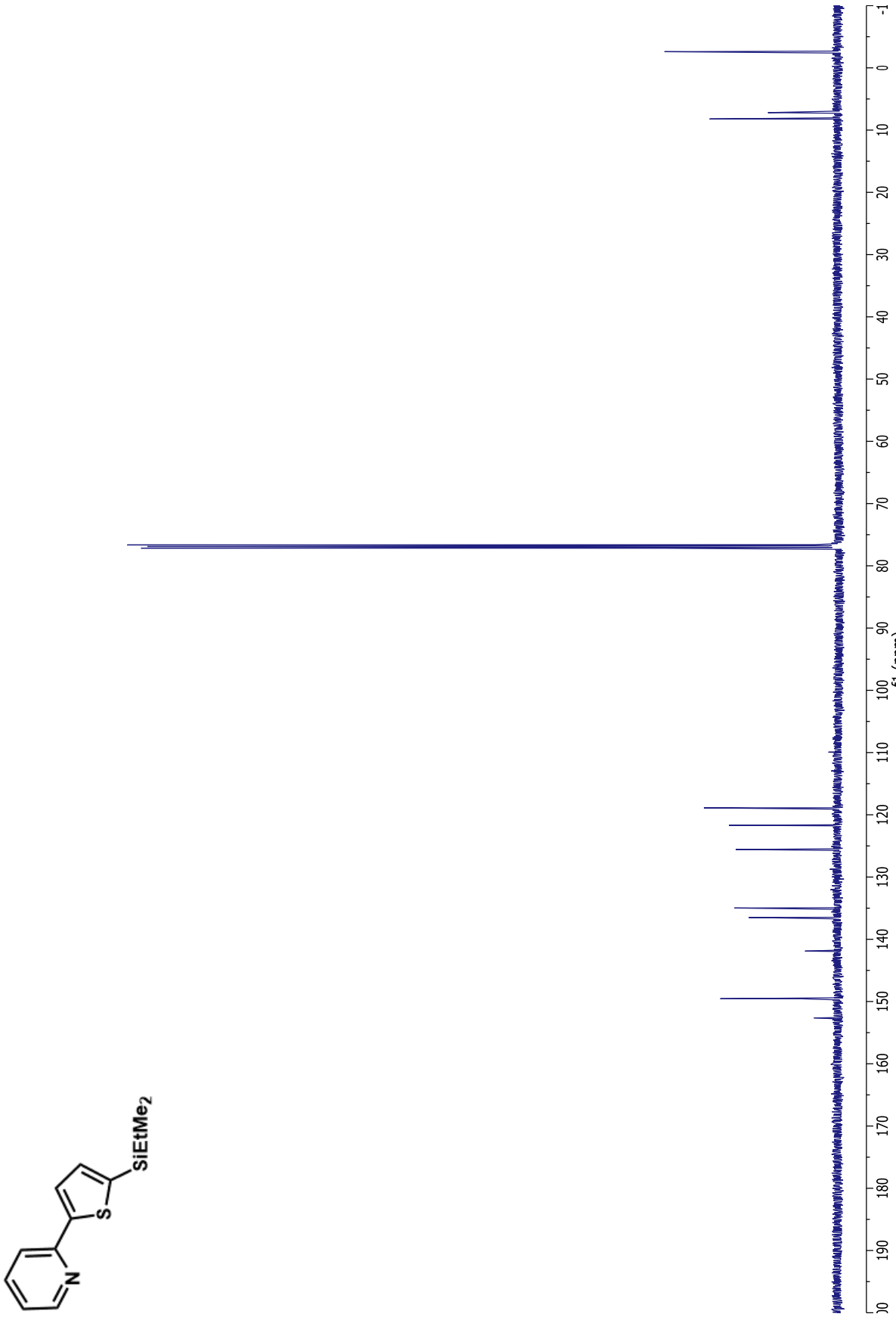
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4j**.



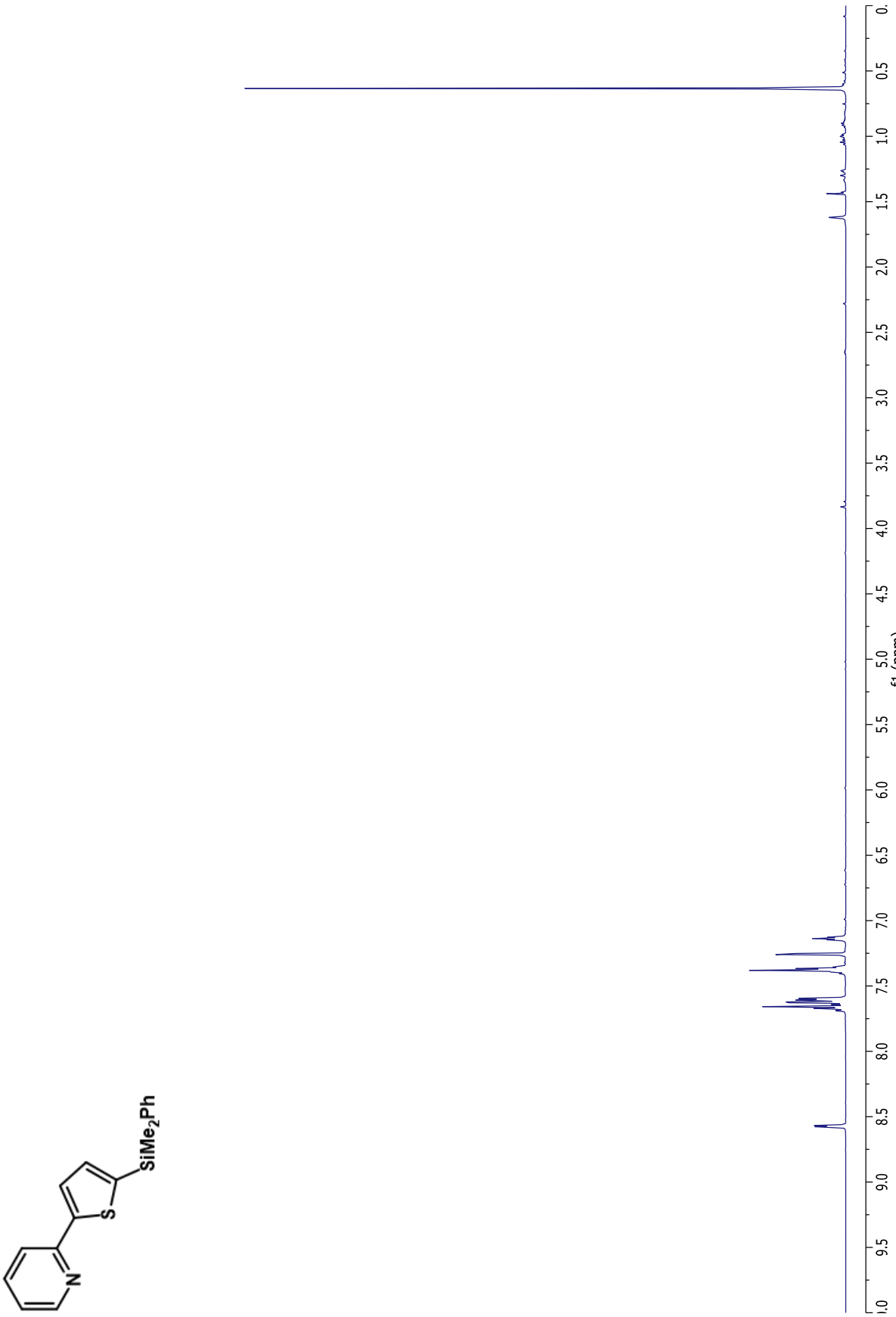
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4j**.



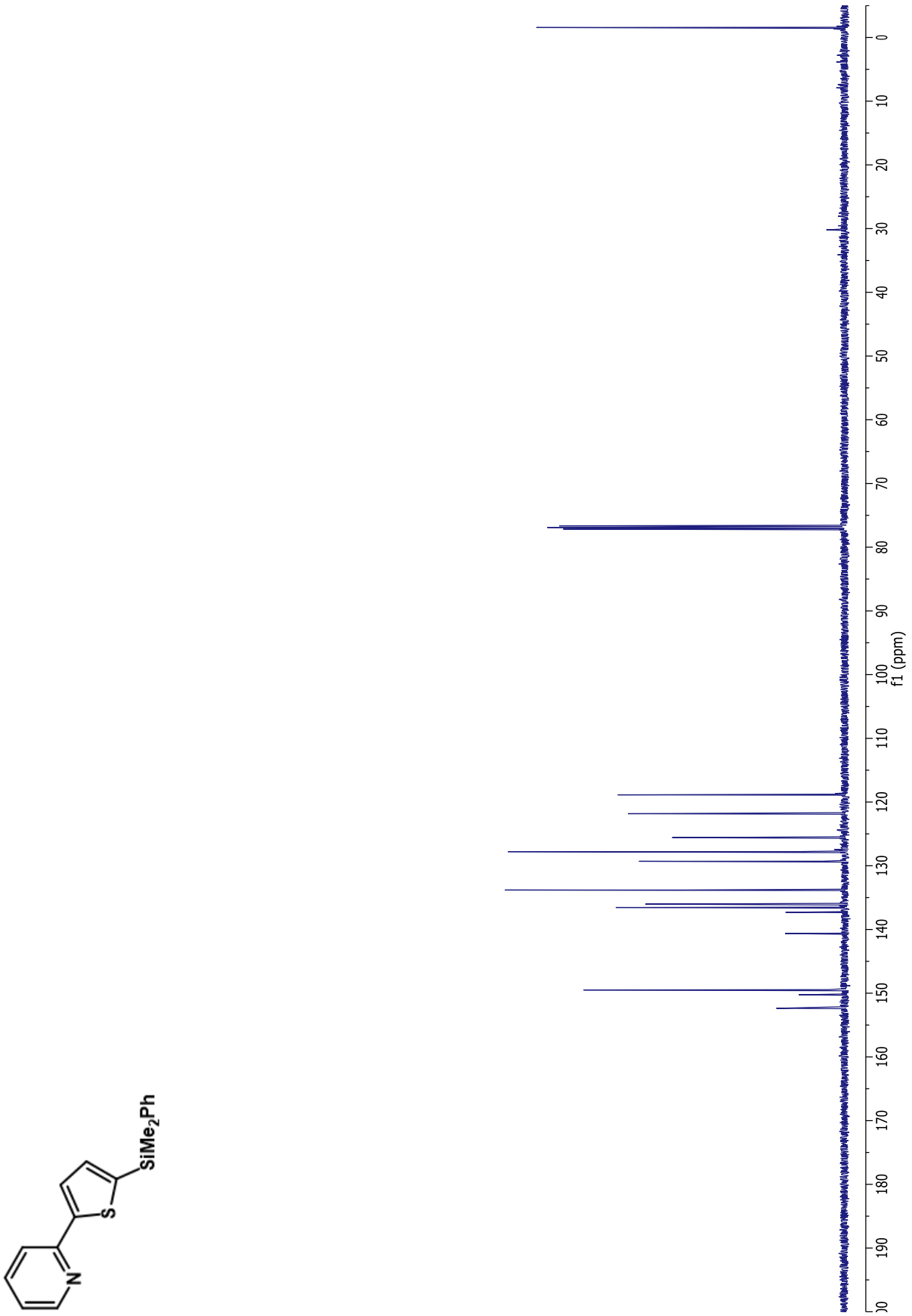
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4k**.



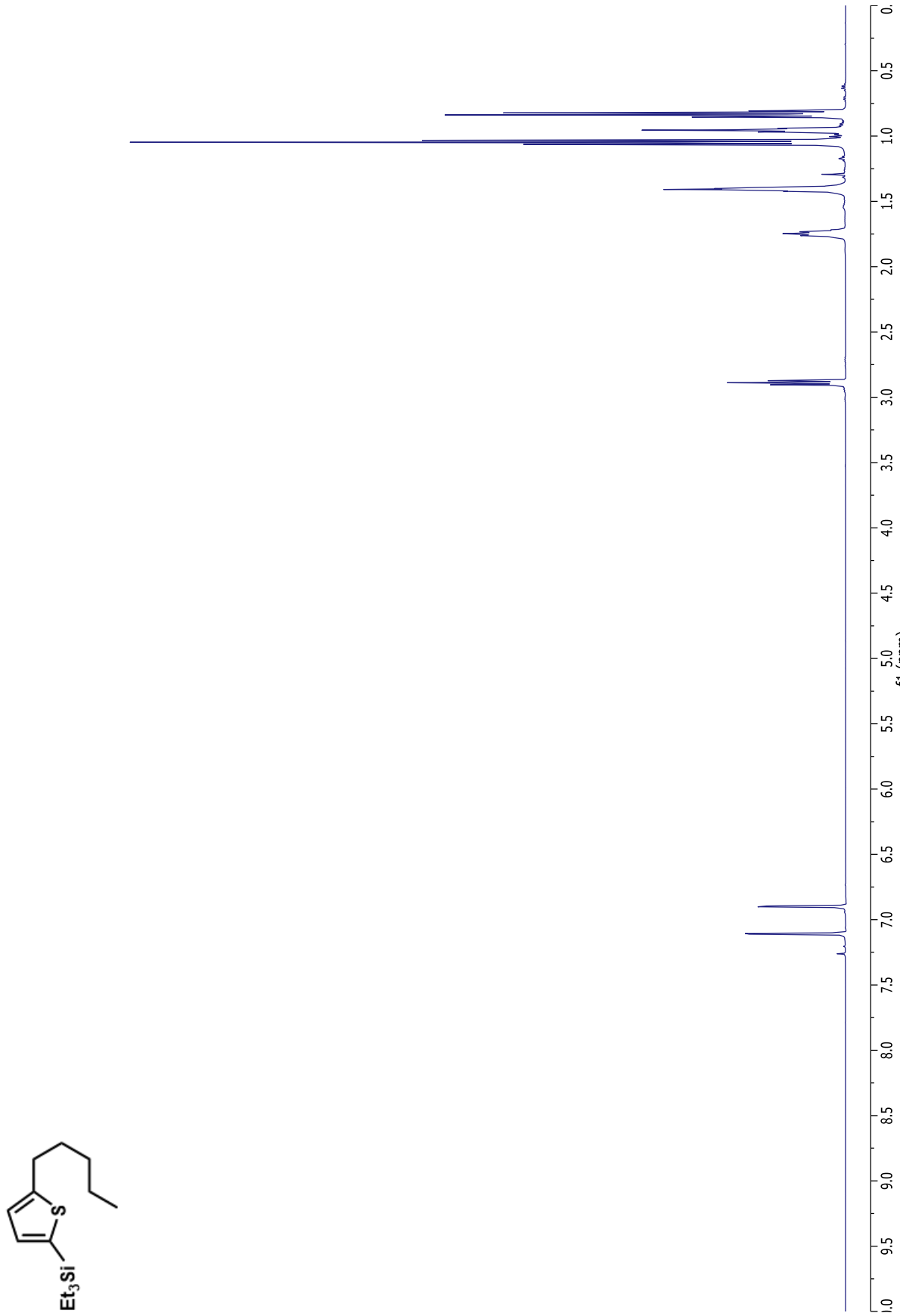
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4k**.



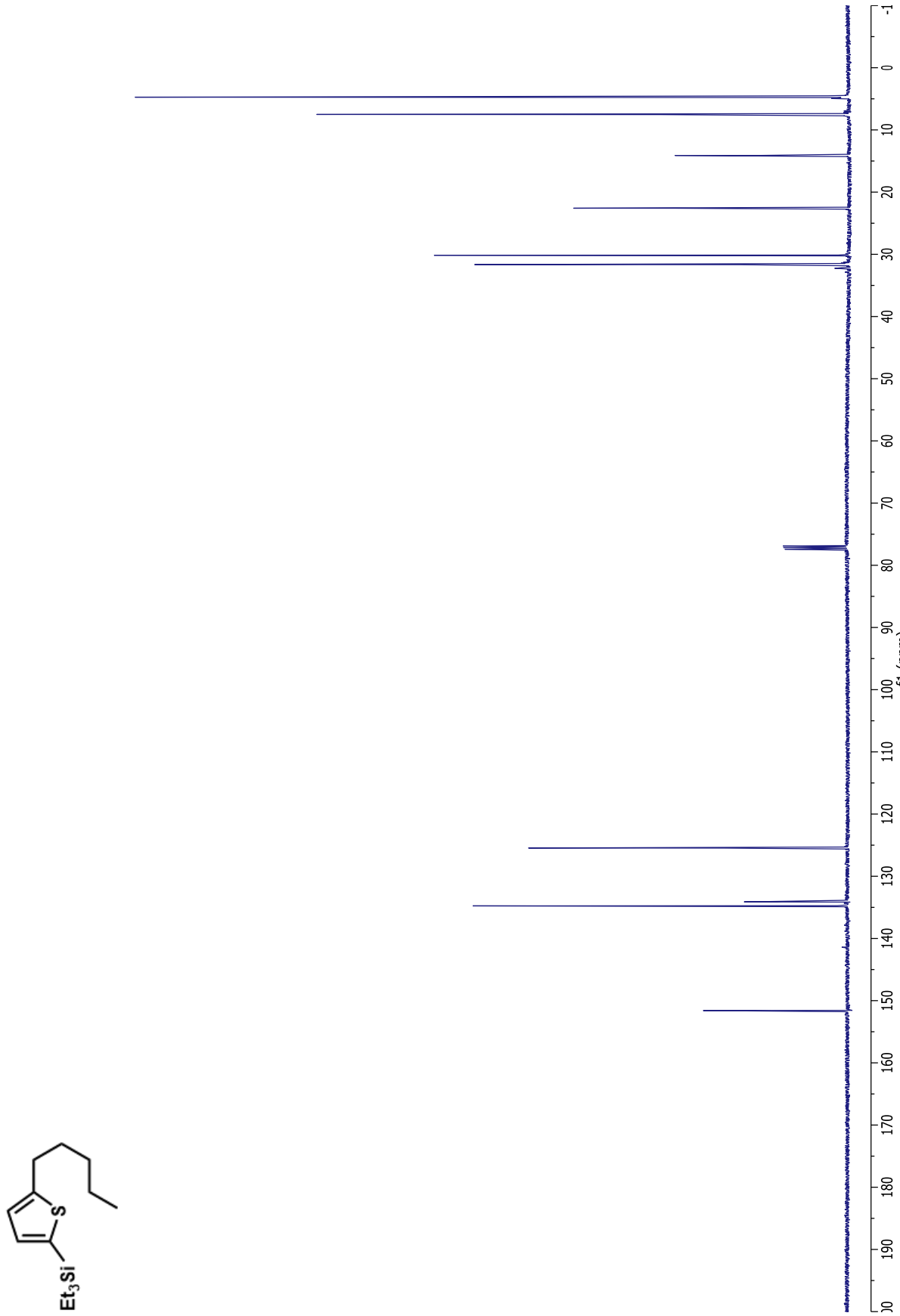
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4l**.



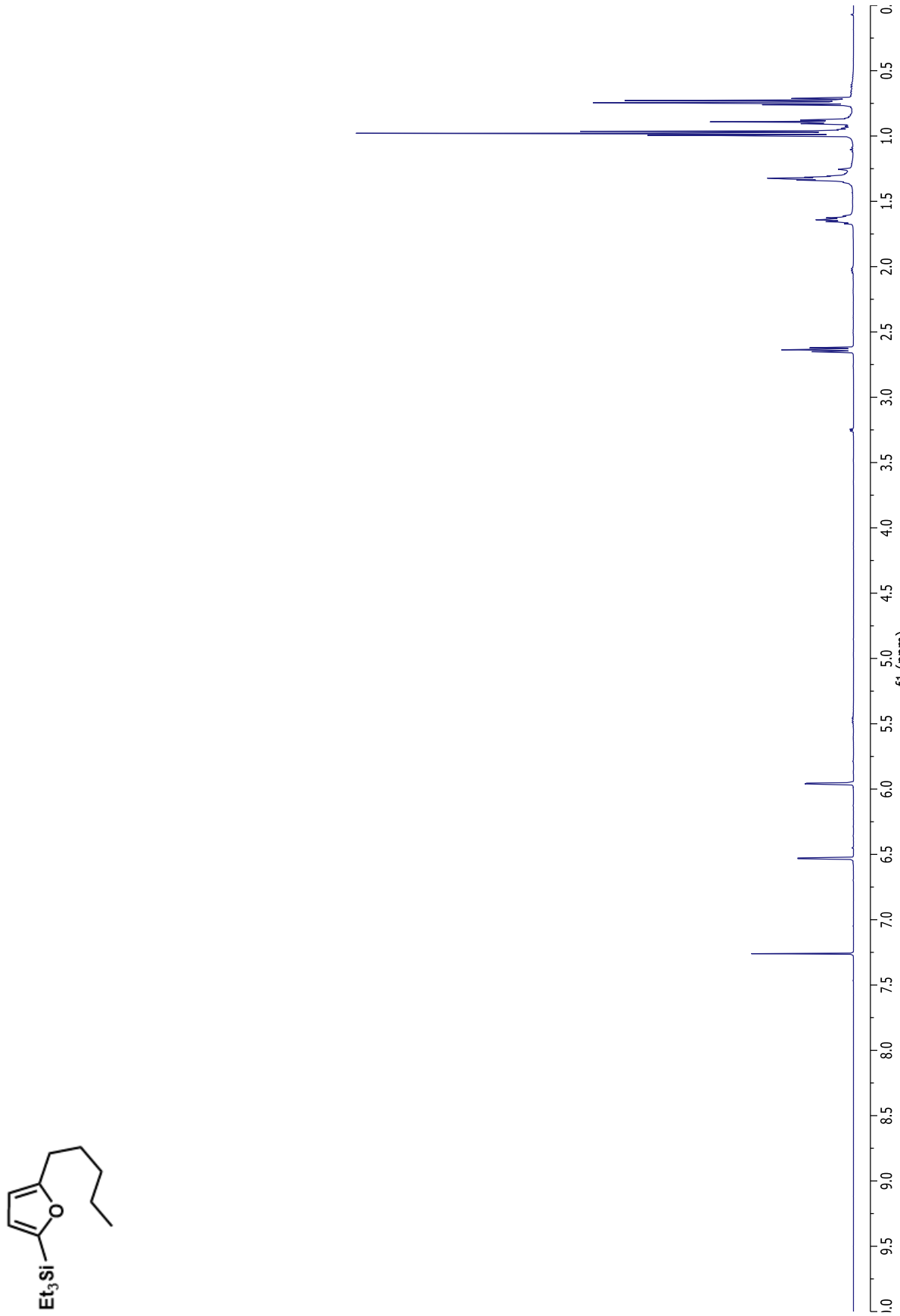
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4l**.



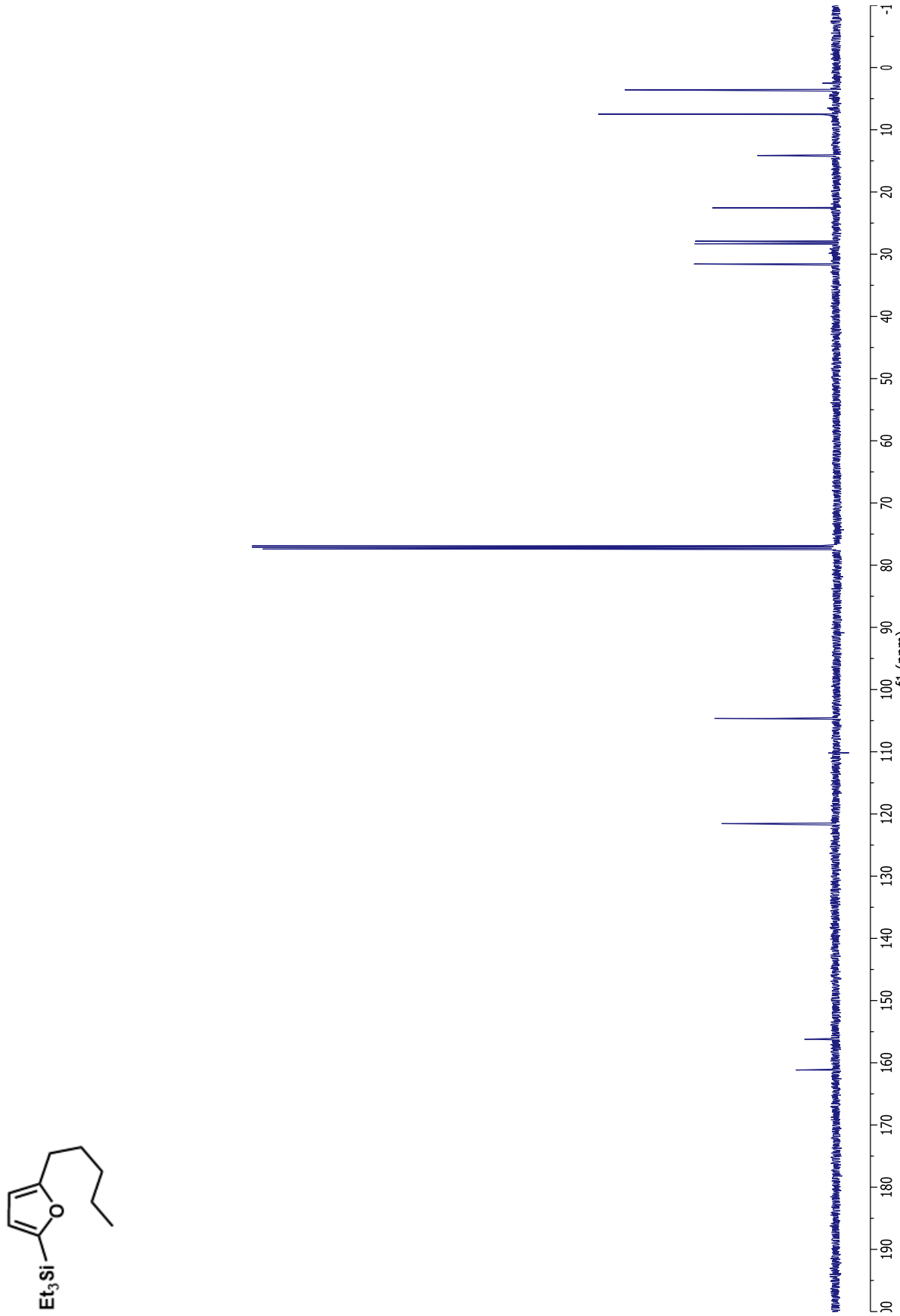
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4m**.



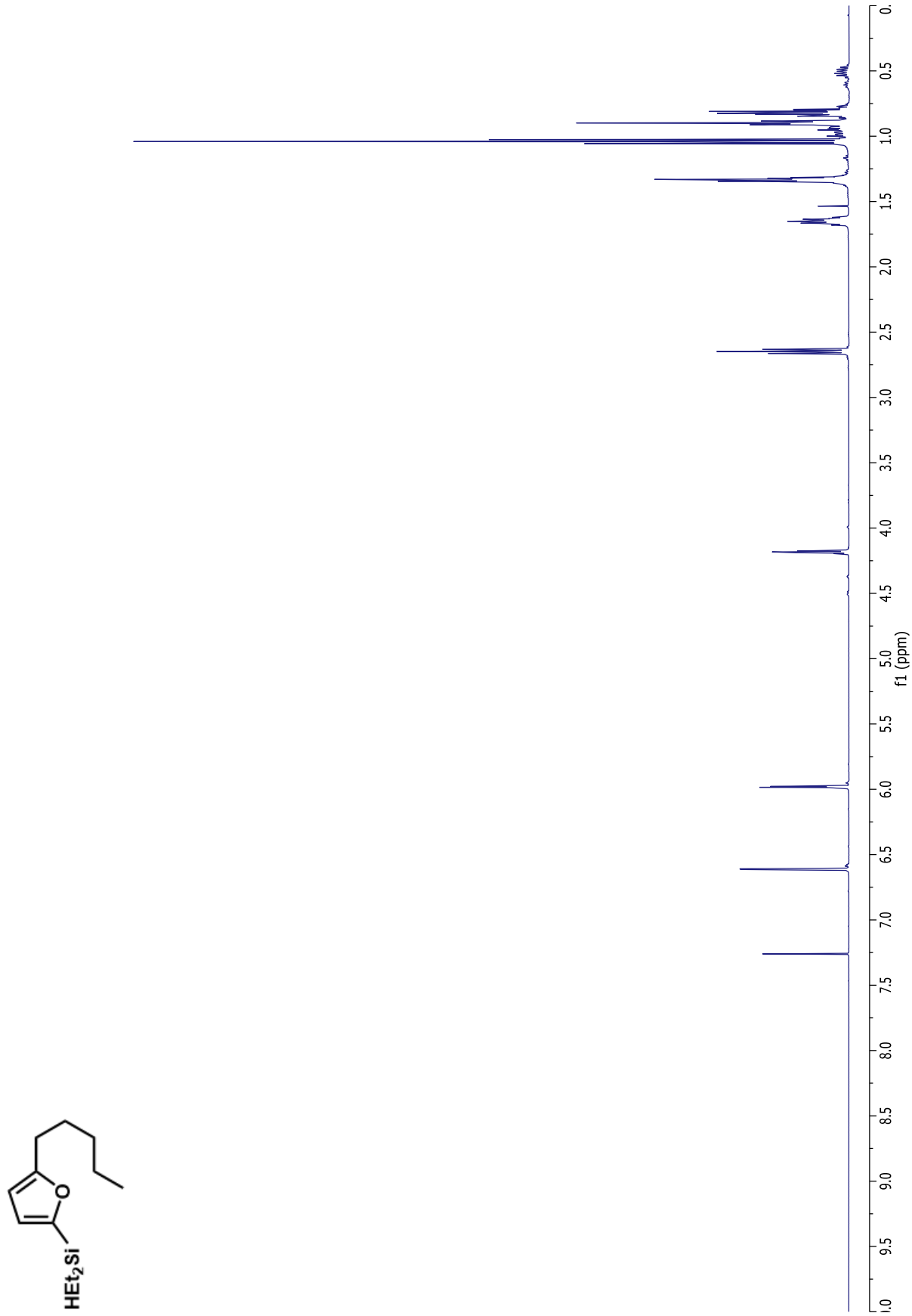
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4m**.



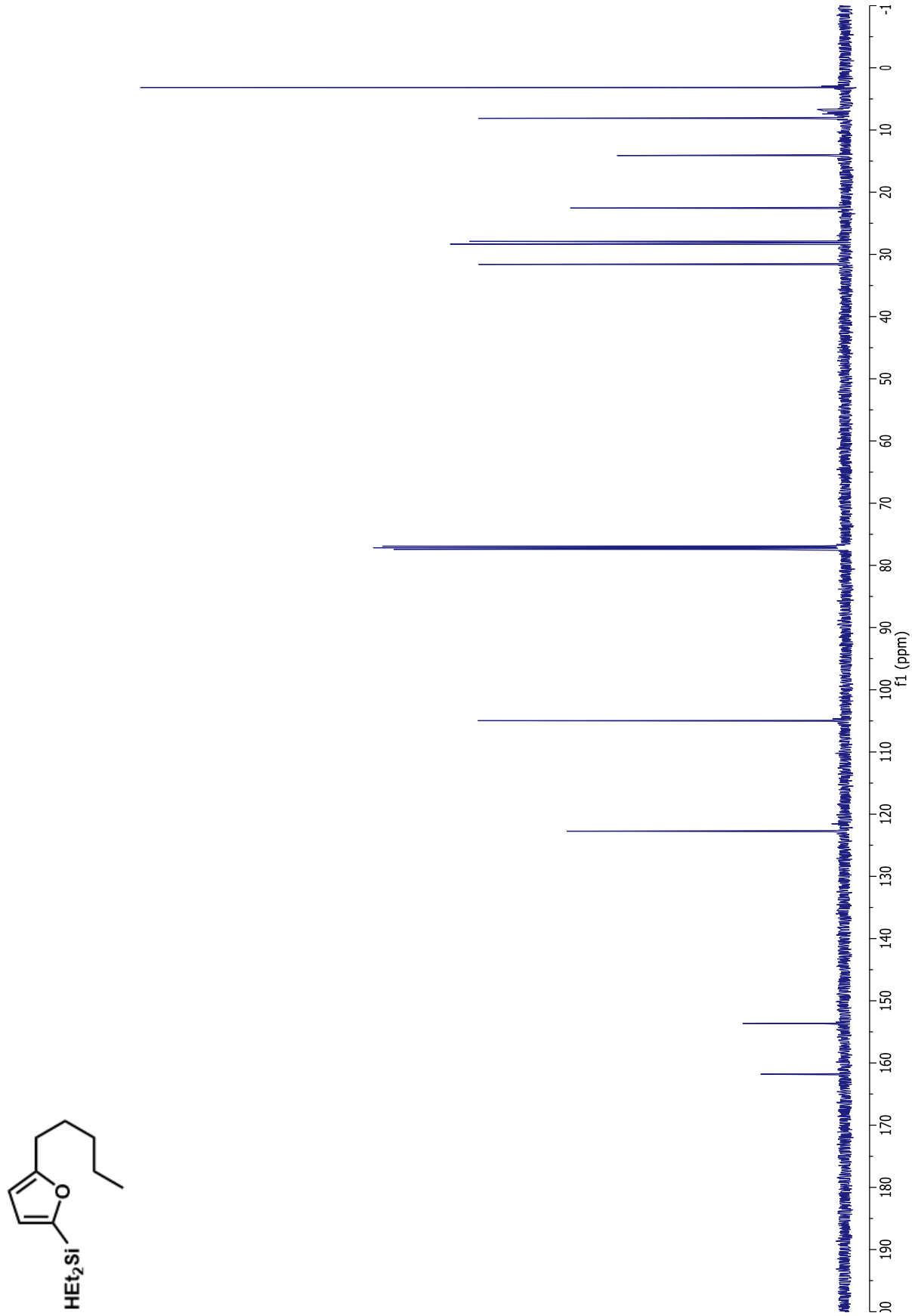
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4n**.



^{13}C NMR (125 MHz, $CDCl_3$) of compound **4n**.

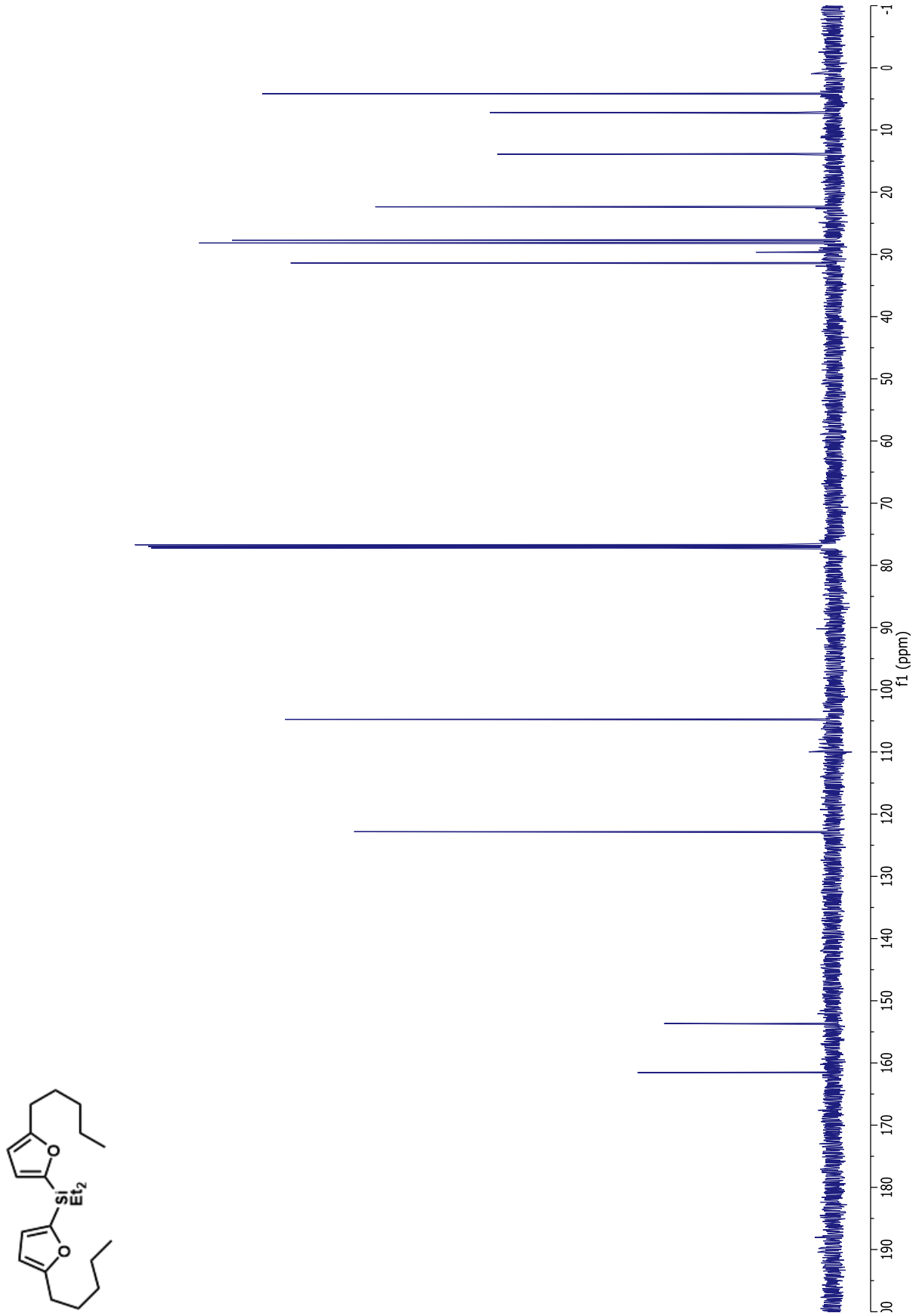


^{1}H NMR (500 MHz, $CDCl_3$) of compound **4o**.

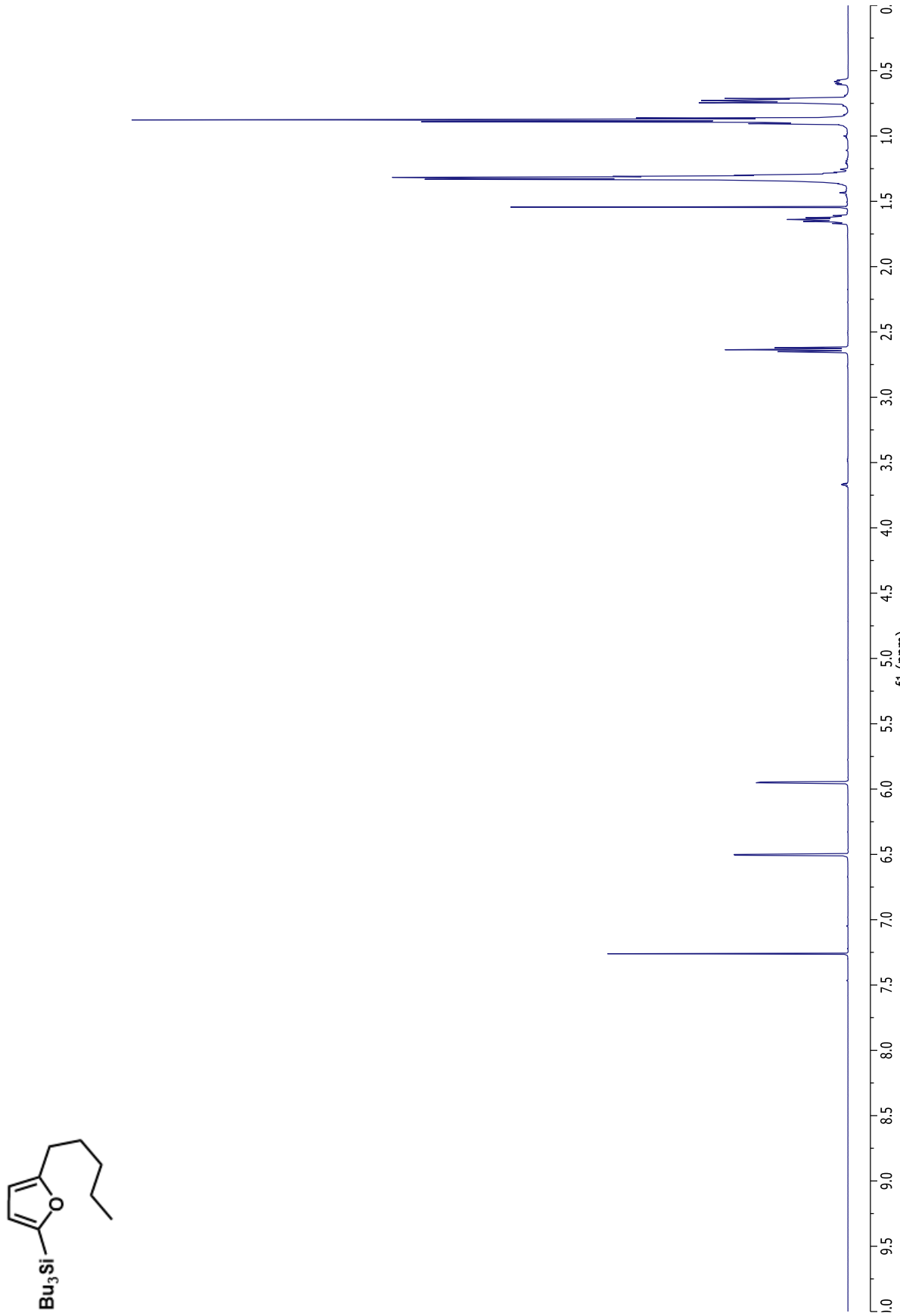


^{13}C NMR (125 MHz, $CDCl_3$) of compound **4o**.

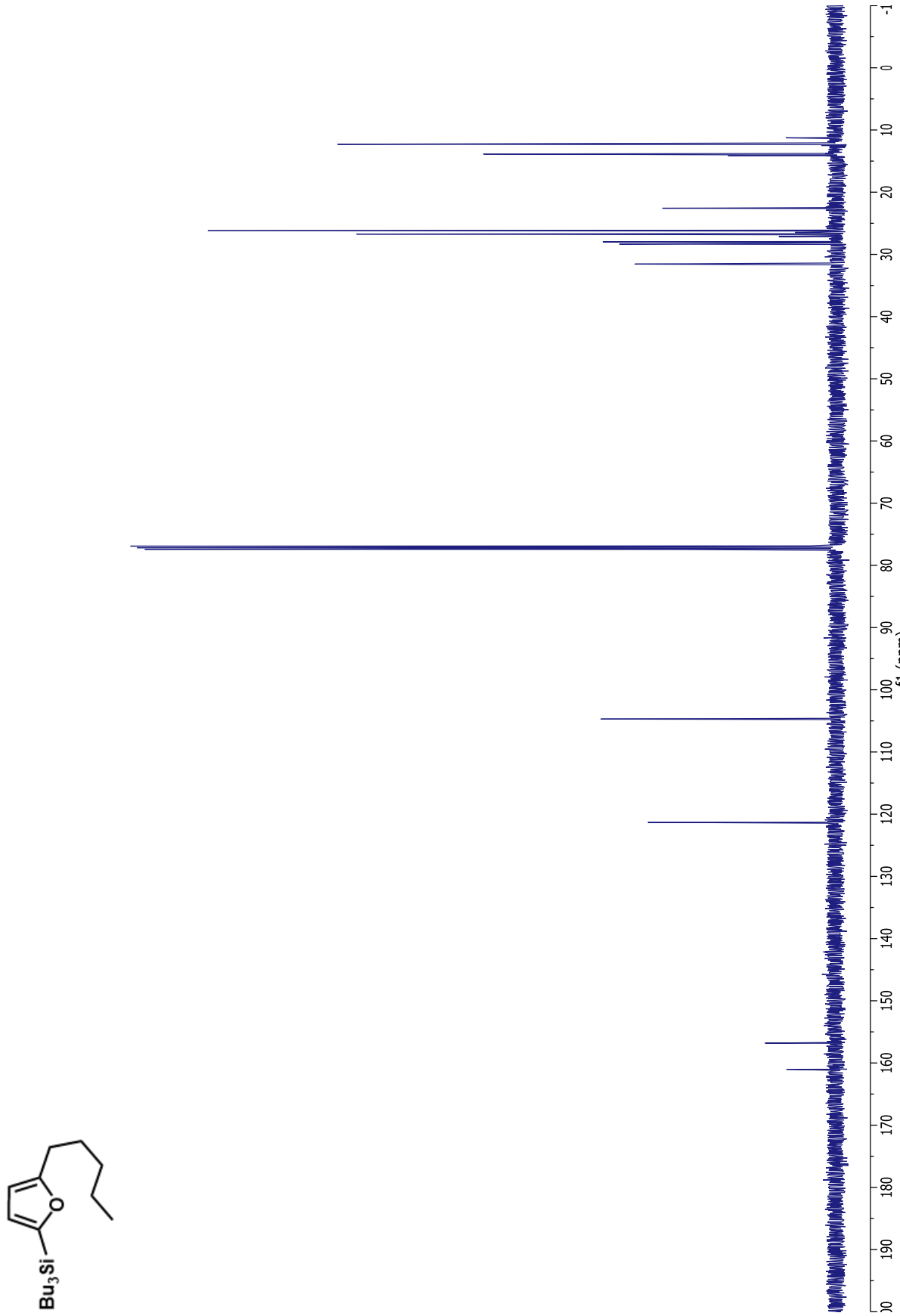
^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-4o**.



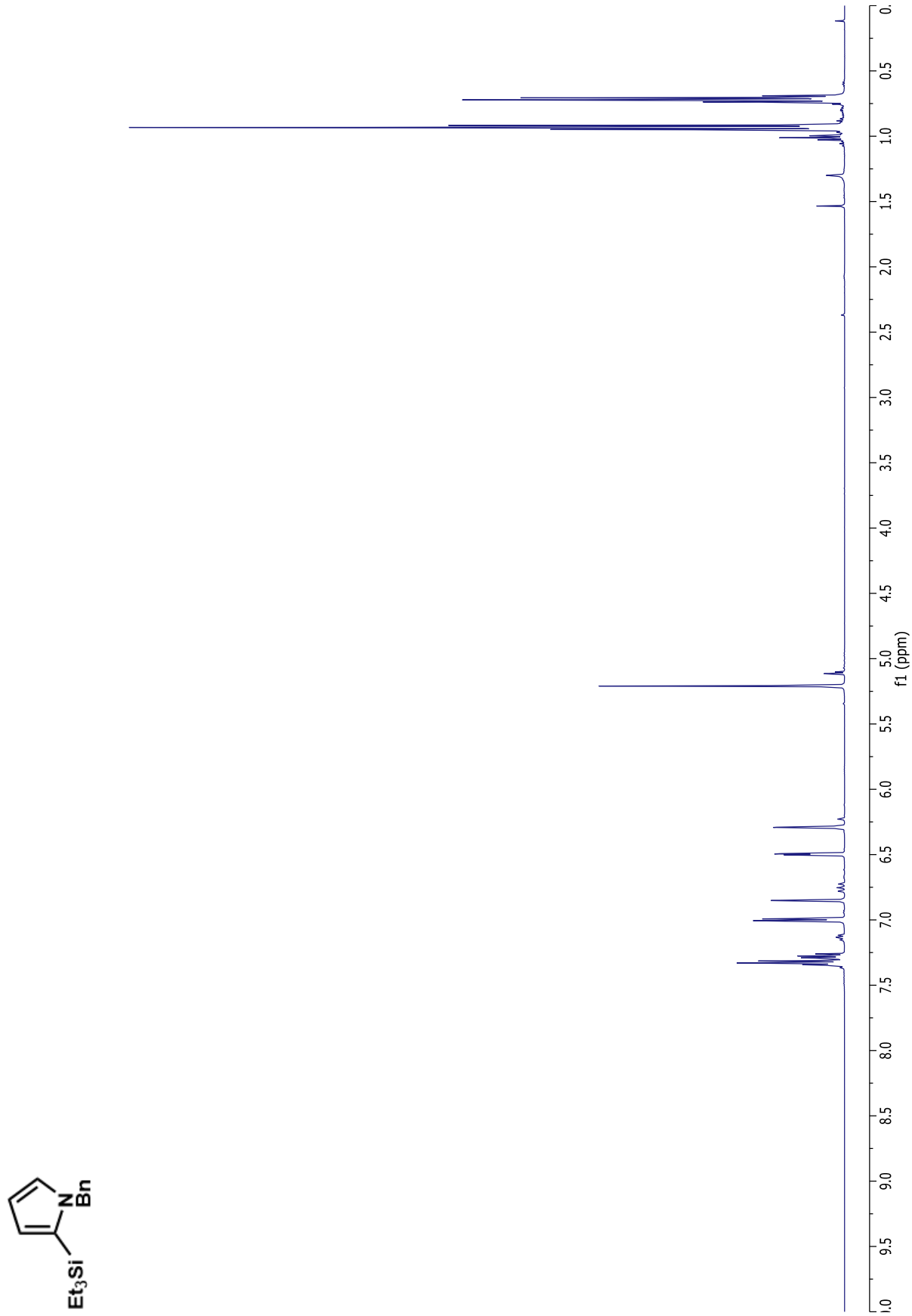
^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-4o**.



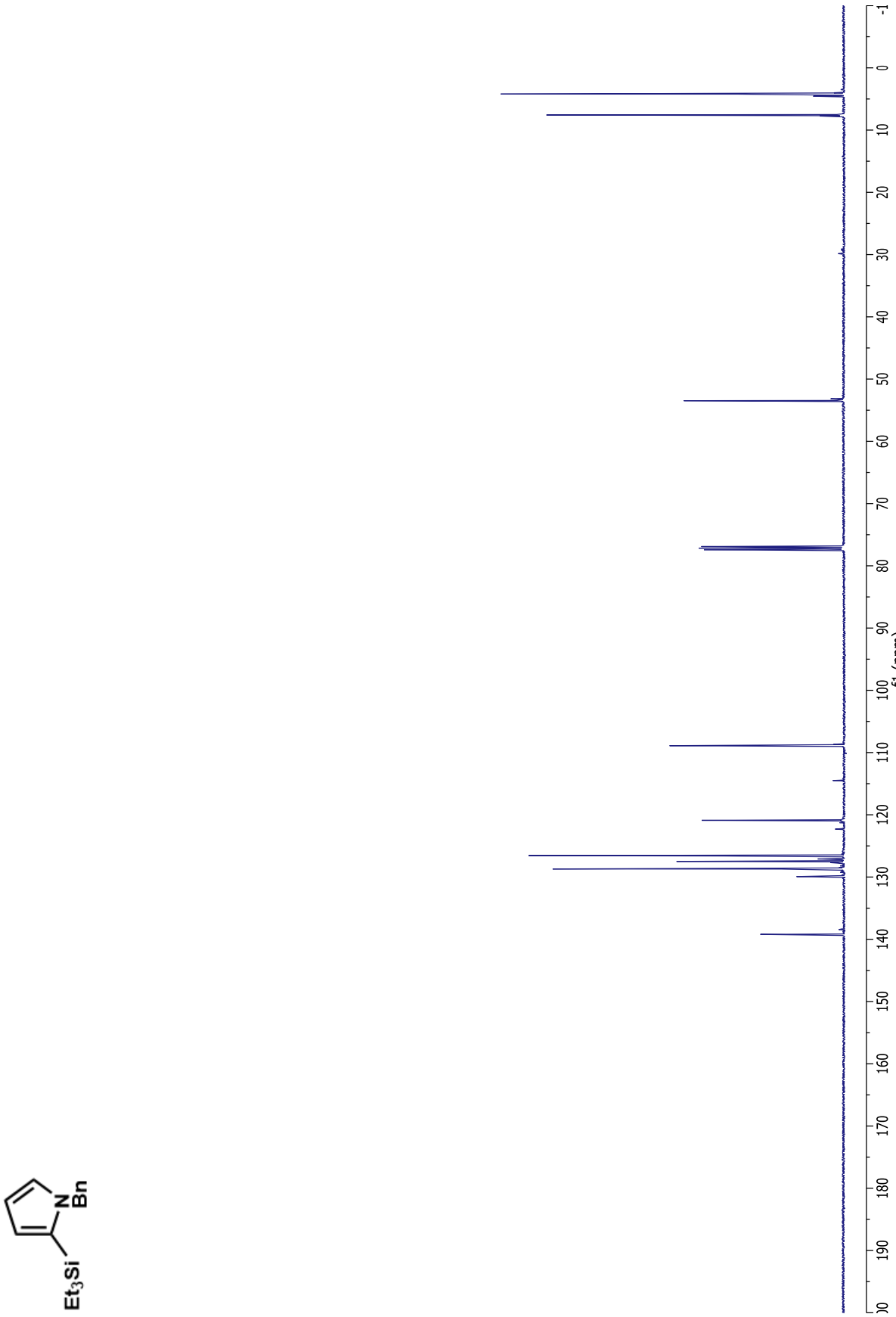
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4p**.



^{13}C NMR (125 MHz, $CDCl_3$) of compound **4p**.

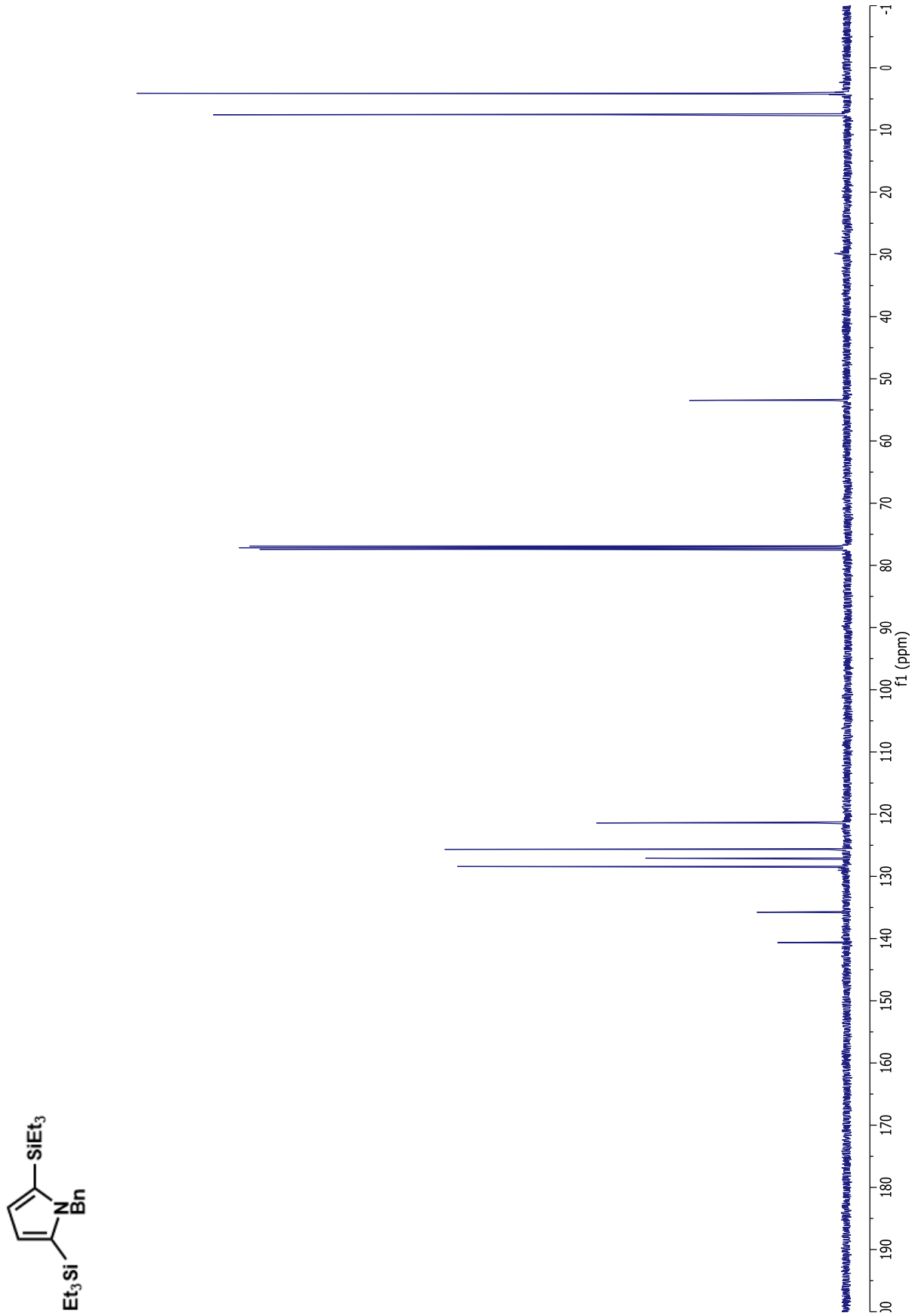


^{1}H NMR (500 MHz, $CDCl_3$) of compound **4s**.

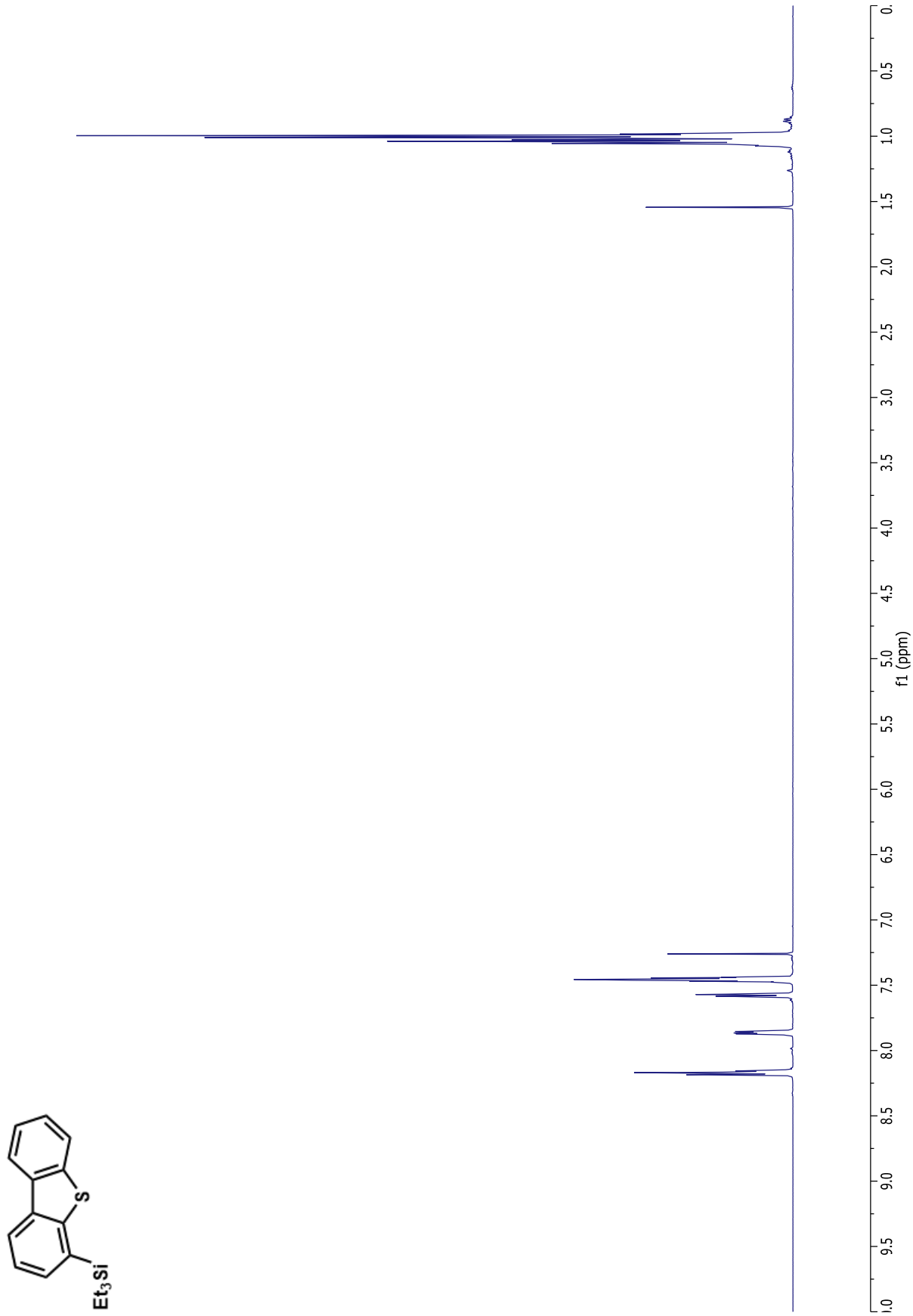


^{13}C NMR (125 MHz, $CDCl_3$) of compound **4s**.

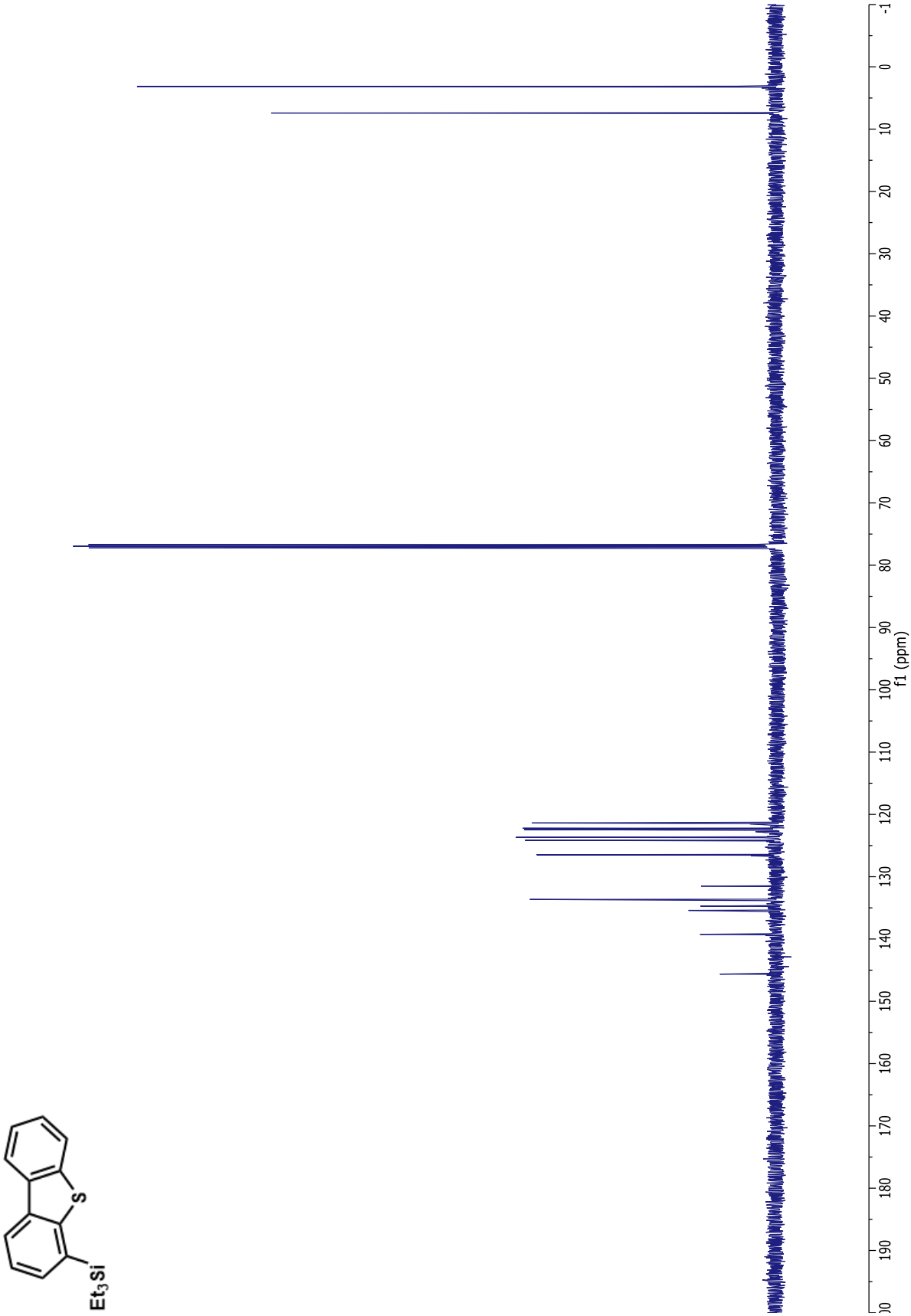
^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-4s**.



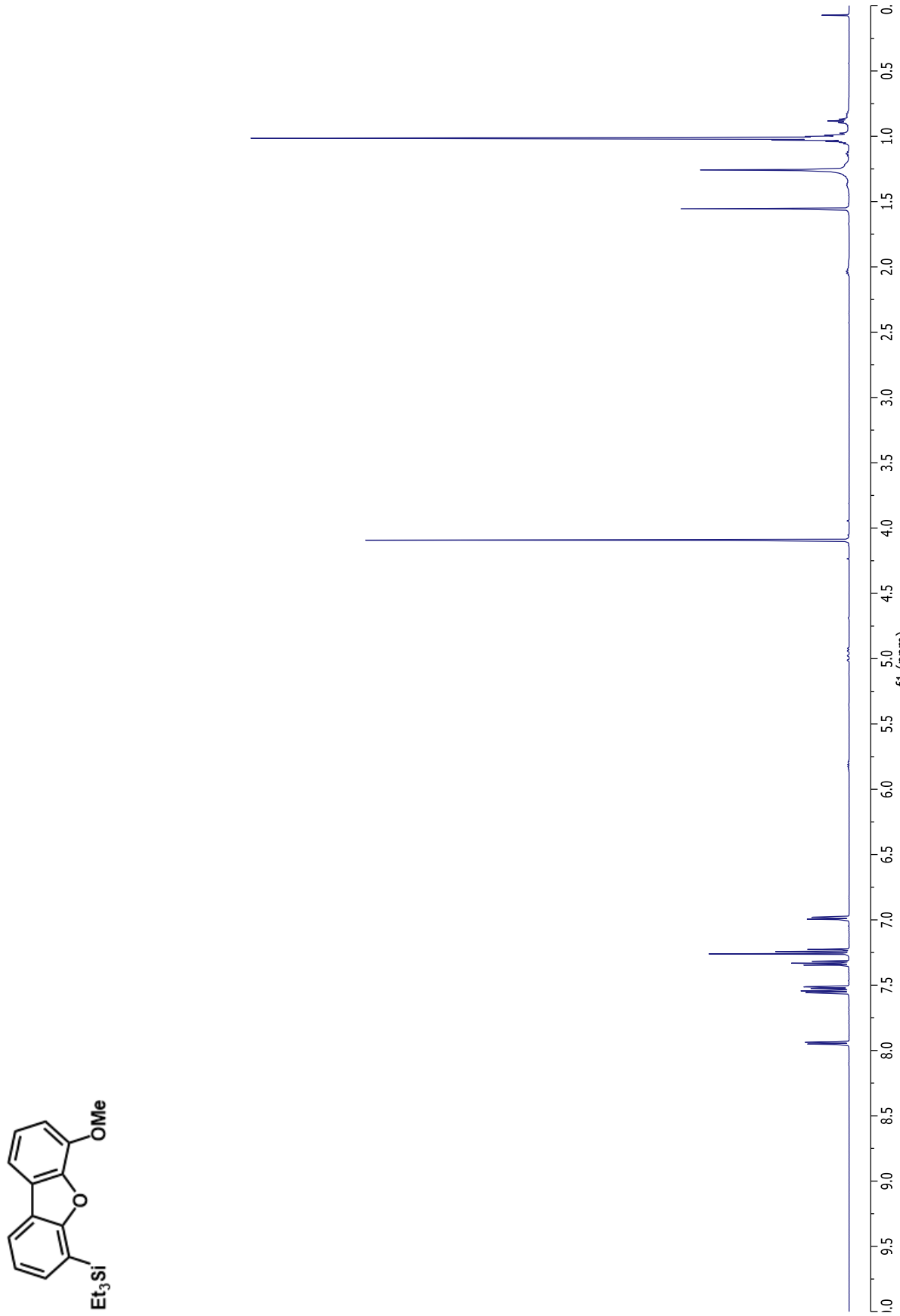
^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-4s**.



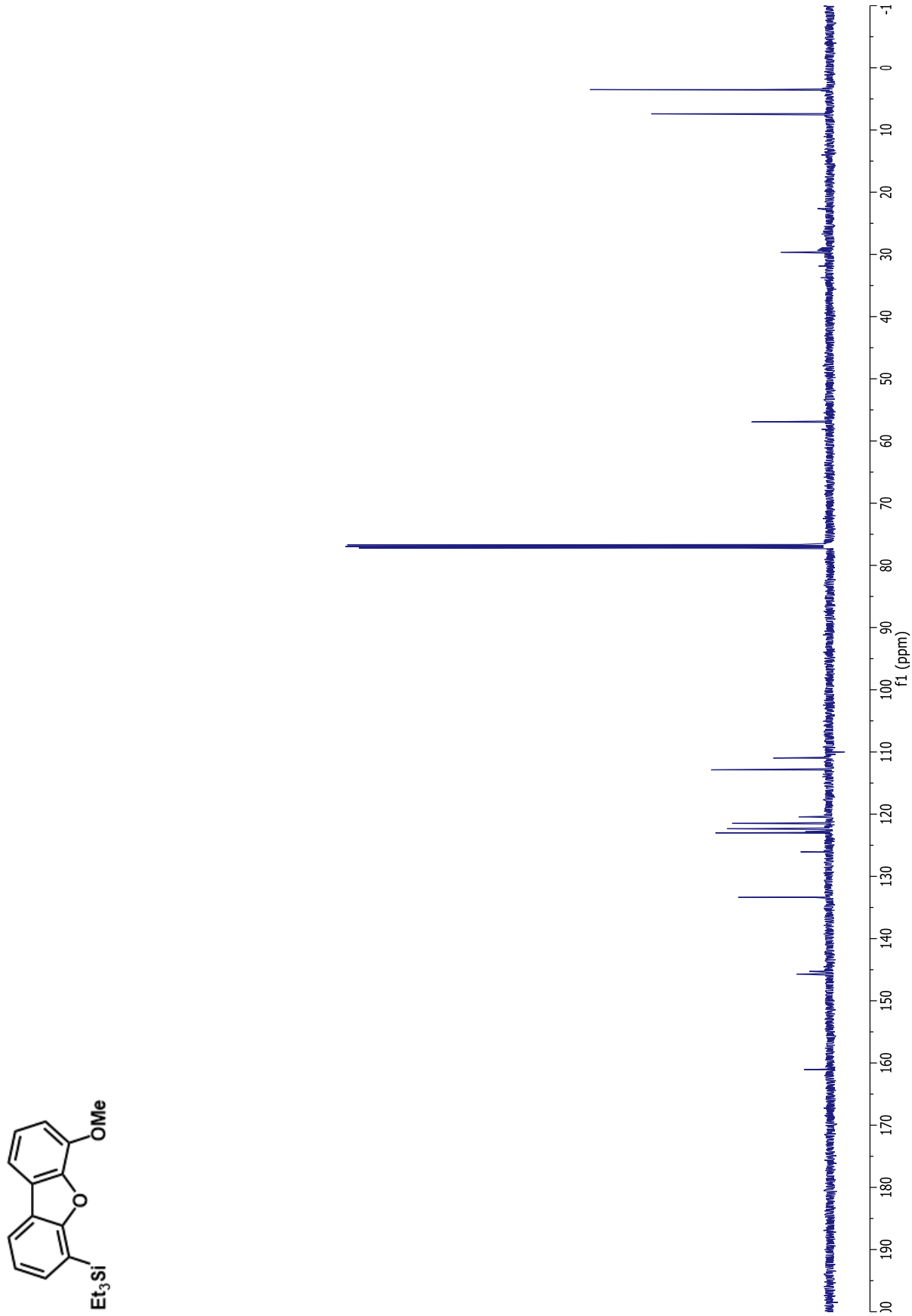
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4u**.



^{13}C NMR (125 MHz, $CDCl_3$) of compound **4u**.

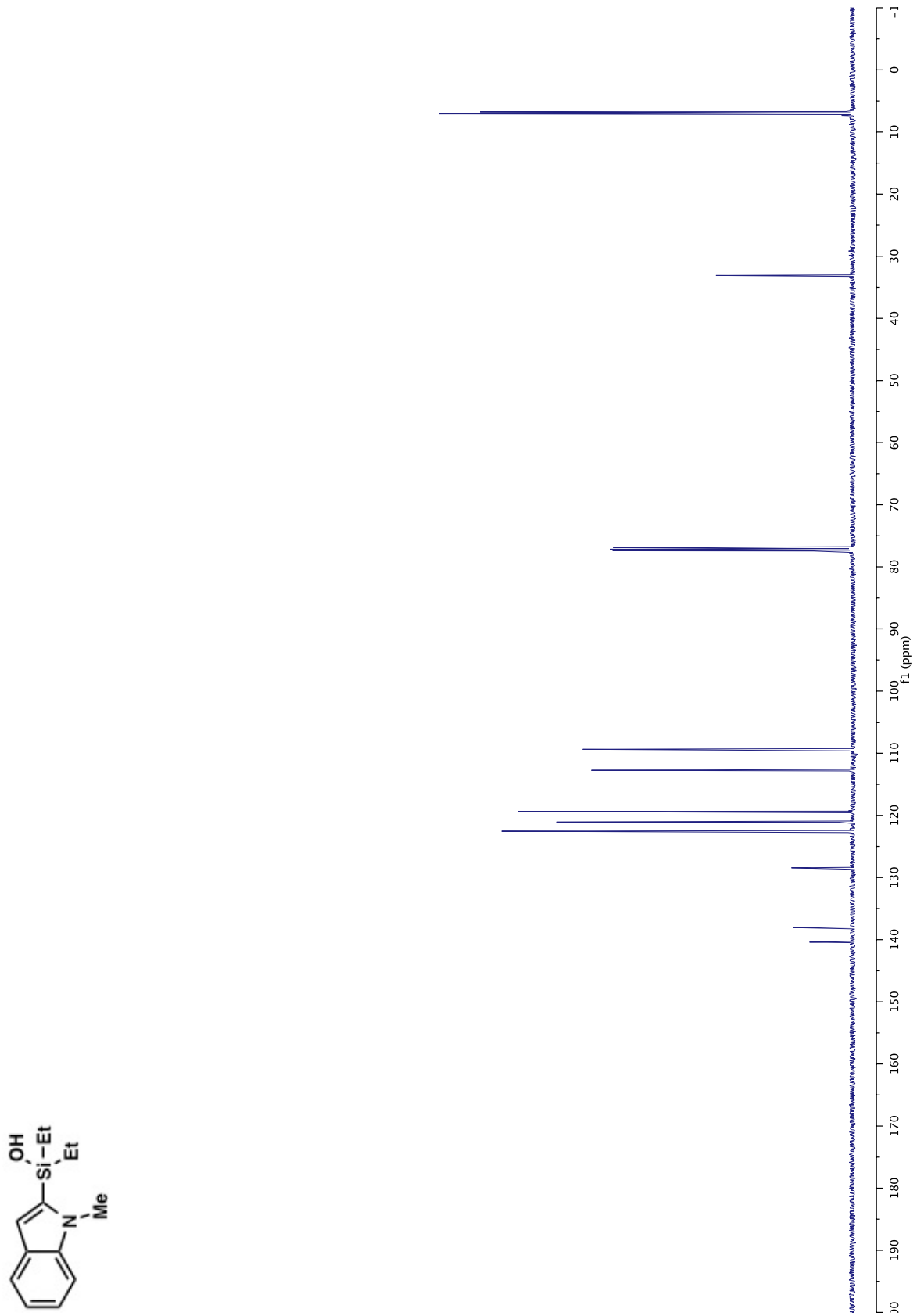


^{1}H NMR (500 MHz, $CDCl_3$) of compound **4w**.



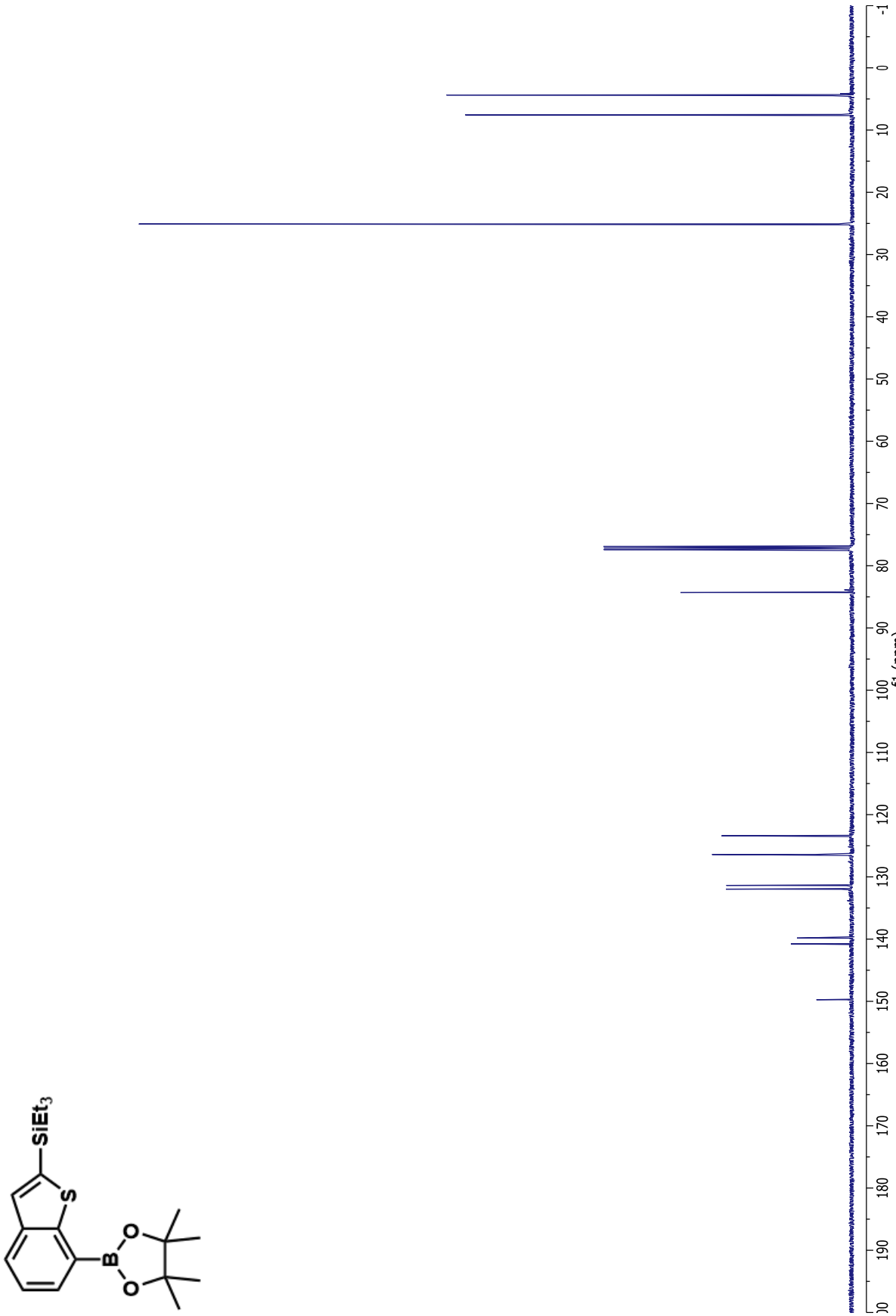
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4w**.

^{1}H NMR (500 MHz, $CDCl_3$) of compound **6**.



