CHAPTER 1

The Evolution of a Unified, Stereodivergent Approach to the Synthesis of Communesin F and Perophoramidine[†]

1.1. Introduction

In 1993, communesin A (**1a**) was isolated along with communesin B (**1b**) from a strain of *Penicillium* sp. found growing on a marine alga by the Numata group (Figure 1.1.1).[1] Communesins A (**1a**) and B (**1b**) exhibit antiproliferative activity against P-388 lymphocytic leukemia cells (ED_{50} = 3.5 μg/mL and 0.45 μg/mL, respectively).[1] In addition, communesin B (**1b**) disrupts actin microfilaments in cultured mammalian cells and shows cytotoxic activity against LoVo and KB cells (MIC values of 2.0 μg/mL and 4.5 μg/mL, respectively).[2] Several other members of the comunesin family, communesins B–H (**1b–1h**), were disclosed from related marine fungal strains of

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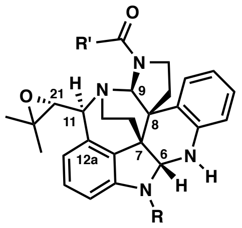
[†] This work was performed in collaboration with Dr. Florian Vogt, Dr. Jeremy A. May, Dr. Shyam Krishnan, Dr. Michele Gatti, and Dr. Scott C. Virgil. Additionally, this work has been published and adapted with permission from Han, S.-J.; Vogt, F.; May, J. A.; Krishnan, S.; Gatti, M.; Virgil, S. C.; Stoltz, B. M. *J. Org. Chem.* **2015**, *80*, 528–547. Copyright 2015 American Chemical Society. Related work has been published and adapted with permission from Han, S.-J.; Vogt, F.; Krishnan, S.; May, J. A.; Gatti, M.; Virgil, S. C.; Stoltz, B. M. *Org. Lett.* **2014**, *16*, 3316–3319. Copyright 2014 American Chemical Society.

Penicillium sp. in the following years.[3] With the exception of communesins G (**1g**) and H (**1h**), the communesins show insecticidal activity and antiproliferative activity against a variety of cancer cells, with communesin B (**1b**) being the most potent.[1–3] These indole alkaloids contain several interesting structural features including vicinal all-carbon quaternary centers, bis-aminal functionalities, and a complex polycyclic core. The communesins are structurally unique when compared against other known microfilament-disrupting agents, which are primarily macrolides. Macrolide microfilament-disrupting agents show considerable structural similarity, and their interactions with actin have been crystallographically characterized, leading to hypotheses regarding their mechanism of action.[4] The unique structure of communesin B (**1b**) suggests that it may exhibit a novel mechanism of action on the cytoskeleton relative to other microfilament-disrupting agents.[5a] The development of a unified synthetic route to the communesins would enable the understanding of their effects on the cellular cytoskeleton, while addressing the scarcity of naturally occurring sources of the compounds.

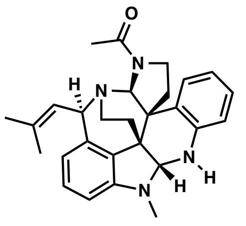
In 2001, an intriguing natural product, nomofungin (**2**) was isolated from an unidentified fungus found on the bark of *Ficus microcarpa* by the Hemscheidt group.[2] Interestingly, the only structural difference between communesin B (**1b**) and nomofungin (**2**) is that communesin B has an aminal moiety instead of the *N,O*-acetal moiety present in nomofungin. A combination of experimental and theoretical exercises led to the independent discovery by our laboratory and the Funk group that the reported structure of nomofungin was incorrect, and that it is actually that of communesin B.[5a,b] Although the structure of nomofungin was erroneously assigned, its isolation and structural revision to that of an older structure can be viewed as the inception point for all synthetic efforts to the communesin family members over the past decade. Interestingly, there were no reports of synthetic efforts toward the communesins from 1993 up to our initial report in 2003.[5i]

A structurally related compound, perophoramidine (**3**), was isolated in 2002 from the ascidian *Perophora namei*.[6] The core is comparable to the one found in the communesins, albeit in a higher oxidation state, with the alternate diastereomeric relationship between the vicinal quaternary carbons and without the azepine ring system. Perophoramidine (**3**) possesses modest cytotoxicity against the HCT 116 human colon carcinoma cell line (IC_{50} = 60 μM) and induces apoptosis.[7]

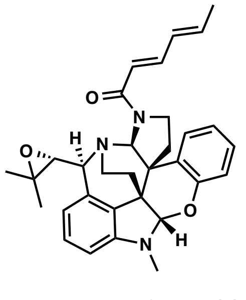
Figure 1.1.1. *Communesins (**1**), Nomofungin (**2**), and Perophoramidine (**3**)*



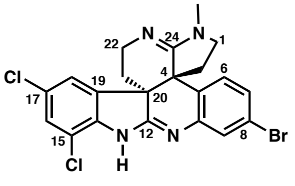
Communesin	*R*	*R'*
A (1a)	CH_3	CH_3
B (1b)	CH_3	pentadienyl
C (1c)	H	pentadienyl
D (1d)	CHO	pentadienyl
E (1e)	H	CH_3
G (1g)	CH_3	CH_2CH_3
H (1h)	CH_3	$CH_2CH_2CH_3$



Communesin F (1f)



Nomofungin (2)
(Original Structure)



Perophoramidine (3)

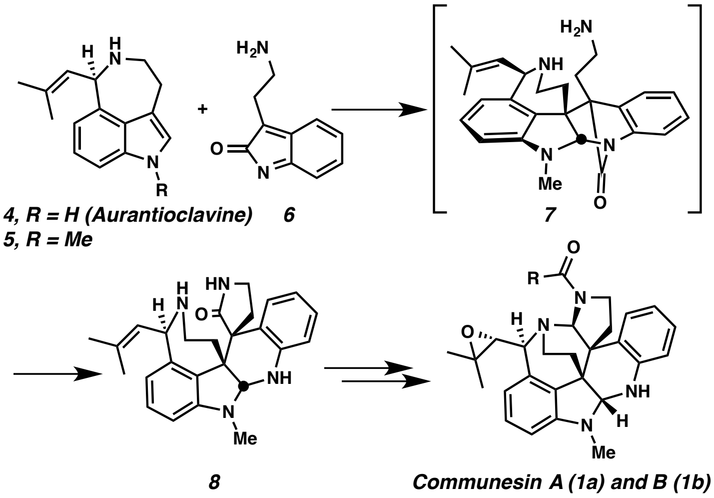
These complex, polycyclic, bioactive alkaloids have been the subject of intense synthetic efforts over the past decade.[5] Numerous approaches have been reported in the literature, including three from our laboratory.[5a,5c,5w] Herein, we report the evolution of an efficient, unified approach toward the synthesis of these unique alkaloids.

1.2. Results and Discussion

1.2.1. Biosynthesis-Inspired Diels–Alder Cycloaddition Strategy to Communesin F

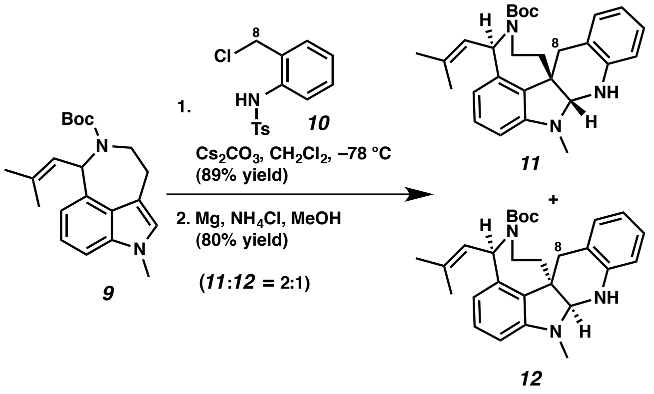
Our early efforts toward the communesin structure centered on the laboratory implementation of our proposed biosynthesis (Scheme 1.2.1).[5a,c,8] As the key step in the process, we envisioned a Diels–Alder cycloaddition to unite the two indole-based fragments by coupling of **5**, an *N*-methylated derivative of the ergot alkaloid aurantioclavine (**4**)[9,10] and an *o*-azaxylylene indolone **6** to generate the bridged lactam **7**. We anticipated that lactam **7** would be highly reactive due to the poor alignment of the nitrogen lone pair with the carbonyl.[11,12,13] As such, the pendant amino group would be expected to easily open the lactam, thus forming spirocycle **8**. Further tailoring would produce communesin A (**1a**) and B (**1b**).

Scheme 1.2.1. Biosynthesis-Inspired Approach



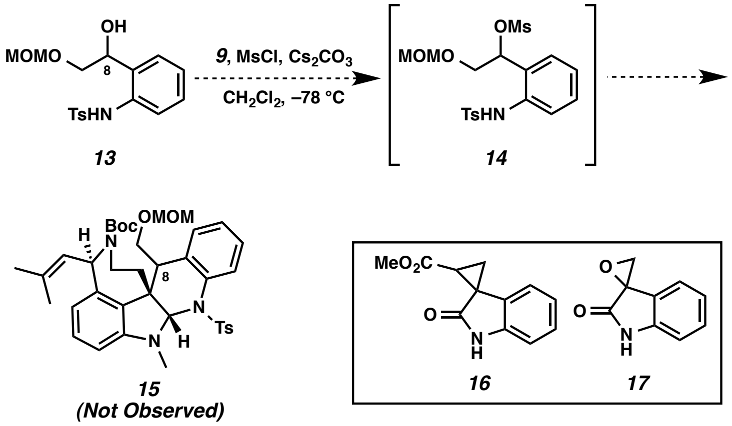
Toward this end, (±)-aurantioclavine was prepared using known methods[5a,14] and an enantioselective synthesis of (–)-aurantioclavine utilizing our oxidative kinetic resolution (OKR) technology was developed.[15] We proceeded to develop an efficient cycloaddition between (±)-indole **9** as a model coupling partner and chlorotoluamide **10** using conditions previously developed by Steinhagen and Corey[16] that resulted in a mixture of pentacyclic diastereomers (89% yield). Removal of the tosyl group with magnesium in methanol produced a 2:1 mixture of diastereomers **11** and **12** in 80% combined yield, with the desired relative stereochemistry evident in the major diastereomer (cf. **11** and **1a**) (Scheme 1.2.2).[5a]

Scheme 1.2.2. *Model Studies for a Diels–Alder Cycloaddtion Strategy To Construct the Pentacyclic Core Structure*



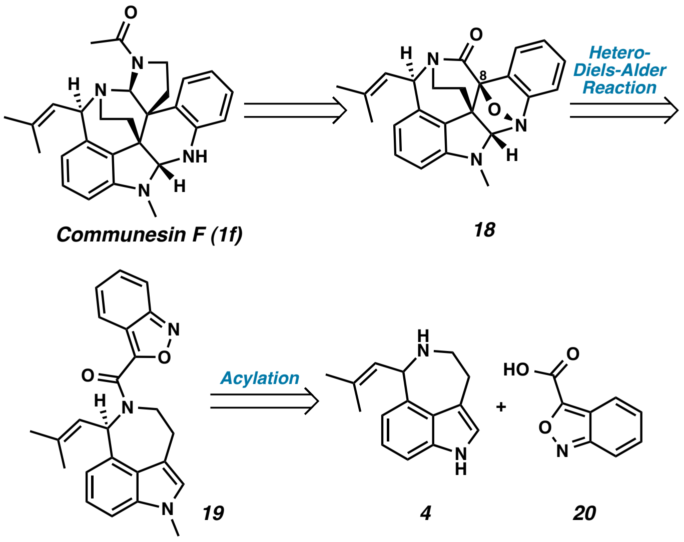
Despite the success of this model system, more advanced electrophiles (e.g., mesylate **14**, cyclopropane **16**, or epoxide **17**[17]) did not succumb to cycloaddition conditions (Scheme 1.2.3). Nor have we been successful in the oxidation of **11** and **12** at C(8), which would provide a functional handle for introduction of the second quaternary stereocenter.

Scheme 1.2.3. *Attempted Diels–Alder Cycloadditions with Advanced Electrophiles*



To obviate the difficulties encountered in our attempts to functionalize C(8), we next considered dienes possessing a functional handle at C(8) that could unite diene and dienophile, such as benzisoxazole **19**, thereby enabling an intramolecular Diels–Alder cycloaddition (Scheme 1.2.4). Thus, when coupled to aurantioclavine **4**, benzisoxazole **20** would offer a stable *o*-methide imine that could react with the indole moiety of compound **19** in a controlled and intramolecular manner.

Scheme 1.2.4. *Retrosynthetic Analysis of Communesin F by an Intramolecular Diels–Alder Cycloaddition*



Fischer esterification of commercially available carboxylic acid **21**, followed by heating in neat sulfuric acid provided the benzisoxazole acid **20** in 44% yield over 2 steps (Scheme 1.2.5).[18] Treatment of benzisoxazole acid **20** with oxalyl chloride provided the corresponding acid chloride, which was smoothly coupled with aurantioclavine **4** to furnish carboxamide **22** (91% yield, 2 steps). Similarly, 1-methylaurantioclavine **5** reacted with the acid chloride to afford carboxamide **19** (77% yield, 2 steps). Substrates **22** and **19** were subjected to an intramolecular Diels–Alder cycloaddition under acidic conditions.[19] Unfortunately, the benzisoxazole reacted with the butenyl side chain of the aurantioclavine core to generate the bridged polycycles **23** and **24**. Nuclear Overhauser Effect NMR spectroscopy (NOESY) studies and X-ray analysis (Figure 1.2.1) demonstrated the relative stereochemistry shown for **24** and that of **23** was assigned by analogy.

Scheme 1.2.5. *Intramolecular Diels–Alder Cycloaddition*

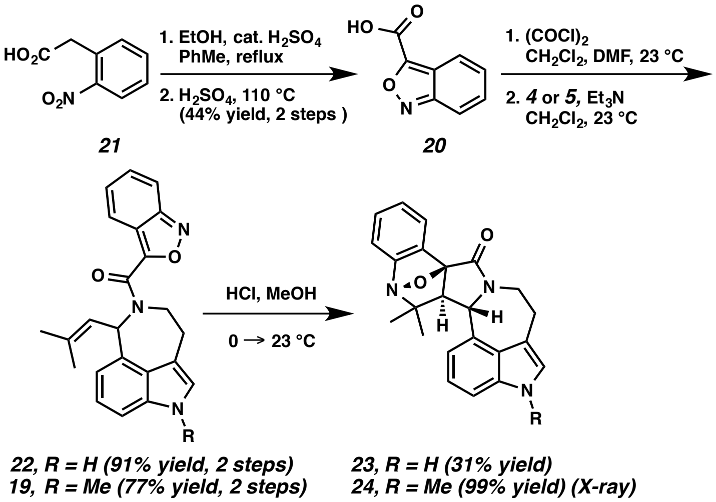
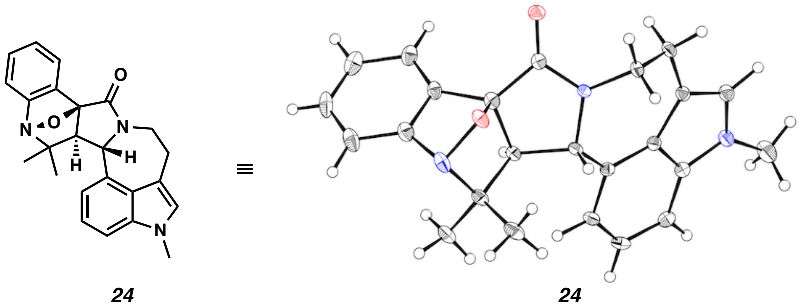


Figure 1.2.1. *X-ray Structure of Bridged Polycycle* ***24***



24 **24**

At this point, we turned our attention to synthesizing 3-bromooxindole **26**, which would be a precursor to an *o*-methide imine such as reactive intermediate **6**, allowing for the construction of the communesin core according to our original biosynthesis-inspired model (Scheme 1.2.1). Aurantioclavine derivative **25** was reacted with bromooxindole **26** in an effort to produce adduct **27** (Scheme 1.2.6a). Interestingly, different reactivity was observed in coordinating and non-coordinating solvents. In THF or acetonitrile, the reaction afforded indole **28** in 69% yield, wherein the oxindole was introduced to position C(2) of the indole nucleus, presumably via rearrangement of the initially formed adduct **27** at C(3) (Scheme 1.2.6b). Sulfonylation of indole **28** with *o*-NsCl under basic conditions was accompanied by unexpected chlorination of the indole moiety to afford chloroindoline **29** (73% yield), the structure of which was unambiguously confirmed by X-ray crystallography (Figure 1.2.2). To the best of our knowledge, this constitutes the first use of *o*-NsCl for chlorination of an indole to provide the 3-chloroindolenine. On the other hand, the same coupling of derivatives **25** and **26** in benzene or dichloromethane furnished indole **28** (24% yield), and two additional undesired products **30** (32% yield) and **31** (24% yield) (Scheme 1.2.6c). Adduct **30** results from nucleophilic attack at C(6) of the aurantioclavine indole core, while double adduct **31** is produced from both C(6) and C(2) functionalization. The structure of **30** was unambiguously determined following preparation of lactam **32** (Scheme 1.2.6d). Subjecting **30** to excess sodium hydride and *o*-NsCl conditions functionalized both the oxindole and indole nitrogens (66% yield) and subsequent reduction of the azide allowed for cyclization to lactam **32** in 66% yield. The structure of **32** was confirmed by single crystal X-ray diffraction (Figure 1.2.3).

Scheme 1.2.6. *Reaction of Aurantioclavine Derivative* ***25*** *with Bromooxindole* ***26***

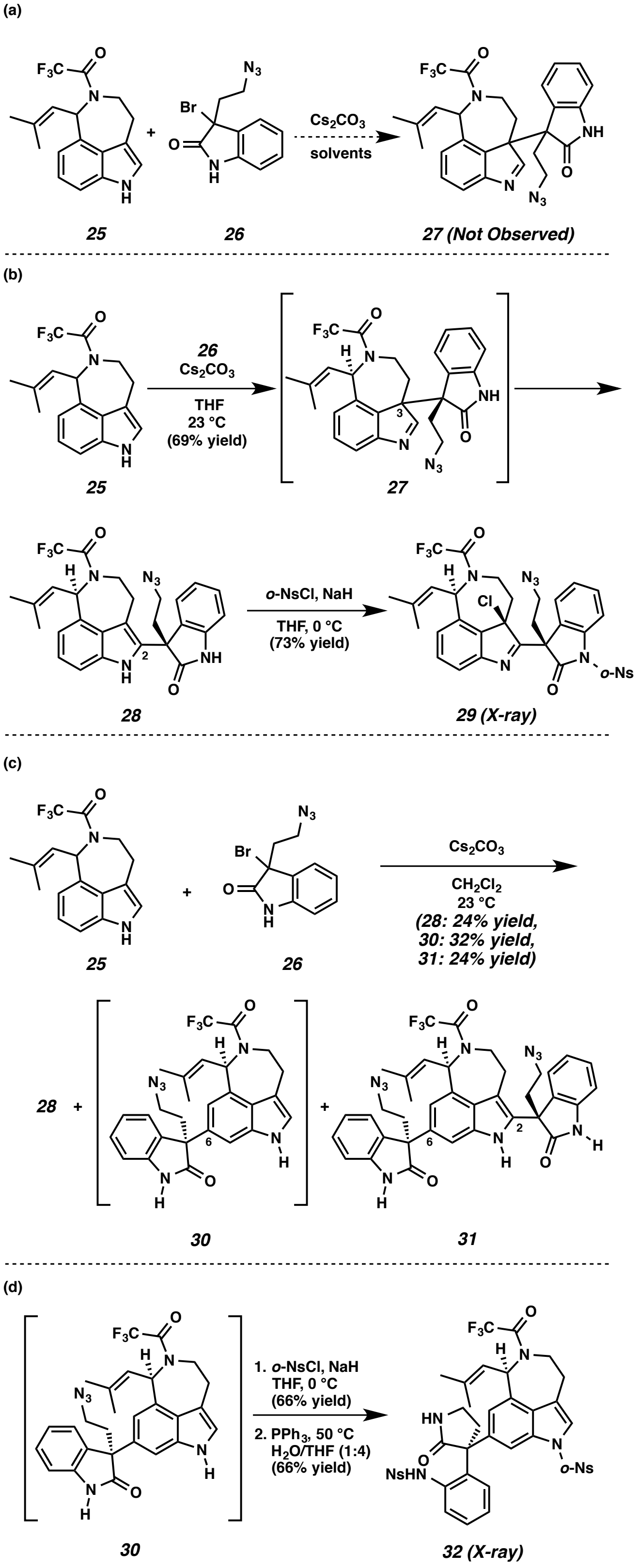
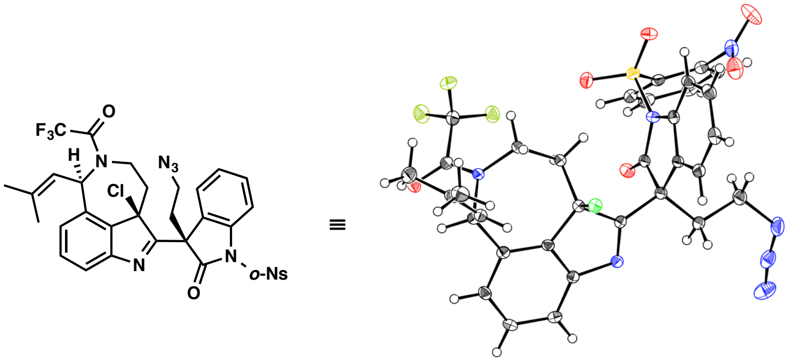
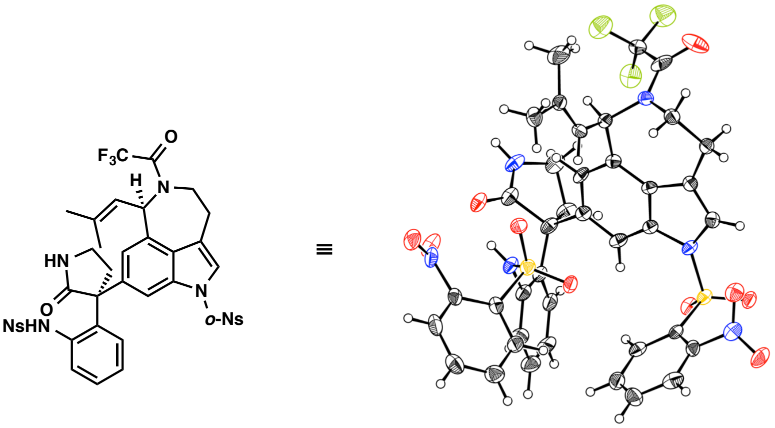


Figure 1.2.2. *X-ray Structure of Chloroindoline **29***



29 ***29***

Figure 1.2.3. *X-ray Structure of Lactam **32***



32 ***32***

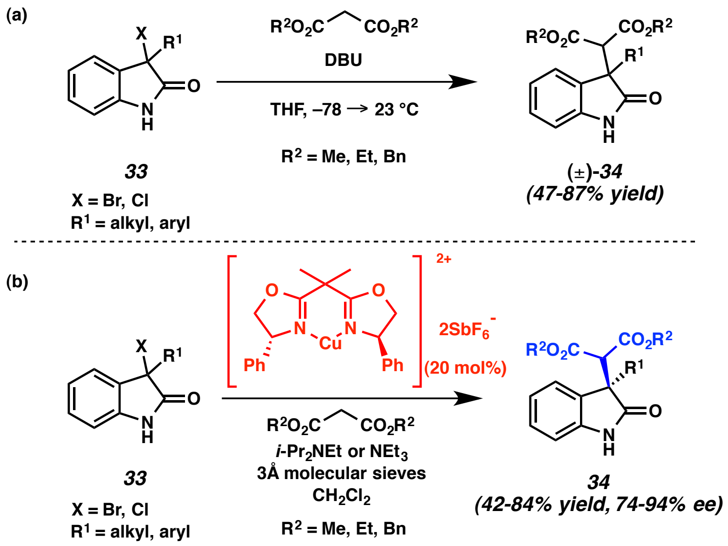
1.2.2. An Alkylation Route to Communesin F

Discouraged by the unsuccessful Diels–Alder cycloaddition-based approaches to communesin F (**1f**), we considered an alternative strategy toward the natural product. In 2007, as a direct result of our efforts toward the communesins and perophoramidine, we developed a method to generate 3,3-disubstituted oxindoles via the base-mediated coupling of oxindole electrophiles with malonate derived nuclophiles. (Scheme 1.2.7a).[20]

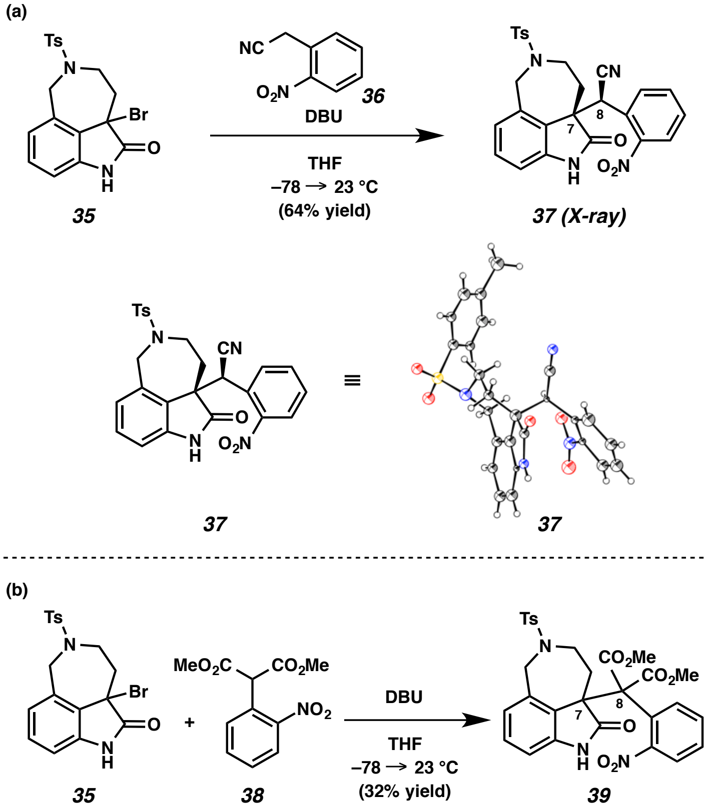
We also developed an asymmetric variant of this reaction utilizing copper bis(oxazoline) complexes (Scheme 1.2.7b).[21]

With the method shown in Scheme 1.2.7, we devised a new synthetic strategy that cast our coupling fragments in an *umpolung* manner, invoking an electrophilic aurantioclavine portion and a nucleophilic right hand fragment. We first pursued this notion in the context of the model azepine **35** (Scheme 1.2.8). Treatment of **35** with DBU and a pronucleophile (e.g., **36**[22] and **38**) produced oxindole adducts (i.e., **37** and **39**) possessing the key C(7)–C(8) linkage in modest but encouraging yields. Importantly, adduct **37** was crystalline, and we confirmed both the new C–C bond as well as the relative stereochemistry of the sole diastereomeric isolate via X-ray analysis.

Scheme 1.2.7. *Construction of 3,3-Disubstituted Oxindoles*

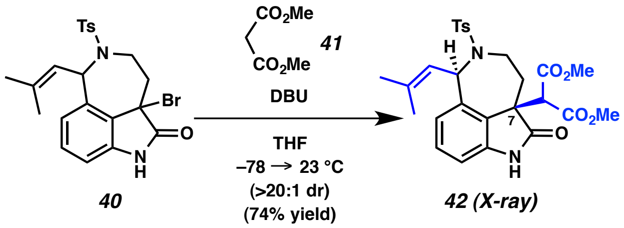


Scheme 1.2.8. *Construction of C(7)–C(8) Linkage by Alkylation Strategy*



Having produced the key C(7)–C(8) linkage via an *umpolung* strategy, we treated aurantioclavine-derived bromooxindole **40** with malonate **41** in the presence of DBU (Scheme 1.2.9). Smooth reactivity under our standard conditions led to the isolation of a single stereoisomeric adduct **42** in 74% yield. To our delight, oxindole adduct **42** was amenable to single crystal X-ray diffraction, however, the X-ray analysis surprisingly revealed that the alkylation occurs with high *syn* selectivity relative to the existing isobutenyl substituent (Figure 1.2.4). This result was intriguing, given that in the Diels–Alder cycloaddition of the corresponding indole **9** with the *o*-azaxylylene derived from chlorotoluamide **10**, the selectivity at C(7) favored the *anti* diastereomer **11** (cf. Schemes 1.2.9. and 1.2.2).[23]

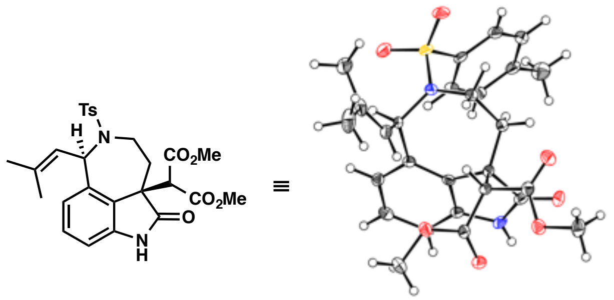
Scheme 1.2.9. *Alkylation of Azepine Bromooxindole* ***40*** *with Malonate* ***41***



40

42 (X-ray)

Figure 1.2.4. *X-ray Structure of Oxindole Adduct* ***42***

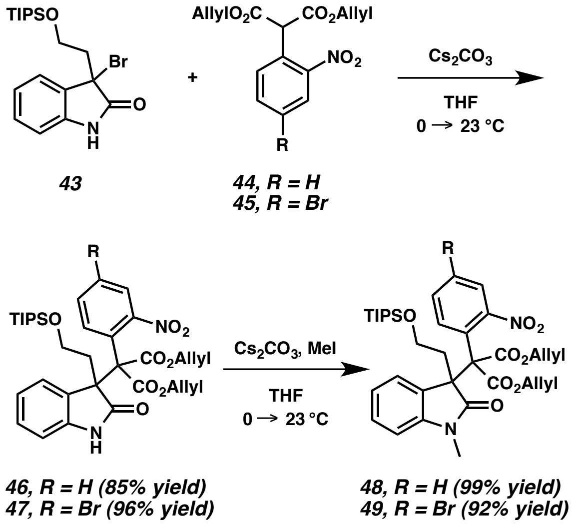


42

42

Since the undesired relative stereochemistry was obtained in adduct **42** from the alkylation of azepine **40** and malonate **41**, we explored our strategy in a model system lacking the azepine ring of the oxindole (Scheme 1.2.10). Known silyl ether **43**[21,22] was converted into malonate adducts **46** and **47** in 85% and 96% yield, respectively, under our previously reported conditions in Scheme 1.2.7. Importantly, in the non-azepine system, the efficiency of those alkylations is increased, even in these cases where vicinal quaternary centers are generated.[24] Methylation of oxindoles **46** and **47** produced **48** and **49** in 99% and 92% yield, respectively.

Scheme 1.2.10. *Alkylation of 3-Bromooxindole* ***43***



43

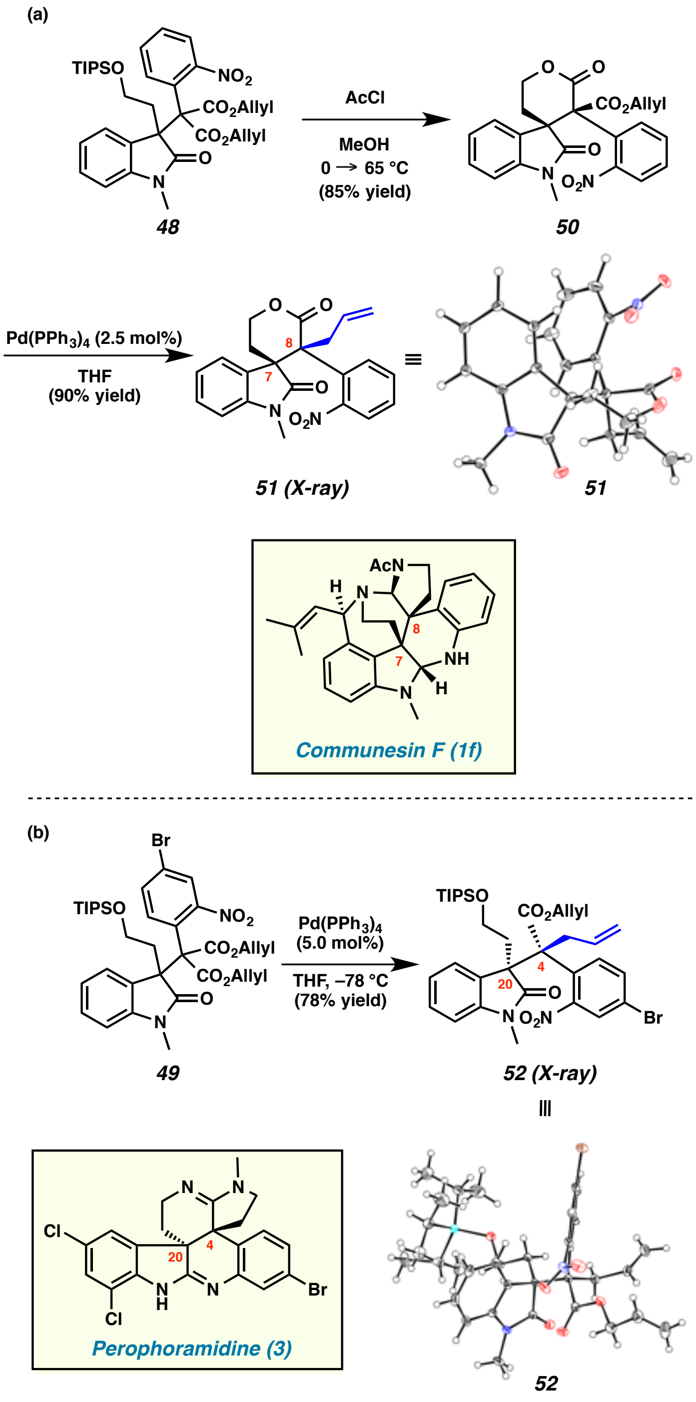
44, R = H
45, R = Br

46, R = H (85% yield)
47, R = Br (96% yield)

48, R = H (99% yield)
49, R = Br (92% yield)

Acid-catalyzed desilylation and cyclization of diester **48** proceeded smoothly to furnish lactone **50** in 85% yield as a single diastereomer (Scheme 1.2.11a).[25] To our delight, lactone **50** underwent decarboxylative allylic alkylation when treated with $Pd(PPh_3)_4$, yielding **51** in 90% yield as a single diastereomer.[26,27] Single crystal X-ray analysis confirmed that lactone **51** possesses the relative stereochemistry at the vicinal quaternary carbon centers C(7) and C(8) that is needed for further elaboration to communesin F (**1f**). Interestingly, direct decarboxylative allylic alkylation of diester **49** again provided an alkylated product (i.e., **52**) as a single diastereomer in 78% yield (Scheme 1.2.11b). Through X-ray analysis, we discovered that the relative stereochemistry at the vicinal quaternary stereocenters C(20) and C(4) of **52** was complementary to that of the lactone **51**, and thus ideal for elaboration to perophoramidine (**3**).

Scheme 1.2.11. *Model Studies for Construction of the Vicinal Quaternary Centers*

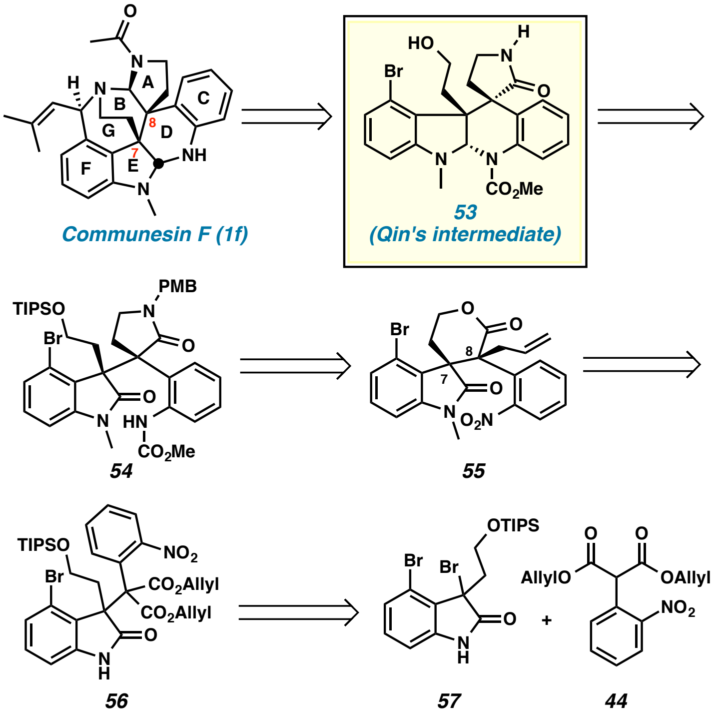


At this time, the underlying reasons for the stereochemical relationships observed in these two alkylation reactions are unclear. The fact that the reactions proceed stereodivergently with high diastereocontrol is quite remarkable. Work toward building reasonable models for stereoinduction of β-quaternary tetrasubstituted enolates in both cyclic and acyclic settings as well as the development of these interesting processes in more general cases is ongoing. Nevertheless, with the promising model systems **51** and **52** completed, we next applied our findings to expedient formal syntheses of communesin F (**1f**) and perophoramidine (**3**).

1.2.3. Formal Synthesis of Communesin F (1f)

As depicted in our retrosynthetic strategy (Scheme 1.2.12), communesin F could be completed from advanced intermediate **53** in Qin's synthesis.[5g] We anticipated the initial disconnection of the aminal linkage in **53**, thereby revealing oxindole and aniline moieties in **54**. Then, the lactam ring in **54** would be excised, affording lactone **55**. We envisioned that the relative stereochemical relationship at C(7) and C(8) of lactone **55** could be established by employing our decarboxylative allylic alkylation. The quaternary center on oxindole **56** was disassembled into 3-bromooxindole **57** and diallyl malonate **44**.

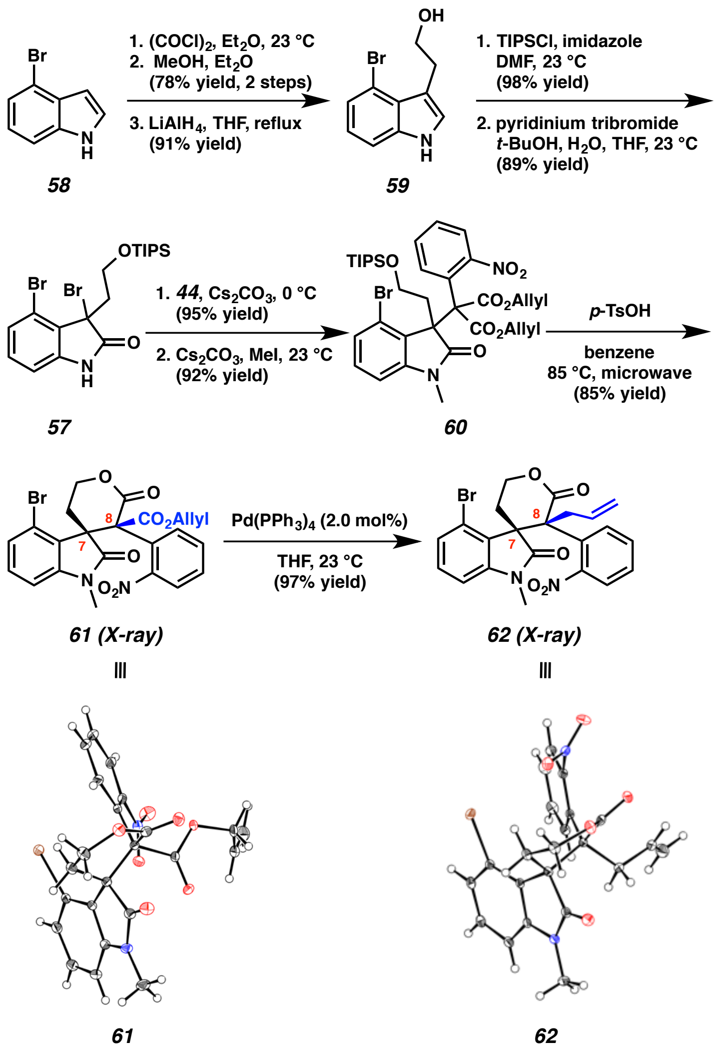
Scheme 1.2.12. *Retrosynthesis of Communesin F (**1f**)*



In the forward synthetic sense, our efforts toward communesin F commenced with the elaboration of 4-bromoindole **58** to diallyl malonate **60** (Scheme 1.2.13). Treatment of 4-bromoindole **58** with oxalyl chloride and methanol provided an oxoacetate (78% yield, 2 steps), which was reduced to the corresponding primary alcohol **59** with $LiAlH_4$ in 91% yield.[5g] Silylation of the primary alcohol with TIPSCl (98% yield) and subsequent oxidation with pyridinium tribromide afforded dibromooxindole **57** in 89% yield.[28] Despite the extra steric encumbrance of C(4) substitution, we were delighted to find that smooth coupling of dibromooxindole **57** with malonate **44** produced a 3,3-disubstituted oxindole in 95% yield. Protection of the oxindole with MeI delivered adduct **60** in 92% yield. Microwave assisted lactonization of diester **60** with *p*-TsOH proceeded smoothly to furnish lactone **61** as a single diastereomer (85% yield).

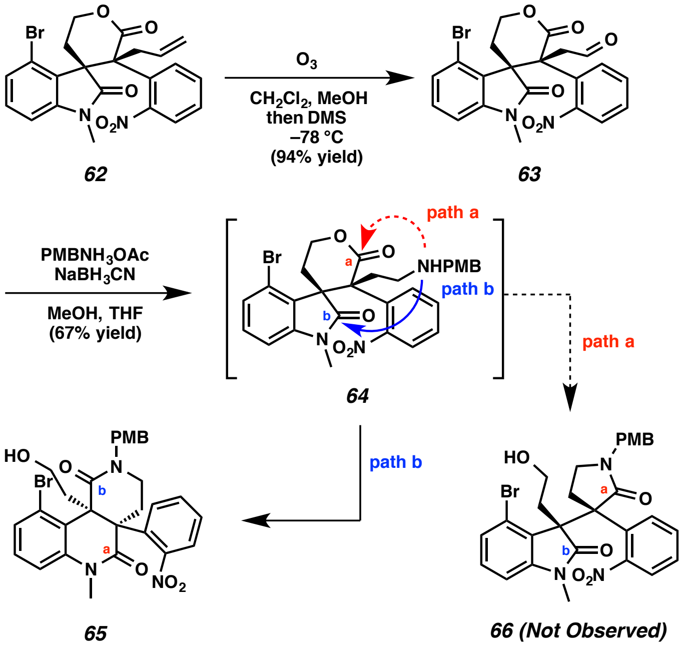
Gratifyingly, decarboxylative allylic alkylation constructed the quaternary center at C(8) of compound **62** as a single diastereomer in 97% yield under $Pd(PPh_3)_4$ catalysis. The relative stereochemistry at C(7) and C(8) of **61** and **62** was unambiguously confirmed by X-ray analysis.

Scheme 1.2.13. *Development of the Vicinal Quaternary Center*



Although ozonolysis of alkene **62** delivered aldehyde **63** in 94% yield, attempted reductive amination of aldehyde **63** did not produce the desired γ-lactam **66** (Scheme 1.2.14). Upon treatment of aldehyde **63** with *p*-methoxybenzylammonium acetate and sodium cyanoborohydride, amine intermediate **64** was likely produced.[29] Instead of opening the lactone directly (path a), nucleophilic attack by the newly generated amine at the oxindole moiety (path b), and subsequent ring-shift tautomerization delivered dihydroquinolinone **65** in 67% yield.

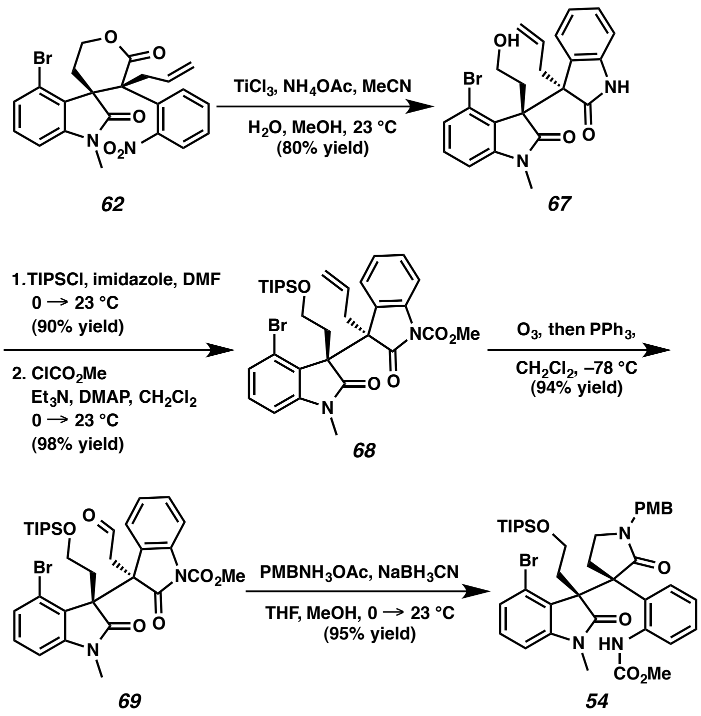
Scheme 1.2.14. *Ozonolysis and Reductive Amination of Lactone* ***62***



Alternatively, we found that lactam **54** (an analogue of **66**) could be obtained via the reaction sequence summarized in Scheme 1.2.15. The nitro group on compound **62** was reduced to the aniline, which resulted in concomitant lactone ring opening to furnish a bis-oxindole **67** in 80% yield. Protection of the primary alcohol with TIPSCl (90%

yield) and protection of the oxindole nitrogen with methyl chloroformate afforded carbamate **68** in 98% yield. Ozonolysis of alkene **68** generated aldehyde **69** (94% yield),[30] which underwent subsequent reductive amination and selective lactamization with the electron deficient oxindole to afford γ-lactam **54** in 95% yield.

Scheme 1.2.15. *Synthesis of Lactam **54***



With lactam **54** in hand, we envisioned that the piperidine D ring of **70** would be prepared by AlH_3-Me_2NEt mediated reductive cyclization (Scheme 1.2.16).[21,31] To our disappointment, treatment of lactam **54** with AlH_3-Me_2NEt produced undesired pyrrolidinoindoline derivative **71** as a single diastereomer in 61% yield, resulting from chemoselective reduction of the *N*-PMB-lactam in the presence of the oxindole. After cleavage of the TIPS group by TBAF (98% yield),[32] the PMB group was removed with

DDQ[33] to provide alcohol **72**. The structure of the pentacyclic heterocycle **72** was confirmed by X-ray analysis (Figure 1.2.5).

Scheme 1.2.16. *Reductive Cyclization of Lactam **54** with AlH$_3$-Me$_2$NEt*

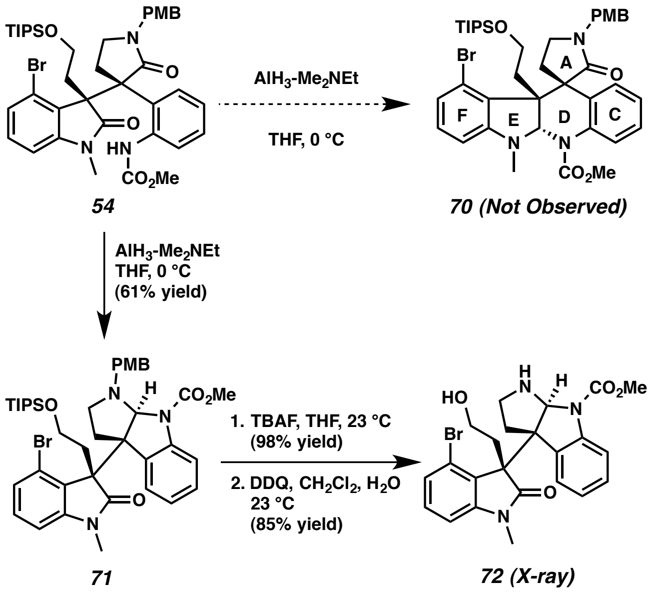
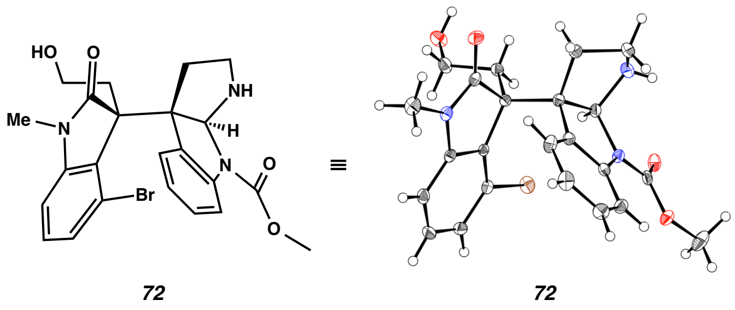
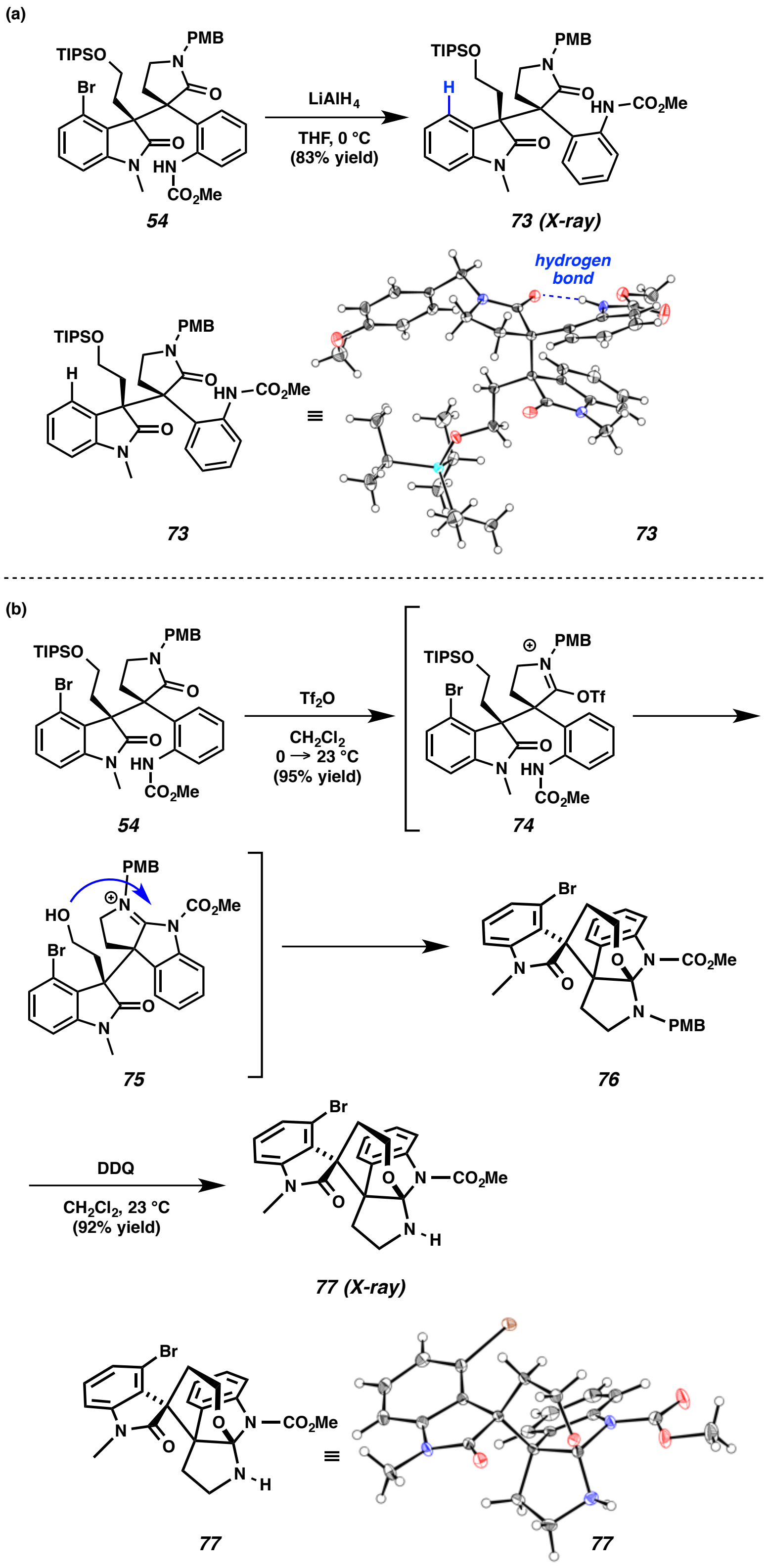


Figure 1.2.5. *X-ray Structure of Pyrrolidinoindoline **72***



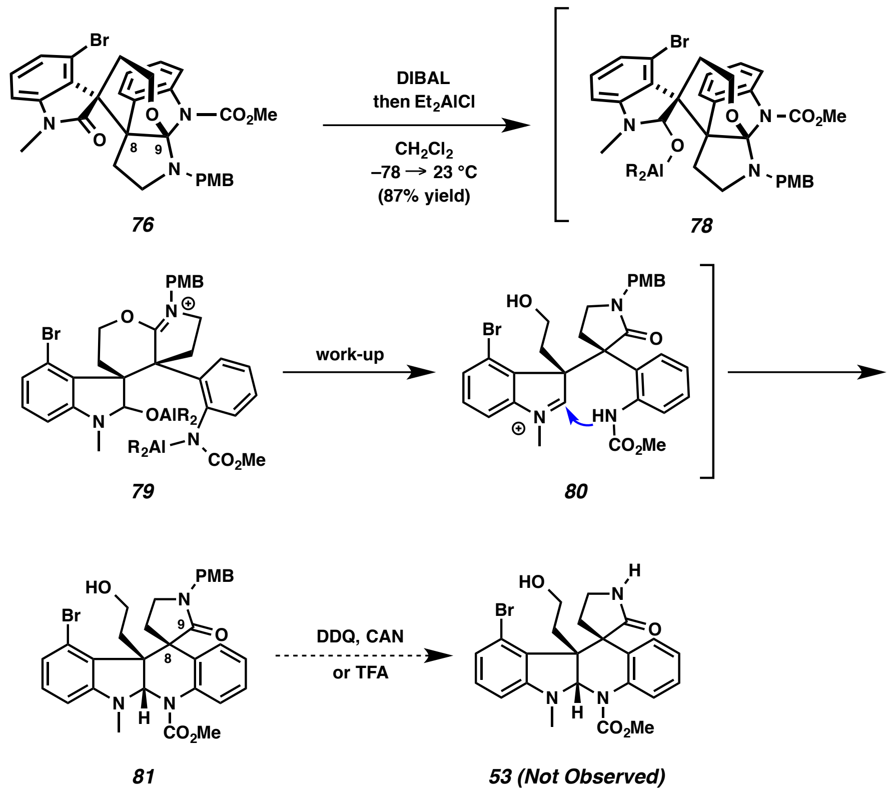
Having failed on our initial exploration, alternative conditions for construction of the piperidine D ring were next explored. Treatment of the lactam **54** with LiAlH$_4$[34] produced debrominated compound **73** in 83% yield (Scheme 1.2.17a). X-ray analysis of compound **73** showed a hydrogen bonding interaction between the carbonyl group of the PMB protected amide and the NH group of the carbamate. We reasoned that the undesired pyrrolidine was formed preferentially to the piperidine due to the close proximity of the carbamate NH and the carbonyl group of the PMB-protected amide. Next, a reductive cyclization reaction was attempted by treatment of **54** with Tf_2O and $NaBH_4$ to construct the piperidine ring. To our surprise, treatment of lactam **54** with Tf_2O provided the PMB-protected hexacyclic oxindole **76** in 95% yield (Scheme 1.2.17b). The PMB-protected amide of **54** was activated by Tf_2O to provide **74**, and nucleophilic attack by the aniline functionality furnished pyrrolidinoindoline derivative **75**. After the TIPS group was removed under the reaction conditions, the resultant hydroxyl group attacked the amidinium to generate the propellane structure of hexacyclic oxindole **76**. After cleavage of the PMB group using DDQ, the propellane structure of hexacyclic oxindole **77** was confirmed using X-ray analysis.

Scheme 1.2.17. *Attempted Reductive Cyclization of Lactam* ***54***



Despite this unexpected turn of events, we envisaged that the desired aminal **81** could be accessed from the propellane compound **76** using suitable conditions, since the oxidation state at C(9) of **76** is identical to that of the desired aminal **81** (Scheme 1.2.18). Moreover, the reactive *N*-PMB-pyrrolidinone in **54** is now protected by the propellane structure of **76**, thus leaving the oxindole as the only reducible carbonyl group. Fortunately, after extensive experimentation, we were pleased to find that reductive cyclization of hexacyclic oxindole **76** could be accomplished with DIBAL and Et_2AlCl to furnish aminal **81** in 87% yield (Scheme 1.2.18). Presumably, the oxindole of **76** was reduced by DIBAL to provide **78**, and rearrangement of the propellane structure generated iminium **79**. After the work-up, water attacked the iminium moiety of **79** to afford aniline **80**, and the resultant aniline group attacked the iminium of **80** to construct aminal **81**. In the last stage of the synthesis, we screened a variety of reaction conditions to remove the PMB group on the lactam **81** (e.g., DDQ, CAN, TFA, etc.) but, surprisingly, removal of the PMB group failed under all conditions attempted. This unexpected turn was particularly insidious since the PMB group was easily removed from hexacyclic oxindole **76** by DDQ (Scheme 1.2.17). The cleavage of allyl or benzyl groups were also examined, but disappointingly, cleavage of these groups on the lactam were similarly unsuccessful under several conditions.[35]

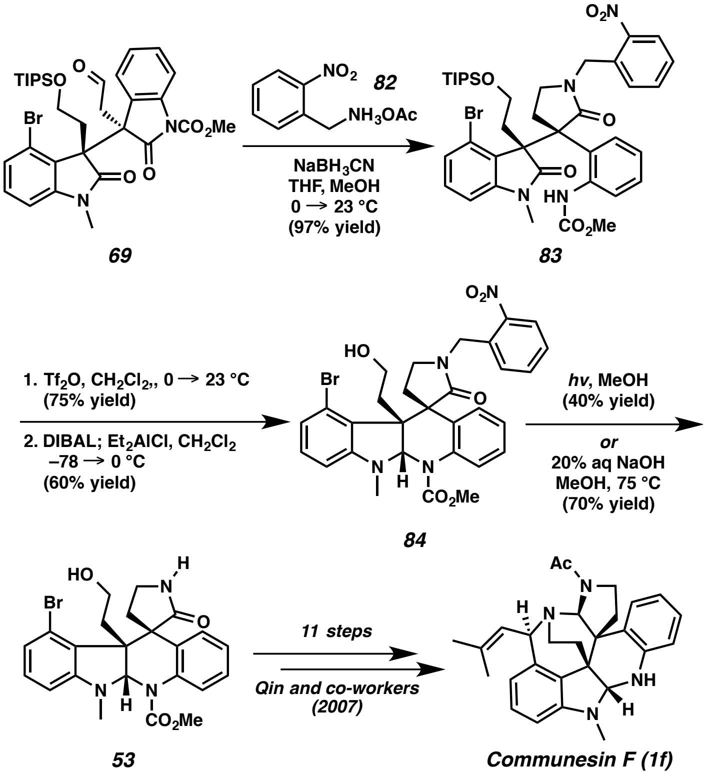
Scheme 1.2.18. *Synthesis of Aminal* ***81***



Given the difficulty of removal of PMB, allyl, and benzyl groups, our attention turned to exploring the *o*-nitrobenzyl group as a protecting group. However, subjecting the hexacyclic oxindole **77** to *o*-nitrobenzyl bromide under basic conditions to produce the *o*-nitrobenzyl protected propellane hexacyclic oxindole turned out to be challenging. Thus, we next investigated reductive amination of aldehyde **69** and were pleased to find that treatment of **69** with *o*-nitrobenzylammonium acetate **82** furnished lactam **83** in 97% yield (Scheme 1.2.19). Formation of the *o*-nitrobenzyl protected propellane hexacyclic oxindole using Tf_2O (75% yield) was followed by reductive cyclization with DIBAL and Et_2AlCl to furnish aminal **84** in 60% yield. To our delight, we found that removal of the *o*-nitrobenzyl group could be achieved by photolysis/irradiation at 350nm in 40% yield.[36]

Surprisingly, we discovered that removal of the *o*-nitrobenzyl group to produce compound **53** was also accomplished using 20% aq NaOH in methanol at 75 °C in 70% yield – a previously unknown deprotection protocol.[37] Aminal **53** has been advanced by the Qin group to communesin F,[5g] thus completing our formal synthesis of the natural product.

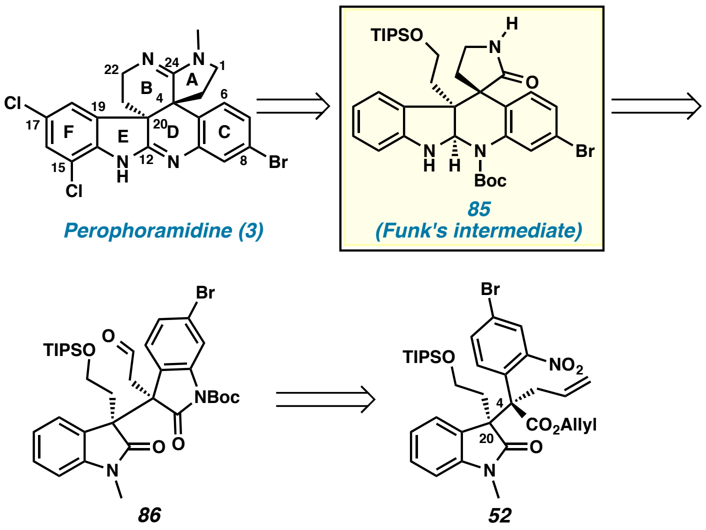
Scheme 1.2.19. *Completion of Formal Synthesis of Communesin F*



1.2.4. Formal Synthesis of Perophoramidine (3)

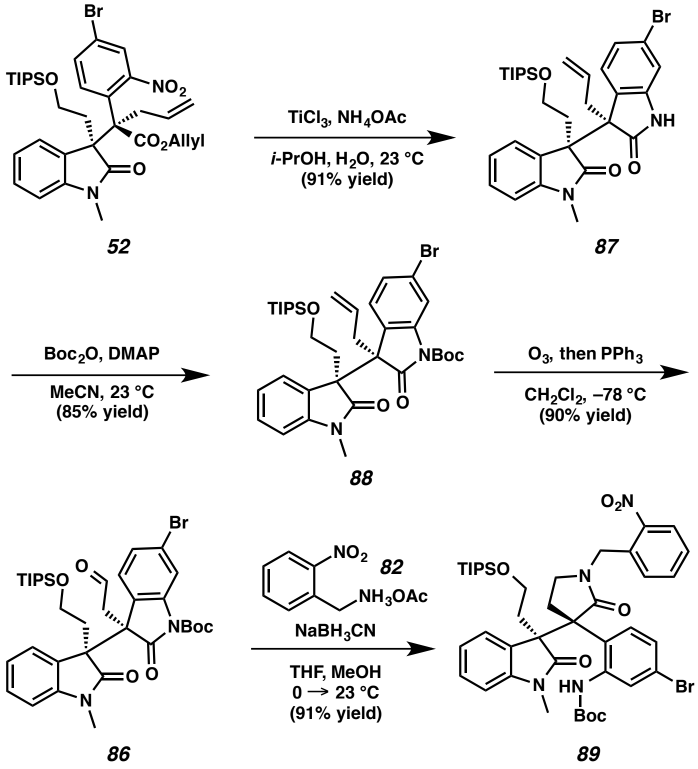
Our retrosynthetic analysis of perophoramidine (**3**) was based on our previously established expedient synthesis of oxindole derivative **52** (Scheme 1.2.20). We speculated that the aminal and lactam ring functionalities of pentacycle **85**, an intermediate in Funk's synthesis,[5o] could be cleaved, thereby leading to aldehyde **86**. The *N–C* bond of the 6-bromooxindole moiety in **86** was excised to arrive at nitroarene **52**. The construction of the contiguous quaternary centers at C(20) and C(4) of allyl ester **52** with the proper relative stereochemistry was accessed by decarboxylative allylic alkylation as previously described (Scheme 1.2.11b).

Scheme 1.2.20. *Retrosynthesis of Perophoramidine (**3**)*



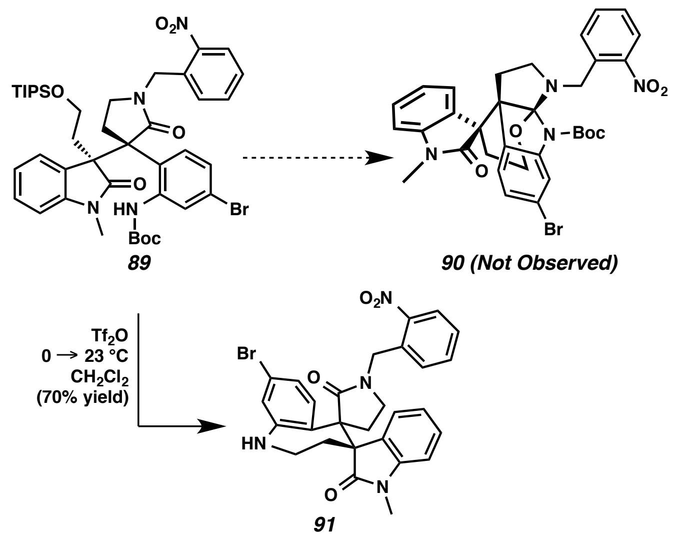
Carbamate **88** was obtained by reduction of nitroarene **52** with titanium chloride and simultaneous oxindole formation[38] to furnish the bis-oxindole moiety **87** in 91% yield followed by protection with Boc anhydride in 85% yield (Scheme 1.2.21). Ozonolysis of olefin **88** produced aldehyde **86** in 90% yield. Reductive amination of aldehyde **86** with *o*-nitrobenzylammonium acetate **82** resulted in an amine that underwent *in situ* lactam formation to afford oxindole lactam **89** in 91% yield.

Scheme 1.2.21. *Synthesis of Amide* ***89***



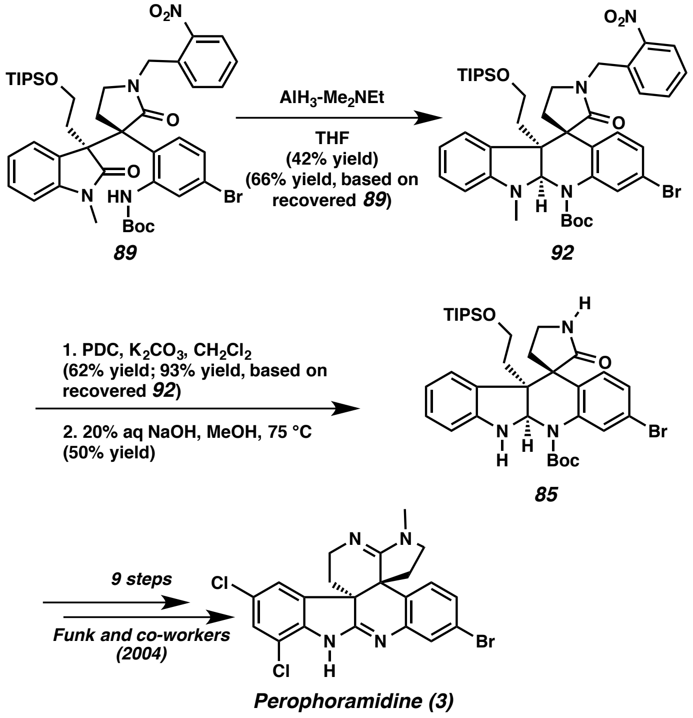
Initially, we attempted to generate the *o*-nitrobenzyl protected propellane hexacyclic oxindole **90** under analogous conditions to those used in our formal synthesis of communesin F on the pseudo diastereomeric series (vide supra). However, treatment of lactam **89** with Tf_2O yielded an unexpected azepine **91** in 70% yield (Scheme 1.2.22). Both the Boc and the TIPS groups on amide **89** were removed under the reaction conditions, and the resulting primary alcohol was presumably converted to the corresponding triflate. Finally, the aniline likely attacked the newly formed triflate to form azepine **91**.

Scheme 1.2.22. Formation of Azepine **91** using Tf_2O



After extensive experimentation, we discovered that in contrast to the communesin system, the desired reductive cyclization in the perophoramidine diastereomer occurred directly with AlH_3-Me_2NEt[31] to furnish cyclization product **92** in 42% yield (66% yield based on recovered starting material) (Scheme 1.2.23). The indoline methyl group was converted to a formyl group using PDC oxidation in 62% yield (93% yield based on recovered starting material).[39] To our delight, an attempt to remove the formyl group with 20% aq NaOH at 75 °C resulted in removal of both the formyl group and the *o*-nitrobenzyl group to produce aminal **85** in 50% yield.[37,40] This molecule was previously advanced by the Funk group to perophoramidine,[5o] and constitutes an expedient formal synthesis of the natural product.

Scheme 1.2.23. *Completion of Formal Synthesis of Perophoramidine*



1.3. Conclusion

In conclusion, we have conducted synthetic studies toward unique polycyclic alkaloids, and completed formal syntheses of communesin F (**1f**) in 9% overall yield over 17 steps and perophoramidine (**3**) in 6% overall yield (13% overall yield, based on recovered starting material) over 10 steps using a unified stereodivergent alkylation approach. The all-carbon quaternary center on the oxindole was established via stabilized enolate alkylation of 3-bromooxindoles, a method previously developed by our laboratory and now shown to be quite versatile even in particularly sterically challenging situations. The complementary relative stereochemistry of the two contiguous quaternary stereogenic centers found in communesin F (**1f**) and perophoramidine (**3**) respectively, was established by substrate controlled diastereoselective decarboxylative allylic alkylation. A reductive amination approach furnished the A ring, and reductive cyclization produced the D ring for both communesin F (**1f**) and perophoramidine (**3**). En route to the evolution of our eventual successful strategy, we have discovered a method to convert an indole to a 3-chloroindolenine using a mild reagent such as *o*-NsCl during the synthesis. In addition, previously unknown, mild and efficient deprotection conditions for the *o*-nitrobenzyl group on the lactam were discovered. Further studies to rationalize unprecedented complementary selectivity by Pd-catalyzed allylic alkylation reactions are currently in progress.

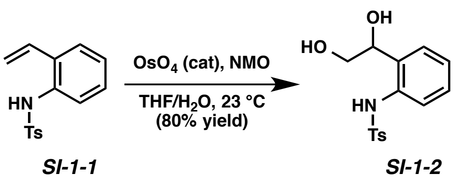
1.4. Experimental Methods and Analytical Data

1.4.1. Materials and Methods

Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Reaction progress was monitored by thin-layer chromatography (TLC). THF, Et_2O, CH_2Cl_2, toluene, benzene, CH_3CN, and dioxane were dried by passage through an activated alumina column under argon. Triethylamine was distilled over CaH_2 prior to use. Purified water was obtained using a Barnstead NANOpure Infinity UV/UF system. Brine solutions are saturated aqueous solutions of sodium chloride. Commercially available reagents were purchased from Sigma-Aldrich, Acros Organics, Strem, or Alfa Aesar and used as received unless otherwise stated. Reaction temperatures were controlled by an IKAmag temperature modulator unless otherwise indicated. Microwave-assisted reactions were performed in a Biotage Initiator 2.5 microwave reactor. Glove box manipulations were performed under a N_2 atmosphere. TLC was performed using E. Merck silica gel 60

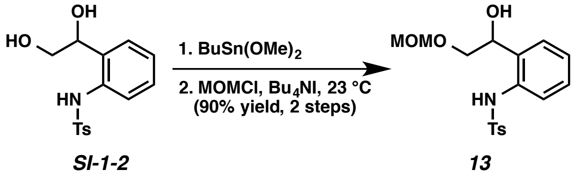
F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, *p*-anisaldehyde, or PMA (phosphomolybdic acid) staining. Silicycle Silia*Flash* P60 Academic Silica gel (particle size 0.040-0.064 mm) was used for flash column chromatography. ^{1}H NMR spectra were recorded on a Varian Inova 500 MHz spectrometer and are reported relative to residual $CHCl_3$ (δ 7.26 ppm), or $(CD_3)_2CO$ (δ 2.05 ppm). ^{13}C NMR spectra are recorded on a Varian Inova 500 MHz spectrometer (125MHz) and are reported relative to $CHCl_3$ (δ 77.16 ppm), or $(CD_3)_2CO$ (δ 29.84 ppm). Data for ^{1}H NMR are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet, br d= broad doublet, app = apparent. Data for ^{13}C are reported in terms of chemical shifts (ppm). IR spectra were obtained using a Perkin Elmer Paragon 1000 spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). High resolution mass spectra (HRMS) were obtained from 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+). X-ray crystallography reports for compounds **29** and **32** can be found in ref 41.[41]

1.4.2. Experimental Procedures



Diol SI-1-2. To a solution of styrene **SI-1-1** (6.11 g, 22.4 mmol, 1.0 equiv) in THF (140 mL) and water (70 mL) were added *N*-methylmorpholine *N*-oxide (5.96 g, 50.8 mmol, 2.3 equiv) and osmium tetroxide (11.6 mg, 43.9 μmol, 0.002 equiv). After addition, reaction was stirred for three days. The reaction was then concentrated to approximately 50 mL under reduced pressure, then extracted with a mixture of ether and THF (1:1) (3 x 45 mL). The organic layers were dried over sodium sulfate, and the solvent was removed under reduced pressure. Impurities were removed by washing solid with dichloromethane to afford diol **SI-1-2** (5.43 g, 80% yield) as a white solid. For spectrum, see ref 41.

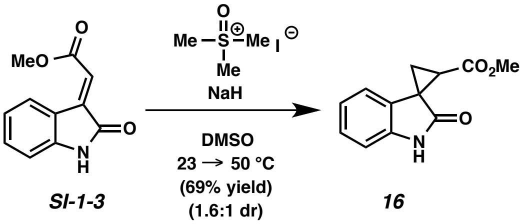
R_f = 0.13 (1:1 hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.78–7.65 (m, 2H), 7.39 (dd, J = 8.1, 1.1 Hz, 1H), 7.25–7.16 (m, 2H), 7.15–7.03 (m, 2H), 4.86–4.79 (m, 1H), 3.66–3.57 (m, 2H), 2.97 (s, 1H), 2.39 (s, 3H), 1.98 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.1, 137.1, 136.3, 129.9, 129.8, 129.2, 128.5, 127.4, 127.0, 122.2, 74.78, 66.0, 21.8; IR (Neat Film NaCl) 3271, 1318, 1150 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{15}H_{18}NO_4S$ [M+H]$^+$: 308.0951; found 308.0967.



Alcohol 13. To a solution of diol **SI-1-2** (500 mg, 1.63 mmol, 1.0 equiv) in toluene (70 mL) was added dibutyltin dimethoxide (410 μL, 1.79 mmol, 1.1 equiv). The flask was fitted with a short path distillation apparatus, and approximately half of the solvent was removed by distillation. To this solution was added MOMCl (136 μL, 1.79 mmol, 1.1 equiv) and tetrabutylammonium iodide (900 mg, 2.44 mmol, 1.5 equiv). After addition, the reaction was stirred for 12 h. Then, brine was added to this solution. The reaction

mixture was extracted with EtOAc (3 x 50 mL). The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography (3:1 → 1:1 hexanes:EtOAc) to afford alcohol **13** (513 mg, 90% yield, 2 steps) as a white solid. For spectrum, see ref 41.

R_f = 0.27 (1:1 hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.27–7.20 (m, 3H), 7.11–7.02 (m, 2H), 4.83–4.78 (m, 1H), 4.64 (s, 2H), 3.60 (dd, *J* = 10.5, 3.5 Hz, 1H), 3.48–3.41 (m, 2H), 3.39 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9, 137.1, 136.3, 129.7, 129.5, 128.9, 128.2, 127.2, 124.7, 122.0, 97.0, 73.3, 72.4, 55.6, 21.6; IR (Neat Film NaCl) 3233, 2932, 1598, 1497, 1335, 1161 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{17}H_{22}NO_5S$ $[M+H]^+$: 352.1213; found 352.1219.

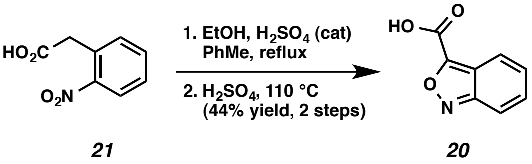


Cyclopropane 16. A flame-dried flask (25 mL) equipped with a teflon stirbar was charged with sodium hydride (60% dispersion in mineral oil, 22 mg, 0.55 mmol, 1.1 equiv), which was washed 3 times with dry hexanes. Then, DMSO (5.5 mL) and trimethyl sulfoxonium iodide (119 mg, 0.58 mmol, 1.2 equiv) were added. To this solution was added oxindole **SI-1-3** (100 mg, 0.49 mmol, 1.0 equiv) in a solution of DMSO (2.5 mL). After addition, the reaction was stirred for 2 h, and then the temperature was raised to 50 °C. The reaction was complete after another hour. Brine

was added and then the mixture was extracted with EtOAc (3 x 5 mL). The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography (3:1 → 1:1 hexanes:EtOAc) to afford oxindole **16** as two diastereomers. Diastereomer 1: (44.7 mg, 42% yield); Diastereomer 2: (28.6 mg, 27% yield). For spectrum, see ref 41.

Diastereomer 1: R_f = 0.52 (1:1 hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.40 (s, 1H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.04–6.97 (m, 2H), 3.70 (s, 3H), 2.74 (t, *J* = 8.0 Hz, 1H), 2.18 (dd, *J* = 4.5, 7.5 Hz, 1H), 2.05 (dd, *J* = 4.5, 8.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.5, 169.3, 141.8, 127.9, 126.4, 123.0, 122.4, 110.3, 52.4, 34.3, 32.9, 21.1; IR (Neat Film NaCl) 3214, 1712, 1622, 1470, 1209 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{12}H_{12}NO_3$ $[M+H]^+$: 218.0812; found 218.0825.

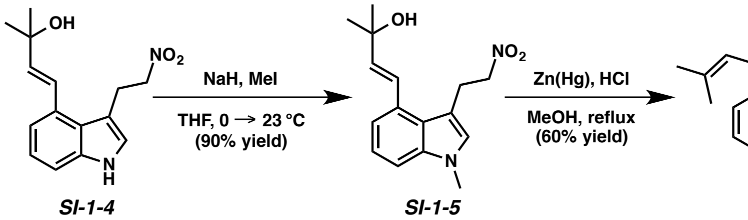
Diastereomer 2: R_f = 0.45 (1:1 hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.06 (s, 1H), 7.27–7.20 (m, 1H), 7.04–6.97 (m, 2H), 6.83 (d, *J* = 7.5 Hz, 1H), 3.75 (s, 3H), 2.68 (t, *J* = 8.0 Hz, 1H), 2.40 (dd, *J* = 5.0, 8.0 Hz, 1H), 1.84 (dd, *J* = 5.0, 8.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 167.7, 141.1, 129.5, 188.0, 122.4, 118.9, 110.3, 52.6, 33.5, 32.9, 21.3; IR (Neat Film NaCl) 3256, 1739, 1710 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{12}H_{12}NO_3$ $[M+H]^+$: 218.0812; found 218.0828.



21 *20*

Acid 20. A flame-dried flask (500 mL) equipped with a teflon stirbar was charged with acid **21** (10.0 g, 55.2 mmol, 1.0 equiv), ethanol (60 mL), sulfuric acid (200 μL), and toluene (280 mL). The flask was fitted with a condenser, and the solution was refluxed for 14 h. The solvent was removed under reduced pressure and sulfuric acid (280 mL) was added. After addition, the reaction was heated to 110 °C and stirred for 90 min. The solution was then poured onto ice (600 g), the mixture was extracted with ether (3 x 200 mL). The combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. Purification was performed via crystallization from water to afford acid **20** (3.94 g, 44% yield, 2 steps) as an off-white solid. For spectrum, see ref 41.

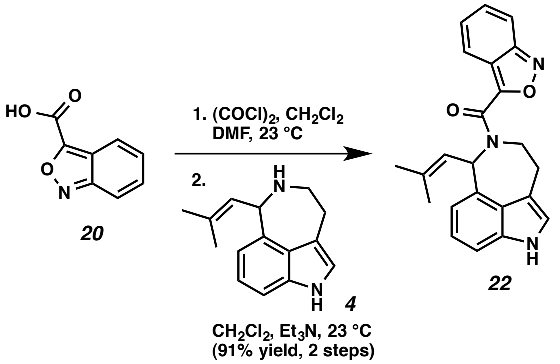
^{1}H NMR (300 MHz, acetone-d$_6$) δ 10.82 (br, s, 1H), 7.94 (d, *J* = 9.0 Hz, 1H), 7.75 (d, *J* = 10.0 Hz, 1H), 7.50 (dd, *J* = 6.5, 9.5 Hz, 1H), 7.34 (dd, *J* = 7.0, 8.5 Hz, 1H); ^{13}C NMR (75 MHz, acetone-d$_6$) δ 158.5, 158.1, 155.3, 132.4, 128.8, 121.4, 121.0, 116.7; IR (Neat Film NaCl) 2360, 1731, 1301, 1231, 1189, 753 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_8H_6NO_3$ $[M+H]^+$: 164.0342; found 164.0341.



1-methylaurantioclavine 5. To a solution of indole **SI-1-4** (386 mg, 1.41 mmol, 1.0 equiv) in THF (14 mL) was added methyl iodide (875 *μ*L, 14.1 mmol, 10 equiv) at 0 °C. Sodium hydride (60% dispersion in mineral oil, 562 mg, 14.5 mmol, 10.3 equiv) was then added to the solution, and the mixture was stirred for 25 min at 23 °C. The reaction was quenched with saturated ammonium hydroxide solution and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, and concentrated *in* *vacuo*. The residue was purified by flash column chromatography (3:1 → 2:1 hexanes:EtOAc) to afford nitro compound **SI-1-5** (363.5 mg, 90% yield) as a yellow solid.

To a solution of nitro compound **SI-1-5** (512 mg, 1.78 mmol, 1.0 equiv) in MeOH (125 mL) and 2N HCl (40 mL) was added amalgamated zinc, which had been formed from zinc dust (6.5 g, 98.3 mmol, 55 equiv) and mercuric chloride (1.10 g, 3.55 mmol, 2.0 equiv) in 2N HCl and subsequently rinsed with MeOH. The mixture was stirred at reflux for 3 h. The reaction was then decanted from the remaining amalgam and then basified to pH >10. The solid was removed by filtration, and the resulting solution was extracted with dichloromethane (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography (18:1 CH_2Cl_2:MeOH) to afford 1-methylaurantioclavine **5** (258 mg, 60% yield) as a yellow oil. For spectrum, see ref 41.

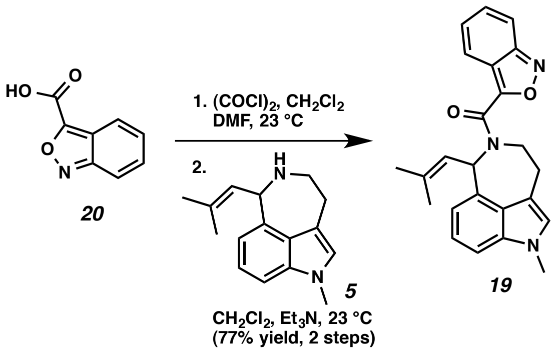
R_f = 0.30 (18:1 CH_2Cl_2:MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19–7.12 (m, 2H), 6.89–6.83 (m, 2H), 5.48 (d, *J* = 9.0 Hz, 1H), 4.92 (d, *J* = 9.0 Hz, 1H), 3.76 (s, 3H), 3.62–3.54 (m, 1H), 3.13–3.02 (m, 3H), 2.26 (br, s, 1H), 1.86 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 137.8, 133.3, 127.7, 125.9, 121.1, 117.4, 114.2, 107.3, 62.6, 48.9, 32.7, 30.8, 25.9, 18.4; IR (Neat Film NaCl) 3332, 2910, 1554, 1455 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{16}H_{21}N_2$ $[M+H]^+$: 241.1699; found 241.1712.



Amide 22. To a solution of acid **20** (262 mg, 1.60 mmol, 1.25 equiv) in dichloromethane (5 mL) was added oxalyl chloride (420 μL, 4.81 mmol, 3.8 equiv) and then a small amount of DMF (~20 μL). The reaction was stirred for 1 h then the solvent was removed under reduced pressure; the residue was evaporated from benzene (2 mL) to remove excess reagent. Dichloromethane (10 mL) and triethylamine (537 μL, 3.85 mmol, 3.0 equiv) were added, and to this solution was added aurantioclavine **4** (290 mg, 1.28 mmol, 1.0 equiv). After addition, the reaction was stirred for 60 min, and then brine was added. The resulting solution was extracted with EtOAc (3 x 7 mL). The combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography (3:1 → 1:1 hexanes:EtOAc) to afford amide **22** (435 mg, 91% yield, 2 steps) as a white solid. For spectrum, see ref 41.

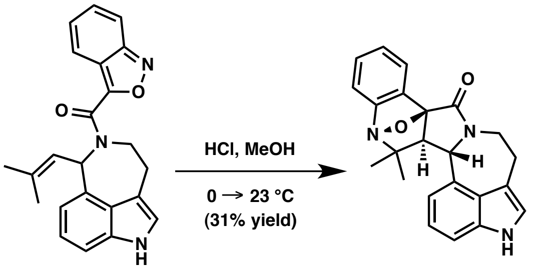
R_f = 0.72 (1:2 hexanes:EtOAc); (Due to the distinct presence of rotameric isomers, the ^{1}H NMR and ^{13}C NMR contained extra peaks. See the attached spectrum), ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00–8.86 (m, 2H), 7.98 (dq, J = 8.9, 0.9 Hz, 1H), 7.71–7.57 (m, 3H), 7.35–7.27 (m, 2H), 7.25–7.22 (m, 1H), 7.22–7.16 (m, 3H), 7.15–7.07 (m, 2H), 7.07–7.01 (m, 2H), 7.01–6.94 (m, 2H), 6.90–6.83 (m, 2H), 6.70 (d, J = 7.5 Hz, 1H), 5.48 (ddq, J = 7.9, 2.8, 1.6 Hz, 2H), 4.82–4.66 (m, 2H), 4.07 (ddd, J = 15.4, 10.0, 5.8 Hz, 1H), 3.82 (td,

J = 13.0, 2.6 Hz, 1H), 3.60–3.46 (m, 1H), 3.23–3.12 (m, 3H), 1.96 (d, *J* = 1.3 Hz, 3H), 1.79 (d, *J* = 1.5 Hz, 3H), 1.73 (d, *J* = 1.6 Hz, 3H), 1.64 (d, *J* = 1.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 158.4, 157.9, 157.8, 156.9, 156.8, 137.7, 137.4, 137.2, 136.9, 135.2, 135.1, 131.5, 131.4, 126.4, 126.1, 124.7, 124.3, 123.9, 123.8, 122.1, 121.9, 121.8, 121.7, 121.1, 121.0, 119.9, 118.3, 117.5, 114.9, 113.3, 112.6, 110.1, 109.9, 61.0, 57.5, 44.5, 43.1, 29.1, 25.9, 25.8, 25.7, 18.9, 18.2; IR (Neat Film NaCl) 3325, 2914, 2246, 1730, 1616, 1447 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{23}H_{22}N_3O_2$ [M+H]$^+$: 372.1707; found: 372.1637.



Amide 19. To a solution of acid **20** (37.5 mg, 0.229 mmol, 1.1 equiv) in dichloromethane (500 μL) was added oxalyl chloride (59 μL, 0.676 mmol, 3.3 equiv) and then a small amount of DMF (~1 μL). The reaction was stirred for 1 h, and then the solvent was removed under reduced pressure. The residue was evaporated from benzene (1 mL) to remove excess reagent. Dichloromethane (1.1 mL) and triethylamine (30 μL, 0.215 mmol, 1.03 equiv) were added, and to this solution was added 1-methylaurantioclavine **5** (50.0 mg, 0.208 mmol, 1.0 equiv). After addition, the reaction was stirred for 60 min, and then brine was added. The resulting solution was extracted with EtOAc (3 x 1.5 mL). The combined organic layers were dried over $MgSO_4$, and

concentrated *in vacuo*. The residue was purified by flash column chromatography (3:1 → 2:1 hexanes:EtOAc) to afford amide **19** (61.6 mg, 77% yield, 2 steps) as a white solid. R_f = 0.79 (1:2 hexanes:EtOAc); (due to the distinct presence of rotameric isomers, the ^{1}H NMR and ^{13}C NMR contained extra peaks. For spectrum, see ref 41), ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, *J* = 9.0 Hz, 1H), 7.68 (d, *J* = 9.0 Hz, 1H), 7.62 (t, *J* = 10.0 Hz, 1H), 7.37–7.30 (m, 1.5H), 7.22–7.18 (m, 2H), 7.13–7.08 (m, 2H), 7.04–6.99 (m, 1H), 6.95 (s, 1H), 6.86–6.84 (m, 2H), 6.67 (d, *J* = 7.5 Hz, 1H), 5.46 (d, *J* = 7.5 Hz, 1H), 4.69 (dd, *J* = 15.0, 38.0 Hz, 1H), 4.04 (dt, *J* = 4.5, 15.5 Hz, 1H), 3.77 (s, 3H), 3.74 (s, 3H), 3.48 (t, *J* = 18.0 Hz, 1H), 3.25 (3.11, m, 2H), 1.92 (s, 3H), 1.78 (s, 3H), 1.72 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 158.5, 157.7, 157.6, 156.9, 156.8, 137.8, 137.7, 137.6, 136.8, 135.7, 135.6, 131.3, 131.2, 126.5, 126.3, 125.9, 124.8, 124.4, 124.3, 124.2, 122.1, 121.6, 121.5, 121.2, 121.1, 120.0, 118.1, 117.3, 115.0, 114.9, 112.3, 111.7, 107.9, 107.7, 60.9, 57.3, 44.5, 43.1, 32.6, 29.0, 25.9, 25.7, 18.9, 18.2; IR (Neat Film NaCl) 2913, 2245, 1615, 1455, 1410 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{24}H_{24}N_3O_2$ $[M+H]^+$: 386.1863; found 386.1775.

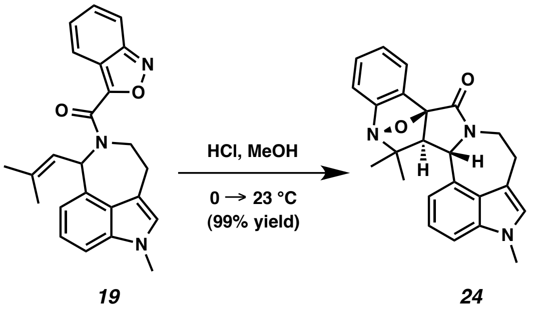


22

23

Indole 23. A flame-dried vial (20 mL) equipped with a teflon stirbar was charged with amide **22** (100 mg, 0.269 mmol, 1.0 equiv) and cooled to 0 °C. To this reaction mixture was added a 0.5 M solution of HCl in MeOH (2.7 mL, generated from addition of acetyl chloride to methanol at 0 ºC) at 0 °C. The mixture was stirred for 1 h and then warmed to 23 ºC over 30 min. The solvent was then removed under reduced pressure. Purification was performed by washing the solid with dichloromethane to afford indole **23** (31.1 mg, 31% yield) as a white solid. For spectrum, see ref 41.

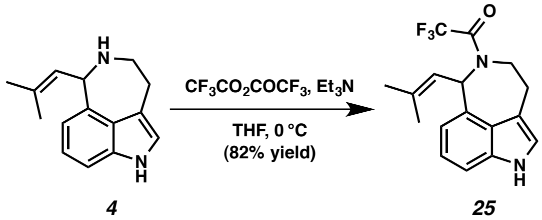
R_f = 0.22 (1:1 hexane:EtOAc); ^{1}H NMR (300 MHz, acetone-d_6) δ 11.05 (s, 1H), 7.34–7.17 (m, 6H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.61 (d, *J* = 7.5 Hz, 1H), 5.47 (d, *J* = 6.5 Hz, 1H), 4.21 (d, *J* = 13.0 Hz, 1H), 3.44 (t, *J* = 11.0 Hz, 1H), 3.18–2.98 (m, 2H), 2.37 (d, *J* = 6.5 Hz, 1H), 1.77 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (75 MHz, DMSO) δ 164.3, 153.0, 139.6, 137.0, 134.6, 127.3, 126.6, 123.7, 122.6, 121.4, 118.6, 118.0, 115.2, 112.7, 110.2, 96.4, 70.1, 63.1, 61.2, 44.4, 26.9, 26.6, 26.0; IR (Neat Film NaCl) 3314, 1681, 753 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{23}H_{22}N_3O_2$ $[M+H]^+$: 372.1707; found 372.1710.



Indole 24. A flame-dried vial (20 mL) equipped with a teflon stirbar was charged with amide **19** (100 mg, 0.259 mmol, 1.0 equiv) and cooled to 0 °C. To this solution was added a 0.5 M solution of HCl in MeOH (2.6 mL, generated from addition of acetyl chloride to methanol at 0 °C) at 0 °C. The mixture was stirred for 1 h and then warmed

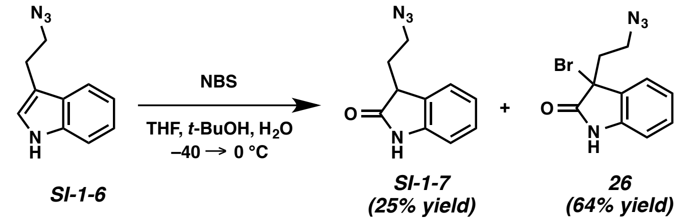
to 23 °C over 30 min. The solvent was then removed under reduced pressure. Purification was performed via flash column chromatography (3:1 → 1:1 hexanes:EtOAc) to afford indole **24** (101 mg, 99% yield) as a white solid. For spectrum, see ref 41.

R_f = 0.29 (1:1 hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.17 (m, 6H), 7.00 (s, 1H), 6.76–6.73 (m, 1H), 5.51 (d, *J* = 6.5 Hz, 1H), 4.57–4.50 (m, 1H), 3.80 (s, 3H), 3.50–3.15 (m, 3H), 2.57 (d, *J* = 6.5 Hz, 1H), 1.95 (s, 3H), 1.18 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 153.5, 139.8, 137.9, 135.6, 127.5, 127.0, 126.9, 124.6, 121.9, 119.1, 118.4, 115.9, 113.4, 108.4, 97.2, 70.9, 64.1, 61.9, 45.2, 33.0, 27.5, 27.2, 26.6; IR (Neat Film NaCl) 3315, 2932, 1699, 1456, 1317, 754 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{24}H_{24}N_3O_2$ [M+H]$^+$: 386.1863; found 386.1809.



***N*-trifluoroacetate-aurantioclavine 25.** To a solution of aurantioclavine **4** (882 mg, 3.90 mmol, 1.0 equiv) in THF (14 mL) were added triethylamine (820 μL, 5.88 mmol, 1.5 equiv) and trifluoroacetic anhydride (606 μL, 4.29 mmol, 1.1 equiv) at 0 ºC. The reaction was complete immediately, so it was quenched with methanol. The solvent was then removed under reduced pressure. Purification was performed via flash column chromatography (9:1 → 3:1 hexanes:EtOAc) to afford the *N*-trifluoroacetate-aurantioclavine **25** (1.03 g, 82% yield) as a yellow foam. For spectrum, see ref 41.

R_f = 0.30 (3:1 hexanes:EtOAc); (Due to the distinct presence of rotameric isomers, the ^{1}H NMR and ^{13}C NMR contained extra peaks. See the attached spectrum), ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (br, s, 1H), 7.29–7.26 (m, 1H), 7.02–6.97 (m, 2H), 6.90 (t, *J* = 7.0 Hz, 1H), 6.23 (d, *J* = 8.0 Hz, 1H), 5.40 (dd, *J* = 7.5, 19.5 Hz, 1H), 4.40 (d, *J* = 13.0 Hz, 1H), 4.16–4.10 (m, 1H), 4.04–3.94 (m, 2H), 3.83 (t, *J* = 13.0 Hz, 1H), 3.43 (t, *J* = 16.5 Hz, 1H), 3.27–3.23 (m, 1H), 3.09 (d, *J* = 16.5 Hz, 1H), 1.91 (s, 3H), 1.86 (s, 3H), 1.78 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5, 157.0, 156.8, 156.3, 138.5, 137.4, 137.2, 137.2, 135.1, 134.4, 124.3, 123.9, 123.5, 123.3, 122.1, 121.9, 121.8, 119.0, 118.8, 118.5, 117.1, 115.2, 115.0, 113.1, 112.6, 110.3, 110.1, 60.7, 60.6, 58.6, 43.7, 43.7, 28.4, 26.2, 25.7, 25.0, 18.9, 18.2; IR (Neat Film NaCl) 3361, 2917, 1667, 1441, 1205 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{17}H_{18}N_2OF_3$ $[M+H]^+$: 323.1366; found 323.1308.



Bromooxindole 26. A flame-dried flask (1000 mL) equipped with a teflon stirbar was charged with azide **SI-1-6**[1] (5.03 g, 30.3 mmol, 1.0 equiv), to which was subsequently added THF (150 mL), *t*-BuOH (150 mL), and water (3.75 mL) and cooled to –40 °C. A 0 °C solution of NBS (8.03 g, 45.1 mmol, 1.5 equiv) in THF (450 mL) was then added via cannula over 30 min, and the resulting solution was allowed to warm to –10 °C over 2 h. Warming continued slowly over 30 min to 0 °C. After 20 min at 0 °C, the solvent was

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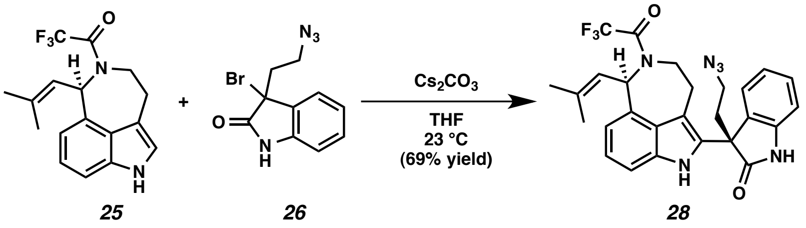
[1] Suzuki, T.; Ota, Y.; Ri, M.; Bando, M.; Gotoh, A.; Itoh, Y.; Tsumoto, H.; Tatum, P. R.; Mizukami, T.; Nakagawa, H.; Iida, S.; Ueda, R.; Shirahige, K.; Miyata, N. *J. Med. Chem.* **2012**, *55*, 9562.

removed under reduced pressure. Purification was performed via flash column chromatography (9:1→1:2 pentanes:ether) to afford bromooxindole **26** (5.46 g, 64% yield) as a yellow solid. Oxindole **SI-1-7** (1.50 g, 25% yield) was also isolated as a light yellow solid. For spectrum, see ref 41.

Bromooxindole **26**: R_f = 0.46 (2:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (br, s, 1H), 7.28–7.23 (m, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 3.61–3.44 (m, 2H), 2.32–2.17 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.5, 141.7, 128.4, 128.1, 123.8, 122.3, 110.2, 48.0, 43.3, 29.5; IR (Neat Film NaCl) 3228, 2100, 1693, 1620, 1470 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{10}H_{10}N_4OBr$ $[M+H]^+$: 281.0033; found 281.0040.

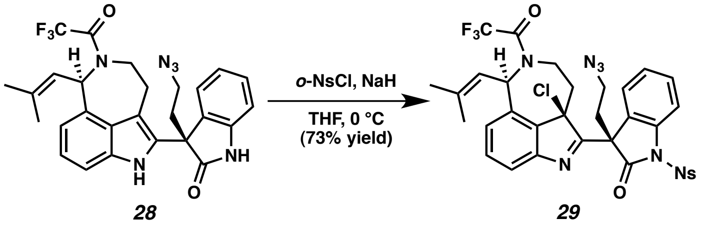
Oxindole **SI-1-7**: R_f = 0.37 (2:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (br, s, 1H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 3.41–3.20 (m, 3H), 2.84–2.57 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.6, 139.8, 130.6, 129.1, 124.6, 123.5, 111.4, 54.5, 47.6, 38.0; IR (Neat Film NaCl) 3252, 2102, 1732, 1619, 1471 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{10}H_{11}N_4O[M+H]^+$: 203.0927; found 203.0933.



Adduct 28. A flame-dried vial (20 mL) equipped with a teflon stirbar was charged with indole **25** (120 mg, 0.372 mmol, 1.0 equiv) and bromooxindole **26** (157 mg, 0.559 mmol,

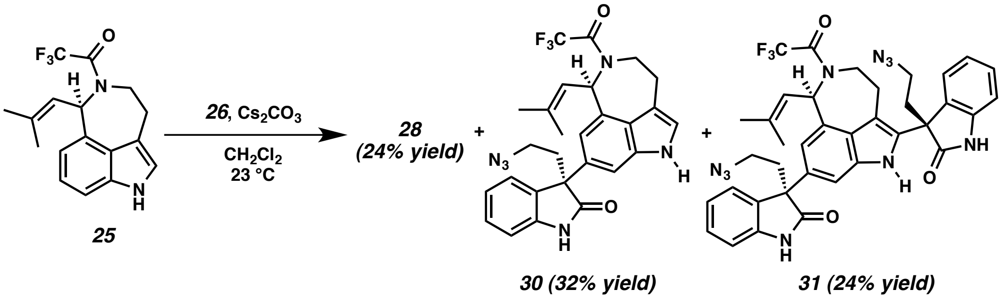
1.5 equiv), which were subsequently dissolved in THF (4 mL). Cesium carbonate (243 mg, 0.746 mmol, 2.0 equiv) was then added. After addition, the reaction was stirred for 12 h, and then water was added. The resulting solution was extracted with EtOAc (3 x 3 mL). The combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography (9:1 → 2:1 hexanes:EtOAc) to afford adduct **28** (134 mg, 69% yield) as a yellow foam. For spectrum, see ref 41.

R_f = 0.34 (2:1 hexanes:EtOAc x2 elutions); (Due to the distinct presence of rotameric isomers, the ^{1}H NMR and ^{13}C NMR contained extra peaks. See the attached spectrum), ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.74 (br, s, 2H), 8.59 (br, s, 1H), 8.97 (br, s, 1H), 7.34–6.86 (m, 12H), 6.78 (t, *J* = 7.0 Hz, 1H), 6.11 (d, *J* = 8.0 Hz, 1H), 5.33 (dd, *J* = 7.5, 20.5 Hz, 2H), 4.16 (d, *J* = 13.5 Hz, 1H), 3.96–3.90 (m, 1H), 3.80 (t, *J* = 16.0 Hz, 1H), 3.63 (t, *J* = 13.5 Hz, 1H), 3.25–3.12 (m, 5H), 3.09–2.86 (m, 3H), 2.65–2.53 (m, 3H), 1.84 (s, 3H), 1.80 (s, 3H), 1.71 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.8, 178.7, 157.1, 156.7, 156.5, 156.0, 141.4, 141.3, 138.4, 137.0, 136.0, 135.6, 135.1, 134.4, 130.1, 129.9, 129.8, 129.5, 129.5, 125.5, 125.0, 124.9, 124.8, 124.4, 123.7, 123.3, 122.4, 122.2, 119.5, 119.0, 118.7, 118.1, 114.9, 111.8, 111.5, 111.2, 111.2, 110.1, 109.8, 60.5, 58.3, 52.7, 52.6, 47.3, 47.3, 43.5, 43.4, 35.0, 34.8, 28.1, 26.3, 25.8, 24.5, 19.0, 18.3; IR (Neat Film NaCl) 3335, 2102, 1713, 1674 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{27}H_{26}N_6O_2F_3$ $[M+H]^+$: 523.2064; found 523.1982.



Chloride 29. To a solution of adduct **28** (183 mg, 0.350 mmol, 1.0 equiv) in THF (4 mL) was added sodium hydride (60% dispersion in mineral oil, 42 mg, 1.05 mmol, 3.0 equiv) at 0 °C. The reaction mixture was stirred for 5 min and *o*-nitrobenzylsulfonyl chloride (116 mg, 0.523 mmol, 1.5 equiv) was added at 0 ºC. The reaction was stirred for 10 min, and then a saturated solution of ammonium chloride was added. The resulting solution was extracted with EtOAc (3 x 3 mL). The combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography (15:1 → 2:1 hexanes:EtOAc) to afford alkyl chloride **29** (142 mg, 73% yield) as a white crystalline solid. For spectrum, see ref 41.

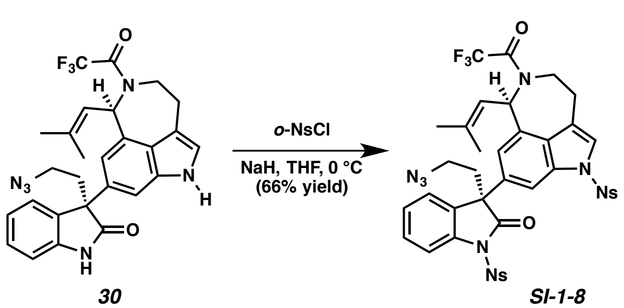
R_f = 0.26 (2:1 hexanes:EtOAc); (Due to the distinct presence of rotameric isomers, the ^{1}H NMR and ^{13}C NMR contained extra peaks. See the attached spectrum), ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64–8.59 (m, 2H), 7.95–7.84 (m, 8H), 7.55–7.47 (m, 6H), 7.37–7.26 (m, 5H), 7.15 (d, *J* = 7.0 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.31 (d, *J* = 7.5 Hz, 2H), 5.76–5.72 (m, 2H), 5.61 (d, *J* = 7.5 Hz, 1H), 4.20–4.08 (m, 2H), 3.94–3.67 (m, 3H), 3.31–3.19 (m, 2H), 2.99–2.74 (m, 6H), 2.29 (dd, *J* = 3.0, 10.5 Hz, 1H), 1.75 (s, 6H), 1.65 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 175.8, 173.8, 173.6, 156.3, 155.9, 151.7, 151.6, 148.2, 147.9, 141.6, 140.7, 139.9, 139.7, 139.2, 138.2, 137.4, 136.9, 136.4, 136.0, 135.3, 135.2, 132.6, 130.9, 130.8, 130.4, 130.4, 128.3, 126.8, 126.6, 126.4, 126.3, 125.8, 125.4, 125.3, 125.2, 124.9, 121.7, 121.6, 120.6, 119.8, 118.6, 115.4, 115.3, 114.8, 77.7, 77.4, 77.2, 76.8, 75.7, 75.5, 60.1, 57.6, 55.7, 55.6, 46.5, 46.4, 40.0, 39.1, 37.8, 37.6, 36.1, 32.6, 26.5, 26.0, 18.6, 18.1; IR (Neat Film NaCl) 2102, 1755, 1686, 1544, 1146 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{33}H_{28}O_7N_7F_3SCl$ $[M+H]^+$: 758.1406; found 758.1442.



Adducts 28, 30, and 31. A flame-dried flask (100 mL) equipped with a teflon stirbar was charged with indole **25** (1.03 g, 3.21 mmol, 1.0 equiv) and bromooxindole **26** (2.25 mg, 8.02 mmol, 2.5 equiv), which were subsequently dissolved in dichloromethane (32 mL). Cesium carbonate (3.14 g, 9.62 mmol, 3.0 equiv) was then added. After addition, the reaction was stirred for 3 h, and then water was added. The resulting solution was extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography (18:1 → 1:2 hexanes:EtOAc) to afford adduct **28** (404 mg, 24% yield), adduct **30** (538 mg, 32% yield), and adduct **31** (548 mg, 24% yield). For spectrum, see ref 41.

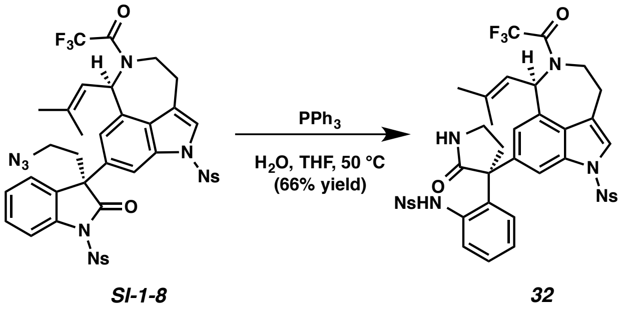
Adduct **30**: R_f = 0.18 (2:1 hexanes:EtOAc x2 elutions); (due to the distinct presence of rotameric isomers, the ^{1}H NMR and ^{13}C NMR contained extra peaks), ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.91 (d, *J* = 13.0 Hz, 2H), 8.33 (d, *J* = 6.0 Hz, 2H), 7.28–6.86 (m, 9H), 6.75 (d, *J* = 7.5 Hz, 1H), 6.11 (d, *J* = 7.5 Hz, 1H), 5.31 (dd, *J* = 7.5, 29.5 Hz, 2H), 4.30 (d, *J* = 13.5 Hz, 1H), 4.06–4.01 (m, 1H), 3.94–3.84 (m, 1H), 3.71 (t, *J* = 13.0 Hz, 1H), 3.29 (t, *J* = 13.0 Hz, 1H), 3.17–3.13 (m, 4H), 2.98 (d, *J* = 16.5 Hz, 1H), 2.89–2.75 (m, 2H), 2.53–2.44 (m, 2H), 1.76 (s, 3H), 1.72 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.1, 180.9, 157.4, 157.0, 156.7, 156.2, 141.1, 138.5, 137.5, 137.3, 137.1, 135.5, 134.8, 133.4, 133.2, 132.2, 132.1, 128.8, 128.7, 125.1, 124.0, 123.6, 123.2, 123.1, 122.8, 122.5, 119.0, 118.7, 117.0, 115.7, 115.1, 114.9, 113.3, 112.6, 110.7, 108.6, 108.5, 60.6, 58.6, 55.5, 55.4, 47.9, 43.8, 43.7, 36.6, 36.3, 28.4, 26.3, 25.8, 25.0, 18.9, 18.3; IR (Neat Film NaCl) 3328, 2100, 1712, 1682 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{27}H_{26}N_6O_2F_3$ $[M+H]^+$: 523.2064, found 523.2002.

Adduct **31**: R_f = 0.09 (2:1 hexanes:EtOAc x2 elutions); (due to the distinct presence of rotameric isomers, the ^{1}H NMR and ^{13}C NMR contained extra peaks), ^{1}H NMR (300 MHz, acetone-d$_6$) δ 10.43 (d, *J* = 11.5 Hz, 1H), 9.80 (d, *J* = 8.0 Hz, 1H), 9.59 (s, 1H), 7.36–7.23 (m, 7H), 7.19–6.97 (m, 8H), 5.36 (dd, *J* = 7.0, 40.0 Hz, 2H), 4.02–3.50 (m, 6H), 3.25–3.10 (m, 8H), 3.04 (s, 2H), 3.01–2.44 (m, 8H), 1.76 (s, 3H), 1.73 (s, 3H), 1.68 (s, 6H); ^{13}C NMR (75 MHz, acetone-d$_6$) δ 180.2, 180.1, 177.9, 177.8, 143.1, 143.0, 142.9, 138.3, 137.4, 137.2, 136.8, 135.3, 134.8, 134.6, 134.4, 133.6, 133.3, 133.2, 133.0, 131.3, 129.9, 129.3, 129.2, 126.1, 125.3, 125.2, 125.0, 124.8, 123.9, 123.6, 122.9, 118.0, 147.1, 111.0, 110.9, 110.3, 109.9, 109.4, 109.2, 61.2, 59.2, 55.8, 55.7, 52.7, 52.7, 48.6, 47.6, 44.0, 37.0, 36.9, 35.4, 28.2, 26.1, 25.7, 24.8, 18.8, 18.3; IR (Neat Film NaCl) 3305, 2101, 1713, 1472 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{37}H_{34}N_{10}F_3O_3$ $[M+H]^+$: 723.2762; found 723.2689.



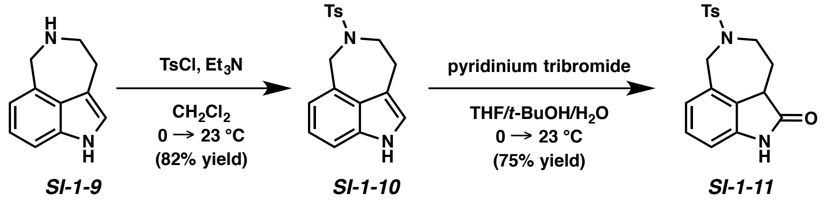
Nosylate SI-1-8. A flame-dried vial (4 mL) equipped with a teflon stirbar was charged with adduct **30** (43.7 mg, 0.0836 mmol), which was subsequently dissolved in THF (800 μL). The solution was cooled to 0 °C, and then sodium hydride (60% dispersion in mineral oil, 17 mg, 0.425 mmol) was added. 5 min after the sodium hydride addition, *o*-nitrobenzylsulfonyl chloride (93 mg, 0.420 mmol) was added. The reaction was stirred for 10 min, and then a saturated solution of ammonium chloride was added. The resulting solution was extracted 3 times with ether, the organic layers were combined and dried over magnesium sulfate, and the solvent was removed under reduced pressure. Purification was performed via flash column chromatography (9:1 →1:1 hexanes:EtOAc) to afford the bisnosylate **SI-1-8** (49.0 mg, 66% yield) as a yellow solid. For spectrum, see ref 41.

R_f = 0.42 (1:1 hexanes:EtOAc); (Due to the distinct presence of rotameric isomers, the ^{1}H NMR and ^{13}C NMR contained extra peaks), ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54–8.51 (m, 2H), 8.03–8.00 (m, 2H), 7.88–7.56 (m, 10H), 7.50 (s, 1H), 7.42–7.35 (m, 5H), 7.18–7.12 (m, 3H), 6.95 (s, 1H), 6.61 (d, *J* = 7.5 Hz, 1H), 5.97 (d, *J* = 7.5 Hz, 1H), 5.23–5.16 (m, 2H), 4.27 (d, *J* = 13.5 Hz, 1H), 4.02 (d, *J* = 15.0 Hz, 1H), 3.89–3.79 (m, 1H), 3.64 (t, *J* = 11.0 Hz, 1H), 3.32–2.80 (m, 10H), 2.48–2.33 (m, 2H), 1.73 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2, 176.0, 157.3, 156.9, 156.5, 148.0, 148.0, 140.2, 140.1, 140.0, 138.6, 137.2, 136.6, 136.2, 136.0, 135.7, 135.5, 134.8, 134.7, 132.8, 132.8, 132.4, 131.2, 131.2, 131.1, 130.9, 130.6, 129.9, 129.8, 129.5, 129.2, 127.4, 127.0, 125.7, 125.7, 125.4, 125.4, 125.2, 125.1, 124.9, 122.8, 121.9, 121.1, 120.0, 118.8, 118.5, 117.9, 115.5, 114.9, 110.6, 60.2, 58.1, 55.0, 55.0, 47.5, 42.8, 42.7, 36.6, 36.6, 39.9, 28.0, 26.3, 25.8, 25.0, 18.9, 18.3; IR (Neat Film NaCl) 2930, 2101, 1754, 1684, 1544 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{39}H_{32}N_8O_{12}F_3S_2$ [M+H]$^+$: 925.1528, found 925.1613.



Lactam 32. To a solution of nosylate **SI-1-8** (43.1 mg, 0.0483 mmol, 1.0 equiv) in THF (1 mL) and water (250 μL) was added triphenylphosphine (25 mg, 0.0953 mmol, 2.0 equiv). The reaction was stirred for 3 h at 50 °C, and then the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (3:1 → 1:1 hexanes:EtOAc) to afford the lactam **32** (49.0 mg, 66% yield) as a yellow crystalline solid. For spectrum, see ref 41.

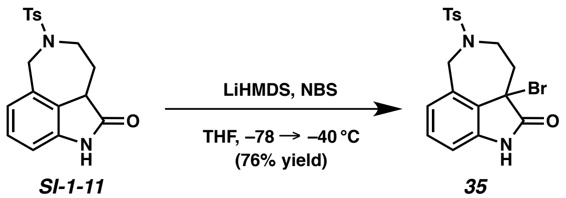
R_f = 0.14 (1:1 hexanes:EtOAc); (due to the distinct presence of rotameric isomers, the ^{1}H NMR and ^{13}C NMR contained extra peaks), ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75–7.50 (m, 6H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.34–7.22 (m, 4H), 7.14 (d, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 7.5 Hz, 2H), 6.55 (d, *J* = 6.5 Hz, 2H), 6.01 (d, *J* = 7.5 Hz, 1H), 5.32 (d, *J* = 8.0 Hz, 1H), 5.20 (d, *J* = 8.0 Hz, 1H), 4.26 (d, *J* = 13.5 Hz, 1H), 4.02 (d, *J* = 15.5 Hz, 1H), 3.81 (t, *J* = 11.5 Hz, 1H), 3.30–3.00 (m, 3H), 2.35–2.28 (m, 2H), 1.67 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.0, 157.3, 156.8, 156.7, 156.2, 147.9, 147.8, 147.7, 139.5, 139.4, 137.8, 137.5, 137.4, 136.9, 136.5, 136.4, 136.2, 136.1, 135.6, 135.3, 135.1, 133.6, 132.9, 132.5, 132.2, 132.0, 131.0, 130.9, 130.5, 129.0, 127.9, 127.8, 126.3, 126.2, 125.2, 125.1, 125.0, 124.9, 124.8, 124.5, 124.4, 124.3, 123.3, 122.4, 121.4, 120.5, 119.2, 118.9, 118.5, 118.4, 115.1, 110.2, 109.7, 77.7, 77.4, 77.2, 76.8, 60.1, 58.2, 57.7, 43.0, 42.8, 39.8, 38.8, 28.5, 26.1, 25.7, 25.3, 18.9, 18.3; IR (Neat Film NaCl) 3098, 2916, 1682, 1545, 1368, 1170, 732 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{39}H_{34}N_6O_{12}F_3S_2$ [M+H]$^+$: 899.1623, found 899.1731.



Oxindole SI-1-11. To a solution of indole **SI-1-9** (106 mg, 0.614 mmol, 1.0 equiv) and Et_3N (0.17 mL, 1.23 mmol, 2.0 equiv) in CH_2Cl_2 (4 mL) cooled to 0 ºC was added a solution of TsCl (117 mg, 0.614 mmol, 1.0 equiv) in CH_2Cl_2 (3 mL) dropwise. The ice bath was removed and the reaction mixture was stirred for 5 h, then diluted with EtOAc (160 mL) and washed with 0.5 N HCl (2 x 30 mL) and brine. The organic layers were combined, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (2:1 hexanes:EtOAc) to afford indole **SI-1-10** (164 mg, 82% yield).

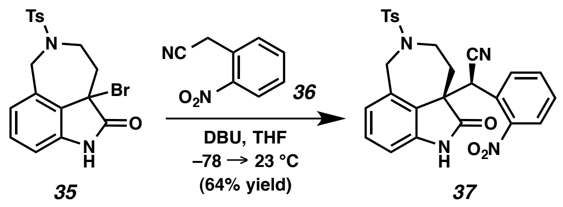
Indole **SI-1-10** was dissolved in THF (10 mL), *t*-BuOH (10 mL) and water (1 mL). The solution was cooled to 0 ºC and pyridinium tribromide (504 mg, 1.54 mmol, 1.02 equiv) was added. The reaction mixture was stirred at 0 ºC for 45 min and then allowed to warm to ambient temperature. The reaction was quenched by addition of 10 mL of 1:1 v/v 1M $Na_2S_2O_3$:sat. $NaHCO_3$. The reaction mixture was diluted with brine (50 mL) and extracted with EtOAc (3 x 50 mL). The combined organic extracts were dried with $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (2:1 hexanes:acetone) to afford oxindole **SI-1-11** (397 mg, 75% yield) of as a white solid.

R_f = 0.15 (1:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (br, s, 1H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.21–7.14 (m, 3H), 6.94 (d, *J* = 7.7 Hz, 1H), 6.80 (d, *J* = 7.7 Hz, 1H), 4.80 (d, *J* = 15.5 Hz, 1H), 4.30 (d, *J* = 13.6 Hz, 1H), 4.15 (d, *J* = 15.5 Hz, 1H), 3.52 (dd, *J* = 12.5, 3.5 Hz, 1H), 3.24 (t, *J* = 12.6 Hz, 1H), 2.38 (s, 3H), 2.30 (m, 1H), 1.53 (m, 1H); ^{13}C (75 MHz, $CDCl_3$) δ 178.4, 143.3, 140.5, 137.1, 135.9, 129.6, 128.4, 128.3, 127.0, 121.5, 109.1, 53.3, 51.6, 46.2, 28.6, 21.5; IR (Neat Film NaCl) 3276, 2925, 2853, 1698, 1618, 1463, 1326, 1153 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{18}H_{19}N_2O_3S$ [M+H]+ : 343.1111; found: 343.1025.



Bromooxindole 35. LiHMDS (429 mg, 2.57 mmol, 2.5 equiv) was dissolved in THF (5 mL). The solution was cooled to –78 ºC and a solution of oxindole **SI-1-11** (352 mg, 1.03 mmol, 1.0 equiv) in THF (20 mL) was added dropwise over 20 min. The reaction mixture was stirred at –78 ºC for 20 min and transferred to a pre-cooled solution of *N*-bromosuccinimide (457 mg, 2.57 mmol, 2.5 equiv) in THF (10 mL) that was protected from light. The resulting reaction mixture was placed in a –40 ºC bath for 1h, while being protected from light, and then quenched with sat. NH_4Cl. The reaction mixture was allowed to warm to ambient temperature, diluted with brine (100 mL) and extracted with EtOAc (3 x 70 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated to afford a yellow oil, which was purified by silica gel chromatography (2:1 hexanes:EtOAc) to afford bromooxindole **35** (334 mg, 76% yield) as a yellow solid.

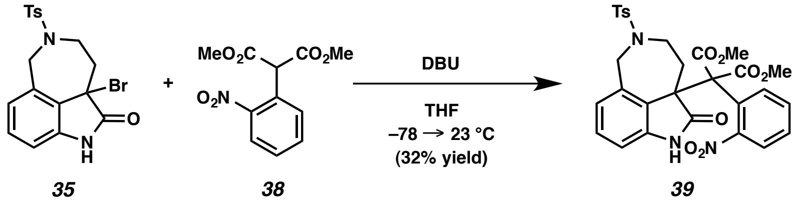
R_f = 0.40 (1:1 hexane:EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ 8.49 (br, s, 1H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.24–7.19 (m, 3H), 6.96 (d, *J* = 7.7 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 4.76 (d, *J* = 15.4 Hz, 1H), 4.32 (m, 2H), 3.80 (t, *J* = 13.2 Hz, 1H), 2.39 (s, 3H), 2.33 (m, 1H), 1.90 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.1, 143.5, 139.0, 137.7, 136.9, 130.7, 129.7, 128.7, 126.9, 122.6, 110.1, 59.2, 51.6, 48.3, 35.2, 21.5; IR (Neat Film NaCl) 3313, 2930, 1734, 1615, 1460, 1334, 1155, 1096, 727 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{18}H_{18}BrN_2O_3S$ $[M+H]^+$: 421.0216; found: 421.0213.



