THE TOTAL SYNTHESIS OF ALEUTIANAMINE, (–)-CROTONOLIDE D, AND (–)-CROTONINE G

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Hao Yu

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Hao Yu
ORCID: 0009-0008-6002-6276

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ABSTRACT

The first chapter describes the total synthesis of aleutianamine, a pyrroloiminoquinone alkaloid that displays potent and selective cytotoxicity towards pancreatic cancer PANC-1 cell line (IC_{50} = 25 nM). An initial α-thioketone derivatization approach was thwarted by a failed enolate functionalization. A second-generation approach employing palladium-catalyzed Barbier addition enabled the successful construction of the [3.3.1]bicyclononane moiety of the natural product, but unsuccessful downstream functionalization and poor material throughput led to the abandonment of this approach. Along the way, a one-pot Larock indolization/Buchwald–Hartwig amination cascade was developed for the synthesis of tricyclic diaminoindole derivatives. Eventually, the total synthesis was accomplished via a novel dearomative arylation of an aminothiophene, which allowed rapid access to the molecular skeleton of aleutianamine including the challenging bridgehead sulfide. Following construction of the core, cerium-mediated oxidative amination and palladium-catalyzed decarboxylative pinacol-type rearrangement enabled chemoselective introduction of the C10 aniline and alkenyl bromide, leading to the total synthesis of aleutianamine.

The second chapter details the total synthesis of crotonolide D and crotonine G. The synthetic approach employs a SmI_2 mediated ketyl radical cyclization to form the highly congested quaternary carbon at the center of these complex molecules. Following the furan introduction, the core structure of the natural product is constructed via oxidative olefin cleavage to install the unusual C19 and C20 oxidation. Finally, palladium-catalyzed carbonylation, furan oxidation and acid mediated condensation/epimerization completes the synthesis.

PUBLISHED CONTENT AND CONTRIBUTIONS

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LIST OF ABBREVIATIONS

Å	Ångstrom
λ	wavelength
μ	micro
$[\alpha]_D$	specific rotation at wavelength of sodium D line
°C	degrees Celsius
Ac	acetyl
AcOH	acetic acid
An	*para*-anisoyl
APCI	atmospheric pressure chemical ionization
aq	aqueous
Ar	aryl
atm	atmosphere
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
bp	boiling point
br	broad
Bu	butyl
Bz	benzoyl
c	concentration for specific rotation measurements (g/100 mL)
calc'd	calculated
CAN	ceric ammonium nitrate
cat	catalytic
CDI	Carbonyl diimidazole

cm^{-1}	wavenumber(s)
Cp^*	Pentamethylcyclopentadienyl
Cy	cyclohexyl
d	doublet
D	deuterium
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DIAD	Diisopropyl azodicarboxylate
DIBAL-H	diisobutylaluminum hydride
DIPEA	diisopropylethylamine
DMA	*N*,*N*-dimethylacetamide
DMAP	4-dimethylaminopyridine
DMF	*N*,*N*-dimethylformamide
DMP	Dess-Martin periodinane
DMSO	dimethyl sulfoxide
DPPA	Diphenylphosphoryl azide
dppe	1,2-Bis(diphenylphosphino)ethane
dr	diastereomeric ratio
e.g.	for example (Latin exempli gratia)
ee	enantiomeric excess
equiv	equivalent(s)
ESI	electrospray ionization
Et	ethyl
EtOAc	ethyl acetate
FAB	fast atom bombardment

FD	field desorption
g	gram(s)
GC	gas chromatography
h	hour(s)
HMDS	1,1,1,3,3,3-hexamethyldisilazane
HMPA	hexamethylphosphoramide
HPLC	high-performance liquid chromatography
HRMS	high-resolution mass spectroscopy
Hz	hertz
i-Bu	isobutyl
IC_{50}	Half-maximal inhibitory concentration
i.e.	that is (Latin id est)
IPA	isopropanol, 2-propanol
i-Pr	isopropyl
IR	infrared (spectroscopy)
J	coupling constant
K	Kelvin(s) (absolute temperature)
kcal	kilocalorie
L	liter; neutral ligand
LC–MS	liquid chromatography–mass spectrometry
LDA	lithium diisopropylamide
m	multiplet; milli
m	meta
M	metal; molar; molecular ion
m/z	mass to charge ratio
m-CPBA	*meta*-chloroperoxybenzoic acid
Me	methyl

mg	milligram(s)
MHz	megahertz
min	minute(s)
MM	mixed method
mol	mole(s)
mp	melting point
Ms	methanesulfonyl (mesyl)
MS	molecular sieves
MTBE	methyl *tert*-butyl ether
NBS	*N*-bromosuccinimide
n-Bu	butyl
NCS	*N*-chlorosuccinimide
ND	not determined
NMO	*N*-methylmorpholine *N*-oxide
NMP	*N*-methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
NR	no reaction detected
Nu^-	nucleophile
o	ortho
p	para
Pd/C	palladium on carbon
PG	protecting group
Ph	phenyl
pH	hydrogen ion concentration in aqueous solution
PIFA	Phenyliodine bis(trifluoroacetate)
Piv	pivolyl
PMA	Phosphomolybdic acid

ppm	parts per million
Pr	propyl
PTSA	*para*-toluenesulfonic acid
Py	pyridine
q	quartet
R	generic for any atom or functional group
Ref.	reference
s	singlet
t	triplet
TBAF	tetrabutylammonium fluoride
TBHP	*Tert*-butyl hydroperoxide
TBS	*tert*-butyldimethylsilyl
t-Bu	*tert*-butyl
Tf	trifluoromethanesulfonyl (triflyl)
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
TLC	thin-layer chromatography
TMS	trimethylsilyl
TOF	time-of-flight
t_R	retention time
Ts	*p*-toluenesulfonyl (tosyl)
TTMSS	Tris-trimethylsilyl silane
UV	ultraviolet
v/v	volume to volume
w	weak
w/v	weight to volume

w/w	weight to weight
X	anionic ligand or electronegative element

CHAPTER 1

Total Synthesis of Aleutianamine [†]

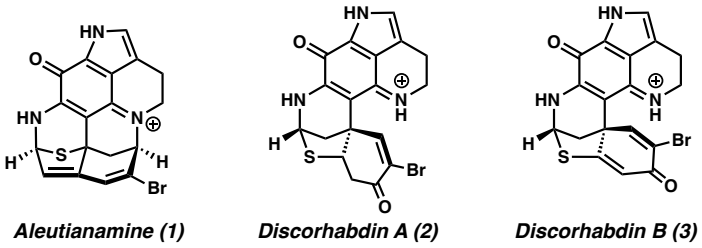
1.1 INTRODUCTION

Discorhabdin alkaloids are a large class of marine natural products characterized by their central pyrroloiminoquinone core.[1] Members of this class generally possess complex multibridged ring systems containing various heteroatoms such as oxygen, nitrogen, sulfur, and bromine. Discorhabdin alkaloids display a wide range of biological activity such as antiviral, antitumor, and immunomodulatory activities.[2] The challenging molecular structure and unique biological activities of discorhabdin alkaloids have stimulated the interest of synthetic chemists over the past five decades. Several members (Figure 1.1.1) of this class have been successfully synthesized.[3] A number of synthetic approaches and methodologies were developed during the synthesis of discorhabdins, pushing the boundaries of synthetic chemistry. Interest in discorhabdin total synthesis was revived after the discovery of aleutianamine (**1**), a rearranged discorhabdin alkaloid isolated by Hamann and coworkers from the marine sponge *Latrunculia (Latrunculia) austini*.[4] Aleutianamine (**1**) was found to possess potent *in vitro* cytotoxicity against a wide variety of cancer cells, with exceptional selectivity toward pancreatic cancer (IC_{50} = 25 nM against PANC–1). The novel structure and promising biological activity of aleutianamine

[†]Portions of this chapter have been reproduced and modified with permission from [*]Yu, H.; [*]Sercel, Z. P.; Rezgui, S. P.; Virgil, S. V.; Stoltz, B. M. *J. Am. Chem. Soc.* **2023**, *145*, 25533–25537. under CC-BY 4.0; © 2023 American Chemical Society.

(**1**) render it an attractive target for total synthesis. This chapter provides a complete account of our synthetic studies toward aleutianamine (**1**), which culminated in a non-biomimetic total synthesis of the natural product.

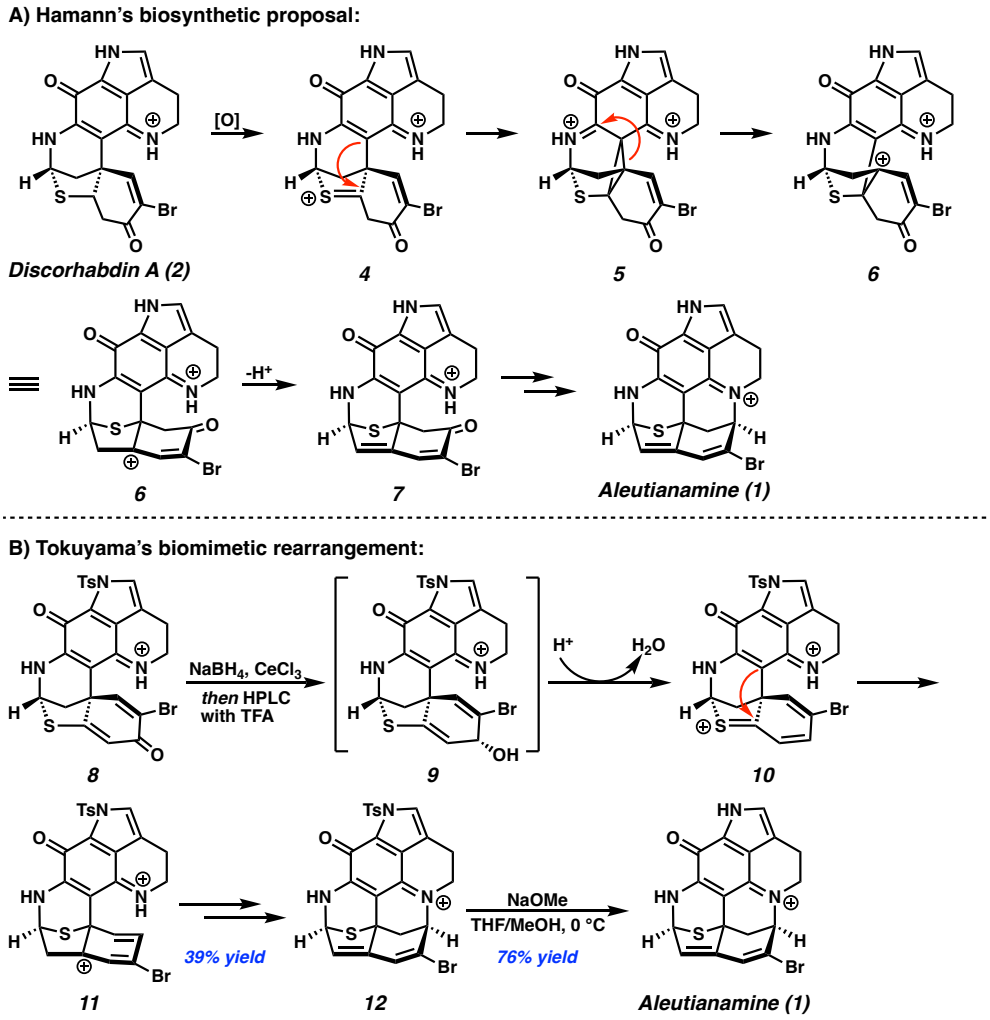
Figure 1.1.1 *Aleutianamine (**1**) and biosynthetically related discorhabdin alkaloids.*



1.2 BIOSYNTHESIS OF ALEUTIANAMINE

Biosynthetically, aleutianamine (**1**) was proposed to arise from discorhabdin A (**2**, Scheme 1.2.1).[4] Initial sulfide oxidation would generate thiocarbenium **4**. Attack on the thiocarbenium ion by the adjacent enamine moiety would deliver cyclopropane **5**, fragmentation of which would lead to allylic carbocation **6**. Finally, deprotonation of cation **6** would provide dienone **7**, then reductive cyclization with the pendant imine would yield aleutianamine (**1**). This cationic skeletal rearrangement was supported by the first total synthesis of aleutianamine (**1**) accomplished by Tokuyama and coworkers.[6] Luche reduction of N-tosyl discorhabdin B (**8**) generated an unstable allylic alcohol **9**, which upon HPLC purification with aqueous trifluoroacetic acid triggered a rearrangement (Scheme 1B) similar with Hamann's biosynthetic hypothesis, furnishing N-tosyl aleutianamine (**12**) in 39% yield. Subsequent tosyl group cleavage completed the synthesis in a remarkable 13-step longest linear sequence.

Scheme 1.2.1. *(A) Hamman's initial biosynthetic proposal. (B) Tokuyama's biomimetic rearrangement.*

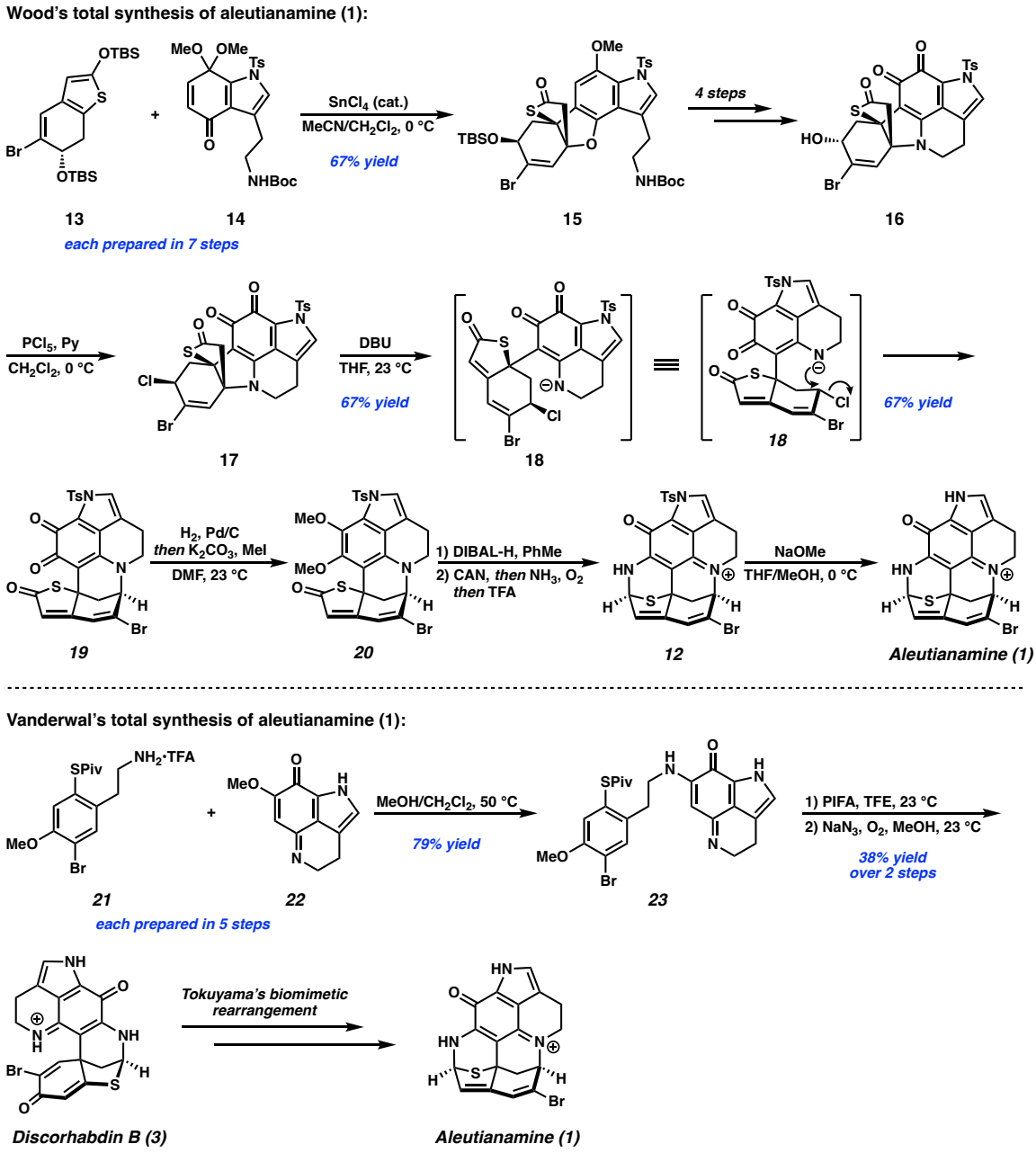


1.3 OTHER TOTAL SYNTHESES OF ALEUTIANAMINE

Following Tokuyama and our initial reports, additional syntheses of aleutianamine (**1**) were disclosed by Wood and Vanderwal.[5] Wood and coworkers utilized a convergent fragment coupling approach (Scheme 1.3.1 A). Vinylogous Mukaiyama–Michael/oxa-Michael cascade between siloxythiophene **13** and quinone monoketal **14** provided oxa-

propellane **15**, which upon 4 steps redox and protecting group manipulations yielded aza-propellane **16**. Chlorination of the secondary alcohol in **16** with PCl_5 proceeded with

Scheme 1.3.1. *(A) Wood's total synthesis of aleutianamine (**1**). (B) Vanderwal's synthesis of aleutianamine (**1**).*



stereoinversion, delivered intermediate **17**. From aza-propellane **17**, skeleton of aleutianamine (**1**) was accessed via an intriguing skeletal rearrangement: treatment of **17** with DBU effected an E1cb elimination to afford **18**, which subsequently underwent intramolecular substitution with the allylic chloride to furnish **19**. Toward the completion of synthesis, they employed a sequence similar to our end-game strategy. Ortho-quinone **19** was hydrogenated and methylated in-situ to provide anisole **20**. Then 1,2-reduction of thiobutenolide followed by ceric ammonium nitrate mediated oxidative amination afforded N-tosyl aleutianamine (**12**). Finally, tosyl deprotection with sodium methoxide completed an elegant abiotic total synthesis of aleutianaine (**1**) in 16 steps (LLS).

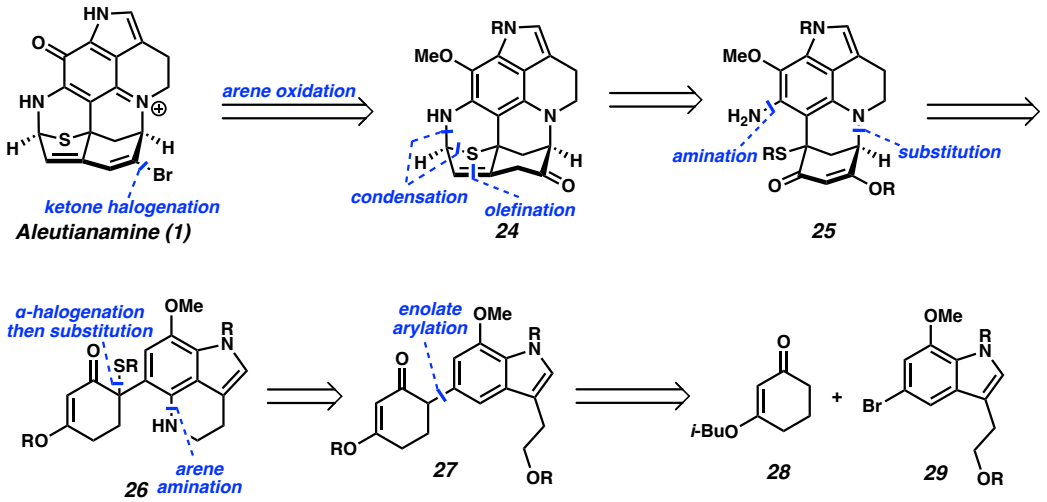
Vanderwal and coworkers took an approach centered on the biomimetic rearrangement reported by the Tokuyama group (Scheme 1.3.1 B). Condensation between Tyramine derivative **21** and iminoquinone **22** (each prepared in 5 steps from commercial material) afforded intermediate **23**. Subsequent oxidative spirocyclization and thioaminal formation provided discorhabdin B (**3**), which upon Tokuyama's biomimetic cascade afforded aleutianamine, completing a biomimetic total synthesis in 9 steps (LLS).

1.4 FIRST-GENERATION APPROACH

We set out to develop a synthetic route to aleutianamine that was orthogonal to the biosynthetic proposal. In our first-generation retrosynthetic analysis (Scheme 1.4.1), we disconnected the alkenyl bromide and reduced the oxidation level of the central quinone down to the corresponding anisole (**24**). This approach is novel compared to previous discorhabdin syntheses, as those typically introduce the quinone at an early stage. Then, release of the thioaminal and removal of the nearby olefin tracked back to protected 1,3-

diketone **25**. Disconnection of the two highlighted C–N bonds through amination guided us back to attached ring system **26**. The sulfide and aniline could be introduced via enolate functionalization and Buchwald-Hartwig amination, resulting in further simplification to functionalized indole **27**. Finally, disconnecting the attached rings suggests readily accessible ketone **28** and tryptophol **29** as starting materials.

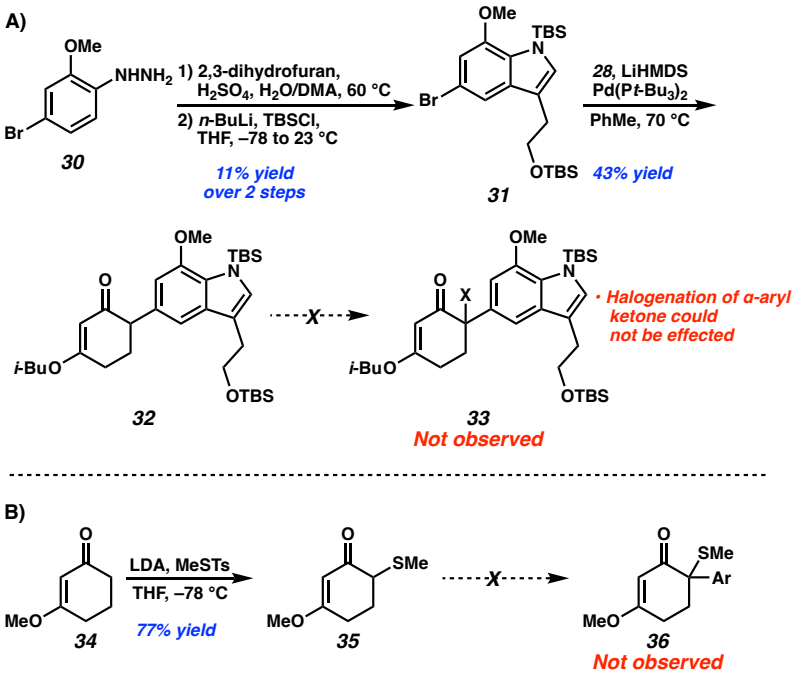
Scheme 1.4.1. *First-generation retrosynthetic analysis.*



We began our synthetic effort by preparation of tryptophol ether **31**. Starting from known hydrazine[7] **30** (Scheme 1.4.2A), Fischer indole synthesis afforded the tryptophol, which upon treatment with excess *n*-BuLi and TBSCl provided the bis-silylated intermediate **31**, albeit in only 11% yield. Subsequent palladium-catalyzed enolate arylation with vinylogous ester afforded tricyclic intermediate **32**.[8] However, despite extensive experimentation, the proposed α-halogenation could never be effected in our hands. Examined conditions either promoted no reaction or led to aromatization of the cyclohexanone. Given the oxidation sensitivity and hindered nature of aryl ketone **32**, we revised the synthetic plan by switching the order of the sulfuration and arylation (Scheme 1.4.2B). Electrophilic sulfuration on vinylogous ester **34** proceeded smoothly to give α-

thioketone **35**, but the following enolate arylation failed under all conditions tested. Given the pitfalls encountered in this vinylogous ester system, due partly to the potential for aromatization, this approach was abandoned.

Scheme 1.4.2. *(A) Failed α-sulfuration of aryl ketone* ***32****. (B)Attempted tertiary sulfide synthesis via ketone arylation.*

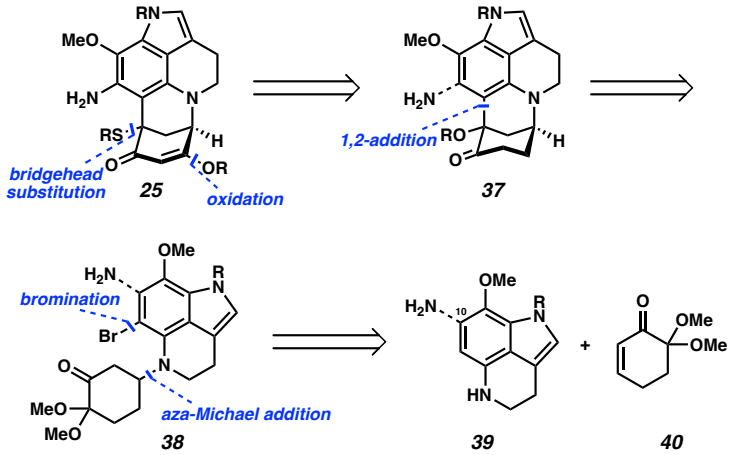


1.5 SECOND-GENERATION RETROSYNTHESIS

Taking the lessons learned from the first-generation approach, a revised retrosynthesis was proposed to circumvent the issues encountered with enolate functionalization. As in the first-generation retrosynthetic analysis, we envisioned that aleutianamine (**1**) would arise from pentacyclic ketone **25**. In contrast to the first retrosynthesis, the bridgehead sulfide in **25** (Scheme 4) was disconnected via bridgehead carbocation substitution,[9] tracing back to oxygenated intermediate **37**. By introducing the

problematic sulfide at a relatively late stage, a wider range of methods could be applied for the bridged ring synthesis. Additionally, as the feasibility of late stage arene amination was uncertain, both the C10 aminated (**37**, Scheme 1.5.1) and non-aminated intermediates would be investigated. The [3.3.1]bicyclononane was disconnected by intramolecular Barbier-type addition, leading back to intermediate **38**, which could be prepared from aniline **39** and enone **40** via aza-Michael addition followed by arene halogenation.

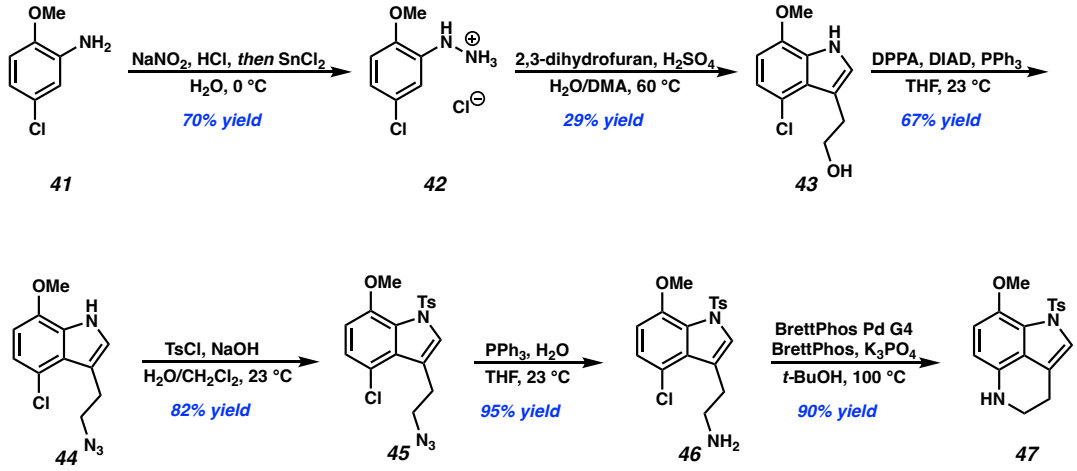
Scheme 1.5.1. *Revised retrosynthetic analysis of key intermediate* ***25****.*



Proceeding forward, we initially investigated the new approach without early-stage incorporation of the C10 nitrogen. Diazotization/reduction of commercially available aniline **41** (Scheme 1.5.2) generated hydrazine **42** in 70% yield on a 50-gram scale.[10] Subsequent Fischer indolization with 2,3-dihydrofuran under aqueous acidic conditions afforded tryptophol **43** in 29% yield.[11] Despite suboptimal yield, this reaction was found to perform consistently even on multidecagram scale; over 15 grams of tryptophol **43** could be readily prepared in one pass. Mitsunobu substitution of the primary alcohol in **43** with azide gave **44**, which upon indole protection and Staudinger azide reduction afforeded amine **46**. Finally, intramolecular Buchwald/Hartwig amination closed the third ring,

furnishing tricyclic aniline **47** in 90% yield.[12] This six-step reaction sequence proved scalable, providing 8 grams of aniline **47** in a single pass.

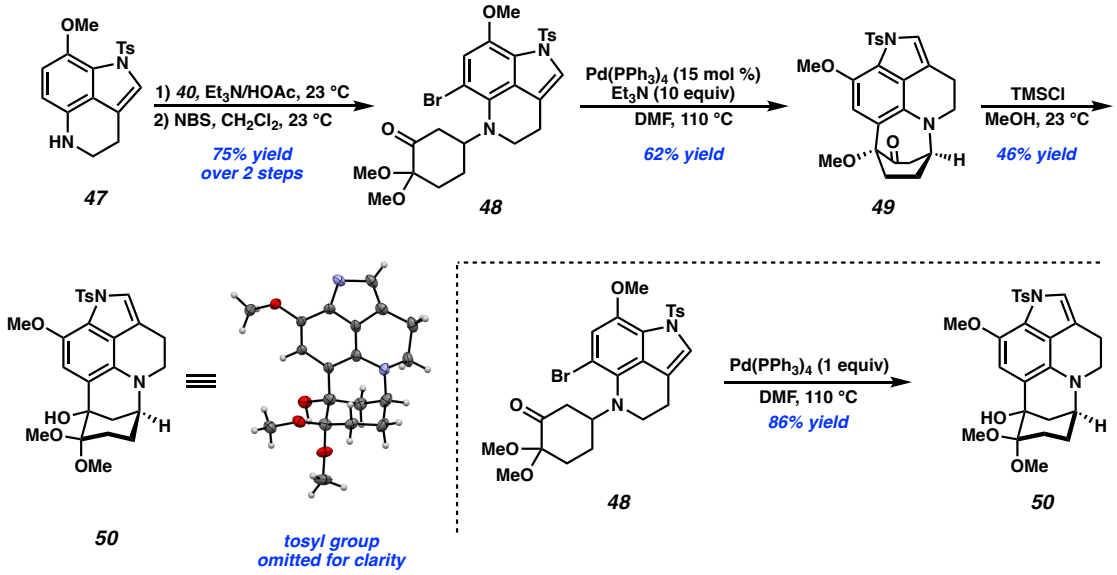
Scheme 1.5.2. *Preparation of aniline* ***47***.



With an ample amount of **47** in hand, we began to investigate strategies to construct the [3.3.1] bicyclic ring system (Scheme 1.5.3). Following optimization, aza-Michael addition between aniline **47** and enone **40** was effected by using partially ionic liquid as a solvent.[13] Arene bromination proceeded smoothly with NBS, delivering intermediate **48** in high yield, primed for the intramolecular 1,2-addition. Interestingly, subjecting **48** to palladium-catalyzed Barbier addition conditions provided [3.2.2]bicyclononane **49** as the sole product.[14] This product likely arises from 1,2-addition into the ketone, followed by acid-mediated 1,2-rearrangement. Treatment of this intermediate with methanolic HCl cleanly effected a 1,2-cationic rearrangement, affording the desired [3.3.1]bicyclononane **50** in 46% yield. Acetal **50** proved to be crystalline, which allowed unambiguous structural determination via X-ray analysis. In contrast to catalytic 1,2-addition, conducting the reaction with stoichiometric palladium afforded dimethyl ketal **50** as the only product,

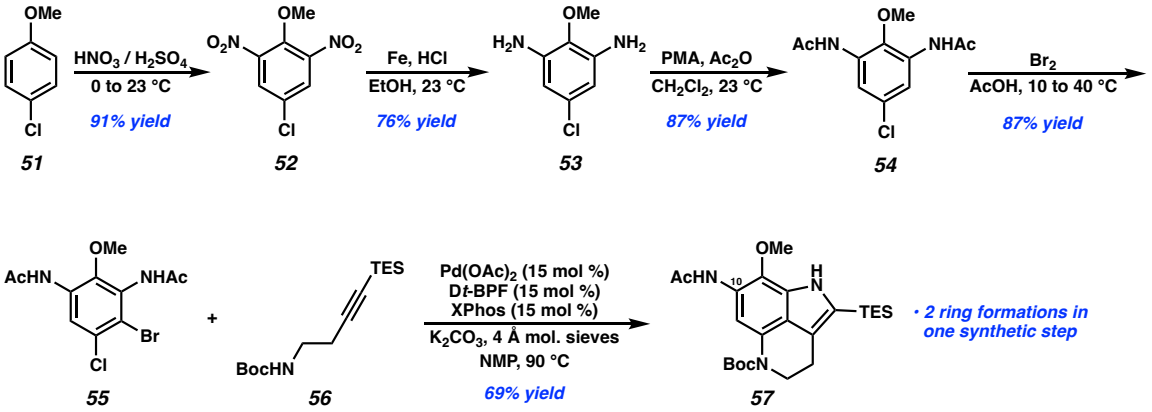
presumably because no Brønsted acid was generated as turning over a Pd (II) intermediate was not necessary.

Scheme 1.5.3. *Palladium catalyzed 1,2-addition.*



Encouraged by the successful synthesis of bridged intermediate **50**, we sought to apply the existing route to access a C10-aminated derivative. Dinitration of commercial anisole **51** (Scheme 1.5.4) afforded nitroarene **52**, which underwent reduction with Fe/HCl

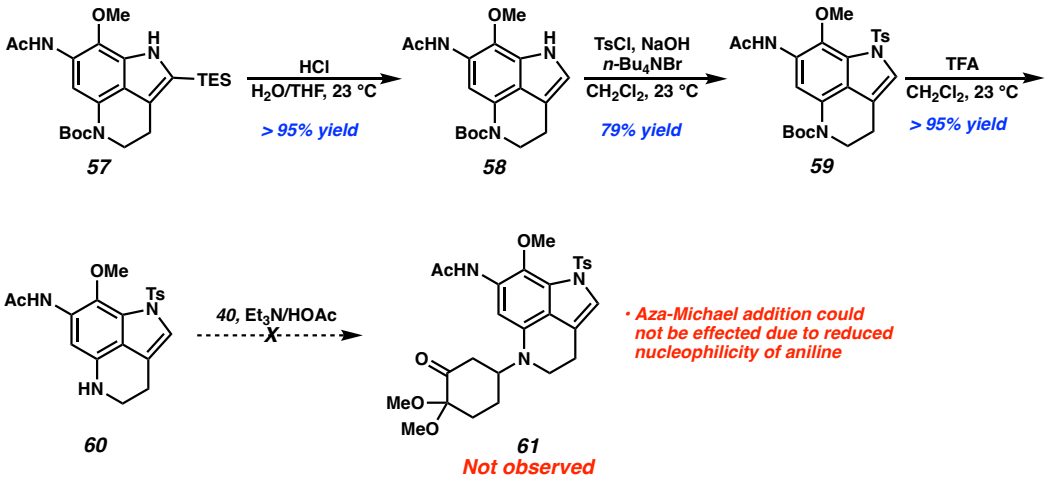
Scheme 1.5.4. *Preparation of aniline **57** via tandem Larock/Buchwald–Hartwig Annulation.*



to yield dianiline **53**. Then phosphomolybdic acid (PMA)-catalyzed acetylation[15] followed by desymmetrizing mono-bromination provided cyclization precursor **55** in high yield. Finally, a tandem Larock indolization/Buchwald–Hartwig amination cascade completed the preparation of tricyclic aniline **57**.[16]

We then focused our efforts toward employing C10-aminated tricycle **57** in the previously developed route to access more advanced [3.3.1]bicyclic intermediates (Scheme 1.5.5). C-2 desilylation with HCl delivers indole **58**, which was tosylated to furnish aniline **59**. Treatment with TFA cleanly removed the Boc protecting group, affording aniline **60** in quantitative yield. Unfortunately, **60** was found not to be competent in aza-Michael addition, possibly owing to the inductive electron-withdrawing effect of the acetamide substituent. Only nonspecific decomposition was observed when **60** was subjected to the previously employed partially ionic liquid conditions.

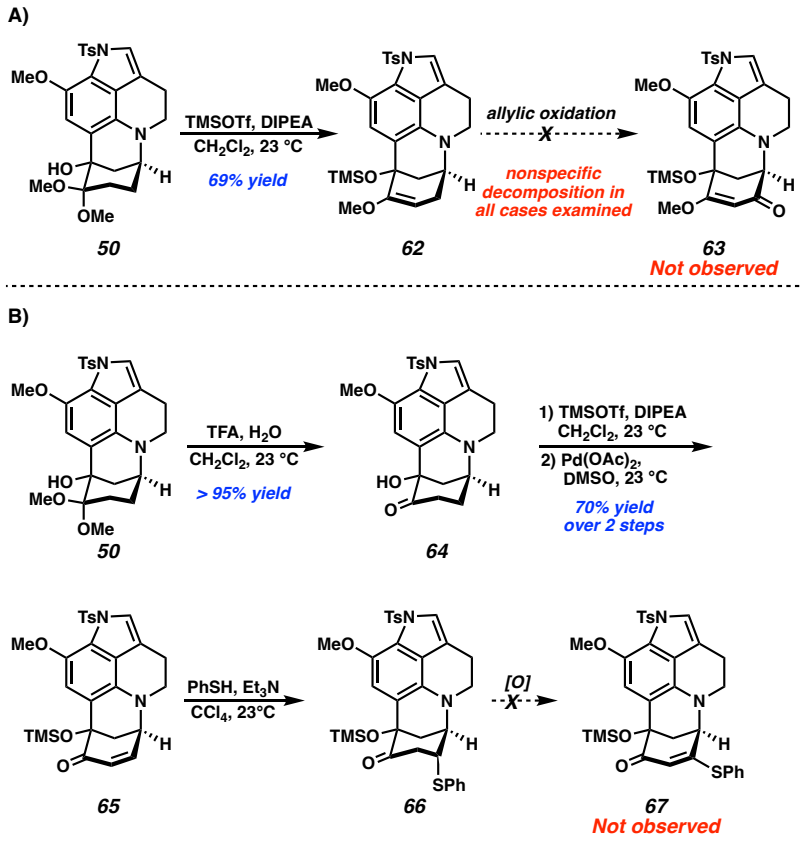
Scheme 1.5.5. *Advancement of tricyclic aniline **57**.*



We therefore turned our attention to evaluate strategies to further elaborate bridged polycycle **50**, more specifically, the installation of a 1,3-diketone moiety. The first route we examined was allylic oxidation (Scheme 1.5.6A). Treatment of dimethyl ketal **50** with

TMSOTf and DIPEA effected an elimination of methanol, producing enol ether **62** in 69% yield.[17] Disappointingly, subjecting enol ether **62** to different allylic oxidation conditions was met with no success, only nonspecific decomposition was observed in all cases. It is possible that the electron-rich nature of the aniline renders it incompatible with the oxidants necessary to achieve allylic oxidation.

Scheme 1.5.6. *Elaboration of 1,2-addition product* ***50****.*



Another precedented, albeit lengthier route to access a 1,3-diketone equivalent involves desaturation followed by thia-Michael addition and further desaturation to vinylogous thioester **67** (Scheme 1.5.6B).[18] Alkaline hydrolysis of thioester **67** would provide a 1,3-diketone. With this proposal in mind, hydrolysis of ketal **50** proceeded smoothly with aqueous acid. Then soft enolization with TMSOTf and DIPEA and Saegusa–

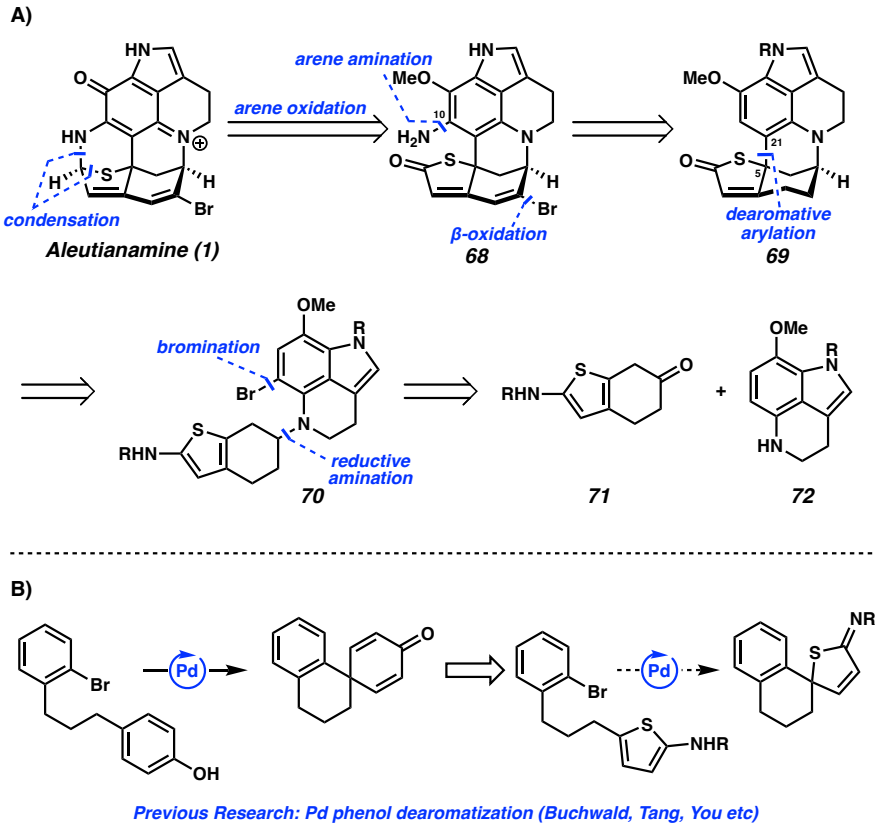
Ito oxidation delivered enone **65**.[19] Treatment of enone **65** with PhSH and catalytic Et_3N afforded sulfide **66** in nearly quantitative yield. However, to our dismay, subjection of sulfide **66** to various halogenating reagents failed to effect the desired desaturation. Only non-specific decomposition was observed. While the evaluation of further reaction conditions could potentially lead to the synthesis of masked 1,3-diketone **67**, the route to sulfide **66** is highly linear, with a longest linear sequence of 13 steps, which was detrimental for material throughput. Additionally, the most advanced intermediate lacks both the bridgehead sulfide and alkenyl bromide. Installation of those challenging motifs from sulfide **66** would likely make the synthetic sequence prohibitively long. Therefore, the second-generation approach was also abandoned.

1.6 THIRD-GENERATION RETROSYNTHETIC ANALYSIS

As we revised our synthetic route yet again, we realized that an ideal synthesis of aleutianamine (**1**) would be convergent and should allow rapid access to the whole molecular skeleton of **1** including the bridgehead sulfide. With these ideas as guidelines, we proposed a third-generation retrosynthesis of aleutianamine (**1**). First, oxidation to the iminoquinone and release of the thioaminal would track back to thiobutenolide **68** (Scheme 1.6.1A). Disconnection of the C10 amino group and alkenyl bromide leads to thiolactone intermediate **69**. Taking inspiration from previous reports of dearomative phenol arylations (Scheme 10B),[20] we then disconnected the C5–C21 bond via thiophene dearomatization, tracing back to haloarene **70**. Haloarene **70** would arise from aniline **72** and aminothiophene **71** via a convergent fragment coupling. The scalable synthesis of aniline

47 we developed in the second-generation approach would facilitate access to material to test the key cyclization step.

Scheme 1.6.1. *Third-generation retrosynthetic analysis of aleutianamine via dearomative thiophene arylation.*

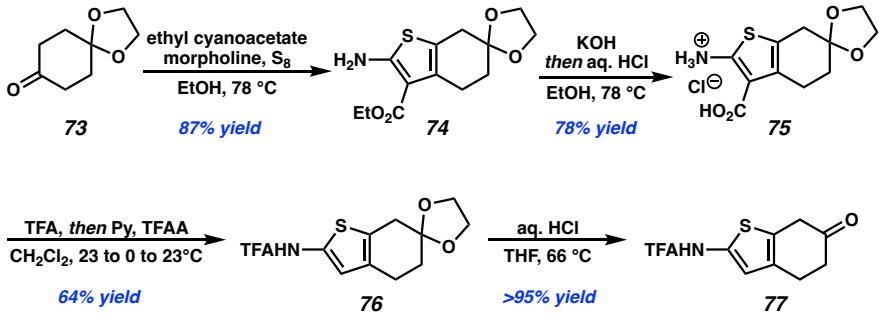


1.7 PALLADIUM-CATALYZED DEAROMATIVE ARYLATION

To realize this synthetic plan, a robust synthesis of aminothiophene **71** would be required. Starting from commercially available 1,4-cyclohexanedione monoethylene ketal (**73**, Scheme 1.7.1), Gewald aminothiophene synthesis under literature conditions provided aminothiophene **74** in 87% yield.[21] Saponification to acid **75**, followed by TFA-mediated decarboxylation, removed the undesired C3 ester group, and the resulting 2-

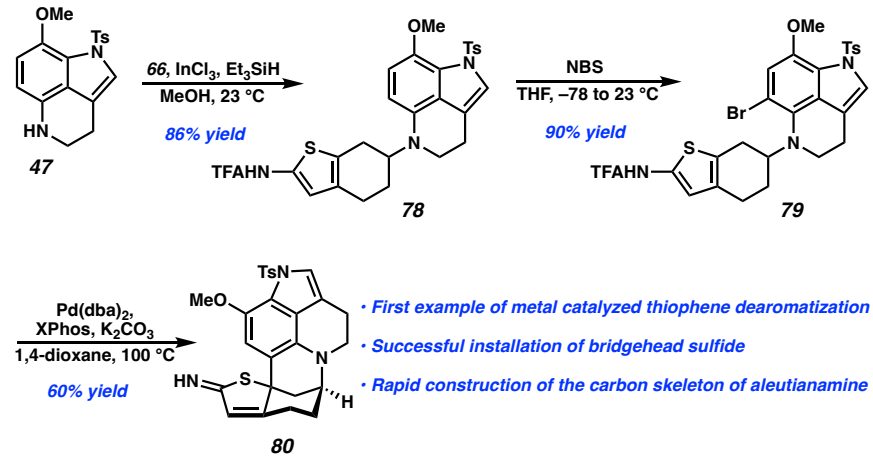
aminothiophene was protected in-situ with TFAA to yield trifluoroacetamide **76**. Finally, aqueous acid-mediated ketal removal generated ketone **77**. This route proved to be highly scalable: Only one chromatographic column was required throughout the 4-step sequence, allowing convenient access to multidecagram quantities of **77**.

Scheme 1.7.1. *Synthesis of aminothiophene **77** via Gewald aminothiophene synthesis.*



Now with access to both fragments, the convergent coupling was tested. We were pleased to find that the reductive amination between **47** and **77** proceeded smoothly using the $InCl_3/Et_3SiH$ system (Scheme 1.7.2) reported by Yang and coworkers,[22] generating **78**

Scheme 1.7.2. *Construction of aleutianamine carbon skeleton.*

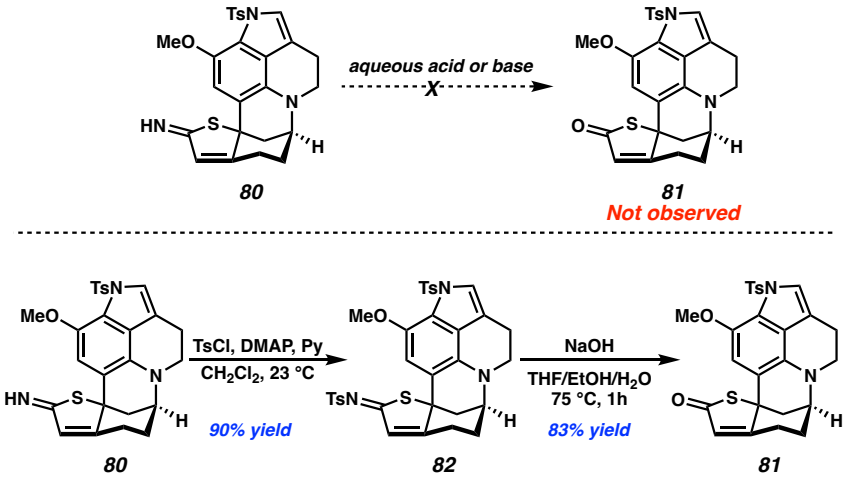


in 86% yield. Subsequent bromination with NBS in THF yielded bromoaniline **79**, the substrate for the planned dearomatization. Gratifyingly, subjecting **79** to modified Buchwald conditions[20a] successfully effected the dearomative cyclization with concomitant hydrolysis of trifluoroacetamide to provide thioimidate **80**. This reaction rapidly assembled of the whole carbon skeleton of aleutianamine (**1**) and the bridgehead sulfide and constitutes the first reported example of transition metal catalyzed dearomative thiophene arylation.

1.8 CONSTRUCTION OF ALEUTIANAMINE CORE STRUCTURE

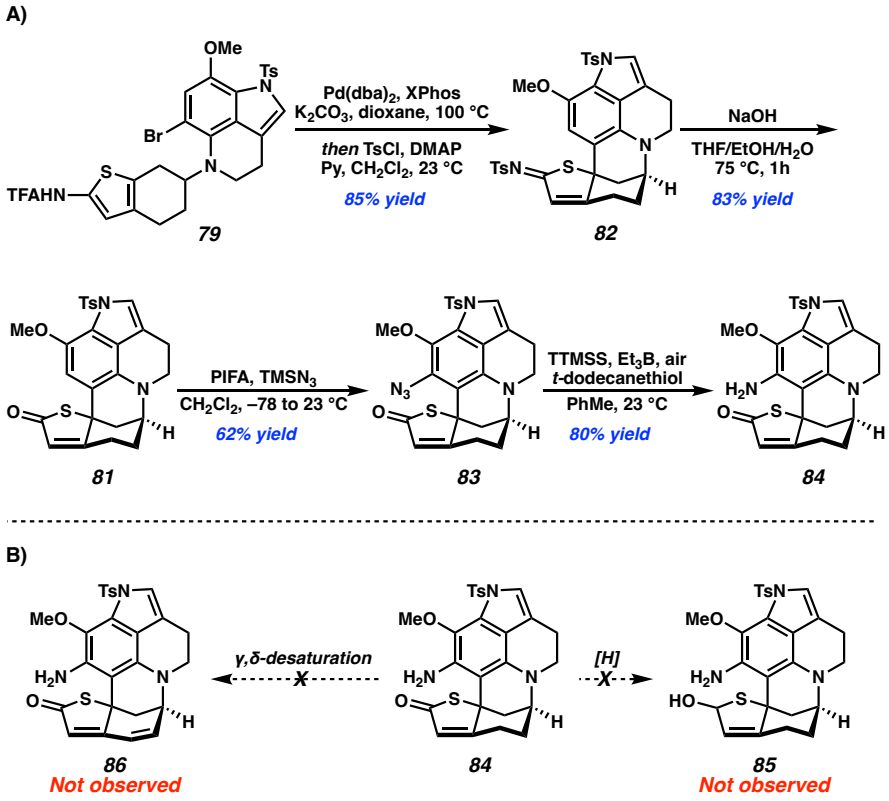
Following the preparation of thioimidate **80**, experiments were conducted to hydrolyze it to the corresponding thiobutenolide **81**, as the imidate nitrogen would likely be problematic for further functionalizations. Surprisingly, thioimidate **80** was found to be recalcitrant to hydrolysis. Treatment with dilute aqueous acid or base at room temperature led to no reaction, while conducting the hydrolysis under more forcing conditions led to nonspecific decomposition (Scheme 1.8.1). This behavior is counterintuitive given the

Scheme 1.8.1. *Hydrolysis of thioimidate* ***80*** *through activation.*



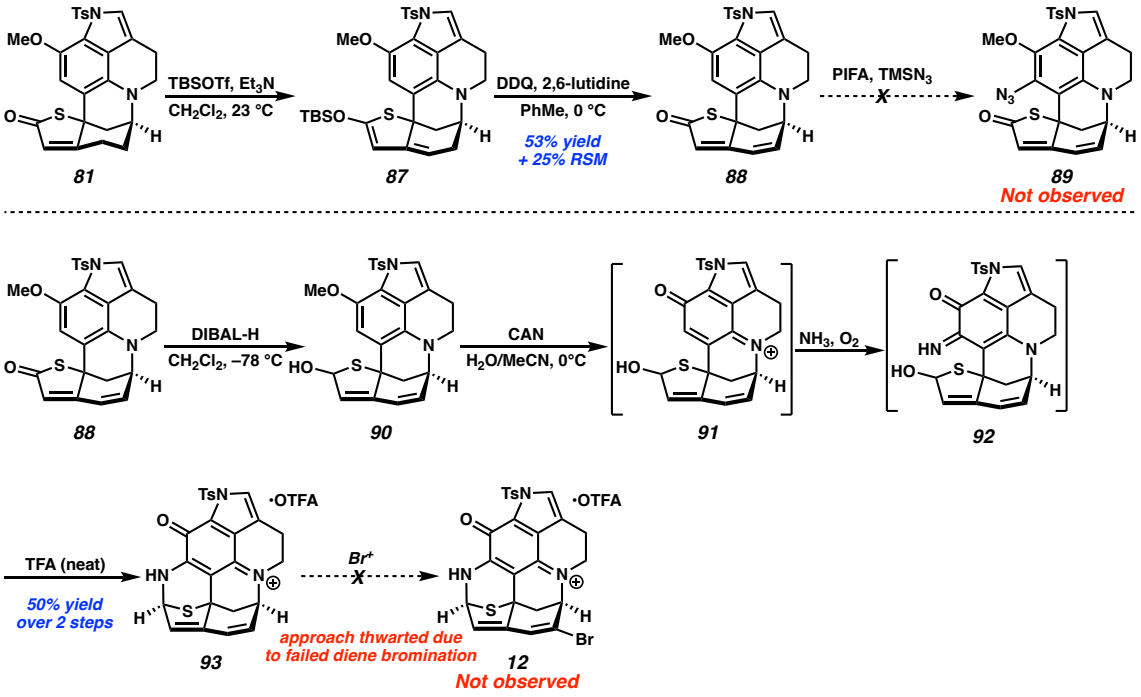
generally facile hydrolysis of imines. We imagined that installation of an electron-withdrawing group on the thioimidate would render it more electrophilic and thus facilitate the hydrolysis. Ultimately, N-tosyl thioimidate **82** was found to be optimal. Subjection of **82** to sodium hydroxide in a mixture of THF/EtOH/H_2O under reflux cleanly effected the hydrolysis, providing thiobutenolide **81** in 83% yield on gram scale. It should be noted that the solvent ratio, temperature, and reaction time all have significant influence on yield. Altering the solvent ratio led to low solubility of thioimidate **82**, and changing the reaction temperature/time resulted in incomplete conversion of **82** or hydrolytic opening of the thiolactone.

Scheme 1.8.2. *(A) Introduction of C10 aniline via electrophilic azidation/reduction. (B) Failed elaboration of aniline* ***84****.*



Having established a route to thiobutenolide **81**, we optimized the preparation of N-tosyl thioimidate **82** (Scheme 1.8.2A). Isolation and purification of free thioimidate **80** is challenging due to its high polarity. We found that the yield can be greatly improved by telescoping the crude **80** directly to tosylation, providing N-tosyl thioimidate in 85% overall yield on multigram scale. With reliable access to thiobutenolide **81**, we next opted to investigate installation of the final nitrogen atom of the natural product. Excitingly, treatment of thiobutenolide **81** with PIFA and $TMSN_3$ under conditions modified from those of Kita effected a chemoselective anisole azidation, affording azide **83** in 62% yield (Scheme 1.8.2A).[23] While Staudinger reduction was unsuccessful, reduction of azide **83** was achieved by employing tris(trimethylsilyl)silane (TTMSS) as reductant under radical conditions, providing aniline **84** in 80% yield.[24] However, attempts to further elaborate

Scheme 1.8.3. *Contruction of aleutianamine core via γ,δ-desaturation and oxidative aromatic amination.*



aniline **84** toward the introduction of the second unsaturation were met with no success (Scheme 1.8.2B). The central arene in aniline **85** was found to be extremely oxidatively sensitive; conditions evaluated for γ,δ-desaturation led to decomposition. Furthermore, treatment of **84** with reductants such as DIBAL-H did not provide the desired thiolactol **85**. Evidently, the Lewis-basic primary aniline could form an ate-complex with the reductant, promoting undesired reactivity.

Since the presence of the C10 amino group proved to be incompatible with downstream functionalization, we instead directed our efforts toward further desaturation of the thiolactone. A wide range of different carbonyl desaturation conditions were explored, most of which led to either no reaction or decomposition of the starting material. After extensive optimization, diene **88** was eventually accessed via a two-step protocol (Scheme 1.8.3). Soft enolization with Et_3N and TBSOTf afforded a somewhat unstable silyl ketene thioacetal **87**, which upon oxidation with DDQ provided diene **88** in 53% yield over two-steps with 25% of recovered thiobutenolide **81**. The choice of silyl group was found to be critical. Silyl ketene acetals generated with a smaller silyl group such as TMS or TES were too unstable to be isolated. Soft enolization with bulkier silyl triflates such as TBDPS and TIPS did not proceed to significant conversion. With the γ,δ-unsaturation incorporated, installation of the final nitrogen atom was again attempted. We were disappointed to find that the anisole azidation was not compatible with diene **88**. Only oxidative decomposition was observed, possibly owing to competing 1,6-addition of azide.

During the course of our synthesis, most intermediates were found to be oxidatively sensitive, indicating that oxidation of those intermediates to the corresponding iminoquinones would likely be facile. The electrophilicity of the iminoquinones could

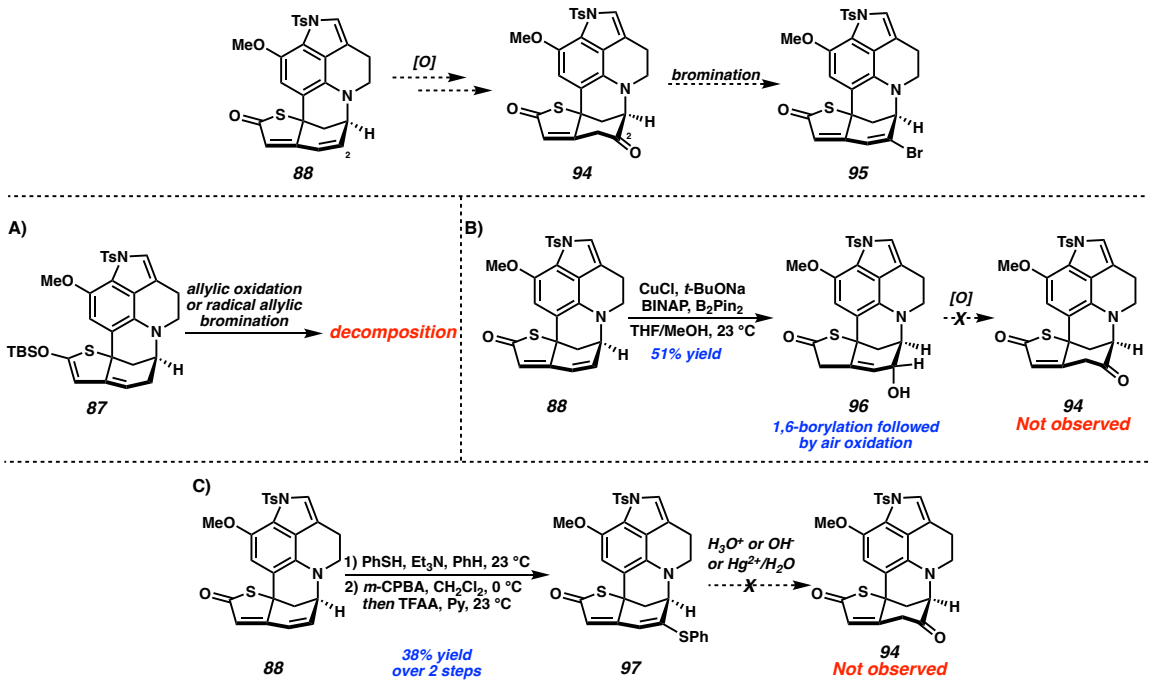
enable a nucleophilic amination to install the final nitrogen atom, circumventing the challenging arene azidation. Moving forward with this plan, we realized that the reduction of the thiolactone should take place before the oxidation of the quinone. Treatment of thiolactone **88** with DIBAL-H at –78 °C effected a 1,2-reduction, providing thiolactol **90** as mixture of epimers in near quantitative yield (Scheme 1.8.3). With thiolactol **90** in hand, we proceeded to evaluate the arene oxidation. We were pleased to find that subjecting **90** to CAN-mediated oxidation conditions indeed led to the formation of cationic iminoquinone **91**.[25] This highly reactive intermediate was not isolated; instead, capture by ammonia provided a putative ortho-aminophenol. Exposure of this extremely electron-rich aminophenol to oxygen promoted clean oxidation to the corresponding iminoquinone **92**. Finally, dissolving the crude iminoquinone **92** in neat TFA led to dehydrative cyclization, yielding N-tosyl desbromoaleutianamine (**93**), which is essentially one bromination and one deprotection away from the natural product.

Bromination of **93** was expected to be relatively straight-forward, as late-stage olefin bromination is precedented in previous pyrolloiminoquinone alkaloid syntheses.[3d, 6] However, this seemingly simple transformation proved not to be feasible. Subjecting N-tosyl desbromoaleutianamine (**93**) to brominating reagents invariably led to decomposition.

1.9 δ-KETONE INSTALLATION VIA PALLADIUM-CATALYZED PINACOL -TYPE REARRANGEMENT AND COMPLETION OF ALEUTIANAMINE SYNTHESIS

To circumvent the unsuccessful bromination, we set out to increase the oxidation level of C2 on diene **88**, which would serve as a functional handle for bromination (Scheme 1.9.1). Various approaches were examined for the ketone installation (Scheme 1.9.1). Direct allylic oxidation or bromination of silyl ketene thioacetal **87** led to decomposition (Scheme 1.9.1A). Subjecting diene **88** to copper catalyzed 1,6-borylation conditions afforded alcohol **96**,[26] presumably via in-situ aerobic oxidation of the resulting borane (Scheme 1.9.1B). Disappointingly, oxidation of secondary alcohol **96** to ketone **94** was not successful. Most oxidants led to decomposition via oxidation of the central arene, and the adjacent thiobutenolide moiety was found to promote elimination of water to regenerate dienyl thiolactone **88**. Eventually, oxidation at C2 was achieved via a two-step sequence

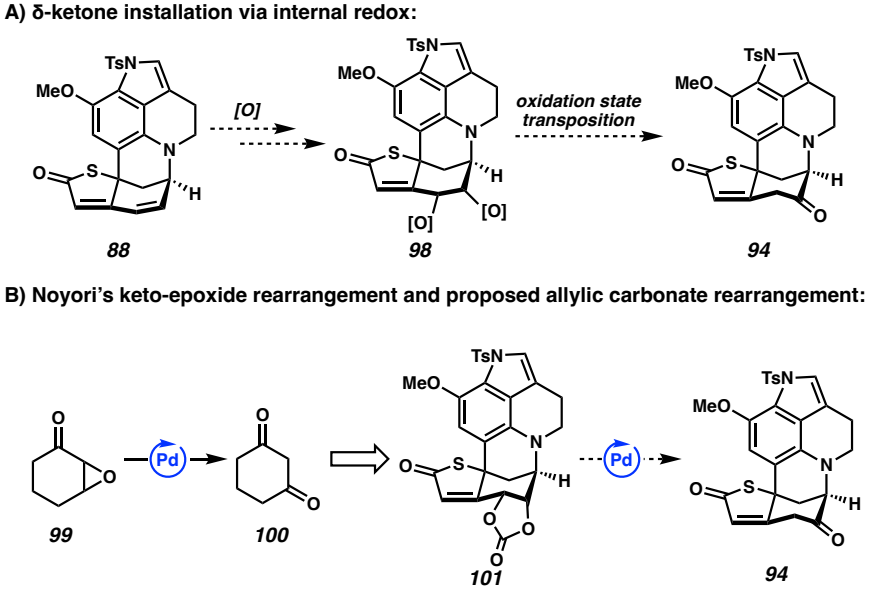
Scheme 1.9.1. *Attempted δ-functionalization.*



(Scheme 1.9.1C). First, treatment of dienyl thiolactone **88** with thiophenol and base induced 1,6-addition, providing a somewhat unstable sulfide. Then, oxidation to the sulfoxide with *m*-CPBA, followed by in-situ Pummerer rearrangement delivered doubly vinylogous dithiocarbonate **97** in 38% yield over two steps. Although C2 of **97** bears the desired oxidation state, to our dismay, sulfide **97** was found to be surprisingly recalcitrant to substitution. Subjection of **97** to aqueous mercury salts, base, or even concentrated hydrochloric acid led to no reaction.

From our efforts toward δ functionalization, it appeared that direct installation of a ketone at C2 would be unfeasible, as common conditions employ strong oxidants, which would not be tolerated by the electron-rich central arene. We addressed this issue with an oxidation relay strategy (Scheme 1.9.2A). Instead of doubly oxidizing C2, oxygenation would be introduced on both C1 and C2. This transformation could be readily achieved via

Scheme 1.9.2. *A) δ-ketone installation via internal oxidation relay. (B)Noyori's keto-epoxide rearrangement and proposed allylic carbonate rearrangement.*

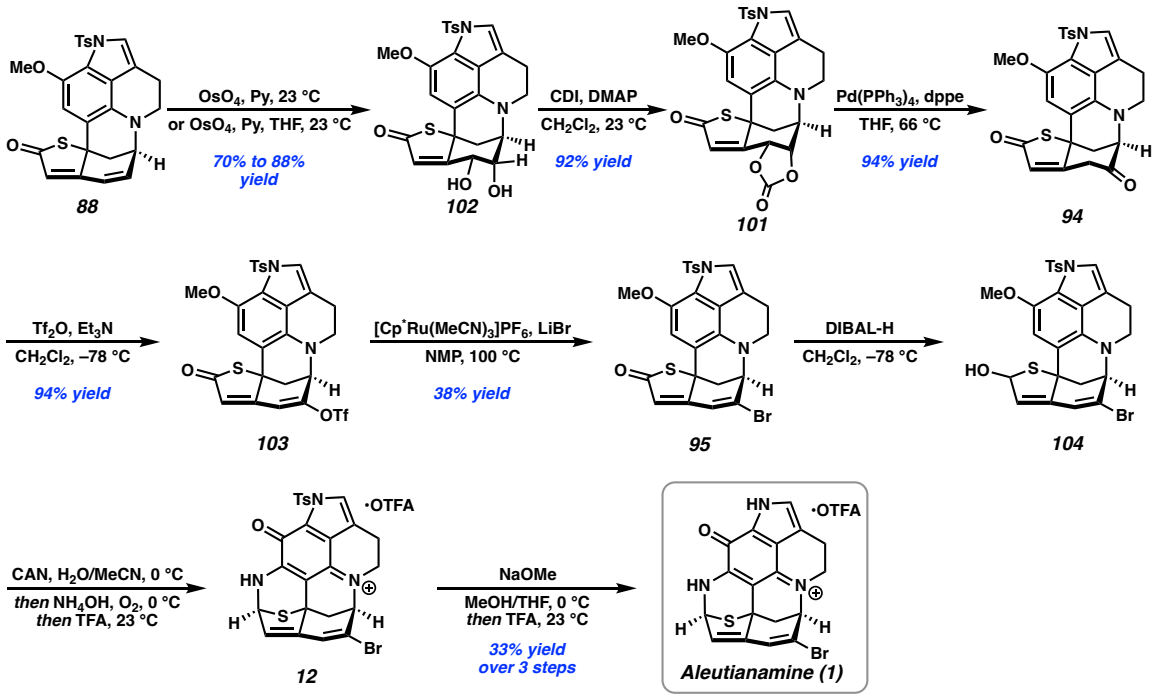


osmium-mediated dihydroxylation, which is known to be selective toward non-aromatic alkenes. With oxygenation installed on both carbons, an internal oxidation state transposition via pinacol-type rearrangement would provide the desired ketone **94**. To realize this transformation, we took inspiration from a report by Noyori and coworkers (Scheme 1.9.2B),[27] where keto-epoxide **99** was rearranged to 1,3-diketone **100** using palladium catalysis. Although the analogous γ,δ-epoxide could not be prepared, we hypothesized that γ,δ-carbonate **101** would serve as an alternative ionizable functional equivalent for the palladium catalyzed rearrangement.

With this new strategy in mind, various conditions for dihydroxylation were evaluated. The electron-poor nature of diene **88** renders the dihydroxylation challenging. No dihydroxylation of **88** was observed even upon subjection to super stoichiometric amount of osmium tetroxide. Eventually, the dihydroxylation was effected by treatment of diene **88** with stoichiometric osmium tetroxide pyridine complex, affording diol **102** in 70 to 88% yield as a single diastereomer (Scheme 1.9.3).[28] Acylation of diol **102** with CDI provided cyclic carbonate **101**. We were delighted to find that the proposed decarboxylative pinacol-type rearrangement proceeded smoothly under Noyori's conditions, delivering ketone **94** in 94% yield. With the C2 ketone installed, we focused our efforts toward completing the synthesis of aleutianamine. Treatment of ketone **94** with triflic anhydride and base provided enol triflate **103**, which upon triflate-halogen exchange[29] delivered alkenyl bromide **95**. We were pleased to observe that alkenyl bromide **95** is compatible with the previously developed reaction sequence. 1,2-reduction of **95** with DIBAL-H followed by CAN-mediated oxidative amination and cyclization yielded N-tosyl

aleutianamine (**12**). Finally, tosyl group cleavage with NaOMe afforded aleutianamine (**1**), completing the synthesis in a longest linear sequence of 20 steps.

Scheme 1.9.3. *Installation of δ-ketone via palladium catalyzed rearrangement and completion of the total synthesis of aleutianamine (**1**).*



1.10 Conclusion

Described above is the full account of our total synthesis of aleutianamine (**1**). An initial α-thioketone derivatization approach was thwarted by unsuccessful enolate functionalization. A second-generation approach employing palladium catalyzed Barbier addition led to the successful installation of the [3.3.1]bicyclononane moiety. However, attempted further elaboration of bicyclic intermediate **39** toward the alkenyl bromide was unfruitful, which led to the abandonment of this approach. The total synthesis was accomplished by employing a novel dearomative arylation of an aminothiophene, which allowed rapid construction of the molecular skeleton of aleutianamine (**1**) including the

challenging bridgehead sulfide. From arylation product **69**, ceric ammonium nitrate-mediated oxidative amination and palladium-catalyzed decarboxylative pinacol-type rearrangement allowed chemoselective introduction of the C10 aniline and alkenyl bromide, leading to a non-biomimetic total synthesis of aleutianamine (**1**).

1.11 EXPERIMENTAL SECTION

1.11.1 MATERIALS AND METHODS

Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon.[30] Reaction progress was monitored by thin-layer chromatography (TLC). 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 $KMnO_4$ staining. Silicycle SiliaFlash® P60 Academic Silica gel (particle size 40–63 μm) was used for flash chromatography. ^1H NMR spectra were recorded on Varian Inova 500 MHz and 600 MHz and Bruker 400 MHz spectrometers and are reported relative to residual $CHCl_3$ (δ 7.26 ppm), C_6D_6 (δ 7.16 ppm) or CD3OD (δ 3.31 ppm). ^{13}C NMR spectra were recorded on a Varian Inova 500 MHz spectrometer (125 MHz) and Bruker 400 MHz spectrometers (100 MHz) and are reported relative to $CHCl_3$ (δ 77.16 ppm), C_6D_6 (δ 128.06 ppm) or CD_3OD (δ 49.01 ppm). Data for ^1H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet, br d = broad doublet. Data for ^{13}C NMR are reported in terms of chemical shifts (δ ppm). IR spectra were obtained by use of a Perkin Elmer Spectrum BXII spectrometer or Nicolet 6700 FTIR spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm path- length cell. High resolution

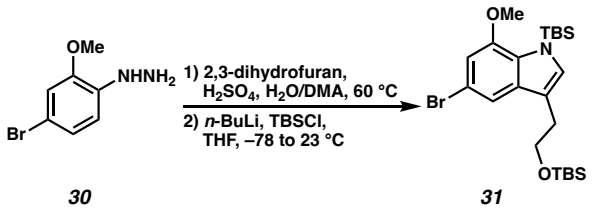
mass spectra (HRMS) were obtained using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+) mode.

1.11.2 EXPERIMENTAL PROCEDURES

Hydrazine 30

Prepared according to literature procedure.[7] All characterization data matched those reported in the literature.

Silyl indole 31



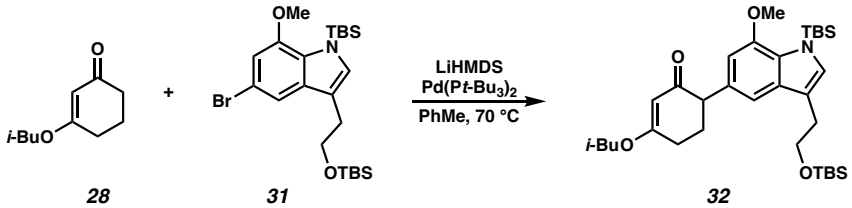
30 *31*

To a 20 mL glass vial was added (4-bromo-2-methoxyphenyl)hydrazine (**31**, 832 mg, 3.83 mmol, 1.0 equiv), DMA (5 mL), deionized water (3.6 mL), and 25% (v/v) aq. H_2SO_4 (1.85 mL, 8.62 mmol, 2.25 equiv). 2,3-dihydrofuran (290 μL, 3.83 mmol, 1.0 equiv) was then added and the vial was sealed and heated to 60 °C in a metal heating block. After 4 h of stirring at 60 °C, the reaction mixture was transferred to a separatory funnel containing 1:1 saturated aq. $NaHCO_3$/brine. The resulting suspension was extracted with EtOAc (4x5 mL). The combined organic extracts were washed with water, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (50% EtOAc/hexanes) to afford an intermediate tryptophol as a viscous brown oil (351 mg, 1.30 mmol, 34% yield);

The intermediate tryptophol (320 mg, 1.18 mmol, 1.0 equiv) was transferred to a 20 mL glass vial. Traces of water were azeotropically removed by addition of three portions

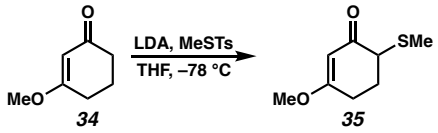
of benzene followed by rotary evaporation, the headspace of the vial was evacuated and flushed with nitrogen, and THF (10 mL) was added. The solution was cooled to –78 °C. *n*-BuLi (2.5 M in hexanes, 0.47 mL, 1.18 mmol, 1.0 equiv) was added slowly and the reaction mixture was subsequently allowed to warm to 23 °C. Then, TBSCl (187 mg, 1.24 mmol, 1.05 equiv) in THF (1 mL) was added and the reaction mixture was allowed to stir at 23 °C for 15 min. After cooling back to –78 °C, additional *n*-BuLi (2.5 M in hexanes, 0.47 mL, 1.18 mmol, 1.0 equiv) was added slowly and the reaction mixture was subsequently allowed to warm back to 23 °C. Additional TBSCl (187 mg, 1.24 mmol, 1.05 equiv) in THF (1 mL) was then added. After an additional 1 h of stirring, the reaction mixture was concentrated under reduced pressure and purified by silica gel flash chromatography (5% EtOAc/hexanes) to afford the title compound as a colorless oil (183 mg, 0.367 mmol, 31% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 1.7 Hz, 1H), 7.04 (s, 1H), 6.69 (d, J = 1.7 Hz, 1H), 3.87 (s, 3H), 3.83 (t, J = 7.0 Hz, 2H), 2.87 (td, J = 7.0, 0.9 Hz, 2H), 0.89 (s, 9H), 0.85 (s, 9H), 0.51 (s, 6H), 0.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 134.6, 131.1, 129.9, 115.0, 114.4, 112.8, 105.6, 63.7, 54.5, 29.0, 26.9, 26.1, 19.7, 18.5, –1.5, –5.2; IR (Neat Film, NaCl) 2927, 2856, 1572, 1462, 1367, 1300, 1254, 1104, 992, 911, 824, 683 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{23}H_{41}BrNO_2Si_2$ $[M+H]^+$: 498.1854, found 498.1844.

Vinylogous ester 32



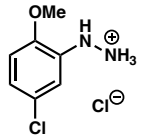
To a 20 mL glass vial were added silyl indole **31** (173 mg, 0.347 mmol, 1.0 equiv) and 3-isobutoxycyclohex-2-en-1-one (**28**, 58 mg, 0.347 mmol, 1.0 equiv). Traces of water were azeotropically removed by addition of three portions of benzene followed by rotary evaporation and the vial was transferred to a nitrogen-filled glovebox. $Pd(t\text{-}Bu_3)_2$ (8.9 mg, 0.0174 mmol, 5 mol %) was added followed by $PhCH_3$ (3.5 mL). A solution of LiHMDS (116 mg, 0.694 mmol, 2.0 equiv) in $PhCH_3$ (1 mL) was added dropwise with manual swirling. Additional $PhCH_3$ (0.2 mL) was used to quantitatively transfer the remaining base. The vial was sealed with a PTFE-lined cap, removed from the glovebox, and heated to 70 °C in a metal heating block for 75 min. The reaction mixture was subsequently cooled to 23 °C and saturated aq. NH_4Cl (5 mL) was added. The layers were separated, and the aqueous layer was extracted with EtOAc (3x2 mL). The combined organic phases were washed with water, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (20% EtOAc/hexanes) to afford the title compound as a colorless film (87.5 mg, 0.149 mmol, 43% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (s, 1H), 6.98 (s, 1H), 6.44 (s, 1H), 5.54 (s, 1H), 3.86 (s, 3H), 3.86 – 3.82 (m, 2H), 3.66 (d, J = 6.5 Hz, 2H), 3.64 – 3.58 (m, 1H), 2.91 (t, J = 7.3 Hz, 2H), 2.55 (t, J = 6.1 Hz, 2H), 2.33 (q, J = 6.6 Hz, 2H), 2.11 – 2.02 (m, 1H), 1.00 (d, J = 6.7 Hz, 6H), 0.91 (s, 9H), 0.90 (s, 9H), 0.51 (s, 6H), 0.05 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.2, 177.6, 147.1, 133.3, 131.8, 130.2, 130.1, 114.8, 110.7, 103.4, 102.7, 74.9, 63.8, 54.0, 52.4, 29.9, 29.2, 28.3, 27.8, 26.9, 26.1, 19.6, 19.2, 18.4, –1.5, –5.1; IR (Neat Film, NaCl) 2927, 2856, 1654, 1609, 1469, 1382, 1313, 1252, 1177, 1098, 994, 910, 838, 682 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{33}H_{56}NO_4Si_2$ $[M+H]^+$: 586.3742, found 586.3752.

3-methoxy-6-(methylthio)cyclohex-2-en-1-one (35)



To a 20 mL glass vial equipped with a septum cap were added THF (8 mL) and *i*-Pr_2NH (0.29 mL, 2.1 mmol, 1.3 equiv). The solution was cooled to –78 °C and *n*-BuLi (2.5 M in hexanes, 0.76 mL, 1.9 mmol, 1.2 equiv) was added slowly with stirring. The mixture was then allowed to warm to 23 °C and cooled back to –78 °C. A solution of 3-methoxycyclohex-2-en-1-one (**34**, 200 mg, 1.59 mmol, 1.0 equiv) in THF (1 mL) was then added dropwise and the resulting light-yellow solution was stirred at –78 °C for 5 min. Subsequently, a solution of methyl thiotosylate[31] (384 mg, 1.90 mmol, 1.2 equiv) in THF (1 mL) was added slowly. After stirring for an additional 5 min at –78 °C, the reaction mixture was warmed to 0 °C in an ice bath, resulting in a pink, milky suspension. Saturated aq. NH_4Cl (5 mL) was then added, and the resulting biphasic suspension was extracted with EtOAc. The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (33% EtOAc/hexanes) to afford the title compound as a yellow solid (210 mg, 1.22 mmol, 77% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.29 (d, J = 0.97 Hz, 1H), 3.69 (s, 3H), 3.25 (t, J = 4.3 Hz, 1H), 2.75 – 2.61 (m, 1H), 2.40 – 2.24 (m, 2H), 2.16 (s, 3H), 2.16 – 2.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 177.2, 100.0, 55.8, 48.4, 27.1, 26.0, 14.6; IR (Neat Film, NaCl) 2920, 2851, 1651, 1607, 1446, 1381, 1317, 1228, 1185, 1075, 1002, 837, 786 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_8H_{13}O_2S$ $[M+H]^+$: 173.0631, found 173.0629.

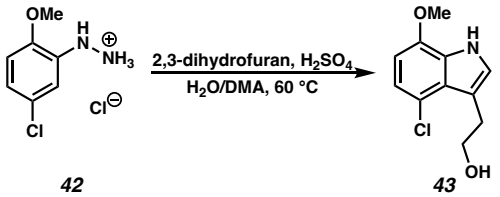
2-(5-chloro-2-methoxyphenyl)hydrazin-1-ium chloride (42)



42

Prepared according to the procedure of Thibeault and coworkers from 4-chloro-2-methoxyaniline.[10] All characterization data matched those reported in the literature.

Tryptophol 43

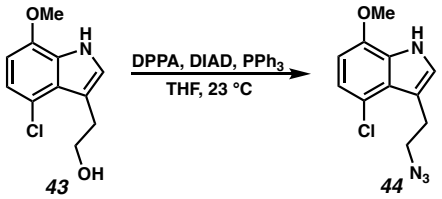


42 ***43***

To a 250 mL round bottom flask were added (5-chloro-2-methoxyphenyl)hydrazine hydrochloride (**42**, 8.60 g, 41.1 mmol, 1.0 equiv), DMA (65 mL), H_2O (65 mL), and 25% (v/v) aq. H_2SO_4 (11.0 mL, 51.4 mmol, 1.25 equiv). 2,3-dihydrofuran (3.42 mL, 45.2 mmol, 1.1 equiv) was added slowly with stirring, resulting in a slow color change to yellow, whereafter the flask was equipped with an air-cooled reflux condenser and heated to 60 °C in an oil bath for 6 h. The reaction mixture was then allowed to cool to 23 °C and transferred to a separatory funnel containing 1:1 saturated aq. $NaHCO_3$/brine (250 mL). The mixture was then extracted with EtOAc (4x100 mL), and the combined organic extracts were washed with water, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (60% EtOAc/hexanes) to afford the title compound as a thick, red-brown syrup that slowly crystallized upon storage at –20 °C (2.66 g, 11.79 mmol, 29% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (br s, 1H), 7.00 (d, J = 2.2 Hz, 1H), 6.96 (d, J = 8.2 Hz, 1H), 6.50 (d, J = 8.2 Hz, 1H), 3.94 (t, J = 6.4

Hz, 2H), 3.91 (s, 3H), 3.23 (td, J = 6.4, 0.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 128.4, 124.8, 123.8, 120.2, 118.2, 113.1, 102.4, 63.7, 55.7, 29.5; IR (Neat Film, NaCl) 3416, 2935, 2580, 1786, 1703, 1626, 1571, 1494, 1452, 1339, 1230, 1115, 1052, 937, 789, 736, 694, 628 cm^{-1}; HRMS (FD+): *m/z* calc'd for $C_{11}H_{13}ClNO_2$ $[M+H]^+$: 225.0557, found 225.0552.

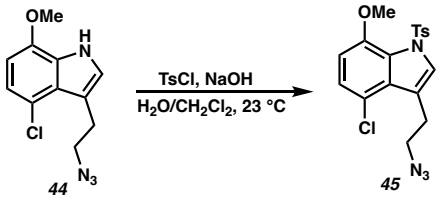
3-(2-azidoethyl)-4-chloro-7-methoxy-1*H*-indole (44)



To a 250 mL round bottom flask was added tryptophol **43** (3.36 g, 14.89 mmol, 1.0 equiv). Traces of water were azeotropically removed by addition of three portions of benzene followed by rotary evaporation. PPh_3 (4.69 g, 17.87 mmol, 1.2 equiv) was added, and the headspace of the flask was evacuated and backfilled with nitrogen. THF (60 mL) was added, and the reaction mixture was cooled to 0 °C. Then, DIAD (3.52 mL, 17.87 mmol, 1.2 equiv) was added dropwise over 4 min. The reaction mixture was stirred at 0 °C for an additional 15 min, after which DPPA (3.85 mL, 17.87 mmol, 1.2 equiv) was added rapidly and the reaction mixture was allowed to warm to 23 °C. The reaction mixture became cloudy over several minutes. TLC analysis after 16 h indicated a high degree of conversion to product. Stirring for another 24 h led to no change in the reaction profile by TLC analysis. The reaction mixture was concentrated under reduced pressure and purified by automated silica gel flash chromatography (Teledyne ISCO, 0→40% EtOAc/hexanes) to afford azide **44** as an orange-brown solid (2.50 g, 9.97 mmol, 67% yield).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.34 (s, 1H), 7.05 (d, *J* = 2.4 Hz, 1H), 6.98 (d, *J* = 8.2 Hz, 1H), 6.53 (d, *J* = 8.2 Hz, 1H), 3.93 (s, 3H), 3.59 (t, *J* = 7.2 Hz, 2H), 3.27 (td, *J* = 7.1, 0.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.2, 128.2, 124.5, 123.5, 120.3, 117.9, 113.2, 102.5, 55.6, 52.8, 25.9. IR (Neat Film, NaCl): 3890, 3864, 3668, 3316, 3132, 3084, 3008, 2938, 2876, 2588, 2492, 2352, 2204, 2106, 1768, 1652, 1630, 1574, 1494, 1464, 1450, 1434, 1380, 1332, 1294, 1272, 1236, 1194, 1172, 1154, 1130, 1070, 1034, 958, 930, 864, 830, 808, 782, 760, 740, 708, 684, 670, 662, 632, cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{11}H_{12}ClN_2O$ $[M+H]^+$: 223.0638, found 223.0630.

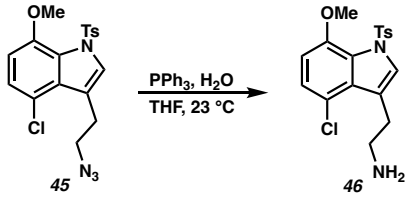
Tosyl indole 45



To a 250 mL round bottom flask under air were added azide **44** (5.11 g, 20.4 mmol, 1.0 equiv), CH_2Cl_2 (41 mL), and Bu_4NHSO_4 (69 mg, 0.204 mmol, 1 mol %), followed by 50% w/v aq. NaOH (14 mL). After stirring for 5 min, TsCl (7.78 g, 40.8 mmol, 2.0 equiv) was added in a single portion. The reaction mixture was subjected to vigorous magnetic stirring for 10 min, then diluted with H_2O (100 mL) and CH_2Cl_2 (30 mL). The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3x50 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by automated silica gel flash chromatography (Teledyne ISCO, 0→45% EtOAc/hexanes) to afford an intermediate tosyl indole as a white solid (6.77 g, 16.7 mmol, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (s, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.29 – 7.26 (m, 2H), 7.08 (d, *J* = 8.5 Hz, 1H), 6.58 (d, *J* = 8.5 Hz, 1H), 3.64 (s, 3H), 3.63 – 3.59 (m, 2H), 3.26 (td, *J* = 7.1, 1.0 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.9, 144.9, 137.6, 129.9, 129.6, 128.6, 127.6, 126.7, 125.0, 118.5, 116.7, 108.0, 56.1, 52.2, 26.7, 22.1. IR (Neat Film, NaCl): 3992, 3892, 3854, 3752, 3630, 3620, 3608, 3586, 3402, 3116, 2926, 2514, 2368, 2098, 1598, 1572, 1540, 1518, 1488, 1464, 1362, 1294, 1252, 1234, 1192, 1172, 1146, 1120, 1092, 1058, 994, 910, 858, 846, 808, 798, 772, 736, 702, 676, 662, 632, 624, cm^{-1}. HRMS (ESI+): m/z calc'd for $C_{18}H_{17}ClN_4O_3SNa$ $[M+Na]^+$: 427.0608, found 427.0603.

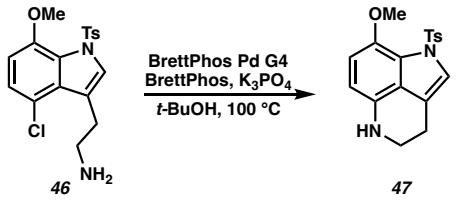
Tryptamine 46



To a 500 mL round bottom flask under air were added azide **45** (11.73 g, 28.97 mmol, 1.0 equiv), PPh_3 (9.88 g, 37.66 mmol, 1.3 equiv), and THF (190 mL). The reaction mixture was stirred at 23 °C for 15 h, whereafter deionized water (9.5 mL) was added. After an additional 30 h, the reaction mixture was concentrated under reduced pressure and purified by silica gel flash chromatography (10% MeOH/CH_2Cl_2 + 1% Et_3N) to afford the title compound as a white solid (10.41 g, 27.48 mmol, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 – 7.65 (m, 3H), 7.29 – 7.23 (m, 2H), 7.05 (d, *J* = 8.5 Hz, 1H), 6.56 (d, *J* = 8.5 Hz, 1H), 3.62 (s, 3H), 3.14 – 3.00 (m, 4H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5, 144.4, 137.4, 129.7, 129.5, 127.4, 127.2, 126.5, 124.6, 118.5, 118.1, 107.5, 55.8,

42.9, 30.7, 21.7. IR (Neat Film, NaCl): 2938, 2686, 2595, 2515, 2363, 1574, 1487, 1366, 1290, 1237, 1171, 1092, 1052, 997, 937, 809, 662 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{18}H_{20}ClN_2O_3S$ $[M+H]^+$: 379.0878, found 379.0877.

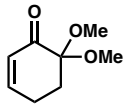
Tricycle 47



A 20 mL glass vial containing tryptamine **46** (1.0 g, 2.64 mmol, 1.0 equiv) was brought into a nitrogen-filled glovebox. To this vial were added BrettPhos Pd G4 (121 mg, 0.132 mmol, 5 mol %), BrettPhos (71 mg, 0.132 mmol, 5 mol %), and K_3PO_4 (784 mg, 3.70 mmol, 1.4 equiv), followed by *t*-BuOH (6.6 mL). The vial was sealed with a PTFE-lined cap and electrical tape, removed from the glovebox, and stirred at 100 °C in a metal heating block. After 3 days, the reaction mixture was partitioned between CH_2Cl_2 and water and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3x), and the combined organic phases were concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (40% EtOAc/hexanes) to afford the title compound as a beige foam (816 mg, 2.38 mmol, 90% yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.4 Hz, 2H), 7.32 (s, 1H), 7.23 (d, J = 7.9 Hz, 2H), 6.56 (d, J = 8.1 Hz, 1H), 6.27 (d, J = 8.1 Hz, 1H), 3.70 (s, 3H), 3.37 (t, J = 5.9 Hz, 2H), 2.91 (t, J = 5.2 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.1, 140.5, 137.1, 135.8, 129.4, 127.7, 124.0, 122.6, 120.2, 115.2, 110.7, 105.0, 57.5, 43.0, 22.8, 21.7. IR (Neat Film, NaCl): 3384,

2956, 2834, 1595, 1512, 1421, 1356, 1260, 1170, 1103, 1035, 977, 937, 795, 664 cm^{-1}. HRMS (ESI+): m/z calc'd for $C_{18}H_{19}N_2O_3S$ $[M+H]^+$: 343.1111, found 343.1127.

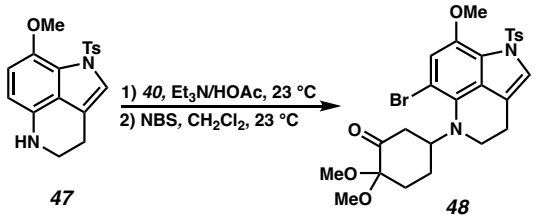
Enone 40



40

Conditions for the synthesis of **40** were adapted from those reported for related compounds by Dong.[32] To a 20 mL glass vial in a nitrogen-filled glovebox were added CuTC (24 mg, 0.126 mmol, 20 mol %), $CyPPh_2$ (34 mg, 0.126 mmol, 20 mol %), benzene (6.3 mL), and a magnetic stir bar. The vial was sealed with a septum cap and removed from the glovebox. 1,2-cyclohexanedione dimethyl ketal (100 mg, 0.632 mmol, 1.0 equiv, prepared according to literature procedure)[33] and di-*tert*-butyl peroxide (0.17 mL, 0.948 mmol, 1.5 equiv) were added by injection. The reaction mixture was then heated to 80 °C in a metal heating block, resulting in a deep green solution. After 23 h, the reaction mixture was allowed to cool to 23 °C, concentrated under reduced pressure, and purified by silica gel flash chromatography (33% EtOAc/hexanes) to afford the title compound as a colorless oil (38.1 mg, 0.244 mmol, 39% yield); ^1H NMR (400 MHz, C_6D_6) δ 6.2 – 6.1 (m, 1H), 5.8 (dtd, *J* = 10.0, 2.0, 0.9 Hz, 1H), 3.1 (d, *J* = 1.0 Hz, 6H), 1.9 – 1.8 (m, 2H), 1.8 – 1.7 (m, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 192.1, 148.9, 128.1, 97.0, 49.6, 31.1, 24.6; IR (Neat Film, NaCl) 2940, 2834, 1694, 1623, 1437, 1388, 1310, 1231, 1160, 1117, 1060, 916, 850, 801 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_8H_{12}NaO_3$ $[M+Na]^+$: 179.0679, found 179.0678.

Bromoarene 48



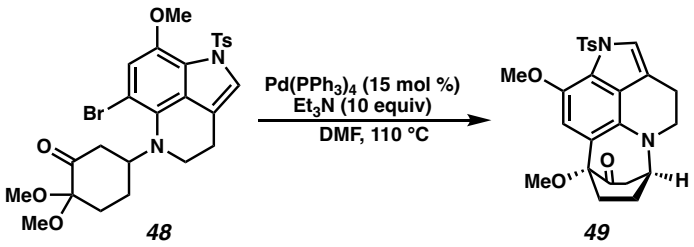
47 *48*

To a 1-dram glass vial under air were added tricycle **47** (50 mg, 0.146 mmol, 1.0 equiv), enone **40** (114 mg, 0.730 mmol, 5.0 equiv), and 1:1 (v/v) Et_3N/HOAc (0.15 mL). The reaction mixture was stirred at 23 °C for 21 h, then partitioned between water and EtOAc. The layers were separated, and the aqueous phase was extracted with EtOAc (3x). The combined organic phases were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (80% Et_2O/hexanes) to afford an intermediate tertiary aniline as a beige foam along with small amount of tricyclic aniline **47** (59 mg, 0.118 mmol, 81% yield by ^1H NMR); The material was used in the next step without further purification.

To a sample of this intermediate aniline (19.5 mg, 0.0391 mmol, 1.0 equiv) also containing secondary aniline **47** as a major impurity (7.6 mg, 0.0222 mmol) in a 1-dram glass vial was added CH_2Cl_2 (2.5 mL). Recrystallized NBS (11 mg, 0.0613 mmol, 1.0 equiv w.r.t. combined total aniline) was added rapidly with stirring, resulting in a brown color. After 10 mins, the reaction mixture was concentrated under reduced pressure and purified by silica gel flash chromatography (80% Et_2O/hexanes) to afford the title compound as an off-white foam (21.1 mg, 0.0365 mmol, 93% yield); ^1H NMR (400 MHz, C_6D_6) δ 7.84 – 7.78 (m, 2H), 7.47 (t, J = 1.5 Hz, 1H), 6.70 (s, 1H), 6.66 – 6.60 (m, 2H), 3.99 (tt, J = 12.4, 4.0 Hz, 1H), 3.28 (s, 3H), 3.18 (s, 3H), 2.97 (s, 3H), 2.96 – 2.91 (m, 1H), 2.88 (ddd, J = 6.6, 5.3, 2.8 Hz, 2H), 2.77 (ddd, J = 11.7, 4.2, 2.2 Hz, 1H), 2.23 – 2.10 (m, 2H), 1.94 (dt,

J = 14.5, 3.4 Hz, 1H), 1.86 – 1.76 (m, 1H), 1.75 (s, 3H), 1.57 (dq, *J* = 13.0, 3.4 Hz, 1H), 1.18 (td, *J* = 14.0, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 202.6, 144.0, 143.1, 137.9, 133.8, 129.4, 127.4, 123.0, 122.5, 114.8, 114.1, 106.2, 100.9, 62.0, 56.3, 49.9, 48.5, 45.8, 42.8, 30.6, 27.4, 22.2, 21.1; IR (Neat Film, NaCl) 2936, 2835, 1732, 1692, 1597, 1490, 1360, 1285, 1222, 1172, 1111, 1057, 992, 933, 806, 666 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{26}H_{30}BrN_2O_6S$ $[M+H]^+$: 577.1002, found 577.1015.

Aza[3.2.2]bicyclononene 49

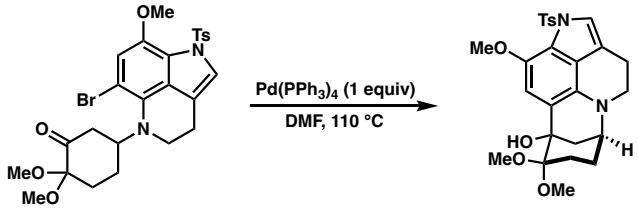


48 ***49***

To a flame-dried 1-dram glass vial was added bromoarene **48** (5 mg, 0.00866 mmol, 1.0 equiv) as a stock solution in benzene. Traces of water were azeotropically removed by addition of two additional portions of benzene followed by rotary evaporation. The vial was transferred to a nitrogen-filled glovebox and $Pd(PPh_3)_4$ (1.5 mg, 0.0013 mmol, 15 mol %), DMF (0.22 mL), and Et_3N (12 μL, 0.0866 mmol, 10 equiv) were added. The vial was sealed with a PTFE-lined cap, removed from the glovebox, and stirred at 110 °C in a metal heating block for 18 h. The reaction mixture was diluted with water (2 mL) and extracted with EtOAc (4x0.5 mL). The combined organic extracts were washed with water, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by preparative TLC on basic alumina (60% EtOAc/hexanes) to afford the title compound as a beige film (2.5 mg, 0.00536 mmol, 62% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* =

8.1 Hz, 2H), 7.32 (d, *J* = 1.3 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.84 (s, 1H), 3.68 (d, *J* = 1.0 Hz, 3H), 3.56 – 3.50 (m, 1H), 3.43 (d, *J* = 1.1 Hz, 3H), 3.32 (qdd, *J* = 11.1, 6.7, 5.1 Hz, 2H), 3.01 – 2.86 (m, 3H), 2.71 – 2.62 (m, 1H), 2.55 (td, *J* = 11.6, 4.7 Hz, 1H), 2.42 (dd, *J* = 10.0, 4.9 Hz, 1H), 2.37 (s, 3H), 2.32 (dd, *J* = 5.2, 2.6 Hz, 1H), 2.04 – 1.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.3, 144.2, 140.7, 137.0, 132.0, 129.4, 127.8, 124.0, 123.6, 120.3, 116.8, 115.0, 106.6, 82.8, 56.8, 56.6, 51.9, 51.8, 44.2, 31.2, 26.3, 23.5, 21.7; IR (Neat Film, NaCl) 2926, 2851, 1727, 1494, 1366, 1285, 1171, 1108, 1019, 807, 670 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{25}H_{27}N_2O_5S$ $[M+H]^+$: 467.1635, found 467.1636.

Bicyclic ketal 50

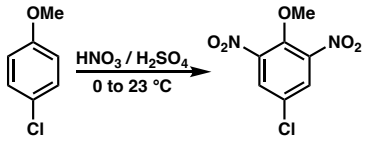


48 ***50***

To a 1-dram glass vial was added bromoarene **48** (53.7 mg, 0.0930 mmol, 1.0 equiv). Traces of water were azeotropically removed by addition of three portions of benzene followed by rotary evaporation. The vial was transferred to a nitrogen-filled glovebox, and $Pd(PPh_3)_4$ (125 mg, 0.108 mmol, 1.16 equiv) and DMF (2.4 mL) were added. The vial was sealed with a PTFE-lined cap, removed from the glovebox, and heated to 110 °C in a metal heating block. After stirring for 17 h, the reaction mixture was allowed to cool to 23 °C, diluted with water and brine, and extracted with EtOAc (3x). The combined organic extracts were dried over Na_2SO_4, concentrated under reduced pressure, and purified by silica gel flash chromatography (45% EtOAc/hexanes) to afford the desired

product as a beige film (40 mg, 0.0802 mmol, 86% yield); ^{1}H NMR (400 MHz, C_6D_6) δ 7.97 – 7.91 (m, 2H), 7.47 (s, 1H), 7.19 (s, 1H), 6.62 – 6.57 (m, 2H), 3.63 (s, 3H), 3.34 (s, 3H), 3.04 (s, 3H), 2.99 (q, *J* = 2.4 Hz, 1H), 2.79 (td, *J* = 9.8, 4.1 Hz, 1H), 2.65 (ddd, *J* = 15.2, 4.8, 1.8 Hz, 1H), 2.58 – 2.46 (m, 2H), 2.11 (dd, *J* = 11.8, 2.9 Hz, 1H), 1.98 (ddd, *J* = 11.9, 3.5, 2.2 Hz, 1H), 1.73 (s, 3H), 1.59 – 1.50 (m, 2H), 1.28 – 1.11 (m, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 143.4, 139.6, 138.1, 133.7, 129.4, 124.3, 121.1, 120.3, 118.0, 114.9, 110.5, 102.7, 75.7, 58.2, 54.7, 51.3, 48.8, 46.7, 38.2, 27.4, 27.0, 23.3, 21.1 (an additional ^{13}C resonance associated with the tosyl group is likely obscured by the solvent signal); IR (Neat Film, NaCl) 2934, 2832, 1504, 1451, 1406, 1360, 1283, 1227, 1169, 1103, 967, 913, 813, 663 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{26}H_{31}N_2O_6S$ $[M+H]^+$: 499.1897, found 499.1890.

5-chloro-2-methoxy-1,3-dinitrobenzene (52).

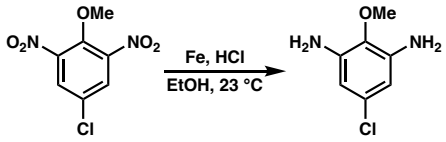


51 ***52***

Behind a safety shield, a flame dried 500 mL 3-neck round-bottom flask equipped with a 100 mL additional funnel was charged with fuming nitric acid (40 mL) and brought to 5 °C. 4-chloroanisole (**51**, 20.0 g, 140.27 mmol, 1.0 equiv) was added dropwise such that the temperature was kept below 30 °C (~ 30 min). The reaction mixture was then brought to 0 °C and concentrated sulfuric acid (20 mL) was added dropwise such that the temperature was kept below 20 °C (~ 30 min). The reaction mixture was then brought to 5 °C and fuming nitric acid (20 mL) was added dropwise such that the temperature was kept

below 20 °C (~ 20 min). The reaction mixture was then stirred for 10 min at 23 °C. The reaction mixture was then poured onto ice (100 mL), and the yellow precipitate was collected via vacuum filtration. The yellow solid was rinsed with cold water and dried under vacuum for 16 h. This yellow solid was taken forward without additional purification. A small sample was purified by column chromatography (SiO_2, 5% EtOAc/Hexanes) for analytical characterization. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (s, 2H), 4.07 (s, 3H). 13C NMR (100 MHz, $CDCl_3$): δ 146.5, 145.7, 129.6, 129.3, 65.2. IR (Neat Film, NaCl): 3082, 2964, 2324, 1608, 1531, 1475, 1421, 1401, 1363, 1254, 1172, 1097, 976, 922, 888, 806, 778, 754, 721 cm^{-1}. HRMS (GCFI+): m/z calc'd for $C_7H_5ClN_2O_5$ $[M]^{+\bullet}$: 231.9887, found 231.9876.

5-chloro-2-methoxybenzene-1,3-diamine (53).

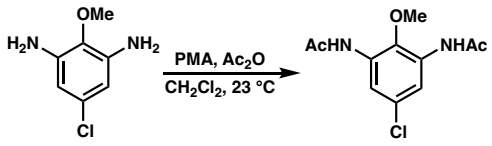


52 ***53***

A flame dried 500 mL 3-neck round-bottom flask equipped with a reflux condenser was charged with dinitro arene **52** (15.0 g, 64.5 mmol, 1.0 equiv) in EtOH (184 mL, 0.35 M) and 1.5% aq. HCl (64.5 mL, 1 M). Iron (21.6 g, 387.0 mmol, 6 equiv) was added in 5 portions over 5 minutes. The reaction mixture was heated to 80 °C for 6 h, at which point TLC indicated consumption of the starting material. The crude reaction mixture was pushed through a pad of celite with EtOAc (200 mL). The filtrate was diluted with water (300 mL), and the product was extracted with EtOAc (3 x 300 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced

pressure. The crude product was purified by column chromatography (SiO_2, 40%-50%-75% EtOAc/Hexanes) to afford the title compound (8.44 g, 76% yield) as an off white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.15 (s, 2H), 3.78 – 3.72 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 133.0, 130.1, 106.2, 58.6. IR (Neat film, NaCl): 3308, 2361, 1675, 1598, 1504, 1435, 1292, 1237, 991, 683 cm1. HRMS (ESI+): *m/z* calc'd for $C_7H_{10}ClN_2O$ $[M+H]^+$: 173.0476, found 173.0478.

Diacetamide 54.

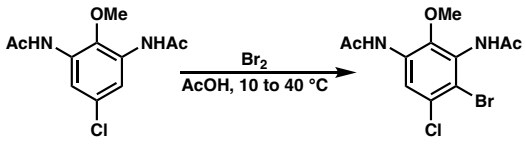


53 ***54***

Prepared using a modified literature procedure.[11] A flame dried 100 mL round-bottom flask was charged with dianline **53** (2.0 g, 11.6 mmol, 1.0 equiv) in CH_2Cl_2 (23 mL, 0.5 M). Acetic anhydride (2.4 mL, 25.52 mmol, 2.2 equiv) and phosphomolybdic acid (PMA, 423.0 mg, 0.23 mmol, 0.02 equiv) were then added. The reaction mixture was stirred at 23 °C for 3 h, at which point TLC indicated complete consumption of the starting material. The reaction mixture was diluted with water (100 mL) and ethyl acetate (150 mL), and the product was extracted with EtOAc (3 x 100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the title compound (2.57 g, 87% yield) as a brown solid which was taken forward without additional purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (s, 2H), 7.47 (s, 2H), 3.77 (s, 3H), 2.23 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.3, 139.4, 132.9, 127.1, 116.8, 60.5, 23.9. IR (Neat film, NaCl): 3413, 3342, 3317, 3220, 2979, 1635, 1592,

1505, 1442, 1322, 1227, 1150,1023, 985, 889, 816, 763, 714, 678 cm^{-1}. HRMS (ESI+): m/z calc'd for $C_{11}H_{14}ClN_2O_3$ $[M+H]^+$: 257.0687, found 257.0689.

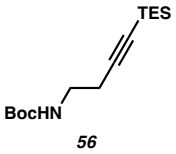
Bromoarene 55.



54 *55*

A flame dried 50 mLround-bottom flask was charged with diacetamide **54** (2.57 g, 10.0 mmol, 1.0 equiv) in glacial acetic acid (14.0 mL, 0.73M). The solution was cooled to 10 °C and Br2 (0.77 mL, 30.0 mmol, 3.0 equiv) was added dropwise over 2 min. The reaction mixture was warmed to 23 °C over 1 h and was then heated to 40 °C for 16 h, at which point LC/MS analysis indicated complete consumption of the starting material. The reaction mixture was poured into ice water (50 mL) and the precipitate was collected via vacuum filtration. The crude product was purified by column chromatography (SiO_2, 100% EtOAc) to afford the title compound (2.7 g, 80% yield) as a brown solid. ^{1}H NMR (600 MHz, DMSO-d_6): δ 9.74 (s, 1H), 9.60 (s, 1H), 8.31 (s, 1H), 3.67 (s, 3H), 2.14 (s,3H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.5, 168.6, 146.7, 132.4, 132.4, 128.0, 120.9, 117.9, 60.9, 23.9, 22.6. IR (Neat film, NaCl): 3902, 3735, 3182, 3002, 2335,1665, 1583, 1514, 1458, 1399, 1370, 1267, 1227, 1165, 1086, 995, 911, 871, 835, 817, 770, 755, 700, 680, 612 cm1. HRMS (ESI+): m/z calc'd for $C_{11}H_{13}BrClN_2O_3$ $[M+H]^+$: 334.9793, found 334. 9794.

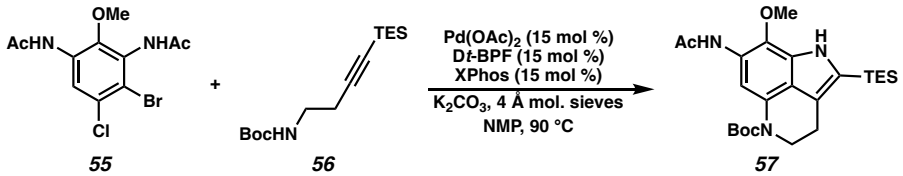
tert-butyl (4-(triethylsilyl)but-3-yn-1-yl)carbamate (56).



56

Prepared according to our previous report.[16]

Tricycle 57.

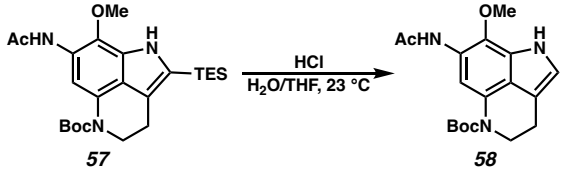


55 ***56*** ***57***

In a nitrogen filled glovebox, to a flame dried 8 mL vial equipped with a magnetic stir bar was sequentially added K_2CO_3 (granular, freshly flame-dried, 303.4 mg, 2.2 mmol, 5.0 equiv), 4Å molecular sieves (powdered, freshly activated, 150 mg, 50 wt% with respect to K_2CO_3), $Pd(OAc)_2$ (Strem, 14.8 mg, 0.066 mmol, 0.15 equiv), XPhos (Combi Blocks, 31.4 mg, 0.066 mmol, 0.15 equiv), D*t*BPF (TCI, 31.3 mg, 0.066 mmol, 0.15 equiv), aryl bromide **55** (147.7 mg, 0.44 mmol, 1.0 equiv), alkyne **56** (622.6 mg, 2.2 mmol, 5.0 equiv), and NMP (4.4 mL, 0.1 M). The vial was sealed with a PTFE cap, removed from the glovebox, stirred at 1000 rpm, andheated at 90 °C for 24 h at which point LC/MS indicated consumption of the starting material. The reaction mixture was pushed through a short pad of celite with EtOAc (20 mL) and was diluted with 1 M aq. LiCl (30 mL). The product was extracted with EtOAc (5 x 30 mL). The combined organic layers were washed with 1M aq. LiCl (3x30 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (SiO_2, 50%-60-70% EtOAc/Hexanes) to afford the title compound (139.7 mg, 0.304 mmol, 69% yield) as a

brown solid. Additionally, unreacted alkyne **56** could be recovered in the first few collected fractions (483 mg). ^{1}H NMR (600 MHz, CD_3OD): δ 10.10 (s, 1H), 7.54 (s, 1H), 3.98 (t, J = 5.7 Hz, 2H), 3.89 (s, 3H), 2.99 (t, J = 5.6 Hz, 2H), 2.18 (s, 3H), 1.56 (s, 9H), 1.00 (t, J = 7.7 Hz, 9H), 0.91 (q, J = 8.0 Hz, 6H).*Note: Two carbon signals are observed as a doublet due to hindered rotation about the C–N bond of the carbamate.* ^{13}C NMR (100 MHz, CD_3OD): δ 172.3, 155.4, 136.0, 131.2 (d, J = 15.0 Hz), 129.8 (d, J = 16.7 Hz), 128.9, 125.0, 123.2, 121.7, 109.2, 82.4, 61.3, 46.8, 28.7, 25.6, 23.3, 7.7, 4.4. IR (Neat film, NaCl): 3307, 2952, 2930, 2873, 2485, 1667, 1622, 1539, 1516, 1456, 1388, 1368, 1312, 1364, 1160, 1077, 1050, 1003, 977, 855, 737 cm1. HRMS (ESI+): m/z calc'd for $C_{24}H_{38}N_3O_4Si$ $[M+H]^+$: 460.2626, found 460.2625.

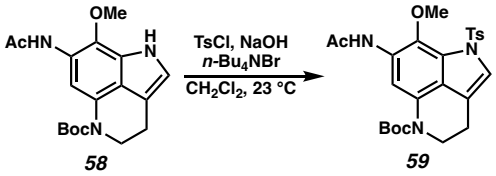
Indole 58.



To a 20 mL vial under an ambient atmosphere was added tricycle **57** (134.0 mg, 0.29 mmol, 1.0 equiv), THF (2.9 mL, 0.1 M), and 2 M aq. HCl (2.9 mL, 0.1 M). The reaction mixture was stirred at 23 °C for 4 h, at which point LC/MS analysis indicated complete consumption of the starting material. aq.saturated $NaHCO_3$ (10 mL) was added, and the reaction mixture was transferred to a separatory funnel with EtOAc. The mixture was further diluted with EtOAc (30 mL) and water (30 mL). The product was extracted with EtOAc (3 x 30 mL), the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the title compound

(97.1 mg, quantitative yield) as a brown solid, which was taken directly forward without further purification. ^{1}H NMR (400 MHz, CD_3OD) δ 7.54 (s, 1H), 6.88 (s, 1H), 3.97 (t, J = 5.6 Hz, 2H), 3.92 (s, 3H), 2.92 (t, J = 5.7 Hz, 2H), 2.17 (s, 3H), 1.56 (s, 9H). ^{13}C NMR (100 MHz, CD_3OD): δ 172.3, 155.4, 136.4, 128.9, 127.7, 124.2, 122.5, 119.4, 111.2, 109.6, 82.4, 60.9, 46.6, 28.7, 23.8, 23.3. IR (Neat film, NaCl): 3317, 2972, 2929, 2444, 1668, 1510, 1389, 1367, 1326, 1264, 1247, 1206, 1160, 1125, 1037, 969, 873 cm^{-1}. HRMS (ESI+): m/z calc'd for $C_{14}H_{16}N_3O_4$ (loss of tBu) [M+H]+: 290.1135, found 290.1135.

Tosyl indole 59.

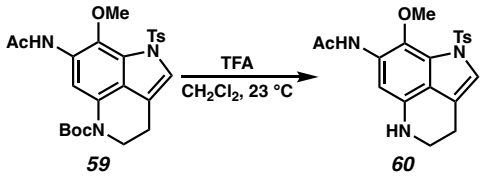


58 ***59***

A flame-dried 1-dram vial was charged with indole **58** (25 mg, 0.0724 mmol, 1.0 equiv), TsCl (28 mg, 0.145 mmol, 2.0 equiv), Bu_4NBr (2.4 mg, 0.00724 mmol, 0.1 equiv), and powdered KOH (13 mg, 0.217 mmol, 3.0 equiv). The vial was evacuated and backfilled with nitrogen, then CH_2Cl_2 (0.72 mL, 0.1M) was added, and the resulting suspension was stirred at 23 °C for 30 min. The reaction was diluted with CH_2Cl_2 (5 mL) and water (5 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3x3 mL), the combined organic extracts were dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (15% EtOAc/hexanes to 50% EtOAc/hexanes) to afford the title compound (28.5 mg, 0.0571 mmol, 79%) as a yellow solid. ^{1}H NMR (400 MHz, C_6D_6): δ 9.11 (s, 1H), 7.85 (d, J = 8.3 Hz, 2H), 7.33 – 7.20 (m, 2H), 6.65 (d, J = 8.3 Hz, 2H), 3.76 (t, J = 5.7 Hz, 2H), 3.66 (s,

3H), 2.29 (m, 2H), 1.67 (s, 3H), 1.64 – 1.46 (m, 12H). ^{13}C NMR (100 MHz, C_6D_6): δ 167.1, 153.5, 144.4, 144.3, 136.6, 132.8, 130.9, 130.5, 129.7, 125.8, 121.7, 121.6, 117.0, 110.5, 81.8, 61.6, 44.3, 28.5, 24.3, 22.5, 21.1. IR (Neat film, NaCl): 3301, 3133, 2978, 2933, 1693, 1681, 1613, 1530, 1470, 1370, 1328, 1306, 1271, 1168, 1094, 849, 800, 766, 735, 703, 681, 667. HRMS (FD+): m/z calc'd for $C_{25}H_{29}N_3O_6S$ $[M+H]^+$: 500.1855, found 500.1866.

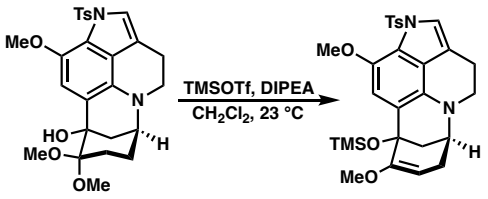
Tricyclic aniline 60.



59 *60*

To a 1-dram vial containing tosyl indole **59** (50 mg, 0.100 mmol, 1.0 equiv) was added CH_2Cl_2 (1 mL, 0.15M) and TFA (0.25 mL, 3.29 mmol, 33 equiv). The resulting mixture was stirred at 23 °C for 30 min, at which point TLC analysis showed full consumption of starting material. The reaction was quenched with sat. $NaHCO_3$ solution (5 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3x3 mL), the combined organic extracts were dried with Na_2SO_4 and concentrated under reduced pressure to afford the title compound (40 mg, 0.100 mmol, >99 %) as a brown foam. ^{1}H NMR (400 MHz, C_6D_6): δ 7.95 (s, 1H), 7.92 (d, J = 8.1 Hz, 2H), 7.43 (s, 1H), 7.28 (s, 1H), 6.63 (d, J = 8.1 Hz, 2H), 3.72 (s, 3H), 3.18 (s, 1H), 2.62 (t, J = 5.9 Hz, 2H), 2.37 (t, J = 5.9 Hz, 2H), 1.66 (s, 3H), 1.57 (s, 3H).^{13}C NMR (100 MHz, C_6D_6): δ 167.4, 144.0, 138.4, 136.7, 131.7, 129.6, 129.3, 128.3, 127.8, 126.4, 120.0, 117.8, 117.2, 100.0, 90.1, 61.7, 42.4, 24.4, 22.6, 21.0. IR (Neat film, NaCl): HRMS (FD+): m/z calc'd for $C_{20}H_{22}N_3O_4S$ $[M+H]^+$: 400.1331, found 400.1332.

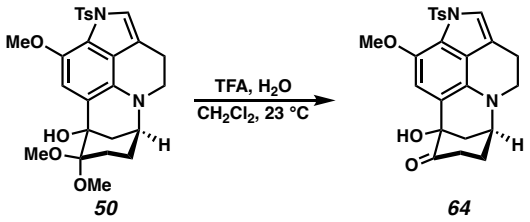
Methyl enol ether 62



50 ***62***

To a 1-dram glass vial was added ketal **50** (5 mg, 0.010 mmol, 1.0 equiv). Traces of water were azeotropically removed by addition of three portions of benzene followed by rotary evaporation. The headspace of the vial was evacuated and backfilled with nitrogen. CH_2Cl_2 (1 mL) and *i*-Pr_2NEt (27 μL, 0.16 mmol, 16 equiv) were added, followed by the addition of TMSOTf (18 μL, 0.10 mmol, 10 equiv). The reaction mixture was stirred at 23 °C for 30 min, then quenched with aq. NaOH (0.3 mL). The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1x). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by preparative TLC on silica gel (50% EtOAc/hexanes) to afford the title compound as a beige film (3.7 mg, 0.00687 mmol, 69% yield); ^{1}H NMR (400 MHz, C_6D_6) δ 7.94 – 7.87 (m, 2H), 7.40 (t, *J* = 1.7 Hz, 1H), 7.27 (s, 1H), 6.58 (d, *J* = 8.2 Hz, 2H), 4.15 (dd, *J* = 4.9, 2.4 Hz, 1H), 3.63 (s, 3H), 3.20 (dt, *J* = 4.6, 2.9 Hz, 1H), 2.94 (s, 3H), 2.91 – 2.84 (m, 1H), 2.68 – 2.55 (m, 2H), 2.53 – 2.43 (m, 1H), 2.20 – 1.99 (m, 4H), 1.73 (s, 3H), 0.29 (s, 9H); ^{13}C NMR (100 MHz, C_6D_6) δ 159.3, 143.2, 139.5, 138.2, 131.5, 129.3, 123.8, 121.5, 121.4, 120.3, 114.8, 109.0, 90.9, 71.6, 58.3, 54.1, 53.6, 47.3, 38.5, 30.3, 23.2, 21.1, 2.1 (an additional ^{13}C resonance associated with the tosyl group is likely obscured by the solvent signal); IR (Neat Film, NaCl) 2932, 2834, 1657, 1597, 1505, 1463, 1406, 1361, 1285, 1249, 1172, 1104, 1024, 932, 843, 682 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{28}H_{35}N_2O_5SSi$ $[M+H]^+$: 539.2030, found 539.2028.

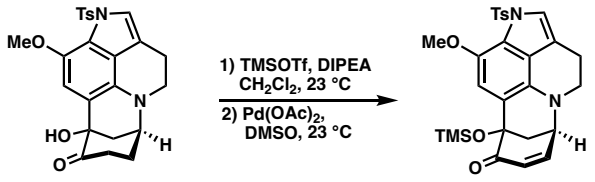
α-Hydroxyketone 64



50 ***64***

To a 1-dram glass vial under air were added ketal **50** (10 mg, 0.020 mmol, 1.0 equiv), CH_2Cl_2 (1 mL), water (0.1 mL), and TFA (6.0 μL, 0.078 mmol, 3.9 equiv). The reaction mixture was stirred at 23 °C for 40 min, then neutralized with saturated aq. $NaHCO_3$ (1 mL) and stirred for an additional 10 min. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3x0.5 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure to afford the title compound as a beige film (9.0 mg, 0.020 mmol, >99% yield); ^{1}H NMR (400 MHz, C_6D_6) δ 7.72 – 7.67 (m, 2H), 7.29 (t, *J* = 1.3 Hz, 1H), 6.66 (s, 1H), 6.44 – 6.36 (m, 2H), 4.55 (s, 1H), 3.20 (s, 3H), 2.61 (td, *J* = 3.6, 1.8 Hz, 1H), 2.55 – 2.46 (m, 1H), 2.45 – 2.33 (m, 1H), 2.32 – 2.23 (m, 2H), 2.15 (dt, *J* = 12.5, 3.4 Hz, 1H), 1.89 – 1.72 (m, 2H), 1.52 (s, 3H), 1.47 (dd, *J* = 12.4, 2.8 Hz, 2H), 0.84 (tdd, *J* = 13.8, 6.0, 2.8 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 209.9, 143.7, 140.4, 138.0, 133.2, 129.4, 124.3, 121.8, 120.9, 116.3, 114.2, 107.0, 75.9, 57.2, 54.6, 46.8, 39.6, 33.5, 32.3, 23.1, 21.1 (an additional ^{13}C resonance associated with the tosyl group is obscured by the solvent signal); IR (Neat Film, NaCl) 3466, 2925, 2853, 1712, 1596, 1505, 1462, 1435, 1367, 1285, 1223, 1171, 1105, 1010, 970, 892, 816, 735, 665 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{24}H_{25}N_2O_5S$ $[M+H]^+$: 453.1479, found 453.1472.

Enone 65



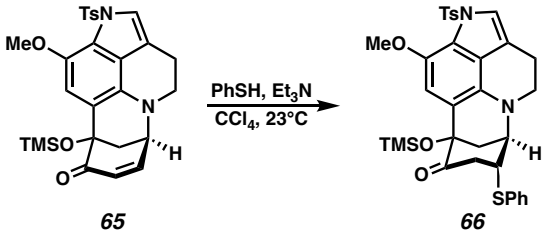
64 *65*

To a 1-dram glass vial was added ketone **64** (9 mg, 0.020 mmol, 1.0 equiv). Traces of water were azeotropically removed by addition of three portions of benzene followed by rotary evaporation. The headspace of the vial was evacuated and backfilled with nitrogen. CH_2Cl_2 (0.5 mL) and *i*-Pr_2NEt (40 µL, 0.23 mmol, 11 equiv) were added, followed by the addition of TMSOTf (28 µL, 0.15 mmol, 7.5 equiv). The reaction mixture was stirred at 23 °C for 1 h, after which LC–MS analysis indicated incomplete conversion. Additional *i*-Pr_2NEt (14 µL, 0.080 mmol, 4 equiv) and TMSOTf (10 µL, 0.055 mmol, 2.8 equiv) were therefore added, and stirring was continued for an additional 40 min, after which LC–MS analysis indicated complete conversion. The reaction mixture was loaded directly onto a silica gel preparative TLC plate. Elution with 25% EtOAc/hexanes afforded a silyl enol ether that was used directly in the following step.

This intermediate was transferred to a 20 mL glass vial and brought into a nitrogen-filled glovebox. $Pd(OAc)_2$ (9 mg, 0.040 mmol, 2.0 equiv) and DMSO (1.2 mL) were added. The reaction mixture was stirred at 28 °C for 4 days, whereafter the vial was removed from the glovebox and the reaction mixture diluted with water and extracted with CH_2Cl_2 (4x). The combined organic extracts were washed with 1 M aq. LiCl, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by preparative TLC on silica gel (70% EtOAc/hexanes) to afford the title compound as a yellow solid (7 mg, 0.013 mmol, 65% yield over 2 steps); ^1H NMR (400 MHz, C_6D_6) δ 7.87 – 7.78 (m, 2H),

7.47 (d, *J* = 1.6 Hz, 1H), 7.04 (s, 1H), 6.57 (d, *J* = 8.0 Hz, 2H), 5.87 (d, *J* = 9.9 Hz, 1H), 5.81 (ddd, *J* = 10.0, 5.1, 1.8 Hz, 1H), 3.43 (s, 3H), 3.32 (td, *J* = 4.4, 2.8 Hz, 1H), 2.65 – 2.57 (m, 2H), 2.41 – 2.29 (m, 1H), 2.23 (ddd, *J* = 12.0, 2.7, 1.8 Hz, 1H), 2.15 – 1.99 (m, 2H), 1.71 (s, 3H), 0.37 (s, 9H); ^{13}C NMR (100 MHz, C_6D_6) δ 196.0, 143.7, 142.0, 141.0, 137.9, 130.8, 129.6, 129.4, 124.5, 123.0, 121.1, 115.7, 114.0, 107.3, 77.0, 56.8, 54.6, 47.2, 38.6, 23.1, 21.1, 2.7 (an additional ^{13}C resonance associated with the tosyl group is likely obscured by the solvent signal); IR (Neat Film, NaCl) 2925, 2854, 1693, 1504, 1463, 1352, 1263, 1173, 1107, 1024, 963, 932, 844, 759, 666 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{27}H_{31}N_2O_5SSi$ $[M+H]^+$: 523.1717, found 523.1718.

Phenyl sulfide 66

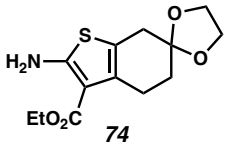


65 *66*

To a 1-dram glass vial was added enone **65** (12.4 mg, 0.024 mmol, 1.0 equiv), CCl_4 (0.1 mL), thiophenol (6 μL, 0.059 mmol, 2.5 equiv), and Et_3N (2.0 μL, 0.014 mmol, 0.6 equiv). The reaction mixture was stirred at 23 °C for 35 min, during which time the yellow color of the starting material disappeared. The reaction mixture was loaded directly onto a silica gel preparative TLC plate. Elution with 40% EtOAc/hexanes afforded the title compound as a colorless film (15.6 mg, 0.024 mmol, >99% yield); ^{1}H NMR (400 MHz, C_6D_6) δ 7.92 – 7.86 (m, 2H), 7.49 (d, *J* = 1.3 Hz, 1H), 7.30 – 7.25 (m, 2H), 7.02 – 6.87 (m, 4H), 6.63 – 6.58 (m, 2H), 3.67 (dq, *J* = 6.1, 2.1 Hz, 1H), 3.46 (s, 3H), 3.31 (dt, *J* = 4.9, 2.3 Hz, 1H), 2.94 (dd, *J* = 12.5, 2.9 Hz, 1H), 2.72 – 2.61 (m, 1H), 2.56 – 2.42 (m, 4H), 2.37

(dt, J = 15.8, 1.8 Hz, 1H), 2.09 (ddd, J = 12.5, 3.4, 2.3 Hz, 1H), 1.72 (s, 3H), 0.51 (s, 9H); ^{13}C NMR (100 MHz, C_6D_6) δ 204.7, 143.8, 140.7, 137.9, 134.1, 132.7, 131.2, 129.5, 129.4, 127.9, 124.3, 121.8, 121.0, 117.3, 114.0, 107.4, 79.4, 58.3, 57.2, 50.2, 46.8, 40.2, 35.2, 23.1, 21.1, 3.0 (an additional ^{13}C resonance associated with the tosyl group is likely obscured by the solvent signal); IR (Neat Film, NaCl) 2934, 2847, 1725, 1502, 1358, 1285, 1249, 1172, 1106, 963, 845, 665 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{33}H_{37}N_2O_5S_2Si$ $[M+H]^+$: 633.1908, found 633.1895.

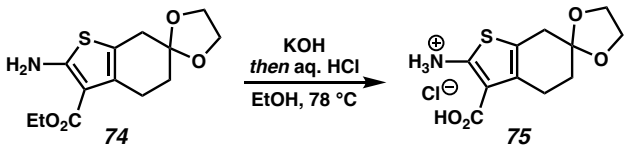
Aminothiophene 74



74

Prepared according to the procedure of Andersen, Møller, and coworkers from 1,4-cyclohexandione monoethylene ketal. All characterization data matched those reported in the literature.

Amino acid hydrochloride 75

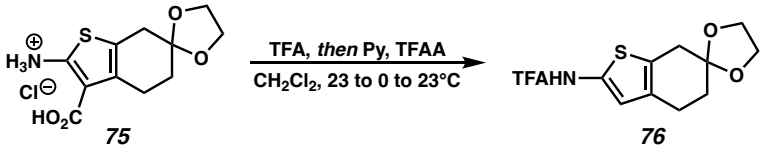


74 ***75***

To a 350 mL glass pressure vessel under air were added aminothiophene **74** (22.2 g, 78.35 mmol, 1.0 equiv), KOH (17.6 g, 313.4 mmol, 4.0 equiv), EtOH (165 mL), and water (33 mL). The flask was sealed, and the reaction mixture was stirred at 75 °C in an oil bath for 12 h. The reaction mixture was subsequently transferred to an Erlenmeyer flask

and cooled to 0 °C in an ice bath. The solution was acidified with 1 N aq. HCl (375 mL), resulting in the formation of a thick precipitate. The product was collected by vacuum filtration and washed with water. The resulting clay-like material was transferred to a round bottom flask with MeOH. The solvent was removed under reduced pressure and the product was dried under high vacuum to afford the title compound as a cream-colored powder (17.95 g, 61.53 mmol, 79% yield assuming complete conversion to hydrochloride); ^{1}H NMR (400 MHz, DMSO) δ 11.81 (br s, 1H), 7.20 (br s, 2H), 3.90 (s, 4H), 2.72 (t, J = 6.4 Hz, 2H), 2.59 (s, 2H), 1.75 (t, J = 6.5 Hz, 2H); ^{13}C NMR (100 MHz, DMSO) δ 166.7, 163.4, 130.9, 112.4, 107.6, 102.6, 63.9, 34.3, 31.0, 25.1; IR (Neat Film, NaCl) 3409, 2890, 1635, 1580, 1474, 1451, 1353, 1294, 1267, 1105, 1054, 1036, 926, 642 cm^{-1}; HRMS (ESI–): *m/z* calc'd for $C_{11}H_{12}NO_4S$ [M–H]$^-$: 254.0493, found 254.0494.

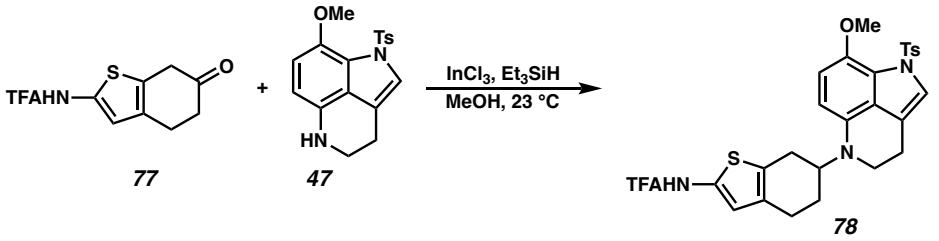
Trifluoroacetamidothiophene 76



To a 500 mL round bottom flask was added hydrochloride salt **75** (14.29 g, 48.98 mmol, 1.0 equiv). Traces of water were azeotropically removed by addition of three portions of benzene followed by rotary evaporation. Then, the headspace of the flask was evacuated and backfilled with nitrogen, and CH_2Cl_2 (150 mL) and TFA (11.2 mL, 146.9 mmol, 3.0 equiv) were added. After 15 min, additional CH_2Cl_2 (50 mL) was added to reduce the viscosity of the mixture. The reaction mixture was stirred for 2.5 h at 23 °C, whereafter it was cooled to 0 °C in an ice bath and pyridine (19.7 mL, 244.9 mmol, 5.0 equiv) was added rapidly. TFAA (10.2 mL, 73.47 mmol, 1.5 equiv) was then added, and

the ice bath was removed. After stirring for an additional 16 h at 23 °C, silica gel was added, and the reaction mixture was concentrated under reduced pressure and purified by silica gel flash chromatography (33% EtOAc/hexanes) to afford the title compound as an orange solid (9.67 g, 31.47 mmol, 64% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 6.59 (s, 1H), 4.06 – 3.98 (m, 4H), 2.91 (d, *J* = 1.5 Hz, 2H), 2.74 (tt, *J* = 6.5, 1.6 Hz, 2H), 1.94 (t, *J* = 6.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 153.8, 153.4, 153.0, 133.4, 131.8, 127.9, 120.1, 117.2, 116.1, 114.4, 111.5, 108.5, 64.8, 34.9, 31.7, 24.0; IR (Neat Film, NaCl) 3248, 3097, 2894, 1713, 1589, 1434, 1362, 1250, 1169, 1060, 946, 905, 842, 739 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{12}H_{13}F_3NO_3S$ $[M+H]^+$: 308.0563, found 308.0561.

Tertiary aniline 78

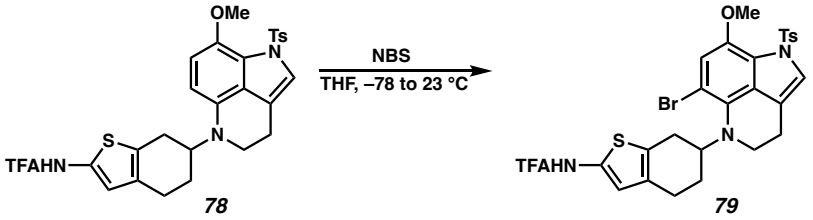


To a 100 mL round bottom flask containing thiophene-ketal **76** (1.64 g, 5.34 mmol, 1.5 equiv) under nitrogen and equipped with a reflux condenser were added THF (27 mL) and 4 N aq. HCl (5.3 mL, 21.2 mmol, 4.0 equiv w.r.t. ketal). The reaction mixture was heated to reflux and stirred for 1.5 h, then allowed to cool to 23 °C and quenched with saturated aq. $NaHCO_3$ (100 mL). The resulting mixture was extracted with CH_2Cl_2 (3x40 mL). The combined organic extracts were washed with brine, and the brine phase was back-extracted once with CH_2Cl_2. The combined organic phases were dried over a mixture

of Na_2SO_4 and $MgSO_4$ and concentrated under reduced pressure to afford crude ketone **77** as an orange solid that was used directly without further purification.

To a 50 mL round bottom flask were added tricyclic aniline **47** (1.22 g, 3.56 mmol, 1.0 equiv), the crude ketone resulting from hydrolysis of ketal **77** (5.34 mmol assuming pure compound), and $InCl_3$ (1.57 g, 7.12 mmol, 2.0 equiv). The headspace of the flask was evacuated and backfilled with nitrogen. MeOH (12 mL) and Et_3SiH (5.7 mL, 35.6 mmol, 10 equiv) were added and the reaction mixture was stirred at 23 °C for 24 h, whereafter it was transferred to a separatory funnel containing saturated aq. $NaHCO_3$ (200 mL). The resulting suspension was extracted with CH_2Cl_2 (3x70 mL). The combined organic extracts (still containing a significant quantity of water and indium salts) were dried over Na_2SO_4, concentrated under reduced pressure, and purified by automated silica gel flash chromatography (Teledyne ISCO, 0→60% EtOAc/hexanes) to afford the title compound as a golden-colored foam of sufficient purity for use in the next step (1.80 g, 3.05 mmol, 86% yield). A sample for analysis was obtained by preparative TLC on silica gel (33% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (br s, 1H), 7.82 – 7.75 (m, 2H), 7.34 (t, *J* = 1.5 Hz, 1H), 7.26 – 7.21 (m, 2H), 6.60 (s, 1H), 6.58 (d, *J* = 8.3 Hz, 1H), 6.30 (d, *J* = 8.8 Hz, 1H), 4.15 – 4.01 (m, 1H), 3.68 (s, 3H), 3.33 (dt, *J* = 11.0, 5.4 Hz, 1H), 3.21 (dt, *J* = 11.5, 6.2 Hz, 1H), 2.99 – 2.92 (m, 3H), 2.91 – 2.66 (m, 3H), 2.37 (s, 3H), 2.07 – 1.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 153.4, 144.2, 140.0, 137.1, 136.3, 133.2, 132.4, 129.5, 129.4, 127.7, 124.2, 123.2, 119.7, 117.2, 116.5, 115.4, 114.4, 110.3, 102.7, 57.3, 53.5, 42.2, 27.0, 26.0, 25.9, 23.5, 21.7; IR (Neat Film, NaCl) 3281, 3126, 3058, 2935, 2841, 1714, 1588, 1510, 1442, 1356, 1251, 1169, 1108, 1056, 996, 903, 739, 663 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{28}H_{27}F_3N_3O_4S_2$ $[M+H]^+$: 590.1390, found 590.1404.

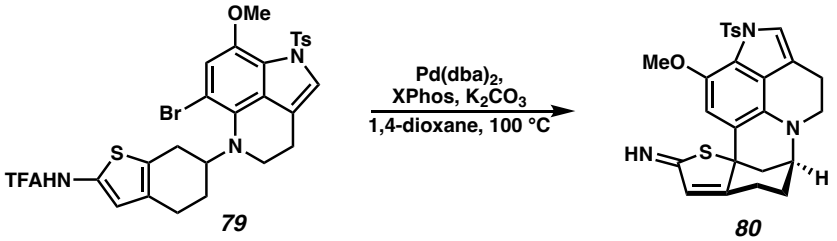
Bromoarene 79



To a 250 mL round bottom flask was added tertiary aniline **78** (2 g, 3.40 mmol, 1.0 equiv). Traces of water were azeotropically removed by addition of three portions of benzene followed by rotary evaporation, and the headspace of the flask was evacuated and backfilled with nitrogen. The starting material was taken up in THF (50 mL), and the flask was cooled to –78 °C and protected from light. A solution of NBS (484 mg, 3.06 mmol, 0.9 equiv) in THF (25 mL) was added as a slow stream with rapid stirring. Following addition, the reaction mixture was allowed to stir at –78 °C for 5 additional min, whereafter the cooling bath was removed and the reaction mixture allowed to warm to 23 °C. The mixture was stirred at room temperature for 10 min before being quenched with sat. $Na_2S_2O_3$ solution (50 mL). The biphasic mixture was transferred to a separatory funnel and the phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (3x50 mL). The combined organic phases were dried over Na_2SO_4, concentrated under reduced pressure and purified by silica gel flash chromatography (0→30% EtOAc/hexanes) to afford the title compound as a brown foam (2.0 g, 3.05 mmol, 90% yield); ^{1}H NMR (400 MHz, C_6D_6) δ 7.86 – 7.80 (m, 2H), 7.54 (t, *J* = 1.5 Hz, 1H), 6.75 (s, 1H), 6.67 – 6.57 (m, 2H), 6.01 (s, 1H), 4.17 (dddd, *J* = 13.7, 11.3, 5.3, 2.6 Hz, 1H), 3.19 (s, 3H), 2.99 – 2.75 (m, 3H), 2.58 (tdd, *J* = 11.7, 3.9, 2.0 Hz, 1H), 2.36 – 2.09 (m, 4H), 1.80 – 1.71 (m, 1H), 1.76 (s, 3H), 1.45 (tdd, *J* = 12.2, 10.7, 6.7 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 153.6, 153.2, 144.1, 143.0, 137.8, 134.6, 133.6, 131.9, 129.6, 129.5, 128.0, 127.7, 123.1, 122.4, 117.7,

116.6, 116.2, 115.2, 114.2, 106.2, 59.5, 56.3, 43.0, 29.5, 28.5, 26.0, 22.6, 21.1; IR (Neat Film, NaCl) 3295, 2931, 1714, 1588, 1490, 1438, 1347, 1251, 1172, 1111, 908, 804, 737, 665 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{28}H_{26}BrF_3N_3O_4S_2$ $[M+H]^+$: 668.0495, found 668.0502.

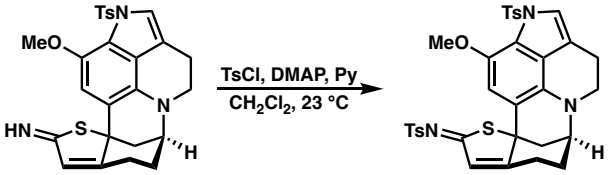
Thioimidate 80



To a 40 mL glass vial was added bromoarene **80** (331 mg, 0.495 mmol, 1.0 equiv). Traces of water were azeotropically removed by addition of three portions of benzene followed by rotary evaporation and the vial was transferred to a nitrogen-filled glovebox. Solid K_2CO_3 (96 mg, 0.695 mmol, 1.4 equiv) was added to the vial. In a separate vial, a stock solution of $Pd(dba)_2$ (46.2 mg) and XPhos (64.2 mg) in 1,4-dioxane (13.3 mL) was prepared and stirred at 28 °C for 10 min. Then, 12.4 mL of this solution were transferred to the vial containing bromoarene **79** (for 43 mg $Pd(dba)_2$ [0.0748 mmol, 15 mol %] and 59.1 mg XPhos [0.124 mmol, 25 mol %]). The vial was sealed with a PTFE/silicone septum cap, removed from the glovebox, and stirred at 100 °C for 6 h. The reaction mixture was then allowed to cool to 23 °C and passed through a PTFE syringe filter, which was subsequently rinsed with EtOAc. The solution was concentrated under reduced pressure and purified by silica gel flash chromatography (100% EtOAc → 100% acetone) to afford the title compound as an off-white solid (145 mg, 0.295 mmol, 60% yield); ^1H NMR (400

MHz, CD_2Cl_2) δ 7.81 – 7.72 (m, 2H), 7.32 – 7.24 (m, 3H), 6.81 (s, 1H), 5.78 (d, *J* = 1.7 Hz, 1H), 3.64 (s, 3H), 3.59 (p, *J* = 2.7 Hz, 1H), 3.35 (ddd, *J* = 11.1, 9.7, 5.7 Hz, 1H), 3.25 (ddd, *J* = 11.1, 4.8, 3.5 Hz, 1H), 3.04 – 2.94 (m, 2H), 2.65 (dt, *J* = 12.5, 2.9 Hz, 1H), 2.54 – 2.47 (m, 1H), 2.40 (qd, *J* = 5.3, 3.1 Hz, 1H), 2.37 (s, 3H), 2.33 (dd, *J* = 12.5, 2.9 Hz, 1H), 2.06 – 1.97 (m, 1H), 1.61 (tdd, *J* = 13.7, 5.3, 2.9 Hz, 1H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 178.5, 168.3, 144.9, 139.3, 137.2, 133.5, 129.7, 128.0, 123.5, 122.3, 121.7, 120.6, 115.2, 114.5, 109.1, 63.5, 57.4, 47.6, 41.9, 31.9, 24.8, 23.2, 21.7 (the bridgehead methine ^{13}C resonance is obscured by the solvent peak); IR (Neat Film, NaCl) 2925, 2851, 1595, 1503, 1462, 1349, 1284, 1226, 1174, 1106, 1011, 898, 808, 738, 704, 672 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{26}H_{26}N_3O_3S_2$ $[M+H]^+$: 492.1410, found 492.1416.

_N_-tosylthioimidate 82

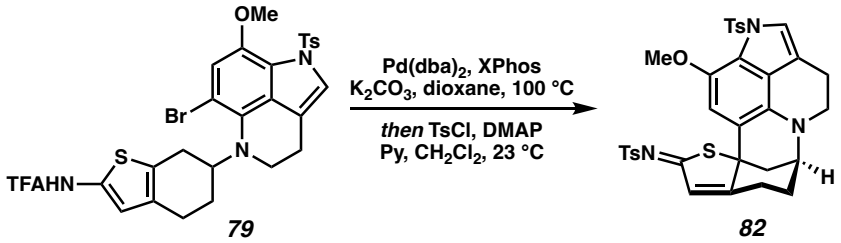


80 ***82***

To a 1-dram glass vial containing TsCl (16 mg, 0.0814 mmol, 2.0 equiv) under nitrogen was added thioimidate **80** (20 mg, 0.0407 mmol, 1.0 equiv) as a stock solution in CH_2Cl_2 (1 mL), followed by pyridine (10 μL, 0.122 mmol, 3.0 equiv). The reaction mixture was stirred at 23 °C for 3 days, after which it was concentrated under reduced pressure and purified by silica gel flash chromatography (50% EtOAc/hexanes) to afford the title compound as an orange film (23.7 mg, 0.0367 mmol, 90% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.1 Hz, 2H), 7.83 – 7.74 (m, 2H), 7.36 – 7.28 (m, 3H), 7.28 – 7.22 (m, 2H), 6.49 (s, 1H), 5.97 (d, *J* = 1.6 Hz, 1H), 3.65 – 3.61 (m, 1H), 3.59 (s, 3H), 3.37 (dt,

J = 10.9, 7.6 Hz, 1H), 3.27 (dt, *J* = 11.1, 4.2 Hz, 1H), 3.06 – 2.97 (m, 2H), 2.83 (dt, *J* = 12.6, 2.8 Hz, 1H), 2.68 – 2.58 (m, 1H), 2.49 – 2.44 (m, 1H), 2.43 (s, 3H), 2.38 (s, 3H), 2.21 – 2.04 (m, 2H), 1.59 – 1.51 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.5, 175.3, 144.4, 144.0, 139.4, 137.3, 136.9, 133.1, 129.6, 129.5, 127.9, 127.6, 123.6, 122.7, 121.6, 120.7, 114.2, 111.1, 107.8, 65.4, 57.2, 53.0, 47.4, 40.4, 31.7, 25.4, 23.0, 21.7; IR (Neat Film, NaCl) 2924, 2850, 1596, 1519, 1449, 1286, 1228, 1167, 1107, 1010, 867, 813, 734, 664 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{33}H_{32}N_3O_5S_3$ $[M+H]^+$: 646.1499, found 646.1500.