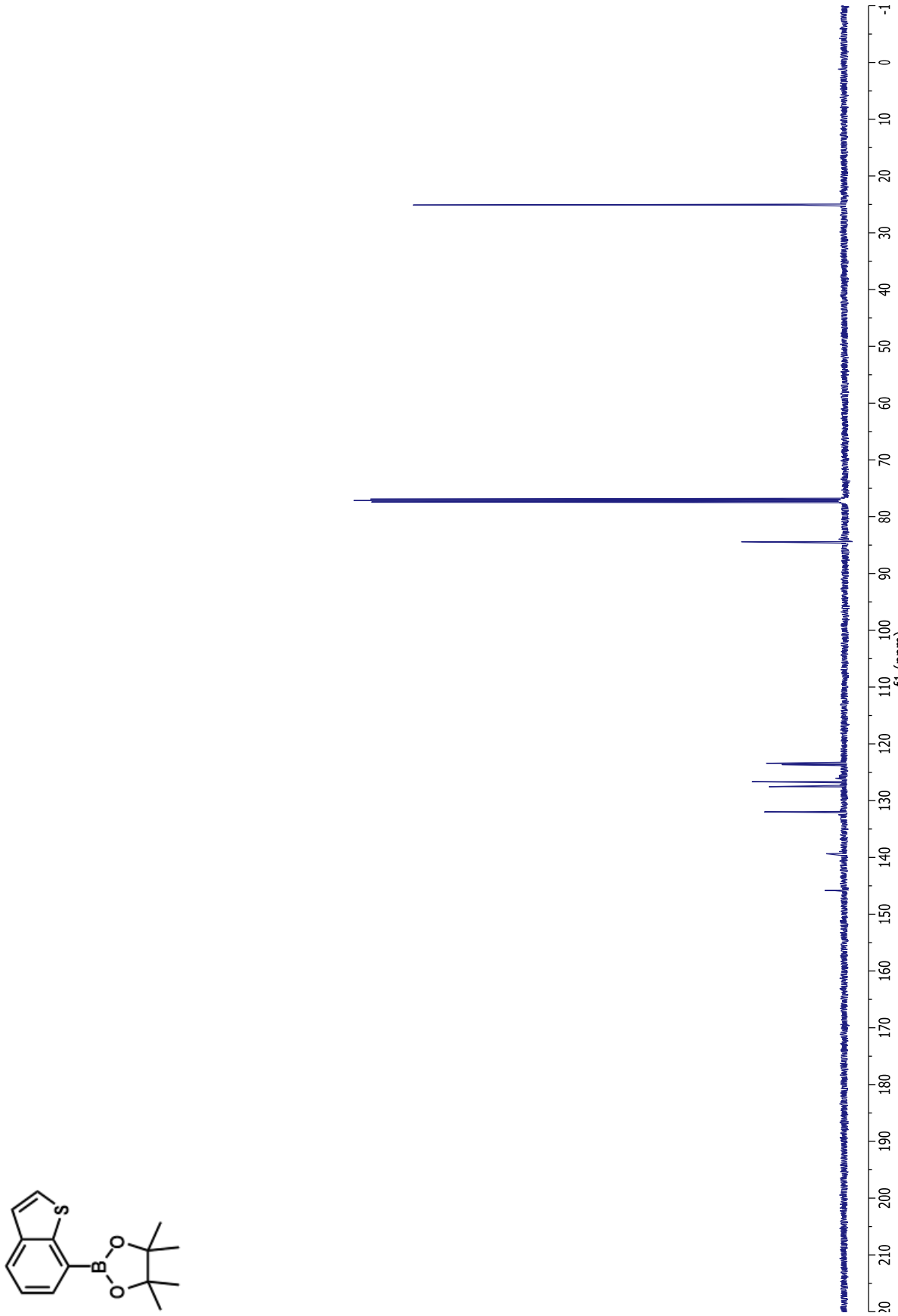
^{13}C NMR (125 MHz, $CDCl_3$) of compound **6**.

^{1}H NMR (500 MHz, $CDCl_3$) of compound **7**.

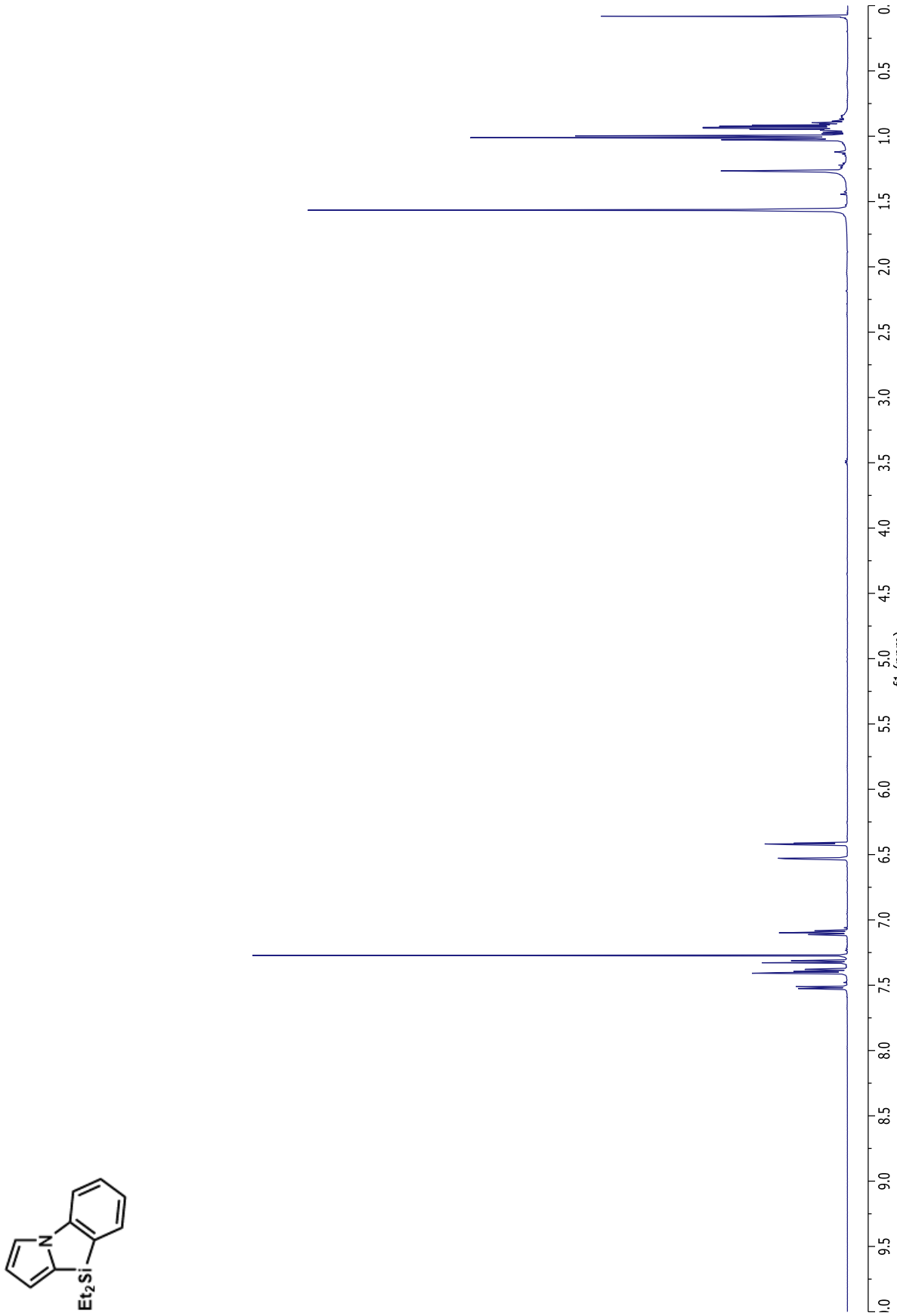


^{13}C NMR (125 MHz, $CDCl_3$) of compound **7**.

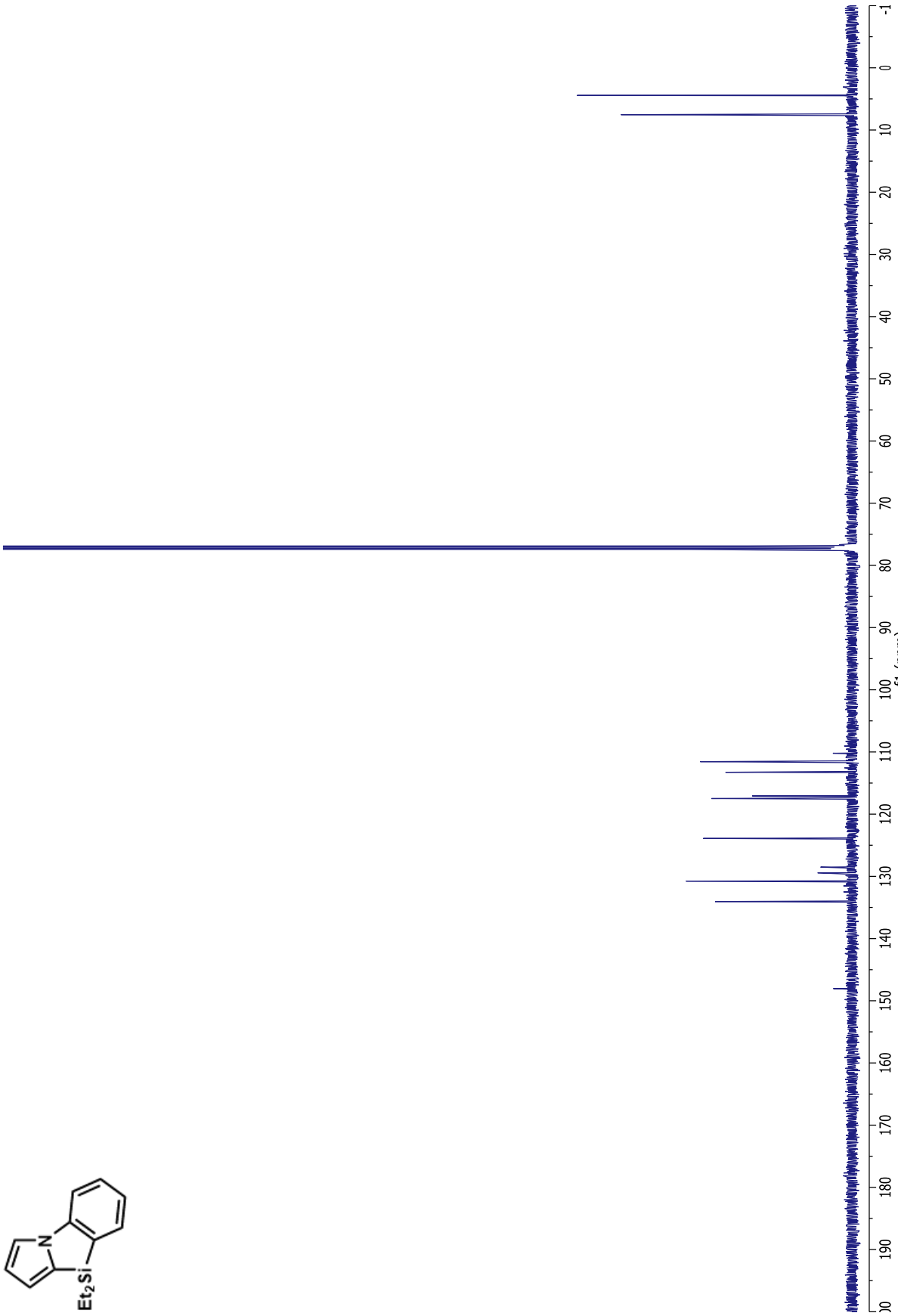
^{1}H NMR (500 MHz, $CDCl_3$) of compound **8**.



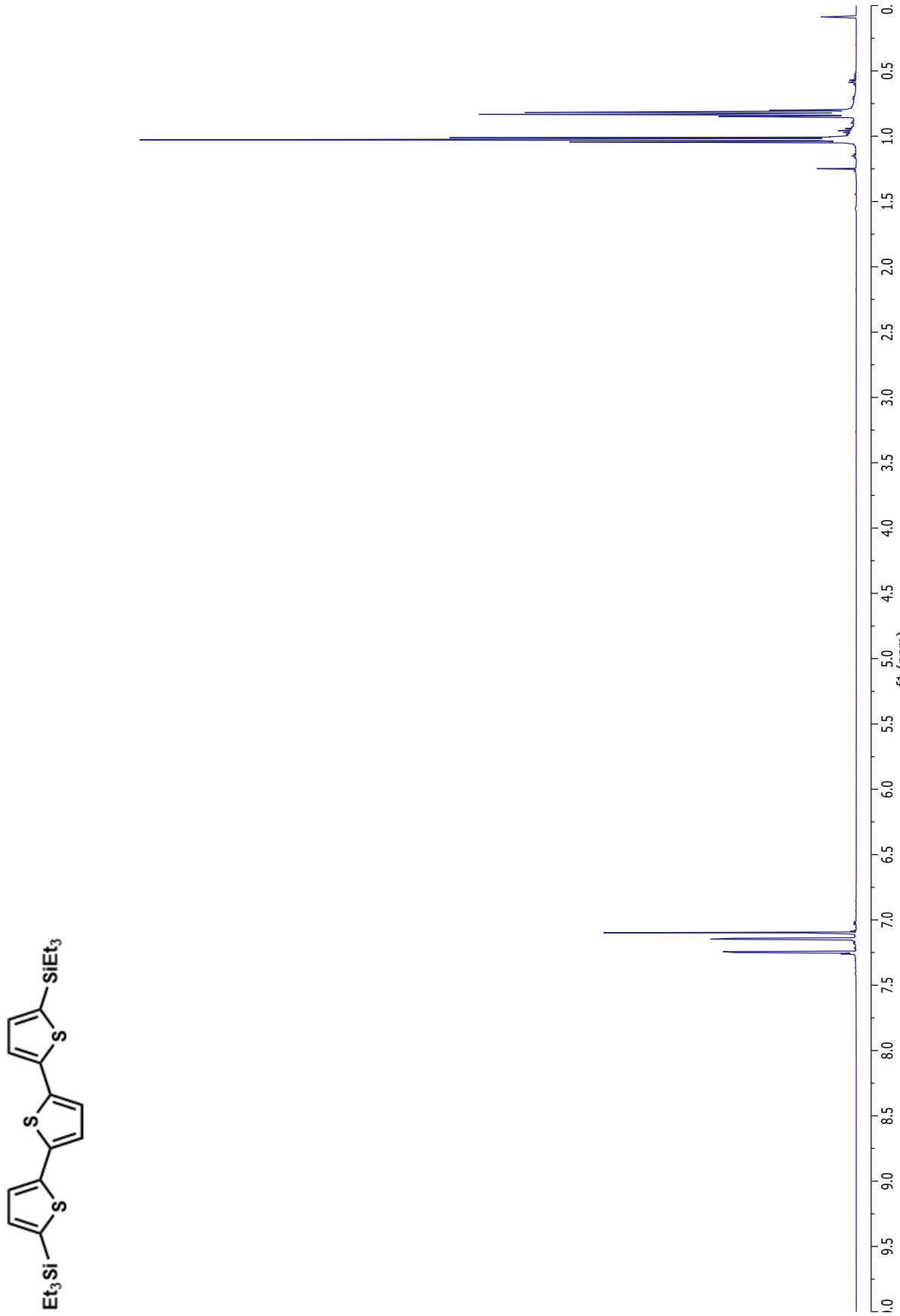
^{13}C NMR (125 MHz, $CDCl_3$) of compound **8**.



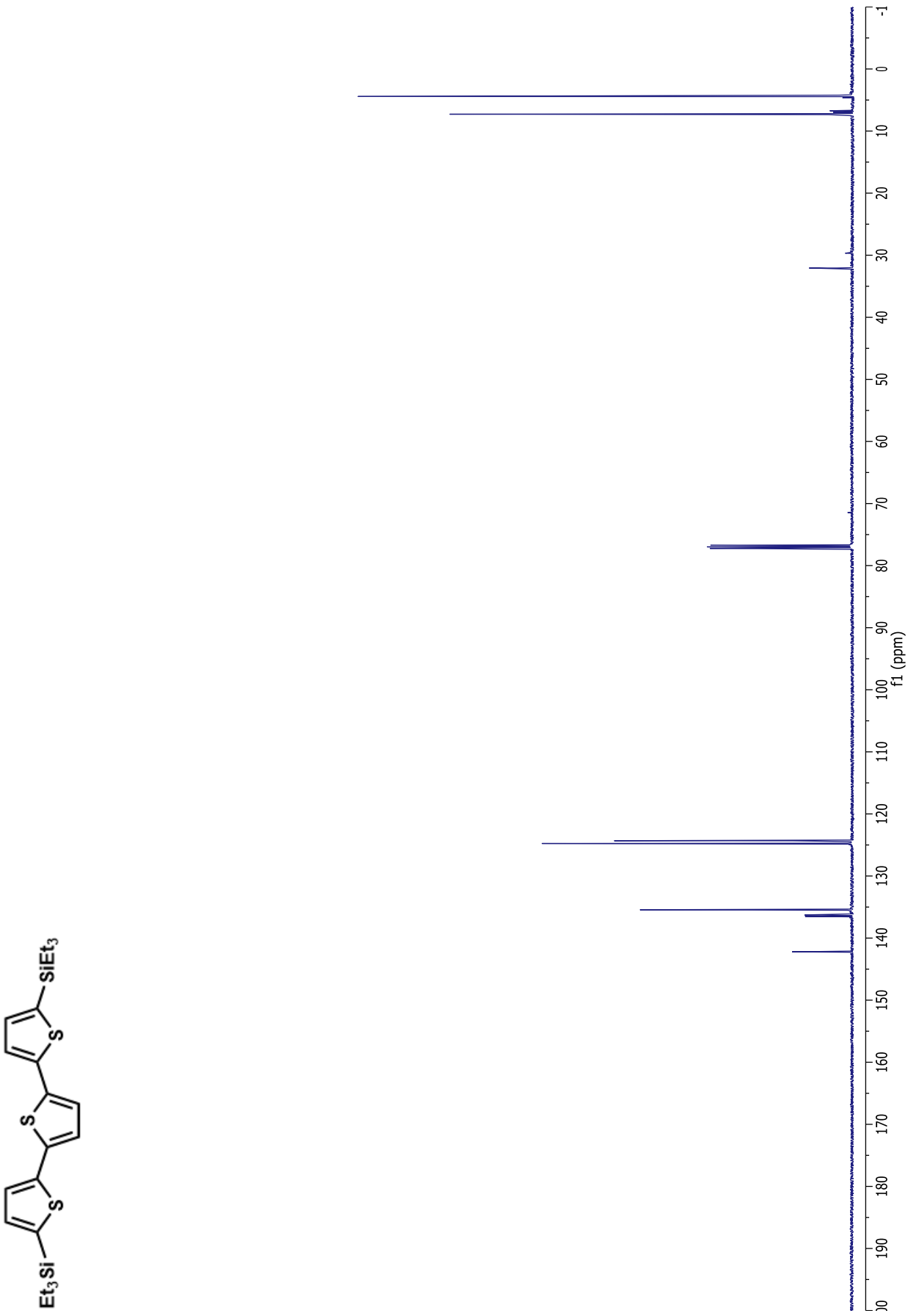
^{1}H NMR (500 MHz, $CDCl_3$) of compound **9**.



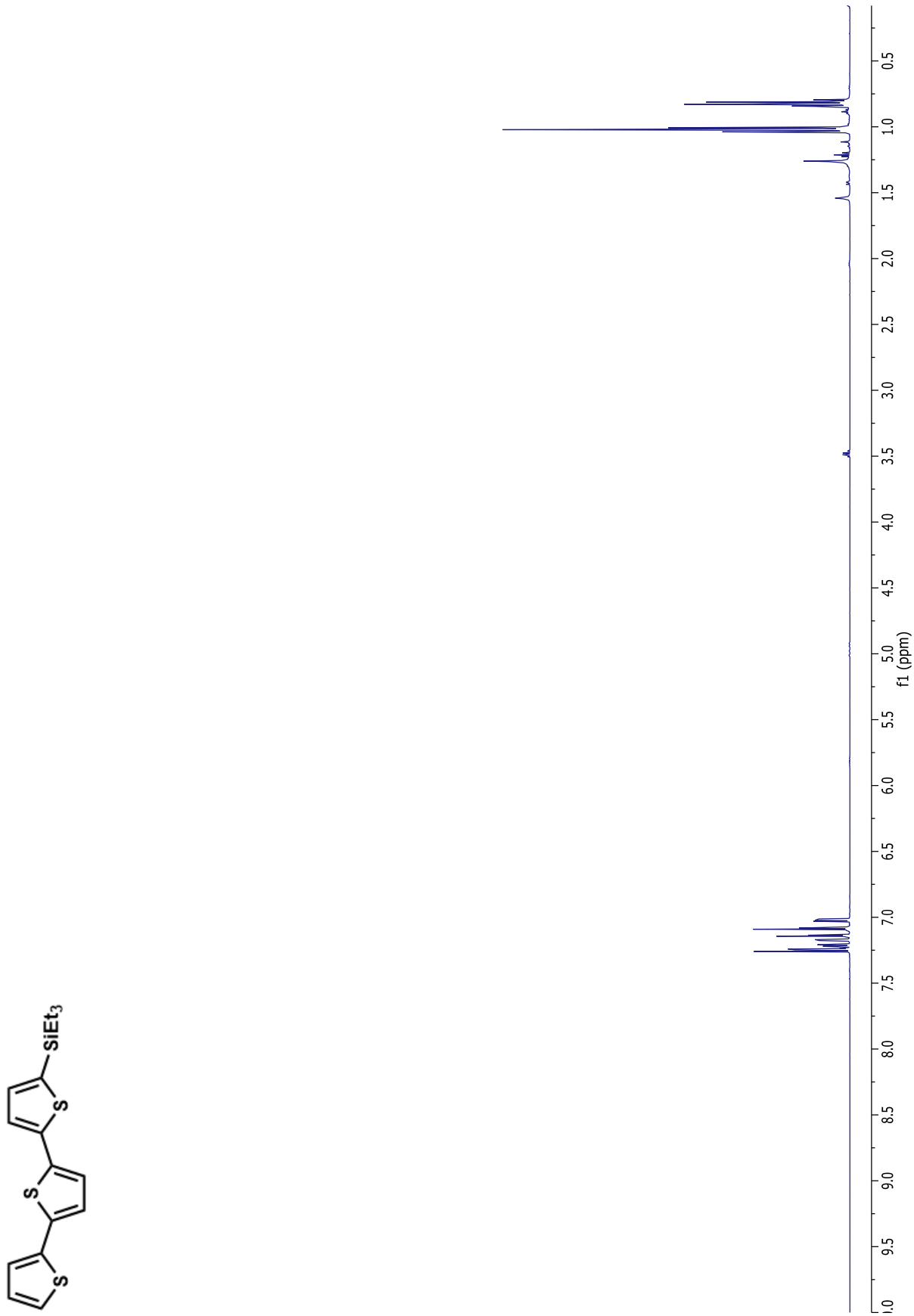
^{13}C NMR (125 MHz, $CDCl_3$) of compound **9**.



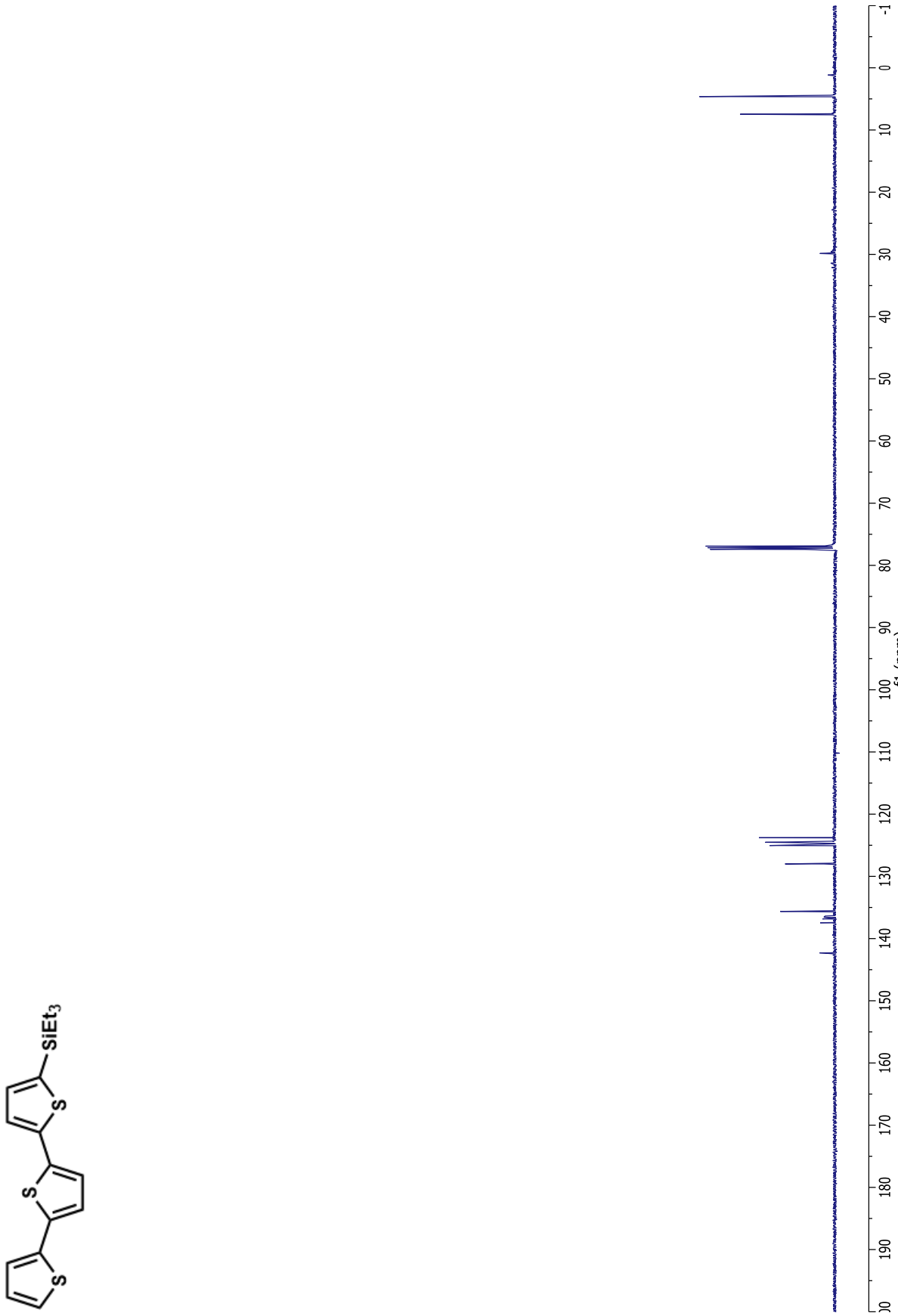
^{1}H NMR (500 MHz, $CDCl_3$) of compound **10**.



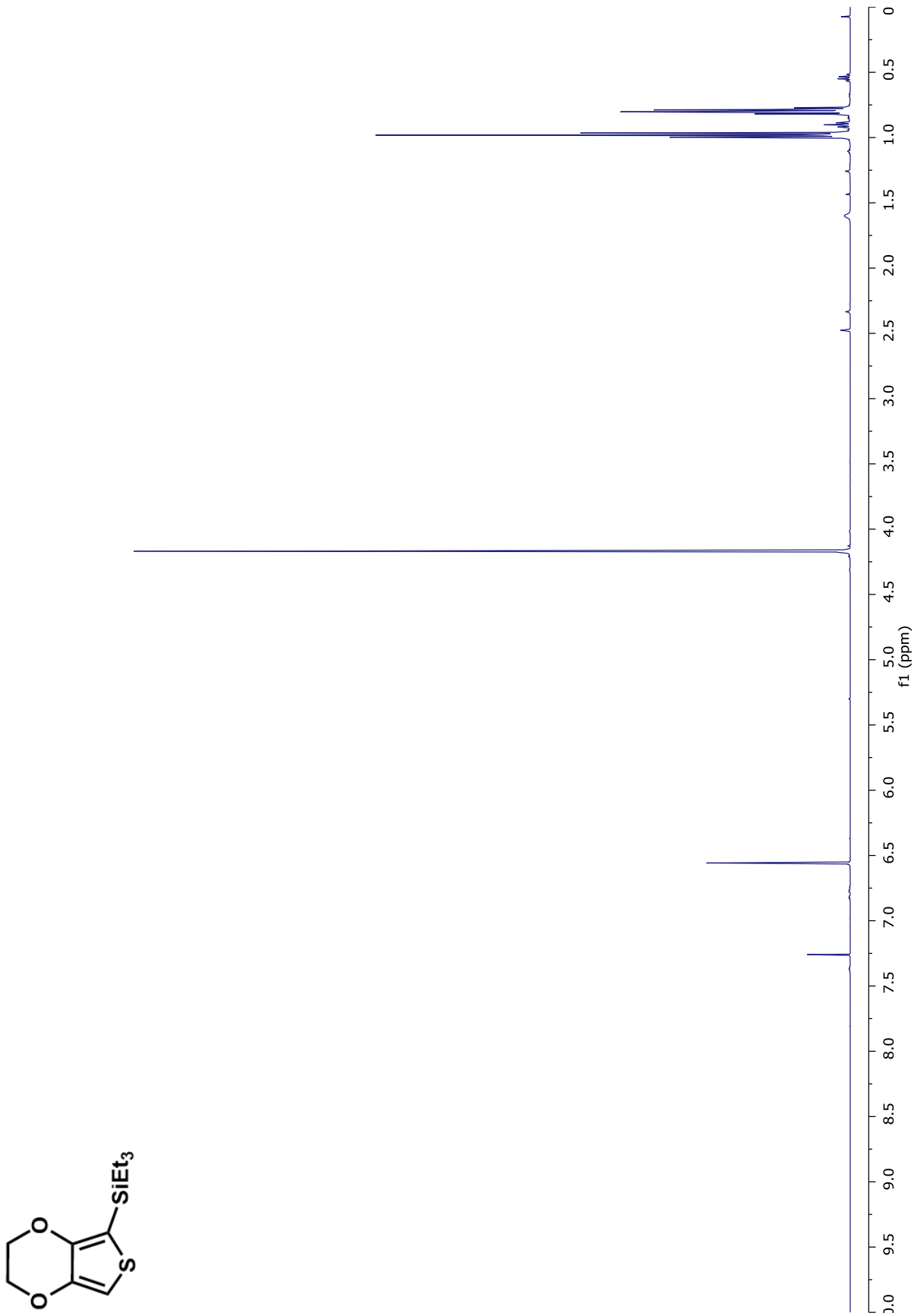
^{13}C NMR (125 MHz, $CDCl_3$) of compound **10**.



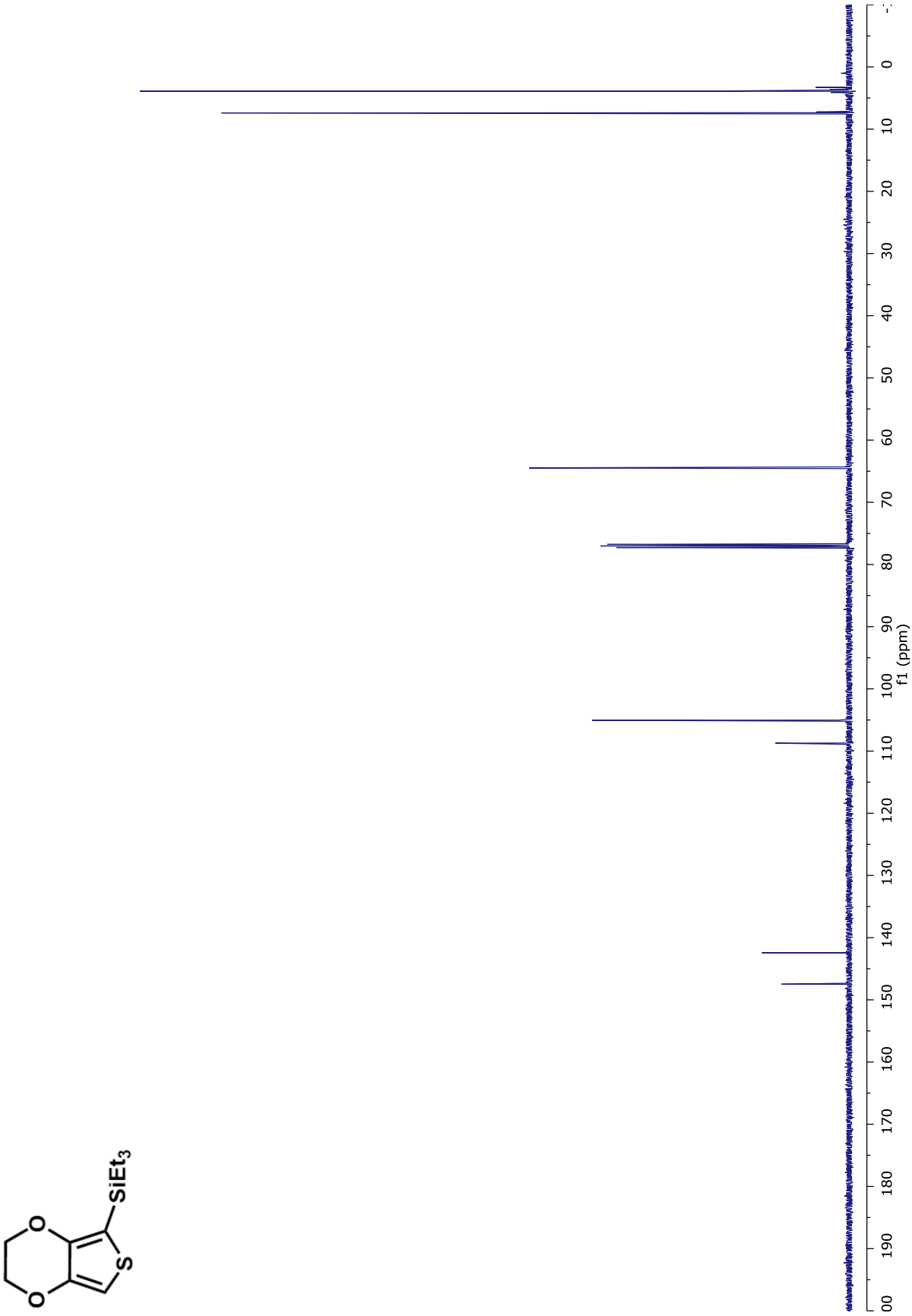
^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-10**.



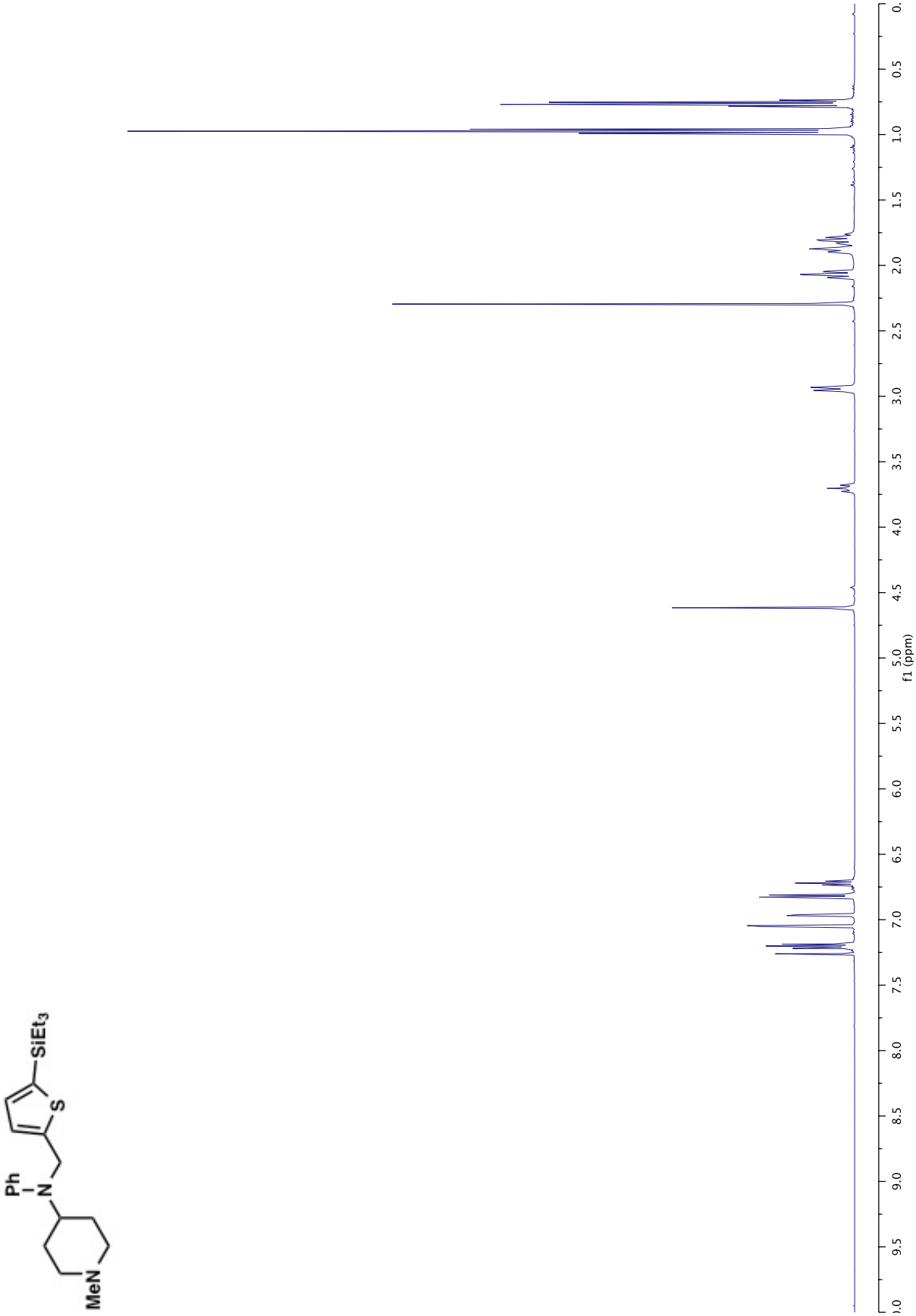
^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-10**.



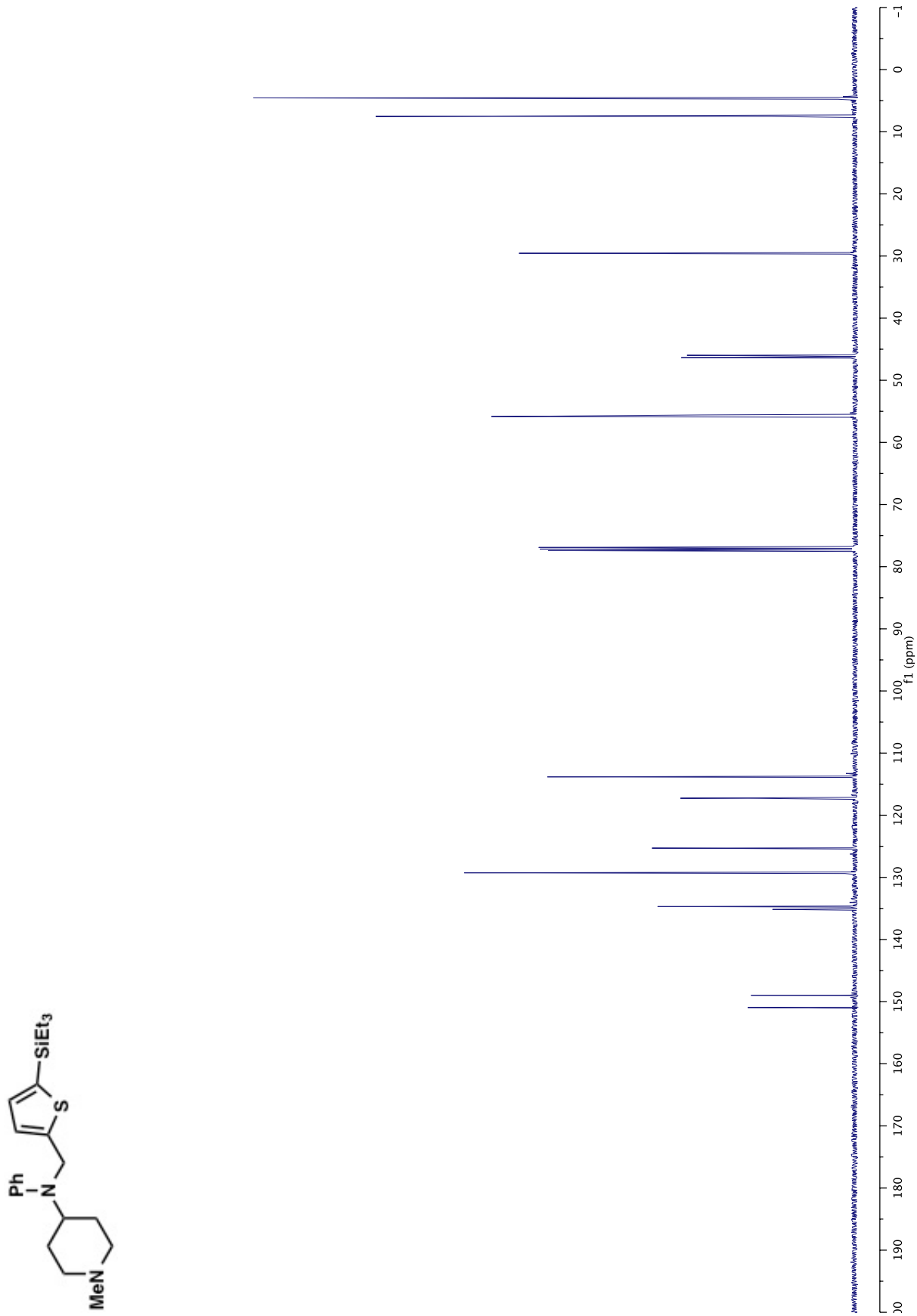
^{1}H NMR (500 MHz, $CDCl_3$) of compound **11**.



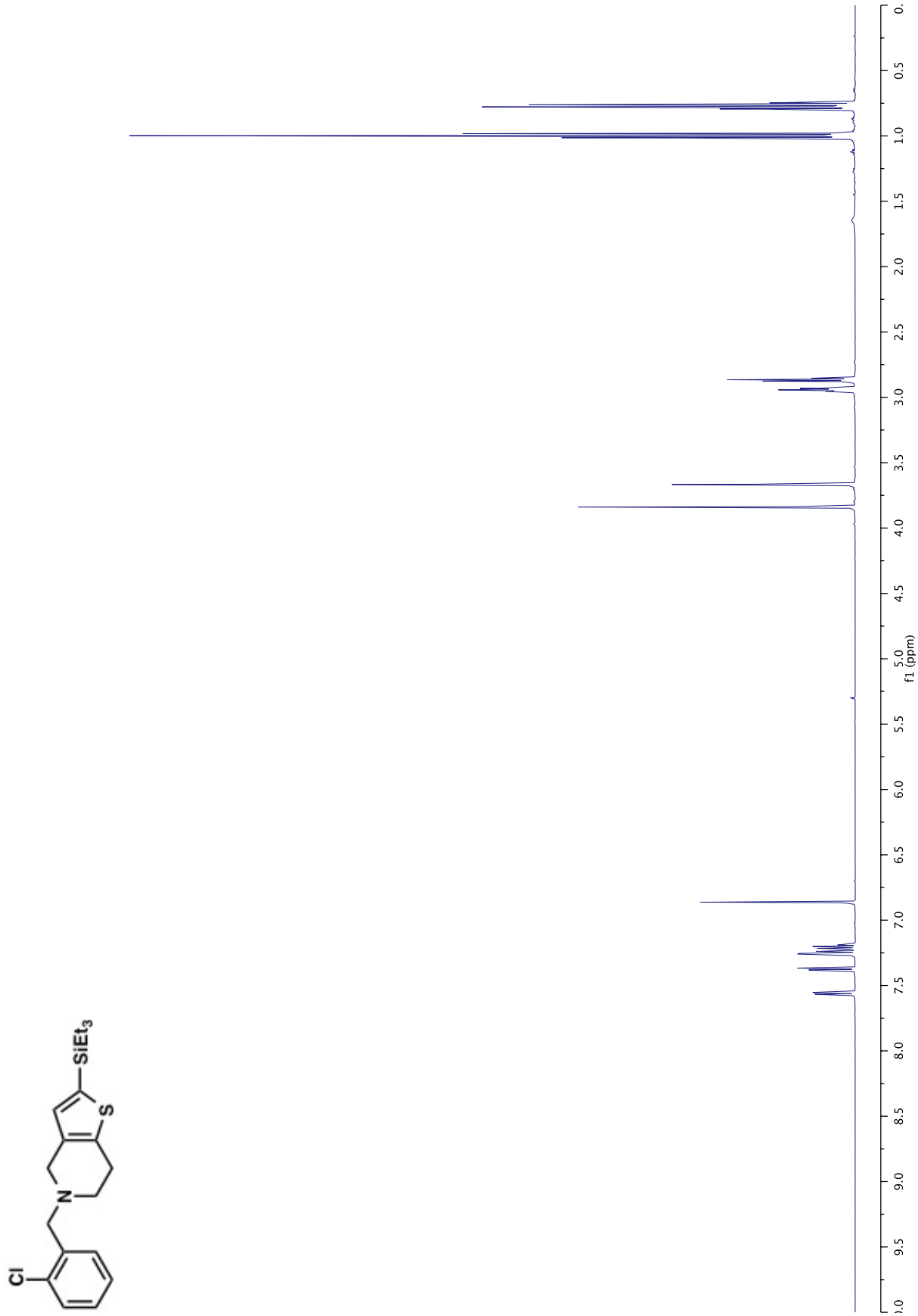
^{13}C NMR (125 MHz, $CDCl_3$) of compound **11**.



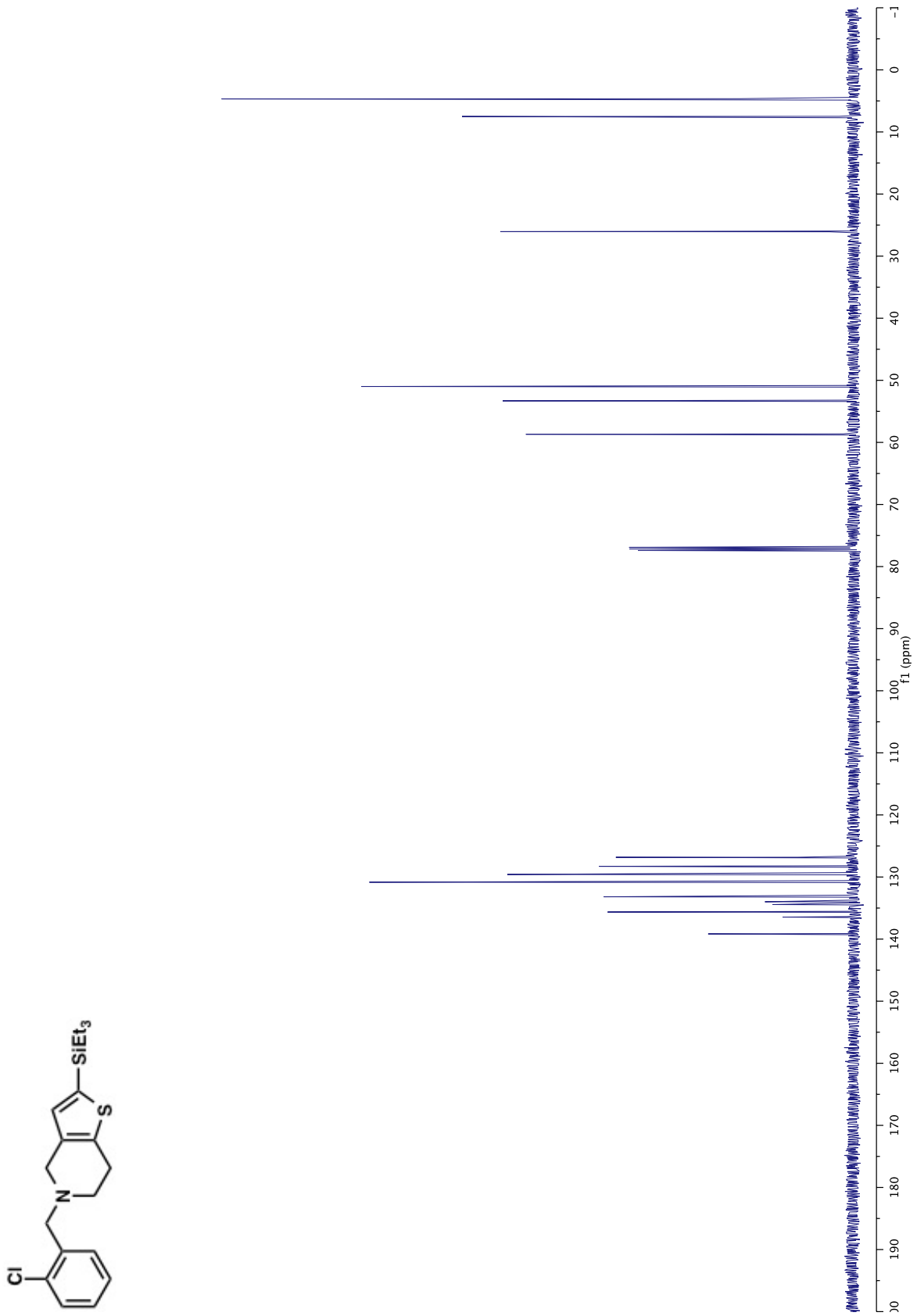
^{1}H NMR (500 MHz, $CDCl_3$) of compound **12**.



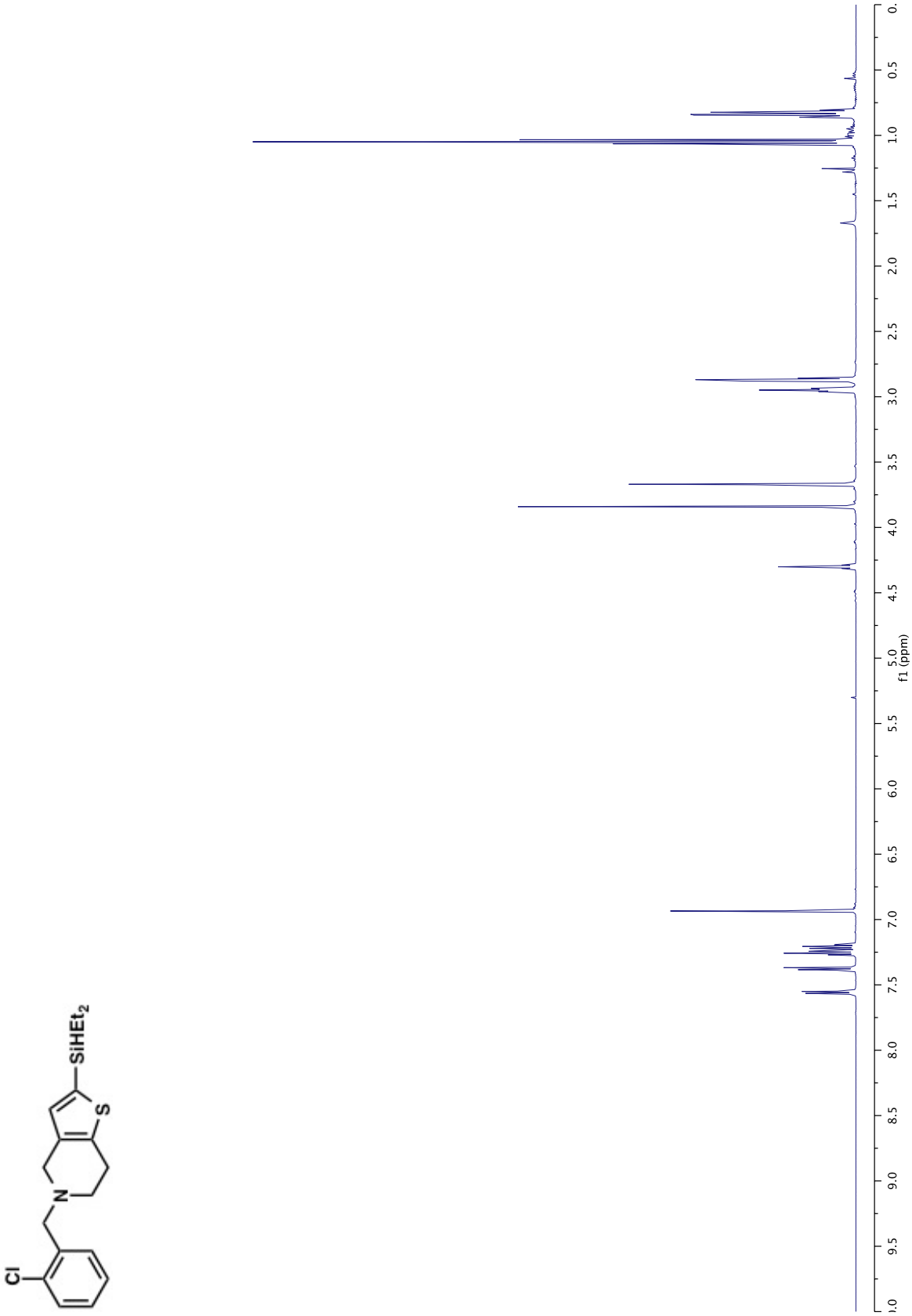
^{13}C NMR (125 MHz, $CDCl_3$) of compound **12**.



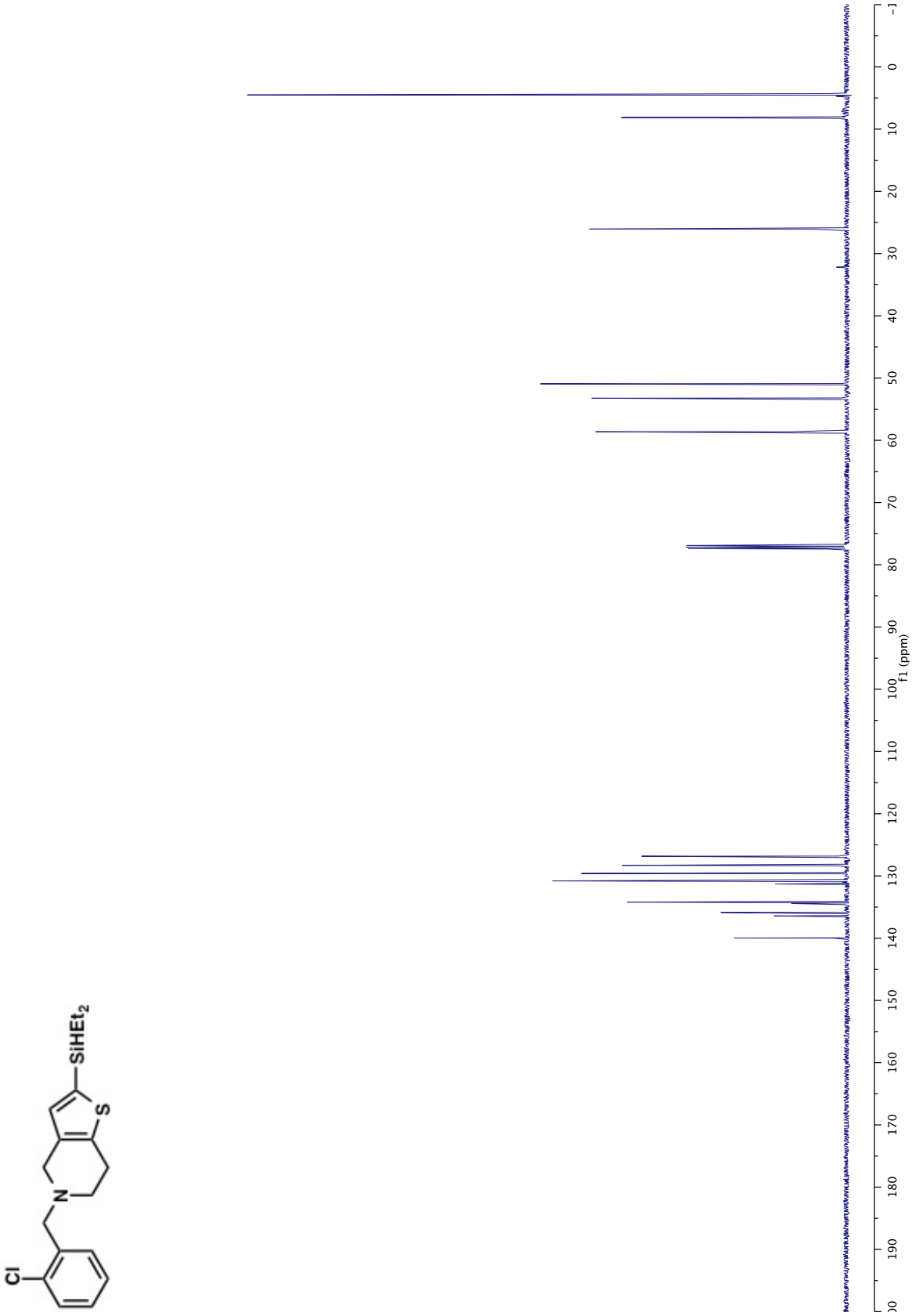
^{1}H NMR (500 MHz, $CDCl_3$) of compound **13a**.



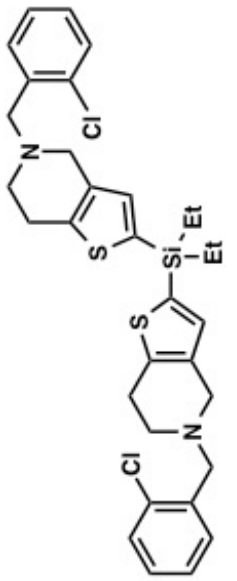
^{13}C NMR (125 MHz, $CDCl_3$) of compound **13a**.

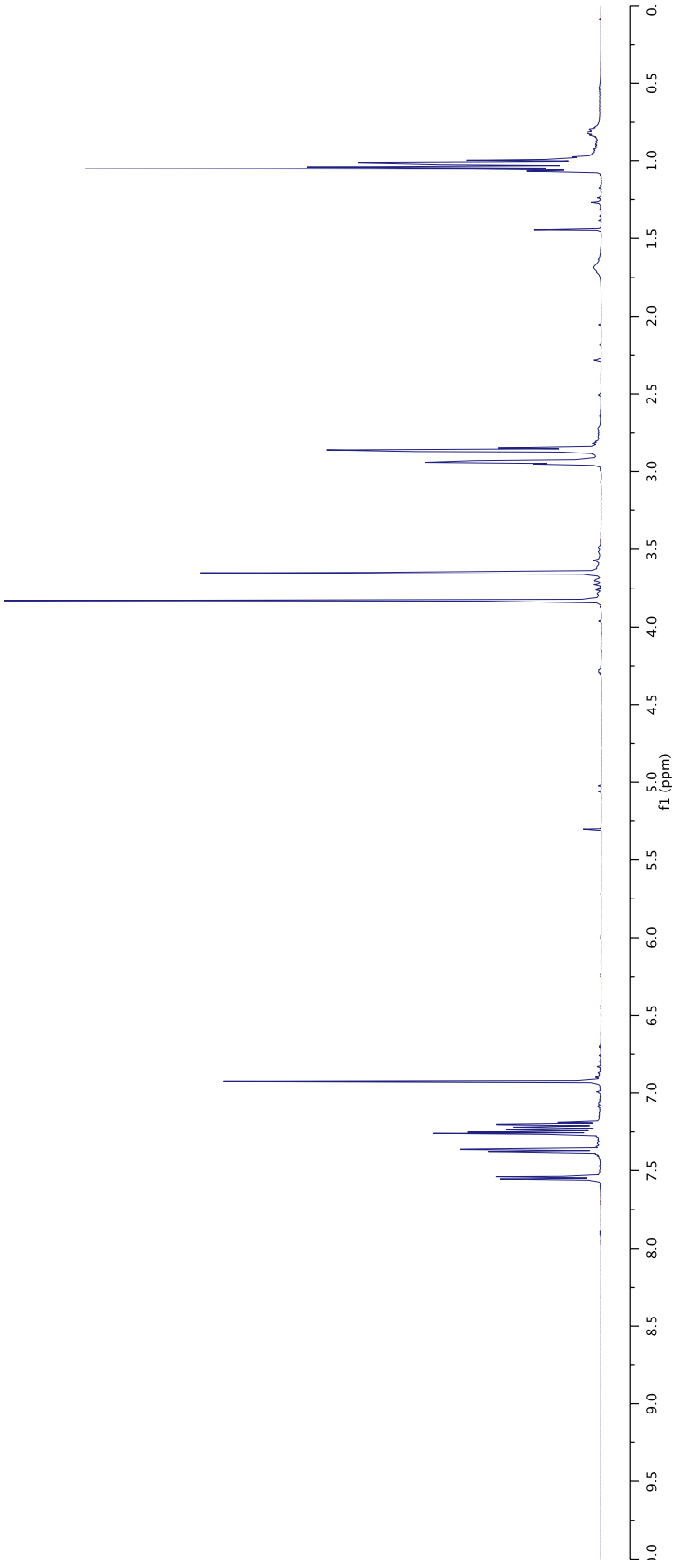


^{1}H NMR (500 MHz, $CDCl_3$) of compound **13b**.

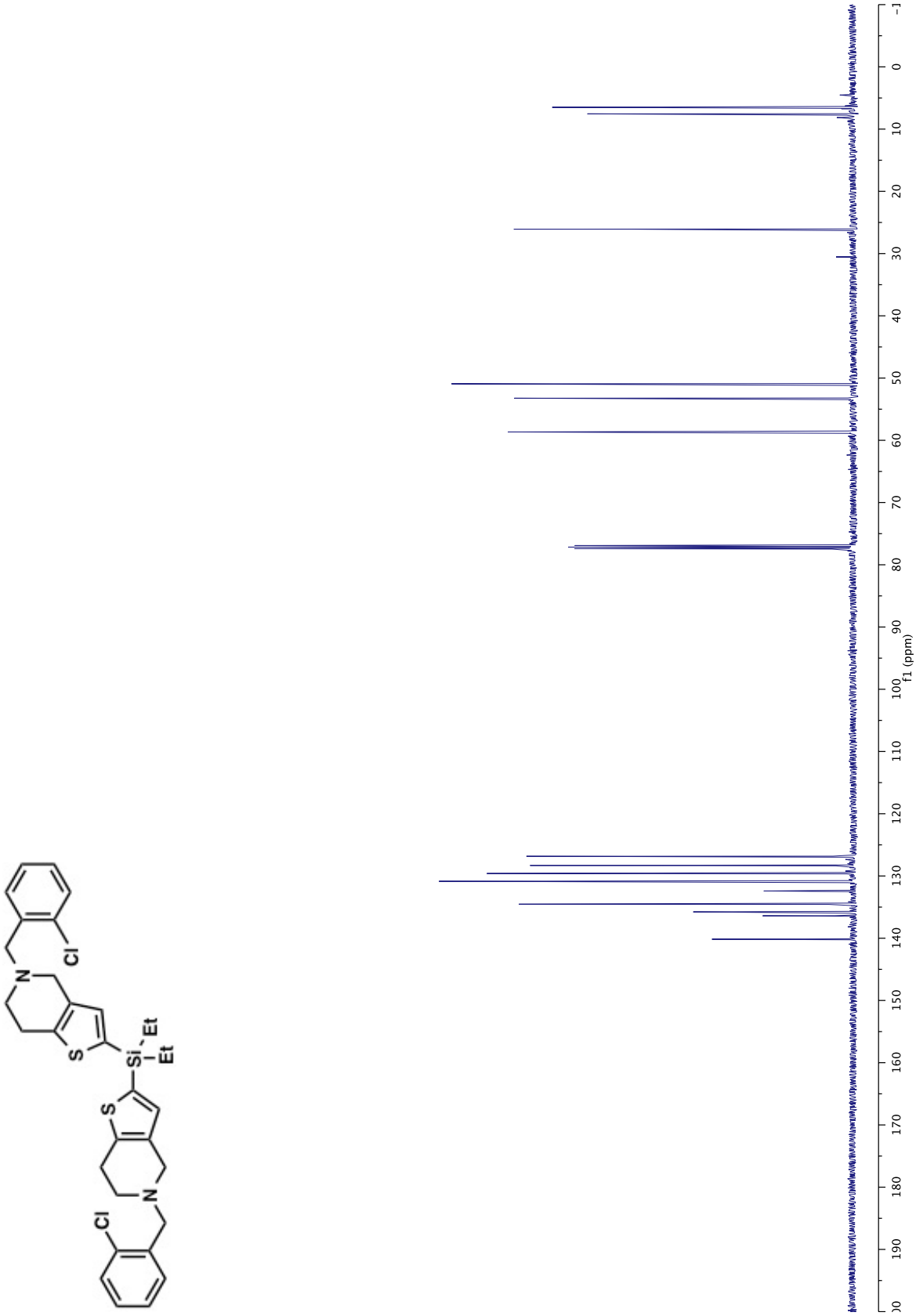


^{13}C NMR (125 MHz, $CDCl_3$) of compound **13b**.

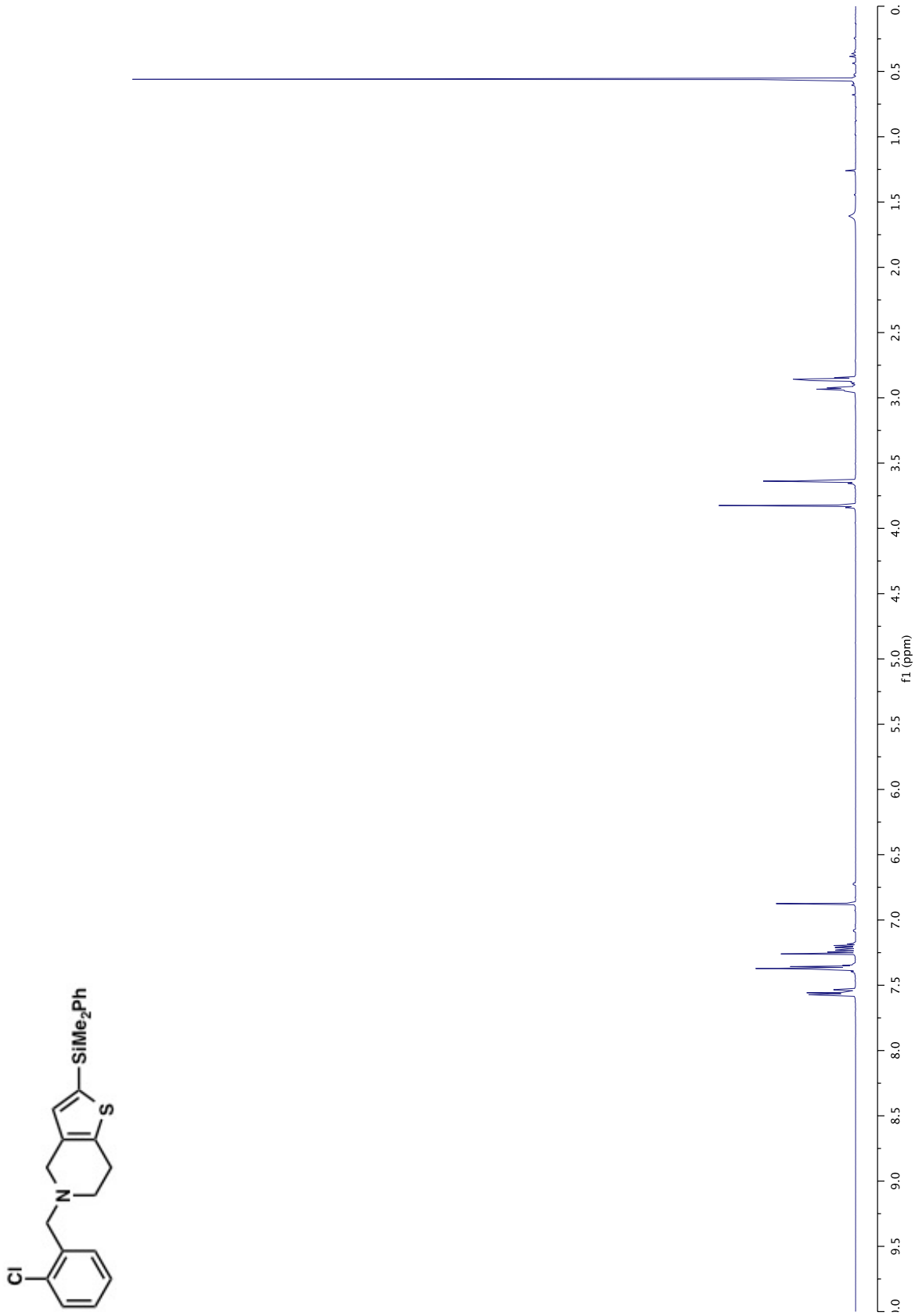




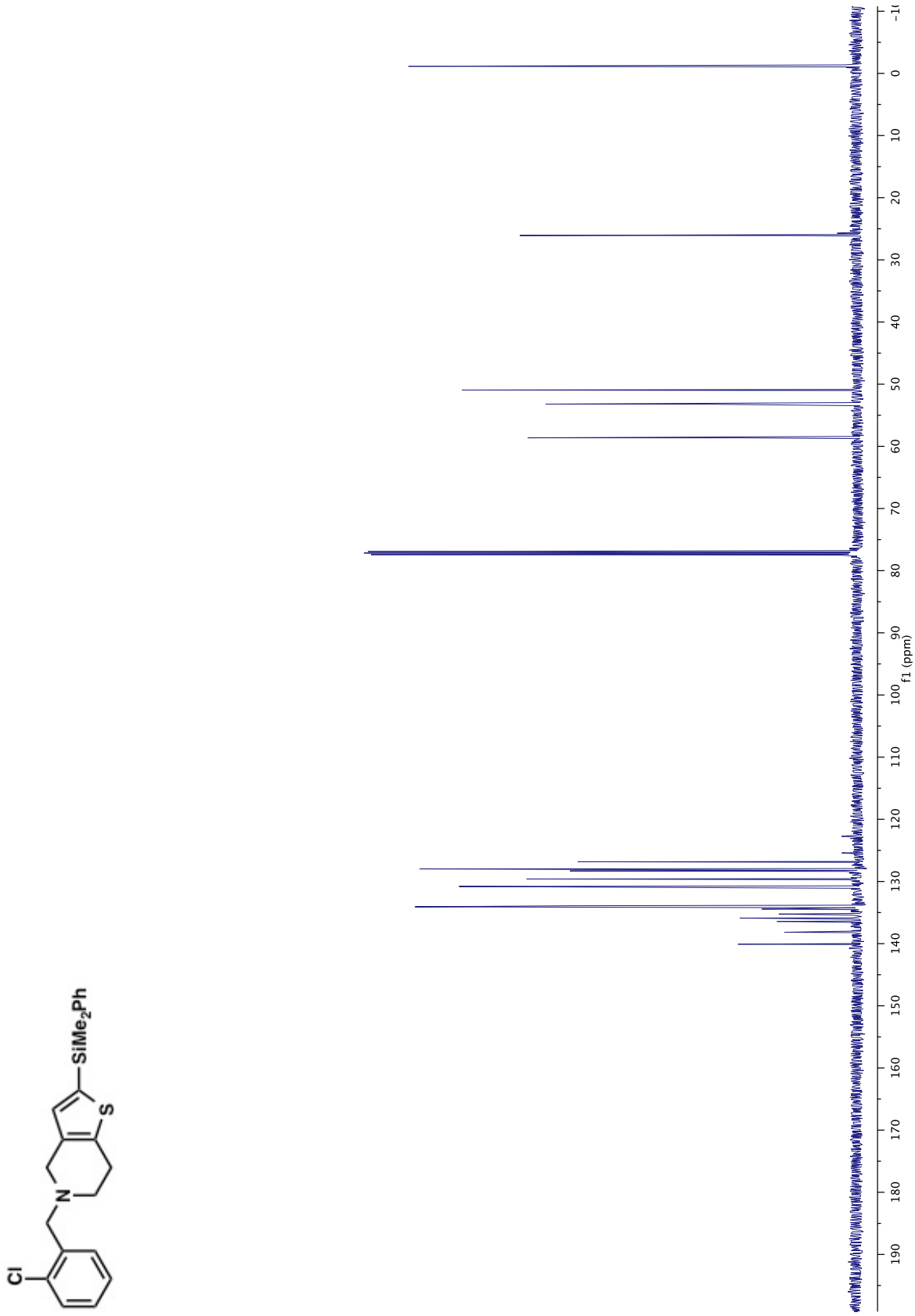
^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-13b**.



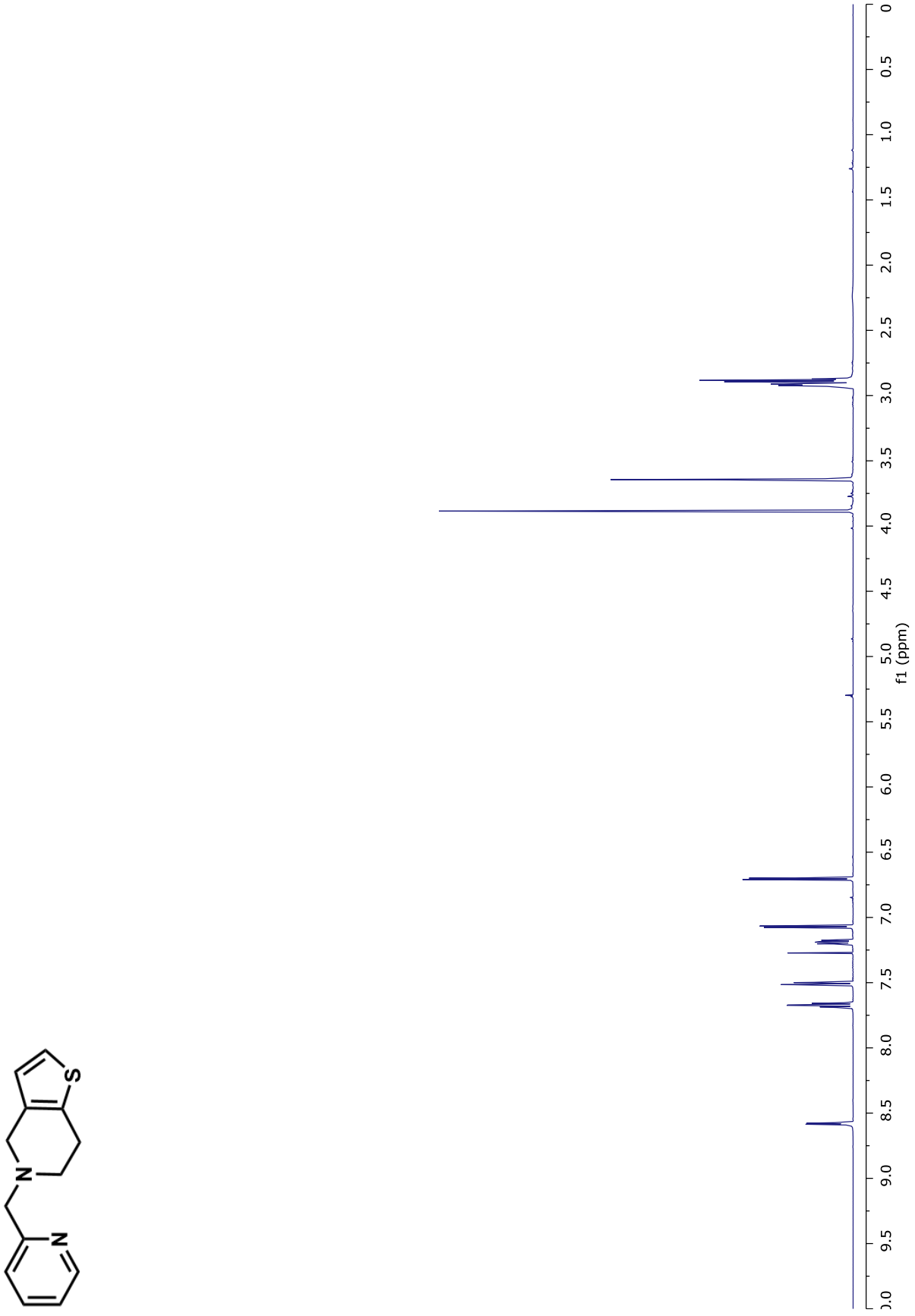
^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-13b**.



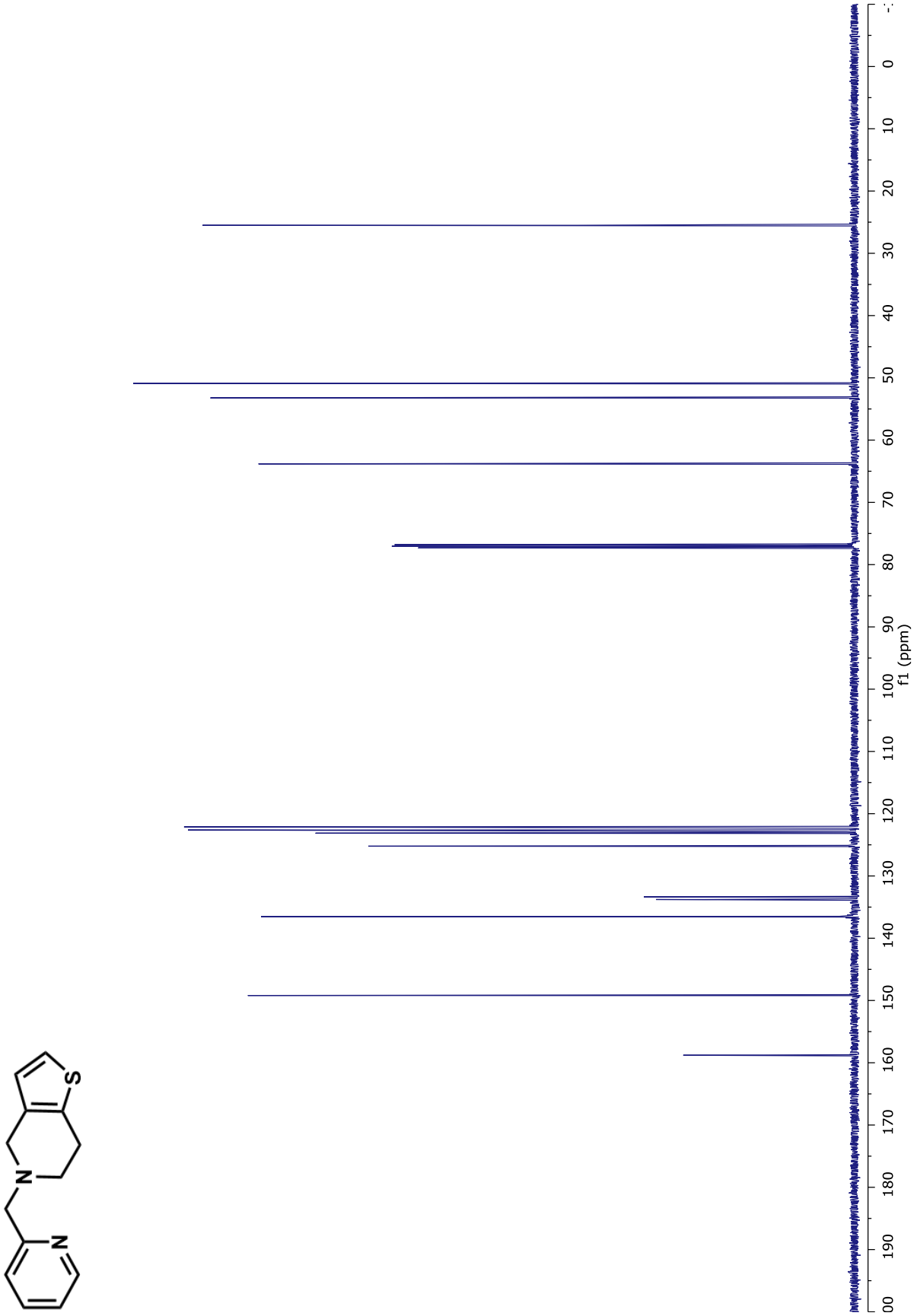
^{1}H NMR (500 MHz, $CDCl_3$) of compound **13c**.