Nitrile 37. A solution of bromooxindole **35** (44.9 mg, 0.107 mmol, 1.0 equiv) and 2-nitrophenylacetonitrile **36** (34.6 mg, 0.213 mmol, 2.0 equiv) in THF (3 mL) was cooled to –78 °C. DBU (64 μL, 0.426 mmol, 4.0 equiv) was added dropwise. The reaction mixture was then allowed to gradually warm to ambient temperature. After 8 h, the reaction mixture was quenched with sat. NH_4Cl (10 mL) and the mixture was extracted with EtOAc (4 x 5 mL). The combined organic extracts were dried over $MgSO_4$ and

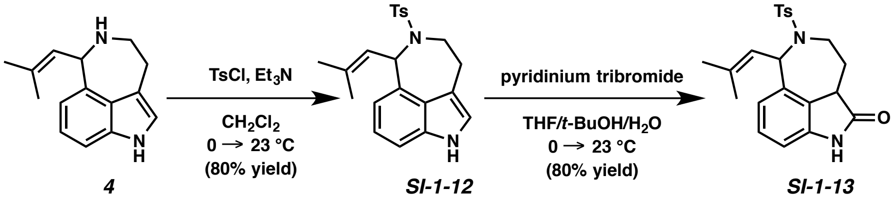
concentrated under reduced pressure to afford a brown oil, which was purified by preparatory thin layer chromatography on silica gel (1:1 hexane:EtOAc x2 elutions) to afford nitrile **37** (34.8 mg, 64% yield) as an orange-yellow solid.

R_f = 0.28 (1:1 hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (m, 1H), 7.63 (m, 2H), 7.55 (m, 2H), 7.43 (m, 2H), 7.29 (d, *J* = 8.0 H, 2H), 7.18 (t, *J* = 7.8 Hz, 1H), 6.97 (d, *J* = 7.7 Hz, 1H), 6.48 (d, *J* = 7.4 Hz, 1H), 6.07 (s, 1H), 4.80 (d, *J* = 16.2 Hz, 1H), 4.29 (m, 2H), 3.45 (app. t, *J* = 13.2 Hz, 1H), 2.74 (app. dd, *J* = 15.0, 2.6 Hz, 1H), 2.43 (s, 3H), 1.94 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2, 147.9, 143.8, 140.3, 137.9, 136.5, 133.5, 132.5, 131.0, 130.3, 130.0, 127.0, 124.8, 124.5, 124.5, 123.7, 116.2, 109.4, 54.4, 52.6, 46.8, 34.2, 32.1, 21.6; IR (Neat Film NaCl) 3302, 2920, 1724, 1527, 1155, 724 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{26}H_{23}N_4O_5S$ [M+H]$^+$: 503.1384; found: 503.1411.



Aryl malonate 39. To a solution of bromooxindole **35** (50.0 mg, 0.119 mmol, 1.0 equiv) and malonate **38** (90.1 mg, 0.356 mmol, 3.0 equiv) in THF (0.6 mL) was added DBU (54.2 mg, 0.356 mmol, 3.0 equiv) at –78 °C. The reaction solution was slowly warmed to 23 °C. The reaction solution was stirred for 12 h, and quenched with sat. NH_4Cl. The mixture was extracted with EtOAc (3 x 1 mL) and brine. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure and then the residue was purified by preparatory thin layer chromatography on silica gel (1:1 hexane:EtOAc) to afford nitrile **39** (23 mg, 32% yield).

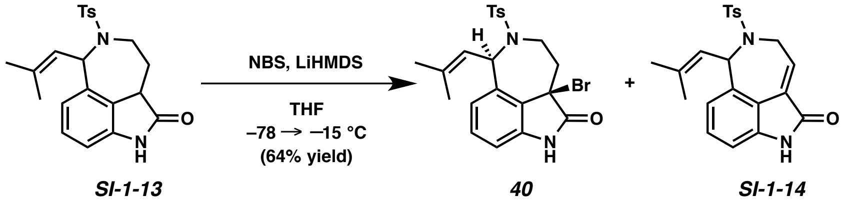
R_f = 0.15 (1:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.85 (br, s, 1H), 8.23 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.58–7.51 (m, 5H), 7.24 (d, *J* = 8.0 Hz, 2H), 6.96 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.76 (d, *J* = 1.5 Hz, 1H), 6.66 (d, *J* = 1.0 Hz, 1H), 4.44 (d, *J* = 15.4 Hz, 1H), 4.15 (d, *J* = 15.4 Hz, 1H), 3.95 (d, *J* = 14.6 Hz, 1H), 3.82 (s, 3H), 3.75 (s, 3H), 3.69 (m, 1H), 2.40 (s, 3H), 1.95 (d, *J* = 14.6 Hz, 1H), 1.66 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.1, 168.8, 148.1, 143.4, 141.2, 138.7, 137.0, 134.7, 133.9, 132.0, 129.7, 129.1, 128.3, 126.8, 125.7, 122.8, 110.7, 74.8, 68.7, 53.7, 53.5, 51.3, 46.0, 33.4, 21.5; IR (Neat Film NaCl) 3313, 1737, 1623, 1530, 1450, 1347, 1241, 1153, 1091, 895, 729 cm^{-1}; HRMS (FAB) *m/z* calc'd for $C_{29}H_{26}N_3O_9S$ $[M-H]^-$: 592.1395; found: 592.1382.



Oxindole SI-1-13. To a solution of aurantioclavine **4** (300 mg, 0.00133 mol, 1.0 equiv) and Et_3N (0.37 mL, 0.00265 mol, 2.0 equiv) in CH_2Cl_2 (4 mL) cooled to 0 °C was added a solution of TsCl (254 mg, 0.00133 mmol, 1.0 equiv) in CH_2Cl_2 (3 mL) dropwise. The ice bath was removed and the reaction mixture was stirred for 5 h, then diluted with EtOAc (200 mL) and washed with 0.5 N HCl (2 x 35 mL) and brine. The organic layers were combined, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (2:1 hexanes:EtOAc) to afford indole **SI-1-12** (405 mg, 80% yield).

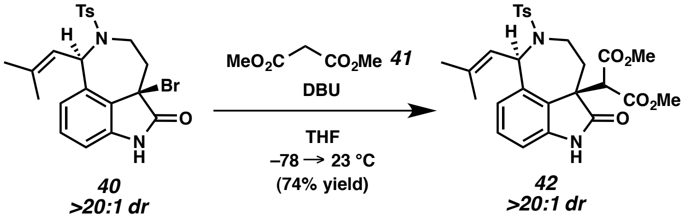
A solution of indole **SI-1-12** (902.2 mg, 2.371 mmol, 1.0 equiv) in THF/*t*-BuOH/H_2O (10:10:1 v/v/v, 52.5 mL) was cooled to 0 ºC and pyridinium tribromide (834.2 mg, 2.608 mmol, 1.1 equiv) was added in small portions over 5 min. The reaction mixture was stirred at 0 ºC for 15 min, and then allowed to warm to ambient temperature. After 5 min at ambient temperature, the reaction mixture was quenched by addition of 1:1 v/v sat. $NaHCO_3$:1M aq $Na_2S_2O_3$ (15 mL), poured into brine (150 mL) and extracted with EtOAc (3 x 100 mL). The combined extracts were dried over Na_2SO_4 and concentrated under reduced pressure to afford a brown solid, which was purified by silica gel chromatography (2:1 → 1:1 hexanes:EtOAc) to afford oxindole **SI-1-13** (747.5 mg, 80% yield).

R_f = 0.22 (5:1 benzene:MeCN); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (br, s, 1H), 7.33 (dd, *J* = 8.5, 2.1 Hz, 2H), 7.03 (m, 1H), 6.96 (d, *J* = 7.2 Hz, 2H), 6.82 (d, *J* = 7.7 Hz, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 5.76 (d, *J* = 8.0 Hz, 1H), 5.31 (m, 1H), 4.00 (dt, *J* = 15.7, 2.8 Hz, 1H), 3.64–3.50 (m, 2H), 2.22 (s, 3H), 2.00 (m, 1H), 1.67 (s, 3H), 1.65 (s, 3H), 1.25 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.4, 142.9, 140.9, 140.5, 138.2, 129.2, 128.3, 128.3, 127.0, 126.7, 121.3, 119.0, 108.7, 59.0, 46.0, 43.8, 27.8, 26.0, 21.4, 18.5; IR (Neat Film NaCl) 3246, 2925, 1713, 1615, 1460, 1326, 1155, 732 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{22}H_{25}N_2O_3S$ $[M+H]^+$: 397.1580; found: 397.1586.



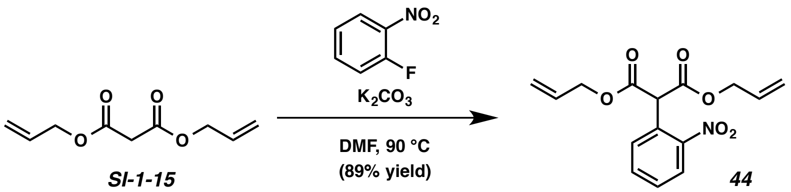
Bromooxindole 40. A solution of oxindole **SI-1-13** (172.0 mg, 0.434 mmol, 1.0 equiv) in THF (5 mL) was added dropwise to a freshly prepared solution of LiHMDS (217.8 mg, 1.301 mmol, 3.0 equiv) in THF (5 mL) that had been pre-cooled to –78 ºC. After 20 min at –78 ºC, the resulting solution was transferred via cannula to a solution of *N*-bromosuccinimide (231.6 mg, 1.301 mmol, 3.0 equiv) in THF (5 mL) that had been pre-cooled to –78 ºC. The resulting yellow reaction mixture was allowed to warm to –15 ºC (the reaction flask was transferred to a bath composed of ethylene glycol and dry ice) and maintained at this temperature for 2 h. The reaction mixture was then cooled to –78 ºC and quenched by addition of sat. NH_4Cl (5 mL). The yellow reaction mixture was allowed to warm to ambient temperature and diluted with H_2O (80 mL), then extracted with EtOAc (3 x 70 mL). The combined organic extracts were washed with brine (100 mL), dried over $MgSO_4$ and concentrated under reduced pressure to afford a yellow oil, which was purified immediately by silica gel chromatography (2:1 hexanes:EtOAc) to afford a 3:1 mixture of bromooxindole **40** (>20:1 dr) and dehydrobromination product **SI-1-14** (131.1 mg, 64% combined yield, 50% yield of bromooxindole **40**). Bromooxindole **40** was stored frozen in benzene and used without further purification. The relative configuration of this bromooxindole was assigned based on the stereochemistry of the malonate adduct obtained (see below). Quenching the reaction prior to completion afforded the bromooxindole **40** as a single diastereomer, which showed greater stability, and could be fully characterized.

R_f = 0.50 (1:1 hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (br, s, 1H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.21 (t, *J* = 8.0, 1H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 7.5 Hz, 1H), 6.79 (dd, *J* = 8.0, 1.0 Hz, 1H), 5.96 (td, *J* = 8.5, 1.5 Hz, 1H), 5.88 (d, *J* = 8.5 Hz, 1H), 4.18–4.02 (m, 2H), 2.35 (s, 3H), 2.27 (m, 1H), 1.97 (m, 1H), 1.76 (d, *J* = 1.0 Hz, 3H), 1.75 (d, *J* = 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 143.2, 142.4, 140.2, 139.2, 137.8, 130.8, 129.4, 126.9, 126.1, 122.7, 120.1, 109.7, 66.8, 59.5, 39.8, 34.4, 26.1, 21.4, 18.4; IR (Neat Film NaCl) 3291, 1734, 1617, 1602, 1457, 1326, 1156, 1092, 738 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{22}H_{23}BrN_2O_3S$ $[M+H]^+$: 475.0686; found: 475.0668.



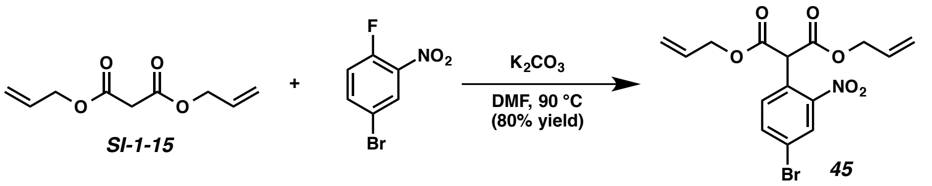
Malonate 42. Bromooxindole **40** (>20:1 dr, 51.3 mg, 0.108 mmol, 1.0 equiv) was dissolved in THF (2 mL). Dimethyl malonate **41** (37 μL, 0.324 mmol, 3.0 equiv) was added and the reaction mixture was cooled to –78 °C. DBU (48 μL, 0.324 mmol, 3.0 equiv) was added dropwise. The reaction mixture was stirred at –78 °C for 15 min and then warmed to 23 °C. After maintaining the reaction mixture at 23 °C for 6 h, sat. NH_4Cl (2 mL) was added and the reaction mixture was warmed to ambient temperature. The reaction mixture was diluted with EtOAc (50 mL) and sat. NH_4Cl (50 mL). The phases were separated and the aqueous phase was extracted with EtOAc (2 x 50 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated to afford colorless oil. Analysis of the crude oil by ^{1}H NMR indicated >20:1 dr of the malonate adduct **42**. The residue was purified by silica gel chromatography (1:1 hexane:EtOAc) to afford malonate **42** (42 mg, 74% yield).

R_f = 0.20 (1:1 hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (br, s, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 2H), 6.91, (d, *J* = 7.5 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 5.92 (d, *J* = 4.5 Hz, 1H), 5.38 (d, *J* = 4.5 Hz, 1H), 4.62 (s, 1H), 4.06 (m, 1H), 3.89 (m, 1H), 3.78 (s, 3H), 3.46 (s, 3H), 2.40 (m, 1H), 2.30 (s, 3H), 1.82 (s, 3H), 1.79 (s, 3H), 1.07 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.8, 166.8, 166.8, 143.0, 141.9, 141.4, 141.0, 137.9, 129.2, 128.9, 127.6, 127.0, 123.0, 124.0, 109.0, 59.6, 53.9, 52.9, 52.3, 51.3, 39.8, 28.9, 26.4, 21.4, 18.6; IR (Neat Film NaCl) 3338, 2953, 1733, 1618, 1597, 1458, 1327, 1158 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{27}H_{31}N_2O_7S$ $[M+H]^+$: 527.1846; found: 527.1848.



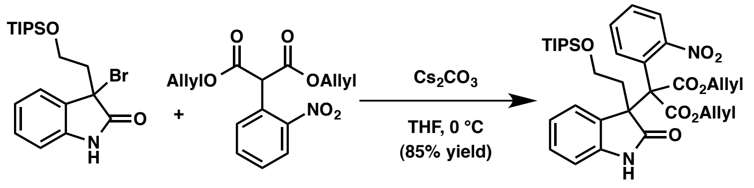
Diallyl 2-(2-nitrophenyl)malonate 44. A 500 mL round-bottom flask with a magnetic stir bar was charged with diallyl malonate **SI-1-15** (22.0 g, 118 mmol, 1.0 equiv), 1-fluoro-2-nitrobenzene (13.7 mL, 129 mmol, 1.1 equiv), and K_2CO_3 (48.9 g, 354 mmol, 3.0 equiv). DMF (120 mL) was added and the brown suspension was heated to 90 ºC for 16 h. The reaction mixture was cooled to ambient temperature and diluted with ice water (250 mL) and Et_2O (300 mL). The aqueous phase was extracted with Et_2O (3 x 300 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography (9:1 hexanes:EtOAc) on silica gel to give arylated malonate **44** (32.1 g, 89% yield).

R_f = 0.51 (1:1 hexane:Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.66 (td, *J* = 7.6, 1.4 Hz, 1H), 7.55–7.51 (m, 2H), 5.90 (ddt, *J* = 17.3, 10.4, 5.7 Hz, 2H), 5.39-5.23 (m, 5H), 4.70 (dt, *J* = 5.8, 1.4 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.8, 148.7, 133.6, 131.4, 131.1, 129.3, 127.9, 125.3, 119.1, 66.8, 54.3; IR (Neat Film NaCl) 3086, 2950, 1738, 1611, 1530, 1447, 1350, 1154, 991, 937, 852, 787, 722 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{15}H_{16}NO_6$ [M+H]$^+$: 306.0972; found: 306.0930.



Diallyl 2-(4-bromo-2-nitrophenyl)malonate 45. A 500 mL round-bottom flask with a magnetic stir bar was charged with diallyl malonate **SI-1-15** (15.0 g, 81.5 mmol, 1.0 equiv), 4-bromo-1-fluoro-2-nitrobenzene (11.0 mL, 89.7 mmol, 1.1 equiv), and K_2CO_3 (33.8 g, 245 mmol, 3.0 equiv). DMF (163 mL) was added and the brown suspension was heated to 90 °C for 16 h. The reaction mixture was cooled to ambient temperature and diluted with ice water (250 mL) and Et_2O (300 mL). The aqueous phase was extracted with Et_2O (3 x 300 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography (9:1 hexanes:EtOAc) on silica gel to give arylated malonate **45** (32.1 g, 80% yield).

R_f = 0.69 (1:1 hexane:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 2.1 Hz, 1H), 7.77 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 5.94–5.84 (m, 2H), 5.37–5.24 (m, 5H), 4.70 (dt, *J* = 5.9, 1.3 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 149.1, 136.5, 132.8, 131.0, 128.2, 126.8, 122.8, 119.3, 66.9, 53.8; IR (Neat Film NaCl) 3085, 2986, 2951, 1733, 1649, 1538, 1348, 1283, 1218, 1148, 989, 936 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{15}H_{15}BrNO_6$ [M+H]$^+$: 384.0077; found: 384.0072.

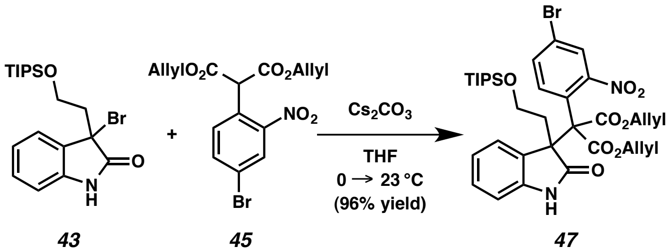


43 44 46

Oxindole 46. To a suspension of Cs_2CO_3 (5.37 g, 16.5 mmol, 3.0 equiv) and bromooxindole **43** (2.27 g, 5.50 mmol, 1.0 equiv) in THF (100 mL) was added malonate **44** (5.04 g, 16.5 mmol, 3.0 equiv) at 0 °C. The reaction mixture was then allowed to slowly warm to 23 ºC and stirred for 16 h. Solids were removed via a filtration through a celite plug (rinsed with EtOAc) and the resulting purple solution was concentrated under reduced pressure. The residue was purified by column chromatography using a Teledyne Isco CombiFlash (SiO_2, 120 g column, 100:0 → 3:1 hexanes:EtOAc) to provide alkylation product **46** (8.9 g, 85% yield) as a colorless oil.

R_f = 0.18 (3:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.0 Hz, 1H), 7.94 (s, 1H), 7.73 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.41 (dt, *J* = 8.0, 1.6 Hz, 1H), 7.38– 7.33 (m, 2H), 7.13 (dt, *J* = 7.7, 1.1 Hz, 1H), 6.89 (dt, *J* = 7.7, 1.0 Hz, 1H), 6.72 (d, *J* = 7.6 Hz, 1H), 5.88–5.73 (m, 2H), 5.25 (ddd, *J* = 17.2, 2.8, 1.4 Hz, 1H), 5.19–5.11 (m, 3H), 4.69 (tdd, *J* = 13.3, 5.7, 1.4 Hz, 1H), 4.64 (tdd, *J* = 13.3, 5.7, 1.3 Hz, 1H), 4.57 (tdd, *J* = 13.4, 5.9, 1.4 Hz, 1H), 4.48 (tdd, *J* = 13.1, 5.9, 1.1 Hz, 1H), 3.35 (ddd, *J* = 9.5, 8.5, 6.9 Hz, 1H), 3.07 (dt, *J* = 9.5, 4.5 Hz, 1H), 2.95 (ddd, *J* = 12.9, 8.7, 7.0 Hz, 1H), 2.63 (ddd, *J* =

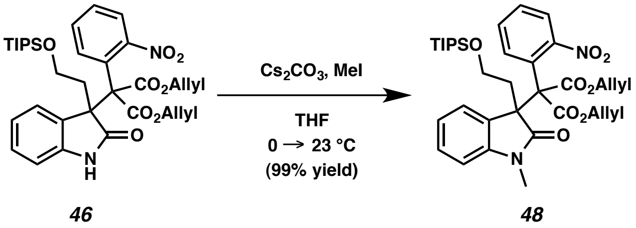
12.9, 8.5, 4.5 Hz, 1H), 0.97–0.77 (m, 21H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 177.8, 166.7, 166.3, 150.2, 140.7, 132.4, 131.3, 131.0, 130.8, 129.5, 129.2, 128.5, 126.9, 125.3, 122.4, 119.2, 118.4, 109.1, 66.8, 66.7, 59.5, 56.7, 38.3, 17.8, 11.8; IR (Neat Film NaCl) 3332, 2942, 1714, 1649, 1618, 1538, 1471, 1356, 1230, 1114, 995, 933, 885, 850, 752, 683 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{34}H_{45}N_2O_8Si$ [M+H]$^+$: 637.2940; found: 637.2945.



Oxindole 47. To a solution of 3-bromooxindole **43** (2.0 g, 4.85 mmol, 1.0 equiv) and malonate **45** (3.7 g, 9.70 mmol, 2.0 equiv) in THF (49 mL) was added Cs_2CO_3 (3.2 g, 9.70 mmol, 2.0 equiv) at 0 ºC. The reaction mixture was warmed to 23 ºC and stirred overnight. Solids were removed via a filtration through a celite plug and the resulting solution was concentrated under reduced pressure. The residue was purified by flash column chromatography (9:1 → 4:1 hexanes:EtOAc) on silica gel to give desired alkylated product **47** (3.3g, 96% yield).

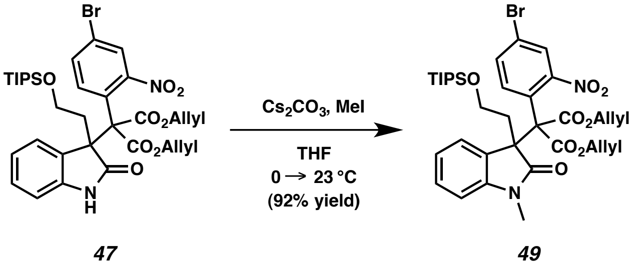
R_f = 0.33 (4:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.00 (br, s, 1H), 7.95 (d, *J* = 8.9 Hz, 1H), 7.86 (d, *J* = 2.3 Hz, 1H), 7.53 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.43–7.39 (m, 1H), 7.16 (td, *J* = 7.7, 1.2 Hz, 1H), 6.92 (td, *J* = 7.7, 1.1 Hz, 1H), 6.75–6.72 (m, 1H), 5.79 (dddt, *J* = 33.6, 17.2, 10.4, 5.9 Hz, 2H), 5.26–5.18 (m, 2H), 5.19–5.14 (m, 2H), 4.66 (qdt, *J* = 13.2, 5.9, 1.4 Hz, 2H), 4.55–4.42 (m, 2H), 3.32 (dt, *J* = 9.7, 7.5 Hz, 1H), 3.09 (ddd, *J*

= 9.8, 8.5, 4.5 Hz, 1H), 2.89–2.82 (m, 1H), 2.63 (ddd, J = 12.7, 8.1, 4.5 Hz, 1H), 0.89 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.0, 166.6, 166.2, 150.9, 140.9, 134.3, 134.1, 131.3, 130.8, 129.0, 129.0, 128.6, 128.3, 127.2, 122.7, 122.2, 119.6, 119.0, 109.5, 67.2, 67.1, 66.9, 59.7, 57.0, 38.4, 18.0, 11.9; IR (Neat Film NaCl) 3203, 2943, 2865, 1716, 1619, 1538, 1471, 1357, 1229, 1111, 992, 935, 753, 735 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{34}H_{44}BrN_2O_8Si$ [M+H]$^+$: 715.2045; found: 715.2090.



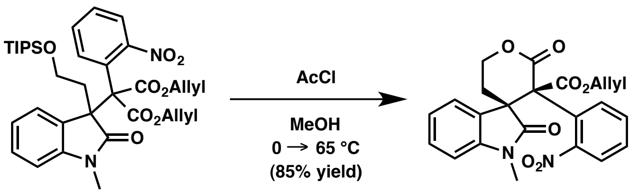
Methyloxindole 48. To a suspension of oxindole **46** (0.50 g, 0.79 mmol, 1.0 equiv) and Cs_2CO_3 (0.77 g, 2.37 mmol, 3.0 equiv) in THF (4.0 mL) was added methyl iodide (0.3 mL, 4.7 mmol, 6.0 equiv) at 0 °C. The reaction mixture was stirred for 12 h at 23 °C. After the reaction was done, sat. NH_4Cl was added. The aqueous phase was extracted with EtOAc (3 x 3 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (3:1 hexanes:EtOAc) to give methylated oxindole **48** (0.51g, 99% yield).

R_f = 0.33 (3:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 8.0 Hz, 1H), 7.54 (dd, J = 7.9, 1.5 Hz, 1H), 7.42 (d, J = 7.6 Hz, 1H), 7.31 (dt, J = 7.7, 1.6 Hz, 1H), 7.25 (dt, J = 7.8, 1.2 Hz, 1H), 7.10 (dt, J = 7.7, 0.9 Hz, 1H), 6.85 (dt, J = 7.8, 0.8 Hz, 1H), 6.57 (d, J = 7.7 Hz, 1H), 5.80 (tdd, J = 16.3, 10.7, 5.8 Hz, 1H), 5.71 (tdd, J = 16.4, 10.5, 5.9 Hz, 1H), 5.22–5.02 (m, 4H), 4.69–4.56 (m, 2H), 4.52 (tdd, *J* = 13.1, 5.8, 1.3 Hz, 1H), 4.36 (tdd, *J* = 13.3, 5.9, 1.3 Hz, 1H), 3.15–3.02 (m, 4H), 2.96 (ddd, *J* = 9.7, 8.3, 4.7 Hz, 1H), 2.85 (td, *J* = 13.2, 7.4 Hz, 1H), 2.67 (ddd, *J* = 12.8, 8.0, 4.7 Hz, 1H), 0.86–0.71 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.3, 166.5, 166.5, 150.3, 143.6, 132.7, 131.3, 130.9, 130.3, 128.8, 128.5, 128.5, 128.3, 126.9, 125.1, 122.3, 119.1, 118.5, 107.3, 66.7, 66.7, 59.6, 56.8, 37.9, 26.1, 17.8, 11.7; IR (Neat Film NaCl) 3421, 3054, 2944, 2866, 1723, 1613, 1539, 1473, 1356, 1253, 1180, 1104, 1068, 935, 862, 840, 752, 690 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{35}H_{47}N_2O_8Si$ $[M+H]^+$: 651.3096; found: 651.3184.



Methyloxindole 49. To a solution of oxindole **47** (14.1 g, 0.0197 mol, 1.0 equiv) in THF (106 mL) was added Cs_2CO_3 (19.3 g, 0.0591 mol, 3.0 equiv) and MeI (7.40 mL, 0.118 mol, 6.0 equiv) at 0 ºC. Then, the reaction mixture was stirred for 12 h at 23 ºC. After the reaction was done, sat. NH_4Cl was added. The aqueous phase was extracted with EtOAc (3 x 100 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography (7:1 hexanes:EtOAc) on silica gel to give methylated oxindole **49** (13.2 g, 92% yield).

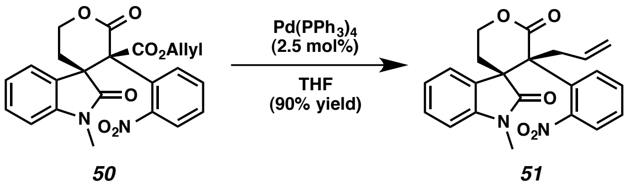
R_f = 0.40 (4:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.89 (d, *J* = 8.9 Hz, 1H), 7.76 (d, *J* = 2.3 Hz, 1H), 7.53–7.48 (m, 2H), 7.21 (td, *J* = 7.7, 1.2 Hz, 1H), 6.95 (td, *J* = 7.6, 1.1 Hz, 1H), 6.69–6.66 (m, 1H), 5.85 (ddt, *J* = 17.2, 10.4, 5.9 Hz, 1H), 5.74 (ddt, *J* = 17.2, 10.4, 5.9 Hz, 1H), 5.26–5.20 (m, 2H), 5.18 (ddt, *J* = 10.4, 2.2, 1.2 Hz, 2H), 4.72–4.63 (m, 2H), 4.54 (ddt, *J* = 13.1, 6.0, 1.4 Hz, 1H), 4.40 (ddt, *J* = 13.0, 6.0, 1.3 Hz, 1H), 3.18–3.13 (m, 1H), 3.13 (s, 3H), 3.05 (ddd, *J* = 9.9, 7.9, 4.7 Hz, 1H), 2.82 (dt, *J* = 13.0, 7.6 Hz, 1H), 2.71 (ddd, *J* = 12.8, 7.6, 4.7 Hz, 1H), 0.90–0.84 (m, 21H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 176.3, 166.3, 166.2, 150.8, 143.7, 134.4, 133.4, 131.1, 130.8, 128.8, 128.1, 128.0, 127.0, 122.5, 122.1, 119.4, 119.0, 107.6, 67.0, 66.9, 66.9, 59.6, 56.8, 37.9, 26.3, 17.8, 17.8, 11.8; IR (Neat Film NaCl) 2943, 2865, 1747, 1713, 1611, 1538, 1471, 1357, 1223, 1103, 993, 935, 882, 752 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{35}H_{46}BrN_2O_8Si$ [M+H]$^+$: 729.2201; found: 729.2253.



48 50

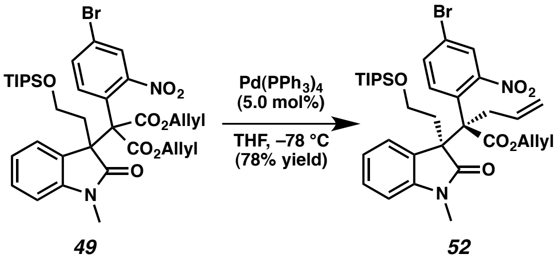
Lactone 50. Acetyl chloride (46.0 μL, 650 μmol, 10.0 equiv) was added to MeOH (1.0 mL) and cooled to 0 °C. The resulting mixture was stirred for 30 min and then the solution of oxindole **48** (21.0 mg, 32.0 μmol, 1.0 equiv) in MeOH (2.0 mL) was added. The reaction was stirred for 2 h at 23 ºC and then heated to 65 °C. The reaction mixture was stirred for 16 h at that temperature. The colorless solution was cooled to ambient temperature, concentrated under reduced pressure and subjected to column chromatography (4:1 hexanes:EtOAc) to afford the desired lactone **50** (12 mg, 85% yield) as a colorless solid.

R$_f$ = 0.29 (50% EtOAc in hexanes); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.80 (d, *J* = 7.4 Hz, 1H), 7.39–7.31 (m, 3H), 7.23–7.15 (m, 2H), 6.82–6.75 (m, 2H), 5.92 (tdd, *J* = 17.1, 10.6, 5.8 Hz, 1H), 5.30 (ddd, *J* = 17.2, 2.7, 1.3 Hz, 1H), 5.21 (ddd, *J* = 10.4, 2.4, 1.2 Hz, 1H), 4.98–4.90 (m, 2H), 4.74 (tdd, *J* = 13.1, 5.8, 1.3 Hz, 1H), 4.71–4.64 (m, 2H), 3.32 (s, 3H), 2.84–2.70 (m, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ 175.8, 166.5, 165.7, 149.2, 142.2, 131.7, 131.4, 131.1, 128.8, 129.7, 129.3, 129.0, 128.9, 125.6, 124.8, 122.5, 118.9, 108.5, 67.5, 65.4, 53.7, 30.2, 26.7; IR (Neat Film NaCl) 2096, 1718, 1637, 1533, 1475, 1358, 1232, 1184, 760 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{23}H_{21}N_2O_7$ [M+H]$^+$: 437.1343; found: 437.1298.



Lactone 51. An oven dried flask was charged with ester **50** (1.3 g, 3.05 mmol, 1.0 equiv), sealed with a rubber stopper and evacuated. The flask was brought in a glove box and Pd(PPh$_3$)$_4$ (84 mg, 75.0 μmol, 0.025 equiv) was added. The flask was brought out of the dry box and THF (60 mL) was added. The reaction mixture was stirred for 5 min and concentrated under reduced pressure. Column chromatography using a Teledyne Isco CombiFlash R$_f$ (SiO$_2$, 80 g column, 25→50% EtOAc in hexanes) afforded the desired protected alkylation product **51** (1.1 g, 90% yield) as a colorless solid.

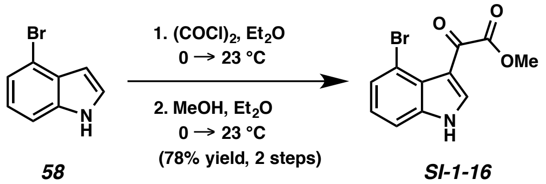
R$_f$ = 0.40 (1:1 hexane:EtOAc); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.63 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.18 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.12 (dt, *J* = 7.5, 1.7 Hz, 1H), 7.07 (dt, *J* = 7.7, 1.1 Hz, 1H), 7.00 (d, *J* = 7.7 Hz, 1H), 6.85 (dd, *J* = 8.0, 1.3 Hz, 1H), 6.68 (d, *J* = 7.7 Hz, 1H), 6.64 (dt, *J* = 7.7, 1.0 Hz, 1H), 5.55 (tdd, *J* = 17.0, 10.2, 6.7 Hz, 1H), 5.33 (ddd, *J* = 11.6, 10.0, 3.4 Hz, 1H), 5.01 (ddd, *J* = 17.1, 3.0, 1.5 Hz, 1H), 4.93 (ddd, *J* = 10.3, 2.7, 1.2 Hz, 1H), 4.68 (td, *J* = 11.6, 4.7 Hz, 1H), 3.45 (tdd, *J* = 15.6, 6.6, 1.3 Hz, 1H), 3.26 (s, 3H), 2.99 (tdd, *J* = 9.0, 6.9, 1.3 Hz, 1H), 2.87 (ddd, *J* = 14.6, 10.0, 4.6 Hz, 1H), 2.21 (ddd, *J* = 14.7, 4.8, 3.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 177.3, 168.5, 149.8, 142.1, 133.9, 133.1, 131.1, 130.6, 130.4, 128.6, 127.8, 125.7, 124.8, 122.2, 119.0, 107.6, 64.8, 54.2, 54.0, 43.7, 30.7, 26.5; IR (Neat Film NaCl) 1701, 1614, 1531, 1473, 1356, 1300, 1259, 1202, 1105, 929, 739 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{22}H_{21}N_2O_5$ [M+H]$^+$: 393.1445; found: 393.1458.



Allyl 52. To a 500 mL round-bottom flask with a magnetic stir bar was added malonate **49** (11.1 g, 15.2 mmol, 1.0 equiv). The flask was brought into a N_2-filled glove box and then $Pd(PPh_3)_4$ (0.88 g, 0.761 mol, 0.05 equiv) was added. The reaction mixture was brought out from the glove box and treated with THF (152 mL). After 1 h stirring, the solvent was evaporated under reduced pressure. The residue was purified by column

chromatography (1:1 hexane:EtOAc) on silica gel to afford allylated product **52** (8.1 g, 78% yield).

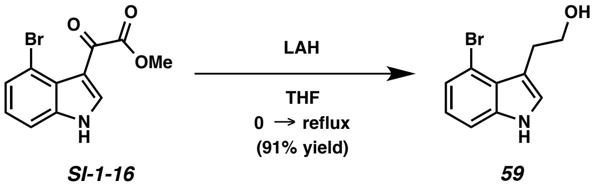
R_f = 0.45 (4:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.7 Hz, 1H), 7.97 (d, *J* = 2.3 Hz, 1H), 7.80 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.22 (td, *J* = 7.7, 1.1 Hz, 1H), 6.83–6.77 (m, 2H), 6.33 (d, *J* = 7.5 Hz, 1H), 5.66 (ddt, *J* = 16.9, 10.3, 6.2 Hz, 1H), 5.56 (ddt, *J* = 17.0, 10.1, 6.9 Hz, 1H), 5.16–5.09 (m, 2H), 4.91 (dq, *J* = 17.1, 1.5 Hz, 1H), 4.84 (ddd, *J* = 10.2, 1.9, 1.1 Hz, 1H), 4.38–4.26 (m, 2H), 3.37 (dd, *J* = 15.3, 7.0 Hz, 1H), 3.23 (s, 3H), 3.21–3.10 (m, 2H), 2.90 (ddd, *J* = 9.5, 8.5, 4.2 Hz, 1H), 2.59–2.51 (m, 1H), 2.16 (ddd, *J* = 12.5, 8.1, 4.3 Hz, 1H), 0.92–0.80 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.7, 169.6, 152.1, 144.3, 134.8, 134.5, 133.7, 131.3, 131.1, 128.9, 128.8, 128.70, 125.13, 121.9, 121.8, 119.5, 118.2, 108.1, 65.7, 60.7, 59.5, 55.5, 39.0, 36.6, 26.5, 18.0, 11.9; IR (Neat Film NaCl) 2942, 2865, 1713, 1610, 1538, 1495, 1471, 1353, 1106, 995, 918, 882, 750, 732 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{34}H_{46}BrN_2O_6Si$ $[M+H]^+$: 685.2303; found: 685.2294.



Oxoacetate SI-1-16. To a solution of 4-bromoindole **58** (8.0 g, 40.8 mmol, 1.0 equiv) in Et_2O (204 mL) was added oxalyl chloride (9.25 mL, 102 mmol, 2.5 equiv) dropwise at 0 °C. The reaction mixture was stirred for 16 h at 23 °C. The resulting suspension was filtered and washed with cold ether. The filter cake was dried *in vacuo* to afford the oxoacetyl chloride, which was used without further purification.

To a solution of oxoacetyl chloride in Et_2O (204 mL) was added MeOH (10 mL) at 0 ºC, and stirred for 2 h. The resulting mixture was concentrated *in vacuo* and purified by flash column chromatography (4:1 hexanes:EtOAc) on silica gel to give oxoacetate **SI-1-16** (9.0 g, 78% yield, 2 steps).

$R_f = 0.23$ (1:1 hexane:EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ 9.01 (br, s, 1H), 8.27 (d, J = 3.2 Hz, 1H), 7.52 (dd, J = 7.6, 0.8 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.16 (t, J = 7.8Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.3, 164.0, 137.8, 136.2, 128.3, 125.3, 125.2, 115.3, 115.0, 111.0, 53.0; IR (Neat Film NaCl) 3206, 1656, 1500, 1410, 1306, 1252, 1196, 1139, 1104, 789, 770, 731 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{11}H_9BrNO_3$ $[M+H]^+$: 281.9760; found: 281.9760.



Alcohol 59. To a solution of oxoacetate **SI-1-16** (6.8 g, 24.1 mmol, 1.0 equiv) in THF (120 mL) was added LAH (2.8 g, 72.3 mmol, 3.0 equiv) in portions at 0 ºC. The reaction mixture was refluxed for 4 h. When the reaction was done, the solution was cooled to 0 ºC, and quenched by Fieser work-up[2]. The suspension was filtered and the filter cake was washed with EtOAc. The combined organic phases were concentrated *in vacuo*, and extracted with EtOAc (3 x 100 mL). The combined organic layer was washed with brine,

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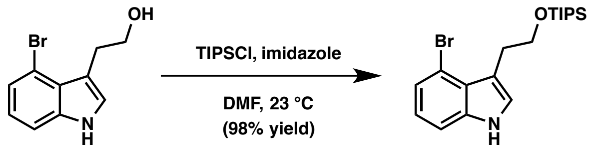
[2] Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis* **1967**, 581-595.

dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography (1:1 hexane:EtOAc) on silica gel to give alcohol **59** (5.3 g, 91% yield).

R_f = 0.27 (1:1 hexane:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (br, s, 1H), 7.31 (dd, J = 7.6, 0.8 Hz, 1H), 7.28 (dd, J = 7.6, 0.8 Hz, 1H), 7.12 (dd, J = 2.8Hz, 1H), 7.01 (t, J = 7.8 Hz, 1H), 3.97 (t, J = 6.4 Hz, 2H), 3.28 (dt, J = 6.4, 0.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.8, 125.4, 124.1, 123.0, 114.4, 113.1, 110.6, 63.6, 29.5 ; IR (Neat Film NaCl) 3369, 2929, 1899, 1613, 1478, 1425, 1335, 1185, 1029, 913, 815, 770, 736 cm $^{-1}$; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{10}H_{11}BrNO$ $[M+H]^+$: 240.0019; found: 240.0021.

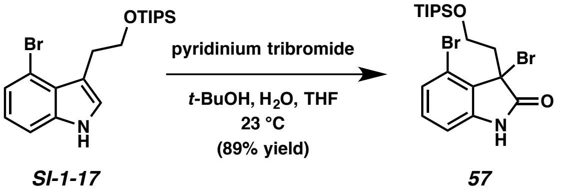


59 *SI-1-17*

TIPS-ether SI-1-17. To a solution of alcohol **59** (8.1 g, 33.7 mmol, 1.0 equiv) in DMF (112 mL) was added imidazole (5.0 g, 74.2 mmol, 2.2 equiv) and TIPSCl (10.7 mL, 50.6 mmol, 1.5 equiv). After stirring for 3 h at 23 °C, water (10 mL) was added. The aqueous phase was extracted with Et_2O (3 x 100 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography (9:1 hexanes:EtOAc) on silica gel to give TIPS-ether **SI-1-17** (13.1 g, 98% yield).

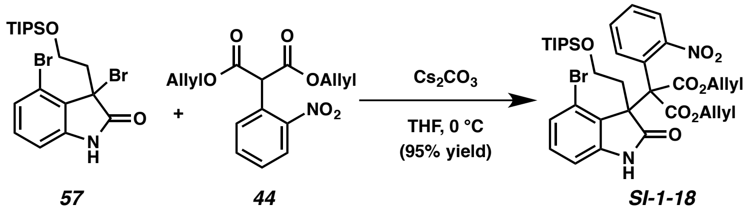
R_f = 0.56 (4:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (br, s, 1H), 7.30–7.25 (m, 2H), 7.12 (d, *J* = 2.4 Hz, 1H), 6.99 (t, *J* = 7.8 Hz, 1H), 4.00 (t, *J* = 7.1 Hz, 2H), 3.27 (t, *J* = 7.1 Hz, 2H), 1.05-1.07 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.4, 125.7, 124.4, 123.9, 122.6, 114.3, 114.1, 110.4, 64.9, 29.9, 18.1, 12.0; IR (Neat Film NaCl)

3425, 3286, 2942, 1614, 1561, 1549, 1463, 1425, 1382, 1336, 1246, 1184, 1102, 1064, 1013, 913, 883, 826, 772, 738 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{19}H_{31}BrNOSi$ $[M+H]^+$: 396.1353; found: 396.1357.



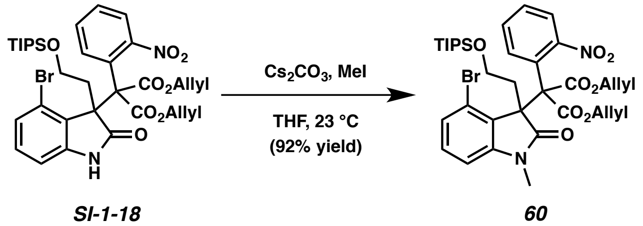
3-Bromooxindole 57. To a solution of indole **SI-1-17** (5.0 g, 12.6 mmol, 1.0 equiv) in *t*-BuOH (100 mL), THF (25 mL), and water (1.1 mL) was added pyridinium tribromide (7.9 g, 24.6 mmol, 1.95 equiv). The reaction mixture was stirred for 30 min and then diluted with EtOAc (50 mL) and water (80 mL). The aqueous phase was extracted with EtOAc (3 x 150 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography (4:1 hexanes:EtOAc) on silica gel to give 3-bromooxindole **57** (5.5 g, 89% yield).

R_f = 0.31 (4:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (br, s, 1H), 7.19 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.13 (t, *J* = 7.9 Hz, 1H), 6.86 (dd, *J* = 7.6, 1.0 Hz, 1H), 3.66 (ddd, *J* = 10.4, 5.5, 3.3 Hz, 1H), 3.46 (td, *J* = 10.5, 3.8 Hz, 1H), 3.08 (dt, *J* = 13.9, 3.5 Hz, 1H), 2.90 (ddd, *J* = 13.9, 10.6, 5.4 Hz, 1H), 0.87 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.8, 142.3, 131.2, 127.5, 127.0, 120.8, 109.5, 60.6, 56.1, 39.6, 17.8, 11.8; IR (Neat Film NaCl) 2941, 2864, 2109, 1728, 1613, 1583, 1312, 1102, 882, 744 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{19}H_{30}Br_2NO_2Si$ $[M+H]^+$: 490.0407; found: 490.0340.



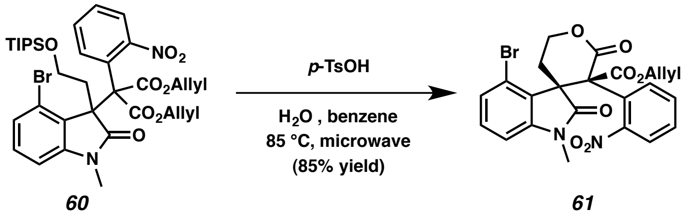
Oxindole SI-1-18. To a solution of 3-bromooxindole **57** (5.6 g, 11.4 mmol, 1.0 equiv) and malonate **44** (5.2 g, 17.1 mmol, 1.5 equiv) in THF was added Cs_2CO_3 (7.4 g, 22.8 mmol, 2.0 equiv) at 0 ºC. The reaction mixture was stirred for 1 h at 0 ºC. Solids were removed via a filtration through a celite plug and the resulting solution was concentrated under reduced pressure. The residue was purified by flash column chromatography (9:1 → 4:1 hexanes:EtOAc) on silica gel to give desired alkylated product **SI-1-18** (5.4 g, 95% yield).

R_f= 0.18 (3:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.01 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.90 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.68 (ddd, *J* = 8.5, 7.4, 1.6 Hz, 1H), 7.55 (d, *J* = 5.3 Hz, 1H), 7.51 (td, *J* = 7.7, 1.2 Hz, 1H), 7.02 (d, *J* = 7.9 Hz, 1H), 6.93 (dd, *J* = 8.1, 1.0 Hz, 1H), 6.78 (dd, *J* = 7.6, 1.0 Hz, 1H), 5.92–5.81 (m, 2H), 5.76–5.68 (m, 1H), 5.26–5.18 (m, 2H), 5.17–5.10 (m, 2H), 4.76-4.69 (m, 1H), 4.68-4.63 (m, 1H), 4.51–4.47 (m, 1H), 4.25–4.20 (m, 1H), 3.33–3.26 (m, 1H), 3.23–3.13 (m, 2H), 2.97-2.90 (m, 1H), 0.91 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.4, 167.0, 166.0, 144.4, 133.8, 131.8, 131.3, 131.1, 129.8, 129.3, 128.3, 127.5, 126.9, 126.5, 121.82, 119.6, 119.0, 118.9, 108.5, 67.6, 66.6, 66.5, 59.5, 58.3, 32.9, 17.9, 11.9; IR (Neat Film NaCl) 3350, 3086, 2943, 1732, 1612, 1574, 1531, 1446, 1354, 1228, 1169, 1104, 992, 931, 789 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{34}H_{44}BrN_2O_8Si$ $[M+H]^+$: 715.2045; found 715.2055.



Methyloxindole 60. To a solution of oxindole **SI-1-18** (5.6 g, 11.2 mmol, 1.0 equiv) in THF (56 mL) was added Cs_2CO_3 (10.9 g, 33.6 mmol, 3.0 equiv) and MeI (4.3 mL, 67.2 mmol, 6.0 equiv) at 0 ºC. Then, the reaction mixture was stirred for 12 h at 23 ºC. After the reaction was done, sat. NH_4Cl was added. The aqueous phase was extracted with EtOAc (3 x 50 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography (7:1 hexanes:EtOAc) on silica gel to give methylated oxindole **60** (7.5 g, 92% yield).

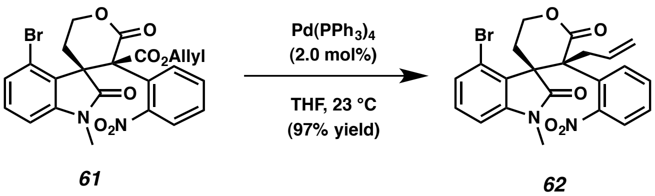
R_f = 0.38 (4:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.01 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.91 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.69 (ddd, *J* = 8.5, 7.3, 1.6 Hz, 1H), 7.54–7.50 (m, 1H), 7.10 (t, *J* = 8.0 Hz, 1H), 6.95 (dd, *J* = 8.1, 1.0 Hz, 1H), 6.78 (dd, *J* = 7.8, 1.0 Hz, 1H), 5.88 (ddt, *J* = 16.5, 10.4, 5.8 Hz, 1H), 5.71 (ddt, *J* = 16.7, 10.2, 6.3 Hz, 1H), 5.27–5.11 (m, 4H), 4.78 (ddt, *J* = 13.1, 6.0, 1.4 Hz, 1H), 4.68 (ddt, *J* = 13.1, 5.6, 1.5 Hz, 1H), 4.47 (ddt, *J* = 12.7, 6.3, 1.2 Hz, 1H), 4.21 (ddt, *J* = 12.8, 6.4, 1.2 Hz, 1H), 3.24 (s, 3H), 3.20–3.15 (m, 3H), 3.00–2.93 (m, 1H), 0.91 (s, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.14, 167.03, 165.81, 152.74, 147.67, 147.67, 133.81, 131.78, 131.42, 131.19, 129.73, 129.21, 128.45, 126.99, 126.85, 126.54, 121.57, 119.44, 106.83, 67.43, 66.37, 65.91, 59.57, 57.96, 32.75, 26.77, 17.90, 11.85; IR (Neat Film NaCl) 2917, 2863, 1721, 1600, 1529, 1450, 1350, 1231, 1088, 923, 883, 852 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{35}H_{46}BrN_2O_8Si$ $[M+H]^+$: 729.2201; found: 729.2240.



Lactone 61. To a 20 mL microwave vial with a magnetic stir bar were added oxindole **60** (500 mg, 0.69 mmol, 1.0 equiv), *p*-TsOH (520 mg, 2.7 mmol, 4.0 equiv), and benzene (20 mL). The reaction was sealed with a microwave crimp cap and subjected to microwave irradiation in a Biotage Initiator microwave reactor (temperature: 85 °C, sensitivity: low) with a gradual temperature increase over 10 min (10 °C increments). After 20 min of stirring, the vial was cooled to ambient temperature and uncapped. The reaction was diluted with EtOAc (10 mL) and quenched by addition of sat. $NaHCO_3$. The phases were separated and the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (1:1 hexane:EtOAc) on silica gel to afford lactone **61** (300 mg, 85% yield).

R_f = 0.23 (1:1 hexane:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (dd, *J* = 8.2, 1.5 Hz, 1H), 8.00–7.98 (m, 1H), 7.71 (dd, *J* = 9.1, 7.6 Hz, 1H), 7.61–7.57 (m, 1H), 7.11 (t, *J* = 8.0 Hz, 1H), 6.96 (dd, *J* = 8.1, 1.0 Hz, 1H), 6.87 (dd, *J* = 7.8, 1.0 Hz, 1H), 5.75–5.66 (m, 1H), 5.18–5.07 (m, 3H), 4.71 (td, *J* = 11.0, 10.4, 7.4 Hz, 1H), 4.55 (ddt, *J* = 12.9, 5.9, 1.3 Hz, 1H), 4.26 (ddt, *J* = 12.9, 6.2, 1.3 Hz, 1H), 3.63 (ddd, *J* = 15.2, 13.1, 7.3 Hz, 1H), 3.34

(s, 3H), 1.69–1.64 (m, 1H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 175.2, 165.3, 152.1, 145.9, 136.8, 133.5, 131.9, 130.9, 130.2, 130.2, 127.7, 127.5, 119.3, 107.9, 70.5, 67.1, 64.9, 60.4, 54.5, 27.0, 24.1, 21.1, 14.2; IR (Neat Film NaCl) 2929, 1742, 1713, 1601, 1532, 1456, 1353, 1192, 1112, 1058, 1033, 993, 936, 856, 767 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{23}H_{20}BrN_2O_7$ [M+H]$^+$: 515.0448; found: 515.0450.



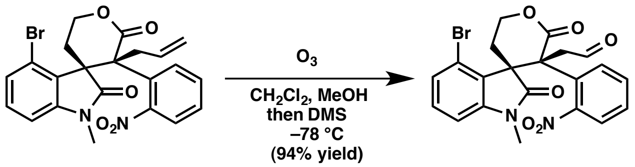
61

62

Allyl 62. To a 250 mL round-bottom flask with a magnetic stir bar was added lactone **61** (2.5 g, 4.9 mmol, 1.0 equiv). The flask was brought into a N$_2$-filled glove box, and then Pd(PPh$_3$)$_4$ (0.1 g, 0.097 mmol, 0.02 equiv) was added. The reaction mixture was brought out from the glove box and treated with THF (97 mL). After 5 min stirring, the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (1:1 hexane:EtOAc) on silica gel to afford allylated product **62** (2.0 g, 97% yield).

R$_f$ = 0.24 (1:1 hexane:EtOAc); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.66 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.40 (t, *J* = 7.7 Hz, 1H), 7.20 (dd, *J* = 9.6, 6.5 Hz, 2H), 7.01 (d, *J* = 8.1 Hz, 1H), 6.92 (d, *J* = 7.7 Hz, 1H), 6.48 (d, *J* = 8.1 Hz, 1H), 5.52 (ddt, *J* = 16.6, 12.0, 6.4 Hz, 1H), 5.43–5.35 (m, 1H), 4.79–4.72 (m, 3H), 4.32 (td, *J* = 13.7, 7.2 Hz, 1H), 3.31 (s, 3H), 3.13 (dd, *J* = 15.6, 5.0 Hz, 1H), 2.43–2.36 (m, 1H), 1.73 (dd, *J* = 14.7, 5.0 Hz, 1H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 175.5, 169.8, 152.4, 146.0, 134.7, 134.3, 130.9, 130.7, 130.4, 128.5, 128.3, 126.0, 125.2, 124.0, 117.8, 107.6, 64.7, 56.7, 54.2, 42.9, 26.4, 23.8; IR (Neat Film

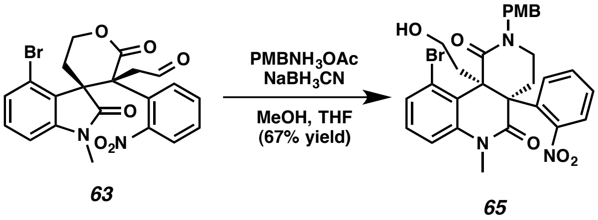
NaCl) 3418, 2923, 1709, 1601, 1532, 1455, 1361, 1292, 1201, 1113, 1069, 986, 917, 777, 736 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{22}H_{20}BrN_2O_5$ $[M+H]^+$: 471.0550; found: 471.0552.



62 *63*

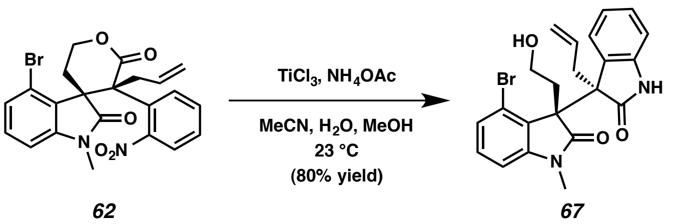
Aldehyde 63. A solution of alkene **62** (47.1 mg, 100 μmol, 1.0 equiv) in a mixture of CH_2Cl_2 (2.5 mL) and MeOH (2.5 mL) in a Schlenk flask hooked up to an ozone generator was purged with oxygen gas at –78 °C (5 min, flow 0.25). Then the ozone generator was turned on (low–medium setting) and an ozone/oxygen gas mixture was bubbled through the reaction. The progress of the reaction was checked via TLC (9:1 hexanes:CH_2Cl_2) in short time intervals (1-2 min). Upon completion of the reaction, the mixture was purged with oxygen gas for 5 min and DMS (36.0 μg, 500 μmol, 5.00 equiv) was added. The reaction mixture was slowly warmed to ambient temperature, and stirred for 16 h. The residue was purified by column chromatography (9:1 CH_2Cl_2:EtOAc) on silica gel to afford aldehyde **63** (44 mg, 94% yield).

R_f = 0.28 (9:1 CH_2Cl_2:EtOAc); ^1H NMR (500 MHz, DMSO-d_6) δ 8.64 (d, *J* = 3.4 Hz, 1H), 7.83–7.79 (m, 1H), 7.65–7.59 (m, 1H), 7.43–7.39 (m, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 7.9 Hz, 1H), 7.05 (d, *J* = 8.1 Hz, 1H), 6.92 (d, *J* = 8.3 Hz, 1H), 5.15 (ddd, *J* = 12.5, 10.8, 4.7 Hz, 1H), 4.59 (dd, *J* = 11.1, 6.9 Hz, 1H), 3.94 (ddd, *J* = 14.5, 12.6, 7.1 Hz, 1H), 3.22 (s, 3H), 3.08 (d, *J* = 17.0 Hz, 1H), 2.67 (dd, *J* = 17.0, 3.5 Hz, 1H), 1.96 (dd, *J* = 14.7, 4.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO) δ 198.0, 174.8, 171.0, 151.5, 146.3, 133.3, 131.9, 131.3, 129.9, 129.7, 127.6, 125.5, 124.6, 122.4, 109.3, 65.4, 55.6, 52.6, 49.8, 26.4, 22.3; IR (Neat Film NaCl) 1695, 1600, 1528, 1458, 1354, 1294, 1222, 1118, 850, 787 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{21}H_{18}BrN_2O_6$ [M+H]$^+$: 473.0343 found:473.0346.



Amide 65. To a suspension of aldehyde **63** (47.3 mg, 100 μmol, 1.0 equiv) and the acetic acid ammonium salt of *para*-methoxybenzylamine (59.2 mg, 300 μmol, 3.0 equiv) in MeOH (4 mL) was added $NaBH_3CN$ (2.60 mg, 300 μmol, 3.0 equiv) in THF (2 mL). The reaction mixture was stirred at ambient temperature for 16 h (conversion of the suspension to a clear, colorless solution usually indicated the completion of the reaction) and then concentrated under reduced pressure. Column chromatography using a Teledyne Isco CombiFlash R_f (SiO_2, 12 g column, 1. 1:1 → 1:4 hexanes:EtOAc) yielded lactam **65** (39.7 mg, 67% yield) as a colorless solid.

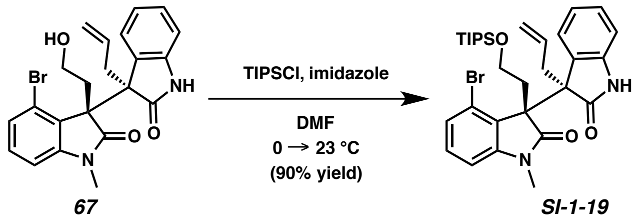
R_f = 0.12 (19:1 CH_2Cl_2:MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.10 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.59–7.55 (m, 1H), 7.43 (ddd, *J* = 8.4, 7.3, 1.3 Hz, 1H), 7.36 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.17 (t, *J* = 7.9 Hz, 1H), 7.10 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.06–7.02 (m, 2H), 6.81–6.76 (m, 3H), 4.71 (d, *J* = 14.6 Hz, 1H), 3.98 (d, *J* = 14.6 Hz, 1H), 3.76 (s, 3H), 3.53–3.49 (m, 1H), 3.18 (s, 3H), 3.16–3.08 (m, 3H), 2.90 (ddd, *J* = 9.6, 8.5, 3.2 Hz, 1H), 2.78 (dt, *J* = 9.6, 7.3 Hz, 1H), 2.25 (ddd, *J* = 14.1, 7.1, 3.1 Hz, 1H), 2.14 (ddd, *J* = 14.0, 8.6, 7.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.7, 171.7, 159.2, 152.6, 147.2, 134.4, 130.9, 130.4, 130.3, 129.9, 129.0, 128.0, 127.9, 126.3, 125.5, 122.4, 114.1, 107.3, 60.1, 58.5, 55.7, 55.4, 47.4, 44.0, 32.1, 27.5, 26.8; IR (Neat Film NaCl) 3459, 2931, 1682, 1601, 1574, 1530, 1457, 1360, 1249, 1176, 1037, 910, 849, 783, 731 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{29}H_{29}BrN_3O_6$ $[M+H]^+$: 594.1234; found: 594.1230.



Bis-oxindole 67. To a solution of lactone **62** (2.4 g, 5.6 mmol, 1.0 equiv) in H_2O (282 mL) and MeOH (565 mL) were added NH_4OAc (43.5 g, 564 mmol, 100.0 equiv) and $TiCl_3$ (10% w/w, 70.3 mL, 56.4 mmol, 10.0 equiv). Then, the reaction was stirred for 12 h at 23 °C. The reaction mixture was diluted with EtOAc (500 mL) and then the phases were separated and the aqueous phase was extracted with EtOAc (3 x 300 mL). The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (1:1 hexane:EtOAc) on silica gel to afford bis-oxindole **67** (1.99 g, 80% yield).

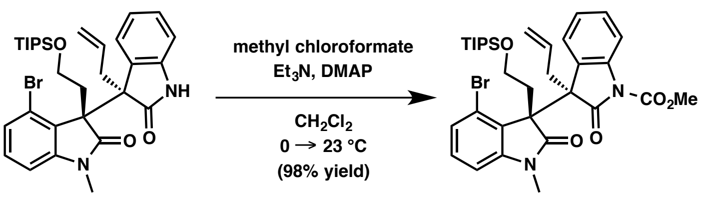
R_f = 0.10 (1:1 hexane:EtOAc); ^{1}H NMR (500 MHz, DMSO) δ 10.33 (s, 1H), 6.98 (dd, *J* = 8.1, 1.0 Hz, 1H), 6.96–6.87 (m, 2H), 6.77–6.67 (m, 2H), 6.58 (dd, *J* = 7.8, 1.0 Hz, 1H), 6.45 (d, *J* = 7.6 Hz, 1H), 4.96 (ddt, *J* = 16.7, 9.7, 6.9 Hz, 1H), 4.86 (dd, *J* = 17.0, 2.5 Hz, 1H), 4.74 (dd, *J* = 9.9, 2.6 Hz, 1H), 4.39 (t, *J* = 5.0 Hz, 1H), 3.41–3.32 (m, 2H), 3.22–3.13 (m, 1H), 3.03 (s, 3H), 2.86 (dtd, *J* = 10.3, 7.9, 5.5 Hz, 1H), 2.76 (dd, *J* = 13.5, 6.8

Hz, 1H), 2.24 (dt, *J* = 13.2, 7.9 Hz, 1H); ^{13}C NMR (125 MHz, DMSO) δ 177.5, 175.8, 146.5, 142.8, 133.4, 130.2, 128.5, 128.1, 126.9, 126.8, 123.5, 120.4, 119.3, 118.9, 108.9, 107.4, 58.4, 57.2, 56.0, 33.5, 28.9, 26.3; IR (Neat Film NaCl) 2917, 2356, 1697, 1599, 1574, 1455, 1349, 1184, 910, 752 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{22}H_{22}BrN_2O_3$ [M+H]$^+$: 441.0808; found 441.0812.



TIPS-ether SI-1-19. Bis-oxindole **67** (1.66 g, 3.76 mmol, 1.0 equiv) was dissolved in DMF (18.8 mL) to which TIPSCl (1.61 mL, 7.52 mmol, 2.0 equiv) and imidazole (1.02 g, 15.0 mmol, 4.0 equiv) were added at 0 °C. The reaction was slowly warmed to 23 °C, and stirred for 12 h. The reaction mixture was extracted with EtOAc (3 x 40 mL), and washed with brine. The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 hexanes:EtOAc) on silica gel to afford TIPS protected compound **SI-1-19** (2.02 g, 90% yield).

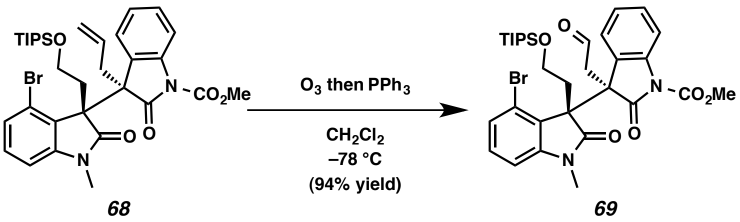
R_f = 0.20 (4:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (s, 1H), 6.99–6.92 (m, 2H), 6.87–6.80 (m, 2H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.49 (d, *J* = 7.8 Hz, 1H), 6.28 (d, *J* = 7.7 Hz, 1H), 5.10 (ddt, *J* = 16.9, 9.9, 7.1 Hz, 1H), 4.97 (dd, *J* = 17.1, 2.1 Hz, 1H), 4.77 (dd, *J* = 9.9, 2.2 Hz, 1H), 3.73 (ddd, *J* = 8.7, 5.7, 2.6 Hz, 1H), 3.57 (dd, *J* = 13.6, 7.1 Hz, 1H), 3.47–3.41 (m, 2H), 3.05 (s, 3H), 2.97 (dd, *J* = 13.6, 7.1 Hz, 1H), 2.60 (ddd, *J* = 15.0, 11.5, 5.6 Hz, 1H), 0.87–0.82 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.1, 175.8, 146.3, 140.9, 132.6, 129.3, 128.2, 127.0, 126.8, 123.7, 120.6, 119.4, 119.1, 108.5, 106.2, 60.9, 57.7, 56.8, 33.0, 28.8, 25.9, 17.8, 17.8, 11.8; IR (Neat Film NaCl) 3191, 3081, 2942, 2865, 2251, 2699, 1602, 1471, 1337, 1236, 1108, 995, 920, 736 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{31}H_{42}BrN_2O_3Si$ $[M+H]^+$: 597.2143; found 597.2141.



SI-1-19 *68*

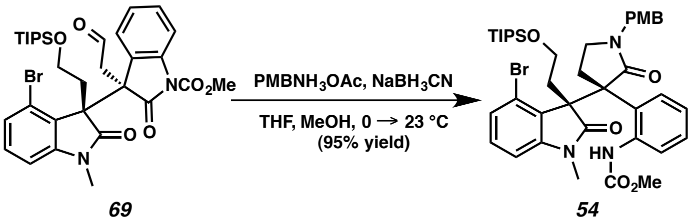
Carbamate 68. To a stirred solution of bis-oxindole **SI-1-19** (350 mg, 0.59 mmol, 1.0 equiv) in CH_2Cl_2 (5.86 mL) were added DMAP (7 mg, 0.059 mmol, 0.1 equiv), Et_3N (0.812 mL, 5.9 mmol, 10.0 equiv), and methyl chloroformate (0.16 mL, 1.76 mmol, 3.0 equiv) at 0 ºC. The reaction was slowly warmed to 23 ºC, and stirred for 12 h. The solvent was concentrated *in vacuo*, and then the residue was purified by column chromatography (4:1 hexanes:EtOAc) to afford carbamate **68** (377 mg, 98% yield).

R_f = 0.61 (4:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (dt, *J* = 8.2, 0.8 Hz, 1H), 7.05 (ddd, *J* = 8.1, 6.1, 2.9 Hz, 1H), 6.96 (dd, *J* = 8.2, 1.0 Hz, 1H), 6.92–6.91 (m, 2H), 6.82 (t, *J* = 7.9 Hz, 1H), 6.25 (dd, *J* = 7.8, 1.0 Hz, 1H), 5.06 (ddt, *J* = 16.6, 9.6, 6.9 Hz, 1H), 5.00 – 4.95 (m, 1H), 4.81–4.78 (m, 1H), 4.00 (s, 3H), 3.72 (ddd, *J* = 10.2, 5.7, 3.1 Hz, 1H), 3.61 (ddt, *J* = 13.8, 6.9, 1.0 Hz, 1H), 3.43 (td, *J* = 10.4, 3.9 Hz, 1H), 3.33–3.28 (m, 1H), 3.04–2.99 (m, 1H), 3.02 (s, 3H), 2.62 (ddd, *J* = 14.0, 10.6, 5.7 Hz, 1H), 0.87–0.81 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.3, 174.2, 151.3, 146.1, 139.5, 132.0, 129.6, 128.6, 127.1, 126.5, 126.2, 123.2, 122.7, 119.9, 119.0, 113.9, 106.3, 60.7, 58.4, 57.3, 53.7, 33.4, 28.9, 26.0, 17.7, 11.8; IR (Neat Film NaCl) 2942, 2865, 2089, 1722, 1602, 1463, 1348, 1201, 1243, 1166, 1104, 1026, 920, 883, 736, 772 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{33}H_{44}BrN_2O_5Si$ $[M+H]^+$: 655.2197; found 655.2199.



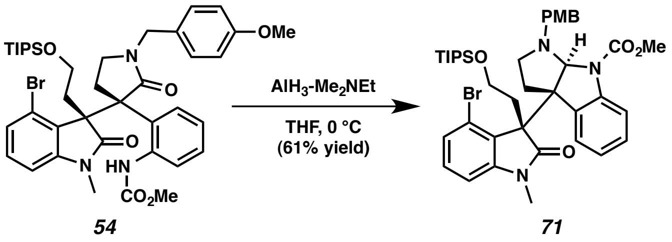
Aldehyde 69. To a 25 mL round bottom flask with magnetic stir bar was added alkene **68** (260 mg, 0.40 mmol, 1.0 equiv) and CH_2Cl_2 (2.0 mL). The flask was connected to an ozone generator, and purged with oxygen gas (flow: 0.5), for 5 min at –78 ºC and then ozone gas (flow: 0.5) was bubbled through into the reaction solution for 10 min at –78 ºC. After the reaction was done, oxygen gas was bubbled into the reaction mixture for 20 min and PPh_3 (313mg, 1.19 mmol, 3.0 equiv) was added. The reaction mixture was slowly warmed to ambient temperature, stirred for 16 h, and then concentrated under reduced pressure. The residue was purified by column chromatography (4:1 hexanes:EtOAc) to afford aldehyde **69** (245 mg, 94% yield).

R_f = 0.13 (4:1 hexanes:EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ 9.46 (d, *J*=1.0 Hz, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.06–7.01 (m, 1H), 6.99 (d, *J* = 8.1 Hz, 1H), 6.88–6.82 (m, 2H), 6.75 (d, *J* = 7.6 Hz, 1H), 6.23 (d, *J* = 7.8 Hz, 1H), 4.33 (d, *J* = 19.4 Hz, 1H), 4.02 (s, 3H), 3.72 (ddd, *J* = 9.3, 5.6, 2.7 Hz, 1H), 3.58 (dd, *J* = 19.3, 1.2 Hz, 1H), 3.42 (td, *J* = 10.3, 3.4 Hz, 1H), 3.23 (dt, *J* = 14.0, 3.4 Hz, 1H), 2.99 (s, 3H), 2.56–2.48 (m, 1H), 0.86–0.79 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.9, 175.4, 174.4, 151.3, 146.0, 140.0, 129.9, 128.8, 127.2, 126.5, 125.2, 122.6, 121.4, 119.3, 114.1, 106.5, 60.6, 58.2, 53.8, 52.8, 44.6, 28.9, 26.0, 17.7, 11.8; IR (Neat Film NaCl) 2942, 2865, 2255, 1773, 1718, 1603, 1576, 1459, 1351, 1295, 1245, 1163, 1108, 914, 883, 771, 732 cm^{-1}; HRMS (MM: ESI-APCI+) *m*/*z* calc'd for $C_{32}H_{41}BrN_2O_6Si$ $[M+H]^+$: 657.1990; found: 657.1991.



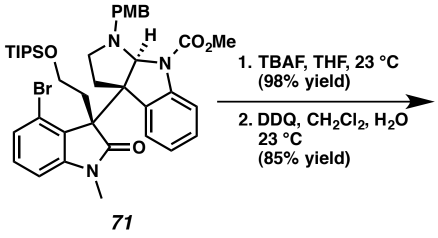
Lactam 54. To a solution of aldehyde **69** (100 mg, 0.15 mmol, 1.0 equiv) and *p*-methoxybenzylammonium acetate (90 mg, 0.46 mmol, 3.0 equiv) in methanol (7.6 mL) was added $NaBH_3CN$ (21 mg, 0.30 mmol, 2.0 equiv) in THF (3.8 mL) at 0 °C. The reaction mixture was slowly warmed to 23 °C and stirred overnight. The reaction mixture was washed with EtOAc (3 x 10 mL), and brine. The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 hexanes:EtOAc) on silica gel to afford lactam **54** (112 mg, 95% yield).

R_f = 0.20 (4:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.14 (s, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.18 (d, *J* = 8.3 Hz, 2H), 7.15–7.10 (m, 2H), 7.05 (q, *J* = 8.5, 7.9 Hz, 2H), 6.88 (t, *J* = 7.7 Hz, 1H), 6.85–6.80 (m, 2H), 6.49 (d, *J* = 7.7 Hz, 1H), 4.80 (d, *J* = 14.4 Hz, 1H), 4.36 (d, *J* = 14.4 Hz, 1H), 3.78 (s, 3H), 3.70 (s, 1H), 3.63 (s, 3H), 3.52 (td, *J* = 6.9, 3.6 Hz, 1H), 3.43–3.36 (m, 1H), 3.27 (td, *J* = 9.3, 5.7 Hz, 1H), 3.17 (t, *J* = 9.6 Hz, 1H), 2.87 (ddd, J = 13.3, 6.1, 3.5 Hz, 1H), 2.66–2.60 (m, 1H), 2.56 (s, 3H), 2.54–2.49 (m, 1H), 0.85 (q, J = 3.8 Hz, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.94, 173.92, 159.34, 154.32, 146.89, 139.65, 132.30, 130.98, 130.07, 129.75, 128.88, 128.50, 127.57, 127.42, 126.71, 126.45, 121.74, 120.99, 120.75, 114.18, 107.15, 68.21, 61.31, 60.86, 60.43, 55.34, 51.42, 47.61, 44.98, 31.20, 25.78, 17.86, 11.88; IR (Neat Film NaCl) 2944, 2865, 2073, 1716, 1667, 1604, 1513, 1455, 1247, 1227, 1109, 1069, 1034, 883, 761 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{40}H_{53}BrN_3O_6Si$ $[M+H]^+$: 778.2882; found: 778.2879.



Aminal 71. To a solution of amide **54** (0.32 g, 0.41 mmol, 1.0 equiv) in THF (41.1 mL) was added AlH_3-Me_2NEt (0.5 M in toluene; 1.64 mL, 0.82 mmol, 2.0 equiv) dropwise at 0 °C. The reaction was stirred for 2 h and quenched with MeOH. The reaction solution was concentrated *in vacuo* and purified by column chromatography (4:1 hexanes:EtOAc) to afford aminal **71** (0.19 g, 61% yield).

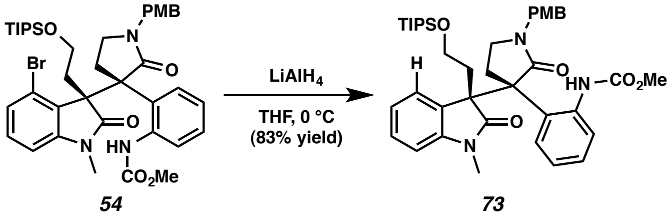
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58–7.47 (m, 1H), 7.21 (d, J = 8.2 Hz, 2H), 7.04–6.93 (m, 3H), 6.80 (dq, J = 14.8, 7.4 Hz, 4H), 6.39–6.24 (m, 2H), 4.00 (d, J = 13.7 Hz, 1H), 3.92–3.79 (m, 4H), 3.78 (s, 3H), 3.68 (dd, J = 10.2, 5.0 Hz, 1H), 3.57–3.43 (m, 1H), 3.03 (s, 3H), 2.65 (m, 4H), 2.26 (dt, J = 15.0, 7.2 Hz, 1H), 2.09 (dd, J = 11.9, 4.6 Hz, 1H), 0.87 (d, J = 3.2 Hz, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.0, 175.7, 160.6, 146.3, 141.7, 133.9, 132.2, 130.3, 130.1, 126.8, 123.6, 123.2, 123.1, 115.1, 114.6, 113.9, 107.3, 107.1, 106.6, 82.4, 60.7, 60.1, 57.2, 55.3, 52.6, 51.0, 31.9, 31.1, 30.7, 29.7, 26.1, 17.7, 11.8; IR (Neat Film NaCl) 2943, 1722, 1604, 1464, 1386, 1344, 1254, 1107, 1033, 885, 760 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{40}H_{53}BrN_3O_5Si$ $[M+H]^+$: 762.2932; found: 762.2936.



Aminal 72. To a solution of silyl ether **71** (98 mg, 0.13 mmol, 1.0 equiv) in THF (1.28 mL) was added TBAF (0.15 mL, 1.0 M solution in THF) at 0 °C. The reaction mixture was stirred for 3 h at 23 °C and quenched with sat. NH_4Cl. The reaction mixture was washed with EtOAc (3 x 1.5 mL), and brine. The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (2:1 hexanes:EtOAc) on silica gel to afford PMB-protected aminal compound (78 mg, 98% yield).

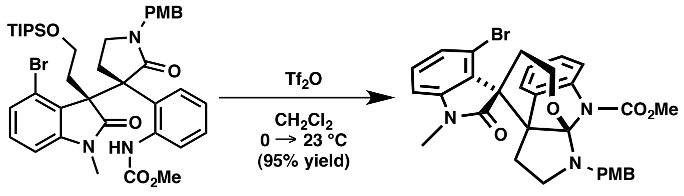
To a solution of PMB-protected aminal compound (96 mg, 0.16 mmol, 1.0 equiv) in CH_2Cl_2 (3.1 mL) and H_2O (0.8 mL) was added DDQ (53 mg, 0.23 mmol, 1.5 equiv) in portions over 30 min at 0 °C. The reaction mixture was stirred for 2 h at 23 °C. The solution was diluted with CH_2Cl_2 and quenched with sat. $NaHCO_3$. The reaction mixture was washed with CH_2Cl_2 (3 x 2.5 mL), and brine. The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 CH_2Cl_2:acetone) on silica gel to afford aminal **72** (64 mg, 85% yield).

R_f = 0.31 (4:1 CH_2Cl_2:acetone); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.1 Hz, 1H), 7.01–6.96 (m, 2H), 6.84 (p, *J* = 8.6 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 6.73 (t, *J* = 7.5 Hz, 1H), 6.48 (s, 1H), 6.35 (d, *J* = 7.8 Hz, 1H), 3.87 (d, *J* = 17.2 Hz, 3H), 3.66 (ddd, *J* = 10.8, 6.8, 3.7 Hz, 1H), 3.35 (dt, *J* = 10.9, 5.3 Hz, 1H), 3.11 (s, 3H), 3.01 (dd, *J* = 10.0, 6.5 Hz, 1H), 2.8–2.76 (m, 1H), 2.76–2.62 (m, 2H), 2.50 (td, *J* = 10.3, 4.7 Hz, 1H), 2.24 (br, s, 1H), 2.20 (dd, *J* = 12.7, 4.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 152.8, 146.1, 142.7, 130.4, 129.7, 128.9, 127.4, 127.2, 122.8, 121.6, 118.5, 113.8, 106.8, 80.5, 63.4, 60.0, 57.2, 52.6, 44.6, 35.1, 31.5, 26.3; IR (Neat Film NaCl) 3417, 2925, 1710, 1604, 1487, 1458, 1392, 1362, 1272, 1093, 756 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{23}H_{25}BrN_3O_4$ $[M+H]^+$: 486.1023; found: 486.1014.



Oxindole 73. To a solution of lactam **54** (10.6 mg, 0.0136 mmol, 1.0 equiv) in THF (1.36 ml) was added $LiAlH_4$ (5.2 mg, 0.136 mmol, 10.0 equiv) in portions at 0 ºC. The reaction was stirred for 1 h and then quenched with sat. NaCl. The reaction mixture was washed with EtOAc (3 x 2 mL) and brine. The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 hexanes:EtOAc) to afford oxindole **73** (7.9 mg, 83% yield).

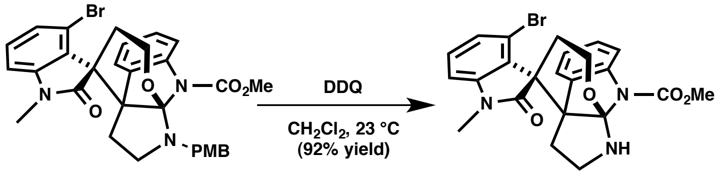
R_f = 0.25 (4:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.64 (br, s, 1H), 8.02 (d, *J* = 7.5 Hz, 1H), 7.60 (s, 1H), 7.13 (d, *J* = 8.4 Hz, 3H), 7.09 (t, *J* = 7.6 Hz, 1H), 7.04 (t, *J* = 7.7 Hz, 1H), 6.97 (s, 1H), 6.83 (d, *J* = 8.3 Hz, 3H), 6.38 (d, *J* = 7.7 Hz, 1H), 4.55 (d, *J* = 14.5 Hz, 1H), 4.44 (d, *J* = 14.5 Hz, 1H), 3.77 (s, 3H), 3.71 (s, 3H), 3.31–3.27 (m, 1H), 3.24 (br, s, 2H), 3.14 (br, s, 1H), 3.05–3.00 (m, 1H), 2.85 (s, 3H), 2.72 (s, 1H), 2.52 (t, *J* = 9.9 Hz, 1H), 2.41 (br, s, 1H), 0.86 (q, *J* = 7.5, 6.2 Hz, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.5, 159.4, 154.7, 143.7, 129.6, 129.4, 129.3, 129.2, 128.6, 128.4, 127.7, 127.5, 127.4, 122.2, 122.0, 121.8, 114.3, 107.3, 60.0, 56.6, 55.4, 52.1, 47.1, 44.0, 34.3, 29.9, 26.0, 18.0, 12.0; IR (Neat Film NaCl) 2941, 1732, 1711, 1610, 1515, 1442, 1375, 1248, 1225, 1105, 1070, 1036, 750 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{40}H_{54}N_3O_6Si$ $[M+H]^+$: 700.3776; found: 700.3776.



54 74

PMB-Propellane hexacycle 74. To a solution of lactam **54** (70 mg, 0.090 mmol, 1.0 equiv) in CH_2Cl_2 (9 mL) was added Tf_2O (45 μL, 0.27 mmol, 3.0 equiv) dropwise at 0 °C. The reaction mixture was slowly warmed to 23 °C and stirred for 2 h. The solution was neutralized by adding sat. $NaHCO_3$. The reaction mixture was washed with CH_2Cl_2 (3 x 5 mL) and brine. The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (2:1 hexanes:EtOAc) on silica gel to afford propellane hexacycle **74** (52 mg, 95% yield).

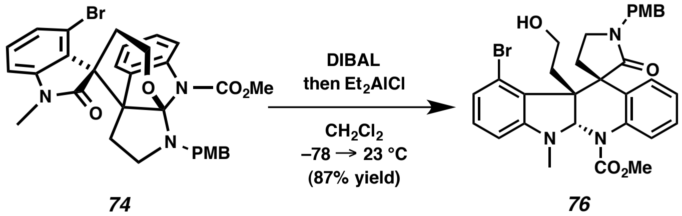
R_f = 0.25 (3:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.16–7.11 (m, 3H), 6.95–6.93 (m, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 6.73 (td, *J* = 7.6, 1.1 Hz, 1H), 6.60 (t, *J* = 4.4 Hz, 1H), 6.36 (dd, *J* = 7.6, 1.5 Hz, 1H), 4.53 (dt, *J* = 11.5, 5.8 Hz, 1H), 4.47 (d, *J* = 14.9 Hz, 1H), 4.23–4.18 (m, 1H), 3.87 (s, 3H), 3.76 (s, 3H), 3.72 (d, *J* = 13.7 Hz, 1H), 3.21 (s, 3H), 3.01 (ddd, *J* = 14.4, 11.7, 8.4 Hz, 1H), 2.77–2.73 (m, 1H), 2.54 (q, *J* = 9.3 Hz, 1H), 2.13 (td, *J* = 8.8, 5.3 Hz, 1H), 1.93 (dd, *J* = 14.2, 6.3 Hz, 1H), 1.80–1.75 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.0, 158.5, 153.7, 145.8, 142.5, 132.0, 130.9, 130.1, 129.5, 129.4, 128.9, 128.1, 124.6, 122.9, 121.5, 116.1, 113.6, 112.1, 106.6, 58.2, 57.0, 55.4, 54.4, 52.7, 50.2, 47.9, 33.7, 26.6, 23.2; IR (Neat Film NaCl) 1718, 1601, 1575, 1513, 1484, 1455, 1365, 1245, 1134, 1099, 1037, 912, 764, 731 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{31}H_{31}BrN_3O_5$ $[M+H]^+$: 604.1442; found: 604.1433.



74 *75*

Propellane hexacycle 75. To a solution of oxindole **74** (46 mg, 0.075 mmol, 1.0 equiv) in CH_2Cl_2 (3.8 mL) and H_2O (0.94 mL) was added DDQ (34 mg, 0.15 mmol, 2.0 equiv) at 0 °C. The reaction mixture was slowly warmed to 23 °C and stirred for 2 h. The solution was quenched with sat. $NaHCO_3$. The reaction mixture was washed with CH_2Cl_2 (3 x 3.0 mL) and brine. The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 CH_2Cl_2:acetone) on silica gel to afford propellane hexacycle **75** (33 mg, 92% yield).

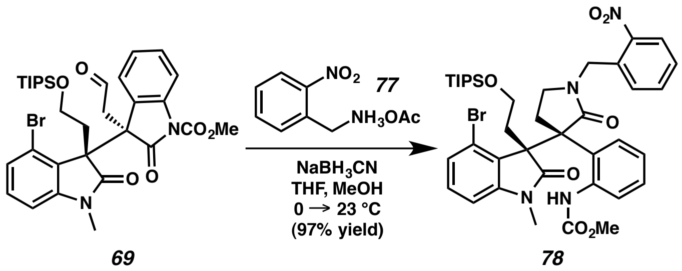
R_f = 0.1 (1:1 hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.3 Hz, 1H), 7.16 (t, *J* = 7.9 Hz, 1H), 6.98 (dd, *J* = 21.2, 8.0 Hz, 2H), 6.71 (d, *J* = 7.7 Hz, 2H), 6.25 (d, *J* = 7.6 Hz, 1H), 4.45 (td, *J* = 11.1, 6.6 Hz, 1H), 4.10–4.02 (m, 1H), 3.92 (s, 3H), 3.23 (s, 3H), 3.14 (dd, *J* = 9.4, 6.0 Hz, 1H), 3.08–2.92 (m, 1H), 2.68–2.51 (m, 2H), 1.82 (td, *J* = 14.2, 12.6, 7.1 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.9, 153.6, 145.8, 142.4, 133.3, 130.4, 129.7, 129.2, 128.1, 125.7, 123.2, 122.5, 114.3, 111.6, 106.9, 58.5, 55.7, 53.8, 53.0, 43.3, 36.5, 26.6, 23.5;IR (Neat Film NaCl) 2958, 1713, 1602, 1485, 1446, 1373, 1242, 1095, 754 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{23}H_{23}BrN_3O_4$ $[M+H]^+$: 484.0866; found: 484.0874.



Aminal 76. To a solution of propellane hexacycle **74** (13 mg, 0.021 mmol, 1.0 equiv) in CH_2Cl_2 (2.14 mL) was added DIBAL (1.0 M in THF; 0.11 mL, 0.11 mmol, 5 equiv) dropwise at –78 °C. The reaction mixture was stirred for 1 h and warmed to 0 °C. DIBAL (1.0 M in THF; 21.4 μL, 21.4 μmol, 1 equiv) was added dropwise at 0 °C and stirred for 1 h. Then, DIBAL (1.0 M in THF; 21.4 mL, 21.4 mmol, 1 equiv) was added one more time dropwise at 0 °C and stirred for another 1 h. The reaction mixture was warmed to 23 °C and Et_2AlCl (1.0 M in hexane; 42.8 mL, 42.8 mmol, 2 equiv) was added dropwise. The mixture was stirred for 30 min and quenched with sat. NH_4Cl and sat. potassium sodium tartrate. The reaction mixture was washed with CH_2Cl_2 (3 x 2.0 mL)

and brine. The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (1:1 hexane:EtOAc) on silica gel to afford propellane aminal **76** (10.5 mg, 87% yield).

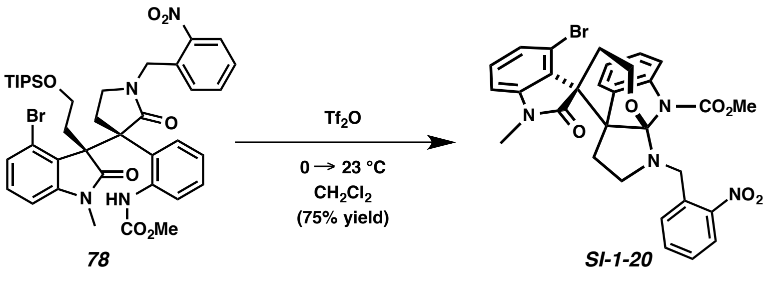
R_f = 0.25 (1:1 hexane:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.7 Hz, 1H), 7.24–7.22 (m, 2H), 7.17 (s, 1H), 7.08–7.03 (m, 1H), 6.87–6.84 (m, 2H), 6.82 (t, *J* = 7.9 Hz, 1H), 6.71 (dd, *J* = 8.0, 1.0 Hz, 1H), 6.23 (br, s, 1H), 6.01 (dd, *J* = 7.9, 1.0 Hz, 1H), 5.15 (d, *J* = 14.5 Hz, 1H), 3.94 (d, *J* = 14.5 Hz, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 3.72–3.63 (m, 2H), 3.40 (dd, *J* = 9.5, 7.7 Hz, 1H), 3.12 (td, *J* = 9.7, 1.5 Hz, 1H), 3.10–3.04 (m, 1H), 2.89–2.82 (m, 1H), 2.48 (s, 3H), 2.32 (dt, *J* = 14.2, 7.2 Hz, 1H), 1.65 (dt, *J* = 14.7, 9.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 159.2, 152.7, 139.2, 136.3, 134.0, 130.4, 129.8, 128.8, 126.8, 126.7, 126.1, 125.2, 125.0, 122.9, 122.4, 114.2, 104.7, 83.3, 61.0, 60.5, 55.4, 53.6, 53.4, 47.1, 44.3, 35.3, 33.0, 31.1; IR (Neat Film NaCl) 2922, 1689, 1597, 1512, 1444, 1334, 1249, 1178, 1032, 754 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{31}H_{33}BrN_3O_5$ $[M+H]^+$: 606.1598; found: 606.1592.



Amide 78. To a solution of aldehyde **69** (100 mg, 0.13 mmol, 1.0 equiv) and *o*-nitrobenzylammonium acetate **77** (97 mg, 0.38 mmol, 3.0 equiv) in MeOH (7.6 mL) was added $NaBH_3CN$ (21 mg, 0.26 mmol, 2.0 equiv) in THF (3.8 mL) at 0 °C. The reaction mixture was slowly warmed to ambient temperature and stirred for 12 h. Then, H_2O (5

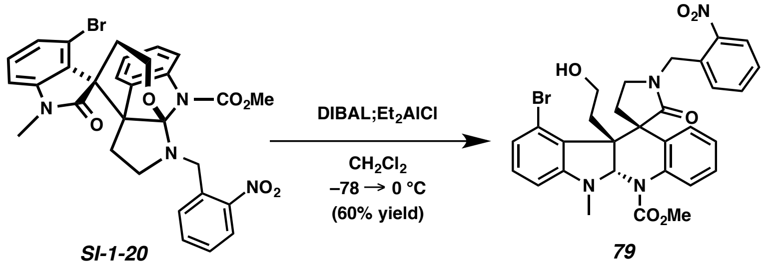
mL) was added and extracted with EtOAc (3 x 20 mL), and washed with brine. The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 hexanes:EtOAc) on silica gel to afford *o*-nitrobenzyl protected amide **78** (116 mg, 97% yield).

R_f = 0.35 (2:1 hexanes:EtOAc); (Due to the distinct presence of rotameric isomers, the ^{1}H NMR and ^{13}C NMR contained extra peaks. See the attached spectrum), ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.63 (s, 1H), 8.06–7.97 (m, 2H), 7.51 (td, *J* = 7.6, 1.5 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.25–7.18 (m, 2H), 7.13 (dd, *J* = 14.1, 8.2 Hz, 2H), 7.05 (t, *J* = 7.9 Hz, 1H), 6.97–6.90 (m, 1H), 6.53 (d, *J* = 7.6 Hz, 1H), 5.32 (d, *J* = 16.5 Hz, 1H), 4.71 (dd, *J* = 16.4, 6.5 Hz, 1H), 3.70–3.63 (m, 2H), 3.57 (td, *J* = 6.3, 2.9 Hz, 1H), 3.55–3.51 (m, 1H), 3.35–3.26 (m, 2H), 2.92 (ddd, *J* = 13.1, 5.4, 3.3 Hz, 1H), 2.84 (s, 1H), 2.69 (ddd, *J* = 19.4, 8.7, 5.3 Hz, 2H), 2.63 (s, 3H), 0.85 (t, *J* = 4.1 Hz, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.0, 175.4, 154.4, 148.7, 147.1, 139.7, 134.1, 132.1, 131.2, 130.0, 129.4, 128.8, 128.7, 127.6, 126.6, 126.0, 125.3, 122.1, 121.8, 121.3, 107.3, 60.9, 60.6, 60.4, 51.6, 46.0, 45.1, 31.8, 31.6, 25.9, 17.9, 11.9; IR (Neat Film NaCl) 3418, 2943, 2865, 2251, 1717, 1601, 1527, 1456, 1338, 1313, 1282, 1227, 1113, 1069, 911, 883, 857, 730 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{39}H_{50}BrN_4O_7Si$ $[M+H]^+$: 793.2627; found: 793.2658.



Propellane hexacycle SI-1-20. To a solution of amide **78** (54.1 mg, 0.087 mmol, 1.0 equiv) in CH_2Cl_2 (6.82 mL), was added Tf_2O (34 mL, 0.26 mmol, 3.0 equiv) dropwise at 0 ºC. The reaction mixture was slowly warmed to 23 ºC, and stirred for 2 h. After the reaction was done, the solution was brought to pH 10.5-11.0 by addition of sat. $NaHCO_3$. The reaction mixture was extracted with EtOAc (3 x 6 mL) and washed with brine. The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (2:1 hexanes:EtOAc) on silica gel to afford propellane hexacycle **SI-1-20** (39.6 mg, 75% yield).

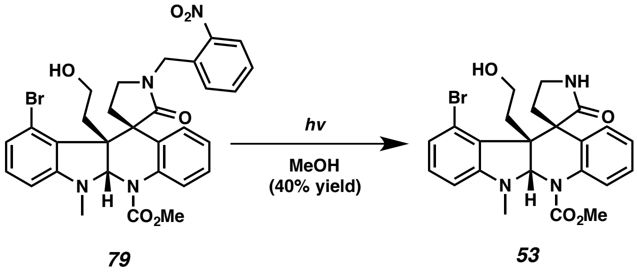
R_f = 0.46 (1:1 hexane:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.72–7.58 (m, 1H), 7.46–7.40 (m, 2H), 7.30 (ddd, *J* = 8.0, 6.7, 2.2 Hz, 1H), 7.21–7.14 (m, 1H), 6.99–6.93 (m, 2H), 6.81–6.76 (m, 1H), 6.64 (dd, *J* = 7.4, 1.4 Hz, 1H), 6.36 (dd, *J* = 7.7, 1.3 Hz, 1H), 4.61 (d, *J* = 16.6 Hz, 1H), 4.54 (d, *J* = 18.2 Hz, 1H), 4.45 (td, *J* = 11.4, 6.5 Hz, 1H), 4.18–4.11 (m, 1H), 3.72 (d, *J* = 9.4 Hz, 3H), 3.21 (s, 3H), 3.11–3.02 (m, 1H), 2.96–2.87 (m, 1H), 2.51 (dt, *J* = 14.4, 9.0 Hz, 2H), 1.94–1.81 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 153.5, 148.9, 145.8, 144.4, 142.1, 136.2, 132.9, 131.0, 130.0, 129.6, 129.1, 128.1, 127.3, 125.1, 124.3, 123.1, 116.1, 111.9, 106.8, 64.5, 58.4, 56.5, 54.5, 52.6, 50.0, 47.9, 33.9, 26.5, 22.8; IR (Neat Film NaCl) 2953, 2360, 1721, 1599, 1573, 1524, 1483, 1455, 1367, 1242, 1134, 1088, 1134, 1088, 947, 856, 761, 733 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{30}H_{28}BrN_4O_6$ $[M+H]^+$: 619.1187; found: 619.1188.



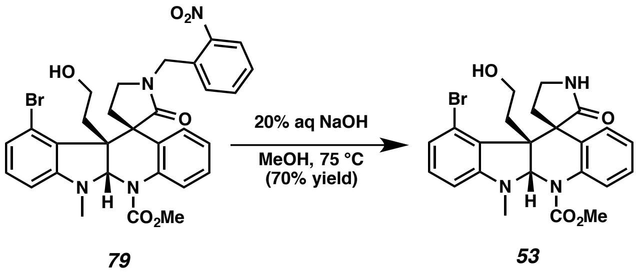
Aminal 79. To a solution of propellane hexacyclic oxindole **SI-1-20** (14.6 mg, 0.024 mmol, 1.0 equiv) in CH_2Cl_2 (2.4 mL) was added DIBAL (1.0 M in THF; 0.12 mL, 0.12 mmol, 5 equiv) dropwise at –78 ºC. After the reaction mixture was stirred for 1 h at –78 ºC, the solution was warmed to 0 ºC and DIBAL (1.0 M in THF; 24 mL, 0.024 mmol, 1.0 equiv) was added dropwise. The mixture was stirred for 1 h at 0 ºC, and more DIBAL (1.0 M in THF; 24 mL, 0.024 mmol, 1.0 equiv) was added dropwise. The reaction mixture was stirred for 1 h at 0 ºC, and warmed to 23 ºC. To the reaction mixture was added Et_2AlCl (1.0 M in hexanes; 48 mL, 0.048 mmol, 2.0 equiv) dropwise. The reaction was stirred for 30 min and quenched with aq NH_4Cl (1 mL) and aq potassium sodium tartrate (1 mL). The reaction mixture was washed with EtOAc (3 x 3 mL), and brine. The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (1:1 hexane:EtOAc) on silica gel to afford aminal **79** (8.9 mg, 60% yield).

R_f = 0.12 (1:1 hexane:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.58 (td, *J* = 7.6, 1.3 Hz, 1H), 7.50–7.48 (m, 1H), 7.44 (ddd, *J* = 8.6, 7.4, 1.5 Hz, 1H), 7.37–7.34 (m, 1H), 7.23–7.19 (m, 1H), 7.09–7.05 (m, 1H), 6.81 (t, *J* = 7.9 Hz, 1H), 6.69 (dd, *J* = 8.0, 1.0 Hz, 1H), 6.26 (s, 1H), 6.01 (dd, *J* = 7.9, 0.9 Hz, 1H), 5.41 (d, *J* = 16.3 Hz, 1H), 4.56 (d, *J* = 16.2 Hz, 1H), 3.86 (s, 3H), 3.73–3.64 (m, 2H), 3.56 (td, *J* = 9.5, 7.4 Hz, 1H), 3.24–3.18 (m, 1H), 3.09 (ddd, *J* = 13.6, 8.6, 5.3 Hz, 1H), 2.95 (ddd, *J* =

14.2, 7.4, 1.7 Hz, 1H), 2.48 (s, 3H), 2.35 (ddd, *J* = 13.2, 8.5, 6.2 Hz, 1H), 1.78 (dt, *J* = 14.2, 9.4 Hz, 1H), 1.74 (br, s, 1H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 171.5, 171.3 152.6, 148.9, 138.8, 136.3, 133.7, 132.1, 130.4, 129.7, 128.4, 126.9, 126.2, 126.0, 125.0, 124.8, 122.7, 122.2, 104.6, 83.2, 64.4, 60.7, 60.4, 53.3, 53.1, 45.3, 44.5, 35.2, 33.0, 31.0; IR (Neat Film NaCl) 2955, 2357, 1694, 1595, 1524, 1444, 1335, 1281, 1073, 1032, 911, 857, 835, 730 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{30}H_{30}BrN_4O_6$ [M+H]$^+$: 621.1343; found: 621.1286.

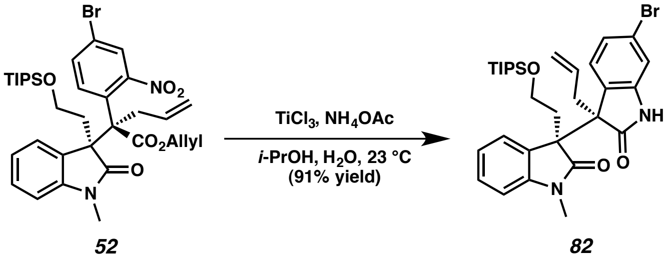


Amide 53. A solution of aminal **79** (21.5 mg, 0.035 mmol, 1.0 equiv) in anhydrous MeOH (3.5 mL) in a Pyrex flask was purged with N_2 for 5 min. The reaction mixture was irradiated in a cylindrical photoreactor with 254 nm lamps under N_2 for 3 h and concentrated. The residue was purified by column chromatography (4:1 CH_2Cl_2:acetone) on silica gel to afford aminal **53** (6.7 mg, 40% yield). See below for characterization data.



Amide 53. To a solution of *o*-nitrobenzyl protected aminal **79** (10.8 mg, 0.017 mmol, 1.0 equiv) in MeOH (0.8 mL) was added 20% aq NaOH (0.2 mL) and the mixture was stirred for 4 h at 75 ºC. After the reaction mixture was cooled to 23 ºC, it was diluted with water and extracted with EtOAc (3 x 2 mL). The organic layer was washed with brine, dried over $MgSO_4$, concentrated *in vacuo*. The residue was purified by column chromatography (4:1 CH_2Cl_2:acetone) to afford compound **53** (5.9 mg, 70% yield).

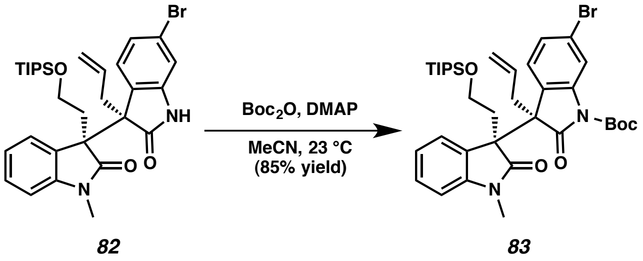
R_f = 0.18 (4:1 CH_2Cl_2:acetone); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51–7.45 (m, 1H), 7.19 (td, *J* = 7.6, 1.4 Hz, 1H), 7.05 (td, *J* = 7.7, 1.4 Hz, 1H), 6.80 (d, *J* = 7.9 Hz, 1H), 6.69 (dt, *J* = 8.0, 1.0 Hz, 1H), 6.60 (br, s, 1H), 6.25 (br, s, 1H), 5.99 (dd, *J* = 7.9, 0.9 Hz, 1H), 3.87 (s, 3H), 3.74–3.63 (m, 2H), 3.55 (td, *J* = 9.4, 7.3 Hz, 1H), 3.33 (ddd, *J* = 9.8, 8.8, 1.5 Hz, 1H), 3.17 (ddd, *J* = 13.6, 8.4, 5.6 Hz, 1H), 3.03–2.96 (m, 1H), 2.49 (s, 3H), 2.36 (ddd, *J* = 13.2, 8.2, 6.3 Hz, 1H), 1.92 (dt, *J* = 14.0, 9.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.8, 155.4, 152.9, 138.6, 136.4, 130.4, 126.9, 126.6, 126.1, 125.0, 123.4, 122.5, 104.6, 83.2, 76.9, 60.9, 60.6, 53.5, 52.3, 40.4, 35.8, 35.2, 31.1; IR (Neat Film NaCl) 3418, 2955, 2357, 1693, 1593, 1446, 1335, 1282, 1032, 836, 754 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{23}H_{25}BrN_3O_4$ $[M+H]^+$: 486.1023; found: 486.1004.



Bis-oxindole 82. To a solution of oxindole **52** (7.65 g, 11.2 mmol, 1.0 equiv) in H_2O (187 mL) and *i*-PrOH (373 mL) were added NH_4OAc (43.2 g, 0.560 mol, 50 equiv) and

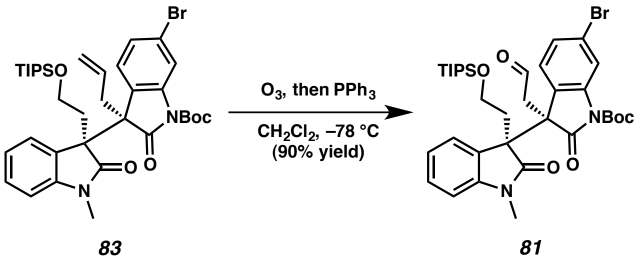
$TiCl_3$ (20% w/w, 69.2 mL, 0.11 mol, 10 equiv). Then, the reaction was stirred for 12 h at 23 ºC. The reaction mixture was diluted with EtOAc (200 mL) and then the phases were separated and the aqueous phase was extracted with EtOAc (3 x 300 mL). The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (2:1 hexanes:EtOAc) on silica gel to afford bis-oxindole **82** (6.10 g, 91% yield).

R_f = 0.68 (1:1 hexane:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (br, s, 1H), 7.31–7.26 (m, 1H), 6.98–6.90 (m, 2H), 6.88 (dd, *J* = 2.7, 1.5 Hz, 1H), 6.82 (s, 1H), 6.73–6.69 (m, 1H), 6.21 (br, s, 1H), 5.14 (ddt, *J* = 17.1, 10.0, 7.1 Hz, 1H), 4.96 (ddd, *J* = 17.1, 2.0, 0.9 Hz, 1H), 4.86–4.80 (m, 1H), 3.42–3.31 (m, 2H), 3.25 (ddd, *J* = 9.9, 7.5, 4.7 Hz, 1H), 3.05 (dt, *J* = 14.5, 7.4 Hz, 1H), 2.90 (s, 3H), 2.79 (dd, *J* = 13.0, 6.9 Hz, 1H), 2.34 (ddd, *J* = 13.4, 6.8, 4.7 Hz, 1H), 0.92–0.81 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.14, 176.05, 144.65, 142.73, 131.37, 128.80, 127.92, 127.73, 125.58, 124.41, 124.20, 121.97, 121.73, 119.88, 112.70, 108.15, 59.61, 56.86, 54.80, 35.16, 32.66, 25.91, 17.82, 11.77; IR (Neat Film NaCl) 3270, 2942, 2865, 1716, 1611, 1471, 1377, 1241, 1105, 916, 883, 791, 734 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{31}H_{42}BrN_2O_3Si$ [M+H]$^+$: 597.2143; found: 597.2187.



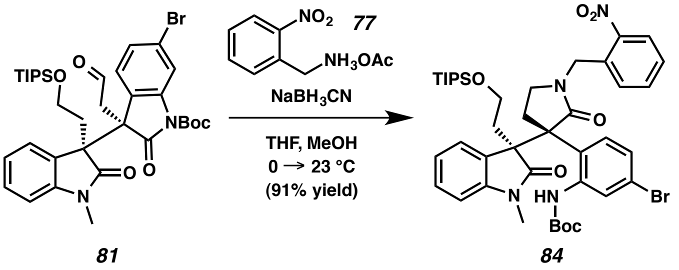
Carbamate 83. To a stirred solution of bis-oxindole **82** (2.63 g, 4.40 mmol, 1.0 equiv) in CH_2Cl_2 (44 mL) were added DMAP (1.08 g, 8.80 mmol, 2.0 equiv) and Boc_2O (1.92 g, 8.80 mmol, 2.0 equiv) at 0 ºC. The reaction was slowly warmed to 23 ºC, and stirred for 12 h. The solvent was concentrated *in vacuo* and then the residue was purified by column chromatography (4:1 hexanes:EtOAc) to afford protected compound **83** (2.6 g, 85% yield).

R_f = 0.52 (4:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 1.9 Hz, 1H), 7.25 (td, *J* = 7.7, 1.3 Hz, 1H), 7.14–7.09 (m, 1H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.71–6.67 (m, 1H), 6.62–6.53 (m, 1H), 6.47 (s, 1H), 5.10 (ddt, *J* = 17.0, 9.9, 7.1 Hz, 1H), 4.99–4.92 (m, 1H), 4.83 (dd, *J* = 10.0, 2.0 Hz, 1H), 3.43 (dd, *J* = 13.3, 7.3 Hz, 1H), 3.35 (dt, *J* = 9.9, 7.2 Hz, 1H), 3.20 (ddd, *J* = 9.9, 7.7, 4.8 Hz, 1H), 2.94 (s, 3H), 2.90 (dd, *J* = 13.9, 8.0 Hz, 1H), 2.81–2.75 (m, 1H), 2.30 (ddd, *J* = 13.2, 7.2, 4.8 Hz, 1H), 1.51 (s, 9H), 0.89–0.84 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.60, 173.73, 148.46, 144.52, 141.67, 131.26, 128.95, 127.19, 126.28, 126.06, 125.32, 124.15, 122.43, 121.69, 120.23, 118.24, 108.06, 84.08, 59.56, 57.36, 55.29, 34.77, 32.70, 27.92, 25.97, 17.82, 11.76; IR (Neat Film NaCl) 2941, 2866, 1770, 1716, 1610, 1471, 1420, 1370, 1342, 1287, 1246, 1153, 1105, 1067, 1023, 919, 882, 845, 752, 733 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{31}H_{42}BrN_2O_3Si$ $[M+H-Boc]^+$: 597.2143 found: 597.2181.



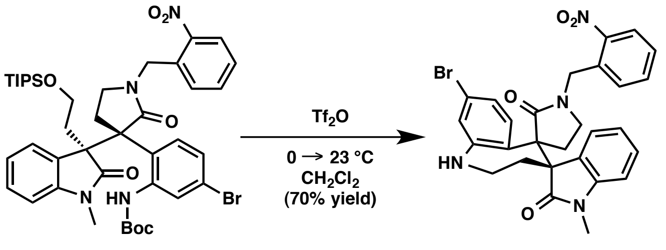
Aldehyde 81. To a 100 mL round bottom flask with magnetic stir bar was added alkene **83** (2.61 g, 0.00374 mol, 1.0 equiv). The flask was connected to an ozone generator and purged with oxygen gas (flow: 0.5) for 5 min at –78 ºC. Then, ozone gas (flow: 0.5) was bubbled through into the reaction solution for 30 min at –78 ºC. After the reaction was done, oxygen gas was bubbled into the reaction mixture for 20 min and PPh_3 (2.95 g, 0.0112 mol, 3.0 equiv) was added. The reaction mixture was slowly warmed to ambient temperature, stirred for 16 h, and then concentrated under reduced pressure. The residue was purified by column chromatography (4:1 hexanes:EtOAc) to afford aldehyde **81** (2.4 g, 90% yield).

R_f = 0.23 (4:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.45 (s, 1H), 8.00 (d, *J* = 1.8 Hz, 1H), 7.31 – 7.26 (m, 1H), 7.21 (td, *J* = 7.8, 1.2 Hz, 1H), 6.93 (br, s, 1H), 6.77 (t, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 5.99 (br, s, 1H), 4.43 (d, *J* = 19.1 Hz, 1H), 3.39 (dd, *J* = 19.2, 1.1 Hz, 1H), 3.31 (dt, *J* = 9.9, 7.3 Hz, 1H), 3.15 (ddd, *J* = 9.9, 8.0, 4.7 Hz, 1H), 3.10 (s, 3H), 2.64 (dt, *J* = 12.8, 7.6 Hz, 1H), 2.20 (ddd, *J* = 12.6, 7.5, 4.7 Hz, 1H), 1.43 (s, 9H), 0.91–0.82 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.38, 175.36, 173.47, 148.07, 144.01, 142.38, 129.18, 126.57, 126.04, 125.73, 124.51, 123.59, 122.99, 121.72, 118.74, 108.14, 83.83, 59.25, 53.78, 53.64, 44.47, 33.42, 27.83, 26.20, 17.80, 11.74; IR (Neat Film NaCl) 1941, 2865, 1771, 1722, 1609, 1471, 1422, 1370, 1345, 1291, 1245, 1152, 1109, 1070, 1015, 882, 845, 793, 749 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{30}H_{40}BrN_2O_4Si$ $[M+H-Boc]^+$: 599.1935 found: 597.1971.



Amide 84. To a solution of aldehyde **81** (200 mg, 0.29 mmol, 1.0 equiv) and *o*-nitrobenzylammonium acetate **77** (182 mg, 0.86 mmol, 3.0 equiv) in MeOH (14.3 mL) was added $NaBH_3CN$ (39 mg, 0.57 mmol, 2.0 equiv) in THF (7.2 mL) at 0 ºC. The reaction mixture was slowly warmed to ambient temperature, and stirred for 12 h. Then, H_2O (10 mL) was added. The mixture was extracted with EtOAc (3 x 20 mL) and washed with brine. The combined organic phases were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 hexanes:EtOAc) on silica gel to afford *o*-nitrobenzyl protected amide **84** (221 mg, 91% yield).

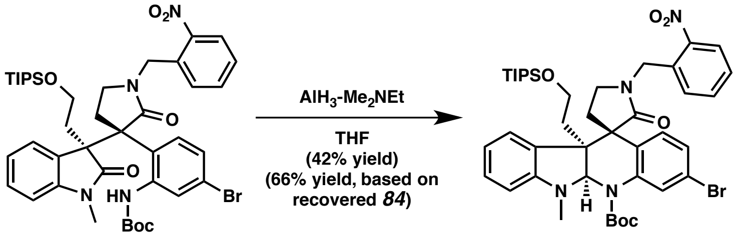
R_f = 0.22 (4:1 hexanes:EtOAc); (due to the distinct presence of rotameric isomers, the ^{1}H NMR and ^{13}C NMR contained extra peaks. See attached the spectrum behind); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (d, *J* = 8.9 Hz, 1H), 8.36 (d, *J* = 2.3 Hz, 1H), 8.09 (s, 1H), 8.06–7.96 (m, 2H), 7.83 (s, 1H), 7.62 (d, *J* = 7.1 Hz, 2H), 7.46 (t, *J* = 8.5 Hz, 1H), 7.42–7.30 (m, 6H), 7.23 (d, *J* = 8.3 Hz, 3H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.93–6.86 (m, 2H), 6.81 (d, *J* = 7.5 Hz, 2H), 6.10 (d, *J* = 7.6 Hz, 1H), 5.00 (d, *J* = 16.9 Hz, 1H), 4.91 (d, *J* = 17.3 Hz, 1H), 4.58 (d, *J* = 17.3 Hz, 1H), 4.27 (s, 1H), 3.75 (s, 1H), 3.37 (t, *J* = 7.4 Hz, 1H), 3.28 (s, 3H), 3.23 (d, *J* = 4.9 Hz, 1H), 3.18 (d, *J* = 7.2 Hz, 4H), 3.14–3.06 (m, 3H), 2.99 (dt, *J* = 9.2, 4.7 Hz, 2H), 2.80 (dd, *J* = 13.3, 9.4 Hz, 3H), 2.43 (t, *J* = 7.8 Hz, 1H), 2.25–2.13 (m, 1H), 2.06 (d, *J* = 8.9 Hz, 2H), 0.87 (d, *J* = 1.9 Hz, 21H), 0.80 (d, *J* = 2.7 Hz, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.3, 176.9, 174.6, 152.9, 148.3, 148.1, 145.0, 144.7, 141.9, 134.5, 134.1, 131.8, 131.0, 129.1, 128.8, 128.8, 128.5, 128.4, 128.4, 128.2, 127.0, 125.3, 125.2, 125.1, 124.9, 123.2, 122.9, 122.1, 121.7, 108.4, 107.9, 79.9, 59.9, 59.2, 59.1, 52.9, 44.6, 44.2, 44.1, 36.4, 34.6, 31.3, 31.1, 28.6, 28.3, 26.5, 26.3, 18.2, 18.0, 17.9, 12.2, 12.1, 11.9; IR (Neat Film NaCl) 3329, 2941, 2866, 1701, 1612, 1531, 1496, 1473, 1344, 1280, 1159, 1103, 1072, 1024, 914, 885, 753, 731, 688 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{42}H_{56}BrN_4O_7Si$ [M+H]$^+$: 835.3096; found: 835.3105.



84 **86**

Tetrahydroazepine 86. To a solution of amide **84** (20 mg, 0.0239 mmol, 1.0 equiv) in CH_2Cl_2 (2.39 mL), was added Tf_2O (0.0121 ml, 0.0718 mmol, 3.0 equiv) dropwise at 0 ºC. The reaction mixture was slowly warmed to 23 ºC, and stirred for 2 h. After the reaction was done, the solution was brought to pH 10.5-11.0 by addition of sat. $NaHCO_3$. The reaction mixture was extracted with EtOAc (3 x 3 mL) and washed with brine. The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (2:1 hexanes:EtOAc) on silica gel to afford tetrahydroazepine **86** (9.4 mg, 70% yield).

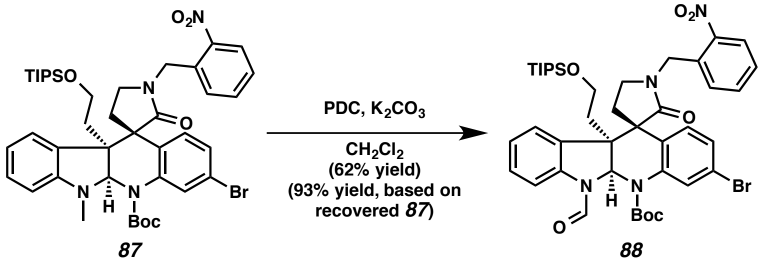
R_f = 0.33 (2:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.2 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.09 (d, *J* = 2.0 Hz, 1H), 6.98 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 6.73 (t, J = 7.7 Hz, 1H), 6.70 (dd, J = 8.4, 1.3 Hz, 1H), 6.18 (d, J = 7.6 Hz, 1H), 5.08 (d, J = 17.1 Hz, 1H), 4.47 (d, J = 17.1 Hz, 1H), 3.89 (s, br, 1H), 3.81–3.75 (m, 1H), 3.31–3.26 (m, 2H), 3.23 (td, J = 9.3, 8.5, 4.1 Hz, 1H), 3.18 (d, J = 1.5 Hz, 3H), 2.97–2.93 (m, 1H), 2.93–2.89 (m, 1H), 2.70 (dt, J = 13.7, 8.6 Hz, 1H), 1.45–1.39 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.4, 175.1, 150.3, 148.3, 143.8, 134.2, 132.5, 131.1, 131.1, 129.4, 129.2, 128.3, 127.7, 126.0, 125.3, 125.0, 124.6, 121.7, 121.3, 108.0, 58.8, 50.3, 44.6, 44.1, 43.4, 36.1, 27.6, 26.4; IR (Neat Film NaCl) 3343, 2942, 1703, 1611, 1588, 1524, 1471, 1357, 1285, 1137, 1106, 1065, 984, 858, 732 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{28}H_{26}BrN_4O_4$ [M+H]$^+$: 561.1132; found: 561.1165.



84 *87*

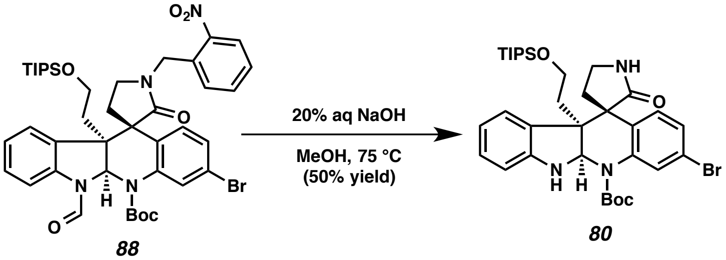
Aminal 87. Oxindole **84** (20 mg, 0.0239 mmol, 1.0 equiv) was dissolved in THF (2.39 mL) and cooled to 0 °C. AlH_3-Me_2NEt (0.5 M in toluene; 0.096 mL, 0.0478 mmol, 2.0 equiv) was added dropwise at 0 °C. The solution was stirred for 2 h and quenched with MeOH. The solution was concentrated under reduced pressure and purified by column chromatography (4:1 hexanes:EtOAc) on silica gel to afford cyclized compound **87** (8.23 mg, 42% yield; 66% yield based on recovered starting material).

R_f = 0.33 (4:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (d, J = 7.9 Hz, 1H), 7.40 (s, 1H), 7.35 (dt, J = 19.0, 7.4 Hz, 2H), 7.06–7.03 (m, 1H), 6.96 (d, J = 7.6 Hz, 1H), 6.93–6.91 (m, 2H), 6.90–6.86 (m, 1H), 6.40 (t, J = 7.4 Hz, 1H), 6.20 (s, 1H), 6.12 (d, J = 7.8 Hz, 1H), 4.75 (q, J = 16.8, 16.1 Hz, 2H), 3.78 (td, J = 10.7, 10.3, 6.0 Hz, 1H), 3.53 (q, J = 8.8 Hz, 1H), 3.46 (t, J = 9.3 Hz, 1H), 3.16–3.07 (m, 2H), 2.84(s, 3H), 2.75 (dd, J = 13.4, 6.0 Hz, 1H), 2.50 (td, J = 11.4, 5.6 Hz, 1H), 2.23–2.16 (m, 1H), 1.47 (s, 9H), 0.95 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 153.6, 150.9, 148.7, 139.9, 133.5, 132.2, 131.0, 130.6, 128.9, 128.5, 128.2, 127.8, 125.2, 124.8, 123.2, 120.6, 116.2, 104.3, 80.9, 79.6, 59.9, 56.9, 54.12, 44.49, 43.5, 39.5, 31.0, 29.6, 28.2, 26.3, 17.9, 11.9; IR (Neat Film NaCl) 2941, 2865, 1697, 1603, 1528, 1491, 1333, 1302, 1168, 1100, 992, 882, 739 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{42}H_{56}BrN_4O_6Si$ [M+H]$^+$: 819.3147; found: 819.3153.



Formyl 88. To a solution of methyl protected compound **87** (11 mg, 0.0161 mmol, 1.0 equiv) in CH_2Cl_2 (1.61 mL) was added PDC (9.1 mg, 0.0241 mmol, 1.5 equiv) at 23 °C. After being stirred at 23 °C for 12 h, the reaction mixture was quenched with water. The reaction mixture was washed with CH_2Cl_2 (3 x 2 mL), and brine. The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 hexanes:EtOAc) on silica gel to afford aldehyde **88** (7.0 mg, 62% yield; 93% yield based on recovered starting material).

R_f = 0.55 (4:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.96 (dd, *J* = 7.8, 2.5 Hz, 2H), 7.38 (q, *J* = 8.5, 8.0 Hz, 2H), 7.33 (s, br, 1H), 7.14–6.99 (m, 4H), 6.96–6.87 (m, 3H), 4.83 (s, br, 1H), 4.70 (d, 15Hz, 1H), 3.64–3.54 (m, 2H), 3.51 (t, *J* = 9.4 Hz, 1H), 3.26 (q, *J* = 10.0, 7.4 Hz, 1H), 3.11 (q, *J* = 10.9 Hz, 1H), 2.79 (dd, *J* = 13.2, 5.8 Hz, 1H), 2.58 (dt, *J* = 13.1, 7.8 Hz, 1H), 2.19 (ddd, *J* = 12.9, 7.9, 4.7 Hz, 1H), 1.44 (s, br, 9H), 0.98–0.76 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 161.4, 153.1, 148.7, 141.3, 138.3, 133.5, 131.8, 131.5, 131.2, 129.3, 128.7, 128.4, 125.1, 124.9, 124.2, 123.5, 121.1, 116.0, 81.9, 75.1, 59.4, 57.2, 54.1, 44.6, 43.6, 39.6, 29.7, 28.1, 26.3, 17.9, 17.9, 11.8; IR (Neat Film NaCl) 2942, 2866, 1683, 1591, 1527, 1489, 1393, 1323, 1280, 1155, 1096, 911, 733 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{42}H_{54}BrN_4O_7Si$ $[M+H]^+$: 833.2940; found: 833.2960.



