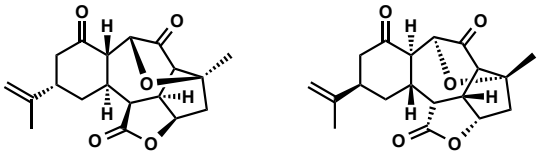
CHAPTER 5

Synthetic Studies Toward Polycyclic Ineleganolide

5.1. Introduction

The complex polycyclic norcembranoid ineleganolide (**238**) was first isolated from the Taiwanese coral *Sinularia inelegans* in 1999 by the Duh group (Figure 5.1.1).[1,2] The relative stereochemistry of ineleganolide (**238**) was unambiguously confirmed by X-ray analysis and spectroscopic method. This complex polycyclic norditerpenoid possesses intriguing architectural features including an ether bridge, which connects two carbocyclic rings and an angular fusion of five-, seven,- and six-membered carbocyclic rings linked with a five-membered lactone ring. Ineleganolide exhibits cytotoxic activity against P-388 murine leukemia cells (ED_{50} = 3.82 μg/mL).[1]

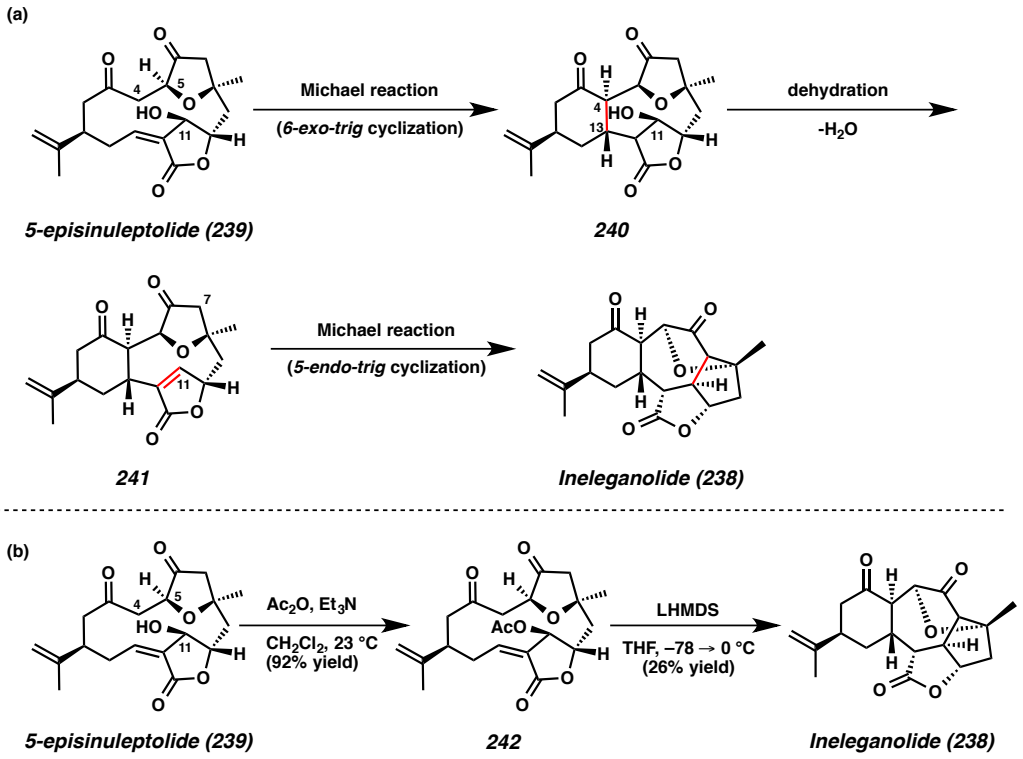
Figure 5.1.1. *Structure of Ineleganolide (**238**). (Originally depicted structure shown on the left-hand side; the proposed actual structure from biosynthetic studies shown on the right-hand side.)*[3]



Ineleganolide (238)

A biosynthetic pathway of ineleganolide was proposed by Pattenden and co-workers (Scheme 5.1.1a).[4] It is hypothesized that ineleganolide (**238**) is biosynthetically constructed by successive transannular Michael reactions of macrocyclic 5-episinuleptolide (**239**). An initial intramolecular Michael reaction of 5-episinuleptolide (**239**) establishes the C4–C13 bond to furnish cyclohexanone **240**. Dehydration of **240** at C11 and subsequent bond formation between C7 and C11 by a second Michael reaction affords ineleganolide (**238**). The Pattenden group proved this biosynthetic route experimentally by a semisynthesis of ineleganolide (**238**) from 5-episinuleptolide (**239**), which was isolated from *Sinularia scabra* species (Scheme 5.1.1b).[5] Acetylation of the hydroxyl group at C11 position of 5-episinuleptolide (**239**) furnished acetate **242**. Ineleganolide (**238**) was obtained in 26% yield by treatment of acetate **242** with LHMDS.

Scheme 5.1.1. *Proposed Biosynthesis of Ineleganolide (**238**)*

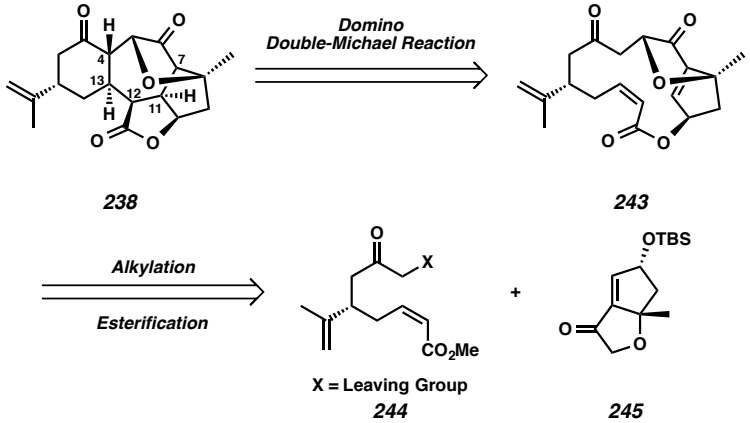


Although this intriguing polycyclic norditerpenoid ineleganolide (**238**) has attracted much attention from the synthetic community over the past decade including extensive efforts from my lab at Caltech,[6] a total synthesis of ineleganolide has not been reported. Herein, we describe new synthetic strategies toward an enantioselective synthesis of ineleganolide (**238**). We chose to pursue the synthesis of the enantiomer of ineleganolide (**238**), which was depicted in the original isolation paper.

5.2. Results and Discussion

We envisioned that a total synthesis of ineleganolide (**238**) could be achieved by successive transannular Michael reactions (Scheme 5.2.1). Disconnections of the C4–C13 and C11–C12 bonds affords domino double-Michael reaction precursor **243**. The 1,4-diketone and ester functional groups of macrocycle **243** can be disassembled into α,β-unsaturated ester **244** and bicycle **245**.

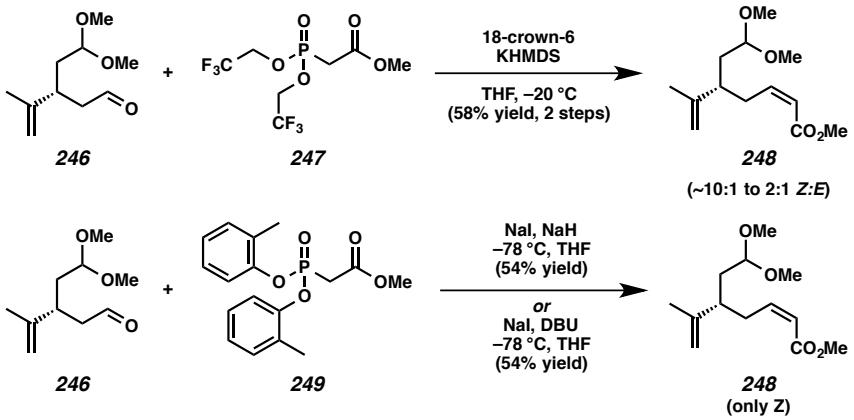
Scheme 5.2.1. *Retrosynthesis of Ineleganolide (**238**)*



Our synthesis began with the known acetal **246**[7] to prepare the α,β-unsaturated ester fragment **248** (Scheme 5.2.2). Subjection of acetal **246** to Still-Gennari

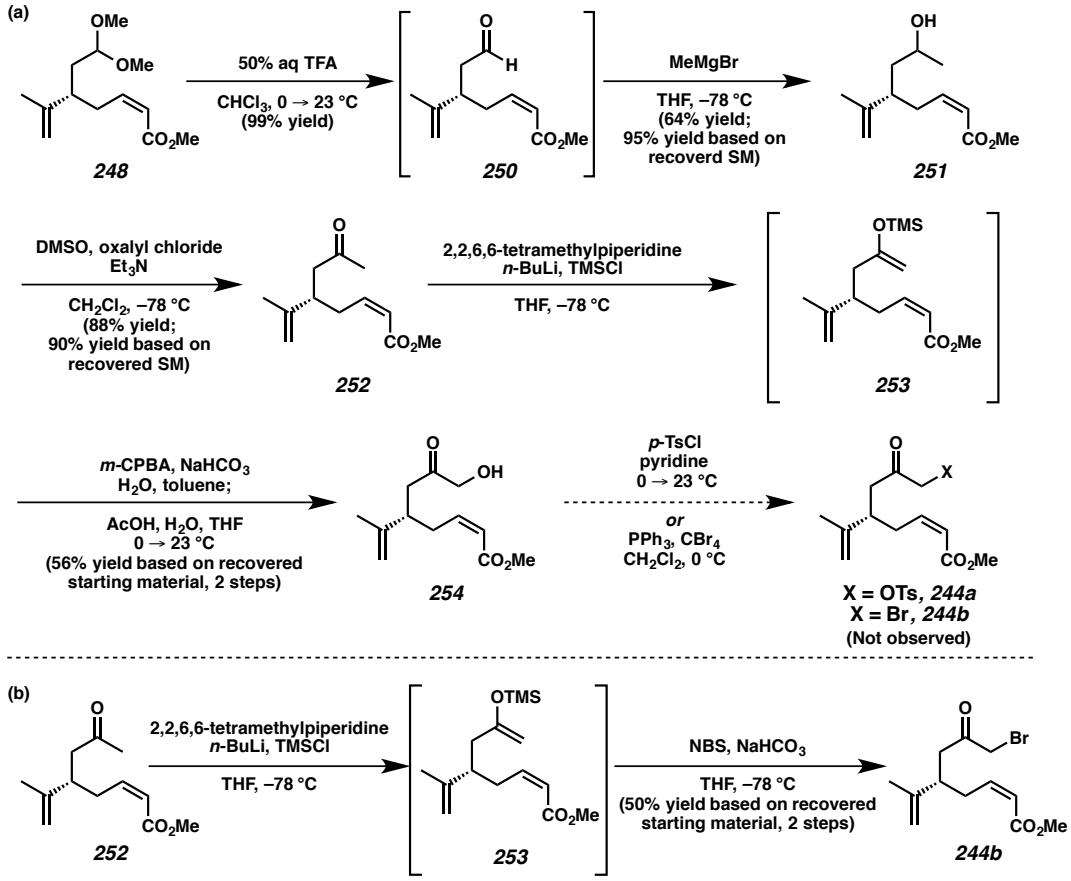
olefination conditions[8,9] afforded the (*Z*)- and (*E*)-isomers of enoate **248** in ratios ranging from 10:1 to 2:1, respectively. We were delighted to find that highly (*Z*)-selective olefination occurred to furnish enoate **248** in 54% yield using conditions developed by the Ando group.[10]

Scheme 5.2.2. *Synthesis of (Z)-Selective Enoate* ***248***



Acid-mediated acetal hydrolysis of **248** furnished aldehyde **250** in quantitative yield (Scheme 5.2.3a). Methyl Grignard addition to aldehyde **250** produced diastereomeric mixtures of alcohol **251**, which was converted to ketone **252** by Swern oxidation. After extensive experimentation, it was found that employing LiTMP (TMP = 2,2,6,6-tetramethylpiperidine) and TMSCl afforded kinetically favored silyl enol ether **253** selectively.[11] Silyl enol ether **253** was subsequently transformed to α-hydroxyketone **254** by Rubottom oxidation.[12] Surprisingly, tosylation and bromination of α-hydroxyketone **254** proved to be challenging. However, we were delighted to find that treatment of silyl enol ether **253** with NBS furnished α-bromoketone **244b** (Scheme 5.2.3b).

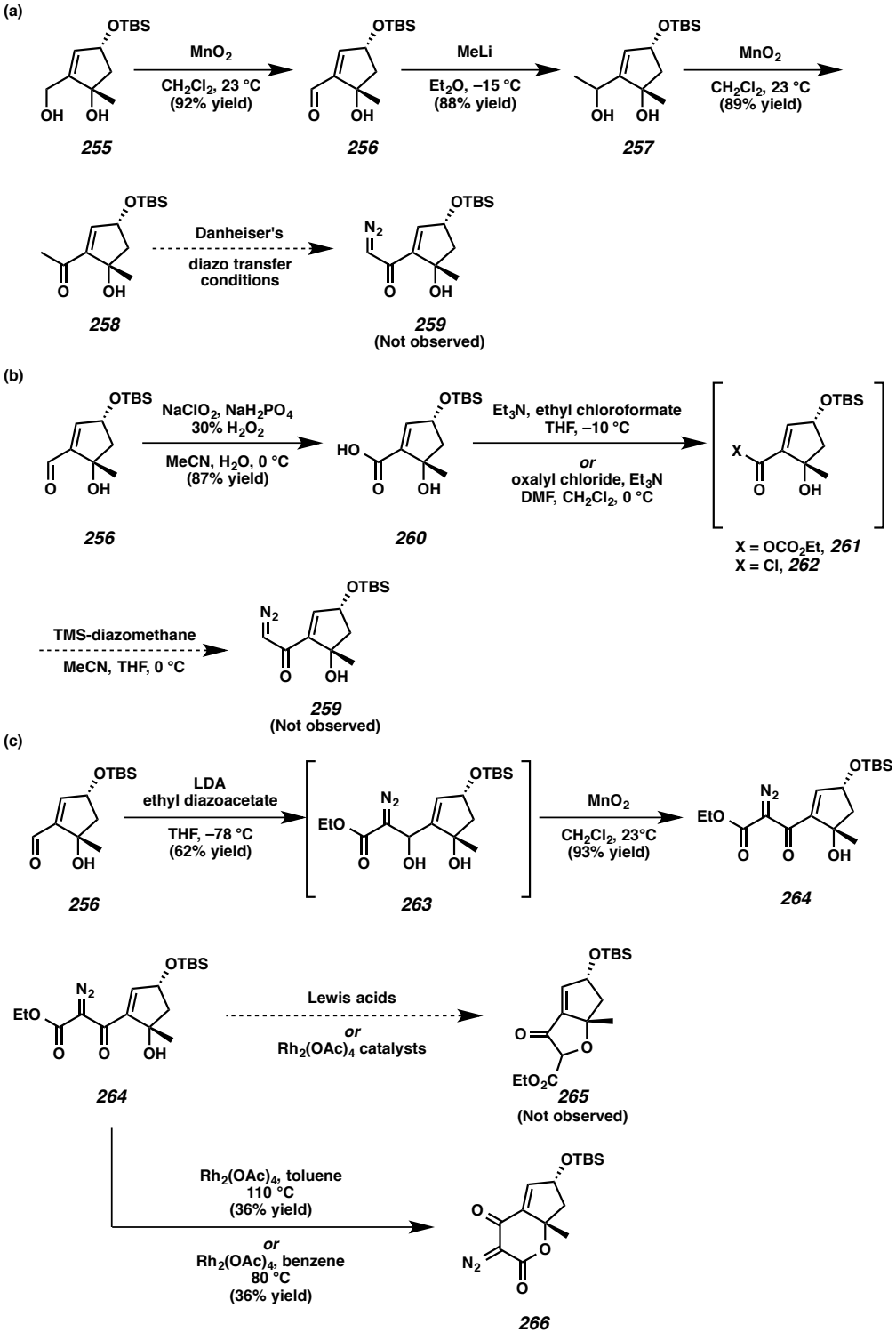
Scheme 5.2.3. *Synthesis of α-Bromoketone* ***244b***



With α,β-unsaturated ester fragment **244b** in hand, we turned our attention to preparing bicyclic fragment **245**. Oxidation of known diol **255**[6a,13] with MnO_2 delivered aldehyde **256** (Scheme 5.2.4a). Methyllithium addition to aldehyde **256** provided secondary alcohol **257**, which was oxidized with MnO_2 to afford ketone **258**. Unfortunately, we explored diazo transfer reactions extensively with various diazo sources (e.g., *p*-ABSA, 4-dodecylbenzenesulfonyl azide) under Danheiser's conditions,[14] but the desired diazo **259** was not observed. Another strategy was devised to obtain diazo ketone **259** by using Pinnick oxidation of aldehyde **256** to furnish acid **260** (Scheme 5.2.4b). Treatment of acid **260** with ethyl chloroformate or oxalyl chloride generated the corresponding intermediates **261** or **262**, respectively. However, attempts to obtain the desired diazo ketone **259** from intermediate **261** or

262 with TMS-diazomethane were unsuccessful.[15,16,17] Alternatively, we envisioned that the diazo functional group could be inserted by addition of ethyl diazoacetate to aldehyde **256** (Scheme 5.2.4c). Deprotonation of ethyl diazoacetate by LDA followed by addition to aldehyde **256** resulted in an alcohol (**263**) that could be oxidized to diazo compound **264**. Disappointingly, intramolecular O–H insertion of the tertiary alcohol to the diazo in **264** was found to be challenging under Lewis acid conditions. Despite screening numerous rhodium catalysts, solvents, and temperature, only undesired lactonization occurred to form **266**.[18]

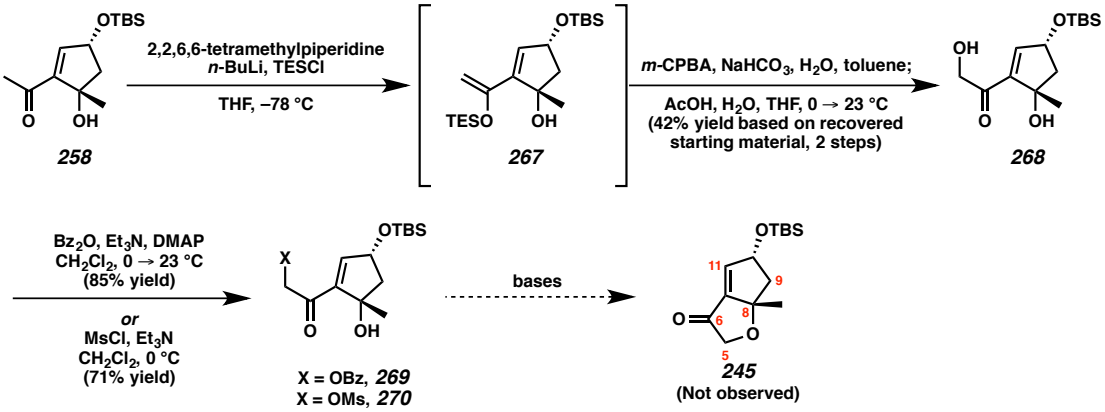
Scheme 5.2.4. *Attempts to Synthesize Bicyclic Fragment via Diazo Compounds*



Having failed to access the bicyclic fragment using diazo strategies, a revised approach was put forward (Scheme 5.2.5). Treatment of methyl ketone **258** with

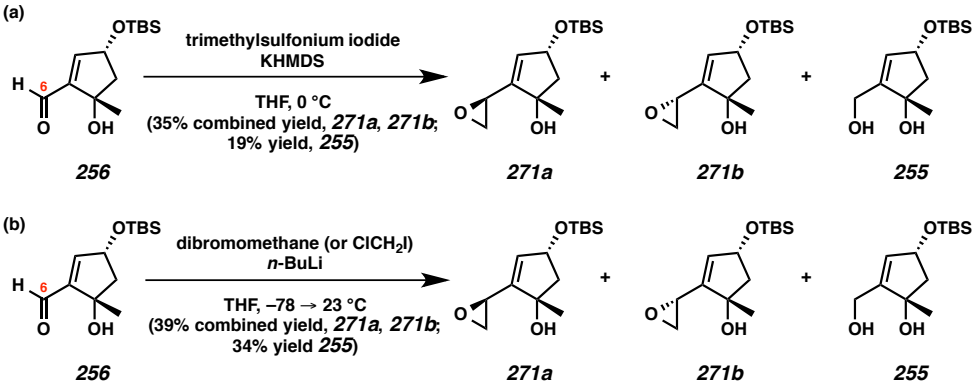
LiTMP (TMP = 2,2,6,6,-tetramethylpiperidine) and TESCl provided silyl ether **267**, which was transformed to α-hydroxyketone **268** by Rubottom oxidation. However, the desired bicycle **245** was not observed under various basic conditions (e.g., NaOH, KO^{t}Bu, NaH, LHMDS, LDA) from benzoate **269** and mesylate **270**, which were prepared from α-hydroxyketone **268**.[19,20]

Scheme 5.2.5. *Attempted Williamson Etherifications*



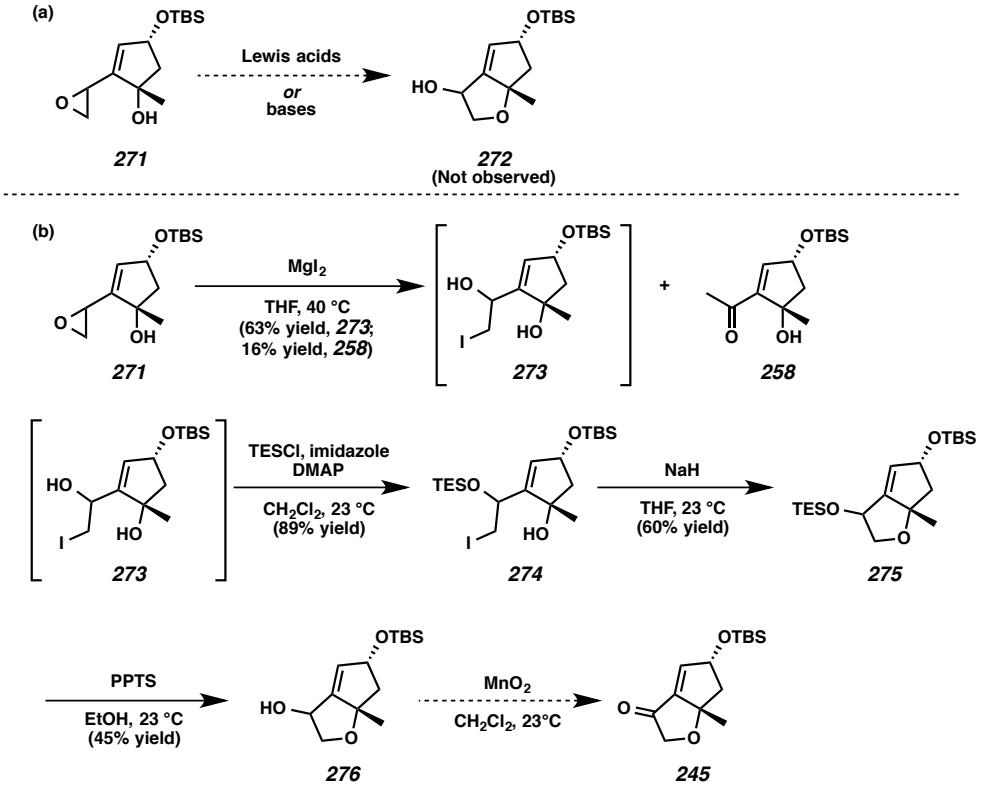
The desired bicycle **245** seemed highly angularly strained due to the α,β-unsaturated ketone at the junction of the bicycle. We envisaged that the strain would be reduced by converting the sp^2-hybridized carbon to the sp^3-hybridized carbon at C6. After considerable experimentation, we found that diastereomeric mixtures of epoxides **271a** and **271b** could be obtained by a Corey-Chaykovsky reaction (Scheme 5.2.6a).[21] Surprisingly, diol **255** was furnished as a major byproduct under these reaction conditions. Treatment of aldehyde **256** with dibromomethane (or chloroiodomethane) and *n*-BuLi also produced diastereomeric mixtures of epoxides **271a** and **271b** along with diol **255** (Scheme 5.2.6b).[22]

Scheme 5.2.6. *Synthesis Epoxides* ***271a*** *and* ***271b***



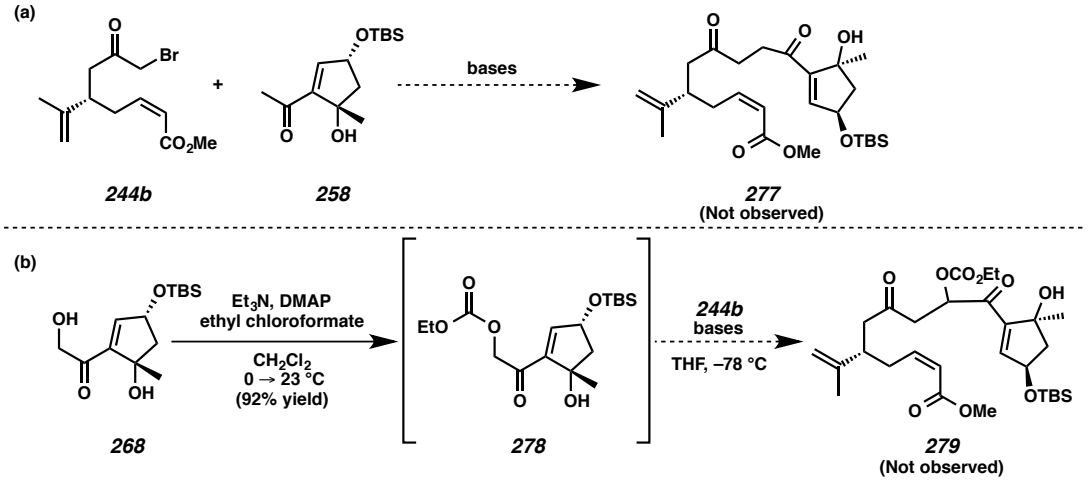
With epoxide **271** in hand, direct epoxide ring opening reactions were conducted to deliver **272** (Scheme 5.2.7a). Unfortunately, 5-membered ring formation to generate **272** was not observed with various Lewis acids (e.g., $CeCl_3$, TMSOTf, $In(OTf)_3$, PPTS) or bases (e.g., KHMDS, NaH).[23] Interestingly, treatment of epoxide **271** with MgI_2 at 40 °C generated iodohydrin **273** along with methyl ketone **258** (Scheme 5.2.7b).[24,25] Protection of secondary alcohol **273** with TESCl and subsequent intramolecular etherification of iodide **274** with NaH afforded bicyclc **275**.[26] Selective removal of TES group in **275** with PPTS furnished mono-silyl ether **276**. An attempt to oxidize secondary alcohol **276** to ketone **245** shows promise by TLC analysis but to date we have not successfully isolated and characterized **245**.[27]

Scheme 5.2.7. *Formation of Bicyclic Fragment*



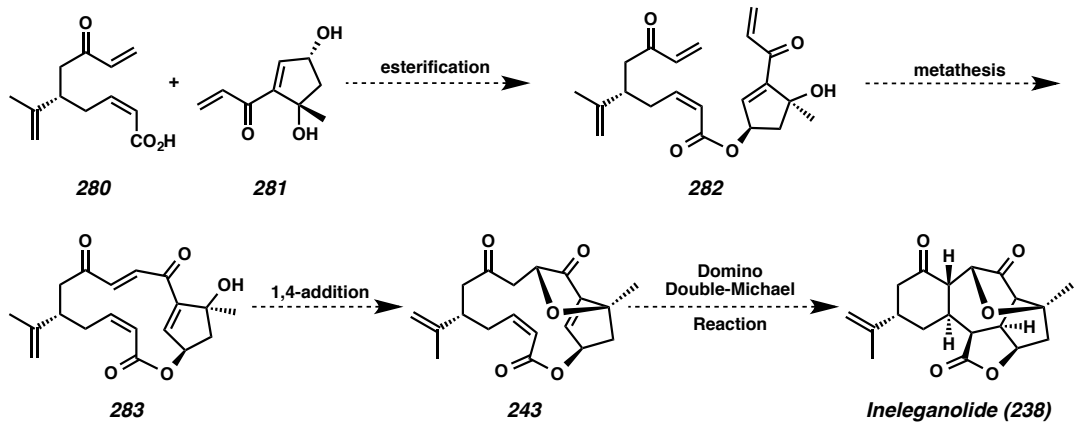
We next investigated coupling reactions of α-bromoketone **244b** and methylketone **258**, which could be easily prepared (Scheme 5.2.8a). Despite extensive experimentation, alkylation of methylketone **258** with α-bromoketone **244b** failed under basic conditions.[28] Treatment of hydroxyketone **268** with ethyl chloroformate afforded the carbonate intermediate, which was subjected to α-bromoketone **244b** to generate 1,4-diketone **279** under basic conditions. However, α-bromoketone **244b** appeared to decompose under the basic conditions and only the unreacted cyclopentene fragment was recovered.

Scheme 5.2.8. *Coupling of the Fragments*



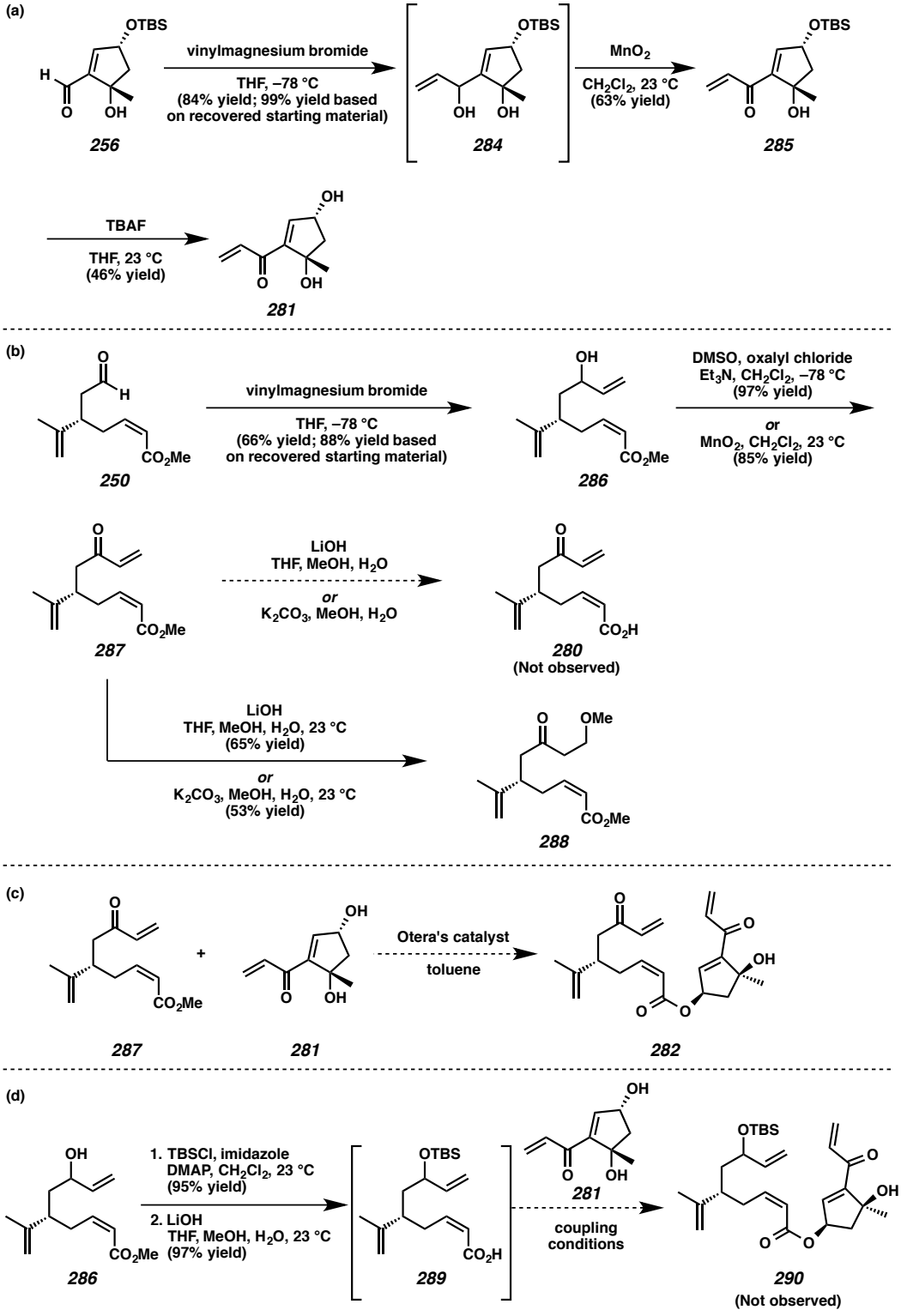
Since coupling reactions of α-bromoketone **244b** and the cyclopentene fragment by alkylation did not proceed, we next chose to focus on metathesis strategies to combine these two fragments (Scheme 5.2.9). We believed that esterification of acid **280** and secondary alcohol **281** would afford metathesis precursor diene **282**. Intramolecular metathesis reaction between the vinyl groups of **282** was expected to produce macrocycle **283**. 1,4-Addition of tertiary alcohol to the α,β-unsaturated ketone could deliver 5-membered ether **243**, which would proceed domino double-Michael reaction to afford ineleganolide (**238**).

Scheme 5.2.9. *Synthetic Plan by Using Metathesis Strategies*



1,2-Addition of vinylmagnesium bromide to aldehyde **256** furnished allyl alcohol **284**, which was oxidized by MnO_2 to deliver vinyl ketone **285** (Scheme 5.2.10a). Removal of silyl group on **285** with TBAF afforded diol **281**. Vinyl Grignard addition to aldehyde **250** and subsequent oxidation of the resultant alcohol **286** produced ketone **287** (Scheme 5.2.10b). However, an attempted hydrolysis of methyl ester **287** afforded Michael adduct **288** instead of the desired acid **280**. Additionally, transesterifications of ester **287** with alcohol **281** were unsuccessful with Otera's catalyst (Scheme 5.2.10c).[29] Therefore, we decided to explore esterification reactions with silyl ether **289** (Scheme 5.2.10d). Silylation of secondary alcohol **286** with TBSCl and subsequent hydrolysis produced acid intermediate **289**. Disappointingly, esterification of acid **289** and alcohol **281** was found to be challenging under several coupling conditions (e.g., EDCI, DCC, BOPCl).[30]

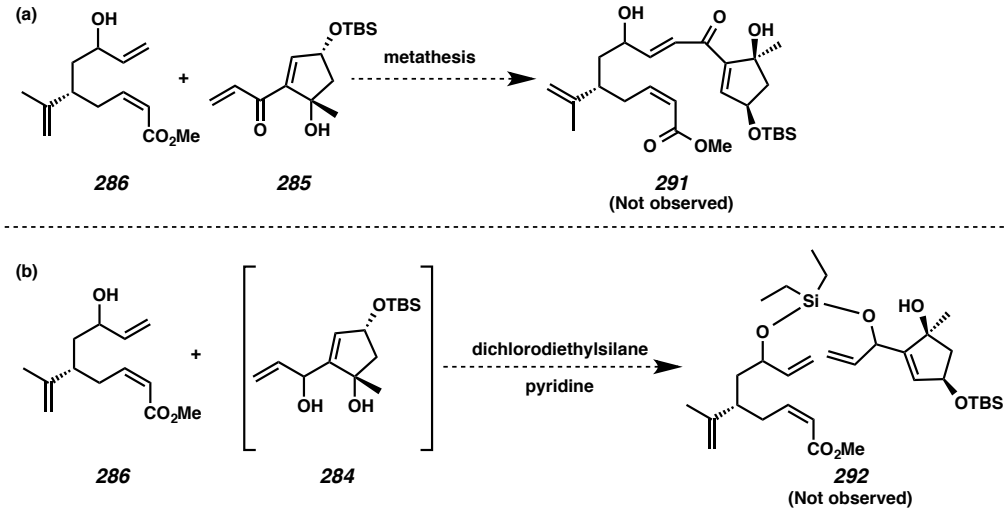
Scheme 5.2.10. *Coupling of the Fragments by Esterification*



At this stage, we began to investigate intermolecular metathesis between allyl alcohol **286** and vinyl ketone **285** with Grubbs' catalysts (Scheme 5.2.11a).[31]

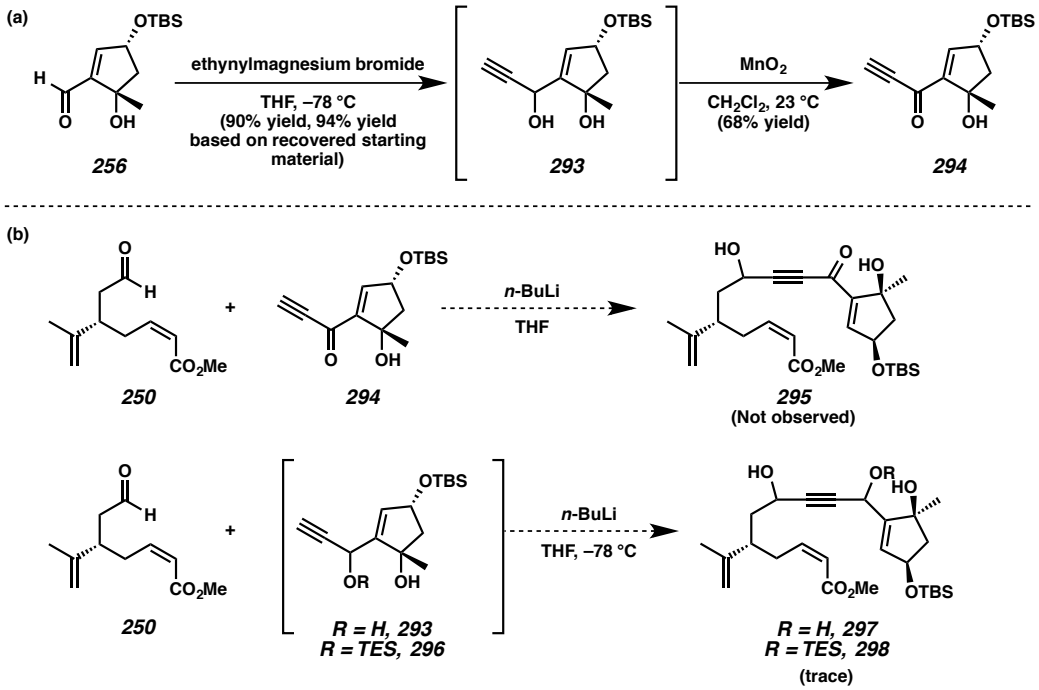
However, intermolecular metathesis of **286** and **285** to deliver **291** proved to be difficult. Alternatively, we attempted to connect allyl alcohol **286** and diol **284** via a silyl tether, but the yield was unsatisfactory (Scheme 5.2.11b).