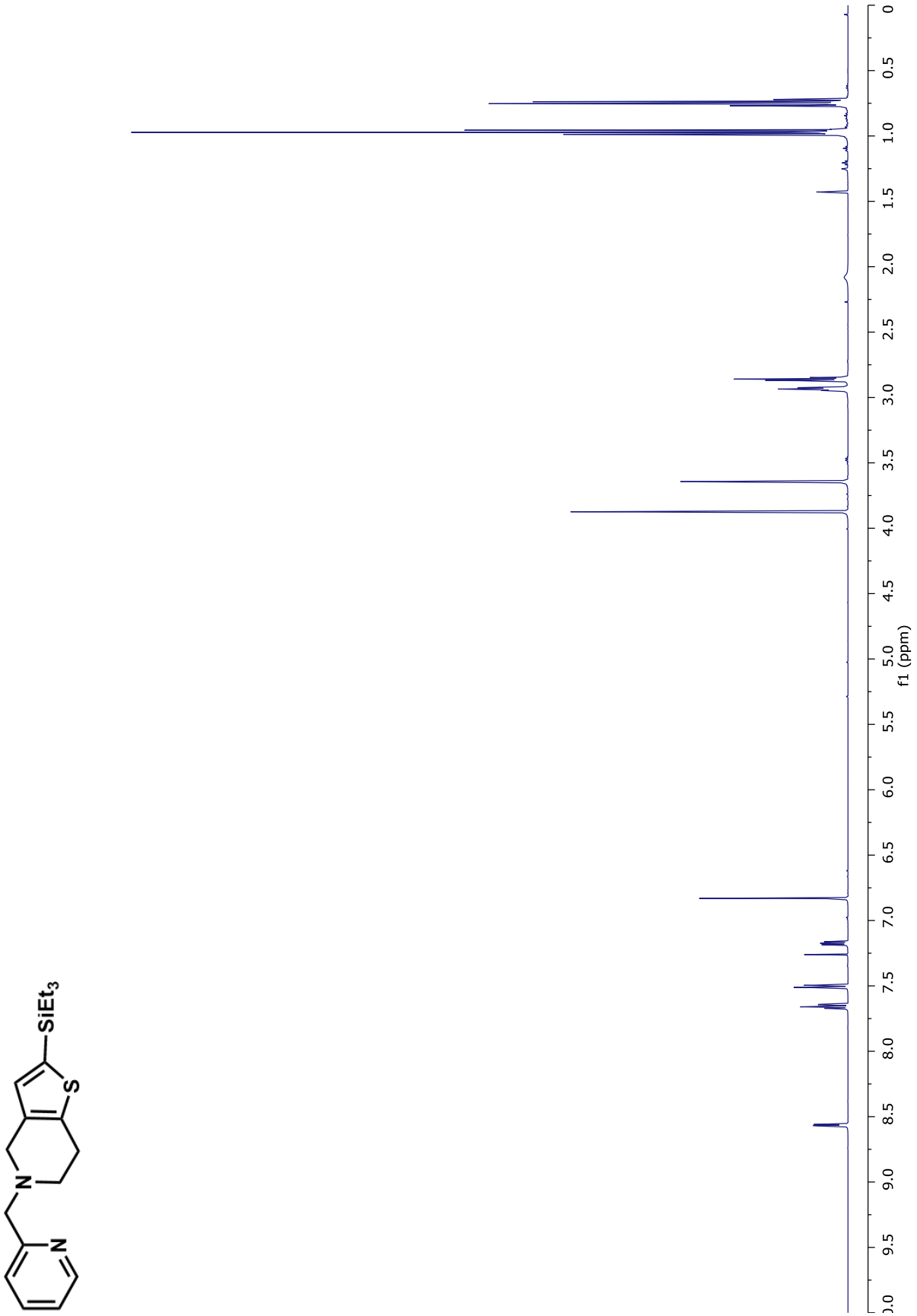
^{13}C NMR (125 MHz, $CDCl_3$) of compound **13c**.



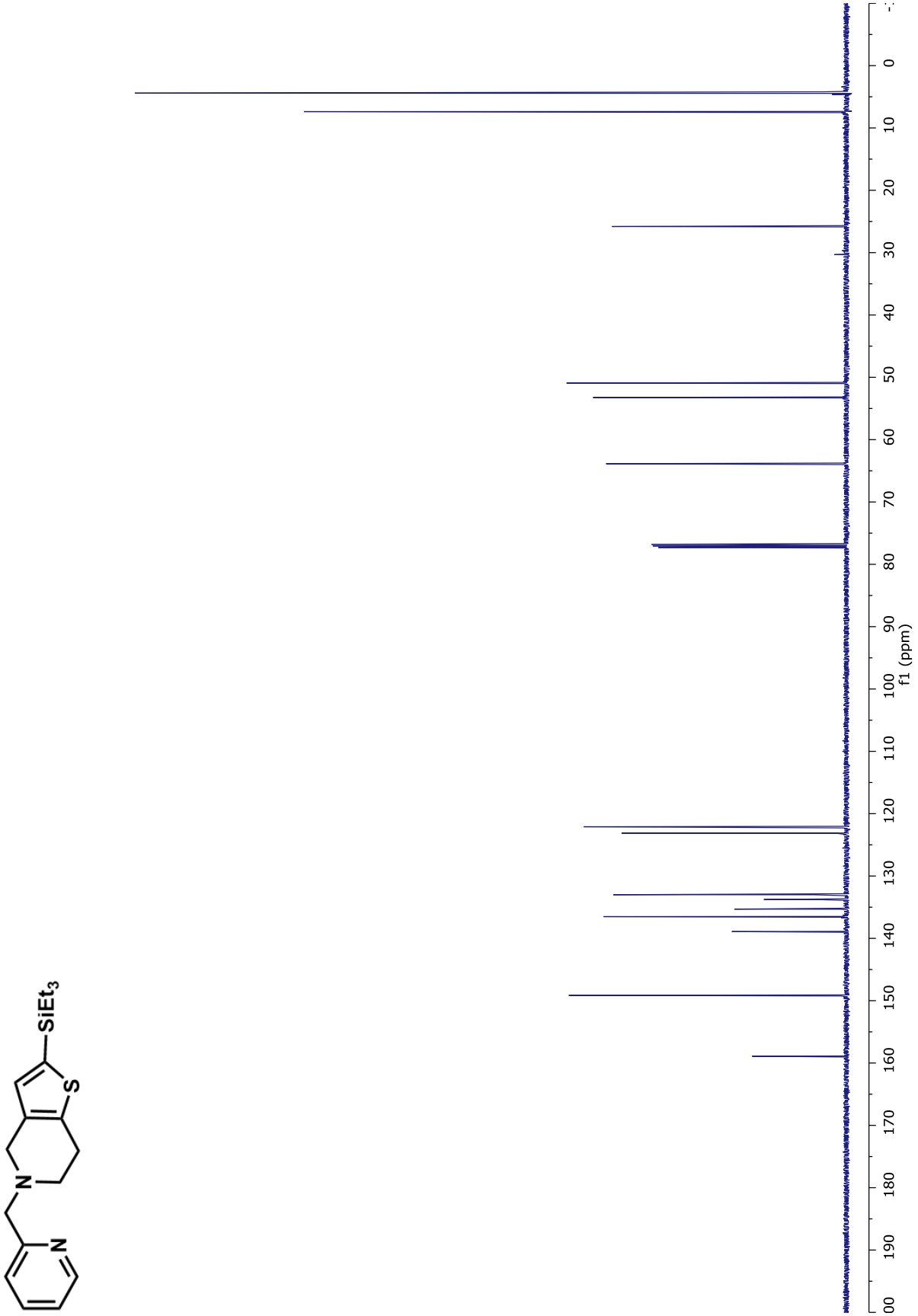
^{1}H NMR (500 MHz, $CDCl_3$) of compound **SM-14**.



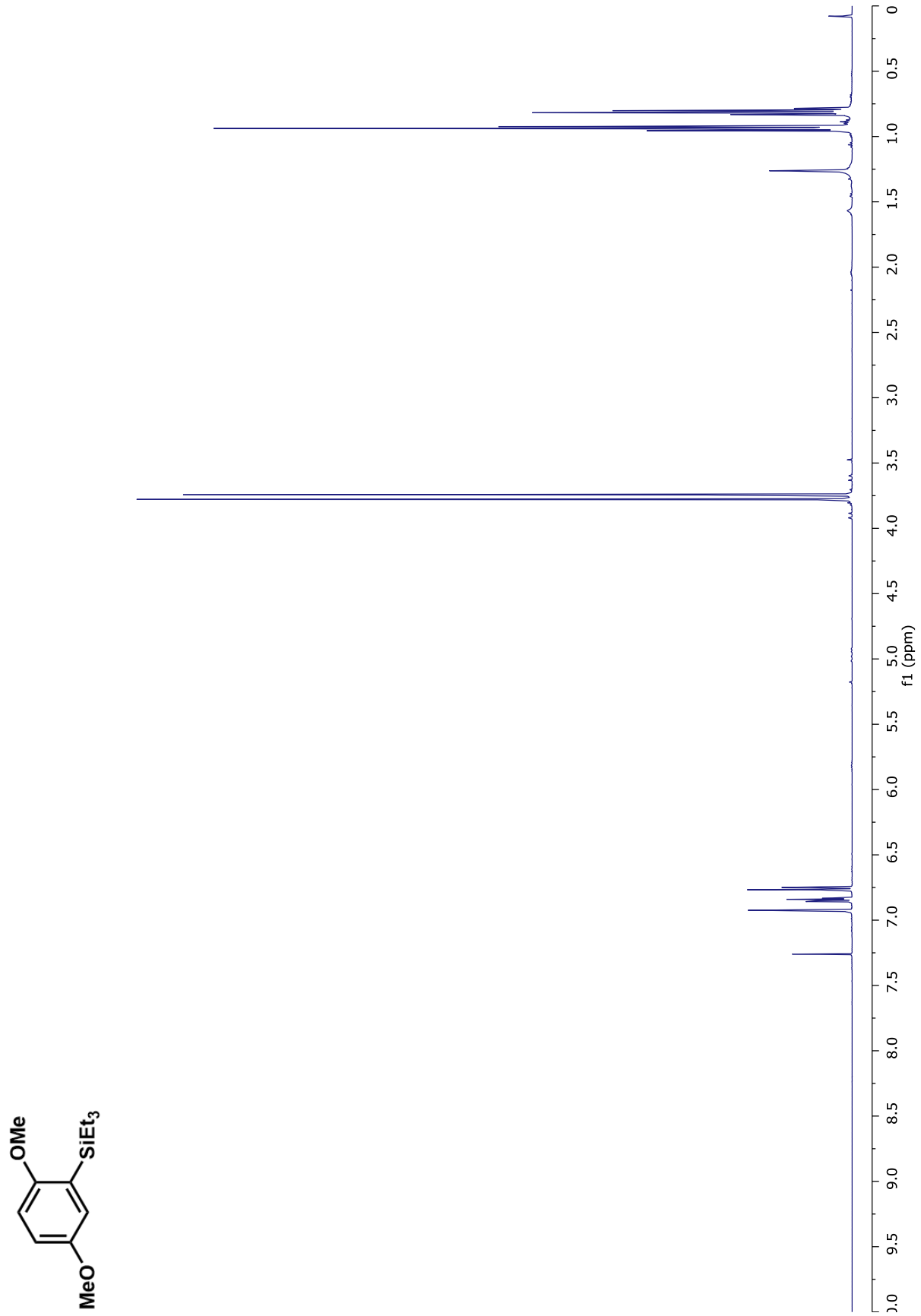
^{13}C NMR (125 MHz, $CDCl_3$) of compound **SM-14.**



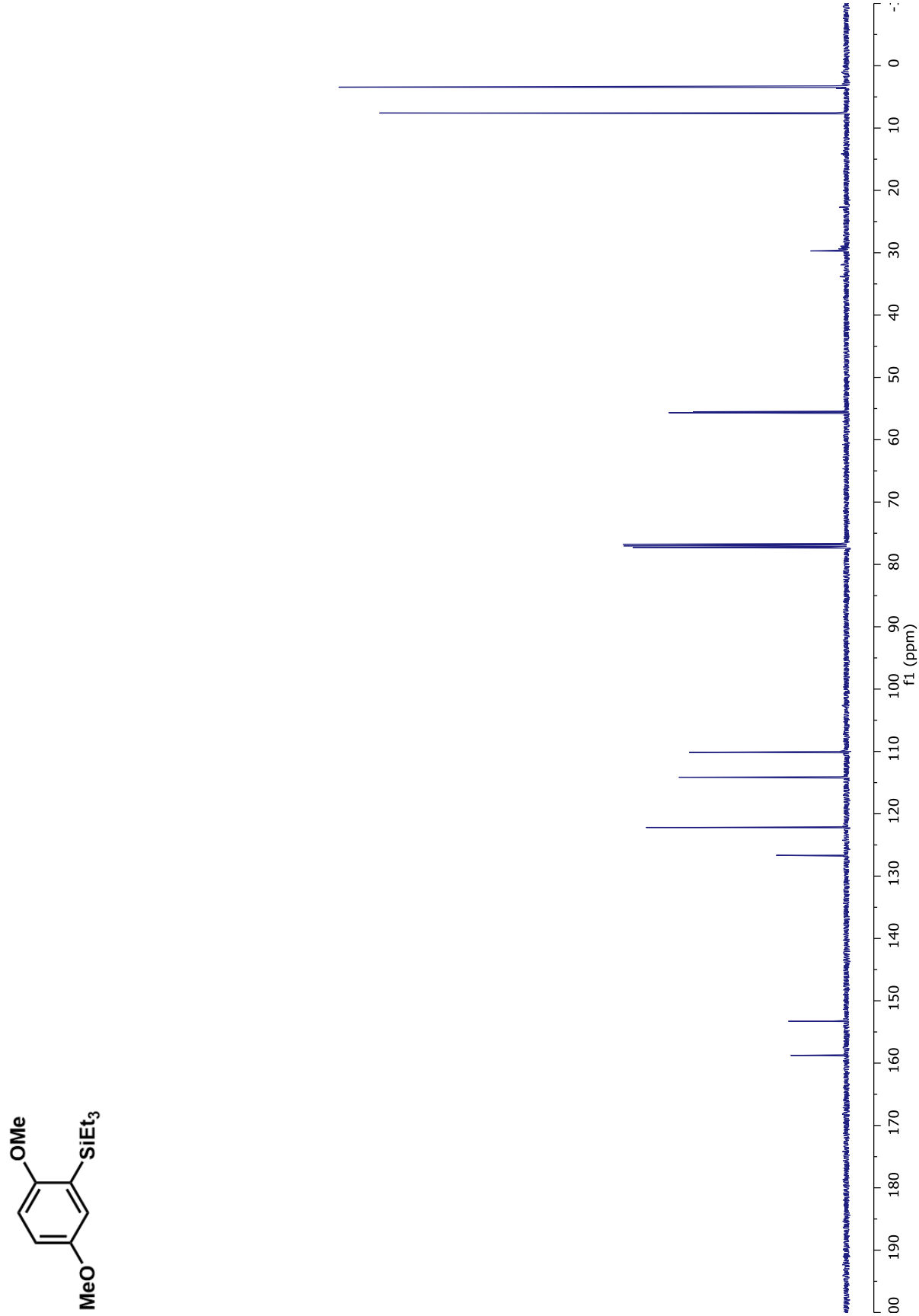
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14**.



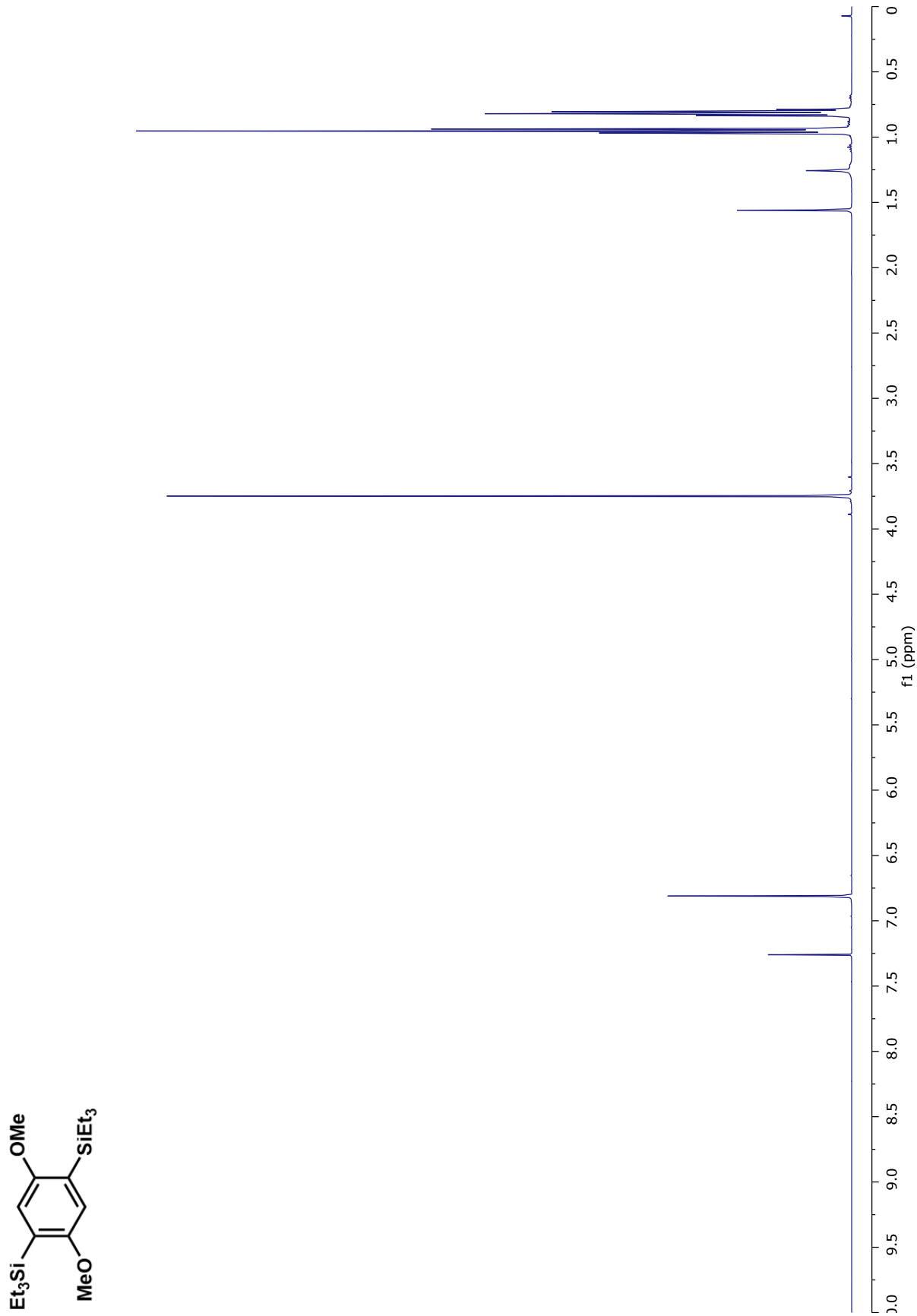
^{13}C NMR (125 MHz, $CDCl_3$) of compound **14**.



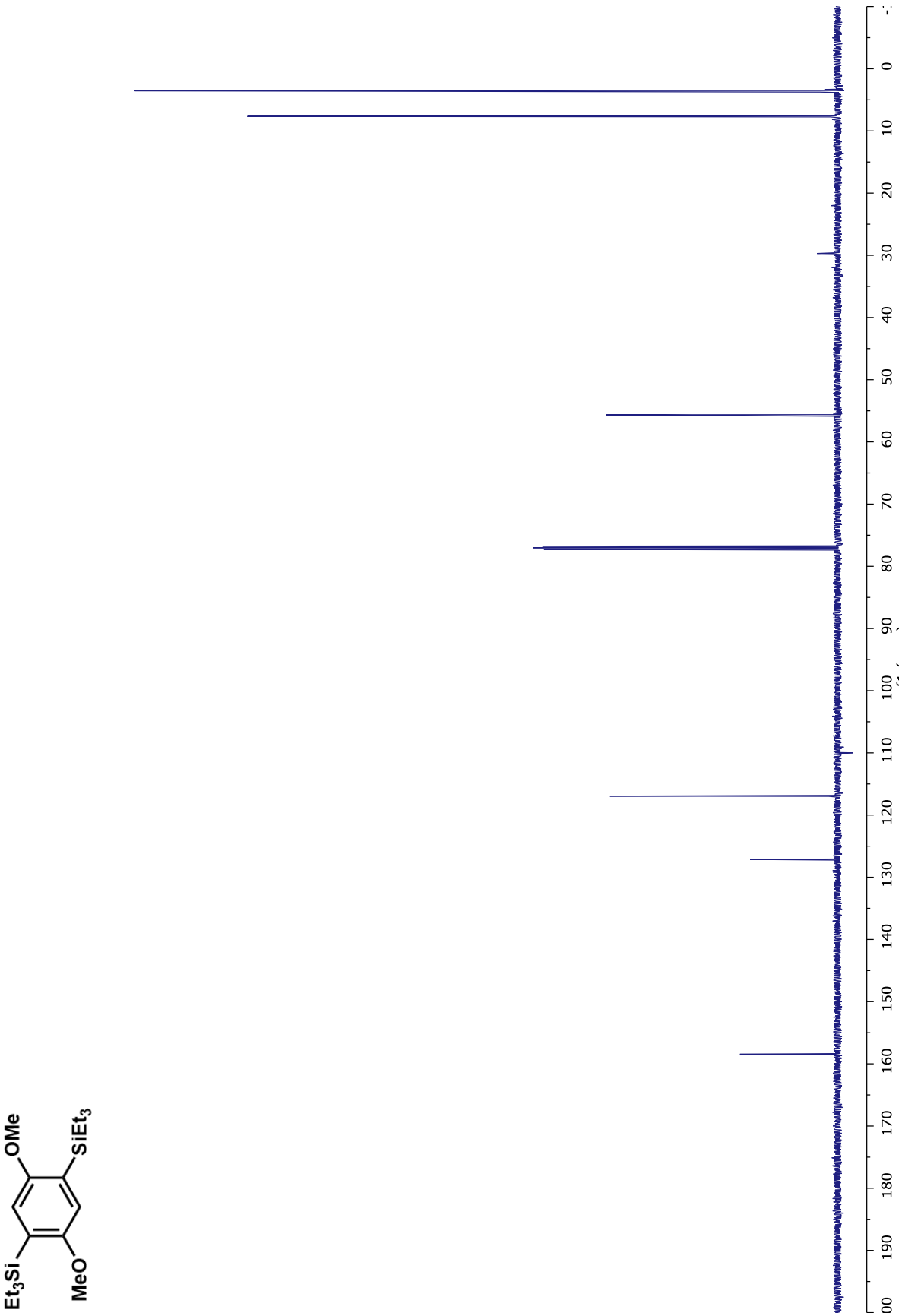
^{1}H NMR (500 MHz, $CDCl_3$) of compound **17c**.



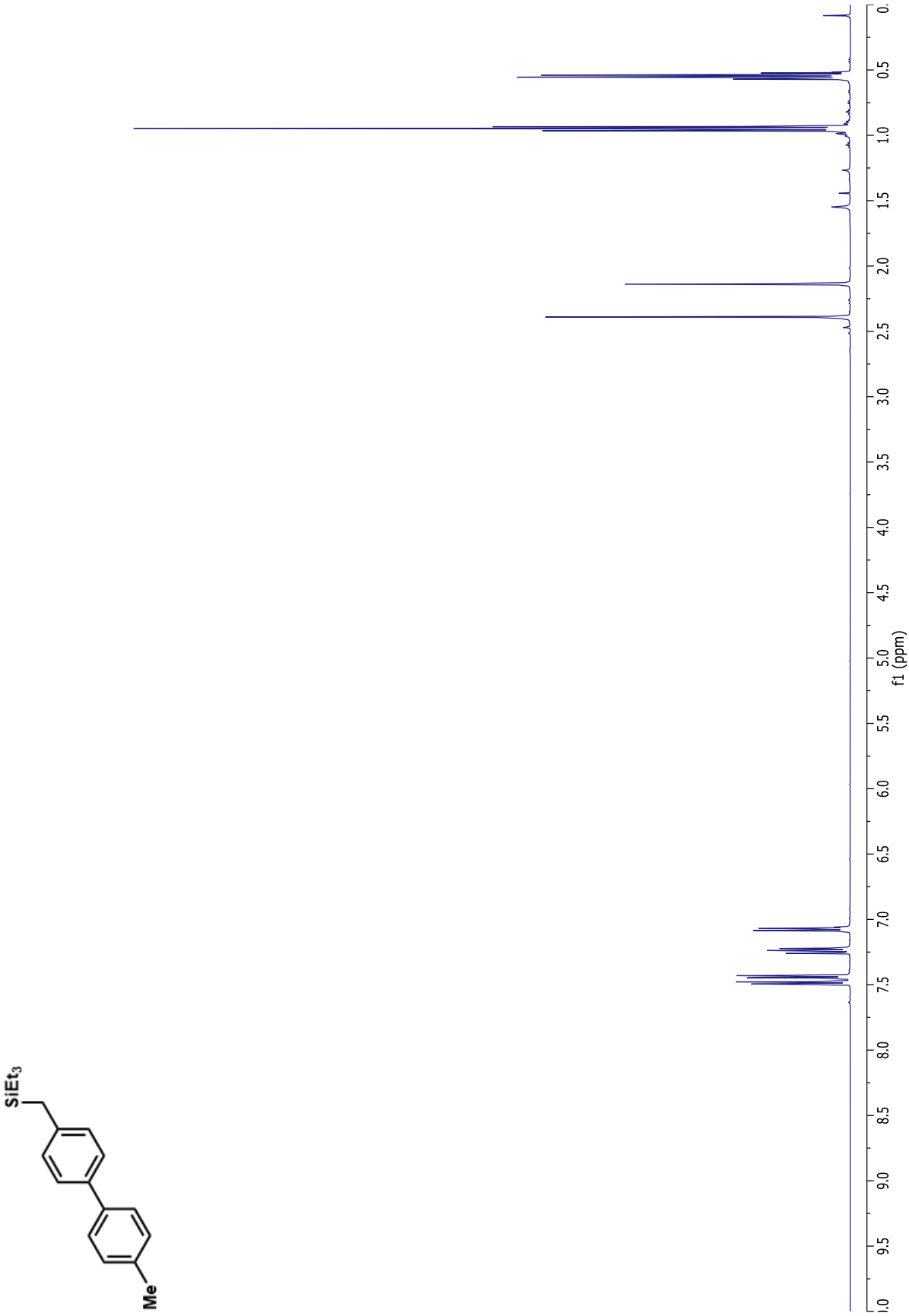
^{13}C NMR (125 MHz, $CDCl_3$) of compound **17c**.



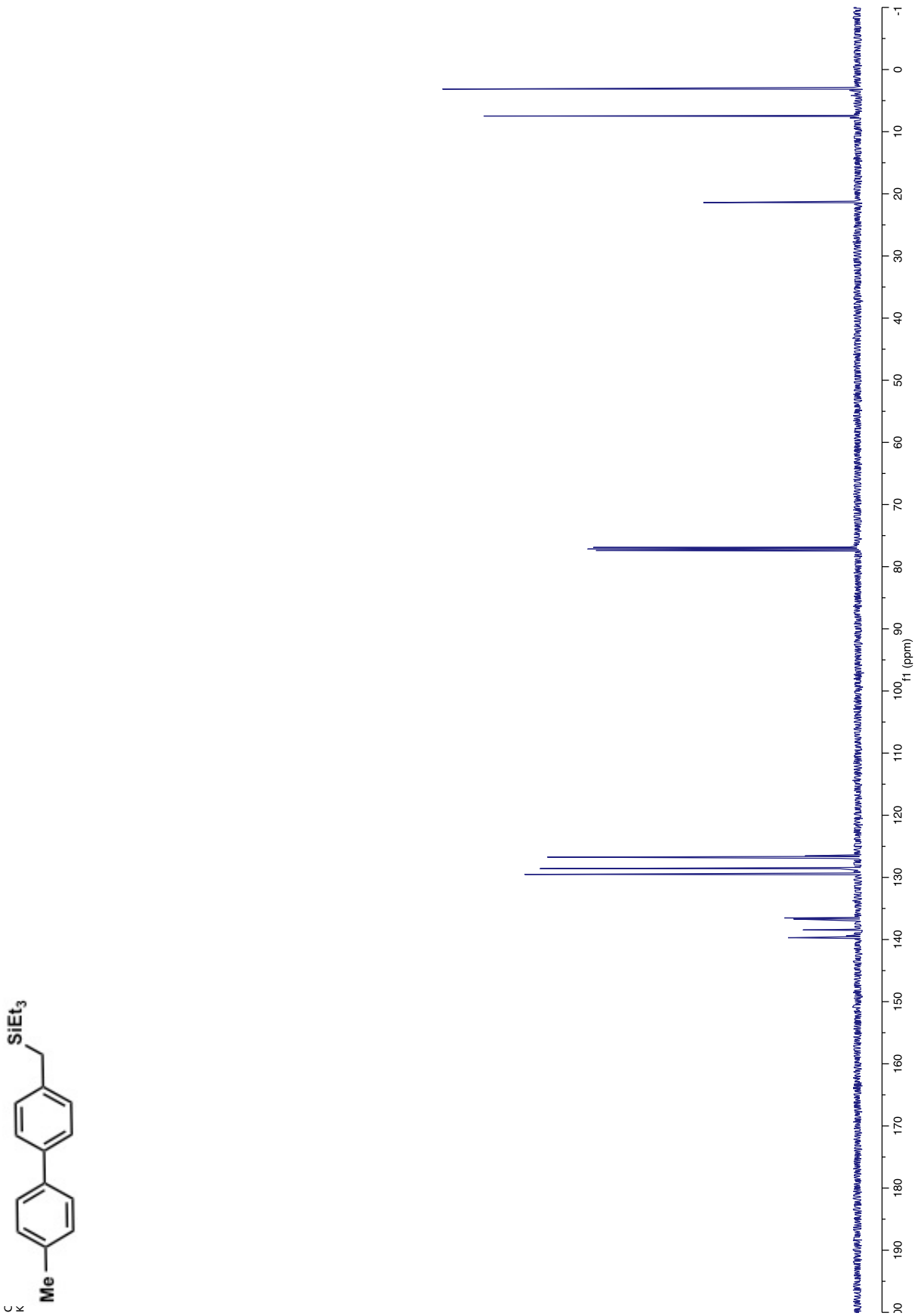
^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-17c**.



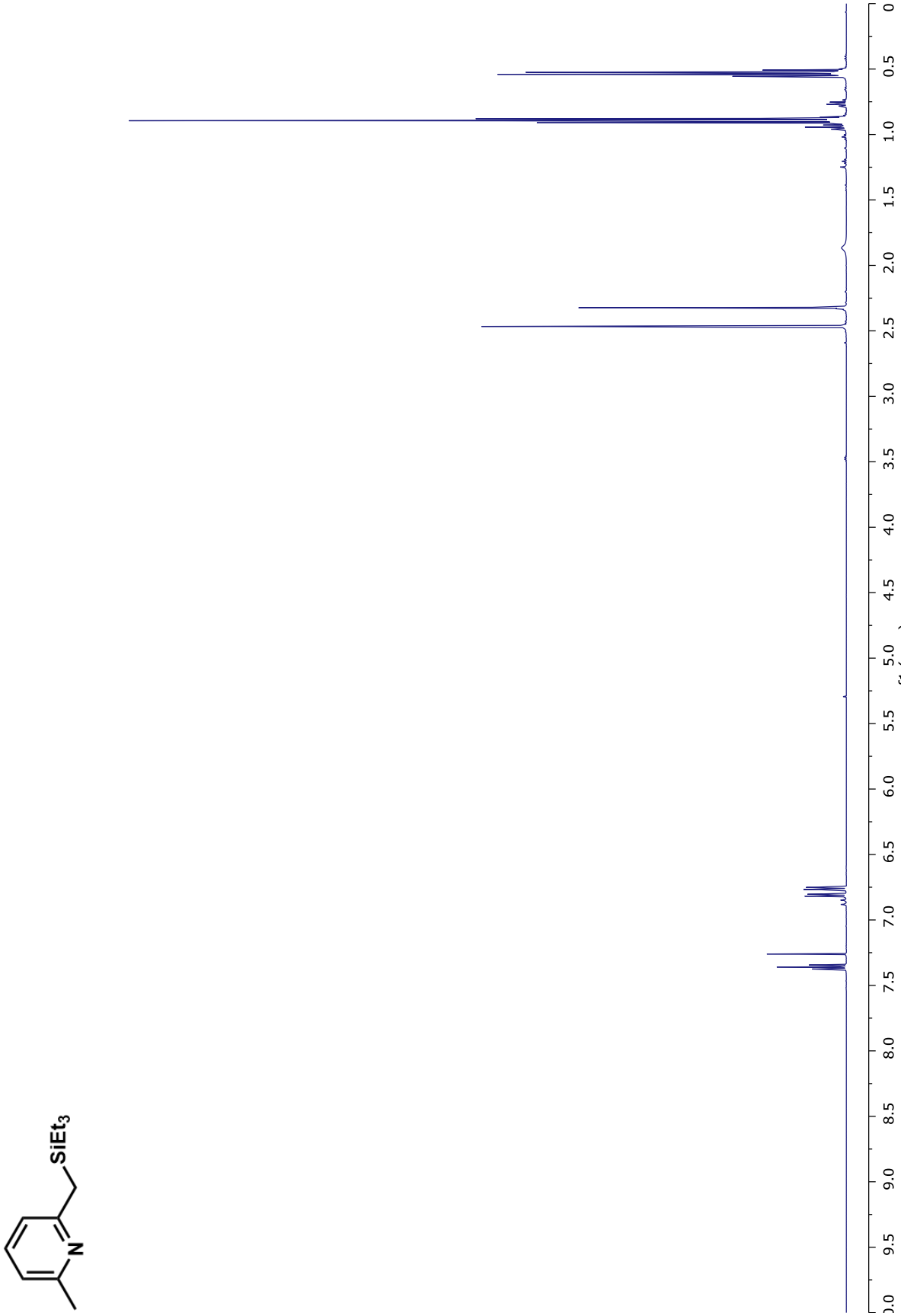
^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-17c**.



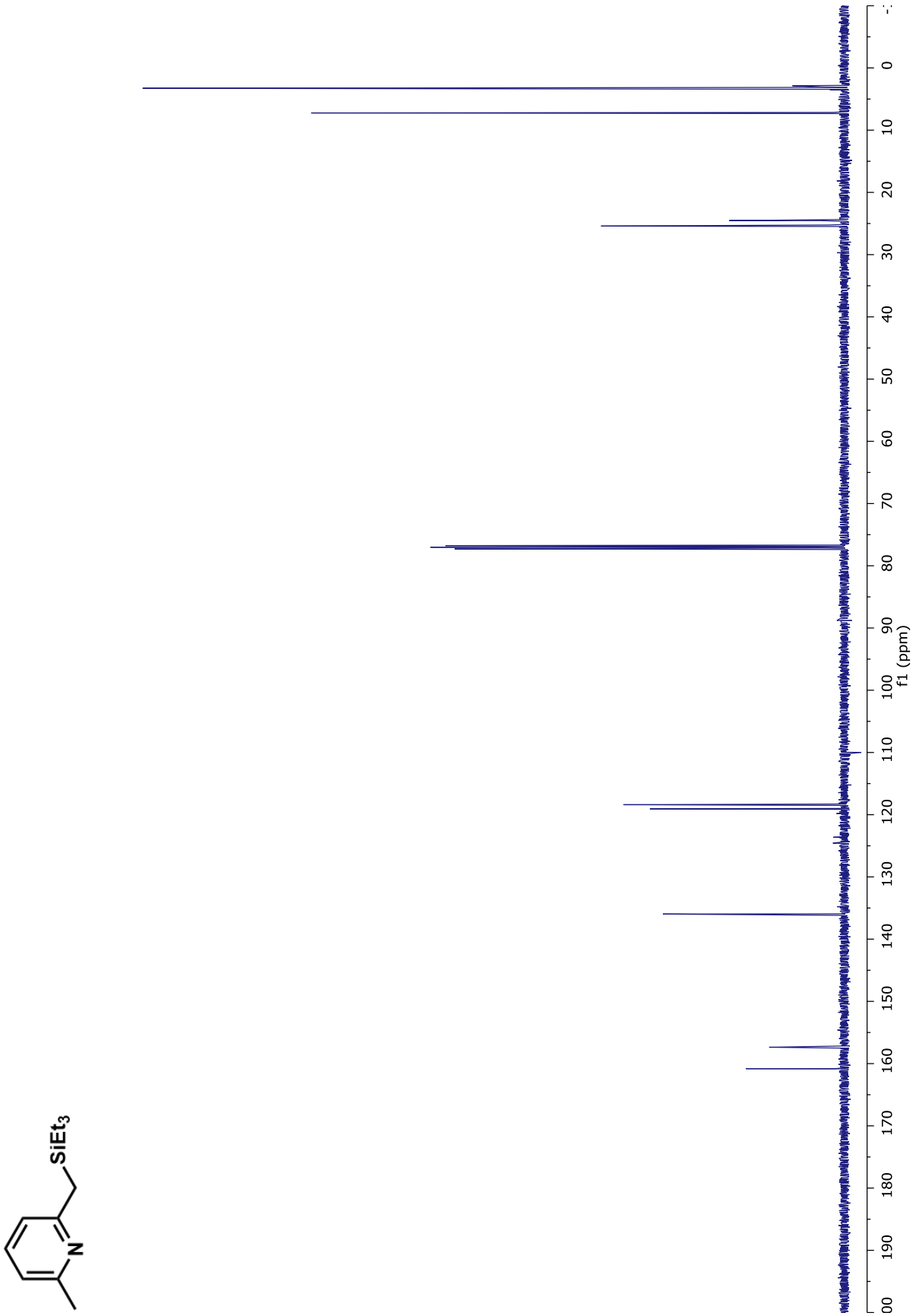
^{1}H NMR (500 MHz, $CDCl_3$) of compound **18b**.



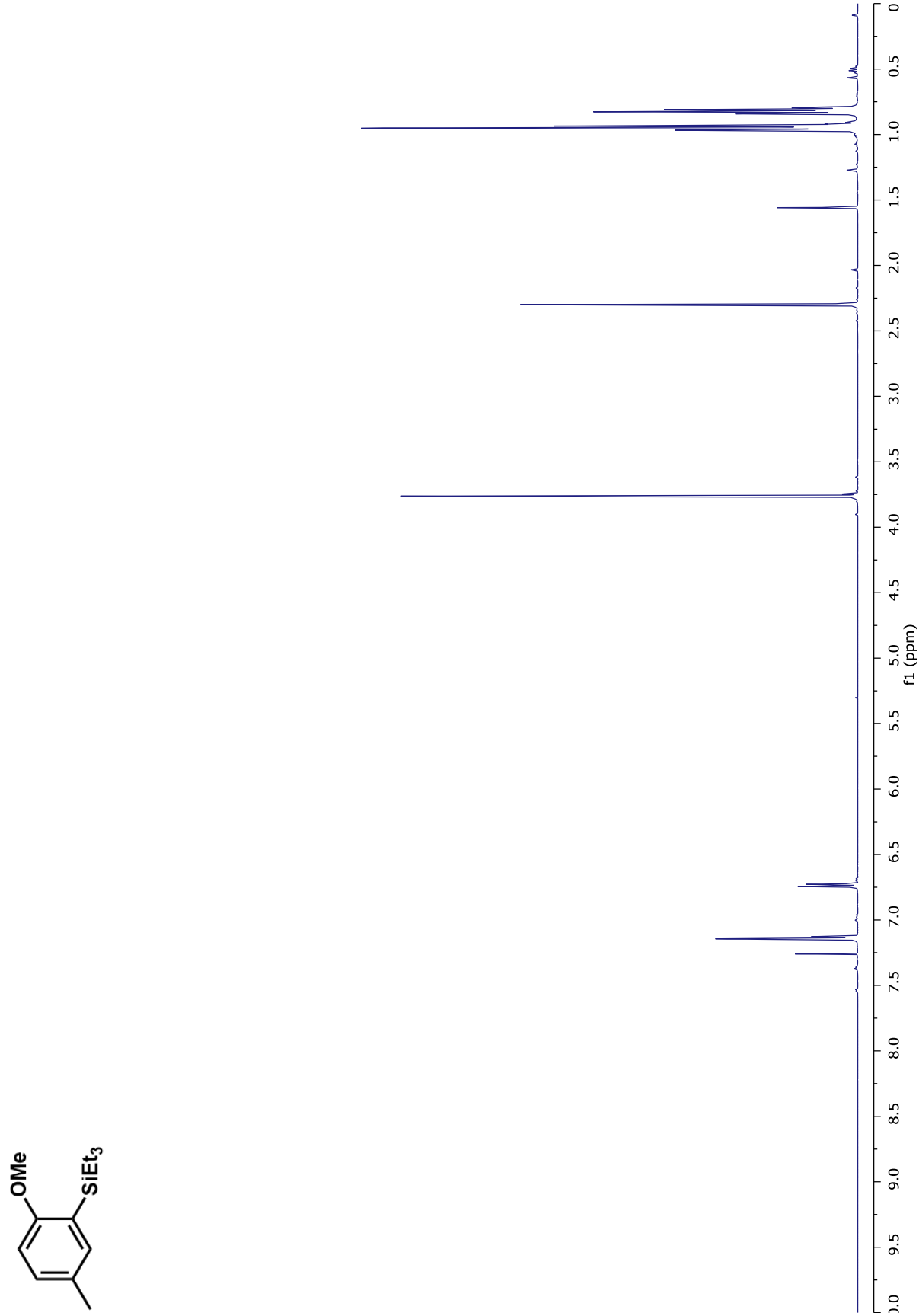
^{13}C NMR (125 MHz, $CDCl_3$) of compound **18b**.



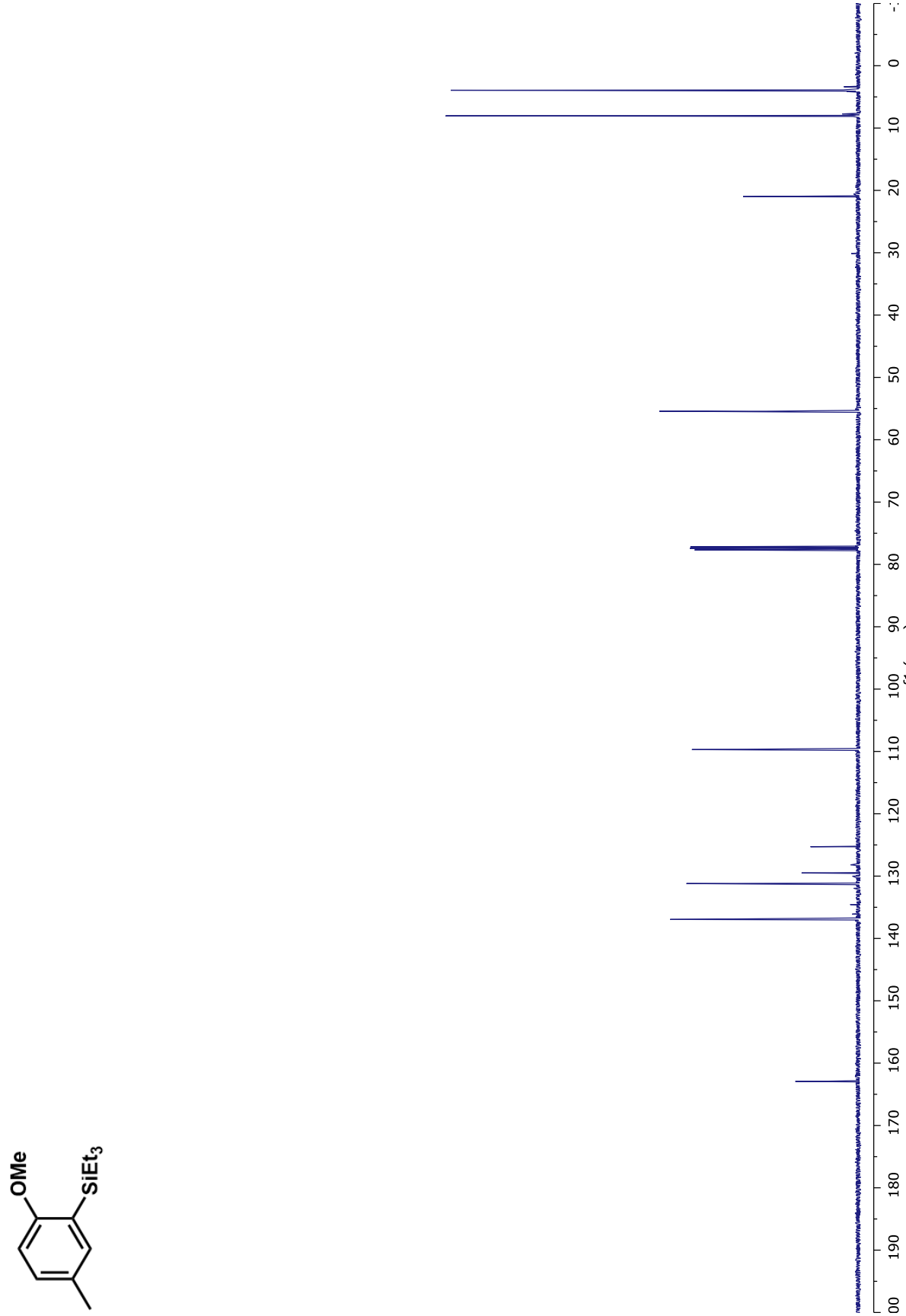
^{1}H NMR (500 MHz, $CDCl_3$) of compound **18c**.



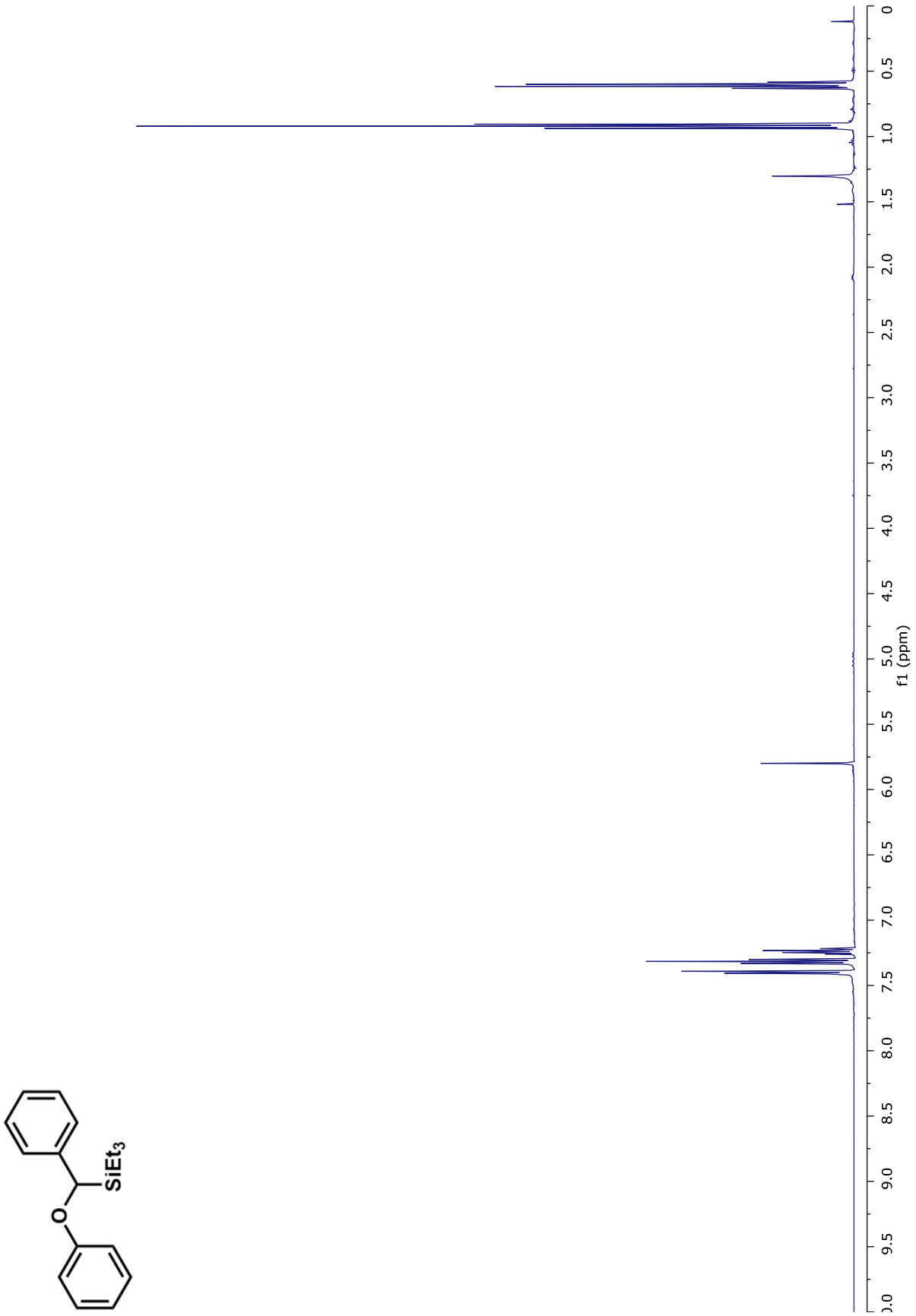
^{13}C NMR (125 MHz, $CDCl_3$) of compound **18c**.



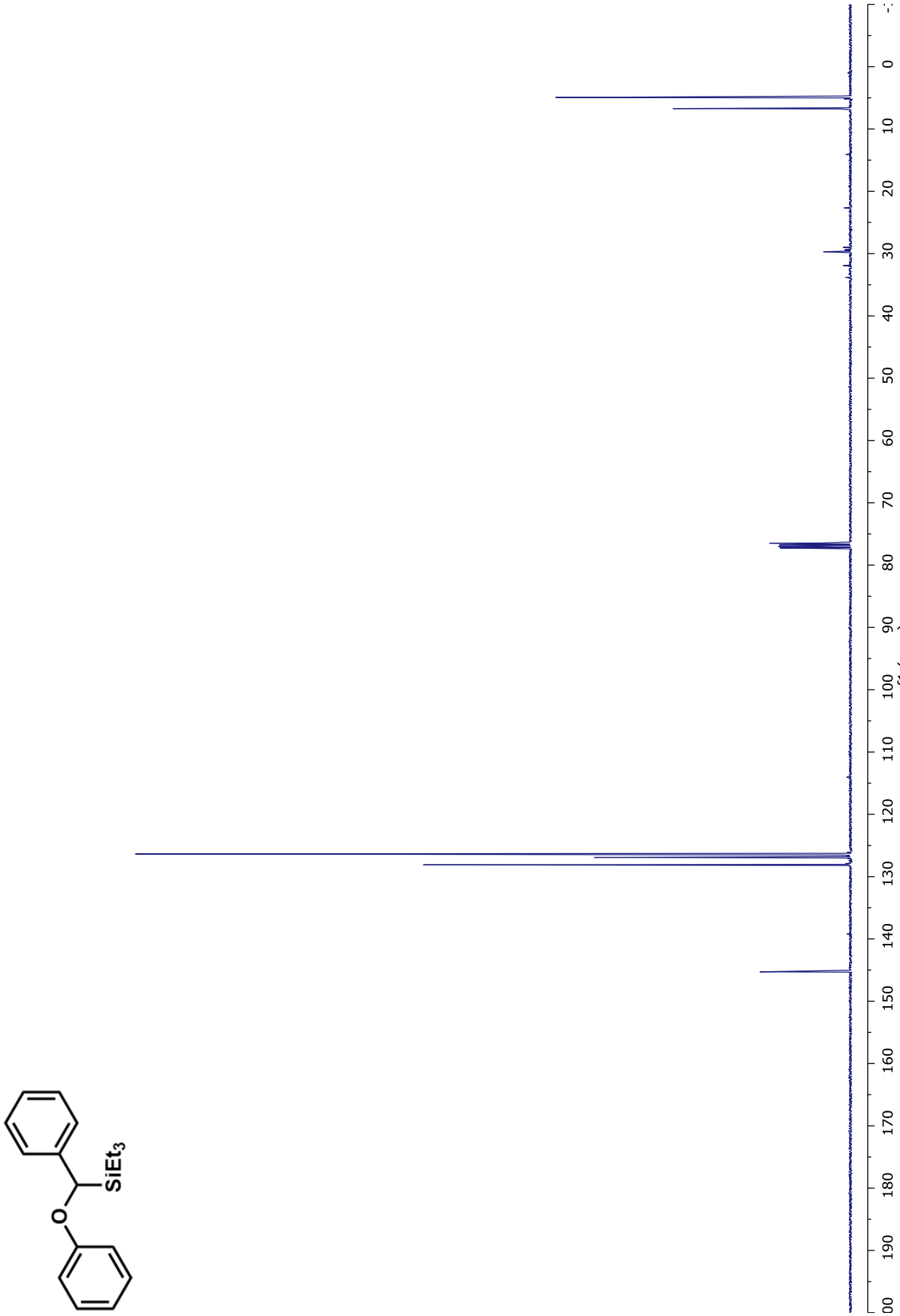
^{1}H NMR (500 MHz, $CDCl_3$) of compound **20**.



^{13}C NMR (125 MHz, $CDCl_3$) of compound **20**.

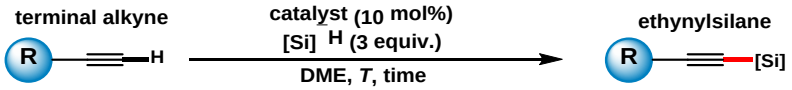


^{1}H NMR (500 MHz, $CDCl_3$) of compound **22**.

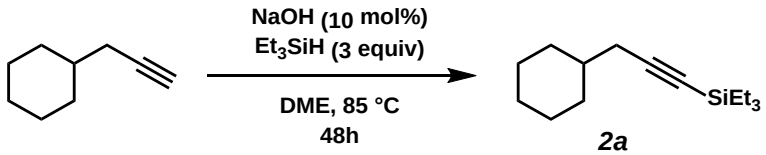


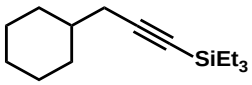
^{13}C NMR (125 MHz, $CDCl_3$) of compound **22**.

1. General procedure for cross-dehydrogenative C(*sp*)–H silylation and characterization data.



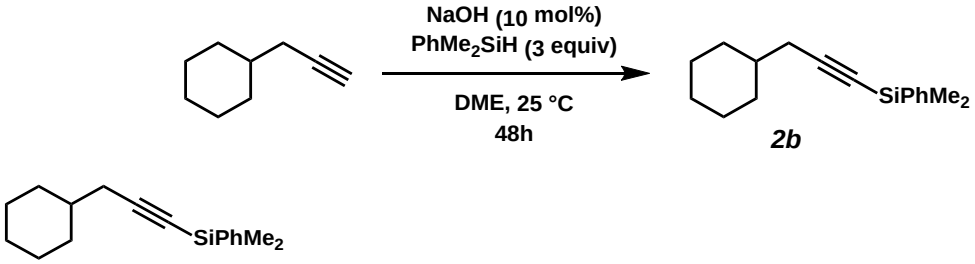
In a nitrogen-filled glove box, catalyst (0.05 mmol, 10 mol%) and alkyne (0.5 mmol, 1 equiv) were added to a 2 dram scintillation vial equipped with a magnetic stirring bar, followed by solvent (0.5 mL), and silane (1.5 mmol, 3 equiv). The vial was then sealed and the mixture was stirred at the indicated 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.



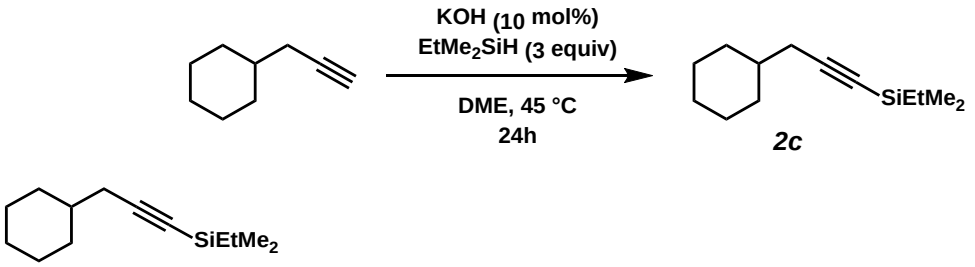


(3-cyclohexylprop-1-yn-1-yl)triethylsilane 2a: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv.), Et_3SiH (174 mg, 240 μL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 85 °C for 48 h. The desired product **2a** (111.9 mg, 95% yield) was obtained after purification by high vacuum (45 mtorr, 2 hours) as a colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

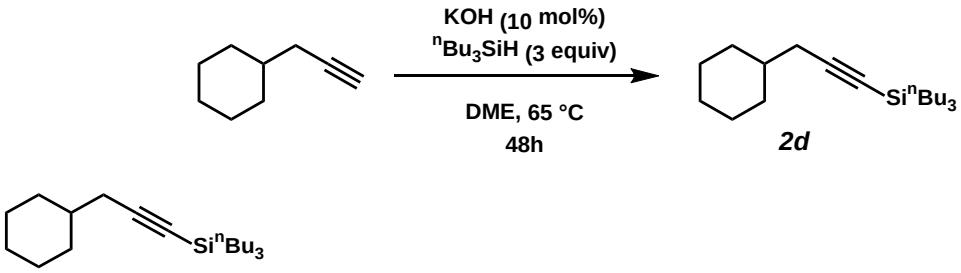


(3-cyclohexylprop-1-yn-1-yl)dimethyl(phenyl)silane 2b: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 25 °C for 48 h. The desired product **2b** (113.6 mg, 89% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **2b** in analytically pure form as a colorless oil. R_f = 0.67 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

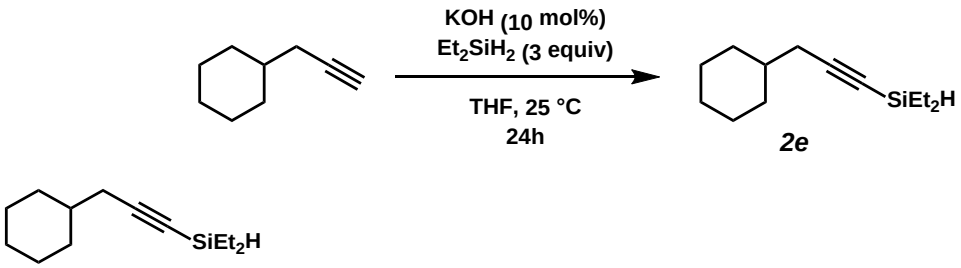


(3-cyclohexylprop-1-yn-1-yl)(ethyl)dimethylsilane 2c: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%),

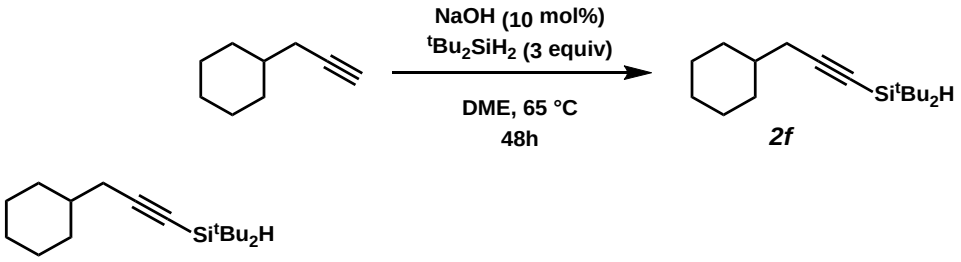
cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv.), $EtMe_2SiH$ (132 mg, 198 μL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 24 h. The desired product **2c** (95.1 mg, 91% yield) was obtained after purification by high vacuum (45 mtorr, 2 hours) as a colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) 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.



tributyl(3-cyclohexylprop-1-yn-1-yl)silane 2d: 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$_3$SiH (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 **2d** (117.2 mg, 73% yield) was obtained by silica gel flash chromatography (100% hexanes) yielded the product **2d** as a colorless oil. R_f = 0.78 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

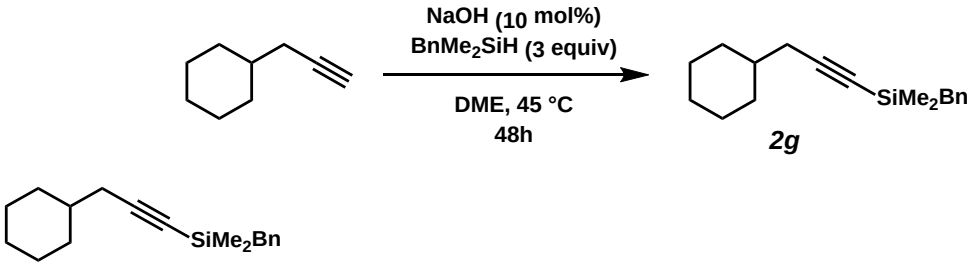


(3-cyclohexylprop-1-yn-1-yl)diethylsilane 2e: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv.), Et_2SiH_2 (132 mg, 194 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of tetrahydrofuran (THF) at 25 °C for 24 h. The desired product **2e** (73.6 mg, 71% yield) was obtained in 90% purity after high vacuum at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **2e** as a colorless oil. R_f = 0.77 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

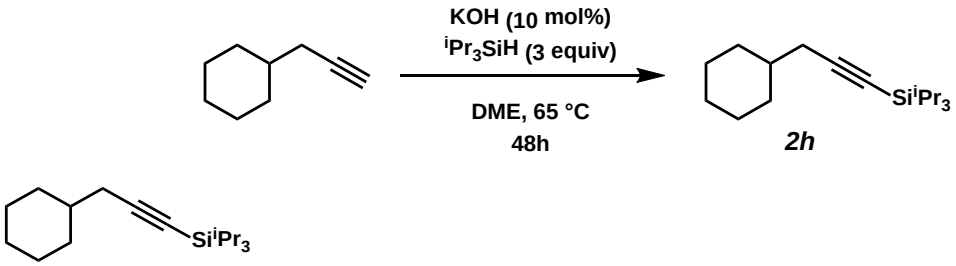


di-tert-butyl(3-cyclohexylprop-1-yn-1-yl)silane 2f: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv.), ^{t}Bu$_2$SiH$_2$ (216 mg, 297 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **2f** (114.5 mg, 87% yield) was obtained in 90% purity after high vacuum at 45

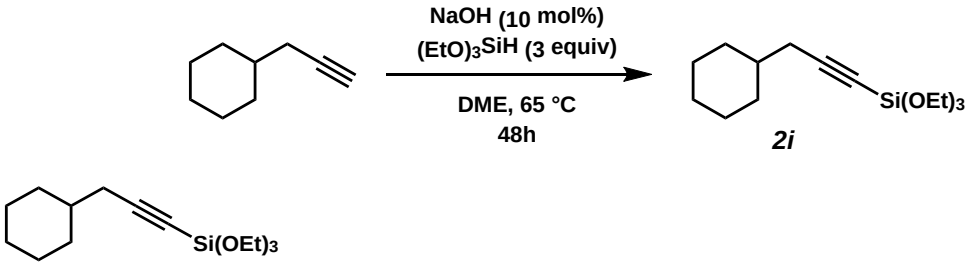
mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **2f** as a colorless oil. R_f = 0.88 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) δ 3.57 (t, J = 1.2 Hz, 1H), 2.17 (dd, J = 6.5, 1.2 Hz, 2H), 1.84 – 1.78 (m, 2H), 1.76 – 1.70 (m, 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.



benzyl(3-cyclohexylprop-1-yn-1-yl)dimethylsilane 2g: 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 **2g** (101.9 mg, 75.3% yield) was obtained by silica gel flash chromatography (100% hexanes) as a colorless oil. R_f = 0.51 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

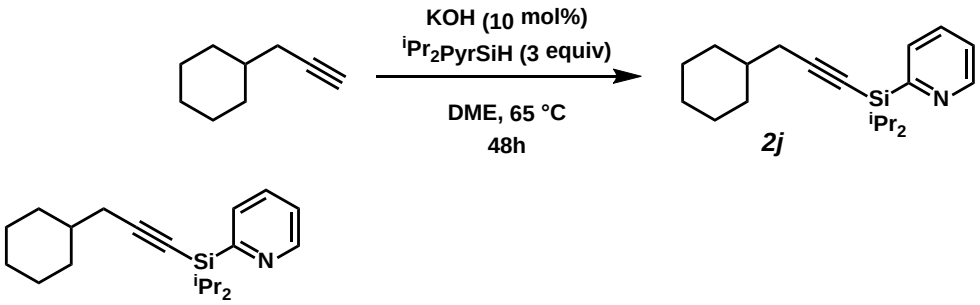


(3-cyclohexylprop-1-yn-1-yl)triisopropylsilane 2h: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv.), $^{i}Pr_3SiH$ (238 mg, 307 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 85 °C for 48 h. The desired product **2h** (95.6 mg, 68.6% yield) was obtained by silica gel flash chromatography (100% hexanes) as a colorless oil. R_f = 0.79 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

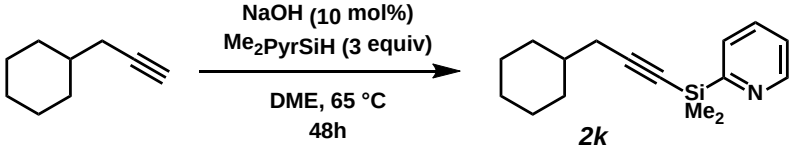


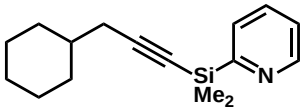
(3-cyclohexylprop-1-yn-1-yl)triethoxysilane 2i: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv.), $(EtO)_3SiH$ (246 mg, 277 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **2i** (97.1 mg, 68.3% yield) was obtained by silica gel flash chromatography (5% Et_2O in hexanes) as a colorless oil. R_f = 0.41 (5% Et_2O in hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

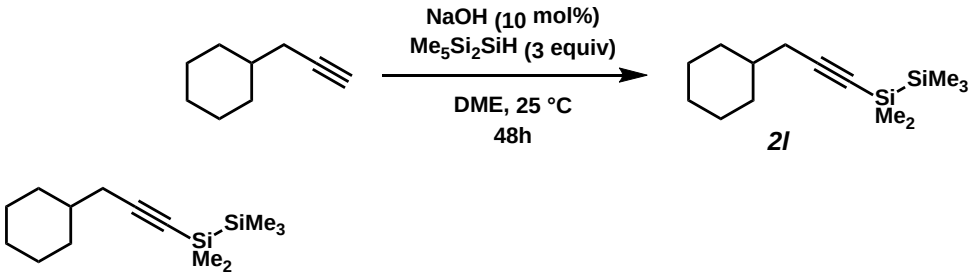


2-((3-cyclohexylprop-1-yn-1-yl)diisopropylsilyl)pyridine 2j: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv.), ^{i}Pr$_2$(Pyr)SiH (290 mg, 322 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **2j** (122.5 mg, 78.1% yield) was obtained by silica gel flash chromatography (10% EtOAc in hexanes) as a colorless oil. R_f = 0.47 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, THF-*d8*) 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) 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 258.1672.



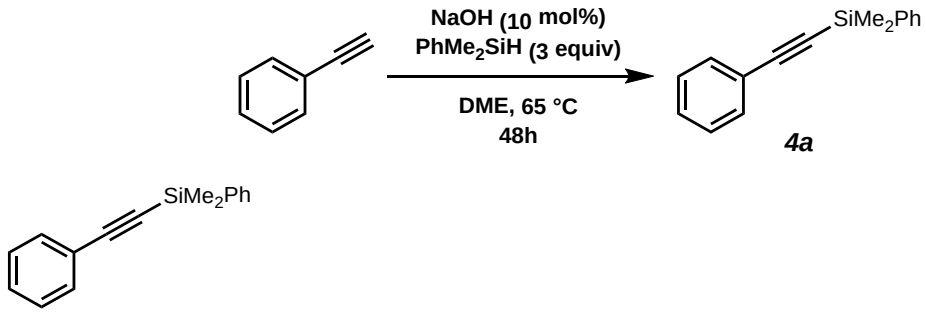


2-((3-cyclohexylprop-1-yn-1-yl)dimethylsilyl)pyridine 2k: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv.), Me_2(Pyr)SiH (206 mg, 225 μL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **2k** (99.9 mg, 77.6% yield) was obtained by silica gel flash chromatography (10% EtOAc in hexanes) as a colorless oil. R_f = 0.42 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, THF-*d8*) 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, 3H), 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) 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.

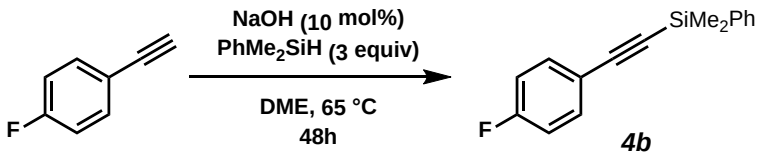


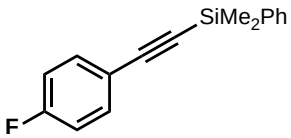
1-(3-cyclohexylprop-1-yn-1-yl)-1,1,2,2,2-pentamethyldisilane 2l: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv.), Me_5Si_2H (246 mg, 277 μL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 25 °C for 48 h. The desired product **2l** (120.0 mg, 95% yield) was obtained as a cloudy, colorless oil after heating to 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, THF-d8) 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) 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.

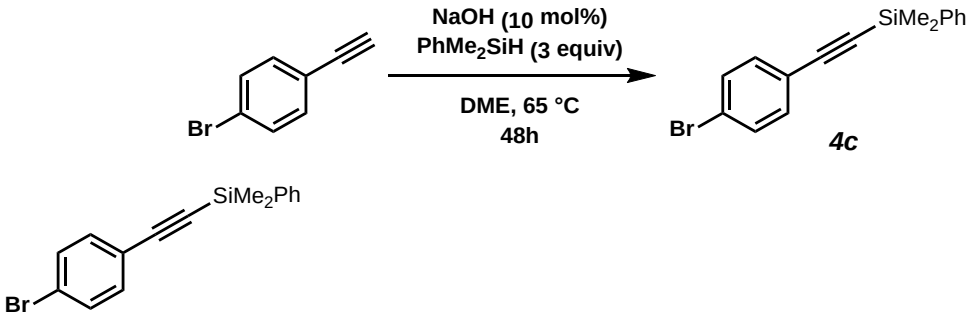


dimethyl(phenyl)(phenylethynyl)silane 4a: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), ethynylbenzene (52 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **4a** (105.7 mg, 89% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **4a** in analytically pure form as a colorless oil. R_f = 0.38 (100% hexanes); ^{1}H NMR (500 MHz, THF-*d8*) 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) 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.



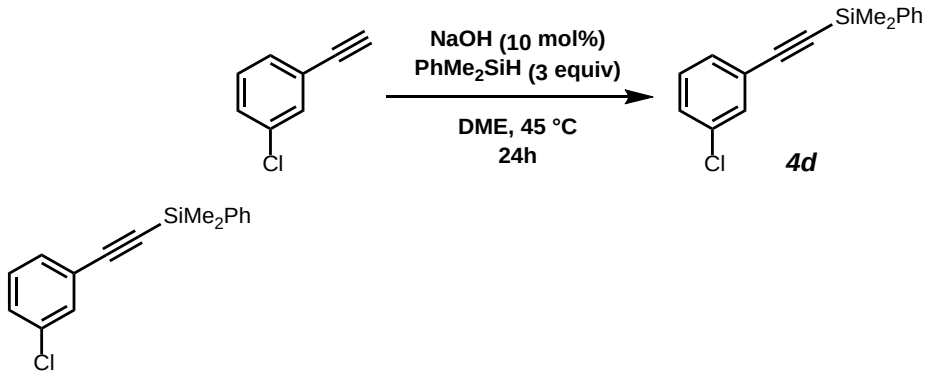


((4-fluorophenyl)ethynyl)dimethyl(phenyl)silanepyridine 4b: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 1-ethynyl-4-fluorobenzene (60 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **4b** (111.9 mg, 88% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **4b** in analytically pure form as a colorless oil. R_f = 0.49 (100% hexanes); ^{1}H NMR (500 MHz, THF-*d8*) 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) δ 163.93 (d, J = 248.7 Hz), 137.74, 135.10 (d, J = 8.5 Hz), 134.65 , 130.39 , 128.81 , 120.43 (d, J = 3.5 Hz), 116.51 (d, J = 22.4 Hz), 106.68 , 92.43 (d, J = 1.3 Hz), -0.56 . 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.

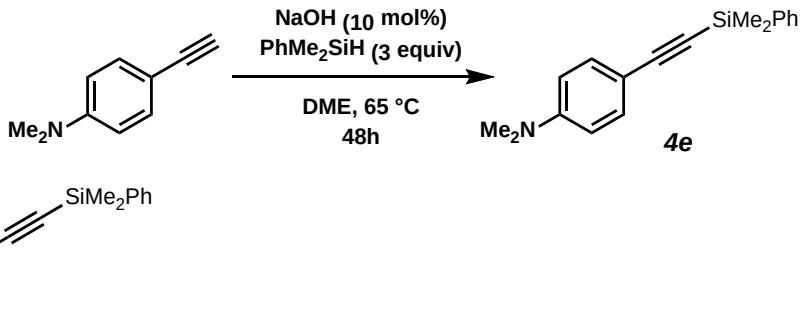


((4-bromophenyl)ethynyl)dimethyl(phenyl)silane 4c: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 1-bromo-4-ethynylbenzene (90 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **4c** (81.3 mg, 52% yield) was obtained in 80% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash

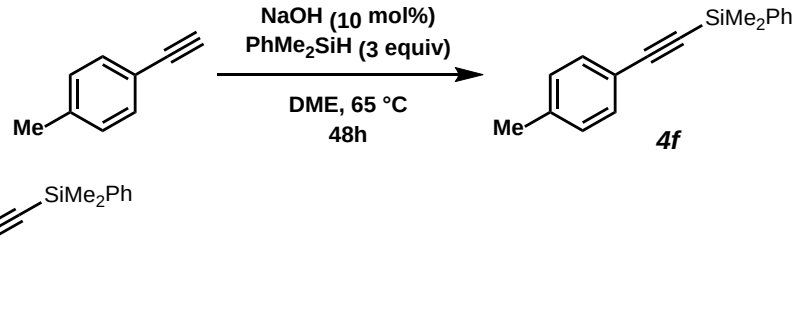
chromatography (100% hexanes) yielded the product **4c** as colourless crystals in a 9:1 mixture with the disiloxane **xx**. R_f = 0.54 (100% hexanes); ^{1}H NMR (500 MHz, THF-*d8*) δ 7.69 – 7.63 (m, 2H), 7.51 (d, J = 8.5 Hz, 2H), 7.39 (d, J = 8.5 Hz, 2H), 7.36 – 7.30 (m, 3H), 0.46 (s, 6H); ^{13}C NMR (126 MHz,thf) 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 $C_{16}H_{16}BrSi$ [M+H]: 317.0184, found 317.0180.



((3-chlorophenyl)ethynyl)dimethyl(phenyl)silane 4d: 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 **4d** (121.6 mg, 90% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **4d** in analytically pure form as a colorless oil. R_f = 0.42 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

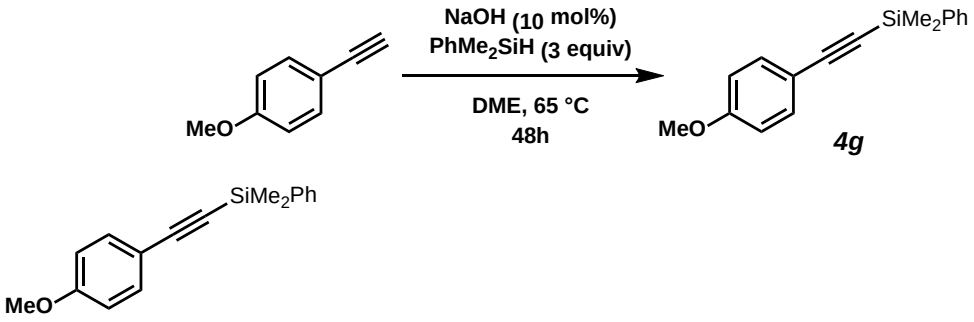


4-((dimethyl(phenyl)silyl)ethynyl)-N,N-dimethylaniline 4e: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 4-ethynyl-N,N-dimethylaniline (73 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **4e** (139.4 mg, 100% yield) was obtained as colourless crystals after heating to 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

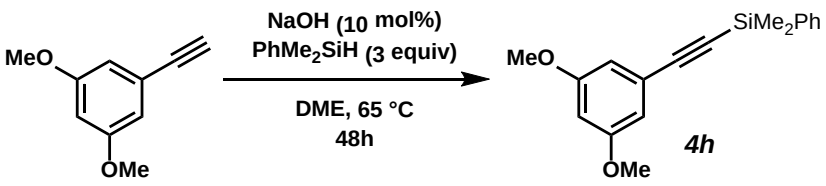


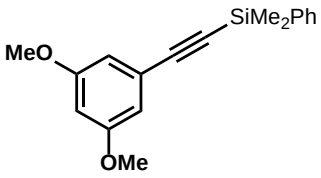
dimethyl(phenyl)(*p*-tolylethynyl)silane 4f: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 1-ethynyl-4-methylbenzene (58 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **4f** (115.5 mg, 92% yield) was obtained as a pale yellow oil after heating to 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

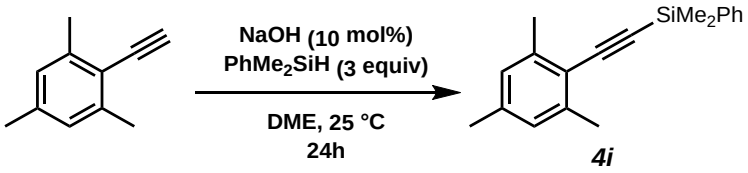


((4-methoxyphenyl)ethynyl)dimethyl(phenyl)silane 4g: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 1-ethynyl-4-methoxybenzene (66 mg, 0.5 mmol, 1.0 equiv.), PhMe$_2$SiH (204 mg, 230 μL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **4g** (121.6 mg, 91% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes → 5% EtOAc in hexanes) yielded the product **4g** in analytically pure form as a yellow oil. R_f = 0.27 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

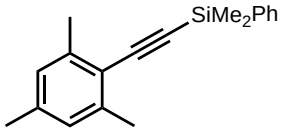




((3,5-dimethoxyphenyl)ethynyl)dimethyl(phenyl)silane 4h: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 1-ethynyl-3,5-dimethoxybenzene (81 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **4h** (140.6 mg, 95% yield) was obtained as a light yellow oil after heating to 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

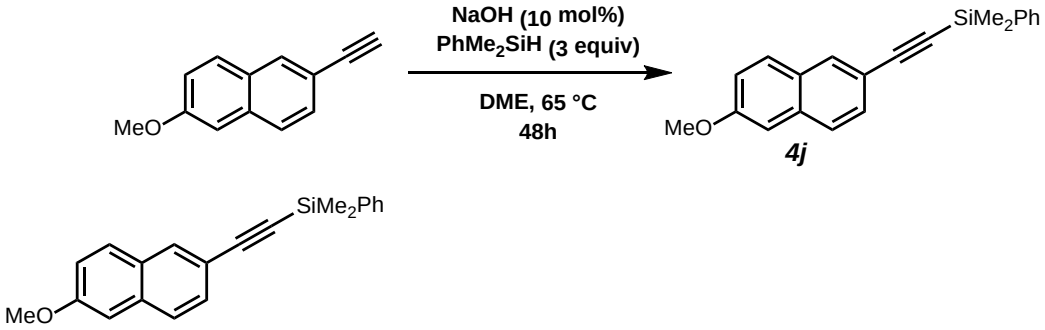


4i

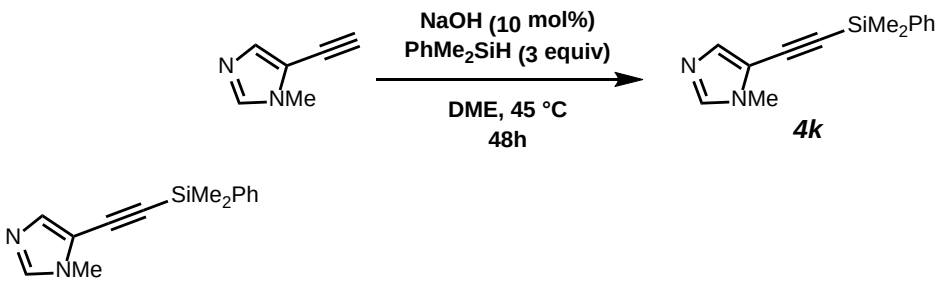


2-ethynyl-1,3,5-trimethylbenzene 4i: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 2-ethynyl-1,3,5-trimethylbenzene (57 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 25 °C for 24 h. The desired product **4i** (119.1 mg, 86% yield) was obtained as a colorless oil after heating to 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, Chloroform-*d*) 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,

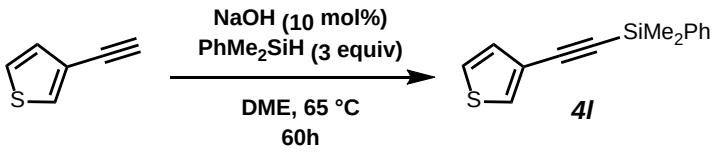
129.45, 127.99, 127.67, 119.94, 104.95, 99.66, 21.51, 21.15, -0.34. IR (Neat Film NaCl) 3440, 3068, 2959, 2146, 1646, 1610, 1474, 1428, 1224, 1117, 841, 825, 779, 753, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{19}H_{23}Si$ [M+H]: 279.1569, found 279.1561.