Amide 80. To a solution of aldehyde **88** (14.8 mg, 0.0177 mmol, 1.0 equiv) in MeOH (0.4 mL) was added 20% aq NaOH (0.2 mL) and the reaction mixture was stirred for 4 h at 75 °C. The reaction mixture was diluted with EtOAc (1 mL) and the aqueous phase was extracted with EtOAc (3 x 1 mL). The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 hexanes:EtOAc) on silica gel to afford desired amide **80** (5.9 mg, 50% yield).

R_f = 0.21 (4:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.14 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.06 (dt, *J* = 7.7, 3.7 Hz, 3H), 6.70 (t, *J* = 7.4 Hz, 1H), 6.60 (d, *J* = 7.7 Hz, 1H), 6.17 (s, 1H), 5.72 (s, 1H), 3.69–3.61 (m, 1H), 3.48 (dt, *J* = 10.8, 5.6 Hz, 1H), 3.07 (m, 1H), 2.85 (m, 1H), 2.77 (m, 2H), 2.33 (d, *J* = 7.9 Hz, 1H), 1.59 (s, 9H), 0.91 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 153.9, 149.2, 138.2, 130.4, 128.9, 127.1, 126.8, 126.5, 124.4, 120.6, 119.5, 109.4, 82.5, 60.3, 55.6, 53.4, 38.9, 35.7, 31.2, 28.6, 18.4, 11.9; IR (Neat Film NaCl) 3401, 2941, 2865, 1696, 1487, 1465, 1314, 1163, 1094, 882, 740 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{34}H_{49}BrN_3O_4Si$ $[M+H]^+$: 670.2670; found: 670.2679.

1.5. References and Notes

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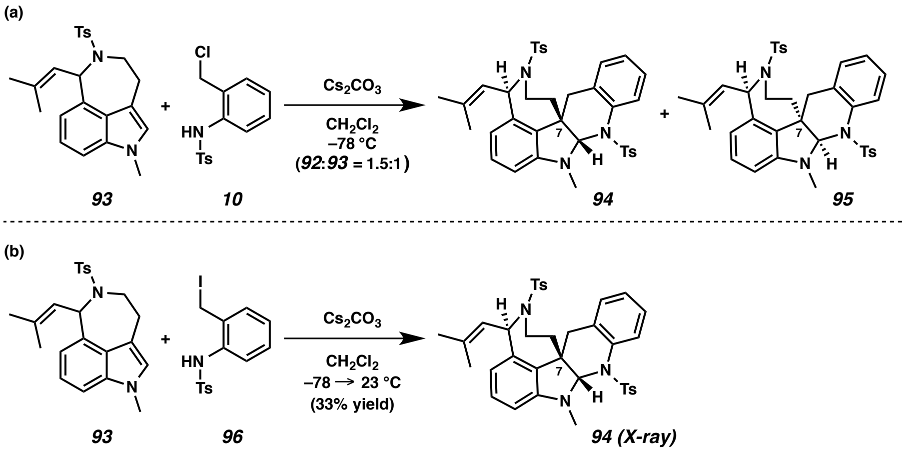
(23) We thought that the diastereoselectivity might be related to protecting groups and attempted the Diels–Alder cycloaddition with tosyl protected aurantioclavine derivative

and *o*-azaxylylene derivative. However, a change of the protecting groups did not significantly affect the diastereoselectivity of the cycloaddition.



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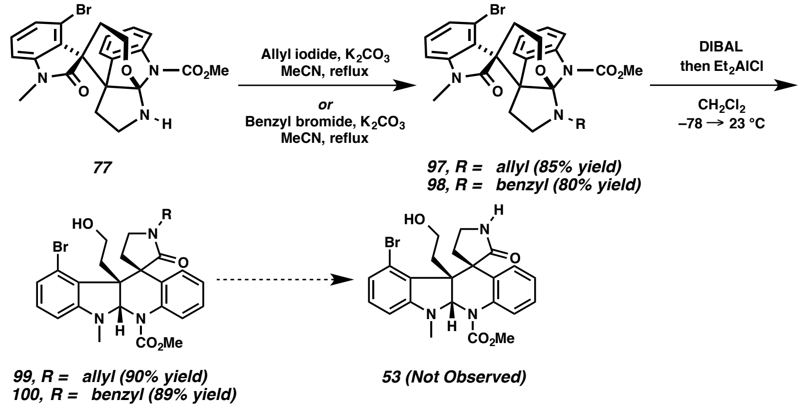
(35) Treatment of hexacyclic oxindole **77** with allyl iodide and benzyl bromide under basic conditions provided **97** and **98** in 85% and 80% yield, respectively. Although smooth reductive cyclization of the propellane hexacyclic oxindole **97** and **98** led to aminal **99** and **100**, respectively, removal of both allyl and benzyl groups on lactam **99** and **100** turned out to be challenging.



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APPENDIX 1

Spectra Relevant to Chapter 1:

The Evolution of a Unified, Stereodivergent Approach to the Synthesis of Communesin F and Perophoramidine

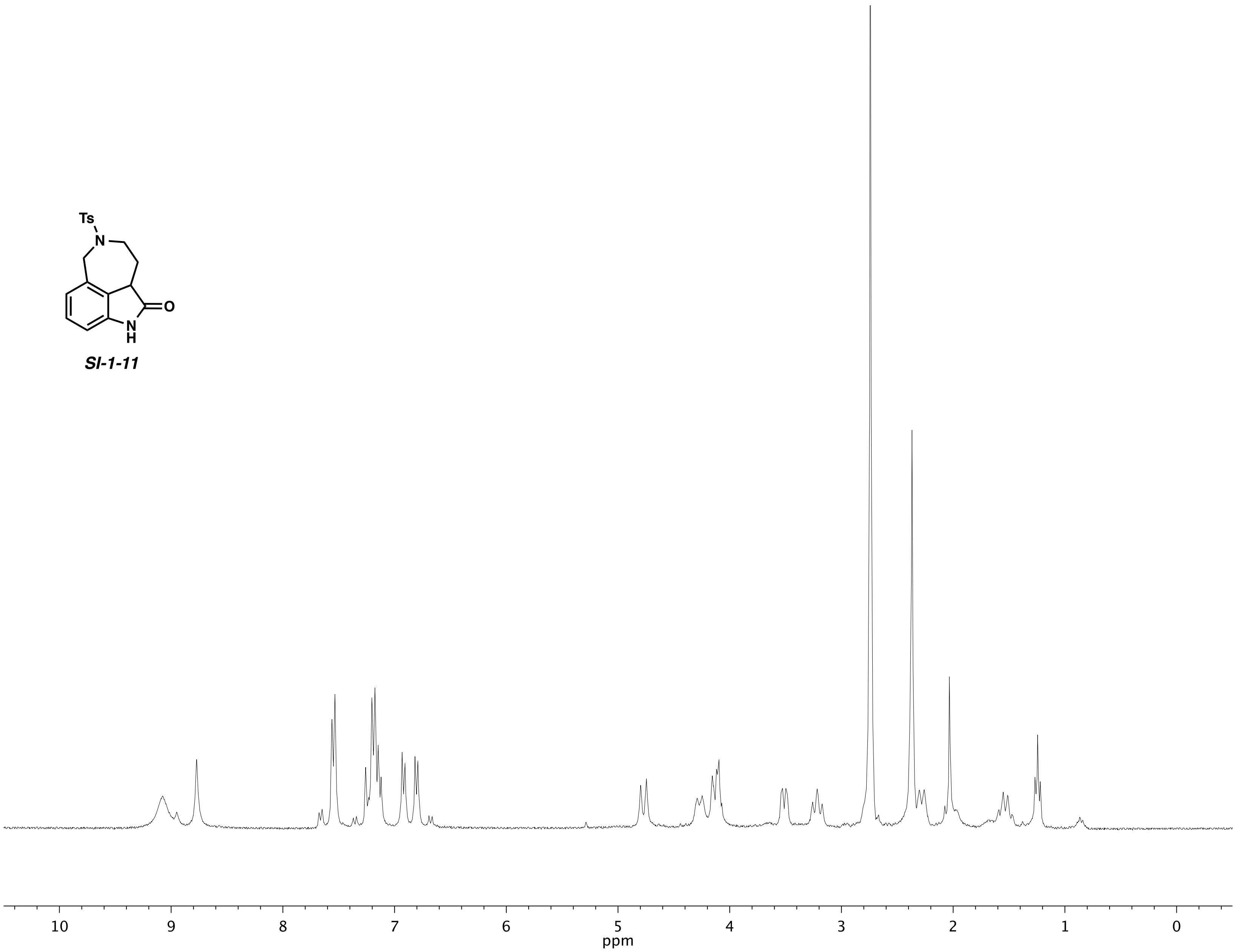


Figure A1.1. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **SI-1-11**.

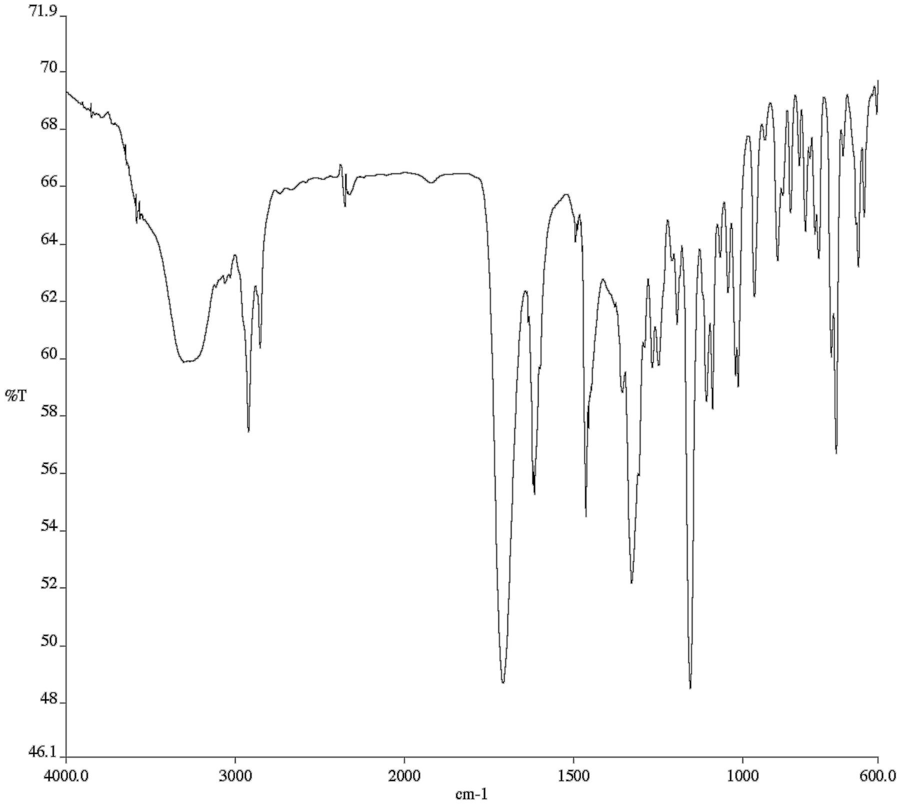


Figure A1.2. Infrared spectrum (Thin Film, NaCl) of compound **SI-1-11**.

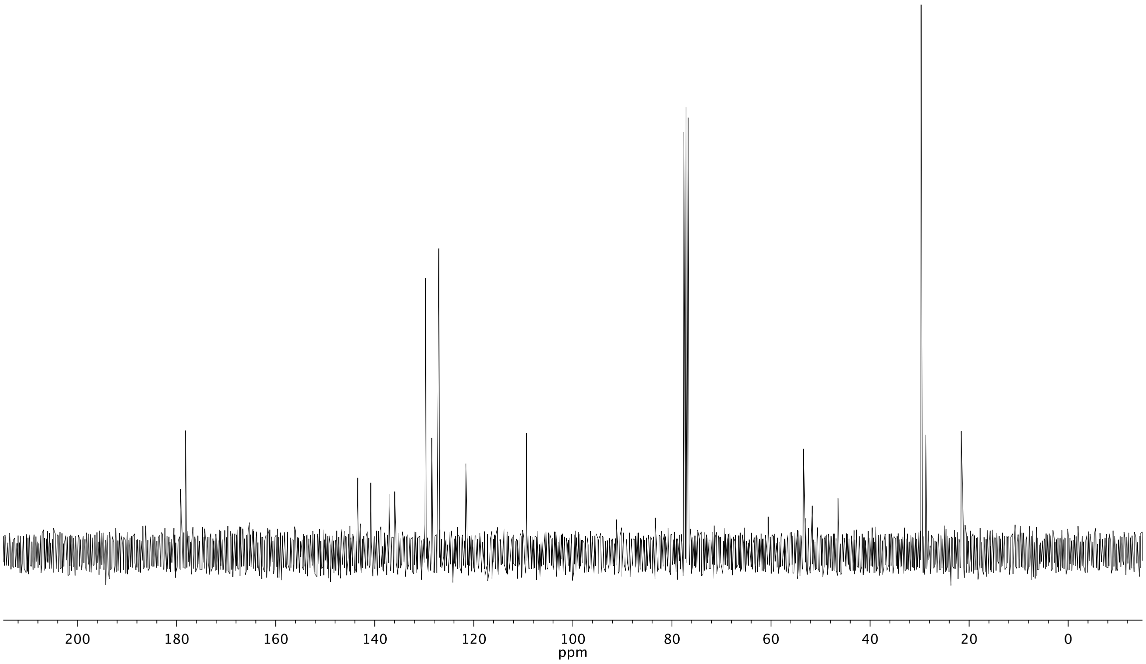


Figure A1.3. ^{13}C NMR (75 MHz, CDCl$_3$) of compound **SI-1-11**.

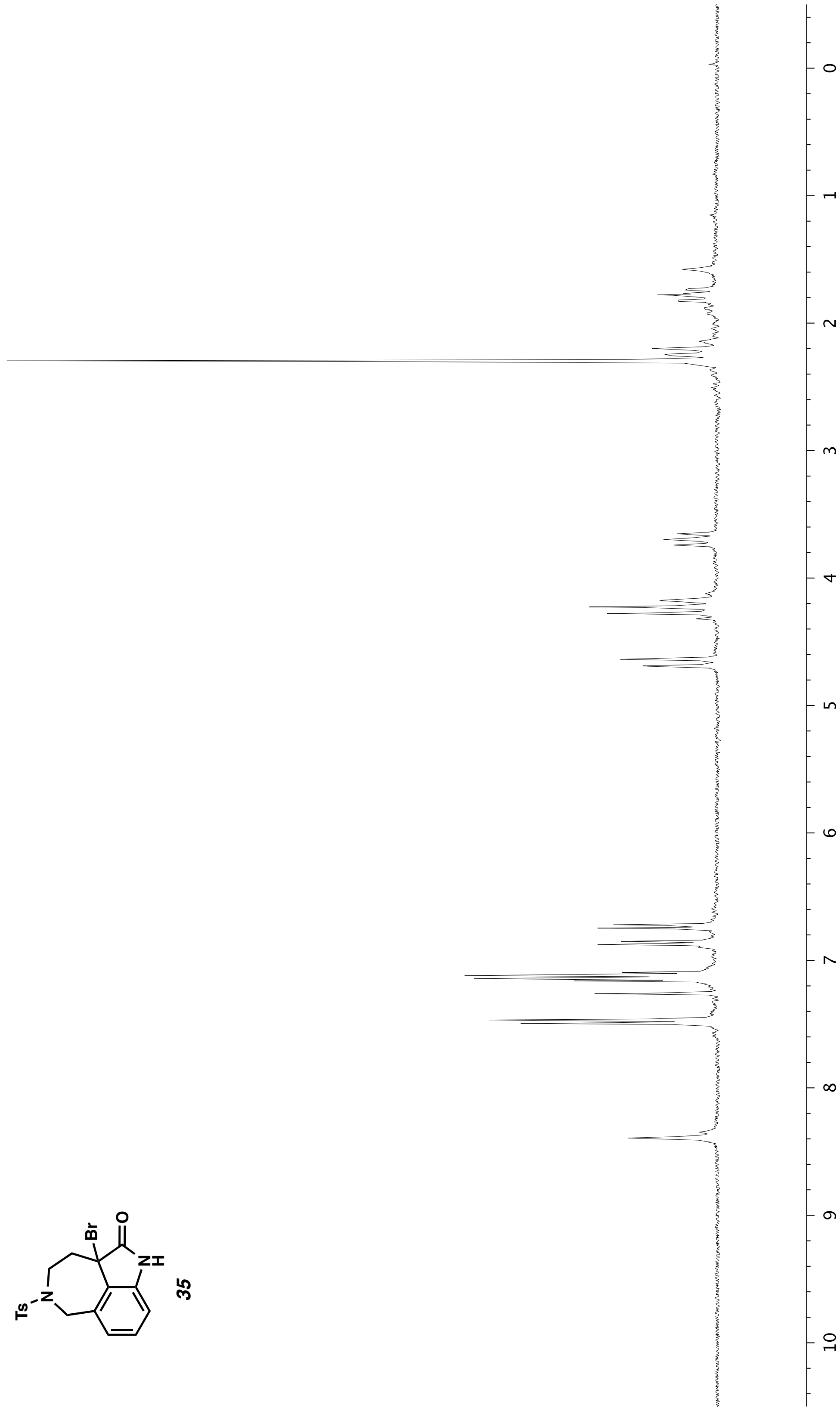


Figure A1.4. ^{1}H NMR (300 MHz, CDCl$_3$) of compound **35**.

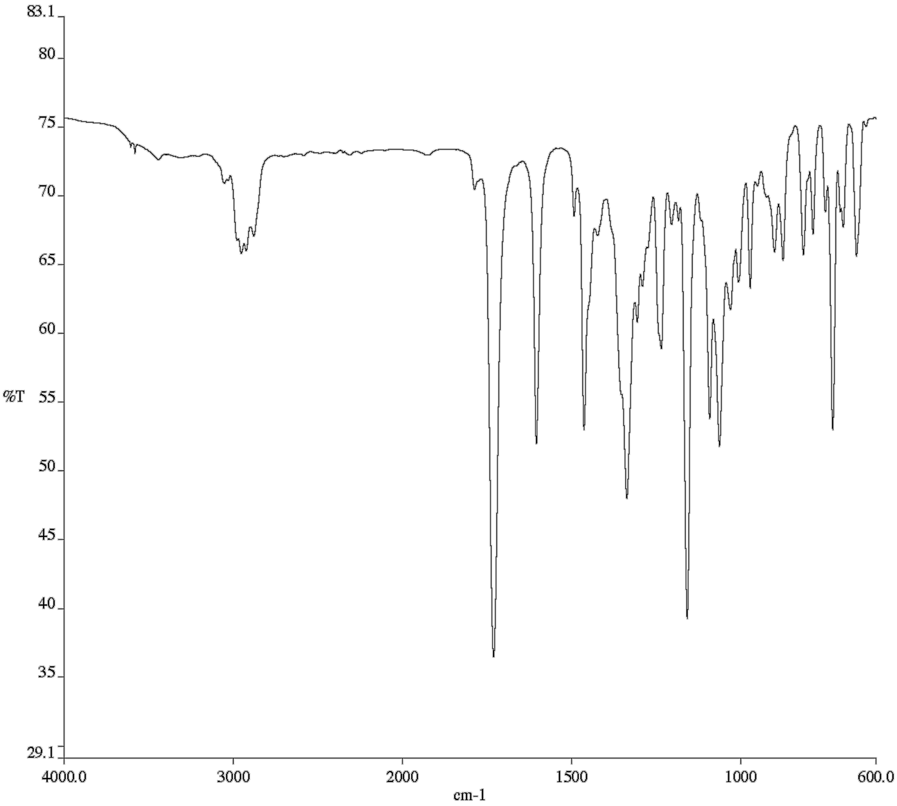


Figure A1.5. Infrared spectrum (Thin Film, NaCl) of compound **35**.

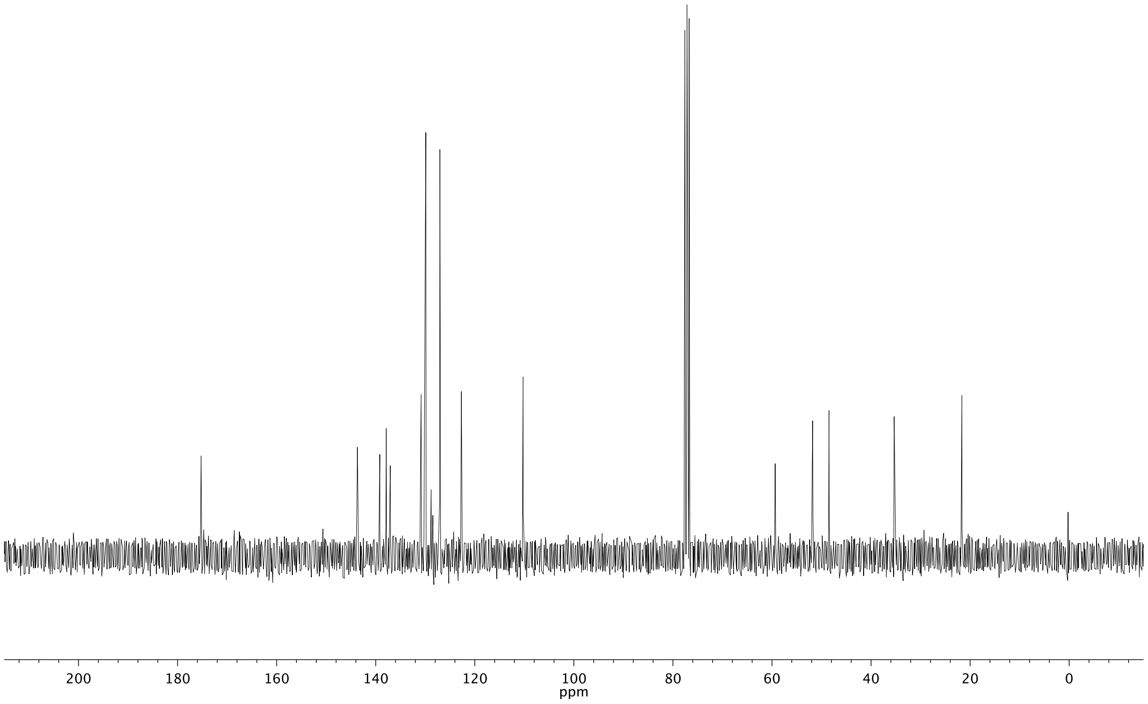


Figure A1.6. ^{13}C NMR (75 MHz, CDCl$_3$) of compound **35**.

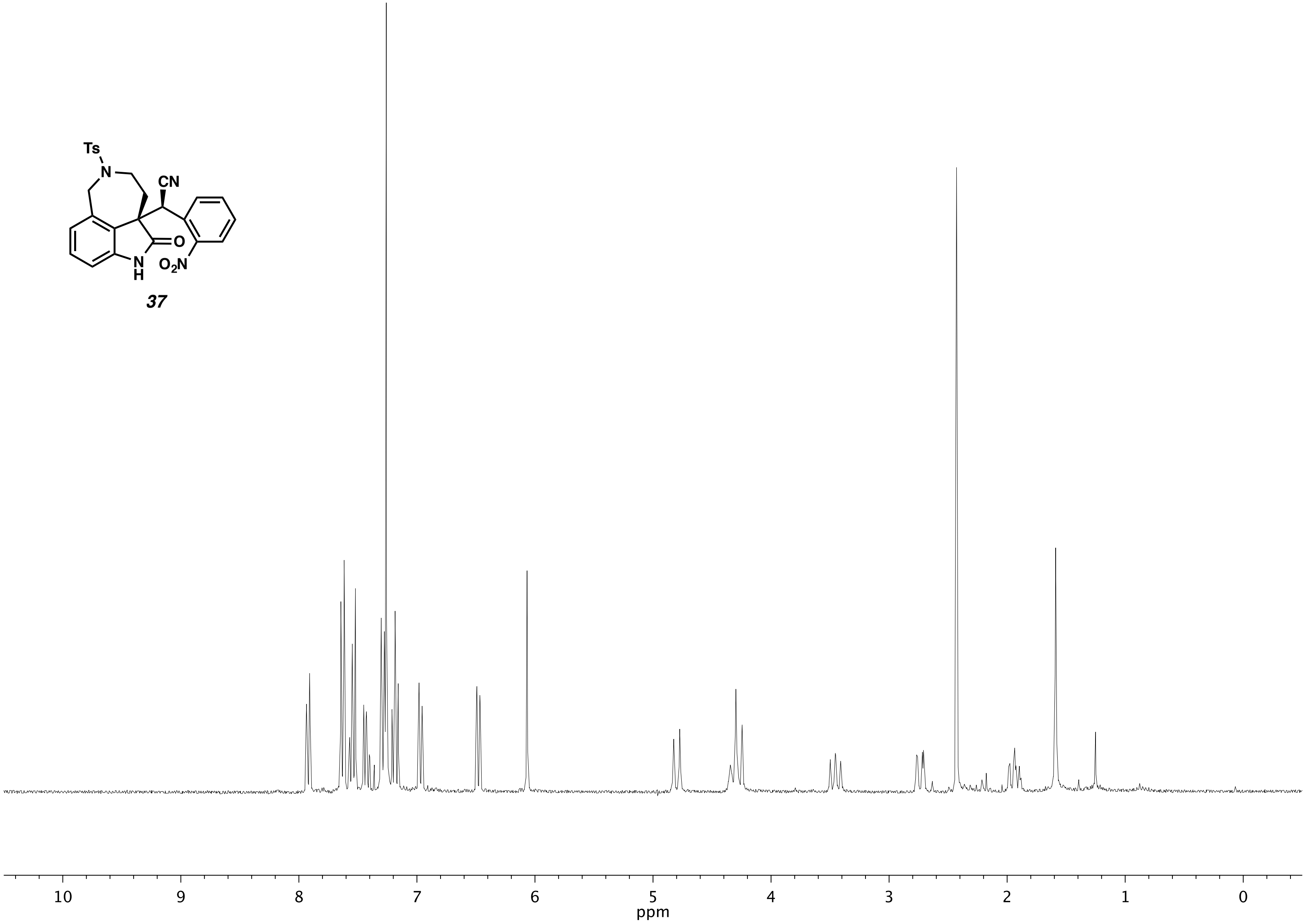


Figure A1.7. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **37**.

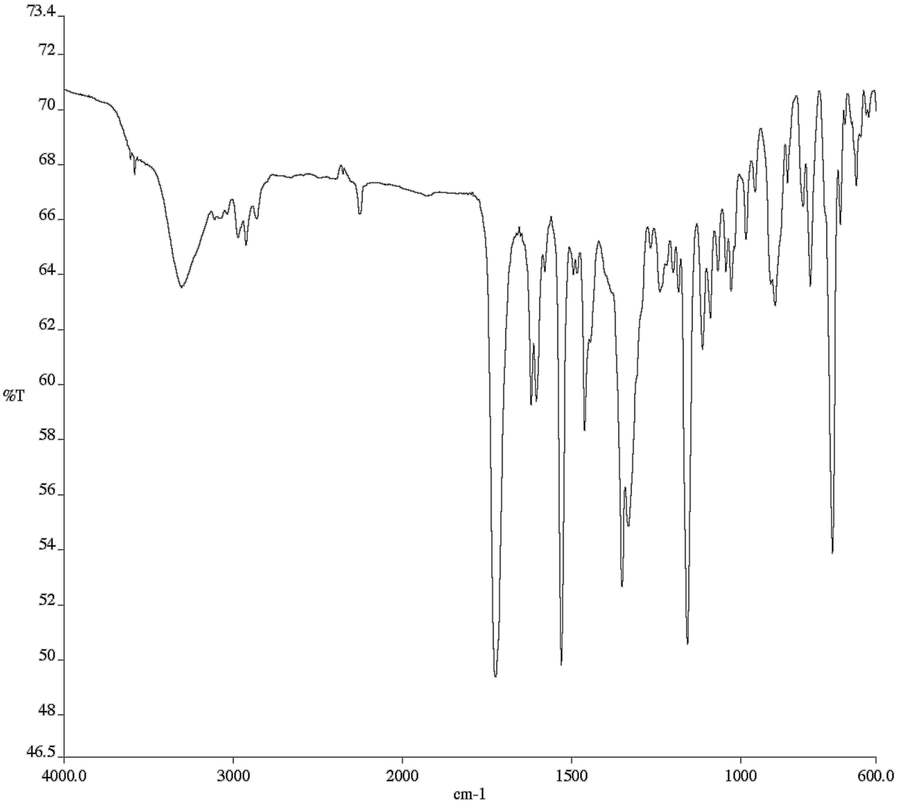


Figure A1.8. Infrared spectrum (Thin Film, NaCl) of compound **37**.

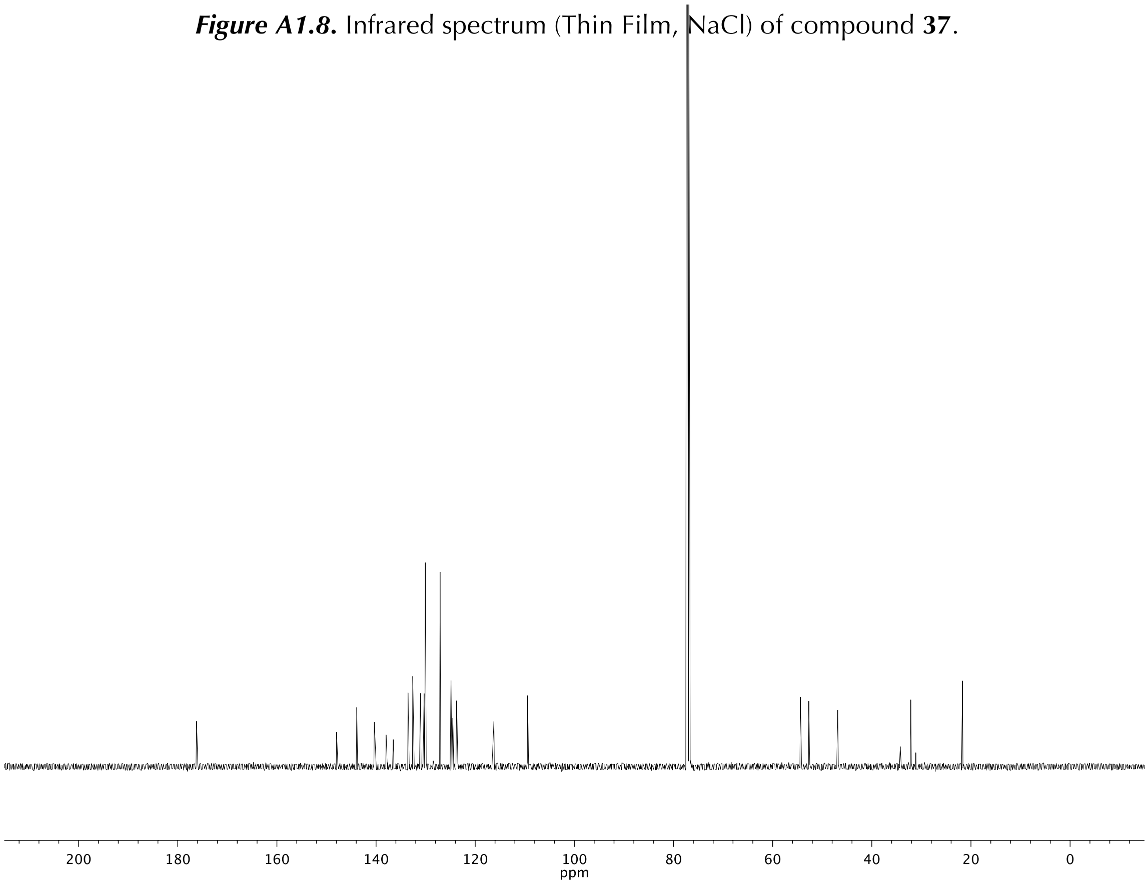
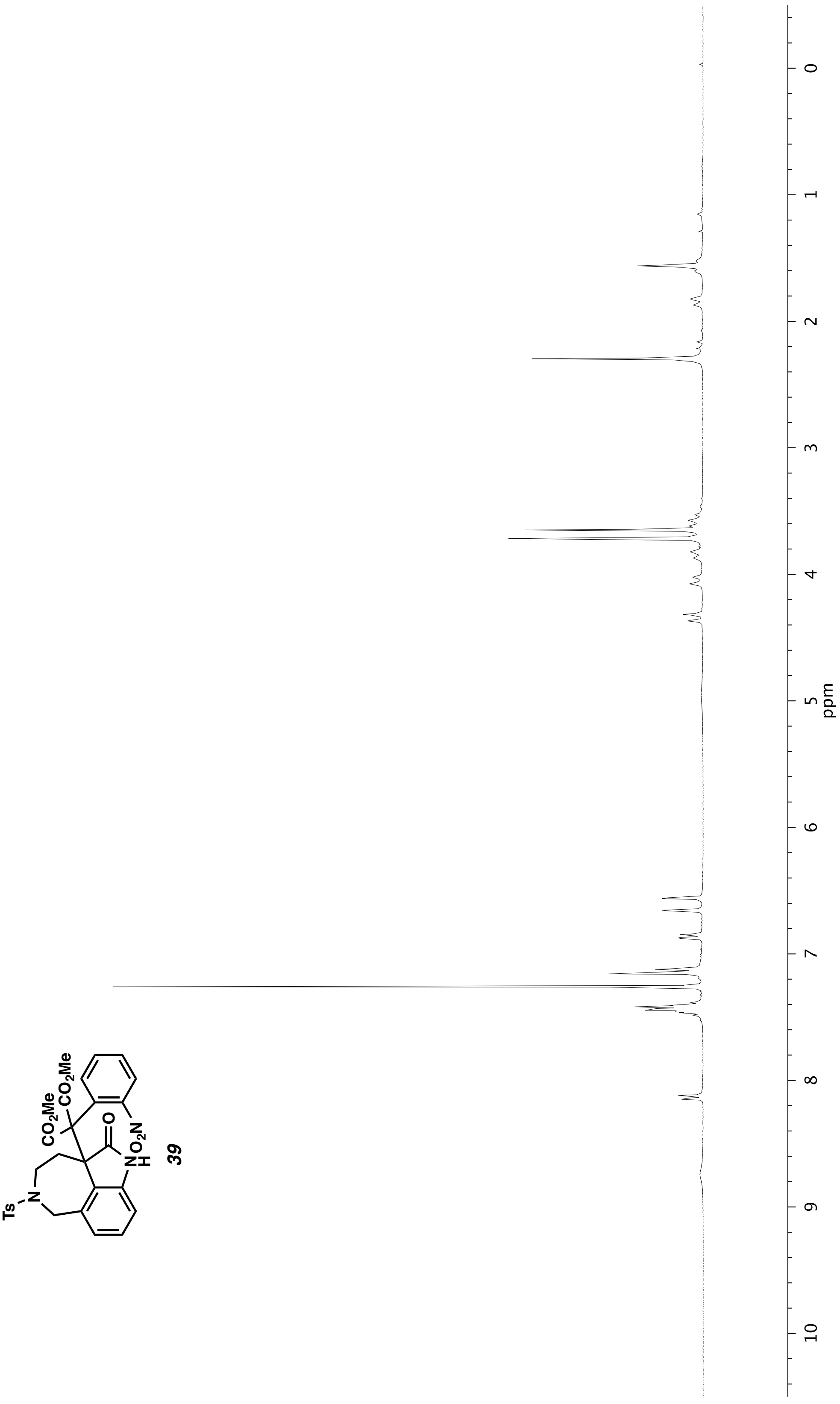


Figure A1.9. ^{13}C NMR (75 MHz, CDCl$_3$) of compound **37**.



39

Figure A1.10. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **39**.

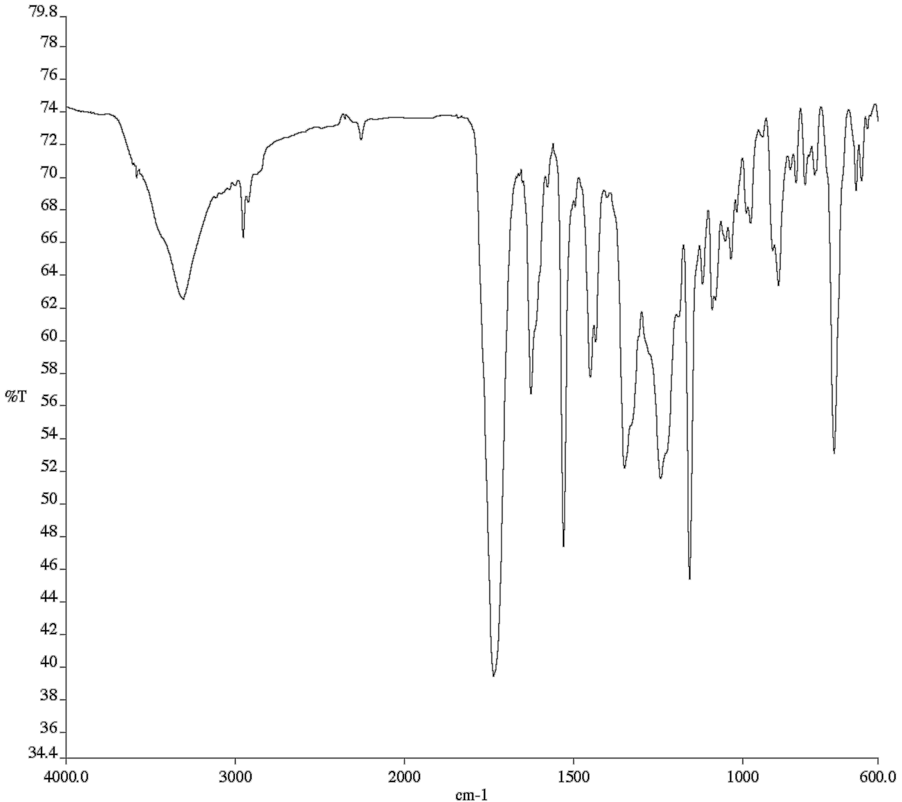


Figure A1.11. Infrared spectrum (Thin Film, NaCl) of compound **39**.

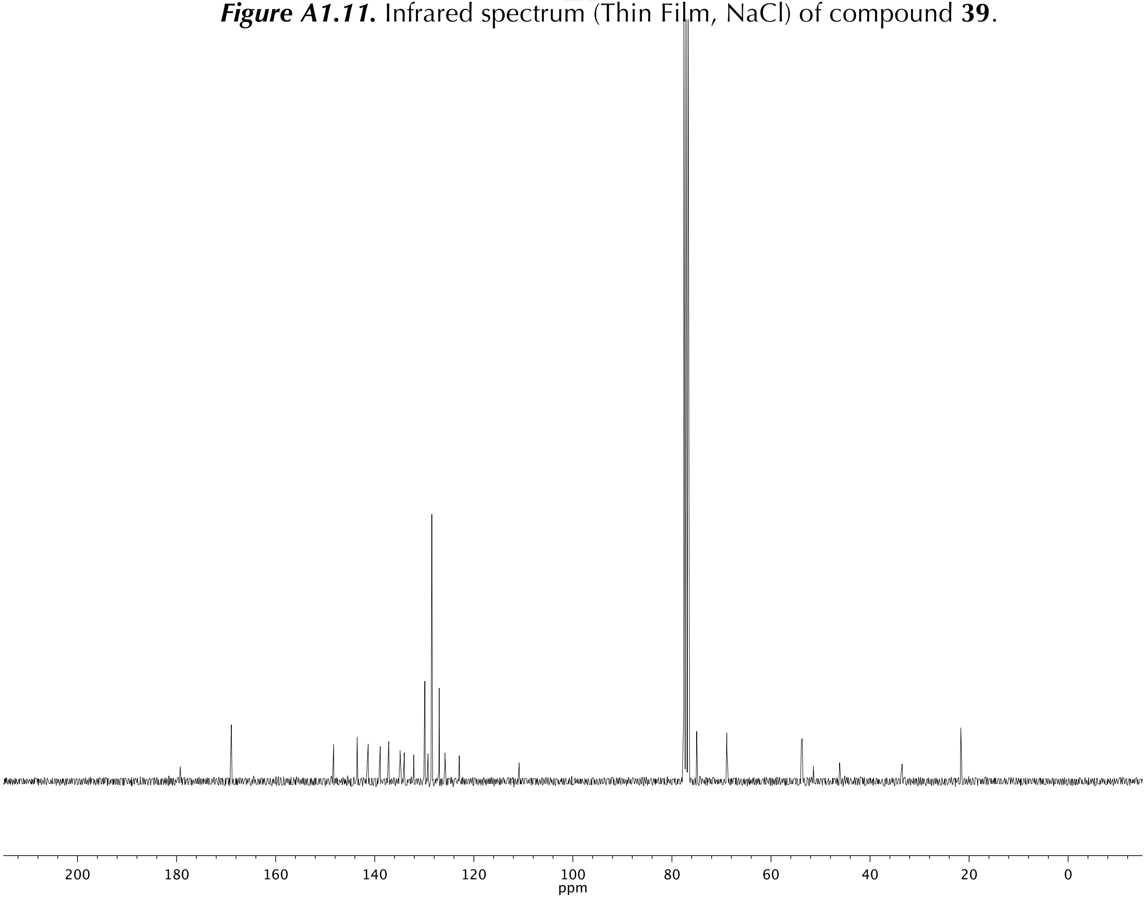
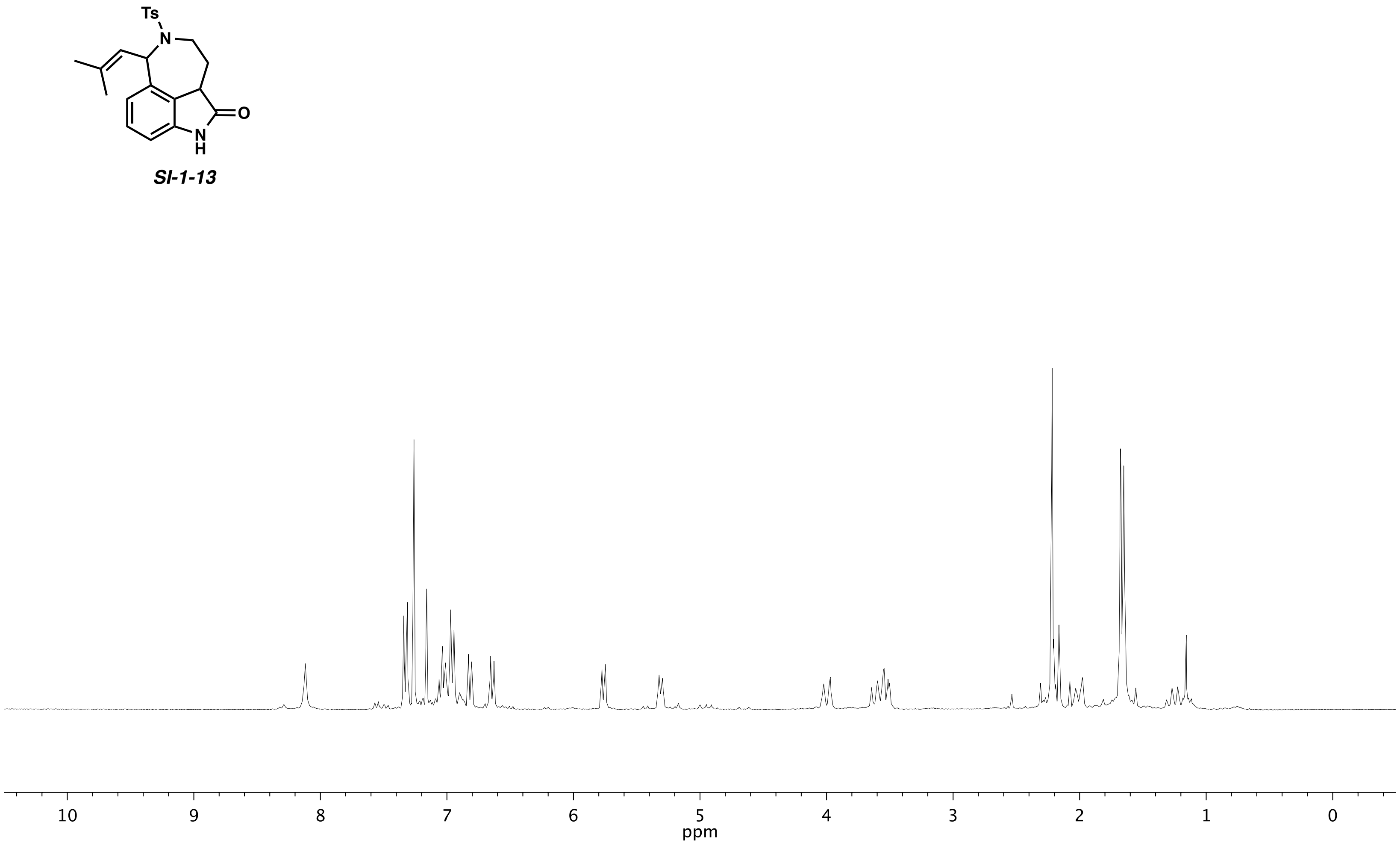


Figure A1.12. ^{13}C NMR (75 MHz, CDCl$_3$) of compound **39**.



SI-1-13

Figure A1.13. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **SI-1-13**.

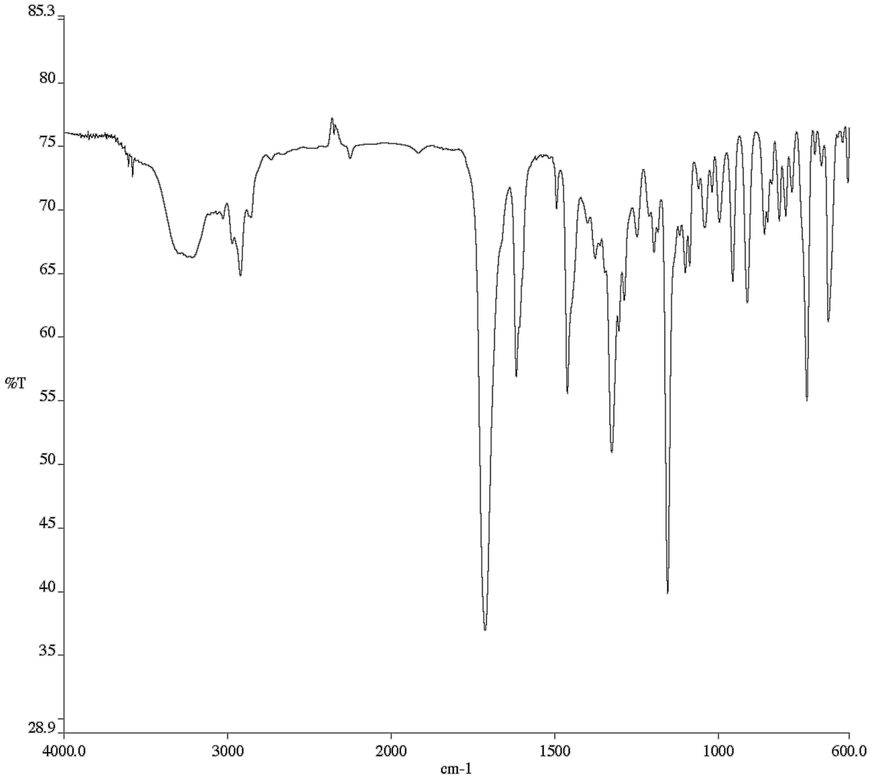


Figure A1.14. Infrared spectrum (Thin Film, NaCl) of compound **SI-1-13**.

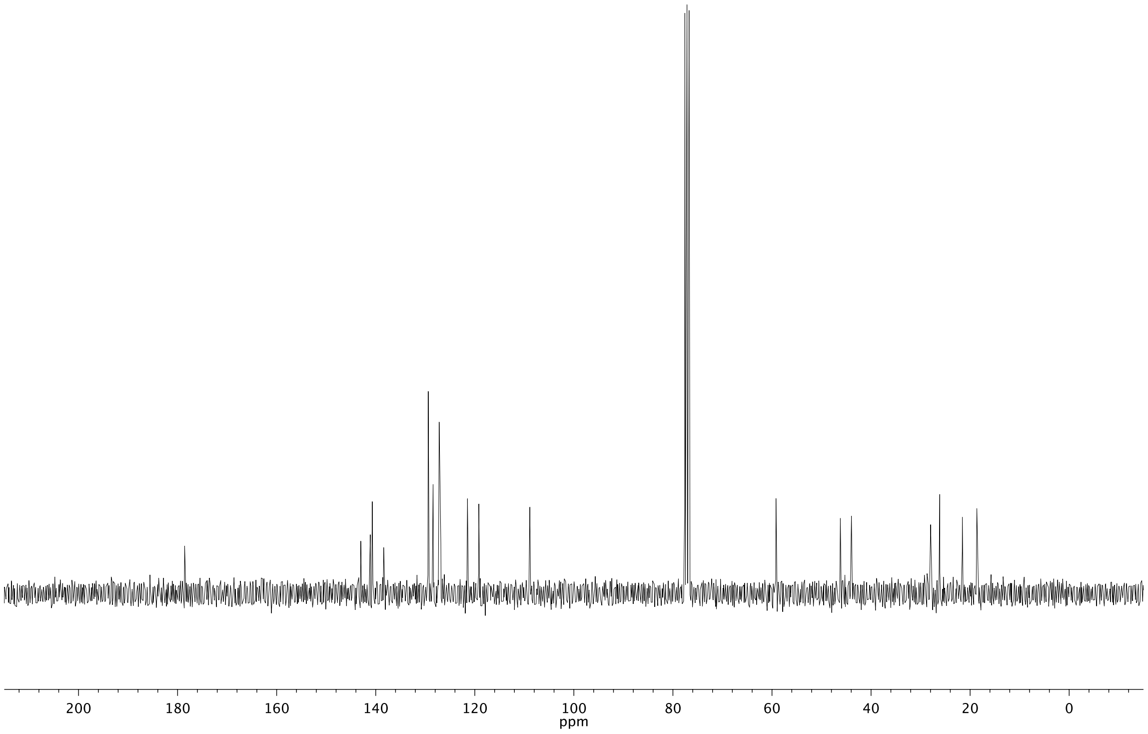
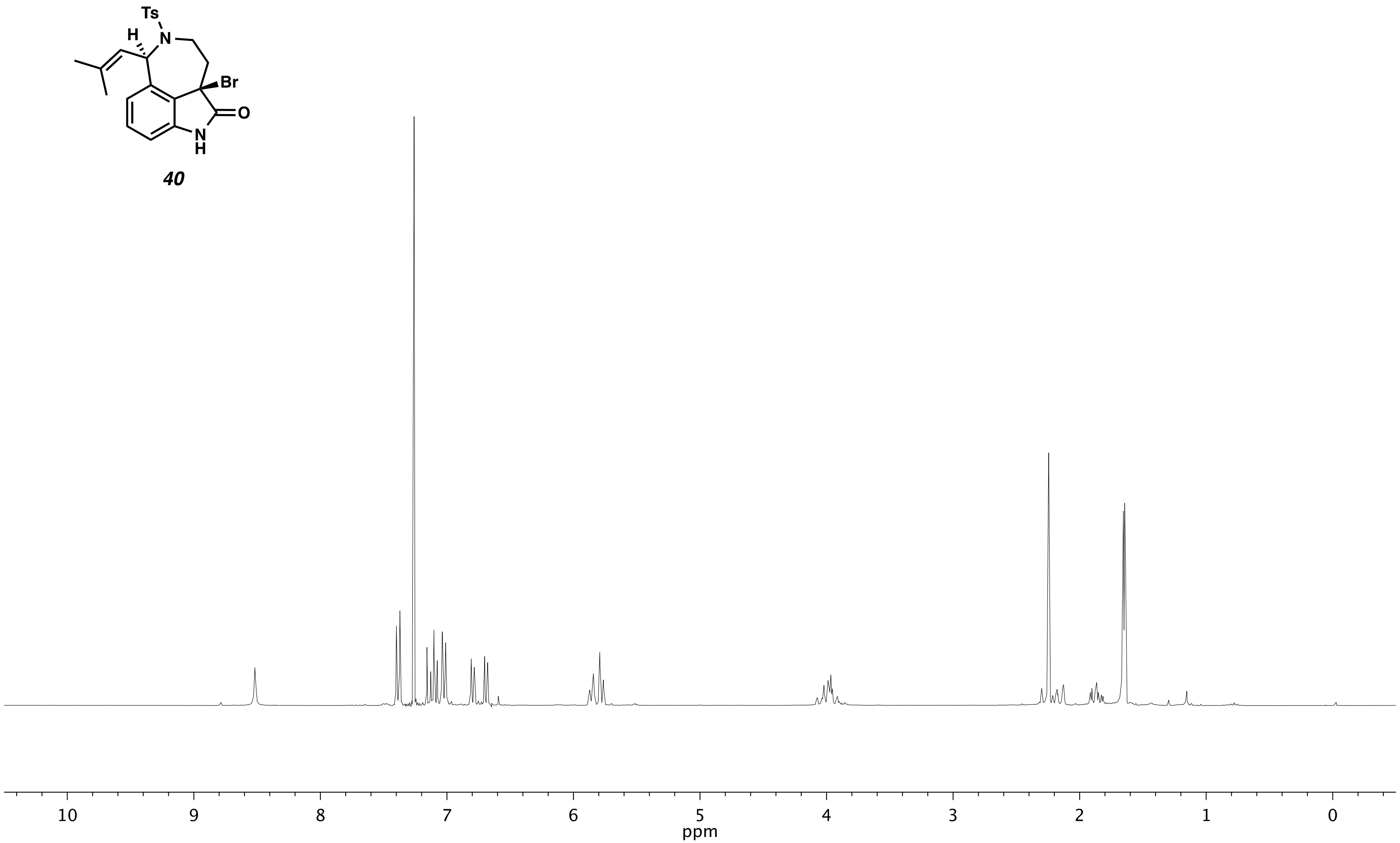


Figure A1.15. ^{13}C NMR (75 MHz, CDCl$_3$) of compound **SI-1-13.**



40

Figure A1.16. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **40**.

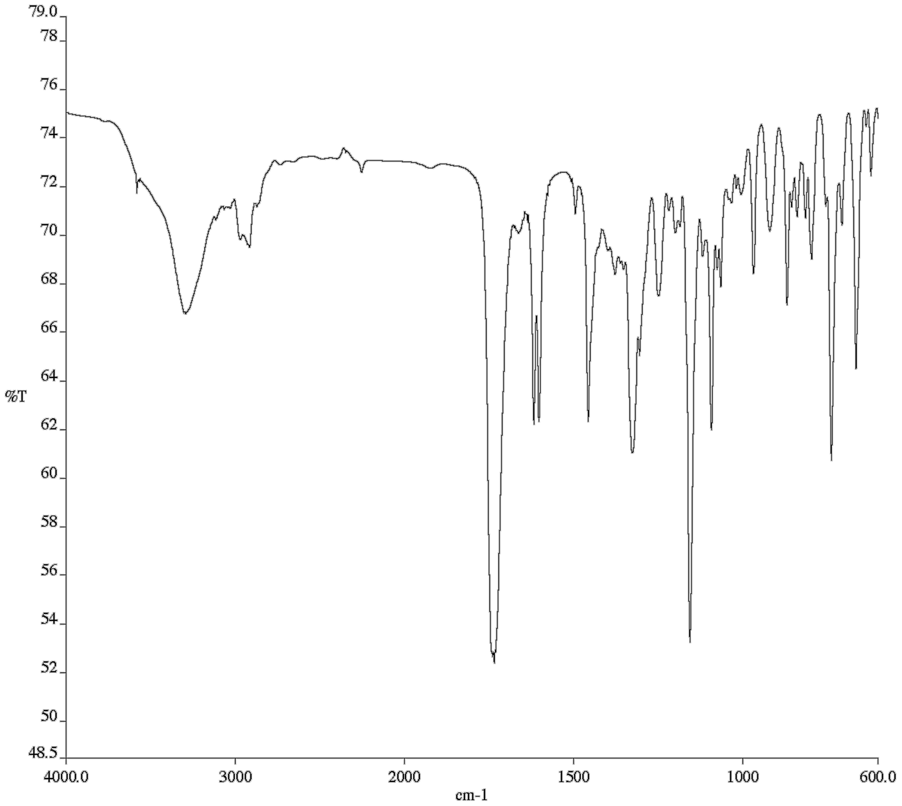


Figure A1.17. Infrared spectrum (Thin Film, NaCl) of compound **40**.

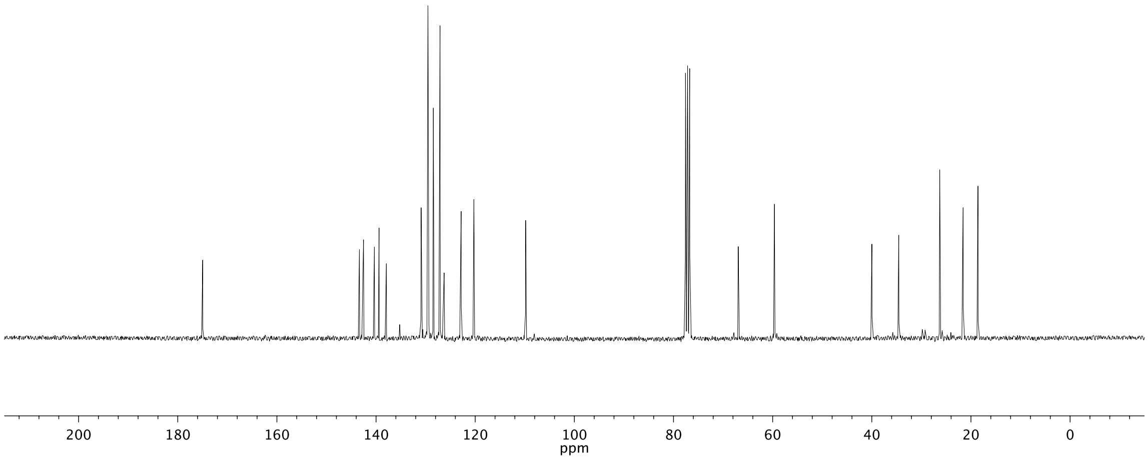
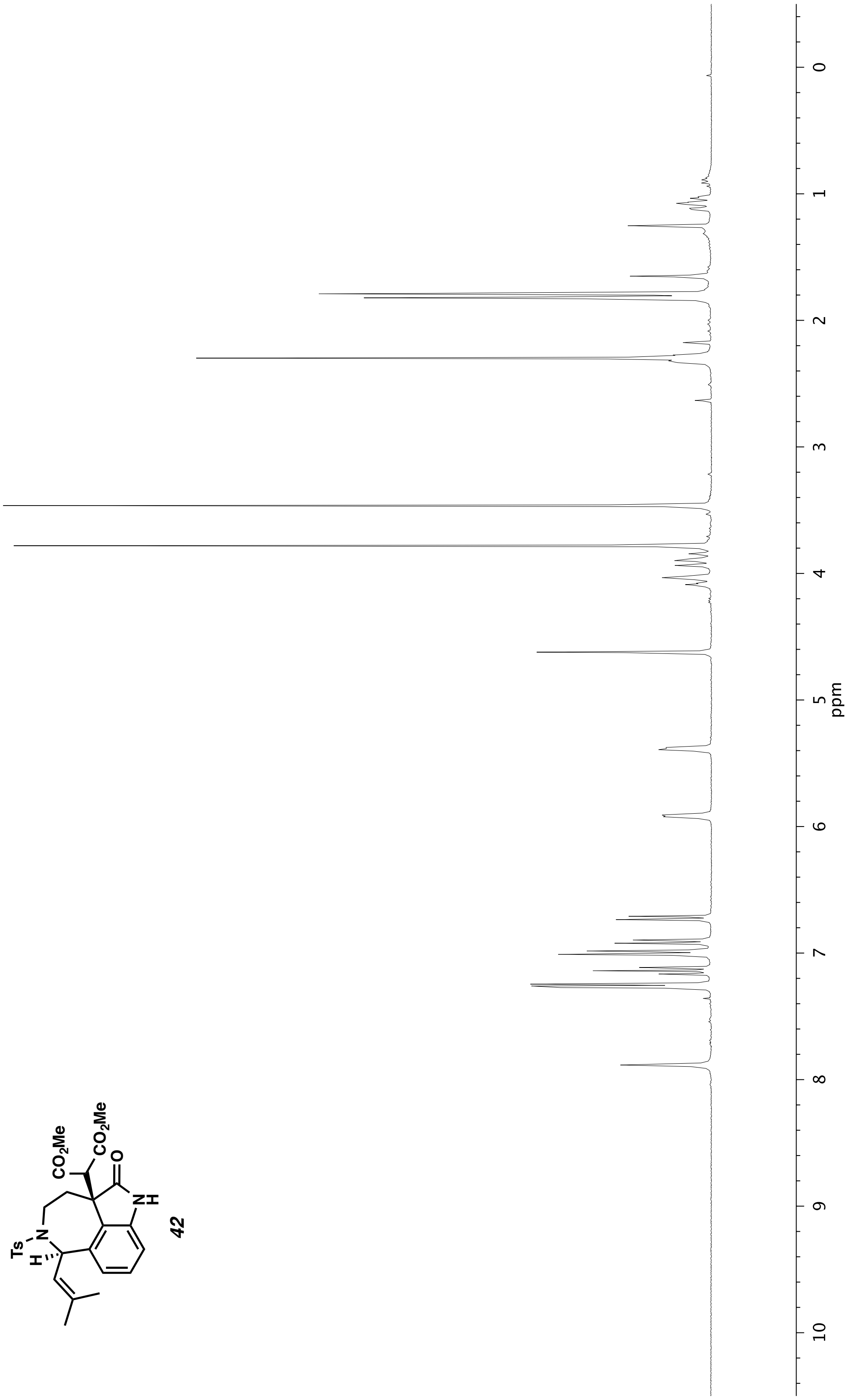


Figure A1.18. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **40.**



42

Figure A1.19. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **42**.

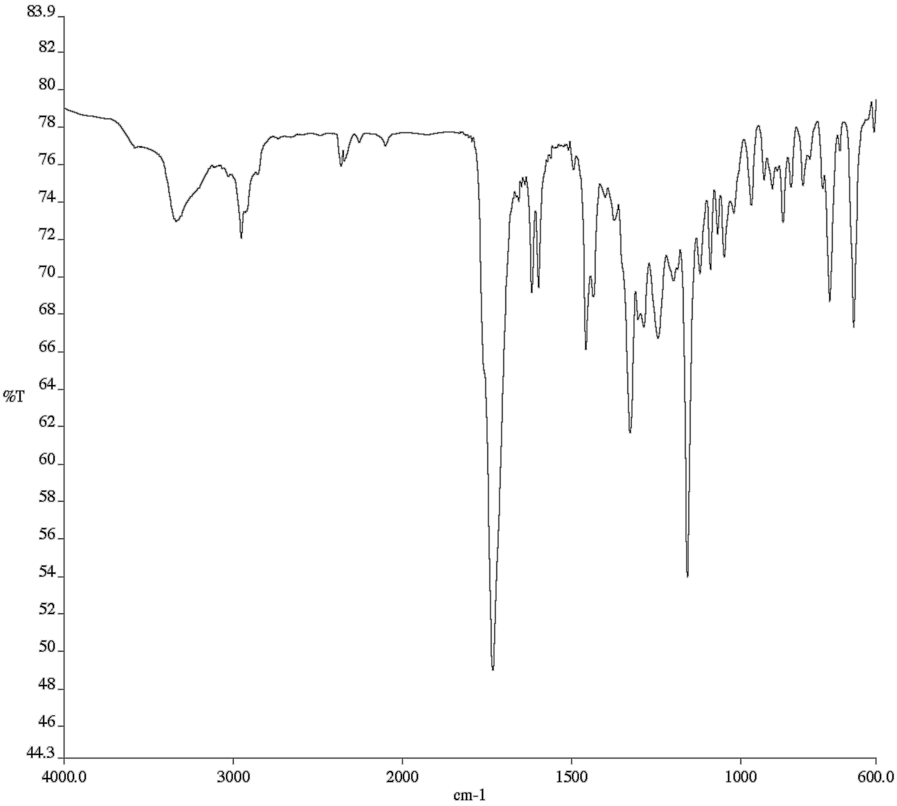


Figure A1.20. Infrared spectrum (Thin Film, NaCl) of compound **42**.

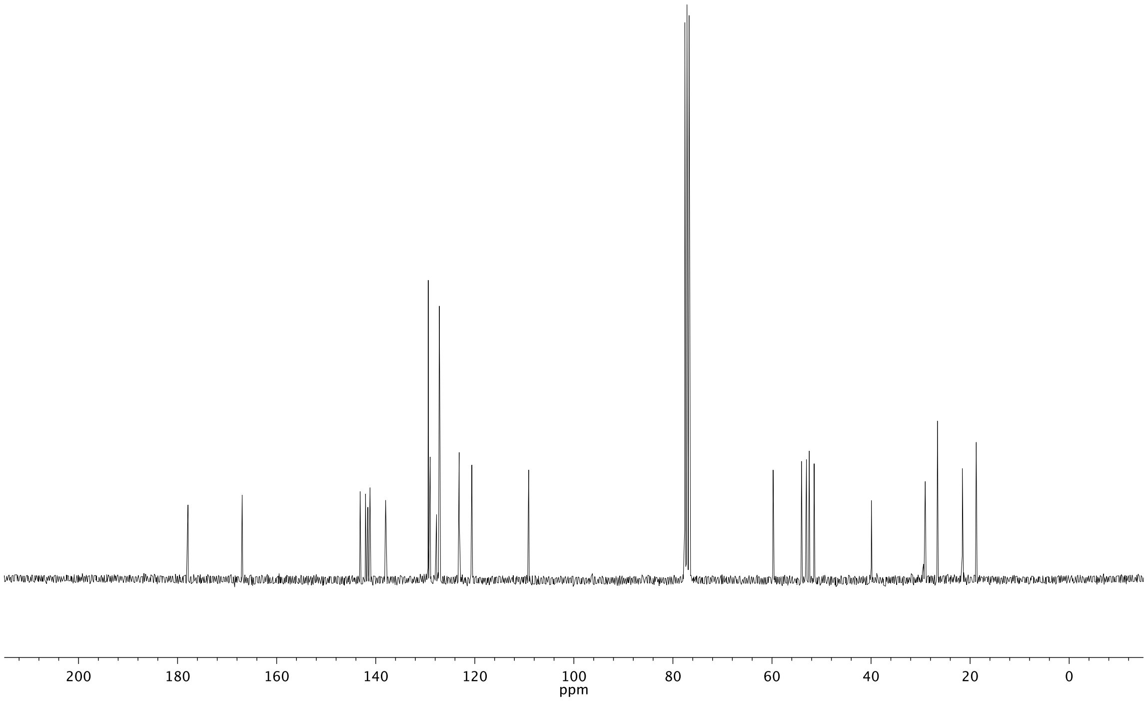


Figure A1.21. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **42.**

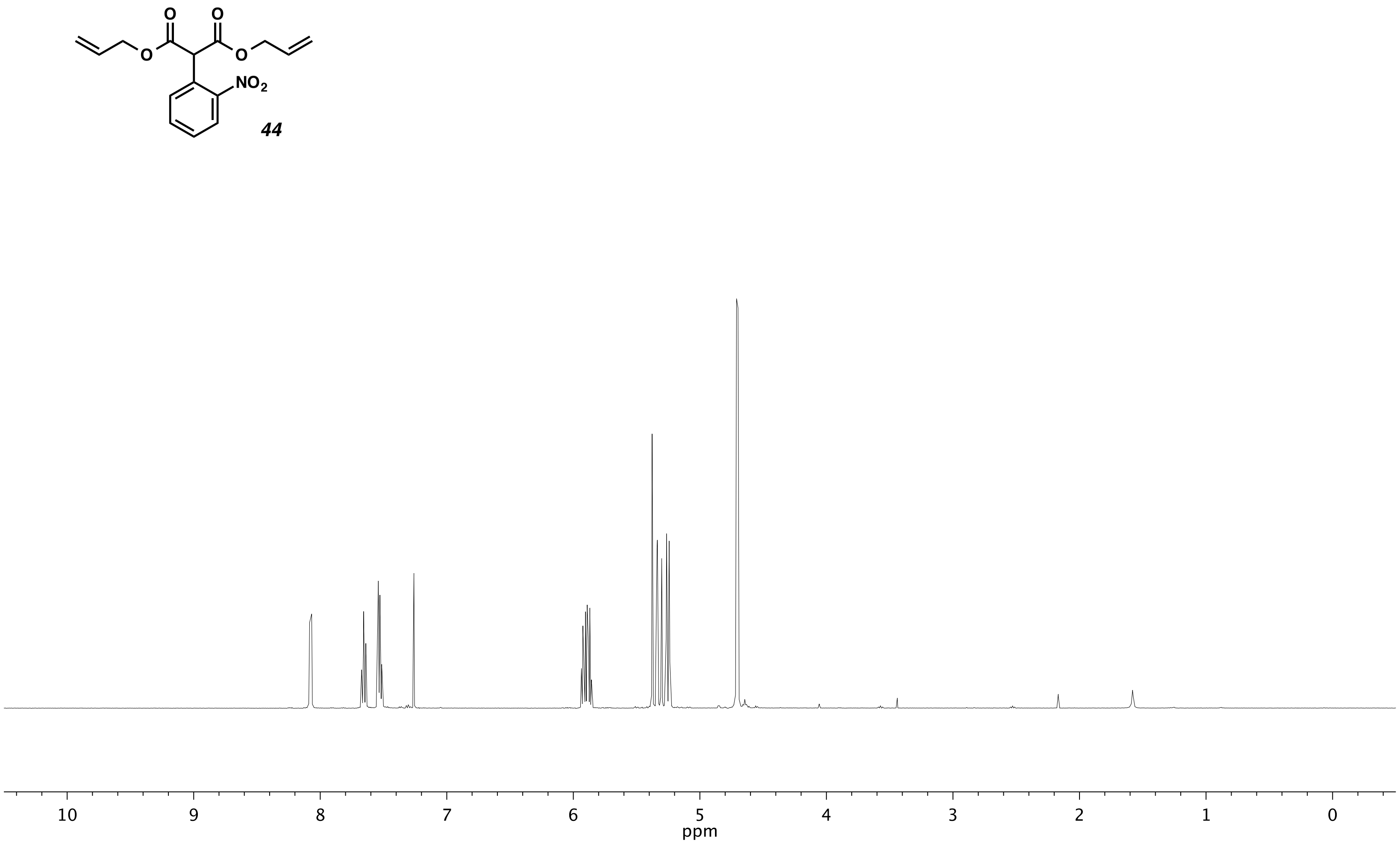


Figure A1.22. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **44**.

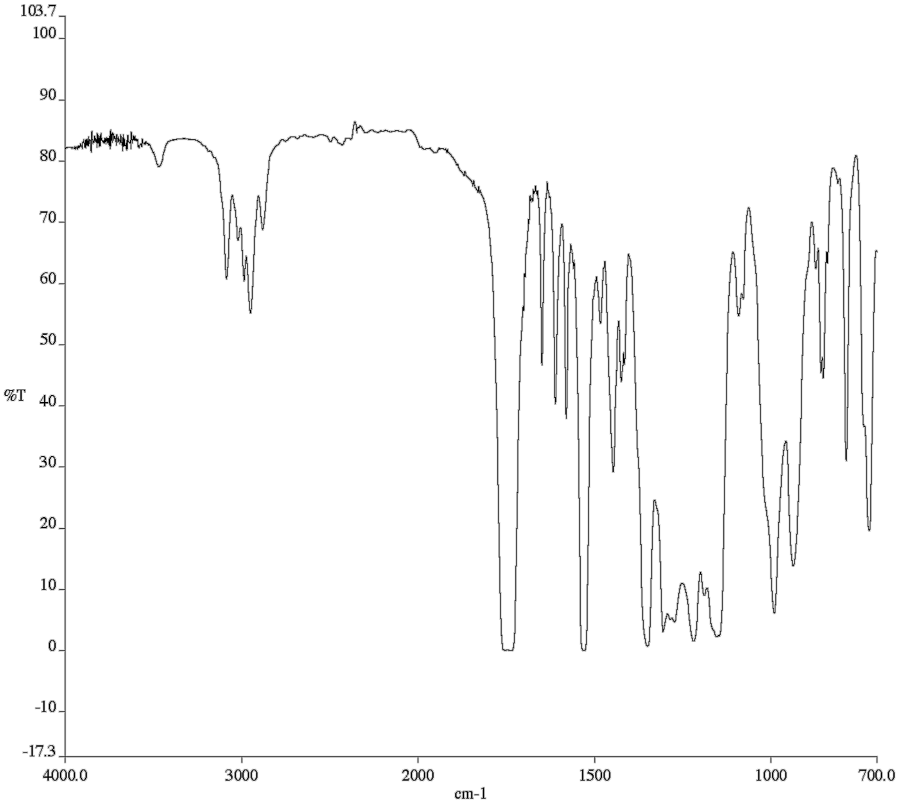


Figure A1.23. Infrared spectrum (Thin Film, NaCl) of compound **44**.

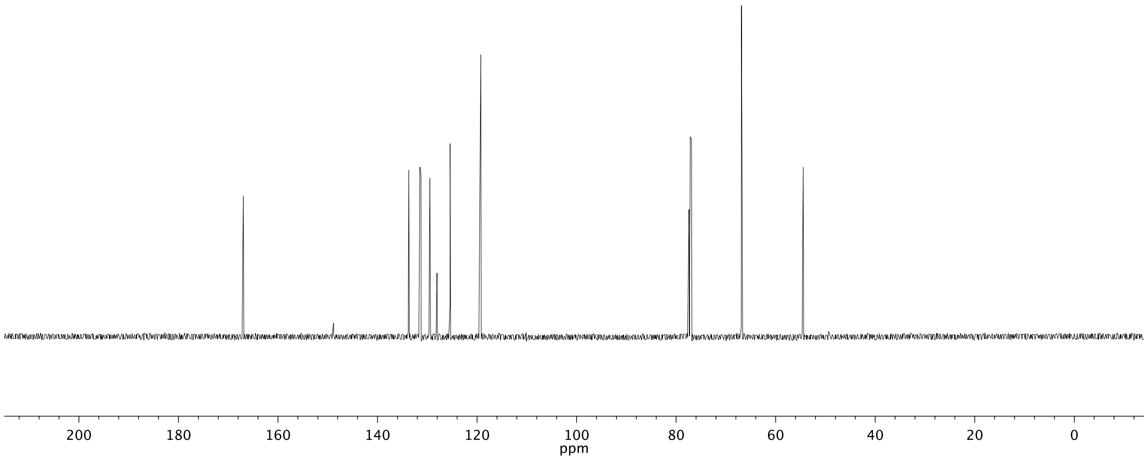


Figure A1.24. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **44**.

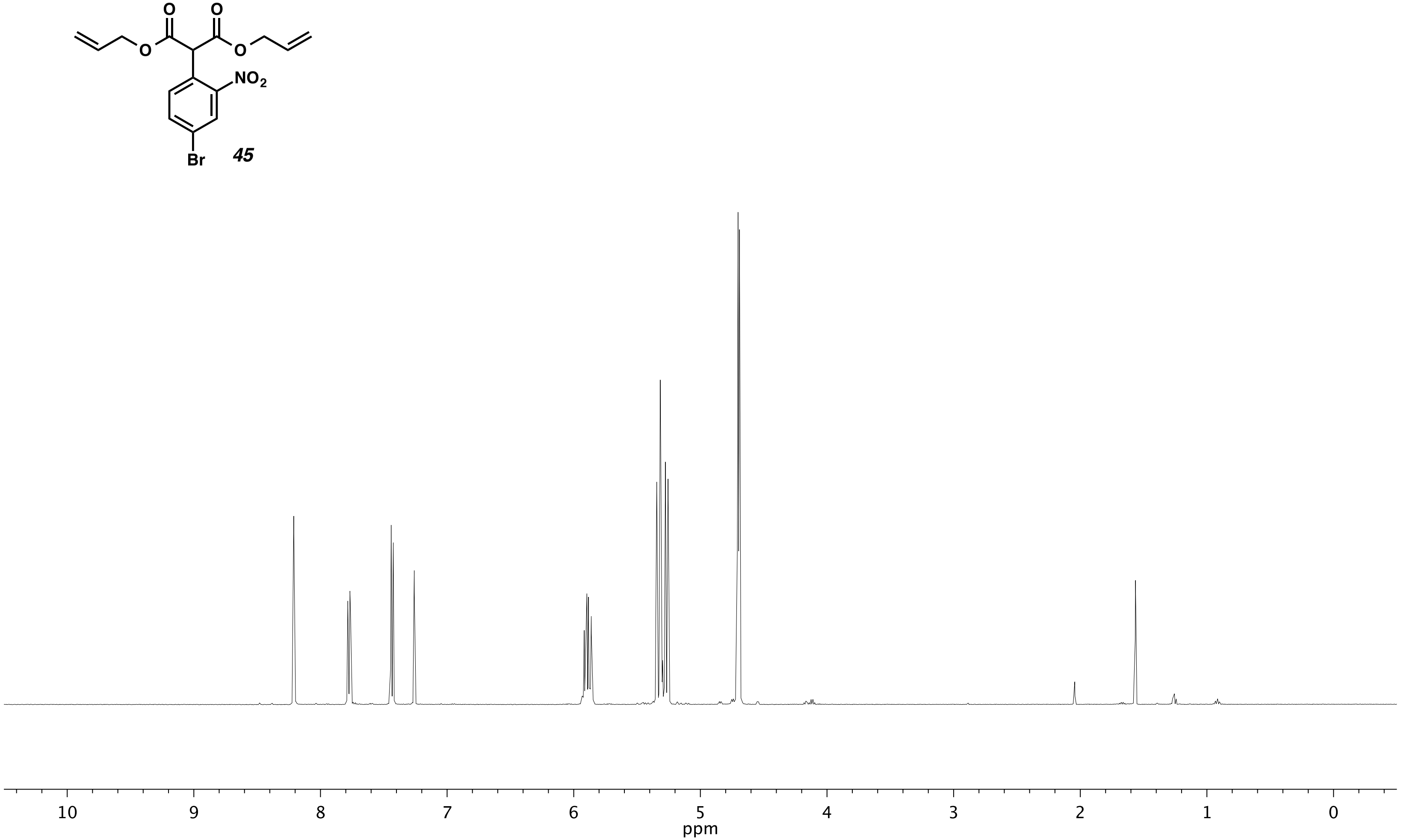


Figure A1.25. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **45**.

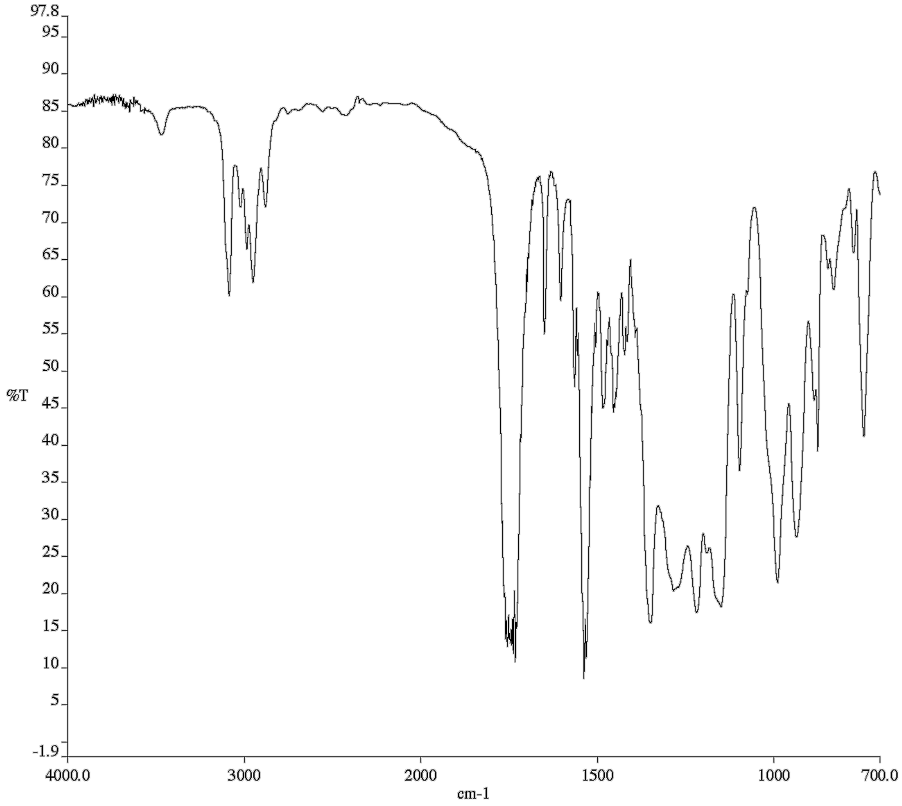


Figure A1.26. Infrared spectrum (Thin Film, NaCl) of compound **45**.

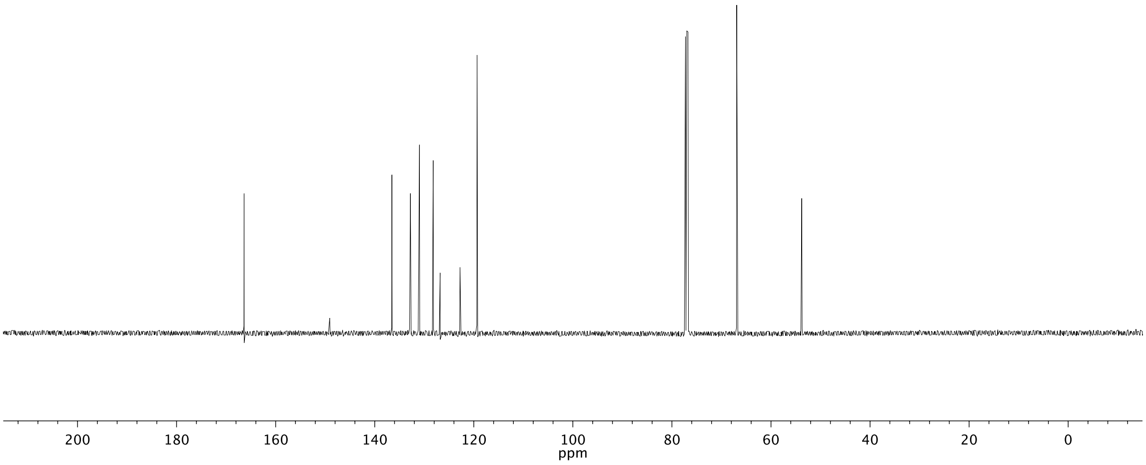


Figure A1.27. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **45**.

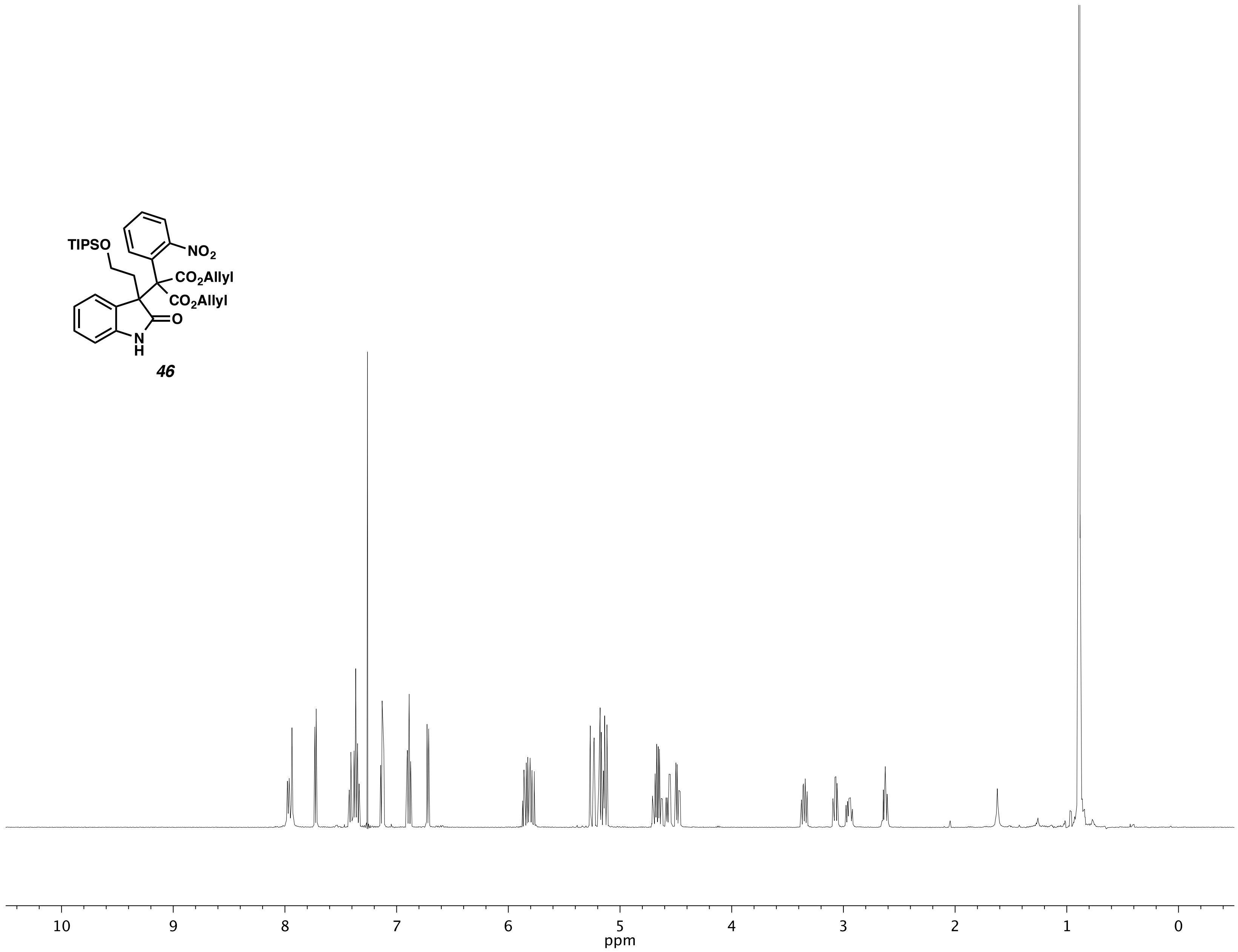


Figure A1.28. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **46**.

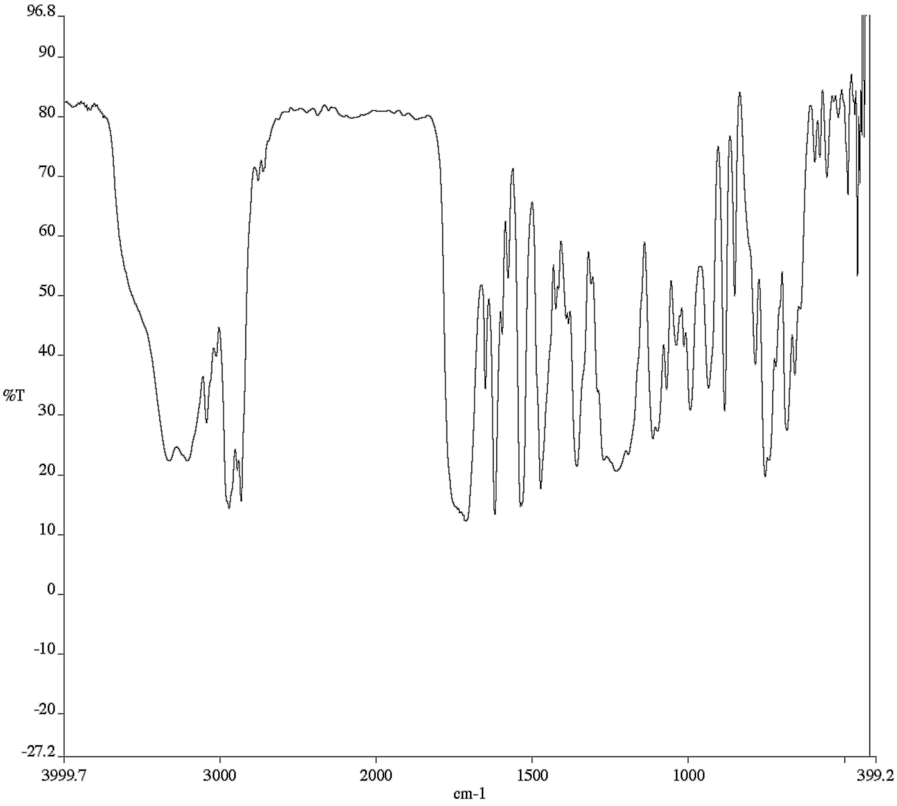


Figure A1.29. Infrared spectrum (Thin Film, NaCl) of compound **46**.

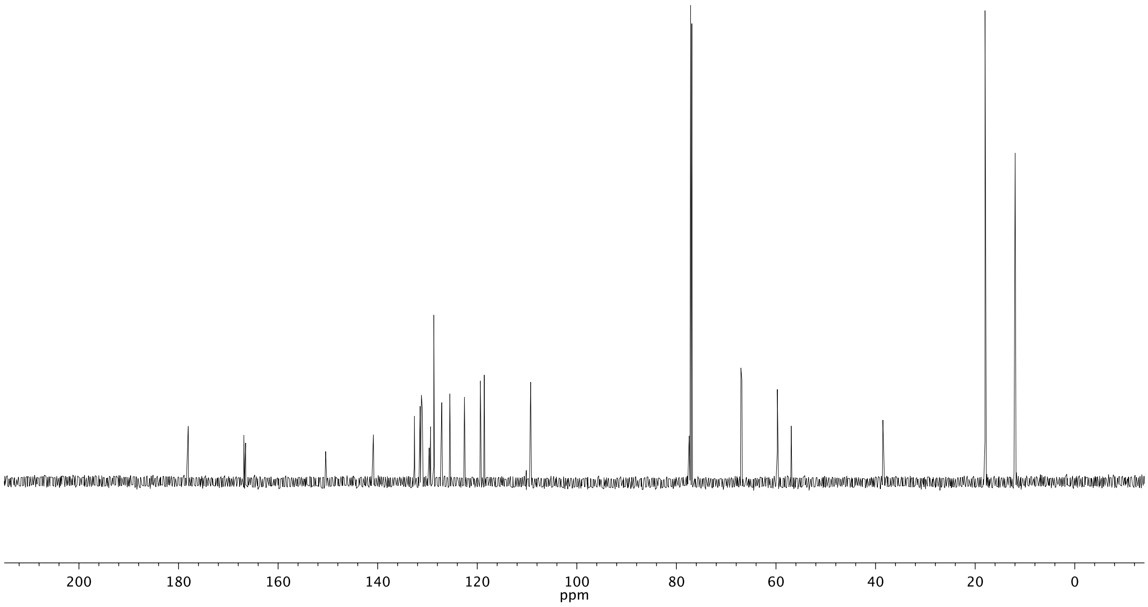


Figure A1.30. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **46**.

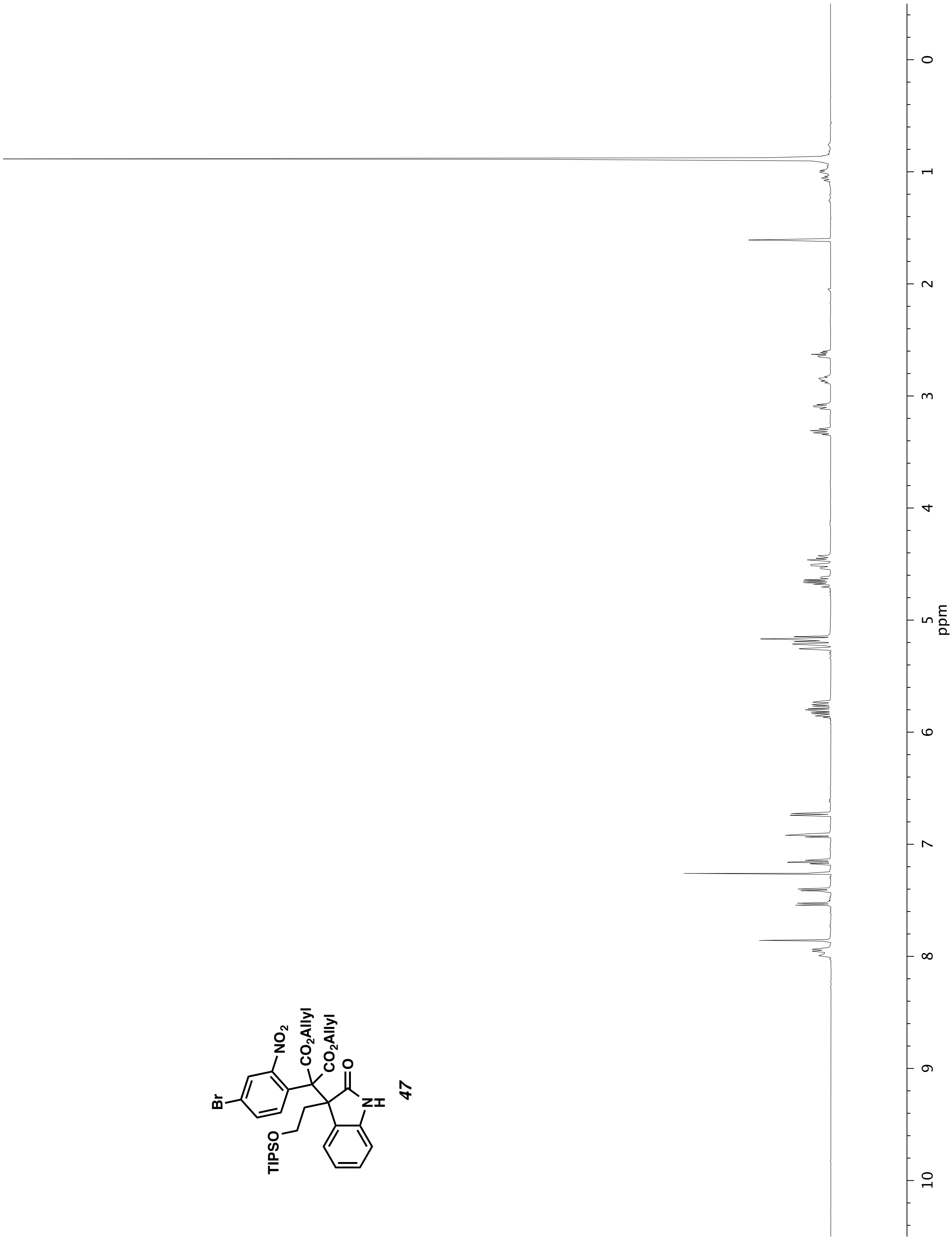


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Figure A1.31. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **47**.

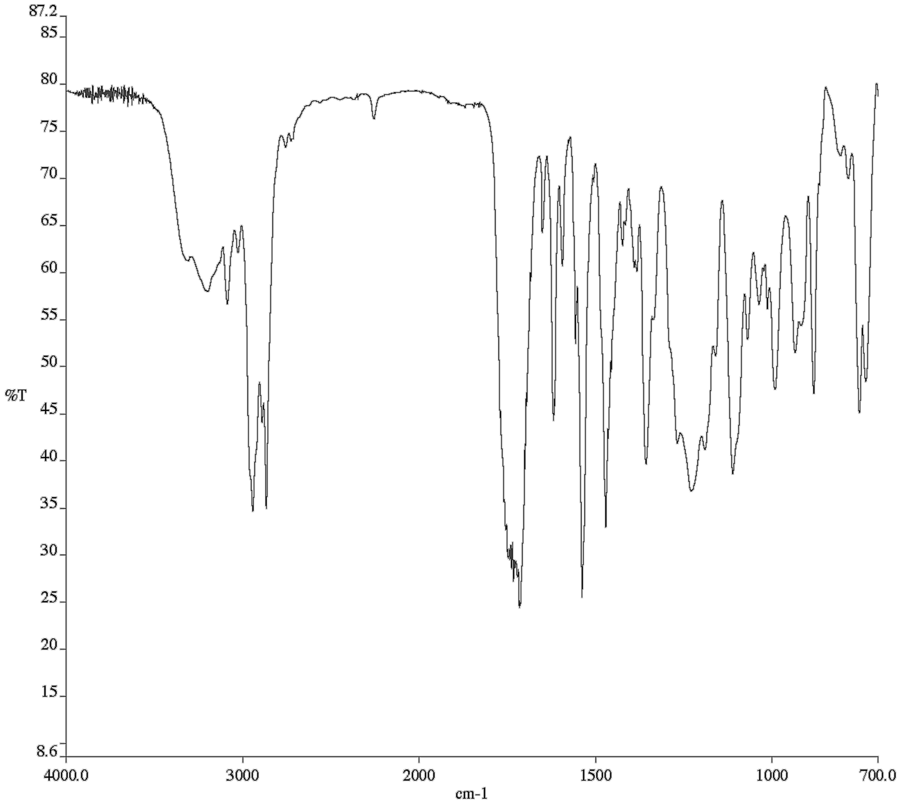


Figure A1.32. Infrared spectrum (Thin Film, NaCl) of compound **47**.

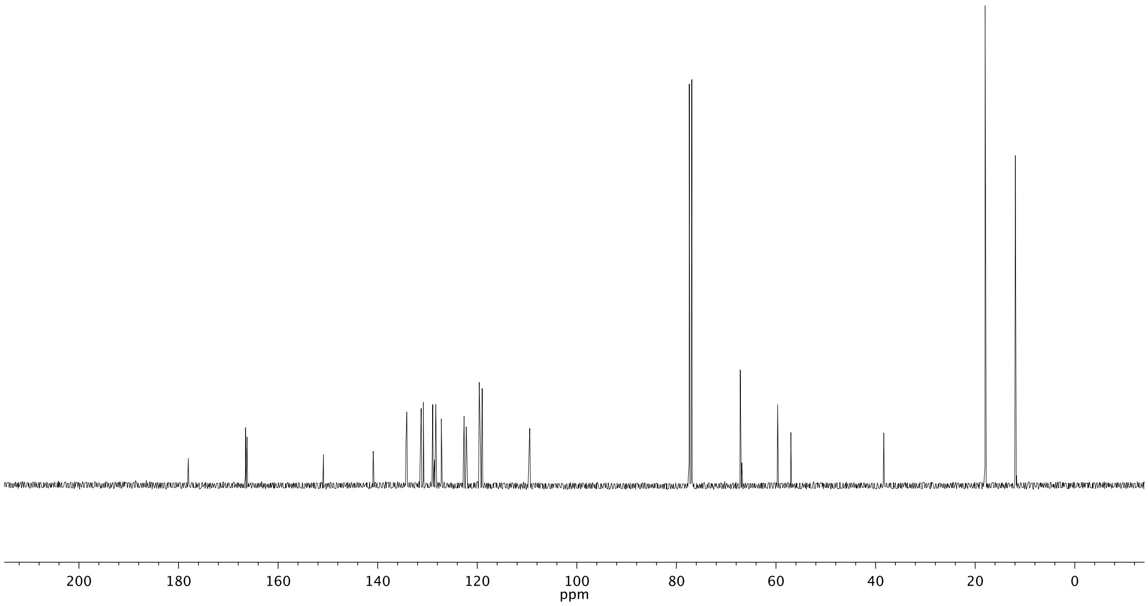
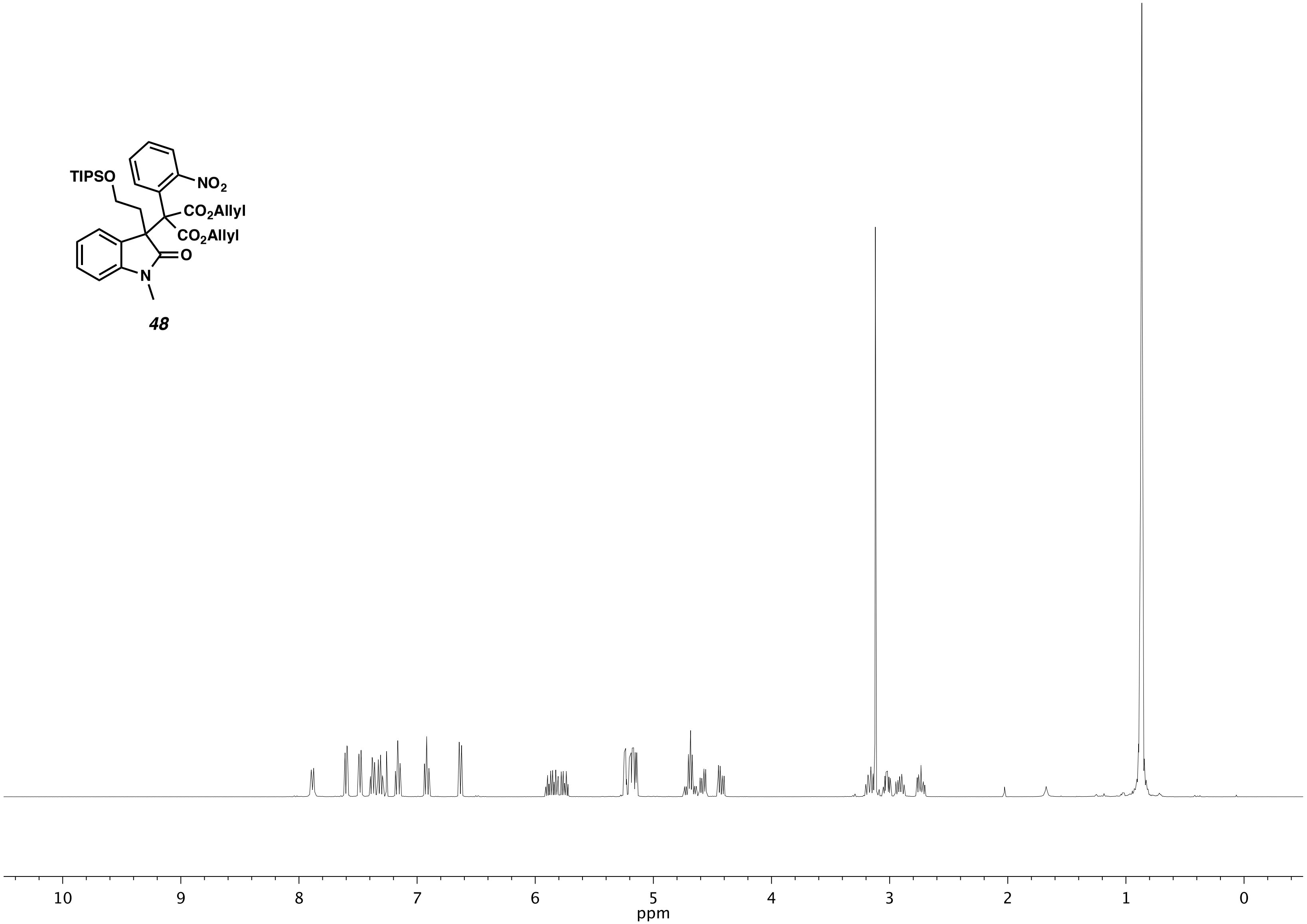


Figure A1.33. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **47**.



48

Figure A1.34. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **48**.

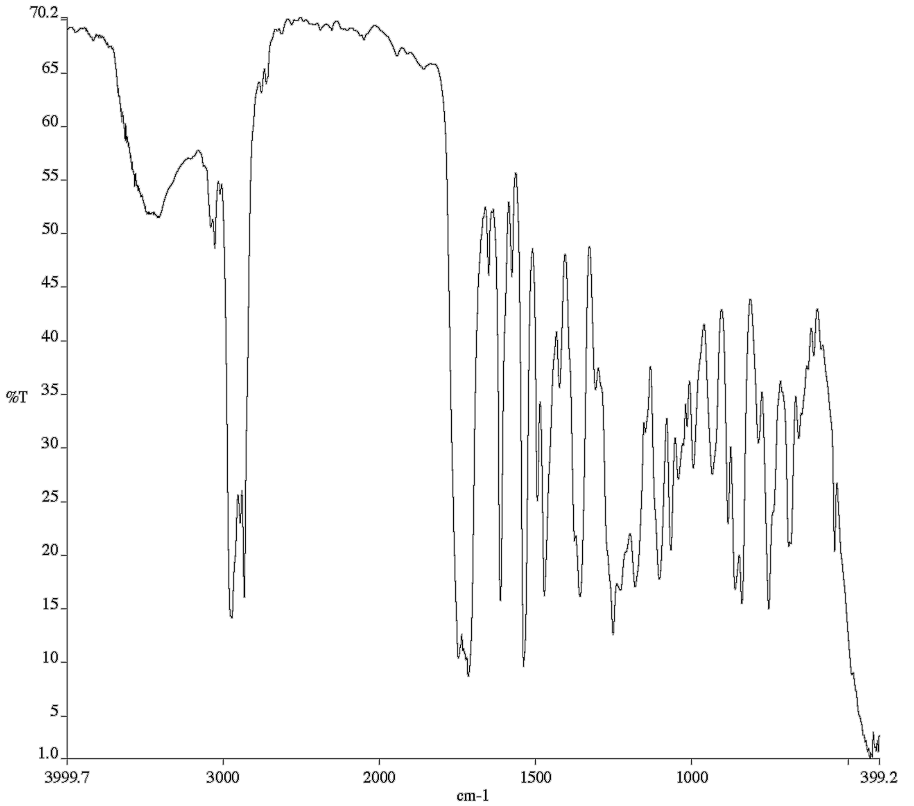


Figure A1.35. Infrared spectrum (Thin Film, NaCl) of compound **48**.

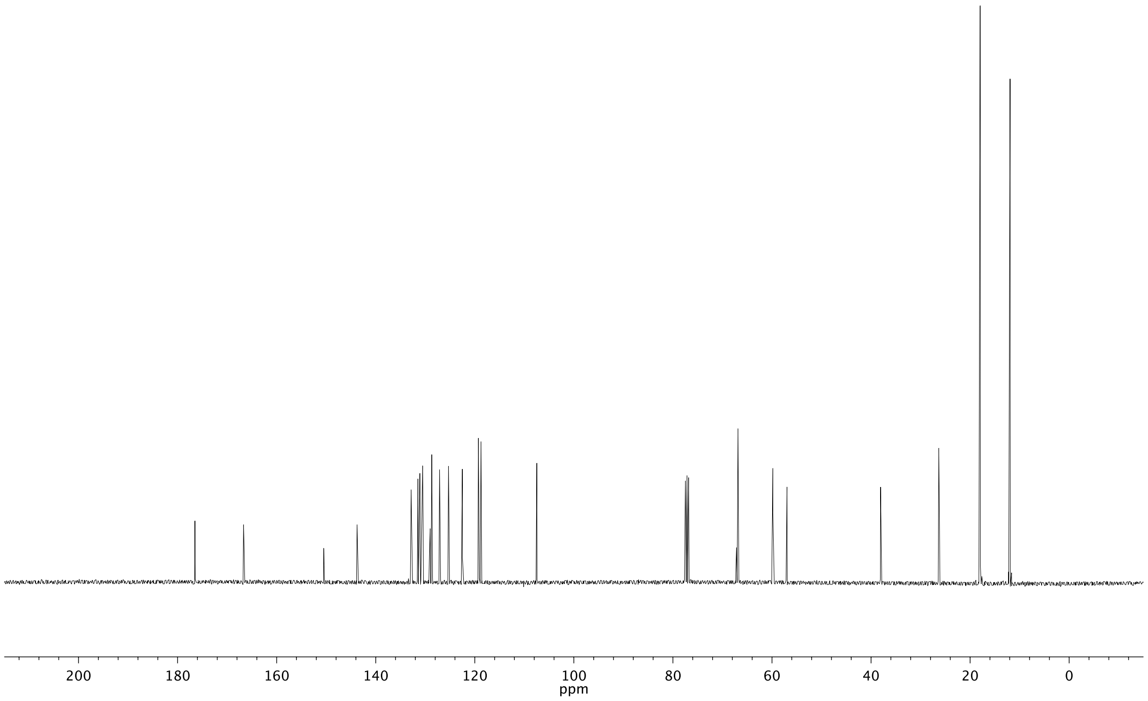


Figure A1.36. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **48**.

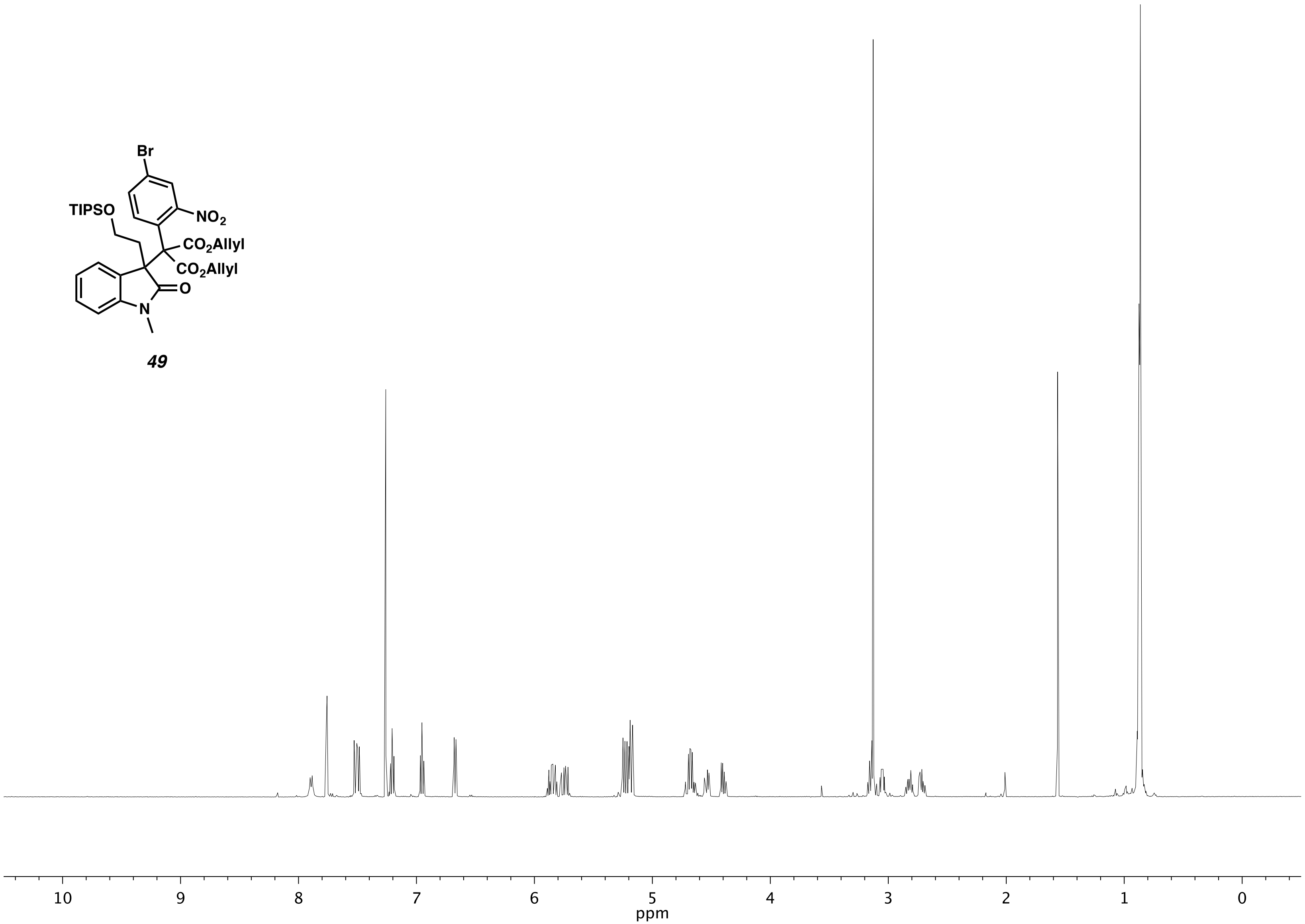


Figure A1.37. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **49**.

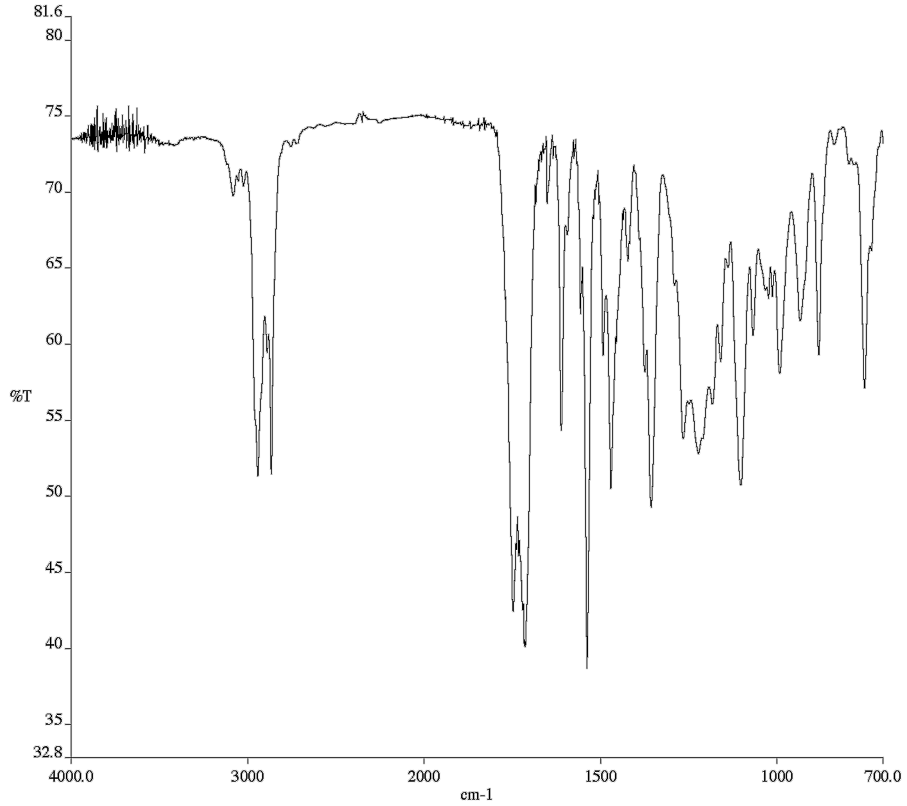


Figure A1.38. Infrared spectrum (Thin Film, NaCl) of compound **49**.

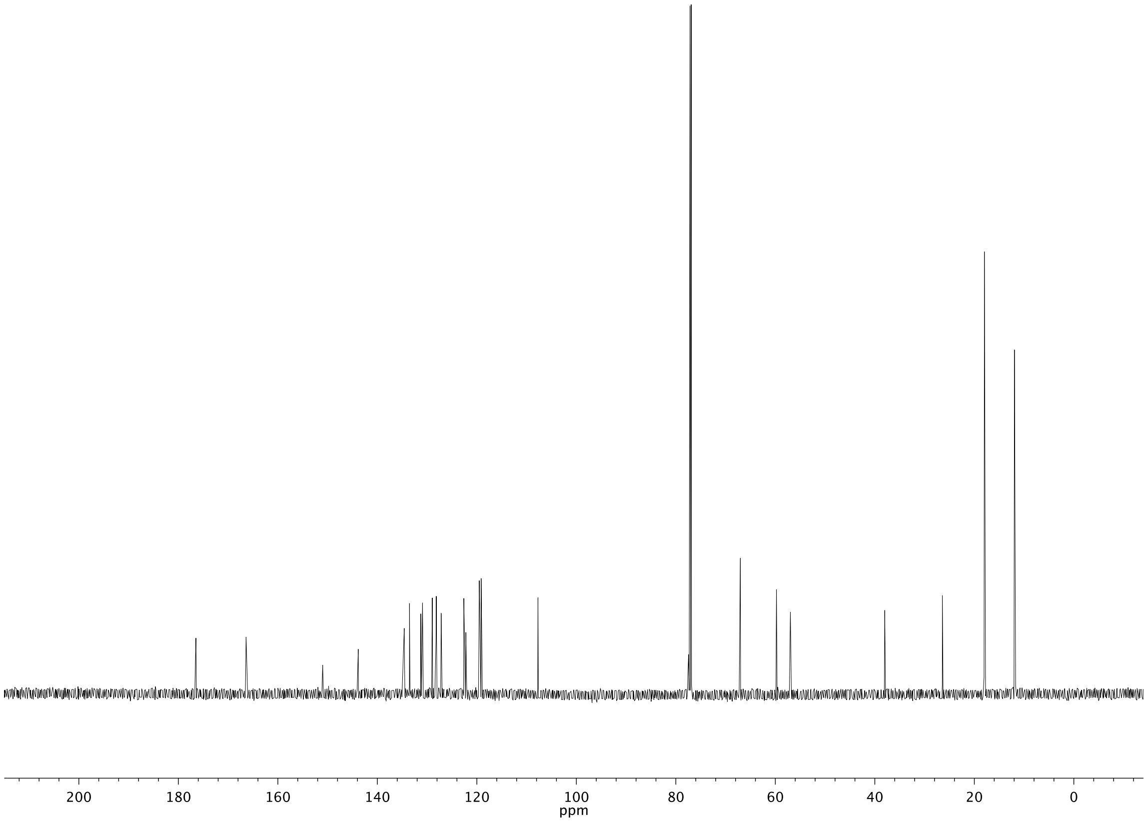


Figure A1.39. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **49**.

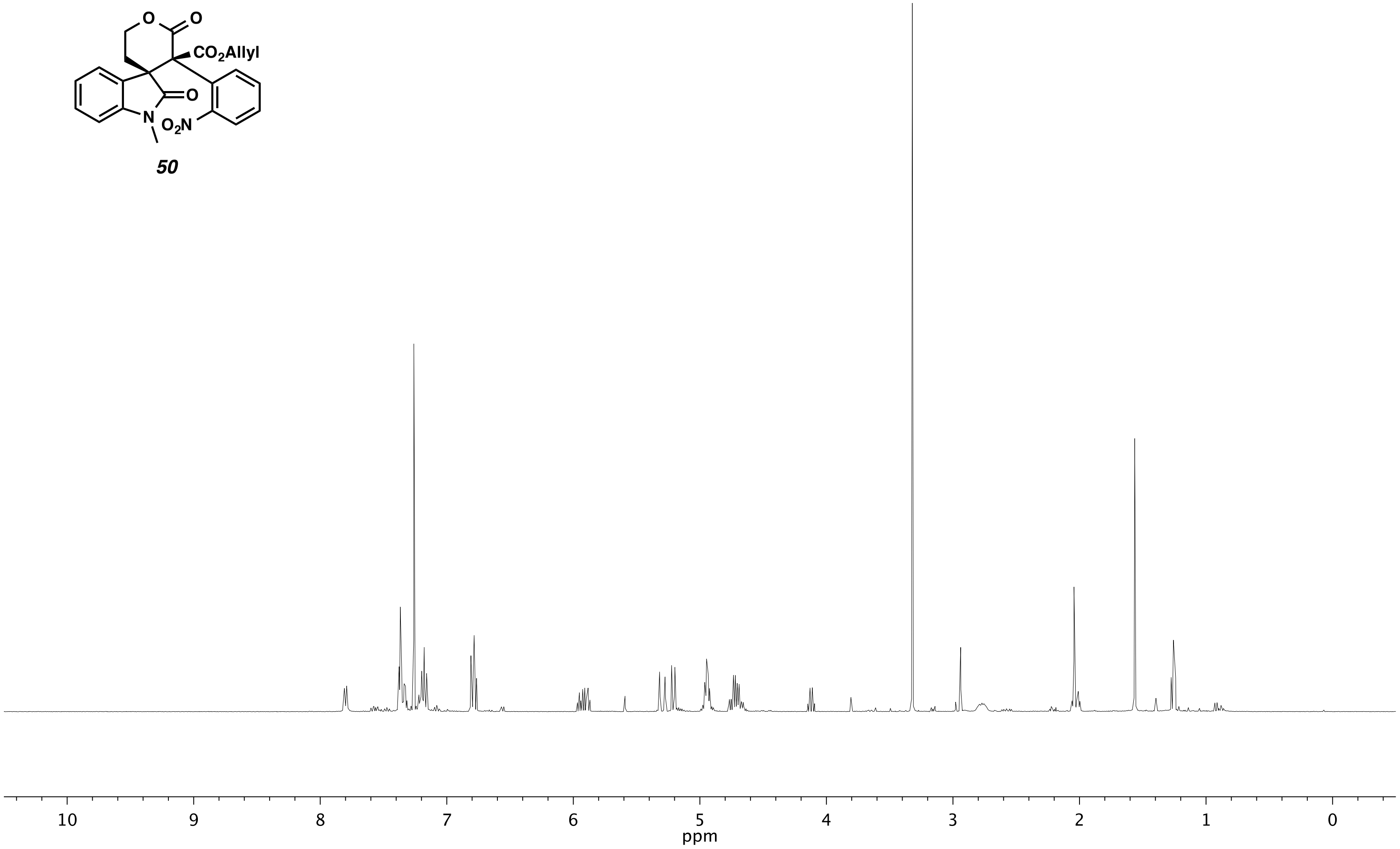


Figure A1.40. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **50**.

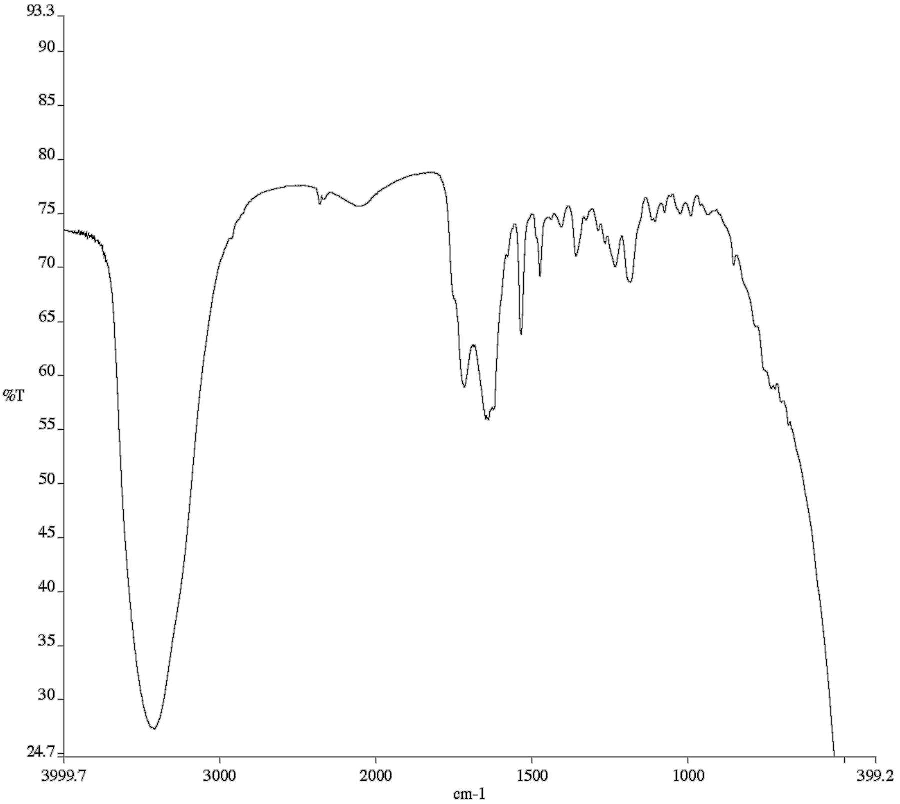


Figure A1.41. Infrared spectrum (Thin Film, NaCl) of compound **50**.