Scheme 5.2.11. *Intermolecular Metathesis*



Since combining the two fragments appeared to be challenging, we devised a new synthetic strategy that utilized an alkyne functionality (Scheme 5.2.12). Addition of ethynylmagnesium bromide to aldehyde **256** provided intermediate **293**, which was oxidized by MnO_2 to generate ynone **294** (Scheme 5.2.12a). Although *n*-BuLi was subjected to alkyne **294** to form lithium acetylide, which was added to aldehyde **250**, little or no conversion was observed (Scheme 5.2.11b). We also attempted the lithium acetylide addition reaction with alcohol **293** or silyl ether **296**,[32] but only trace amounts of the respective coupling products **297** or **298** were observed.

Scheme 5.2.12. *Alkyne Addition*



5.3. Conclusion

We have described our efforts toward the synthesis of ineleganolide. Highly (*Z*)-selective olefination at C12–C13 was achieved by a method developed by the Ando group. The C–O bond formation at C5, which proved to be challenging in the other strategy investigated in our group,[6a] was accomplished. Although the entire fragmented carbon framework was constructed from this work, unfortunately, coupling of the two fragments was unsuccessful. We will further investigate a total synthesis of ineleganolide using modified strategies.

5.4. Experimental Methods and Analytical Data

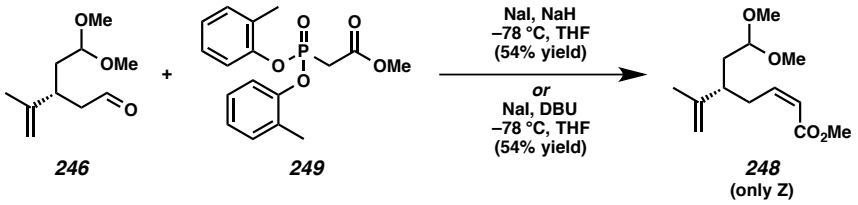
5.4.1. Materials and Methods

Unless stated otherwise, reactions were performed at ambient temperature (23 °C) in flame-dried glassware under an argon atmosphere using dry, deoxygentated solvents

(distilled or passed over a column of activated alumina) using a Teflon®-coated magnetic stirring bar. Commercially available reagents were used as received unless otherwise noted. Et_3N was distilled from calcium hydride immediately prior to use. MeOH was distilled from magnesium methoxide immediately prior to use. Reactions requiring external heat were modulated to the specified temperatures using an IKAmag temperature controller. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (250 nm) and visualized by UV fluorescence quenching, potassium permanganate, or *p*-anisaldehyde staining. Silicycle SiliaFlash P60 Academic Silica gel (particle size 40-63 nm) was used for flash chromatography. ^{1}H NMR spectra were recorded on a Varian Mercury 300 MHz, a Bruker AV III HD 400 MHz spectrometer equipped with a Prodigy liquid nitrogen temperature cryoprobe, Varian Inova 500 MHz, and 600 MHz spectrometers and are reported relative to residual $CHCl_3$ (δ 7.26 ppm), $CHDCl_2$ (δ 5.32) or C_6HD_6 (δ 7.16 ppm). ^{13}C NMR spectra are recorded on a Varian Mercury 300 MHz, a Bruker AV III HD 400 MHz spectrometer equipped with a Prodigy liquid nitrogen temperature cryoprobe, Varian Inova 500 MHz, and 600 MHz spectrometers (75 MHz, 126 MHz, and 151 MHz, respectively) and are reported relative to $CHCl_3$ (δ 77.16 ppm), $CHDCl_2$ (δ 53.84) or C_6HD_5 (δ 128.06 ppm). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Infrared (IR) spectra were recorded on a Perkin Elmer Paragon 1000 Spectrometer and are reported in frequency of absorption (cm^{-1}). High resolution mass spectra (HRMS) were obtained from the Caltech Mass Spectral Facility using a JEOL JMS-600H High Resolution Mass Spectrometer in fast atom bombardment (FAB+) or electron ionization (EI+) mode or acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in atmospheric pressure

chemical ionization (APCI) or mixed (MultiMode ESI/APCI) ionization mode. Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path length cell at 589 nm.

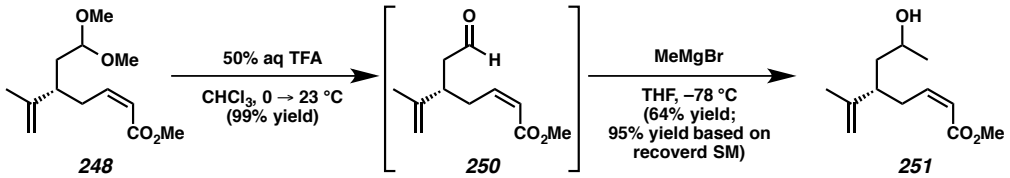
5.4.2. Experimental Procedures



246 ***249*** ***248*** (only Z)

A solution of phosphate **249** (108 mg, 0.322 mmol, 1.20 equiv) in THF (2.68 mL) was treated with NaI (52.0 mg, 0.349 mmol, 1.30 equiv) and DBU (53.0 mg, 0.348 mmol, 1.30 equiv) at 0 °C and stirred for 10 min. After the mixture was cooled to –78 °C, aldehyde **246** was added. The reaction was done in 3 min, and quenched with sat. aq NH_4Cl. The aqueous phase was extracted with EtOAc (3 x 3.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford α,β-unsaturated ester **248** (35.5 mg, 54% yield). (The same result was obtained by using 1.05 equiv NaH instead of DBU.)

R_f = 0.62 (1:4 EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.16 (dt, *J* = 11.5, 7.2 Hz, 1H), 5.79 (dt, *J* = 11.5, 1.9 Hz, 1H), 4.79 (ddt, *J* = 13.6, 2.1, 1.1 Hz, 2H), 4.35 (dd, *J* = 7.0, 4.7 Hz, 1H), 3.70 (s, 3H), 3.31 (s, 3H), 3.30 (s, 3H), 2.80 – 2.71 (m, 2H), 2.37 (tt, *J* = 8.5, 6.5 Hz, 1H), 1.76 – 1.64 (m, 2H), 1.65 (dd, *J* = 1.5, 0.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 148.9, 146.3, 120.0, 112.7, 103.0, 53.2, 52.7, 51.2, 43.2, 35.9, 32.6, 18.4; IR (Neat Film NaCl) 2949, 2830, 1723, 1646, 1437, 1408, 1203, 1127, 1053, 892, 819 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{13}H_{21}O_4$ $[M+H]^+$-H_2 : 241.1440; found: 241.1431; $[\alpha]_D^{25.0}$ 3.04° (*c* 0.30, $CHCl_3$).

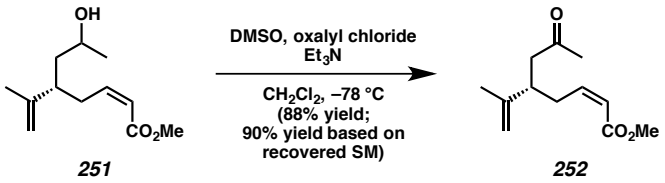


To a solution of acetal **248** (129 mg, 0.494 mmol, 1.00 equiv) in $CHCl_3$ (2.47 mL) was added 50% aq TFA (1.23 mL) at 0 °C. The reaction mixture was stirred for 3 h at 23 °C before it was quenched by the addition of sat. aq $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2 (3 x 4.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to afford aldehyde **250** (95.0 mg, 99% yield), which was used without further purification.

To a solution of aldehyde **250** (95.0 mg, 0.484 mmol, 1.00 equiv) in THF (5.00 mL) was added MeMgBr (3.0 M solution in diethyl ether; 0.21 mL, 0.629 mmol, 1.30 equiv) at –78 °C. The mixture was stirred for 1 h at –78 °C. Then, the solution was quenched by the addition of sat. aq $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 x 5.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford secondary alcohol **251** (65.5 mg, 64% yield).

R_f = 0.22 (1:4 EtOAc:hexanes); (due to the presence of diastereomeric mixtures, the ^1H NMR and ^{13}C NMR contained extra peaks. See the attached spectrum) ^1H NMR (400 MHz, $CDCl_3$) δ 6.18 (ddt, *J* = 11.5, 9.8, 7.4 Hz, 2H), 5.82 – 5.76 (m, 2H), 4.86 – 4.76 (m, 4H), 3.92 – 3.83 (m, 1H), 3.77 (ddt, *J* = 9.4, 6.3, 3.1 Hz, 1H), 3.70 (s, 6H), 2.87 (dddd, *J* = 15.1, 7.3, 5.0, 1.8 Hz, 1H), 2.74 (dddd, *J* = 8.3, 7.3, 5.1, 1.8 Hz, 2H), 2.64 – 2.55 (m, 1H), 2.49 (dddd, *J* = 10.0, 8.6, 6.5, 4.9 Hz, 1H), 2.37 (dddd, *J* = 9.8, 8.1, 6.7, 5.0 Hz, 1H), 1.68 (t, *J* = 1.2 Hz, 3H), 1.63 (dd, *J* = 1.5, 0.8 Hz, 3H), 1.55 – 1.42 (m, 4H), 1.19 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 149.2,

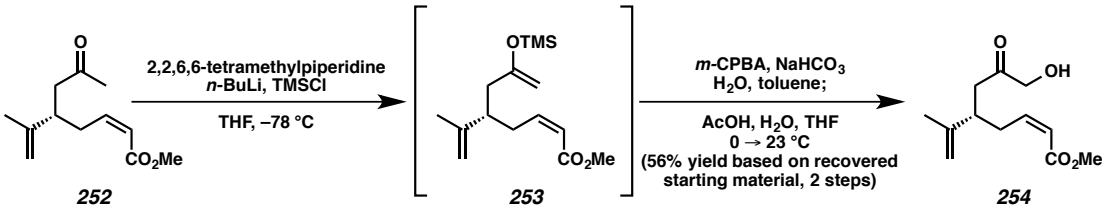
149.1, 147.7, 146.8, 119.9, 112.9, 112.4, 66.6, 65.9, 51.3, 51.2, 45.1, 44.1, 43.1, 42.4, 33.0, 32.0, 24.2, 23.5, 18.5, 18.1; IR (Neat Film NaCl) 3421, 2966, 2928, 1724, 1646, 1438, 1408, 1203, 1170, 892, 819 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{12}H_{21}O_3$ $[M+H]^+$: 213.1491; found 213.1489; $[\alpha]_D^{25.0}$ –9.52° (*c* 0.11, $CHCl_3$).



251 ***252***

To a stirred solution of oxalyl chloride (0.21 mL, 2.40 mmol, 1.50 equiv) in CH_2Cl_2 (8.00 mL) was added DMSO (0.34 mL, 4.79 mmol, 3.00 equiv) dropwise at –78 °C. The reaction mixture was stirred for 15 min, and alcohol **251** (339 mg, 1.60 mmol, 1.00 equiv) in CH_2Cl_2 (1.00 mL) was added dropwise. The solution was stirred for 2 h and 30 min at –78 °C, then Et_3N (1.56 mL, 7.00 equiv) was added. After 90 min at –78 °C, the solution was warmed to 23 °C over 30 min and quenched with H_2O. The aqueous phase was extracted with CH_2Cl_2 (3 x 10.0 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford ketone **252** (295 mg, 88% yield).

R_f = 0.35 (1:4 EtOAc:hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 6.19 – 6.10 (m, 1H), 5.81 (dt, *J* = 11.6, 1.7 Hz, 1H), 4.79 (p, *J* = 1.5 Hz, 1H), 4.74 (dt, *J* = 1.7, 0.8 Hz, 1H), 3.70 (s, 3H), 2.84 – 2.73 (m, 3H), 2.61 – 2.46 (m, 2H), 2.12 (d, *J* = 0.5 Hz, 3H), 1.68 (dd, *J* = 1.5, 0.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.8, 166.9, 148.3, 146.2, 120.4, 112.3, 51.3, 47.6, 42.1, 32.4, 30.6, 19.5; IR (Neat Film NaCl) 2951, 1718, 1647, 1437, 1204, 1272, 821 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{12}H_{19}O_3$ $[M+H]^+$: 211.1329; found: 211.1327; $[\alpha]_D^{25.0}$ –9.42° (*c* 0.15, $CHCl_3$).



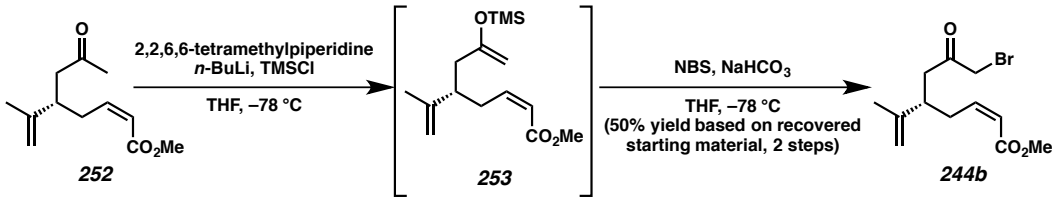
252 ***253*** ***254***

To a solution of 2,2,6,6-tetramethylpiperidine (50 μL, 0.296 mmol, 1.50 equiv) in THF (2.00 mL) was added *n*-BuLi (2.5 M in hexane; 0.12 mL, 0.296 mmol, 1.50 equiv) at 0 °C. The reaction mixture was stirred for 15 min at 0 °C, and TMSCl (0.13 mL, 0.990 mmol, 5.00 equiv) was added at –78 °C. Then, methyl ketone **252** (42.0 mg, 0.198 mmol, 1.00 equiv) in THF (1.00 mL) was added dropwise at –78 °C. The solution was stirred for 1 h and quenched with Et_3N, followed by sat. aq $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 x 2.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was quickly filtered by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford silyl ether **253**, which was used without further purification.

To a solution of *m*-CPBA (75%; 41.0 mg, 0.178 mmol, 0.90 equiv) in toluene (2.74 mL) was added solid $NaHCO_3$ (35.0 mg, 0.411 mmol, 2.08 equiv). The heterogeneous mixture was stirred for 15 min at 23 °C, then H_2O (0.40 mL) was added. Silyl ether **253** in toluene (0.50 mL) was added dropwise to the reaction mixture at 0 °C. After the solution was stirred for 30 min at 0 °C, sat. aq $NaHCO_3$ was added and stirred for 10 min at 0 °C. The aqueous phase was extracted with EtOAc (3 x 3.00 mL). The combined organic phases were washed with $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. To the residue dissolved in THF (0.30 mL) and H_2O (0.17 mL) was added AcOH (0.17 mL). The mixture was stirred for 2 h at 23 °C. Then, the solution was diluted with EtOAc and H_2O, and solid $NaHCO_3$ was added until the gas evolution ceased. The aqueous phase was extracted with EtOAc (3 x 1.00 mL). The combined organic phases were washed with brine,

dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford α-hydoxyketone **254** (12.0 mg, 56% yield based on recovered starting material, 2 steps).

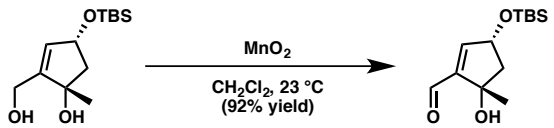
R_f = 0.35 (1:4 EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.13 (dt, *J* = 11.5, 7.1 Hz, 1H), 5.83 (ddd, *J* = 11.6, 2.0, 1.3 Hz, 1H), 4.82 (p, *J* = 1.5 Hz, 1H), 4.75 (dt, *J* = 1.6, 0.8 Hz, 1H), 4.20 (d, *J* = 3.0 Hz, 2H), 3.71 (s, 3H), 3.05 (s, br, 1H), 2.91 – 2.71 (m, 3H), 2.62 – 2.43 (m, 2H), 1.69 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.6, 166.8, 147.6, 145.5, 120.8, 112.8, 68.8, 51.3, 42.3, 42.1, 32.4, 19.5; IR (Neat Film NaCl) 2917, 1716, 1440, 1205, 1172 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{12}H_{19}O_4$ $[M+H]^+$: 227.1283; found: 227.1288; $[\alpha]_D^{25.0}$ –4.11° (*c* 0.09, $CHCl_3$).



To a solution of 2,2,6,6-tetramethylpiperidine (0.23 mL, 1.39 mmol, 1.60 equiv) in THF (8.70 mL) was added *n*-BuLi (1.98 M in hexane; 0.70 mL, 1.39 mmol, 1.60 equiv) at 0 °C. The reaction mixture was stirred for 15 min at 0 °C, and TMSCl (0.55 mL, 4.35 mmol, 5.00 equiv) was added at –78 °C. Then, methyl ketone **252** (183 mg, 0.870 mmol, 1.00 equiv) in THF (1.00 mL) was added dropwise at –78 °C. The solution was stirred for 1 h and quenched with Et_3N, followed by sat. aq $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 x 10.0 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was quickly filtered by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford silyl ether **253**, which was used without further purification.

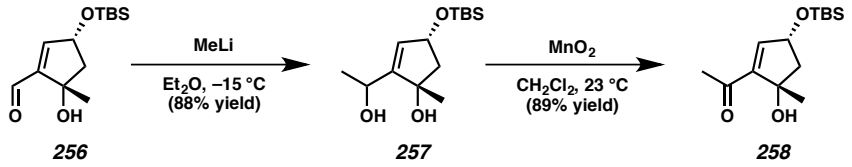
A solution of silyl ether **253** in THF (8.70 mL) at –78 °C was treated with solid $NaHCO_3$ (132 mg, 1.57 mmol, 1.80 equiv) and stirred for 10 min at –78 °C. NBS (248 mg, 1.39 mmol, 1.60 equiv) was then added portionwise and stirred for 15 min at –78 °C. The solvent was evaporated and the residue was purified by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford α-bromoketone **244b** (55.0 mg, 50% yield based on recovered starting material, 2 steps).

R_f = 0.65 (1:4 EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.14 (dt, *J* = 11.5, 7.2 Hz, 1H), 5.83 (dt, *J* = 11.6, 1.6 Hz, 1H), 4.82 (p, *J* = 1.5 Hz, 1H), 4.77 (dt, *J* = 1.5, 0.8 Hz, 1H), 3.87 (d, *J* = 1.0 Hz, 2H), 3.71 (s, 3H), 2.89 – 2.68 (m, 6H), 1.72 – 1.69 (m, 3H), 1.56 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.9, 166.9, 147.8, 145.7, 120.7, 112.7, 51.3, 43.7, 42.1, 34.8, 32.2, 19.7; IR (Neat Film NaCl) 2949, 2360, 1716, 1645, 1439, 1203, 1172 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{11}H_{14}O_2Br$ [M-OMe]$^+$: 257.0177; found: 257.0170; $[\alpha]_D^{25.0}$ –4.06° (*c* 0.09, $CHCl_3$).



255 ***256***

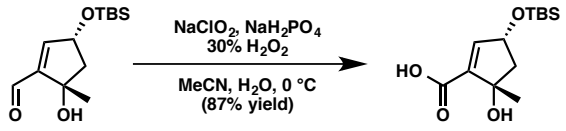
To a stirred solution of diol **255** (20.0 mg, 0.0774 mmol, 1.00 equiv) in CH_2Cl_2 (0.80 mL) was added MnO_2 (85%; 119 mg, 1.16 mmol, 15.0 equiv). The solution was stirred for 12 h at 23 °C. Solids were removed via a filtration through a celite plug (rinsed with CH_2Cl_2) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford aldehyde **256** (18.3 mg, 92% yield). All the spectrum data matched with those reported in ref 6a.



256 ***257*** ***258***

To a solution of aldehyde **256** (100 mg, 0.390 mmol, 1.00 equiv) in Et_2O (2.00 mL) was added MeLi (1.6 M in diethyl ether; 1.95 mL, 3.12 mmol, 8.00 equiv) at –10 °C. The solution was stirred for 2 h and quenched with sat. aq NH_4Cl. The solution was poured into H_2O. The aqueous phase was extracted with EtOAc (3 x 3.00 mL), washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:2 EtOAc:hexanes) on silica gel to afford alcohol **257** (93.4 mg, 88% yield).

To a stirred solution of alcohol **257** (162 mg, 0.594 mmol, 1.00 equiv) in CH_2Cl_2 (6.00 mL) was added MnO_2 (85%; 1.20 g, 11.9 mmol, 20.0 equiv). The solution was stirred for 12 h at 23 °C. Solids were removed via a filtration through a celite plug (rinsed with CH_2Cl_2) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford ketone **258** (143 mg, 89% yield). All the spectrum data matched with those reported in ref 6a.

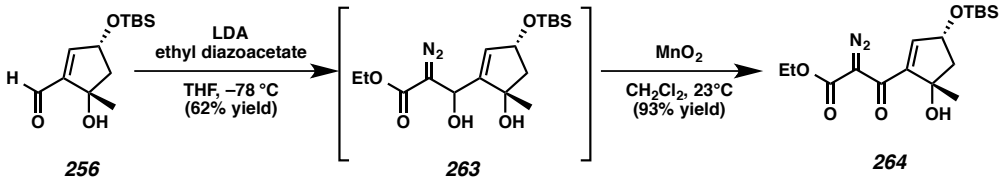


256 ***260***

To a stirred solution of aldehyde **256** (18.3 mg, 0.0714 mmol, 1.00 equiv) in MeCN (0.70 mL) were added NaH_2PO_4 (30.0 mg, 0.25 mmol, 3.50 equiv) in H_2O (0.50 mL) and 30% H_2O_2 (10 μL) at 0 °C. Then, a solution of $NaClO_2$ (23.0 mg, 0.25 mmol, 3.50 equiv) in H_2O (0.70 mL) was added dropwise in 1 h at 0 °C. The reaction

mixture was stirred for 10 min and quenched with sat. aq Na_2SO_3. The aqueous phase was extracted with EtOAc (2.00 mL). The combined aqueous phases were acidified with 2N HCl to make the solution pH 5–6. The aqueous phase was extracted with EtOAc (3 x 4.00 mL) washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to afford acid **260** (17.0 mg, 87% yield).

R_f = 0.15 (1:1 EtOAc:hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77 (d, *J* = 1.8 Hz, 1H), 4.75 (td, *J* = 6.7, 1.9 Hz, 1H), 2.50 (dd, *J* = 12.9, 6.9 Hz, 1H), 2.09 – 2.03 (m, 1H), 1.48 (d, *J* = 0.7 Hz, 3H), 0.90 (s, 9H), 0.10 (d, *J* = 3.0 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.2, 147.9, 139.6, 79.5, 72.7, 51.3, 27.7, 25.9, 18.2, -4.5, -4.6; IR (Neat Film NaCl) 2929, 2857, 1701, 1362, 1258, 1097, 898, 837, 778 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{12}H_{19}O_4$ $[M+H]^+$-H_2: 271.1366; found: 271.1357; $[\alpha]_D^{25.0}$ 185.9° (*c* 0.31, $CHCl_3$).



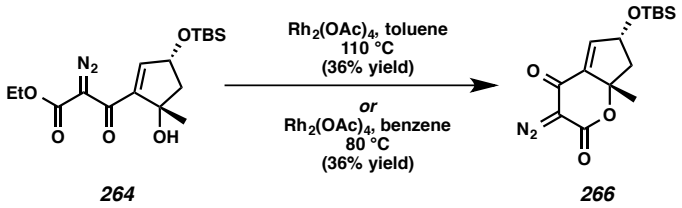
256 ***263*** ***264***

To a solution of aldehyde **256** (15.0 mg, 0.0585 mmol, 1.00 equiv) and ethyl diazoacetate (22 μL, 0.205 mmol, 3.50 equiv) in THF (0.60 mL) was added LDA (0.20 M solution in THF; 0.44 mL, 0.088 mmol, 1.50 equiv) at –78 °C. The reaction mixture was stirred for 10 min and quenched with sat. aq NH_4Cl. The aqueous phase was extracted with EtOAc (3 x 1.00 mL) washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to afford alcohol **263**, which was used without further purification (13.5 mg, 62% yield).

To a solution of alcohol **263** (13.0 mg, 0.0351 mmol, 1.00 equiv) in CH_2Cl_2 (0.40 mL) was added MnO_2 (85%; 72.0 mg, 0.702 mmol, 20.0 equiv) at 23 °C. The reaction

mixture was stirred overnight. Solids were removed via a filtration through a celite plug (rinsed with CH_2Cl_2) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford diazo **264** (12.0 mg, 93% yield).

R_f = 0.56 (1:2 EtOAc:hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.27 (d, *J* = 2.0 Hz, 1H), 4.79 (ddd, *J* = 6.9, 5.6, 2.0 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.45 (dd, *J* = 13.0, 6.9 Hz, 1H), 2.01 (dd, *J* = 13.0, 5.7 Hz, 1H), 1.39 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.4, 161.4, 145.4, 141.0, 82.3, 73.8, 62.0, 51.7, 27.3, 26.0, 25.8, 18.3, 14.4, -4.5, -4.6; IR (Neat Film NaCl) 3499, 2930, 2857, 2141, 1728, 1471, 1370, 1300, 1259, 1094, 906, 837 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{17}H_{29}O_5N_2Si$ $[M+H]^+$: 369.1846; found 369.1845; $[\alpha]_D^{25.0}$ 14.2° (*c* 0.25, $CHCl_3$).

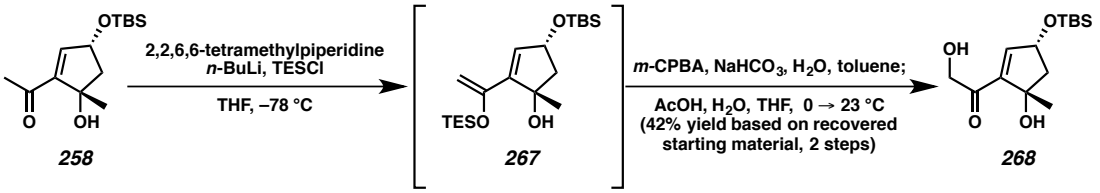


264 ***266***

To a solution of diazo **264** (12.0 mg, 0.0326 mmol, 1.00 equiv) in toluene (0.30 mL), was added dirhodium tetraacetate (0.70 mg, 0.00163 mmol, 0.05 equiv). The solution was refluxed under argon for 10 min. Solids were removed via a filtration through a celite plug (rinsed with EtOAc) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford lactone **266** (4.0 mg, 36% yield). (Similar result was obtained with benzene solvent at 80 °C.)

R_f = 0.30 (1:2 EtOAc:hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.75 (d, *J* = 1.6 Hz, 1H), 4.85 (ddd, *J* = 7.1, 6.4, 1.7 Hz, 1H), 2.72 (dd, *J* = 12.6, 6.4 Hz, 1H), 2.40 – 2.30

(m, 1H), 1.58 (s, 3H), 0.90 (s, 9H), 0.11 (d, J = 4.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.7, 175.1, 142.6, 138.1, 87.6, 73.5, 51.1, 26.9, 25.8, 18.2, 14.3, -4.6, -4.7; IR (Neat Film NaCl) 2953, 2856, 2146, 1713, 1661, 1330, 1302, 1097, 1066, 837 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{15}H_{23}O_4N_2Si$ $[M+H]^+$: 323.1427; found 323.1417; $[\alpha]_D^{25.0}$ 7.77° (*c* 0.20, $CHCl_3$).

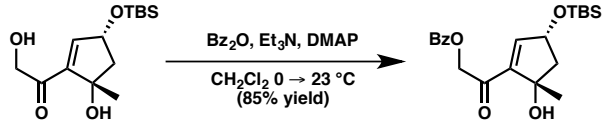


To a solution of 2,2,6,6-tetramethylpiperidine (0.20 mL, 1.19 mmol, 5.00 equiv) in THF (2.40 mL) was added *n*-BuLi (1.96 M in hexane; 0.61 mL, 1.19 mmol, 5.00 equiv) at 0 °C. The reaction mixture was stirred for 30 min at 0 °C, and TMSCl (0.20 mL, 1.19 mmol, 5.00 equiv) was added at –78 °C. Methyl ketone **258** (50.0 mg, 0.238 mmol, 1.00 equiv) in THF (0.60 mL) was added dropwise at –78 °C. The solution was stirred for 30 min and quenched with Et_3N, followed by sat. aq $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 x 3.50 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was quickly filtered by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford silyl ether **267**, which was used without further purification.

To a solution of *m*-CPBA (75%; 50.0 mg, 0.217 mmol, 0.91 equiv) in toluene (3.34 mL) was added $NaHCO_3$ (55.0 mg, 0.651 mmol, 2.74 equiv). The heterogeneous mixture was stirred for 15 min at 23 °C, then H_2O (0.56 mL) was added. Silyl ether **267** in toluene (0.50 mL) was added dropwise to the reaction mixture at 0 °C. After the solution was stirred for 45 min at 0 °C, sat. aq $NaHCO_3$ was added and stirred for 10 min at 0 °C. The aqueous phase was extracted with EtOAc (3 x 3.00 mL). The

combined organic phases were washed with $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. To the residue dissolved in THF (0.42 mL) and H_2O (0.21 mL) was added AcOH (0.21 mL). The mixture was stirred for 2 h at 23 °C. After the solution was diluted with EtOAc and H_2O, solid $NaHCO_3$ was added until the gas evolution ceased. The aqueous phase was extracted with EtOAc (3 x 2.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford α-hydoxyketone **268** (12.0 mg, 42% yield based on recovered starting material, 2 steps).

R_f = 0.30 (1:2 EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.55 (d, *J* = 1.9 Hz, 1H), 4.79 (td, *J* = 6.9, 1.9 Hz, 1H), 4.59 (d, *J* = 18.6 Hz, 1H), 4.51 (d, *J* = 18.6 Hz, 1H), 3.12 (s, br, 1H), 2.44 (dd, *J* = 12.8, 7.0 Hz, 1H), 2.05 – 1.99 (m, 1H), 1.47 (s, 3H), 0.90 (s, 9H), 0.10 (d, *J* = 4.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.4, 145.8, 143.8, 80.5, 73.4, 65.8, 50.9, 28.0, 25.9, 18.2, -4.5, -4.6; IR (Neat Film NaCl) 3418, 2929, 2857, 1682, 1361, 1259, 1093, 912, 835 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{14}H_{27}O_4Si$ $[M+H]^+$:287.1679; found: 287.1677; $[\alpha]_D^{25.0}$ 78.9° (*c* 0.10, $CHCl_3$).

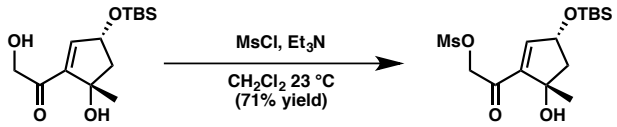


268 ***269***

To a solution of α-hydroxyketone **268** (9.80 mg, 0.0342 mmol, 1.00 equiv) in CH_2Cl_2 (0.30 mL) were added DMAP (8.40 mg, 0.0684 mmol, 2.00 equiv) and Et_3N (38 μL, 0.274 mmol, 8.00 equiv). The solution was cooled to 0 °C and benzoic anhydride (15.0 mg, 0.0684 mmol, 2.00 equiv) was added in one portion. After 30 min, the

solution was warmed to 23 °C and stirred for 2 h. After the reaction was done, water was added. The aqueous phase was extracted with CH_2Cl_2 (3 x 1.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford benzoate **269** (11.4 mg, 85% yield).

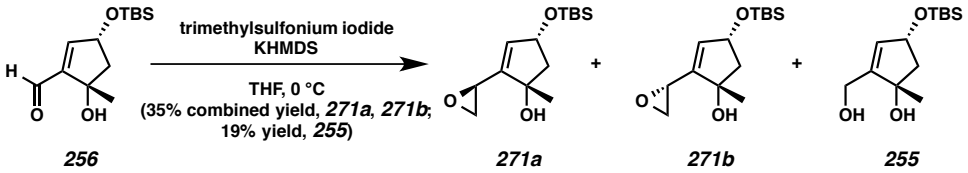
R_f = 0.75 (1:2 EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 – 8.07 (m, 2H), 7.65 – 7.55 (m, 1H), 7.51 – 7.42 (m, 2H), 6.65 (d, *J* = 1.9 Hz, 1H), 5.30 (d, *J* = 16.4 Hz, 1H), 5.18 (d, *J* = 16.4 Hz, 1H), 4.81 (td, *J* = 7.1, 1.9 Hz, 1H), 2.44 (dd, *J* = 12.7, 7.0 Hz, 1H), 2.07 – 1.97 (m, 1H), 1.47 (s, 3H), 0.91 (s, 9H), 0.11 (d, *J* = 4.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.6, 166.0, 145.5, 144.2, 133.6, 130.1, 129.3, 128.7, 80.6, 73.4, 66.3, 50.7, 28.1, 25.9, 18.3, -4.5, -4.6; IR (Neat Film NaCl) 2928, 1728, 1691, 1259, 1098, 836 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{21}H_{29}O_5Si$ $[M+H]^+$-H_2: 389.1784; found: 389.1783; $[\alpha]_D^{25.0}$ 40.9° (*c* 0.16, $CHCl_3$).



268 ***270***

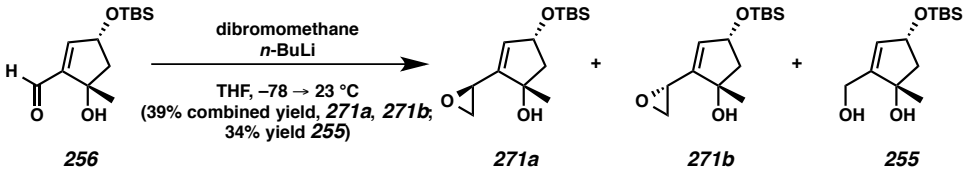
To a stirred solution of α-hydroxyketone **268** (49.0 mg, 0.171 mmol, 1.00 equiv) in CH_2Cl_2 (1.71 mL) were added Et_3N (72 μL, 0.513 mmol, 3.00 equiv) and MsCl (20 μL, 0.257 mmol, 1.50 equiv) at 0 °C. The solution was stirred at 0 °C for 2 h and quenched with H_2O. The aqueous phase was extracted with CH_2Cl_2 (3 x 2.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford mesylate **270** (44.0 mg, 71% yield).

R_f = 0.43 (1:4 EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.58 (d, *J* = 1.9 Hz, 1H), 5.15 (s, 2H), 4.78 (td, *J* = 7.0, 1.9 Hz, 1H), 3.23 (s, 3H), 2.44 (dd, *J* = 12.8, 7.0 Hz, 1H), 2.05 – 1.95 (m, 1H), 1.95 (s, br, 1H), 1.46 (s, 3H), 0.90 (s, 9H), 0.11 (d, *J* = 4.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.2, 146.5, 143.8, 80.6, 73.3, 69.8, 50.7, 39.3, 27.9, 25.9, 18.2, -4.5, -4.7; IR (Neat Film NaCl) 2930, 2856, 1693, 1354, 1259, 1173, 1091, 1042, 959, 912, 835, 777 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{15}H_{27}O_5SiS$ [M-OH]$^•$: 347.1348; found: 347.1357; $[\alpha]_D^{25.0}$ 36.3° (*c* 0.12, $CHCl_3$).



256 ***271a*** ***271b*** ***255***

To a solution of trimethylsulfonium iodide (18.0 mg, 0.0877 mmol, 1.50 equiv) in THF (0.60 mL) was added dry KHMDS (17.0 mg, 0.0877 mmol, 1.50 equiv) in portions over 30 min at 0 °C. The mixture was stirred for 1 h. Then, a solution of aldehyde **256** in THF (0.30 mL) was added to a reaction vessel. The solution was stirred for 30 min and quenched with H_2O. The aqueous phase was extracted with EtOAc (3 x 1.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford epoxide **271a** and **271b** (5.50 mg, 35% yield). See below for characterization data.