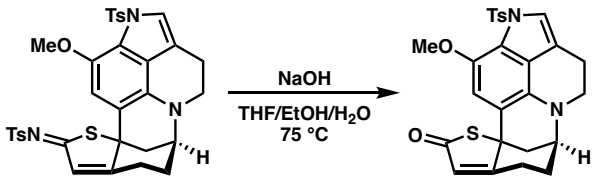
Procedure for the direct preparation of *N*-tosylthioimidate 82 from bromoarene 79



To a 500 mL Schlenk bomb in a nitrogen-filled glovebox was added bromoarene **79** (2.00 g, 3.1 mmol, 1.0 equiv) as a solution in a minimal amount of benzene. The benzene was removed under reduced pressure, and K_2CO_3 (600 mg, 4.34 mmol, 1.4 equiv) and 1,4-dioxane (60 mL) were added. In a separate vial, $Pd(dba)_2$ (270 mg, 0.465 mmol, 15 mol %) and XPhos (691 mg, 0.775 mmol, 25 mol %) were combined. 1,4-dioxane (20 mL) was added and the mixture was stirred at 28 °C for 10 min. Then, the Pd/ligand solution was transferred by pipette to the Schlenk bomb. The vessel was sealed, removed from the glovebox, and stirred at 100 °C for 7 h, at which point LC/MS analysis showed full consumption of starting material. Then water (2 mL) was added via syringe. The resulting

mixture was stirred at 100 °C for 1 h. The reaction mixture was allowed to cool to 23 °C, filtered through a Celite plug with EtOAc, and concentrated under reduced pressure. Traces of water were azeotropically removed by addition of three portions of $PhCH_3$ followed by rotary evaporation. DMAP (39 mg, 0.31 mmol, 10 mol %) was added and the headspace of the flask was evacuated and backfilled with nitrogen. CH_2Cl_2 (62 mL) was added, followed by pyridine (0.75 mL, 9.3 mmol, 3.0 equiv). TsCl (1.2 g, 6.2 mmol, 2.0 equiv) was added in a single portion under a stream of nitrogen. The reaction mixture was stirred at 23 °C for 58 h, then concentrated under reduced pressure. The crude product was purified by automated silica gel flash chromatography (Teledyne ISCO, 0→40→75% EtOAc/hexanes) to afford *N*-tosylthioimidate **82** as an orange foam that crystallized upon standing (1.7 g, 4.12 mmol, 85% yield). For characterization data, see above.

Thiolactone 81

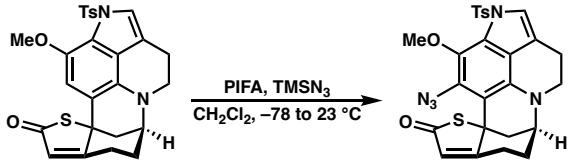


82 ***81***

To a 250 mL round bottom flask were added thioimidate **82** (940 mg, 1.46 mmol, 1.0 equiv), THF (30 mL), water (10 mL), degassed ethanol (50 mL), and 2 N aq. NaOH (6 mL, 12 mmol, 8.2 equiv). The headspace of the vial was purged with nitrogen and the vial was sealed with a PTFE/silicone septum. The reaction mixture was stirred at 80 °C for 1 hour, at which point the solution became homogenous and was immediately removed from the oil bath and allowed to cool to 23 °C. The reaction mixture was quenched with glacial acetic acid (2 mL) and partitioned between water and EtOAc. The layers were separated,

and the aqueous phase was extracted with EtOAc (3x). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo* to afford the crude product. Purification by silica gel flash chromatography (0→2% EtOAc/CH_2Cl_2) afforded the title compound (591 mg, 1.21 mmol, 83% yield). ^{1}H NMR (400 MHz, C_6D_6): δ 7.86 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 1.6 Hz, 1H), 6.89 (t, *J* = 1.3 Hz, 1H), 6.67 – 6.59 (m, 2H), 5.50 (d, *J* = 1.7 Hz, 1H), 3.32 (s, 3H), 2.87 – 2.78 (m, 1H), 2.78 – 2.59 (m, 2H), 2.59 – 2.45 (m, 2H), 2.40 (dt, *J* = 12.4, 2.8 Hz, 1H), 1.91 – 1.81 (m, 1H), 1.81 – 1.76 (m, 1H), 1.74 (s, 3H), 1.73 – 1.66 (m, 1H), 1.66 – 1.56 (m, 1H), 0.97 – 0.81 (m, 1H). ^{13}C NMR (100 MHz, C_6D_6): δ 196.3, 177.3, 143.9, 140.0, 137.8, 133.5, 129.4, 124.2, 121.9, 121.7, 121.0, 114.6, 112.8, 108.9, 60.8, 57.0, 53.0, 47.1, 40.9, 31.4, 24.8, 23.0, 21.1 (*Note: an additional ^{13}C resonance associated with the tosyl group is likely obscured by the solvent signal*). IR (Neat Film, NaCl): 2931, 2851, 1682, 1504, 1348, 1284, 1227, 1169, 1107, 1011, 897, 851, 814, 738, 662 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{26}H_{25}N_2O_4S_2$ $[M+H]^+$: 493.1250, found 493.1251.

Azide 83

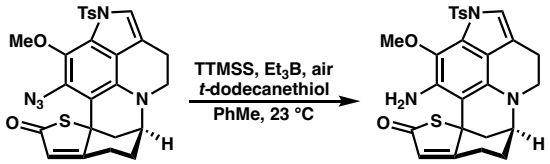


81 ***83***

To a 1-dram glass vial containing thiolactone **81** (22.6 mg, 0.0459 mmol, 1.0 equiv) under nitrogen were added CH_2Cl_2 (2.3 mL) and $TMSN_3$ (30 μL, 0.23 mmol, 5.0 equiv). The reaction mixture was cooled to –78 °C and a solution of PIFA (18.8 mg, 0.0437 mmol, 0.95 equiv) in CH_2Cl_2 (0.5 mL) was added dropwise. After stirring for 10 min at –78 °C, the reaction mixture was allowed to warm to 23 °C, concentrated under reduced pressure,

and purified by preparative TLC on silica gel (90% Et_2O/hexanes, eluted twice) to afford an intermediate aryl azide as a brown film (15.3 mg, 0.0287 mmol, 62% yield); ^{1}H NMR (600 MHz, C_6D_6) 7.94 (s, 1H), 7.34 (s, 1H), 6.56 (d, J = 7.9 Hz, 2H), 5.66 (s, 1H), 3.81 (s, 1H), 2.62 – 2.54 (m, 2H), 2.50 (td, J = 13.5, 4.9 Hz, 2H), 2.43 – 2.33 (m, 2H), 2.24 (dt, J = 12.6, 3.0 Hz, 1H), 1.80 (dd, J = 14.3, 5.8 Hz, 1H), 1.66 – 1.59 (m, 2H), 1.58 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ (three ^{13}C resonances associated with aromatic carbons are likely obscured by the solvent signal) 196.7, 173.5, 144.7, 136.6, 136.1, 135.1, 130.7, 129.8, 126.5, 123.2, 120.7, 118.4, 115.5, 107.0, 62.1, 58.6, 52.7, 47.6, 42.3, 30.7, 24.6, 22.6, 21.0. IR (Neat Film, NaCl): 2926, 2854, 2104, 1740, 1682, 1634, 1618, 1596, 1520, 1488, 1454, 1435, 1416, 1398, 1370, 1342, 1290, 1270, 1226, 1188, 1174, 1140, 1112, 1094, 962, 916, 894, 650 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{26}H_{25}N_2O_4S_2$ $[M+H]^+$: 534.1270, found 534.1260.

Primary aniline 84

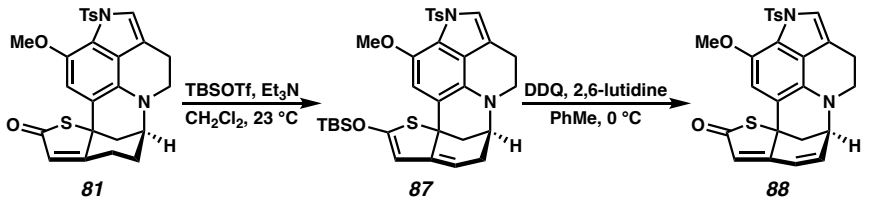


83 ***84***

To a ½-dram glass vial under air was added this intermediate aryl azide **83** (7.3 mg, 0.0137 mmol, 1.0 equiv) as a stock solution in CH_2Cl_2. The solvent was removed by blowing a stream of nitrogen over the surface of the solution. Then, $PhCH_3$ (0.36 mL), tris(trimethylsilyl)silane (21 µL, 0.0684 mmol, 5.0 equiv), *tert*-dodecanethiol (1.6 µL, 0.0069 mmol, 0.5 equiv), and triethylborane (1 M in hexanes, 41 µL, 0.0411 mmol, 3.0 equiv) were added under air. After 5 min, the reaction mixture was concentrated under

reduced pressure and purified by preparative TLC on silica gel (100% EtOAc) to afford the title compound as a brown film (5.5 mg, 0.0108 mmol, 79% yield); ^{1}H NMR (400 MHz, C_6D_6) δ 8.02 – 7.97 (m, 2H), 7.26 (d, *J* = 1.6 Hz, 1H), 6.59 – 6.54 (m, 2H), 5.60 (d, *J* = 1.5 Hz, 1H), 4.53 (s, 2H), 3.77 (s, 3H), 2.63 – 2.50 (m, 3H), 2.42 – 2.34 (m, 3H), 1.75 – 1.67 (m, 2H), 1.65 (s, 3H), 1.58 – 1.53 (m, 2H), 0.75 – 0.63 (m, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 194.9, 175.9, 143.9, 139.9, 136.8, 136.6, 129.6, 127.5, 127.2, 122.7, 117.8, 116.5, 112.2, 100.0, 60.3, 60.3, 52.8, 48.0, 44.0, 30.9, 25.2, 22.9, 21.0 (an additional ^{13}C resonance associated with the tosyl group is likely obscured by the solvent signal); IR (Neat Film, NaCl) 3440, 3347, 2921, 2854, 1682, 1486, 1367, 1294, 1177, 1136, 1094, 967, 828, 738, 683 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{26}H_{26}N_3O_4S_2$ $[M+H]^+$: 508.1359, found 508.1374.

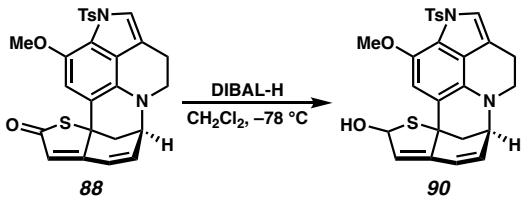
Diene 88



To a 20 mL glass vial containing thiobutenolide **81** (50 mg, 0.102 mmol, 1.0 equiv) under nitrogen was added CH_2Cl_2 (1 mL), triethylamine (0.15 mL, 1.02 mmol, 10 equiv), and TBSOTf (0.16 mL, 0.711 mmol, 7.0 equiv). The reaction mixture was stirred at 23 °C for 14 hours before being loaded on to a silica gel column. The column was flushed with 10% EtOAc/hexanes (200 mL), followed by 40% EtOAc/hexanes (150 mL) to afford an intermediate silyl ketene thioacetal and starting material (12.7 mg, 0.0258 mmol, 25% recovery). The silyl ketene thioacetal was transferred to an 8 mL vial, evacuated and

backfilled 3 times with N_2, and PhMe (0.76 mL) was added. The resulting mixture was cooled to 0 °C in an ice bath, whereafter 2,6-lutidine (17.5 μL, 0.152 mmol, 2.0 equiv) and DDQ (17.3 mg, 0.0761 mmol, 1.0 equiv, as a solution in 0.76 mL PhMe) were sequentially added. The reaction mixture was stirred at 0 °C and the reaction was monitored by LC/MS. Upon the completion of the reaction (*ca*. ~5 min), the reaction mixture was loaded directly onto silica gel. Purification by silica gel flash chromatography (0→35% EtOAc/hexanes) afforded diene **88** (26.3 mg, 0.0537 mmol, 53% over 2 steps) as an orange solid. ^{1}H NMR (400 MHz, C_6D_6): δ 7.83 – 7.78 (m, 2H), 7.44 (d, *J* = 1.6 Hz, 1H), 6.92 (s, 1H), 6.62 – 6.53 (m, 2H), 5.87 (ddd, *J* = 9.7, 1.9, 0.9 Hz, 1H), 5.52 (s, 1H), 5.46 – 5.38 (m, 1H), 3.29 (s, 3H), 3.19 (dtt, *J* = 4.7, 3.3, 2.0 Hz, 1H), 2.67 – 2.55 (m, 3H), 2.40 – 2.32 (m, 2H), 1.93 (dd, *J* = 12.3, 3.9 Hz, 1H), 1.71 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 196.1, 171.8, 143.8, 141.3, 137.8, 132.8, 131.8, 129.4, 128.0, 125.1, 124.1, 123.4, 121.6, 121.2, 114.3, 113.6, 108.7, 58.2, 56.8, 53.0, 47.9, 37.6, 23.0, 21.1. IR (Neat Film, NaCl): 3060, 2934, 2841, 1681, 1622, 1504, 1347, 1287, 1226, 1177, 1106, 1016, 967, 898, 856, 813, 732, 662, 623 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{26}H_{23}N_2O_4S_2$ $[M+H]^+$: 491.1094, found 491.1098.

Thiolactol 90

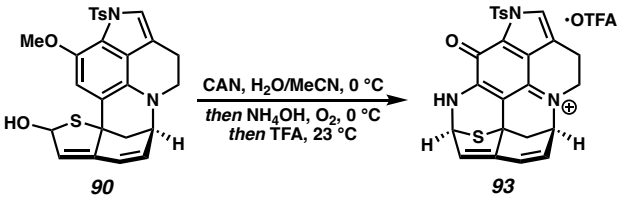


88 ***90***

To a 20 mL glass vial containing diene **88** (20 mg, 0.0408 mmol, 1.0 equiv) under nitrogen was added CH_2Cl_2 (1.9 mL). The solution was cooled to –78 °C in a dry ice/acetone bath. To the resulting mixture was added DIBAL (70 μL, 0.408 mmol, 10

equiv) as a freshly prepared solution in CH_2Cl_2 (1 mL). The reaction was quenched at –78 °C by the addition of 2 mL saturated aqueous Rochelle's salt solution immediately following the addition of DIBAL. The resulting mixture was allowed to warm up to 23 °C and was stirred vigorously for 45 min. The layers were then separated, and the aqueous phase was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo* to afford crude thiolactol **90** as a yellow oil, which was used immediately in next step without further purification.

N-tosyl desbromoaleutianamine (93)

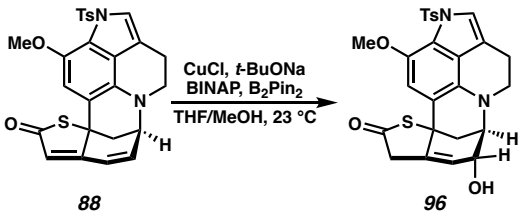


90 *93*

To a 20 mL vial containing thiolactol **90** (20 mg, 0.0408 mmol, 1.0 equiv) under nitrogen was added MeCN (2.7 mL). The vial was cooled to 0 °C in an ice bath and CAN (44.8 mg, 0.0816 mmol, 2 equiv) was added dropwise as a freshly prepared solution in 1.3 mL water. The resulting mixture was stirred at 0 °C for 5 min, after which aqueous ammonia (27% w/w, 34 μL, 0.408 mmol, 10 equiv) was added. The reaction vessel was flushed with O_2, and the resulting mixture was stirred for 7 min under an O_2 atmosphere at 0 °C. The reaction mixture was warmed to 23 °C and was diluted with EtOAc (5 mL) and water (3 mL). The layers were separated, and the aqueous phase was extracted with EtOAc (4x4 mL). The combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. The residue was taken up in TFA (4 mL), and the mixture was allowed to stand at 23 °C for 10 min before being concentrated by rotary evaporation. The crude N-tosyl

desbromoaleutianamine (**93**) was purified by preparative reverse phase HPLC (Eclipse XDB-C18, 5 μm, 9.4 x 250 mm, MeCN-H_2O (0.1% TFA) = 32.5:67.5 to 100:0, linear gradient for 6 min, flow rate = 5 mL/min) to afford N-tosyl desbromoaleutianamine (**93**) as the TFA salt (12 mg, 0.0204 mmol, 50% yield). ^{1}H NMR (400 MHz, CD_3OD): δ 8.09 – 8.01 (m, 2H), 7.78 (d, *J* = 1.4 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 2H), 6.72 (d, *J* = 9.4 Hz, 1H), 6.16 (dd, *J* = 9.5, 5.9 Hz, 1H), 5.94 (d, *J* = 3.3 Hz, 1H), 5.31 (d, *J* = 3.3 Hz, 1H), 4.95 (dt, *J* = 6.0, 2.9 Hz, 1H), 4.26 – 4.16 (m, 1H), 4.15 – 3.97 (m, 1H), 3.22 (td, *J* = 15.4, 7.1 Hz, 1H), 3.16 – 3.04 (m, 1H), 2.51 – 2.31 (m, 5H). ^{13}C NMR (100 MHz, MeOD): δ 167.4, 148.7, 147.4, 141.9, 140.7, 134.6, 131.1, 130.1, 129.3, 127.8, 124.4, 123.7, 118.8, 112.3, 102.5, 64.8, 57.6, 51.9, 50.9, 30.9, 21.7, 20.3. (*Note: two ^{13}C signals overlap*.) IR (Neat Film, NaCl): 3136, 2932, 1682, 1622, 1524, 1442, 1420, 1378, 1346, 1268, 1194, 1180, cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{25}H_{20}N_3O_3S_2$ $[M+H]^+$: 474.0941, found 474.0959.

Alcohol 96

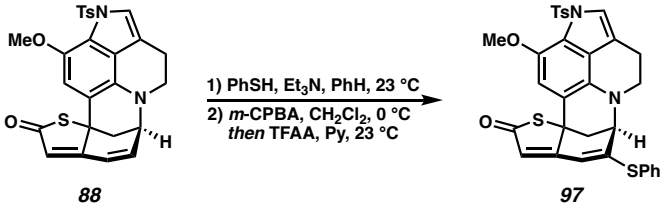


88 ***96***

To a flame dried 1 dram vial in a nitrogen filled glove box was added CuCl (1.5 mg, 0.0155 mmol, 0.38 equiv), BINAP (9.65 mg, 0.0155 mmol, 0.38 equiv), NaO*t*-Bu (1.5 mg, 0.0155 mmol, 0.38 equiv) and THF (1 mL, 0.04 M). The vial was sealed and stirred for 10 min at 23 °C. Then, diene **88** (20.0 mg, 0.04 mmol, 1.0 equiv) and B_2Pin_2 (81.3 mg, 0.32 mmol, 8.0 equiv) as a solution in THF (1 mL, 0.04M) were added to the CuCl solution. The vial was sealed with a septa cap and removed for the glovebox. MeOH (0.024 mL, 0.6

mmol, 15.0 equiv) was then added, and the reaction mixture was stirred for 10 min at 23 °C, at which point LC/MS analysis indicated complete consumption of the starting material. The reaction mixture was diluted with EtOAc (5 mL) and a saturated solution of NH_4Cl (3 mL). The layers were separated, and the aqueous phase was extracted with EtOAc (4x4 mL). The combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. The crude solid was purified by preparatory TLC (60% EtOAc/hexanes) to afford the titled compound (10.3 mg, 50% yield) as a yellow solid. Suitable crystals for X-Ray diffraction were grown via layer diffusion (CH2Cl2/hexanes)^{1}H NMR (400 MHz, C_6D_6): δ 7.88 (d, J = 8.4 Hz, 2H), 7.40 (s, 1H), 7.00 (s, 1H), 6.79 – 6.47 (m, 2H), 4.92 (ddd, J = 3.9, 2.6, 1.2 Hz, 1H), 3.72 (s, 1H), 3.46 (s, 3H), 3.23 (td, J = 2.7, 1.2 Hz, 1H), 2.99 (dt, J = 19.4, 2.7 Hz, 1H), 2.80 – 2.58 (m, 2H), 2.56 (s, 1H), 2.49 – 2.27 (m, 2H), 2.15 (dd, J = 12.0, 2.5 Hz, 1H), 1.80 (dd, J = 12.1, 4.0 Hz, 1H), 1.71 (s, 3H). ^{13}C NMR (100 MHz, C6D6): δ 201.2, 143.8, 141.4, 139.8, 137.8, 130.0, 129.4, 121.8, 121.0, 120.9, 114.4, 114.3, 108.7, 66.1, 59.9, 58.1, 56.1, 47.6, 45.6, 32.4, 30.7, 22.8, 21.1. IR (Neat Film, NaCl): 3315, 2919, 1712, 1503, 1355, 1286, 1173, 1104 cm^{-1}. HRMS (ESI+): m/z calc'd for $C_{26}H_{25}N_2O_5S_2$ $[M+H]^+$: 509.1199, found 509.1196.

Doubly vinylogous dithiocarbonate 97



88 ***97***

To a ½-dram glass vial containing diene **88** (5.0 mg, 0.0102 mmol, 1.0 equiv) under nitrogen were added benzene (0.2 mL), thiophenol (5.2 µL, 0.051 mmol, 5.0 equiv), and

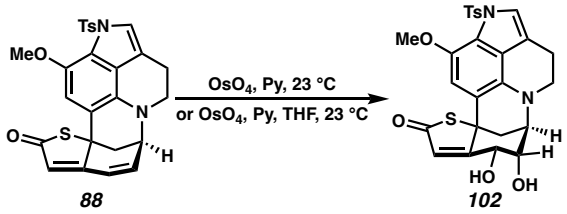
Et_3N (14.2 μL, 0.102 mmol, 10 equiv). The reaction mixture was stirred at 23 °C for 75 min, whereafter it was loaded directly onto a silica gel flash column. Elution (10 → 25% EtOAc/hexanes) provided an intermediate sulfide as a colorless film (4.7 mg, 0.00782 mmol, 77% yield) along with small amount of impurity; Intermediate sulfide was used in the next step without further purification.

To a 1-dram glass vial containing this intermediate sulfide (3.2 mg, 0.00533 mmol, 1.0 equiv) under nitrogen was added CH_2Cl_2 (133 μL), and the vial was cooled to 0 °C in an ice bath. *m*-CPBA (77 wt %, 1.2 mg, 0.00535 mmol, 1.0 equiv) was added dropwise as a solution in CH_2Cl_2 (133 μL) and the reaction mixture was allowed to stir at 0 °C for 100 min. The solution was then diluted with EtOAc (1 mL), washed with saturated aq. K_2CO_3 (3x), dried over Na_2SO_4, and concentrated to provide a crude sulfoxide that was used directly in the next step.

To a ½-dram glass vial was added the crude sulfoxide as a solution in dry CH_2Cl_2 (0.25 mL). The vial was cooled to 0 °C, and pyridine (7.0 μL, 0.087 mmol, 16 equiv) and TFAA (7.5 μL, 0.054 mmol, 10 equiv) were added. The reaction mixture was stirred for 5 min at 0 °C, then allowed to warm to 23 °C and stirred for an additional 14 h. MeOH (7 μL) was then added to quench excess TFAA, and the reaction mixture was loaded directly onto a silica gel flash column and eluted (25% EtOAc/hexanes). The product was combined with the product of another reaction conducted on a 0.0118 mmol scale to provide the title compound as an orange-red film (5.0 mg, 0.00835 mmol, 49% combined yield); ^{1}H NMR (400 MHz, C_6D_6) δ 7.83 – 7.76 (m, 2H), 7.47 (d, J = 1.7 Hz, 1H), 7.08 – 7.01 (m, 2H), 6.96 – 6.86 (m, 4H), 6.55 (d, J = 8.1 Hz, 2H), 5.80 (s, 1H), 5.11 (s, 1H), 3.54 (t, J = 3.2 Hz, 1H), 3.46 (td, J = 11.6, 3.9 Hz, 1H), 3.25 (s, 3H), 2.93 (ddd, J = 11.1, 4.9, 2.6 Hz, 1H), 2.68 –

2.57 (m, 1H), 2.53 (dt, J = 15.6, 3.3 Hz, 1H), 2.34 (dd, J = 12.2, 2.6 Hz, 1H), 2.00 (dd, J = 12.3, 3.8 Hz, 1H), 1.72 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 195.4, 171.3, 145.0, 143.7, 141.4, 137.8, 134.4, 130.1, 129.8, 129.6, 129.3, 124.2, 123.0, 121.3, 118.5, 118.4, 114.3, 112.9, 108.8, 57.1, 56.8, 56.8, 50.1, 37.8, 23.2, 21.1 (2 additional aryl ^{13}C resonances are likely obscured by the solvent signal); IR (Neat Film, NaCl) 2924, 2853, 1678, 1593, 1503, 1348, 1281, 1173, 1108, 1022, 897, 810, 675 cm^{-1}; HRMS (ESI+): *m/z* calc'd for $C_{32}H_{27}N_2O_4S_3$ $[M+H]^+$: 599.1127, found 599.1120.

Diol 102



88 *102*

Preparation on <20 mg scale: To a 20 mL glass vial equipped with a septum cap was added diene **88** (20 mg, 0.041 mmol, 1.0 equiv), and the vial was evacuated and backfilled with nitrogen 3 times. Freshly distilled pyridine (1 mL) was added, followed by OsO_4 (11.4 mg, 0.0449 mmol, 1.1 equiv) as a solution in pyridine (0.3 mL). The reaction mixture was stirred at 23 °C for 30 min, after which LC–MS analysis indicated complete consumption of the starting material. The reaction was quenched by addition of saturated aqueous Na_2SO_3 (0.5 mL) and water (5 mL). The mixture was extracted with EtOAc (4 x 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude osmate ester was dissolved in THF (1.5 mL), then saturated aqueous Na_2SO_3 (0.5 mL) and water (1 mL) were sequentially added. The resulting mixture was vigorously stirred for 15 h before water (5 mL) was added. The mixture was extracted with

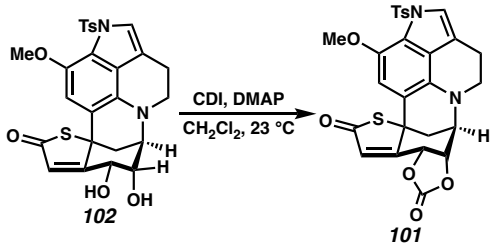
EtOAc (3x7 mL), dried with Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by silica gel flash chromatography (40→80% EtOAc/hexanes) to afford diol **102** as a light-yellow foam (18.9 mg, 0.0361 mmol, 88% yield). ^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.75 (d, *J* = 8.4 Hz, 2H), 7.31 (s, 1H), 7.27 (d, *J* = 7.7 Hz, 2H), 6.77 (s, 1H), 5.98 (d, *J* = 2.0 Hz, 1H), 4.37 (t, *J* = 3.8 Hz, 1H), 4.26 (dd, *J* = 4.3, 1.9 Hz, 1H), 3.72 (q, *J* = 3.2 Hz, 1H), 3.62 (s, 3H), 3.42 (t, *J* = 5.8 Hz, 2H), 3.07 – 2.93 (m, 2H), 2.83 (br, 1H), 2.58 (dd, *J* = 12.7, 3.0 Hz, 1H), 2.45 (ddd, *J* = 12.7, 3.0, 1.0 Hz, 1H), 2.37 (s, 3H), 1.64 (br, 1H). ^{13}C NMR (100 MHz, CD_2Cl_2): δ 197.1, 178.6, 145.1, 139.7, 137.0, 131.6, 129.8, 127.9, 123.7, 123.1, 122.1, 121.1, 114.7, 112.4, 108.4, 73.7, 69.2, 60.3, 58.1, 57.2, 48.4, 34.6, 23.3, 21.7. IR (Neat Film, NaCl): 2920, 1832, 1814, 1690, 1504, 1440, 1404, 1354, 1288, 1230, 1168, 1138, 1106, 1056, 838, 814, 666 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{26}H_{25}N_2O_6S_2$ $[M+H]^+$: 525.1154, found 525.1144.

Note: The above procedure was found to give much lower yield on >20 mg scale. The following procedure was employed when conducting this reaction on larger scale.

50 mg scale preparation: To a 20 mL glass vial containg diene **88** (50 mg, 0.102 mmol, 1.0 equiv) was added THF (1.5 mL) followed by OsO_4 (77 mg, 0.306 mmol, 3.0 equiv) and pyridine (0.05 mL, 0.612 mmol, 6.0 equiv) as a solution in THF (1 mL). The reaction mixture was stirred at 23 °C for 1h, after which LC–MS analysis indicated complete consumption of the starting material. The reaction was quenched with sat. Na_2SO_3 solution (2.5 mL), and the resulting mixture was stirred vigorously (1500 rpm) at 23 °C for 24h. The mixture was extracted with EtOAc (3x5 mL), dried with Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by silica gel flash

chromatography (40→80% EtOAc/hexanes) to afford diol **102** as a light-yellow foam (37 mg, 0.0714 mmol, 70% yield). For characterization data, see above.

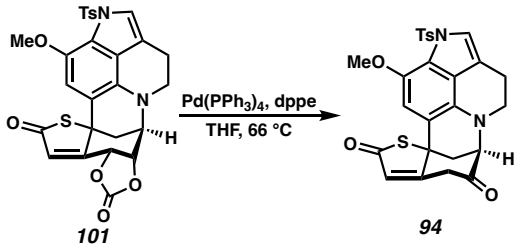
Carbonate 101.



To a 20 mL glass vial equipped with a septum cap was added diol **102** (20.8 mg, 0.0397 mmol, 1.0 equiv) and DMAP (0.1 mg, 0.8 μmol, 0.02 equiv). The vial was evacuated and backfilled with nitrogen 3 times. CDI (18.6 mg, 0.119 mmol, 3.0 equiv) was added as a solution in CH_2Cl_2 (4 mL). The reaction mixture was stirred at 23 °C for 30 min, after which TLC analysis indicated full consumption of starting material. The reaction mixture was washed with 5% aqueous citric acid (3x5 mL), dried with Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by silica gel flash chromatography (0→35% EtOAc/hexanes) to afford cyclic carbonate **101** as a yellow foam (20 mg, 0.0363 mmol, 92%). ^{1}H NMR (400 MHz, C_6D_6): δ 7.88 – 7.80 (m, 2H), 7.46 (d, *J* = 1.2 Hz, 1H), 6.64 – 6.62 (m, 2H), 6.61 (s, 1H), 5.97 (d, *J* = 2.0 Hz, 1H), 3.73 (dt, *J* = 6.7, 1.8 Hz, 1H), 3.59 (ddd, *J* = 6.6, 2.1, 0.7 Hz, 1H), 3.28 (s, 3H), 2.92 (q, *J* = 2.8 Hz, 1H), 2.49 – 2.27 (m, 4H), 1.96 (ddd, *J* = 13.4, 2.7, 1.4 Hz, 1H), 1.74 (dd, *J* = 13.4, 3.5 Hz, 1H), 1.70 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 193.9, 170.4, 152.1, 144.3, 141.2, 137.5, 130.7, 129.5, 124.8, 124.3, 122.5, 121.5, 113.6, 109.5, 108.3, 75.9, 73.3, 57.8, 56.7, 53.0, 47.4, 34.1, 22.7, 21.1. (*Note: an additional ^{13}C resonance associated with the tosyl group is likely*

obscured by the solvent signal.) IR (Neat Film, NaCl): 3442, 2920, 1832, 1814, 1690, 1504, 1440, 1404, 1354, 1288, 1230, 1168, 1138, 1106, 1056, 838, 814, 666 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{27}H_{23}N_2O_7S_2$ $[M+H]^+$: 551.0947, found 551.0937.

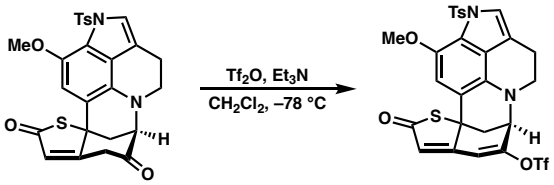
Ketone 94.



Procedure adopted from a report by Noyori.[27] A 20 mL glass vial containing cyclic carbonate **101** (20.6 mg, 0.0375 mmol, 1.0 equiv) was transferred to a nitrogen-filled glovebox. In a separate vial, a stock solution of $Pd(PPh_3)_4$ (7.7 mg) and dppe (2.7 mg) in THF (2.6 mL) was prepared and stirred at 28 °C for 10 min. Then, 1.5 mL of the catalyst solution was transferred to the vial containing cyclic carbonate **101** (for 4.4 mg of $Pd(PPh_3)_4$ [0.00375 mmol, 10 mol %] and 1.5 mg dppe [0.00375 mmol, 10 mol %]). The vial was sealed with a PTFE/silicone septum cap and electrical tape, removed from the glovebox, and stirred at 66 °C for 5 h. The reaction mixture was concentrated *in vacuo* and purified by silica gel flash chromatography (0→40% EtOAc/hexanes) to afford ketone **94** as a yellow oil (18 mg, 0.036, 94% yield). ^{1}H NMR (400 MHz, C_6D_6): δ 7.88 – 7.79 (m, 2H), 7.42 (s, 1H), 6.80 (s, 1H), 6.62 (d, *J* = 8.1 Hz, 2H), 5.20 (d, *J* = 2.2 Hz, 1H), 3.29 (s, 3H), 3.17 – 3.10 (m, 1H), 2.86 (dd, *J* = 17.0, 1.6 Hz, 1H), 2.73 – 2.64 (m, 1H), 2.60 – 2.43 (m, 2H), 2.38 – 2.25 (m, 2H), 2.11 (dd, *J* = 17.0, 2.4 Hz, 1H), 1.72 (s, 3H), 1.51 (dd, *J* = 13.3, 3.2 Hz, 1H). ^{13}C NMR (100 MHz, C_6D_6): δ 198.5, 195.5, 172.9, 144.1, 141.3, 137.7,

130.3, 129.4, 124.4, 122.9, 122.6, 121.7, 113.8, 112.0, 108.0, 62.9, 58.7, 56.7, 48.1, 43.9, 35.2, 22.6, 21.1. (*Note: an additional ^{13}C resonance associated with the tosyl group is likely obscured by the solvent signal.*) IR (Neat Film, NaCl): 2920, 1832, 1814, 1690, 1504, 1440, 1404, 1354, 1288, 1230, 1168, 1138, 1106, 1056, 838, 814, 666 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{26}H_{23}N_2O_5S_2$ $[M+H]^+$: 507.1048, found 507.1051.

Enol triflate 103.

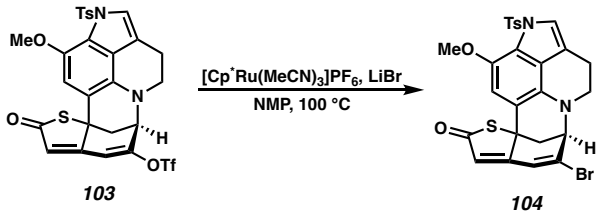


94 ***103***

To a 20 mL glass vial containing ketone **94** (12 mg, 0.024 mmol, 1.0 equiv) under nitrogen was added CH_2Cl_2 (2.4 mL). The mixture was cooled to –78 °C in a dry ice/acetone bath, then triethyl amine (34 μL, 0.24 mmol, 10 equiv) and triflic anhydride (20 μL, 0.12 mmol, 5.0 equiv) were sequentially added. The reaction mixture was stirred at –78 °C and the reaction progress was monitored by LC–MS. The reaction was quenched by addition of water (2 mL) at –78 °C upon completion (*ca*. 5–10 min). The resulting mixture was allowed to warm up to 23 °C, then the layers were separated. The organic phase was washed with water (2 x 2 mL), dried with Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by silica gel flash chromatography (0→10% EtOAc/CH_2Cl_2) to afford enol triflate **103** as a red film (14.2 mg, 0.0222 mmol, 94% yield). ^1H NMR (400 MHz, C_6D_6): δ 7.83 – 7.75 (m, 2H), 7.41 (d, *J* = 1.7 Hz, 1H), 6.75 (s, 1H), 6.61 – 6.53 (m, 2H), 5.71 (s, 1H), 5.28 (s, 1H), 3.49 (ddd, *J* = 3.8, 2.5, 1.1 Hz, 1H), 3.29 (s, 3H), 2.82 – 2.72 (m, 2H), 2.52 (dddd, *J* = 15.7, 10.8, 6.7, 2.0 Hz, 1H), 2.31 (dt, *J* = 15.7,

2.9 Hz, 1H), 2.15 (dd, J = 12.5, 2.5 Hz, 1H), 1.79 (dd, J = 12.5, 3.9 Hz, 1H), 1.67 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 195.1, 167.5, 150.2, 144.1, 141.9, 137.5, 130.4, 129.4, 128.0, 124.8, 124.3, 123.5, 121.8, 118.9 (q, J = 322.2 Hz), 116.3, 114.1, 112.1, 108.1, 56.8, 56.6, 56.5, 49.2, 36.4, 22.8, 21.0. IR (Neat Film, NaCl): 2920, 1832, 1814, 1690, 1504, 1440, 1404, 1354, 1288, 1230, 1168, 1138, 1106, 1056, 838, 814, 666 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{27}H_{21}F_3N_2O_7S_3$ $[M]^+$: 638.0463, found 638.0547.

Alkenyl bromide 104.

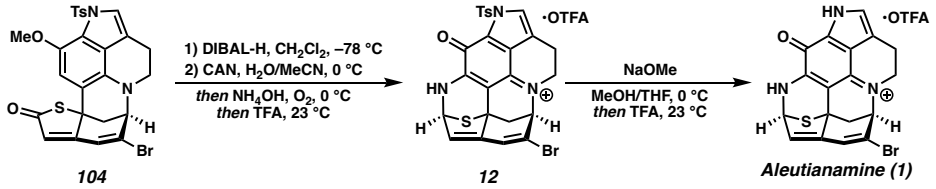


103 *104*

A 4 mL vial containing enol triflate **103** (18 mg, 0.028 mmol, 1.0 equiv) was brought into a nitrogen-filled glovebox. In a separate vial, a stock solution of $[Cp^*Ru(MeCN)_3]PF_6$ (10.2 mg) and LiBr (17.7 mg) in NMP (2.3 mL) was prepared and stirred at 28 °C for 10 mins. Then, 0.94 mL of the catalyst solution (for 4.3 mg of $[Cp^*Ru(MeCN)_3]PF_6$ [0.00852 mmol, 30 mol %] and 7.3 mg LiBr [0.0852 mmol, 3 equiv]) was transferred to the vial containing enol triflate **103**. The vial was sealed with a PTFE/silicone septum cap and electrical tape, removed from glovebox, and stirred at 100 °C for 5 h. Then the reaction mixture was diluted with Et_2O (2 mL) and water (2 mL) and filtered through a PTFE syringe filter. The layers were separated, and the aqueous layer was extracted with Et_2O (4x2 mL). The combined organic phased were dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by silica gel flash chromatography (100% hexane→100% CH_2Cl_2) to afford alkenyl bromide **104** (6.8 mg,

0.012 mmol, 38% yield) as an orange film. ^{1}H NMR (400 MHz, C_6D_6): δ 7.84 – 7.76 (m, 2H), 7.41 (d, *J* = 1.7 Hz, 1H), 6.83 (s, 1H), 6.61 – 6.53 (m, 2H), 6.15 (s, 1H), 5.34 (s, 1H), 3.48 – 3.42 (m, 1H), 3.29 (s, 3H), 3.17 (ddd, *J* = 12.2, 11.1, 3.7 Hz, 1H), 2.90 (ddd, *J* = 11.1, 4.9, 2.5 Hz, 1H), 2.55 (dddd, *J* = 15.6, 12.1, 4.9, 1.9 Hz, 1H), 2.40 (dt, *J* = 15.6, 3.2 Hz, 1H), 2.14 (dd, *J* = 12.3, 2.5 Hz, 1H), 1.83 – 1.73 (m, 1H), 1.70 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 195.5, 170.3, 143.9, 141.6, 137.7, 130.7, 129.4, 127.6, 124.3, 123.3, 121.4, 121.1, 114.2, 112.1, 108.4, 61.4, 56.8, 56.5, 49.7, 38.3, 23.2, 21.1. (*Note: additional ^{13}C resonances associated with the tosyl group and the alkenyl bromide carbon are likely obscured by the solvent signal.*) IR (Neat Film, NaCl): 2920, 1832, 1814, 1690, 1504, 1440, 1404, 1354, 1288, 1230, 1168, 1138, 1106, 1056, 838, 814, 666 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{26}H_{22}BrN_2O_4S_2$ $[M+H]^+$: 571.0184, found 571.0154.

Aleutianamine (1).



To an 8 mL vial containing alkenyl bromide **104** (6.8 mg, 0.012 mmol, 1.0 equiv) under nitrogen was added CH_2Cl_2 (0.9 mL). The resulting mixture was cooled to –78 °C in a dry ice/acetone bath, then DIBAL (21 μL, 0.12 mmol, 10 equiv) was added as a freshly prepared solution in CH_2Cl_2 (0.3 mL, 0.4 M). The reaction was quenched at –78 °C by addition of 1 mL saturated aqueous Rochelle's salt solution immediately after the addition of DIBAL. The resulting mixture was allowed to warm up to 23 °C and was stirred

vigorously for 45 min. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 1 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo* to afford crude thiolactol as a yellow oil, which was used directly in the next step without further purification.

To an 8 mL vial containing crude thiolactol (6.8 mg, 0.012 mmol, 1.0 equiv) under nitrogen was added MeCN (0.8 mL). The resulting solution was cooled to 0 °C in an ice water bath, and CAN (13.2 mg, 0.024 mmol, 2.0 equiv) was added as a freshly prepared solution in 0.3 mL of water. The resulting mixture was stirred at 0 °C for 5 min, whereafter concentrated aqueous ammonia (27% w/w, 35 μL, 0.42 mmol, 35 equiv) was added. The reaction vessel was flushed with O_2, and the resulting mixture was stirred for 7 min under an O_2 atmosphere at 0 °C. The reaction mixture was then warmed to 23 °C and was diluted with EtOAc (2 mL) and water (1.5 mL). The layers were separated, and the aqueous phase was extracted with EtOAc (4 x 2 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was taken up in trifluoroacetic acid (1 mL), and the mixture was allowed to stand at 23 °C for 10 min before being concentrated *in vacuo*. The crude N-tosyl aleutianamine (**12**) was used directly in the next step without further purification.

To a 4 mL vial containing crude N-tosyl aleutianamine (**12**, 0.012 mmol, 1.0 equiv) under nitrogen was added THF (0.78 mL). The resulting mixture was cooled to 0 °C in an ice bath and NaOMe in MeOH (0.2 M, 0.42 mL, 0.084 mmol, 7 equiv) was added. The reaction mixture was stirred at 0 °C for 10 min, after which TFA in MeOH (0.2 M, 0.42 mL) was added and the reaction mixture was allowed to warm to 23 °C. The mixture was concentrated *in vacuo* and the residue was purified by preparative reverse-phase HPLC

(Eclipse XDB-C18, 5 μm, 9.4 x 250 mm, MeCN-H_2O (0.1% TFA) = 0:100 to 100:0, linear gradient for 6 min, flow rate = 5 mL/min) to afford aleutianamine (**1**) as TFA salt (2 mg, 0.00391 mmol, 33% over three steps). ^{1}H NMR (500 MHz, CD_3OD): δ 7.14 (s, 1H), 7.08 (d, *J* = 1.1 Hz, 1H), 5.97 (d, *J* = 3.4 Hz, 1H), 5.43 – 5.38 (m, 1H), 5.13 (t, *J* = 3.0 Hz, 1H), 4.29 – 4.22 (m, 2H), 3.29 – 3.18 (m, 1H), 3.14 – 3.05 (m, 1H), 2.67 (dd, *J* = 12.8, 3.1 Hz, 1H), 2.57 (ddd, *J* = 12.8, 3.0, 1.2 Hz, 1H). ^{13}C NMR (100 MHz, CD_3OD): δ 168.6, 149.8, 142.9, 142.2, 129.2, 126.5, 125.8, 122.7, 119.3, 118.1, 112.5, 101.8, 65.4, 64.9, 54.1, 49.8, 32.5, 21.2. IR (Neat film, NaCl): 3106, 2928, 1674, 1616, 1520, 1410, 1342, 1170, 996, 800, 720 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{18}H_{13}BrN_3OS$ $[M+H]^+$: 399.9937, found 399.9945.

1.12 REFERENCES AND NOTES

(1) Hu, J.-F.; Fan, H.; Xiong, J.; Wu, S.-B. Discorhabdins and Pyrroloiminoquinone-Related Alkaloids. *Chem. Rev*. **2011**, *111*, 5465−5491.

(2) For selected examples, see: (a) Perry, N. B.; Blunt, J. W.; McCombs, J. D.; Munro, M. H. G. Discorhabdin C, a Highly Cytotoxic Pigment from a Sponge of the Genus Latrunculia. *J. Org. Chem.* **1986**, *51*, 5476−5478. (b) Na, M.;Ding, Y.; Wang, B.; Tekwani, B. L.; Schinazi, R. F.; Franzblau, S.; Kelly, M.; Stone, R.; Li, X.-C.; Ferreira, D.; Hamann, M. T. Anti-infective Discorhabdins from a Deep-Water Alaskan Sponge of the Genus Latrunculia. *J. Nat. Prod.* **2010**, *73*, 383−387.

(3) For representative discorhabdin total syntheses, see: (a)Nishiyama, S.; Cheng, J.-F.; Tao, X.-L.; Yamamura, S.; Synthetic studies on novel sulfur-containing alkaloids, prianosins and discorhabdins: total synthesis of discorhabdin C. *Tetrahedron. Lett.* **1991**, *32*, 4151–4154. (b) Tohma, H.; Harayama, Y.; Hashizume, M.; Iwata, M.; Kiyono, Y.; Egi, M.; Kita, Y. The First Total Synthesis of Discorhabdin A. *J. Am. Chem. Soc.* **2003**, *125*, 11235–11240. (c) Aubart, K. M.; Heathcock, C. H. A Biomimetic Approach to the Discorhabdin Alkaloids: Total Syntheses of Discorhabdins C and E and Dethiadiscorhabdin D. *J. Org. Chem.* **1999**, *64*, 16–22. (d) Derstine, B.; Cook, A.; Collings, J.; Gair, J.; Saurí, J.; Kwan, E.; Burns, N. Total Synthesis of (−)-Discorhabdin V. *Angew. Chem. Int. Ed.* **2024**, 63, e202315284. (e) Kita, Y.; Tohma, H.; Inagaki, M.; Hatanaka, K.; Yakura, T. Total synthesis of discorhabdin C: a general aza spiro dienone formation from O-silylated phenol derivatives using a hypervalent iodine reagent. *J. Am. Chem. Soc.* **1992**, *114*, 6, 2175–2180.

(4) (a) Zou, Y.; Wang, X.; Sims, J.; Wang, B.; Pandey, P.; Welsh, C. L.; Stone, R. P.; Avery, M. A.; Doerksen, R. J.; Ferreira, D.; Anklin, C.; Valeriote, F. A.; Kelly, M.; Hamann, M. T. Computationally Assisted Discovery and Assignment of a Highly Strained and PANC-1 Selective Alkaloid from Alaska's Deep Ocean. *J. Am. Chem. Soc.* **2019**, *141*, 4338–4344. (b)Dickinson, C. F.; Potluri, A.; Bland, A. M.; Flipse, S. M.; Hanna, G. S.; Wagner, R. T.; Robertson, K. D.; Ho, T. H.; Sprague, D. J.; Hoff, G. R.; Stone, R. P.; Tius, M. A.; Tantillo, D. J.; Hamann, M. T. On the Discorhabdins Leading to the Aleutianamine Ring System: A One-Step in Situ Transformation Characterized Through Computational and Experimental Studies and Its Implications on Biosynthesis, Synthesis, and Pharmacology. *Angew. Chem. Int. Ed.* **2026**, e7864883.

(5) (a) Tuccinardi, J. P.; Wood, J. L.; Convergent Total Synthesis of Aleutianamine. *J. Am. Chem. Soc.* **2025**, *147*, 7, 611–633. (b) Magann, N.; Barnes, G.; Schioldager, R.; Hörmann, F.; Muñoz, R.; Han, H.-Y.; Von Hoff, D.; Vanderwal, C. Optimized Biomimetic Syntheses of Discorhabdin B and Aleutianamine Drives a Deeper Exploration of their Anticancer Activities. *Chemrxiv.* **2025**, DOI: 10.26434/chemrxiv-2025-djk90

(6) Shimomura, M.; Ide, K.; Sakata, J.; Tokuyama, H. Unified Divergent Total Synthesis of Discorhabdin B, H, K, and Aleutianamine via the Late-Stage Oxidative N,S-Acetal Formation. *J. Am. Chem. Soc.* **2023**, *145*, 18233–18239.

(7) Koike, T.; Hoashi, Y.; Tomata, Y. Heterocyclic Compound and Use Thereof. US Patent Application 20120142672A1, June 7, 2012.

(8) Johnson, T.; Pultar, F.; Menke, F.; Lautens, M. Palladium-Catalyzed α-Arylation of Vinylogous Esters for the Synthesis of γ,γ-Disubstituted Cyclohexenones. *Org. Lett.* **2016**, *18,* 6488–6491.

(9) Nishimoto, Y.; Okita, A.; Yasuda, M.; Baba, A. Synthesis of a Wide Range of Thioethers by Indium Triiodide Catalyzed Direct Coupling between Alkyl Acetates and Thiosilanes. *Org. Lett.* **2012**, *14*, 1846–1849.

(10) Thibeault, C.; Clark, C. G.; DeLucca, I.; Hu, C. H.; Jeon, Y.; Lam, P. Y. S.; Qiao, J. X.; Yang, W.; Wang, Y.; Wang, T. C. 7-hydroxy-spiropipiperidine indolinyl antagonists of p2y1 receptor. U.S. Patent 9428504B2, August 30, 2016.

(11) Campos, K. R.; Woo, J. C. S.; Lee, S.; Tillyer, R. D. A General Synthesis of Substituted Indoles from Cyclic Enol Ethers and Enol Lactones. *Org. Lett.* **2004**, *6*, 79–82.

(12) Surry, S. D.; Buchwald, L. S. Dialkylbiaryl phosphines in Pd-catalyzed amination: a user's guide. *Chem. Sci.* **2011**, *2*, 27–50.

(13) Verma, A. K.; Attri, P.; Chopra, V.; Tiwari, R. K.; Chandra, R.Triethylammonium acetate (TEAA): a recyclable inexpensive ionic liquid promotes the chemoselective aza- and thia-Michael reactions. *Monatsh. Chem.*

2008, *139*, 1041–1047.

(14) Saadi, J.; Bentz, C.; Redies, K.; Lentz, D.; Zimmer. R.; Reissig, H. Stereoselective synthesis of tricyclic compounds by intramolecular palladium-catalyzed addition of aryl iodides to carbonyl groups. *Beilstein J. Org. Chem.* **2016**, *12*, 1236–1242.

(15) S. T. Kadam.; S. S. Kim. *Synthesis*, **2008**, *2*, 267–271.

(16) Rezgui, S. P.; Farhi, J.; Yu, H.; Sercel, Z. P.; Virgil, S. C.; Stoltz, B. M. Divergent Total Syntheses of Pyrroloiminoquinone Alkaloids Enabled by the Development of a Larock/Buchwald–Hartwig Annulation/Cyclization. *Chem. Sci.* **2024**, *15*, 12284– 12290, DOI: 10.1039/D4SC02981J

(17) Miller, R. D.; McKean, D. R. A facile preparation of methyl enol ethers from acetals and ketals using trimethylsilyl iodide. *Tetrahedron. Lett.* **1982**, *23*, 323–326.

(18) Inouye, Y.; Kojima, T.; Owada, J.; Kakisawa, H. Preparation of Bicyclo[3.3.1]nonane-2,4-dione Derivatives. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 4369–4375.

(19) Ito, Y.; Hirao, T.; Saegusa, T. Synthesis of .alpha.,.beta.-unsaturated carbonyl compounds by palladium(II)-catalyzed dehydrosilylation of silyl enol ethers. *J. Org. Chem.* **1978**, *43*, 5, 1011–1031.

(20) Phenol dearomatization: (a) Rousseaux, S.; García-Fortanet, J.; Sanchez, M. A. D. A.; Buchwald, S. L.; Palladium(0)-Catalyzed Arylative Dearomatization of Phenols. *J. Am. Chem. Soc.* **2011**, *133*, 9282–9285. (b) Xu, R.; Gu, Q.; Wu, W.; Zhao, Z.; You, S. Construction of Erythrinane Skeleton via Pd(0)-Catalyzed Intramolecular Dearomatization of *para*-Aminophenols. *J. Am. Chem. Soc.* **2014**, *136*, 15469−15472. (c) Du, K.; Guo, P.; Chen, Y.; Cao, Z.; Wang, Z.; Tang, W. Enantioselective Palladium-Catalyzed Dearomative Cyclization for the Efficient Synthesis of Terpenes and Steroids. *Angew. Chem. Int. Ed.* **2015**, *54*, 3033−3037. For examples of furan dearomatizations see: (d) Liu, J.; Xu, X.; Li, J.; Liu, B.; Jiang, H.; Yin, B. Palladium-catalyzed dearomatizing 2,5-alkoxyarylation of

furan rings: diastereospecific access to spirooxindoles. *Chem. Commun.* **2016**, *52*, 9550–9553. (e) Li, J.; Peng, H.; Wang, F.; Wang, X.; Jiang, H.; Yin, B. 2,5-Oxyarylation of Furans: Synthesis of Spiroacetals via Palladium-Catalyzed Aerobic Oxidative Coupling of Boronic Acids with α-Hydroxyalkylfurans. *Org. Lett.* **2016**, *18*, 3226−3229. For examples of an radical dearomative thiophene spirocyclization see: (f) Shi, Z.; Wang, W.; Li, N.; Yuan, Y.; Ye, K. Electrochemical Dearomative Spirocyclization of N-Acyl Thiophene-2-sulfonamide. *Org. Lett.* **2022**, *24*, 6321−6325. (g) Crich, D.; Patel, M. Facile Dearomatizing Radical Arylation of Furan and Thiophene. *Org. Lett.* **2005**, *7*, 17, 3625–3628. (h) Crich, D.; Patel, M. *Tetradedron*, **2006**, *62*, 7824–7837. Reviews on dearomative cyclization of phenols and heteroarenes: (i) Wang, Z. Palladium-catalyzed asymmetric dearomative cyclization in natural product synthesis. *Org. Biomol. Chem*. **2020**, *18*, 4354–4370. (j) Zheng, C.; You, S. L. Catalytic asymmetric dearomatization by transition-metal catalysis: a method for transformations of aromatic compounds. *Chem*. **2016**, *1*, 830–857.

(21) Andersen, H. S; Olsen, O. H.; Iversen, L. F.; Sørensen, A. L. P.; Mortensen, S. B.; Christensen, M. S.; Branner, S.; Hansen, T. K.; Lau, J. F.; Jeppesen, L.; Moran, E. J.; Su, J.; Bakir, F.; Judge, L.; Shahbaz, M.; Collins, T.; Vo, T.; Newman, M. J.; Ripka, W. C.; Møller, N. P. H. Discovery and SAR of a Novel Selective and Orally Bioavailable Nonpeptide Classical Competitive Inhibitor Class of Protein-Tyrosine Phosphatase 1B. *J. Med. Chem.* **2002**, *45*, 4443–4459.

(22) Lee, O.; Law, K.; Ho, C.; Yang, D. Highly Chemoselective Reductive Amination of Carbonyl Compounds Promoted by $InCl_3/Et_3SiH$/ MeOH System. *J. Org. Chem.* **2008**, *73*, 8829–8837.

(23) a) Kita, Y.; Tohma, H.; Inagaki, M.; Hatanaka, K.; Yakura, T. A novel oxidative azidation of aromatic compounds with hypervalent iodine reagent, phenyliodine(III) bis(trifluoroacetate) (PIFA) and trimethylsilyl azide. *Tetrahedron Lett.* **1991**, *32*, 4321–4324. b) Kita, Y.; Tohma, H.; Hatanaka, K.; Takada, T.; Fujita, S.; Mitoh, S.; Sakurai, H.; Oka, S. Hypervalent Iodine-Induced Nucleophilic Substitution of para-Substituted Phenol Ethers. Generation of Cation Radicals as Reactive Intermediates. *J. Am. Chem. Soc.* **1994**, *116*, 3684–3691.

(24) Benati, L.; Bencivenni, G.; Leardini, R.; Minozzi, M.; Nanni, D.; Scialpi, R.; Spagnolo, P.; Zanardi, G. Radical Reduction of Aromatic Azides to Amines with Triethylsilane. *J. Org. Chem.* **2006**, *71*, 5822–5825.

(25) White, J. D.; Yager, K. M.; Yakura, T. Synthetic Studies of the Pyrroloquinoline Nucleus of the Makaluvamine Alkaloids. Synthesis of the Topoisomerase II Inhibitor Makaluvamine D. *J. Am. Chem. Soc.* **1994**, *116*, 1831–1838.

(26) Solé, C.; Tatla, A.; Mata, J. A.; Whiting, A.; Gulyás, H.; Fernádez, E. Catalytic 1,3-Difunctionalisation of Organic Backbones through a Highly Stereoselective, One-Pot, Boron Conjugate-Addition/Reduction/Oxidation Process. *Chem. Eur. J.* **2011**, *17*, 14248–14257.

(27) Suzuki, M.; Watanabe, A.; Noyori, R. Palladium (0)-Catalyzed Reaction of a,b-Epoxy Ketones Leading to b-Diketones. *J. Am. Chem. Soc.* **1980**, *102*, 2095–2096.

(28) (a) Criegee, R. Die Oxidative Spaltung der C–C-Bindung. *Angew. Chem.* **1937**, *50*, 153–172. (b) Criegee, R. Organische Osmiumverbindungen. *Angew. Chem.* **1938**, *51*, 519-530.

(29) Imazaki, Y.; Shirakawa, E.; Ueno, R.; Hayashi, T. Ruthenium-Catalyzed Transformation of Aryl and Alkenyl Triflates to Halides. *J. Am. Chem. Soc.* **2012**, *134*, 14760–14763.

(30) Pangborn, A. M.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. Safe and Convenient Procedure for Solvent Purification. *Organometallics* **1996**, *15*, 1518–1520.

(31) Fujiki, K.; Tanifuji, N.; Sasaki, Y.; Yokoyama, T. New and Facile Synthesis of Thiosulfonates from Sulfinate/Disulfide/I_2 System. *Synthesis* **2002**, 343–348.

(32) Chen, M.; Dong, G. Copper-Catalyzed Desaturation of Lactones, Lactams, and Ketones under pH-Neutral Conditions. *J. Am. Chem. Soc.* **2019**, *141*, 14889–14897.

(33) Gregoire, B.; Carre, M. C.; Caubere, P. Arynic condensation of ketone enolates. 17. New general access to benzocyclobutene derivatives. *J. Org. Chem.* **1986**, *51*, 1419–1427.

APPENDIX 1

Spectra Relevant to Chapter 1:

Total Synthesis of Aleutianamine

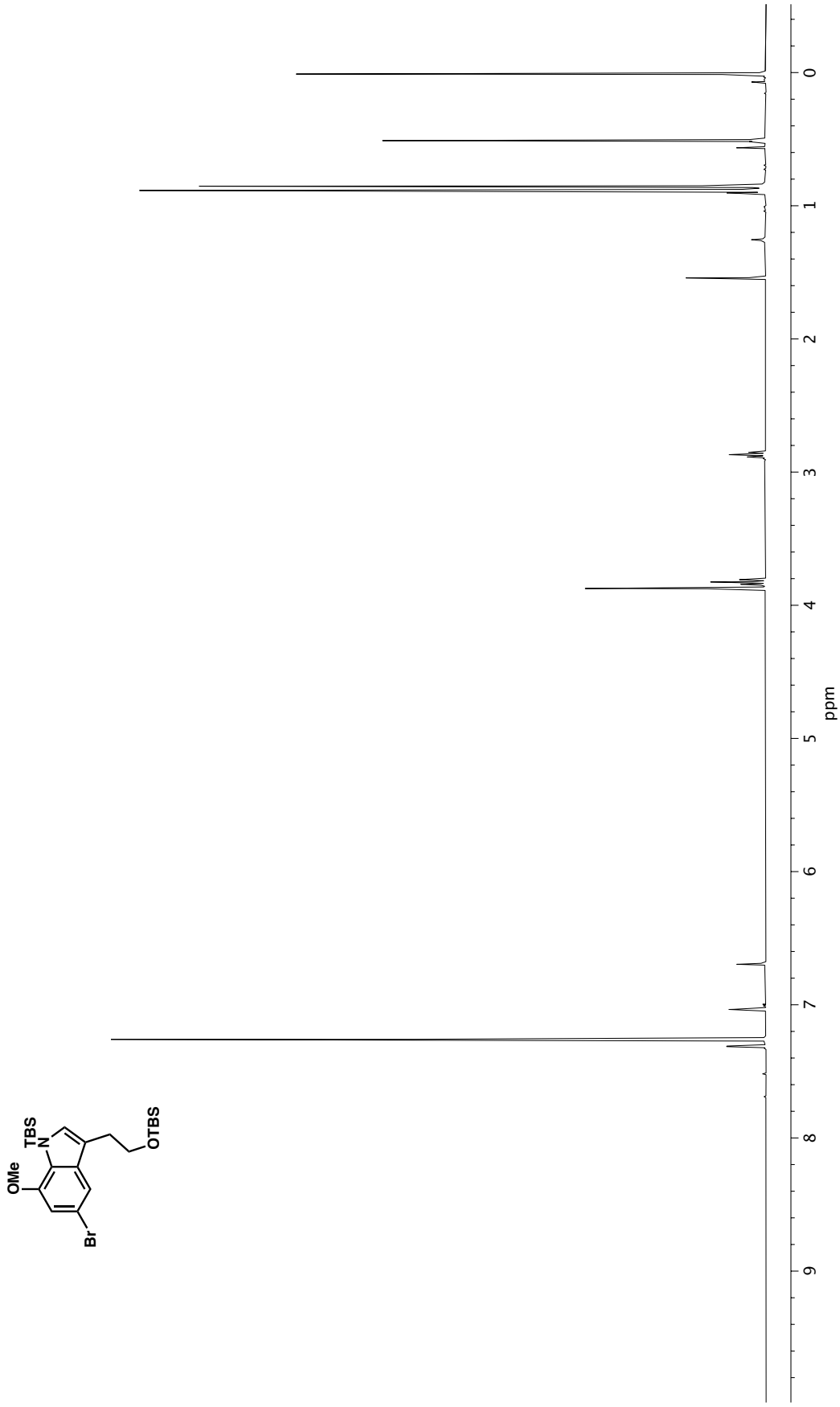


Figure A1.1. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **31**.

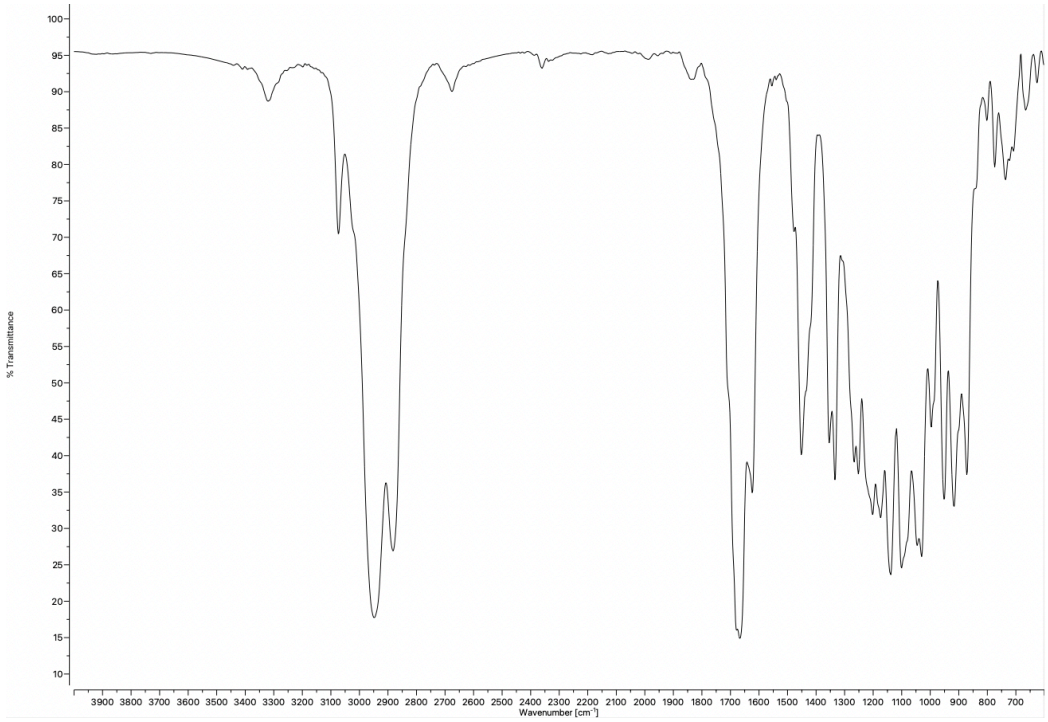


Figure A1.2. Infrared spectrum (Thin Film, NaCl) of compound **31**.

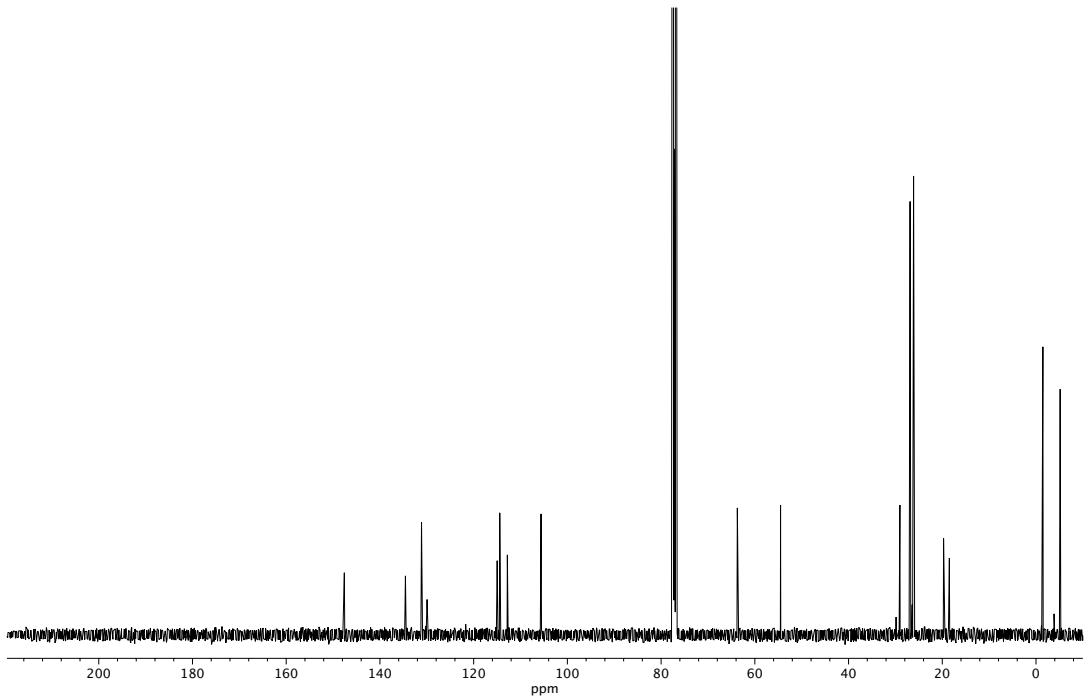


Figure A1.3. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **31**.

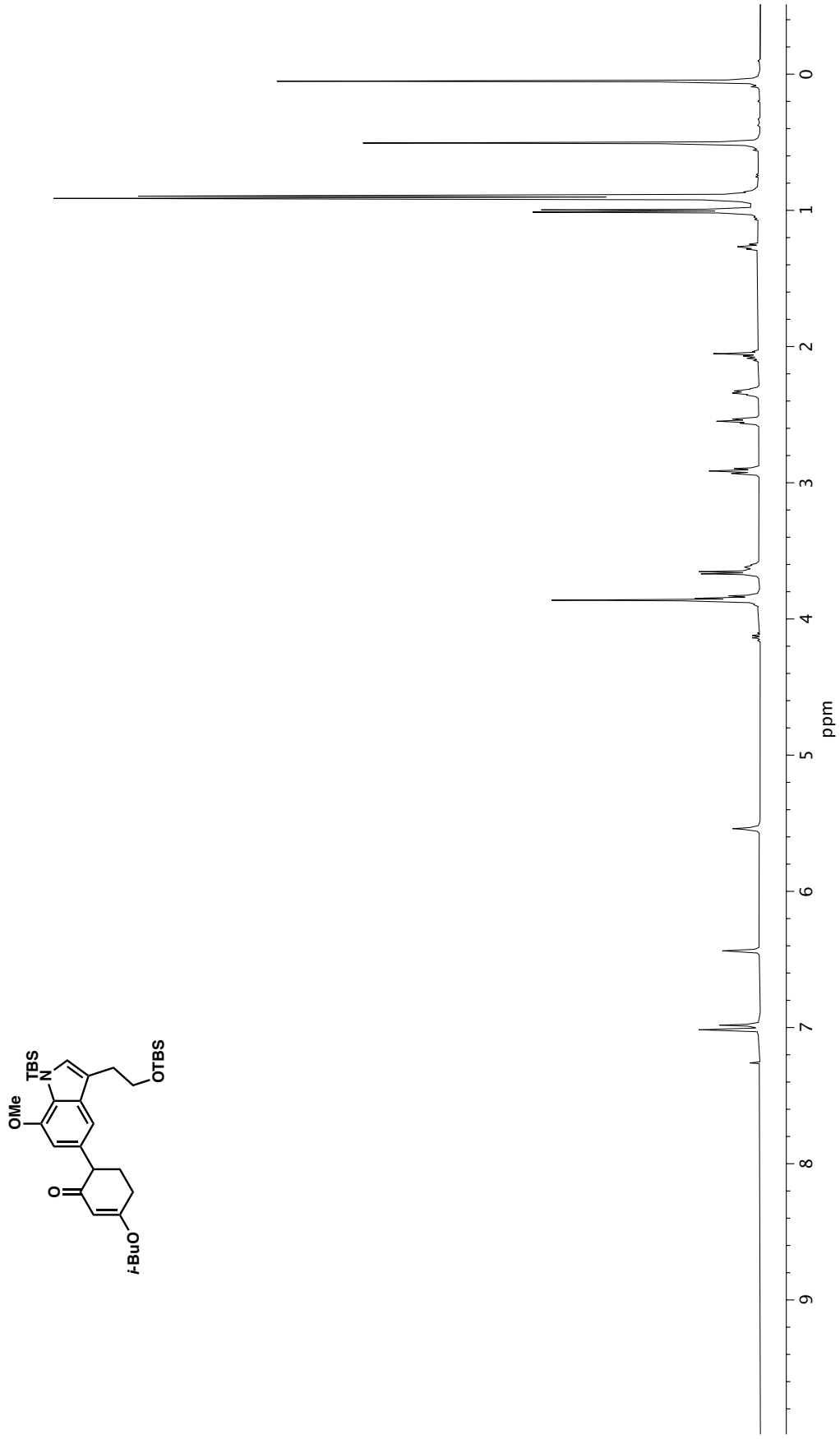


Figure A1.4. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **32**.

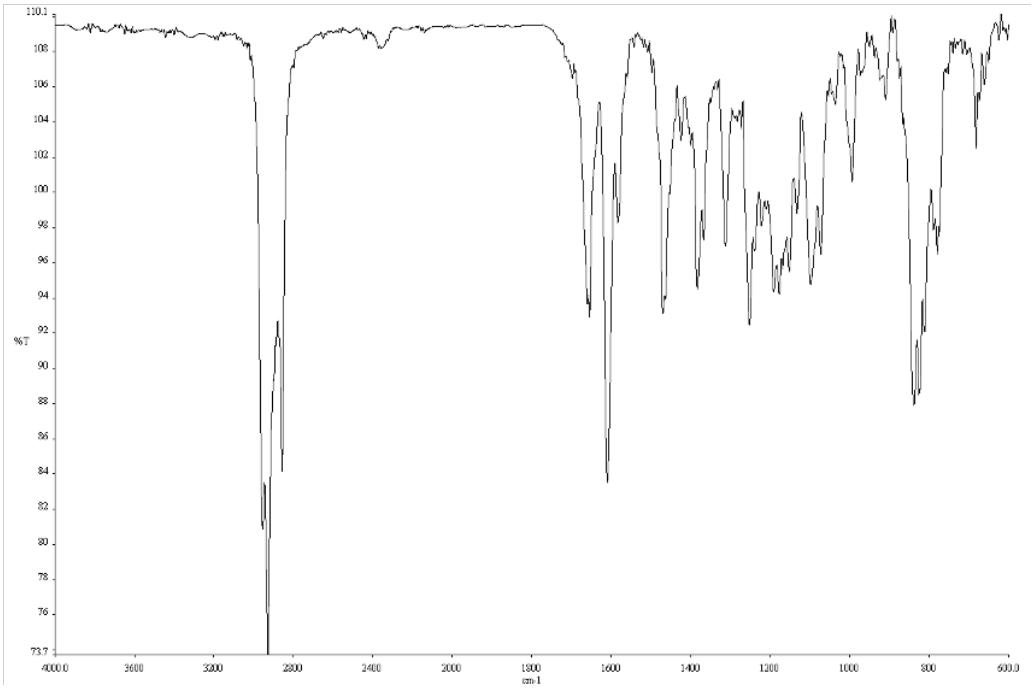


Figure A1.5. Infrared spectrum (Thin Film, NaCl) of compound **32**.

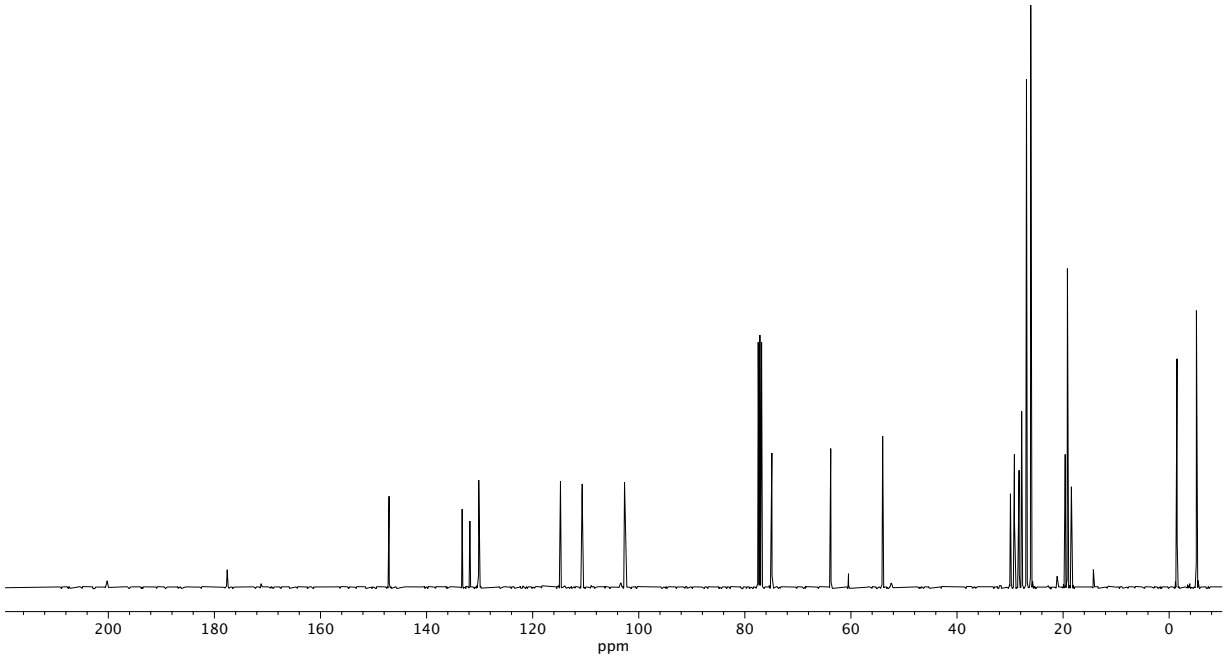


Figure A1.6. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **32.**

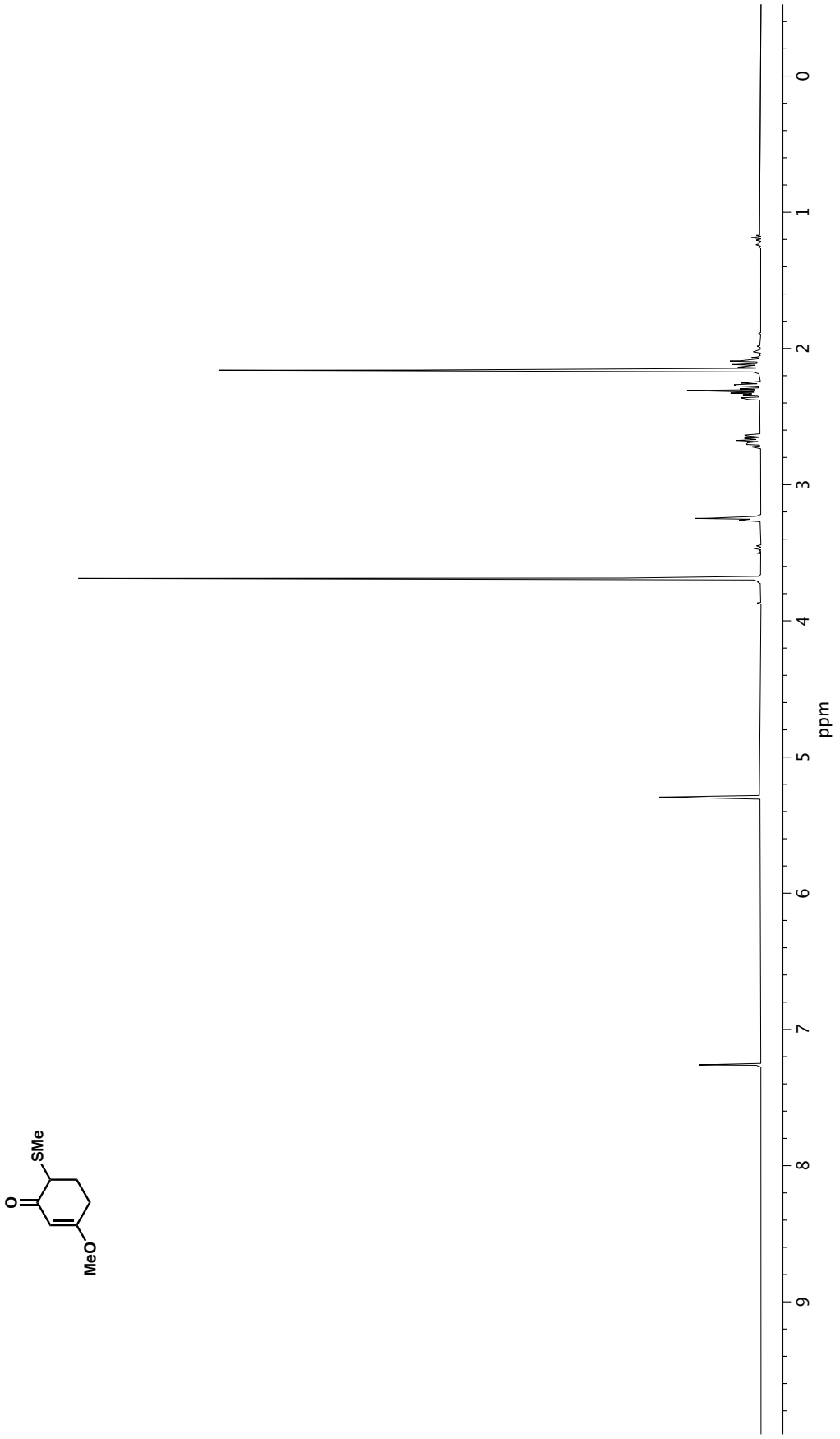


Figure A1.7. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **35**.

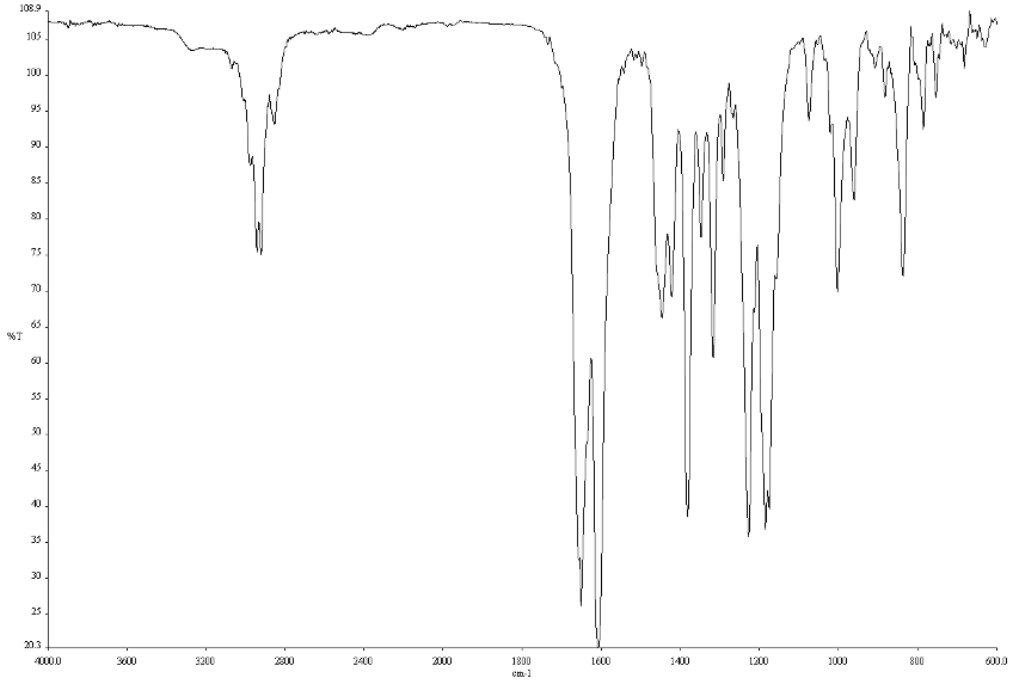


Figure A1.8. Infrared spectrum (Thin Film, NaCl) of compound **35**.

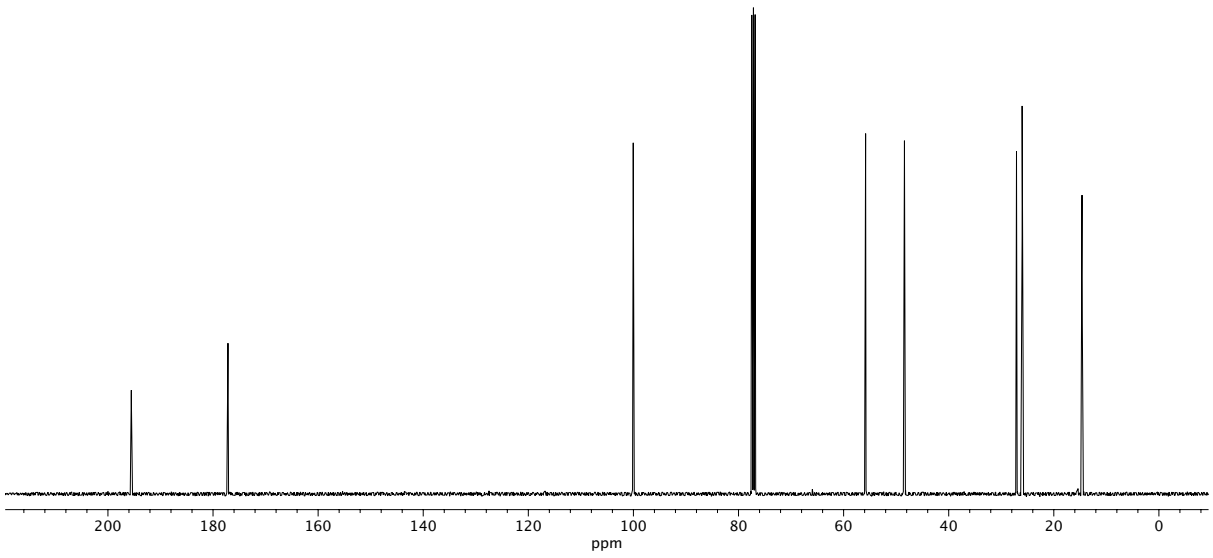


Figure A1.9. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **35.**

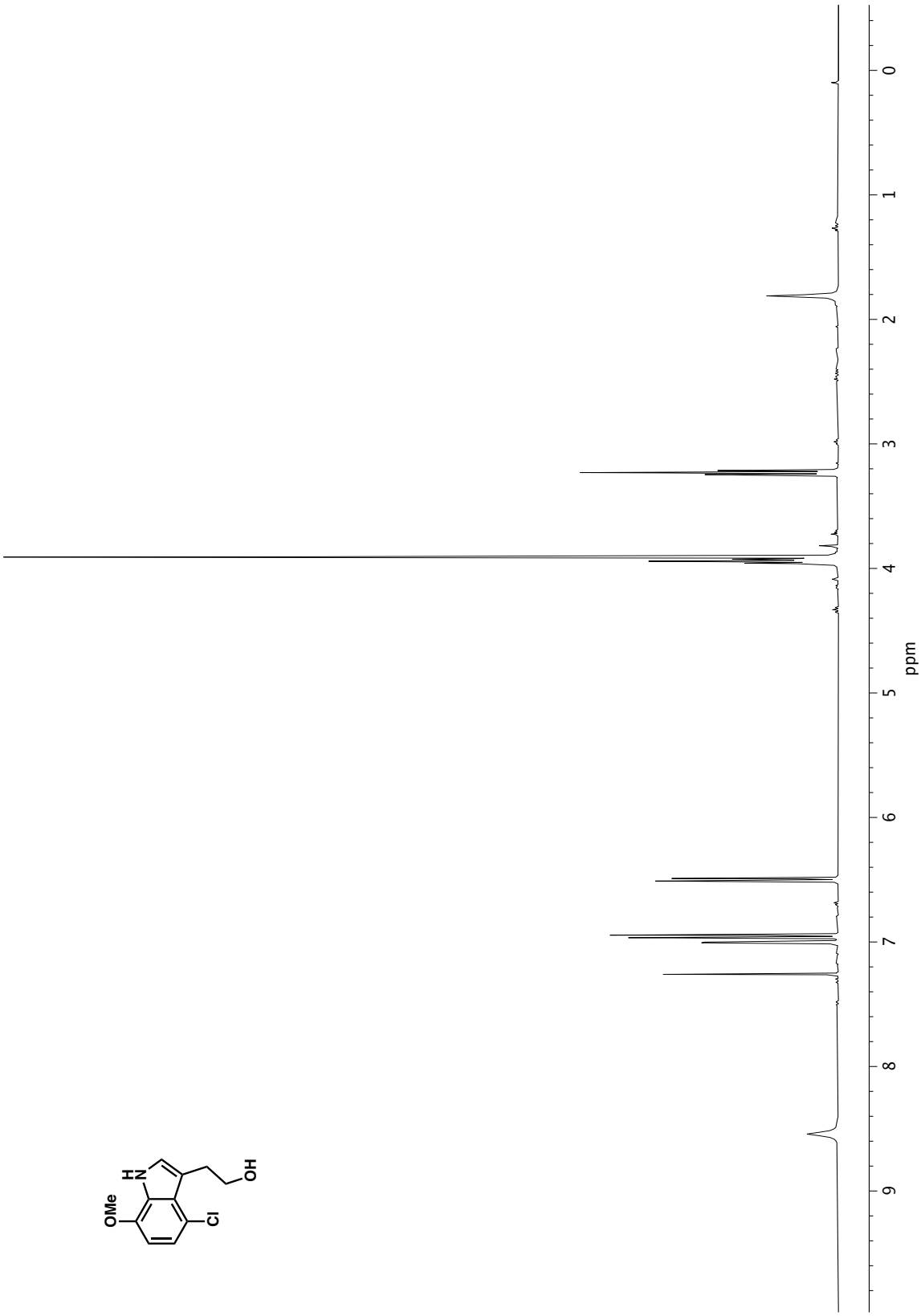


Figure A1.10. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **43**.

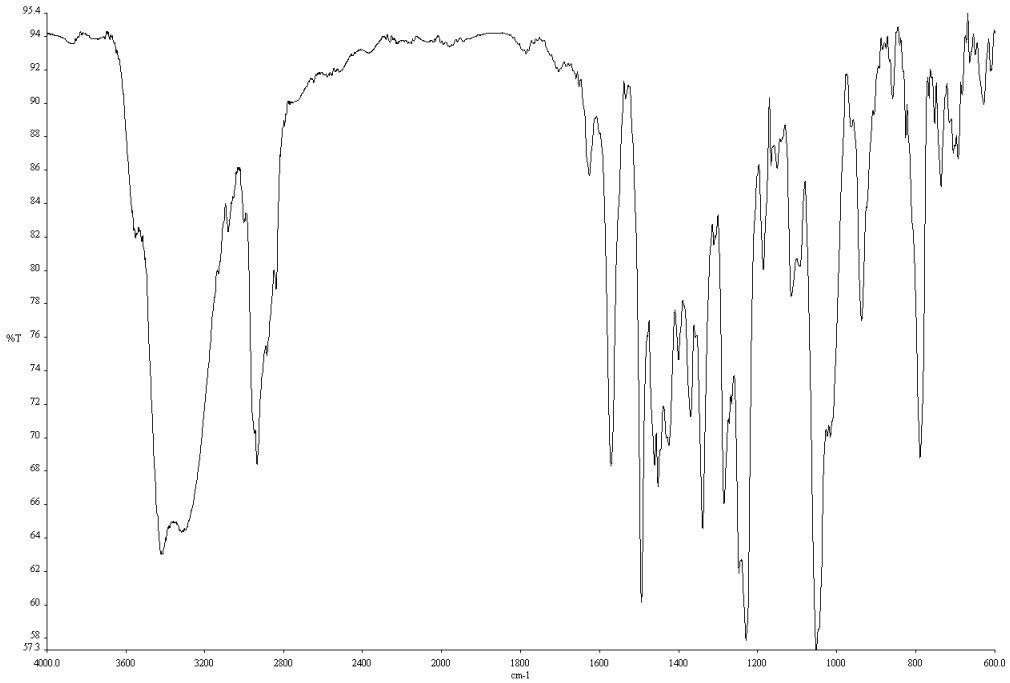


Figure A1.11. Infrared spectrum (Thin Film, NaCl) of compound **43**.

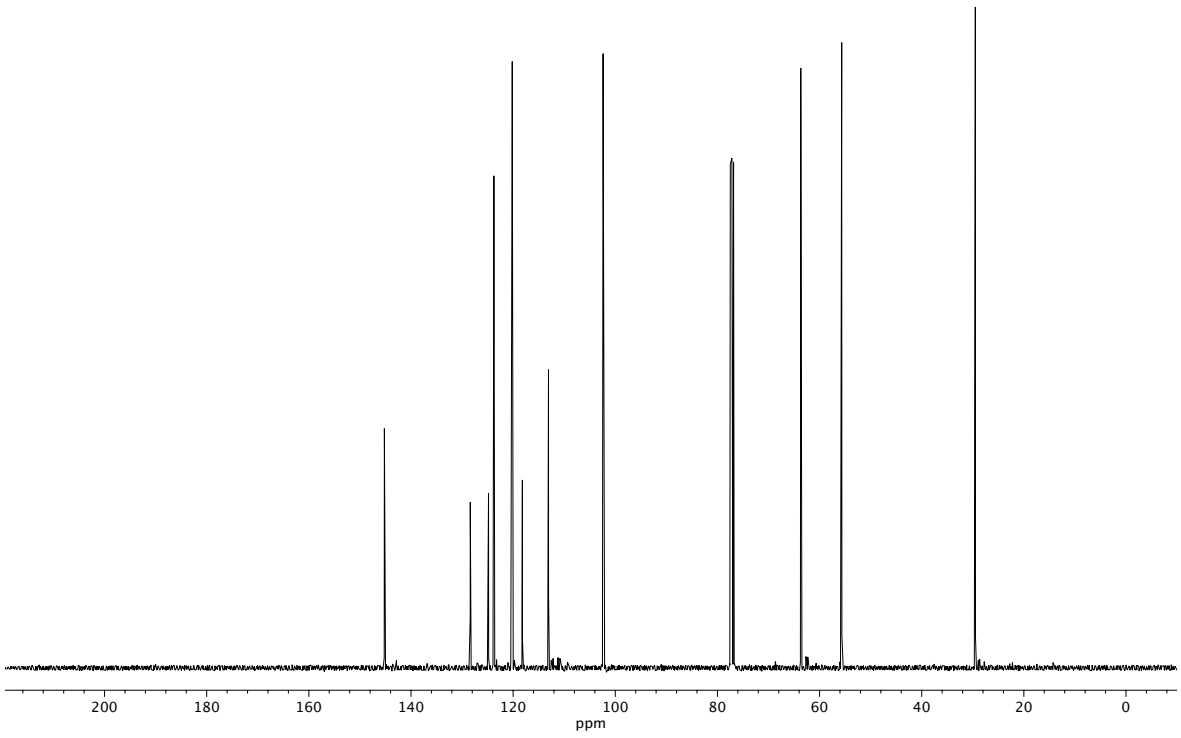


Figure A1.12. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **43.**

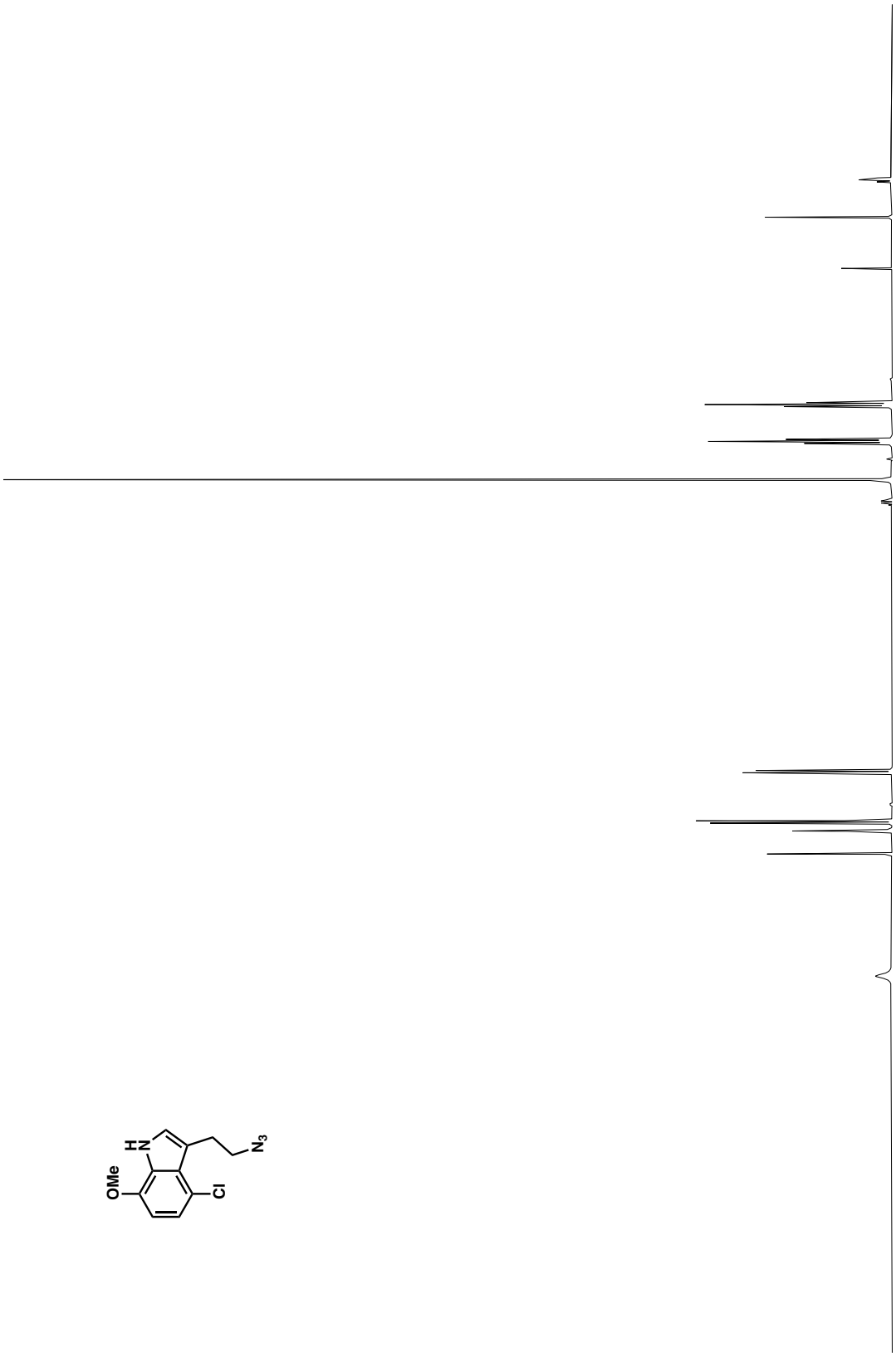


Figure A1.13. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **44**.

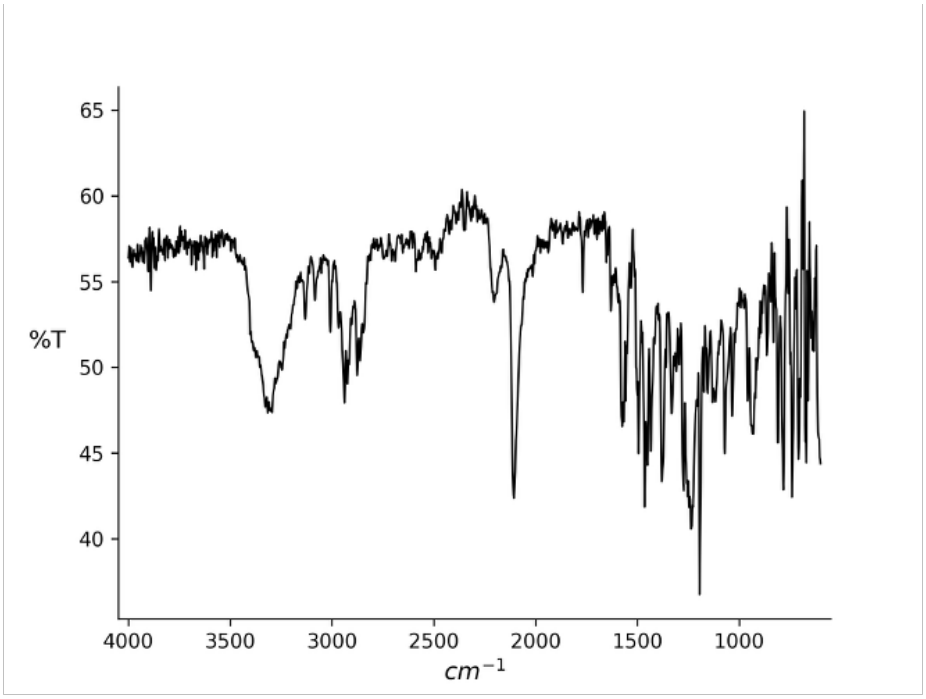


Figure A1.14. Infrared spectrum (Thin Film, NaCl) of compound **44**.

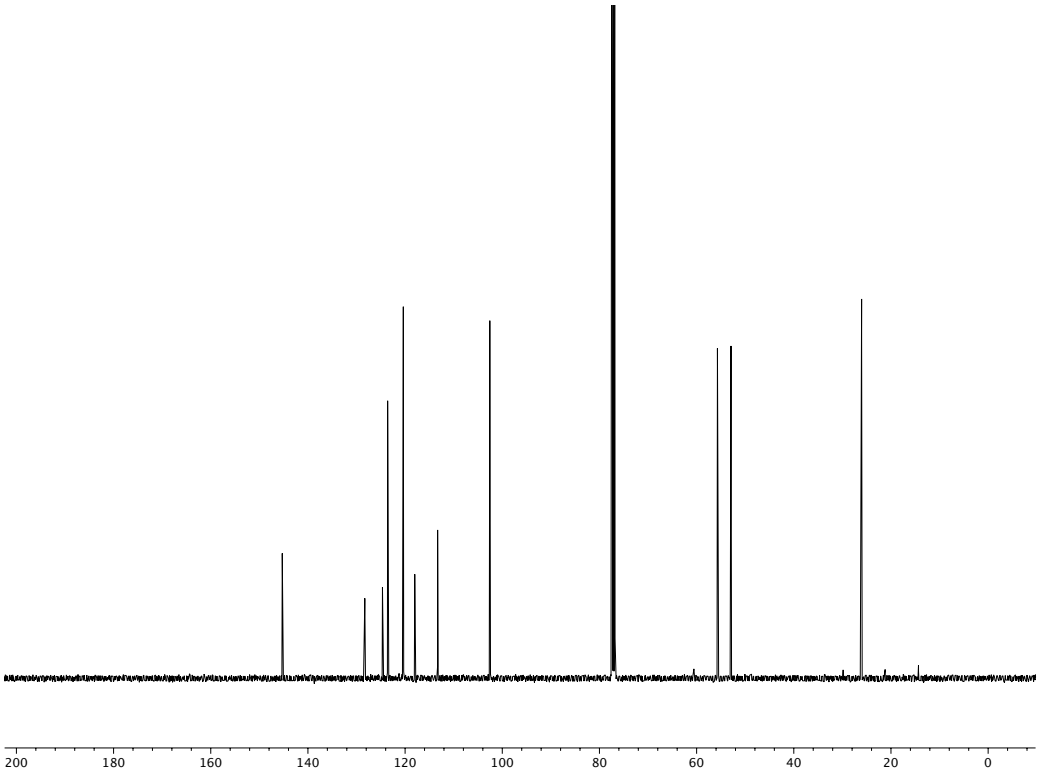


Figure A1.15. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **44.**

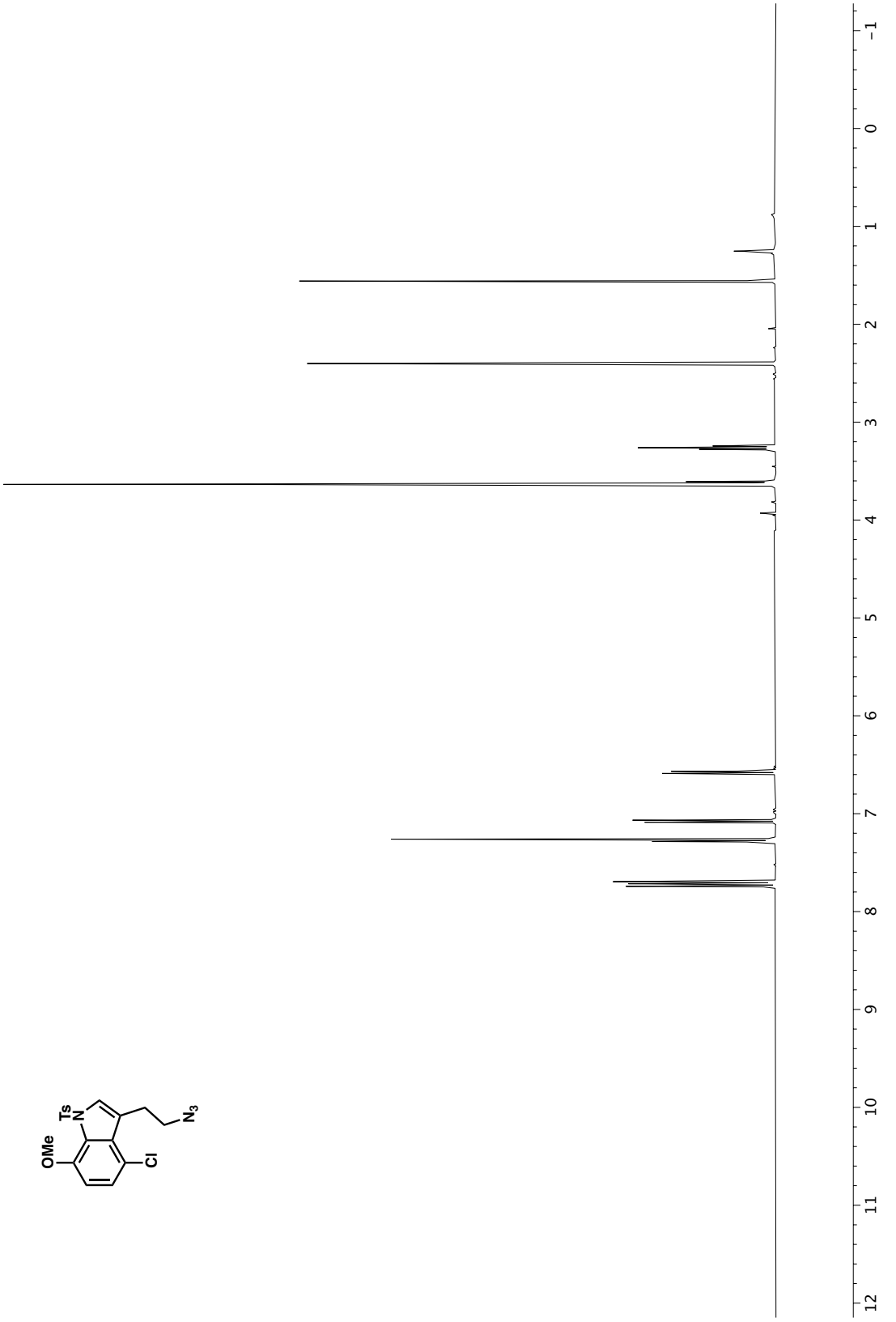


Figure A1.16. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **45**.

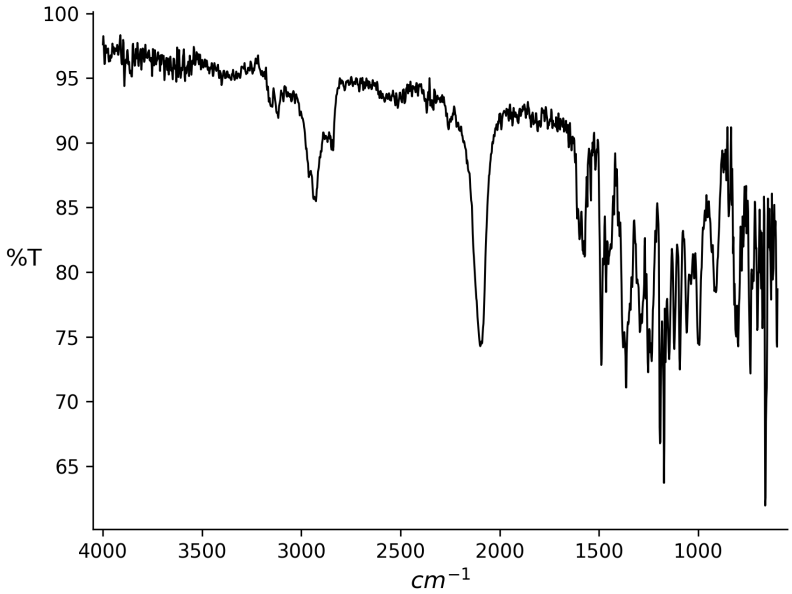


Figure A1.17. Infrared spectrum (Thin Film, NaCl) of compound **45**.

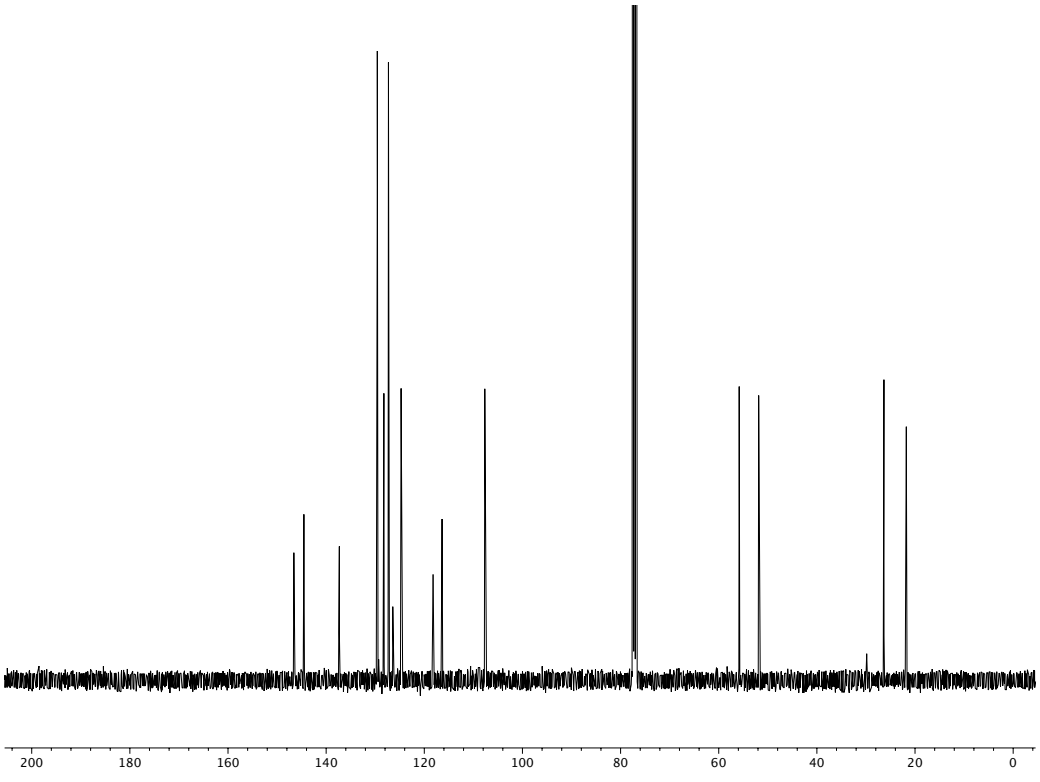


Figure A1.18. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **45.**

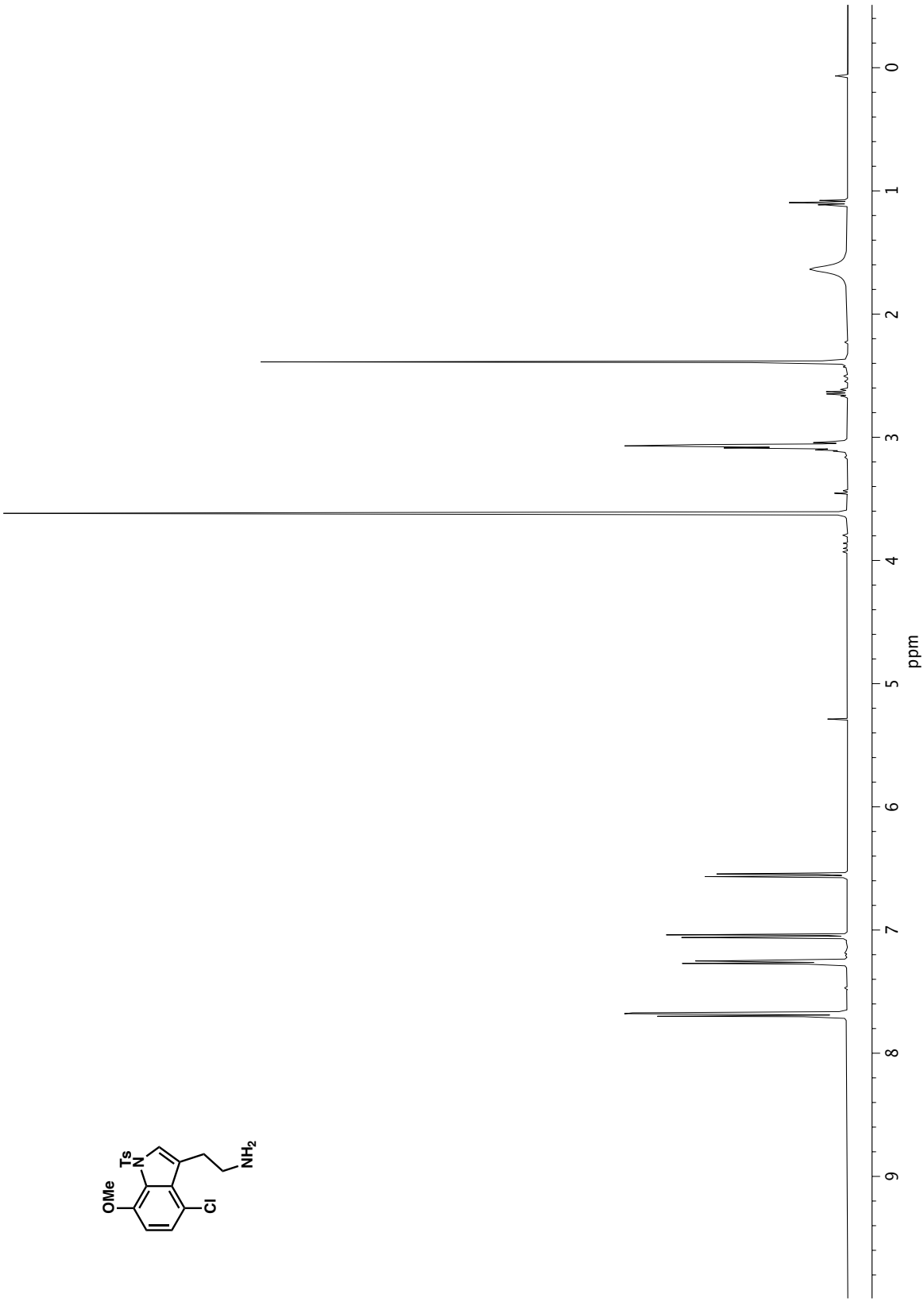


Figure A1.19. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **46**.

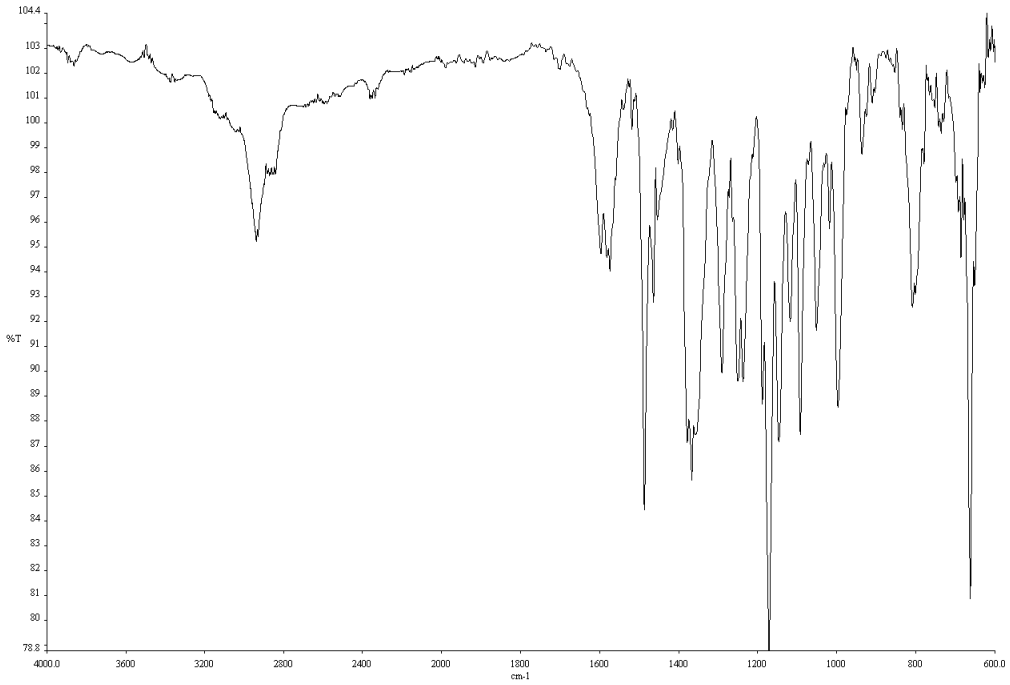


Figure A1.20. Infrared spectrum (Thin Film, NaCl) of compound **46**.

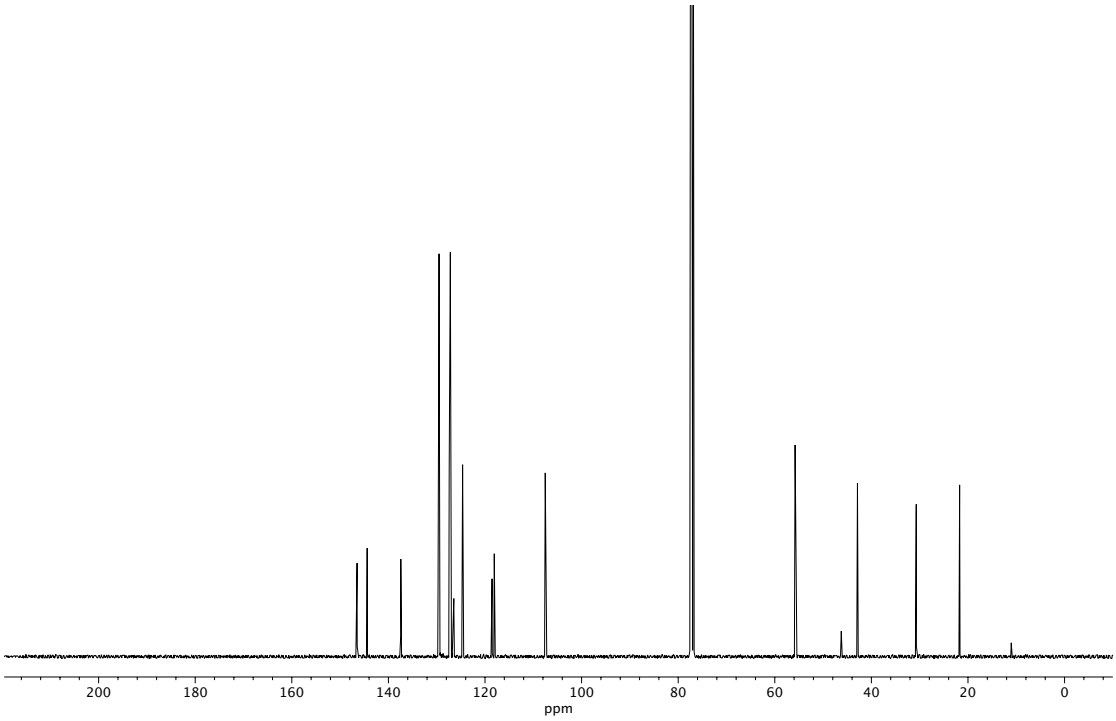


Figure A1.21. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **46.**

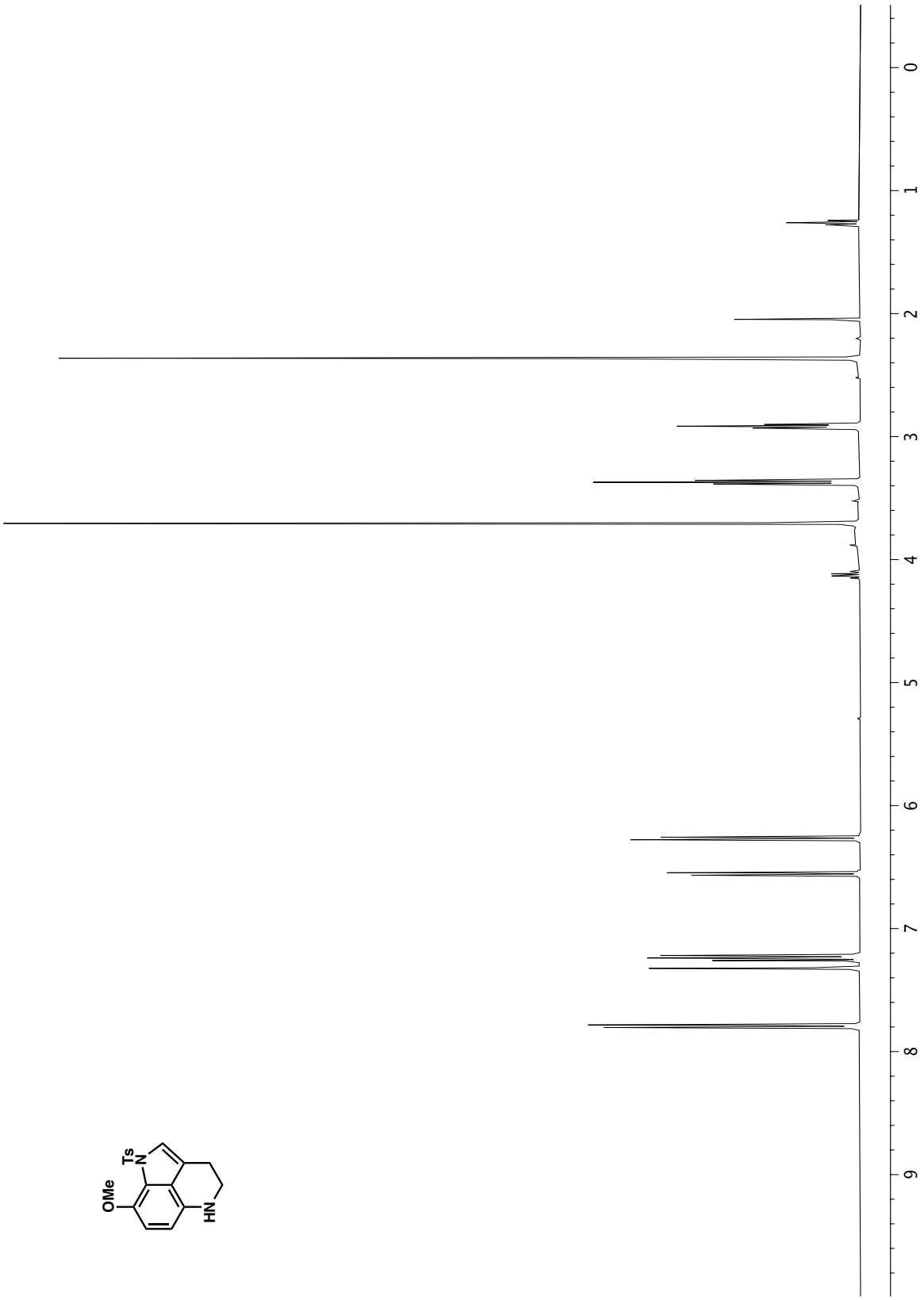


Figure A1.22. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **47**.

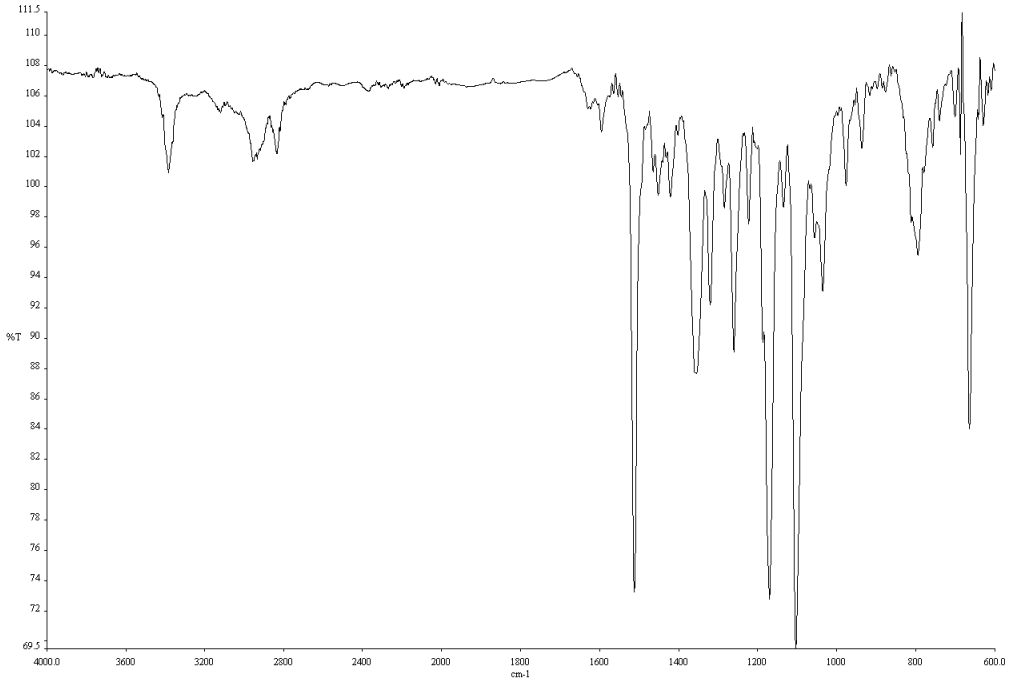


Figure A1.23. Infrared spectrum (Thin Film, NaCl) of compound **47**.

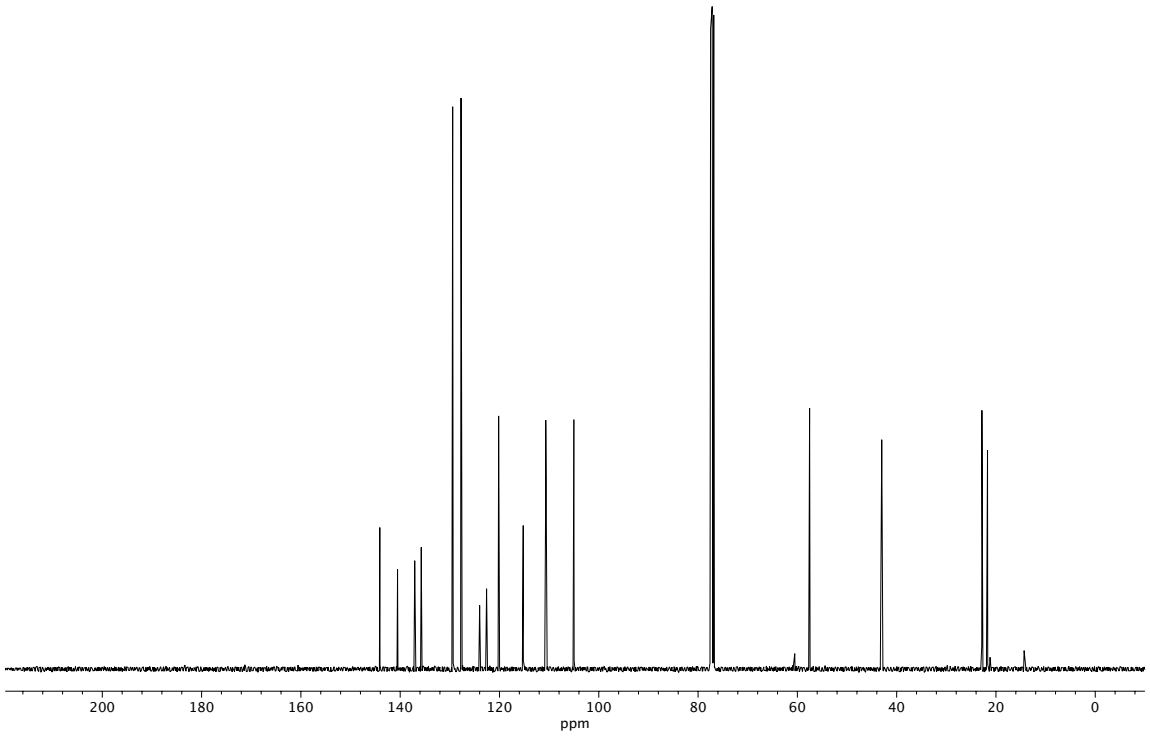


Figure A1.24. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **47.**

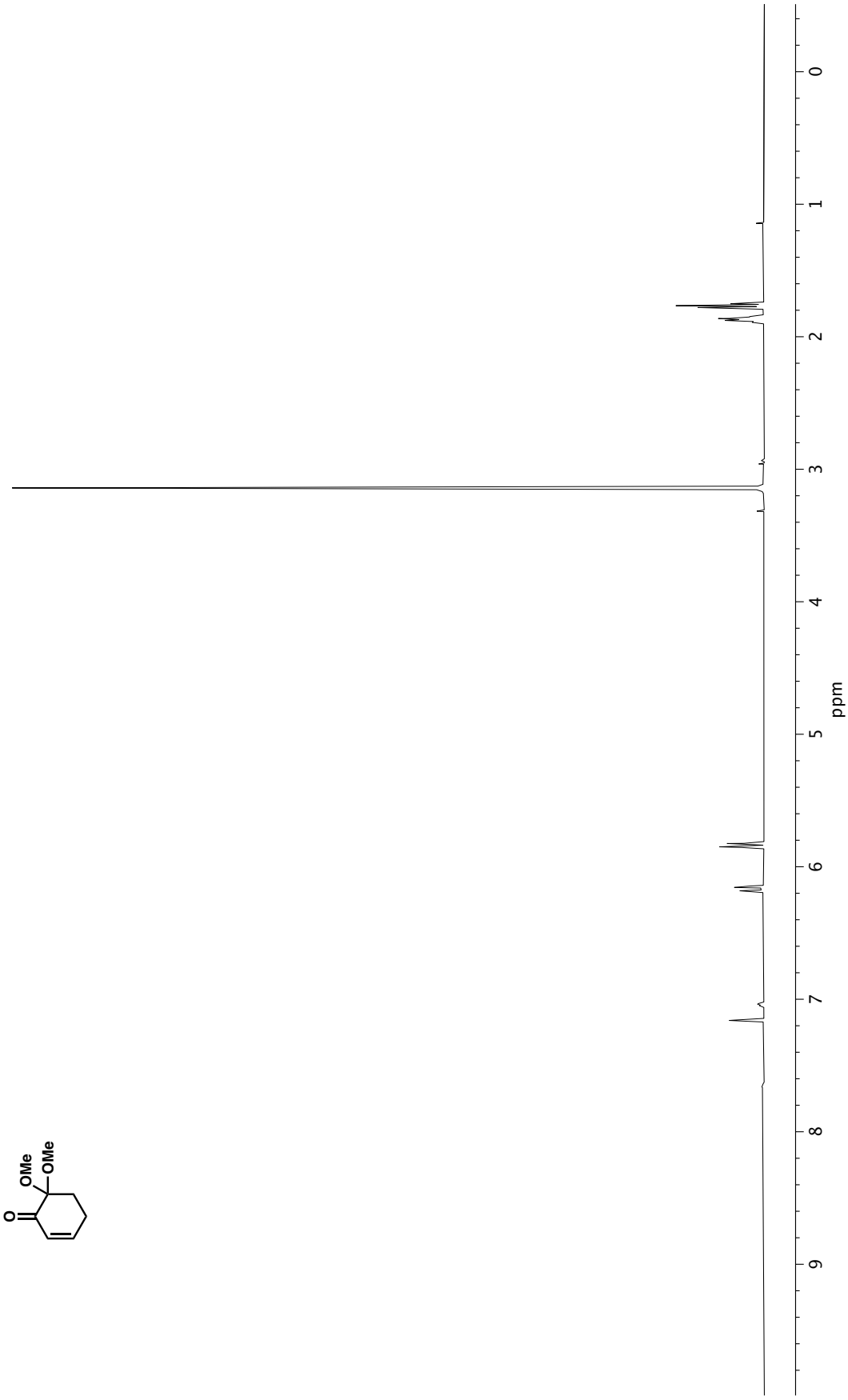


Figure A1.25. ^{1}H NMR (400 MHz, C_6D_6) of compound **40**.

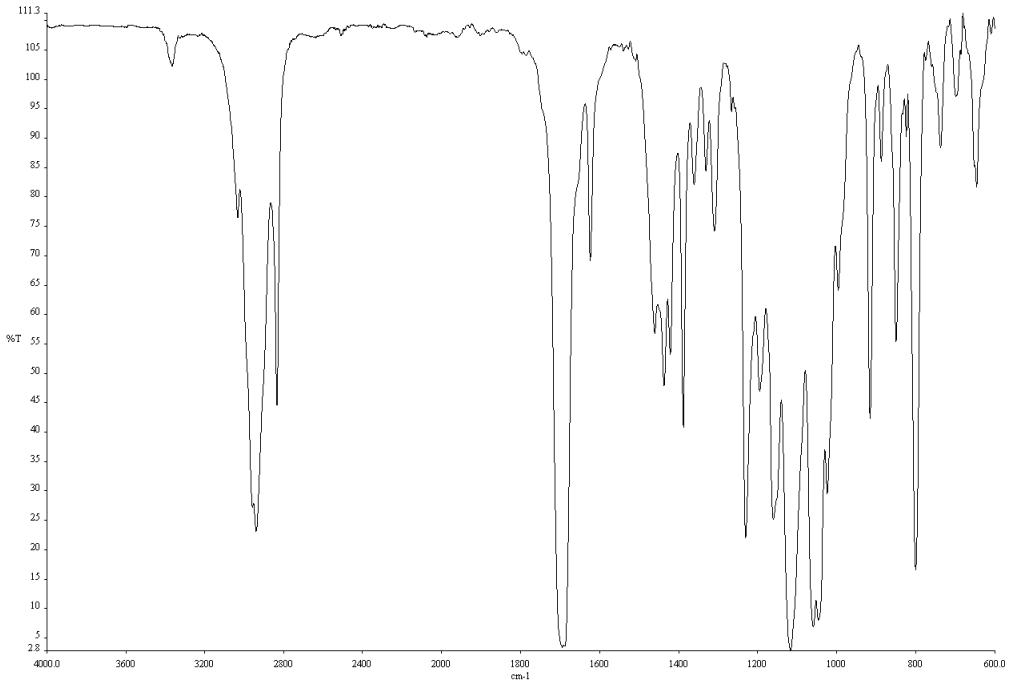


Figure A1.26. Infrared spectrum (Thin Film, NaCl) of compound **40**.

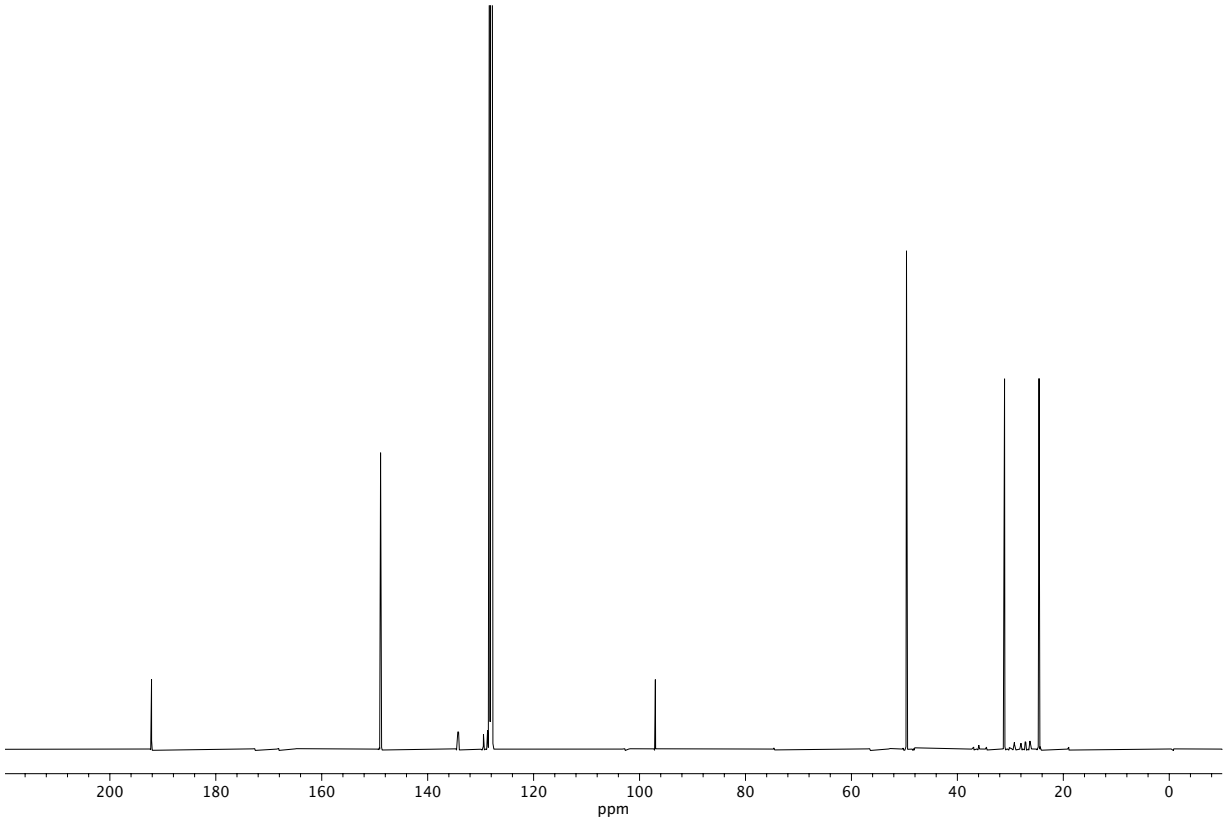


Figure A1.27. ^{13}C NMR (101 MHz, C_6D_6) of compound **40.**

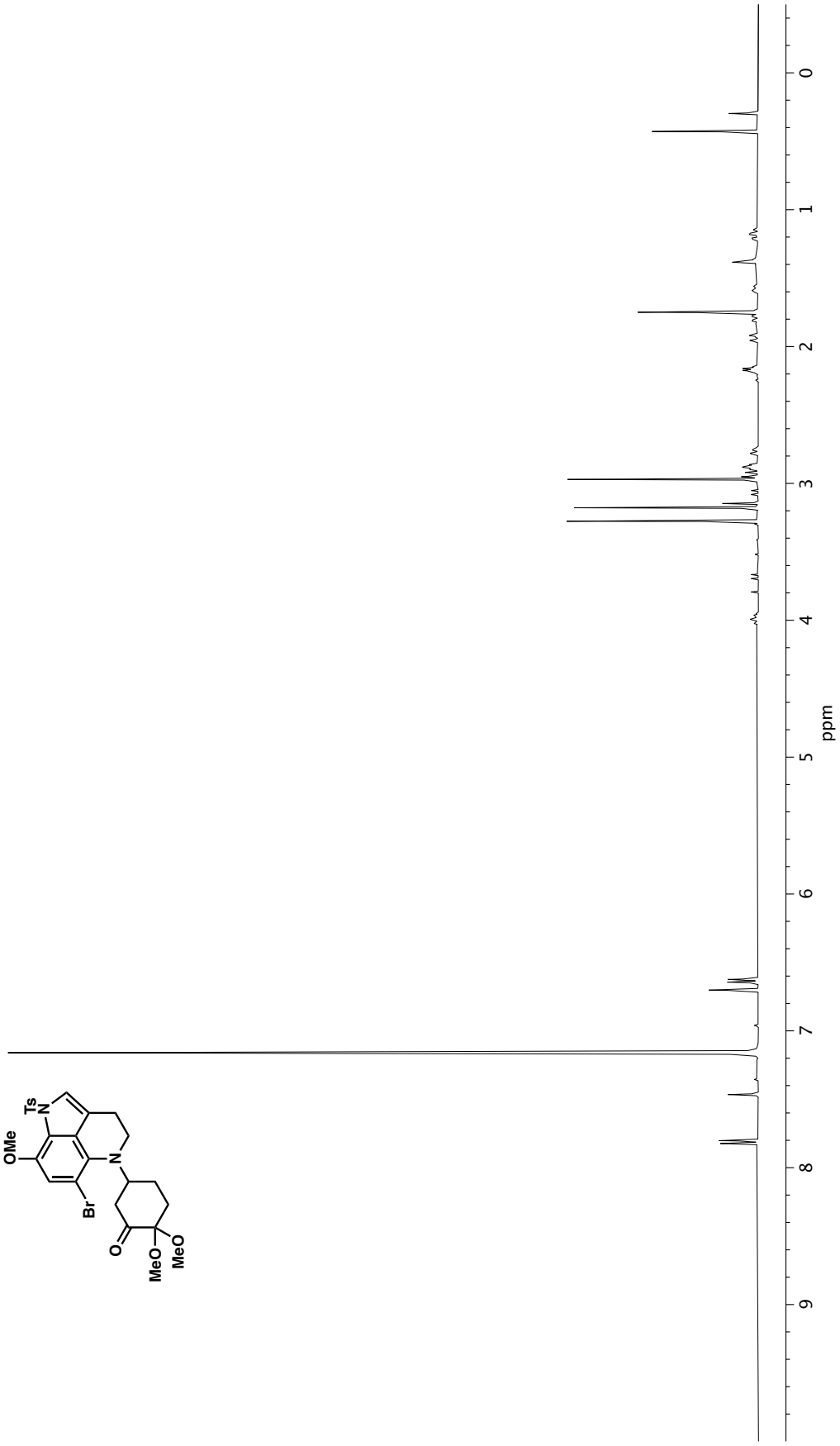


Figure A1.28. ^{1}H NMR (400 MHz, C_6D_6) of compound **48**.

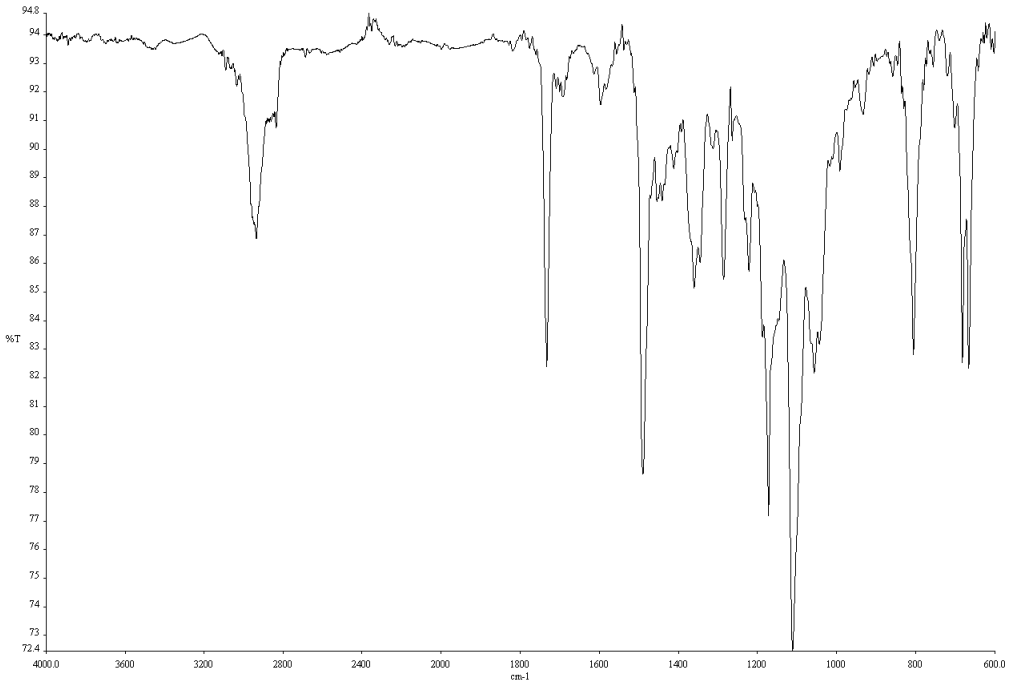


Figure A1.29. Infrared spectrum (Thin Film, NaCl) of compound **48**.

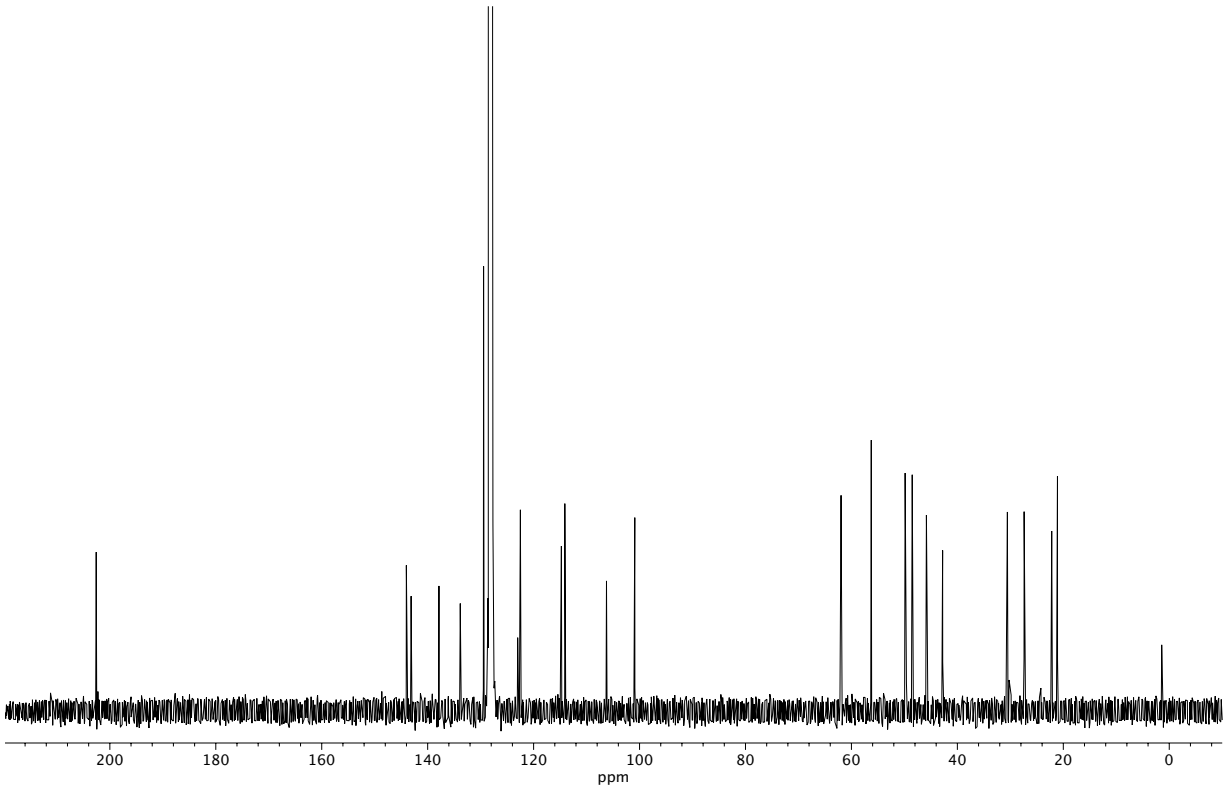


Figure A1.30. ^{13}C NMR (101 MHz, C_6D_6) of compound **48.**

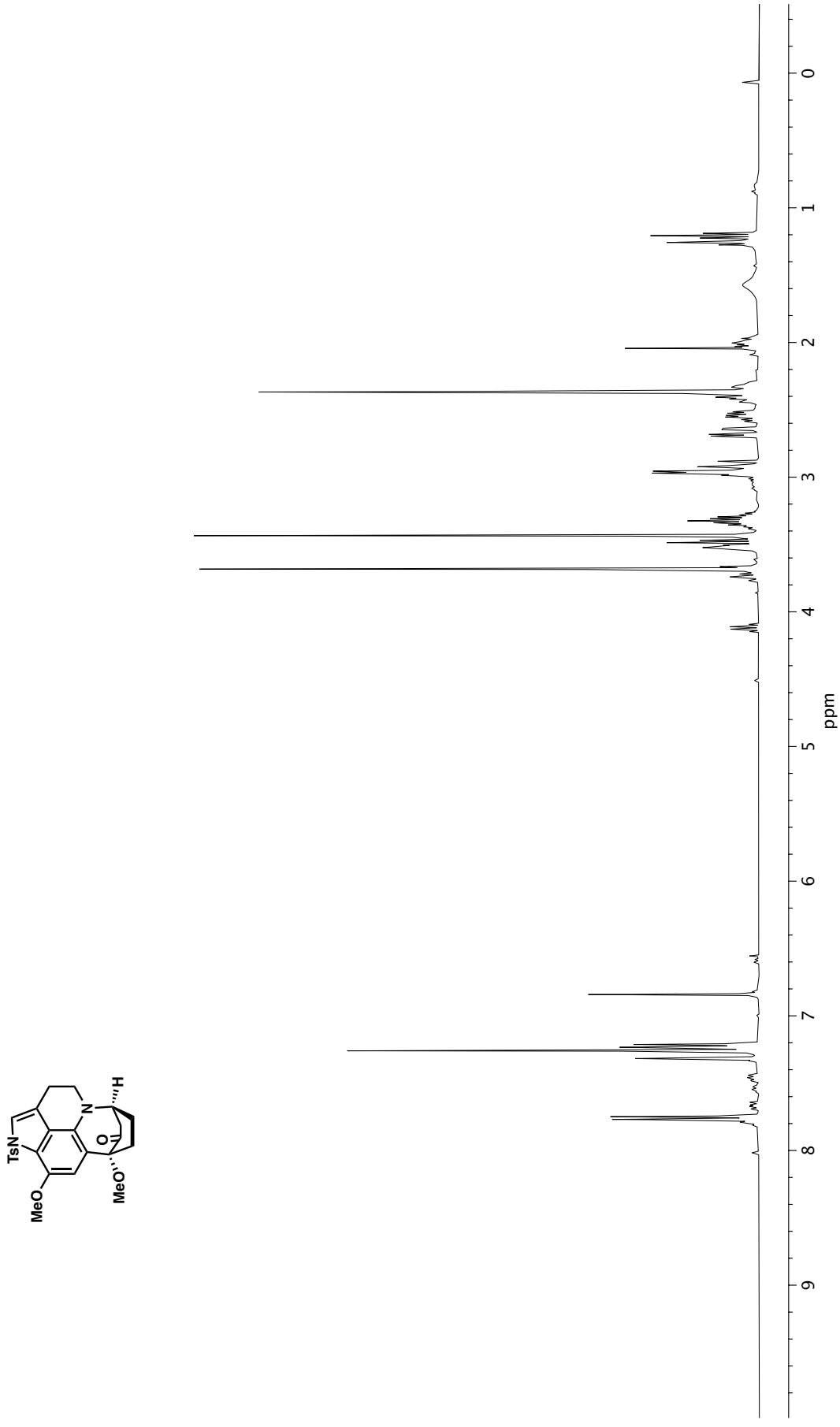


Figure A1.31. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **49**.

