

Ring Contraction Strategy for the Practical, Scalable, Catalytic Asymmetric Synthesis of Versatile γ -Quaternary Acylcyclopentenones

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Supporting Information (Experimental Procedures)

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Materials and Methods. Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Reaction progress was monitored by thin-layer chromatography (TLC). THF was distilled over sodium/fluorenone or dried by passage through an activated alumina column under argon prior to use. *p*-Dioxane was distilled over sodium or dried by passage through an activated alumina column under argon prior to use. Methanol was distilled over Mg(OMe)₂ prior to use. Other solvents were dried by passage through an activated alumina column under argon. Diisopropylamine and triethylamine were distilled over CaH₂ prior to use. Iodomethane, iodoethane, acrylonitrile, and acrolein were distilled prior to use. Purified water was obtained using a Barnstead NANOpure Infinity UV/UF system. Brine solutions are saturated aqueous solutions of sodium chloride. MePh₃PBr from Sigma-Aldrich was stored in a glove box prior to use. NaH (60% wt. dispersion in mineral oil) from Sigma-Aldrich was purified by trituration with hexanes under a N₂ atmosphere and removal of residual solvent under vacuum. LiOCH₂CF₃ was prepared according to the method of Shreeve.^[1] Allyl cyanofornate was prepared according to the method of Mander or Rattigan.^[2] Gramine methiodide was prepared according to the method of Armen.^[3] The procedure of Maruyama and Naruta was used to prepare 1-chloro-2,4-pentadiene (92:8 *E:Z*).^[4] Phosphinooxazoline (PHOX) ligands were prepared by methods described in our previous work.^[5] Tris(4,4'-methoxydibenzylideneacetone)dipalladium(0) (Pd₂(pmdba)₃) was prepared according to the method of Ibers^[6] or Fairlamb.^[7] Herrmann's catalyst was prepared according to a literature procedure.^[8] All other reagents were purchased from Sigma-Aldrich, Acros Organics, Strem, or Alfa Aesar and used as received unless otherwise stated. Reaction temperatures were controlled by an IKAmag temperature modulator. Microwave-assisted reactions were performed in a Biotage Initiator 2.5 microwave reactor. Glove box manipulations were performed under a N₂ atmosphere. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, *p*-anisaldehyde, or KMnO₄ staining. ICN silica gel (particle size 0.032–0.0653 mm) was used for flash column chromatography. Automated flash column chromatography was performed on a Teledyne Isco CombiFlash R_f system. ¹H NMR spectra were recorded on a Varian Mercury 300 MHz, a Varian 400 MR 400 MHz, or a Varian Inova 500 MHz spectrometer and are reported relative to residual CHCl₃ (δ 7.26 ppm). ¹³C NMR spectra are recorded on a Varian Mercury 300 MHz, a Varian 400 MR 400 MHz, or a Varian Inova 500 MHz spectrometer (at 75 MHz, 100 MHz, and 125 MHz respectively) and are reported relative to CDCl₃ (δ 77.16 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, app = apparent. Data for ¹³C are reported in terms of chemical shifts (δ ppm). IR spectra were obtained using a Perkin Elmer Paragon 1000 or Perkin Elmer Spectrum BXII spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm⁻¹). Optical rotations were measured with a Jasco P-1010 or Jasco P-2000 polarimeter operating on the sodium D-line (589 nm) using a 100 mm path-length cell and are reported as: [α]_D^T (concentration in g/100 mL, solvent, ee). Melting points were measured using a Thomas-Hoover capillary melting point apparatus and the reported values are uncorrected. Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC utilizing a Chiralcel AD or OD-H columns (4.6 mm x 25 cm) obtained from Daicel Chemical Industries Ltd. with visualization at 254 nm. Analytical chiral SFC was performed with a Mettler Toledo SFC supercritical CO₂ analytical chromatography system with a Chiralcel AD-H column (4.6 mm x 25 cm) with visualization at 254 nm/210 nm. Analytical chiral GC was performed with an Agilent 6850 GC utilizing a G-TA (30 m x 0.25 mm) column (1.0 mL/min carrier gas flow). High-resolution mass

spectra (HRMS) were obtained from the Caltech Mass Spectral Facility (EI+ or FAB+) or on a Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed (MM: ESI-APCI+) ionization mode.

List of Abbreviations. The following abbreviations are used in experimental procedures:

CDI = 1,1'-carbonyldiimidazole

DDQ = 2,3-dichloro-5,6-dicyano-*p*-benzoquinone

DMA = *N,N'*-dimethylacetamide

DMAD = dimethyl acetylenedicarboxylate

DMAP = 4-(dimethylamino)pyridine

DMF = *N,N'*-dimethylformamide

HFIP = 1,1,1,3,3,3-hexafluoro-2-propanol

i-Bu = isobutyl

IPA = isopropanol

LDA = lithium diisopropylamide

Pd₂(pmdba)₃ = tris(4,4'-methoxydibenzylideneacetone)dipalladium(0)

PHOX = phosphinooxazoline

PPTS = pyridinium *p*-toluenesulfonate

TBAA = tetrabutylammonium acetate

TBAF = tetrabutylammonium fluoride

TBAI = tetrabutylammonium iodide

TBDPS = *tert*-butyldiphenylsilyl

TBDPSCl = *tert*-butyl(chloro)diphenylsilane

TBSOTf = *tert*-butyldimethylsilyl trifluoromethanesulfonate

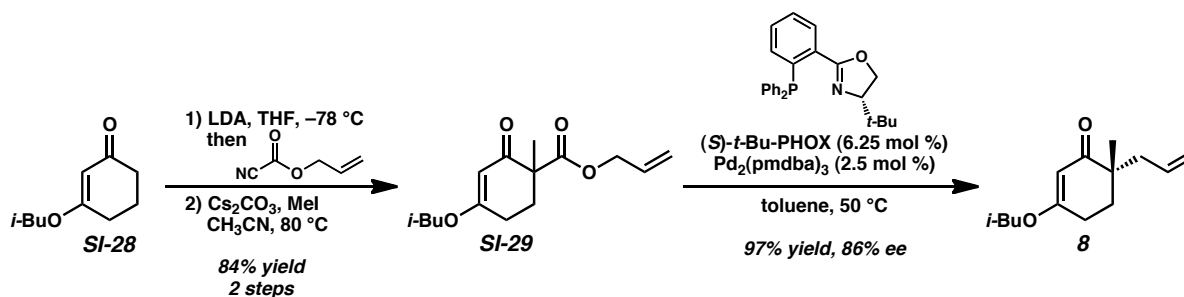
TFE = 2,2,2-trifluoroethanol

TMS = trimethylsilyl

TMSCl = chlorotrimethylsilane

μ waves = microwave irradiation

Procedure for the Synthesis of Cyclohexenone 9

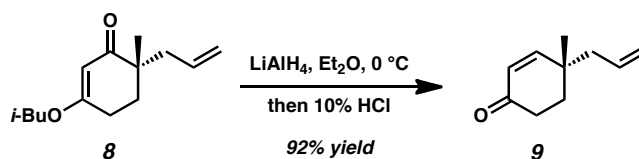


β -Ketoester SI-29. To a solution of diisopropylamine (0.49 mL, 3.47 mmol, 1.17 equiv) in THF (10 mL) in a 50 mL round-bottom flask at $0\text{ }^{\circ}\text{C}$ was added *n*-BuLi (1.70 mL, 3.40 mmol, 2.1 M in hexanes, 1.15 equiv) dropwise over 10 min. After 15 min of stirring at $0\text{ }^{\circ}\text{C}$, the reaction was cooled to $-78\text{ }^{\circ}\text{C}$ using an acetone/CO₂(s) bath. A solution of vinylogous ester **SI-28**^[9] (0.50 g, 2.97 mmol, 1.00 equiv) in THF (5.0 mL) was added dropwise using positive pressure cannulation. After an additional 1 h of stirring at $-78\text{ }^{\circ}\text{C}$, allyl cyanoformate (0.37 mL, 3.40 mmol, 1.15 equiv) was added dropwise. The reaction was stirred at $-78\text{ }^{\circ}\text{C}$ for 2.5 h, quenched by addition of sat aqueous NH₄Cl and H₂O (5 mL each), and then allowed to warm to ambient temperature. The reaction was diluted with Et₂O (25 mL) and the phases were separated. The aqueous phase was extracted with Et₂O (2 x 25 mL) and the combined organic phases were dried over MgSO₄, filtered, and concentrated under reduced pressure to afford a pale red oil.

The crude oil was added to a 25 mL Schlenk flask and dissolved in CH₃CN (10 mL). MeI (0.56 mL, 8.90 mmol, 3.00 equiv) was added, followed by Cs₂CO₃ (1.26 g, 3.90 mmol, 1.30 equiv). The flask was sealed with a Teflon valve, immersed in an oil bath, and heated to $80\text{ }^{\circ}\text{C}$. After 14 h of vigorous stirring, the suspension was allowed to cool to ambient temperature, diluted with EtOAc (25 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO₂, 3 x 20 cm, 19:1→9:1→4:1, Hexanes:EtOAc) to afford β -ketoester **SI-29** (0.67 g, 2.52 mmol, 84% yield over 2 steps) as a pale yellow oil; $R_f = 0.36$ (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 5.81 (dddd, $J = 17.2, 10.7, 5.5, 5.5\text{ Hz}$, 1H), 5.30 (s, 1H), 5.22 (app dq, $J = 17.2, 1.5\text{ Hz}$, 1H), 5.14 (app dq, $J = 10.5, 1.3\text{ Hz}$, 1H), 4.65–4.46 (m, 2H), 3.55 (d, $J = 6.5\text{ Hz}$, 2H), 2.60–2.23 (m, 3H), 1.97 (app sept, $J = 6.6\text{ Hz}$, 1H), 1.89–1.70 (m, 1H), 1.35 (s, 3H), 0.91 (d, $J = 6.7\text{ Hz}$, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 196.4, 176.7, 172.5, 131.9, 118.0, 101.7, 74.9, 65.5, 52.3, 31.7, 27.7, 26.3, 20.6, 19.0; IR (Neat Film NaCl) 2961, 2937, 2876, 1733, 1660, 1608, 1457, 1427, 1406, 1385, 1369, 1346, 1319, 1248, 1199, 1176, 1113, 1039, 991, 928, 837, 818, 772, 751 cm⁻¹; HRMS (EI+) m/z calc'd for C₁₅H₂₂O₄ [M]⁺: 266.1518; found 266.1510.

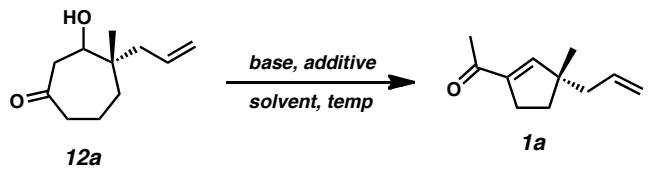
Vinylogous Ester 8. β -Ketoester **SI-29** (180 mg, 0.68 mmol, 1.00 equiv) in a 20 mL scintillation vial and a septum-fitted screw cap were evacuated/backfilled with N₂ (3 cycles, 5 min evacuation per cycle) in a glove box antechamber before being transferred into a glove box. A separate 20 mL scintillation vial in the glove box was loaded with (S)-*t*-Bu-PHOX (16.4 mg, 0.042 mmol, 6.25 mol %), Pd₂(pmdba)₃ (18.5 mg, 0.017 mmol, 2.5 mol %), and a magnetic stir bar. Toluene (4 mL) was added and the black suspension was stirred at $30\text{ }^{\circ}\text{C}$ in a heating block for 30 min. β -Ketoester **SI-29** was dissolved in toluene (2.8 mL) and added to the orange catalyst solution, causing an immediate color change to olive green. The vial was capped with the septum-fitted screw cap and the edges were sealed with electrical tape. The vial was removed from the glove box, connected to a N₂-filled Schlenk manifold, and immersed in a $50\text{ }^{\circ}\text{C}$ oil bath.

After 22 h, the reaction was an orange-brown solution. The mixture was concentrated under reduced pressure and purified by flash column chromatography (SiO₂, 2 x 25 cm, 20:1→10:1, Hexanes:EtOAc) to afford vinylogous ester **8** (146 mg, 0.66 mmol, 97% yield) as a clear, colorless oil; $R_f = 0.57$ (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 5.81–5.63 (m, 1H), 5.22 (s, 1H), 5.08–4.98 (m, 2H), 3.56 (d, $J = 6.5$ Hz, 2H), 2.40 (app t, $J = 6.4$ Hz, 2H), 2.33 (dddd, $J = 13.8, 7.6, 1.0, 1.0$ Hz, 1H), 2.16 (dddd, $J = 13.8, 7.6, 1.0, 1.0$ Hz, 1H), 2.00 (app sept, $J = 6.7$ Hz, 1H), 1.90 (ddd, $J = 13.4, 6.6, 6.6$ Hz, 1H), 1.68 (ddd, $J = 13.6, 6.2, 6.2$ Hz, 1H), 1.06 (s, 3H), 0.95 (d, $J = 6.7$ Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 203.5, 176.1, 134.4, 117.9, 101.4, 74.8, 43.3, 41.6, 31.9, 27.9, 26.0, 22.3, 19.2; IR (Neat Film NaCl) 3074, 2962, 2932, 2875, 1655, 1611, 1470, 1464, 1429, 1404, 1384, 1368, 1327, 1307, 1299, 1240, 1195, 1178, 1123, 1080, 1032, 996, 968, 951, 913, 862, 840, 806, 786, 736 cm⁻¹; HRMS (EI+) m/z calc'd for C₁₄H₂₂O₂ [M]⁺: 222.1620; found 222.1627; $[\alpha]_D^{25.0} -10.67$ (c 0.98, CHCl₃, 86.3% ee); HPLC conditions: 5% IPA in Hexanes, OD-H column, t_R (min): major = 5.80, minor = 6.53.



Cyclohexenone 9. A 50 mL round-bottom flask was charged with Et₂O (11.1 mL) and cooled to 0 °C. LiAlH₄ (13.6 mg, 0.36 mmol, 0.55 equiv) was added in one portion. After 10 min, a solution of vinylogous ester **8** (146 mg, 0.66 mmol, 1.00 equiv) in Et₂O (2.0 mL) was added dropwise using positive pressure cannulation. After 30 min of stirring at 0 °C, an additional portion of LiAlH₄ (2.5 mg, 0.066 mmol, 0.10 equiv) was added. After 60 min of stirring, the reaction was quenched by slow addition of aqueous HCl (1.0 mL, 10% w/w). The resulting biphasic system was allowed to warm to ambient temperature and stirred vigorously for 8.5 h. The phases were separated and the aqueous phase was extracted with Et₂O (3 x 15 mL). The combined organic phases were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified using flash column chromatography (SiO₂, 2 x 25 cm, 10:1→4:1→1:1→1:2 Hexanes:Et₂O) to afford cyclohexenone **9** (90.5 mg, 0.60 mmol, 92% yield) as a yellow oil; $R_f = 0.51$ (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 6.67 (d, $J = 10.2$ Hz, 1H), 5.88 (d, $J = 10.2$ Hz, 1H), 5.79 (dddd, $J = 16.8, 10.3, 7.4, 7.4$ Hz, 1H), 5.20–5.01 (m, 2H), 2.54–2.36 (m, 2H), 2.29–2.10 (m, 2H), 2.05–1.89 (m, 1H), 1.85–1.69 (m, 1H), 1.14 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 199.4, 158.4, 133.4, 127.6, 118.6, 45.2, 35.7, 34.1, 33.6, 24.7; IR (Neat Film NaCl) 3077, 3005, 2960, 2917, 2868, 2849, 1682, 1639, 1616, 1459, 1419, 1390, 1373, 1332, 1250, 1223, 1193, 1115, 996, 961, 918, 871, 803, 757 cm⁻¹; HRMS (EI+) m/z calc'd for C₁₀H₁₄O [M]⁺: 150.1045; found 150.1056; $[\alpha]_D^{25.0} +26.72$ (c 1.02, CHCl₃, 86.3% ee).

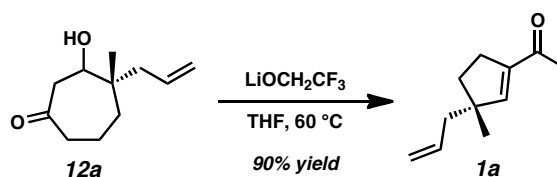
Ring Contraction Screening Protocol

Table SI-1. Ring Contraction Screen of β -Hydroxyketone **12a**^a


Entry	Base	Additive	Solvent	T (°C)	time (h)	Yield (%) ^b
1	LiOt-Bu	—	<i>t</i> -BuOH	40	9	71
2	LiOt-Bu	—	THF	40	8	60
3	NaOt-Bu	—	THF	40	5	81
4	KOt-Bu	—	THF	40	5	85
5	NaOH	—	THF	60	4	89
6	KOH	—	THF	60	4	87
7	LiOH	—	THF	60	24	19 ^d
8	LiOH	<i>t</i> -BuOH	THF	60	24	78
9	LiOH	HFIP ^c	THF	60	12.5	87
10	LiOH	TFE ^c	THF	60	12.5	96
11	LiOCH ₂ CF ₃	—	THF	60	10	90 ^e

^a Conditions: β -hydroxyketone (1.0 equiv), additive (1.5 equiv), base (1.5 equiv) in solvent (0.1 M) at indicated temperature. ^b GC yield using an internal standard, unless otherwise stated. ^c HFIP = 1,1,1,3,3,3-hexafluoro-2-propanol; TFE = 2,2,2-trifluoroethanol. ^d Several reaction intermediates observed by TLC and GC analysis. ^e Isolated yield.

Ring Contraction Screen to Produce Acylcyclopentene **1a (0.10 mmol scale, Table 1, entries 1–4 and Table SI-1, entries 1–10).** A benzene solution of β -hydroxyketone **12a** was transferred to a dry 1 dram vial and concentrated under reduced pressure to obtain a starting mass. To this vial was added a magnetic stir bar and 1,4-diisopropylbenzene (internal standard). The contents were solvated in either *t*-BuOH or THF (0.1 M). After complete solvation, an appropriate additive (*t*-BuOH, TFE, or HFIP; 1.50 equiv) was added, followed by base (1.50 equiv). The head space of the vial was purged with N₂, and the vial was capped with a teflon-lined hard cap and stirred the appropriate temperature (40 or 60 °C) in a heating block. Reaction progress was initially followed by TLC analysis and when necessary aliquots were removed and flushed through a small SiO₂ plug with EtOAc for GC analysis. GC conditions: 90 °C isothermal for 5 min, then ramp 10 °C/min to 250 °C, DB-WAX column, *t_R* (min): 1,4-diisopropylbenzene = 5.3, acylcyclopentene **1a** = 9.3, β -hydroxyketone **12a** = 17.1 and 17.2 (two diastereomers). (For characterization data, see p. 33).

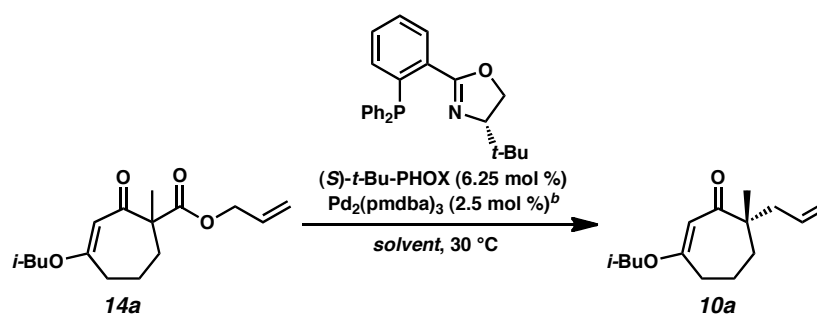


Ring Contraction using LiOCH₂CF₃ (Table SI-1, entry 11). β -Hydroxyketone **12a** (30.0 mg, 0.16 mmol, 1.00 equiv) was measured into a 1 dram vial with magnetic stir bar with a septum-fitted screw cap. LiOCH₂CF₃^[1] (26.0 mg, 0.25 mmol, 1.50 equiv) was measured into a separate 1

dram vial, capped with a septum, evacuated/backfilled with N₂ (3 cycles, 5 min evacuation per cycle), and dissolved in THF (0.5 mL). The solution was cannulated into the vial containing β-hydroxyketone along with additional THF rinses (2 x 0.5 mL). The yellow solution was stirred at 60 °C in a heating block. After 10 h, the reaction was cooled to ambient temperature. The turbid brown solution was diluted with Et₂O and stirred with Na₂SO₄ for 30 min. The reaction was filtered and concentrated in vacuo at 0 °C in an ice/water bath. The residue was purified by flash column chromatography (SiO₂, 1 x 20 cm, 15:1 Hexanes:Et₂O) to afford acylcyclopentene **1a** (24.4 mg, 0.149 mmol, 90% yield) as a clear, colorless oil. (For characterization data, see p. 33).

Enantioselective Pd-Catalyzed Decarboxylative Alkylation Screening Protocol

Table SI-2. Solvent Screen for the Enantioselective Alkylation of **14a^a**



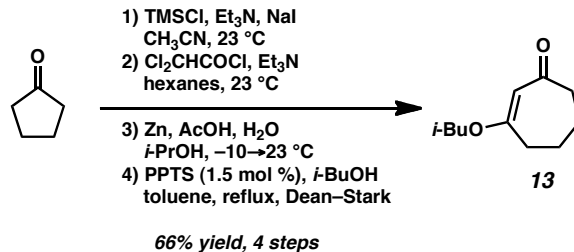
Entry	Solvent	Yield (%) ^c	ee (%) ^d
1	THF	94	84
2	TBME ^e	88	85
3	Et ₂ O	93	86
4	benzene	84	86
5	toluene	91	88

^a Conditions: β-ketoester (1.0 equiv), Pd₂(pmdba)₃ (2.5 mol %), (S)-t-Bu-PHOX (6.25 mol %) in solvent (0.1 M) at 30 °C.

^b pmdba = 4,4'-methoxydibenzylideneacetone. ^c Isolated yield.

^d Determined by chiral HPLC. ^e TBME = *tert*-butyl methyl ether.

Enantioselective Allylation Screen to Produce Vinylogous Ester **10a (0.20 mmol scale).** To a 25 mL flask was added Pd₂(pmdba)₃ (5.00 μmol, 2.5 mol %) and (S)-t-Bu-PHOX (12.5 μmol, 6.25 mol %). The flask was evacuated/backfilled with N₂ (3 cycles, 5 min evacuation per cycle). Solvent (most of total volume, 0.1 M final concentration) was added and the black suspension was stirred for 30 min at 30 °C using an oil bath. A solution of β-ketoester **14a** (0.20 mmol, 1.00 equiv) in solvent (remainder of total volume) was transferred to the catalyst solution using positive pressure cannulation. When judged complete by TLC analysis, the reaction was filtered through a small plug of SiO₂, eluted with Et₂O, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, 1.5 x 15 cm, 9:1→6:1 Hexanes:EtOAc) or preparative TLC (SiO₂, 2:1 Hexanes:EtOAc) provided ketone **10a** for analysis. HPLC conditions: 1% IPA in Hexanes, 1.0 mL/min, OD-H column, t_R (min): major = 6.30, minor = 7.26. (For characterization data, see p. 22).

Procedures for the Synthesis of Parent Vinylogous Ester **13**^[10]

Vinylogous ester 13. NaI (157 g, 1.05 mol, 1.25 equiv) was placed in a 3 L 3-neck round-bottom flask, dried under high vacuum at 90 °C for 12 h, and allowed to cool to ambient temperature under N₂. CH₃CN (1.3 L) was added to dissolve the NaI. To the solution was added cyclopentanone (74.3 mL, 0.84 mol, 1.00 equiv), followed by Et₃N (146 mL, 1.05 mol, 1.25 equiv). The flask was fitted with an addition funnel, and the funnel was charged with TMSCl (122 mL, 0.96 mmol, 1.14 equiv), which was added dropwise over 30 min. The resulting suspension was stirred for an additional 1 h at ambient temperature. Pentane (1.0 L) was added, and the biphasic system was stirred vigorously for 10 min. The phases were separated and the CH₃CN layer was extracted with pentane (3 x 400 mL). The combined pentane phases were washed with H₂O (2 x 500 mL) and brine (500 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure to afford the desired product (131 g, quantitative) as a colorless oil.

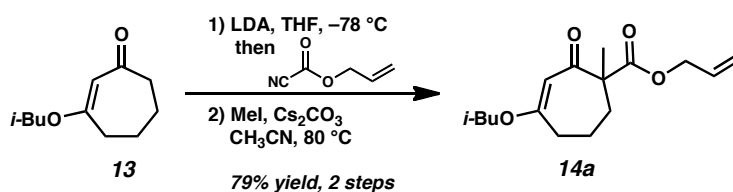
A portion of the above trimethylsilylether (89.7 g, 0.57 mol, 1.00 equiv) was placed in a 3 L 3-neck round-bottom flask fitted with a stopper, an addition funnel, and an overhead stirrer. Hexanes (900 mL) was added followed by Et₃N (111 mL, 0.80 mol, 1.39 equiv). Dichloroacetyl chloride (66.4 mL, 0.69 mol, 1.21 equiv) was dissolved in hexanes (400 mL) and added dropwise over 9.5 h. After 18 h of stirring at ambient temperature, the brown suspension was filtered, rinsing with EtOAc (3 x 500 mL). The clear brown solution was concentrated under reduced pressure and then filtered through a pad of Al₂O₃ (7 x 18 cm, neutral) using EtOAc as eluent. The solution was concentrated under reduced pressure to afford the desired product (125 g, 0.47 mol, 82% yield) as a brown oil that crystallized in the freezer (-20 °C).

A portion of the above dichlorocyclobutanone (53.4 g, 0.20 mol, 1.00 equiv) was placed in a 3 L 3-neck round-bottom flask fitted with a thermometer, an addition funnel, and an overhead stirrer. Isopropyl alcohol and purified water (170 mL each) were added and the suspension was cooled to -10 °C (internal temperature) using a MeOH/ice bath. Zn dust (58.8 g, 0.90 mol, 4.50 equiv) was added in four portions (5 min between each) and AcOH (63 mL, 1.10 mol, 5.50 equiv) dissolved in H₂O (130 mL) was added dropwise while keeping the internal temperature below 0 °C (usually added over 1.5 h). The reaction was stirred for an additional 30 min at -10 °C (internal temperature) before the cooling bath was removed and the reaction was allowed to warm to ambient temperature. After 8.5 h, the reaction was filtered, rinsing with isopropyl alcohol (100 mL). The mixture was cooled to 0 °C and neutralized by portionwise addition of K₂CO₃ (74.6 g, 0.54 mol, 5.50 equiv). The viscous suspension was filtered, rinsing with H₂O (100 mL) and EtOAc (300 mL). The biphasic system was concentrated under reduced pressure to ~200 mL and extracted with CH₂Cl₂. The combined organics were dried over MgSO₄, filtered, and concentrated under reduced pressure to afford the desired product (24.2 g, 0.19 mol, 96% yield) as a pale orange oil.

To a solution of 1,3-cycloheptanedione (35.8 g, 0.28 mol, 1.00 equiv) in toluene (280 mL) in a 1 L flask fitted with a reflux condenser and Dean-Stark trap was added isobutanol (208

mL, 2.27 mol, 8.11 equiv) and pyridinium *p*-toluenesulfonate (1.07 g, 4.26 mmol, 1.50 mol %). The solution was immersed in an oil bath at 130 °C and monitored by TLC. When the starting material was consumed (typically within 4–6 h), the reaction was allowed to cool to ambient temperature. The resulting dark orange solution was washed with sat aqueous NaHCO₃ (200 mL). The aqueous phase was extracted with EtOAc (3 x 150 mL) and the combined organics were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure to afford a thick dark orange oil. The crude oil was flushed through a silica gel plug (SiO₂, 7 x 9 cm, 1:4→3:7→1:1 Et₂O-Hexanes) to afford vinylogous ester **13** (43.5 g, 0.24 mol, 84% yield, 66% yield over 4 steps) as a pale orange oil; *R_f* = 0.22 (2:1 Hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 5.37 (s, 1H), 3.49 (d, *J* = 6.6 Hz, 2H), 2.60–2.56 (m, 4H), 2.00 (sept, *J* = 6.6 Hz, 1H), 1.88–1.77 (m, 4H), 0.96 (d, *J* = 6.8 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 202.5, 176.6, 106.0, 75.0, 41.9, 33.1, 27.9, 23.7, 21.5, 19.3; IR (Neat Film NaCl) 2958, 2872, 1646, 1607, 1469, 1237, 1190, 1174 cm⁻¹; HRMS (EI+) *m/z* calc'd for C₁₁H₁₈O₂ [M]⁺: 182.1307; found 182.1310.

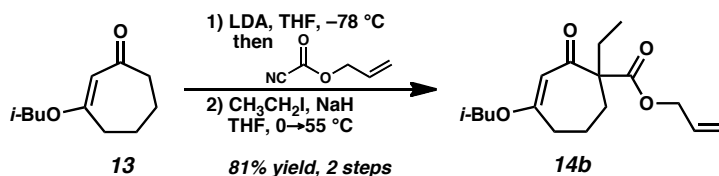
Procedures for the Preparation of β-Ketoesters 14



β-Ketoester 14a. To a solution of diisopropylamine (6.46 mL, 46.1 mmol, 1.20 equiv) in THF (180 mL) in a 500 mL round-bottom flask at 0 °C was added *n*-BuLi (17.2 mL, 44.2 mmol, 2.57 M in hexanes, 1.15 equiv) dropwise over 15 min using a syringe pump. After 15 min of stirring at 0 °C, the mixture was cooled to –78 °C using an acetone/CO₂(s) bath. A solution of vinylogous ester **13** (7.01 g, 38.4 mmol, 1.00 equiv) in THF (20 mL) was added dropwise over 20 min using a syringe pump. After an additional 1 h of stirring at –78 °C, allyl cyanofornate (4.60 mL, 42.2 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at –78 °C for 2.5 h, quenched by addition of sat aqueous NH₄Cl and H₂O (30 mL each), and allowed to warm to ambient temperature. The reaction was diluted with Et₂O (100 mL) and the phases were separated. The aqueous phase was extracted with Et₂O (2 x 100 mL). The combined organic phases were dried over MgSO₄, filtered, and concentrated under reduced pressure to afford a pale orange oil.

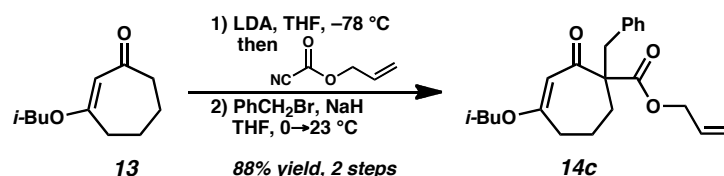
The crude oil was dissolved in CH₃CN (130 mL) in a 500 mL round-bottom flask and treated with MeI (7.2 mL, 115 mmol, 3.00 equiv) and Cs₂CO₃ (16.76 g, 49.9 mmol, 1.30 equiv). The flask was fitted with a condenser, immersed in an oil bath, and heated to 80 °C with vigorous stirring. After 12 h of stirring at 80 °C, the reaction was allowed to cool to ambient temperature, diluted with EtOAc (100 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure to afford an orange oil. The crude product was purified by flash column chromatography (SiO₂, 5 x 15 cm, 19:1→9:1 Hexanes:EtOAc, dry-loaded using Celite) to afford β-ketoester **14a** (8.51 g, 30.4 mmol, 79% yield over 2 steps) as a pale yellow oil; *R_f* = 0.43 (4:1 Hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 5.86 (dddd, *J* = 17.1, 10.7, 5.6, 5.6 Hz, 1H), 5.39 (s, 1H), 5.29 (app dq, *J* = 17.1, 1.5 Hz, 1H), 5.20 (app dq, *J* = 10.5, 1.4 Hz, 1H), 4.62 (dddd, *J* = 13.3, 5.6, 1.2, 1.2 Hz, 1H), 4.56 (dddd, *J* = 13.4, 5.6, 1.2, 1.2 Hz, 1H), 3.54–3.42 (m, 2H),

2.59 (ddd, $J = 17.8, 9.8, 3.9$ Hz, 1H), 2.45–2.38 (m, 2H), 2.02–1.94 (m, 2H), 1.84–1.75 (m, 1H), 1.70 (ddd, $J = 14.4, 7.3, 4.4$ Hz, 1H), 1.43 (s, 3H), 0.94 (d, $J = 6.6$ Hz, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 199.1, 174.0, 173.5, 132.0, 118.4, 105.2, 74.8, 65.8, 59.1, 34.3, 33.9, 27.9, 24.2, 21.4, 19.3; IR (Neat Film NaCl) 2959, 2936, 2875, 1734, 1650, 1613, 1456, 1384, 1233, 1170, 1115, 994 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{16}\text{H}_{24}\text{O}_4$ $[\text{M}]^+$: 280.1675; found 280.1686.



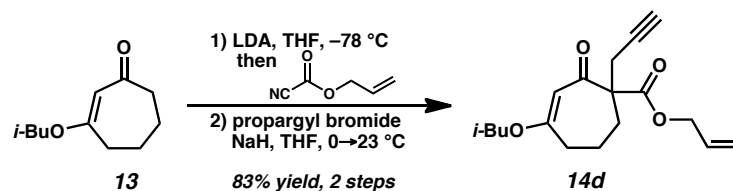
β -Ketoester 14b. To a solution of diisopropylamine (0.92 mL, 6.58 mmol, 1.20 equiv) in THF (27 mL) in a 100 mL round-bottom flask at 0 $^\circ\text{C}$ was added *n*-BuLi (2.56 mL, 6.30 mmol, 2.46 M in hexanes, 1.15 equiv) dropwise over 10 min. After 15 min of stirring at 0 $^\circ\text{C}$, the mixture was cooled to -78 $^\circ\text{C}$ using an acetone/ $\text{CO}_2(\text{s})$ bath. A solution of vinylogous ester **13** (1.00 g, 5.48 mmol, 1.00 equiv) in THF (2 mL) was added dropwise using positive pressure cannulation. After an additional 1 h of stirring at -78 $^\circ\text{C}$, allyl cyanoformate (0.67 mL, 6.02 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at -78 $^\circ\text{C}$ for 2.5 h, quenched by addition of 50% sat aqueous NH_4Cl (8 mL), and allowed to warm to ambient temperature. The reaction was diluted with Et_2O (25 mL) and the phases were separated. The aqueous phase was extracted with Et_2O (3 x 25 mL). The combined organic phases were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure to afford a pale orange oil.