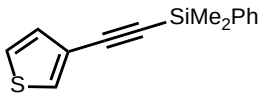


((6-methoxynaphthalen-2-yl)ethynyl)dimethyl(phenyl)silane 4j: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 2-ethynyl-6-methoxynaphthalene (91 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 48 h. The desired product **4j** (134.8 mg, 85% yield) was obtained in 95% purity as a colorless oil after heating to 85°C at 45 mtorr for 30 minutes. This product decomposes on silica. ^{1}H NMR (500 MHz, Chloroform-*d*) 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.



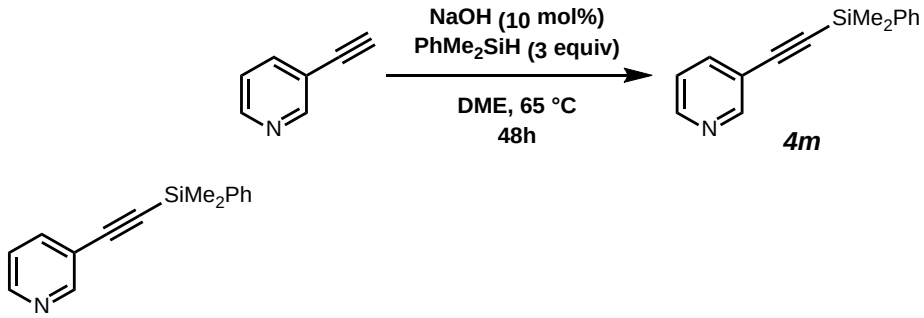
5-((dimethyl(phenyl)silyl)ethynyl)-1-methyl-1*H*-imidazole 4k: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 5-ethynyl-1-methyl-1*H*-imidazole (53 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **4k** (98.7 mg, 82% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% EtOAc) yielded the product **4k** in analytically pure form as a colorless oil. R_f = 0.45 (100% EtOAc); ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.68 – 7.65 (m, 2H), 7.40 (ddd, J = 5.4, 4.4, 1.8 Hz, 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.



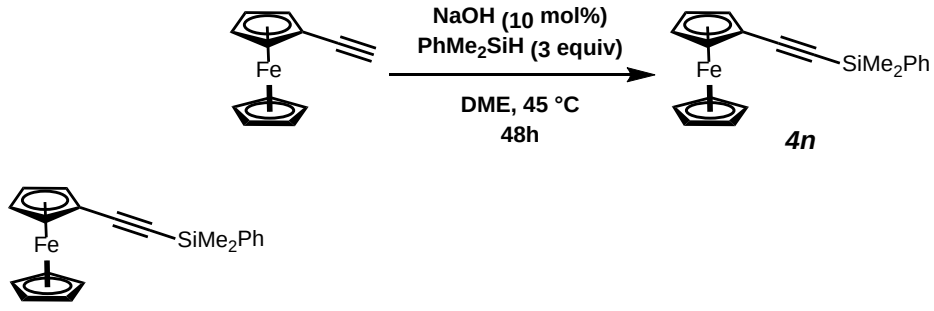


dimethyl(phenyl)(thiophen-3-ylethynyl)silane 4l: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 3-ethynylthiophene (54 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 65 °C for 60 h. The desired product **4l** (113.2 mg, 93% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **4l** in analytically pure form as a colorless oil. R_f = 0.39 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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,

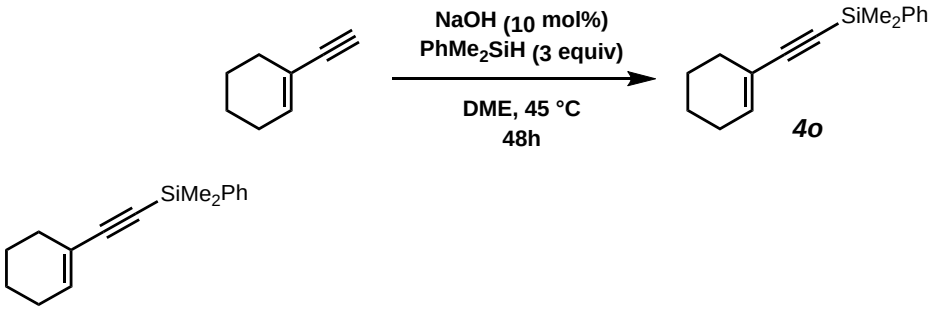
2152, 1427, 1356, 1249, 1163, 1116, 944, 870, 781, 753, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{14}SSi$ [M+•]: 242.0586, found 242.0576.



3-((dimethyl(phenyl)silyl)ethynyl)pyridine 4m: 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 **4m** (91.8 mg, 77% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **4m** in analytically pure form as a colorless oil. R_f = 0.31 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

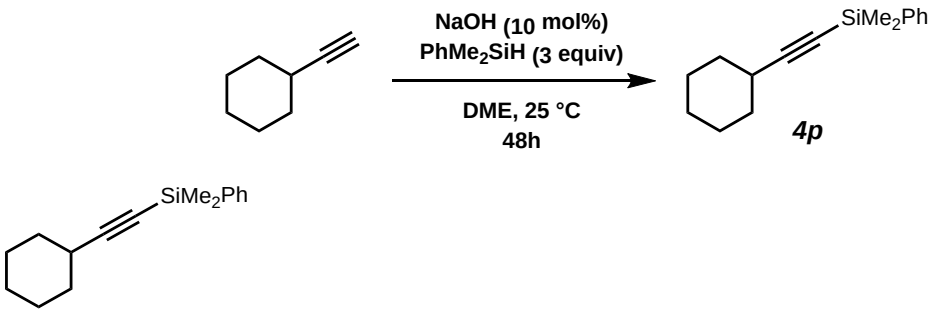


((dimethyl(phenyl)silyl)ethynyl)ferrocene 4n: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), ethynylferrocene (105 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **4n** (170.1 mg, 99% yield) was obtained as a red crystalline solid after heating to 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.70 (dd, J = 6.1, 3.1 Hz, 2H), 7.43 – 7.37 (m, 3H), 4.48 (s, 2H), 4.21 (m, 7H), 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.

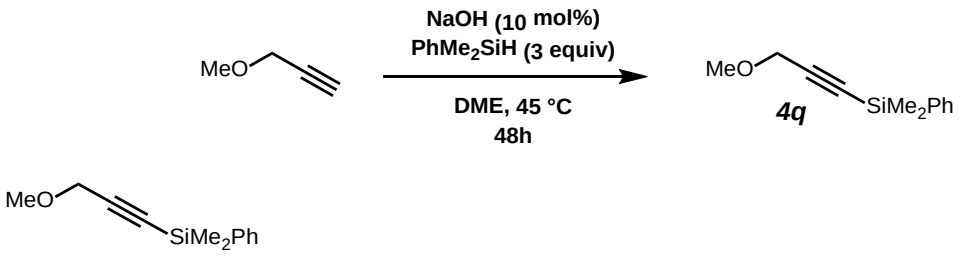


(cyclohex-1-en-1-ylethynyl)dimethyl(phenyl)silane 4o: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 1-ethynylcyclohex-1-ene (53 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **4o** (102.7 mg, 85% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 15 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **4o** in analytically pure form as a colorless oil. R_f = 0.50 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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,

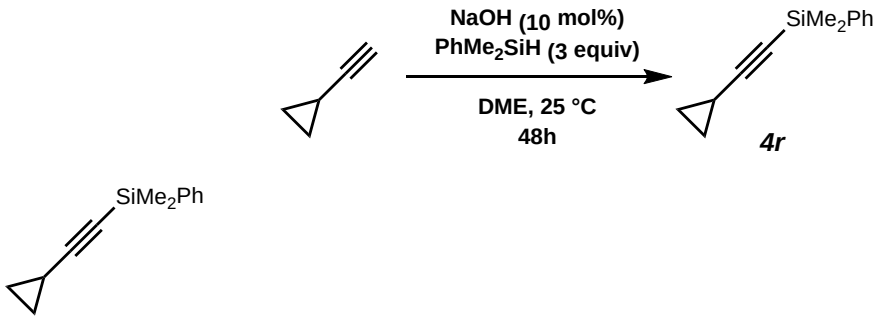
1249, 1116, 863, 819, 779, 730, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{16}H_{21}Si$ [M+H]: 241.1413, found 241.1402.



(cyclohexylethynyl)dimethyl(phenyl)silane 4p: 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 **4p** (97.4 mg, 80% yield) was obtained in 80% purity after heating to 85°C at 45 mtorr for 15 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **4p** as a colorless oil in a 9:1 mixture with the disiloxane **xx**. R_f = 0.53 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

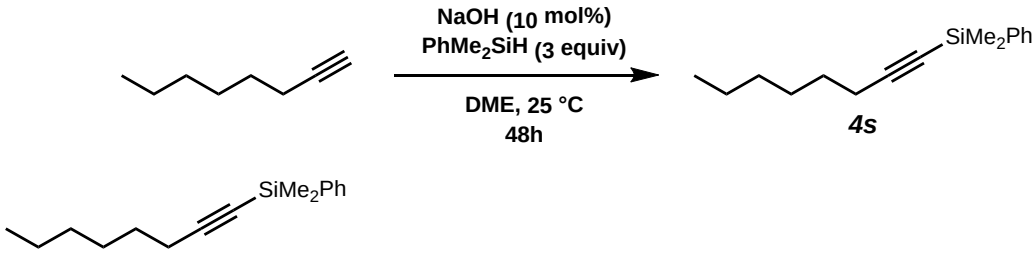


(3-methoxyprop-1-yn-1-yl)dimethyl(phenyl)silane 4q: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 3-methoxyprop-1-yne (35 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **4q** (61.0 mg, 60% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 15 minutes; careful heating is necessary, as the product is volatile. Subsequent purification by silica gel flash chromatography (50% DCM in hexanes) yielded the product **4q** in analytically pure form as a colorless oil. R_f = 0.38 (50% DCM in hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

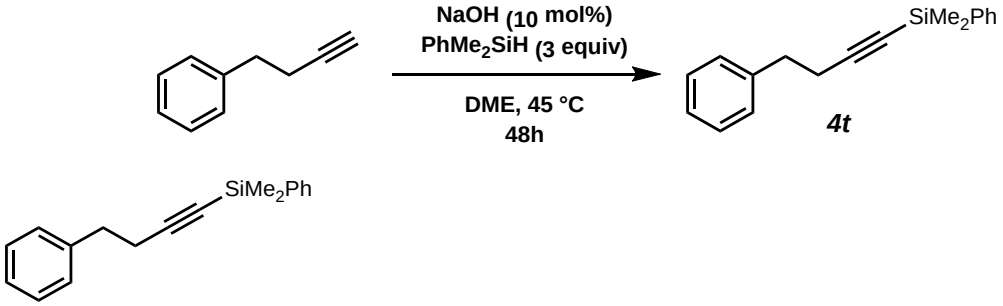


(cyclopropylethynyl)dimethyl(phenyl)silane 4r: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), ethynylcyclopropane (33 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 25 °C for 48 h. The desired product **4r** (70.1 mg, 70% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **4r** in analytically pure form as a colorless oil. Careful heating is necessary since this product is volatile. R_f = 0.38 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

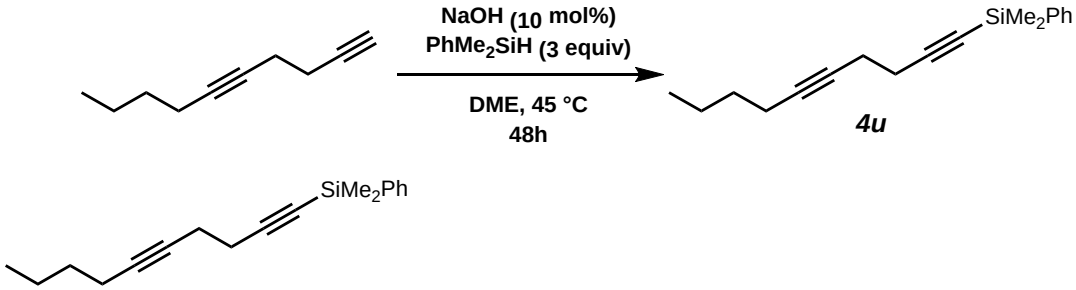


dimethyl(oct-1-yn-1-yl)(phenyl)silane 4s: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), oct-1-yne (55 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 25 °C for 48 h. The desired product **4s** (101.0 mg, 83% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 15 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **4s** in analytically pure form as a colorless oil. R_f = 0.53 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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)-H_2]: 245.1726, found 245.1727.

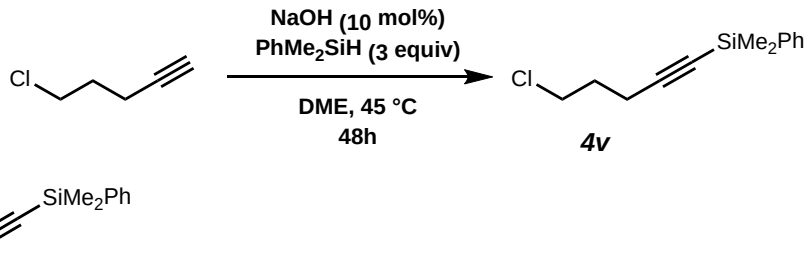


dimethyl(phenyl)(4-phenylbut-1-yn-1-yl)silane 4t: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), but-3-yn-1-ylbenzene (65 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol,

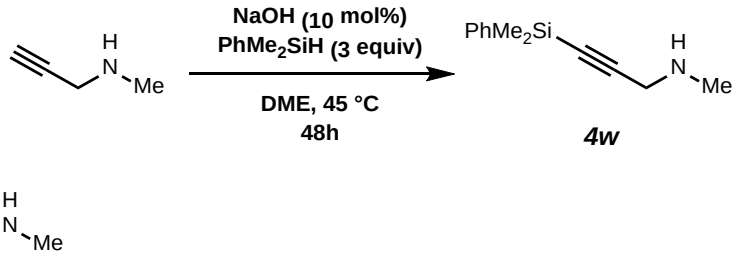
3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **4t** (130.0 mg, 98% yield) was obtained as a pale yellow oil after heating to 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.64 – 7.59 (m, 2H), 7.42 – 7.37 (m, 3H), 7.31 (dd, J = 8.0, 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 4u: 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 **4u** (131.3 mg, 98% yield) was obtained as a colorless oil after heating to 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, Chloroform-*d*) 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); ^{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.

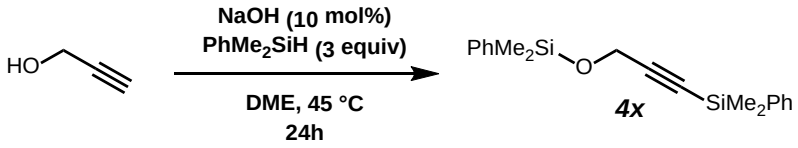


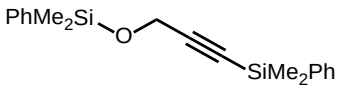
(5-chloropent-1-yn-1-yl)dimethyl(phenyl)silane 4v: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), 5-chloropent-1-yne (51 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **4v** (93.3 mg, 79% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **4v** in analytically pure form as a colorless oil. Careful heating is necessary since this product is volatile. R_f = 0.31 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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 4w: 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 **4w** (81.8 mg, 80% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 15 minutes; careful heating is necessary, as the product is volatile.

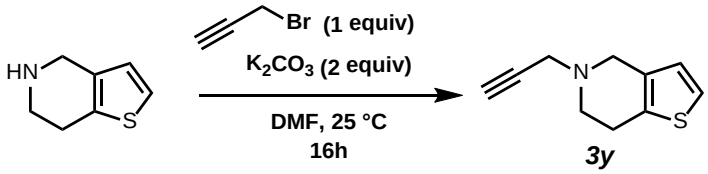
Subsequent purification by silica gel flash chromatography (100% EtOAc) yielded the product **4w** in analytically pure form as a colorless oil. R_f = 0.32 (100% EtOAc); ^{1}H NMR (500 MHz, THF-*d8*) δ 7.63 – 7.59 (m, 2H), 7.33 – 7.29 (m, 3H), 3.36 (s, 2H), 2.39 (s, 3H), 0.36 (s, 6H); ^{13}C NMR (126 MHz, thf) 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.

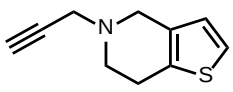




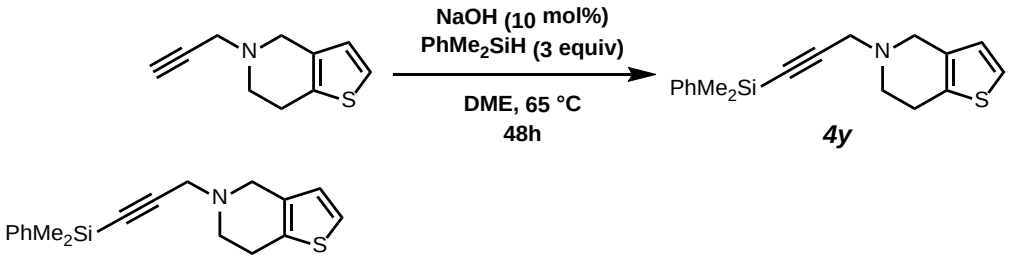
KNB-III-075

(3-((dimethyl(phenyl)silyl)oxy)prop-1-yn-1-yl)dimethyl(phenyl)silane 4x: 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 **4x** (142.9 mg, 88% yield) was obtained as a colorless oil after heating to 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, Chloroform-*d*) 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.





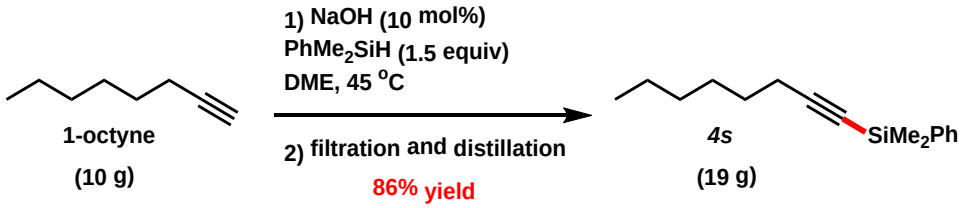
5-(prop-2-yn-1-yl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine 3y: To a mixture of tetrahydrothieno[3,2-*c*]pyridine hydrochloride (1.40 g, 10 mmol, 1 equiv) and K_2CO_3 (2.76 g, 20 mmol, 2 equiv) in DMF (30 ml), was added 1-propyne-3-bromide (1.18 g, 10 mmol, 1 equiv) and the mixture was stirred at room 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 **3y** as a yellow liquid (1.27 g, 72% yield). R_f = 0.35 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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 4y: 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 **4y** (120.4 mg, 77% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 15 minutes; subsequent purification by silica gel flash chromatography (10% EtOAc in hexanes) yielded the product **4y** in analytically pure form as a yellow oil. R_f = 0.40 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

2. Procedure for the multi-gram scale synthesis of *4s*.



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) (degassed, 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:

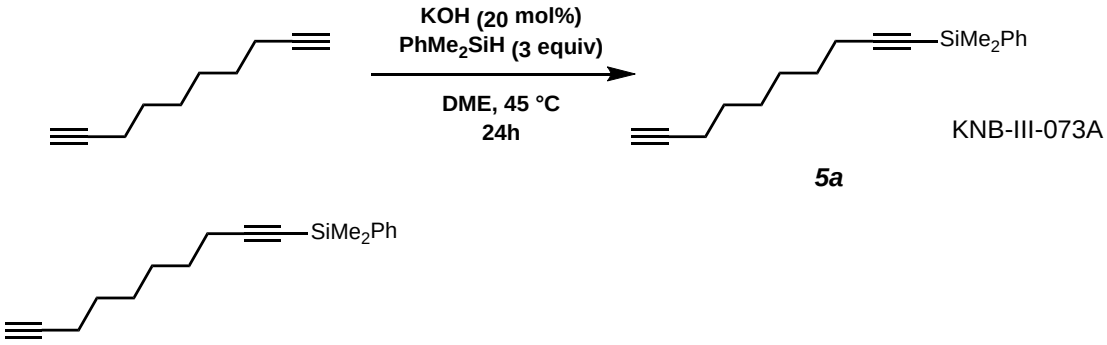
a) Heating bath to 80 °C, vacuum stabilizes at 200 millitorr as a small amount of droplets condense into the forerun. Forerun comes off as a colorless liquid. Thermometer reads 22 °C.

b) Vacuum stays at 200 millitorr. Heating bath set to 85 °C as the last of the remaining silane boils off.

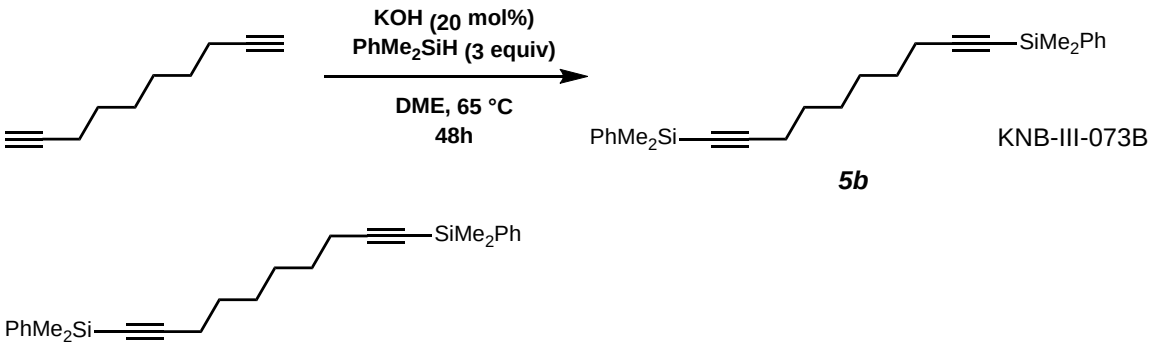
c) Heating bath temperature increased to 125 °C. The solution starts to boil slowly. Thermometer reads 60 °C. Vacuum stays at 200 millitorr.

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 ***4s*** is obtained as a colorless oil (19.0 g, 86% yield).

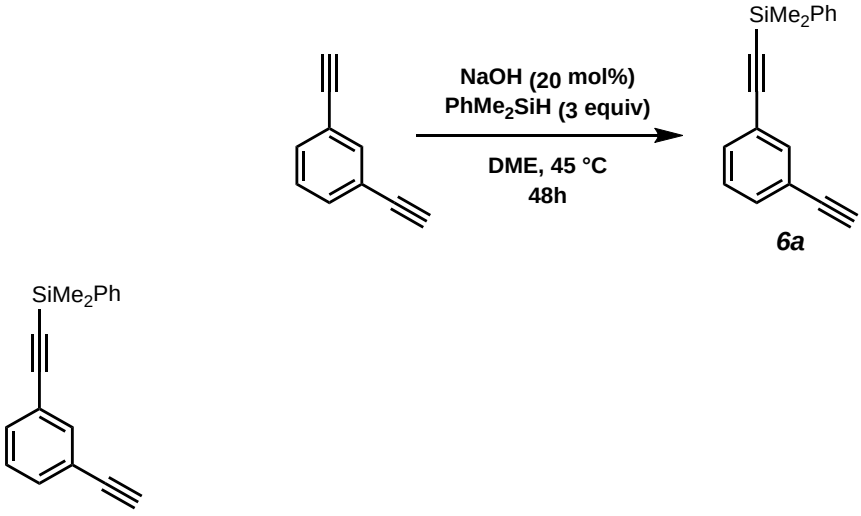
3. Synthesis of *mono*- and *bis*-silylated diynes.



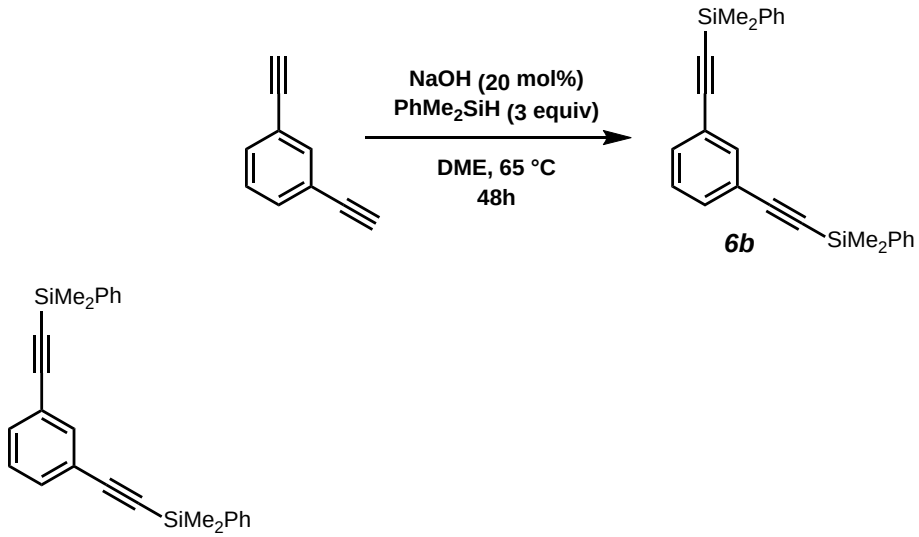
deca-1,9-diyn-1-yldimethyl(phenyl)silane 5a: The general procedure was followed. The reaction was performed with KOH (5.6 mg, 0.1 mmol, 20 mol%), deca-1,9-diyne (67 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 µL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 24 h. The desired product **5a** (126.2 mg, 94% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 20 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **5a** in analytically pure form as a colorless oil. R_f = 0.48 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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, 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.



1,10-bis(dimethyl(phenyl)silyl)deca-1,9-diyne 5b: 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 **5b** (190.9 mg, 95% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **5b** in analytically pure form as a colorless oil. R_f = 0.43 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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 (m, 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.



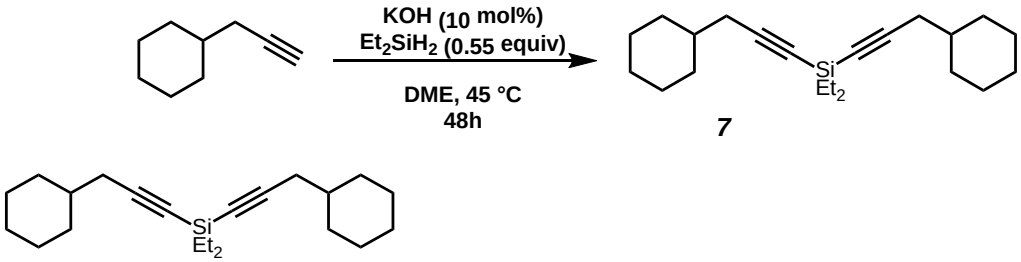
((3-ethynylphenyl)ethynyl)dimethyl(phenyl)silane 6a: The general procedure was followed. The reaction was performed with NaOH (4.0 mg, 0.1 mmol, 20 mol%), 1,3-diethynylbenzene (63 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **6a** (99.2 mg, 76% yield) was obtained in 85% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes → 3% EtOAc in hexanes) yielded the product **6a** in analytically pure form as a colorless oil. R_f = 0.27 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.70 – 7.68 (m, 2H), 7.64 (t, J = 1.6 Hz, 1H), 7.46 (ddt, J = 14.2, 7.8, 1.4 Hz, 2H), 7.41 (dd, J = 4.9, 1.9 Hz, 3H), 7.29 (dd, J = 7.7, 0.6 Hz, 1H), 3.09 (s, 1H), 0.51 (d, J = 0.5 Hz, 6H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 136.86, 135.71, 133.86, 132.38, 132.35, 129.66, 128.48, 128.09, 123.43, 122.51, 105.63, 93.20, 82.78, 77.99, -0.75. IR (Neat Film NaCl) 3294, 2950, 2152, 1474, 1428, 1249, 1118, 924, 838, 818, 781, 731, 698 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{17}Si$ [M+H]: 261.1100, found 261.1093.



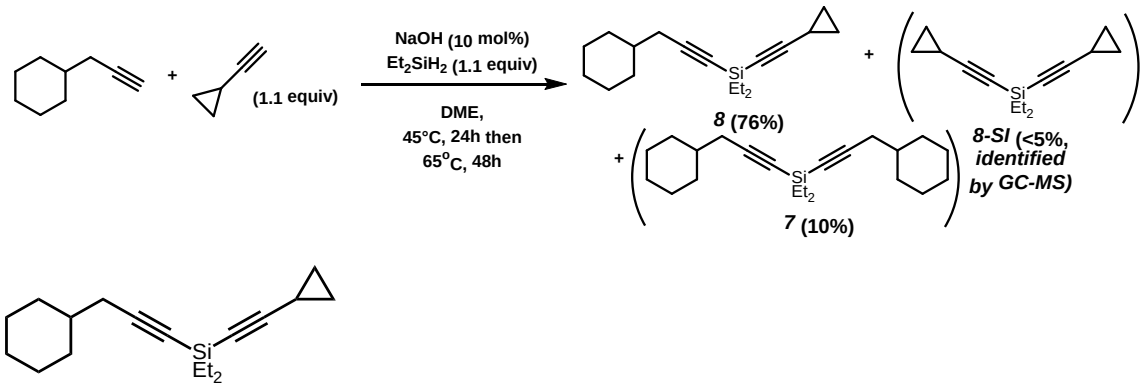
1,3-bis((dimethyl(phenyl)silyl)ethynyl)benzene 6b: The general procedure was followed. The reaction was performed with NaOH (4.0 mg, 0.1 mmol, 20 mol%), 1,3-diethynylbenzene (63 mg, 0.5 mmol, 1.0 equiv.), $PhMe_2SiH$ (204 mg, 230 μL, 1.5 mmol, 3.0 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 48 h. The desired product **6b** (173.5 mg, 88% yield) was obtained in 95% purity after heating to 85°C at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100%

hexanes → 3% EtOAc in hexanes) yielded the product **6b** in analytically pure form as a light yellow oil. R_f = 0.26 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

4. Synthesis of symmetric and unsymmetric diethynylsilanes.

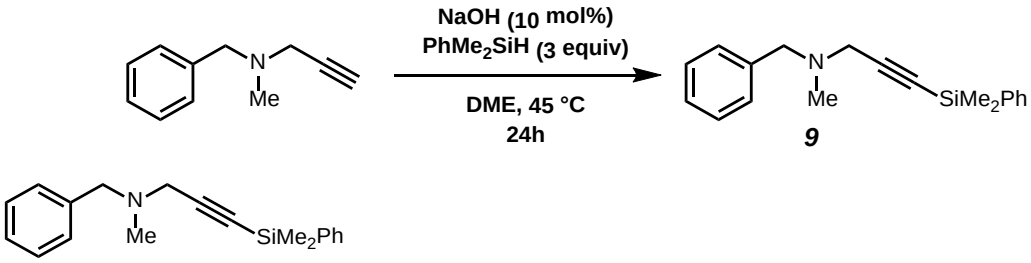


bis(3-cyclohexylprop-1-yn-1-yl)diethylsilane 7: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv.), Et_2SiH_2 (24 mg, 36 μL, 0.275 mmol, 0.55 equiv.), and 0.5 mL of tetrahydrofuran (THF) at 45 °C for 48 h. The desired product **7** (125.0 mg, 76% yield) was obtained in 90% purity after high vacuum at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **7** as a colorless oil. R_f = 0.51 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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, 4H), 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.

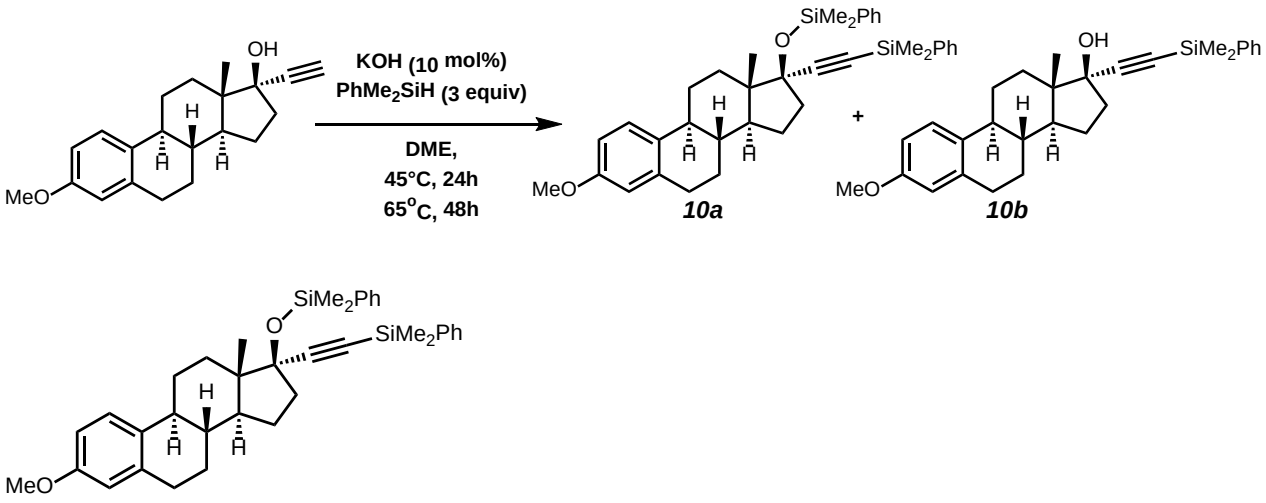


(3-cyclohexylprop-1-yn-1-yl)(cyclopropylethynyl)diethylsilane 8: The general procedure was followed. The reaction was performed with NaOH (2.0 mg, 0.05 mmol, 10 mol%), cyclohexylpropyne (61 mg, 0.5 mmol, 1.0 equiv.), cyclopropylacetylene (36 mg, 0.55 mmol, 1.1 equiv.), Et_2SiH_2 (49 mg, 71 μL, 0.55 mmol, 1.1 equiv.), and 0.5 mL of 1,2-dimethoxyethane (DME) at 45 °C for 24 h, then 65 °C for 48 h. The desired product **8** (102.8 mg, 76% yield) was obtained in 90% purity after high vacuum at 45 mtorr for 30 minutes; subsequent purification by silica gel flash chromatography (100% hexanes) yielded the product **8** as a colorless oil. Also isolated was 10% yield of the homocoupled 3-cyclohexyl-1-propyne product **7**; <5% of the homocoupled cyclopropylacetylene **8-SI** was identified by GC-MS. This same product **xx** can be achieved in comparable yield (106.4 mg, 78% yield) in a 2-step process by first isolating the silylated cyclohexylpropyne **2e** and then combining this pre-silylated product with cyclopropylacetylene (1.1 equiv.) and NaOH (10 mol %). R_f = 0.34 (100% hexanes); ^{1}H NMR (500 MHz, Chloroform-*d*) 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.

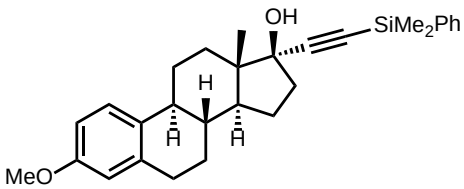
5. Late-stage silylation of pharmaceuticals.



N-benzyl-3-(dimethyl(phenyl)silyl)-N-methylprop-2-yn-1-amine 9: 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 **9** (140.4 mg, 95.7% yield) was obtained as a pale yellow oil after heating to 85°C at 45 mtorr for 30 minutes. ^{1}H NMR (500 MHz, Chloroform-*d*) 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.



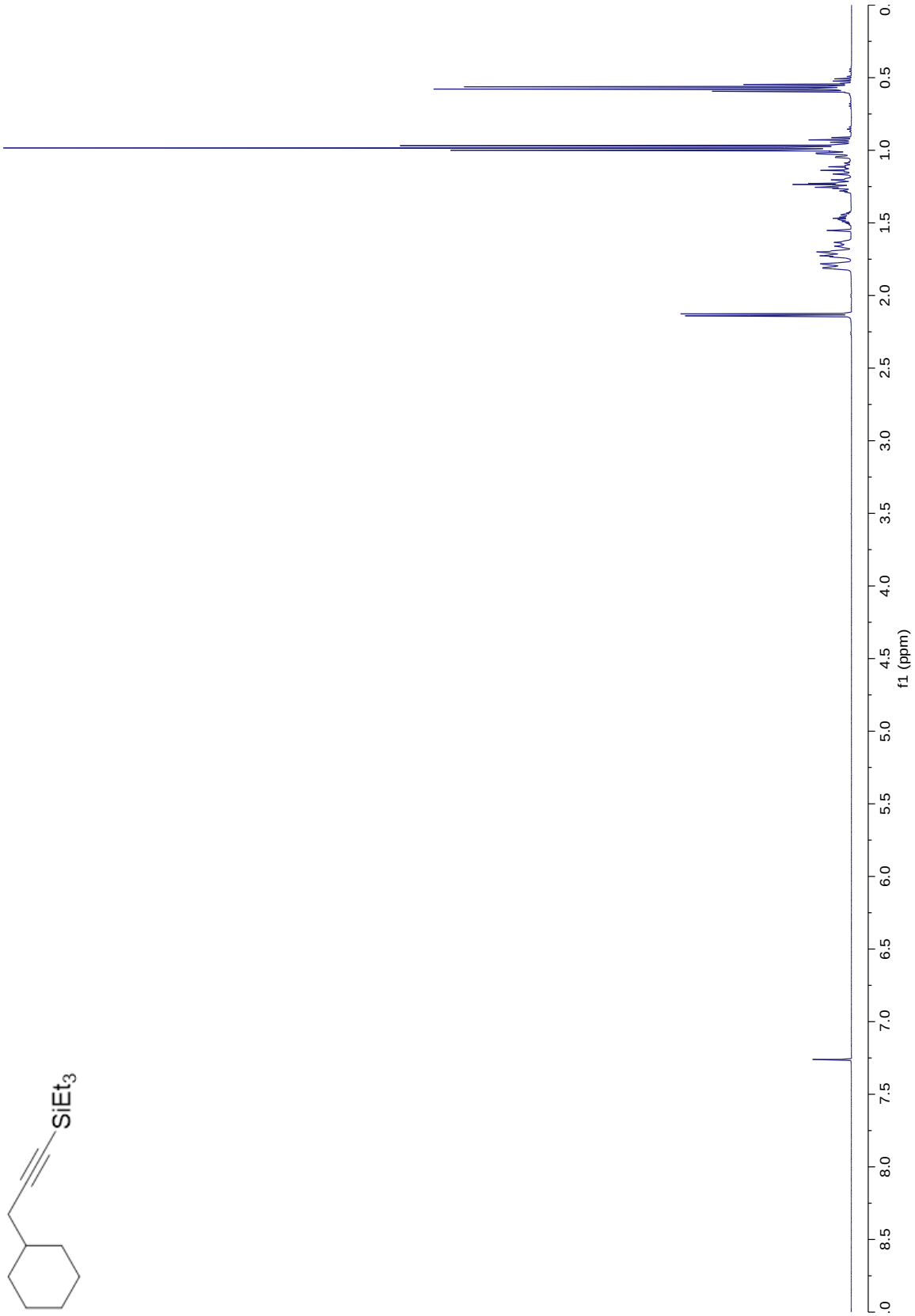
(((8R,9S,13S,14S,17S)-17-((dimethyl(phenyl)silyl)ethynyl)-3-methoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-17-yl)oxy)dimethyl(phenyl)silane 10a: The general procedure was followed. The reaction was performed with KOH (2.8 mg, 0.05 mmol, 20 mol%), mestranol ((8R,9S,13S,14S,17R)-17-ethynyl-3-methoxy-13-methyl- 7,8,9,11,12,13,14,15,16,17- decahydro -6H-cyclopenta[a]phenanthren-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 **10a** (62.7 mg, 28.2% yield) was obtained as a colorless oil by silica gel flash chromatography (1% → 5% EtOAc in hexanes). R_f = 0.52 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, THF-*d8*) δ 7.62 – 7.56 (m, 4H), 7.30 (dtq, J = 9.6, 5.1, 2.2 Hz, 6H), 7.16 (d, J = 8.6 Hz, 1H), 6.63 (dd, J = 8.5, 2.7 Hz, 1H), 6.59 – 6.55 (m, 1H), 3.69 (d, J = 1.0 Hz, 3H), 2.88 – 2.75 (m, 2H), 2.42 – 2.23 (m, 2H), 2.18 (qd, J = 10.8, 10.1, 3.5 Hz, 1H), 2.11 – 1.95 (m, 2H), 1.94 – 1.85 (m, 1H), 1.83 – 1.74 (m, 2H), 1.54 – 1.38 (m, 3H), 1.34 (ddt, J = 24.2, 12.3, 5.9 Hz, 1H), 0.94 (d, J = 2.0 Hz, 3H), 0.52 – 0.43 (m, 6H), 0.38 – 0.32 (m, 6H).^{13}C NMR (126 MHz, thf) δ 158.87, 140.78, 138.42, 134.65, 134.38, 133.09, 130.31, 129.98, 128.73, 128.45, 127.12, 114.47, 112.88, 112.37, 90.44, 82.68, 55.34, 51.46, 49.86, 49.47, 45.16, 41.66, 40.95, 34.17, 30.86, 28.64, 27.69, 24.01, 17.10, 13.81, 1.44, -0.61. 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.



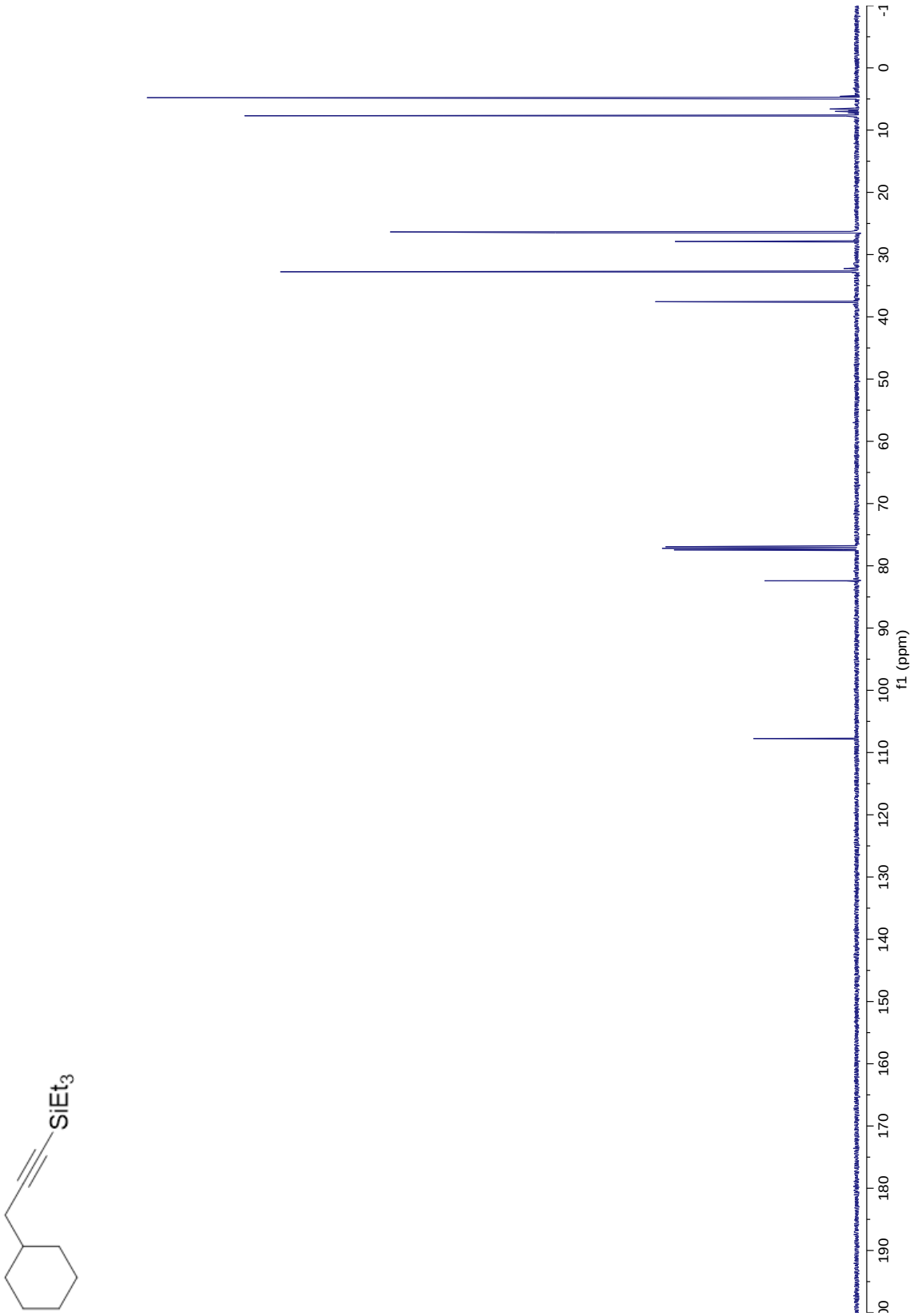
(8R,9S,13S,14S,17S)-17-((dimethyl(phenyl)silyl)ethynyl)-3-methoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-17-ol 10b: The desired product **10b** (137.4 mg, 61.8% yield) was also obtained from this reaction as a white solid foam by silica gel flash chromatography (1% → 5% EtOAc in hexanes). R_f = 0.39 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, THF-*d8*) δ 7.62 – 7.56 (m, 2H), 7.32 –

7.27 (m, 3H), 7.05 (dd, J = 8.8, 0.9 Hz, 1H), 6.60 (dd, J = 8.5, 2.8 Hz, 1H), 6.57 (d, J = 2.7 Hz, 1H), 5.68 (s, 1H), 3.71 (s, 3H), 2.82 – 2.78 (m, 2H), 2.33 – 2.26 (m, 1H), 2.24 – 2.16 (m, 3H), 2.00 (ddd, J = 13.3, 11.9, 4.1 Hz, 1H), 1.90 – 1.81 (m, 3H), 1.68 – 1.60 (m, 1H), 1.40 (ddd, J = 10.3, 7.7, 3.0 Hz, 3H), 1.33 – 1.27 (m, 1H), 0.91 (s, 3H), 0.44 (d, J = 1.5 Hz, 6H); ^{13}C NMR (126 MHz, thf) δ 158.91, 140.86, 138.41, 134.21, 132.92, 130.05, 128.59, 127.30, 114.45, 112.45, 91.04, 82.87, 55.37, 49.97, 49.45, 48.26, 45.20, 40.94, 40.81, 37.16, 34.18, 30.91, 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]: 455.2563, found 455.2575.

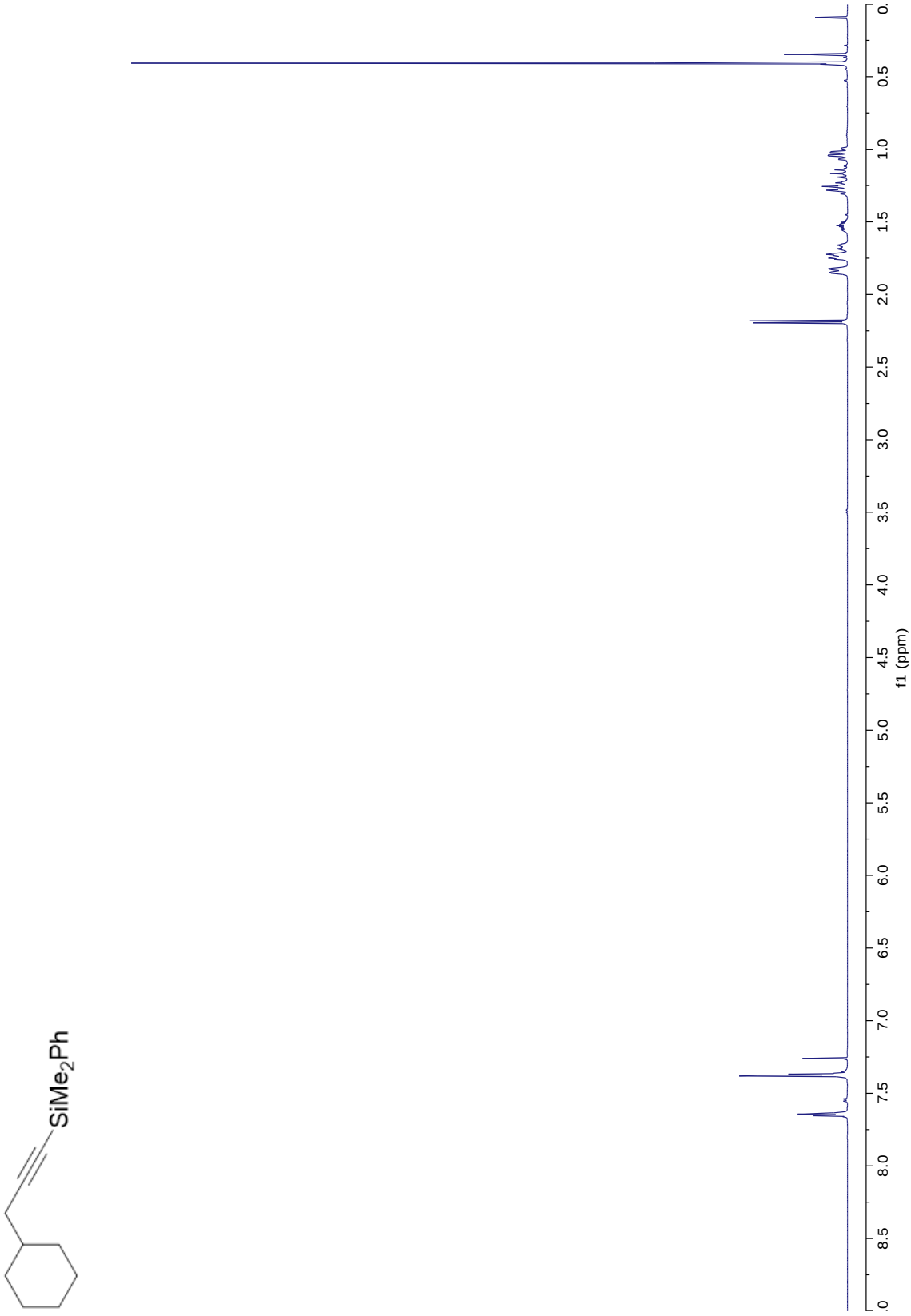
Part III. ^{1}H NMR and ^{13}C NMR Spectra of New Compounds



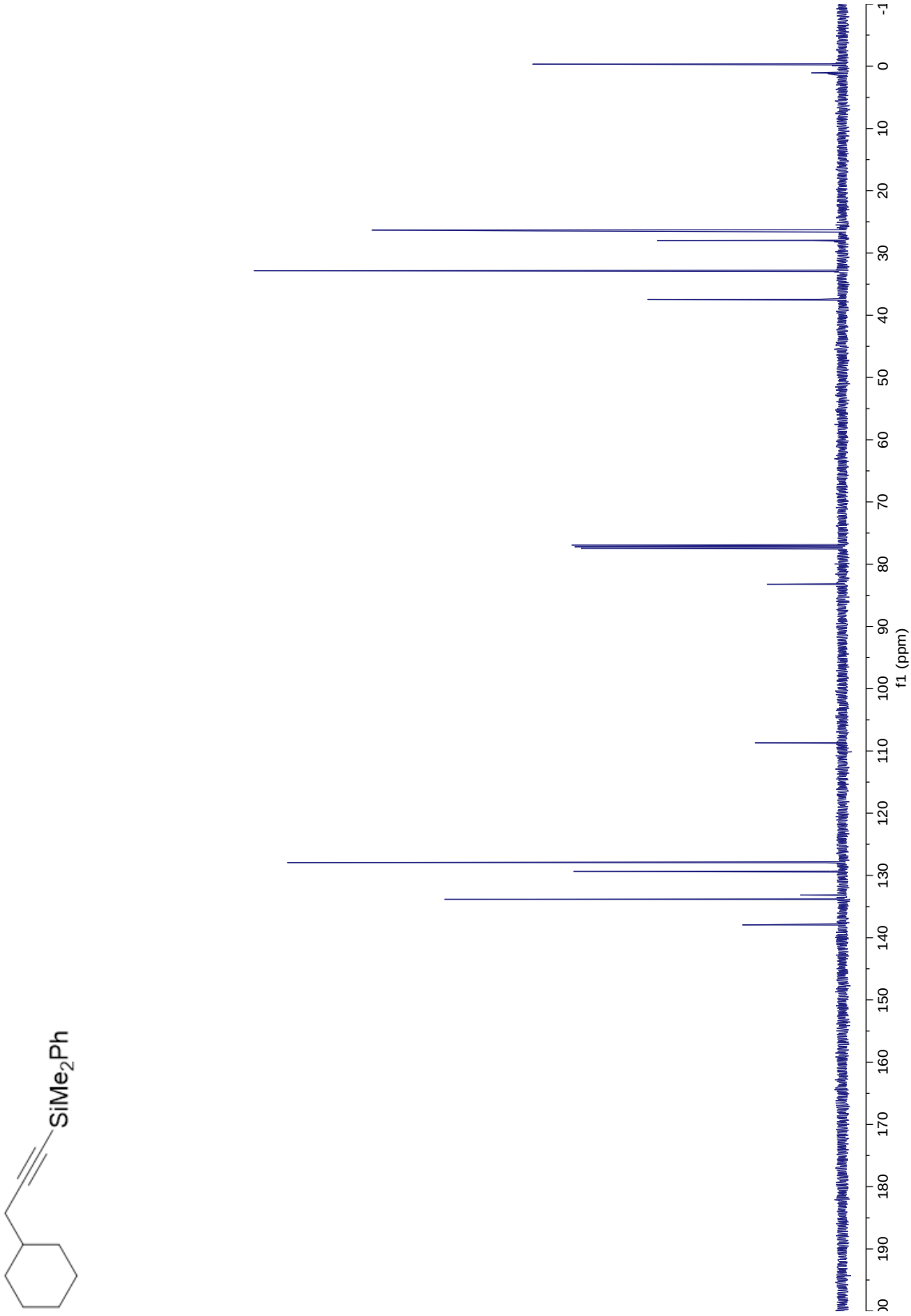
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2a**.



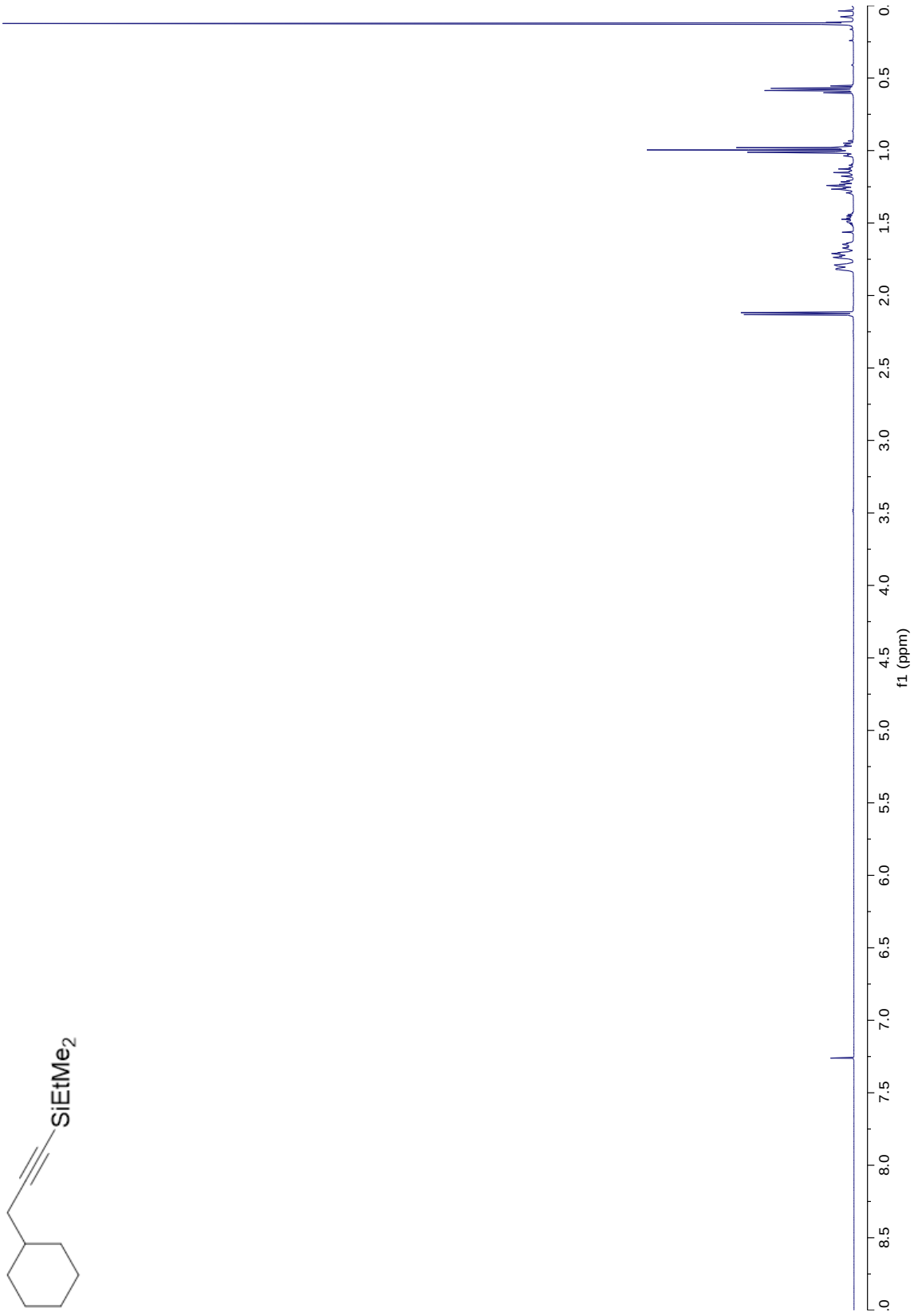
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2a.**



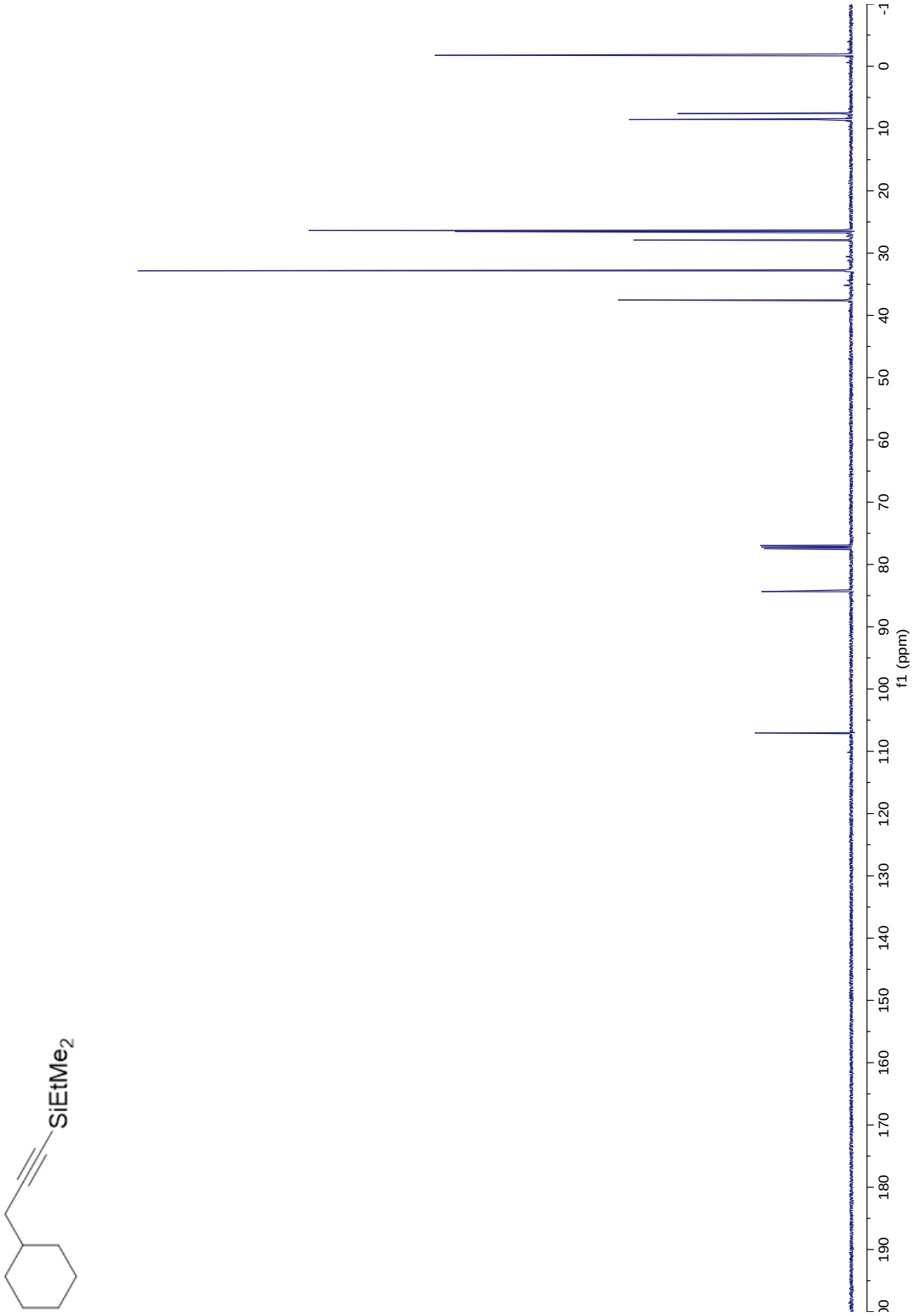
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2b.**



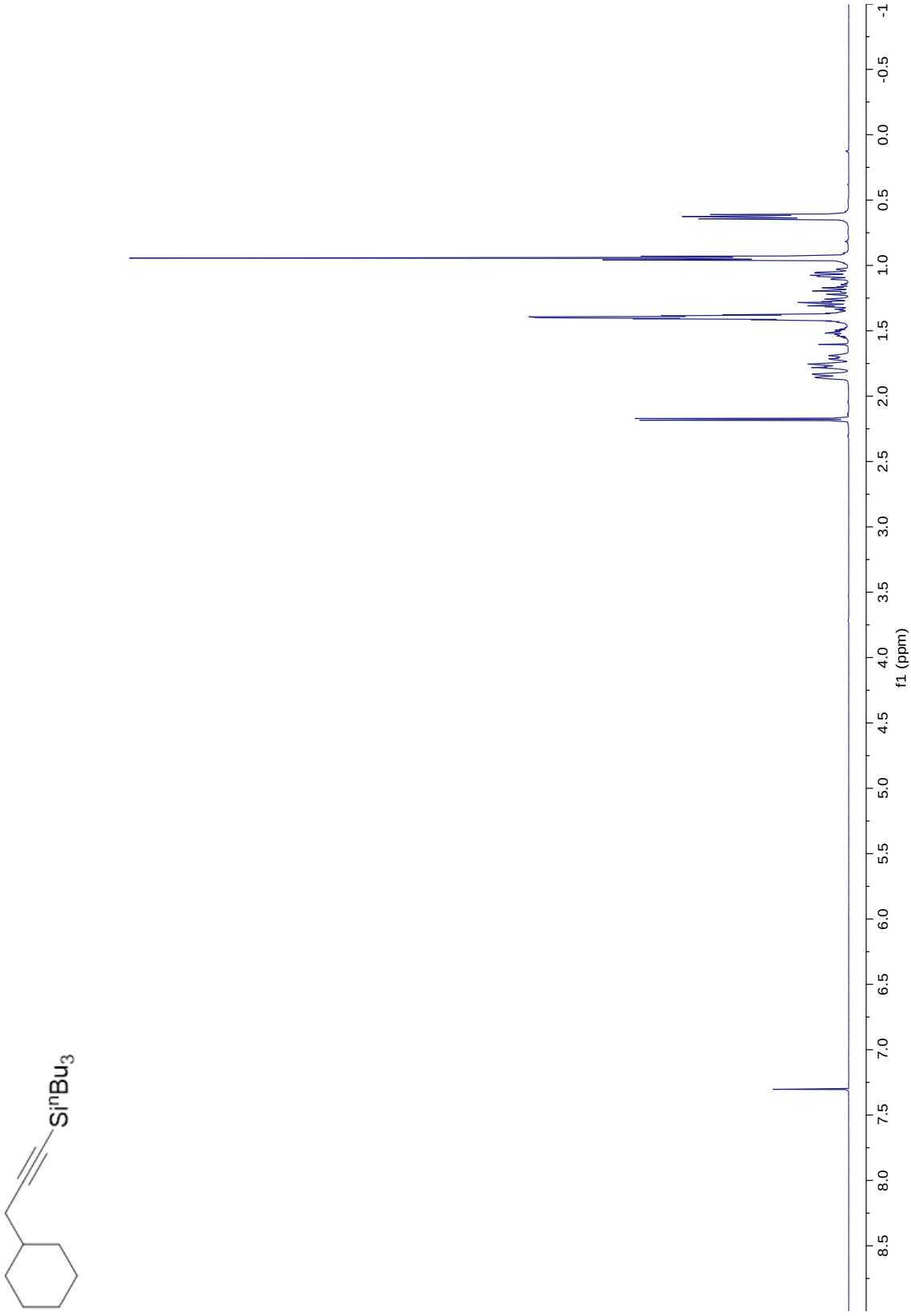
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2b.**



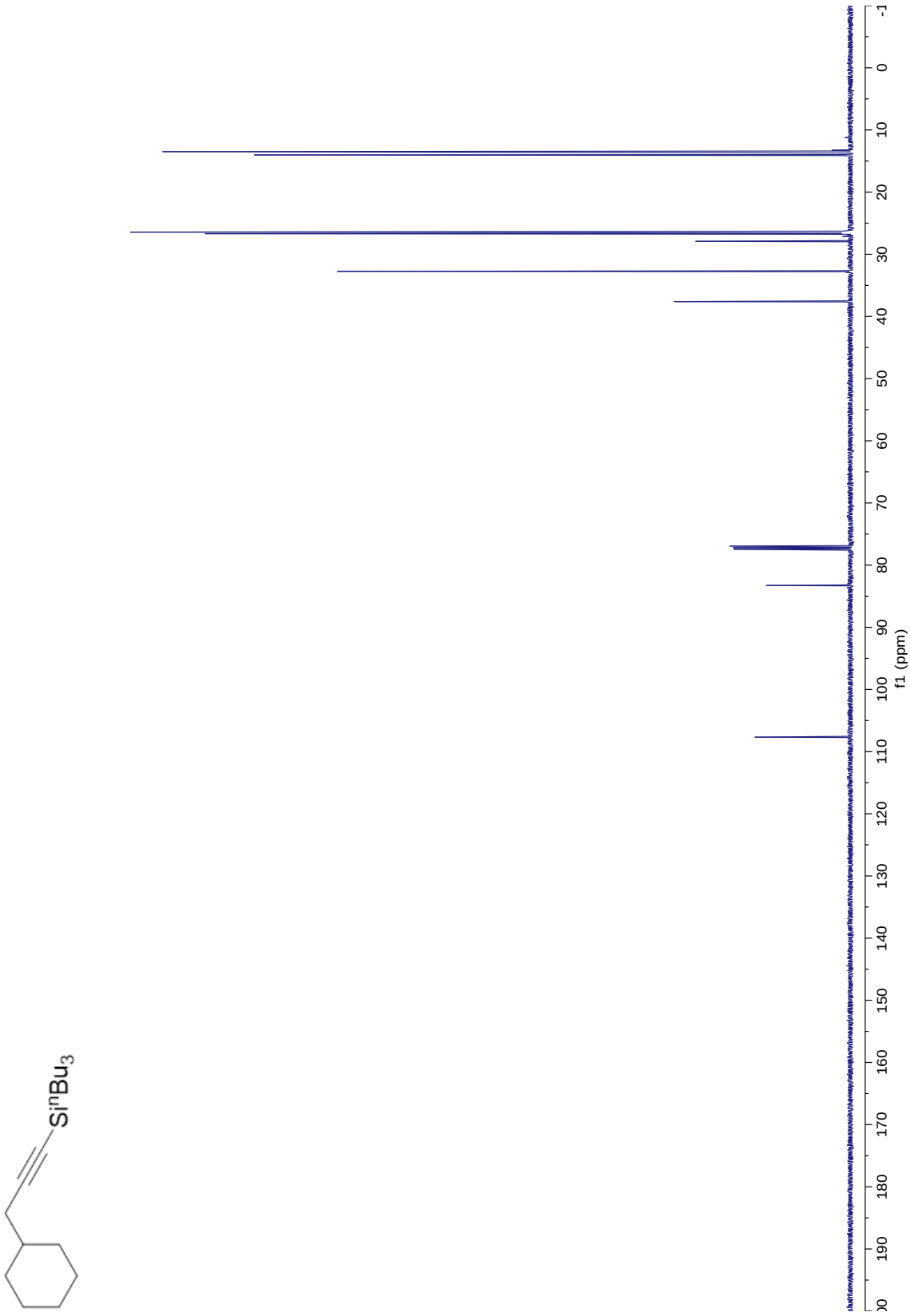
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2c.**



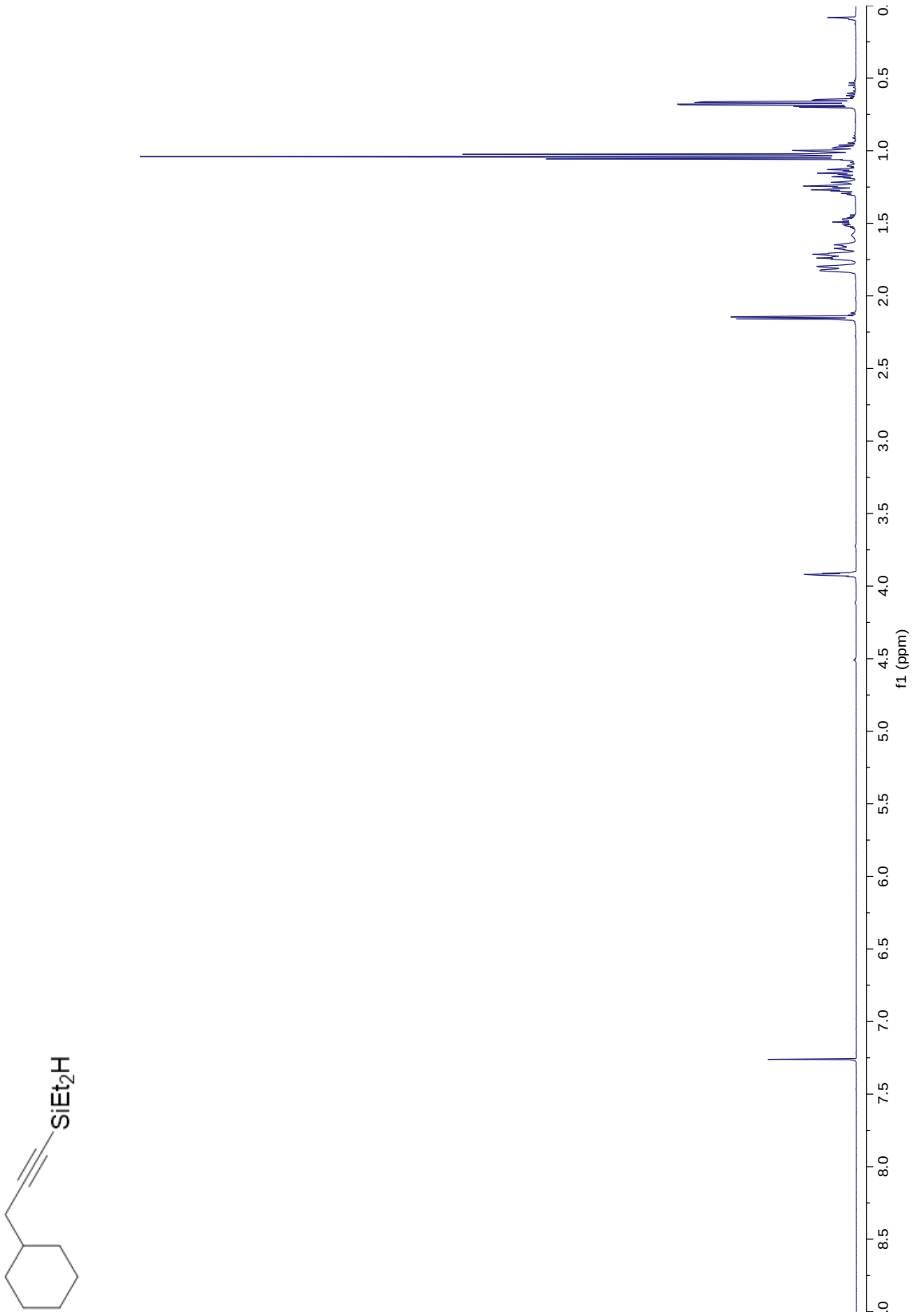
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2c.**



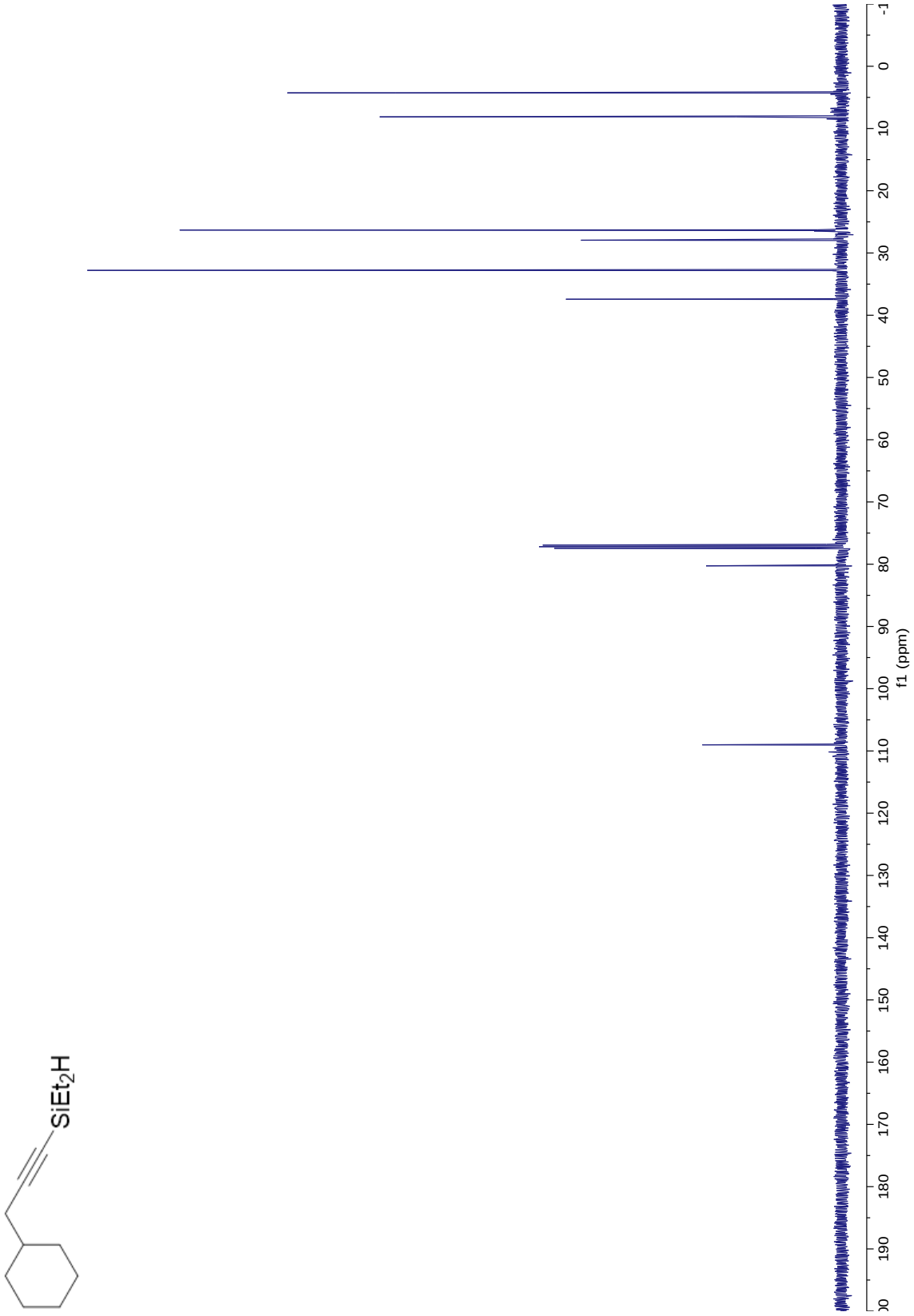
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2d.**



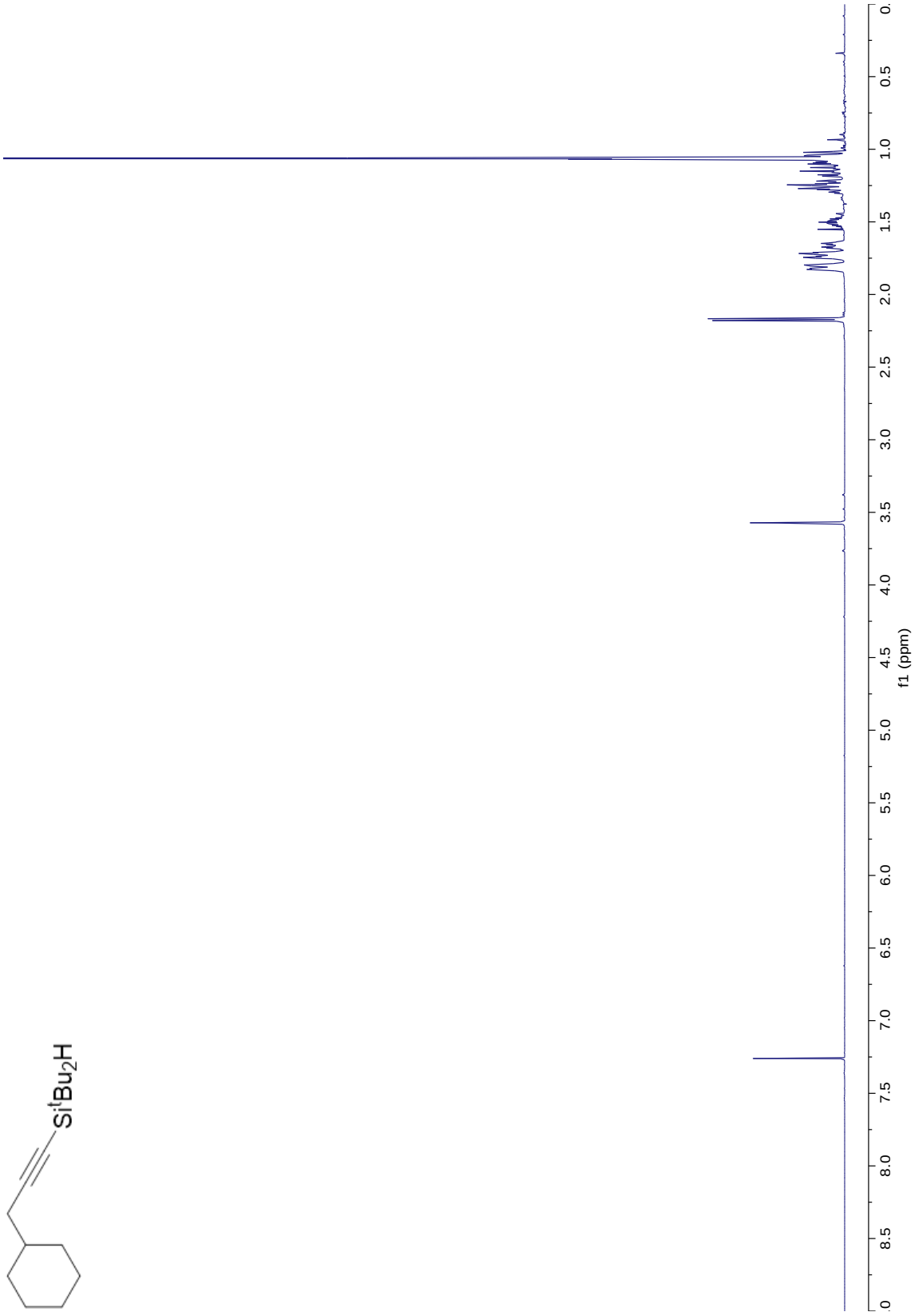
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2d.**