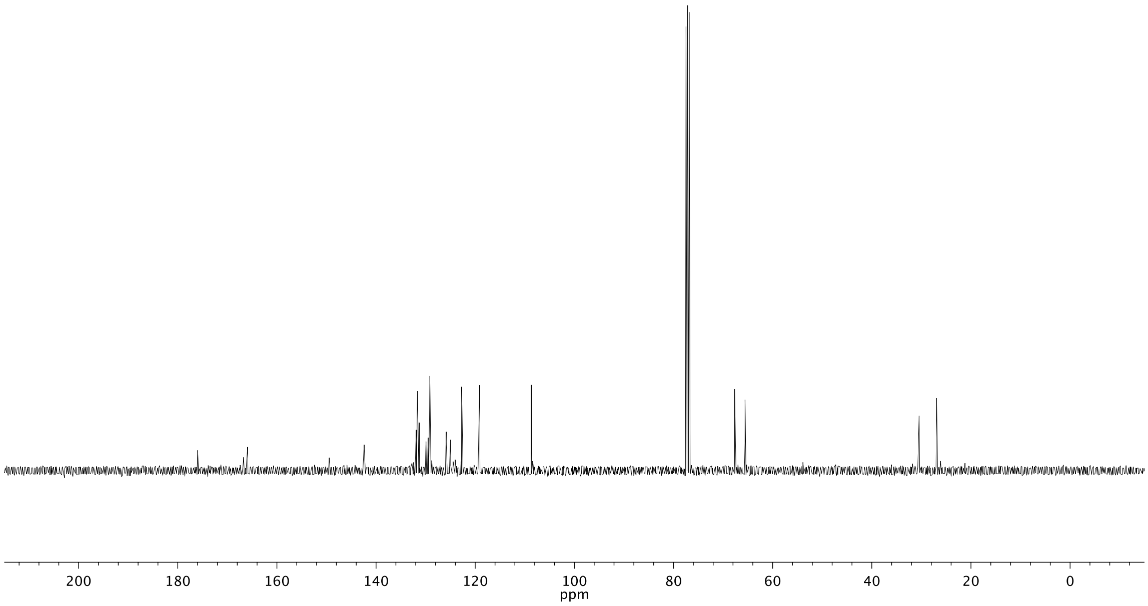


Figure A1.42. ^{13}C NMR (100 MHz, CDCl$_3$) of compound **50**.

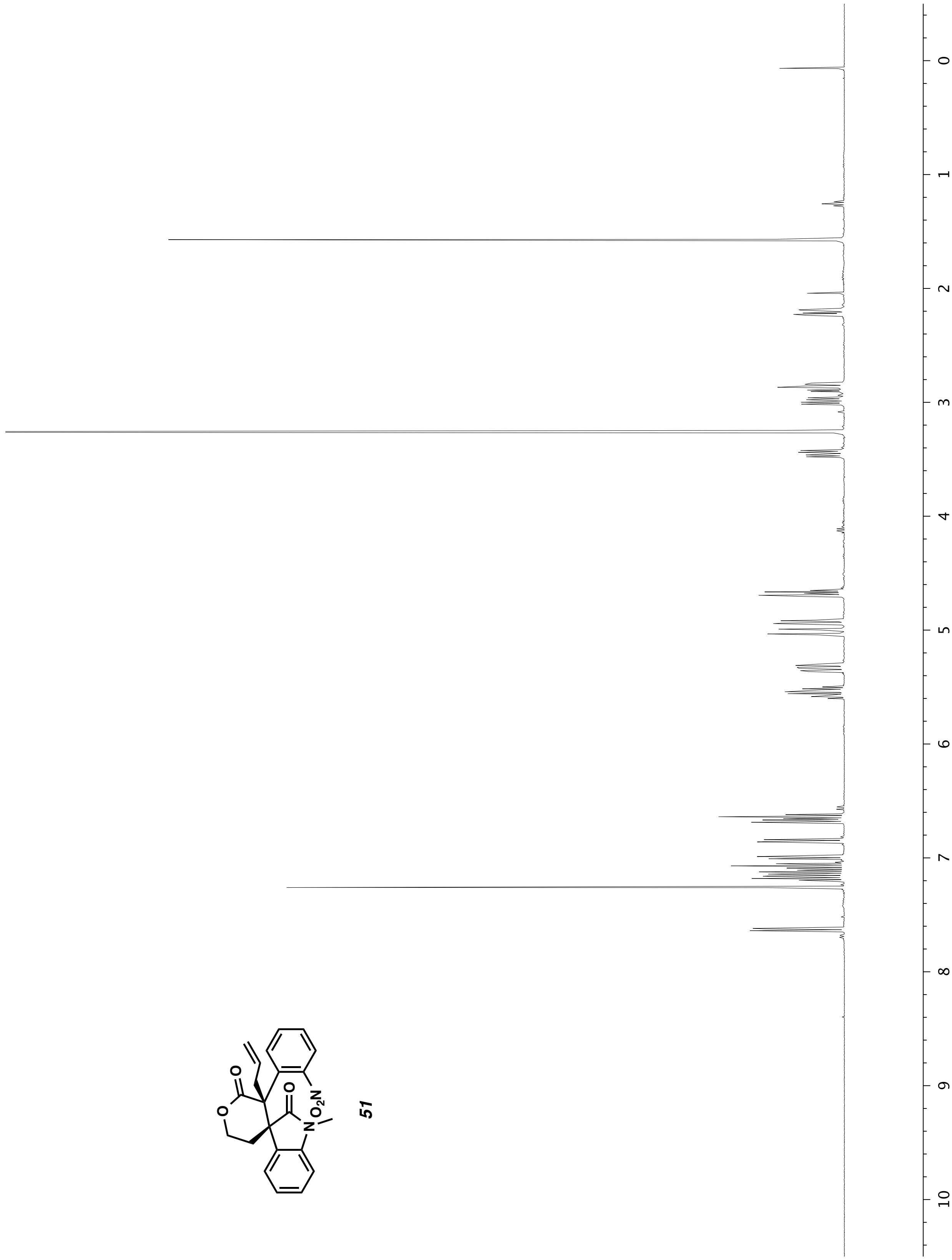


Figure A1.43. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **51**.

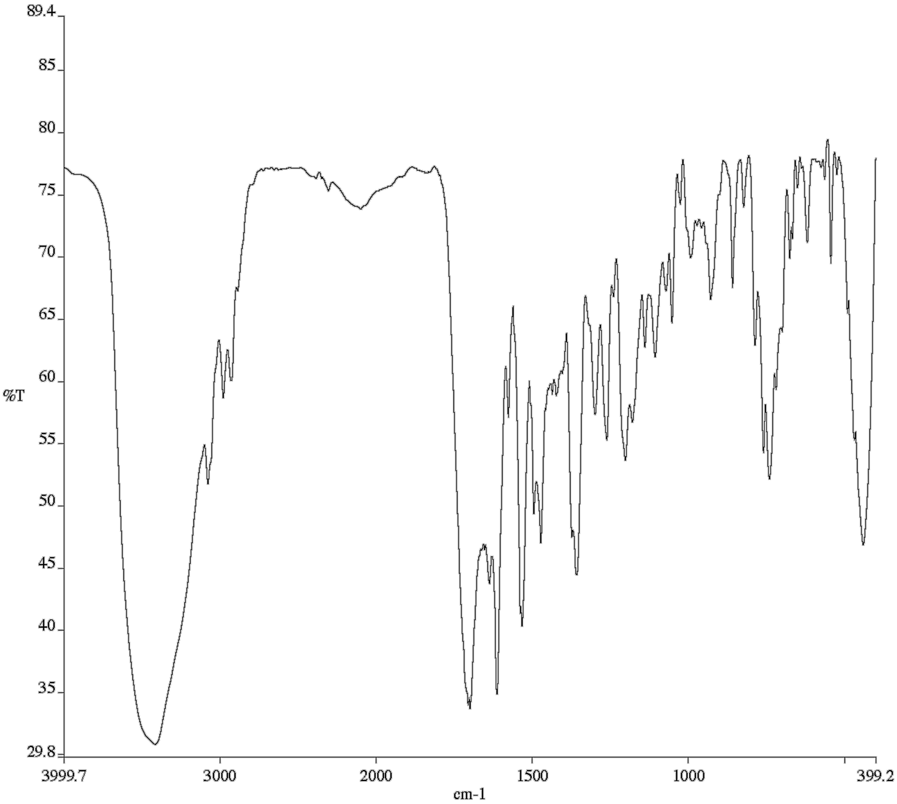


Figure A1.44. Infrared spectrum (Thin Film, NaCl) of compound **51**.

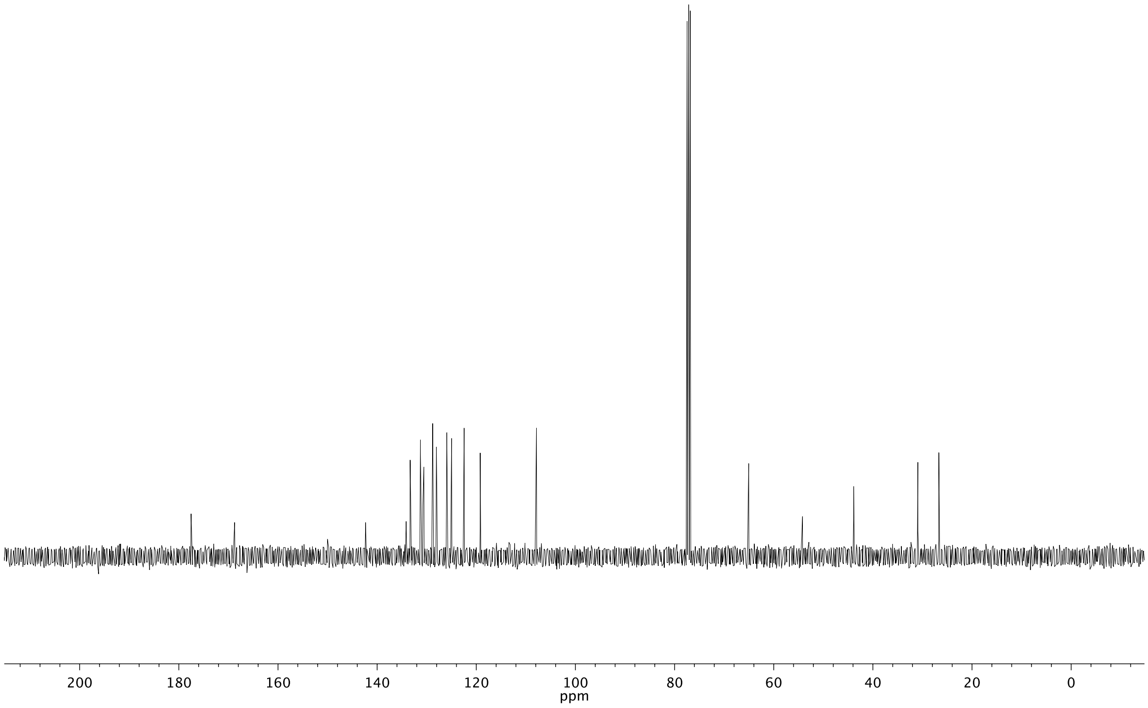


Figure A1.45. ^{13}C NMR (100 MHz, CDCl$_3$) of compound **51**.

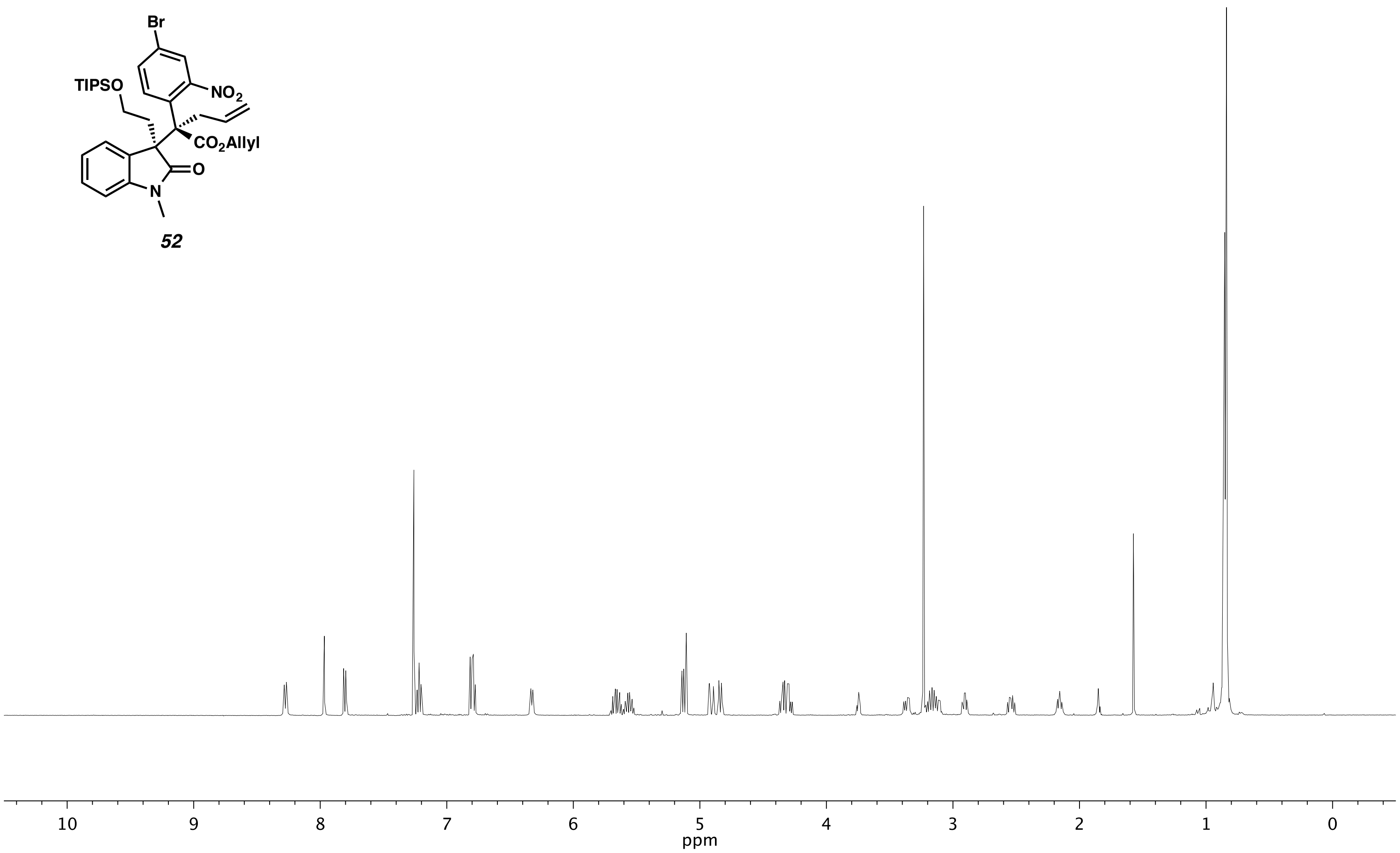


Figure A1.46. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **52**.

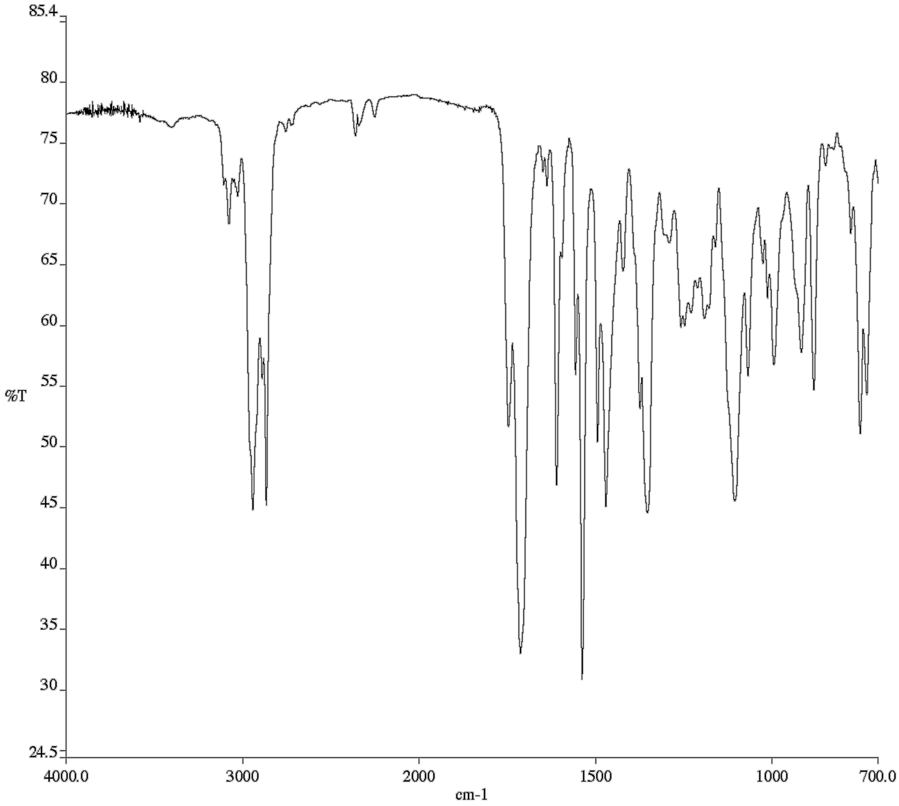


Figure A1.47. Infrared spectrum (Thin Film, NaCl) of compound **52**.

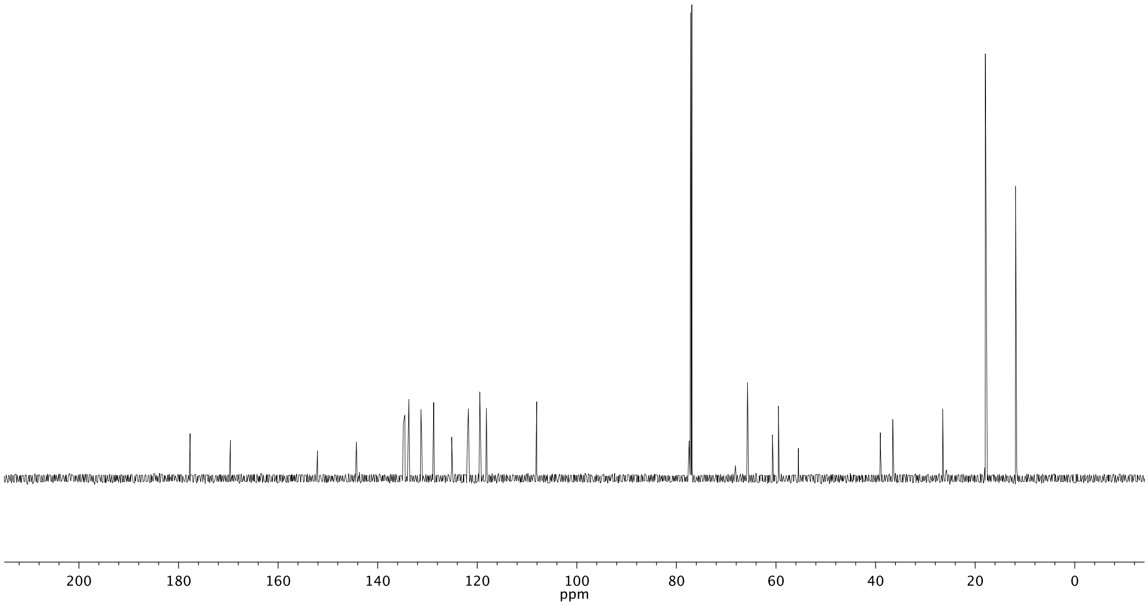
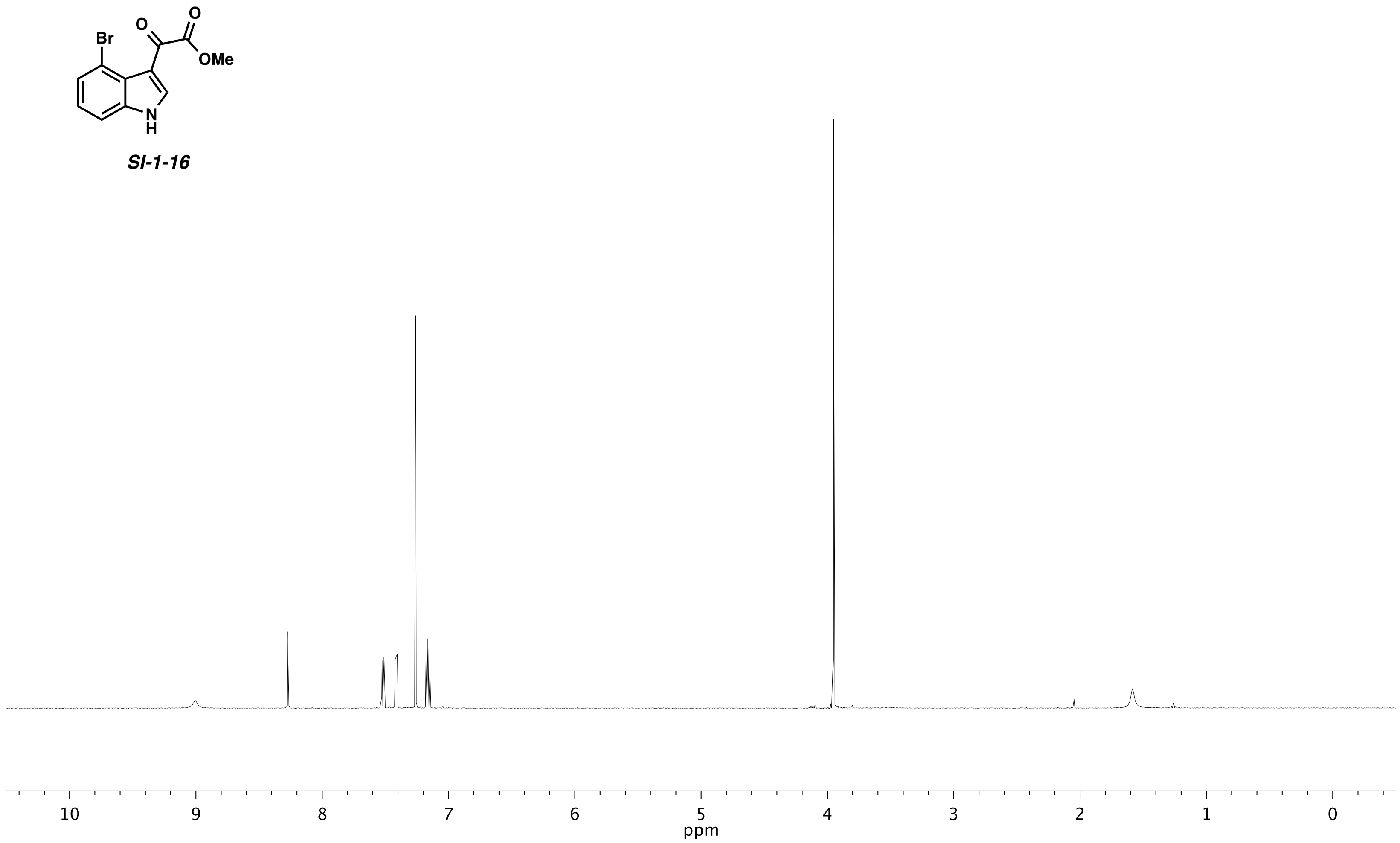


Figure A1.48. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **52**.



_SI-1-16_

Figure A1.49. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-1-16**.

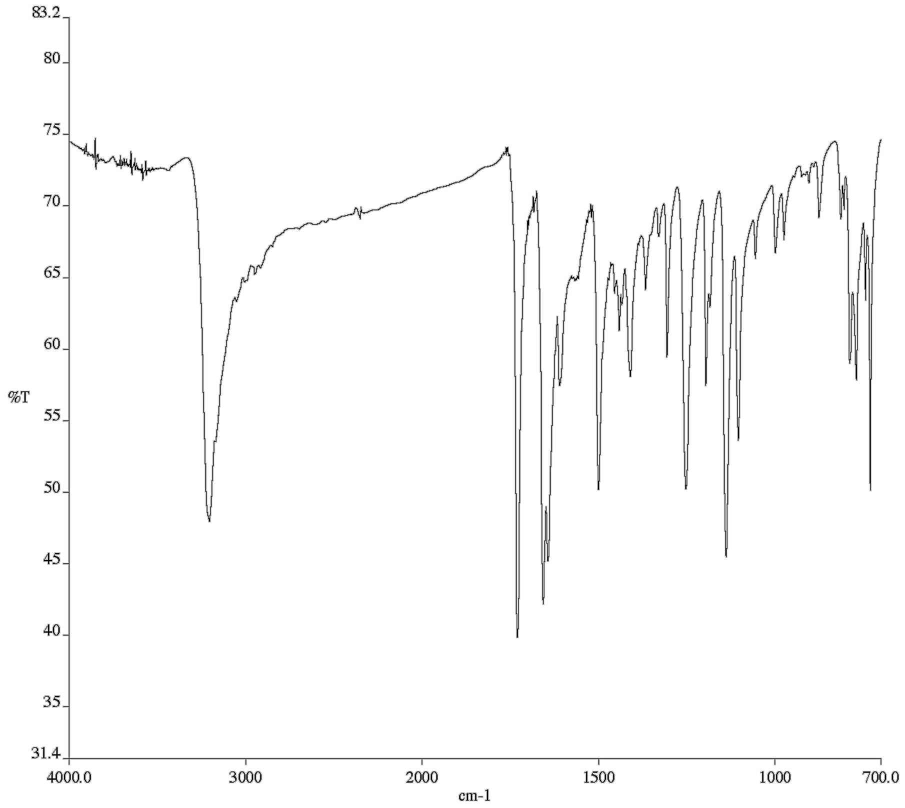


Figure A1.50. Infrared spectrum (Thin Film, NaCl) of compound **SI-1-16**.

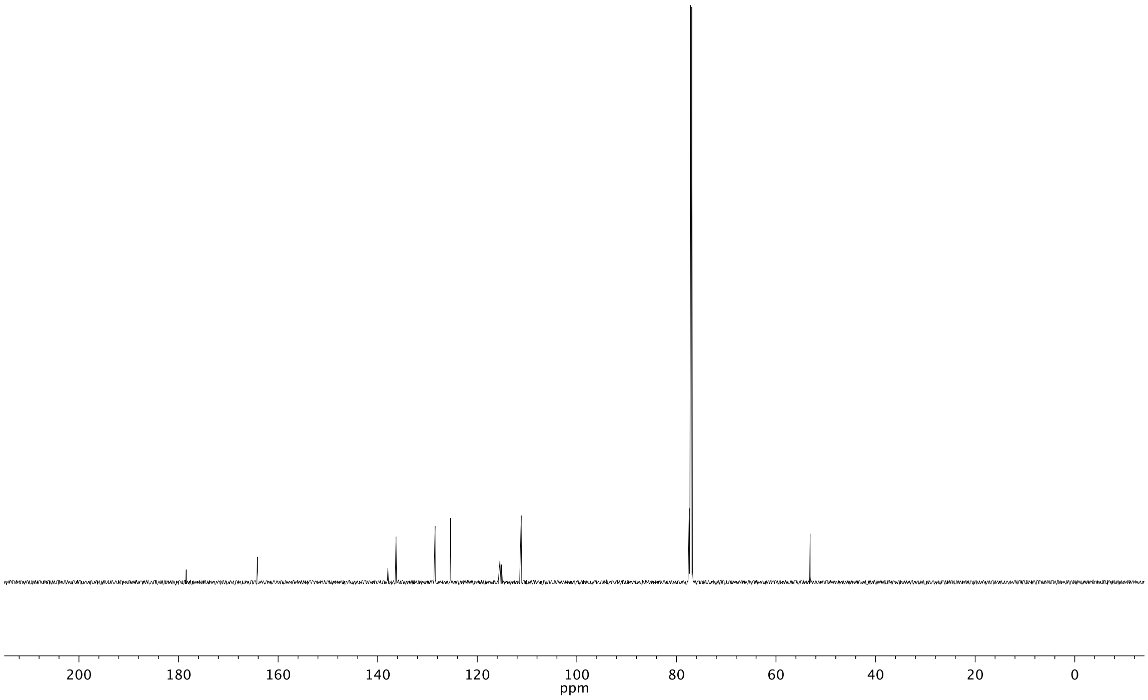


Figure A1.51. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **SI-1-16**.

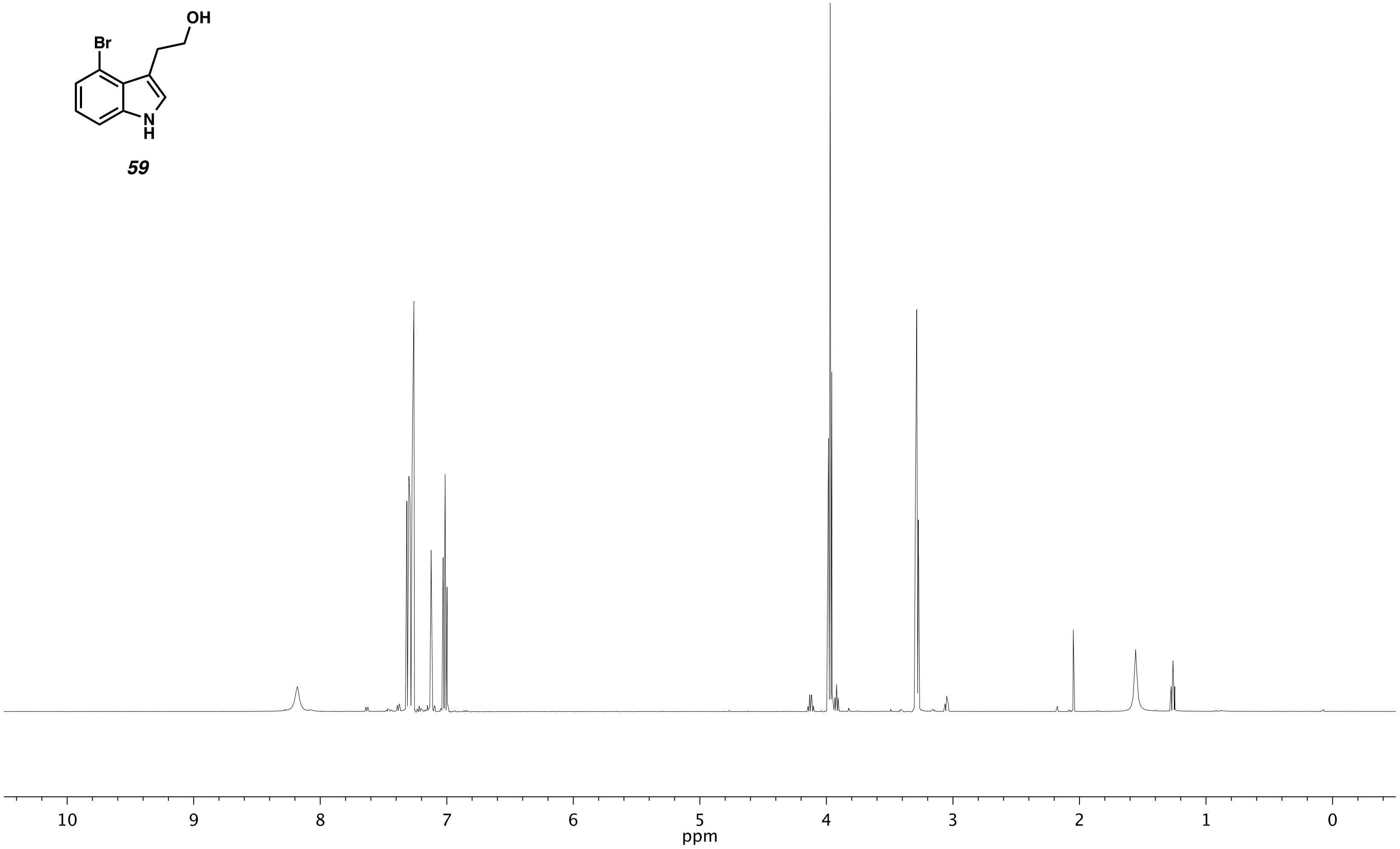


Figure A1.52. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **59**.

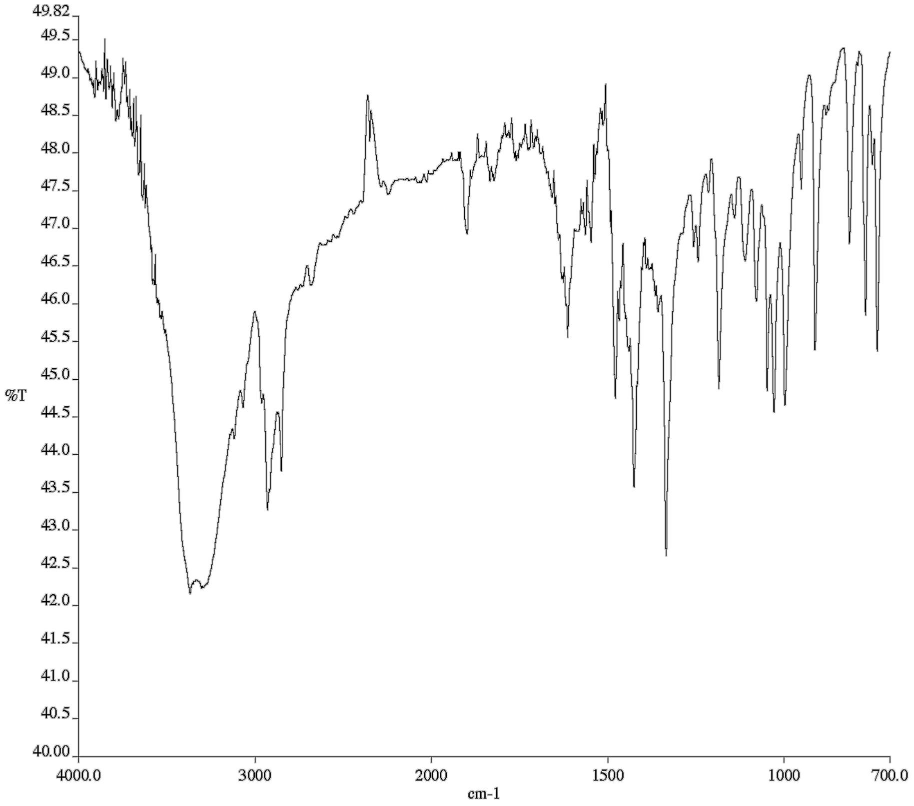


Figure A1.53. Infrared spectrum (Thin Film, NaCl) of compound **59**.

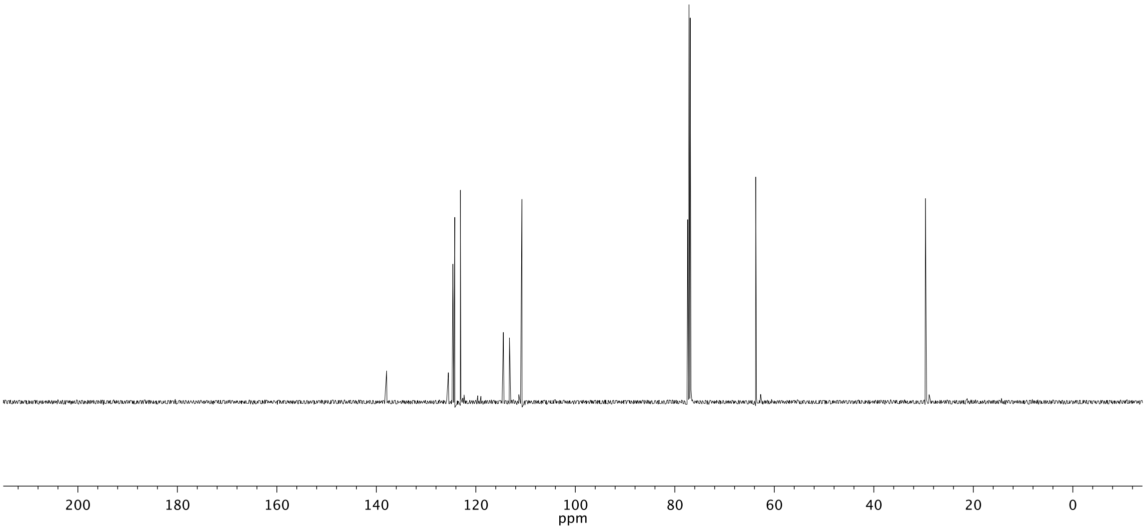


Figure A1.54. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **59**.

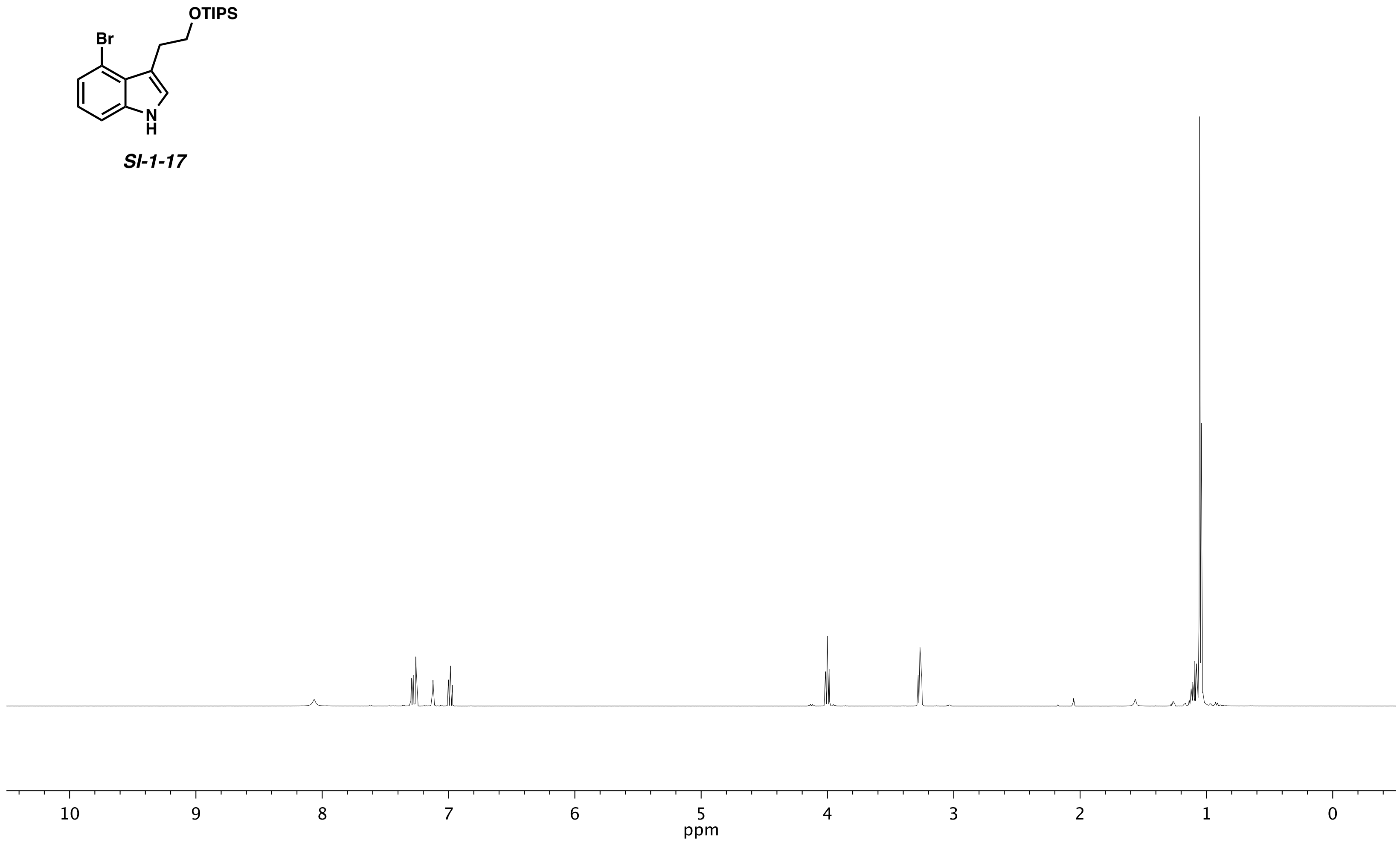


Figure A1.55. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-1-17**.

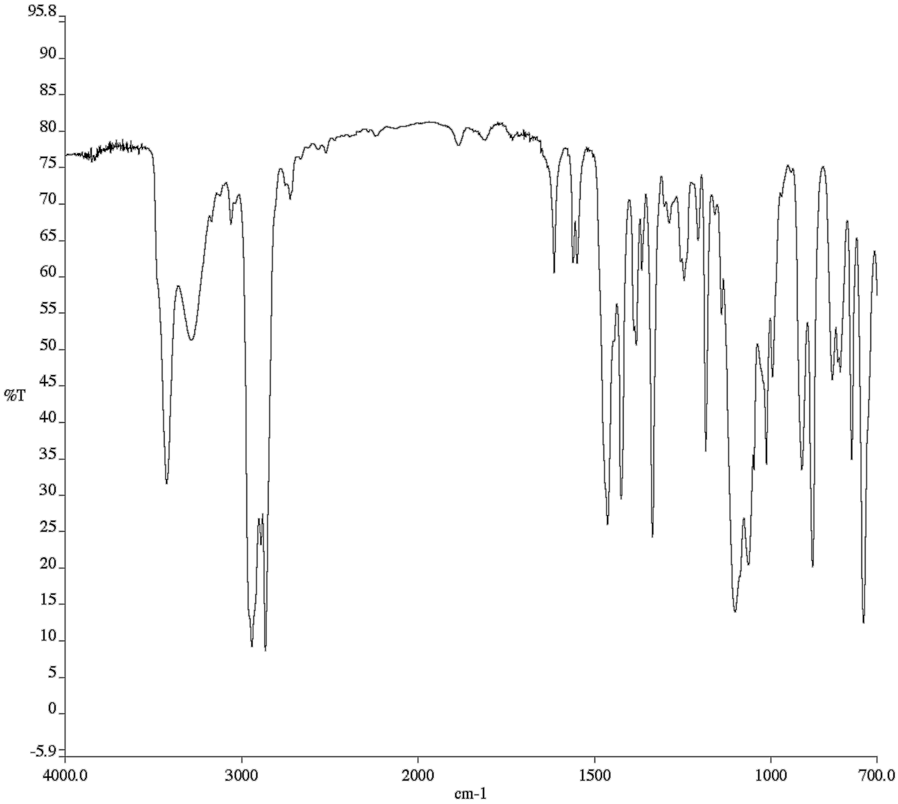


Figure A1.56. Infrared spectrum (Thin Film, NaCl) of compound **SI-1-17**.

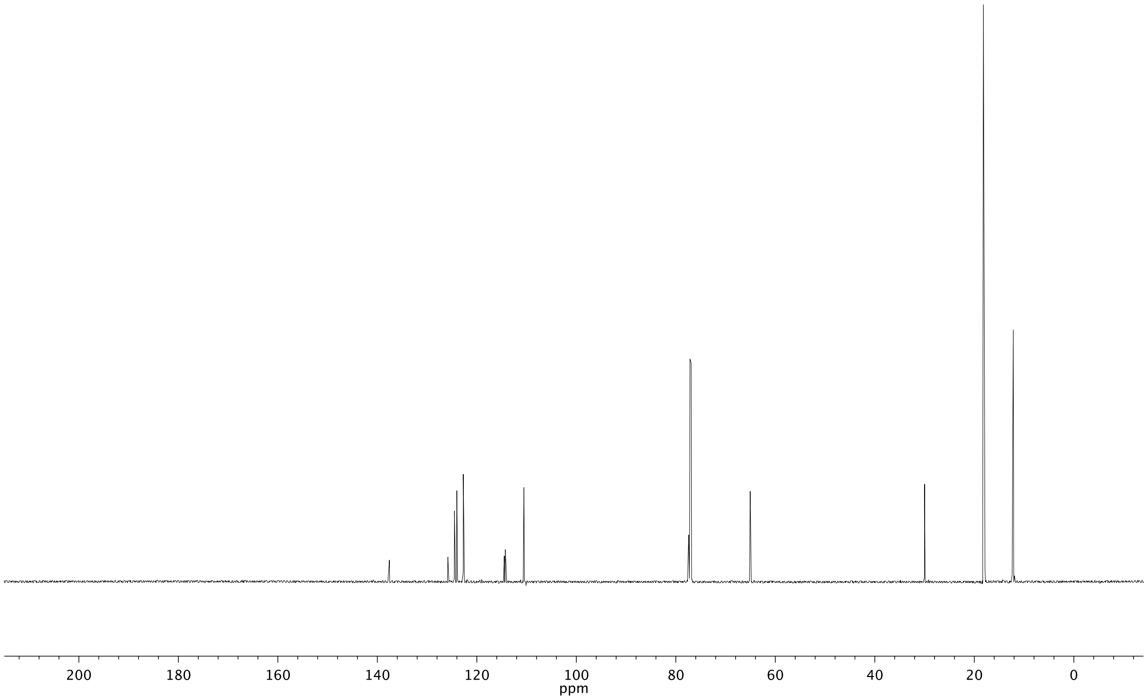


Figure A1.57. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **SI-1-17.**

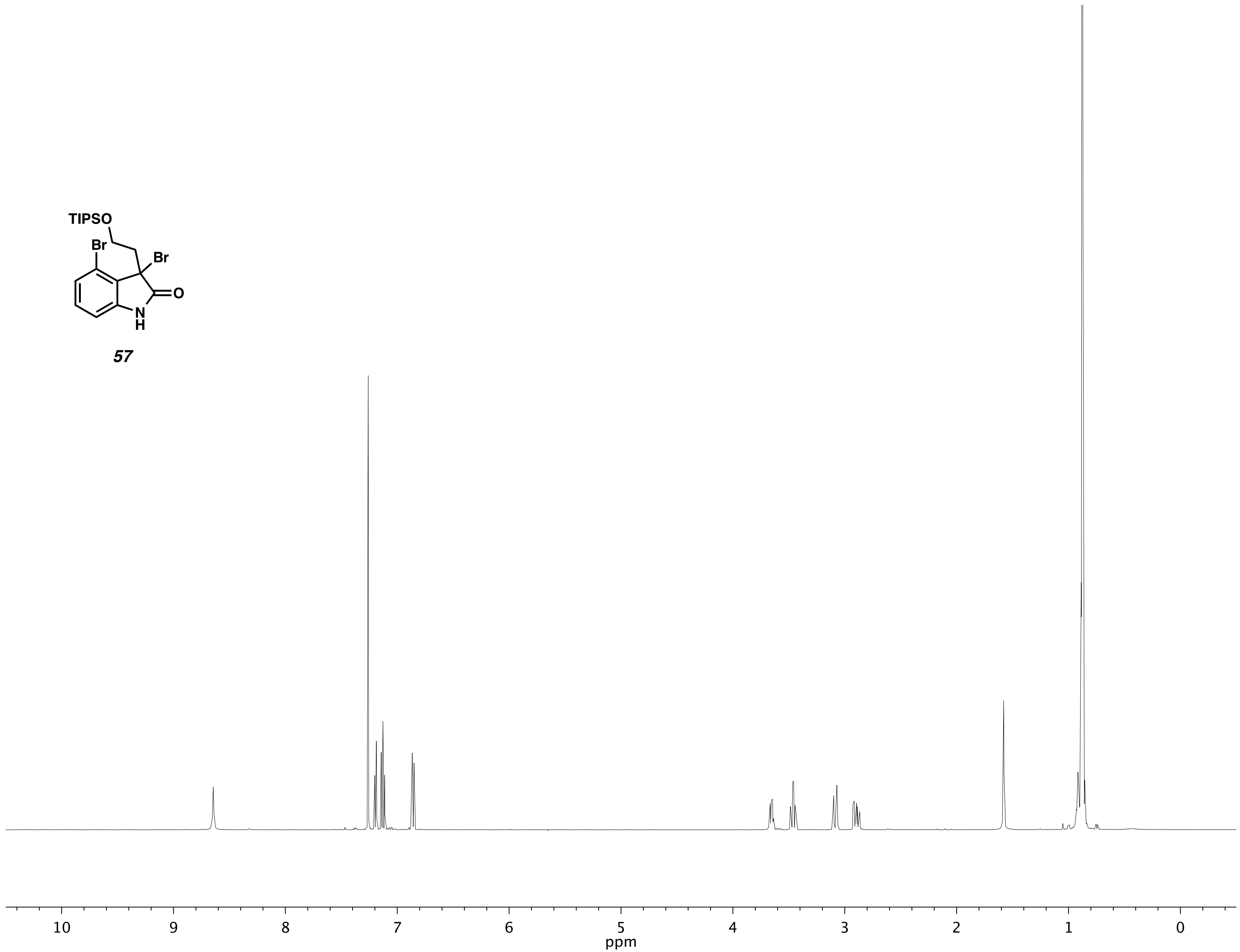


Figure A1.58. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **57**.

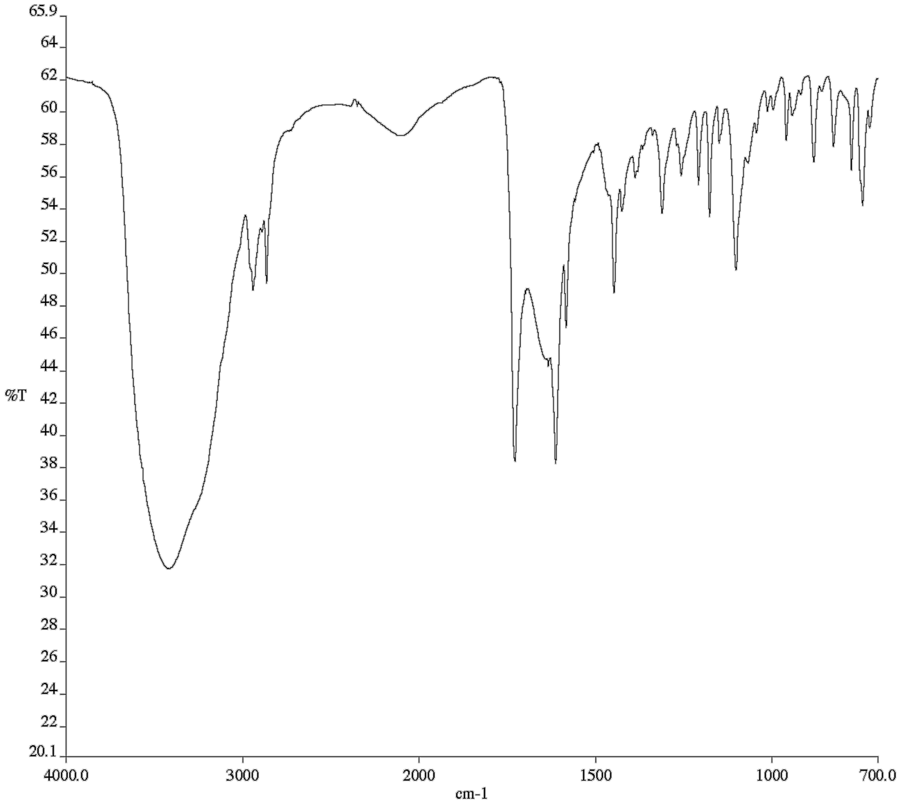


Figure A1.59. Infrared spectrum (Thin Film, NaCl) of compound **57**.

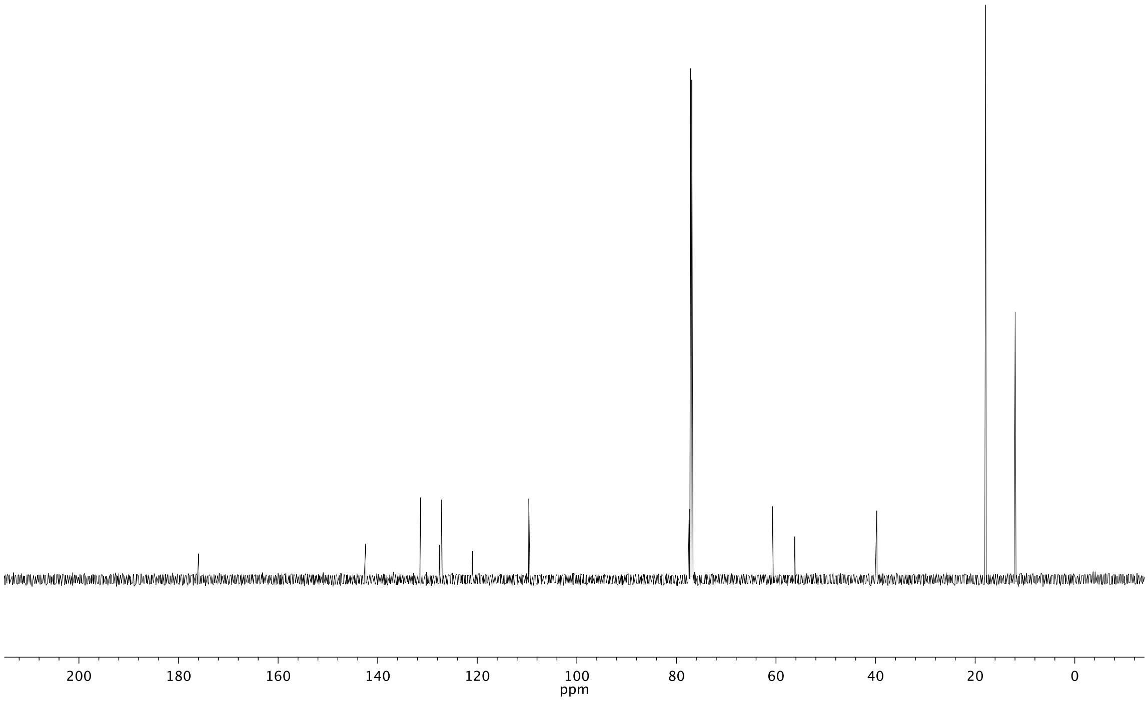


Figure A1.60. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **57.**

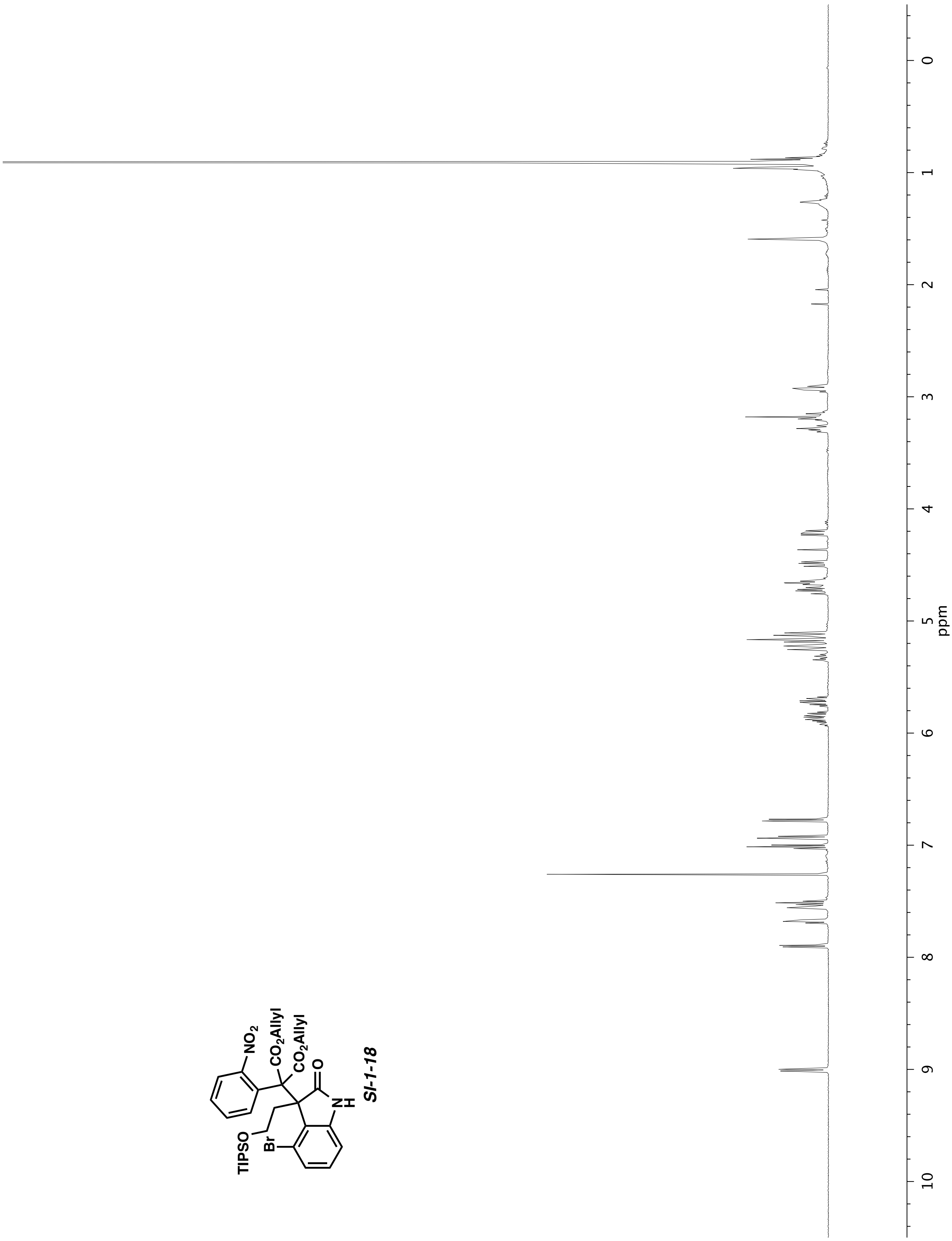


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Figure A1.61. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **SI-1-18**.

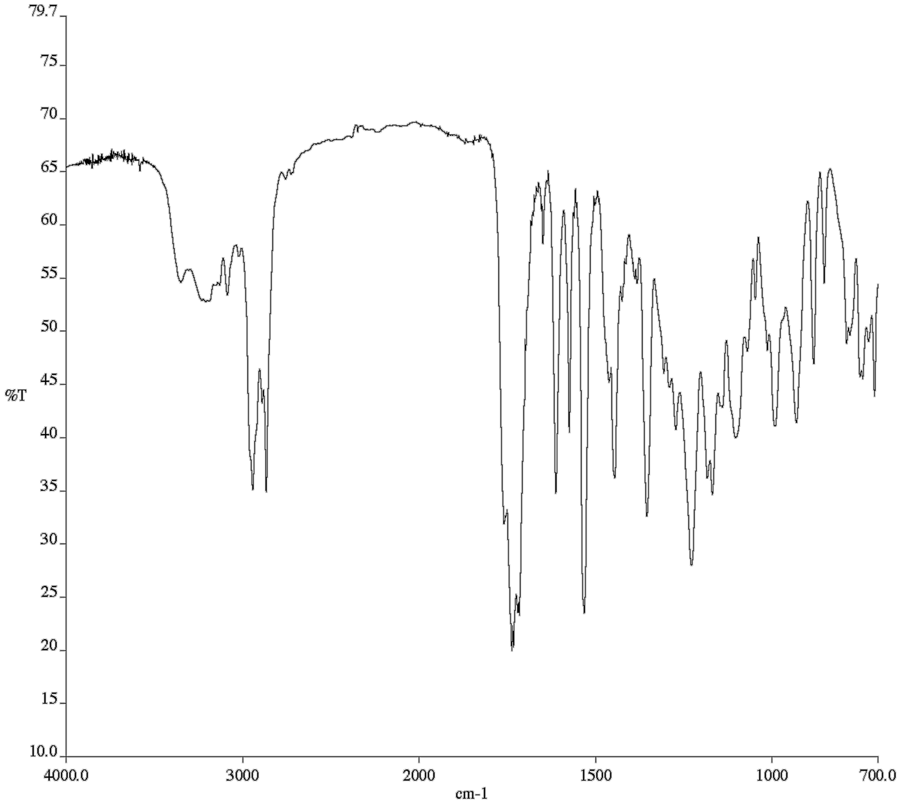

Figure A1.62. Infrared spectrum (Thin Film, NaCl) of compound **SI-1-18**.

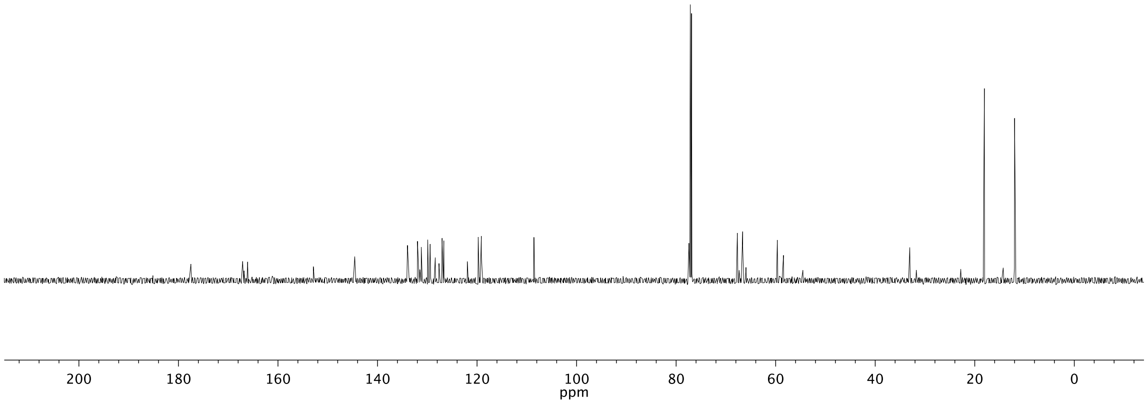

Figure A1.63. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **SI-1-18.**

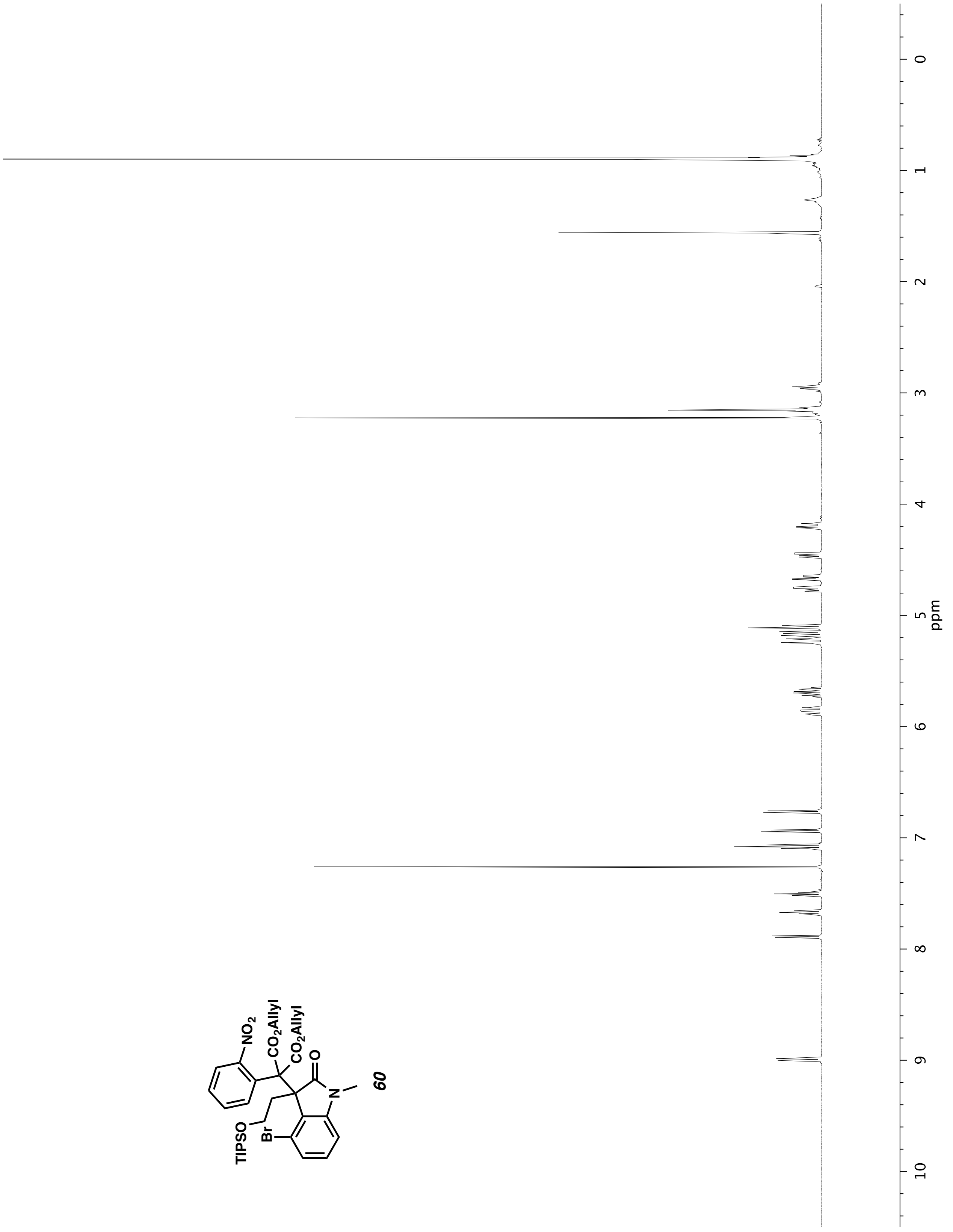

Figure A1.64. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **60**.

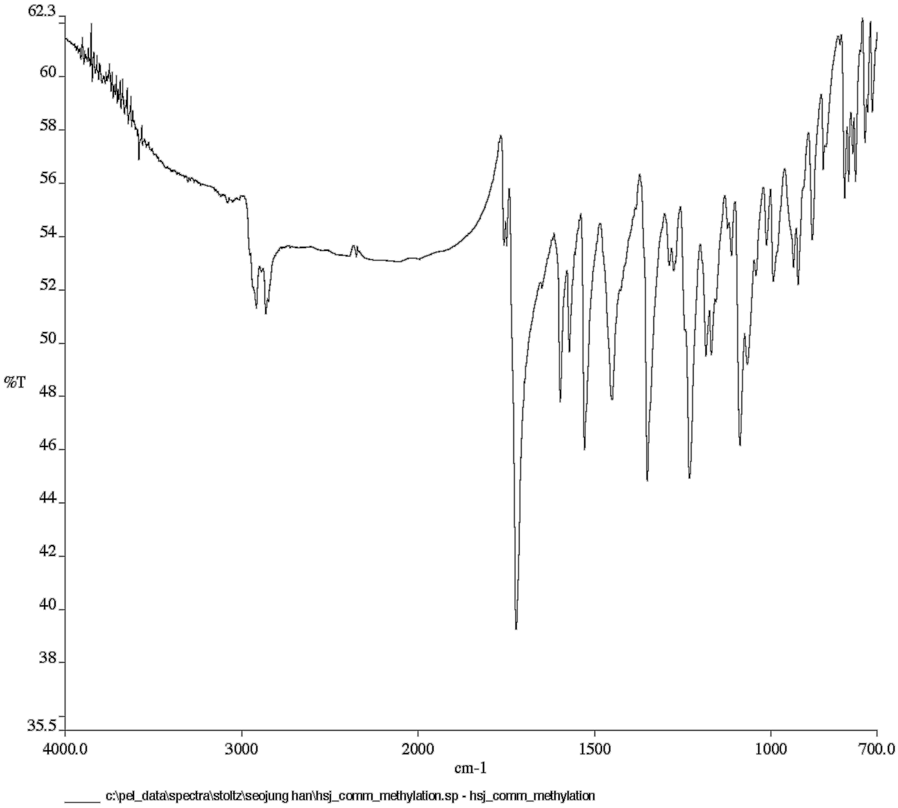

Figure A1.65. Infrared spectrum (Thin Film, NaCl) of compound **60**.

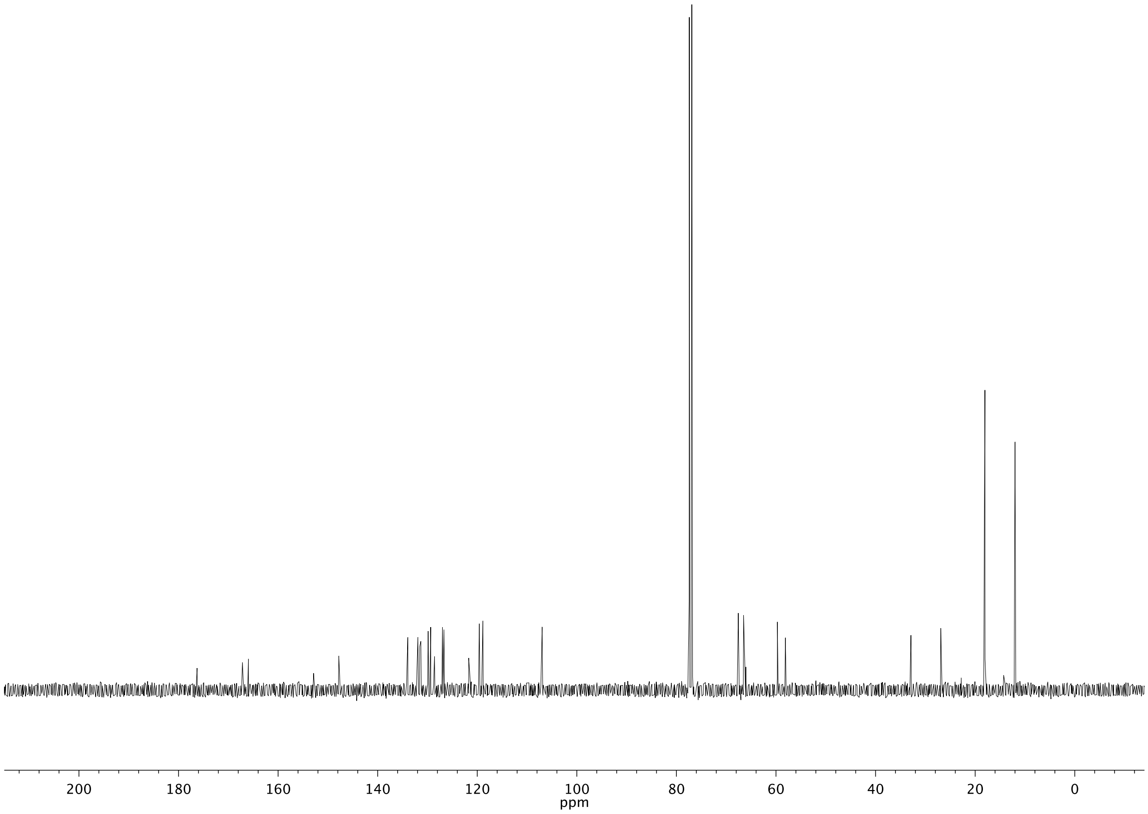

Figure A1.66. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **60**

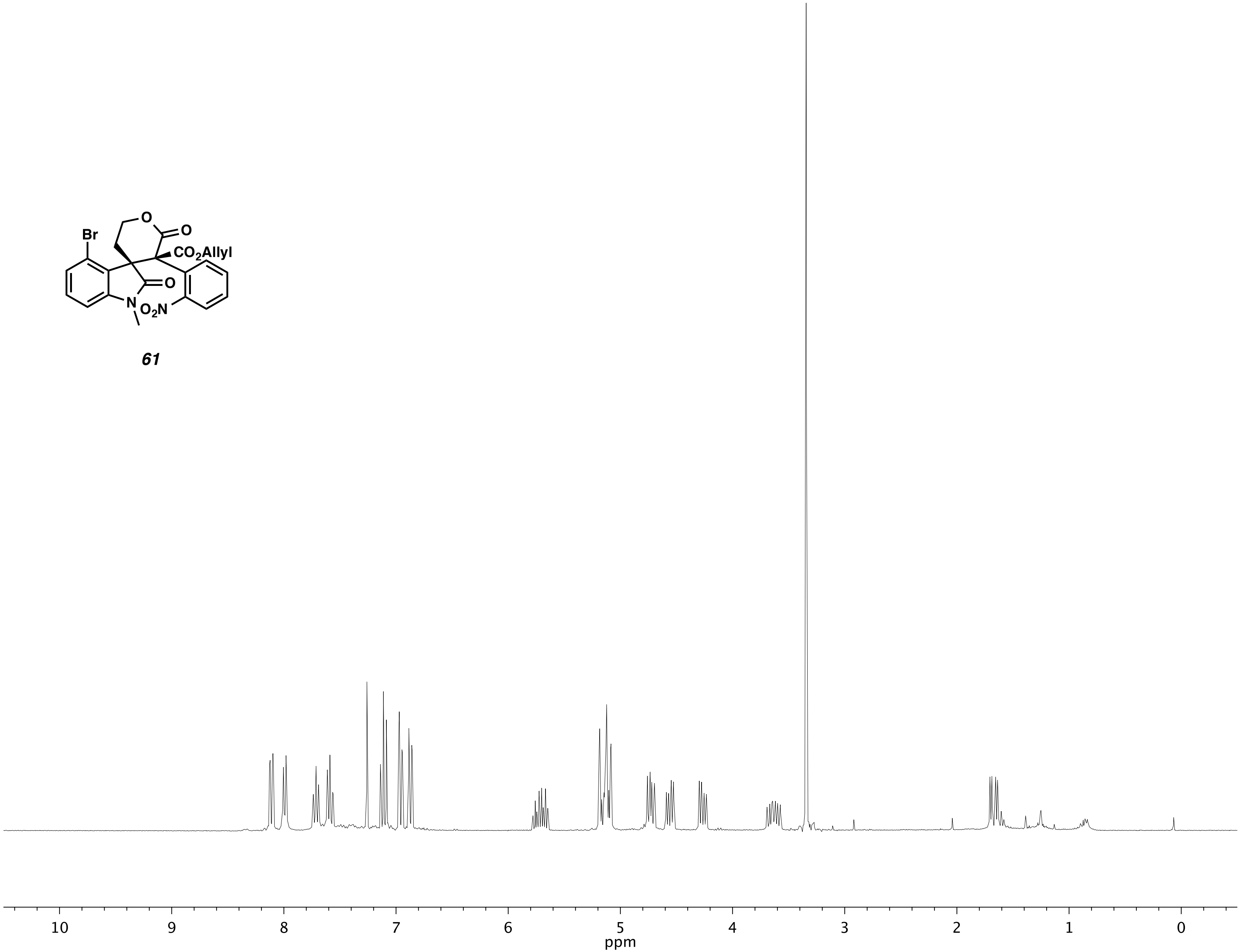

Figure A1.67. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **61**.

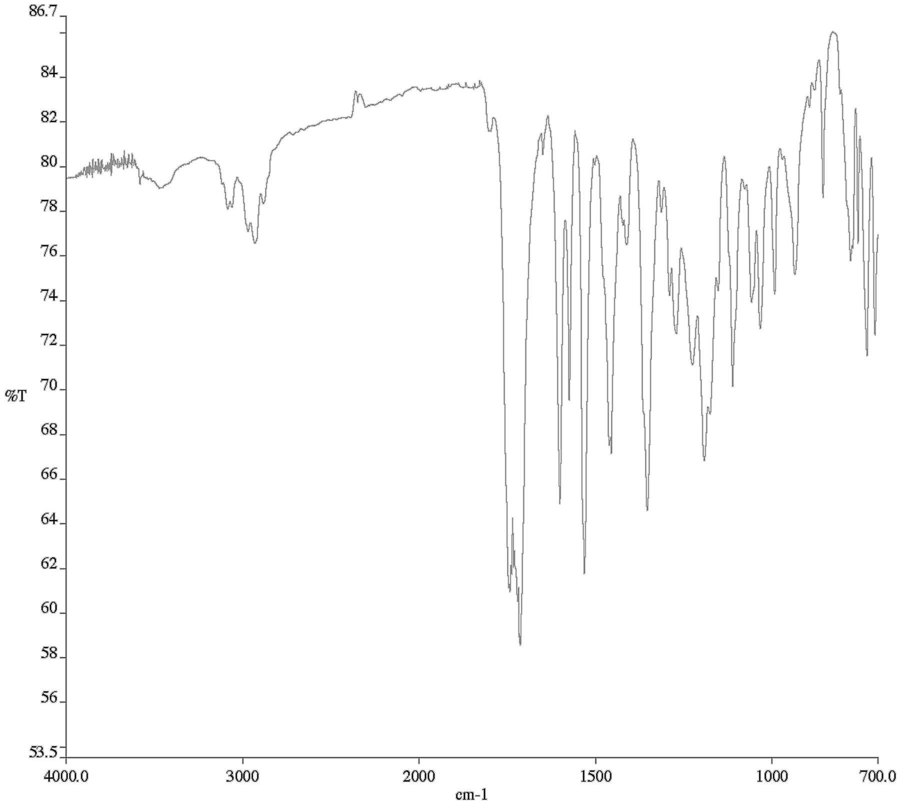

Figure A1.68. Infrared spectrum (Thin Film, NaCl) of compound **61**.

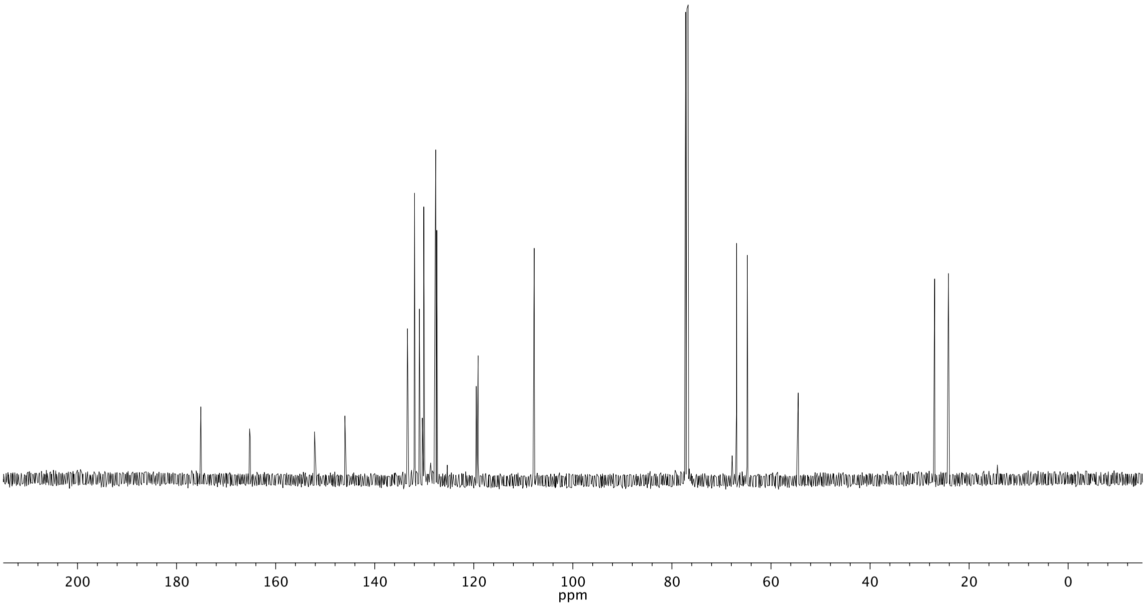

Figure A1.69. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **61.**

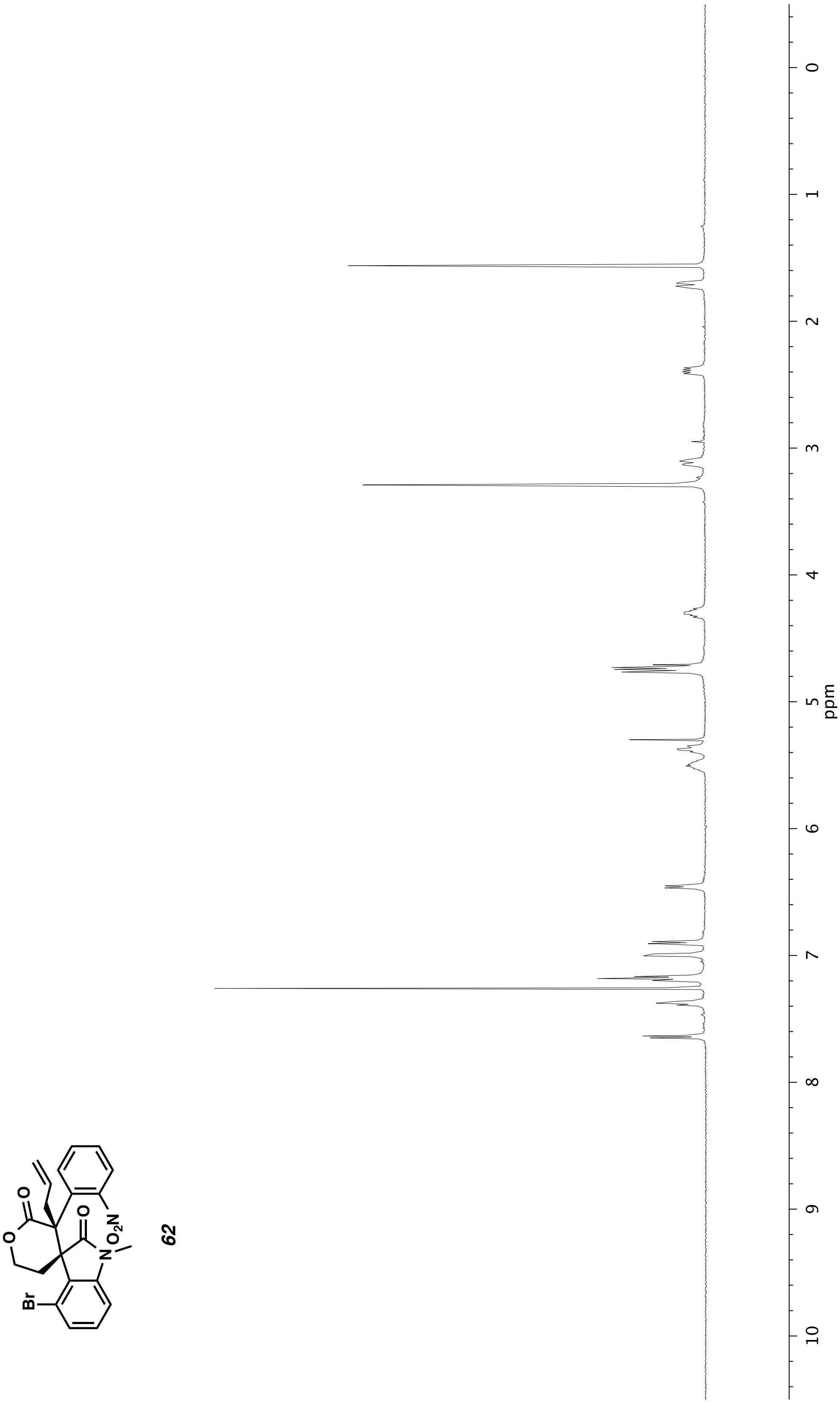

Figure A1.70. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **62**.

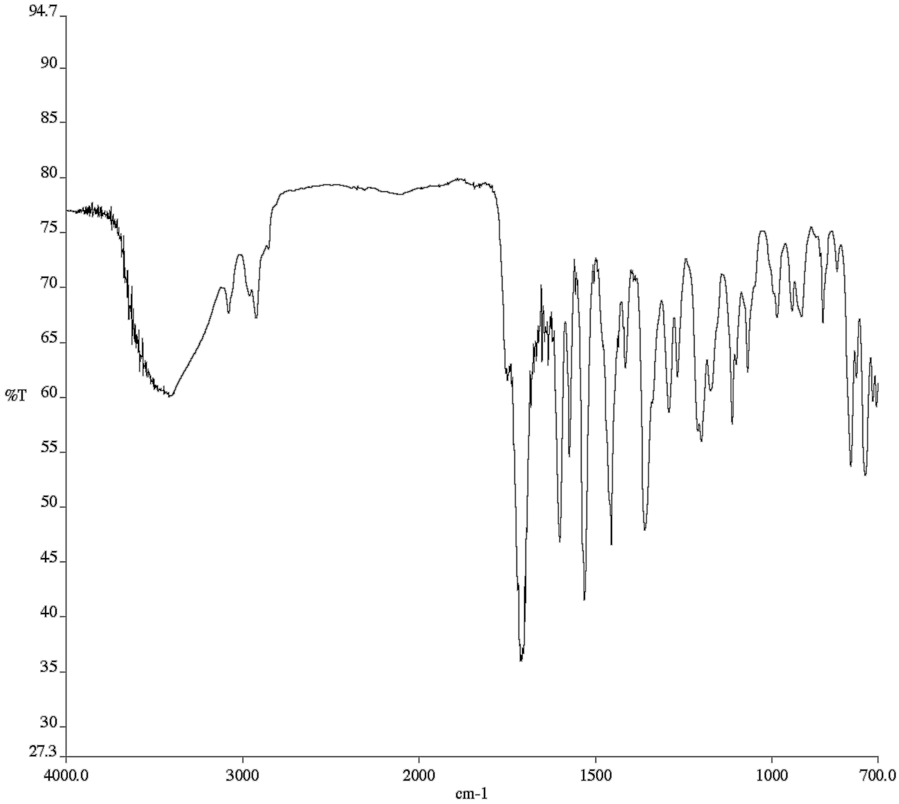

Figure A1.71. Infrared spectrum (Thin Film, NaCl) of compound **62**.

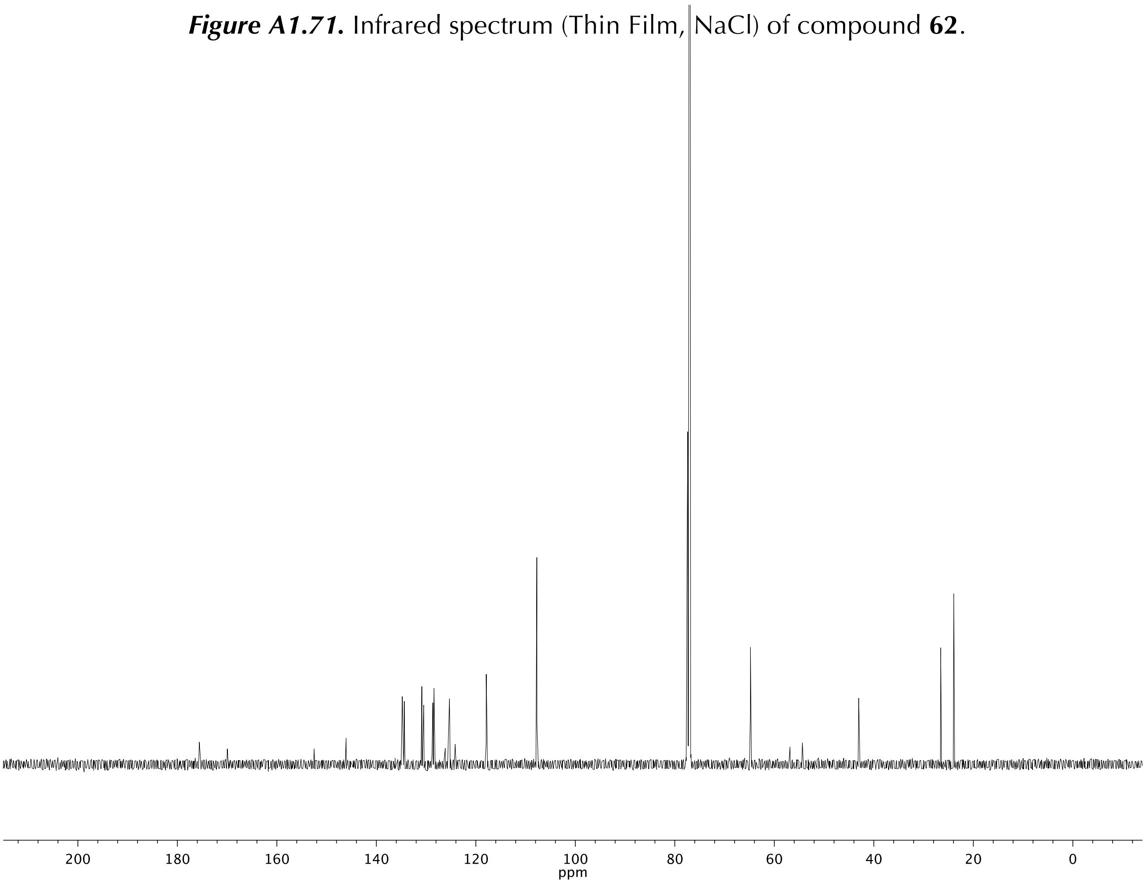

Figure A1.72. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **62.**

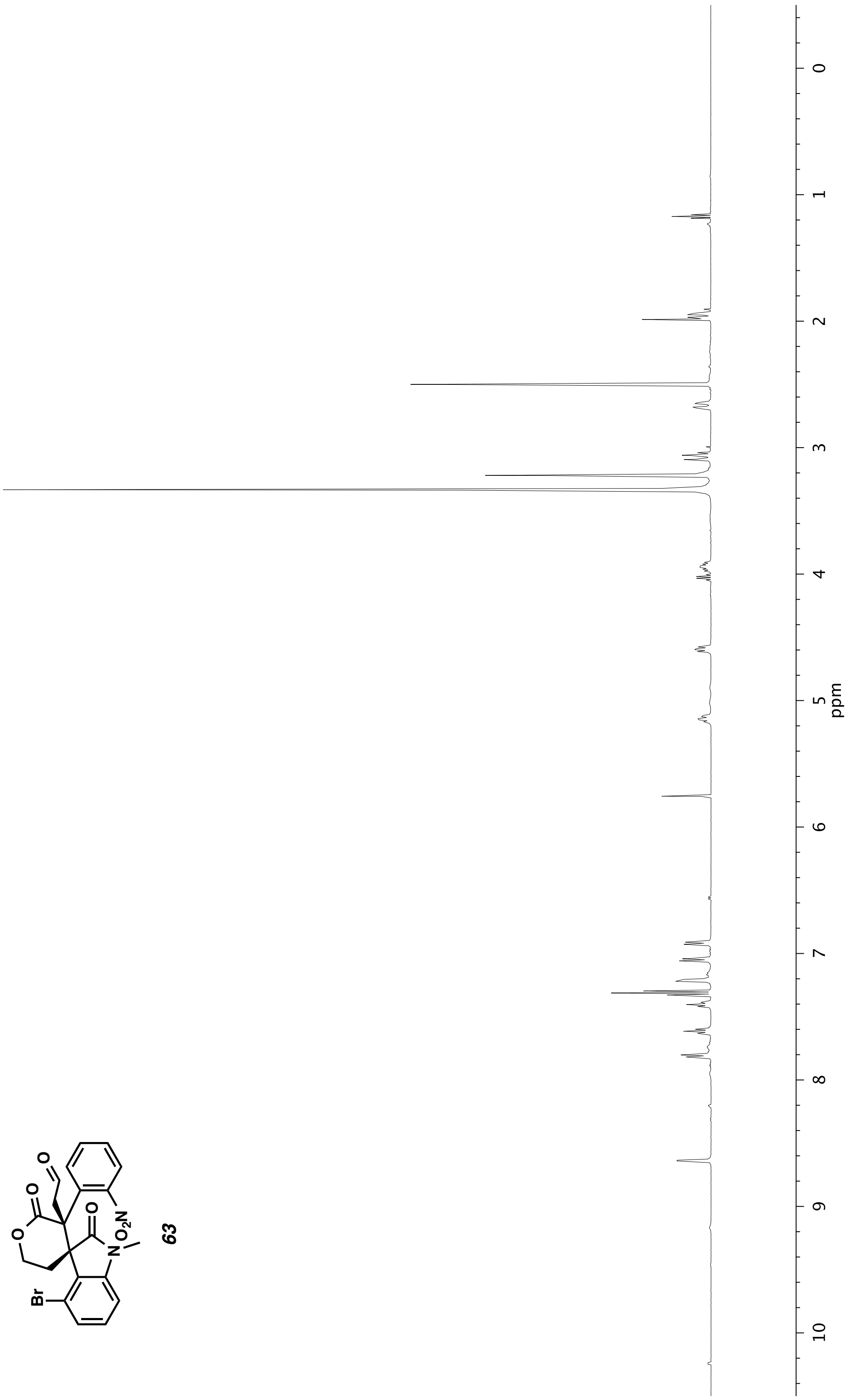

Figure A1.73. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **63**.

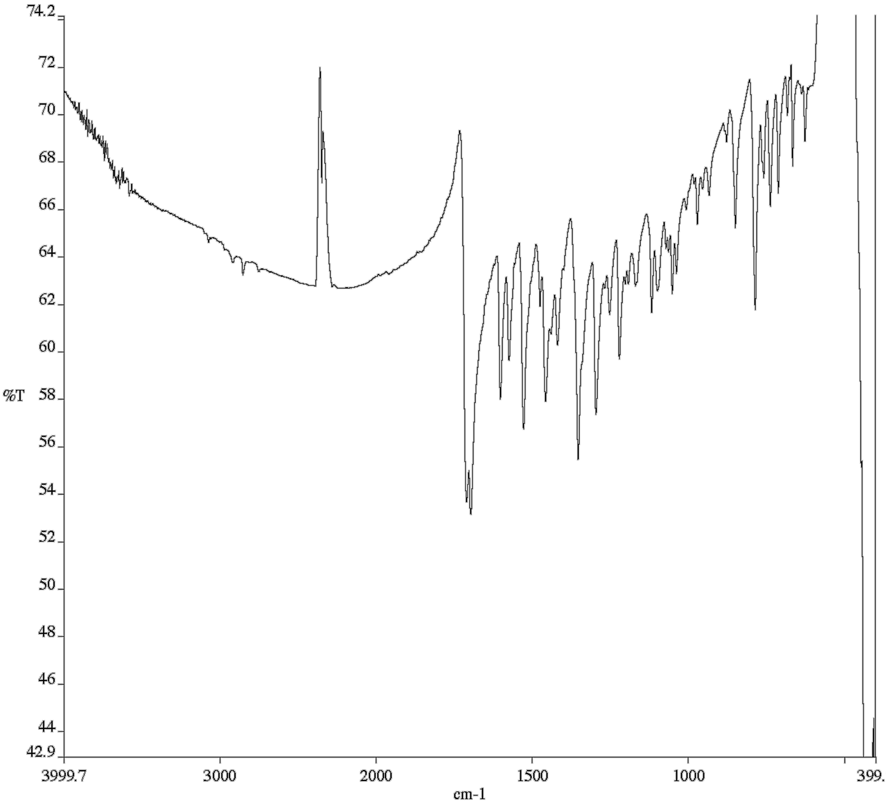

Figure A1.74. Infrared spectrum (Thin Film, NaCl) of compound **63**.

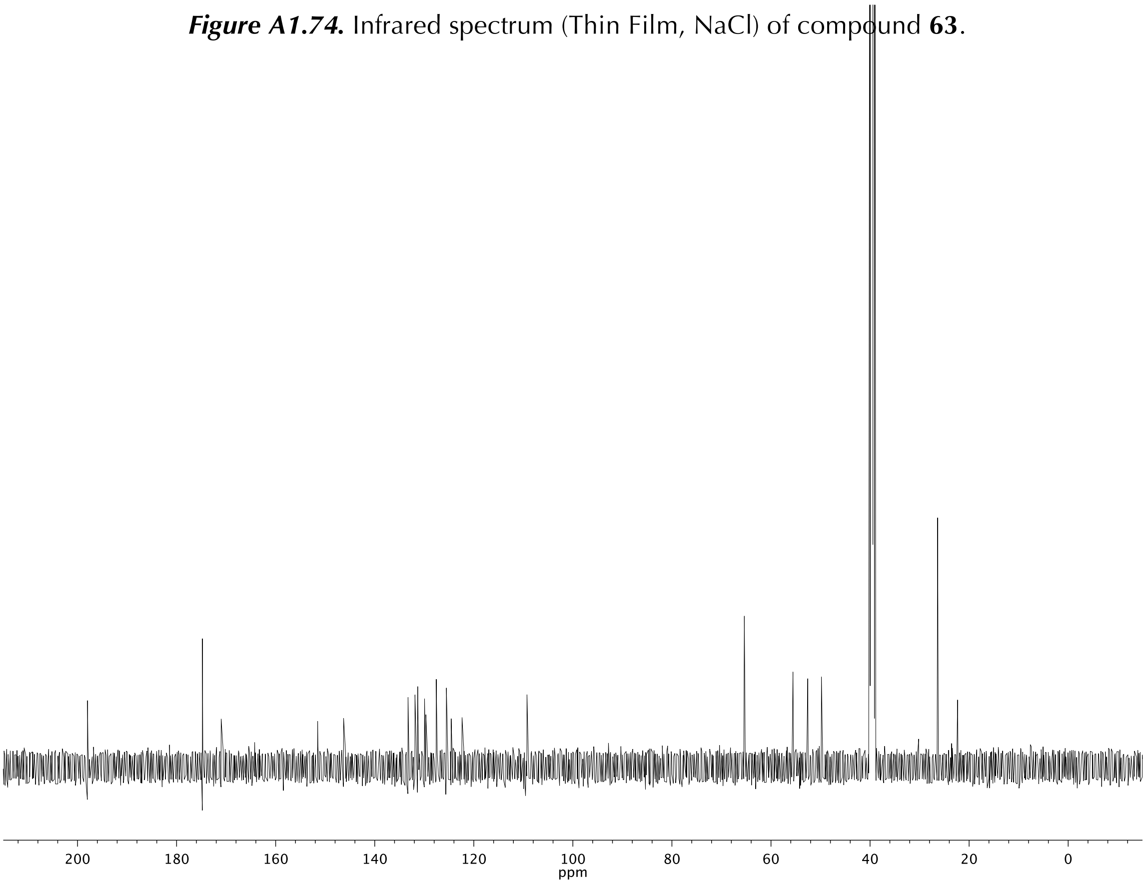

Figure A1.75. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **63.**

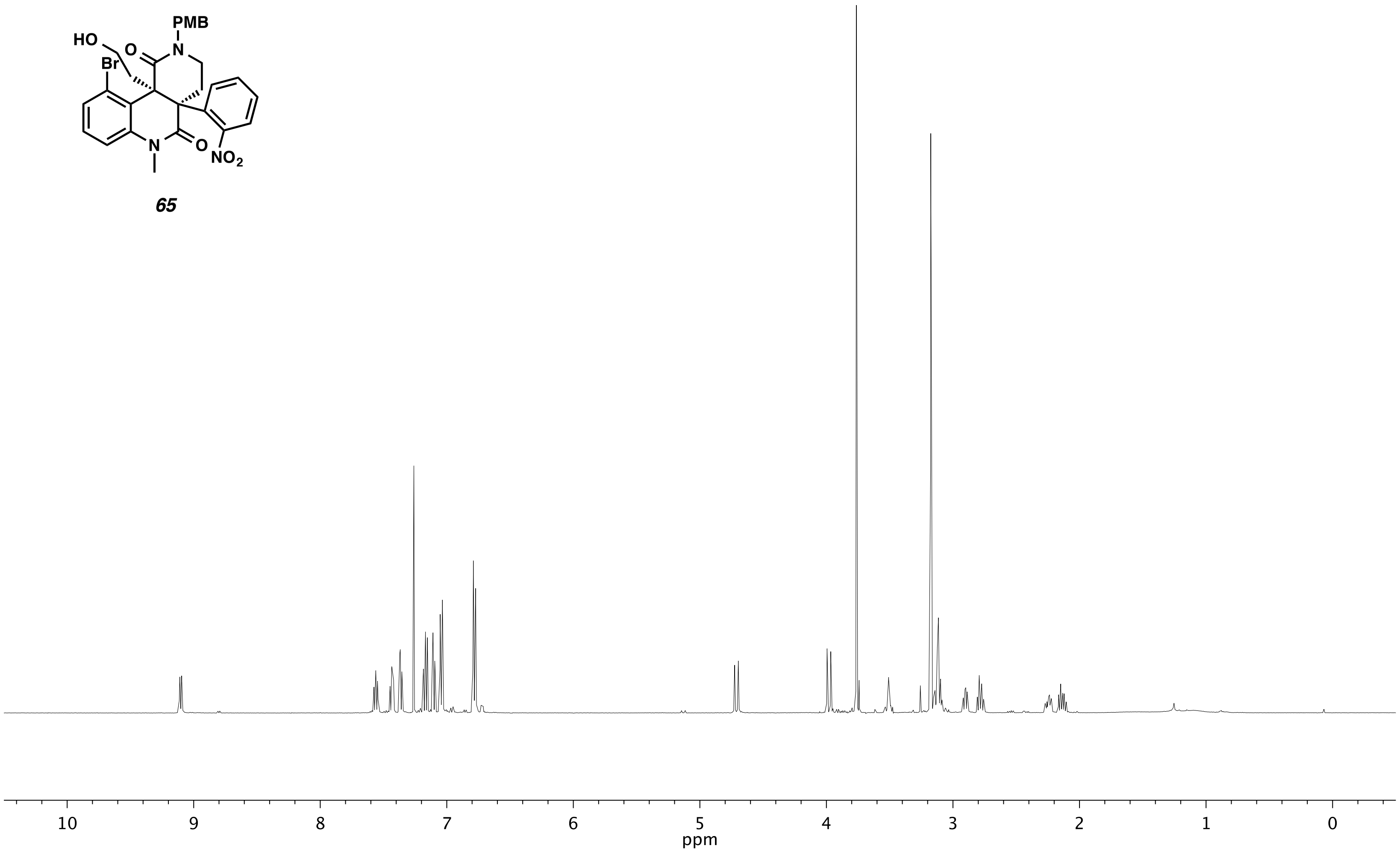
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Figure A1.76. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **65**.

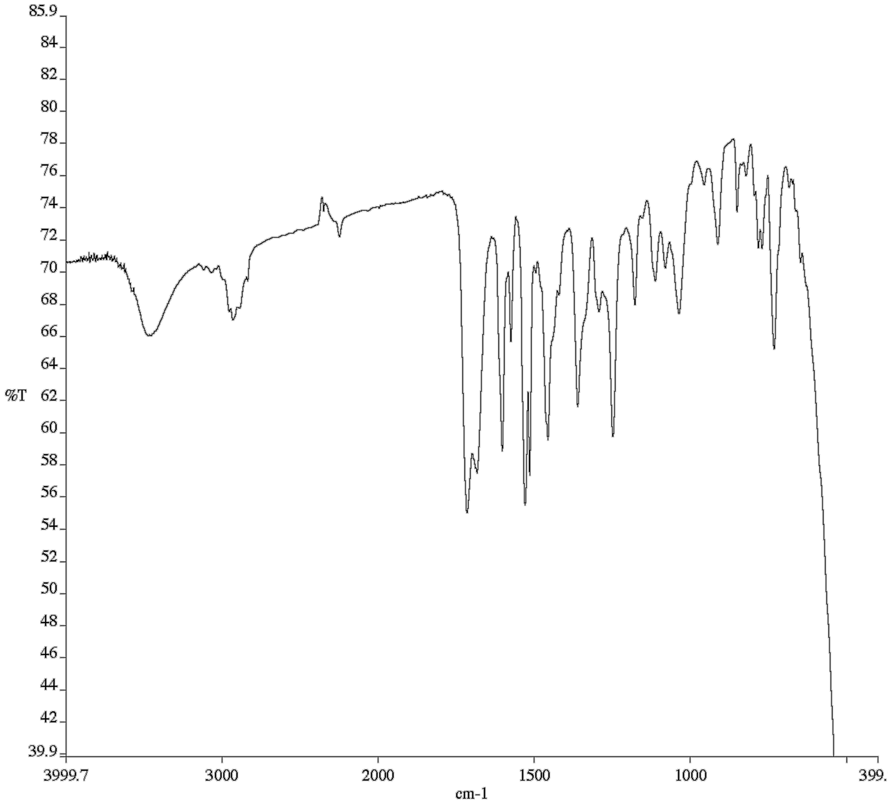

Figure A1.77. Infrared spectrum (Thin Film, NaCl) of compound **65**.

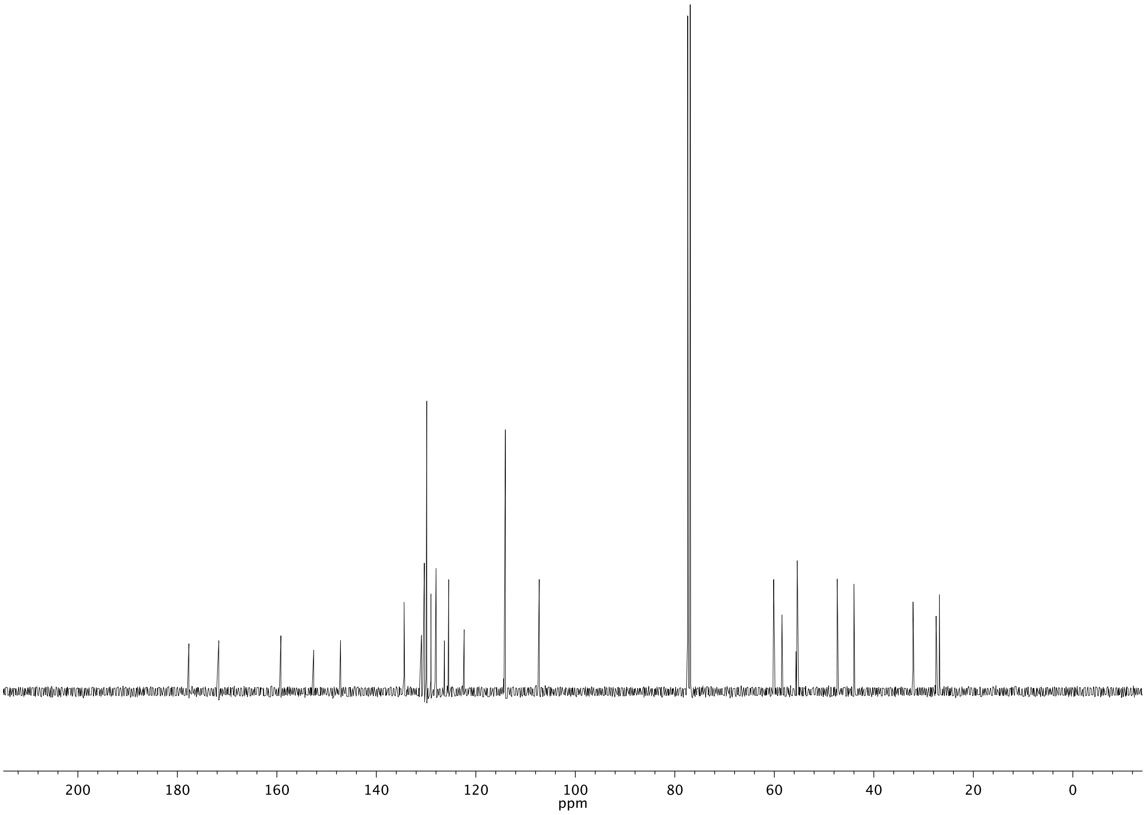

Figure A1.78. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **65.**

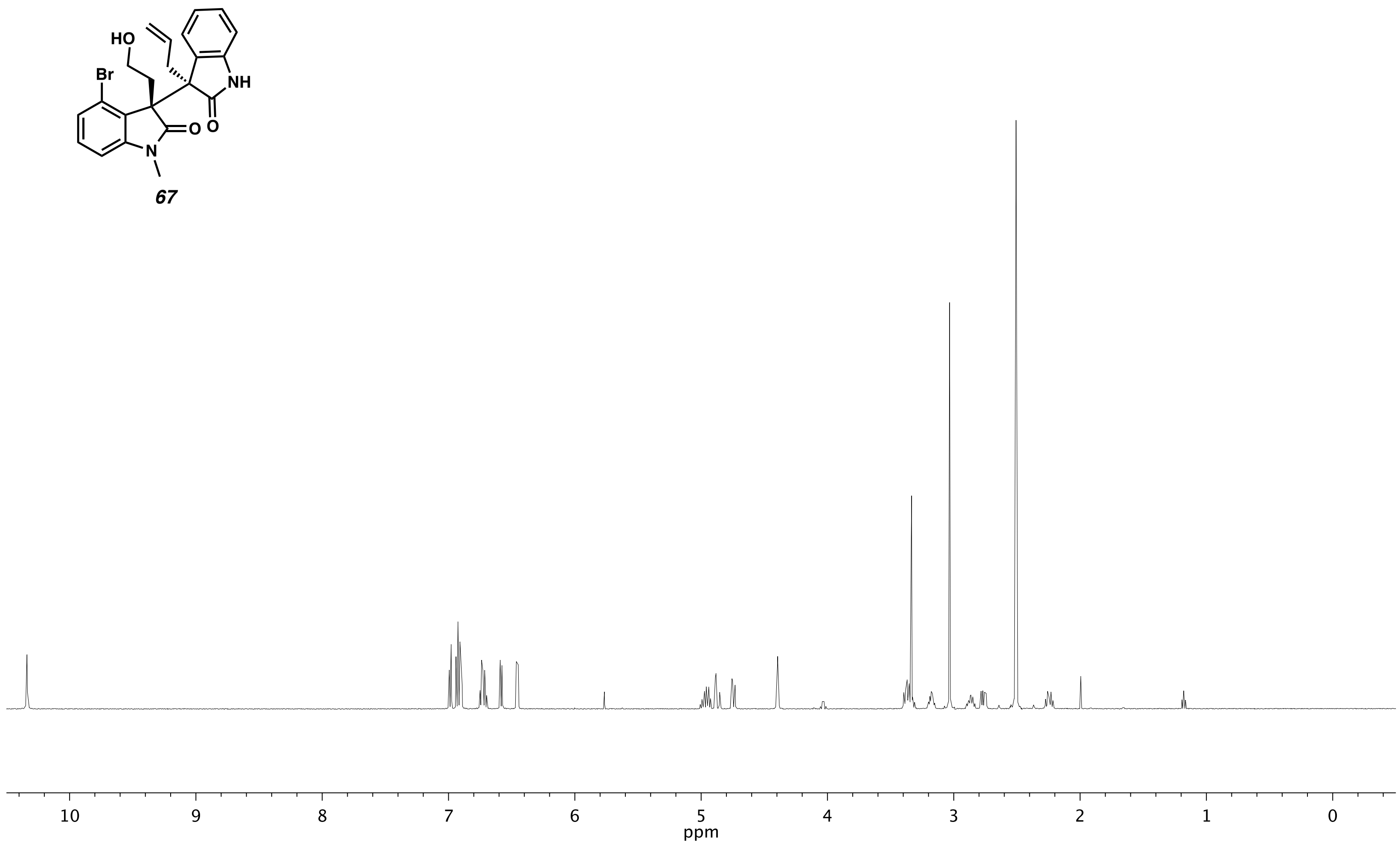

Figure A1.79. ^{1}H NMR (500 MHz, DMSO) of compound **67**.

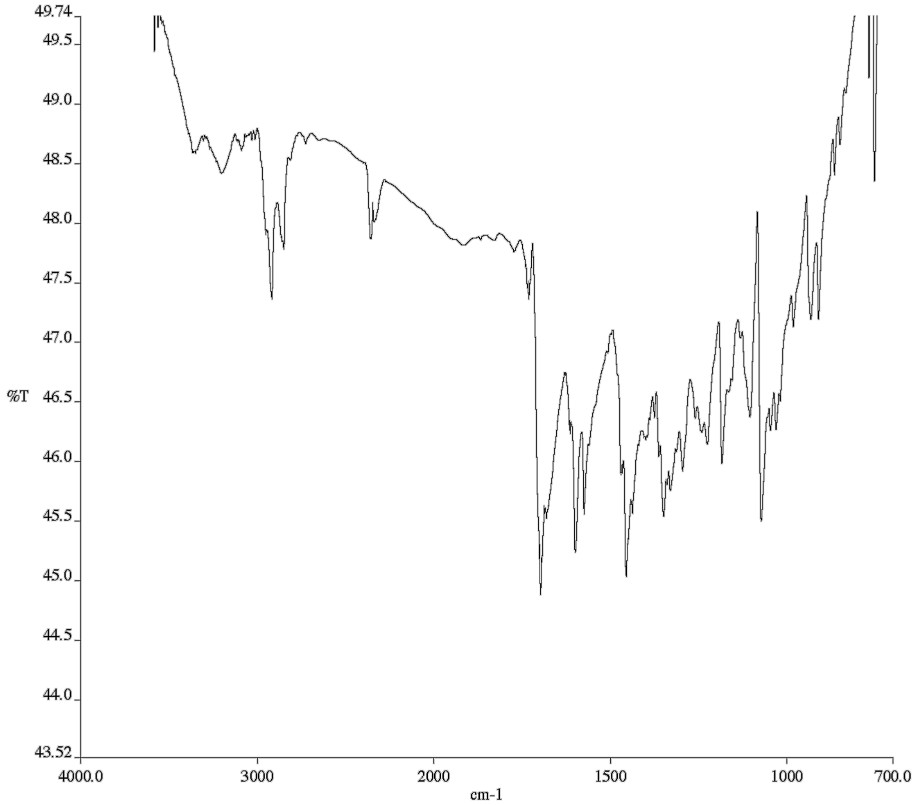

Figure A1.80. Infrared spectrum (Thin Film, NaCl) of compound **67**.

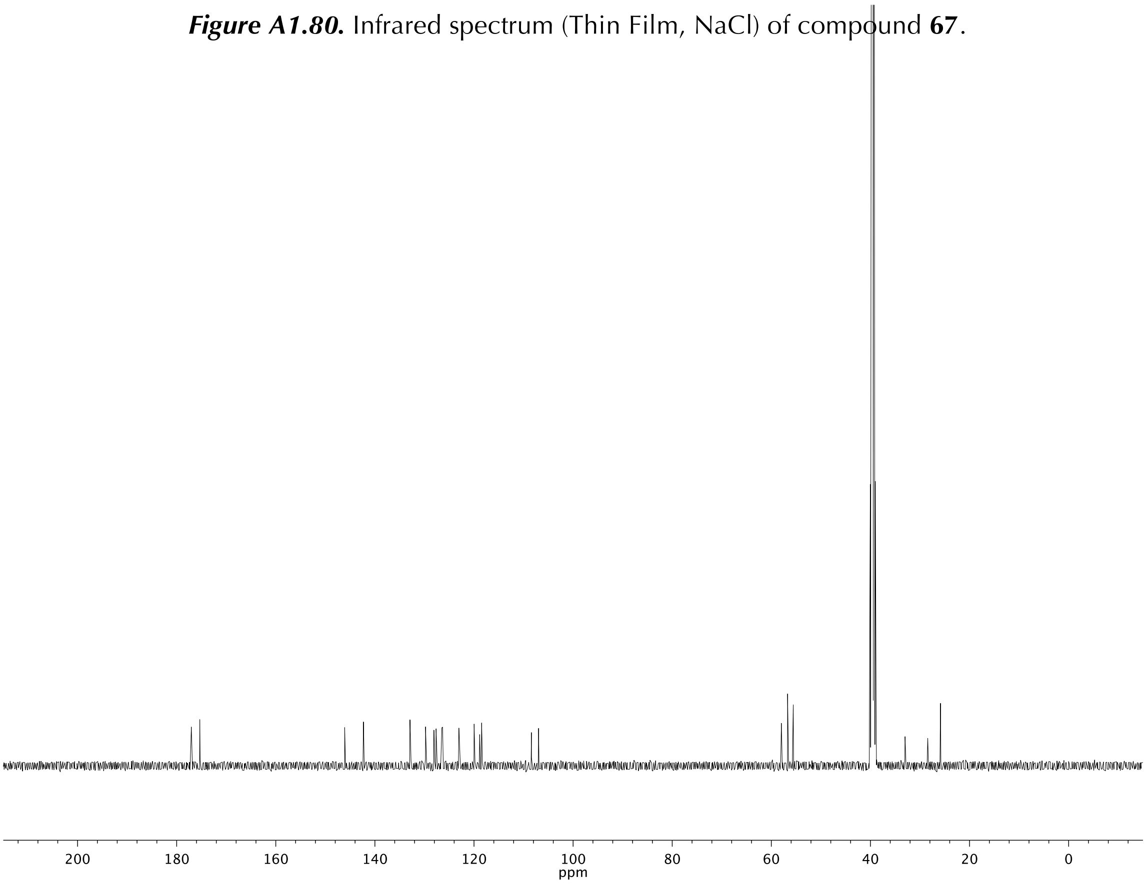

Figure A1.81. ^{13}C NMR (125 MHz, DMSO) of compound **67**.

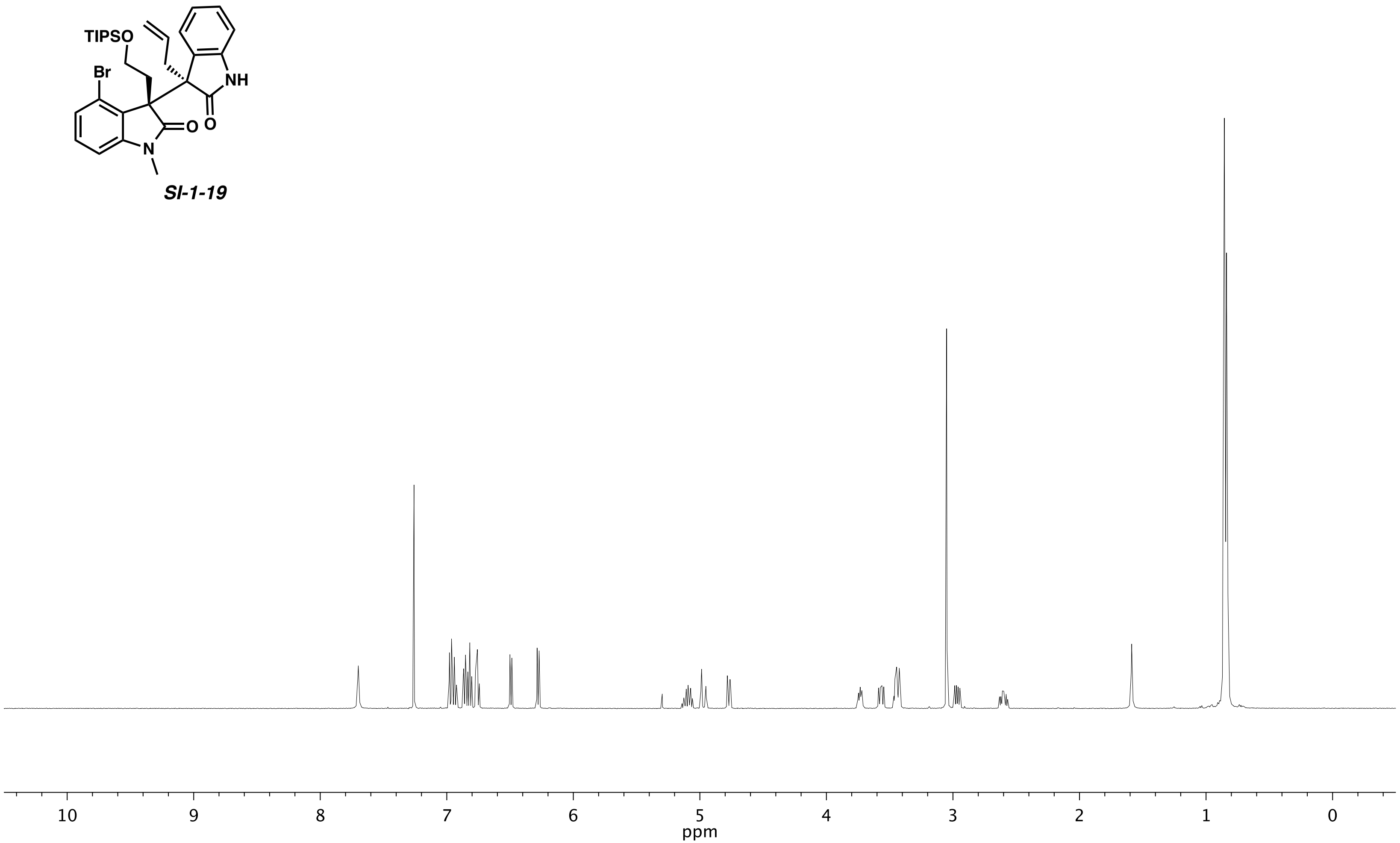

Figure A1.82. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **SI-1-19**.

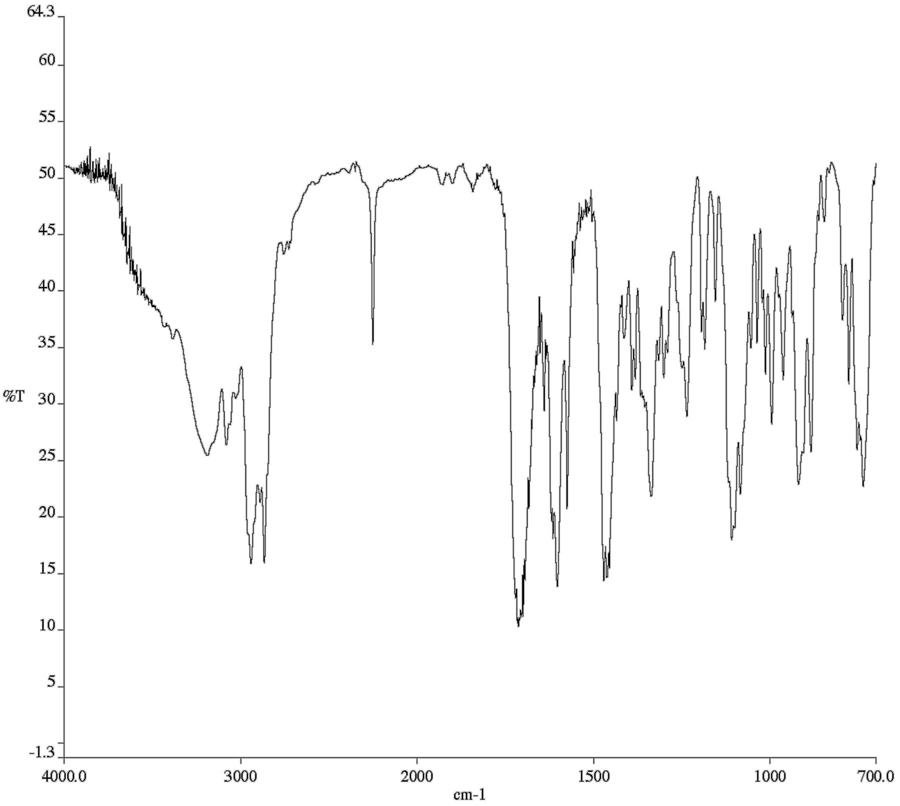

Figure A1.83. Infrared spectrum (Thin Film, NaCl) of compound **SI-1-19**.

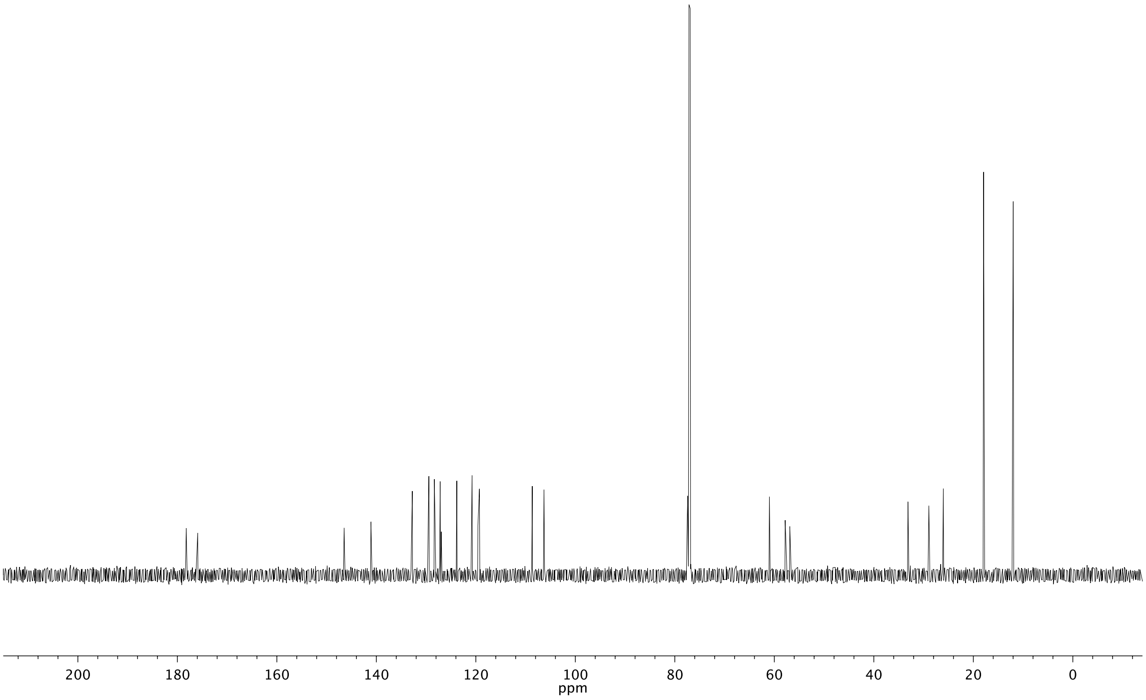

Figure A1.84. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-1-19**.