The crude oil was dissolved in THF (8 mL) in a 100 mL round-bottom flask, cooled to 0 $^\circ\text{C}$, and stirred vigorously as hexane-washed NaH (158 mg, 6.58 mmol, 1.20 equiv) was added in one portion. Evolution of gas was observed and the reaction was stirred at 0 $^\circ\text{C}$ for 30 min to give a yellow-orange solution. $\text{CH}_3\text{CH}_2\text{I}$ (1.31 mL, 16.4 mmol, 3.00 equiv) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 4.5 h. The mixture was heated to 45 $^\circ\text{C}$ and stirred for 1.5 h. Additional $\text{CH}_3\text{CH}_2\text{I}$ (0.65 mL, 8.22 mmol, 1.50 equiv) was added dropwise and the mixture was stirred at 45 $^\circ\text{C}$ for 6 h. A third portion of $\text{CH}_3\text{CH}_2\text{I}$ (0.33 mL, 4.11 mmol, 0.75 equiv) was added dropwise and the reaction was warmed to 55 $^\circ\text{C}$ and stirred for 1.5 h. The flask was cooled to ambient temperature and quenched by addition of 50% sat aqueous NH_4Cl (10 mL). The phases were separated and the aqueous layer was extracted with Et_2O (3 x 15 mL). The combined organic phases were washed with brine, dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2 , 5 x 20 cm, 9:1 \rightarrow 6:1 \rightarrow 3:1 \rightarrow 2:1 Hexanes: EtOAc) to afford β -ketoester **14b** (1.31 g, 4.44 mmol, 81% yield over 2 steps) as a yellow oil; $R_f = 0.53$ (4:1 Hexanes: EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 5.85 (dddd, $J = 17.5, 10.2, 5.7, 5.7$ Hz, 1H), 5.35 (s, 1H), 5.29 (app dq, $J = 17.2, 1.5$ Hz, 1H), 5.19 (app dq, $J = 10.4, 1.3$ Hz, 1H), 4.62 (dddd, $J = 13.2, 5.7, 1.4, 1.4$ Hz, 1H), 4.54 (dddd, $J = 13.2, 5.7, 1.4, 1.4$ Hz, 1H), 3.57–3.34 (m, 2H), 2.60 (dddd, $J = 17.9, 9.9, 3.7, 1.2$ Hz, 1H), 2.49–2.26 (m, 2H), 2.12–1.85 (m, 4H), 1.85–1.57 (m, 2H), 0.93 (d, $J = 6.7$ Hz, 6H), 0.84 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 198.7, 173.7, 173.2, 132.0, 118.5, 105.5, 74.7, 65.7, 63.1, 34.1, 31.0, 30.6, 27.9, 22.0, 19.3, 9.0; IR (Neat Film NaCl) 3085, 2960, 2937, 2876, 1731, 1663, 1613, 1471, 1461, 1453, 1424, 1383, 1369, 1328, 1304, 1278, 1229, 1199, 1170, 1121, 1006, 988, 931, 875, 858, 813 cm^{-1} ; HRMS (MM: ESI-APCI+) m/z calc'd for $\text{C}_{17}\text{H}_{27}\text{O}_4$ $[\text{M}+\text{H}]^+$: 295.1904; found 295.1918.



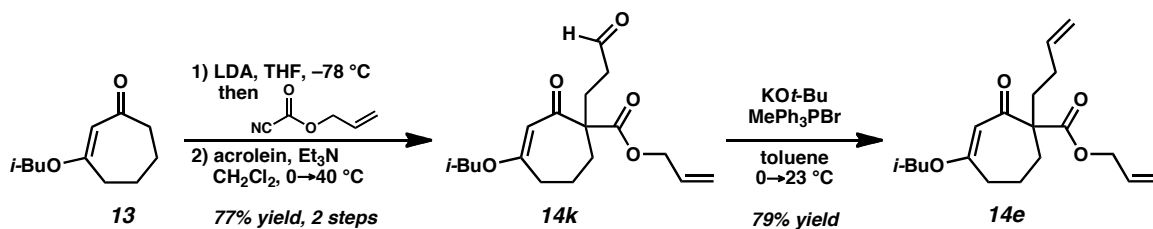
β -Ketoester 14c. To a solution of diisopropylamine (0.92 mL, 6.58 mmol, 1.20 equiv) in THF (27 mL) in a 100 mL round-bottom flask at 0 °C was added *n*-BuLi (2.56 mL, 6.30 mmol, 2.46 M in hexanes, 1.15 equiv) dropwise over 10 min. After 15 min of stirring at 0 °C, the mixture was cooled to -78 °C using an acetone/ $\text{CO}_2(\text{s})$ bath. A solution of vinylogous ester **13** (1.00 g, 5.48 mmol, 1.00 equiv) in THF (2 mL) was added dropwise using positive pressure cannulation. After an additional 1 h of stirring at -78 °C, allyl cyanoformate (0.67 mL, 6.02 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at -78 °C for 2.5 h, quenched by addition of 50% sat aqueous NH_4Cl (8 mL), and allowed to warm to ambient temperature. The reaction was diluted with Et_2O (25 mL) and the phases were separated. The aqueous phase was extracted with Et_2O (3 x 25 mL). The combined organic phases were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure to afford a pale orange oil.

The crude oil was dissolved in THF (8 mL) in a 100 mL round-bottom flask, cooled to 0 °C, and stirred vigorously as hexane-washed NaH (197 mg, 8.22 mmol, 1.50 equiv) was added in one portion. Evolution of gas was observed and the reaction was stirred at 0 °C for 30 min to give a yellow-orange solution. Benzyl bromide (1.96 mL, 16.44 mmol, 3.00 equiv) was added dropwise. The reaction was allowed to warm to ambient temperature and stirred for 3 h. The reaction was quenched by addition of 50% sat aqueous NH_4Cl (10 mL). The phases were separated and the aqueous layer was extracted with Et_2O (3 x 15 mL). The combined organic phases were washed with brine, dried over MgSO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2 , 3 x 23 cm, Hexanes \rightarrow 10:1 Hexanes:EtOAc) to afford β -ketoester **14c** (1.72 g, 4.83 mmol, 88% yield over 2 steps) as a pale yellow oil; $R_f = 0.26$ (10:1 Hexanes:EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 7.30–7.15 (m, 3H), 7.15–7.06 (m, 2H), 5.85 (dddd, $J = 17.1, 10.4, 5.8, 5.8$ Hz, 1H), 5.36 (s, 1H), 5.30 (app dq, $J = 17.2, 1.5$ Hz, 1H), 5.21 (app dq, $J = 10.4, 1.3$ Hz, 1H), 4.63 (dddd, $J = 13.2, 5.7, 1.3, 1.3$ Hz, 1H), 4.52 (dddd, $J = 13.2, 5.8, 1.3, 1.3$ Hz, 1H), 3.42 (d, $J = 6.5$ Hz, 2H), 3.30 (d, $J = 13.5$ Hz, 1H), 3.23 (d, $J = 13.5$ Hz, 1H), 2.54 (ddd, $J = 12.1, 10.0, 3.5$ Hz, 1H), 2.38–2.18 (m, 2H), 2.04–1.83 (m, 2H), 1.81–1.64 (m, 2H), 0.92 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 198.0, 174.0, 172.7, 137.0, 131.8, 130.7, 128.1, 126.8, 118.8, 105.7, 74.8, 66.0, 64.0, 43.1, 34.0, 31.3, 27.9, 22.0, 19.2; IR (Neat Film NaCl) 3085, 3062, 3029, 2959, 2934, 2873, 1736, 1732, 1661, 1652, 1611, 1495, 1471, 1454, 1423, 1383, 1368, 1270, 1235, 1173, 1088, 1007, 957, 992, 930, 862, 815, 741 cm^{-1} ; HRMS (APCI+) m/z calc'd for $\text{C}_{22}\text{H}_{29}\text{O}_4$ $[\text{M}+\text{H}]^+$: 357.2060; found 357.2051.



β -Ketoester 14d. To a solution of diisopropylamine (0.92 mL, 6.58 mmol, 1.20 equiv) in THF (27 mL) in a 100 mL round-bottom flask at 0 °C was added *n*-BuLi (2.56 mL, 6.30 mmol, 2.46 M in hexanes, 1.15 equiv) dropwise over 10 min. After 15 min of stirring at 0 °C, the mixture was cooled to -78 °C using an acetone/CO₂(s) bath. A solution of vinylogous ester **13** (1.00 g, 5.48 mmol, 1.00 equiv) in THF (2 mL) was added dropwise using positive pressure cannulation. After an additional 1 h of stirring at -78 °C, allyl cyanoformate (0.67 mL, 6.02 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at -78 °C for 2.5 h, quenched by addition of 50% sat aqueous NH₄Cl (8 mL), and then allowed to warm to ambient temperature. The reaction was diluted with Et₂O (25 mL) and the phases were separated. The aqueous phase was extracted with Et₂O (3 x 25 mL). The combined organic phases were dried over Na₂SO₄, filtered, and concentrated under reduced pressure to afford a pale orange oil.

The crude oil was dissolved in THF (8 mL) in a 100 mL round-bottom flask, cooled to 0 °C, and stirred vigorously as hexane-washed NaH (197 mg, 8.22 mmol, 1.5 equiv) was added in one portion. Evolution of gas was observed and the reaction was stirred at 0 °C for 30 min to give a yellow-orange solution. Propargyl bromide (1.22 mL, 10.96 mmol, 80% wt in toluene, 2.00 equiv) was added dropwise and the reaction was allowed to warm to ambient temperature and stirred for 5.5 h. The reaction was quenched by addition of 50% sat aqueous NH₄Cl (10 mL). The phases were separated and the aqueous layer was extracted with Et₂O (3 x 15 mL). The combined organic phases were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO₂, 3 x 24 cm, Hexanes→20:1→15:1→10:1 Hexanes:EtOAc) to afford β -ketoester **14d** (1.38 g, 4.53 mmol, 83% yield over 2 steps) as a pale yellow oil; R_f = 0.55 (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 5.85 (dddd, J = 17.2, 10.4, 5.7, 5.7 Hz, 1H), 5.38 (s, 1H), 5.29 (app dq, J = 17.2, 1.5 Hz, 1H), 5.19 (app dq, J = 10.4, 1.3 Hz, 1H), 4.63 (dddd, J = 13.2, 5.6, 1.4, 1.4 Hz, 1H), 4.56 (dddd, J = 13.2, 5.7, 1.4, 1.4 Hz, 1H), 3.56–3.38 (m, 2H), 2.79 (dd, J = 2.7, 0.6 Hz, 1H), 2.72–2.32 (m, 4H), 2.15–1.89 (m, 4H), 1.89–1.71 (m, 1H), 0.93 (d, J = 6.7 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 196.5, 174.8, 171.7, 131.7, 118.7, 105.0, 80.2, 74.9, 71.4, 66.1, 62.0, 34.3, 31.2, 27.9, 27.5, 21.7, 19.2; IR (Neat Film NaCl) 3289, 3085, 2959, 2933, 2874, 2120, 1740, 1735, 1654, 1649, 1470, 1452, 1424, 1402, 1384, 1369, 1309, 1291, 1272, 1232, 1187, 1173, 1133, 1085, 1066, 1007, 968, 930, 863, 820 cm⁻¹; HRMS (EI+) m/z calc'd for C₁₈H₂₅O₄ [M+H]⁺: 305.1753; found 305.1746.

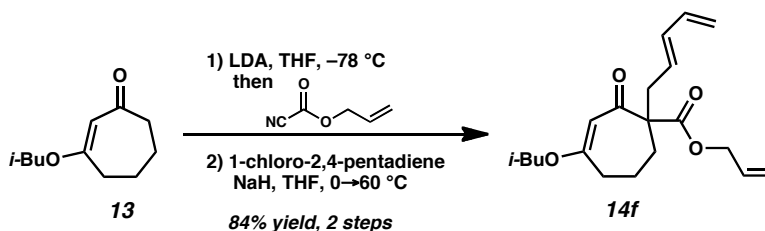


β -Ketoester 14k. To a solution of diisopropylamine (1.49 mL, 10.63 mmol, 1.20 equiv) in THF (43 mL) in a 250 mL round-bottom flask at 0 °C was added *n*-BuLi (4.74 mL, 10.19 mmol, 2.51 M in hexanes, 1.15 equiv) dropwise over 10 min. After 15 min of stirring at 0 °C, the mixture was cooled to -78 °C using an acetone/CO₂(s) bath. A solution of vinylogous ester **13** (1.61 g, 8.86 mmol, 1.00 equiv) in THF (3 mL) was added dropwise using positive pressure cannulation. After an additional 1 h of stirring at -78 °C, allyl cyanoformate (1.06 mL, 9.74 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at -78 °C for 2.5 h, quenched by addition of 50% sat aqueous NH₄Cl (12.9 mL), and then allowed to warm to ambient temperature. The reaction was diluted with Et₂O (50 mL) and the phases were separated. The aqueous phase was extracted with Et₂O (3 x 100 mL). The combined organic phases were dried over Na₂SO₄, filtered, and concentrated under reduced pressure to afford a pale orange oil. The crude oil was purified by automated flash column chromatography using a Teledyne Isco CombiFlash R_f (SiO₂, 25 g loading cartridge, 330 g column, hold 0% [3 min]→ramp to 20% [10 min]→hold 20% [10 min]→ramp to 50% [4 min]→hold 50% EtOAc in Hexanes [5 min]) to afford the intermediate β -ketoester (2.02 g, 7.58 mmol, 86% yield).

A portion of the intermediate β -ketoester (990 mg, 3.72 mmol, 1.00 equiv) was dissolved in CH₂Cl₂ (10 mL) in a 100 mL round-bottom flask, cooled to 0 °C, and treated with Et₃N (0.518 mL, 3.72 mmol, 1.00 equiv). Acrolein (0.248 mL, 3.72 mmol, 1.00 equiv) was added dropwise and the reaction was allowed to warm to ambient temperature. After 51 h, the reaction was cooled to 0 °C and an additional portion of acrolein (0.125 mL, 1.86 mmol, 0.50 equiv) was added. After 100 h, the reaction was concentrated under reduced pressure, dissolved in Et₂O, and filtered through a cotton plug to remove salts. The filtrate was concentrated under reduced pressure and the crude product was purified by flash column chromatography (SiO₂, 3 x 25 cm, 10:1→6:1→4:1 Hexanes:EtOAc) to afford β -ketoester **14k** (1.07 g, 3.34 mmol, 90% yield, 77% yield over 2 steps) as a clear oil; *R*_f = 0.23, broad (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 9.73 (t, *J* = 1.3 Hz, 1H), 5.86 (dddd, *J* = 17.1, 10.4, 5.8, 5.8 Hz, 1H), 5.36 (s, 1H), 5.30 (app dq, *J* = 17.2, 1.5 Hz, 1H), 5.22 (app dq, *J* = 10.4, 1.2 Hz, 1H), 4.63 (dddd, *J* = 13.1, 5.7, 1.3, 1.3 Hz, 1H), 4.55 (dddd, *J* = 13.2, 5.8, 1.3, 1.3 Hz, 1H), 3.55–3.40 (m, 2H), 2.66–2.29 (m, 5H), 2.29–2.08 (m, 2H), 2.08–1.89 (m, 2H), 1.89–1.59 (m, 2H), 0.94 (d, *J* = 6.7 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 201.6, 197.9, 173.9, 172.7, 131.7, 119.0, 105.3, 74.9, 66.0, 61.8, 39.7, 34.2, 32.1, 29.6, 27.9, 21.5, 19.2; IR (Neat Film NaCl) 3084, 2960, 2936, 2875, 2829, 2723, 1727, 1649, 1611, 1471, 1454, 1422, 1403, 1385, 1369, 1306, 1270, 1234, 1191, 1173, 1104, 1004, 990, 931, 877, 862, 822 cm⁻¹; HRMS (FAB+) *m/z* calc'd for C₁₈H₂₇O₅ [M+H]⁺: 323.1858; found 323.1860.

β -Ketoester 14e. MePh₃PBr (1.33 g, 3.72 mmol, 1.26 equiv) was suspended in toluene (20 mL) in 100 mL round-bottom flask and cooled to 0 °C. KO^t-Bu (0.348 g, 3.10 mmol, 1.05 equiv) was added in one portion and the bright yellow mixture was stirred at 0 °C for 30 min, warmed to ambient temperature, and stirred for an additional 2 h. The mixture was cooled to 0 °C and a solution of aldehyde **14k** (0.95 g, 2.94 mmol, 1.00 equiv) in toluene (2 mL) was added to the

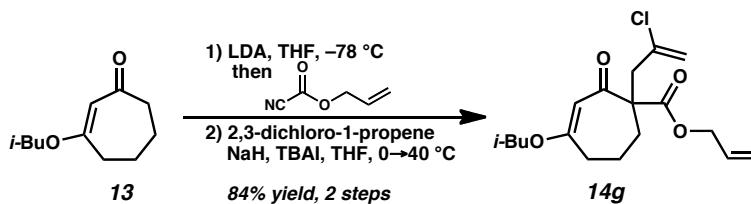
reaction using positive pressure cannulation. The mixture turned brown. The reaction was maintained at 0 °C for 1.5 h, warmed to ambient temperature, and stirred for 4 h. The reaction was quenched by addition of 50% sat aqueous NH₄Cl (4 mL). The phases were separated and the aqueous phase was extracted with Et₂O (3 x 100 mL). The combined organic phases were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO₂, 3 x 25 cm, 20:1→15:1 Hexanes:EtOAc) to afford β -ketoester **14e** (747 mg, 2.33 mmol, 79% yield) as a pale yellow oil; *R*_f = 0.66 (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 5.85 (dddd, *J* = 17.2, 10.4, 5.7, 5.7 Hz, 1H), 5.84–5.69 (m, 1H), 5.35 (s, 1H), 5.29 (app dq, *J* = 17.2, 1.5 Hz, 1H), 5.20 (app dq, *J* = 10.4, 1.3 Hz, 1H), 5.08–4.96 (m, 1H), 4.96–4.87 (m, 1H), 4.62 (dddd, *J* = 13.1, 5.7, 1.4, 1.4 Hz, 1H), 4.54 (dddd, *J* = 13.1, 5.7, 1.4, 1.4 Hz, 1H), 3.53–3.38 (m, 2H), 2.59 (dddd, *J* = 17.9, 9.8, 3.7, 1.1 Hz, 1H), 2.51–2.29 (m, 2H), 2.09–1.87 (m, 6H), 1.87–1.66 (m, 2H), 0.94 (d, *J* = 6.7, 3H), 0.94 (d, *J* = 6.7, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 198.4, 173.7, 173.0, 138.2, 131.9, 118.6, 114.9, 105.4, 74.8, 65.8, 62.6, 36.8, 34.1, 31.5, 28.8, 27.9, 22.0, 19.3; IR (Neat Film NaCl) 3078, 2959, 2935, 2874, 1732, 1662, 1612, 1471, 1453, 1423, 1401, 1384, 1369, 1307, 1270, 1231, 1194, 1170, 1091, 993, 913, 874, 817, 766 cm⁻¹; HRMS (EI+) *m/z* calc'd for C₁₉H₂₈O₄ [M]⁺: 320.1988; found 320.1977.



β -Ketoester 14f. To a solution of diisopropylamine (0.406 mL, 2.90 mmol, 1.20 equiv) in THF (12 mL) in a 50 mL round-bottom flask at 0 °C was added *n*-BuLi (1.10 mL, 2.77 mmol, 2.51 M in hexanes, 1.15 equiv) dropwise over 10 min. After 15 min of stirring at 0 °C, the mixture was cooled to -78 °C using an acetone/CO₂(s) bath. A solution of vinylogous ester **13** (0.44 g, 2.41 mmol, 1.00 equiv) in THF (2 mL) was added dropwise using positive pressure cannulation. After an additional 1 h of stirring at -78 °C, allyl cyanoformate (0.288 mL, 2.65 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at -78 °C for 2.5 h, quenched by addition of 50% sat aqueous NH₄Cl (4 mL), and then allowed to warm to ambient temperature. The reaction was diluted with Et₂O (15 mL) and the phases were separated. The aqueous phase was extracted with Et₂O (3 x 15 mL). The combined organic phases were dried over Na₂SO₄, filtered, and concentrated under reduced pressure to afford a pale orange oil. The crude oil was purified by automated flash column chromatography using a Teledyne Isco CombiFlash R_f (SiO₂, 5 g loading cartridge, 40 g column, hold 0% [1 min]→ramp to 20% [8 min]→hold 20% [5 min]→ramp to 50% [4 min]→50% EtOAc in Hexanes [6 min]) to afford the intermediate β -ketoester (590 mg, 2.21 mmol, 92% yield).

A portion of the intermediate β -ketoester (250 mg, 0.94 mmol, 1.00 equiv) was dissolved in THF (5 mL) in a 50 mL round-bottom flask, cooled to 0 °C, and stirred vigorously as hexane-washed NaH (33.8 mg, 6.58 mmol, 1.50 equiv) was added in one portion. Evolution of gas was observed and the reaction was stirred at 0 °C for 30 min to give a yellow-orange solution. 1-chloro-2,4-pentadiene^[4] (144 mg, 1.41 mmol, 1.50 equiv) was added dropwise and the reaction was allowed to warm to ambient temperature and then heated to 40 °C. After 10.5 h, an

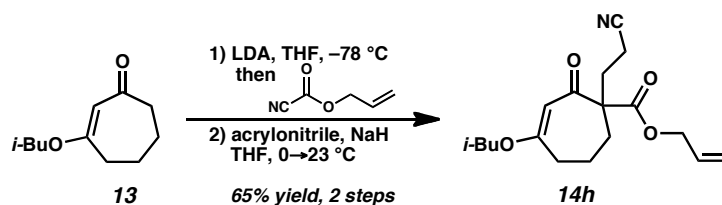
additional portion of 1-chloro-2,4-pentadiene (144 mg, 1.41 mmol, 1.50 equiv) was added and the reaction was heated at 50 °C for 11.5 h. The flask was cooled to ambient temperature and the reaction was quenched by addition of 50% sat aqueous NH₄Cl (2 mL). The phases were separated and the aqueous layer was extracted with Et₂O (3 x 10 mL). The combined organic phases were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO₂, 3 x 25 cm, 20:1→15:1→10:1 Hexanes:EtOAc) to afford β -ketoester **14f** (286 mg, 0.86 mmol, 91% yield, 84% yield over 2 steps) as a pale yellow oil; R_f = 0.59 (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 6.25 (ddd, J = 16.7, 10.3, 10.3 Hz, 1H), 6.11–5.98 (m, 1H), 5.83 (dddd, J = 17.2, 10.4, 5.7, 5.7 Hz, 1H), 5.58 (ddd, J = 15.1, 7.7, 7.7 Hz, 1H), 5.36 (s, 1H), 5.27 (app dq, J = 17.2, 1.5 Hz, 1H), 5.18 (app dq, J = 10.4, 1.2 Hz, 1H), 5.08 (dd, J = 16.9, 1.6 Hz, 1H), 4.96 (dd, J = 16.9, 1.6 Hz, 1H), 4.60 (dddd, J = 13.2, 5.8, 1.4, 1.4 Hz, 1H), 4.52 (dddd, J = 13.2, 5.8, 1.4, 1.4 Hz, 1H), 3.57–3.35 (m, 2H), 2.65 (d, J = 7.7 Hz, 2H), 2.56 (ddd, J = 12.7, 6.8, 2.3 Hz, 1H), 2.48–2.19 (m, 2H), 2.10–1.85 (m, 2H), 1.85–1.63 (m, 2H), 0.92 (d, J = 6.7, 3H), 0.92 (d, J = 6.7, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 197.9, 174.0, 172.7, 136.9, 134.6, 131.9, 129.7, 118.6, 116.1, 105.4, 74.8, 65.9, 62.9, 41.0, 34.1, 31.4, 27.9, 21.8, 19.2; IR (Neat Film NaCl) 3085, 2959, 2933, 2874, 1733, 1650, 1612, 1471, 1453, 1434, 1402, 1384, 1369, 1307, 1272, 1234, 1194, 1171, 1093, 1006, 968, 955, 929, 900, 864, 822, 761 cm⁻¹; HRMS (FAB+) m/z calc'd for C₂₀H₂₉O₄ [M+H]⁺: 333.2066; found 333.2052.



β -Ketoester 14g. To a solution of diisopropylamine (0.92 mL, 6.58 mmol, 1.20 equiv) in THF (27 mL) in a 100 mL round-bottom flask at 0 °C was added *n*-BuLi (2.56 mL, 6.30 mmol, 2.46 M in hexanes, 1.15 equiv) dropwise over 10 min. After 15 min of stirring at 0 °C, the mixture was cooled to -78 °C using an acetone/CO₂(s) bath. A solution of vinyllogous ester **13** (1.00 g, 5.48 mmol, 1.00 equiv) in THF (2 mL) was added dropwise using positive pressure cannulation. After an additional 1 h of stirring at -78 °C, allyl cyanoformate (0.67 mL, 6.02 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at -78 °C for 2.5 h, quenched by addition of 50% sat aqueous NH₄Cl (8 mL), and allowed to warm to ambient temperature. The reaction was diluted with Et₂O (25 mL) and the phases were separated. The aqueous phase was extracted with Et₂O (3 x 25 mL). The combined organic phases were dried over Na₂SO₄, filtered, and concentrated under reduced pressure to afford a pale orange oil.

The crude oil was dissolved in THF (8 mL) in a 100 mL round-bottom flask, cooled to 0 °C, and stirred vigorously as hexane-washed NaH (197 mg, 8.22 mmol, 1.50 equiv) was added in one portion. Evolution of gas was observed and the reaction was stirred at 0 °C for 30 min to give a yellow-orange solution. 2,3-dichloro-1-propene (1.00 mL, 10.96 mmol, 2.0 equiv) was added dropwise and the reaction was allowed to warm to ambient temperature. After 10 h, TBAI (202 mg, 0.548 mmol, 0.10 equiv) was added and the reaction was heated to 40 °C. After 41 h, the reaction was cooled to ambient temperature and quenched by addition of 50% sat aqueous NH₄Cl (10 mL). The phases were separated and the aqueous layer was extracted with Et₂O (3 x 15 mL). The combined organic phases were washed with brine, dried over Na₂SO₄, filtered, and

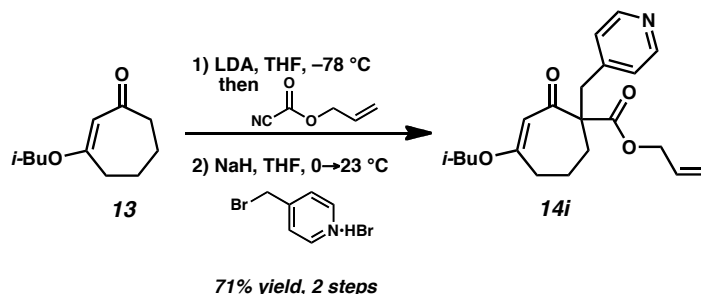
concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO₂, 3 x 25 cm, 20:1→15:1 Hexanes:EtOAc) to afford β -ketoester **14g** (1.57 g, 4.61 mmol, 84% yield over 2 steps) as a yellow oil; R_f = 0.60 (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 5.87 (dddd, J = 17.1, 10.4, 5.8, 5.8 Hz, 1H), 5.38–5.25 (m, 3H), 5.25–5.16 (m, 2H), 4.65 (dddd, J = 13.2, 5.8, 1.3, 1.3 Hz, 1H), 4.52 (dddd, J = 13.1, 5.8, 1.3, 1.3 Hz, 1H), 3.45 (ddd, J = 21.1, 9.3, 6.5 Hz, 2H), 3.04 (s, 2H), 2.71 (dddd, J = 18.2, 10.2, 3.0, 1.3 Hz, 1H), 2.62–2.47 (m, 1H), 2.39 (ddd, J = 17.2, 6.9, 2.6 Hz, 1H), 2.10–1.90 (m, 2H), 1.89–1.65 (m, 2H), 0.94 (d, J = 6.7 Hz, 3H), 0.94 (d, J = 6.7 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 196.6, 174.8, 172.1, 138.1, 131.7, 118.8, 117.1, 104.9, 74.8, 66.2, 62.2, 46.1, 33.9, 30.7, 27.8, 22.6, 19.2; IR (Neat Film NaCl) 3085, 2960, 2935, 2875, 1737, 1662, 1610, 1471, 1452, 1427, 1384, 1369, 1298, 1272, 1229, 1198, 1171, 1153, 1079, 1008, 967, 930, 890, 862, 813 cm⁻¹; HRMS (EI+) m/z calc'd for C₁₈H₂₅O₄ [M–Cl]⁺: 305.1753; found 305.1742.



β -Ketoester 14h. To a solution of diisopropylamine (1.53 mL, 10.93 mmol, 1.20 equiv) in THF (45 mL) in a 250 mL round-bottom flask at 0 °C was added *n*-BuLi (4.17 mL, 10.47 mmol, 2.51 M in hexanes, 1.15 equiv) dropwise over 10 min. After 15 min of stirring at 0 °C, the mixture was cooled to –78 °C using an acetone/CO₂(s) bath. A solution of vinylogous ester **13** (1.66 g, 9.11 mmol, 1.00 equiv) in THF (2 mL) was added dropwise over 10 min. After an additional 1 h of stirring at –78 °C, allyl cyanofornate (1.09 mL, 10.0 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at –78 °C for 2.5 h, quenched by addition of 50% sat aqueous NH₄Cl (13.5 mL), and then allowed to warm to ambient temperature. The reaction was diluted with Et₂O (50 mL) and the phases were separated. The aqueous phase was extracted with Et₂O (3 x 100 mL). The combined organic phases were dried over Na₂SO₄, filtered, and concentrated under reduced pressure to afford a pale orange oil. The crude oil was purified by automated flash column chromatography using a Teledyne Isco CombiFlash R_f (SiO₂, 25 g loading cartridge, 80 g column, multi-step gradient, hold 0% [2 min]→ramp to 20% [4 min]→hold 20% [15 min]→ramp to 50% [7 min]→hold 50% EtOAc in Hexanes [5 min]) to afford the intermediate β -ketoester (2.08 g, 7.80 mmol, 86% yield).

One third of the intermediate β -ketoester (694 mg, 2.60 mmol, 1.00 equiv) was dissolved in THF (5 mL) in a 50 mL round-bottom flask, cooled to 0 °C, and stirred vigorously as hexane-washed NaH (15.6 mg, 0.65 mmol, 0.25 equiv) was added in one portion. Evolution of gas was observed and the reaction was stirred at 0 °C for 30 min to give a yellow-orange solution. Acrylonitrile (0.256 mL, 3.90 mmol, 1.50 equiv) was added dropwise and the reaction was allowed to warm to ambient temperature. After 40 h, the reaction was diluted with Et₂O (30 mL) and washed with H₂O (5 mL) and brine (5 mL). The aqueous layer was extracted with Et₂O (3 x 20 mL). The combined organic phases were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO₂, 3 x 25 cm, 10:1→6:1→4:1 Hexanes:EtOAc) to afford β -ketoester **14h** (620 mg, 1.94 mmol, 75% yield, 65% yield over 2 steps) as a clear, colorless oil; R_f = 0.29 (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 5.87 (dddd, J = 16.2, 10.4, 5.8, 5.8 Hz, 1H),

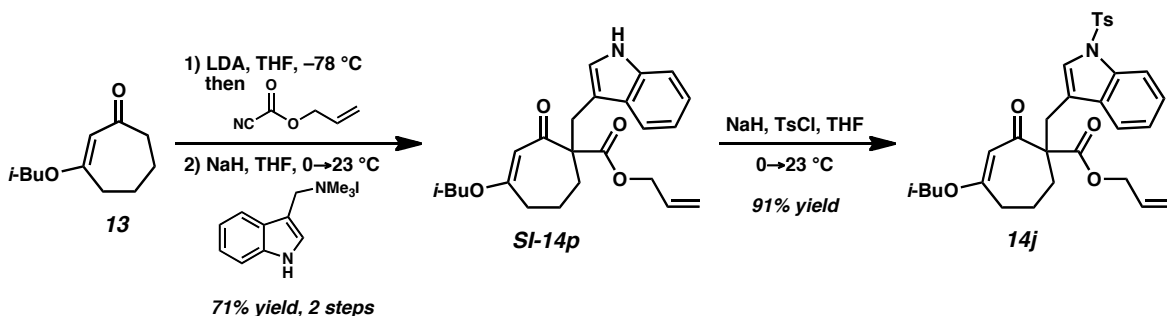
5.38 (s, 1H), 5.32 (app dq, $J = 17.2, 1.4$ Hz, 1H), 5.25 (app dq, $J = 10.4, 1.1$ Hz, 1H), 4.67 (dddd, $J = 13.0, 5.8, 1.2, 1.2$ Hz, 1H), 4.58 (dddd, $J = 13.1, 5.9, 1.2, 1.2$ Hz, 1H), 3.57–3.39 (m, 2H), 2.58 (ddd, $J = 13.1, 9.6, 3.9$ Hz, 1H), 2.51–2.32 (m, 4H), 2.32–2.11 (m, 2H), 2.11–1.90 (m, 2H), 1.90–1.64 (m, 2H), 0.95 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 196.9, 174.4, 172.0, 131.4, 119.7, 119.3, 105.1, 75.0, 66.3, 61.5, 34.1, 33.1, 32.0, 27.9, 21.4, 19.2, 13.3; IR (Neat Film NaCl) 3081, 2959, 2936, 2875, 2247, 1733, 1648, 1609, 1471, 1454, 1423, 1403, 1385, 1369, 1297, 1269, 1235, 1192, 1173, 1096, 996, 932, 874, 824, 764 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{18}\text{H}_{25}\text{O}_4\text{N}$ $[\text{M}]^+$: 319.1784; found 319.1777.



β -Ketoester 14i. To a solution of diisopropylamine (3.54 mL, 25.27 mmol, 1.20 equiv) in THF (108 mL) in a 250 mL round-bottom flask at 0 °C was added *n*-BuLi (10.26 mL, 24.22 mmol, 2.36 M in hexanes, 1.15 equiv) dropwise over 10 min. After 15 min of stirring at 0 °C, the mixture was cooled to –78 °C using an acetone/ $\text{CO}_2(\text{s})$ bath. A solution of vinylogous ester **13** (3.84 g, 21.06 mmol, 1.00 equiv) in THF (10 mL) was added dropwise using positive pressure cannulation. After an additional 1 h of stirring at –78 °C, allyl cyanoformate (2.52 mL, 9.74 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at –78 °C for 2.5 h, quenched by addition of 50% sat aqueous NH_4Cl (30.7 mL), and then allowed to warm to ambient temperature. The reaction was diluted with Et_2O (100 mL) and the phases were separated. The aqueous phase was extracted with Et_2O (3 x 100 mL). The combined organic phases were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure to afford a pale orange oil. The crude oil was purified by automated flash column chromatography using a Teledyne Isco CombiFlash R_f (SiO_2 , 32 g loading cartridge, 330 g column, multi-step gradient, hold 0% [2 min]→ramp to 20% [10 min]→hold 20% [6 min]→ramp to 50% [3 min]→hold 50% EtOAc in Hexanes [11 min]) to afford the intermediate β -ketoester (4.66 g, 17.50 mmol, 83% yield) as a pale orange oil.