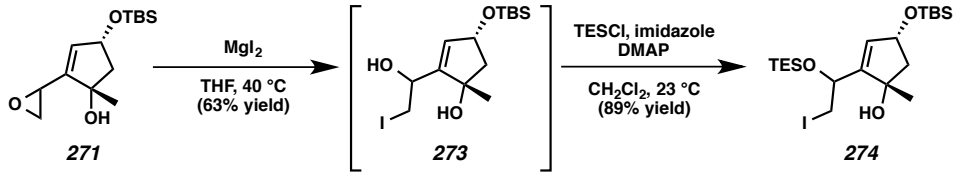


256 ***271a*** ***271b*** ***255***

To a solution of aldehyde **256** (155 mg, 0.604 mmol, 1.00 equiv) and dibromomethane (51.0 μL, 0.725 mmol, 1.20 equiv) in THF (3.02 mL) was added *n*-BuLi (2.4 M solution in hexane; 0.28 mL, 0.665 mmol, 1.10 equiv) dropwise over 30 min at –78 °C. The reaction mixture was slowly warmed to 23 °C and stirred overnight. Then, the reaction was quenched with sat. aq NH_4Cl. The aqueous phase was extracted with EtOAc (3 x 3.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford epoxide **271a** and **271b** (64.0 mg, 39% yield).

R_f = 0.56 (1:2 EtOAc:hexanes); Diastereomer 1: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72 (dd, *J* = 2.2, 1.0 Hz, 1H), 4.61 (ddd, *J* = 6.5, 3.8, 2.3 Hz, 1H), 3.55 (ddt, *J* = 4.3, 2.7, 0.8 Hz, 1H), 2.97 (dd, *J* = 6.0, 4.2 Hz, 1H), 2.74 (dd, *J* = 6.0, 2.7 Hz, 1H), 2.36 (dd, *J* = 13.5, 6.5 Hz, 1H), 2.06 (d, *J* = 15.5 Hz, 1H), 1.89 (dd, *J* = 13.5, 3.8 Hz, 1H), 1.37 (s, 3H), 0.88 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.4, 131.1, 81.3, 73.3, 52.6, 49.7, 48.2, 26.1, 26.0, 18.3, -4.6; IR (Neat Film NaCl) 3408, 2929, 2856, 1361, 1252, 1085, 835 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{14}H_{25}O_3Si$ $[M+H]^+$-H_2: 269.1573; found: 269.1568; $[\alpha]_D^{25.0}$ 44.7° (*c* 0.08, $CHCl_3$).

Diastereomer 2: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.71 (dd, *J* = 2.1, 1.0 Hz, 1H), 4.65 (dddd, *J* = 6.4, 4.4, 2.1, 1.1 Hz, 1H), 3.50 (ddt, *J* = 3.7, 2.7, 1.0 Hz, 1H), 3.04 (dd, *J* = 5.7, 4.2 Hz, 1H), 2.88 (dd, *J* = 5.7, 2.7 Hz, 1H), 2.44 (dd, *J* = 13.3, 6.5 Hz, 1H), 2.15 (s, 1H), 1.90 (dd, *J* = 13.3, 4.4 Hz, 1H), 1.44 (s, 3H), 0.90 (s, 9H), 0.09 (d, *J* = 1.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.2, 131.1, 81.1, 73.2, 52.8, 49.5, 47.5, 26.1, 26.0, 18.3, -4.6; IR (Neat Film NaCl) 2956, 2929, 2856, 1361, 1253, 1086, 836, 776 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{14}H_{25}O_3Si$ $[M+H]^+$-H_2: 269.1573; found: 269.1577; $[\alpha]_D^{25.0}$ 11.5° (*c* 0.15, $CHCl_3$).



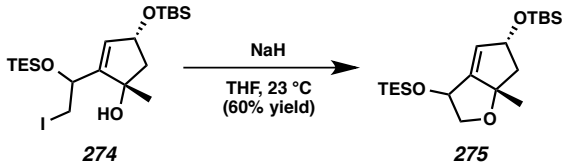
271 *273* *274*

To a solution of epoxide **271** (64.0 mg, 0.237 mmol, 1.00 equiv) in THF (1.19 mL) was added MgI_2 (69.0 mg, 0.248 mmol, 1.05 equiv). The reaction mixture was stirred overnight at 40 °C and then quenched with H_2O. The aqueous phase was extracted with EtOAc (3 x 2.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford iodohydrin **273** (59.0 mg, 63% yield).

To a solution of iodohydrin **273** (13.5 mg, 0.0338 mmol, 1.00 equiv) in CH_2Cl_2 (0.20 mL) were added imidazole (11.5 mg, 0.169 mmol, 5.00 equiv), DMAP (0.20 mg, 0.0016 mmol, 0.05 equiv), and TESCl (6.20 μL, 0.0371 mmol, 1.10 equiv). The reaction mixture was stirred overnight at 23 °C and then H_2O was added. The aqueous phase was extracted with CH_2Cl_2 (3 x 0.50 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford silyl ether **274** (11.5 mg, 89% yield).

R_f = 0.80 (1:4 EtOAc:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.89 (ddd, *J* = 2.1, 1.3, 0.5 Hz, 1H), 4.57 (dtd, *J* = 5.4, 3.0, 1.4 Hz, 1H), 4.30 (ddt, *J* = 6.5, 3.9, 1.3 Hz, 1H), 3.59 (dd, *J* = 10.2, 3.8 Hz, 1H), 3.35 (dd, *J* = 10.2, 6.4 Hz, 1H), 2.26 – 2.20 (m, 1H), 1.91 – 1.84 (m, 1H), 1.33 (s, 3H), 0.99 – 0.95 (m, 9H), 0.88 (s, 9H), 0.65 – 0.60 (m, 6H), 0.08 (d, *J* = 0.8 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.8, 132.3, 80.6, 72.8, 69.2, 52.5, 26.0, 25.4, 18.2, 15.4, 7.1, 5.0, -4.4, -4.6; IR (Neat Film NaCl) 2955, 1256,

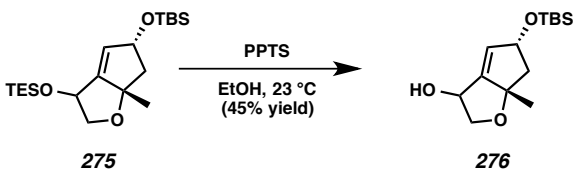
1088, 836, 740 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{20}H_{40}O_3Si_2I$ $[M+H]^+-H_2$: 511.1561; found: 511.1573; $[\alpha]_D^{25.0}$ 4.31° (*c* 0.20, $CHCl_3$).



274 ***275***

To a solution of NaH (60%, 1.00 mg, 0.0246 mmol, 1.10 equiv) in THF (1.12 mL) was added silyl ether **274** (11.5 mg, 0.0224 mmol, 1.00 equiv) in THF (0.50 mL) at 23 °C. The solution was stirred overnight and then H_2O was added. The aqueous phase was extracted with EtOAc (3 x 1.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford ether **275** (5.20 mg, 60% yield).

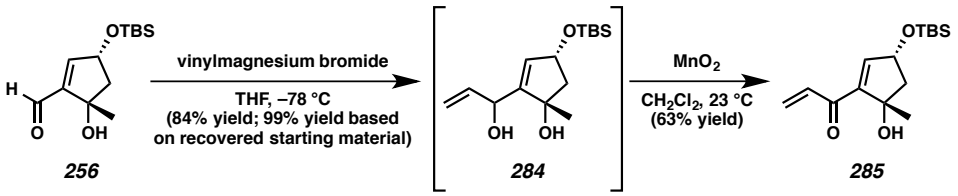
R_f = 0.23 (1:8 EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.56 (dd, *J* = 2.2, 1.1 Hz, 1H), 4.99 (dddd, *J* = 7.4, 5.4, 3.2, 1.1 Hz, 1H), 4.84 (tdd, *J* = 7.5, 3.2, 2.2 Hz, 1H), 4.16 (t, *J* = 7.9 Hz, 1H), 3.56 (dd, *J* = 8.2, 7.2 Hz, 1H), 2.40 (dd, *J* = 11.5, 5.4 Hz, 1H), 2.00 (ddd, *J* = 11.5, 7.3, 1.0 Hz, 1H), 1.21 (d, *J* = 0.9 Hz, 3H), 0.97 (t, *J* = 8.0 Hz, 9H), 0.90 (s, 9H), 0.68 – 0.52 (m, 6H), 0.10 – 0.06 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 126.0, 89.1, 79.3, 73.6, 68.2, 54.4, 26.0, 6.9, 4.8, -4.5; IR (Neat Film NaCl) 2955, 2927, 2875, 2360, 1459, 1256, 1089, 835 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{20}H_{39}O_3Si_2$ $[M+H]^+-H_2$: 383.2438; found: 383.2409; $[\alpha]_D^{25.0}$ 12.7° (*c* 0.15, $CHCl_3$).



275 ***276***

To a solution of ether **275** (5.10 mg, 0.0132 mmol, 1.00 equiv) in EtOH (0.13 mL) was added PPTS (0.30 mg, 0.00132 mmol, 0.10 equiv) and stirred at 23 °C for 30 min. The reaction was quenched with sat. aq $NaHCO_3$ and the aqueous phase was extracted with EtOAc (3 x 0.70 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford alcohol **276** (1.61 mg, 45% yield).

R_f = 0.23 (1:8 EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.66 (dd, *J* = 2.2, 1.2 Hz, 1H), 5.14 – 5.03 (m, 1H), 4.86 (m, br, 1H), 4.35 (dd, *J* = 9.4, 7.5 Hz, 1H), 3.69 (dd, *J* = 9.4, 5.5 Hz, 1H), 2.43 (dd, *J* = 11.7, 5.5 Hz, 1H), 2.02 (ddd, *J* = 11.7, 7.3, 1.0 Hz, 1H), 1.22 (s, 3H), 0.90 (s, 9H), 0.09 (d, *J* = 5.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7, 126.3, 90.2, 79.9, 75.1, 68.6, 54.0, 26.0, 24.1, -4.5, -4.6; IR (Neat Film NaCl) 2929, 2857, 1361, 1256, 1084, 835, 776 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{14}H_{27}O_3Si$ $[M+H]^+$: 271.1730; found: 271.1734; $[\alpha]_D^{25.0}$ 33.7° (*c* 0.06, $CHCl_3$).

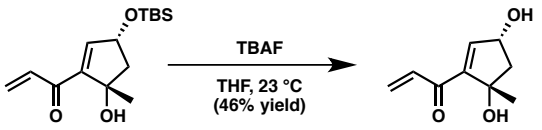


A flame-dried flask was charged with aldehyde **256** (399 mg, 1.56 mmol, 1.00 equiv) and THF (7.80 mL). Then, vinylmagnesium bromide (1.0 M solution in THF; 20.5 mL, 20.3 mmol, 13.0 equiv) was added to the solution at –78 °C and stirred for 3 h. The reaction was quenched with sat. aq NH_4Cl and the aqueous phase was extracted with EtOAc (3 x 10.0 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column

chromatography (1:2 EtOAc:hexanes) on silica gel to afford allyl alcohol **284** (371 mg, 84% yield).

To a solution of allyl alcohol **284** (371 mg, 1.30 mmol, 1.00 equiv) in CH_2Cl_2 (13.0 mL) was added MnO_2 (85%; 4.00 g, 39.1 mmol, 30.0 equiv). The mixture was stirred for 12 h. Solids were removed via a filtration through a celite plug (rinsed with CH_2Cl_2) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford vinyl ketone **285** (230 mg, 63% yield).

R_f = 0.55 (1:2 EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (dd, *J* = 17.1, 10.5 Hz, 1H), 6.60 (d, *J* = 1.9 Hz, 1H), 6.35 (dd, *J* = 17.1, 1.6 Hz, 1H), 5.80 (dd, *J* = 10.5, 1.6 Hz, 1H), 4.79 (td, *J* = 7.1, 1.9 Hz, 1H), 3.67 (s, 1H), 2.44 (dd, *J* = 12.7, 7.0 Hz, 1H), 2.04 (ddd, *J* = 12.6, 7.1, 0.9 Hz, 1H), 1.46 (s, 3H), 0.91 (s, 9H), 0.11 (d, *J* = 4.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.7, 147.0, 145.9, 132.3, 129.4, 80.4, 73.2, 51.0, 28.2, 25.9, 18.3, -4.4, -4.6; IR (Neat Film NaCl) 2955, 2929, 2856, 1658, 1605, 1361, 1259, 1091, 911, 837, 777 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{15}H_{25}O_3Si$ $[M+H]^+$-H_2: 281.1573; found: 281.1569; $[\alpha]_D^{25.0}$ 33.3° (*c* 0.06, $CHCl_3$).

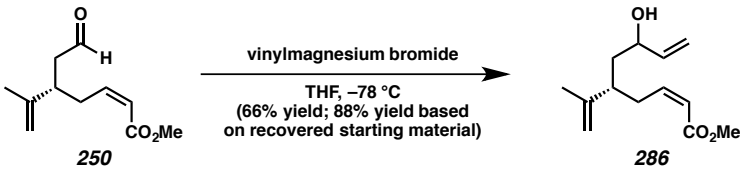


285 ***281***

To a solution of ketone **285** (22.1 mg, 0.0782 mmol, 1.00 equiv) in THF (0.80 mL) was added TBAF (1.0 M solution in THF; 0.16 mL, 0.156 mmol, 2.00 equiv) at 23 °C and stirred for 30 min. The reaction was quenched with sat. aq NH_4Cl. The aqueous phase was extracted with EtOAc (3 x 1.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was

purified by column chromatography (1:1 EtOAc:hexanes) on silica gel to afford diol **281** (6.00 mg, 46% yield).

R_f = 0.15 (1:1 EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (dd, *J* = 17.1, 10.5 Hz, 1H), 6.68 (d, *J* = 2.1 Hz, 1H), 6.36 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.85 (dd, *J* = 10.5, 1.6 Hz, 1H), 4.82 (ddd, *J* = 7.4, 5.8, 2.1 Hz, 1H), 3.62 (s, br, 1H), 2.51 (dd, *J* = 13.4, 7.1 Hz, 1H), 2.01 (dd, *J* = 13.4, 5.7 Hz, 1H), 1.48 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.3, 148.2, 144.3, 132.6, 130.0, 81.2, 73.5, 50.2, 27.7; IR (Neat Film NaCl) 2922, 1657, 1605, 1407, 1264, 1223, 1148, 1067, 961, 796 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_9H_{13}O_3$ $[M+H]^+$: 169.0865; found: 169.0864; $[\alpha]_D^{25.0}$ 25.8° (*c* 0.10, $CHCl_3$).

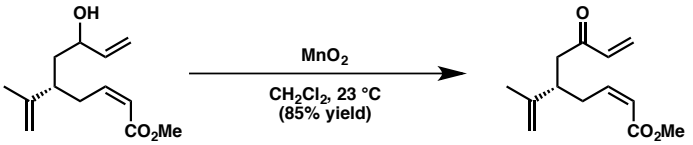


250 ***286***

To a stirred solution of aldehyde **250** (300 mg, 1.53 mmol, 1.00 equiv) in THF (15.3 mL) was added vinylmagnesium bromide (1.0 M solution in THF; 2.29 mmol, 1.50 equiv) at –78 °C. The reaction was stirred for 1 h at –78 °C and quenched with sat. aq NH_4Cl. The aqueous phase was extracted with EtOAc (3 x 6.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford allyl alcohol **286** (227 mg, 66% yield).

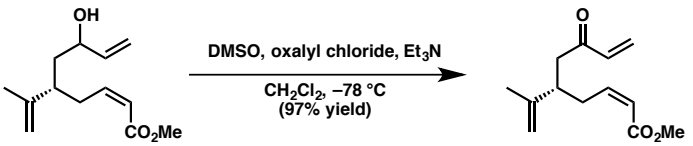
R_f = 0.32 (1:4 EtOAc:hexanes); (due to the presence of diastereomeric mixtures, the ^{1}H NMR and ^{13}C NMR contained extra peaks. See the attached spectrum) ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.23 – 6.14 (m, 2H), 5.92 – 5.82 (m, 2H), 5.82 – 5.77 (m, 2H), 5.23 (ddt, *J* = 17.2, 5.0, 1.5 Hz, 2H), 5.10 (ddt, *J* = 13.4, 10.4, 1.4 Hz, 2H), 4.86 –

4.74 (m, 4H), 4.17 (q, *J* = 6.7 Hz, 1H), 4.13 – 4.07 (m, 1H), 3.71 – 3.68 (m, 6H), 2.91 – 2.81 (m, 1H), 2.76 (ddd, *J* = 7.3, 6.2, 1.8 Hz, 2H), 2.69 – 2.62 (m, 1H), 2.54 (dtd, *J* = 9.8, 7.6, 4.6 Hz, 2H), 2.37 (ddd, *J* = 15.1, 9.2, 5.8 Hz, 1H), 1.65 (dq, *J* = 1.5, 0.8 Hz, 3H), 1.63 – 1.51 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 149.1, 149.0, 147.1, 146.5, 141.5, 140.9, 119.9, 115.2, 114.3, 113.2, 112.6, 71.6, 70.9, 51.3, 51.2, 44.2, 40.7, 40.2, 32.9, 32.1, 18.6, 18.2; IR (Neat Film NaCl) 2929, 1722, 1644, 1439, 1202, 1168, 1124, 993 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{13}H_{21}O_3$ $[M+H]^+$: 225.1491; found: 225.1491.



286 ***287***

To a solution of allyl alcohol **286** (10.0 mg, 0.0446 mmol, 1.00 equiv) in CH_2Cl_2 (0.45 mL) was added MnO_2 (85%; 182 mg, 1.78 mmol, 40.0 equiv). The mixture was stirred for 12 h at 23 °C. Solids were removed via a filtration through a celite plug (rinsed with CH_2Cl_2) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:6 EtOAc:hexanes) on silica gel to afford ketone **287** (8.41 mg, 85% yield). See below for characterization data.

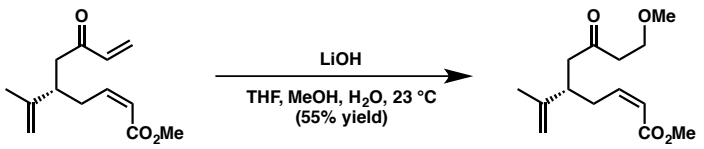


286 ***287***

To a stirred solution of oxalyl chloride (29 μL, 0.335 mmol, 1.50 equiv) in CH_2Cl_2 (1.10 mL) was added DMSO (47 μL, 0.669 mmol, 3.00 equiv) at –78 °C. The

solution was stirred for 15 min, then alcohol **286** (50.0 mg, 0.223 mmol, 1.00 equiv) in CH_2Cl_2 (0.6 mL) was added at –78 °C. The mixture was stirred for 3 h and 30 min at –78 °C, and then Et_3N (0.22 mL, 1.56 mmol, 7.00 equiv) was added. After 90 min at –78 °C, the solution was slowly warmed to 23 °C over 30 min and H_2O was added. The aqueous phase was extracted with CH_2Cl_2 (3 x 2.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:6 EtOAc:hexanes) on silica gel to afford ketone **287** (47.9 mg, 97% yield).

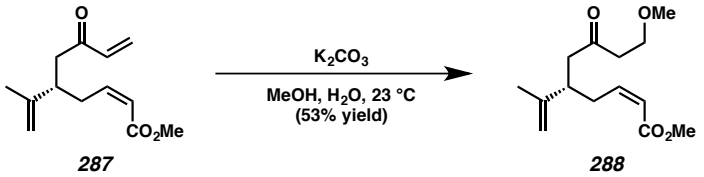
R_f = 0.55 (1:4 EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.34 (dd, *J* = 17.7, 10.4 Hz, 1H), 6.23 – 6.12 (m, 2H), 5.84 – 5.78 (m, 2H), 4.78 (p, *J* = 1.5 Hz, 1H), 4.74 (dt, *J* = 1.7, 0.8 Hz, 1H), 3.70 (s, 3H), 2.88 – 2.77 (m, 3H), 2.73 – 2.61 (m, 2H), 1.69 (dd, *J* = 1.5, 0.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.6, 166.9, 148.4, 146.1, 136.8, 128.4, 120.4, 112.3, 51.2, 43.5, 42.2, 32.4, 19.6; IR (Neat Film NaCl) 2950, 1716, 1645, 1439, 1407, 1204, 1173, 992, 895, 818 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{13}H_{19}O_3$ $[M+H]^+$: 223.1334; found: 223.1325; $[\alpha]_D^{25.0}$ –0.98° (*c* 0.28, $CHCl_3$).



287 ***288***

To a solution of ester **287** (10.0 mg, 0.0449 mmol, 1.00 equiv) in THF (0.50 mL) was added a solution of LiOH (2.20 mg, 0.0898 mmol, 2.00 equiv) in H_2O (0.20 mL). After 2 h at 23 °C, the aqueous phase was extracted with EtOAc (3 x 1.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4

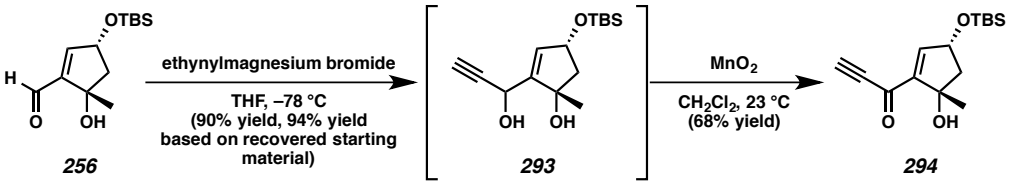
EtOAc:hexanes) on silica gel to afford Michael adduct **288** (6.28 mg, 55% yield). See below for characterization data.



287 ***288***

To a stirred solution of ester **287** (6.80 mg, 0.00306 mmol, 1.00 equiv) in MeOH (0.10 mL) and H_2O (0.10 mL) was added K_2CO_3 (17.0 mg, 0.122 mmol, 4.00 equiv). After 7 h, the aqueous phase was extracted with EtOAc (3 x 0.50 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford Michael adduct **288** (4.11 mg, 53% yield).

R_f = 0.25 (1:4 EtOAc:hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.14 (dt, *J* = 11.6, 7.1 Hz, 1H), 5.80 (dt, *J* = 11.6, 1.7 Hz, 1H), 4.78 (p, *J* = 1.5 Hz, 1H), 4.77 – 4.70 (m, 1H), 3.70 (s, 3H), 3.61 (t, *J* = 6.3 Hz, 2H), 3.31 (s, 3H), 2.88 – 2.71 (m, 3H), 2.63 (t, *J* = 6.3 Hz, 2H), 2.61 – 2.45 (m, 2H), 1.68 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.0, 166.9, 148.4, 146.2, 120.3, 112.2, 67.6, 59.0, 51.2, 47.3, 43.3, 41.8, 32.3, 19.6; IR (Neat Film NaCl) 2922, 1719, 1646, 1438, 1203, 1172, 1117, 894, 820 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{14}H_{23}O_4$ $[M+H]^+$: 255.1596; found: 255.1604; $[\alpha]_D^{25.0}$ – 3.01° (*c* 0.36, $CHCl_3$).



256 ***293*** ***294***

A flame-dried flask was charged with aldehyde **256** (53.4 mg, 0.208 mmol, 1.00 equiv) and THF (1.04 mL). Then, ethynylmagnesium bromide (0.4M solution in THF; 5.20 mL, 2.08 mmol, 10.0 equiv) was added at –78 °C and stirred for 3 h. The reaction mixture was slowly warmed to 23 °C and stirred for 5 h. The reaction was quenched by adding sat. aq NH_4Cl. The aqueous phase was extracted with EtOAc (3 x 1.50 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:2 EtOAc:hexanes) on silica gel to afford diol **293** (53.0 mg, 90% yield).

To a solution of diol **293** (11.1 mg, 0.0392 mmol, 1.00 equiv) in CH_2Cl_2 (0.40 mL) was added MnO_2 (85%; 52.0 mg, 0.510 mmol, 13.0 equiv). The mixture was stirred for 12 h. Solids were removed via a filtration through a celite plug (rinsed with CH_2Cl_2) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford ketone **294** (7.50 mg, 68% yield).

R_f = 0.56 (1:2 EtOAc:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 (d, *J* = 1.9 Hz, 1H), 4.79 (tdd, *J* = 7.2, 1.9, 0.7 Hz, 1H), 3.29 (s, 1H), 3.09 (s, 1H), 2.47 (dd, *J* = 12.8, 7.0 Hz, 1H), 2.07 (ddt, *J* = 12.8, 7.1, 0.8 Hz, 1H), 1.58 (s, br, 1H), 1.46 (s, 3H), 0.91 (s, 9H), 0.11 (d, *J* = 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 151.9, 147.9, 79.9, 79.5, 79.3, 72.9, 51.5, 27.8, 25.9, 18.2, -4.6; IR (Neat Film NaCl) 2929, 2955, 2857, 2097, 1638, 1361, 1272, 1259, 1209, 1093, 837, 777 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{15}H_{25}O_3Si$ $[M+H]^+$: 281.1567; found: 281.1569; $[\alpha]_D^{25.0}$ 13.3° (*c* 0.06, $CHCl_3$).

5.5. References and Notes

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(3) The absolute stereochemistry has yet to be confirmed.

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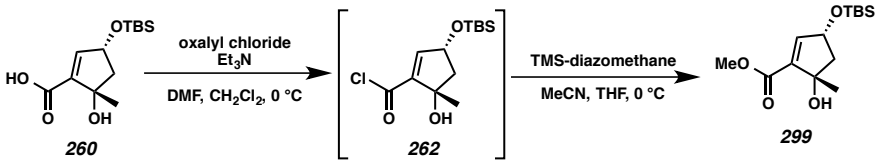
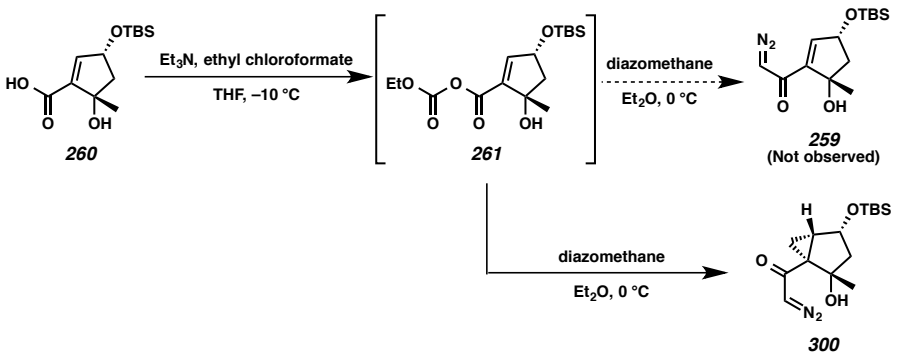
(15) Treatment of TMS-diazomethane to acid chloride **262** afforded only methyl ester **299**.



(16) Addition of diazomethane to intermediate **261** furnished cyclopropane **300**.



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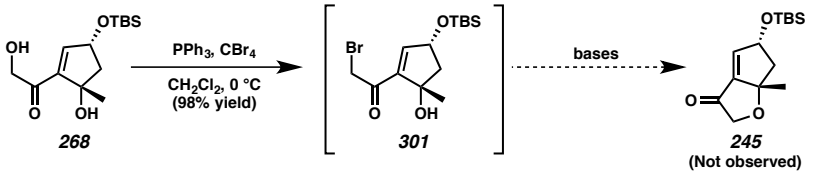
(20) Attempted etherifications of α-bromoketone **301**, which was prepared from α-hydroxyketone **268**, was also unsuccessful.



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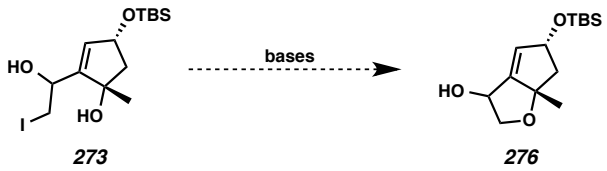
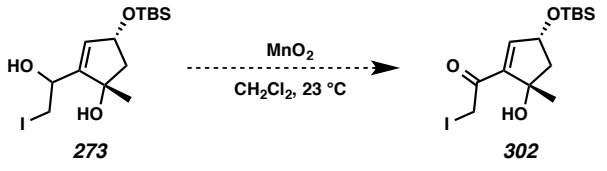
(25) Only ketone **258** was observed when the reaction was conducted at 80 °C.

(26) Attempts on direct intramolecular etherification of iodohydrin **273** under basic conditions failed to produce **276**. In addition, oxidation of iodohydrin **273** with MnO_2 produced complex mixtures of byproducts.



273 ***276***



273 ***302***

(27) Because oxidation of secondary alcohol **276** with MnO_2 was conducted on small scale, the amount of the obtained ketone **245** was too little to be characterized by NMR analysis.

(28) Nevar, N. M.; Kel'in, A. V.; Kulinkovich, O. L. *Synthesis* **2000**, *9*, 1259–1262.

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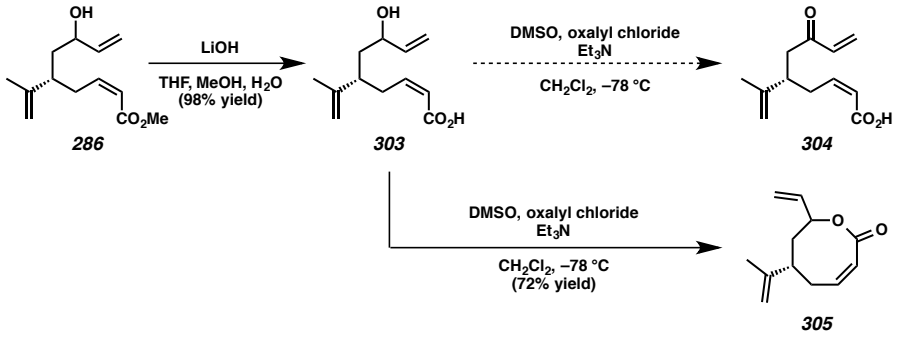
(30) An attempt to oxidize secondary alcohol **303**, which was prepared by hydrolysis of ester **286** using Swern oxidation conditions, caused lactonization to give **305** instead of the desired **304**.



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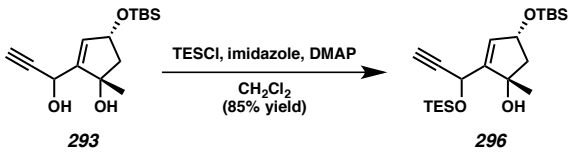
(32) Silyl ether **296** was prepared from diol **293** with TESCl.



APPENDIX 13

Spectra Relevant to Chapter 5:

Synthetic Studies Toward Polycyclic Ineleganolide

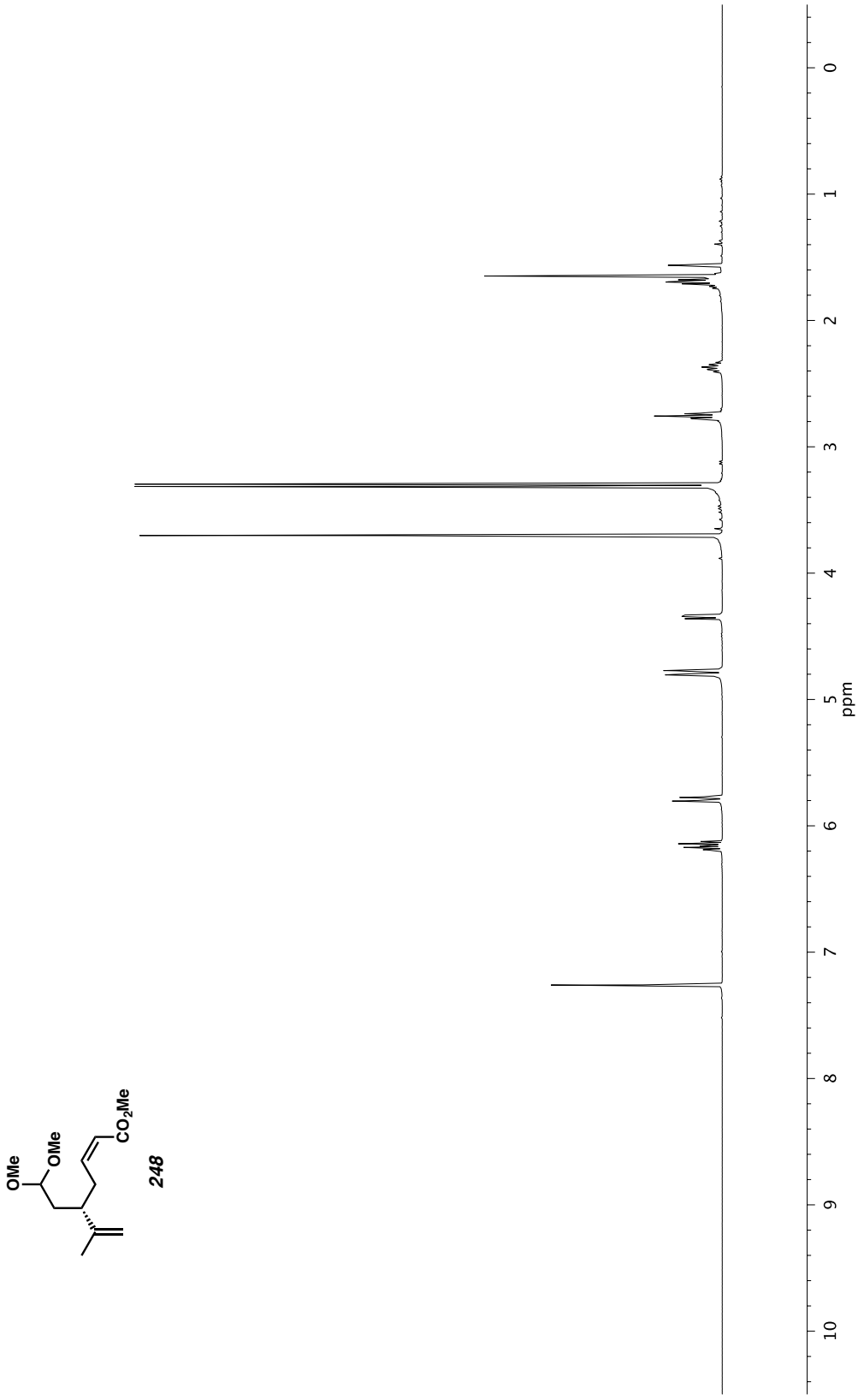


Figure A13.1. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **248**.

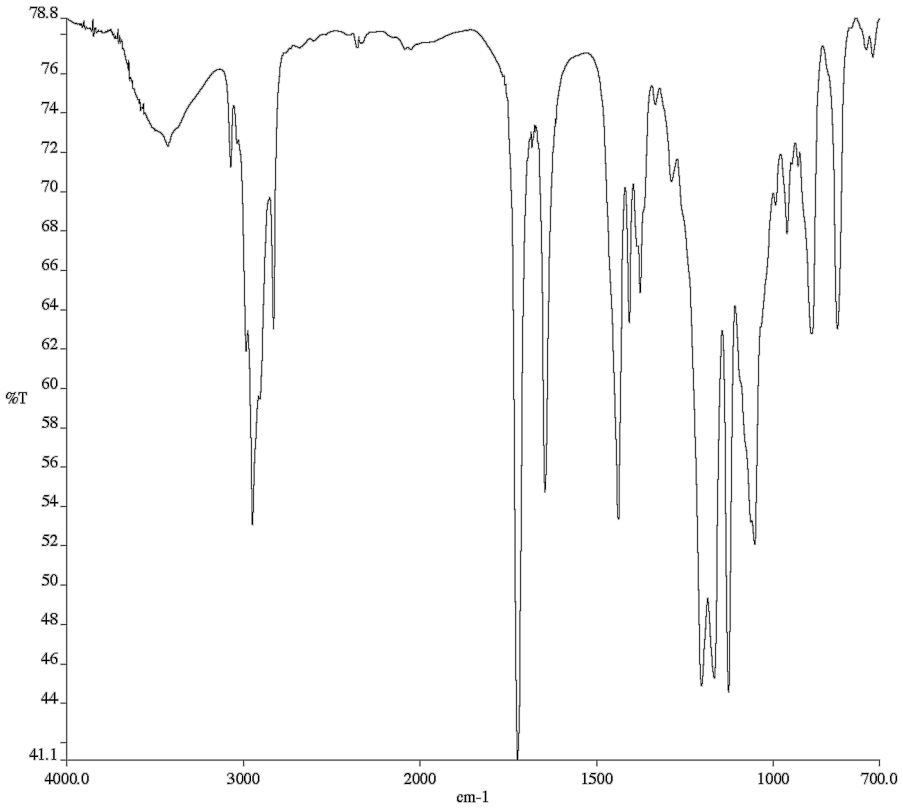


Figure A13.2. Infrared spectrum (Thin Film, NaCl) of compound **248**.