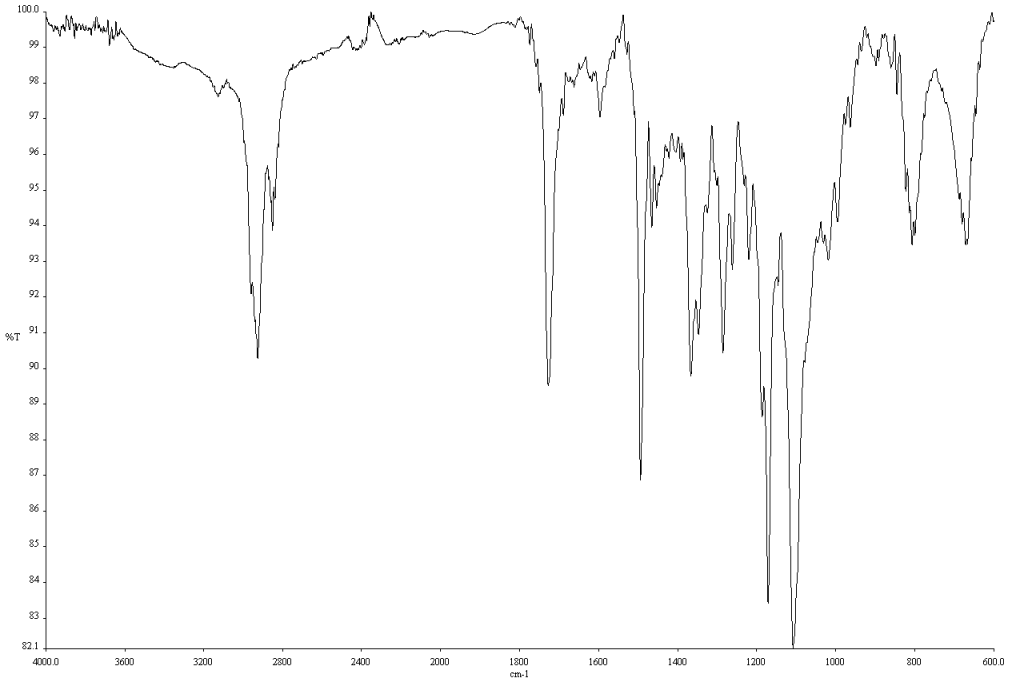


Figure A1.32. Infrared spectrum (Thin Film, NaCl) of compound **49**.

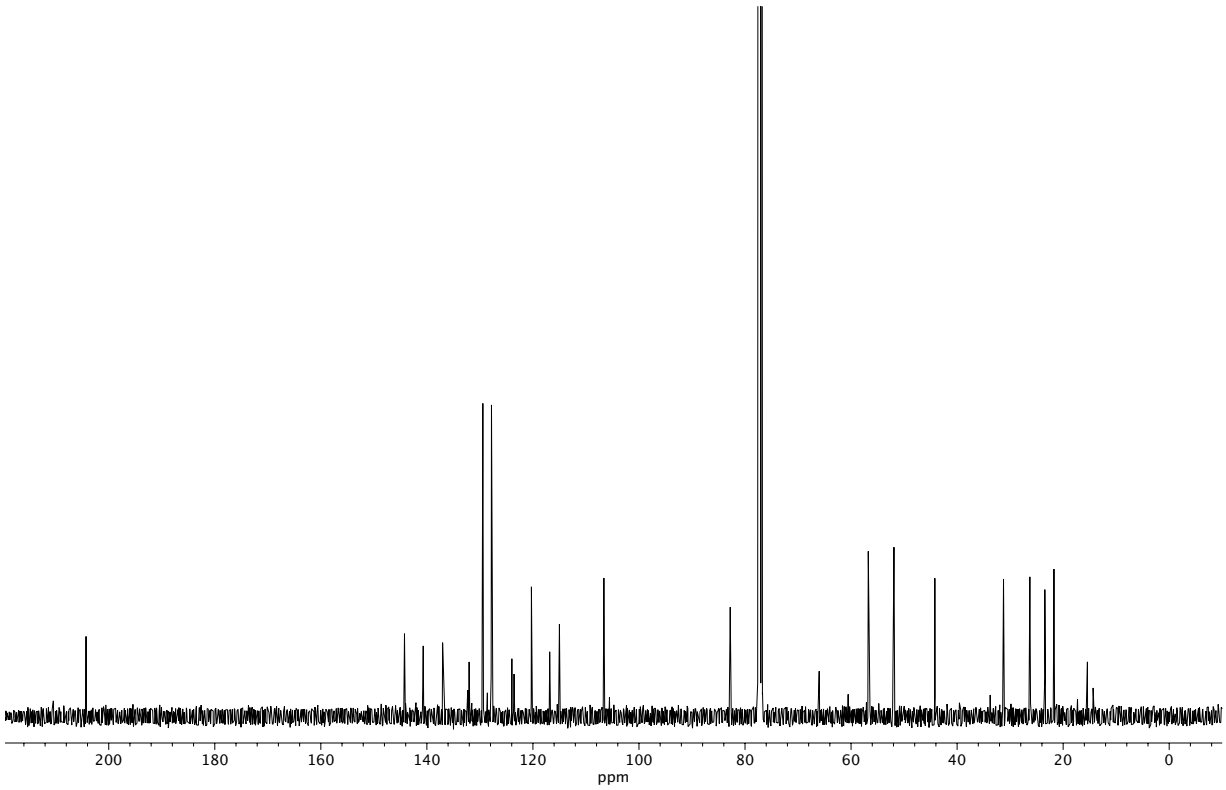


Figure A1.33. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **49.**

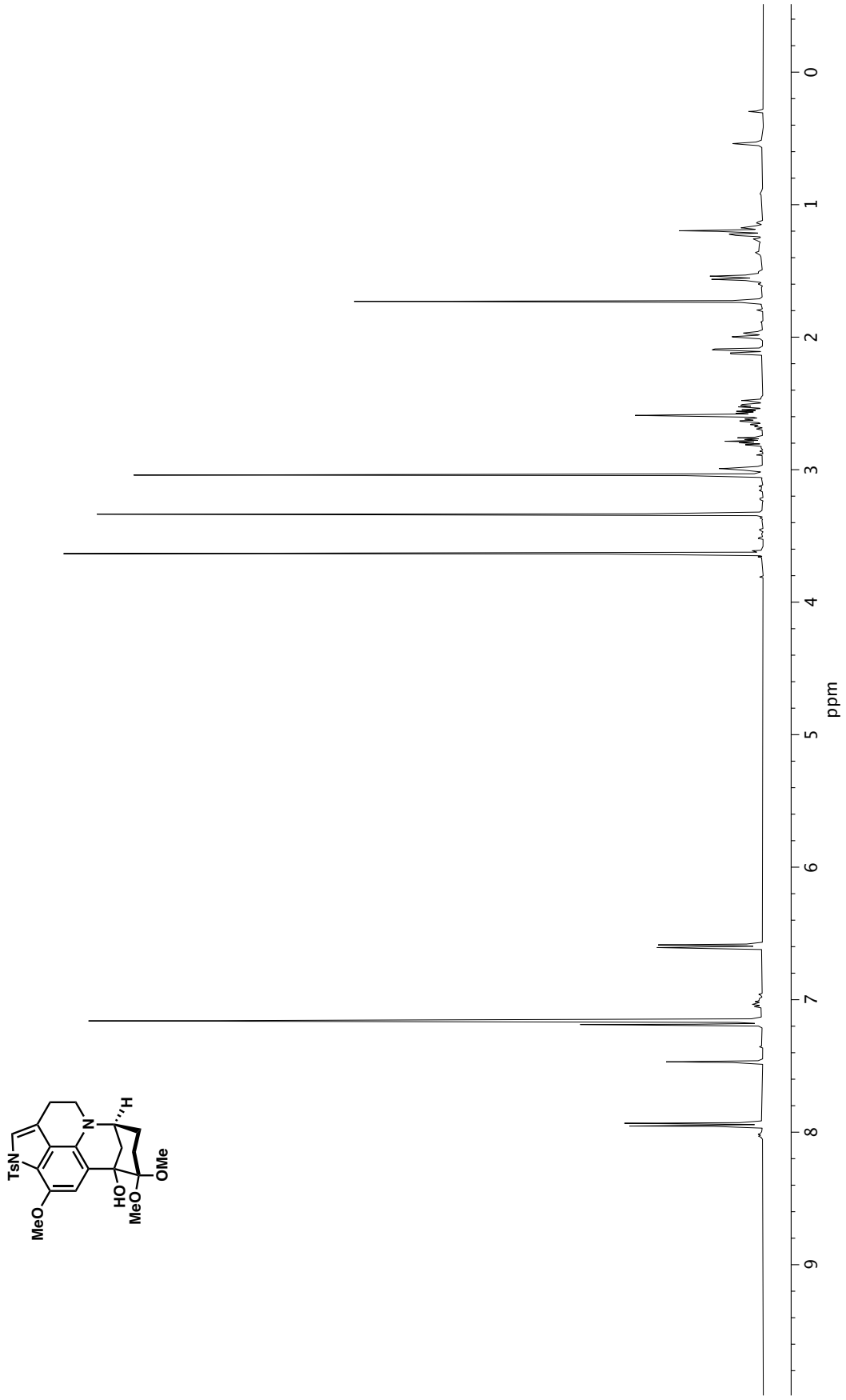


Figure A1.34. ^{1}H NMR (400 MHz, C_6D_6) of compound **50**.

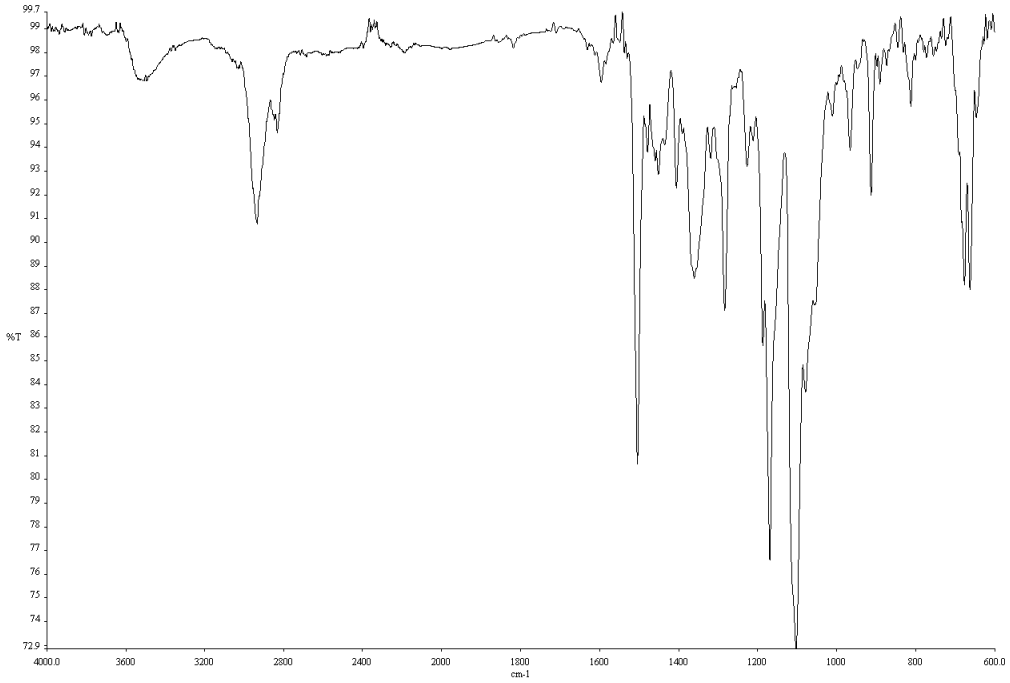


Figure A1.35. Infrared spectrum (Thin Film, NaCl) of compound **50**.

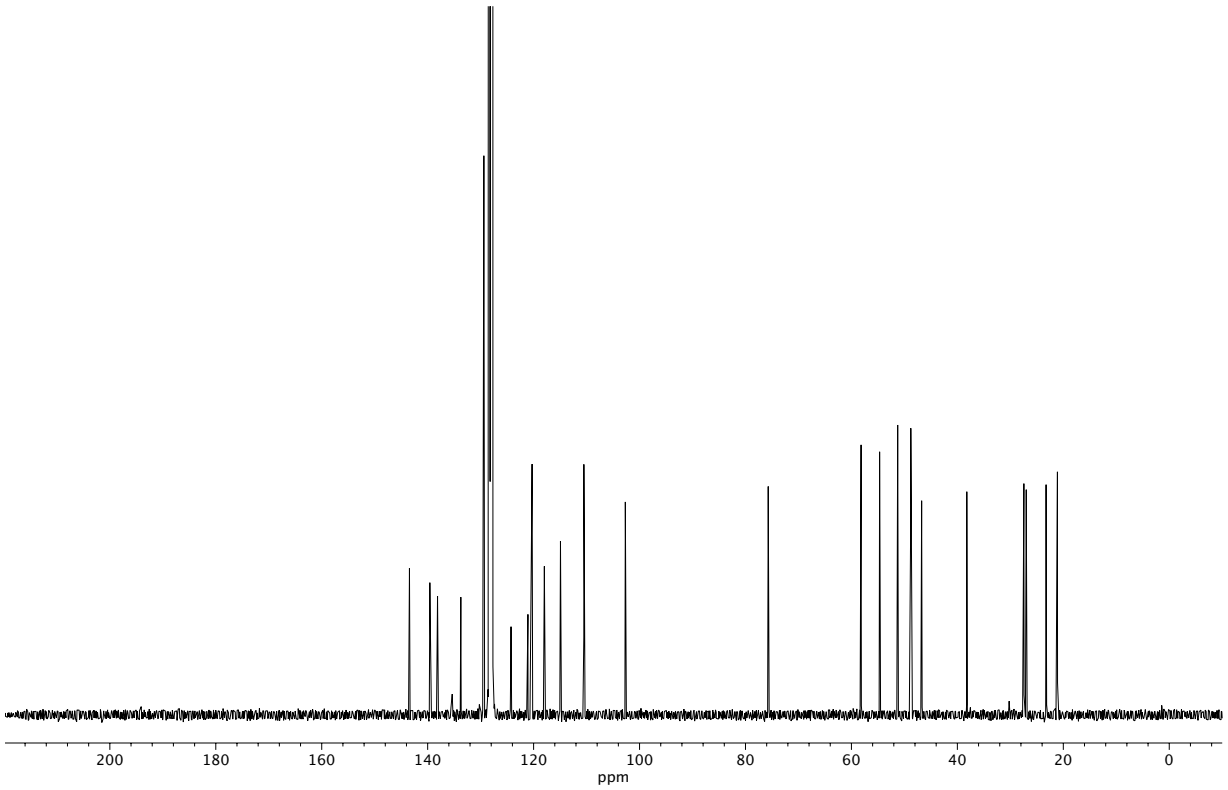


Figure A1.36. ^{13}C NMR (101 MHz, C_6D_6) of compound **50.**

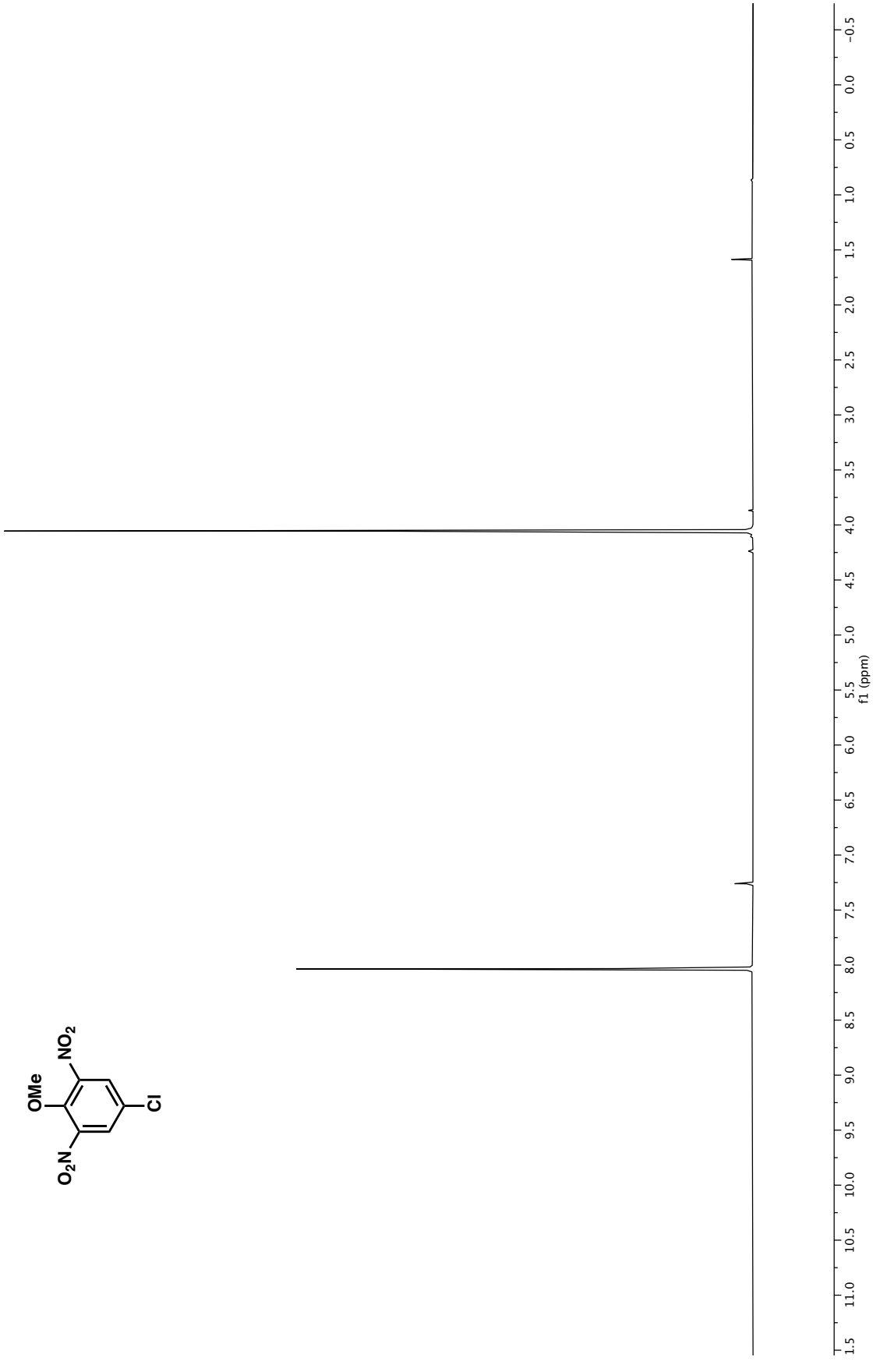


Figure A1.37. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **52**.

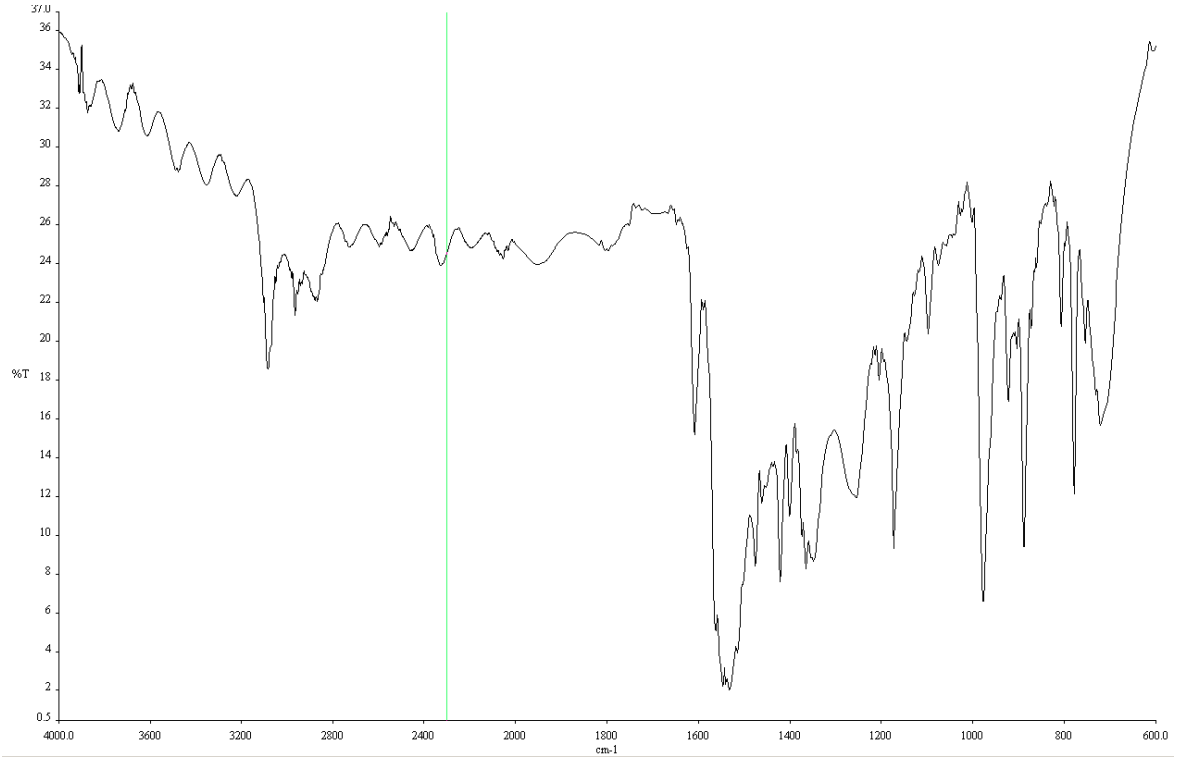


Figure A1.38. Infrared spectrum (Thin Film, NaCl) of compound **52**.

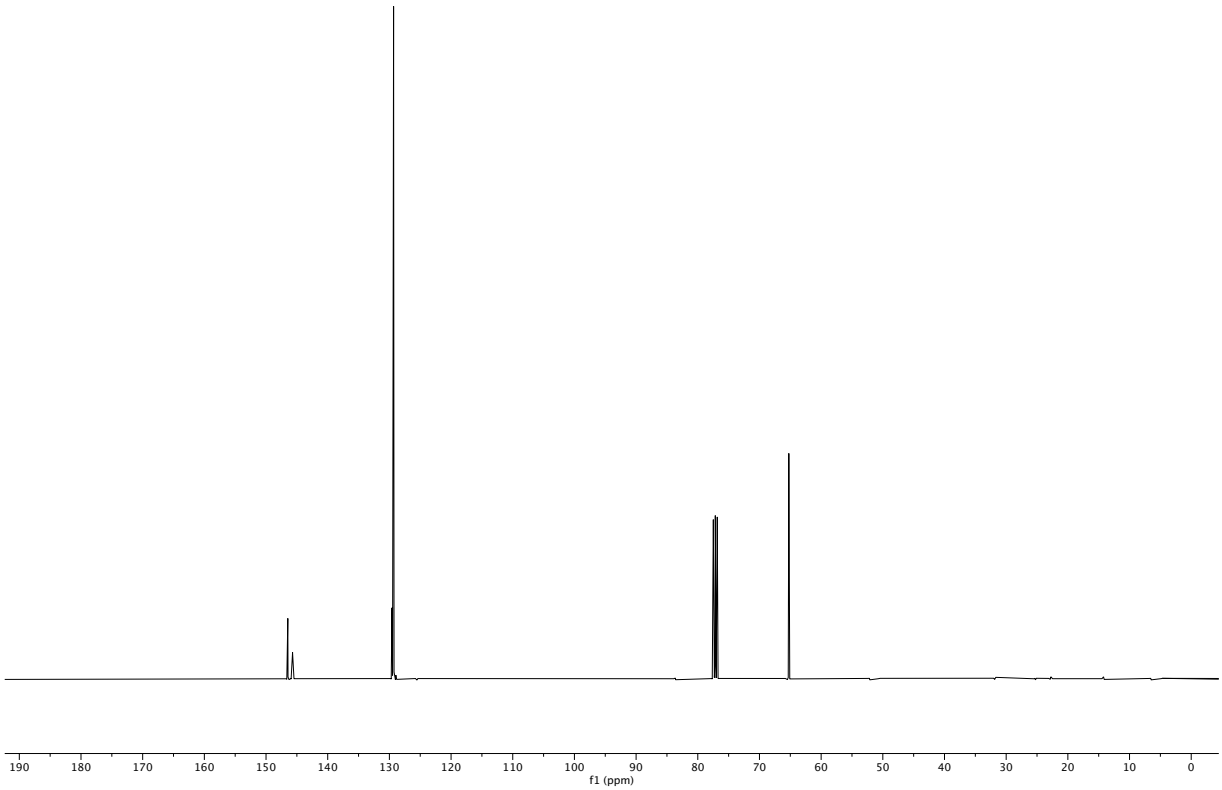


Figure A1.39. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **52.**

Figure A1.40. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **53**.

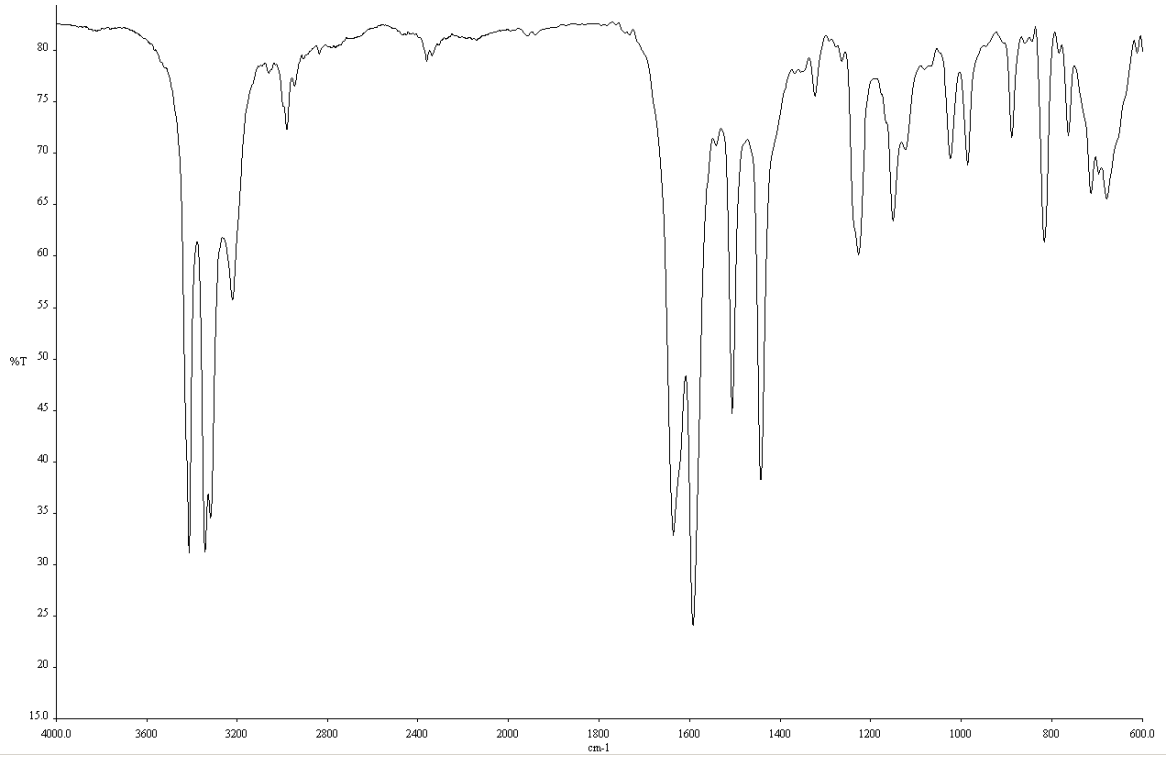


Figure A1.41. Infrared spectrum (Thin Film, NaCl) of compound **53**.

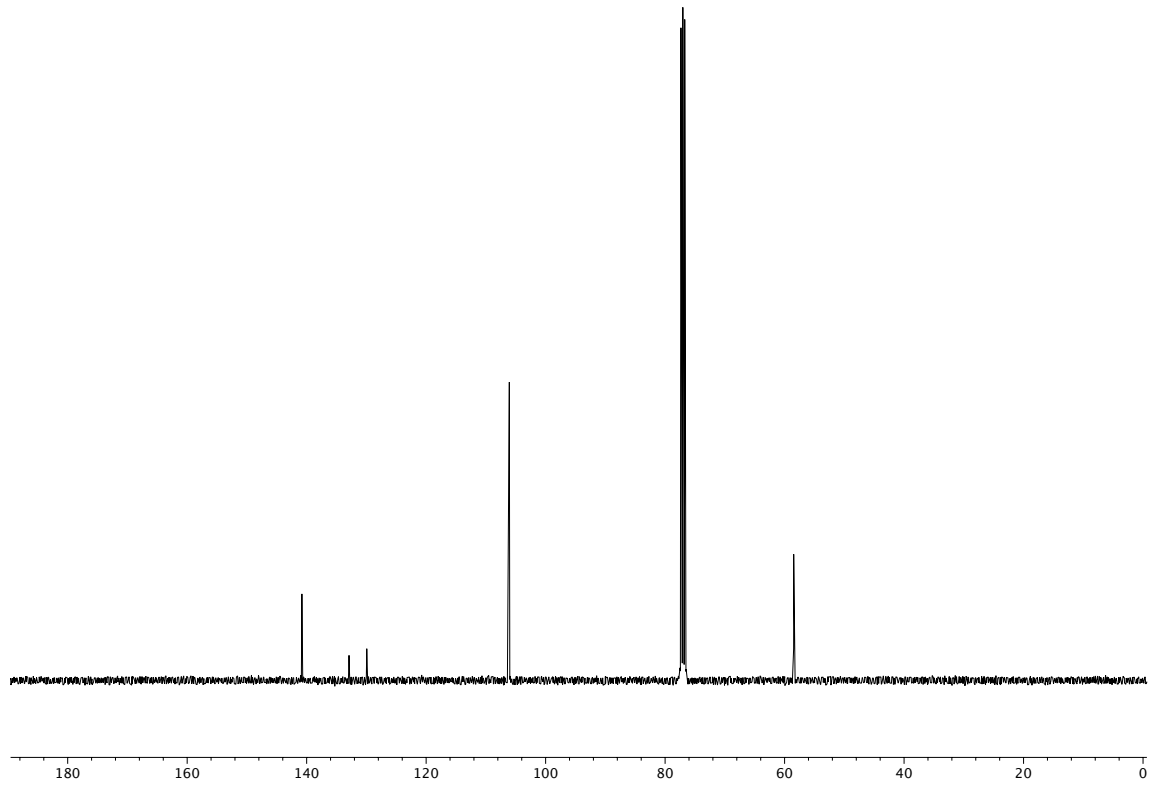


Figure A1.42. ^{13}C NMR (151 MHz, $CDCl_3$) of compound **53.**

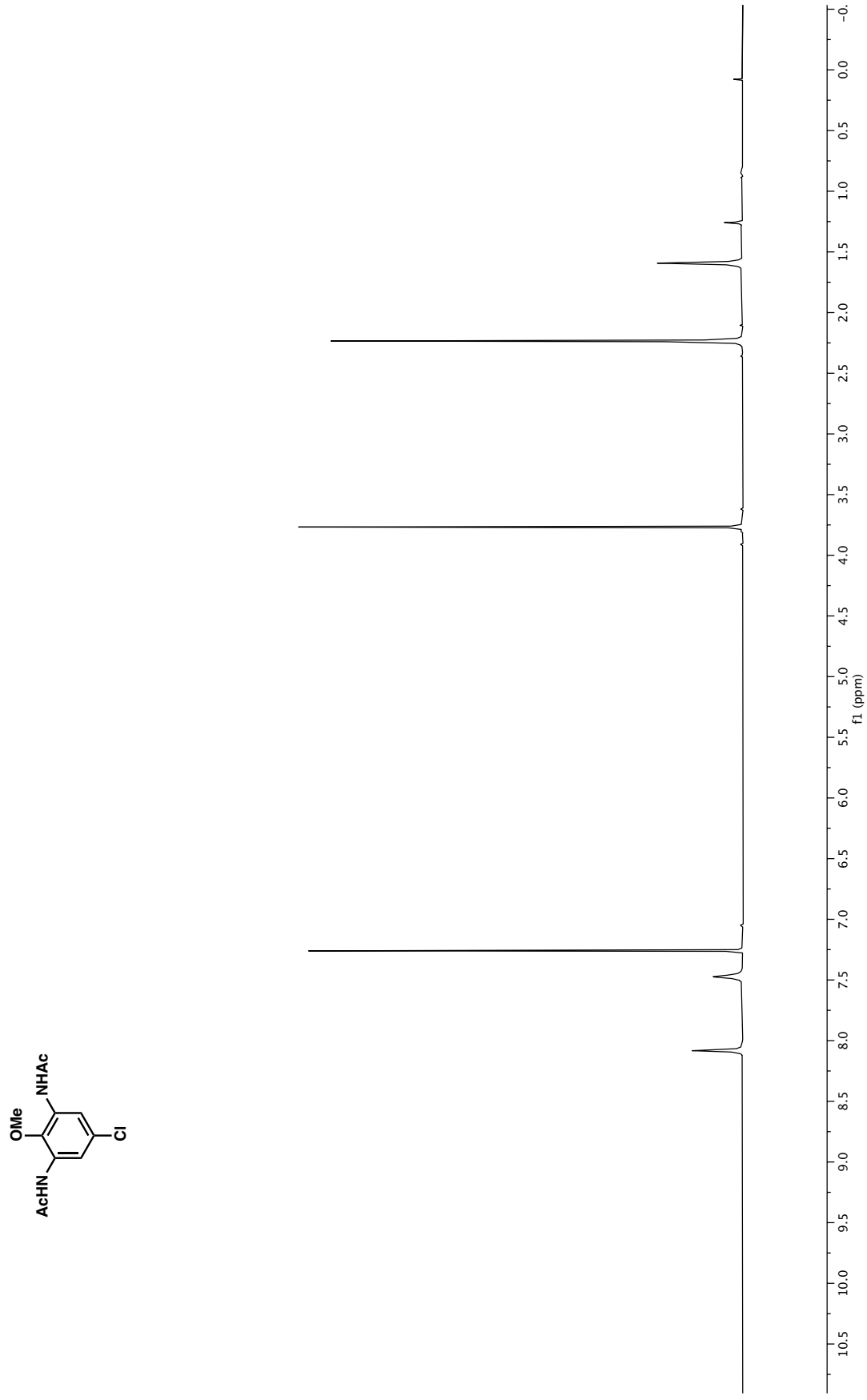


Figure A1.43. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **54**.

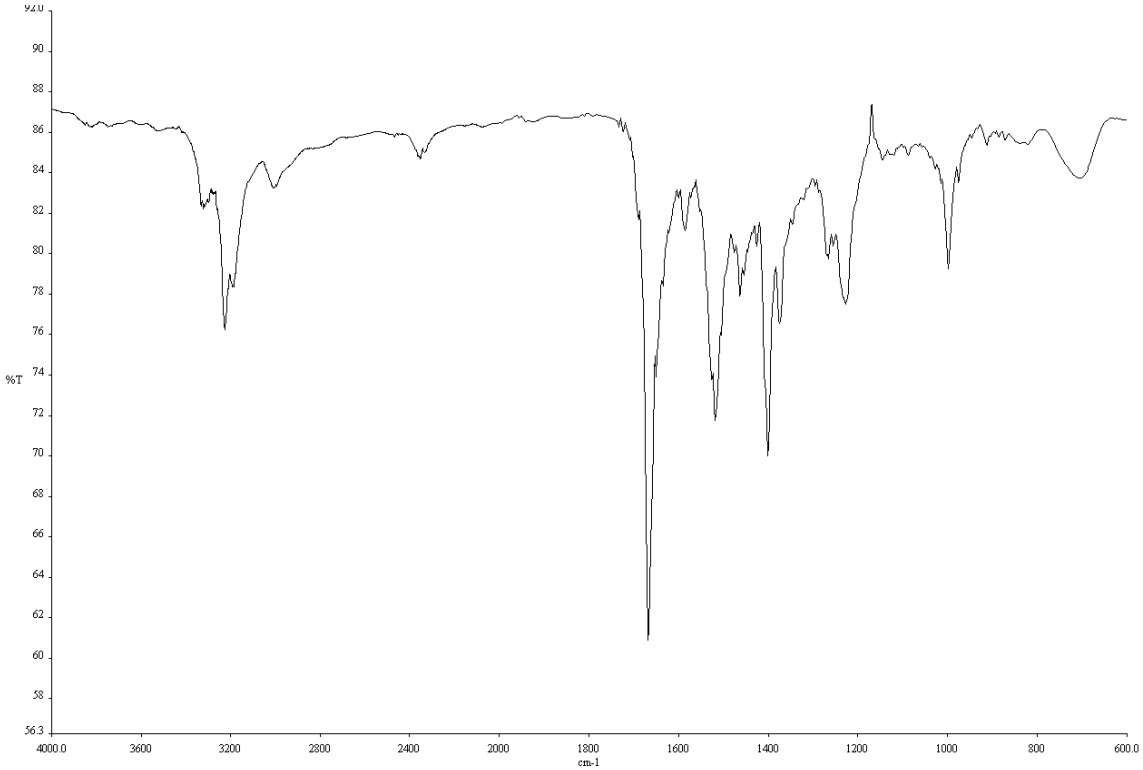


Figure A1.44. Infrared spectrum (Thin Film, NaCl) of compound **54**.

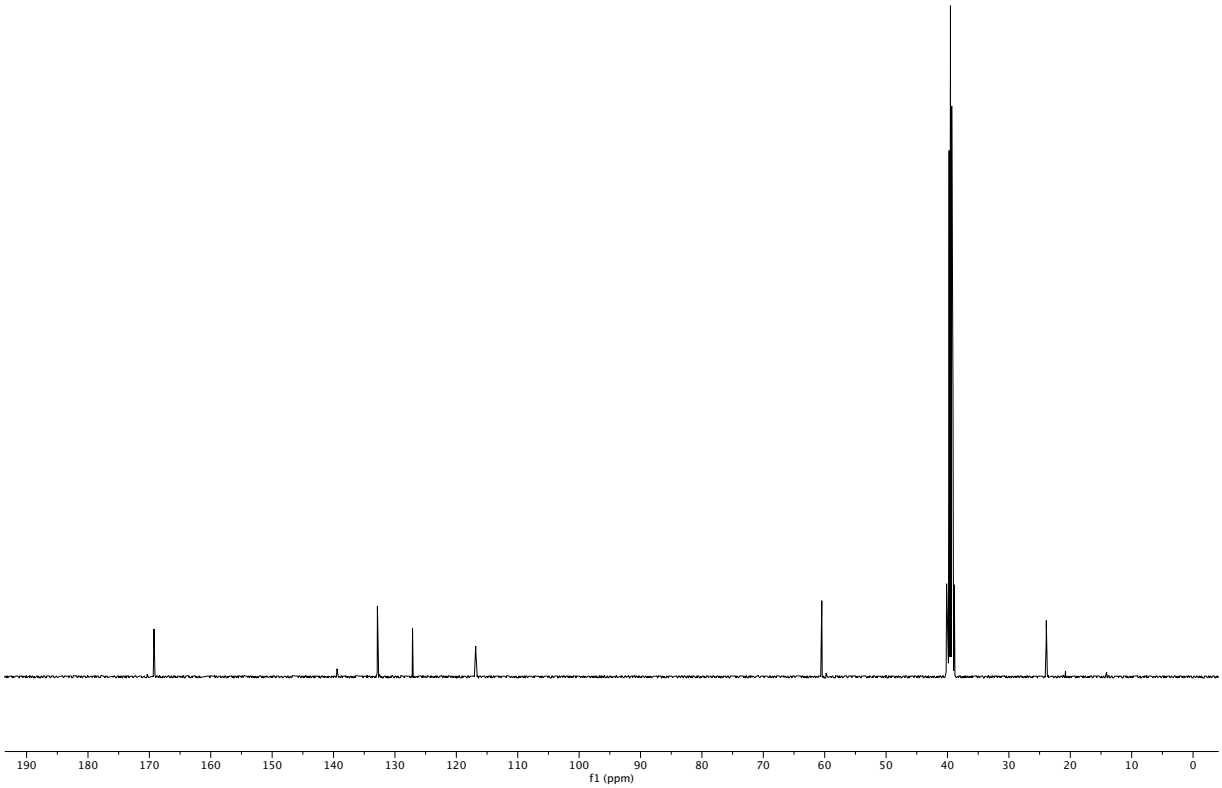


Figure A1.45. ^{13}C NMR (101 MHz, DMSO-d_6) of compound **54.**

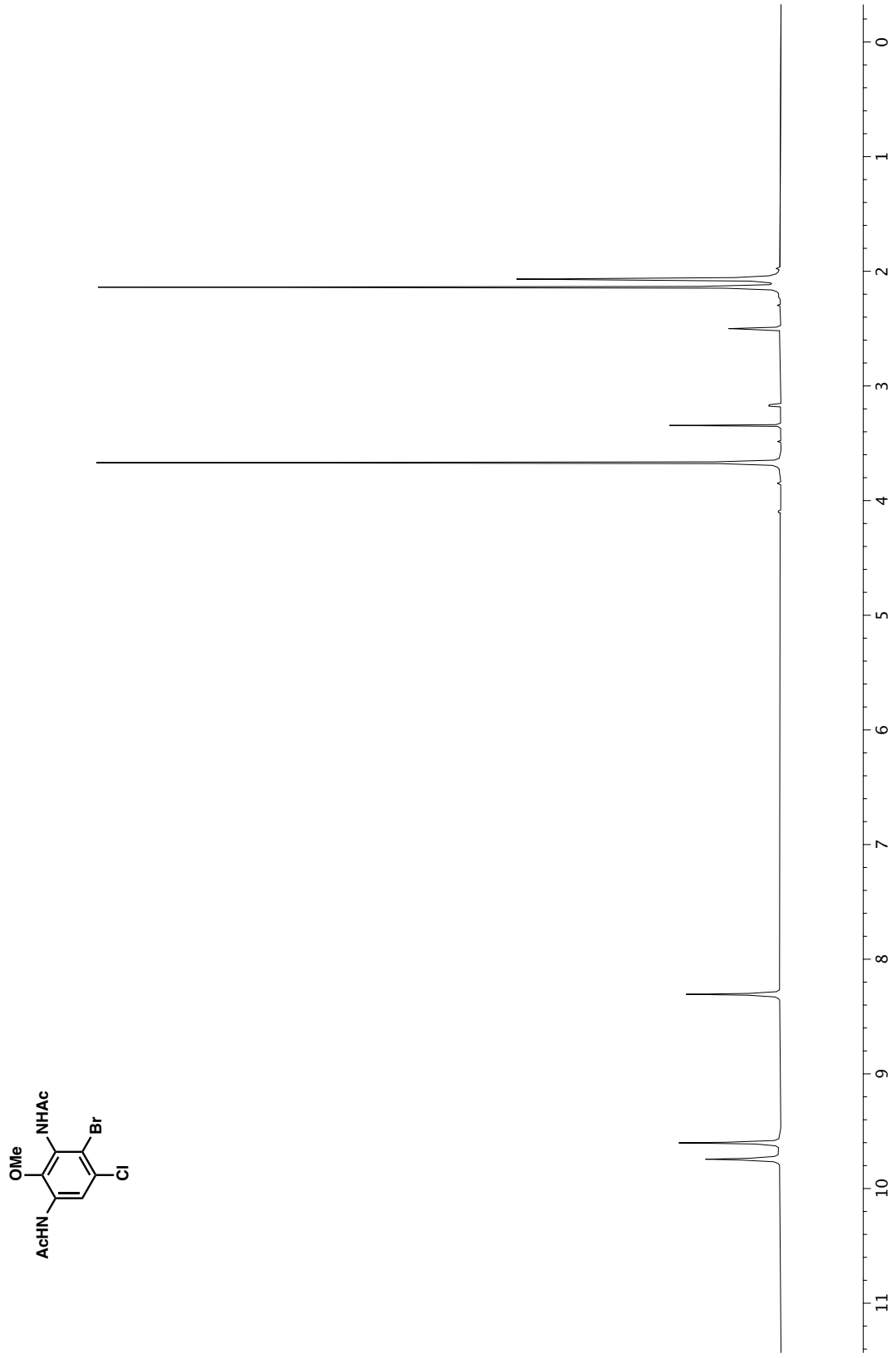


Figure A1.46. ^{1}H NMR (600 MHz, DMSO-d_6) of compound **55**.

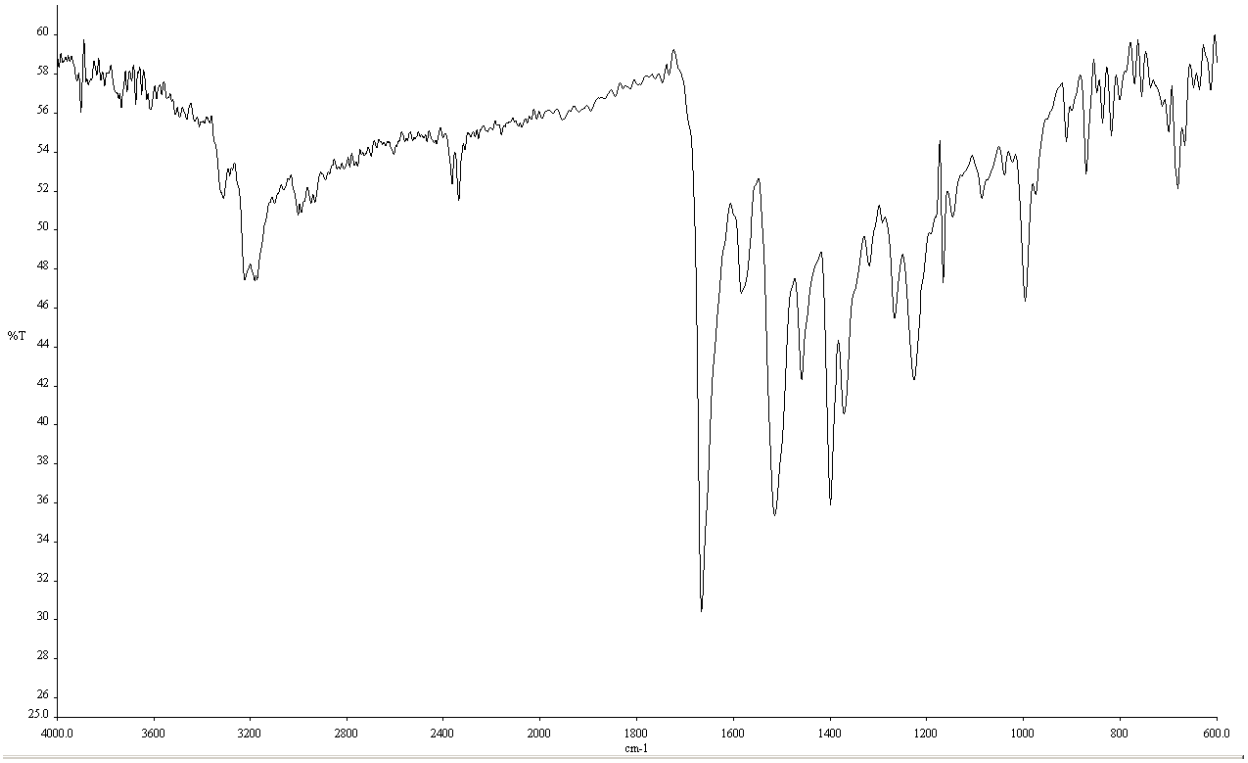


Figure A1.47. Infrared spectrum (Thin Film, NaCl) of compound **55**.

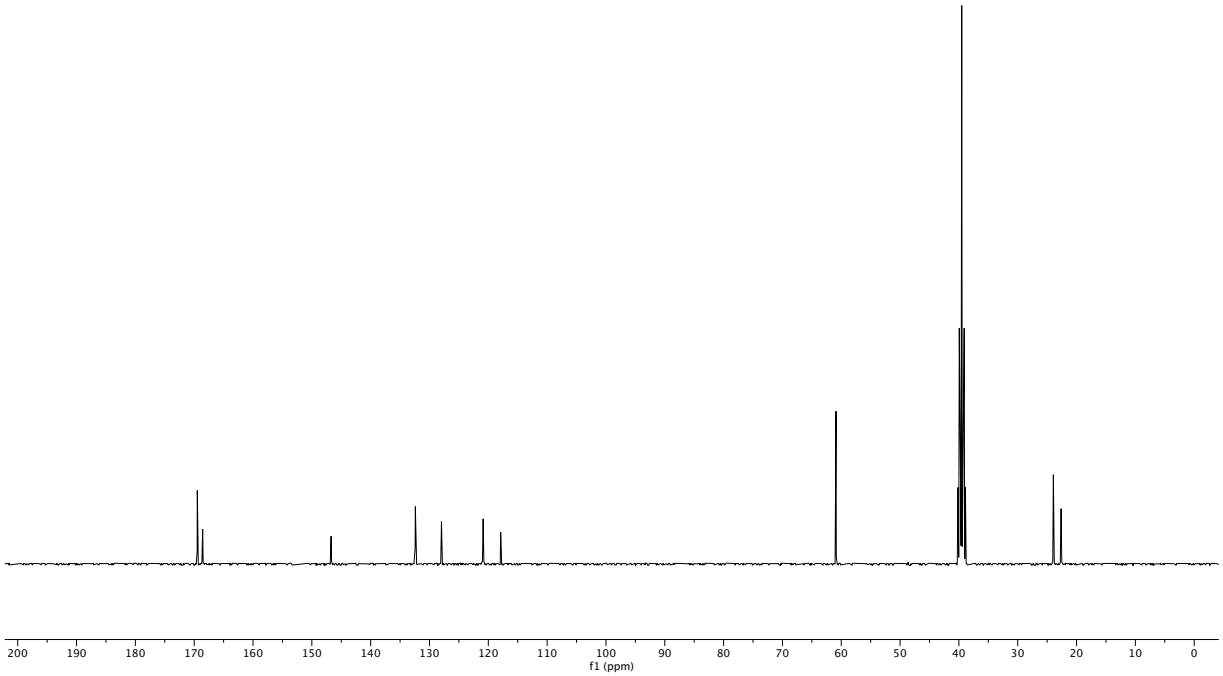


Figure A1.48. ^{13}C NMR (101 MHz, DMSO-d_6) of compound **55.**

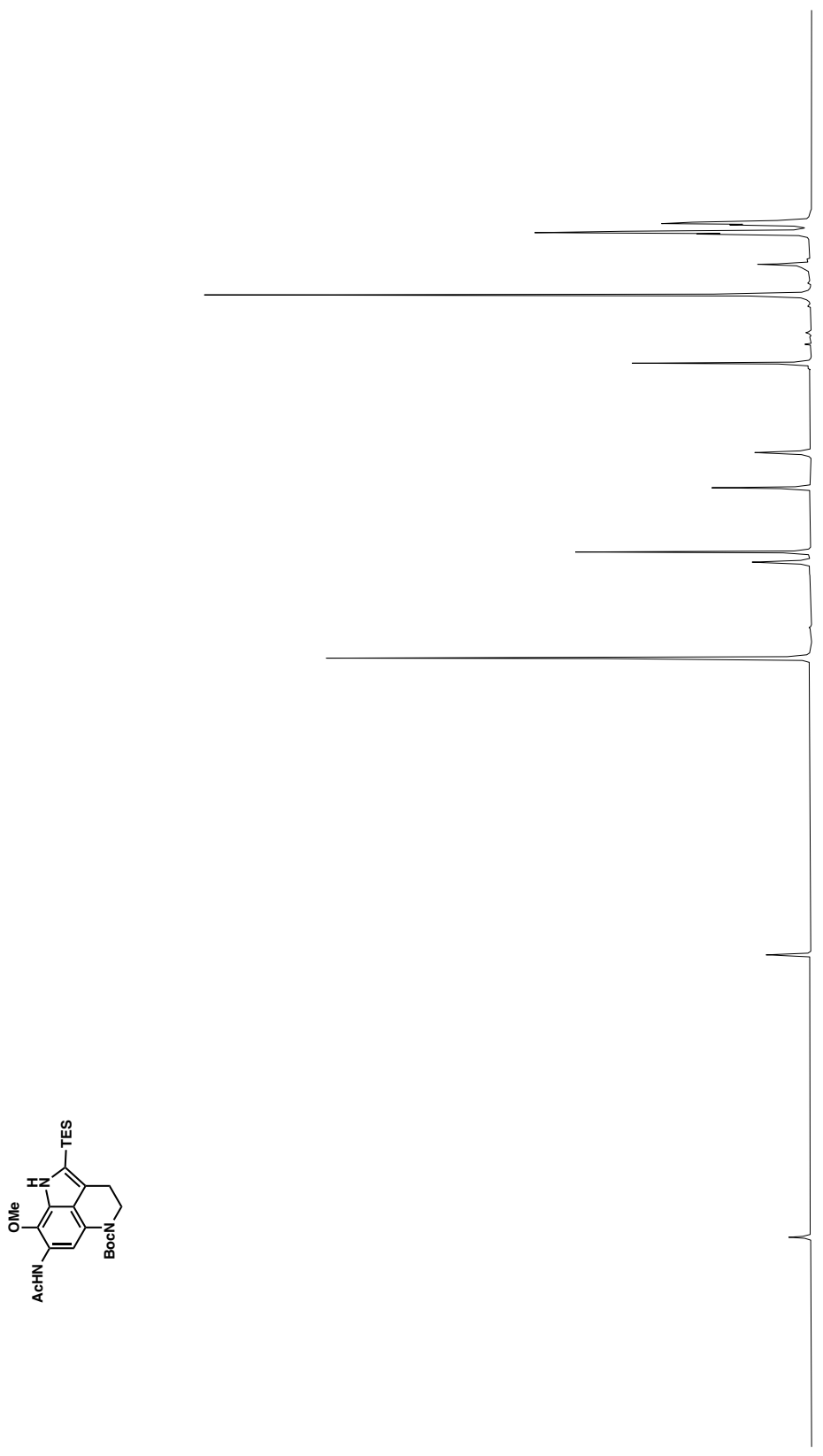


Figure A1.49. ^{1}H NMR (600 MHz, CD_3OD) of compound **57**.

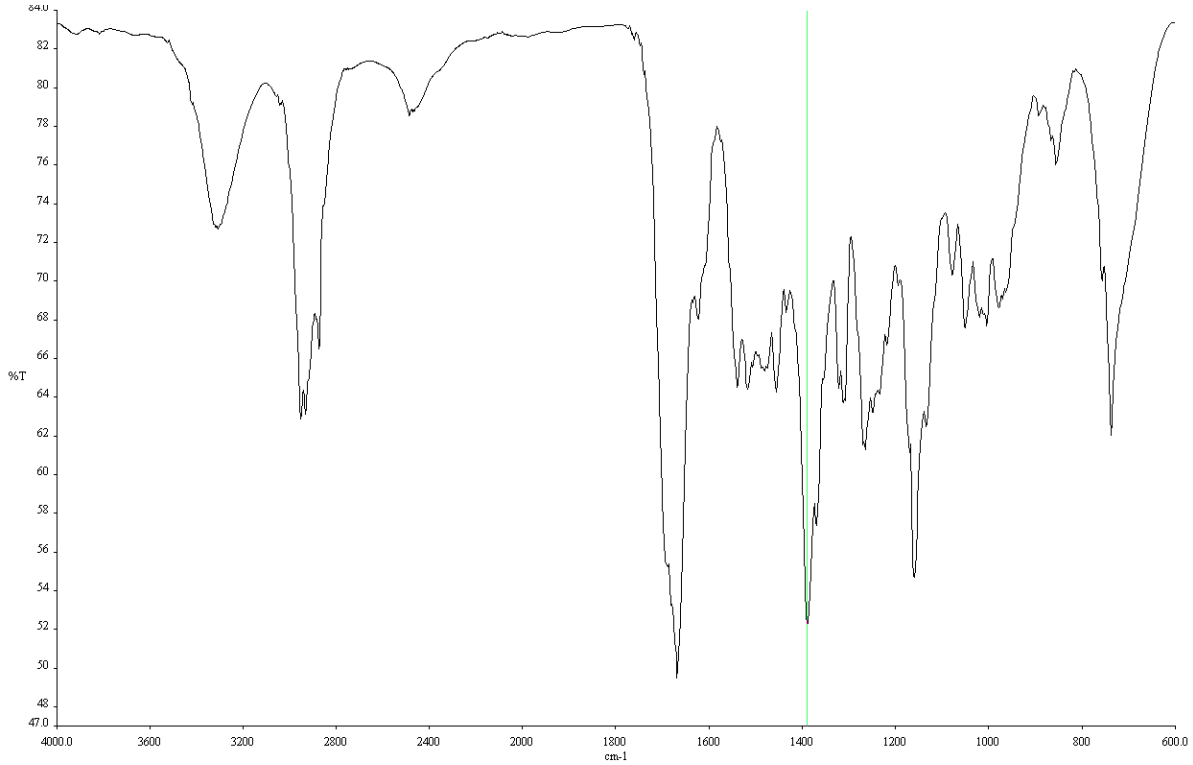


Figure A1.50. Infrared spectrum (Thin Film, NaCl) of compound **57**.

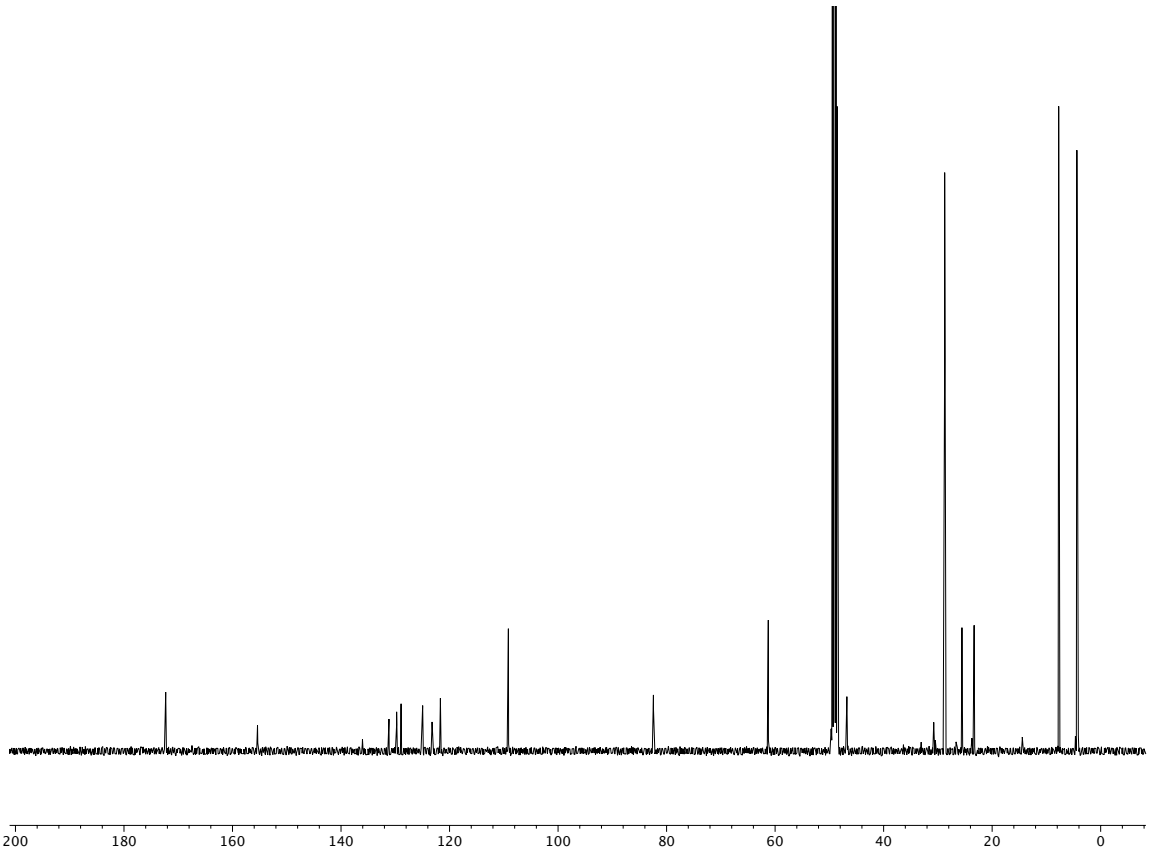


Figure A1.51. ^{13}C NMR (101 MHz, CD_3OD) of compound **57.**

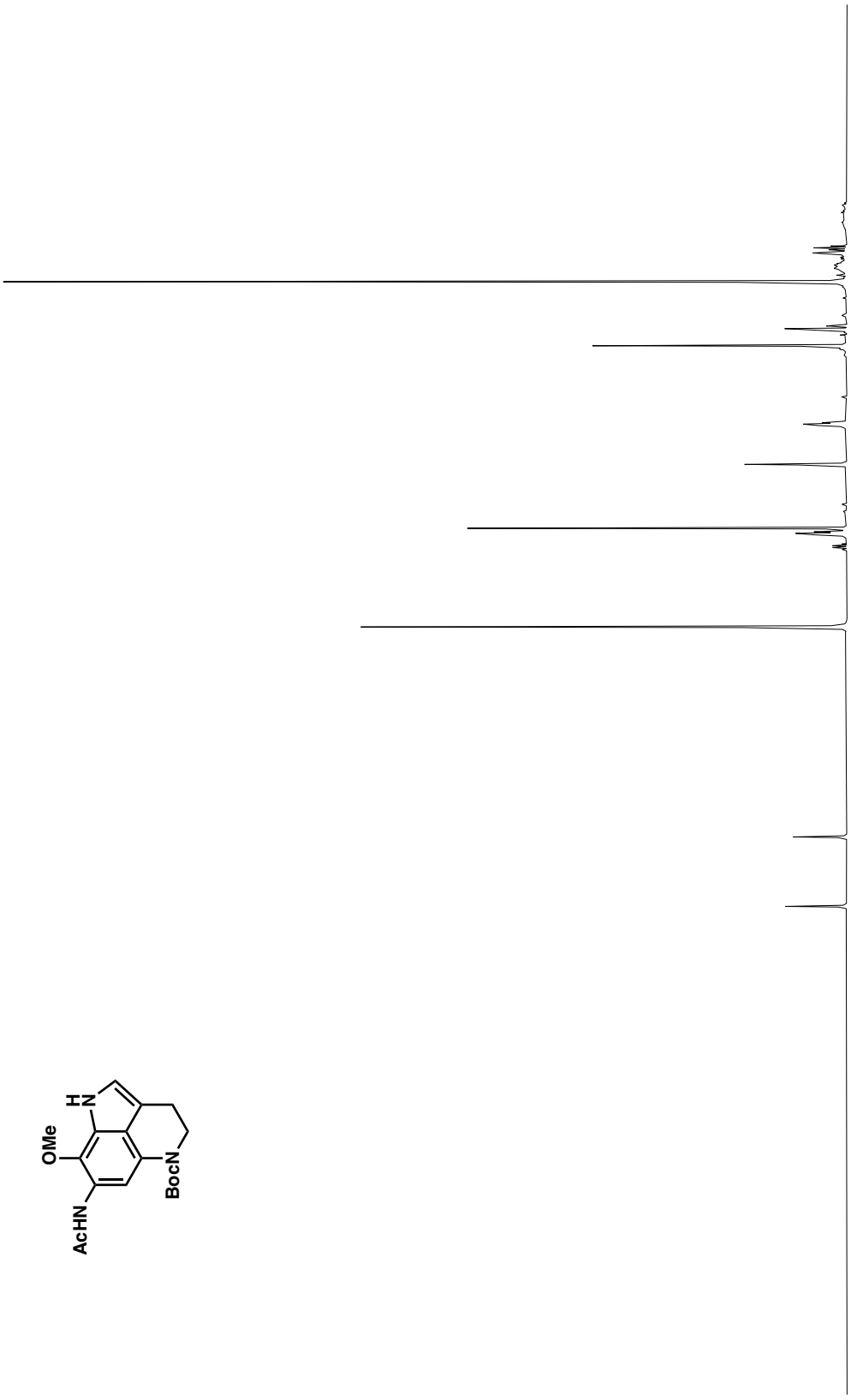


Figure A1.52. ^{1}H NMR (400 MHz, CD_3OD) of compound **58**.

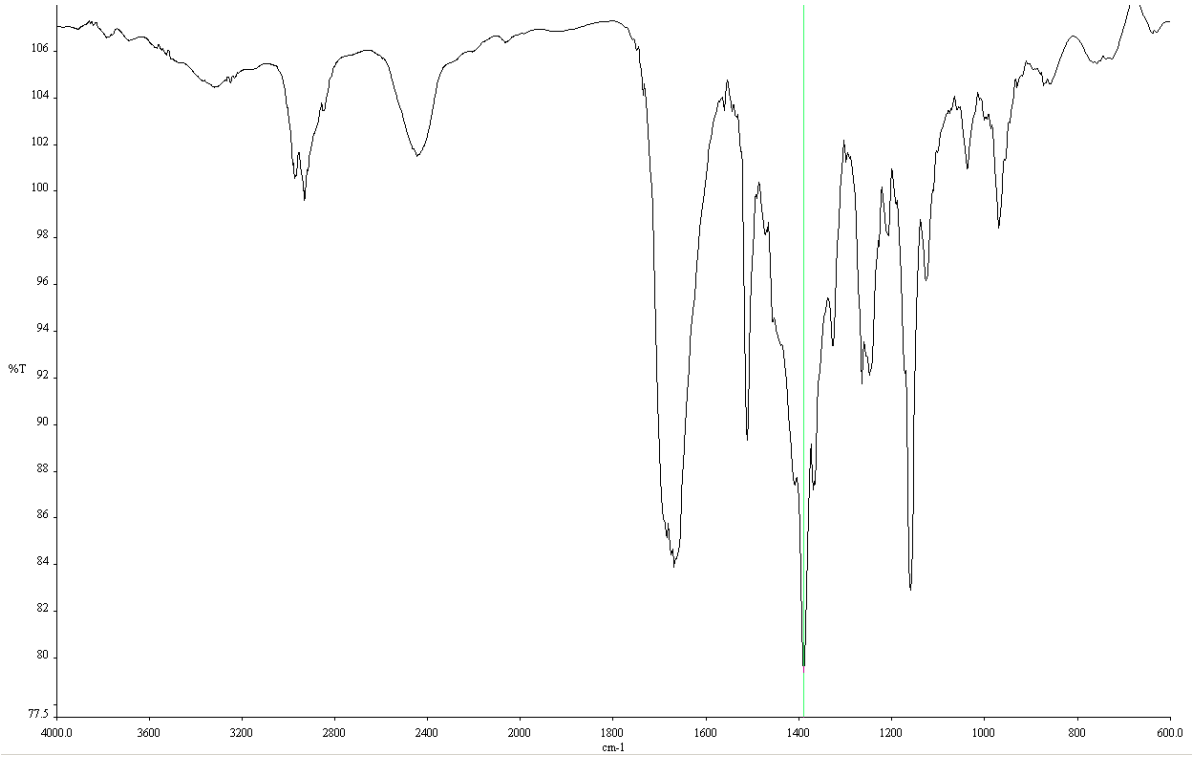


Figure A1.53. Infrared spectrum (Thin Film, NaCl) of compound **58**.

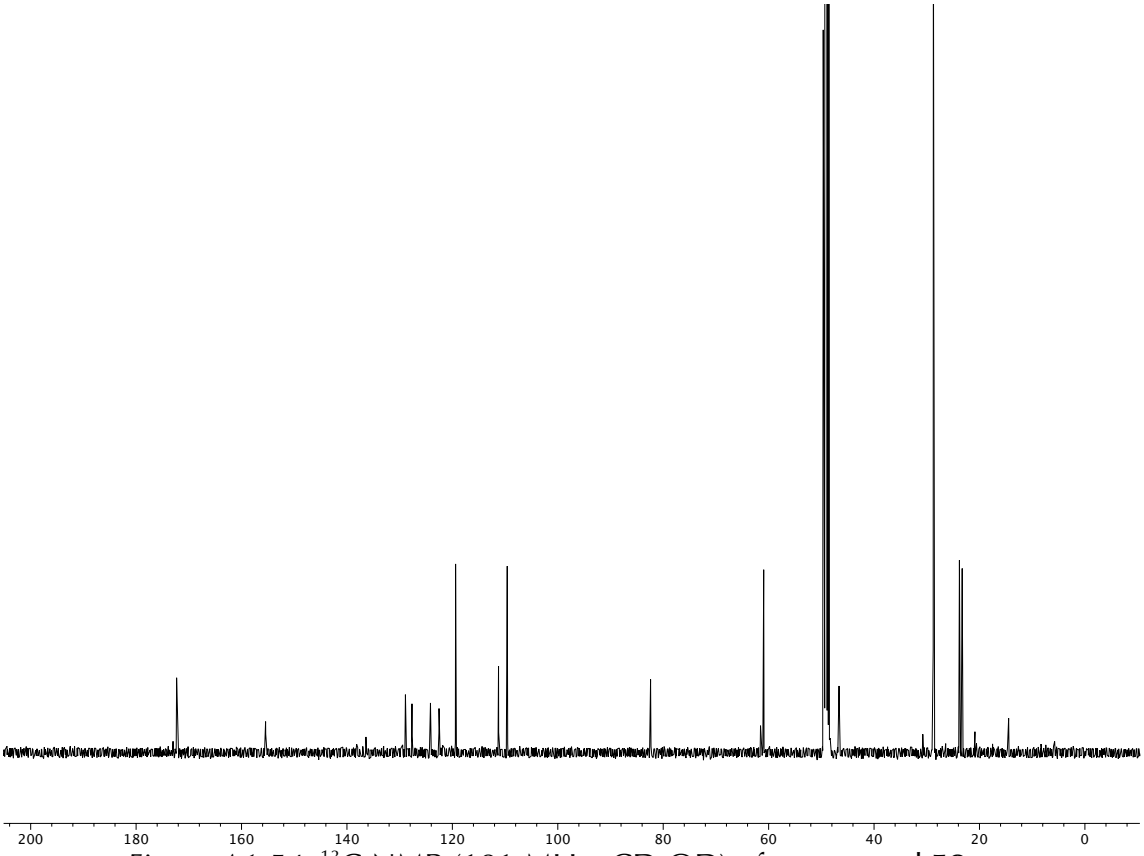


Figure A1.54. ^{13}C NMR (101 MHz, CD_3OD) of compound **58.**

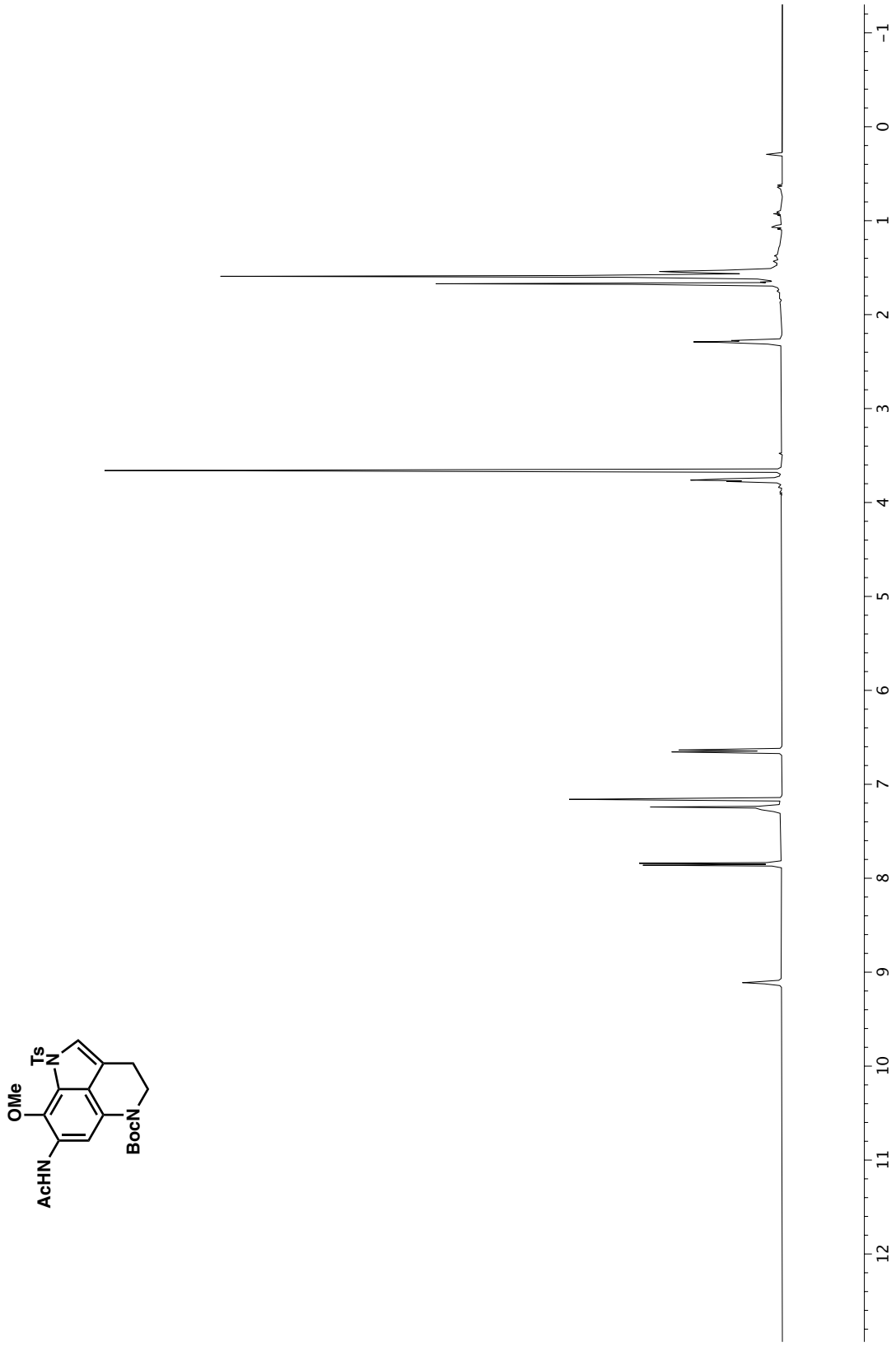


Figure A1.55. ^{1}H NMR (400 MHz, C_6D_6) of compound **59**.

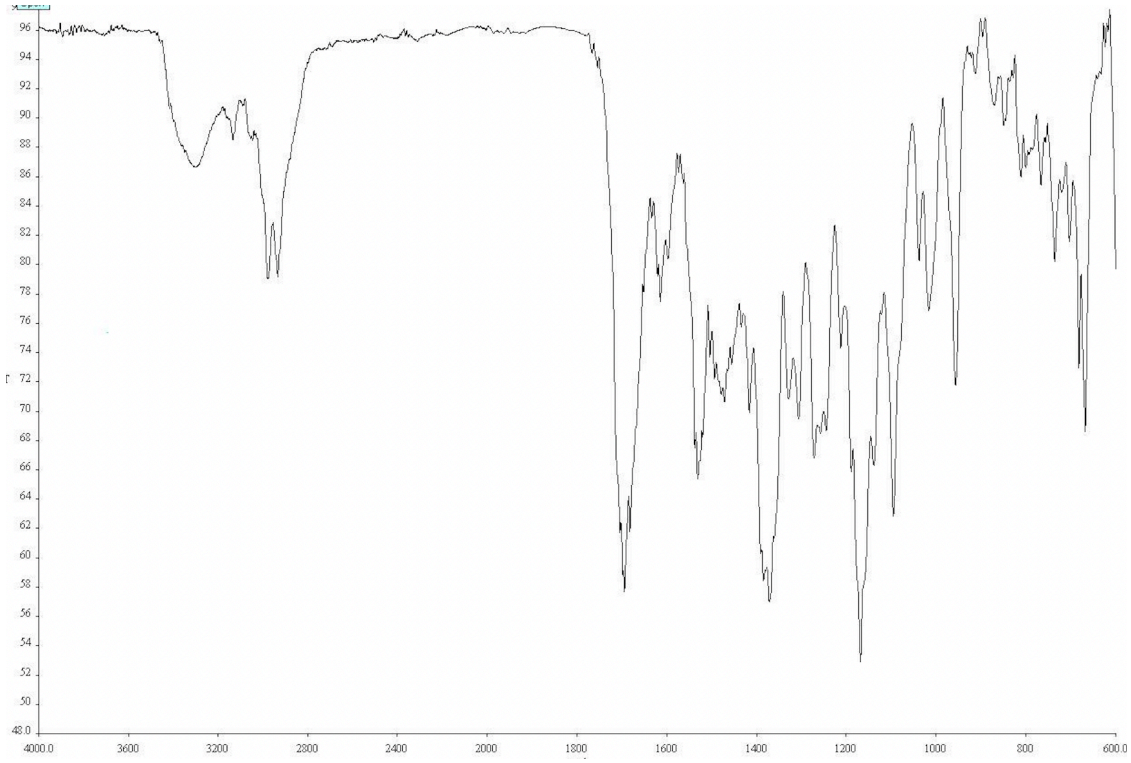


Figure A1.56. Infrared spectrum (Thin Film, NaCl) of compound **59**.

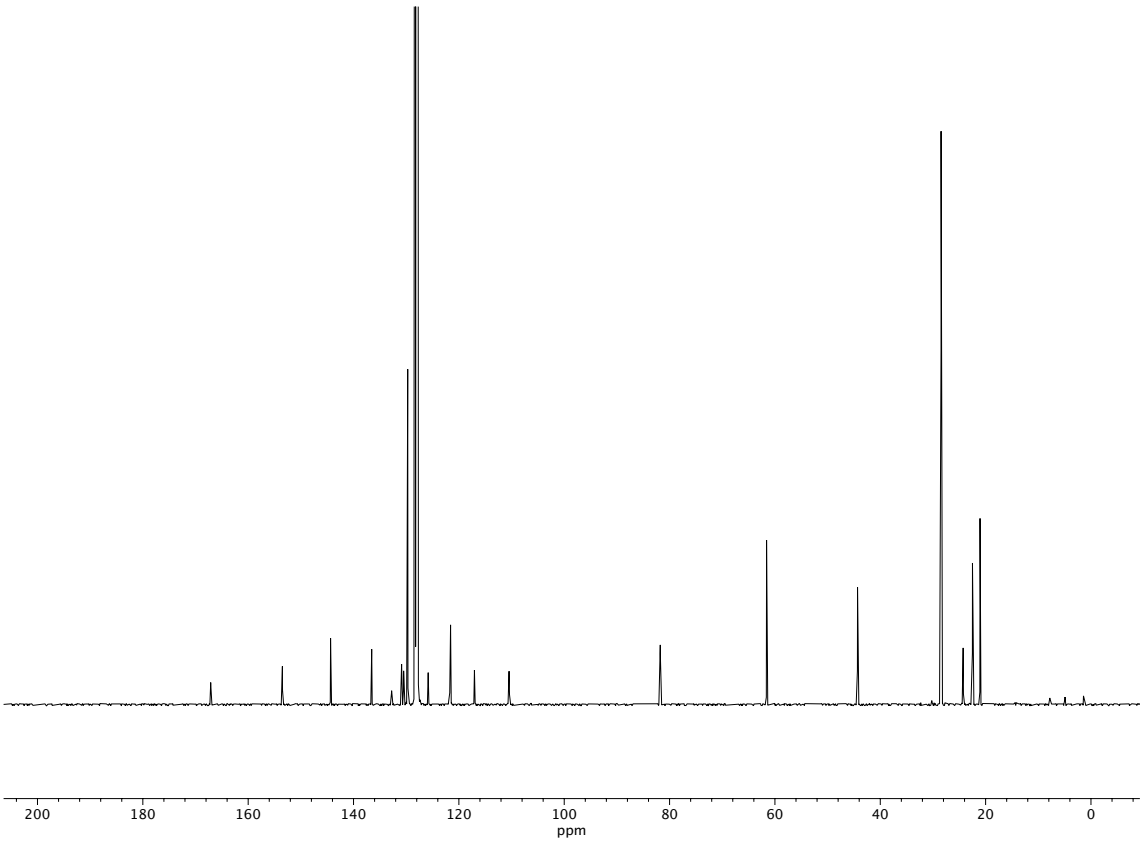


Figure A1.57. ^{13}C NMR (101 MHz, C_6D_6) of compound **59.**

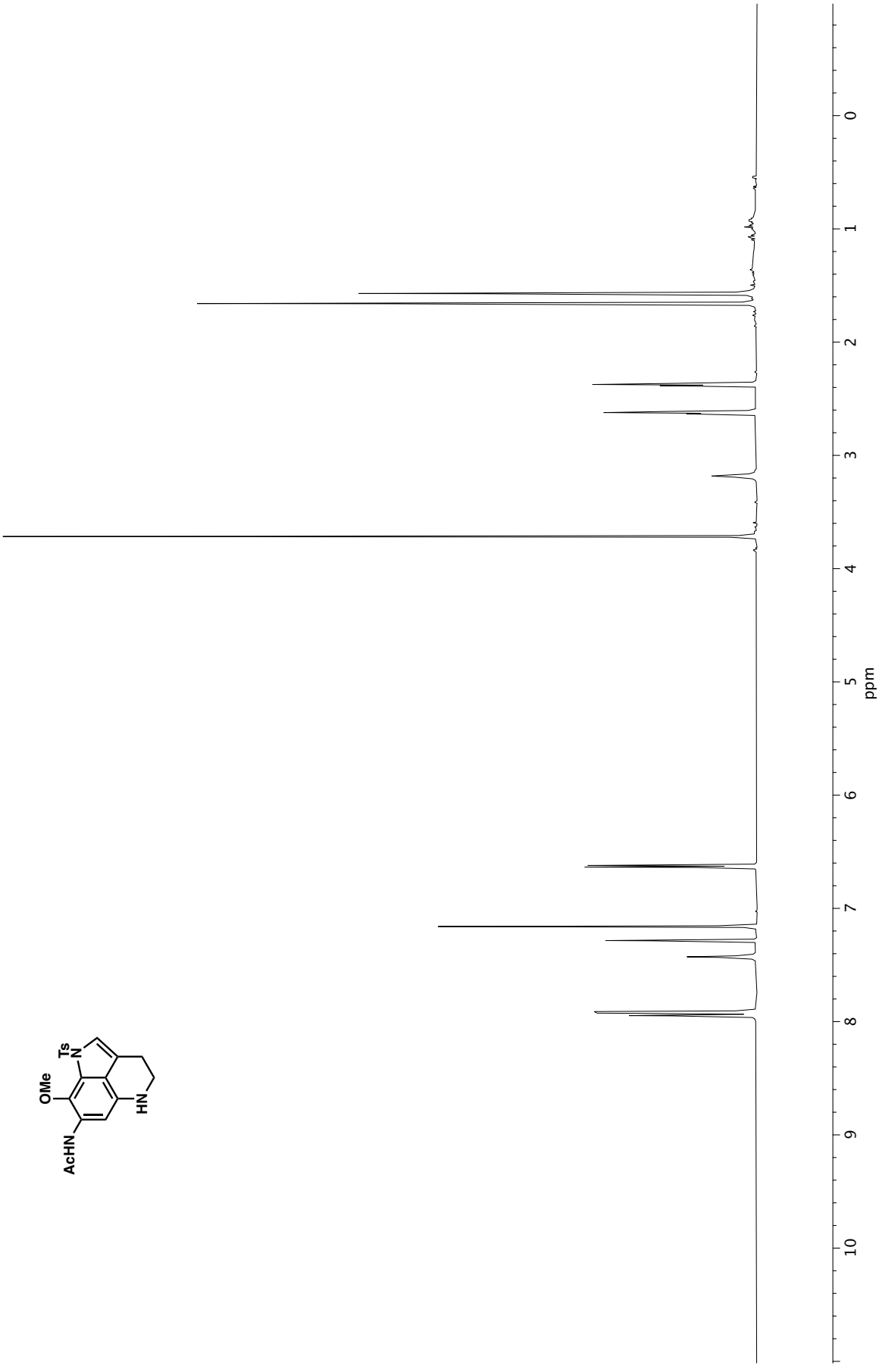


Figure A1.58. ^{1}H NMR (600 MHz, C_6D_6) of compound **60**.

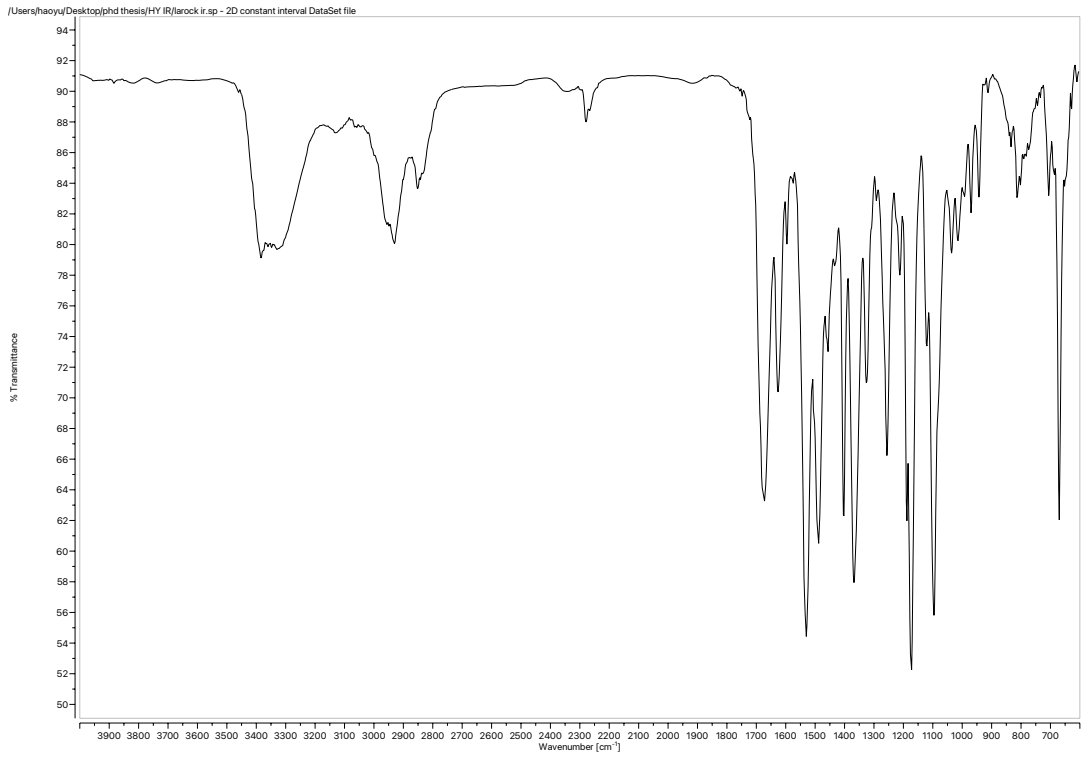


Figure A1.59. Infrared spectrum (Thin Film, NaCl) of compound **60**.

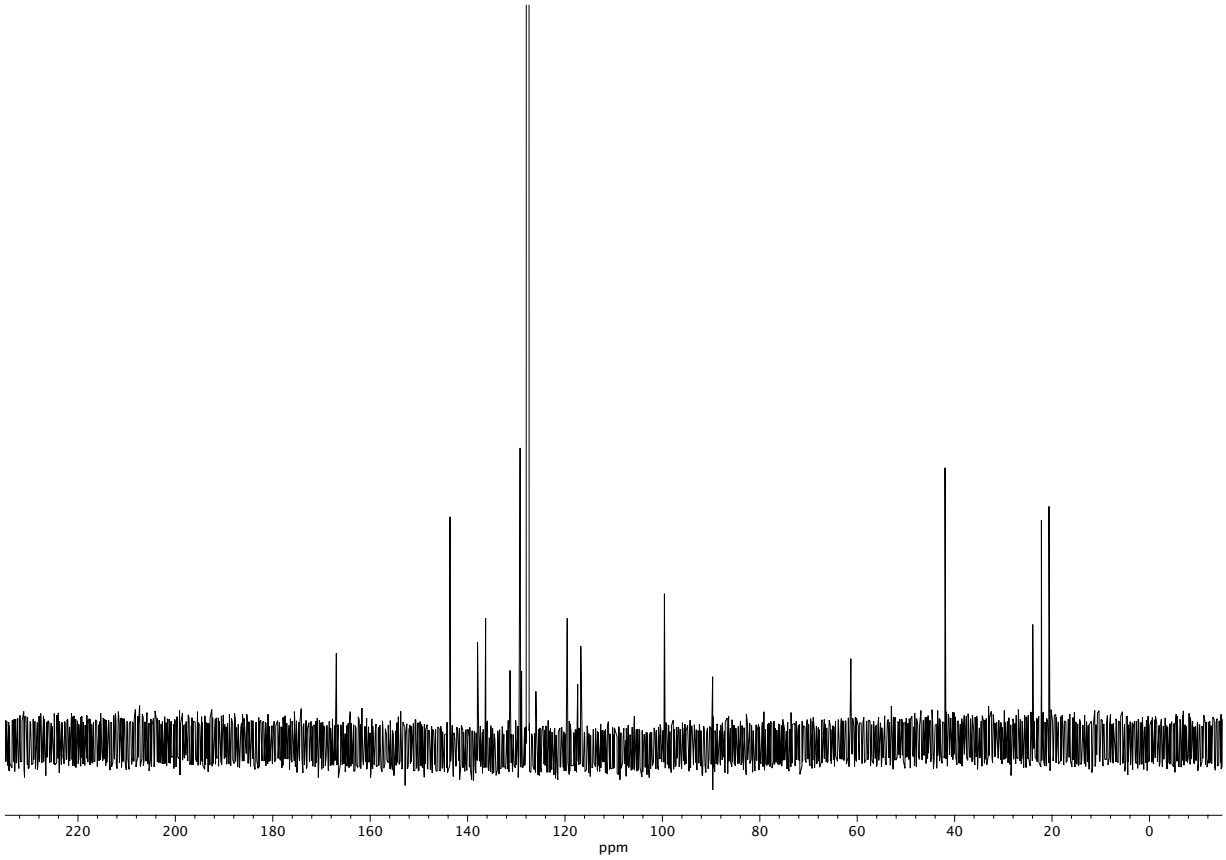


Figure A1.60. ^{13}C NMR (151 MHz, C_6D6) of compound **60.**

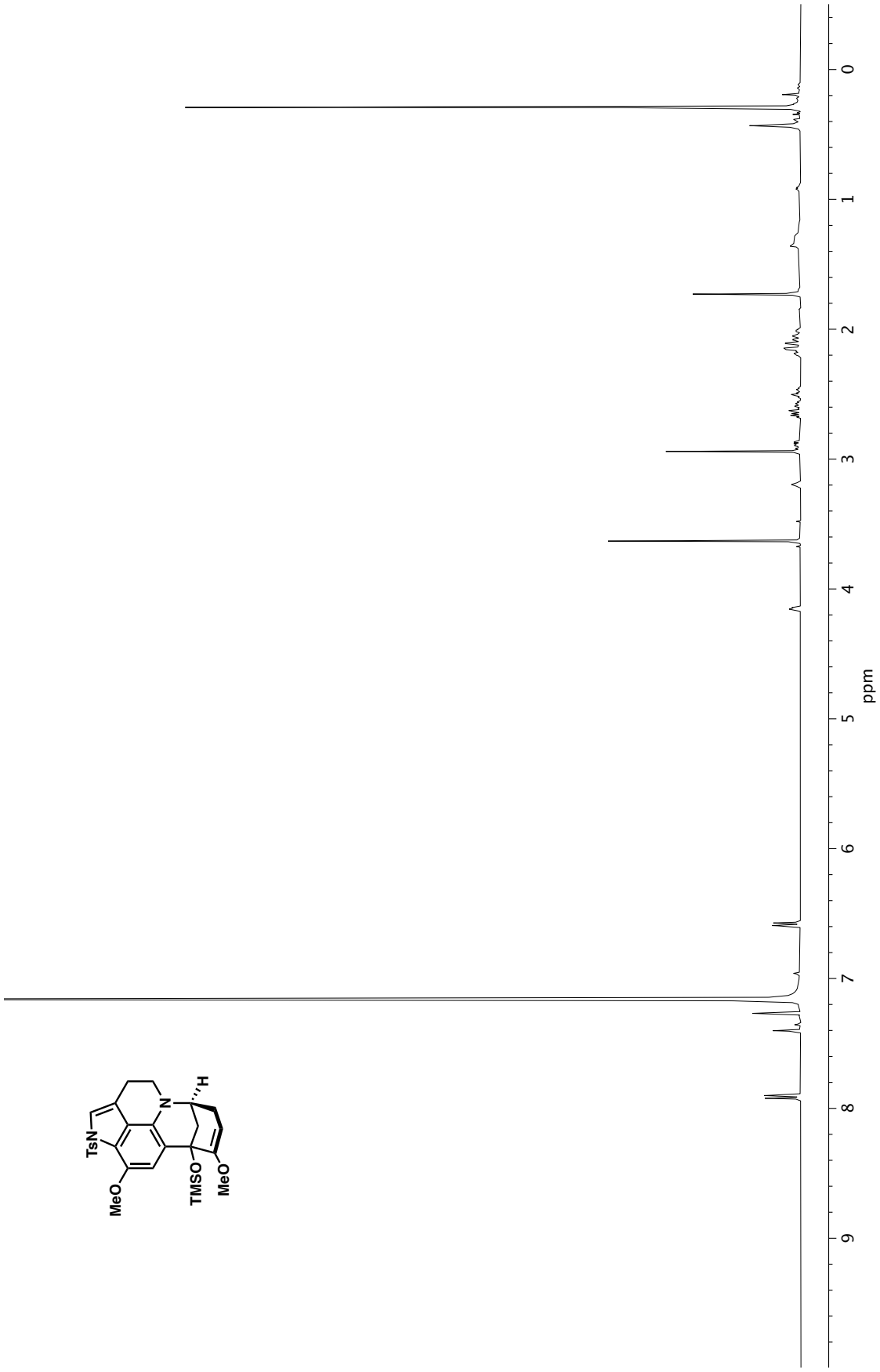


Figure A1.61. ^{1}H NMR (400 MHz, C_6D_6) of compound **62**.

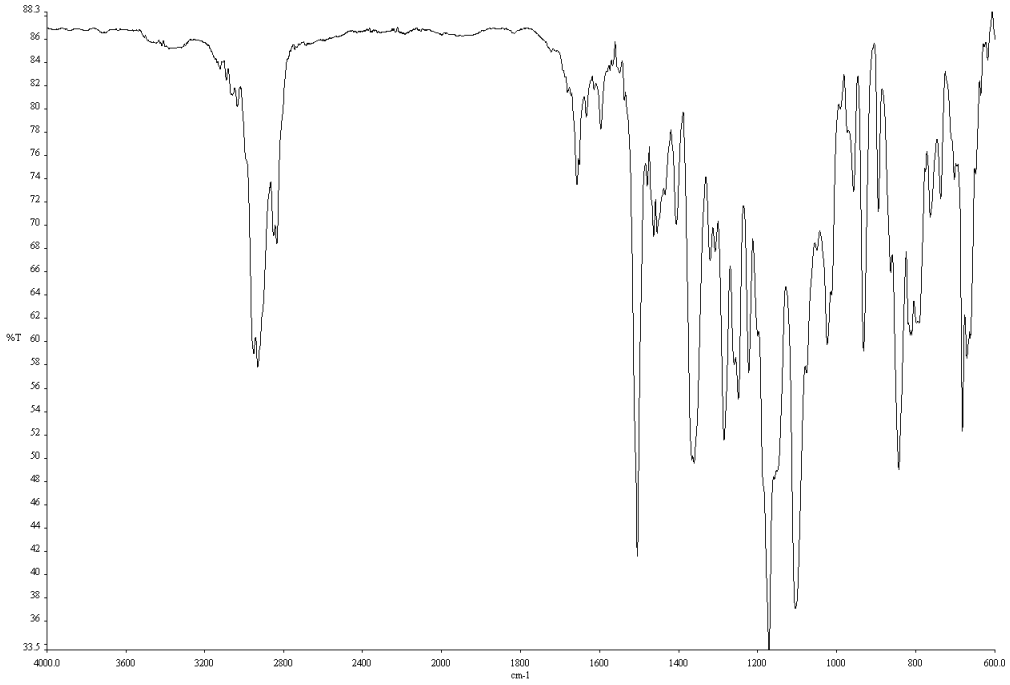


Figure A1.62. Infrared spectrum (Thin Film, NaCl) of compound **62**.

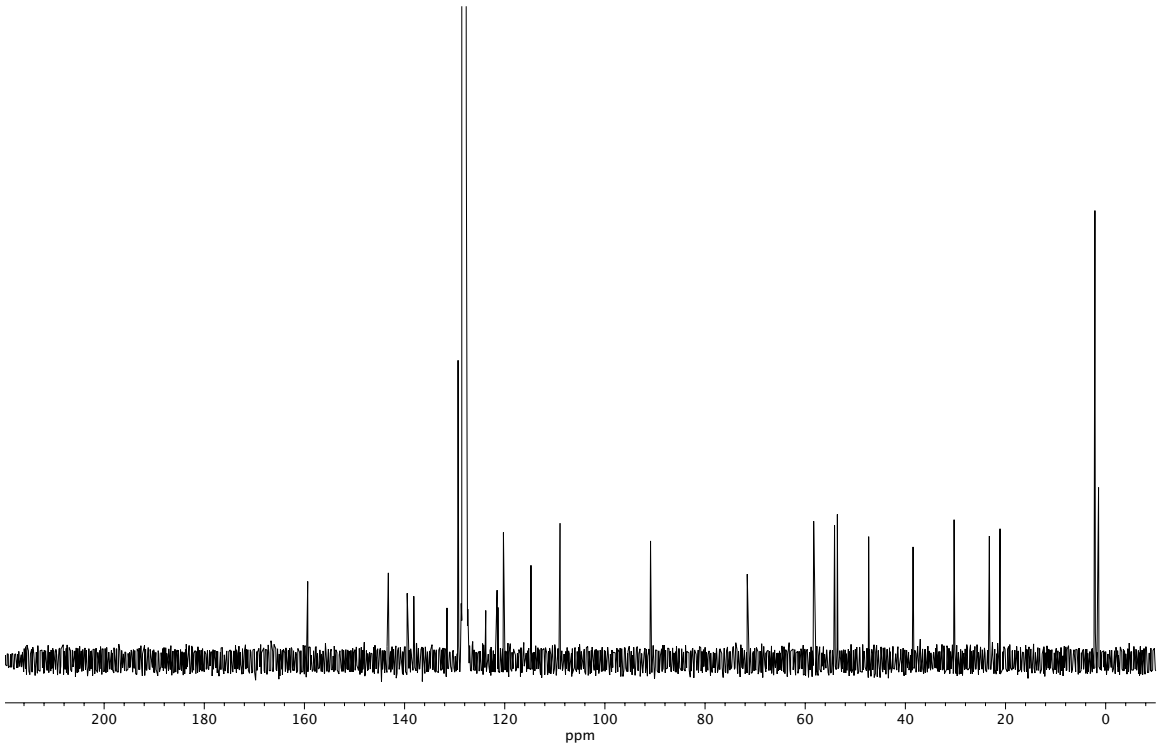


Figure A1.63. ^{13}C NMR (101 MHz, C_6D_6) of compound **62**.

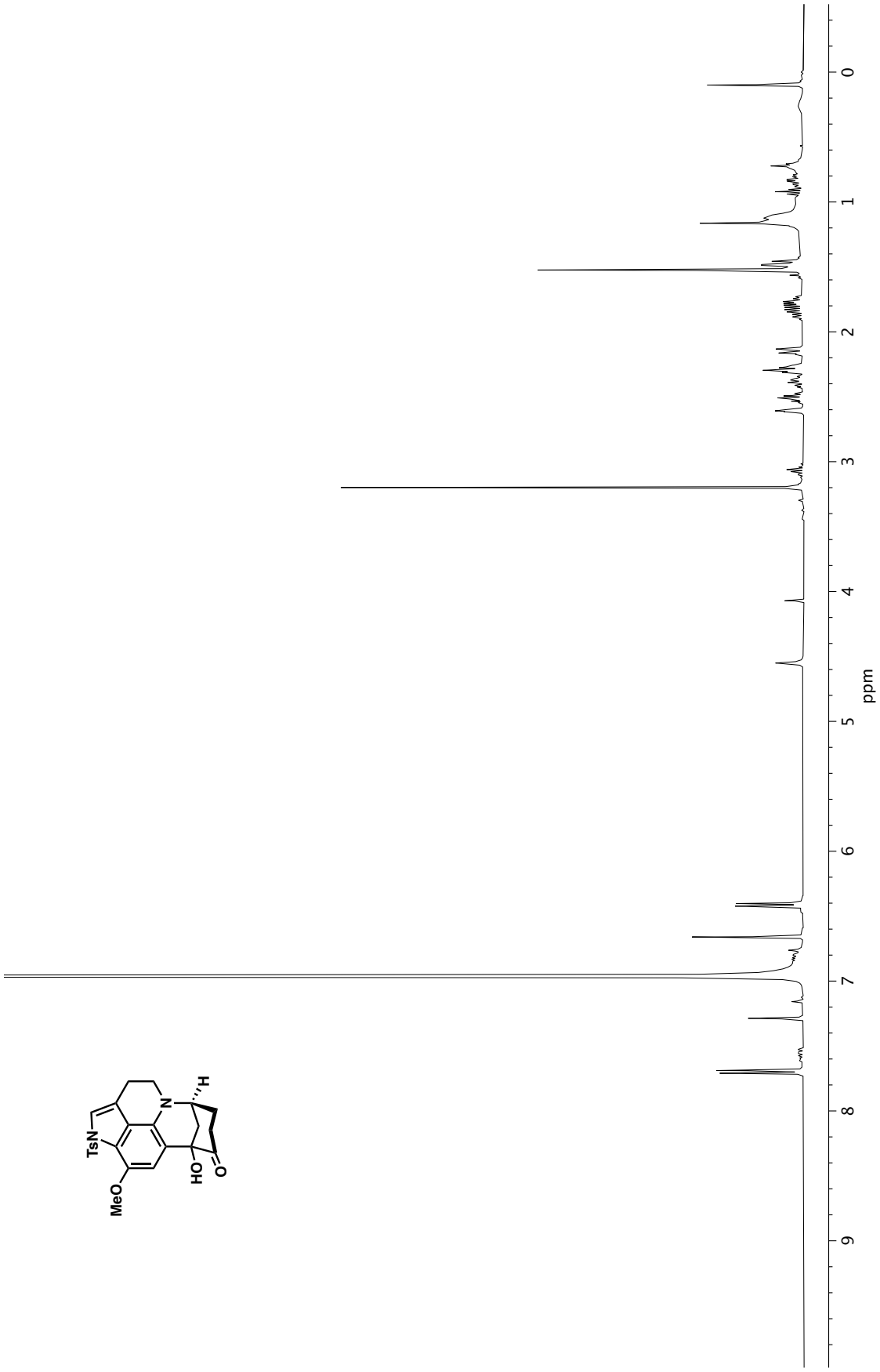


Figure A1.64. ^{1}H NMR (400 MHz, C_6D_6) of compound **64**.

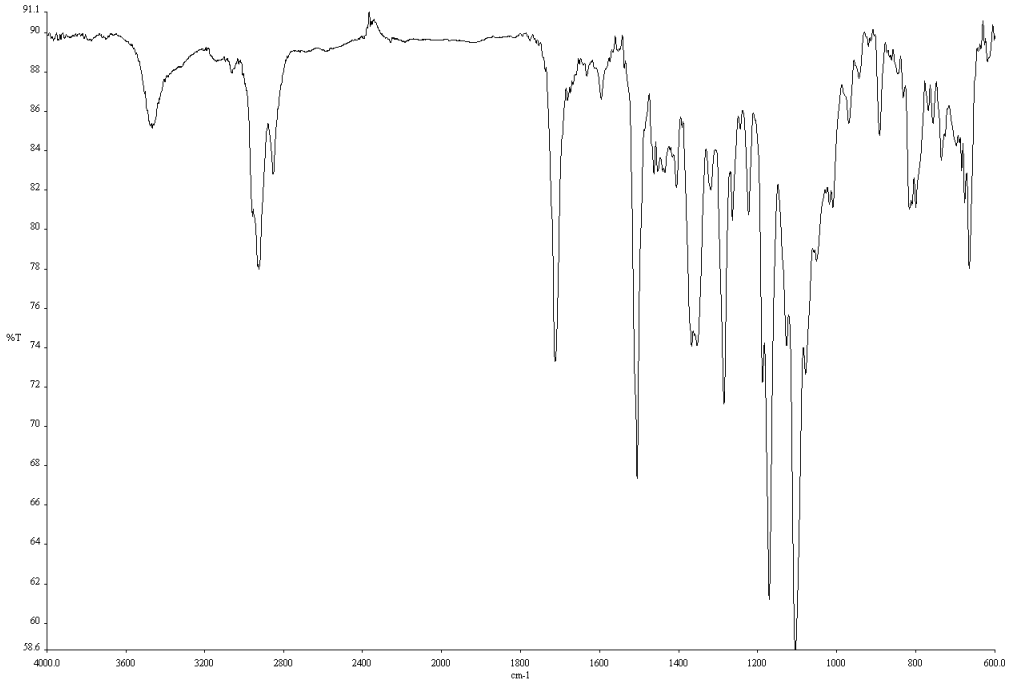


Figure A1.65. Infrared spectrum (Thin Film, NaCl) of compound **64**.

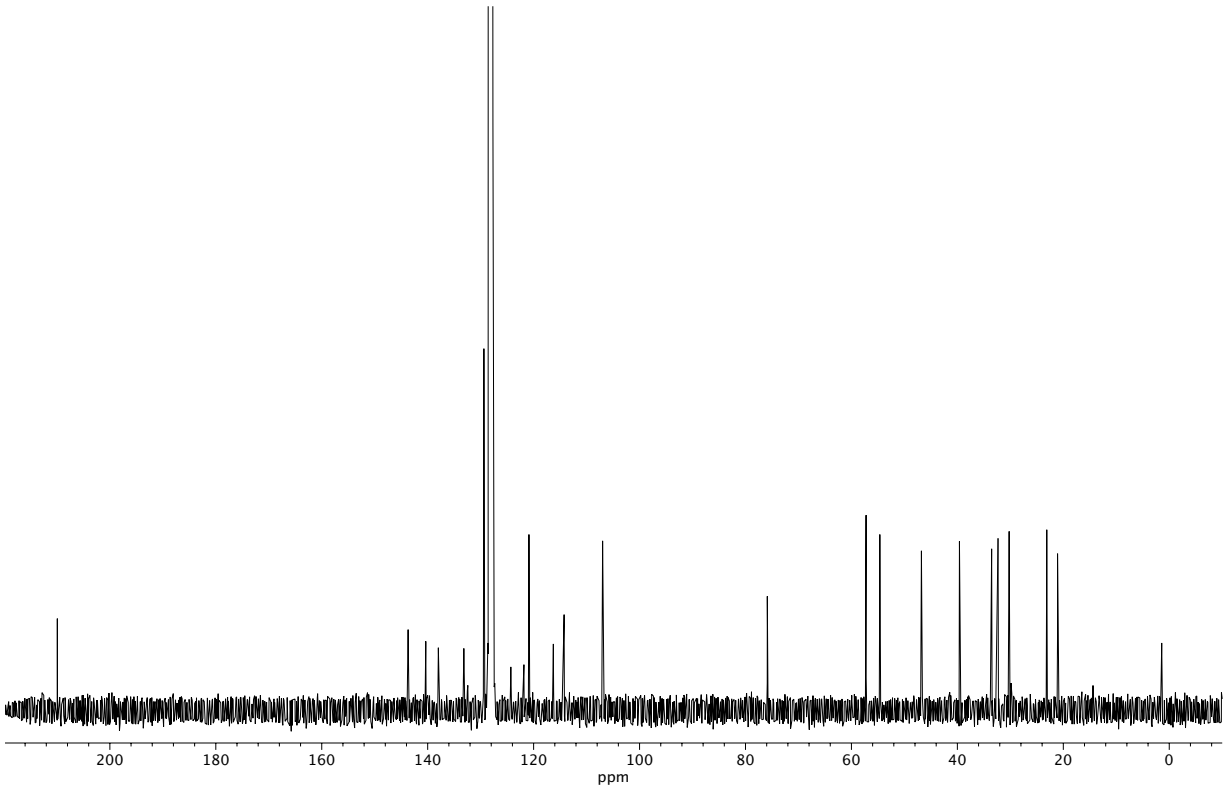


Figure A1.66. ^{13}C NMR (101 MHz, C_6D_6) of compound **64.**

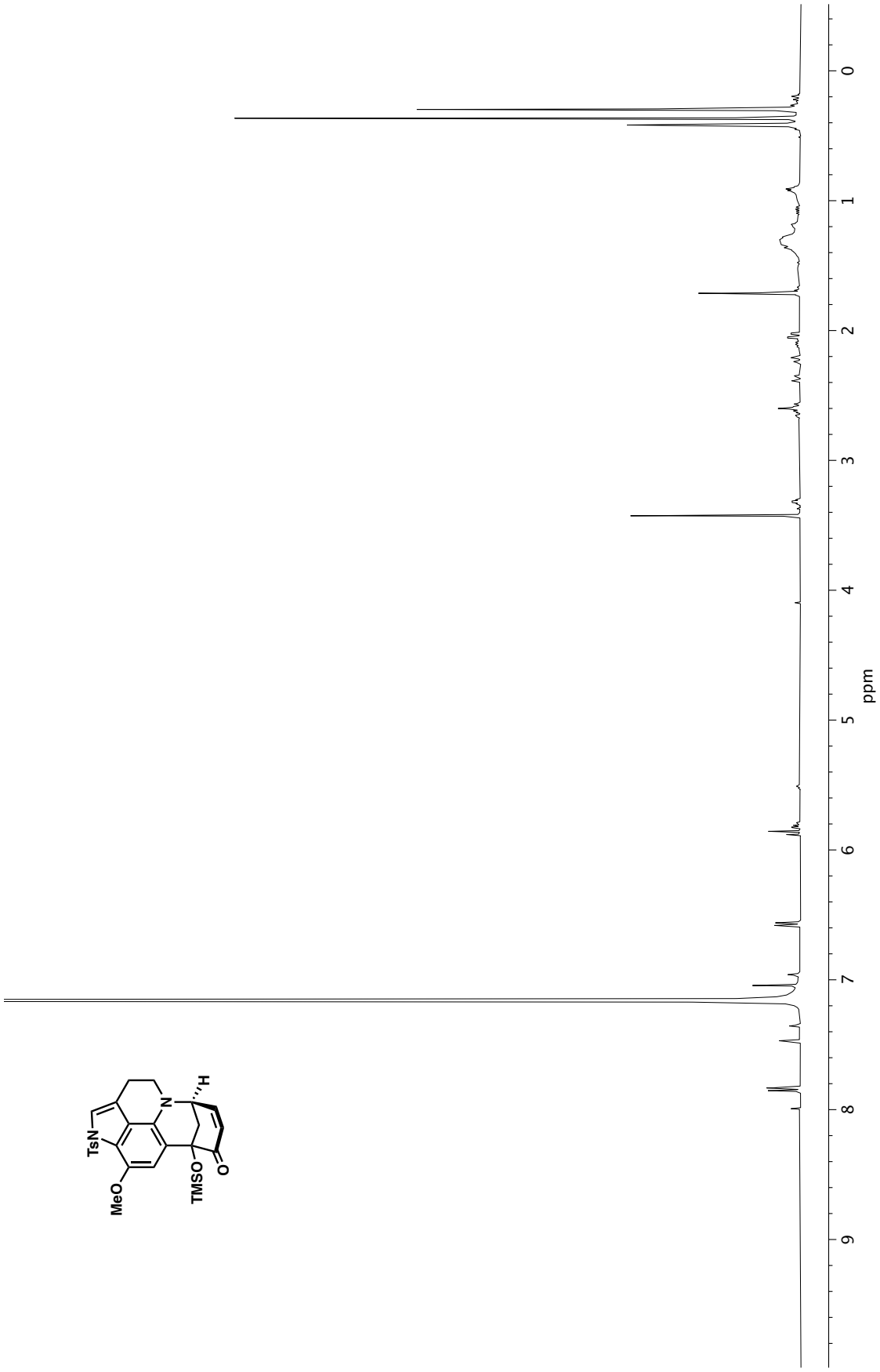


Figure A1.67. ^{1}H NMR (400 MHz, C_6D_6) of compound **65**.

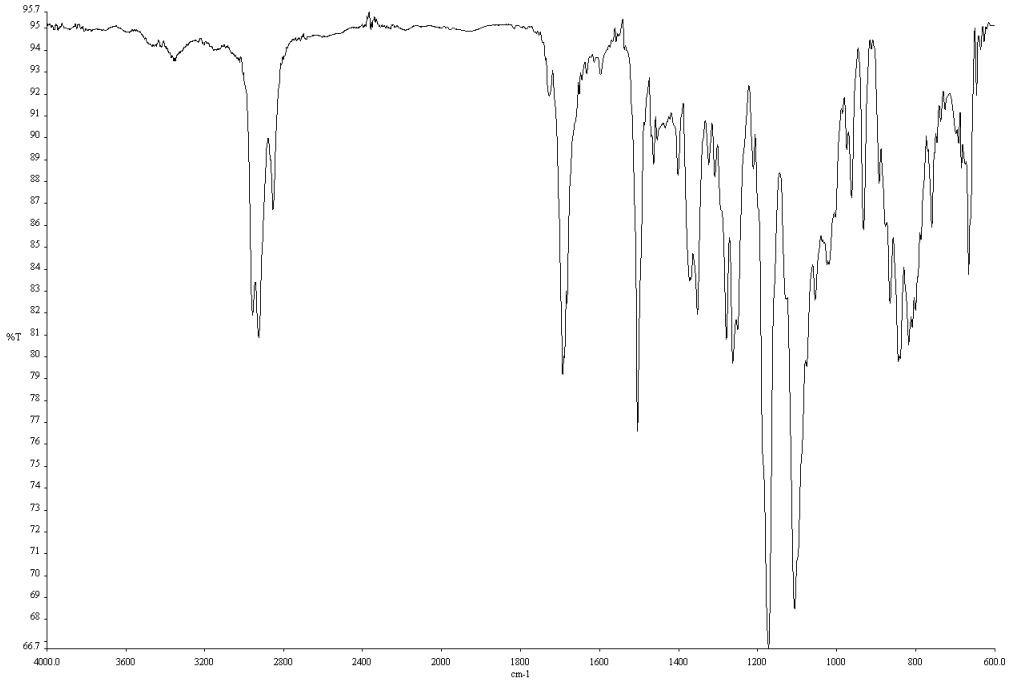


Figure A1.68. Infrared spectrum (Thin Film, NaCl) of compound **65**.

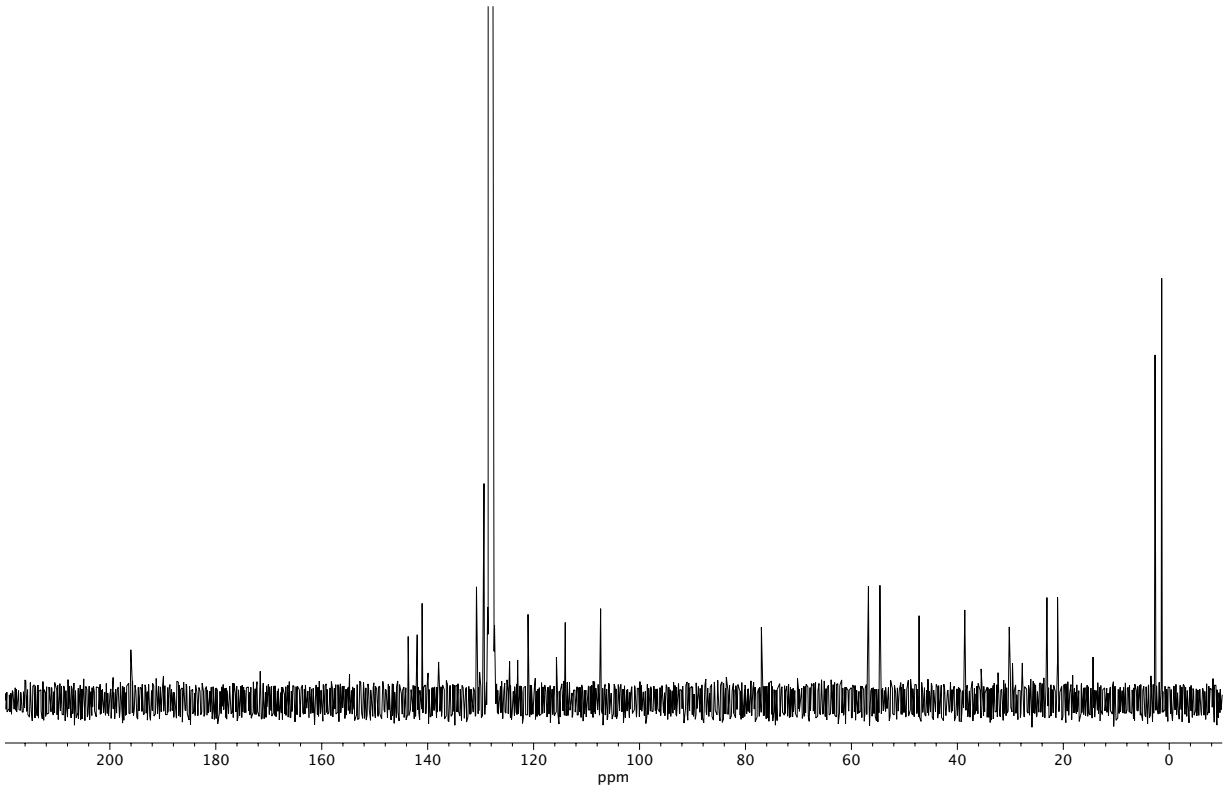


Figure A1.69. ^{13}C NMR (101 MHz, C_6D_6) of compound **65.**

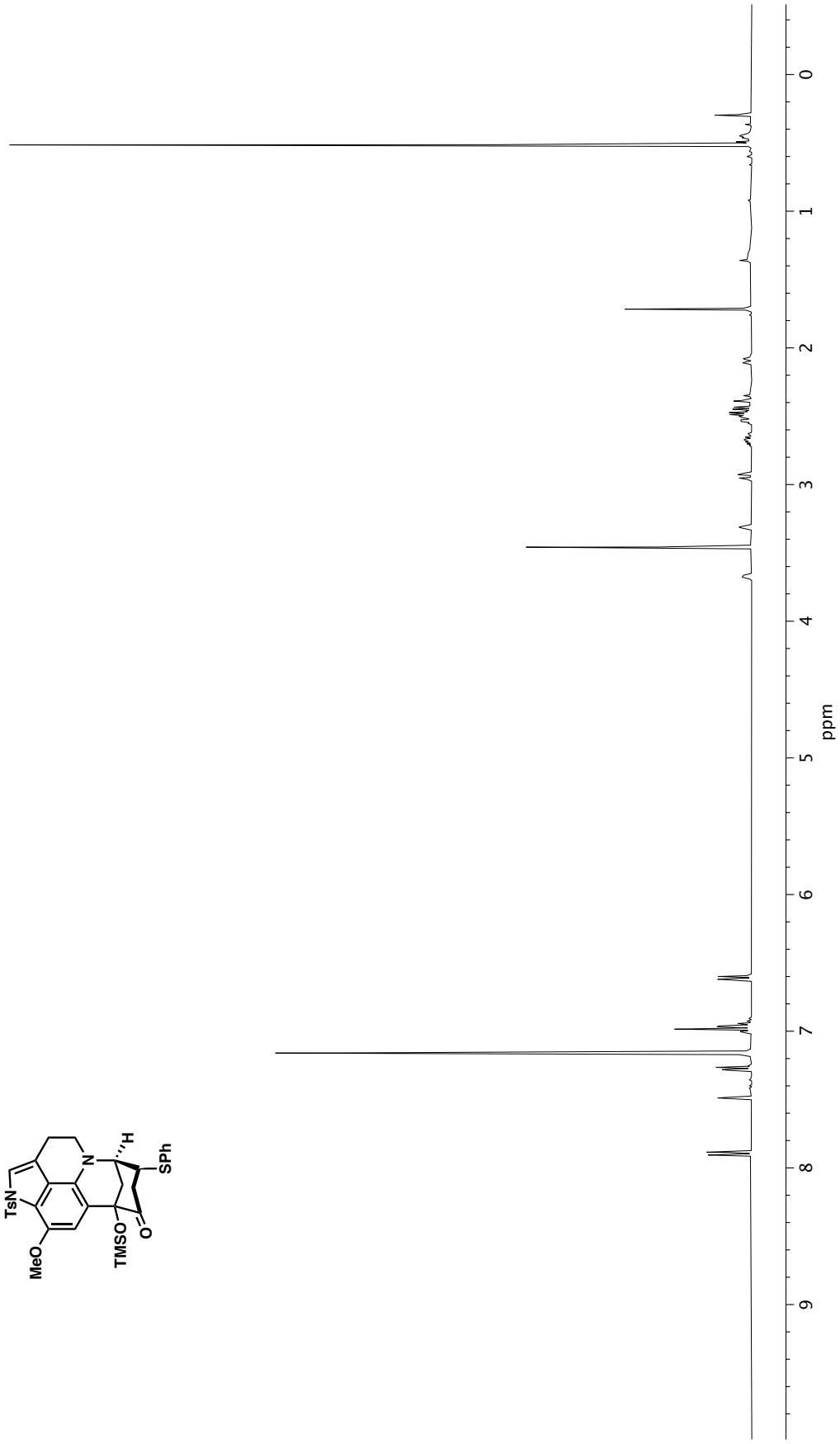


Figure A1.70. ^{1}H NMR (400 MHz, C_6D_6) of compound **66**.

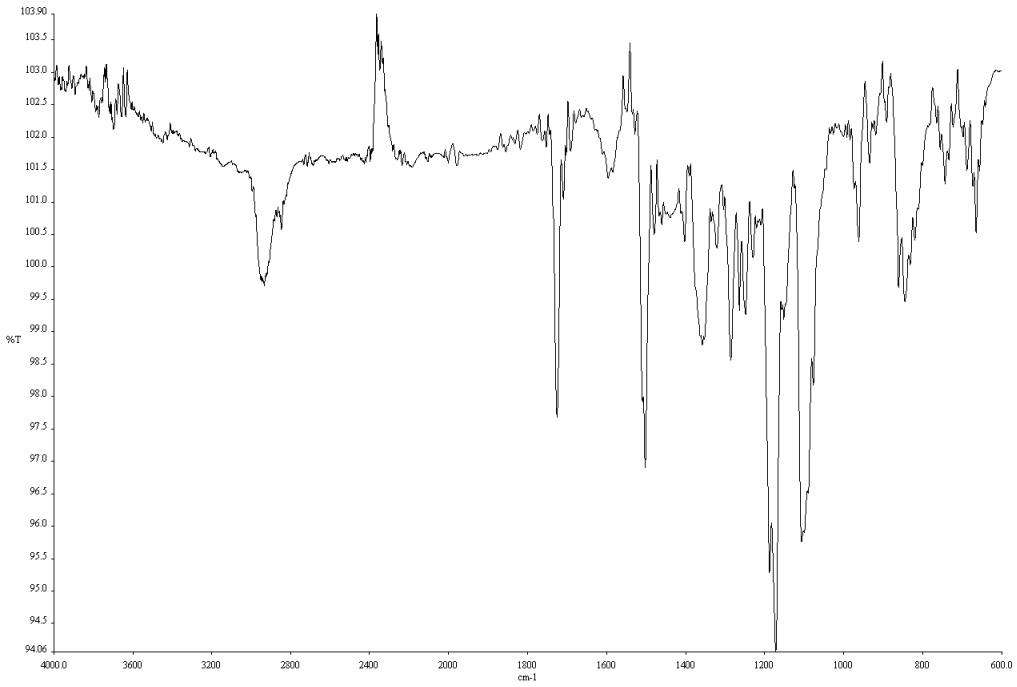


Figure A1.71. Infrared spectrum (Thin Film, NaCl) of compound **66**.

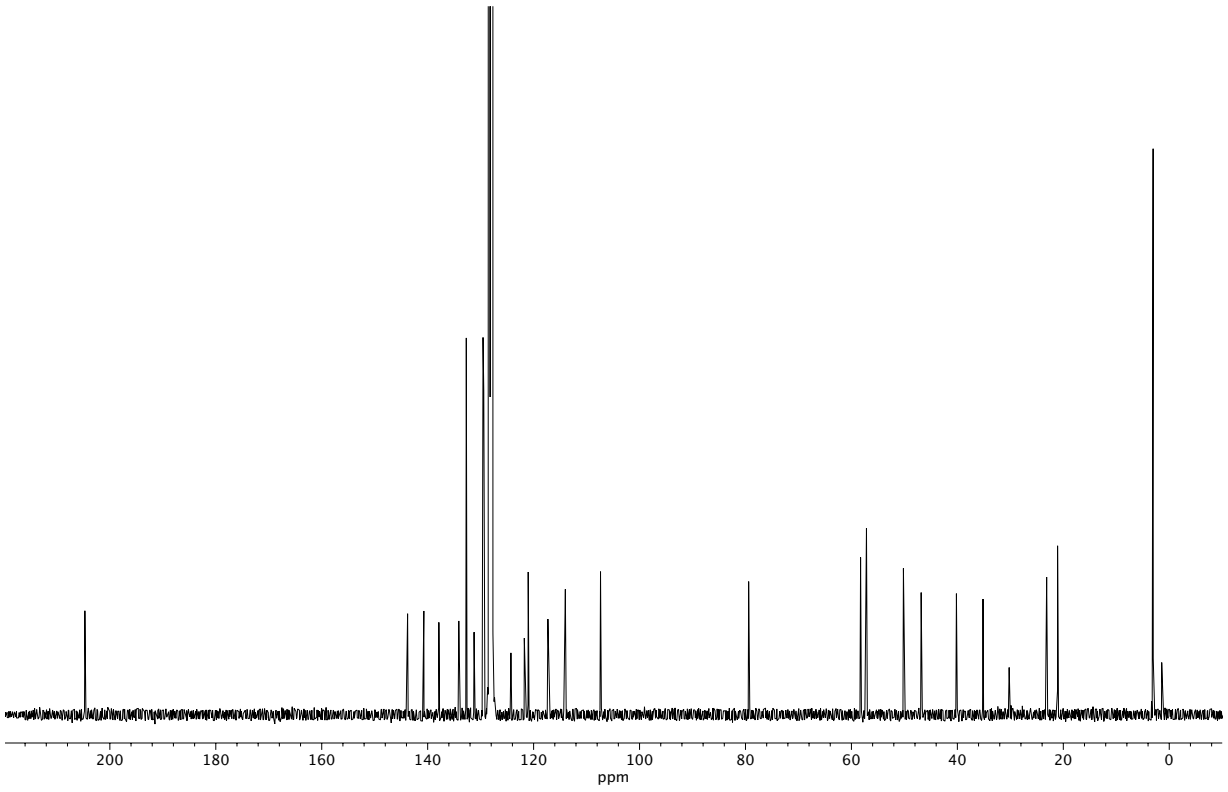


Figure A1.72. ^{13}C NMR (101 MHz, C_6D_6) of compound **66.**

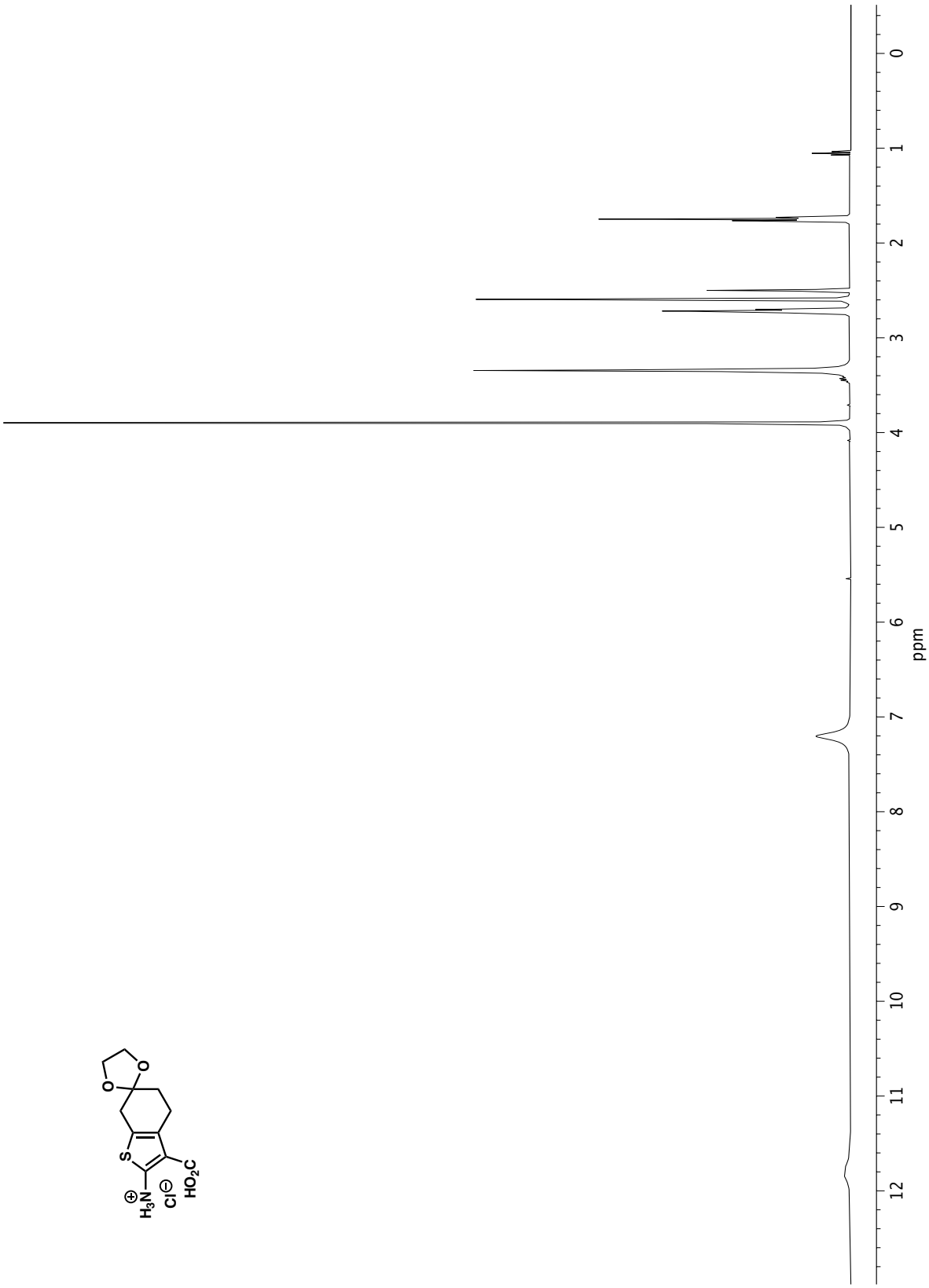


Figure A1.73. ^{1}H NMR (400 MHz, DMSO-d_6) of compound **75**.

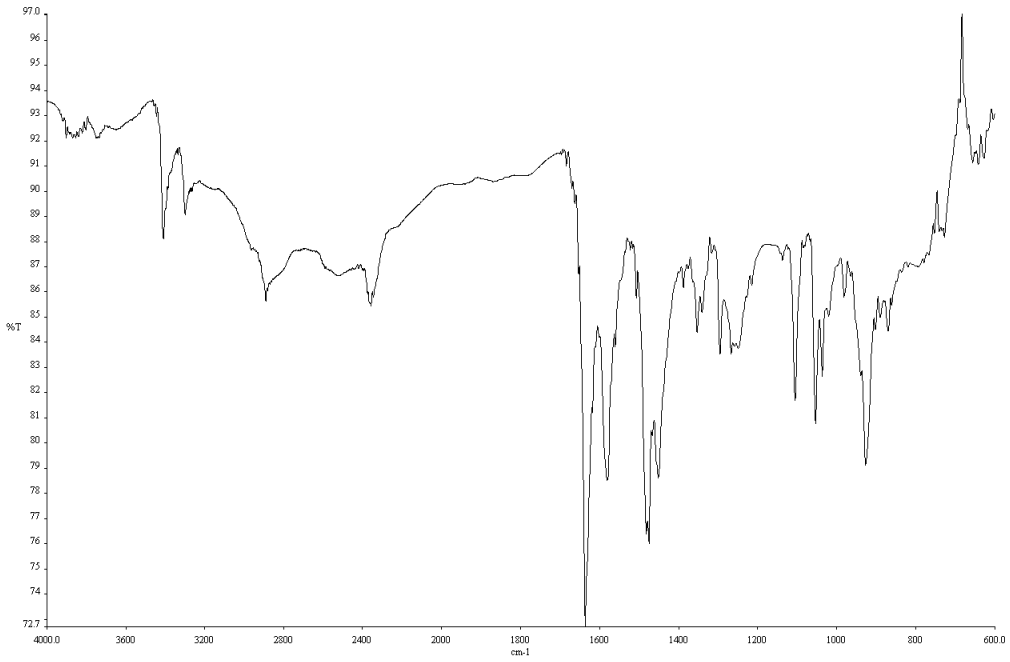


Figure A1.74. Infrared spectrum (Thin Film, NaCl) of compound **75**.

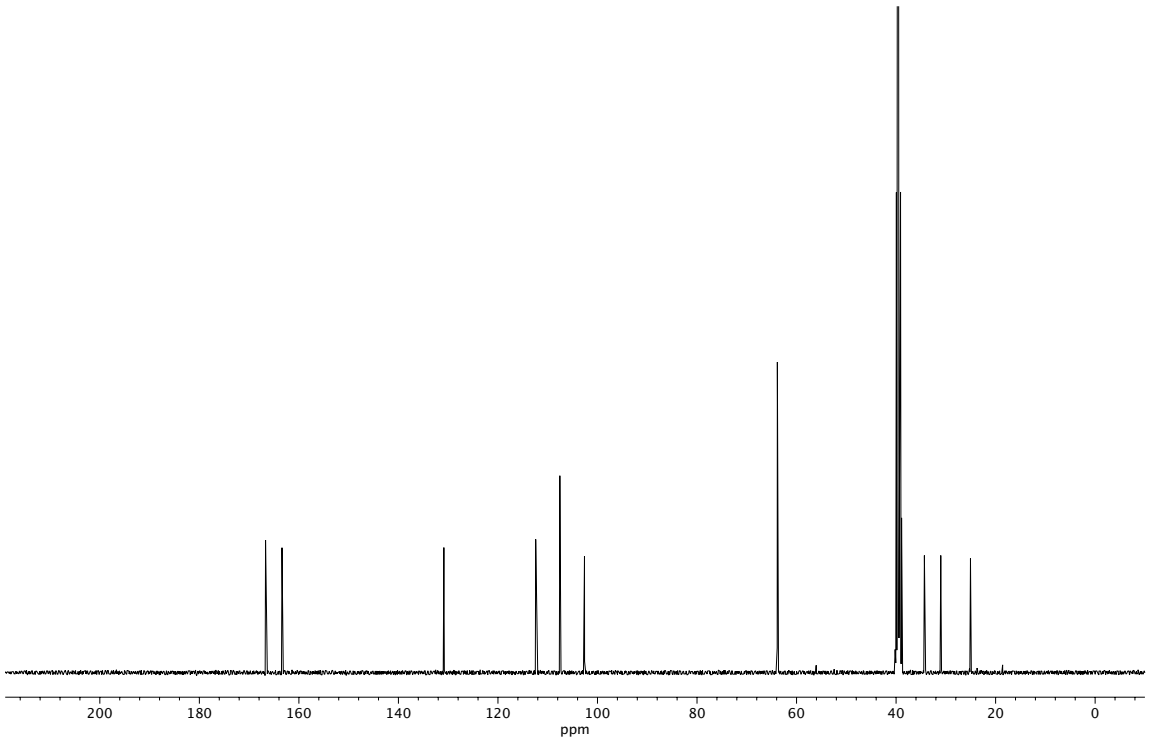


Figure A1.75. ^{13}C NMR (101 MHz, DMSO-d_6) of compound **75.**

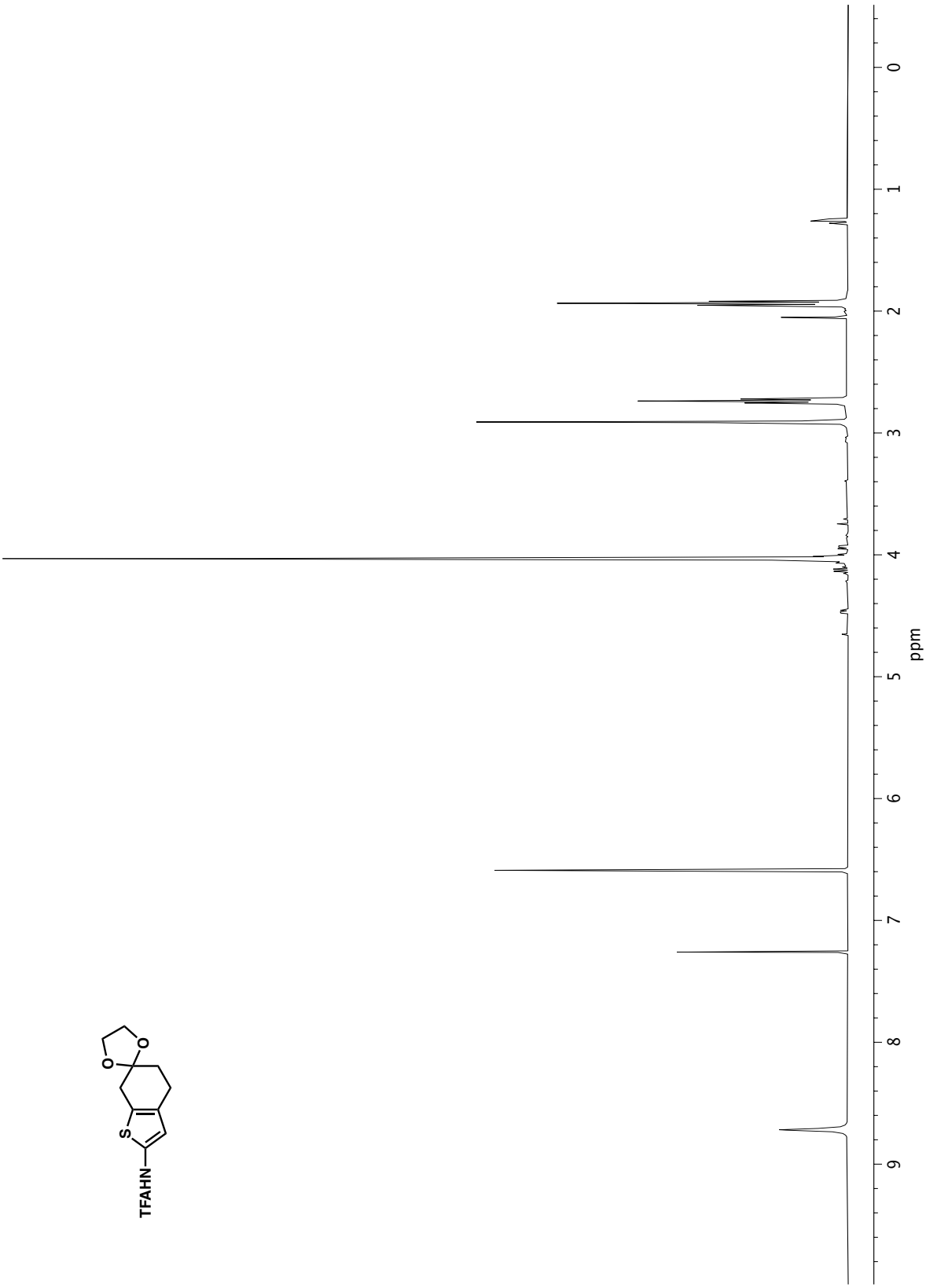


Figure A1.76. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **76**.

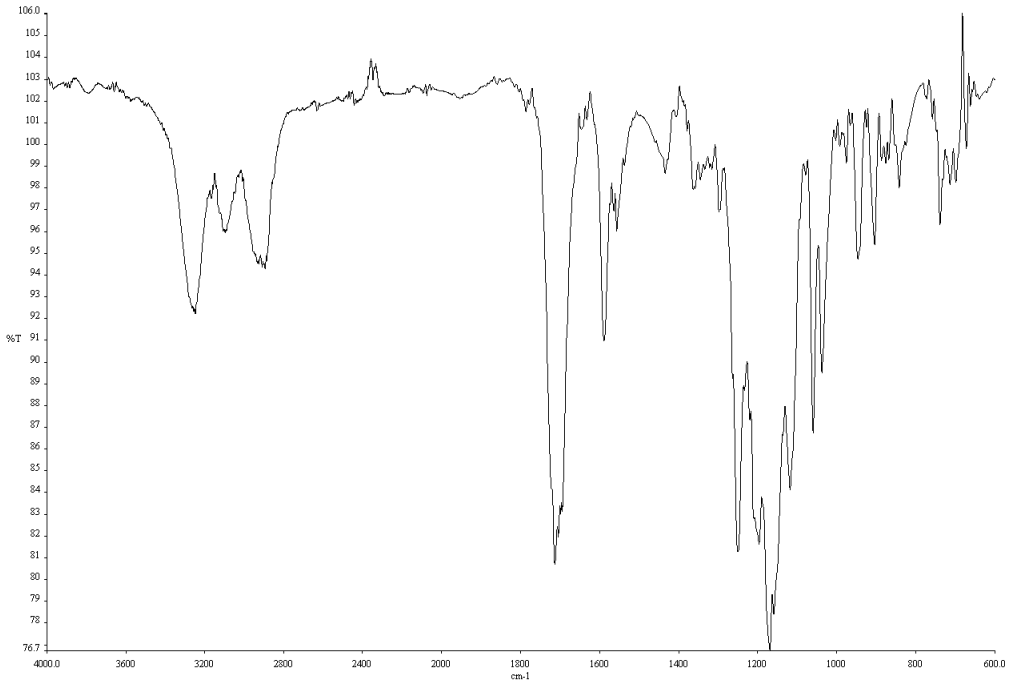


Figure A1.77. Infrared spectrum (Thin Film, NaCl) of compound **76**.

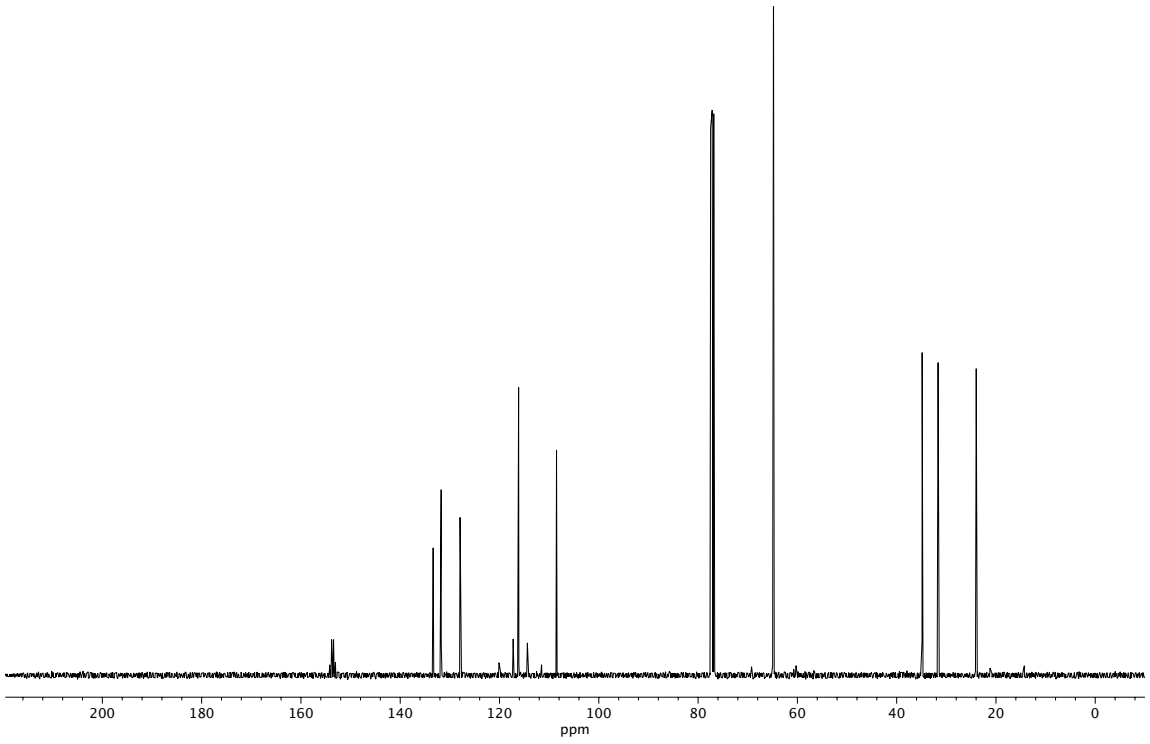


Figure A1.78. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **76.**

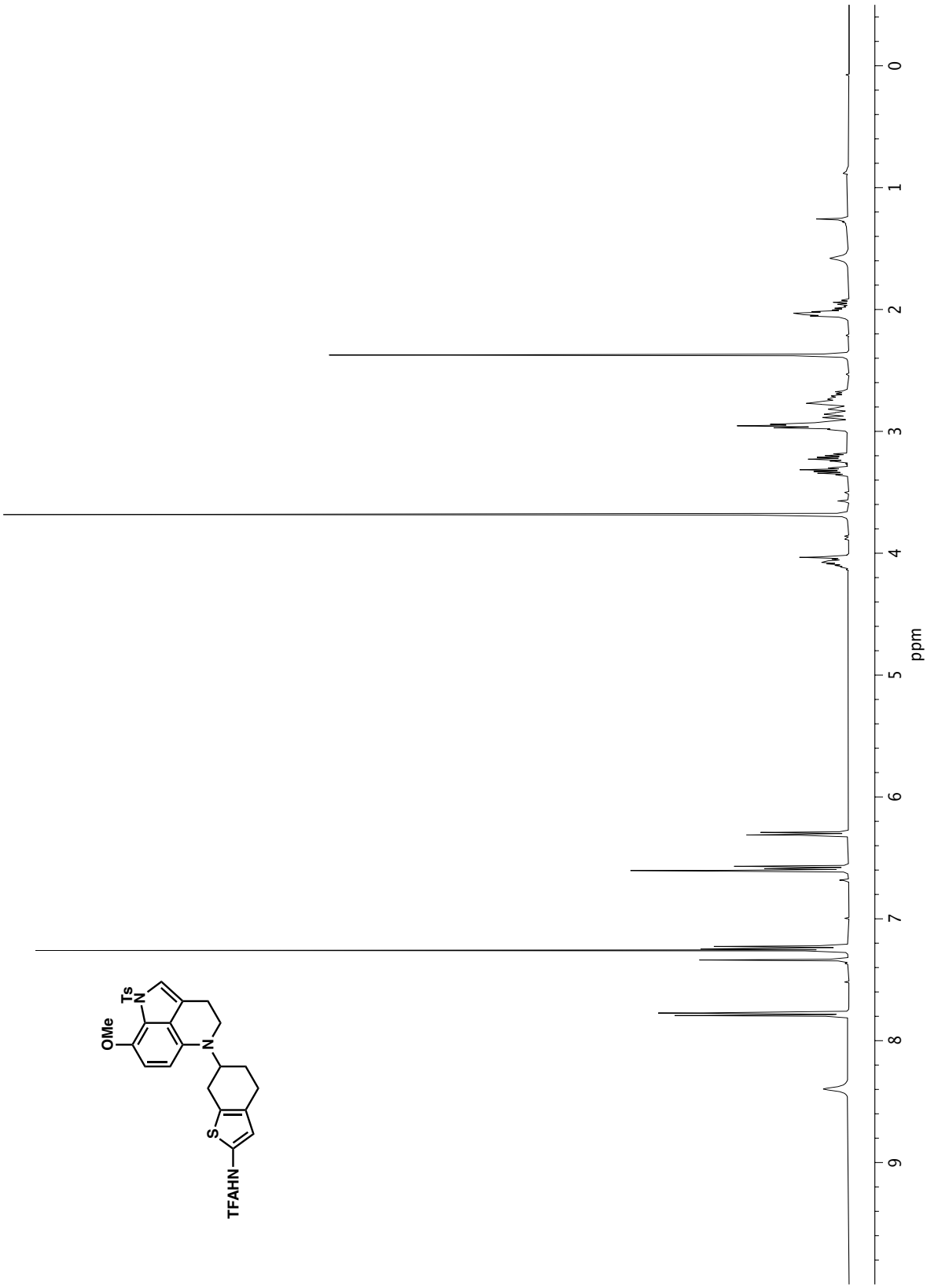


Figure A1.79. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **78**.