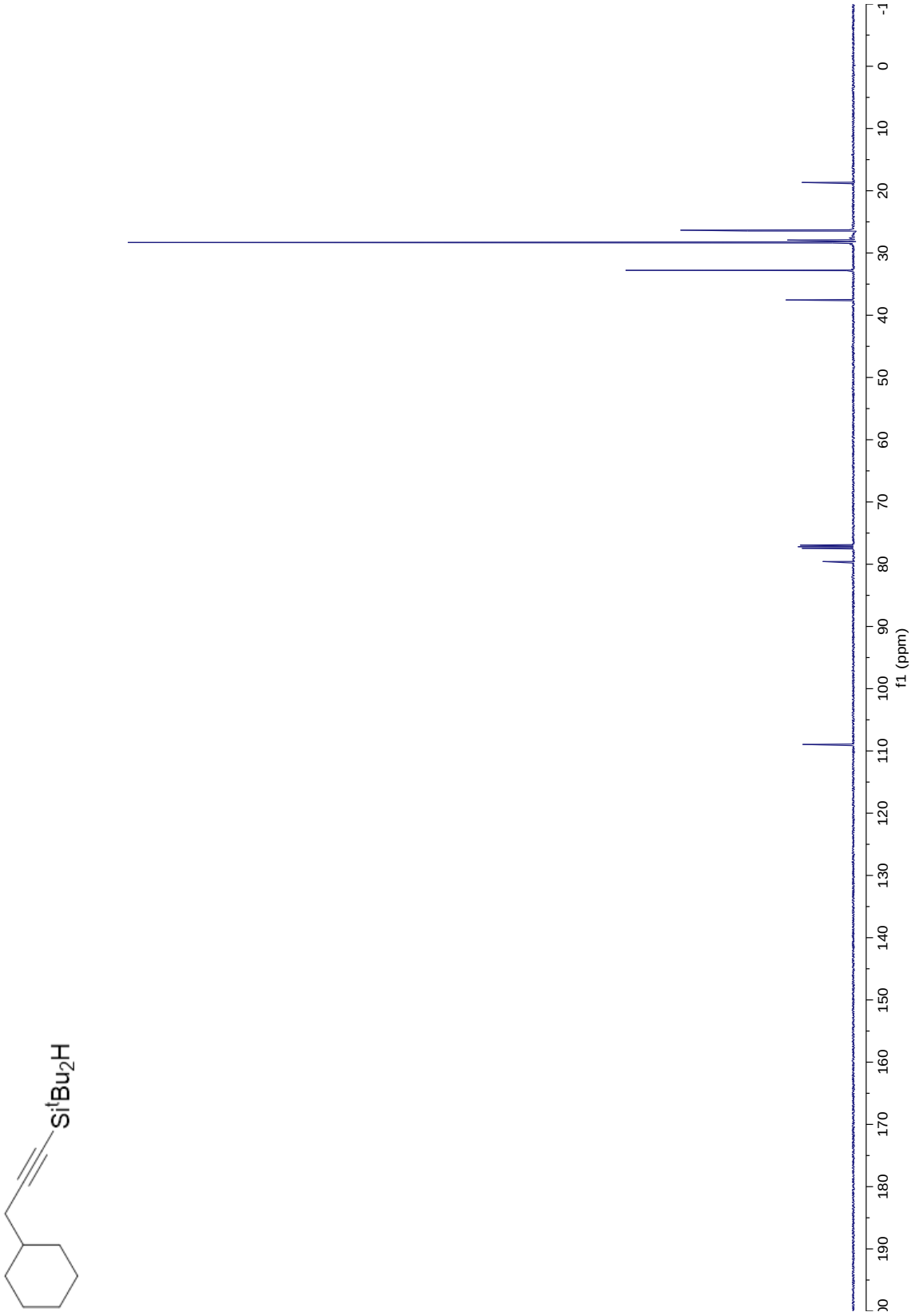
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2e.**



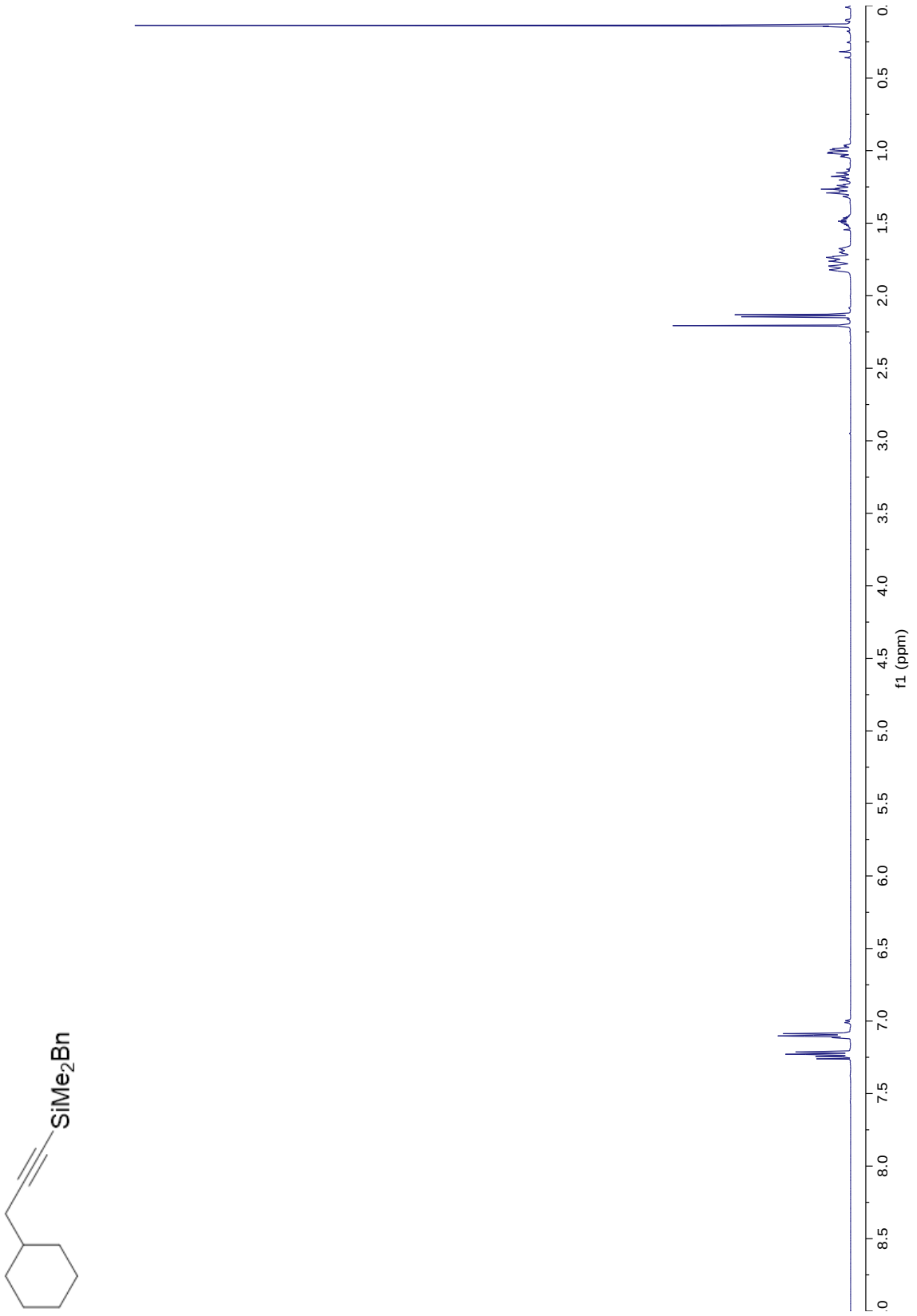
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2e.**



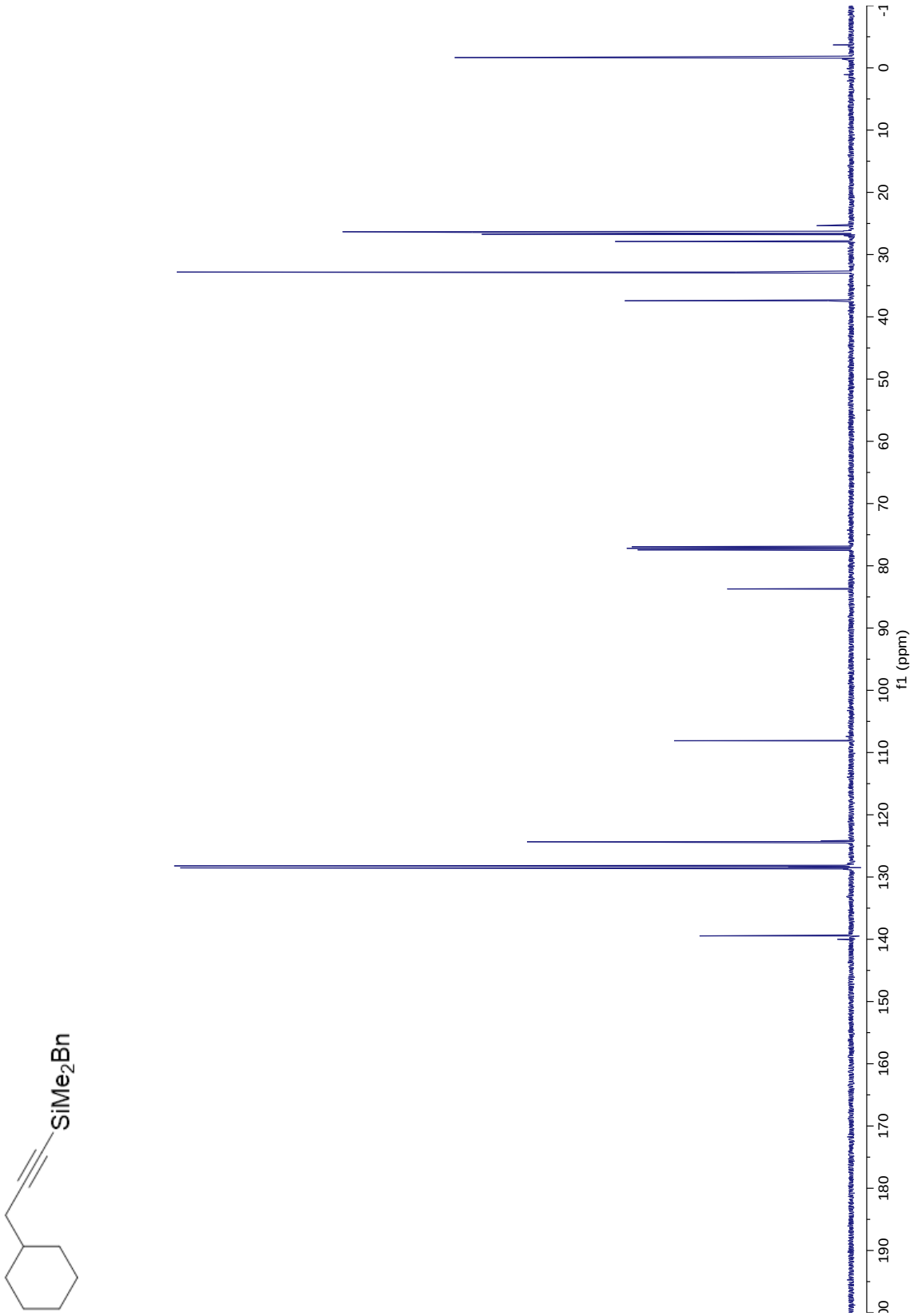
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2f.**



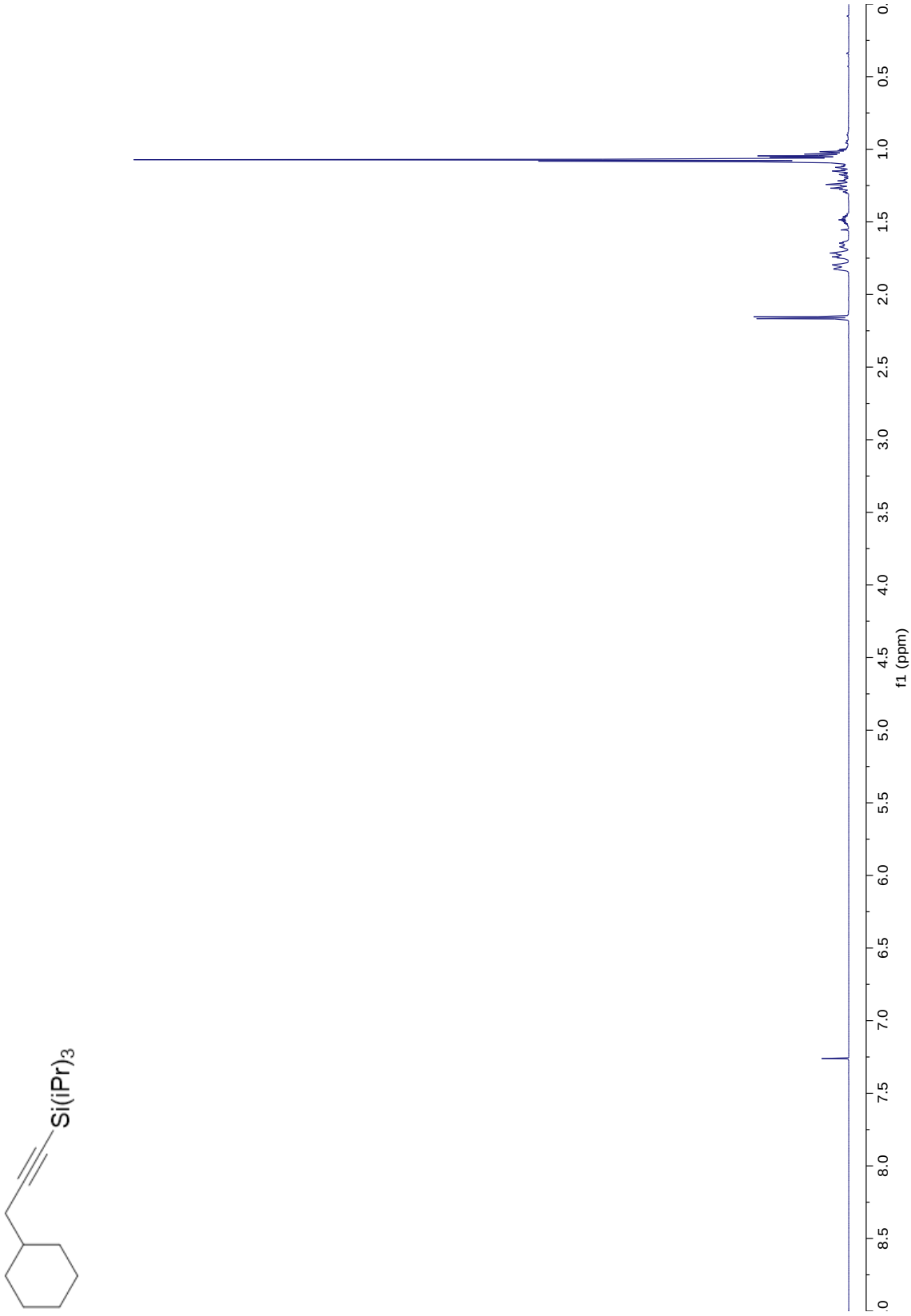
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2f.**



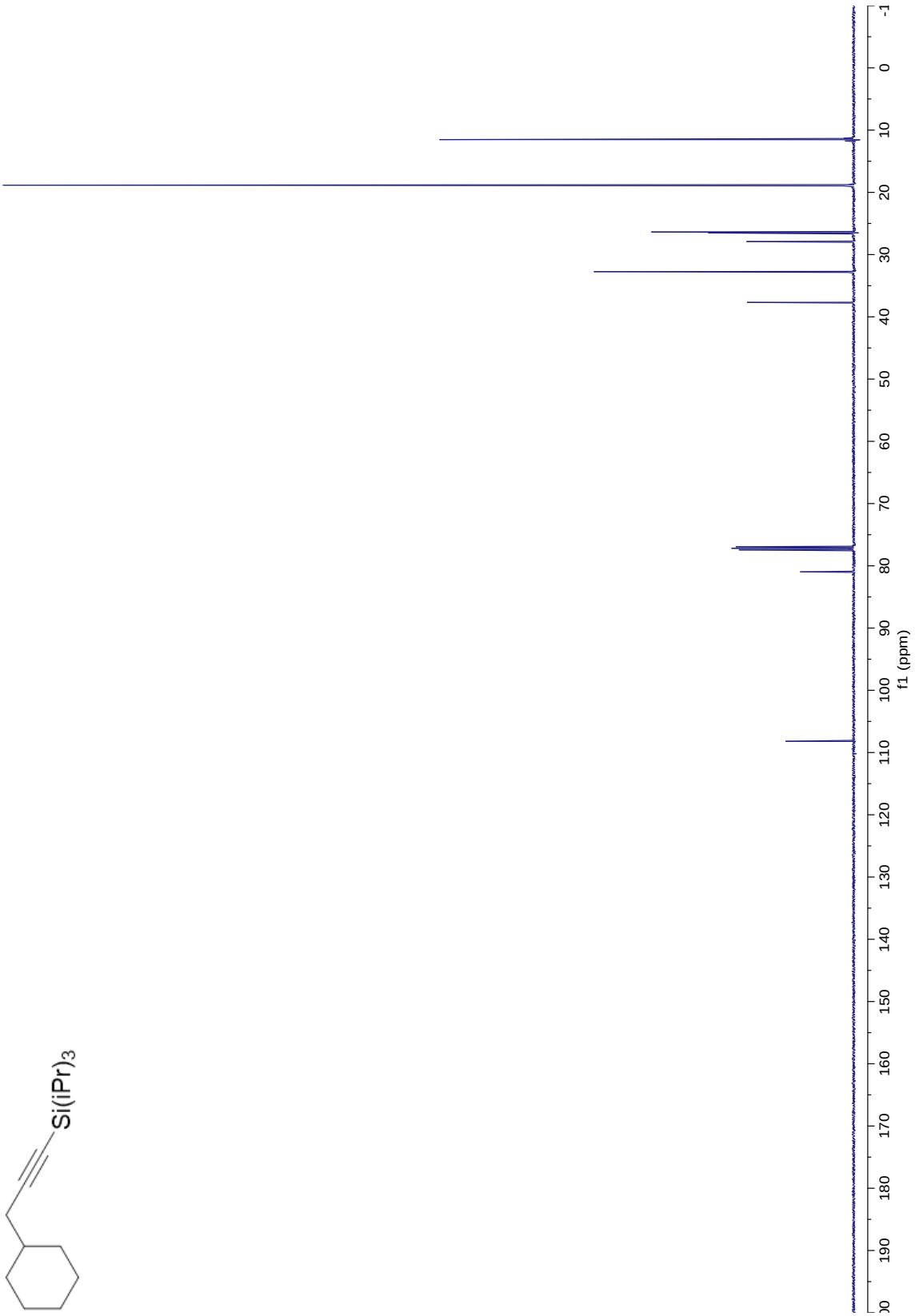
^{1}H NMR (500 MHz, $CDCl_3$ of compound **2g.**



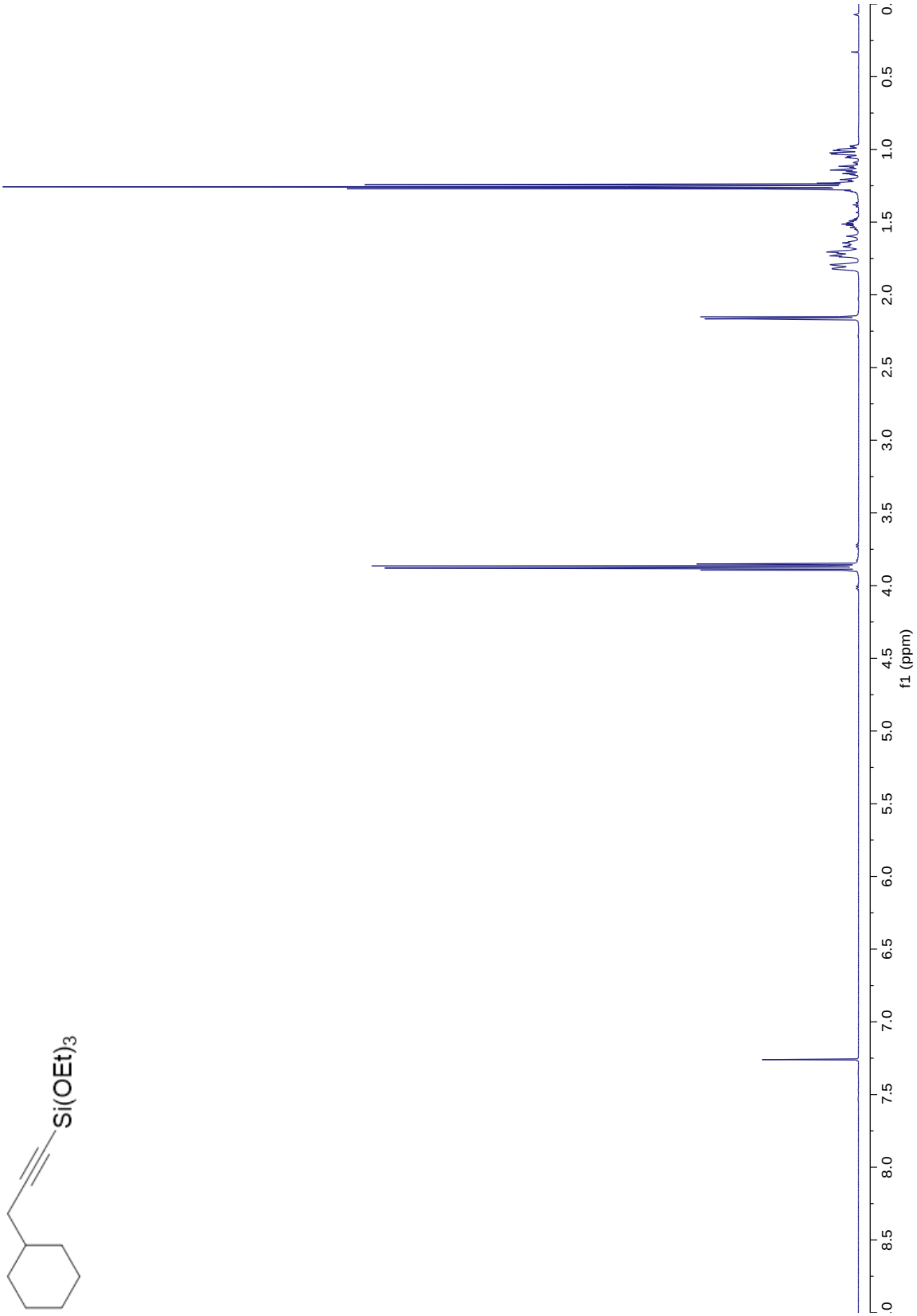
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2g.**



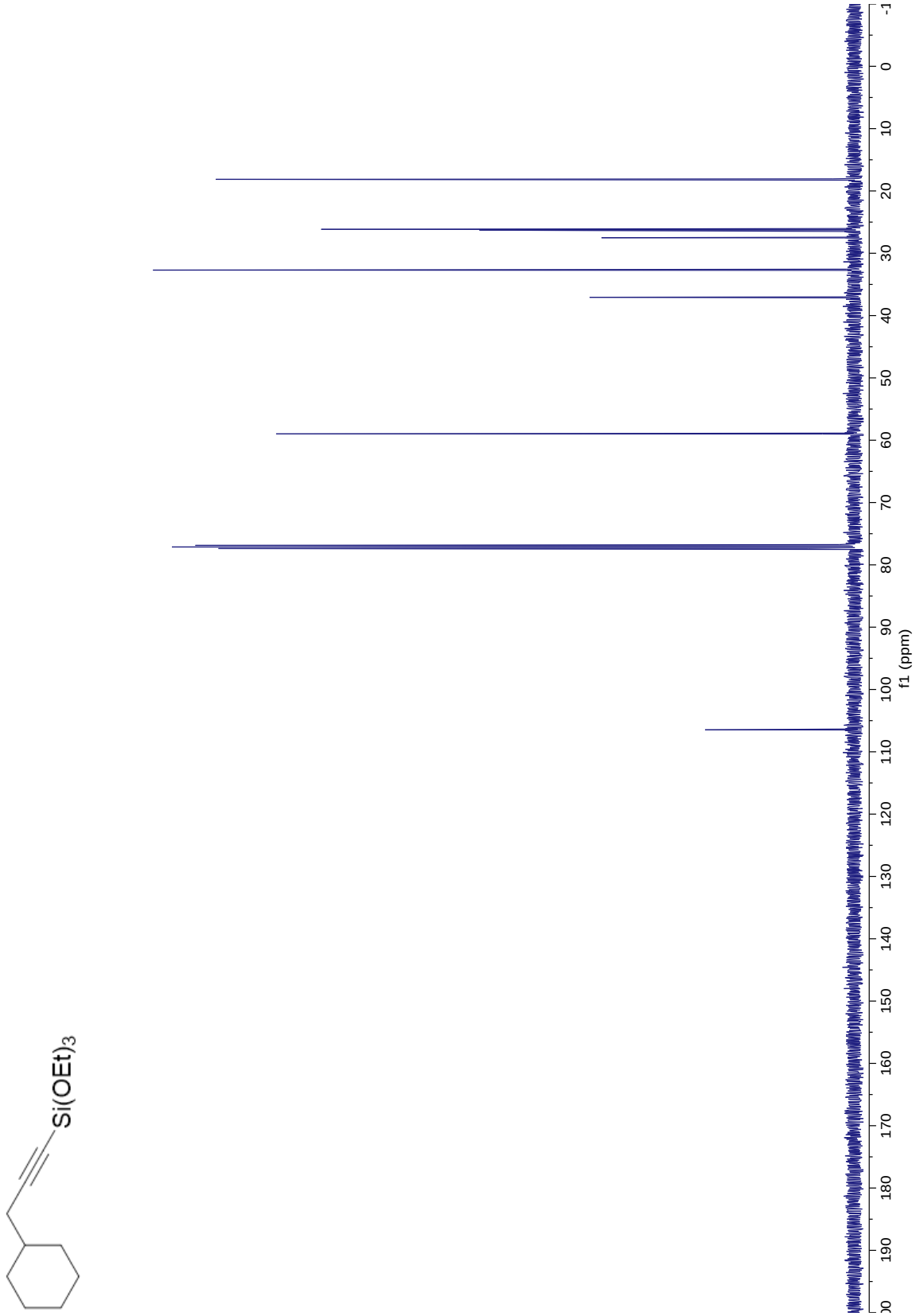
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2h.**



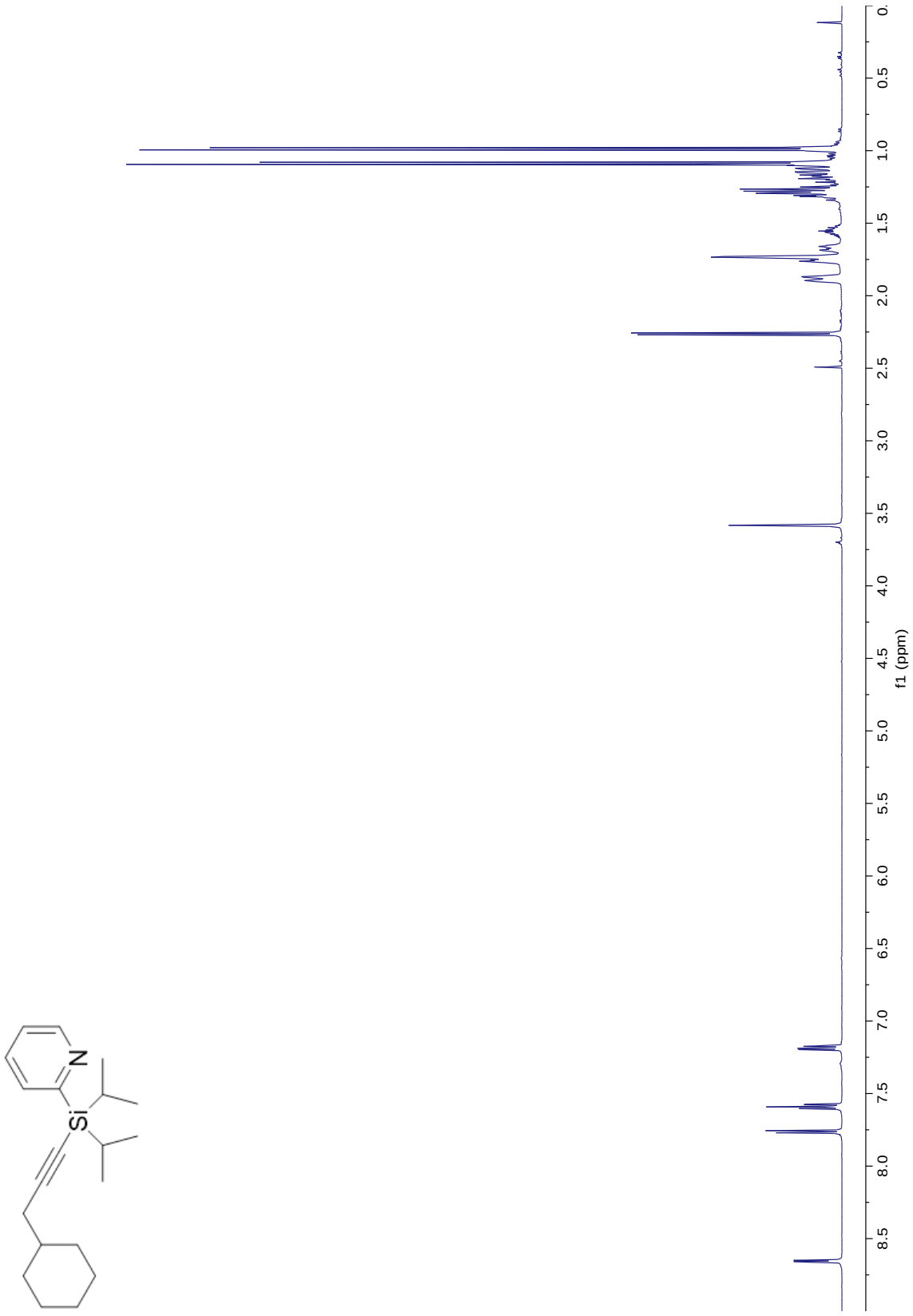
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2h.**



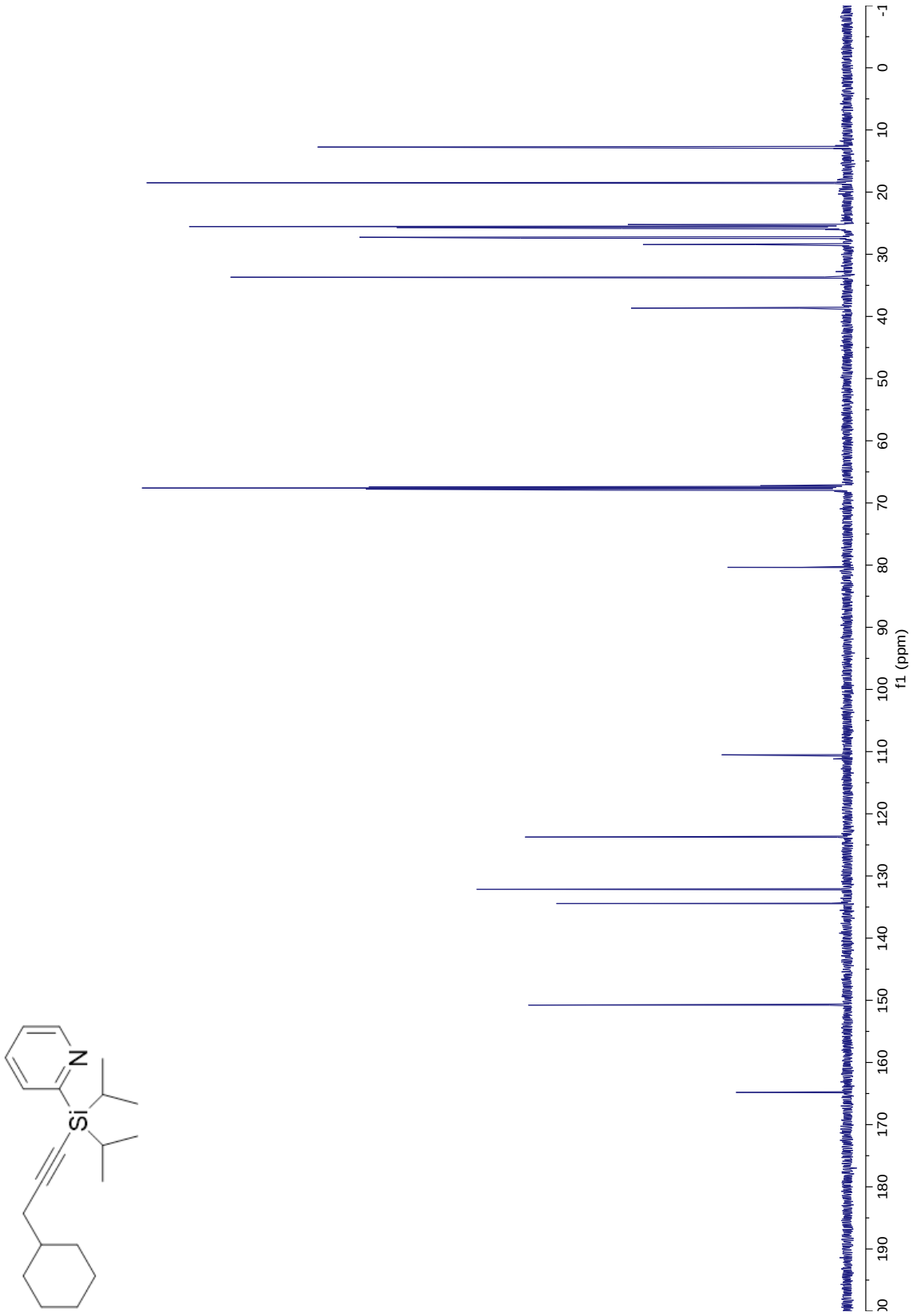
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2i.**



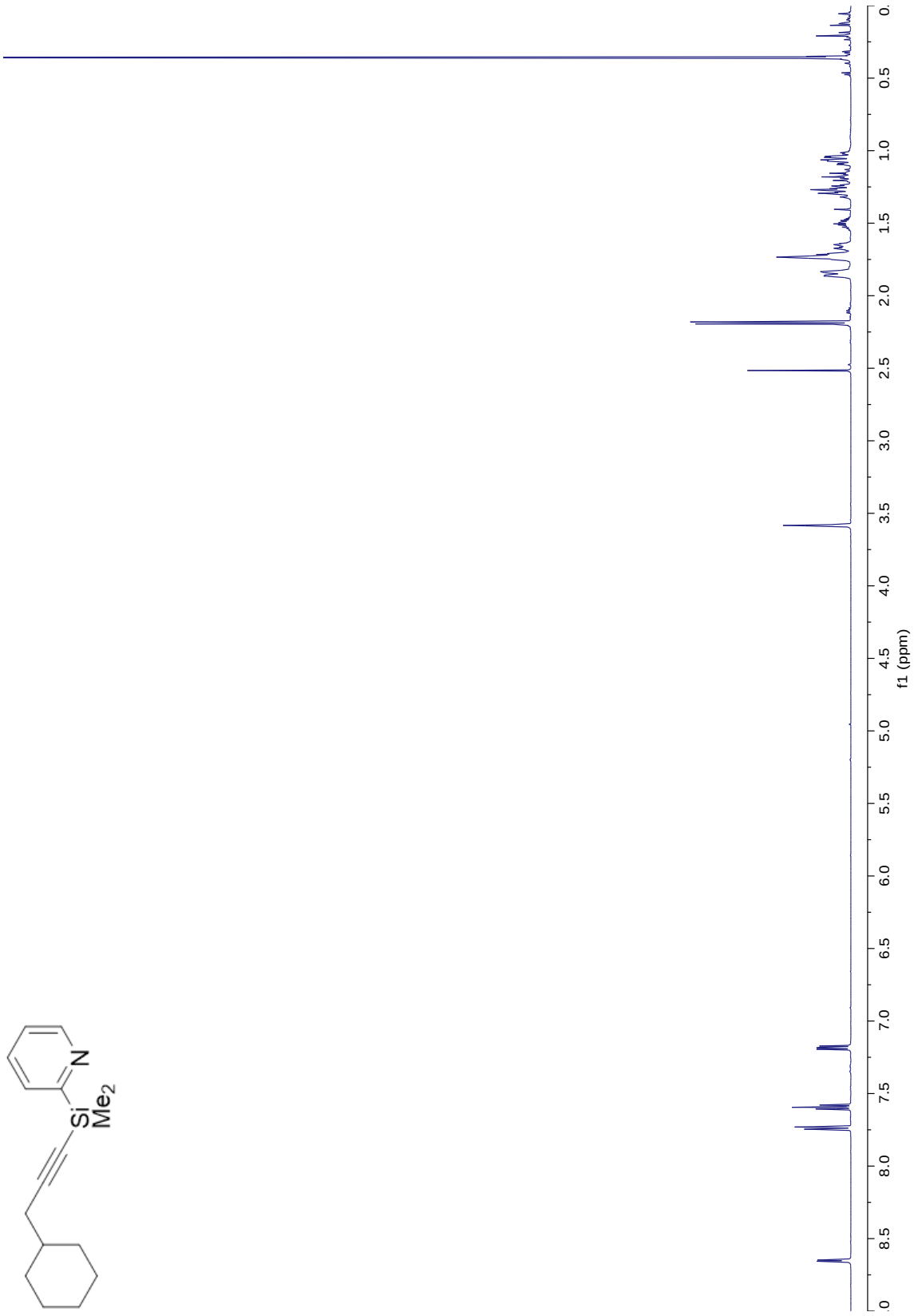
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2i.**



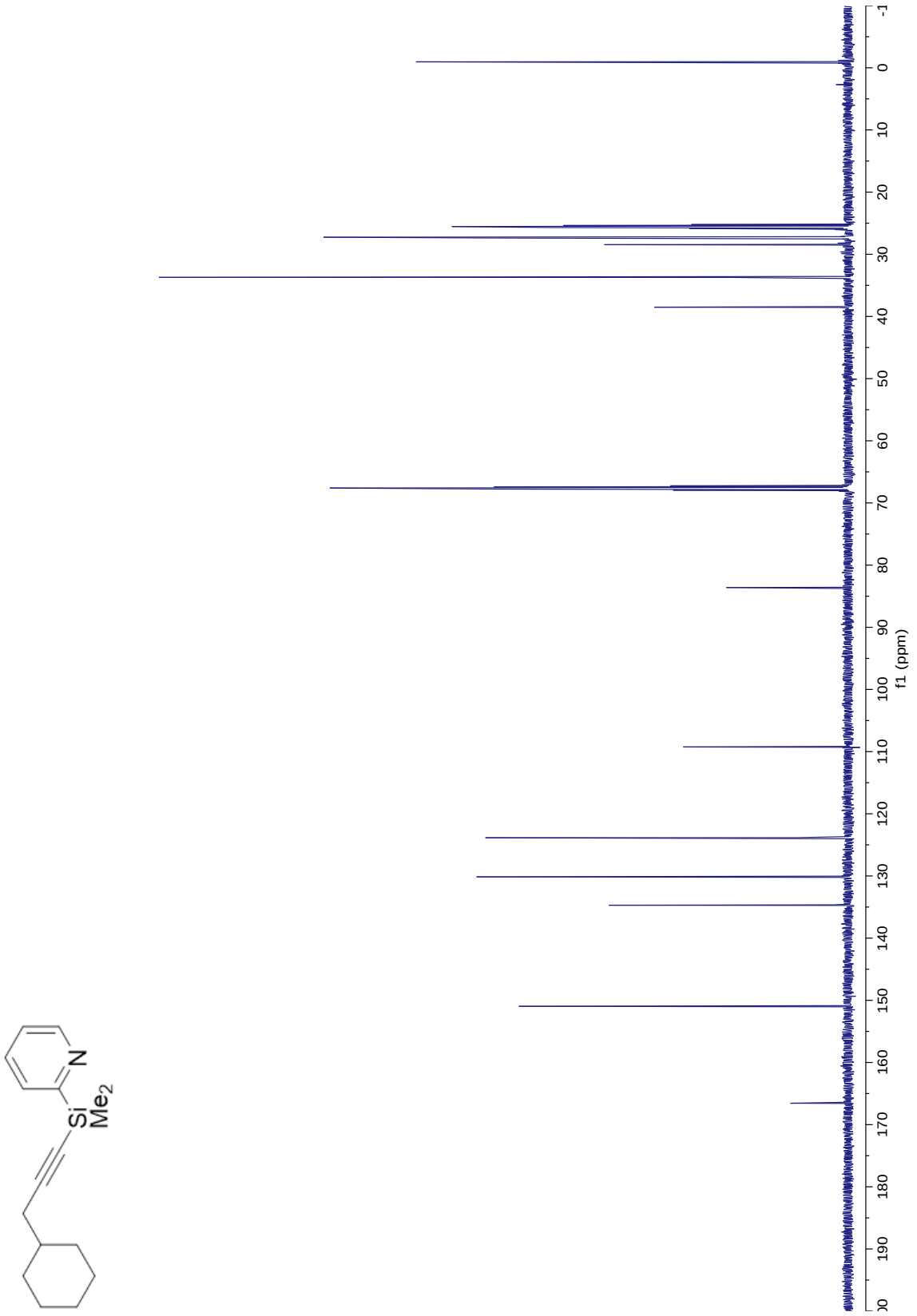
^{1}H NMR (500 MHz, THF-*d8*) of compound **2j.**



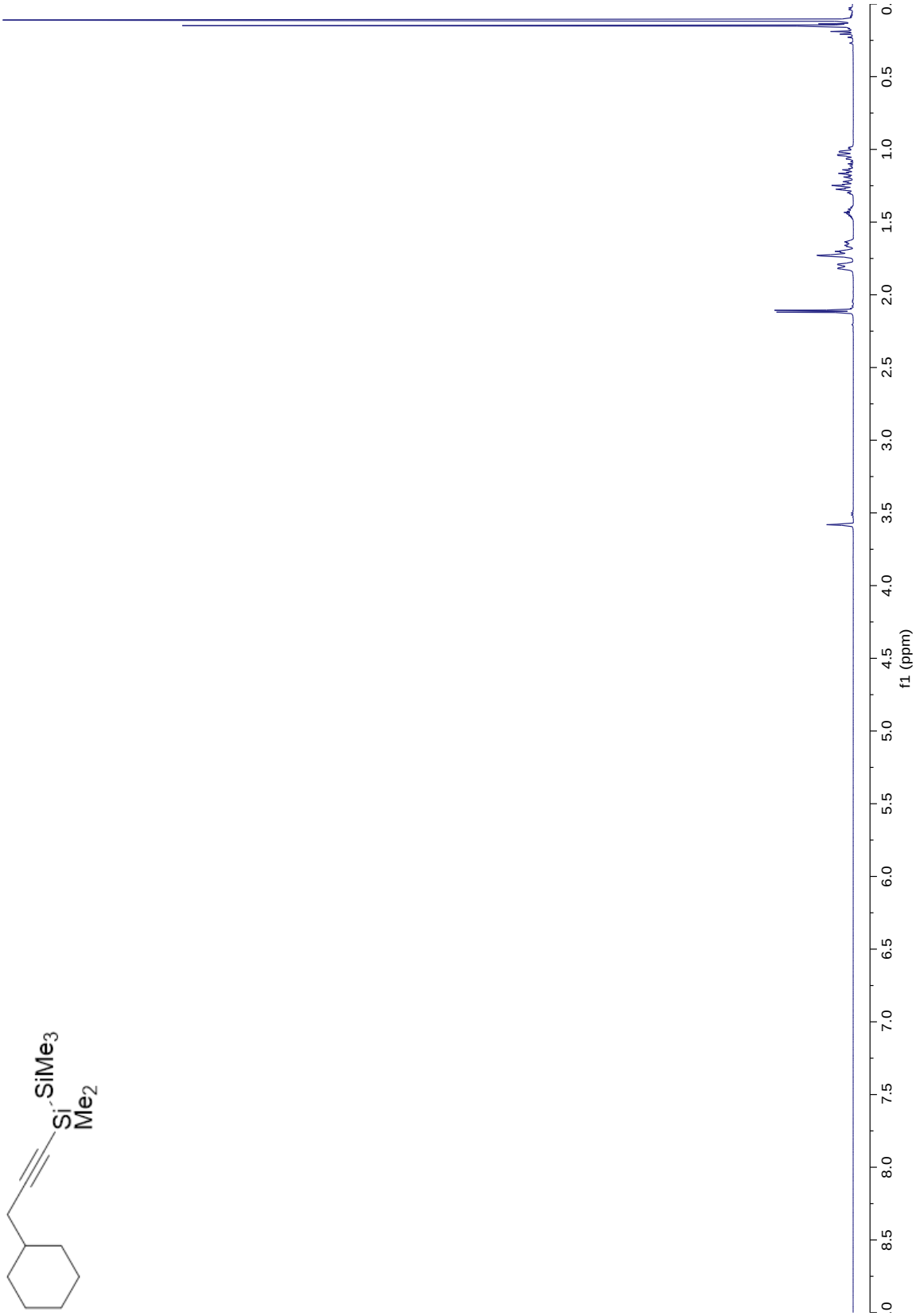
^{13}C NMR (126 MHz, THF-*d8*) of compound **2j.**



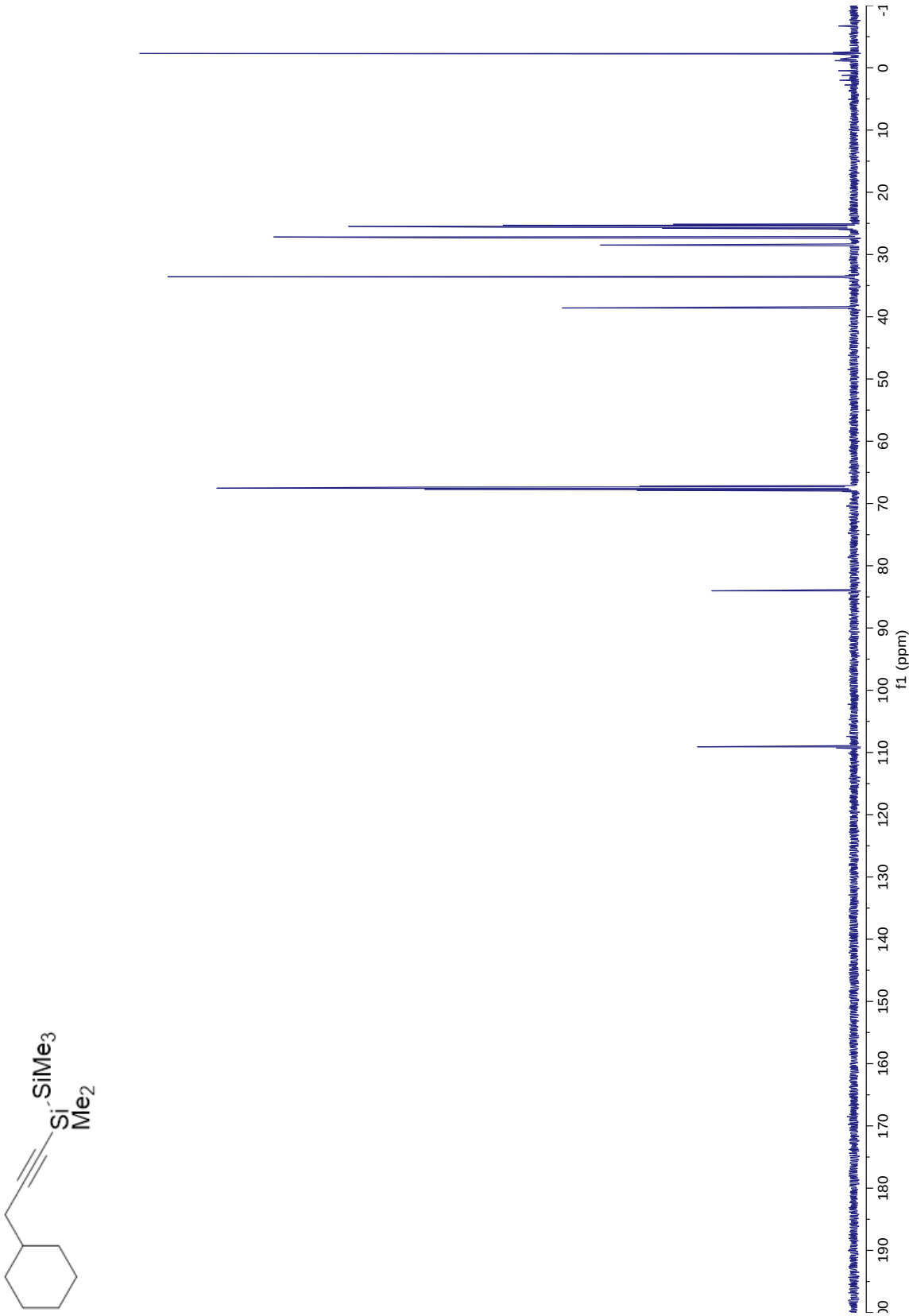
^{1}H NMR (500 MHz, THF-*d8*) of compound **2k.**



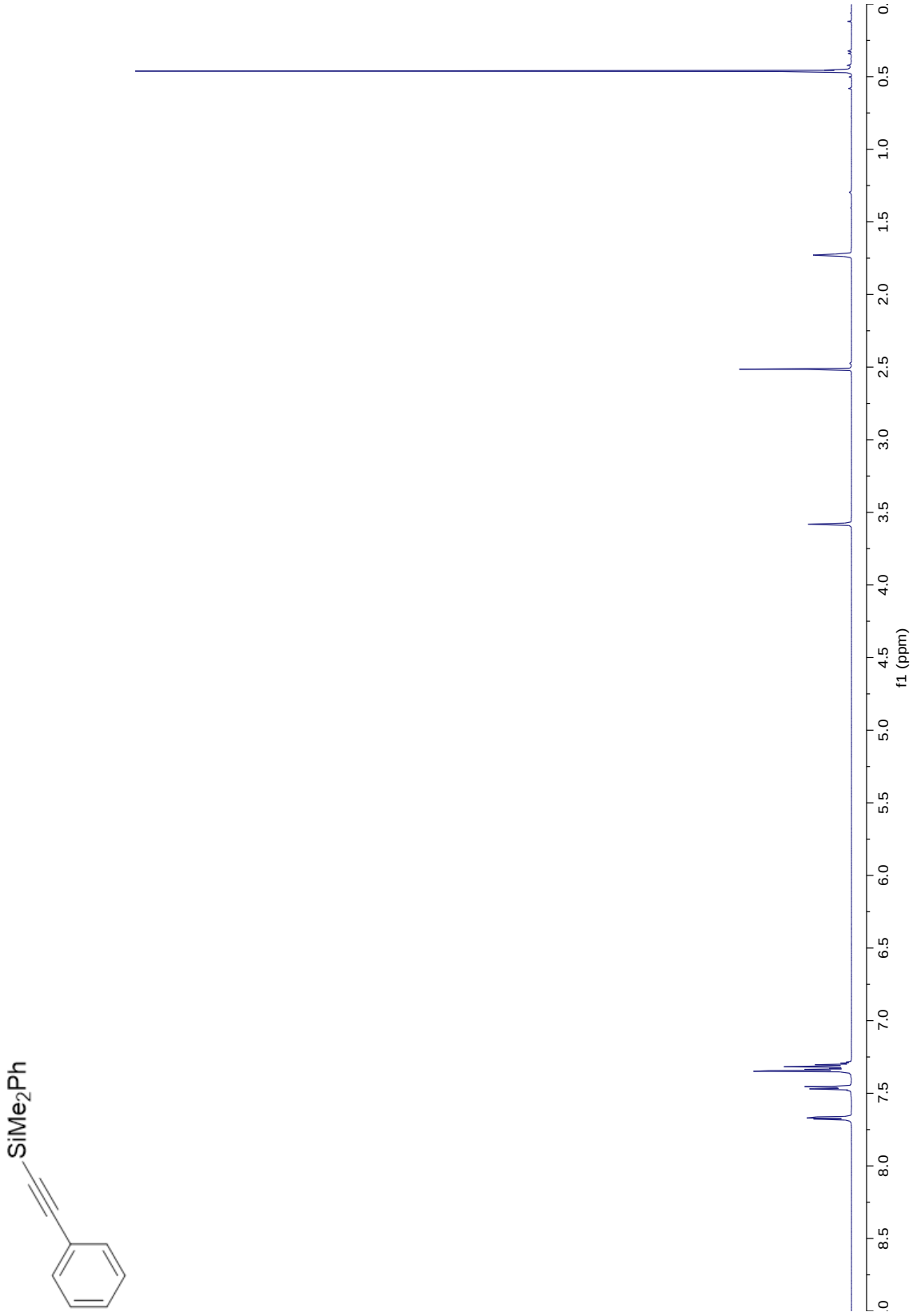
^{13}C NMR (126 MHz, THF-*d8*) of compound **2k.**



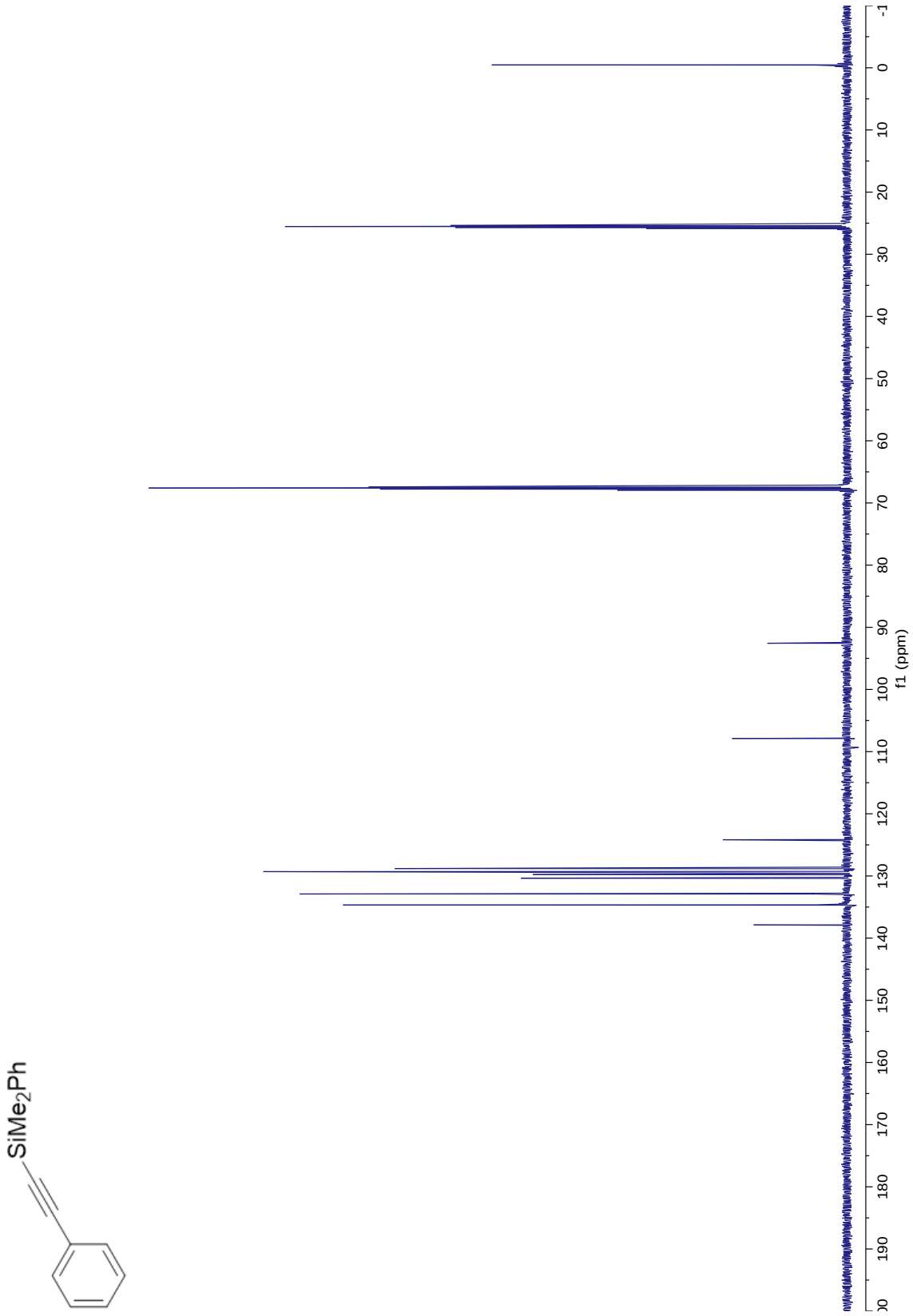
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2l.**



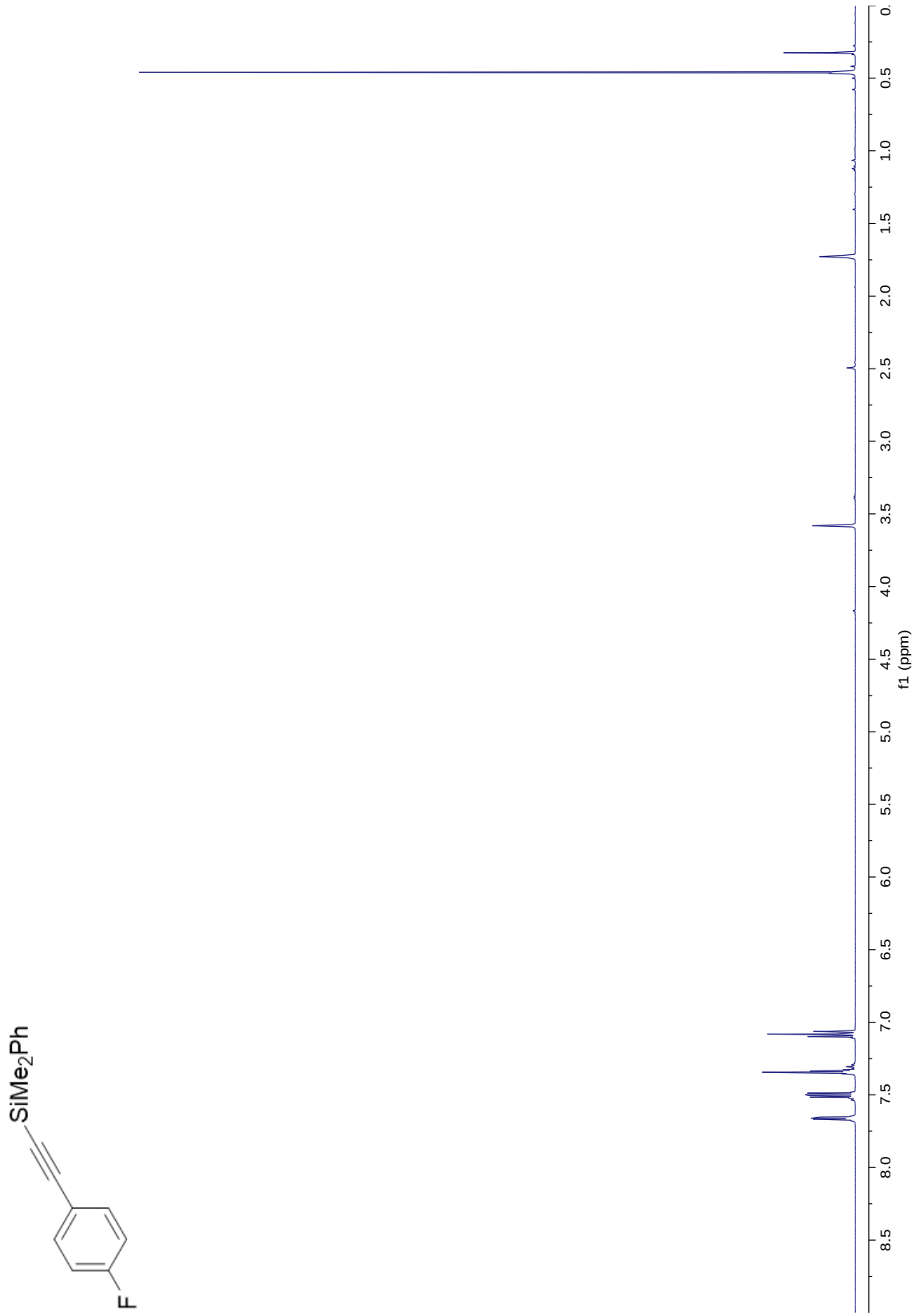
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2l.**



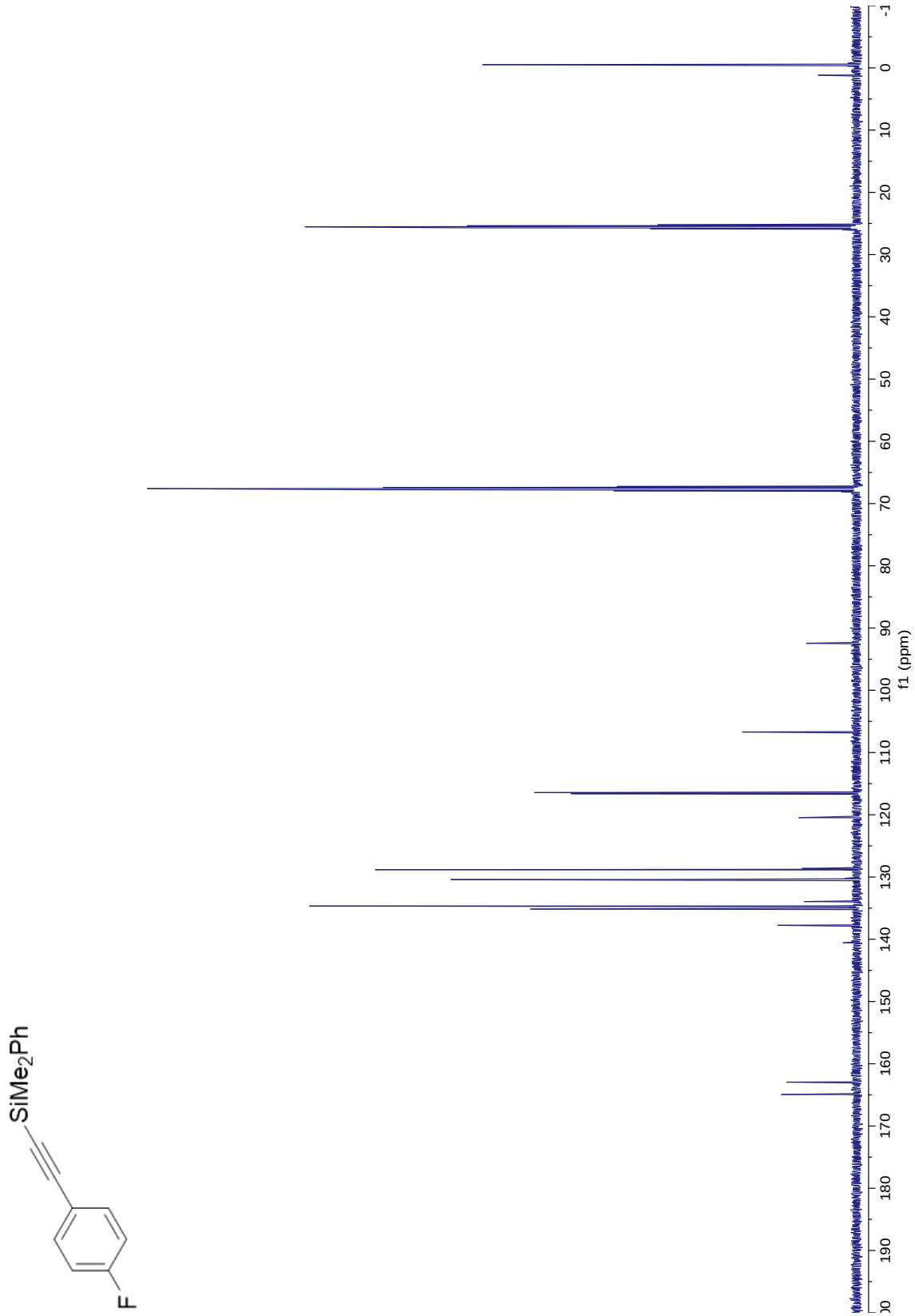
^{1}H NMR (500 MHz, THF-*d8*) of compound **4a.**



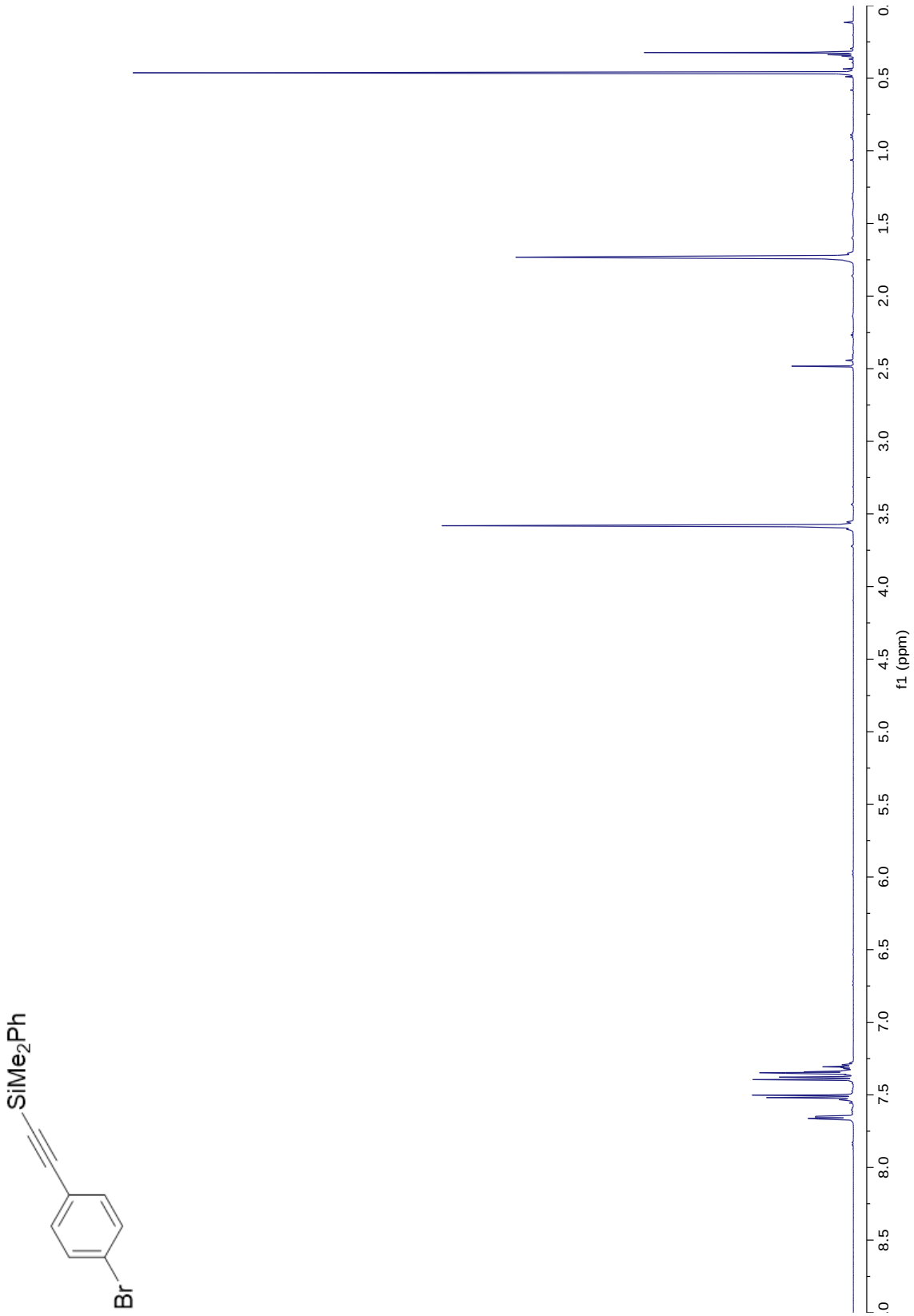
^{13}C NMR (126 MHz, THF-*d8*) of compound **4a.**



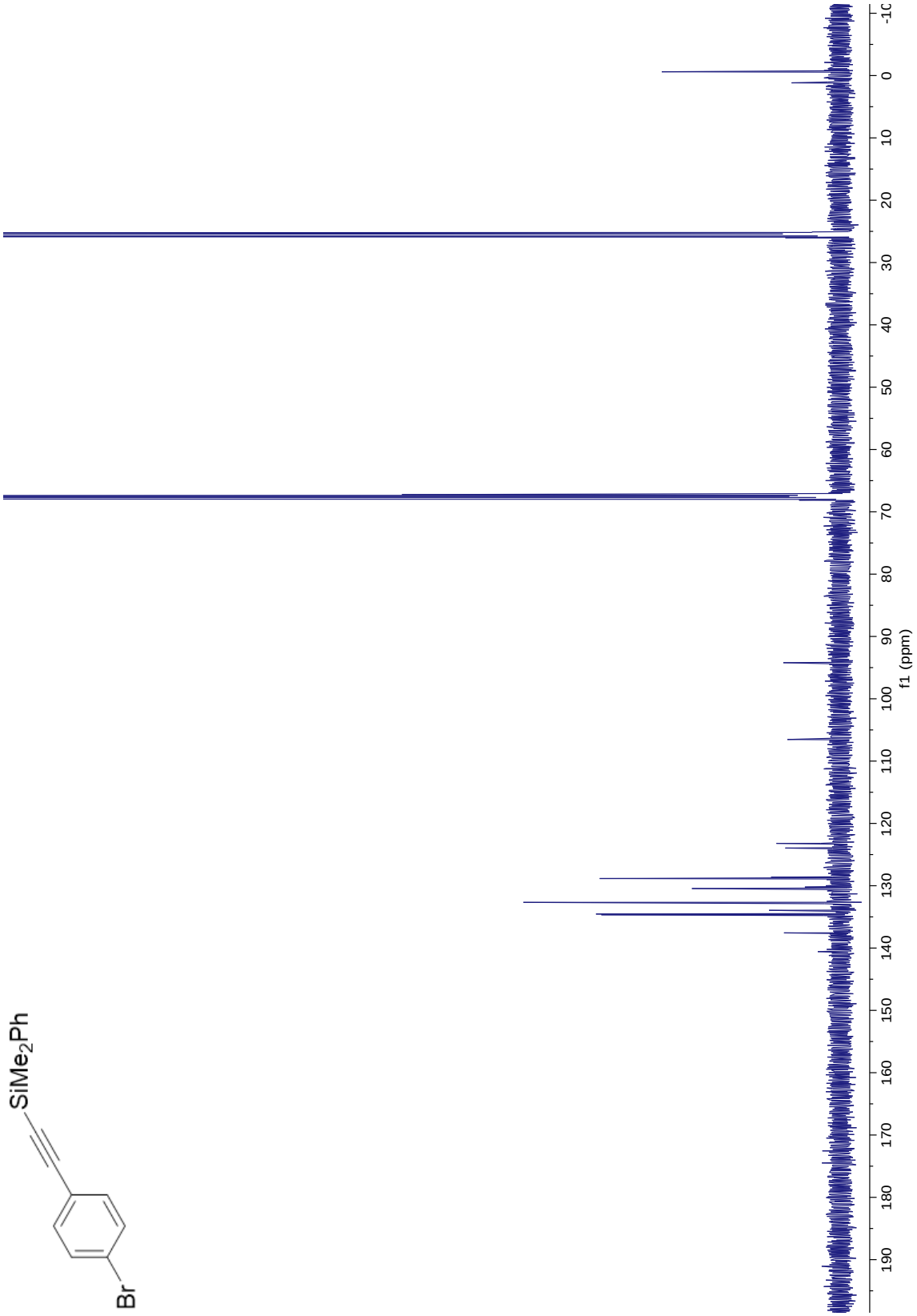
^{1}H NMR (500 MHz, THF-*d8*) of compound **4b.**



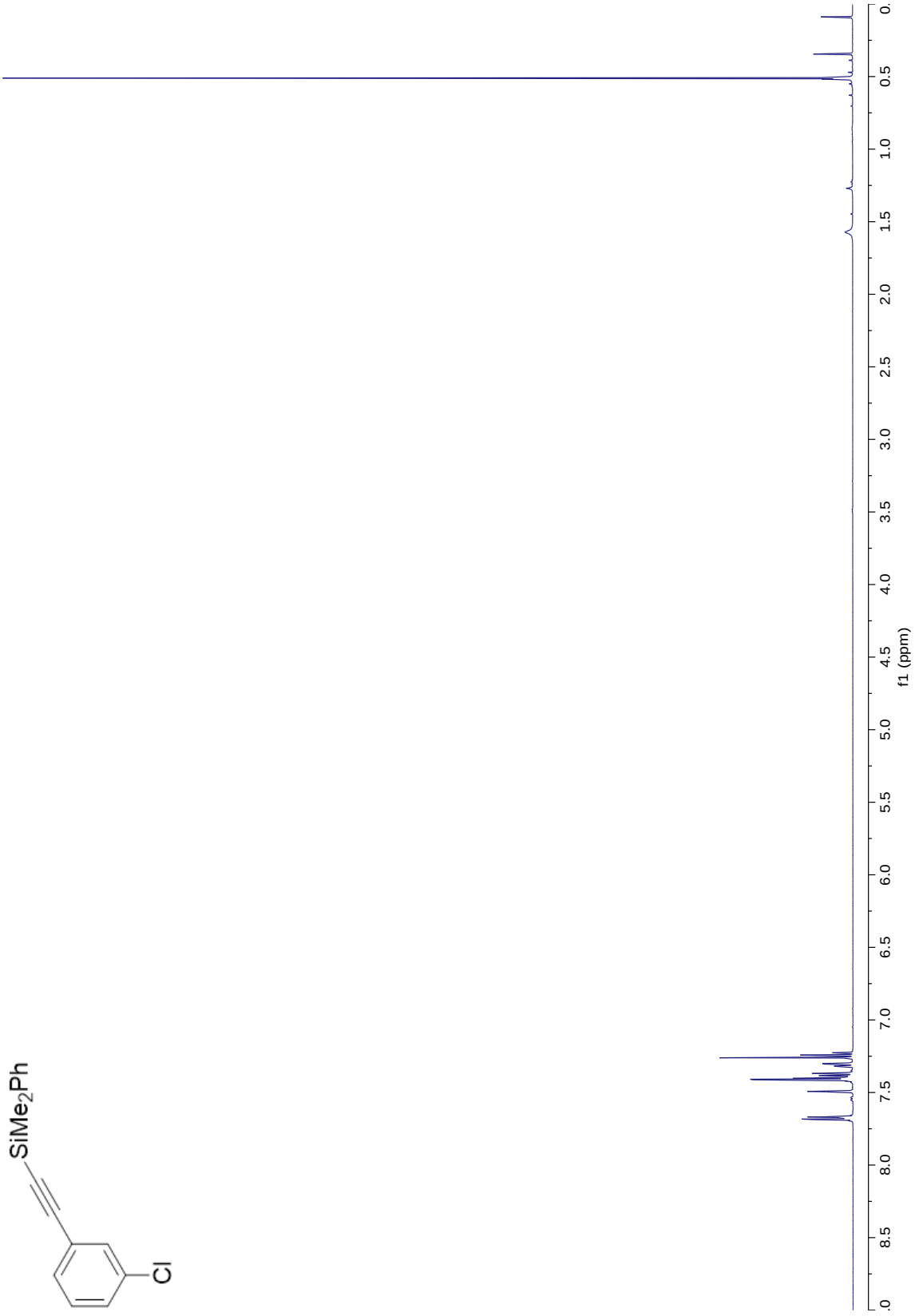
^{13}C NMR (126 MHz, THF-*d8*) of compound **4b.**



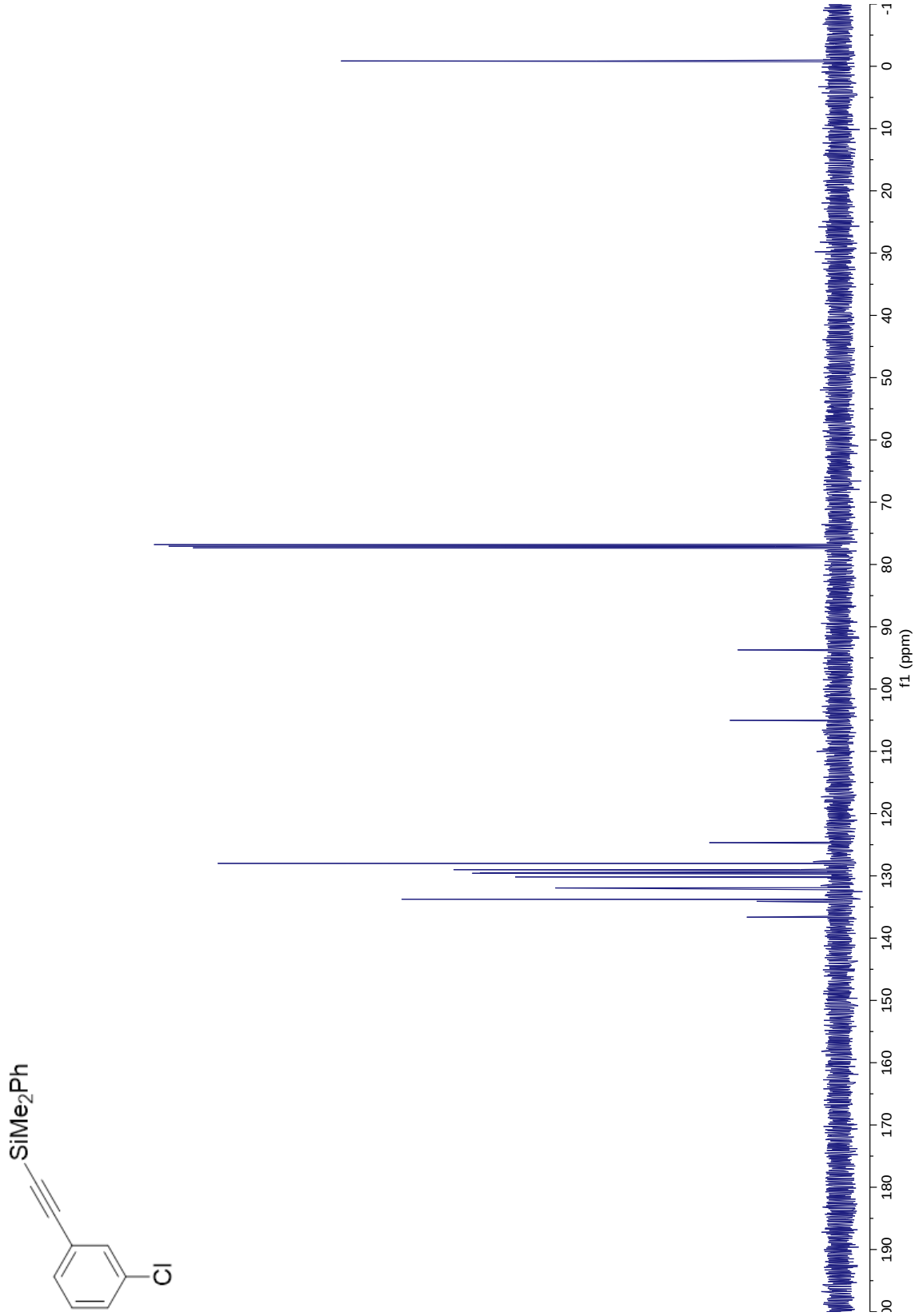
^{1}H NMR (500 MHz, THF-*d8*) of compound **4c.**