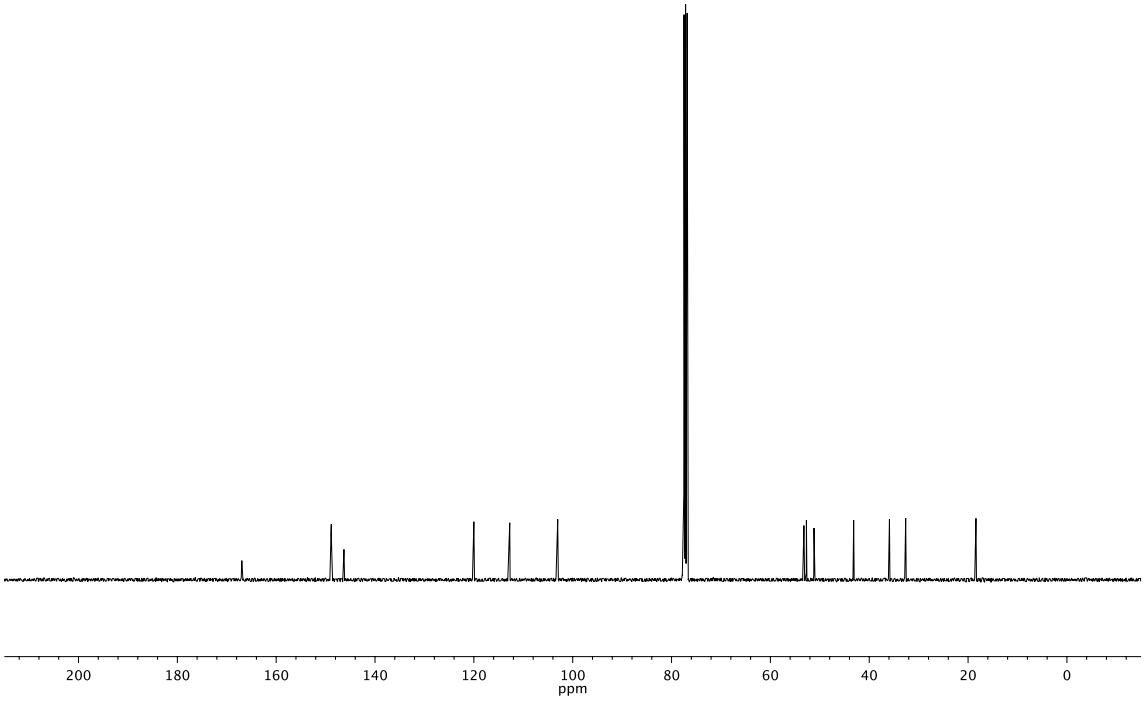


Figure A13.3. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **248**.

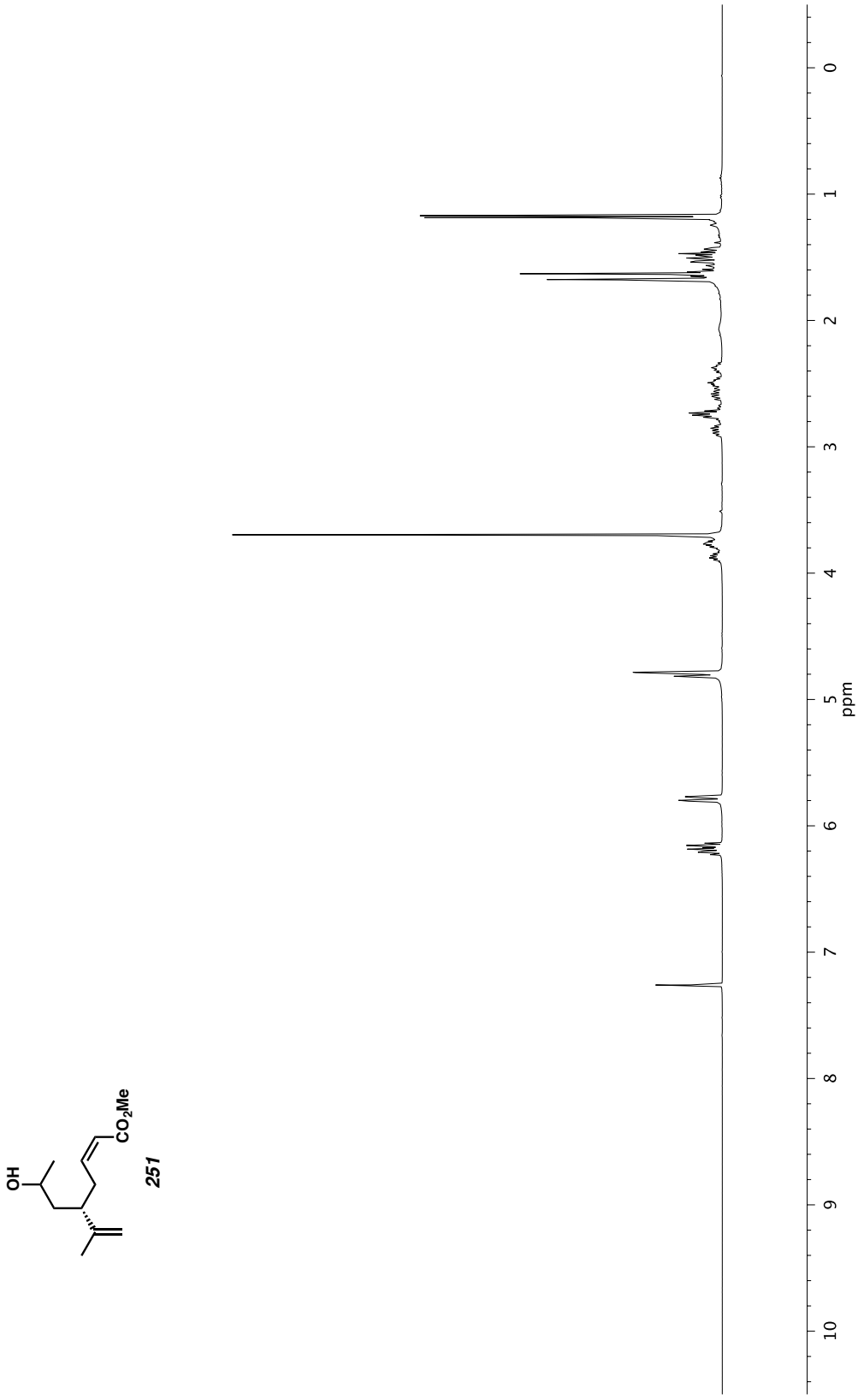


Figure A13.4. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **251**.

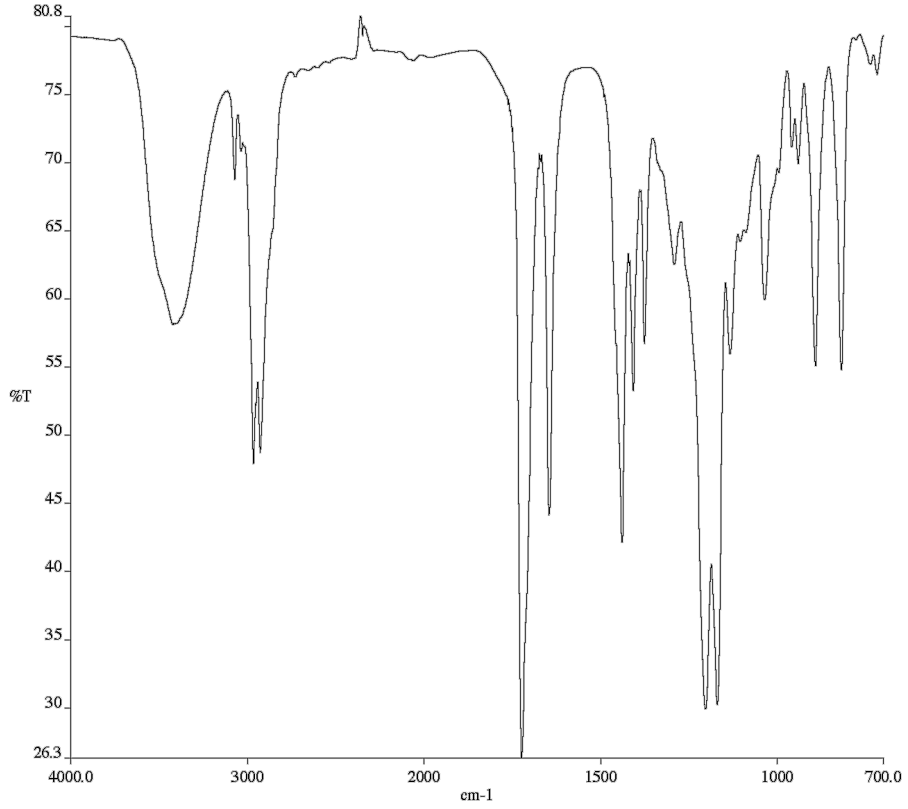


Figure A13.5. Infrared spectrum (Thin Film, NaCl) of compound **251**.

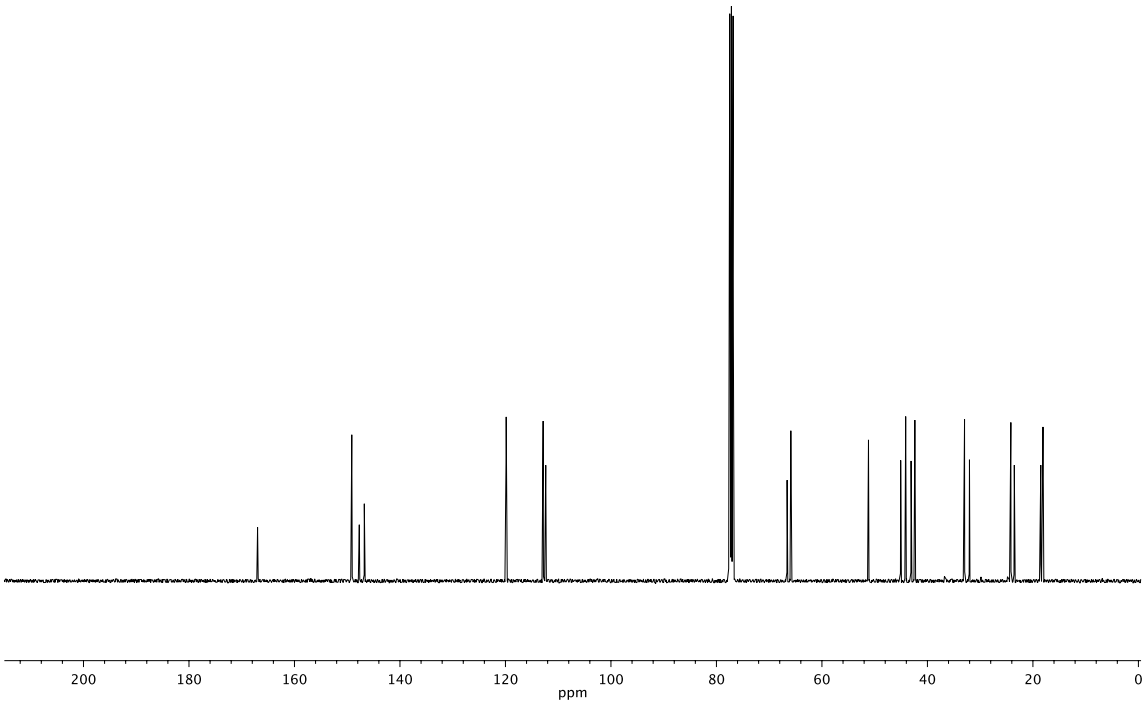


Figure A13.6. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **251**.

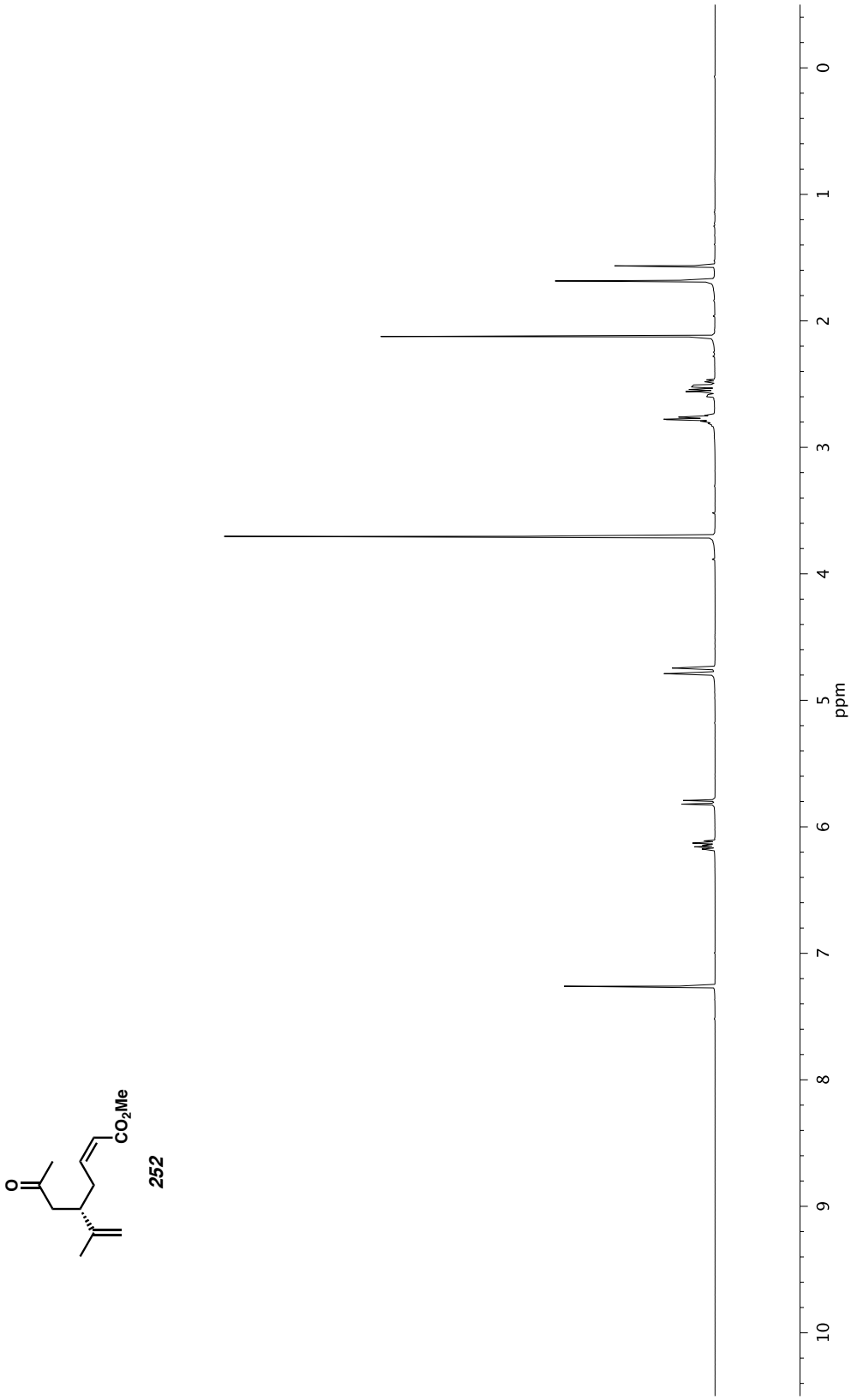


Figure A13.7. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **252**.

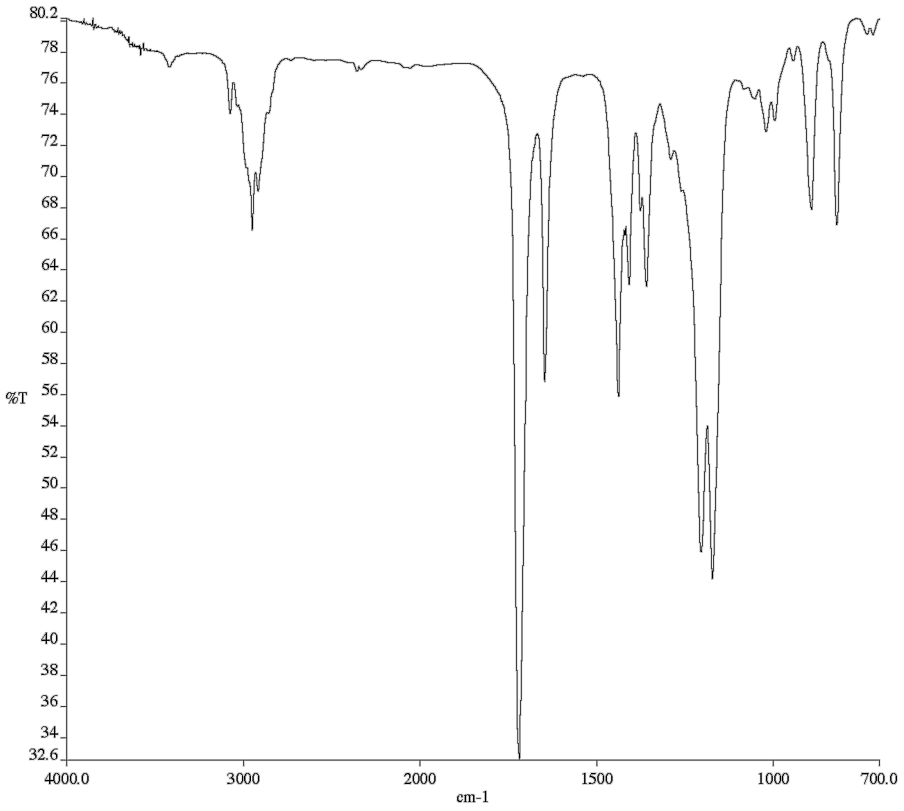


Figure A13.8. Infrared spectrum (Thin Film, NaCl) of compound **252**.

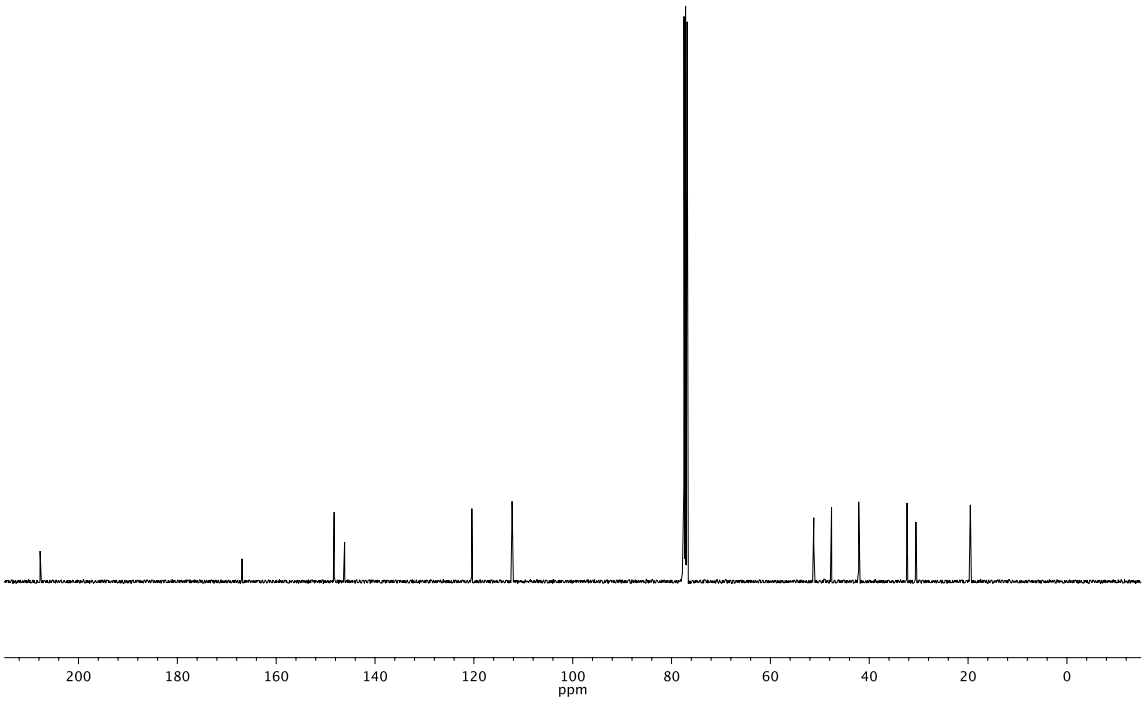


Figure A13.9. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **252**.

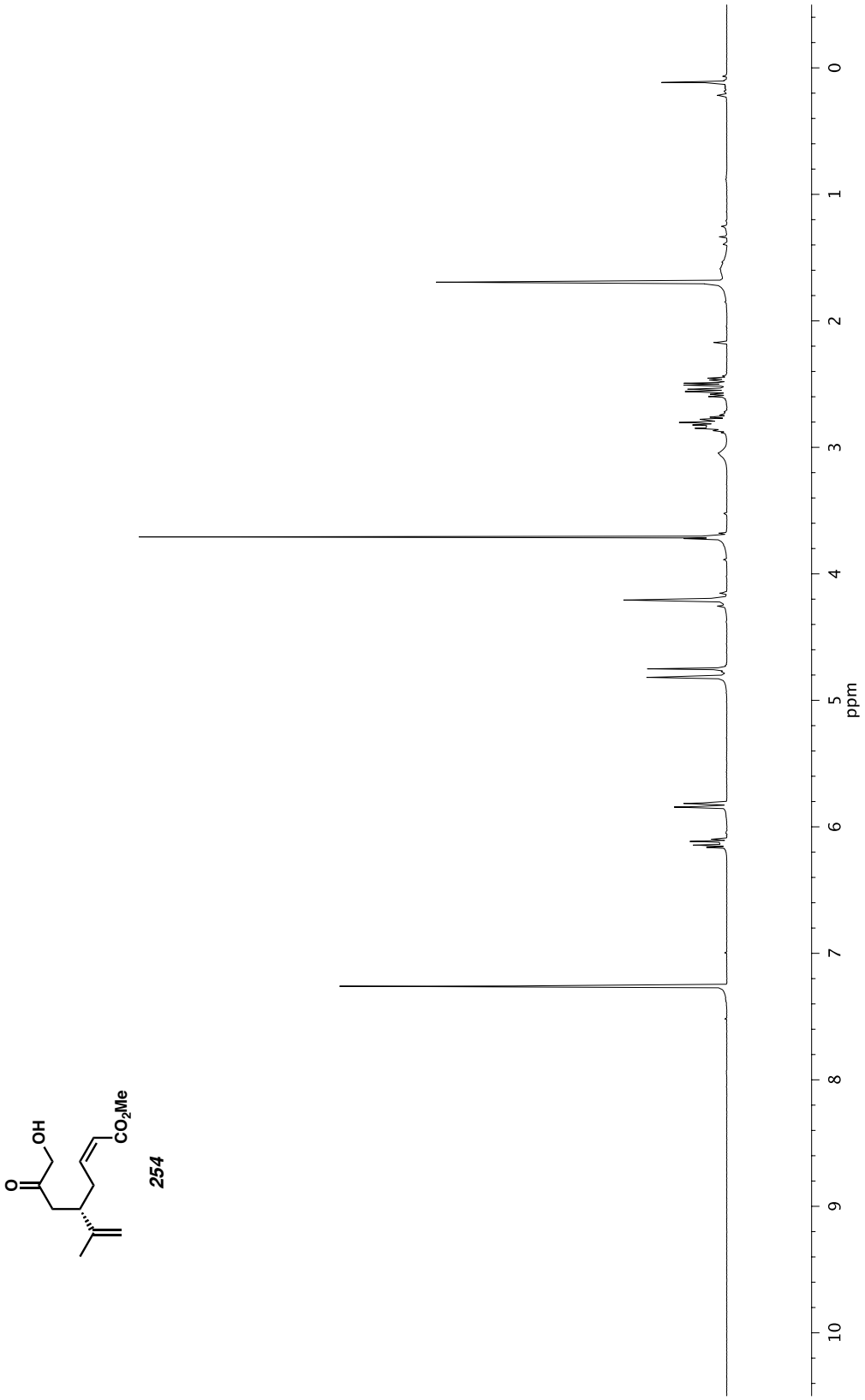


Figure A13.10. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **254**.

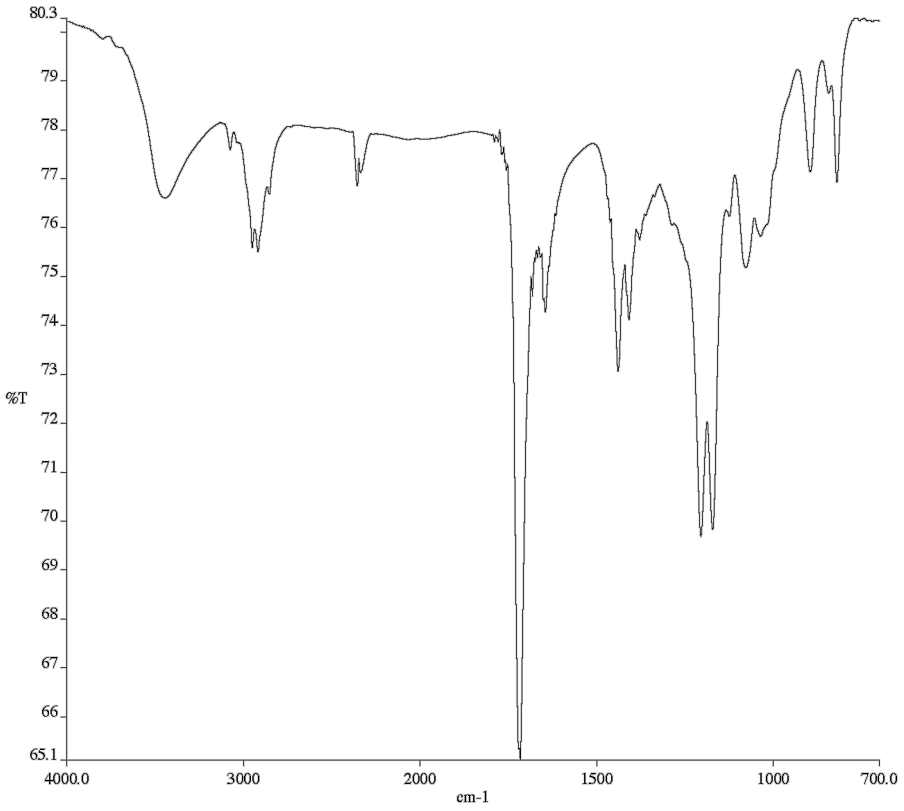


Figure A13.11. Infrared spectrum (Thin Film, NaCl) of compound **254**.

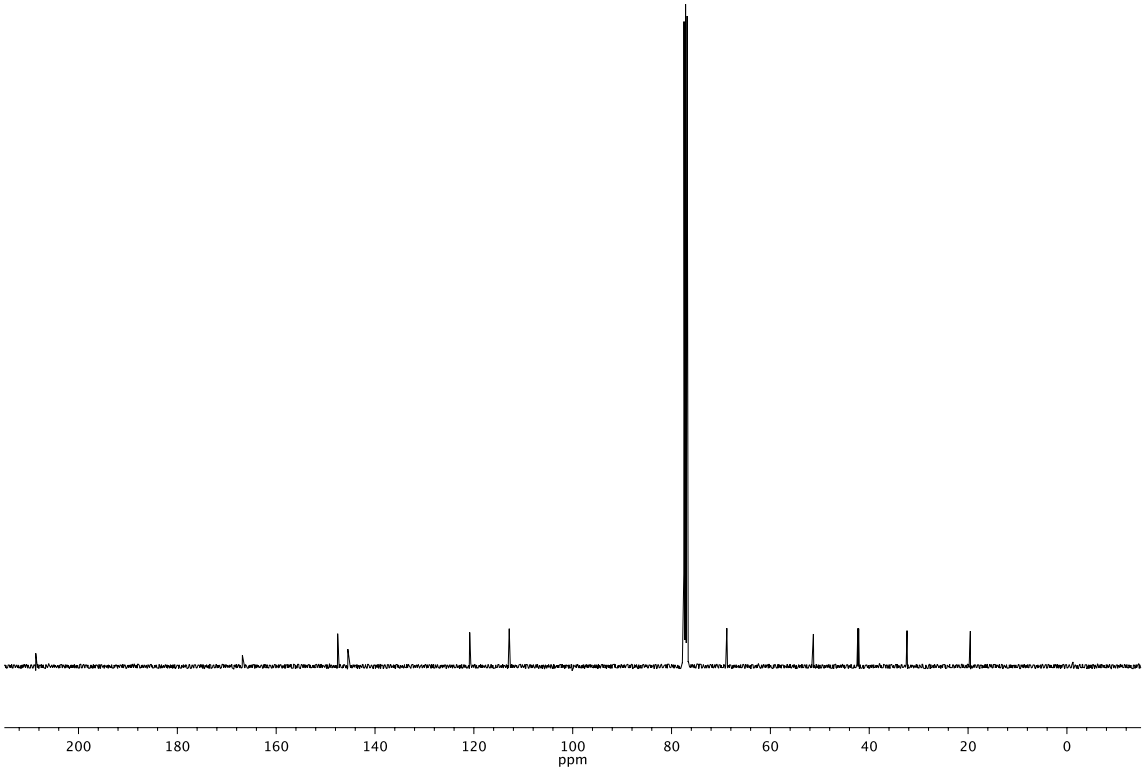


Figure A13.12. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **254**.

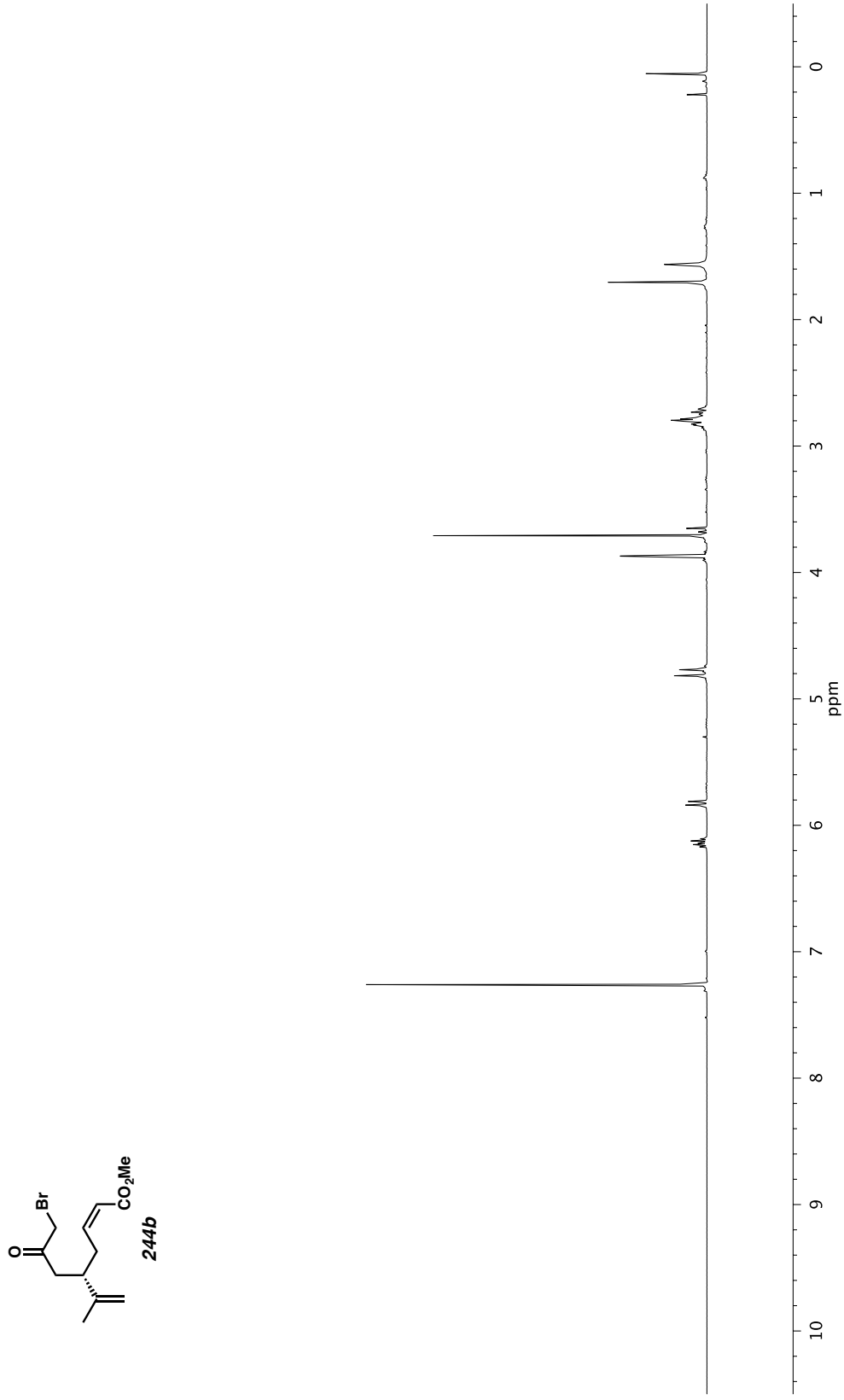


Figure A13.13. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **244b**.

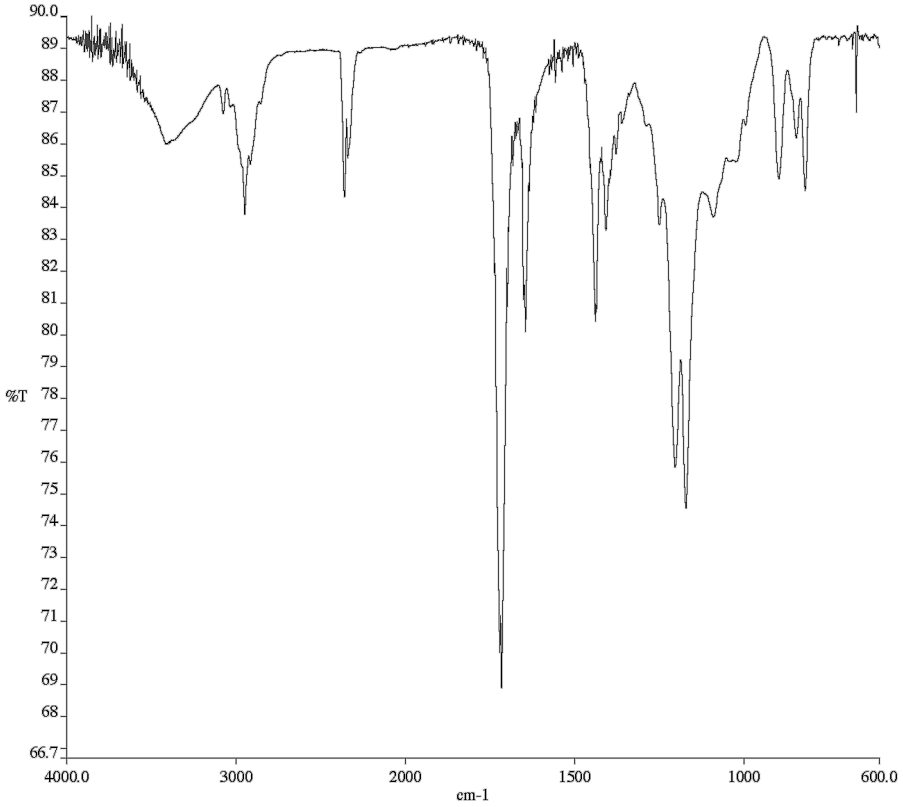


Figure A13.14. Infrared spectrum (Thin Film, NaCl) of compound **244b**.

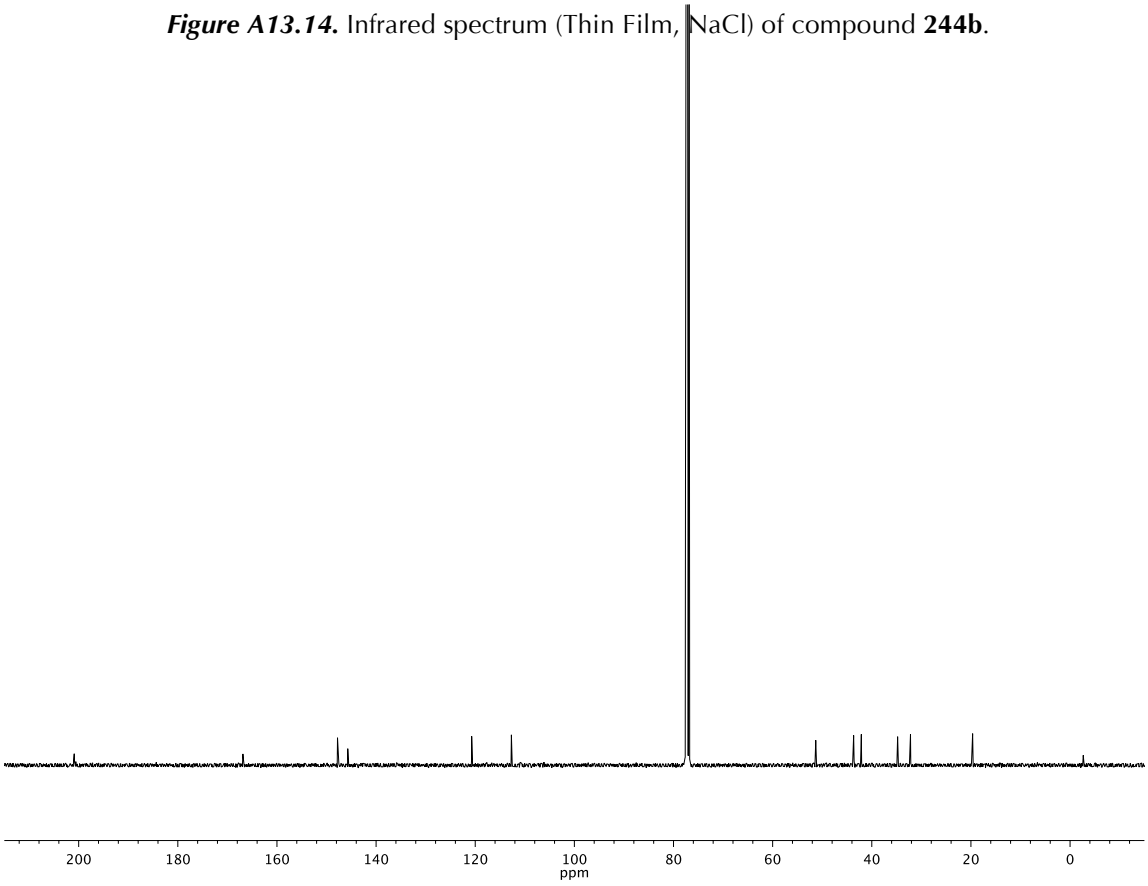


Figure A13.15. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **244b**.