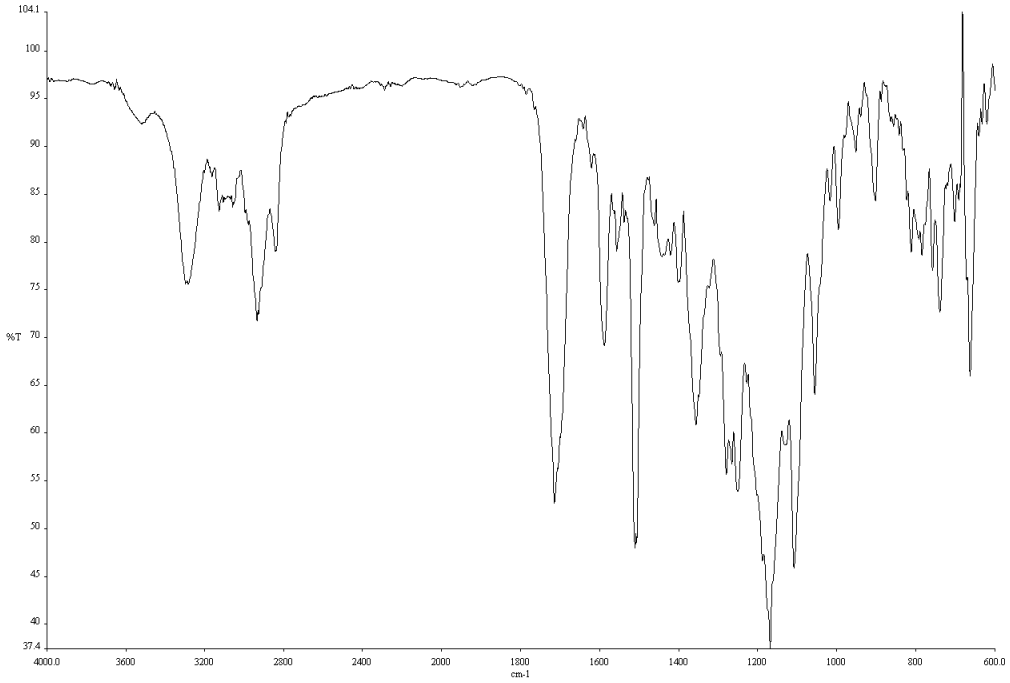


Figure A1.80. Infrared spectrum (Thin Film, NaCl) of compound **78**.

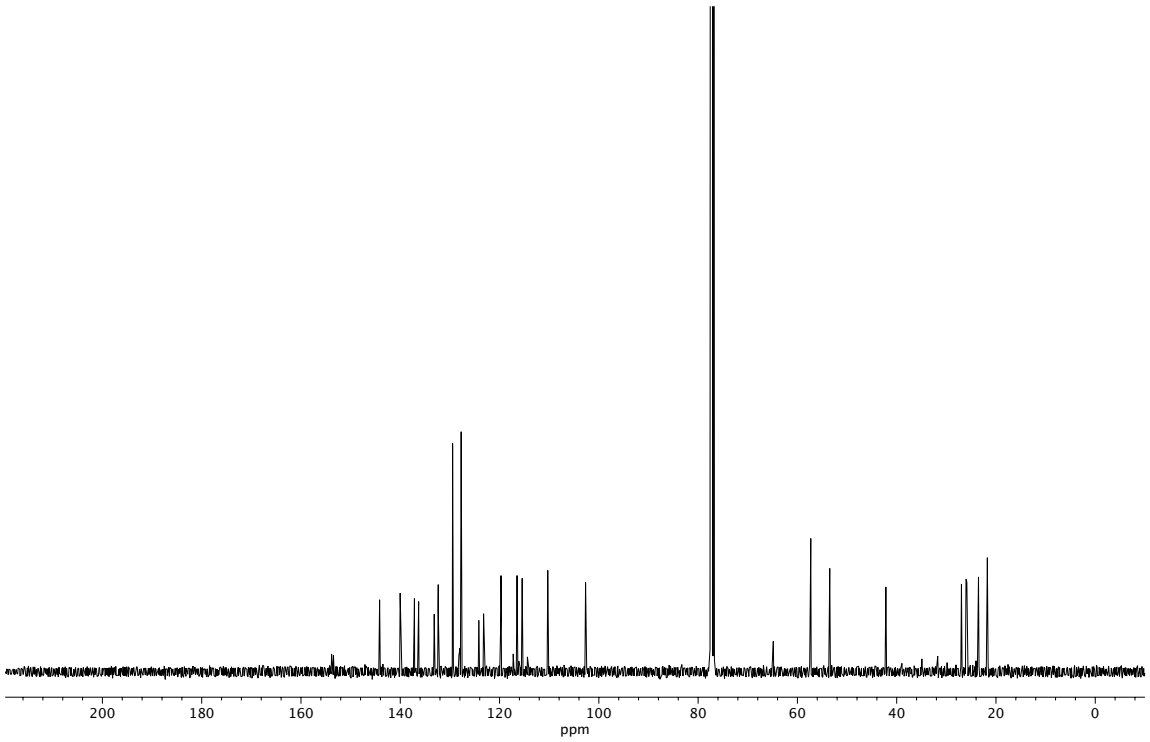


Figure A1.81. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **78.**

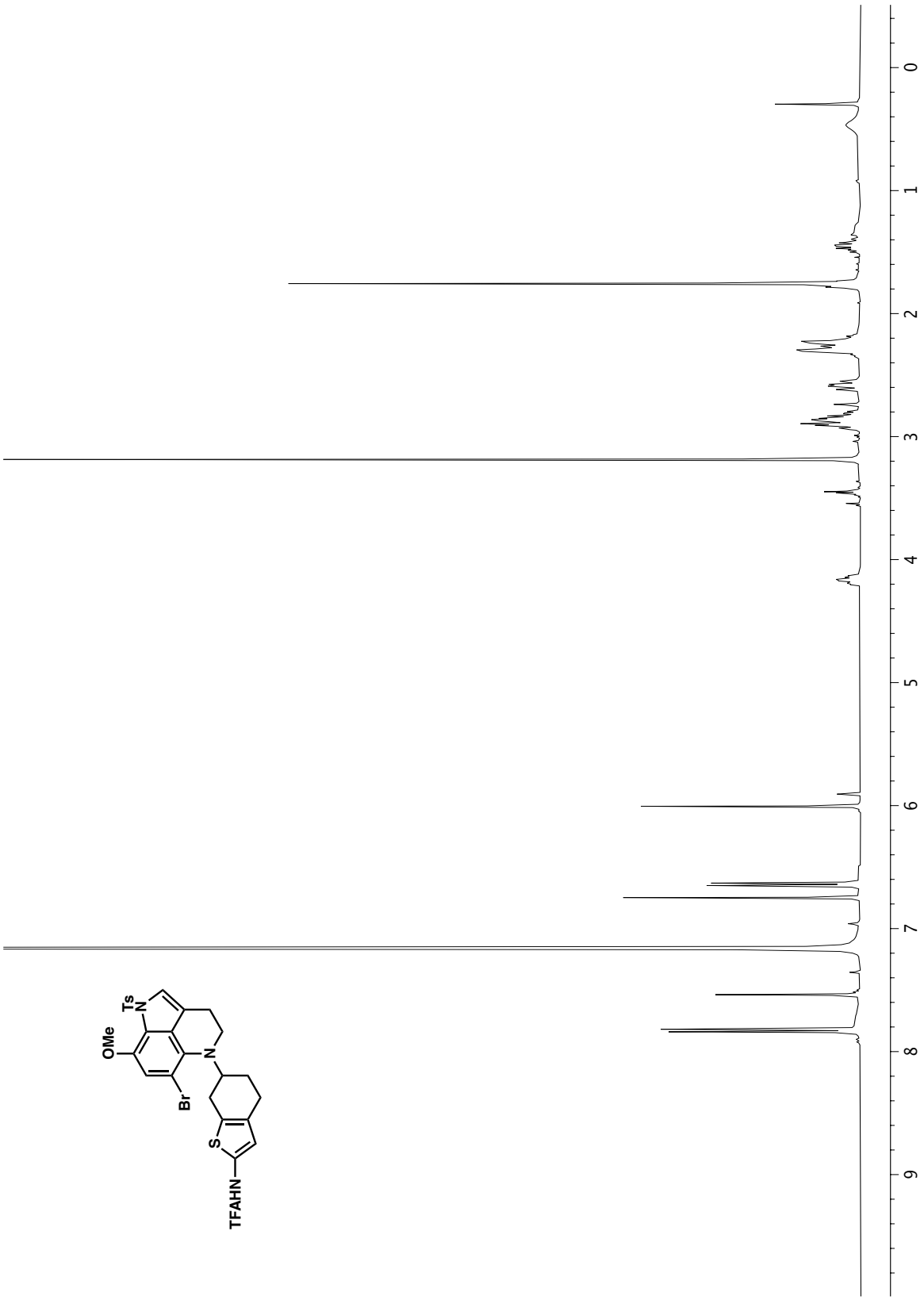


Figure A1.82. ^{1}H NMR (400 MHz, C_6D_6) of compound **79**.

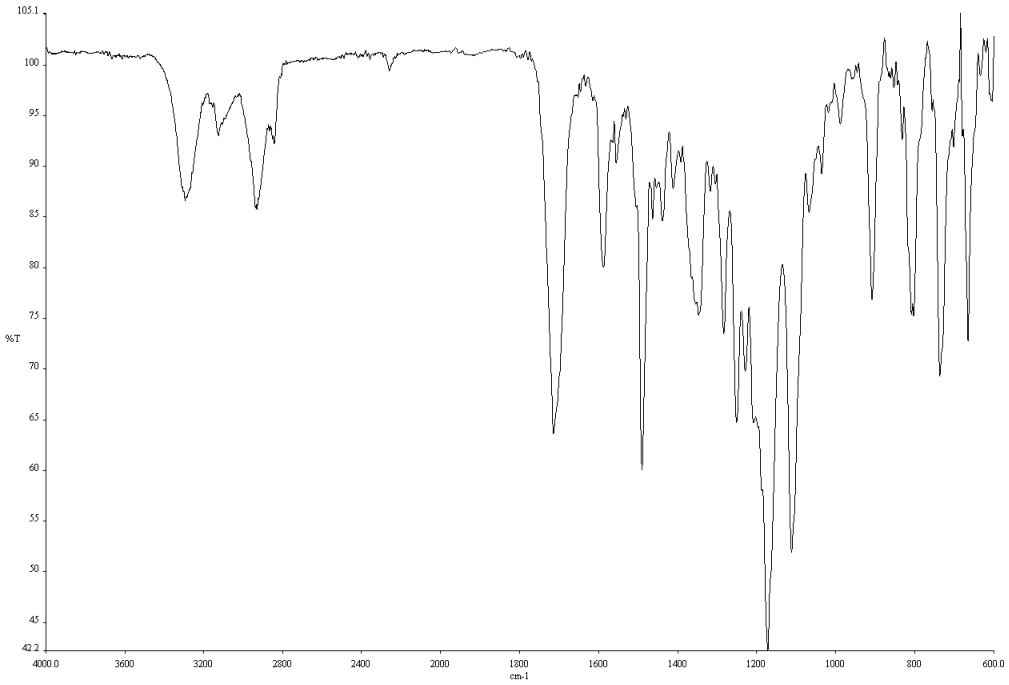


Figure A1.83. Infrared spectrum (Thin Film, NaCl) of compound **79**.

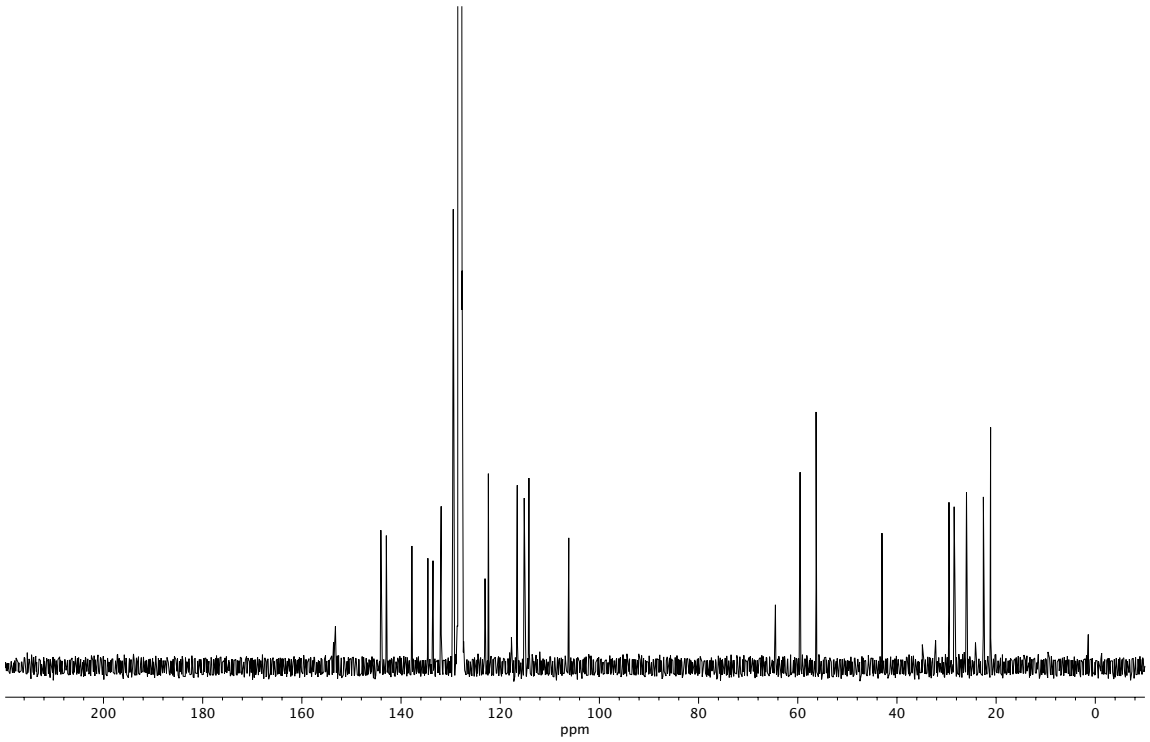


Figure A1.84. ^{13}C NMR (101 MHz, C_6D_6) of compound **79.**

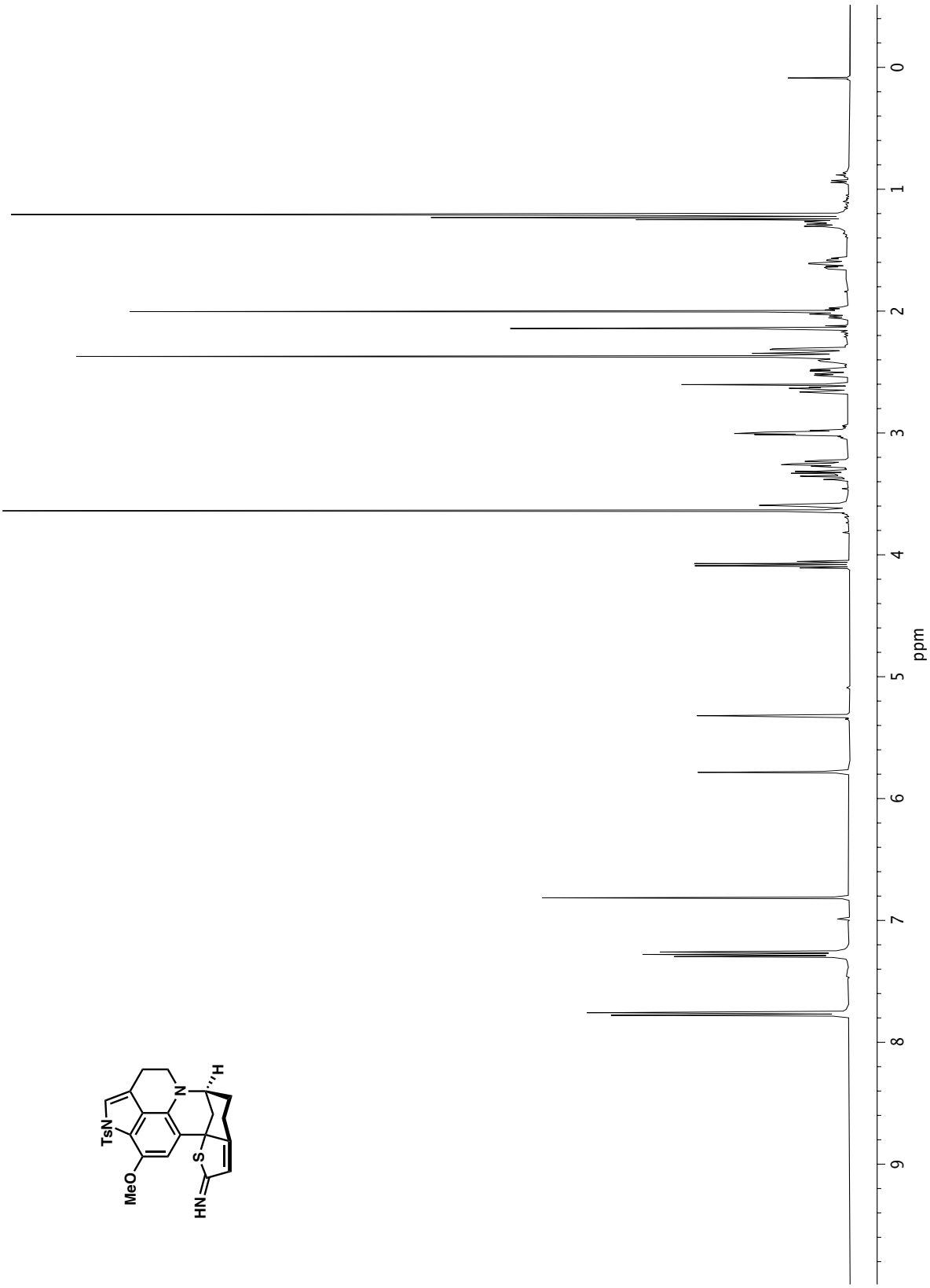


Figure A1.85. ^{1}H NMR (400 MHz, CD_2Cl_2) of compound **80**.

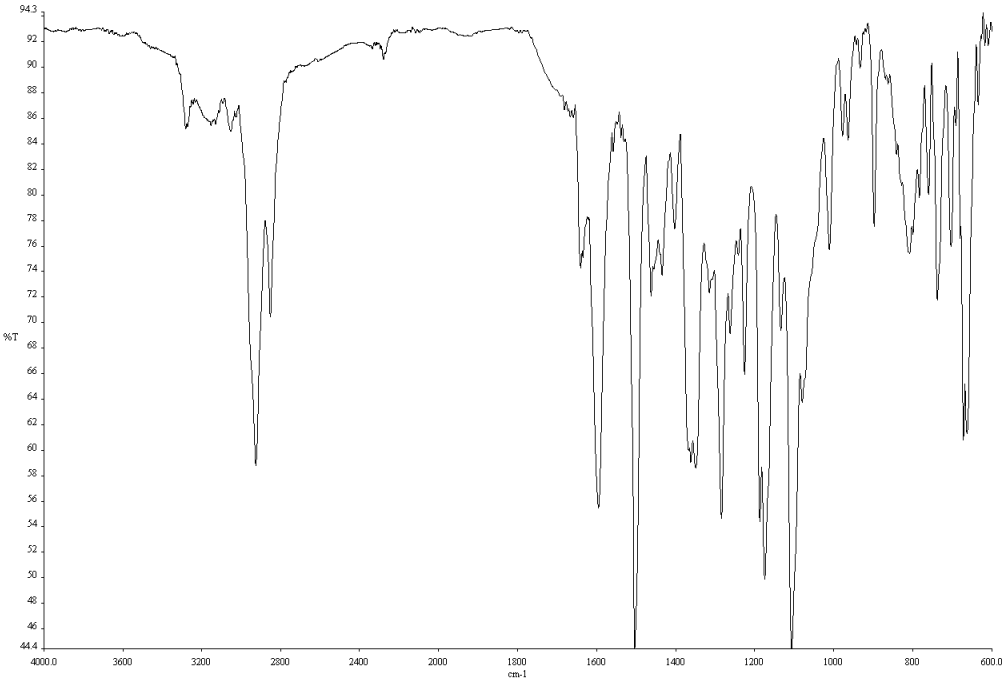


Figure A1.86. Infrared spectrum (Thin Film, NaCl) of compound **80**.

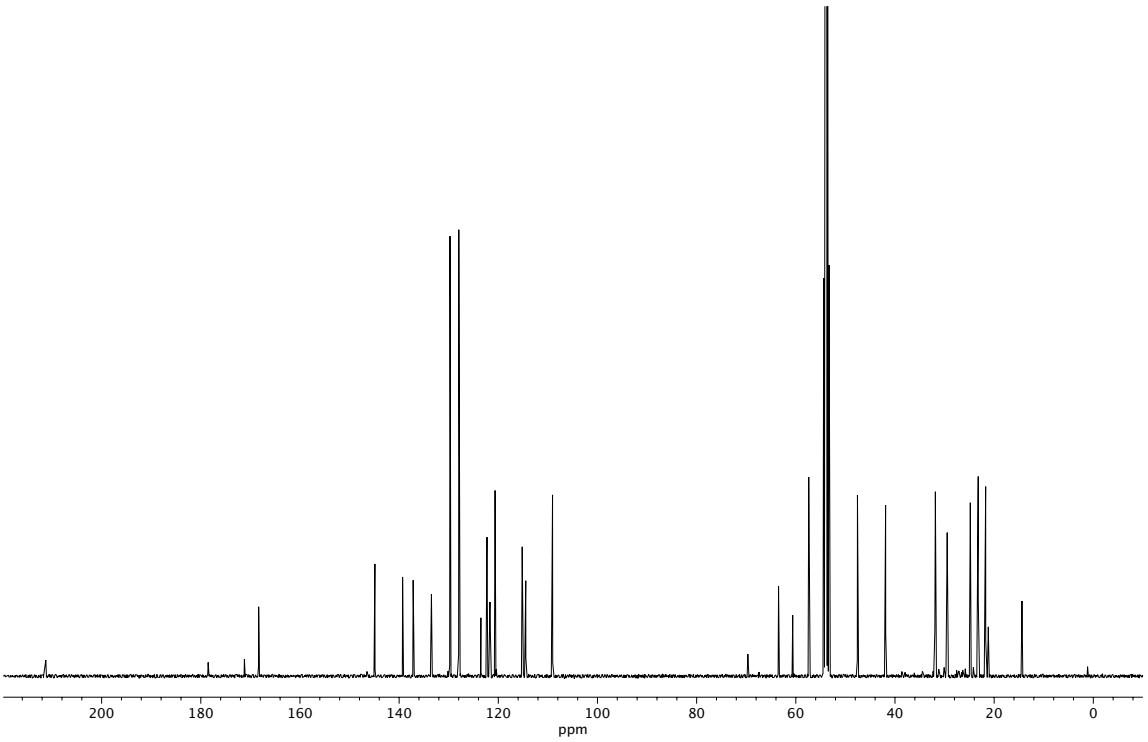


Figure A1.87. ^{13}C NMR (101 MHz, CD_2Cl_2) of compound **80.**

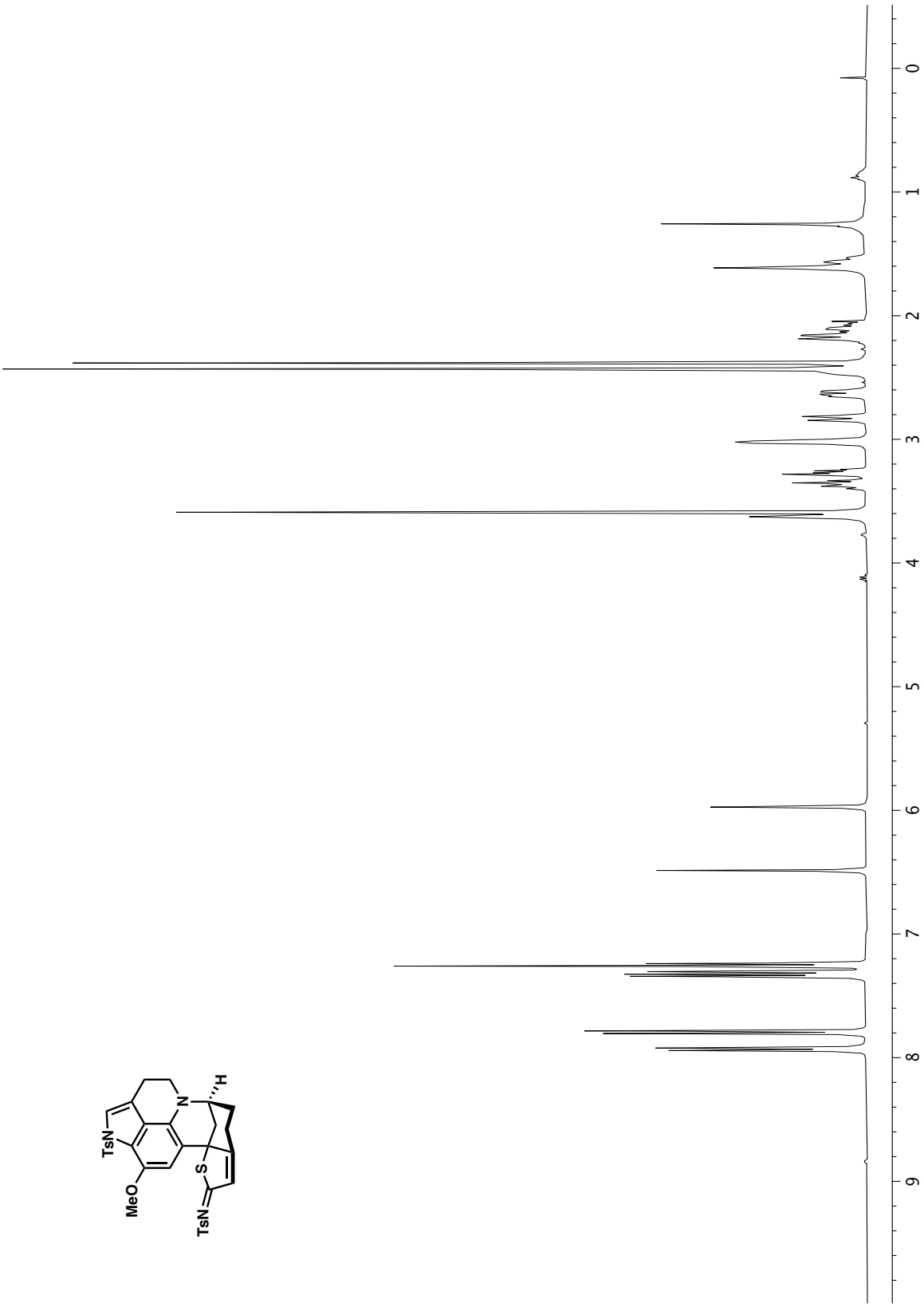


Figure A1.88. ^{1}H NMR (400 MHz, C_6D_6) of compound **82**.

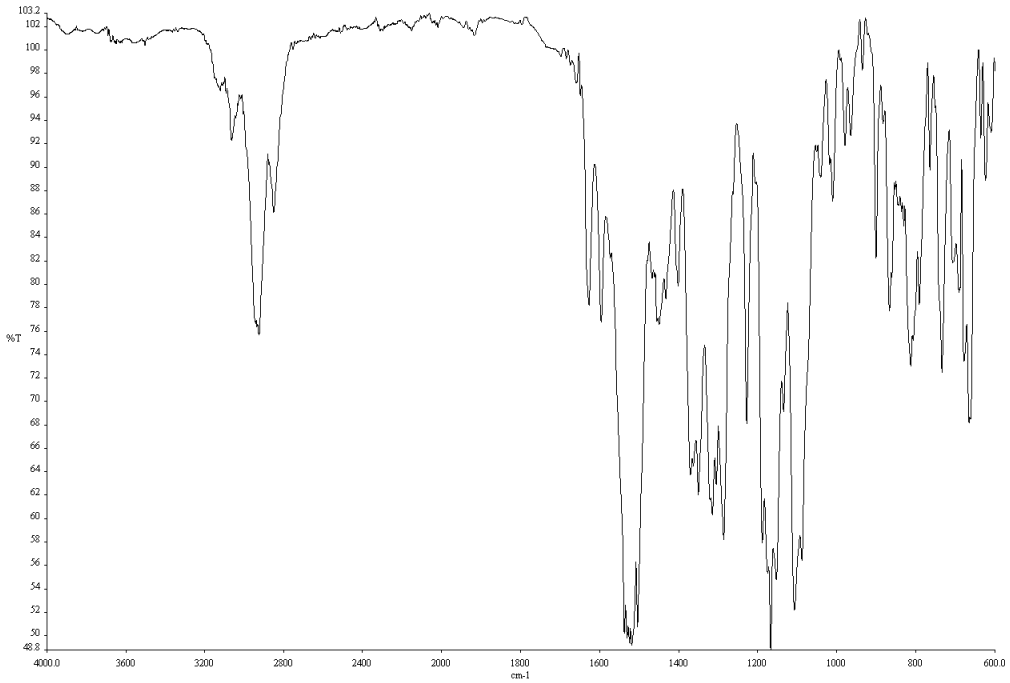


Figure A1.89. Infrared spectrum (Thin Film, NaCl) of compound **82**.

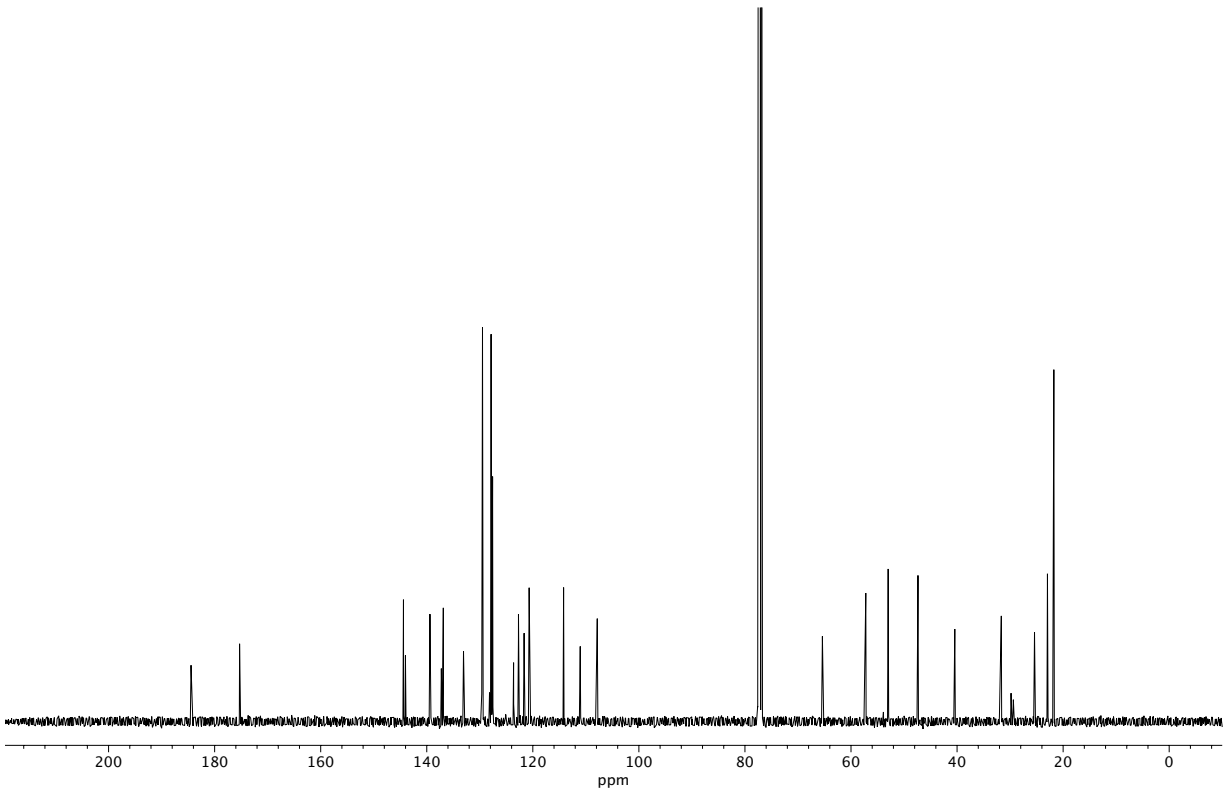


Figure A1.90. ^{13}C NMR (101 MHz, C_6D_6) of compound **82.**

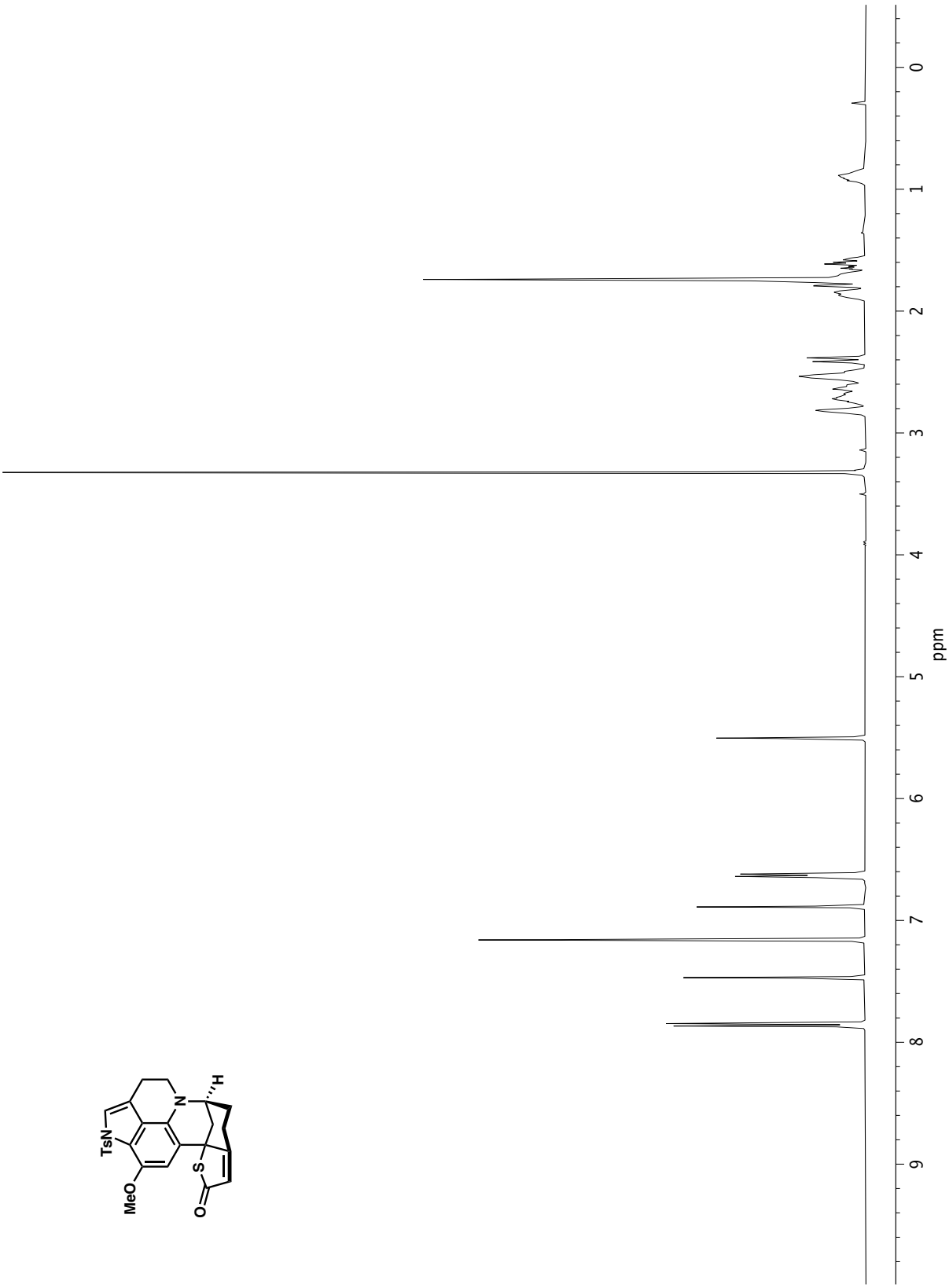


Figure A1.91. ^{1}H NMR (400 MHz, C_6D_6) of compound **81**.

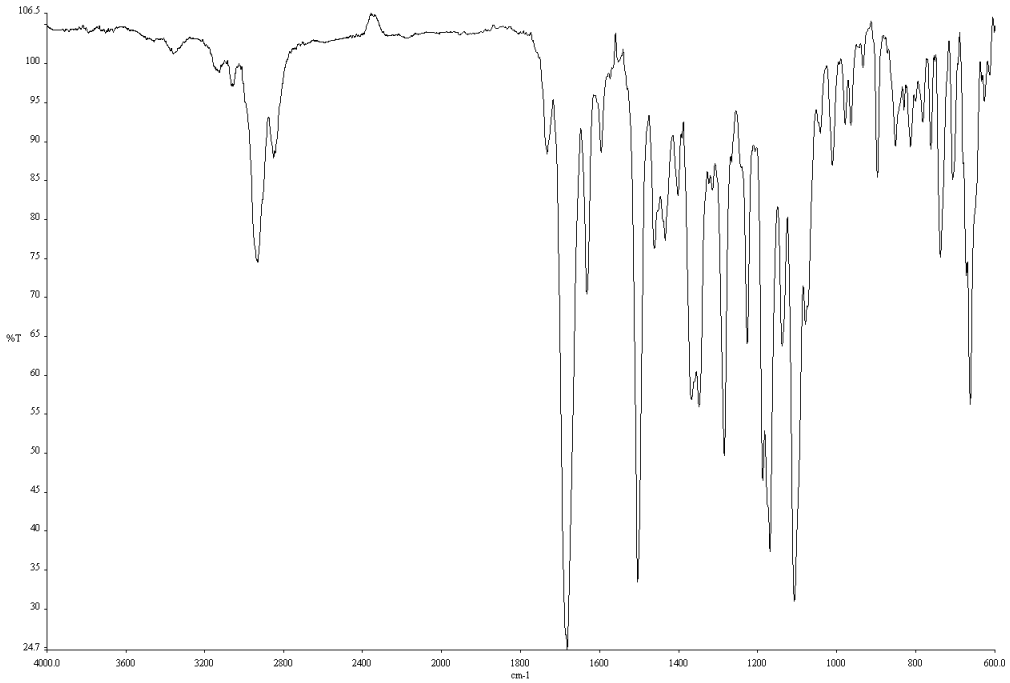


Figure A1.92. Infrared spectrum (Thin Film, NaCl) of compound **81**.

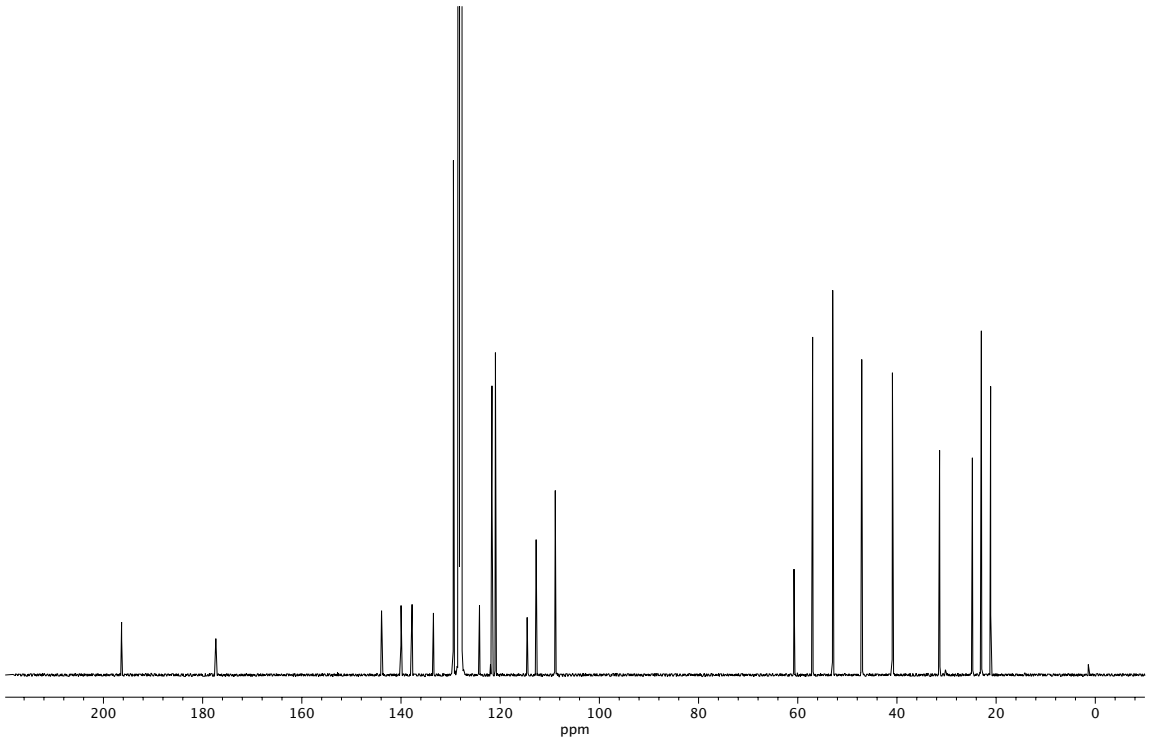


Figure A1.93. ^{13}C NMR (101 MHz, C_6D_6) of compound **81.**

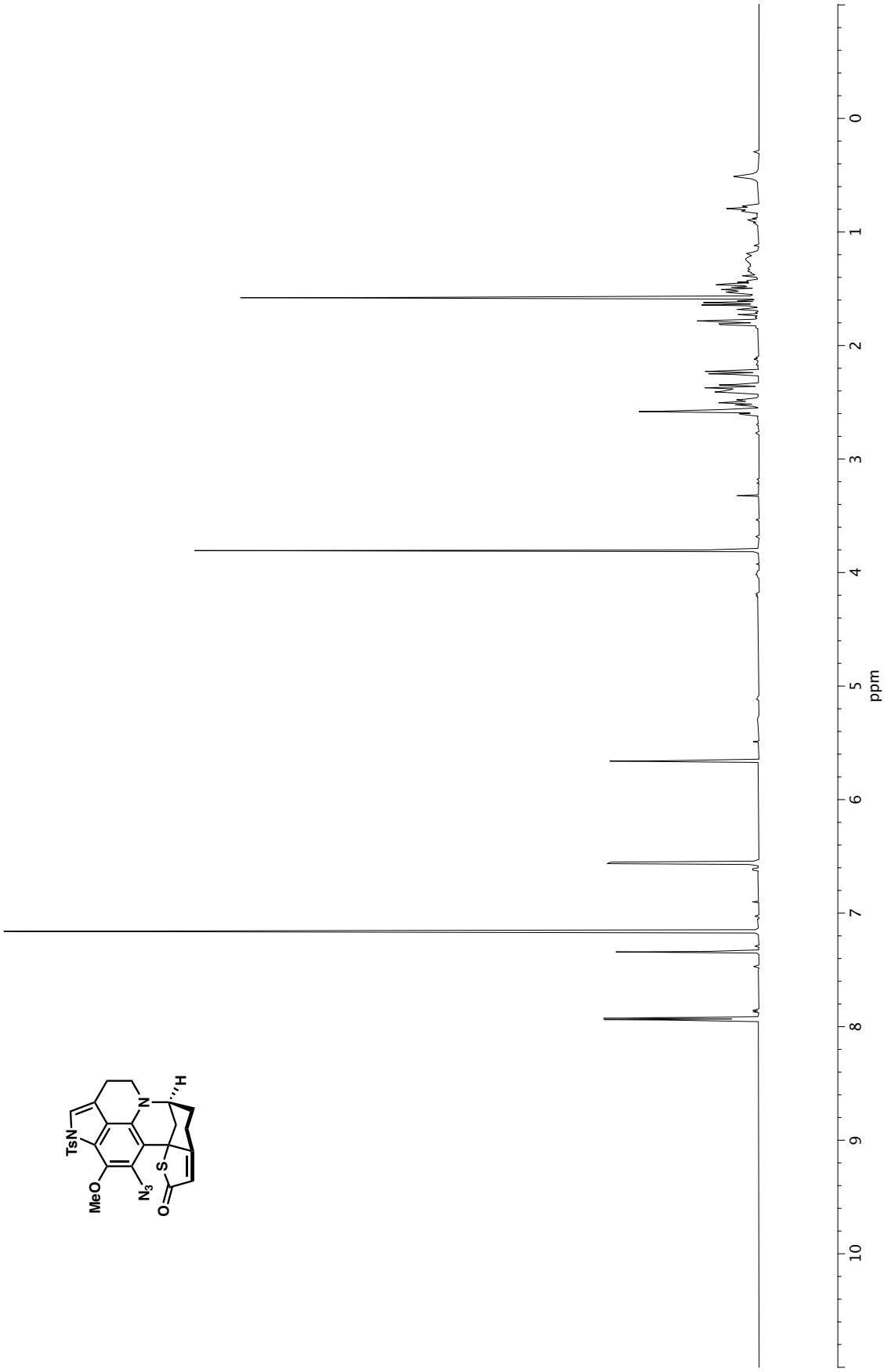


Figure A1.94. ^{1}H NMR (600 MHz, C_6D_6) of compound **83**.

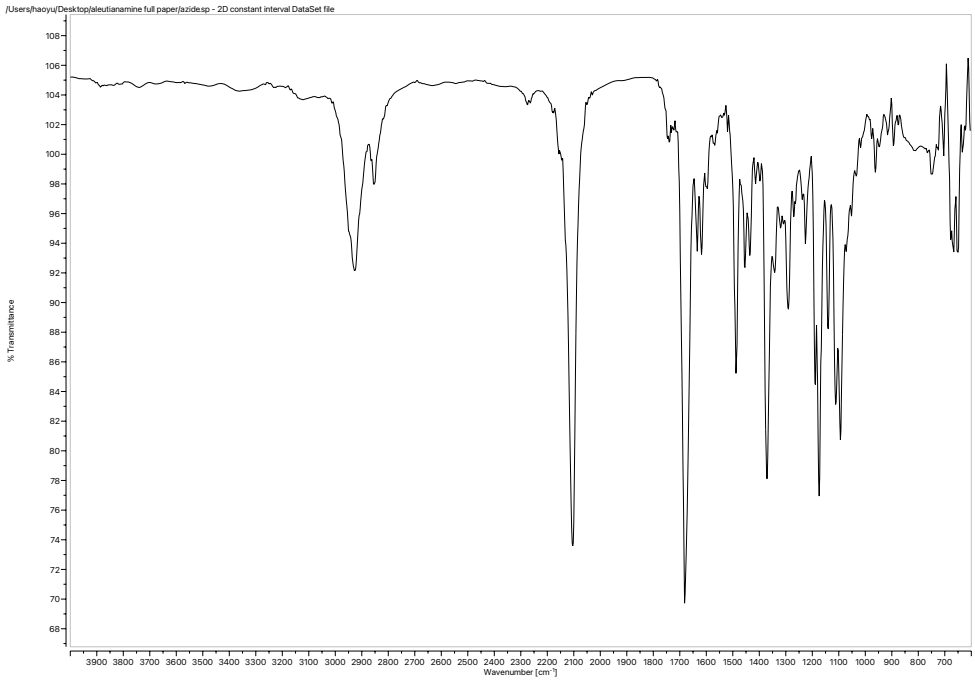


Figure A1.95. Infrared spectrum (Thin Film, NaCl) of compound **83**.

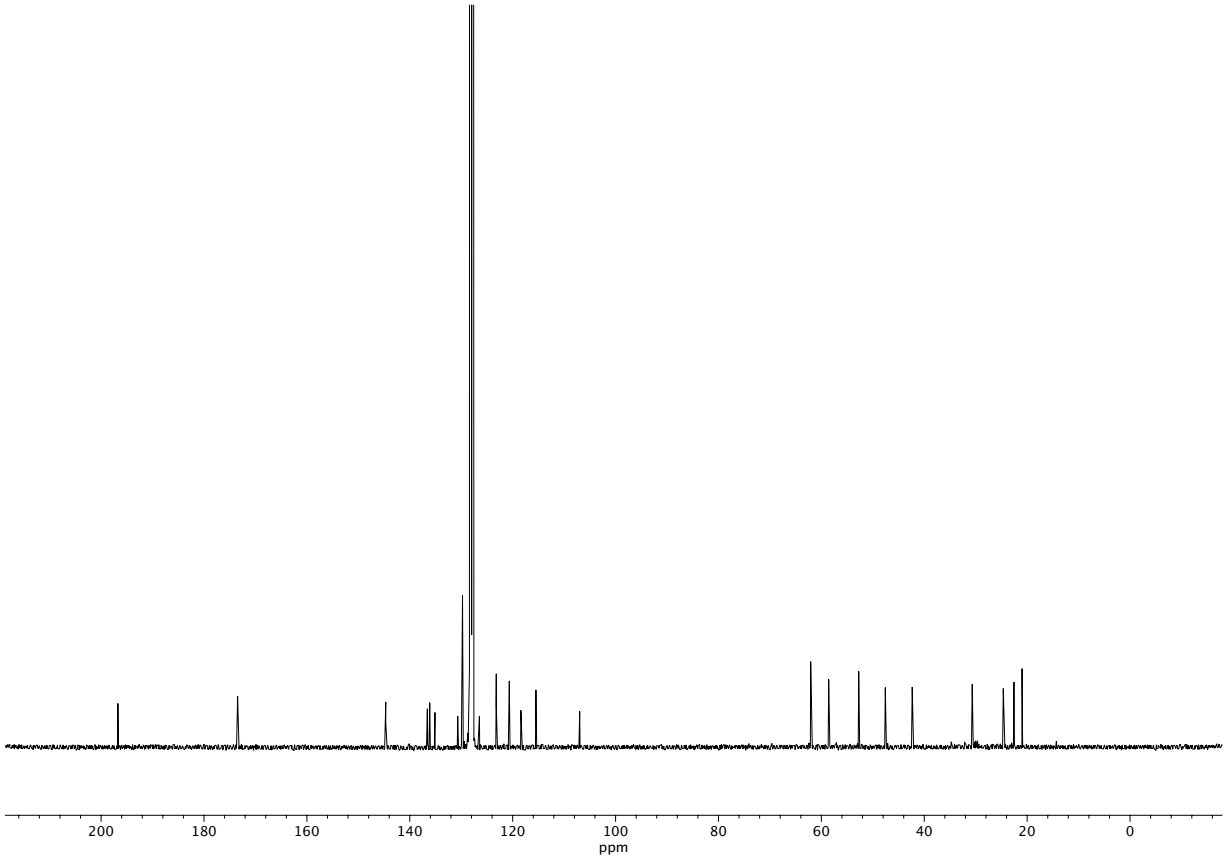


Figure A1.96. ^{13}C NMR (101 MHz, C_6D_6) of compound **83.**

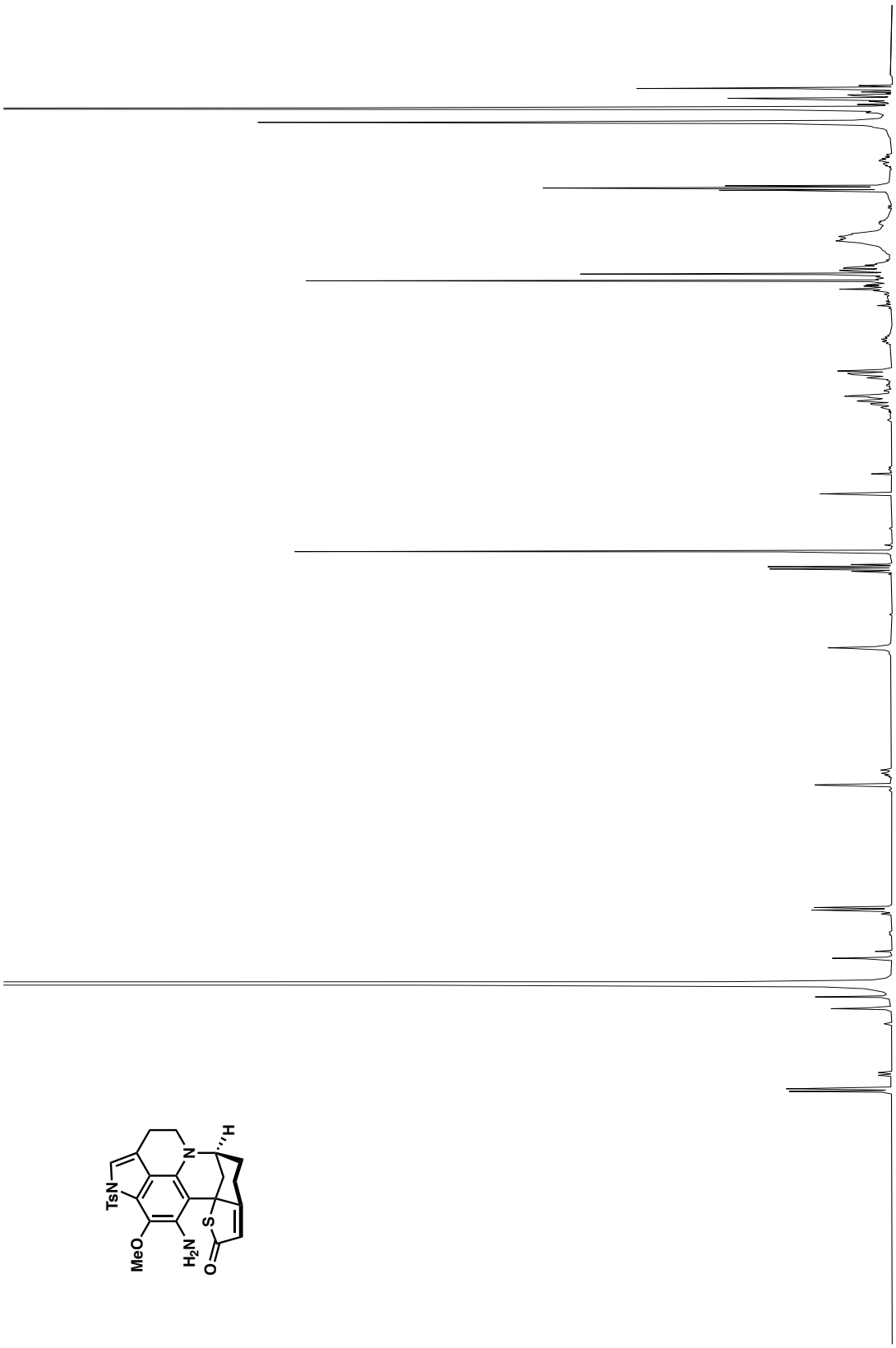


Figure A1.97. ^{1}H NMR (400 MHz, C_6D_6) of compound **84**.

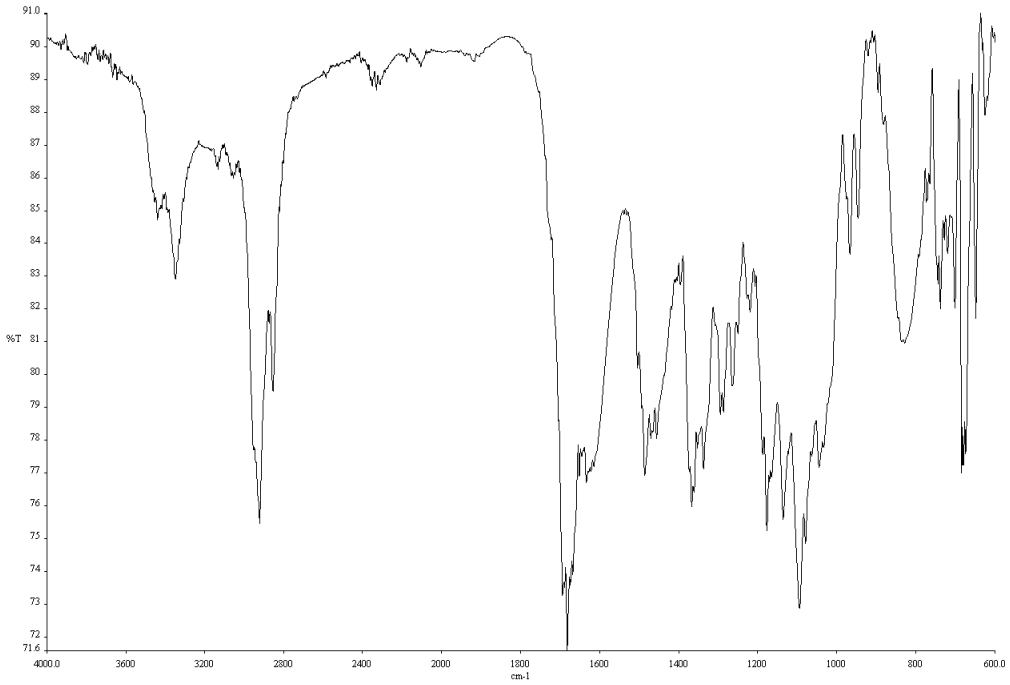


Figure A1.98. Infrared spectrum (Thin Film, NaCl) of compound **84**.

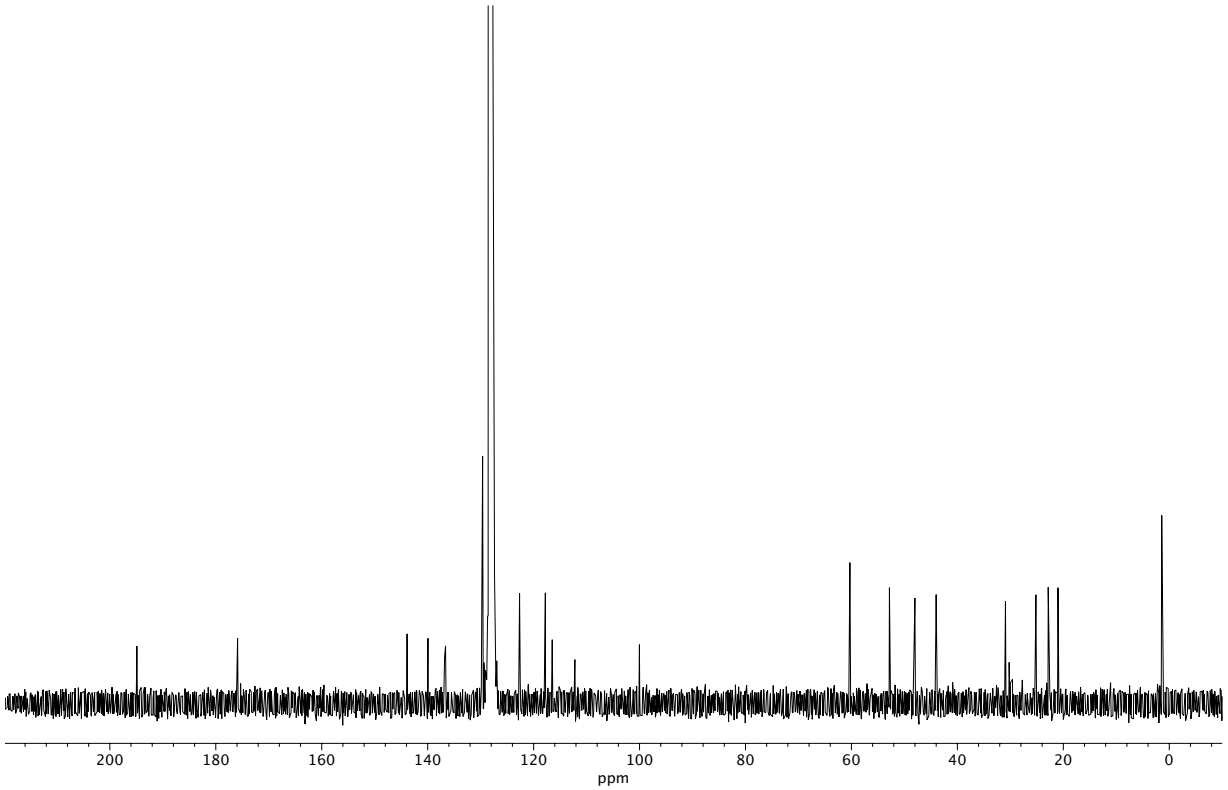


Figure A1.99. ^{13}C NMR (151 MHz, C_6D_6) of compound **84.**

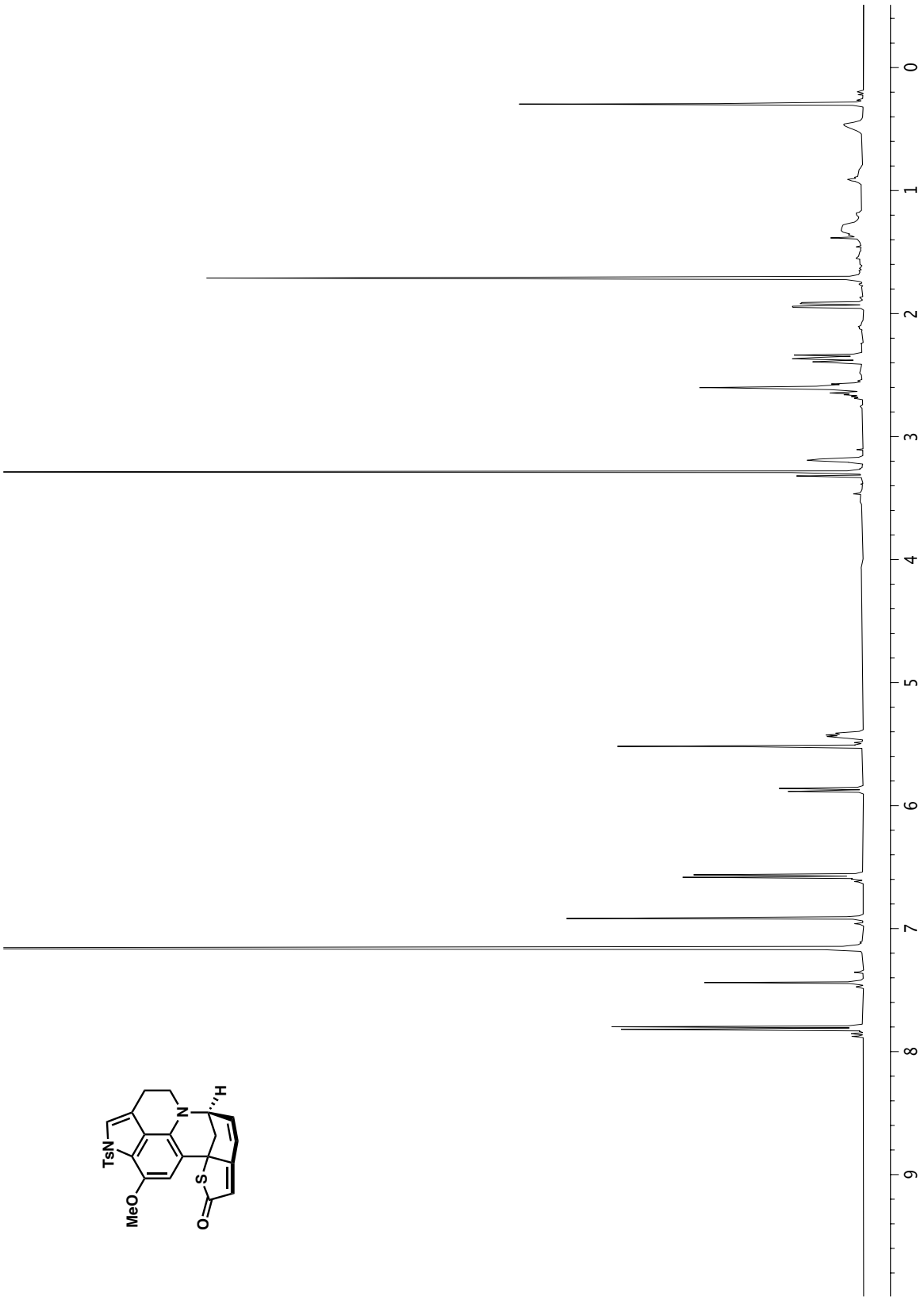


Figure A1.100. ^{1}H NMR (400 MHz, C_6D_6) of compound **88**.

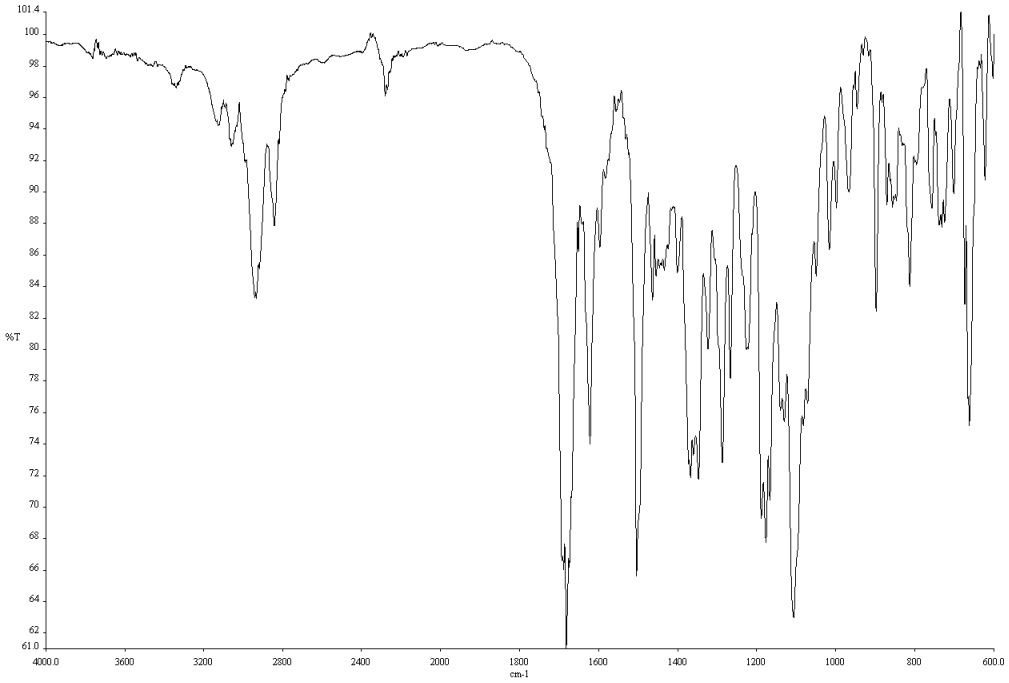


Figure A1.101. Infrared spectrum (Thin Film, NaCl) of compound **88**.

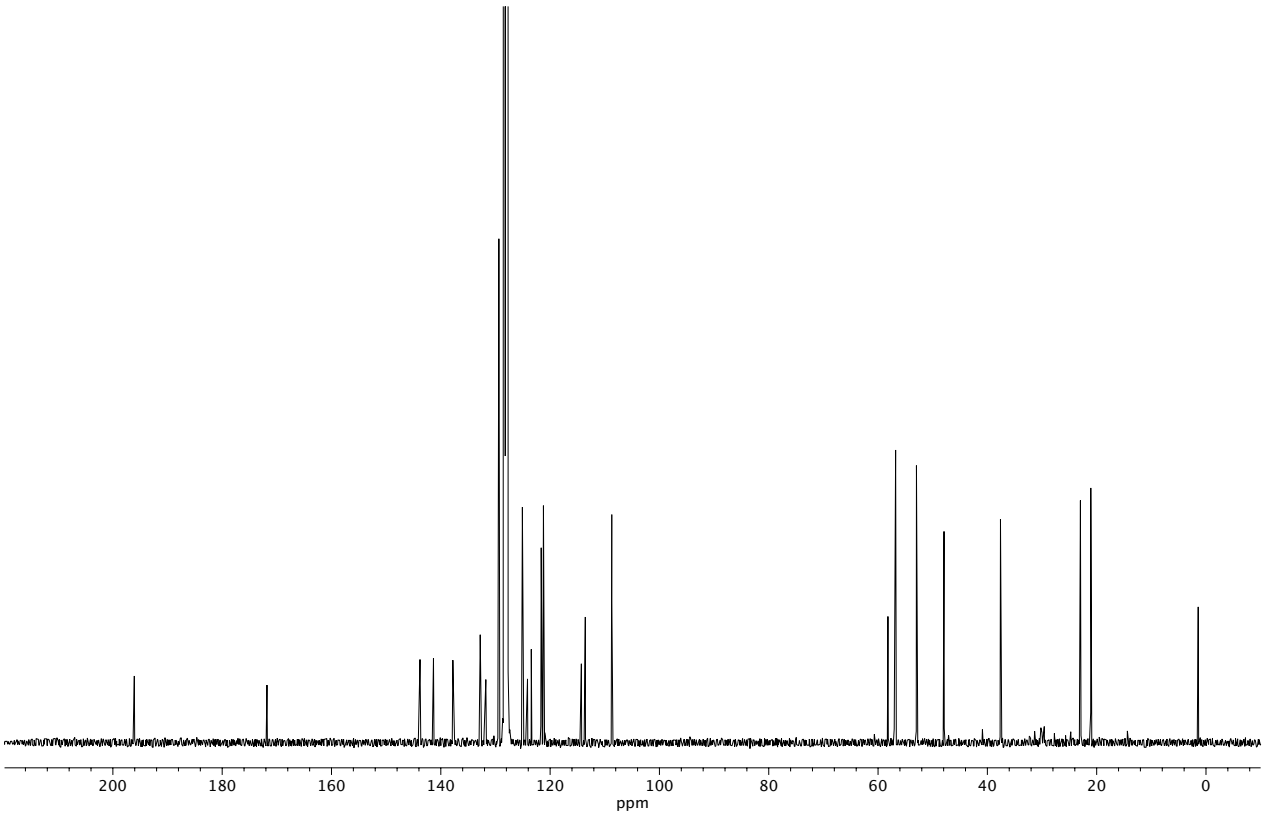


Figure A1.102. ^{13}C NMR (101 MHz, C_6D_6) of compound **88.**

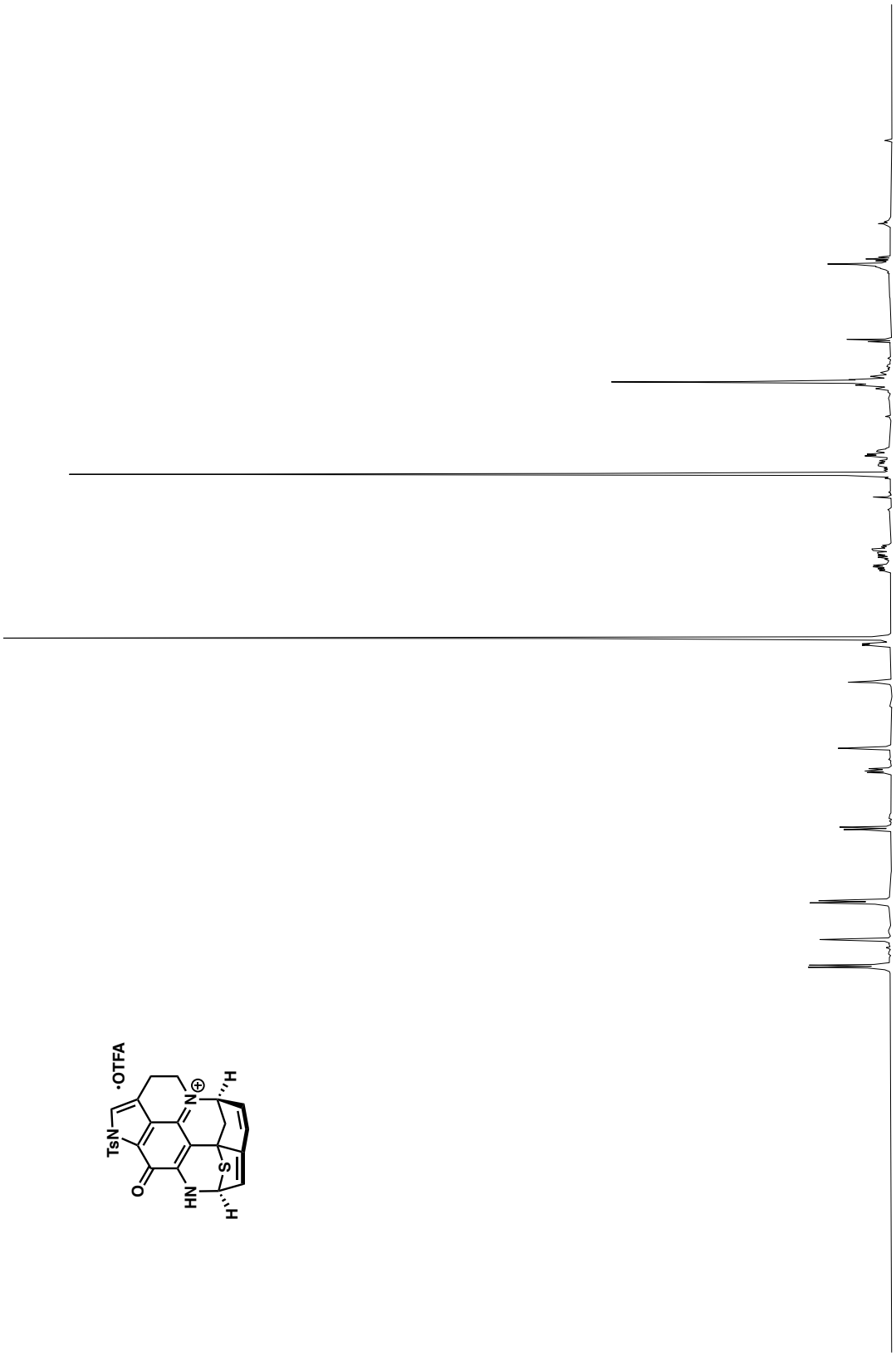


Figure A1.103. ^{1}H NMR (400 MHz, CD_3OD) of compound **93**.

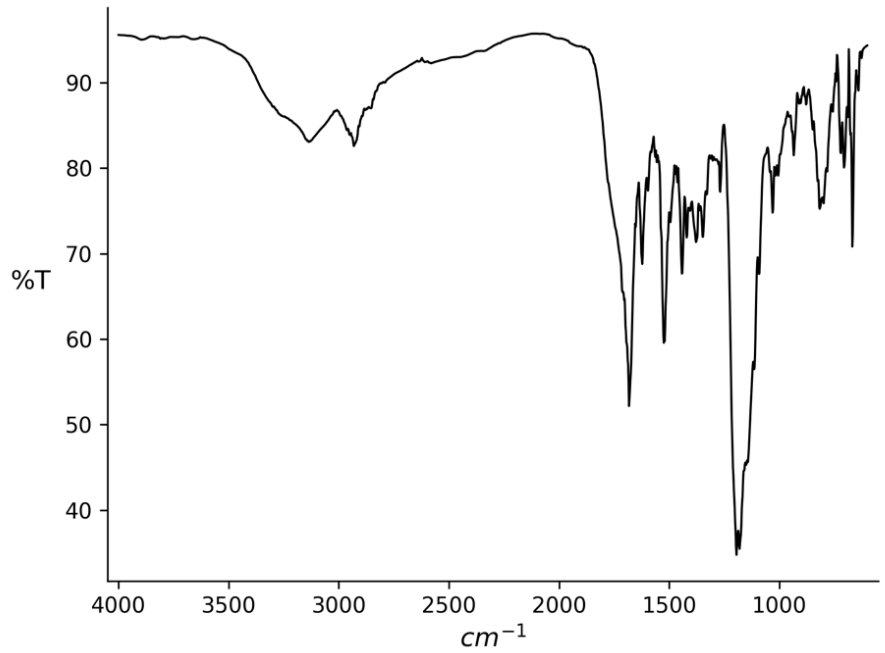


Figure A1.104. Infrared spectrum (Thin Film, NaCl) of compound **93**.

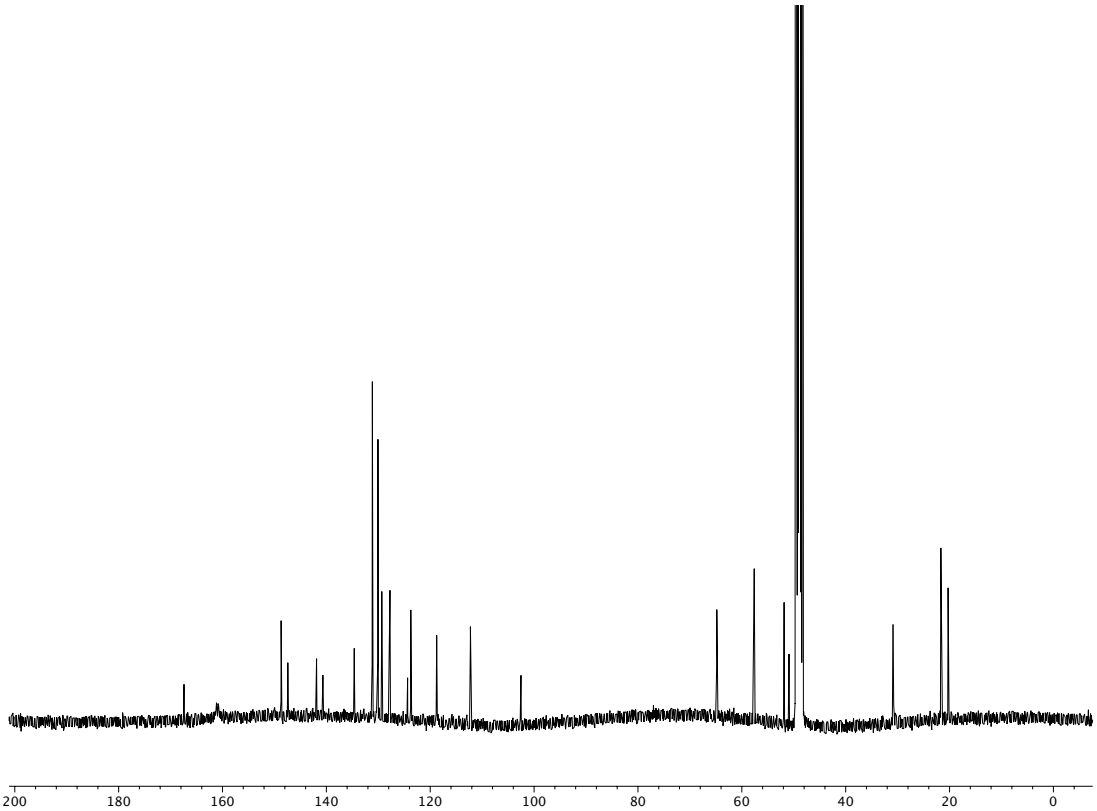


Figure A1.105. ^{13}C NMR (101 MHz, CD_3OD) of compound **93.**

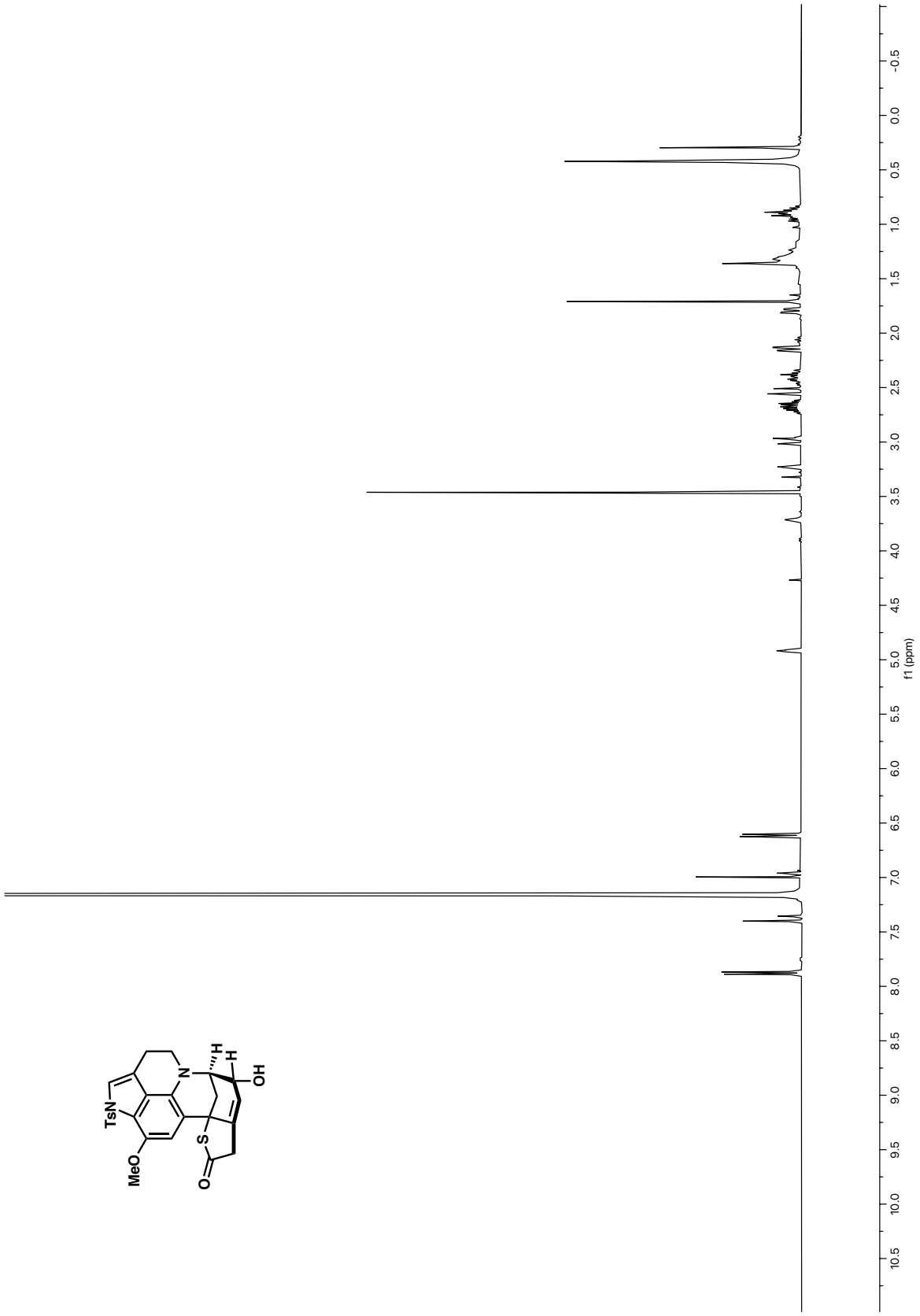


Figure A1.106. ^{1}H NMR (400 MHz, C_6D_6) of compound **96**.

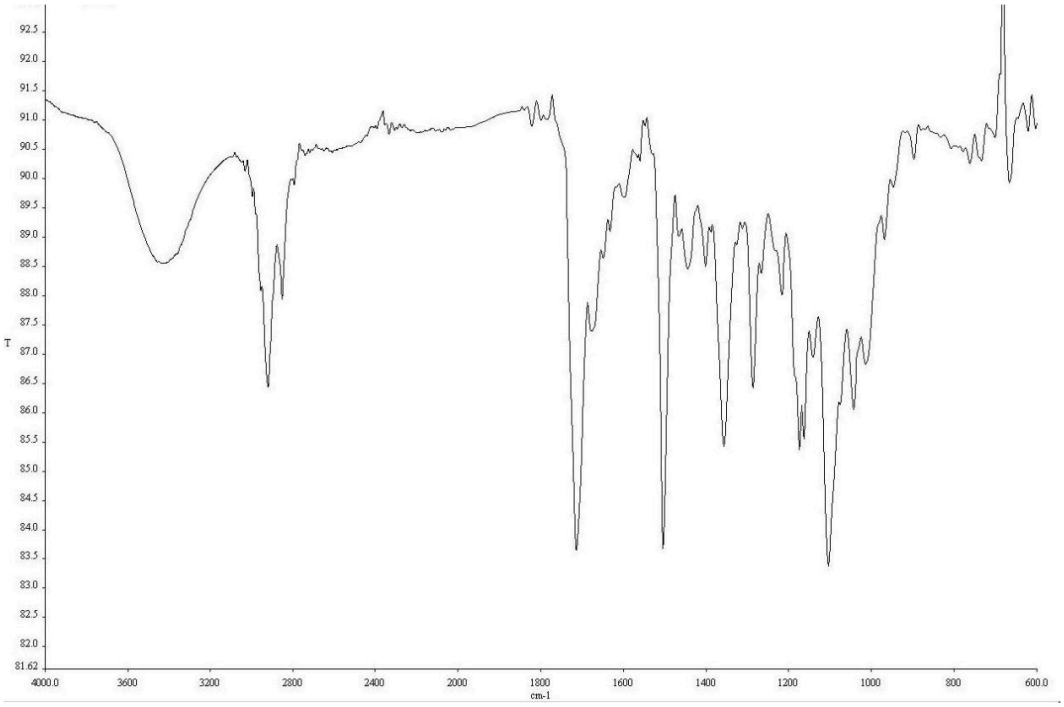


Figure A1.107. Infrared spectrum (Thin Film, NaCl) of compound **96**.

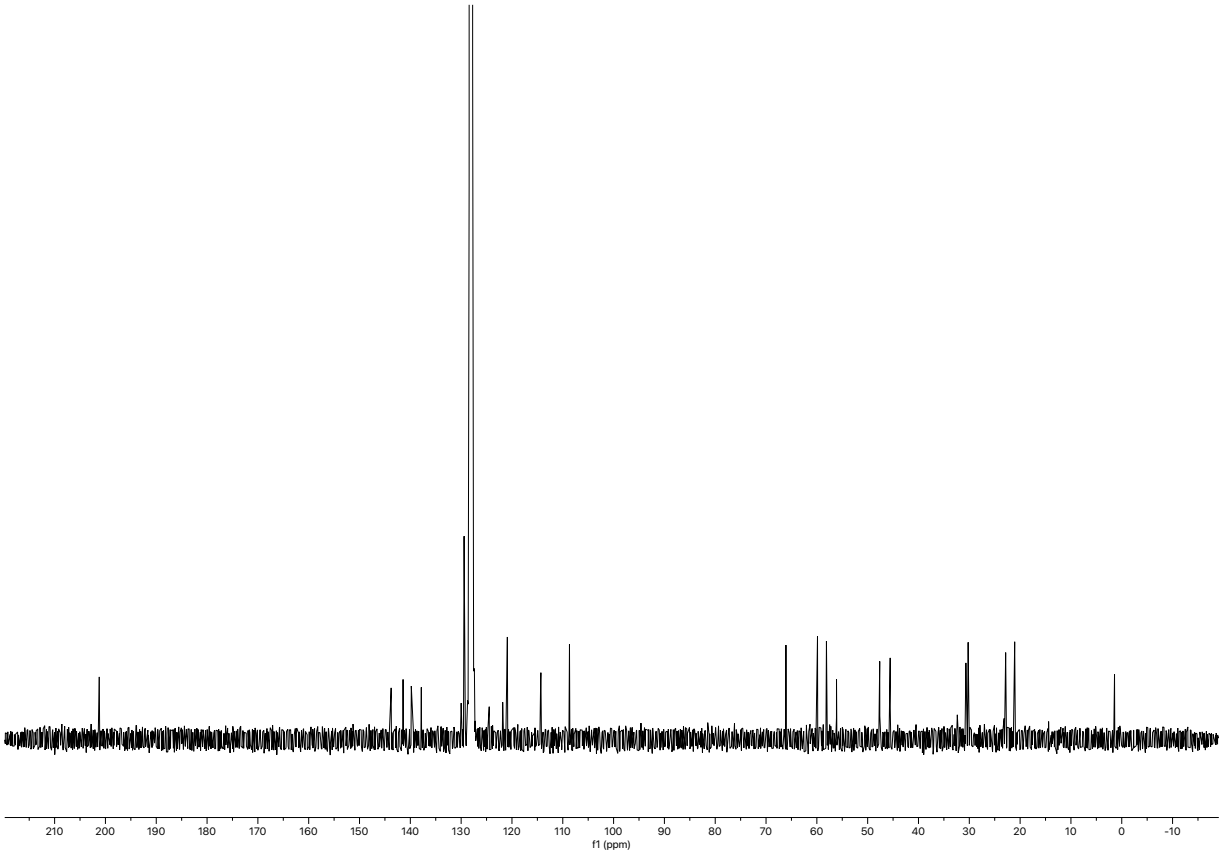


Figure A1.108. ^{13}C NMR (101 MHz, C_6D_6) of compound **96.**

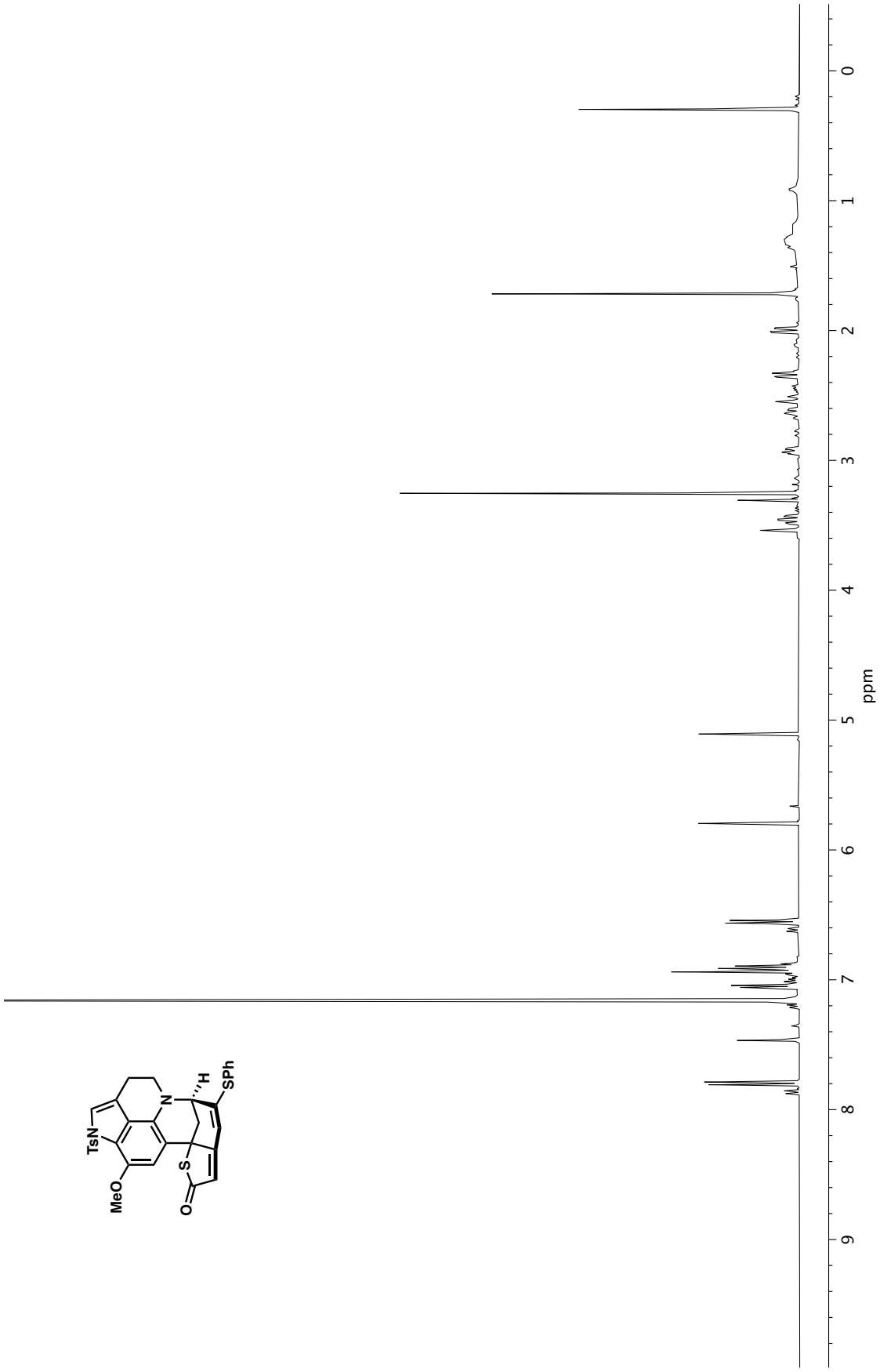


Figure A1.109. ^{1}H NMR (400 MHz, C_6D_6) of compound **97**.

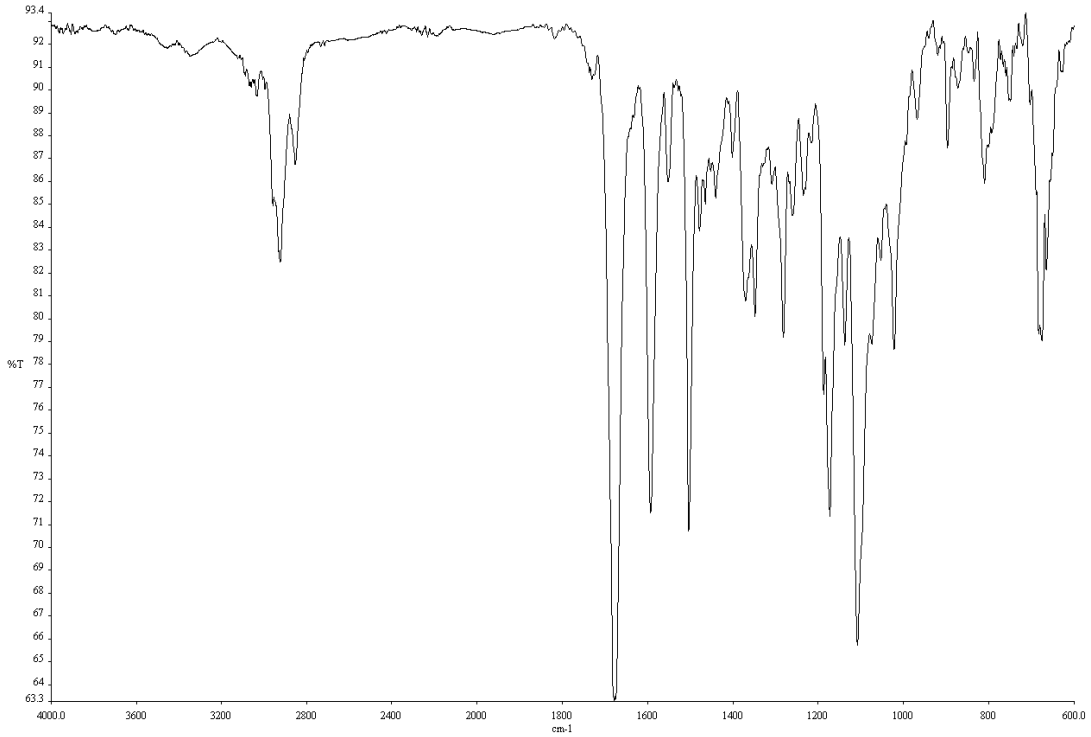


Figure A1.110. Infrared spectrum (Thin Film, NaCl) of compound **97**.

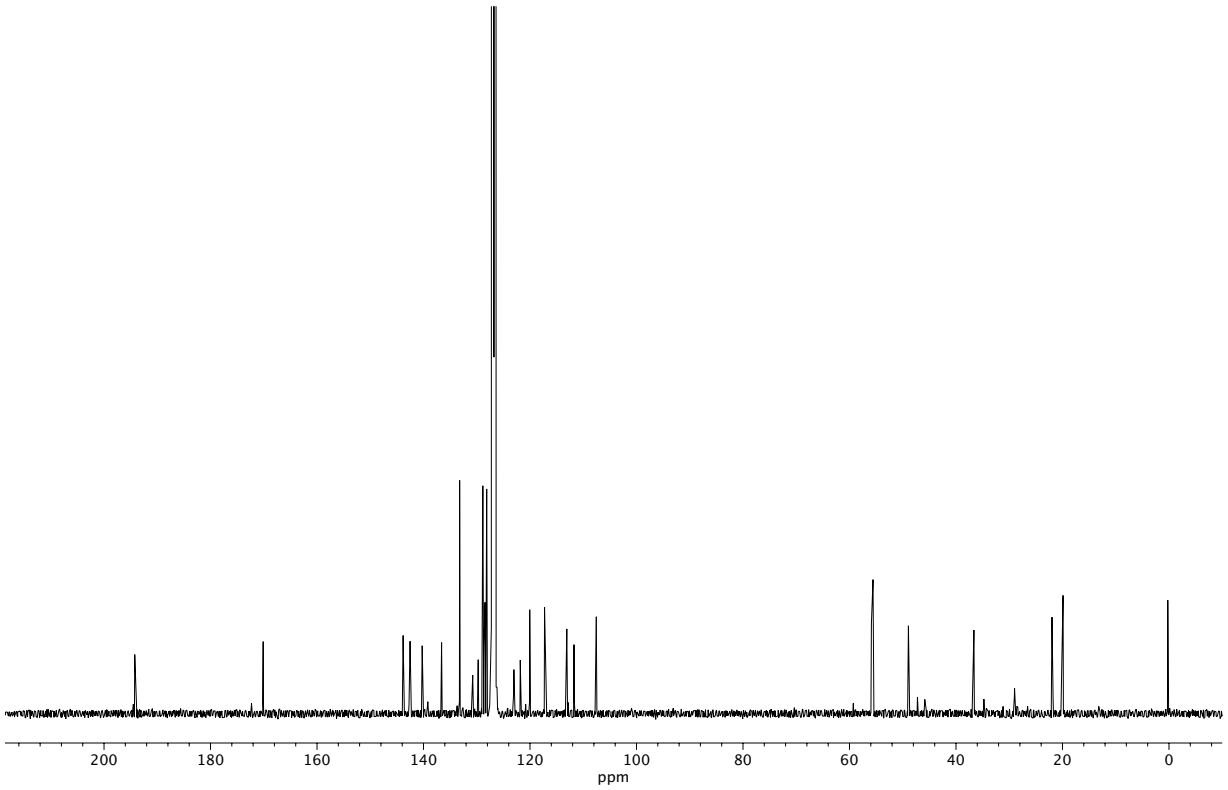


Figure A1.111. ^{13}C NMR (101 MHz, C_6D_6) of compound **97.**

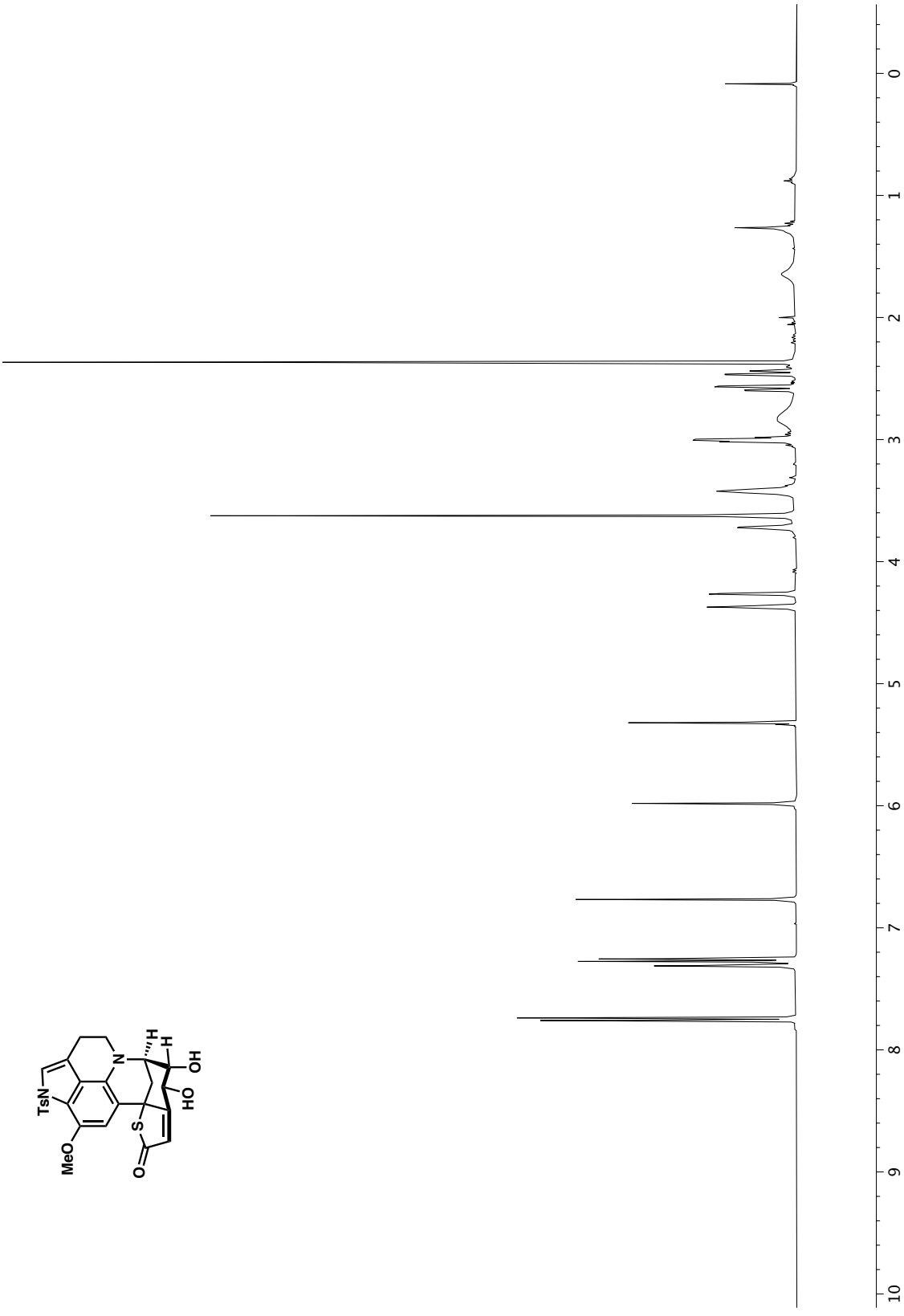


Figure A1.112. ^{1}H NMR (400 MHz, CD_2Cl_2) of compound **102**.

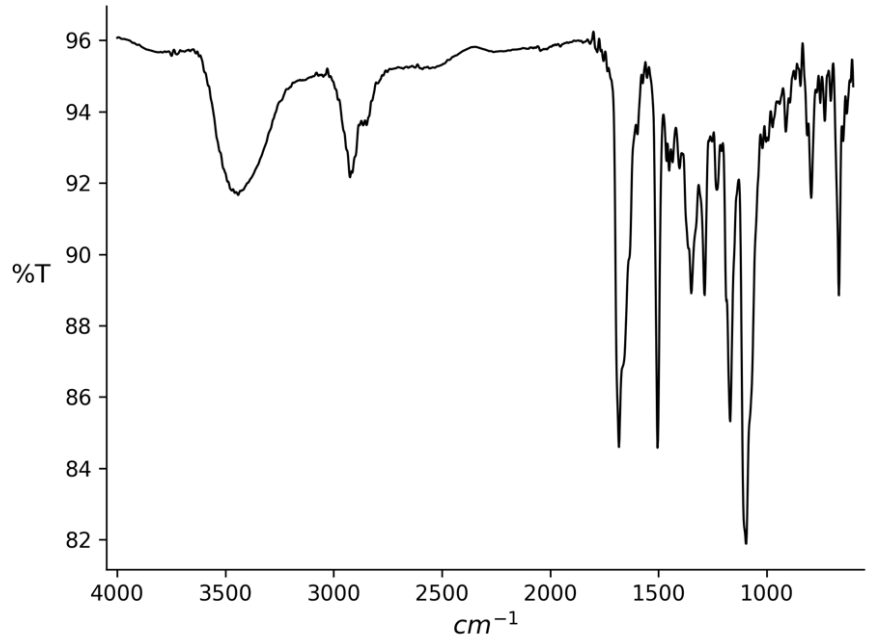


Figure A1.113. Infrared spectrum (Thin Film, NaCl) of compound **102**.

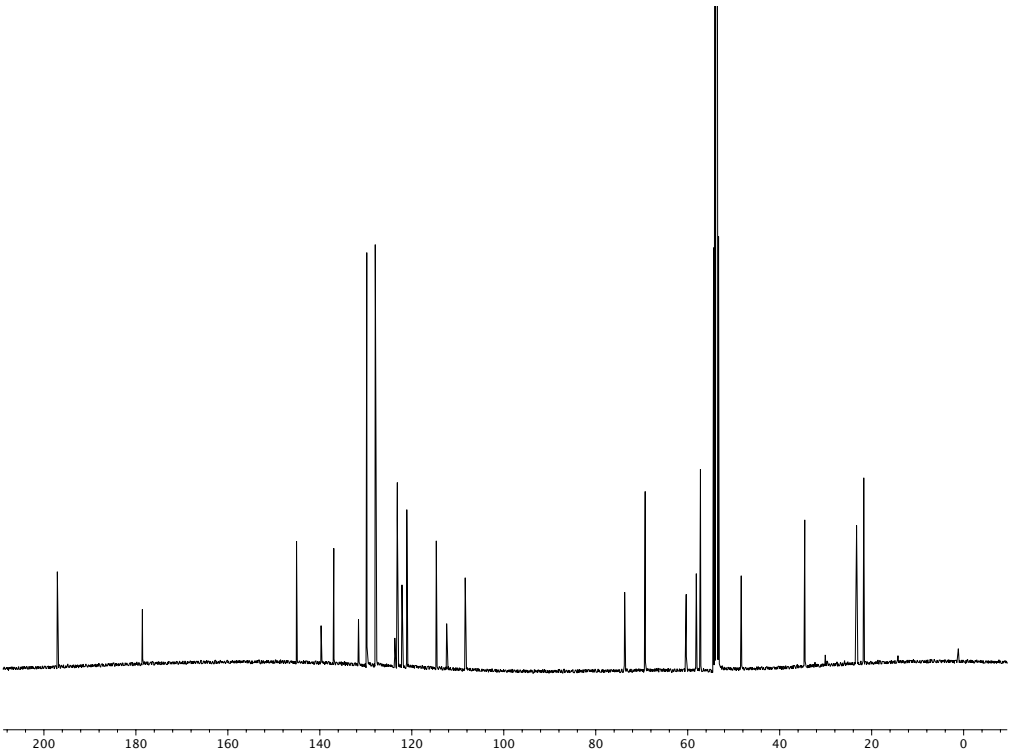


Figure A1.114. ^{13}C NMR (101 MHz, CD_2Cl_2) of compound **102.**

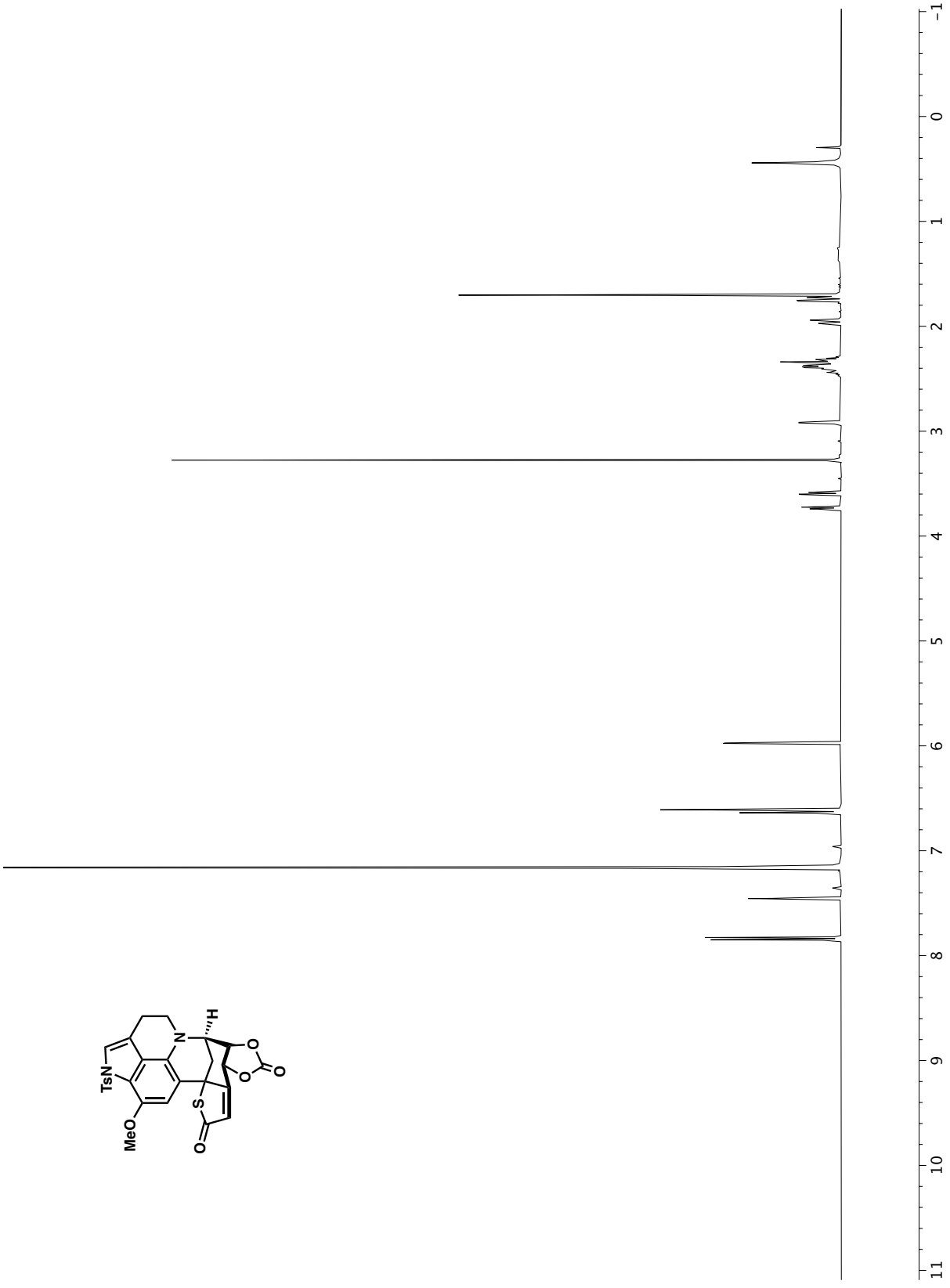


Figure A1.115. ^{1}H NMR (400 MHz, C_6D_6) of compound **101**.

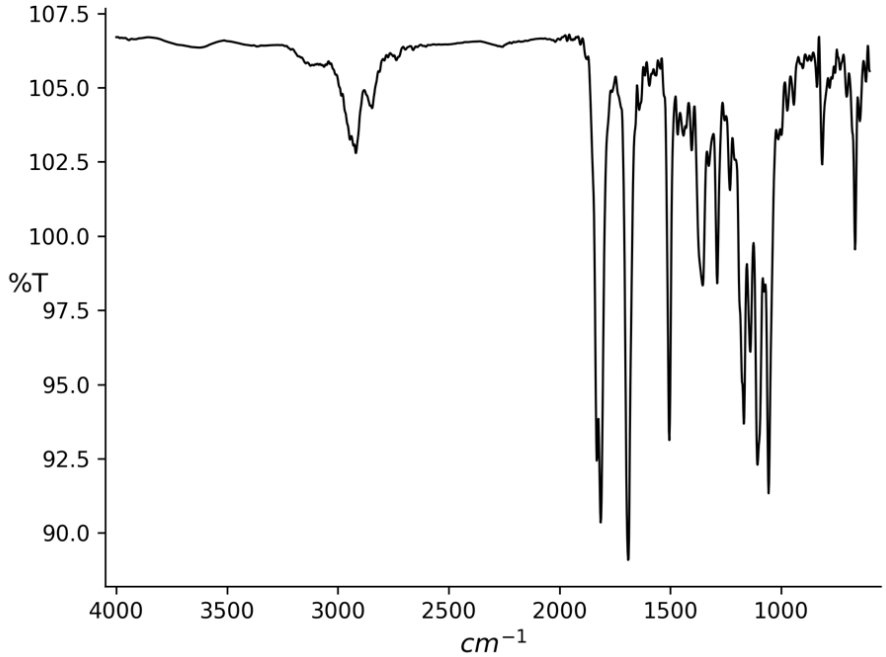


Figure A1.116. Infrared spectrum (Thin Film, NaCl) of compound **101**.

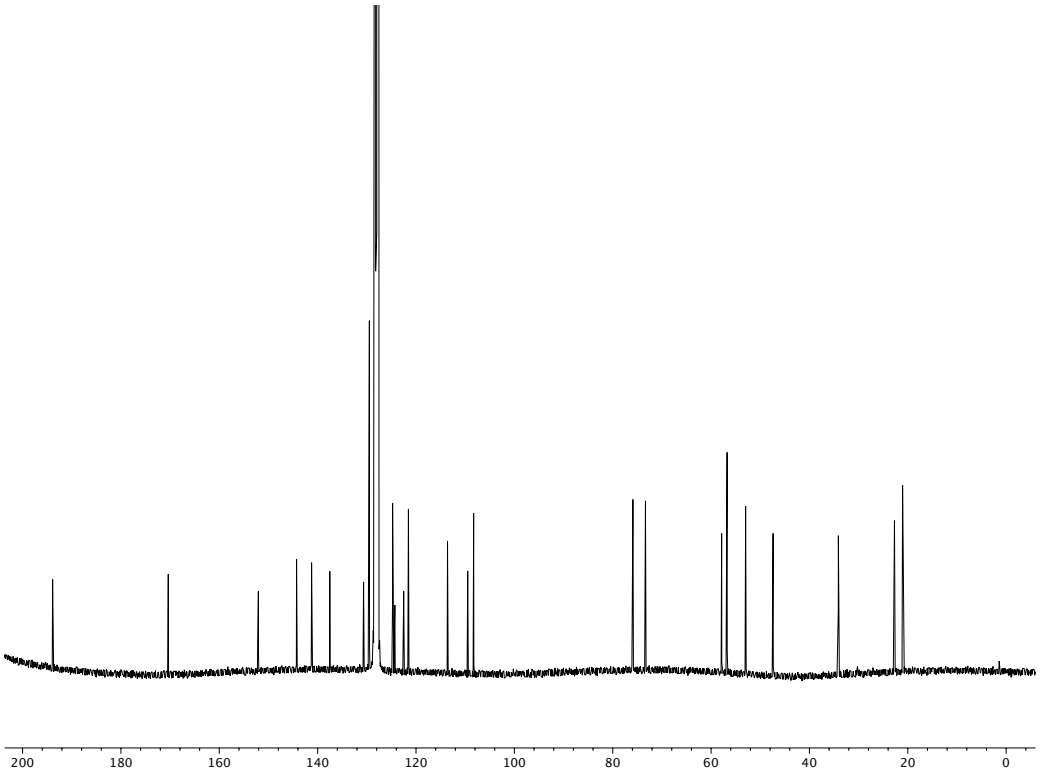


Figure A1.117. ^{13}C NMR (101 MHz, C_6D_6) of compound **101.**

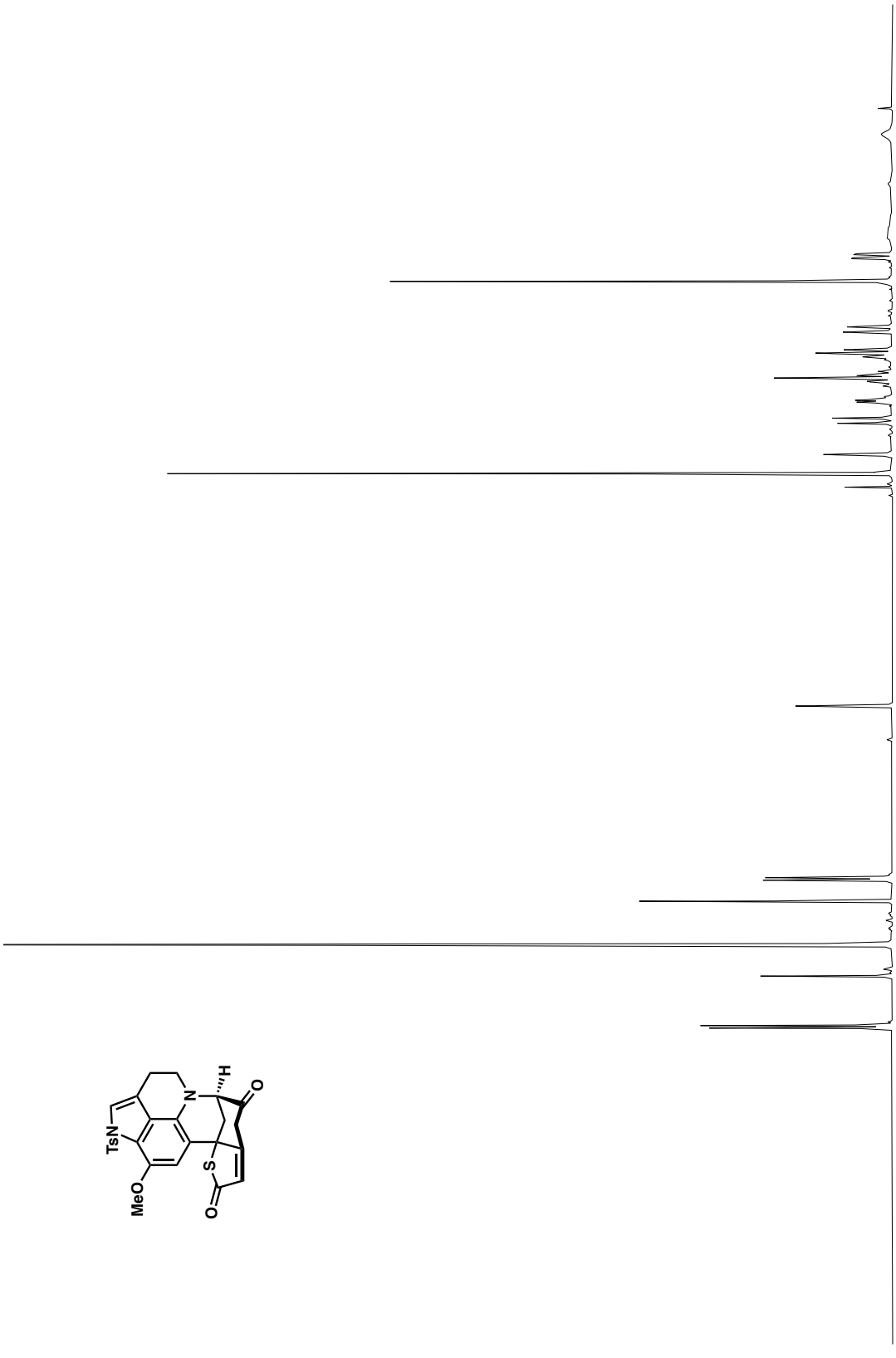


Figure A1.118. ^{1}H NMR (400 MHz, C_6D_6) of compound **94**.

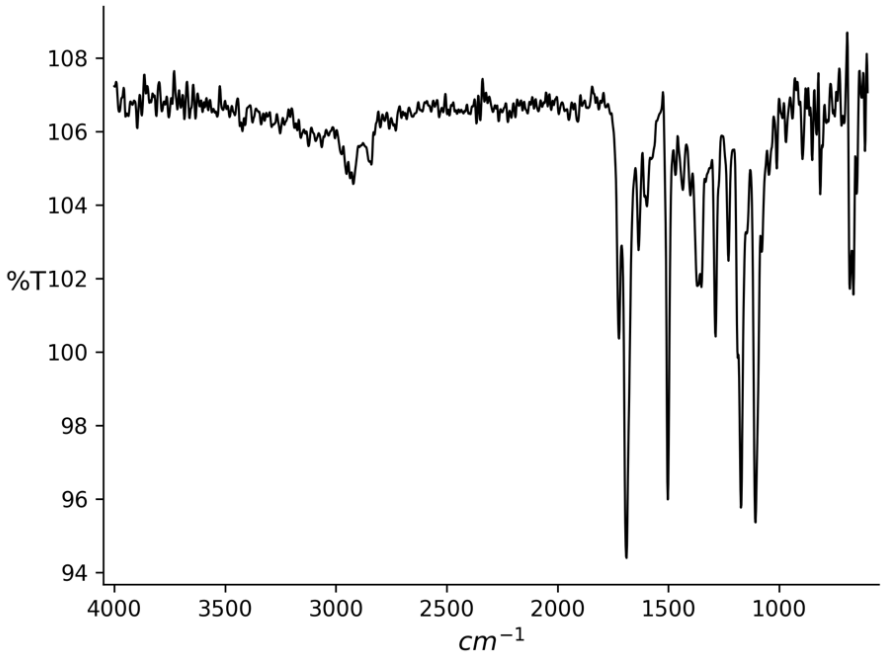


Figure A1.119. Infrared spectrum (Thin Film, NaCl) of compound **94**.

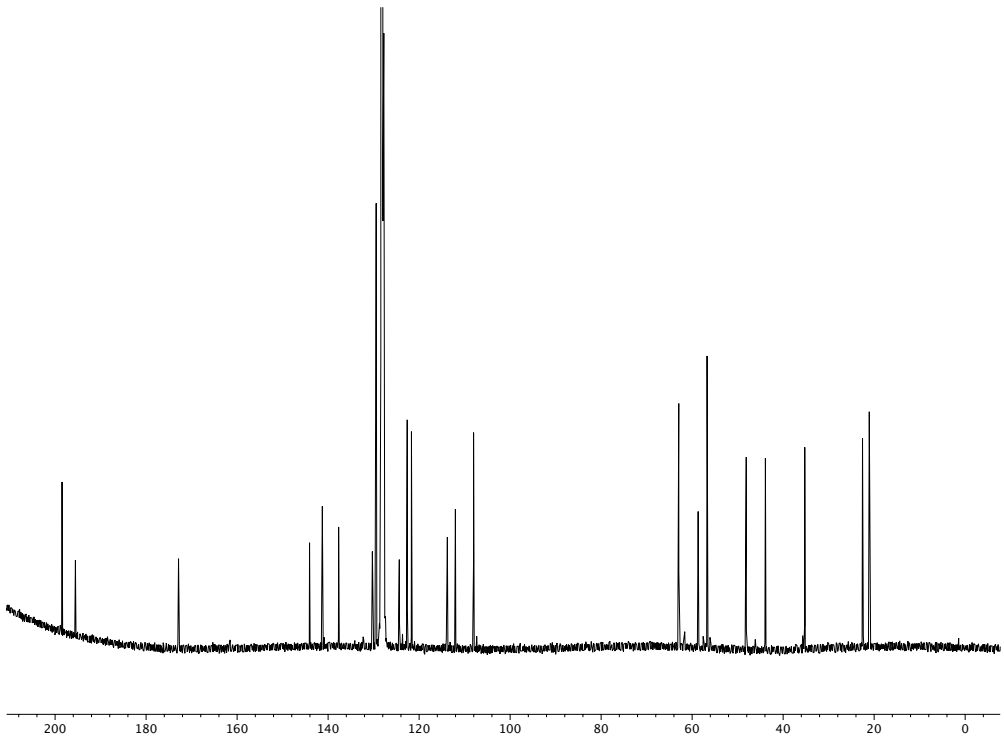


Figure A1.120. ^{13}C NMR (101 MHz, C_6D_6) of compound **94.**

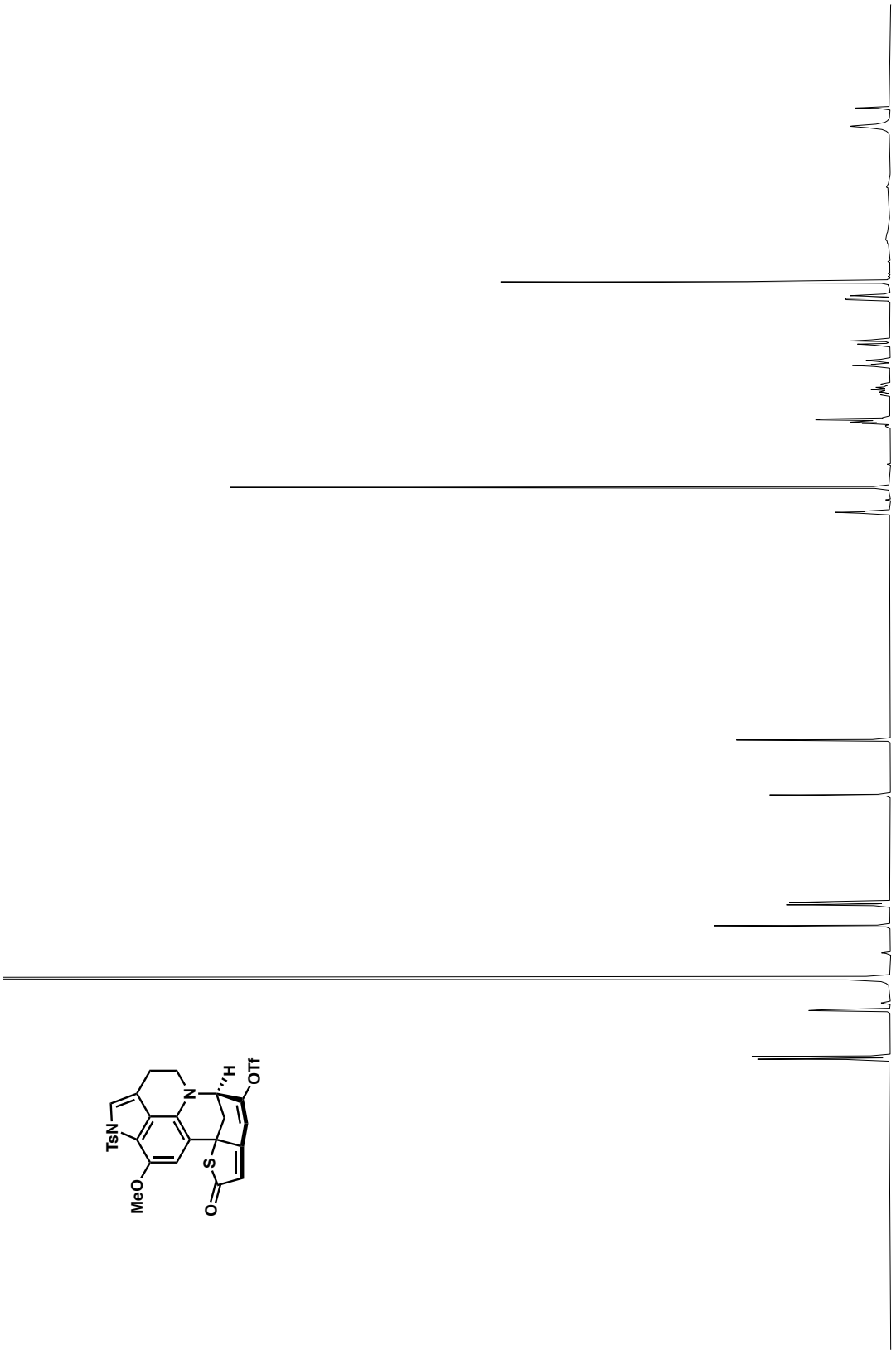


Figure A1.121. ^{1}H NMR (400 MHz, C_6D_6) of compound **103.**

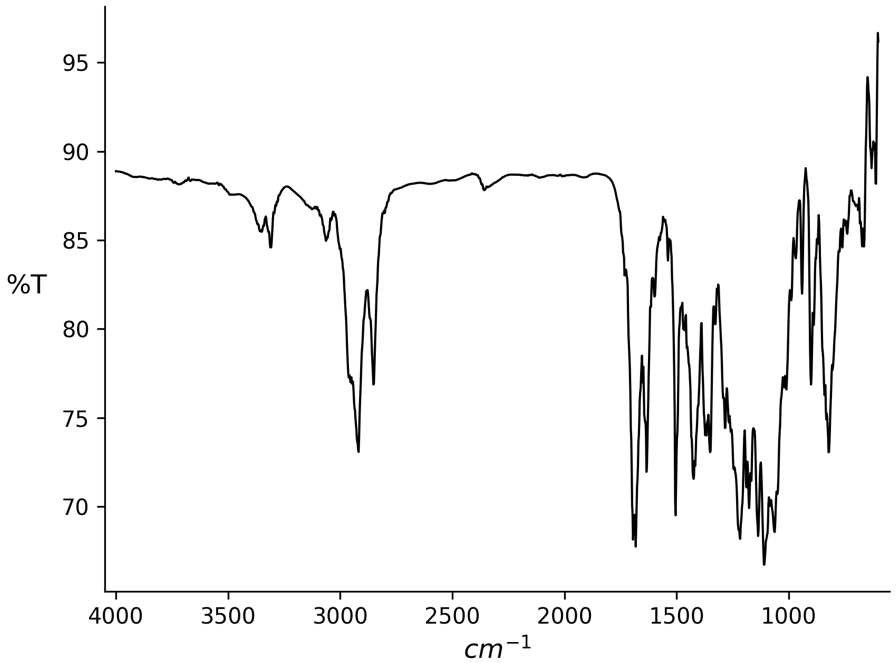


Figure A1.122. Infrared spectrum (Thin Film, NaCl) of compound **103**.

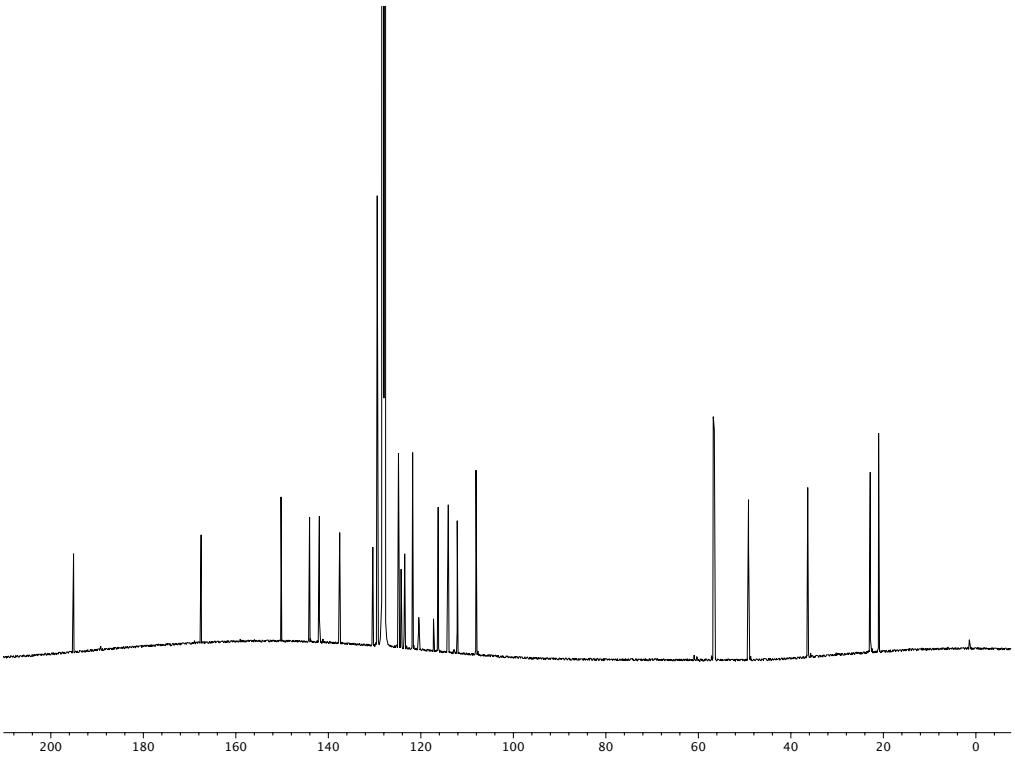


Figure A1.123. ^{13}C NMR (101 MHz, C_6D_6) of compound **103.**

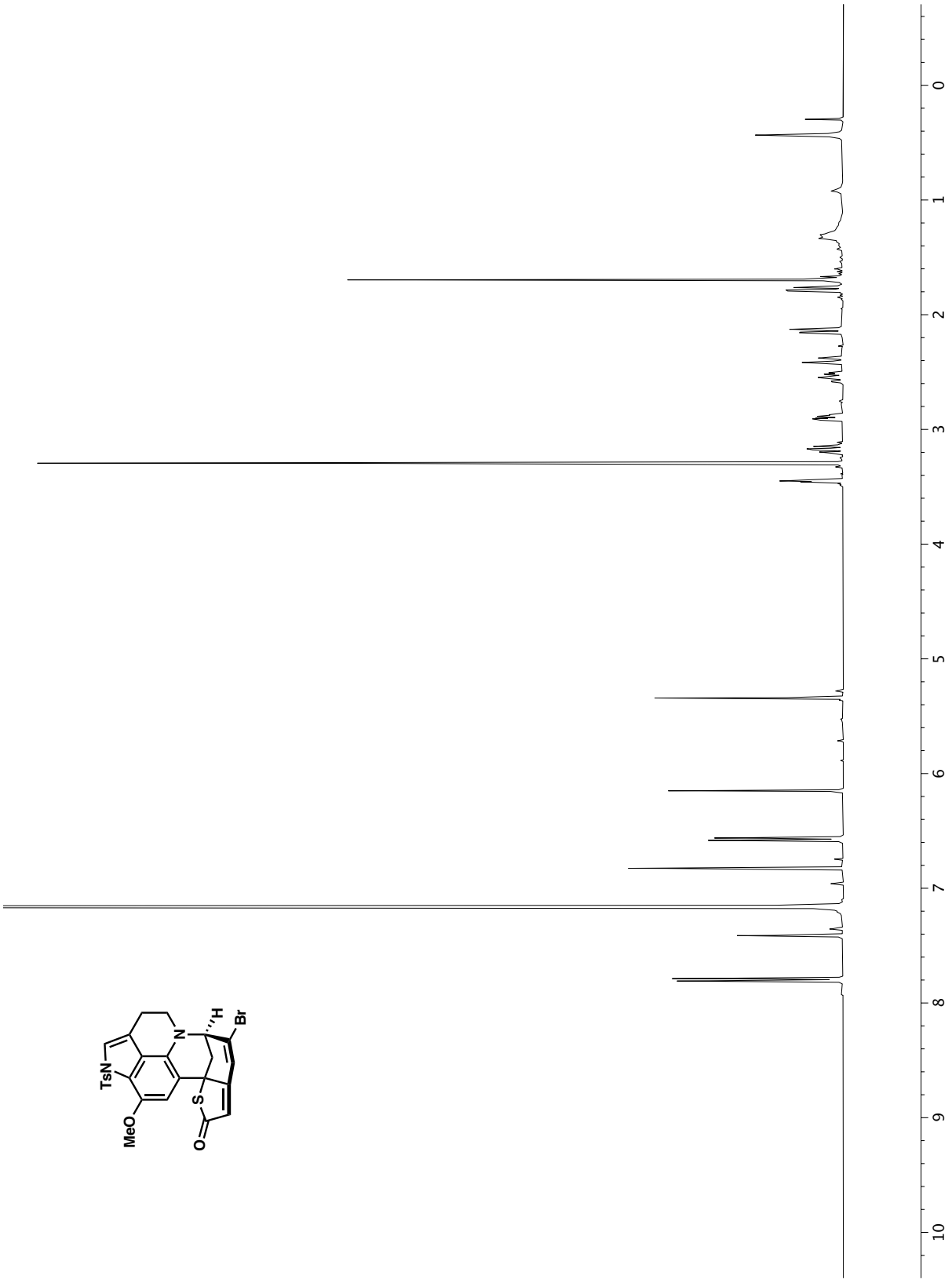


Figure A1.124. ^{1}H NMR (400 MHz, C_6D_6) of compound **95**.

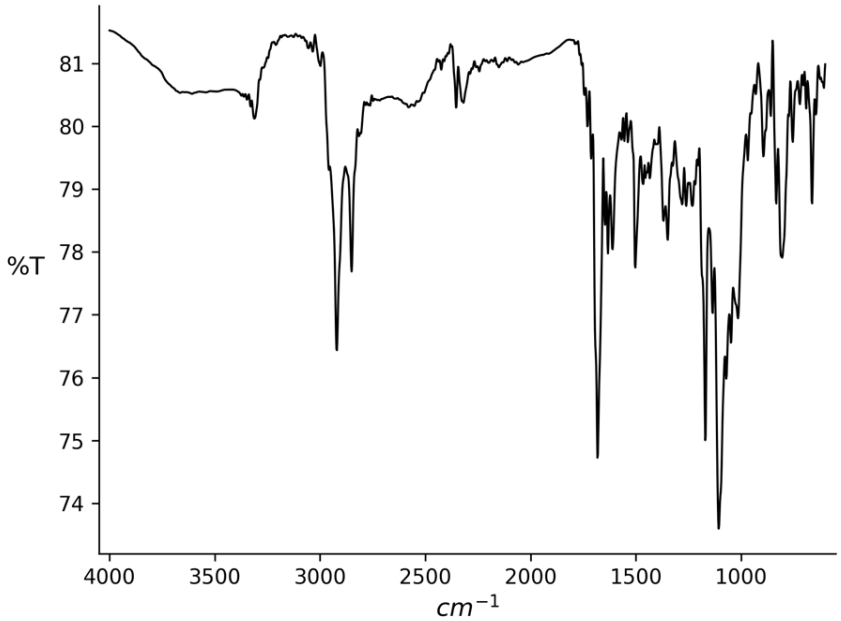


Figure A1.125. Infrared spectrum (Thin Film, NaCl) of compound **95**.

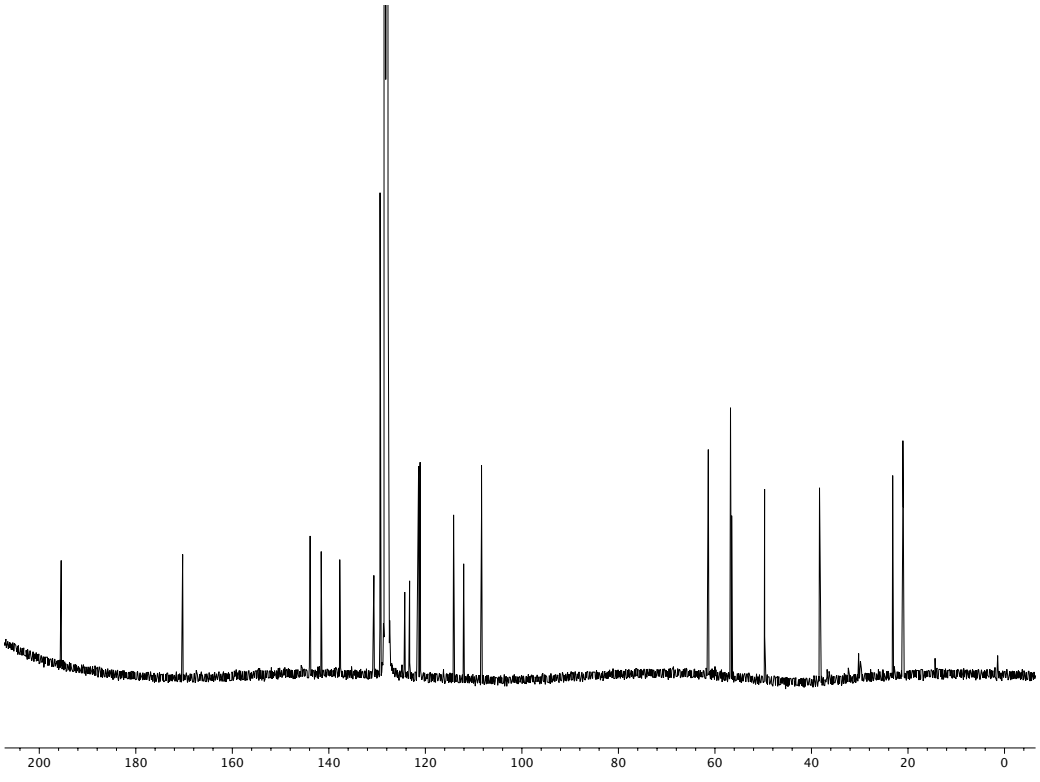


Figure A1.126. ^{13}C NMR (101 MHz, C_6D_6) of compound **95.**

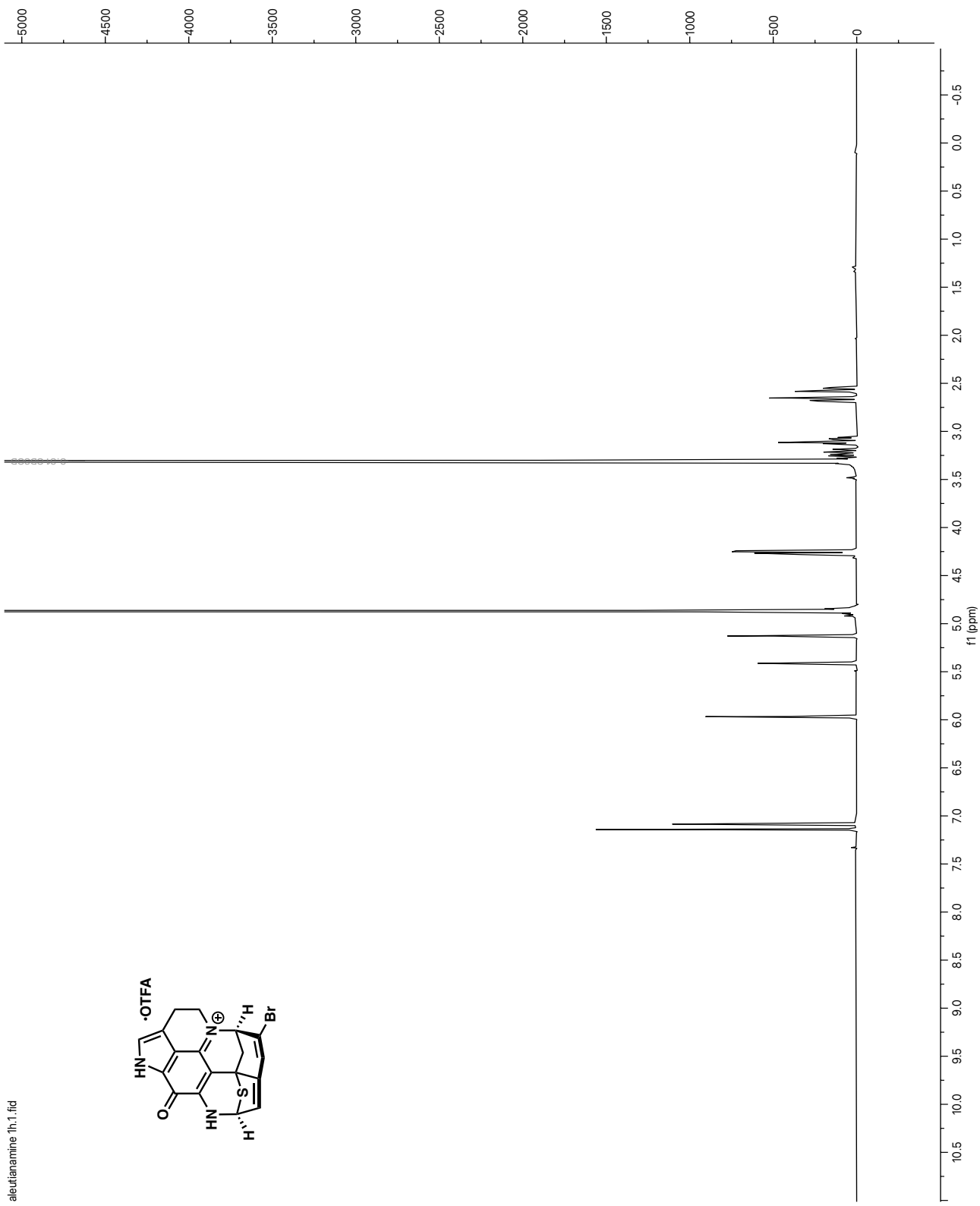


Figure A1.127. ^{1}H NMR (600 MHz, CD_3OD) of compound **1**.

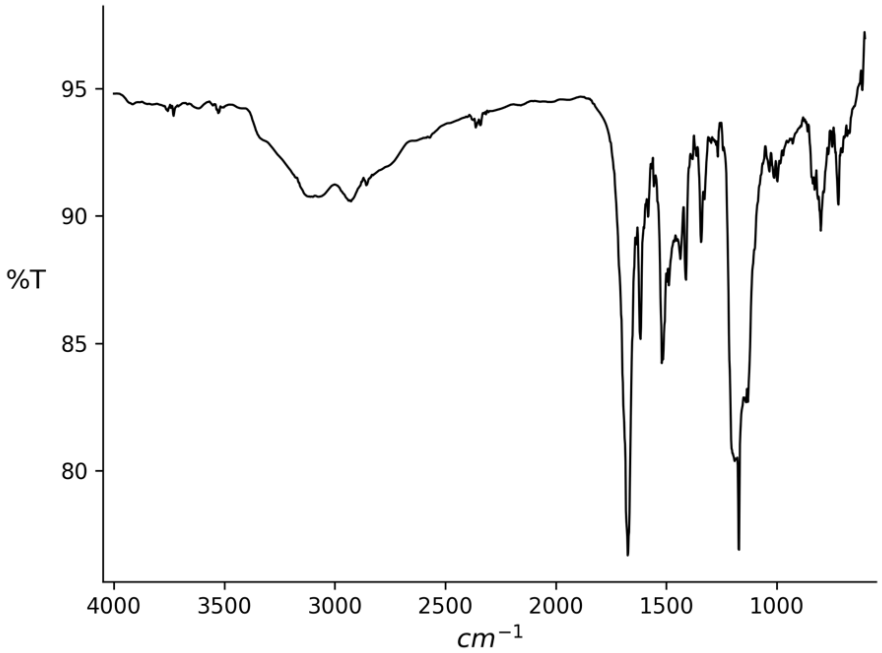


Figure A1.128. Infrared spectrum (Thin Film, NaCl) of compound **1**.