A portion of the intermediate β -ketoester (1.00 g, 3.75 mmol, 1.00 equiv) was dissolved in THF (25 mL) in a 100 mL round-bottom flask, cooled to 0 °C, and stirred vigorously as hexane-washed NaH (90 mg, 3.75 mmol, 1.00 equiv) was added in one portion. Evolution of gas was observed and the reaction was stirred at 0 °C for 30 min to give a yellow-orange solution. Additional NaH (202 mg, 8.43 mmol, 2.25 equiv) was added, giving a thick yellow suspension. After 5 min, 4-(bromomethyl)pyridine hydrogen bromide (996 mg, 3.94 mmol, 1.05 equiv) was added portionwise and the reaction was allowed to warm to ambient temperature. After 14 h, the reaction was quenched by addition of 50% sat aqueous NH_4Cl (16 mL) to give a brown biphasic mixture. The phases were separated and the aqueous layer was extracted with Et_2O (3 x 25 mL). The combined organic phases were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2 , 3 x 25 cm, 1:1→1:4 Hexanes:EtOAc→EtOAc) to afford β -ketoester **14i** (1.16 g, 3.23 mmol, 86% yield, 71% yield over 2 steps) as a yellow oil; $R_f = 0.28$, broad (1:2 Hexanes:EtOAc); ^1H NMR (300

MHz, CDCl₃) δ 8.44 (dd, J = 4.4, 1.6 Hz, 2H), 7.06 (dd, J = 4.4, 1.6 Hz, 2H), 5.82 (dddd, J = 17.1, 10.4, 5.8, 5.8 Hz, 1H), 5.37 (s, 1H), 5.28 (app dq, J = 17.2, 1.5 Hz, 1H), 5.21 (app dq, J = 10.4, 1.2 Hz, 1H), 4.61 (dddd, J = 13.1, 5.9, 1.3, 1.3 Hz, 1H), 4.50 (dddd, J = 13.1, 5.9, 1.3, 1.3 Hz, 1H), 3.42 (d, J = 6.5 Hz, 2H), 3.27 (d, J = 13.3 Hz, 1H), 3.18 (d, J = 13.3 Hz, 1H), 2.54 (ddd, J = 17.2, 9.3, 3.0 Hz, 1H), 2.38–2.21 (m, 2H), 2.03–1.86 (m, 2H), 1.83–1.59 (m, 2H), 0.91 (d, J = 6.7 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 197.0, 174.3, 172.3, 149.6, 146.1, 131.4, 126.0, 119.2, 105.6, 74.9, 66.1, 63.5, 42.4, 33.9, 31.5, 27.8, 21.8, 19.2; IR (Neat Film NaCl) 3072, 3026, 2959, 2935, 2874, 1733, 1660, 1608, 1557, 1496, 1470, 1452, 1415, 1384, 1369, 1293, 1272, 1232, 1201, 1172, 1095, 1074, 1005, 994, 956, 935, 862, 823, 773 cm⁻¹; HRMS (EI+) m/z calc'd for C₂₁H₂₇O₄N [M]⁺: 357.1940; found 357.1945.

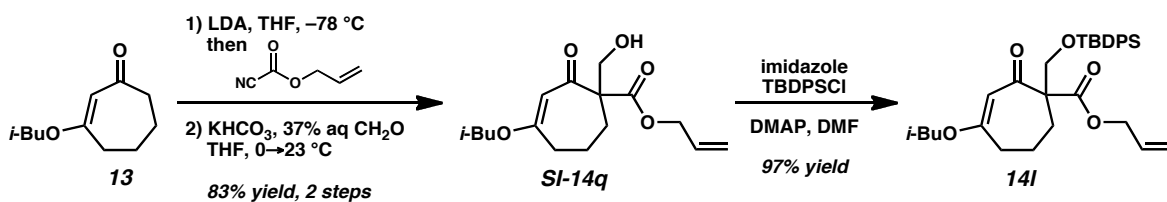


Indolyl β -Ketoester SI-14p. To a solution of diisopropylamine (3.54 mL, 25.27 mmol, 1.20 equiv) in THF (108 mL) in a 250 mL round-bottom flask at 0 °C was added *n*-BuLi (10.26 mL, 24.22 mmol, 2.36 M in hexanes, 1.15 equiv) dropwise over 10 min. After 15 min of stirring at 0 °C, the mixture was cooled to -78 °C using an acetone/CO₂(s) bath. A solution of vinylogous ester **13** (3.84 g, 21.06 mmol, 1.00 equiv) in THF (10 mL) was added dropwise using positive pressure cannulation. After an additional 1 h of stirring at -78 °C, allyl cyanoformate (2.52 mL, 9.74 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at -78 °C for 2.5 h, quenched by addition of 50% sat aqueous NH₄Cl (30.7 mL), and then allowed to warm to ambient temperature. The reaction was diluted with Et₂O (100 mL) and the phases were separated. The aqueous phase was extracted with Et₂O (3 x 100 mL). The combined organic phases were dried over Na₂SO₄, filtered, and concentrated under reduced pressure to afford a pale orange oil. The crude oil was purified by automated flash column chromatography using a Teledyne Isco CombiFlash R_f (SiO₂, 32 g loading cartridge, 330 g column, multi-step gradient, hold 0% [2 min]→ramp to 20% [10 min]→hold 20% [6 min]→ramp to 50% [3 min]→hold 50% EtOAc in Hexanes [11 min]) to afford the intermediate β -ketoester (4.66 g, 17.50 mmol, 83% yield) as a pale orange oil.

A portion of the intermediate β -ketoester (0.85 g, 3.19 mmol, 1.00 equiv) was dissolved in THF (32 mL) in a 100 mL round-bottom flask, cooled to 0 °C, and stirred vigorously as hexane-washed NaH (84 mg, 3.51 mmol, 1.10 equiv) was added in one portion. Evolution of gas was observed and the reaction was stirred at 0 °C for 30 min to give a yellow-orange solution. Gramine methiodide^[3] (1.06 g, 3.35 mmol, 1.05 equiv) was added portionwise to give a suspension. After 11.5 h, the reaction was a brown-orange solution. Additional gramine methiodide (212 mg, 0.67 mmol, 0.31 equiv) was added. After 30 min, the reaction was quenched by addition of 50% sat aqueous NH₄Cl (4.3 mL) to give a brown biphasic mixture. Volatiles were removed under reduced pressure. The residue was extracted with EtOAc (3 x 40 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was

dissolved in a minimal amount of 1:1 Hexanes:EtOAc and filtered through a silica gel pad (1.5 x 10 cm, 1:1 Hexanes:EtOAc). The filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO₂, 5 x 20 cm, 6:1→4:1→2:1 Hexanes:EtOAc) to afford β -ketoester **SI-14p** (1.09 g, 2.75 mmol, 86% yield, 71% yield over 2 steps) as an orange-brown semi-solid; $R_f = 0.21$ (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 8.08 (s, 1H), 7.67–7.54 (m, 1H), 7.38–7.29 (m, 1H), 7.21–7.04 (m, 2H), 7.00 (d, $J = 2.4$ Hz, 1H), 5.84 (dddd, $J = 17.2, 10.4, 5.7, 5.7$ Hz, 1H), 5.37 (s, 1H), 5.29 (app dq, $J = 17.2, 1.5$ Hz, 1H), 5.20 (app dq, $J = 10.4, 1.3$ Hz, 1H), 4.60 (dddd, $J = 13.2, 5.6, 1.4, 1.4$ Hz, 1H), 4.50 (dddd, $J = 13.2, 5.8, 1.4, 1.4$ Hz, 1H), 3.52 (dd, $J = 14.3, 0.5$ Hz, 1H), 3.47–3.31 (m, 3H), 2.63–2.34 (m, 2H), 2.28 (ddd, $J = 17.8, 7.7, 4.0$ Hz, 1H), 2.02–1.63 (m, 4H), 0.90 (d, $J = 6.7$ Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 198.8, 173.7, 173.2, 135.8, 131.9, 128.8, 124.3, 121.8, 119.5, 119.2, 118.6, 111.1, 111.0, 106.0, 74.7, 65.9, 64.3, 34.0, 32.8, 31.6, 27.8, 21.7, 19.2; IR (Neat Film NaCl) 3785, 3584, 3392, 3079, 3057, 2958, 2930, 2874, 1729, 1641, 1607, 1457, 1457, 1433, 1423, 1384, 1368, 1341, 1233, 1191, 1174, 1127, 1085, 1010, 932, 879, 863, 822, 742 cm⁻¹; HRMS (EI+) m/z calc'd for C₂₄H₂₉O₄N [M]⁺: 395.2097; found 395.2097.

Tosylindolyl β -Ketoester 14j. To a solution of indole **SI-14p** (250 mg, 0.63 mmol, 1.00 equiv) in THF (9 mL) in a 100 mL round-bottom flask was added TsCl (241 mg, 1.26 mmol, 2.00 equiv). The mixture was cooled to 0 °C and stirred vigorously as hexane-washed NaH (61 mg, 2.53 mmol, 4.00 equiv) was added in one portion. The reaction was maintained at 0 °C for 5 min before warming to ambient temperature. After 24 h, the white suspension was cooled to 0 °C and additional TsCl (241 mg, 1.26 mmol, 2.00 equiv) was added, followed by hexane-washed NaH (121 mg, 5.06 mmol, 8.00 equiv) in one portion. The reaction was allowed to warm to ambient temperature. After 46 h, the reaction was quenched by addition of 50% sat aqueous NH₄Cl (3 mL). The phases were separated and the aqueous phase was extracted with Et₂O (3 x 15 mL). The combined organic phases were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO₂, 3 x 25 cm, 10:1→6:1→4:1 Hexanes:EtOAc) to afford β -ketoester **14j** (317 mg, 5.76 mmol, 91% yield) as a yellow foam; $R_f = 0.40$ (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 7.97–7.89 (m, 1H), 7.75–7.66 (m, 2H), 7.53–7.44 (m, 1H), 7.35 (s, 1H), 7.31–7.13 (m, 4H), 5.77 (dddd, $J = 17.1, 10.4, 5.8$ Hz, 1H), 5.39 (s, 1H), 5.25 (app dq, $J = 17.2, 1.5$ Hz, 1H), 5.18 (app dq, $J = 10.4, 1.2$ Hz, 1H), 4.52 (dddd, $J = 13.1, 5.7, 1.3, 1.3$ Hz, 1H), 4.42 (dddd, $J = 13.2, 5.9, 1.3, 1.3$ Hz, 1H), 3.48–3.32 (m, 3H), 3.26 (d, $J = 14.4$ Hz, 1H), 2.52 (ddd, $J = 17.7, 9.2, 3.3$ Hz, 1H), 2.41–2.19 (m, 5H), 2.02–1.82 (m, 2H), 1.78–1.58 (m, 2H), 0.92 (d, $J = 6.7$ Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 197.8, 174.0, 172.8, 144.8, 135.4, 134.9, 132.1, 131.6, 129.9, 127.0, 125.8, 124.6, 123.2, 119.9, 118.9, 118.0, 113.7, 105.9, 74.8, 66.1, 63.6, 34.1, 32.2, 31.7, 27.9, 21.7, 21.6, 19.2; IR (Neat Film NaCl) 3854, 3401, 2959, 2931, 2874, 1731, 1657, 1650, 1609, 1448, 1368, 1279, 1233, 1188, 1173, 1121, 1098, 1087, 1019, 1007, 992, 976, 938, 864, 813, 748 cm⁻¹; HRMS (FAB+) m/z calc'd for C₃₁H₃₆O₆N [M+H]⁺: 550.2263; found 550.2250.



Hydroxy β -Ketoester SI-14q. To a solution of diisopropylamine (1.84 mL, 13.15 mmol, 1.20 equiv) in THF (54 mL) in a 250 mL round-bottom flask at $0\text{ }^\circ\text{C}$ was added *n*-BuLi (5.12 mL, 12.60 mmol, 2.51 M in hexanes, 1.15 equiv) dropwise over 10 min. After 15 min of stirring at $0\text{ }^\circ\text{C}$, the mixture was cooled to $-78\text{ }^\circ\text{C}$ using an acetone/ $\text{CO}_2(\text{s})$ bath. A solution of vinylogous ester **13** (2.00 g, 10.96 mmol, 1.00 equiv) in THF (4 mL) was added dropwise using positive pressure cannulation. After an additional 1 h of stirring at $-78\text{ }^\circ\text{C}$, allyl cyanoformate (1.34 mL, 12.06 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at $-78\text{ }^\circ\text{C}$ for 2.5 h, quenched by addition of 50% sat aqueous NH_4Cl (16 mL), and then allowed to warm to ambient temperature. The reaction was diluted with Et_2O (200 mL) and the phases were separated. The aqueous phase was extracted with Et_2O (3 x 100 mL). The combined organic phases were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure to afford a pale orange oil (2.92 g).

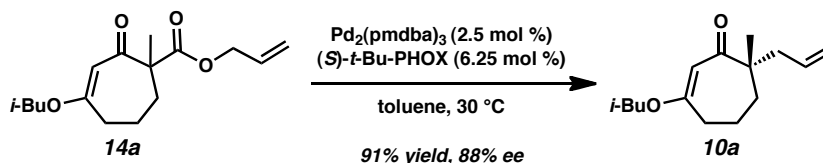
Half of the crude oil (1.46 g) was dissolved in THF (10 mL) in a 50 mL round-bottom flask and cooled to $0\text{ }^\circ\text{C}$. KHCO_3 (1.65 g, 16.44 mmol, 3.00 equiv) and 37% wt. aqueous formaldehyde (2.81 mL, 37.73 mmol, 6.9 equiv) were added. The reaction was allowed to warm to ambient temperature. After 11 h, the reaction was diluted with H_2O and CH_2Cl_2 (25 mL each). The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (4 x 12 mL). The combined organic phases were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2 , 3 x 25 cm, 4:1 \rightarrow 2:1 \rightarrow 1:1 Hexanes:EtOAc) to afford β -ketoester **SI-14q** (1.35 g, 4.55 mmol, 83% yield over 2 steps) as a pale yellow oil; $R_f = 0.21$ (4:1 Hexanes:EtOAc); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 5.89 (dddd, $J = 17.2, 10.4, 5.7, 5.7$ Hz, 1H), 5.43 (s, 1H), 5.32 (app dq, $J = 17.2, 1.5$ Hz, 1H), 5.23 (app dq, $J = 10.4, 1.3$ Hz, 1H), 4.76–4.54 (m, 2H), 3.93–3.72 (m, 2H), 3.51 (d, $J = 6.5$ Hz, 2H), 3.59–3.45 (m, 1H), 2.68–2.50 (m, 1H), 2.50–2.35 (m, 1H), 2.31–2.12 (m, 1H), 2.10–1.91 (m, 2H), 1.91–1.71 (m, 2H), 0.96 (d, $J = 6.7$ Hz, 6H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 200.2, 175.1, 171.9, 131.6, 118.9, 105.6, 75.1, 68.7, 66.1, 63.6, 33.7, 28.6, 27.9, 20.9, 19.2; IR (Neat Film NaCl) 3448, 3083, 2959, 2937, 2875, 1733, 1646, 1608, 1471, 1457, 1420, 1404, 1385, 1369, 1298, 1235, 1195, 1171, 1099, 1044, 998, 928, 869, 825 cm^{-1} ; HRMS (FAB+) m/z calc'd for $\text{C}_{16}\text{H}_{25}\text{O}_5$ $[\text{M}+\text{H}]^+$: 297.1702; found 297.1715.

Siloxy β -Ketoester 14I. Alcohol **SI-14q** (895 mg, 3.02 mmol, 1.00 equiv), DMAP (553 mg, 4.53 mmol, 1.50 equiv), and imidazole (308 mg, 4.53 mmol, 1.50 equiv) were dissolved in DMF (11 mL) in a 20 mL scintillation vial with magnetic stir bar and septum fitted screw cap. TBDPSCI (0.942 mL, 3.62 mmol, 1.20 equiv) was added dropwise. The stirred mixture turned into a turbid white suspension within 5 min. After 54 h, the reaction was poured into H_2O (35 mL) and 2:1 CH_2Cl_2 /Hexanes (75 mL). The phases were separated and the aqueous layer was further extracted with 2:1 CH_2Cl_2 /Hexanes (4 x 35 mL). The combined organics were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2 , 5 x 25 cm, 40:1 \rightarrow 20:1 Hexanes:EtOAc) to afford siloxy β -ketoester **14I** (1.567 g, 2.93 mmol, 97% yield) as a clear, colorless oil; $R_f = 0.58$ (4:1 Hexanes:EtOAc); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.70–7.61 (m, 4H), 7.47–7.32 (m, 6H), 5.86

(dddd, $J = 17.1, 10.5, 5.7, 5.7$ Hz, 1H), 5.39 (s, 1H), 5.29 (app dq, $J = 17.2, 1.5$ Hz, 1H), 5.19 (app dq, $J = 10.4, 1.2$ Hz, 1H), 4.65 (dddd, $J = 13.2, 5.7, 1.3, 1.3$ Hz, 1H), 4.52 (dddd, $J = 13.3, 5.7, 1.3, 1.3$ Hz, 1H), 4.15 (d, $J = 9.6$ Hz, 1H), 4.05 (d, $J = 9.6$ Hz, 1H), 3.47 (d, $J = 6.5$ Hz, 2H), 2.80–2.51 (m, 2H), 2.43 (ddd, $J = 11.0, 7.4, 2.9$ Hz, 1H), 2.17–1.89 (m, 3H), 1.89–1.68 (m, 1H), 1.04 (s, 9H), 0.95 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 197.5, 174.8, 171.6, 135.8, 135.7, 133.3, 133.2, 131.89, 129.8, 129.7, 127.8, 127.7, 118.5, 105.8, 74.8, 69.0, 65.9, 65.1, 34.5, 30.0, 27.8, 26.8, 21.9, 19.4, 19.2; IR (Neat Film NaCl) 3460, 3071, 3049, 2958, 2931, 2890, 2857, 1738, 1650, 1609, 1472, 1429, 1384, 1362, 1299, 1236, 1200, 1173, 1113, 1007, 998, 936, 864, 822, 740 cm^{-1} ; HRMS (FAB+) m/z calc'd for $\text{C}_{32}\text{H}_{43}\text{O}_5\text{Si}$ $[\text{M}+\text{H}]^+$: 535.2880; found 535.2880.

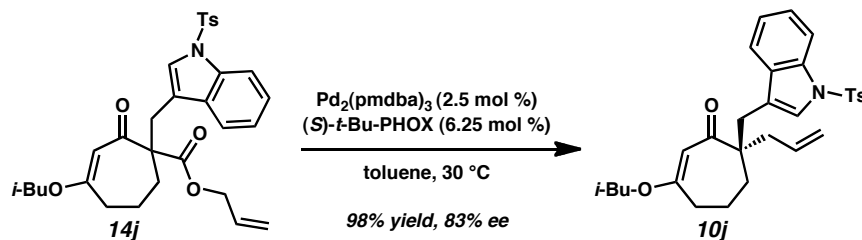
Procedures for Synthesis of Enantioenriched Vinylogous Esters 10 using Enantioselective Decarboxylative Alkylation Reactions

General Method SI-A: Schlenk Manifold Method



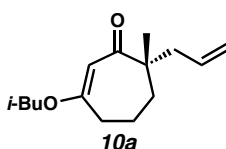
Vinylogous Ester 10a. $\text{Pd}_2(\text{pmdba})_3$ (5.0 mg, 4.5 μmol , 2.5 mol %) and $(S)\text{-}t\text{-Bu-PHOX}$ (4.4 mg, 11 μmol , 6.25 mol %) were placed in a 1 dram vial. The flask was evacuated/backfilled with N_2 (3 cycles, 10 min evacuation per cycle). Toluene (1.3 mL, sparged with N_2 for 1 h immediately before use) was added and the black suspension was immersed in an oil bath preheated to 30 °C. After 30 min of stirring, β -ketoester **14a** (50.7 mg, 0.181 mmol, 1.00 equiv) was added as a solution in toluene (0.5 mL, sparged with N_2 immediately before use) using positive pressure cannulation. The dark orange catalyst solution turned olive green immediately upon addition of β -ketoester **14a**. The reaction was stirred at 30 °C for 21 h, allowed to cool to ambient temperature, filtered through a silica gel plug (2 x 2 cm, Et_2O), and concentrated under reduced pressure. The crude oil was purified by preparative TLC (SiO_2 , 4:1 Hexanes:EtOAc) to afford vinylogous ester **10a** (38.8 mg, 0.164 mmol, 91% yield, 88% ee) as a pale yellow oil. (For characterization data, see p. 22).

General Method SI-B: Glove Box Method

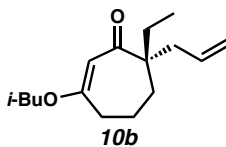


Vinylogous Ester 10j. A 20 mL scintillation vial was loaded with β -ketoester **14j** (447 mg, 0.81 mmol, 1.00 equiv). A separate 20 mL scintillation vial was loaded with $\text{Pd}_2(\text{pmdba})_3$ (19.7 mg,

0.051 mmol, 6.25 mol %), (*S*)-*t*-Bu-PHOX (22.3 mg, 0.020 mmol, 2.5 mol %), and magnetic stir bar. The two vials and a teflon-lined hard cap were evacuated/backfilled with N₂ in a glove box antechamber (3 cycles, 5 min evacuation per cycle) before being transferred into the glove box. Toluene (5 mL) was added to the vial containing Pd₂(pmdba)₃ and (*S*)-*t*-BuPHOX. The vial was capped and heated to 30 °C for 30 min. During this time, the mixture developed a dark orange color. β-Ketoester **14j** was dissolved in toluene (3 mL) and added to the catalyst solution dropwise, causing the solution to turn olive green. The solution was stirred at 30 °C in a heating block. The capped vial was removed from the glove box after 29 h of stirring. The crude product was concentrated under reduced pressure and purified by flash column chromatography (SiO₂, 5 x 25 cm, 15:1→10:1→8:1→6:1 Hexanes:EtOAc) to afford vinylogous ester **10j** (403 mg, 0.796 mmol, 98% yield, 82.9% ee) as a thick, white semi-solid. (For characterization data, see p. 26).

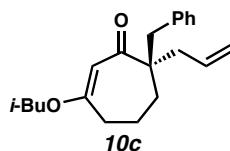


Vinylogous Ester 10a (Table 2, entry 1). Prepared using General Method SI-A. 38.8 mg, 0.164 mmol, 91% yield. Preparative TLC (SiO₂, 4:1 Hexanes:EtOAc); R_f = 0.31 (3:1 Hexanes:Et₂O); ¹H NMR (500 MHz, CDCl₃) δ 5.72 (dddd, *J* = 16.6, 10.5, 7.3, 7.3 Hz, 1H), 5.31 (s, 1H), 5.05–5.00 (m, 2H), 3.50 (dd, *J* = 9.3, 6.6 Hz, 1H), 3.47 (dd, *J* = 9.3, 6.6 Hz, 1H), 2.53–2.42 (m, 2H), 2.38 (dd, *J* = 13.7, 7.1 Hz, 1H), 2.20 (dd, *J* = 13.7, 7.8 Hz, 1H), 1.98 (app sept, *J* = 6.6 Hz, 1H), 1.86–1.70 (m, 3H), 1.62–1.56 (m, 1H), 1.14 (s, 3H), 0.95 (d, *J* = 6.6 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 206.7, 171.3, 134.6, 117.9, 105.0, 74.5, 51.5, 45.4, 36.1, 35.2, 28.0, 25.2, 19.9, 19.3, 19.3; IR (Neat Film NaCl) 2960, 2933, 2873, 1614, 1470, 1387, 1192, 1171, 998, 912 cm⁻¹; HRMS (EI+) *m/z* calc'd for C₁₅H₂₄O₂ [M]⁺: 236.1776; found 236.1767; [α]_D^{25.6} –69.04 (*c* 1.08, CHCl₃, 88.0% ee); HPLC conditions: 1% IPA in Hexanes, 1.0 mL/min, OD-H column, t_R (min): major = 6.30, minor = 7.26.

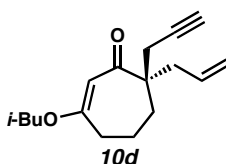


Vinylogous Ester 10b (Table 2, entry 2). Prepared using General Method SI-A. 226.3 mg, 0.90 mmol, 89% yield. Flash column chromatography (SiO₂, 3 x 24 cm, 20:1→15:1→10:1 Hexanes:EtOAc); R_f = 0.43 (10:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 5.82–5.62 (m, 1H), 5.29 (s, 1H), 5.06–4.98 (m, 2H), 3.48 (dd, *J* = 11.1, 6.6 Hz, 1H), 3.45 (dd, *J* = 11.2, 6.6 Hz, 1H), 2.49–2.42 (m, 2H), 2.40 (dddd, *J* = 13.8, 7.1, 1.2 Hz, 1H), 2.23 (dddd, *J* = 13.8, 7.7, 1.1, 1.1 Hz, 1H), 1.97 (app sept, *J* = 6.7 Hz, 1H), 1.84–1.44 (m, 6H), 0.98–0.91 (d, *J* = 6.7 Hz, 6H), 0.79 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 206.2, 171.0, 135.1, 117.6, 105.5, 74.4, 54.8, 41.9, 36.1, 32.3, 31.3, 28.0, 20.0, 19.3, 8.6; IR (Neat Film NaCl) 3073, 2960, 2933, 2876, 1617, 1613, 1459, 1400, 1387, 1369, 1314, 1220, 1190, 1173, 996, 969, 954, 912, 883, 873, 856, 782 cm⁻¹; HRMS (EI+) *m/z* calc'd for C₁₆H₂₆O₂ [M]⁺: 250.1933; found 250.1909;

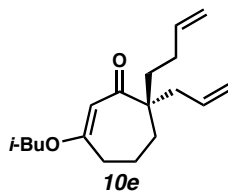
$[\alpha]_D^{25.0} +25.83$ (*c* 1.04, CHCl₃, 91.6% ee); HPLC conditions: 0.25% IPA in Hexanes, 1.0 mL/min, AD column, *t_R* (min): minor = 16.23, major = 18.08.



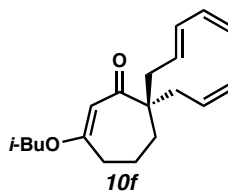
Vinylogous Ester 10c (Table 2, entry 3). Prepared using General Method SI-A. 172.5 mg, 0.552 mmol, 98% yield. Flash column chromatography (SiO₂, 3 x 24 cm, 20:1→15:1→10:1 Hexanes:EtOAc); *R_f* = 0.50 (10:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 7.28–7.14 (m, 3H), 7.14–7.08 (m, 2H), 5.85–5.68 (m, 1H), 5.31 (s, 1H), 5.10–4.99 (m, 2H), 3.44 (dd, *J* = 14.7, 6.6 Hz, 1H), 3.41 (dd, *J* = 14.7, 6.6 Hz, 1H), 3.14 (d, *J* = 13.3 Hz, 1H), 2.71 (d, *J* = 13.3 Hz, 1H), 2.51 (dddd, *J* = 13.7, 6.8, 1.2, 1.2 Hz, 1H), 2.45–2.32 (m, 2H), 2.16 (dddd, *J* = 13.7, 7.9, 1.1, 1.1 Hz, 1H), 1.93 (app sept, *J* = 6.7 Hz, 1H), 1.83–1.56 (m, 4H), 0.92 (d, *J* = 6.7 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 205.5, 171.4, 138.3, 134.5, 130.8, 128.0, 126.3, 118.2, 106.3, 74.5, 56.2, 44.1, 43.9, 36.3, 31.3, 27.9, 19.5, 19.3; IR (Neat Film NaCl) 3072, 3061, 3027, 3002, 2957, 2931, 2871, 1610, 1495, 1471, 1454, 1422, 1403, 1387, 1368, 1318, 1280, 1217, 1189, 1173, 1081, 1031, 1007, 969, 957, 913, 875, 856, 831, 760, 746, 733 cm⁻¹; HRMS (EI+) *m/z* calc'd for C₂₁H₂₈O₂ [M]⁺: 312.2089; found 312.2083; $[\alpha]_D^{25.0} +2.91$ (*c* 0.98, CHCl₃, 86.3% ee); HPLC conditions: 0.5% IPA in Hexanes, 1.0 mL/min, OD-H column, *t_R* (min): minor = 13.96, major = 15.70.



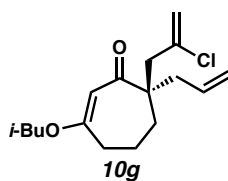
Vinylogous Ester 10d (Table 2, entry 4). Prepared using General Method SI-A. 224.7 mg, 0.86 mmol, 88% yield. Flash column chromatography (SiO₂, 3 x 25 cm, 20:1→15:1 Hexanes:EtOAc); *R_f* = 0.44 (10:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 5.74–5.59 (m, 1H), 5.32 (s, 1H), 5.12–5.02 (m, 2H), 3.50 (dd, *J* = 14.9, 6.5 Hz, 1H), 3.47 (dd, *J* = 14.7, 6.6 Hz, 1H), 2.53–2.48 (m, 4H), 2.46 (dddd, *J* = 13.7, 7.3, 1.2, 1.2 Hz, 1H), 2.35 (dddd, *J* = 13.7, 7.6, 1.1, 1.1 Hz, 1H), 2.09–1.67 (m, 5H), 1.57 (s, 1H), 0.95 (d, *J* = 6.7 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 204.0, 171.7, 133.7, 118.5, 105.0, 81.7, 74.6, 70.8, 54.2, 42.9, 36.1, 32.5, 28.0, 27.1, 20.0, 19.3; IR (Neat Film NaCl) 3301, 3075, 2957, 2930, 2873, 2116, 1612, 1471, 1457, 1435, 1423, 1402, 1387, 1368, 1320, 1221, 1191, 1175, 995, 969, 916, 874, 845 cm⁻¹; HRMS (EI+) *m/z* calc'd for C₁₇H₂₄O₂ [M]⁺: 260.1776; found 260.1737; $[\alpha]_D^{25.0} -26.51$ (*c* 1.03, CHCl₃, 88.5% ee); HPLC conditions: 0.5% IPA in Hexanes, 1.0 mL/min, OD-H column, *t_R* (min): major = 12.35, minor = 13.43.



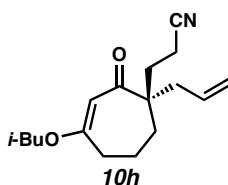
Vinylogous Ester 10e (Table 2, entry 5). Prepared using General Method SI-B. 287.5 mg, 1.04 mmol, 95% yield. Flash column chromatography (SiO₂, 2 x 25 cm, 20:1 Hexanes:EtOAc); R_f = 0.44 (10:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 5.84–5.64 (m, 2H), 5.30 (s, 1H), 5.09–4.87 (m, 4H), 3.49 (dd, *J* = 11.2, 6.6 Hz, 1H), 3.46 (dd, *J* = 11.1, 6.6 Hz, 1H), 2.54–2.37 (m, 3H), 2.27 (dddd, *J* = 13.8, 7.7, 1.2, 1.2 Hz, 1H), 2.07–1.89 (m, 3H), 1.86–1.45 (m, 6H), 0.95 (d, *J* = 6.7 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 205.8, 171.1, 138.9, 134.8, 117.9, 114.5, 105.5, 74.8, 54.4, 42.3, 38.0, 36.1, 32.7, 28.6, 28.0, 19.9, 19.3; IR (Neat Film NaCl) 3076, 2958, 2932, 2874, 1639, 1614, 1471, 1455, 1434, 1424, 1402, 1387, 1368, 1317, 1280, 1216, 1190, 1174, 1086, 996, 969, 955, 910, 878, 853, 829, 771 cm⁻¹; HRMS (EI+) *m/z* calc'd for C₁₈H₂₈O₂ [M]⁺: 276.2089; found 276.2060; [α]_D^{25.0} +15.28 (*c* 0.97, CHCl₃, 86.9% ee); HPLC conditions: 0.8% IPA in Hexanes, 2.0 mL/min, AD column, t_R (min): major = 5.03, minor = 6.06.



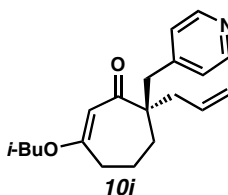
Vinylogous Ester 10f (Table 2, entry 6). Prepared using General Method SI-A. 232.9 mg, 0.81 mmol, 90% yield. Flash column chromatography (SiO₂, 3 x 25 cm, 20:1→15:1 Hexanes:EtOAc); R_f = 0.45 (10:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 6.30 (dt, *J* = 16.9, 10.3 Hz, 1H), 6.04 (dd, *J* = 15.1, 10.4 Hz, 1H), 5.82–5.53 (m, 2H), 5.31 (s, 1H), 5.15–4.92 (m, 4H), 3.48 (d, *J* = 6.5 Hz, 2H), 2.55–2.36 (m, 4H), 2.30–2.16 (m, 2H), 1.98 (app sept, *J* = 6.7 Hz, 1H), 1.84–1.67 (m, 4H), 0.95 (d, *J* = 6.7 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 205.3, 171.4, 137.2, 134.5, 134.1, 130.8, 118.0, 115.5, 105.5, 74.5, 55.1, 43.1, 41.6, 36.1, 32.5, 28.0, 19.9, 19.3; IR (Neat Film NaCl) 3075, 3036, 3007, 2958, 2931, 2873, 1726, 1635, 1611, 1471, 1456, 1436, 1402, 1387, 1368, 1312, 1277, 1219, 1190, 1173, 1085, 1005, 954, 911, 874, 831 cm⁻¹; HRMS (FAB+) *m/z* calc'd for C₁₉H₂₉O₂ [M+H]⁺: 289.2168; found 289.2172; [α]_D^{25.0} -20.62 (*c* 1.05, CHCl₃, 89.6% ee); SFC conditions: 5.0% IPA in Hexanes, 2.5 mL/min, AD-H column, t_R (min): minor = 6.31, major = 6.99.



Vinylogous Ester 10g (Table 2, entry 7). Prepared using General Method SI-A. 259.5 mg, 0.87 mmol, 99% yield. Flash column chromatography (SiO₂, 3 x 25 cm, 20:1→15:1 Hexanes:EtOAc); R_f = 0.36 (10:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 5.78–5.62 (m, 1H), 5.36 (s, 1H), 5.25 (s, 1H), 5.14 (s, 1H), 5.11–5.01 (m, 2H), 3.54–3.43 (m, 2H), 2.95 (dd, *J* = 14.4, 0.7 Hz, 1H), 2.54–2.41 (m, 4H), 2.25 (dddd, *J* = 13.9, 7.9, 1.1, 1.1 Hz, 1H), 2.07–1.89 (m, 2H), 1.88–1.70 (m, 3H), 0.95 (d, *J* = 6.7 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 204.3, 171.6, 139.4, 133.9, 118.7, 116.6, 105.9, 74.6, 54.7, 46.7, 43.7, 36.3, 31.5, 28.0, 19.6, 19.3; IR (Neat Film NaCl) 3075, 2958, 2934, 2874, 1612, 1471, 1458, 1424, 1403, 1388, 1368, 1339, 1321, 1297, 1222, 1192, 1175, 1082, 1010, 995, 968, 956, 916, 875, 847, 746 cm⁻¹; HRMS (FAB+) *m/z* calc'd for C₁₇H₂₆O₂Cl [M+H]⁺: 297.1621; found 297.1623; [α]_D^{25.0} +4.20 (*c* 1.02, CHCl₃, 85.7% ee); HPLC conditions: 0.1% IPA in Hexanes, 1.0 mL/min, OD-H column, t_R (min): minor = 24.19, major = 27.22.

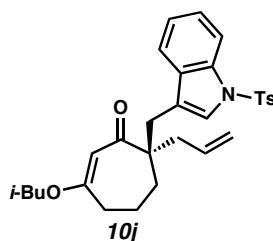


Vinylogous Ester 10h (Table 2, entry 8). Prepared using General Method SI-A. 292.8 mg, 1.06 mmol, 96% yield. (SiO₂, 3 x 25 cm, 20:1→10:1→8:1→6:1 Hexanes:EtOAc); R_f = 0.39 broad (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 5.75–5.58 (m, 1H), 5.31 (s, 1H), 5.15–5.04 (m, 2H), 3.48 (d, *J* = 6.5 Hz, 2H), 2.51 (t, *J* = 6.1 Hz, 2H), 2.40 (dddd, *J* = 14.0, 7.0, 1.2, 1.2 Hz, 1H), 2.35–2.22 (m, 3H), 2.11–1.93 (m, 2H), 1.93–1.62 (m, 5H), 0.96 (d, *J* = 6.7 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 203.9, 172.1, 133.1, 120.3, 119.2, 104.9, 74.7, 53.6, 41.8, 36.1, 33.9, 32.8, 28.0, 19.8, 19.3, 12.8; IR (Neat Film NaCl) 3076, 2958, 2933, 2874, 2246, 1635, 1609, 1472, 1458, 1420, 1404, 1388, 1368, 1319, 1281, 1214, 1192, 1175, 1084, 1003, 917, 880, 854, 827, 766 cm⁻¹; HRMS (EI+) *m/z* calc'd for C₁₇H₂₅O₂N [M]⁺: 275.1885; found 275.1893; [α]_D^{25.0} -20.97 (*c* 1.06, CHCl₃, 87.4% ee); HPLC conditions: 5.0% IPA in Hexanes, 1.0 mL/min, OD-H column, t_R (min): major = 10.67, minor = 14.66.