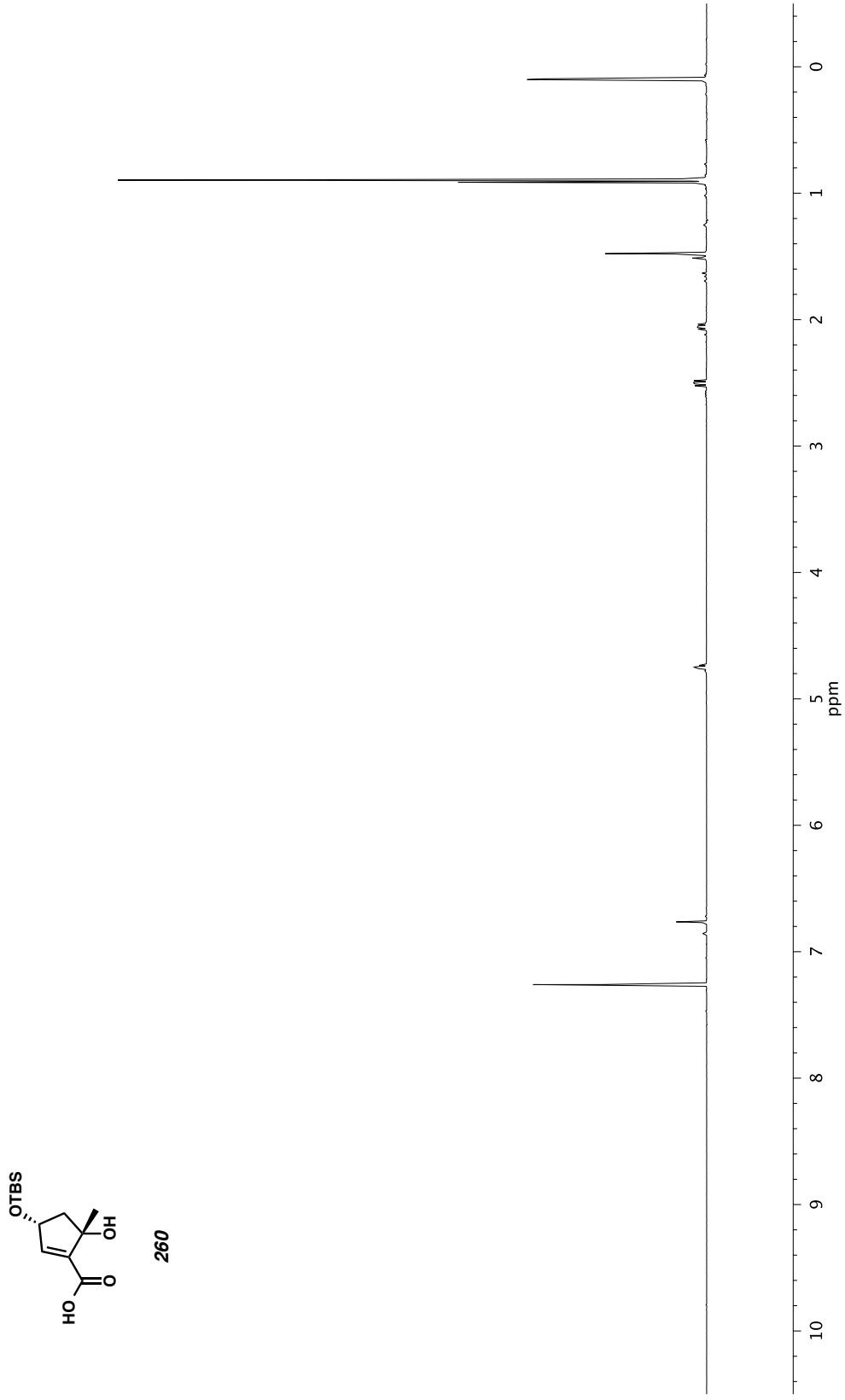


Figure A13.16. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **260**.

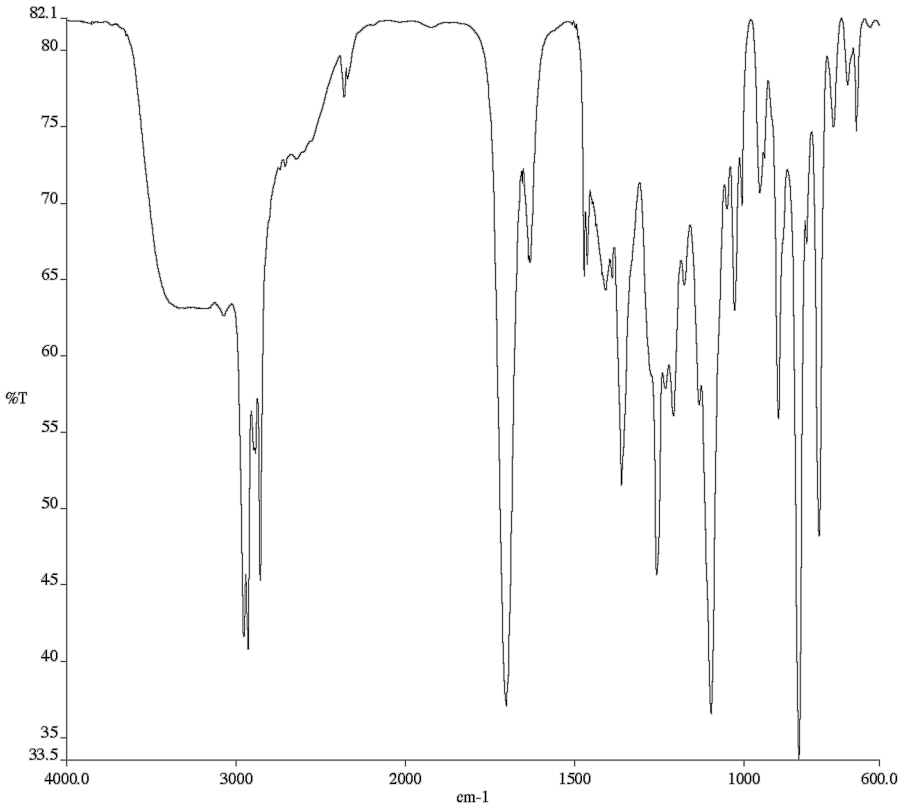


Figure A13.17. Infrared spectrum (Thin Film, NaCl) of compound **260**.

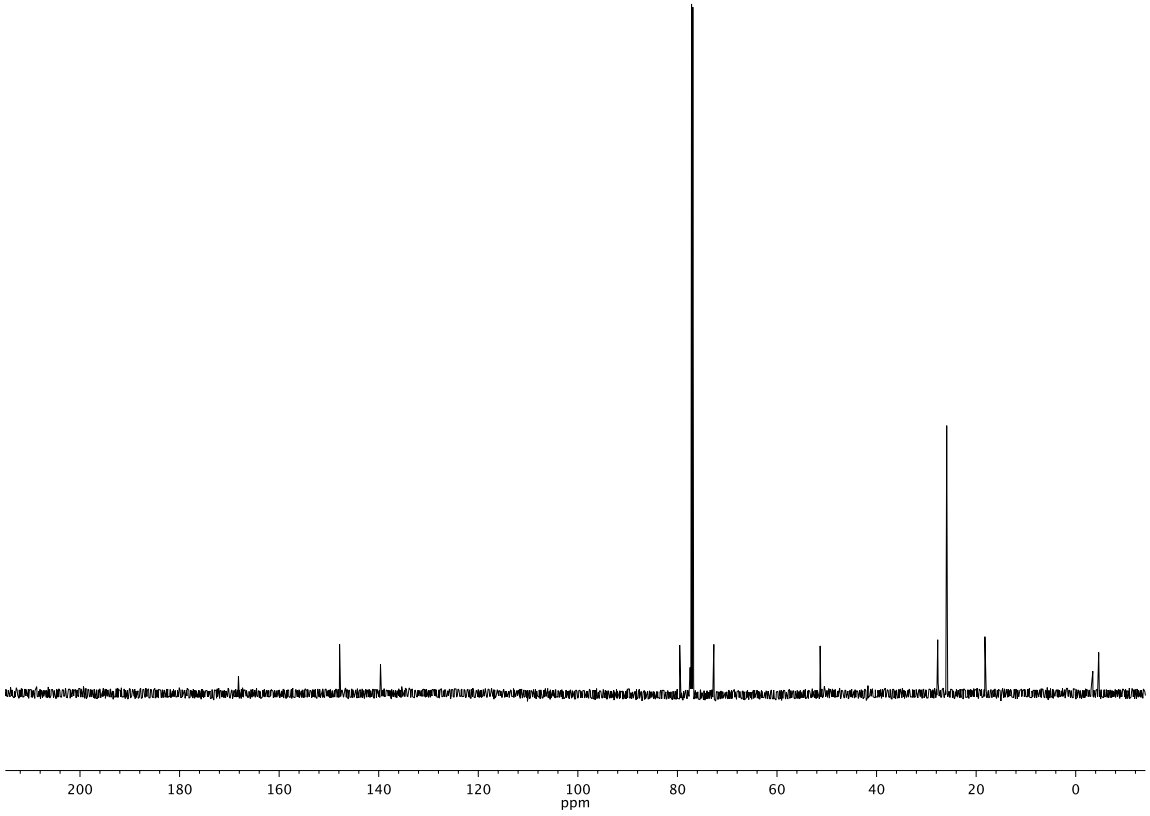
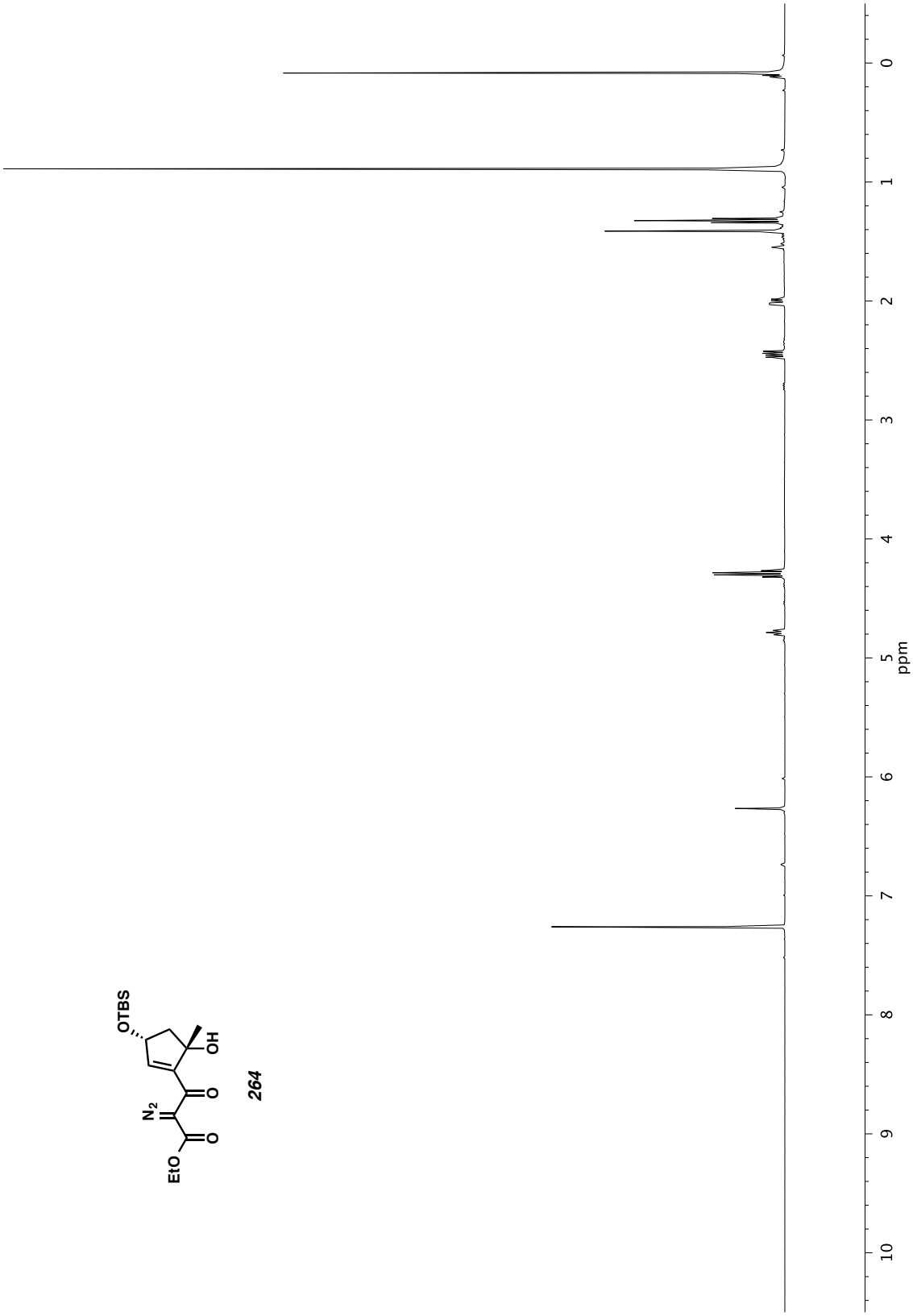


Figure A13.18. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **260**.



264

Figure A13.19. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **264**.

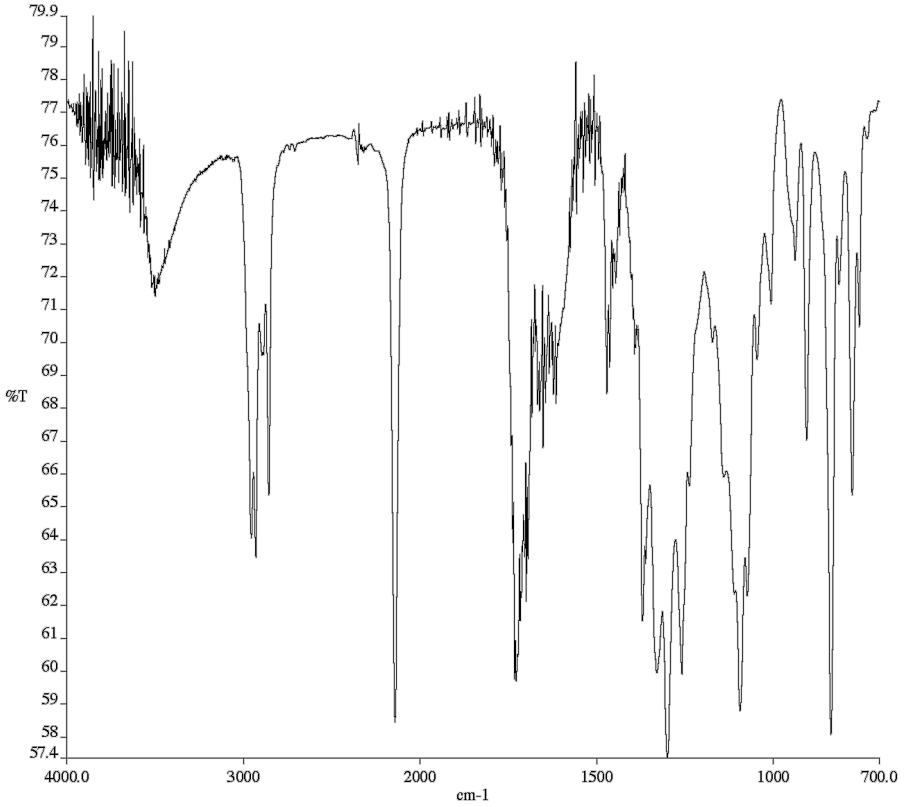


Figure A13.20. Infrared spectrum (Thin Film, NaCl) of compound **264**.

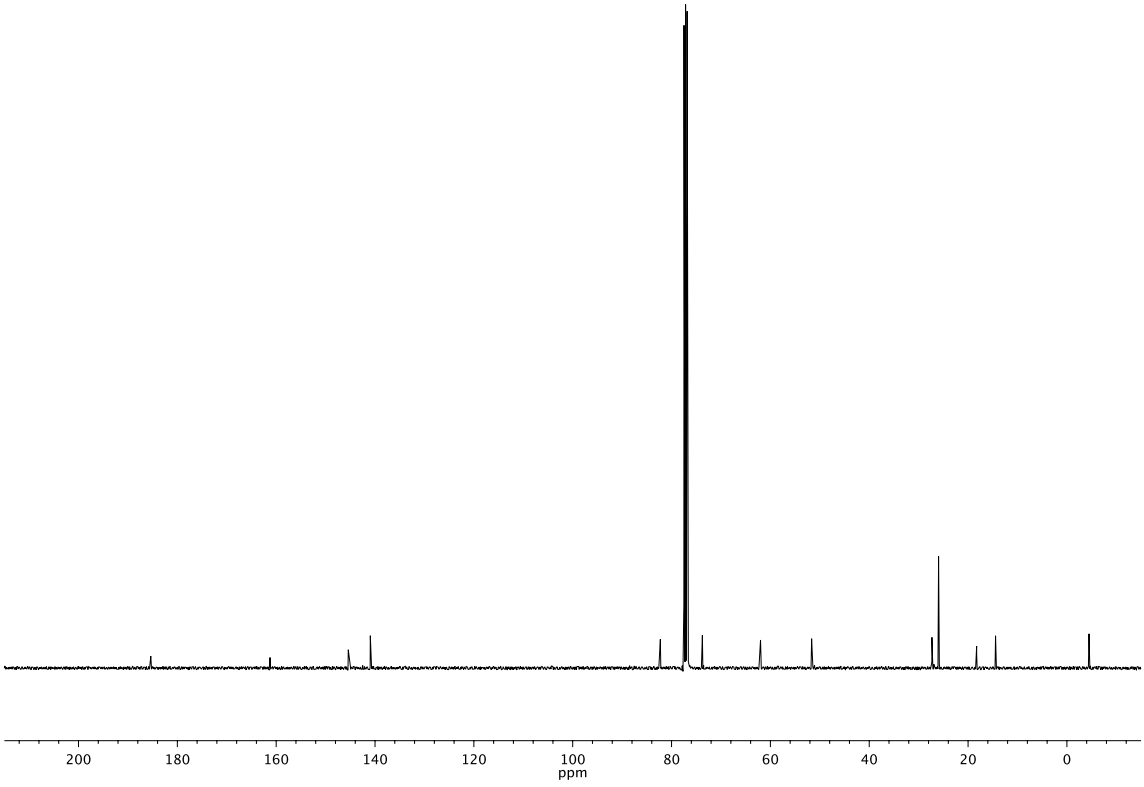


Figure A13.21. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **264**.

Figure A13.22. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **266**.

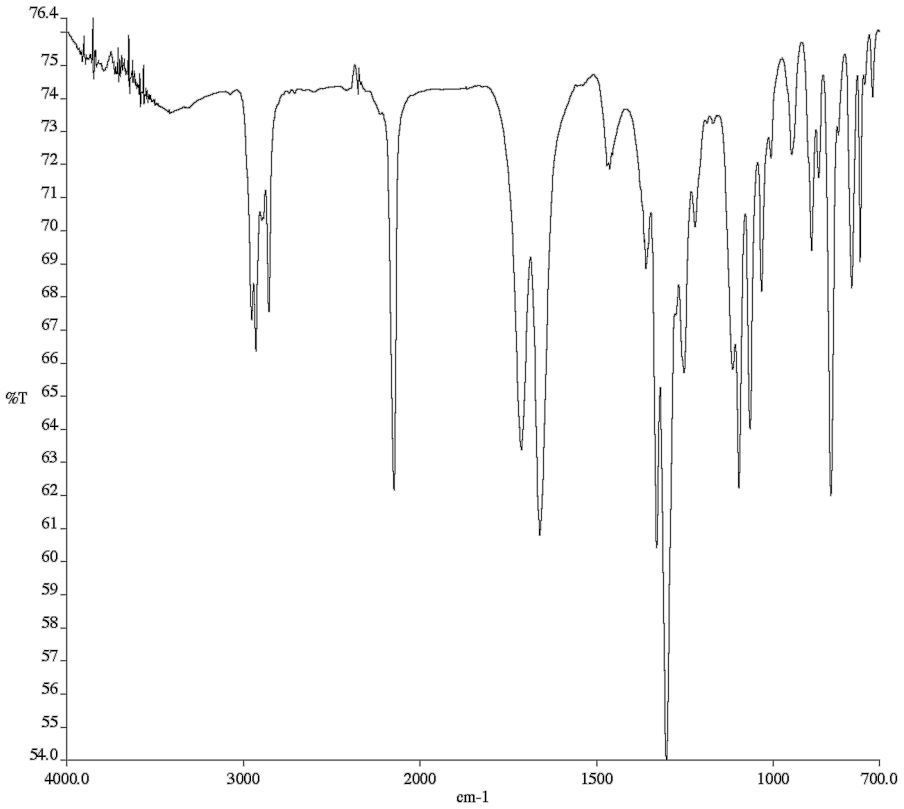


Figure A13.23. Infrared spectrum (Thin Film, NaCl) of compound **266**.

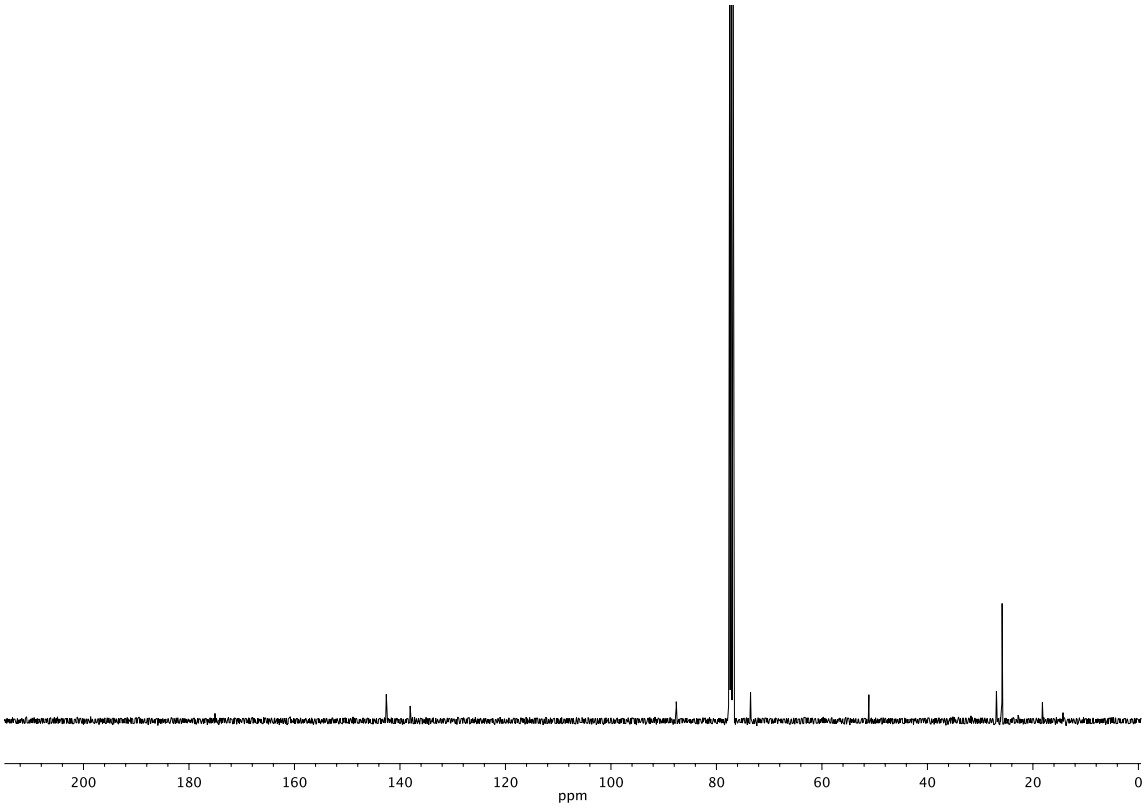


Figure A13.24. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **266**.

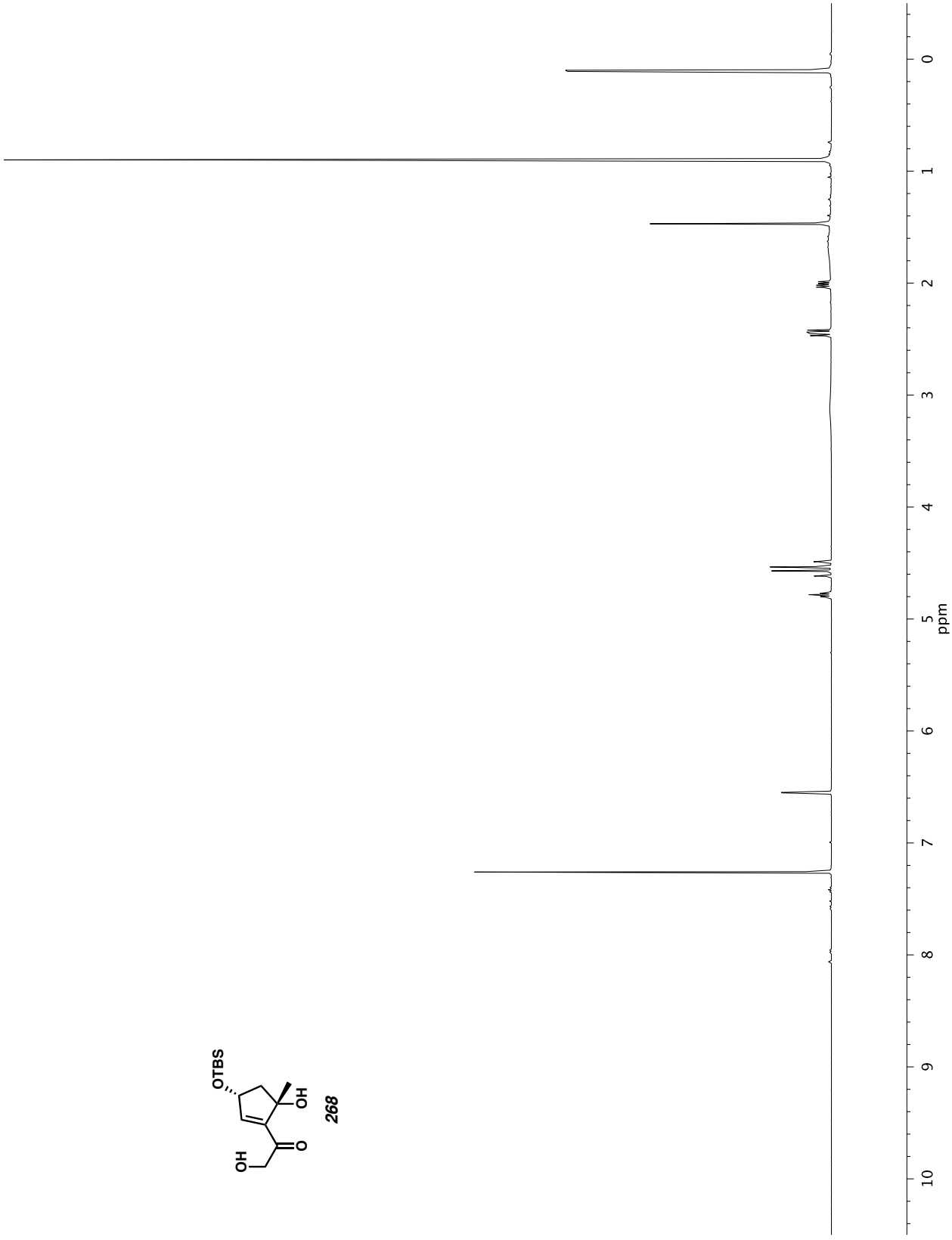


Figure A13.25. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **268**.

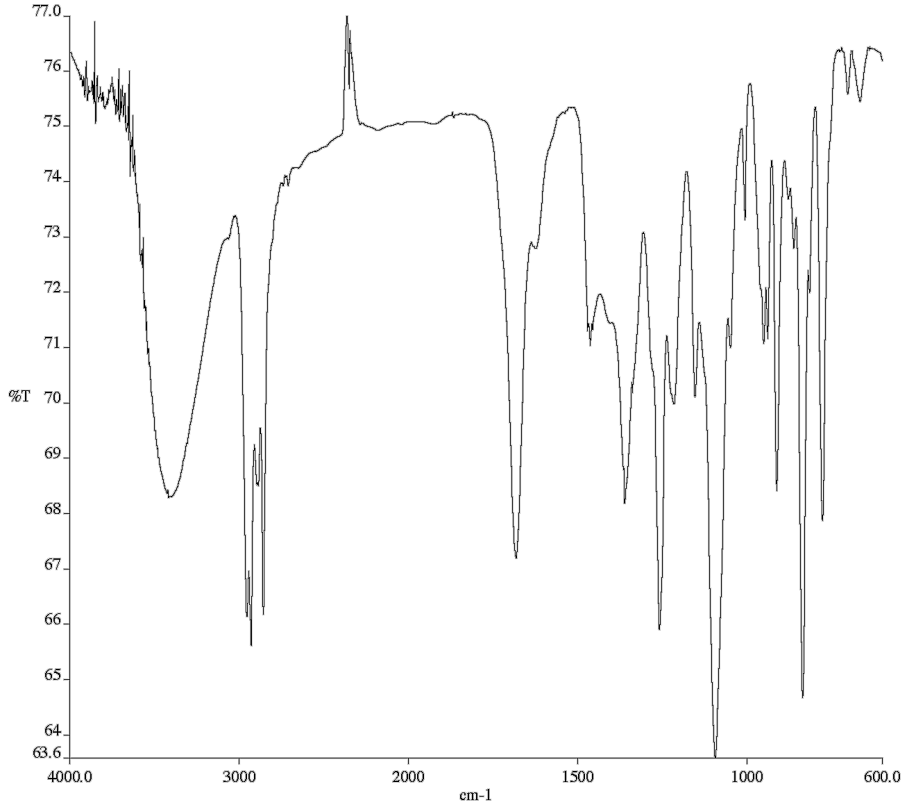


Figure A13.26. Infrared spectrum (Thin Film, NaCl) of compound **268**.

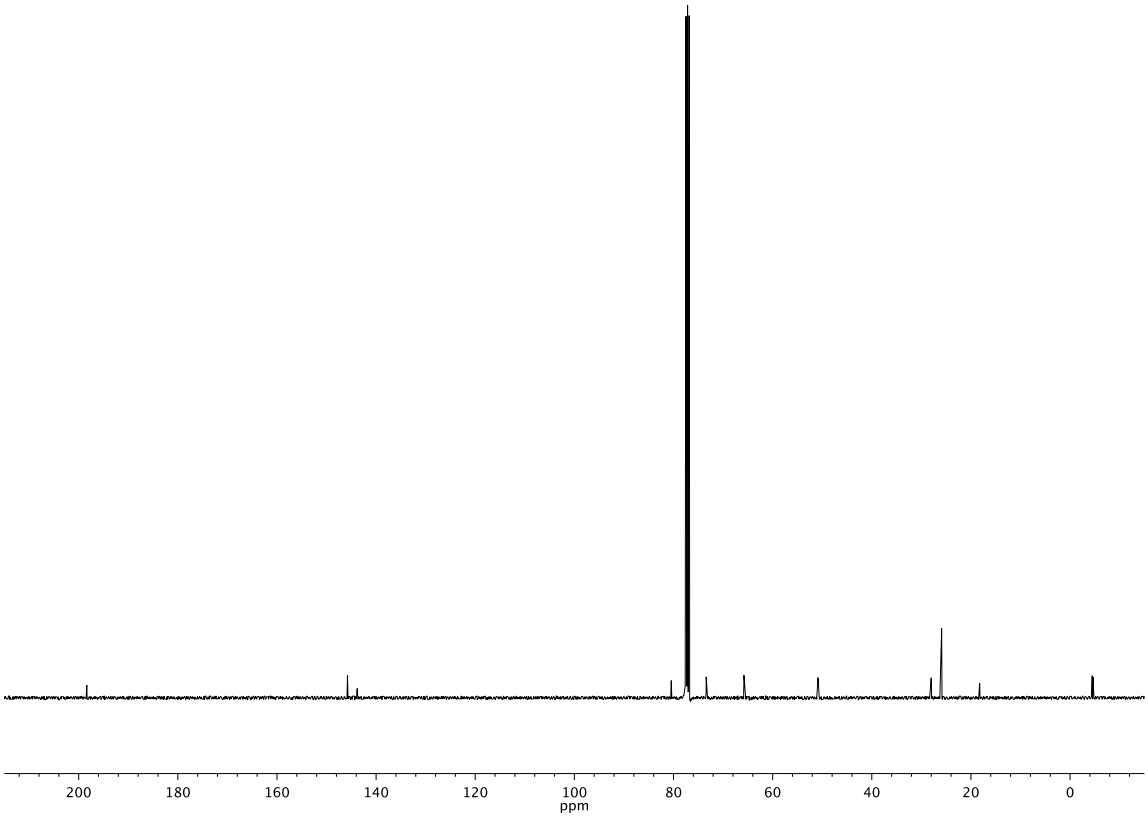


Figure A13.27. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **268**.

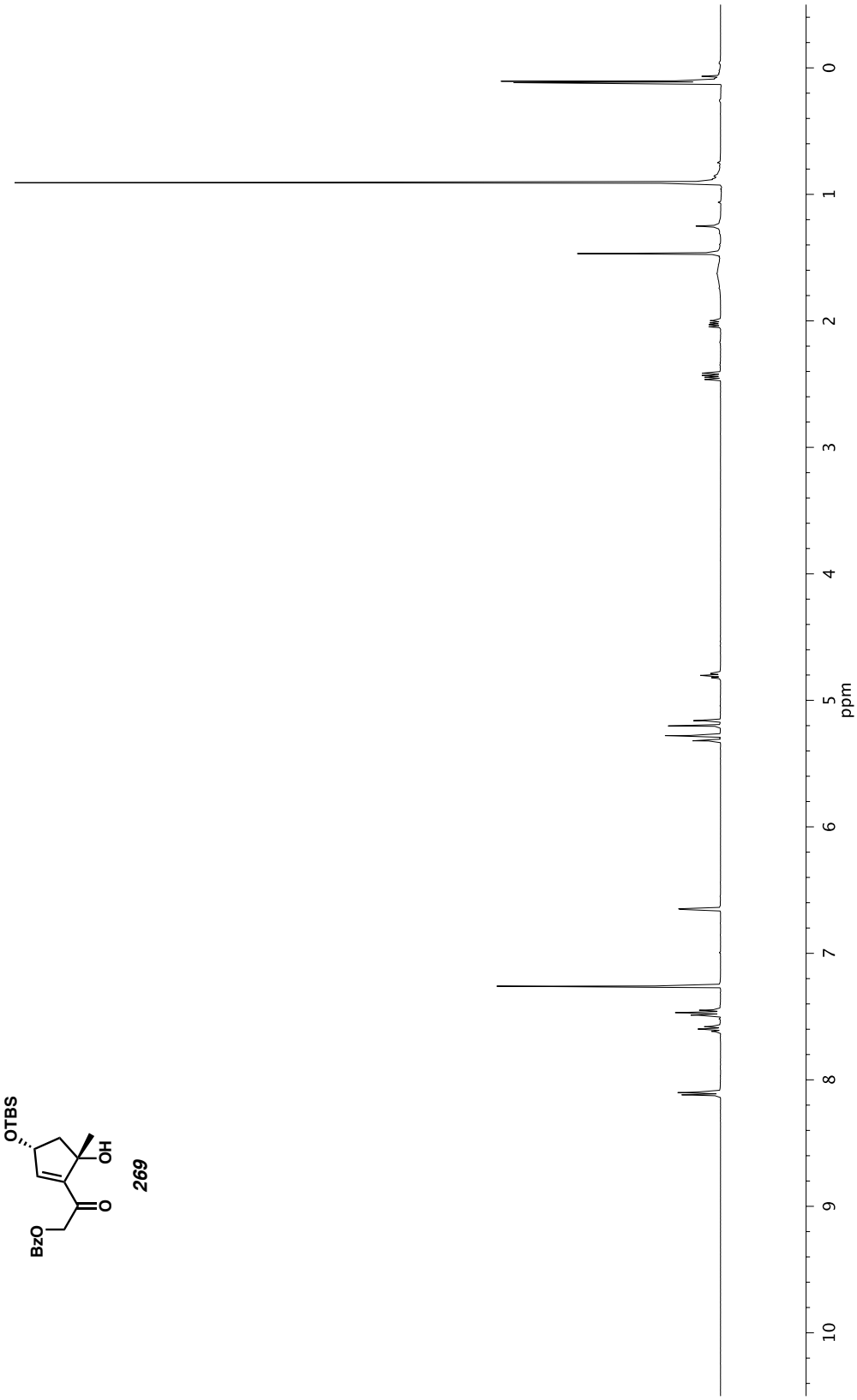


Figure A13.28. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **269**.