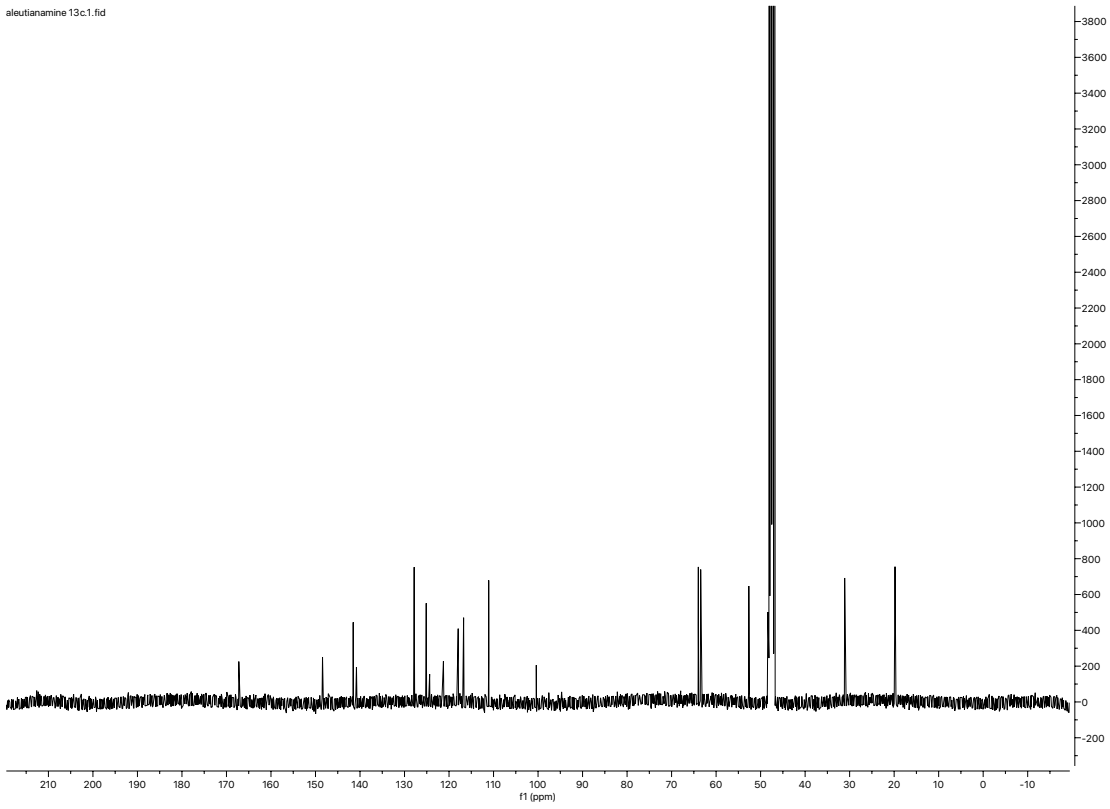


Figure A1.129. ^{13}C NMR (101 MHz, CD_3OD) of compound **1.**

APPENDIX 2

X-Ray Crystallography Reports Relevant to Chapter 1:

Total Synthesis of Aleutianamine

A2.1 GENERAL EXPERIMENTAL INFORMATION

Low-temperature diffraction data (ϕ-and ω-scans) were collected a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON II CPAD detector with Cu *K*a radiation (l = 1.54178 Å) from an IμS micro-source. The structure was solved by direct methods using SHELXS and refined against F^2 on all data by full-matrix least squares with SHELXL-2019 using established refinement techniques. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the *U* value of the atoms they are linked to (1.5 times for methyl groups).

A2.2 X-RAY CRYSTAL STRUCTURE OF COMPOUND 50

Figure A2.2.1 *X-ray crystal structure of compound* ***50****.*

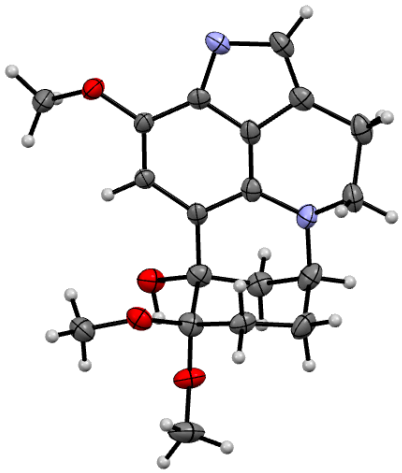


Table A2.2.1. Crystal data and structure refinement for compound **50**.

Empirical formula	C104 H120 N8 O24 S4
Formula weight	1994.31
Temperature	100(2) K
Wavelength	1.54178 Å

Crystal system	Monoclinic	
Space group	Pn	
Unit cell dimensions	a = 13.0642(17) Å	a= 90°.
	b = 10.4450(14) Å	b= 96.540(9)°.
	c = 35.025(5) Å	g = 90°.
Volume	4748.2(11) $Å^3$	
Z	2	
Density (calculated)	1.395 Mg/m^3	
Absorption coefficient	1.600 mm^{-1}	
F(000)	2112	
Crystal size	0.100 x 0.100 x 0.050 mm^3	
Theta range for data collection	2.539 to 74.648°.	
Index ranges	-16<=h<=16, -8<=k<=11, -41<=l<=43	
Reflections collected	56428	
Independent reflections	17264 [R(int) = 0.0782]	
Completeness to theta = 67.679°	97.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7538 and 0.6417	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	17264 / 6 / 1289	
Goodness-of-fit on F^2	1.020	
Final R indices [I>2sigma(I)]	R1 = 0.0606, wR2 = 0.1505	
R indices (all data)	R1 = 0.0741, wR2 = 0.1583	
Absolute structure parameter	0.039(16)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.574 and -0.509 $e.Å^{-3}$	

Table 2.2.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for compound **50**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	5663(1)	10872(2)	6716(1)	20(1)
C(1)	7000(5)	10692(7)	6836(2)	20(1)
C(2)	7370(6)	9855(9)	7124(2)	29(2)
C(3)	8423(6)	9751(9)	7220(2)	30(2)
C(4)	9110(5)	10482(8)	7032(2)	24(2)
C(7)	10262(5)	10346(10)	7139(2)	38(2)
C(5)	8720(5)	11312(8)	6751(2)	26(2)
C(6)	7654(5)	11428(8)	6645(2)	22(2)
O(1)	5218(3)	11319(5)	7046(1)	24(1)
O(2)	5465(4)	11538(5)	6362(1)	25(1)
N(1)	5219(4)	9385(6)	6656(2)	19(1)
C(8)	5273(4)	8583(7)	6332(2)	18(1)
C(21)	4514(5)	7671(7)	6342(2)	19(1)
C(22)	4379(5)	6650(7)	6082(2)	20(1)
C(9)	5970(4)	8500(7)	6056(2)	17(1)
O(3)	6744(3)	9387(5)	6076(1)	22(1)
C(24)	7562(5)	9158(8)	5849(2)	27(2)
C(10)	5835(5)	7493(7)	5796(2)	20(1)
C(11)	5045(5)	6567(6)	5802(2)	18(1)
C(12)	4874(5)	5506(7)	5510(2)	19(1)
C(23)	4389(5)	4376(7)	5707(2)	24(1)
O(4)	5825(3)	5154(5)	5387(1)	24(1)
C(13)	4093(5)	5959(7)	5161(2)	22(1)
O(5)	4385(3)	7110(5)	4990(1)	23(1)
C(25)	5274(5)	7107(7)	4785(2)	26(2)
O(6)	4053(4)	4927(5)	4895(1)	26(1)
C(26)	3407(6)	5140(8)	4540(2)	32(2)
C(14)	3040(5)	6263(8)	5291(2)	26(2)
C(15)	2608(5)	5177(8)	5519(2)	27(2)
C(16)	3394(5)	4765(7)	5858(2)	26(2)

N(2)	3625(4)	5764(6)	6147(2)	23(1)
C(17)	2780(5)	6275(8)	6348(2)	28(2)
C(18)	3167(6)	6893(8)	6737(2)	27(2)
C(19)	3991(5)	7862(7)	6672(2)	20(1)
C(20)	4419(5)	8897(7)	6861(2)	23(1)
S(101)	5050(1)	3488(2)	1853(1)	29(1)
C(101)	3783(6)	4025(8)	1893(2)	24(2)
C(102)	2961(6)	3313(9)	1732(2)	31(2)
C(103)	1971(6)	3728(9)	1767(2)	33(2)
C(104)	1794(6)	4856(8)	1961(2)	29(2)
C(107)	706(6)	5312(9)	1995(2)	37(2)
C(105)	2643(6)	5554(8)	2124(2)	29(2)
C(106)	3642(6)	5132(9)	2096(2)	29(2)
O(101)	5543(4)	3100(6)	2220(2)	38(1)
O(102)	5030(4)	2649(6)	1535(2)	36(1)
N(101)	5673(4)	4835(7)	1759(2)	30(1)
C(108)	5462(5)	5690(7)	1455(2)	22(1)
C(121)	6167(5)	6695(8)	1528(2)	24(1)
C(122)	6175(5)	7785(8)	1298(2)	28(2)
C(109)	4704(5)	5786(7)	1133(2)	22(1)
O(103)	4043(3)	4770(5)	1067(1)	26(1)
C(124)	3051(5)	5070(8)	875(2)	30(2)
C(110)	4701(5)	6866(7)	909(2)	23(1)
C(111)	5433(5)	7869(7)	978(2)	24(1)
C(112)	5457(5)	9051(8)	738(2)	28(2)
C(123)	5874(6)	10162(9)	1001(3)	38(2)
O(104)	4431(4)	9334(6)	566(2)	32(1)
C(113)	6172(5)	8888(8)	415(2)	28(2)
O(105)	6045(4)	10061(6)	210(2)	39(1)
C(125)	6652(8)	10226(10)	-97(3)	53(3)
O(106)	5941(4)	7819(5)	171(1)	32(1)
C(126)	4997(6)	7873(10)	-84(2)	40(2)
C(114)	7292(5)	8679(8)	587(2)	31(2)
C(115)	7684(6)	9713(9)	877(3)	39(2)
C(116)	6953(6)	9864(8)	1187(3)	38(2)
N(102)	6895(4)	8723(7)	1424(2)	30(1)

C(117)	7826(6)	8262(10)	1655(3)	38(2)
C(118)	7599(6)	7458(9)	2003(2)	37(2)
C(119)	6801(5)	6459(8)	1878(2)	30(2)
C(120)	6491(5)	5338(9)	2017(2)	31(2)
S(201)	4407(1)	6586(2)	3279(1)	21(1)
C(201)	3058(5)	6777(8)	3185(2)	20(1)
C(202)	2423(6)	5901(8)	3337(2)	28(2)
C(203)	1376(6)	5995(8)	3247(2)	29(2)
C(204)	945(5)	6960(9)	3004(2)	29(2)
C(207)	-205(6)	7083(9)	2905(2)	34(2)
C(205)	1600(6)	7850(9)	2862(2)	28(2)
C(206)	2662(6)	7751(8)	2947(2)	22(2)
O(201)	4805(4)	6208(5)	2933(1)	29(1)
O(202)	4634(4)	5852(5)	3621(1)	27(1)
N(201)	4851(4)	8088(6)	3354(2)	20(1)
C(208)	4790(4)	8850(6)	3683(2)	17(1)
C(221)	5535(5)	9785(7)	3673(2)	19(1)
C(222)	5666(5)	10790(7)	3937(2)	20(1)
C(209)	4101(4)	8908(6)	3963(2)	17(1)
O(203)	3358(3)	7989(5)	3944(1)	22(1)
C(224)	2532(5)	8170(8)	4168(2)	27(2)
C(210)	4235(4)	9890(7)	4227(2)	17(1)
C(211)	5011(5)	10835(7)	4223(2)	20(1)
C(212)	5194(5)	11886(7)	4518(2)	22(1)
C(223)	5649(5)	13045(7)	4321(2)	25(2)
O(204)	4217(4)	12236(5)	4639(1)	23(1)
C(213)	5964(5)	11412(7)	4866(2)	23(1)
O(205)	5665(3)	10262(5)	5030(1)	22(1)
C(225)	4778(5)	10280(7)	5238(2)	24(1)
O(206)	5994(3)	12458(4)	5132(1)	22(1)
C(226)	6650(6)	12227(8)	5491(2)	30(2)
C(214)	7018(5)	11127(7)	4734(2)	23(1)
C(215)	7433(5)	12221(8)	4511(2)	29(2)
C(216)	6668(5)	12653(7)	4175(2)	24(1)
N(202)	6434(4)	11674(6)	3878(2)	24(1)
C(217)	7280(5)	11178(8)	3679(2)	29(2)

C(218)	6900(6)	10579(9)	3288(2)	29(2)
C(219)	6076(5)	9607(7)	3345(2)	23(1)
C(220)	5658(5)	8577(7)	3154(2)	23(1)
S(301)	-41(1)	10959(2)	3152(1)	30(1)
C(301)	1207(6)	11465(9)	3101(2)	29(2)
C(302)	1385(6)	12483(9)	2864(2)	30(2)
C(303)	2376(7)	12886(8)	2845(2)	30(2)
C(304)	3207(6)	12326(8)	3059(2)	29(2)
C(307)	4295(6)	12824(9)	3045(2)	36(2)
C(305)	3040(6)	11302(9)	3291(2)	32(2)
C(306)	2039(7)	10874(8)	3316(2)	32(2)
O(301)	-541(5)	10570(6)	2786(2)	38(1)
O(302)	-33(5)	10110(6)	3470(2)	39(1)
N(301)	-636(5)	12311(6)	3247(2)	28(1)
C(308)	-423(5)	13159(7)	3558(2)	24(2)
C(321)	-1126(5)	14146(8)	3492(2)	27(2)
C(322)	-1131(5)	15231(7)	3723(2)	25(2)
C(309)	329(5)	13225(7)	3878(2)	24(2)
O(303)	992(4)	12198(5)	3943(1)	29(1)
C(324)	1966(6)	12460(9)	4156(2)	35(2)
C(310)	343(5)	14304(7)	4102(2)	24(1)
C(311)	-378(5)	15327(8)	4039(2)	24(2)
C(312)	-394(6)	16500(8)	4286(2)	29(2)
C(323)	-812(6)	17615(8)	4033(2)	32(2)
O(304)	642(4)	16755(6)	4455(2)	34(1)
C(313)	-1087(5)	16302(8)	4615(2)	28(2)
O(305)	-843(4)	15237(5)	4850(1)	30(1)
C(325)	103(6)	15258(9)	5103(2)	38(2)
O(306)	-943(4)	17461(5)	4828(2)	34(1)
C(326)	-1546(7)	17606(11)	5139(3)	49(2)
C(314)	-2214(5)	16091(8)	4451(2)	28(2)
C(315)	-2617(6)	17127(9)	4169(2)	38(2)
C(316)	-1916(6)	17290(8)	3850(2)	35(2)
N(302)	-1856(5)	16164(7)	3609(2)	31(1)
C(317)	-2807(6)	15713(9)	3386(2)	35(2)
C(318)	-2588(5)	14938(9)	3028(2)	35(2)

C(319)	-1777(5)	13937(8)	3143(2)	28(2)
C(320)	-1463(5)	12845(9)	2993(2)	32(2)

Table 2.2.3. Bond lengths [Å] and angles [°] for compound **50**.

S(1)-O(2)	1.417(5)
S(1)-O(1)	1.431(5)
S(1)-N(1)	1.663(6)
S(1)-C(1)	1.760(7)
C(1)-C(6)	1.378(10)
C(1)-C(2)	1.379(11)
C(2)-C(3)	1.383(11)
C(2)-H(2)	0.9500
C(3)-C(4)	1.398(10)
C(3)-H(3)	0.9500
C(4)-C(5)	1.366(11)
C(4)-C(7)	1.515(10)
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(5)-C(6)	1.406(10)
C(5)-H(5)	0.9500
C(6)-H(6)	0.9500
N(1)-C(8)	1.418(8)
N(1)-C(20)	1.430(8)
C(8)-C(21)	1.377(9)
C(8)-C(9)	1.403(8)
C(21)-C(22)	1.399(10)
C(21)-C(19)	1.423(8)
C(22)-N(2)	1.388(9)
C(22)-C(11)	1.388(9)
C(9)-O(3)	1.367(8)
C(9)-C(10)	1.389(9)
O(3)-C(24)	1.424(8)
C(24)-H(24A)	0.9800
C(24)-H(24B)	0.9800
C(24)-H(24C)	0.9800
C(10)-C(11)	1.416(9)
C(10)-H(10)	0.9500

C(11)-C(12)	1.508(9)
C(12)-O(4)	1.407(7)
C(12)-C(23)	1.541(10)
C(12)-C(13)	1.572(9)
C(23)-C(16)	1.513(10)
C(23)-H(23A)	0.9900
C(23)-H(23B)	0.9900
O(4)-H(4O)	0.83(3)
C(13)-O(5)	1.416(9)
C(13)-O(6)	1.422(8)
C(13)-C(14)	1.529(9)
O(5)-C(25)	1.433(8)
C(25)-H(25A)	0.9800
C(25)-H(25B)	0.9800
C(25)-H(25C)	0.9800
O(6)-C(26)	1.439(8)
C(26)-H(26A)	0.9800
C(26)-H(26B)	0.9800
C(26)-H(26C)	0.9800
C(14)-C(15)	1.533(11)
C(14)-H(14A)	0.9900
C(14)-H(14B)	0.9900
C(15)-C(16)	1.539(10)
C(15)-H(15A)	0.9900
C(15)-H(15B)	0.9900
C(16)-N(2)	1.462(9)
C(16)-H(16)	1.0000
N(2)-C(17)	1.474(9)
C(17)-C(18)	1.541(11)
C(17)-H(17A)	0.9900
C(17)-H(17B)	0.9900
C(18)-C(19)	1.514(10)
C(18)-H(18A)	0.9900
C(18)-H(18B)	0.9900
C(19)-C(20)	1.356(10)
C(20)-H(20)	0.9500

S(101)-O(102)	1.416(6)
S(101)-O(101)	1.431(6)
S(101)-N(101)	1.677(7)
S(101)-C(101)	1.769(7)
C(101)-C(102)	1.374(12)
C(101)-C(106)	1.379(12)
C(102)-C(103)	1.383(12)
C(102)-H(102)	0.9500
C(103)-C(104)	1.393(12)
C(103)-H(103)	0.9500
C(104)-C(105)	1.394(11)
C(104)-C(107)	1.517(11)
C(107)-H(10A)	0.9800
C(107)-H(10B)	0.9800
C(107)-H(10C)	0.9800
C(105)-C(106)	1.391(12)
C(105)-H(105)	0.9500
C(106)-H(106)	0.9500
N(101)-C(108)	1.393(9)
N(101)-C(120)	1.419(10)
C(108)-C(121)	1.401(10)
C(108)-C(109)	1.417(9)
C(121)-C(122)	1.394(11)
C(121)-C(119)	1.422(9)
C(122)-N(102)	1.393(9)
C(122)-C(111)	1.400(10)
C(109)-O(103)	1.371(9)
C(109)-C(110)	1.373(10)
O(103)-C(124)	1.425(8)
C(124)-H(12A)	0.9800
C(124)-H(12B)	0.9800
C(124)-H(12C)	0.9800
C(110)-C(111)	1.420(10)
C(110)-H(110)	0.9500
C(111)-C(112)	1.496(11)
C(112)-O(104)	1.436(9)

C(112)-C(123)	1.542(11)
C(112)-C(113)	1.558(10)
C(123)-C(116)	1.517(12)
C(123)-H(12D)	0.9900
C(123)-H(12E)	0.9900
O(104)-H(104)	0.86(3)
C(113)-O(106)	1.417(10)
C(113)-O(105)	1.419(10)
C(113)-C(114)	1.532(10)
O(105)-C(125)	1.417(10)
C(125)-H(12F)	0.9800
C(125)-H(12G)	0.9800
C(125)-H(12H)	0.9800
O(106)-C(126)	1.439(9)
C(126)-H(12I)	0.9800
C(126)-H(12J)	0.9800
C(126)-H(12K)	0.9800
C(114)-C(115)	1.531(12)
C(114)-H(11A)	0.9900
C(114)-H(11B)	0.9900
C(115)-C(116)	1.534(12)
C(115)-H(11C)	0.9900
C(115)-H(11D)	0.9900
C(116)-N(102)	1.459(11)
C(116)-H(116)	1.0000
N(102)-C(117)	1.465(11)
C(117)-C(118)	1.535(13)
C(117)-H(11E)	0.9900
C(117)-H(11F)	0.9900
C(118)-C(119)	1.504(11)
C(118)-H(11G)	0.9900
C(118)-H(11H)	0.9900
C(119)-C(120)	1.348(12)
C(120)-H(120)	0.9500
S(201)-O(202)	1.425(5)
S(201)-O(201)	1.428(5)

S(201)-N(201)	1.683(6)
S(201)-C(201)	1.767(7)
C(201)-C(206)	1.378(11)
C(201)-C(202)	1.382(11)
C(202)-C(203)	1.372(11)
C(202)-H(202)	0.9500
C(203)-C(204)	1.394(12)
C(203)-H(203)	0.9500
C(204)-C(205)	1.394(12)
C(204)-C(207)	1.509(10)
C(207)-H(20A)	0.9800
C(207)-H(20B)	0.9800
C(207)-H(20C)	0.9800
C(205)-C(206)	1.389(11)
C(205)-H(205)	0.9500
C(206)-H(206)	0.9500
N(201)-C(208)	1.409(8)
N(201)-C(220)	1.426(8)
C(208)-C(221)	1.382(9)
C(208)-C(209)	1.405(8)
C(221)-C(222)	1.396(10)
C(221)-C(219)	1.428(9)
C(222)-C(211)	1.391(9)
C(222)-N(202)	1.395(8)
C(209)-O(203)	1.362(7)
C(209)-C(210)	1.381(9)
O(203)-C(224)	1.417(8)
C(224)-H(22A)	0.9800
C(224)-H(22B)	0.9800
C(224)-H(22C)	0.9800
C(210)-C(211)	1.417(9)
C(210)-H(210)	0.9500
C(211)-C(212)	1.508(10)
C(212)-O(204)	1.438(8)
C(212)-C(223)	1.543(10)
C(212)-C(213)	1.569(9)

C(223)-C(216)	1.537(10)
C(223)-H(22D)	0.9900
C(223)-H(22E)	0.9900
O(204)-H(204)	0.83(3)
C(213)-O(205)	1.406(9)
C(213)-O(206)	1.434(8)
C(213)-C(214)	1.530(9)
O(205)-C(225)	1.437(8)
C(225)-H(22F)	0.9800
C(225)-H(22G)	0.9800
C(225)-H(22H)	0.9800
O(206)-C(226)	1.458(8)
C(226)-H(22I)	0.9800
C(226)-H(22J)	0.9800
C(226)-H(22K)	0.9800
C(214)-C(215)	1.519(10)
C(214)-H(21A)	0.9900
C(214)-H(21B)	0.9900
C(215)-C(216)	1.523(10)
C(215)-H(21C)	0.9900
C(215)-H(21D)	0.9900
C(216)-N(202)	1.467(9)
C(216)-H(216)	1.0000
N(202)-C(217)	1.467(9)
C(217)-C(218)	1.536(10)
C(217)-H(21E)	0.9900
C(217)-H(21F)	0.9900
C(218)-C(219)	1.511(10)
C(218)-H(21G)	0.9900
C(218)-H(21H)	0.9900
C(219)-C(220)	1.348(10)
C(220)-H(220)	0.9500
S(301)-O(302)	1.423(6)
S(301)-O(301)	1.428(6)
S(301)-N(301)	1.664(7)
S(301)-C(301)	1.742(9)

C(301)-C(302)	1.384(12)
C(301)-C(306)	1.395(12)
C(302)-C(303)	1.370(12)
C(302)-H(302)	0.9500
C(303)-C(304)	1.378(12)
C(303)-H(303)	0.9500
C(304)-C(305)	1.374(12)
C(304)-C(307)	1.519(12)
C(307)-H(30A)	0.9800
C(307)-H(30B)	0.9800
C(307)-H(30C)	0.9800
C(305)-C(306)	1.394(12)
C(305)-H(305)	0.9500
C(306)-H(306)	0.9500
N(301)-C(308)	1.405(9)
N(301)-C(320)	1.432(10)
C(308)-C(321)	1.382(10)
C(308)-C(309)	1.407(9)
C(321)-C(322)	1.393(11)
C(321)-C(319)	1.424(9)
C(322)-N(302)	1.385(10)
C(322)-C(311)	1.397(9)
C(309)-C(310)	1.373(10)
C(309)-O(303)	1.380(9)
O(303)-C(324)	1.427(9)
C(324)-H(32A)	0.9800
C(324)-H(32B)	0.9800
C(324)-H(32C)	0.9800
C(310)-C(311)	1.426(10)
C(310)-H(310)	0.9500
C(311)-C(312)	1.501(11)
C(312)-O(304)	1.438(9)
C(312)-C(323)	1.527(11)
C(312)-C(313)	1.559(10)
C(323)-C(316)	1.547(11)
C(323)-H(32D)	0.9900

C(323)-H(32E)	0.9900
O(304)-H(304)	0.86(3)
C(313)-O(305)	1.397(10)
C(313)-O(306)	1.423(9)
C(313)-C(314)	1.535(9)
O(305)-C(325)	1.438(9)
C(325)-H(32F)	0.9800
C(325)-H(32G)	0.9800
C(325)-H(32H)	0.9800
O(306)-C(326)	1.423(9)
C(326)-H(32I)	0.9800
C(326)-H(32J)	0.9800
C(326)-H(32K)	0.9800
C(314)-C(315)	1.518(12)
C(314)-H(31A)	0.9900
C(314)-H(31B)	0.9900
C(315)-C(316)	1.533(11)
C(315)-H(31C)	0.9900
C(315)-H(31D)	0.9900
C(316)-N(302)	1.455(11)
C(316)-H(316)	1.0000
N(302)-C(317)	1.469(10)
C(317)-C(318)	1.543(12)
C(317)-H(31E)	0.9900
C(317)-H(31F)	0.9900
C(318)-C(319)	1.511(11)
C(318)-H(31G)	0.9900
C(318)-H(31H)	0.9900
C(319)-C(320)	1.341(12)
C(320)-H(320)	0.9500

O(2)-S(1)-O(1)	119.8(3)
O(2)-S(1)-N(1)	108.7(3)
O(1)-S(1)-N(1)	103.9(3)
O(2)-S(1)-C(1)	109.8(3)
O(1)-S(1)-C(1)	108.9(3)

N(1)-S(1)-C(1)	104.6(3)
C(6)-C(1)-C(2)	121.6(7)
C(6)-C(1)-S(1)	118.5(6)
C(2)-C(1)-S(1)	119.9(6)
C(1)-C(2)-C(3)	118.9(7)
C(1)-C(2)-H(2)	120.5
C(3)-C(2)-H(2)	120.5
C(2)-C(3)-C(4)	121.2(8)
C(2)-C(3)-H(3)	119.4
C(4)-C(3)-H(3)	119.4
C(5)-C(4)-C(3)	118.5(7)
C(5)-C(4)-C(7)	121.0(7)
C(3)-C(4)-C(7)	120.4(7)
C(4)-C(7)-H(7A)	109.5
C(4)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
C(4)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(4)-C(5)-C(6)	121.6(7)
C(4)-C(5)-H(5)	119.2
C(6)-C(5)-H(5)	119.2
C(1)-C(6)-C(5)	118.2(7)
C(1)-C(6)-H(6)	120.9
C(5)-C(6)-H(6)	120.9
C(8)-N(1)-C(20)	107.3(5)
C(8)-N(1)-S(1)	127.3(5)
C(20)-N(1)-S(1)	122.2(5)
C(21)-C(8)-C(9)	120.0(6)
C(21)-C(8)-N(1)	106.7(5)
C(9)-C(8)-N(1)	132.9(6)
C(8)-C(21)-C(22)	123.3(6)
C(8)-C(21)-C(19)	109.7(6)
C(22)-C(21)-C(19)	126.7(6)
N(2)-C(22)-C(11)	126.0(6)
N(2)-C(22)-C(21)	116.2(6)

C(11)-C(22)-C(21)	117.6(6)
O(3)-C(9)-C(10)	125.8(5)
O(3)-C(9)-C(8)	117.2(6)
C(10)-C(9)-C(8)	116.9(6)
C(9)-O(3)-C(24)	117.1(5)
O(3)-C(24)-H(24A)	109.5
O(3)-C(24)-H(24B)	109.5
H(24A)-C(24)-H(24B)	109.5
O(3)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5
C(9)-C(10)-C(11)	123.1(6)
C(9)-C(10)-H(10)	118.4
C(11)-C(10)-H(10)	118.4
C(22)-C(11)-C(10)	119.0(6)
C(22)-C(11)-C(12)	118.0(6)
C(10)-C(11)-C(12)	123.0(6)
O(4)-C(12)-C(11)	109.3(5)
O(4)-C(12)-C(23)	111.1(5)
C(11)-C(12)-C(23)	107.2(5)
O(4)-C(12)-C(13)	111.1(5)
C(11)-C(12)-C(13)	109.7(5)
C(23)-C(12)-C(13)	108.4(5)
C(16)-C(23)-C(12)	111.4(6)
C(16)-C(23)-H(23A)	109.4
C(12)-C(23)-H(23A)	109.4
C(16)-C(23)-H(23B)	109.4
C(12)-C(23)-H(23B)	109.4
H(23A)-C(23)-H(23B)	108.0
C(12)-O(4)-H(4O)	107(6)
O(5)-C(13)-O(6)	110.9(5)
O(5)-C(13)-C(14)	104.1(5)
O(6)-C(13)-C(14)	112.6(5)
O(5)-C(13)-C(12)	113.7(5)
O(6)-C(13)-C(12)	104.6(5)
C(14)-C(13)-C(12)	111.1(5)

C(13)-O(5)-C(25)	118.9(5)
O(5)-C(25)-H(25A)	109.5
O(5)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25B)	109.5
O(5)-C(25)-H(25C)	109.5
H(25A)-C(25)-H(25C)	109.5
H(25B)-C(25)-H(25C)	109.5
C(13)-O(6)-C(26)	115.1(5)
O(6)-C(26)-H(26A)	109.5
O(6)-C(26)-H(26B)	109.5
H(26A)-C(26)-H(26B)	109.5
O(6)-C(26)-H(26C)	109.5
H(26A)-C(26)-H(26C)	109.5
H(26B)-C(26)-H(26C)	109.5
C(13)-C(14)-C(15)	113.4(6)
C(13)-C(14)-H(14A)	108.9
C(15)-C(14)-H(14A)	108.9
C(13)-C(14)-H(14B)	108.9
C(15)-C(14)-H(14B)	108.9
H(14A)-C(14)-H(14B)	107.7
C(14)-C(15)-C(16)	110.9(5)
C(14)-C(15)-H(15A)	109.5
C(16)-C(15)-H(15A)	109.5
C(14)-C(15)-H(15B)	109.5
C(16)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	108.0
N(2)-C(16)-C(23)	108.4(5)
N(2)-C(16)-C(15)	113.7(6)
C(23)-C(16)-C(15)	109.4(6)
N(2)-C(16)-H(16)	108.4
C(23)-C(16)-H(16)	108.4
C(15)-C(16)-H(16)	108.4
C(22)-N(2)-C(16)	117.2(5)
C(22)-N(2)-C(17)	114.8(6)
C(16)-N(2)-C(17)	118.8(5)
N(2)-C(17)-C(18)	112.7(6)

N(2)-C(17)-H(17A)	109.1
C(18)-C(17)-H(17A)	109.1
N(2)-C(17)-H(17B)	109.1
C(18)-C(17)-H(17B)	109.1
H(17A)-C(17)-H(17B)	107.8
C(19)-C(18)-C(17)	108.2(6)
C(19)-C(18)-H(18A)	110.1
C(17)-C(18)-H(18A)	110.1
C(19)-C(18)-H(18B)	110.1
C(17)-C(18)-H(18B)	110.1
H(18A)-C(18)-H(18B)	108.4
C(20)-C(19)-C(21)	107.5(6)
C(20)-C(19)-C(18)	136.0(6)
C(21)-C(19)-C(18)	116.4(6)
C(19)-C(20)-N(1)	108.8(5)
C(19)-C(20)-H(20)	125.6
N(1)-C(20)-H(20)	125.6
O(102)-S(101)-O(101)	119.9(4)
O(102)-S(101)-N(101)	109.3(3)
O(101)-S(101)-N(101)	103.7(3)
O(102)-S(101)-C(101)	109.0(4)
O(101)-S(101)-C(101)	110.3(3)
N(101)-S(101)-C(101)	103.3(3)
C(102)-C(101)-C(106)	121.4(7)
C(102)-C(101)-S(101)	119.4(6)
C(106)-C(101)-S(101)	119.2(6)
C(101)-C(102)-C(103)	119.3(8)
C(101)-C(102)-H(102)	120.4
C(103)-C(102)-H(102)	120.4
C(102)-C(103)-C(104)	121.2(8)
C(102)-C(103)-H(103)	119.4
C(104)-C(103)-H(103)	119.4
C(103)-C(104)-C(105)	118.3(8)
C(103)-C(104)-C(107)	120.9(7)
C(105)-C(104)-C(107)	120.9(8)
C(104)-C(107)-H(10A)	109.5

C(104)-C(107)-H(10B)	109.5
H(10A)-C(107)-H(10B)	109.5
C(104)-C(107)-H(10C)	109.5
H(10A)-C(107)-H(10C)	109.5
H(10B)-C(107)-H(10C)	109.5
C(106)-C(105)-C(104)	121.0(8)
C(106)-C(105)-H(105)	119.5
C(104)-C(105)-H(105)	119.5
C(101)-C(106)-C(105)	118.9(7)
C(101)-C(106)-H(106)	120.5
C(105)-C(106)-H(106)	120.5
C(108)-N(101)-C(120)	108.6(6)
C(108)-N(101)-S(101)	129.0(5)
C(120)-N(101)-S(101)	122.2(5)
N(101)-C(108)-C(121)	105.8(6)
N(101)-C(108)-C(109)	135.5(7)
C(121)-C(108)-C(109)	118.5(6)
C(122)-C(121)-C(108)	123.7(6)
C(122)-C(121)-C(119)	126.6(7)
C(108)-C(121)-C(119)	109.5(7)
N(102)-C(122)-C(121)	116.3(6)
N(102)-C(122)-C(111)	126.1(7)
C(121)-C(122)-C(111)	117.5(6)
O(103)-C(109)-C(110)	125.4(6)
O(103)-C(109)-C(108)	116.6(6)
C(110)-C(109)-C(108)	117.9(6)
C(109)-O(103)-C(124)	115.5(6)
O(103)-C(124)-H(12A)	109.5
O(103)-C(124)-H(12B)	109.5
H(12A)-C(124)-H(12B)	109.5
O(103)-C(124)-H(12C)	109.5
H(12A)-C(124)-H(12C)	109.5
H(12B)-C(124)-H(12C)	109.5
C(109)-C(110)-C(111)	123.4(6)
C(109)-C(110)-H(110)	118.3
C(111)-C(110)-H(110)	118.3

C(122)-C(111)-C(110)	118.8(7)
C(122)-C(111)-C(112)	116.4(6)
C(110)-C(111)-C(112)	124.8(6)
O(104)-C(112)-C(111)	109.1(6)
O(104)-C(112)-C(123)	110.1(6)
C(111)-C(112)-C(123)	108.3(6)
O(104)-C(112)-C(113)	109.1(6)
C(111)-C(112)-C(113)	111.8(6)
C(123)-C(112)-C(113)	108.5(6)
C(116)-C(123)-C(112)	110.5(7)
C(116)-C(123)-H(12D)	109.6
C(112)-C(123)-H(12D)	109.6
C(116)-C(123)-H(12E)	109.6
C(112)-C(123)-H(12E)	109.6
H(12D)-C(123)-H(12E)	108.1
C(112)-O(104)-H(104)	104(7)
O(106)-C(113)-O(105)	111.8(6)
O(106)-C(113)-C(114)	104.7(6)
O(105)-C(113)-C(114)	111.9(6)
O(106)-C(113)-C(112)	114.8(6)
O(105)-C(113)-C(112)	103.1(6)
C(114)-C(113)-C(112)	110.7(6)
C(125)-O(105)-C(113)	116.4(6)
O(105)-C(125)-H(12F)	109.5
O(105)-C(125)-H(12G)	109.5
H(12F)-C(125)-H(12G)	109.5
O(105)-C(125)-H(12H)	109.5
H(12F)-C(125)-H(12H)	109.5
H(12G)-C(125)-H(12H)	109.5
C(113)-O(106)-C(126)	116.9(6)
O(106)-C(126)-H(12I)	109.5
O(106)-C(126)-H(12J)	109.5
H(12I)-C(126)-H(12J)	109.5
O(106)-C(126)-H(12K)	109.5
H(12I)-C(126)-H(12K)	109.5
H(12J)-C(126)-H(12K)	109.5

C(115)-C(114)-C(113)	113.1(7)
C(115)-C(114)-H(11A)	109.0
C(113)-C(114)-H(11A)	109.0
C(115)-C(114)-H(11B)	109.0
C(113)-C(114)-H(11B)	109.0
H(11A)-C(114)-H(11B)	107.8
C(114)-C(115)-C(116)	110.8(6)
C(114)-C(115)-H(11C)	109.5
C(116)-C(115)-H(11C)	109.5
C(114)-C(115)-H(11D)	109.5
C(116)-C(115)-H(11D)	109.5
H(11C)-C(115)-H(11D)	108.1
N(102)-C(116)-C(123)	107.8(6)
N(102)-C(116)-C(115)	113.3(7)
C(123)-C(116)-C(115)	109.8(7)
N(102)-C(116)-H(116)	108.6
C(123)-C(116)-H(116)	108.6
C(115)-C(116)-H(116)	108.6
C(122)-N(102)-C(116)	118.2(6)
C(122)-N(102)-C(117)	115.5(7)
C(116)-N(102)-C(117)	119.3(6)
N(102)-C(117)-C(118)	113.4(7)
N(102)-C(117)-H(11E)	108.9
C(118)-C(117)-H(11E)	108.9
N(102)-C(117)-H(11F)	108.9
C(118)-C(117)-H(11F)	108.9
H(11E)-C(117)-H(11F)	107.7
C(119)-C(118)-C(117)	109.7(6)
C(119)-C(118)-H(11G)	109.7
C(117)-C(118)-H(11G)	109.7
C(119)-C(118)-H(11H)	109.7
C(117)-C(118)-H(11H)	109.7
H(11G)-C(118)-H(11H)	108.2
C(120)-C(119)-C(121)	107.0(6)
C(120)-C(119)-C(118)	136.4(7)
C(121)-C(119)-C(118)	116.6(7)

C(119)-C(120)-N(101)	109.1(6)
C(119)-C(120)-H(120)	125.4
N(101)-C(120)-H(120)	125.4
O(202)-S(201)-O(201)	120.2(3)
O(202)-S(201)-N(201)	109.5(3)
O(201)-S(201)-N(201)	103.8(3)
O(202)-S(201)-C(201)	109.0(3)
O(201)-S(201)-C(201)	109.0(3)
N(201)-S(201)-C(201)	104.1(3)
C(206)-C(201)-C(202)	121.4(7)
C(206)-C(201)-S(201)	119.5(6)
C(202)-C(201)-S(201)	118.9(6)
C(203)-C(202)-C(201)	119.3(7)
C(203)-C(202)-H(202)	120.3
C(201)-C(202)-H(202)	120.3
C(202)-C(203)-C(204)	121.0(7)
C(202)-C(203)-H(203)	119.5
C(204)-C(203)-H(203)	119.5
C(205)-C(204)-C(203)	118.6(7)
C(205)-C(204)-C(207)	119.8(8)
C(203)-C(204)-C(207)	121.6(7)
C(204)-C(207)-H(20A)	109.5
C(204)-C(207)-H(20B)	109.5
H(20A)-C(207)-H(20B)	109.5
C(204)-C(207)-H(20C)	109.5
H(20A)-C(207)-H(20C)	109.5
H(20B)-C(207)-H(20C)	109.5
C(206)-C(205)-C(204)	120.8(7)
C(206)-C(205)-H(205)	119.6
C(204)-C(205)-H(205)	119.6
C(201)-C(206)-C(205)	118.8(7)
C(201)-C(206)-H(206)	120.6
C(205)-C(206)-H(206)	120.6
C(208)-N(201)-C(220)	108.2(5)
C(208)-N(201)-S(201)	127.2(4)
C(220)-N(201)-S(201)	121.2(5)

C(221)-C(208)-C(209)	119.7(6)
C(221)-C(208)-N(201)	105.9(5)
C(209)-C(208)-N(201)	134.0(6)
C(208)-C(221)-C(222)	123.3(6)
C(208)-C(221)-C(219)	110.0(6)
C(222)-C(221)-C(219)	126.5(6)
C(211)-C(222)-N(202)	126.6(6)
C(211)-C(222)-C(221)	117.5(6)
N(202)-C(222)-C(221)	115.8(6)
O(203)-C(209)-C(210)	126.2(5)
O(203)-C(209)-C(208)	116.5(6)
C(210)-C(209)-C(208)	117.3(5)
C(209)-O(203)-C(224)	117.6(5)
O(203)-C(224)-H(22A)	109.5
O(203)-C(224)-H(22B)	109.5
H(22A)-C(224)-H(22B)	109.5
O(203)-C(224)-H(22C)	109.5
H(22A)-C(224)-H(22C)	109.5
H(22B)-C(224)-H(22C)	109.5
C(209)-C(210)-C(211)	123.0(6)
C(209)-C(210)-H(210)	118.5
C(211)-C(210)-H(210)	118.5
C(222)-C(211)-C(210)	119.1(6)
C(222)-C(211)-C(212)	117.1(6)
C(210)-C(211)-C(212)	123.8(6)
O(204)-C(212)-C(211)	108.1(5)
O(204)-C(212)-C(223)	109.4(6)
C(211)-C(212)-C(223)	107.8(5)
O(204)-C(212)-C(213)	111.2(5)
C(211)-C(212)-C(213)	109.8(6)
C(223)-C(212)-C(213)	110.4(5)
C(216)-C(223)-C(212)	109.4(6)
C(216)-C(223)-H(22D)	109.8
C(212)-C(223)-H(22D)	109.8
C(216)-C(223)-H(22E)	109.8
C(212)-C(223)-H(22E)	109.8

H(22D)-C(223)-H(22E)	108.2
C(212)-O(204)-H(204)	123(6)
O(205)-C(213)-O(206)	111.8(5)
O(205)-C(213)-C(214)	105.0(6)
O(206)-C(213)-C(214)	112.6(5)
O(205)-C(213)-C(212)	113.9(5)
O(206)-C(213)-C(212)	103.5(5)
C(214)-C(213)-C(212)	110.3(5)
C(213)-O(205)-C(225)	118.3(5)
O(205)-C(225)-H(22F)	109.5
O(205)-C(225)-H(22G)	109.5
H(22F)-C(225)-H(22G)	109.5
O(205)-C(225)-H(22H)	109.5
H(22F)-C(225)-H(22H)	109.5
H(22G)-C(225)-H(22H)	109.5
C(213)-O(206)-C(226)	113.9(5)
O(206)-C(226)-H(22I)	109.5
O(206)-C(226)-H(22J)	109.5
H(22I)-C(226)-H(22J)	109.5
O(206)-C(226)-H(22K)	109.5
H(22I)-C(226)-H(22K)	109.5
H(22J)-C(226)-H(22K)	109.5
C(215)-C(214)-C(213)	113.2(6)
C(215)-C(214)-H(21A)	108.9
C(213)-C(214)-H(21A)	108.9
C(215)-C(214)-H(21B)	108.9
C(213)-C(214)-H(21B)	108.9
H(21A)-C(214)-H(21B)	107.7
C(214)-C(215)-C(216)	112.3(5)
C(214)-C(215)-H(21C)	109.2
C(216)-C(215)-H(21C)	109.2
C(214)-C(215)-H(21D)	109.2
C(216)-C(215)-H(21D)	109.2
H(21C)-C(215)-H(21D)	107.9
N(202)-C(216)-C(215)	114.1(6)
N(202)-C(216)-C(223)	107.7(5)

C(215)-C(216)-C(223)	109.8(6)
N(202)-C(216)-H(216)	108.4
C(215)-C(216)-H(216)	108.4
C(223)-C(216)-H(216)	108.4
C(222)-N(202)-C(217)	115.5(6)
C(222)-N(202)-C(216)	116.8(5)
C(217)-N(202)-C(216)	118.4(5)
N(202)-C(217)-C(218)	112.5(6)
N(202)-C(217)-H(21E)	109.1
C(218)-C(217)-H(21E)	109.1
N(202)-C(217)-H(21F)	109.1
C(218)-C(217)-H(21F)	109.1
H(21E)-C(217)-H(21F)	107.8
C(219)-C(218)-C(217)	108.5(6)
C(219)-C(218)-H(21G)	110.0
C(217)-C(218)-H(21G)	110.0
C(219)-C(218)-H(21H)	110.0
C(217)-C(218)-H(21H)	110.0
H(21G)-C(218)-H(21H)	108.4
C(220)-C(219)-C(221)	107.1(6)
C(220)-C(219)-C(218)	136.4(6)
C(221)-C(219)-C(218)	116.4(6)
C(219)-C(220)-N(201)	108.8(5)
C(219)-C(220)-H(220)	125.6
N(201)-C(220)-H(220)	125.6
O(302)-S(301)-O(301)	119.1(4)
O(302)-S(301)-N(301)	109.5(3)
O(301)-S(301)-N(301)	104.2(3)
O(302)-S(301)-C(301)	110.2(4)
O(301)-S(301)-C(301)	109.4(3)
N(301)-S(301)-C(301)	103.1(4)
C(302)-C(301)-C(306)	119.3(8)
C(302)-C(301)-S(301)	121.2(7)
C(306)-C(301)-S(301)	119.5(6)
C(303)-C(302)-C(301)	119.3(8)
C(303)-C(302)-H(302)	120.3

C(301)-C(302)-H(302)	120.3
C(302)-C(303)-C(304)	122.2(8)
C(302)-C(303)-H(303)	118.9
C(304)-C(303)-H(303)	118.9
C(305)-C(304)-C(303)	118.9(8)
C(305)-C(304)-C(307)	119.8(7)
C(303)-C(304)-C(307)	121.2(8)
C(304)-C(307)-H(30A)	109.5
C(304)-C(307)-H(30B)	109.5
H(30A)-C(307)-H(30B)	109.5
C(304)-C(307)-H(30C)	109.5
H(30A)-C(307)-H(30C)	109.5
H(30B)-C(307)-H(30C)	109.5
C(304)-C(305)-C(306)	120.0(8)
C(304)-C(305)-H(305)	120.0
C(306)-C(305)-H(305)	120.0
C(305)-C(306)-C(301)	120.2(7)
C(305)-C(306)-H(306)	119.9
C(301)-C(306)-H(306)	119.9
C(308)-N(301)-C(320)	107.7(6)
C(308)-N(301)-S(301)	129.4(5)
C(320)-N(301)-S(301)	122.8(5)
C(321)-C(308)-N(301)	105.8(6)
C(321)-C(308)-C(309)	119.1(7)
N(301)-C(308)-C(309)	135.0(7)
C(308)-C(321)-C(322)	123.9(6)
C(308)-C(321)-C(319)	110.4(7)
C(322)-C(321)-C(319)	125.5(7)
N(302)-C(322)-C(321)	117.0(6)
N(302)-C(322)-C(311)	125.1(7)
C(321)-C(322)-C(311)	117.9(6)
C(310)-C(309)-O(303)	125.1(6)
C(310)-C(309)-C(308)	117.4(6)
O(303)-C(309)-C(308)	117.5(6)
C(309)-O(303)-C(324)	116.3(6)
O(303)-C(324)-H(32A)	109.5

O(303)-C(324)-H(32B)	109.5
H(32A)-C(324)-H(32B)	109.5
O(303)-C(324)-H(32C)	109.5
H(32A)-C(324)-H(32C)	109.5
H(32B)-C(324)-H(32C)	109.5
C(309)-C(310)-C(311)	124.1(6)
C(309)-C(310)-H(310)	118.0
C(311)-C(310)-H(310)	118.0
C(322)-C(311)-C(310)	117.6(7)
C(322)-C(311)-C(312)	117.4(6)
C(310)-C(311)-C(312)	125.0(6)
O(304)-C(312)-C(311)	108.3(6)
O(304)-C(312)-C(323)	110.8(6)
C(311)-C(312)-C(323)	108.3(6)
O(304)-C(312)-C(313)	108.6(6)
C(311)-C(312)-C(313)	111.4(6)
C(323)-C(312)-C(313)	109.4(6)
C(312)-C(323)-C(316)	109.2(6)
C(312)-C(323)-H(32D)	109.8
C(316)-C(323)-H(32D)	109.8
C(312)-C(323)-H(32E)	109.8
C(316)-C(323)-H(32E)	109.8
H(32D)-C(323)-H(32E)	108.3
C(312)-O(304)-H(304)	92(7)
O(305)-C(313)-O(306)	111.2(6)
O(305)-C(313)-C(314)	104.6(6)
O(306)-C(313)-C(314)	112.5(6)
O(305)-C(313)-C(312)	115.3(6)
O(306)-C(313)-C(312)	102.8(6)
C(314)-C(313)-C(312)	110.8(6)
C(313)-O(305)-C(325)	118.3(6)
O(305)-C(325)-H(32F)	109.5
O(305)-C(325)-H(32G)	109.5
H(32F)-C(325)-H(32G)	109.5
O(305)-C(325)-H(32H)	109.5
H(32F)-C(325)-H(32H)	109.5

H(32G)-C(325)-H(32H)	109.5
C(313)-O(306)-C(326)	116.1(6)
O(306)-C(326)-H(32I)	109.5
O(306)-C(326)-H(32J)	109.5
H(32I)-C(326)-H(32J)	109.5
O(306)-C(326)-H(32K)	109.5
H(32I)-C(326)-H(32K)	109.5
H(32J)-C(326)-H(32K)	109.5
C(315)-C(314)-C(313)	112.9(6)
C(315)-C(314)-H(31A)	109.0
C(313)-C(314)-H(31A)	109.0
C(315)-C(314)-H(31B)	109.0
C(313)-C(314)-H(31B)	109.0
H(31A)-C(314)-H(31B)	107.8
C(314)-C(315)-C(316)	111.2(6)
C(314)-C(315)-H(31C)	109.4
C(316)-C(315)-H(31C)	109.4
C(314)-C(315)-H(31D)	109.4
C(316)-C(315)-H(31D)	109.4
H(31C)-C(315)-H(31D)	108.0
N(302)-C(316)-C(315)	114.1(7)
N(302)-C(316)-C(323)	107.9(6)
C(315)-C(316)-C(323)	109.2(7)
N(302)-C(316)-H(316)	108.5
C(315)-C(316)-H(316)	108.5
C(323)-C(316)-H(316)	108.5
C(322)-N(302)-C(316)	118.8(6)
C(322)-N(302)-C(317)	115.9(7)
C(316)-N(302)-C(317)	118.0(6)
N(302)-C(317)-C(318)	112.1(7)
N(302)-C(317)-H(31E)	109.2
C(318)-C(317)-H(31E)	109.2
N(302)-C(317)-H(31F)	109.2
C(318)-C(317)-H(31F)	109.2
H(31E)-C(317)-H(31F)	107.9
C(319)-C(318)-C(317)	109.6(6)

C(319)-C(318)-H(31G)	109.7
C(317)-C(318)-H(31G)	109.7
C(319)-C(318)-H(31H)	109.7
C(317)-C(318)-H(31H)	109.7
H(31G)-C(318)-H(31H)	108.2
C(320)-C(319)-C(321)	106.8(7)
C(320)-C(319)-C(318)	136.1(7)
C(321)-C(319)-C(318)	117.1(7)
C(319)-C(320)-N(301)	109.2(6)
C(319)-C(320)-H(320)	125.4
N(301)-C(320)-H(320)	125.4

Symmetry transformations used to generate equivalent atoms:

Table 2.2.4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for compound **50**. 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)	20(1)	17(1)	22(1)	-2(1)	3(1)	0(1)
C(1)	25(3)	14(4)	21(3)	-2(3)	1(2)	-3(3)
C(2)	23(3)	41(5)	22(3)	3(3)	6(3)	-3(3)
C(3)	30(4)	35(5)	24(3)	5(3)	6(3)	-3(3)
C(4)	21(3)	26(4)	25(3)	-7(3)	3(3)	-3(3)
C(7)	19(3)	61(6)	32(4)	-7(4)	2(3)	-7(3)
C(5)	17(3)	29(5)	33(4)	-3(3)	1(3)	-13(3)
C(6)	23(3)	19(4)	26(3)	2(3)	3(3)	-1(3)
O(1)	23(2)	21(3)	26(2)	-3(2)	5(2)	3(2)
O(2)	27(2)	21(3)	28(2)	1(2)	2(2)	1(2)
N(1)	18(2)	19(3)	21(2)	-3(2)	2(2)	2(2)
C(8)	16(3)	18(4)	20(3)	-1(2)	1(2)	2(2)
C(21)	17(3)	16(4)	23(3)	0(2)	1(2)	2(2)
C(22)	17(3)	17(4)	26(3)	3(3)	1(2)	4(2)
C(9)	15(3)	19(4)	18(3)	1(2)	1(2)	1(2)
O(3)	18(2)	22(3)	28(2)	-6(2)	8(2)	-7(2)
C(24)	26(3)	26(4)	30(3)	-5(3)	8(3)	-3(3)
C(10)	18(3)	21(4)	22(3)	-1(3)	4(2)	4(2)
C(11)	22(3)	7(4)	24(3)	2(2)	-1(2)	1(2)
C(12)	18(3)	14(4)	23(3)	-3(3)	0(2)	2(2)
C(23)	30(3)	15(4)	26(3)	-3(3)	-1(3)	0(3)
O(4)	19(2)	23(3)	29(2)	-6(2)	0(2)	4(2)
C(13)	22(3)	15(4)	26(3)	-8(3)	-2(2)	3(3)
O(5)	23(2)	19(3)	27(2)	1(2)	2(2)	3(2)
C(25)	29(3)	25(4)	25(3)	0(3)	7(3)	-1(3)
O(6)	31(2)	17(3)	26(2)	-3(2)	-6(2)	-1(2)
C(26)	38(4)	25(5)	30(4)	-8(3)	-12(3)	3(3)
C(14)	22(3)	24(4)	31(3)	-5(3)	-3(3)	-2(3)
C(15)	19(3)	29(5)	33(4)	-3(3)	-1(3)	-4(3)
C(16)	28(3)	18(4)	32(3)	-2(3)	2(3)	-8(3)

N(2)	23(3)	16(3)	30(3)	1(2)	4(2)	-6(2)
C(17)	20(3)	28(5)	37(4)	3(3)	5(3)	-3(3)
C(18)	22(4)	26(5)	35(4)	-2(3)	7(3)	-4(3)
C(19)	19(3)	21(4)	23(3)	2(2)	7(2)	-1(2)
C(20)	19(3)	31(4)	19(3)	2(3)	4(2)	-2(3)
S(101)	31(1)	31(1)	27(1)	5(1)	9(1)	6(1)
C(101)	23(3)	22(5)	26(4)	6(3)	6(3)	5(3)
C(102)	32(4)	25(5)	38(4)	-7(3)	13(3)	-9(3)
C(103)	30(4)	32(5)	36(4)	-10(3)	3(3)	-9(3)
C(104)	34(4)	32(5)	22(3)	4(3)	4(3)	-4(3)
C(107)	30(4)	32(5)	49(5)	2(4)	3(3)	4(3)
C(105)	35(4)	22(5)	30(4)	-6(3)	5(3)	-6(3)
C(106)	25(4)	32(5)	29(4)	-4(3)	3(3)	-4(3)
O(101)	37(3)	44(4)	35(3)	17(3)	9(2)	5(3)
O(102)	38(3)	38(4)	35(3)	3(2)	13(2)	4(2)
N(101)	21(3)	43(4)	26(3)	1(3)	4(2)	2(3)
C(108)	16(3)	28(4)	23(3)	-2(3)	6(2)	3(3)
C(121)	18(3)	30(4)	24(3)	-5(3)	4(2)	1(3)
C(122)	18(3)	34(5)	32(4)	-10(3)	6(3)	-3(3)
C(109)	20(3)	26(4)	22(3)	-3(3)	4(2)	1(3)
O(103)	20(2)	24(3)	31(2)	3(2)	-1(2)	-3(2)
C(124)	18(3)	31(5)	39(4)	4(3)	-3(3)	-3(3)
C(110)	19(3)	27(4)	23(3)	-7(3)	3(2)	4(3)
C(111)	17(3)	24(4)	31(3)	-1(3)	8(2)	2(3)
C(112)	21(3)	28(5)	37(4)	-2(3)	5(3)	6(3)
C(123)	38(4)	25(5)	50(5)	-7(4)	11(3)	0(3)
O(104)	22(2)	31(3)	43(3)	8(2)	7(2)	7(2)
C(113)	26(3)	22(4)	36(4)	5(3)	8(3)	-3(3)
O(105)	38(3)	32(4)	51(3)	13(2)	17(2)	7(2)
C(125)	52(5)	45(6)	65(6)	28(5)	26(4)	13(4)
O(106)	27(2)	33(3)	36(3)	1(2)	8(2)	0(2)
C(126)	31(4)	58(6)	31(4)	0(4)	2(3)	-3(4)
C(114)	23(3)	31(5)	41(4)	5(3)	10(3)	4(3)
C(115)	33(4)	32(5)	52(5)	-1(4)	3(3)	-6(3)
C(116)	33(4)	30(5)	50(5)	-9(4)	3(3)	-10(3)
N(102)	23(3)	26(4)	42(3)	-11(3)	5(2)	-4(2)

C(117)	23(4)	36(6)	55(5)	-16(4)	1(3)	-7(3)
C(118)	24(3)	48(6)	35(4)	-16(4)	-5(3)	0(3)
C(119)	22(3)	41(5)	26(3)	-11(3)	1(2)	4(3)
C(120)	24(3)	46(5)	22(3)	-2(3)	3(3)	6(3)
S(201)	21(1)	19(1)	24(1)	-3(1)	1(1)	-1(1)
C(201)	18(3)	22(4)	19(3)	-5(3)	0(2)	1(3)
C(202)	29(4)	24(5)	31(4)	3(3)	-2(3)	0(3)
C(203)	39(4)	15(4)	35(4)	2(3)	13(3)	-7(3)
C(204)	24(3)	44(5)	18(3)	-5(3)	-2(3)	-3(3)
C(207)	29(4)	45(6)	29(4)	2(3)	2(3)	-6(3)
C(205)	29(4)	34(5)	19(3)	5(3)	-2(3)	6(3)
C(206)	21(3)	22(4)	24(3)	2(3)	3(2)	-6(3)
O(201)	31(2)	28(3)	26(2)	-9(2)	2(2)	-4(2)
O(202)	24(2)	24(3)	32(2)	-1(2)	0(2)	4(2)
N(201)	18(2)	23(4)	20(2)	-1(2)	2(2)	-3(2)
C(208)	17(3)	15(4)	19(3)	1(2)	0(2)	-2(2)
C(221)	19(3)	18(4)	20(3)	5(2)	2(2)	4(2)
C(222)	20(3)	18(4)	21(3)	1(2)	0(2)	-6(2)
C(209)	11(2)	15(4)	24(3)	1(2)	1(2)	-2(2)
O(203)	19(2)	20(3)	28(2)	-5(2)	9(2)	-8(2)
C(224)	19(3)	30(5)	33(3)	6(3)	9(3)	3(3)
C(210)	14(3)	18(4)	19(3)	5(2)	0(2)	3(2)
C(211)	18(3)	21(4)	22(3)	2(2)	2(2)	4(2)
C(212)	20(3)	19(4)	25(3)	0(3)	0(2)	-1(3)
C(223)	32(3)	18(4)	24(3)	-1(3)	-4(3)	0(3)
O(204)	28(2)	20(3)	22(2)	-3(2)	0(2)	6(2)
C(213)	22(3)	21(4)	27(3)	1(3)	2(2)	-3(3)
O(205)	27(2)	15(3)	24(2)	0(2)	0(2)	1(2)
C(225)	24(3)	23(4)	26(3)	0(3)	1(3)	0(3)
O(206)	26(2)	11(3)	27(2)	-3(2)	-6(2)	6(2)
C(226)	37(4)	18(4)	31(4)	-5(3)	-8(3)	3(3)
C(214)	19(3)	17(4)	31(3)	-3(3)	-1(2)	1(2)
C(215)	22(3)	30(5)	36(4)	-5(3)	4(3)	-8(3)
C(216)	25(3)	17(4)	32(3)	2(3)	6(3)	-10(3)
N(202)	23(3)	21(4)	30(3)	-4(2)	5(2)	-8(2)
C(217)	28(4)	33(5)	28(4)	-4(3)	7(3)	-10(3)

C(218)	21(4)	34(5)	33(4)	0(3)	12(3)	-8(3)
C(219)	18(3)	28(4)	24(3)	0(3)	3(2)	-3(3)
C(220)	22(3)	25(4)	21(3)	-3(3)	5(2)	0(3)
S(301)	38(1)	29(1)	25(1)	-5(1)	10(1)	-5(1)
C(301)	37(4)	29(5)	22(4)	-3(3)	10(3)	2(3)
C(302)	29(4)	32(5)	29(4)	6(3)	4(3)	5(3)
C(303)	43(5)	19(4)	31(4)	8(3)	12(3)	-3(3)
C(304)	38(4)	25(5)	25(3)	-3(3)	9(3)	6(3)
C(307)	41(4)	37(5)	33(4)	5(3)	6(3)	3(3)
C(305)	34(4)	31(5)	31(4)	3(3)	8(3)	13(3)
C(306)	44(5)	28(5)	26(4)	10(3)	9(3)	-2(4)
O(301)	53(3)	33(4)	28(3)	-9(2)	9(2)	-11(3)
O(302)	49(3)	38(4)	32(3)	-1(2)	14(2)	-15(3)
N(301)	28(3)	34(4)	21(3)	-3(2)	4(2)	-7(3)
C(308)	20(3)	31(5)	22(3)	3(3)	9(2)	-1(3)
C(321)	20(3)	39(5)	22(3)	8(3)	4(2)	1(3)
C(322)	24(3)	27(4)	24(3)	7(3)	4(2)	-1(3)
C(309)	20(3)	31(4)	23(3)	2(3)	4(2)	6(3)
O(303)	25(2)	28(3)	34(3)	-5(2)	1(2)	5(2)
C(324)	34(4)	35(5)	36(4)	-5(3)	-3(3)	12(3)
C(310)	19(3)	31(5)	21(3)	0(3)	4(2)	2(3)
C(311)	18(3)	34(5)	20(3)	5(3)	5(2)	1(3)
C(312)	25(3)	34(5)	30(4)	0(3)	7(3)	-3(3)
C(323)	33(4)	28(5)	36(4)	0(3)	6(3)	-3(3)
O(304)	26(2)	40(4)	37(3)	-8(2)	6(2)	-6(2)
C(313)	24(3)	29(4)	31(4)	-3(3)	4(3)	-8(3)
O(305)	34(3)	32(3)	26(2)	0(2)	6(2)	-6(2)
C(325)	40(4)	44(6)	28(4)	-3(3)	1(3)	1(4)
O(306)	32(3)	29(3)	43(3)	-12(2)	16(2)	-6(2)
C(326)	45(5)	56(7)	48(5)	-25(4)	18(4)	-3(4)
C(314)	18(3)	28(4)	37(4)	-6(3)	9(3)	-5(3)
C(315)	24(3)	39(5)	50(5)	-2(4)	3(3)	9(3)
C(316)	32(4)	27(5)	46(4)	7(3)	6(3)	5(3)
N(302)	36(3)	26(4)	31(3)	3(3)	-1(3)	7(3)
C(317)	31(4)	43(6)	30(4)	9(4)	-4(3)	2(4)
C(318)	24(3)	50(6)	30(4)	9(3)	-1(3)	-6(3)

C(319)	25(3)	35(5)	25(3)	2(3)	6(2)	-7(3)
C(320)	27(3)	46(5)	21(3)	1(3)	0(2)	-9(3)

Table 2.2.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for compound **50**.

	x	y	z	U(eq)
H(2)	6909	9357	7254	34
H(3)	8684	9173	7416	35
H(7A)	10591	10140	6909	56
H(7B)	10398	9659	7328	56
H(7C)	10544	11153	7249	56
H(5)	9180	11823	6625	31
H(6)	7391	11999	6446	27
H(24A)	7815	8281	5892	40
H(24B)	8124	9763	5922	40
H(24C)	7311	9274	5577	40
H(10)	6295	7421	5606	24
H(23A)	4252	3666	5522	29
H(23B)	4881	4063	5923	29
H(4O)	5710(60)	4560(60)	5230(20)	36
H(25A)	5898	7073	4969	39
H(25B)	5281	7888	4631	39
H(25C)	5251	6357	4616	39
H(26A)	2684	5164	4589	48
H(26B)	3506	4443	4360	48
H(26C)	3591	5957	4428	48
H(14A)	2547	6446	5061	31
H(14B)	3100	7045	5451	31
H(15A)	2437	4435	5348	33
H(15B)	1967	5467	5618	33
H(16)	3112	4005	5985	31
H(17A)	2298	5572	6390	34
H(17B)	2395	6923	6182	34
H(18A)	2589	7320	6846	33
H(18B)	3455	6229	6920	33
H(20)	4220	9242	7093	27

H(102)	3071	2544	1598	37
H(103)	1401	3236	1656	39
H(10A)	260	5095	1760	56
H(10B)	708	6242	2032	56
H(10C)	446	4895	2215	56
H(105)	2538	6329	2256	34
H(106)	4217	5598	2214	34
H(12A)	2781	5832	993	44
H(12B)	2584	4347	899	44
H(12C)	3106	5237	603	44
H(110)	4183	6946	697	27
H(12D)	5885	10958	848	45
H(12E)	5413	10301	1203	45
H(104)	4520(80)	9790(80)	369(18)	48
H(12F)	7333	10551	4	79
H(12G)	6314	10838	-282	79
H(12H)	6728	9401	-224	79
H(12I)	4412	7718	62	60
H(12J)	5009	7217	-284	60
H(12K)	4927	8720	-205	60
H(11A)	7349	7834	715	38
H(11B)	7737	8664	376	38
H(11C)	7738	10539	741	47
H(11D)	8379	9479	999	47
H(116)	7199	10596	1358	45
H(11E)	8253	9007	1747	46
H(11F)	8231	7739	1491	46
H(11G)	8240	7038	2119	44
H(11H)	7345	8020	2200	44
H(120)	6774	4947	2250	37
H(202)	2708	5241	3503	34
H(203)	937	5393	3350	34
H(20A)	-519	6230	2894	51
H(20B)	-353	7506	2655	51
H(20C)	-491	7594	3103	51
H(205)	1316	8534	2705	33

H(206)	3107	8344	2843	27
H(22A)	2793	8128	4441	41
H(22B)	2015	7499	4107	41
H(22C)	2217	9010	4110	41
H(210)	3784	9935	4422	20
H(22D)	5156	13341	4104	30
H(22E)	5771	13758	4507	30
H(204)	4160(70)	12660(70)	4836(16)	35
H(22F)	4929	10794	5472	37
H(22G)	4608	9404	5308	37
H(22H)	4193	10655	5076	37
H(22I)	6565	11340	5573	44
H(22J)	6455	12811	5689	44
H(22K)	7371	12376	5452	44
H(21A)	7514	10940	4963	27
H(21B)	6962	10352	4570	27
H(21C)	8079	11945	4413	35
H(21D)	7598	12954	4687	35
H(216)	6961	13418	4054	29
H(21E)	7664	10524	3842	35
H(21F)	7762	11885	3640	35
H(21G)	6617	11252	3107	34
H(21H)	7480	10158	3178	34
H(220)	5867	8234	2924	27
H(302)	826	12897	2716	36
H(303)	2494	13575	2678	36
H(30A)	4549	13203	3294	55
H(30B)	4291	13476	2844	55
H(30C)	4745	12115	2989	55
H(305)	3607	10887	3434	38
H(306)	1924	10177	3480	39
H(32A)	2300	13169	4035	53
H(32B)	2402	11696	4160	53
H(32C)	1864	12696	4420	53
H(310)	867	14373	4313	29
H(32D)	-361	17767	3828	38

H(32E)	-823	18403	4189	38
H(304)	440(70)	17370(70)	4590(20)	51
H(32F)	682	15084	4956	57
H(32G)	78	14601	5302	57
H(32H)	192	16102	5225	57
H(32I)	-2188	18054	5049	73
H(32J)	-1158	18104	5344	73
H(32K)	-1707	16760	5238	73
H(31A)	-2276	15250	4320	33
H(31B)	-2647	16067	4665	33
H(31C)	-2659	17947	4307	45
H(31D)	-3320	16898	4053	45
H(316)	-2179	18023	3683	42
H(31E)	-3244	16459	3303	42
H(31F)	-3194	15170	3551	42
H(31G)	-3229	14518	2913	42
H(31H)	-2346	15519	2834	42
H(320)	-1744	12482	2755	38

Table 2.2.6. Torsion angles [°] for compound **50**.

O(2)-S(1)-C(1)-C(6)	15.2(7)
O(1)-S(1)-C(1)-C(6)	-117.8(6)
N(1)-S(1)-C(1)-C(6)	131.6(6)
O(2)-S(1)-C(1)-C(2)	-166.7(6)
O(1)-S(1)-C(1)-C(2)	60.4(7)
N(1)-S(1)-C(1)-C(2)	-50.2(7)
C(6)-C(1)-C(2)-C(3)	-0.4(12)
S(1)-C(1)-C(2)-C(3)	-178.4(6)
C(1)-C(2)-C(3)-C(4)	0.4(12)
C(2)-C(3)-C(4)-C(5)	0.2(12)
C(2)-C(3)-C(4)-C(7)	-179.4(8)
C(3)-C(4)-C(5)-C(6)	-0.9(12)
C(7)-C(4)-C(5)-C(6)	178.7(7)
C(2)-C(1)-C(6)-C(5)	-0.3(12)
S(1)-C(1)-C(6)-C(5)	177.8(6)
C(4)-C(5)-C(6)-C(1)	1.0(12)
O(2)-S(1)-N(1)-C(8)	39.4(6)
O(1)-S(1)-N(1)-C(8)	168.0(5)
C(1)-S(1)-N(1)-C(8)	-77.8(6)
O(2)-S(1)-N(1)-C(20)	-117.8(5)
O(1)-S(1)-N(1)-C(20)	10.8(5)
C(1)-S(1)-N(1)-C(20)	125.0(5)
C(20)-N(1)-C(8)-C(21)	1.3(7)
S(1)-N(1)-C(8)-C(21)	-158.6(5)
C(20)-N(1)-C(8)-C(9)	-171.5(7)
S(1)-N(1)-C(8)-C(9)	28.6(10)
C(9)-C(8)-C(21)-C(22)	-1.3(10)
N(1)-C(8)-C(21)-C(22)	-175.2(6)
C(9)-C(8)-C(21)-C(19)	172.7(6)
N(1)-C(8)-C(21)-C(19)	-1.2(7)
C(8)-C(21)-C(22)-N(2)	175.7(6)
C(19)-C(21)-C(22)-N(2)	2.7(10)
C(8)-C(21)-C(22)-C(11)	-0.3(9)
C(19)-C(21)-C(22)-C(11)	-173.2(6)

C(21)-C(8)-C(9)-O(3)	-176.0(6)
N(1)-C(8)-C(9)-O(3)	-4.0(10)
C(21)-C(8)-C(9)-C(10)	1.6(9)
N(1)-C(8)-C(9)-C(10)	173.6(6)
C(10)-C(9)-O(3)-C(24)	-9.5(9)
C(8)-C(9)-O(3)-C(24)	167.9(6)
O(3)-C(9)-C(10)-C(11)	176.9(6)
C(8)-C(9)-C(10)-C(11)	-0.5(9)
N(2)-C(22)-C(11)-C(10)	-174.1(6)
C(21)-C(22)-C(11)-C(10)	1.4(9)
N(2)-C(22)-C(11)-C(12)	7.3(10)
C(21)-C(22)-C(11)-C(12)	-177.2(5)
C(9)-C(10)-C(11)-C(22)	-1.0(9)
C(9)-C(10)-C(11)-C(12)	177.5(6)
C(22)-C(11)-C(12)-O(4)	-150.2(6)
C(10)-C(11)-C(12)-O(4)	31.3(8)
C(22)-C(11)-C(12)-C(23)	-29.7(7)
C(10)-C(11)-C(12)-C(23)	151.8(6)
C(22)-C(11)-C(12)-C(13)	87.8(7)
C(10)-C(11)-C(12)-C(13)	-90.7(7)
O(4)-C(12)-C(23)-C(16)	177.1(5)
C(11)-C(12)-C(23)-C(16)	57.8(7)
C(13)-C(12)-C(23)-C(16)	-60.6(7)
O(4)-C(12)-C(13)-O(5)	-66.4(7)
C(11)-C(12)-C(13)-O(5)	54.6(7)
C(23)-C(12)-C(13)-O(5)	171.3(5)
O(4)-C(12)-C(13)-O(6)	54.8(7)
C(11)-C(12)-C(13)-O(6)	175.8(5)
C(23)-C(12)-C(13)-O(6)	-67.5(6)
O(4)-C(12)-C(13)-C(14)	176.5(6)
C(11)-C(12)-C(13)-C(14)	-62.5(7)
C(23)-C(12)-C(13)-C(14)	54.3(7)
O(6)-C(13)-O(5)-C(25)	-49.5(7)
C(14)-C(13)-O(5)-C(25)	-170.9(5)
C(12)-C(13)-O(5)-C(25)	68.1(7)
O(5)-C(13)-O(6)-C(26)	-54.6(7)

C(14)-C(13)-O(6)-C(26)	61.6(8)
C(12)-C(13)-O(6)-C(26)	-177.7(6)
O(5)-C(13)-C(14)-C(15)	-174.8(5)
O(6)-C(13)-C(14)-C(15)	65.0(7)
C(12)-C(13)-C(14)-C(15)	-52.0(7)
C(13)-C(14)-C(15)-C(16)	53.0(8)
C(12)-C(23)-C(16)-N(2)	-62.2(7)
C(12)-C(23)-C(16)-C(15)	62.3(7)
C(14)-C(15)-C(16)-N(2)	64.5(8)
C(14)-C(15)-C(16)-C(23)	-56.7(8)
C(11)-C(22)-N(2)-C(16)	-10.7(10)
C(21)-C(22)-N(2)-C(16)	173.7(6)
C(11)-C(22)-N(2)-C(17)	-157.2(6)
C(21)-C(22)-N(2)-C(17)	27.2(8)
C(23)-C(16)-N(2)-C(22)	36.9(8)
C(15)-C(16)-N(2)-C(22)	-84.9(7)
C(23)-C(16)-N(2)-C(17)	-178.0(6)
C(15)-C(16)-N(2)-C(17)	60.2(8)
C(22)-N(2)-C(17)-C(18)	-56.5(8)
C(16)-N(2)-C(17)-C(18)	157.6(6)
N(2)-C(17)-C(18)-C(19)	52.5(9)
C(8)-C(21)-C(19)-C(20)	0.6(8)
C(22)-C(21)-C(19)-C(20)	174.4(6)
C(8)-C(21)-C(19)-C(18)	-176.8(6)
C(22)-C(21)-C(19)-C(18)	-3.1(10)
C(17)-C(18)-C(19)-C(20)	159.5(8)
C(17)-C(18)-C(19)-C(21)	-23.9(9)
C(21)-C(19)-C(20)-N(1)	0.2(7)
C(18)-C(19)-C(20)-N(1)	176.9(8)
C(8)-N(1)-C(20)-C(19)	-0.9(7)
S(1)-N(1)-C(20)-C(19)	160.2(5)
O(102)-S(101)-C(101)-C(102)	22.3(7)
O(101)-S(101)-C(101)-C(102)	-111.3(7)
N(101)-S(101)-C(101)-C(102)	138.4(6)
O(102)-S(101)-C(101)-C(106)	-159.4(6)
O(101)-S(101)-C(101)-C(106)	66.9(7)

N(101)-S(101)-C(101)-C(106)	-43.3(7)
C(106)-C(101)-C(102)-C(103)	1.3(12)
S(101)-C(101)-C(102)-C(103)	179.5(7)
C(101)-C(102)-C(103)-C(104)	0.2(13)
C(102)-C(103)-C(104)-C(105)	-0.6(12)
C(102)-C(103)-C(104)-C(107)	179.4(8)
C(103)-C(104)-C(105)-C(106)	-0.5(12)
C(107)-C(104)-C(105)-C(106)	179.5(7)
C(102)-C(101)-C(106)-C(105)	-2.3(12)
S(101)-C(101)-C(106)-C(105)	179.5(6)
C(104)-C(105)-C(106)-C(101)	1.9(12)
O(102)-S(101)-N(101)-C(108)	57.2(7)
O(101)-S(101)-N(101)-C(108)	-173.8(6)
C(101)-S(101)-N(101)-C(108)	-58.7(7)
O(102)-S(101)-N(101)-C(120)	-128.7(6)
O(101)-S(101)-N(101)-C(120)	0.3(7)
C(101)-S(101)-N(101)-C(120)	115.4(6)
C(120)-N(101)-C(108)-C(121)	1.1(7)
S(101)-N(101)-C(108)-C(121)	175.8(5)
C(120)-N(101)-C(108)-C(109)	-173.8(7)
S(101)-N(101)-C(108)-C(109)	0.9(12)
N(101)-C(108)-C(121)-C(122)	-176.6(6)
C(109)-C(108)-C(121)-C(122)	-0.7(10)
N(101)-C(108)-C(121)-C(119)	-0.6(7)
C(109)-C(108)-C(121)-C(119)	175.3(6)
C(108)-C(121)-C(122)-N(102)	176.7(6)
C(119)-C(121)-C(122)-N(102)	1.4(10)
C(108)-C(121)-C(122)-C(111)	-0.1(10)
C(119)-C(121)-C(122)-C(111)	-175.3(6)
N(101)-C(108)-C(109)-O(103)	-7.0(11)
C(121)-C(108)-C(109)-O(103)	178.6(5)
N(101)-C(108)-C(109)-C(110)	174.2(7)
C(121)-C(108)-C(109)-C(110)	-0.2(9)
C(110)-C(109)-O(103)-C(124)	-29.3(9)
C(108)-C(109)-O(103)-C(124)	152.0(6)
O(103)-C(109)-C(110)-C(111)	-176.9(6)

C(108)-C(109)-C(110)-C(111)	1.8(9)
N(102)-C(122)-C(111)-C(110)	-174.9(6)
C(121)-C(122)-C(111)-C(110)	1.6(9)
N(102)-C(122)-C(111)-C(112)	3.4(10)
C(121)-C(122)-C(111)-C(112)	179.8(6)
C(109)-C(110)-C(111)-C(122)	-2.5(10)
C(109)-C(110)-C(111)-C(112)	179.4(6)
C(122)-C(111)-C(112)-O(104)	-149.8(6)
C(110)-C(111)-C(112)-O(104)	28.3(9)
C(122)-C(111)-C(112)-C(123)	-29.9(8)
C(110)-C(111)-C(112)-C(123)	148.2(6)
C(122)-C(111)-C(112)-C(113)	89.5(8)
C(110)-C(111)-C(112)-C(113)	-92.4(8)
O(104)-C(112)-C(123)-C(116)	179.4(6)
C(111)-C(112)-C(123)-C(116)	60.2(8)
C(113)-C(112)-C(123)-C(116)	-61.3(9)
O(104)-C(112)-C(113)-O(106)	-65.8(8)
C(111)-C(112)-C(113)-O(106)	55.0(8)
C(123)-C(112)-C(113)-O(106)	174.3(6)
O(104)-C(112)-C(113)-O(105)	56.1(7)
C(111)-C(112)-C(113)-O(105)	176.8(6)
C(123)-C(112)-C(113)-O(105)	-63.8(7)
O(104)-C(112)-C(113)-C(114)	175.9(6)
C(111)-C(112)-C(113)-C(114)	-63.4(8)
C(123)-C(112)-C(113)-C(114)	56.0(8)
O(106)-C(113)-O(105)-C(125)	-59.1(9)
C(114)-C(113)-O(105)-C(125)	58.0(10)
C(112)-C(113)-O(105)-C(125)	177.0(7)
O(105)-C(113)-O(106)-C(126)	-47.6(8)
C(114)-C(113)-O(106)-C(126)	-169.0(6)
C(112)-C(113)-O(106)-C(126)	69.4(8)
O(106)-C(113)-C(114)-C(115)	-177.4(6)
O(105)-C(113)-C(114)-C(115)	61.3(8)
C(112)-C(113)-C(114)-C(115)	-53.1(9)
C(113)-C(114)-C(115)-C(116)	53.0(9)
C(112)-C(123)-C(116)-N(102)	-61.8(8)

C(112)-C(123)-C(116)-C(115)	62.0(9)
C(114)-C(115)-C(116)-N(102)	64.1(9)
C(114)-C(115)-C(116)-C(123)	-56.5(9)
C(121)-C(122)-N(102)-C(116)	178.2(6)
C(111)-C(122)-N(102)-C(116)	-5.3(10)
C(121)-C(122)-N(102)-C(117)	27.4(9)
C(111)-C(122)-N(102)-C(117)	-156.1(7)
C(123)-C(116)-N(102)-C(122)	33.9(9)
C(115)-C(116)-N(102)-C(122)	-87.9(8)
C(123)-C(116)-N(102)-C(117)	-176.5(7)
C(115)-C(116)-N(102)-C(117)	61.8(9)
C(122)-N(102)-C(117)-C(118)	-53.7(9)
C(116)-N(102)-C(117)-C(118)	155.8(7)
N(102)-C(117)-C(118)-C(119)	48.6(9)
C(122)-C(121)-C(119)-C(120)	175.8(6)
C(108)-C(121)-C(119)-C(120)	-0.1(8)
C(122)-C(121)-C(119)-C(118)	-3.4(10)
C(108)-C(121)-C(119)-C(118)	-179.3(6)
C(117)-C(118)-C(119)-C(120)	159.9(8)
C(117)-C(118)-C(119)-C(121)	-21.2(9)
C(121)-C(119)-C(120)-N(101)	0.7(8)
C(118)-C(119)-C(120)-N(101)	179.7(8)
C(108)-N(101)-C(120)-C(119)	-1.2(8)
S(101)-N(101)-C(120)-C(119)	-176.3(5)
O(202)-S(201)-C(201)-C(206)	160.1(6)
O(201)-S(201)-C(201)-C(206)	-66.9(7)
N(201)-S(201)-C(201)-C(206)	43.4(6)
O(202)-S(201)-C(201)-C(202)	-23.2(7)
O(201)-S(201)-C(201)-C(202)	109.8(6)
N(201)-S(201)-C(201)-C(202)	-139.9(6)
C(206)-C(201)-C(202)-C(203)	0.7(12)
S(201)-C(201)-C(202)-C(203)	-176.0(6)
C(201)-C(202)-C(203)-C(204)	-0.2(12)
C(202)-C(203)-C(204)-C(205)	-1.4(12)
C(202)-C(203)-C(204)-C(207)	-179.4(7)
C(203)-C(204)-C(205)-C(206)	2.5(12)

C(207)-C(204)-C(205)-C(206)	-179.5(7)
C(202)-C(201)-C(206)-C(205)	0.4(11)
S(201)-C(201)-C(206)-C(205)	177.0(6)
C(204)-C(205)-C(206)-C(201)	-2.0(11)
O(202)-S(201)-N(201)-C(208)	-41.9(6)
O(201)-S(201)-N(201)-C(208)	-171.5(5)
C(201)-S(201)-N(201)-C(208)	74.5(6)
O(202)-S(201)-N(201)-C(220)	114.8(5)
O(201)-S(201)-N(201)-C(220)	-14.8(5)
C(201)-S(201)-N(201)-C(220)	-128.8(5)
C(220)-N(201)-C(208)-C(221)	1.0(7)
S(201)-N(201)-C(208)-C(221)	160.1(5)
C(220)-N(201)-C(208)-C(209)	172.9(7)
S(201)-N(201)-C(208)-C(209)	-27.9(10)
C(209)-C(208)-C(221)-C(222)	1.7(9)
N(201)-C(208)-C(221)-C(222)	175.0(6)
C(209)-C(208)-C(221)-C(219)	-174.2(6)
N(201)-C(208)-C(221)-C(219)	-0.9(7)
C(208)-C(221)-C(222)-C(211)	0.4(9)
C(219)-C(221)-C(222)-C(211)	175.6(6)
C(208)-C(221)-C(222)-N(202)	-177.9(6)
C(219)-C(221)-C(222)-N(202)	-2.7(10)
C(221)-C(208)-C(209)-O(203)	177.1(5)
N(201)-C(208)-C(209)-O(203)	6.0(10)
C(221)-C(208)-C(209)-C(210)	-2.4(9)
N(201)-C(208)-C(209)-C(210)	-173.5(6)
C(210)-C(209)-O(203)-C(224)	12.2(9)
C(208)-C(209)-O(203)-C(224)	-167.2(6)
O(203)-C(209)-C(210)-C(211)	-178.2(6)
C(208)-C(209)-C(210)-C(211)	1.2(9)
N(202)-C(222)-C(211)-C(210)	176.5(6)
C(221)-C(222)-C(211)-C(210)	-1.6(9)
N(202)-C(222)-C(211)-C(212)	-4.9(10)
C(221)-C(222)-C(211)-C(212)	177.0(6)
C(209)-C(210)-C(211)-C(222)	0.9(9)
C(209)-C(210)-C(211)-C(212)	-177.7(6)

C(222)-C(211)-C(212)-O(204)	148.3(6)
C(210)-C(211)-C(212)-O(204)	-33.1(8)
C(222)-C(211)-C(212)-C(223)	30.2(8)
C(210)-C(211)-C(212)-C(223)	-151.3(6)
C(222)-C(211)-C(212)-C(213)	-90.2(7)
C(210)-C(211)-C(212)-C(213)	88.4(7)
O(204)-C(212)-C(223)-C(216)	-177.4(5)
C(211)-C(212)-C(223)-C(216)	-60.1(7)
C(213)-C(212)-C(223)-C(216)	59.9(7)
O(204)-C(212)-C(213)-O(205)	65.9(8)
C(211)-C(212)-C(213)-O(205)	-53.8(7)
C(223)-C(212)-C(213)-O(205)	-172.5(5)
O(204)-C(212)-C(213)-O(206)	-55.7(7)
C(211)-C(212)-C(213)-O(206)	-175.4(5)
C(223)-C(212)-C(213)-O(206)	65.9(6)
O(204)-C(212)-C(213)-C(214)	-176.4(6)
C(211)-C(212)-C(213)-C(214)	63.9(7)
C(223)-C(212)-C(213)-C(214)	-54.8(8)
O(206)-C(213)-O(205)-C(225)	47.5(7)
C(214)-C(213)-O(205)-C(225)	170.0(5)
C(212)-C(213)-O(205)-C(225)	-69.3(7)
O(205)-C(213)-O(206)-C(226)	55.4(7)
C(214)-C(213)-O(206)-C(226)	-62.5(7)
C(212)-C(213)-O(206)-C(226)	178.4(5)
O(205)-C(213)-C(214)-C(215)	174.4(5)
O(206)-C(213)-C(214)-C(215)	-63.7(7)
C(212)-C(213)-C(214)-C(215)	51.3(8)
C(213)-C(214)-C(215)-C(216)	-53.3(8)
C(214)-C(215)-C(216)-N(202)	-63.9(8)
C(214)-C(215)-C(216)-C(223)	57.1(8)
C(212)-C(223)-C(216)-N(202)	64.2(7)
C(212)-C(223)-C(216)-C(215)	-60.5(7)
C(211)-C(222)-N(202)-C(217)	154.9(7)
C(221)-C(222)-N(202)-C(217)	-26.9(8)
C(211)-C(222)-N(202)-C(216)	8.8(10)
C(221)-C(222)-N(202)-C(216)	-173.1(6)

C(215)-C(216)-N(202)-C(222)	84.7(7)
C(223)-C(216)-N(202)-C(222)	-37.4(8)
C(215)-C(216)-N(202)-C(217)	-60.5(8)
C(223)-C(216)-N(202)-C(217)	177.4(6)
C(222)-N(202)-C(217)-C(218)	56.0(9)
C(216)-N(202)-C(217)-C(218)	-158.4(6)
N(202)-C(217)-C(218)-C(219)	-52.4(9)
C(208)-C(221)-C(219)-C(220)	0.5(8)
C(222)-C(221)-C(219)-C(220)	-175.3(6)
C(208)-C(221)-C(219)-C(218)	178.4(6)
C(222)-C(221)-C(219)-C(218)	2.6(10)
C(217)-C(218)-C(219)-C(220)	-158.5(8)
C(217)-C(218)-C(219)-C(221)	24.4(9)
C(221)-C(219)-C(220)-N(201)	0.2(7)
C(218)-C(219)-C(220)-N(201)	-177.1(8)
C(208)-N(201)-C(220)-C(219)	-0.7(7)
S(201)-N(201)-C(220)-C(219)	-161.3(5)
O(302)-S(301)-C(301)-C(302)	-166.9(6)
O(301)-S(301)-C(301)-C(302)	60.3(8)
N(301)-S(301)-C(301)-C(302)	-50.1(7)
O(302)-S(301)-C(301)-C(306)	10.0(8)
O(301)-S(301)-C(301)-C(306)	-122.7(7)
N(301)-S(301)-C(301)-C(306)	126.8(7)
C(306)-C(301)-C(302)-C(303)	0.2(12)
S(301)-C(301)-C(302)-C(303)	177.2(7)
C(301)-C(302)-C(303)-C(304)	-1.2(13)
C(302)-C(303)-C(304)-C(305)	2.2(13)
C(302)-C(303)-C(304)-C(307)	-177.5(8)
C(303)-C(304)-C(305)-C(306)	-2.2(12)
C(307)-C(304)-C(305)-C(306)	177.5(8)
C(304)-C(305)-C(306)-C(301)	1.3(12)
C(302)-C(301)-C(306)-C(305)	-0.3(12)
S(301)-C(301)-C(306)-C(305)	-177.3(6)
O(302)-S(301)-N(301)-C(308)	55.9(7)
O(301)-S(301)-N(301)-C(308)	-175.6(6)
C(301)-S(301)-N(301)-C(308)	-61.4(7)

O(302)-S(301)-N(301)-C(320)	-127.9(6)
O(301)-S(301)-N(301)-C(320)	0.6(6)
C(301)-S(301)-N(301)-C(320)	114.9(6)
C(320)-N(301)-C(308)-C(321)	1.5(7)
S(301)-N(301)-C(308)-C(321)	178.2(5)
C(320)-N(301)-C(308)-C(309)	-174.4(7)
S(301)-N(301)-C(308)-C(309)	2.3(12)
N(301)-C(308)-C(321)-C(322)	-175.7(6)
C(309)-C(308)-C(321)-C(322)	1.0(10)
N(301)-C(308)-C(321)-C(319)	-0.3(7)
C(309)-C(308)-C(321)-C(319)	176.4(6)
C(308)-C(321)-C(322)-N(302)	177.0(6)
C(319)-C(321)-C(322)-N(302)	2.3(10)
C(308)-C(321)-C(322)-C(311)	0.2(10)
C(319)-C(321)-C(322)-C(311)	-174.5(6)
C(321)-C(308)-C(309)-C(310)	-2.3(10)
N(301)-C(308)-C(309)-C(310)	173.2(7)
C(321)-C(308)-C(309)-O(303)	177.5(6)
N(301)-C(308)-C(309)-O(303)	-7.0(11)
C(310)-C(309)-O(303)-C(324)	-24.8(10)
C(308)-C(309)-O(303)-C(324)	155.4(6)
O(303)-C(309)-C(310)-C(311)	-177.2(6)
C(308)-C(309)-C(310)-C(311)	2.6(10)
N(302)-C(322)-C(311)-C(310)	-176.5(6)
C(321)-C(322)-C(311)-C(310)	0.0(9)
N(302)-C(322)-C(311)-C(312)	3.6(10)
C(321)-C(322)-C(311)-C(312)	-179.9(6)
C(309)-C(310)-C(311)-C(322)	-1.4(10)
C(309)-C(310)-C(311)-C(312)	178.4(7)
C(322)-C(311)-C(312)-O(304)	-151.2(6)
C(310)-C(311)-C(312)-O(304)	29.0(9)
C(322)-C(311)-C(312)-C(323)	-30.9(8)
C(310)-C(311)-C(312)-C(323)	149.3(7)
C(322)-C(311)-C(312)-C(313)	89.4(8)
C(310)-C(311)-C(312)-C(313)	-90.4(8)
O(304)-C(312)-C(323)-C(316)	178.8(6)

C(311)-C(312)-C(323)-C(316)	60.1(8)
C(313)-C(312)-C(323)-C(316)	-61.6(8)
O(304)-C(312)-C(313)-O(305)	-64.3(8)
C(311)-C(312)-C(313)-O(305)	54.9(8)
C(323)-C(312)-C(313)-O(305)	174.6(6)
O(304)-C(312)-C(313)-O(306)	56.8(7)
C(311)-C(312)-C(313)-O(306)	176.0(6)
C(323)-C(312)-C(313)-O(306)	-64.2(7)
O(304)-C(312)-C(313)-C(314)	177.2(6)
C(311)-C(312)-C(313)-C(314)	-63.6(8)
C(323)-C(312)-C(313)-C(314)	56.2(8)
O(306)-C(313)-O(305)-C(325)	-46.9(8)
C(314)-C(313)-O(305)-C(325)	-168.6(6)
C(312)-C(313)-O(305)-C(325)	69.6(8)
O(305)-C(313)-O(306)-C(326)	-60.3(8)
C(314)-C(313)-O(306)-C(326)	56.6(9)
C(312)-C(313)-O(306)-C(326)	175.8(7)
O(305)-C(313)-C(314)-C(315)	-177.1(6)
O(306)-C(313)-C(314)-C(315)	62.0(8)
C(312)-C(313)-C(314)-C(315)	-52.4(9)
C(313)-C(314)-C(315)-C(316)	53.5(9)
C(314)-C(315)-C(316)-N(302)	63.2(9)
C(314)-C(315)-C(316)-C(323)	-57.7(9)
C(312)-C(323)-C(316)-N(302)	-62.1(8)
C(312)-C(323)-C(316)-C(315)	62.4(8)
C(321)-C(322)-N(302)-C(316)	177.6(6)
C(311)-C(322)-N(302)-C(316)	-5.9(10)
C(321)-C(322)-N(302)-C(317)	27.9(9)
C(311)-C(322)-N(302)-C(317)	-155.5(7)
C(315)-C(316)-N(302)-C(322)	-87.1(8)
C(323)-C(316)-N(302)-C(322)	34.5(9)
C(315)-C(316)-N(302)-C(317)	61.9(9)
C(323)-C(316)-N(302)-C(317)	-176.5(6)
C(322)-N(302)-C(317)-C(318)	-54.6(9)
C(316)-N(302)-C(317)-C(318)	155.5(7)
N(302)-C(317)-C(318)-C(319)	49.0(9)

C(308)-C(321)-C(319)-C(320)	-1.1(8)
C(322)-C(321)-C(319)-C(320)	174.2(7)
C(308)-C(321)-C(319)-C(318)	-179.7(6)
C(322)-C(321)-C(319)-C(318)	-4.4(10)
C(317)-C(318)-C(319)-C(320)	160.7(8)
C(317)-C(318)-C(319)-C(321)	-21.3(9)
C(321)-C(319)-C(320)-N(301)	2.1(8)
C(318)-C(319)-C(320)-N(301)	-179.8(7)
C(308)-N(301)-C(320)-C(319)	-2.3(8)
S(301)-N(301)-C(320)-C(319)	-179.2(5)

Symmetry transformations used to generate equivalent atoms:

Table 2.2.7. Hydrogen bonds for compound **50** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(24)-H(24B)...O(104)#1	0.98	2.42	3.158(9)	132.0
O(4)-H(4O)...O(206)#2	0.83(3)	2.26(6)	2.970(7)	143(8)
C(25)-H(25A)...O(4)	0.98	2.49	2.963(9)	109.3
C(26)-H(26B)...O(204)#2	0.98	2.63	3.218(10)	118.6
C(17)-H(17A)...N(101)#3	0.99	2.64	3.450(9)	138.9
C(20)-H(20)...O(301)#1	0.95	2.42	3.281(8)	150.5
C(106)-H(106)...O(201)	0.95	2.63	3.340(9)	132.3
O(104)-H(104)...O(105)	0.86(3)	2.15(9)	2.679(7)	120(8)
C(224)-H(22B)...O(304)#2	0.98	2.41	3.140(9)	131.0
O(204)-H(204)...O(6)#4	0.83(3)	2.39(7)	2.966(7)	128(8)
C(225)-H(22G)...O(5)	0.98	2.64	3.447(9)	139.3
C(225)-H(22H)...O(204)	0.98	2.25	2.960(9)	128.0
C(217)-H(21F)...N(301)#5	0.99	2.67	3.469(9)	138.0
O(304)-H(304)...O(306)	0.86(3)	2.07(9)	2.675(7)	127(9)

Symmetry transformations used to generate equivalent atoms:

#1 x+1/2,-y+2,z+1/2 #2 x,y-1,z #3 x-1/2,-y+1,z+1/2

#4 x,y+1,z #5 x+1,y,z

A2.3 X-RAY CRYSTAL STRUCTURE OF COMPOUND 96

Figure A2.3.1 *X-ray crystal structure of compound* ***96***.

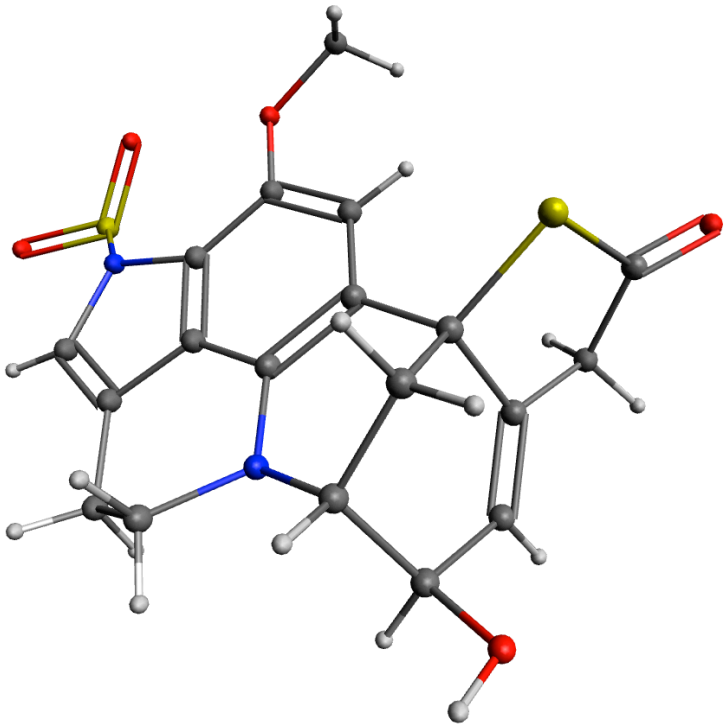


Table A2.3.1 *Crystal data and structure refinement for compound* ***96***.

Empirical formula	C27 H26 Cl2 N2 O5 S2	
Formula weight	593.52	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.9341(11) Å	a= 68.752(6)°.
	b = 11.1021(10) Å	b= 79.513(6)°.
	c = 12.9734(11) Å	g = 81.600(8)°.
Volume	1306.3(2) $Å^3$	
Z	2	
Density (calculated)	1.509 Mg/m^3	
Absorption coefficient	4.093 mm^{-1}	
F(000)	616	
Crystal size	0.100 x 0.100 x 0.050 mm^3	

Theta range for data collection	3.692 to 74.612°.
Index ranges	-12<=h<=12, -13<=k<=13, -16<=l<=16
Reflections collected	39783
Independent reflections	5328 [R(int) = 0.0583]
Completeness to theta = 67.679°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7538 and 0.5834
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5328 / 1 / 348
Goodness-of-fit on F^2	1.027
Final R indices [I>2sigma(I)]	R1 = 0.0411, wR2 = 0.1048
R indices (all data)	R1 = 0.0480, wR2 = 0.1098
Extinction coefficient	n/a
Largest diff. peak and hole	0.455 and -0.444 e.$Å^{-3}$

Table 2.3.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for compound **96**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	7922(1)	4539(1)	6722(1)	23(1)
C(1)	6124(2)	4537(2)	7229(2)	26(1)
O(1)	5678(2)	3996(2)	8190(1)	37(1)
C(2)	5301(2)	5258(2)	6296(2)	21(1)
C(3)	6226(2)	6161(2)	5370(2)	20(1)
C(4)	5886(2)	7375(2)	4750(2)	22(1)
C(5)	6901(2)	8273(2)	3936(2)	23(1)
O(2)	7099(2)	9158(2)	4456(1)	26(1)
C(6)	8269(2)	7527(2)	3686(2)	22(1)
N(1)	8121(2)	6857(2)	2926(1)	22(1)
C(7)	8781(2)	7422(2)	1760(2)	24(1)
C(8)	8283(2)	6921(2)	951(2)	24(1)
C(9)	8385(2)	5464(2)	1411(2)	19(1)
C(10)	8541(2)	4501(2)	987(2)	20(1)
N(2)	8515(2)	3278(2)	1874(1)	18(1)
C(11)	8269(2)	3522(2)	2905(2)	18(1)
C(12)	8128(2)	2759(2)	4046(2)	18(1)
O(3)	8242(2)	1436(1)	4369(1)	24(1)
C(19)	8383(3)	731(2)	5520(2)	28(1)
C(13)	7897(2)	3424(2)	4803(2)	19(1)
C(14)	7886(2)	4776(2)	4484(2)	20(1)
C(17)	8095(2)	5520(2)	3353(2)	19(1)
C(18)	8241(2)	4863(2)	2595(2)	18(1)
C(15)	7692(2)	5535(2)	5277(2)	20(1)
C(16)	8709(2)	6586(2)	4790(2)	22(1)
S(2)	8012(1)	2056(1)	1606(1)	18(1)
O(4)	8542(2)	2268(2)	459(1)	24(1)
O(5)	8426(2)	873(1)	2439(1)	23(1)
C(20)	6215(2)	2304(2)	1746(2)	19(1)
C(21)	5601(2)	3059(2)	807(2)	23(1)

C(22)	4178(2)	3258(2)	908(2)	24(1)
C(23)	3364(2)	2712(2)	1929(2)	22(1)
C(24)	4009(2)	1973(2)	2861(2)	22(1)
C(26)	1817(2)	2887(2)	2036(2)	28(1)
C(25)	5427(2)	1766(2)	2780(2)	21(1)
C(1S)	6900(3)	913(3)	9056(3)	44(1)
Cl(1S)	5618(1)	831(1)	8303(1)	66(1)
Cl(2S)	8520(1)	274(1)	8573(1)	47(1)

Table 2.3.3. Bond lengths [Å] and angles [°] for compound **96**.

S(1)-C(1)	1.788(2)
S(1)-C(15)	1.836(2)
C(1)-O(1)	1.202(3)
C(1)-C(2)	1.497(3)
C(2)-C(3)	1.512(3)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(4)	1.326(3)
C(3)-C(15)	1.523(3)
C(4)-C(5)	1.506(3)
C(4)-H(4)	0.9500
C(5)-O(2)	1.430(3)
C(5)-C(6)	1.531(3)
C(5)-H(5)	1.0000
O(2)-H(2)	0.831(18)
C(6)-N(1)	1.472(3)
C(6)-C(16)	1.530(3)
C(6)-H(6)	1.0000
N(1)-C(17)	1.386(3)
N(1)-C(7)	1.477(3)
C(7)-C(8)	1.533(3)
C(7)-H(7A)	0.9900
C(7)-H(7B)	0.9900
C(8)-C(9)	1.502(3)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(10)	1.348(3)
C(9)-C(18)	1.425(3)
C(10)-N(2)	1.426(3)
C(10)-H(10)	0.9500
N(2)-C(11)	1.430(2)
N(2)-S(2)	1.6779(17)
C(11)-C(18)	1.391(3)
C(11)-C(12)	1.407(3)

C(12)-O(3)	1.367(2)
C(12)-C(13)	1.398(3)
O(3)-C(19)	1.435(2)
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
C(13)-C(14)	1.404(3)
C(13)-H(13)	0.9500
C(14)-C(17)	1.392(3)
C(14)-C(15)	1.521(3)
C(17)-C(18)	1.399(3)
C(15)-C(16)	1.536(3)
C(16)-H(16A)	0.9900
C(16)-H(16B)	0.9900
S(2)-O(5)	1.4274(15)
S(2)-O(4)	1.4305(15)
S(2)-C(20)	1.752(2)
C(20)-C(21)	1.393(3)
C(20)-C(25)	1.394(3)
C(21)-C(22)	1.388(3)
C(21)-H(21)	0.9500
C(22)-C(23)	1.395(3)
C(22)-H(22)	0.9500
C(23)-C(24)	1.398(3)
C(23)-C(26)	1.508(3)
C(24)-C(25)	1.385(3)
C(24)-H(24)	0.9500
C(26)-H(26A)	0.9800
C(26)-H(26B)	0.9800
C(26)-H(26C)	0.9800
C(25)-H(25)	0.9500
C(1S)-Cl(2S)	1.762(3)
C(1S)-Cl(1S)	1.771(3)
C(1S)-H(1S1)	0.9900
C(1S)-H(1S2)	0.9900

C(1)-S(1)-C(15)	94.70(10)
O(1)-C(1)-C(2)	126.5(2)
O(1)-C(1)-S(1)	122.89(19)
C(2)-C(1)-S(1)	110.57(15)
C(1)-C(2)-C(3)	107.52(17)
C(1)-C(2)-H(2A)	110.2
C(3)-C(2)-H(2A)	110.2
C(1)-C(2)-H(2B)	110.2
C(3)-C(2)-H(2B)	110.2
H(2A)-C(2)-H(2B)	108.5
C(4)-C(3)-C(2)	126.70(19)
C(4)-C(3)-C(15)	122.10(19)
C(2)-C(3)-C(15)	111.04(17)
C(3)-C(4)-C(5)	123.85(19)
C(3)-C(4)-H(4)	118.1
C(5)-C(4)-H(4)	118.1
O(2)-C(5)-C(4)	105.94(17)
O(2)-C(5)-C(6)	110.21(17)
C(4)-C(5)-C(6)	111.42(17)
O(2)-C(5)-H(5)	109.7
C(4)-C(5)-H(5)	109.7
C(6)-C(5)-H(5)	109.7
C(5)-O(2)-H(2)	109(2)
N(1)-C(6)-C(16)	112.28(17)
N(1)-C(6)-C(5)	109.53(17)
C(16)-C(6)-C(5)	108.85(17)
N(1)-C(6)-H(6)	108.7
C(16)-C(6)-H(6)	108.7
C(5)-C(6)-H(6)	108.7
C(17)-N(1)-C(6)	118.34(17)
C(17)-N(1)-C(7)	116.63(17)
C(6)-N(1)-C(7)	115.90(16)
N(1)-C(7)-C(8)	113.24(17)
N(1)-C(7)-H(7A)	108.9
C(8)-C(7)-H(7A)	108.9
N(1)-C(7)-H(7B)	108.9

C(8)-C(7)-H(7B)	108.9
H(7A)-C(7)-H(7B)	107.7
C(9)-C(8)-C(7)	109.09(17)
C(9)-C(8)-H(8A)	109.9
C(7)-C(8)-H(8A)	109.9
C(9)-C(8)-H(8B)	109.9
C(7)-C(8)-H(8B)	109.9
H(8A)-C(8)-H(8B)	108.3
C(10)-C(9)-C(18)	106.64(18)
C(10)-C(9)-C(8)	136.23(19)
C(18)-C(9)-C(8)	117.08(18)
C(9)-C(10)-N(2)	109.70(17)
C(9)-C(10)-H(10)	125.2
N(2)-C(10)-H(10)	125.2
C(10)-N(2)-C(11)	107.76(16)
C(10)-N(2)-S(2)	116.34(13)
C(11)-N(2)-S(2)	128.04(14)
C(18)-C(11)-C(12)	119.17(18)
C(18)-C(11)-N(2)	104.89(17)
C(12)-C(11)-N(2)	135.87(18)
O(3)-C(12)-C(13)	123.14(18)
O(3)-C(12)-C(11)	120.22(18)
C(13)-C(12)-C(11)	116.63(18)
C(12)-O(3)-C(19)	116.52(16)
O(3)-C(19)-H(19A)	109.5
O(3)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
O(3)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
C(12)-C(13)-C(14)	123.78(18)
C(12)-C(13)-H(13)	118.1
C(14)-C(13)-H(13)	118.1
C(17)-C(14)-C(13)	119.17(19)
C(17)-C(14)-C(15)	115.17(18)
C(13)-C(14)-C(15)	125.64(18)

N(1)-C(17)-C(14)	125.07(19)
N(1)-C(17)-C(18)	117.91(18)
C(14)-C(17)-C(18)	116.99(19)
C(11)-C(18)-C(17)	124.06(18)
C(11)-C(18)-C(9)	110.89(18)
C(17)-C(18)-C(9)	125.05(19)
C(14)-C(15)-C(3)	110.45(16)
C(14)-C(15)-C(16)	107.04(17)
C(3)-C(15)-C(16)	110.01(17)
C(14)-C(15)-S(1)	114.32(14)
C(3)-C(15)-S(1)	104.17(14)
C(16)-C(15)-S(1)	110.85(14)
C(6)-C(16)-C(15)	107.42(16)
C(6)-C(16)-H(16A)	110.2
C(15)-C(16)-H(16A)	110.2
C(6)-C(16)-H(16B)	110.2
C(15)-C(16)-H(16B)	110.2
H(16A)-C(16)-H(16B)	108.5
O(5)-S(2)-O(4)	119.18(9)
O(5)-S(2)-N(2)	107.64(9)
O(4)-S(2)-N(2)	104.87(9)
O(5)-S(2)-C(20)	110.06(9)
O(4)-S(2)-C(20)	109.04(9)
N(2)-S(2)-C(20)	105.02(9)
C(21)-C(20)-C(25)	121.14(19)
C(21)-C(20)-S(2)	118.54(16)
C(25)-C(20)-S(2)	120.31(16)
C(22)-C(21)-C(20)	118.99(19)
C(22)-C(21)-H(21)	120.5
C(20)-C(21)-H(21)	120.5
C(21)-C(22)-C(23)	121.06(19)
C(21)-C(22)-H(22)	119.5
C(23)-C(22)-H(22)	119.5
C(22)-C(23)-C(24)	118.73(19)
C(22)-C(23)-C(26)	121.33(19)
C(24)-C(23)-C(26)	119.93(19)

C(25)-C(24)-C(23)	121.18(19)
C(25)-C(24)-H(24)	119.4
C(23)-C(24)-H(24)	119.4
C(23)-C(26)-H(26A)	109.5
C(23)-C(26)-H(26B)	109.5
H(26A)-C(26)-H(26B)	109.5
C(23)-C(26)-H(26C)	109.5
H(26A)-C(26)-H(26C)	109.5
H(26B)-C(26)-H(26C)	109.5
C(24)-C(25)-C(20)	118.88(19)
C(24)-C(25)-H(25)	120.6
C(20)-C(25)-H(25)	120.6
Cl(2S)-C(1S)-Cl(1S)	111.24(16)
Cl(2S)-C(1S)-H(1S1)	109.4
Cl(1S)-C(1S)-H(1S1)	109.4
Cl(2S)-C(1S)-H(1S2)	109.4
Cl(1S)-C(1S)-H(1S2)	109.4
H(1S1)-C(1S)-H(1S2)	108.0

Symmetry transformations used to generate equivalent atoms:

Table 2.3.4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for compound **96**. 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)	26(1)	25(1)	18(1)	-7(1)	-6(1)	-1(1)
C(1)	31(1)	26(1)	22(1)	-10(1)	0(1)	-4(1)
O(1)	42(1)	42(1)	20(1)	-5(1)	2(1)	-6(1)
C(2)	19(1)	28(1)	18(1)	-10(1)	3(1)	-6(1)
C(3)	19(1)	25(1)	19(1)	-10(1)	-2(1)	-5(1)
C(4)	17(1)	26(1)	24(1)	-9(1)	-4(1)	-2(1)
C(5)	26(1)	20(1)	22(1)	-6(1)	-5(1)	-2(1)
O(2)	35(1)	19(1)	24(1)	-7(1)	-2(1)	-6(1)
C(6)	22(1)	21(1)	21(1)	-6(1)	-1(1)	-6(1)
N(1)	27(1)	20(1)	18(1)	-6(1)	0(1)	-6(1)
C(7)	28(1)	23(1)	18(1)	-4(1)	0(1)	-8(1)
C(8)	28(1)	23(1)	17(1)	-4(1)	-1(1)	-5(1)
C(9)	15(1)	25(1)	16(1)	-5(1)	0(1)	-4(1)
C(10)	18(1)	25(1)	15(1)	-4(1)	0(1)	-6(1)
N(2)	18(1)	22(1)	14(1)	-6(1)	0(1)	-4(1)
C(11)	14(1)	23(1)	17(1)	-8(1)	-1(1)	-4(1)
C(12)	19(1)	20(1)	17(1)	-5(1)	-4(1)	-4(1)
O(3)	36(1)	19(1)	17(1)	-4(1)	-6(1)	-5(1)
C(19)	44(1)	21(1)	18(1)	-3(1)	-9(1)	-5(1)
C(13)	18(1)	23(1)	15(1)	-4(1)	-3(1)	-4(1)
C(14)	16(1)	24(1)	19(1)	-8(1)	-2(1)	-4(1)
C(17)	17(1)	22(1)	19(1)	-7(1)	-1(1)	-4(1)
C(18)	14(1)	22(1)	17(1)	-5(1)	0(1)	-4(1)
C(15)	20(1)	21(1)	18(1)	-5(1)	-4(1)	-2(1)
C(16)	18(1)	22(1)	24(1)	-7(1)	-3(1)	-5(1)
S(2)	18(1)	21(1)	17(1)	-8(1)	0(1)	-2(1)
O(4)	24(1)	30(1)	18(1)	-12(1)	2(1)	-4(1)
O(5)	24(1)	23(1)	22(1)	-9(1)	-2(1)	0(1)
C(20)	19(1)	21(1)	20(1)	-10(1)	-2(1)	-3(1)
C(21)	24(1)	27(1)	16(1)	-7(1)	-1(1)	-6(1)

C(22)	24(1)	26(1)	21(1)	-6(1)	-6(1)	-3(1)
C(23)	20(1)	25(1)	24(1)	-13(1)	-3(1)	-3(1)
C(24)	22(1)	27(1)	19(1)	-9(1)	1(1)	-7(1)
C(26)	20(1)	37(1)	30(1)	-15(1)	-3(1)	-3(1)
C(25)	22(1)	24(1)	17(1)	-6(1)	-3(1)	-3(1)
C(1S)	43(2)	52(2)	43(2)	-23(1)	-11(1)	3(1)
Cl(1S)	47(1)	102(1)	67(1)	-49(1)	-13(1)	-6(1)
Cl(2S)	41(1)	39(1)	61(1)	-19(1)	-2(1)	-4(1)

Table 2.3.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for compound **96**.

	x	y	z	U(eq)
H(2A)	4492	5761	6557	26
H(2B)	4974	4642	6023	26
H(4)	4947	7698	4824	26
H(5)	6509	8760	3226	27
H(2)	7520(30)	9770(20)	3980(20)	39
H(6)	8980	8160	3311	26
H(7A)	9788	7219	1733	28
H(7B)	8592	8377	1511	28
H(8A)	7318	7263	856	28
H(8B)	8855	7221	211	28
H(10)	8651	4619	215	24
H(19A)	9137	1042	5721	42
H(19B)	8583	-196	5634	42
H(19C)	7526	865	5991	42
H(13)	7739	2932	5577	23
H(16A)	8692	7052	5315	26
H(16B)	9655	6189	4659	26
H(21)	6147	3432	109	27
H(22)	3752	3774	272	28
H(24)	3464	1607	3562	26
H(26A)	1525	3763	1557	42
H(26B)	1432	2765	2815	42
H(26C)	1487	2246	1805	42
H(25)	5856	1266	3419	25
H(1S1)	6951	1828	8974	53
H(1S2)	6649	419	9860	53

Table 2.3.6. Torsion angles [°] for compound **96**.

C(15)-S(1)-C(1)-O(1)	-179.4(2)
C(15)-S(1)-C(1)-C(2)	2.08(16)
O(1)-C(1)-C(2)-C(3)	159.8(2)
S(1)-C(1)-C(2)-C(3)	-21.8(2)
C(1)-C(2)-C(3)-C(4)	-138.7(2)
C(1)-C(2)-C(3)-C(15)	36.7(2)
C(2)-C(3)-C(4)-C(5)	172.32(19)
C(15)-C(3)-C(4)-C(5)	-2.6(3)
C(3)-C(4)-C(5)-O(2)	-104.9(2)
C(3)-C(4)-C(5)-C(6)	15.0(3)
O(2)-C(5)-C(6)-N(1)	-166.80(16)
C(4)-C(5)-C(6)-N(1)	75.9(2)
O(2)-C(5)-C(6)-C(16)	70.1(2)
C(4)-C(5)-C(6)-C(16)	-47.2(2)
C(16)-C(6)-N(1)-C(17)	13.4(3)
C(5)-C(6)-N(1)-C(17)	-107.6(2)
C(16)-C(6)-N(1)-C(7)	-132.47(19)
C(5)-C(6)-N(1)-C(7)	106.5(2)
C(17)-N(1)-C(7)-C(8)	48.8(3)
C(6)-N(1)-C(7)-C(8)	-164.74(18)
N(1)-C(7)-C(8)-C(9)	-50.8(2)
C(7)-C(8)-C(9)-C(10)	-153.7(2)
C(7)-C(8)-C(9)-C(18)	29.3(2)
C(18)-C(9)-C(10)-N(2)	-0.6(2)
C(8)-C(9)-C(10)-N(2)	-177.9(2)
C(9)-C(10)-N(2)-C(11)	2.6(2)
C(9)-C(10)-N(2)-S(2)	154.30(14)
C(10)-N(2)-C(11)-C(18)	-3.5(2)
S(2)-N(2)-C(11)-C(18)	-150.84(15)
C(10)-N(2)-C(11)-C(12)	179.9(2)
S(2)-N(2)-C(11)-C(12)	32.5(3)
C(18)-C(11)-C(12)-O(3)	-175.70(17)
N(2)-C(11)-C(12)-O(3)	0.6(3)
C(18)-C(11)-C(12)-C(13)	3.2(3)

N(2)-C(11)-C(12)-C(13)	179.5(2)
C(13)-C(12)-O(3)-C(19)	-11.8(3)
C(11)-C(12)-O(3)-C(19)	166.97(19)
O(3)-C(12)-C(13)-C(14)	174.76(18)
C(11)-C(12)-C(13)-C(14)	-4.1(3)
C(12)-C(13)-C(14)-C(17)	1.0(3)
C(12)-C(13)-C(14)-C(15)	-177.57(19)
C(6)-N(1)-C(17)-C(14)	15.4(3)
C(7)-N(1)-C(17)-C(14)	161.03(19)
C(6)-N(1)-C(17)-C(18)	-166.98(18)
C(7)-N(1)-C(17)-C(18)	-21.3(3)
C(13)-C(14)-C(17)-N(1)	-179.40(19)
C(15)-C(14)-C(17)-N(1)	-0.7(3)
C(13)-C(14)-C(17)-C(18)	2.9(3)
C(15)-C(14)-C(17)-C(18)	-178.37(17)
C(12)-C(11)-C(18)-C(17)	0.7(3)
N(2)-C(11)-C(18)-C(17)	-176.63(18)
C(12)-C(11)-C(18)-C(9)	-179.45(17)
N(2)-C(11)-C(18)-C(9)	3.2(2)
N(1)-C(17)-C(18)-C(11)	178.31(18)
C(14)-C(17)-C(18)-C(11)	-3.8(3)
N(1)-C(17)-C(18)-C(9)	-1.5(3)
C(14)-C(17)-C(18)-C(9)	176.34(18)
C(10)-C(9)-C(18)-C(11)	-1.7(2)
C(8)-C(9)-C(18)-C(11)	176.17(17)
C(10)-C(9)-C(18)-C(17)	178.13(19)
C(8)-C(9)-C(18)-C(17)	-4.0(3)
C(17)-C(14)-C(15)-C(3)	79.9(2)
C(13)-C(14)-C(15)-C(3)	-101.5(2)
C(17)-C(14)-C(15)-C(16)	-39.9(2)
C(13)-C(14)-C(15)-C(16)	138.7(2)
C(17)-C(14)-C(15)-S(1)	-163.02(15)
C(13)-C(14)-C(15)-S(1)	15.6(3)
C(4)-C(3)-C(15)-C(14)	-95.1(2)
C(2)-C(3)-C(15)-C(14)	89.2(2)
C(4)-C(3)-C(15)-C(16)	22.8(3)

C(2)-C(3)-C(15)-C(16)	-152.83(17)
C(4)-C(3)-C(15)-S(1)	141.69(18)
C(2)-C(3)-C(15)-S(1)	-33.97(19)
C(1)-S(1)-C(15)-C(14)	-102.83(15)
C(1)-S(1)-C(15)-C(3)	17.81(15)
C(1)-S(1)-C(15)-C(16)	136.09(15)
N(1)-C(6)-C(16)-C(15)	-53.1(2)
C(5)-C(6)-C(16)-C(15)	68.3(2)
C(14)-C(15)-C(16)-C(6)	65.7(2)
C(3)-C(15)-C(16)-C(6)	-54.4(2)
S(1)-C(15)-C(16)-C(6)	-169.05(14)
C(10)-N(2)-S(2)-O(5)	163.49(14)
C(11)-N(2)-S(2)-O(5)	-51.47(18)
C(10)-N(2)-S(2)-O(4)	35.63(16)
C(11)-N(2)-S(2)-O(4)	-179.33(16)
C(10)-N(2)-S(2)-C(20)	-79.25(16)
C(11)-N(2)-S(2)-C(20)	65.79(18)
O(5)-S(2)-C(20)-C(21)	-154.32(16)
O(4)-S(2)-C(20)-C(21)	-21.85(19)
N(2)-S(2)-C(20)-C(21)	90.09(17)
O(5)-S(2)-C(20)-C(25)	26.4(2)
O(4)-S(2)-C(20)-C(25)	158.91(16)
N(2)-S(2)-C(20)-C(25)	-89.15(18)
C(25)-C(20)-C(21)-C(22)	-1.0(3)
S(2)-C(20)-C(21)-C(22)	179.81(16)
C(20)-C(21)-C(22)-C(23)	-0.2(3)
C(21)-C(22)-C(23)-C(24)	1.1(3)
C(21)-C(22)-C(23)-C(26)	-177.9(2)
C(22)-C(23)-C(24)-C(25)	-0.8(3)
C(26)-C(23)-C(24)-C(25)	178.2(2)
C(23)-C(24)-C(25)-C(20)	-0.3(3)
C(21)-C(20)-C(25)-C(24)	1.2(3)
S(2)-C(20)-C(25)-C(24)	-179.59(16)

Symmetry transformations used to generate equivalent atoms:

Table 2.3.7. Hydrogen bonds for compound **96** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(2)-H(2)...O(3)#1	0.831(18)	2.32(3)	2.878(2)	125(3)
O(2)-H(2)...O(5)#1	0.831(18)	2.06(2)	2.842(2)	158(3)
C(8)-H(8B)...O(4)#2	0.99	2.65	3.411(3)	134.0
C(16)-H(16B)...S(1)#3	0.99	2.93	3.843(2)	154.2
C(21)-H(21)...O(1)#4	0.95	2.45	3.160(3)	131.2
C(25)-H(25)...O(2)#5	0.95	2.51	3.348(3)	147.6
C(1S)-H(1S1)...O(1)	0.99	2.50	3.308(4)	139.1

Symmetry transformations used to generate equivalent atoms:

#1 x,y+1,z #2 -x+2,-y+1,-z #3 -x+2,-y+1,-z+1

#4 x,y,z-1 #5 x,y-1,z

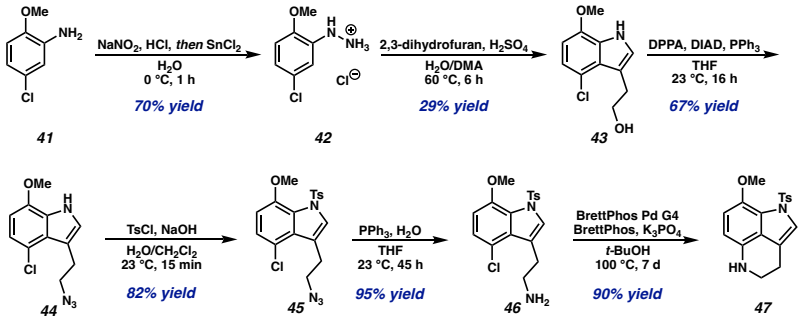
APPENDIX 3

Synthetic Summary for Chapter 1:

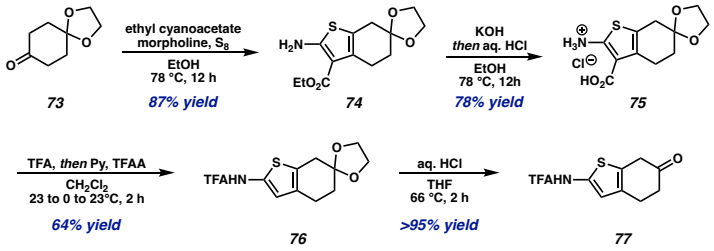
Total Synthesis of Aleutianamine

Scheme A3.1. *Synthetic summary of the total synthesis of aleutianamine.*

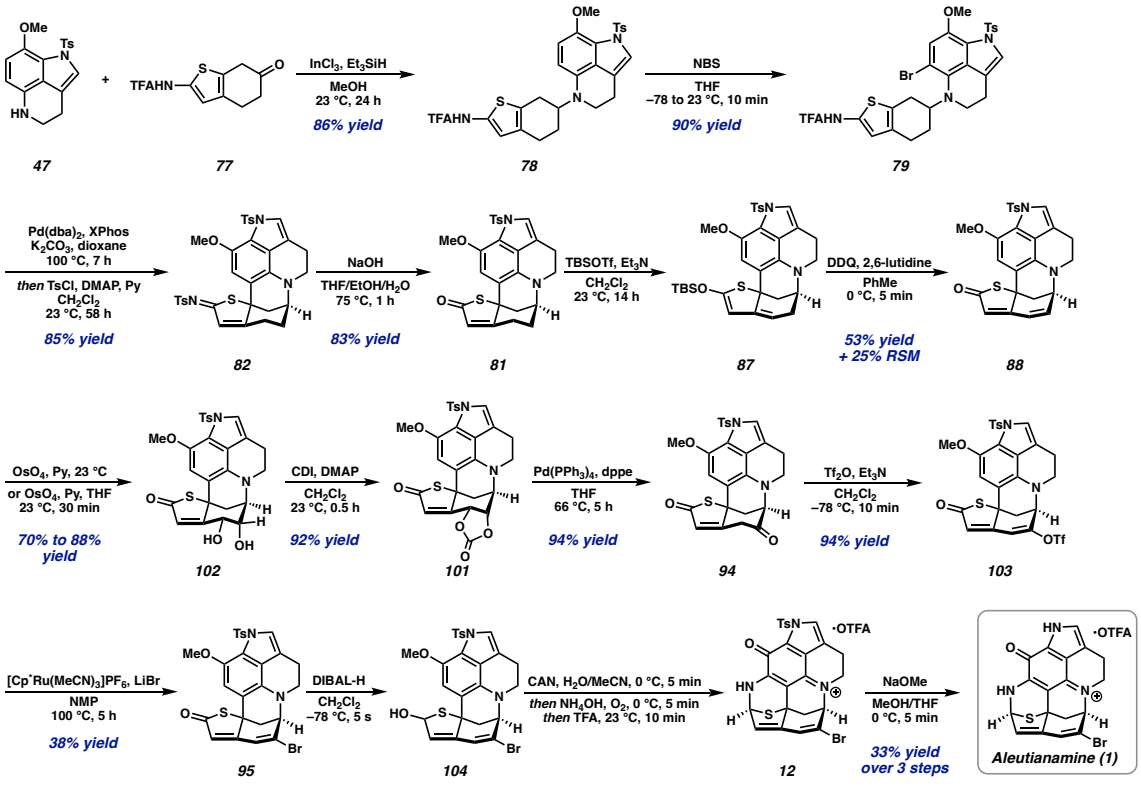
A) Synthesis of fragment 47.



B) Synthesis of fragment 77.



C) Synthesis of aleutianamine (1).



CHAPTER 2

Total Synthesis of Crotonine G and Crotonolide D †

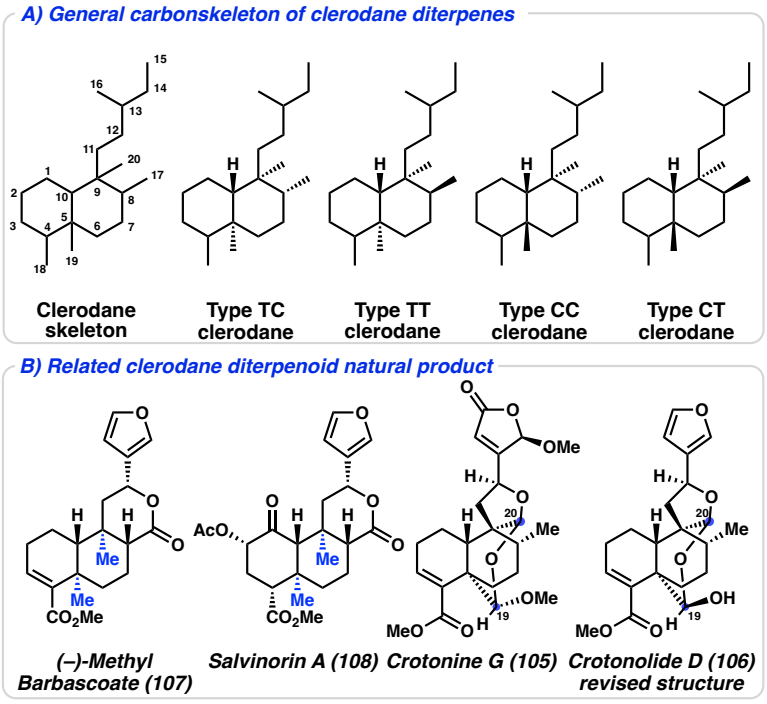
2.1 INTRODUCTION

Clerodane diterpenoids represent a large class of natural products isolated from different plant species.[1] Clerodane diterpenoids all share a similar 20-carbon core with a central decalin moiety and are further classified by the relative stereochemistry of the stereodiads defined by the decalin ring junction (C5 and C10) and the neighboring C9 and C8 stereocenters (Figure 2.1.1A). Natural products in this class display diverse biological activity and thus have stimulated the interest of synthetic organic chemists. Many elegant synthetic approaches have been disclosed, such as the total synthesis of type TC clerodane methylbarbascoate (**107**) [2] and salvinorin A (**108**, Figure 2.1.1B).[3,4,5]

Crotonine G (**105**)[6] and crotonolide D (**106**)[7] are novel two type TC clerodane diterpenoids recently isolated from medicinal plants *Croton yunanensis* and *Croton laui*. Structurally, crotononine G (**105**) and crotonolide D (**106**) contain a tetracyclic core bearing multiple stereocenters, in which four of those are contiguous. Compared to other clerodane diterpenoids that have been synthesized, crotonine G (**105**) and crotonolide D (**106**) possess unprecedented C-19 and C-20 oxidation, which would be difficult to access using established synthetic approaches. The densely functionalized decalin core along with the

unique oxidation pattern present significant synthetic challenges. Additionally, crotonine G (**105**) was found to promote glucose uptake activity in insulin-resistant 3T3-L1 adipocytes.[6] Unfortunately, further investigation of the biological activities of these molecules has been limited due to extremely low isolation efficiency (0.76 mg/kg). Because of the structural complexity and intriguing biological activity, we were motivated to pursue the total syntheses of these molecules.

Figure 2.1.1. *A) General skeleton of clerodane diterpenoids. (B) Crotonine G (**105**), crotonolide D (**106**) and related natural products.*

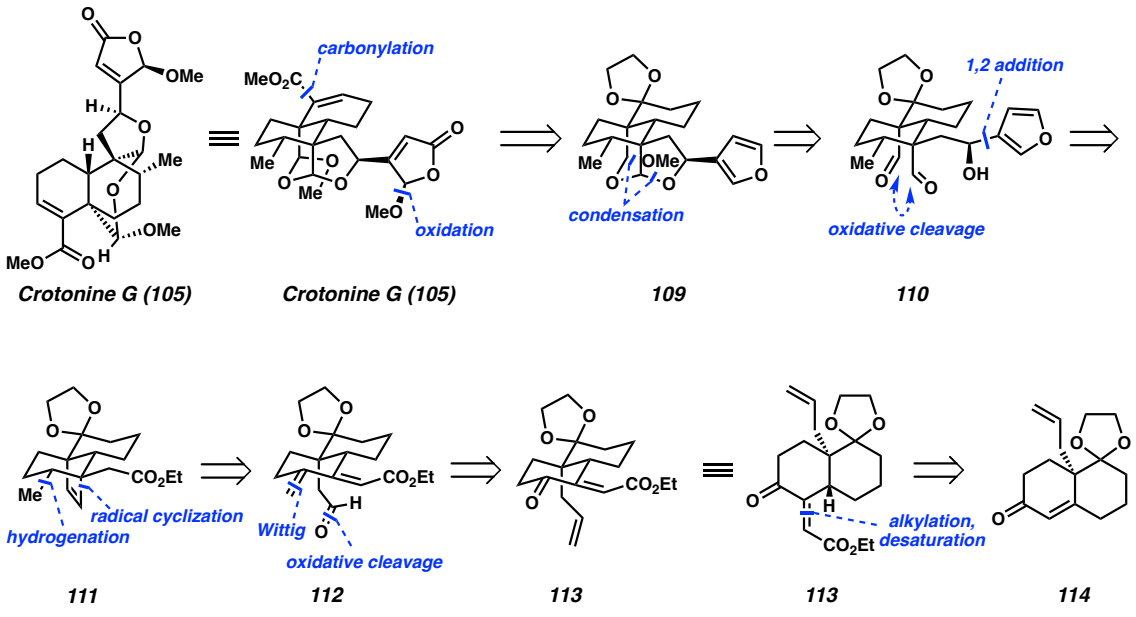


2.2 RETROSYNTHETIC ANALYSIS

Given the structural similarity between crotonine G (**105**) and crotonolide D (**106**), we envision that they could be accessed from the same or similar intermediates and thus we began our retrosynthetic analysis from crotonine G (**105**). Disconnection of the α,β-

unsaturated ester using palladium-catalyzed carbonylation, and redox manipulation of the butenolide ring would lead to intermediate **109** (Scheme 2.2.1). Revealing the diacetal guided us back to dialdehyde **110**, which was retrosynthetically converted to alkene **111** by oxidative olefin cleavage and organometallic addition. The highlighted C-C bond in **111** was disconnected by ketyl radical cyclization, resulting in further simplification to aldehyde **112**. Finally, functional group interconversions on aldehyde **112** led us back to enoate **113**, which could be accessed by reductive alkylation and desaturation from enone **114**.[8]

Scheme 2.2.1. *Retrosynthetic analysis of crotonine G (**105**).*

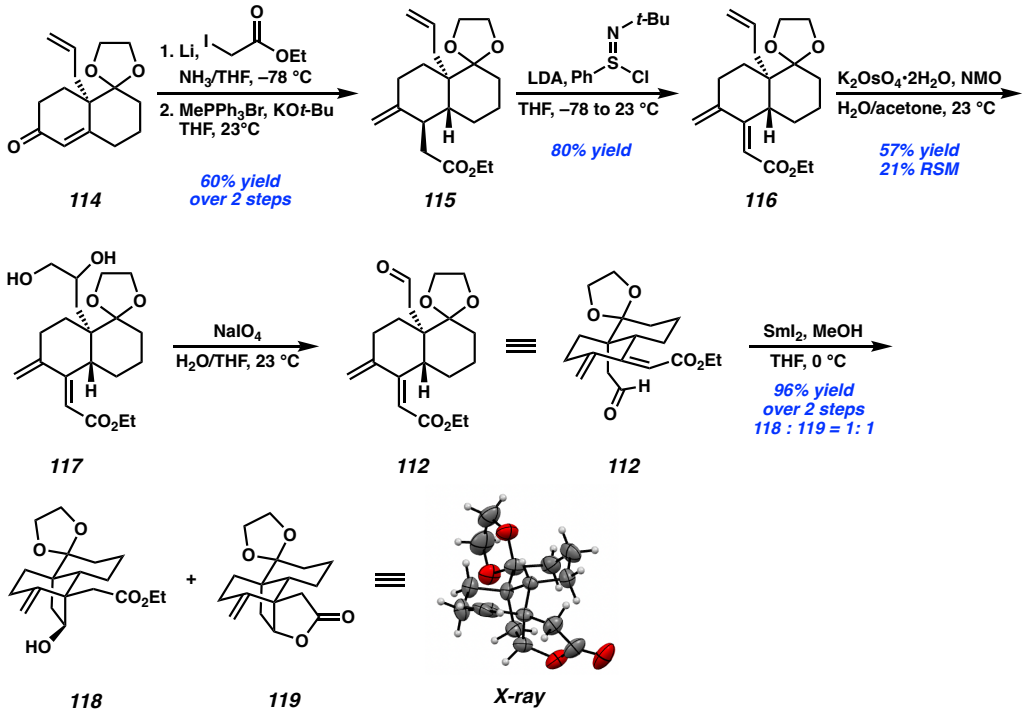


2.3 SAMARIUM DIIODIDE MEDIATED KETYL RADICAL CYCLIZATION

Starting from enantioenriched enone **114** (prepared in 4 steps from commercially available materials), dissolving metal-mediated reductive alkylation and Wittig olefination afforded ester **115** as a single diastereomer. Desaturation of ester **115** was achieved by treatment

with LDA and Mukaiyama's reagent,[9] giving dienyl ester **116** in good yield and stereoselectivity. Osmium-mediated dihydroxylation followed by oxidative diol cleavage provided aldehyde **112** as the cyclization precusor. Gratifyingly, treatment of aldehyde **112** with SmI_2 enabled the proposed ketyl radical cyclization to proceed smoothly, providing a1:1 mixture of hydroxy ester **118** and and lactone **119** in near quantitative yield. Suitable crystals for X-ray analysis of lactone **119** were obtained, confirming the absolute and relative stereochemistry.

Scheme 2.3.1. *Synthesis of hydroxyl ester* ***118*** *and lactone* ***119***.

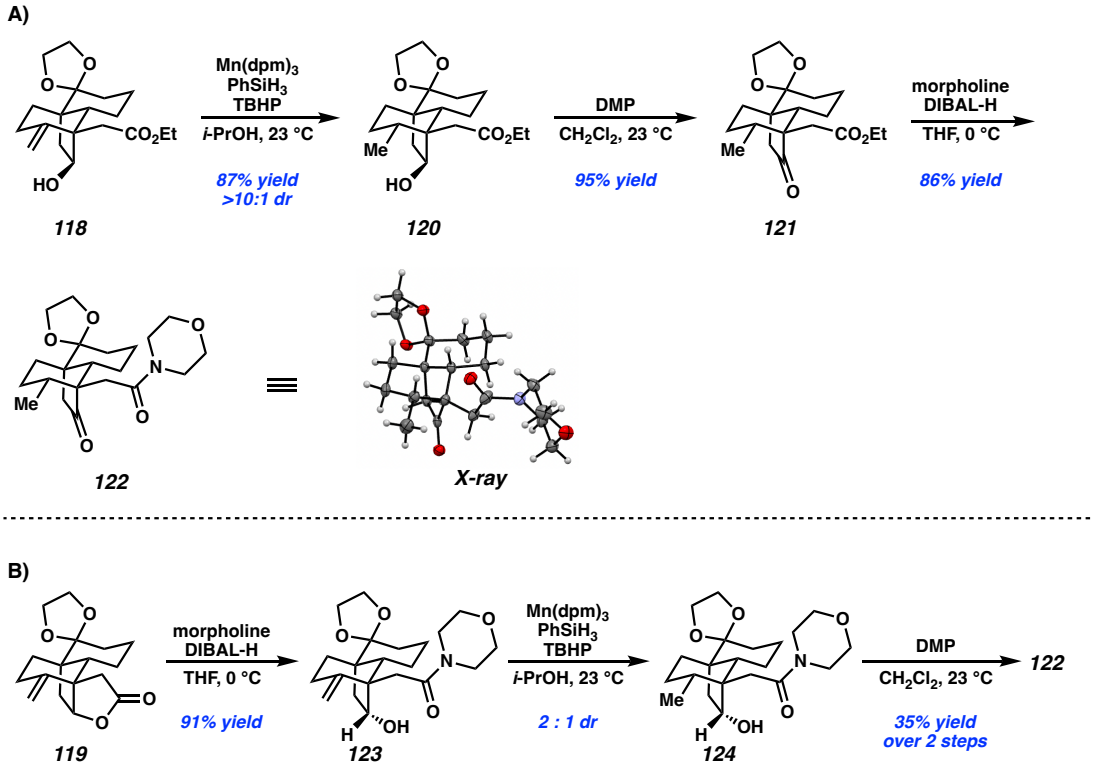


2.4 CONSTRUCTION OF CAGE-LIKE CORE

Proceeding forward, we envisioned a plan to utilize both products of the SmI_2 cyclization in our synthesis. To this end, initially we sought to hydrogenate the exocyclic

olefin to diastereoselectively install the equatorial methyl group (Scheme 2.4.1). This transformation proved to be surprisingly challenging, as transition metal or diimide mediated hydrogenation of hydroxy ester **118** or lactone **119** gave the undesired axial diastereomer or no reaction. Ultimately, we found that subjecting hydroxy ester **118** to the HAT hydrogenation conditions developed by the Shenvi group delivered alkane **120** as the only diastereomer in excellent yield.[10] Oxidation of the secondary alcohol followed by transamidation with aluminum morpholine amide[11] gave ketone **122**, which proved to be crystalline and allowed unambiguous determination of the methyl group configuration by X-ray analysis. As for lactone **119**, a slightly modified synthetic sequence was established, where lactone opening was conducted first to produce morpholine amide **123**. HAT

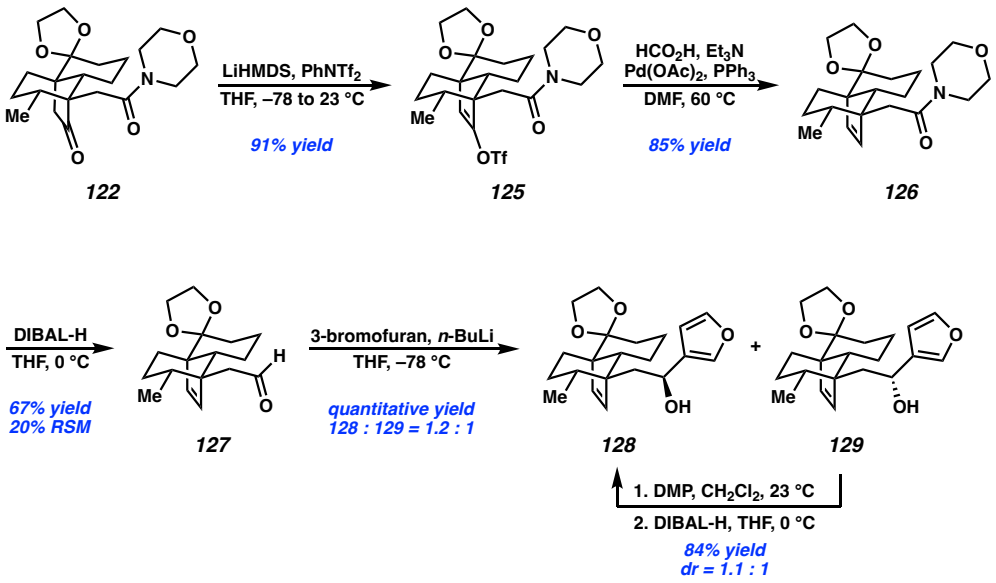
Scheme 2.4.1. *Morpholine amide (**122**) synthesis from hydroxy ester **118** and lactone **119**.*



hydrogenation of olefin **123** gave the saturated intermediate **124**, albeit in diminished diastereoseletivity (i.e. 2:1). DMP oxidation of secondary alcohol **124** produced the common intermediate **122**.

With access to ample amounts of ketone **122**, treatment with LiHMDS and $PhNTf_2$ affected selective ketone triflation (Scheme 2.4.2), which was reduced under palladium catalysis in the presence of formic acid to afford olefin **126** in an overall 77% yield.[12] With amide **126** in hand, efforts were directed toward introducing the 3-furyl group by nucleophilic addition. This transformation proved to be surprisingly challenging, as different 3-furylmetallic reagents (Li, Mg, Ce, La)[13,14,15] all failed to react. After extensive optimization, we found that treatment of amide **126** with 1 equivalent of DIBAL-H at low temperature provided aldehyde **127** in satisfactory yield. Subsequent 3-furyl lithium addition proceeded smoothly, generating 3-furfuryl alcohols **128** and **129** as a diastereomeric mixture. Importantly, we were able to recycle the undesired diastereomer

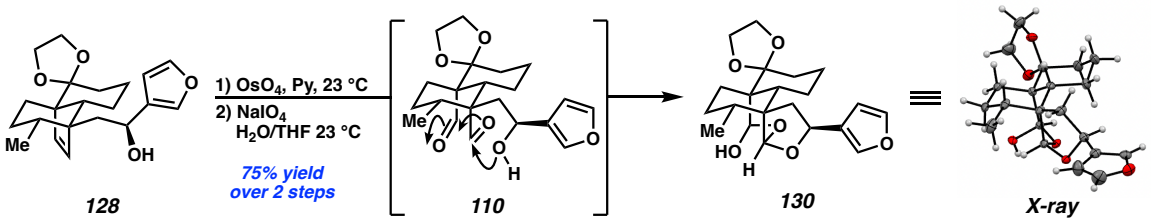
Scheme 2.4.2. *Preparation of furfuryl alcohol* ***128****.*



129 via an oxidation-reduction sequence. This route proved to be reproducible and scalable, providing access to sufficient quantities of alcohol **128** (>300 mg prepared).

With the 3-furyl group introduced, we next investigated the formation of the tetrahydropyran ring (Scheme 2.4.3). Oxidative cleavage of intermediate **128** proved to be challenging as the disubstituted olefin is flanked by two neighboring quaternary carbons and is extremely hindered. Eventually, we found that treatment of olefin **128** with a stoichiometric amount of osmium tetroxide pyridine complex affected the dihydroxylation in high conversion.[16] Subjecting the resultant diol to sodium periodate generated dialdehyde **110**, which spontaneously cyclized with the appended furfuryl alcohol to give hemiacetal **130**. X-ray analysis of hemiacetal **130** indicated that the tetrahydropyran resides in a boat conformation in the solid state, possibly to avoid introducing strain to the adjacent tetrahydrofuran ring.