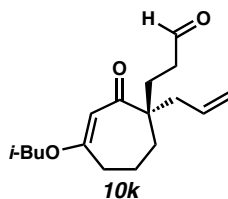


Vinylogous Ester 10i (Table 2, entry 9). Prepared using General Method SI-B. 339.6 mg, 1.08 mmol, 97% yield. Flash column chromatography (SiO₂, 3 x 20 cm, 1:1→ 1:4

Hexanes:EtOAc→EtOAc); $R_f = 0.28$, broad (1:2 Hexanes:EtOAc); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 8.45 (dd, $J = 4.5, 1.5$ Hz, 2H), 7.05 (dd, $J = 4.5, 1.6$ Hz, 2H), 5.84–5.66 (m, 1H), 5.31 (s, 1H), 5.15–5.02 (m, 2H), 3.44 (dd, $J = 15.1, 6.3$ Hz, 1H), 3.41 (dd, $J = 15.0, 6.3$ Hz, 1H), 3.20 (d, $J = 12.9$ Hz, 1H), 2.60 (d, $J = 12.9$ Hz, 1H), 2.48 (dddd, $J = 13.8, 6.9, 1.2, 1.2$ Hz, 1H), 2.43–2.29 (m, 2H), 2.23 (dddd, $J = 13.8, 7.8, 1.1, 1.1$ Hz, 1H), 1.94 (app sept, $J = 6.7$ Hz, 1H), 1.84–1.67 (m, 2H), 1.67–1.51 (m, 2H), 0.92 (d, $J = 6.7$ Hz, 6H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 204.4, 171.8, 149.5, 147.6, 133.7, 126.2, 118.9, 106.0, 74.6, 55.8, 43.8, 43.5, 36.2, 31.5, 27.9, 19.4, 19.3; IR (Neat Film NaCl) 3072, 3024, 2957, 2931, 2873, 1608, 1558, 1496, 1471, 1458, 1438, 1415, 1388, 1368, 1320, 1220, 1190, 1173, 1072, 994, 957, 916, 876, 844, 796 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{20}\text{H}_{27}\text{O}_2\text{N}$ $[\text{M}]^+$: 313.2042; found 313.2045; $[\alpha]_{\text{D}}^{25.0} +22.44$ (c 1.16, CHCl_3 , 84.6% ee); HPLC conditions: 5.0% EtOH in Hexanes, 1.0 mL/min, AD column, t_{R} (min): major = 13.22, minor = 15.13.

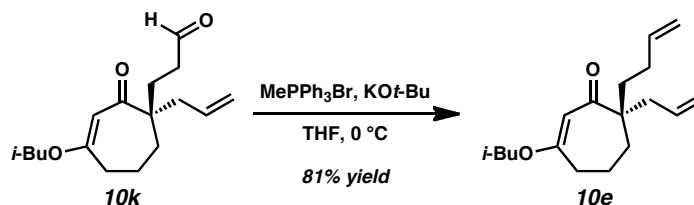


Vinylogous Ester 10j (Table 2, entry 10). Prepared using General Method SI-B. 403 mg, 0.796 mmol, 98% yield. Flash column chromatography (SiO_2 , 5 x 25 cm, 15:1→10:1→8:1→6:1 Hexanes:EtOAc); $R_f = 0.49$ (4:1 Hexanes:EtOAc); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.96 (dm, $J = 8.4$ Hz, 1H), 7.70 (dm, $J = 8.4$ Hz, 2H), 7.48 (dm, $J = 7.9$ Hz, 1H), 7.31–7.13 (m, 5H), 5.86–5.68 (m, 1H), 5.32 (s, 1H), 5.13–5.00 (m, 2H), 3.42 (dd, $J = 17.0, 7.7$ Hz, 1H), 3.38 (dd, $J = 17.0, 7.6$ Hz, 1H), 3.20 (dd, $J = 14.2, 0.7$ Hz, 1H), 2.73 (d, $J = 14.1$ Hz, 1H), 2.51 (dddd, $J = 13.7, 6.9, 1.3, 1.3$ Hz, 1H), 2.44–2.15 (m, 6H), 1.92 (app sept, $J = 6.7$ Hz, 1H), 1.76–1.46 (m, 4H), 0.92 (d, $J = 6.7$ Hz, 6H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 205.2, 171.7, 144.8, 135.4, 135.0, 134.1, 132.4, 129.8, 126.9, 125.4, 124.5, 123.2, 120.1, 119.6, 118.6, 113.8, 106.4, 74.6, 55.9, 44.1, 36.3, 33.0, 31.9, 27.9, 21.7, 19.5, 19.3; IR (Neat Film NaCl) 3584, 3401, 2068, 2958, 2930, 2873, 1609, 1494, 1470, 1448, 1422, 1402, 1368, 1306, 1279, 1215, 1188, 1174, 1120, 1097, 1020, 975, 916, 876, 813, 782, 747 cm^{-1} ; HRMS (FAB+) m/z calc'd for $\text{C}_{30}\text{H}_{36}\text{O}_4\text{NS}$ $[\text{M}+\text{H}]^+$: 506.2365; found 506.2358; $[\alpha]_{\text{D}}^{25.0} +9.10$ (c 1.00, CHCl_3 , 82.9% ee); HPLC conditions: 5.0% EtOH in Hexanes, 1.0 mL/min, AD column, t_{R} (min): major = 11.11, minor = 16.64.

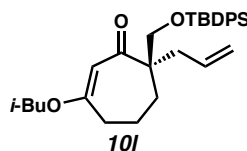


Vinylogous Ester 10k (Table 2, entry 11). Prepared using General Method SI-B. 77.3 mg, 0.278 mmol, 90% yield. Flash column chromatography (SiO_2 , 2 x 25 cm, 6:1→4:1 Hexanes:EtOAc); $R_f = 0.35$, broad (4:1 Hexanes:EtOAc); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 9.73

(t, $J = 1.5$ Hz, 1H), 5.78–5.61 (m, 1H), 5.29 (s, 1H), 5.11–5.02 (m, 2H), 3.47 (m, 2H), 2.54–2.33 (m, 5H), 2.28 (dddd, $J = 14.0, 7.6, 1.2, 1.2$ Hz, 1H), 2.07–1.73 (m, 5H), 1.73–1.56 (m, 2H), 0.95 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 205.0, 202.3, 171.7, 134.0, 118.5, 105.2, 74.6, 53.6, 42.1, 39.4, 36.1, 33.1, 30.3, 28.0, 19.9, 19.3; IR (Neat Film NaCl) 3075, 2958, 2931, 2719, 1724, 1611, 1471, 1458, 1421, 1403, 1388, 1368, 1213, 1191, 1175, 998, 915, 878 cm^{-1} ; HRMS (FAB+) m/z calc'd for $\text{C}_{17}\text{H}_{27}\text{O}_3$ $[\text{M}+\text{H}]^+$: 279.1960; found 279.1969; $[\alpha]_{\text{D}}^{25.0} +15.37$ (c 1.03, CHCl_3 , 79.5% ee); Compound **10k** was derivatized using procedure below to determine ee using the corresponding chiral HPLC assay for vinylogous ester **10e**.

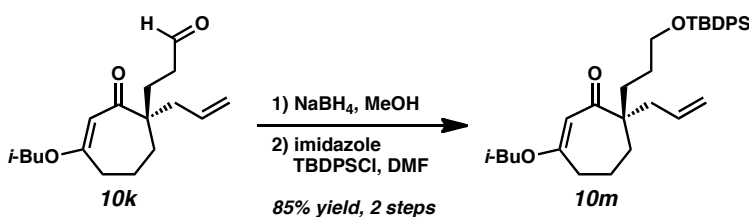


Vinylogous Ester 10e. To a solution of MePh_3PBr (323.2 mg, 0.905 mmol, 0.84 equiv) in THF (14.0 mL) in a 50 mL round-bottom flask at 0°C was added $\text{KO}t\text{-Bu}$ (84.6 mg, 0.754 mmol, 0.699 equiv) to give a bright yellow suspension. Aldehyde **10k** (299.9 mg, 1.078 mmol, 1.00 equiv) in THF (2 mL) was added to the suspension using positive pressure cannulation and maintained at 0°C . The reaction faded to an off-white suspension. After 1.5 h of stirring, an additional portion of Wittig reagent was prepared in a 20 mL scintillation vial. MePPh_3Br (323.2 mg, 0.905 mmol, 0.84 equiv) was added to the vial. The vial was sealed with a septum, evacuated/backfilled with N_2 (3 cycles, 5 min evacuation per cycle). Anhydrous THF (3 mL) was added and the vial was cooled to 0°C . $\text{KO}t\text{-Bu}$ (84.6 mg, 0.754 mmol, 0.699 equiv) was added in one portion, giving a bright yellow suspension which was added to the reaction flask using positive pressure cannulation. The tan suspension was stirred at 0°C for 1 h. An additional portion of Wittig reagent using MePPh_3Br (323.2 mg, 0.905 mmol, 0.84 equiv), $\text{KO}t\text{-Bu}$ (84.6 mg, 0.754 mmol, 0.699 equiv) and THF (3 mL) was prepared at 0°C and added using positive pressure cannulation as previously described. The reaction showed a persistent yellow color. After 30 min of stirring at 0°C , the reaction was quenched by addition of sat aqueous NH_4Cl (5 mL) and stirred for 30 min while the mixture was allowed to warm to ambient temperature. The mixture was extracted with Et_2O (3 x 20 mL), dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2 , 3 x 25 cm, 1% \rightarrow 2% \rightarrow 3% \rightarrow 5% EtOAc in Hexanes) to afford vinylogous ester **10e** (243.7 mg, 0.882 mmol, 81% yield) as a yellow liquid; HPLC conditions: 0.8% IPA in Hexanes, 2.0 mL/min, AD column, t_{R} (min): major = 4.39, minor = 3.17. (For characterization data, see p. 24).



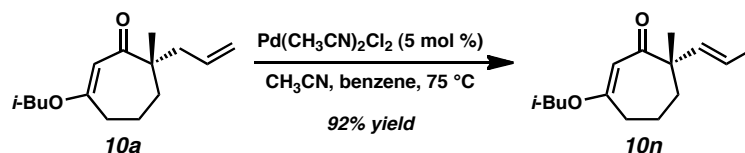
Vinylogous Ester 10l. Prepared using General Method SI-B. 242.0 mg, 0.493 mmol, 66% yield. Flash column chromatography (SiO_2 , 3 x 25 cm, 2% \rightarrow 5% \rightarrow 10% EtOAc in Hexanes); $R_f = 0.44$ (10:1 Hexanes: EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 7.67–7.61 (m, 4H), 7.46–7.33 (m,

6H), 5.78–5.60 (m, 1H), 5.32 (s, 1H), 5.08–4.96 (m, 2H), 3.78 (d, $J = 9.7$ Hz, 1H), 3.67 (d, $J = 9.7$ Hz, 1H), 3.46 (dd, $J = 14.7, 6.5$ Hz, 1H), 3.43 (dd, $J = 14.6, 6.5$ Hz, 1H), 2.49 (dddd, $J = 13.7, 6.6, 1.3, 1.3$ Hz, 1H), 2.48–2.41 (m, 2H), 2.33 (dddd, $J = 13.8, 7.8, 1.2, 1.2$ Hz, 1H), 2.09–1.88 (m, 2H), 1.82–1.65 (m, 3H), 1.04 (s, 9H), 0.95 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 204.5, 171.5, 135.9, 135.8, 134.7, 133.7, 133.5, 129.7, 127.8, 127.7, 117.8, 106.1, 74.5, 69.0, 57.4, 41.0, 36.3, 30.3, 28.0, 27.0, 20.0, 19.5, 19.3; IR (Neat Film NaCl) 3071, 3050, 2957, 2930, 2857, 1731, 1614, 1472, 1428, 1402, 1388, 1368, 1315, 1261, 1222, 1190, 1174, 1112, 1007, 998, 969, 955, 938, 914, 880, 824, 810, 740 cm^{-1} ; HRMS (FAB+) m/z calc'd for $\text{C}_{31}\text{H}_{43}\text{O}_3\text{Si}$ $[\text{M}+\text{H}]^+$: 491.2982; found 491.2993; $[\alpha]_{\text{D}}^{25.0} -6.72$ (c 1.09, CHCl_3 , 57.8% ee); HPLC conditions: 0.2% IPA in Hexanes, 1.0 mL/min, OD-H column, t_{R} (min): major = 21.74, minor = 25.53.

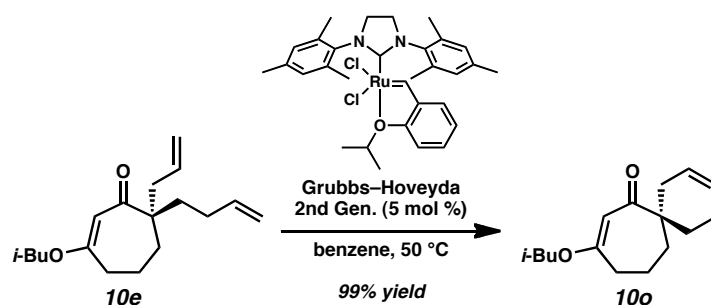


Vinylogous Ester 10m. A round-bottom flask with magnetic stir bar was charged with aldehyde **10k** (40.2 mg, 0.14 mmol, 1.00 equiv) and MeOH (3.0 mL). The flask was cooled to 0 °C and NaBH_4 (5.5 mg, 0.14 mmol, 1.00 equiv) was added slowly portionwise. The mixture was stirred for 1 h at 0 °C. Sat aqueous NaHCO_3 (3 mL) was added, followed by CH_2Cl_2 (10 mL). The mixture was stirred vigorously for 5 min. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). Combined organic phases were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude alcohol was used directly in the next step without further purification. $R_f = 0.29$ (2:1 Hexanes:EtOAc).

To a 2 dram vial with a solution of crude alcohol and imidazole (11.8 mg, 0.17 mmol, 1.20 equiv) in DMF (0.7 mL) at 0 °C was added TBDPSCl (39.6 μL , 0.14 mmol, 1.00 equiv) dropwise. After 2 h of stirring, the reaction was quenched by addition of H_2O (0.3 mL) and extracted with Et_2O (5 x 5 mL). The combined organics were dried over MgSO_4 , filtered, and concentrated under reduced pressure. The residue was purified by automated flash column chromatography using a Teledyne Isco CombiFlash R_f (SiO_2 , 12 g loading cartridge, 80 g column, multi-step gradient, hold 2% [2 min]→ramp to 5% [10 min]→hold 5% [10 min]→ramp to 10% [32 min]→hold 10% Et_2O in Hexanes [5 min]) to afford vinylogous ester **10m** (63.3 mg, 0.12 mmol, 85% yield over 2 steps) as a pale, white oil; $R_f = 0.42$ (10:1 Hexanes:EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 7.69–7.62 (m, 4H), 7.46–7.33 (m, 6H), 5.82–5.62 (m, 1H), 5.29 (s, 1H), 5.08–4.96 (m, 2H), 3.61 (t, $J = 6.1$ Hz, 2H), 3.48 (dd, $J = 13.7, 6.6$ Hz, 1H), 3.45 (dd, $J = 13.7, 6.6$ Hz, 1H), 2.50–2.43 (m, 2H), 2.40 (dddd, $J = 13.8, 7.0, 1.2$ Hz, 1H), 2.25 (dddd, $J = 13.9, 7.8, 1.1$ Hz, 1H), 1.98 (app sept, $J = 6.7$ Hz, 1H), 1.86–1.38 (m, 8H), 1.04 (s, 9H), 0.95 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 206.0, 171.0, 135.7, 134.9, 134.1, 129.6, 127.7, 117.7, 105.2, 74.4, 64.4, 54.2, 42.1, 36.1, 34.8, 32.8, 28.0, 27.3, 27.0, 20.0, 19.3; IR (Neat Film NaCl) 3071, 3051, 3013, 2998, 2956, 2930, 2858, 1614, 1471, 1428, 1401, 1387, 1368, 1311, 1214, 1188, 1174, 1111, 1028, 1007, 998, 966, 913, 872, 823, 780, 740, 725 cm^{-1} ; HRMS (FAB+) m/z calc'd for $\text{C}_{33}\text{H}_{47}\text{O}_3\text{Si}$ $[\text{M}+\text{H}]^+$: 519.3295; found 519.3275; $[\alpha]_{\text{D}}^{25.0} +9.06$ (c 0.95, CHCl_3 , 88.0% ee).



Vinylogous Ester 10n. $\text{Pd}(\text{CH}_3\text{CN})_2\text{Cl}_2$ (49.1 mg, 0.189 mmol, 5 mol %) was placed in a 50 mL round-bottom Schlenk flask and evacuated/backfilled with N_2 (3 cycles, 5 min per cycle). Benzene (10 mL) was added, followed by acetonitrile (90 μL). A solution of vinylogous ester **10a** (895 mg, 3.79 mmol, 1.00 equiv) in benzene (5.0 mL) was added using positive pressure cannulation. The resulting orange solution was heated to 75 °C in an oil bath. After 11 h of stirring, the reaction was cooled to ambient temperature, filtered through a Celite plug (eluted with Et_2O), and concentrated carefully under reduced pressure, allowing for a film of ice to form on the outside of the flask, to afford a pale yellow oil. The crude oil was purified by automated flash column chromatography using a Teledyne Isco CombiFlash R_f (SiO_2 , 25 g loading cartridge, 80 g column, linear gradient, 0 \rightarrow 10% EtOAc in Hexanes [33 min]) to afford vinylogous ester **10n** (823.6 mg, 3.48 mmol, 92% yield) in a 20:1 ratio to isomeric starting material **10a**. Analytically pure samples could be obtained using the above column conditions; R_f = 0.56 (4:1 Hexanes: EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 5.56 (dq, J = 15.7, 1.4 Hz, 1H), 5.41 (dq, J = 15.7, 6.2, Hz, 1H), 5.34 (s, 1H), 3.48 (d, J = 6.5 Hz, 2H), 2.63–2.33 (m, 2H), 2.04–1.91 (m, 1H), 1.90–1.70 (m, 4H), 1.67 (dd, J = 6.2, 1.4 Hz, 3H), 1.22 (s, 3H), 0.95 (d, J = 6.7 Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 205.3, 171.6, 136.5, 123.9, 105.2, 74.5, 53.9, 36.2, 33.3, 28.0, 27.2, 20.2, 19.3, 18.4; IR (Neat Film NaCl) 3022, 2960, 2873, 1614, 1471, 1455, 1423, 1402, 1387, 1370, 1212, 1192, 1173, 1120, 967, 883, 858, 827 cm^{-1} ; HRMS (MM: ESI-APCI+) m/z calc'd for $\text{C}_{15}\text{H}_{25}\text{O}_2$ $[\text{M}+\text{H}]^+$: 237.1849; found 237.1848; $[\alpha]_D^{25.0}$ +4.05 (c 1.39, CHCl_3 , 88.0 % ee).



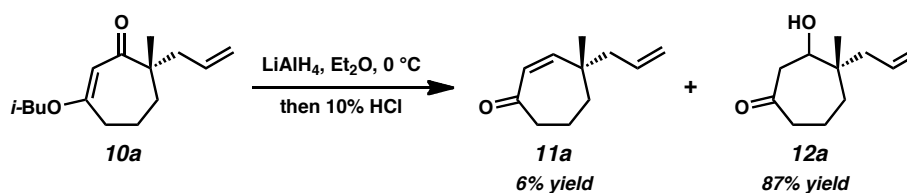
Vinylogous Ester 10o. Vinylogous ester **10e** (100 mg, 0.362 mmol, 1.00 equiv) was added to a 50 mL 2-neck flask fitted with a rubber septum and oven-dried reflux condenser. The flask was evacuated/backfilled with Ar (3 cycles, 5 min evacuation per cycle). Dry degassed benzene (36.2 mL, sparged with N_2 for 1 h immediately before use) was added. Grubbs–Hoveyda 2nd Generation catalyst (11.3 mg, 18.1 μmol , 5 mol %) was added to the reaction, giving the solution an olive green color. The mixture was kept under Ar , stirred until homogeneous, and heated to 50 °C using an oil bath. After 30 min of stirring, the reaction was cooled to ambient temperature and several drops of ethyl vinyl ether were added. After 30 min, the reaction developed a deep brown color. The mixture was concentrated under reduced pressure and filtered through a silica

gel plug (3 x 5 cm, 1:1 Hexanes:Et₂O). The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (SiO₂, 3 x 25 cm, 20:1→15:1→10:1 Hexanes:EtOAc) to afford vinylogous ester **10o** (89.2 mg, 0.359 mmol, 99% yield) as a white solid. $R_f = 0.39$ (10:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 5.69–5.58 (m, 2H), 5.30 (s, 1H), 3.49 (dd, $J = 14.4, 6.5$ Hz, 1H), 3.46 (dd, $J = 14.3, 6.5$ Hz, 1H), 2.70–2.57 (m, 1H), 2.54–2.44 (m, 2H), 2.08–1.91 (m, 3H), 1.91–1.57 (m, 7H), 0.95 (d, $J = 6.7$ Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 207.2, 171.3, 125.6, 125.4, 104.0, 74.4, 50.5, 35.9, 33.9, 32.3, 32.2, 28.0, 22.4, 20.6, 19.3; IR (Neat Film NaCl) 3050, 3023, 2981, 2958, 2928, 2890, 2874, 2837, 1726, 1633, 1610, 1470, 1457, 1435, 1416, 1406, 1392, 1364, 1327, 1295, 1270, 1218, 1178, 1189, 1117, 1096, 1045, 1028, 1003, 953, 935, 917, 888, 850, 837, 807, 758, 731 cm⁻¹; HRMS (EI+) m/z calc'd for C₁₆H₂₄O₂ [M]⁺: 248.1776; found 248.1774; [α]_D^{25.0} -32.18 (c 0.97, CHCl₃, 78.4% ee).

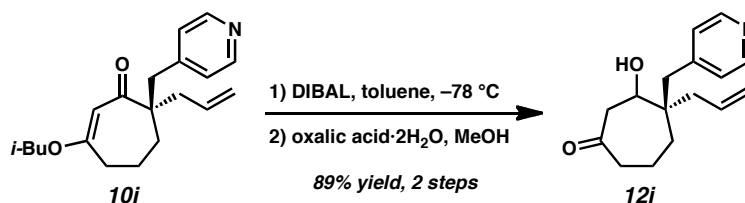
Procedures for the Synthesis of Acylcyclopentenes **1** by Ring Contraction

Full characterization data is reported for acylcyclopentenes **1**, cycloheptenone **11a**, and β -hydroxyketone intermediate **12a** (mixture of diastereomers). For all other β -hydroxyketone intermediates (**12b–j**, **l–o**, mixtures of diastereomers), R_f , IR, and HRMS data are reported and ¹H NMR and IR spectra are provided for reference in **Figures SI-35–SI-48**.

General Method A: Lithium Aluminum Hydride Reduction / 10% Aq HCl Hydrolysis

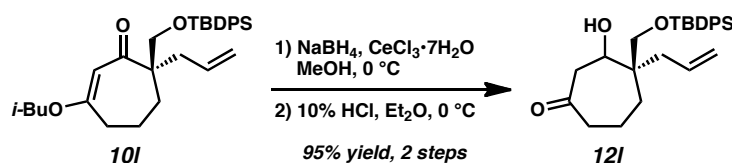


Cycloheptenone 11a and β -**Hydroxyketone 12a**. A 500 mL round-bottom flask with magnetic stir bar was charged with Et₂O (150 mL) and cooled to 0 °C. LiAlH₄ (806 mg, 21.2 mmol) was added in one portion. After 10 min, a solution of vinylogous ester **10a** (9.13 g, 38.6 mmol) in Et₂O (43 mL) was added dropwise using positive pressure cannulation. The grey suspension was stirred for 40 min and additional LiAlH₄ (148 mg, 3.9 mmol) was added in one portion. After an additional 30 min of stirring at 0 °C, the reaction was quenched by slow addition of aqueous HCl (110 mL, 10% w/w). The resulting biphasic system was allowed to warm to ambient temperature and stirred vigorously for 8.5 h. The phases were separated and the aqueous phase was extracted with Et₂O (3 x 100 mL). The combined organic phases were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was azeotroped with toluene (3 x 20 mL) and purified using flash column chromatography (SiO₂, 5 x 15 cm, 9:1→3:1 Hexanes:EtOAc, dry-loaded using Celite) to afford β -hydroxyketone **12a** (6.09 g, 87% yield, 1.3:1 dr) as a colorless semi-solid and cycloheptenone **11a** (387 mg, 6% yield) as a colorless oil. (For characterization data, see p. 32–33).

General Method B: DIBAL Reduction / Oxalic Acid Hydrolysis

β -Hydroxyketone 12i. A 25 mL pear shaped flask was charged with vinylogous ester **10i** (29.4 mg, 0.094 mmol, 1.00 equiv) and toluene (3.0 mL). The solution was cooled to $-78 \text{ }^\circ\text{C}$ using an acetone/ $\text{CO}_2(\text{s})$ bath. A 1.0 M solution of DIBAL in toluene (112.6 μL , 0.113 mmol, 1.00 equiv) was added dropwise and the solution was stirred for 10 min. MeOH (180 μL), $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$ (1.08 g), and Celite (360 mg) were added. The reaction was stirred vigorously and allowed to warm slowly to ambient temperature. The mixture was filtered through a Celite plug (3 x 3 cm, EtOAc), and concentrated in vacuo. $R_f = 0.28$, broad (1:2 Hexanes:EtOAc).

The crude hydroxy isobutyl enol ether was added to a 25 mL round-bottom flask and dissolved in MeOH (4.0 mL). Oxalic acid dihydrate (354.9 mg, 2.82 mmol, 30.0 equiv) was added in one portion. After 1 h of stirring, the reaction was neutralized to pH 7 with 1 M aqueous pH 7 $\text{NaH}_2\text{PO}_4/\text{Na}_2\text{HPO}_4$ buffer (6 mL). The biphasic mixture was stirred vigorously for 10 min and the phases were separated. The aqueous layer was extracted with Et_2O (4 x 15 mL). The combined organic phases were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude product was purified using flash column chromatography (SiO_2 , 1.5 x 25 cm, 4:1 \rightarrow 2:1 \rightarrow 1:2 Hexanes-Acetone) to afford β -hydroxyketone **12i** as a mixture of diastereomers (21.6 mg, 0.083 mmol, 89% yield over 2 steps, 2.8:1 dr) as a clear, colorless residue which solidified upon standing. $R_f = 0.10$ (4:1 Hexanes-Acetone). (For characterization data, see p. 38).

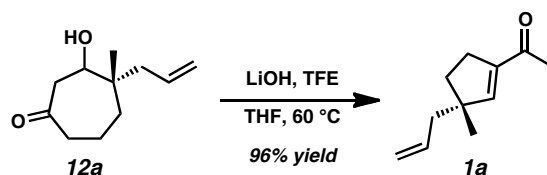
General Method C: Luche Reduction / 10% Aq HCl Hydrolysis

β -Hydroxyketone 12l. A 100 mL round-bottom flask with magnetic stir bar was charged with vinylogous ester **10l** (65.6 mg, 0.134 mmol, 1.00 equiv) and anhydrous MeOH (8.3 mL). The solution was cooled to $0 \text{ }^\circ\text{C}$. $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (78.2 mg, 0.21 mmol, 1.56 equiv) was added in one portion and the mixture was stirred for 5 min. Addition of NaBH_4 (23.8 mg, 0.63 mmol, 4.70 equiv) led to the evolution of gas and a turbid solution that became clear after several minutes. The reaction was stirred at $0 \text{ }^\circ\text{C}$. After 15 min, the reaction was diluted with CH_2Cl_2 (20 mL) until turbid, filtered through a Celite plug (3 x 3 cm, CH_2Cl_2), and concentrated in vacuo. The residue was taken up in CH_2Cl_2 , filtered through a Celite plug (3 x 5 cm, CH_2Cl_2), and concentrated in vacuo a second time. $R_f = 0.33$ (10:1 Hexanes:EtOAc).

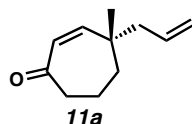
The crude hydroxy isobutyl enol ether was added to a 25 mL round-bottom flask with amagnetic stir bar and dissolved in Et_2O (3.8 mL). The vigorously stirred solution was cooled to $0 \text{ }^\circ\text{C}$ and aqueous HCl (384 μL , 10% w/w) was added dropwise via syringe. After 30 min, the reaction was allowed to warm to ambient temperature and extracted with Et_2O (3 x 5 mL). The

combined organic phases were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude product was purified using flash column chromatography (SiO_2 , 1.5 x 25 cm, 6:1→4:1 Hexanes:EtOAc) to afford β -hydroxyketone **12l** as a mixture of diastereomers (55.6 mg, 0.13 mmol, 95% yield over 2 steps, 3.5:1 dr) as a colorless oil; $R_f = 0.22, 0.28$ (two diastereomers) (4:1 Hexanes:EtOAc); (For characterization data, see p. 40).

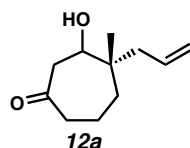
General Method D: β -Hydroxyketone Ring Contraction



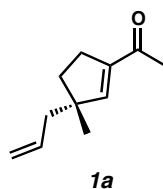
Acylcyclopentene 1a. Alcohol **12a** (6.09 g, 33.4 mmol, 1.00 equiv) was dissolved in THF (334 mL) in a 500 mL round-bottom flask. The solution was treated with 2,2,2-trifluoroethanol (3.67 mL, 50.1 mmol, 1.50 equiv) and anhydrous LiOH (1.20 g, 50.1 mmol, 1.50 equiv). The flask was fitted with a condenser, purged with N_2 , and heated to 60 °C using an oil bath. After 18 h of stirring, the suspension was allowed to cool to ambient temperature, diluted with Et_2O (150 mL), dried over Na_2SO_4 (30 min of stirring), filtered, and concentrated carefully under reduced pressure, allowing for a film of ice to form on the outside of the flask. The crude product was purified using flash column chromatography (SiO_2 , 5 x 15 cm, 15:1 Hexanes:Et₂O) to afford acylcyclopentene **1a** (5.29 g, 32.2 mmol, 96% yield) as a colorless fragrant oil. (For characterization data, see p. 33).



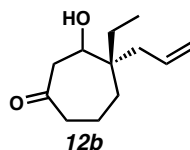
Cycloheptenone 11a. Prepared using General Method A. 387 mg, 2.36 mmol, 6.1% yield. $R_f = 0.54$ (7:3 Hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 6.04 (dd, $J = 12.9, 0.7$ Hz, 1H), 5.82 (d, $J = 12.9$ Hz, 1H), 5.75 (dddd, $J = 17.1, 10.3, 7.8, 7.1$ Hz, 1H), 5.10 (dddd, $J = 10.3, 1.2, 1.2, 1.2$ Hz, 1H), 5.08–5.03 (m, 1H), 2.65–2.52 (m, 2H), 2.19 (app dd, $J = 13.7, 6.8$ Hz, 1H), 2.11 (app dd, $J = 13.7, 8.1$ Hz, 1H), 1.84–1.76 (m, 3H), 1.68–1.63 (m, 1H), 1.10 (s, 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 204.7, 152.5, 133.8, 128.6, 118.6, 47.2, 45.1, 42.7, 38.2, 27.1, 18.4; IR (Neat Film NaCl) 3076, 3011, 2962, 2934, 2870, 1659, 1454, 1402, 1373, 1349, 1335, 1278, 1208, 1172, 997, 916, 874, 822, 772 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{11}\text{H}_{16}\text{O}$ $[\text{M}]^+$: 164.1201; found 164.1209; $[\alpha]_D^{21.0} -9.55$ (c 1.07, CHCl_3 , 88.0% ee).



β -Hydroxyketone 12a (Table 3, entry 1). Prepared using General Method A. 6.09 g, 33.41 mmol, 87% yield. $R_f = 0.23$ (7:3 Hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ **major epimer**; 5.88 (dddd, $J = 15.1, 9.0, 7.6, 7.6$ Hz, 1H), 5.12–5.08 (m, 2H), 3.70 (dd, $J = 4.9, 3.9$ Hz, 1H), 2.86 (dd, $J = 15.6, 1.7$ Hz, 1H), 2.65 (dd, $J = 15.6, 7.3$ Hz, 1H), 2.54–2.43 (m, 2H), 2.24 (dd, $J = 13.7, 7.8$ Hz, 1H), 2.07 (dd, $J = 13.4, 7.3$ Hz, 1H), 1.99 (dd, $J = 15.9, 4.4$ Hz, 1H), 1.82–1.69 (m, 2H), 1.45–1.41 (m, 1H), 0.96 (s, 3H); **minor epimer** 5.83 (dddd, $J = 14.9, 10.3, 7.6, 7.6$ Hz, 1H), 5.12–5.06 (m, 2H), 3.68 (dd, $J = 4.1, 2.4$ Hz, 1H) 2.80 (dd, $J = 15.4, 2.4$ Hz, 1H), 2.74 (dd, $J = 15.4, 8.1$ Hz 1H), 2.46–2.38 (m, 2H), 2.18 (dd, $J = 13.9, 7.3$ Hz, 1H), 2.09 (dd, $J = 12.9, 7.8$ Hz, 1H), 1.82–1.65 (m, 3H) 1.50–1.47 (m, 1H), 1.02 (s, 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ **major epimer**; 213.2, 135.0, 118.1, 72.9, 46.7, 44.9, 44.2, 41.0, 36.3, 21.9, 18.9; **minor epimer**; 212.6, 134.2, 118.3, 73.3, 47.2, 42.8, 41.0, 35.9, 22.6, 18.7; IR (Neat Film NaCl) 3436, 3074, 2932, 1692, 1638, 1443, 1403, 1380, 1352, 1318, 1246, 1168, 1106, 1069, 999, 913, 840 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{11}\text{H}_{18}\text{O}_2$ $[\text{M}]^{+}$: 182.1313; found 182.1307; $[\alpha]_{\text{D}}^{22.8} -57.10$ (c 2.56, CHCl_3 , 88.0% ee).

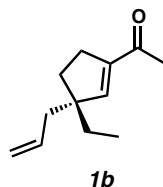


Acylcyclopentene 1a (Table 3, entry 1). Prepared using General Method D. 5.29 g, 32.2 mmol, 96% yield. $R_f = 0.67$ (8:2 Hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 6.45 (app t, $J = 1.7$ Hz, 1H), 5.76 (dddd, $J = 16.4, 10.7, 7.3, 7.3$ Hz, 1H), 5.07–5.03 (m, 2H), 2.59–2.48 (m, 2H), 2.30 (s, 3H), 2.21–2.14 (m, 2H), 1.85 (ddd, $J = 12.9, 8.3, 6.3$ Hz, 1H), 1.64 (ddd, $J = 12.9, 8.5, 6.1$ Hz, 1H), 1.11 (s, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 197.5, 151.9, 143.8, 134.9, 117.8, 50.0, 45.3, 36.0, 29.7, 26.8, 25.6; IR (Neat Film NaCl) 3077, 2956, 2863, 1668, 1635, 1616, 1454, 1435, 1372, 1366, 1309, 1265, 1213, 1177, 993, 914, 862 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{11}\text{H}_{17}\text{O}$ $[\text{M}+\text{H}]^{+}$: 165.1279; found 165.1281; $[\alpha]_{\text{D}}^{21.4} +17.30$ (c 0.955, CHCl_3 , 88.0% ee).