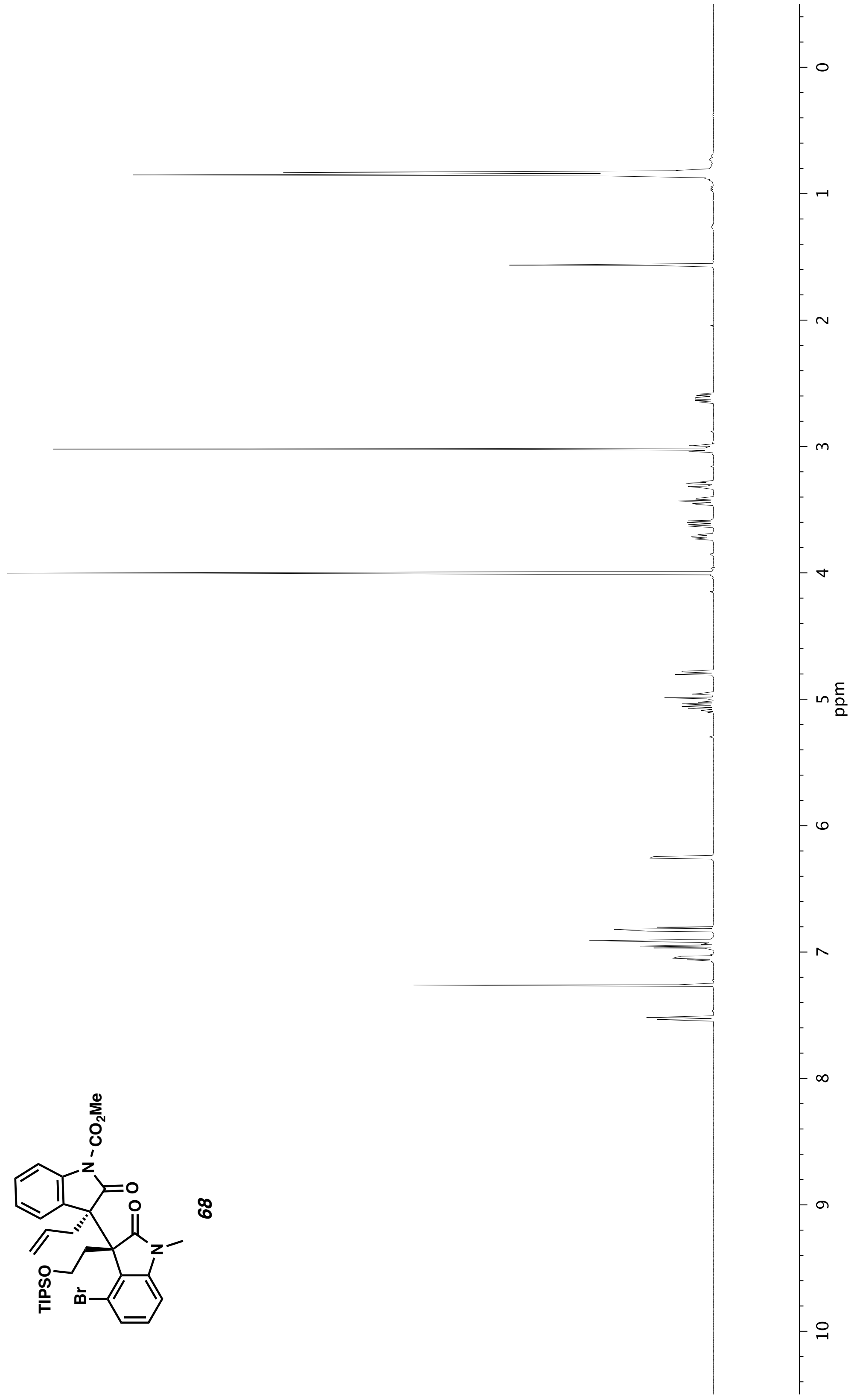

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Figure A1.85. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **68**.

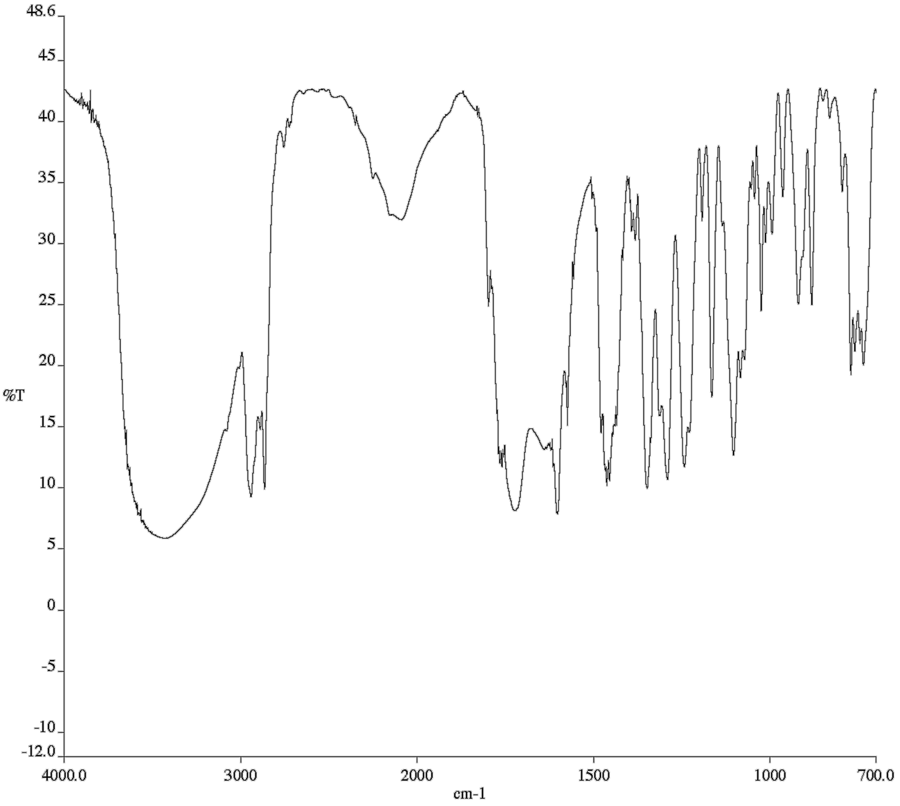

Figure A1.86. Infrared spectrum (Thin Film, NaCl) of compound **68**.

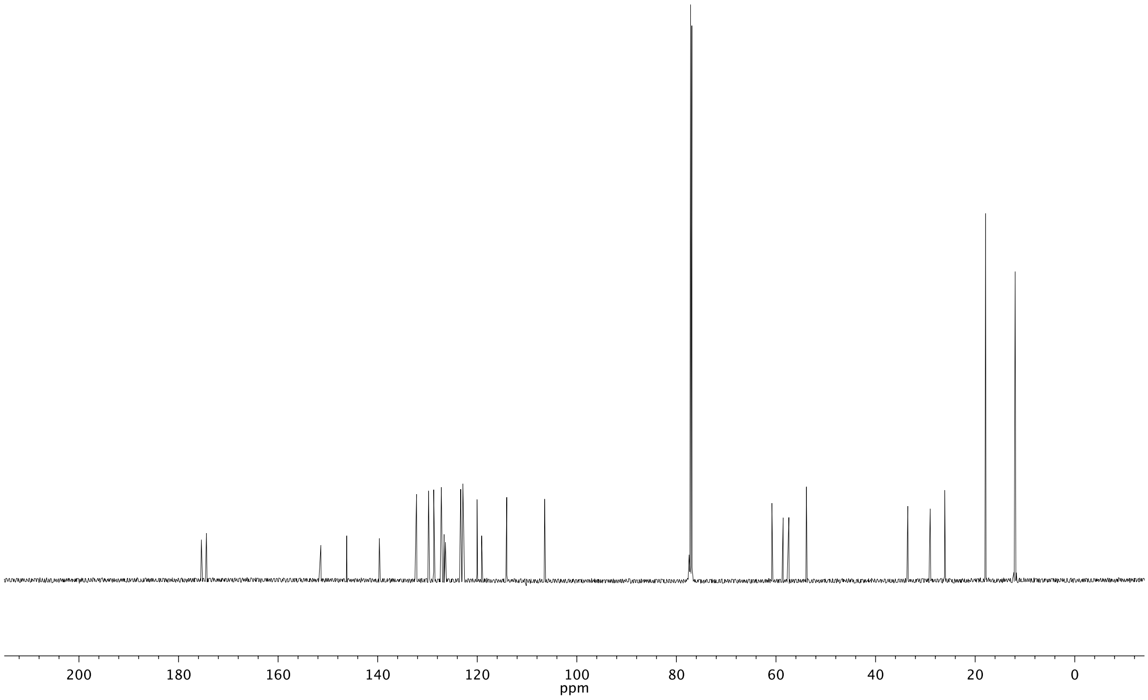

Figure A1.87. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **68**.

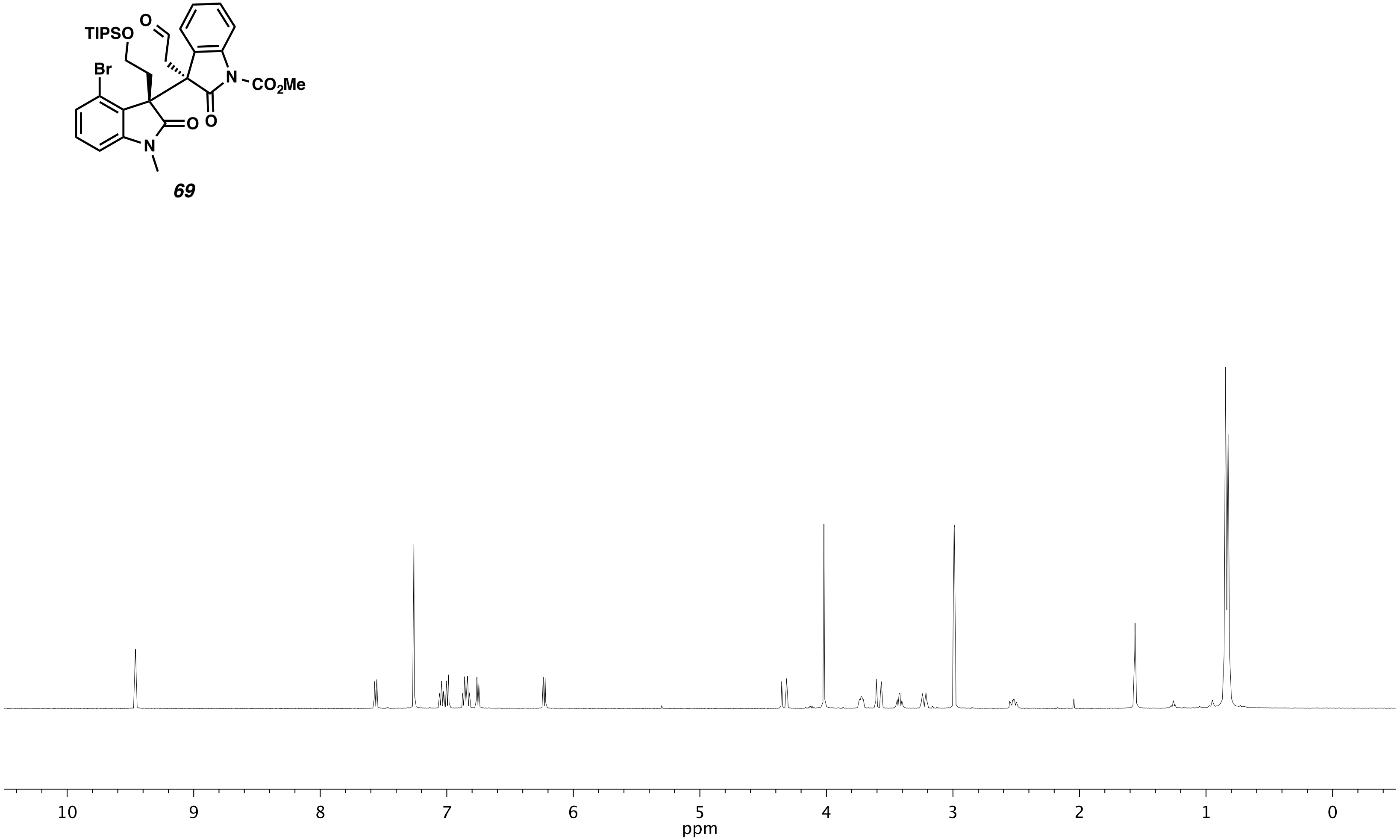

Figure A1.88. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **69**.

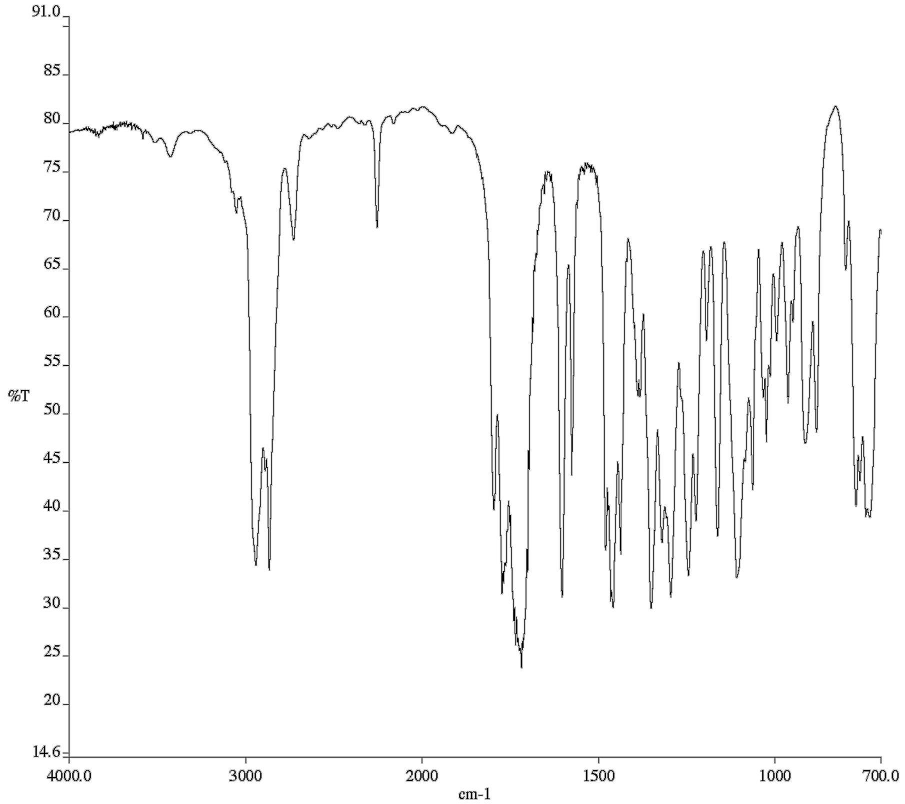

Figure A1.89. Infrared spectrum (Thin Film, NaCl) of compound **69**.

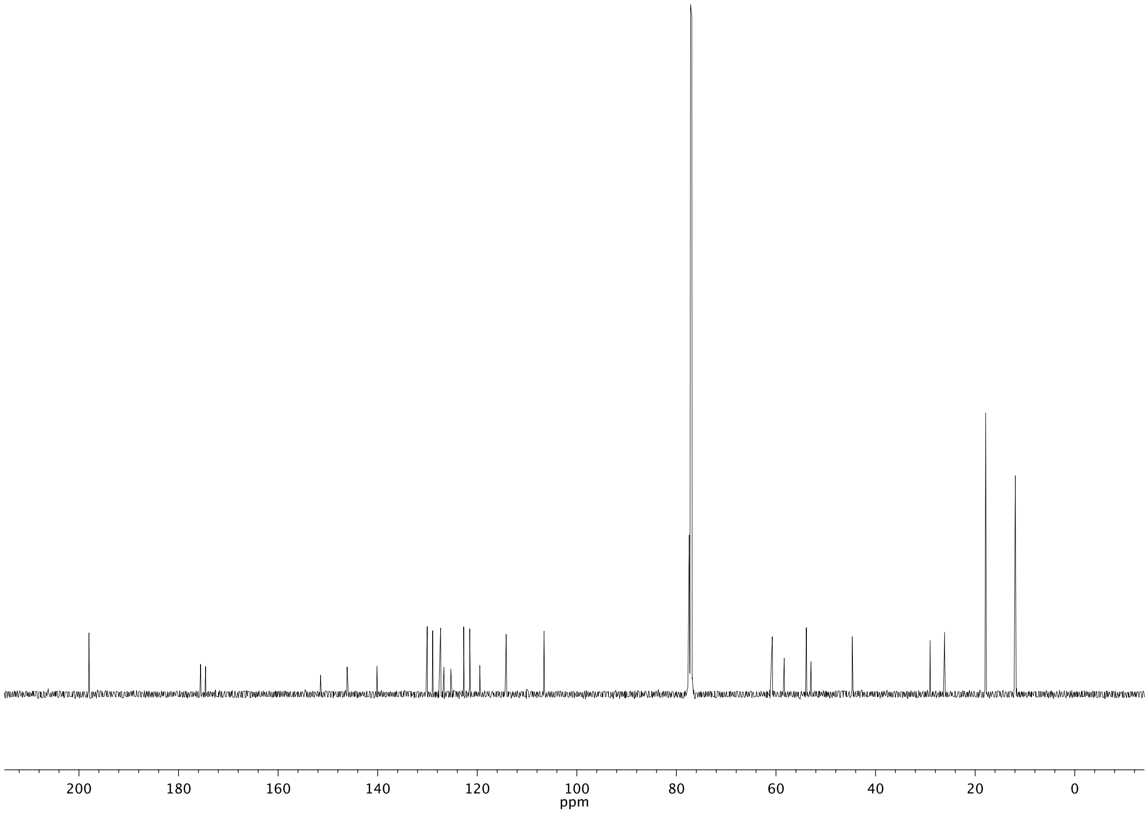

Figure A1.90. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **69**.

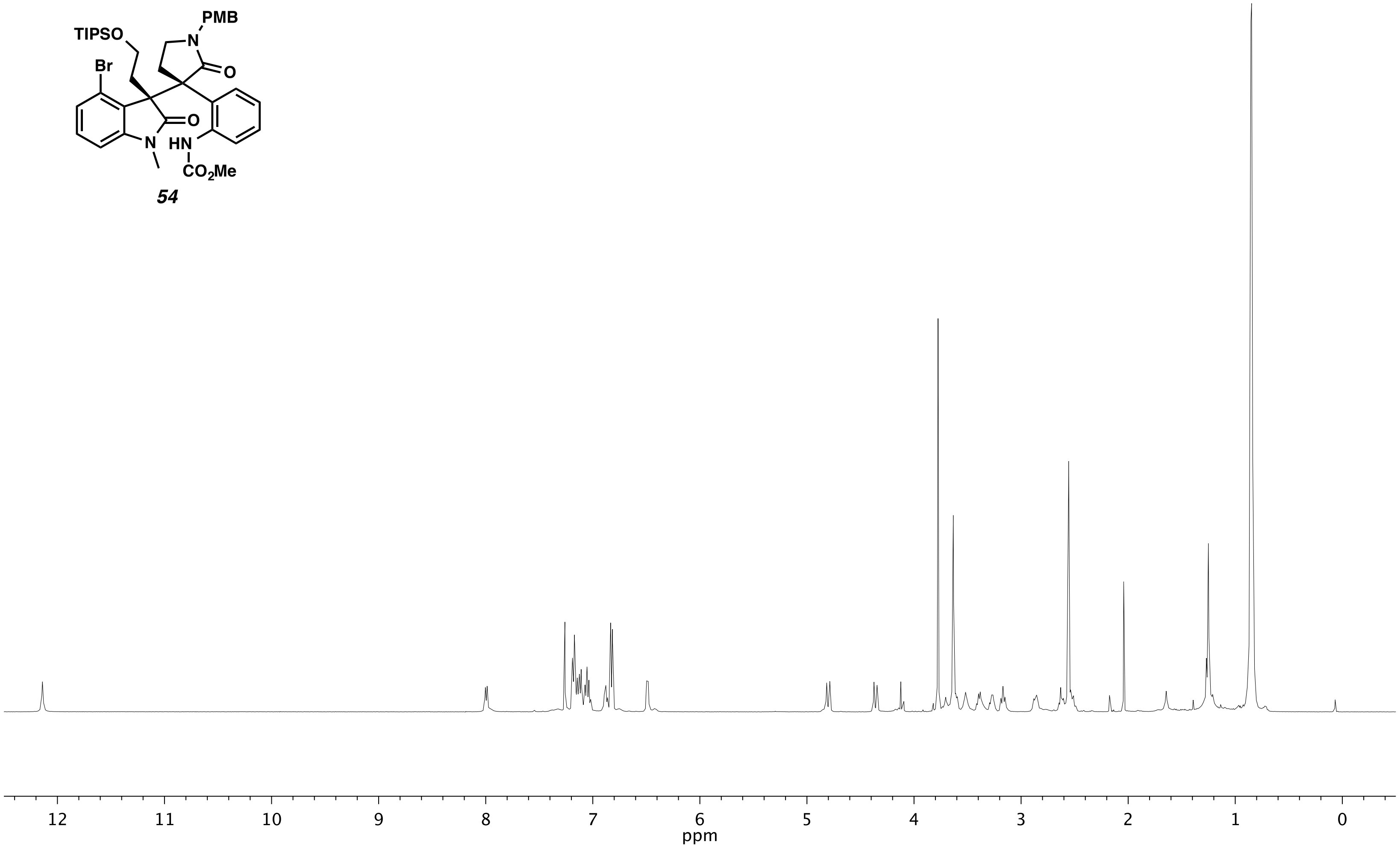

Figure A1.91. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **54**.

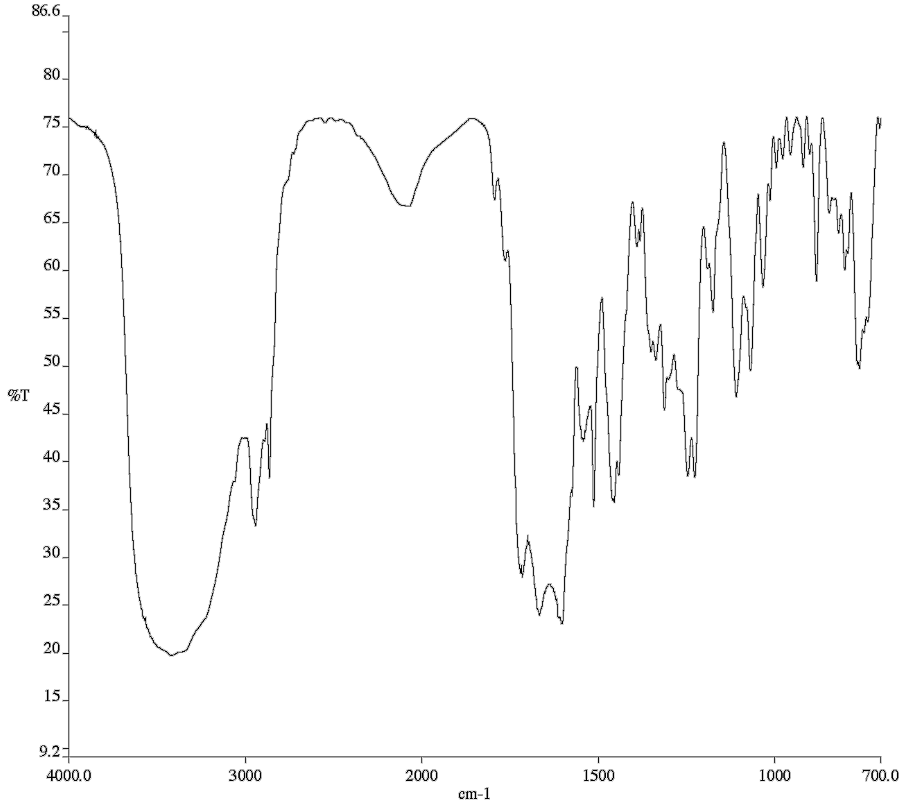

Figure A1.92. Infrared spectrum (Thin Film, NaCl) of compound **54**.

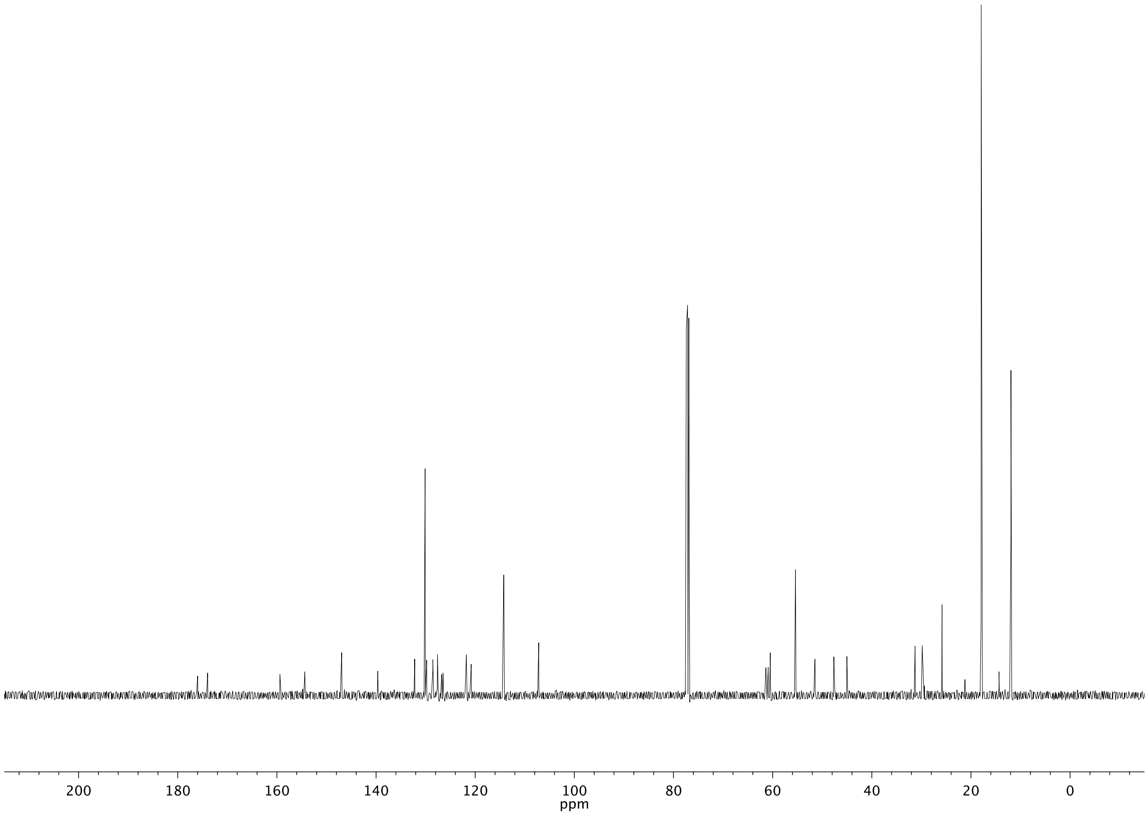

Figure A1.93. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **54**.

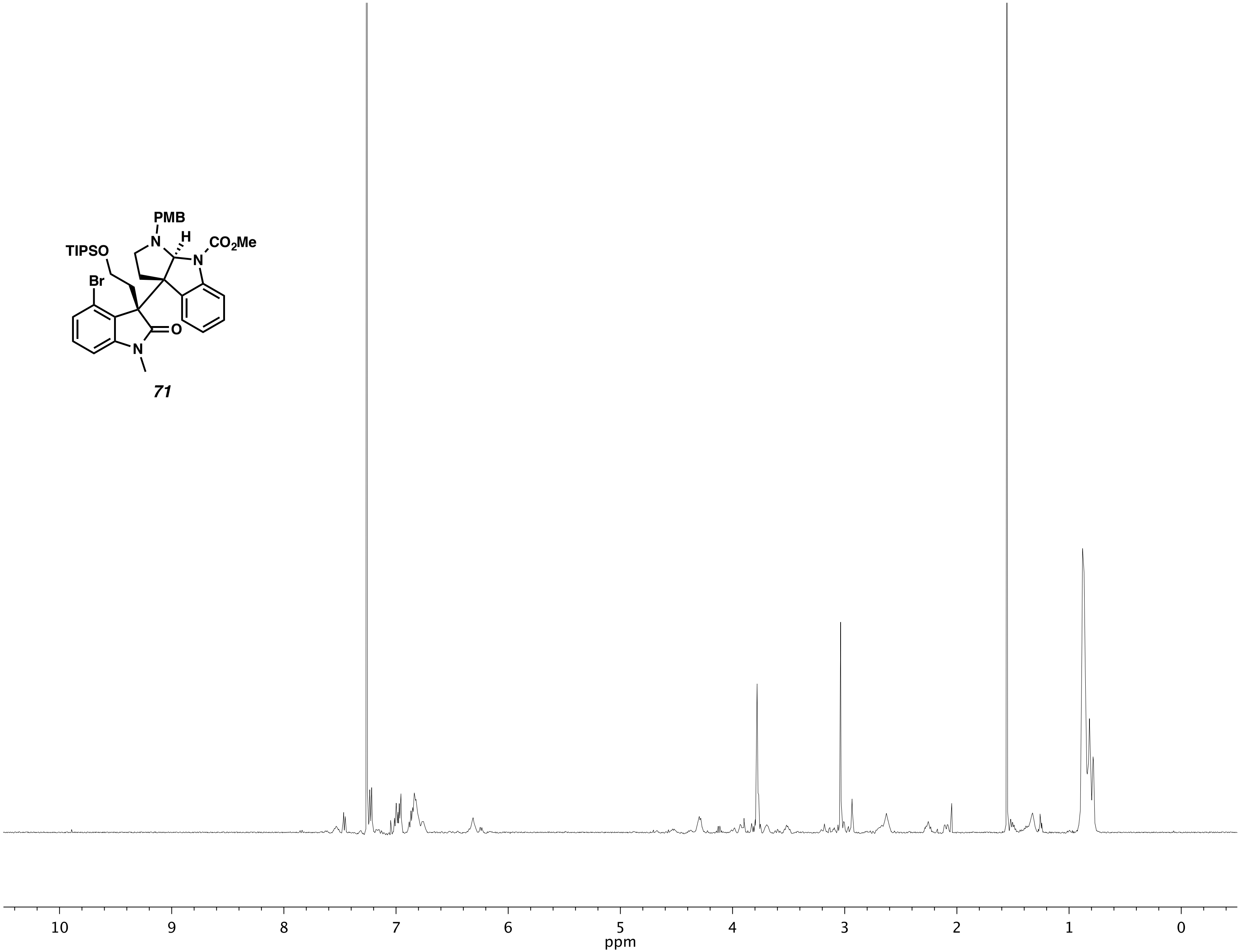

Figure A1.94. ^{1}H NMR (300 MHz, CDCl$_3$) of compound **71**.

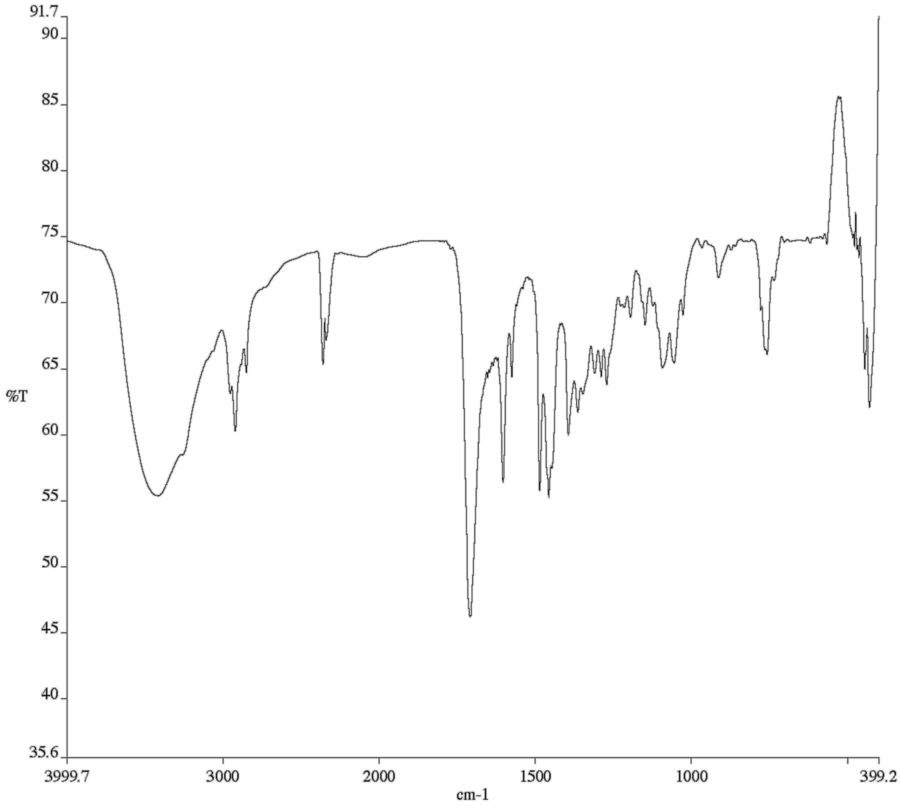

Figure A1.95. Infrared spectrum (Thin Film, NaCl) of compound **71**.

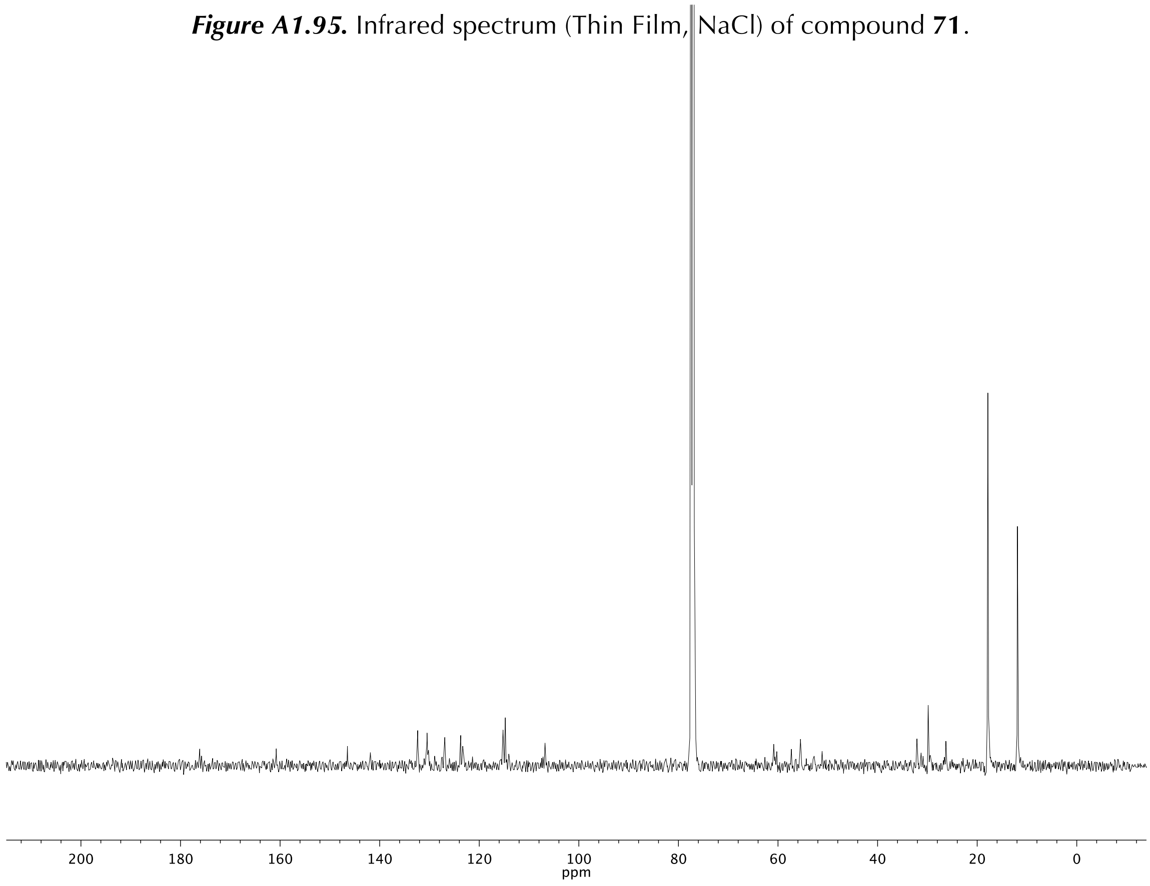

Figure A1.96. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **71**.

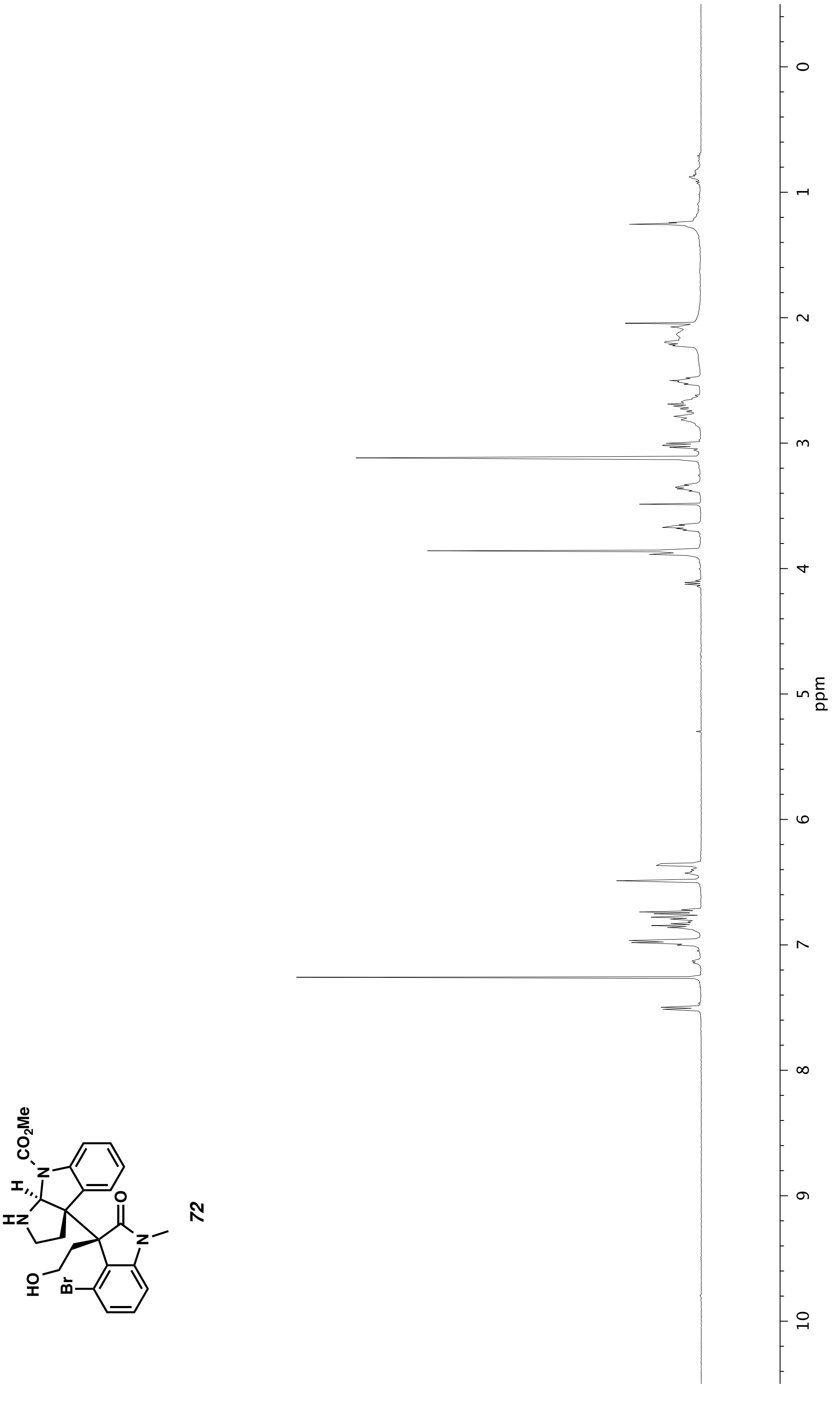

Figure A1.97. ^{1}H NMR (600 MHz, CDCl$_3$) of compound **72**.

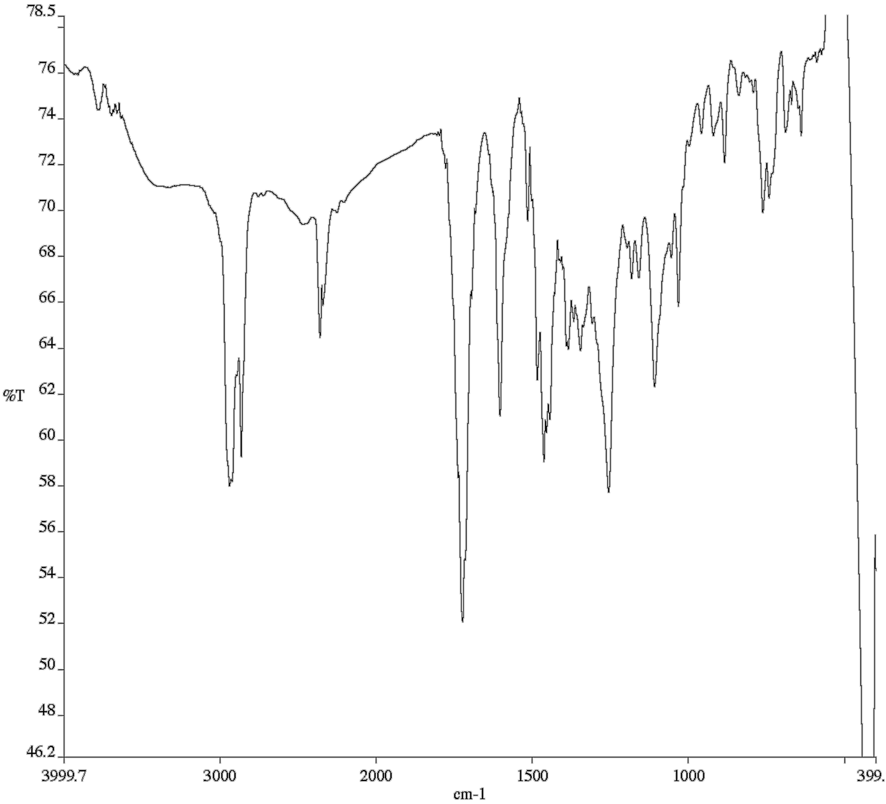

Figure A1.98. Infrared spectrum (Thin Film, NaCl) of compound **72**.

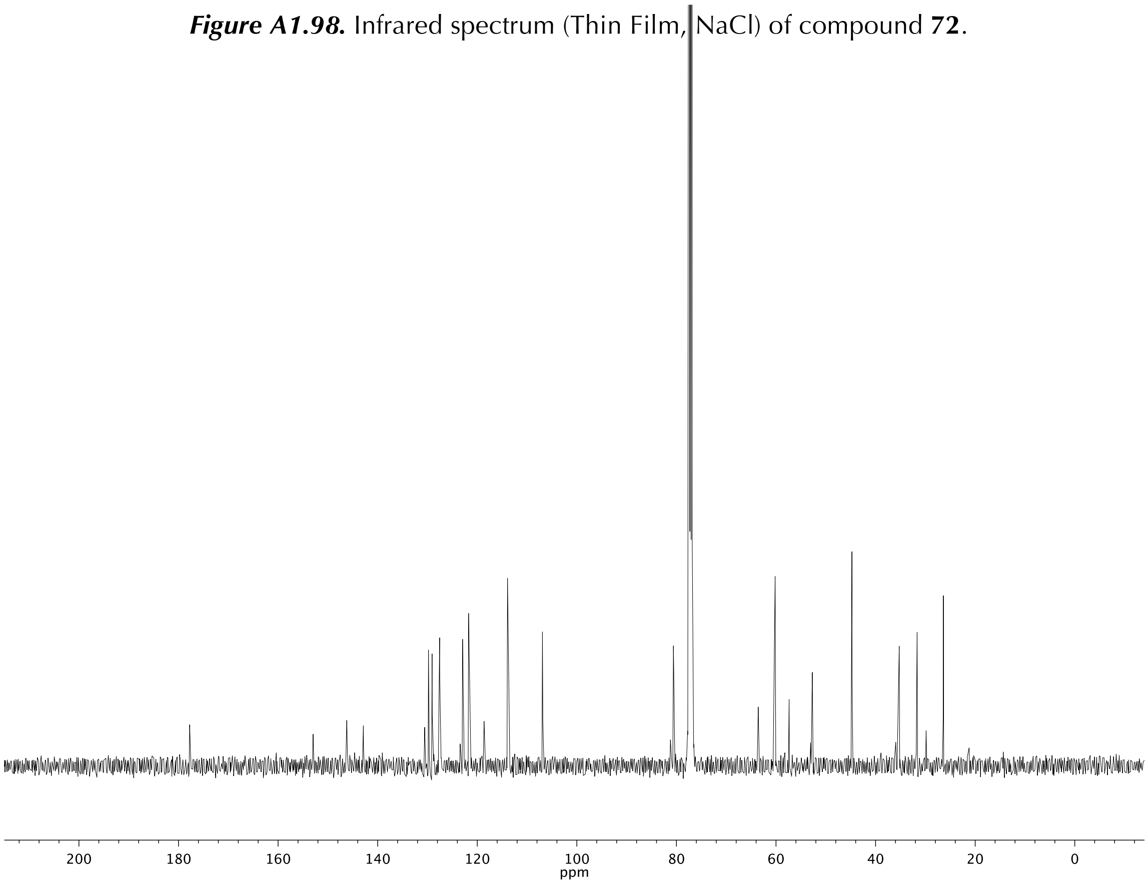

Figure A1.99. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **72**.

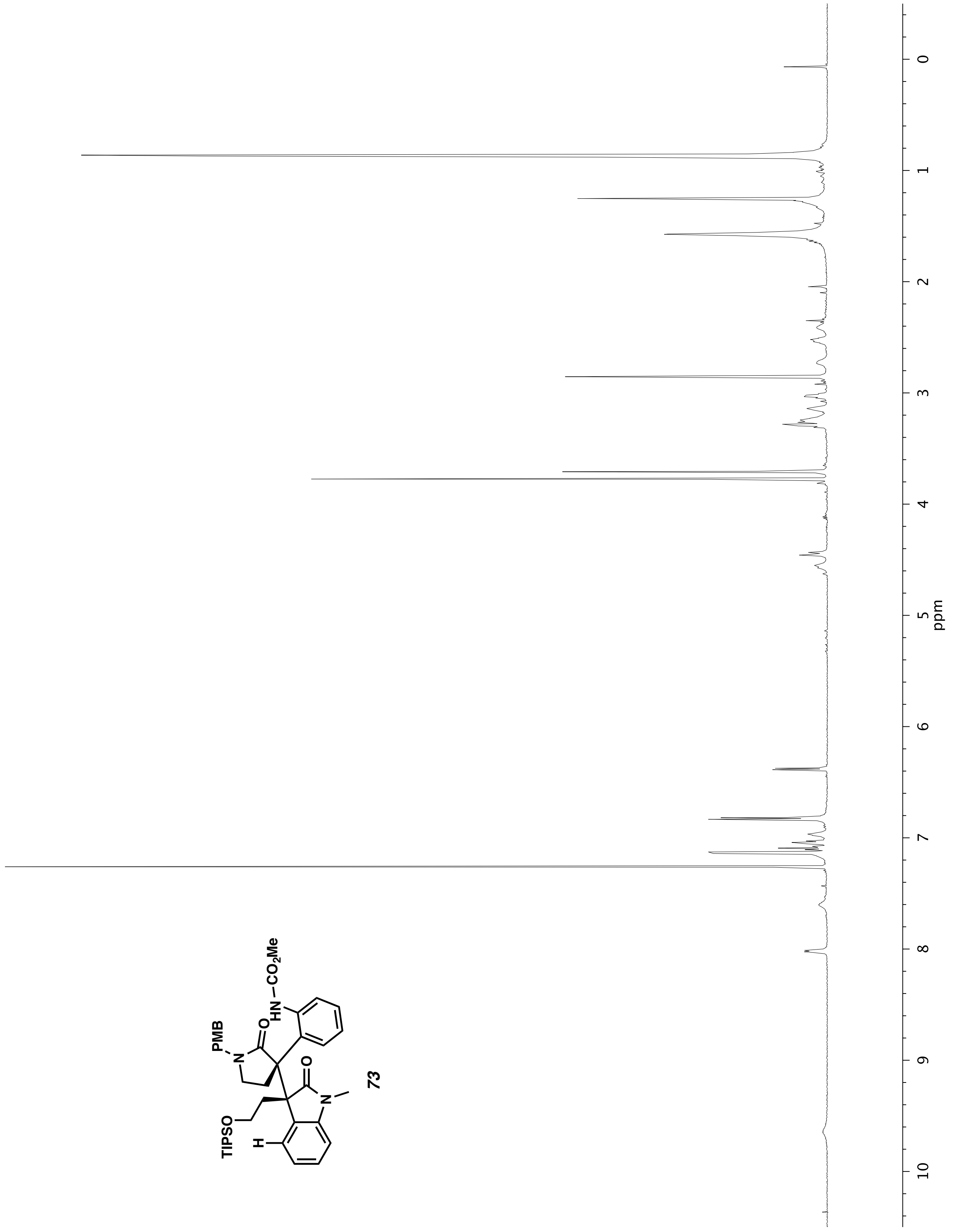

Figure A1.100. ^{1}H NMR (600 MHz, CDCl$_3$) of compound **73**.

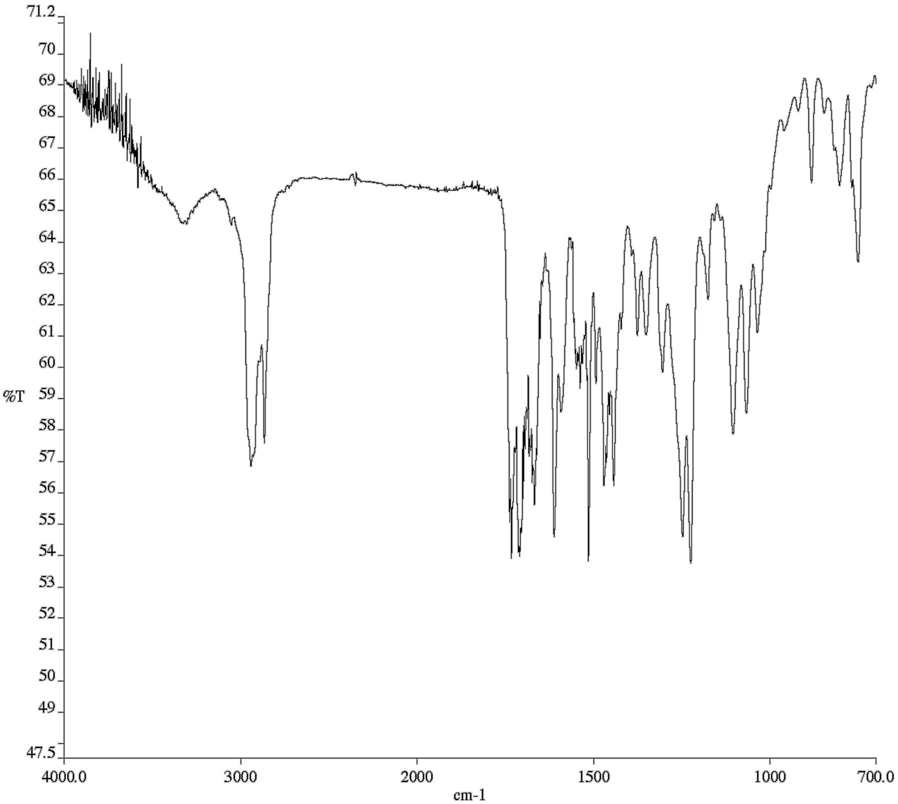

Figure A1.101. Infrared spectrum (Thin Film, NaCl) of compound **73**.

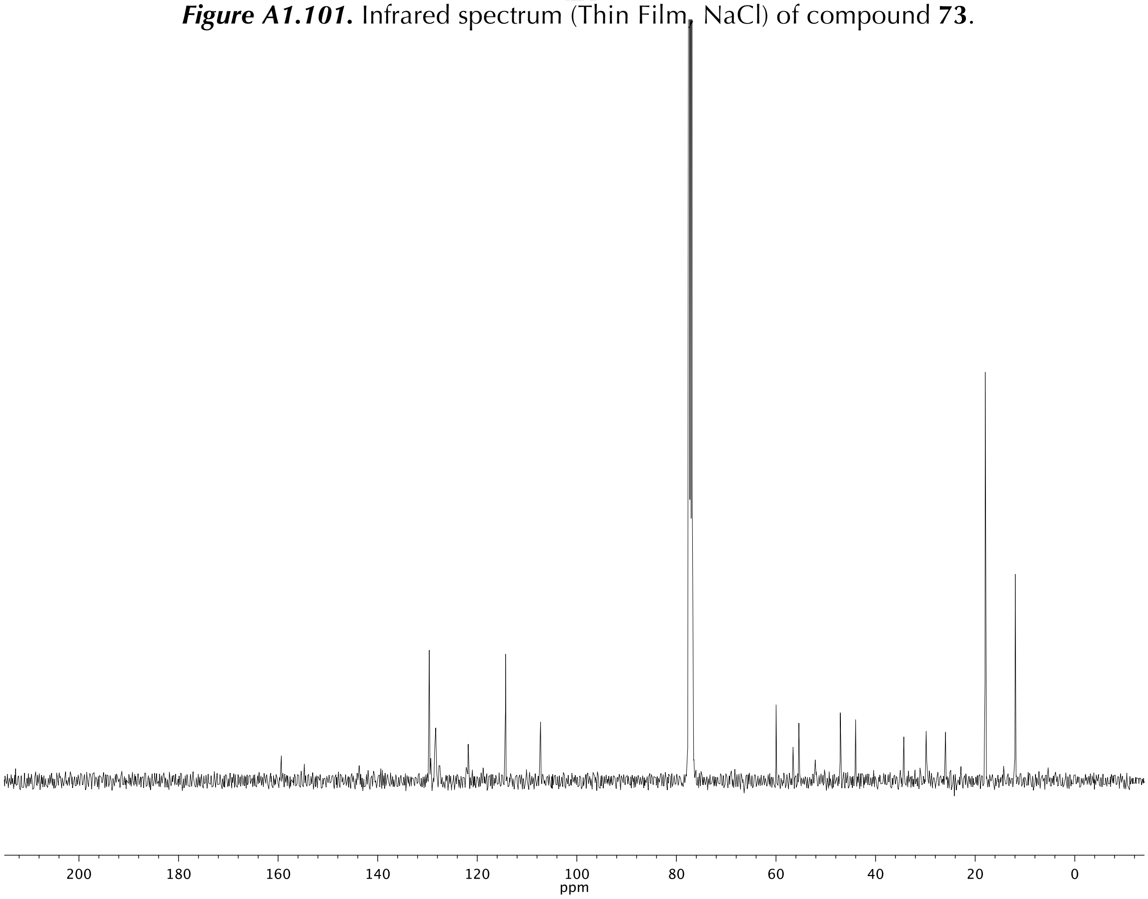

Figure A1.102. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **73**.

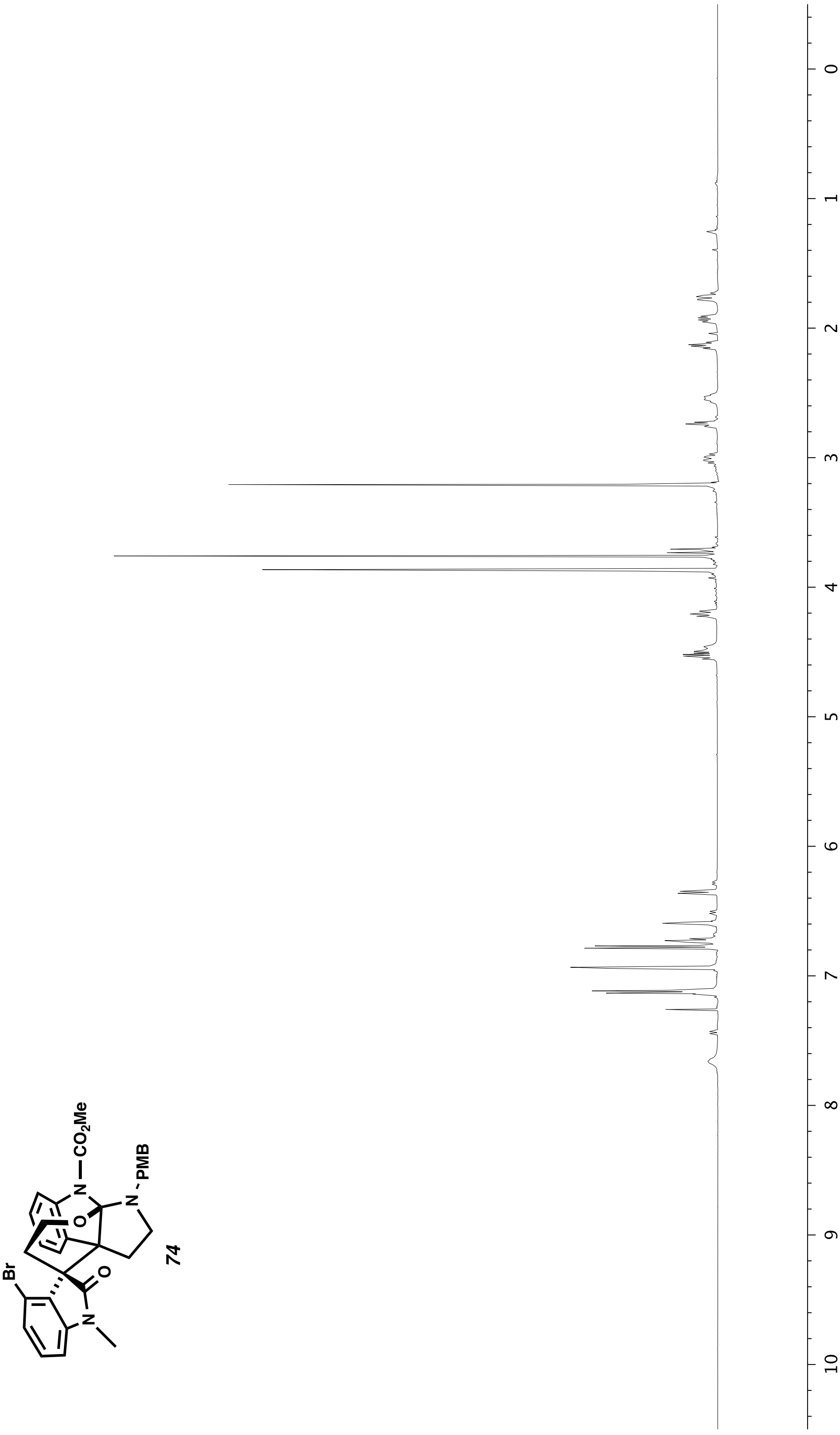

Figure A1.103. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **74**.

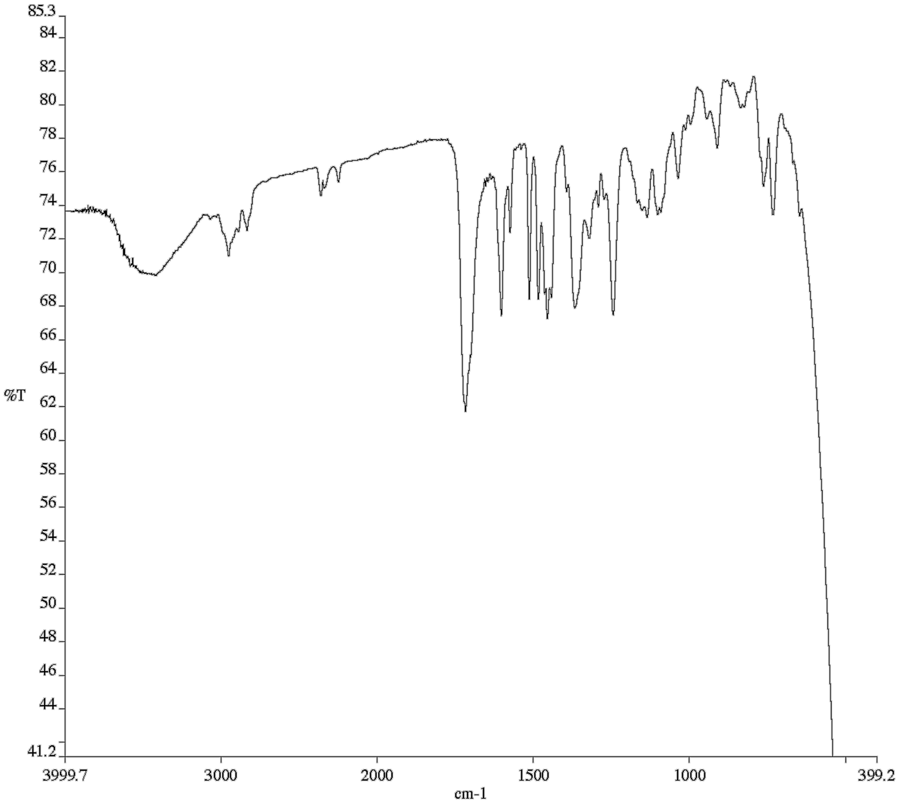

Figure A1.104. Infrared spectrum (Thin Film, NaCl) of compound **74**.

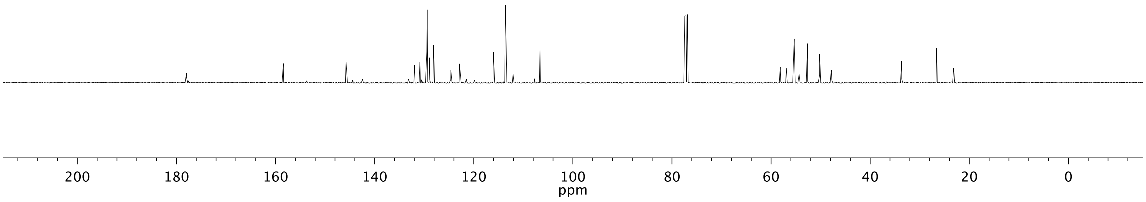

Figure A1.105. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **74**.

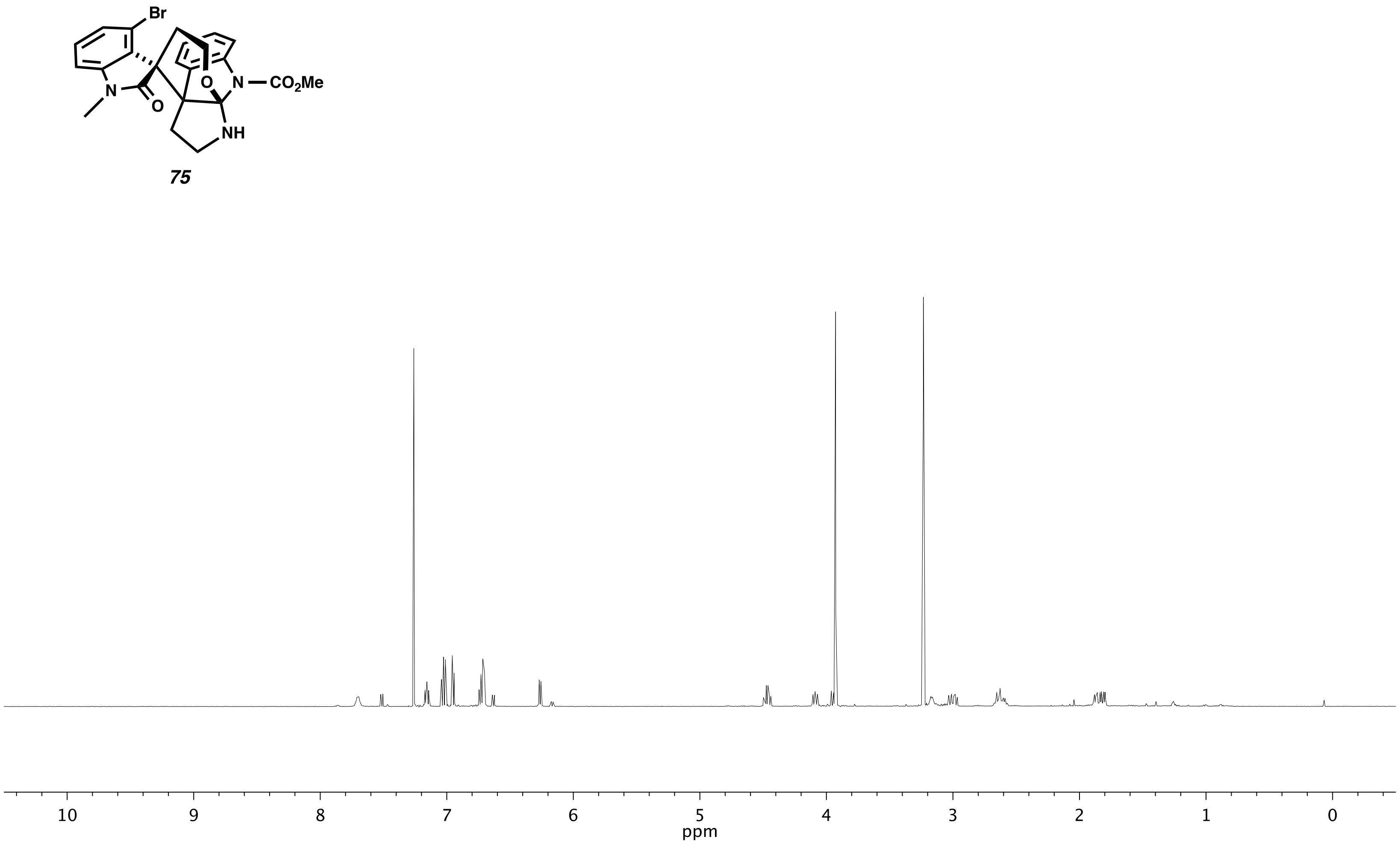

Figure A1.106. ^{1}H NMR (300 MHz, CDCl$_3$) of compound **75**.

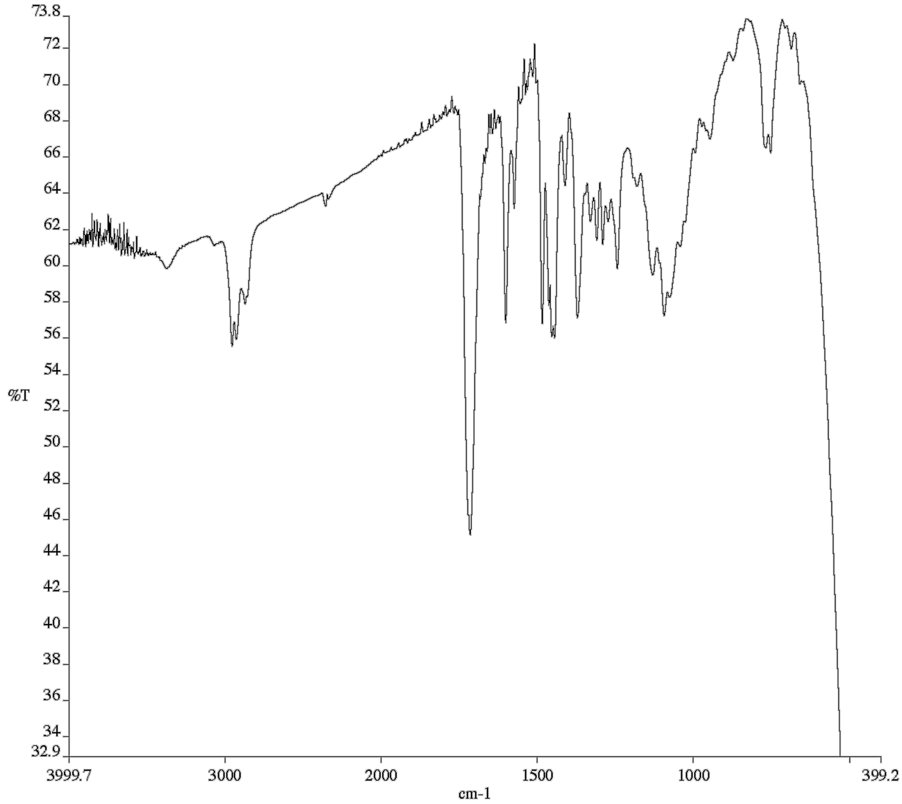

Figure A1.107. Infrared spectrum (Thin Film, NaCl) of compound **75**.

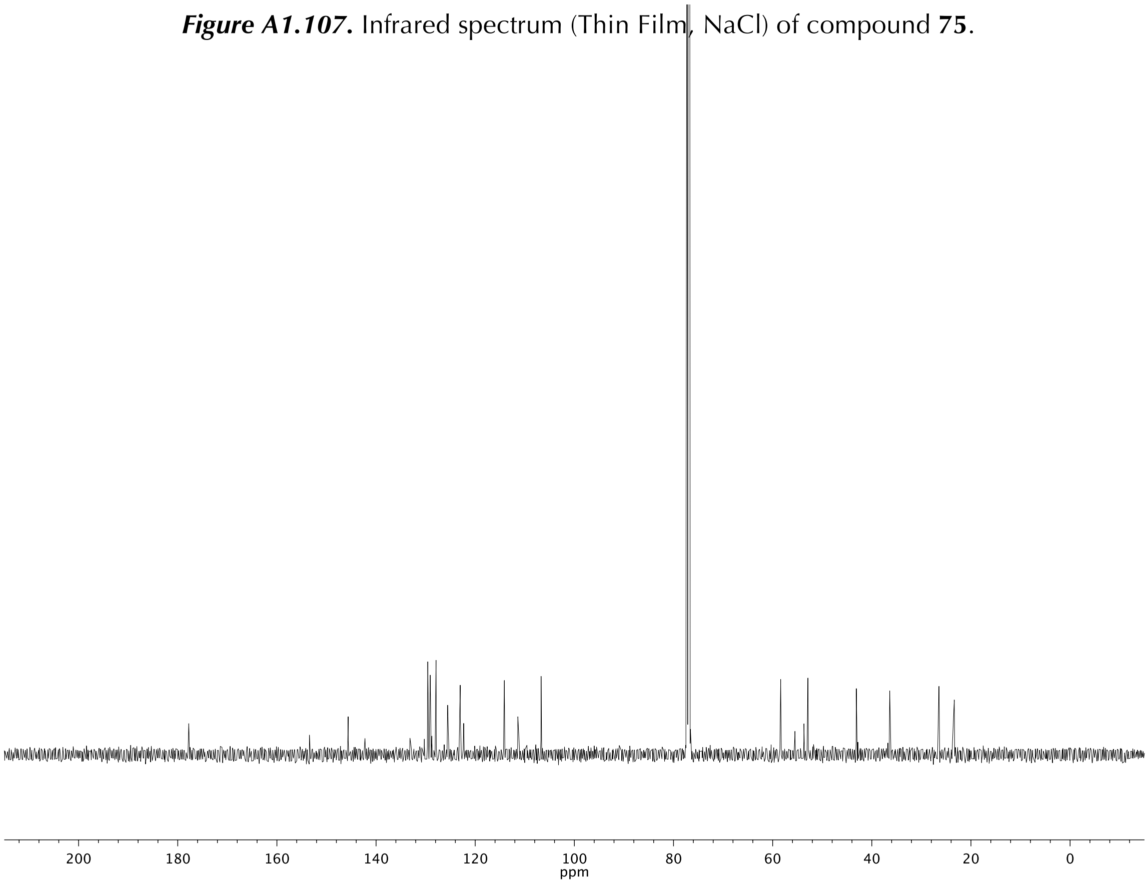

Figure A1.108. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **75**.

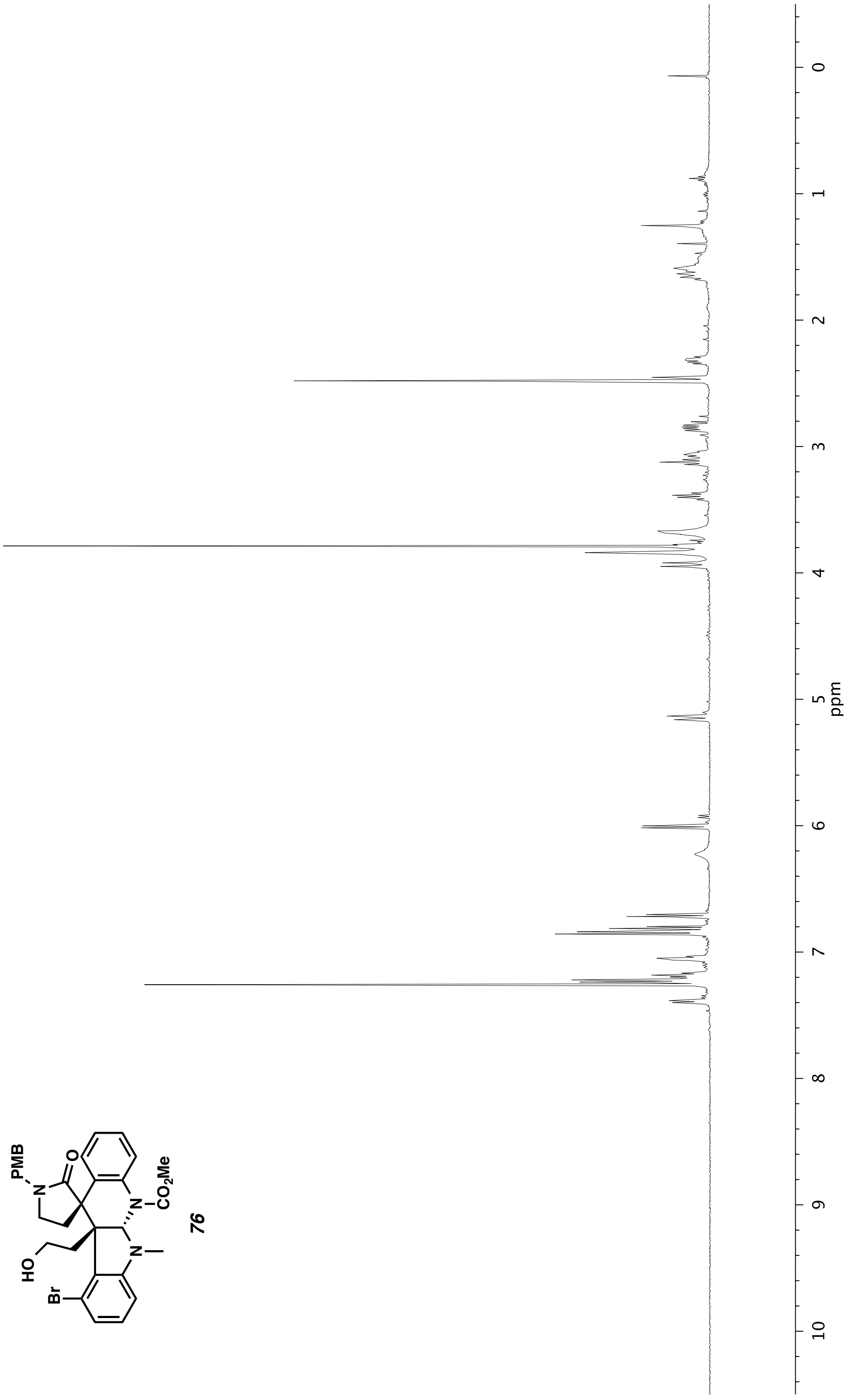

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Figure A1.109. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **76**.

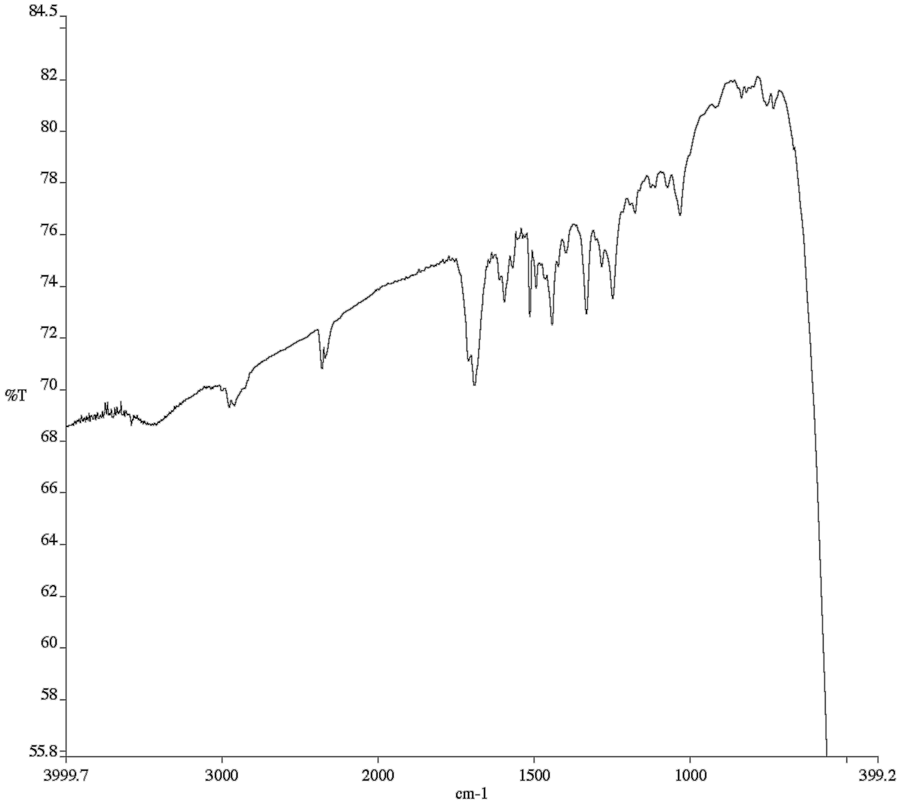

Figure A1.110. Infrared spectrum (Thin Film, NaCl) of compound **76**.

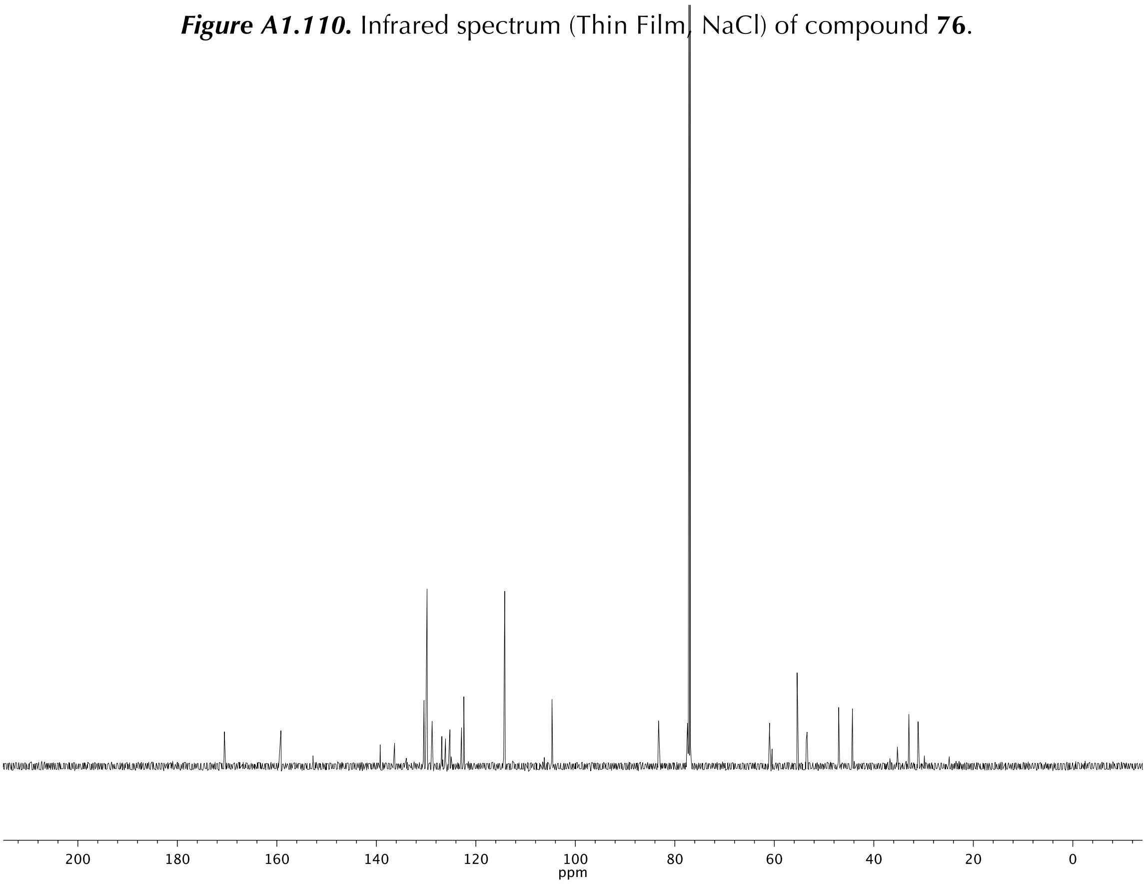

Figure A1.111. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **76**.

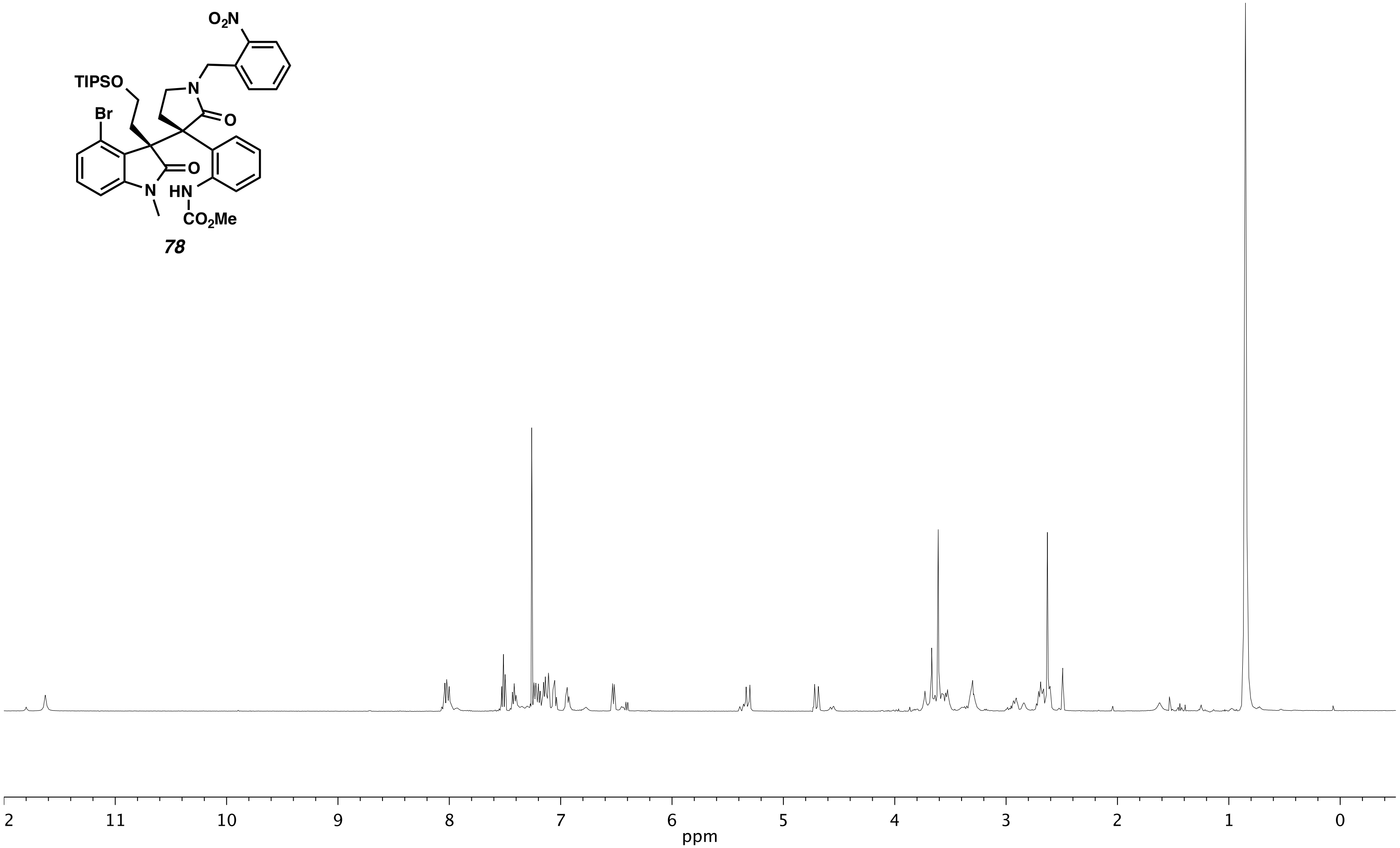

Figure A1.112. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **78**.

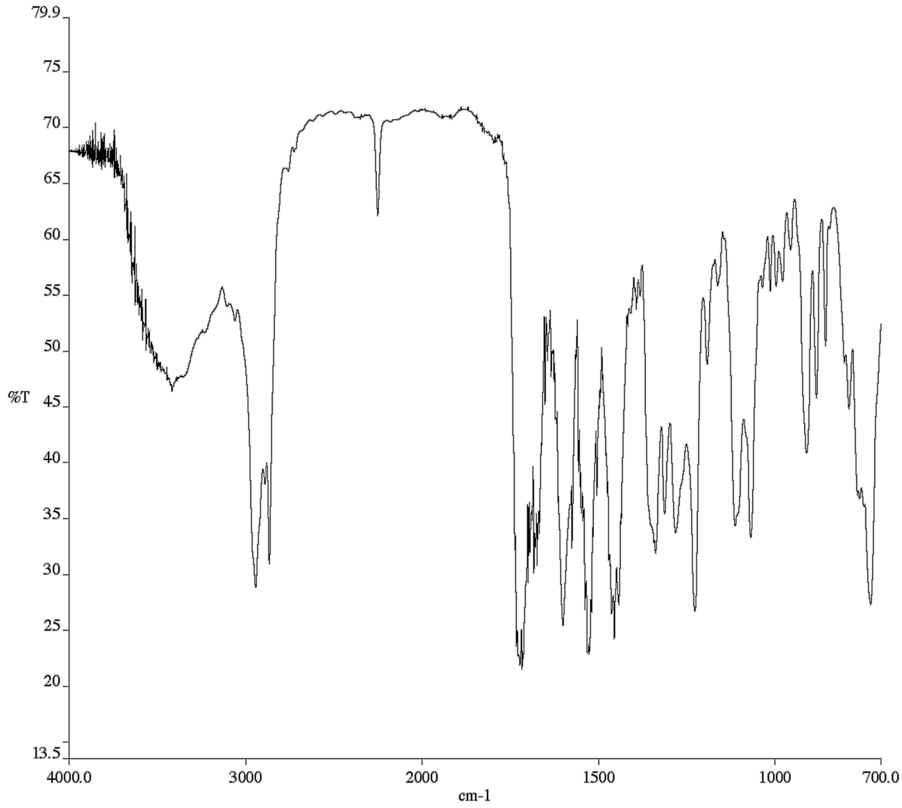

Figure A1.113. Infrared spectrum (Thin Film, NaCl) of compound **78**.

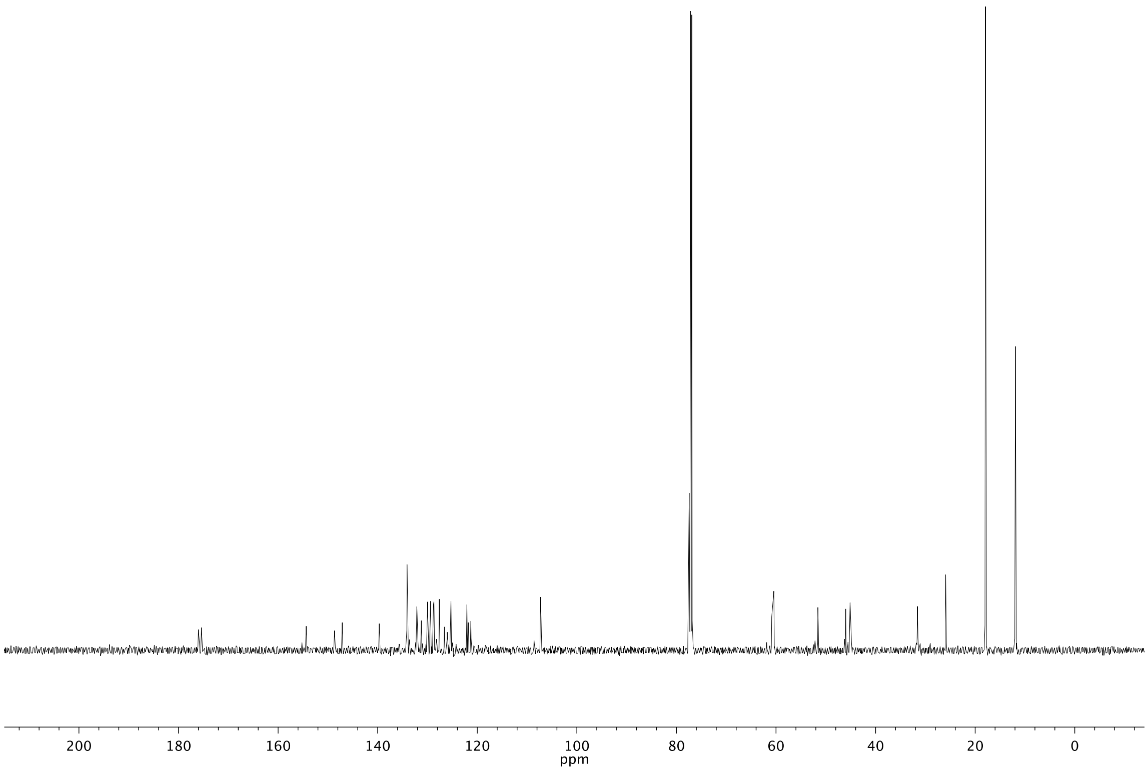

Figure A1.114. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **78**.

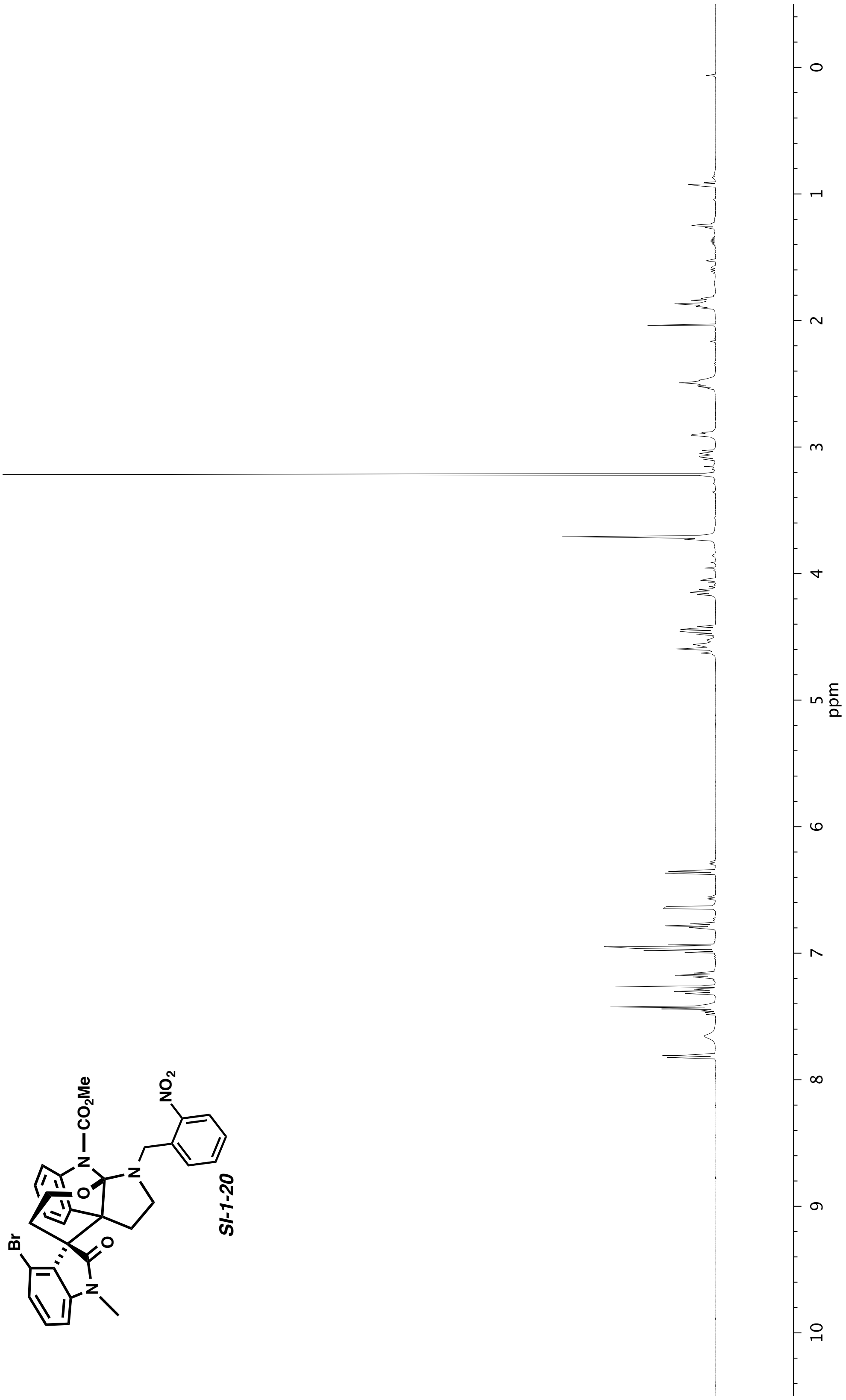

Figure A1.115. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **SI-1-20**.

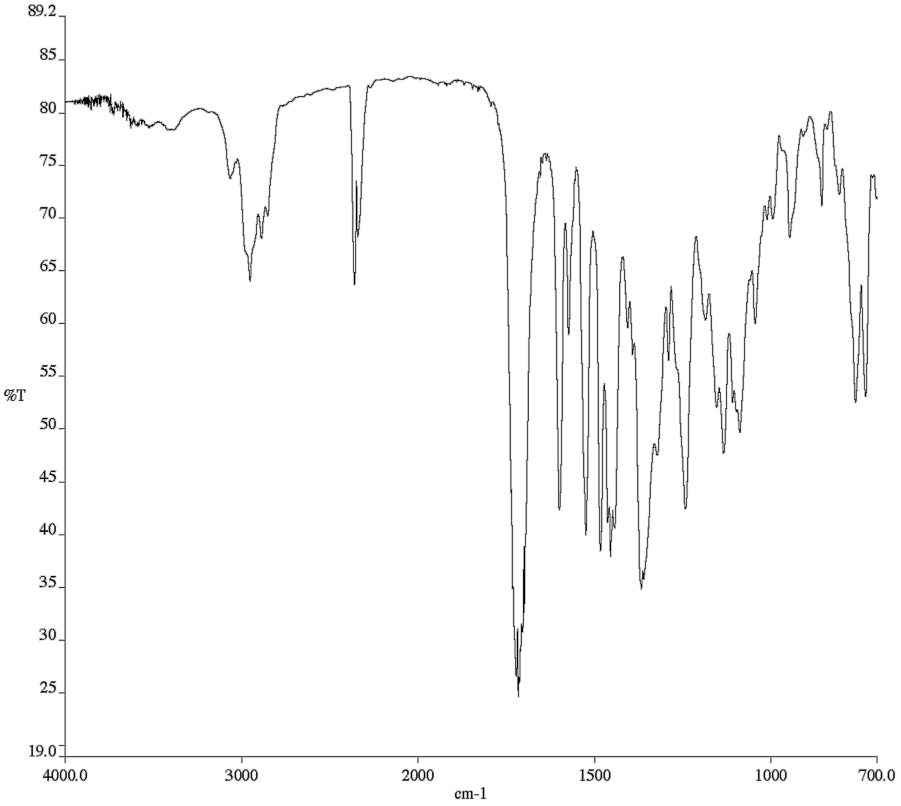

Figure A1.116. Infrared spectrum (Thin Film, NaCl) of compound **SI-1-20**.

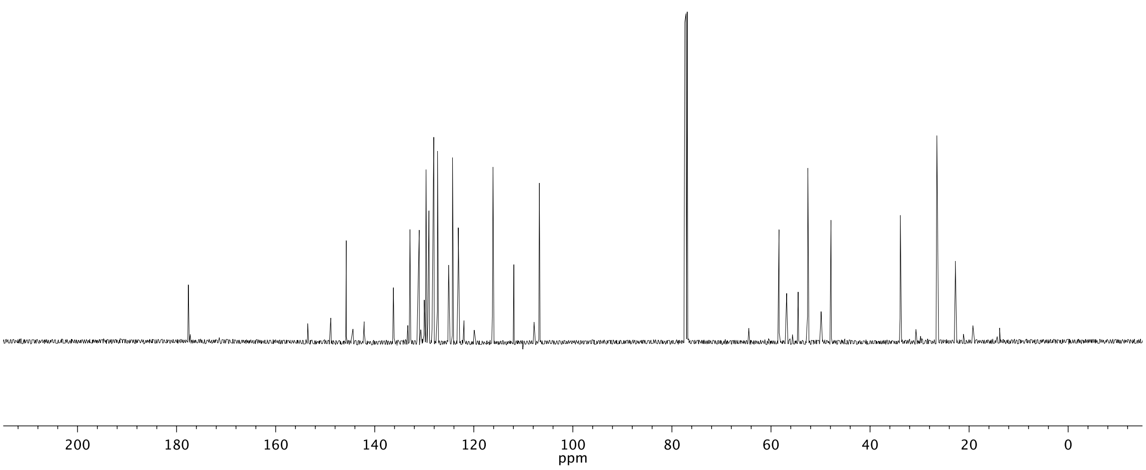

Figure A1.117. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **SI-1-20**.

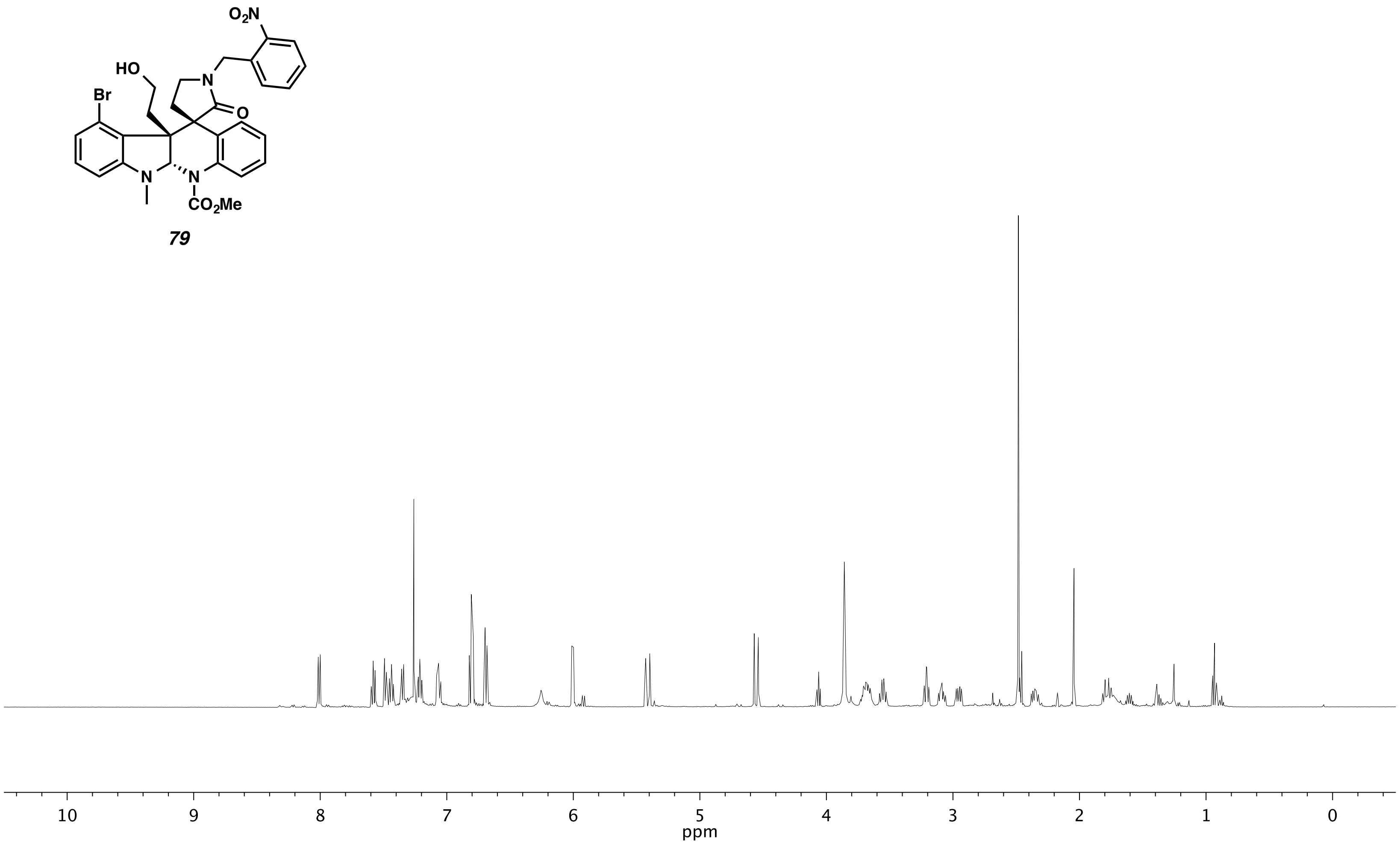

Figure A1.118. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **79**.

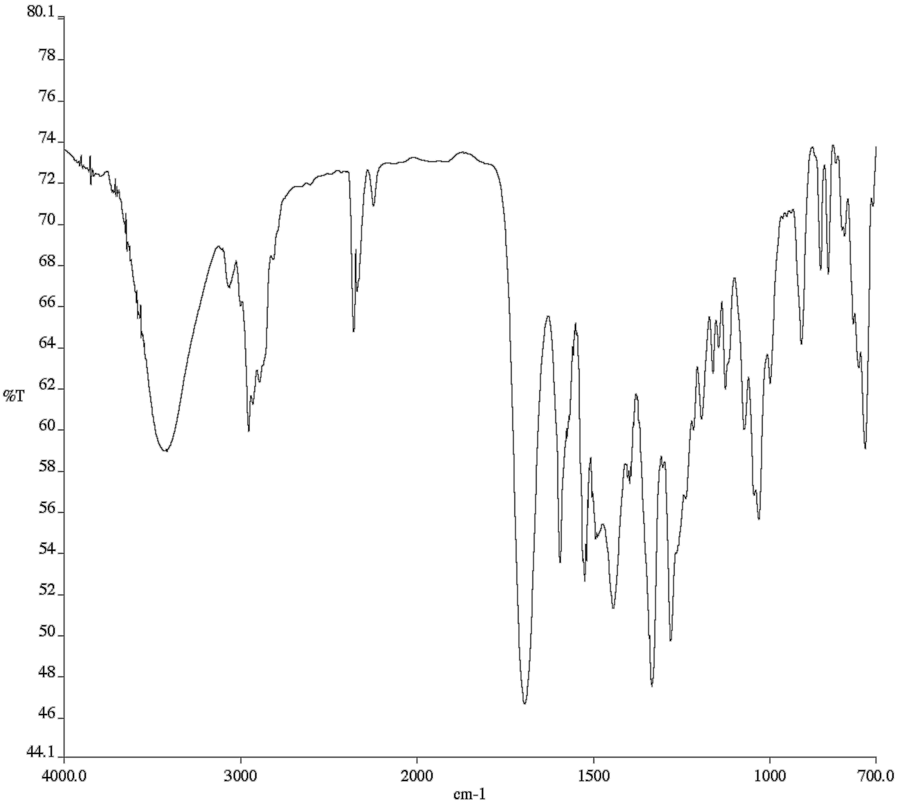

Figure A1.119. Infrared spectrum (Thin Film, NaCl) of compound **79**.

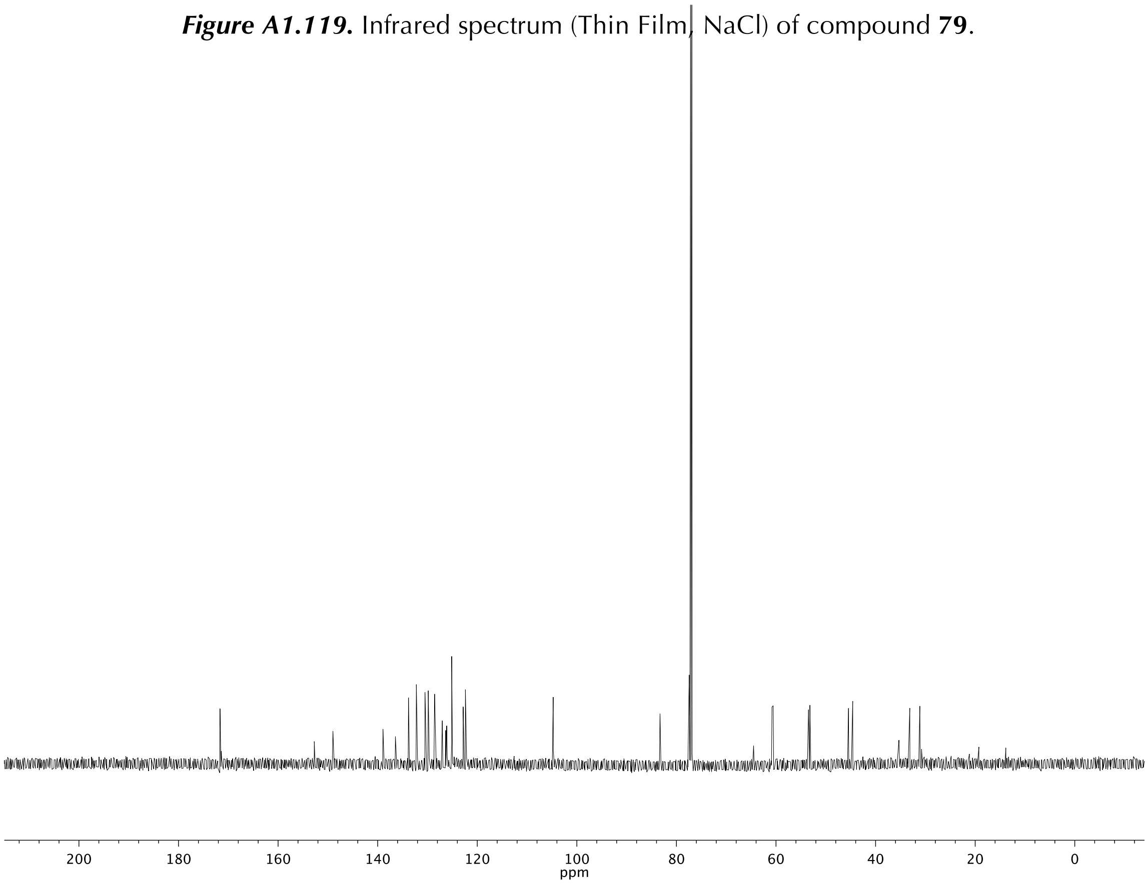

Figure A1.120. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **79**.

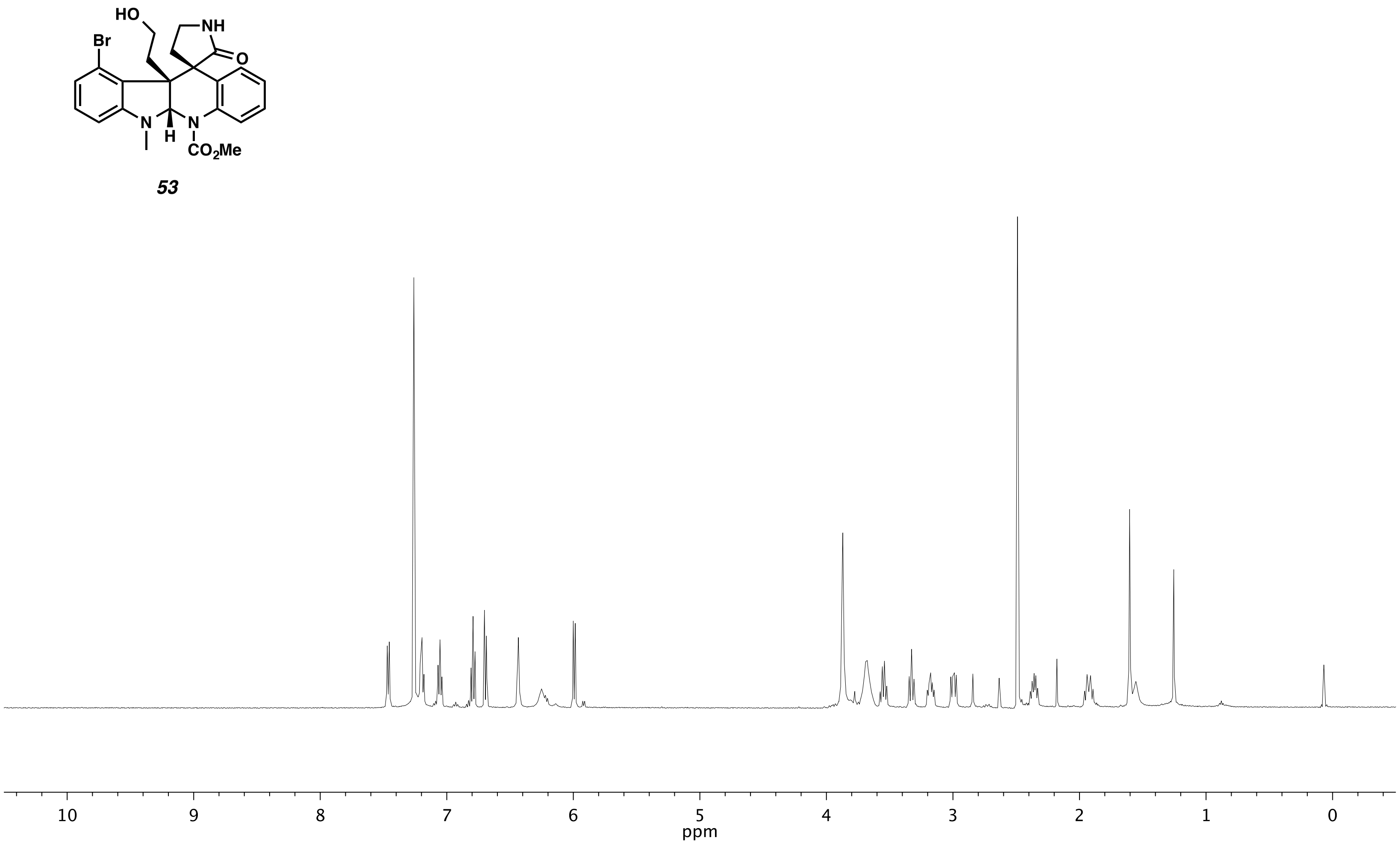

Figure A1.121. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **53**.

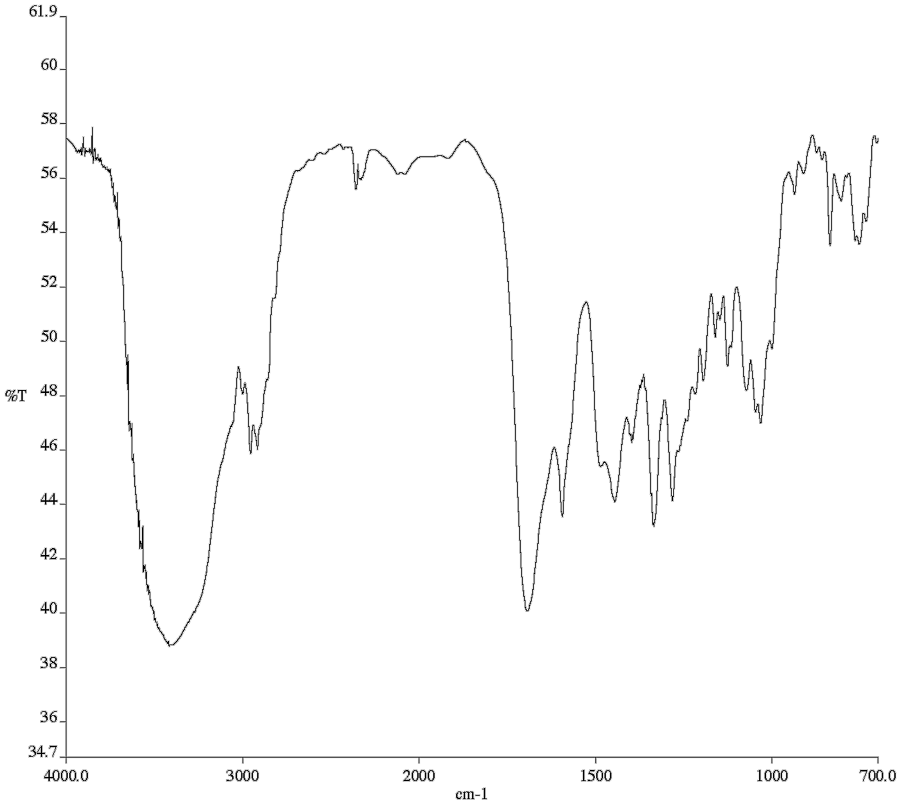

Figure A1.122. Infrared spectrum (Thin Film, NaCl) of compound **53**.

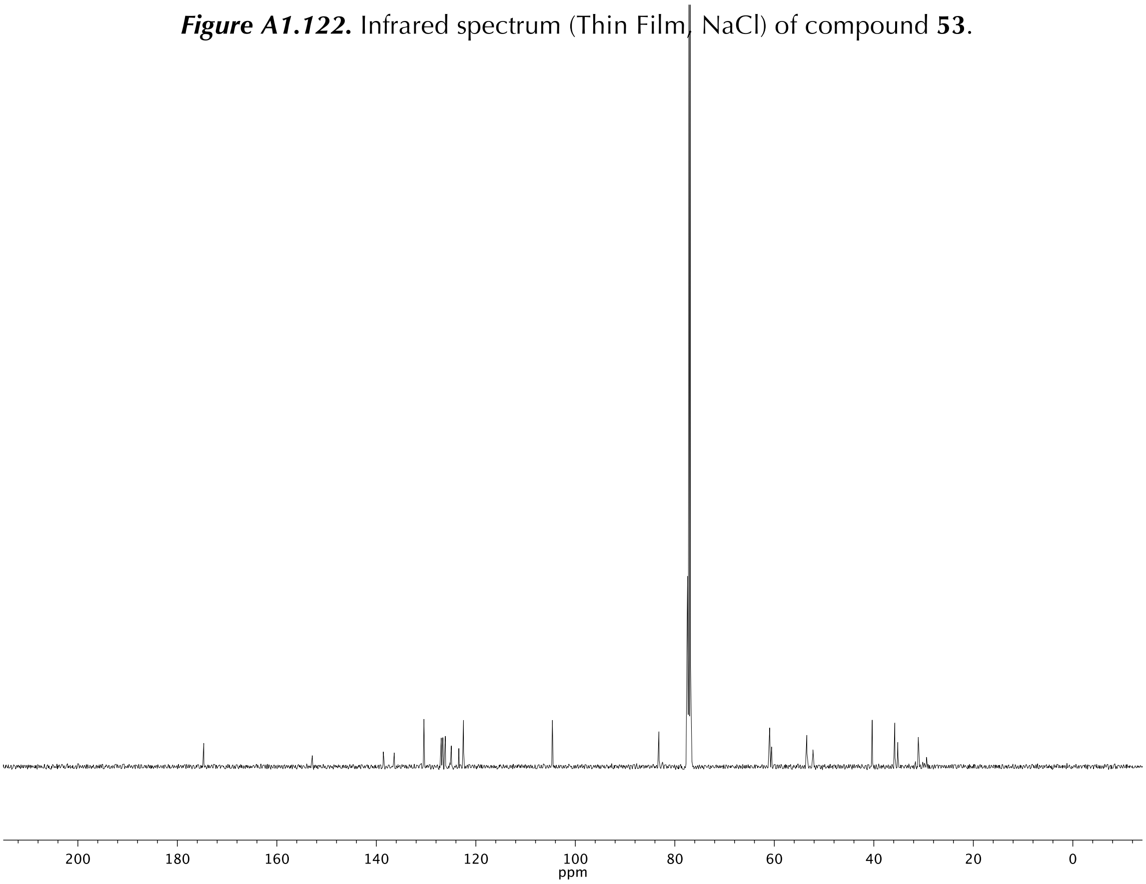

Figure A1.123. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **53**.

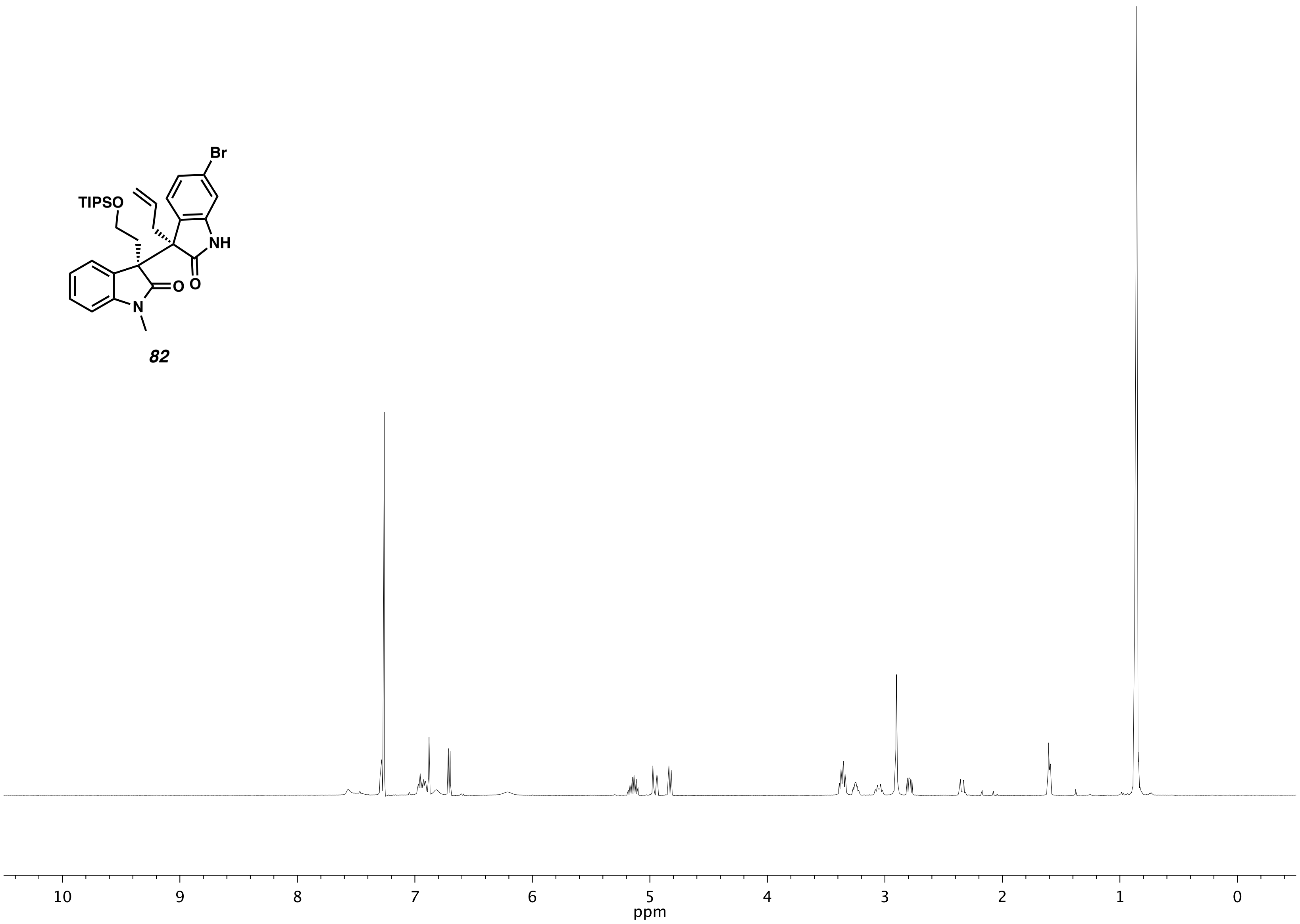

Figure A1.124. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **82**.

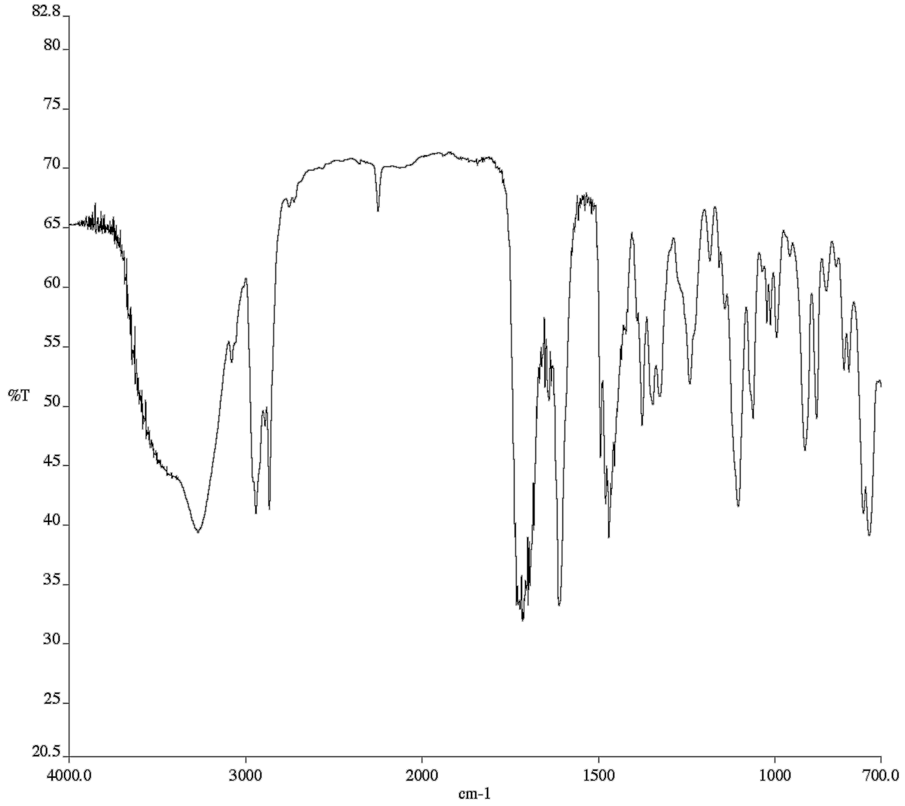

Figure A1.125. Infrared spectrum (Thin Film, NaCl) of compound **82**.