Figure 2.4.3. *Construction of cage-like core via olefin cleavage.*

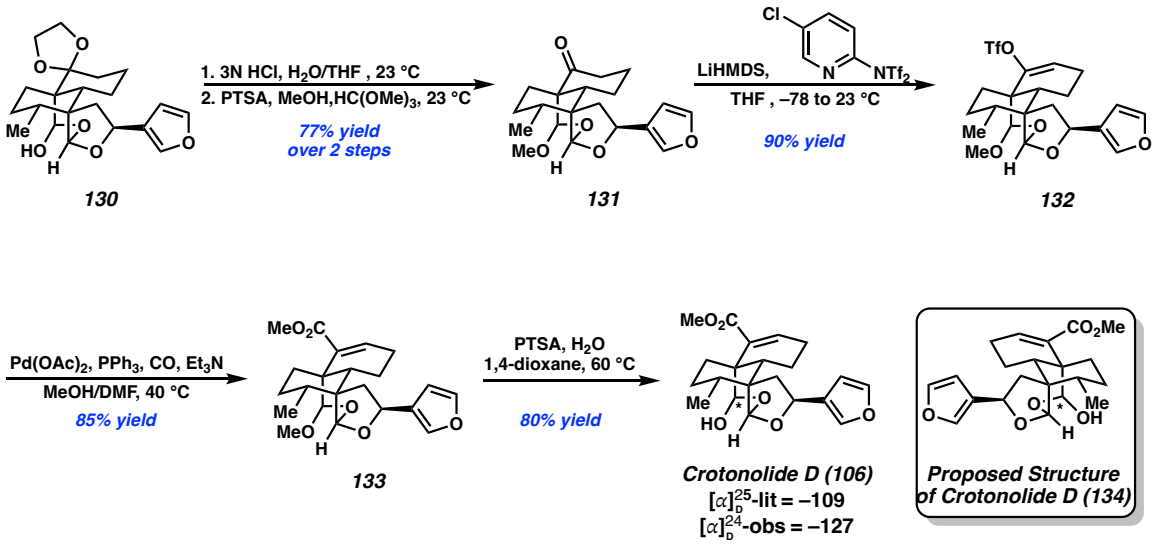


2.5 COMPLETION OF THE TOTAL SYNTHESES OF CROTONINE G AND CROTONOLIDE D.

Despite the presence of the furan and 3-furfuryl ether, intermediate **130** proved to be reasonably acid stable, as hydrolysis of the ketal with aqueous acid and acid catalyzed acetalization proceeded smoothly, giving methyl acetal **131** in 77% yield. At this stage, the remaining objectives included the introduction of the α,β-unsaturated ester and

manipulation of the acetal or furan moiety. Triflation with LiHMDS and Comins' reagent[17] afforded triflate **132**, which upon carefully optimized carbonylation gave methyl enoate **133** in excellent yield. Hydrolysis of the methyl acetal in enoate **133** completed the synthesis of crotonolide D (**106**). Crotonolide D (**106**) was obtained as a mixture of C-19 epimers with a similar diastereomeric ratio compared to the isolation report (4.5 : 1 vs 3.6 : 1).[7] Although being the enantiomer of what the isolation chemists proposed, we found that our synthetic crotonolide D (**106**) matched the reported optical rotation (Scheme 2.5.1). This observation suggested that **106** is the actual natural enantiomer of crotonolide D (**106**), which is consistent with other natural products in this class.[18]

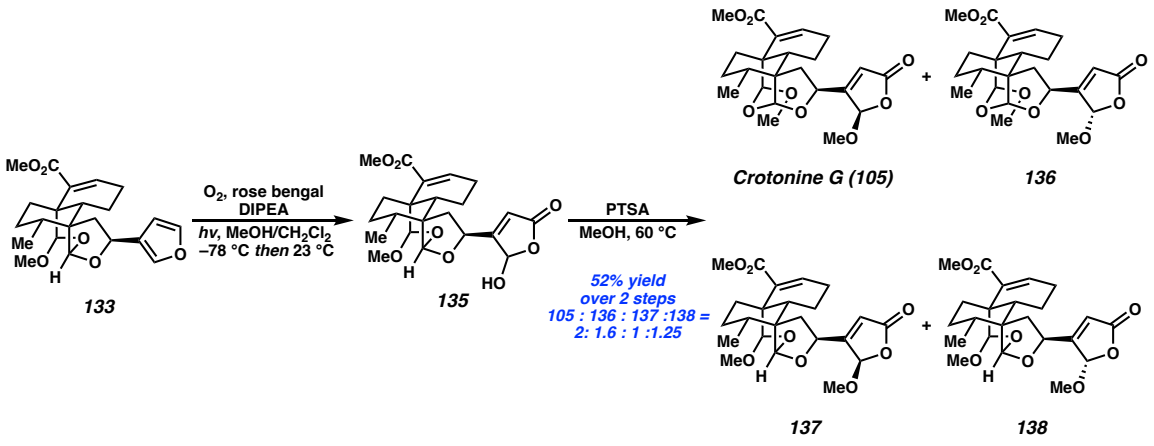
Scheme 2.5.1. *Completion of the total synthesis of crotonolide D (**106**) and configuration reassignement.*



To complete the synthesis of crotonine G (**105**), we attempted various oxidations of the furan. Ultimately, we found that exposing furan **133** to singlet oxygen smoothly induced the hetero–Diels–Alder reaction.[19] Subsequent concentration of the reaction mixture at 23 °C promoted the Kornblum–DeLaMare rearrangement to afford hydroxy

butenolide **134**. With butenolide **134** in hand, all that remained was formation of the methoxy butenolide and inversion of the methyl acetal stereocenter. After some optimization, we found that subjecting butenolide **134** to excess methanolic acid at 60 °C generated a diastereomeric mixture of four compounds with crotonine G (**105**) as the slightly dominate species. Performing the reaction for shorter or longer amount of time had no influence on the diastereomeric ratio, and subjection of a single isomer to methanolic acid produced an epimeric mixture of all four isomers. These experiments suggested that the reaction was under thermodynamic control. Computational studies revealed that the free energies of the four isomers (**105**, **136**–**138**) are within 0.6 kcal/mol difference at the M06-2X/def2-TZVPP, ma-def2-TZVPP(O)/CPCM(Methanol)//M06-2X/def2-SVP,ma-def2-SVP(O)/CPCM (Methanol) level of theory, which is consistent with the experimental observation that a mixture of stereoisomers is obtained. Given the similarity in thermodynamic stability, we hypothesize that **136**, **137**, and **138** could be natural products that have yet to be isolated.[20]

Scheme 2.5.2. *Completion of the total synthesis of crotonine G (**1**) via furan oxidation.*



2.6 CONCLUSION

In conclusion, we have developed asymmetric total syntheses of crotonine G (**105**) and crotonolide D (**106**). Starting from a known enantioenriched building block, we rapidly constructed a bridged bicycle bearing two all-carbon quaternary centers, via a SmI_2 mediated radical cyclization. From the cyclized intermediate, introduction of the furan ring and oxidative olefin cleavage afforded the skeleton of the natural products. Finally, carbonylation, acetal formation and redox manipulation completed the total syntheses. Efforts to apply similar radical cyclization strategies to the synthesis of other clerodane diterpenoids are currently ongoing in our laboratory.

2.7 EXPERIMENTAL SECTION

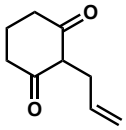
2.7.1 MATERIALS AND METHODS

Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon.[21] Reaction progress was monitored by thin-layer chromatography (TLC). 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 $KMnO_4$ staining. Silicycle SiliaFlash® P60 Academic Silica gel (particle size 40–63 μm) was used for flash chromatography. ^1H NMR spectra were recorded on Varian Inova 500 MHz and 600 MHz and Bruker 400 MHz spectrometers and are reported relative to residual $CHCl_3$ (δ 7.26 ppm), C_6D_6 (δ 7.16 ppm) or CD3OD (δ 3.31 ppm). ^{13}C NMR spectra were recorded on a Varian Inova 500 MHz spectrometer (125 MHz) and Bruker 400 MHz spectrometers (100 MHz) and are reported relative to $CHCl_3$ (δ 77.16 ppm), C_6D_6 (δ 128.06 ppm) or CD_3OD (δ 49.01 ppm). Data for ^1H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet, br d = broad doublet. Data for ^{13}C NMR are reported in terms of chemical shifts (δ ppm). IR spectra were obtained by use of a Perkin Elmer Spectrum BXII spectrometer or Nicolet 6700 FTIR spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm path- length cell. High resolution

mass spectra (HRMS) were obtained using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+) mode.

2.7.2 EXPERIMENTAL PROCEDURES

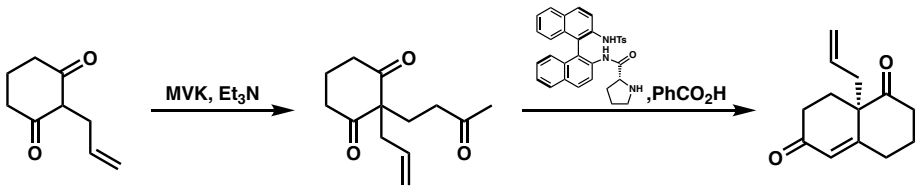
2-Allyl-1,3-cyclohexanedione (139)



139

Prepared according to the procedure of Assound and coworkers from 1,3-cyclohexanedione.[8a] The crude product was used in the next reaction without any further purification.

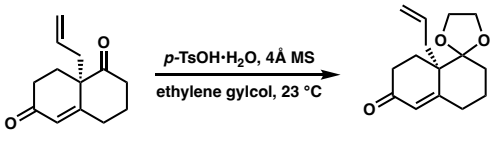
Diketone 141



139 ***140*** ***141***

Prepared in 2 steps according to the procedure of Nàjera and coworkers from 2-Allyl-1,3-cyclohexanedione (**139**) with the alternative enantiomer of the BINAM catalyst.[8b] All characterization data matched those reported in the literature.

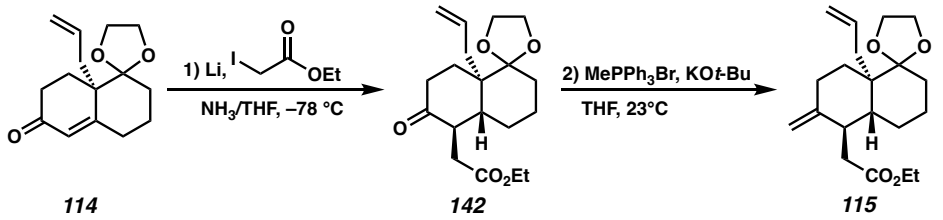
Ketal 114



141 ***114***

To a 1L round bottom flask was added diketone **141** (26.0 g, 127 mmol, 1 equiv), ethylene glycol (424 mL), followed by freshly activated 4Å molecular sieve (24.2 g), and *p*-TsOH•H_2O (24.2 g, 127 mmol, 1 equiv). The resulting suspension was stirred at 23 °C for 1h before being quenched with *aq*. $NaHCO_3$ (500 mL). The mixture was extracted with Et_2O (3 x 500 mL). The combined organic extracts were washed with brine (200 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by silica gel flash column chromatography (30% to 50% Et_2O/Hexane) to afford ketal **114** (22.0 g, 88.9 mmol, 70% yield) as a colorless oil, which upon standing at 23 °C solidified as a white solid. ***Note****: 50 min to 1h was found to be the optimal reaction time. Extended reaction time results in formation of large amount of bisketalized product.* ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.90 (d, *J* = 1.8 Hz, 1H), 5.77 (dddd, *J* = 16.7, 10.0, 8.1, 6.5 Hz, 1H), 5.09 (dq, *J* = 17.0, 1.6 Hz, 1H), 5.03 (ddt, *J* = 10.0, 2.1, 1.1 Hz, 1H), 4.18 – 3.70 (m, 4H), 2.73 – 2.59 (m, 1H), 2.53 – 2.35 (m, 4H), 2.23 (ddt, *J* = 16.1, 9.7, 4.2 Hz, 2H), 1.93 (td, *J* = 13.6, 4.6 Hz, 1H), 1.88 – 1.77 (m, 2H), 1.74 – 1.57 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 199.8, 165.2, 134.3, 127.1, 118.0, 113.5, 65.4, 64.9, 48.2, 40.6, 35.0, 32.0, 30.2, 24.8, 22.7. IR (Neat Film, NaCl): 3321, 2948, 2882, 1667, 1623, 1451, 1353, 1333, 1266, 1251, 1201, 1173, 1139, 1100, 1030, 996, 951, 916, 871, 801, 773, 736, 665, 625 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{15}H_{21}O_3$ $[M+H]^+$: 249.1491, found 249.1484. $[\alpha]_D^{23}$: –39 (*c* = 0.50, $CHCl_3$)

Ester 115



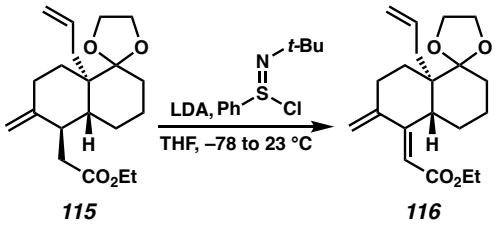
114 ***142*** ***115***

To a 1 L round bottom flask was condensed liquid ammonia (200 mL), then lithium (559 mg, 80.5 mmol, 4 equiv.) was added at ‑78 °C under argon atmosphere and stirred for 0.5 h. Solution of enone **114** (5.00 g, 20.1 mmol, 1 equiv.) in THF (200 mL) was added to the above dark-blue reaction mixture slowly at ‑78 °C and stirred for 1 h. After 1 h, isoprene (4.03 mL, 40.3 mmol, 2 equiv.) was added dropwise to the above mixture until the mixture turned from deep blue to light grey. Then the resulting mixture was warmed to 23 °C, allowing ammonia to evaporate under a stream of nitrogen. Upon the completion of ammonia evaporation, the reaction mixture was diluted with anhydrous THF (200 mL) and cooled to –78 °C. Ethyl iodoacetate (11.9 mL, 101 mmol, 5 equiv.) was added at ‑78 °C and stirred for 1 h before quenching the reaction with *aq*. NH_4Cl (200 mL). The mixture was then extracted with Et_2O (3 x 100 mL). The combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (25% Et_2O/hexanes) to afford compound **142** as a yellow oil mixed with some byproduct (total 6.10 g), which was used for the next transformation without further purification.

To a flame dried 1 L round bottom flask was added KO*t*-Bu (2.44 g, 21.8 mmol, 1.2 equiv.) and $MePPh_3Br$ (8.10 g, 22.7 mmol, 1.25 equiv.), and the headspace of the flask was evacuated and backfilled with nitrogen three times. THF (181 mL) was added at 23 °C

under nitrogen atmosphere and the resulting bright yellow mixture stirred for 30 min. Then a solution of **142** (6.10 g, 18.1 mmol, 1 equiv.) in THF (181 mL) was added to the mixture at 23 °C and stirred for 1 h. The reaction was quenched by the addition of *aq*. NH_4Cl (200 mL) before extracting with Et_2O (3 x 100 mL). The combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (5% Et_2O/Hexanes) to afford ester **115** as a colorless oil (4.00 g, 12.0 mmol, 60% yield over 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.16 (dddd, *J* = 16.8, 10.0, 8.0, 6.4 Hz, 1H), 5.15 – 5.01 (m, 1H), 5.01 – 4.92 (m, 1H), 4.68 (d, *J* = 1.4 Hz, 1H), 4.61 – 4.42 (m, 1H), 4.13 (qq, *J* = 7.3, 3.6 Hz, 2H), 3.96 – 3.67 (m, 4H), 2.69 (ddd, *J* = 12.2, 7.7, 6.0 Hz, 1H), 2.61 – 2.37 (m, 3H), 2.33 – 2.08 (m, 2H), 1.87 – 1.39 (m, 9H), 1.26 (td, *J* = 7.5, 5.0 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 152.0, 137.0, 115.5, 113.2, 104.8, 65.5, 64.5, 60.5, 48.6, 45.8, 39.0, 35.5, 33.4, 31.9, 30.1, 28.6, 23.6, 22.9, 14.3. IR (Neat Film, NaCl): 3072, 2943, 2875, 1734, 1641, 1449, 1374, 1297, 1238, 1207, 1184, 1153, 1122, 1092, 1035, 983, 950, 889, 800, 751, 690, 653 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{20}H_{31}O_4$ $[M+H]^+$: 335.2222, found 335.2220. $[\alpha]_D^{23}$: –8 (*c* = 0.32, $CHCl_3$)

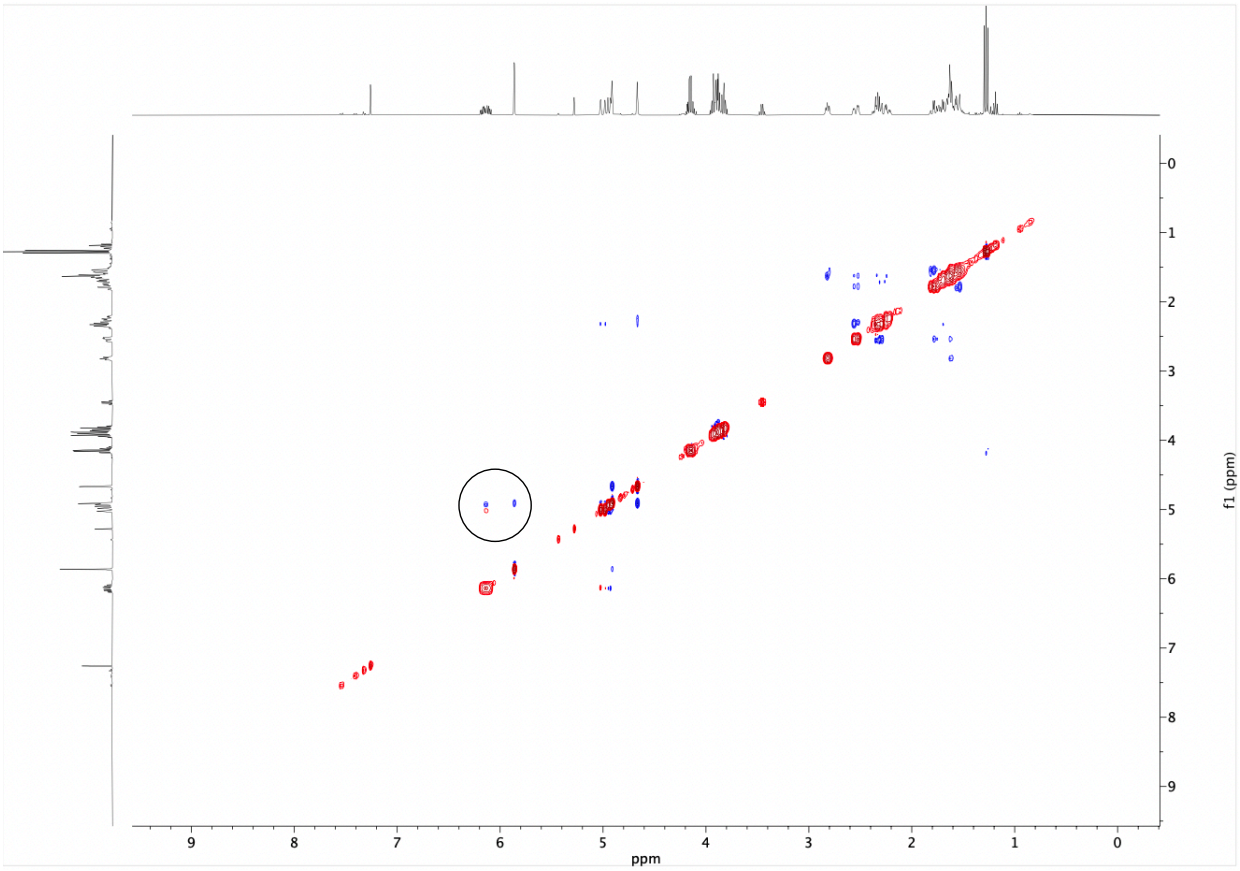
Enoate 116

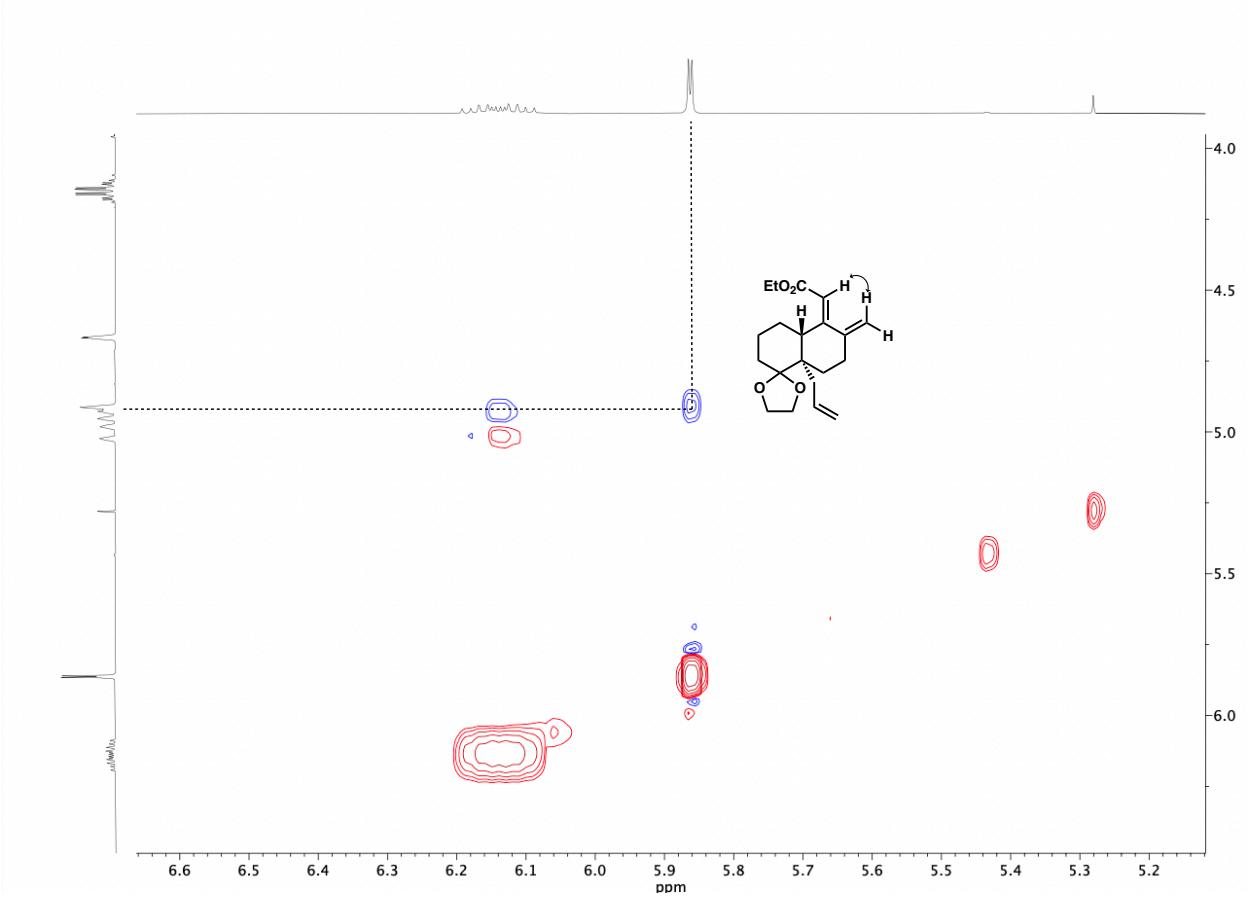


To a flame dried 250 mL round bottom flask under nitrogen was added THF (111 mL) and *i*-Pr_2NH (39.8 mmol, 5.62 mL, 1.2 equiv). The resulting mixture was cooled to –78 °C before *n*-BuLi (2.09 M in hexane, 17.5 mL, 36.5 mmol, 1.1 equiv) was added dropwise. After stirring at –78 °C for 30 min, the solution of ester **115** (11.1 g, 33.2 mmol, 1.0 equiv) in THF (111 mL) was added to the above mixture at ‑78 °C and stirred for 1 h. Freshly prepared solution of *N*-tert-butylbenzenesulfinimidoyl chloride (14.3 g, 66.4 mmol, 2 equiv) in THF (111 mL) was added to the mixture at ‑78 °C. The mixture was allowed to warm to 23 °C and stirred at that temperature for 1 h. Then the reaction was quenched by the addition of *aq*. $NaHCO_3$ (300 mL) before extracting with Et_2O (3 x 200 mL). The combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (50% CH_2Cl_2/Hexanes) to afford Enoate **116** as a brown-red oil (8.83 g, 26.6 mmol, 80% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.16 (dddd, *J* = 17.1, 10.1, 9.4, 5.0 Hz, 1H), 5.88 (d, *J* = 2.0 Hz, 1H), 5.03 (dtd, *J* = 17.1, 2.1, 1.0 Hz, 1H), 4.99 – 4.94 (m, 1H), 4.93 (s, 1H), 4.69 (dt, *J* = 2.1, 1.1 Hz, 1H), 4.17 (qd, *J* = 7.2, 2.3 Hz, 2H), 4.00 – 3.77 (m, 4H), 2.99 – 2.75 (m, 1H), 2.63 – 2.50 (m, 1H), 2.45 – 2.17 (m, 3H), 1.87 – 1.70 (m, 2H), 1.70 – 1.48 (m, 6H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 154.3, 151.3, 137.1, 116.8, 115.5, 113.0, 108.8, 65.6, 64.7, 60.5, 48.6, 46.7, 34.3, 30.6,

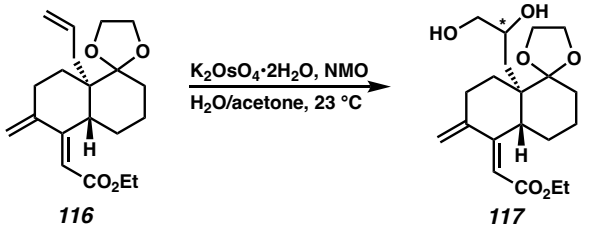
29.5, 25.9, 23.8, 23.1, 14.3. IR (Neat Film, NaCl): 3072, 2940, 2876, 1724, 1636, 1448, 1366, 1336, 1284, 1208, 1175, 1132, 1090, 1034, 948, 902, 870, 750, 716, 684 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{20}H_{29}O_4$ $[M+H]^+$: 333.2066, found 333.2059. $[\alpha]_D^{23}$: 44 (*c* = 0.39, $CHCl_3$)

Figure 2.7.1. Noesy spectra of ester **116**.





Diol 117



116 ***117***

To a 1 L round bottom flask containing unsaturated ester **116** (8.00 g, 24.1 mmol, 1 equiv) was added acetone (241 mL), deionized water (48 mL) followed by $K_2OsO_4 \cdot 2H_2O$ (443 mg, 1.20 mmol, 5 mol%), and $NMO \cdot H_2O$ (3.25 g, 24.1 mmol, 1 equiv),. The reaction mixture was stirred at 23 °C for 15 h, whereafter 1:1 mixture of *aq*. $Na_2S_2O_3$ and

aq. $NaHCO_3$ (300 mL) was added before extracted with EtOAc (3 x 200 mL). The combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (50% EtOAc / hexanes) to afford diol **117** as a mixture of diastereomers (5.00 g, 13.6 mmol, 57% yield, 2 : 1 dr) and recovered SM (**116**) (1.70 g, 5.10 mmol, 21% yield). Analytical samples of each diastereomers were obtained by preparative TLC (50% EtOAc/Hexane).

Characterizations of minor isomer (faster eluting isomer):

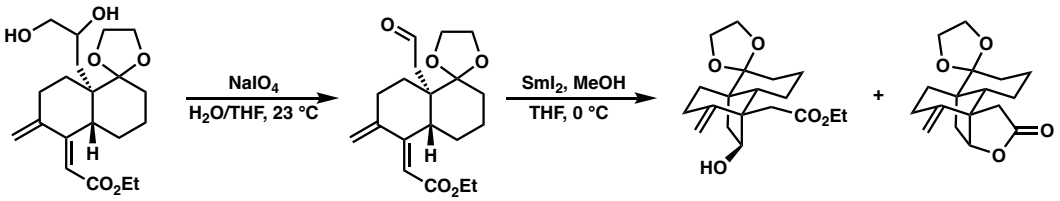
^{1}H NMR (600 MHz, $CDCl_3$): δ 5.88 (d, *J* = 1.8 Hz, 1H), 4.92 (s, 1H), 4.68 (d, *J* = 1.0 Hz, 1H), 4.17 (dqt, *J* = 14.5, 7.3, 4.0 Hz, 3H), 4.04 – 3.80 (m, 4H), 3.58 (d, *J* = 7.3 Hz, 1H), 3.46 (t, *J* = 9.1 Hz, 1H), 2.93 (d, *J* = 4.2 Hz, 1H), 2.75 (ddd, *J* = 12.6, 3.3, 1.8 Hz, 1H), 2.61 – 2.50 (m, 1H), 2.37 (ddd, *J* = 14.8, 5.7, 3.0 Hz, 1H), 2.22 – 2.14 (m, 1H), 1.94 (ddd, *J* = 13.3, 5.7, 2.9 Hz, 1H), 1.85 – 1.67 (m, 4H), 1.67 – 1.49 (m, 5H), 1.29 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.5, 152.7, 151.0, 116.6, 113.0, 108.6, 70.0, 67.8, 65.4, 64.5, 60.6, 49.2, 47.0, 31.6, 30.5, 30.5, 27.8, 23.5, 22.7, 14.3. IR (Neat Film, NaCl): 3402, 2927, 1721, 1636, 1454, 1170, 1082, 1026, 950, 891, 733 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{20}H_{30}NaO_6$ $[M+Na]^+$: 389.1940, found 389.1936. $[\alpha]_D^{24}$: 17 (*c* = 0.20, $CHCl_3$)

Characterizations of major isomer (slower eluting isomer):

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.87 (d, *J* = 2.0 Hz, 1H), 4.96 (d, *J* = 1.5 Hz, 1H), 4.85 (s, 1H), 4.70 (d, *J* = 1.6 Hz, 1H), 4.16 (qd, *J* = 7.1, 5.0 Hz, 2H), 4.09 – 4.01 (m, 1H), 4.02 – 3.93 (m, 3H), 3.92 – 3.84 (m, 1H), 3.48 (qt, *J* = 10.3, 4.9 Hz, 2H), 2.95 (ddd, *J* = 9.1, 5.1, 2.0 Hz, 1H), 2.49 – 2.32 (m, 1H), 2.29 (dd, *J* = 8.3, 4.0 Hz, 1H), 2.19 (dddd, *J* = 15.0, 13.1, 6.9, 4.0 Hz, 1H), 1.95 – 1.83 (m, 3H), 1.81 – 1.70 (m, 2H), 1.71 – 1.54 (m, 5H), 1.29 (t, *J*

= 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 167.8, 154.1, 150.0, 117.5, 112.9, 109.5, 67.8, 67.5, 65.5, 64.8, 60.5, 48.6, 45.9, 33.2, 30.4, 29.5, 25.3, 23.5, 23.0, 14.3. IR (Neat Film, NaCl): 3463, 2933, 1718, 1637, 1448, 1367, 1176, 1088, 1055, 1030, 951,887, 828, 739 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{20}H_{30}NaO_6$ $[M+Na]^+$: 389.1940, found 389.1935. $[\alpha]_D^{24}$: 42 (*c* = 0.31, $CHCl_3$)

Ester 118 and lactone 119



117 ***112*** ***118*** ***119***

To a 1 L round bottom flask containing the diol **117** (mixture of diastereomers, 5.00 g, 13.6 mmol, 1 equiv), was added deionized water (68 mL), and THF (271 mL) followed by $NaIO_4$ (14.5 g, 67.8 mmol, 5 equiv). The mixture was stirred at 23 °C for 0.5 h before being quenched by 1:1 mixture of *aq*. $Na_2S_2O_3$ and *aq*. $NaHCO_3$ (300 mL) at 0 °C. The resulting mixture was additionally stirred for 0.5 h, and then extracted with Et_2O (3 x 200 mL). The combined organic extracts were washed with brine (100 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude aldehyde **112** (4.54 g, 13.6 mmol, quantitative yield) was used without further purification.

To a 2 L round bottom flask containing the crude aldehyde **112** under nitrogen was added MeOH (2.72 mL, 67.3 mmol, 5 equiv) and THF (135 mL). The resulting solution was cooled to 0 °C before SmI_2 (0.1 M in THF, 336 mL, 33.6 mmol, 2.5 equiv) was added via cannulation. The resulting deep blue solution was stirred at 0 °C for 10 mins before

being quenched by the addition of *aq*. $Na_2S_2O_3$ (300mL) and extracted with EtOAc (3 x 200 mL). The combined organic extracts were washed with brine (200 mL), dried over $MgSO_4$, and filtered through a plug of silica. The residue was concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (20% Et_2O/Hexanes) to afford the lactone **119** as white solid (1.88 g, 6.46 mmol, 48% yield) and the hydroxyester **118** as colorless oil (2.17 g, 6.46 mmol, 48% yield). X-ray quality crystals of lactone **119** were obtained by slow evaporation from 1:1 Et_2O/Hexane at 23 °C.

Characterization of lactone 119:

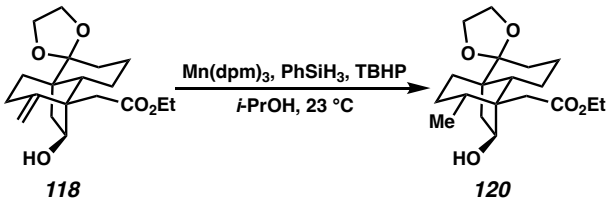
^{1}H NMR (600 MHz, $CDCl_3$): δ 4.64 (d, *J* = 2.0 Hz, 1H), 4.55 (ddd, *J* = 7.6, 3.2, 1.0 Hz, 1H), 4.49 (d, *J* = 2.0 Hz, 1H), 3.93 – 3.78 (m, 4H), 2.68 (d, *J* = 17.8 Hz, 1H), 2.59 (d, *J* = 17.7 Hz, 1H), 2.40 – 2.27 (m, 2H), 2.12 (ddd, *J* = 15.1, 7.6, 1.2 Hz, 1H), 2.02 (tdt, *J* = 15.2, 7.1, 2.2 Hz, 1H), 1.70 (tdd, *J* = 13.1, 6.3, 1.8 Hz, 2H), 1.66 – 1.60 (m, 1H), 1.61 – 1.57 (m, 2H), 1.52 (dddd, *J* = 13.3, 12.0, 6.5, 2.3 Hz, 2H), 1.45 – 1.36 (m, 1H), 1.28 – 1.20 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 176.9, 150.6, 110.9, 104.6, 86.9, 65.1, 65.0, 57.9, 54.1, 53.7, 38.4, 33.7, 31.1, 30.8, 29.7, 23.5, 22.6. IR (Neat Film, NaCl): 2946, 2872, 1778, 1649, 1448, 1419, 1299, 1262, 1200, 1170, 1108, 1078, 1039, 1001, 936, 889, 845, 739 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{17}H_{23}O_4$ $[M+H]^+$: 291.1596, found 291.1589. $[\alpha]_D^{23}$: 43 (*c* = 0.58, $CHCl_3$)

Characterization of hydroxyl ester 118:

^{1}H NMR (600 MHz, $CDCl_3$): δ 4.65 (d, *J* = 2.0 Hz, 1H), 4.44 (dd, *J* = 10.9, 4.3 Hz, 1H), 4.37 (d, *J* = 2.0 Hz, 1H), 4.27 (s, 1H), 4.15 – 4.00 (m, 2H), 3.90 – 3.77 (m, 4H), 2.87 (dddd, *J* = 12.5, 10.6, 8.1, 3.9 Hz, 1H), 2.72 (d, *J* = 16.7 Hz, 1H), 2.56 – 2.37 (m, 2H), 2.19 (ddd, *J* = 14.7, 5.8, 2.1 Hz, 1H), 1.69 – 1.49 (m, 7H), 1.50 – 1.43 (m, 1H), 1.38 (ddd, *J* = 16.1,

9.9, 3.2 Hz, 1H), 1.19 (td, *J* = 7.2, 0.8 Hz, 3H), 1.01 (qd, *J* = 13.0, 3.7 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.3, 152.1, 111.4, 105.9, 77.2, 65.0, 65.0, 60.9, 56.5, 54.4, 49.1, 39.4, 38.5, 32.5, 30.6, 30.5, 24.7, 22.3, 14.0. IR (Neat Film, NaCl): 3473, 3078, 2934, 2873, 2677, 1783, 1714, 1640, 1452, 1371, 1340, 1297, 1251, 1202, 1168, 1109, 1079, 1039, 998, 948, 892, 846, 805, 736, 682, 651 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{19}H_{29}O_5$ $[M+H]^+$: 337.2015, found 337.2014. $[\alpha]_D^{24}$: 21 (*c* = 0.58, $CHCl_3$)

Alcohol 120

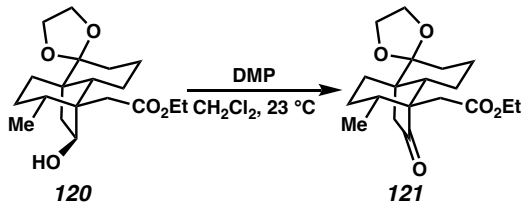


118 *120*

Procedure adopted from a report by Shenvi.[10] To a 500 mL round bottom flask was added hydroxyester **118** (1.95 g, 5.80 mmol, 1 equiv), and the headspace was evacuated and backfilled with argon three times. *i*-PrOH (degassed, 116 mL) $PhSiH_3$ (1.08 mL, 8.69 mmol, 1.5 equiv), and TBHP (5 M in decane, 2.32 mL, 2 equiv) were added sequentially under argon atmosphere. After stirring the mixture at 23 ℃ with bubbling argon for 10 mins, $Mn(dpm)_3$ (0.1 M solution in *i*-PrOH, 2.90 mL, 5 mol%) was added and the mixture was stirred at 23 °C under argon atmosphere for 4 h at which point LC/MS analysis showed full conversion of starting material. The mixture was concentrated under reduced pressure and purified by silica gel flash chromatography (30% Et_2O/Hexanes) to afford the product as colorless oil (1.70 g, 5.02 mmol, 87% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.35 (dd, *J* = 11.2, 4.9 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.93 – 3.81 (m, 4H), 2.85 (s, 1H), 2.62 (d, *J* = 16.1 Hz, 1H), 2.39 (ddd, *J* = 14.6, 11.1, 1.5 Hz, 1H), 2.25 (d, *J* = 16.1 Hz, 1H), 1.91

(qd, J = 13.1, 6.0 Hz, 1H), 1.73 – 1.48 (m, 10H), 1.47 – 1.37 (m, 1H), 1.21 (t, J = 7.1 Hz, 3H), 1.00 (d, J = 7.0 Hz, 3H), 0.89 (qd, J = 13.2, 4.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 174.2, 111.9, 79.6, 65.1, 65.0, 60.4, 55.2, 50.3, 48.7, 41.6, 40.0, 38.1, 31.6, 30.8, 28.7, 24.9, 22.3, 18.9, 14.2. IR (Neat Film, NaCl): 3495, 2935, 2873, 2132, 1729, 1450, 1370, 1341, 1259, 1187, 1162, 1102, 1051, 946, 872, 804, 735, 703 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{19}H_{31}O_5$ $[M+H]^+$: 339.2171, found 339.2167. $[\alpha]_D^{24}$: 37 (c = 0.25, $CHCl_3$)

Ketone 121

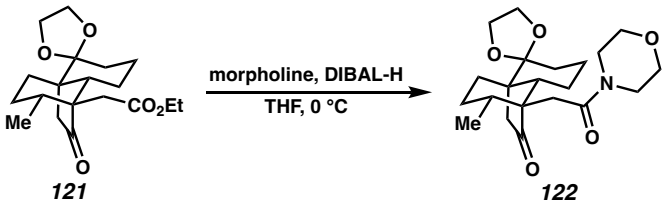


120 ***121***

To a 500 mL round bottom flask was added alcohol **120** (2.20 g, 6.50 mmol, 1 equiv), CH_2Cl_2 (130 mL) and Dess-Martin periodinane (4.14 g, 9.75 mmol, 1.5 equiv). The resulting suspension was stirred at 23 °C for 0.5h at which point TLC showed full conversion of starting material. The reaction was quenched with 1:1 mixture of *aq*. $Na_2S_2O_3$ and aq. $NaHCO_3$ (100 mL), and the resulting biphasic mixture was stirred vigorously (1200 rpm) at 23°C for 0.5h. Then the two layers were separated, and the aqueous phase was extracted with EtOAc (3 x 100 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (20% Et_2O/Hexanes) to afford the title compound as a colorless oil (2.08 g, 6.18 mmol, 95% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.01 (qq, J = 10.8, 7.1 Hz, 2H), 3.93 – 3.81 (m, 4H), 2.65 (d, J = 16.7 Hz, 1H), 2.35 (dd, J = 19.2, 1.4 Hz, 1H), 2.13 (ddd, J = 12.8, 5.3, 2.0 Hz, 1H), 2.05 (d, J = 16.7 Hz, 1H), 2.01

– 1.92 (m, 2H), 1.75 (tdd, *J* = 13.3, 5.6, 1.4 Hz, 1H), 1.70 – 1.61 (m, 2H), 1.62 – 1.42 (m, 5H), 1.15 (t, *J* = 7.2 Hz, 3H), 0.97 (qd, *J* = 13.6, 5.6 Hz, 1H), 0.71 (d, *J* = 6.6 Hz, 3H), 0.69 – 0.62 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 217.7, 171.4, 110.8, 65.2, 65.0, 60.1, 58.8, 50.2, 45.4, 43.5, 37.2, 31.7, 30.2, 29.7, 29.1, 24.8, 21.8, 16.3, 14.2. IR (Neat Film, NaCl): 3447, 2934, 2874, 2677, 1729, 1446, 1372, 1300, 1162, 1107, 1082, 1049, 975, 944, 878, 806, 735, 701, 652, 610 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{19}H_{29}O_5$ $[M+H]^+$: 337.2015, found 337.2007. $[\alpha]_D^{24}$: 38 (*c* = 0.67, $CHCl_3$)

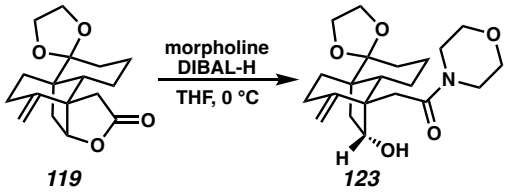
Amide 122



Procedure adopted from a report by An.[11] To a flame dried 500 mL round bottom flask under nitrogen was added morpholine (3.85 mL, 44.6 mmol, 10 equiv) and THF (122 mL). The resulting solution was cooled to 0 °C before DIBAL-H (6.98 mL, 40.1 mmol, 9 equiv) was slowly added. The resulting mixture was stirred for 3h at 0 °C to afford 0.32 M solution of diisobutyl aluminum morpholine amide. Separately, to a 1 L flask under nitrogen were added ketone **121** (1.50 g, 4.46 mmol, 1 equiv) and THF (89 mL). The resulting solution was cooled to 0 °C before aluminum amide solution (122 mL) was transferred by cannulation. The mixture was stirred at 0 °C for 0.5h, at which point TLC analysis showed full conversion of starting material. The reaction mixture was quenched with *aq*. Rochelle's salt (200 mL) and the resulting biphasic mixture was stirred for 1h at 23 °C. The mixture was then extracted with EtOAc (3 x 100 mL) and the combined organic

extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (50% EtOAc/Hexanes) to afford the title compound as a white solid (1.45 g, 3.84 mmol, 86% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.91 – 3.77 (m, 4H), 3.60 – 3.32 (m, 8H), 2.71 (d, *J* = 17.6 Hz, 1H), 2.44 (ddd, *J* = 12.8, 5.3, 2.0 Hz, 1H), 1.94 (dd, *J* = 19.2, 2.0 Hz, 2H), 1.88 (d, *J* = 17.6 Hz, 2H), 1.79 (tdd, *J* = 13.3, 5.6, 1.4 Hz, 1H), 1.64 – 1.38 (m, 7H), 0.92 (qd, *J* = 13.6, 5.5 Hz, 1H), 0.67 – 0.61 (m, 1H), 0.60 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 219.7, 169.1, 110.7, 66.8, 66.5, 65.1, 65.0, 59.2, 50.1, 46.0, 45.6, 43.5, 41.6, 36.5, 30.3, 29.8, 29.0, 28.9, 24.9, 21.8, 16.3. IR (Neat Film, NaCl): 3358, 2922, 2853, 1729, 1647, 1451, 1377, 1229, 1111, 1035, 948 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{21}H_{32}NO_5$ $[M+H]^+$: 378.2280, found 378.2272. $[\alpha]_D^{24}$: 33 (*c* = 0.04, $CHCl_3$)

Alcohol 123

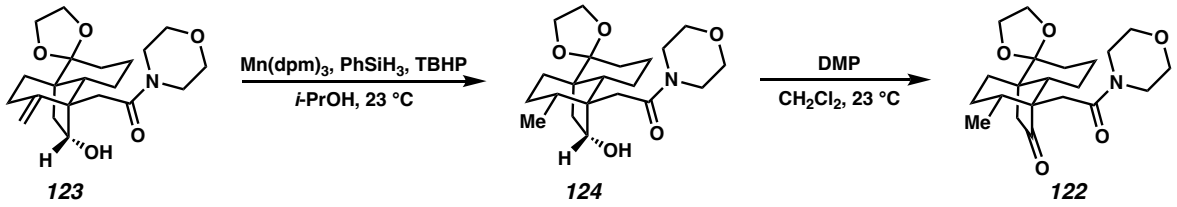


119 ***123***

To a 500 mL round bottom flask were added morpholine (2.97 mL, 34.4 mmol, 10 equiv) and THF (94 mL). DIBAL-H (5.39 mL, 31.0 mmol, 9 equiv) was slowly added to the above solution at 0 °C and stirred for 3 h. Separately, to a 1 L flask were added lactone **119** (1.00 g, 3.44 mmol, 1 equiv) and THF (69 mL). The morpholine-DIBAL-H solution was transferred to the solution of ketone slowly at 0 °C. The mixture was stirred for 0.5 h and quenched with *aq*. Rochelle's salt (200 mL) and stirred for further 1 h. The mixture was extracted with EtOAc (3 x 100 mL). The combined organic extracts were washed with

brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (50% EtOAc / hexanes) to afford the title compound as a white solid (1.18 g, 3.13 mmol, 91% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.55 (d, *J* = 1.6 Hz, 1H), 4.45 – 4.39 (m, 1H), 4.25 (t, *J* = 1.3 Hz, 1H), 4.02 (d, *J* = 3.2 Hz, 1H), 3.98 – 3.82 (m, 4H), 3.78 – 3.45 (m, 8H), 2.78 (d, *J* = 15.7 Hz, 1H), 2.65 (d, *J* = 15.7 Hz, 1H), 2.30 – 2.11 (m, 4H), 1.84 – 1.64 (m, 3H), 1.64 – 1.52 (m, 3H), 1.57 – 1.34 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.7, 153.5, 111.7, 102.0, 75.2, 66.7, 66.4, 64.9, 64.9, 57.1, 55.6, 50.3, 46.6, 41.9, 41.0, 31.5, 30.4, 30.3, 30.0, 24.0, 22.5. IR (Neat Film, NaCl): 3443, 2944, 2865, 1619, 1443, 1227, 1165, 1115, 1047, 929, 882, 754 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{21}H_{32}NO_5$ $[M+H]^+$: 378.2280, found 378.2279. $[\alpha]_D^{22}$: –72 (*c* = 1.1, $CHCl_3$)

Ketone 122

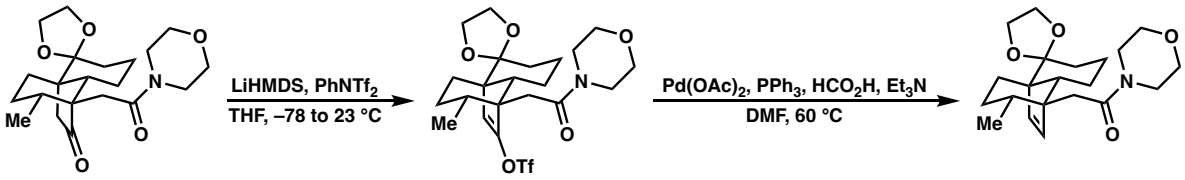


To a 500 mL round bottom flask containing amide **123** (1.00 g, 2.65 mmol, 1 equiv) under argon was added *i*-PrOH (degassed, 88 mL), $PhSiH_3$ (493 µL, 3.97 mmol, 1.5 equiv), and TBHP (5 M in decane, 1.06 mL, 0.530 mmol, 2 equiv). The resulting mixture was stirred at 23 ℃ for 10 min with bubbling argon, then $Mn(dpm)_3$ (0.1 M in *i*-PrOH, 5.30 mL, 20 mol%) was added and the mixture was stirred at 23 °C for 1 h. The mixture was concentrated under reduced pressure and purified by silica gel flash chromatography (50%

EtOAc / hexanes) to afford the alkane **124** as a mixture of the inseparable diastereomers as colorless oil, which was used directly in the next step without further purification.

To a 500 mL round bottom flask under nitrogen was added HAT product **124** as a mixture of diastereomer (844 mg, 2.22 mmol, 1 equiv), CH_2Cl_2 (45 mL) followed by Dess-Martin periodinane (1.41 g, 3.34 mmol, 1.5 equiv). The suspension was stirred at 23 °C for 0.5h, at which point TLC analysis showed full consumption of starting material. The reaction was quenched by addition of 1:1 mixture of *aq*. $Na_2S_2O_3$ and *aq*. $NaHCO_3$ (100 mL) and the resulting mixture was stirred vigorously (1200 rpm) at 23 °C for 0.5h. Then two layers were separated, and the aqueous phase was extracted with EtOAc (3 x 100 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (30% EtOAc/Hexanes) to afford the title compound as a colorless oil (353 mg, 0.934 mmol, 35% yield over 2 steps).

Cyclopentene 126



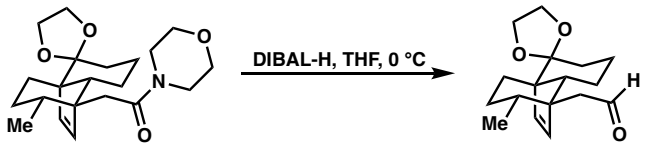
To a 250 mL round bottom flask under nitrogen was added ketone **122** (1.30 g, 3.44 mmol, 1 equiv) and THF (43 mL). The solution was cooled to –78 °C before LiHMDS (1.5 M in THF, 10.3 mL, 15.5 mmol, 4.5 equiv) was added dropwise. The resulting mixture was stirred at –78 °C for 1h, then $PhNTf_2$ (1.85 g, 5.17 mmol, 1.5 equiv) in THF (43 mL) was added slowly. Upon the completion of addition, the mixture was warmed to 23 °C and

stirred for 0.5 h. The reaction was quenched with *aq*. NH_4Cl (50 mL) and extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (10% to 35% Et_2O / hexanes) to afford triflate **125** as a colorless oil (1.60 g, 3.14 mmol, 91% yield). ^1H NMR (600 MHz, $CDCl_3$): δ 5.57 (s, 1H), 3.96 – 3.82 (m, 4H), 3.70 – 3.39 (m, 8H), 2.56 (d, *J* = 17.0 Hz, 1H), 2.38 (dd, *J* = 11.5, 5.2 Hz, 1H), 2.32 – 2.22 (m, 2H), 1.72 – 1.38 (m, 7H), 1.35 – 1.21 (m, 2H), 1.12 (qd, *J* = 12.7, 6.3 Hz, 1H), 0.73 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.5, 150.5, 118.6 (*J* = 318 Hz), 116.9, 109.5, 67.0, 66.7, 65.4, 65.0, 55.8, 54.9, 52.9, 46.1, 41.7, 33.0, 31.4, 29.2, 28.2, 25.1, 23.7, 21.3, 17.7. IR (Neat Film, NaCl): 2934, 2869, 1655, 1423, 1214, 1182, 1141, 1114, 1035, 953, 897, 857, 769, 738, 685 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{22}H_{31}F_3NO_7S$ $[M+H]^+$: 510.1773, found 510.1779. $[\alpha]_D^{24}$: 41 (*c* = 0.22, $CHCl_3$)

To a 250 mL round bottom flask was added triflate **125** (1.60 g, 3.14 mmol, 1 equiv), $Pd(OAc)_2$ (70.5 mg, 0.314 mmol, 10 mol%), PPh_3 (165 mg, 0.628 mmol, 20 mol%). The flask was evacuated and backfilled with nitrogen three times before DMF (63 mL) was added. The mixture was bubbled with nitrogen for 10 minutes before addition of Et_3N (3.50 mL, 25.1 mmol, 8 equiv) and HCO_2H (592 μL, 15.7 mmol, 5 equiv). The mixture heated to 60 °C by a preheated metal heating block, and was stirred at that temperature for 30 min, at which point TLC analysis showed full consumption of starting material. The reaction was quenched with *aq*. NH_4Cl (50 mL) and was extracted with Et_2O (3 x 50 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (60% Et_2O / hexanes) to afford the cyclopentene **126** as a colorless oil (965 mg, 2.67 mmol,

85% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.66 (d, *J* = 5.7 Hz, 1H), 5.30 (d, *J* = 5.7 Hz, 1H), 3.95 – 3.82 (m, 4H), 3.69 – 3.40 (m, 8H), 2.54 (d, *J* = 17.1 Hz, 1H), 2.28 – 2.17 (m, 2H), 2.09 (dt, *J* = 12.2, 5.6 Hz, 1H), 1.60 (dt, *J* = 12.3, 2.4 Hz, 1H), 1.56 – 1.44 (m, 4H), 1.40 (td, *J* = 8.5, 4.1 Hz, 1H), 1.34 – 1.24 (m, 2H), 1.15 (qd, *J* = 11.6, 7.1 Hz, 1H), 1.04 – 0.94 (m, 1H), 0.63 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.0, 133.1, 132.7, 110.7, 67.1, 66.7, 65.2, 64.9, 56.9, 56.6, 55.1, 46.2, 41.6, 33.1, 31.7, 31.5, 29.5, 24.6, 24.0, 21.9, 18.4. IR (Neat Film, NaCl): 2926, 2860, 1651, 1425, 1212, 1178, 1113, 1035, 944 cm^{-1} HRMS (ESI+): *m/z* calc'd for $C_{21}H_{32}NO_4$ $[M+H]^+$: 362.2331, found 362.2328. $[\alpha]_D^{22}$: 34 (*c* = 0.14, $CHCl_3$)

Aldehyde 127

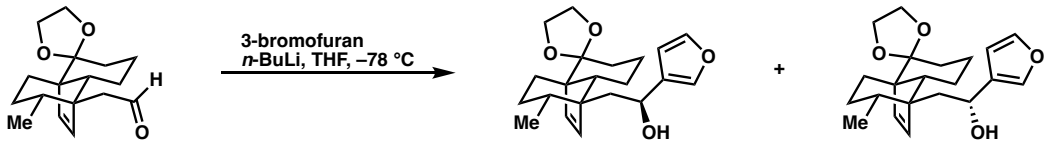


126 ***127***

To a 500 mL round bottom flask containing cyclopentene **126** (900 mg, 2.49 mmol, 1 equiv) under nitrogen was added THF (124 mL) and the resulting solution was cooled to 0 °C. Freshly prepared DIBAL-H solution (0.2 M in THF, 18.7 mL, 3.74 mmol, 1.5 equiv) was added to the above mixture dropwise and the mixture was stirred at 0 °C for 1 h. The reaction was quenched with *aq*. Rochelle's salt (100 mL), warmed to 23 °C, and stirred for 1 h. The resulting mixture was extracted with Et_2O (3 x 100 mL). The combined organic extracts were washed with brine (100 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (10% to 60% Et_2O / hexanes) to afford aldehyde **127** as a colorless oil (461 mg, 1.67 mmol, 67%

yield) with recovery of starting material **126** (180 mg, 0.498 mmol, 20% yield). ^{1}H NMR (600 MHz, C_6D_6): δ 9.50 (dd, *J* = 1.7 Hz, 1.7Hz 1H), 5.87 (dd, *J* = 5.7, 1.0 Hz, 1H), 5.10 (dd, *J* = 5.7, 1.0 Hz, 1H), 3.58 – 3.42 (m, 4H), 2.26 (dd, *J* = 16.5, 3.2 Hz, 1H), 2.13 (dd, *J* = 16.4, 1.6 Hz, 1H), 1.93 (dd, *J* = 11.6, 5.5 Hz, 1H), 1.69 – 1.30 (m, 9H), 1.18 – 1.06 (m, 2H), 0.61 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (150 MHz, C_6D_6): δ 200.6, 133.7, 132.1, 110.4, 65.2, 64.9, 57.2, 57.0, 54.8, 44.1, 33.4, 33.2, 29.8, 24.8, 24.8, 22.1, 18.4. IR (Neat Film, NaCl): 2934, 2868, 2717, 1720, 1440, 1343, 1295, 1180, 1108, 1072, 1049, 943, 878, 740 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{17}H_{25}O_3$ $[M+H]^+$: 277.1804, found 277.1795. $[\alpha]_D^{24}$: 55 (*c* = 0.17, $CHCl_3$)

Furyl alcohol 128 and 129



127 ***128*** ***129***

To a 500 mL round bottom flask under nitrogen was added 3-bromofuran (521 µL, 5.57 mmol, 5.5 equiv) and Et_2O (50 mL). The solution was cooled to –78 °C, before *n*-BuLi (2.09 M in hexane, 2.42 mL, 5.07 mmol, 5 equiv) was added dropwise. The resulting mixture was stirred at –78 °C for 0.5 h, then the solution of aldehyde **127** (280 mg, 1.01 mmol, 1 equiv) in Et_2O (50 mL) was added slowly and stirring was continued for 10 minutes. The reaction was quenched with *aq*. NH_4Cl (50 mL) and extracted with Et_2O (3 x 50 mL). The combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (2% Et_2O / CH_2Cl_2) to afford furfuryl alcohol **128** as a colorless

solid (188 mg, 0.547 mmol, 54% yield) and undesired diastereomer **129** as colorless solid (161 mg, 0.466 mmol, 46% yield).

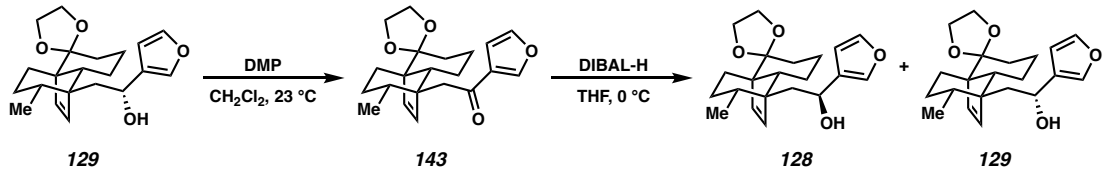
Characterization of furfuryl alcohol 128 (slower eluting diastereomer):

^{1}H NMR (600 MHz, C_6D_6): δ 7.10 (p, *J* = 0.8 Hz, 1H), 7.08 (t, *J* = 1.7 Hz, 1H), 6.22 (dd, *J* = 1.9, 0.9 Hz, 1H), 6.00 (d, *J* = 1.0 Hz, 1H), 5.29 (dd, *J* = 5.7, 0.9 Hz, 1H), 4.62 (dt, *J* = 10.3, 3.3 Hz, 1H), 3.60 – 3.51 (m, 4H), 2.17 (ddd, *J* = 12.8, 4.3, 1.8 Hz, 1H), 2.11 (dd, *J* = 11.2, 5.4 Hz, 1H), 2.02 (dd, *J* = 15.0, 10.3 Hz, 1H), 1.82 (qt, *J* = 13.8, 3.3 Hz, 1H), 1.77 – 1.65 (m, 4H), 1.65 – 1.51 (m, 4H), 1.45 – 1.32 (m, 1H), 1.32 – 1.21 (m, 1H), 1.04 (d, *J* = 3.9 Hz, 1H), 0.66 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, C_6D_6): δ 143.3, 138.6, 135.0, 133.2, 131.9, 111.2, 109.0, 65.1, 64.8, 64.0, 58.2, 57.4, 55.6, 37.5, 33.3, 31.9, 30.3, 25.1, 25.0, 22.5, 18.7. IR (Neat Film, NaCl): 3466, 2928, 2868, 1722, 1501, 1438, 1343, 1294, 1179, 1105, 1048, 1025, 939, 873, 793, 762, 737, 679 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{21}H_{29}O_4$ $[M+H]^+$: 345.2066, found 345.2057. $[\alpha]_D^{23}$: –3 (*c* = 0.33, $CHCl_3$)

Characterization of furfuryl alcohol 129 (faster eluting diastereomer):

^{1}H NMR (600 MHz, C_6D_6): δ 7.12 (p, *J* = 0.8 Hz, 1H), 7.09 (t, *J* = 1.7 Hz, 1H), 6.25 (dd, *J* = 1.8, 0.9 Hz, 1H), 5.93 (dd, *J* = 5.7, 1.0 Hz, 1H), 5.32 (dd, *J* = 5.8, 1.0 Hz, 1H), 4.53 (dd, *J* = 8.9, 2.2 Hz, 1H), 3.58 – 3.47 (m, 4H), 2.11 (dd, *J* = 15.1, 8.9 Hz, 1H), 1.86 (td, *J* = 11.8, 6.2 Hz, 2H), 1.75 – 1.61 (m, 6H), 1.61 – 1.53 (m, 1H), 1.51 – 1.42 (m, 2H), 1.33 – 1.18 (m, 3H), 1.01 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (150 MHz, C_6D_6): δ 143.4, 138.6, 134.1, 132.8, 131.8, 110.8, 109.0, 65.2, 64.9, 64.8, 56.9, 56.6, 56.5, 38.0, 33.5, 33.3, 30.4, 25.3, 24.4, 22.4, 19.4. IR (Neat Film, NaCl): 3467, 3142, 3034, 2936, 2867, 1719, 1501, 1438, 1344, 1295, 1220, 1180, 1158, 1106, 1049, 1024, 970, 944, 874, 840, 792, 737, 683 cm^{-1}.

HRMS (ESI+): *m/z* calc'd for $C_{21}H_{27}O_3$ $[M–OH]^+$: 327.1955, found 327.1954. $[\alpha]_D^{23}$: 14 (*c* = 1.2, $CHCl_3$)



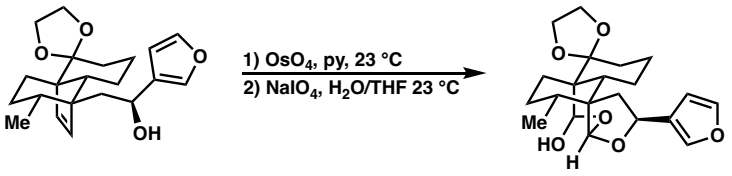
129 ***143*** ***128*** ***129***

To a 100 mL round bottom flask was added undesired diastereomer **129** (15 mg, 0.0438 mmol, 1 equiv), then the headspace was evacuated and backfilled with nitrogen three times. CH_2Cl_2 (1.5 mL) and Dess-Martin periodinane (37.2 mg, 0.0876 mmol, 2 equiv) was added and the resulting suspension was stirred at 23 °C for 0.5 h. The reaction was quenched with 1:1 mixture of *aq*. $Na_2S_2O_3$ and *aq*. $NaHCO_3$ (2 mL), and the resulting biphasic mixture was stirred vigorously (1200 rpm) at 23 °C for 0.5h. Then the layers were separated, and the aqueous layer was extracted with Et_2O (3 x 1 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure to afford ketone **143**. The crude product was used directly in the next step without further purification.

To a 100 mL round bottom flask under nitrogen was added crude furyl ketone **143** and THF (2.2 mL) and the resulting solution was cooled to 0 °C. Freshly prepared DIBAL-H (0.2 M in THF, 0.66 mL, 0.131 mmol, 3 equiv) was added to the above solution at 0 °C and the mixture was stirred for 1h. The reaction was quenched with *aq*. Rochelle's salt (2 mL), warmed to 23 °C and stirred for 1h. The mixture was extracted with Et_2O (3 x 1 mL). The combined organic extracts were washed with brine (2 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash

chromatography (2% Et_2O / CH_2Cl_2) to afford the desired diastereomer **128** as a colorless solid (6.0 mg, 0.0175 mmol, 40% yield over 2 steps) and undesired diastereomer **129** as colorless solid (6.6 mg, 0.0193 mmol, 44% yield over 2 steps).

Diacetal 130



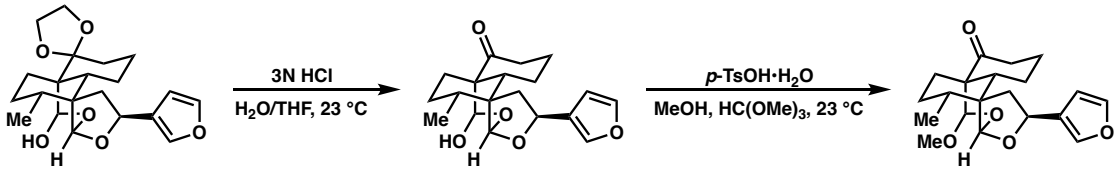
128 ***130***

To a 100 mL round bottom flask containing furyl alcohol **128** (110 mg, 0.319 mmol, 1 equiv) was added pyridine (5.3 mL), followed by a freshly prepared solution of OsO_4 (81.2 mg, 0.319 mmol, 1 equiv) in pyridine (5.3 mL). The resulting mixture was stirred at 23 °C for 1h before being concentrated under reduced pressure to afford intermediate osmate ester as a brown foam. To the residue was added THF (10.6 mL) and saturated *aq*. Na_2SO_3 (10.6 mL) and stirred vigorously (1500 rpm) at 23 °C for 48 h. The mixture was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure to afford the crude diol. The crude diol was used in the next reaction without further purification. ***Note****: The hydrolysis of osmate ester is very slow, thus vigorous stirring for 2-3 days is necessary. Incomplete hydrolysis of osmate ester will result in greatly diminished yield (~30%).*

To a 50 mL round bottom flask containing crude diol was added THF (8.0 mL) and deionized H_2O (2.0 mL), followed by $NaIO_4$ (341 mg, 1.60 mmol, 5 equiv). The mixture was stirred at 23 °C for 0.5 h, at which point TLC analysis showed full conversion of starting material. The reaction was quenched with 1:1 mixture of aq. $Na_2S_2O_3$ and aq.

$NaHCO_3$ (10 mL) and was then extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (30% EtOAc/hexanes) to afford the title compound as white crystals (90.4 mg, 0.240 mmol, 75% yield over 2 steps). ^{1}H NMR (600 MHz, C_6D_6): δ 7.28 (dt, *J* = 1.6, 0.8 Hz, 1H), 7.11 (t, *J* = 1.7 Hz, 1H), 6.35 (dd, *J* = 1.9, 0.8 Hz, 1H), 5.66 (d, *J* = 2.6 Hz, 1H), 5.58 (s, 1H), 5.11 (dd, *J* = 10.4, 5.8 Hz, 1H), 3.42 (dddd, *J* = 10.3, 8.1, 6.3, 4.9 Hz, 4H), 2.51 (s, 1H), 2.08 – 1.98 (m, 1H), 1.98 – 1.84 (m, 3H), 1.76 (dd, *J* = 13.1, 5.8 Hz, 1H), 1.65 – 1.52 (m, 8H), 1.42 (ddd, *J* = 11.9, 6.6, 4.5 Hz, 1H), 0.83 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 143.5, 139.5, 111.8, 109.3, 100.2, 94.4, 73.9, 65.1, 65.0, 50.0, 48.6, 47.2, 39.4, 38.2, 32.4, 31.5, 25.7, 25.5, 22.9, 17.3. (one of the furan ^{13}C resonance is obscured by the solvent peak). IR (Neat Film, NaCl): 3450, 2924, 1450, 1103, 1011, 943, 874, 758 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{21}H_{27}O_5$ $[M–OH]^+$: 359.1853, found 359.1853. $[\alpha]_D^{23}$: –9 (*c* = 0.13, $CHCl_3$)

Ketone 131

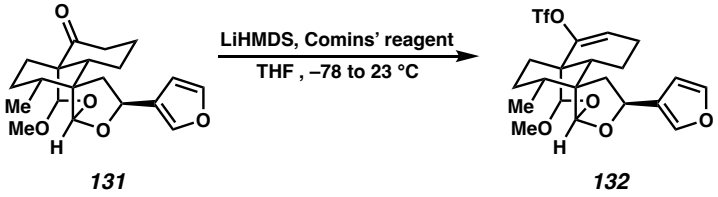


To a 50 mL round bottom flask containing hemiacetal **130** (90.7 mg, 0.241 mmol, 1 equiv) under nitrogen was added THF (12 mL), deionized H_2O (1.9 mL) followed by 3 M *aq*. HCl (964 µL, 2.89 mmol). The resulting mixture was stirred at 23 °C for 18 h, at which point LC/MS analysis showed full conversion to product. The reaction was

quenched with *aq*. $NaHCO_3$ (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4 and concentrated under reduced pressure to afford crude ketone **144**. The crude product was used in the next reaction without further purification.

To a 50 mL round bottom flask were added the crude product (**144**), MeOH (0.96 mL), $CH(OMe)_3$ (9.6 mL). PTSA (22.9 mg, 0.120 mmol, 50 mol%) was added to the above solution and the mixture was stirred for 10 minutes. The reaction was quenched with *aq.* $NaHCO_3$ (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (5% to 10% EtOAc/Hexanes) to afford the title compound as colorless oil (64.0 mg, 0.185 mmol, 77% yield over 2 steps). ^{1}H NMR (600 MHz, C_6D_6): δ 7.28 (dt, *J* = 1.7, 0.9 Hz, 1H), 7.12 (t, *J* = 1.7 Hz, 1H), 6.29 (dd, *J* = 1.9, 0.9 Hz, 1H), 5.36 (s, 1H), 5.03 (s, 1H), 4.97 (dd, *J* = 9.7, 6.4 Hz, 1H), 3.21 (s, 3H), 2.74 (ddd, *J* = 14.1, 5.3, 1.6 Hz, 1H), 2.29 – 2.22 (m, 1H), 2.17 (td, *J* = 14.2, 6.0 Hz, 1H), 1.93 (qd, *J* = 13.2, 3.7 Hz, 1H), 1.86 (dd, *J* = 13.2, 9.7 Hz, 1H), 1.76 (qd, *J* = 13.4, 5.3 Hz, 1H), 1.58 (ddd, *J* = 13.3, 6.2, 2.4 Hz, 2H), 1.51 – 1.39 (m, 3H), 1.25 (dd, *J* = 13.1, 4.0 Hz, 1H), 1.20 (ddd, *J* = 12.9, 6.6, 4.7 Hz, 1H), 1.12 (qt, *J* = 13.6, 4.3 Hz, 1H), 0.70 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 209.1, 143.8, 139.2, 128.6, 109.1, 100.3, 99.3, 72.5, 56.3, 53.2, 52.8, 48.1, 38.7, 38.6, 37.7, 30.9, 28.2, 26.0, 24.7, 16.9. IR (Neat Film, NaCl): 3464, 2924, 2867, 1706, 1549, 1500, 1459, 1383, 1338, 1210, 1131, 1100, 1075, 1018, 988, 947, 874, 793, 735 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{19}H_{23}O_4$ $[M–OMe]^+$: 315.1591, found 315.1591. $[\alpha]_D^{23}$: –37 (*c* = 0.17, $CHCl_3$)

Triflate 132

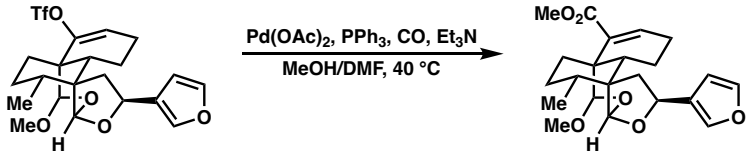


131 ***132***

To a 100 mL round bottom flask containing ketone **131** (64.0 mg, 0.185 mmol, 1 equiv) under nitrogen was added THF (9 mL) and the solution was cooled to –78 °C. Then LiHMDS (1.5 M in THF, 554 µL, 0.831 mmol, 4.5 equiv) was added slowly and the resulting mixture was stirred at –78 °C. After 1h, Comins' reagent (218 mg, 0.554 mmol, 3 equiv) in THF (9 mL) was added dropwise ‑78 °C. Upon the completion of addition, the mixture was warmed to 23 °C and stirred for 0.5 h. The reaction was quenched with *aq*. $NaHCO_3$ (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (3% to 5% to 10% Et_2O/hexanes) to afford triflate **132** as a colorless oil (79.8 mg, 0.167 mmol, 90% yield). ^1H NMR (600 MHz, C_6D_6): δ 7.28 – 7.24 (m, 1H), 7.11 (t, *J* = 1.7 Hz, 1H), 6.30 (dd, *J* = 2.0, 0.9 Hz, 1H), 5.56 (dd, *J* = 5.6, 2.4 Hz, 1H), 5.28 (s, 1H), 5.12 (s, 1H), 4.91 (dd, *J* = 10.1, 5.9 Hz, 1H), 3.36 (s, 3H), 2.56 (ddd, *J* = 13.1, 5.3, 1.9 Hz, 1H), 1.85 (dd, *J* = 13.1, 10.1 Hz, 1H), 1.78 – 1.67 (m, 2H), 1.62 (dtd, *J* = 17.9, 5.5, 1.5 Hz, 1H), 1.56 – 1.47 (m, 2H), 1.40 – 1.33 (m, 2H), 1.27 (dd, *J* = 13.1, 6.1 Hz, 1H), 1.16 (ddd, *J* = 12.3, 6.7, 5.1 Hz, 1H), 1.09 (dd, *J* = 13.3, 2.6 Hz, 1H), 1.02 (td, *J* = 13.3, 5.8 Hz, 1H), 0.69 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 154.2, 143.8, 139.4, 127.3, 119.1 (*J* = 320 Hz), 117.3, 109.1, 102.2, 99.2, 72.9, 55.9, 49.7, 48.8, 42.7, 38.7, 37.9, 30.6, 29.8, 24.4, 21.3, 16.7. IR (Neat Film, NaCl): 2923, 2854, 1730, 1460, 1415, 1378, 1274, 1210, 1141, 1023, 945, 882,

825, 794, 743 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{20}H_{22}F_3O_6S$ $[M–OMe]^+$: 447.1084, found 447.1086. $[\alpha]_D^{24}$: –13 (*c* = 0.06, $CHCl_3$)

Ester 133

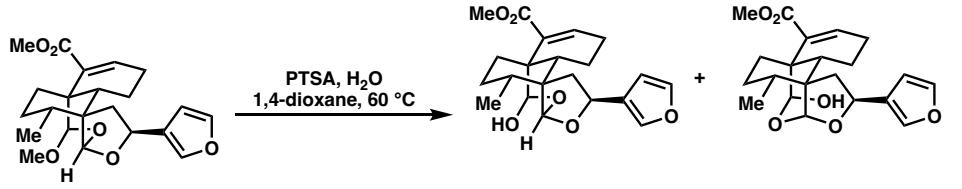


132 ***133***

To a 2-dram vial containing triflate **132** (15 mg, 0.0314 mmol, 1 equiv) was added $Pd(OAc)_2$ (1.5 mg, 0.00628 mmol, 20 mol %), and PPh_3 (3.3 mg, 0.0126 mmol, 40 mol %), and the headspace of the vial was evacuated and refilled with nitrogen three times. DMF (0.75 mL), MeOH (0.75 mL), and Et_3N (14 μL, 0.0941 mmol, 3 equiv) were added sequentially. The resulting solution was bubbled CO for 10 mins at 23 °C, before being transferred to a preheated heating block. The solution was stirred at 40 °C under CO atmosphere for 3h, at which point TLC analysis showed full conversion. The reaction was quenched by addition of deionized water (5 mL), and the resulting mixture was extracted with EtOAc (3 x 3 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (5% to 10% to 15% EtOAc/Hexane) to afford ester **133** as colorless oil (10.5 mg, 0.0271 mmol, 85% yield). ^1H NMR (600 MHz, C_6D_6): δ 7.31 – 7.29 (m, 1H), 7.12 (t, *J* = 1.7 Hz, 1H), 6.71 – 6.68 (m, 1H), 6.38 (dd, *J* = 1.9, 0.8 Hz, 1H), 5.48 (s, 1H), 5.11 (dd, *J* = 11.0, 5.1 Hz, 1H), 4.99 (s, 1H), 3.43 (s, 3H), 3.43 (s, 3H), 2.72 (ddd, *J* = 12.7, 5.4, 1.9 Hz, 1H), 2.04 – 1.92 (m, 2H), 1.91 – 1.83 (m, 2H), 1.73 – 1.63 (m, 2H), 1.54 – 1.46 (m, 2H), 1.30 (ddd, *J* = 12.4, 6.5, 5.1 Hz, 1H), 1.11 (dd, *J* = 12.9, 2.5 Hz, 1H), 0.99

(td, J = 13.0, 5.7 Hz, 1H), 0.83 (d, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 167.5, 143.6, 139.6, 139.5, 137.2, 126.8, 109.3, 104.9, 98.8, 74.1, 56.2, 50.9, 50.8, 50.2, 41.5, 39.7, 38.4, 33.0, 31.7, 26.8, 22.3, 17.0. IR (Neat Film, NaCl): 2923, 2854, 1719, 1503, 1459, 1376, 1252, 1212, 1160, 1132, 1094, 1050, 1021, 996, 940, 873, 802, 748 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{21}H_{25}O_5$ $[M–OMe]^+$: 357.1697, found 357.1697. $[\alpha]_D^{23}$: –48 (c = 0.07, $CHCl_3$)

(–)-Crotonolide D (106) and (–)-iso-corotonolide D (145)



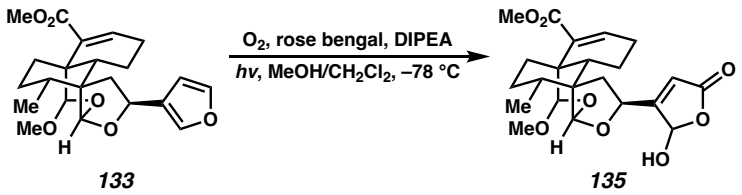
133 ***Crotonolide D (106)*** ***iso-Crotonolide D (145)***

To a 1-dram vial containing ester **133** (5mg, 0.0129 mmol, 1 equiv) under nitrogen was added 1,4-dioxane (0.4 mL), deionized water (0.14 mL), and *p*-TsOH•H_2O (12 mg, 0.0644 mmol, 5 equiv). The vial was sealed and placed in a preheated metal heating block. The reaction mixture was stirred at 60 °C for 2h, at which point TLC analysis showed full consumption of starting material. The reaction was quenched by *aq*. $NaHCO_3$ (1 mL), and the mixture was extracted with EtOAc (3 x 2 mL). The combined organic extracts were washed with brine (2 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (10% to 20% to 30% EtOAc/Hexane) to afford crotonolide D **106** and iso-crotonolide D (**145**) as a 4.5 : 1 mixture of anomeric isomer (4 mg, 0.0107, 83% yield). All characterization data matched literature report.[7]

Characterization of (–)-crotonolide D (106) and (–)-iso-crotonolide D (145):

^{1}H NMR of (–)-crotonolide D (600 MHz, $CDCl_3$): δ 7.42 (m, 1H), 7.39 (t, *J* = 1.8 Hz, 1H), 6.94 (dd, *J* = 5.7, 2.3 Hz, 1H), 6.43 (dd, *J* = 1.9, 0.9 Hz, 1H), 5.41 (s, 1H), 5.40 (d, *J* = 2.0 Hz, 1H), 5.11 (dd, *J* = 10.2, 5.8 Hz, 1H), 4.40 (d, *J* = 2.1 Hz, 1H), 3.75 (s, 3H), 2.46 – 2.31 (m, 2H), 2.23 – 2.10 (m, 3H), 2.02 – 1.87 (m, 2H), 1.73 – 1.63 (m, 3H), 1.53-1.49 (m, 1H), 1.04 (td, *J* = 13.5, 5.4 Hz, 1H), 1.00 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR of (–)-crotonolide D (150 MHz, $CDCl_3$): δ 168.9, 143.5, 140.2, 137.5, 139.6, 126.3, 108.9, 99.5, 97.3, 73.1, 52.2, 49.5, 49.4, 41.5, 38.8, 38.5, 31.8, 31.0, 27.0, 21.6, 17.0. ^{1}H NMR of (–)-iso-crotonolide D (600 MHz, $CDCl_3$): δ 7.41 (dt, *J* = 1.7, 0.9 Hz, 1H), 7.39 (overlapped, 1H), 7.05 (dd, *J* = 5.5, 2.4 Hz, 1H), 6.39 (dd, *J* = 1.9, 0.9 Hz, 1H), 5.47 (d, *J* = 3.7 Hz, 1H), 5.26 (s, 1H), 5.15 (overlapped, 1H), 3.73 (s, 3H), 3.05 (d, *J* = 3.9 Hz, 1H), 2.46 – 2.31 (overlapped, 2H), 2.23 – 2.10 (overlapped, 2H), 2.02 – 1.87 (overlapped, 2H), 1.73 – 1.63 (overlapped, 3H), 1.53-1.49 (overlapped, 1H), 1.04 (overlapped, 1H), 1.00 (overlapped, 3H). ^{13}C NMR of (–)-iso-crotonolide D (150 MHz, $CDCl_3$): δ 168.9, 143.5, 140.2, 137.5, 139.6, 126.3, 108.9, 99.5, 97.3, 73.1, 52.2, 49.5, 49.4, 41.5, 38.8, 38.5, 31.8, 31.0, 27.0, 21.6, 17.0. IR of the mixture (Neat Film, NaCl): 3480, 2922, 2857, 1687, 1502, 1436, 1360, 1275, 1255, 1215, 1093, 1055, 1020, 938, 873, 785 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{21}H_{26}NaO_6$ $[M+Na]^+$: 397.1627, found 397.1622. $[\alpha]_D^{24}$: –127 (*c* = 0.04, MeOH)

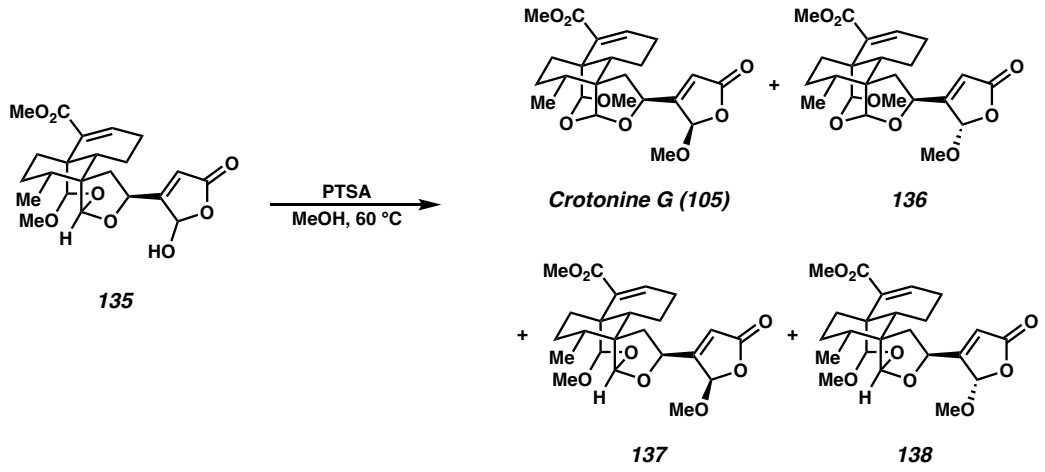
Crotonine G (105)



133 ***135***

To a 2-dram vial containing ester **133** (10 mg, 0.0258 mmol, 1 equiv) was added rose bengal (0.9 mg, 0.000885 mmol, 3.5 mol %), CH_2Cl_2 (2 mL), MeOH (2 mL), and

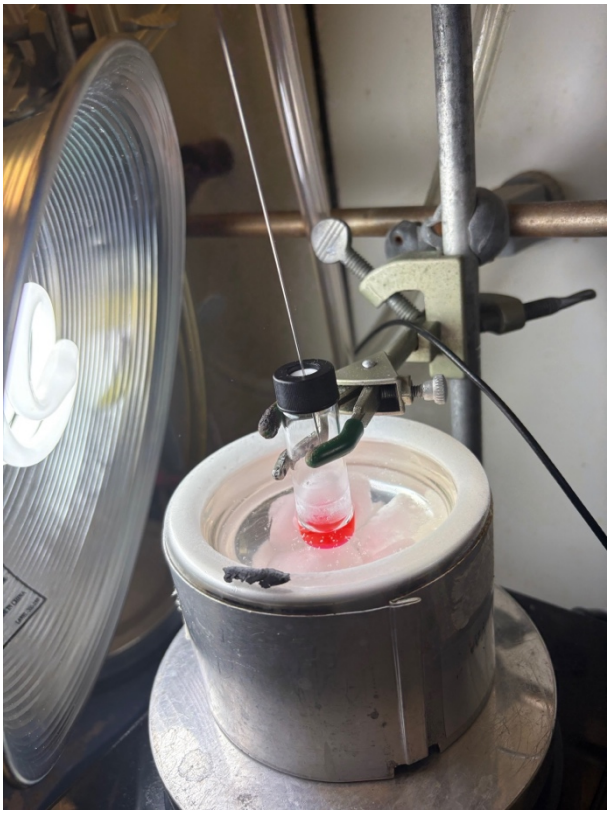
DIPEA (45 μL, 0.258 mmol, 10 equiv). The resulting pink solution was cooled to –78 °C, and sparged with O_2 for 20 min. Then the mixture was irradiated with a 150 W tungsten lamp (see attached picture for set up) under O_2 atmosphere at –78 °C for 30 min, at which point TLC analysis showed full consumption of starting material. Irridiation was stopped, and the mixture was allowed to warm up to 23 °C before being concentrated under reduced pressure. The crude residue was purified by silica gel flash column chromatography to afford butenolide **135** as a colorless oil, which was used directly in next step.



To a 2 dram vial containing butanolide **135** (*ca*. 0.0258 mmol) under nitrogen was added *p*-TsOH•H_2O (22.6 mg, 0.119 mmol, 5 equiv) in MeOH (1 mL). The resulting solution was stirred at 60 °C for 1h, before being quenched with *aq*. $NaHCO_3$ (3mL). The mixture was extracted with EtOAc (3 x 2 mL). The combined organic extracts were washed with brine (2 mL), dried over Na_2SO_4, and concentrated under reduced pressure to afford a crude residue. The above-mentioned process was repeated once with another 10 mg of butanolide **135**, and the crude product obtained was combined. The crude product was purified by preparative HPLC (Agilent Zorbax RX-SIL 5μm (SiO_2), *i*-PrOH / Hexane (8%,

isocratic), flowrate: 5 mL/min, monitor wavelength = 230 nm, retention time of **105** = 4.7 min, retention time of **136** = 5.5 min, retention time of **137** = 5.8 min, retention time of **138** = 6.8 min) to yield crotonine G (**105**, 4.0 mg, 18% over 2 steps), and **138** (3.1 mg, 14% over 2 steps). The mixed fractions were combined and repurified by preparative HPLC (Agilent Zorbax RX-SIL 5µm (SiO2), *i*-PrOH / Hexane (8%, isocratic), flowrate: 5 mL/min, monitor wavelength = 230 nm, to yield **136** (2.0 mg, 9% over 2 steps), and **137** (2.5 mg, 11% over 2 steps).

Figure 2.7.2. Experimental set up of the singlet oxygen Diels-Alder reaction.



Characterization of Crotonine G (105):

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.99 (dd, *J* = 5.5, 2.2 Hz, 1H), 6.01 (t, *J* = 1.1 Hz, 1H), 5.84 (d, *J* = 1.0 Hz, 1H), 5.22 (s, 1H), 5.08 (d, *J* = 0.7 Hz, 1H), 4.97 (t, *J* = 7.9 Hz, 1H), 3.71 (s, 3H), 3.60 (s, 3H), 3.38 (s, 3H), 2.49 – 2.43 (m, 1H), 2.41 – 2.32 (m, 2H), 2.24 (dd, *J* =

13.1, 9.1 Hz, 1H), 2.20 – 2.11 (m, 1H), 2.08 (dd, *J* = 13.1, 8.2 Hz, 1H), 1.80 – 1.67 (m, 3H), 1.66 – 1.61 (m, 1H), 1.39 – 1.36 (m, 1H), 1.22 – 1.19 (m, 1H), 0.95 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 167.9, 167.0, 140.3, 134.7, 117.5, 103.1, 102.6, 99.5, 71.1, 57.3, 56.5, 51.3, 46.0, 45.0, 40.4, 37.9, 35.7, 34.9, 29.9, 26.8, 20.9, 16.4. IR (Neat Film, NaCl): 3359, 2922, 2854, 1792, 1765, 1710, 1456, 1379, 1257, 1212, 1093, 1045, 967, 931, 896, 732 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{22}H_{27}O_7$ $[M\text{-}OMe]^+$: 403.1751, found 403.1752. $[\alpha]_D^{23}$: –71 (*c* = 0.05, $CHCl_3$)

Characterization of isomer 136:

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.99 (dd, *J* = 5.4, 2.2 Hz, 1H), 6.09 (dd, *J* = 1.6, 0.9 Hz, 1H), 5.75 (d, *J* = 0.7 Hz, 1H), 5.17 (s, 1H), 5.04 (d, *J* = 0.7 Hz, 1H), 4.77 (t, *J* = 8.2 Hz, 1H), 3.71 (s, 3H), 3.61 (s, 3H), 3.39 (s, 3H), 2.51 – 2.45 (m, 1H), 2.39 – 2.30 (m, 2H), 2.21 – 2.08 (m, 3H), 1.79 – 1.68 (m, 3H), 1.64 (dd, *J* = 12.0, 6.2 Hz, 1H), 1.36 (d, *J* = 12.7 Hz, 1H), 1.23 – 1.17 (m, 1H), 0.94 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 168.0, 164.9, 138.6, 137.6, 118.5, 104.6, 103.3, 99.1, 75.4, 57.2, 56.5, 51.6, 49.8, 41.1, 38.2, 37.3, 32.4, 31.4, 29.9, 26.7, 22.0, 16.9. IR (Neat Film, NaCl): 3359, 3193, 2922, 2853, 1793, 1765, 1711, 1660, 1458, 1377, 1257, 1213, 1141, 1045, 970, 935, 899, 762 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{22}H_{27}O_7$ $[M+H]^+$: 403.1751, found 403.1750. $[\alpha]_D^{22}$: –17 (*c* = 0.1, $CHCl_3$)

Characterization of isomer 137:

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.74 (dd, *J* = 5.7, 2.3 Hz, 1H), 6.10 (t, *J* = 1.2 Hz, 1H), 5.80 (d, *J* = 1.0 Hz, 1H), 5.28 (s, 1H), 5.00 (ddd, *J* = 11.3, 5.7, 1.4 Hz, 1H), 4.88 (s, 1H), 3.73

(s, 3H), 3.57 (s, 3H), 3.49 (s, 3H), 2.37 (dd, *J* = 13.2, 4.7 Hz, 1H), 2.35 – 2.29 (m, 1H), 2.23 (dd, *J* = 12.8, 11.4 Hz, 1H), 2.18 – 2.11 (m, 1H), 2.09 (dd, *J* = 12.7, 5.7 Hz, 1H), 1.95 – 1.87 (m, 2H), 1.78 (td, *J* = 14.1, 5.3 Hz, 1H), 1.64 (dt, *J* = 8.8, 5.2 Hz, 2H), 1.43 (dd, *J* = 12.1, 3.2 Hz, 1H), 1.01 (td, *J* = 13.2, 5.5 Hz, 1H), 0.92 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.2, 168.0, 167.2, 140.4, 134.9, 117.6, 103.7, 102.8, 99.4, 71.0, 58.0, 56.8, 51.5, 46.5, 45.6, 40.7, 37.9, 36.0, 35.1, 30.0, 27.0, 21.1, 16.7. IR (Neat Film, NaCl): 3359, 3200, 2923, 2853, 1794, 1766, 1718, 1661, 1460, 1377, 1252, 1211, 1096, 1023, 979, 891, 818, 761, 718, 661 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{23}H_{23}NaO_8$ $[M+Na]^+$: 457.1838, found 457.1835. $[\alpha]_D^{24}$: –60 (*c* = 0.15, $CHCl_3$)

Characterization of isomer 138:

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.74 (dd, *J* = 5.7, 2.2 Hz, 1H), 6.13 (dd, *J* = 1.6, 0.9 Hz, 1H), 5.77 (d, *J* = 1.0 Hz, 1H), 5.26 (s, 1H), 4.88 (s, 1H), 4.85 – 4.80 (m, 1H), 3.73 (s, 3H), 3.62 (s, 3H), 3.49 (s, 3H), 2.36 (dd, *J* = 13.2, 4.8 Hz, 1H), 2.34 – 2.28 (m, 1H), 2.24 (dd, *J* = 13.3, 5.5 Hz, 1H), 2.17 – 2.09 (m, 1H), 2.02 (dd, *J* = 13.3, 11.1 Hz, 1H), 1.92 – 1.83 (m, 2H), 1.77 (td, *J* = 14.0, 5.0 Hz, 1H), 1.70 – 1.58 (m, 2H), 1.42 (dd, *J* = 12.2, 3.3 Hz, 1H), 1.00 (td, *J* = 13.1, 5.4 Hz, 1H), 0.91 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.1, 168.0, 165.6, 138.7, 137.6, 118.3, 104.7, 103.5, 98.7, 75.2, 57.9, 56.5, 51.6, 50.8, 49.8, 41.1, 38.1, 38.0, 32.5, 31.4, 26.7, 22.1, 16.9. IR (Neat Film, NaCl): 3360, 2924, 2853, 1794, 1764, 1718, 1659, 1463, 1361, 1251, 1208, 1113, 1023, 979, 874, 826, 716 cm^{-1}. HRMS (ESI+): *m/z* calc'd for $C_{22}H_{27}O_7$ $[M+H]^+$: 403.1751, found 403.1753. $[\alpha]_D^{22}$: –150 (*c* = 0.02, $CHCl_3$)

2.8 REFERENCES AND NOTES

(1) Salatino, A.; Salatino, M. L. F.; Negri, G. Traditional uses, chemistry and pharmacology of Croton species (Euphorbiaceae). *J. Braz Chem. Soc.* **2007**, *18*, 11–33.

(2) Hagiwara, H.; Hamano, K.; Nozawa, M.; Hoshi, T.; Suzuki, T.; Kido, F. The First Total Synthesis of (−)-Methyl Barbascoate. *J. Org. Chem.* **2005**, *70*, 2250–2255.

(3) (a) Scheerer, J. R.; Lawrence, J. F.; Wang, G. C.; Evans, D. A. Asymmetric Synthesis of Salvinorin A, A Potent κ Opioid Receptor Agonist. *J. Am. Chem. Soc.* **2007**, *129*, 8968–8969. (b) Wang, Y.; Metz, P. Total Synthesis of the Neoclerodane Diterpenoids Salvinorin A via an Intramolecular Diels–Alder Strategy. *Org. Lett.* **2018**, *20*, 3418–3421. (c) Nozawa, M.; Suka, Y.; Hoshi, T.; Suzuki, T.; Hagisawa, H. Total Synthesis of the Hallucinogenic Neoclerodane Diterpenoid Salvinorin A. *Org. Lett.* **2008**, *10*, 1365–1368. (d) Hagisawa, H.; Suka, Y.; Nojima, T.; Hoshi, T.; Suzuki, T. Second-generation Synthesis of Salvinorin A. *Tetrahedron*, **2009**, *65*, 4820–4825. (e) Line, N. J.; Burns, A. C.; Butler, S. C.; Casbohm, J.; Forsyth, C. J. Total Synthesis of (–)-Salvinorin A. *Chem. Eur. J.* **2016**, *22*, 17983–17986.

(4) Representative syntheses of related clerodane diterpenoids: (a) Liu, H.; Zhu, J.; Chen, I.; Jankowska, R.; Han, Y.; Shia, K. The Total Synthesis of Racemic Teucvin and 12-*epi*-Reucvin. *Angew. Chem. Int. Ed.* **2003**, *42*, 1851–1853. (b) Zeiler, M. J.; Connors, G. M.; Durling, G. M.; Oliver, A. G.; Marquez, L.; Melander, R. J.; Quave, C. L.; Melander, C. Synthesis, Stereochemical Confirmation, and Derivatization of 12(S),16ϵ-Dihydroxycleroda-3,13-dien-15,16-olide, a Clerodane Diterpene That Sensitizes Methicillin-Resistant Staphylococcus aureus to β-Lactam Antibiotics.

Angew. Chem. Int. Ed. **2022**, e202117458. (c) Ye, Q.; Qu, P.; Snyder, S. A. Total Syntheses of Scaparvins B, C, and D Enabled by a Key C–H Functionalization. *J. Am. Chem. Soc.* **2017**, *139*, 18428–18431. (d) Roach, J. J.; Sasano, Y.; Schmid, C. L.; Zaidi, S.; Katritch, V.; Stevens, R. C.; Bohn, L. M.; Shenvi, R. A. Dynamic Strategic Bond Analysis Yields a Ten-Step Synthesis of 20-nor-Salvinorin A, a Potent κ-OR Agonist. *ACS. Cent. Sci.* **2017**, *3*, 1329–1336.

(5) For reviews on salvinorin analogs and their biological activity, see: (a) Tokoroyama, T. Synthesis of Clerodane Diterpenoids and Related Compounds - Stereoselective Construction of the Decalin Skeleton with Multiple Contiguous Stereogenic Centers. *Synthesis*, **2000**, 611–633. (b) Roach, J. J.; Shenvi, R. A. Mechanism of Action of the Cytotoxic Asmarine Alkaloids. *Bioorg. Med. Chem. Lett.* **2018**, *28*, 1436–1445.

(6) Jiang, Z.; Liu, C.; Niu, Q.; Yan, X.; Xiao, D.; Zhang, H.; Huang, C.; Shi, C.; He, H. In Vitro Hypoglycemic Diterpenoids from the Roots of Crotonyunnanensis. *J. Nat. Prod.* **2023**, *86*, 199–208.

(7) Liu, C.; Xu, J.; Zhao, J.; Xu, C.; Dong, L.; Ding, J.; Yue, J. Diterpenoids from Croton laui and Their Cytotoxic and AntimicrobialActivities. *J. Nat. Prod.* **2014**, *77*, 1013–1020.

(8) (a) Gao, J.; Simon, J. O.; Rodrigo, R.; Assoud, A. From Chiral ortho-Benzoquinone Monoketals to Nonracemic Indolinocodeines through Diels−Alder and Cope Reactions. *J. Org. Chem.* **2013**, *78*, 48–58. (b) Bradshaw, B.; Etxebarría-Jardi, G.; Bonjoch, J.; Viózquez, S.F.; Guillena, G.; Nàjera, C. Efficient Solvent-Free Robinson Annulation Protocols for the Highly Enantioselective Synthesis of the Wieland–Miescher Ketone and Analogues. *Adv. Synth. Cayal.* **2009**, *351*, 2482–2490.

(9) Mukaiyama, T.; Matsuo, J.–i.; Kitagawa, H. A New and One-Pot Synthesis of α,β-Unsaturated Ketones by Dehydrogenation of Various Ketones with N-tert-Butyl Phenylsulfinimidoyl Chloride. *Chem. Lett.* **2000**, *29*, 1250–1251.

(10) Iwasaki, K.; Wan, K. K.; Oppedisano, A.; Crossley, S. W. M.; Shenvi, R. A. Simple, Chemoselective Hydrogenation with Thermodynamic Stereocontrol. *J. Am. Chem. Soc.* **2014**, *136*, 1300–1303.

(11) Jeon, A. R.; Kim, M. E.; Park, J. K.; Shin, W. K.; An, D. K. Mild and direct conversion of esters to morpholine amides using diisobutyl(morpholino)aluminum: application to efficient one-pot synthesis of ketones and aldehydes from esters. *Tetrahedron*. **2014**, *70*, 4420–4424.

(12) Direct dehydration of **118**, **120**, and **123** was attempted but none of the investigated conditions gave desired product.

(13) Imamoto, T.; Sugiura, Y.; Takiyama, N. Organocerium reagents. Nucleophilic addition to easily enolizable ketones. *Tetrahedron. Lett.* **1984**, *25*, 4233–4236.

(14) Krasovskiy, A.; Kopp, F.; Knochel, P. Soluble Lanthanide Salts ($LnCl_3$•2 LiCl) for the Improved Addition of Organomagnesium Reagents to Carbonyl Compounds. *Angew. Chem. Int. Ed.* **2006**, *45*, 497–500.

(15) Benischke, A. D.; Anthore-Dalion, L.; Berionni, G.; Knochel, P. Preparation of Functionalized Diaryl- and Diheteroaryllanthanum Reagents by Fast Halogen-Lanthanum Exchange. *Angew. Chem. Int. Ed.* **2017**, *56*, 16390–16394.

(16) (a) Criegee, R. *Angew. Chem.* **1937**, *50*, 153–172. (b) Criegee, R. *Angew. Chem.* **1938**, *51*, 519-530.

(17) Comins, D. L.; Dehghani, A. Pyridine-derived triflating reagents: An improved preparation of vinyl triflates from metallo enolates. *Tetrahedron. Lett.* **1992**, *33*, 6299–6302.

(18) The two C-19 epimers of crotonolide D (**2**) could not be separated by either silica gel flash column chromatography or reverse phase HPLC. Therefore, the optical rotation measurement was conducted on the epimeric mixture. The small difference in optical rotation compared to isolation report might be attributed to the difference in diastereomeric ratio (4.5 : 1 vs 3.6 : 1).

(19) Corey, E. J.; Roberts, B. E. Total Synthesis of Dysidiolide. *J. Am. Chem. Soc.* **1997**, *119*, 12425–12431.

(20) During the isolation of crotonine G, methanol was employed as a solvent for preparative HPLC. Therefore, it's also possible that the C-16 and C-19 hydroxylated **1** is the actual natural product.

(21) Pangborn, A. M.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. Safe and Convenient Procedure for Solvent Purification. *Organometallics* **1996**, *15*, 1518–1520.

APPENDIX 4

Spectra Relevant to Chapter 2:

Total Synthesis of Crotonine G and Crotonolide D

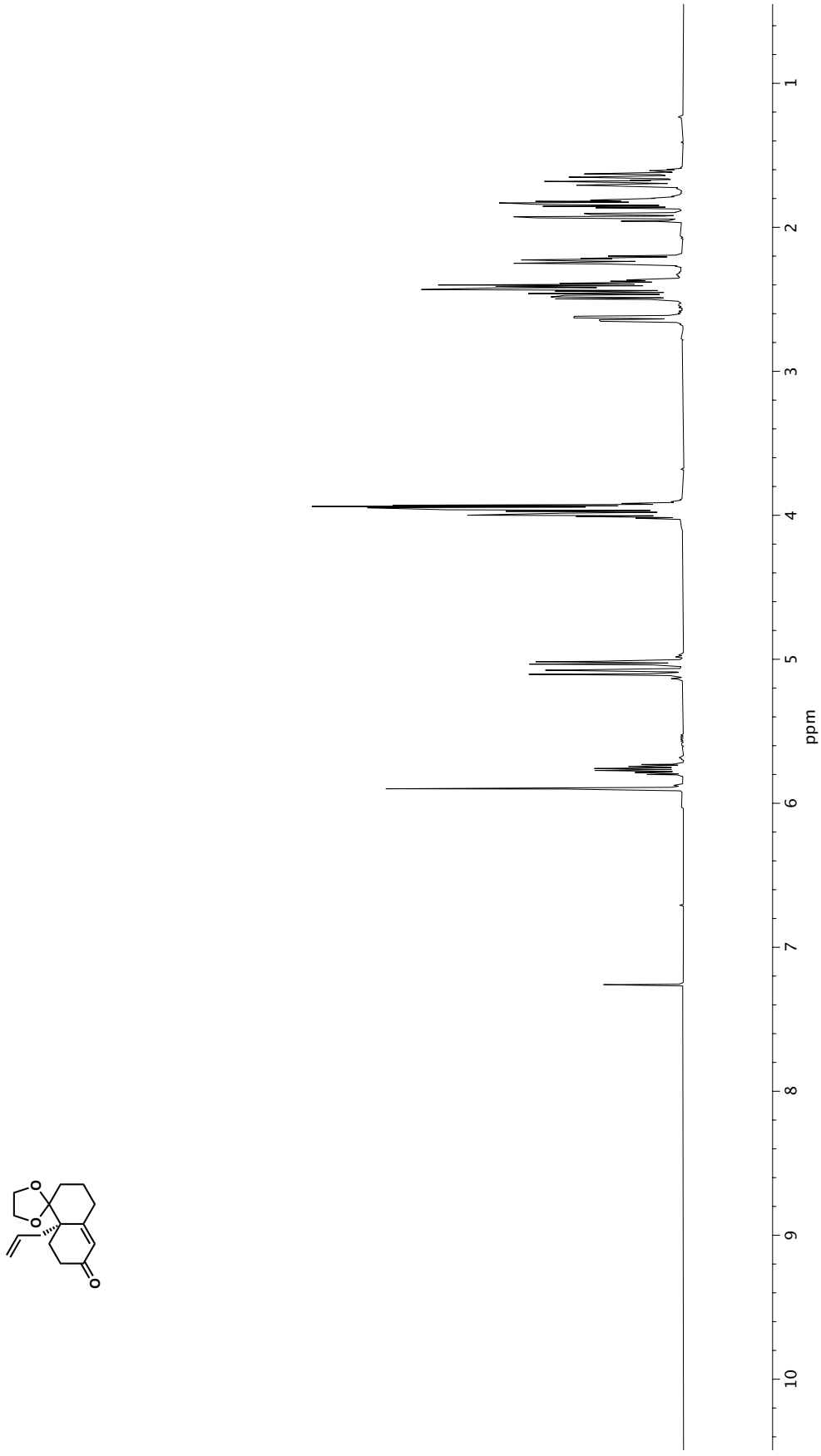


Figure 4.1. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **114**.

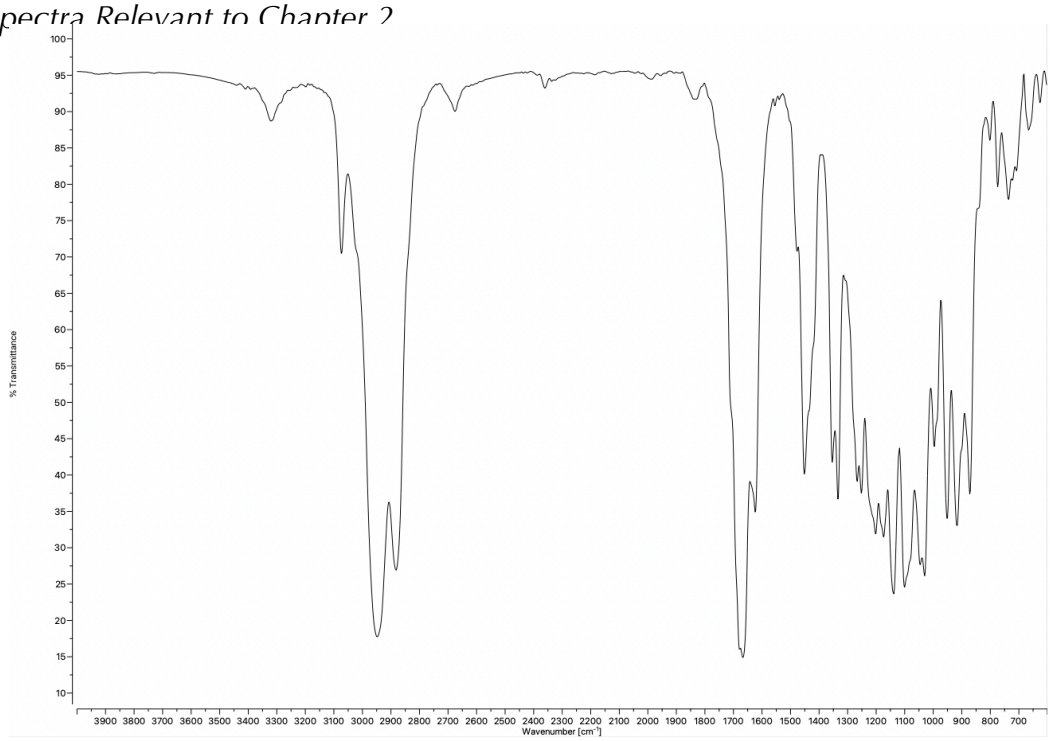


Figure 4.2. Infrared spectrum (Thin Film, NaCl) of compound **114**.

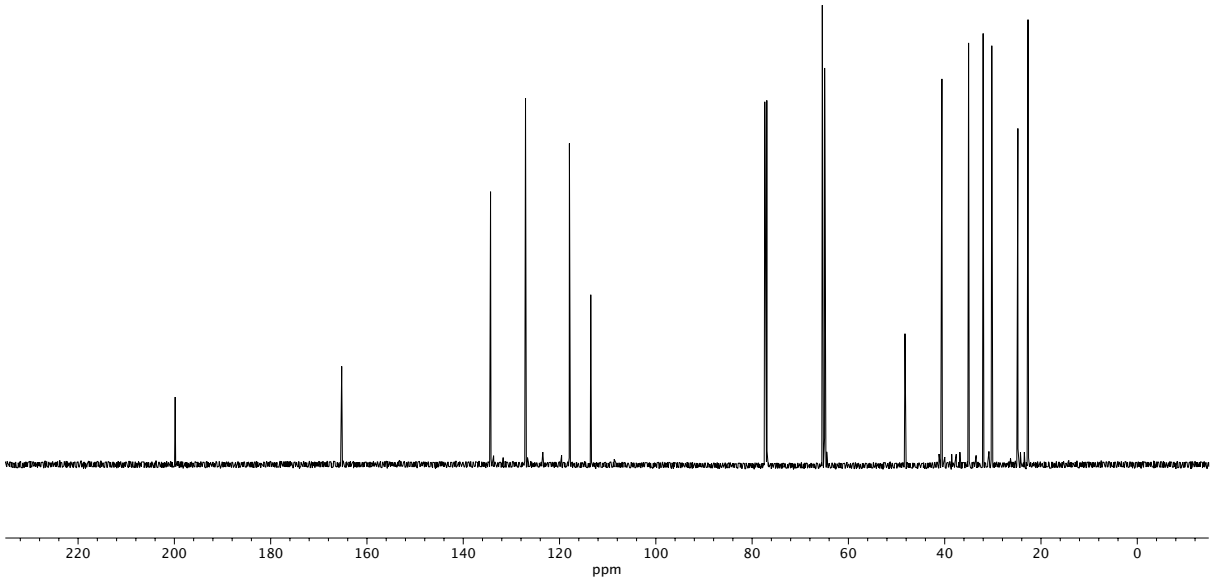


Figure 4.3. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **114**.

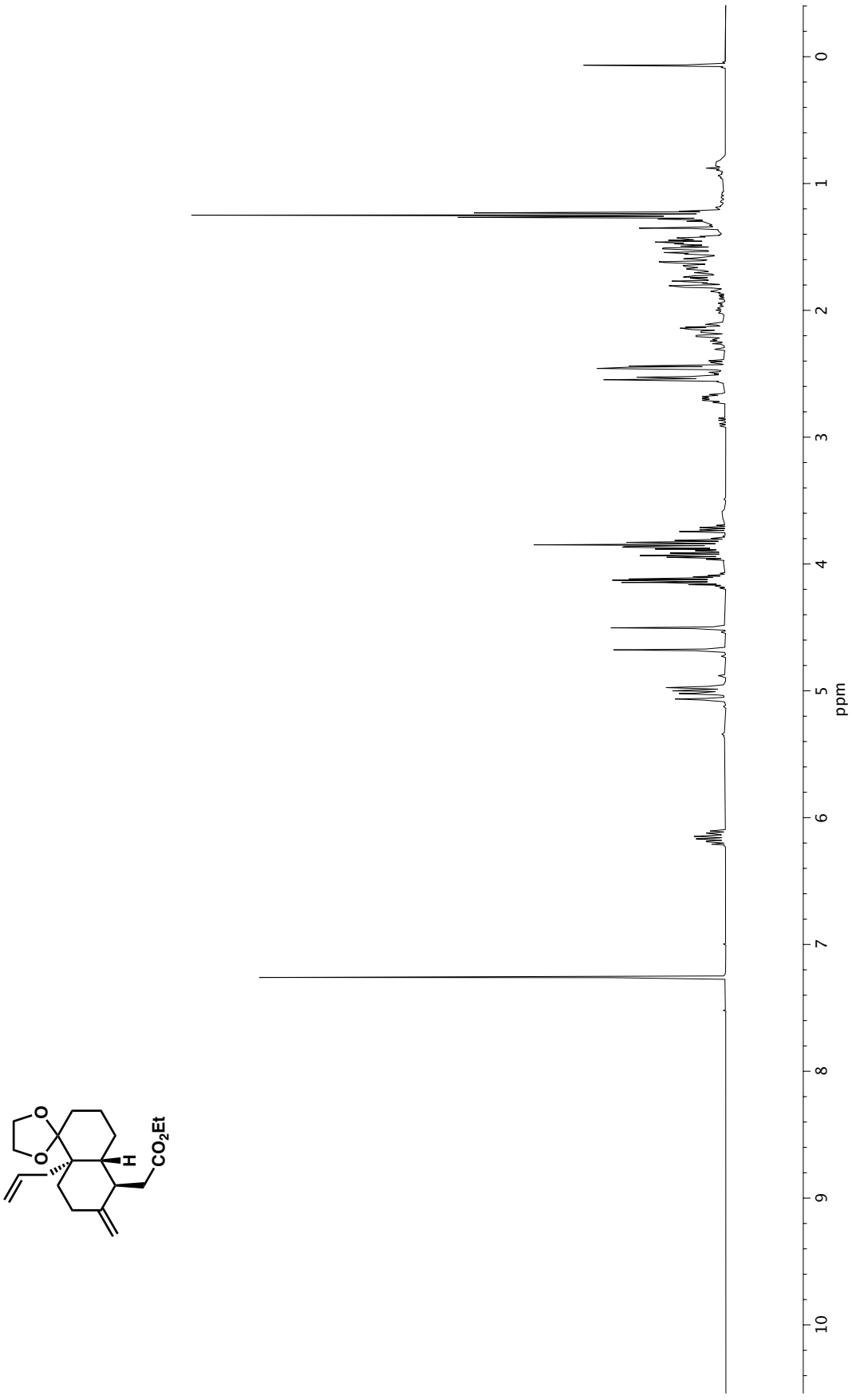


Figure 4.4. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **115**.

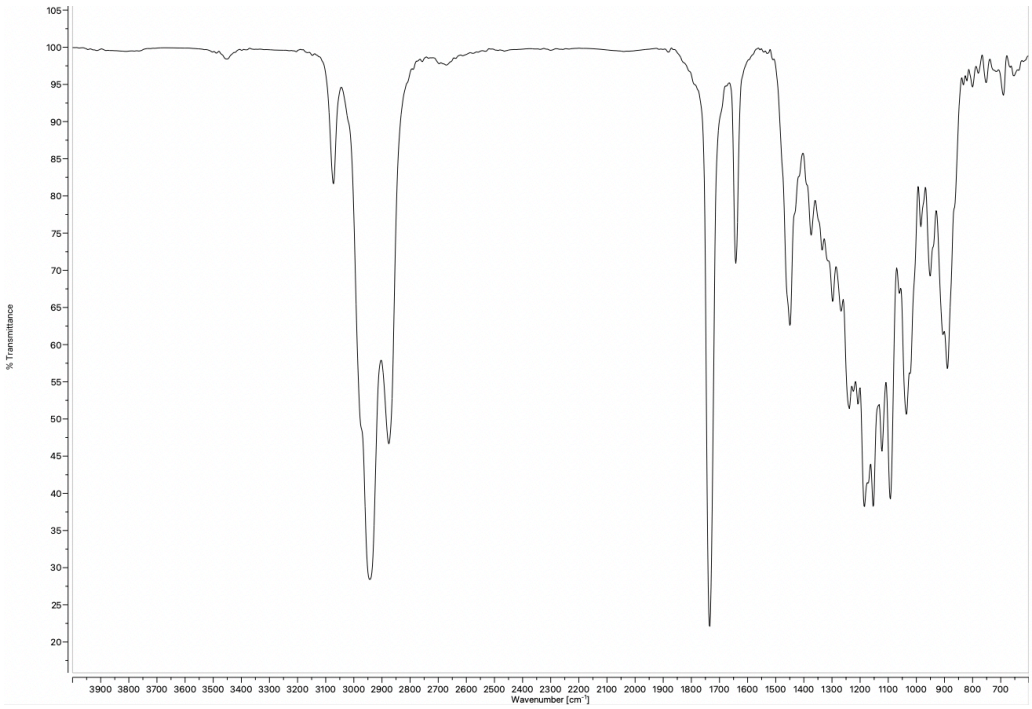


Figure 4.5. Infrared spectrum (Thin Film, NaCl) of compound **115**.

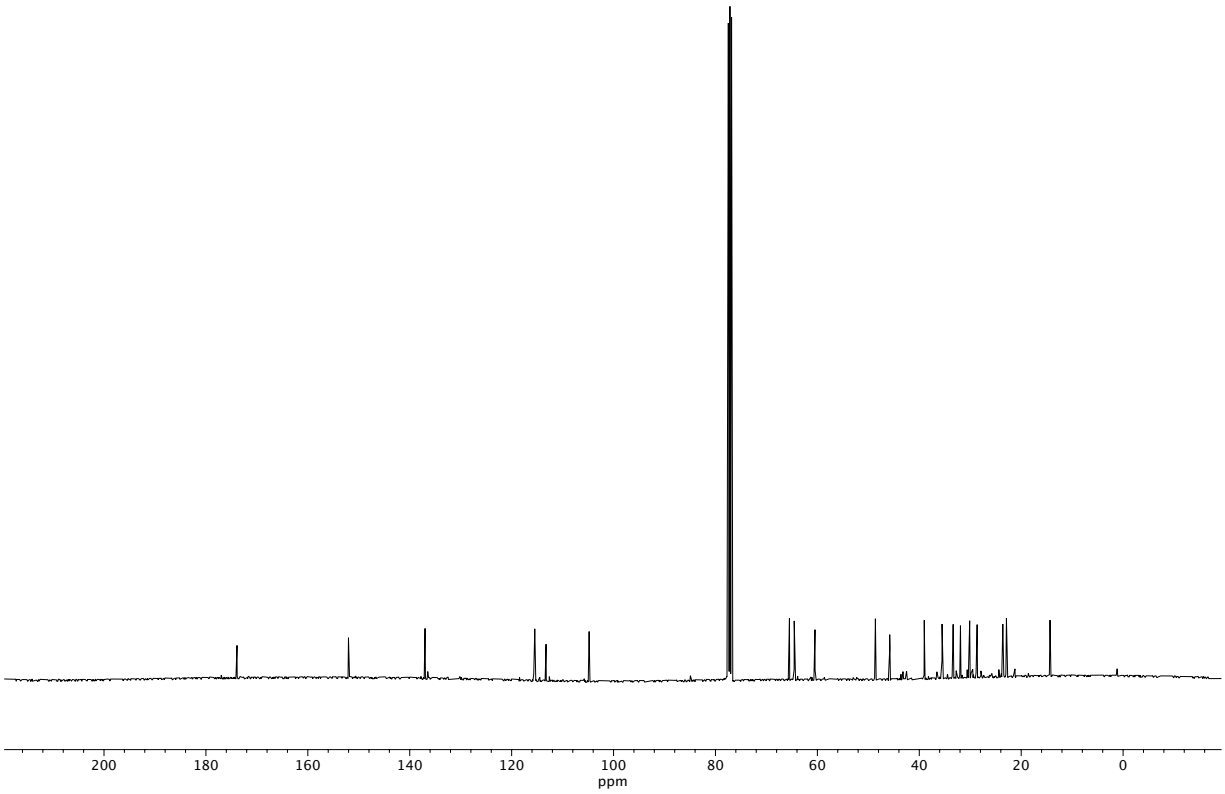


Figure 4.6. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **115.**

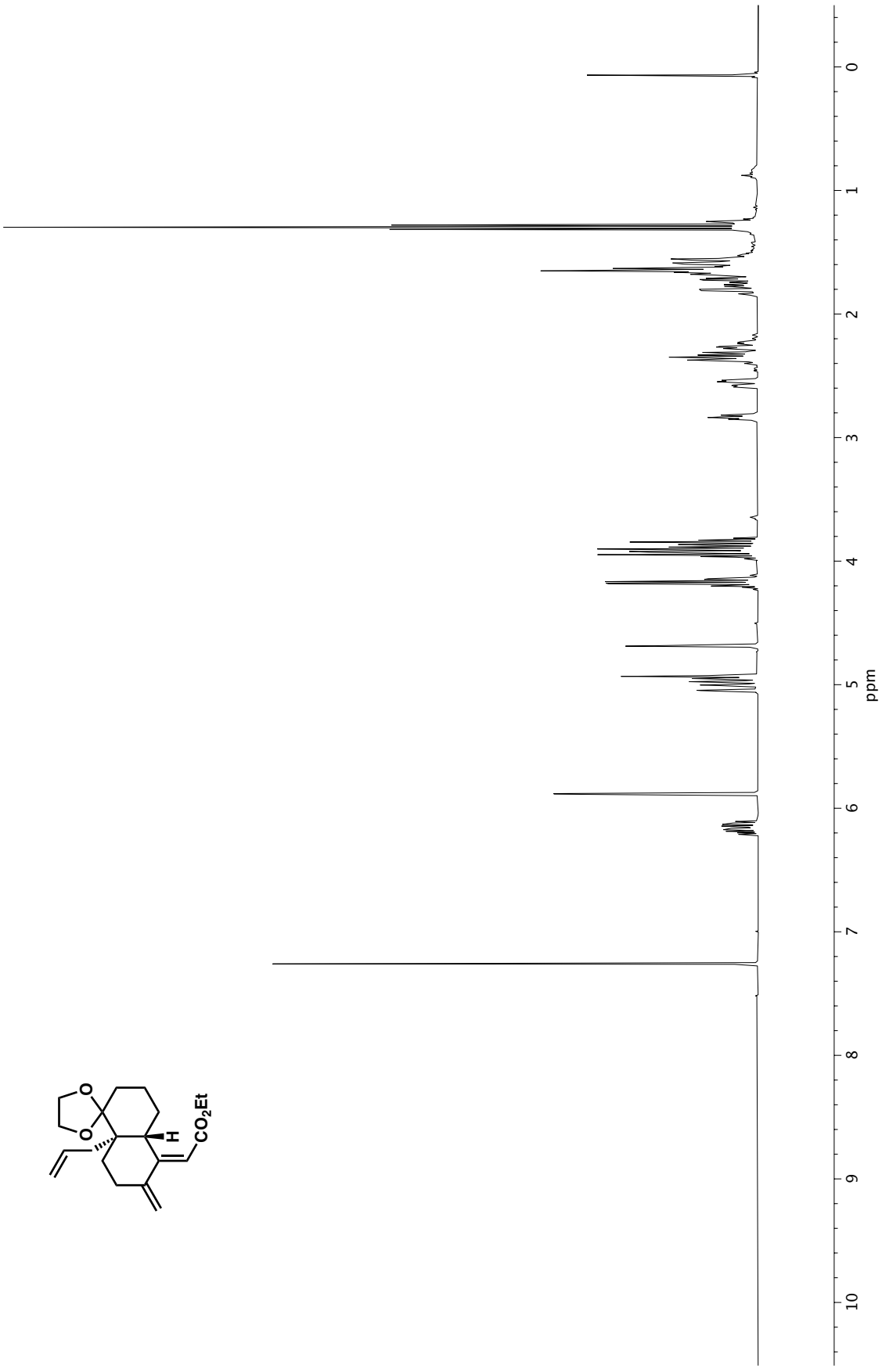


Figure 4.7. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **116**.

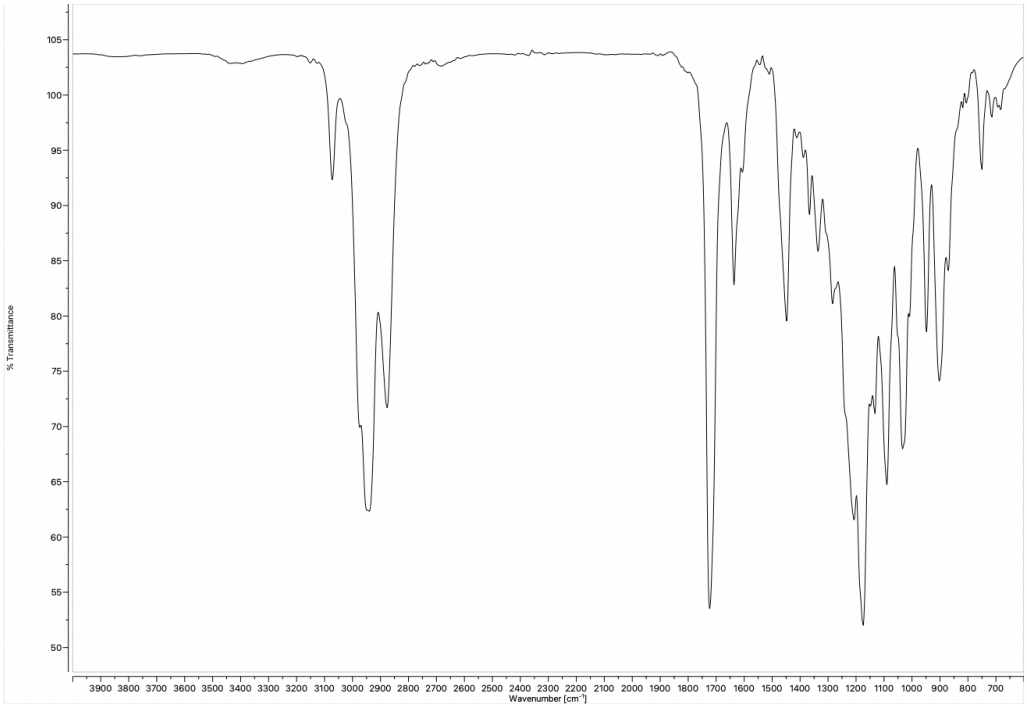


Figure 4.8. Infrared spectrum (Thin Film, NaCl) of compound **116**.

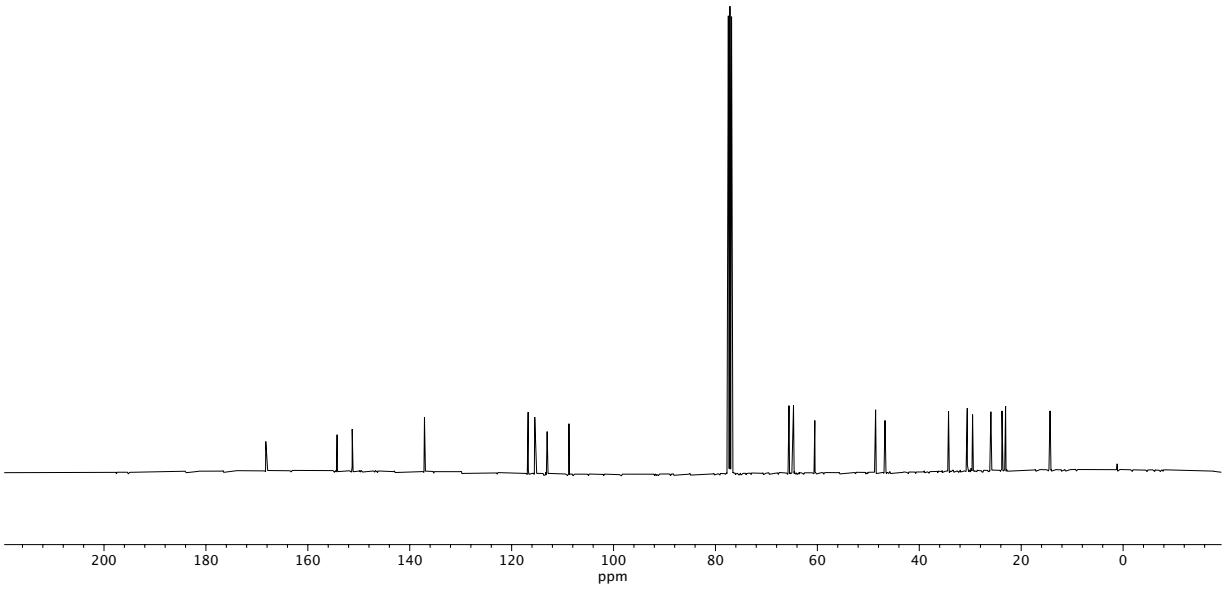


Figure 4.9. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **116.**

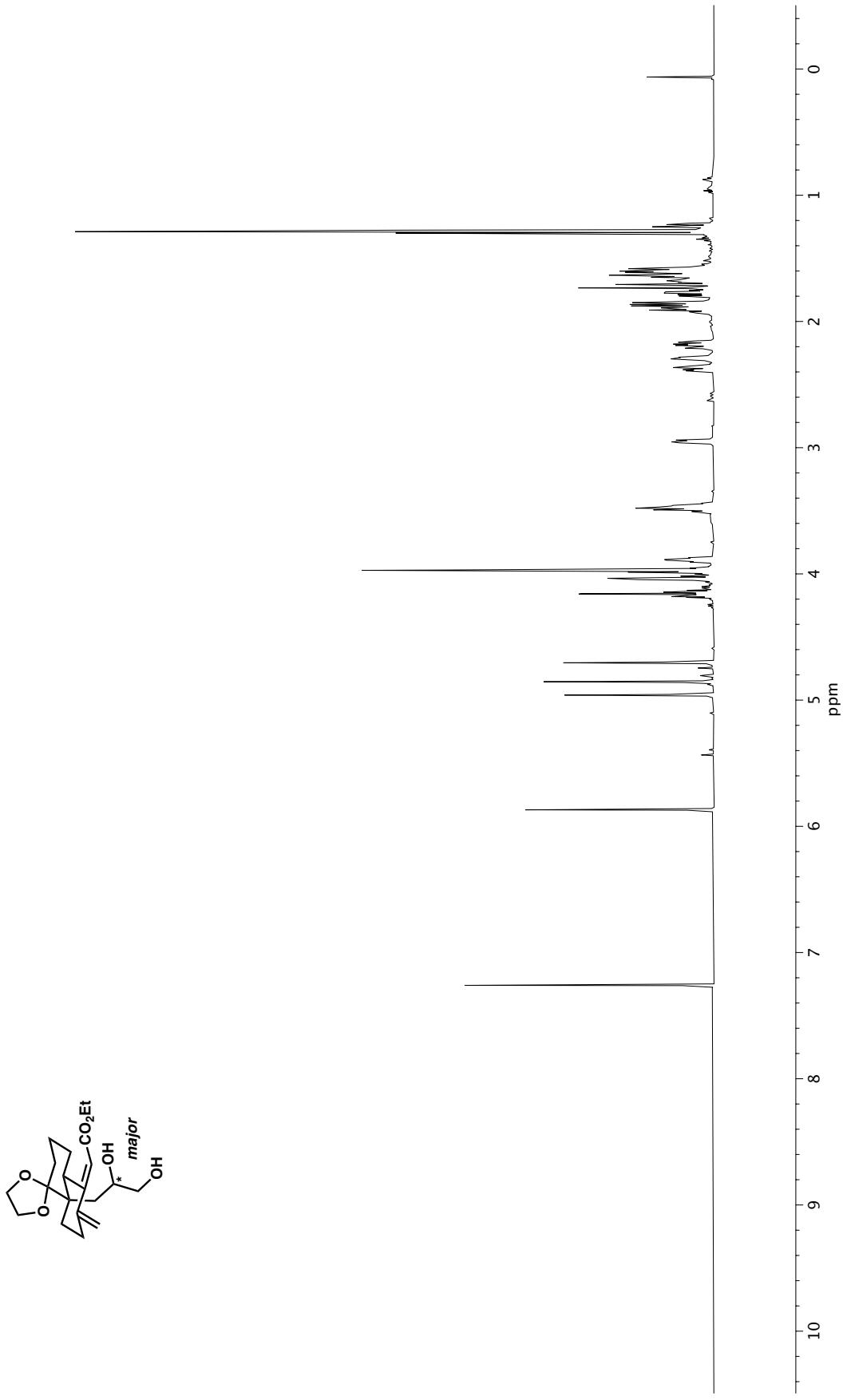


Figure 4.10. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **117** (major).

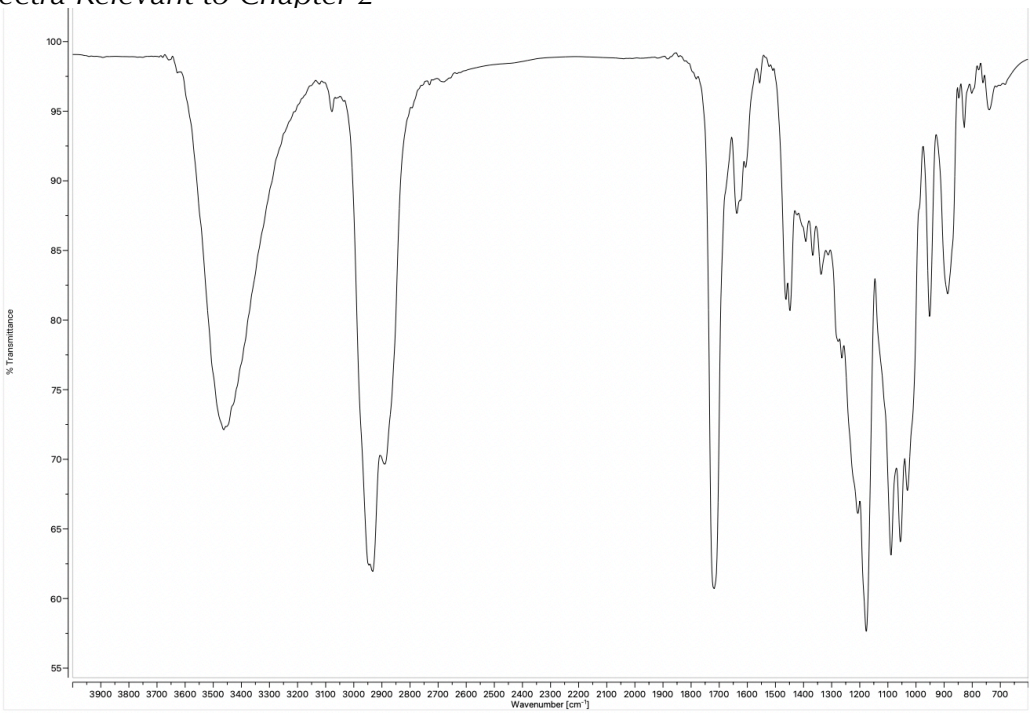


Figure 4.11. Infrared spectrum (Thin Film, NaCl) of compound **117** (major).

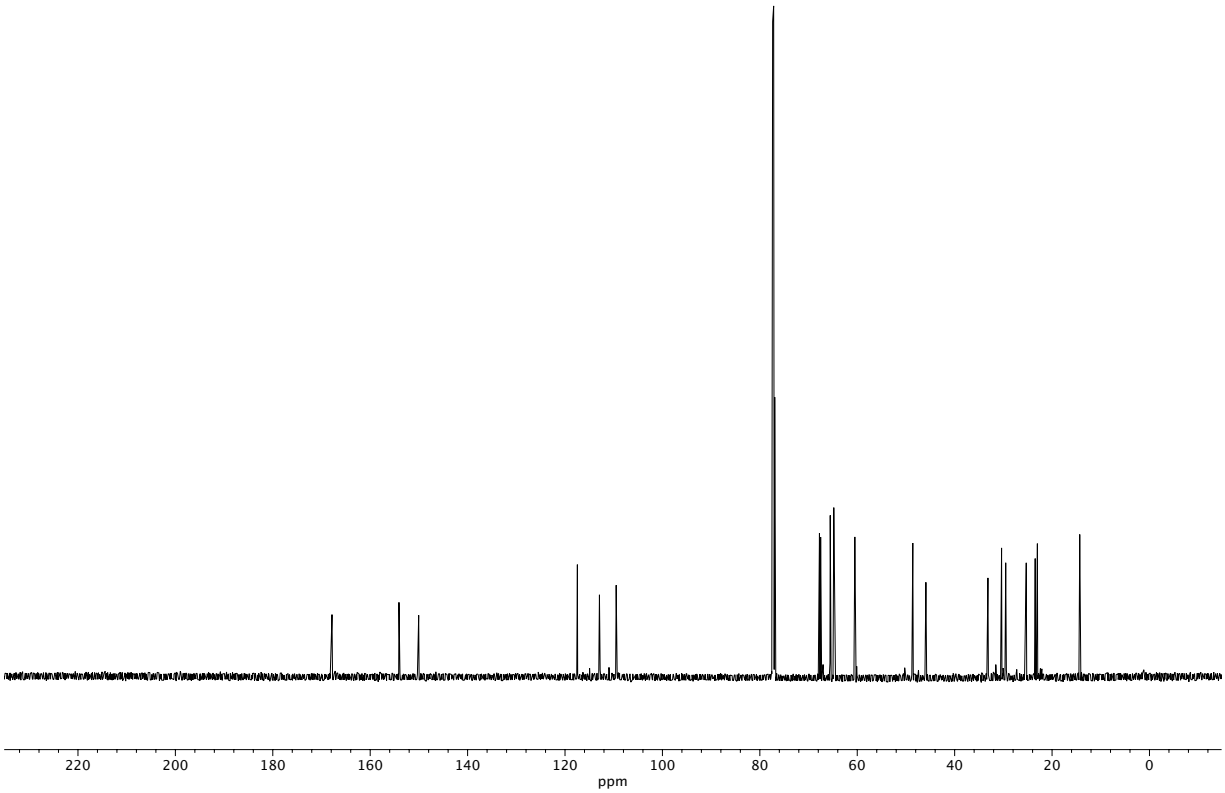


Figure 4.12. ^{13}C NMR (151 MHz, $CDCl_3$) of compound **117** (major)**.**

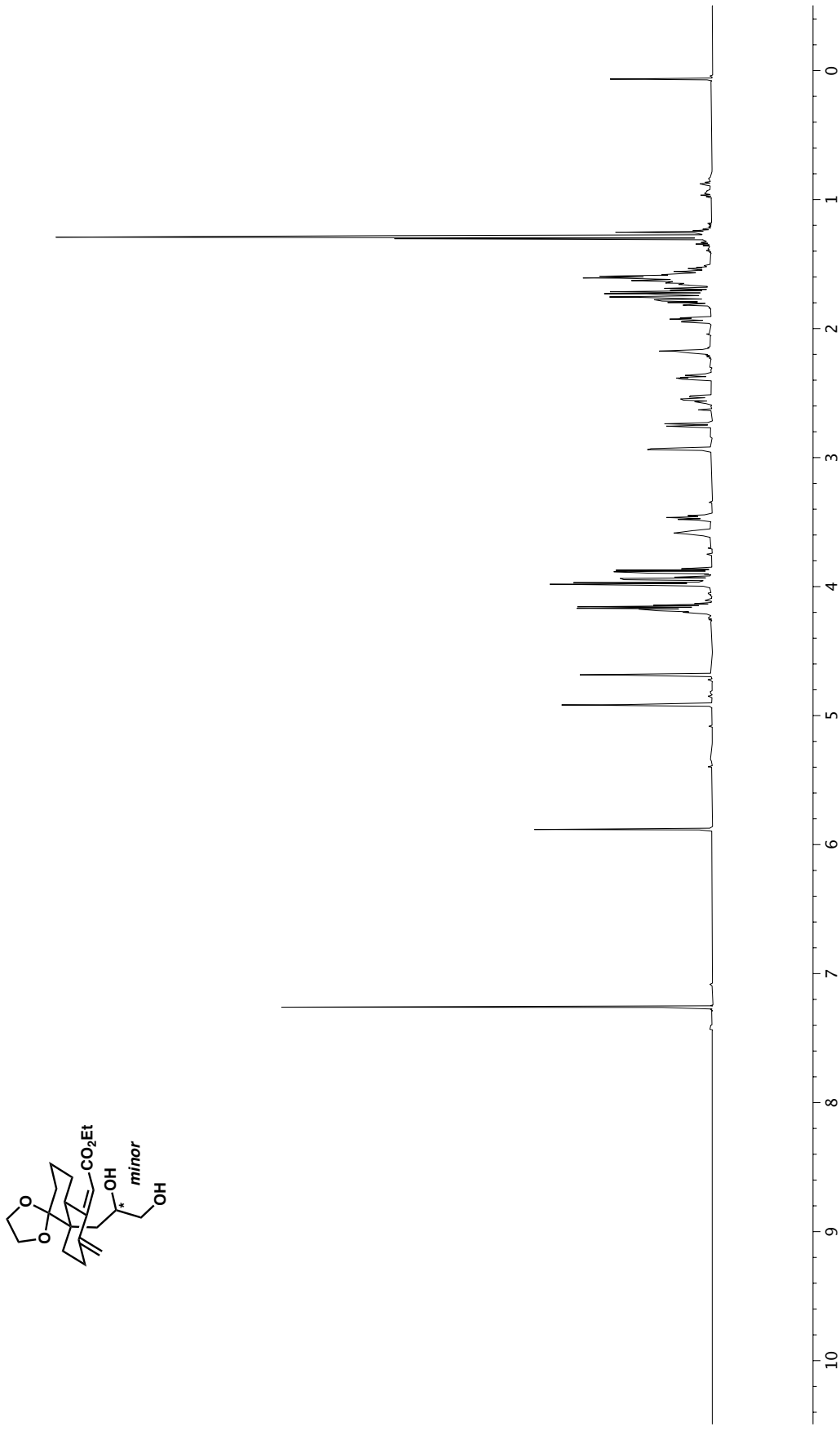


Figure 4.13. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **117** (minor).

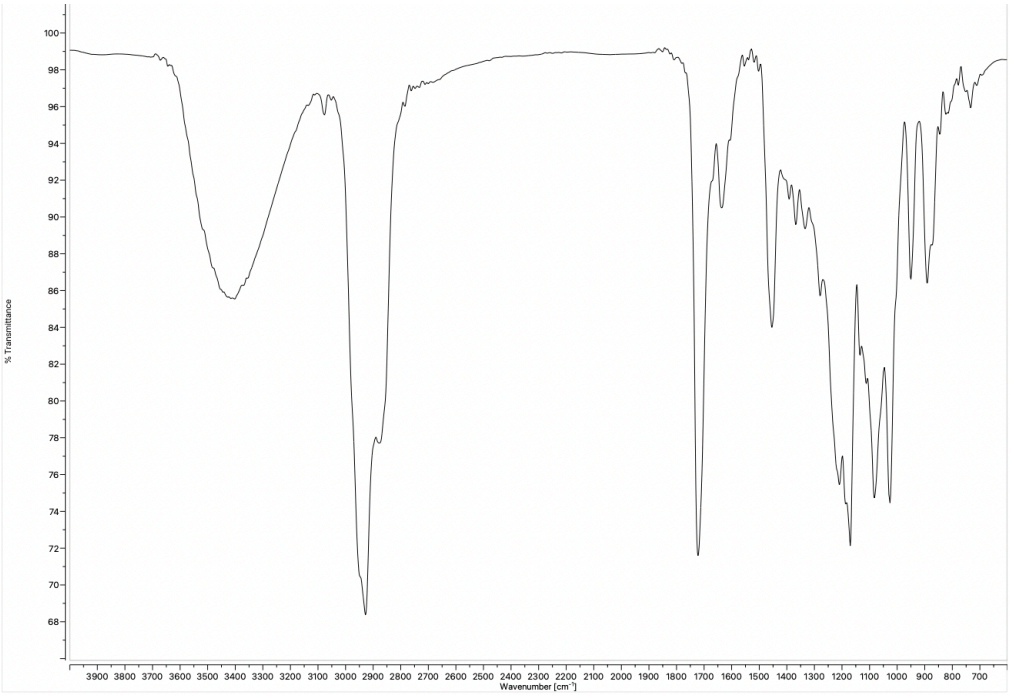


Figure 4.14. Infrared spectrum (Thin Film, NaCl) of compound **117** (minor).

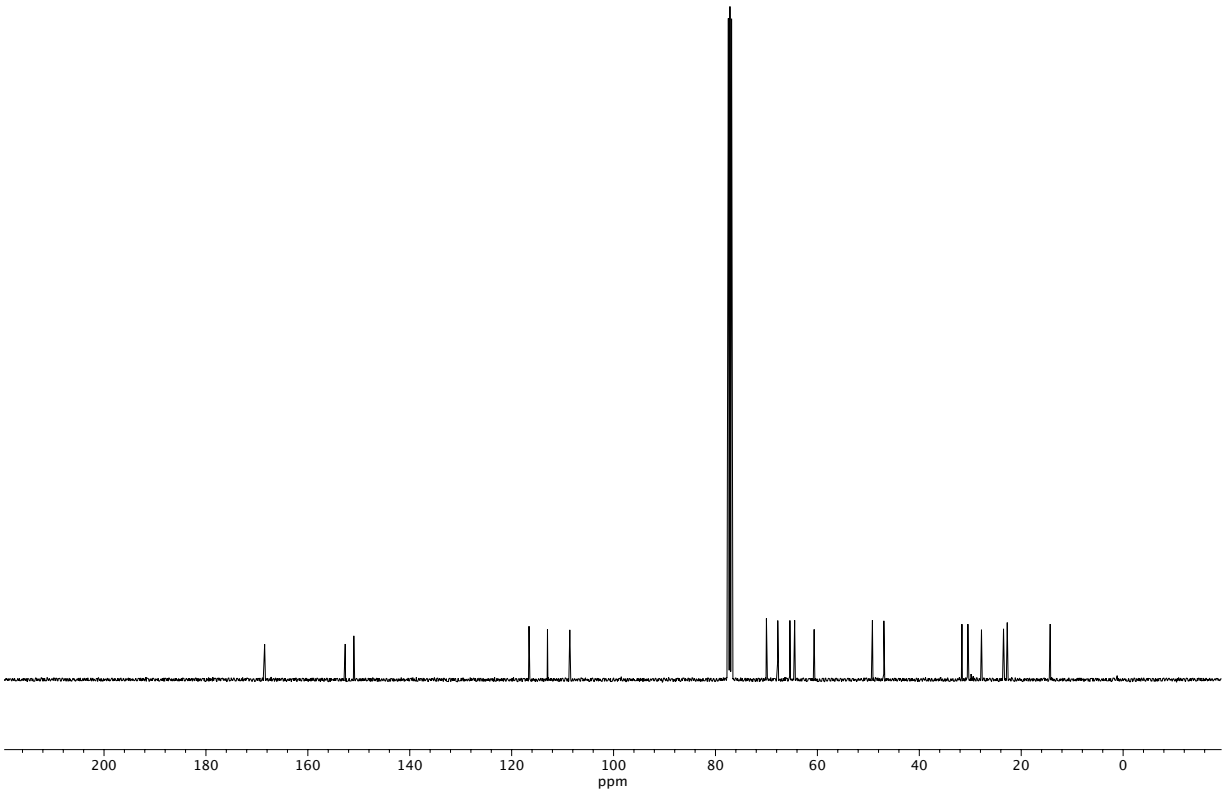


Figure 4.15. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **117** (minor)**.**

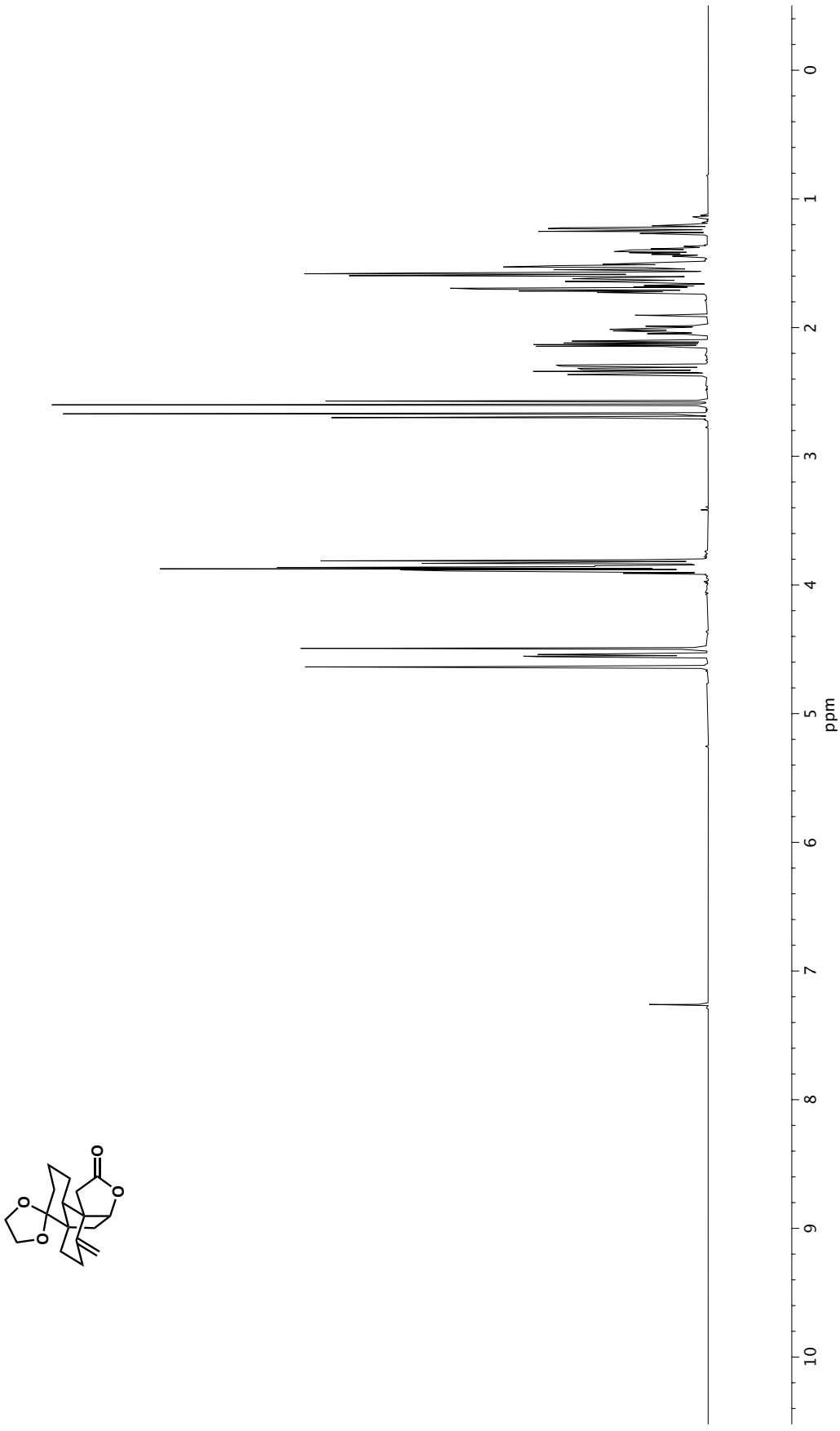


Figure 4.16. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **119**.