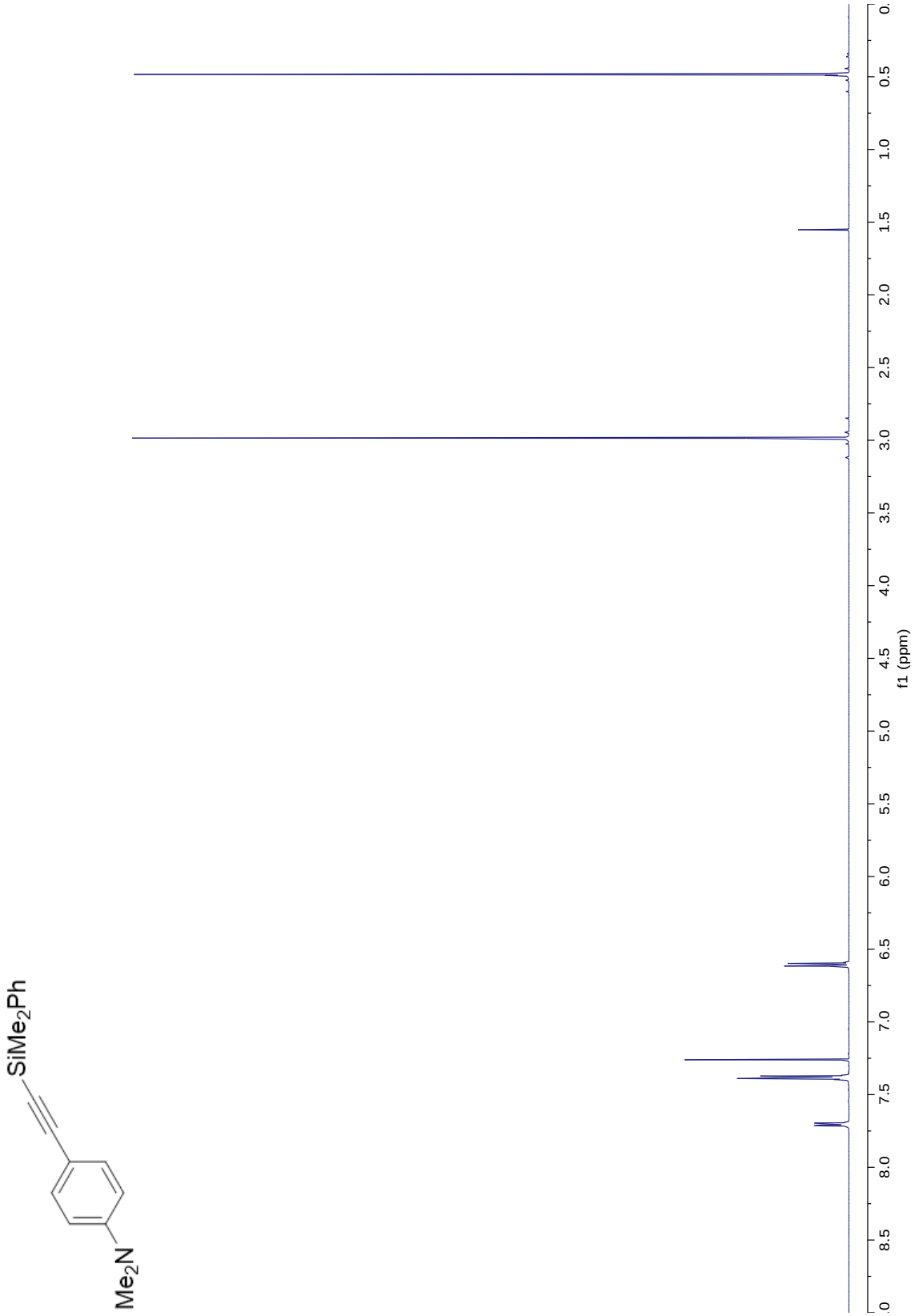
^{13}C NMR (126 MHz, THF-*d8*) of compound **4c.**



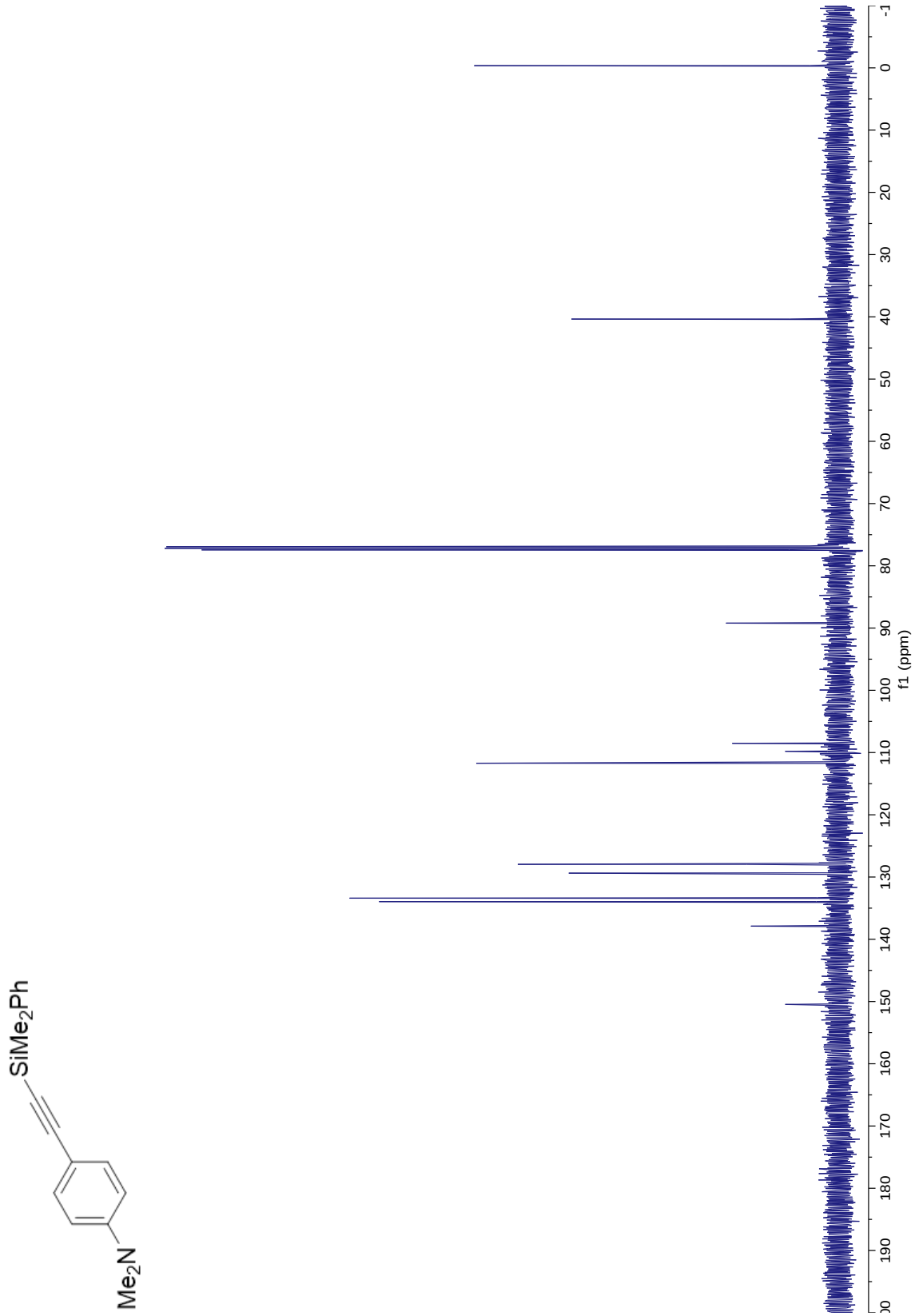
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4d.**



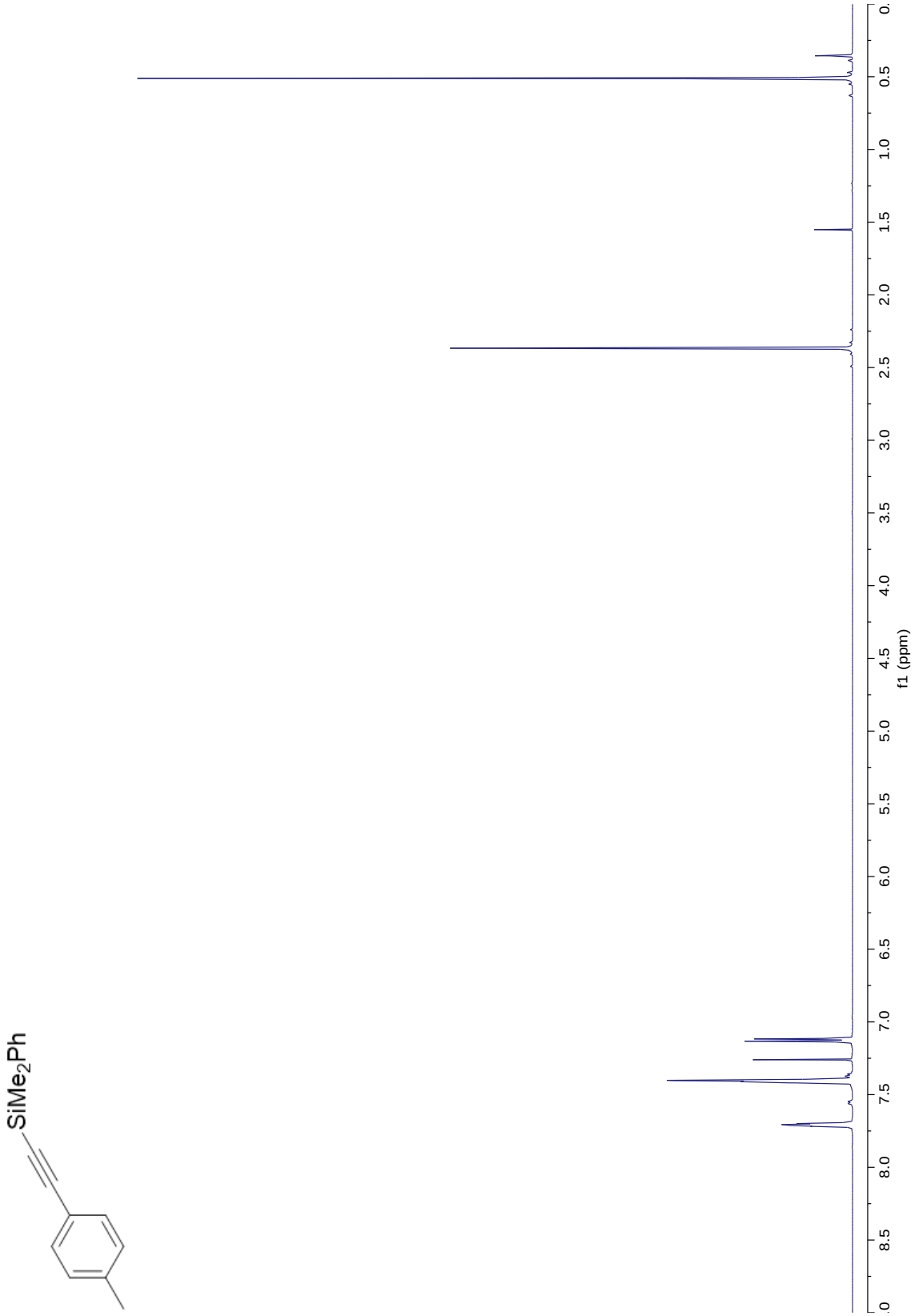
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4d.**



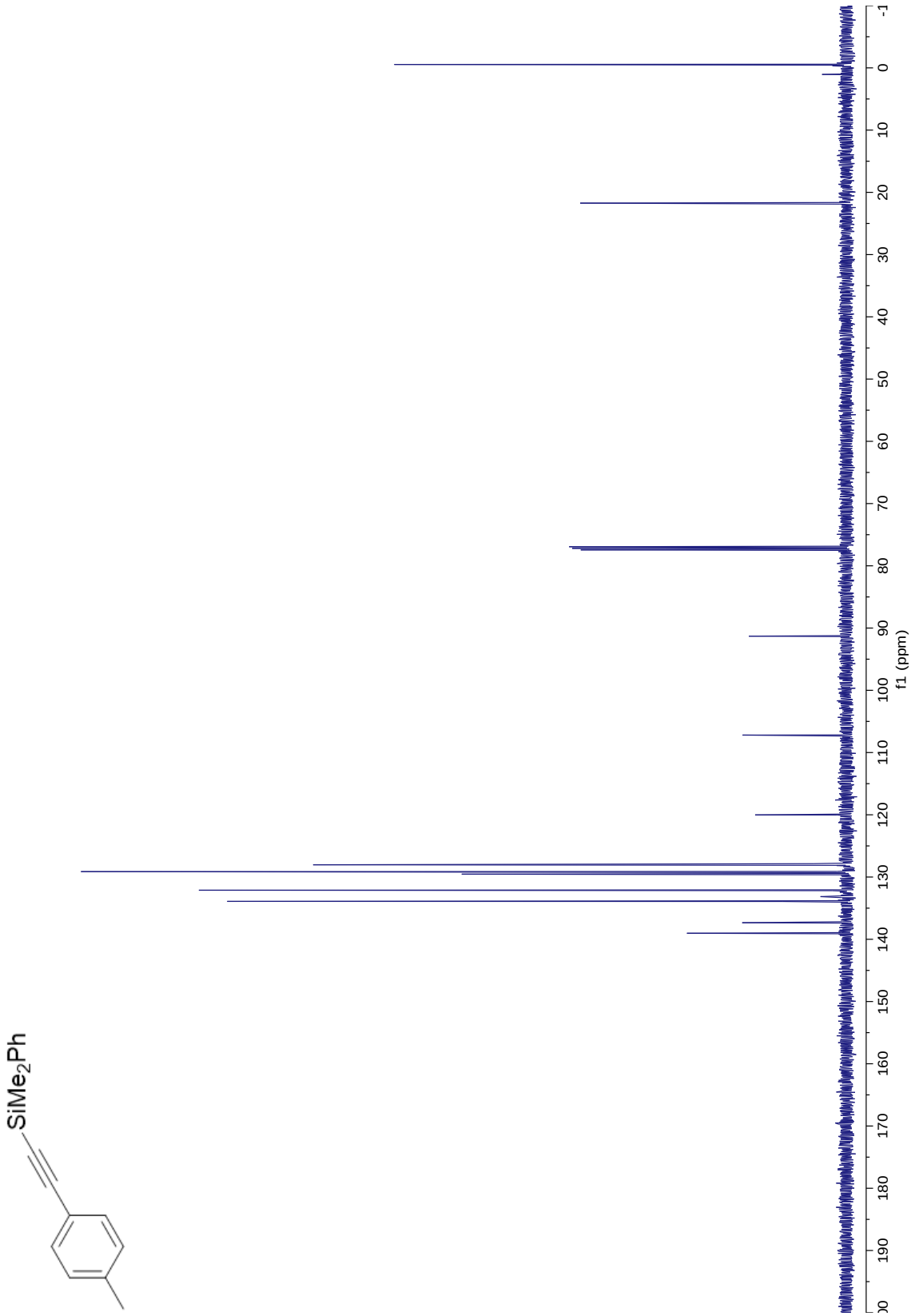
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4e.**



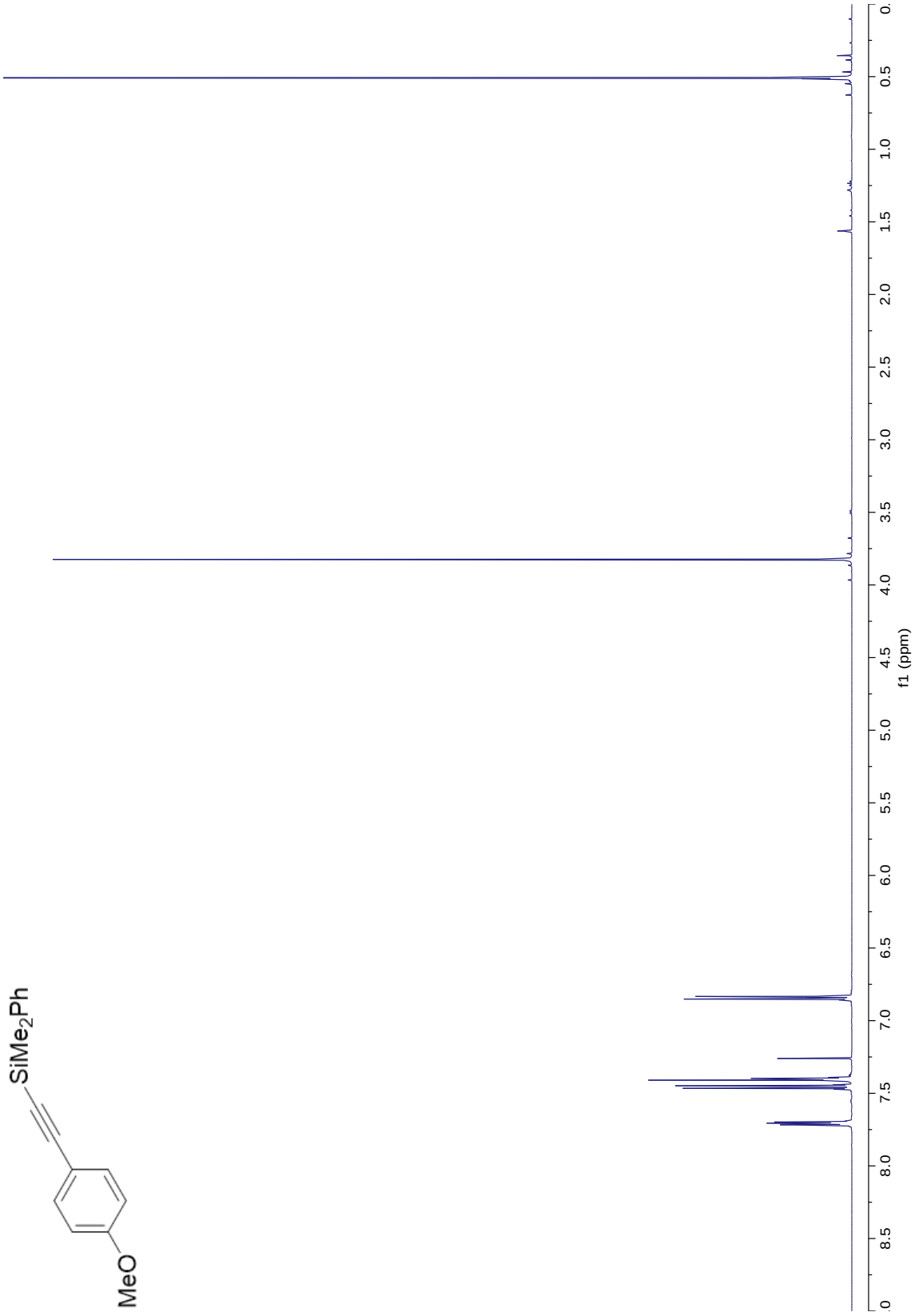
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4e.**



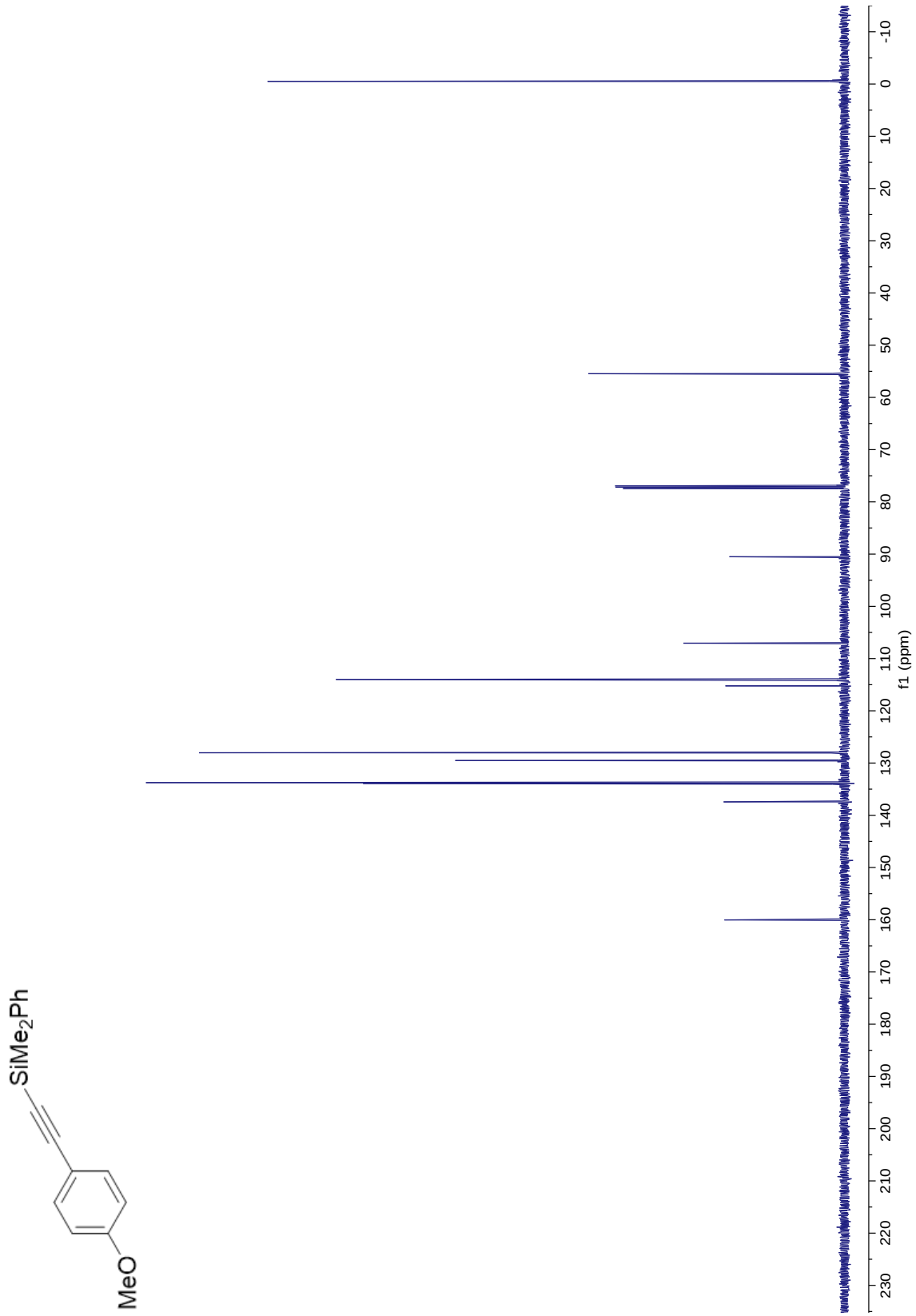
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4f.**



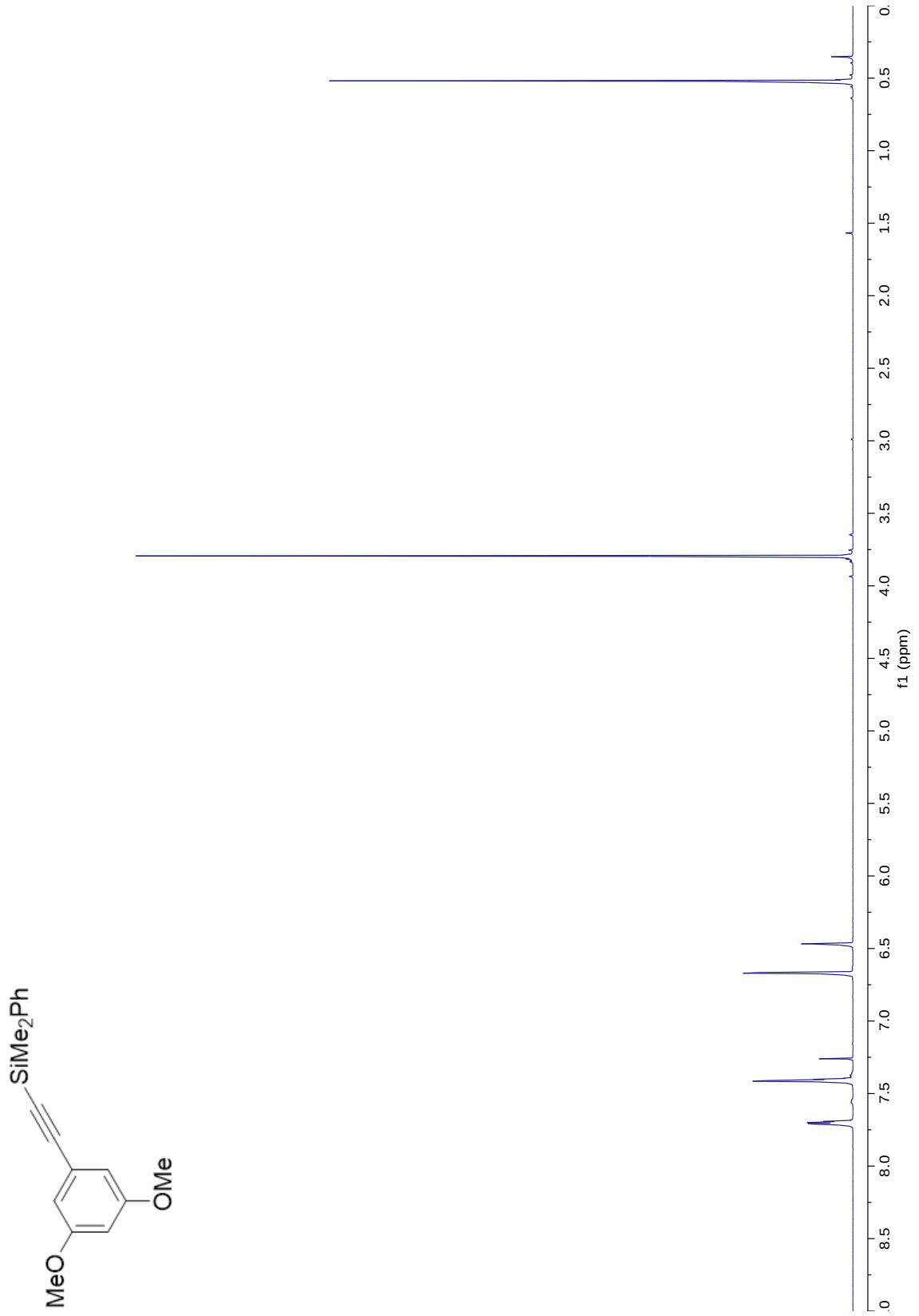
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4f.**



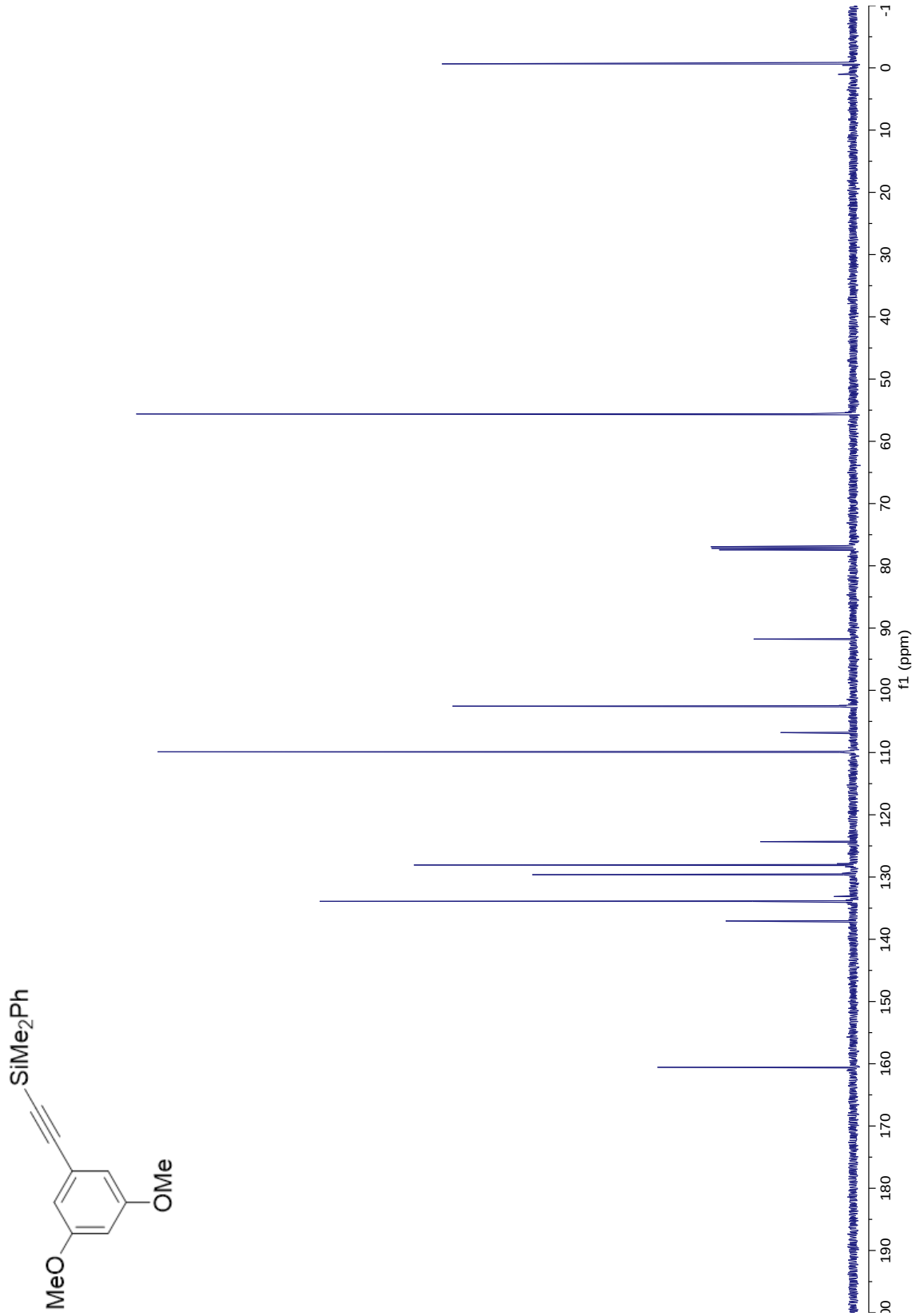
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4g.**



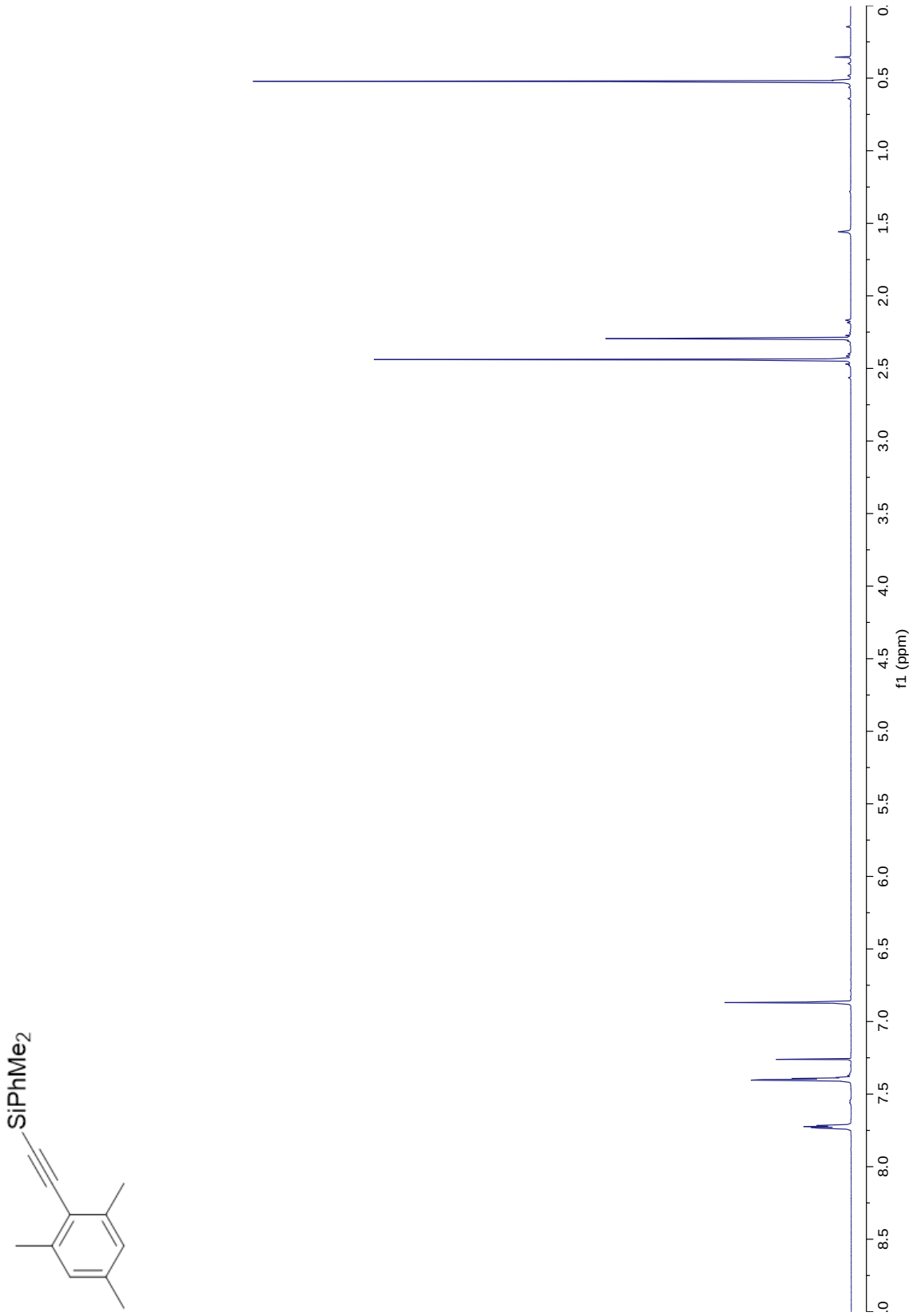
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4g.**



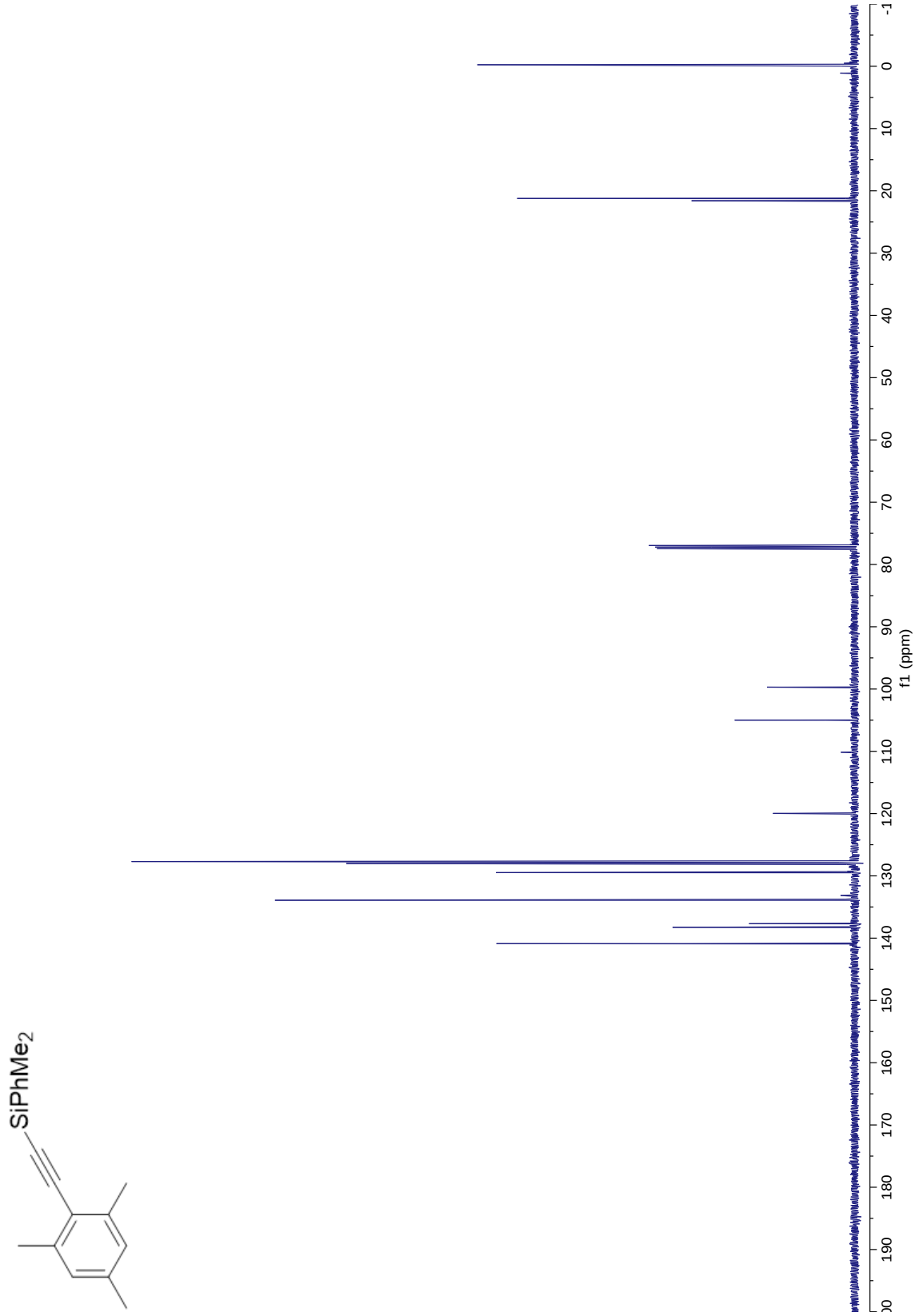
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4h.**



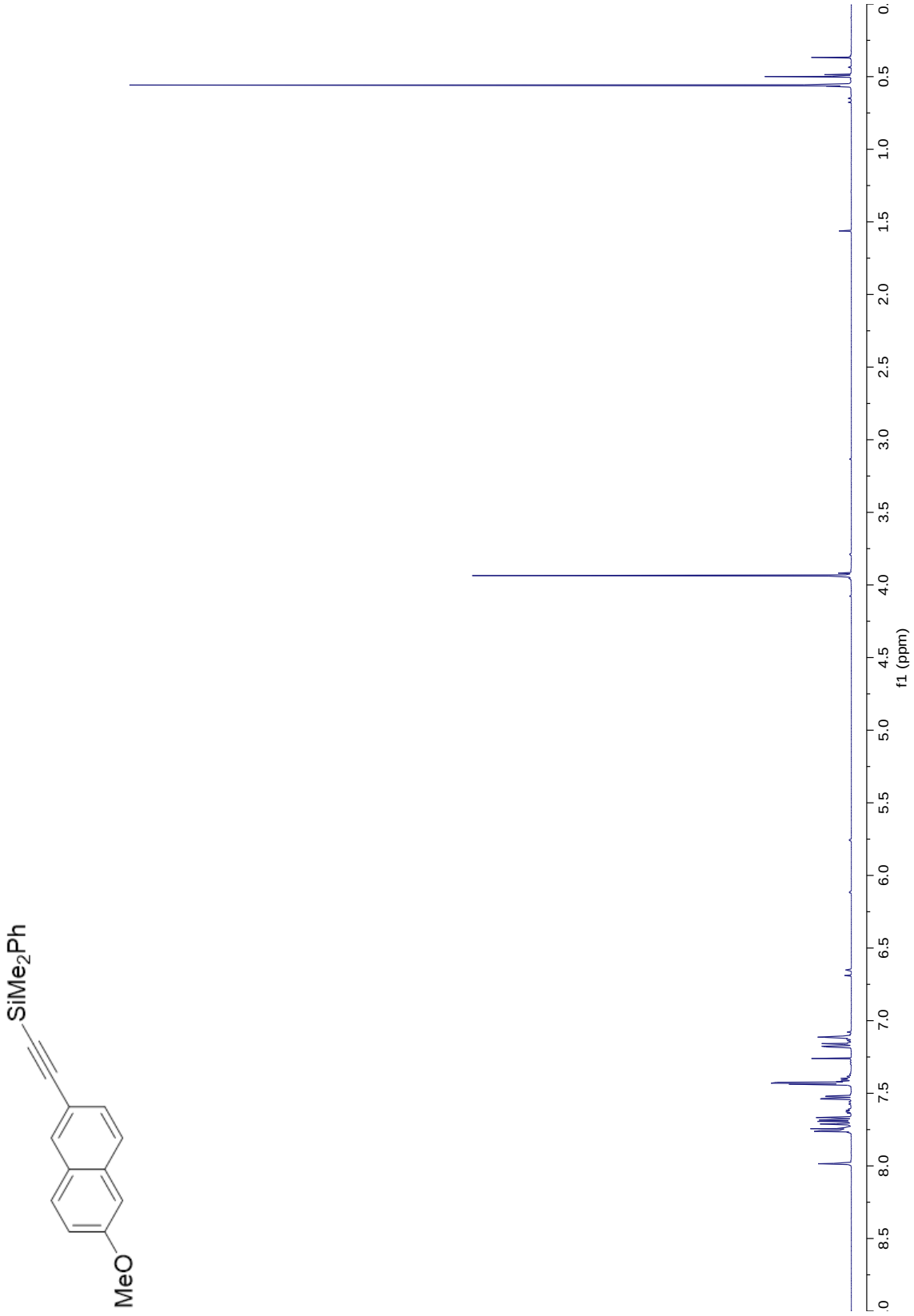
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4h.**



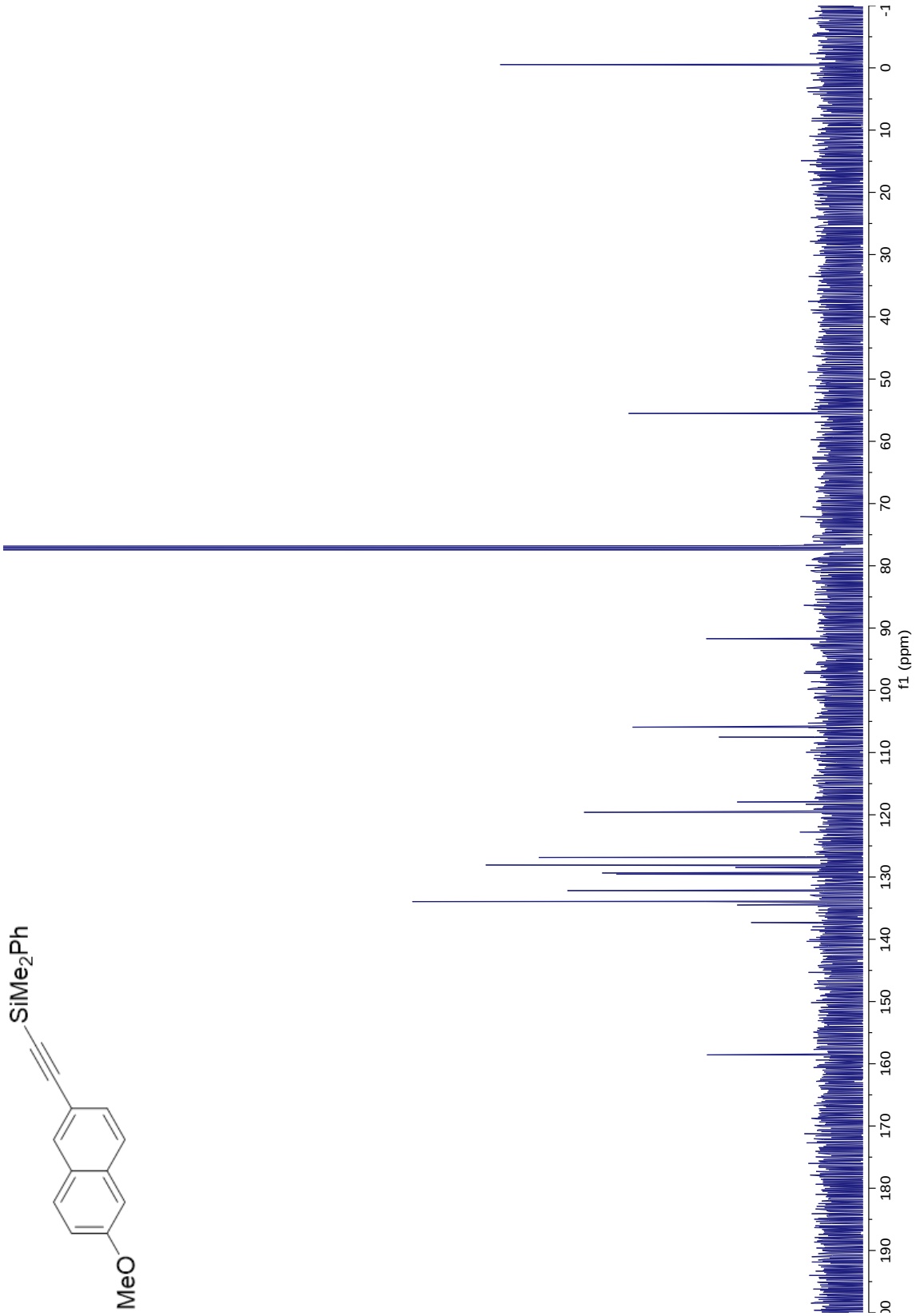
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4i.**



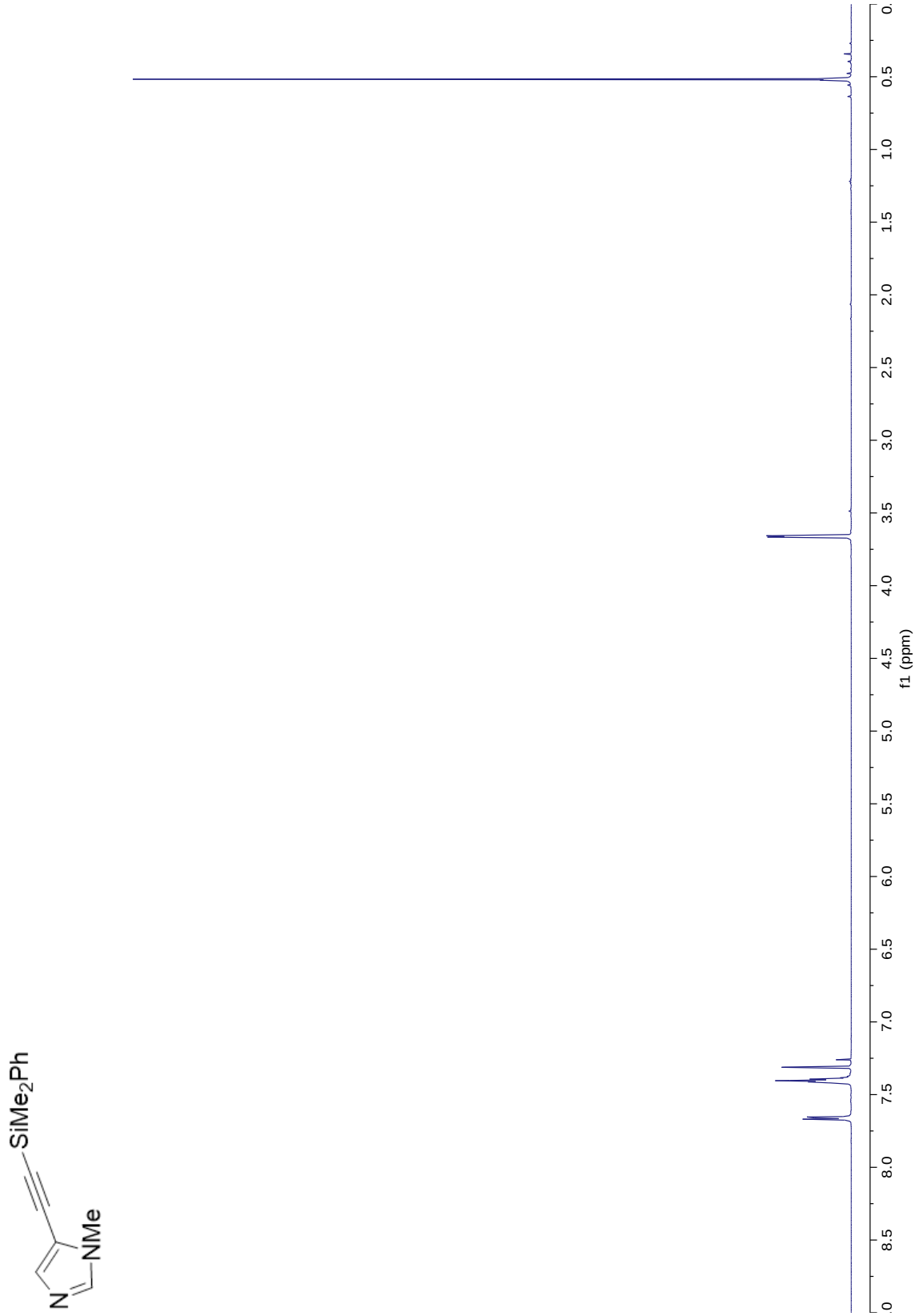
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4i.**



^{1}H NMR (500 MHz, $CDCl_3$) of compound **4j.**



^{13}C NMR (126 MHz, $CDCl_3$) of compound **4j.**



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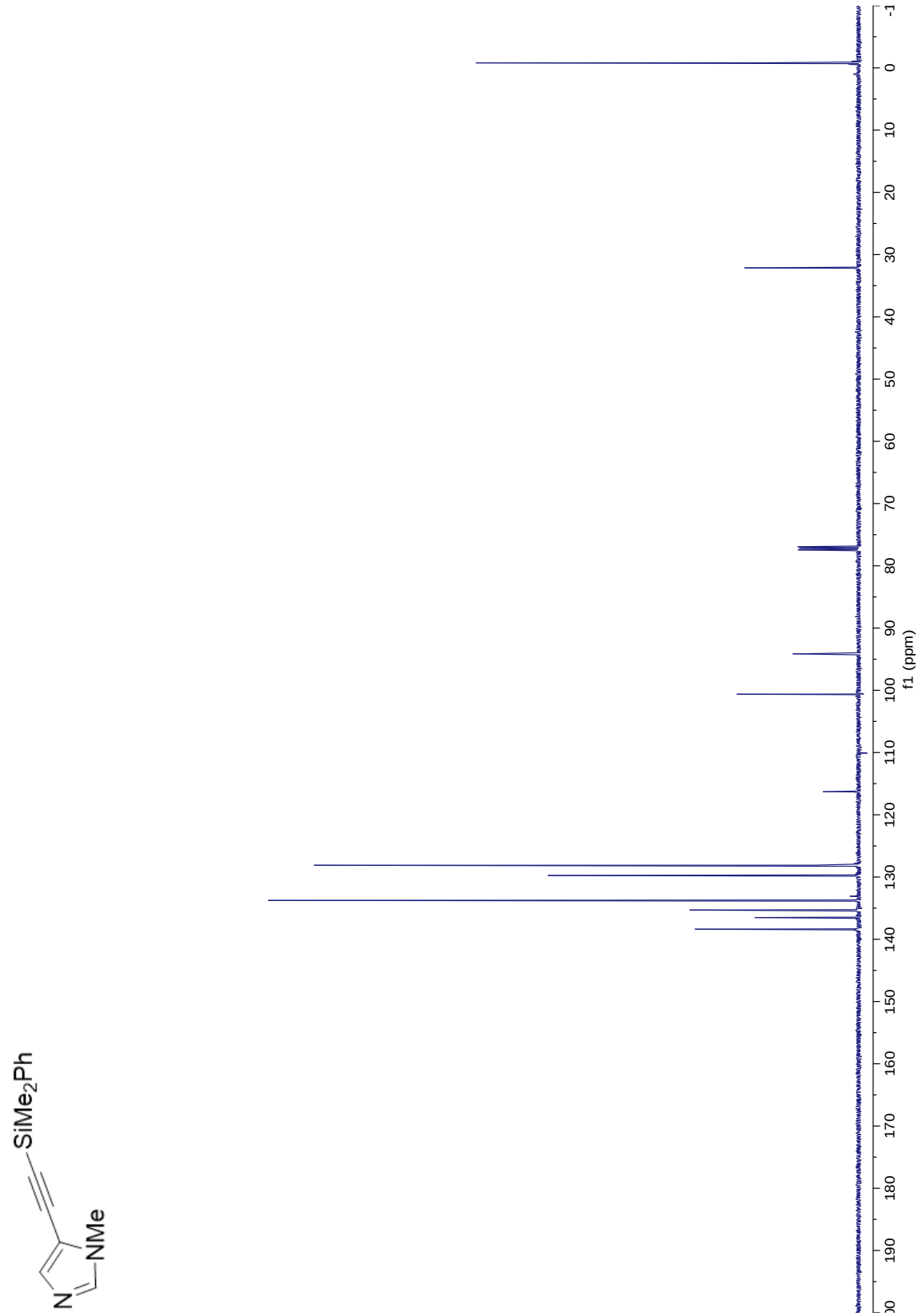
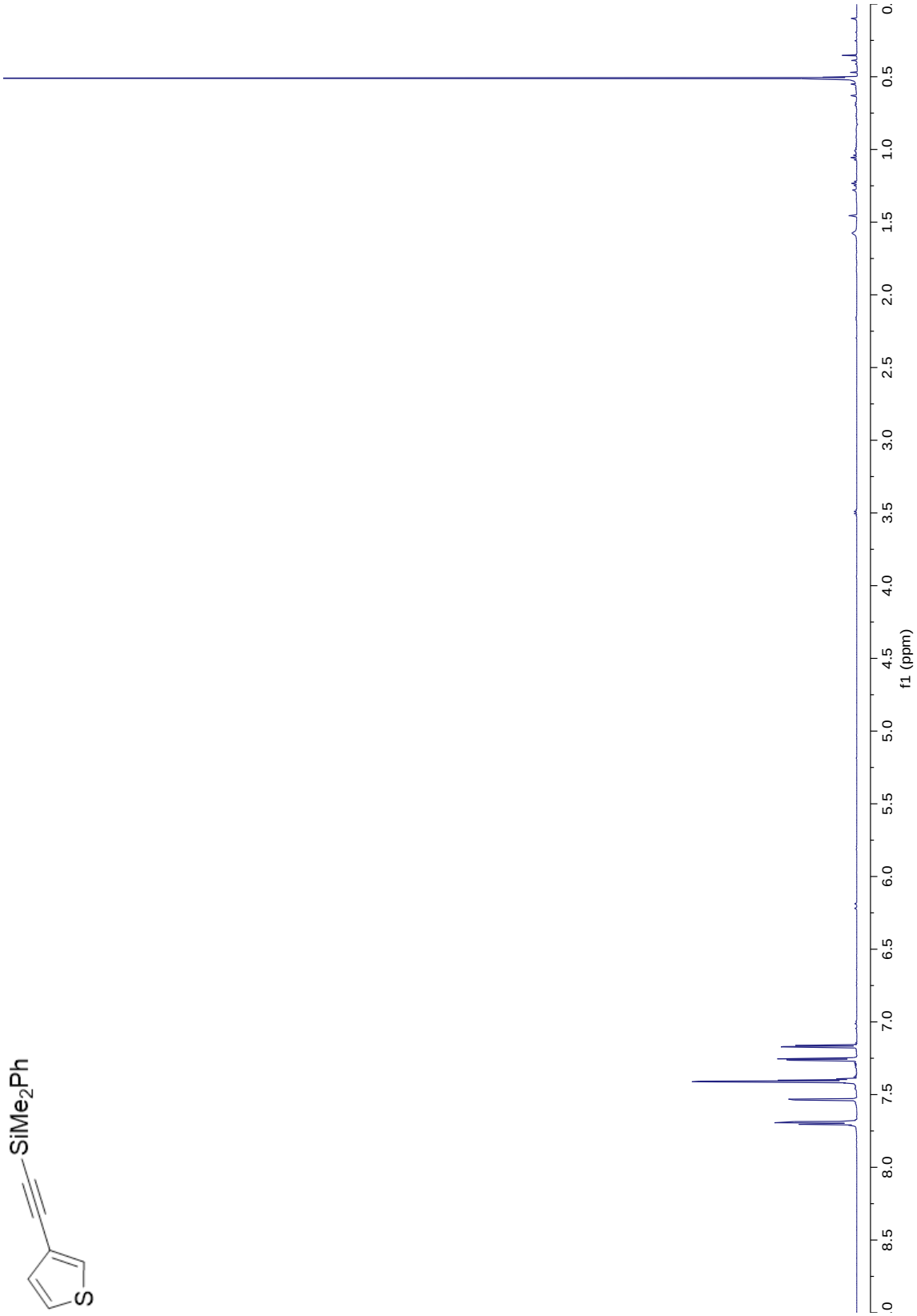
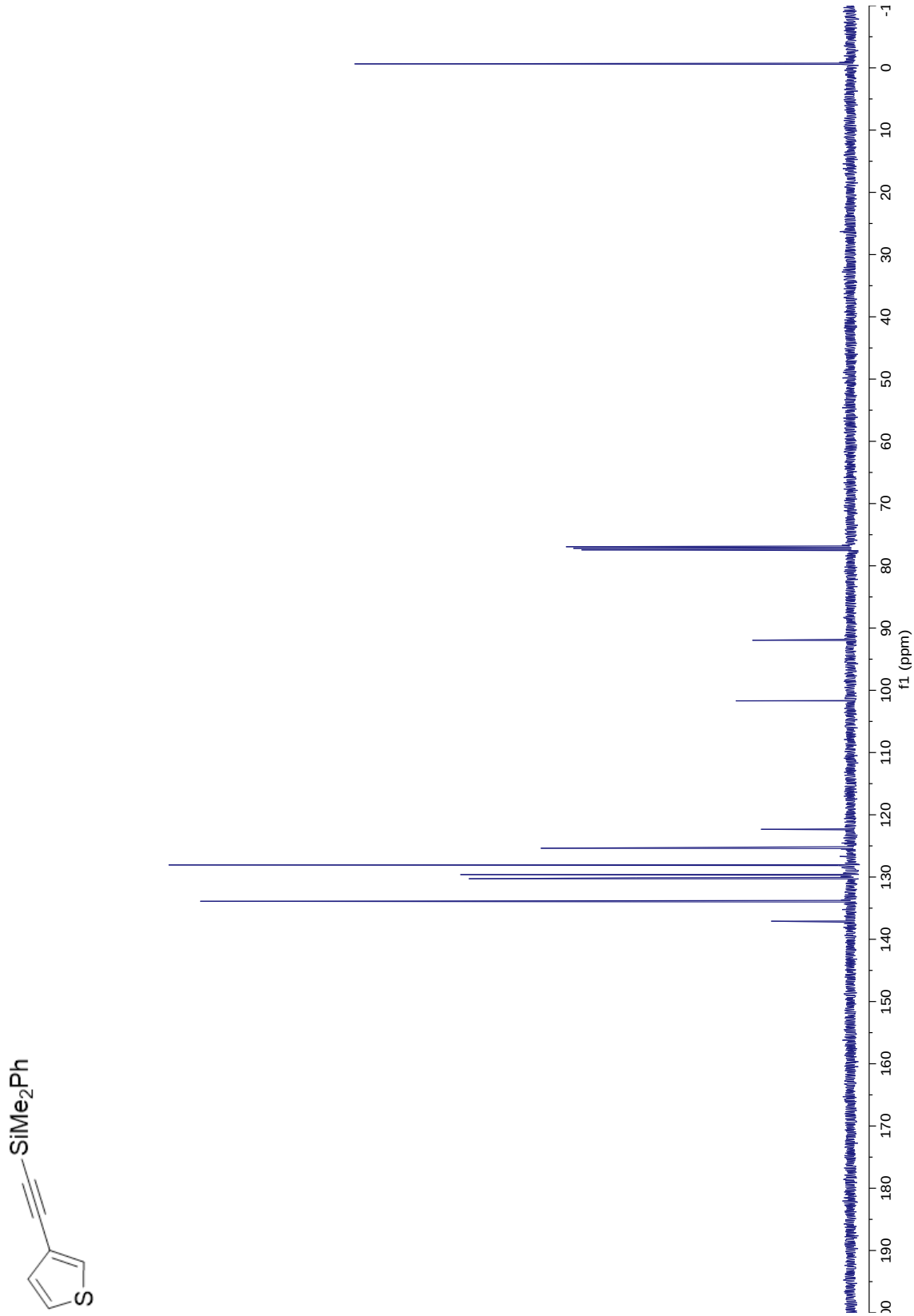


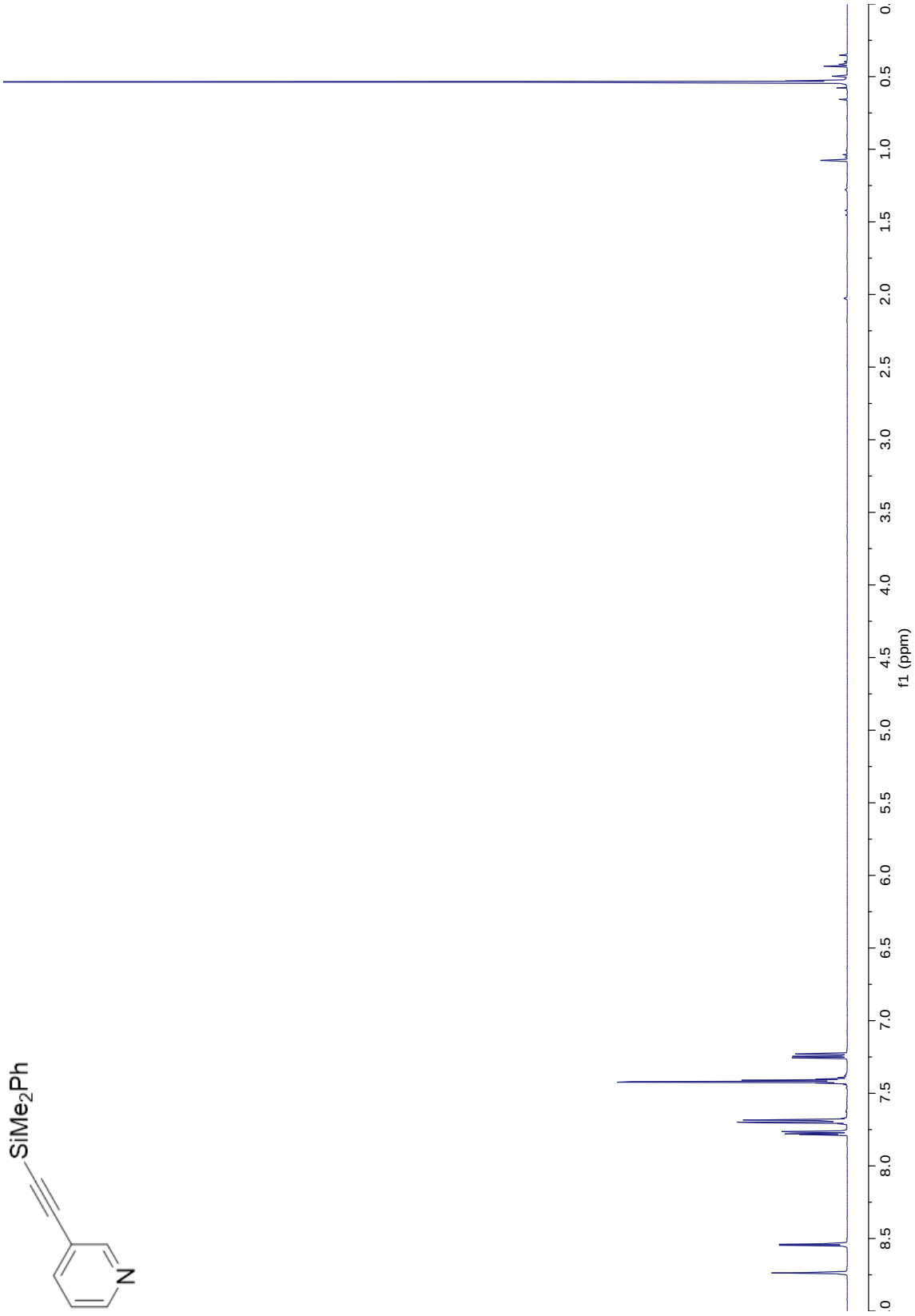
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4k.**



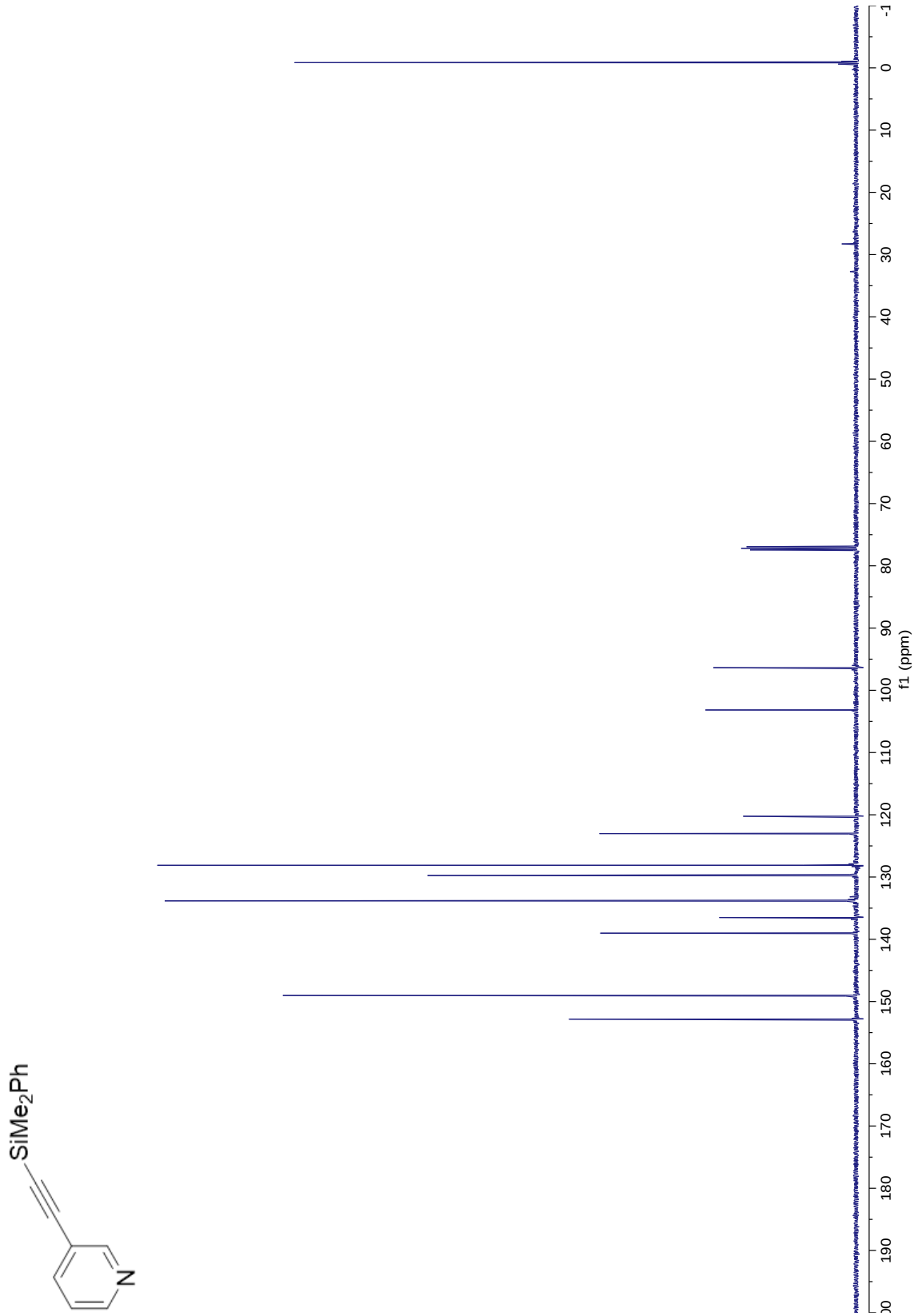
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4l.**



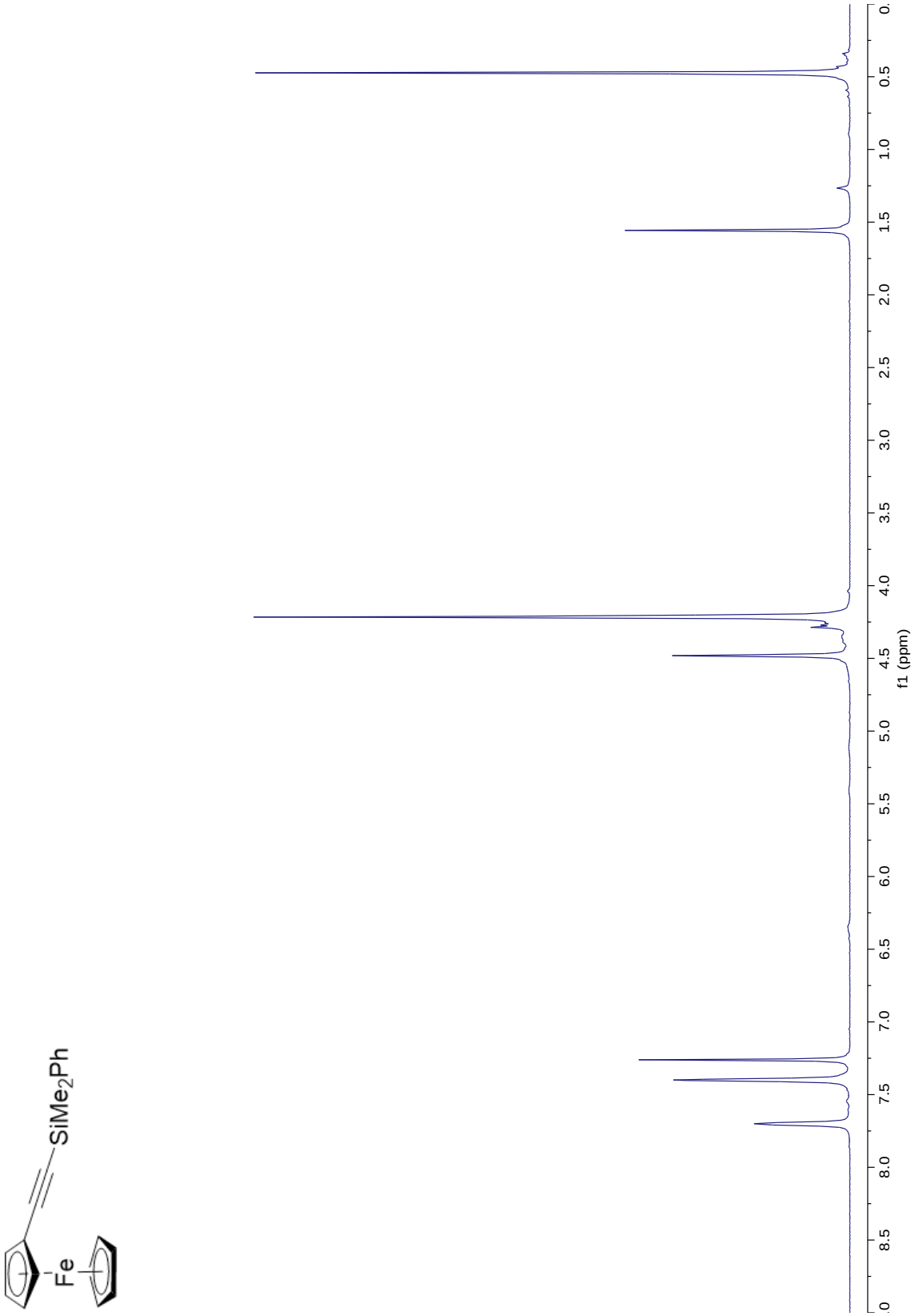
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4l.**



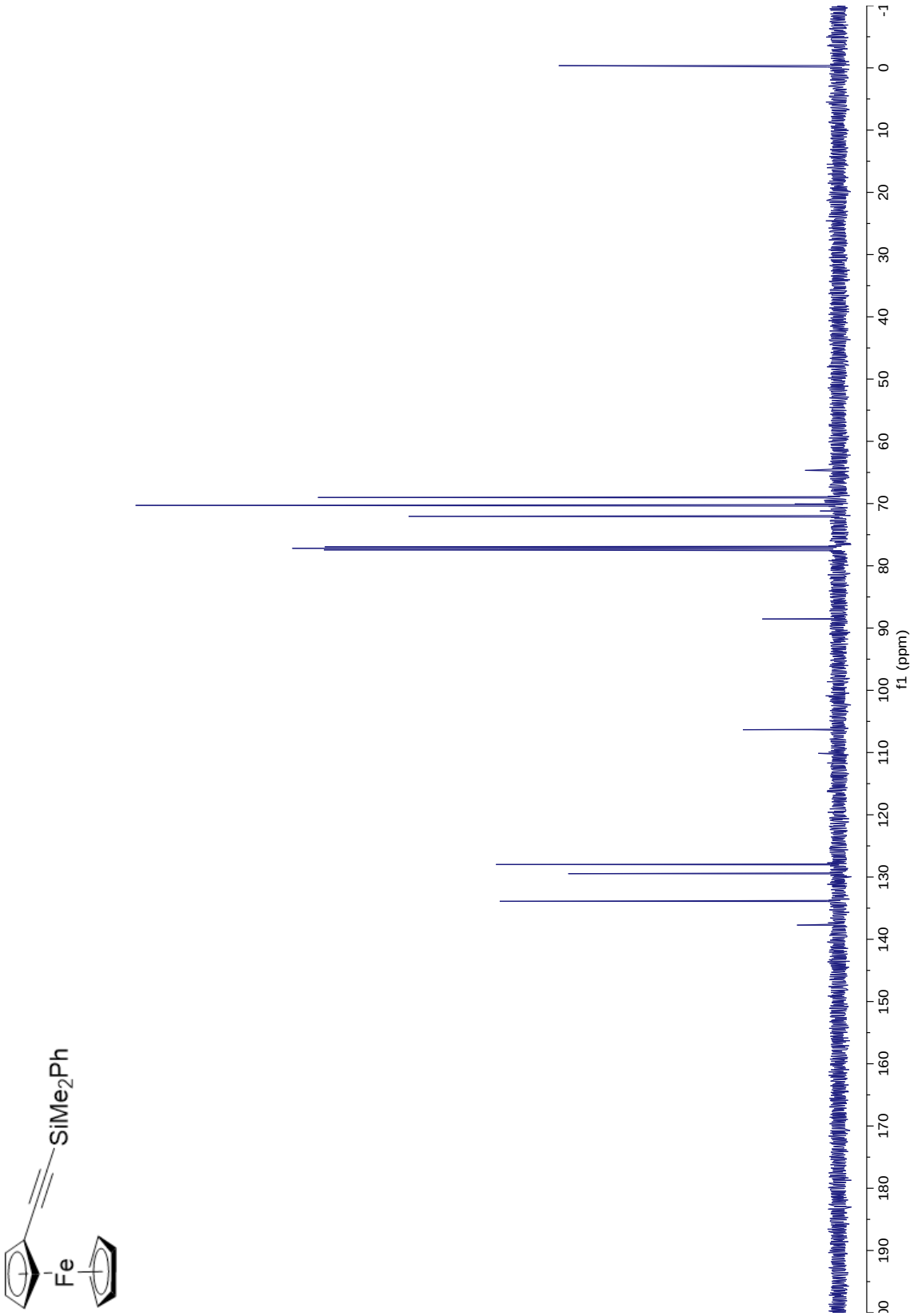
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4m.**



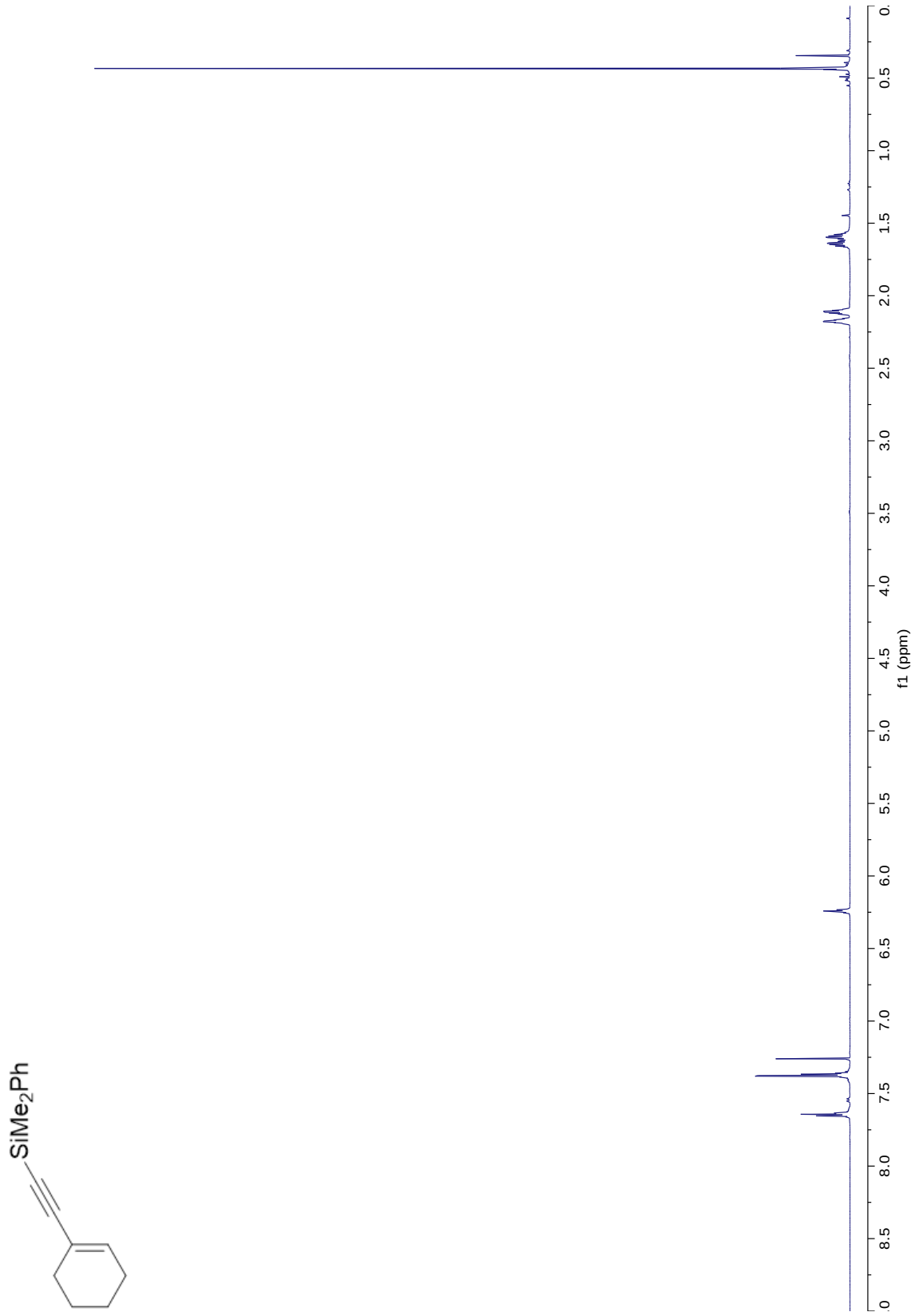
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4m.**



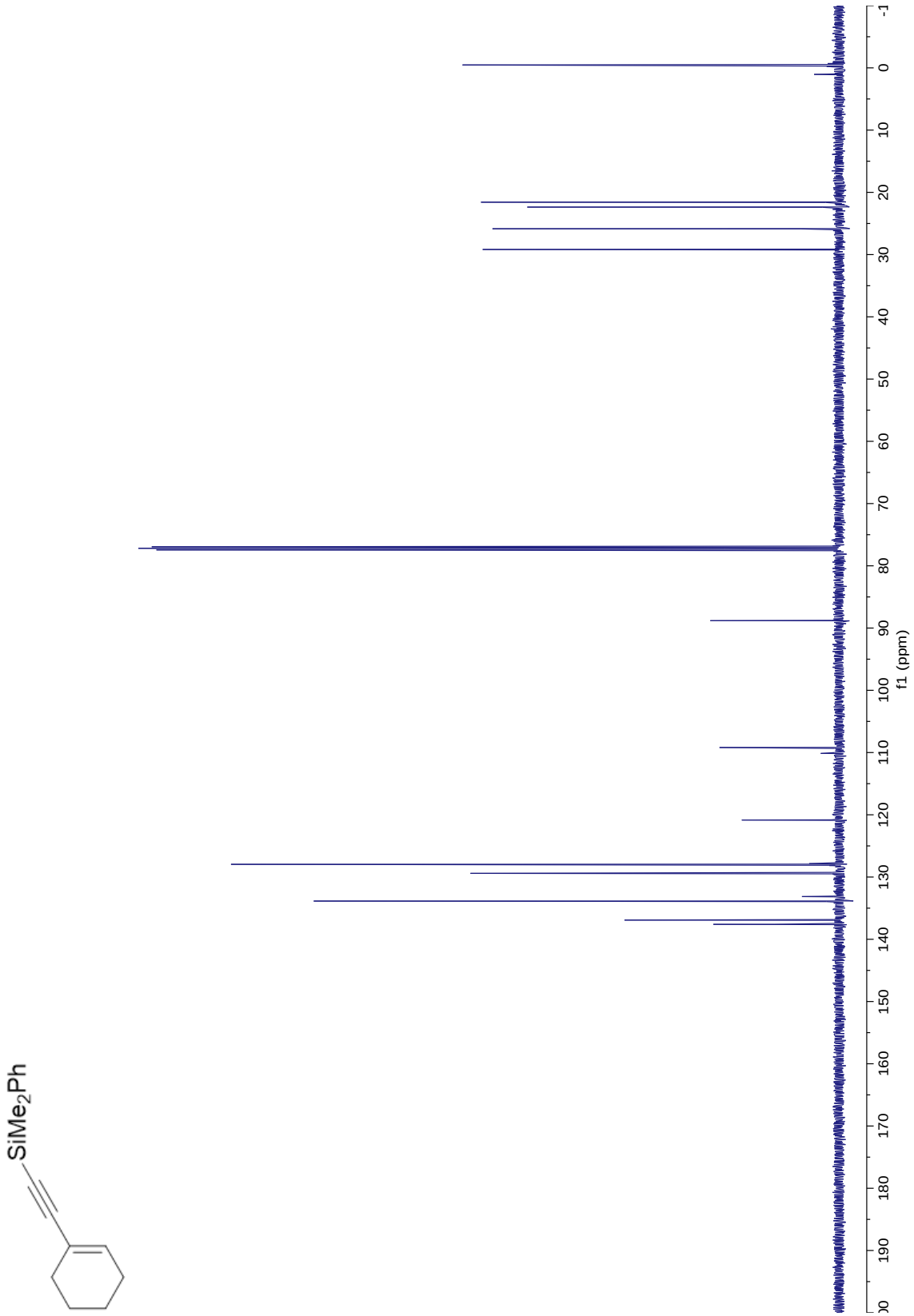
^{1}H NMR (500 MHz, $CDCl_3$ of compound **4n.**