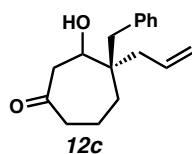


β -Hydroxyketone 12b (Table 3, entry 2). Prepared using General Method A. 111.5 mg, 0.57 mmol, 95% yield. Flash column chromatography (SiO_2 , 2 x 25 cm, 10:1→3:1 Hexanes:EtOAc); $R_f = 0.36$ (2:1 Hexanes:EtOAc); $^1\text{H NMR}$ (300 MHz, CDCl_3) mixture of two diastereomers, see **Figure SI-36**; IR (Neat Film NaCl) 3448, 3073, 2965, 2933, 1832, 1696, 1691, 1673, 1459,

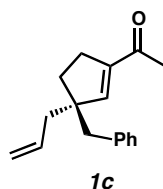
1413, 1381, 1352, 1334, 1323, 1306, 1269, 1252, 1269, 1252, 1172, 1138, 1111, 1084, 1071, 1050, 997, 955, 930, 912, 876, 825, 777, 737 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{12}\text{H}_{20}\text{O}_2$ $[\text{M}]^+$: 196.1463; found 196.1480.



Acylcyclopentene 1b (Table 3, entry 2). Prepared using General Method D. 21.8 mg, 0.12 mmol, 95% yield. Flash column chromatography (SiO_2 , 1 x 20 cm, 15:1 Hexanes: Et_2O); R_f = 0.73 (2:1 Hexanes: EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 6.44 (dd, J = 1.8, 1.8 Hz, 1H), 5.80–5.64 (m, 1H), 5.08–5.04 (m, 1H), 5.03–5.00 (m, 1H), 2.55–2.46 (m, 2H), 2.30 (s, 3H), 2.19–2.16 (m, 2H), 1.81–1.68 (m, 2H), 1.52–1.41 (m, 2H), 0.85 (dd, J = 7.5, 7.5 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) 197.4, 150.7, 144.6, 134.8, 117.7, 54.0, 43.1, 32.9, 31.3, 30.1, 26.9, 9.1; IR (Neat Film NaCl) 3075, 2962, 2922, 2878, 2855, 1669, 1639, 1617, 1459, 1437, 1372, 1319, 1266, 1207, 1052, 995, 913, 868, 784 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{12}\text{H}_{19}\text{O}$ $[\text{M}+\text{H}]^+$: 179.1436; found 179.1401; $[\alpha]_D^{25.0}$ +7.06 (c 0.98, CHCl_3 , 91.6% ee).

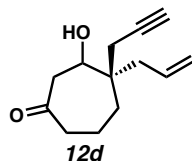


β -Hydroxyketone 12c (Table 3, entry 3). Prepared using General Method A. 109.9 mg, 0.43 mmol, 89% yield. Flash column chromatography (SiO_2 , 2 x 25 cm, 10:1 \rightarrow 3:1 Hexanes: EtOAc); R_f = 0.11 (4:1 Hexanes: EtOAc); ^1H NMR (300 MHz, CDCl_3) mixture of two diastereomers, see Figure SI-37; IR (Neat Film NaCl) 3443, 3072, 3028, 3003, 2930, 2865, 1696, 1692, 1685, 1636, 1601, 1582, 1495, 1453, 1413, 1400, 1352, 1340, 1255, 1182, 1163, 1118, 1058, 1031, 995, 970, 916, 885, 848, 809, 754 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{17}\text{H}_{22}\text{O}_2$ $[\text{M}]^+$: 258.1620; found 258.1642.

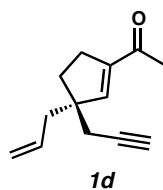


Acylcyclopentene 1c (Table 3, entry 3). Prepared using General Method D. 22.7 mg, 0.094 mmol, 97% yield. Flash column chromatography (SiO_2 , 1 x 20 cm, 15:1 Hexanes: Et_2O); R_f = 0.54 (4:1 Hexanes: EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 7.30–7.18 (m, 3H), 7.14–7.08 (m, 2H), 6.45 (dd, J = 1.8, 1.8 Hz, 1H), 5.78 (dddd, J = 16.3, 10.8, 7.7, 7.0 Hz, 1H), 5.13–5.10 (m,

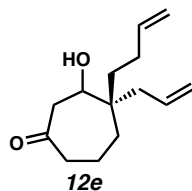
1H), 5.07 (dddd, $J = 9.1, 2.2, 1.2, 1.2$ Hz, 1H), 2.79 (d, $J = 13.3$ Hz, 1H), 2.73 (d, $J = 13.3$ Hz, 1H), 2.43 (dddd, $J = 16.5, 8.6, 5.7, 1.7$ Hz, 1H), 2.27–2.17 (m, 3H), 2.21 (s, 3H), 1.91–1.75 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) 197.1, 150.1, 144.9, 138.2, 134.7, 130.4, 128.1, 126.4, 118.3, 54.6, 45.2, 43.3, 33.3, 30.0, 26.9; IR (Neat Film NaCl) 3061 3027, 3002, 2920, 2853, 1668, 1638. 1617, 1495, 1453, 1442, 1371, 1314, 1264, 1197, 1089, 1030, 995, 914, 861, 734 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{17}\text{H}_{20}\text{O}$ $[\text{M}]^{+}$: 240.1514; found 240.1530; $[\alpha]_{\text{D}}^{25.0} -20.63$ (c 0.83, CHCl_3 , 86.3% ee).



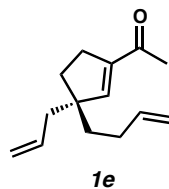
β -Hydroxyketone 12d (Table 3, entry 4). Prepared using General Method A. 117 mg, 0.56 mmol, 98% yield. Flash column chromatography (SiO_2 , 2 x 25 cm, 10:1→3:1 Hexanes:EtOAc); $R_f = 0.35$ (10:1 Hexanes:EtOAc); ^1H NMR (300 MHz, CDCl_3) mixture of two diastereomers, see **Figure SI-38**; IR (Neat Film NaCl) 3434, 3295, 3074, 3002, 2932, 2114, 1690, 1684, 1637, 1447, 1354, 1252, 1166, 1124, 1064, 977, 917, 886, 838 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{13}\text{H}_{18}\text{O}_2$ $[\text{M}]^{+}$: 206.1307; found 206.1311.



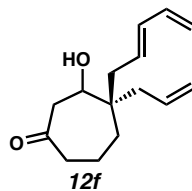
Acylcyclopentene 1d (Table 3, entry 4). Prepared using General Method D. 22.5 mg, 0.12 mmol, 97% yield. Flash column chromatography (SiO_2 , 1 x 20 cm, 15:1 Hexanes:Et₂O); $R_f = 0.74$ (2:1 Hexanes:EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 6.51 (dd, $J = 1.8, 1.8$ Hz, 1H), 5.73 (dddd, $J = 16.9, 10.2, 7.4, 7.4$ Hz, 1H), 5.13 (dm, $J = 10.2$ Hz, 1H), 5.10–5.07 (m, 1H), 2.66–2.46 (m, 2H), 2.34–2.33 (m, 1H), 2.33–2.32 (m, 1H), 2.32 (s, 3H), 2.32–2.30 (m, 2H), 1.99 (dd, $J = 2.7, 2.7$ Hz, 1H), 1.93–1.75 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) 197.3, 148.6, 145.2, 133.9, 118.6, 81.4, 70.3, 53.2, 42.4, 33.4, 30.0, 28.5, 26.9; IR (Neat Film NaCl) 3298, 3075, 3001, 2924, 2857, 2116, 1669, 1639, 1617, 1457, 1437, 1372, 1318, 1265, 1222, 1204, 996, 919, 867 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{13}\text{H}_{16}\text{O}$ $[\text{M}]^{+}$: 188.1201; found 188.1211; $[\alpha]_{\text{D}}^{25.0} -58.65$ (c 0.71, CHCl_3 , 88.5% ee).



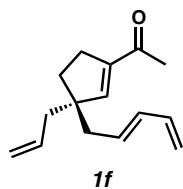
β -Hydroxyketone 12e (Table 3, entry 5). Prepared using General Method A. 116.7 mg, 0.52 mmol, 97% yield. Flash column chromatography (SiO₂, 2 x 25 cm, 10:1→3:1 Hexanes:EtOAc); R_f = 0.15 (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) mixture of two diastereomers, see **Figure SI-39**; IR (Neat Film NaCl) 3447, 3075, 3001, 2975, 2931, 2866, 1827, 1693, 1639, 1456, 1415, 1352, 1336, 1250, 1169, 1116, 1073, 995, 910, 855, 763, 714 cm⁻¹; HRMS (EI+) *m/z* calc'd for C₁₈H₂₈O₂ [M]⁺: 276.2089; found 276.2060.



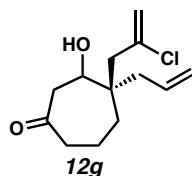
Acylcyclopentene 1e (Table 3, entry 5). Prepared using General Method D. 19.1 mg, 0.093 mmol, 90% yield. Flash column chromatography (SiO₂, 1 x 20 cm, 15:1 Hexanes:Et₂O); R_f = 0.62 (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 6.45 (dd, *J* = 1.8, 1.8 Hz, 1H), 5.79 (dddd, *J* = 16.8, 10.2, 6.5, 6.5 Hz, 1H), 5.72 (dddd, *J* = 16.8, 9.5, 7.3, 7.3 Hz, 1H), 5.09–5.07 (m, 1H), 5.05–4.97 (m, 2H), 4.94 (dm, *J* = 10.2 Hz, 1H), 2.56–2.49 (m, 2H), 2.30 (s, 3H), 2.23–2.17 (m, 2H), 2.15–1.91 (m, 2H), 1.85–1.70 (m, 2H), 1.58–1.50 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) 197.3, 150.4, 144.6, 138.8, 134.6, 117.9, 114.6, 53.5, 43.6, 38.1, 33.3, 30.1, 29.2, 26.9; IR (Neat Film NaCl) 3076, 3001, 2976, 2919, 2854, 1670, 1640, 1618, 1437, 1372, 1314, 1265, 1204, 995, 911, 865 cm⁻¹; HRMS (EI+) *m/z* calc'd for C₁₄H₂₁O [M+H]⁺: 205.1592; found 205.1588; [α]_D^{25.0} –30.08 (*c* 0.92, CHCl₃, 86.9% ee).



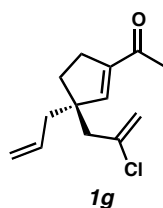
β -Hydroxyketone 12f (Table 3, entry 6). Prepared using General Method A. 117.5 mg, 0.50 mmol, 96% yield. Flash column chromatography (SiO₂, 2 x 25 cm, 10:1→3:1 Hexanes:EtOAc); R_f = 0.19 (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) mixture of two diastereomers, see **Figure SI-40**; IR (Neat Film NaCl) 3448, 3075, 3035, 3007, 2972, 2929, 2865, 1700, 1696, 1691, 1685, 1648, 1637, 1600, 1449, 1415, 1352, 1333, 1245, 1171, 1120, 1068, 1052, 1005, 969, 954, 912, 855, 838, 817, 720 cm⁻¹; HRMS (FAB+) *m/z* calc'd for C₁₅H₂₃O₂ [M+H]⁺: 235.1698; found 235.1697.



Acylcyclopentene 1f (Table 3, entry 6). Prepared using General Method D. 25.2 mg, 0.12 mmol, 95% yield. Flash column chromatography (SiO₂, 1 x 20 cm, 15:1 Hexanes:Et₂O); R_f = 0.65 (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 6.45 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.30 (ddd, *J* = 16.9, 10.2, 10.2 Hz, 1H), 6.08 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.73 (dddd, *J* = 16.4, 11.6, 8.9, 7.5 Hz, 1H), 5.63 (ddd, *J* = 15.0, 7.6, 7.6 Hz, 1H), 5.14–5.09 (m, 2H), 5.06–5.02 (m, 1H), 5.00 (dm, *J* = 10.1 Hz, 1H), 2.54–2.46 (m, 2H), 2.30 (s, 3H), 2.25–2.17 (m, 4H), 1.80–1.74 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) 197.3, 150.0, 144.8, 137.0, 134.5, 134.3, 130.4, 118.1, 115.9, 54.0, 43.3, 42.0, 33.2, 30.0, 26.9; IR (Neat Film NaCl) 3079, 3006, 2929, 2857, 1735, 1670, 1640, 1617, 1439, 1371, 1318, 1267, 1201, 1175, 1084, 1004, 952, 912 cm⁻¹; HRMS (FAB+) *m/z* calc'd for C₁₅H₂₁O [M+H]⁺: 217.1592; found 217.1568; [α]_D^{25.0} -32.14 (c 1.26, CHCl₃, 89.6% ee).

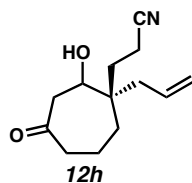


β-Hydroxyketone 12g (Table 3, entry 7). Prepared using General Method A. 114.9 mg, 0.47 mmol, 93% yield. Flash column chromatography (SiO₂, 2 x 25 cm, 10:1→3:1 Hexanes:EtOAc); R_f = 0.15 (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) mixture of two diastereomers, see Figure SI-41; IR (Neat Film NaCl) 3436, 3075, 2931, 2869, 1695, 1627, 1452, 1414, 1352, 1297, 1251, 1222, 1151, 1064, 1021, 997, 974, 915, 887, 839 cm⁻¹; HRMS (EI+) *m/z* calc'd for C₁₃H₁₉O₂Cl [M]⁺: 242.1074; found 242.1063.

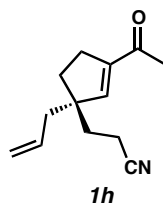


Acylcyclopentene 1g (Table 3, entry 7). Prepared using General Method D. 23.8 mg, 0.11 mmol, 99% yield. Flash column chromatography (SiO₂, 1 x 20 cm, 15:1 Hexanes:Et₂O); R_f = 0.55 (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 6.61 (dd, *J* = 1.8, 1.8 Hz, 1H), 5.73 (dddd, *J* = 15.9, 11.1, 7.9, 7.3 Hz, 1H), 5.29 (d, *J* = 1.2 Hz, 1H), 5.15–5.14 (m, 1H), 5.11–5.10 (m, 1H), 5.08–5.04 (m, 1H), 2.56–2.48 (m, 4H), 2.31 (s, 3H), 2.28–2.25 (m, 2H), 1.93 (ddd, *J* = 13.3, 8.4, 6.6 Hz, 1H), 1.84 (ddd, *J* = 13.3, 8.1, 6.4 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) 197.3,

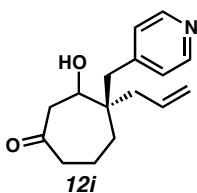
149.6, 144.4, 139.4, 134.0, 118.7, 116.4, 53.4, 48.0, 43.4, 33.3, 29.8, 26.9; IR (Neat Film NaCl) 3076, 2946, 2857, 1669, 1629, 1434, 1372, 1320, 1266, 1230, 1206, 1167, 996, 917, 886 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{13}\text{H}_{18}\text{OCl}$ $[\text{M}+\text{H}]^+$: 225.1046; found 225.1053; $[\alpha]_{\text{D}}^{25.0}$ +46.29 (c 1.06, CHCl_3 , 85.7% ee).



β -Hydroxyketone 12h (Table 3, entry 8). Prepared using General Method A. 72.4 mg, 0.33 mmol, 90% yield. Flash column chromatography (SiO_2 , 2 x 25 cm, 4:1 \rightarrow 2:1 \rightarrow 1:1 Hexanes:EtOAc); R_f = 0.40, broad (1:1 Hexanes:EtOAc); ^1H NMR (300 MHz, CDCl_3) mixture of two diastereomers, see **Figure SI-42**; IR (Neat Film NaCl) 3468, 3075, 2932, 2871, 2247, 1696, 1458, 1437, 1420, 1352, 1319, 1252, 1169, 1122, 1070, 999, 921, 853, 754 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{13}\text{H}_{19}\text{O}_2\text{N}$ $[\text{M}]^{+}$: 221.1416; found 221.1411.

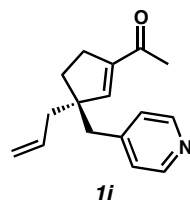


Acylcyclopentene 1h (Table 3, entry 8). Prepared using General Method D. 19.4 mg, 0.095 mmol, 94% yield. Flash column chromatography (SiO_2 , 1 x 20 cm, 2:1 \rightarrow 3:2 \rightarrow 1:1 Hexanes:Et₂O); R_f = 0.84, broad (1:1 Hexanes:EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 6.42 (dd, J = 1.8, 1.8 Hz, 1H), 5.70 (dddd, J = 16.4, 10.6, 7.4, 7.4 Hz, 1H), 5.15–5.12 (m, 1H), 5.15–5.06 (m, 1H), 2.60–2.52 (m, 2H), 2.37–2.22 (m, 2H), 2.32 (s, 3H), 2.23–2.20 (m, 2H), 1.93–1.82 (m, 3H), 1.73 (ddd, J = 13.6, 8.2, 7.0 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) 196.8, 147.2, 146.0, 133.3, 120.0, 119.0, 53.2, 43.5, 34.2, 32.7, 30.2, 27.0, 13.1; IR (Neat Film NaCl) 3074, 2923, 2857, 2245, 1667, 1640, 1618, 1423, 1373, 1308, 1264, 1202, 1090, 996, 918, 867 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{13}\text{H}_{18}\text{NO}$ $[\text{M}+\text{H}]^+$: 204.1388; found 204.1385; $[\alpha]_{\text{D}}^{25.0}$ -31.11 (c 0.90, CHCl_3 , 87.4% ee).

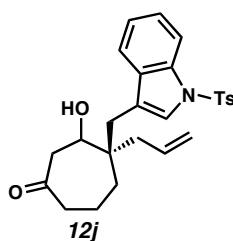


β -Hydroxyketone 12i (Table 3, entry 9). Prepared using General Method B. 21.6 mg, 0.083 mmol, 89% yield over 2 steps. Flash column chromatography (SiO_2 , 1.5 x 25 cm, 4:1 \rightarrow 2:1 \rightarrow 1:2

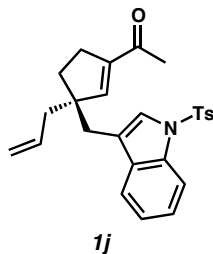
Hexanes-Acetone); $R_f = 0.10$ (2:1 Hexanes-Acetone); $^1\text{H NMR}$ (300 MHz, CDCl_3) mixture of two diastereomers, see **Figure SI-43**; IR (Neat Film NaCl) 3391, 3201, 3073, 2929, 2865, 1699, 1636, 1603, 1557, 1497, 1456, 1418, 1352, 1332, 1297, 1258, 1222, 1187, 1161, 1113, 1069, 1005, 995, 972, 915, 886, 851, 802, 735 cm^{-1} ; HRMS (FAB+) m/z calc'd for $\text{C}_{16}\text{H}_{22}\text{O}_2\text{N}$ $[\text{M}+\text{H}]^+$: 260.1650; found 260.1649.



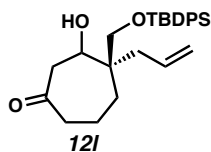
Acylcyclopentene 1i (**Table 3, entry 9**). Prepared using General Method D. 15.7 mg, 0.065 mmol, 90% yield. Flash column chromatography (SiO_2 , 1.5 x 16 cm, 2:1→1:1 Hexanes-Acetone); $R_f = 0.47$ (2:1 Hexanes-Acetone); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 8.49 (br d, $J = 3.8$ Hz, 2H), 7.04 (d, $J = 5.7$ Hz, 2H), 6.40 (dd, $J = 1.7, 1.7$ Hz, 1H), 5.75 (dddd, $J = 17.3, 10.3, 7.3, 7.3$ Hz, 1H), 5.16–5.04 (m, 2H), 2.77 (d, $J = 13.0$ Hz, 1H), 2.71 (d, $J = 13.0$ Hz, 1H), 2.52–2.39 (m, 1H), 2.33–2.35 (m, 1H), 2.28 (s, 3H), 2.24–2.20 (m, 2H), 1.85–1.80 (m, 2H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) 196.8, 149.6, 148.6, 147.3, 145.4, 134.0, 125.7, 118.8, 54.2, 44.4, 43.3, 33.3, 30.0, 27.0; IR (Neat Film NaCl) 3401, 3071, 3025, 2922, 2856, 1668, 1640, 1618, 1600, 1557, 1495, 1441, 1415, 1373, 1318, 1277, 1265, 1220, 1194, 1071, 994, 917, 874, 844, 810, 763 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{16}\text{H}_{19}\text{ON}$ $[\text{M}]^+$: 176.1467; found 176.1458; $[\alpha]_D^{25.0} -8.58$ (c 0.77, CHCl_3 , 84.6% ee).



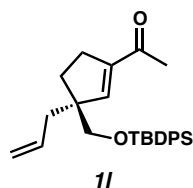
β -Hydroxyketone 12j (**Table 3, entry 10**). Prepared using General Method A. 300.1 mg, 0.67 mmol, 94% yield. Flash column chromatography (SiO_2 , 3 x 25 cm, 4:1→3:1→2:1→1:1 Hexanes:EtOAc); $R_f = 0.20, 0.26$ (two diastereomers) (2:1 Hexanes:EtOAc); $^1\text{H NMR}$ (300 MHz, CDCl_3) mixture of two diastereomers, see **Figure SI-44**; IR (Neat Film NaCl) 3436, 3068, 2930, 2873, 1693, 1639, 1597, 1494, 1447, 1365, 1402, 1365, 1279, 1211, 1188, 1172, 1133, 1121, 1095, 1063, 1020, 995, 975, 913, 813, 778, 747 cm^{-1} ; HRMS (FAB+) m/z calc'd for $\text{C}_{26}\text{H}_{30}\text{O}_4\text{NS}$ $[\text{M}+\text{H}]^+$: 452.1896; found 452.1896.



Acylcyclopentene 1j (Table 3, entry 10). Prepared using General Method D. 55.7 mg, 0.10 mmol, 93% yield. Flash column chromatography (SiO₂, 2 x 25 cm, 10:1→8:1→6:1→4:1 Hexanes:EtOAc); R_f = 0.67 (2:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 7.98 (br d, *J* = 8.2 Hz, 1H), 7.63 (dm, *J* = 8.4 Hz, 2H), 7.40 (dd, *J* = 7.3, 0.8 Hz, 1H), 7.33 (br s, 1H), 7.30 (ddd, *J* = 8.2, 8.2, 1.3 Hz, 1H), 7.21 (ddd, *J* = 7.5, 7.5, 1.1 Hz, 1H), 7.17 (dm, *J* = 8.2 Hz, 2H), 6.35 (dd, *J* = 1.8, 1.8 Hz, 1H), 5.75 (dddd, *J* = 16.9, 10.3, 7.7, 6.9 Hz, 1H), 5.13–5.10 (m, 1H), 5.10–5.04 (m, 1H), 2.82 (s, 3H), 2.44 (dddd, *J* = 14.7, 8.8, 5.9, 1.7 Hz, 1H), 2.33 (br s, 2H), 2.31–2.18 (m, 3H), 2.16 (s, 3H), 1.86 (ddd, *J* = 14.6, 8.6, 6.1 Hz, 1H), 1.79 (ddd, *J* = 14.8, 7.6, 5.8 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) 196.9, 149.9, 145.1, 144.9, 135.2, 135.1, 134.3, 131.9, 130.0, 126.7, 124.8, 124.7, 123.2, 119.9, 119.4, 118.5, 113.9, 54.5, 43.5, 33.8, 33.4, 30.0, 26.8, 21.7; IR (Neat Film NaCl) 3316, 3129, 3101, 3068, 3001, 2974, 2922, 2855, 1667, 1639, 1618, 1597, 1562, 1493, 1448, 1400, 1372, 1307, 1293, 1277, 1211, 1188, 1174, 1121, 1094, 1020, 978, 916, 853, 813, 747 cm⁻¹; HRMS (EI+) *m/z* calc'd for C₂₆H₂₇O₃NS [M]⁺: 433.1712; found 433.1694; [α]_D^{25.0} +0.35 (*c* 1.09, CHCl₃, 82.9% ee).

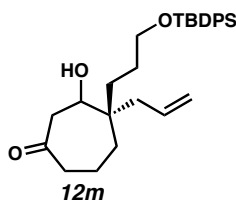


β-Hydroxyketone 12l (Table 3, entry 11). Prepared using General Method C. 55.6 mg, 0.13 mmol, 95% yield over 2 steps. Flash column chromatography (SiO₂, 1.5 x 25 cm, 6:1→4:1 Hexanes:EtOAc); R_f = 0.22, 0.28 (two diastereomers) (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) mixture of two diastereomers, see **Figure SI-45**; IR (Neat Film NaCl) 3468, 3072, 3050, 2999, 3013, 2931, 2895, 2858, 2248, 1960, 1891, 1823, 1772, 1698, 1638, 1590, 1472, 1462, 1446, 1428, 1391, 1361, 1337, 1260, 1222, 1186, 1172, 1158, 1113, 1088, 1030, 1006, 999, 976, 914, 841, 823, 810, 740 cm⁻¹; HRMS (FAB+) *m/z* calc'd for C₂₇H₃₇O₃Si [M+H]⁺: 437.2512; found 437.2517.

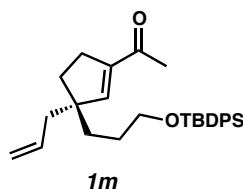


Acylcyclopentene 1l (Table 3, entry 11). Prepared using General Method D. 32.6 mg, 0.078 mmol, 96% yield. Flash column chromatography (SiO₂, 1 x 20 cm, 15:1 Hexanes:Et₂O); R_f =

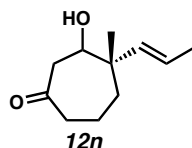
0.60 (4:1 Hexanes:EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 7.67–7.60 (m, 4H), 7.47–7.34 (m, 6H), 6.50 (dd, $J = 1.8, 1.8$ Hz, 1H), 5.71 (dddd, $J = 17.0, 10.1, 7.8, 6.9$ Hz, 1H), 5.12–5.08 (m, 1H), 5.06–5.02 (m, 1H), 3.57 (d, $J = 9.8$ Hz, 1H), 3.53 (d, $J = 9.8$ Hz, 1H), 2.54–2.48 (m, 2H), 2.38 (ddd, $J = 13.8, 6.9, 1.1$ Hz, 1H), 2.31–2.25 (m, 1H), 2.29 (s, 3H), 1.81–1.72 (m, 2H), 1.07 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) 197.2, 148.5, 145.7, 135.8, 135.7, 134.5, 133.6, 133.6, 129.9, 129.9, 127.8, 118.0, 69.1, 56.5, 40.4, 30.7, 30.0, 27.0, 26.8, 19.5; IR (Neat Film NaCl) 3072, 3050, 2999, 2956, 2931, 2896, 2857, 1671, 1639, 1618, 1472, 1463, 1427m 1367, 1320, 1266, 1232, 1188, 1112, 998, 936, 915, 864, 824, 740 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{27}\text{H}_{34}\text{O}_2\text{Si}$ $[\text{M}]^+$: 433.1712; found 433.1694; $[\alpha]_{\text{D}}^{25.0} -17.58$ (c 0.94, CHCl_3 , 51.4% ee).



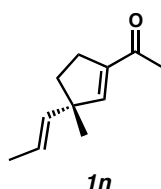
β -Hydroxyketone 12m (Table 3, entry 12). Prepared using General Method C. 110.6 mg, 0.24 mmol, 92% yield over 2 steps. Flash column chromatography (SiO_2 , 2 x 25 cm, 6:1 \rightarrow 4:1 Hexanes:EtOAc); $R_f = 0.15$ (4:1 Hexanes:EtOAc); ^1H NMR (300 MHz, CDCl_3) mixture of two diastereomers, see Figure SI-46; IR (Neat Film NaCl) 3436, 3071, 3050, 3013, 2999, 2931, 2896, 2859, 1960, 1891, 1826, 1694, 1638, 1589, 1472, 1461, 1428, 1390, 1360, 1325, 1307, 1251, 1218, 1188, 1168, 1111, 1092, 1007, 998, 973, 934, 914, 823, 798, 740 cm^{-1} ; HRMS (FAB+) m/z calc'd for $\text{C}_{29}\text{H}_{41}\text{O}_3\text{Si}$ $[\text{M}+\text{H}]^+$: 465.2825; found 465.2810.



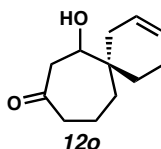
Acylcyclopentene 1m (Table 3, entry 12). Prepared using General Method D. 92.2 mg, 0.21 mmol, 92% yield. Flash column chromatography (SiO_2 , 2 x 25 cm, 15:1 Hexanes:Et₂O); $R_f = 0.64$ (4:1 Hexanes:EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 7.71–7.64 (m, 4H), 7.48–7.35 (m, 6H), 6.44 (dd, $J = 1.7, 1.7$ Hz, 1H), 5.81–5.65 (m, 1H), 5.10–5.07 (m, 1H), 5.05–5.02 (m, 1H), 3.69–3.64 (m, 2H), 2.55–2.49 (m, 2H), 2.31 (s, 3H), 2.20–2.18 (m, 2H), 1.84–1.67 (m, 2H), 1.53–1.48 (m, 4H), 1.07 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) 197.3, 150.7, 144.4, 135.7, 134.7, 134.0, 129.7, 127.7, 117.8, 64.3, 53.3, 43.5, 34.8, 33.3, 30.0, 28.0, 27.0, 26.8, 19.3; IR (Neat Film NaCl) 3071, 3050, 3013, 2999, 2931, 2897, 2857, 1670, 638, 1618, 1589, 1472, 1461, 1448, 1428, 1388, 1372, 1316, 1263, 1201, 1157, 1111, 1093, 1030, 1008, 998, 937, 915, 865, 823, 803, 741, 726 cm^{-1} ; HRMS (FAB+) m/z calc'd for $\text{C}_{25}\text{H}_{29}\text{O}_2\text{Si}$ $[\text{M}-\text{C}_4\text{H}_9]^+$: 389.1968; found 389.1958; $[\alpha]_{\text{D}}^{25.0} -14.19$ (c 0.92, CHCl_3 , 78.4% ee).



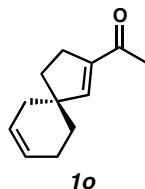
β -Hydroxyketone 12n (Table 3, entry 13). Prepared using General Method A. 429.5 mg, 2.36 mmol, 87% yield. Flash column chromatography (SiO₂, 3 x 20 cm, 9:1→3:1 Hexanes:EtOAc); R_f = 0.14 (4:1 Hexanes:EtOAc); ¹H NMR (400 MHz, CDCl₃) mixture of two diastereomers, see **Figure SI-47**; IR (Neat Film NaCl) 3449, 3027, 2963, 2928, 2873, 1694, 1454, 1404, 1350, 1320, 1251, 1170, 1066, 969 cm⁻¹; HRMS (MM: ESI-APCI+) *m/z* calc'd for C₁₁H₁₉O₂ [M+H]⁺: 165.1274; found 165.1278.



Acylcyclopentene 1n (Table 3, entry 13). Prepared using General Method D. Due to the volatility of acylcyclopentene **1n**, the work-up solvent (Et₂O) was removed using ambient pressure distillation (50→80 °C). 323.8 mg, 1.97 mmol, 93% yield. The crude oil was purified by automated flash column chromatography using a Teledyne Isco CombiFlash R_f (SiO₂, 32 g loading cartridge, 80 g column, linear gradient, 0→30% Et₂O in Pentane [33 min]) and solvent was removed using ambient pressure distillation (60 °C); R_f = 0.55 (4:1 Hexanes:EtOAc); ¹H NMR (400 MHz, CDCl₃) δ 6.41 (dd, *J* = 1.7, 1.7 Hz, 1H), 5.50 (dq, *J* = 15.5, 1.3 Hz, 1H), 5.39 (dq, *J* = 15.6, 6.2 Hz, 1H), 2.58–2.52 (m, 2H), 2.31–2.28 (m, 1H), 2.30 (s, 3H), 1.91 (ddd, *J* = 12.8, 7.4, 7.4 Hz, 1H), 1.74 (ddd, *J* = 12.8, 7.2, 7.2 Hz, 1H), 1.68–1.64 (m, 2H), 1.19 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 197.5, 151.4, 143.8, 137.5, 122.3, 51.5, 38.1, 29.6, 26.8, 25.4, 18.2; IR (Neat Film NaCl) 3022, 2958, 2859, 1674, 1617, 1451, 1377, 1365, 1310, 1271, 1229, 1165, 967 cm⁻¹; HRMS (MM: ESI-APCI+) *m/z* calc'd for C₁₁H₁₇O [M+H]⁺: 165.1279; found 165.1278; [α]_D^{25.0} +89.82 (*c* 1.04, CHCl₃, 88.0 % ee).

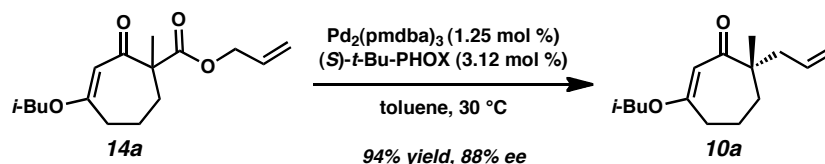


β -Hydroxyketone 12o (Table 3, entry 14). Prepared using General Method A. 29.1 mg, 0.150 mmol, 96% yield. Flash column chromatography (SiO₂, 2 x 20 cm, 9:1→3:1 Hexanes:EtOAc); R_f = 0.09 (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) mixture of two diastereomers, see **Figure SI-48**; IR (Neat Film NaCl) 3436, 3021, 2922, 2873, 2842, 2697, 1692, 1656, 1436, 1402, 1353, 1318, 1256, 1202, 1184, 1172, 1152, 1093, 1071, 1050, 1000, 981, 970, 949, 932, 876, 850, 834, 798, 750 cm⁻¹; HRMS (EI+) *m/z* calc'd for C₁₂H₁₈O₂ [M]⁺: 194.1307; found 194.1315.

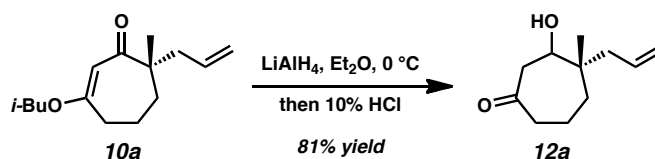


Acylcyclopentene 10 (Table 3, entry 14). Prepared using General Method D. 21.7 mg, 0.123 mmol, 91% yield. Flash column chromatography (SiO₂, 1 x 20 cm, 15:1 Hexanes:Et₂O); $R_f = 0.65$ (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 6.58 (dd, $J = 1.8, 1.8$ Hz, 1H), 5.72 (dm, $J = 10.0$ Hz, 1H), 5.65 (dm, $J = 10.0$ Hz, 1H), 2.59–2.52 (m, 2H), 2.30 (s, 3H), 2.13–2.04 (m, 2H), 2.02–1.98 (m, 2H), 1.77–1.70 (m, 2H), 1.69 (ddd, $J = 12.8, 6.3, 6.3$ Hz, 1H), 1.56 (ddd, $J = 12.8, 6.5, 6.5$ Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) 197.8, 151.4, 143.9, 127.0, 125.5, 48.7, 35.8, 35.8, 32.5, 28.9, 26.8, 23.1; IR (Neat Film NaCl) 3320, 3023, 2918, 2856, 1704, 1669, 1616, 1436, 1371, 1436, 1371, 1316, 1269, 1231, 11945, 1116, 1086, 1045, 1020, 980, 962, 935, 864, 763 cm⁻¹; HRMS (EI+) m/z calc'd for C₁₂H₁₆O [M]⁺: 176.1201; found 176.1234; $[\alpha]_D^{25.0} -10.42$ (c 1.08, CHCl₃, 78.4% ee).