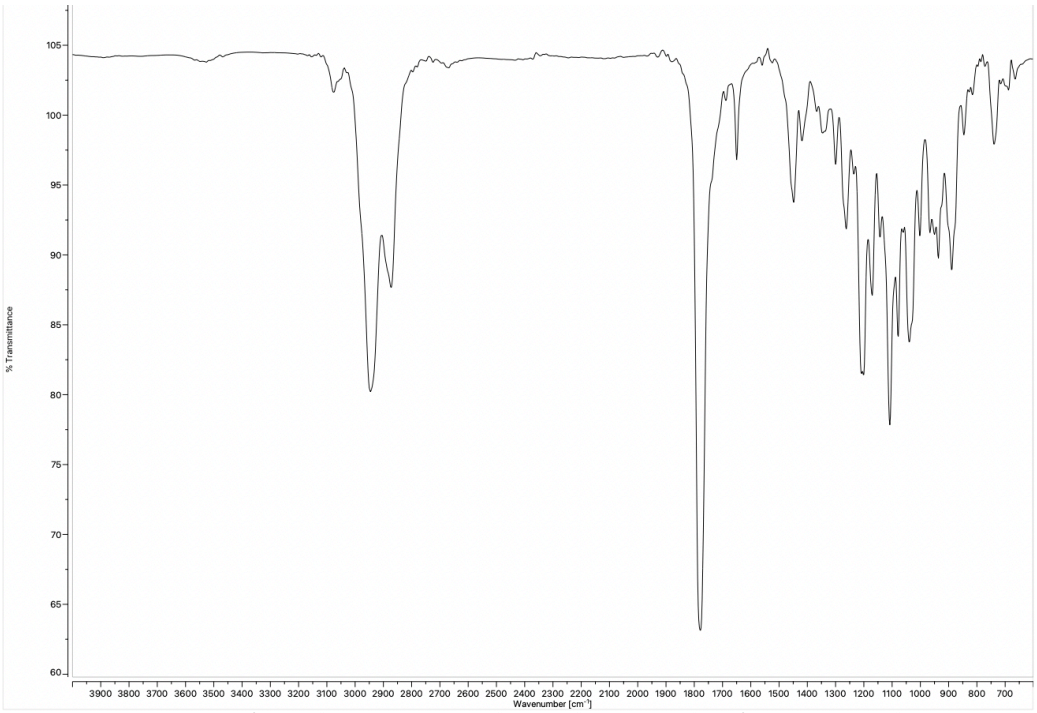


Figure 4.17. Infrared spectrum (Thin Film, NaCl) of compound **119**.

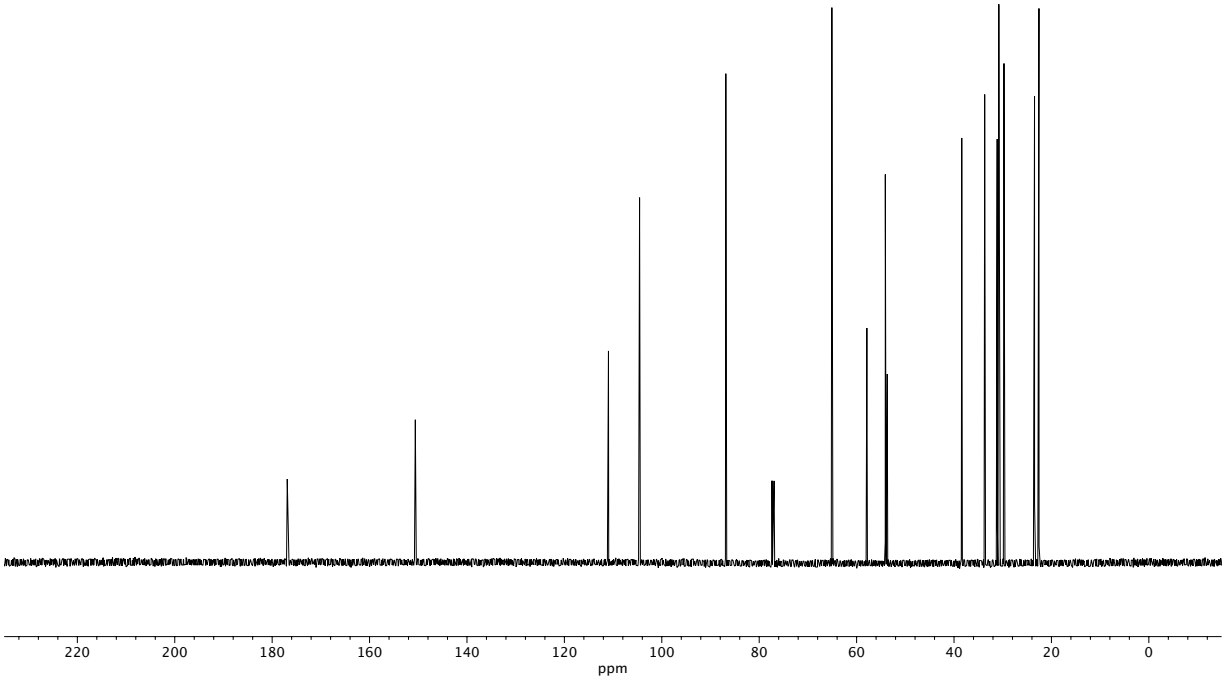


Figure 4.18. ^{13}C NMR (151 MHz, $CDCl_3$) of compound **119.**

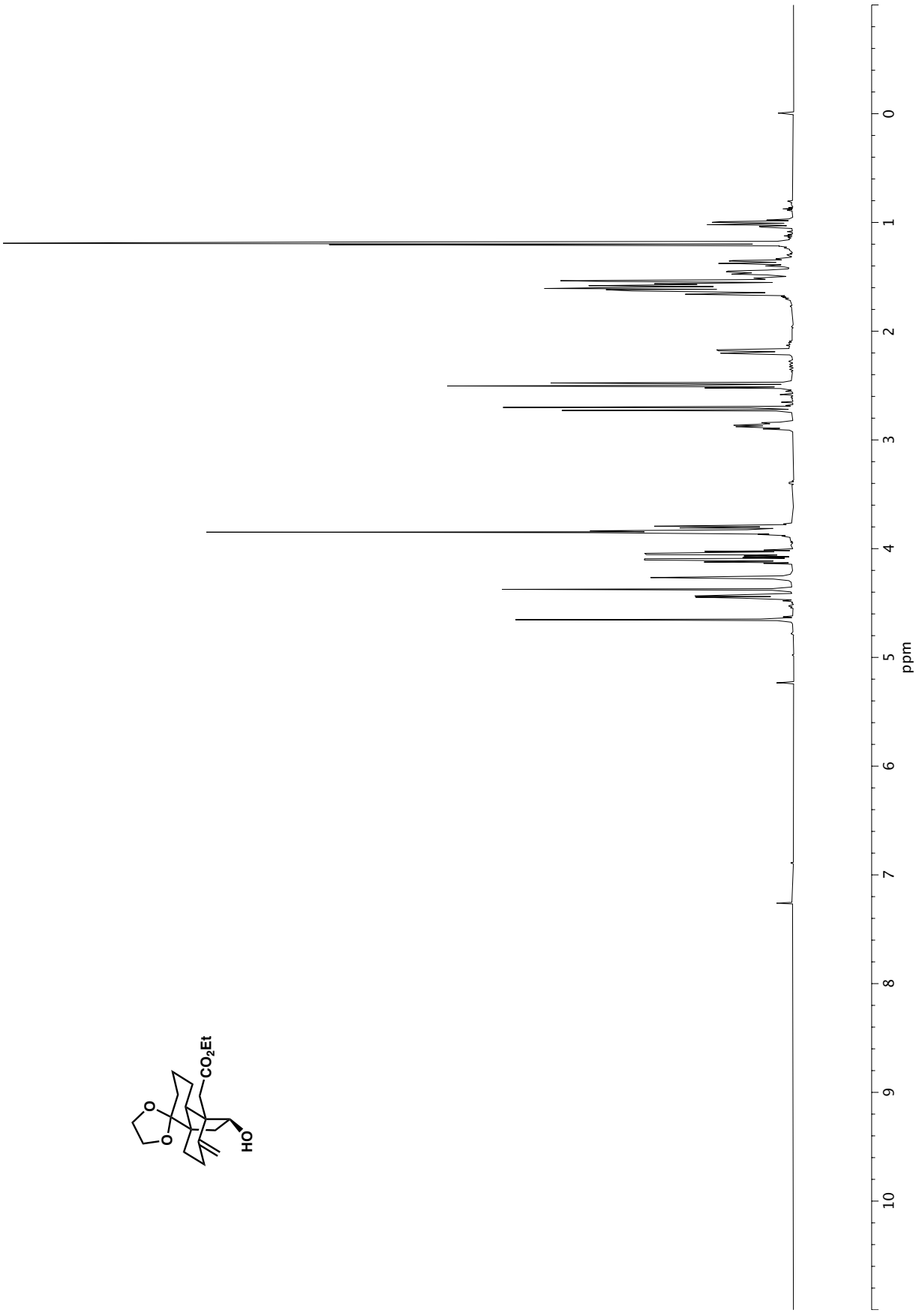


Figure 4.19. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **118**.

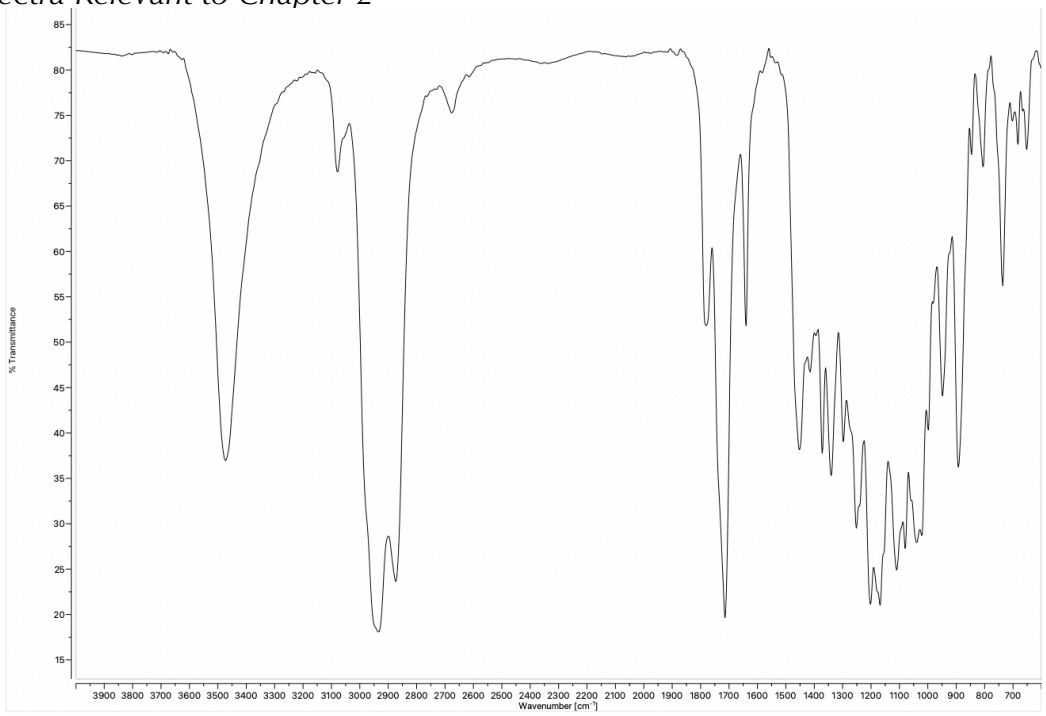


Figure 4.20. Infrared spectrum (Thin Film, NaCl) of compound **118**.

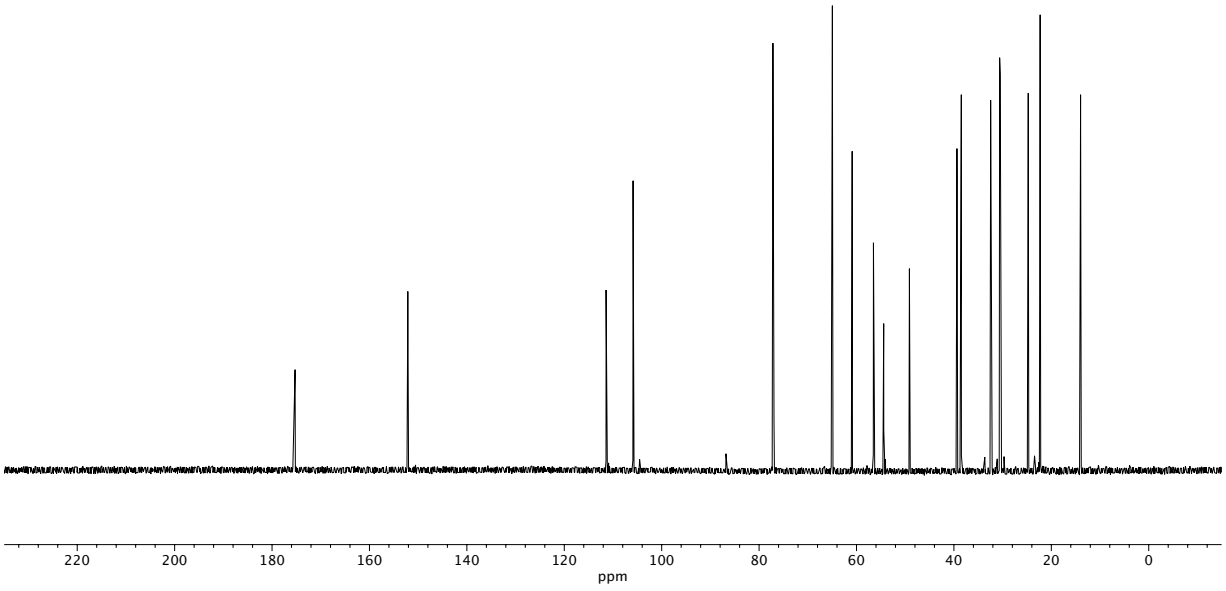


Figure 4.21. ^{13}C NMR (151 MHz, $CDCl_3$) of compound **118.**

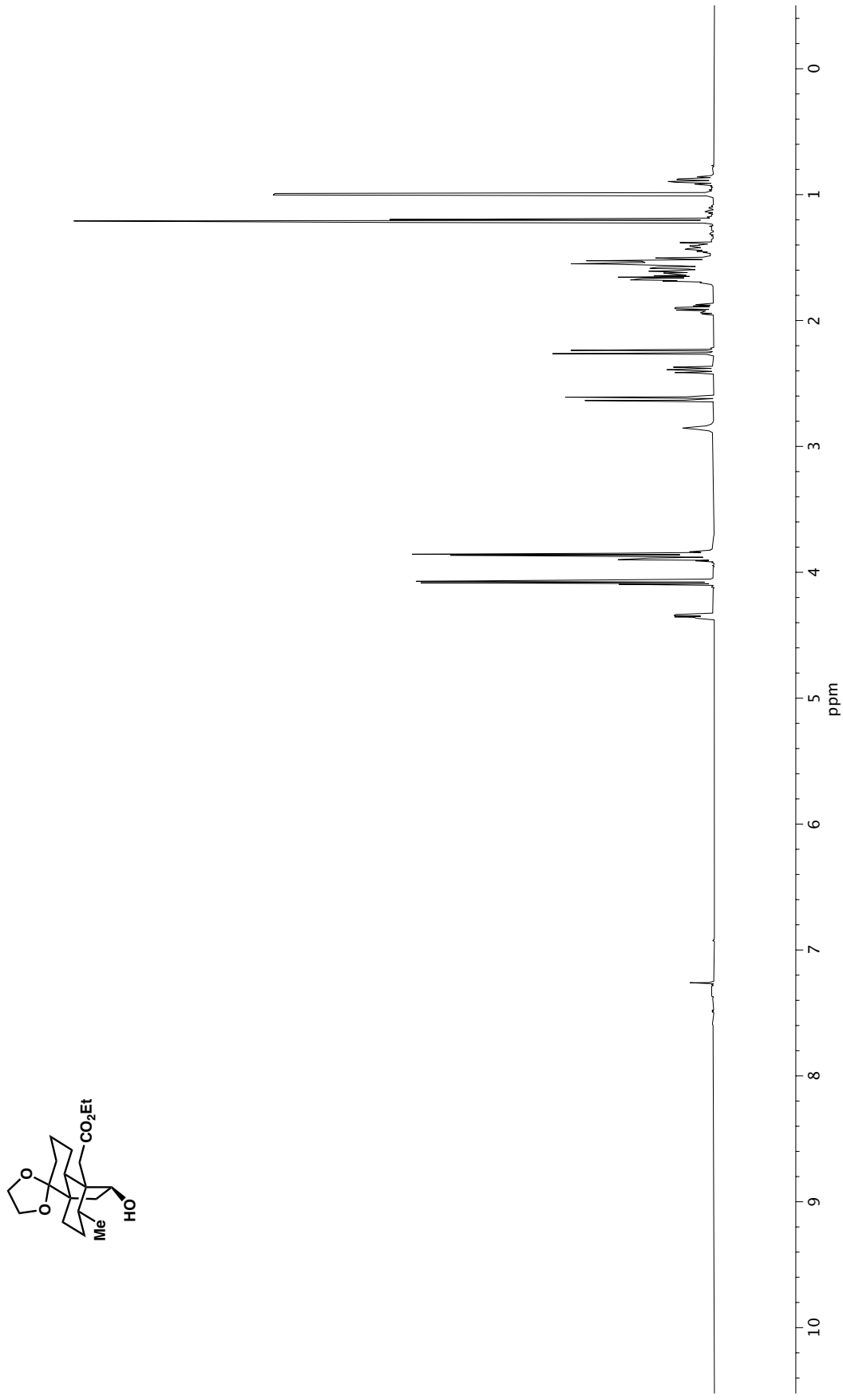


Figure 4.22. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **120**.

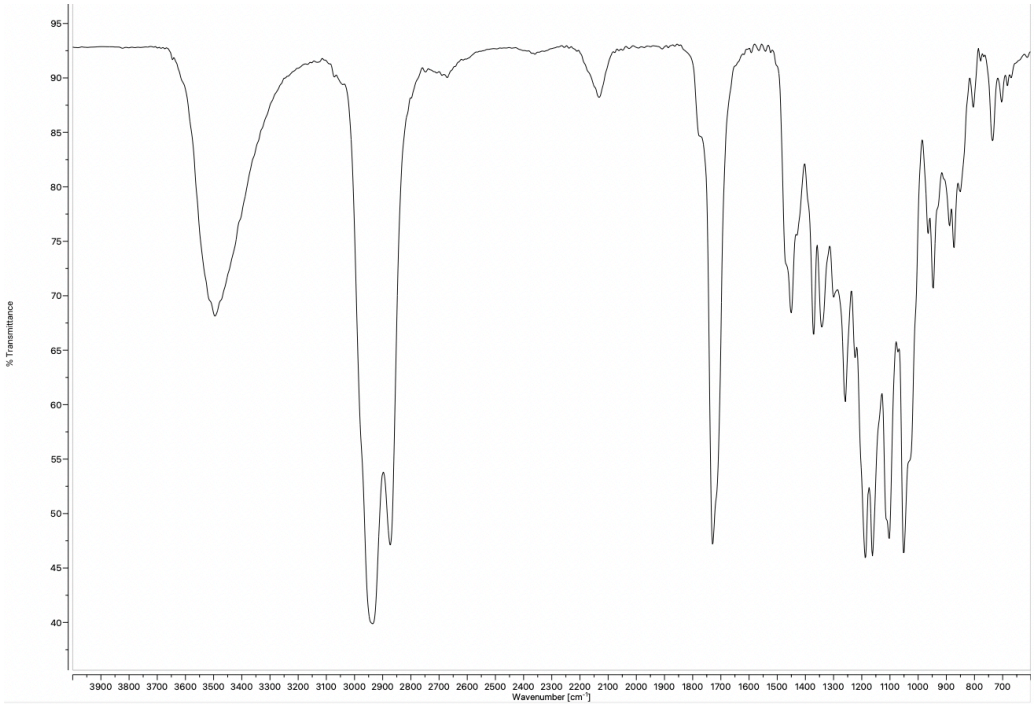


Figure 4.23. Infrared spectrum (Thin Film, NaCl) of compound **120**.

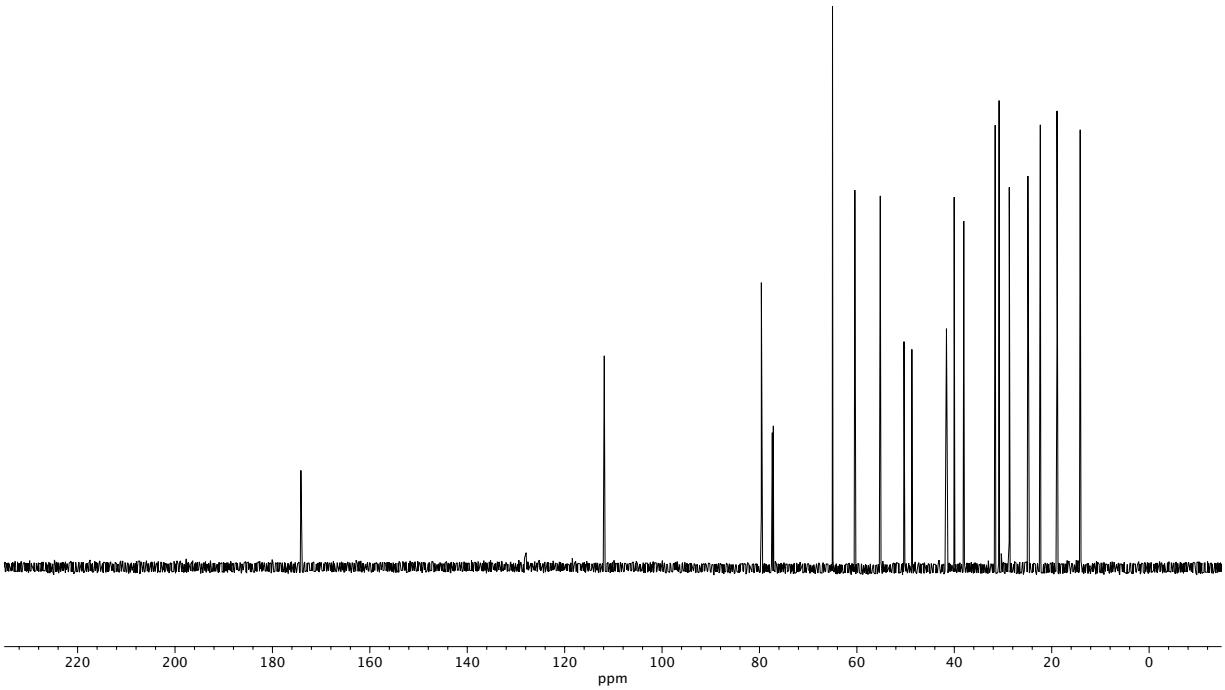


Figure 4.24. ^{13}C NMR (151 MHz, $CDCl_3$) of compound **120.**

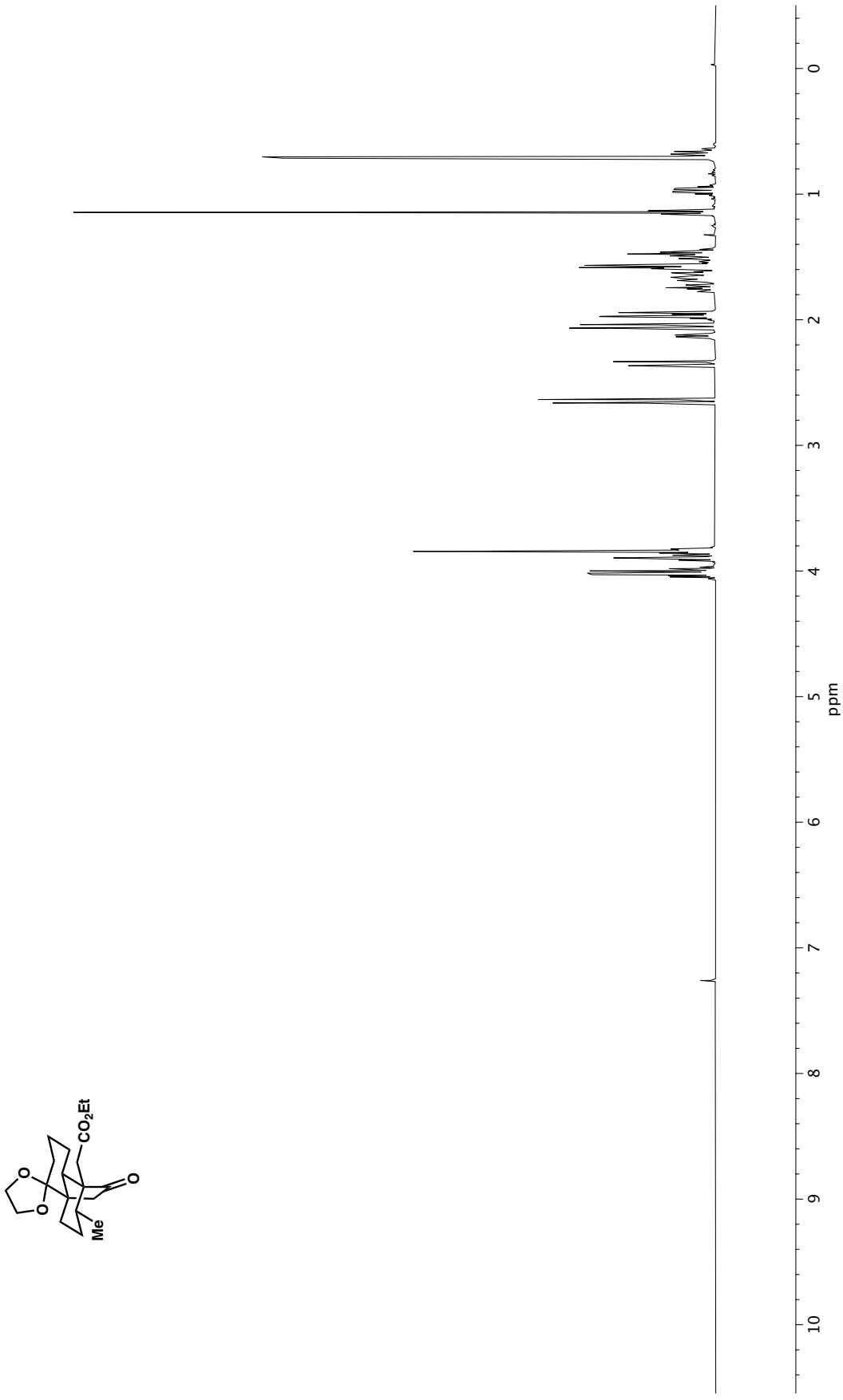


Figure 4.25. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **121**.

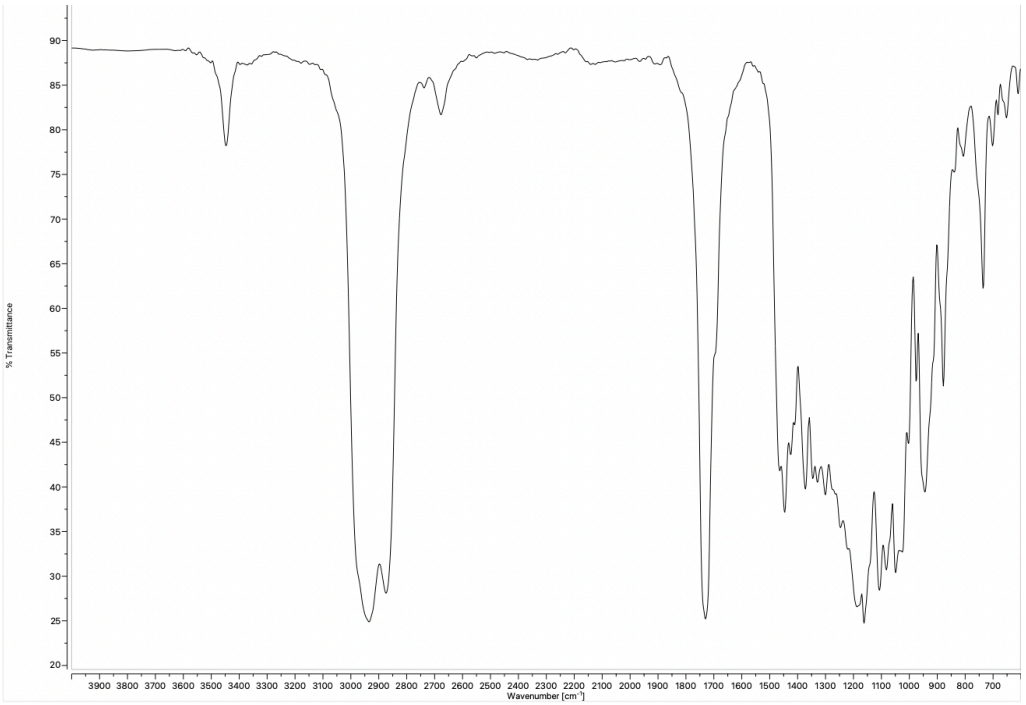


Figure 4.26. Infrared spectrum (Thin Film, NaCl) of compound **121**.

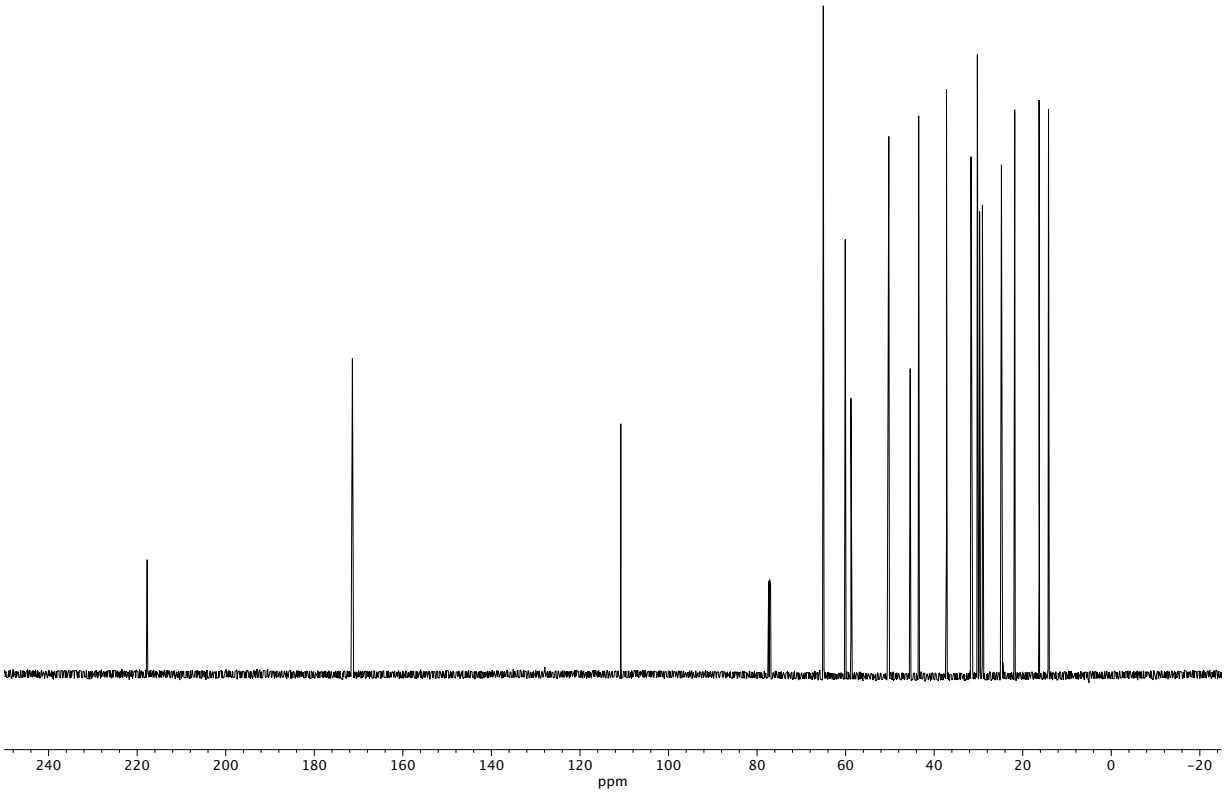


Figure 4.27. ^{13}C NMR (151 MHz, $CDCl_3$) of compound **121.**

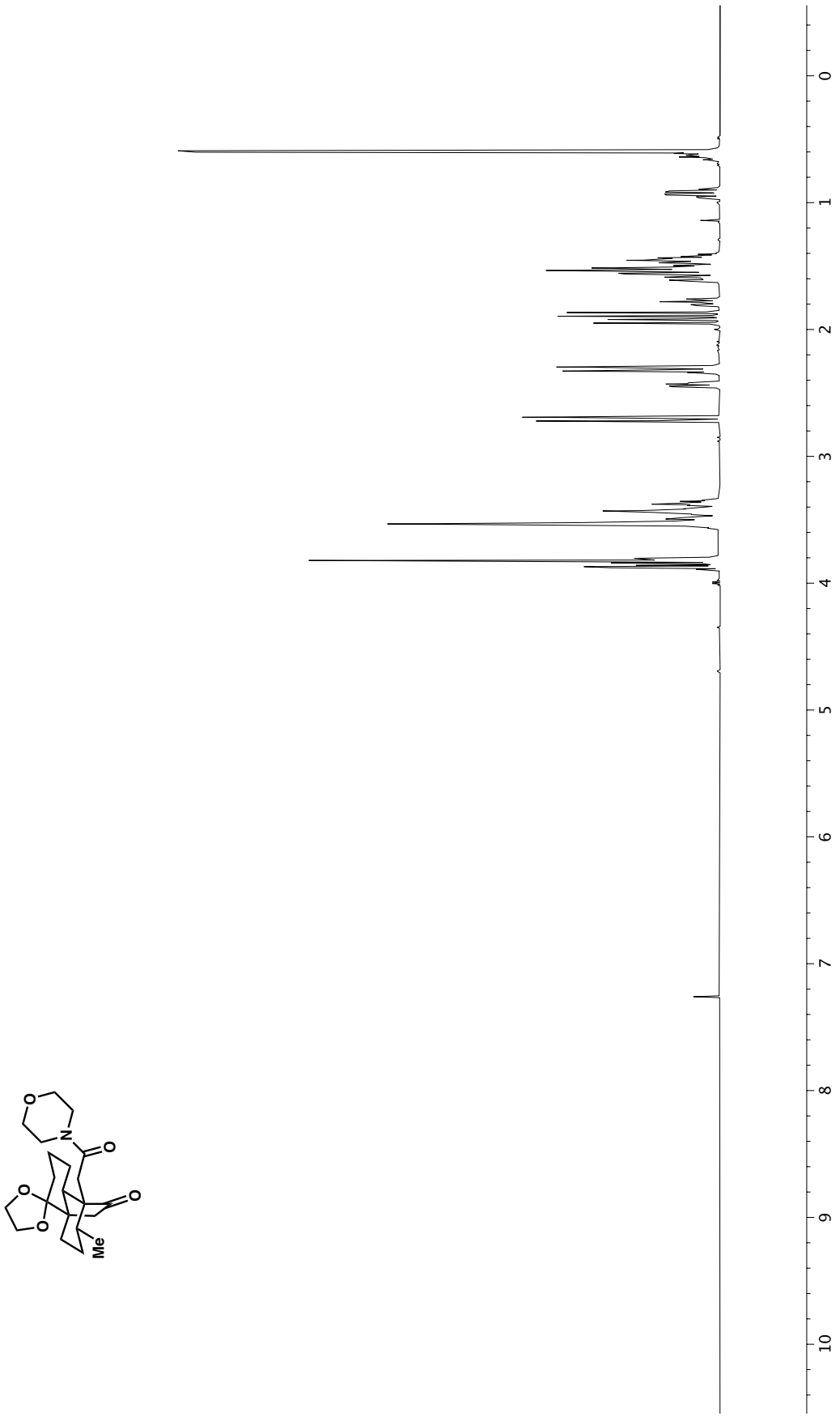


Figure 4.28. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **122**.

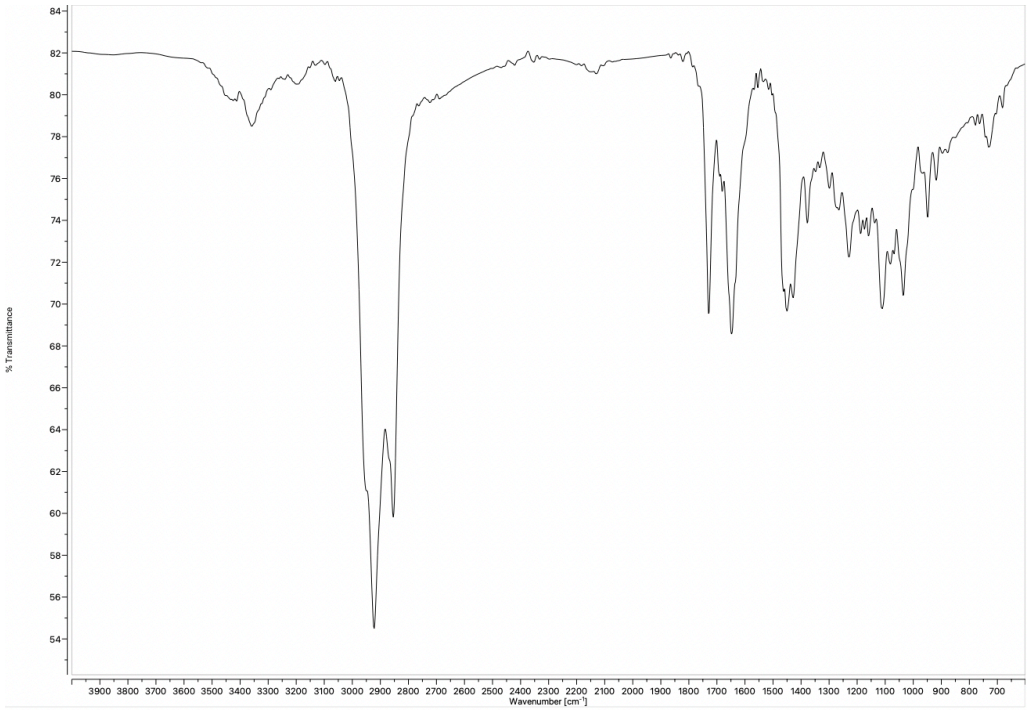


Figure 4.29. Infrared spectrum (Thin Film, NaCl) of compound **122**.

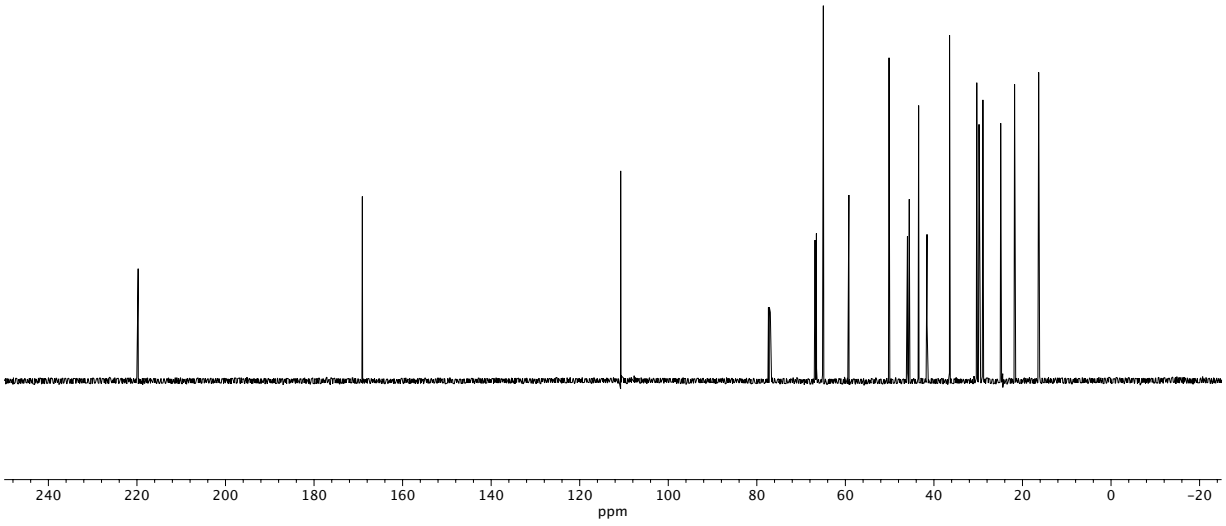


Figure 4.30. ^{13}C NMR (151 MHz, $CDCl_3$) of compound **122.**

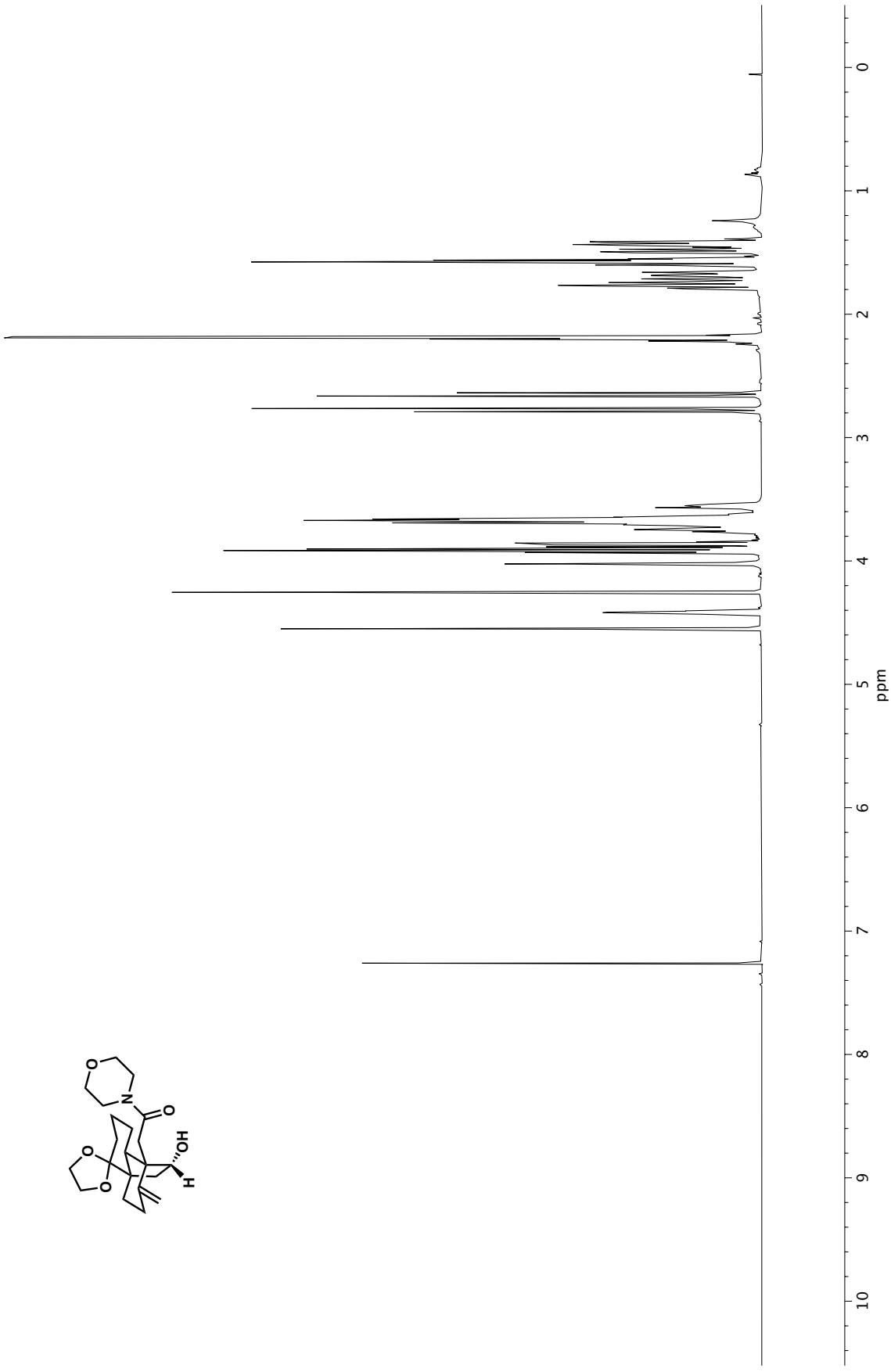


Figure 4.31. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **123**.

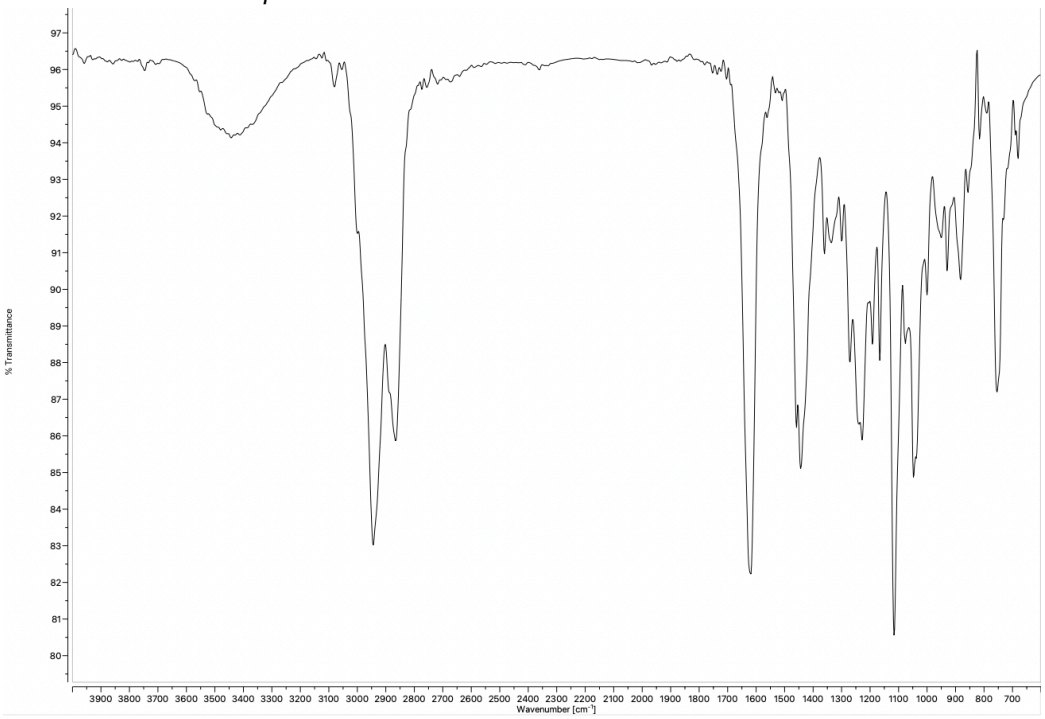


Figure 4.32. Infrared spectrum (Thin Film, NaCl) of compound **123**.

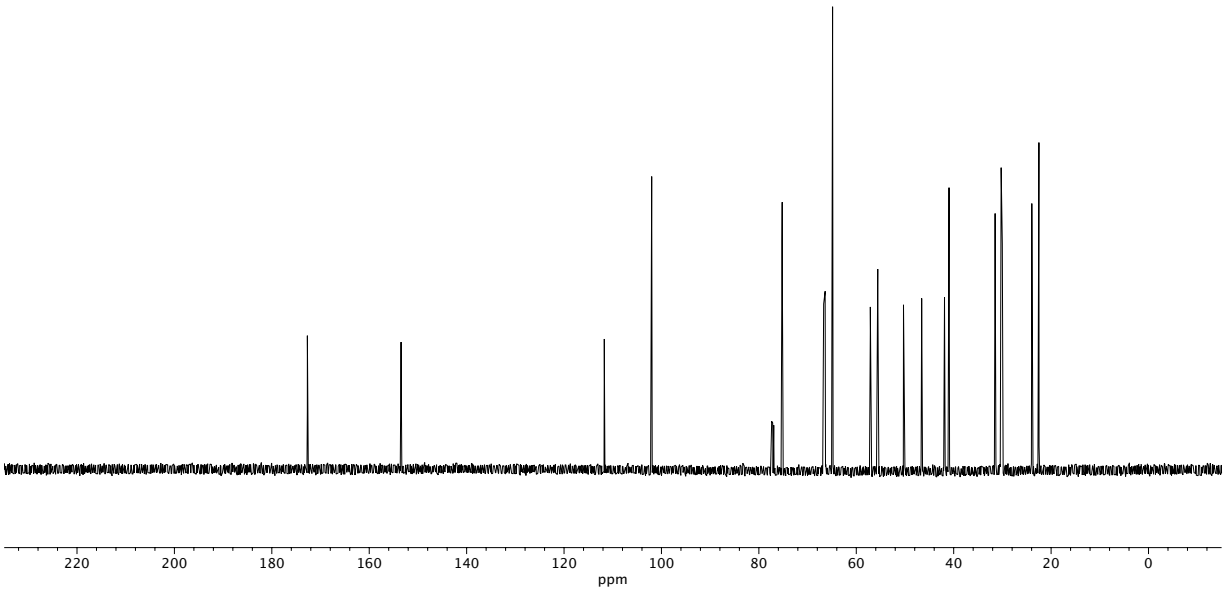


Figure 4.33. ^{13}C NMR (151 MHz, $CDCl_3$) of compound **123.**

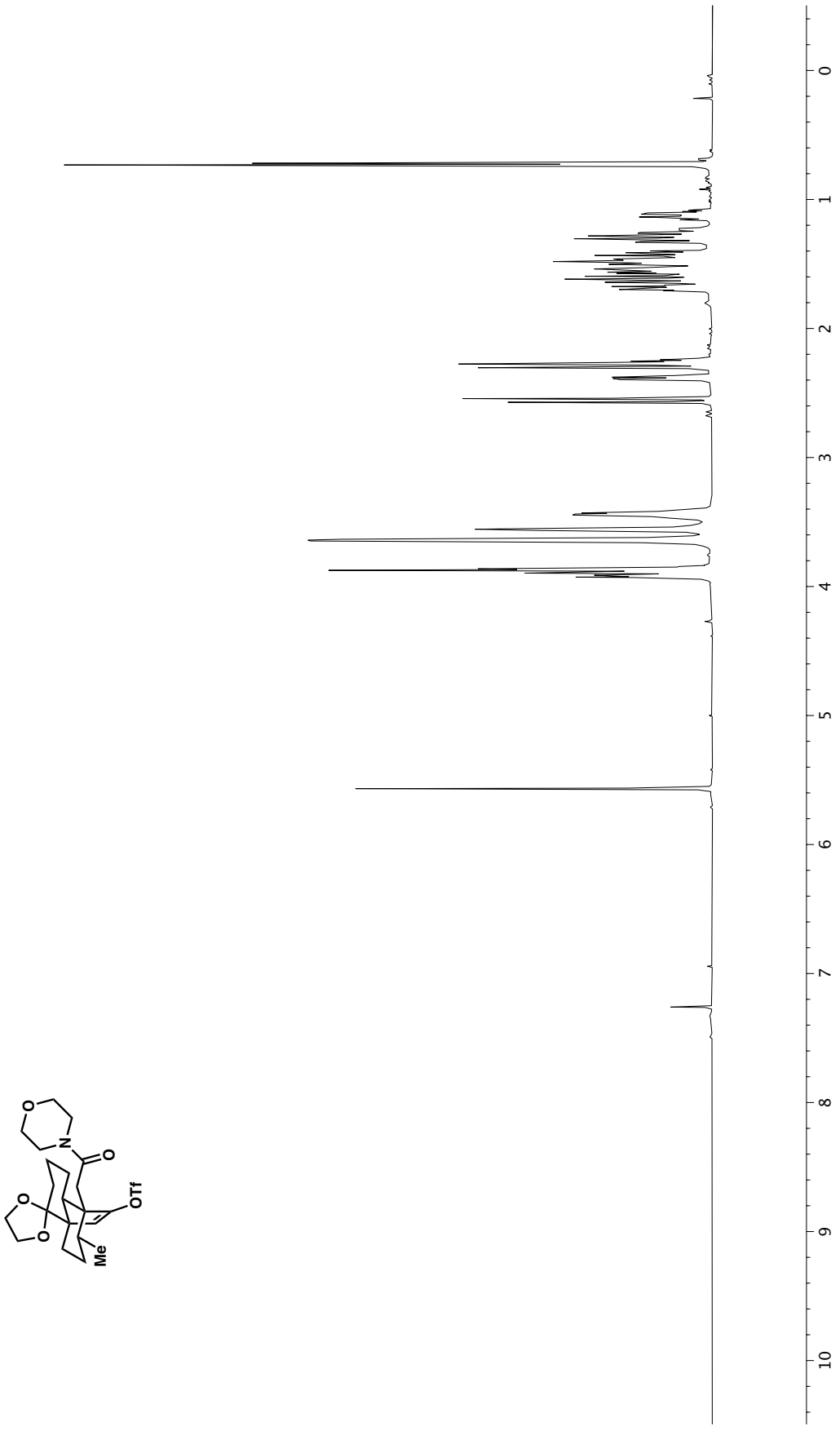


Figure 4.34. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **125**.

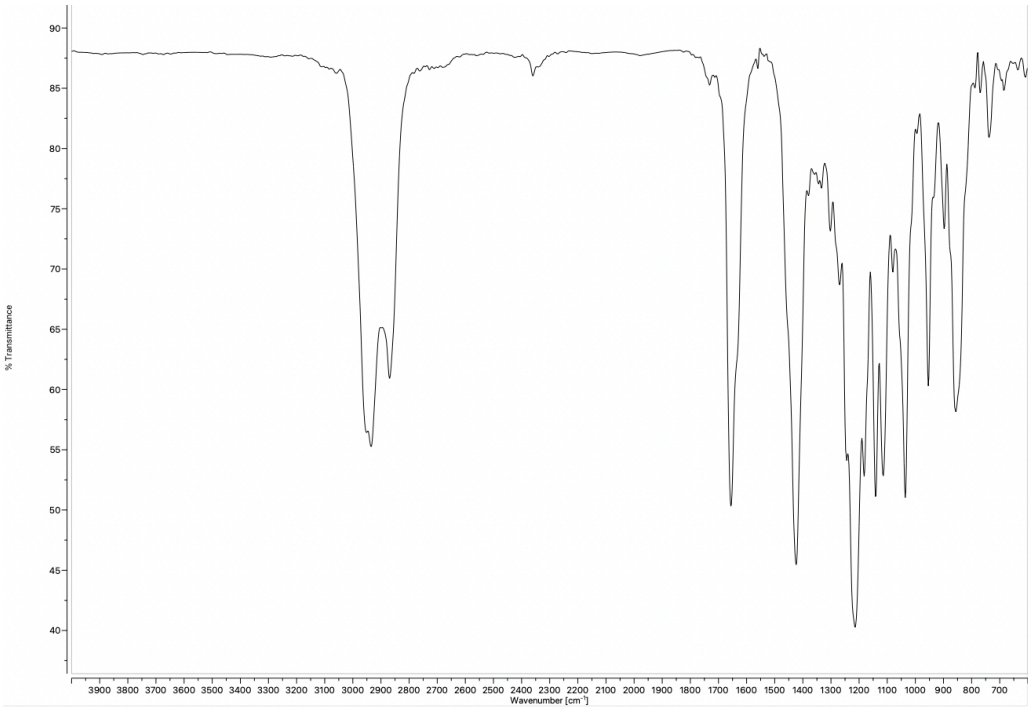


Figure 4.35. Infrared spectrum (Thin Film, NaCl) of compound **125**.

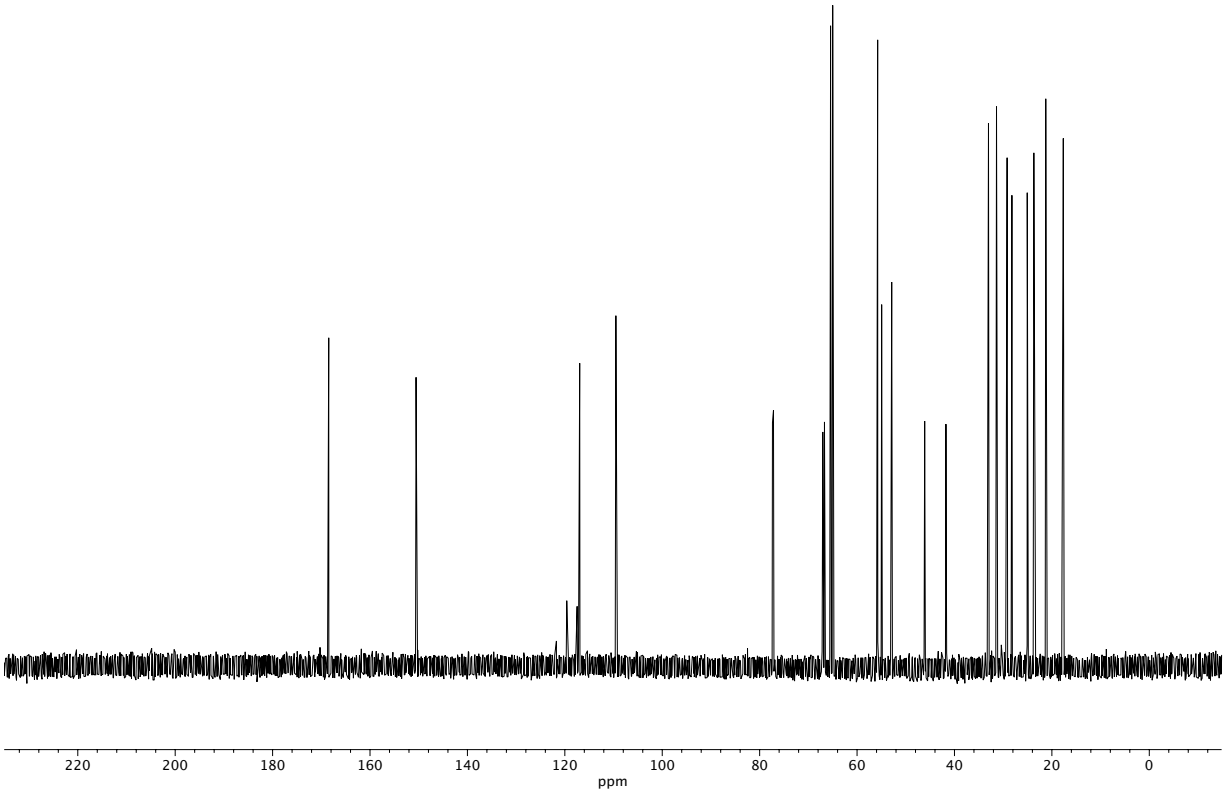


Figure 4.36. ^{13}C NMR (151 MHz, $CDCl_3$) of compound **125.**

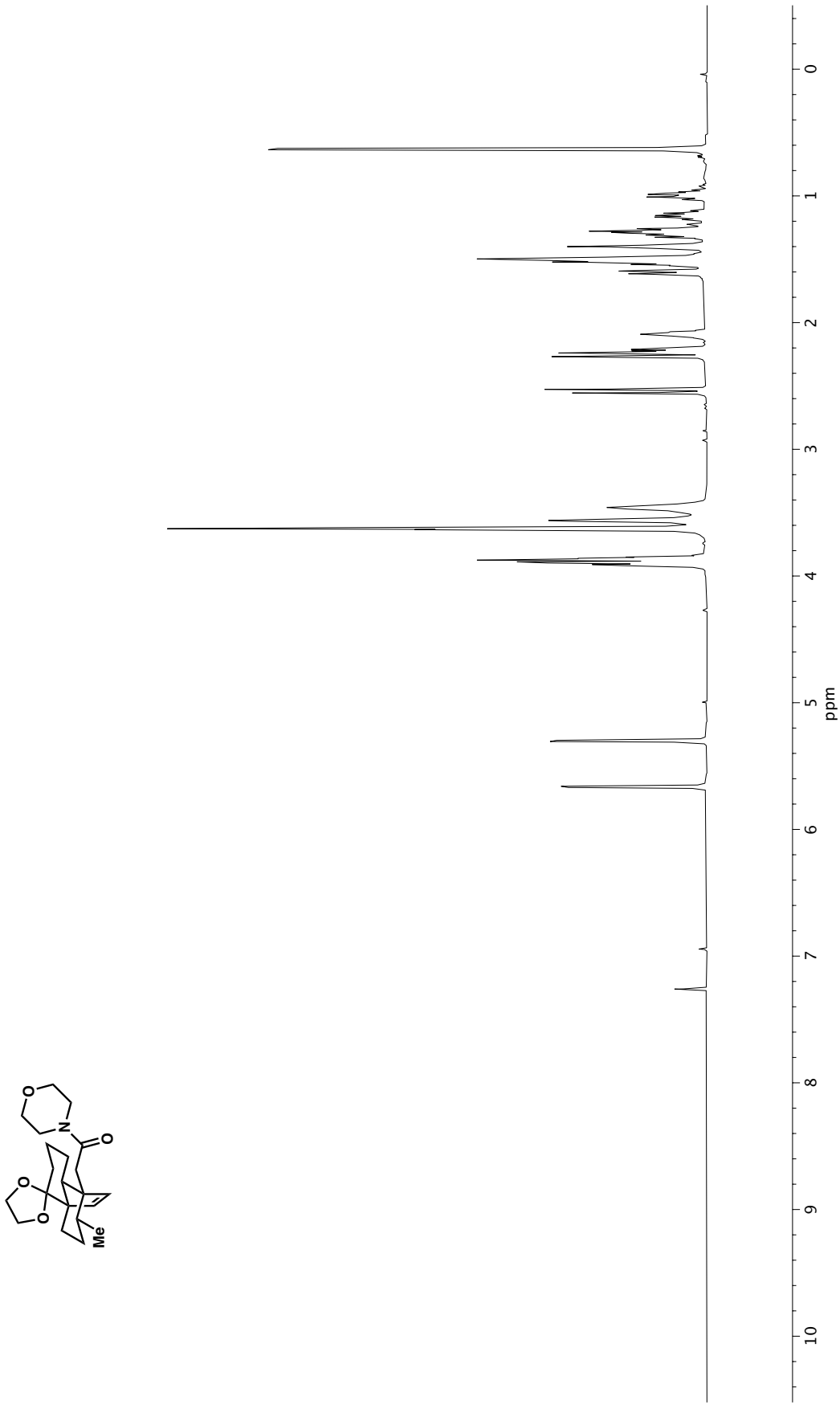


Figure 4.37. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **126**.

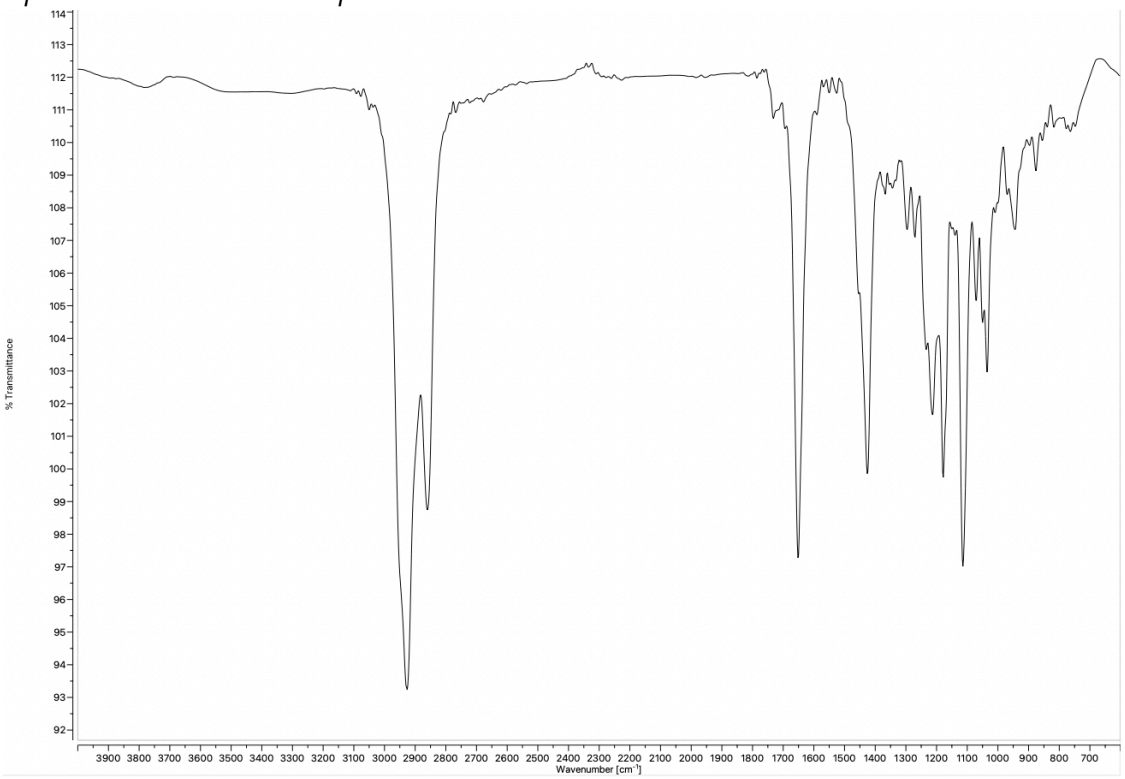


Figure 4.38. Infrared spectrum (Thin Film, NaCl) of compound **126**.

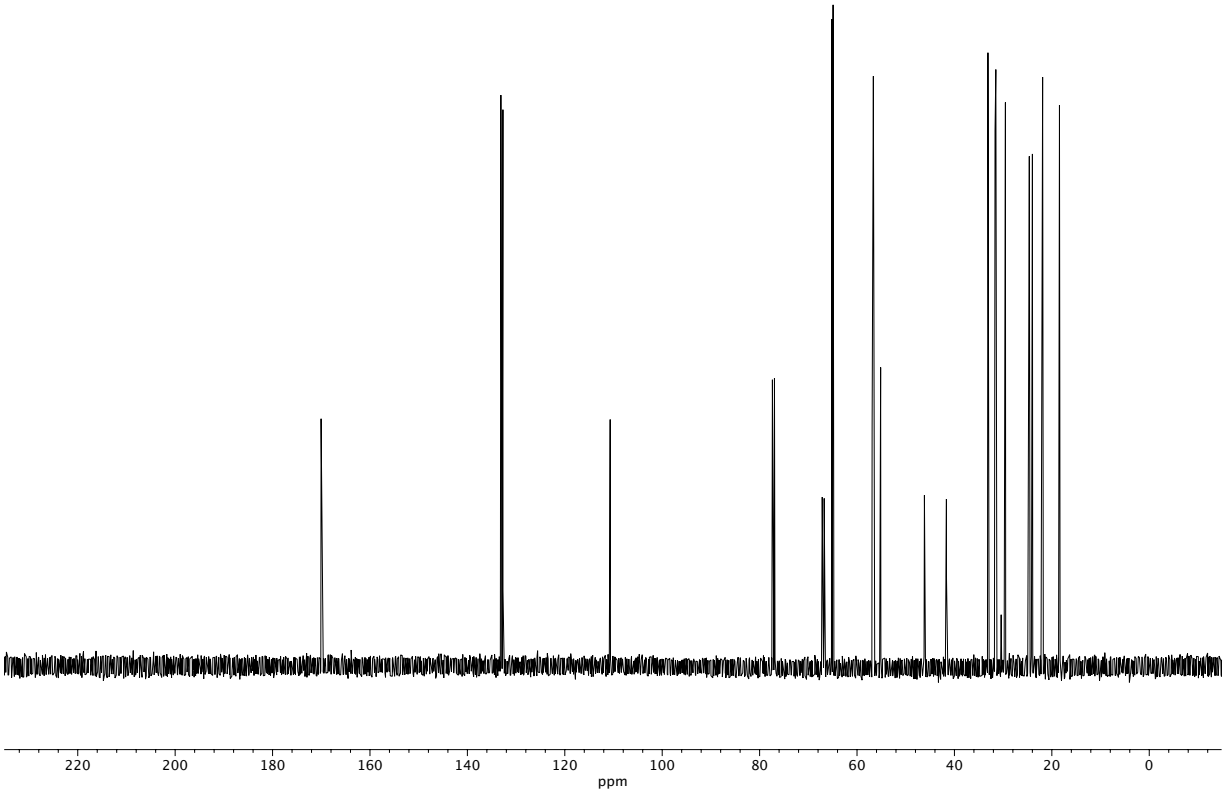


Figure 4.39. ^{13}C NMR (151 MHz, $CDCl_3$) of compound **126.**

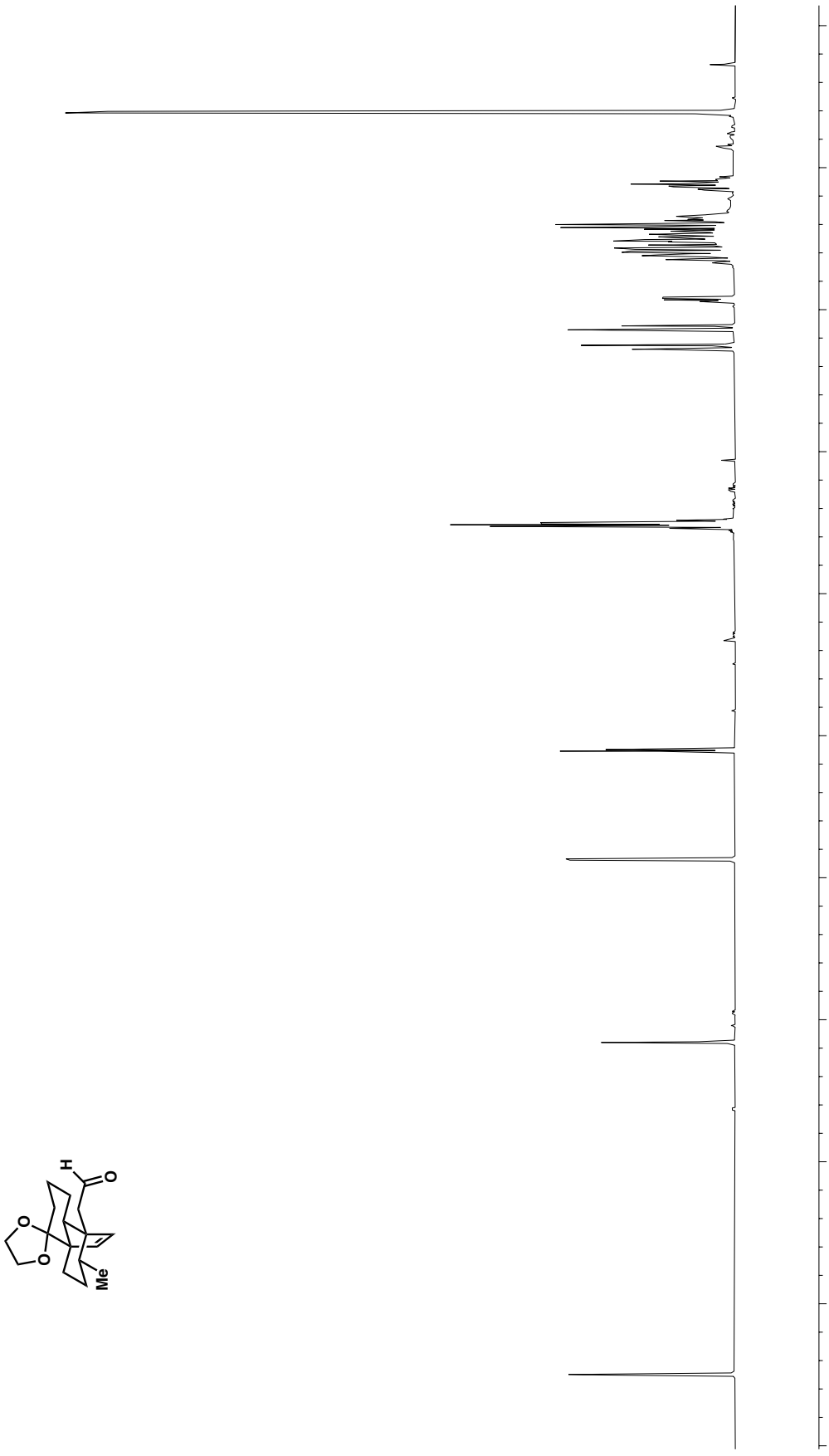


Figure 4.40. ^{1}H NMR (600 MHz, C_6D_6) of compound **127**.

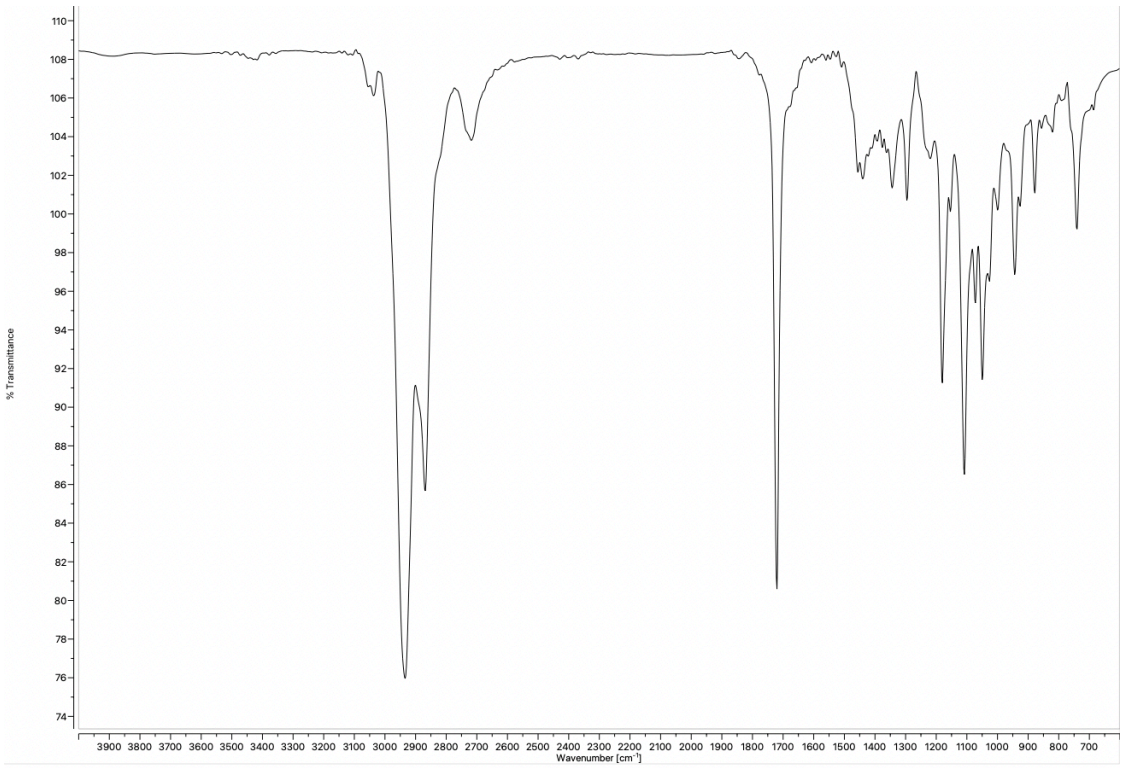


Figure 4.41. Infrared spectrum (Thin Film, NaCl) of compound **127**.

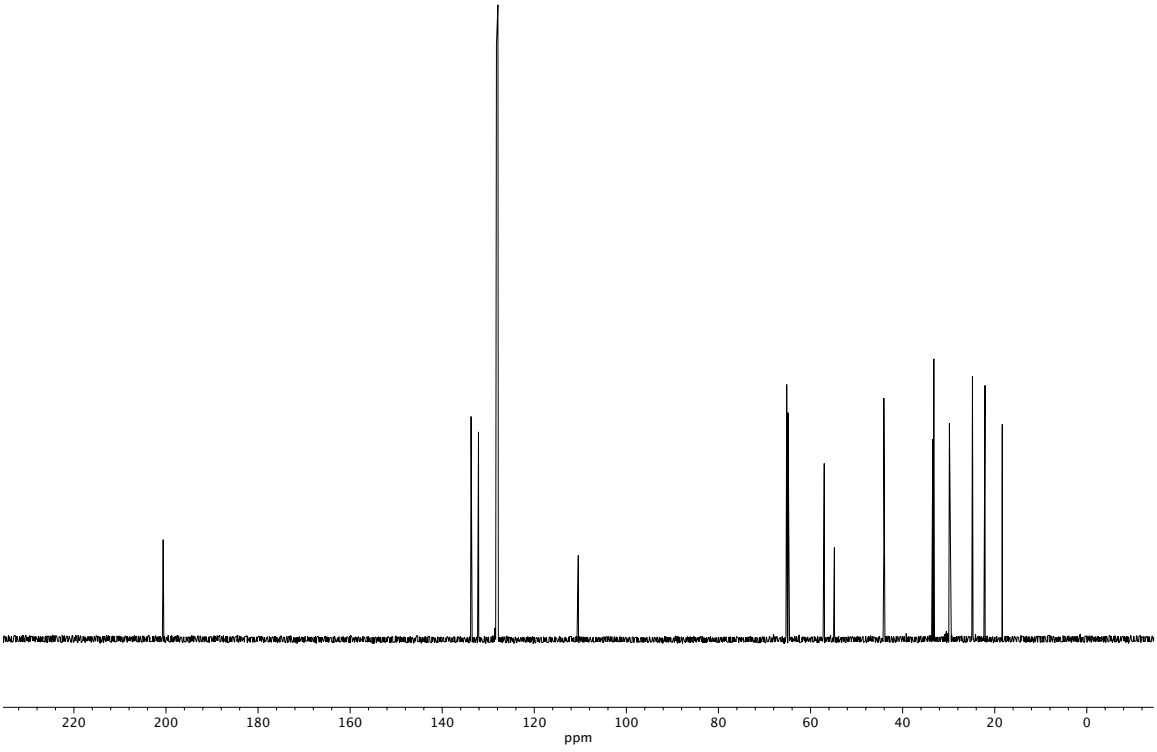


Figure 4.42. ^{13}C NMR (151 MHz, C_6D_6) of compound **127.**

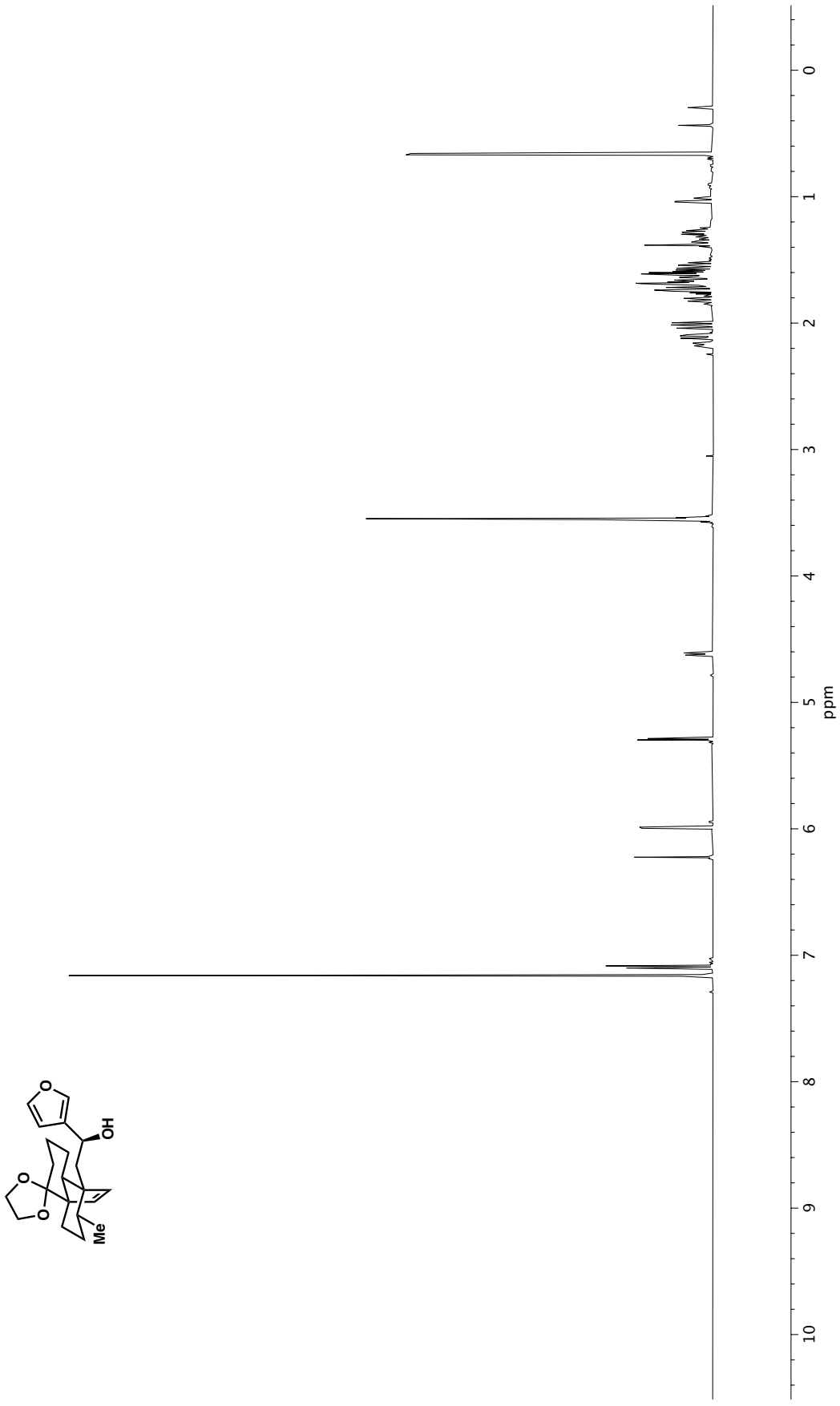


Figure 4.43. ^{1}H NMR (600 MHz, C_6D_6) of compound **128**.

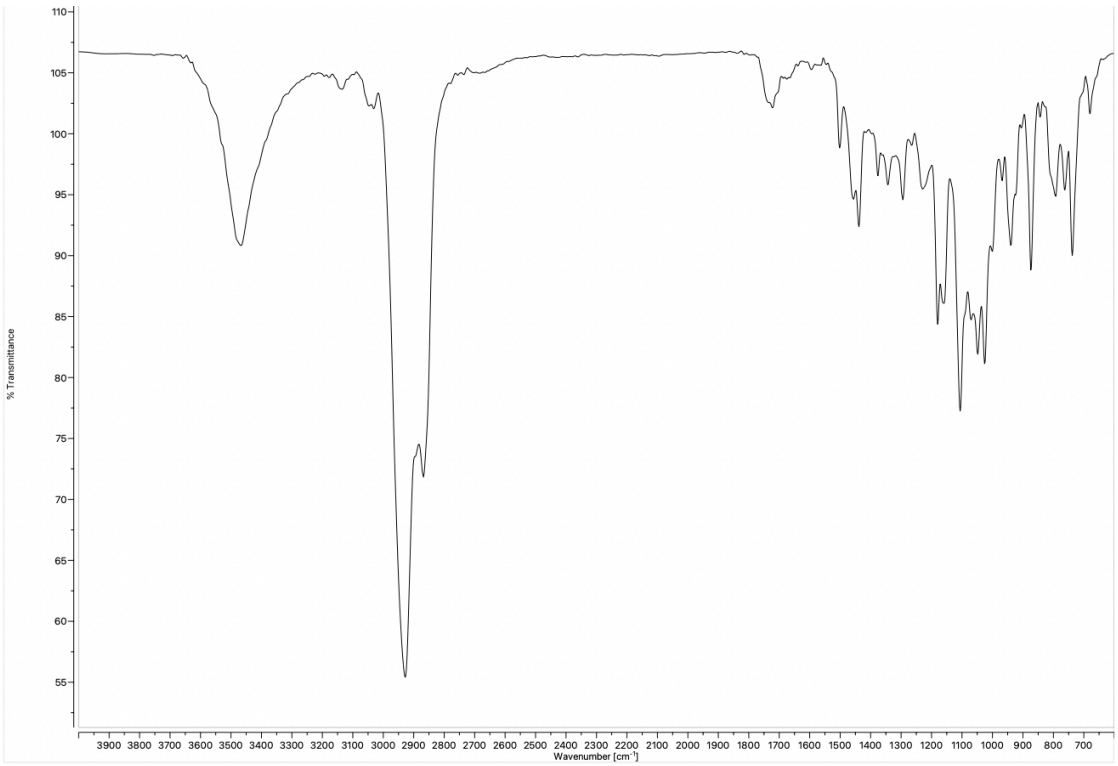


Figure 4.44. Infrared spectrum (Thin Film, NaCl) of compound **128**.

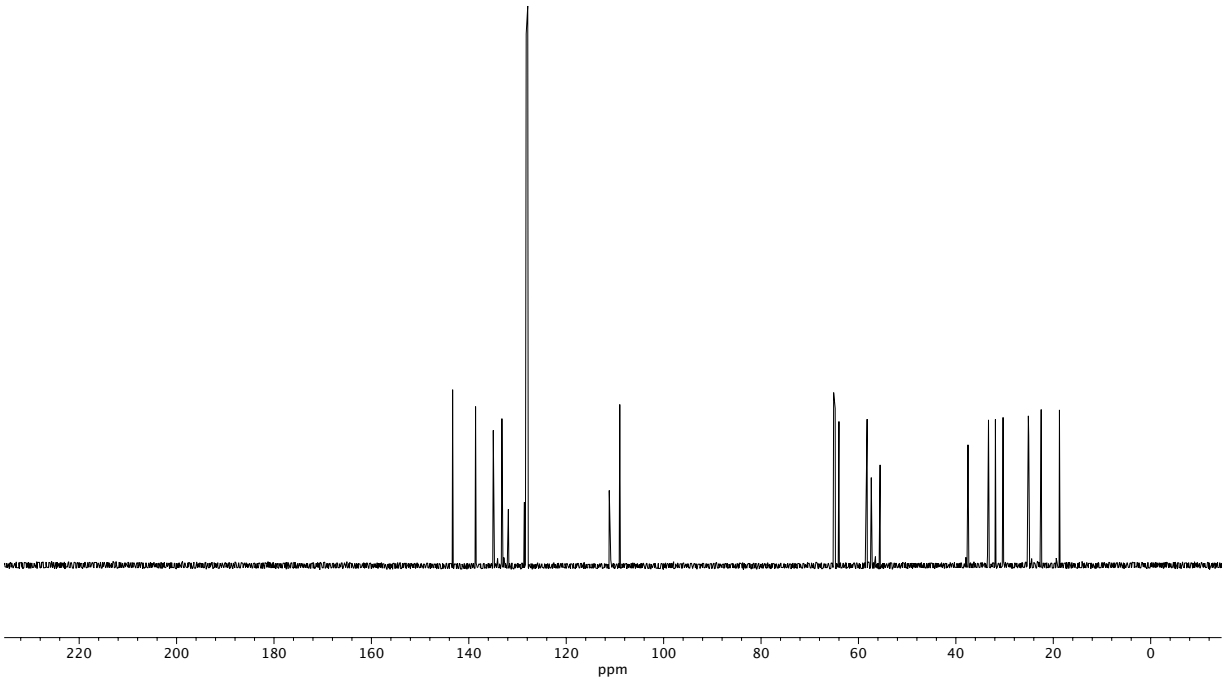


Figure 4.45. ^{13}C NMR (151 MHz, C_6D_6) of compound **128.**

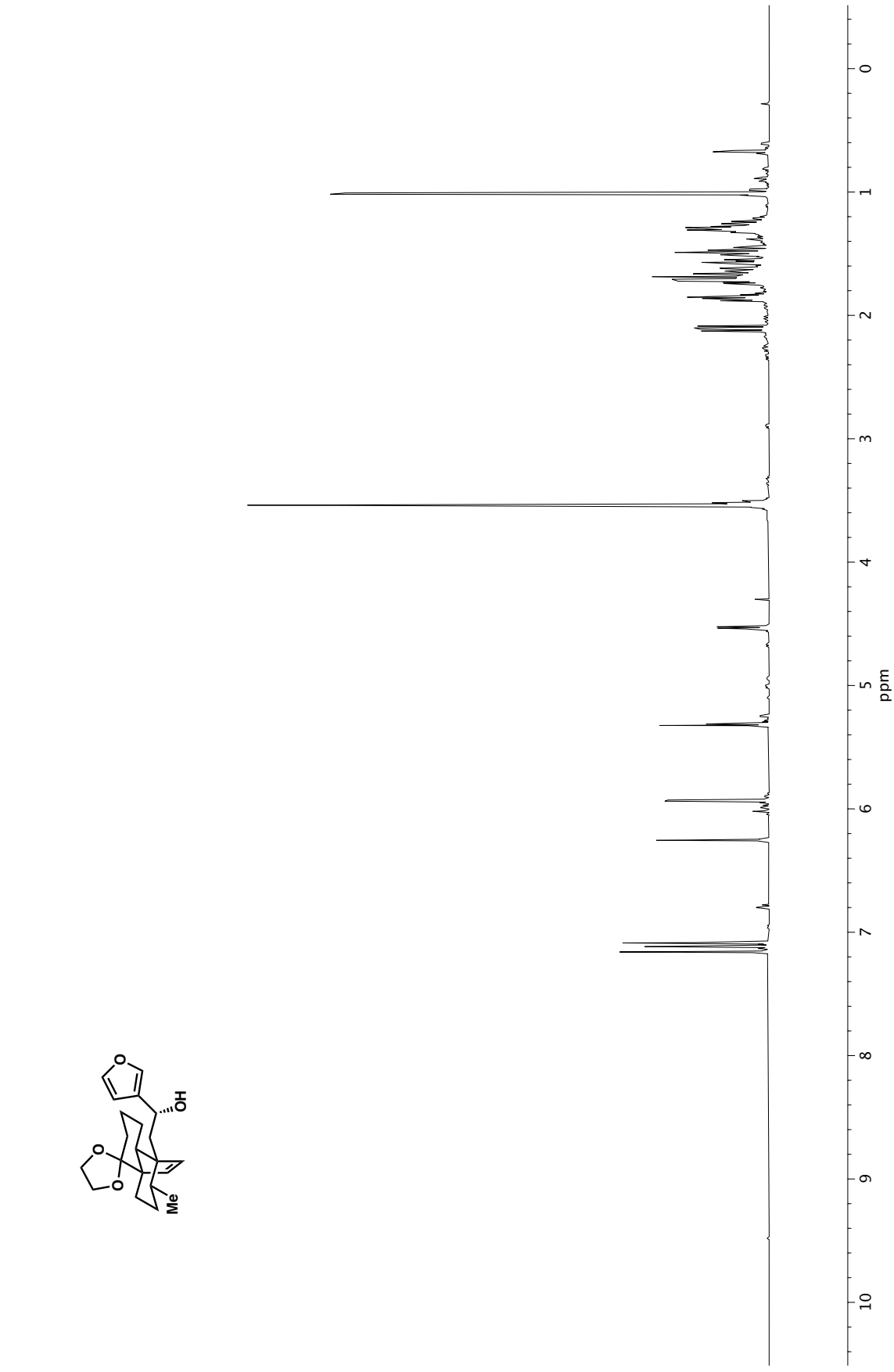


Figure 4.46. ^{1}H NMR (600 MHz, C_6D_6) of compound **129**.

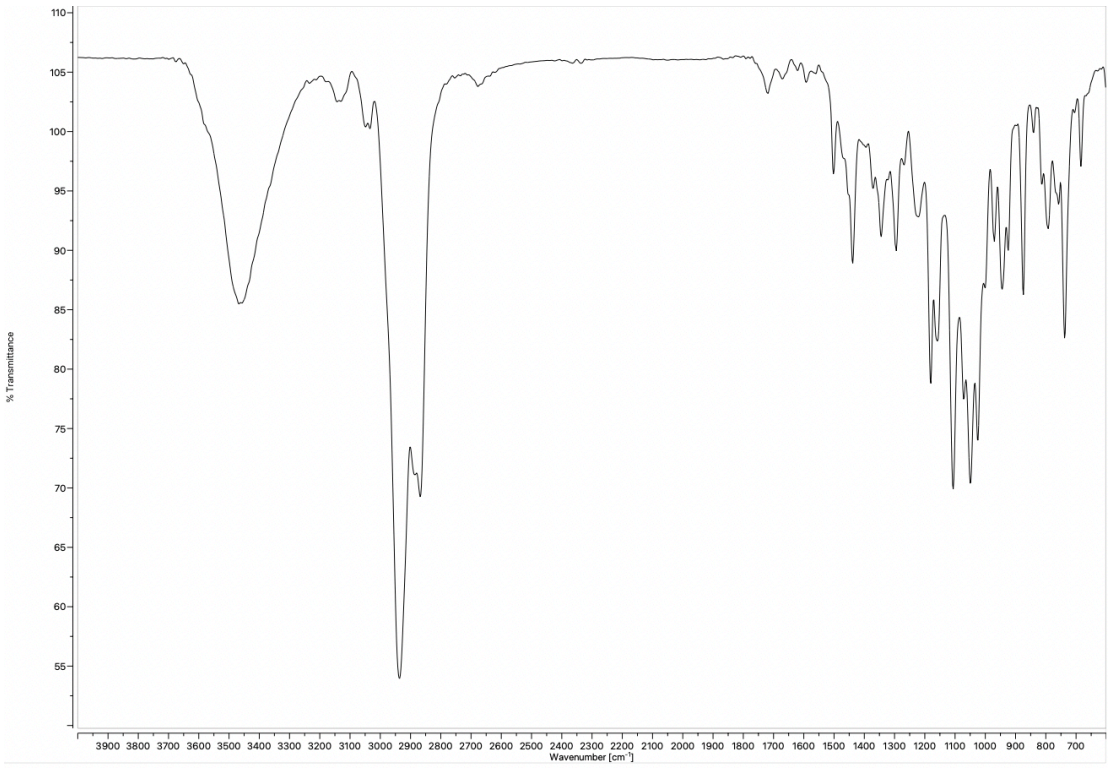


Figure 4.47. Infrared spectrum (Thin Film, NaCl) of compound **129**.

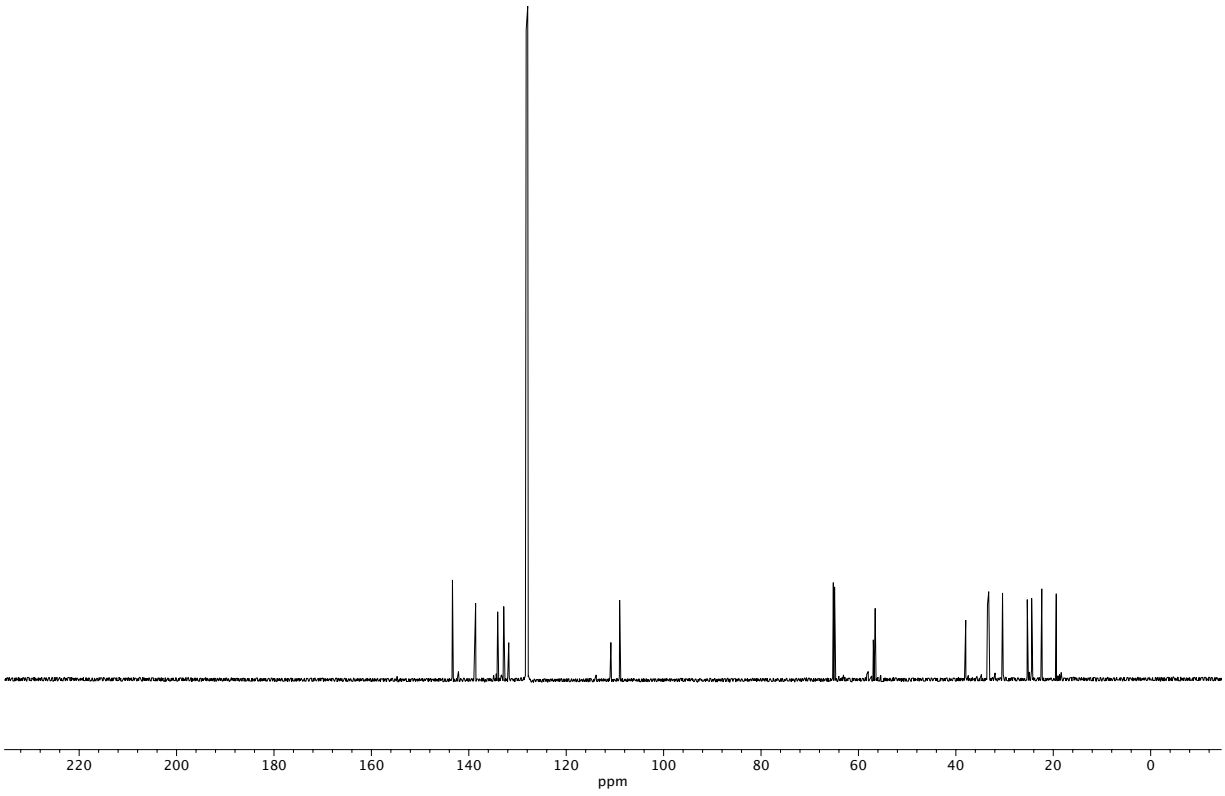


Figure 4.48. ^{13}C NMR (151 MHz, C_6D_6) of compound **129.**

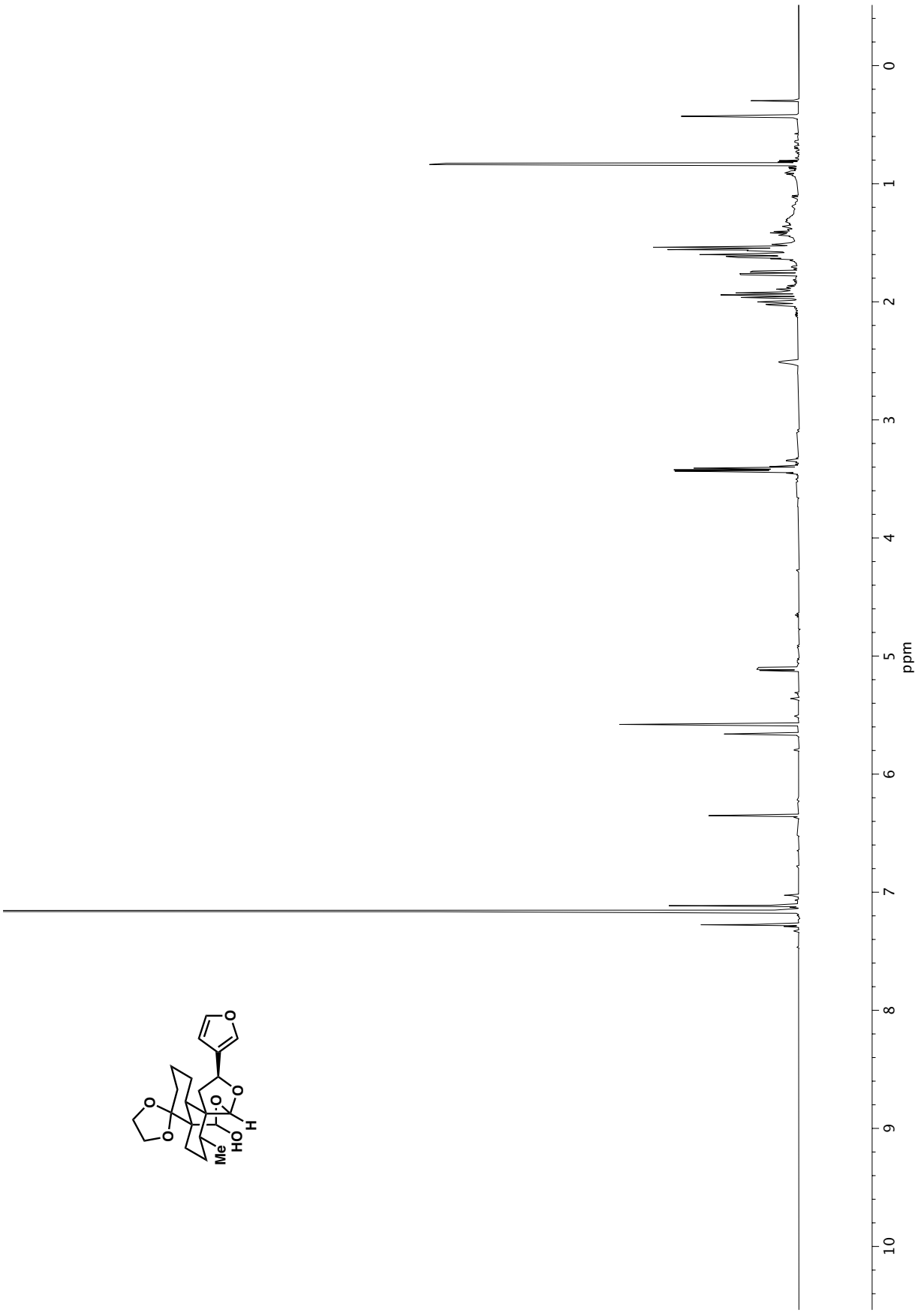


Figure 4.49. ^{1}H NMR (600 MHz, C_6D_6) of compound **130**.

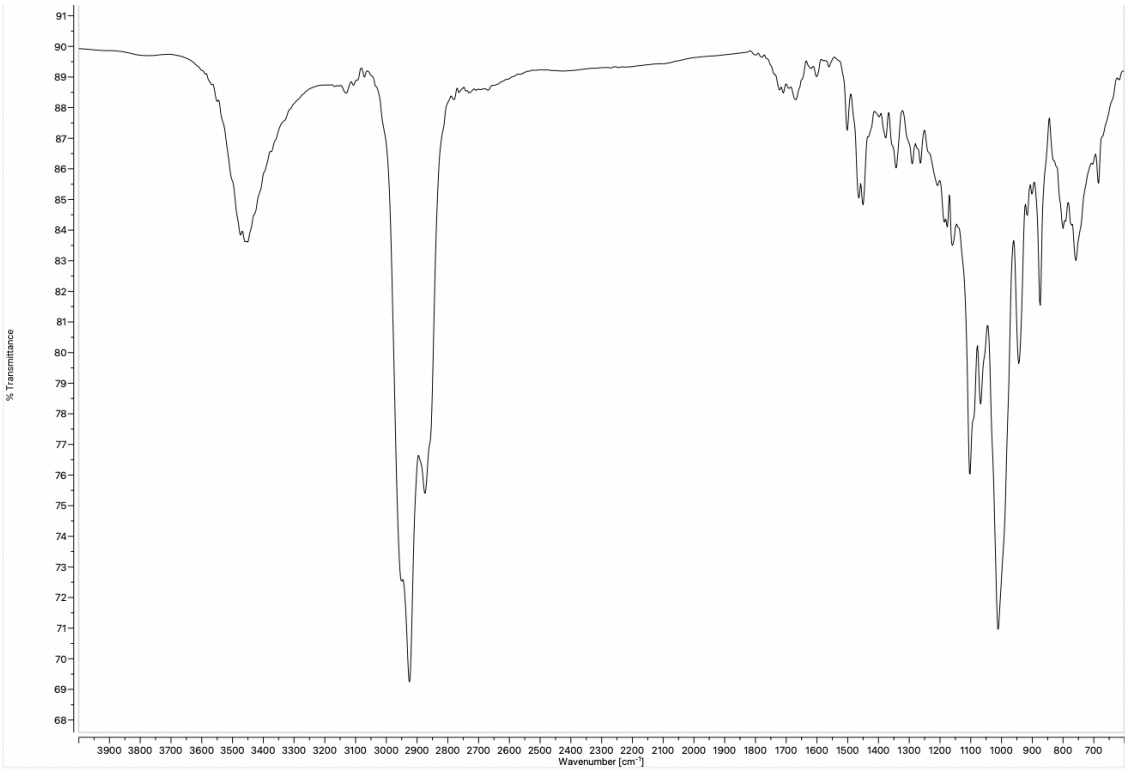


Figure 4.50. Infrared spectrum (Thin Film, NaCl) of compound **130**.

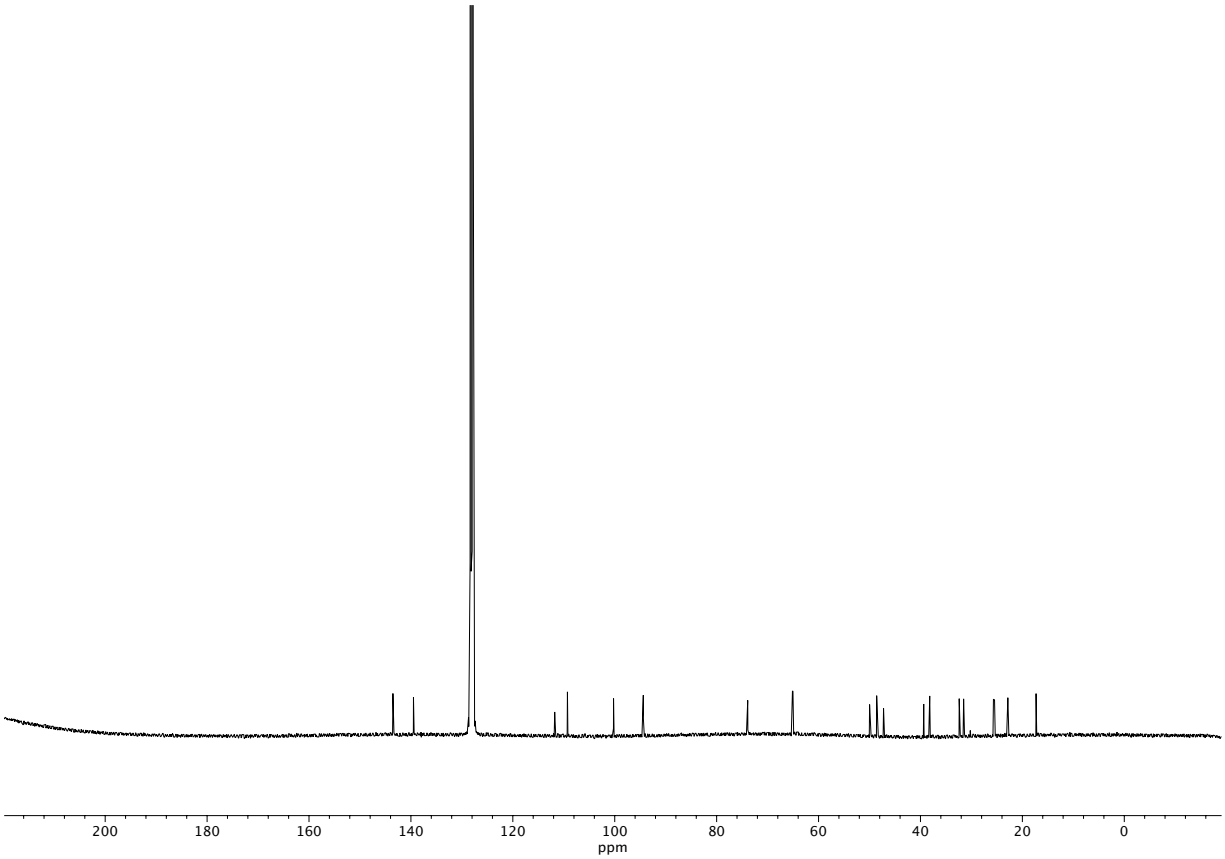


Figure 4.51. ^{13}C NMR (101 MHz, C_6D_6) of compound **130.**

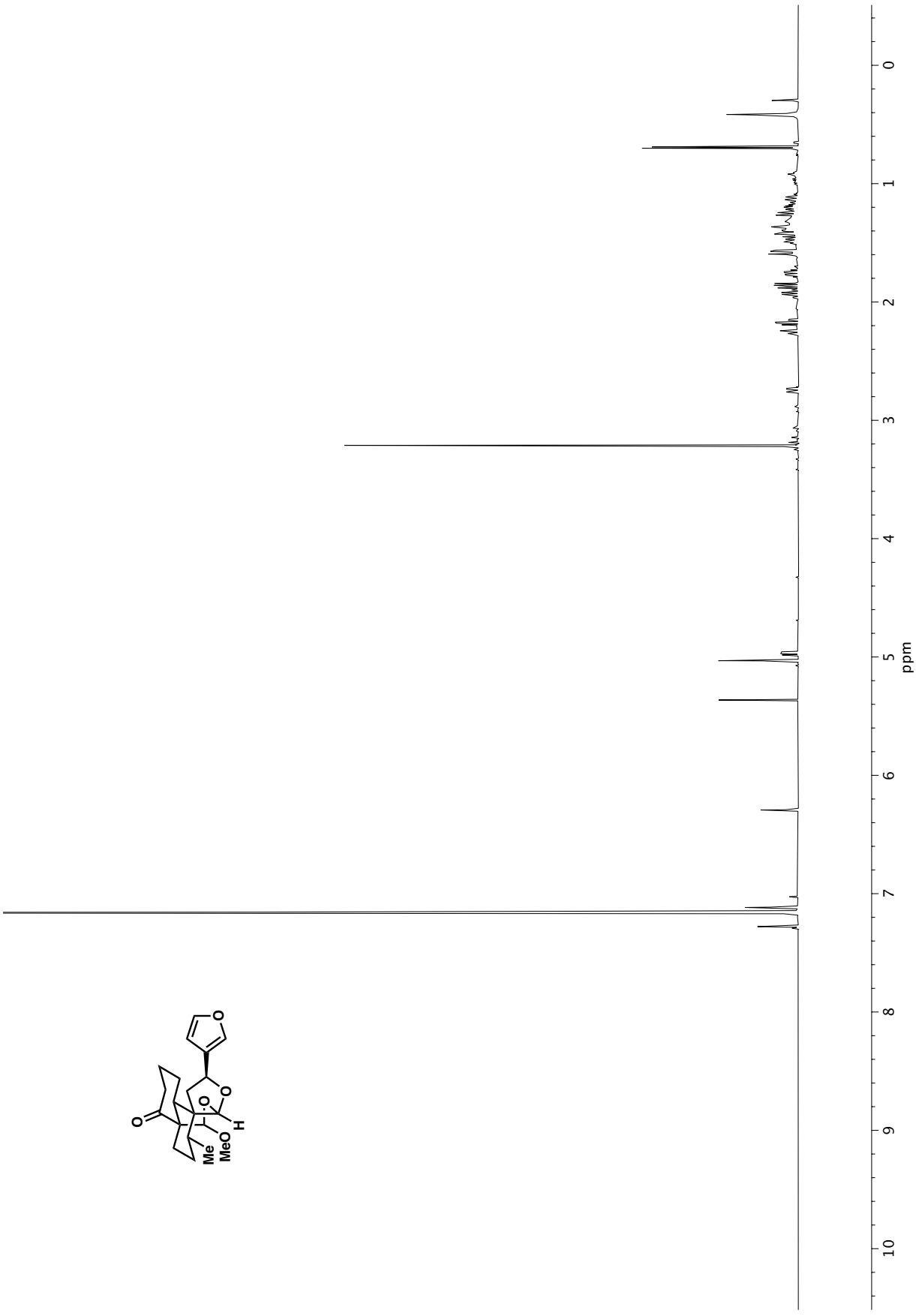


Figure 4.52. ^{1}H NMR (600 MHz, C_6D_6) of compound **131**.

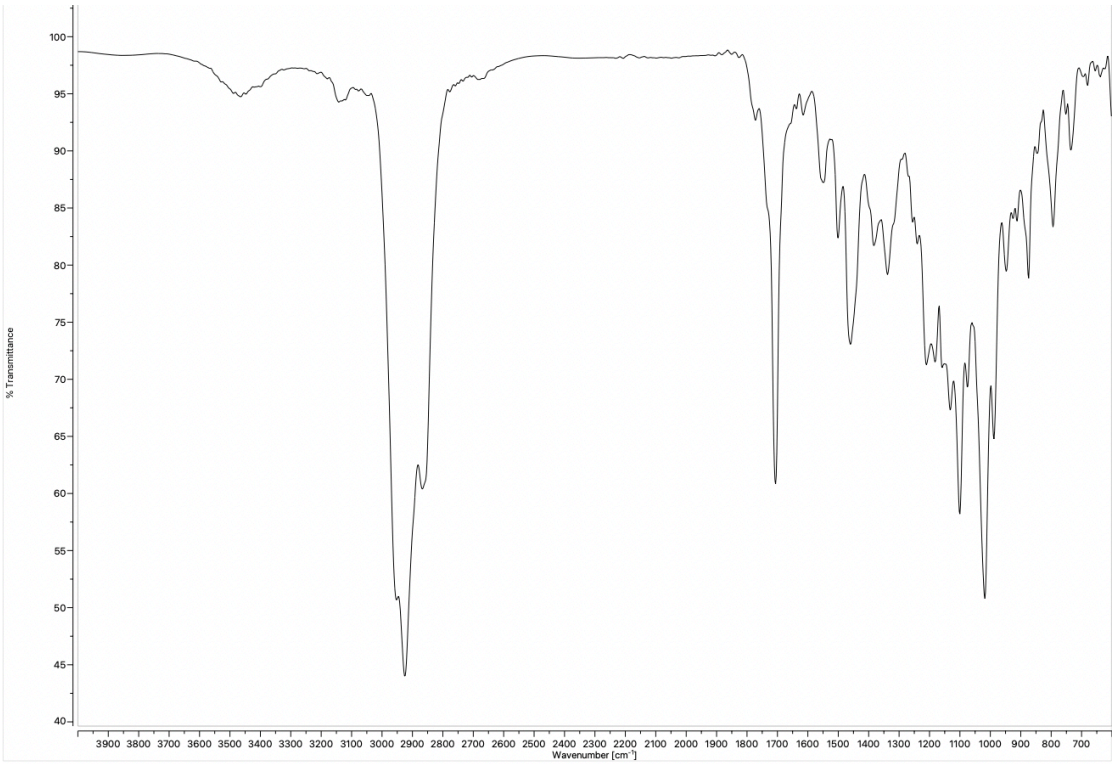


Figure 4.53. Infrared spectrum (Thin Film, NaCl) of compound **131**.

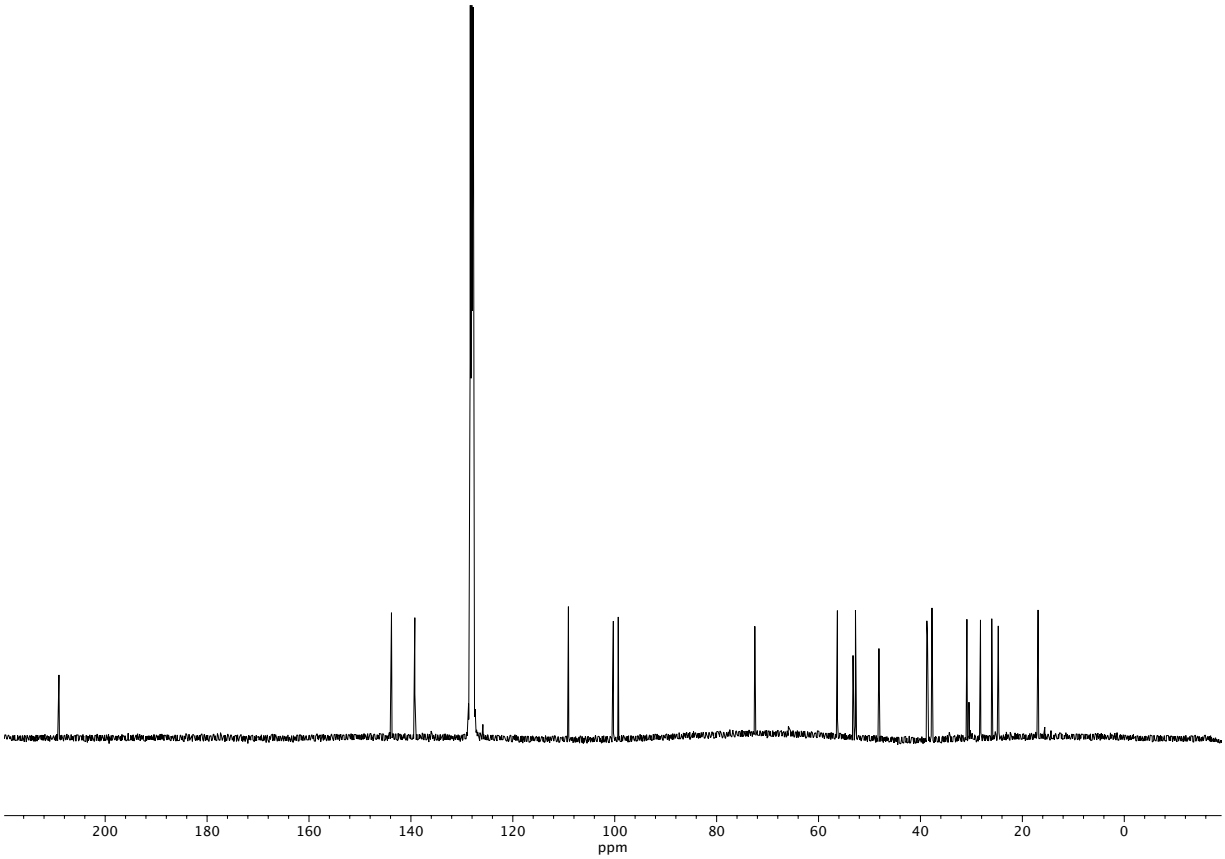


Figure 4.54. ^{13}C NMR (101 MHz, C_6D_6) of compound **131.**

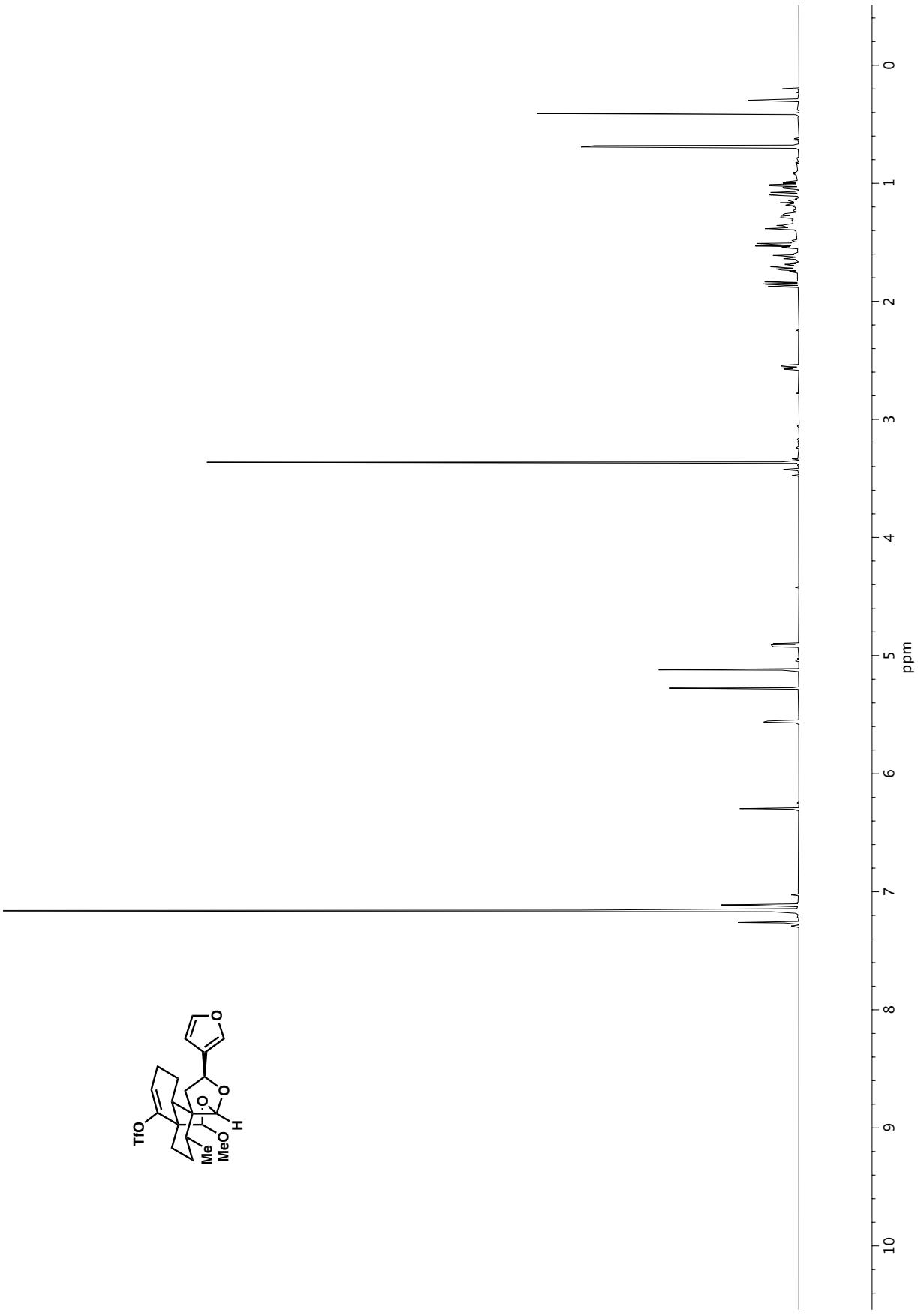


Figure 4.55. ^{1}H NMR (600 MHz, C_6D_6) of compound **132**.

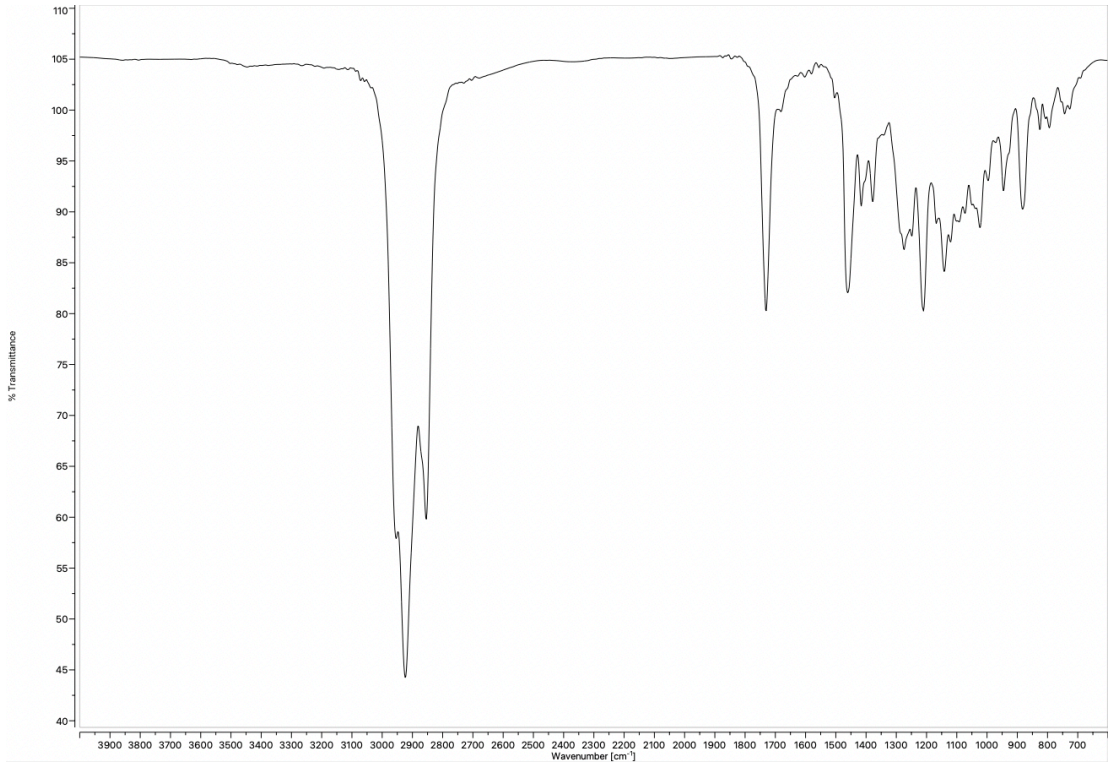


Figure 4.56. Infrared spectrum (Thin Film, NaCl) of compound **132**.

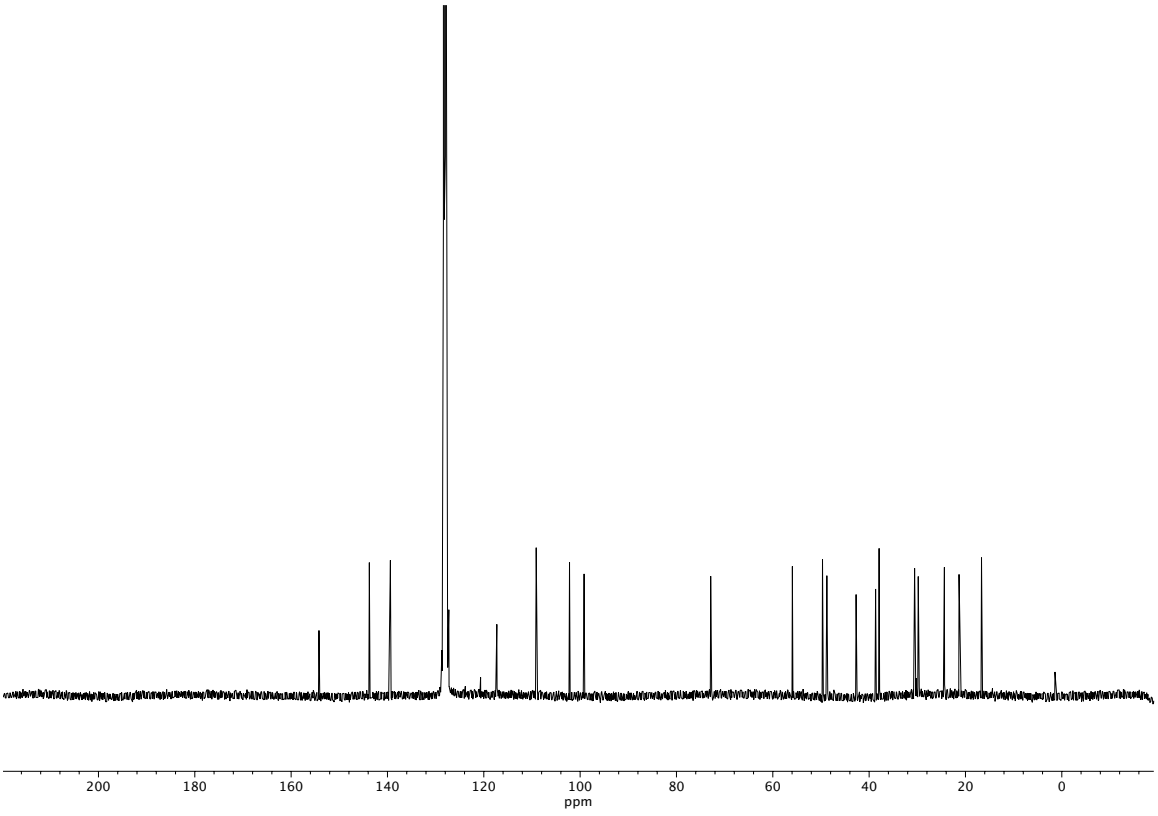


Figure 4.57. ^{13}C NMR (101 MHz, C_6D_6) of compound **132.**

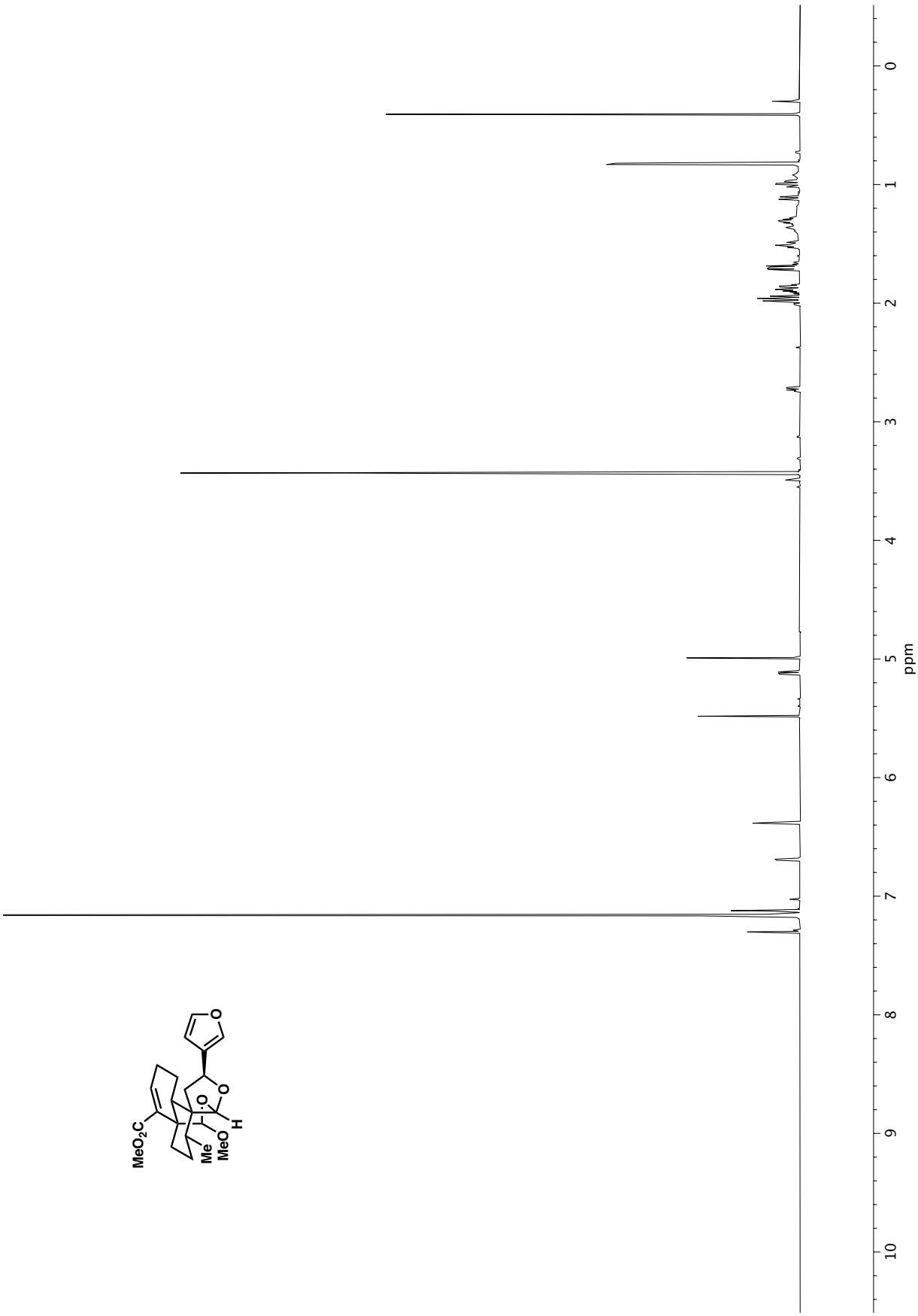


Figure 4.58. ^{1}H NMR (600 MHz, C_6D_6) of compound **133**.

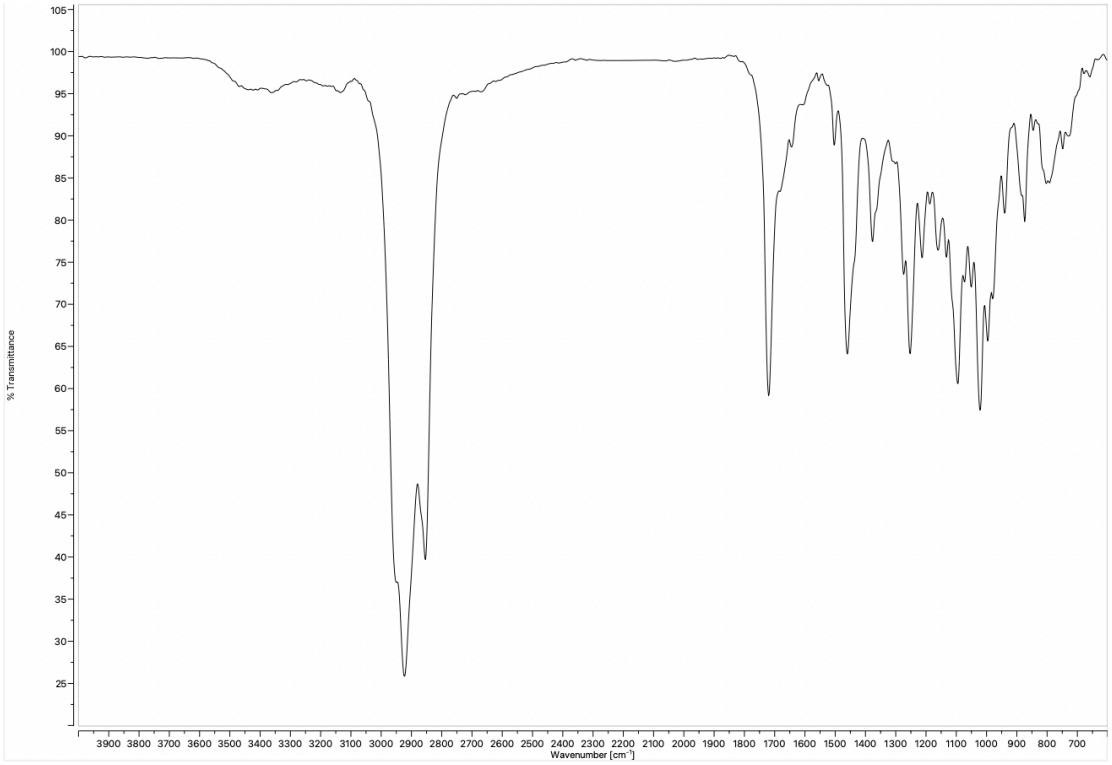


Figure 4.59. Infrared spectrum (Thin Film, NaCl) of compound **133**.

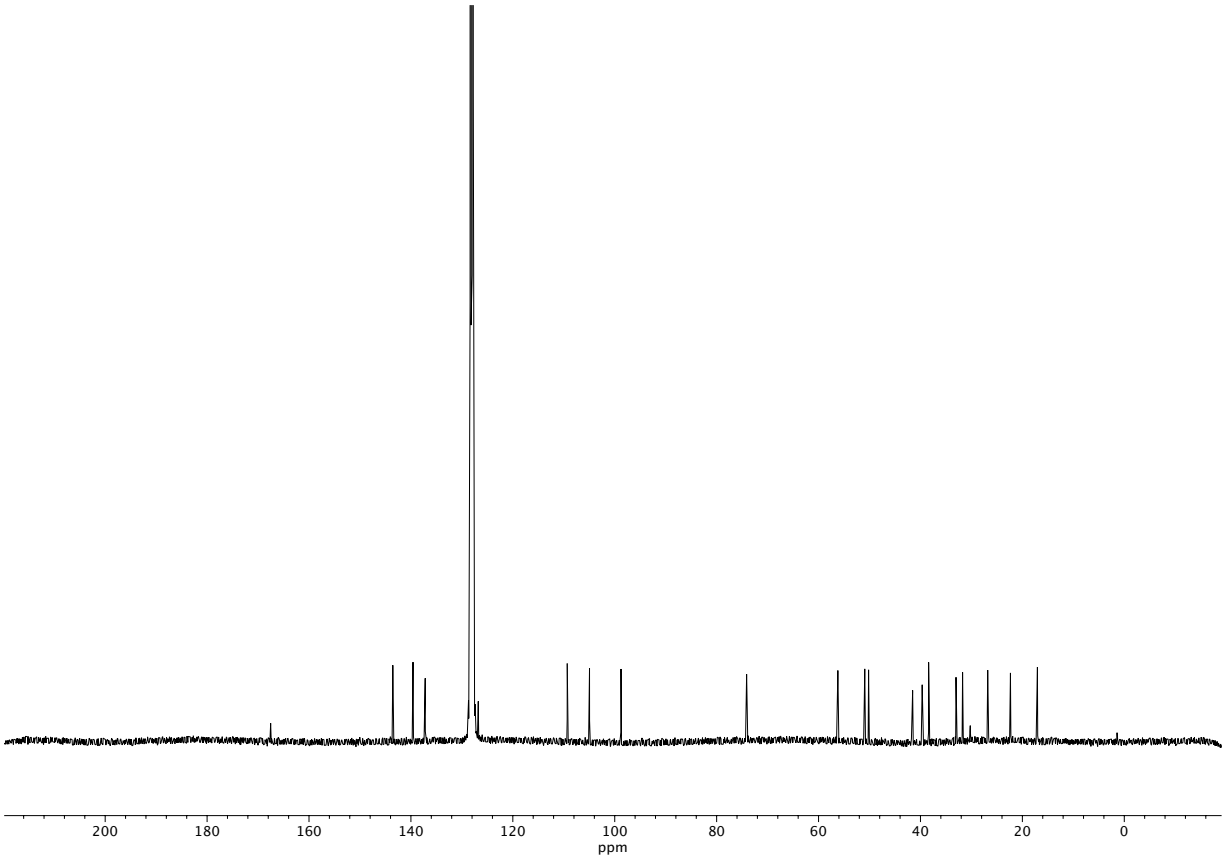


Figure 4.60. ^{13}C NMR (101 MHz, C_6D6) of compound **133.**

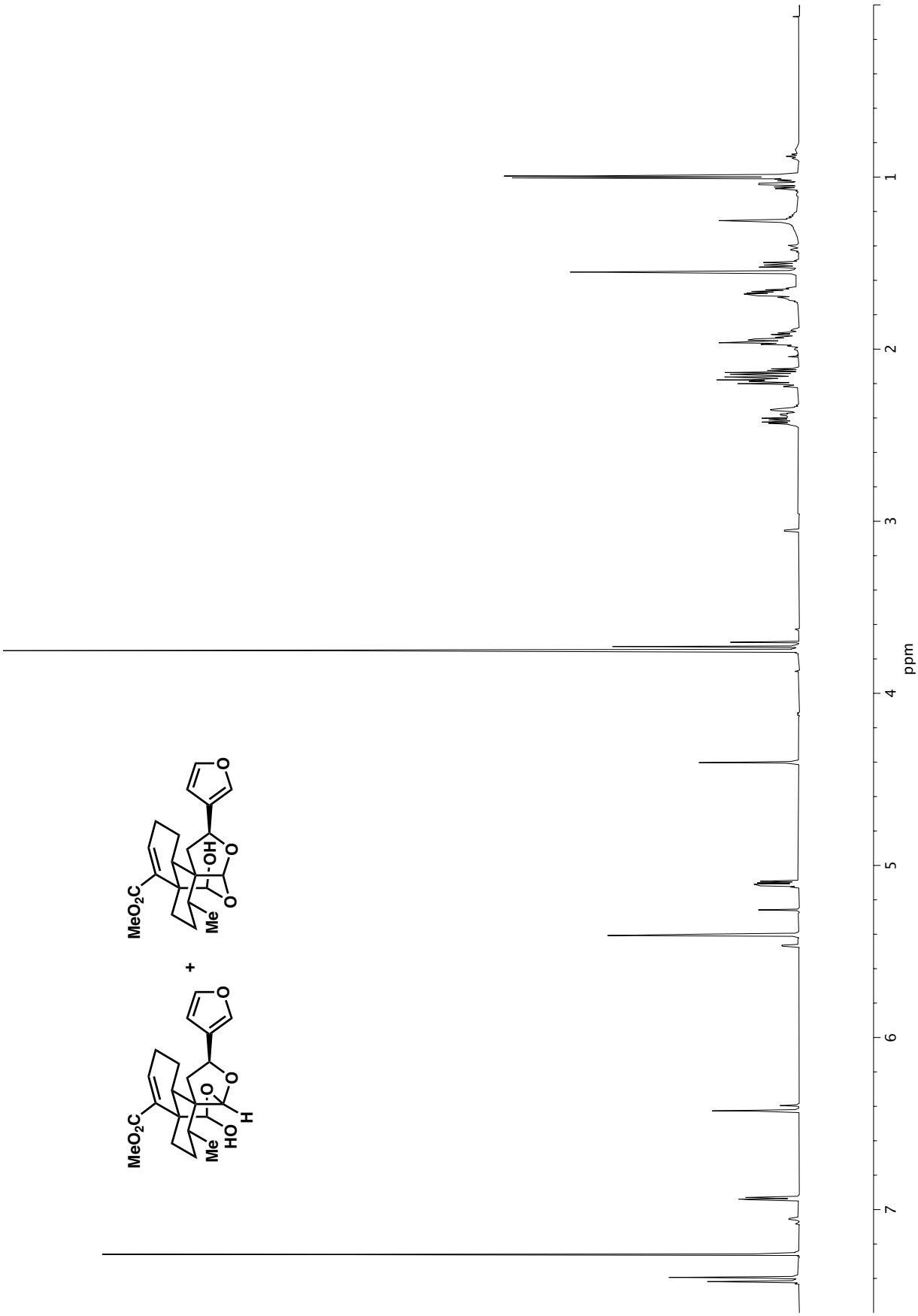


Figure 4.61. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **106**.

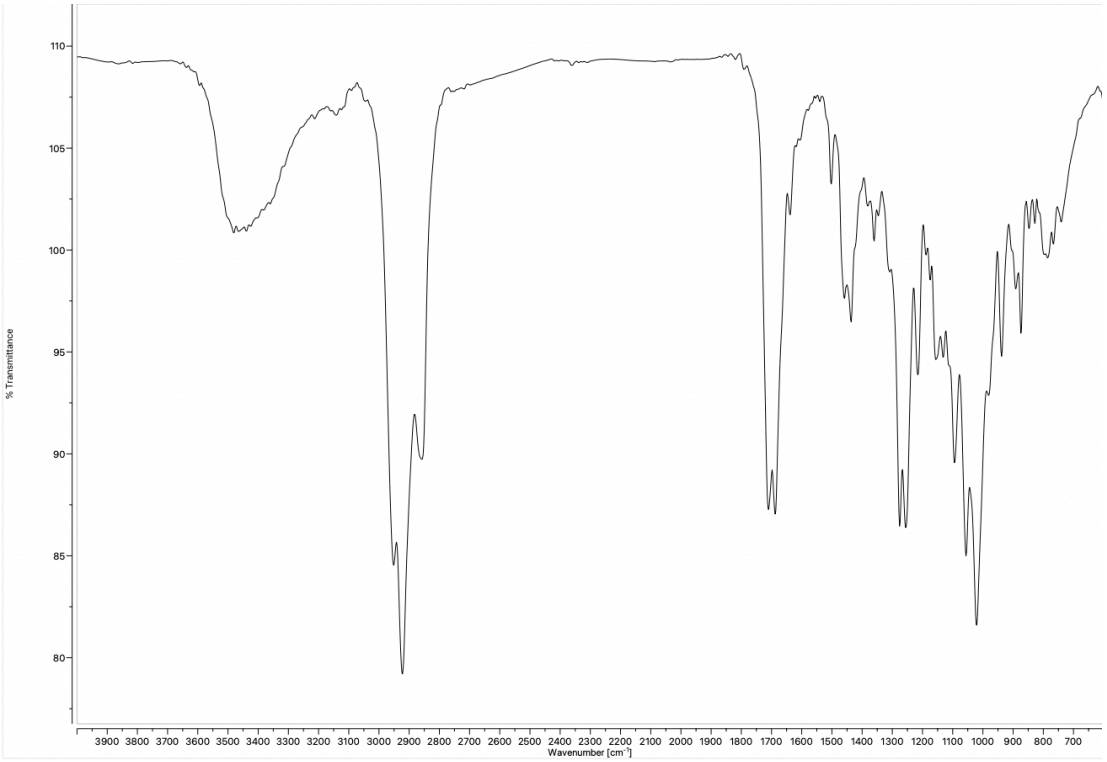


Figure 4.62. Infrared spectrum (Thin Film, NaCl) of compound **106**.