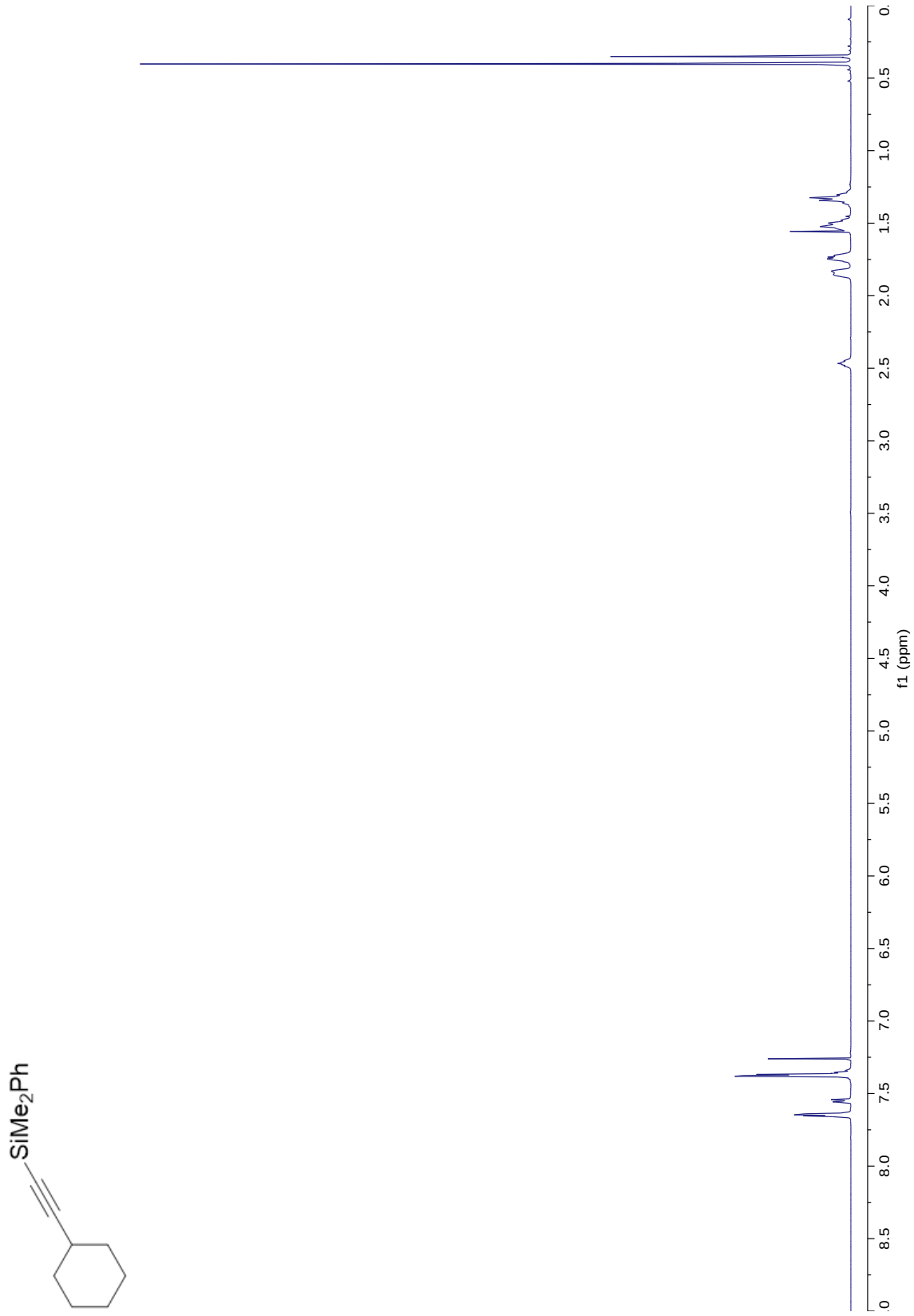
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4n.**



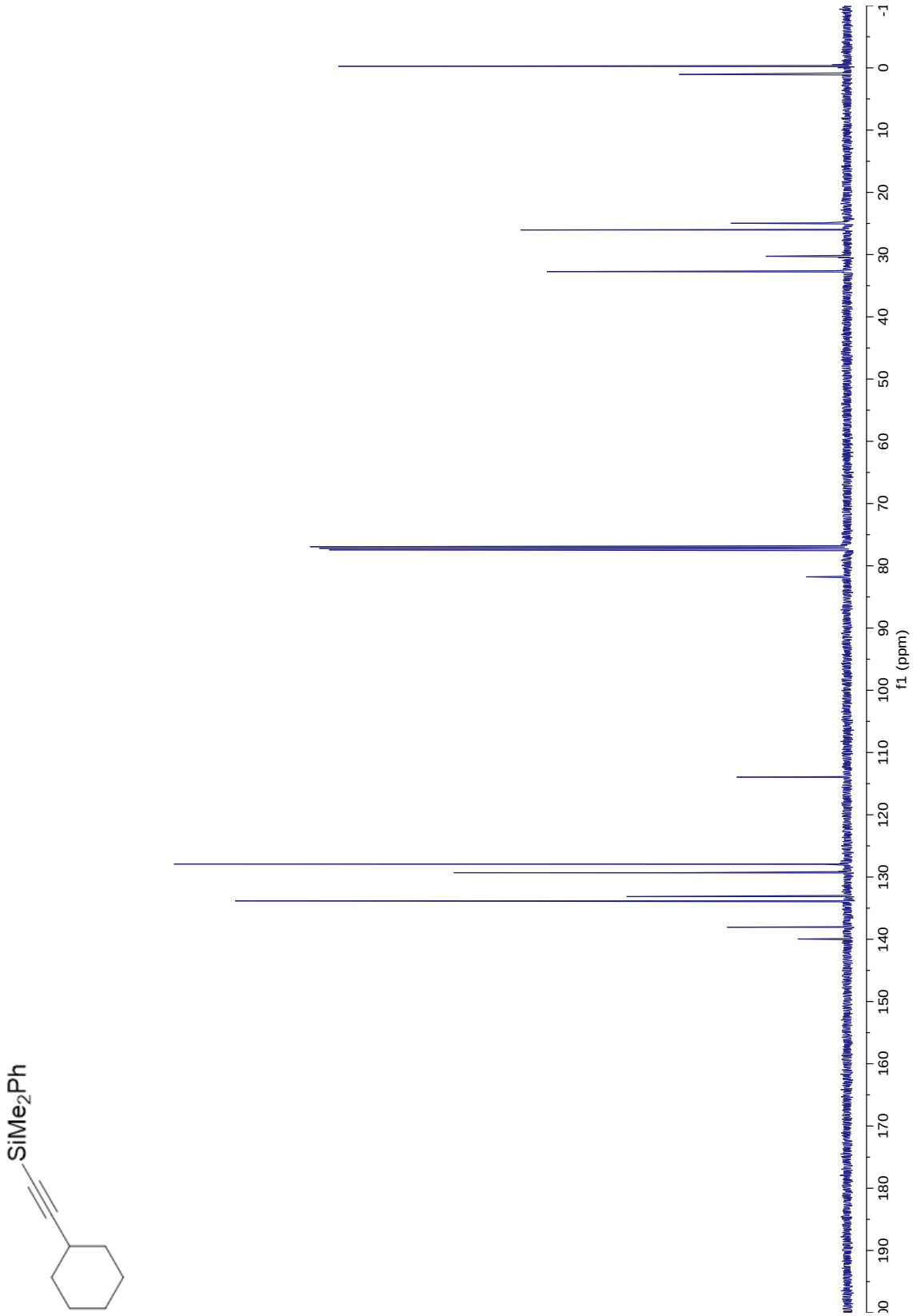
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4o.**



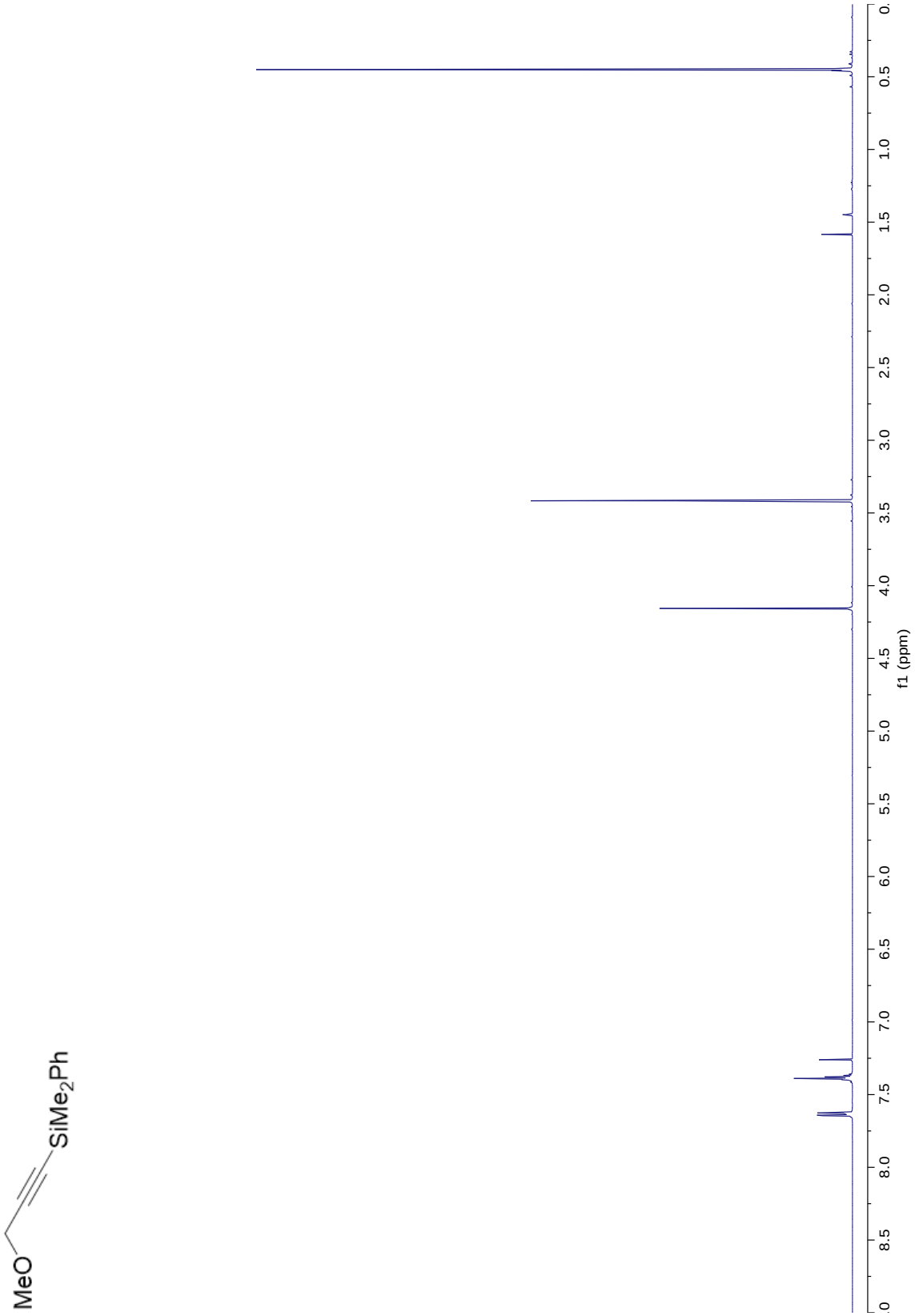
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4o.**



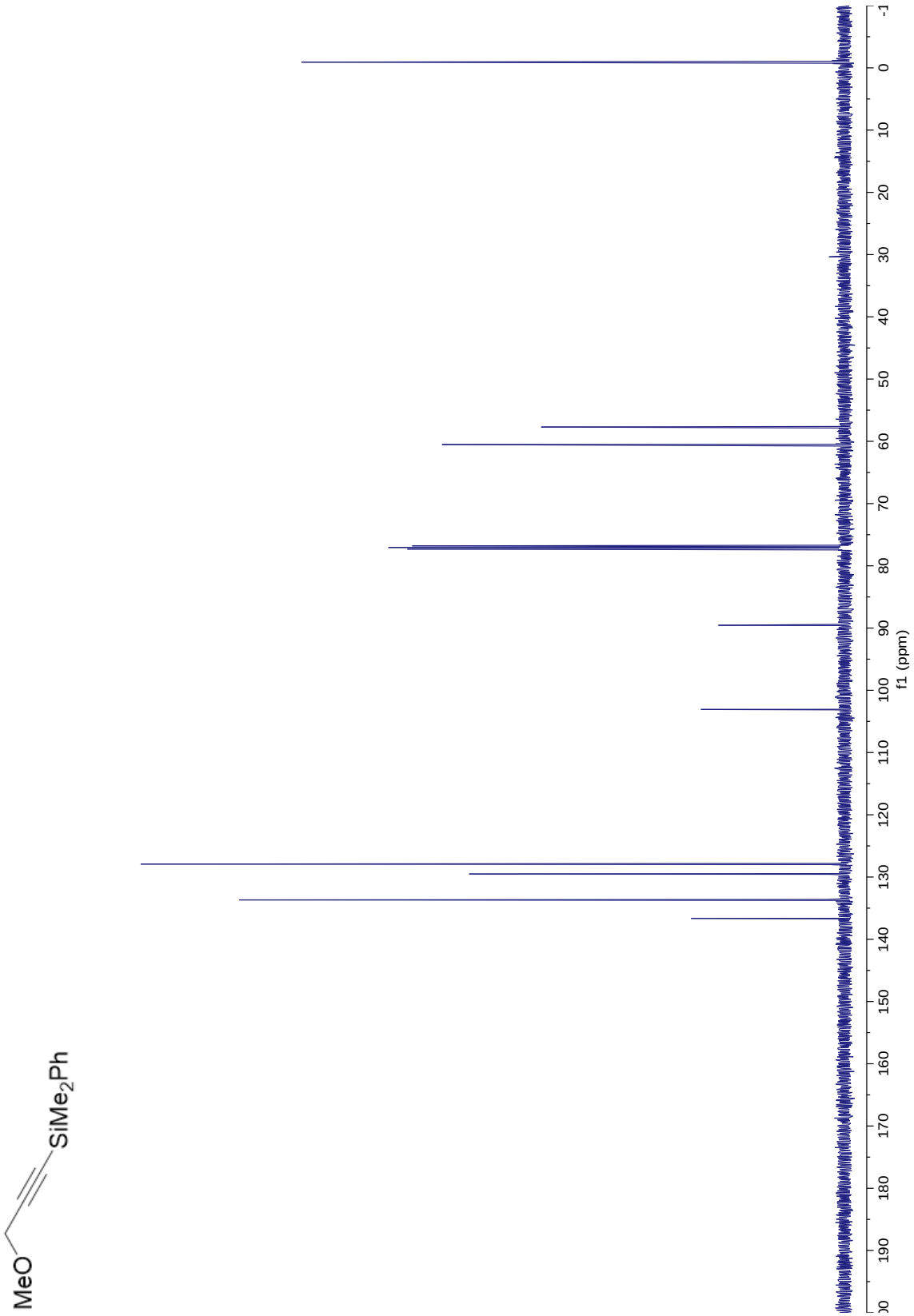
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4p.**



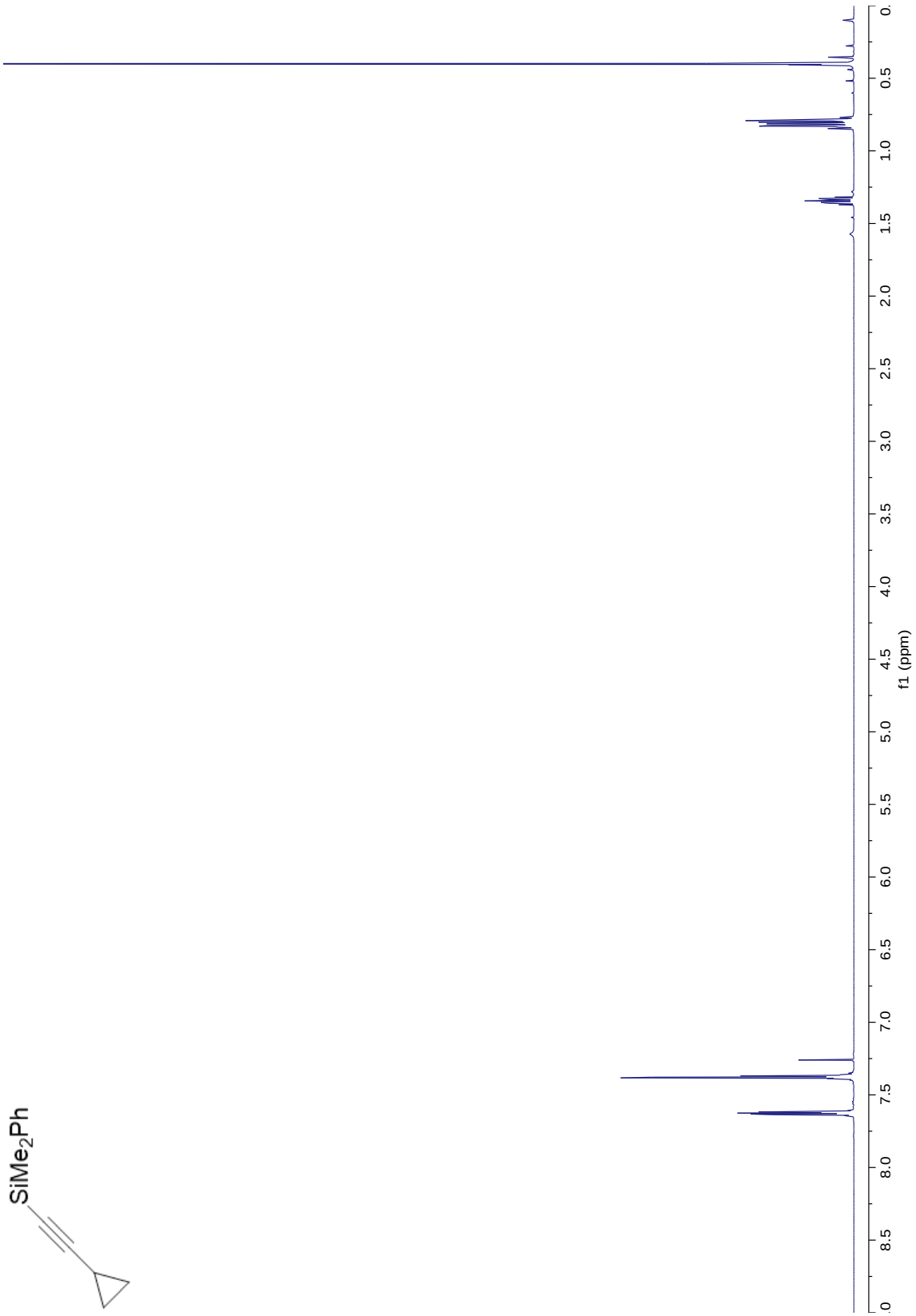
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4p.**



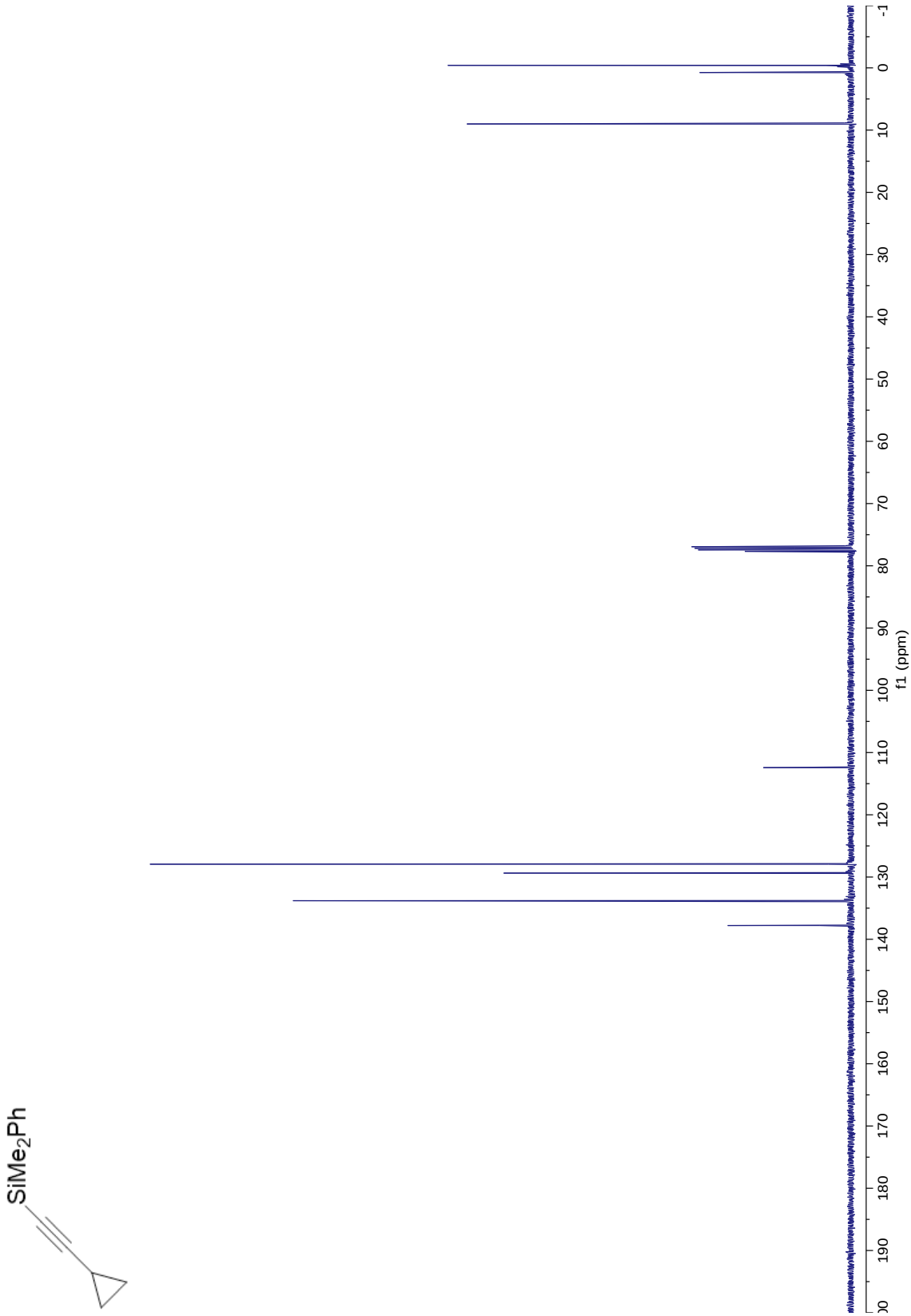
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4q.**



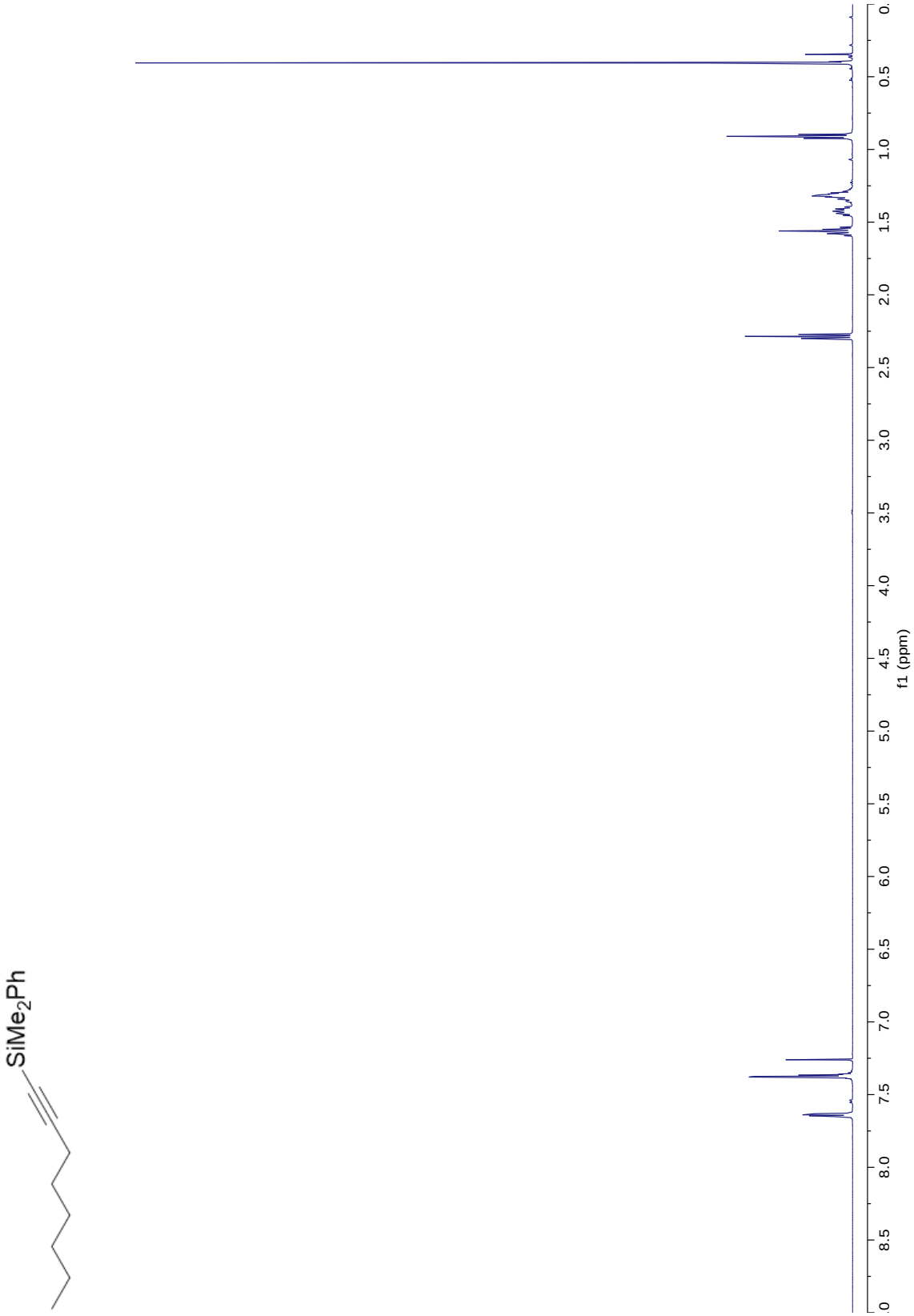
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4q.**



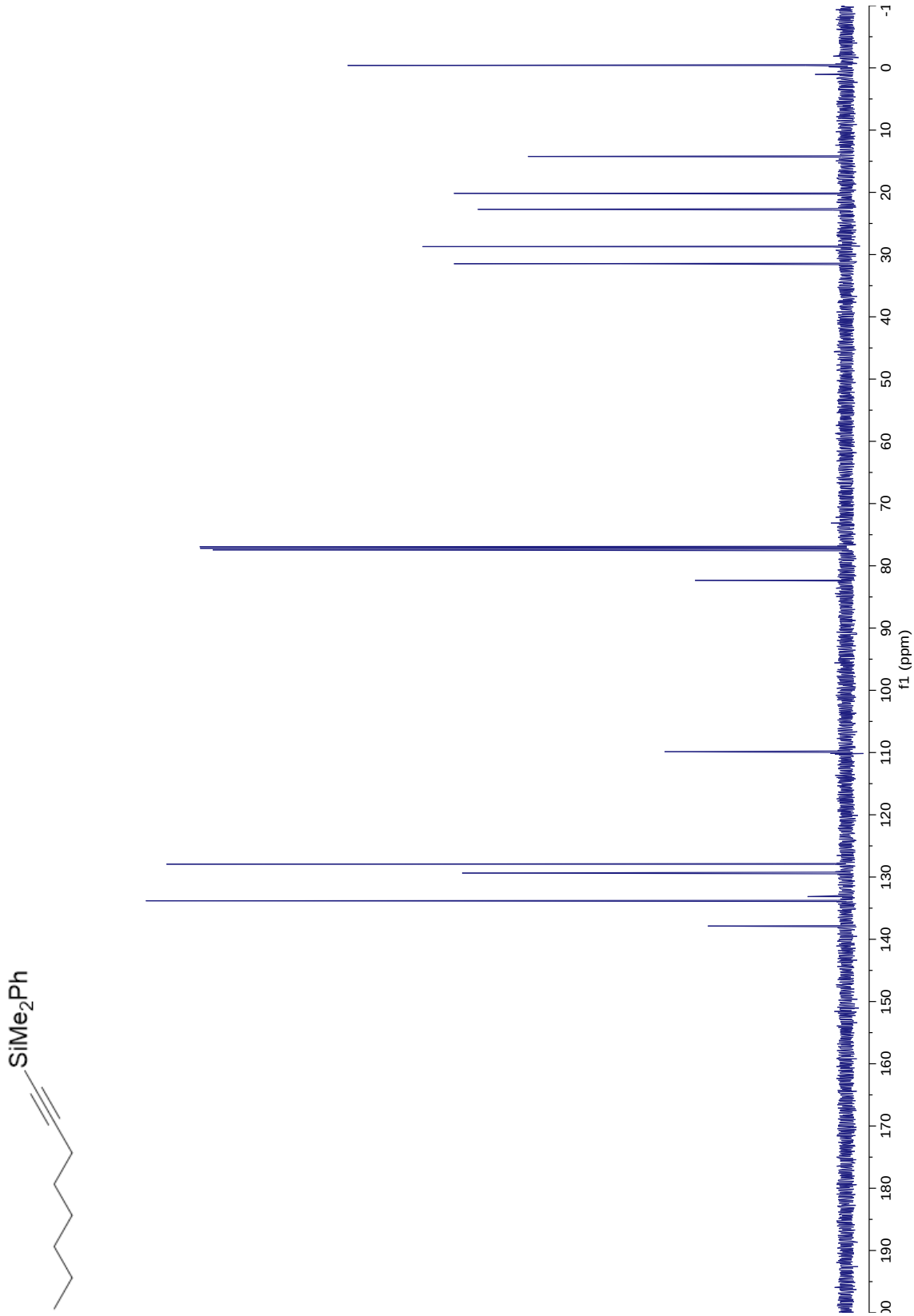
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4r.**



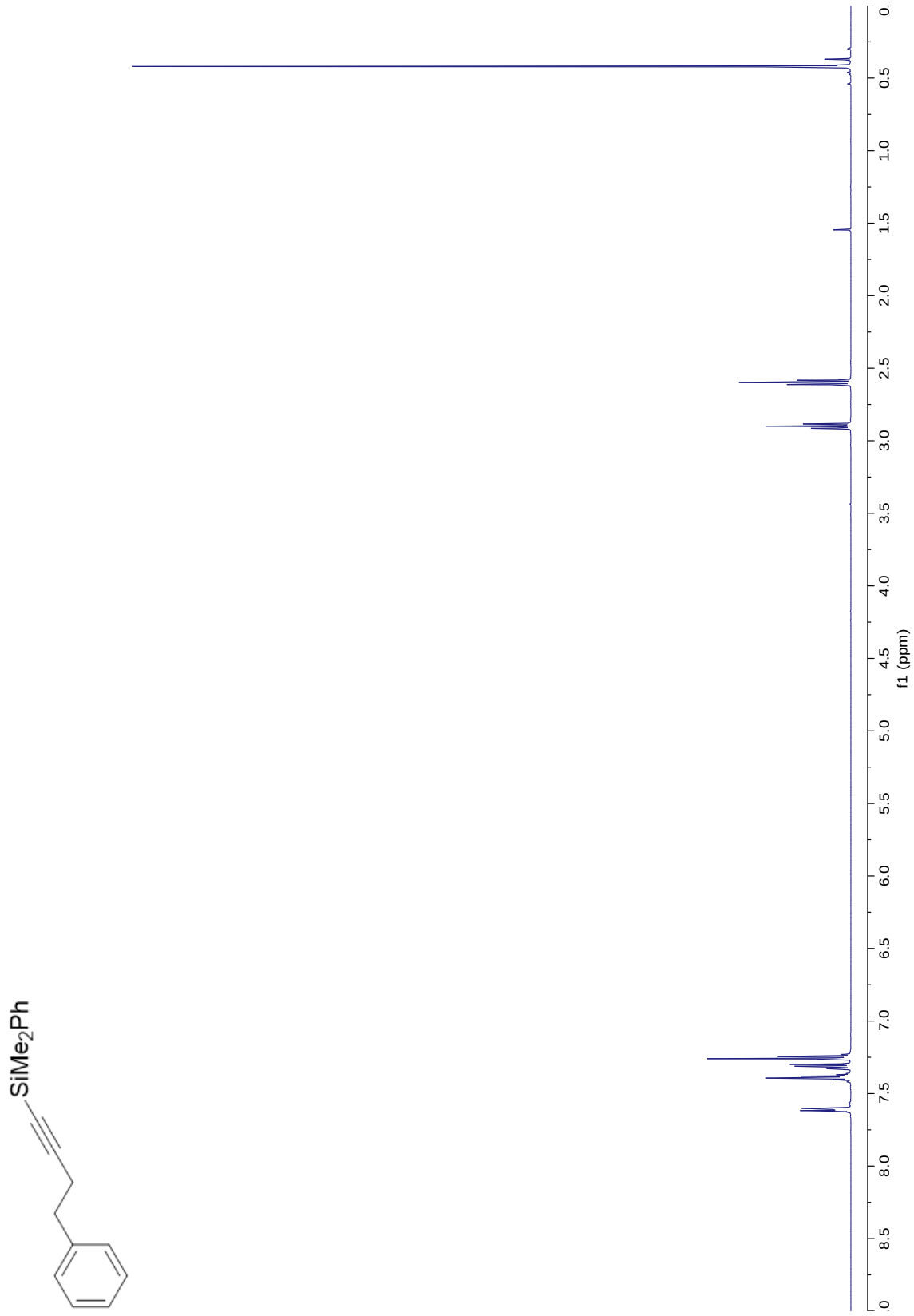
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4r.**



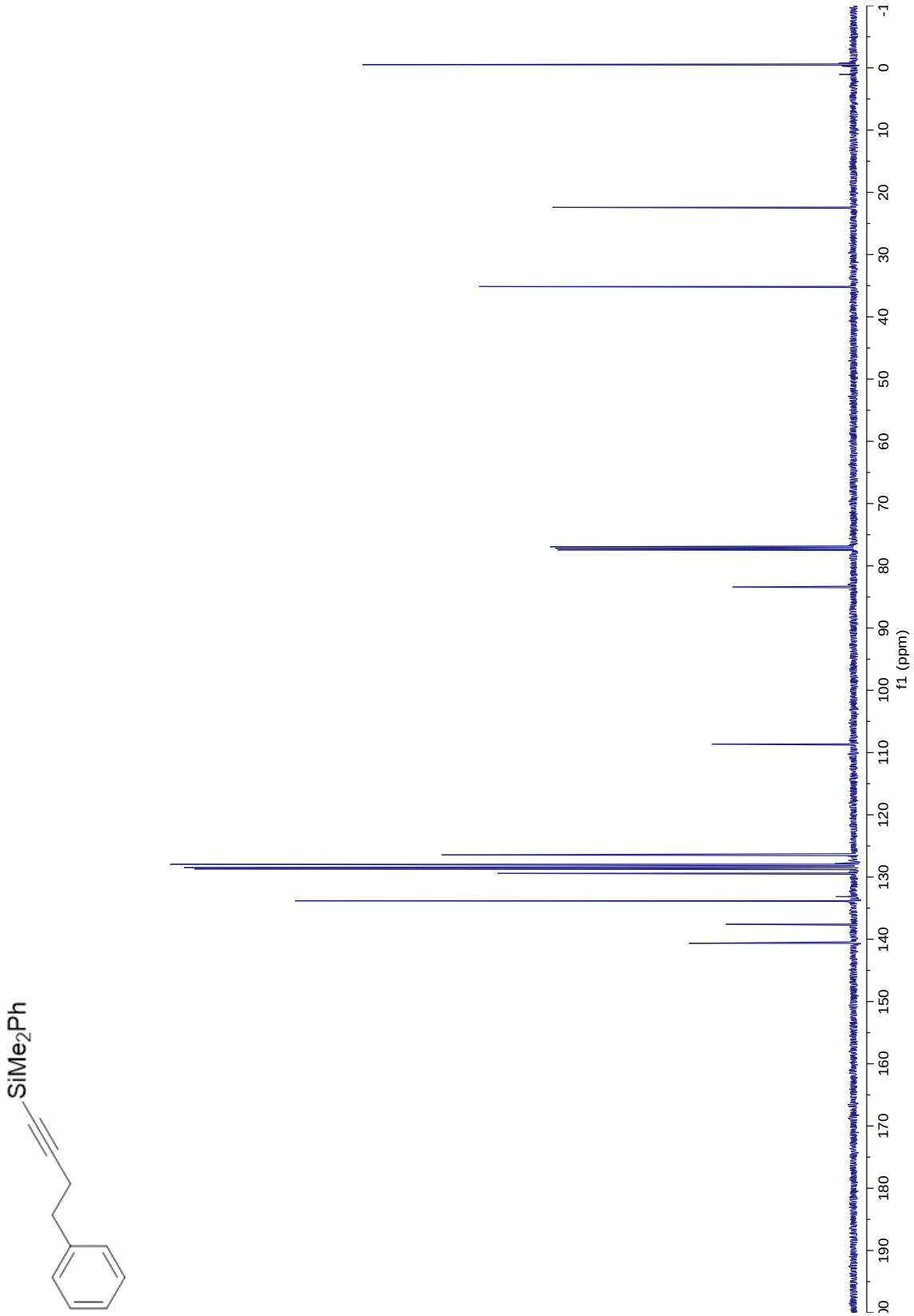
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4s.**



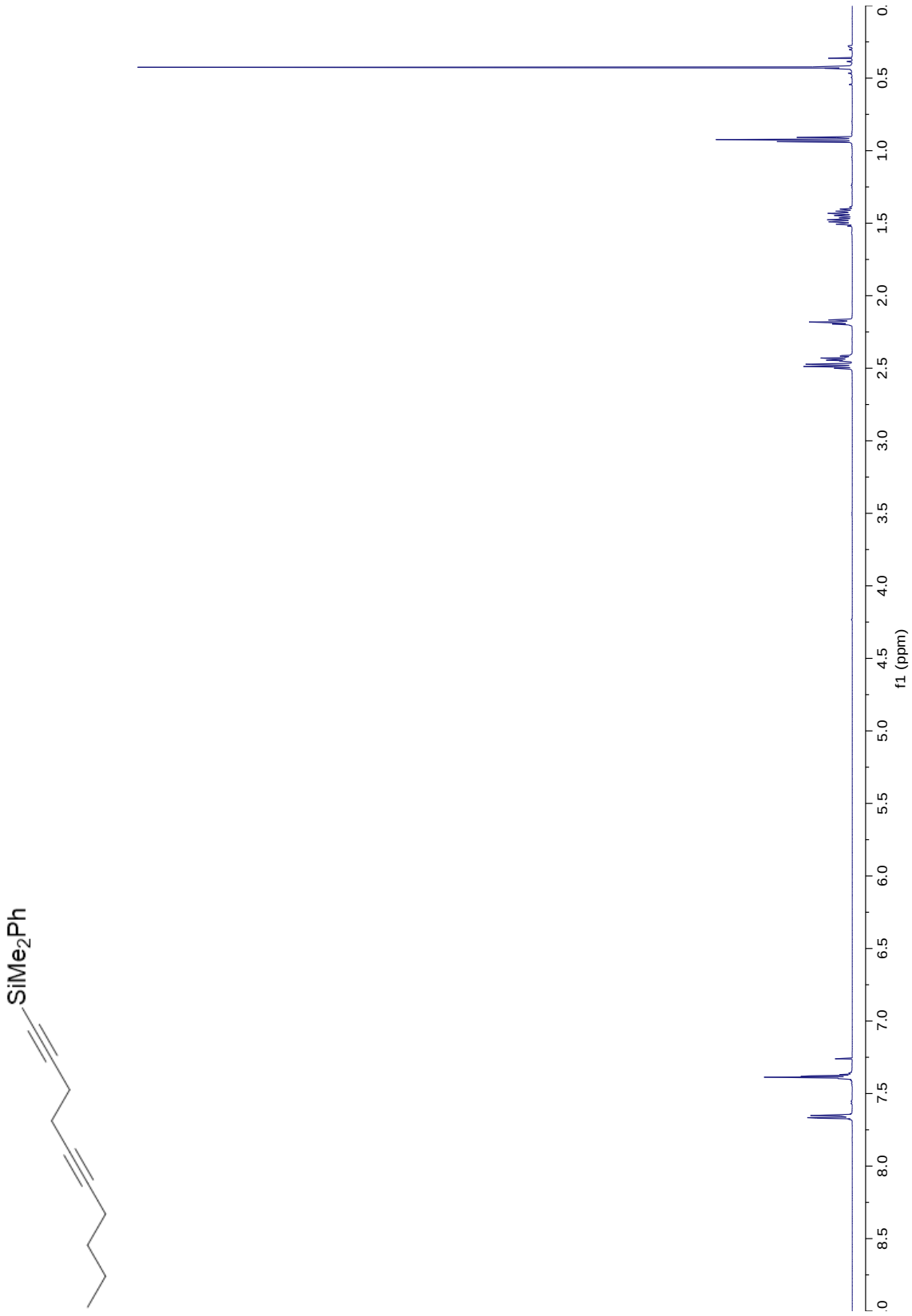
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4s.**



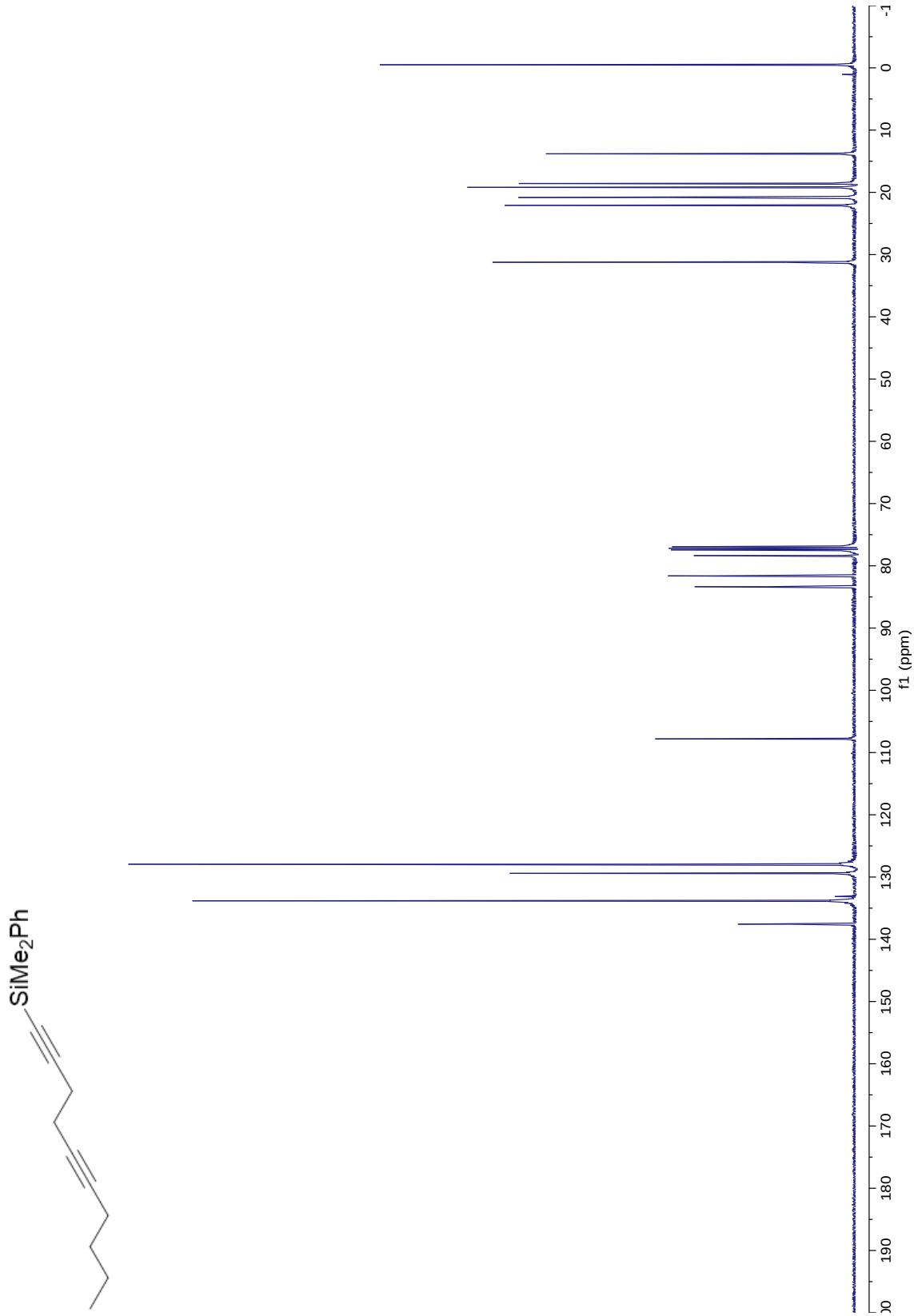
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4t.**



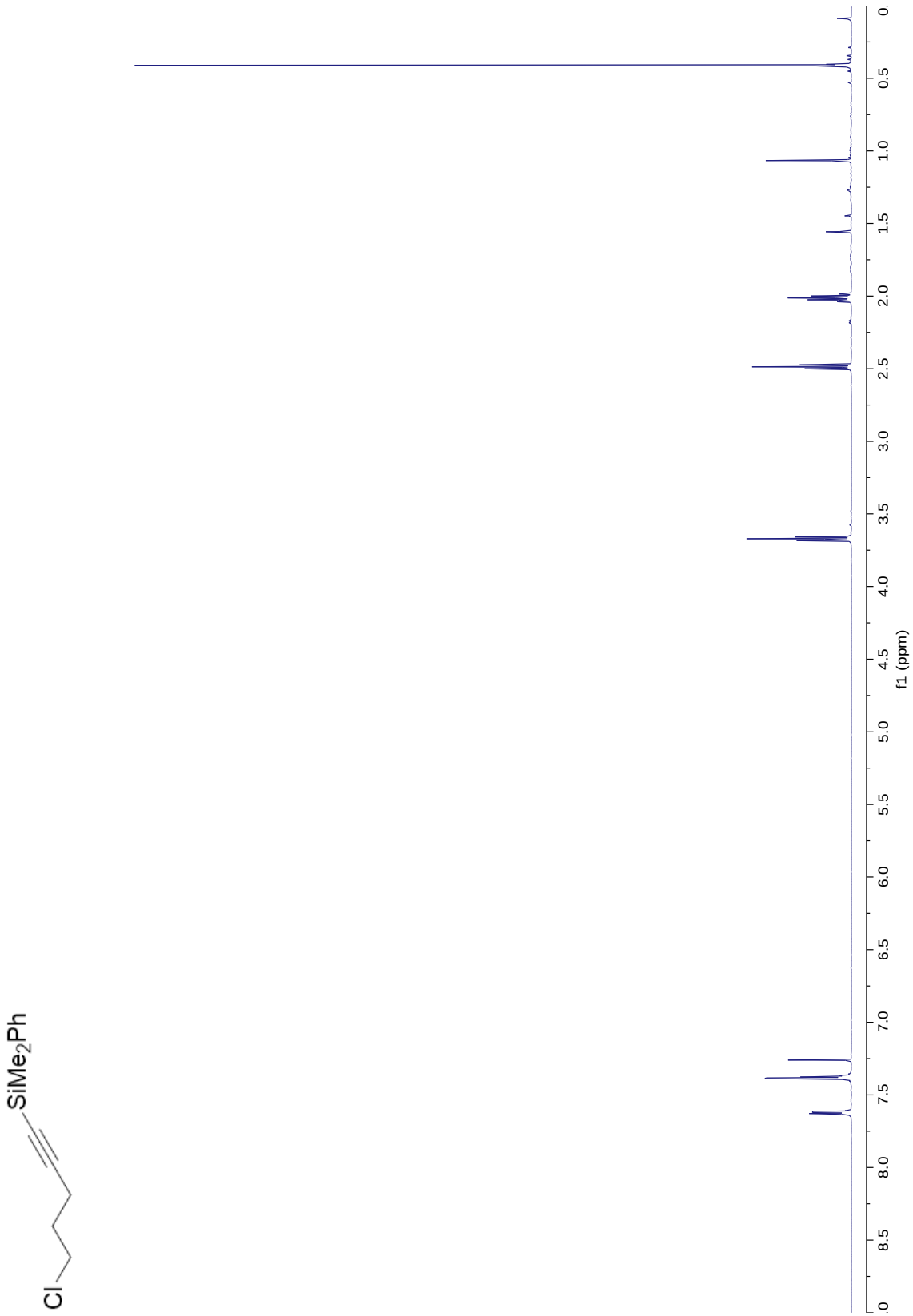
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4t.**



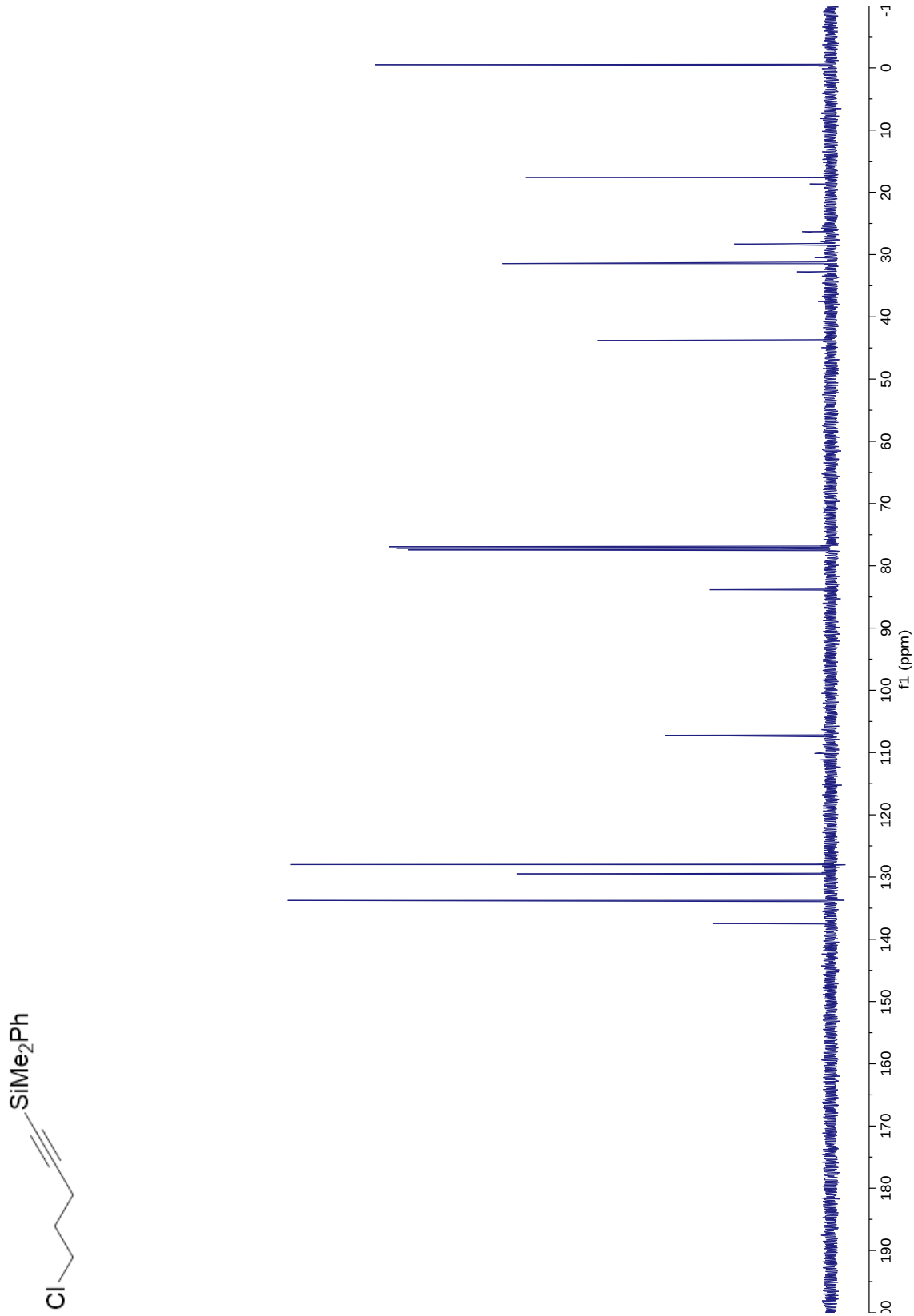
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4u.**



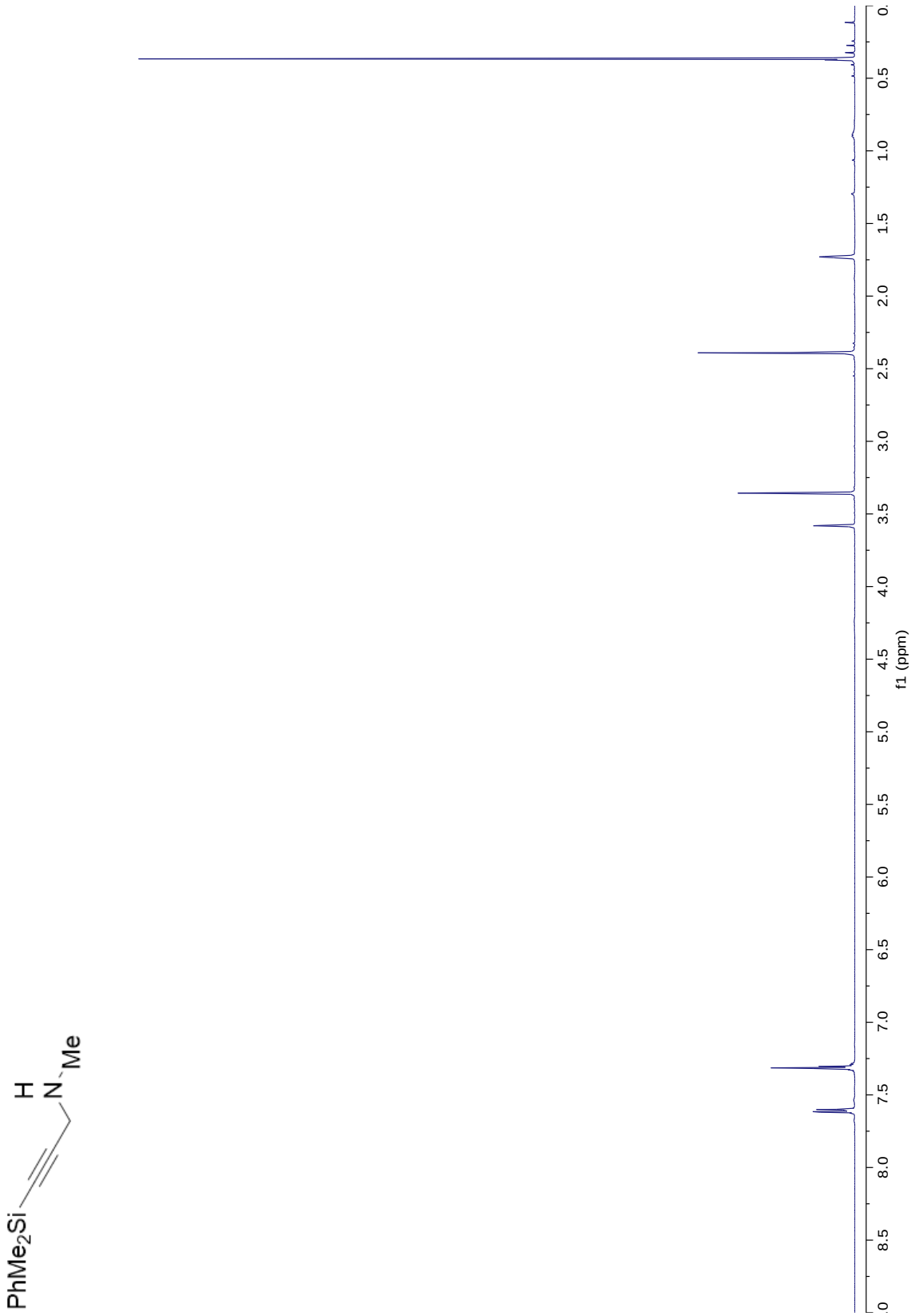
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4u.**



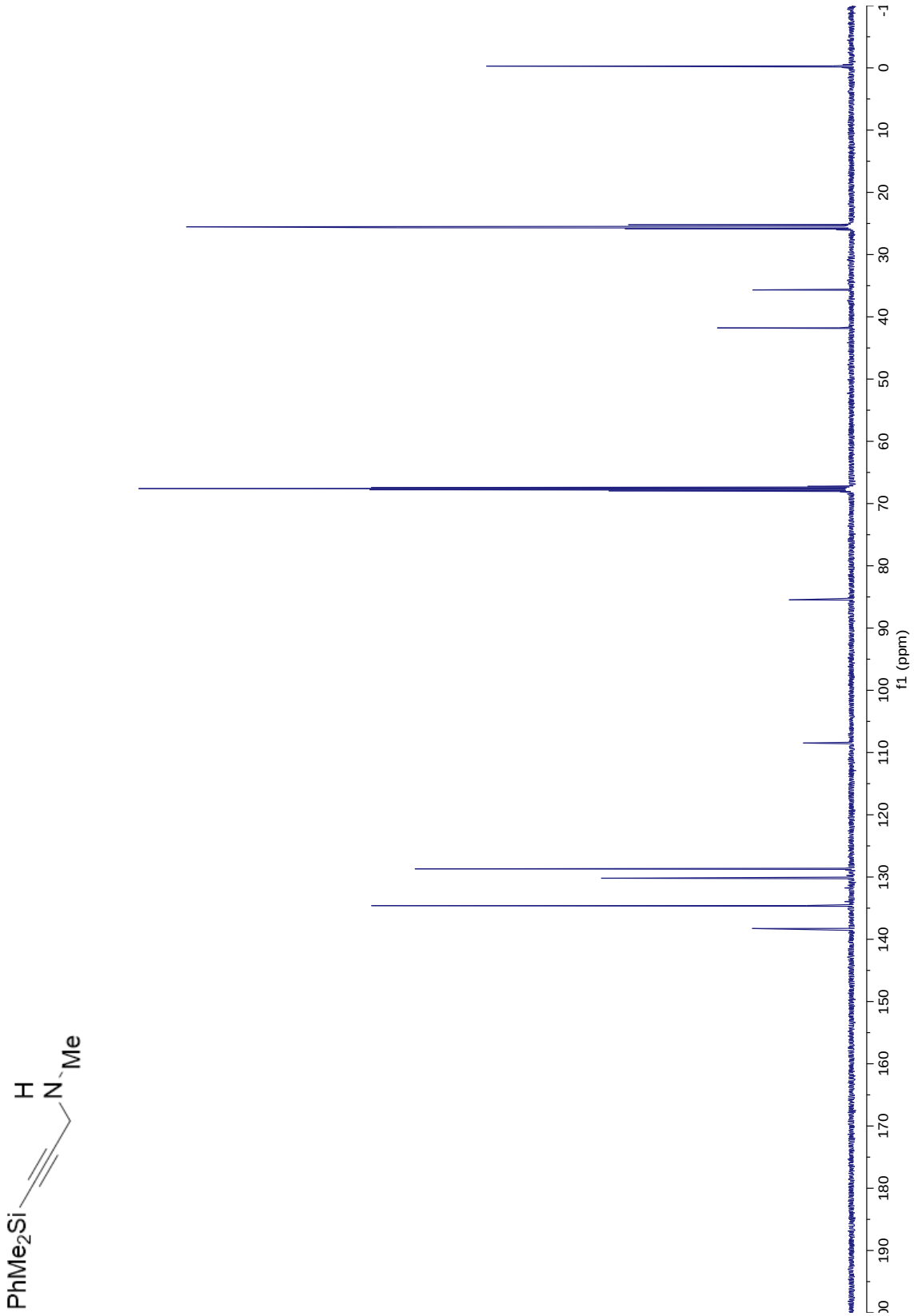
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4v.**



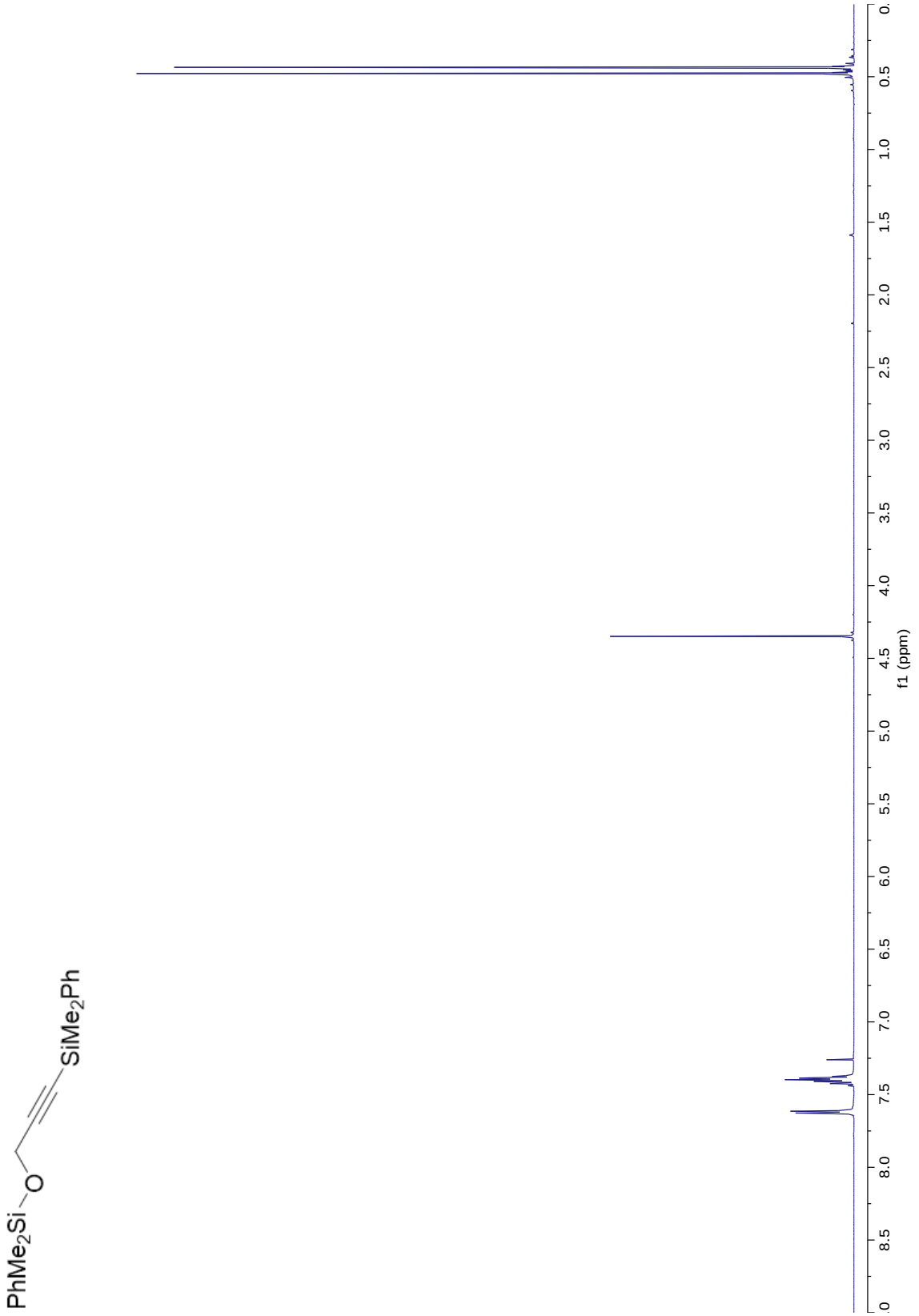
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4v.**



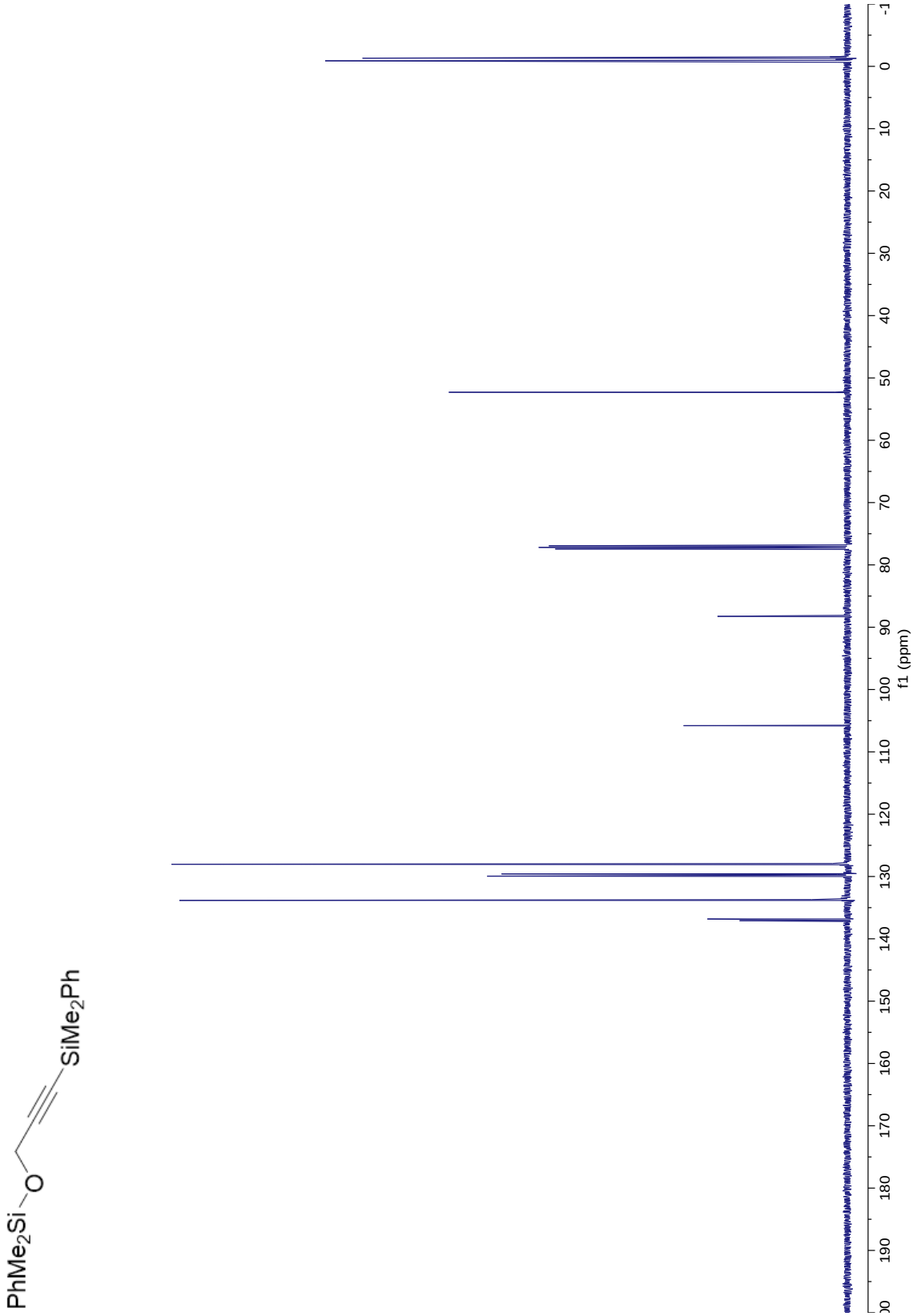
^{1}H NMR (500 MHz, THF-*d8*) of compound **4w.**



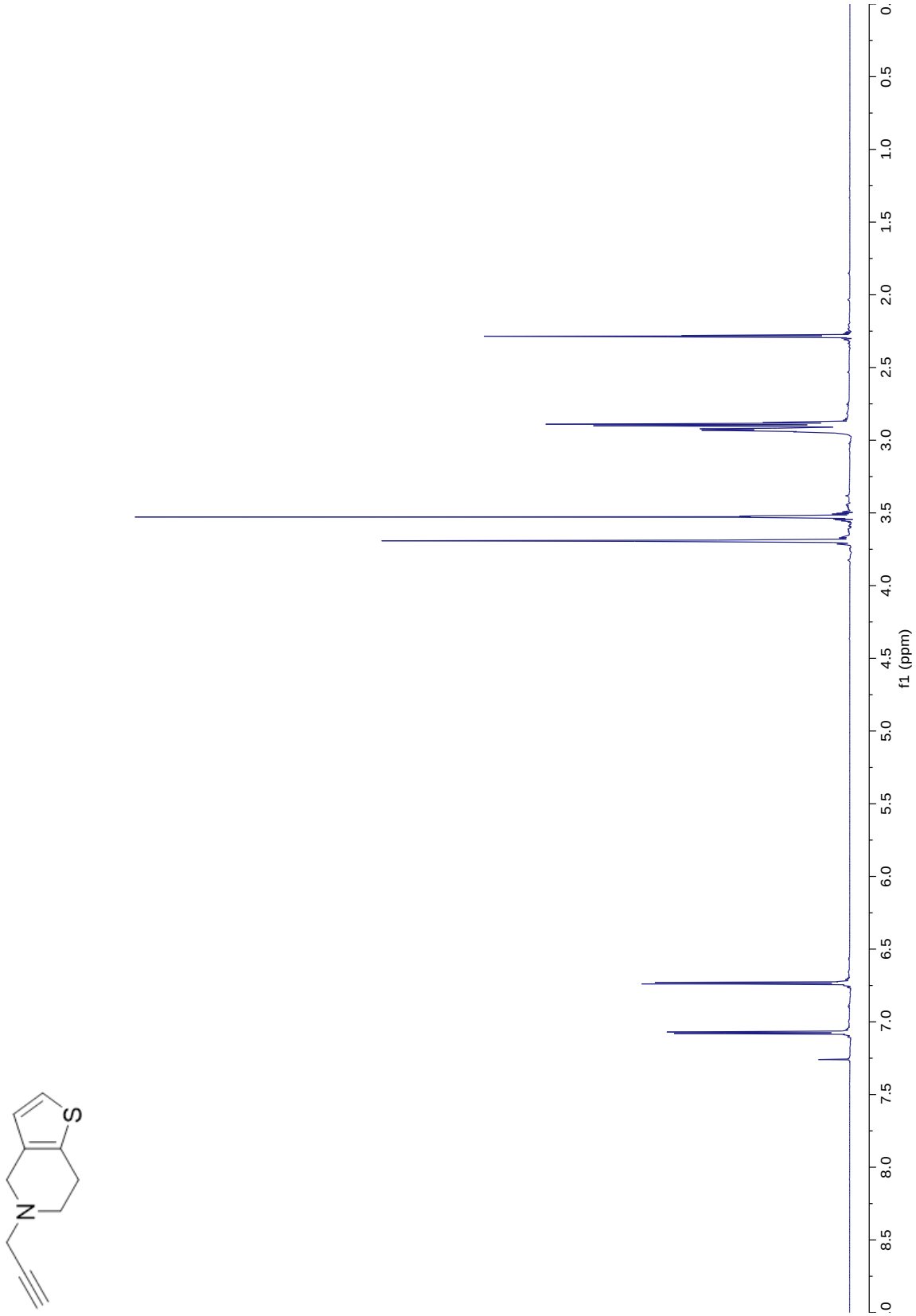
^{13}C NMR (126 MHz, THF-*d8*) of compound **4w.**



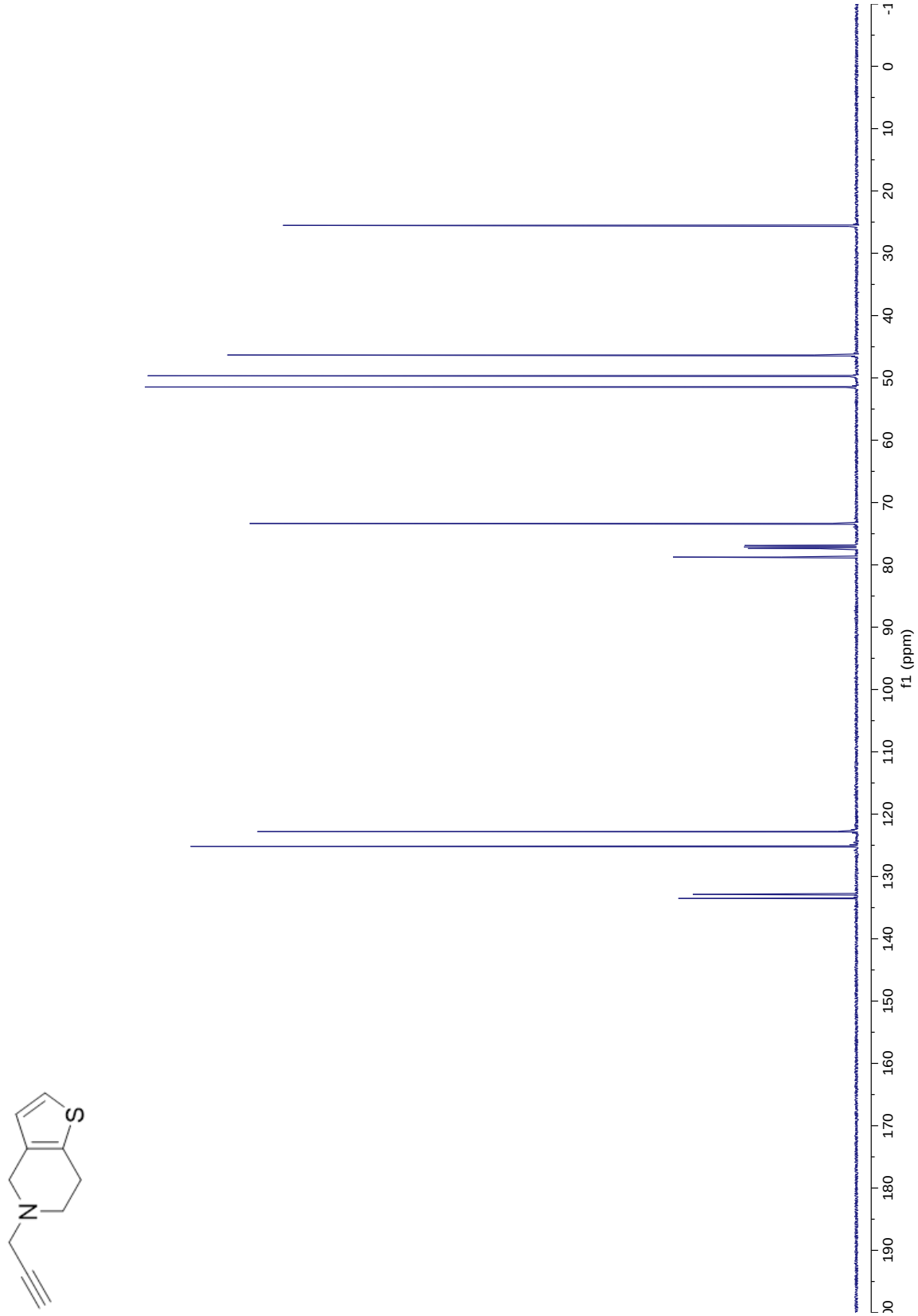
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4x.**



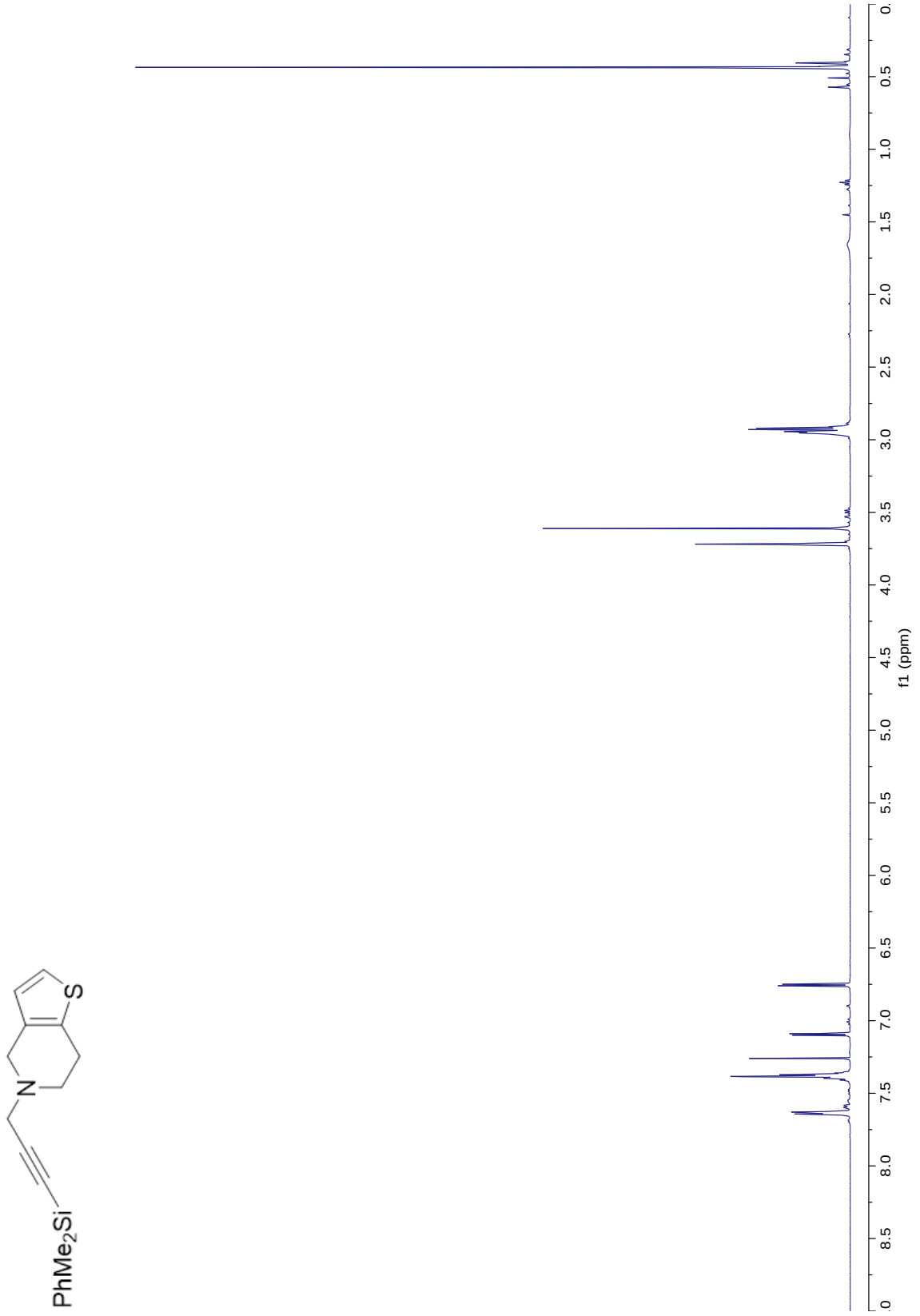
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4x.**