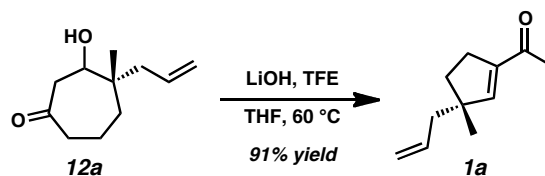
Procedure for the Large Scale Synthesis of Acylcyclopentene 1a



Vinylogous Ester 10a. Pd₂(pmdba)₃ (733.1 mg, 0.67 mmol, 0.0125) and (S)-*t*-BuPHOX (647.0 mg, 1.67 mmol, 0.0312 equiv) were placed in a 500 mL round-bottom flask. The flask was evacuated/backfilled with N₂ (3 cycles, 10 min evacuation per cycle). Toluene (222 mL, sparged with N₂ for 1 h immediately before use) was added and the black suspension was immersed in an oil bath preheated to 30 °C. After 30 min of stirring, the vinylogous ester **14a** (15.0 g, 53.5 mmol, 1.0 equiv) in toluene (46 mL, sparged with N₂ immediately before use) was added using positive pressure cannulation. The dark orange catalyst solution turned olive green immediately after the addition of β -ketoester **14a**. The solution was stirred at 30 °C for 32 h, allowed to cool to ambient temperature, filtered through a silica gel plug (2 x 5.5 cm SiO₂, Et₂O), and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO₂, 8 x 12 cm, 19:1 Hexanes:EtOAc, dry-loaded using SiO₂) to afford vinylogous ester **10a** (11.83 g, 50.1 mmol, 94% yield, 88% ee) as a pale yellow oil. (For characterization data, see p. 22).

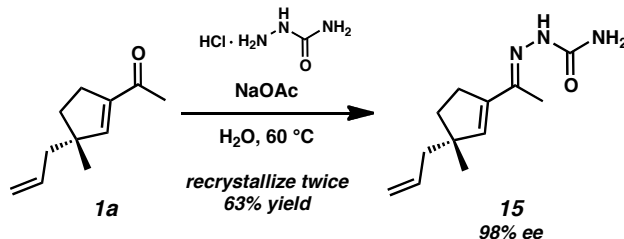


β -Hydroxyketone 12a. A 500 mL round-bottom flask with magnetic stir bar was charged with Et_2O (150 mL) and cooled to $0\text{ }^\circ\text{C}$. LiAlH_4 (1.04 g, 0.0275 mol, 0.55 equiv) was added in one portion. After 10 min, a solution of vinyllogous ester **10a** (11.83 g, 50 mmol, 1.0 equiv) in Et_2O (50 and 25 mL for quantitative transfer) was added dropwise using positive pressure cannulation. The grey suspension was stirred for 60 min after which LiAlH_4 (190 mg, 5.0 mmol, 0.1 equiv) was added in one portion. After an additional 10 min of stirring at $0\text{ }^\circ\text{C}$, the reaction was quenched by slow addition of aqueous HCl (143 mL, 10% w/w). The resulting biphasic system was allowed to warm to ambient temperature and stirred vigorously for 10 h. The reaction was diluted with Et_2O , the phases were separated and the aqueous phase was extracted with Et_2O (3 x 150 mL). The combined organic phases were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude product was azeotroped with toluene (50 mL) and purified using flash column chromatography (SiO_2 , 8 x 13 cm, 9:1 \rightarrow 3:1 Hexanes: EtOAc , dry-loaded using Celite) to afford β -hydroxyketone **12a** (7.25 g, 39.8 mmol, 81% yield) as a colorless semi-solid. (For characterization data, see p. 33).



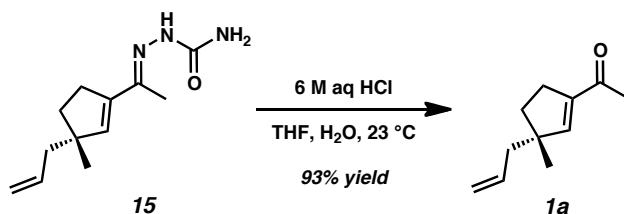
Acylcyclopentene 1a. Alcohol **12a** (7.25 g, 39.8 mmol, 1.0 equiv) was dissolved in THF (400 mL) in a 1 L round-bottom flask. The solution was treated with 2,2,2-trifluoroethanol (5.99 g, 4.36 mL, 59.7 mmol, 1.5 equiv) and LiOH (1.43 g, 59.7 mmol, 1.5 equiv). The flask was fitted with a reflux condenser, purged with N_2 , and heated to $60\text{ }^\circ\text{C}$ using an oil bath. After 18 h of stirring, the suspension was allowed to cool to ambient temperature, diluted with Et_2O (200 mL), stirred with Na_2SO_4 for 30 min, filtered, and concentrated carefully under reduced pressure, allowing for a film of ice to form on the outside of the flask. The crude product was purified using flash column chromatography (SiO_2 , 8 x 12 cm, 15:1 \rightarrow 9:1 Pentane: Et_2O) to afford acylcyclopentene **1a** (5.93 g, 36.1 mmol, 91% yield) as a colorless fragrant oil. (For characterization data, see p. 33).

Procedures for the Synthesis of Acylcyclopentene Derivatives



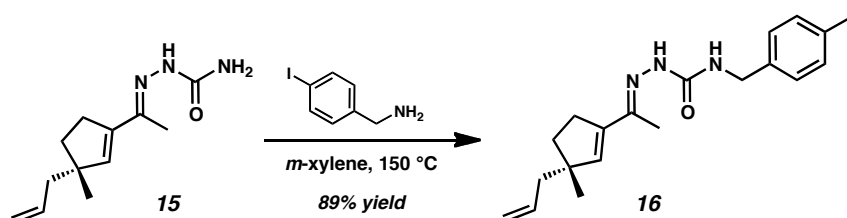
Semicarbazone 1a. A 15 mL round-bottom flask was charged with sodium acetate (150 mg, 1.83 mmol, 1.20 equiv), semicarbazide hydrochloride (204 mg, 1.83 mmol, 1.20 equiv), and a magnetic stir bar. Purified water (1.7 mL) was added and the mixture was stirred until all the solids had dissolved. Acylcyclopentene **1a** (250 mg, 1.52 mmol, 1.00 equiv) was added neat and the mixture was heated to 60 °C for 4 h. The slurry was allowed to cool to ambient temperature while stirring and vacuum filtered (water aspirator). The white solid was dried under reduced pressure to afford semicarbazone **15** (311 mg, 1.40 mmol, 92% yield). The ee of the semicarbazone at this point was found to be 91% (measured by hydrolysis to ketone **1a**, GC conditions: 80 °C isothermal for 90 min, G-TA column, t_r (min): acylcyclopentene **1a** = 54.98).

The semicarbazone **15** (300 mg, 1.36 mmol) was transferred to a round-bottom flask, the solids were suspended in toluene-hexanes (50:50), and the mixture was heated to 90 °C while stirring. After a few min of stirring, the solids had dissolved completely to afford a clear, colorless solution. Heating was discontinued and the stirring mixture was allowed to cool to ambient temperature while still immersed in the oil bath. After 10 h had elapsed, the slurry was vacuum filtered to afford **15** (246 mg, 1.11 mmol, 82% yield, 63% overall yield after recrystallizing twice). The ee at this point was found to be 94.5% (measured by hydrolysis to ketone **1a**). A second recrystallization following the above procedure employing **15** (241 mg, 1.09 mmol) afforded **15** (201 mg, 0.91 mmol, 83% yield). The ee at this point was found to be 97.9% (measured by hydrolysis to ketone **1a**); R_f = 0.30 (9:1 CHCl_3 -MeOH); ^1H NMR (300 MHz, CDCl_3) δ 8.52 (br s, 1H), 6.06 (br s, 1H), 5.85 (app t, J = 1.6 Hz, 1H), 5.76 (dddd, J = 16.7, 9.3, 7.4, 7.4 Hz, 1H), 5.47 (br s, 1H), 5.06–4.98 (m, 2H), 2.67–2.49 (m, 2H), 2.15–2.12 (m, 2H), 1.98 (s, 3H), 1.82 (ddd, J = 12.8, 8.2, 6.9 Hz, 1H), 1.62 (ddd, J = 12.8, 8.5, 6.4 Hz, 1H), 1.07 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.1, 145.0, 141.7, 141.2, 135.6, 117.2, 49.2, 45.9, 36.2, 30.8, 26.3, 12.8; IR (Neat Film NaCl) 3473, 3266, 3189, 2946, 2858, 1698, 1579, 1478, 1437, 1377, 1349, 1321, 1130, 1109, 993, 910, 845, 768 cm^{-1} ; HRMS (ESI+) m/z calc'd for $\text{C}_{12}\text{H}_{20}\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$: 222.1606; found 222.1610; $[\alpha]_D^{22.6}$ +39.80 (c 0.84, CHCl_3 , 97.9% ee); mp = 145–146 °C (1:1 toluene-hexanes).

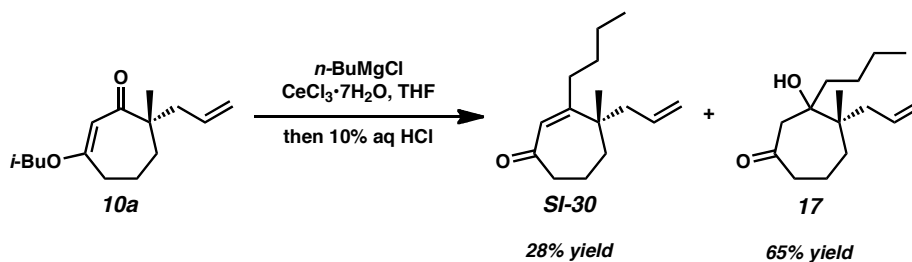


Acylcyclopentene 1a. A solution of semicarbazone **15** (191.8 mg, 0.867 mmol, 1.00 equiv) in THF (1.92 mL) was treated with aqueous HCl (3.84 mL, 6.0 M, in H_2O) was added. The

resulting biphasic mixture was stirred vigorously at ambient temperature for 30 h. The reaction was diluted with Et₂O (10 mL), the phases were separated, and the aqueous phase was extracted with Et₂O (2 x 10 mL). The combined organics were dried over MgSO₄, filtered, and concentrated carefully under reduced pressure, allowing for a film of ice to form on the outside of the flask. The residue was filtered through a short silica gel plug (1 x 10 cm SiO₂, 4:1 Hexanes:Et₂O) to afford acylcyclopentene **1a** (132.6 mg, 0.81 mmol, 93% yield); [α]_D^{22.6} +39.80° (*c* 0.84, CHCl₃, 97.9% ee). (For characterization data, see p. 33).



Iodoarene 16. To a solution of semicarbazone **15** (50 mg, 0.23 mmol, 1.00 equiv) in *m*-xylene (2.2 mL) was added 4-iodo-benzylamine (63 mg, 0.27 mmol, 1.17 equiv). The resulting pale yellow solution was immersed in an oil bath and heated to 150 °C. After 9 h of stirring at 150 °C, the reaction was allowed to cool to ambient temperature and concentrated under reduced pressure to afford a pale yellow solid. The crude solid was purified by flash column chromatography (1.0 x 15 cm SiO₂, 9:1→7:3 Hexanes:EtOAc) to afford iodoarene **16** (88 mg, 0.20 mmol, 89% yield) as a white solid. X-ray quality crystals were obtained by slow vapor diffusion of pentane into a chloroform solution of **16**; *R*_f = 0.52 (9:1 CHCl₃-MeOH); ¹H NMR (500 MHz, CDCl₃) δ 7.88 (s, 1H), 7.66–7.64 (m, 2H), 7.08 (d, *J* = 8.5 Hz, 2H), 6.50 (t, *J* = 6.1 Hz, 1H), 5.86 (app t, *J* = 1.5 Hz, 1H), 5.76 (dddd, *J* = 16.9, 9.0, 7.6, 7.6 Hz, 1H), 5.04–5.01 (m, 2H), 4.46 (d, *J* = 6.3 Hz, 2H), 2.60–2.49 (m, 2H), 2.18–2.10 (m, 2H); 1.95 (s, 3H), 1.82 (ddd, *J* = 12.9, 8.5, 6.3 Hz, 1H), 1.62 (ddd, *J* = 12.9, 8.5, 6.1 Hz, 1H), 1.07 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 156.3, 144.5, 141.5, 141.4, 139.2, 137.8, 135.6, 129.4, 117.2, 92.6, 49.3, 45.9, 43.2, 36.2, 30.9, 26.3, 12.5; IR (Neat Film NaCl) 3411, 3194, 3075, 2946, 2920, 2863, 1677, 1528, 1486, 1401, 1323, 1259, 1142, 1114, 1057, 1000, 913, 845 cm⁻¹; HRMS (FAB+) *m/z* calc'd for C₁₉H₂₅N₃OI [M+H]⁺: 438.1043; found 438.1036; [α]_D^{22.2} +31.43 (*c* 0.36, CHCl₃, 91.0% ee); mp = 123–124 °C (CHCl₃-*n*-pentane).

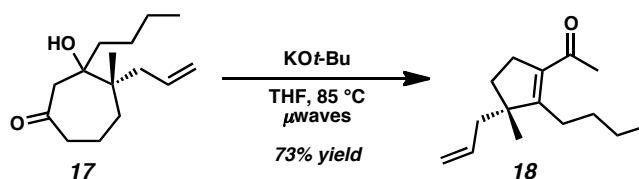


Acylcyclopentene SI-30 and β -Hydroxyketone 17. CeCl₃·7H₂O (419 mg, 1.13 mmol, 2.55 equiv) in a 100 mL round-bottom flask was immersed in a preheated oil bath at 150 °C and placed under vacuum for 4 h while stirring. The flask was cooled to ambient temperature, backfilled with N₂, and charged with THF (4 mL). After 15 h of stirring, additional THF (4 mL)

and *n*-butylmagnesium chloride solution (1.2 mL, 1.86 M in THF, 2.23 mmol, 5.02 equiv) were added to the flask. The resulting slurry was stirred for 4.25 h before vinylogous ester **10a** (105 mg, 0.444 mmol, 1.00 equiv) dissolved in THF (1 mL) was added using positive pressure cannulation followed by two THF rinses (2 x 0.5 mL). After 45 min of stirring, the reaction was quenched by addition of 10% w/w HCl (10 mL). The phases were separated and the aqueous layer was extracted with ethyl acetate (3 x 15 mL). The combined organic phases were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography using a Teledyne Isco CombiFlash R_f system (SiO₂, 25 g loading cartridge, 12 g column, multi-step gradient, hold 0% [1 min]→ramp to 10% [5 min]→hold 10% [31 min]→100% EtOAc in Hexanes [10 min]) to afford acylcyclopentene **30** (28 mg, 0.13 mmol, 28% yield) and β-hydroxyketone **17** (69 mg, 0.29 mmol, 65% yield) as pale yellow oils.

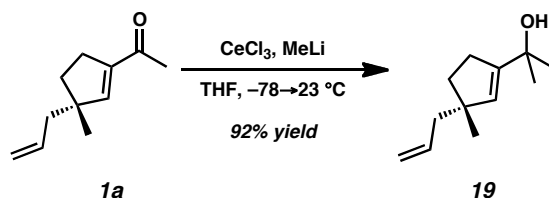
Acylcyclopentene SI-30. R_f = 0.68 (30% EtOAc in Hexanes); ¹H NMR (500 MHz, CDCl₃) δ 5.89 (s, 1H), 5.63 (dddd, *J* = 16.9, 10.3, 7.9, 6.7 Hz, 1H), 5.10–4.98 (m, 2H), 2.61–2.54 (m, 2H), 2.37 (dddd, *J* = 14.1, 6.7, 1.3, 1.3 Hz, 1H), 2.18–2.03 (m, 3H), 1.85–1.72 (m, 3H), 1.66–1.56 (m, 1H), 1.53–1.43 (m, 2H), 1.37 (app. septuplet, *J* = 7.3 Hz, 2H), 1.15 (s, 3H), 0.92 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 205.4, 163.0, 134.2, 128.7, 118.1, 45.7, 45.3, 44.4, 38.8, 34.0, 32.4, 25.7, 23.0, 17.6, 14.1; IR (Neat Film NaCl) 3076, 2957, 2933, 2872, 1652, 1611, 1467, 1414, 1379, 1342, 1263, 1218, 1178, 1109, 1072, 996, 962, 914, 841, 780, 713 cm⁻¹; HRMS (MM: ESI–APCI+) calc'd for C₁₅H₂₅O [M+H]⁺: 221.1900; found 221.1905; [α]_D^{25.0} –33.17 (*c* 1.17, CHCl₃, 88.0% ee).

β-Hydroxyketone 17. R_f = 0.48 (30% EtOAc in Hexanes); ¹H NMR (500 MHz, CDCl₃) mixture of two diastereomers, see **Figure SI-66**; IR (Neat Film NaCl) 3502, 3073, 2956, 2871, 1695, 1638, 1468, 1404, 1380, 1341, 1286, 1181, 1125, 1052, 1028, 998, 913, 868, 796, 732 cm⁻¹; HRMS (MM: ESI–APCI+) calc'd for C₁₅H₂₇O₂ [M+H]⁺: 239.2006; found 239.2013.

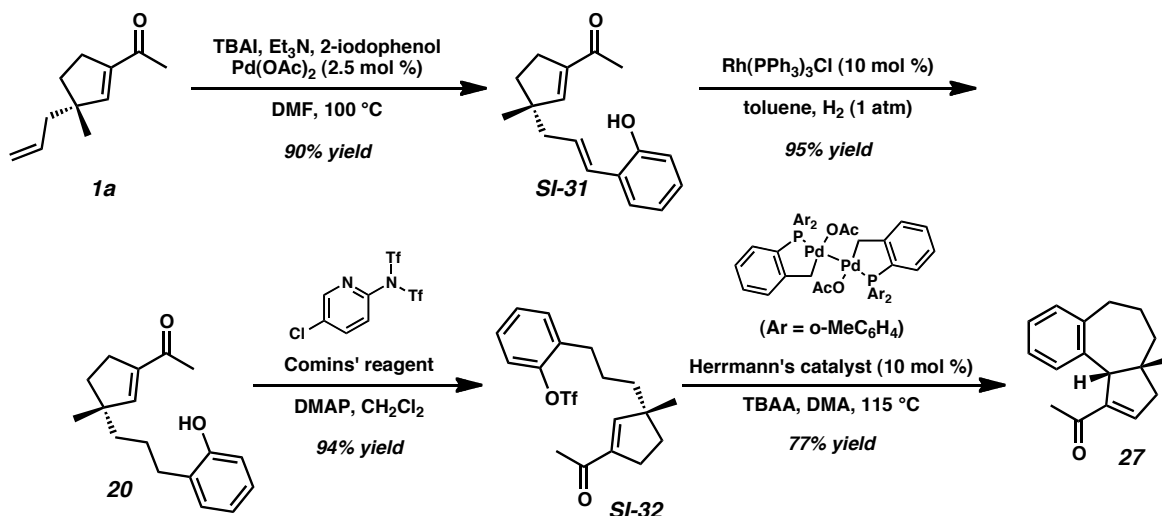


Acylcyclopentene 18. KO^t-Bu (32 mg, 0.283 mmol, 1.62 equiv), THF (1.75 mL), and β-hydroxyketone **17** (175 μL, 1.0 M in benzene, 0.175 mmol, 1.00 equiv) were added to a 0.5–2.0 mL microwave vial with a magnetic spin vane. The pale yellow solution was subjected to microwave irradiation in a Biotage Initiator microwave reactor (temperature: 85 °C, sensitivity: normal). After 5 min of irradiation, the crimp cap was removed and Na₂SO₄ was added to the vial. The contents were filtered through a silica gel plug with Et₂O, concentrated under reduced pressure, and purified by flash column chromatography (5% Et₂O in Pentane) to yield acylcyclopentene **18** (31 mg, 0.14 mmol, 73% yield) as a pale yellow oil; R_f = 0.81 (30% EtOAc in Hexanes); ¹H NMR (500 MHz, CDCl₃) δ 5.77–5.65 (m, 1H), 5.08–5.00 (m, 2H), 2.60–2.49 (m, 2H), 2.45–2.37 (m, 1H), 2.24–2.17 (m, 4H), 2.15–2.10 (m, 2H), 1.85 (ddd, *J* = 12.8, 7.7, 6.2 Hz, 1H), 1.60–1.51 (m, 1H), 1.47–1.34 (m, 4H), 1.06 (s, 3H), 0.93 (t, *J* = 7.1 Hz, 3H); ¹³C NMR

(125 MHz, CDCl₃) δ 198.8, 164.2, 135.0, 134.7, 117.6, 52.6, 43.8, 35.0, 32.1, 31.5, 30.4, 27.6, 24.7, 23.8, 14.0; IR (Neat film NaCl) 3075, 3002, 2957, 2930, 2870, 2859, 1677, 1653, 1639, 1602, 1456, 1432, 1373, 1355, 1311, 1275, 1258, 1188, 1141, 1089, 995, 959, 913, 848, 801, 726 cm⁻¹; HRMS (MM: ESI-APCI+) calc'd for C₁₅H₂₅O [M+H]⁺: 221.1900; found 221.1900; $[\alpha]_D^{25.0}$ -1.44 (*c* 1.35, CHCl₃, 88.0% ee).



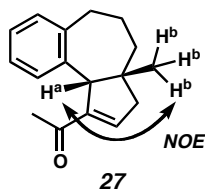
Alcohol 19. CeCl₃ (187 mg, 0.759 mmol, 2.50 equiv) was weighed out in a glovebox and placed in a 25 mL round-bottom flask. The flask was sealed with a septum and removed from the glovebox. THF (3 mL) was added to the flask, the suspension was cooled to -78 °C using an acetone/CO₂ (s) bath, and MeLi (326 μ L, 0.912 mmol, 2.80 M in DME, 3.00 equiv) was added in a dropwise manner. The resulting pale brown suspension was stirred at -78 °C for 30 min. Acylcyclopentene **1a** (50.0 mg, 0.304 mmol, 1.00 equiv) was added neat to the reaction in a dropwise manner. After 30 min of stirring at -78 °C, the reaction was quenched by dropwise addition of sat aqueous NH₄Cl (1.0 mL), the cooling bath was removed, and the reaction was allowed to warm to ambient temperature. The reaction was diluted with Et₂O (10 mL) and H₂O (10 mL) and the phases were separated. The aqueous phase was extracted with Et₂O (3 x 15 mL) and the combined organic phases were washed with brine (10 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by automated flash column chromatography using a Teledyne Isco CombiFlash R_f (SiO₂, 5 g loading cartridge, 12 g column, multi-step gradient, 5% [5 min]→10% Et₂O in Pentane) to afford alcohol **19** (50.4 mg, 0.280 mmol, 92% yield) as a pale yellow oil; *R_f* = 0.31 (4:1 Hexanes:EtOAc); ¹H NMR (400 MHz, CDCl₃) δ 5.78 (dddd, *J* = 14.7, 11.8, 9.3, 7.4 Hz, 1H), 5.34 (dd, *J* = 1.8, 1.8 Hz, 1H), 5.04–5.00 (m, 1H), 5.00–4.97 (m, 1H), 2.45–2.29 (m, 2H), 2.18–2.00 (m, 2H), 1.81 (ddd, *J* = 12.7, 8.3, 6.0 Hz, 1H), 1.60 (ddd, *J* = 12.7, 8.5, 6.1 Hz, 1H), 1.44 (br s, 1H), 1.34 (s, 6H), 1.02 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 149.7, 136.21, 131.6, 116.7, 70.9, 48.2, 46.2, 36.9, 30.9, 29.3, 29.3, 26.5; IR (Neat Film NaCl) 3370, 3077, 2973, 2943, 2859, 1637, 1454, 1412, 1367, 1328, 1254, 1212, 1162, 1137, 997, 960, 940, 910, 853, 806 cm⁻¹; HRMS (MM: ESI-APCI+) *m/z* calc'd for C₁₂H₁₉ [M-OH]⁺: 163.1481; found 163.1482; $[\alpha]_D^{25.0}$ +5.34 (*c* 1.16, CHCl₃, 88.0% ee).



Phenol 20. DMF (1.52 mL) was sparged with N₂ in a 25 mL Schlenk flask for 1 h. Et₃N (0.849 mL, 6.09 mmol, 5.0 equiv), TBAI (450 mg, 1.22 mmol, 1.0 equiv) and 2-iodophenol (282.2 mg, 1.28 mmol, 1.05 equiv) were added, followed by Pd(OAc)₂ (6.84 mg, 0.030 mmol, 2.5 mol %). The flask was carefully evacuated/backfilled with N₂ (3 cycles, 1 min evacuation per cycle) followed by addition of acylcyclopentene **1a** (200 mg, 1.22 mmol, 1.0 equiv). The suspension was immersed in an oil bath at 100 °C. The reaction turned orange within 15 min of stirring. After 5 h of stirring, the reaction was allowed to cool to ambient temperature, diluted with EtOAc (10 mL), and poured into aqueous HCl (10 mL, 1.0 M). The phases were separated and the aqueous phase was extracted with EtOAc (2 x 10 mL). The combined organic phases were washed with brine (10 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography using a Teledyne Isco CombiFlash R_f system (SiO₂, 12 g loading cartridge, 40 g column, linear gradient, 5%→30% EtOAc in Hexanes [25 min]) to afford styrenyl phenol **SI-31** (283.0 mg, 1.10 mmol, 90% yield) as a colorless oil. R_f = 0.17 (4:1 Hexanes:EtOAc).

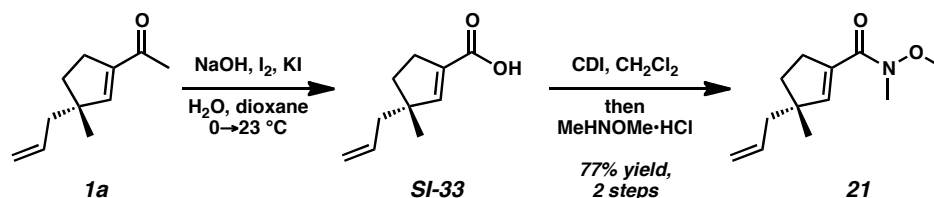
Rh(PPh₃)₃Cl (22.2 mg, 0.024 mmol, 0.10 equiv) was weighed out in a glove box and added to a long reaction tube with magnetic stir bar. Styrenyl phenol **SI-31** (61.5 mg, 0.240 mmol, 1.0 equiv) was dissolved in toluene (4.8 mL) and added to the reaction tube using positive pressure cannulation. H₂ was bubbled through the suspension for 5 min and the reaction tube was fitted with a balloon containing H₂ (1 atm). The reaction was stirred for an additional 6 h at which point TLC analysis indicated complete conversion of the starting material. The resulting clear orange reaction mixture was adsorbed onto a 12 g Isco loading cartridge and purified by flash column chromatography using a Teledyne Isco CombiFlash R_f system (SiO₂, 12 g loading cartridge, 24 g column, linear gradient, 5%→50% Et₂O in Hexanes [40 min]) to afford phenol **20** (58.9 mg, 0.228 mmol, 95% yield) as a pale yellow oil; R_f = 0.18 (4:1 Hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 7.13–7.04 (m, 2H), 6.87 (t, *J* = 7.4 Hz, 1H), 6.75 (d, *J* = 7.9 Hz, 1H), 6.46 (app t, *J* = 1.7 Hz, 1H), 4.82 (bs, 1H), 2.60 (t, *J* = 7.3 Hz, 2H), 2.56–2.50 (m, 2H), 2.29 (s, 3H), 1.87–1.75 (m, 1H), 1.71–1.42 (m, 5H), 1.09 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 197.9, 153.6, 152.8, 143.4, 130.4, 128.4, 127.3, 120.9, 115.3, 50.1, 40.8, 36.2, 30.8, 29.7, 26.8, 25.8, 25.5; IR (Neat Film NaCl) 3344, 3054, 3039, 2951, 2863, 1651, 1610, 1592, 1507, 1455, 1377, 1365, 1313, 1272, 1238, 1179, 1155, 1127, 1106, 1042, 907, 853, 752 cm⁻¹; HRMS (MM: ESI-APCI+) *m/z* calc'd for C₁₇H₂₃O₂ [M+H]⁺: 259.1693; found 259.1691; [α]_D^{25.0} +28.73 (c 0.74, CHCl₃, 88.0% ee).

Triflate SI-32. To a solution of phenol **20** (104.2 mg, 0.40 mmol, 1.00 equiv) in CH₂Cl₂ (8.0 mL) in a 20 mL vial was added DMAP (97.8 mg, 0.80 mmol, 2.0 equiv) in one portion, followed by *N,N*-Bis(trifluoromethylsulfonyl)-5-chloro-2-pyridylamine (172.8 mg, 0.44 mmol, 1.1 equiv). After 15 min of stirring at ambient temperature, TLC revealed full conversion of phenol **20**. The reaction mixture was adsorbed onto a 12 g Isco loading cartridge and purified by flash column chromatography using a Teledyne Isco CombiFlash R_f system (SiO₂, 12 g loading cartridge, 40 g column, linear gradient, 5→20% EtOAc in Hexanes [25 min]) to afford triflate **SI-32** (146.2 mg, 0.374 mmol, 94% yield) as a clear, colorless oil; R_f = 0.44. (4:1 Hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 7.32–7.30 (m, 2H), 7.28 (dd, *J* = 8.5, 4.0 Hz, 1H), 7.24 (dm, *J* = 7.8 Hz, 1H), 6.44 (app t, *J* = 1.8 Hz, 1H), 2.69 (t, *J* = 7.7 Hz, 2H), 2.61–2.46 (m, 2H), 2.29 (s, 3H), 1.80 (ddd, *J* = 13.0, 8.7, 6.5 Hz, 1H), 1.66 (ddd, *J* = 11.8, 8.0, 5.2 Hz, 1H), 1.64–1.45 (m, 3H), 1.50 (ddd, *J* = 11.4, 7.5, 5.1 Hz, 1H), 1.10 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 197.6, 152.0, 148.1, 143.7, 135.1, 131.3, 128.5, 128.0, 121.5, 118.7 (q, *J* = 320 Hz, 1C), 50.0, 40.7, 36.1, 30.8, 29.8, 26.8, 25.8, 25.7; IR (Neat Film NaCl) 3032, 2958, 2868, 1671, 1617, 1486, 1454, 1420, 1365, 1303, 1251, 1217, 1140, 1100, 1073, 893, 814, 767 cm⁻¹; HRMS (MM: ESI-APCI+) *m/z* calc'd for C₁₈H₂₂F₃O₄S [M+H]⁺: 391.1188; found 391.1193; [α]_D^{25.0} +22.00 (c 1.31, CHCl₃, 88.0% ee).



Acylcyclopentene 27. To a solution of triflate **SI-32** (30.0 mg, 0.077 mmol, 1.0 equiv) in dry DMA (1.54 mL) in a 4 dram vial was added TBAA (57.9 mg, 0.19 mmol, 2.5 equiv, stored and weighed out in a glovebox). The resulting clear, colorless solution was degassed by bubbling Ar through the solution for 1 h. Herrmann's catalyst^[81] (7.2 mg, 7.7 μmol, 0.10 equiv) was placed in a reaction tube which was subsequently evacuated/backfilled with Ar (3 cycles, 1 min evacuation per cycle). The solution containing triflate **SI-32** was added to the catalyst using positive pressure cannulation. The resulting pale green-yellow solution was immersed in an oil bath at ambient temperature and heated to 115 °C. After 2 h of stirring, the reaction was allowed to cool to ambient temperature, diluted with EtOAc (10 mL), and poured into aqueous HCl (1.0 M, 5.0 mL). The phases were separated and the aqueous phase was extracted with EtOAc (10 mL). The combined organics were washed with brine (5.0 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography using a Teledyne Isco CombiFlash R_f system (SiO₂, 2.5 g loading cartridge, 4 g column, multi-step gradient, hold 5% [10 min]→hold 10% [4 min]→hold 20% [3 min]→hold 60% EtOAc in Hexanes [3 min]) to afford acylcyclopentene **27** (14.3 mg, 0.0595 mmol, 77% yield, 62% yield over 4 steps) as a pale yellow solid. The relative stereochemistry was assigned based on strong NOE interaction between H^a and H^b; R_f = 0.46 (4:1 Hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 7.17–7.06 (m, 3H), 6.95 (app t, *J* = 2.4 Hz, 1H), 6.63 (bd, *J* = 6.2 Hz, 1H), 3.86 (s, 1H), 2.92–2.84 (m, 1H), 2.66 (app dd, *J* = 13.5, 7.9 Hz, 1H), 2.41 (s, 3H), 2.32–2.18 (m, 2H) 1.84 (app ddt, *J* = 13.5, 7.7, 5.6 Hz, 1H), 1.58–1.43 (m, 1H), 1.30 (ddd, *J* = 14.0, 5.1, 2.3 Hz, 1H), 1.18 (s, 3H), 0.85 (app dt, *J* = 13.5, 5.6 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 196.7, 146.2, 144.6, 139.6, 139.2, 128.5, 126.7, 126.2, 125.0, 55.5, 48.4, 43.9, 34.1, 30.6, 26.9, 25.9,

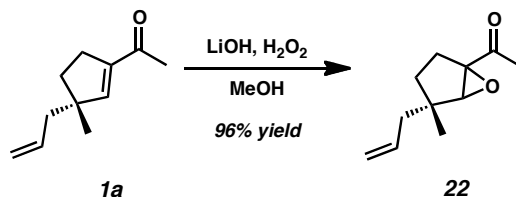
21.4; IR (Neat Film NaCl) 3062, 3012, 2933, 2893, 2859, 1659, 1617, 1476, 1456, 1446, 1370, 1278, 1266, 1244, 1199, 1123, 997, 935, 794, 757, 752, 730 cm^{-1} ; HRMS (MM: ESI-APCI+) m/z calc'd for $\text{C}_{17}\text{H}_{21}\text{O}$ $[\text{M}+\text{H}]^+$: 241.1587; found 241.1591; $[\alpha]_{\text{D}}^{25.0} +3.88$ (c 1.43, CHCl_3 , 88.0% ee).