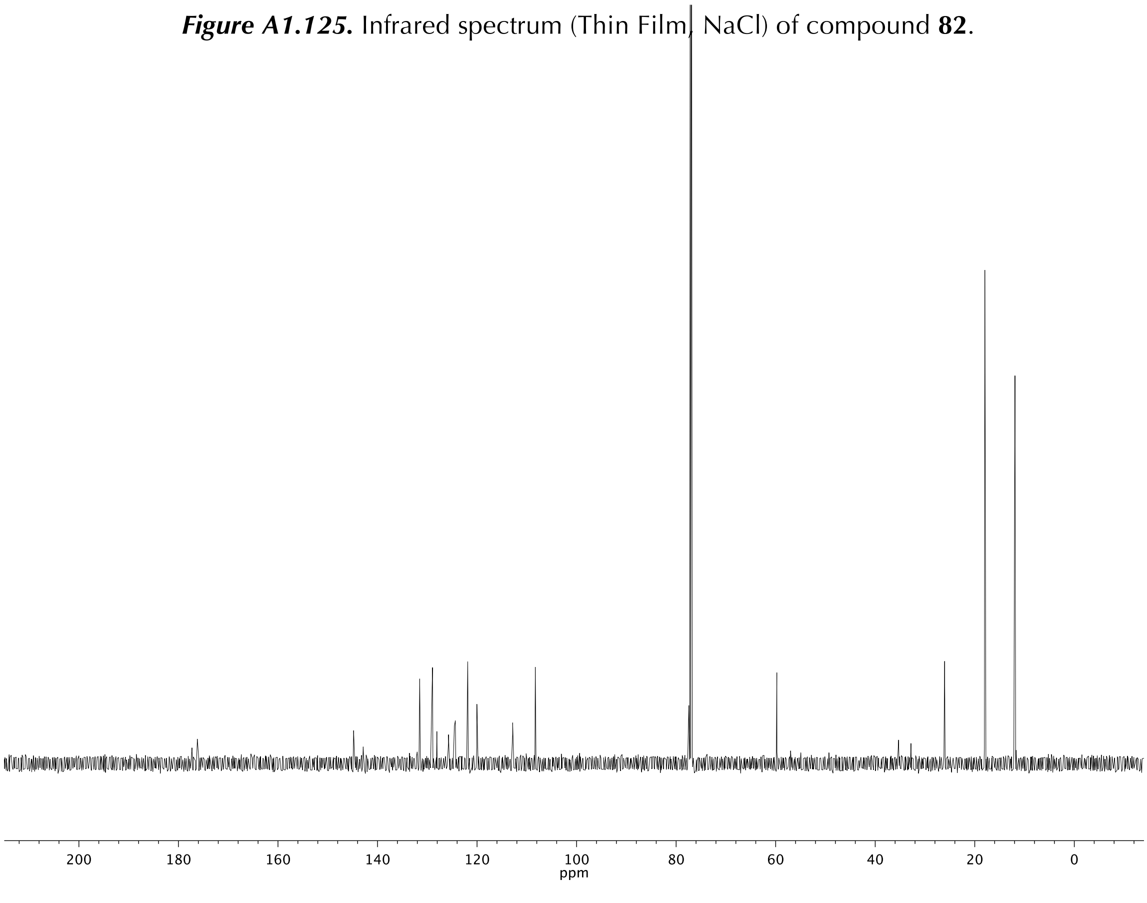

Figure A1.126. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **82**.

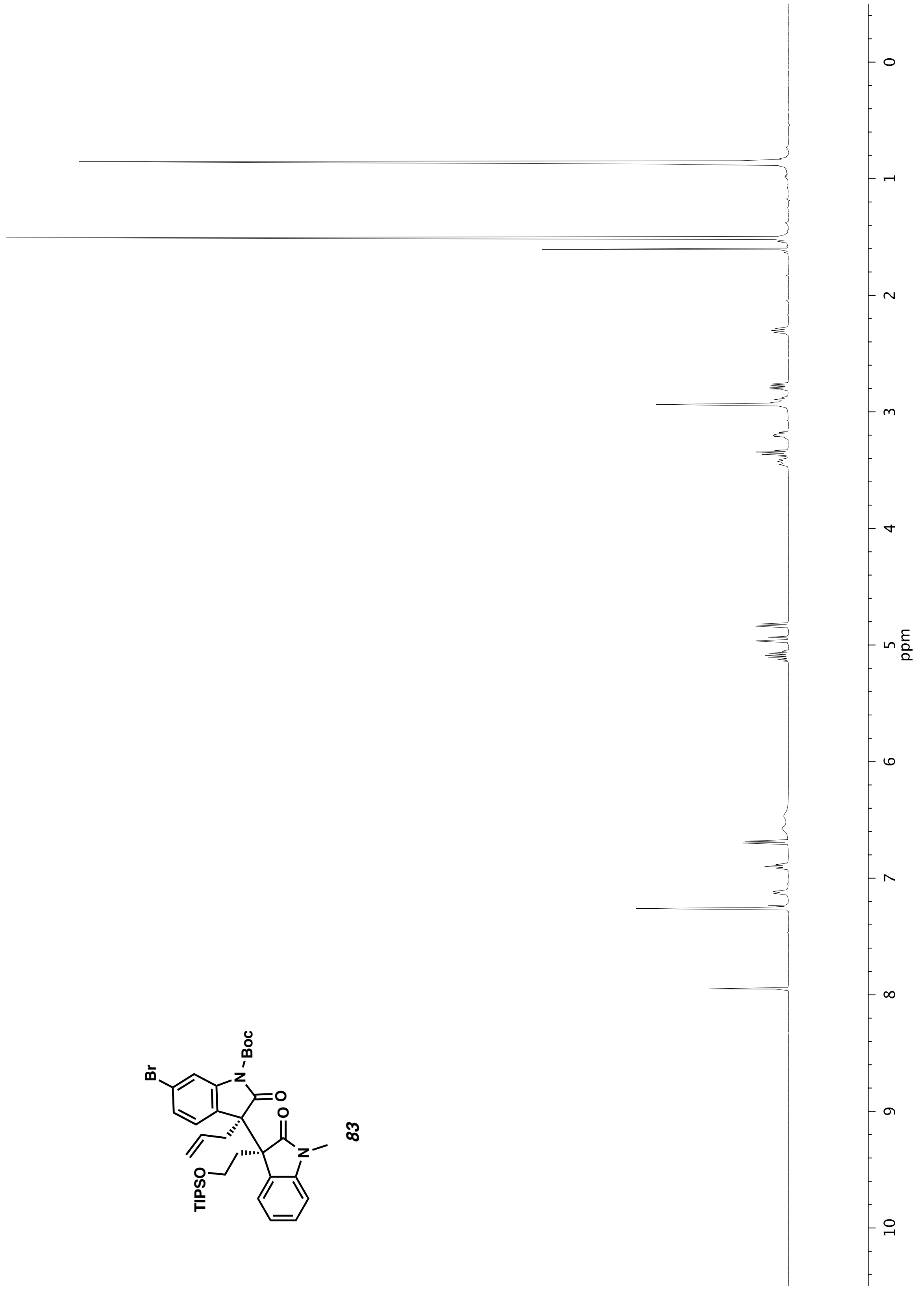

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Figure A1.127. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **83**.

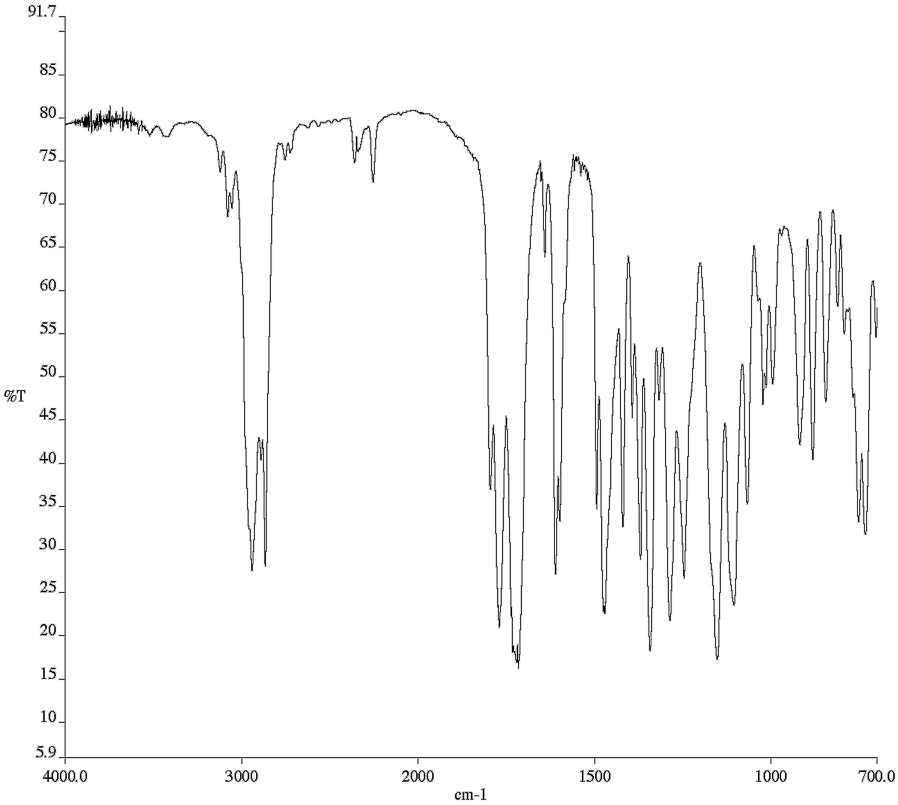

Figure A1.128. Infrared spectrum (Thin Film, NaCl) of compound **83**.

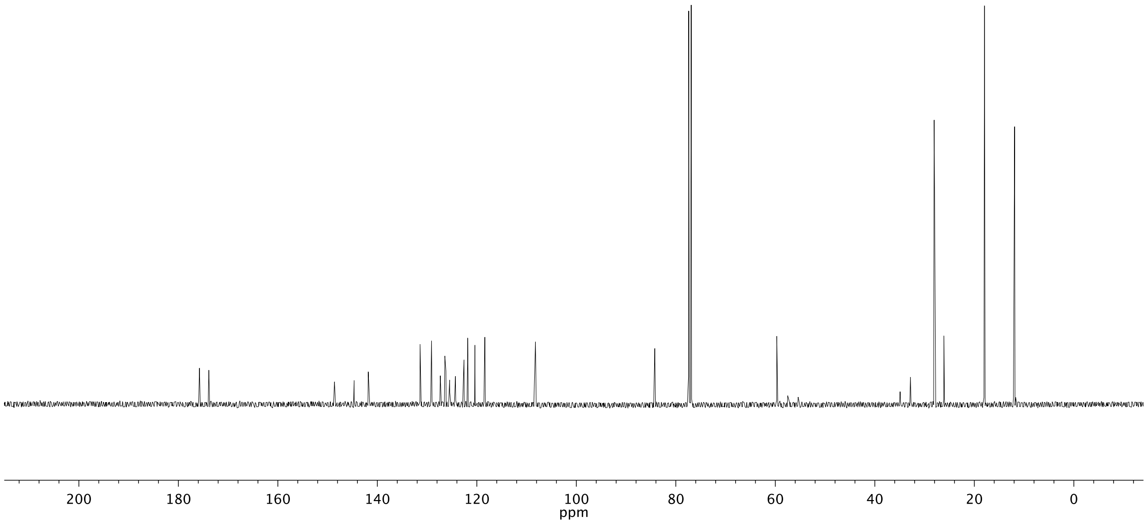

Figure A1.129. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **83**.

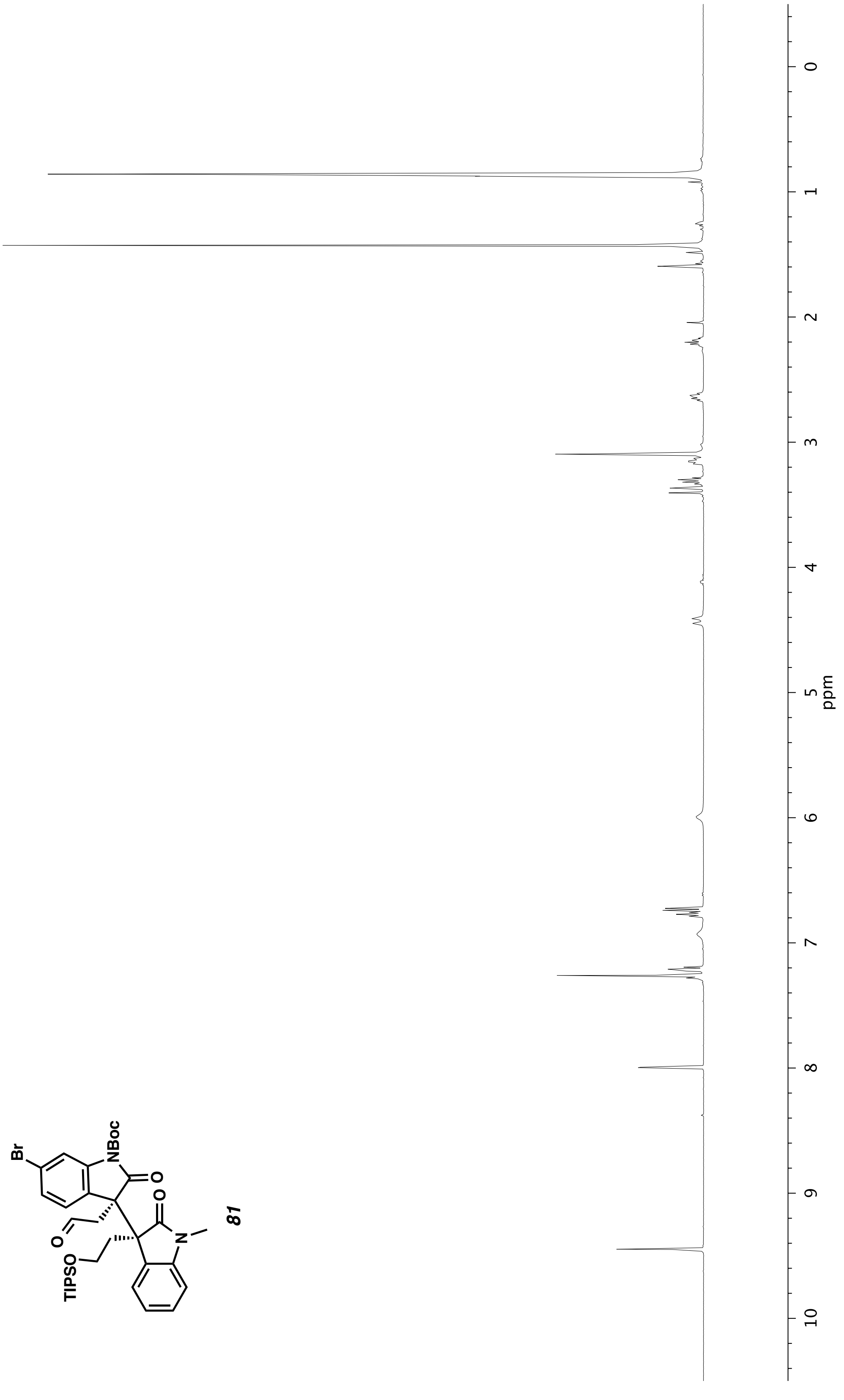

Figure A1.130. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **81**.

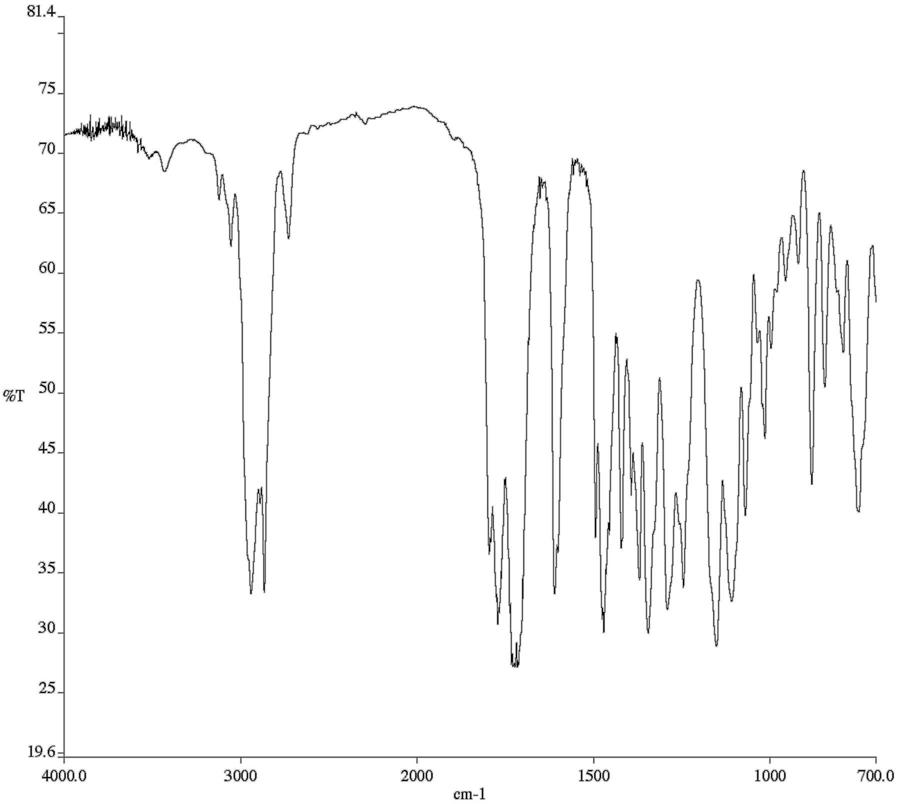

Figure A1.131. Infrared spectrum (Thin Film, NaCl) of compound **81**.

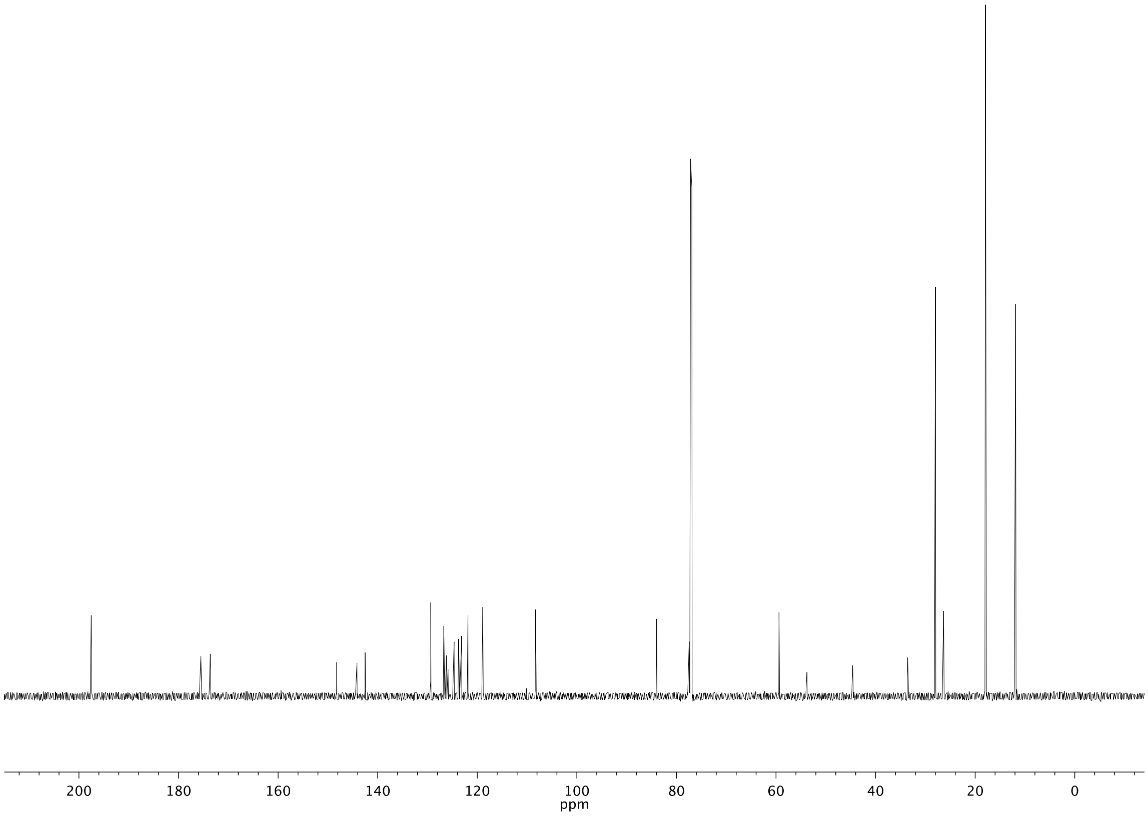

Figure A1.132. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **81**.

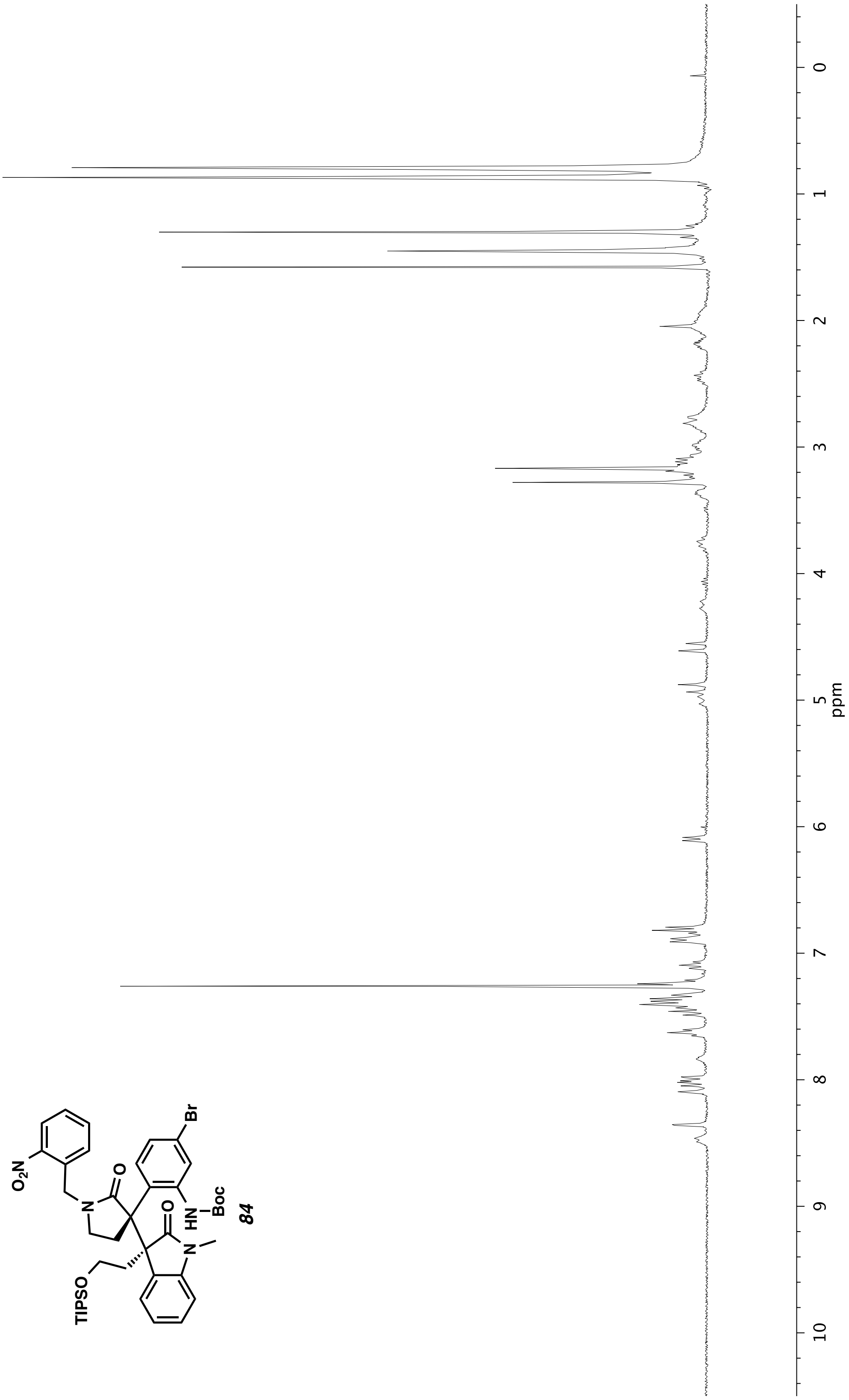

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Figure A1.133. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **84**.

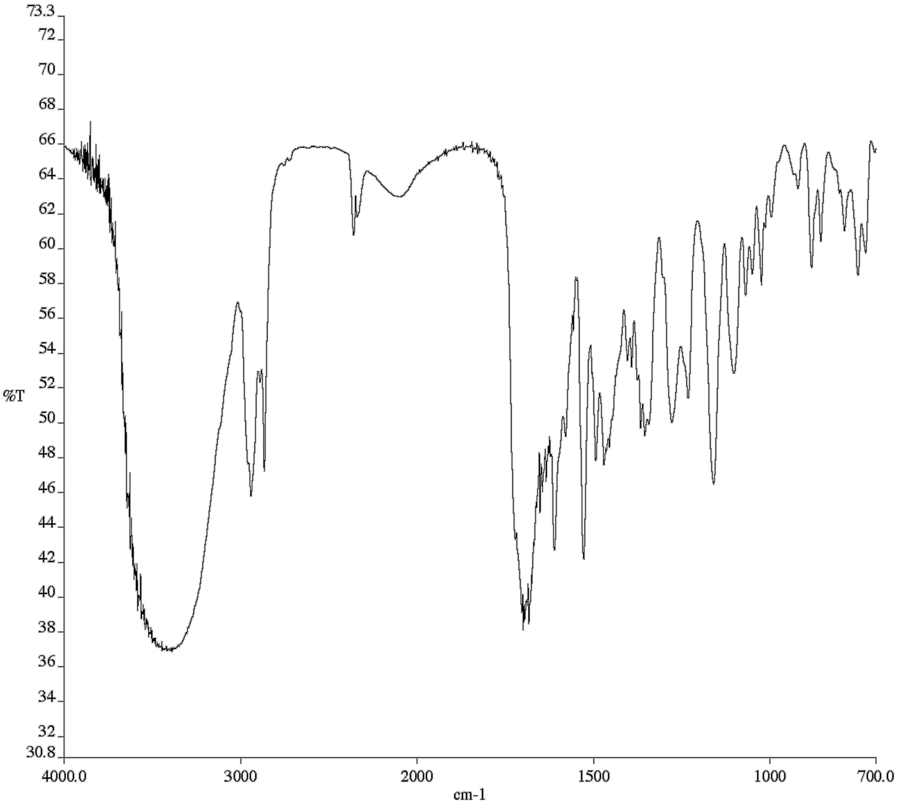

Figure A1.134. Infrared spectrum (Thin Film, NaCl) of compound **84**.

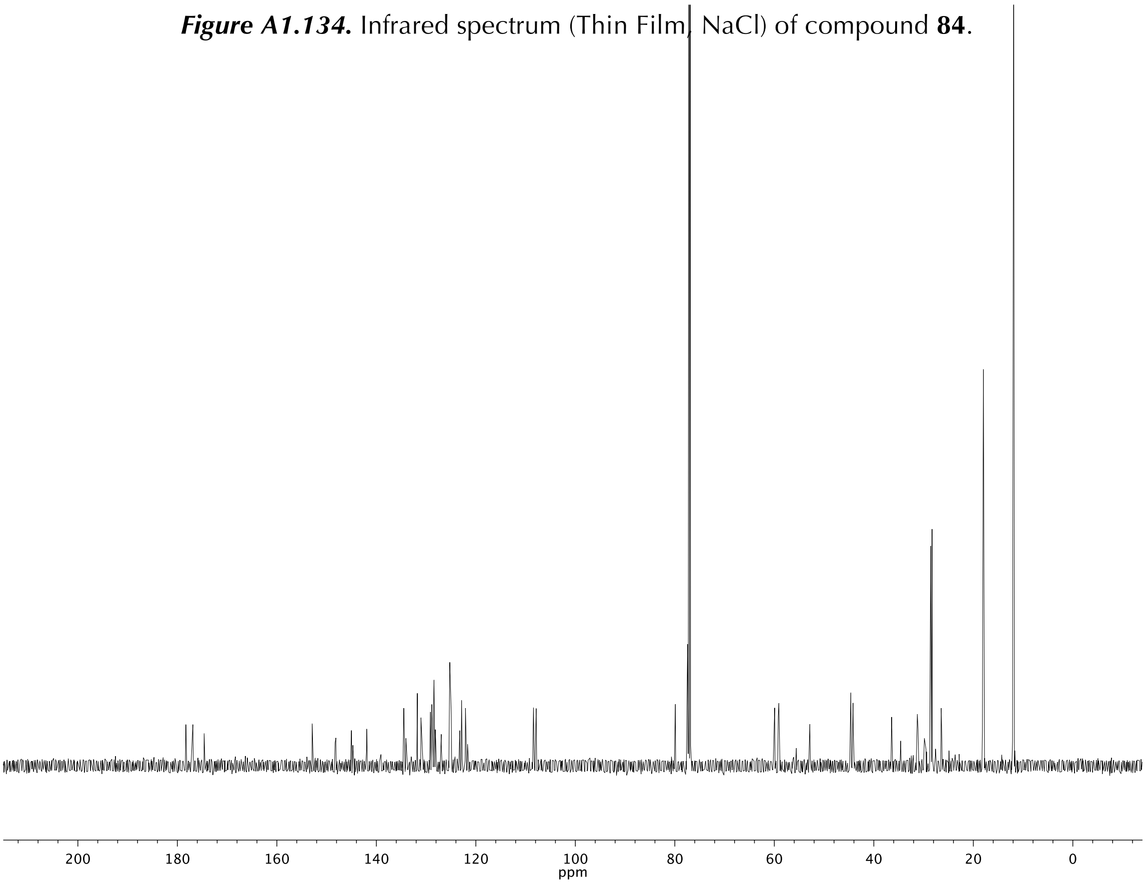

Figure A1.135. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **84**.

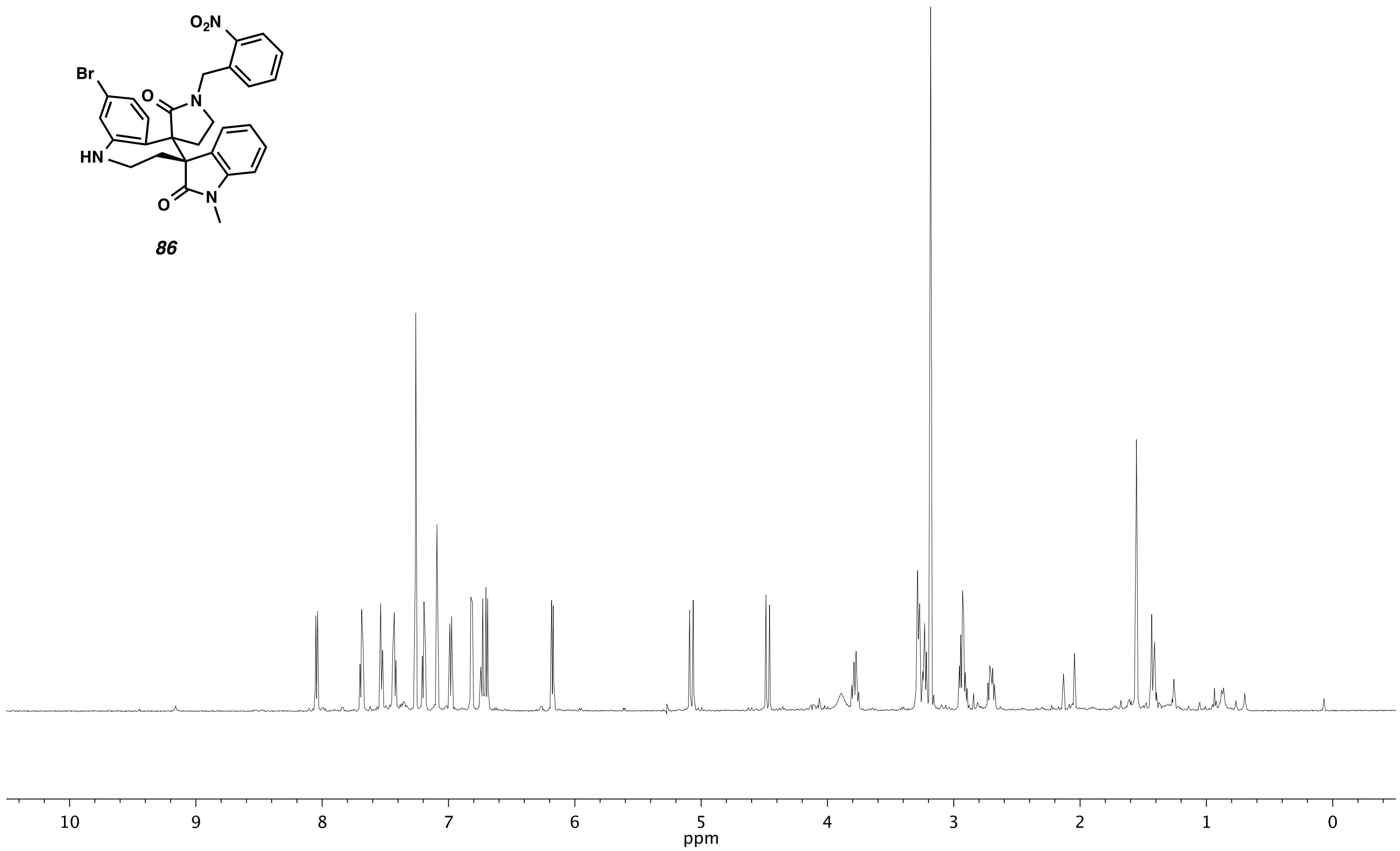

Figure A1.136. ^{1}H NMR (600 MHz, CDCl$_3$) of compound **86**.

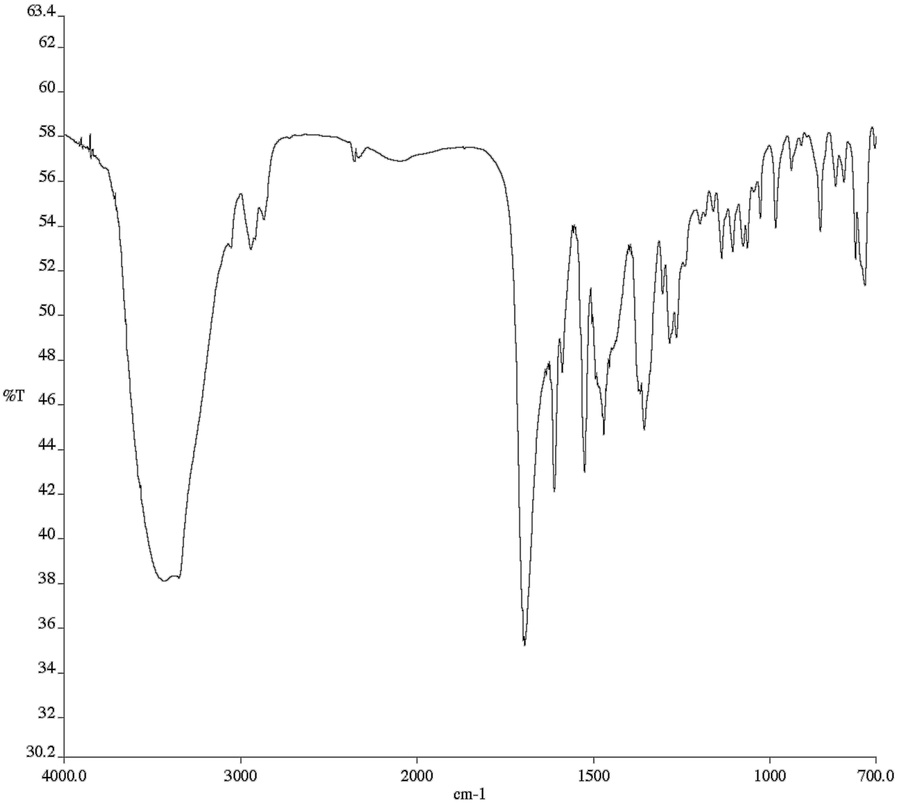

Figure A1.137. Infrared spectrum (Thin Film, NaCl) of compound **86**.

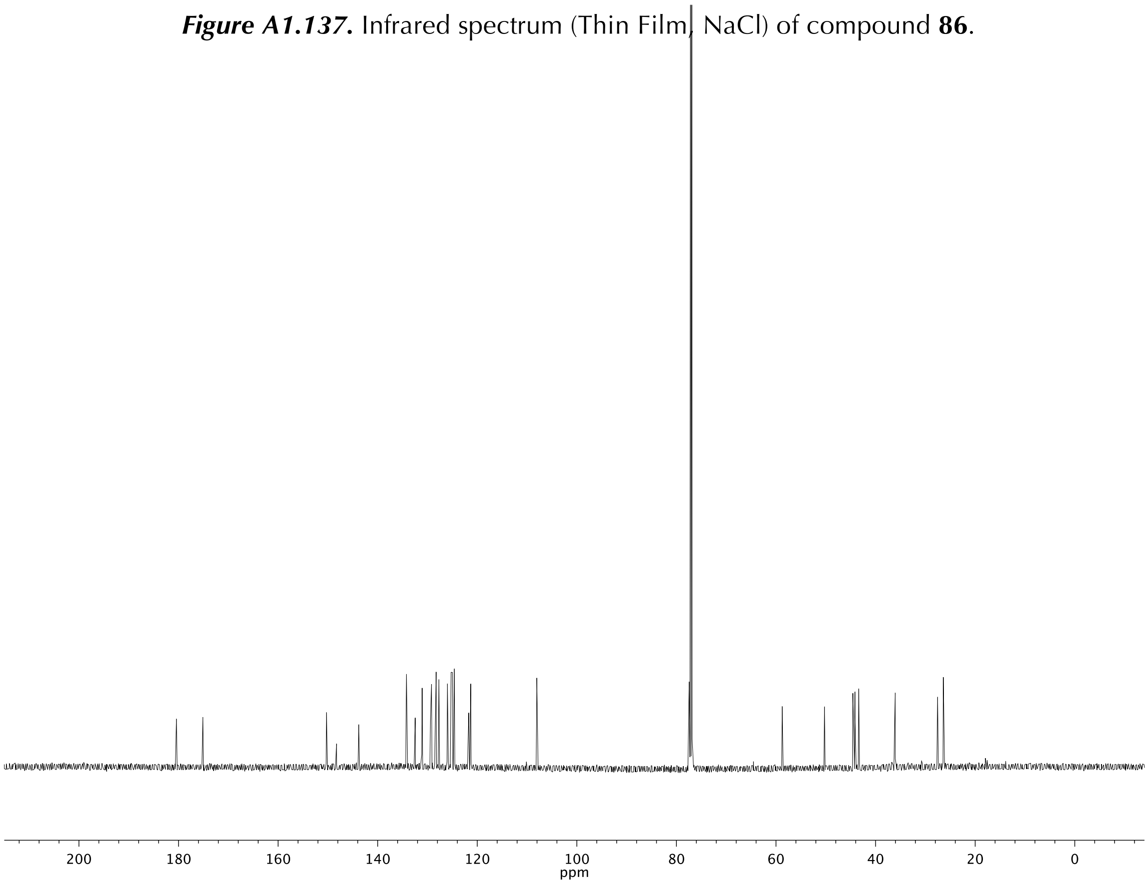

Figure A1.138. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **86**.

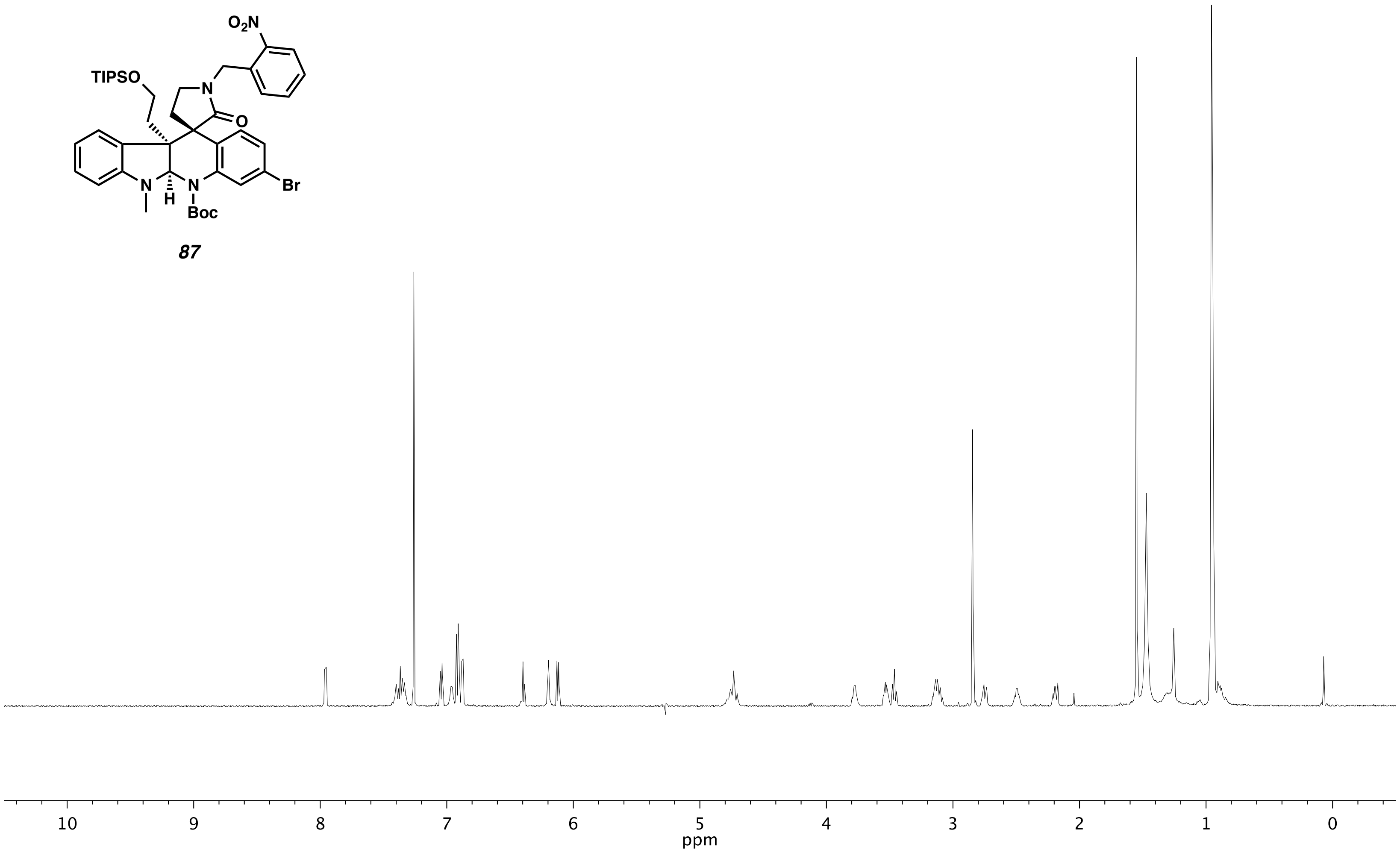

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Figure A1.139. ^{1}H NMR (600 MHz, CDCl$_3$) of compound **87**.

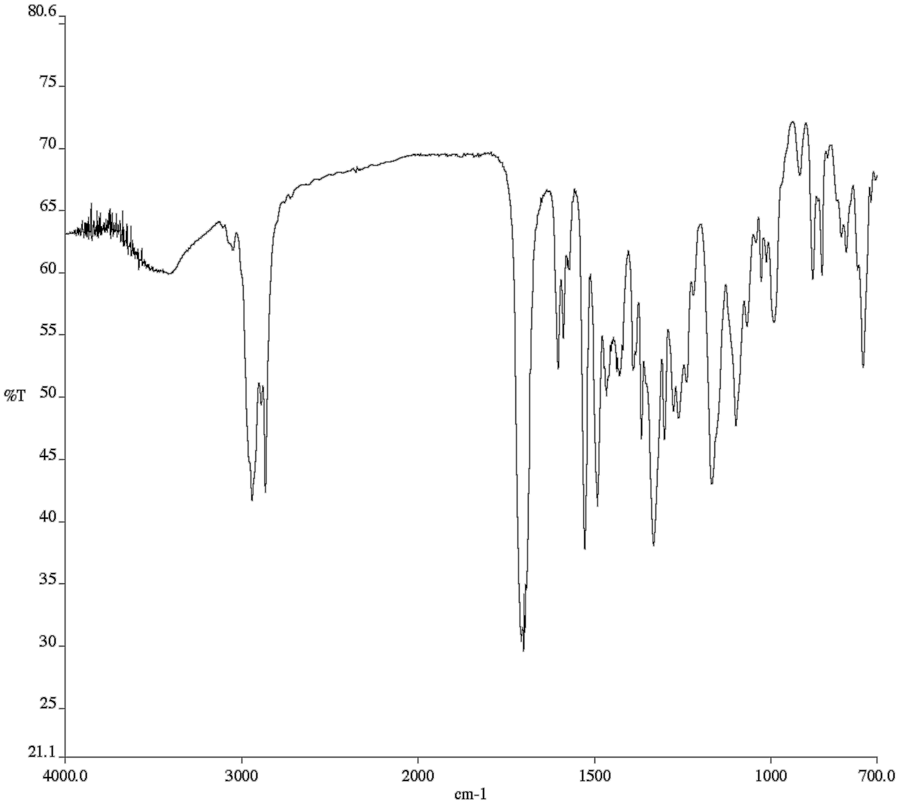

Figure A1.140. Infrared spectrum (Thin Film, NaCl) of compound **87**.

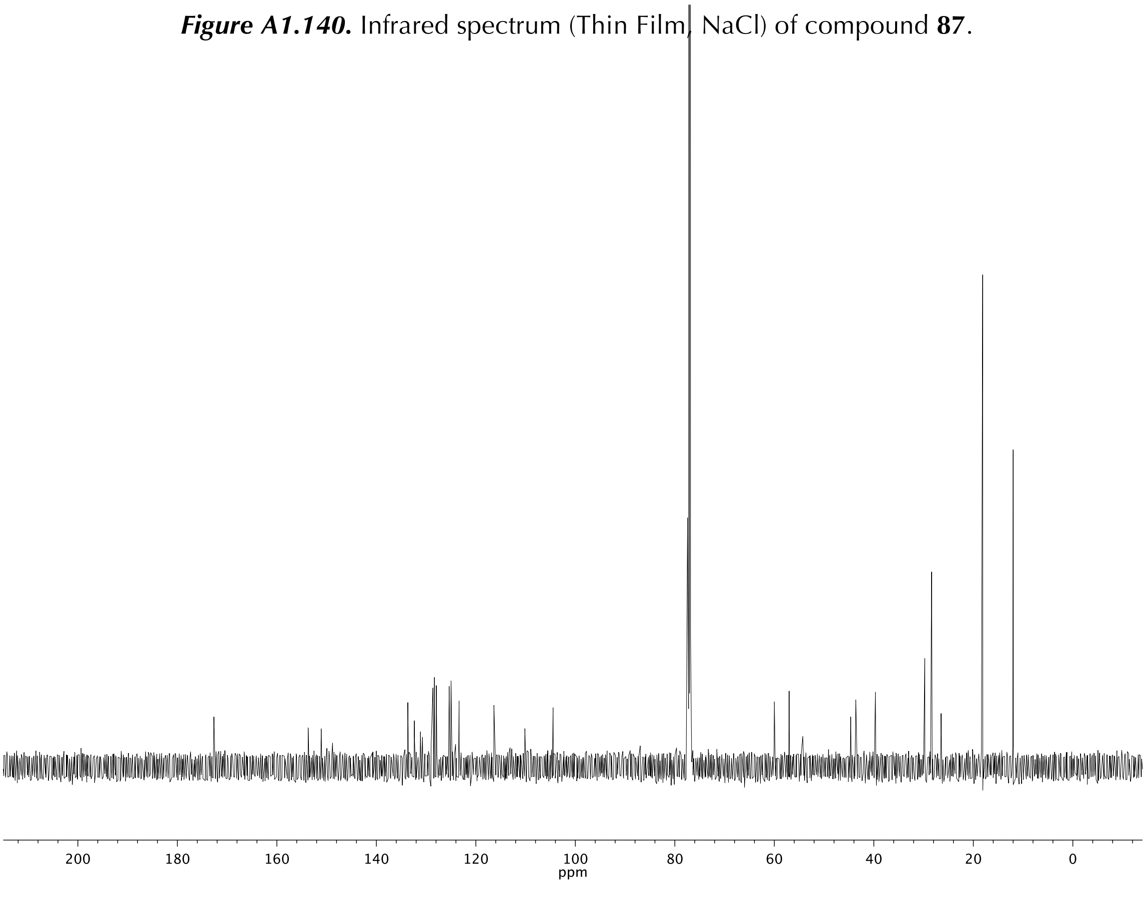

Figure A1.141. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **87**.

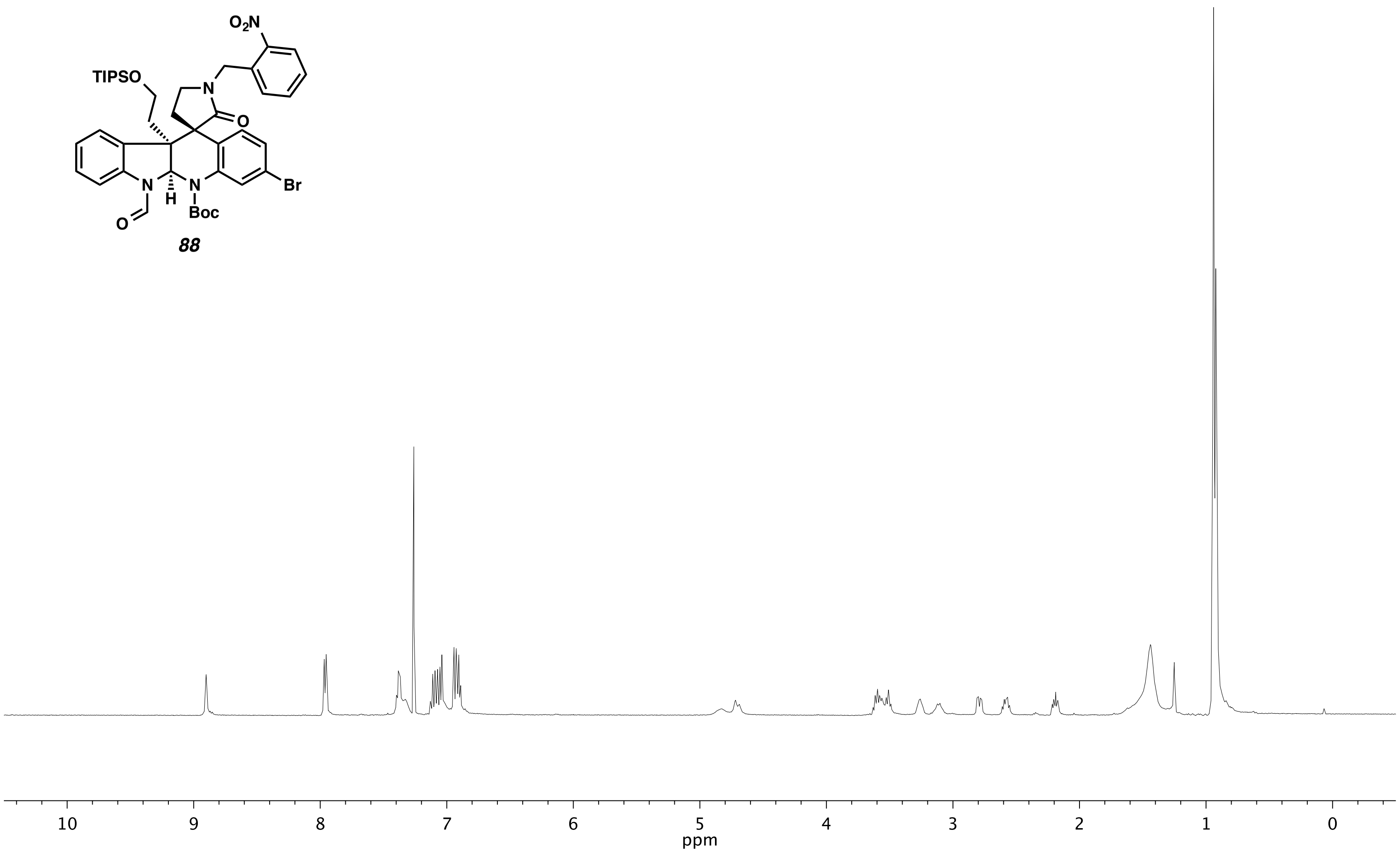

Figure A1.142. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **88**.

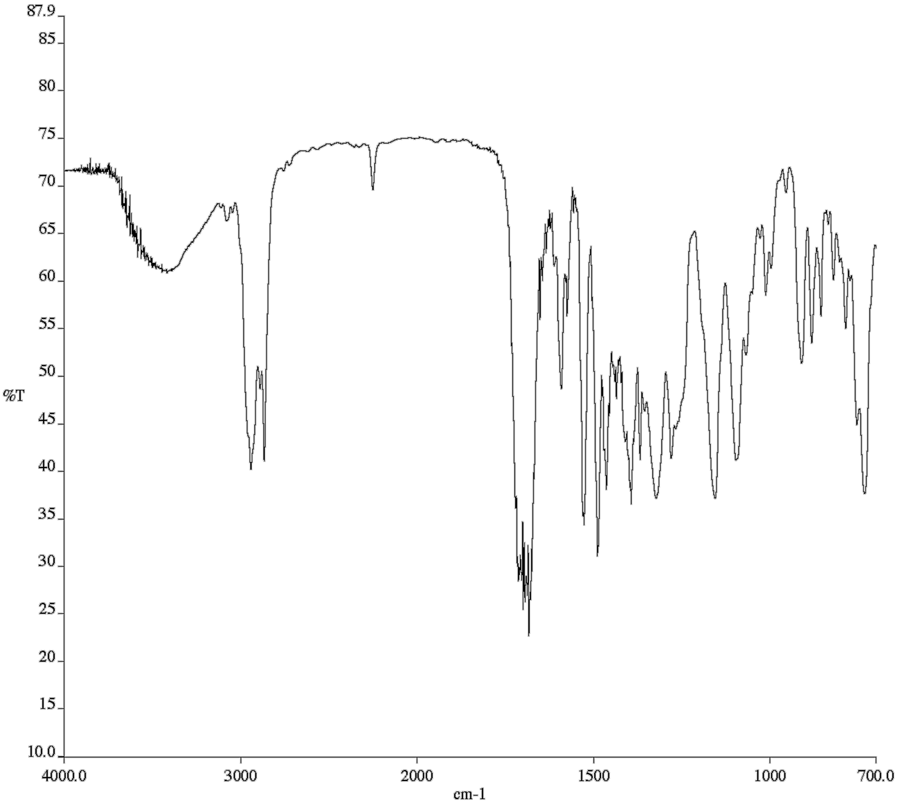

Figure A1.143. Infrared spectrum (Thin Film, NaCl) of compound **88**.

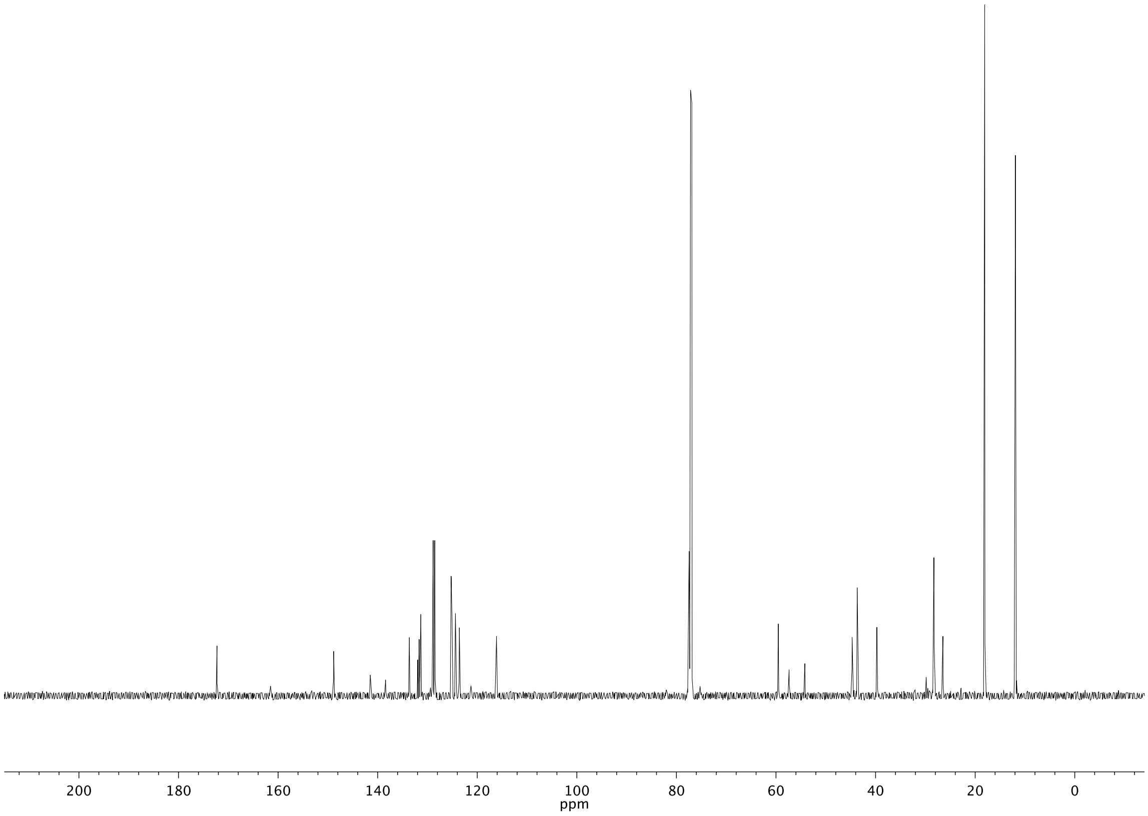

Figure A1.144. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **88**.

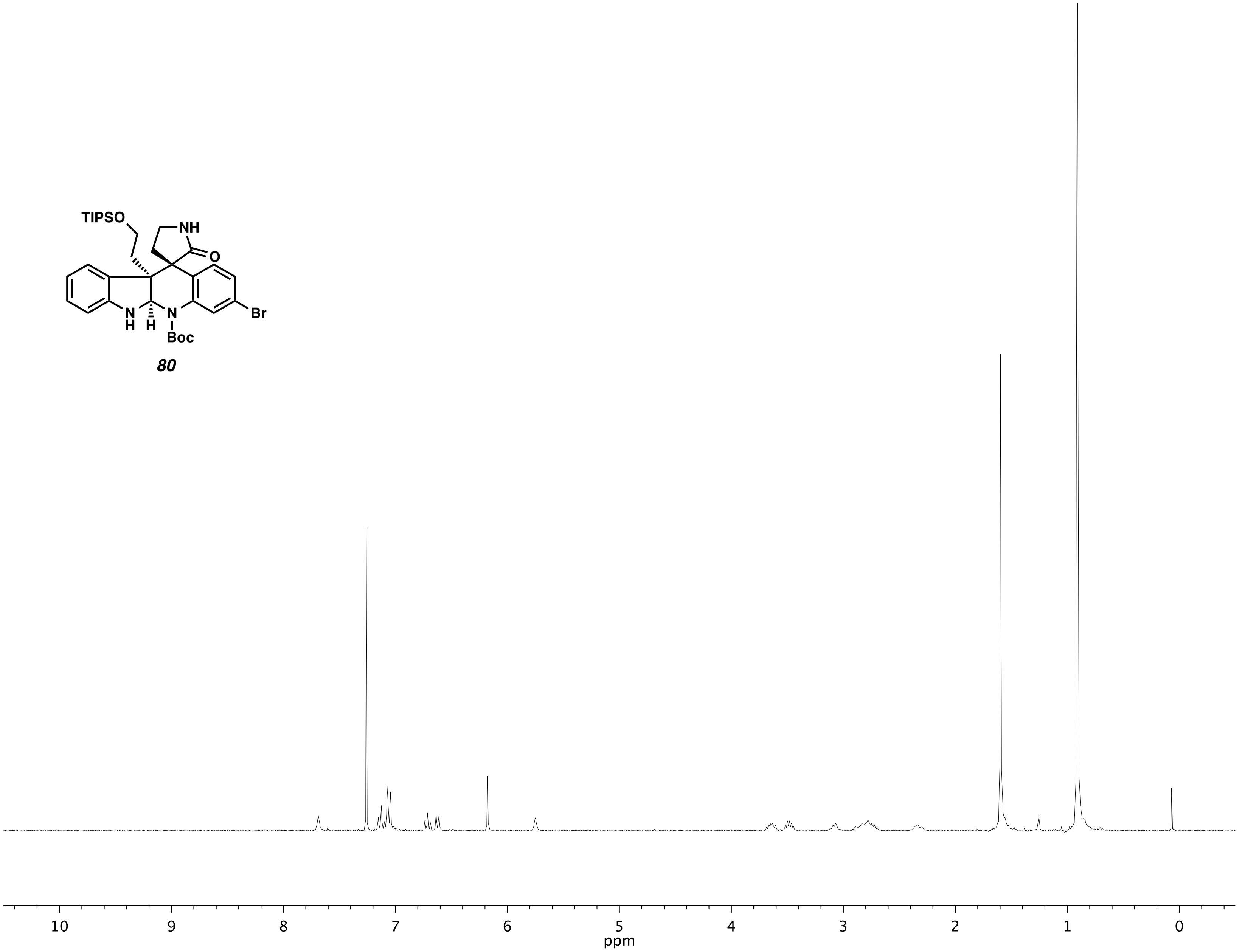

Figure A1.145. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **80**.

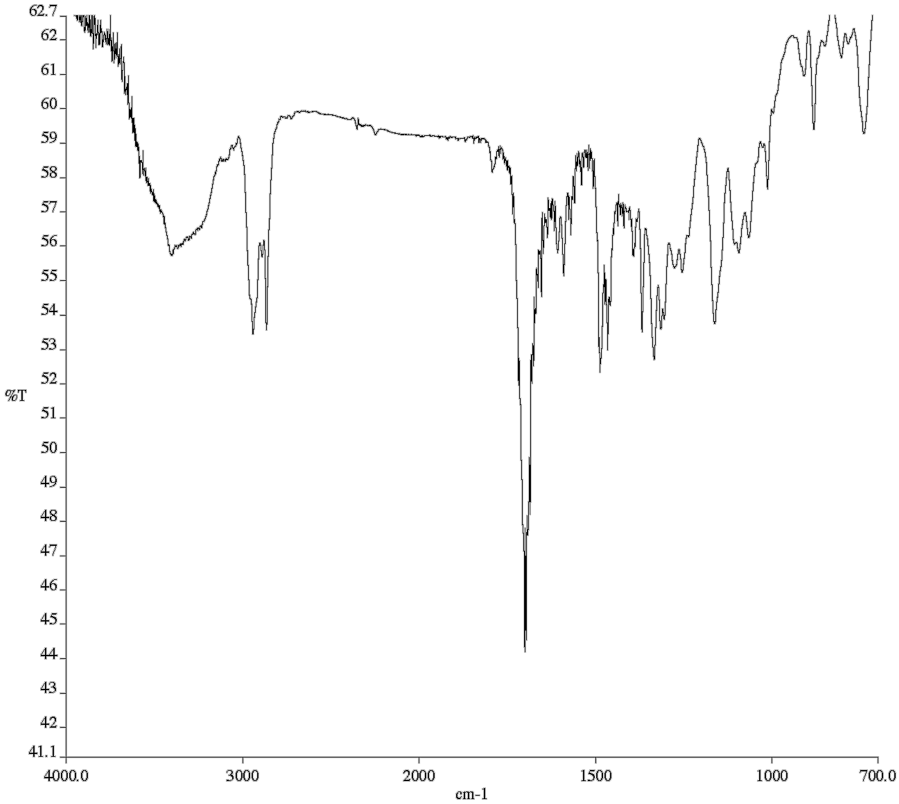

Figure A1.146. Infrared spectrum (Thin Film, NaCl) of compound **80**.

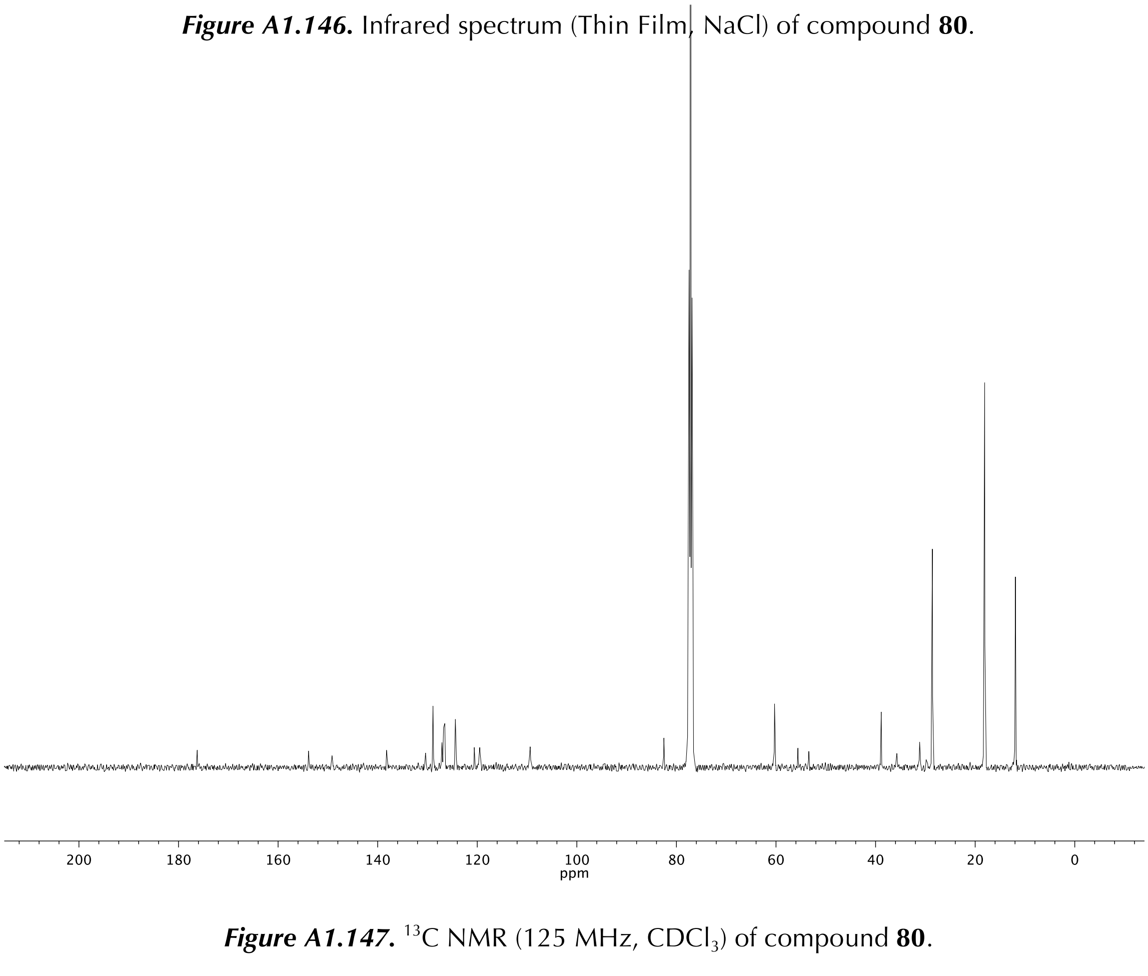

Figure A1.147. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **80**.

APPENDIX 2

X-Ray Crystallography Reports Relevant to Chapter 1: The Evolution of a Unified, Stereodivergent Approach to the Synthesis of Communesin F and Perophoramidine

A2.1. X-Ray Crystal Structure Analysis of 24

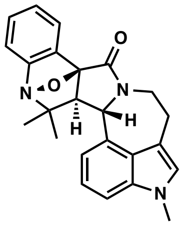

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Figure A2.1.1. *X-ray Crystal Structure of **24***

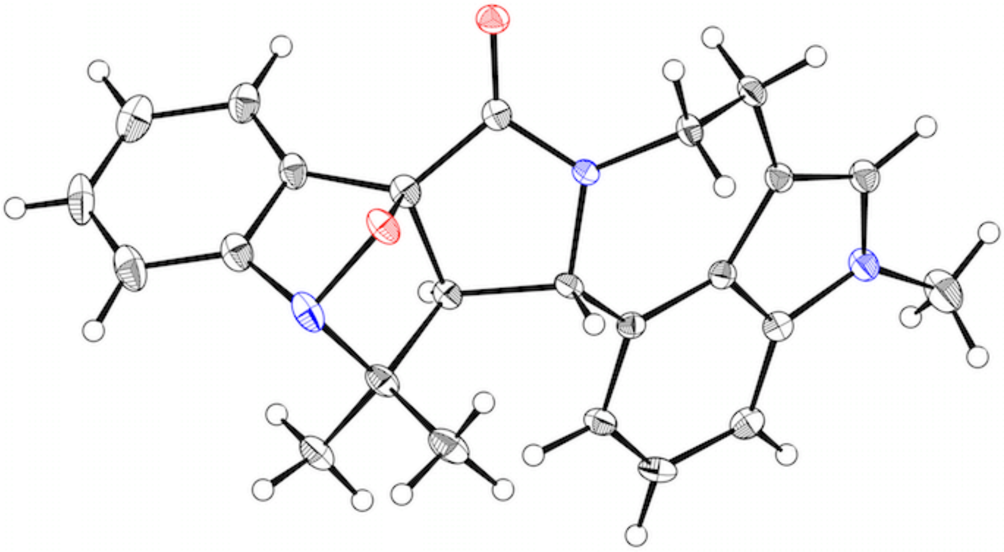

Table A2.1.1. *Crystal Data and Structure Analysis Details for **24***

Empirical formula	C25 H25 Cl2 N3 O2
Formula weight	470.38
Crystallization solvent	???Solvent???
Crystal shape	chunk
Crystal color	colourless
Crystal size	0.09 x 0.14 x 0.14 mm

Data Collection

Preliminary photograph(s)	rotation
Type of diffractometer	Bruker APEX-II CCD
Wavelength	0.71073 Å MoK
Data collection temperature	100 K

Theta range for 6076 reflections used in lattice determination	2.60 to 23.34°	
Unit cell dimensions	a = 8.2203(10) Å	a= 90°
	b = 26.018(3) Å	b= 90°
	c = 10.2431(12) Å	g = 90°
Volume	2190.8(5) Å^3	
Z	4	
Crystal system	orthorhombic	
Space group	P n a 21 (# 33)	
Density (calculated)	1.426 g/cm^3	
F(000)	984	
Theta range for data collection	1.6 to 32.9°	
Completeness to theta = 25.000°	100.0%	
Index ranges	-12 £ h £ 12, -39 £ k £ 39, -15 £ l £ 15	
Data collection scan type	and scans	
Reflections collected	54235	
Independent reflections	7838 [R$_{int}$= 0.0905]	
Reflections > 2s(I)	5779	
Average s(I)/(net I)	0.0696	
Absorption coefficient	0.33 mm^{-1}	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.9032	

Structure Solution and Refinement

Primary solution method	direct
Secondary solution method	?
Hydrogen placement	difmap
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7838 / 1 / 365
Treatment of hydrogen atoms	refxyz
Goodness-of-fit on F^2	1.13
Final R indices [I>2s(I), 5779 reflections]	R1 = 0.0490, wR2 = 0.0781
R indices (all data)	R1 = 0.0843, wR2 = 0.0857
Type of weighting scheme used	calc
Weighting scheme used	w=1/[^2^(Fo^2^)+(0.0300P)^2^] where
P=(Fo^2^+2Fc^2^)/3	
Max shift/error	0.000
Average shift/error	0.000
Absolute structure parameter	0.44(6)
Extinction coefficient	n/a

Largest diff. peak and hole	0.36 and -0.32 e·Å^{-3}

Programs Used

Cell refinement	SAINT V8.34A (Bruker-AXS, 2007)
Data collection	APEX2 2013.10-0 (Bruker-AXS, 2007)
Data reduction	SAINT V8.34A (Bruker-AXS, 2007)
Structure solution	XT (Sheldrick, 2012)
Structure refinement	SHELXL-2013/2 (Sheldrick, 2013)
Graphics	DIAMOND 3 (Crystal Impact, 1999)

References

Special Refinement Details

Table A2.1.2. *Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **24**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor*

	x	y	z	U_{eq}
O(1)	4(2)	2120(1)	6508(2)	16(1)
O(2)	85(2)	911(1)	6456(2)	16(1)
N(1)	1141(2)	1782(1)	4648(2)	12(1)
N(2)	1982(3)	2496(1)	117(2)	16(1)
N(3)	-836(3)	449(1)	6069(2)	20(1)
C(1)	-798(3)	1282(1)	5638(2)	15(1)
C(2)	110(3)	1784(1)	5675(2)	13(1)
C(3)	2535(3)	2130(1)	4609(3)	14(1)
C(4)	2247(3)	2582(1)	3706(2)	16(1)
C(5)	2045(3)	2430(1)	2314(2)	14(1)
C(6)	2387(3)	2738(1)	1267(2)	16(1)
C(7)	2210(4)	2702(1)	-1189(3)	29(1)
C(8)	1399(3)	2015(1)	413(2)	14(1)
C(9)	862(3)	1636(1)	-448(2)	16(1)
C(10)	332(3)	1183(1)	92(3)	17(1)
C(11)	350(3)	1105(1)	1455(2)	16(1)
C(12)	898(3)	1479(1)	2324(2)	12(1)
C(13)	1425(3)	1954(1)	1793(2)	13(1)
C(14)	997(3)	1336(1)	3766(2)	13(1)
C(15)	-526(3)	1052(1)	4272(2)	13(1)
C(16)	-460(3)	459(1)	4594(3)	17(1)
C(17)	1216(4)	220(1)	4435(3)	22(1)
C(18)	-1727(4)	147(1)	3860(3)	20(1)
C(19)	-2483(3)	644(1)	6275(2)	19(1)
C(20)	-3860(4)	373(1)	6614(3)	26(1)
C(21)	-5287(4)	655(1)	6750(3)	27(1)
C(22)	-5336(4)	1177(1)	6574(3)	25(1)
C(23)	-3924(3)	1452(1)	6225(2)	20(1)
C(24)	-2515(3)	1175(1)	6080(2)	16(1)
Cl(1)	5159(1)	1123(1)	2694(1)	28(1)
Cl(2)	5970(1)	875(1)	1(1)	44(1)
C(25)	4688(4)	1234(1)	1034(3)	25(1)

Table A2.1.3. *Bond lengths [Å] and angles [°] for* ***24***

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O(1)-C(2)	1.224(3)
O(2)-N(3)	1.475(3)
O(2)-C(1)	1.471(3)
N(1)-C(2)	1.352(3)
N(1)-C(3)	1.460(3)
N(1)-C(14)	1.475(3)
N(2)-C(6)	1.376(3)
N(2)-C(7)	1.453(4)
N(2)-C(8)	1.375(3)
N(3)-C(16)	1.542(3)
N(3)-C(19)	1.461(3)
C(1)-C(2)	1.504(3)
C(1)-C(15)	1.538(3)
C(1)-C(24)	1.508(3)
C(3)-H(3A)	0.96(3)
C(3)-H(3B)	0.99(3)
C(3)-C(4)	1.514(4)
C(4)-H(4A)	0.95(3)
C(4)-H(4B)	0.97(3)
C(4)-C(5)	1.490(3)
C(5)-C(6)	1.368(3)
C(5)-C(13)	1.440(3)
C(6)-H(6)	1.00(3)
C(7)-H(7A)	0.95(4)
C(7)-H(7B)	0.90(4)
C(7)-H(7C)	1.02(4)
C(8)-C(9)	1.393(3)
C(8)-C(13)	1.422(3)
C(9)-H(9)	0.95(3)
C(9)-C(10)	1.373(4)
C(10)-H(10)	0.95(3)
C(10)-C(11)	1.411(4)
C(11)-H(11)	1.03(3)
C(11)-C(12)	1.393(3)
C(12)-C(13)	1.419(3)
C(12)-C(14)	1.525(3)
C(14)-H(14)	0.96(3)
C(14)-C(15)	1.543(3)
C(15)-H(15)	0.95(3)
C(15)-C(16)	1.579(3)
C(16)-C(17)	1.520(4)
C(16)-C(18)	1.519(4)
C(17)-H(17A)	0.98(3)
C(17)-H(17B)	1.00(3)
C(17)-H(17C)	1.01(3)
C(18)-H(18A)	0.98(3)
C(18)-H(18B)	0.91(3)
C(18)-H(18C)	0.97(3)
C(19)-C(20)	1.378(4)
C(19)-C(24)	1.396(4)
C(20)-H(20)	0.98(3)
C(20)-C(21)	1.390(4)
C(21)-H(21)	0.86(3)
C(21)-C(22)	1.370(4)
C(22)-H(22)	0.95(3)

C(22)-C(23)	1.410(4)
C(23)-H(23)	0.99(3)
C(23)-C(24)	1.373(4)
Cl(1)-C(25)	1.768(3)
Cl(2)-C(25)	1.762(3)
C(25)-H(25A)	1.05(3)
C(25)-H(25B)	0.91(3)

C(1)-O(2)-N(3)	97.38(16)
C(2)-N(1)-C(3)	120.7(2)
C(2)-N(1)-C(14)	115.4(2)
C(3)-N(1)-C(14)	122.2(2)
C(6)-N(2)-C(7)	126.1(2)
C(8)-N(2)-C(6)	108.2(2)
C(8)-N(2)-C(7)	125.7(2)
O(2)-N(3)-C(16)	98.47(17)
C(19)-N(3)-O(2)	98.84(18)
C(19)-N(3)-C(16)	108.8(2)
O(2)-C(1)-C(2)	108.11(19)
O(2)-C(1)-C(15)	100.99(18)
O(2)-C(1)-C(24)	99.71(19)
C(2)-C(1)-C(15)	106.81(19)
C(2)-C(1)-C(24)	128.1(2)
C(24)-C(1)-C(15)	109.7(2)
O(1)-C(2)-N(1)	126.1(2)
O(1)-C(2)-C(1)	127.1(2)
N(1)-C(2)-C(1)	106.7(2)
N(1)-C(3)-H(3A)	105.4(16)
N(1)-C(3)-H(3B)	104.5(16)
N(1)-C(3)-C(4)	112.0(2)
H(3A)-C(3)-H(3B)	111(2)
C(4)-C(3)-H(3A)	112.9(17)
C(4)-C(3)-H(3B)	110.5(17)
C(3)-C(4)-H(4A)	109.4(17)
C(3)-C(4)-H(4B)	108.2(17)
H(4A)-C(4)-H(4B)	105(2)
C(5)-C(4)-C(3)	113.3(2)
C(5)-C(4)-H(4A)	109.6(18)
C(5)-C(4)-H(4B)	110.7(18)
C(6)-C(5)-C(4)	124.9(2)
C(6)-C(5)-C(13)	106.6(2)
C(13)-C(5)-C(4)	128.5(2)
N(2)-C(6)-H(6)	117.3(16)
C(5)-C(6)-N(2)	110.7(2)
C(5)-C(6)-H(6)	131.9(16)
N(2)-C(7)-H(7A)	110(2)
N(2)-C(7)-H(7B)	109(2)
N(2)-C(7)-H(7C)	101(2)
H(7A)-C(7)-H(7B)	116(3)
H(7A)-C(7)-H(7C)	116(3)
H(7B)-C(7)-H(7C)	103(3)
N(2)-C(8)-C(9)	127.9(2)
N(2)-C(8)-C(13)	108.3(2)
C(9)-C(8)-C(13)	123.7(2)
C(8)-C(9)-H(9)	120.8(17)
C(10)-C(9)-C(8)	116.9(2)
C(10)-C(9)-H(9)	122.3(17)
C(9)-C(10)-H(10)	116.5(18)

C(9)-C(10)-C(11)	121.3(2)
C(11)-C(10)-H(10)	122.2(18)
C(10)-C(11)-H(11)	122.5(17)
C(12)-C(11)-C(10)	122.3(2)
C(12)-C(11)-H(11)	115.2(17)
C(11)-C(12)-C(13)	117.6(2)
C(11)-C(12)-C(14)	117.8(2)
C(13)-C(12)-C(14)	124.5(2)
C(8)-C(13)-C(5)	106.2(2)
C(12)-C(13)-C(5)	135.6(2)
C(12)-C(13)-C(8)	118.2(2)
N(1)-C(14)-C(12)	113.95(19)
N(1)-C(14)-H(14)	106.4(16)
N(1)-C(14)-C(15)	103.67(18)
C(12)-C(14)-H(14)	107.2(17)
C(12)-C(14)-C(15)	113.51(19)
C(15)-C(14)-H(14)	111.9(15)
C(1)-C(15)-C(14)	103.71(19)
C(1)-C(15)-H(15)	106.3(17)
C(1)-C(15)-C(16)	101.28(18)
C(14)-C(15)-H(15)	110.2(16)
C(14)-C(15)-C(16)	120.7(2)
C(16)-C(15)-H(15)	112.7(15)
N(3)-C(16)-C(15)	102.36(19)
C(17)-C(16)-N(3)	106.3(2)
C(17)-C(16)-C(15)	114.1(2)
C(18)-C(16)-N(3)	109.8(2)
C(18)-C(16)-C(15)	113.2(2)
C(18)-C(16)-C(17)	110.5(2)
C(16)-C(17)-H(17A)	112.8(18)
C(16)-C(17)-H(17B)	111.4(19)
C(16)-C(17)-H(17C)	110.4(19)
H(17A)-C(17)-H(17B)	110(3)
H(17A)-C(17)-H(17C)	103(2)
H(17B)-C(17)-H(17C)	109(3)
C(16)-C(18)-H(18A)	109.3(18)
C(16)-C(18)-H(18B)	108(2)
C(16)-C(18)-H(18C)	113.1(19)
H(18A)-C(18)-H(18B)	111(3)
H(18A)-C(18)-H(18C)	105(3)
H(18B)-C(18)-H(18C)	111(3)
C(20)-C(19)-N(3)	128.3(2)
C(20)-C(19)-C(24)	121.8(3)
C(24)-C(19)-N(3)	109.9(2)
C(19)-C(20)-H(20)	121.3(19)
C(19)-C(20)-C(21)	116.7(3)
C(21)-C(20)-H(20)	121.3(19)
C(20)-C(21)-H(21)	121(2)
C(22)-C(21)-C(20)	122.3(3)
C(22)-C(21)-H(21)	117(2)
C(21)-C(22)-H(22)	120.7(19)
C(21)-C(22)-C(23)	120.8(3)
C(23)-C(22)-H(22)	118.5(19)
C(22)-C(23)-H(23)	118.4(17)
C(24)-C(23)-C(22)	117.1(3)
C(24)-C(23)-H(23)	124.4(17)
C(19)-C(24)-C(1)	102.0(2)
C(23)-C(24)-C(1)	136.5(2)

C(23)-C(24)-C(19)	121.3(2)
Cl(1)-C(25)-H(25A)	110.2(17)
Cl(1)-C(25)-H(25B)	107(2)
Cl(2)-C(25)-Cl(1)	111.07(16)
Cl(2)-C(25)-H(25A)	106.5(17)
Cl(2)-C(25)-H(25B)	108(2)
H(25A)-C(25)-H(25B)	113(3)

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Symmetry transformations used to generate equivalent atoms:

Table A2.1.4. *Anisotropic displacement parameters ($Å^2$x 10^4) for **24**. The anisotropic displacement factor exponent takes the form: $-2p^2$ [h^2 $a^{*2}U^{11}$ + ... + 2 h k a* b* U^{12}]*

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	206(9)	155(8)	131(8)	-22(7)	-1(7)	-14(7)
O(2)	207(10)	124(8)	161(8)	51(7)	-61(7)	-31(7)
N(1)	126(10)	118(9)	127(9)	-25(8)	-2(8)	-24(8)
N(2)	203(11)	166(10)	125(9)	9(9)	-8(9)	-46(9)
N(3)	212(12)	166(11)	214(11)	57(9)	-55(9)	-61(9)
C(1)	171(12)	142(12)	126(11)	41(9)	-26(9)	3(10)
C(2)	146(12)	138(12)	117(10)	32(9)	-22(9)	3(9)
C(3)	126(12)	149(12)	159(11)	7(10)	-10(9)	-34(10)
C(4)	177(13)	139(12)	148(11)	-8(10)	-12(10)	-51(10)
C(5)	119(12)	133(12)	160(11)	-4(9)	-4(9)	-5(9)
C(6)	153(12)	172(12)	166(12)	1(10)	-11(10)	-24(9)
C(7)	420(20)	280(16)	154(13)	27(12)	-28(13)	-139(15)
C(8)	143(12)	150(12)	139(11)	0(9)	-5(9)	8(10)
C(9)	169(13)	201(13)	121(10)	-4(10)	-15(10)	24(10)
C(10)	212(13)	137(12)	167(11)	-54(10)	-42(10)	14(10)
C(11)	193(13)	109(11)	173(12)	-16(10)	-4(10)	-1(10)
C(12)	116(11)	119(11)	131(10)	-7(9)	-4(8)	17(9)
C(13)	102(12)	136(12)	141(11)	-3(9)	-3(9)	8(9)
C(14)	132(12)	97(11)	153(11)	-15(9)	-13(10)	-8(9)
C(15)	148(12)	118(12)	112(11)	17(9)	-27(9)	-10(9)
C(16)	191(13)	99(11)	221(12)	26(10)	-30(10)	1(9)
C(17)	227(15)	118(12)	329(16)	7(12)	-65(12)	5(11)
C(18)	215(14)	129(13)	264(14)	3(11)	-22(11)	-38(11)
C(19)	216(13)	199(12)	146(11)	44(10)	-28(10)	-40(10)
C(20)	297(17)	272(15)	199(13)	74(12)	-32(12)	-122(13)
C(21)	214(15)	394(17)	194(13)	80(12)	3(11)	-141(13)
C(22)	181(14)	404(17)	172(13)	48(12)	-9(11)	10(13)
C(23)	178(13)	276(14)	133(11)	30(11)	-6(10)	-30(11)
C(24)	169(12)	194(12)	123(11)	32(10)	-11(9)	-46(10)
Cl(1)	219(3)	371(4)	261(3)	-11(3)	-21(3)	63(3)
Cl(2)	350(5)	605(5)	360(4)	-126(4)	68(4)	131(4)
C(25)	205(14)	276(15)	265(14)	-15(12)	8(12)	51(12)

Table A2.1.5. *Hydrogen coordinates (x 10^3) and isotropic displacement parameters ($Å^2$x 10^3) for **24***

	x	y	z	U_{iso}

H(3A)	344(4)	192(1)	435(3)	17
H(3B)	266(3)	225(1)	552(3)	17
H(4A)	131(4)	277(1)	399(3)	19
H(4B)	315(3)	282(1)	380(3)	19
H(6)	291(3)	308(1)	120(3)	20
H(7A)	249(4)	305(1)	-114(4)	43
H(7B)	133(5)	262(1)	-168(3)	43
H(7C)	309(5)	246(1)	-155(3)	43
H(9)	86(4)	169(1)	-136(3)	20
H(10)	-5(3)	93(1)	-50(3)	21
H(11)	-4(3)	77(1)	188(3)	19
H(14)	197(3)	114(1)	388(3)	15
H(15)	-145(3)	114(1)	377(3)	15
H(17A)	204(4)	38(1)	500(3)	34
H(17B)	159(4)	23(1)	350(3)	34
H(17C)	121(4)	-15(1)	474(3)	34
H(18A)	-185(4)	-19(1)	428(3)	30
H(18B)	-138(4)	11(1)	302(3)	30
H(18C)	-280(4)	30(1)	389(3)	30
H(20)	-387(4)	0(1)	662(3)	31
H(21)	-620(4)	50(1)	691(3)	32
H(22)	-632(4)	136(1)	671(3)	30
H(23)	-402(4)	183(1)	605(3)	23
H(25A)	349(4)	112(1)	83(3)	30
H(25B)	486(4)	158(1)	87(3)	30

Table A2.1.6. *Hydrogen bonds for **24** [Å and °]*

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(7)-H(7B)...O(1)#1	0.90(4)	2.52(4)	3.338(4)	151(3)
C(7)-H(7C)...O(1)#2	1.02(4)	2.76(4)	3.325(4)	115(2)
C(9)-H(9)...O(1)#1	0.95(3)	2.55(3)	3.436(3)	156(2)

Symmetry transformations used to generate equivalent atoms:
#1 x,y,z-1 #2 x+1/2,-y+1/2,z-1

A2.2. X-Ray Crystal Structure Analysis of 37

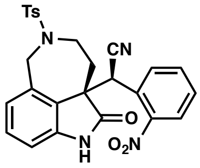

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Figure A2.2.1. *X-ray Crystal Structure of **37***

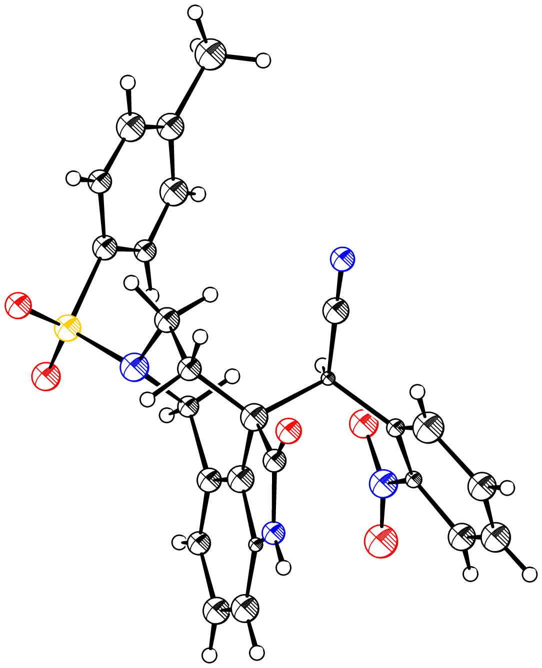

Table A2.2.1. *Crystal data and structure refinement for **37***

Empirical formula	C26 H22 N4 O5 S
Formula weight	502.54
Crystal Habit	Needle
Crystal size	0.30 x 0.07 x 0.07 mm^3
Crystal color	Colorless

Data Collection

Preliminary Photos	
Type of diffractometer	Bruker SMART 1000
Wavelength	0.71073 Å MoK⟨
Data Collection Temperature	100(2) K
\ range for 1342 reflections used	

in lattice determination	2.17 to 18.91°	
Unit cell dimensions	a = 13.243(2) Å	〈= 90°
	b = 14.115(2) Å	®= 90°
	c = 25.059(4) Å	© = 90°
Volume	4684.2(13) Å^3	
Z	8	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Density (calculated)	1.425 Mg/m^3	
F(000)	2096	
Data collection program	Bruker SMART v5.630	
\ range for data collection	1.63 to 22.98°	
Completeness to \ = 22.98°	83.9 %	
Index ranges	-12<=h<=13, -14<=k<=10, -27<=l<=21	
Data collection scan type	scans at 2 settings	
Data reduction program	Bruker SAINT v6.45A	
Reflections collected	10767	
Independent reflections	5122 [R_{int}= 0.1652]	
Absorption coefficient	0.185 mm^{-1}	
Absorption correction	None	
Max. and min. transmission	0.9871 and 0.9465	
Number of standards	? reflections measured every ?min.	
Variation of standards ?%.		

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 1990)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric positions
Structure refinement program	SHELXL-97 (Sheldrick, 1997)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	5122 / 0 / 291
Treatment of hydrogen atoms	Riding
Goodness-of-fit on F^2	1.294
Final R indices [I>2ʃ(I), 2377 reflections]	R1 = 0.1085, wR2 = 0.1814
R indices (all data)	R1 = 0.2168, wR2 = 0.2078
Type of weighting scheme used	Sigma
Weighting scheme used	w=1/s^2^(Fo^2^)
Max shift/error	0.015
Average shift/error	0.000

Absolute structure determination	?
Absolute structure parameter	0.5(3)
Largest diff. peak and hole	0.868 and -1.060 e.Å^{-3}

Special Refinement Details

Table A2.2.2. *Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **37**. U(eq) is defined asthe trace of the orthogonalized U^{ij} tensor*

	x	y	z	U_{eq}
S(1A)	2444(3)	6752(3)	3762(2)	24(1)
O(1A)	1847(8)	6830(7)	4221(4)	35(3)
O(2A)	2120(8)	7120(7)	3248(4)	25(3)
O(3A)	3062(8)	2592(7)	2393(4)	22(3)
O(4A)	4152(8)	3228(8)	4567(4)	26(3)
O(5A)	2979(9)	2243(8)	4804(4)	34(3)
N(1A)	2662(8)	5605(8)	3672(5)	10(3)
N(2A)	2007(9)	2282(9)	3084(5)	19(4)
N(3A)	3661(10)	2523(10)	4514(5)	27(4)
N(4A)	5462(11)	3745(9)	2693(6)	31(4)
C(1A)	3644(12)	7259(11)	3917(6)	19(4)
C(2A)	3980(11)	7265(11)	4429(6)	20(5)
C(3A)	4958(12)	7621(11)	4550(7)	31(5)
C(4A)	5605(14)	8037(13)	4166(7)	40(6)
C(5A)	5147(11)	8041(10)	3649(7)	21(5)
C(6A)	4202(11)	7655(10)	3519(6)	12(4)
C(7A)	6579(12)	8456(12)	4253(7)	36(5)
C(8A)	2748(12)	5013(10)	4169(6)	21(4)
C(9A)	2094(14)	4095(11)	4086(7)	36(5)
C(10A)	1349(11)	3803(11)	4439(6)	13(4)
C(11A)	810(12)	3025(11)	4359(6)	24(5)
C(12A)	966(12)	2434(12)	3927(6)	26(5)
C(13A)	1776(11)	2644(10)	3576(6)	19(4)
C(14A)	2313(11)	3475(10)	3645(6)	13(4)
C(15A)	3070(11)	3547(10)	3202(6)	17(4)
C(16A)	3010(11)	4510(10)	2925(6)	14(4)
C(17A)	3383(11)	5395(10)	3235(6)	15(4)
C(18A)	2703(12)	2749(11)	2827(6)	21(5)
C(19A)	4146(10)	3299(9)	3415(5)	3(4)
C(20A)	4911(12)	3517(11)	2992(6)	16(4)
C(21A)	4200(12)	2245(11)	3559(6)	23(5)
C(22A)	4506(10)	1615(10)	3185(6)	10(4)
C(23A)	4374(13)	614(12)	3276(7)	38(5)
C(24A)	4002(12)	326(12)	3754(7)	33(5)
C(25A)	3778(12)	949(11)	4169(7)	26(5)
C(26A)	3877(10)	1874(10)	4071(6)	8(4)
S(1B)	7184(3)	1177(3)	3593(2)	24(1)
O(1B)	6473(8)	1114(7)	4015(4)	28(3)
O(2B)	6953(8)	839(7)	3074(4)	24(3)
O(3B)	8347(8)	5377(7)	2346(4)	23(3)
O(4B)	9055(8)	4456(8)	4514(4)	28(3)
O(5B)	8036(9)	5576(8)	4787(5)	39(3)
N(1B)	7443(10)	2316(9)	3495(5)	28(4)

N(2B)	7154(9)	5718(9)	3014(5)	18(3)
N(3B)	8648(10)	5277(10)	4471(6)	28(4)
N(4B)	10569(10)	4005(9)	2678(5)	20(4)
C(1B)	8339(12)	633(11)	3783(7)	21(4)
C(2B)	8674(11)	682(11)	4310(6)	17(4)
C(3B)	9535(12)	304(11)	4441(7)	28(5)
C(4B)	10165(13)	-92(12)	4072(7)	26(5)
C(5B)	9804(12)	-94(11)	3538(7)	29(5)
C(6B)	8964(11)	227(10)	3393(7)	19(5)
C(7B)	11271(11)	-495(12)	4220(7)	34(5)
C(8B)	7549(12)	2872(9)	4003(6)	15(4)
C(9B)	7020(12)	3849(11)	3944(6)	20(4)
C(10B)	6276(11)	4107(10)	4280(6)	19(5)
C(11B)	5776(12)	4987(11)	4225(7)	25(5)
C(12B)	6092(12)	5574(12)	3800(6)	27(5)
C(13B)	6847(10)	5316(10)	3459(6)	7(4)
C(14B)	7352(12)	4461(11)	3542(7)	25(5)
C(15B)	8118(12)	4327(11)	3101(7)	26(5)
C(16B)	7989(12)	3429(10)	2779(6)	20(5)
C(17B)	8247(12)	2492(10)	3090(6)	22(5)
C(18B)	7896(12)	5207(11)	2769(6)	18(4)
C(19B)	9211(10)	4501(10)	3372(6)	7(4)
C(20B)	9978(12)	4216(11)	2978(7)	24(5)
C(21B)	9361(11)	5538(10)	3556(6)	11(4)
C(22B)	9696(13)	6156(11)	3175(7)	34(5)
C(23B)	9622(12)	7178(12)	3311(7)	28(5)
C(24B)	9228(12)	7468(12)	3774(7)	31(5)
C(25B)	8888(12)	6840(11)	4145(7)	26(5)
C(26B)	9000(11)	5871(10)	4031(6)	9(4)

Table A2.2.3. *Bond lengths [Å] and angles [°] for **37***

S(1A)-O(1A)	1.399(11)
S(1A)-O(2A)	1.455(11)
S(1A)-N(1A)	1.659(12)
S(1A)-C(1A)	1.786(16)
O(3A)-C(18A)	1.206(16)
O(4A)-N(3A)	1.196(14)
O(5A)-N(3A)	1.225(16)
N(1A)-C(17A)	1.484(17)
N(1A)-C(8A)	1.504(17)
N(2A)-C(18A)	1.305(17)
N(2A)-C(13A)	1.369(18)
N(3A)-C(26A)	1.469(18)
N(4A)-C(20A)	1.094(17)
C(1A)-C(2A)	1.357(19)
C(1A)-C(6A)	1.361(19)
C(2A)-C(3A)	1.42(2)
C(3A)-C(4A)	1.42(2)
C(4A)-C(5A)	1.43(2)
C(4A)-C(7A)	1.44(2)
C(5A)-C(6A)	1.403(19)
C(8A)-C(9A)	1.57(2)
C(9A)-C(10A)	1.39(2)
C(9A)-C(14A)	1.44(2)
C(10A)-C(11A)	1.32(2)

C(11A)-C(12A)	1.38(2)
C(12A)-C(13A)	1.42(2)
C(13A)-C(14A)	1.382(18)
C(14A)-C(15A)	1.50(2)
C(15A)-C(16A)	1.528(18)
C(15A)-C(18A)	1.55(2)
C(15A)-C(19A)	1.562(19)
C(16A)-C(17A)	1.552(18)
C(19A)-C(20A)	1.50(2)
C(19A)-C(21A)	1.532(19)
C(21A)-C(22A)	1.354(19)
C(21A)-C(26A)	1.45(2)
C(22A)-C(23A)	1.44(2)
C(23A)-C(24A)	1.36(2)
C(24A)-C(25A)	1.39(2)
C(25A)-C(26A)	1.336(19)
S(1B)-O(2B)	1.418(11)
S(1B)-O(1B)	1.418(11)
S(1B)-N(1B)	1.662(13)
S(1B)-C(1B)	1.776(16)
O(3B)-C(18B)	1.241(17)
O(4B)-N(3B)	1.282(14)
O(5B)-N(3B)	1.209(16)
N(1B)-C(17B)	1.493(18)
N(1B)-C(8B)	1.501(17)
N(2B)-C(13B)	1.316(17)
N(2B)-C(18B)	1.365(18)
N(3B)-C(26B)	1.463(18)
N(4B)-C(20B)	1.126(18)
C(1B)-C(2B)	1.40(2)
C(1B)-C(6B)	1.40(2)
C(2B)-C(3B)	1.301(19)
C(3B)-C(4B)	1.36(2)
C(4B)-C(5B)	1.42(2)
C(4B)-C(7B)	1.61(2)
C(5B)-C(6B)	1.254(19)
C(8B)-C(9B)	1.55(2)
C(9B)-C(10B)	1.35(2)
C(9B)-C(14B)	1.40(2)
C(10B)-C(11B)	1.41(2)
C(11B)-C(12B)	1.41(2)
C(12B)-C(13B)	1.36(2)
C(13B)-C(14B)	1.396(19)
C(14B)-C(15B)	1.51(2)
C(15B)-C(16B)	1.51(2)
C(15B)-C(18B)	1.52(2)
C(15B)-C(19B)	1.62(2)
C(16B)-C(17B)	1.572(19)
C(19B)-C(20B)	1.47(2)
C(19B)-C(21B)	1.547(19)
C(21B)-C(26B)	1.365(19)
C(21B)-C(22B)	1.37(2)
C(22B)-C(23B)	1.49(2)
C(23B)-C(24B)	1.34(2)
C(24B)-C(25B)	1.36(2)
C(25B)-C(26B)	1.41(2)
O(1A)-S(1A)-O(2A)	122.2(7)

O(1A)-S(1A)-N(1A)	106.7(7)
O(2A)-S(1A)-N(1A)	106.2(6)
O(1A)-S(1A)-C(1A)	107.0(7)
O(2A)-S(1A)-C(1A)	108.2(7)
N(1A)-S(1A)-C(1A)	105.4(7)
C(17A)-N(1A)-C(8A)	116.8(11)
C(17A)-N(1A)-S(1A)	114.1(9)
C(8A)-N(1A)-S(1A)	116.3(9)
C(18A)-N(2A)-C(13A)	114.5(13)
O(4A)-N(3A)-O(5A)	127.2(15)
O(4A)-N(3A)-C(26A)	119.8(14)
O(5A)-N(3A)-C(26A)	113.0(13)
C(2A)-C(1A)-C(6A)	120.8(16)
C(2A)-C(1A)-S(1A)	120.0(12)
C(6A)-C(1A)-S(1A)	119.2(12)
C(1A)-C(2A)-C(3A)	120.1(16)
C(4A)-C(3A)-C(2A)	123.5(17)
C(3A)-C(4A)-C(5A)	111.2(16)
C(3A)-C(4A)-C(7A)	127.6(17)
C(5A)-C(4A)-C(7A)	121.2(17)
C(6A)-C(5A)-C(4A)	125.9(16)
C(1A)-C(6A)-C(5A)	118.3(15)
N(1A)-C(8A)-C(9A)	107.8(12)
C(10A)-C(9A)-C(14A)	116.9(15)
C(10A)-C(9A)-C(8A)	123.5(16)
C(14A)-C(9A)-C(8A)	119.5(15)
C(11A)-C(10A)-C(9A)	122.1(16)
C(10A)-C(11A)-C(12A)	122.6(17)
C(11A)-C(12A)-C(13A)	118.2(16)
N(2A)-C(13A)-C(14A)	108.4(14)
N(2A)-C(13A)-C(12A)	130.5(15)
C(14A)-C(13A)-C(12A)	119.2(15)
C(13A)-C(14A)-C(9A)	120.6(14)
C(13A)-C(14A)-C(15A)	108.0(13)
C(9A)-C(14A)-C(15A)	131.4(13)
C(14A)-C(15A)-C(16A)	111.2(12)
C(14A)-C(15A)-C(18A)	101.0(12)
C(16A)-C(15A)-C(18A)	110.8(12)
C(14A)-C(15A)-C(19A)	110.0(12)
C(16A)-C(15A)-C(19A)	113.8(12)
C(18A)-C(15A)-C(19A)	109.4(11)
C(15A)-C(16A)-C(17A)	118.1(12)
N(1A)-C(17A)-C(16A)	109.0(12)
O(3A)-C(18A)-N(2A)	129.1(15)
O(3A)-C(18A)-C(15A)	123.9(15)
N(2A)-C(18A)-C(15A)	106.8(14)
C(20A)-C(19A)-C(21A)	109.5(13)
C(20A)-C(19A)-C(15A)	109.2(12)
C(21A)-C(19A)-C(15A)	109.9(12)
N(4A)-C(20A)-C(19A)	174.7(18)
C(22A)-C(21A)-C(26A)	117.6(14)
C(22A)-C(21A)-C(19A)	119.3(14)
C(26A)-C(21A)-C(19A)	123.0(14)
C(21A)-C(22A)-C(23A)	119.9(15)
C(24A)-C(23A)-C(22A)	118.5(17)
C(23A)-C(24A)-C(25A)	123.1(17)
C(26A)-C(25A)-C(24A)	117.4(17)
C(25A)-C(26A)-C(21A)	123.0(16)

C(25A)-C(26A)-N(3A)	116.9(14)
C(21A)-C(26A)-N(3A)	120.1(13)
O(2B)-S(1B)-O(1B)	121.3(7)
O(2B)-S(1B)-N(1B)	103.6(7)
O(1B)-S(1B)-N(1B)	107.9(7)
O(2B)-S(1B)-C(1B)	106.6(7)
O(1B)-S(1B)-C(1B)	110.2(7)
N(1B)-S(1B)-C(1B)	106.2(7)
C(17B)-N(1B)-C(8B)	115.0(12)
C(17B)-N(1B)-S(1B)	114.1(11)
C(8B)-N(1B)-S(1B)	113.6(10)
C(13B)-N(2B)-C(18B)	112.1(13)
O(5B)-N(3B)-O(4B)	122.8(14)
O(5B)-N(3B)-C(26B)	120.5(13)
O(4B)-N(3B)-C(26B)	116.6(13)
C(2B)-C(1B)-C(6B)	119.5(15)
C(2B)-C(1B)-S(1B)	120.4(13)
C(6B)-C(1B)-S(1B)	119.9(13)
C(3B)-C(2B)-C(1B)	119.8(16)
C(2B)-C(3B)-C(4B)	122.2(17)
C(3B)-C(4B)-C(5B)	115.7(16)
C(3B)-C(4B)-C(7B)	122.9(15)
C(5B)-C(4B)-C(7B)	121.4(15)
C(6B)-C(5B)-C(4B)	124.7(17)
C(5B)-C(6B)-C(1B)	118.0(17)
N(1B)-C(8B)-C(9B)	110.0(12)
C(10B)-C(9B)-C(14B)	120.9(15)
C(10B)-C(9B)-C(8B)	120.8(15)
C(14B)-C(9B)-C(8B)	118.3(14)
C(9B)-C(10B)-C(11B)	121.3(17)
C(12B)-C(11B)-C(10B)	116.8(16)
C(13B)-C(12B)-C(11B)	122.1(15)
N(2B)-C(13B)-C(12B)	130.0(15)
N(2B)-C(13B)-C(14B)	110.6(14)
C(12B)-C(13B)-C(14B)	119.2(15)
C(13B)-C(14B)-C(9B)	119.4(15)
C(13B)-C(14B)-C(15B)	108.7(15)
C(9B)-C(14B)-C(15B)	131.3(15)
C(16B)-C(15B)-C(14B)	114.8(14)
C(16B)-C(15B)-C(18B)	111.7(13)
C(14B)-C(15B)-C(18B)	99.6(13)
C(16B)-C(15B)-C(19B)	116.9(13)
C(14B)-C(15B)-C(19B)	105.9(13)
C(18B)-C(15B)-C(19B)	106.2(12)
C(15B)-C(16B)-C(17B)	114.6(12)
N(1B)-C(17B)-C(16B)	108.8(12)
O(3B)-C(18B)-N(2B)	128.9(14)
O(3B)-C(18B)-C(15B)	122.1(15)
N(2B)-C(18B)-C(15B)	108.9(13)
C(20B)-C(19B)-C(21B)	111.7(13)
C(20B)-C(19B)-C(15B)	107.0(13)
C(21B)-C(19B)-C(15B)	112.6(12)
N(4B)-C(20B)-C(19B)	179(2)
C(26B)-C(21B)-C(22B)	120.2(14)
C(26B)-C(21B)-C(19B)	122.6(14)
C(22B)-C(21B)-C(19B)	116.0(14)
C(21B)-C(22B)-C(23B)	115.9(16)
C(24B)-C(23B)-C(22B)	121.5(18)

C(23B)-C(24B)-C(25B)	121.5(17)
C(24B)-C(25B)-C(26B)	117.3(16)
C(21B)-C(26B)-C(25B)	123.3(15)
C(21B)-C(26B)-N(3B)	124.9(13)
C(25B)-C(26B)-N(3B)	111.7(13)

Symmetry transformations used to generate equivalent atoms:

Table A2.2.4. *Hydrogen bonds for* ***37*** *[Å and °]*

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2A)-H(2A)...O(3B)#1	0.88	2.11	2.933(16)	155.2
N(2B)-H(2B)...O(3A)#2	0.88	2.02	2.849(16)	157.3

Symmetry transformations used to generate equivalent atoms:
#1 -x+1,y-1/2,-z+1/2 #2 -x+1,y+1/2,-z+1/2

A2.3. X-Ray Crystal Structure Analysis of 42

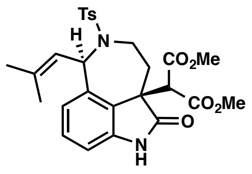

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Figure A2.3.1. *X-ray Crystal Structure of **42***

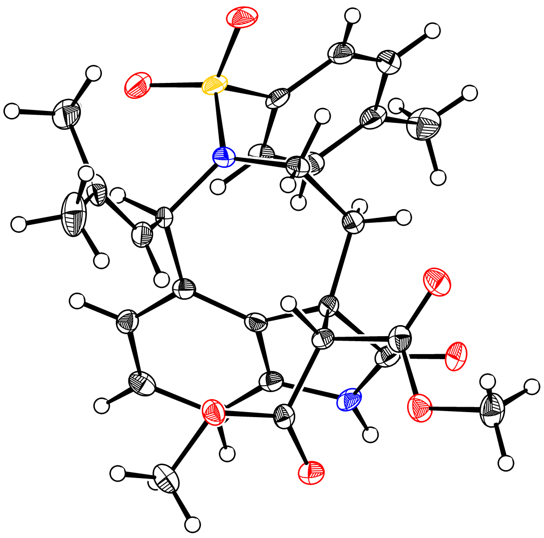

Table A2.3.1. *Crystal data and structure refinement for **42***

Empirical formula	C27 H30 N2 O7 S
Formula weight	526.59
Crystal Habit	Blade
Crystal size	0.33 x 0.26 x 0.07 mm^3
Crystal color	Colorless

Data Collection

Preliminary Photos		
Type of diffractometer	Bruker SMART 1000	
Wavelength	0.71073 Å MoKa	
Data Collection Temperature	100(2) K	
q range for 9727 reflections used in lattice determination	2.40 to 33.11°	
Unit cell dimensions	a = 9.5308(8) Å	a= 90°
	b = 9.7901(9) Å	b= 100.914(2)°
	c = 13.8253(12) Å	g = 90°
Volume	1266.67(19) $Å^3$	
Z	2	
Crystal system	Monoclinic	

Space group	Pn
Density (calculated)	1.381 Mg/m^3
F(000)	556
Data collection program	Bruker SMART v5.630
q range for data collection	2.08 to 33.37°
Completeness to q = 33.37°	79.2 %
Index ranges	-12<=h<=12, -12<=k<=14, -20<=l<=18
Data collection scan type	scans at 5 settings
Data reduction program	Bruker SAINT v6.45A
Reflections collected	17354
Independent reflections	6630 [R$_{int}$= 0.0627]
Absorption coefficient	0.178 mm^{-1}
Absorption correction	None
Max. and min. transmission	0.9876 and 0.9436
Number of standards	? reflections measured every ?min.
Variation of standards	?%.