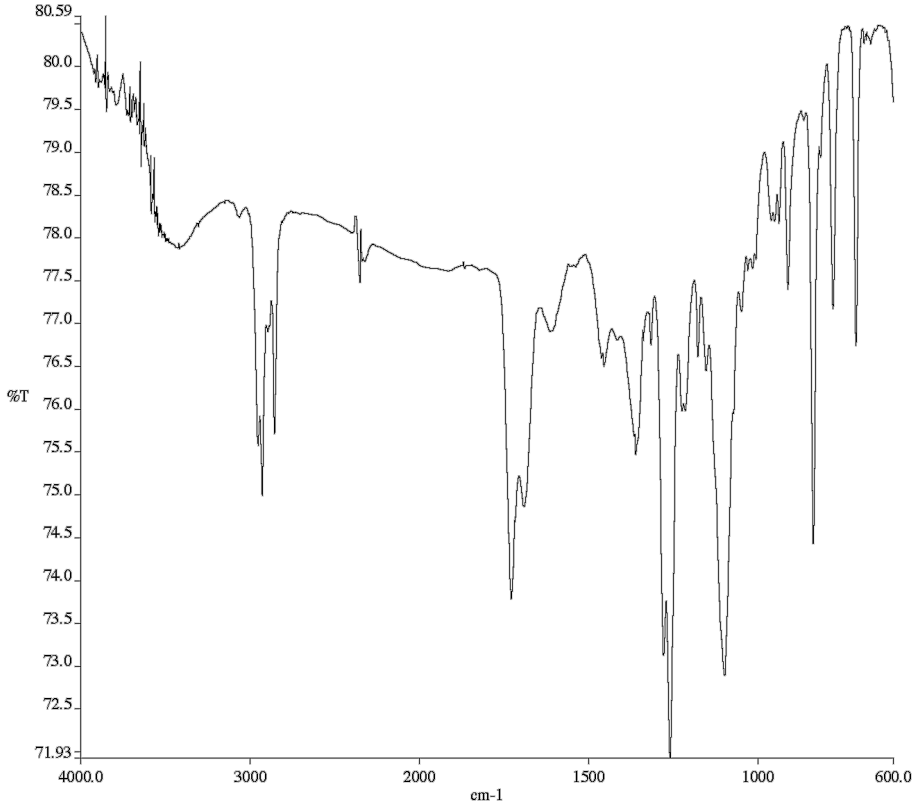


Figure A13.29. Infrared spectrum (Thin Film, NaCl) of compound **269**.

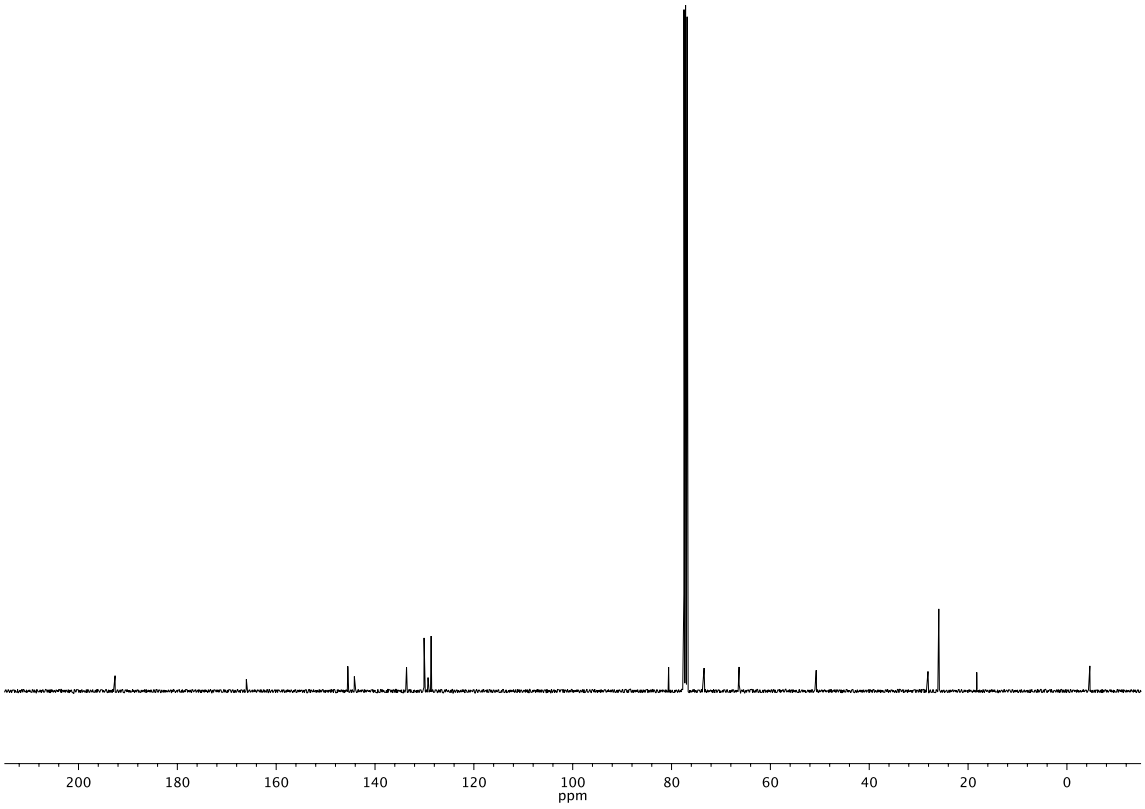


Figure A13.30. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **269**.

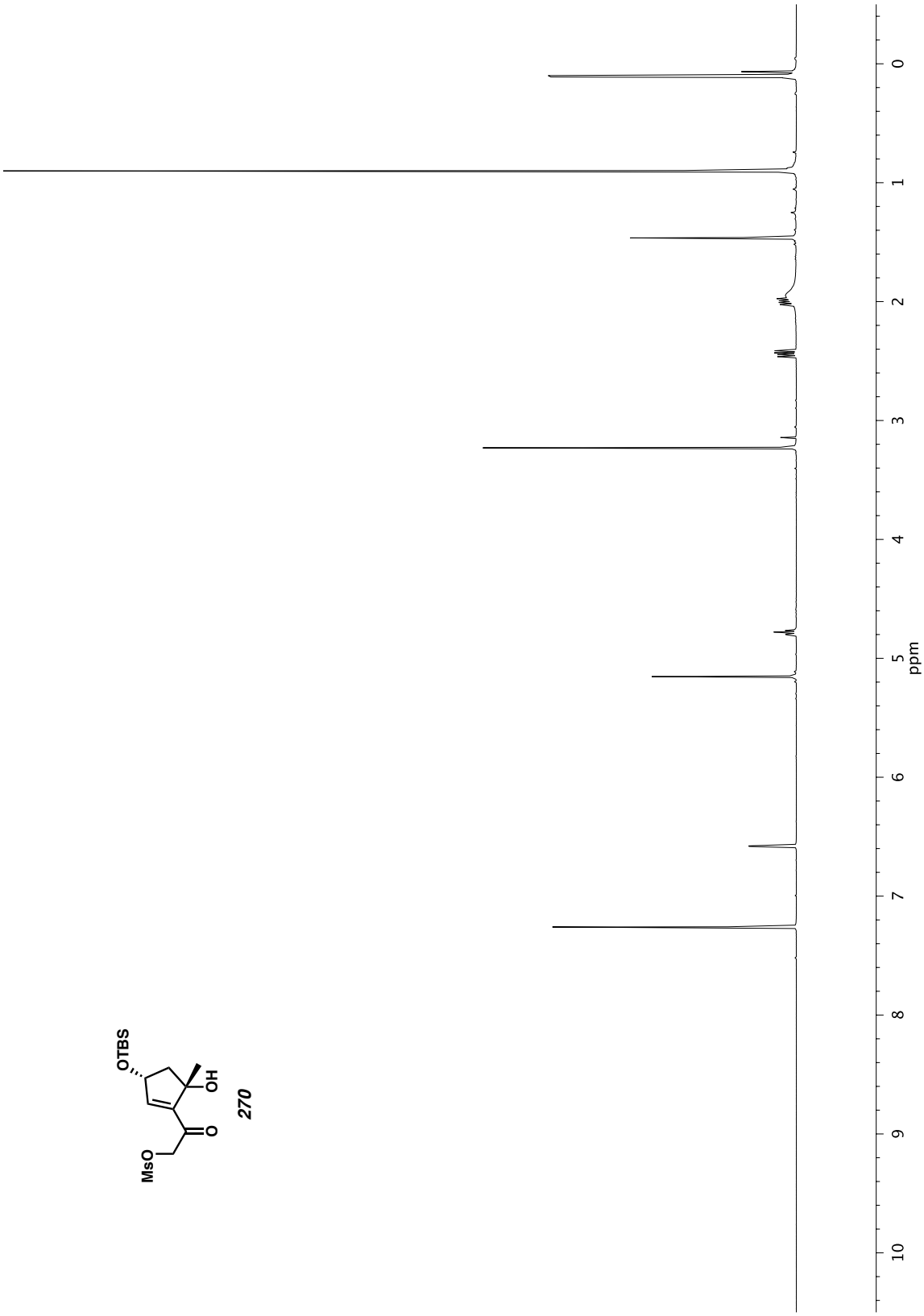


Figure A13.31. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **270**.

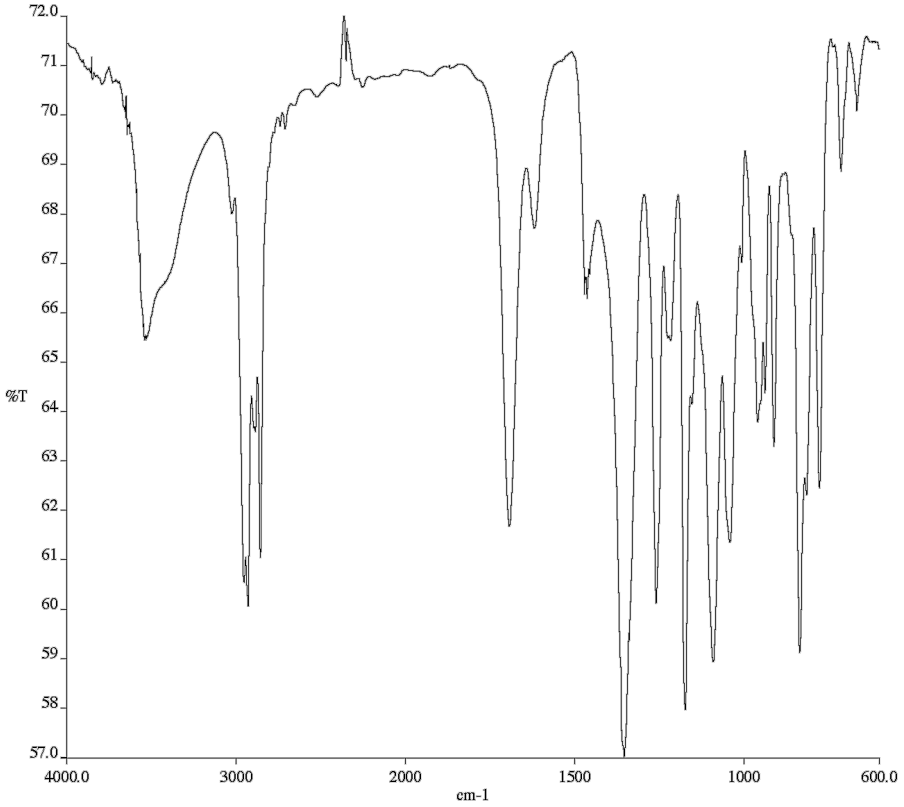


Figure A13.32. Infrared spectrum (Thin Film, NaCl) of compound **270**.

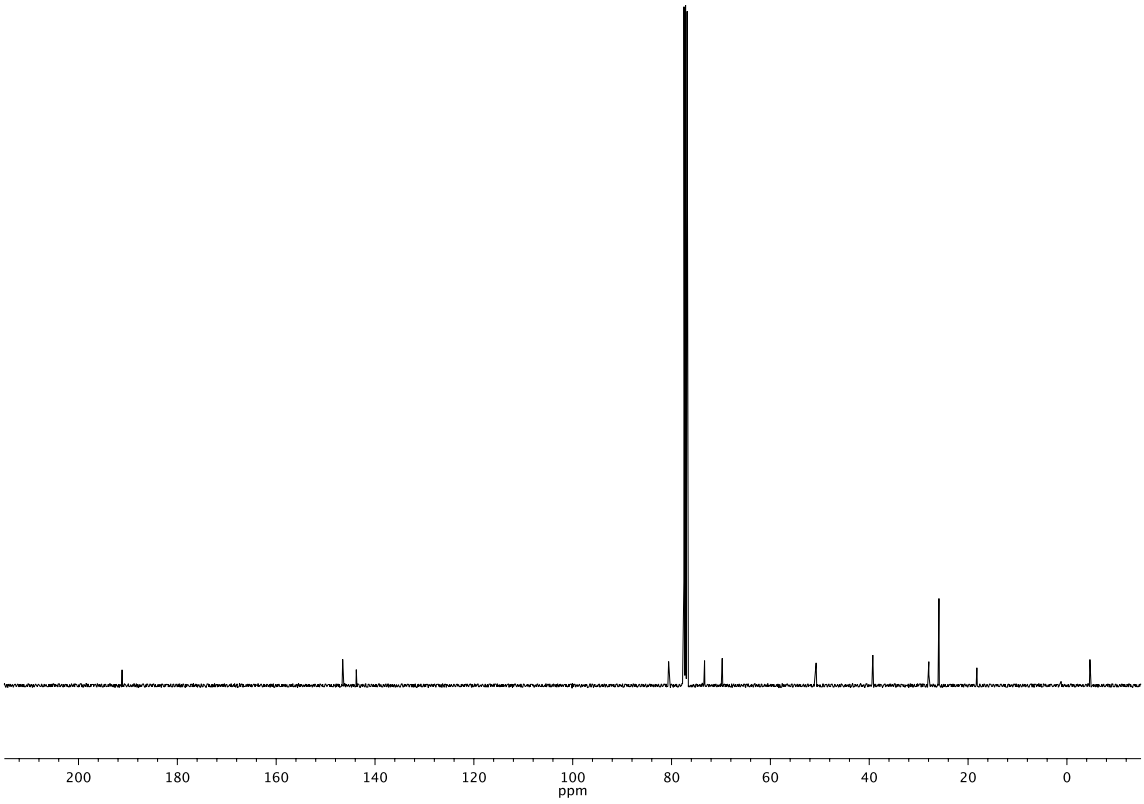


Figure A13.33. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **270**.

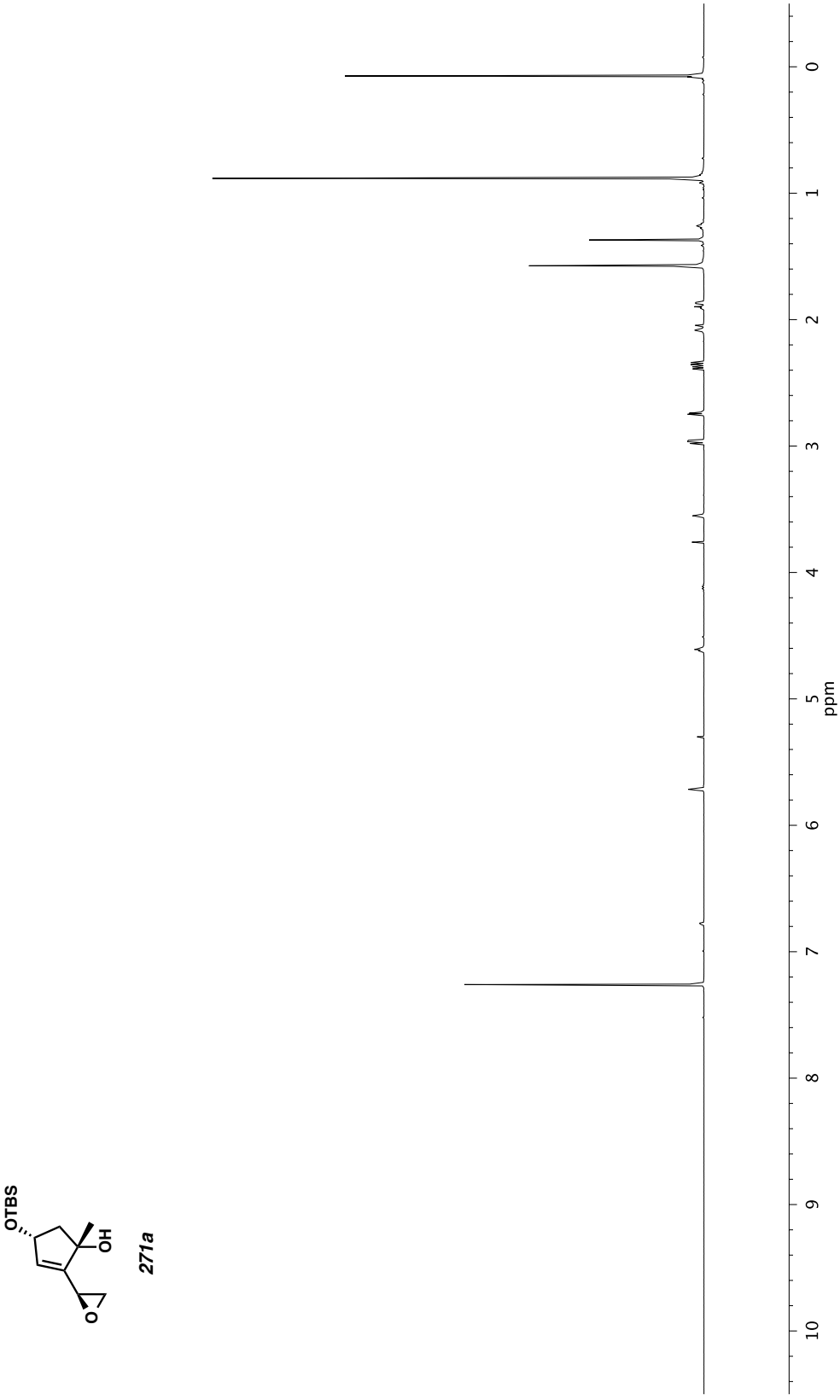


Figure A13.34. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **271a**.

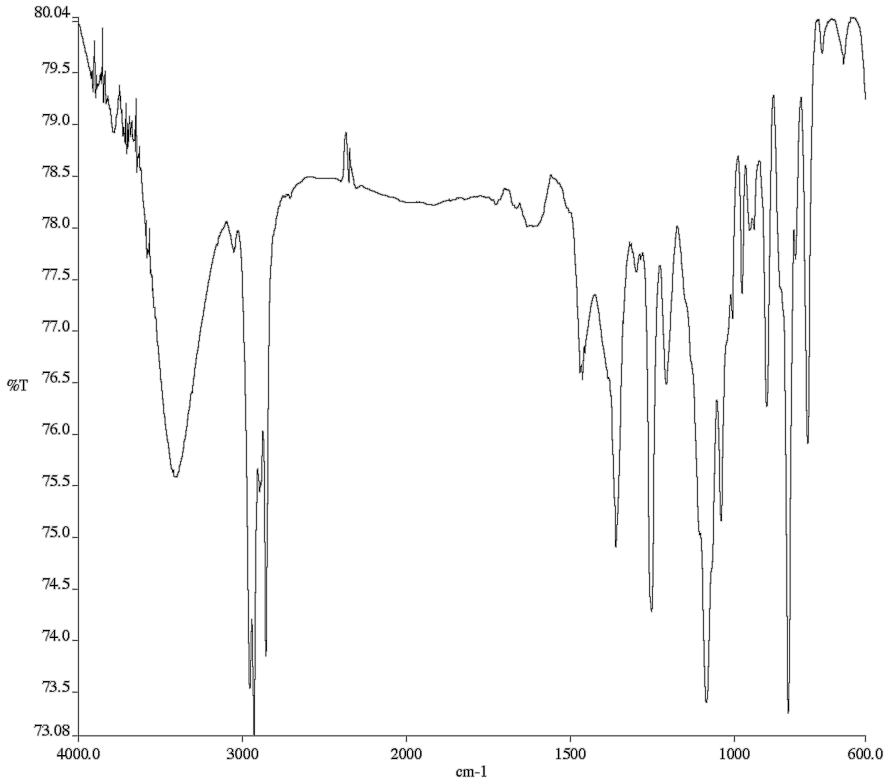


Figure A13.35. Infrared spectrum (Thin Film, NaCl) of compound **271a**.

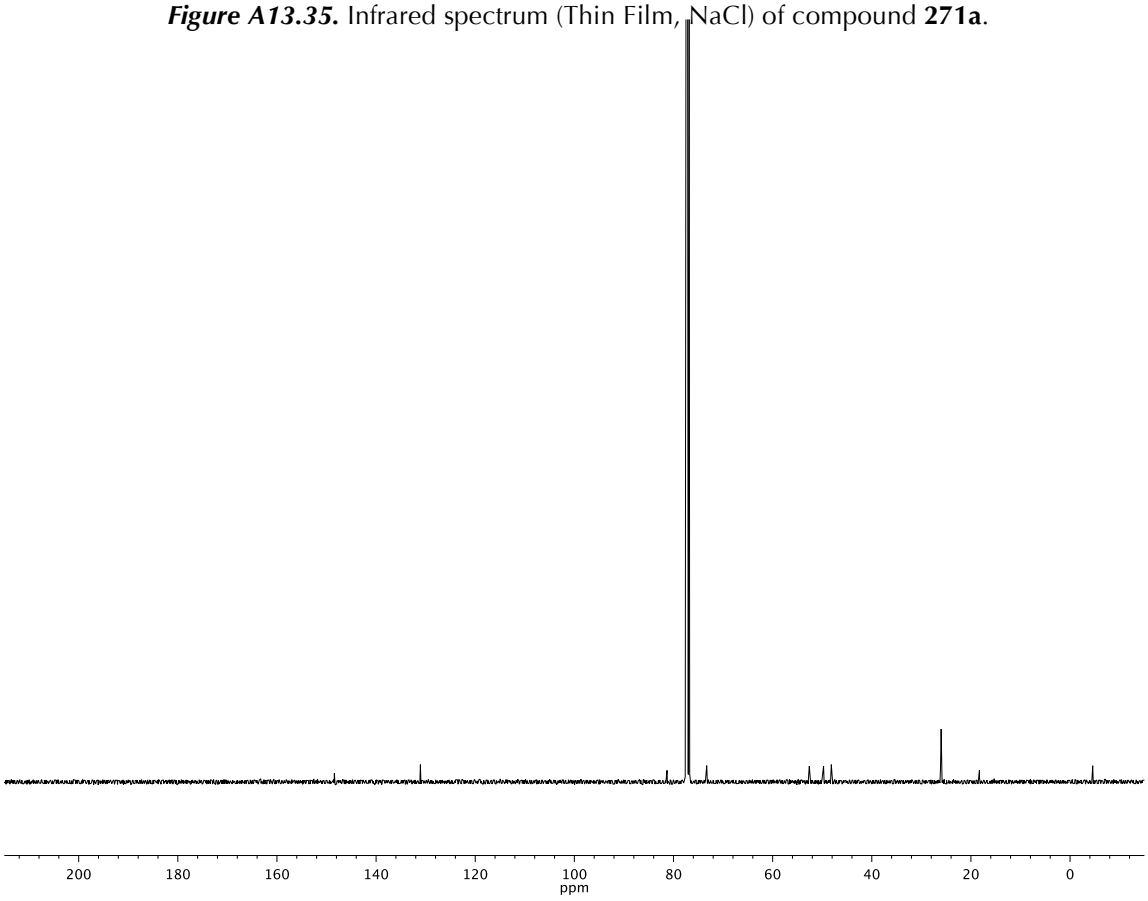


Figure A13.36. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **271a**.

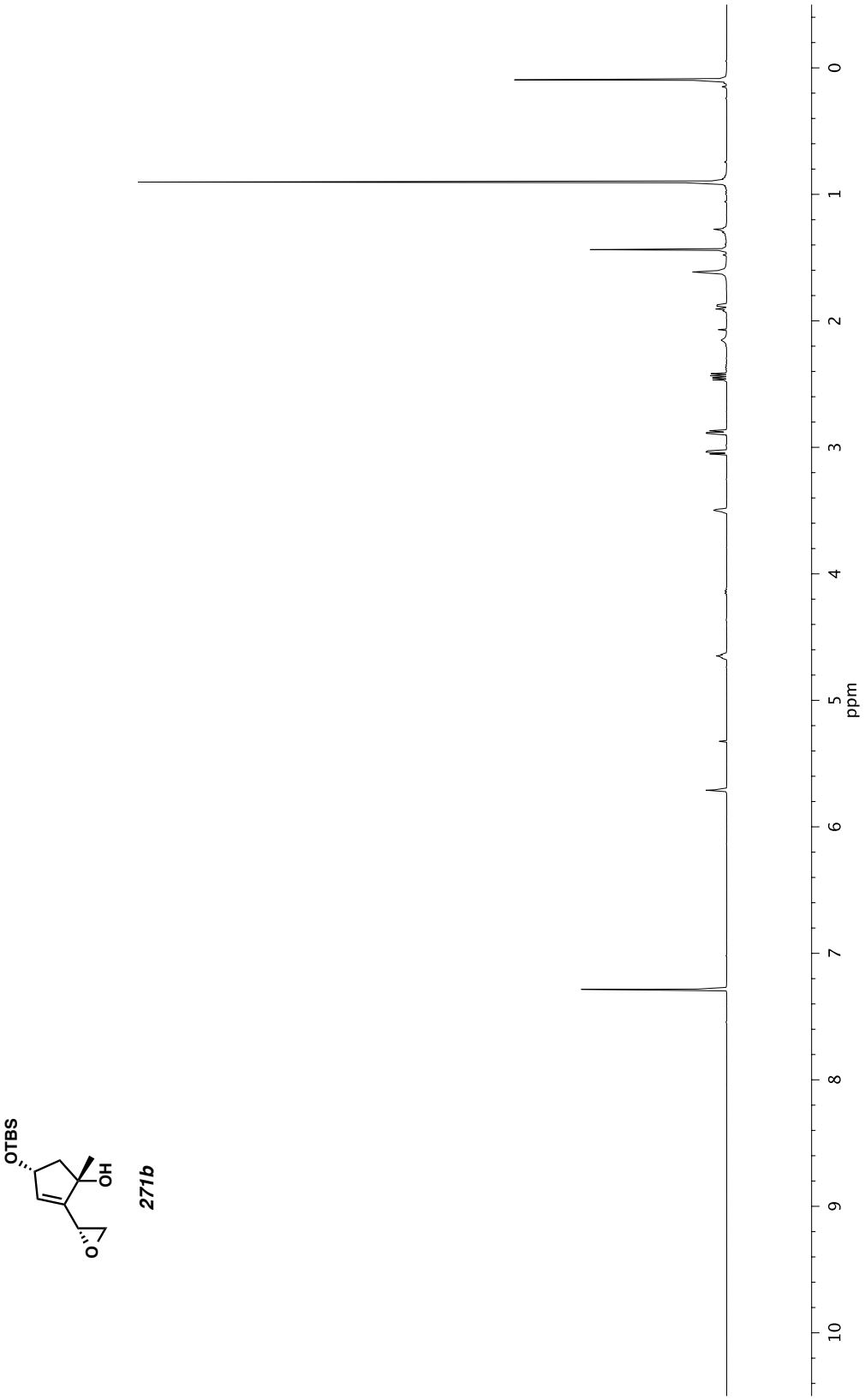


Figure A13.37. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **271b**.

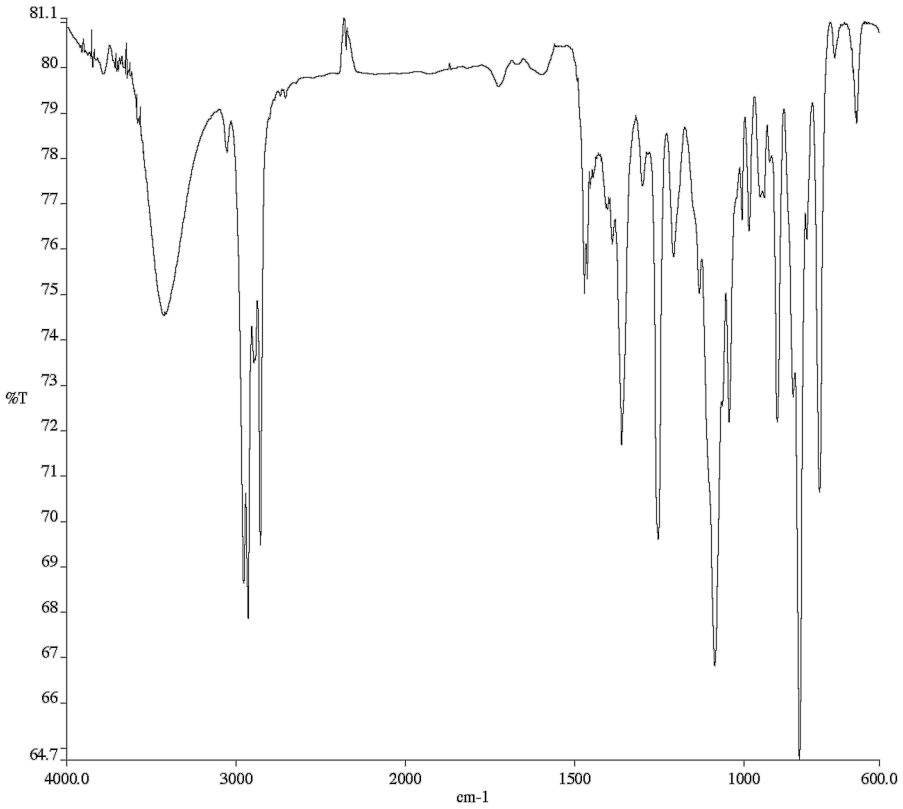


Figure A13.38. Infrared spectrum (Thin Film, NaCl) of compound **271b**.

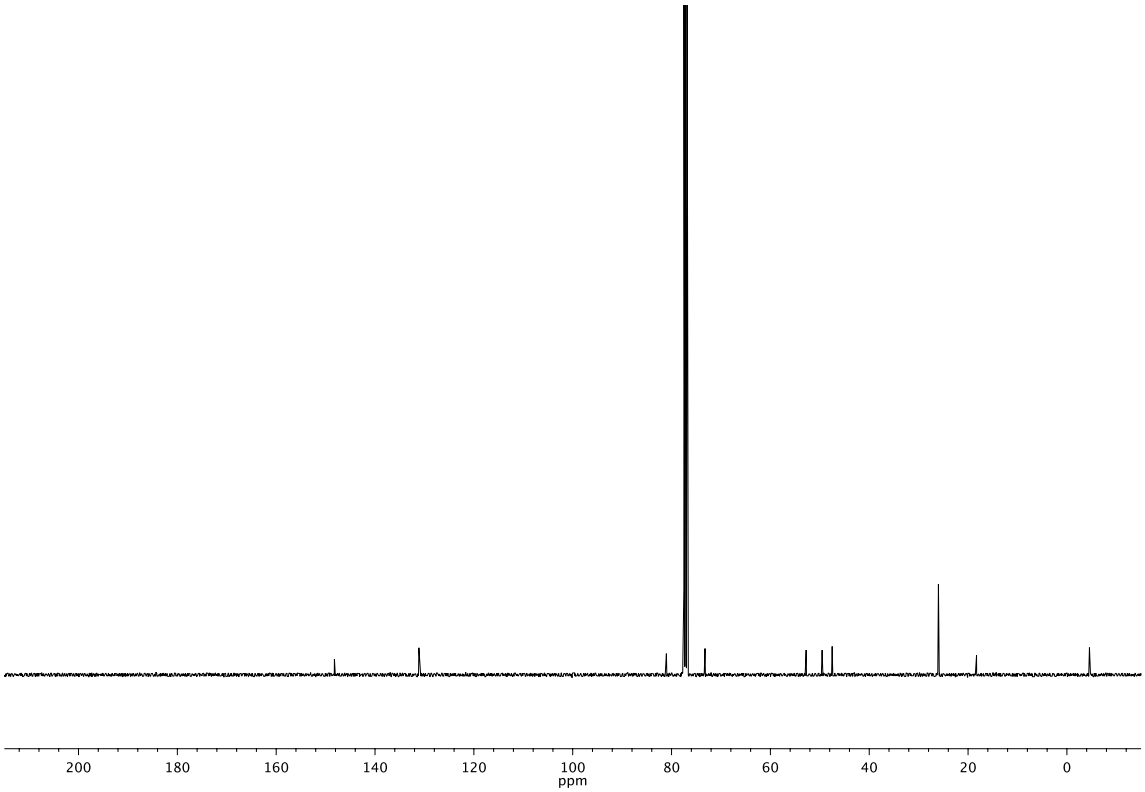


Figure A13.39. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **271b**.

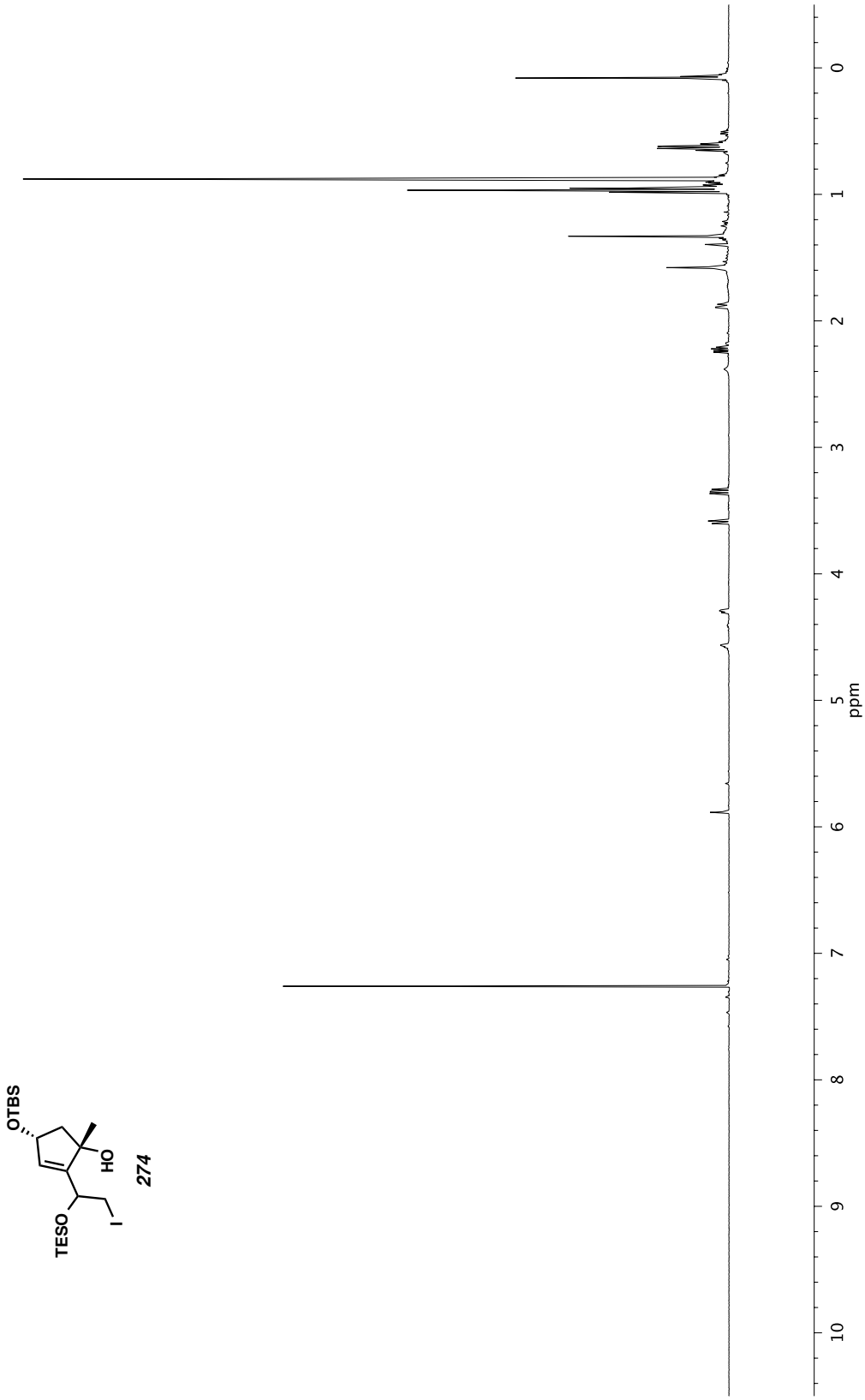


Figure A13.40. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **274**.