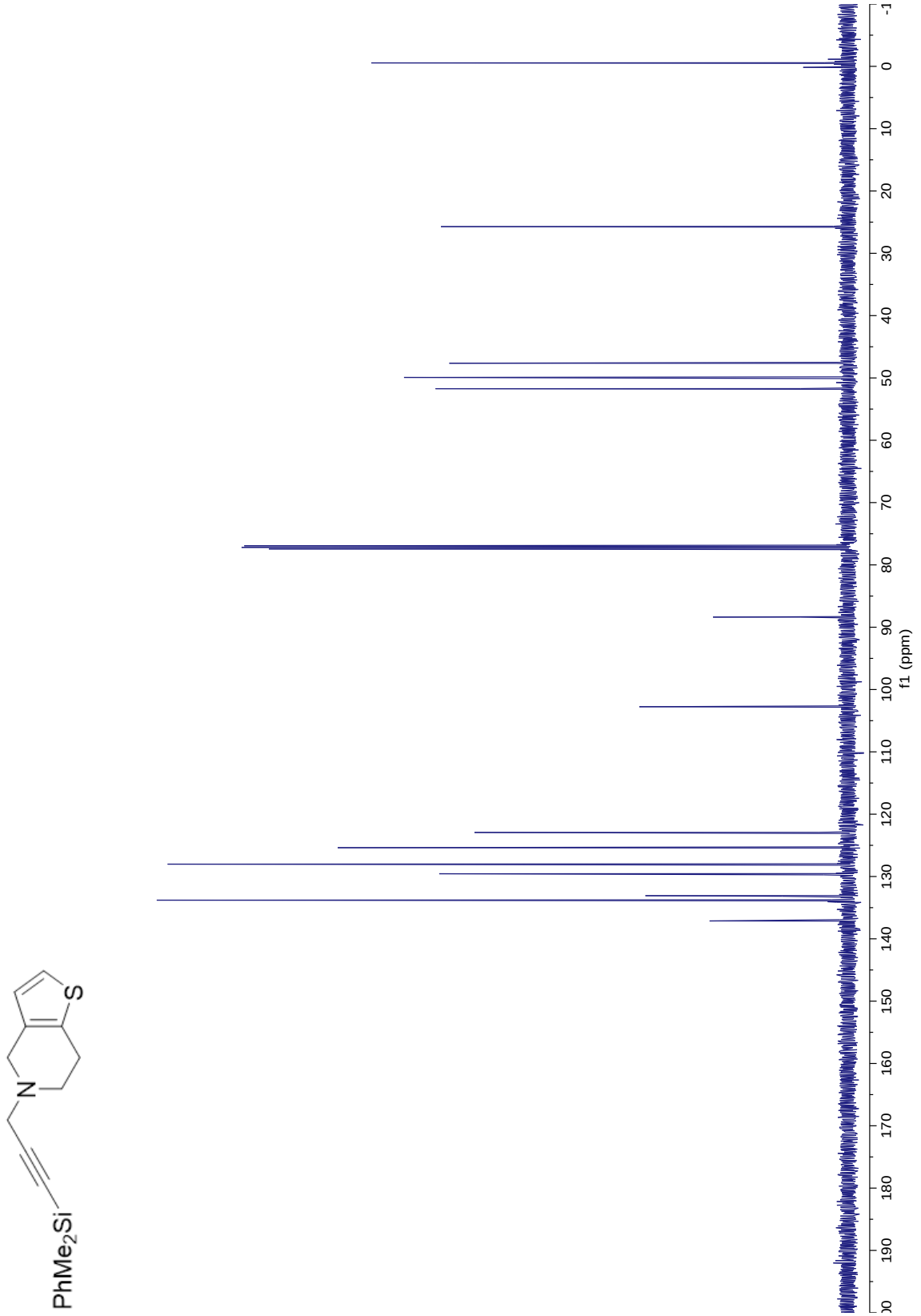
^{1}H NMR (500 MHz, $CDCl_3$) of compound **3y.**



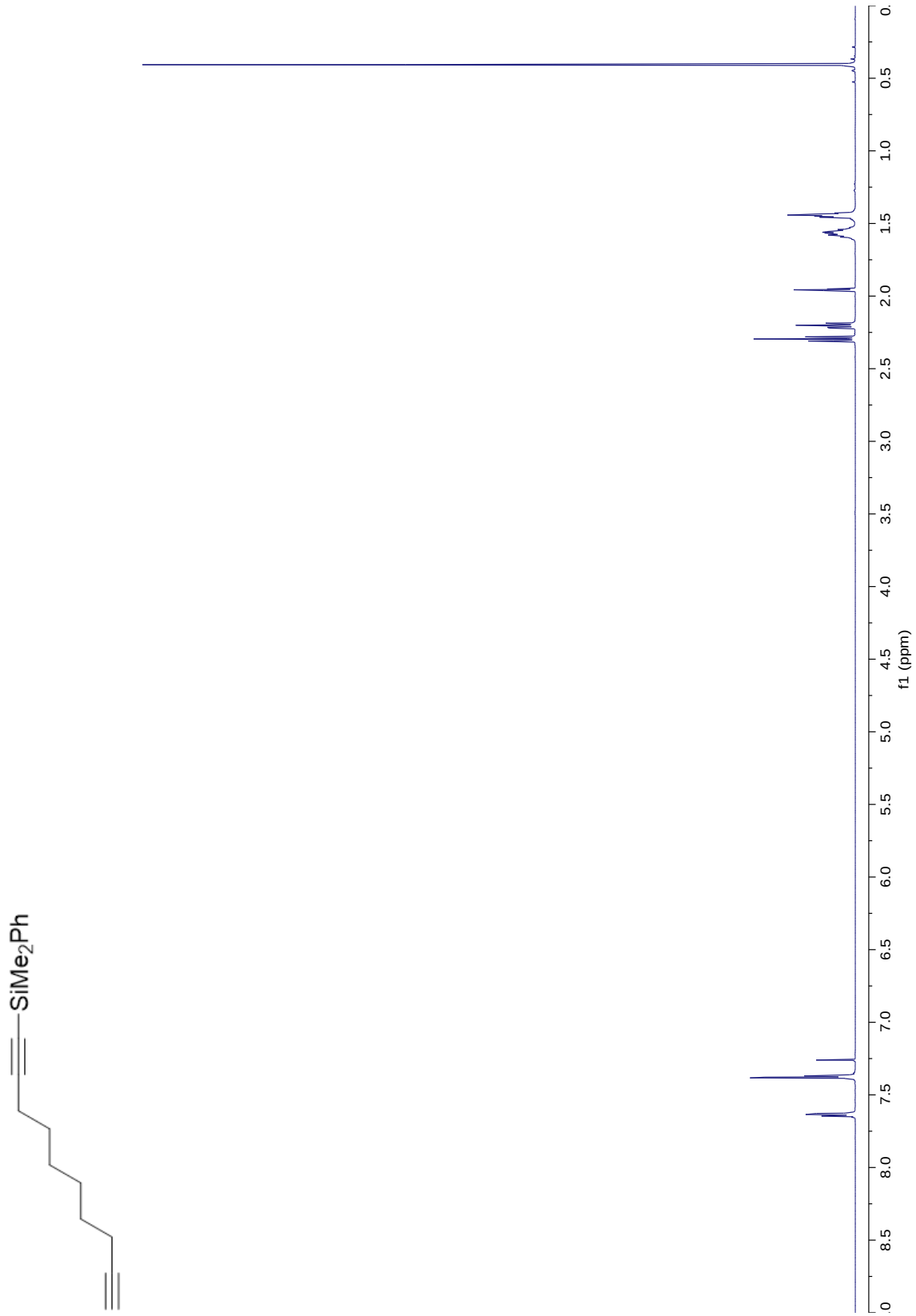
^{13}C NMR (126 MHz, $CDCl_3$) of compound **3y.**



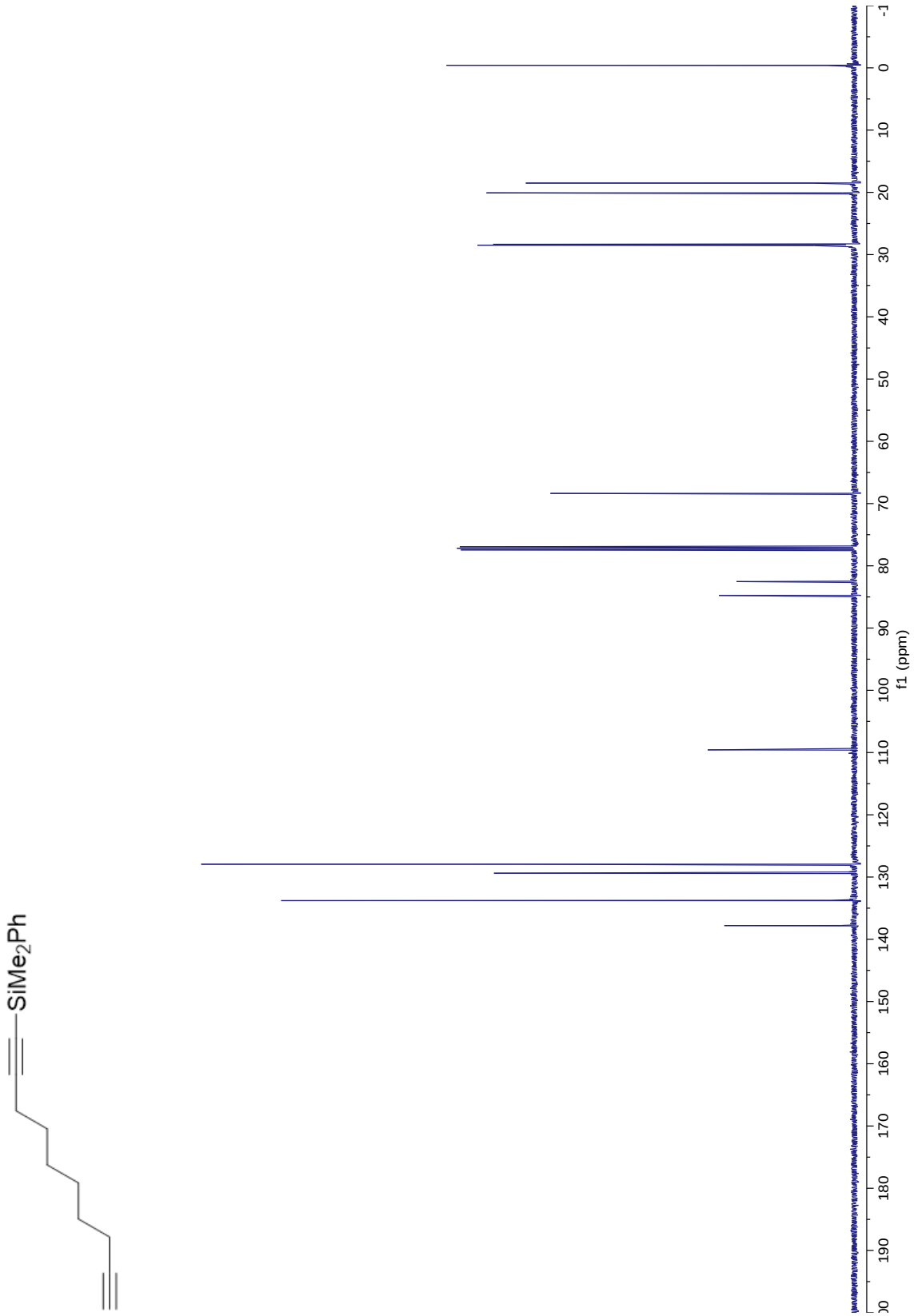
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4y.**



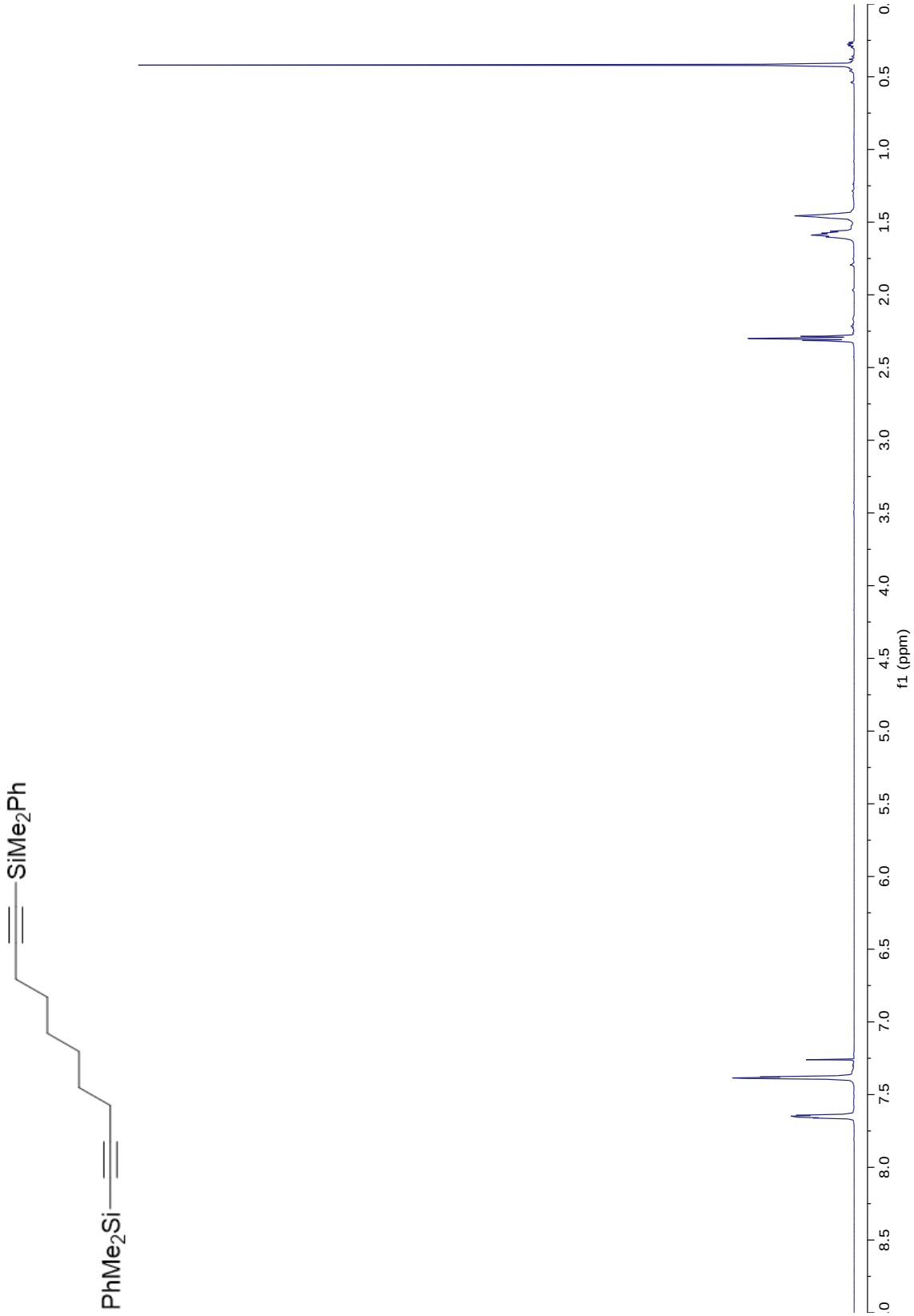
^{13}C NMR (126 MHz, $CDCl_3$) of compound **4y.**



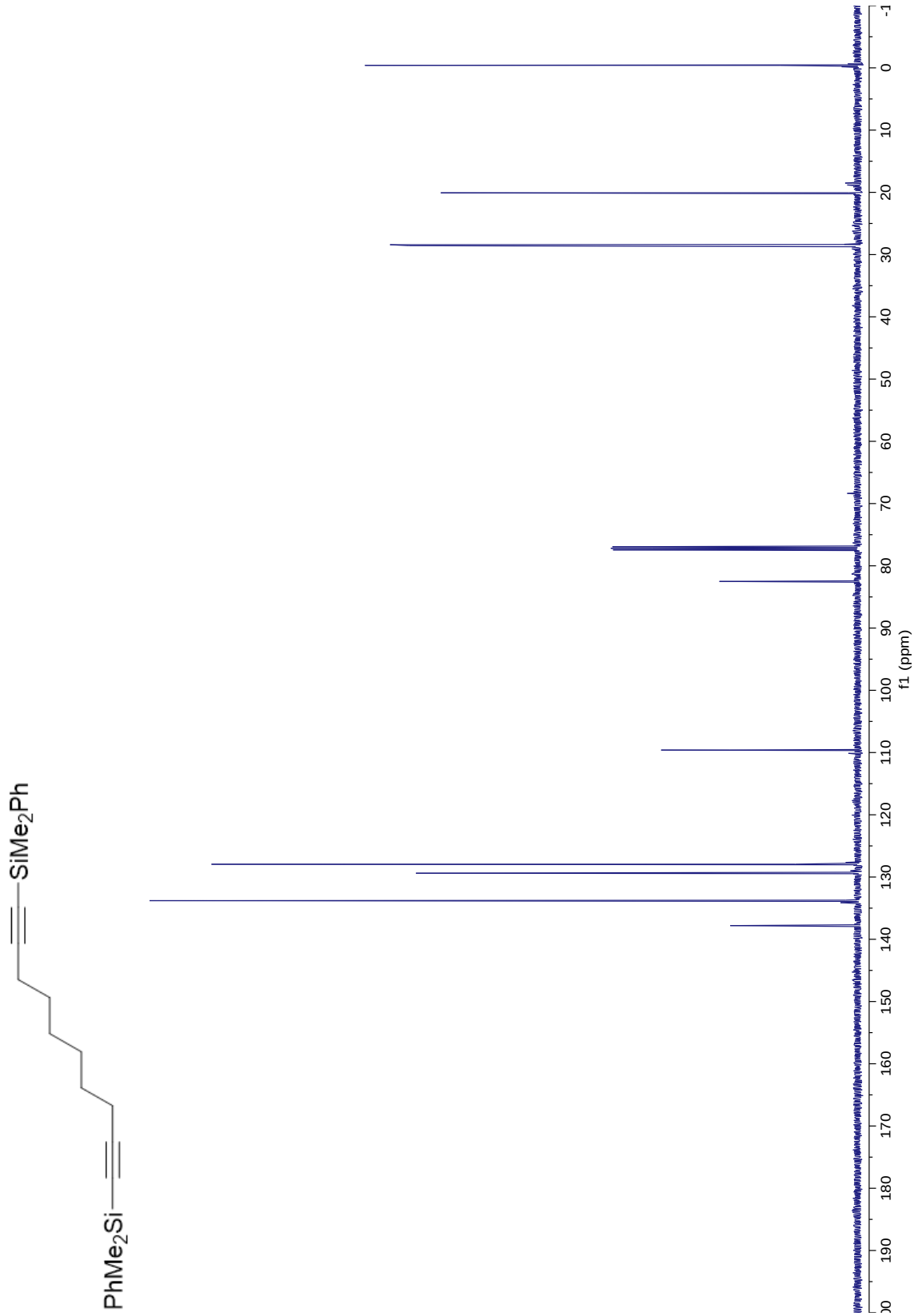
^{1}H NMR (500 MHz, $CDCl_3$) of compound **5a.**



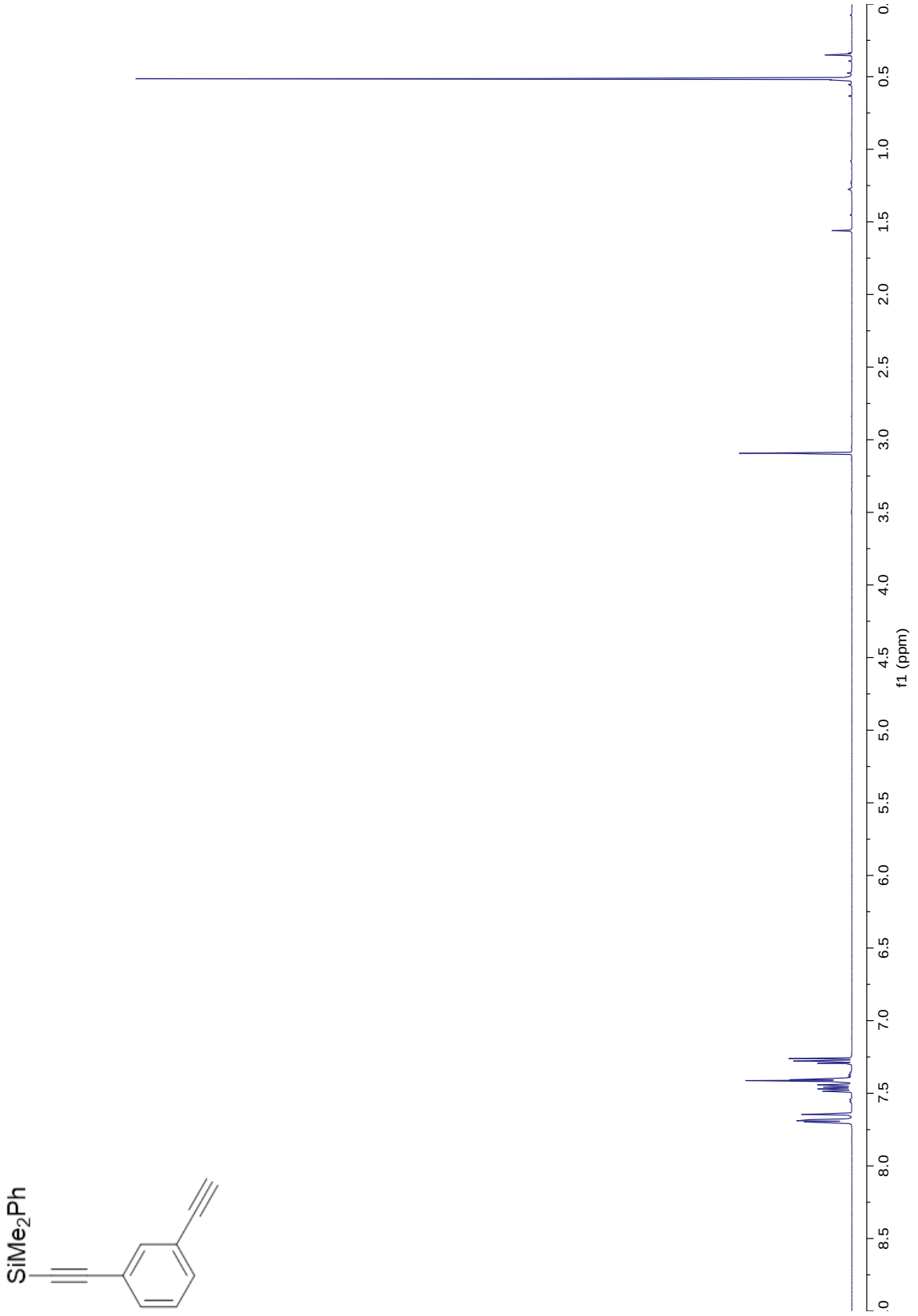
^{13}C NMR (126 MHz, $CDCl_3$) of compound **5a.**



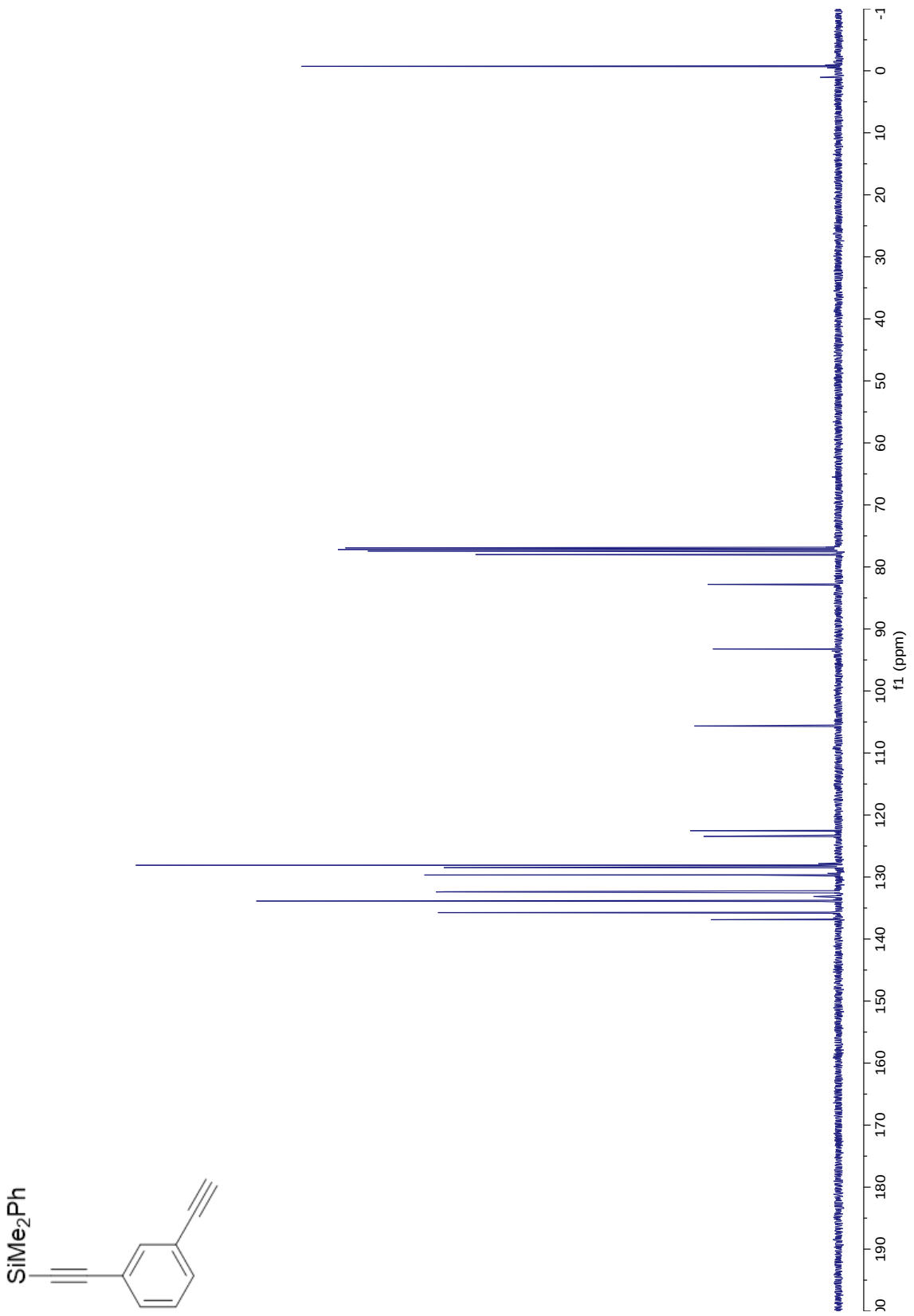
^{1}H NMR (500 MHz, $CDCl_3$) of compound **5b.**



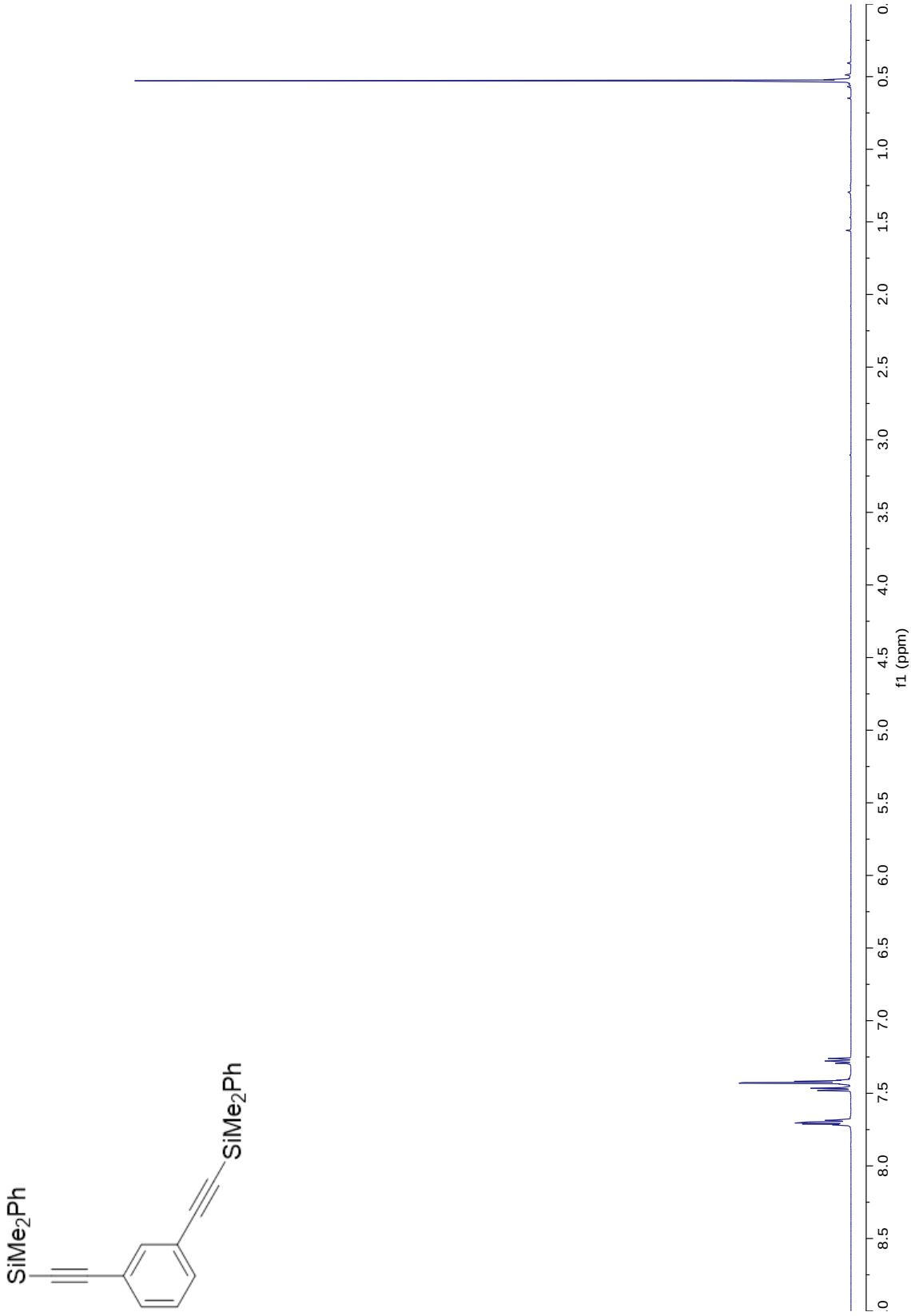
^{13}C NMR (126 MHz, $CDCl_3$) of compound **5b.**



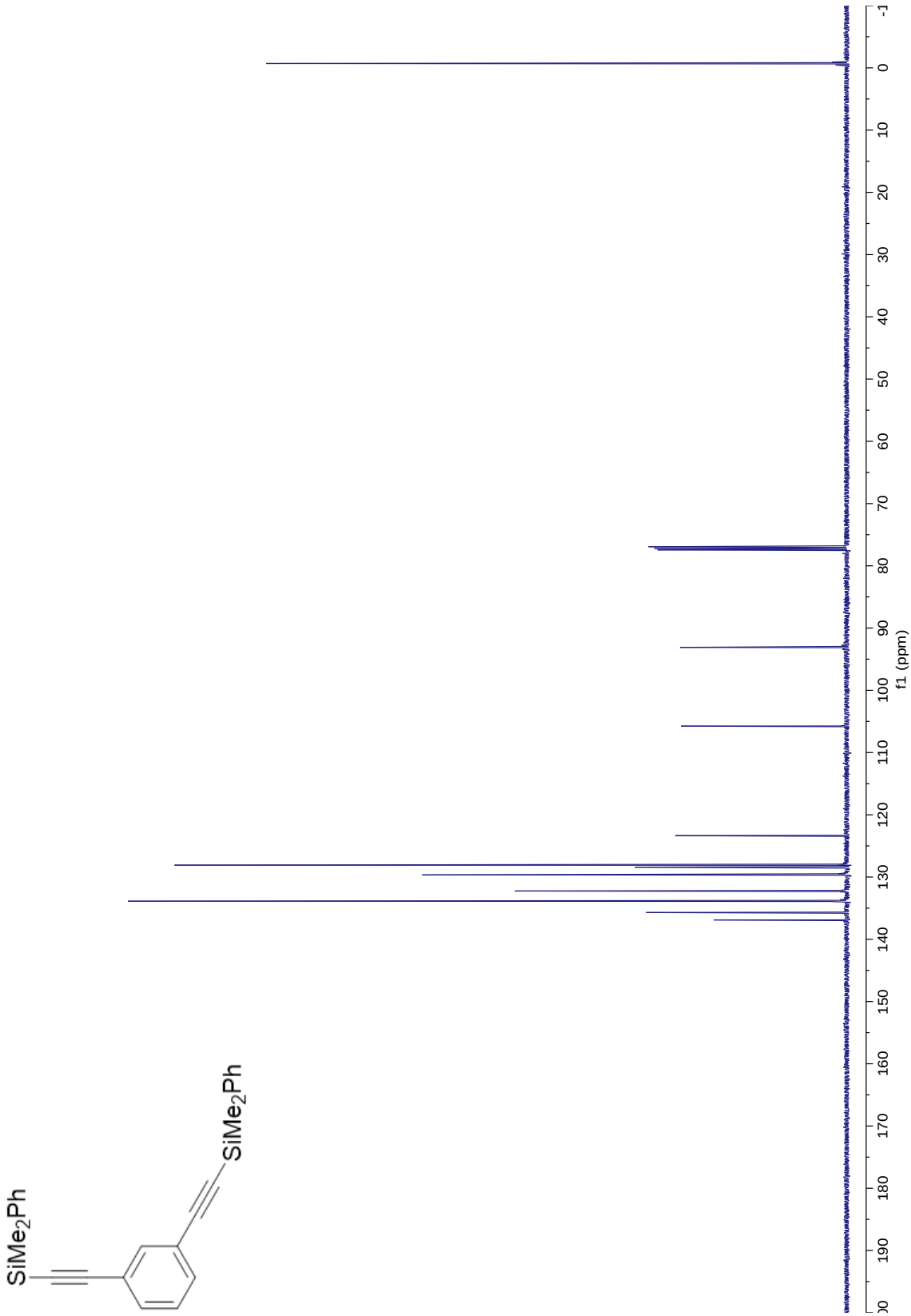
^{1}H NMR (500 MHz, $CDCl_3$) of compound **6a.**



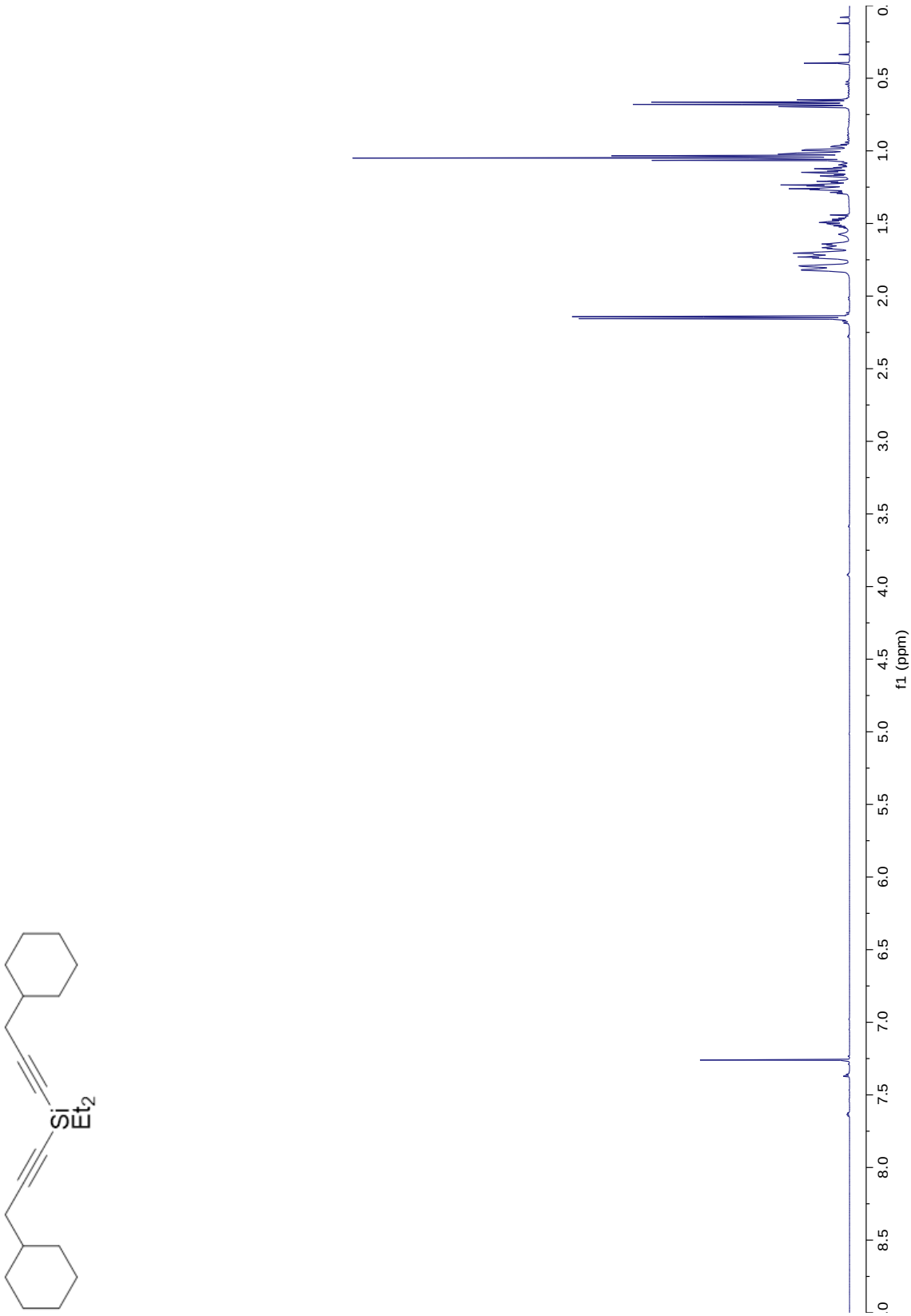
^{13}C NMR (126 MHz, $CDCl_3$) of compound **6a.**



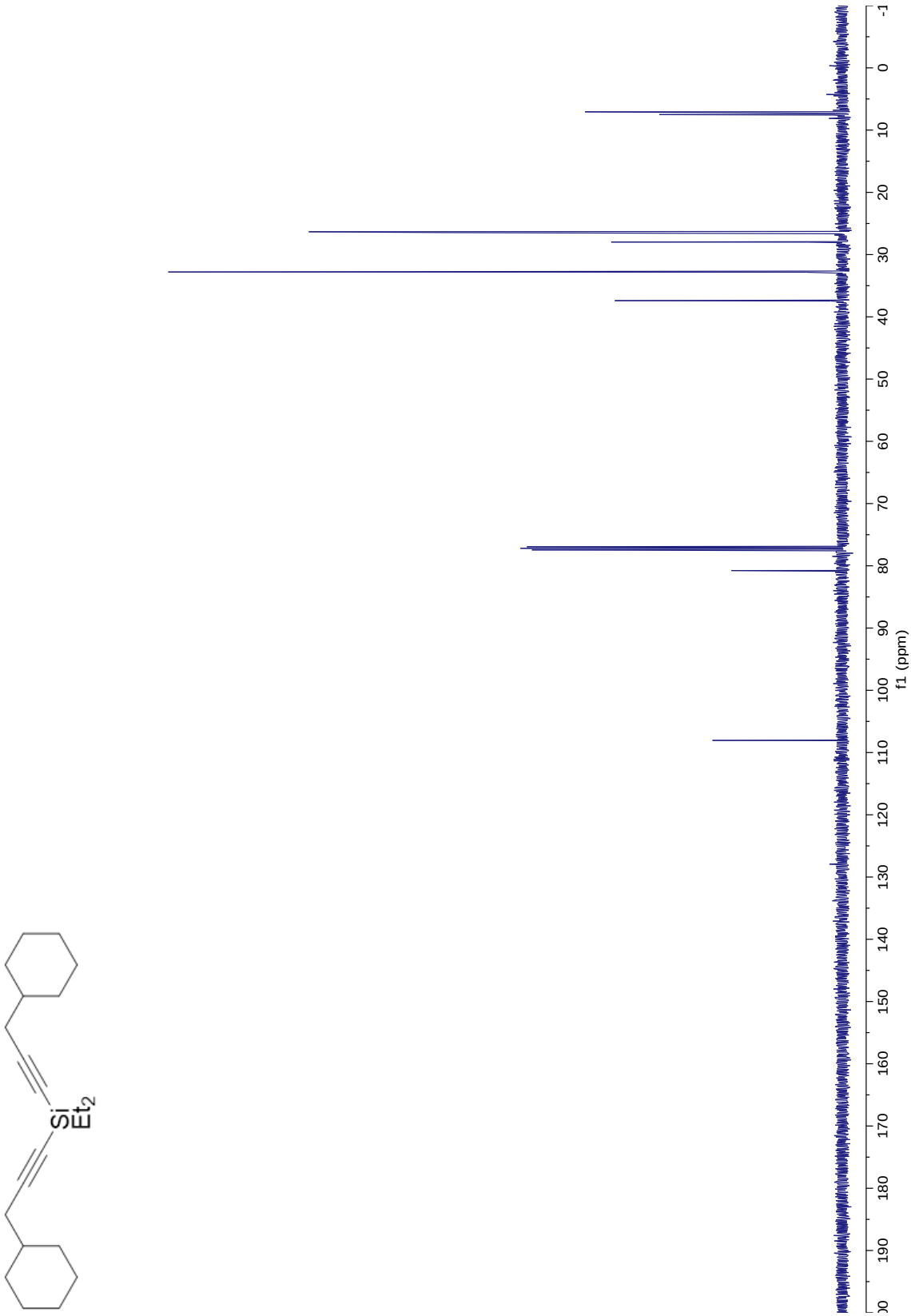
^{1}H NMR (500 MHz, $CDCl_3$) of compound **6b.**



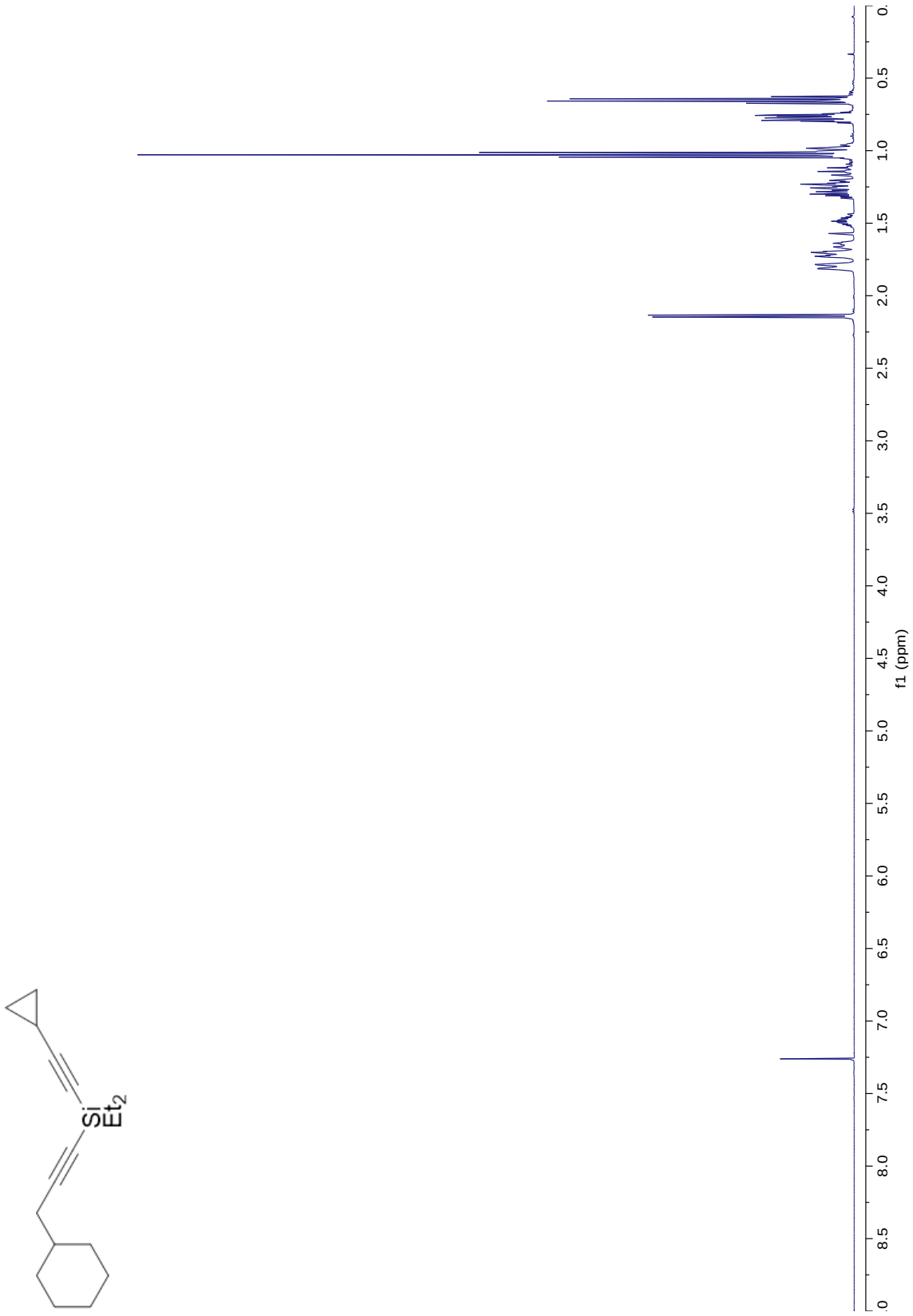
^{13}C NMR (126 MHz, $CDCl_3$) of compound **6b.**



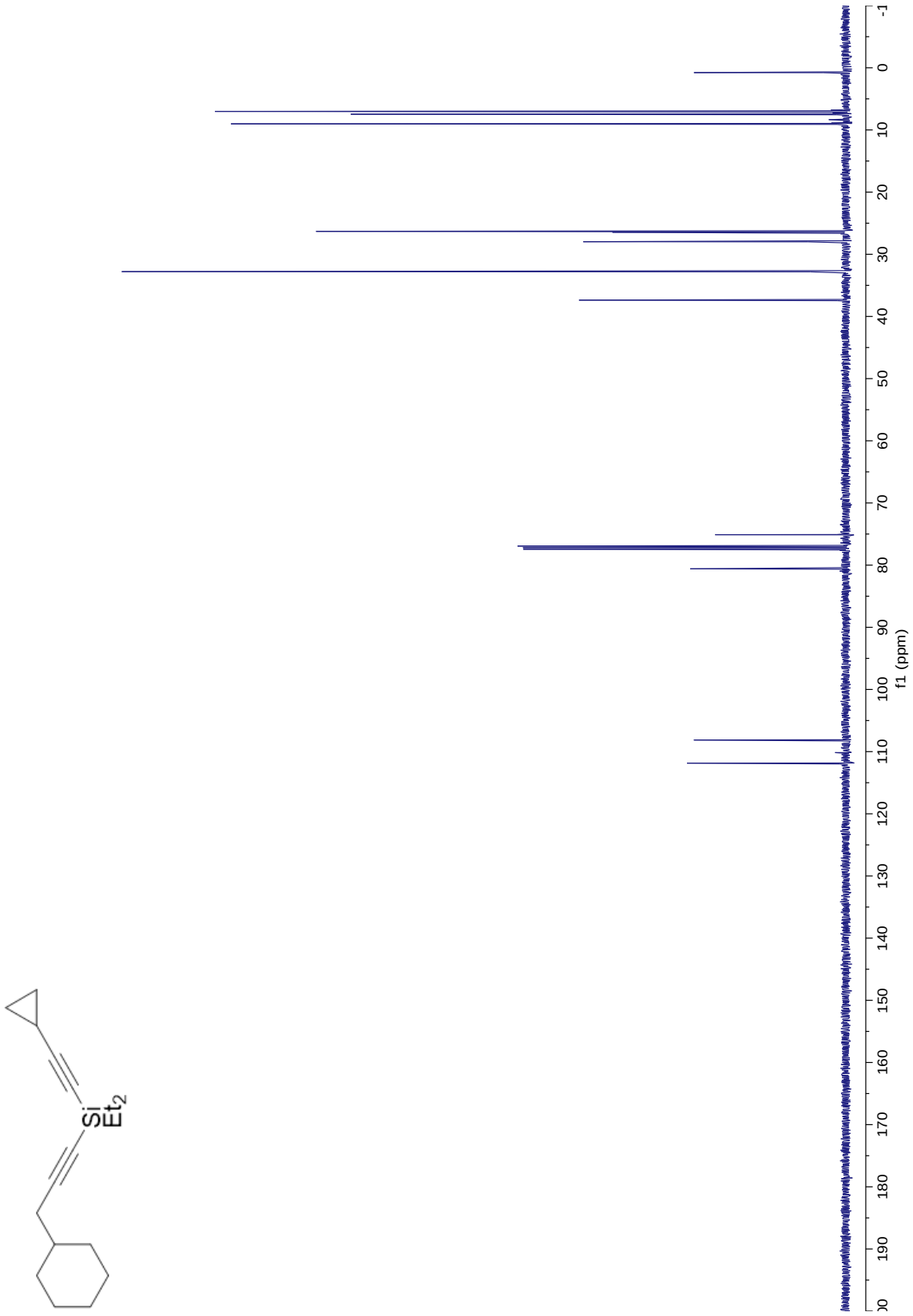
^{1}H NMR (500 MHz, $CDCl_3$) of compound **7.**



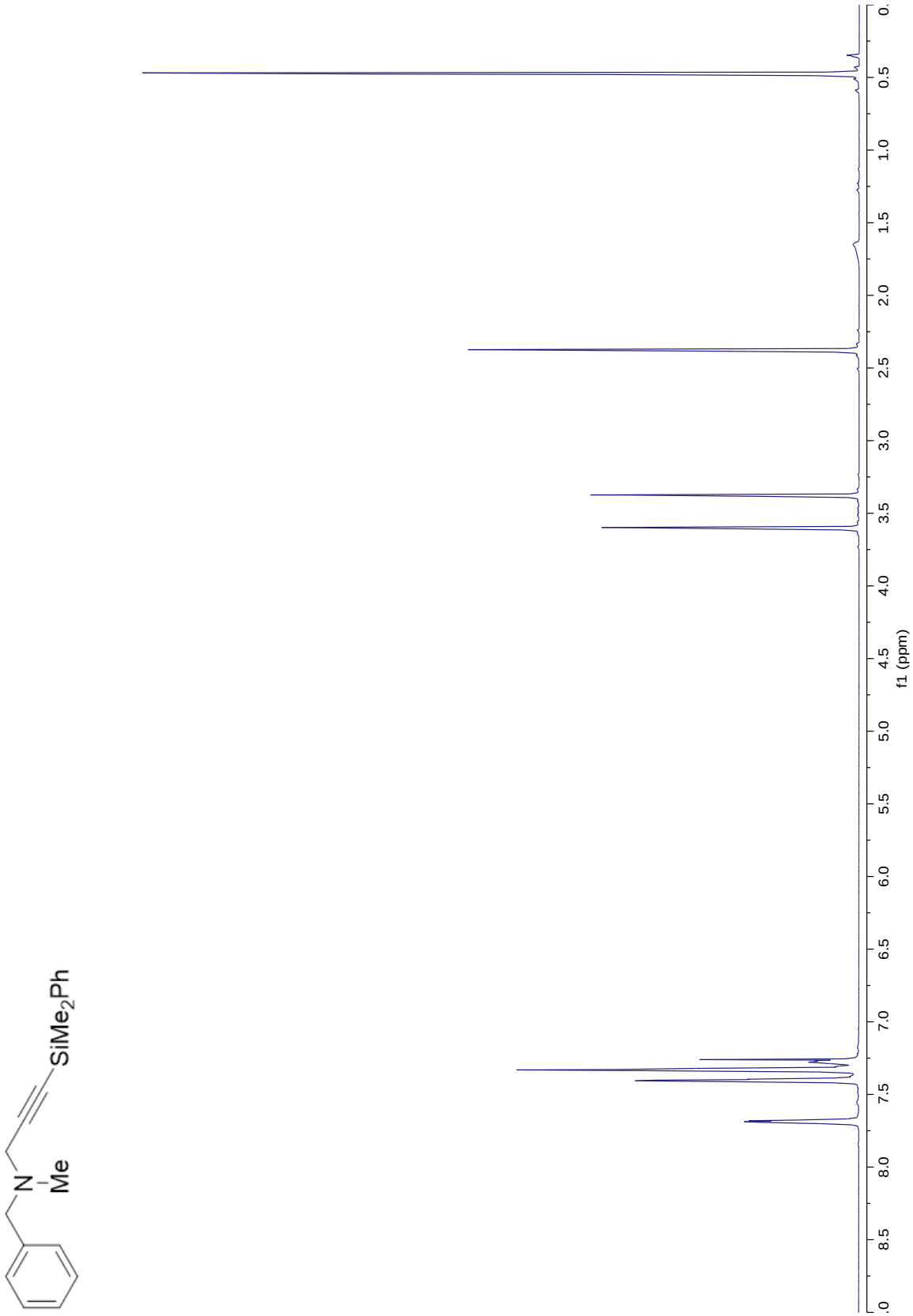
^{13}C NMR (126 MHz, $CDCl_3$) of compound **7.**



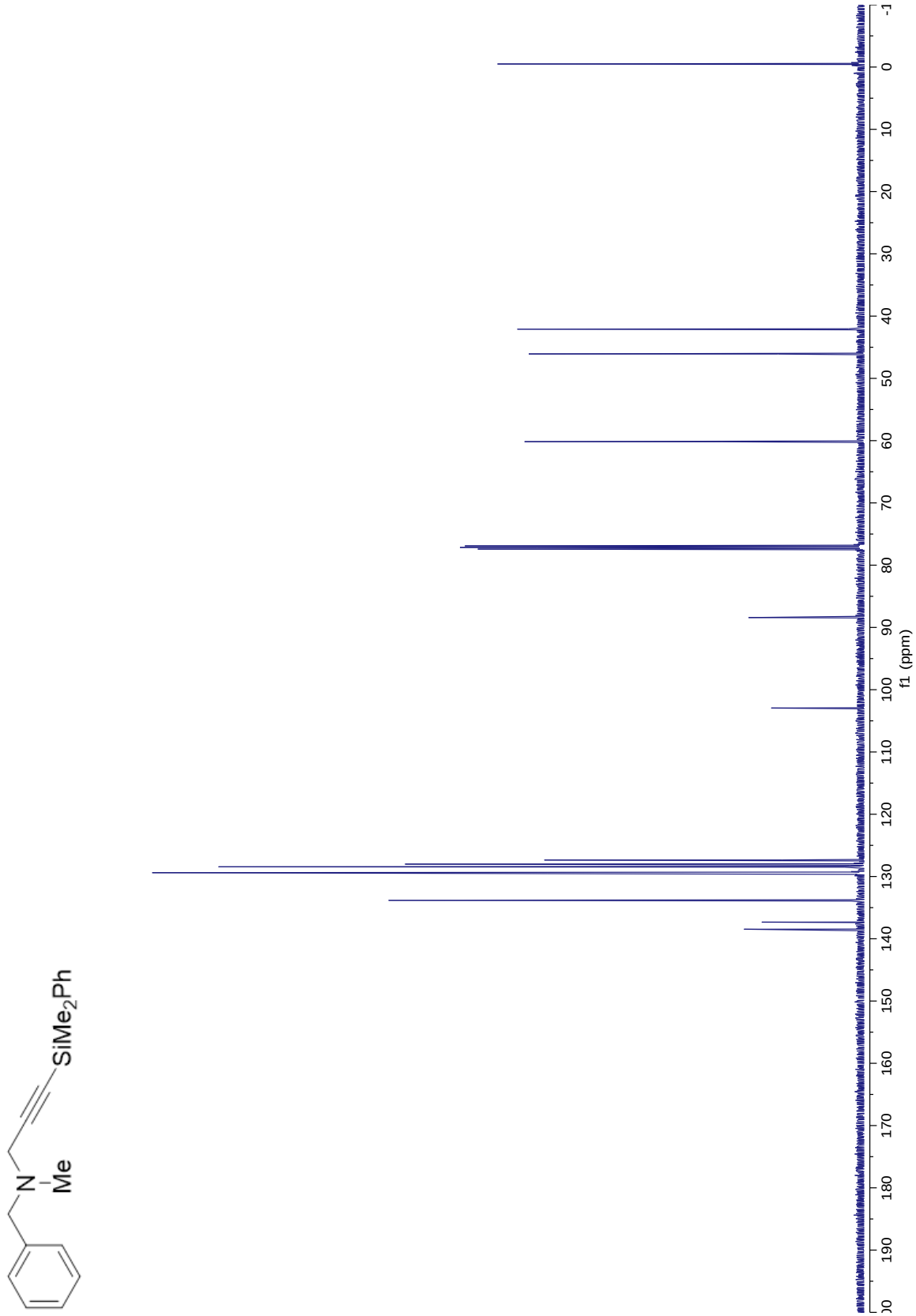
^{1}H NMR (500 MHz, $CDCl_3$) of compound **8.**



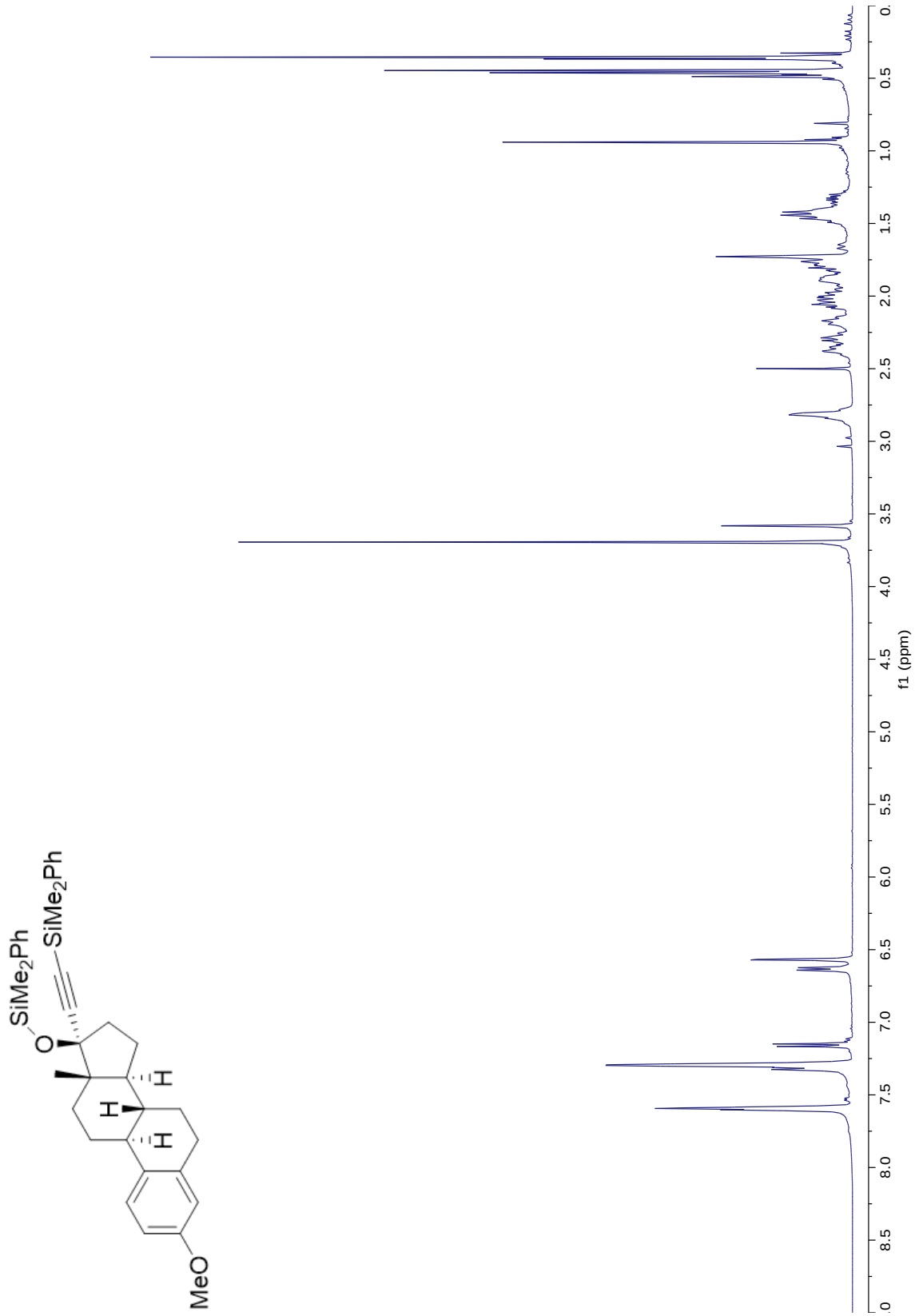
^{13}C NMR (126 MHz, $CDCl_3$) of compound **8.**



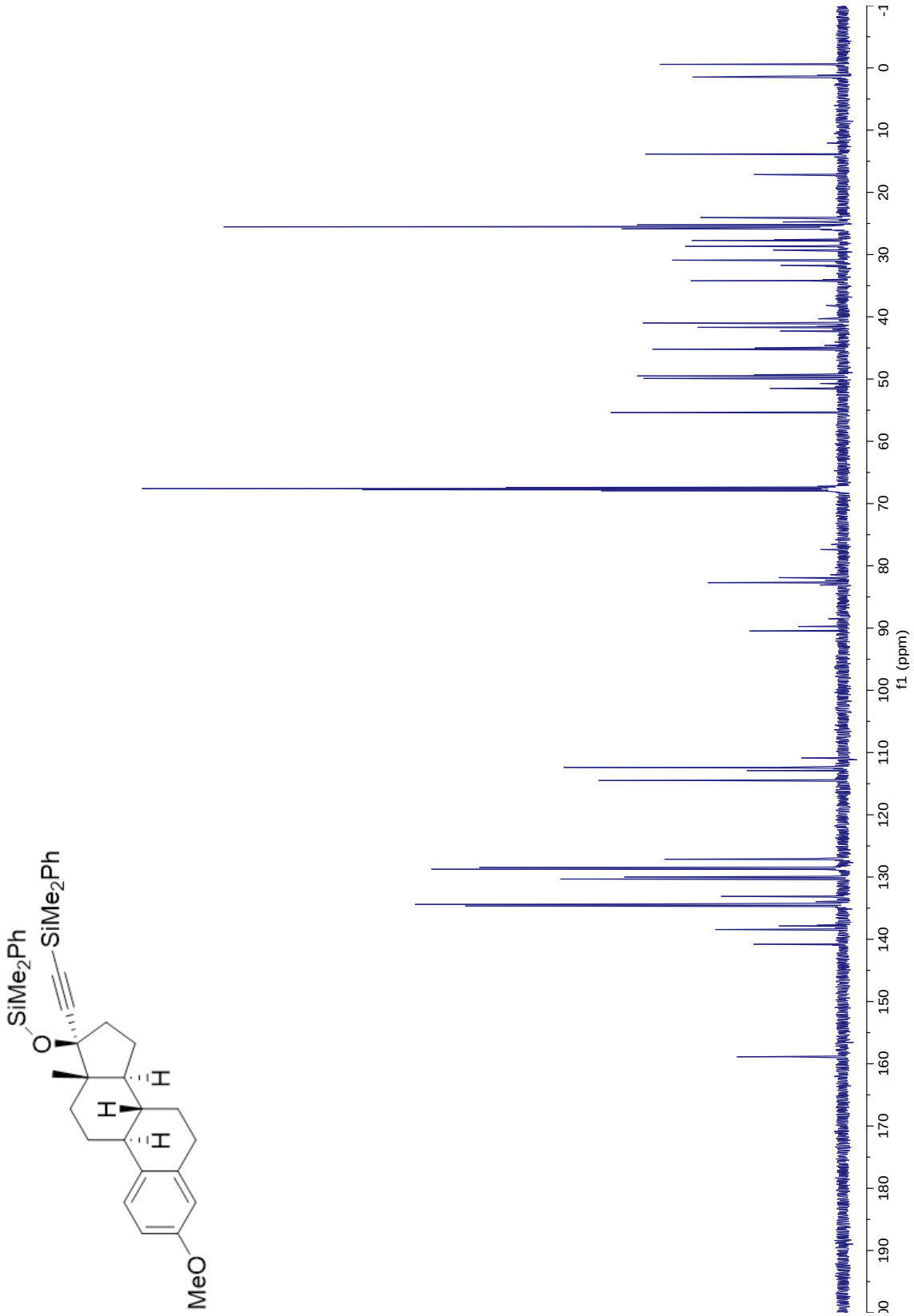
^{1}H NMR (500 MHz, $CDCl_3$) of compound **9.**



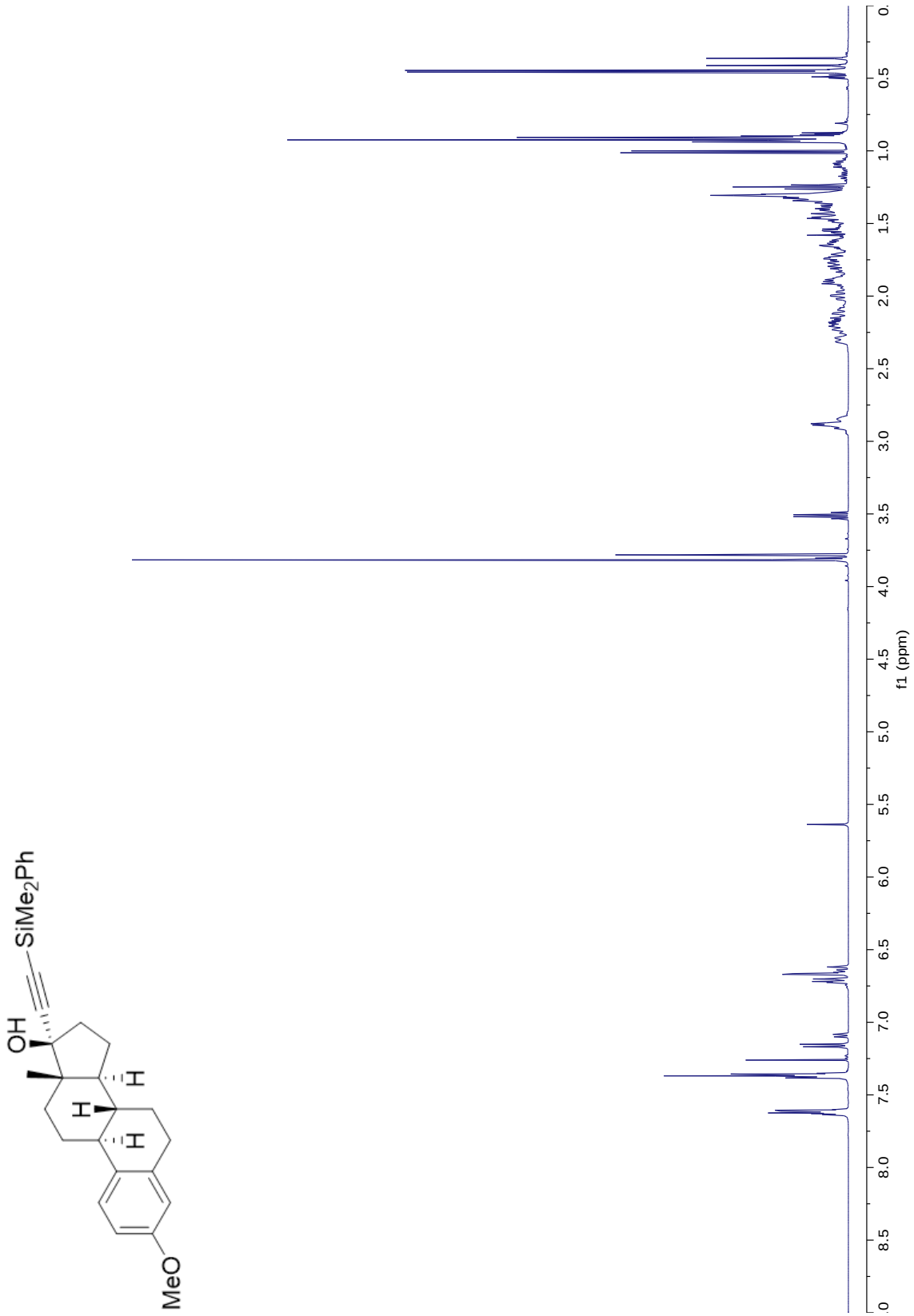
^{13}C NMR (126 MHz, $CDCl_3$) of compound **9.**



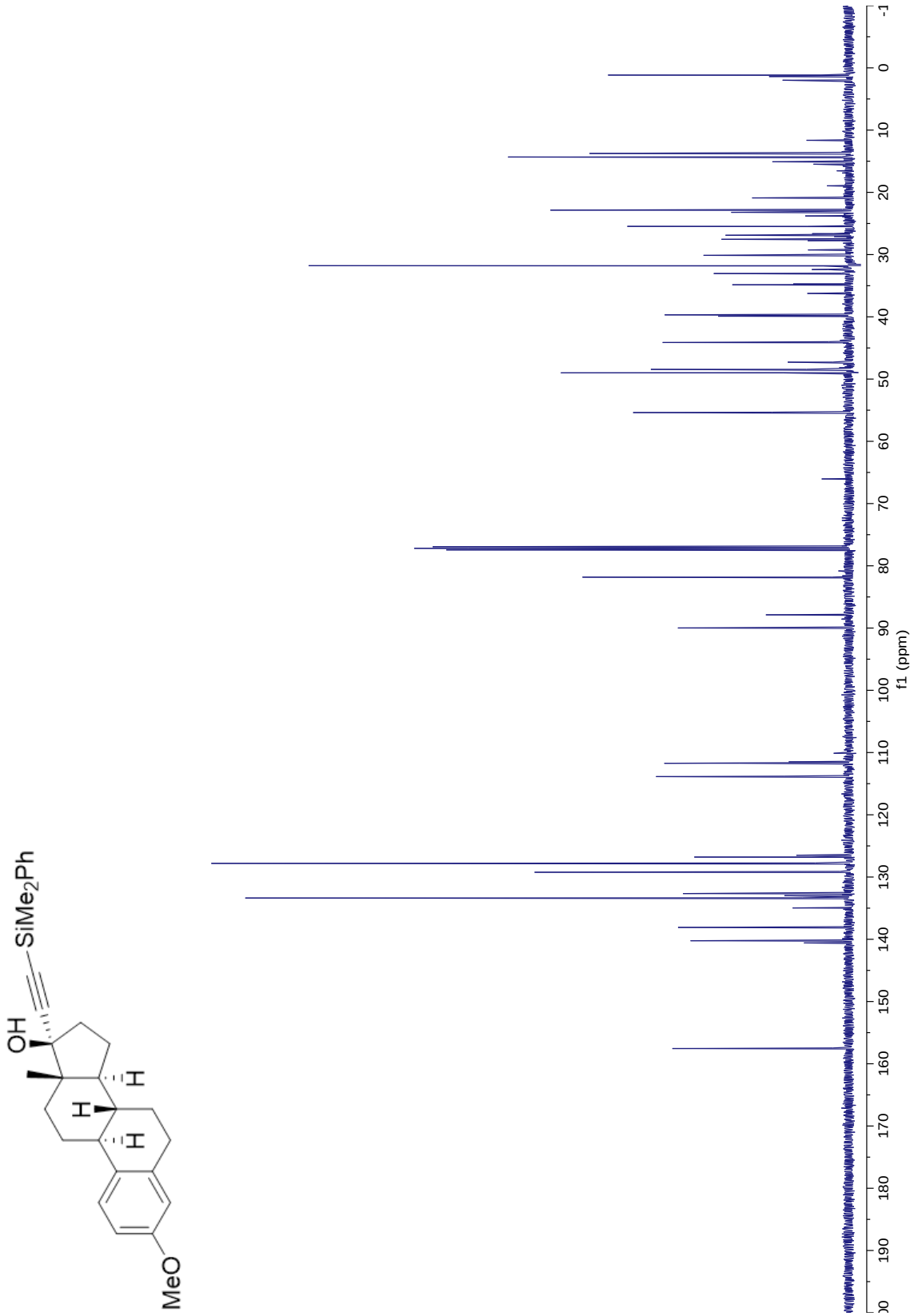
^{1}H NMR (500 MHz, THF-*d8*) of compound **10a.**



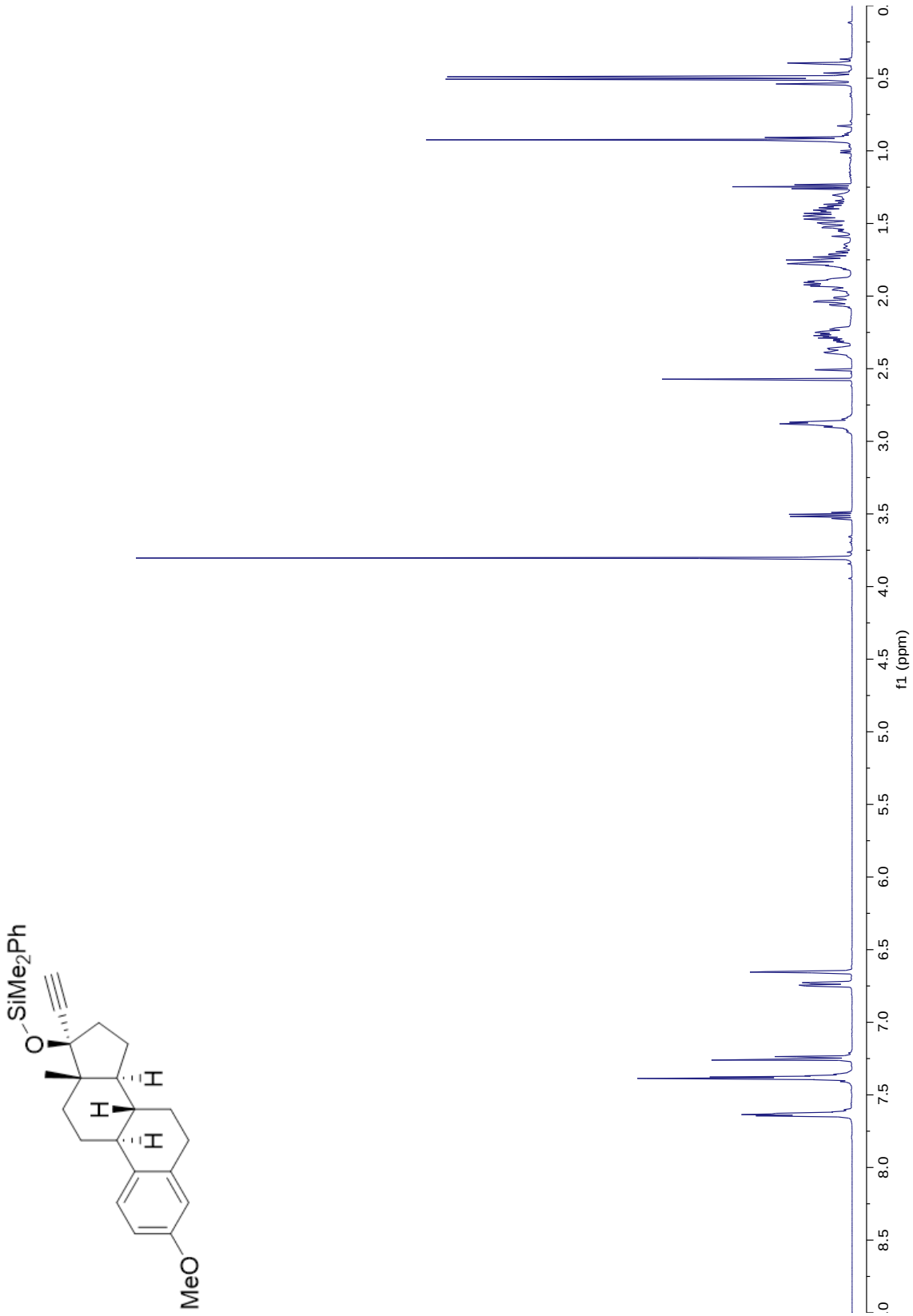
^{13}C NMR (126 MHz, THF-*d8*) of compound **10a.**



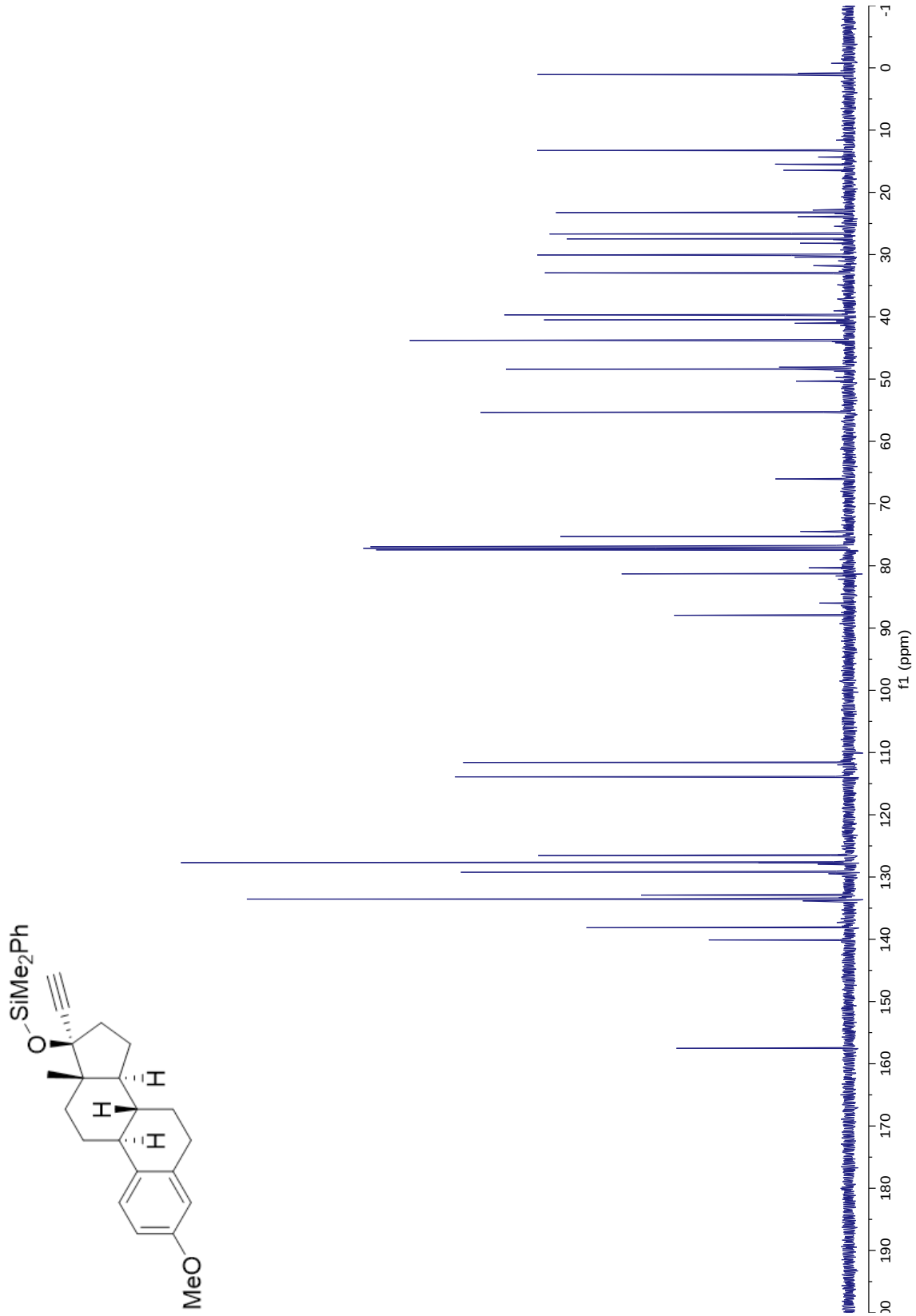
^{1}H NMR (500 MHz, $CDCl_3$) of compound **10b.**



^{13}C NMR (126 MHz, $CDCl_3$) of compound **10b.**



^{1}H NMR (500 MHz, $CDCl_3$) of compound **10-SI.**



^{13}C NMR (126 MHz, $CDCl_3$) of compound **10-SI.**