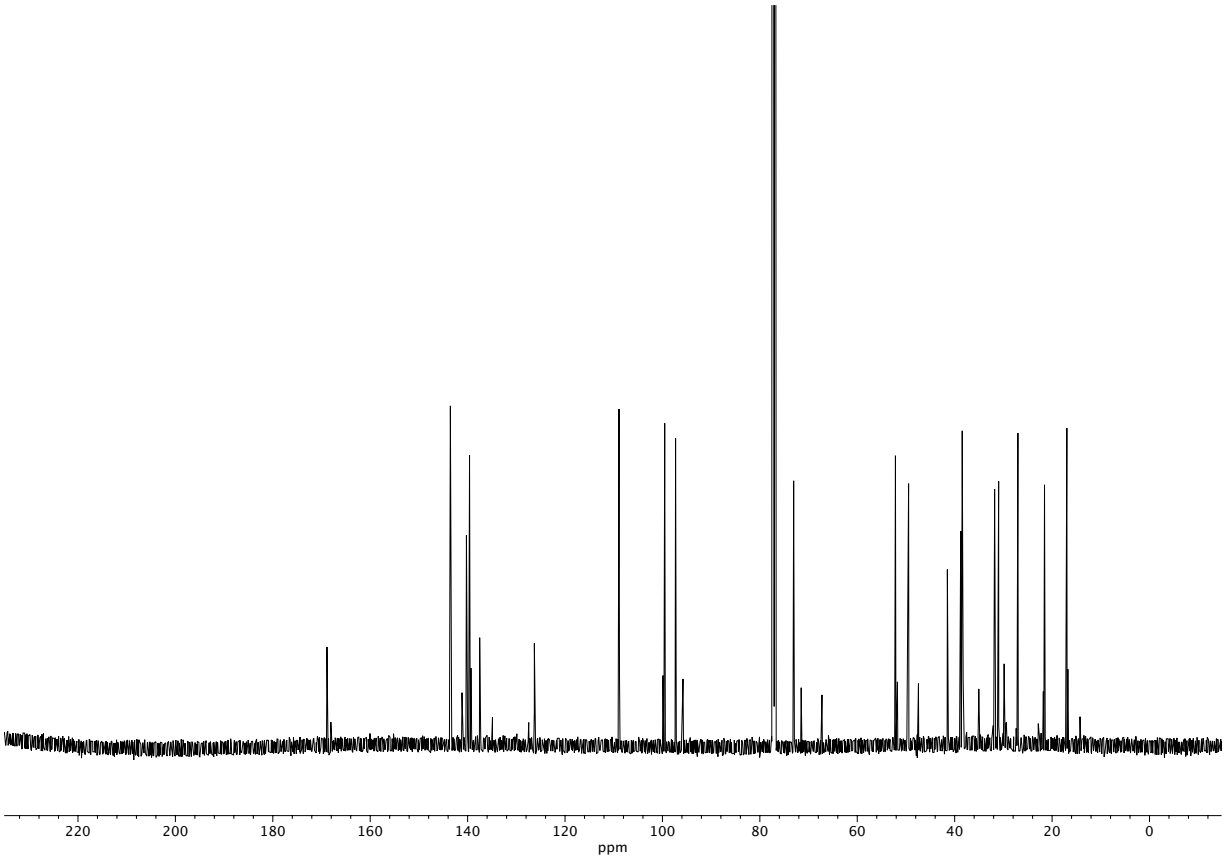


Figure 4.63. ^{13}C NMR (151 MHz, $CDCl_3$) of compound **106.**

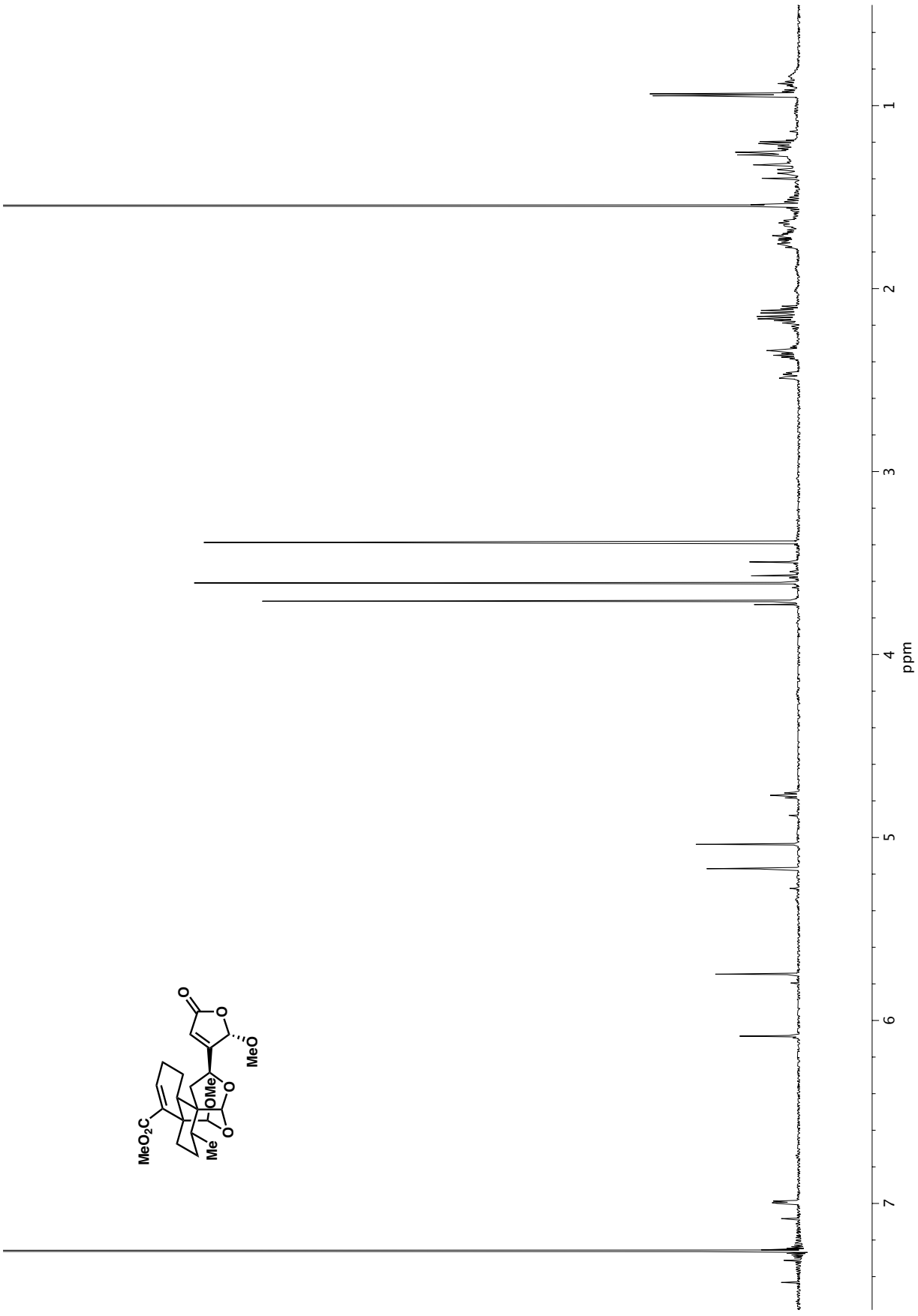


Figure 4.64. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **136**.

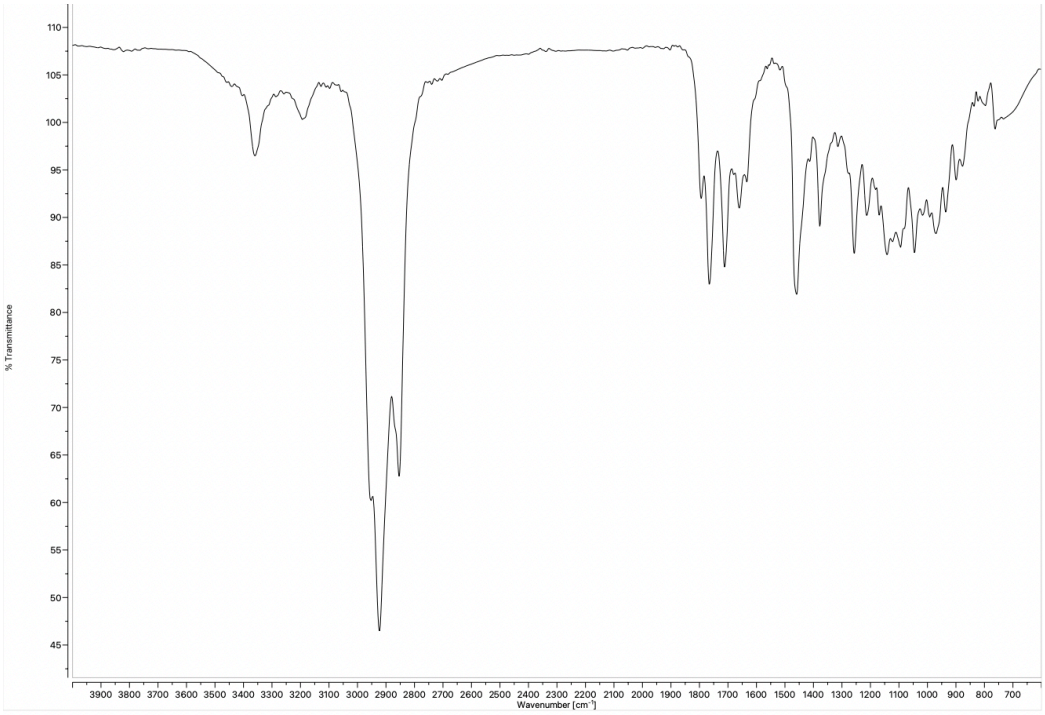


Figure 4.65. Infrared spectrum (Thin Film, NaCl) of compound **136**.

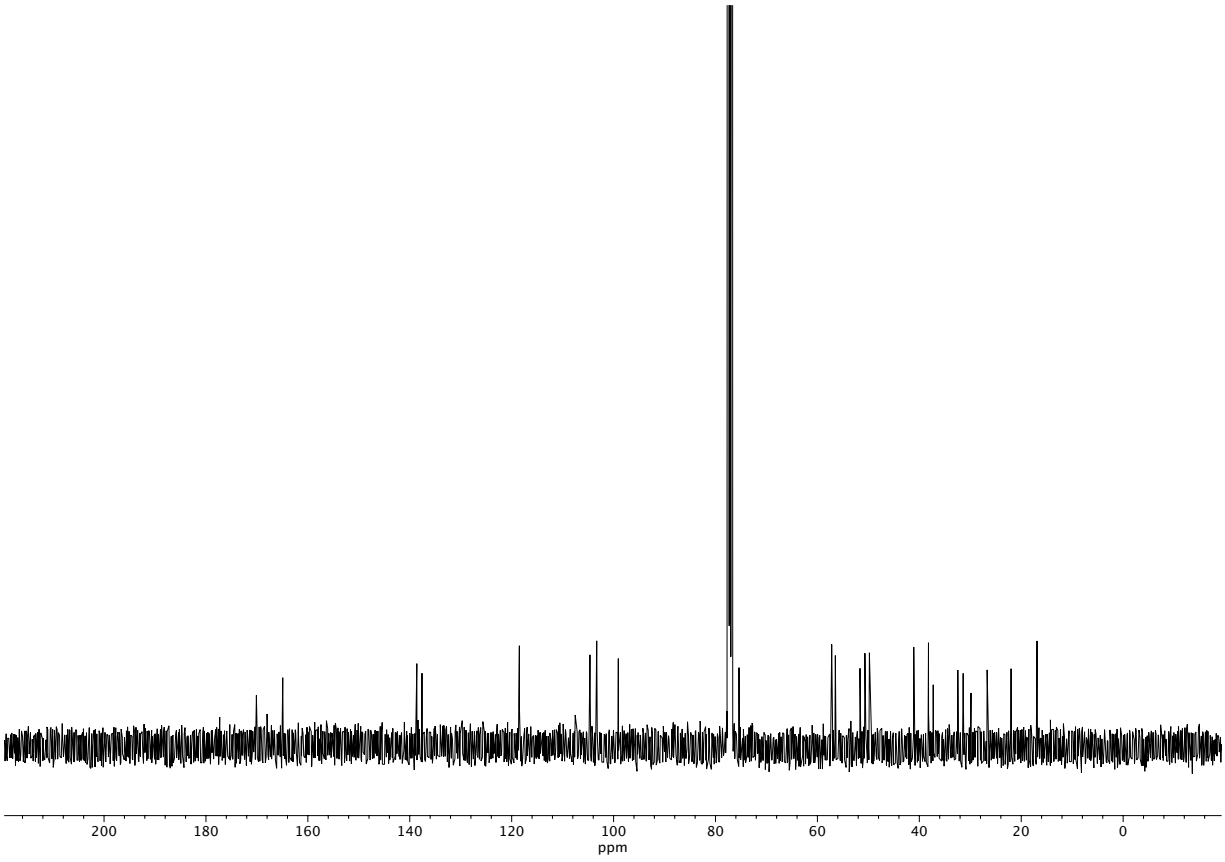


Figure 4.66. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **136.**

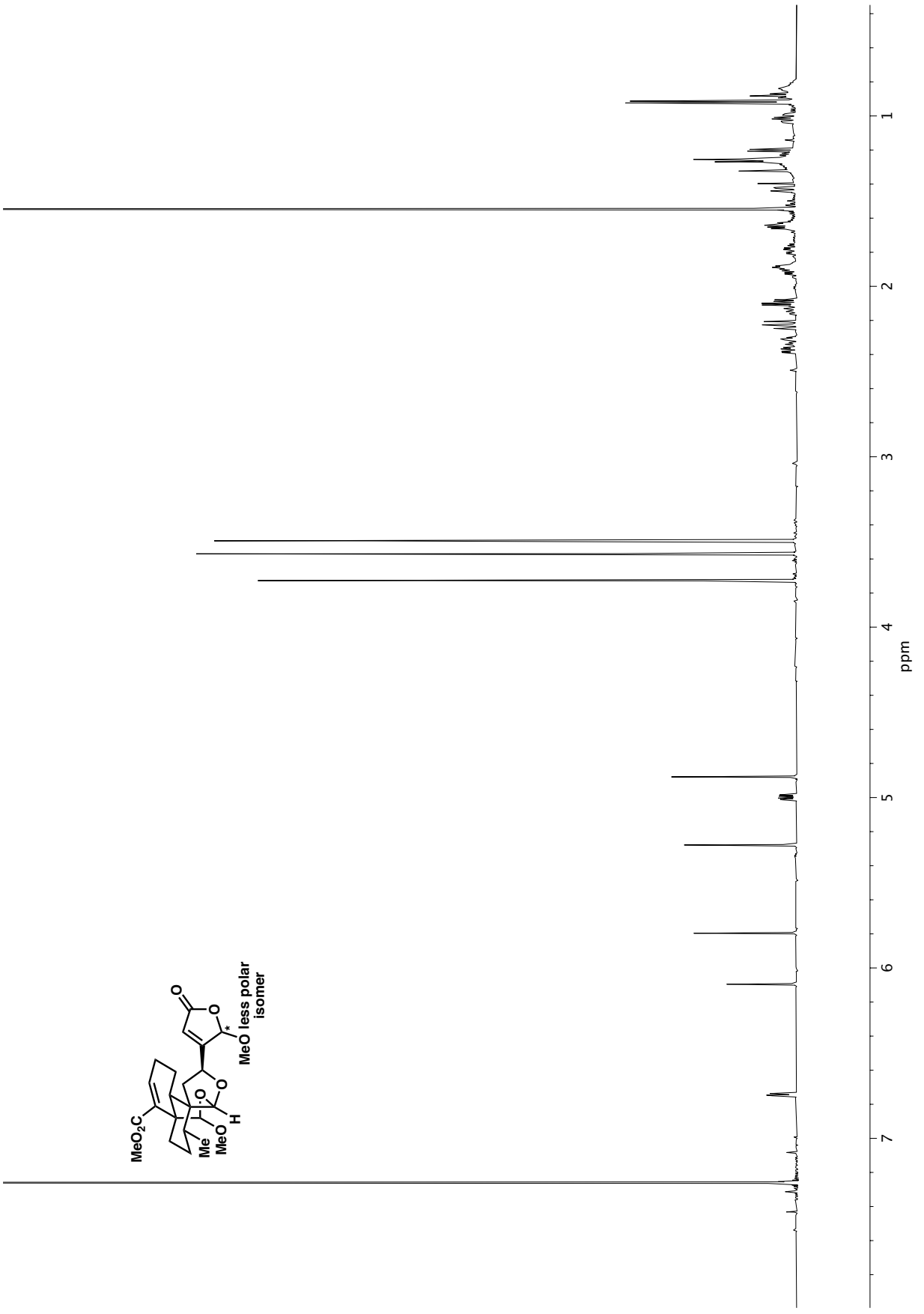


Figure 4.67. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **137**.

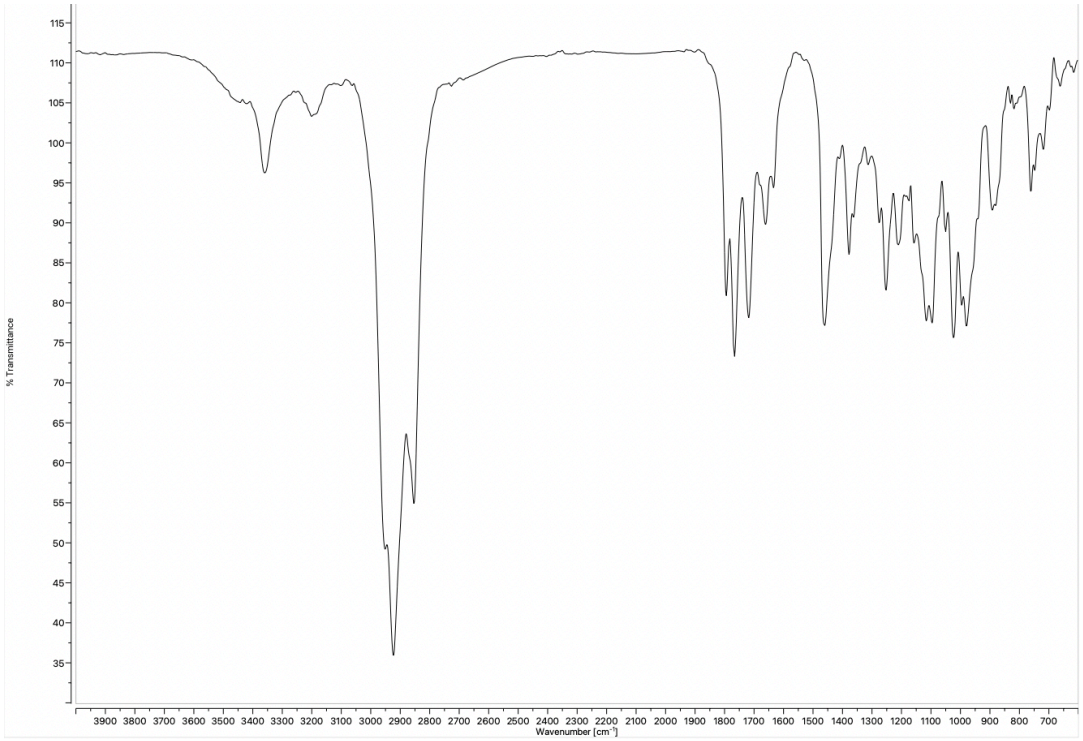


Figure 4.68. Infrared spectrum (Thin Film, NaCl) of compound **137**.

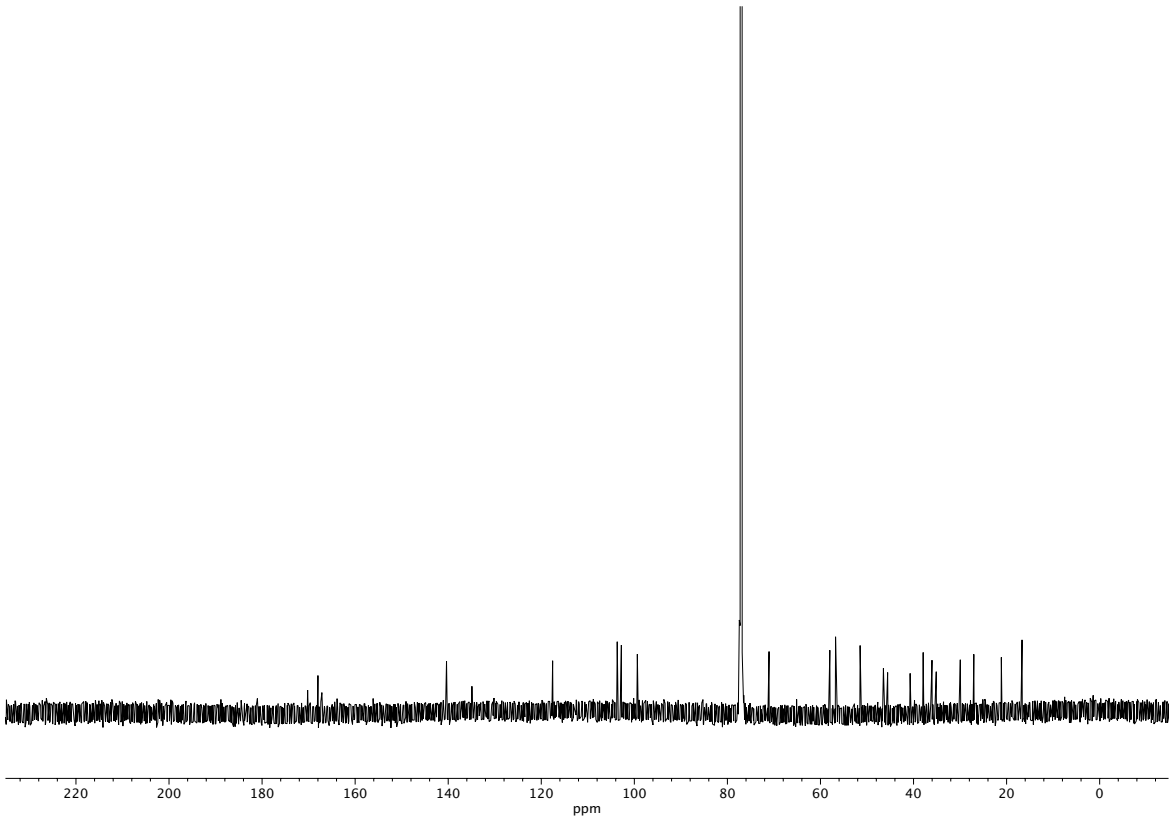


Figure 4.69. ^{13}C NMR (151 MHz, $CDCl_3$) of compound **137.**

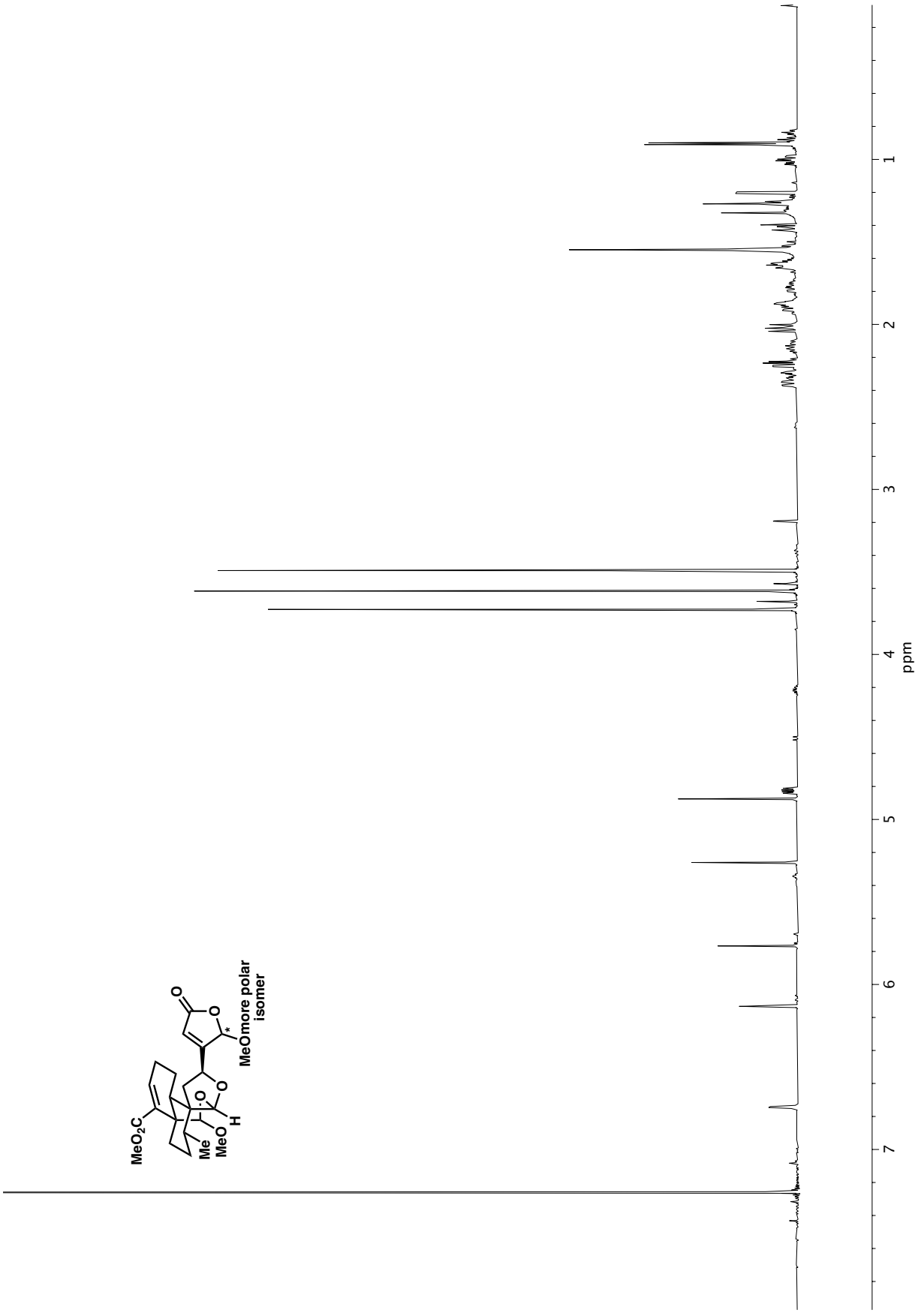


Figure 4.70. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **138**.

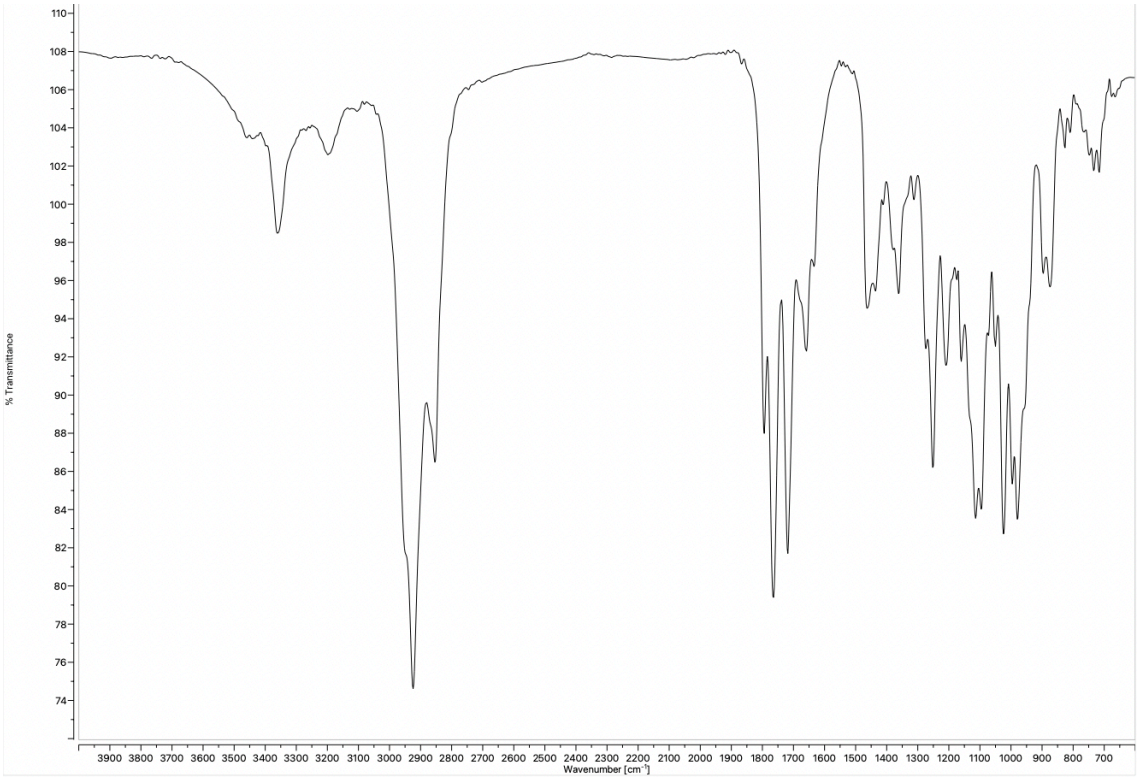


Figure 4.71. Infrared spectrum (Thin Film, NaCl) of compound **138**.

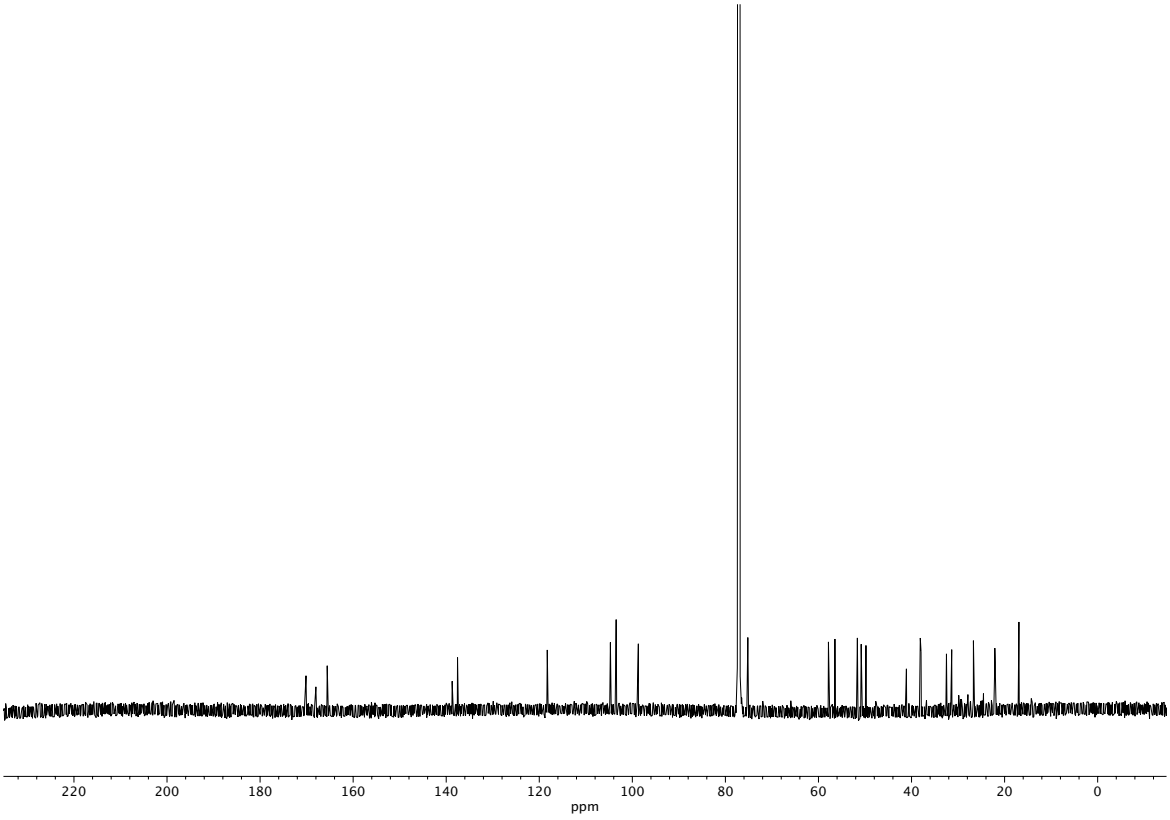


Figure 4.72. ^{13}C NMR (151 MHz, $CDCl_3$) of compound **138.**

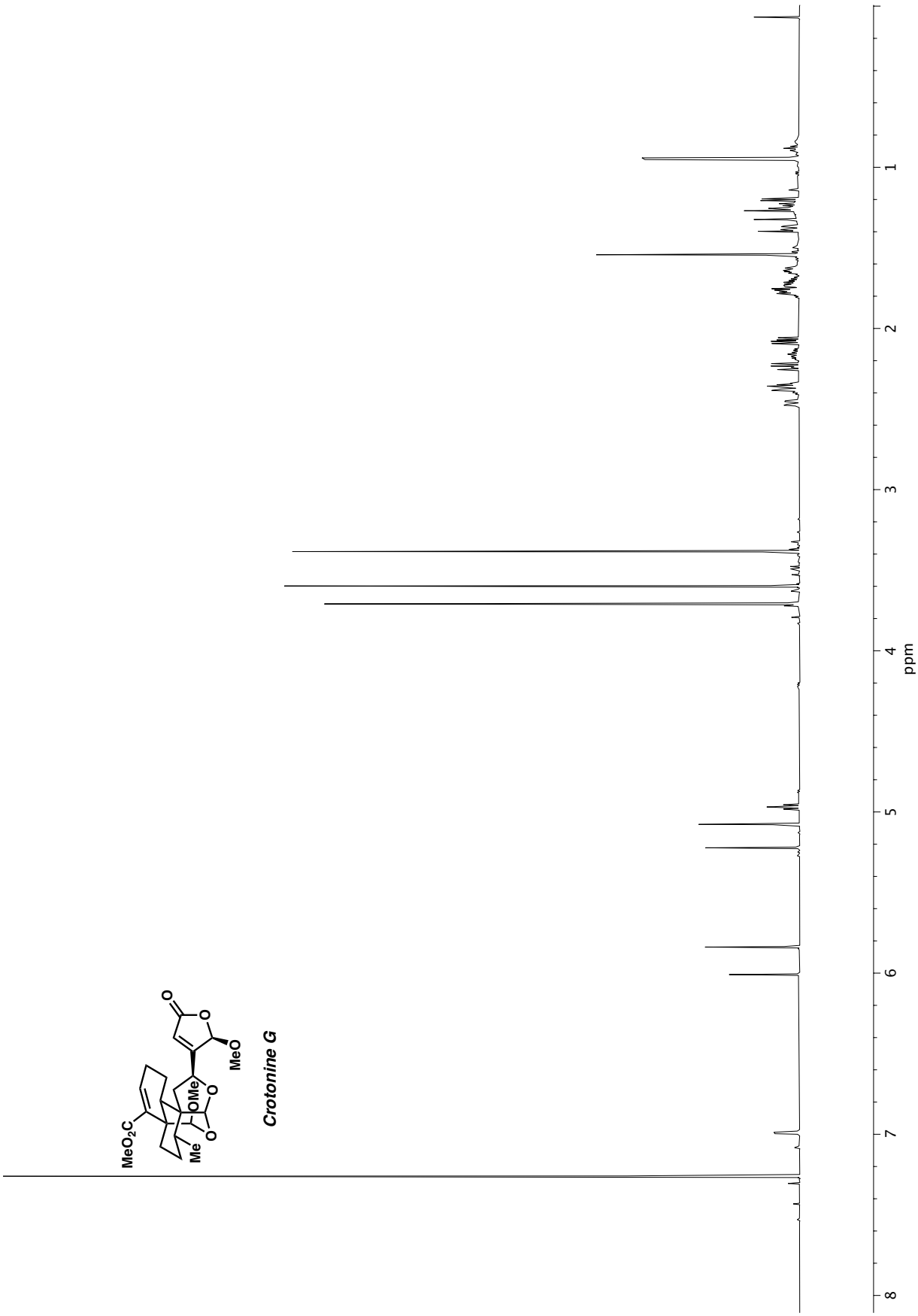


Figure 4.73. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **1**.

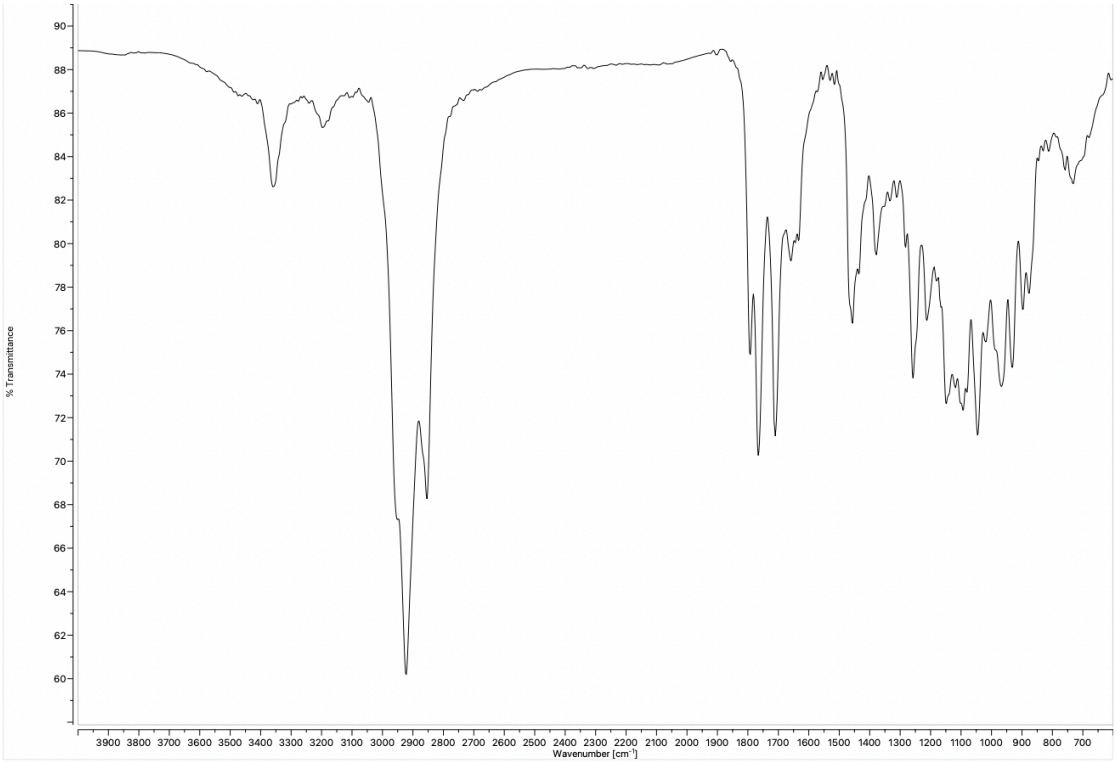


Figure 4.74. Infrared spectrum (Thin Film, NaCl) of compound **1**.

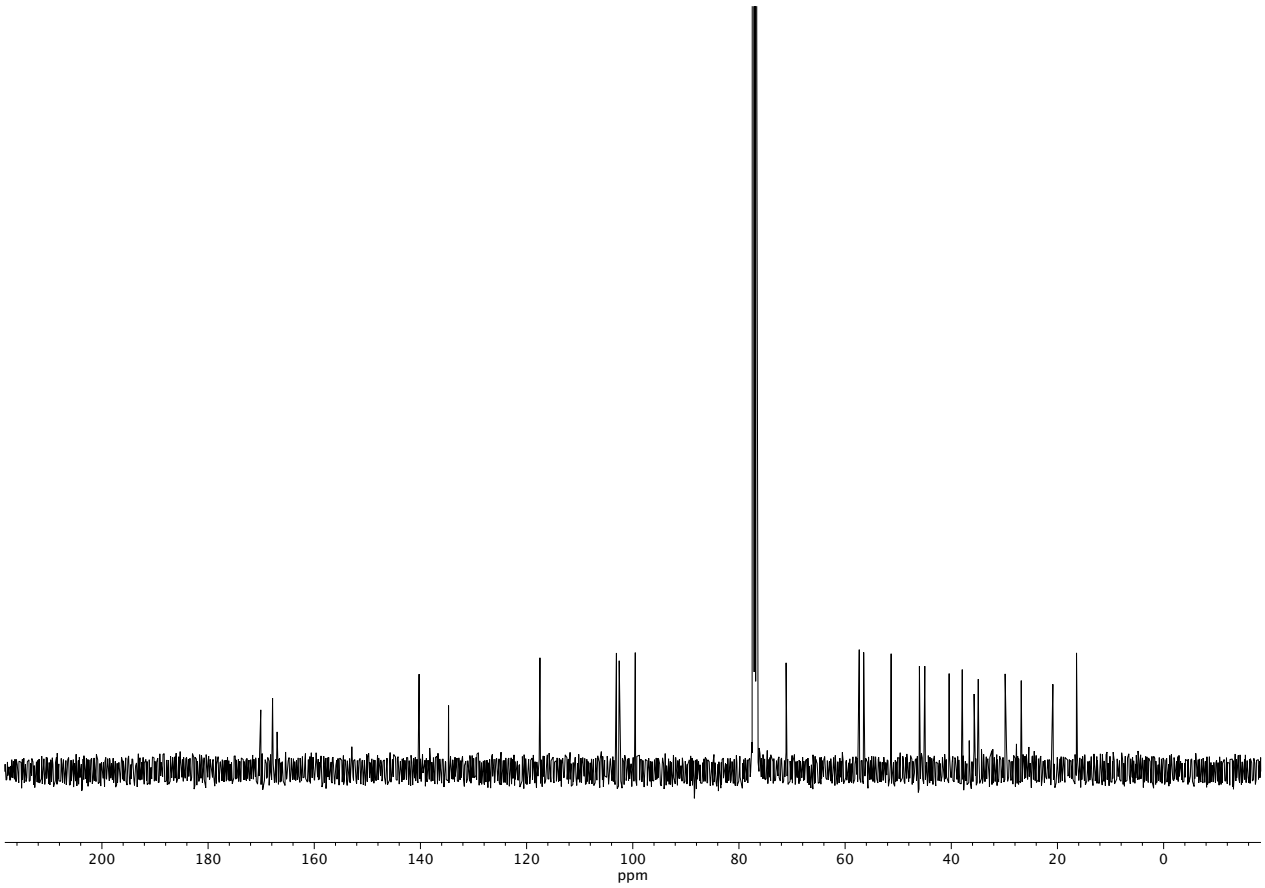


Figure 4.75. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **1.**

APPENDIX 5

X-Ray Crystallography Reports Relevant to Chapter 2:

Total Synthesis of Crotonine G and Crotonolide D

A4.1 GENERAL EXPERIMENTAL INFORMATION

Low-temperature diffraction data (ϕ-and ω-scans) were collected a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON II CPAD detector with Cu *K*a radiation (l = 1.54178 Å) from an IμS micro-source. The structure was solved by direct methods using SHELXS and refined against F^2 on all data by full-matrix least squares with SHELXL-2019 using established refinement techniques. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the *U* value of the atoms they are linked to (1.5 times for methyl groups).

A5.2 X-RAY CRYSTAL STRUCTURE OF COMPOUND 119

Figure A5.2.1 *X-ray crystal structure of compound* ***119***.

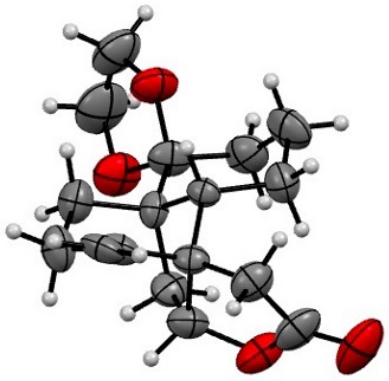


Table A5.2.1. Crystal data and structure refinement for compound **119**.

Empirical formula	C17 H22 O4
Formula weight	290.34
Temperature	200(2) K
Wavelength	1.54178 Å
Crystal system	Orthorhombic

Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.6471(12) Å	a= 90°.
	b = 9.7099(10) Å	b= 90°.
	c = 19.694(2) Å	g = 90°.
Volume	1462.4(3) $Å^3$	
Z	4	
Density (calculated)	1.319 Mg/m^3	
Absorption coefficient	0.755 mm^{-1}	
F(000)	624	
Crystal size	0.150 x 0.100 x 0.100 mm^3	
Theta range for data collection	4.490 to 74.407°.	
Index ranges	-9<=h<=9, -12<=k<=12, -23<=l<=24	
Reflections collected	34947	
Independent reflections	2994 [R(int) = 0.0625]	
Completeness to theta = 67.679°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7538 and 0.6778	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2994 / 1231 / 382	
Goodness-of-fit on F^2	1.063	
Final R indices [I>2sigma(I)]	R1 = 0.0315, wR2 = 0.0789	
R indices (all data)	R1 = 0.0421, wR2 = 0.0887	
Absolute structure parameter	-0.08(11)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.149 and -0.123 $e.Å^{-3}$	

Table A5.2.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for compound **119**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	8275(13)	7008(7)	7668(3)	66(2)
C(1)	9566(13)	7873(9)	7480(5)	68(2)
O(2)	11014(11)	7745(6)	7716(5)	94(2)
C(2)	8927(13)	8905(11)	6972(5)	59(2)
C(3)	7271(16)	8261(11)	6696(6)	39(2)
C(4)	5830(20)	9236(12)	6508(12)	49(3)
C(15)	5880(30)	10610(14)	6471(10)	55(3)
C(5)	4080(18)	8490(14)	6439(8)	62(3)
C(6)	4224(17)	7159(13)	6028(7)	56(3)
C(7)	5859(16)	6302(13)	6205(6)	40(2)
C(8)	7466(15)	7237(12)	6093(7)	35(2)
C(9)	9177(15)	6420(12)	6099(5)	55(2)
C(10)	9137(18)	5216(13)	5613(6)	69(3)
C(11)	7683(18)	4251(17)	5811(11)	62(3)
C(12)	6005(17)	5011(11)	5754(6)	51(3)
O(3)	4397(17)	4291(14)	5848(6)	70(3)
C(16)	4020(20)	3658(16)	5210(7)	94(4)
C(17)	4862(14)	4548(12)	4699(5)	81(3)
O(4)	5996(14)	5453(12)	5047(5)	67(2)
C(13)	6682(13)	7335(11)	7290(5)	52(2)
C(14)	5918(13)	6023(11)	6972(5)	51(2)
O(1A)	7466(11)	6918(7)	7788(3)	60(2)
C(1A)	8874(14)	7739(9)	7730(5)	67(2)
O(2A)	10132(13)	7576(7)	8089(6)	108(3)
C(2A)	8600(13)	8816(11)	7200(6)	62(2)
C(3A)	7031(16)	8269(12)	6794(6)	43(2)
C(4A)	5740(20)	9308(13)	6506(12)	49(3)
C(15A)	6200(30)	10596(13)	6383(11)	58(3)
C(5A)	4070(20)	8674(15)	6285(7)	55(2)
C(6A)	4366(18)	7351(14)	5866(6)	51(2)

C(7A)	5761(17)	6435(13)	6169(6)	40(2)
C(8A)	7500(17)	7223(15)	6223(7)	44(3)
C(9A)	9124(15)	6319(12)	6347(5)	56(2)
C(10A)	9167(16)	5111(13)	5850(5)	61(2)
C(11A)	7491(16)	4248(14)	5926(10)	52(3)
C(12A)	5827(16)	5057(12)	5790(6)	49(3)
O(3A)	4496(18)	4123(13)	6022(6)	63(2)
C(16A)	3860(20)	3389(11)	5443(6)	76(3)
C(17A)	4090(20)	4404(11)	4883(6)	92(4)
O(4A)	5517(15)	5261(11)	5080(5)	65(2)
C(13A)	6108(12)	7328(10)	7314(5)	43(2)
C(14A)	5364(12)	6112(10)	6928(5)	41(2)

Table A5.2.3. Bond lengths [Å] and angles [°] for compound **119**.

O(1)-C(1)	1.347(9)
O(1)-C(13)	1.463(10)
C(1)-O(2)	1.208(8)
C(1)-C(2)	1.499(10)
C(2)-C(3)	1.513(12)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(4)	1.502(12)
C(3)-C(13)	1.542(11)
C(3)-C(8)	1.557(11)
C(4)-C(15)	1.336(13)
C(4)-C(5)	1.525(13)
C(15)-H(15A)	0.9500
C(15)-H(15B)	0.9500
C(5)-C(6)	1.530(13)
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-C(7)	1.542(12)
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(14)	1.534(12)
C(7)-C(12)	1.541(11)
C(7)-C(8)	1.544(12)
C(8)-C(9)	1.530(11)
C(8)-H(8)	1.0000
C(9)-C(10)	1.511(11)
C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(10)-C(11)	1.506(14)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(11)-C(12)	1.485(13)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900

C(12)-O(3)	1.426(12)
C(12)-O(4)	1.457(12)
O(3)-C(16)	1.428(11)
C(16)-C(17)	1.472(13)
C(16)-H(16A)	0.9900
C(16)-H(16B)	0.9900
C(17)-O(4)	1.412(10)
C(17)-H(17A)	0.9900
C(17)-H(17B)	0.9900
C(13)-C(14)	1.535(11)
C(13)-H(13)	1.0000
C(14)-H(14A)	0.9900
C(14)-H(14B)	0.9900
O(1A)-C(1A)	1.345(9)
O(1A)-C(13A)	1.452(9)
C(1A)-O(2A)	1.205(8)
C(1A)-C(2A)	1.493(11)
C(2A)-C(3A)	1.537(11)
C(2A)-H(2A1)	0.9900
C(2A)-H(2A2)	0.9900
C(3A)-C(4A)	1.522(12)
C(3A)-C(13A)	1.544(12)
C(3A)-C(8A)	1.556(12)
C(4A)-C(15A)	1.322(14)
C(4A)-C(5A)	1.482(13)
C(15A)-H(15C)	0.9500
C(15A)-H(15D)	0.9500
C(5A)-C(6A)	1.544(13)
C(5A)-H(5A1)	0.9900
C(5A)-H(5A2)	0.9900
C(6A)-C(7A)	1.511(12)
C(6A)-H(6A1)	0.9900
C(6A)-H(6A2)	0.9900
C(7A)-C(12A)	1.533(12)
C(7A)-C(8A)	1.538(13)
C(7A)-C(14A)	1.557(12)

C(8A)-C(9A)	1.541(12)
C(8A)-H(8A)	1.0000
C(9A)-C(10A)	1.527(11)
C(9A)-H(9A1)	0.9900
C(9A)-H(9A2)	0.9900
C(10A)-C(11A)	1.539(12)
C(10A)-H(10C)	0.9900
C(10A)-H(10D)	0.9900
C(11A)-C(12A)	1.519(12)
C(11A)-H(11C)	0.9900
C(11A)-H(11D)	0.9900
C(12A)-O(4A)	1.432(11)
C(12A)-O(3A)	1.437(13)
O(3A)-C(16A)	1.430(11)
C(16A)-C(17A)	1.488(11)
C(16A)-H(16C)	0.9900
C(16A)-H(16D)	0.9900
C(17A)-O(4A)	1.427(10)
C(17A)-H(17C)	0.9900
C(17A)-H(17D)	0.9900
C(13A)-C(14A)	1.515(10)
C(13A)-H(13A)	1.0000
C(14A)-H(14C)	0.9900
C(14A)-H(14D)	0.9900

C(1)-O(1)-C(13)	109.6(6)
O(2)-C(1)-O(1)	120.2(7)
O(2)-C(1)-C(2)	128.6(8)
O(1)-C(1)-C(2)	111.2(6)
C(1)-C(2)-C(3)	103.7(7)
C(1)-C(2)-H(2A)	111.0
C(3)-C(2)-H(2A)	111.0
C(1)-C(2)-H(2B)	111.0
C(3)-C(2)-H(2B)	111.0
H(2A)-C(2)-H(2B)	109.0
C(4)-C(3)-C(2)	116.4(9)

C(4)-C(3)-C(13)	109.9(11)
C(2)-C(3)-C(13)	102.3(7)
C(4)-C(3)-C(8)	106.5(10)
C(2)-C(3)-C(8)	117.2(9)
C(13)-C(3)-C(8)	103.5(8)
C(15)-C(4)-C(3)	128.3(13)
C(15)-C(4)-C(5)	119.8(13)
C(3)-C(4)-C(5)	111.5(9)
C(4)-C(15)-H(15A)	120.0
C(4)-C(15)-H(15B)	120.0
H(15A)-C(15)-H(15B)	120.0
C(4)-C(5)-C(6)	112.7(12)
C(4)-C(5)-H(5A)	109.1
C(6)-C(5)-H(5A)	109.1
C(4)-C(5)-H(5B)	109.1
C(6)-C(5)-H(5B)	109.1
H(5A)-C(5)-H(5B)	107.8
C(5)-C(6)-C(7)	113.2(10)
C(5)-C(6)-H(6A)	108.9
C(7)-C(6)-H(6A)	108.9
C(5)-C(6)-H(6B)	108.9
C(7)-C(6)-H(6B)	108.9
H(6A)-C(6)-H(6B)	107.8
C(14)-C(7)-C(12)	114.9(10)
C(14)-C(7)-C(6)	110.0(9)
C(12)-C(7)-C(6)	111.5(9)
C(14)-C(7)-C(8)	102.8(9)
C(12)-C(7)-C(8)	109.8(9)
C(6)-C(7)-C(8)	107.2(10)
C(9)-C(8)-C(7)	112.0(9)
C(9)-C(8)-C(3)	114.1(9)
C(7)-C(8)-C(3)	101.0(8)
C(9)-C(8)-H(8)	109.8
C(7)-C(8)-H(8)	109.8
C(3)-C(8)-H(8)	109.8
C(10)-C(9)-C(8)	112.3(9)

C(10)-C(9)-H(9A)	109.1
C(8)-C(9)-H(9A)	109.1
C(10)-C(9)-H(9B)	109.1
C(8)-C(9)-H(9B)	109.1
H(9A)-C(9)-H(9B)	107.9
C(11)-C(10)-C(9)	109.4(10)
C(11)-C(10)-H(10A)	109.8
C(9)-C(10)-H(10A)	109.8
C(11)-C(10)-H(10B)	109.8
C(9)-C(10)-H(10B)	109.8
H(10A)-C(10)-H(10B)	108.2
C(12)-C(11)-C(10)	108.0(12)
C(12)-C(11)-H(11A)	110.1
C(10)-C(11)-H(11A)	110.1
C(12)-C(11)-H(11B)	110.1
C(10)-C(11)-H(11B)	110.1
H(11A)-C(11)-H(11B)	108.4
O(3)-C(12)-O(4)	105.4(8)
O(3)-C(12)-C(11)	119.4(11)
O(4)-C(12)-C(11)	102.9(11)
O(3)-C(12)-C(7)	105.1(10)
O(4)-C(12)-C(7)	108.1(9)
C(11)-C(12)-C(7)	115.0(10)
C(12)-O(3)-C(16)	105.6(9)
O(3)-C(16)-C(17)	105.1(8)
O(3)-C(16)-H(16A)	110.7
C(17)-C(16)-H(16A)	110.7
O(3)-C(16)-H(16B)	110.7
C(17)-C(16)-H(16B)	110.7
H(16A)-C(16)-H(16B)	108.8
O(4)-C(17)-C(16)	107.6(8)
O(4)-C(17)-H(17A)	110.2
C(16)-C(17)-H(17A)	110.2
O(4)-C(17)-H(17B)	110.2
C(16)-C(17)-H(17B)	110.2
H(17A)-C(17)-H(17B)	108.5

C(17)-O(4)-C(12)	106.4(8)
O(1)-C(13)-C(14)	110.2(8)
O(1)-C(13)-C(3)	105.6(6)
C(14)-C(13)-C(3)	106.6(8)
O(1)-C(13)-H(13)	111.4
C(14)-C(13)-H(13)	111.4
C(3)-C(13)-H(13)	111.4
C(7)-C(14)-C(13)	105.4(8)
C(7)-C(14)-H(14A)	110.7
C(13)-C(14)-H(14A)	110.7
C(7)-C(14)-H(14B)	110.7
C(13)-C(14)-H(14B)	110.7
H(14A)-C(14)-H(14B)	108.8
C(1A)-O(1A)-C(13A)	110.8(6)
O(2A)-C(1A)-O(1A)	120.8(8)
O(2A)-C(1A)-C(2A)	128.0(9)
O(1A)-C(1A)-C(2A)	111.3(6)
C(1A)-C(2A)-C(3A)	103.4(7)
C(1A)-C(2A)-H(2A1)	111.1
C(3A)-C(2A)-H(2A1)	111.1
C(1A)-C(2A)-H(2A2)	111.1
C(3A)-C(2A)-H(2A2)	111.1
H(2A1)-C(2A)-H(2A2)	109.1
C(4A)-C(3A)-C(2A)	118.1(10)
C(4A)-C(3A)-C(13A)	110.0(11)
C(2A)-C(3A)-C(13A)	102.5(8)
C(4A)-C(3A)-C(8A)	108.3(11)
C(2A)-C(3A)-C(8A)	114.9(9)
C(13A)-C(3A)-C(8A)	101.5(9)
C(15A)-C(4A)-C(5A)	124.7(13)
C(15A)-C(4A)-C(3A)	121.5(13)
C(5A)-C(4A)-C(3A)	113.1(10)
C(4A)-C(15A)-H(15C)	120.0
C(4A)-C(15A)-H(15D)	120.0
H(15C)-C(15A)-H(15D)	120.0
C(4A)-C(5A)-C(6A)	112.2(13)

C(4A)-C(5A)-H(5A1)	109.2
C(6A)-C(5A)-H(5A1)	109.2
C(4A)-C(5A)-H(5A2)	109.2
C(6A)-C(5A)-H(5A2)	109.2
H(5A1)-C(5A)-H(5A2)	107.9
C(7A)-C(6A)-C(5A)	112.4(9)
C(7A)-C(6A)-H(6A1)	109.1
C(5A)-C(6A)-H(6A1)	109.1
C(7A)-C(6A)-H(6A2)	109.1
C(5A)-C(6A)-H(6A2)	109.1
H(6A1)-C(6A)-H(6A2)	107.8
C(6A)-C(7A)-C(12A)	110.2(9)
C(6A)-C(7A)-C(8A)	110.2(10)
C(12A)-C(7A)-C(8A)	116.1(10)
C(6A)-C(7A)-C(14A)	111.1(9)
C(12A)-C(7A)-C(14A)	107.3(9)
C(8A)-C(7A)-C(14A)	101.7(8)
C(7A)-C(8A)-C(9A)	115.1(11)
C(7A)-C(8A)-C(3A)	100.1(9)
C(9A)-C(8A)-C(3A)	116.3(9)
C(7A)-C(8A)-H(8A)	108.3
C(9A)-C(8A)-H(8A)	108.3
C(3A)-C(8A)-H(8A)	108.3
C(10A)-C(9A)-C(8A)	110.7(9)
C(10A)-C(9A)-H(9A1)	109.5
C(8A)-C(9A)-H(9A1)	109.5
C(10A)-C(9A)-H(9A2)	109.5
C(8A)-C(9A)-H(9A2)	109.5
H(9A1)-C(9A)-H(9A2)	108.1
C(9A)-C(10A)-C(11A)	109.8(10)
C(9A)-C(10A)-H(10C)	109.7
C(11A)-C(10A)-H(10C)	109.7
C(9A)-C(10A)-H(10D)	109.7
C(11A)-C(10A)-H(10D)	109.7
H(10C)-C(10A)-H(10D)	108.2
C(12A)-C(11A)-C(10A)	113.5(10)

C(12A)-C(11A)-H(11C)	108.9
C(10A)-C(11A)-H(11C)	108.9
C(12A)-C(11A)-H(11D)	108.9
C(10A)-C(11A)-H(11D)	108.9
H(11C)-C(11A)-H(11D)	107.7
O(4A)-C(12A)-O(3A)	106.2(8)
O(4A)-C(12A)-C(11A)	112.4(11)
O(3A)-C(12A)-C(11A)	102.2(10)
O(4A)-C(12A)-C(7A)	110.4(9)
O(3A)-C(12A)-C(7A)	111.9(10)
C(11A)-C(12A)-C(7A)	113.2(10)
C(16A)-O(3A)-C(12A)	107.6(9)
O(3A)-C(16A)-C(17A)	102.8(8)
O(3A)-C(16A)-H(16C)	111.2
C(17A)-C(16A)-H(16C)	111.2
O(3A)-C(16A)-H(16D)	111.2
C(17A)-C(16A)-H(16D)	111.2
H(16C)-C(16A)-H(16D)	109.1
O(4A)-C(17A)-C(16A)	105.9(8)
O(4A)-C(17A)-H(17C)	110.6
C(16A)-C(17A)-H(17C)	110.6
O(4A)-C(17A)-H(17D)	110.6
C(16A)-C(17A)-H(17D)	110.6
H(17C)-C(17A)-H(17D)	108.7
C(17A)-O(4A)-C(12A)	108.1(8)
O(1A)-C(13A)-C(14A)	112.2(7)
O(1A)-C(13A)-C(3A)	105.2(6)
C(14A)-C(13A)-C(3A)	107.4(8)
O(1A)-C(13A)-H(13A)	110.6
C(14A)-C(13A)-H(13A)	110.6
C(3A)-C(13A)-H(13A)	110.6
C(13A)-C(14A)-C(7A)	104.6(7)
C(13A)-C(14A)-H(14C)	110.8
C(7A)-C(14A)-H(14C)	110.8
C(13A)-C(14A)-H(14D)	110.8
C(7A)-C(14A)-H(14D)	110.8

H(14C)-C(14A)-H(14D) 108.9

Symmetry transformations used to generate equivalent atoms:

Table A5.2.4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for compound **119**. 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)	85(4)	60(3)	53(3)	9(2)	-25(3)	-14(3)
C(1)	80(4)	63(3)	60(4)	-5(3)	-30(3)	-13(3)
O(2)	94(4)	90(3)	99(5)	-9(3)	-56(4)	-5(3)
C(2)	66(4)	52(3)	59(4)	-4(3)	-12(3)	-10(3)
C(3)	49(4)	36(3)	34(3)	3(2)	4(3)	-3(2)
C(4)	61(5)	45(4)	41(7)	-8(4)	12(4)	-4(4)
C(15)	71(6)	53(4)	40(4)	-7(3)	23(5)	7(3)
C(5)	49(4)	55(4)	80(8)	1(4)	1(4)	11(3)
C(6)	47(3)	53(4)	68(7)	2(4)	-9(4)	2(3)
C(7)	34(3)	36(3)	49(4)	4(3)	-4(3)	2(2)
C(8)	40(3)	32(3)	34(4)	-2(2)	3(2)	0(2)
C(9)	45(3)	57(3)	64(5)	-3(4)	3(4)	5(2)
C(10)	77(4)	57(4)	71(6)	-12(4)	18(5)	19(3)
C(11)	78(5)	51(5)	57(6)	-14(4)	-2(4)	16(4)
C(12)	66(5)	37(4)	49(4)	-13(3)	-1(3)	-12(3)
O(3)	73(4)	69(5)	69(5)	-16(4)	-8(3)	-28(4)
C(16)	98(5)	90(8)	95(8)	-33(6)	-30(6)	-18(6)
C(17)	97(6)	75(5)	70(5)	-20(4)	-32(4)	5(4)
O(4)	81(4)	74(5)	46(3)	-15(3)	-6(2)	-8(3)
C(13)	61(5)	55(3)	39(3)	-4(2)	4(3)	-8(3)
C(14)	49(5)	57(4)	47(3)	9(2)	4(3)	-13(3)
O(1A)	78(4)	52(2)	49(3)	-2(2)	-26(3)	-5(3)
C(1A)	72(5)	59(4)	70(5)	-9(4)	-28(3)	-9(4)
O(2A)	103(5)	105(4)	116(6)	-22(4)	-68(5)	2(4)
C(2A)	57(4)	51(3)	76(6)	-10(4)	-14(4)	-12(3)
C(3A)	44(3)	41(3)	43(4)	-7(3)	3(3)	-4(2)
C(4A)	59(5)	46(5)	41(7)	1(4)	6(4)	19(3)
C(15A)	79(7)	44(3)	51(7)	7(3)	29(4)	19(3)
C(5A)	60(4)	60(5)	45(4)	4(3)	-3(3)	17(3)
C(6A)	49(4)	62(5)	41(4)	0(3)	-9(3)	4(3)

C(7A)	51(5)	40(4)	30(3)	-4(3)	-4(3)	-5(3)
C(8A)	45(3)	46(4)	40(5)	8(3)	3(3)	-2(3)
C(9A)	46(3)	50(3)	70(5)	-9(4)	-5(4)	1(2)
C(10A)	60(3)	59(4)	65(6)	-1(4)	6(4)	13(3)
C(11A)	64(4)	35(4)	57(6)	-6(3)	1(3)	0(3)
C(12A)	54(4)	54(5)	39(4)	2(3)	-16(3)	7(3)
O(3A)	77(3)	43(2)	68(5)	3(3)	-22(3)	-14(2)
C(16A)	95(6)	46(3)	86(6)	-1(4)	-48(5)	-4(3)
C(17A)	139(8)	54(4)	83(6)	13(4)	-71(6)	-26(5)
O(4A)	107(6)	44(2)	44(3)	1(2)	-32(3)	-10(3)
C(13A)	50(4)	43(3)	35(3)	6(2)	-6(3)	-7(3)
C(14A)	42(4)	42(3)	39(3)	0(2)	0(3)	-11(3)

Table A5.2.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{3}) for compound **119**.

	x	y	z	U(eq)
H(2A)	9798	9045	6606	71
H(2B)	8678	9801	7191	71
H(15A)	6933	11086	6572	66
H(15B)	4863	11111	6344	66
H(5A)	3228	9110	6217	74
H(5B)	3630	8270	6898	74
H(6A)	4255	7393	5538	67
H(6B)	3168	6593	6109	67
H(8)	7346	7742	5653	42
H(9A)	10154	7039	5973	66
H(9B)	9398	6075	6564	66
H(10A)	8947	5551	5144	82
H(10B)	10270	4723	5627	82
H(11A)	7674	3439	5507	74
H(11B)	7854	3927	6283	74
H(16A)	2745	3608	5133	113
H(16B)	4513	2714	5192	113
H(17A)	5529	3982	4371	97
H(17B)	3965	5077	4447	97
H(13)	5804	7812	7583	62
H(14A)	6670	5219	7072	61
H(14B)	4729	5842	7150	61
H(2A1)	9646	8911	6907	74
H(2A2)	8331	9719	7408	74
H(15C)	5438	11185	6136	69
H(15D)	7293	10933	6541	69
H(5A1)	3409	9346	6007	66
H(5A2)	3357	8451	6690	66
H(6A1)	3254	6831	5839	61
H(6A2)	4711	7607	5398	61

H(8A)	7680	7747	5792	52
H(9A1)	10194	6881	6290	67
H(9A2)	9104	5965	6818	67
H(10C)	10202	4529	5943	74
H(10D)	9259	5462	5380	74
H(11C)	7546	3461	5607	62
H(11D)	7442	3869	6392	62
H(16C)	2616	3133	5499	91
H(16D)	4557	2547	5359	91
H(17C)	4350	3928	4451	110
H(17D)	3013	4959	4824	110
H(13A)	5157	7840	7555	52
H(14C)	4089	6030	7005	49
H(14D)	5937	5244	7070	49

Table A5.2.6. Torsion angles [°] for compound **119**.

C(13)-O(1)-C(1)-O(2)	-177.3(9)
C(13)-O(1)-C(1)-C(2)	2.2(9)
O(2)-C(1)-C(2)-C(3)	160.6(10)
O(1)-C(1)-C(2)-C(3)	-18.9(10)
C(1)-C(2)-C(3)-C(4)	146.0(12)
C(1)-C(2)-C(3)-C(13)	26.2(10)
C(1)-C(2)-C(3)-C(8)	-86.2(10)
C(2)-C(3)-C(4)-C(15)	9(3)
C(13)-C(3)-C(4)-C(15)	125(2)
C(8)-C(3)-C(4)-C(15)	-124(2)
C(2)-C(3)-C(4)-C(5)	-163.2(13)
C(13)-C(3)-C(4)-C(5)	-47.5(18)
C(8)-C(3)-C(4)-C(5)	64.0(17)
C(15)-C(4)-C(5)-C(6)	140.8(18)
C(3)-C(4)-C(5)-C(6)	-46.1(19)
C(4)-C(5)-C(6)-C(7)	42.5(15)
C(5)-C(6)-C(7)-C(14)	54.2(13)
C(5)-C(6)-C(7)-C(12)	-177.1(11)
C(5)-C(6)-C(7)-C(8)	-56.9(13)
C(14)-C(7)-C(8)-C(9)	76.8(10)
C(12)-C(7)-C(8)-C(9)	-46.0(13)
C(6)-C(7)-C(8)-C(9)	-167.3(9)
C(14)-C(7)-C(8)-C(3)	-45.0(10)
C(12)-C(7)-C(8)-C(3)	-167.7(9)
C(6)-C(7)-C(8)-C(3)	71.0(11)
C(4)-C(3)-C(8)-C(9)	164.1(11)
C(2)-C(3)-C(8)-C(9)	31.7(13)
C(13)-C(3)-C(8)-C(9)	-80.1(11)
C(4)-C(3)-C(8)-C(7)	-75.6(12)
C(2)-C(3)-C(8)-C(7)	152.0(9)
C(13)-C(3)-C(8)-C(7)	40.3(10)
C(7)-C(8)-C(9)-C(10)	52.5(12)
C(3)-C(8)-C(9)-C(10)	166.4(9)
C(8)-C(9)-C(10)-C(11)	-60.3(13)

C(9)-C(10)-C(11)-C(12)	62.0(16)
C(10)-C(11)-C(12)-O(3)	173.8(11)
C(10)-C(11)-C(12)-O(4)	57.6(14)
C(10)-C(11)-C(12)-C(7)	-59.7(17)
C(14)-C(7)-C(12)-O(3)	70.0(12)
C(6)-C(7)-C(12)-O(3)	-56.1(13)
C(8)-C(7)-C(12)-O(3)	-174.8(11)
C(14)-C(7)-C(12)-O(4)	-177.8(9)
C(6)-C(7)-C(12)-O(4)	56.1(13)
C(8)-C(7)-C(12)-O(4)	-62.6(12)
C(14)-C(7)-C(12)-C(11)	-63.5(14)
C(6)-C(7)-C(12)-C(11)	170.4(12)
C(8)-C(7)-C(12)-C(11)	51.7(15)
O(4)-C(12)-O(3)-C(16)	32.2(14)
C(11)-C(12)-O(3)-C(16)	-82.7(16)
C(7)-C(12)-O(3)-C(16)	146.3(11)
C(12)-O(3)-C(16)-C(17)	-27.9(15)
O(3)-C(16)-C(17)-O(4)	13.1(15)
C(16)-C(17)-O(4)-C(12)	6.5(14)
O(3)-C(12)-O(4)-C(17)	-23.8(13)
C(11)-C(12)-O(4)-C(17)	102.1(11)
C(7)-C(12)-O(4)-C(17)	-135.8(10)
C(1)-O(1)-C(13)-C(14)	130.0(8)
C(1)-O(1)-C(13)-C(3)	15.2(10)
C(4)-C(3)-C(13)-O(1)	-150.0(10)
C(2)-C(3)-C(13)-O(1)	-25.7(10)
C(8)-C(3)-C(13)-O(1)	96.6(9)
C(4)-C(3)-C(13)-C(14)	92.9(10)
C(2)-C(3)-C(13)-C(14)	-142.9(8)
C(8)-C(3)-C(13)-C(14)	-20.6(10)
C(12)-C(7)-C(14)-C(13)	151.9(9)
C(6)-C(7)-C(14)-C(13)	-81.2(10)
C(8)-C(7)-C(14)-C(13)	32.7(10)
O(1)-C(13)-C(14)-C(7)	-121.5(8)
C(3)-C(13)-C(14)-C(7)	-7.3(10)
C(13A)-O(1A)-C(1A)-O(2A)	178.8(9)

C(13A)-O(1A)-C(1A)-C(2A)	0.2(9)
O(2A)-C(1A)-C(2A)-C(3A)	165.1(10)
O(1A)-C(1A)-C(2A)-C(3A)	-16.4(10)
C(1A)-C(2A)-C(3A)-C(4A)	145.5(13)
C(1A)-C(2A)-C(3A)-C(13A)	24.4(10)
C(1A)-C(2A)-C(3A)-C(8A)	-84.7(11)
C(2A)-C(3A)-C(4A)-C(15A)	24(3)
C(13A)-C(3A)-C(4A)-C(15A)	141(2)
C(8A)-C(3A)-C(4A)-C(15A)	-109(2)
C(2A)-C(3A)-C(4A)-C(5A)	-165.1(14)
C(13A)-C(3A)-C(4A)-C(5A)	-48.0(19)
C(8A)-C(3A)-C(4A)-C(5A)	62.1(19)
C(15A)-C(4A)-C(5A)-C(6A)	125(2)
C(3A)-C(4A)-C(5A)-C(6A)	-46(2)
C(4A)-C(5A)-C(6A)-C(7A)	43.3(16)
C(5A)-C(6A)-C(7A)-C(12A)	172.4(11)
C(5A)-C(6A)-C(7A)-C(8A)	-58.3(13)
C(5A)-C(6A)-C(7A)-C(14A)	53.6(13)
C(6A)-C(7A)-C(8A)-C(9A)	-164.9(9)
C(12A)-C(7A)-C(8A)-C(9A)	-38.8(14)
C(14A)-C(7A)-C(8A)-C(9A)	77.2(11)
C(6A)-C(7A)-C(8A)-C(3A)	69.7(11)
C(12A)-C(7A)-C(8A)-C(3A)	-164.3(10)
C(14A)-C(7A)-C(8A)-C(3A)	-48.2(11)
C(4A)-C(3A)-C(8A)-C(7A)	-70.5(12)
C(2A)-C(3A)-C(8A)-C(7A)	155.0(10)
C(13A)-C(3A)-C(8A)-C(7A)	45.3(10)
C(4A)-C(3A)-C(8A)-C(9A)	164.8(11)
C(2A)-C(3A)-C(8A)-C(9A)	30.3(14)
C(13A)-C(3A)-C(8A)-C(9A)	-79.4(11)
C(7A)-C(8A)-C(9A)-C(10A)	48.8(12)
C(3A)-C(8A)-C(9A)-C(10A)	165.4(10)
C(8A)-C(9A)-C(10A)-C(11A)	-58.1(12)
C(9A)-C(10A)-C(11A)-C(12A)	59.5(15)
C(10A)-C(11A)-C(12A)-O(4A)	77.5(15)
C(10A)-C(11A)-C(12A)-O(3A)	-169.0(12)

C(10A)-C(11A)-C(12A)-C(7A)	-48.5(17)
C(6A)-C(7A)-C(12A)-O(4A)	36.8(14)
C(8A)-C(7A)-C(12A)-O(4A)	-89.2(13)
C(14A)-C(7A)-C(12A)-O(4A)	157.9(10)
C(6A)-C(7A)-C(12A)-O(3A)	-81.3(12)
C(8A)-C(7A)-C(12A)-O(3A)	152.7(11)
C(14A)-C(7A)-C(12A)-O(3A)	39.8(12)
C(6A)-C(7A)-C(12A)-C(11A)	163.9(11)
C(8A)-C(7A)-C(12A)-C(11A)	37.8(15)
C(14A)-C(7A)-C(12A)-C(11A)	-75.0(13)
O(4A)-C(12A)-O(3A)-C(16A)	21.6(14)
C(11A)-C(12A)-O(3A)-C(16A)	-96.3(13)
C(7A)-C(12A)-O(3A)-C(16A)	142.2(11)
C(12A)-O(3A)-C(16A)-C(17A)	-30.4(14)
O(3A)-C(16A)-C(17A)-O(4A)	28.1(15)
C(16A)-C(17A)-O(4A)-C(12A)	-15.6(14)
O(3A)-C(12A)-O(4A)-C(17A)	-3.1(14)
C(11A)-C(12A)-O(4A)-C(17A)	107.8(11)
C(7A)-C(12A)-O(4A)-C(17A)	-124.7(11)
C(1A)-O(1A)-C(13A)-C(14A)	132.6(7)
C(1A)-O(1A)-C(13A)-C(3A)	16.1(9)
C(4A)-C(3A)-C(13A)-O(1A)	-151.3(10)
C(2A)-C(3A)-C(13A)-O(1A)	-24.9(10)
C(8A)-C(3A)-C(13A)-O(1A)	94.2(9)
C(4A)-C(3A)-C(13A)-C(14A)	89.0(11)
C(2A)-C(3A)-C(13A)-C(14A)	-144.6(8)
C(8A)-C(3A)-C(13A)-C(14A)	-25.5(9)
O(1A)-C(13A)-C(14A)-C(7A)	-119.2(8)
C(3A)-C(13A)-C(14A)-C(7A)	-4.1(9)
C(6A)-C(7A)-C(14A)-C(13A)	-84.6(10)
C(12A)-C(7A)-C(14A)-C(13A)	155.0(8)
C(8A)-C(7A)-C(14A)-C(13A)	32.7(10)

Symmetry transformations used to generate equivalent atoms:

A5.3 X-RAY CRYSTAL STRUCTURE OF COMPOUND 122

Figure A5.3.1 *X-ray crystal structure of compound* ***122****.*

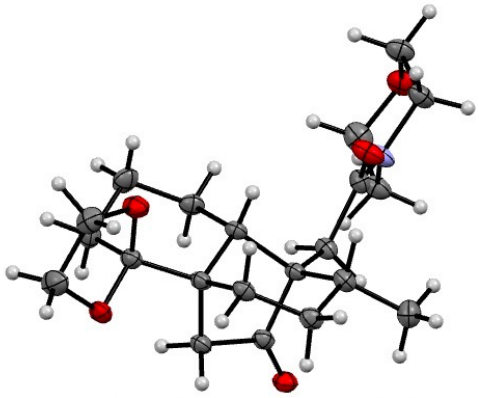


Table A5.3.1 *Crystal data and structure refinement for compound* ***122****.*

Empirical formula	C21 H31 N O5	
Formula weight	377.47	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 6.4595(6) Å	a= 80.654(7)°.
	b = 11.2008(8) Å	b= 77.081(12)°.
	c = 14.2221(8) Å	g = 75.133(7)°.
Volume	963.32(14) $Å^3$	
Z	2	
Density (calculated)	1.301 Mg/m^3	
Absorption coefficient	0.748 mm^{-1}	
F(000)	408	
Crystal size	0.100 x 0.100 x 0.020 mm^3	
Theta range for data collection	3.208 to 74.420°.	
Index ranges	-8<=h<=8, -13<=k<=13, -17<=l<=17	
Reflections collected	41844	
Independent reflections	7574 [R(int) = 0.0498]	
Completeness to theta = 67.679°	100.0 %	
Absorption correction	Semi-empirical from equivalents	

Max. and min. transmission	0.7538 and 0.6414
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7574 / 42 / 544
Goodness-of-fit on F^2	1.075
Final R indices [I>2sigma(I)]	R1 = 0.0379, wR2 = 0.0967
R indices (all data)	R1 = 0.0410, wR2 = 0.0994
Absolute structure parameter	-0.07(9)
Extinction coefficient	n/a
Largest diff. peak and hole	0.237 and -0.187 e.$Å^{-3}$

Table 5.3.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for compound **122**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	2538(3)	4282(2)	2313(1)	25(1)
C(1)	2732(4)	5204(2)	2586(2)	20(1)
C(2)	2243(4)	5484(2)	3634(2)	21(1)
C(3)	3021(4)	6688(2)	3583(2)	19(1)
C(4)	1802(5)	7461(2)	4424(2)	22(1)
O(2)	2005(4)	6686(2)	5308(1)	26(1)
O(3)	2853(3)	8440(2)	4423(1)	28(1)
C(5)	-585(5)	8025(3)	4375(2)	27(1)
C(6)	-789(5)	8803(3)	3397(2)	30(1)
C(7)	210(4)	7992(3)	2562(2)	23(1)
C(8)	2617(4)	7371(2)	2571(2)	19(1)
C(9)	3529(4)	6294(2)	1920(2)	18(1)
C(10)	6074(4)	5953(3)	1800(2)	22(1)
C(21)	7227(5)	4998(3)	1087(2)	29(1)
C(11)	6713(4)	5498(3)	2790(2)	23(1)
C(12)	5482(4)	6363(2)	3562(2)	21(1)
C(13)	1900(6)	7501(3)	6001(2)	35(1)
C(14)	3040(5)	8486(3)	5400(2)	30(1)
C(15)	2670(4)	6474(2)	972(2)	21(1)
C(16)	3302(4)	7527(3)	234(2)	22(1)
O(4)	4626(4)	8076(2)	341(2)	31(1)
N(1)	2360(4)	7816(2)	-563(2)	26(1)
C(17)	3135(5)	8700(3)	-1361(2)	28(1)
C(18)	1230(5)	9567(3)	-1747(2)	30(1)
O(5)	-73(4)	8896(2)	-2036(2)	32(1)
C(19)	-925(5)	8124(3)	-1223(2)	33(1)
C(20)	864(5)	7180(3)	-806(2)	28(1)
O(101)	2633(3)	4958(2)	7509(2)	28(1)
C(101)	4211(4)	4193(2)	7170(2)	22(1)
C(102)	4838(4)	3908(2)	6123(2)	22(1)

C(103)	7076(4)	3000(2)	6063(2)	21(1)
C(104)	7587(5)	2132(3)	5268(2)	23(1)
O(102)	7420(3)	2880(2)	4366(1)	27(1)
O(103)	9803(3)	1430(2)	5181(2)	28(1)
C(105)	6125(5)	1206(3)	5469(2)	27(1)
C(106)	6280(5)	452(3)	6455(2)	28(1)
C(107)	5533(5)	1312(3)	7258(2)	24(1)
C(108)	6908(4)	2284(3)	7101(2)	22(1)
C(109)	5891(4)	3357(2)	7746(2)	21(1)
C(110)	7664(5)	4102(3)	7694(2)	28(1)
C(121)	6968(6)	5117(3)	8379(3)	40(1)
C(111)	8339(5)	4675(3)	6645(2)	29(1)
C(112)	8859(5)	3734(3)	5911(2)	27(1)
C(113)	9138(5)	2270(3)	3651(2)	29(1)
C(114)	10945(5)	1704(3)	4212(2)	29(1)
C(115)	4652(5)	3012(3)	8766(2)	26(1)
O(104)	7950(3)	2042(2)	9369(2)	32(1)
C(116)	5987(5)	2170(3)	9464(2)	31(1)
N(101)	4952(7)	1304(5)	10120(3)	27(1)
C(117)	6042(9)	540(5)	10885(4)	30(1)
C(118)	4900(10)	1021(6)	11855(4)	39(2)
O(105)	2650(15)	1013(8)	12054(6)	38(2)
C(119)	1602(10)	1777(7)	11313(4)	32(1)
C(120)	2605(8)	1319(5)	10336(4)	30(1)
N(01A)	4793(10)	1985(7)	10367(5)	25(2)
C(17A)	5909(13)	1318(8)	11152(6)	29(2)
C(18A)	4919(14)	247(8)	11641(6)	33(2)
O(05A)	2630(20)	619(10)	11981(10)	36(3)
C(19A)	1595(16)	1189(10)	11183(6)	32(2)
C(20A)	2419(12)	2328(7)	10685(5)	29(2)

Table 5.3.3. Bond lengths [Å] and angles [°] for compound **122**.

O(1)-C(1)	1.205(3)
C(1)-C(2)	1.520(4)
C(1)-C(9)	1.543(3)
C(2)-C(3)	1.541(4)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(12)	1.532(4)
C(3)-C(4)	1.538(4)
C(3)-C(8)	1.561(4)
C(4)-O(2)	1.419(3)
C(4)-O(3)	1.429(3)
C(4)-C(5)	1.522(4)
O(2)-C(13)	1.429(4)
O(3)-C(14)	1.432(4)
C(5)-C(6)	1.530(4)
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-C(7)	1.536(4)
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(8)	1.533(4)
C(7)-H(7A)	0.9900
C(7)-H(7B)	0.9900
C(8)-C(9)	1.554(3)
C(8)-H(8)	1.0000
C(9)-C(15)	1.535(4)
C(9)-C(10)	1.565(4)
C(10)-C(21)	1.527(4)
C(10)-C(11)	1.527(4)
C(10)-H(10)	1.0000
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(11)-C(12)	1.528(4)

C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(14)	1.523(5)
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-H(14A)	0.9900
C(14)-H(14B)	0.9900
C(15)-C(16)	1.521(4)
C(15)-H(15A)	0.9900
C(15)-H(15B)	0.9900
C(16)-O(4)	1.222(3)
C(16)-N(1)	1.359(4)
N(1)-C(20)	1.464(4)
N(1)-C(17)	1.467(3)
C(17)-C(18)	1.509(4)
C(17)-H(17A)	0.9900
C(17)-H(17B)	0.9900
C(18)-O(5)	1.422(4)
C(18)-H(18A)	0.9900
C(18)-H(18B)	0.9900
O(5)-C(19)	1.422(4)
C(19)-C(20)	1.510(4)
C(19)-H(19A)	0.9900
C(19)-H(19B)	0.9900
C(20)-H(20A)	0.9900
C(20)-H(20B)	0.9900
O(101)-C(101)	1.213(3)
C(101)-C(102)	1.517(4)
C(101)-C(109)	1.533(4)
C(102)-C(103)	1.533(4)
C(102)-H(10A)	0.9900
C(102)-H(10B)	0.9900
C(103)-C(104)	1.536(4)
C(103)-C(112)	1.538(4)

C(103)-C(108)	1.556(4)
C(104)-O(102)	1.424(3)
C(104)-O(103)	1.434(3)
C(104)-C(105)	1.528(4)
O(102)-C(113)	1.437(3)
O(103)-C(114)	1.436(3)
C(105)-C(106)	1.525(4)
C(105)-H(10C)	0.9900
C(105)-H(10D)	0.9900
C(106)-C(107)	1.529(4)
C(106)-H(10E)	0.9900
C(106)-H(10F)	0.9900
C(107)-C(108)	1.534(4)
C(107)-H(10G)	0.9900
C(107)-H(10H)	0.9900
C(108)-C(109)	1.549(4)
C(108)-H(108)	1.0000
C(109)-C(115)	1.533(4)
C(109)-C(110)	1.565(4)
C(110)-C(121)	1.531(4)
C(110)-C(111)	1.539(4)
C(110)-H(110)	1.0000
C(121)-H(12C)	0.9800
C(121)-H(12D)	0.9800
C(121)-H(12E)	0.9800
C(111)-C(112)	1.527(4)
C(111)-H(11C)	0.9900
C(111)-H(11D)	0.9900
C(112)-H(11E)	0.9900
C(112)-H(11F)	0.9900
C(113)-C(114)	1.507(4)
C(113)-H(11G)	0.9900
C(113)-H(11H)	0.9900
C(114)-H(11I)	0.9900
C(114)-H(11J)	0.9900
C(115)-C(116)	1.510(4)

C(115)-H(11K)	0.9900
C(115)-H(11L)	0.9900
O(104)-C(116)	1.217(4)
C(116)-N(01A)	1.356(7)
C(116)-N(101)	1.421(5)
N(101)-C(117)	1.464(6)
N(101)-C(120)	1.474(6)
C(117)-C(118)	1.523(8)
C(117)-H(11M)	0.9900
C(117)-H(11N)	0.9900
C(118)-O(105)	1.419(10)
C(118)-H(11O)	0.9900
C(118)-H(11P)	0.9900
O(105)-C(119)	1.424(10)
C(119)-C(120)	1.507(8)
C(119)-H(11Q)	0.9900
C(119)-H(11R)	0.9900
C(120)-H(12F)	0.9900
C(120)-H(12G)	0.9900
N(01A)-C(17A)	1.463(9)
N(01A)-C(20A)	1.466(9)
C(17A)-C(18A)	1.501(10)
C(17A)-H(17C)	0.9900
C(17A)-H(17D)	0.9900
C(18A)-O(05A)	1.421(14)
C(18A)-H(18C)	0.9900
C(18A)-H(18D)	0.9900
O(05A)-C(19A)	1.425(14)
C(19A)-C(20A)	1.516(11)
C(19A)-H(19C)	0.9900
C(19A)-H(19D)	0.9900
C(20A)-H(20C)	0.9900
C(20A)-H(20D)	0.9900

O(1)-C(1)-C(2)	125.9(2)
O(1)-C(1)-C(9)	125.1(2)

C(2)-C(1)-C(9)	109.0(2)
C(1)-C(2)-C(3)	104.4(2)
C(1)-C(2)-H(2A)	110.9
C(3)-C(2)-H(2A)	110.9
C(1)-C(2)-H(2B)	110.9
C(3)-C(2)-H(2B)	110.9
H(2A)-C(2)-H(2B)	108.9
C(12)-C(3)-C(4)	110.4(2)
C(12)-C(3)-C(2)	109.3(2)
C(4)-C(3)-C(2)	112.9(2)
C(12)-C(3)-C(8)	108.1(2)
C(4)-C(3)-C(8)	113.0(2)
C(2)-C(3)-C(8)	102.8(2)
O(2)-C(4)-O(3)	106.2(2)
O(2)-C(4)-C(5)	110.9(2)
O(3)-C(4)-C(5)	108.8(2)
O(2)-C(4)-C(3)	108.0(2)
O(3)-C(4)-C(3)	109.6(2)
C(5)-C(4)-C(3)	113.2(2)
C(4)-O(2)-C(13)	105.5(2)
C(4)-O(3)-C(14)	108.1(2)
C(4)-C(5)-C(6)	110.4(2)
C(4)-C(5)-H(5A)	109.6
C(6)-C(5)-H(5A)	109.6
C(4)-C(5)-H(5B)	109.6
C(6)-C(5)-H(5B)	109.6
H(5A)-C(5)-H(5B)	108.1
C(5)-C(6)-C(7)	110.5(2)
C(5)-C(6)-H(6A)	109.6
C(7)-C(6)-H(6A)	109.6
C(5)-C(6)-H(6B)	109.6
C(7)-C(6)-H(6B)	109.6
H(6A)-C(6)-H(6B)	108.1
C(8)-C(7)-C(6)	111.5(2)
C(8)-C(7)-H(7A)	109.3
C(6)-C(7)-H(7A)	109.3

C(8)-C(7)-H(7B)	109.3
C(6)-C(7)-H(7B)	109.3
H(7A)-C(7)-H(7B)	108.0
C(7)-C(8)-C(9)	113.2(2)
C(7)-C(8)-C(3)	113.1(2)
C(9)-C(8)-C(3)	101.48(19)
C(7)-C(8)-H(8)	109.6
C(9)-C(8)-H(8)	109.6
C(3)-C(8)-H(8)	109.6
C(15)-C(9)-C(1)	108.6(2)
C(15)-C(9)-C(8)	116.1(2)
C(1)-C(9)-C(8)	101.97(19)
C(15)-C(9)-C(10)	115.0(2)
C(1)-C(9)-C(10)	105.9(2)
C(8)-C(9)-C(10)	108.0(2)
C(21)-C(10)-C(11)	110.2(2)
C(21)-C(10)-C(9)	114.1(2)
C(11)-C(10)-C(9)	109.7(2)
C(21)-C(10)-H(10)	107.5
C(11)-C(10)-H(10)	107.5
C(9)-C(10)-H(10)	107.5
C(10)-C(21)-H(21A)	109.5
C(10)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(10)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(10)-C(11)-C(12)	113.0(2)
C(10)-C(11)-H(11A)	109.0
C(12)-C(11)-H(11A)	109.0
C(10)-C(11)-H(11B)	109.0
C(12)-C(11)-H(11B)	109.0
H(11A)-C(11)-H(11B)	107.8
C(11)-C(12)-C(3)	111.4(2)
C(11)-C(12)-H(12A)	109.3
C(3)-C(12)-H(12A)	109.3

C(11)-C(12)-H(12B)	109.3
C(3)-C(12)-H(12B)	109.3
H(12A)-C(12)-H(12B)	108.0
O(2)-C(13)-C(14)	103.1(2)
O(2)-C(13)-H(13A)	111.2
C(14)-C(13)-H(13A)	111.2
O(2)-C(13)-H(13B)	111.2
C(14)-C(13)-H(13B)	111.2
H(13A)-C(13)-H(13B)	109.1
O(3)-C(14)-C(13)	104.7(2)
O(3)-C(14)-H(14A)	110.8
C(13)-C(14)-H(14A)	110.8
O(3)-C(14)-H(14B)	110.8
C(13)-C(14)-H(14B)	110.8
H(14A)-C(14)-H(14B)	108.9
C(16)-C(15)-C(9)	115.2(2)
C(16)-C(15)-H(15A)	108.5
C(9)-C(15)-H(15A)	108.5
C(16)-C(15)-H(15B)	108.5
C(9)-C(15)-H(15B)	108.5
H(15A)-C(15)-H(15B)	107.5
O(4)-C(16)-N(1)	121.3(2)
O(4)-C(16)-C(15)	121.6(2)
N(1)-C(16)-C(15)	117.1(2)
C(16)-N(1)-C(20)	126.5(2)
C(16)-N(1)-C(17)	119.3(2)
C(20)-N(1)-C(17)	113.4(2)
N(1)-C(17)-C(18)	110.2(2)
N(1)-C(17)-H(17A)	109.6
C(18)-C(17)-H(17A)	109.6
N(1)-C(17)-H(17B)	109.6
C(18)-C(17)-H(17B)	109.6
H(17A)-C(17)-H(17B)	108.1
O(5)-C(18)-C(17)	111.2(2)
O(5)-C(18)-H(18A)	109.4
C(17)-C(18)-H(18A)	109.4

O(5)-C(18)-H(18B)	109.4
C(17)-C(18)-H(18B)	109.4
H(18A)-C(18)-H(18B)	108.0
C(18)-O(5)-C(19)	109.7(2)
O(5)-C(19)-C(20)	111.9(2)
O(5)-C(19)-H(19A)	109.2
C(20)-C(19)-H(19A)	109.2
O(5)-C(19)-H(19B)	109.2
C(20)-C(19)-H(19B)	109.2
H(19A)-C(19)-H(19B)	107.9
N(1)-C(20)-C(19)	109.7(2)
N(1)-C(20)-H(20A)	109.7
C(19)-C(20)-H(20A)	109.7
N(1)-C(20)-H(20B)	109.7
C(19)-C(20)-H(20B)	109.7
H(20A)-C(20)-H(20B)	108.2
O(101)-C(101)-C(102)	125.9(3)
O(101)-C(101)-C(109)	124.7(2)
C(102)-C(101)-C(109)	109.3(2)
C(101)-C(102)-C(103)	104.3(2)
C(101)-C(102)-H(10A)	110.9
C(103)-C(102)-H(10A)	110.9
C(101)-C(102)-H(10B)	110.9
C(103)-C(102)-H(10B)	110.9
H(10A)-C(102)-H(10B)	108.9
C(102)-C(103)-C(104)	113.6(2)
C(102)-C(103)-C(112)	109.4(2)
C(104)-C(103)-C(112)	110.2(2)
C(102)-C(103)-C(108)	102.4(2)
C(104)-C(103)-C(108)	112.5(2)
C(112)-C(103)-C(108)	108.4(2)
O(102)-C(104)-O(103)	106.6(2)
O(102)-C(104)-C(105)	111.3(2)
O(103)-C(104)-C(105)	107.5(2)
O(102)-C(104)-C(103)	108.1(2)
O(103)-C(104)-C(103)	109.8(2)

C(105)-C(104)-C(103)	113.3(2)
C(104)-O(102)-C(113)	106.4(2)
C(104)-O(103)-C(114)	108.6(2)
C(106)-C(105)-C(104)	109.9(2)
C(106)-C(105)-H(10C)	109.7
C(104)-C(105)-H(10C)	109.7
C(106)-C(105)-H(10D)	109.7
C(104)-C(105)-H(10D)	109.7
H(10C)-C(105)-H(10D)	108.2
C(105)-C(106)-C(107)	110.3(2)
C(105)-C(106)-H(10E)	109.6
C(107)-C(106)-H(10E)	109.6
C(105)-C(106)-H(10F)	109.6
C(107)-C(106)-H(10F)	109.6
H(10E)-C(106)-H(10F)	108.1
C(106)-C(107)-C(108)	111.7(2)
C(106)-C(107)-H(10G)	109.3
C(108)-C(107)-H(10G)	109.3
C(106)-C(107)-H(10H)	109.3
C(108)-C(107)-H(10H)	109.3
H(10G)-C(107)-H(10H)	107.9
C(107)-C(108)-C(109)	113.4(2)
C(107)-C(108)-C(103)	112.8(2)
C(109)-C(108)-C(103)	101.8(2)
C(107)-C(108)-H(108)	109.5
C(109)-C(108)-H(108)	109.5
C(103)-C(108)-H(108)	109.5
C(101)-C(109)-C(115)	107.3(2)
C(101)-C(109)-C(108)	101.5(2)
C(115)-C(109)-C(108)	116.5(2)
C(101)-C(109)-C(110)	106.3(2)
C(115)-C(109)-C(110)	115.8(2)
C(108)-C(109)-C(110)	108.1(2)
C(121)-C(110)-C(111)	109.7(3)
C(121)-C(110)-C(109)	114.0(2)
C(111)-C(110)-C(109)	110.1(2)

C(121)-C(110)-H(110)	107.6
C(111)-C(110)-H(110)	107.6
C(109)-C(110)-H(110)	107.6
C(110)-C(121)-H(12C)	109.5
C(110)-C(121)-H(12D)	109.5
H(12C)-C(121)-H(12D)	109.5
C(110)-C(121)-H(12E)	109.5
H(12C)-C(121)-H(12E)	109.5
H(12D)-C(121)-H(12E)	109.5
C(112)-C(111)-C(110)	112.5(2)
C(112)-C(111)-H(11C)	109.1
C(110)-C(111)-H(11C)	109.1
C(112)-C(111)-H(11D)	109.1
C(110)-C(111)-H(11D)	109.1
H(11C)-C(111)-H(11D)	107.8
C(111)-C(112)-C(103)	112.0(2)
C(111)-C(112)-H(11E)	109.2
C(103)-C(112)-H(11E)	109.2
C(111)-C(112)-H(11F)	109.2
C(103)-C(112)-H(11F)	109.2
H(11E)-C(112)-H(11F)	107.9
O(102)-C(113)-C(114)	102.9(2)
O(102)-C(113)-H(11G)	111.2
C(114)-C(113)-H(11G)	111.2
O(102)-C(113)-H(11H)	111.2
C(114)-C(113)-H(11H)	111.2
H(11G)-C(113)-H(11H)	109.1
O(103)-C(114)-C(113)	103.6(2)
O(103)-C(114)-H(11I)	111.0
C(113)-C(114)-H(11I)	111.0
O(103)-C(114)-H(11J)	111.0
C(113)-C(114)-H(11J)	111.0
H(11I)-C(114)-H(11J)	109.0
C(116)-C(115)-C(109)	116.7(2)
C(116)-C(115)-H(11K)	108.1
C(109)-C(115)-H(11K)	108.1

C(116)-C(115)-H(11L)	108.1
C(109)-C(115)-H(11L)	108.1
H(11K)-C(115)-H(11L)	107.3
O(104)-C(116)-N(01A)	119.0(4)
O(104)-C(116)-N(101)	119.1(3)
O(104)-C(116)-C(115)	123.3(3)
N(01A)-C(116)-C(115)	112.8(4)
N(101)-C(116)-C(115)	116.1(3)
C(116)-N(101)-C(117)	119.7(4)
C(116)-N(101)-C(120)	126.6(4)
C(117)-N(101)-C(120)	111.0(4)
N(101)-C(117)-C(118)	108.9(4)
N(101)-C(117)-H(11M)	109.9
C(118)-C(117)-H(11M)	109.9
N(101)-C(117)-H(11N)	109.9
C(118)-C(117)-H(11N)	109.9
H(11M)-C(117)-H(11N)	108.3
O(105)-C(118)-C(117)	111.3(6)
O(105)-C(118)-H(11O)	109.4
C(117)-C(118)-H(11O)	109.4
O(105)-C(118)-H(11P)	109.4
C(117)-C(118)-H(11P)	109.4
H(11O)-C(118)-H(11P)	108.0
C(118)-O(105)-C(119)	110.3(7)
O(105)-C(119)-C(120)	111.0(6)
O(105)-C(119)-H(11Q)	109.4
C(120)-C(119)-H(11Q)	109.4
O(105)-C(119)-H(11R)	109.4
C(120)-C(119)-H(11R)	109.4
H(11Q)-C(119)-H(11R)	108.0
N(101)-C(120)-C(119)	109.2(5)
N(101)-C(120)-H(12F)	109.8
C(119)-C(120)-H(12F)	109.8
N(101)-C(120)-H(12G)	109.8
C(119)-C(120)-H(12G)	109.8
H(12F)-C(120)-H(12G)	108.3

C(116)-N(01A)-C(17A)	119.1(6)
C(116)-N(01A)-C(20A)	128.5(5)
C(17A)-N(01A)-C(20A)	112.4(6)
N(01A)-C(17A)-C(18A)	110.3(6)
N(01A)-C(17A)-H(17C)	109.6
C(18A)-C(17A)-H(17C)	109.6
N(01A)-C(17A)-H(17D)	109.6
C(18A)-C(17A)-H(17D)	109.6
H(17C)-C(17A)-H(17D)	108.1
O(05A)-C(18A)-C(17A)	112.7(8)
O(05A)-C(18A)-H(18C)	109.1
C(17A)-C(18A)-H(18C)	109.1
O(05A)-C(18A)-H(18D)	109.1
C(17A)-C(18A)-H(18D)	109.1
H(18C)-C(18A)-H(18D)	107.8
C(18A)-O(05A)-C(19A)	109.3(11)
O(05A)-C(19A)-C(20A)	111.5(8)
O(05A)-C(19A)-H(19C)	109.3
C(20A)-C(19A)-H(19C)	109.3
O(05A)-C(19A)-H(19D)	109.3
C(20A)-C(19A)-H(19D)	109.3
H(19C)-C(19A)-H(19D)	108.0
N(01A)-C(20A)-C(19A)	109.7(7)
N(01A)-C(20A)-H(20C)	109.7
C(19A)-C(20A)-H(20C)	109.7
N(01A)-C(20A)-H(20D)	109.7
C(19A)-C(20A)-H(20D)	109.7
H(20C)-C(20A)-H(20D)	108.2

Symmetry transformations used to generate equivalent atoms:

Table 5.3.4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for compound **122**. 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)	31(1)	20(1)	25(1)	0(1)	-5(1)	-10(1)
C(1)	18(1)	20(1)	21(1)	2(1)	-4(1)	-4(1)
C(2)	22(1)	20(1)	18(1)	2(1)	-3(1)	-6(1)
C(3)	24(1)	18(1)	15(1)	2(1)	-4(1)	-6(1)
C(4)	28(1)	19(1)	18(1)	1(1)	-4(1)	-5(1)
O(2)	40(1)	23(1)	15(1)	2(1)	-4(1)	-7(1)
O(3)	40(1)	23(1)	23(1)	-2(1)	-8(1)	-11(1)
C(5)	27(1)	29(2)	23(1)	-5(1)	-2(1)	-1(1)
C(6)	30(2)	26(2)	29(2)	-3(1)	-9(1)	4(1)
C(7)	25(1)	21(1)	23(1)	2(1)	-9(1)	-3(1)
C(8)	22(1)	18(1)	16(1)	2(1)	-5(1)	-6(1)
C(9)	23(1)	17(1)	15(1)	2(1)	-4(1)	-8(1)
C(10)	22(1)	24(1)	19(1)	1(1)	-3(1)	-8(1)
C(21)	27(1)	32(2)	27(1)	-6(1)	-2(1)	-6(1)
C(11)	21(1)	24(1)	23(1)	2(1)	-6(1)	-5(1)
C(12)	24(1)	23(1)	18(1)	3(1)	-7(1)	-6(1)
C(13)	53(2)	29(2)	21(1)	-2(1)	-10(1)	-5(1)
C(14)	38(2)	29(2)	26(2)	-6(1)	-13(1)	-4(1)
C(15)	23(1)	23(1)	18(1)	-1(1)	-4(1)	-9(1)
C(16)	23(1)	26(1)	16(1)	-2(1)	-2(1)	-6(1)
O(4)	40(1)	34(1)	26(1)	9(1)	-15(1)	-22(1)
N(1)	29(1)	29(1)	20(1)	8(1)	-10(1)	-13(1)
C(17)	28(1)	30(1)	24(1)	8(1)	-6(1)	-9(1)
C(18)	34(2)	28(2)	27(2)	6(1)	-12(1)	-8(1)
O(5)	37(1)	34(1)	26(1)	4(1)	-15(1)	-7(1)
C(19)	30(2)	42(2)	30(2)	-1(1)	-11(1)	-13(1)
C(20)	34(2)	30(2)	23(1)	4(1)	-9(1)	-13(1)
O(101)	30(1)	26(1)	24(1)	-2(1)	-2(1)	-3(1)
C(101)	26(1)	21(1)	19(1)	4(1)	-4(1)	-9(1)
C(102)	27(1)	20(1)	19(1)	4(1)	-5(1)	-5(1)

C(103)	27(1)	19(1)	17(1)	2(1)	-3(1)	-6(1)
C(104)	28(1)	22(1)	17(1)	2(1)	-5(1)	-2(1)
O(102)	36(1)	22(1)	17(1)	3(1)	-4(1)	2(1)
O(103)	30(1)	26(1)	19(1)	4(1)	-2(1)	2(1)
C(105)	37(2)	20(1)	25(1)	-2(1)	-10(1)	-6(1)
C(106)	38(2)	20(1)	28(2)	3(1)	-9(1)	-10(1)
C(107)	29(1)	22(1)	22(1)	4(1)	-6(1)	-8(1)
C(108)	24(1)	22(1)	19(1)	2(1)	-6(1)	-6(1)
C(109)	23(1)	24(1)	16(1)	0(1)	-3(1)	-6(1)
C(110)	26(1)	32(2)	27(1)	-7(1)	-4(1)	-11(1)
C(121)	43(2)	46(2)	37(2)	-16(2)	-3(1)	-19(2)
C(111)	31(2)	29(2)	30(2)	1(1)	-3(1)	-16(1)
C(112)	29(2)	28(1)	23(1)	2(1)	-2(1)	-11(1)
C(113)	38(2)	23(1)	18(1)	3(1)	-2(1)	-2(1)
C(114)	33(2)	25(1)	23(1)	3(1)	-2(1)	-4(1)
C(115)	24(1)	33(2)	18(1)	2(1)	-4(1)	-6(1)
O(104)	25(1)	38(1)	30(1)	2(1)	-6(1)	-5(1)
C(116)	27(2)	45(2)	18(1)	4(1)	-5(1)	-6(1)
N(101)	28(2)	32(3)	20(2)	3(2)	-8(2)	-6(2)
C(117)	37(3)	27(3)	26(3)	4(2)	-12(2)	-4(2)
C(118)	52(4)	40(4)	21(3)	-1(2)	-17(2)	0(3)
O(105)	49(3)	41(5)	17(2)	4(3)	-5(2)	-2(3)
C(119)	34(3)	33(3)	25(3)	3(3)	-4(2)	-4(3)
C(120)	29(2)	35(3)	25(3)	2(2)	-5(2)	-11(2)
N(01A)	26(3)	27(4)	20(3)	5(3)	-4(2)	-7(3)
C(17A)	37(4)	28(4)	26(4)	5(3)	-13(3)	-12(3)
C(18A)	51(5)	26(4)	27(4)	5(3)	-18(4)	-14(3)
O(05A)	51(5)	35(6)	22(4)	3(4)	-3(3)	-20(5)
C(19A)	44(5)	32(5)	24(4)	4(4)	-6(4)	-20(4)
C(20A)	28(4)	35(4)	21(4)	-1(3)	-5(3)	-6(3)

Table 5.3.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for compound **122**.

	x	y	z	U(eq)
H(2A)	3048	4798	4040	25
H(2B)	661	5610	3906	25
H(5A)	-1258	8556	4906	33
H(5B)	-1375	7353	4462	33
H(6A)	-30	9487	3317	36
H(6B)	-2348	9175	3380	36
H(7A)	-617	7343	2621	28
H(7B)	85	8513	1936	28
H(8)	3512	8009	2358	23
H(10)	6597	6731	1547	26
H(21A)	8795	4777	1092	44
H(21B)	6989	5352	433	44
H(21C)	6638	4252	1280	44
H(11A)	8299	5422	2723	28
H(11B)	6422	4661	3008	28
H(12A)	6023	7136	3425	25
H(12B)	5769	5955	4207	25
H(13A)	2673	7058	6530	42
H(13B)	369	7874	6286	42
H(14A)	2317	9318	5609	36
H(14B)	4591	8293	5461	36
H(15A)	3216	5690	667	25
H(15B)	1058	6629	1133	25
H(17A)	4130	8241	-1888	33
H(17B)	3958	9187	-1125	33
H(18A)	324	10090	-1239	36
H(18B)	1779	10124	-2311	36
H(19A)	-1877	7685	-1423	39
H(19B)	-1828	8648	-715	39
H(20A)	220	6700	-216	34

H(20B)	1673	6593	-1286	34
H(10A)	4934	4674	5673	27
H(10B)	3762	3522	5962	27
H(10C)	4595	1658	5461	32
H(10D)	6585	640	4955	32
H(10E)	7806	-11	6458	34
H(10F)	5354	-158	6576	34
H(10G)	5647	810	7893	29
H(10H)	3983	1740	7275	29
H(108)	8405	1870	7224	26
H(110)	8980	3499	7883	33
H(12C)	8133	5561	8291	59
H(12D)	6689	4737	9052	59
H(12E)	5636	5702	8231	59
H(11C)	7142	5376	6479	35
H(11D)	9639	5010	6600	35
H(11E)	10270	3147	5971	32
H(11F)	9010	4177	5246	32
H(11G)	9592	2873	3101	34
H(11H)	8684	1623	3400	34
H(11I)	11884	938	3949	35
H(11J)	11857	2299	4194	35
H(11K)	3904	3791	9059	31
H(11L)	3509	2605	8699	31
H(11M)	7594	582	10750	36
H(11N)	5979	-338	10906	36
H(11O)	5603	495	12379	46
H(11P)	5060	1880	11843	46
H(11Q)	1732	2643	11292	39
H(11R)	31	1773	11467	39
H(12F)	2401	472	10341	35
H(12G)	1882	1873	9829	35
H(17C)	5788	1892	11633	35
H(17D)	7477	1006	10887	35
H(18C)	5204	-371	11176	40
H(18D)	5632	-159	12195	40

H(19C)	-2	1433	11417	38
H(19D)	1876	583	10709	38
H(20C)	1719	2684	10118	34
H(20D)	2034	2967	11141	34

Table 5.3.6. Torsion angles [°] for compound **122**.

O(1)-C(1)-C(2)-C(3)	173.5(3)
C(9)-C(1)-C(2)-C(3)	-6.4(3)
C(1)-C(2)-C(3)-C(12)	-83.1(2)
C(1)-C(2)-C(3)-C(4)	153.5(2)
C(1)-C(2)-C(3)-C(8)	31.5(3)
C(12)-C(3)-C(4)-O(2)	-67.8(3)
C(2)-C(3)-C(4)-O(2)	54.9(3)
C(8)-C(3)-C(4)-O(2)	171.0(2)
C(12)-C(3)-C(4)-O(3)	47.4(3)
C(2)-C(3)-C(4)-O(3)	170.2(2)
C(8)-C(3)-C(4)-O(3)	-73.8(3)
C(12)-C(3)-C(4)-C(5)	169.0(2)
C(2)-C(3)-C(4)-C(5)	-68.2(3)
C(8)-C(3)-C(4)-C(5)	47.8(3)
O(3)-C(4)-O(2)-C(13)	33.8(3)
C(5)-C(4)-O(2)-C(13)	-84.2(3)
C(3)-C(4)-O(2)-C(13)	151.3(2)
O(2)-C(4)-O(3)-C(14)	-18.4(3)
C(5)-C(4)-O(3)-C(14)	100.9(3)
C(3)-C(4)-O(3)-C(14)	-134.9(2)
O(2)-C(4)-C(5)-C(6)	-177.0(2)
O(3)-C(4)-C(5)-C(6)	66.6(3)
C(3)-C(4)-C(5)-C(6)	-55.4(3)
C(4)-C(5)-C(6)-C(7)	60.2(3)
C(5)-C(6)-C(7)-C(8)	-58.1(3)
C(6)-C(7)-C(8)-C(9)	165.2(2)
C(6)-C(7)-C(8)-C(3)	50.5(3)
C(12)-C(3)-C(8)-C(7)	-167.7(2)
C(4)-C(3)-C(8)-C(7)	-45.2(3)
C(2)-C(3)-C(8)-C(7)	76.8(3)
C(12)-C(3)-C(8)-C(9)	70.7(2)
C(4)-C(3)-C(8)-C(9)	-166.8(2)
C(2)-C(3)-C(8)-C(9)	-44.8(2)
O(1)-C(1)-C(9)-C(15)	35.7(4)

C(2)-C(1)-C(9)-C(15)	-144.4(2)
O(1)-C(1)-C(9)-C(8)	158.9(3)
C(2)-C(1)-C(9)-C(8)	-21.3(3)
O(1)-C(1)-C(9)-C(10)	-88.3(3)
C(2)-C(1)-C(9)-C(10)	91.6(2)
C(7)-C(8)-C(9)-C(15)	36.2(3)
C(3)-C(8)-C(9)-C(15)	157.8(2)
C(7)-C(8)-C(9)-C(1)	-81.6(2)
C(3)-C(8)-C(9)-C(1)	40.0(2)
C(7)-C(8)-C(9)-C(10)	167.1(2)
C(3)-C(8)-C(9)-C(10)	-71.3(2)
C(15)-C(9)-C(10)-C(21)	-42.3(3)
C(1)-C(9)-C(10)-C(21)	77.6(3)
C(8)-C(9)-C(10)-C(21)	-173.8(2)
C(15)-C(9)-C(10)-C(11)	-166.5(2)
C(1)-C(9)-C(10)-C(11)	-46.6(3)
C(8)-C(9)-C(10)-C(11)	62.0(3)
C(21)-C(10)-C(11)-C(12)	-175.6(2)
C(9)-C(10)-C(11)-C(12)	-49.2(3)
C(10)-C(11)-C(12)-C(3)	49.4(3)
C(4)-C(3)-C(12)-C(11)	174.9(2)
C(2)-C(3)-C(12)-C(11)	50.1(3)
C(8)-C(3)-C(12)-C(11)	-61.0(3)
C(4)-O(2)-C(13)-C(14)	-34.7(3)
C(4)-O(3)-C(14)-C(13)	-3.1(3)
O(2)-C(13)-C(14)-O(3)	23.1(3)
C(1)-C(9)-C(15)-C(16)	179.6(2)
C(8)-C(9)-C(15)-C(16)	65.5(3)
C(10)-C(9)-C(15)-C(16)	-62.0(3)
C(9)-C(15)-C(16)-O(4)	9.0(4)
C(9)-C(15)-C(16)-N(1)	-172.2(2)
O(4)-C(16)-N(1)-C(20)	175.9(3)
C(15)-C(16)-N(1)-C(20)	-2.8(4)
O(4)-C(16)-N(1)-C(17)	7.3(4)
C(15)-C(16)-N(1)-C(17)	-171.5(2)
C(16)-N(1)-C(17)-C(18)	-138.9(3)

C(20)-N(1)-C(17)-C(18)	51.0(3)
N(1)-C(17)-C(18)-O(5)	-55.6(3)
C(17)-C(18)-O(5)-C(19)	60.9(3)
C(18)-O(5)-C(19)-C(20)	-61.2(3)
C(16)-N(1)-C(20)-C(19)	140.2(3)
C(17)-N(1)-C(20)-C(19)	-50.6(3)
O(5)-C(19)-C(20)-N(1)	55.4(3)
O(101)-C(101)-C(102)-C(103)	173.4(3)
C(109)-C(101)-C(102)-C(103)	-6.8(3)
C(101)-C(102)-C(103)-C(104)	153.5(2)
C(101)-C(102)-C(103)-C(112)	-82.9(3)
C(101)-C(102)-C(103)-C(108)	31.9(3)
C(102)-C(103)-C(104)-O(102)	56.6(3)
C(112)-C(103)-C(104)-O(102)	-66.5(3)
C(108)-C(103)-C(104)-O(102)	172.4(2)
C(102)-C(103)-C(104)-O(103)	172.6(2)
C(112)-C(103)-C(104)-O(103)	49.4(3)
C(108)-C(103)-C(104)-O(103)	-71.6(3)
C(102)-C(103)-C(104)-C(105)	-67.1(3)
C(112)-C(103)-C(104)-C(105)	169.7(2)
C(108)-C(103)-C(104)-C(105)	48.6(3)
O(103)-C(104)-O(102)-C(113)	23.8(3)
C(105)-C(104)-O(102)-C(113)	-93.2(3)
C(103)-C(104)-O(102)-C(113)	141.8(2)
O(102)-C(104)-O(103)-C(114)	-3.0(3)
C(105)-C(104)-O(103)-C(114)	116.4(2)
C(103)-C(104)-O(103)-C(114)	-119.9(2)
O(102)-C(104)-C(105)-C(106)	-178.0(2)
O(103)-C(104)-C(105)-C(106)	65.6(3)
C(103)-C(104)-C(105)-C(106)	-55.9(3)
C(104)-C(105)-C(106)-C(107)	60.4(3)
C(105)-C(106)-C(107)-C(108)	-58.8(3)
C(106)-C(107)-C(108)-C(109)	166.3(2)
C(106)-C(107)-C(108)-C(103)	51.3(3)
C(102)-C(103)-C(108)-C(107)	76.5(3)
C(104)-C(103)-C(108)-C(107)	-45.9(3)

C(112)-C(103)-C(108)-C(107)	-168.0(2)
C(102)-C(103)-C(108)-C(109)	-45.3(2)
C(104)-C(103)-C(108)-C(109)	-167.7(2)
C(112)-C(103)-C(108)-C(109)	70.2(3)
O(101)-C(101)-C(109)-C(115)	36.1(4)
C(102)-C(101)-C(109)-C(115)	-143.8(2)
O(101)-C(101)-C(109)-C(108)	158.8(3)
C(102)-C(101)-C(109)-C(108)	-21.1(3)
O(101)-C(101)-C(109)-C(110)	-88.4(3)
C(102)-C(101)-C(109)-C(110)	91.8(3)
C(107)-C(108)-C(109)-C(101)	-81.2(3)
C(103)-C(108)-C(109)-C(101)	40.2(2)
C(107)-C(108)-C(109)-C(115)	34.9(3)
C(103)-C(108)-C(109)-C(115)	156.3(2)
C(107)-C(108)-C(109)-C(110)	167.3(2)
C(103)-C(108)-C(109)-C(110)	-71.3(3)
C(101)-C(109)-C(110)-C(121)	77.6(3)
C(115)-C(109)-C(110)-C(121)	-41.4(4)
C(108)-C(109)-C(110)-C(121)	-174.1(3)
C(101)-C(109)-C(110)-C(111)	-46.2(3)
C(115)-C(109)-C(110)-C(111)	-165.3(2)
C(108)-C(109)-C(110)-C(111)	62.0(3)
C(121)-C(110)-C(111)-C(112)	-174.9(3)
C(109)-C(110)-C(111)-C(112)	-48.6(3)
C(110)-C(111)-C(112)-C(103)	48.4(3)
C(102)-C(103)-C(112)-C(111)	50.5(3)
C(104)-C(103)-C(112)-C(111)	176.1(2)
C(108)-C(103)-C(112)-C(111)	-60.4(3)
C(104)-O(102)-C(113)-C(114)	-34.1(3)
C(104)-O(103)-C(114)-C(113)	-17.7(3)
O(102)-C(113)-C(114)-O(103)	31.4(3)
C(101)-C(109)-C(115)-C(116)	179.3(2)
C(108)-C(109)-C(115)-C(116)	66.4(3)
C(110)-C(109)-C(115)-C(116)	-62.3(4)
C(109)-C(115)-C(116)-O(104)	21.0(5)
C(109)-C(115)-C(116)-N(01A)	175.6(5)

C(109)-C(115)-C(116)-N(101)	-144.7(4)
O(104)-C(116)-N(101)-C(117)	19.8(7)
C(115)-C(116)-N(101)-C(117)	-173.9(4)
O(104)-C(116)-N(101)-C(120)	179.3(4)
C(115)-C(116)-N(101)-C(120)	-14.4(7)
C(116)-N(101)-C(117)-C(118)	106.5(6)
C(120)-N(101)-C(117)-C(118)	-56.0(6)
N(101)-C(117)-C(118)-O(105)	57.5(7)
C(117)-C(118)-O(105)-C(119)	-59.7(8)
C(118)-O(105)-C(119)-C(120)	60.0(8)
C(116)-N(101)-C(120)-C(119)	-104.3(6)
C(117)-N(101)-C(120)-C(119)	56.6(6)
O(105)-C(119)-C(120)-N(101)	-58.0(7)
O(104)-C(116)-N(01A)-C(17A)	-16.6(9)
C(115)-C(116)-N(01A)-C(17A)	-172.5(6)
O(104)-C(116)-N(01A)-C(20A)	166.0(7)
C(115)-C(116)-N(01A)-C(20A)	10.2(10)
C(116)-N(01A)-C(17A)-C(18A)	-126.2(8)
C(20A)-N(01A)-C(17A)-C(18A)	51.6(10)
N(01A)-C(17A)-C(18A)-O(05A)	-55.2(11)
C(17A)-C(18A)-O(05A)-C(19A)	59.6(11)
C(18A)-O(05A)-C(19A)-C(20A)	-60.2(11)
C(116)-N(01A)-C(20A)-C(19A)	125.0(9)
C(17A)-N(01A)-C(20A)-C(19A)	-52.5(9)
O(05A)-C(19A)-C(20A)-N(01A)	57.0(11)

Symmetry transformations used to generate equivalent atoms:

A5.4 X-RAY CRYSTAL STRUCTURE OF COMPOUND 130

Figure A5.4.1 *X-ray crystal structure of compound* ***130***.

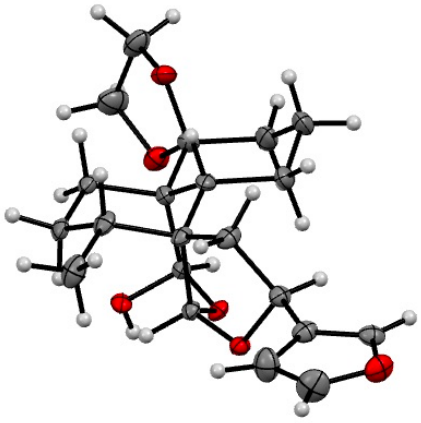


Table A5.4.1. *Crystal data and structure refinement for compound* ***130***.

Empirical formula	C21 H28 O6	
Formula weight	376.43	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 10.5284(6) Å	a= 90°.
	b = 7.5847(7) Å	b= 97.585(7)°.
	c = 11.5215(9) Å	g = 90°.
Volume	912.00(12) $Å^3$	
Z	2	
Density (calculated)	1.371 Mg/m^3	
Absorption coefficient	0.818 mm^{-1}	
F(000)	404	
Crystal size	0.200 x 0.200 x 0.200 mm^3	
Theta range for data collection	3.870 to 74.452°.	
Index ranges	-13<=h<=13, -9<=k<=9, -14<=l<=14	
Reflections collected	22241	
Independent reflections	3674 [R(int) = 0.0399]	
Completeness to theta = 67.679°	100.0 %	

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7538 and 0.6781
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3674 / 2 / 248
Goodness-of-fit on F^2	1.045
Final R indices [I>2sigma(I)]	R1 = 0.0328, wR2 = 0.0812
R indices (all data)	R1 = 0.0337, wR2 = 0.0818
Absolute structure parameter	0.14(6)
Extinction coefficient	n/a
Largest diff. peak and hole	0.613 and -0.305 e.$Å^{-3}$

Table A5.4.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for compound **130**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	3902(2)	7200(3)	3671(2)	21(1)
C(17)	2439(2)	7387(4)	3541(2)	30(1)
C(2)	4490(2)	9033(3)	3564(2)	19(1)
C(3)	5947(2)	8977(3)	3654(2)	17(1)
C(4)	6441(2)	7621(3)	2829(2)	16(1)
C(5)	6056(2)	8088(3)	1510(2)	15(1)
O(1)	5647(2)	9846(2)	1381(1)	17(1)
O(2)	5106(1)	6913(2)	931(1)	16(1)
C(6)	4027(2)	6555(3)	1525(2)	15(1)
O(3)	3327(1)	5206(2)	881(1)	17(1)
C(7)	3550(2)	3527(3)	1496(2)	19(1)
C(18)	2411(2)	2367(3)	1164(2)	21(1)
C(19)	1096(3)	2651(4)	1293(3)	35(1)
C(20)	466(3)	1177(4)	905(3)	37(1)
O(6)	1289(2)	-32(2)	533(2)	29(1)
C(21)	2469(2)	746(3)	702(2)	21(1)
C(8)	3761(2)	4070(3)	2787(2)	22(1)
C(9)	4404(2)	5899(3)	2799(2)	17(1)
C(10)	5886(2)	5784(3)	3074(2)	18(1)
C(11)	6523(2)	4272(3)	2467(2)	23(1)
C(12)	7977(2)	4285(3)	2789(2)	30(1)
C(13)	8535(2)	6045(3)	2479(2)	28(1)
C(14)	7930(2)	7557(3)	3082(2)	21(1)
O(4)	8453(2)	9186(2)	2738(1)	24(1)
C(15)	9110(3)	9987(4)	3774(3)	38(1)
C(16)	9319(2)	8564(4)	4644(2)	31(1)
O(5)	8287(2)	7391(2)	4322(1)	26(1)

Table A5.4.3. Bond lengths [Å] and angles [°] for compound **130**.

C(1)-C(2)	1.533(3)
C(1)-C(17)	1.534(3)
C(1)-C(9)	1.550(3)
C(1)-H(1)	1.0000
C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(2)-C(3)	1.525(3)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(4)	1.537(3)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(10)	1.551(3)
C(4)-C(14)	1.556(3)
C(4)-C(5)	1.561(3)
C(5)-O(1)	1.403(2)
C(5)-O(2)	1.436(2)
C(5)-H(5)	1.0000
O(1)-H(1O)	0.83(2)
O(2)-C(6)	1.427(3)
C(6)-O(3)	1.412(3)
C(6)-C(9)	1.552(3)
C(6)-H(6)	1.0000
O(3)-C(7)	1.461(3)
C(7)-C(18)	1.496(3)
C(7)-C(8)	1.531(3)
C(7)-H(7)	1.0000
C(18)-C(21)	1.345(3)
C(18)-C(19)	1.428(4)
C(19)-C(20)	1.345(4)
C(19)-H(19)	0.9500
C(20)-O(6)	1.369(4)
C(20)-H(20)	0.9500

O(6)-C(21)	1.366(3)
C(21)-H(21)	0.9500
C(8)-C(9)	1.543(3)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(10)	1.554(3)
C(10)-C(11)	1.542(3)
C(10)-H(10)	1.0000
C(11)-C(12)	1.527(3)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(12)-C(13)	1.519(4)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(14)	1.523(3)
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-O(4)	1.430(3)
C(14)-O(5)	1.435(3)
O(4)-C(15)	1.433(3)
C(15)-C(16)	1.470(4)
C(15)-H(15A)	0.9900
C(15)-H(15B)	0.9900
C(16)-O(5)	1.415(3)
C(16)-H(16A)	0.9900
C(16)-H(16B)	0.9900

C(2)-C(1)-C(17)	108.60(19)
C(2)-C(1)-C(9)	110.40(17)
C(17)-C(1)-C(9)	114.79(19)
C(2)-C(1)-H(1)	107.6
C(17)-C(1)-H(1)	107.6
C(9)-C(1)-H(1)	107.6
C(1)-C(17)-H(17A)	109.5
C(1)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5

C(1)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(3)-C(2)-C(1)	112.50(18)
C(3)-C(2)-H(2A)	109.1
C(1)-C(2)-H(2A)	109.1
C(3)-C(2)-H(2B)	109.1
C(1)-C(2)-H(2B)	109.1
H(2A)-C(2)-H(2B)	107.8
C(2)-C(3)-C(4)	113.36(17)
C(2)-C(3)-H(3A)	108.9
C(4)-C(3)-H(3A)	108.9
C(2)-C(3)-H(3B)	108.9
C(4)-C(3)-H(3B)	108.9
H(3A)-C(3)-H(3B)	107.7
C(3)-C(4)-C(10)	108.76(17)
C(3)-C(4)-C(14)	108.67(17)
C(10)-C(4)-C(14)	109.39(17)
C(3)-C(4)-C(5)	112.64(17)
C(10)-C(4)-C(5)	108.98(16)
C(14)-C(4)-C(5)	108.37(16)
O(1)-C(5)-O(2)	110.78(16)
O(1)-C(5)-C(4)	110.81(16)
O(2)-C(5)-C(4)	112.74(16)
O(1)-C(5)-H(5)	107.4
O(2)-C(5)-H(5)	107.4
C(4)-C(5)-H(5)	107.4
C(5)-O(1)-H(1O)	107(2)
C(6)-O(2)-C(5)	116.48(15)
O(3)-C(6)-O(2)	106.26(15)
O(3)-C(6)-C(9)	108.37(16)
O(2)-C(6)-C(9)	113.20(16)
O(3)-C(6)-H(6)	109.6
O(2)-C(6)-H(6)	109.6
C(9)-C(6)-H(6)	109.6
C(6)-O(3)-C(7)	109.73(15)

O(3)-C(7)-C(18)	108.43(17)
O(3)-C(7)-C(8)	103.28(17)
C(18)-C(7)-C(8)	114.56(18)
O(3)-C(7)-H(7)	110.1
C(18)-C(7)-H(7)	110.1
C(8)-C(7)-H(7)	110.1
C(21)-C(18)-C(19)	105.9(2)
C(21)-C(18)-C(7)	124.2(2)
C(19)-C(18)-C(7)	129.8(2)
C(20)-C(19)-C(18)	106.4(2)
C(20)-C(19)-H(19)	126.8
C(18)-C(19)-H(19)	126.8
C(19)-C(20)-O(6)	110.8(2)
C(19)-C(20)-H(20)	124.6
O(6)-C(20)-H(20)	124.6
C(21)-O(6)-C(20)	105.52(19)
C(18)-C(21)-O(6)	111.3(2)
C(18)-C(21)-H(21)	124.3
O(6)-C(21)-H(21)	124.3
C(7)-C(8)-C(9)	104.95(17)
C(7)-C(8)-H(8A)	110.8
C(9)-C(8)-H(8A)	110.8
C(7)-C(8)-H(8B)	110.8
C(9)-C(8)-H(8B)	110.8
H(8A)-C(8)-H(8B)	108.8
C(8)-C(9)-C(1)	113.06(18)
C(8)-C(9)-C(6)	102.87(16)
C(1)-C(9)-C(6)	110.07(18)
C(8)-C(9)-C(10)	112.27(18)
C(1)-C(9)-C(10)	108.85(17)
C(6)-C(9)-C(10)	109.57(16)
C(11)-C(10)-C(4)	112.90(18)
C(11)-C(10)-C(9)	115.75(18)
C(4)-C(10)-C(9)	107.77(17)
C(11)-C(10)-H(10)	106.6
C(4)-C(10)-H(10)	106.6

C(9)-C(10)-H(10)	106.6
C(12)-C(11)-C(10)	111.50(19)
C(12)-C(11)-H(11A)	109.3
C(10)-C(11)-H(11A)	109.3
C(12)-C(11)-H(11B)	109.3
C(10)-C(11)-H(11B)	109.3
H(11A)-C(11)-H(11B)	108.0
C(13)-C(12)-C(11)	110.81(19)
C(13)-C(12)-H(12A)	109.5
C(11)-C(12)-H(12A)	109.5
C(13)-C(12)-H(12B)	109.5
C(11)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	108.1
C(12)-C(13)-C(14)	110.9(2)
C(12)-C(13)-H(13A)	109.5
C(14)-C(13)-H(13A)	109.5
C(12)-C(13)-H(13B)	109.5
C(14)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	108.0
O(4)-C(14)-O(5)	106.96(18)
O(4)-C(14)-C(13)	108.97(19)
O(5)-C(14)-C(13)	108.51(19)
O(4)-C(14)-C(4)	109.66(18)
O(5)-C(14)-C(4)	108.30(17)
C(13)-C(14)-C(4)	114.18(18)
C(14)-O(4)-C(15)	107.29(19)
O(4)-C(15)-C(16)	105.6(2)
O(4)-C(15)-H(15A)	110.6
C(16)-C(15)-H(15A)	110.6
O(4)-C(15)-H(15B)	110.6
C(16)-C(15)-H(15B)	110.6
H(15A)-C(15)-H(15B)	108.8
O(5)-C(16)-C(15)	104.0(2)
O(5)-C(16)-H(16A)	111.0
C(15)-C(16)-H(16A)	110.9
O(5)-C(16)-H(16B)	111.0

C(15)-C(16)-H(16B)	110.9
H(16A)-C(16)-H(16B)	109.0
C(16)-O(5)-C(14)	107.27(19)

Symmetry transformations used to generate equivalent atoms:

Table A5.4.4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for compound **130**. 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}
C(1)	27(1)	22(1)	14(1)	-1(1)	7(1)	-3(1)
C(17)	28(1)	35(1)	30(1)	-9(1)	14(1)	-7(1)
C(2)	24(1)	18(1)	14(1)	-4(1)	5(1)	1(1)
C(3)	23(1)	16(1)	12(1)	-2(1)	2(1)	0(1)
C(4)	19(1)	14(1)	15(1)	0(1)	1(1)	3(1)
C(5)	16(1)	14(1)	14(1)	-1(1)	2(1)	0(1)
O(1)	24(1)	14(1)	14(1)	4(1)	4(1)	2(1)
O(2)	20(1)	18(1)	11(1)	-1(1)	4(1)	-3(1)
C(6)	19(1)	14(1)	12(1)	0(1)	3(1)	0(1)
O(3)	22(1)	14(1)	14(1)	1(1)	0(1)	-1(1)
C(7)	22(1)	15(1)	18(1)	2(1)	2(1)	-2(1)
C(18)	25(1)	20(1)	17(1)	3(1)	3(1)	-4(1)
C(19)	30(1)	33(1)	44(2)	-6(1)	12(1)	0(1)
C(20)	22(1)	47(2)	44(2)	-5(1)	8(1)	-8(1)
O(6)	33(1)	24(1)	28(1)	0(1)	1(1)	-11(1)
C(21)	21(1)	21(1)	21(1)	6(1)	0(1)	-2(1)
C(8)	31(1)	19(1)	16(1)	2(1)	3(1)	-7(1)
C(9)	25(1)	15(1)	12(1)	1(1)	2(1)	-3(1)
C(10)	25(1)	14(1)	13(1)	3(1)	-1(1)	3(1)
C(11)	29(1)	14(1)	24(1)	0(1)	-2(1)	4(1)
C(12)	30(1)	23(1)	34(1)	-5(1)	-6(1)	12(1)
C(13)	20(1)	30(1)	31(1)	-9(1)	-2(1)	8(1)
C(14)	20(1)	20(1)	20(1)	-1(1)	-3(1)	4(1)
O(4)	21(1)	27(1)	25(1)	-3(1)	1(1)	-5(1)
C(15)	40(2)	31(1)	38(2)	-3(1)	-11(1)	-6(1)
C(16)	24(1)	42(2)	27(1)	-12(1)	-1(1)	-3(1)
O(5)	29(1)	24(1)	22(1)	0(1)	-9(1)	2(1)

Table A5.4.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for compound **130**.

	x	y	z	U(eq)
H(1)	4193	6758	4481	25
H(17A)	2112	7639	2722	45
H(17B)	2210	8355	4037	45
H(17C)	2061	6287	3781	45
H(2A)	4138	9556	2801	22
H(2B)	4241	9803	4190	22
H(3A)	6305	8691	4470	20
H(3B)	6263	10160	3471	20
H(5)	6842	7968	1114	18
H(1O)	5790(30)	10170(40)	720(20)	26
H(6)	3484	7636	1526	18
H(7)	4339	2951	1277	22
H(19)	737	3677	1592	42
H(20)	-429	1000	892	45
H(21)	3233	210	516	26
H(8A)	4324	3215	3257	26
H(8B)	2935	4140	3108	26
H(10)	6087	5578	3936	22
H(11A)	6179	3130	2702	27
H(11B)	6309	4389	1608	27
H(12A)	8195	4066	3639	36
H(12B)	8358	3328	2364	36
H(13A)	8381	6217	1621	33
H(13B)	9472	6042	2724	33
H(15A)	8584	10939	4055	45
H(15B)	9938	10492	3618	45
H(16A)	10151	7972	4608	37
H(16B)	9301	9024	5446	37

Table A5.4.6. Torsion angles [°] for compound **130**.

C(17)-C(1)-C(2)-C(3)	-178.67(17)
C(9)-C(1)-C(2)-C(3)	-52.0(2)
C(1)-C(2)-C(3)-C(4)	50.9(2)
C(2)-C(3)-C(4)-C(10)	-55.7(2)
C(2)-C(3)-C(4)-C(14)	-174.69(17)
C(2)-C(3)-C(4)-C(5)	65.2(2)
C(3)-C(4)-C(5)-O(1)	15.5(2)
C(10)-C(4)-C(5)-O(1)	136.33(17)
C(14)-C(4)-C(5)-O(1)	-104.72(19)
C(3)-C(4)-C(5)-O(2)	-109.3(2)
C(10)-C(4)-C(5)-O(2)	11.5(2)
C(14)-C(4)-C(5)-O(2)	130.47(18)
O(1)-C(5)-O(2)-C(6)	-77.6(2)
C(4)-C(5)-O(2)-C(6)	47.2(2)
C(5)-O(2)-C(6)-O(3)	-172.14(15)
C(5)-O(2)-C(6)-C(9)	-53.3(2)
O(2)-C(6)-O(3)-C(7)	103.86(18)
C(9)-C(6)-O(3)-C(7)	-18.1(2)
C(6)-O(3)-C(7)-C(18)	153.43(18)
C(6)-O(3)-C(7)-C(8)	31.5(2)
O(3)-C(7)-C(18)-C(21)	124.1(2)
C(8)-C(7)-C(18)-C(21)	-121.1(2)
O(3)-C(7)-C(18)-C(19)	-58.6(3)
C(8)-C(7)-C(18)-C(19)	56.1(3)
C(21)-C(18)-C(19)-C(20)	0.3(3)
C(7)-C(18)-C(19)-C(20)	-177.3(2)
C(18)-C(19)-C(20)-O(6)	-0.2(3)
C(19)-C(20)-O(6)-C(21)	-0.1(3)
C(19)-C(18)-C(21)-O(6)	-0.4(3)
C(7)-C(18)-C(21)-O(6)	177.4(2)
C(20)-O(6)-C(21)-C(18)	0.3(3)
O(3)-C(7)-C(8)-C(9)	-32.1(2)
C(18)-C(7)-C(8)-C(9)	-149.81(19)
C(7)-C(8)-C(9)-C(1)	140.1(2)

C(7)-C(8)-C(9)-C(6)	21.4(2)
C(7)-C(8)-C(9)-C(10)	-96.3(2)
C(2)-C(1)-C(9)-C(8)	-175.07(17)
C(17)-C(1)-C(9)-C(8)	-51.9(3)
C(2)-C(1)-C(9)-C(6)	-60.7(2)
C(17)-C(1)-C(9)-C(6)	62.5(2)
C(2)-C(1)-C(9)-C(10)	59.4(2)
C(17)-C(1)-C(9)-C(10)	-177.42(19)
O(3)-C(6)-C(9)-C(8)	-2.9(2)
O(2)-C(6)-C(9)-C(8)	-120.52(18)
O(3)-C(6)-C(9)-C(1)	-123.67(18)
O(2)-C(6)-C(9)-C(1)	118.73(18)
O(3)-C(6)-C(9)-C(10)	116.66(18)
O(2)-C(6)-C(9)-C(10)	-0.9(2)
C(3)-C(4)-C(10)-C(11)	-168.87(17)
C(14)-C(4)-C(10)-C(11)	-50.3(2)
C(5)-C(4)-C(10)-C(11)	68.0(2)
C(3)-C(4)-C(10)-C(9)	62.0(2)
C(14)-C(4)-C(10)-C(9)	-179.43(16)
C(5)-C(4)-C(10)-C(9)	-61.1(2)
C(8)-C(9)-C(10)-C(11)	41.8(2)
C(1)-C(9)-C(10)-C(11)	167.71(18)
C(6)-C(9)-C(10)-C(11)	-71.9(2)
C(8)-C(9)-C(10)-C(4)	169.23(17)
C(1)-C(9)-C(10)-C(4)	-64.8(2)
C(6)-C(9)-C(10)-C(4)	55.6(2)
C(4)-C(10)-C(11)-C(12)	54.8(2)
C(9)-C(10)-C(11)-C(12)	179.6(2)
C(10)-C(11)-C(12)-C(13)	-57.1(3)
C(11)-C(12)-C(13)-C(14)	56.9(3)
C(12)-C(13)-C(14)-O(4)	-178.26(19)
C(12)-C(13)-C(14)-O(5)	65.6(2)
C(12)-C(13)-C(14)-C(4)	-55.3(3)
C(3)-C(4)-C(14)-O(4)	-67.6(2)
C(10)-C(4)-C(14)-O(4)	173.80(17)
C(5)-C(4)-C(14)-O(4)	55.1(2)

C(3)-C(4)-C(14)-O(5)	48.8(2)
C(10)-C(4)-C(14)-O(5)	-69.8(2)
C(5)-C(4)-C(14)-O(5)	171.49(17)
C(3)-C(4)-C(14)-C(13)	169.80(19)
C(10)-C(4)-C(14)-C(13)	51.2(2)
C(5)-C(4)-C(14)-C(13)	-67.5(2)
O(5)-C(14)-O(4)-C(15)	-0.4(2)
C(13)-C(14)-O(4)-C(15)	-117.5(2)
C(4)-C(14)-O(4)-C(15)	116.8(2)
C(14)-O(4)-C(15)-C(16)	18.0(3)
O(4)-C(15)-C(16)-O(5)	-28.8(3)
C(15)-C(16)-O(5)-C(14)	28.8(3)
O(4)-C(14)-O(5)-C(16)	-18.2(2)
C(13)-C(14)-O(5)-C(16)	99.3(2)
C(4)-C(14)-O(5)-C(16)	-136.29(19)

Symmetry transformations used to generate equivalent atoms:

Table A5.4.7. Hydrogen bonds for compound **130** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1O)...O(2)#1	0.83(2)	2.40(3)	3.103(2)	142(3)
O(1)-H(1O)...O(3)#1	0.83(2)	2.17(2)	2.963(2)	158(3)
C(21)-H(21)...O(1)#2	0.95	2.62	3.403(3)	140.1

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y+1/2,-z #2 x,y-1,z

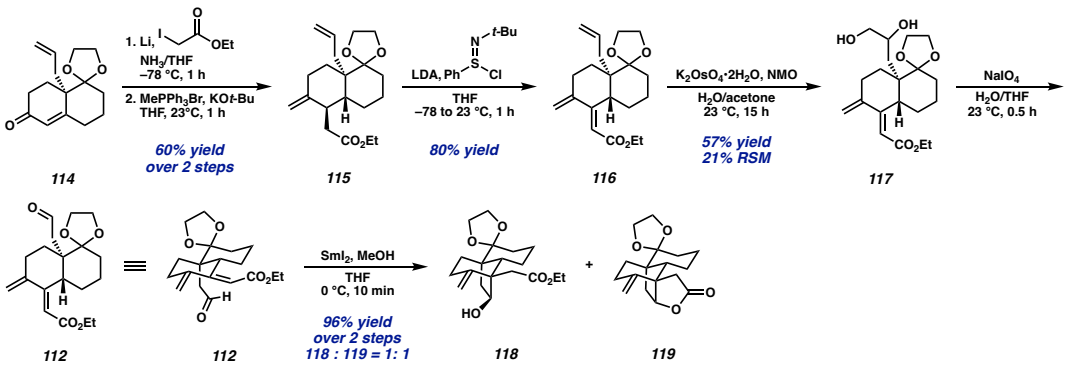
APPENDIX 6

Synthetic Summary for Chapter 2:

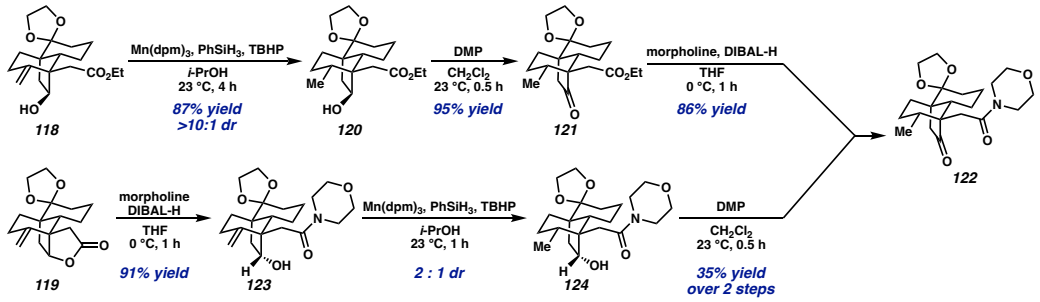
Total Synthesis of Crotonine G and Crotonolide D

Scheme A6.1. *Synthetic summary of the total synthesis of crotonolide D.*

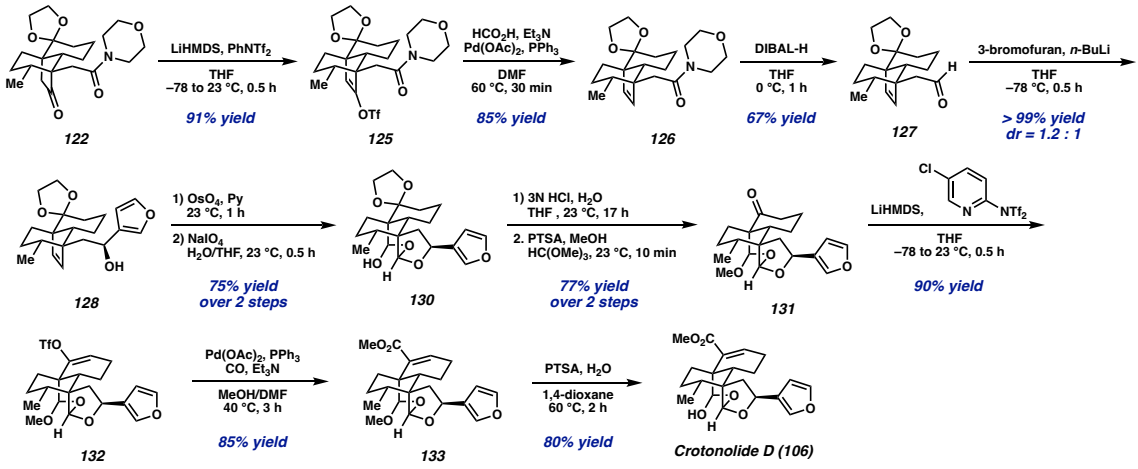
A) Synthesis of 118 and 119 via SmI_2 mediated cyclization.



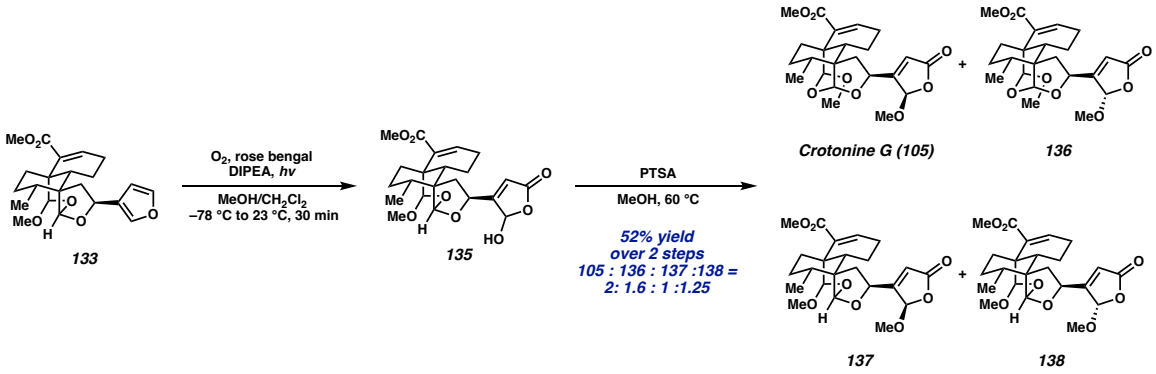
B) Synthesis of amide 122.



C) Synthesis of crotonolide D (106) from amide 122.



Scheme A6.2. *Synthesis of crotonolide G.*



ABOUT THE AUTHOR

Hao Yu was born in Jinan, China on May 31st, 1996. He spent his entire childhood in Jinan, where he attended elementary to high school. He participated in the chemistry olympiad in high school, where he developed interest in chemistry (although he did not get any prize).

Hao moved to Vancouver, Canada in 2016, where he attended the University of British Columbia. He chose to major in chemistry because that was the only subject he was somewhat good at. He became interested in organic synthesis after taking a second-year organic chemistry course taught by Prof. Marco Ciufolini, and he joined the Ciufolini lab at the beginning of his third year, working on the synthesis of tanshinone analogs. At the beginning of his fourth year, he joined the lab of Prof. Glenn Sammis working on sulfuryl fluoride mediated reactions.

In 2020, Hao was admitted to Caltech, but he decided to defer his enrollment by a year because of the COVID pandemic. He came to Pasadena in September 2021, to begin graduate studies at Caltech under the guidance of Prof. Brian M. Stoltz. During his PhD, Hao's research primarily focused on the total synthesis of bioactive natural products.

Upon completing his PhD, Hao will travel to New Jersey to conduct postdoctoral research at Princeton University with Professor David W. C. MacMillan.