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 1990)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric positions
Structure refinement program	SHELXL-97 (Sheldrick, 1997)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	6630 / 2 / 339
Treatment of hydrogen atoms	Riding
Goodness-of-fit on F^2	1.413
Final R indices [I>2s(I), 5764 reflections]	R1 = 0.0412, wR2 = 0.0772
R indices (all data)	R1 = 0.0487, wR2 = 0.0785
Type of weighting scheme used	Sigma
Weighting scheme used	w=1/s^2^(Fo^2^)
Max shift/error	0.003
Average shift/error	0.000
Absolute structure determination	?
Absolute structure parameter	-0.06(5)
Largest diff. peak and hole	0.698 and -0.437 e.Å^{-3}

Special Refinement Details

Table A2.3.2. *Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for* ***42****. U(eq) is defined as the trace of the orthogonalized U^{ij} tensor*

	x	y	z	U_{eq}
S(1)	2561(1)	4166(1)	5901(1)	20(1)
O(1)	1091(2)	3868(1)	5901(1)	28(1)
O(2)	3543(2)	3041(1)	5888(1)	26(1)
O(3)	5953(1)	9815(1)	6612(1)	23(1)
O(4)	7590(1)	7652(1)	8168(1)	25(1)
O(5)	7214(1)	9500(1)	9044(1)	22(1)
O(6)	4387(1)	10398(1)	8732(1)	21(1)
O(7)	3629(1)	8558(1)	9457(1)	19(1)
N(1)	3154(2)	5091(2)	6868(1)	18(1)
N(2)	3555(2)	10204(2)	6558(1)	18(1)
C(1)	2669(2)	5158(2)	4849(2)	17(1)
C(2)	3664(2)	4837(2)	4284(2)	21(1)
C(3)	3700(2)	5589(2)	3436(2)	23(1)
C(4)	2753(2)	6670(2)	3153(2)	21(1)
C(5)	1775(2)	6993(2)	3757(2)	24(1)
C(6)	1722(2)	6249(2)	4595(2)	22(1)
C(7)	2775(3)	7430(2)	2213(2)	33(1)
C(8)	4669(2)	5481(2)	7050(2)	19(1)
C(9)	4988(2)	6898(2)	6675(2)	17(1)
C(10)	4451(2)	8092(2)	7224(1)	15(1)
C(11)	2834(2)	8156(2)	7105(1)	15(1)
C(12)	1822(2)	7184(2)	7242(1)	15(1)
C(13)	2158(2)	5683(2)	7468(1)	16(1)
C(14)	2653(2)	5409(2)	8558(2)	18(1)
C(15)	2510(2)	4205(2)	8993(2)	23(1)
C(16)	1948(2)	2934(2)	8454(2)	32(1)
C(17)	2943(2)	4057(3)	10088(2)	37(1)
C(18)	404(2)	7610(2)	7130(1)	17(1)
C(19)	-10(2)	8938(2)	6853(1)	19(1)
C(20)	980(2)	9888(2)	6632(1)	18(1)
C(21)	2385(2)	9461(2)	6761(1)	15(1)
C(22)	4787(2)	9468(2)	6759(1)	18(1)
C(23)	5191(2)	8149(2)	8355(1)	16(1)
C(24)	6788(2)	8399(2)	8493(1)	18(1)
C(25)	8742(2)	9752(2)	9212(2)	27(1)
C(26)	4392(2)	9188(2)	8867(1)	15(1)
C(27)	2603(2)	9418(2)	9817(2)	25(1)

Table A2.3.3. *Bond lengths [Å] and angles [°] for* ***42***

S(1)-O(1)	1.4313(14)
S(1)-O(2)	1.4482(14)
S(1)-N(1)	1.6255(17)
S(1)-C(1)	1.767(2)
O(3)-C(22)	1.215(2)
O(4)-C(24)	1.204(2)
O(5)-C(24)	1.338(2)
O(5)-C(25)	1.451(2)

O(6)-C(26)	1.199(2)
O(7)-C(26)	1.341(2)
O(7)-C(27)	1.449(2)
N(1)-C(8)	1.469(2)
N(1)-C(13)	1.491(2)
N(2)-C(22)	1.361(2)
N(2)-C(21)	1.403(2)
C(1)-C(2)	1.374(3)
C(1)-C(6)	1.400(3)
C(2)-C(3)	1.390(3)
C(3)-C(4)	1.398(3)
C(4)-C(5)	1.401(3)
C(4)-C(7)	1.501(3)
C(5)-C(6)	1.377(3)
C(8)-C(9)	1.531(2)
C(9)-C(10)	1.532(2)
C(10)-C(11)	1.519(3)
C(10)-C(22)	1.551(2)
C(10)-C(23)	1.590(2)
C(11)-C(12)	1.393(2)
C(11)-C(21)	1.402(2)
C(12)-C(18)	1.395(2)
C(12)-C(13)	1.524(2)
C(13)-C(14)	1.515(3)
C(14)-C(15)	1.341(3)
C(15)-C(16)	1.496(3)
C(15)-C(17)	1.499(3)
C(18)-C(19)	1.392(3)
C(19)-C(20)	1.398(3)
C(20)-C(21)	1.382(3)
C(23)-C(24)	1.517(2)
C(23)-C(26)	1.524(3)

O(1)-S(1)-O(2)	118.70(9)
O(1)-S(1)-N(1)	107.55(8)
O(2)-S(1)-N(1)	107.99(8)
O(1)-S(1)-C(1)	108.78(9)
O(2)-S(1)-C(1)	105.60(9)
N(1)-S(1)-C(1)	107.79(8)
C(24)-O(5)-C(25)	114.58(15)
C(26)-O(7)-C(27)	114.87(15)
C(8)-N(1)-C(13)	120.84(15)
C(8)-N(1)-S(1)	117.58(12)
C(13)-N(1)-S(1)	121.04(13)
C(22)-N(2)-C(21)	111.90(15)
C(2)-C(1)-C(6)	120.90(18)
C(2)-C(1)-S(1)	119.74(14)
C(6)-C(1)-S(1)	119.35(16)
C(1)-C(2)-C(3)	119.21(17)
C(2)-C(3)-C(4)	121.30(19)
C(3)-C(4)-C(5)	118.11(18)
C(3)-C(4)-C(7)	120.25(18)
C(5)-C(4)-C(7)	121.62(17)
C(6)-C(5)-C(4)	121.13(18)
C(5)-C(6)-C(1)	119.32(19)
N(1)-C(8)-C(9)	115.42(15)
C(8)-C(9)-C(10)	114.69(15)
C(11)-C(10)-C(9)	113.86(15)

C(11)-C(10)-C(22)	101.80(14)
C(9)-C(10)-C(22)	110.06(14)
C(11)-C(10)-C(23)	110.93(14)
C(9)-C(10)-C(23)	112.65(14)
C(22)-C(10)-C(23)	106.77(14)
C(12)-C(11)-C(21)	119.60(16)
C(12)-C(11)-C(10)	132.16(16)
C(21)-C(11)-C(10)	108.20(15)
C(11)-C(12)-C(18)	117.54(16)
C(11)-C(12)-C(13)	124.25(16)
C(18)-C(12)-C(13)	118.17(15)
N(1)-C(13)-C(14)	111.94(14)
N(1)-C(13)-C(12)	113.07(14)
C(14)-C(13)-C(12)	112.87(15)
C(15)-C(14)-C(13)	124.25(18)
C(14)-C(15)-C(16)	124.3(2)
C(14)-C(15)-C(17)	120.4(2)
C(16)-C(15)-C(17)	115.24(18)
C(19)-C(18)-C(12)	121.84(17)
C(18)-C(19)-C(20)	120.92(17)
C(21)-C(20)-C(19)	116.63(16)
C(20)-C(21)-C(11)	123.04(17)
C(20)-C(21)-N(2)	127.26(16)
C(11)-C(21)-N(2)	109.68(16)
O(3)-C(22)-N(2)	126.81(16)
O(3)-C(22)-C(10)	125.37(16)
N(2)-C(22)-C(10)	107.82(15)
C(24)-C(23)-C(26)	114.28(15)
C(24)-C(23)-C(10)	112.17(14)
C(26)-C(23)-C(10)	108.22(14)
O(4)-C(24)-O(5)	123.72(18)
O(4)-C(24)-C(23)	123.19(17)
O(5)-C(24)-C(23)	113.04(15)
O(6)-C(26)-O(7)	124.28(17)
O(6)-C(26)-C(23)	125.06(17)
O(7)-C(26)-C(23)	110.58(15)

Symmetry transformations used to generate equivalent atoms:

Table A2.3.4. *Anisotropic displacement parameters (Å^{2}x 10^4) for* ***42***. *The anisotropic displacement factor exponent takes the form: -2p^2 [h^2 a*^{2}U ^{11} + ... + 2 h k a* b* U^{12}]*

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	284(3)	91(2)	237(3)	-5(2)	94(2)	-26(2)
O(1)	333(8)	219(7)	297(9)	-67(6)	115(7)	-105(6)
O(2)	421(9)	99(6)	292(8)	25(6)	140(7)	25(6)
O(3)	230(7)	208(7)	267(8)	36(6)	97(6)	-55(6)
O(4)	187(7)	262(7)	301(9)	1(6)	61(6)	54(6)
O(5)	167(7)	267(7)	229(8)	-24(6)	36(6)	-9(5)
O(6)	212(7)	155(7)	276(8)	-7(6)	63(6)	11(5)
O(7)	199(7)	208(7)	180(7)	20(5)	78(5)	10(5)
N(1)	208(8)	126(8)	211(9)	-7(6)	88(6)	4(6)
N(2)	222(9)	96(7)	224(9)	48(6)	46(7)	-3(6)
C(1)	230(10)	101(8)	185(10)	-8(7)	38(8)	-49(7)
C(2)	201(10)	138(9)	284(12)	-18(8)	41(8)	15(7)
C(3)	239(11)	185(10)	280(12)	-13(8)	109(9)	0(7)

C(4)	235(10)	133(9)	252(11)	12(8)	34(8)	-12(7)
C(5)	241(10)	157(9)	309(12)	12(8)	25(8)	47(8)
C(6)	230(11)	164(10)	292(12)	-33(8)	84(9)	10(8)
C(7)	399(13)	255(11)	324(13)	85(10)	58(10)	33(10)
C(8)	196(10)	139(9)	246(11)	-4(7)	82(8)	25(7)
C(9)	172(10)	165(9)	189(10)	3(7)	60(7)	4(7)
C(10)	164(9)	124(8)	167(10)	21(7)	54(7)	-9(6)
C(11)	192(9)	133(9)	127(9)	-19(7)	52(7)	9(7)
C(12)	194(9)	132(9)	117(9)	9(7)	42(7)	9(7)
C(13)	139(9)	134(9)	213(10)	-13(7)	89(8)	-22(7)
C(14)	151(9)	169(9)	240(11)	33(8)	59(8)	1(7)
C(15)	146(9)	252(10)	302(12)	115(9)	93(8)	48(8)
C(16)	328(12)	154(10)	524(16)	127(10)	173(11)	49(8)
C(17)	283(12)	474(14)	361(14)	223(11)	103(10)	-17(10)
C(18)	185(10)	177(9)	151(10)	-8(7)	42(8)	-33(7)
C(19)	167(9)	221(10)	172(10)	-8(8)	10(8)	59(7)
C(20)	229(10)	141(9)	167(10)	25(7)	20(8)	50(7)
C(21)	225(10)	128(9)	107(9)	-1(7)	38(8)	-1(7)
C(22)	251(10)	130(9)	152(10)	1(7)	42(8)	-25(7)
C(23)	177(9)	105(8)	192(10)	30(7)	50(8)	12(7)
C(24)	186(10)	179(9)	179(10)	64(8)	37(8)	10(7)
C(25)	173(10)	374(12)	244(12)	-17(9)	12(8)	-73(8)
C(26)	97(8)	196(9)	151(10)	-6(7)	-8(7)	-9(7)
C(27)	231(10)	306(11)	241(11)	-9(9)	104(9)	37(8)

Table A2.3.5. *Hydrogen bonds for **42** [Å and °]*

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2)...O(2)#1	0.88	2.05	2.928(2)	174.5

Symmetry transformations used to generate equivalent atoms:
#1 x,y+1,z

A2.4. X-Ray Crystal Structure Analysis of 51

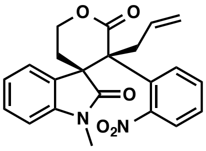

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Figure A2.4.1. *X-ray Crystal Structure of* ***51***

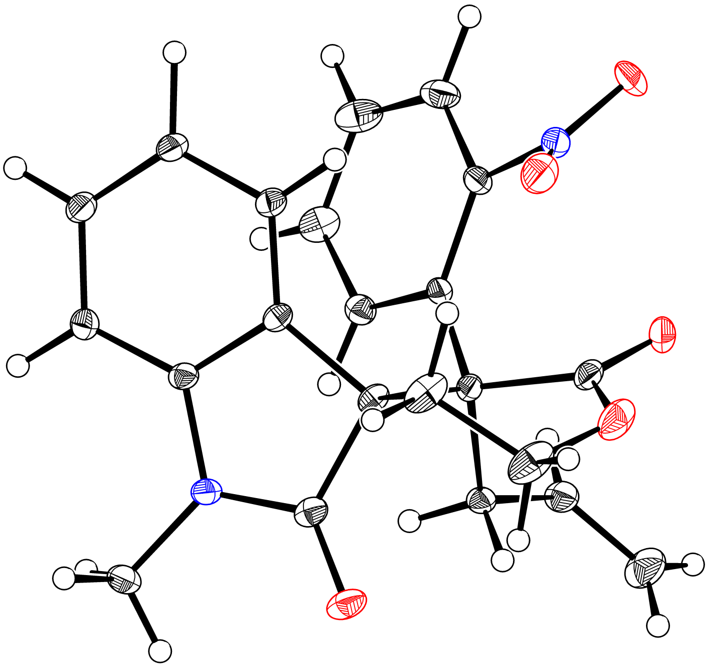

Table A2.4.1. *Crystal Data and Structure Analysis Details for* ***51***

Empirical formula	C22 H20 N2 O5
Formula weight	392.40
Crystal shape	plate
Crystal color	colourless
Crystal size	0.08 x 0.39 x 0.40 mm

Data Collection

Preliminary photograph(s)	rotation
Type of diffractometer	Bruker APEX-II CCD
Wavelength	0.71073 Å MoK

Data collection temperature	100 K
Theta range for 9925 reflections used in lattice determination	2.59 to 33.53°
Unit cell dimensions	a = 7.5798(3) Å ⟨= 90° b = 30.0522(12) Å ®= 103.6098(19)° c = 8.3663(3) Å © = 90°
Volume	1852.24(12) Å^3
Z	4
Crystal system	monoclinic
Space group	P 1 21/c 1 (# 14)
Density (calculated)	1.407 g/cm^3
F(000)	824
Theta range for data collection	2.6 to 36.7°
Completeness to theta = 25.000°	99.9%
Index ranges	-12 ″ h ″ 12, -48 ″ k ″ 48, -13 ″ l ″ 13
Data collection scan type	and scans
Reflections collected	90271
Independent reflections	8678 [R_{int}= 0.0550]
Reflections > 2 ʃ(I)	6686
Average ʃ(I)/(net I)	0.0317
Absorption coefficient	0.10 mm^{-1}
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.9172

Structure Solution and Refinement

Primary solution method	?
Secondary solution method	?
Hydrogen placement	difmap
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8678 / 0 / 322
Treatment of hydrogen atoms	refxyz
Goodness-of-fit on F^2	1.63
Final R indices [I>2 ʃ(I), 6686 reflections]	R1 = 0.0491, wR2 = 0.1139
R indices (all data)	R1 = 0.0700, wR2 = 0.1189
Type of weighting scheme used	calc
Weighting scheme used	w=1/[^2^(Fo^2^)+(0.0400P)^2^] where
P=(Fo^2^+2Fc^2^)/3	
Max shift/error	0.001
Average shift/error	0.000
Extinction coefficient	n/a

Largest diff. peak and hole	0.63 and -0.32 e·Å^{-3}

Programs Used

Cell refinement	SAINT V8.32B (Bruker-AXS, 2007)
Data collection	APEX2 2013.6-2 (Bruker-AXS, 2007)
Data reduction	SAINT V8.32B (Bruker-AXS, 2007)
Structure solution	SHELXT (Sheldrick, 2012)
Structure refinement	SHELXL-2013/2 (Sheldrick, 2013)
Graphics	DIAMOND 3 (Crystal Impact, 1999)

References

Special Refinement Details

Table A2.4.2. *Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **51**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor*

	x	y	z	U_{eq}
O(1)	12316(1)	2035(1)	9127(1)	32(1)
O(2)	9477(1)	1887(1)	8963(1)	25(1)
O(3)	8678(1)	936(1)	10051(1)	25(1)
O(4)	11278(1)	1051(1)	9408(1)	24(1)
O(5)	5030(1)	428(1)	6376(1)	19(1)
N(1)	10836(1)	1886(1)	8401(1)	21(1)
N(2)	4779(1)	893(1)	4161(1)	15(1)
C(1)	8719(1)	1022(1)	7103(1)	12(1)
C(2)	9732(1)	1325(1)	6146(1)	12(1)
C(3)	9631(1)	1230(1)	4488(1)	14(1)
C(4)	10336(1)	1512(1)	3480(1)	19(1)
C(5)	11238(1)	1898(1)	4107(1)	22(1)
C(6)	11443(1)	1996(1)	5750(1)	20(1)
C(7)	10675(1)	1717(1)	6726(1)	15(1)
C(8)	8953(1)	519(1)	6658(1)	12(1)
C(9)	10876(1)	364(1)	6877(1)	17(1)
C(10)	11560(1)	15(1)	7771(2)	26(1)
C(11)	9646(1)	1021(1)	8938(1)	17(1)
C(12)	6715(2)	923(1)	9579(1)	25(1)
C(13)	5976(2)	1265(1)	8268(1)	21(1)
C(14)	6589(1)	1160(1)	6682(1)	13(1)
C(15)	6136(1)	1526(1)	5402(1)	12(1)
C(16)	6548(1)	1975(1)	5472(1)	14(1)
C(17)	6062(1)	2230(1)	4037(1)	15(1)
C(18)	5154(1)	2036(1)	2563(1)	15(1)
C(19)	4645(1)	1588(1)	2488(1)	14(1)
C(20)	5154(1)	1343(1)	3922(1)	13(1)
C(21)	5401(1)	776(1)	5771(1)	14(1)
C(22)	3576(1)	613(1)	2963(1)	21(1)

Table A2.4.3. *Bond lengths [Å] and angles [°] for* ***51***

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O(1)-N(1)	1.2271(10)
O(2)-N(1)	1.2294(12)
O(3)-C(11)	1.3390(12)
O(3)-C(12)	1.4477(14)
O(4)-C(11)	1.2094(12)
O(5)-C(21)	1.2218(10)
N(1)-C(7)	1.4689(12)
N(2)-C(20)	1.4069(10)
N(2)-C(21)	1.3641(11)
N(2)-C(22)	1.4538(11)
C(1)-C(2)	1.5329(12)
C(1)-C(8)	1.5766(11)
C(1)-C(11)	1.5307(11)
C(1)-C(14)	1.6236(11)
C(2)-C(3)	1.4007(12)
C(2)-C(7)	1.4025(11)
C(3)-H(3)	0.978(12)
C(3)-C(4)	1.3876(13)
C(4)-H(4)	0.997(12)
C(4)-C(5)	1.3847(14)
C(5)-H(5)	0.971(13)
C(5)-C(6)	1.3777(15)
C(6)-H(6)	0.998(13)
C(6)-C(7)	1.3900(13)
C(8)-H(8A)	0.987(11)
C(8)-H(8B)	0.950(11)
C(8)-C(9)	1.4994(12)
C(9)-H(9)	0.991(12)
C(9)-C(10)	1.3224(13)
C(10)-H(10A)	0.966(14)
C(10)-H(10B)	0.964(14)
C(12)-H(12A)	0.995(13)
C(12)-H(12B)	0.963(14)
C(12)-C(13)	1.5109(14)
C(13)-H(13A)	1.014(13)
C(13)-H(13B)	1.006(13)
C(13)-C(14)	1.5372(12)
C(14)-C(15)	1.5167(11)
C(14)-C(21)	1.5506(12)
C(15)-C(16)	1.3832(11)
C(15)-C(20)	1.3979(11)
C(16)-H(16)	0.966(12)
C(16)-C(17)	1.3987(12)
C(17)-H(17)	1.136(12)
C(17)-C(18)	1.3904(12)
C(18)-H(18)	0.950(12)
C(18)-C(19)	1.3995(12)
C(19)-H(19)	0.987(12)
C(19)-C(20)	1.3821(11)
C(22)-H(22A)	0.984(13)
C(22)-H(22B)	0.962(13)
C(22)-H(22C)	0.999(13)
C(11)-O(3)-C(12)	120.79(7)
O(1)-N(1)-O(2)	124.15(9)

O(1)-N(1)-C(7)	117.31(9)
O(2)-N(1)-C(7)	118.48(7)
C(20)-N(2)-C(22)	124.99(7)
C(21)-N(2)-C(20)	110.73(7)
C(21)-N(2)-C(22)	123.14(7)
C(2)-C(1)-C(8)	110.41(7)
C(2)-C(1)-C(14)	109.21(6)
C(8)-C(1)-C(14)	110.84(6)
C(11)-C(1)-C(2)	110.91(7)
C(11)-C(1)-C(8)	100.61(6)
C(11)-C(1)-C(14)	114.61(7)
C(3)-C(2)-C(1)	118.59(7)
C(3)-C(2)-C(7)	114.70(8)
C(7)-C(2)-C(1)	126.55(7)
C(2)-C(3)-H(3)	120.3(7)
C(4)-C(3)-C(2)	122.62(8)
C(4)-C(3)-H(3)	117.0(7)
C(3)-C(4)-H(4)	121.5(7)
C(5)-C(4)-C(3)	120.40(9)
C(5)-C(4)-H(4)	118.1(7)
C(4)-C(5)-H(5)	121.2(8)
C(6)-C(5)-C(4)	119.15(9)
C(6)-C(5)-H(5)	119.6(8)
C(5)-C(6)-H(6)	119.9(7)
C(5)-C(6)-C(7)	119.50(8)
C(7)-C(6)-H(6)	120.5(7)
C(2)-C(7)-N(1)	122.81(8)
C(6)-C(7)-N(1)	113.54(8)
C(6)-C(7)-C(2)	123.53(8)
C(1)-C(8)-H(8A)	108.4(6)
C(1)-C(8)-H(8B)	108.6(7)
H(8A)-C(8)-H(8B)	105.1(10)
C(9)-C(8)-C(1)	115.38(7)
C(9)-C(8)-H(8A)	110.1(6)
C(9)-C(8)-H(8B)	108.7(7)
C(8)-C(9)-H(9)	116.9(7)
C(10)-C(9)-C(8)	123.80(9)
C(10)-C(9)-H(9)	119.2(7)
C(9)-C(10)-H(10A)	119.8(8)
C(9)-C(10)-H(10B)	120.9(8)
H(10A)-C(10)-H(10B)	119.2(12)
O(3)-C(11)-C(1)	120.03(8)
O(4)-C(11)-O(3)	118.26(8)
O(4)-C(11)-C(1)	121.28(8)
O(3)-C(12)-H(12A)	102.7(8)
O(3)-C(12)-H(12B)	108.1(8)
O(3)-C(12)-C(13)	111.22(8)
H(12A)-C(12)-H(12B)	108.5(11)
C(13)-C(12)-H(12A)	112.8(8)
C(13)-C(12)-H(12B)	112.9(8)
C(12)-C(13)-H(13A)	107.2(7)
C(12)-C(13)-H(13B)	108.4(7)
C(12)-C(13)-C(14)	110.64(8)
H(13A)-C(13)-H(13B)	107.4(10)
C(14)-C(13)-H(13A)	111.1(7)
C(14)-C(13)-H(13B)	111.9(7)
C(13)-C(14)-C(1)	110.64(7)
C(13)-C(14)-C(21)	108.51(7)

C(15)-C(14)-C(1)	112.77(7)
C(15)-C(14)-C(13)	113.42(7)
C(15)-C(14)-C(21)	100.57(6)
C(21)-C(14)-C(1)	110.42(6)
C(16)-C(15)-C(14)	131.73(8)
C(16)-C(15)-C(20)	119.23(7)
C(20)-C(15)-C(14)	109.02(7)
C(15)-C(16)-H(16)	121.0(7)
C(15)-C(16)-C(17)	119.14(8)
C(17)-C(16)-H(16)	119.8(7)
C(16)-C(17)-H(17)	115.2(6)
C(18)-C(17)-C(16)	120.51(8)
C(18)-C(17)-H(17)	124.2(6)
C(17)-C(18)-H(18)	119.0(7)
C(17)-C(18)-C(19)	121.07(8)
C(19)-C(18)-H(18)	119.9(7)
C(18)-C(19)-H(19)	120.2(7)
C(20)-C(19)-C(18)	117.12(8)
C(20)-C(19)-H(19)	122.7(7)
C(15)-C(20)-N(2)	109.59(7)
C(19)-C(20)-N(2)	127.61(8)
C(19)-C(20)-C(15)	122.79(7)
O(5)-C(21)-N(2)	124.73(8)
O(5)-C(21)-C(14)	126.63(8)
N(2)-C(21)-C(14)	108.62(7)
N(2)-C(22)-H(22A)	112.4(8)
N(2)-C(22)-H(22B)	110.5(8)
N(2)-C(22)-H(22C)	111.4(8)
H(22A)-C(22)-H(22B)	112.9(11)
H(22A)-C(22)-H(22C)	106.0(11)
H(22B)-C(22)-H(22C)	103.2(11)

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Symmetry transformations used to generate equivalent atoms:

Table A2.4.4. *Anisotropic displacement parameters ($Å^2$x 10^4) for* ***51****. The anisotropic displacement factor exponent takes the form: -2ð^2 [h^2 $a^{*2}$$U^{11}$ + ... + 2 h k a* b* U^{12}]*

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	343(4)	179(3)	323(4)	-43(3)	-181(3)	-49(3)
O(2)	381(4)	184(3)	153(3)	-24(2)	26(3)	42(3)
O(3)	415(4)	203(3)	116(3)	34(2)	60(3)	40(3)
O(4)	282(4)	167(3)	184(3)	7(2)	-95(3)	12(3)
O(5)	154(3)	142(3)	293(4)	70(2)	79(3)	1(2)
N(1)	276(4)	106(3)	178(3)	-16(3)	-71(3)	6(3)
N(2)	131(3)	102(3)	205(3)	17(2)	0(3)	-11(2)
C(1)	136(3)	101(3)	105(3)	0(2)	10(3)	10(3)
C(2)	105(3)	102(3)	128(3)	-4(3)	-1(3)	1(2)
C(3)	137(3)	137(3)	146(3)	-12(3)	30(3)	-2(3)
C(4)	213(4)	182(4)	211(4)	8(3)	106(3)	10(3)
C(5)	216(4)	171(4)	321(5)	22(4)	156(4)	-11(3)
C(6)	144(4)	134(4)	310(5)	-10(3)	39(3)	-25(3)
C(7)	137(3)	114(3)	169(4)	-19(3)	-18(3)	-1(3)
C(8)	121(3)	95(3)	153(3)	-9(3)	21(3)	7(3)

C(9)	136(3)	132(3)	222(4)	-2(3)	30(3)	14(3)
C(10)	192(4)	206(4)	367(6)	75(4)	47(4)	61(3)
C(11)	280(4)	98(3)	112(3)	0(3)	-5(3)	22(3)
C(12)	397(6)	217(5)	195(4)	55(4)	171(4)	69(4)
C(13)	310(5)	177(4)	201(4)	38(3)	147(4)	78(4)
C(14)	148(3)	108(3)	143(3)	18(3)	51(3)	31(3)
C(15)	126(3)	103(3)	136(3)	11(3)	38(3)	24(3)
C(16)	154(3)	108(3)	152(4)	1(3)	29(3)	18(3)
C(17)	158(4)	111(3)	176(4)	23(3)	28(3)	4(3)
C(18)	148(4)	133(3)	168(4)	34(3)	28(3)	9(3)
C(19)	126(3)	138(3)	157(4)	5(3)	8(3)	12(3)
C(20)	103(3)	98(3)	176(4)	8(3)	25(3)	9(2)
C(21)	101(3)	123(3)	210(4)	27(3)	53(3)	23(3)
C(22)	166(4)	128(4)	281(5)	-6(3)	-38(3)	-19(3)

Table A2.4.5. *Hydrogen coordinates (x 10^3) and isotropic displacement parameters (Å^{2}x 10^3) for* ***51***

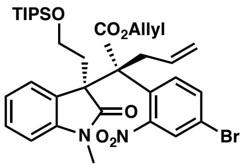
	x	y	z	U_{iso}
H(3)	900(2)	96(1)	398(1)	17
H(4)	1022(2)	144(1)	229(2)	23
H(5)	1177(2)	209(1)	342(2)	26
H(6)	1209(2)	227(1)	622(2)	24
H(8A)	832(2)	33(1)	732(1)	15
H(8B)	833(2)	47(1)	555(1)	15
H(9)	1164(2)	53(1)	626(2)	20
H(10A)	1081(2)	-15(1)	835(2)	31
H(10B)	1279(2)	-8(1)	784(2)	31
H(12A)	637(2)	98(1)	1064(2)	30
H(12B)	635(2)	62(1)	924(2)	30
H(13A)	644(2)	157(1)	873(2)	26
H(13B)	461(2)	127(1)	808(2)	26
H(16)	722(2)	211(1)	648(1)	17
H(17)	651(2)	259(1)	417(1)	18
H(18)	484(2)	222(1)	160(2)	18
H(19)	394(2)	146(1)	145(1)	17
H(22A)	232(2)	73(1)	268(2)	31
H(22B)	365(2)	31(1)	333(2)	31
H(22C)	398(2)	60(1)	191(2)	31

Table A2.4.6. *Hydrogen bonds for* ***51*** *[Å and °].*

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(12)-H(12B)...O(5)	0.963(14)	2.442(13)	3.0678(14)	122.4(10)
C(13)-H(13A)...O(2)	1.014(13)	2.460(13)	3.1858(14)	128.0(9)
C(19)-H(19)...O(4)#1	0.987(12)	2.622(12)	3.5589(11)	158.7(9)
C(22)-H(22B)...O(5)#2	0.962(13)	2.418(13)	3.3085(12)	153.8(10)

Symmetry transformations used to generate equivalent atoms:
#1 x-1,y,z-1   #2 -x+1,-y,-z+1

A2.5. X-Ray Crystal Structure Analysis of 52



52

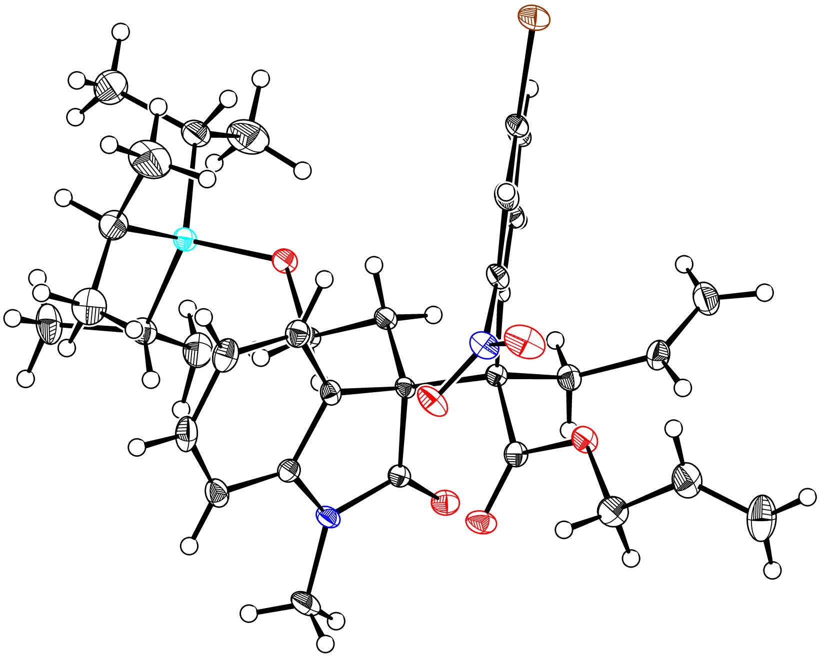


Figure A2.5.1. *X-ray Crystal Structure of **52***

Table A2.5.1. *Crystal Data and Structure Analysis Details for **52***

Empirical formula	C34 H45 Br N2 O6 Si
Formula weight	685.72
Crystal shape	block
Crystal color	colourless
Crystal size	0.11 x 0.16 x 0.24 mm

Data Collection

Preliminary photograph(s)	rotation
Type of diffractometer	Bruker APEX-II CCD
Wavelength	0.71073 Å MoK
Data collection temperature	100 K

Theta range for 9950 reflections used in lattice determination	2.54 to 27.86°
Unit cell dimensions	a = 8.0482(4) Å ⟨= 99.073(2)° b = 14.1277(8) Å ®= 94.101(3)° c = 15.3665(8) Å © = 91.448(2)°
Volume	1719.75(16) Å^{3}
Z	2
Crystal system	triclinic
Space group	P -1 (# 2)
Density (calculated)	1.324 g/cm^{3}
F(000)	720
Theta range for data collection	1.8 to 35.3°
Completeness to theta = 25.000°	100.0%
Index ranges	-13 ″ h ″ 11, -20 ″ k ″ 21, -22 ″ l ″ 23
Data collection scan type	and scans
Reflections collected	70933
Independent reflections	11961 [R_{int}= 0.0565]
Reflections > 2 ⌠(I)	8549
Average ⌠(I)/(net I)	0.0555
Absorption coefficient	1.27 mm^{-1}
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.8989

Structure Solution and Refinement

Primary solution method	?
Secondary solution method	?
Hydrogen placement	difmap
Refinement method	Full-matrix least-squares on F^{2}
Data / restraints / parameters	11961 / 0 / 577
Treatment of hydrogen atoms	refall
Goodness-of-fit on F^{2}	1.12
Final R indices [I>2 ⌠(I), 8549 reflections]	R1 = 0.0402, wR2 = 0.0805
R indices (all data)	R1 = 0.0754, wR2 = 0.0892
Type of weighting scheme used	calc
Weighting scheme used	w=1/[^2^(Fo^2^)+(0.0400P)^2^] where
P=(Fo^2^+2Fc^2^)/3	
Max shift/error	0.003
Average shift/error	0.000
Extinction coefficient	n/a
Largest diff. peak and hole	0.55 and -0.51 e·Å^{-3}

Programs Used

Cell refinement	SAINT V8.32B (Bruker-AXS, 2007)
Data collection	APEX2 2013.6-2 (Bruker-AXS, 2007)
Data reduction	SAINT V8.32B (Bruker-AXS, 2007)
Structure solution	SHELXT (Sheldrick, 2012)
Structure refinement	SHELXL-2013/2 (Sheldrick, 2013)
Graphics	DIAMOND 3 (Crystal Impact, 1999)

References

Refinement Details

Table A2.5.2. *Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **52**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor*

	x	y	z	U_{eq}
Br(1)	3260(1)	-6095(1)	-8561(1)	25(1)
Si(1)	380(1)	-12429(1)	-8560(1)	14(1)
O(1)	-2560(1)	-5767(1)	-7181(1)	28(1)
O(2)	-3551(1)	-7223(1)	-7270(1)	22(1)
O(3)	-3839(1)	-8167(1)	-5718(1)	20(1)
O(4)	-2148(1)	-6852(1)	-5561(1)	17(1)
O(5)	-2199(1)	-10064(1)	-5391(1)	17(1)
O(6)	666(1)	-11489(1)	-7758(1)	16(1)
N(1)	-2394(2)	-6634(1)	-7234(1)	18(1)
N(2)	-4168(1)	-10184(1)	-6562(1)	15(1)
C(1)	-1041(2)	-8300(1)	-6228(1)	12(1)
C(2)	-118(2)	-7745(1)	-6847(1)	12(1)
C(3)	-688(2)	-6993(1)	-7276(1)	14(1)
C(4)	290(2)	-6508(1)	-7788(1)	17(1)
C(5)	1901(2)	-6790(1)	-7907(1)	16(1)
C(6)	2528(2)	-7532(1)	-7516(1)	17(1)
C(7)	1541(2)	-7977(1)	-6986(1)	14(1)
C(8)	-2544(2)	-7788(1)	-5839(1)	14(1)
C(9)	-3446(2)	-6292(1)	-5130(1)	24(1)
C(10)	-2758(2)	-5286(1)	-4906(1)	26(1)
C(11)	-2702(3)	-4786(1)	-4109(1)	34(1)
C(12)	142(2)	-8376(1)	-5382(1)	16(1)
C(13)	1021(2)	-7471(1)	-4906(1)	19(1)
C(14)	2624(2)	-7382(1)	-4698(1)	26(1)
C(15)	-1646(2)	-9346(1)	-6719(1)	11(1)
C(16)	-2895(2)	-9359(1)	-7511(1)	12(1)
C(17)	-2761(2)	-9042(1)	-8310(1)	17(1)
C(18)	-4123(2)	-9176(1)	-8938(1)	21(1)
C(19)	-5578(2)	-9640(1)	-8775(1)	22(1)
C(20)	-5714(2)	-9997(1)	-7988(1)	19(1)
C(21)	-4352(2)	-9853(1)	-7369(1)	14(1)
C(22)	-2666(2)	-9882(1)	-6111(1)	13(1)
C(23)	-5490(2)	-10648(1)	-6173(1)	26(1)
C(24)	-176(2)	-9986(1)	-7005(1)	13(1)
C(25)	-693(2)	-11038(1)	-7320(1)	16(1)

C(26)	-826(2)	-13397(1)	-8136(1)	18(1)
C(27)	28(2)	-13713(1)	-7308(1)	26(1)
C(28)	-1340(3)	-14267(1)	-8838(1)	27(1)
C(29)	2572(2)	-12703(1)	-8851(1)	24(1)
C(30)	3670(2)	-13040(2)	-8115(2)	36(1)
C(31)	2672(3)	-13392(2)	-9724(2)	47(1)
C(32)	-836(2)	-12104(1)	-9559(1)	21(1)
C(33)	-47(3)	-11230(2)	-9867(2)	40(1)
C(34)	-2704(2)	-11962(1)	-9483(1)	28(1)

Table A2.5.3. *Bond lengths [Å] and angles [°] for* ***52***

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Br(1)-C(5)	1.8927(14)
Si(1)-O(6)	1.6623(10)
Si(1)-C(26)	1.8817(15)
Si(1)-C(29)	1.8856(16)
Si(1)-C(32)	1.8850(17)
O(1)-N(1)	1.2263(16)
O(2)-N(1)	1.2245(16)
O(3)-C(8)	1.1986(17)
O(4)-C(8)	1.3462(16)
O(4)-C(9)	1.4600(18)
O(5)-C(22)	1.2110(17)
O(6)-C(25)	1.4361(16)
N(1)-C(3)	1.4782(18)
N(2)-C(21)	1.3931(19)
N(2)-C(22)	1.3727(18)
N(2)-C(23)	1.4476(19)
C(1)-C(2)	1.5425(19)
C(1)-C(8)	1.5348(19)
C(1)-C(12)	1.576(2)
C(1)-C(15)	1.5971(18)
C(2)-C(3)	1.4053(19)
C(2)-C(7)	1.4058(19)
C(3)-C(4)	1.392(2)
C(4)-H(4)	0.929(17)
C(4)-C(5)	1.382(2)
C(5)-C(6)	1.377(2)
C(6)-H(6)	0.921(19)
C(6)-C(7)	1.386(2)
C(7)-H(7)	0.966(18)
C(9)-H(9A)	0.982(19)
C(9)-H(9B)	0.986(19)
C(9)-C(10)	1.491(2)
C(10)-H(10)	0.99(2)
C(10)-C(11)	1.311(3)
C(11)-H(11A)	0.97(2)
C(11)-H(11B)	0.95(2)
C(12)-H(12A)	0.889(18)
C(12)-H(12B)	0.979(17)
C(12)-C(13)	1.502(2)
C(13)-H(13)	0.945(19)
C(13)-C(14)	1.305(2)
C(14)-H(14A)	0.94(2)
C(14)-H(14B)	0.951(19)

C(15)-C(16)	1.5199(19)
C(15)-C(22)	1.5552(19)
C(15)-C(24)	1.5539(19)
C(16)-C(17)	1.382(2)
C(16)-C(21)	1.3977(19)
C(17)-H(17)	0.954(18)
C(17)-C(18)	1.397(2)
C(18)-H(18)	0.945(19)
C(18)-C(19)	1.385(2)
C(19)-H(19)	0.93(2)
C(19)-C(20)	1.391(2)
C(20)-H(20)	0.946(18)
C(20)-C(21)	1.388(2)
C(23)-H(23A)	1.01(2)
C(23)-H(23B)	0.93(2)
C(23)-H(23C)	0.91(2)
C(24)-H(24A)	0.964(17)
C(24)-H(24B)	0.946(17)
C(24)-C(25)	1.5258(19)
C(25)-H(25A)	0.962(17)
C(25)-H(25B)	0.974(17)
C(26)-H(26)	0.946(17)
C(26)-C(27)	1.536(2)
C(26)-C(28)	1.529(2)
C(27)-H(27A)	1.003(19)
C(27)-H(27B)	1.03(2)
C(27)-H(27C)	0.94(2)
C(28)-H(28A)	0.97(2)
C(28)-H(28B)	1.02(2)
C(28)-H(28C)	0.99(2)
C(29)-H(29)	0.972(19)
C(29)-C(30)	1.527(3)
C(29)-C(31)	1.537(3)
C(30)-H(30A)	1.01(2)
C(30)-H(30B)	0.98(3)
C(30)-H(30C)	1.00(2)
C(31)-H(31A)	0.88(3)
C(31)-H(31B)	0.96(2)
C(31)-H(31C)	0.99(3)
C(32)-H(32)	0.953(19)
C(32)-C(33)	1.529(2)
C(32)-C(34)	1.533(2)
C(33)-H(33A)	1.03(3)
C(33)-H(33B)	0.96(2)
C(33)-H(33C)	0.94(2)
C(34)-H(34A)	0.94(2)
C(34)-H(34B)	1.01(2)
C(34)-H(34C)	0.95(2)

O(6)-Si(1)-C(26)	108.45(6)
O(6)-Si(1)-C(29)	102.78(6)
O(6)-Si(1)-C(32)	111.24(6)
C(26)-Si(1)-C(29)	116.69(7)
C(26)-Si(1)-C(32)	108.76(7)
C(32)-Si(1)-C(29)	108.83(8)
C(8)-O(4)-C(9)	115.62(11)
C(25)-O(6)-Si(1)	122.38(9)
O(1)-N(1)-C(3)	117.69(12)

O(2)-N(1)-O(1)	124.37(12)
O(2)-N(1)-C(3)	117.93(12)
C(21)-N(2)-C(23)	124.40(13)
C(22)-N(2)-C(21)	111.59(11)
C(22)-N(2)-C(23)	123.24(13)
C(2)-C(1)-C(12)	109.54(11)
C(2)-C(1)-C(15)	111.12(11)
C(8)-C(1)-C(2)	114.19(11)
C(8)-C(1)-C(12)	102.89(11)
C(8)-C(1)-C(15)	108.71(11)
C(12)-C(1)-C(15)	110.07(11)
C(3)-C(2)-C(1)	128.63(12)
C(3)-C(2)-C(7)	113.94(12)
C(7)-C(2)-C(1)	117.37(12)
C(2)-C(3)-N(1)	123.50(12)
C(4)-C(3)-N(1)	112.78(12)
C(4)-C(3)-C(2)	123.72(13)
C(3)-C(4)-H(4)	119.1(10)
C(5)-C(4)-C(3)	118.92(14)
C(5)-C(4)-H(4)	121.9(10)
C(4)-C(5)-Br(1)	118.87(11)
C(6)-C(5)-Br(1)	120.73(11)
C(6)-C(5)-C(4)	120.31(13)
C(5)-C(6)-H(6)	121.7(12)
C(5)-C(6)-C(7)	119.26(13)
C(7)-C(6)-H(6)	118.9(12)
C(2)-C(7)-H(7)	118.4(10)
C(6)-C(7)-C(2)	123.79(13)
C(6)-C(7)-H(7)	117.8(10)
O(3)-C(8)-O(4)	123.79(13)
O(3)-C(8)-C(1)	125.80(12)
O(4)-C(8)-C(1)	110.08(11)
O(4)-C(9)-H(9A)	109.4(10)
O(4)-C(9)-H(9B)	107.4(10)
O(4)-C(9)-C(10)	106.28(13)
H(9A)-C(9)-H(9B)	110.0(15)
C(10)-C(9)-H(9A)	109.9(11)
C(10)-C(9)-H(9B)	113.6(11)
C(9)-C(10)-H(10)	113.0(12)
C(11)-C(10)-C(9)	123.47(19)
C(11)-C(10)-H(10)	123.5(12)
C(10)-C(11)-H(11A)	121.9(13)
C(10)-C(11)-H(11B)	121.7(14)
H(11A)-C(11)-H(11B)	116.4(19)
C(1)-C(12)-H(12A)	106.2(12)
C(1)-C(12)-H(12B)	111.1(10)
H(12A)-C(12)-H(12B)	105.2(15)
C(13)-C(12)-C(1)	117.48(12)
C(13)-C(12)-H(12A)	109.4(12)
C(13)-C(12)-H(12B)	106.9(10)
C(12)-C(13)-H(13)	117.6(12)
C(14)-C(13)-C(12)	124.11(15)
C(14)-C(13)-H(13)	118.0(12)
C(13)-C(14)-H(14A)	120.7(13)
C(13)-C(14)-H(14B)	120.4(11)
H(14A)-C(14)-H(14B)	118.9(17)
C(16)-C(15)-C(1)	114.67(11)
C(16)-C(15)-C(22)	101.34(11)

C(16)-C(15)-C(24)	108.87(11)
C(22)-C(15)-C(1)	110.99(11)
C(24)-C(15)-C(1)	112.86(11)
C(24)-C(15)-C(22)	107.29(11)
C(17)-C(16)-C(15)	131.56(13)
C(17)-C(16)-C(21)	119.36(13)
C(21)-C(16)-C(15)	108.89(12)
C(16)-C(17)-H(17)	119.5(11)
C(16)-C(17)-C(18)	119.06(15)
C(18)-C(17)-H(17)	121.4(11)
C(17)-C(18)-H(18)	120.6(12)
C(19)-C(18)-C(17)	120.73(15)
C(19)-C(18)-H(18)	118.7(12)
C(18)-C(19)-H(19)	120.8(12)
C(18)-C(19)-C(20)	121.03(15)
C(20)-C(19)-H(19)	118.1(12)
C(19)-C(20)-H(20)	121.0(11)
C(21)-C(20)-C(19)	117.51(14)
C(21)-C(20)-H(20)	121.4(11)
N(2)-C(21)-C(16)	110.02(12)
C(20)-C(21)-N(2)	127.73(13)
C(20)-C(21)-C(16)	122.21(14)
O(5)-C(22)-N(2)	124.97(13)
O(5)-C(22)-C(15)	126.91(12)
N(2)-C(22)-C(15)	107.94(12)
N(2)-C(23)-H(23A)	109.3(13)
N(2)-C(23)-H(23B)	110.9(14)
N(2)-C(23)-H(23C)	115.0(15)
H(23A)-C(23)-H(23B)	103.8(18)
H(23A)-C(23)-H(23C)	104.9(19)
H(23B)-C(23)-H(23C)	112(2)
C(15)-C(24)-H(24A)	108.7(10)
C(15)-C(24)-H(24B)	107.9(10)
H(24A)-C(24)-H(24B)	112.9(14)
C(25)-C(24)-C(15)	113.74(11)
C(25)-C(24)-H(24A)	106.1(10)
C(25)-C(24)-H(24B)	107.7(10)
O(6)-C(25)-C(24)	107.63(11)
O(6)-C(25)-H(25A)	109.7(10)
O(6)-C(25)-H(25B)	111.7(10)
C(24)-C(25)-H(25A)	110.4(10)
C(24)-C(25)-H(25B)	109.9(10)
H(25A)-C(25)-H(25B)	107.5(14)
Si(1)-C(26)-H(26)	104.7(11)
C(27)-C(26)-Si(1)	113.72(11)
C(27)-C(26)-H(26)	104.7(11)
C(28)-C(26)-Si(1)	114.04(11)
C(28)-C(26)-H(26)	108.3(11)
C(28)-C(26)-C(27)	110.66(13)
C(26)-C(27)-H(27A)	113.3(11)
C(26)-C(27)-H(27B)	108.8(11)
C(26)-C(27)-H(27C)	111.1(12)
H(27A)-C(27)-H(27B)	106.3(15)
H(27A)-C(27)-H(27C)	108.5(16)
H(27B)-C(27)-H(27C)	108.7(15)
C(26)-C(28)-H(28A)	112.5(12)
C(26)-C(28)-H(28B)	112.6(12)
C(26)-C(28)-H(28C)	112.8(12)

H(28A)-C(28)-H(28B)	100.8(16)
H(28A)-C(28)-H(28C)	110.9(16)
H(28B)-C(28)-H(28C)	106.5(16)
Si(1)-C(29)-H(29)	103.4(10)
C(30)-C(29)-Si(1)	114.40(13)
C(30)-C(29)-H(29)	107.0(11)
C(30)-C(29)-C(31)	110.15(17)
C(31)-C(29)-Si(1)	114.10(13)
C(31)-C(29)-H(29)	107.0(11)
C(29)-C(30)-H(30A)	114.8(13)
C(29)-C(30)-H(30B)	110.0(15)
C(29)-C(30)-H(30C)	111.3(13)
H(30A)-C(30)-H(30B)	109.4(19)
H(30A)-C(30)-H(30C)	106.0(18)
H(30B)-C(30)-H(30C)	104.8(19)
C(29)-C(31)-H(31A)	112.5(17)
C(29)-C(31)-H(31B)	110.3(14)
C(29)-C(31)-H(31C)	112.4(14)
H(31A)-C(31)-H(31B)	111(2)
H(31A)-C(31)-H(31C)	101(2)
H(31B)-C(31)-H(31C)	109(2)
Si(1)-C(32)-H(32)	105.3(11)
C(33)-C(32)-Si(1)	111.67(13)
C(33)-C(32)-H(32)	103.1(11)
C(33)-C(32)-C(34)	109.47(16)
C(34)-C(32)-Si(1)	116.52(12)
C(34)-C(32)-H(32)	109.8(11)
C(32)-C(33)-H(33A)	111.4(16)
C(32)-C(33)-H(33B)	111.6(14)
C(32)-C(33)-H(33C)	110.4(14)
H(33A)-C(33)-H(33B)	112(2)
H(33A)-C(33)-H(33C)	108(2)
H(33B)-C(33)-H(33C)	102.1(19)
C(32)-C(34)-H(34A)	111.1(13)
C(32)-C(34)-H(34B)	109.4(12)
C(32)-C(34)-H(34C)	114.4(13)
H(34A)-C(34)-H(34B)	105.6(18)
H(34A)-C(34)-H(34C)	110.8(18)
H(34B)-C(34)-H(34C)	104.9(17)

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Symmetry transformations used to generate equivalent atoms:

Table A2.5.4. *Anisotropic displacement parameters (Å^{2}x 10^4) for* ***52***. *The anisotropic displacement factor exponent takes the form: $-2\pi^2$ [h^2 $a^{*2}U^{11}$ + ... + 2 h k a* b* U^{12}]*

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	260(1)	269(1)	233(1)	77(1)	68(1)	-97(1)
Si(1)	147(2)	92(2)	183(2)	-2(2)	37(2)	-4(1)
O(1)	246(6)	146(5)	478(8)	137(5)	54(5)	60(4)
O(2)	126(5)	203(6)	324(6)	62(5)	-30(4)	-23(4)
O(3)	173(5)	134(5)	296(6)	8(4)	99(4)	3(4)
O(4)	150(5)	92(5)	260(6)	-20(4)	38(4)	19(4)
O(5)	189(5)	162(5)	179(5)	61(4)	30(4)	-3(4)
O(6)	137(5)	103(5)	237(6)	-30(4)	52(4)	19(4)

N(1)	146(6)	161(6)	228(7)	73(5)	-6(5)	15(5)
N(2)	124(5)	122(6)	189(6)	12(5)	34(5)	-27(4)
C(1)	119(6)	84(6)	141(6)	13(5)	17(5)	11(5)
C(2)	118(6)	90(6)	135(6)	0(5)	-8(5)	-26(5)
C(3)	115(6)	109(6)	184(7)	17(5)	-6(5)	-10(5)
C(4)	193(7)	130(7)	176(7)	44(6)	-14(6)	-27(5)
C(5)	178(7)	149(7)	156(7)	17(5)	29(6)	-69(5)
C(6)	121(7)	152(7)	211(7)	-11(6)	18(6)	-26(5)
C(7)	131(6)	105(6)	175(7)	7(5)	-5(5)	-7(5)
C(8)	163(7)	100(6)	164(7)	14(5)	17(5)	8(5)
C(9)	204(8)	150(7)	354(10)	-50(7)	71(7)	54(6)
C(10)	249(8)	145(7)	351(10)	-36(7)	14(7)	48(6)
C(11)	428(11)	201(9)	350(11)	-42(8)	-88(9)	60(8)
C(12)	171(7)	147(7)	154(7)	38(6)	-7(6)	-14(6)
C(13)	211(7)	156(7)	173(7)	-21(6)	1(6)	12(6)
C(14)	212(8)	230(8)	300(9)	-44(7)	-8(7)	-31(7)
C(15)	112(6)	76(6)	135(6)	10(5)	14(5)	-10(5)
C(16)	131(6)	83(6)	153(7)	-2(5)	-1(5)	13(5)
C(17)	193(7)	142(7)	169(7)	15(5)	8(6)	3(6)
C(18)	263(8)	207(8)	163(7)	16(6)	-30(6)	36(6)
C(19)	199(8)	222(8)	209(8)	-60(6)	-67(6)	44(6)
C(20)	139(7)	160(7)	251(8)	-51(6)	6(6)	6(6)
C(21)	139(6)	106(6)	170(7)	-22(5)	39(5)	17(5)
C(22)	133(6)	65(6)	174(7)	-8(5)	40(5)	7(5)
C(23)	201(8)	344(10)	239(9)	43(8)	41(7)	-137(7)
C(24)	112(6)	104(6)	175(7)	0(5)	22(5)	6(5)
C(25)	140(7)	104(6)	223(8)	-4(6)	68(6)	17(5)
C(26)	195(7)	115(7)	216(8)	23(6)	28(6)	-9(6)
C(27)	359(10)	214(8)	209(8)	59(7)	-3(7)	-47(7)
C(28)	409(10)	136(7)	254(9)	45(6)	-68(8)	-75(7)
C(29)	182(7)	175(8)	326(9)	-49(7)	84(7)	-9(6)
C(30)	214(9)	371(11)	519(13)	75(10)	60(8)	67(8)
C(31)	297(11)	476(14)	534(15)	-272(11)	171(10)	-23(10)
C(32)	273(8)	168(7)	207(8)	46(6)	35(6)	-14(6)
C(33)	459(13)	424(12)	378(12)	245(10)	12(10)	-117(10)
C(34)	300(9)	259(9)	283(9)	88(8)	-20(7)	56(7)

Table A2.5.5. *Hydrogen coordinates (x 10^3) and isotropic displacement parameters (Å^{2}x 10^3) for* ***52***

	x	y	z	U_{iso}
H(4)	-15(2)	-600(1)	-803(1)	15(4)
H(6)	362(2)	-770(1)	-756(1)	31(5)
H(7)	203(2)	-847(1)	-669(1)	22(4)
H(9A)	-369(2)	-654(1)	-459(1)	24(5)
H(9B)	-445(2)	-636(1)	-555(1)	24(5)
H(10)	-237(2)	-503(1)	-542(1)	35(5)
H(11A)	-313(3)	-504(2)	-362(2)	41(6)
H(11B)	-227(3)	-414(2)	-399(2)	51(7)
H(12A)	-48(2)	-862(1)	-501(1)	22(5)
H(12B)	100(2)	-884(1)	-552(1)	16(4)
H(13)	36(2)	-696(1)	-469(1)	34(5)
H(14A)	333(2)	-788(2)	-490(1)	37(6)
H(14B)	309(2)	-682(1)	-432(1)	28(5)

H(17)	-174(2)	-874(1)	-842(1)	20(4)
H(18)	-408(2)	-893(1)	-948(1)	28(5)
H(19)	-647(2)	-976(1)	-920(1)	32(5)
H(20)	-670(2)	-1033(1)	-788(1)	18(4)
H(23A)	-633(3)	-1016(2)	-596(2)	50(6)
H(23B)	-509(3)	-1086(2)	-566(2)	45(6)
H(23C)	-609(3)	-1111(2)	-655(2)	53(7)
H(24A)	29(2)	-976(1)	-750(1)	17(4)
H(24B)	60(2)	-996(1)	-651(1)	12(4)
H(25A)	-93(2)	-1135(1)	-682(1)	16(4)
H(25B)	-171(2)	-1108(1)	-771(1)	17(4)
H(26)	-180(2)	-1310(1)	-794(1)	21(4)
H(27A)	98(2)	-1415(1)	-744(1)	29(5)
H(27B)	-83(2)	-1410(1)	-702(1)	36(5)
H(27C)	42(2)	-1318(1)	-689(1)	28(5)
H(28A)	-199(2)	-1409(1)	-934(1)	33(5)
H(28B)	-216(3)	-1472(2)	-863(1)	39(6)
H(28C)	-38(3)	-1465(2)	-903(1)	37(6)
H(29)	304(2)	-1208(1)	-893(1)	24(5)
H(30A)	359(3)	-1266(2)	-751(2)	47(6)
H(30B)	483(3)	-1304(2)	-826(2)	65(8)
H(30C)	338(3)	-1372(2)	-806(2)	48(6)
H(31A)	218(3)	-1395(2)	-972(2)	57(8)
H(31B)	381(3)	-1347(2)	-986(2)	48(6)
H(31C)	203(3)	-1317(2)	-1023(2)	59(8)
H(32)	-67(2)	-1261(1)	-1003(1)	27(5)
H(33A)	-6(3)	-1063(2)	-940(2)	81(9)
H(33B)	-54(3)	-1113(2)	-1043(2)	48(6)
H(33C)	106(3)	-1134(2)	-999(2)	50(7)
H(34A)	-322(3)	-1249(2)	-929(1)	44(6)
H(34B)	-327(3)	-1193(2)	-1009(2)	45(6)
H(34C)	-296(3)	-1138(2)	-913(1)	41(6)

Table A2.5.6. *Hydrogen bonds for* ***52*** *[Å and °]*

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(6)-H(6)...O(2)#1	0.921(19)	2.353(19)	3.1624(18)	146.6(16)
C(23)-H(23A)...O(5)#2	1.01(2)	2.45(2)	3.197(2)	129.9(17)

Symmetry transformations used to generate equivalent atoms:
#1 x+1,y,z #2 -x-1,-y-2,-z-1

A2.6. X-Ray Crystal Structure Analysis of 61

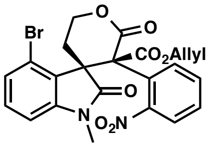

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Figure A2.6.1. *X-ray Crystal Structure of **61***

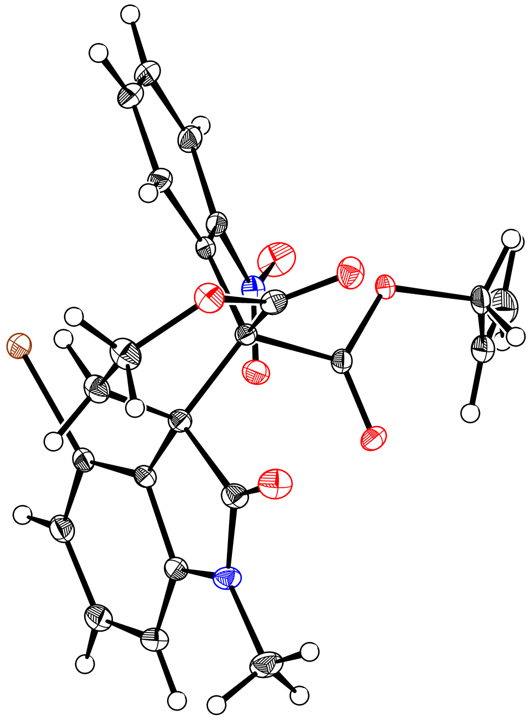

Table A2.6.1. *Crystal Data and Structure Analysis Details for **61***

Empirical formula	C23 H19 Br N2 O7.20
Formula weight	518.54
Crystallization solvent	???Solvent???
Crystal shape	plate
Crystal color	colourless
Crystal size	0.17 x 0.24 x 0.25 mm

Data Collection

Preliminary photograph(s)	rotation
Type of diffractometer	Bruker APEX-II CCD
Wavelength	0.71073 Å MoK

Data collection temperature	100 K	
Theta range for 9593 reflections used in lattice determination	2.62 to 36.54°	
Unit cell dimensions	a = 10.1321(5) Å	〈= 90°
	b = 14.3644(6) Å	®= 104.647(3)°
	c = 14.6551(6) Å	© = 90°
Volume	2063.61(16) Å^3	
Z	4	
Crystal system	monoclinic	
Space group	P 1 21/c 1 (# 14)	
Density (calculated)	1.669 g/cm^3	
F(000)	1054	
Theta range for data collection	2.0 to 42.9°	
Completeness to theta = 25.000°	100.0%	
Index ranges	-19 ″ h ″ 19, -27 ″ k ″ 27, -27 ″ l ″ 28	
Data collection scan type	and scans	
Reflections collected	166238	
Independent reflections	15005 [R_{int}= 0.0848]	
Reflections > 2 ⌠(I)	9726	
Average ⌠(I)/(net I)	0.0622	
Absorption coefficient	2.05 mm^{-1}	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.9002	

Structure Solution and Refinement

Primary solution method	?
Secondary solution method	?
Hydrogen placement	mixed
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	15005 / 0 / 309
Treatment of hydrogen atoms	constr
Goodness-of-fit on F^2	1.03
Final R indices [I>2 ⌠(I), 9726 reflections]	R1 = 0.0534, wR2 = 0.1233
R indices (all data)	R1 = 0.1009, wR2 = 0.1398
Type of weighting scheme used	calc
Weighting scheme used	w=1/[^2^(Fo^2^)+(0.0618P)^2^+1.7296P] where
P=(Fo^2^+2Fc^2^)/3	
Max shift/error	0.000
Average shift/error	0.000
Extinction coefficient	n/a

Largest diff. peak and hole	5.40 and -1.57 e·Å^{-3}

Programs Used

Cell refinement	SAINT V8.32B (Bruker-AXS, 2007)
Data collection	APEX2 2012.10-0 (Bruker-AXS, 2007)
Data reduction	SAINT V8.32B (Bruker-AXS, 2007)
Structure solution	SHELXT (Sheldrick, 2012)
Structure refinement	SHELXL-2013/2 (Sheldrick, 2013)
Graphics	DIAMOND 3 (Crystal Impact, 1999)

References

Special Refinement Details

Table A2.6.2. *Atomic coordinates (x 10^{4}) and equivalent isotropic displacement parameters (Å^{2}x 10^{3}) for **61**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor*

	x	y	z	U$_{eq}$
Br(1)	2176(1)	3795(1)	4422(1)	16(1)
O(1)	4484(1)	6914(1)	2590(1)	19(1)
O(2)	4806(1)	5100(1)	1849(1)	17(1)
O(3)	3104(1)	5662(1)	752(1)	18(1)
O(4)	-1522(1)	4433(1)	2271(1)	22(1)
O(5)	142(1)	5360(1)	2886(1)	16(1)
O(6)	1437(1)	6845(1)	2016(1)	15(1)
O(7)	490(1)	5659(1)	1068(1)	13(1)
O(8)	1317(5)	4704(4)	5932(3)	13(1)
C(4)	1722(2)	5406(1)	5379(1)	15(1)
N(1)	3573(1)	7168(1)	3851(1)	14(1)
N(2)	-318(1)	4658(1)	2439(1)	13(1)
C(1)	3379(1)	5631(1)	3242(1)	11(1)
C(2)	2724(1)	5722(1)	4069(1)	12(1)
C(3)	2202(2)	5102(1)	4617(1)	12(1)
C(5)	1834(2)	6343(1)	5635(1)	17(1)
C(6)	2449(2)	6977(1)	5154(1)	16(1)
C(7)	2877(2)	6651(1)	4388(1)	12(1)
C(8)	3878(2)	6644(1)	3160(1)	14(1)
C(9)	3948(2)	8140(1)	4012(1)	20(1)
C(10)	4635(2)	4985(1)	3515(1)	15(1)
C(11)	5536(2)	5040(1)	2835(1)	19(1)
C(12)	3523(2)	5408(1)	1558(1)	14(1)
C(13)	2536(1)	5327(1)	2228(1)	10(1)
C(14)	1976(1)	4321(1)	2117(1)	10(1)
C(15)	2786(2)	3606(1)	1902(1)	14(1)
C(16)	2314(2)	2703(1)	1684(1)	16(1)
C(17)	985(2)	2474(1)	1652(1)	17(1)
C(18)	150(2)	3150(1)	1888(1)	15(1)
C(19)	644(2)	4040(1)	2126(1)	12(1)
C(20)	1417(2)	6040(1)	1779(1)	11(1)
C(21)	-565(2)	6275(1)	517(1)	15(1)
C(22)	-1606(2)	6519(1)	1041(1)	16(1)
C(23)	-2852(2)	6167(1)	839(1)	24(1)

Table A2.6.3. *Bond lengths [Å] and angles [°] for* ***61***

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Br(1)-C(3)	1.8983(15)
O(1)-C(8)	1.2173(19)
O(2)-C(11)	1.450(2)
O(2)-C(12)	1.3369(19)
O(3)-C(12)	1.2057(19)
O(4)-N(2)	1.2258(18)
O(5)-N(2)	1.2285(17)
O(6)-C(20)	1.2060(18)
O(7)-C(20)	1.3313(18)
O(7)-C(21)	1.4626(18)
O(8)-C(4)	1.419(5)
O(8)-H(4)	0.5001
O(8)-H(8)	0.8315
C(4)-H(4)	0.9497
C(4)-C(3)	1.396(2)
C(4)-C(5)	1.394(2)
N(1)-C(7)	1.3965(19)
N(1)-C(8)	1.358(2)
N(1)-C(9)	1.451(2)
N(2)-C(19)	1.4738(19)
C(1)-C(2)	1.528(2)
C(1)-C(8)	1.555(2)
C(1)-C(10)	1.544(2)
C(1)-C(13)	1.5768(19)
C(2)-C(3)	1.389(2)
C(2)-C(7)	1.410(2)
C(5)-H(5)	0.9500
C(5)-C(6)	1.391(2)
C(6)-H(6)	0.9500
C(6)-C(7)	1.383(2)
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(10)-C(11)	1.514(2)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(12)-C(13)	1.573(2)
C(13)-C(14)	1.5460(19)
C(13)-C(20)	1.5455(19)
C(14)-C(15)	1.400(2)
C(14)-C(19)	1.412(2)
C(15)-H(15)	0.9500
C(15)-C(16)	1.391(2)
C(16)-H(16)	0.9500
C(16)-C(17)	1.376(2)
C(17)-H(17)	0.9500
C(17)-C(18)	1.387(2)
C(18)-H(18)	0.9500
C(18)-C(19)	1.385(2)
C(21)-H(21A)	0.9900
C(21)-H(21B)	0.9900

C(21)-C(22)	1.494(2)
C(22)-H(22)	0.9500
C(22)-C(23)	1.322(3)
C(23)-H(23A)	0.9500
C(23)-H(23B)	0.9500

C(12)-O(2)-C(11)	123.19(13)
C(20)-O(7)-C(21)	117.17(12)
C(4)-O(8)-H(4)	16.4
C(4)-O(8)-H(8)	107.5
H(4)-O(8)-H(8)	113.1
O(8)-C(4)-H(4)	8.5
C(3)-C(4)-O(8)	116.4(3)
C(3)-C(4)-H(4)	120.1
C(5)-C(4)-O(8)	123.3(3)
C(5)-C(4)-H(4)	120.1
C(5)-C(4)-C(3)	119.77(14)
C(7)-N(1)-C(9)	124.62(13)
C(8)-N(1)-C(7)	111.67(12)
C(8)-N(1)-C(9)	123.70(14)
O(4)-N(2)-O(5)	123.20(14)
O(4)-N(2)-C(19)	118.81(13)
O(5)-N(2)-C(19)	117.95(12)
C(2)-C(1)-C(8)	101.37(11)
C(2)-C(1)-C(10)	109.88(12)
C(2)-C(1)-C(13)	122.06(12)
C(8)-C(1)-C(13)	107.22(11)
C(10)-C(1)-C(8)	108.64(12)
C(10)-C(1)-C(13)	106.98(11)
C(3)-C(2)-C(1)	135.18(13)
C(3)-C(2)-C(7)	116.15(13)
C(7)-C(2)-C(1)	108.06(12)
C(4)-C(3)-Br(1)	115.80(11)
C(2)-C(3)-Br(1)	122.67(11)
C(2)-C(3)-C(4)	121.47(14)
C(4)-C(5)-H(5)	119.6
C(6)-C(5)-C(4)	120.74(14)
C(6)-C(5)-H(5)	119.6
C(5)-C(6)-H(6)	121.2
C(7)-C(6)-C(5)	117.54(14)
C(7)-C(6)-H(6)	121.2
N(1)-C(7)-C(2)	110.18(12)
C(6)-C(7)-N(1)	125.78(13)
C(6)-C(7)-C(2)	123.98(14)
O(1)-C(8)-N(1)	125.78(14)
O(1)-C(8)-C(1)	125.49(14)
N(1)-C(8)-C(1)	108.69(12)
N(1)-C(9)-H(9A)	109.5
N(1)-C(9)-H(9B)	109.5
N(1)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(1)-C(10)-H(10A)	109.0
C(1)-C(10)-H(10B)	109.0
H(10A)-C(10)-H(10B)	107.8
C(11)-C(10)-C(1)	113.13(13)
C(11)-C(10)-H(10A)	109.0

C(11)-C(10)-H(10B)	109.0
O(2)-C(11)-C(10)	114.73(13)
O(2)-C(11)-H(11A)	108.6
O(2)-C(11)-H(11B)	108.6
C(10)-C(11)-H(11A)	108.6
C(10)-C(11)-H(11B)	108.6
H(11A)-C(11)-H(11B)	107.6
O(2)-C(12)-C(13)	119.80(13)
O(3)-C(12)-O(2)	119.04(14)
O(3)-C(12)-C(13)	120.80(14)
C(12)-C(13)-C(1)	106.83(11)
C(14)-C(13)-C(1)	117.09(11)
C(14)-C(13)-C(12)	106.13(11)
C(20)-C(13)-C(1)	112.41(11)
C(20)-C(13)-C(12)	101.50(11)
C(20)-C(13)-C(14)	111.34(11)
C(15)-C(14)-C(13)	119.25(13)
C(15)-C(14)-C(19)	114.17(13)
C(19)-C(14)-C(13)	126.32(12)
C(14)-C(15)-H(15)	118.4
C(16)-C(15)-C(14)	123.26(14)
C(16)-C(15)-H(15)	118.4
C(15)-C(16)-H(16)	119.8
C(17)-C(16)-C(15)	120.48(14)
C(17)-C(16)-H(16)	119.8
C(16)-C(17)-H(17)	120.7
C(16)-C(17)-C(18)	118.53(14)
C(18)-C(17)-H(17)	120.7
C(17)-C(18)-H(18)	119.8
C(19)-C(18)-C(17)	120.34(15)
C(19)-C(18)-H(18)	119.8
C(14)-C(19)-N(2)	122.70(12)
C(18)-C(19)-N(2)	114.14(13)
C(18)-C(19)-C(14)	123.08(14)
O(6)-C(20)-O(7)	125.14(13)
O(6)-C(20)-C(13)	123.77(13)
O(7)-C(20)-C(13)	110.96(12)
O(7)-C(21)-H(21A)	109.3
O(7)-C(21)-H(21B)	109.3
O(7)-C(21)-C(22)	111.77(12)
H(21A)-C(21)-H(21B)	107.9
C(22)-C(21)-H(21A)	109.3
C(22)-C(21)-H(21B)	109.3
C(21)-C(22)-H(22)	118.2
C(23)-C(22)-C(21)	123.59(16)
C(23)-C(22)-H(22)	118.2
C(22)-C(23)-H(23A)	120.0
C(22)-C(23)-H(23B)	120.0
H(23A)-C(23)-H(23B)	120.0

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Symmetry transformations used to generate equivalent atoms:

Table A2.6.4. *Anisotropic displacement parameters ($Å^2 x 10^4$) for **61**. The anisotropic displacement factor exponent takes the form: $-2ð^2 [h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$*

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	228(1)	114(1)	135(1)	15(1)	21(1)	-20(1)
O(1)	183(5)	191(5)	217(5)	-12(4)	88(4)	-53(4)
O(2)	132(5)	207(5)	178(5)	-9(4)	52(4)	16(4)
O(3)	210(5)	193(5)	160(5)	40(4)	75(4)	13(4)
O(4)	116(5)	227(6)	338(7)	-22(5)	88(5)	-29(4)
O(5)	147(5)	162(5)	144(4)	-30(4)	14(4)	16(4)
O(6)	165(5)	101(4)	174(5)	-5(3)	25(4)	13(3)
O(7)	127(4)	124(4)	111(4)	5(3)	-16(3)	29(3)
O(8)	60(20)	270(30)	63(19)	92(17)	11(14)	-36(18)
C(4)	168(6)	170(6)	118(5)	11(5)	26(5)	-2(5)
N(1)	152(5)	112(5)	154(5)	-21(4)	37(4)	-42(4)
N(2)	117(5)	145(5)	130(5)	20(4)	28(4)	5(4)
C(1)	98(5)	112(5)	124(5)	-8(4)	11(4)	-8(4)
C(2)	107(5)	118(5)	105(5)	-9(4)	-2(4)	-3(4)
C(3)	129(6)	122(5)	107(5)	7(4)	-1(4)	-6(4)
C(5)	199(7)	183(6)	128(5)	-12(5)	44(5)	11(5)
C(6)	176(6)	140(6)	145(6)	-30(5)	29(5)	0(5)
C(7)	114(5)	120(5)	124(5)	-6(4)	5(4)	-7(4)
C(8)	116(5)	143(6)	150(5)	-13(4)	20(4)	-31(4)
C(9)	210(7)	129(6)	247(7)	-32(5)	39(6)	-55(5)
C(10)	101(5)	195(6)	149(6)	-8(5)	0(4)	22(5)
C(11)	107(6)	262(8)	188(6)	-20(6)	22(5)	12(5)
C(12)	130(6)	125(5)	157(6)	-9(4)	50(5)	-3(4)
C(13)	94(5)	101(5)	109(5)	-8(4)	12(4)	3(4)
C(14)	98(5)	105(5)	96(5)	4(4)	-1(4)	8(4)
C(15)	129(6)	121(5)	155(5)	-10(4)	19(4)	24(4)
C(16)	187(7)	114(5)	180(6)	-7(5)	22(5)	29(5)
C(17)	218(7)	99(5)	179(6)	7(5)	22(5)	-10(5)
C(18)	161(6)	115(5)	156(5)	24(4)	21(5)	-21(4)
C(19)	120(5)	107(5)	117(5)	16(4)	18(4)	5(4)
C(20)	111(5)	113(5)	113(5)	14(4)	17(4)	10(4)
C(21)	156(6)	164(6)	120(5)	31(4)	-3(4)	50(5)
C(22)	170(6)	154(6)	146(6)	10(5)	6(5)	39(5)
C(23)	183(7)	275(8)	256(8)	14(7)	26(6)	15(6)

Table A2.6.5. *Hydrogen coordinates (x 10^3) and isotropic displacement parameters ($Å^2 x 10^3$) for **61***

	x	y	z	U_{iso}
H(4)	132	498	572	18
H(8)	171	481	649	23
H(5)	149	655	614	20
H(6)	257	761	534	19
H(9A)	316	850	409	30
H(9B)	425	838	347	30
H(9C)	469	820	459	30
H(10A)	518	515	415	18
H(10B)	432	434	354	18

H(11A)	614	559	300	23
H(11B)	613	448	292	23
H(15)	370	374	191	17
H(16)	292	224	156	20
H(17)	65	187	147	20
H(18)	-76	300	189	18
H(21A)	-102	596	-8	18
H(21B)	-13	685	36	18
H(22)	-136	695	155	20
H(23A)	-313	573	34	29
H(23B)	-347	635	120	29

Table A2.6.6. *Hydrogen bonds for* ***61*** *[Å and °]*

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(8)-H(8)...O(4)#1	0.83	2.16	2.870(6)	143.3
O(8)-H(8)...N(2)#1	0.83	2.47	2.964(5)	118.6
C(5)-H(5)...O(6)#2	0.95	2.64	3.382(2)	135.3
C(6)-H(6)...O(3)#2	0.95	2.58	3.524(2)	173.5
C(9)-H(9A)...O(4)#3	0.98	2.62	3.270(2)	124.3
C(10)-H(10B)...Br(1)	0.99	2.90	3.5462(16)	123.5
C(18)-H(18)...O(6)#4	0.95	2.52	3.1613(19)	124.5

Symmetry transformations used to generate equivalent atoms:
#1 -x,-y+1,-z+1 #2 x,-y+3/2,z+1/2 #3 -x,y+1/2,-z+1/2
#4 -x,y-1/2,-z+1/2

A2.7. X-Ray Crystal Structure Analysis of 62

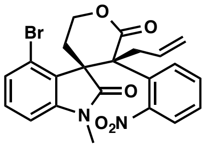

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Figure A2.7.1. *X-ray Crystal Structure of* ***62***

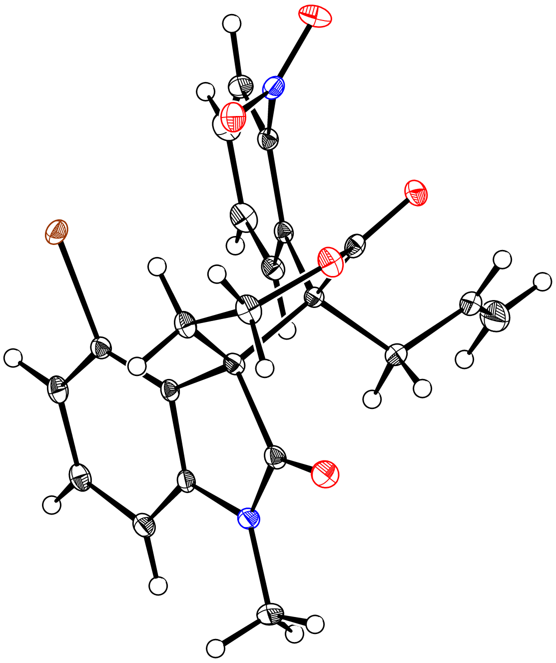


Table A2.7.1. *Crystal data and structure refinement for* ***62***

Empirical formula	C22 H19 Br N2 O5
Formula weight	471.30
Crystallization Solvent	???Solvent???
Crystal Habit	Block
Crystal size	0.25 x 0.25 x 0.22 mm^3
Crystal color	Light yellow

Data Collection

Preliminary Photos	
Type of diffractometer	Bruker SMART 1000
Wavelength	0.71073 Å MoKa
Data Collection Temperature	100(2) K

q range for 9803 reflections used in lattice determination	2.44 to 37.44°	
Unit cell dimensions	a = 9.1581(2) Å	a= 90°
	b = 12.6857(3) Å	b= 90°
	c = 16.7030(3) Å	g = 90°
Volume	1940.50(7) Å^3	
Z	4	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Density (calculated)	1.613 Mg/m^3	
F(000)	960	
Data collection program	Bruker SMART v5.630	
q range for data collection	2.02 to 38.73°	
Completeness to q = 38.73°	98.0 %	
Index ranges	-15<=h<=15, -22<=k<=22, -29<=l<=29	
Data collection scan type	scans at 9 settings	
Data reduction program	Bruker SAINT v6.45A	
Reflections collected	61657	
Independent reflections	10781 [R$_{int}$= 0.0854]	
Absorption coefficient	2.157 mm^{-1}	
Absorption correction	None	
Max. and min. transmission	0.6482 and 0.6146	

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 2008)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric positions
Structure refinement program	SHELXL-97 (Sheldrick, 2008)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	10781 / 0 / 272
Treatment of hydrogen atoms	Riding
Goodness-of-fit on F^2	1.035
Final R indices [I>2s(I), 9216 reflections]	R1 = 0.0252, wR2 = 0.0489
R indices (all data)	R1 = 0.0337, wR2 = 0.0500
Type of weighting scheme used	Sigma
Weighting scheme used	w=1/s^2^(Fo^2^)
Max shift/error	0.002
Average shift/error	0.000
Absolute structure determination	ad

Absolute structure parameter	-0.009(3)
Largest diff. peak and hole	0.506 and -0.302 e.Å^{-3}

Special Refinement Details

Table A2.7.2. *Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **62**. U(eq) is defined asthe trace of the orthogonalized U^{ij} tensor*

	x	y	z	U_{eq}
Br(1)	6172(1)	8240(1)	8167(1)	15(1)
O(1)	3907(1)	9672(1)	4985(1)	17(1)
O(2)	6918(1)	8349(1)	5024(1)	15(1)
O(3)	8739(1)	9434(1)	5191(1)	14(1)
O(4)	8625(1)	7737(1)	6394(1)	15(1)
O(5)	10809(1)	8399(1)	6452(1)	19(1)
N(1)	3093(1)	10408(1)	6153(1)	12(1)
N(2)	9490(1)	8431(1)	6587(1)	12(1)
C(1)	4851(1)	9334(1)	7882(1)	11(1)
C(2)	4150(1)	9836(1)	8519(1)	13(1)
C(3)	3074(1)	10582(1)	8369(1)	13(1)
C(4)	2660(1)	10820(1)	7588(1)	13(1)
C(5)	3393(1)	10316(1)	6972(1)	10(1)
C(6)	4553(1)	9605(1)	7092(1)	9(1)
C(7)	5158(1)	9288(1)	6276(1)	10(1)
C(8)	3998(1)	9786(1)	5710(1)	12(1)
C(9)	1825(1)	10950(1)	5827(1)	16(1)
C(10)	5199(1)	8087(1)	6152(1)	12(1)
C(11)	5626(1)	7790(1)	5306(1)	15(1)
C(12)	7535(1)	9152(1)	5408(1)	11(1)
C(13)	6734(1)	9783(1)	6067(1)	9(1)
C(14)	6523(1)	10915(1)	5677(1)	12(1)
C(15)	7876(1)	11577(1)	5570(1)	14(1)
C(16)	8070(1)	12508(1)	5908(1)	22(1)
C(17)	7685(1)	9912(1)	6823(1)	9(1)
C(18)	7318(1)	10731(1)	7352(1)	12(1)
C(19)	8056(1)	10912(1)	8064(1)	15(1)
C(20)	9254(1)	10302(1)	8269(1)	17(1)
C(21)	9707(1)	9521(1)	7747(1)	14(1)
C(22)	8925(1)	9334(1)	7045(1)	11(1)

Table A2.7.3*.   Bond lengths [Å] and angles [°] for **62***

Br(1)-C(1)	1.9017(10)
O(1)-C(8)	1.2218(12)
O(2)-C(12)	1.3289(12)
O(2)-C(11)	1.4580(13)
O(3)-C(12)	1.2142(12)
O(4)-N(2)	1.2271(11)
O(5)-N(2)	1.2300(11)
N(1)-C(8)	1.3625(13)
N(1)-C(5)	1.3999(12)
N(1)-C(9)	1.4553(13)
N(2)-C(22)	1.4720(12)
C(1)-C(6)	1.3911(14)
C(1)-C(2)	1.3962(14)

C(2)-C(3)	1.3888(15)
C(3)-C(4)	1.3917(15)
C(4)-C(5)	1.3854(14)
C(5)-C(6)	1.4079(14)
C(6)-C(7)	1.5248(13)
C(7)-C(10)	1.5383(13)
C(7)-C(8)	1.5561(14)
C(7)-C(13)	1.6122(13)
C(10)-C(11)	1.5149(14)
C(12)-C(13)	1.5460(13)
C(13)-C(17)	1.5433(13)
C(13)-C(14)	1.5885(13)
C(14)-C(15)	1.5070(14)
C(15)-C(16)	1.3208(15)
C(17)-C(22)	1.4016(14)
C(17)-C(18)	1.4049(14)
C(18)-C(19)	1.3862(14)
C(19)-C(20)	1.3857(16)
C(20)-C(21)	1.3836(15)
C(21)-C(22)	1.3936(14)

C(12)-O(2)-C(11)	124.26(8)
C(8)-N(1)-C(5)	111.30(8)
C(8)-N(1)-C(9)	123.71(8)
C(5)-N(1)-C(9)	124.18(9)
O(4)-N(2)-O(5)	124.19(9)
O(4)-N(2)-C(22)	117.92(8)
O(5)-N(2)-C(22)	117.81(8)
C(6)-C(1)-C(2)	121.36(9)
C(6)-C(1)-Br(1)	122.86(7)
C(2)-C(1)-Br(1)	115.75(7)
C(3)-C(2)-C(1)	119.98(9)
C(2)-C(3)-C(4)	120.64(9)
C(5)-C(4)-C(3)	117.69(9)
C(4)-C(5)-N(1)	126.35(9)
C(4)-C(5)-C(6)	123.75(9)
N(1)-C(5)-C(6)	109.89(8)
C(1)-C(6)-C(5)	116.17(9)
C(1)-C(6)-C(7)	135.37(9)
C(5)-C(6)-C(7)	108.42(8)
C(6)-C(7)-C(10)	112.93(8)
C(6)-C(7)-C(8)	100.84(7)
C(10)-C(7)-C(8)	109.74(8)
C(6)-C(7)-C(13)	114.61(8)
C(10)-C(7)-C(13)	109.51(8)
C(8)-C(7)-C(13)	108.78(7)
O(1)-C(8)-N(1)	124.44(9)
O(1)-C(8)-C(7)	126.88(9)
N(1)-C(8)-C(7)	108.66(8)
C(11)-C(10)-C(7)	112.23(8)
O(2)-C(11)-C(10)	112.87(8)
O(3)-C(12)-O(2)	117.89(9)
O(3)-C(12)-C(13)	119.40(8)
O(2)-C(12)-C(13)	122.54(8)
C(17)-C(13)-C(12)	111.72(8)
C(17)-C(13)-C(14)	107.93(7)
C(12)-C(13)-C(14)	103.53(7)
C(17)-C(13)-C(7)	111.69(7)

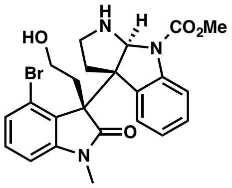
C(12)-C(13)-C(7)	112.19(7)
C(14)-C(13)-C(7)	109.36(7)
C(15)-C(14)-C(13)	116.88(8)
C(16)-C(15)-C(14)	123.95(11)
C(22)-C(17)-C(18)	114.45(9)
C(22)-C(17)-C(13)	128.21(8)
C(18)-C(17)-C(13)	117.30(8)
C(19)-C(18)-C(17)	123.03(10)
C(20)-C(19)-C(18)	120.40(10)
C(21)-C(20)-C(19)	118.74(10)
C(20)-C(21)-C(22)	119.86(10)
C(21)-C(22)-C(17)	123.37(9)
C(21)-C(22)-N(2)	112.90(9)
C(17)-C(22)-N(2)	123.65(8)

Symmetry transformations used to generate equivalent atoms:

Table A2.7.4. *Anisotropic displacement parameters (*$Å^2$*x* 10^4*) for* **62**. *The anisotropic displacement factorexponent takes the form:* $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	163(1)	167(1)	105(1)	41(1)	8(1)	33(1)
O(1)	154(3)	265(4)	81(3)	-9(3)	-27(3)	-9(3)
O(2)	166(3)	173(3)	96(3)	-45(3)	20(3)	-31(3)
O(3)	132(3)	170(3)	115(3)	6(2)	34(3)	1(3)
O(4)	182(4)	119(3)	161(3)	-8(2)	7(3)	-30(3)
O(5)	111(3)	226(4)	235(4)	-21(3)	9(3)	43(3)
N(1)	92(4)	177(4)	92(3)	20(3)	-10(3)	-1(3)
N(2)	135(4)	122(4)	108(3)	24(3)	-5(3)	14(3)
C(1)	99(4)	128(4)	92(4)	7(3)	0(3)	-8(3)
C(2)	148(5)	155(4)	88(4)	-3(3)	29(3)	-19(3)
C(3)	145(4)	134(4)	113(4)	-20(3)	41(3)	-17(3)
C(4)	115(4)	120(4)	141(4)	-1(3)	28(4)	-2(3)
C(5)	96(4)	118(4)	85(4)	12(3)	10(3)	-20(3)
C(6)	94(4)	120(4)	70(3)	1(3)	8(3)	-15(3)
C(7)	92(4)	138(4)	69(4)	-13(3)	2(3)	-7(3)
C(8)	96(4)	164(4)	102(4)	7(3)	-10(3)	-31(3)
C(9)	113(5)	217(5)	157(5)	36(4)	-33(4)	13(4)
C(10)	130(4)	137(4)	107(4)	-16(3)	13(3)	-34(3)
C(11)	160(5)	158(4)	120(4)	-43(3)	4(4)	-41(4)
C(12)	137(4)	119(4)	60(4)	2(3)	-3(3)	7(3)
C(13)	91(4)	105(4)	70(4)	-3(3)	-2(3)	-1(3)
C(14)	113(4)	134(4)	122(4)	26(3)	-8(3)	5(3)
C(15)	130(4)	142(5)	158(4)	45(3)	1(3)	0(3)
C(16)	203(6)	169(5)	299(6)	19(4)	21(5)	-23(4)
C(17)	91(4)	109(3)	75(3)	-1(3)	2(3)	-17(3)
C(18)	116(4)	137(4)	106(4)	-16(3)	9(3)	-9(3)
C(19)	159(4)	181(4)	114(5)	-54(3)	6(4)	-37(4)
C(20)	147(4)	262(5)	103(5)	-28(4)	-31(3)	-48(4)
C(21)	114(4)	189(5)	124(4)	21(3)	-30(3)	-10(4)
C(22)	104(4)	119(4)	93(3)	4(3)	2(3)	-3(3)

A2.8. X-Ray Crystal Structure Analysis of 72



72

Figure A2.8.1. *X-ray Crystal Structure of **72***

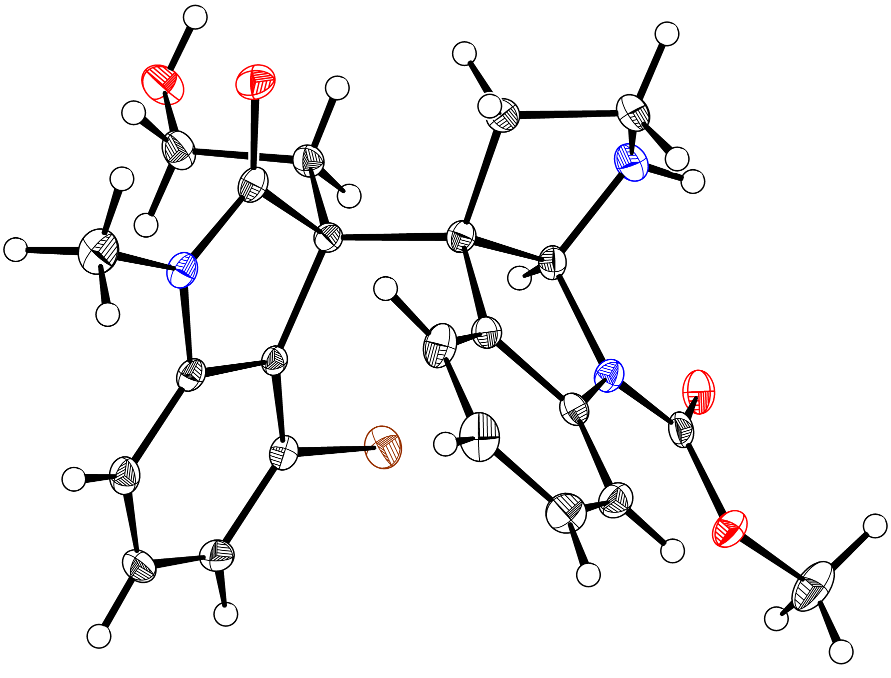


Table A2.8.1. *Crystal Data and Structure Analysis Details for **72***

Empirical formula	C23 H24 Br N3 O4
Formula weight	486.36
Crystal shape	plate
Crystal color	colourless
Crystal size	0.07 x 0.31 x 0.38 mm

Data Collection

Preliminary photograph(s)	rotation
Type of diffractometer	Bruker APEX-II CCD
Wavelength	0.71073 Å MoK
Data collection temperature	100 K
Theta range for 9871 reflections used	

in lattice determination	2.39 to 31.55°	
Unit cell dimensions	a = 8.9320(3) Å b = 27.1836(10) Å c = 9.0145(3) Å	a= 90° b= 107.683(2)° g = 90°
Volume	2085.34(13) $Å^3$	
Z	4	
Crystal system	monoclinic	
Space group	P 1 21/c 1 (# 14)	
Density (calculated)	1.549 g/cm^3	
F(000)	1000	
Theta range for data collection	2.4 to 37.5°	
Completeness to theta = 25.000°	99.9%	
Index ranges	-15 £ h £ 14, -46 £ k £ 45, -15 £ l £ 15	
Data collection scan type	and scans	
Reflections collected	104508	
Independent reflections	10606 [R_{int}= 0.0574]	
Reflections > 2s(I)	8291	
Average s(I)/(net I)	0.0362	
Absorption coefficient	2.01 mm^{-1}	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.8324	

Structure Solution and Refinement

Primary solution method	dual
Secondary solution method	?
Hydrogen placement	?
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	10606 / 0 / 376
Treatment of hydrogen atoms	refall
Goodness-of-fit on F^2	2.53
Final R indices [I>2s(I), 8291 reflections]	R1 = 0.0470, wR2 = 0.0646
R indices (all data)	R1 = 0.0694, wR2 = 0.0654
Type of weighting scheme used	calc
Weighting scheme used	
Max shift/error	0.001
Average shift/error	0.000
Extinction coefficient	0
Largest diff. peak and hole	1.86 and -1.09 e·$Å^{-3}$

Programs Used

Cell refinement	SAINT V8.27B (Bruker-AXS, 2007)
Data collection	APEX2 2012.4-3 (Bruker-AXS, 2007)
Data reduction	SAINT V8.27B (Bruker-AXS, 2007)
Structure solution	SHELXT (Sheldrick, 2012)
Structure refinement	SHELXL-2012/6 (Sheldrick, 2012)
Graphics	DIAMOND 3 (Crystal Impact, 1999)

References

Special Refinement Details

Table A2.8.2. *Atomic coordinates ($x\ 10^4$) and equivalent isotropic displacement parameters ($Å^2 x\ 10^3$) for **72**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor*

	x	y	z	U_{eq}
Br(1)	5616(1)	9528(1)	3588(1)	20(1)
O(1)	3320(1)	7660(1)	145(1)	19(1)
O(2)	2094(1)	8263(1)	4223(1)	22(1)
O(3)	10340(1)	9430(1)	2851(1)	18(1)
O(4)	9696(1)	9118(1)	4907(1)	18(1)
N(1)	2670(1)	8410(1)	-1033(1)	14(1)
N(2)	8487(1)	8844(1)	2459(1)	13(1)
N(3)	8419(2)	8060(1)	3813(1)	22(1)
C(1)	4542(1)	8418(1)	1464(1)	11(1)
C(2)	4040(1)	8938(1)	883(1)	11(1)
C(3)	4320(1)	9405(1)	1519(1)	14(1)
C(4)	3606(2)	9819(1)	682(2)	17(1)
C(5)	2602(2)	9765(1)	-815(2)	19(1)
C(6)	2257(2)	9306(1)	-1492(2)	16(1)
C(7)	2966(1)	8906(1)	-616(1)	12(1)
C(8)	3461(1)	8107(1)	138(1)	13(1)
C(9)	1534(2)	8243(1)	-2468(2)	21(1)
C(10)	4148(2)	8288(1)	2965(2)	14(1)
C(11)	2418(2)	8357(1)	2804(2)	19(1)
C(12)	6299(1)	8286(1)	1562(1)	12(1)
C(13)	6798(1)	8517(1)	248(1)	13(1)
C(14)	6207(2)	8430(1)	-1338(2)	18(1)
C(15)	6884(2)	8664(1)	-2346(2)	22(1)
C(16)	8156(2)	8973(1)	-1769(2)	20(1)
C(17)	8787(2)	9058(1)	-176(2)	17(1)
C(18)	8085(1)	8827(1)	816(1)	13(1)
C(19)	7546(1)	8484(1)	3051(1)	13(1)
C(20)	8360(2)	7697(1)	2606(2)	23(1)
C(21)	6642(2)	7726(1)	1632(2)	17(1)
C(22)	9528(1)	9132(1)	3521(2)	14(1)
C(23)	11536(2)	9722(1)	3929(2)	27(1)

Table A2.8.3. *Bond lengths [Å] and angles [°] for **72***

Br(1)-C(3)	1.9025(13)
O(1)-C(8)	1.2203(15)

O(2)-H(2)	0.856(18)
O(2)-C(11)	1.4180(16)
O(3)-C(22)	1.3461(15)
O(3)-C(23)	1.4446(17)
O(4)-C(22)	1.2132(15)
N(1)-C(7)	1.4020(16)
N(1)-C(8)	1.3567(16)
N(1)-C(9)	1.4531(16)
N(2)-C(18)	1.4145(15)
N(2)-C(19)	1.4905(16)
N(2)-C(22)	1.3609(16)
N(3)-H(3)	0.760(18)
N(3)-C(19)	1.4455(17)
N(3)-C(20)	1.457(2)
C(1)-C(2)	1.5279(16)
C(1)-C(8)	1.5399(17)
C(1)-C(10)	1.5387(17)
C(1)-C(12)	1.5856(17)
C(2)-C(3)	1.3835(17)
C(2)-C(7)	1.4026(16)
C(3)-C(4)	1.3978(18)
C(4)-H(4)	0.939(15)
C(4)-C(5)	1.3829(19)
C(5)-H(5)	0.921(16)
C(5)-C(6)	1.381(2)
C(6)-H(6)	0.925(14)
C(6)-C(7)	1.3800(18)
C(9)-H(9A)	0.960(17)
C(9)-H(9B)	0.961(16)
C(9)-H(9C)	0.996(17)
C(10)-H(10A)	0.897(13)
C(10)-H(10B)	0.984(15)
C(10)-C(11)	1.5195(18)
C(11)-H(11A)	0.946(16)
C(11)-H(11B)	0.983(15)
C(12)-C(13)	1.5211(17)
C(12)-C(19)	1.5569(17)
C(12)-C(21)	1.5515(17)
C(13)-C(14)	1.3857(17)
C(13)-C(18)	1.3912(17)
C(14)-H(14)	0.954(15)
C(14)-C(15)	1.3886(19)
C(15)-H(15)	0.888(15)
C(15)-C(16)	1.382(2)
C(16)-H(16)	0.952(13)
C(16)-C(17)	1.3941(19)
C(17)-H(17)	0.913(14)
C(17)-C(18)	1.3892(17)
C(19)-H(19)	0.943(12)
C(20)-H(20A)	0.974(15)
C(20)-H(20B)	0.997(14)
C(20)-C(21)	1.5206(19)
C(21)-H(21A)	0.939(13)
C(21)-H(21B)	0.956(14)
C(23)-H(23A)	0.931(16)
C(23)-H(23B)	0.962(15)
C(23)-H(23C)	1.013(16)

C(11)-O(2)-H(2)	108.4(11)
C(22)-O(3)-C(23)	114.73(11)
C(7)-N(1)-C(9)	124.25(11)
C(8)-N(1)-C(7)	111.34(10)
C(8)-N(1)-C(9)	124.10(11)
C(18)-N(2)-C(19)	111.20(10)
C(22)-N(2)-C(18)	131.13(11)
C(22)-N(2)-C(19)	117.66(10)
C(19)-N(3)-H(3)	110.4(14)
C(19)-N(3)-C(20)	107.07(11)
C(20)-N(3)-H(3)	110.6(14)
C(2)-C(1)-C(8)	101.12(9)
C(2)-C(1)-C(10)	113.01(10)
C(2)-C(1)-C(12)	114.20(10)
C(8)-C(1)-C(12)	107.26(9)
C(10)-C(1)-C(8)	107.47(10)
C(10)-C(1)-C(12)	112.73(10)
C(3)-C(2)-C(1)	135.27(11)
C(3)-C(2)-C(7)	116.19(11)
C(7)-C(2)-C(1)	108.38(10)
C(2)-C(3)-Br(1)	123.18(9)
C(2)-C(3)-C(4)	121.36(12)
C(4)-C(3)-Br(1)	115.42(9)
C(3)-C(4)-H(4)	117.3(9)
C(5)-C(4)-C(3)	119.63(13)
C(5)-C(4)-H(4)	123.1(9)
C(4)-C(5)-H(5)	117.6(10)
C(6)-C(5)-C(4)	121.31(12)
C(6)-C(5)-H(5)	121.0(10)
C(5)-C(6)-H(6)	123.9(9)
C(7)-C(6)-C(5)	117.20(12)
C(7)-C(6)-H(6)	118.9(9)
N(1)-C(7)-C(2)	109.69(10)
C(6)-C(7)-N(1)	126.00(11)
C(6)-C(7)-C(2)	124.23(12)
O(1)-C(8)-N(1)	125.30(12)
O(1)-C(8)-C(1)	125.66(11)
N(1)-C(8)-C(1)	109.04(10)
N(1)-C(9)-H(9A)	105.5(10)
N(1)-C(9)-H(9B)	108.1(10)
N(1)-C(9)-H(9C)	111.5(10)
H(9A)-C(9)-H(9B)	108.5(13)
H(9A)-C(9)-H(9C)	112.9(13)
H(9B)-C(9)-H(9C)	110.0(13)
C(1)-C(10)-H(10A)	110.7(8)
C(1)-C(10)-H(10B)	110.0(8)
H(10A)-C(10)-H(10B)	108.0(12)
C(11)-C(10)-C(1)	112.66(10)
C(11)-C(10)-H(10A)	108.2(8)
C(11)-C(10)-H(10B)	107.2(8)
O(2)-C(11)-C(10)	111.85(11)
O(2)-C(11)-H(11A)	104.6(9)
O(2)-C(11)-H(11B)	109.4(8)
C(10)-C(11)-H(11A)	110.7(9)
C(10)-C(11)-H(11B)	110.9(8)
H(11A)-C(11)-H(11B)	109.2(12)
C(13)-C(12)-C(1)	112.53(10)
C(13)-C(12)-C(19)	103.10(10)

C(13)-C(12)-C(21)	109.61(10)
C(19)-C(12)-C(1)	114.00(10)
C(21)-C(12)-C(1)	113.78(10)
C(21)-C(12)-C(19)	102.92(10)
C(14)-C(13)-C(12)	128.56(11)
C(14)-C(13)-C(18)	119.71(11)
C(18)-C(13)-C(12)	111.60(10)
C(13)-C(14)-H(14)	119.7(9)
C(13)-C(14)-C(15)	119.53(13)
C(15)-C(14)-H(14)	120.6(9)
C(14)-C(15)-H(15)	116.8(10)
C(16)-C(15)-C(14)	120.22(13)
C(16)-C(15)-H(15)	122.9(10)
C(15)-C(16)-H(16)	116.3(8)
C(15)-C(16)-C(17)	121.18(13)
C(17)-C(16)-H(16)	122.5(8)
C(16)-C(17)-H(17)	120.7(8)
C(18)-C(17)-C(16)	117.89(12)
C(18)-C(17)-H(17)	121.4(8)
C(13)-C(18)-N(2)	108.90(10)
C(17)-C(18)-N(2)	129.64(11)
C(17)-C(18)-C(13)	121.45(11)
N(2)-C(19)-C(12)	104.58(9)
N(2)-C(19)-H(19)	104.9(8)
N(3)-C(19)-N(2)	114.37(10)
N(3)-C(19)-C(12)	105.97(11)
N(3)-C(19)-H(19)	111.9(8)
C(12)-C(19)-H(19)	115.2(8)
N(3)-C(20)-H(20A)	109.9(9)
N(3)-C(20)-H(20B)	116.1(8)
N(3)-C(20)-C(21)	101.40(11)
H(20A)-C(20)-H(20B)	107.2(11)
C(21)-C(20)-H(20A)	113.9(9)
C(21)-C(20)-H(20B)	108.4(8)
C(12)-C(21)-H(21A)	110.3(8)
C(12)-C(21)-H(21B)	113.5(9)
C(20)-C(21)-C(12)	103.11(11)
C(20)-C(21)-H(21A)	108.7(8)
C(20)-C(21)-H(21B)	112.2(8)
H(21A)-C(21)-H(21B)	108.8(12)
O(3)-C(22)-N(2)	112.08(11)
O(4)-C(22)-O(3)	124.48(12)
O(4)-C(22)-N(2)	123.44(12)
O(3)-C(23)-H(23A)	112.0(11)
O(3)-C(23)-H(23B)	103.6(9)
O(3)-C(23)-H(23C)	107.6(9)
H(23A)-C(23)-H(23B)	106.2(13)
H(23A)-C(23)-H(23C)	112.2(13)
H(23B)-C(23)-H(23C)	115.1(12)

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Symmetry transformations used to generate equivalent atoms:

Table A2.8.4. *Anisotropic displacement parameters* ($Å^2 x 10^4$) *for* ***72***. *The anisotropic displacement factor exponent takes the form:* $-2p^2 [h^2 a*^2 U^{11} + ... + 2 h k a* b* U^{12}]$

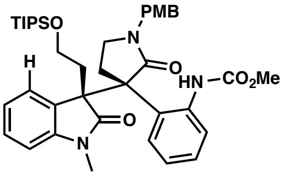
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	189(1)	189(1)	183(1)	-71(1)	-12(1)	-6(1)
O(1)	199(5)	132(5)	234(5)	-45(4)	54(4)	-35(4)
O(2)	251(5)	251(6)	230(5)	92(4)	159(4)	86(4)
O(3)	150(4)	180(5)	203(5)	-31(4)	41(4)	-51(3)
O(4)	139(4)	245(5)	136(4)	-30(4)	9(4)	8(4)
N(1)	123(5)	170(5)	100(5)	-24(4)	12(4)	-24(4)
N(2)	114(5)	152(5)	116(5)	-3(4)	26(4)	-17(4)
N(3)	163(6)	211(6)	235(6)	66(5)	-25(5)	12(5)
C(1)	110(5)	111(5)	115(5)	-8(4)	25(4)	-6(4)
C(2)	88(5)	125(6)	111(5)	6(4)	42(4)	0(4)
C(3)	108(5)	153(6)	143(6)	-18(5)	37(4)	-9(5)
C(4)	161(6)	126(6)	236(7)	6(5)	71(5)	-2(5)
C(5)	161(6)	181(7)	218(7)	86(5)	54(5)	38(5)
C(6)	124(6)	231(7)	134(6)	43(5)	30(5)	3(5)
C(7)	109(5)	158(6)	111(6)	-2(5)	49(4)	-19(4)
C(8)	114(6)	165(6)	126(6)	-23(5)	56(5)	-15(4)
C(9)	216(7)	265(8)	122(6)	-53(6)	-6(5)	-40(6)
C(10)	134(6)	151(6)	119(6)	20(5)	39(5)	9(5)
C(11)	160(6)	247(7)	188(7)	78(6)	91(5)	60(6)
C(12)	115(6)	135(6)	128(6)	-6(4)	45(5)	-1(4)
C(13)	121(6)	129(6)	142(6)	-3(5)	55(5)	11(4)
C(14)	144(6)	250(7)	165(6)	-53(5)	55(5)	-14(5)
C(15)	216(7)	320(8)	112(6)	-31(6)	57(5)	15(6)
C(16)	222(7)	242(7)	177(7)	32(6)	118(6)	20(6)
C(17)	153(6)	171(6)	191(7)	-5(5)	74(5)	-13(5)
C(18)	119(6)	128(6)	131(6)	-2(4)	40(5)	25(4)
C(19)	103(5)	172(6)	119(6)	19(5)	29(5)	4(5)
C(20)	158(7)	180(7)	362(9)	62(6)	77(6)	53(5)
C(21)	155(6)	137(6)	235(7)	-3(5)	78(5)	13(5)
C(22)	91(5)	142(6)	188(6)	-16(5)	28(5)	31(4)
C(23)	209(8)	299(8)	313(9)	-133(7)	93(7)	-119(6)

Table A2.8.5. *Hydrogen coordinates (x 10^3) and isotropic displacement parameters (Å^{2}x 10^3) for **72***

	x	y	z	U_{iso}
H(2)	241(2)	797(1)	452(2)	42(5)
H(3)	926(2)	813(1)	424(2)	37(5)
H(4)	383(2)	1013(1)	119(2)	20(4)
H(5)	219(2)	1005(1)	-136(2)	30(4)
H(6)	159(2)	925(1)	-249(2)	18(4)
H(9A)	172(2)	790(1)	-252(2)	33(5)
H(9B)	176(2)	840(1)	-332(2)	32(5)
H(9C)	44(2)	832(1)	-248(2)	36(5)
H(10A)	441(1)	798(1)	324(2)	9(3)
H(10B)	475(2)	850(1)	382(2)	21(4)
H(11A)	211(2)	869(1)	257(2)	26(4)
H(11B)	176(2)	814(1)	198(2)	21(4)
H(14)	539(2)	819(1)	-172(2)	21(4)
H(15)	645(2)	861(1)	-336(2)	23(4)
H(16)	856(2)	913(1)	-252(2)	15(4)
H(17)	963(2)	926(1)	20(2)	12(3)

H(19)	714(1)	867(1)	373(1)	7(3)
H(20A)	868(2)	738(1)	308(2)	23(4)
H(20B)	902(2)	777(1)	192(2)	15(4)
H(21A)	603(2)	756(1)	216(2)	10(3)
H(21B)	646(2)	758(1)	63(2)	18(4)
H(23A)	1111(2)	996(1)	442(2)	35(5)
H(23B)	1202(2)	990(1)	327(2)	21(4)
H(23C)	1226(2)	949(1)	470(2)	30(4)

A2.9. X-Ray Crystal Structure Analysis of 73



73

Figure A2.9.1. *X-ray Crystal Structure of **73***

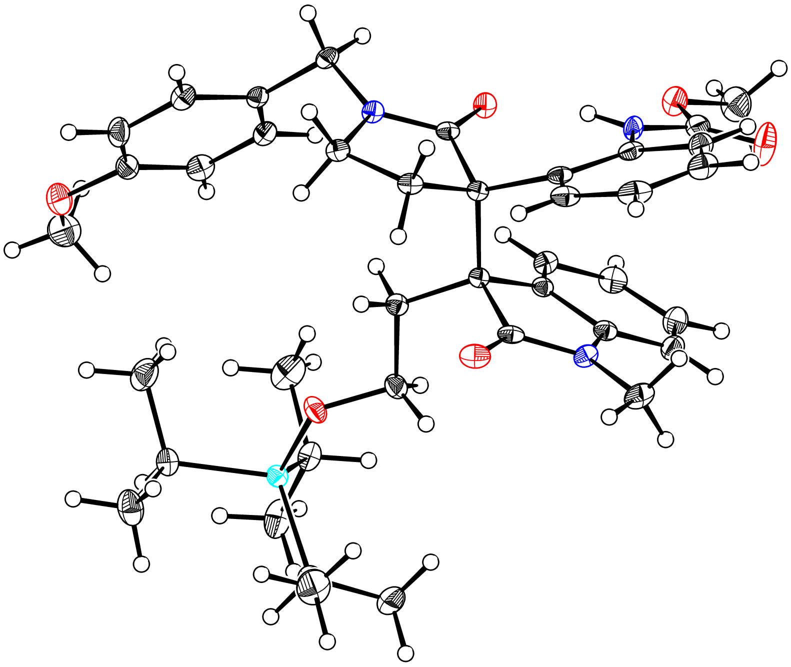


Table A2.9.1. *Crystal Data and Structure Analysis Details for **73***

Empirical formula	C40 H53 N3 O6 Si
Formula weight	699.94
Crystal shape	plate
Crystal color	colourless
Crystal size	0.04 x 0.20 x 0.20 mm

Data Collection

Preliminary photograph(s)	rotation
Type of diffractometer	Bruker APEX-II CCD
Wavelength	0.71073 Å MoK
Data collection temperature	100 K

Theta range for 9937 reflections used in lattice determination	2.40 to 30.23°	
Unit cell dimensions	a = 23.3177(12) Å b = 8.7021(4) Å c = 37.035(2) Å	a= 90° b= 94.394(3)° g = 90°
Volume	7492.8(7) Å^3	
Z	8	
Crystal system	monoclinic	
Space group	I 1 2/a 1 (# 15)	
Density (calculated)	1.241 g/cm^3	
F(000)	3008	
Theta range for data collection	2.4 to 35.0°	
Completeness to theta = 25.000°	99.9%	
Index ranges	-36 £ h £ 37, -13 £ k £ 13, -59 £ l £ 58	
Data collection scan type	and scans	
Reflections collected	146937	
Independent reflections	15890 [R_{int}= 0.1927]	
Reflections > 2s(I)	8277	
Average s(I)/(net I)	0.1381	
Absorption coefficient	0.11 mm^{-1}	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.9156	

Structure Solution and Refinement

Primary solution method	dual
Secondary solution method	?
Hydrogen placement	geom
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	15890 / 0 / 460
Treatment of hydrogen atoms	constr
Goodness-of-fit on F^2	1.25
Final R indices [I>2s(I), 8277 reflections]	R1 = 0.0718, wR2 = 0.1071
R indices (all data)	R1 = 0.1715, wR2 = 0.1233
Type of weighting scheme used	calc
Weighting scheme used	
Max shift/error	0.000
Average shift/error	0.000
Extinction coefficient	n/a
Largest diff. peak and hole	0.55 and -0.53 e·Å^{-3}

Programs Used

Cell refinement	SAINT V8.27B (Bruker-AXS, 2007)
Data collection	APEX2 2012.4-3 (Bruker-AXS, 2007)
Data reduction	SAINT V8.27B (Bruker-AXS, 2007)
Structure solution	SHELXT (Sheldrick, 2012)
Structure refinement	SHELXL-2013/2 (Sheldrick, 2013)
Graphics	DIAMOND 3 (Crystal Impact, 1999)

References

Special Refinement Details

Table A2.9.2. *Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **73**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor*

	x	y	z	U_{eq}
Si(1)	3732(1)	673(1)	2268(1)	13(1)
O(1)	2790(1)	-3775(1)	1228(1)	19(1)
O(2)	3562(1)	-65(1)	1866(1)	18(1)
O(3)	793(1)	2007(1)	470(1)	20(1)
O(4)	337(1)	-285(1)	450(1)	34(1)
O(5)	2274(1)	1556(1)	486(1)	16(1)
O(6)	5052(1)	5085(1)	1358(1)	26(1)
N(1)	1864(1)	-2960(1)	1280(1)	14(1)
N(2)	1318(1)	-73(1)	418(1)	14(1)
N(3)	3199(1)	803(1)	470(1)	13(1)
C(1)	2509(1)	-1080(2)	1090(1)	12(1)
C(2)	1946(1)	-370(2)	1189(1)	12(1)
C(3)	1770(1)	1145(2)	1210(1)	15(1)
C(4)	1220(1)	1458(2)	1310(1)	19(1)
C(5)	854(1)	271(2)	1390(1)	20(1)
C(6)	1027(1)	-1258(2)	1380(1)	18(1)
C(7)	1575(1)	-1538(2)	1283(1)	14(1)
C(8)	2421(1)	-2773(2)	1207(1)	13(1)
C(9)	1600(1)	-4446(2)	1329(1)	21(1)
C(10)	3042(1)	-416(2)	1301(1)	14(1)
C(11)	2999(1)	-378(2)	1707(1)	18(1)
C(12)	2572(1)	-1120(2)	660(1)	11(1)
C(13)	2066(1)	-2081(2)	478(1)	13(1)
C(14)	2184(1)	-3655(2)	434(1)	18(1)
C(15)	1776(1)	-4714(2)	307(1)	23(1)
C(16)	1224(1)	-4227(2)	207(1)	24(1)
C(17)	1084(1)	-2692(2)	246(1)	20(1)
C(18)	1491(1)	-1618(2)	387(1)	14(1)
C(19)	2649(1)	553(2)	526(1)	12(1)
C(20)	3583(1)	-490(2)	547(1)	14(1)
C(21)	3161(1)	-1825(2)	574(1)	14(1)
C(22)	776(1)	440(2)	446(1)	19(1)
C(23)	254(1)	2706(2)	538(1)	31(1)
C(24)	3582(1)	-777(2)	2628(1)	21(1)
C(25)	3734(1)	-2424(2)	2519(1)	34(1)
C(26)	2957(1)	-746(2)	2726(1)	29(1)
C(27)	3303(1)	2471(2)	2331(1)	19(1)

C(28)	3433(1)	3174(2)	2709(1)	28(1)
C(29)	3380(1)	3672(2)	2034(1)	31(1)
C(30)	4519(1)	1125(2)	2262(1)	17(1)
C(31)	4674(1)	1762(2)	1896(1)	28(1)
C(32)	4920(1)	-219(2)	2369(1)	28(1)
C(33)	3412(1)	2292(2)	352(1)	14(1)
C(34)	3837(1)	3026(2)	627(1)	13(1)
C(35)	4426(1)	2770(2)	618(1)	18(1)
C(36)	4818(1)	3460(2)	866(1)	21(1)
C(37)	4626(1)	4444(2)	1127(1)	18(1)
C(38)	4044(1)	4715(2)	1142(1)	19(1)
C(39)	3654(1)	3996(2)	894(1)	16(1)
C(40)	4878(1)	6187(2)	1612(1)	32(1)

Table A2.9.3. Bond lengths [Å] and angles [°] for **73**

_

Si(1)-O(2)	1.6433(11)
Si(1)-C(24)	1.8858(17)
Si(1)-C(27)	1.8806(17)
Si(1)-C(30)	1.8786(16)
O(1)-C(8)	1.2233(18)
O(2)-C(11)	1.4245(18)
O(3)-C(22)	1.367(2)
O(3)-C(23)	1.437(2)
O(4)-C(22)	1.2031(19)
O(5)-C(19)	1.2376(17)
O(6)-C(37)	1.3796(18)
O(6)-C(40)	1.425(2)
N(1)-C(7)	1.4092(19)
N(1)-C(8)	1.358(2)
N(1)-C(9)	1.4496(19)
N(2)-H(2)	0.8800
N(2)-C(18)	1.4106(19)
N(2)-C(22)	1.353(2)
N(3)-C(19)	1.3318(19)
N(3)-C(20)	1.4511(19)
N(3)-C(33)	1.4668(18)
C(1)-C(2)	1.519(2)
C(1)-C(8)	1.554(2)
C(1)-C(10)	1.530(2)
C(1)-C(12)	1.609(2)
C(2)-C(3)	1.385(2)
C(2)-C(7)	1.397(2)
C(3)-H(3)	0.9500
C(3)-C(4)	1.390(2)
C(4)-H(4)	0.9500
C(4)-C(5)	1.385(2)
C(5)-H(5)	0.9500
C(5)-C(6)	1.392(2)
C(6)-H(6)	0.9500
C(6)-C(7)	1.375(2)
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-H(10A)	0.9900

C(10)-H(10B)	0.9900
C(10)-C(11)	1.513(2)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(12)-C(13)	1.558(2)
C(12)-C(19)	1.553(2)
C(12)-C(21)	1.560(2)
C(13)-C(14)	1.409(2)
C(13)-C(18)	1.416(2)
C(14)-H(14)	0.9500
C(14)-C(15)	1.381(2)
C(15)-H(15)	0.9500
C(15)-C(16)	1.377(2)
C(16)-H(16)	0.9500
C(16)-C(17)	1.386(2)
C(17)-H(17)	0.9500
C(17)-C(18)	1.404(2)
C(20)-H(20A)	0.9900
C(20)-H(20B)	0.9900
C(20)-C(21)	1.529(2)
C(21)-H(21A)	0.9900
C(21)-H(21B)	0.9900
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
C(24)-H(24)	1.0000
C(24)-C(25)	1.537(2)
C(24)-C(26)	1.529(2)
C(25)-H(25A)	0.9800
C(25)-H(25B)	0.9800
C(25)-H(25C)	0.9800
C(26)-H(26A)	0.9800
C(26)-H(26B)	0.9800
C(26)-H(26C)	0.9800
C(27)-H(27)	1.0000
C(27)-C(28)	1.536(2)
C(27)-C(29)	1.538(2)
C(28)-H(28A)	0.9800
C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800
C(29)-H(29A)	0.9800
C(29)-H(29B)	0.9800
C(29)-H(29C)	0.9800
C(30)-H(30)	1.0000
C(30)-C(31)	1.533(2)
C(30)-C(32)	1.531(2)
C(31)-H(31A)	0.9800
C(31)-H(31B)	0.9800
C(31)-H(31C)	0.9800
C(32)-H(32A)	0.9800
C(32)-H(32B)	0.9800
C(32)-H(32C)	0.9800
C(33)-H(33A)	0.9900
C(33)-H(33B)	0.9900
C(33)-C(34)	1.507(2)
C(34)-C(35)	1.394(2)
C(34)-C(39)	1.391(2)
C(35)-H(35)	0.9500

C(35)-C(36)	1.383(2)
C(36)-H(36)	0.9500
C(36)-C(37)	1.389(2)
C(37)-C(38)	1.382(2)
C(38)-H(38)	0.9500
C(38)-C(39)	1.388(2)
C(39)-H(39)	0.9500
C(40)-H(40A)	0.9800
C(40)-H(40B)	0.9800
C(40)-H(40C)	0.9800

O(2)-Si(1)-C(24)	109.49(7)
O(2)-Si(1)-C(27)	110.14(7)
O(2)-Si(1)-C(30)	103.79(7)
C(27)-Si(1)-C(24)	109.92(8)
C(30)-Si(1)-C(24)	112.46(7)
C(30)-Si(1)-C(27)	110.87(7)
C(11)-O(2)-Si(1)	126.94(10)
C(22)-O(3)-C(23)	114.30(13)
C(37)-O(6)-C(40)	116.98(14)
C(7)-N(1)-C(9)	125.13(13)
C(8)-N(1)-C(7)	111.14(12)
C(8)-N(1)-C(9)	123.66(13)
C(18)-N(2)-H(2)	116.7
C(22)-N(2)-H(2)	116.7
C(22)-N(2)-C(18)	126.52(13)
C(19)-N(3)-C(20)	115.41(12)
C(19)-N(3)-C(33)	122.84(12)
C(20)-N(3)-C(33)	121.72(12)
C(2)-C(1)-C(8)	100.58(12)
C(2)-C(1)-C(10)	113.97(12)
C(2)-C(1)-C(12)	113.17(11)
C(8)-C(1)-C(12)	106.16(11)
C(10)-C(1)-C(8)	109.56(12)
C(10)-C(1)-C(12)	112.38(12)
C(3)-C(2)-C(1)	131.70(14)
C(3)-C(2)-C(7)	119.12(14)
C(7)-C(2)-C(1)	109.13(13)
C(2)-C(3)-H(3)	120.5
C(2)-C(3)-C(4)	119.00(15)
C(4)-C(3)-H(3)	120.5
C(3)-C(4)-H(4)	119.8
C(5)-C(4)-C(3)	120.47(15)
C(5)-C(4)-H(4)	119.8
C(4)-C(5)-H(5)	119.2
C(4)-C(5)-C(6)	121.55(15)
C(6)-C(5)-H(5)	119.2
C(5)-C(6)-H(6)	121.6
C(7)-C(6)-C(5)	116.89(15)
C(7)-C(6)-H(6)	121.6
C(2)-C(7)-N(1)	109.37(13)
C(6)-C(7)-N(1)	127.66(14)
C(6)-C(7)-C(2)	122.89(14)
O(1)-C(8)-N(1)	125.48(14)
O(1)-C(8)-C(1)	125.94(14)
N(1)-C(8)-C(1)	108.58(13)
N(1)-C(9)-H(9A)	109.5
N(1)-C(9)-H(9B)	109.5

N(1)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(1)-C(10)-H(10A)	108.8
C(1)-C(10)-H(10B)	108.8
H(10A)-C(10)-H(10B)	107.7
C(11)-C(10)-C(1)	113.76(13)
C(11)-C(10)-H(10A)	108.8
C(11)-C(10)-H(10B)	108.8
O(2)-C(11)-C(10)	106.68(13)
O(2)-C(11)-H(11A)	110.4
O(2)-C(11)-H(11B)	110.4
C(10)-C(11)-H(11A)	110.4
C(10)-C(11)-H(11B)	110.4
H(11A)-C(11)-H(11B)	108.6
C(13)-C(12)-C(1)	108.45(12)
C(13)-C(12)-C(21)	110.47(12)
C(19)-C(12)-C(1)	108.49(11)
C(19)-C(12)-C(13)	117.86(12)
C(19)-C(12)-C(21)	100.20(12)
C(21)-C(12)-C(1)	111.17(11)
C(14)-C(13)-C(12)	115.09(13)
C(14)-C(13)-C(18)	116.05(14)
C(18)-C(13)-C(12)	128.49(13)
C(13)-C(14)-H(14)	118.2
C(15)-C(14)-C(13)	123.52(16)
C(15)-C(14)-H(14)	118.2
C(14)-C(15)-H(15)	120.3
C(16)-C(15)-C(14)	119.42(16)
C(16)-C(15)-H(15)	120.3
C(15)-C(16)-H(16)	120.3
C(15)-C(16)-C(17)	119.44(15)
C(17)-C(16)-H(16)	120.3
C(16)-C(17)-H(17)	119.2
C(16)-C(17)-C(18)	121.51(16)
C(18)-C(17)-H(17)	119.2
N(2)-C(18)-C(13)	121.55(13)
C(17)-C(18)-N(2)	118.41(14)
C(17)-C(18)-C(13)	119.97(14)
O(5)-C(19)-N(3)	123.16(14)
O(5)-C(19)-C(12)	126.97(14)
N(3)-C(19)-C(12)	109.83(12)
N(3)-C(20)-H(20A)	111.3
N(3)-C(20)-H(20B)	111.3
N(3)-C(20)-C(21)	102.24(12)
H(20A)-C(20)-H(20B)	109.2
C(21)-C(20)-H(20A)	111.3
C(21)-C(20)-H(20B)	111.3
C(12)-C(21)-H(21A)	110.3
C(12)-C(21)-H(21B)	110.3
C(20)-C(21)-C(12)	107.14(12)
C(20)-C(21)-H(21A)	110.3
C(20)-C(21)-H(21B)	110.3
H(21A)-C(21)-H(21B)	108.5
O(4)-C(22)-O(3)	122.93(16)
O(4)-C(22)-N(2)	128.98(16)
N(2)-C(22)-O(3)	108.09(13)

O(3)-C(23)-H(23A)	109.5
O(3)-C(23)-H(23B)	109.5
O(3)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
Si(1)-C(24)-H(24)	107.6
C(25)-C(24)-Si(1)	112.36(12)
C(25)-C(24)-H(24)	107.6
C(26)-C(24)-Si(1)	112.77(11)
C(26)-C(24)-H(24)	107.6
C(26)-C(24)-C(25)	108.78(14)
C(24)-C(25)-H(25A)	109.5
C(24)-C(25)-H(25B)	109.5
C(24)-C(25)-H(25C)	109.5
H(25A)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25C)	109.5
H(25B)-C(25)-H(25C)	109.5
C(24)-C(26)-H(26A)	109.5
C(24)-C(26)-H(26B)	109.5
C(24)-C(26)-H(26C)	109.5
H(26A)-C(26)-H(26B)	109.5
H(26A)-C(26)-H(26C)	109.5
H(26B)-C(26)-H(26C)	109.5
Si(1)-C(27)-H(27)	107.0
C(28)-C(27)-Si(1)	111.98(12)
C(28)-C(27)-H(27)	107.0
C(28)-C(27)-C(29)	110.83(14)
C(29)-C(27)-Si(1)	112.62(12)
C(29)-C(27)-H(27)	107.0
C(27)-C(28)-H(28A)	109.5
C(27)-C(28)-H(28B)	109.5
C(27)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
C(27)-C(29)-H(29A)	109.5
C(27)-C(29)-H(29B)	109.5
C(27)-C(29)-H(29C)	109.5
H(29A)-C(29)-H(29B)	109.5
H(29A)-C(29)-H(29C)	109.5
H(29B)-C(29)-H(29C)	109.5
Si(1)-C(30)-H(30)	106.8
C(31)-C(30)-Si(1)	112.51(11)
C(31)-C(30)-H(30)	106.8
C(32)-C(30)-Si(1)	114.51(11)
C(32)-C(30)-H(30)	106.8
C(32)-C(30)-C(31)	108.92(14)
C(30)-C(31)-H(31A)	109.5
C(30)-C(31)-H(31B)	109.5
C(30)-C(31)-H(31C)	109.5
H(31A)-C(31)-H(31B)	109.5
H(31A)-C(31)-H(31C)	109.5
H(31B)-C(31)-H(31C)	109.5
C(30)-C(32)-H(32A)	109.5
C(30)-C(32)-H(32B)	109.5
C(30)-C(32)-H(32C)	109.5
H(32A)-C(32)-H(32B)	109.5

H(32A)-C(32)-H(32C)	109.5
H(32B)-C(32)-H(32C)	109.5
N(3)-C(33)-H(33A)	109.0
N(3)-C(33)-H(33B)	109.0
N(3)-C(33)-C(34)	113.08(12)
H(33A)-C(33)-H(33B)	107.8
C(34)-C(33)-H(33A)	109.0
C(34)-C(33)-H(33B)	109.0
C(35)-C(34)-C(33)	120.88(14)
C(39)-C(34)-C(33)	121.12(14)
C(39)-C(34)-C(35)	117.99(14)
C(34)-C(35)-H(35)	119.4
C(36)-C(35)-C(34)	121.12(15)
C(36)-C(35)-H(35)	119.4
C(35)-C(36)-H(36)	120.1
C(35)-C(36)-C(37)	119.81(15)
C(37)-C(36)-H(36)	120.1
O(6)-C(37)-C(36)	115.14(15)
O(6)-C(37)-C(38)	124.72(15)
C(38)-C(37)-C(36)	120.14(15)
C(37)-C(38)-H(38)	120.3
C(37)-C(38)-C(39)	119.46(15)
C(39)-C(38)-H(38)	120.3
C(34)-C(39)-H(39)	119.3
C(38)-C(39)-C(34)	121.46(15)
C(38)-C(39)-H(39)	119.3
O(6)-C(40)-H(40A)	109.5
O(6)-C(40)-H(40B)	109.5
O(6)-C(40)-H(40C)	109.5
H(40A)-C(40)-H(40B)	109.5
H(40A)-C(40)-H(40C)	109.5
H(40B)-C(40)-H(40C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table A2.9.4. *Anisotropic displacement parameters ($Å^2 \times 10^4$) for **73**. The anisotropic displacement factor exponent takes the form: $-2p^2 [h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$*

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Si(1)	140(2)	116(2)	135(2)	-12(2)	-3(2)	-6(2)
O(1)	266(6)	110(6)	194(6)	21(4)	21(5)	56(5)
O(2)	148(6)	238(6)	160(6)	-47(5)	-28(5)	6(5)
O(3)	166(6)	153(6)	292(7)	27(5)	31(5)	30(5)
O(4)	176(7)	275(7)	581(10)	-33(7)	54(6)	-87(6)
O(5)	154(6)	93(5)	220(6)	19(4)	7(5)	9(4)
O(6)	238(7)	285(7)	265(7)	-39(5)	-34(5)	-83(6)
N(1)	184(7)	74(6)	169(7)	7(5)	26(5)	-15(5)
N(2)	131(7)	104(6)	192(7)	9(5)	3(5)	-40(5)
N(3)	144(7)	68(6)	167(6)	14(5)	13(5)	5(5)
C(1)	132(7)	96(7)	117(7)	-3(6)	7(6)	0(6)
C(2)	142(8)	120(8)	102(7)	-10(6)	-1(6)	-8(6)
C(3)	181(8)	120(8)	151(8)	-15(6)	22(6)	-9(6)
C(4)	223(9)	149(8)	192(8)	-26(6)	29(7)	46(7)
C(5)	163(8)	221(9)	228(9)	-17(7)	53(7)	30(7)

C(6)	183(9)	184(9)	182(8)	0(6)	30(7)	-44(7)
C(7)	179(8)	117(8)	110(7)	-9(6)	-6(6)	-6(6)
C(8)	222(9)	92(7)	86(7)	-9(6)	2(6)	8(6)
C(9)	306(10)	103(8)	230(9)	16(7)	47(7)	-59(7)
C(10)	158(8)	136(8)	139(7)	-9(6)	4(6)	-4(6)
C(11)	164(8)	206(9)	153(8)	-24(6)	-15(6)	-19(7)
C(12)	143(8)	75(7)	117(7)	-6(5)	4(6)	4(6)
C(13)	215(8)	87(7)	94(7)	5(6)	13(6)	-23(6)
C(14)	279(9)	122(8)	123(8)	-3(6)	8(7)	-14(7)
C(15)	412(11)	106(8)	165(8)	-31(6)	36(8)	-64(8)
C(16)	362(11)	167(9)	189(9)	-36(7)	10(8)	-149(8)
C(17)	221(9)	201(9)	169(8)	-19(7)	5(7)	-78(7)
C(18)	219(8)	115(8)	103(7)	-1(6)	28(6)	-44(6)
C(19)	178(8)	90(7)	85(7)	-16(5)	6(6)	-11(6)
C(20)	151(8)	137(8)	150(7)	9(6)	31(6)	37(6)
C(21)	196(8)	84(7)	134(7)	-6(6)	18(6)	25(6)
C(22)	202(9)	208(9)	162(8)	10(7)	-8(7)	-47(7)
C(23)	218(10)	308(11)	402(12)	41(9)	43(8)	87(8)
C(24)	216(9)	186(9)	209(8)	36(7)	-21(7)	-49(7)
C(25)	378(12)	160(9)	488(13)	99(9)	-31(10)	-54(8)
C(26)	284(10)	310(10)	265(10)	55(8)	31(8)	-112(8)
C(27)	163(8)	170(9)	240(9)	-27(7)	47(7)	-15(7)
C(28)	233(10)	234(10)	378(11)	-146(8)	87(8)	-49(8)
C(29)	299(10)	205(10)	443(12)	72(8)	128(9)	89(8)
C(30)	147(8)	146(8)	211(8)	-31(6)	7(7)	2(6)
C(31)	200(9)	309(11)	341(11)	33(8)	94(8)	23(8)
C(32)	189(9)	215(9)	412(12)	4(8)	-35(8)	35(7)
C(33)	161(8)	92(7)	169(8)	30(6)	32(6)	-11(6)
C(34)	142(8)	91(7)	164(8)	29(6)	17(6)	0(6)
C(35)	170(8)	152(8)	211(8)	2(7)	50(7)	20(7)
C(36)	121(8)	237(9)	285(10)	19(7)	18(7)	16(7)
C(37)	185(8)	140(8)	206(8)	27(7)	-19(7)	-44(7)
C(38)	241(9)	117(8)	205(8)	-13(6)	34(7)	-7(7)
C(39)	146(8)	119(8)	207(8)	33(6)	43(6)	27(6)
C(40)	406(12)	303(11)	260(10)	-76(8)	-16(9)	-120(9)

Table A2.9.5. *Hydrogen coordinates (x 10^3) and isotropic displacement parameters (Å^{2}x 10^3) for* ***73***

	x	y	z	U_{iso}
H(2)	159	63	42	17
H(3)	202	196	116	18
H(4)	109	249	132	22
H(5)	48	51	145	24
H(6)	78	-207	144	22
H(9A)	135	-470	111	32
H(9B)	137	-441	154	32
H(9C)	190	-523	137	32
H(10A)	338	-104	125	17
H(10B)	311	64	122	17
H(11A)	273	44	177	21
H(11B)	286	-138	179	21
H(14)	256	-401	50	21
H(15)	187	-577	29	27

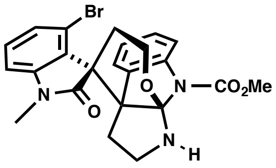
H(16)	94	-494	11	29
H(17)	70	-236	18	24
H(20A)	382	-34	78	17
H(20B)	384	-65	35	17
H(21A)	330	-254	77	17
H(21B)	312	-240	34	17
H(23A)	-3	250	33	46
H(23B)	31	382	57	46
H(23C)	12	228	76	46
H(24)	383	-51	285	25
H(25A)	367	-313	272	52
H(25B)	414	-246	246	52
H(25C)	349	-273	231	52
H(26A)	270	-96	251	43
H(26B)	287	27	282	43
H(26C)	290	-153	291	43
H(27)	289	217	231	23
H(28A)	384	351	274	42
H(28B)	337	240	289	42
H(28C)	318	406	274	42
H(29A)	311	451	206	47
H(29B)	331	319	180	47
H(29C)	377	408	206	47
H(30)	460	196	244	20
H(31A)	508	203	191	42
H(31B)	444	268	184	42
H(31C)	460	98	171	42
H(32A)	485	-106	220	41
H(32B)	484	-58	261	41
H(32C)	532	12	237	41
H(33A)	308	300	30	17
H(33B)	360	215	12	17
H(35)	456	211	44	21
H(36)	522	326	86	26
H(38)	391	539	132	22
H(39)	326	417	91	19
H(40A)	468	704	148	49
H(40B)	522	658	176	49
H(40C)	462	570	177	49