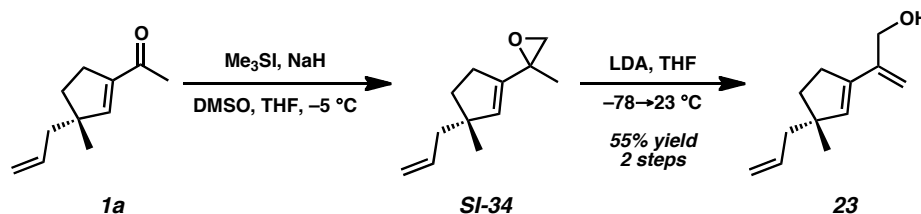
Carboxylic acid SI-33. A 50 mL round-bottom flask with magnetic stir bar was charged with acylcyclopentene **1a** (200 mg, 1.22 mmol, 1.00 equiv) and dioxane (10 mL). The solution was cooled to 0 °C and 5 M aqueous NaOH (10 mL) was added dropwise. The white suspension was stirred for 5 min at 0 °C. A dark brown solution of I_2 (1.37 g, 5.40 mmol, 4.40 equiv) and KI (2.09 g, 12.59 mmol, 10.50 equiv) in purified H_2O (10 mL) was added to the reaction dropwise, causing the reaction to become a yellow suspension. After 6.5 h of stirring at 0 °C, an additional portion of I_2 (343 mg, 1.35 mmol, 1.11 equiv) in dioxane (2 mL) was added to the reaction. After 30 min of stirring at 0 °C, the reaction was acidified to pH 2 using 2 M aqueous HCl. The reaction was extracted with Et_2O (3 x 30 mL) until the organic layer was clear. The combined organic phases were washed with sat aqueous $\text{K}_2\text{S}_2\text{O}_3$ (2 x 10 mL), H_2O (2 x 10 mL), and brine (2 x 10 mL). The combined organic phases were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure to give a yellow semi-solid. The residue was taken up in EtOAc, filtered through a silica gel plug (3 x 3 cm, EtOAc), and concentrated to give carboxylic acid **SI-33** as a pale yellow oil which was used directly in the next step; $R_f = 0.35$, broad (2:1 Hexanes:EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 6.69 (app t, $J = 1.9$ Hz, 1H), 5.89–5.62 (m, 1H), 5.11–4.99 (m, 2H), 2.68–2.47 (m, 2H), 2.26–2.09 (m, 2H), 1.91 (ddd, $J = 13.0, 8.2, 7.0$ Hz, 1H), 1.69 (ddd, $J = 13.0, 8.2, 6.2$ Hz, 1H), 1.10 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.7, 154.3, 134.8, 133.9, 117.8, 49.8, 45.2, 36.3, 30.3, 25.5; IR (Neat Film NaCl) 3076, 3004, 2956, 2926, 2865, 2610, 1687, 1634, 1454, 1424, 1374, 1348, 1306, 1280, 1216, 1180, 1083, 995, 915, 745, 720 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_7\text{H}_9\text{O}_2$ $[\text{M}-\text{C}_3\text{H}_5]^+$: 125.0603; found 125.0629; $[\alpha]_{\text{D}}^{25.0} +1.43$ (c 0.80, CHCl_3 , 88.0% ee).

Amide 21. A 50 mL flask with magnetic stir bar was charged with carboxylic acid **SI-33** (202.7 mg, 1.22 mmol, 1.00 equiv) and anhydrous CH_2Cl_2 (4.0 mL). To the vigorously stirred reaction was added 1,1'-carbonyldiimidazole (217 mg, 1.34 mmol, 1.10 equiv) in a portionwise manner. After 15 min, anhydrous *N,O*-dimethylhydroxylamine hydrochloride (143 mg, 1.46 mmol, 1.20 equiv) was added portionwise. The reaction became turbid after several min. After 21 h, an additional portion of *N,O*-dimethylhydroxylamine hydrochloride (14.3 mg, 0.146 mmol, 0.12 equiv) was added. At 23.5 h, the reaction was transferred to a separatory funnel, washed with 0.25 M HCl (2 x 2 mL), sat aqueous NaHCO_3 , and brine. The combined organic phases were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2 , 3 x 25 cm, 4:1 \rightarrow 3:1 Hexanes:EtOAc) to afford amide **21** as a clear oil (196.7 mg, 0.94 mmol, 77% yield over 2 steps); $R_f = 0.41$ (2:1 Hexanes:EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 6.26 (app t, $J = 1.9$ Hz, 1H), 5.87–5.68 (m, 1H), 5.09–4.97 (m, 2H), 3.63 (s, 3H), 3.23 (s, 3H), 2.77–2.55 (m, 2H), 2.21–2.11 (m, 2H), 1.83 (ddd, $J = 12.8, 8.3,$

6.4 Hz, 1H), 1.62 (ddd, $J = 12.7, 8.4, 6.0$ Hz, 1H), 1.08 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 167.5, 147.0, 135.4, 135.3, 117.4, 61.2, 49.4, 45.4, 35.9, 33.3, 32.9, 25.6; IR (Neat Film NaCl) 3584, 3401, 3078, 2954, 2930, 2864, 1641, 1609, 1454, 1441, 1414, 1378, 1329, 1198, 1177, 1152, 1105, 1043, 997, 969, 914, 812, 723 cm^{-1} ; HRMS (EI+) m/z calc'd for $\text{C}_{12}\text{H}_{20}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 210.1494; found 210.1498; $[\alpha]_{\text{D}}^{25.0} +1.41$ (c 0.98, CHCl_3 , 88.0% ee).



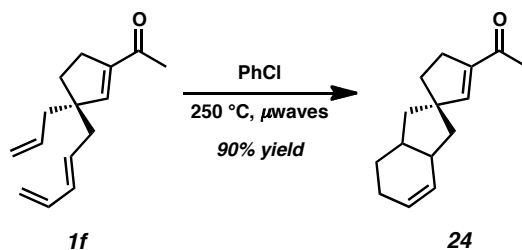
Epoxide 22. A solution of acylcyclopentene **1a** (100 mg, 0.609 mmol, 1.00 equiv) in MeOH (6.1 mL) in a 25 mL round-bottom flask was treated with LiOH (7.3 mg, 0.30 mmol, 0.50 equiv) in one portion. Aqueous H_2O_2 (75.0 μL , 83.3 mg, 2.00 equiv, 50% in H_2O) was added dropwise. After 12 h of stirring at ambient temperature additional aqueous H_2O_2 (75.0 μL , 83.3 mg, 2.00 equiv, 50% in H_2O) was added. The reaction was stirred for an additional 8 h, diluted with CH_2Cl_2 (10 mL), sat aqueous NaHCO_3 (1.0 mL), and water (1.0 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 . The combined organic phases were dried over Mg_2SO_4 , filtered, and concentrated carefully under reduced pressure. The crude product was purified by automated flash column chromatography using a Teledyne Isco CombiFlash R_f (SiO_2 , 12 g loading cartridge, 25 g column, linear gradient, 5% \rightarrow 30% Et_2O in Pentane [15 min]) to afford epoxide **22** (106 mg, 0.588 mmol, 96% yield) as a colorless fragrant oil and as a 1:1.1 mixture of diastereomers; $R_f = 0.54$ (4:1 Hexanes:EtOAc); ^1H NMR (400 MHz, CDCl_3) 5.90–5.68 (m, 2H), 5.14–5.01 (m, 4H), 3.32 (s, 1H), 3.30 (s, 1H), 2.35–2.21 (m, 4H), 2.07 (s, 3H), 2.07 (s, 3H), 2.05–1.99 (m, 2H), 1.96–1.85 (m, 2H), 1.54–1.49 (m, 1H), 1.33–1.29 (m, 2H), 1.20–1.16 (m, 1H), 1.13 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) 205.8, 205.6, 134.7, 133.6, 118.4, 117.8, 70.3, 70.2, 69.4, 69.3, 42.7, 42.7, 42.4, 42.3, 41.3, 31.9, 31.4, 25.0, 24.8, 24.1, 21.7, 20.5; IR (Neat Film NaCl) 3072, 3002, 2958, 2878, 1706, 1642, 1459, 1444, 1419, 1397, 1360, 1325, 1286, 1261, 1115, 922, 856, 831 cm^{-1} ; HRMS (MM: ESI-APCI+) m/z calc'd for $\text{C}_{11}\text{H}_{17}$ $[\text{M}+\text{H}]^+$: 181.1223; found 181.1226; $[\alpha]_{\text{D}}^{25.0} -6.94$ (c 1.40, CHCl_3 , 88.0 % ee).



Allylic alcohol 23. NaH (36.5 mg, 0.91 mmol, 3.0 equiv, 60% w/w in mineral oil) was suspended in DMSO (1.2 mL) in a 25 mL round-bottom flask. After 20 min of stirring at ambient temperature, THF (3.7 mL) was added and the resulting mixture was cooled to $-5\text{ }^\circ\text{C}$ using a water/NaCl/ice bath. Me_3SiI (192.3 mg, 0.95 mmol, 3.1 equiv) was dissolved in DMSO (1.2 mL) and added dropwise to the stirred reaction. After an additional 5 min of stirring, acylcyclopentene **1a** (50 mg, 0.30 mmol, 1.0 equiv) was added neat dropwise. After 1.5 h of

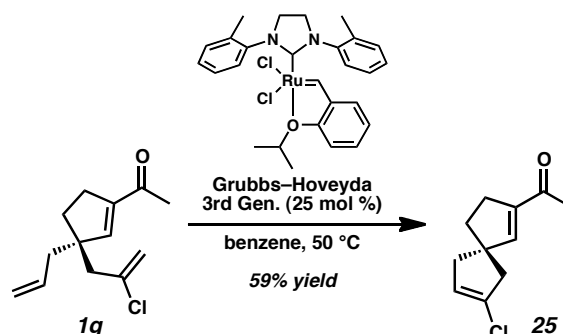
stirring at $-5\text{ }^{\circ}\text{C}$, the reaction was diluted with Et_2O (15 mL) and quenched by pouring the reaction over 10 g of ice. The phases were separated and the aqueous layer was extracted with Et_2O (2 x 10 mL). The combined organic phases were washed with brine (10 mL), dried over MgSO_4 , filtered, and concentrated carefully under reduced pressure, allowing for a film of ice to form on the outside of the flask, to give the volatile crude epoxide **SI-34** as a colorless oil; $R_f = 0.60$ (4:1 Hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3) mixture of two diastereomers, see **Figure SI-75**; $^{13}\text{C NMR}$ (100 MHz, CDCl_3) mixture of two diastereomers, see **Figure SI-75**; IR (Neat Film NaCl) 3072, 3037, 2953, 2923, 2864, 1637, 1451, 1437, 1385, 1370, 1338, 1259, 1140, 1105, 1066, 994, 910, 856, 846, 806, 730 cm^{-1} ; HRMS (APCI+) calc'd for $\text{C}_{12}\text{H}_{19}\text{O}$ $[\text{M}+\text{H}]^+$: 179.1435; found 179.1430.

To a solution of diisopropylamine (0.11 mL, 0.76 mmol, 2.5 equiv) in THF (2.0 mL) in a 10 mL round-bottom flask at $0\text{ }^{\circ}\text{C}$ was added $n\text{-BuLi}$ (370 μL , 0.76 mmol, 2.05 M in cyclohexane, 2.5 equiv) dropwise over 10 min. After 15 min of stirring, the reaction was cooled to $-78\text{ }^{\circ}\text{C}$ using an acetone/ $\text{CO}_2(\text{s})$ bath and crude epoxide **SI-34** in THF (1.0 mL) was added dropwise using positive pressure cannulation. The cooling bath was allowed to warm to ambient temperature and the reaction was stirred for 18 h. The reaction was diluted with Et_2O (10 mL) and quenched by addition of a 50:50 (v/v) mixture of sat aqueous NH_4Cl and water (2.0 mL each). The phases were separated and the aqueous phase was extracted with Et_2O (2 x 10 mL). The combined organic phases were washed with brine (10 mL), dried over MgSO_4 , filtered, and concentrated carefully under reduced pressure, allowing for a film of ice to form on the outside of the flask, to afford a pale yellow oil. The residue was purified by flash column chromatography (SiO_2 , 1 x 22 cm, 20% Et_2O in Pentane) to afford allylic alcohol **23** (29.9 mg, 0.17 mmol, 55% yield over 2 steps) as a colorless oil; $R_f = 0.25$ (4:1 Hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 5.82–5.72 (m, 1H), 5.60 (dd, $J = 1.7, 1.7$ Hz, 1H), 5.22 (app q, $J = 1.4$ Hz, 1H), 5.05–5.04 (m, 1H), 5.04–5.01 (m, 1H), 5.01–4.99 (m, 1H), 4.33 (br s, 2H), 2.58–2.45 (m, 2H), 2.17–2.08 (m, 2H), 1.82 (ddd, $J = 12.7, 8.8, 5.9$ Hz, 1H), 1.62 (ddd, $J = 12.7, 8.8, 5.8$ Hz, 1H), 1.51 (br s, 1H), 1.06 (s, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 143.6, 139.1, 136.0, 135.9, 116.9, 111.9, 64.3, 49.3, 46.2, 35.9, 32.0, 26.4; IR (Neat Film NaCl) 3325, 3071, 3032, 2948, 2859, 1639, 1600, 1451, 1437, 1414, 1370, 1320, 1226, 1194, 1078, 1029, 994, 910, 848 cm^{-1} ; HRMS (MM: ESI-APCI+) m/z calc'd for $\text{C}_{12}\text{H}_{17}$ $[\text{M}-\text{OH}]^+$: 161.1325; found 161.1324; $[\alpha]_{\text{D}}^{25.0} +17.59$ (c 1.38, CHCl_3 , 88.0% ee).

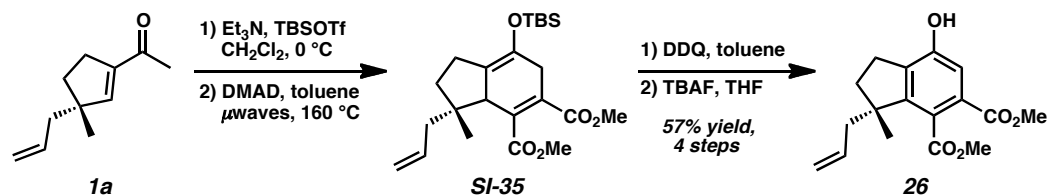


Cyclohexene 24. Acylcyclopentene **1f** (25.2 mg, 0.12 mmol, 1.00 equiv) was added to a 2.0–5.0 mL microwave vial with magnetic stir bar and sealed with a septum-fitted crimp cap. Chlorobenzene (5 mL) was added via syringe. The clear, colorless solution was subjected to microwave irradiation in a Biotage Initiator microwave reactor (temperature: $250\text{ }^{\circ}\text{C}$, sensitivity: low). After 2 h of irradiation, the vial was uncapped and the solvent was removed under reduced pressure. The yellow residue was purified by flash column chromatography (SiO_2 , 1.5 x 15 cm,

15:1 Hexanes:Et₂O) to afford cyclohexene **24** as a yellow oil (22.5 mg, 0.104 mmol, 90% yield); $R_f = 0.65$ (4:1 Hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃) mixture of four diastereomers (2:2:1:1), see **Figure SI-77**; ¹³C NMR (125 MHz, CDCl₃) mixture of four diastereomers, see **Figure SI-77**; IR (Neat Film NaCl) 3014, 2921, 2855, 1666, 1611, 1448, 1437, 1369, 1339, 1303, 1268, 1190, 1093, 1075, 1051, 1037, 1024, 935, 868, 798, 733, 703 cm⁻¹; HRMS (EI+) m/z calc'd for C₁₅H₂₀O [M]⁺: 216.1514; found 216.1518; $[\alpha]_D^{25.0} -15.57$ (*c* 1.01, CHCl₃, 88.0% ee).



Spirocycle 25. A 2-neck flask fitted with rubber septum and reflux condenser under N₂ was charged with Grubbs–Hoveyda 3rd Generation catalyst (2.2 mg, 0.035 mmol, 6.1 mol %). Dry degassed benzene (4 mL, sparged with N₂ for 1 h immediately before use) was added to give a pale green solution. The flask was evacuated/backfilled with N₂ (3 cycles, 5 min evacuation per cycle). Acylcyclopentene **1g** (14.2 mg, 0.063 mmol, 1.0 equiv) in dry, degassed benzene (4 mL) under N₂ was added to the catalyst solution using positive pressure cannulation. The flask was rinsed with benzene (2 mL) and washes were added into the catalyst solution. The reaction was immersed in a preheated 50 °C oil bath and stirred for 44 h. An additional portion of Grubbs–Hoveyda 3rd Generation catalyst (4.4 mg, 0.070 mmol, 12.2 mol %) in degassed benzene (2 mL) was added into the reaction using positive pressure cannulation. After stirring for an additional 15 h, a third portion of Grubbs–Hoveyda 3rd Generation catalyst (2.2 mg, 0.035 mmol, 6.1 mol %) in degassed benzene (2 mL) was added into the reaction using positive pressure cannulation. After 31 h, the reaction was treated with several drops of ethyl vinyl ether and allowed to cool to ambient temperature. The solution was diluted with Et₂O (15 mL) and filtered through a short silica gel plug (2 x 10 cm, Et₂O). The orange filtrate was purified by flash column chromatography (SiO₂, 2 x 25 cm, 1%→3%→5%→6.5% Et₂O in Hexanes) to give volatile spirocycle **25** (7.3 mg, 0.0376 mmol, 59% yield); $R_f = 0.49$ (4:1 Hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 6.61 (app t, $J = 1.7$ Hz, 1H), 5.64 (app p, $J = 2.2$ Hz, 1H), 2.66 (ddd, $J = 16.2, 4.5, 2.1$ Hz, 1H), 2.62–2.53 (m, 3H), 2.51 (ddd, $J = 16.2, 4.6, 2.4$ Hz, 1H), 2.43 (ddd, $J = 16.3, 4.6, 2.4$ Hz, 1H), 2.31 (s, 3H), 2.09–1.95 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 197.3, 150.2, 144.2, 130.7, 125.2, 56.2, 49.7, 44.3, 39.4, 29.6, 26.8; IR (Neat Film NaCl) 2929, 2845, 1726, 1668, 1616, 1436, 1370, 1340, 1314, 1276, 1193, 1079, 1052, 990, 966, 936, 905, 866, 822, 804 cm⁻¹; HRMS (EI+) m/z calc'd for C₁₁H₁₃OCl [M]⁺: 196.0655; found 196.0655; $[\alpha]_D^{25.0} -19.80$ (*c* 0.53, CHCl₃, 88.0% ee).



Phenol 26. A 15 mL flask with magnetic stir bar was charged with acylcyclopentene **1a** (50 mg, 0.274 mmol, 1.00 equiv) and anhydrous CH_2Cl_2 (3.0 mL). The flask was cooled to 0°C and Et_3N (152.8 μL , 1.096 mmol, 4.00 equiv) was added, followed by dropwise addition of TBSOTf (125.8 μL , 0.548 mmol, 2.00 equiv). The reaction became a pale yellow solution. After 1 h of stirring at 0°C , the reaction was quenched by the addition of sat aqueous NaHCO_3 and slowly allowed to warm to ambient temperature. The mixture was extracted with CH_2Cl_2 (3 x 10 mL) and the combined organics were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was filtered through a silica gel plug (2 x 3 cm, 5:1 H:Et₂O) and concentrated under reduced pressure to give crude silyl enol ether as a pale yellow oil. $R_f = 0.79$ (10:1 Hexanes:EtOAc).

The silyl enol ether was added to a 2.0–5.0 mL microwave vial with magnetic stir bar and sealed with a septum-fitted crimp cap. Toluene (5 mL) was added, followed by dimethyl acetylenedicarboxylate (101 μL , 0.822 mmol, 3.00 equiv). The clear, colorless solution was subjected to microwave irradiation in a Biotage Initiator microwave reactor (temperature: 160°C , sensitivity: low). After 2.5 h of irradiation, the vial was uncapped and solvent was removed under reduced pressure. The yellow residue was purified by flash column chromatography (SiO_2 , 3 x 25 cm, 15:1 \rightarrow 10:1 \rightarrow 4:1 \rightarrow 2:1 Hexanes:EtOAc) to afford siloxydiene **SI-35**. $R_f = 0.31$ (10:1 Hexanes:EtOAc).

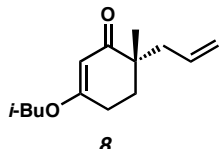
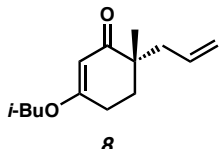
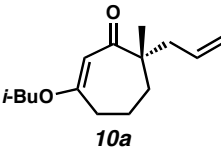
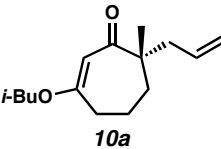
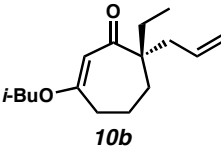
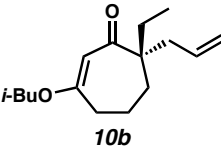
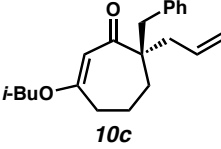
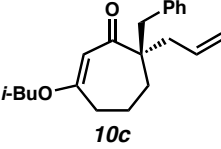
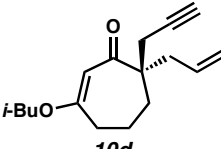
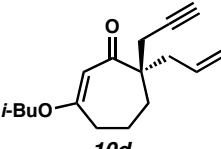
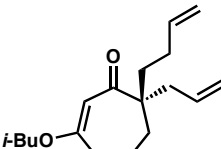
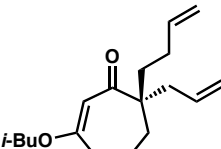
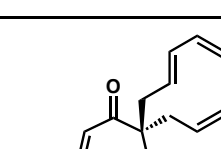
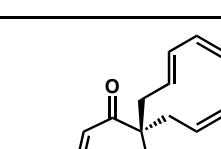
A 20 mL scintillation vial with magnetic stir bar was charged with siloxydiene **SI-35** and toluene (3.0 mL). DDQ (63.5 mg, 0.280 mmol, 1.02 equiv) was added portionwise. Upon complete addition, the solution became a turbid red suspension. After 2 h, the reaction was diluted with CH_2Cl_2 and filtered through a Celite plug (2 x 3 cm, CH_2Cl_2). The clear yellow solution was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2 , 2 x 25 cm, 20:1 \rightarrow 15:1 \rightarrow 10:1 \rightarrow 4:1 \rightarrow 2:1 Hexanes:EtOAc) to afford the intermediate silyl aryl ether. $R_f = 0.31$ (10:1 Hexanes:EtOAc).

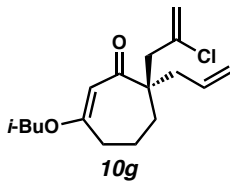
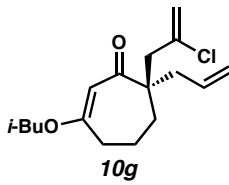
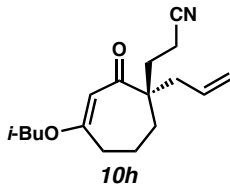
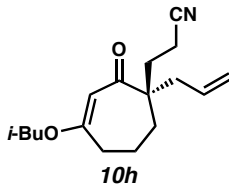
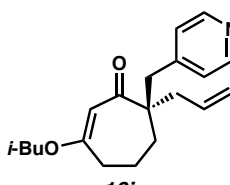
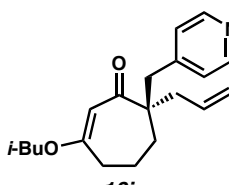
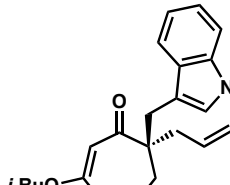
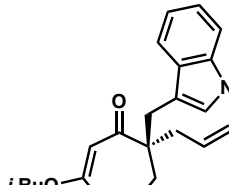
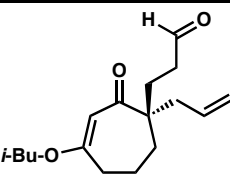
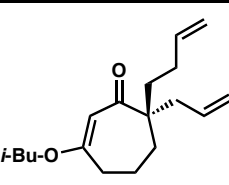
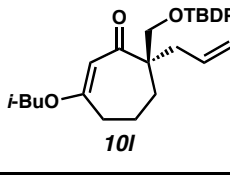
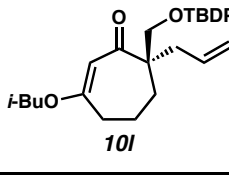
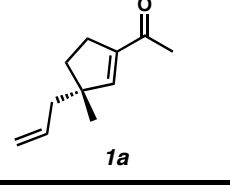
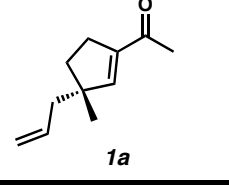
A 20 mL scintillation vial with magnetic stir bar was charged with silyl aryl ether. The vial was evacuated, and backfilled with N_2 . Anhydrous THF (3 mL) was added and a TBAF solution (300 μL , 1.0 M in THF) was added dropwise, giving a bright red solution. After 10 min, the reaction was quenched by the addition of sat aqueous NH_4Cl (600 μL) and H_2O (600 μL). The mixture was stirred vigorously for 20 min and extracted with Et₂O (3 x 5 mL). The combined organics were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2 , 2 x 25 cm, 5:1 \rightarrow 4:1 Hexanes:EtOAc) to afford phenol **26** as a pale yellow oil (52.6 mg, 0.173 mmol, 57% yield over 4 steps); $R_f = 0.11$ (2:1 Hexanes:EtOAc); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.30 (s, 1H), 5.89 (br s, $J = 1.9$ Hz, 1H), 5.66 (dddd, $J = 17.3, 10.2, 7.9, 7.9$ Hz, 1H), 5.09–4.91 (m, 2H), 3.88 (s, 3H), 3.83 (s, 3H), 2.76 (t, $J = 7.3$ Hz, 2H), 2.47–2.26 (m, 2H), 2.24–2.08 (ddd, $J = 12.0, 7.0, 7.0$ Hz, 1H), 1.85–1.70 (ddd, $J = 12.7, 7.6, 7.6$ Hz, 1H), 1.26 (s, 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 170.4, 166.7, 152.5, 150.0, 135.8, 135.3, 128.3, 124.0, 117.7, 115.4, 52.7, 52.5, 49.4, 44.1, 38.3, 26.1, 25.6; IR (Neat Film NaCl) 3401, 3075, 2953, 2871, 1723, 1639, 1588, 1435, 1418, 1376, 1330, 1311, 1258, 1192, 1175, 1142, 1047, 995, 964, 916, 884, 857, 794, 769, 738, 719

cm⁻¹; HRMS (EI+) *m/z* calc'd for C₁₇H₂₀O₅ [M]⁺: 304.1311; found 304.1317; [α]_D^{25.0} -45.63 (c 0.91, CHCl₃, 88.0% ee).

Methods for Determination of Enantiomeric Excess

Table SI-3. Methods for the Determination of Enantiomeric Excess.

entry	product	compound assayed	assay conditions	retention time of major isomer (min)	retention time of minor isomer (min)	% ee
1	 8	 8	HPLC Chiralcel OD-H 5% IPA in hexane isocratic, 1.0 mL/min	5.80	6.53	86
2	 10a	 10a	HPLC Chiralcel OD-H 1% IPA in hexane isocratic, 1.0 mL/min	6.30	7.26	88
3	 10b	 10b	HPLC Chiralcel AD 0.25% IPA in hexane isocratic, 1.0 mL/min	18.08	16.23	92
4	 10c	 10c	HPLC Chiralcel OD-H 0.5% IPA in hexane isocratic, 1.0 mL/min	15.70	13.96	86
5	 10d	 10d	HPLC Chiralcel OD-H 0.5% IPA in hexane isocratic, 1.0 mL/min	12.35	13.43	89
6	 10e	 10e	HPLC Chiralcel AD 0.8% IPA in hexane isocratic, 2.0 mL/min	5.03	6.06	87
7	 10f	 10f	SFC Chiralcel AD-H 5% IPA in hexane isocratic, 2.5 mL/min	6.99	6.31	90

entry	product	compound assayed	assay conditions	retention time of major isomer (min)	retention time of minor isomer (min)	% ee
8	 10g	 10g	HPLC Chiralcel OD-H 0.1% IPA in hexane isocratic, 1.0 mL/min	27.22	24.19	86
9	 10h	 10h	HPLC Chiralcel OD-H 5% IPA in hexane isocratic, 1.0 mL/min	10.67	14.66	87
10	 10i	 10i	HPLC Chiralcel AD 5% EtOH in hexane isocratic, 1.0 mL/min	13.22	15.13	85
11	 10j	 10j	HPLC Chiralcel AD 5% EtOH in hexane isocratic, 1.0 mL/min	11.11	16.64	83
12	 10k	 10e	HPLC Chiralcel AD 0.8% IPA in hexane isocratic, 2.0 mL/min	4.39	5.17	80
13	 10l	 10l	HPLC Chiralcel OD-H 0.2% IPA in hexane isocratic, 1.0 mL/min	21.74	25.53	58
14	 1a	 1a	GC G-TA 80 °C isotherm	54.74	60.24	98

References:

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CALIFORNIA INSTITUTE OF TECHNOLOGY
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X-RAY CRYSTALLOGRAPHY LABORATORY

Crystal Structure Analysis of 16

THJ03

(686849)

Contents:

Table 1. Crystal data

Table 2. Atomic Coordinates

Table 3. Full bond distances and angles

Table 4. Anisotropic displacement parameters

Table 5. Hydrogen bond distances and angles

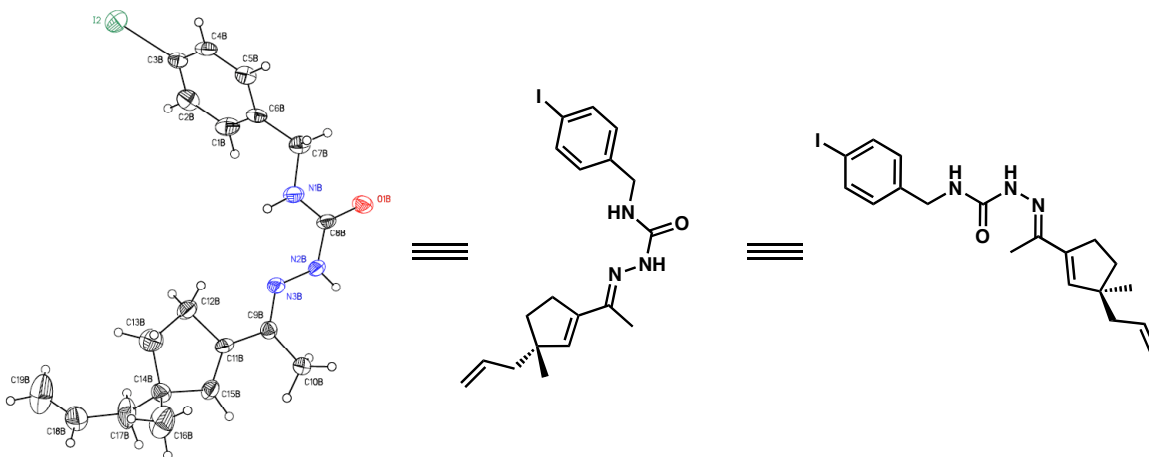


Table 1. Crystal data and structure refinement for THJ03 (CCDC 686849).

Empirical formula	C ₁₉ H ₂₄ N ₃ OI
Formula weight	437.31
Crystallization Solvent	Dichloromethane/pentane
Crystal Habit	Needle
Crystal size	0.28 x 0.11 x 0.07 mm ³
Crystal color	Colorless

Data Collection

Type of diffractometer	Bruker KAPPA APEX II	
Wavelength	0.71073 Å MoK α	
Data Collection Temperature	100(2) K	
θ range for 9911 reflections used in lattice determination	2.57 to 28.78°	
Unit cell dimensions	a = 17.160(4) Å b = 5.5921(14) Å c = 19.984(5) Å	β = 90.689(6)°
Volume	1917.6(8) Å ³	
Z	4	
Crystal system	Monoclinic	
Space group	P2 ₁	
Density (calculated)	1.515 Mg/m ³	
F(000)	880	
Data collection program	Bruker APEX2 v2.1-0	
θ range for data collection	1.55 to 29.84°	
Completeness to θ = 29.84°	88.9 %	
Index ranges	-23 ≤ h ≤ 23, -7 ≤ k ≤ 7, -26 ≤ l ≤ 25	
Data collection scan type	ω scans; 16 settings	
Data reduction program	Bruker SAINT-Plus v7.34A	
Reflections collected	8962	
Independent reflections	8962 [R _{int} = 0.0000]	
Absorption coefficient	1.680 mm ⁻¹	
Absorption correction	Semi-empirical from equivalents (TWNABS)	
Max. and min. transmission	0.7460 and 0.5010	

Table 1 (cont.)**Structure solution and Refinement**

Structure solution program	SHELXS-97 (Sheldrick, 2008)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric positions
Structure refinement program	SHELXL-97 (Sheldrick, 2008)
Refinement method	Full matrix least-squares on F ²
Data / restraints / parameters	8962 / 1 / 437
Treatment of hydrogen atoms	Riding
Goodness-of-fit on F ²	1.609
Final R indices [I>2σ(I), 7203 reflections]	R1 = 0.0409, wR2 = 0.0481
R indices (all data)	R1 = 0.0619, wR2 = 0.0493
Type of weighting scheme used	Sigma
Weighting scheme used	w=1/σ ² (Fo ²)
Max shift/error	0.002
Average shift/error	0.000
Absolute structure determination	Anomalous differences
Absolute structure parameter	0.003(11)
Largest diff. peak and hole	0.807 and -0.967 e.Å ⁻³

Special Refinement Details

The structure was refined as a single component, although the crystals were twins, using an HKLF4 format reflection file prepared with TWINABS (see below). The two orientations were separated using CELL_NOW as follows.

Rotated from first domain by 178.9 degrees about reciprocal axis -0.032 1.000 0.104 and real axis -0.001 1.000 0.007. Twin law to convert hkl from first to this domain (SHELXL TWIN matrix):

```
-1.000 -0.065 0.016
-0.003 0.998 0.014
-0.022 0.207 -0.999
```

From Saint integration; Twin Law, Sample 1 of 1 transforms h1.1(1)->h1.2(2)

```
-0.99897 -0.07583 0.01646
-0.00750 0.99693 0.01538
-0.02464 0.19596 -0.99910
```

Twinabs;

PART 1 - Refinement of parameters to model systematic errors

```
18757 data ( 4443 unique ) involve domain 1 only, mean I/sigma 13.7
18551 data ( 4364 unique ) involve domain 2 only, mean I/sigma 7.1
10342 data ( 4106 unique ) involve 2 domains, mean I/sigma 19.2
```

```
HKLF 4 dataset constructed from all observations involving domains 1..2
8970 Corrected reflections written to file twin4.hkl
Reflections merged according to point-group 2
Minimum and maximum apparent transmission: 0.501007 0.745969
Additional spherical absorption correction applied with mu*r = 0.2000
```

Crystals were mounted on a glass fiber using Paratone oil then placed on the diffractometer under a nitrogen stream at 100K.