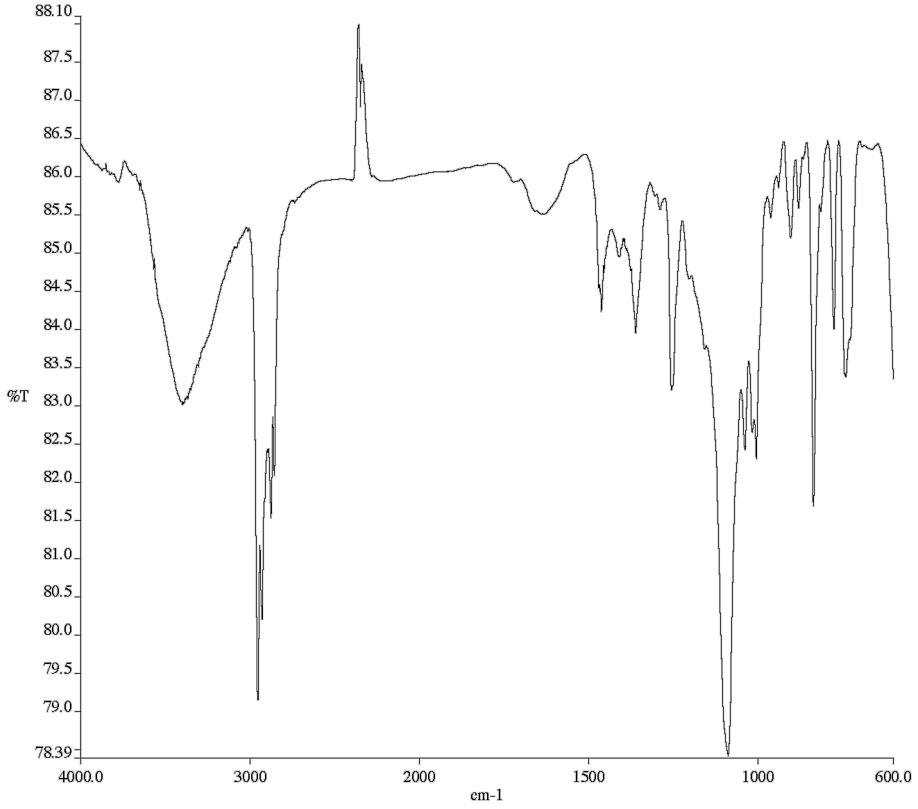


Figure A13.41. Infrared spectrum (Thin Film, NaCl) of compound **274**.

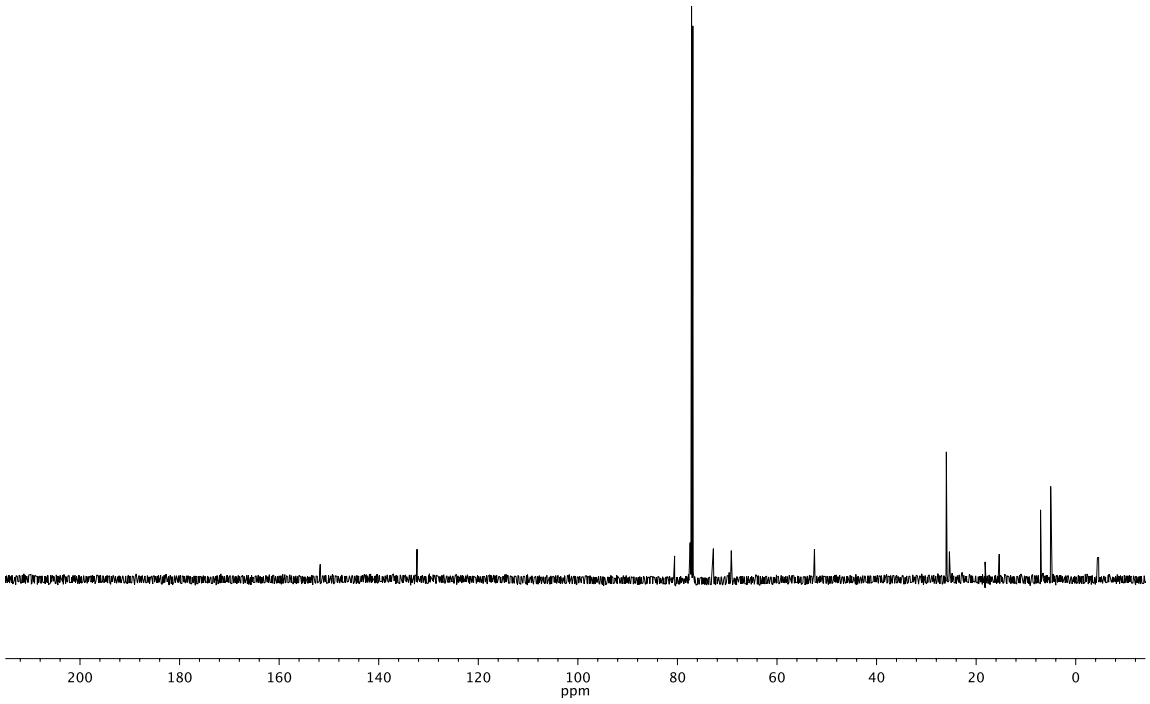


Figure A13.42. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **274**.

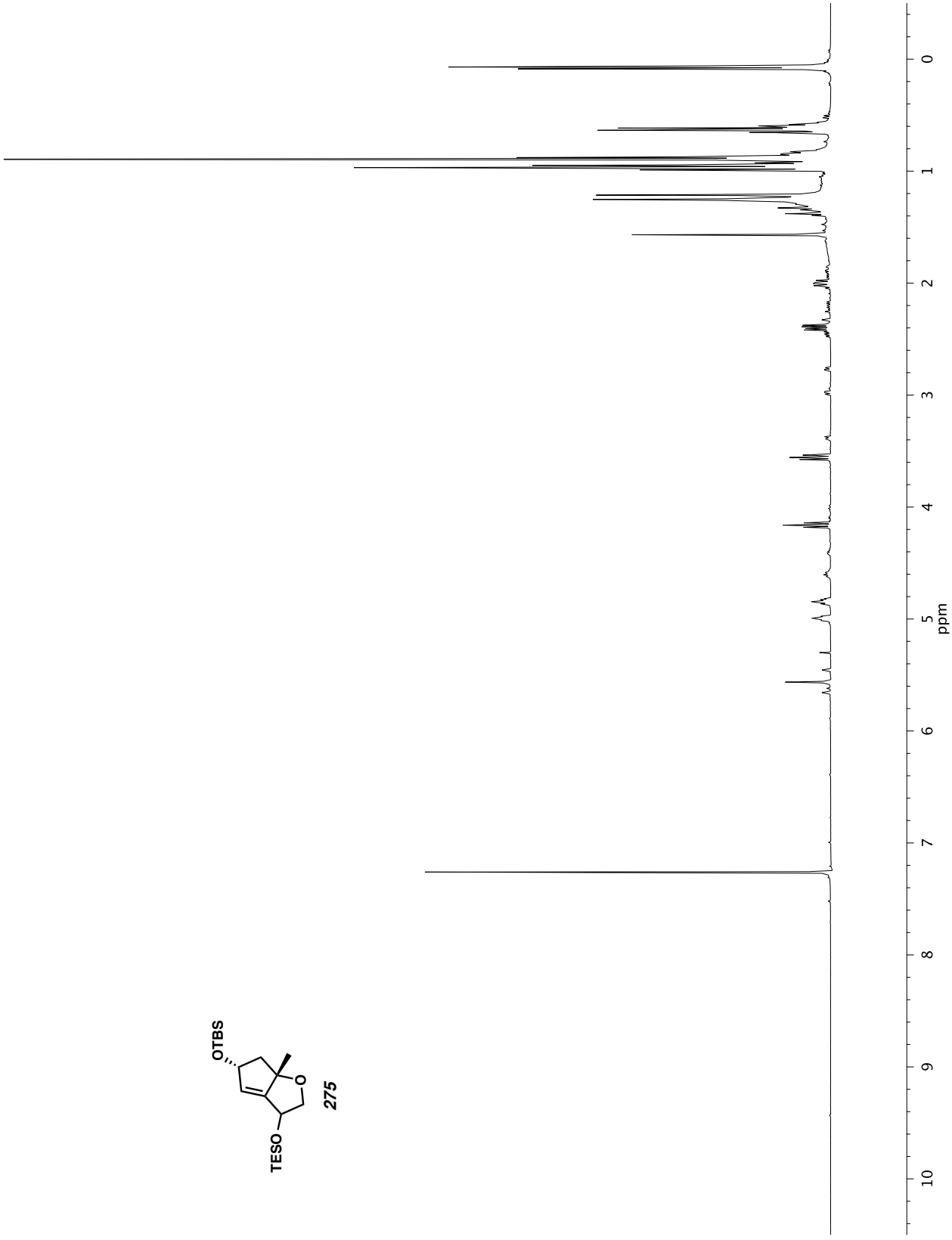


Figure A13.43. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **275**.

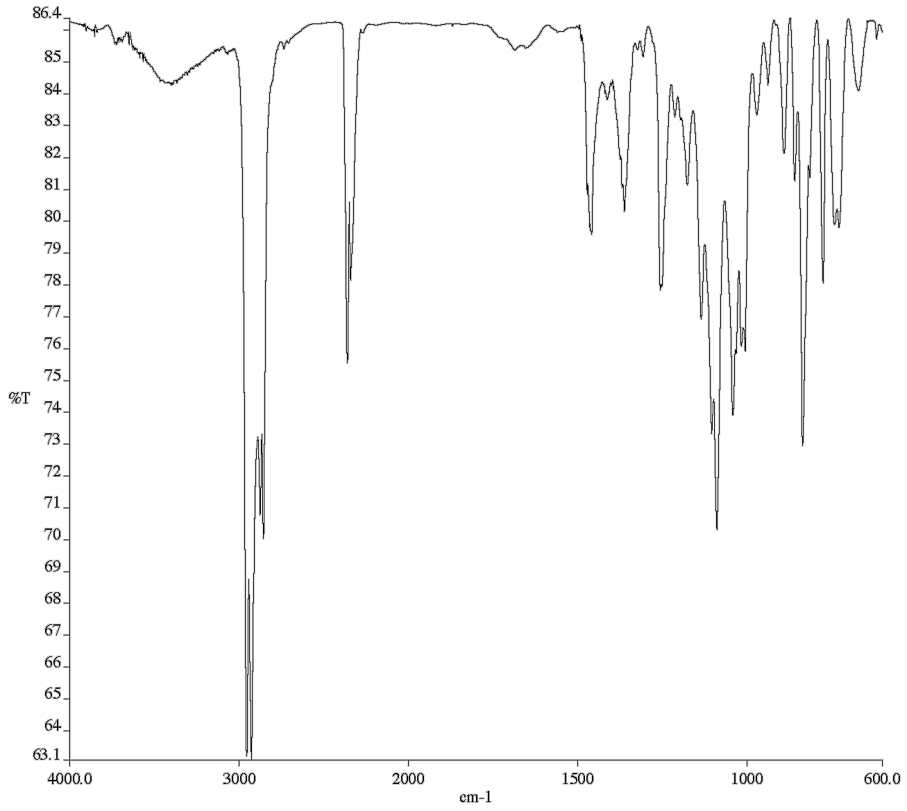


Figure A13.44. Infrared spectrum (Thin Film, NaCl) of compound **275.**

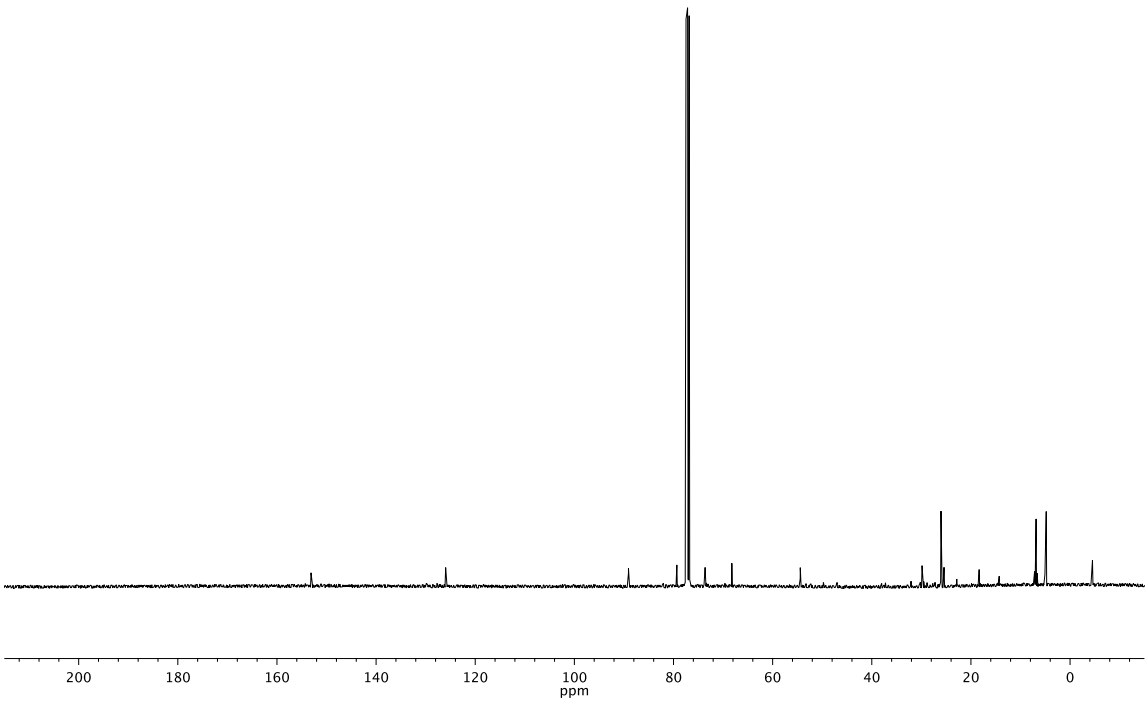


Figure A13.45. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **275**.

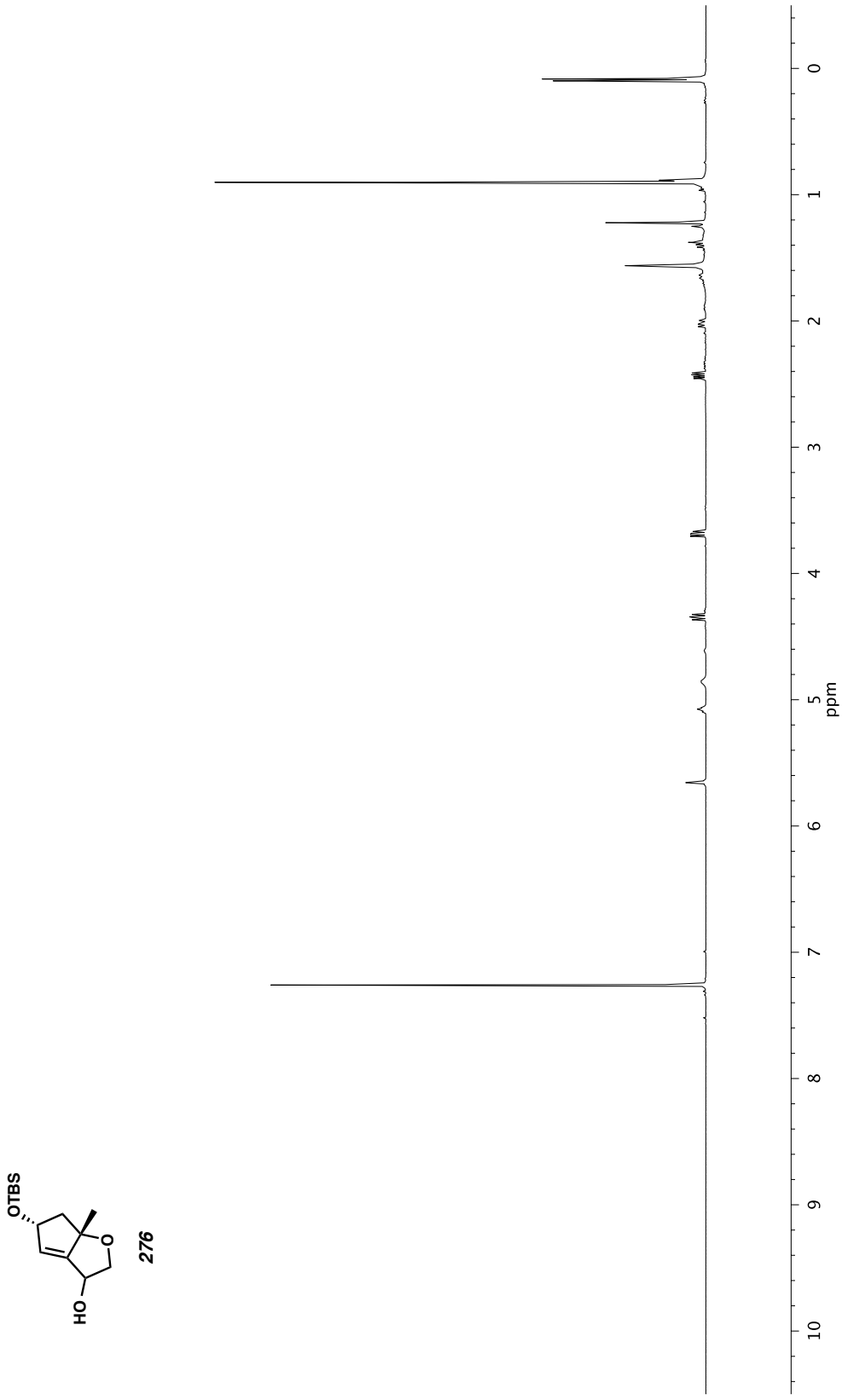


Figure A13.46. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **276**.

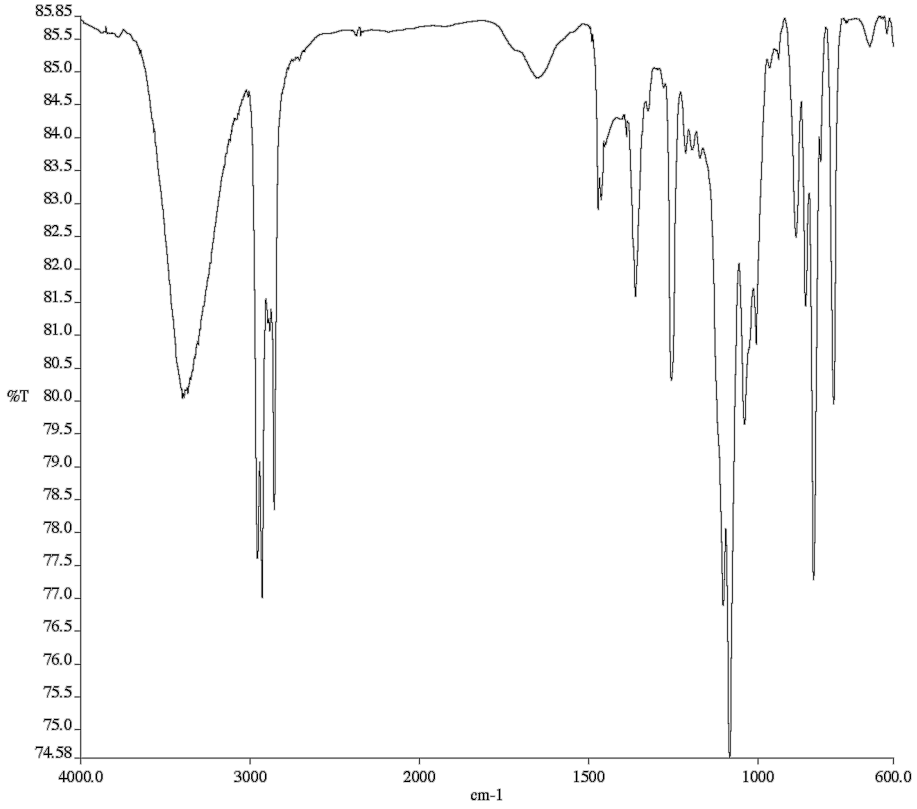


Figure A13.47. Infrared spectrum (Thin Film, NaCl) of compound **276**.

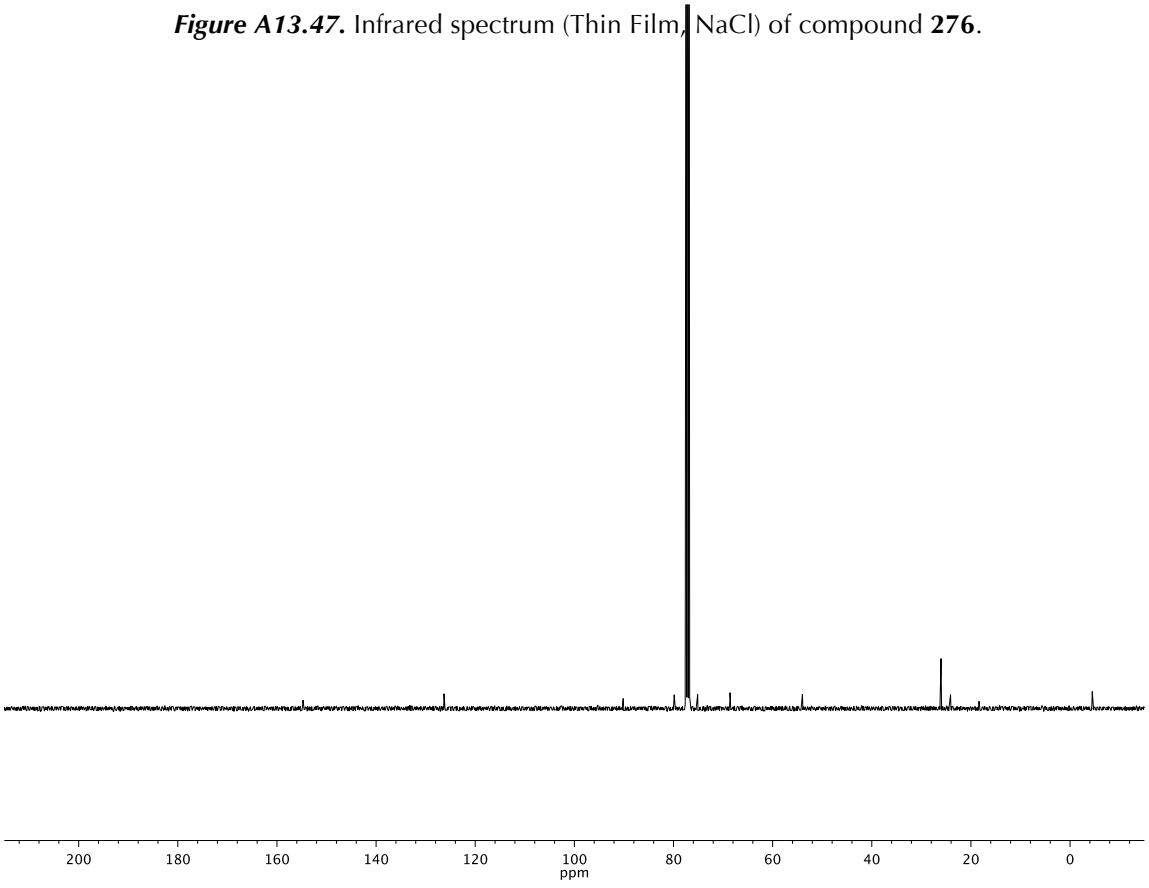


Figure A13.48. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **276**.

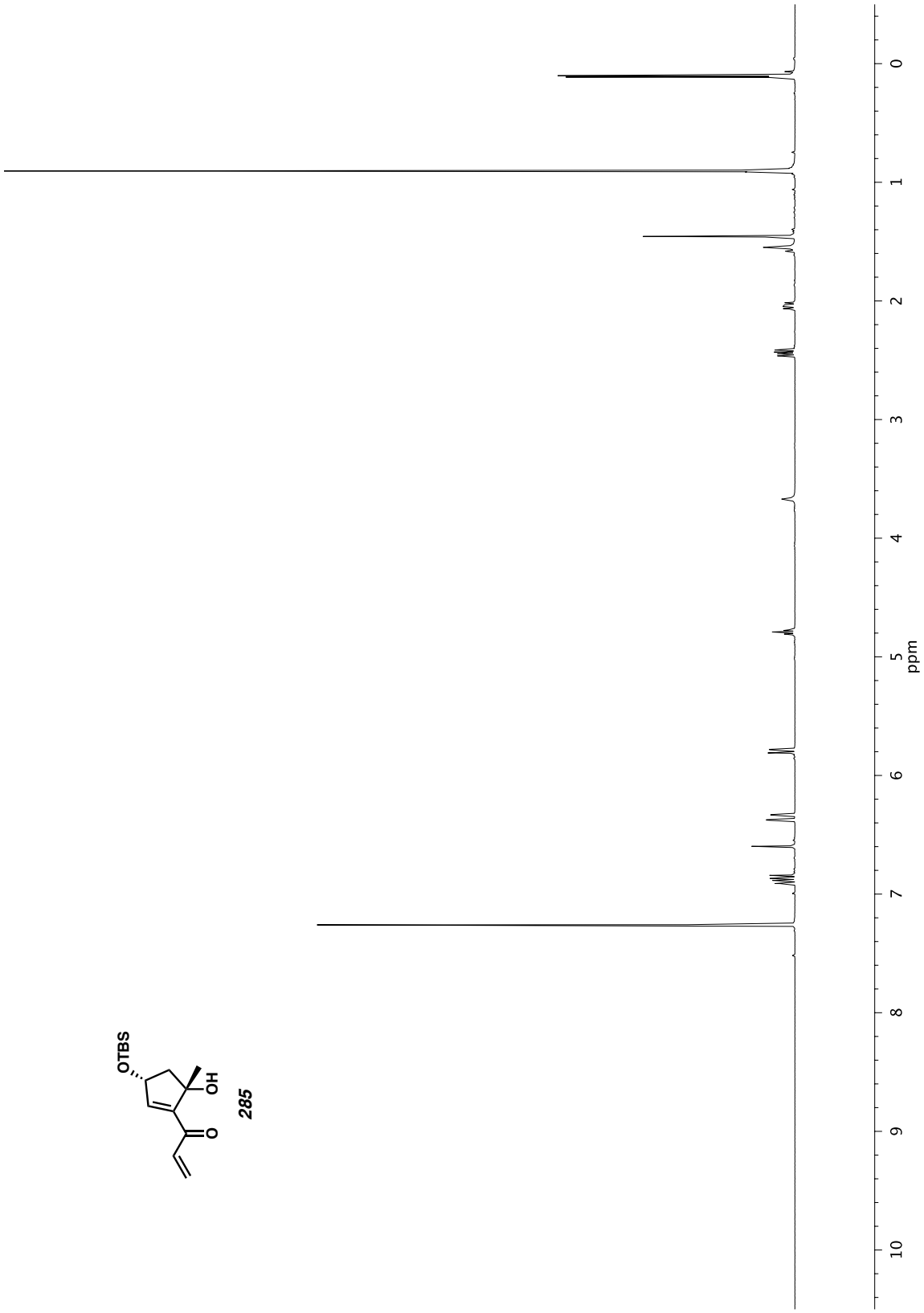


Figure A13.49. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **285**.

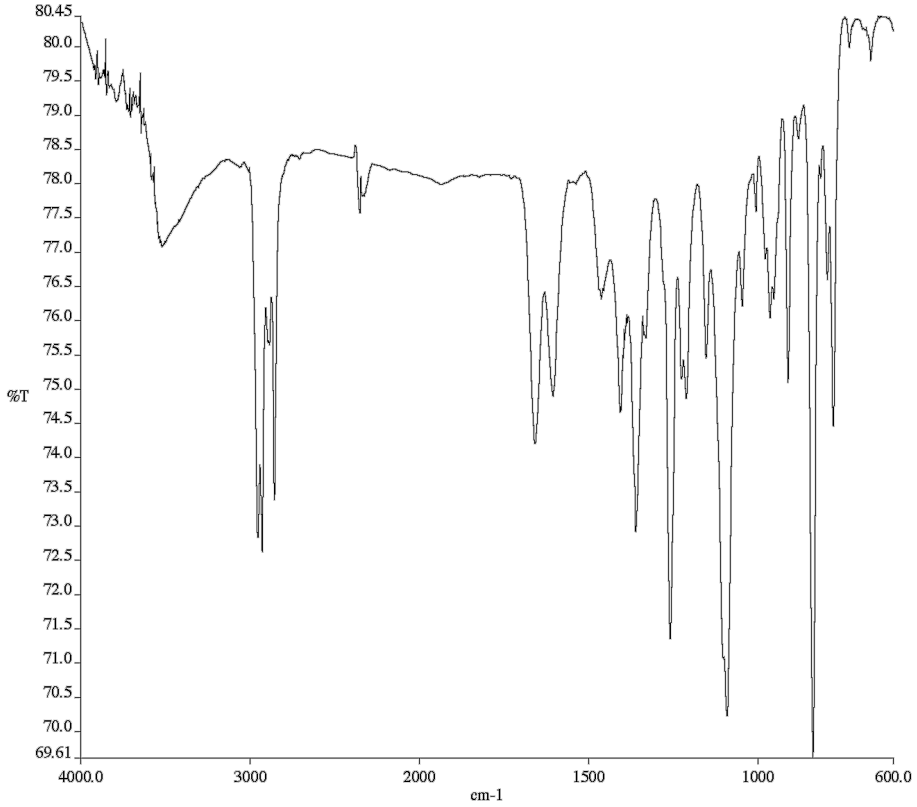


Figure A13.50. Infrared spectrum (Thin Film, NaCl) of compound **285**.

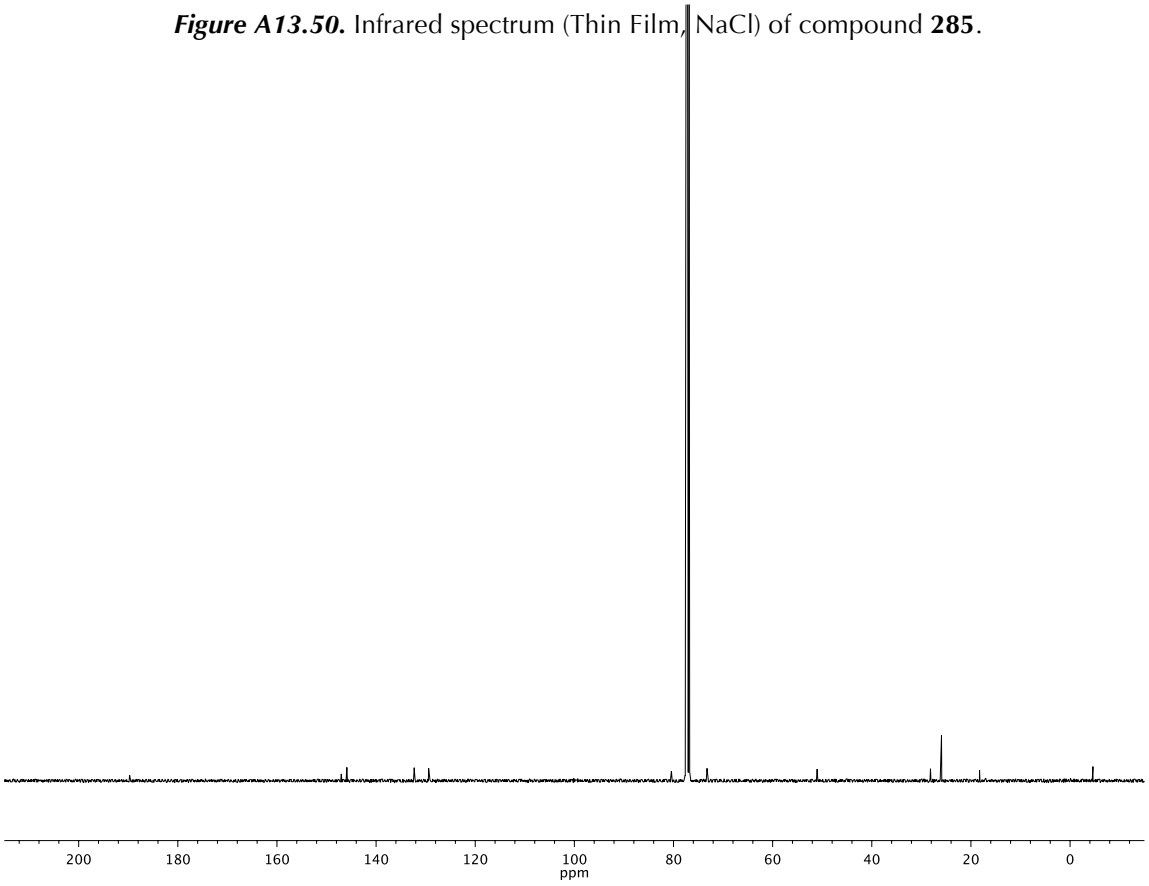


Figure A13.51. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **285**.

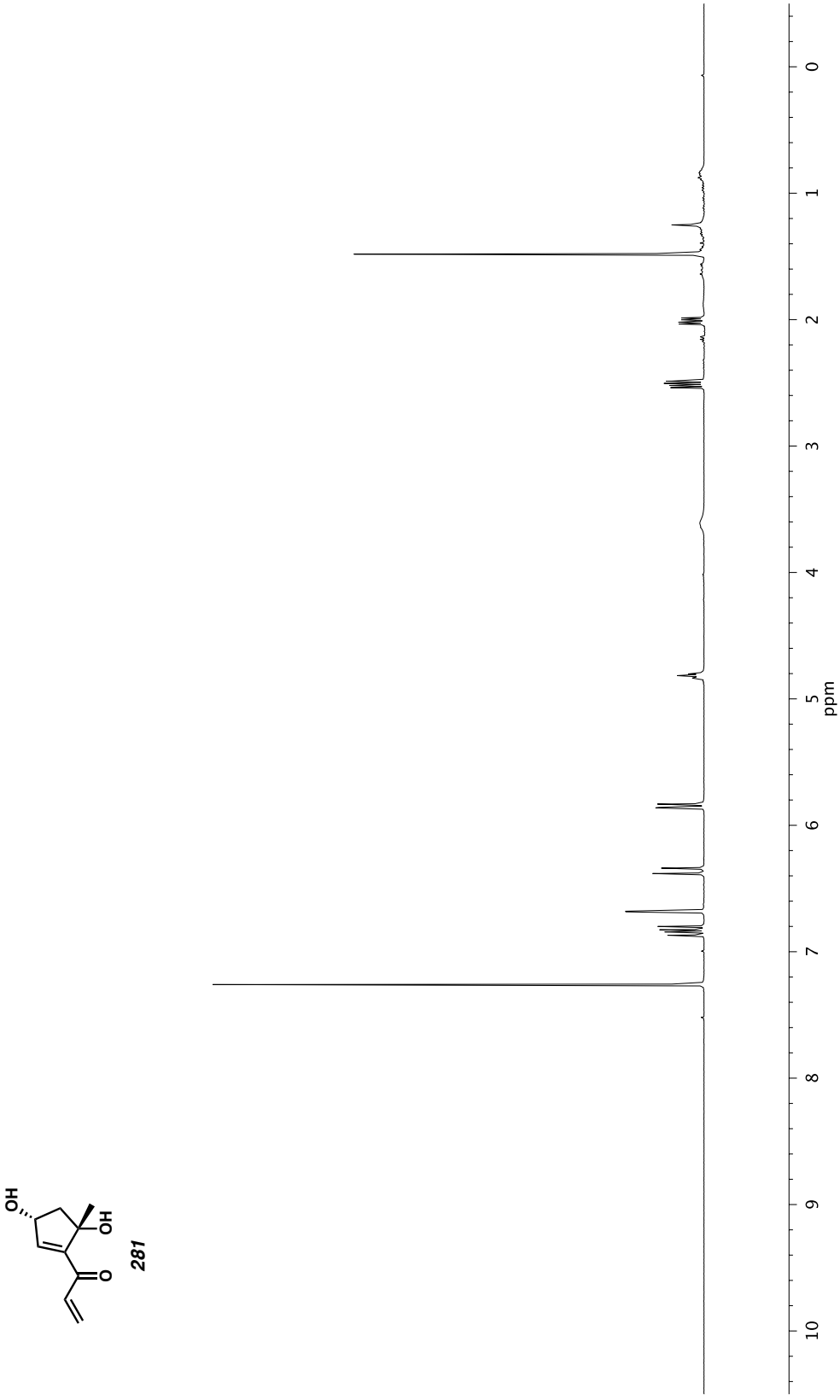


Figure A13.52. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **281**.