Table A2.9.6. *Hydrogen bonds for* ***73*** *[**Å and °**]*

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2)...O(5)	0.88	1.79	2.6356(16)	161.8
C(17)-H(17)...O(4)	0.95	2.27	2.862(2)	119.8
C(21)-H(21A)...O(1)	0.99	2.41	3.1343(19)	129.8

Symmetry transformations used to generate equivalent atoms:

A2.10. X-Ray Crystal Structure Analysis of 77



77

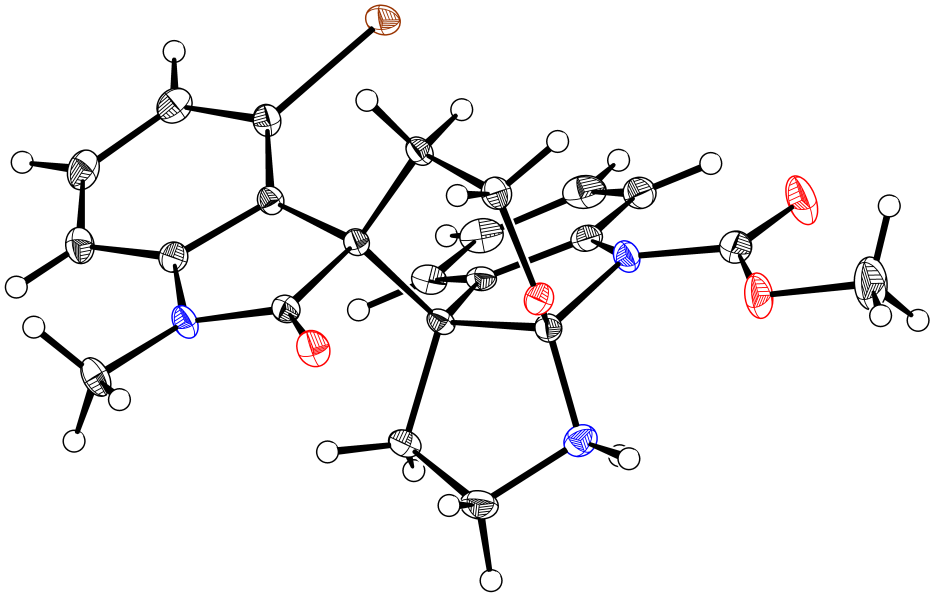


Figure A2.10.1. *X-ray Crystal Structure of **77***

Table A2.10.1. *Crystal data and structure analysis details for **77***

Empirical formula	C46.40 H47.20 Br2 Cl0.80 N6 O8.20
Formula weight	1008.40
Crystallization solvent	isopropanol/hexane (dichloromethane)
Crystal shape	plate
Crystal color	colourless
Crystal size	0.05 x 0.20 x 0.46 mm

Data Collection

Preliminary photograph(s)	rotation
Type of diffractometer	Bruker APEX-II CCD
Wavelength	0.71073 Å MoK

Data collection temperature	100 K	
Theta range for 9880 reflections used in lattice determination	2.32 to 33.69°	
Unit cell dimensions	a = 17.6618(8) Å b = 17.4368(7) Å c = 13.5068(5) Å	〈= 90° ®= 96.873(2)° © = 90°
Volume	4129.7(3) Å^3	
Z	4	
Crystal system	monoclinic	
Space group	P 1 21/c 1 (# 14)	
Density (calculated)	1.622 g/cm^3	
F(000)	2067	
Theta range for data collection	2.1 to 37.6°	
Completeness to theta = 25.000°	99.9%	
Index ranges	-29 ″ h ″ 30, -29 ″ k ″ 29, -23 ″ l ″ 22	
Data collection scan type	and scans	
Reflections collected	213592	
Independent reflections	21060 [R$_{int}$= 0.0668]	
Reflections > 2 ⌠(I)	14742	
Average ⌠(I)/(net I)	0.0422	
Absorption coefficient	2.08 mm^{-1}	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.8480	

Structure Solution and Refinement

Primary solution method	dual
Secondary solution method	?
Hydrogen placement	mixed
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	21060 / 3 / 592
Treatment of hydrogen atoms	mixed
Goodness-of-fit on F^2	3.31
Final R indices [I>2⌠(I), 14742 reflections]	R1 = 0.0585, wR2 = 0.0955
R indices (all data)	R1 = 0.0953, wR2 = 0.0967
Type of weighting scheme used	calc
Weighting scheme used	
Max shift/error	0.002
Average shift/error	0.000
Extinction coefficient	0
Largest diff. peak and hole	3.94 and -2.05 e·Å^{-3}

Programs Used

Cell refinement	SAINT V8.27B (Bruker-AXS, 2007)
Data collection	APEX2 2012.4-3 (Bruker-AXS, 2007)
Data reduction	SAINT V8.27B (Bruker-AXS, 2007)
Structure solution	SHELXT (Sheldrick, 2012)
Structure refinement	SHELXL-2012/6 (Sheldrick, 2012)
Graphics	DIAMOND 3 (Crystal Impact, 1999)

References

Special Refinement Details

Table A2.10.2. *Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **77**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor*

	x	y	z	U_{eq}
Br(1A)	4275(1)	4155(1)	4546(1)	17(1)
O(1A)	4849(1)	1093(1)	2821(1)	18(1)
O(2A)	3534(1)	1156(1)	3905(1)	14(1)
O(3A)	1677(1)	2261(1)	5024(1)	28(1)
O(4A)	2118(1)	1113(1)	4589(1)	24(1)
N(1A)	5279(1)	2188(1)	2142(1)	14(1)
N(2A)	2640(1)	2178(1)	4034(1)	14(1)
N(3A)	2591(1)	1331(1)	2600(1)	17(1)
C(1A)	4767(1)	3863(1)	3418(1)	14(1)
C(2A)	5155(1)	4451(1)	2990(1)	18(1)
C(3A)	5568(1)	4292(1)	2204(1)	20(1)
C(4A)	5638(1)	3544(1)	1865(1)	17(1)
C(5A)	5246(1)	2978(1)	2315(1)	14(1)
C(6A)	4769(1)	3120(1)	3055(1)	12(1)
C(7A)	4390(1)	2370(1)	3293(1)	11(1)
C(8A)	4859(1)	1789(1)	2758(1)	13(1)
C(9A)	5816(1)	1822(1)	1554(1)	19(1)
C(10A)	4427(1)	2208(1)	4414(1)	13(1)
C(11A)	4123(1)	1422(1)	4643(1)	16(1)
C(12A)	3085(1)	1712(1)	3373(1)	13(1)
C(13A)	3527(1)	2321(1)	2811(1)	11(1)
C(14A)	3397(1)	2045(1)	1702(1)	15(1)
C(15A)	3031(1)	1255(1)	1744(1)	20(1)
C(16A)	3091(1)	3045(1)	2962(1)	12(1)
C(17A)	2609(1)	2950(1)	3695(1)	14(1)
C(18A)	2158(1)	3551(1)	3966(1)	18(1)
C(19A)	2193(1)	4244(1)	3462(1)	21(1)
C(20A)	2647(1)	4337(1)	2706(1)	20(1)
C(21A)	3102(1)	3731(1)	2452(1)	16(1)
C(22A)	2101(1)	1885(1)	4585(1)	19(1)
C(23A)	1594(2)	770(1)	5202(2)	34(1)
Br(1B)	7671(1)	4207(1)	1850(1)	25(1)
O(1B)	9584(1)	1388(1)	2258(1)	28(1)
O(2B)	8160(1)	1198(1)	2987(1)	20(1)
O(3B)	6232(1)	1864(1)	4406(1)	29(1)

O(4B)	6979(1)	869(1)	4083(1)	23(1)
N(1B)	10134(1)	2569(1)	2268(1)	19(1)
N(2B)	7383(1)	2057(1)	3810(1)	18(1)
N(3B)	8495(1)	1439(1)	4657(1)	22(1)
C(1B)	8749(1)	4072(1)	2061(1)	21(1)
C(2B)	9187(2)	4725(1)	1973(2)	29(1)
C(3B)	9977(2)	4672(1)	2042(2)	32(1)
C(4B)	10341(1)	3971(1)	2150(2)	25(1)
C(5B)	9885(1)	3336(1)	2235(1)	20(1)
C(6B)	9091(1)	3365(1)	2251(1)	17(1)
C(7B)	8814(1)	2560(1)	2462(1)	16(1)
C(8B)	9533(1)	2080(1)	2309(1)	19(1)
C(9B)	10900(1)	2317(1)	2149(2)	29(1)
C(10B)	8104(1)	2283(1)	1797(1)	18(1)
C(11B)	7945(1)	1441(1)	1974(1)	21(1)
C(12B)	8160(1)	1753(1)	3723(1)	16(1)
C(13B)	8665(1)	2476(1)	3597(1)	16(1)
C(14B)	9393(1)	2339(1)	4357(1)	20(1)
C(15B)	9317(1)	1506(1)	4664(1)	22(1)
C(16B)	8167(1)	3112(1)	3924(1)	17(1)
C(17B)	7437(1)	2860(1)	4005(1)	17(1)
C(18B)	6878(1)	3355(1)	4264(1)	22(1)
C(19B)	7080(1)	4112(1)	4481(1)	24(1)
C(20B)	7819(2)	4353(1)	4474(1)	27(1)
C(21B)	8373(1)	3854(1)	4203(1)	22(1)
C(22B)	6812(1)	1614(1)	4130(1)	20(1)
C(23B)	6407(1)	360(1)	4393(2)	26(1)
Cl(1)	10468(1)	4314(1)	5067(1)	59(1)
C(1)	9892(3)	4837(3)	5573(4)	28(1)
O(1)	9448(4)	4184(4)	5213(5)	16(2)

Table A2.10.3. Bond lengths [Å] and angles [°] for **77**

_

Br(1A)-C(1A)	1.9116(18)
O(1A)-C(8A)	1.217(2)
O(2A)-C(11A)	1.430(2)
O(2A)-C(12A)	1.396(2)
O(3A)-C(22A)	1.204(2)
O(4A)-C(22A)	1.345(2)
O(4A)-C(23A)	1.443(2)
N(1A)-C(5A)	1.398(2)
N(1A)-C(8A)	1.370(2)
N(1A)-C(9A)	1.455(2)
N(2A)-C(12A)	1.496(2)
N(2A)-C(17A)	1.421(2)
N(2A)-C(22A)	1.376(2)
N(3A)-H(3AA)	0.9200
N(3A)-H(3AB)	0.9200
N(3A)-C(12A)	1.440(2)
N(3A)-C(15A)	1.475(2)
C(1A)-C(2A)	1.397(3)
C(1A)-C(6A)	1.385(2)
C(2A)-H(2A)	0.9500
C(2A)-C(3A)	1.386(3)
C(3A)-H(3A)	0.9500

C(3A)-C(4A)	1.392(3)
C(4A)-H(4A)	0.9500
C(4A)-C(5A)	1.387(2)
C(5A)-C(6A)	1.405(2)
C(6A)-C(7A)	1.520(2)
C(7A)-C(8A)	1.543(2)
C(7A)-C(10A)	1.534(2)
C(7A)-C(13A)	1.586(3)
C(9A)-H(9AA)	0.9800
C(9A)-H(9AB)	0.9800
C(9A)-H(9AC)	0.9800
C(10A)-H(10A)	0.9900
C(10A)-H(10B)	0.9900
C(10A)-C(11A)	1.517(2)
C(11A)-H(11A)	0.9900
C(11A)-H(11B)	0.9900
C(12A)-C(13A)	1.567(2)
C(13A)-C(14A)	1.564(2)
C(13A)-C(16A)	1.504(2)
C(14A)-H(14A)	0.9900
C(14A)-H(14B)	0.9900
C(14A)-C(15A)	1.524(3)
C(15A)-H(15A)	0.9900
C(15A)-H(15B)	0.9900
C(16A)-C(17A)	1.392(3)
C(16A)-C(21A)	1.383(2)
C(17A)-C(18A)	1.391(3)
C(18A)-H(18A)	0.9500
C(18A)-C(19A)	1.392(3)
C(19A)-H(19A)	0.9500
C(19A)-C(20A)	1.381(3)
C(20A)-H(20A)	0.9500
C(20A)-C(21A)	1.394(3)
C(21A)-H(21A)	0.9500
C(23A)-H(23A)	0.9800
C(23A)-H(23B)	0.9800
C(23A)-H(23C)	0.9800
Br(1B)-C(1B)	1.906(2)
O(1B)-C(8B)	1.212(2)
O(2B)-C(11B)	1.439(2)
O(2B)-C(12B)	1.387(2)
O(3B)-C(22B)	1.212(2)
O(4B)-C(22B)	1.336(2)
O(4B)-C(23B)	1.444(2)
N(1B)-C(5B)	1.407(2)
N(1B)-C(8B)	1.368(3)
N(1B)-C(9B)	1.449(3)
N(2B)-C(12B)	1.489(3)
N(2B)-C(17B)	1.426(2)
N(2B)-C(22B)	1.379(3)
N(3B)-H(3BA)	0.9200
N(3B)-H(3BB)	0.9200
N(3B)-C(12B)	1.436(2)
N(3B)-C(15B)	1.456(3)
C(1B)-C(2B)	1.389(3)
C(1B)-C(6B)	1.383(3)
C(2B)-H(2B)	0.9500
C(2B)-C(3B)	1.390(3)

C(3B)-H(3B)	0.9500
C(3B)-C(4B)	1.380(3)
C(4B)-H(4B)	0.9500
C(4B)-C(5B)	1.381(3)
C(5B)-C(6B)	1.407(3)
C(6B)-C(7B)	1.524(3)
C(7B)-C(8B)	1.556(3)
C(7B)-C(10B)	1.532(3)
C(7B)-C(13B)	1.592(3)
C(9B)-H(9BA)	0.9800
C(9B)-H(9BB)	0.9800
C(9B)-H(9BC)	0.9800
C(10B)-H(10C)	0.9900
C(10B)-H(10D)	0.9900
C(10B)-C(11B)	1.519(3)
C(11B)-H(11C)	0.9900
C(11B)-H(11D)	0.9900
C(12B)-C(13B)	1.567(3)
C(13B)-C(14B)	1.565(3)
C(13B)-C(16B)	1.515(3)
C(14B)-H(14C)	0.9900
C(14B)-H(14D)	0.9900
C(14B)-C(15B)	1.521(3)
C(15B)-H(15C)	0.9900
C(15B)-H(15D)	0.9900
C(16B)-C(17B)	1.379(3)
C(16B)-C(21B)	1.384(3)
C(17B)-C(18B)	1.386(3)
C(18B)-H(18B)	0.9500
C(18B)-C(19B)	1.388(3)
C(19B)-H(19B)	0.9500
C(19B)-C(20B)	1.373(3)
C(20B)-H(20B)	0.9500
C(20B)-C(21B)	1.391(3)
C(21B)-H(21B)	0.9500
C(23B)-H(23D)	0.9800
C(23B)-H(23E)	0.9800
C(23B)-H(23F)	0.9800
Cl(1)-C(1)#1	1.794(6)
Cl(1)-C(1)	1.581(6)
C(1)-Cl(1)#1	1.794(6)
C(1)-C(1)#1	1.734(10)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
O(1)-H(1C)	0.848(10)
O(1)-H(1D)	0.855(10)

C(12A)-O(2A)-C(11A)	116.99(13)
C(22A)-O(4A)-C(23A)	113.72(16)
C(5A)-N(1A)-C(9A)	124.50(16)
C(8A)-N(1A)-C(5A)	111.22(14)
C(8A)-N(1A)-C(9A)	122.96(15)
C(17A)-N(2A)-C(12A)	108.96(13)
C(22A)-N(2A)-C(12A)	124.67(15)
C(22A)-N(2A)-C(17A)	121.53(16)
H(3AA)-N(3A)-H(3AB)	108.7
C(12A)-N(3A)-H(3AA)	110.5
C(12A)-N(3A)-H(3AB)	110.5

C(12A)-N(3A)-C(15A)	106.25(15)
C(15A)-N(3A)-H(3AA)	110.5
C(15A)-N(3A)-H(3AB)	110.5
C(2A)-C(1A)-Br(1A)	115.20(13)
C(6A)-C(1A)-Br(1A)	123.47(13)
C(6A)-C(1A)-C(2A)	121.29(17)
C(1A)-C(2A)-H(2A)	120.1
C(3A)-C(2A)-C(1A)	119.89(17)
C(3A)-C(2A)-H(2A)	120.1
C(2A)-C(3A)-H(3A)	119.5
C(2A)-C(3A)-C(4A)	120.96(17)
C(4A)-C(3A)-H(3A)	119.5
C(3A)-C(4A)-H(4A)	121.5
C(5A)-C(4A)-C(3A)	117.09(17)
C(5A)-C(4A)-H(4A)	121.5
N(1A)-C(5A)-C(6A)	109.47(15)
C(4A)-C(5A)-N(1A)	126.49(17)
C(4A)-C(5A)-C(6A)	123.99(16)
C(1A)-C(6A)-C(5A)	116.32(16)
C(1A)-C(6A)-C(7A)	135.22(16)
C(5A)-C(6A)-C(7A)	108.41(14)
C(6A)-C(7A)-C(8A)	101.00(14)
C(6A)-C(7A)-C(10A)	113.54(14)
C(6A)-C(7A)-C(13A)	112.66(14)
C(8A)-C(7A)-C(13A)	108.40(14)
C(10A)-C(7A)-C(8A)	112.28(14)
C(10A)-C(7A)-C(13A)	108.74(14)
O(1A)-C(8A)-N(1A)	124.26(16)
O(1A)-C(8A)-C(7A)	127.54(16)
N(1A)-C(8A)-C(7A)	108.13(14)
N(1A)-C(9A)-H(9AA)	109.5
N(1A)-C(9A)-H(9AB)	109.5
N(1A)-C(9A)-H(9AC)	109.5
H(9AA)-C(9A)-H(9AB)	109.5
H(9AA)-C(9A)-H(9AC)	109.5
H(9AB)-C(9A)-H(9AC)	109.5
C(7A)-C(10A)-H(10A)	109.0
C(7A)-C(10A)-H(10B)	109.0
H(10A)-C(10A)-H(10B)	107.8
C(11A)-C(10A)-C(7A)	113.14(14)
C(11A)-C(10A)-H(10A)	109.0
C(11A)-C(10A)-H(10B)	109.0
O(2A)-C(11A)-C(10A)	113.43(14)
O(2A)-C(11A)-H(11A)	108.9
O(2A)-C(11A)-H(11B)	108.9
C(10A)-C(11A)-H(11A)	108.9
C(10A)-C(11A)-H(11B)	108.9
H(11A)-C(11A)-H(11B)	107.7
O(2A)-C(12A)-N(2A)	112.12(14)
O(2A)-C(12A)-N(3A)	108.01(14)
O(2A)-C(12A)-C(13A)	115.79(15)
N(2A)-C(12A)-C(13A)	104.45(13)
N(3A)-C(12A)-N(2A)	111.50(16)
N(3A)-C(12A)-C(13A)	104.77(14)
C(12A)-C(13A)-C(7A)	110.33(14)
C(14A)-C(13A)-C(7A)	115.73(14)
C(14A)-C(13A)-C(12A)	103.34(13)
C(16A)-C(13A)-C(7A)	112.41(14)

C(16A)-C(13A)-C(12A)	102.11(14)
C(16A)-C(13A)-C(14A)	111.64(14)
C(13A)-C(14A)-H(14A)	110.8
C(13A)-C(14A)-H(14B)	110.8
H(14A)-C(14A)-H(14B)	108.8
C(15A)-C(14A)-C(13A)	104.90(14)
C(15A)-C(14A)-H(14A)	110.8
C(15A)-C(14A)-H(14B)	110.8
N(3A)-C(15A)-C(14A)	102.31(14)
N(3A)-C(15A)-H(15A)	111.3
N(3A)-C(15A)-H(15B)	111.3
C(14A)-C(15A)-H(15A)	111.3
C(14A)-C(15A)-H(15B)	111.3
H(15A)-C(15A)-H(15B)	109.2
C(17A)-C(16A)-C(13A)	111.31(15)
C(21A)-C(16A)-C(13A)	128.41(16)
C(21A)-C(16A)-C(17A)	120.22(17)
C(16A)-C(17A)-N(2A)	109.75(15)
C(18A)-C(17A)-N(2A)	129.11(17)
C(18A)-C(17A)-C(16A)	121.06(17)
C(17A)-C(18A)-H(18A)	121.1
C(17A)-C(18A)-C(19A)	117.73(18)
C(19A)-C(18A)-H(18A)	121.1
C(18A)-C(19A)-H(19A)	119.1
C(20A)-C(19A)-C(18A)	121.80(18)
C(20A)-C(19A)-H(19A)	119.1
C(19A)-C(20A)-H(20A)	120.1
C(19A)-C(20A)-C(21A)	119.74(18)
C(21A)-C(20A)-H(20A)	120.1
C(16A)-C(21A)-C(20A)	119.37(18)
C(16A)-C(21A)-H(21A)	120.3
C(20A)-C(21A)-H(21A)	120.3
O(3A)-C(22A)-O(4A)	123.93(18)
O(3A)-C(22A)-N(2A)	125.17(18)
O(4A)-C(22A)-N(2A)	110.89(17)
O(4A)-C(23A)-H(23A)	109.5
O(4A)-C(23A)-H(23B)	109.5
O(4A)-C(23A)-H(23C)	109.5
H(23A)-C(23A)-H(23B)	109.5
H(23A)-C(23A)-H(23C)	109.5
H(23B)-C(23A)-H(23C)	109.5
C(12B)-O(2B)-C(11B)	116.97(14)
C(22B)-O(4B)-C(23B)	114.79(16)
C(5B)-N(1B)-C(9B)	125.24(17)
C(8B)-N(1B)-C(5B)	110.68(17)
C(8B)-N(1B)-C(9B)	123.67(17)
C(17B)-N(2B)-C(12B)	108.85(16)
C(22B)-N(2B)-C(12B)	122.68(15)
C(22B)-N(2B)-C(17B)	121.78(16)
H(3BA)-N(3B)-H(3BB)	108.6
C(12B)-N(3B)-H(3BA)	110.5
C(12B)-N(3B)-H(3BB)	110.5
C(12B)-N(3B)-C(15B)	106.38(15)
C(15B)-N(3B)-H(3BA)	110.5
C(15B)-N(3B)-H(3BB)	110.5
C(2B)-C(1B)-Br(1B)	116.23(17)
C(6B)-C(1B)-Br(1B)	122.96(16)
C(6B)-C(1B)-C(2B)	120.8(2)

C(1B)-C(2B)-H(2B)	119.9
C(1B)-C(2B)-C(3B)	120.3(2)
C(3B)-C(2B)-H(2B)	119.9
C(2B)-C(3B)-H(3B)	119.5
C(4B)-C(3B)-C(2B)	121.1(2)
C(4B)-C(3B)-H(3B)	119.5
C(3B)-C(4B)-H(4B)	121.6
C(3B)-C(4B)-C(5B)	116.8(2)
C(5B)-C(4B)-H(4B)	121.6
C(4B)-C(5B)-N(1B)	125.6(2)
C(4B)-C(5B)-C(6B)	124.3(2)
C(6B)-C(5B)-N(1B)	110.01(17)
C(1B)-C(6B)-C(5B)	116.31(18)
C(1B)-C(6B)-C(7B)	135.46(19)
C(5B)-C(6B)-C(7B)	108.21(16)
C(6B)-C(7B)-C(8B)	100.70(15)
C(6B)-C(7B)-C(10B)	116.13(16)
C(6B)-C(7B)-C(13B)	110.98(15)
C(8B)-C(7B)-C(13B)	108.03(15)
C(10B)-C(7B)-C(8B)	112.10(15)
C(10B)-C(7B)-C(13B)	108.51(16)
O(1B)-C(8B)-N(1B)	123.69(19)
O(1B)-C(8B)-C(7B)	127.66(19)
N(1B)-C(8B)-C(7B)	108.63(16)
N(1B)-C(9B)-H(9BA)	109.5
N(1B)-C(9B)-H(9BB)	109.5
N(1B)-C(9B)-H(9BC)	109.5
H(9BA)-C(9B)-H(9BB)	109.5
H(9BA)-C(9B)-H(9BC)	109.5
H(9BB)-C(9B)-H(9BC)	109.5
C(7B)-C(10B)-H(10C)	109.3
C(7B)-C(10B)-H(10D)	109.3
H(10C)-C(10B)-H(10D)	108.0
C(11B)-C(10B)-C(7B)	111.50(16)
C(11B)-C(10B)-H(10C)	109.3
C(11B)-C(10B)-H(10D)	109.3
O(2B)-C(11B)-C(10B)	113.68(15)
O(2B)-C(11B)-H(11C)	108.8
O(2B)-C(11B)-H(11D)	108.8
C(10B)-C(11B)-H(11C)	108.8
C(10B)-C(11B)-H(11D)	108.8
H(11C)-C(11B)-H(11D)	107.7
O(2B)-C(12B)-N(2B)	112.64(16)
O(2B)-C(12B)-N(3B)	109.16(15)
O(2B)-C(12B)-C(13B)	115.73(15)
N(2B)-C(12B)-C(13B)	105.33(14)
N(3B)-C(12B)-N(2B)	110.71(15)
N(3B)-C(12B)-C(13B)	102.81(16)
C(12B)-C(13B)-C(7B)	109.92(15)
C(14B)-C(13B)-C(7B)	115.40(16)
C(14B)-C(13B)-C(12B)	103.86(15)
C(16B)-C(13B)-C(7B)	112.48(15)
C(16B)-C(13B)-C(12B)	101.45(16)
C(16B)-C(13B)-C(14B)	112.39(15)
C(13B)-C(14B)-H(14C)	111.1
C(13B)-C(14B)-H(14D)	111.1
H(14C)-C(14B)-H(14D)	109.0
C(15B)-C(14B)-C(13B)	103.47(16)

C(15B)-C(14B)-H(14C)	111.1
C(15B)-C(14B)-H(14D)	111.1
N(3B)-C(15B)-C(14B)	101.24(16)
N(3B)-C(15B)-H(15C)	111.5
N(3B)-C(15B)-H(15D)	111.5
C(14B)-C(15B)-H(15C)	111.5
C(14B)-C(15B)-H(15D)	111.5
H(15C)-C(15B)-H(15D)	109.3
C(17B)-C(16B)-C(13B)	111.82(16)
C(17B)-C(16B)-C(21B)	119.68(18)
C(21B)-C(16B)-C(13B)	128.31(19)
C(16B)-C(17B)-N(2B)	109.92(17)
C(16B)-C(17B)-C(18B)	121.42(18)
C(18B)-C(17B)-N(2B)	128.6(2)
C(17B)-C(18B)-H(18B)	120.9
C(17B)-C(18B)-C(19B)	118.2(2)
C(19B)-C(18B)-H(18B)	120.9
C(18B)-C(19B)-H(19B)	119.7
C(20B)-C(19B)-C(18B)	120.7(2)
C(20B)-C(19B)-H(19B)	119.7
C(19B)-C(20B)-H(20B)	119.7
C(19B)-C(20B)-C(21B)	120.6(2)
C(21B)-C(20B)-H(20B)	119.7
C(16B)-C(21B)-C(20B)	119.0(2)
C(16B)-C(21B)-H(21B)	120.5
C(20B)-C(21B)-H(21B)	120.5
O(3B)-C(22B)-O(4B)	124.24(19)
O(3B)-C(22B)-N(2B)	124.87(18)
O(4B)-C(22B)-N(2B)	110.89(17)
O(4B)-C(23B)-H(23D)	109.5
O(4B)-C(23B)-H(23E)	109.5
O(4B)-C(23B)-H(23F)	109.5
H(23D)-C(23B)-H(23E)	109.5
H(23D)-C(23B)-H(23F)	109.5
H(23E)-C(23B)-H(23F)	109.5
C(1)-Cl(1)-C(1)#1	61.5(3)
Cl(1)-C(1)-Cl(1)#1	118.5(3)
Cl(1)-C(1)-C(1)#1	65.3(3)
Cl(1)#1-C(1)-H(1A)	92.2
Cl(1)-C(1)-H(1A)	117.2
Cl(1)#1-C(1)-H(1B)	92.2
Cl(1)-C(1)-H(1B)	117.2
C(1)#1-C(1)-Cl(1)#1	53.2(3)
C(1)#1-C(1)-H(1A)	117.2
C(1)#1-C(1)-H(1B)	117.2
H(1A)-C(1)-H(1B)	114.2
H(1C)-O(1)-H(1D)	100(2)

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Symmetry transformations used to generate equivalent atoms:

#1 +2

Table A2.10.4. *Anisotropic displacement parameters (Å^{2}x 10^4) for* ***77****. The anisotropic displacement factor exponent takes the form:* $-2\pi^2 [h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}

Br(1A)	221(1)	127(1)	183(1)	-63(1)	55(1)	-12(1)
O(1A)	226(8)	99(6)	216(7)	-16(5)	81(6)	8(5)
O(2A)	139(7)	115(6)	164(6)	11(5)	19(5)	-6(5)
O(3A)	290(10)	282(8)	321(8)	-16(7)	201(7)	27(7)
O(4A)	256(9)	212(7)	285(8)	29(6)	150(7)	-49(6)
N(1A)	159(9)	123(7)	149(7)	-7(6)	77(6)	14(6)
N(2A)	144(9)	142(7)	154(7)	-18(6)	62(6)	2(6)
N(3A)	158(9)	142(7)	200(8)	-24(6)	14(7)	-6(6)
C(1A)	142(10)	127(8)	156(9)	4(7)	41(7)	3(7)
C(2A)	203(11)	111(8)	217(10)	13(7)	19(8)	-21(7)
C(3A)	203(11)	161(9)	228(10)	62(7)	36(8)	-51(8)
C(4A)	171(11)	184(9)	168(9)	36(7)	51(8)	-15(8)
C(5A)	139(10)	128(8)	145(8)	6(7)	19(7)	-5(7)
C(6A)	128(10)	105(7)	117(8)	8(6)	28(7)	2(7)
C(7A)	130(9)	72(7)	121(8)	-10(6)	38(7)	-4(6)
C(8A)	133(10)	128(8)	123(8)	-12(6)	24(7)	2(7)
C(9A)	182(11)	221(9)	193(9)	-12(8)	97(8)	53(8)
C(10A)	157(10)	124(8)	108(8)	1(6)	43(7)	-5(7)
C(11A)	175(11)	157(8)	138(8)	24(7)	28(7)	-15(7)
C(12A)	134(10)	115(8)	133(8)	-11(6)	34(7)	-10(7)
C(13A)	148(10)	93(7)	95(8)	-7(6)	29(7)	4(7)
C(14A)	183(11)	154(8)	111(8)	-14(7)	21(7)	2(7)
C(15A)	242(12)	181(9)	163(9)	-55(7)	21(8)	-19(8)
C(16A)	133(10)	112(8)	115(8)	-30(6)	4(7)	4(7)
C(17A)	122(10)	152(8)	145(8)	-37(7)	-6(7)	2(7)
C(18A)	139(10)	209(9)	200(9)	-67(8)	29(8)	22(8)
C(19A)	212(11)	161(9)	252(10)	-74(8)	-15(8)	65(8)
C(20A)	245(12)	132(9)	218(10)	-1(7)	-30(8)	31(8)
C(21A)	192(11)	156(8)	136(9)	-8(7)	5(7)	16(7)
C(22A)	184(11)	236(10)	159(9)	-2(8)	20(8)	-43(8)
C(23A)	339(15)	331(12)	380(13)	62(11)	178(11)	-93(11)
Br(1B)	308(1)	227(1)	224(1)	10(1)	22(1)	96(1)
O(1B)	288(10)	184(7)	394(9)	21(6)	144(7)	48(6)
O(2B)	263(9)	140(6)	210(7)	-28(5)	91(6)	7(6)
O(3B)	227(9)	276(8)	397(9)	-11(7)	150(7)	15(7)
O(4B)	265(9)	159(6)	294(8)	25(6)	131(6)	-22(6)
N(1B)	177(10)	212(8)	205(8)	5(7)	71(7)	0(7)
N(2B)	208(10)	138(7)	212(8)	9(6)	101(7)	7(7)
N(3B)	275(11)	186(8)	198(8)	31(7)	82(7)	36(7)
C(1B)	251(12)	227(10)	161(9)	-3(8)	43(8)	4(9)
C(2B)	490(17)	152(9)	240(11)	7(8)	77(10)	-23(10)
C(3B)	484(17)	207(10)	272(12)	-32(9)	97(11)	-143(10)
C(4B)	272(13)	276(11)	204(10)	-27(8)	56(9)	-99(9)
C(5B)	255(12)	200(9)	141(9)	5(7)	53(8)	-31(8)
C(6B)	201(11)	162(9)	144(9)	5(7)	36(8)	-17(8)
C(7B)	174(11)	140(8)	179(9)	0(7)	56(8)	6(7)
C(8B)	201(12)	211(10)	174(9)	19(8)	62(8)	7(8)
C(9B)	167(12)	343(12)	381(13)	2(10)	67(10)	-1(10)
C(10B)	209(12)	199(9)	137(9)	7(7)	51(8)	2(8)
C(11B)	239(12)	188(9)	199(10)	-38(8)	21(8)	-20(8)
C(12B)	180(11)	136(8)	181(9)	3(7)	51(8)	11(7)
C(13B)	181(11)	139(8)	179(9)	0(7)	40(8)	-6(7)
C(14B)	193(12)	226(10)	192(10)	-22(8)	29(8)	-2(8)
C(15B)	241(12)	227(10)	178(10)	31(8)	17(8)	70(9)
C(16B)	208(11)	161(9)	150(9)	4(7)	26(8)	22(8)
C(17B)	262(12)	146(8)	111(8)	13(7)	35(8)	46(8)
C(18B)	279(13)	227(10)	166(9)	1(8)	78(9)	72(9)

C(19B)	342(14)	211(10)	178(9)	-17(8)	36(9)	85(9)
C(20B)	470(16)	174(9)	162(10)	-35(8)	25(10)	54(9)
C(21B)	305(14)	189(9)	178(10)	-7(8)	42(9)	3(9)
C(22B)	228(12)	216(10)	176(9)	2(8)	63(8)	-3(8)
C(23B)	267(13)	225(10)	294(11)	39(9)	105(9)	-90(9)
Cl(1)	275(5)	605(6)	881(8)	237(5)	39(5)	-52(4)
C(1)	240(30)	410(30)	190(20)	-110(20)	40(20)	-110(30)

Table A2.10.5. *Hydrogen coordinates (x 10^3) and isotropic displacement parameters (Å^{2}x 10^3) for **77***

	x	y	z	U_{iso}
H(3AA)	216	162	243	20
H(3AB)	245	86	281	20
H(2A)	514	496	324	21
H(3A)	581	470	189	24
H(4A)	594	343	135	21
H(9AA)	632	204	173	29
H(9AB)	565	191	84	29
H(9AC)	583	127	169	29
H(10A)	496	225	472	15
H(10B)	413	260	472	15
H(11A)	455	105	470	19
H(11B)	392	144	530	19
H(14A)	306	240	129	18
H(14B)	389	201	142	18
H(15A)	269	114	112	23
H(15B)	342	85	186	23
H(18A)	184	349	448	22
H(19A)	190	466	364	25
H(20A)	265	481	236	24
H(21A)	342	379	193	19
H(23A)	170	97	588	51
H(23B)	166	21	521	51
H(23C)	107	89	493	51
H(3BA)	836	93	471	26
H(3BB)	834	171	518	26
H(2B)	895	521	186	35
H(3B)	1027	513	202	38
H(4B)	1088	393	216	30
H(9BA)	1094	176	225	44
H(9BB)	1127	258	264	44
H(9BC)	1101	244	147	44
H(10C)	766	259	194	22
H(10D)	818	236	109	22
H(11C)	739	134	179	25
H(11D)	823	113	153	25
H(14C)	986	242	404	24
H(14D)	940	269	494	24
H(15C)	951	115	418	26
H(15D)	959	141	534	26
H(18B)	637	318	429	26
H(19B)	670	447	464	29
H(20B)	795	487	466	32

H(21B)	889	402	421	27
H(23D)	627	53	504	38
H(23E)	661	-16	446	38
H(23F)	596	37	390	38
H(1A)	1010	513	617	33
H(1B)	937	463	560	33
H(1C)	993(1)	423(6)	536(7)	24
H(1D)	929(5)	441(5)	572(5)	24

Table A2.10.6. *Hydrogen bonds for* ***77*** *[Å and °]*

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(3A)-H(3AB)...Br(1B)#2	0.92	2.92	3.8165(15)	164.2
N(3B)-H(3BB)...Br(1B)#3	0.92	3.11	3.6325(16)	118.2
C(9B)-H(9BC)...O(3A)#4	0.98	2.46	3.406(3)	163.4
C(15B)-H(15C)...O(1B)	0.99	2.65	3.346(2)	127.8
C(23B)-H(23F)...O(1A)	0.98	2.62	3.510(3)	151.5

Symmetry transformations used to generate equivalent atoms:
#1 +2 #2 +1
#3 #4 +1

A2.11. X-Ray Crystal Structure Analysis of 94

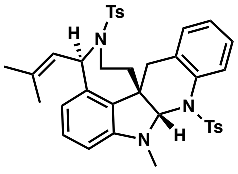

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Figure A2.11.1. *X-ray Crystal Structure of* ***94***

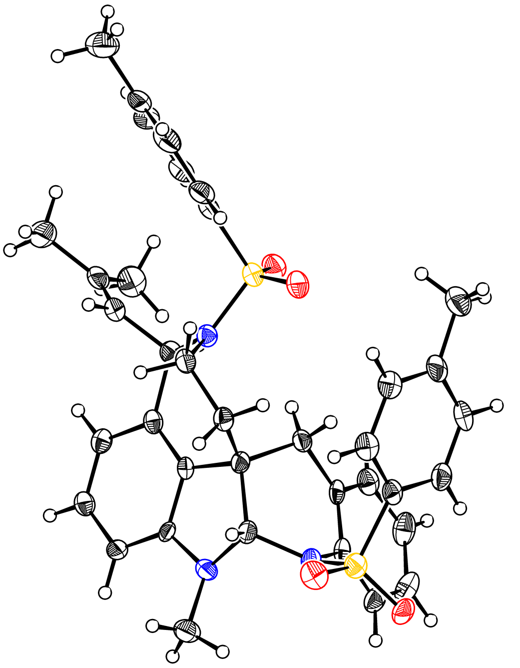


Table A2.11.1. *Crystal data and structure refinement for* ***94***

Empirical formula	C37 H39 N3 O4 S2
Formula weight	653.83
Crystallization Solvent	???Solvent???
Crystal Habit	Fragment
Crystal size	0.25 x 0.24 x 0.17 mm^3
Crystal color	Colorless

Data Collection

Preliminary Photos	
Type of diffractometer	Bruker SMART 1000
Wavelength	0.71073 Å MoK〈
Data Collection Temperature	100(2) K

\ range for 8943 reflections used in lattice determination	2.22 to 27.43°	
Unit cell dimensions	a = 15.5078(13) Å	〈= 90°
	b = 11.2221(10) Å	®= 94.7250(10)°
	c = 18.4268(16) Å	© = 90°
Volume	3195.9(5) Å^3	
Z	4	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Density (calculated)	1.359 Mg/m^3	
F(000)	1384	
Data collection program	Bruker SMART v5.630	
\ range for data collection	1.65 to 28.34°	
Completeness to \ = 28.34°	94.1 %	
Index ranges	-20<=h<=20, -14<=k<=14, -24<=l<=24	
Data collection scan type	scans at 5 settings	
Data reduction program	Bruker SAINT v6.45A	
Reflections collected	44083	
Independent reflections	7500 [R$_{int}$= 0.1020]	
Absorption coefficient	0.213 mm^{-1}	
Absorption correction	None	
Max. and min. transmission	0.9647 and 0.9487	
Number of standards	? reflections measured every ?min.	
Variation of standards	?%.	

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 1990)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric positions
Structure refinement program	SHELXL-97 (Sheldrick, 1997)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	7500 / 0 / 420
Treatment of hydrogen atoms	Riding
Goodness-of-fit on F^2	1.394
Final R indices [I>2 ʃ(I), 4434 reflections]	R1 = 0.0531, wR2 = 0.0888
R indices (all data)	R1 = 0.0982, wR2 = 0.0932
Type of weighting scheme used	Sigma
Weighting scheme used	w=1/s^2^(Fo^2^)
Max shift/error	0.001

Average shift/error	0.000
Absolute structure determination	?
Largest diff. peak and hole	0.629 and -0.498 e.Å^{-3}

Special Refinement Details

Table A2.11.2. *Atomic coordinates (x 10^{4}) and equivalent isotropic displacement parameters (Å^{2}x 10^{3}) for* ***94****. U(eq) is defined as the trace of the orthogonalized U^{ij} tensor*

	x	y	z	U_{eq}
S(1)	7430(1)	6065(1)	847(1)	26(1)
S(2)	7110(1)	2404(1)	-2197(1)	26(1)
O(1)	7087(1)	5440(1)	1441(1)	30(1)
O(2)	6897(1)	6283(1)	191(1)	31(1)
O(3)	7723(1)	2951(1)	-2627(1)	31(1)
O(4)	6624(1)	1390(1)	-2471(1)	30(1)
N(1)	8248(1)	5286(2)	622(1)	21(1)
N(2)	7649(1)	1964(2)	-1428(1)	20(1)
N(3)	9053(1)	1794(2)	-836(1)	25(1)
C(1)	7803(1)	7460(2)	1173(1)	24(1)
C(2)	7883(2)	8387(2)	687(1)	29(1)
C(3)	8173(2)	9490(2)	943(1)	33(1)
C(4)	8386(2)	9698(2)	1672(1)	31(1)
C(5)	8312(2)	8744(2)	2161(1)	29(1)
C(6)	8016(1)	7645(2)	1910(1)	27(1)
C(7)	8701(2)	10883(2)	1936(2)	46(1)
C(8)	8655(1)	5616(2)	-41(1)	24(1)
C(9)	8357(2)	4792(2)	-673(1)	22(1)
C(10)	8247(1)	3487(2)	-452(1)	20(1)
C(11)	8970(1)	3097(2)	114(1)	18(1)
C(12)	9226(1)	3566(2)	796(1)	21(1)
C(13)	8757(1)	4558(2)	1172(1)	22(1)
C(14)	9352(1)	5326(2)	1652(1)	25(1)
C(15)	9436(2)	5322(2)	2377(1)	28(1)
C(16)	10029(2)	6186(2)	2792(1)	40(1)
C(17)	8968(2)	4500(2)	2843(1)	39(1)
C(18)	9956(1)	3058(2)	1182(1)	24(1)
C(19)	10392(1)	2119(2)	898(1)	23(1)
C(20)	10133(1)	1653(2)	218(1)	22(1)
C(21)	9429(1)	2138(2)	-162(1)	17(1)
C(22)	8404(1)	2657(2)	-1116(1)	22(1)
C(23)	7170(1)	1365(2)	-902(1)	22(1)
C(24)	6883(2)	213(2)	-1018(1)	27(1)
C(25)	6385(2)	-308(2)	-509(1)	35(1)
C(26)	6207(2)	313(2)	108(1)	33(1)
C(27)	6542(2)	1444(2)	235(1)	26(1)
C(28)	7023(1)	1991(2)	-273(1)	20(1)
C(29)	7332(1)	3253(2)	-188(1)	21(1)
C(30)	9532(2)	1163(2)	-1354(1)	31(1)
C(31)	6376(2)	3476(2)	-1938(1)	23(1)
C(32)	6582(2)	4681(2)	-1968(1)	27(1)
C(33)	6067(2)	5512(2)	-1643(1)	27(1)
C(34)	5362(2)	5159(2)	-1284(1)	29(1)
C(35)	5149(2)	3940(2)	-1281(1)	30(1)

C(36)	5649(2)	3115(2)	-1606(1)	29(1)
C(37)	4847(2)	6041(2)	-885(1)	37(1)

Table A2.11.3. *Bond lengths [Å] and angles [°] for* ***94***

S(1)-O(2)	1.4297(15)
S(1)-O(1)	1.4381(16)
S(1)-N(1)	1.6227(18)
S(1)-C(1)	1.757(2)
S(2)-O(3)	1.4257(16)
S(2)-O(4)	1.4330(16)
S(2)-N(2)	1.6596(18)
S(2)-C(31)	1.750(2)
N(1)-C(8)	1.468(3)
N(1)-C(13)	1.479(3)
N(2)-C(23)	1.437(3)
N(2)-C(22)	1.482(3)
N(3)-C(21)	1.383(3)
N(3)-C(30)	1.443(3)
N(3)-C(22)	1.460(3)
C(1)-C(2)	1.385(3)
C(1)-C(6)	1.387(3)
C(2)-C(3)	1.387(3)
C(3)-C(4)	1.376(3)
C(4)-C(5)	1.409(3)
C(4)-C(7)	1.485(3)
C(5)-C(6)	1.382(3)
C(8)-C(9)	1.527(3)
C(9)-C(10)	1.533(3)
C(10)-C(11)	1.531(3)
C(10)-C(29)	1.559(3)
C(10)-C(22)	1.573(3)
C(11)-C(12)	1.391(3)
C(11)-C(21)	1.407(3)
C(12)-C(18)	1.406(3)
C(12)-C(13)	1.527(3)
C(13)-C(14)	1.497(3)
C(14)-C(15)	1.331(3)
C(15)-C(17)	1.490(3)
C(15)-C(16)	1.501(3)
C(18)-C(19)	1.379(3)
C(19)-C(20)	1.386(3)
C(20)-C(21)	1.362(3)
C(23)-C(24)	1.378(3)
C(23)-C(28)	1.390(3)
C(24)-C(25)	1.391(3)
C(25)-C(26)	1.380(3)
C(26)-C(27)	1.384(3)
C(27)-C(28)	1.387(3)
C(28)-C(29)	1.498(3)
C(31)-C(36)	1.386(3)
C(31)-C(32)	1.391(3)
C(32)-C(33)	1.395(3)
C(33)-C(34)	1.381(3)
C(34)-C(35)	1.408(3)
C(34)-C(37)	1.501(3)
C(35)-C(36)	1.375(3)

O(2)-S(1)-O(1)	120.13(10)
O(2)-S(1)-N(1)	106.61(9)
O(1)-S(1)-N(1)	106.12(9)
O(2)-S(1)-C(1)	106.75(10)
O(1)-S(1)-C(1)	107.87(10)
N(1)-S(1)-C(1)	109.02(10)
O(3)-S(2)-O(4)	120.13(10)
O(3)-S(2)-N(2)	106.90(10)
O(4)-S(2)-N(2)	106.10(9)
O(3)-S(2)-C(31)	109.52(11)
O(4)-S(2)-C(31)	107.86(11)
N(2)-S(2)-C(31)	105.34(10)
C(8)-N(1)-C(13)	117.95(18)
C(8)-N(1)-S(1)	118.38(15)
C(13)-N(1)-S(1)	120.44(15)
C(23)-N(2)-C(22)	114.75(17)
C(23)-N(2)-S(2)	117.62(15)
C(22)-N(2)-S(2)	120.12(15)
C(21)-N(3)-C(30)	121.98(19)
C(21)-N(3)-C(22)	111.09(17)
C(30)-N(3)-C(22)	117.99(18)
C(2)-C(1)-C(6)	119.6(2)
C(2)-C(1)-S(1)	119.49(18)
C(6)-C(1)-S(1)	120.90(18)
C(1)-C(2)-C(3)	119.6(2)
C(4)-C(3)-C(2)	121.9(2)
C(3)-C(4)-C(5)	118.0(2)
C(3)-C(4)-C(7)	121.2(2)
C(5)-C(4)-C(7)	120.8(2)
C(6)-C(5)-C(4)	120.5(2)
C(5)-C(6)-C(1)	120.4(2)
N(1)-C(8)-C(9)	110.94(18)
C(8)-C(9)-C(10)	114.14(18)
C(11)-C(10)-C(9)	111.28(17)
C(11)-C(10)-C(29)	112.00(18)
C(9)-C(10)-C(29)	111.58(18)
C(11)-C(10)-C(22)	102.01(17)
C(9)-C(10)-C(22)	109.37(18)
C(29)-C(10)-C(22)	110.18(17)
C(12)-C(11)-C(21)	120.0(2)
C(12)-C(11)-C(10)	130.2(2)
C(21)-C(11)-C(10)	109.72(18)
C(11)-C(12)-C(18)	117.4(2)
C(11)-C(12)-C(13)	125.12(19)
C(18)-C(12)-C(13)	117.4(2)
N(1)-C(13)-C(14)	110.77(18)
N(1)-C(13)-C(12)	109.80(17)
C(14)-C(13)-C(12)	113.23(18)
C(15)-C(14)-C(13)	126.6(2)
C(14)-C(15)-C(17)	124.6(2)
C(14)-C(15)-C(16)	120.9(2)
C(17)-C(15)-C(16)	114.5(2)
C(19)-C(18)-C(12)	121.2(2)
C(18)-C(19)-C(20)	121.1(2)
C(21)-C(20)-C(19)	118.3(2)
C(20)-C(21)-N(3)	127.6(2)
C(20)-C(21)-C(11)	121.9(2)

N(3)-C(21)-C(11)	110.44(19)
N(3)-C(22)-N(2)	106.80(17)
N(3)-C(22)-C(10)	105.32(17)
N(2)-C(22)-C(10)	116.47(18)
C(24)-C(23)-C(28)	122.0(2)
C(24)-C(23)-N(2)	120.8(2)
C(28)-C(23)-N(2)	117.1(2)
C(23)-C(24)-C(25)	118.7(2)
C(26)-C(25)-C(24)	120.2(2)
C(25)-C(26)-C(27)	120.3(2)
C(26)-C(27)-C(28)	120.4(2)
C(27)-C(28)-C(23)	118.2(2)
C(27)-C(28)-C(29)	122.2(2)
C(23)-C(28)-C(29)	119.5(2)
C(28)-C(29)-C(10)	114.72(18)
C(36)-C(31)-C(32)	120.0(2)
C(36)-C(31)-S(2)	119.38(19)
C(32)-C(31)-S(2)	120.01(18)
C(31)-C(32)-C(33)	119.4(2)
C(34)-C(33)-C(32)	121.2(2)
C(33)-C(34)-C(35)	118.4(2)
C(33)-C(34)-C(37)	121.3(2)
C(35)-C(34)-C(37)	120.3(2)
C(36)-C(35)-C(34)	120.8(2)
C(35)-C(36)-C(31)	120.2(2)

Symmetry transformations used to generate equivalent atoms:

Table A2.11.4. *Anisotropic displacement parameters (Å^{2}x 10^4) for **94**. The anisotropic displacement factor exponent takes the form: -2ð^2 [h^2 a*^{2}U ^{11} + ... + 2 h k a* b* U^{12}]*

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	189(3)	284(4)	294(4)	-20(3)	14(3)	21(3)
S(2)	246(3)	321(4)	197(3)	2(3)	-38(3)	18(3)
O(1)	246(10)	297(10)	350(10)	-9(8)	77(8)	-2(8)
O(2)	229(10)	365(11)	334(10)	-4(8)	-69(8)	60(8)
O(3)	337(11)	387(11)	202(9)	68(8)	65(8)	12(8)
O(4)	281(10)	335(10)	266(10)	-58(8)	-110(8)	-5(8)
N(1)	193(11)	241(11)	202(11)	-2(9)	2(9)	7(9)
N(2)	195(11)	252(11)	158(10)	20(8)	-18(8)	-7(9)
N(3)	203(11)	288(12)	255(12)	-58(9)	-4(9)	60(9)
C(1)	175(13)	266(14)	284(14)	12(12)	26(11)	57(11)
C(2)	272(15)	297(15)	290(15)	-13(12)	22(12)	94(12)
C(3)	293(15)	290(16)	409(17)	75(13)	106(13)	77(13)
C(4)	218(14)	308(15)	429(17)	-103(13)	133(12)	-2(12)
C(5)	299(15)	327(16)	252(14)	-62(12)	57(12)	6(12)
C(6)	253(14)	272(15)	285(14)	31(12)	75(11)	67(12)
C(7)	497(19)	324(17)	580(20)	-79(14)	231(16)	-43(14)
C(8)	179(13)	249(14)	281(14)	19(11)	8(11)	3(11)
C(9)	186(13)	272(14)	211(13)	14(11)	-2(10)	3(11)
C(10)	177(13)	242(14)	187(13)	-22(10)	-11(10)	-10(11)
C(11)	128(12)	221(13)	198(13)	13(10)	4(10)	-22(10)
C(12)	170(13)	222(13)	224(13)	47(11)	22(10)	-17(11)
C(13)	214(13)	235(13)	194(13)	6(11)	1(10)	10(11)
C(14)	187(13)	269(14)	294(15)	-11(12)	14(11)	18(11)
C(15)	207(14)	332(15)	300(15)	-54(12)	-47(12)	101(12)

C(16)	389(17)	484(18)	316(15)	-121(14)	-89(13)	67(14)
C(17)	384(17)	587(19)	206(14)	-17(13)	4(12)	30(15)
C(18)	224(14)	250(14)	223(13)	18(11)	-25(11)	-24(11)
C(19)	197(13)	253(14)	243(14)	30(11)	-17(11)	28(11)
C(20)	204(13)	175(13)	280(14)	-29(11)	41(11)	-15(11)
C(21)	152(12)	187(13)	181(12)	-39(10)	8(10)	-62(10)
C(22)	182(13)	276(14)	214(13)	-28(11)	8(10)	-33(11)
C(23)	146(13)	270(14)	228(14)	45(11)	-52(10)	-26(11)
C(24)	264(14)	283(15)	250(14)	-21(12)	-77(11)	-23(12)
C(25)	365(16)	307(15)	340(16)	57(13)	-107(13)	-127(13)
C(26)	277(15)	454(17)	268(15)	84(13)	-10(12)	-111(13)
C(27)	217(14)	366(16)	204(13)	34(12)	-9(11)	16(12)
C(28)	128(12)	245(14)	216(13)	33(11)	-66(10)	-4(10)
C(29)	163(13)	255(14)	220(13)	-6(11)	0(10)	21(11)
C(30)	312(15)	320(15)	287(15)	-39(12)	5(12)	88(12)
C(31)	189(13)	308(15)	185(13)	30(11)	-42(10)	26(11)
C(32)	269(15)	350(16)	178(13)	75(12)	-11(11)	1(13)
C(33)	279(15)	293(15)	213(13)	90(11)	-58(11)	28(12)
C(34)	198(14)	354(16)	286(14)	25(12)	-81(11)	83(12)
C(35)	148(13)	412(17)	345(15)	48(13)	11(11)	14(13)
C(36)	217(14)	303(15)	324(15)	21(12)	-69(12)	-12(12)
C(37)	281(15)	370(16)	443(17)	52(13)	17(13)	61(13)

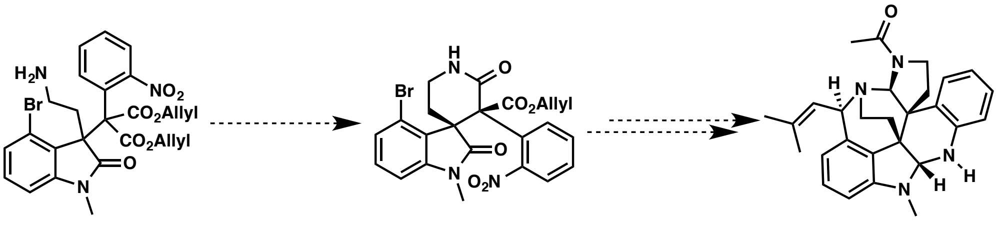
APPENDIX 3

Synthetic Studies Toward the Total Synthesis of Communesin F

A3.1. Direct Lactam-Forming Strategy

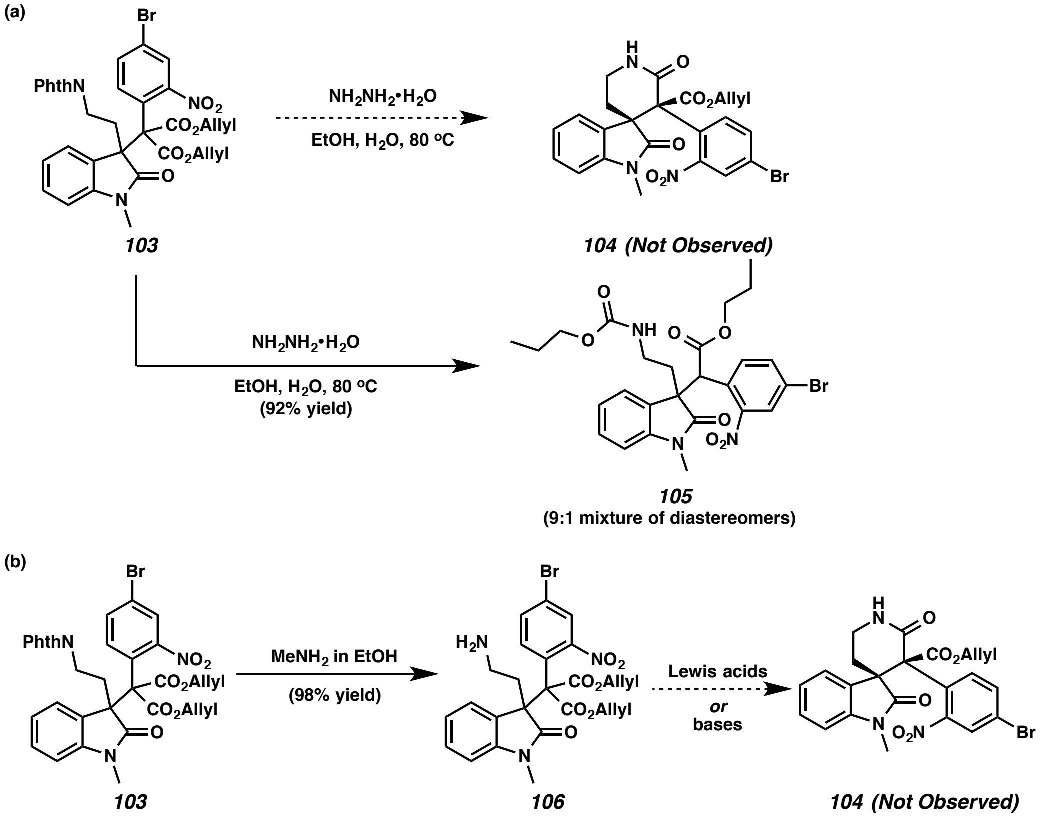
Having successfully completed our formal synthesis of communesin F (**1f**) and perophoramidine (**3**), our attention turned to a total synthesis of communesin F (**1f**). We envisioned that direct lactamization of malonate **101** would afford allyl ester **102**, which could be a potential precursor toward the efficient synthesis of communesin F (**1f**) (Scheme A3.1.1). Since lactonization of diester **60** afforded lactone **61** as a single diastereomer (Scheme 1.2.13, **60** → **61**), we believed that the diastereomer needed for elaboration to communesin F (**1f**) could be selectively formed by lactamization of malonate **101**.

Scheme A3.1.1. *Direct Lactam-Forming Strategy Toward Communesin F (**1f**)*



To examine diastereoselective lactam formation, we chose phthalimide **103** as a model substrate. Interestingly, an attempt to remove the phthalyl protecting group and simultaneously construct lactam **104** from malonate **103** furnished a 9:1 diastereomeric mixture of **105** (Scheme A3.1.2a). The double bonds of the allyl groups were reduced and one of the resultant propyl esters was transferred to the amine. Treatment of phthalimide **103** with methylamine generated the desired amine **106** (Scheme A3.1.2b). Despite extensive screening of Lewis acids, acids, and bases (e.g., $AlMe_3$, KO*t*-Bu, *p*-TsOH), lactamization of malonate **106** proved to be challenging.

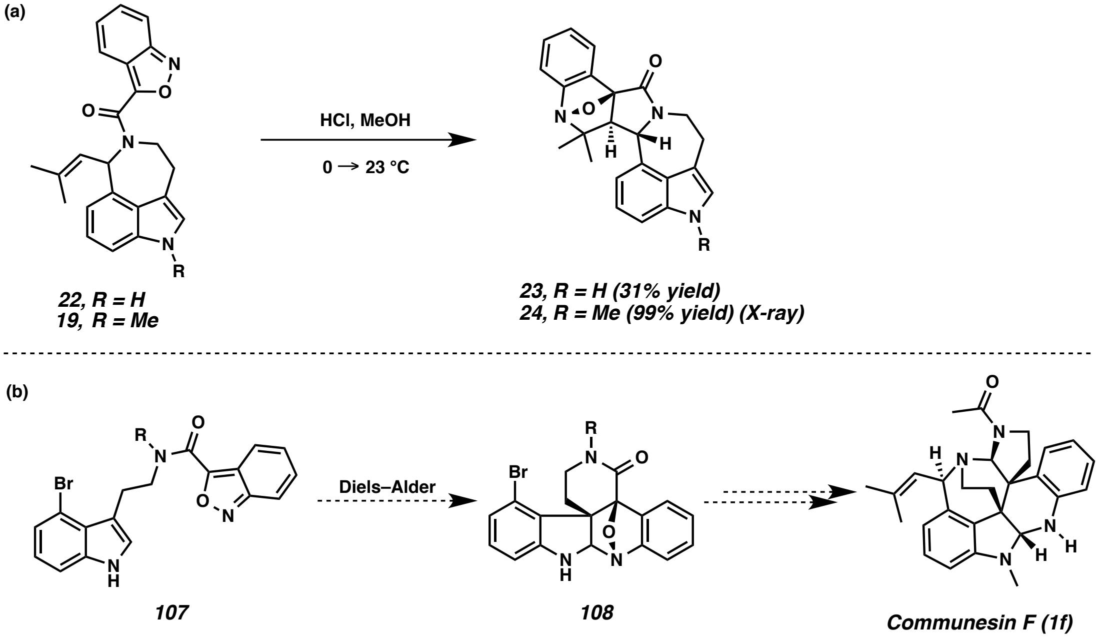
Scheme A3.1.2. *Attempted Lactam-Forming Reactions*



A3.2. Diels–Alder Strategy

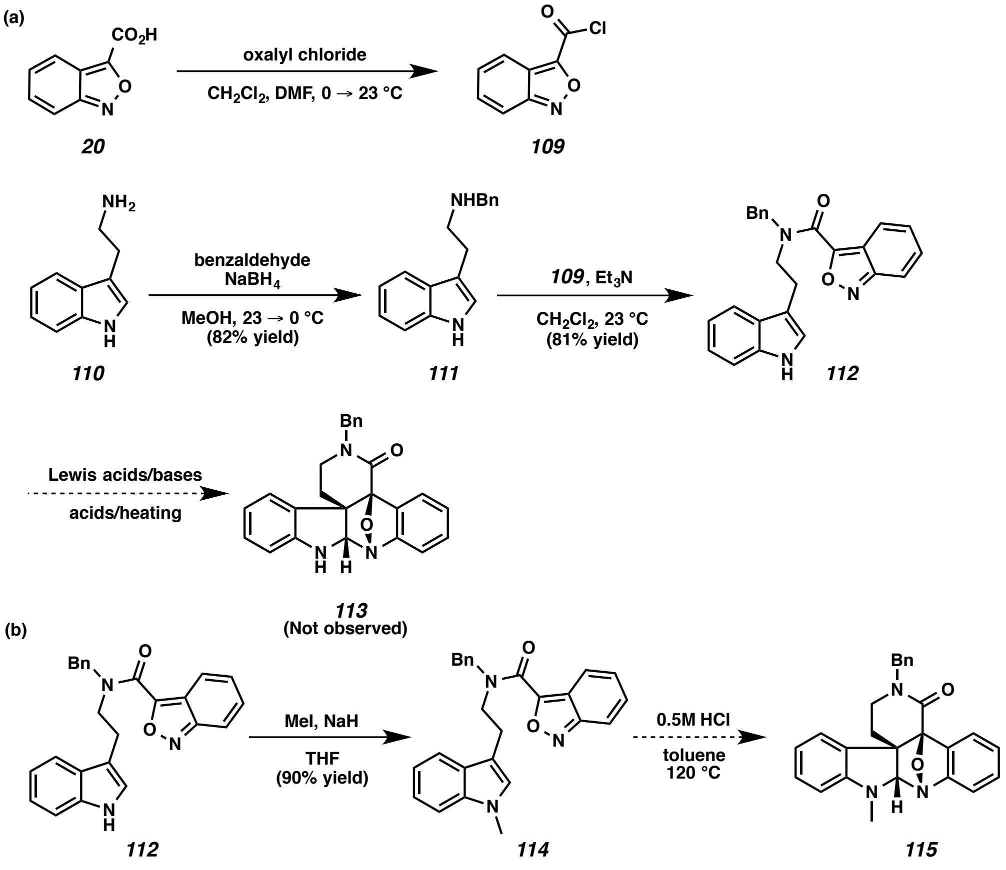
Next, we investigated a Diels–Alder strategy toward the total synthesis of communesin F (**1f**). As described in Schemes A3.2.1a and 1.2.5, the benzisoxazole in **19** and **22** reacted with the butenyl side chain by an intramolecular Diels–Alder cycloaddtion to afford the undesired bridged polycycles **24** and **23**, respectively. We expected that the desired core structure could be constructed via an intramolecular Diels–Alder reaction with substrates, which possess no butenyl side chain (Scheme A3.2.1b).

Scheme A3.2.1. *Diels–Alder Strategy Toward Communesin F (**1f**)*



Treatment of acid **20** with oxalyl chloride produced acyl chloride **109**, which was used directly without further purification (Scheme A3.2.2a). Tryptamine (**110**) was used as the model substrate to explore a Diels–Alder strategy. Reductive amination of tryptamine (**110**) with benzaldehyde furnished benzyl amine **111**, which was coupled with acid chloride **109** to afford amide **112**. However, all attempts at intramolecular Diels–Alder reactions using a wide variety of conditions (e.g., HCl, $BF_3{\cdot}OEt_2$, Et_2AlCl, $SnCl_4$, KO*t*-Bu, SiO_2, MeMgBr, $AgClO_4$, heating) to provide the communesin F core structure were unsuccessful.[1] Indole **112** was protected with methyl iodide to produce **114**, but the desired Diels–Alder cycloaddition product was not observed (Scheme A3.2.2b).

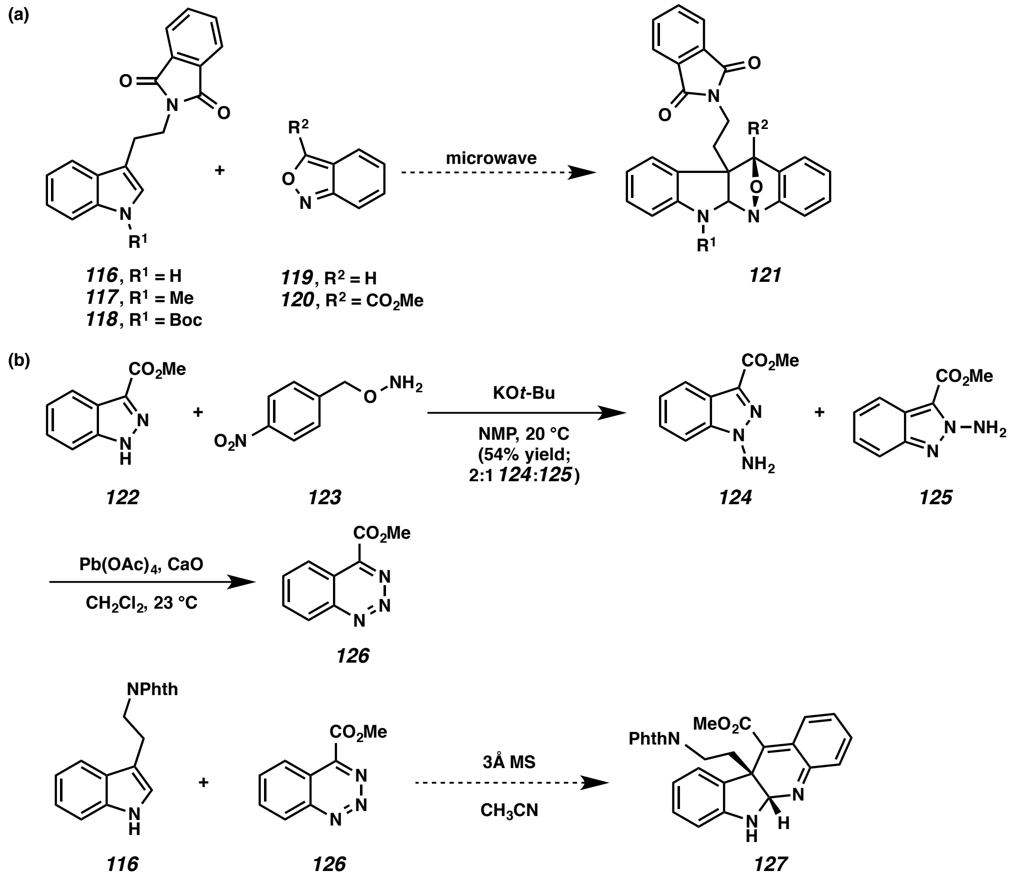
Scheme A3.2.2. *Intramolecular Diels–Alder Reactions*



Having failed to access the communesin F core by intramolecular Diels–Alder reactions, we chose to examine intermolecular Diels–Alder reactions (Scheme A3.2.3).

Intermolecular Diels–Alder reactions between phthalimide **116–118** and benzisoxazole **119–120** did not proceed below 150 °C and the anthranil fragment decomposed at a higher temperature (Scheme A3.2.3a). Addition of Lewis acids did not improve the reactivities. Alternatively, we envisioned that a Diels–Alder reaction of 1,2,3-benzotriazine with phthalimide **116** would afford **127** by loss of N_2 (Scheme A3.2.3b).[2] Amination of indazole **122** followed by oxidation with lead tetraacetate furnished 1,2,3-benzotriazine **126**. Disappointingly, the desired adduct (**127**) was not observed by intermolecular Diels–Alder reactions under several conditions.

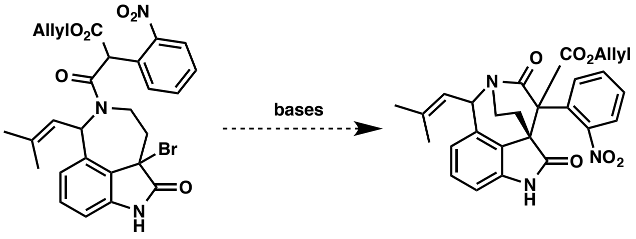
Scheme A3.2.3. *Intermolecular Diels–Alder Reactions*



A3.3. Intramolecular Alkylation of 3-Bromooxindole Strategy

A plausible rationale for forming *syn*-selective adduct **42** from alkylation of 3-bromooxindole **40** and malonate **41** is that the tosyl group would be located far from the isobutenyl group due to steric hindrance and thus, malonate **41** would approach *syn* to the isobutenyl group to reduce the steric interaction with the tosyl group (Scheme 1.2.9). We believed that intramolecular alkylation of the 3-bromooxindole with a tethered malonate derivative in **128** could deliver the stereochemistry needed for the synthesis of communesin F (**1f**).

Scheme A3.3.1. *Intramolecular Alkylation Strategy*

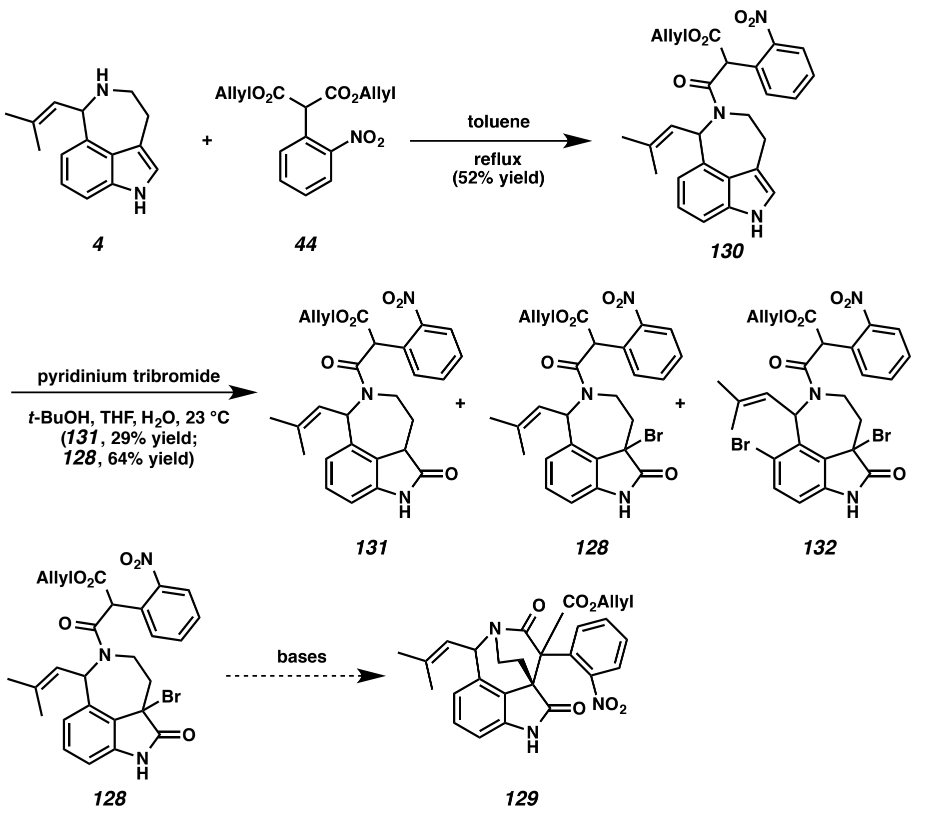


128

129

Coupling of aurantioclavine (**4**) and malonate **44** afforded amide **130**, which was oxidized with pyridinium tribromide to furnish a mixture of **131**, **128**, and **132** (Scheme A3.3.2). Unfortunately, intramolecular alkylation of 3-bromooxindole **128** provided a complex mixture of the unisolable desired product and byproducts even after extensive screening of the reaction parameters.

Scheme A3.3.2. *Intramolecular Alkylation of 3-Bromooxindole*



Although our synthetic efforts toward the total synthesis of communesin F were unsuccessful, we believe that these routes are one of the most expedient routes to complex communesin F.

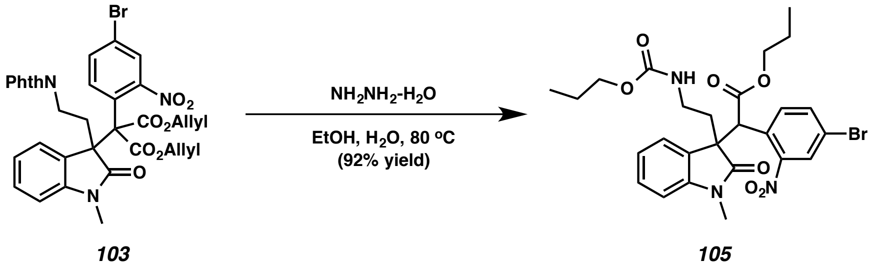
A3.4. Experimental Methods and Analytical Data

A3.4.1. Materials and Methods

Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Reaction progress was monitored by thin-layer chromatography (TLC). THF, Et_2O, CH_2Cl_2, toluene, benzene, CH_3CN, and dioxane were dried by passage through an activated alumina column under argon. Triethylamine was distilled over CaH_2 prior to use. Purified water was obtained using a Barnstead NANOpure Infinity UV/UF system. Brine solutions are saturated aqueous solutions of sodium chloride. Commercially available reagents were purchased from Sigma-Aldrich, Acros Organics, Strem, or Alfa Aesar and used as received unless otherwise stated. Reaction temperatures were controlled by an IKAmag temperature modulator unless otherwise indicated. Microwave-assisted reactions were performed in a Biotage Initiator 2.5 microwave reactor. Glove box manipulations were performed under a N_2 atmosphere. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, *p*-anisaldehyde, or PMA (phosphomolybdic acid) staining. Silicycle Silia*Flash* P60 Academic Silica gel (particle size 0.040-0.064 mm) was used for flash column chromatography. ^1H NMR spectra were recorded on a Varian Inova 500 MHz spectrometer and are reported relative to residual $CHCl_3$ (δ 7.26 ppm), or $(CD_3)_2CO$ (δ 2.05 ppm). ^{13}C NMR spectra are recorded on a Varian Inova 500 MHz spectrometer (125MHz) and are reported relative to $CHCl_3$ (δ 77.16 ppm), or $(CD_3)_2CO$ (δ 29.84 ppm). Data for ^1H NMR are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet, br d= broad doublet, app = apparent. Data for ^{13}C are reported in terms of chemical shifts (ppm). IR spectra were obtained using a Perkin Elmer Paragon 1000 spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). High resolution mass spectra (HRMS) were obtained from Agilent 6200 Series TOF with an Agilent G1978A

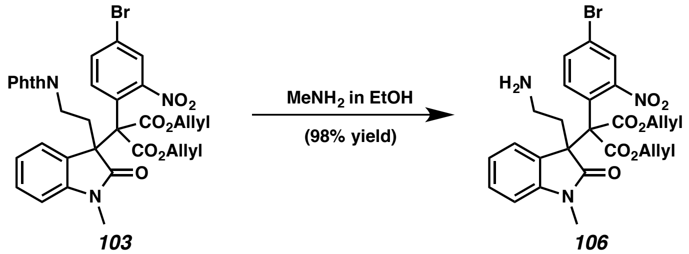
Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed ionization mode (MM: ESI-APCI+).

A3.4.2. Experimental Procedures



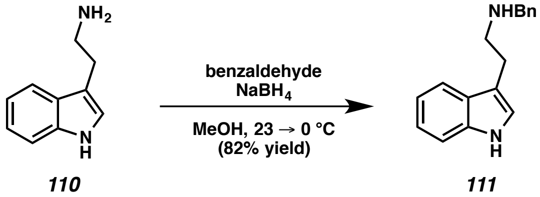
To a solution of phthalimide **103** (20.0 mg, 0.0285 mmol, 1.00 equiv) in EtOH (3.00 mL) and H_2O (2.40 μL) was added hydrazine monohydrate (28.0 μL, 0.577 mmol, 20.0 equiv). The reaction mixture was heated to 80 °C for 1 h. The reaction mixture was then cooled to 23 °C and the resulting solid was filtered through a plug of celite. The residue was purified by column chromatography using mixtures of EtOAc and hexanes to provide oxindole **105** (15.1 mg, 92% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 2.1 Hz, 1H), 7.50 (d, *J* = 7.4 Hz, 1H), 7.47 – 7.42 (m, 1H), 7.35 (d, *J* = 8.6 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 5.07 (s, 1H), 4.35 (s, br, 1H), 3.96 (dt, *J* = 9.9, 6.7 Hz, 2H), 3.86 (t, *J* = 6.7 Hz, 2H), 3.02 (s, 3H), 2.81 – 2.70 (m, 2H), 2.29 (s, br, 1H), 2.08 – 2.03 (m, 1H), 1.55 – 1.47 (m, 4H), 0.88 (dd, *J* = 14.0, 7.0 Hz, 3H), 0.76 (t, *J* = 7.4 Hz, 3H).

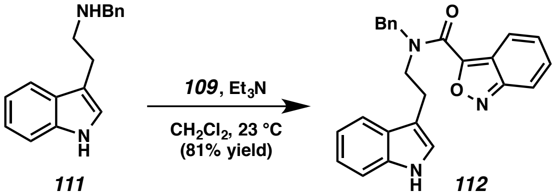


To a solution of $MeNH_2$ (8M in EtOH; 9.5 mL) was added phthalimide **103** (20.0 mg, 0.0285 mmol). The solution was stirred for 12 h at 23 °C. Then, the solution was concentrated to afford amine **106** (16.0 mg, 98% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (q, *J* = 2.2 Hz, 1H), 7.49 (dd, *J* = 7.5, 2.5 Hz, 1H), 7.41 (dt, *J* = 8.7, 2.4 Hz, 1H), 7.32 – 7.25 (m, 2H), 7.12 (ddd, *J* = 9.5, 7.6, 2.5 Hz, 1H), 6.70 (dd, *J* = 7.8, 2.5 Hz, 1H), 5.79 (ddq, *J* = 15.1, 9.3, 4.6, 4.2 Hz, 1H), 5.68 (ddtd, *J* = 16.9, 11.4, 5.7, 2.6 Hz, 1H), 5.19 (d, *J* = 17.1 Hz, 1H), 5.15 – 5.07 (m, 4H), 4.47 (pd, *J* = 12.2, 11.3, 4.9 Hz, 3H), 4.39 (d, *J* = 5.3 Hz, 2H), 2.97 (s, 3H), 2.75 (dp, *J* = 27.3, 6.8 Hz, 2H), 2.29 (dt, *J* = 12.6, 6.8 Hz, 1H), 2.09 – 2.01 (m, 1H).



To a solution of tryptamine (**110**) (500 mg, 3.12 mmol, 1.00 equiv) in MeOH (15.6 mL) at 23 °C was added benzaldehyde (0.350 mL, 3.43 mmol, 1.10 equiv). After 4 h, the reaction mixture was cooled to 0 °C. Then, $NaBH_4$ (177 mg, 4.68 mmol, 1.50 equiv) was added and the reaction mixture was stirred for an additional 1 h. The reaction was quenched with sat. aq $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2 (3 x 7.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to afford amine **111** (640 mg, 82% yield). Data for the compound matches reported data.[1]



To a solution of acid chloride **109** (0.613 mmol) and Et_3N (0.26 mL, 1.84 mmol, 3.00 equiv) in CH_2Cl_2 (3.10 mL) was added indole **111** (154 mg, 0.613 mmol, 1.00 equiv) at 23 °C. The reaction mixture was stirred for 6 h at 23 °C. After the reaction was done, water was added. The aqueous phase was extracted with CH_2Cl_2 (3 x 3.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel chromatography with mixtures of EtOAc and hexanes to afford amide **112** (197 mg, 81% yield).

(Due to the distinct presence of rotameric isomers, the ^{1}H NMR contained extra peaks.) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.81 (d, *J* = 8.9 Hz, 1H), 7.64 – 7.53 (m, 3H), 7.47 – 7.41 (m, 1H), 7.38 – 7.35 (m, 4H), 7.33 – 7.28 (m, 5H), 7.23 – 7.14 (m, 4H), 7.13 – 7.02 (m, 5H), 6.94 (d, *J* = 2.4 Hz, 1H), 4.85 (s, 4H), 4.01 (t, *J* = 7.4 Hz, 2H), 3.82 (t, *J* = 7.6 Hz, 2H), 3.14 (dt, *J* = 14.5, 7.6 Hz, 4H).

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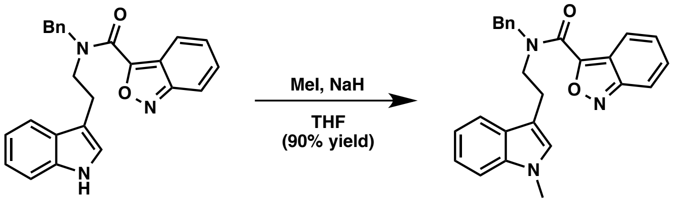
[1] Martin, D. B. C.; Vanderwal, C. D. *J. Am. Chem. Soc.* **2009**, *131*, 3472–3473.

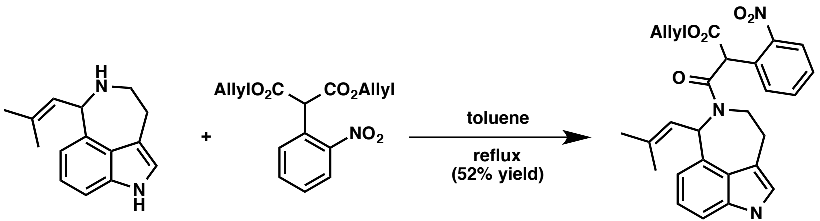


112 **114**

To a solution of indole **112** (68.4 mg, 0.173 mmol, 1.00 equiv) in THF (0.900 mL) were added MeI (0.110 mL, 1.73 mmol, 10.0 equiv) and NaH (60%; 14.0 mg, 0.346 mmol, 2.00 equiv) at 0 °C. The reaction mixture was stirred at 23 °C for 4 h. The reaction was quenched with sat. aq NH_4Cl. The aqueous phase was extracted with EtOAc (3 x 1.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel chromatography with mixtures of EtOAc and hexanes to afford amide **114** (64.0 mg, 90% yield).

(Due to the distinct presence of rotameric isomers, the ^{1}H NMR contained extra peaks.)

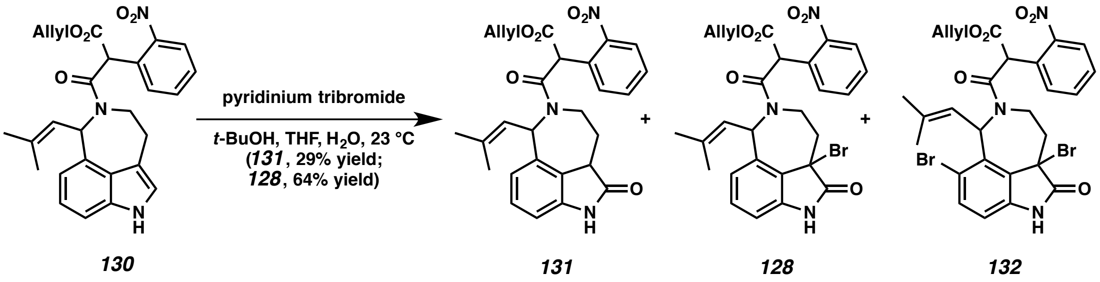
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.9 Hz, 0.5H), 7.69 (dt, *J* = 8.9, 1.1 Hz, 1H), 7.61 (dd, *J* = 12.1, 8.5 Hz, 1H), 7.54 (dt, *J* = 9.1, 1.0 Hz, 1H), 7.44 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.41 – 7.36 (m, 4H), 7.31 (tdd, *J* = 7.3, 4.0, 1.8 Hz, 5H), 7.12 – 7.05 (m, 4H), 6.91 (s, br, 0.5H), 6.76 (s, 1H), 4.88 (d, *J* = 2.3 Hz, 3.5H), 4.04 (t, *J* = 7.2 Hz, 2H), 3.86 – 3.78 (m, 1H), 3.74 (s, 1.5H), 3.57 (s, 3H), 3.16 (d, *J* = 8.2 Hz, 1H), 3.09 (t, *J* = 7.1 Hz, 2H).



4 **44** **130**

To a solution of aurantioclavine (**4**) (10.0 mg, 0.0442 mmol, 1.00 equiv) in toluene (0.200

mL) was added malonate **44** (15.0 mg, 0.0486 mmol, 1.10 equiv). The reaction mixture was refluxed for 12 h. Then, the reaction was quenched with water. The aqueous phase was extracted with EtOAc (3 x 1.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel chromatography with mixtures of EtOAc and hexanes to afford indole **130** (10.8 mg, 52% yield). Due to the distinct presence of rotameric isomers and diastereomeric mixtures, the ^1H NMR contained extra peaks.



To a solution of indole **130** (10.9 mg, 0.0230 mmol, 1.00 equiv) in *t*-BuOH (0.230 mL) and THF (0.06 mL), H_2O (2.10 μL) was added. Then, pyridinium tribromide (14.3 mg, 0.0448 mmol, 1.95 equiv) was added at 23 °C. The reaction was stirred at 23 °C for 6 h. Then, the reaction was quenched with water. The aqueous phase was extracted with EtOAc (3 x 0.50 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel chromatography with mixtures of EtOAc and hexanes to afford mixtures of **131** (3.30 mg, 29% yield), **128** (8.35 mg, 64% yield), and trace amounts of **132**. Due to the distinct presence of rotameric isomers and diastereomeric mixtures, the ^1H NMR contained extra peaks.

A3.5. References and Notes

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(1) (a) Boger, D. L.; Cassidy, K. C.; Nakahara, S. *J. Am. Chem. Soc.* **1993**, *115*, 10733–10741. (b) Suzuki, T.; Kobayashi, S. *Org. Lett.* **2010**, *12*, 2920–2923. (c) Asao, N.; Sato, K.; Menggenbateer; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 3682–3685. (d) Martin, D. B. C.; Nguyen, L. Q.; Vanderwal, C. D. *J. Org. Chem.* **2012**, *77*, 17–46. (e) Chen, Y.; Wang, L.; Liu, Y.; Li, Y. *Chem. Eur. J.* **2011**, *17*, 12582–12586.

(2) Koyama, J.; Toyokuni, I.; Tagahara, K. *Chem. Pharm. Bull.* **1998**, *46*, 332–334.

APPENDIX 4

Stereochemical Evaluation of Bisphosphine Copper Catalysts for the Asymmetric Alkylation of 3-Bromooxindoles with α-Arylated Malonate Esters[†]

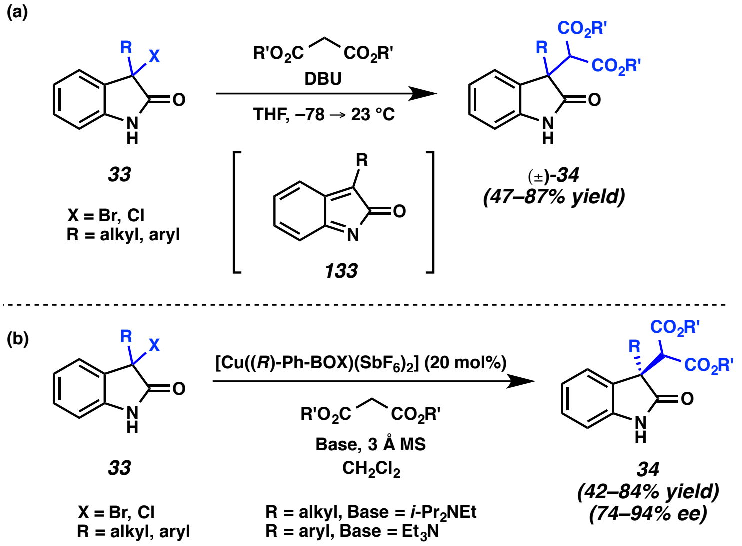
A4.1. Introduction

3,3-Disubstituted oxindole moieties are present in a wide variety of natural products and pharmaceutical agents.[1] Accordingly, methods for the asymmetric construction of 3,3-disubstituted oxindoles have attracted considerable attention from the synthetic community, and a number of catalytic stereoselective approaches to provide C3 quaternary stereocenters on oxindoles have been reported.[2,3] In 2007, we discovered that 3,3-disubstituted oxidoles **34** were furnished efficiently by base-mediated alkylation of reactive electrophilic *o*-azaxylyxene **133**, generated from 3-halooxindole **33**, with nucleophilic malonate esters (Scheme A4.1.1a).[3a] Additionally, we developed a method for the enantioselective alkylation of 3-bromooxindoles **33** by using a copper (*R*)-Ph-BOX ligand complex (Scheme A4.1.1b).[3b]

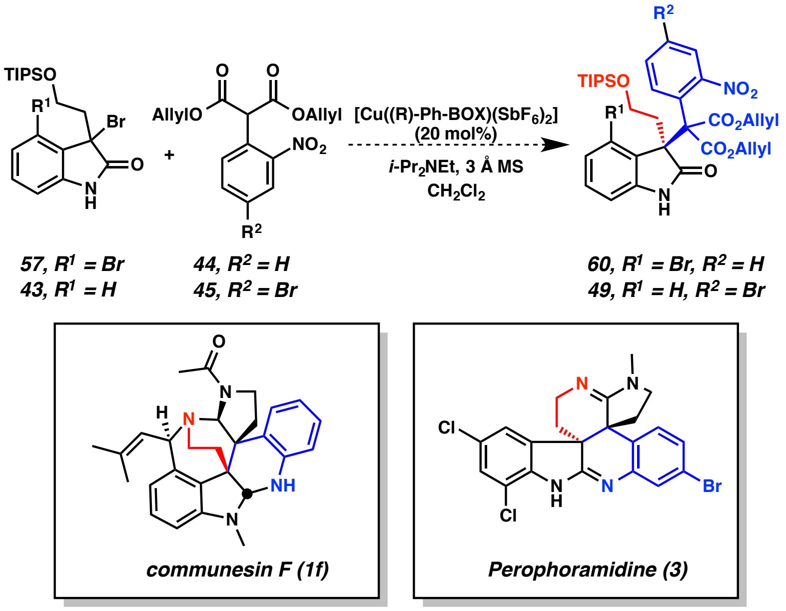
[†] This work was performed in collaboration with Dr. Chung Whan Lee and Dr. Scott C. Virgil. Additionally, this work has been published and adapted with permission from Lee, C. W.; Han, S.-J.; Virgil, S. C.; Stoltz, B. M. *Tetrahedron* **2014**, *71*, 3666–3670. Copyright 2014 Elsevier.

Following our development of these methods, our attention turned to the syntheses of the polycyclic alkaloids communesin F (**1f**) and perophoramidine (**3**).[4] We envisioned that the stereochemistry at the vicinal quaternary centers on communesin F and perophoramidine could be installed utilizing the conditions described in Scheme A4.1.1b. However, attempts to produce diesters **60** and **49** via copper catalyzed enantioselective alkylation of 3-bromooxindoles **57** and **43** with α-arylated malonate esters **44** and **45** were unsuccessful (Scheme A4.1.2). Therefore, we pursued the development of an alternative catalytic system.

Scheme A4.1.1. *Construction of 3,3-Disubstituted Oxindoles by Alkylation of 3-Halooxindoles*



Scheme A4.1.2. Attempts for Alkylation of 3-Bromooxindoles with α-Arylated Malonate Esters



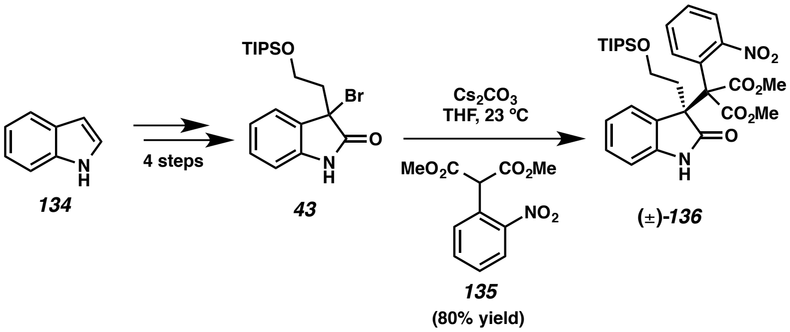
In our previous studies, we tested a variety of metal catalysts (e.g. Cu^{II}, Mg^{II}, La^{III}, and Ni^{II}) and discovered that the combination of Cu^{II} and a chiral bisoxazoline ligand effectively promoted the catalytic reaction. Chiral Cu(II) bisphosphine complexes have also found use in stereoselective synthesis.[5] Since the catalytic system can be formed with a number of different chiral bisphosphine ligands, quite a few options would be available for developing a stereoselective reaction. Herein, we describe several screening studies designed and undertaken to optimize the reaction conditions for the alkylation of 3-bromooxindoles with α-arylated malonate esters using a copper(II) bisphosphine catalyst.

A4.2. Results and Discussion

A4.2.1. Initial Screening Results

To develop a stereoselective alkylation method, we chose simple substrates for optimization studies; specifically, we used bromooxindole **43** without a substituent on the aromatic ring and *o*-nitrophenyl dimethylmalonate **135** as a coupling partner. Bromooxindole **43** was easily prepared from indole (**134**) in four steps by a known sequence,[4] which was then added to *o*-nitrophenyl dimethylmalonate **135** and cesium carbonate in THF solvent to afford a racemic product **136** in good yield. (Scheme A4.2.1).

Scheme A4.2.1. *Synthesis of the Racemic Product*

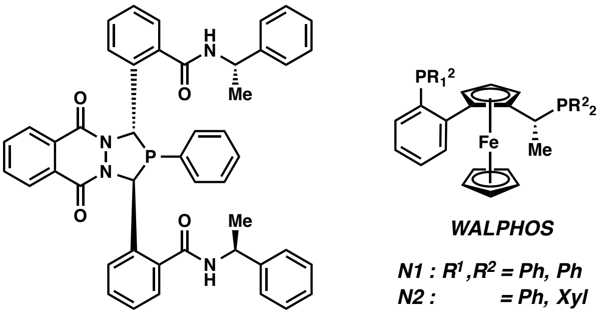


Choosing (*R*)-BINAP as a chiral ligand, we began our research by screening various copper sources, bases, and solvents. For instance we attempted the following variations of copper ions: Copper(II) triflate, copper(II) chloride with silver hexafluoroantimodate, copper(II) isobutyrate, copper(II) *tert*-butoxide (generated *in situ* by adding lithium *tert*-butoxide to copper(II) isobutyrate and ligand mixture), copper(II) ethylhexanoate, and copper(II) trifluoroacetylacetonate. We explored both organic and inorganic bases, including diisopropylethylamine, pyridine, tetramethylenediamine (TMEDA), triethylamine, diisopropylamine, 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU), sodium carbonate, potassium acetate, sodium ethylhexanoate and cesium carbonate. The various reactions combinations were attempted in the following solvents: dichloromethane, tetrahydrofuran, benzene, acetonitrile, and dioxane. Evaluating the 93 reactions that were explored,[6] we found that copper(II) *tert*-butoxide and the ligand complex generated in THF, which was similar to Fandrick's conditions for asymmetric propargylation[5], exhibited the best reactivity without generation of side products for the coupling of the arylated malonate **135** and bromooxindole **43** in CH_2Cl_2 (high conversion, 20% ee).

A4.2.2. Ligand Screening and Optimization Studies

Based on previous studies, we selected copper(II) *iso*-butyrate, lithium *tert*-butoxide and THF solvent for generation of the catalytic species with chiral ligands, diisopropylamine as the base and CH_2Cl_2 as solvent. We have screened 69 chiral bisphosphine ligands[6] under similar condition, finding WALPHOS and DiazaPHOS to give the best enantioselectivities (Figure A4.2.1).

***Figure A4.2.1**. Results with DiazaPHOS and WALPHOS*

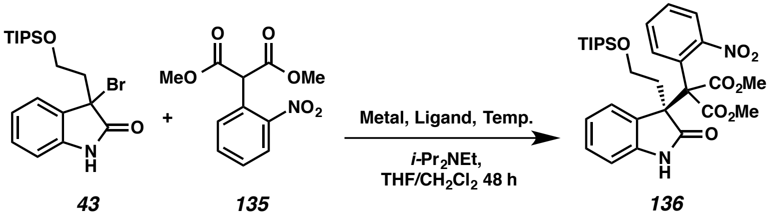


***W1* : (S,S,S)-DiazaPHOS-PPE**
40% ee

27% ee

Having identified the most effective ligands, we next screened several copper sources under lower temperatures. Although none of these sources exhibited better results than the combination of copper(II) isobutyrate and lithium *tert*-butoxide for WALPHOS (**N1** and **N2**), we were able to observe better stereoselectivity at low temperature (Table A4.2.1, entries 6 and 16). With DiazaPHOS (**W1**), copper(II) triflate showed better selectivity at 0 °C (Table A4.2.1, entries 22 and 23).

Table A4.2.1. *Further investigations using WALPHOS and DiazaPHOS in the alkylation reaction*

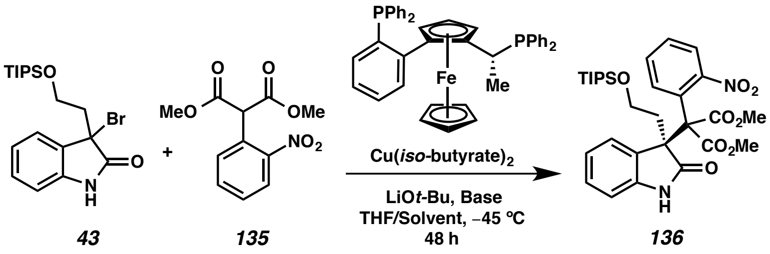


Entry	Metal Sources	Ligand	Additive	Temp.	ee[a]
1	CuCl$_2$	**N1**	AgBF$_4$	–45 °C	–
2	CuCl$_2$	**N1**	AgNTf$_2$	–45 °C	–
3	CuCl$_2$	**N1**	AgPF$_6$	–45 °C	–
4	CuCl$_2$	**N1**	AgSbF$_6$	–45 °C	–
5	CuCl$_2$	**N1**	LiO*t*-Bu	–45 °C	–
6	Cu(*iso*-butyrate)$_2$	**N1**	LiO*t*-Bu	–45 °C	44%
7	Cu(*iso*-butyrate)$_2$	**N1**	AgSbF$_6$	–45 °C	–
8	Cu(hfacac)$_2$	**N1**		–45 °C	trace
9	Cu(OTf)$_2$	**N1**		–45 °C	trace
10	Cu(OTf)$_2$	**N1**	LiO*t*-Bu	–45 °C	23%
11	Cu(EH)$_2$	**N1**		–45 °C	trace
12	CuCl$_2$	**N2**	AgBF$_4$	–45 °C	–
13	CuCl$_2$	**N2**	AgNTf$_2$	–45 °C	–
14	CuCl$_2$	**N2**	AgPF$_6$	–45 °C	–
15	CuCl$_2$	**N2**	AgSbF$_6$	–45 °C	–
16	Cu(*iso*-butyrate)$_2$	**N2**	LiO*t*-Bu	–45 °C	54%
17	Cu(hfacac)$_2$	**N2**		–45 °C	30%
18	Cu(OTf)$_2$	**N2**		–45 °C	45%
19	Cu(EH)$_2$	**N2**		–45 °C	trace
20	Cu(*iso*-butyrate)$_2$	**W1**	LiO*t*-Bu	0 °C	trace
21	Cu(*iso*-butyrate)$_2$	**W1**[b]	LiO*t*-Bu	0 °C	trace
22	Cu(OTf)$_2$	**W1**		0 °C	40%
23	Cu(OTf)$_2$	**W1**[b]		0 °C	50%

Conditions: 0.0049 mmol **43**, 0.0145 mmol **135**, Cu (20 mol %), Ligand (22 mol %), Additive (20 mol %), *i*-Pr$_2$NEt (3 equiv.), 0.1 mL CH$_2$Cl$_2$ (0.049 M). Metal catalyst, ligand and additives were mixed in THF. THF was removed *in vacuo*, and the resultant was diluted with the reaction solvent. The reaction was initiated by addition of base. Cu(hfacac)$_2$: Copper(II) hexafluoroacetylacetonate, Cu(EH)$_2$: Copper(II) ethylhexanoate. [a] enantiomeric excess was measured by chiral SFC. [b] 44 mol % of ligand was used.

With a suitable bisphosphine ligand in hand (**N1**), we tested multiple solvents and bases. However, amine bases weaker than Hünig's base (Table A4.2.2, entries 1-12) could not initiate the reaction, whereas stronger bases (entries 13-18) decreased the stereoselectivity. The copper bisphosphine complex demonstrated similar selectivity in dichloromethane (entry 19), THF (entry 20), and chloroform (entry 22), however it showed worse selectivity in acetonitrile (entry 21) and failed to proceed at all in toluene and 1,2-dimethoxyethane (DME).

Table A4.2.2. *Investigation of reaction solvents and bases with WALPHOS in the alkylation reaction*

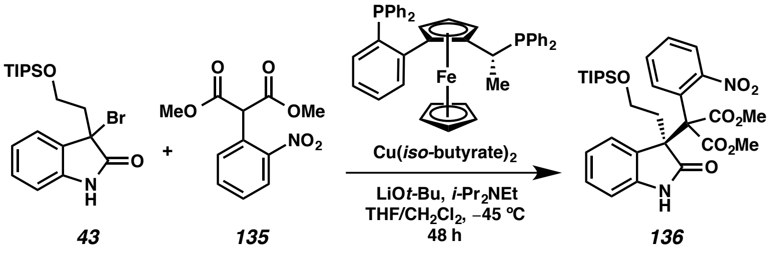


Entry	Solvent	Base	ee
1	CH_2Cl_2	DABCO	–
2	THF	DABCO	–
3	CH_3CN	DABCO	–
4	$CHCl_3$	DABCO	–
5	Toluene	DABCO	–
6	DME	DABCO	–
7	CH_2Cl_2	DMAP	–
8	THF	DMAP	–
9	CH_3CN	DMAP	–
10	$CHCl_3$	DMAP	–
11	Toluene	DMAP	–
12	DME	DMAP	–
13	CH_2Cl_2	Cs_2CO_3	35%
14	THF	Cs_2CO_3	15%
15	CH_3CN	Cs_2CO_3	20%
16	$CHCl_3$	Cs_2CO_3	20%
17	Toluene	Cs_2CO_3	–
18	DME	Cs_2CO_3	10%
19	CH_2Cl_2	*i*-Pr_2NEt	40%
20	THF	*i*-Pr_2NEt	50%
21	CH_3CN	*i*-Pr_2NEt	30%
22	$CHCl_3$	*i*-Pr_2NEt	40%
23	Toluene	*i*-Pr_2NEt	–
24	DME	*i*-Pr_2NEt	–

Conditions: 0.0024 mmol **43**, 0.0072 mmol **135**, Cu (20 mol %), Ligand (22 mol %), LiO*t*-Bu (20 mol %), Base (3 equiv), 0.06 mL CH_2Cl_2 (0.04 M).

In addition to these studies, we examined the effect of the catalyst and ligand loading on the stereoselectivity of our alkylation reaction. Unsatisfactory results were produced with low catalyst or ligand loading (Table A4.2.3, entries 1,2 and 4), but 20 mol % of copper(II) isobutyrate and 40 mol % of the ligand gave the product in 56% ee (Table A4.2.3, entry 3). Stoichiometric amounts of the copper presursor and ligand produced only a slight increase in ee (Table A4.2.3, entry 5). Additionally, we investigated the impact of the equivalents of Hünig's base on the selectivity of the reaction. Results showed the amount of Hünig's base had little effect on the stereoselectivity of the product (Table A4.2.3, entries 6-13). Subsequent examination of concentration effects showed lowering the concentration of the reaction mixture from 0.05 M to 0.02 M resulted in increase stereoselectivity (Table A4.2.4).

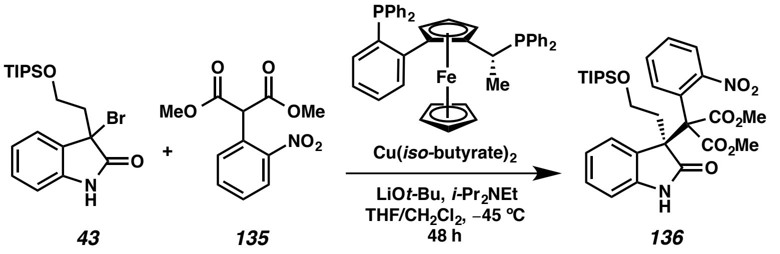
Table A4.2.3. *Examination of the amount of catalyst and ligand loading in the alkylation reaction*



Entry	Cu(*iso*-butyrate)$_2$	Ligand	*i*-Pr$_2$NEt	ee
1	10 mol %	10 mol %	3.0 equiv	25%
2	10 mol %	20 mol %	3.0 equiv	28%
3	20 mol %	40 mol %	3.0 equiv	56%
4	20 mol %	10 mol %	3.0 equiv	35%
5	1 equiv	1 equiv	3.0 equiv	60%
6	20 mol %	20 mol %	1.0 equiv	33%
7	20 mol %	20 mol %	1.5 equiv	35%
8	20 mol %	20 mol %	2.0 equiv	38%
9	20 mol %	20 mol %	2.5 equiv	37%
10	20 mol %	20 mol %	4.0 equiv	36%
11	20 mol %	20 mol %	5.0 equiv	37%
12	20 mol %	20 mol %	6.0 equiv	36%
13	20 mol %	20 mol %	20 equiv	36%

Conditions: 0.0049 mmol **43**, 0.0145 mmol **135**, LiO*t*-Bu (10 mol %), 0.1 mL CH_2Cl_2 (0.049 M).

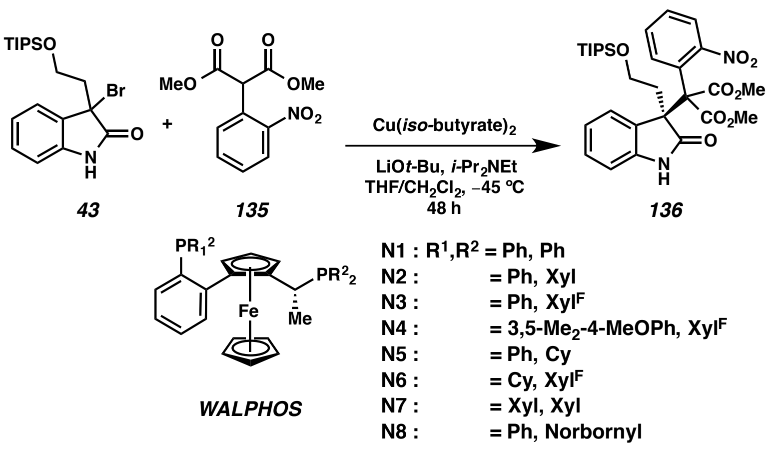
Table A4.2.4. *Examination of concentration in the malonate addition reaction*



Entry	Concentration	ee
1	0.005 M	53%
2	0.01 M	63%
3	0.02 M	64%
4	0.05 M	55%
5	0.25 M	40%

Conditions: 0.0049 mmol **43**, 0.0145 mmol **135**, Cu (20 mol %), Ligand (40 mol %), LiO*t*-Bu (20 mol %), *i*-Pr$_2$NEt (3 equiv).

Table A4.2.5. *The effect of WALPHOS substituents under optimized conditions in the alkylation reaction*



N1 : R^1,R^2 = Ph, Ph
N2 : = Ph, Xyl
N3 : = Ph, Xyl^F
N4 : = 3,5-Me_2-4-MeOPh, Xyl^F
N5 : = Ph, Cy
N6 : = Cy, Xyl^F
N7 : = Xyl, Xyl
N8 : = Ph, Norbornyl

Entry	Ligand	ee
1	**N1**	60%
2	**N2**	trace
3	**N3**	25%
4	**N4**	25%
5	**N5**	70%
6	**N6**	–
7	**N7**	–
8	**N8**	–

Conditions: 0.0049 mmol **43**, 0.0145 mmol **135**, Cu (20 mol %), Ligand (40 mol %), LiO*t*-Bu (20 mol %), *i*-Pr_2NEt (3 equiv), 0.25 mL CH_2Cl_2 (0.02 M).

Finally, we explored a set of WALPHOS ligands (**N1** – **N8**) under our optimized conditions. Gratifyingly, we observed improved ee by using (Ph,Cy)-WALPHOS (Table A4.2.5, entry 5), leading to product formation in 70% ee, whereas other ligands showed diminished selectivity. To date, this is the best result we have, which is a great improvement over the starting point.

A4.3. Conclusion

Asymmetric alkylation of 3-halooxindoles with malonate esters is an effective method to construct 3,3,-disubstituted oxindole moieties. Herein, we have reported that copper(II) chiral bisphosphine complex demonstrated reactivity with an α-arylated malonate ester, which was an unreactive substrate in previously developed conditions. This method could be applied to the installation of vicinal quaternary centers on communesin F and perophoramidine and could be useful in the synthesis of a variety of other natural products.

A4.4. Selected Experiments

A4.4.1. Synthesis of (±)-136

To a flame-dried round-bottomed flask, equipped with a stirbar, was added bromooxindole **43** (20 mg, 0.045 mmol), *o*-nitrophenyl dimethylmalonate **135** (37 mg, 0.135 mmol) and THF (0.5 mL). To the mixture was added cesium carbonate (47.4 mg, 0.045 mmol) at ambient temperature and the reaction mixture was then stirred for 3 h. The reaction mixture was then treated with saturated NH_4Cl aqueous solution, extracted with EtOAc, washed with brine and dried over $MgSO_4$. After concentration *in vacuo*, the crude product was obtained. Chromatography (6:1 hexanes : ethyl acetate) on silica gel afforded the title compound **136** (23 mg, 80% yield) as colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.0 (d, J = 8.1 Hz, 1H), 7.85 (s, 1H), 7.74 (dd, J = 7.9, 1.7 Hz, 1H), 7.40 (dtd, J = 26.6, 7.4, 1.5 Hz, 2H), 7.30 (d, J = 7.8 Hz, 1H), 7.14 (td, J = 7.7, 1.3 Hz, 1H), 6.90 (td, J = 7.7, 1.2 Hz ,1H), 6.75 (dd, J = 7.8, 1.1 Hz, 1H), 3.74 (s, 3H), 3.65 (s, 3H), 3.35 (ddd, J = 9.5, 8.4, 6.9 Hz, 1H), 3.06 (td, J = 9.3, 4.5, 1H), 2.93 (ddd, J = 12.6, 8.8, 6.7 Hz, 1H), 2.54 (ddd, J = 12.8, 8.4, 4.4 Hz, 1H), 0.89 (s, 21H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.86, 167.63, 167.27, 150.34, 140.67, 132.46, 131.12, 129.49, 129.23, 128.63, 128.61, 126.73, 125.39, 122.45, 109.98, 109.12, 59.52, 56.71, 52.81, 52.80, 38.34, 29.70, 17.85, 17,84, 11.80. IR (Neat Film, NaCl) 2923, 2852, 1722, 1617, 1532, 1463, 1353, 1259, 1097, 992, 799, 753 cm^{-1}; HRMS (MM) *m/z* calc'd for $C_{30}H_{40}N_2O_8Si$ $[M+H]^+$: 585.2627, found 585.2636.

A4.4.2. Ligand Screening Procedure

Every step was performed in a nitrogen-filled glove box. Solutions of Copper(II) isoburtyrate (8 mg, 0.034 mmol) in THF (3.5 mL), lithium *tert*-butoxide (2.72 mg, 0.034 mmol) in THF (3.5 mL), bromooxindole **43** (70 mg, 0.17 mmol) and malonate **135** (129 mg, 0.51 mmol) in CH_2Cl_2 (1.75 mL), *i*-Pr_2NEt (0.1 ml, 0.57 mmol) in CH_2Cl_2 (2 mL) were prepared in 2 dram vials prior to reaction setup. To a ligand (1.1 μmol, 22 mol %) in a 1 dram vial equipped with a stirbar was added copper(II) isobutyrate in THF (0.1 mL, 0.97 μmol, 20 mol %). The heterogeneous solution was agitated at room temperature for 10-20 min until a clear homogeneous solution was generated. The reaction mixtures were charged with lithium *tert*-butoxide in THF (0.1 mL, 0.97 μmol, 20 mol %). Reaction mixtures were allowed to stir for 5 min and concentrated under reduced pressure. A mixture of bromooxindole **43** and malonate **135** in CH_2Cl_2 (0.05 mL, 4.85 μmol, 14.55 μmol) was dispensed to each vial and allowed to stir for 10 min. After setting the reaction temperature, *i*-Pr_2NEt in CH_2Cl_2 (0.05 mL, 14.55 μmol, 3 equiv) was added to the reaction vials and allowed to stir for 48 h. Upon completion, sat. aq ammonium chloride solution (0.1 mL) was added, and the mixture was filtered through silica gel. Each filtrate was diluted by 1 mL of solvent (ethyl acetate or isopropanol) and analyzed by chiral SFC. The mixture was separated by an AD-H column with 20% isopropanol as eluent.

A4.5. References and Notes

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APPENDIX 5

Spectra Relevant to Appendix 4:

Stereochemical Evaluation of Bisphosphine Copper Catalysts for the Asymmetric Alkylation of 3-Bromooxindoles with α-Arylated Malonate Esters

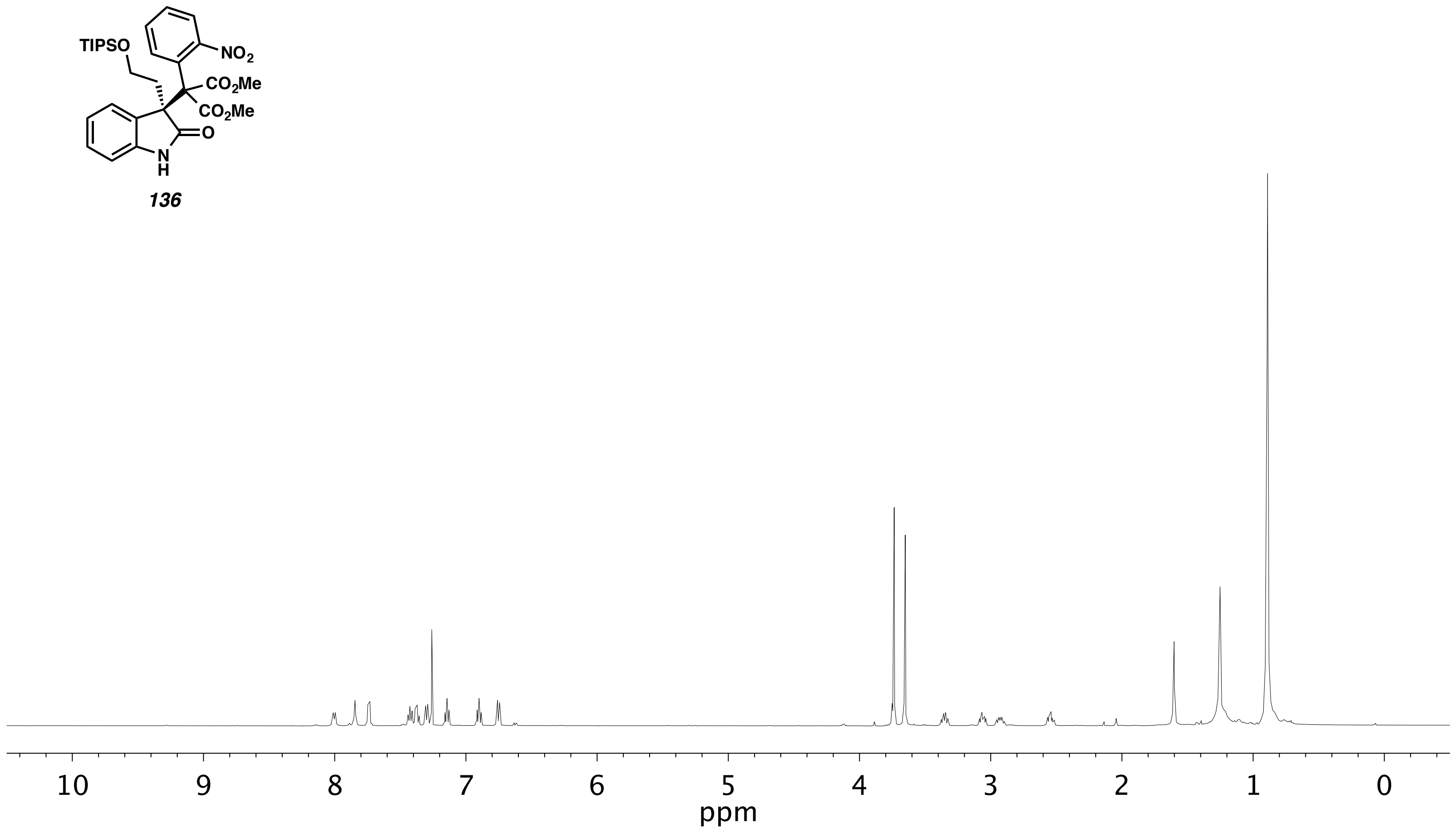

Figure A5.1. ^{1}H NMR (500 MHz, CDCl$_3$) of compound **136**.

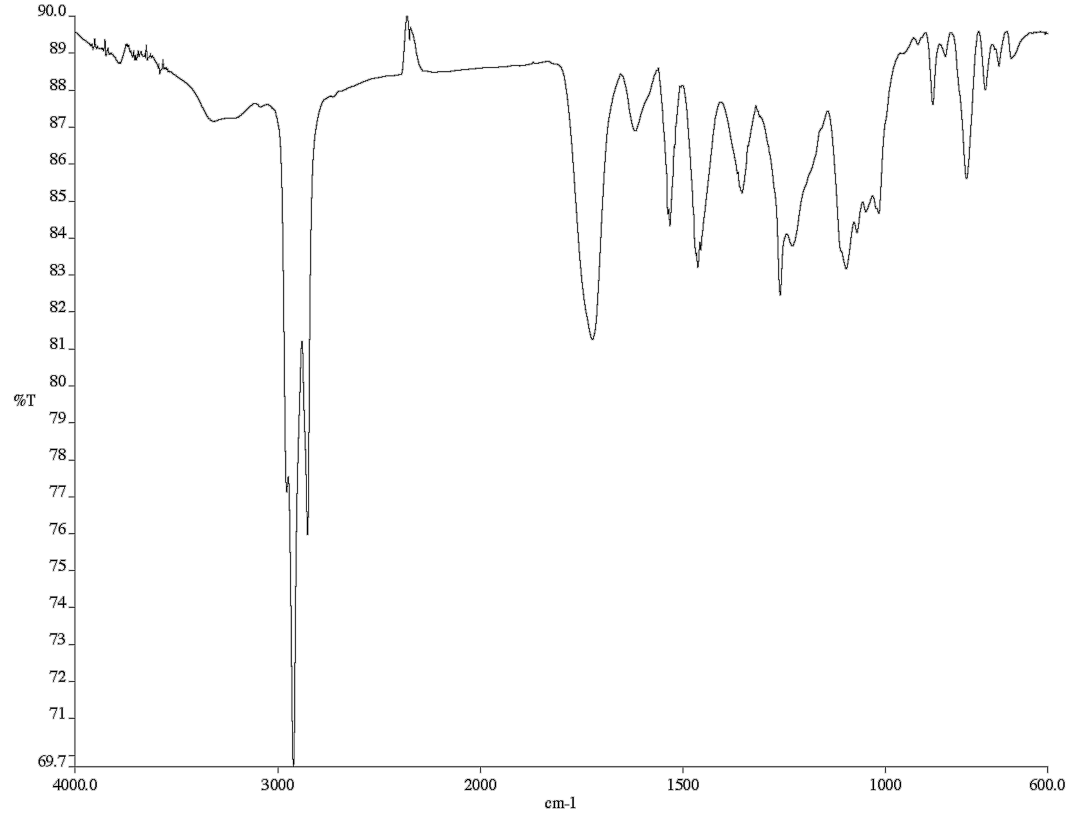

Figure A5.2. Infrared spectrum (Thin Film, NaCl) of compound **136**.

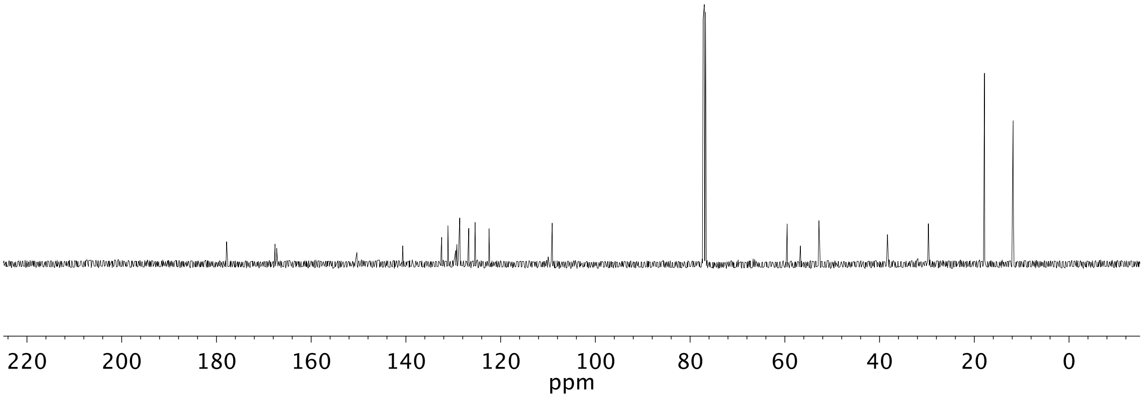

Figure A5.3. ^{13}C NMR (125 MHz, CDCl$_3$) of compound **136**.