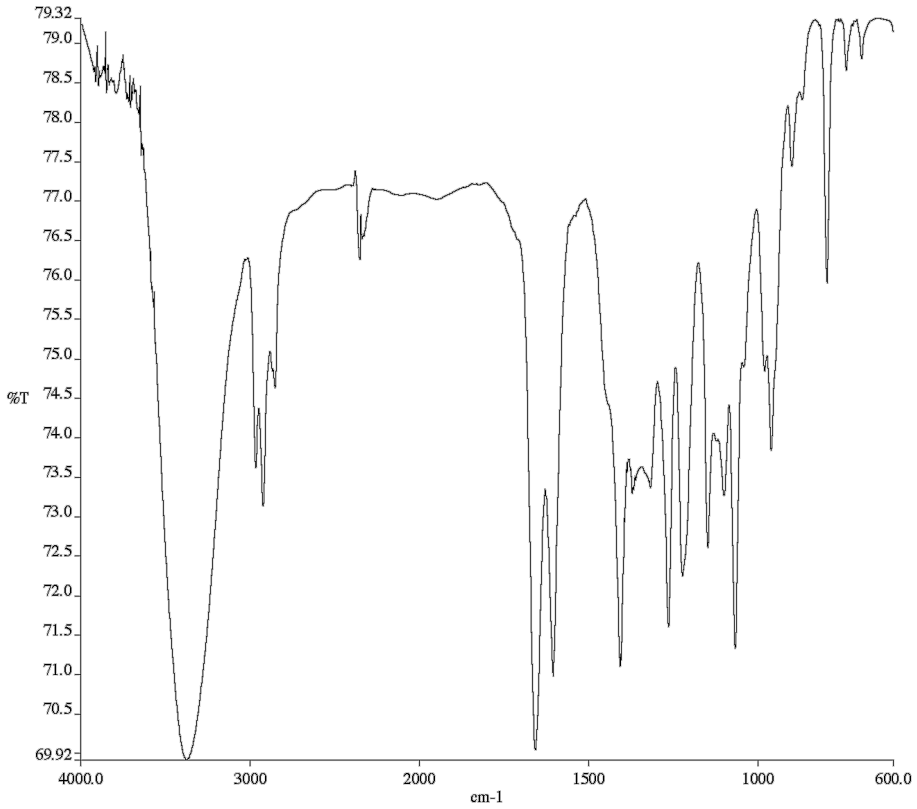


Figure A13.53. Infrared spectrum (Thin Film, NaCl) of compound **281**.

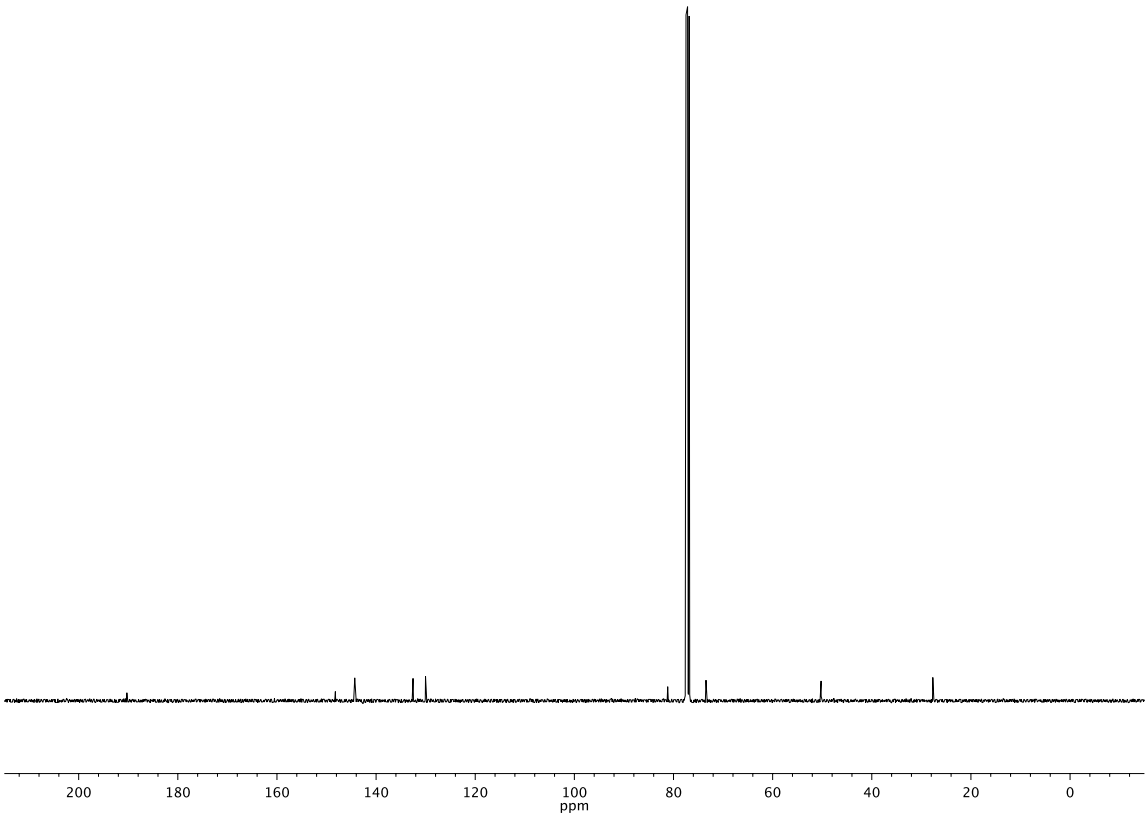


Figure A13.54. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **281**.

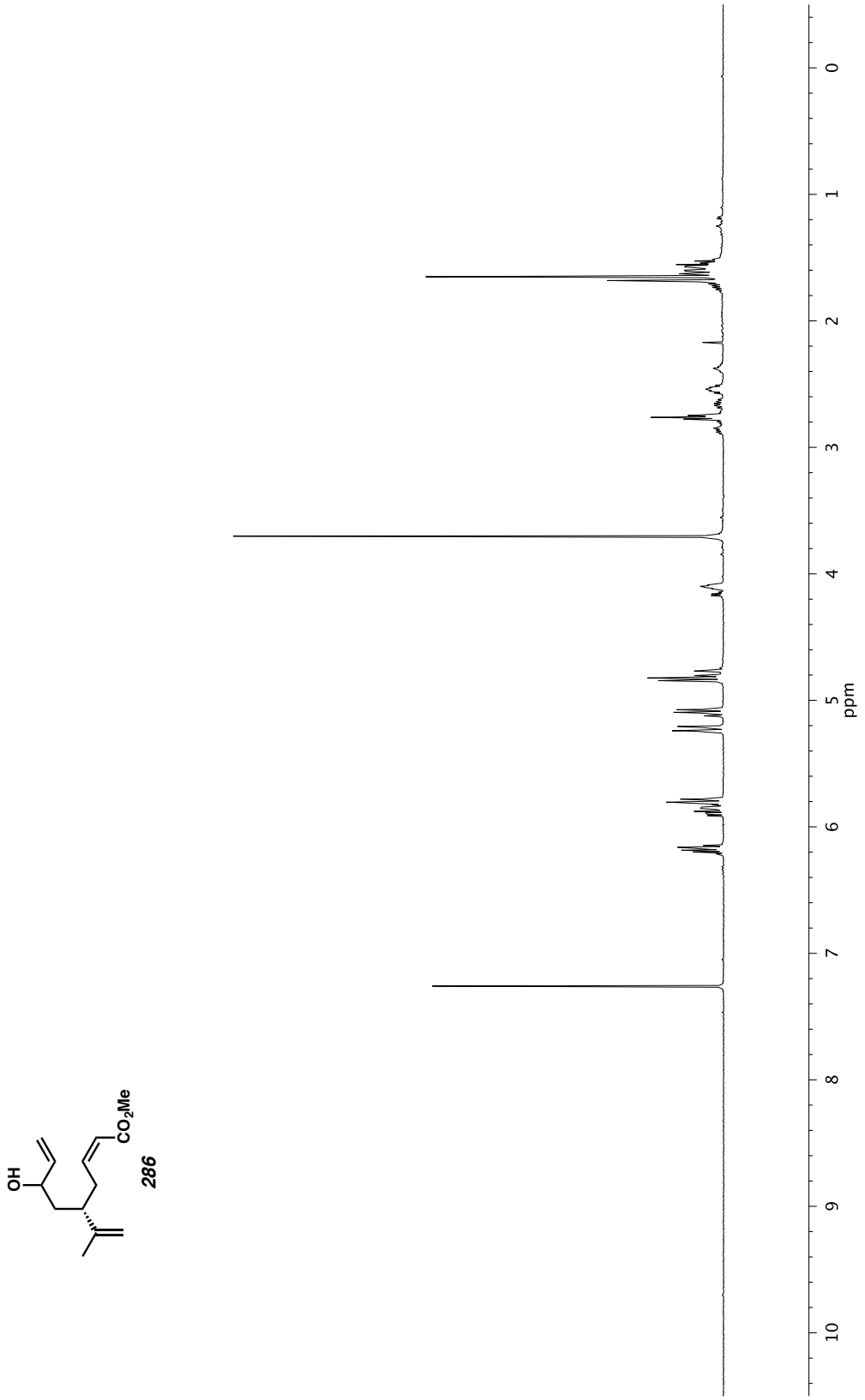


Figure A13.55. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **286**.

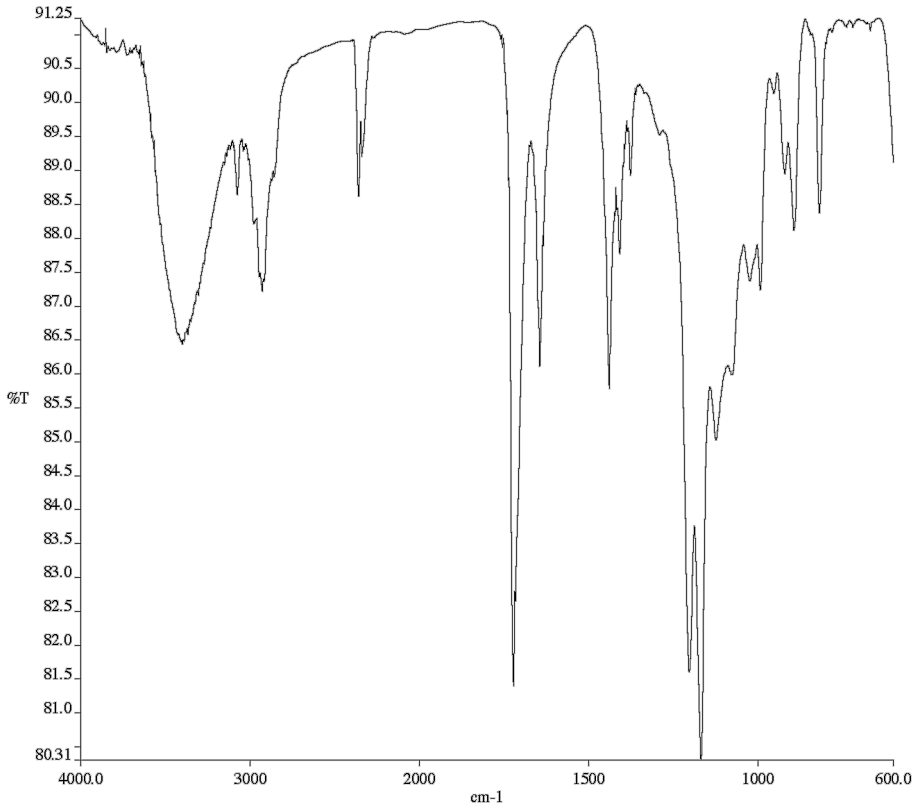


Figure A13.56. Infrared spectrum (Thin Film, NaCl) of compound **286**.

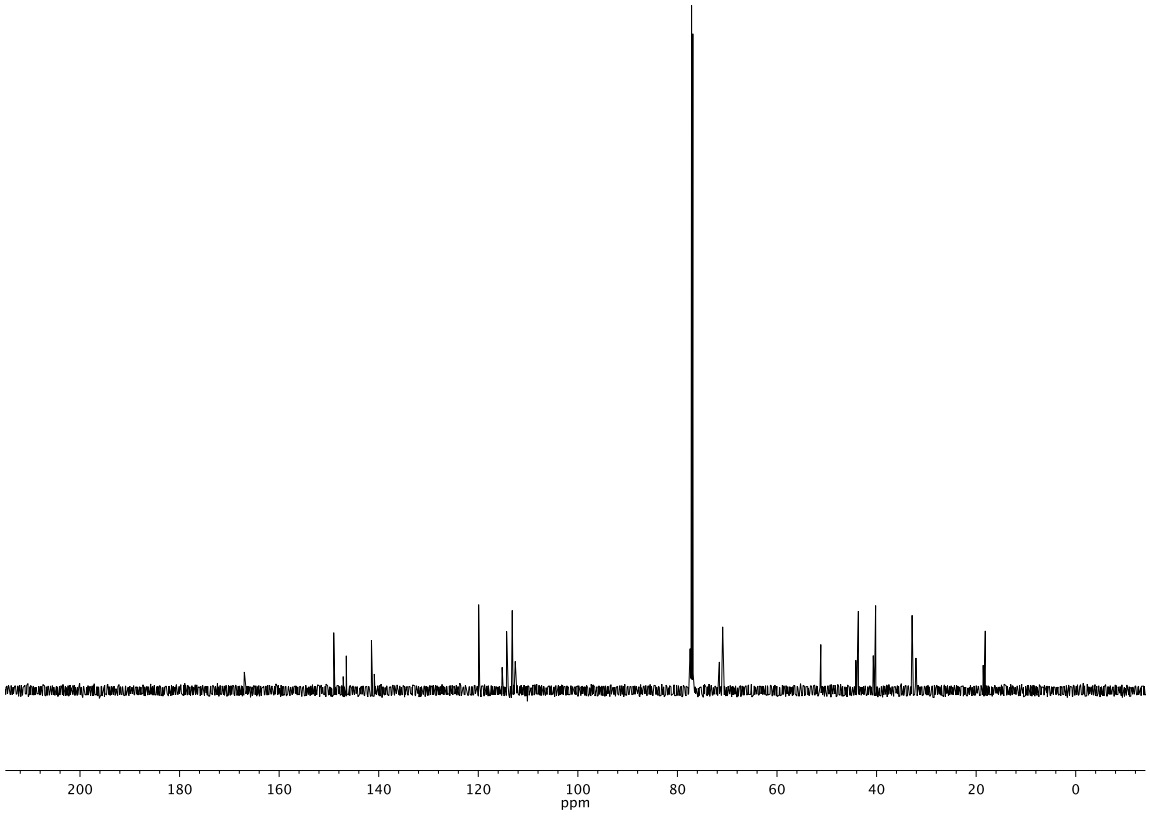


Figure A13.57. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **286**.

Figure A13.58. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **287**.

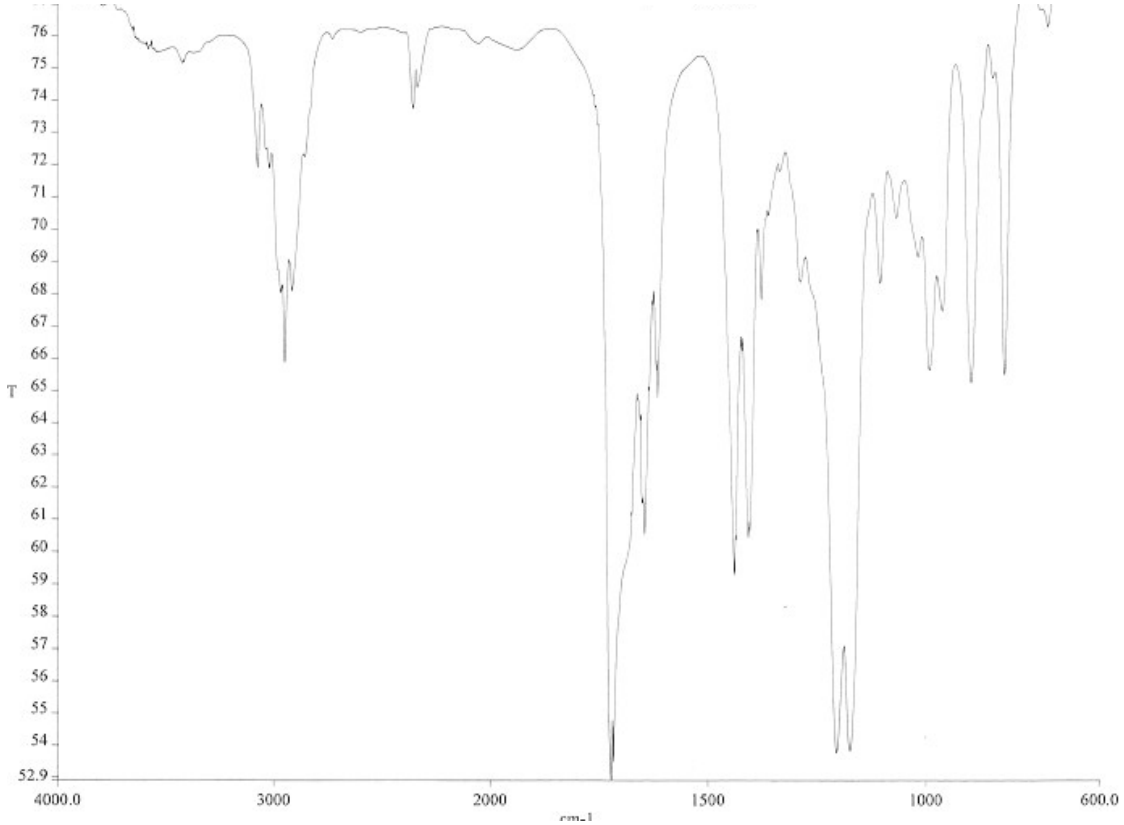


Figure A13.59. Infrared spectrum (Thin Film, NaCl) of compound **287**.

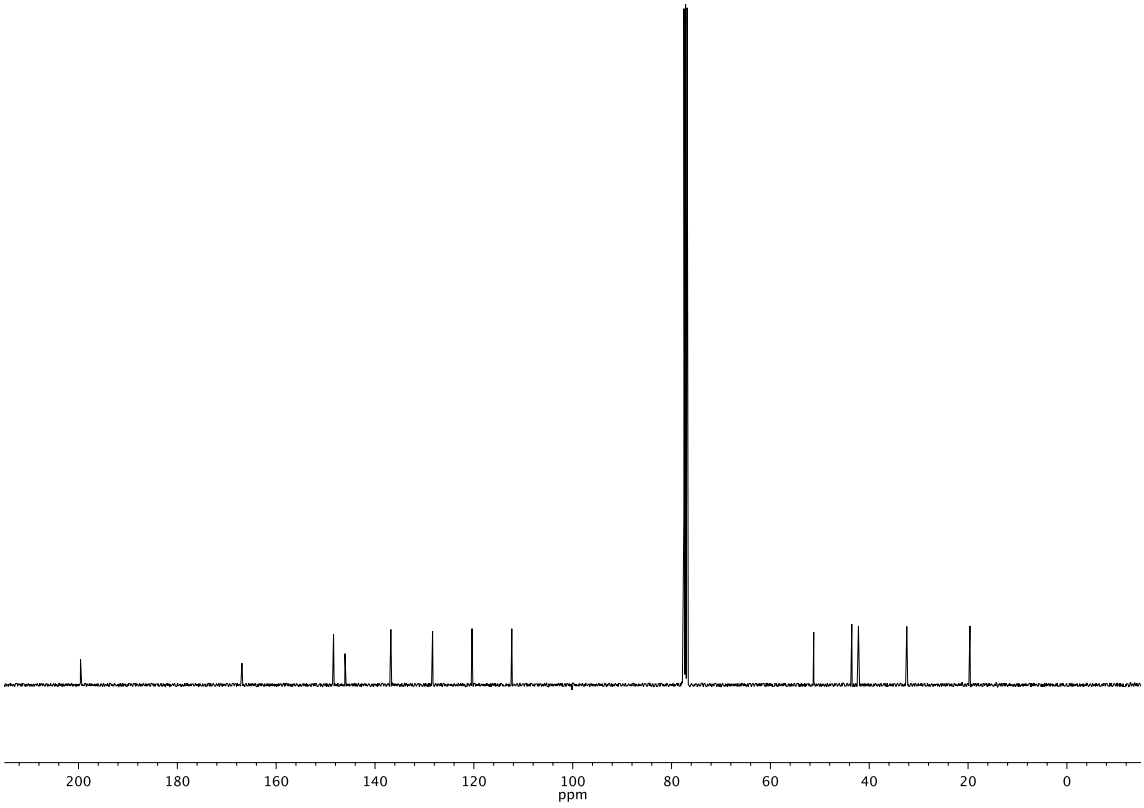


Figure A13.60. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **287**.

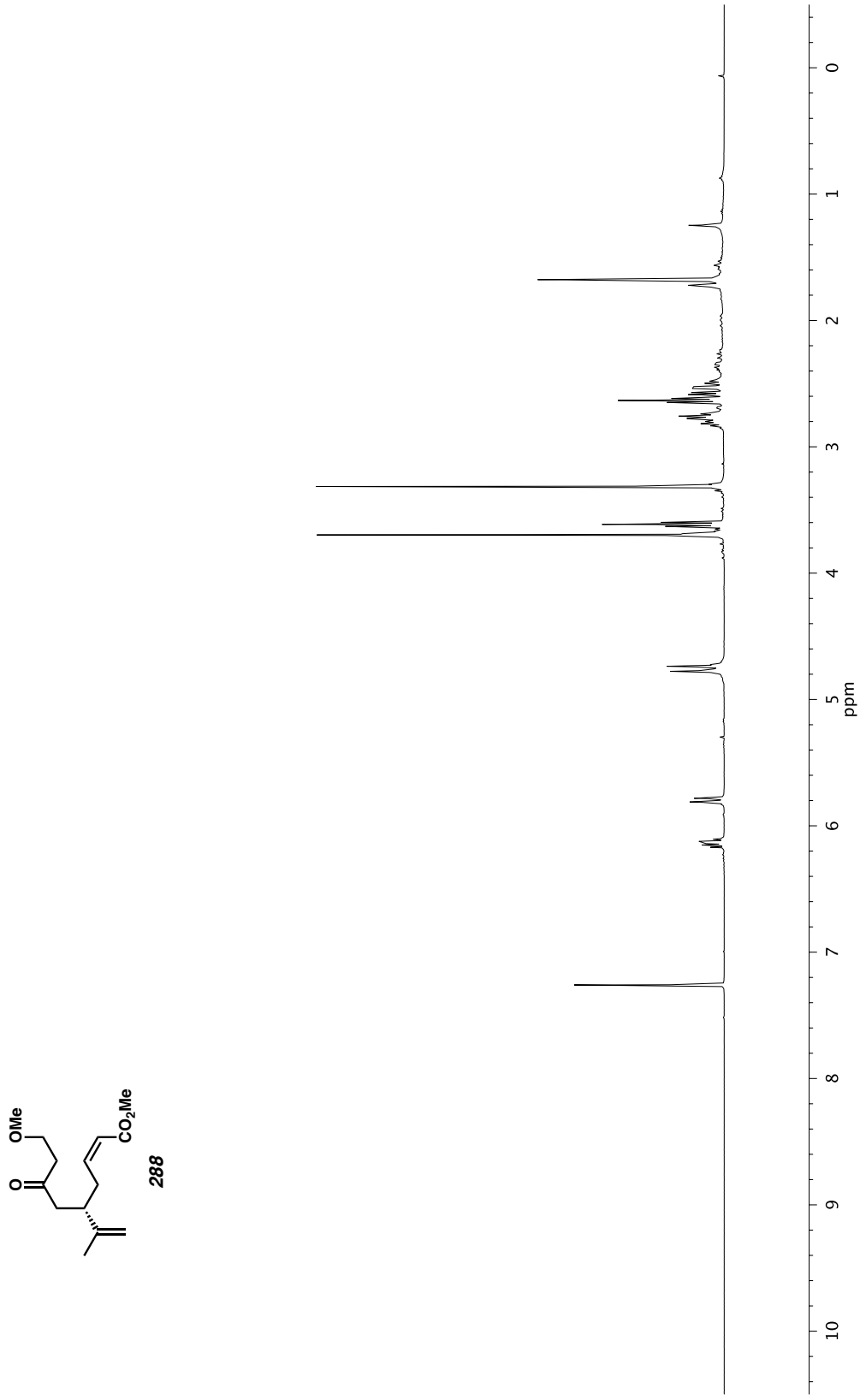


Figure A13.61. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **288**.

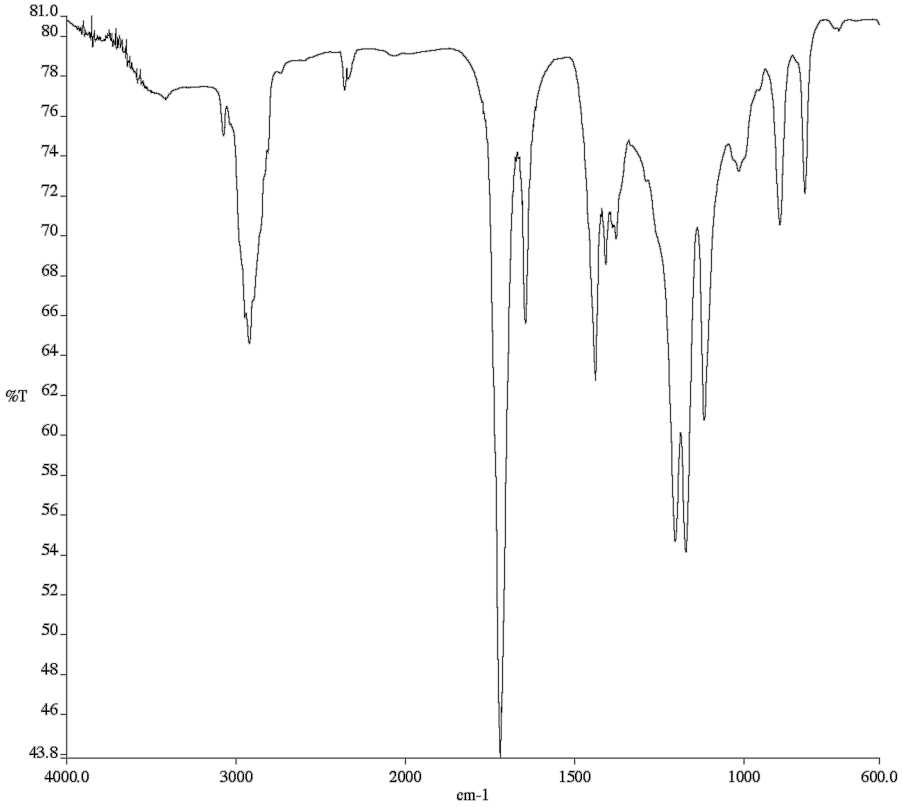


Figure A13.62. Infrared spectrum (Thin Film, NaCl) of compound **288**.

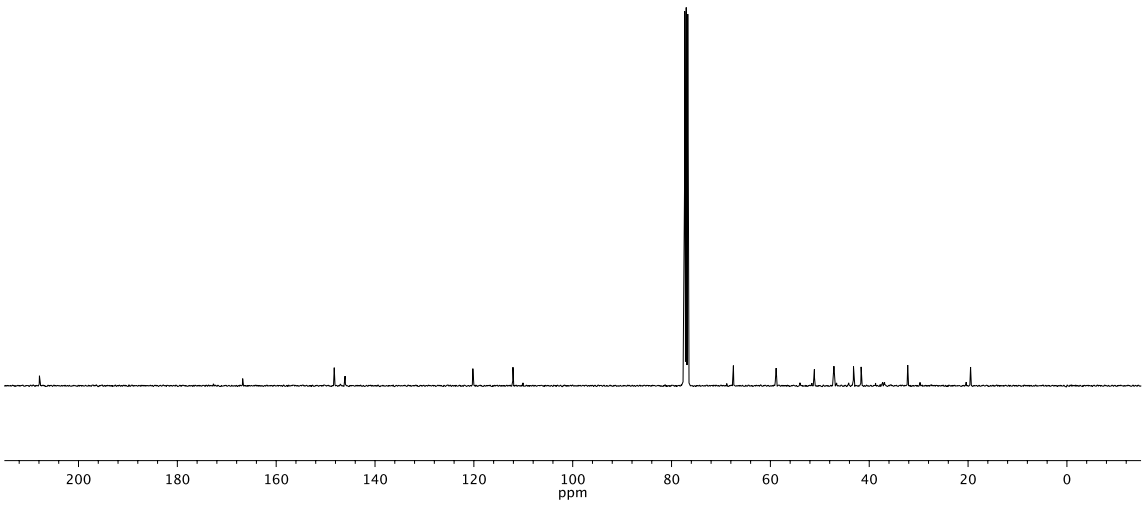


Figure A13.63. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **288**.

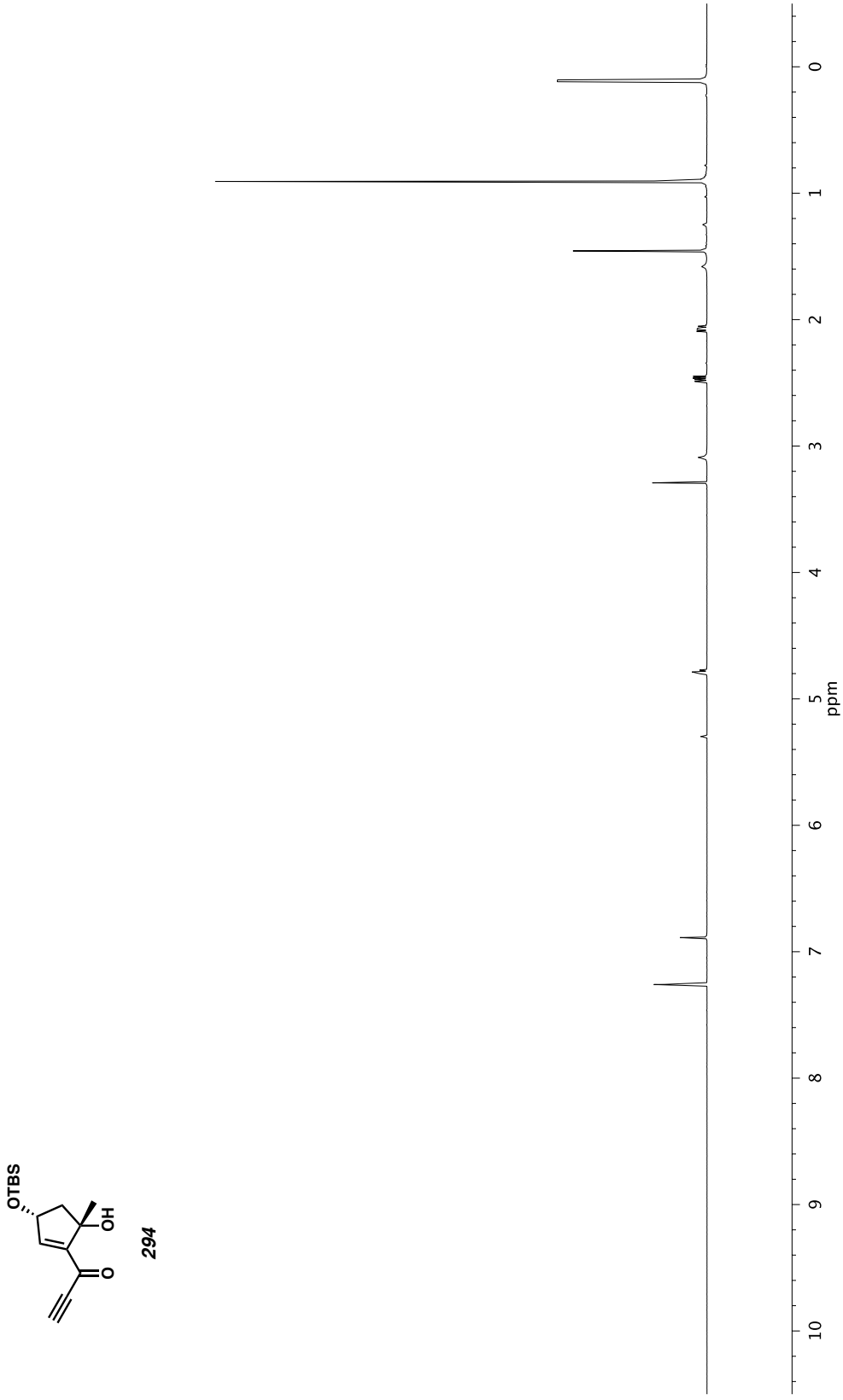


Figure A13.64. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **294**.

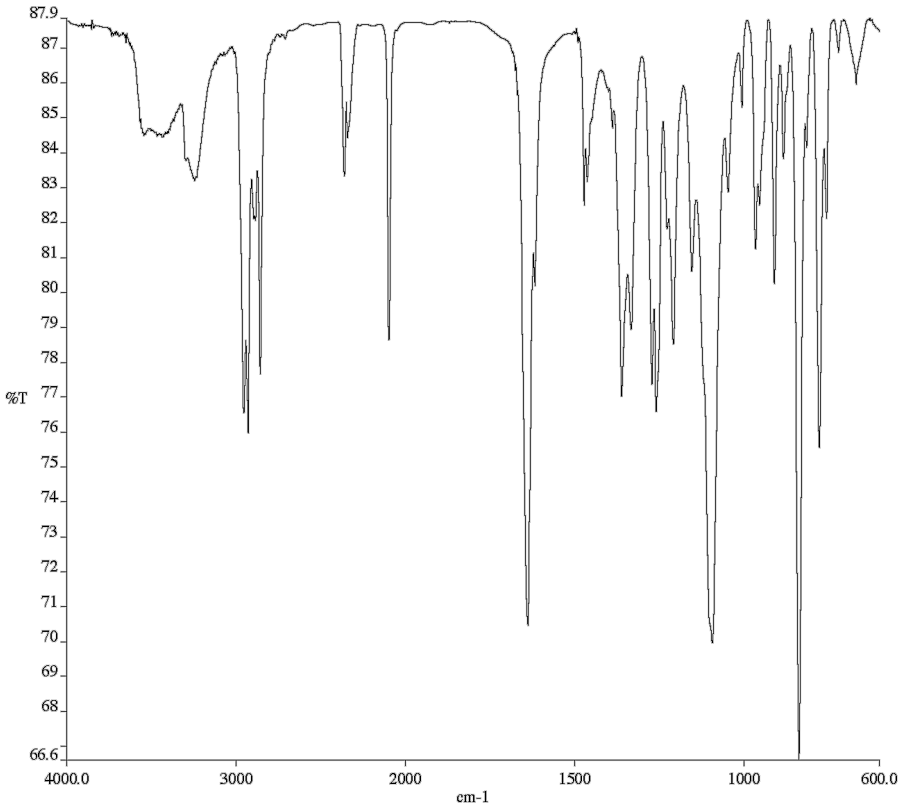


Figure A13.65. Infrared spectrum (Thin Film, NaCl) of compound **294**.

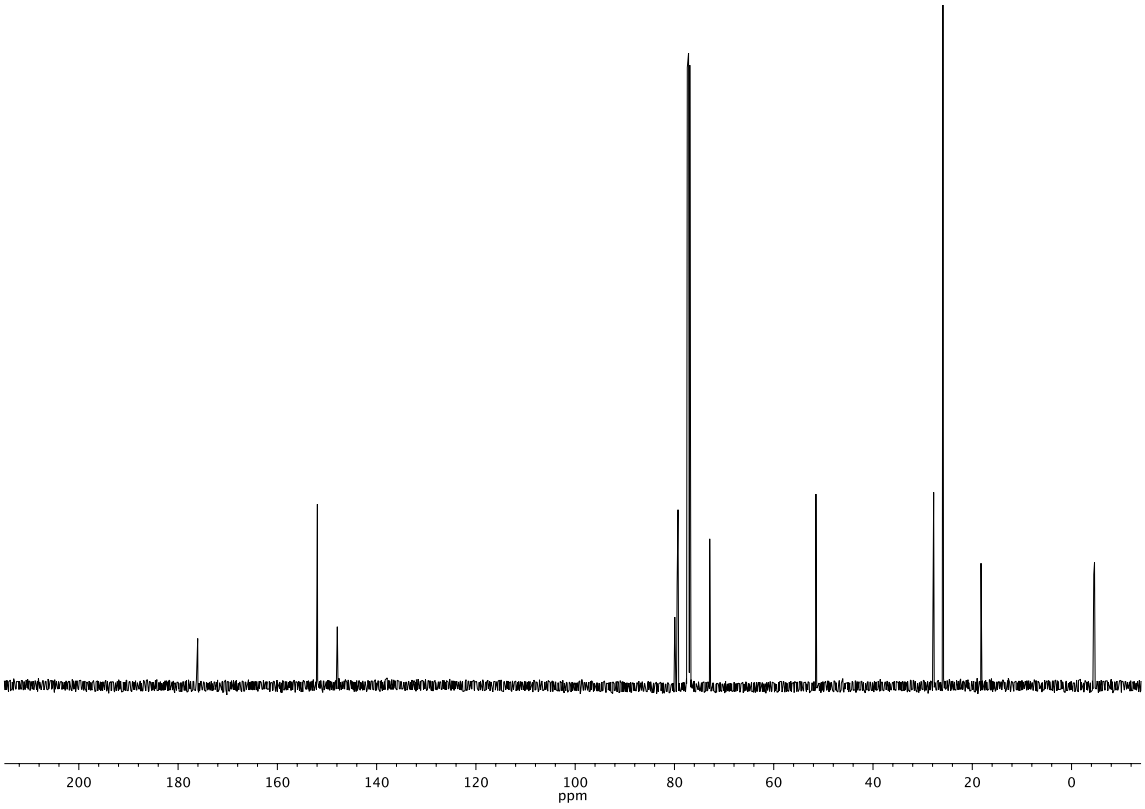


Figure A13.66. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **294**.