Refinement of F^2 against ALL reflections. The weighted R-factor (wR) and goodness of fit (S) are based on F^2 , conventional R-factors (R) are based on F , with F set to zero for negative F^2 . The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F , and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

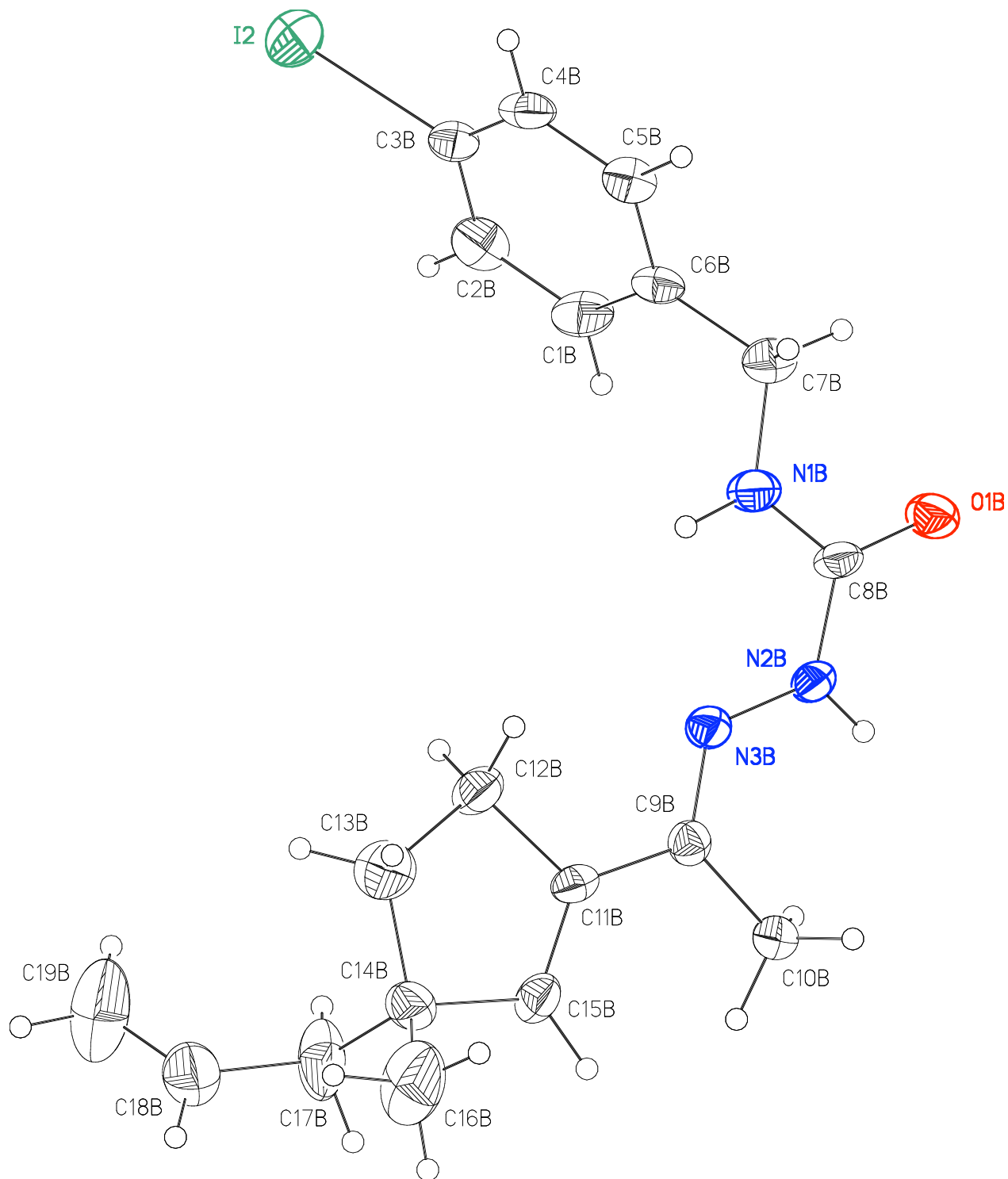


Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for THJ03 (CCDC 686849). $U(\text{eq})$ is defined as the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
I(1)	9525(1)	8297(1)	6590(1)	36(1)
O(1A)	7955(1)	941(3)	3051(1)	30(1)
N(1A)	7500(2)	3872(4)	3727(1)	30(1)
N(2A)	6670(2)	1070(4)	3270(1)	28(1)
N(3A)	6059(2)	2296(4)	3562(1)	28(1)
C(1A)	8489(2)	4383(5)	4938(2)	26(1)
C(2A)	8786(2)	5006(6)	5555(2)	27(1)
C(3A)	9158(2)	7186(5)	5637(2)	24(1)
C(4A)	9240(2)	8700(6)	5094(2)	23(1)
C(5A)	8934(2)	8049(6)	4481(2)	24(1)
C(6A)	8541(2)	5886(5)	4389(2)	21(1)
C(7A)	8214(2)	5251(6)	3716(2)	29(1)
C(8A)	7411(2)	1915(5)	3335(2)	24(1)
C(9A)	5356(2)	1676(5)	3411(2)	25(1)
C(10A)	5153(2)	-221(5)	2912(2)	34(1)
C(11A)	4738(2)	3016(6)	3736(2)	25(1)
C(12A)	4902(2)	5012(5)	4229(2)	30(1)
C(13A)	4096(2)	6199(5)	4302(2)	34(1)
C(14A)	3501(2)	4222(5)	4130(2)	33(1)
C(15A)	3985(2)	2625(5)	3693(2)	32(1)
C(16A)	3271(2)	2838(6)	4771(2)	47(1)
C(17A)	2751(2)	5160(6)	3793(2)	36(1)
C(18A)	2864(2)	6198(6)	3116(2)	39(1)
C(19A)	2612(2)	8233(8)	2900(2)	51(1)
I(2)	5760(1)	351(1)	-1541(1)	52(1)
O(1B)	6661(1)	7118(3)	2275(1)	34(1)
N(1B)	7173(2)	4167(4)	1625(1)	34(1)
N(2B)	7955(2)	7040(4)	2098(1)	27(1)
N(3B)	8578(2)	5882(4)	1807(1)	26(1)
C(1B)	6496(2)	3858(5)	289(2)	33(1)
C(2B)	6341(2)	3322(8)	-374(2)	35(1)
C(3B)	5958(2)	1240(6)	-534(2)	29(1)
C(4B)	5742(2)	-303(6)	-40(2)	31(1)
C(5B)	5895(2)	235(6)	618(2)	28(1)
C(6B)	6287(2)	2329(5)	795(2)	26(1)
C(7B)	6454(2)	2863(6)	1519(2)	32(1)
C(8B)	7233(2)	6143(5)	2016(2)	25(1)
C(9B)	9266(2)	6619(5)	1925(2)	24(1)
C(10B)	9471(2)	8670(6)	2382(2)	33(1)
C(11B)	9892(2)	5325(6)	1586(2)	25(1)
C(12B)	9704(2)	3469(7)	1051(2)	34(1)
C(13B)	10499(2)	2401(6)	903(2)	54(1)
C(14B)	11131(2)	4019(5)	1204(2)	33(1)
C(15B)	10659(2)	5558(6)	1666(2)	30(1)
C(16B)	11736(3)	2543(7)	1600(2)	67(2)
C(17B)	11522(2)	5571(7)	690(2)	58(1)
C(18B)	12017(3)	4302(6)	194(2)	52(1)
C(19B)	11859(3)	3982(7)	-416(2)	77(2)

Table 3. Bond lengths [Å] and angles [°] for THJ03 (CCDC 686849).

I(1)-C(3A)	2.092(3)	C(9A)-N(3A)-N(2A)	118.6(3)
O(1A)-C(8A)	1.226(4)	C(2A)-C(1A)-C(6A)	122.1(3)
N(1A)-C(8A)	1.354(4)	C(1A)-C(2A)-C(3A)	119.6(3)
N(1A)-C(7A)	1.449(4)	C(2A)-C(3A)-C(4A)	119.8(3)
N(2A)-C(8A)	1.361(4)	C(2A)-C(3A)-I(1)	120.1(2)
N(2A)-N(3A)	1.388(3)	C(4A)-C(3A)-I(1)	119.9(2)
N(3A)-C(9A)	1.289(4)	C(5A)-C(4A)-C(3A)	119.7(3)
C(1A)-C(2A)	1.375(5)	C(4A)-C(5A)-C(6A)	121.7(3)
C(1A)-C(6A)	1.386(4)	C(1A)-C(6A)-C(5A)	117.2(3)
C(2A)-C(3A)	1.385(4)	C(1A)-C(6A)-C(7A)	122.8(3)
C(3A)-C(4A)	1.384(4)	C(5A)-C(6A)-C(7A)	120.1(3)
C(4A)-C(5A)	1.376(4)	N(1A)-C(7A)-C(6A)	115.0(3)
C(5A)-C(6A)	1.397(5)	O(1A)-C(8A)-N(1A)	123.1(3)
C(6A)-C(7A)	1.494(4)	O(1A)-C(8A)-N(2A)	121.2(3)
C(9A)-C(11A)	1.457(4)	N(1A)-C(8A)-N(2A)	115.8(3)
C(9A)-C(10A)	1.494(4)	N(3A)-C(9A)-C(11A)	116.2(3)
C(11A)-C(15A)	1.312(4)	N(3A)-C(9A)-C(10A)	123.9(3)
C(11A)-C(12A)	1.514(5)	C(11A)-C(9A)-C(10A)	119.8(3)
C(12A)-C(13A)	1.542(4)	C(15A)-C(11A)-C(9A)	127.4(3)
C(13A)-C(14A)	1.542(5)	C(15A)-C(11A)-C(12A)	109.9(3)
C(14A)-C(15A)	1.505(4)	C(9A)-C(11A)-C(12A)	122.6(3)
C(14A)-C(17A)	1.538(5)	C(11A)-C(12A)-C(13A)	102.6(3)
C(14A)-C(16A)	1.552(5)	C(12A)-C(13A)-C(14A)	105.2(2)
C(17A)-C(18A)	1.487(5)	C(15A)-C(14A)-C(17A)	114.4(3)
C(18A)-C(19A)	1.290(5)	C(15A)-C(14A)-C(13A)	100.7(3)
I(2)-C(3B)	2.096(3)	C(17A)-C(14A)-C(13A)	113.7(3)
O(1B)-C(8B)	1.242(4)	C(15A)-C(14A)-C(16A)	109.3(3)
N(1B)-C(8B)	1.356(4)	C(17A)-C(14A)-C(16A)	108.2(3)
N(1B)-C(7B)	1.447(4)	C(13A)-C(14A)-C(16A)	110.3(3)
N(2B)-C(8B)	1.346(4)	C(11A)-C(15A)-C(14A)	114.4(3)
N(2B)-N(3B)	1.383(3)	C(18A)-C(17A)-C(14A)	114.4(3)
N(3B)-C(9B)	1.270(4)	C(19A)-C(18A)-C(17A)	127.0(3)
C(1B)-C(6B)	1.376(4)	C(8B)-N(1B)-C(7B)	123.6(3)
C(1B)-C(2B)	1.380(5)	C(8B)-N(2B)-N(3B)	119.3(3)
C(2B)-C(3B)	1.373(5)	C(9B)-N(3B)-N(2B)	119.4(3)
C(3B)-C(4B)	1.366(4)	C(6B)-C(1B)-C(2B)	121.4(3)
C(4B)-C(5B)	1.372(4)	C(3B)-C(2B)-C(1B)	119.6(3)
C(5B)-C(6B)	1.394(5)	C(4B)-C(3B)-C(2B)	120.0(3)
C(6B)-C(7B)	1.501(5)	C(4B)-C(3B)-I(2)	120.1(3)
C(9B)-C(11B)	1.467(4)	C(2B)-C(3B)-I(2)	119.8(2)
C(9B)-C(10B)	1.504(4)	C(3B)-C(4B)-C(5B)	120.3(3)
C(11B)-C(15B)	1.330(4)	C(4B)-C(5B)-C(6B)	120.9(3)
C(11B)-C(12B)	1.522(4)	C(1B)-C(6B)-C(5B)	117.7(3)
C(12B)-C(13B)	1.521(5)	C(1B)-C(6B)-C(7B)	122.4(3)
C(13B)-C(14B)	1.530(5)	C(5B)-C(6B)-C(7B)	119.8(3)
C(14B)-C(15B)	1.505(4)	N(1B)-C(7B)-C(6B)	113.3(3)
C(14B)-C(17B)	1.509(5)	O(1B)-C(8B)-N(2B)	121.1(3)
C(14B)-C(16B)	1.537(6)	O(1B)-C(8B)-N(1B)	123.0(3)
C(17B)-C(18B)	1.493(5)	N(2B)-C(8B)-N(1B)	115.9(3)
C(18B)-C(19B)	1.260(5)	N(3B)-C(9B)-C(11B)	116.0(3)
		N(3B)-C(9B)-C(10B)	124.7(3)
C(8A)-N(1A)-C(7A)	120.7(3)	C(11B)-C(9B)-C(10B)	119.3(3)
C(8A)-N(2A)-N(3A)	119.8(3)	C(15B)-C(11B)-C(9B)	128.7(3)

Supporting Information for Hong, Krout, Jensen, Bennett, Harned, and Stolt SI 67

C(15B)-C(11B)-C(12B)	110.6(3)	C(15B)-C(14B)-C(16B)	110.9(3)
C(9B)-C(11B)-C(12B)	120.7(3)	C(17B)-C(14B)-C(16B)	110.8(3)
C(13B)-C(12B)-C(11B)	102.9(3)	C(13B)-C(14B)-C(16B)	110.9(3)
C(12B)-C(13B)-C(14B)	108.9(3)	C(11B)-C(15B)-C(14B)	114.2(3)
C(15B)-C(14B)-C(17B)	109.6(3)	C(18B)-C(17B)-C(14B)	116.1(3)
C(15B)-C(14B)-C(13B)	101.3(3)	C(19B)-C(18B)-C(17B)	126.3(5)
C(17B)-C(14B)-C(13B)	112.9(3)		

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^4$) for THJ03 (CCDC 686849). The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^2 U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
I(1)	340(2)	433(1)	310(1)	1(1)	-116(1)	-2(1)
O(1A)	177(14)	294(13)	431(15)	-131(10)	-15(11)	35(10)
N(1A)	166(17)	377(19)	352(17)	-168(12)	3(13)	-6(12)
N(2A)	150(17)	315(15)	378(18)	-133(12)	-22(13)	22(12)
N(3A)	186(19)	310(15)	328(18)	-35(12)	-35(15)	38(13)
C(1A)	190(20)	176(16)	420(20)	13(15)	-22(18)	9(13)
C(2A)	250(20)	237(18)	320(20)	88(15)	-7(16)	-4(16)
C(3A)	170(20)	261(17)	270(20)	-18(14)	-7(16)	69(14)
C(4A)	180(20)	200(20)	310(20)	-23(14)	-29(15)	-13(14)
C(5A)	240(20)	201(19)	275(19)	26(16)	5(15)	34(16)
C(6A)	171(19)	195(18)	269(19)	-26(14)	-8(15)	64(14)
C(7A)	260(20)	280(18)	330(20)	-40(17)	-16(16)	-38(18)
C(8A)	200(20)	257(18)	260(20)	-33(14)	-61(17)	19(16)
C(9A)	200(20)	231(17)	330(20)	-9(14)	-9(18)	-26(15)
C(10A)	200(20)	410(20)	430(20)	-69(17)	3(18)	-44(17)
C(11A)	190(20)	240(20)	330(20)	21(16)	-31(15)	-26(17)
C(12A)	250(20)	283(18)	360(20)	-23(16)	-60(16)	-30(16)
C(13A)	260(20)	305(19)	440(20)	-99(15)	-50(18)	42(16)
C(14A)	190(20)	305(19)	490(30)	-7(15)	9(19)	19(15)
C(15A)	260(20)	240(20)	460(20)	-48(14)	-26(19)	-18(15)
C(16A)	360(30)	500(30)	540(30)	114(18)	30(20)	88(19)
C(17A)	250(20)	390(20)	450(20)	-34(18)	9(18)	40(20)
C(18A)	270(20)	480(20)	420(30)	-75(18)	-70(20)	77(18)
C(19A)	410(30)	600(20)	510(20)	40(20)	-88(19)	120(30)
I(2)	431(2)	791(2)	333(2)	-69(1)	-57(1)	-30(2)
O(1B)	227(16)	346(12)	447(16)	-105(10)	2(13)	9(11)
N(1B)	220(19)	350(17)	440(20)	-151(12)	-38(16)	9(12)
N(2B)	230(20)	301(15)	272(17)	-106(12)	-29(14)	3(13)
N(3B)	208(18)	309(16)	277(16)	-57(12)	-23(14)	26(14)
C(1B)	340(30)	190(20)	470(30)	-9(15)	-50(20)	-62(15)
C(2B)	310(20)	404(19)	350(20)	130(20)	-22(16)	20(20)
C(3B)	190(20)	370(20)	310(20)	-17(16)	-51(17)	17(16)
C(4B)	200(20)	270(20)	450(30)	-58(16)	-50(18)	-39(15)
C(5B)	270(20)	236(18)	340(20)	71(16)	-20(16)	-10(17)
C(6B)	170(20)	246(18)	350(20)	8(15)	-46(17)	-2(14)
C(7B)	300(20)	310(20)	360(20)	-12(15)	-23(17)	-59(16)
C(8B)	200(20)	282(19)	270(20)	-34(14)	-76(16)	-6(16)
C(9B)	250(20)	257(18)	220(20)	11(14)	2(17)	11(16)
C(10B)	260(20)	400(20)	330(20)	-104(16)	37(16)	-60(18)
C(11B)	250(20)	241(17)	253(19)	-25(16)	-45(15)	-52(18)
C(12B)	340(20)	341(18)	330(20)	-105(19)	-60(16)	10(20)
C(13B)	450(30)	450(20)	730(30)	-310(20)	70(30)	-4(19)
C(14B)	250(20)	350(20)	390(20)	-54(15)	20(19)	25(15)
C(15B)	340(20)	290(18)	266(19)	-75(16)	-25(16)	33(18)
C(16B)	720(40)	680(30)	610(30)	-170(20)	-50(30)	380(30)
C(17B)	840(30)	400(20)	510(30)	-150(20)	330(20)	-90(20)
C(18B)	500(30)	540(30)	520(30)	-104(19)	110(30)	-49(19)
C(19B)	1060(50)	830(40)	420(30)	40(20)	60(30)	500(30)

Table 5. Hydrogen bonds for THJ03 (CCDC 686849) [\AA and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	$\angle(\text{DHA})$
N(2A)-H(2A)...O(1B)#1	0.88	2.13	2.972(3)	159.7
N(2B)-H(2B)...O(1A)#2	0.88	2.04	2.895(3)	163.1

Symmetry transformations used to generate equivalent atoms:

#1 $x, y-1, z$

#2 $x, y+1, z$

Ring Contraction Strategy for the Practical, Scalable, Catalytic Asymmetric Synthesis of Versatile γ -Quaternary Acylcyclopentenones

Allen Y. Hong, Michael R. Krout, Thomas Jensen, Nathan B. Bennett,
Andrew M. Harned, Brian M. Stoltz*

Supporting Information (^1H , ^{13}C NMR and IR Spectra)

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Division of Chemistry and Chemical Engineering, California Institute of Technology,
Pasadena, California 91125, USA*

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β-Ketoesters 14a–l and SI-14p–SI-14q	SI 79
Enantioenriched Vinylogous Esters 10a–o	SI 107
Cycloheptenone 11a	SI 137
β-Hydroxyketones 12a–j, l–o	SI 139
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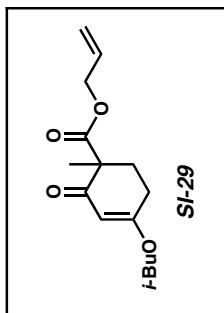
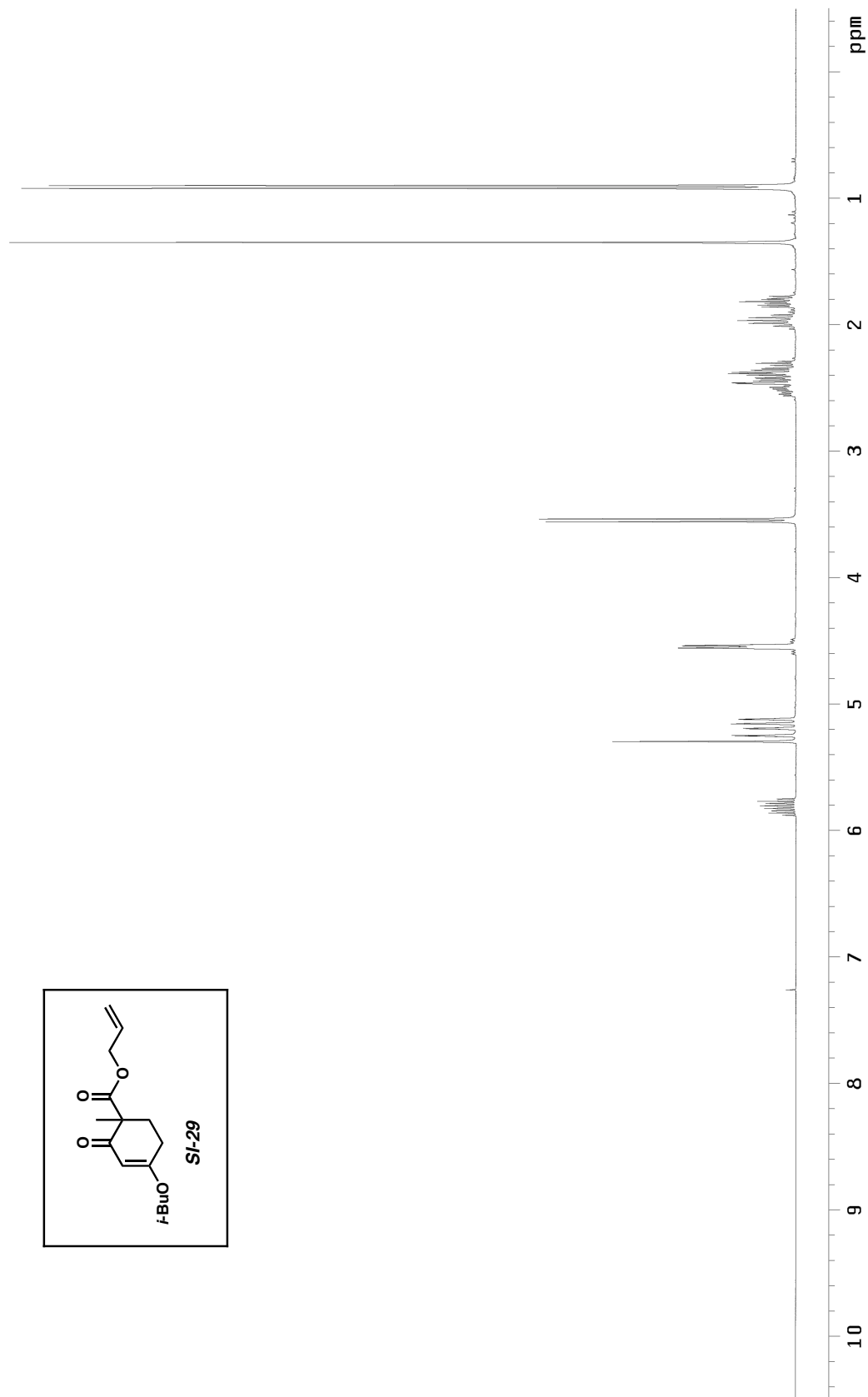


Figure SI-1A. ¹H NMR (300 MHz, CDCl₃) of compound SI-29.

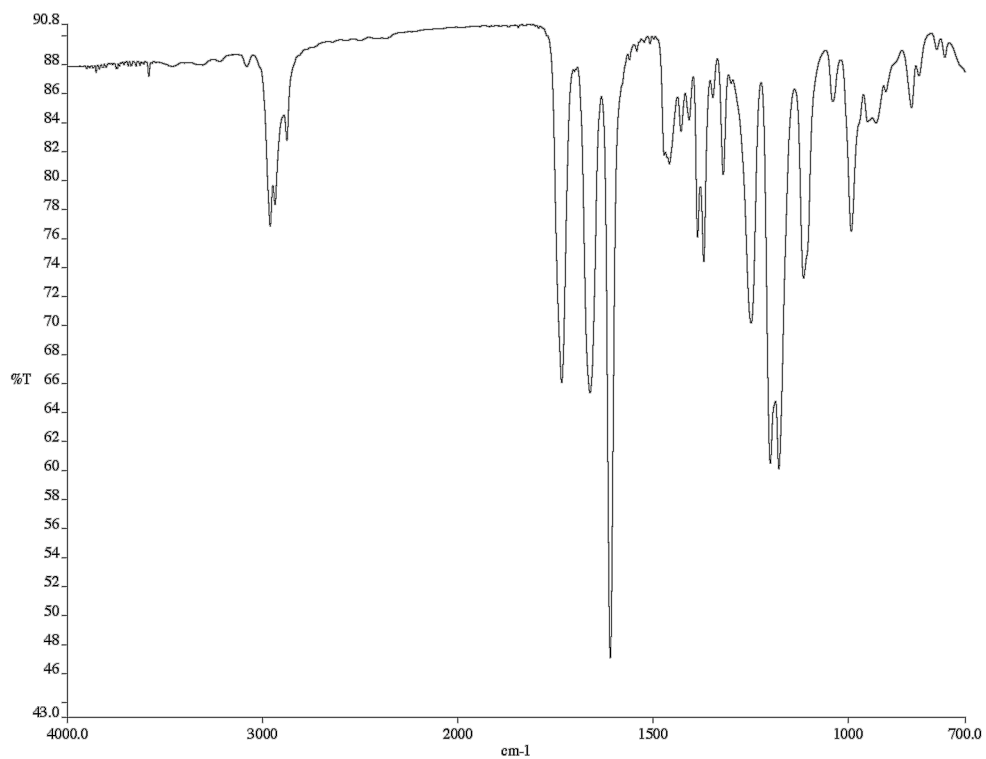


Figure SI-1B. Infrared spectrum (thin film/NaCl) of compound **SI-29**.

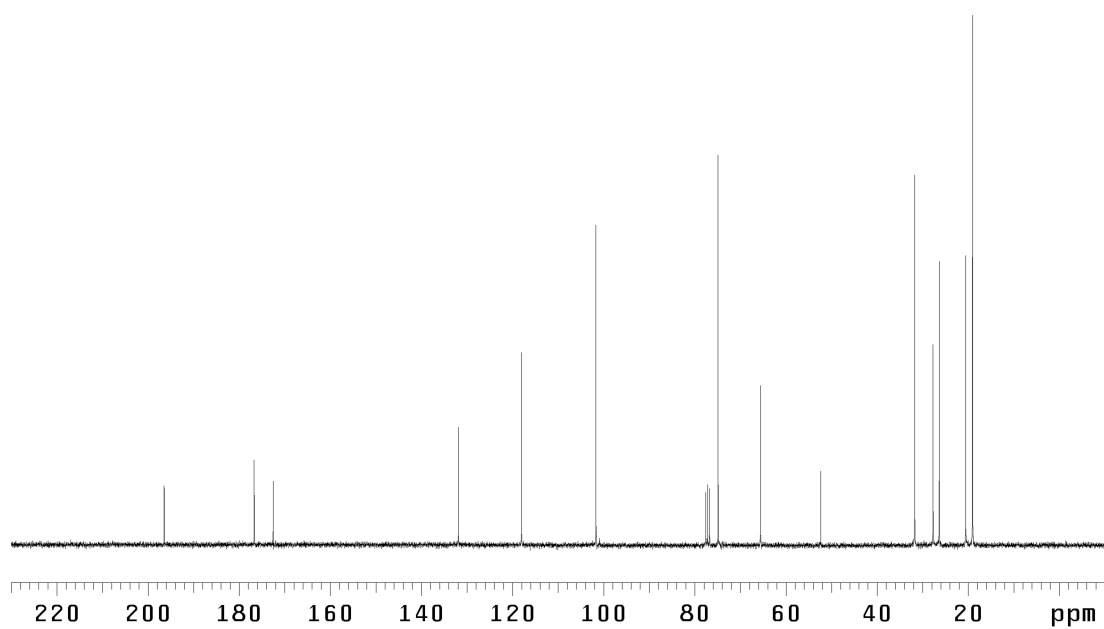


Figure SI-1C. ¹³C NMR (75 MHz, CDCl₃) of compound **SI-29**.

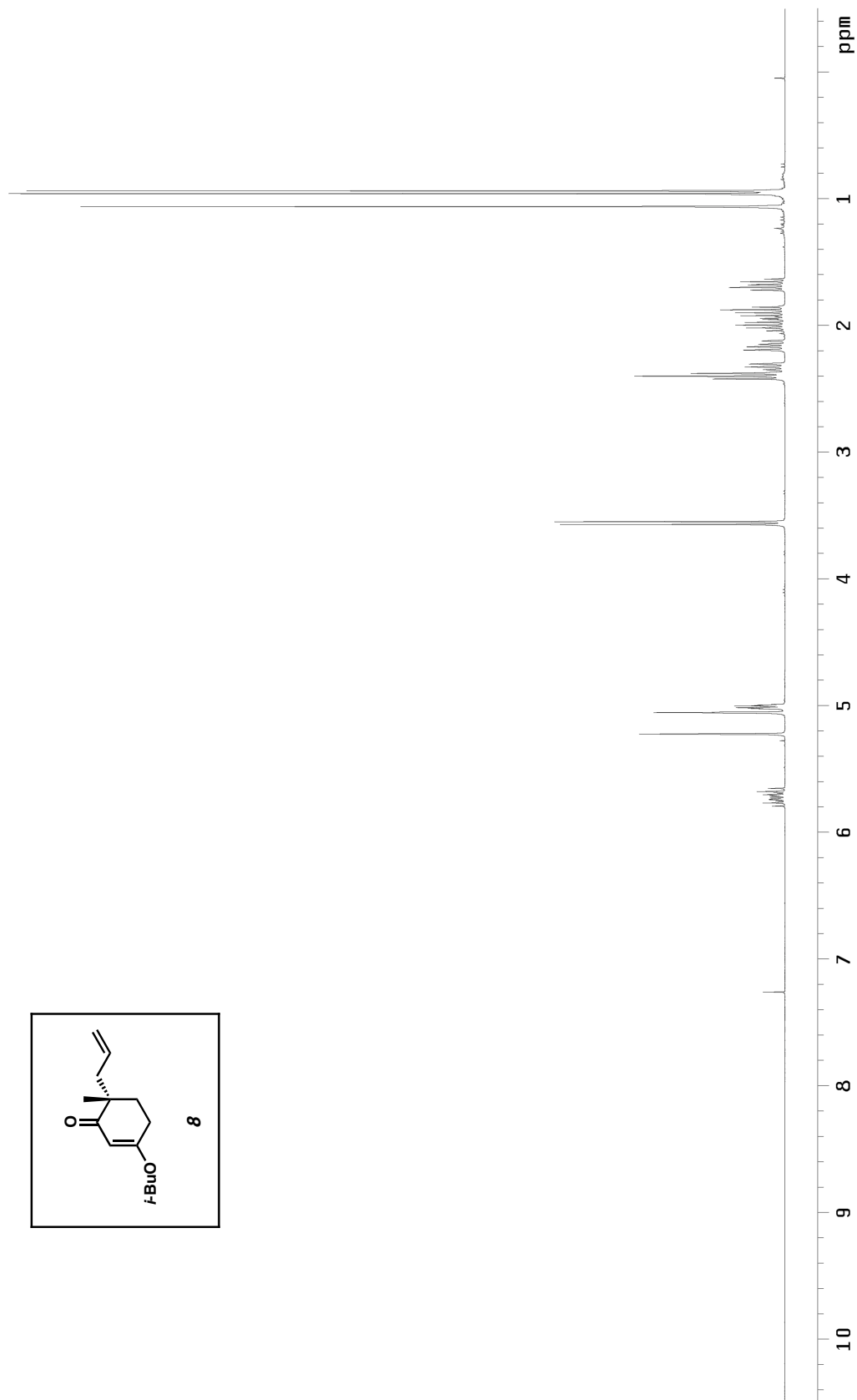


Figure SI-2A. ¹H NMR (300 MHz, CDCl₃) of compound **8**.

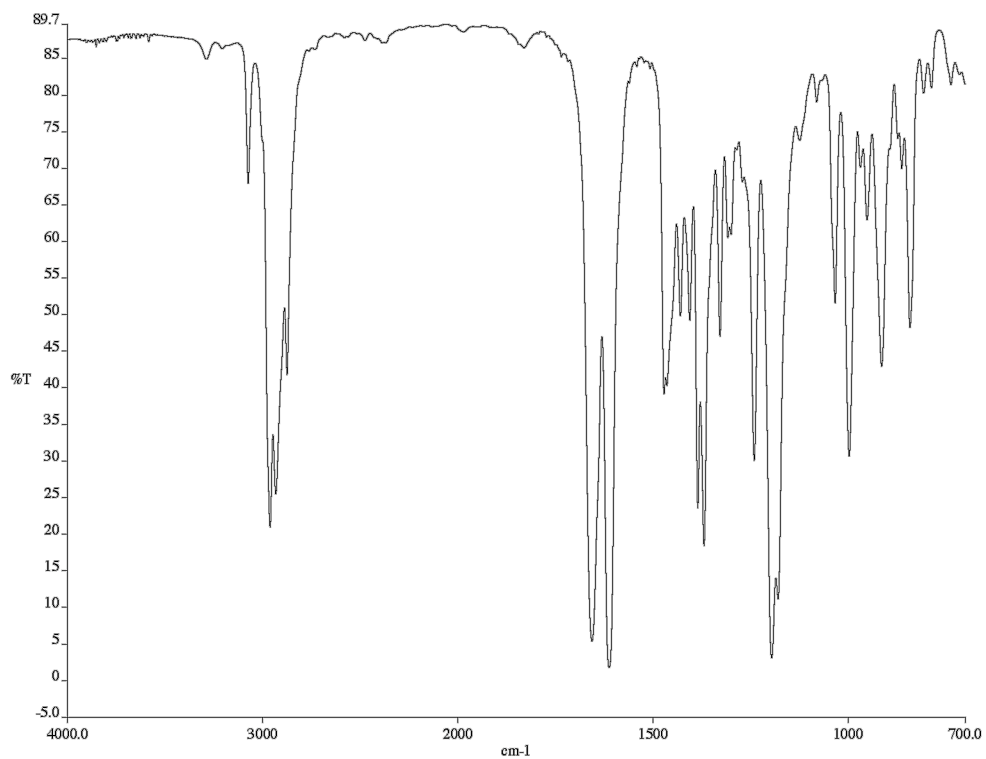


Figure SI-2B. Infrared spectrum (thin film/NaCl) of compound **8**.

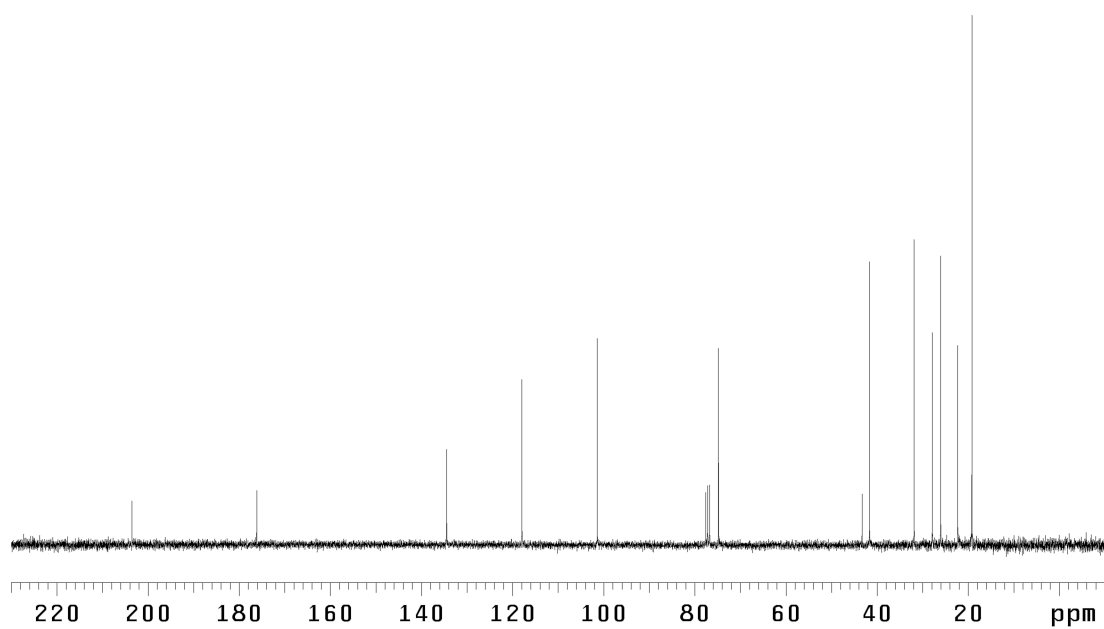


Figure SI-2C. ¹³C NMR (75 MHz, CDCl₃) of compound **8**.

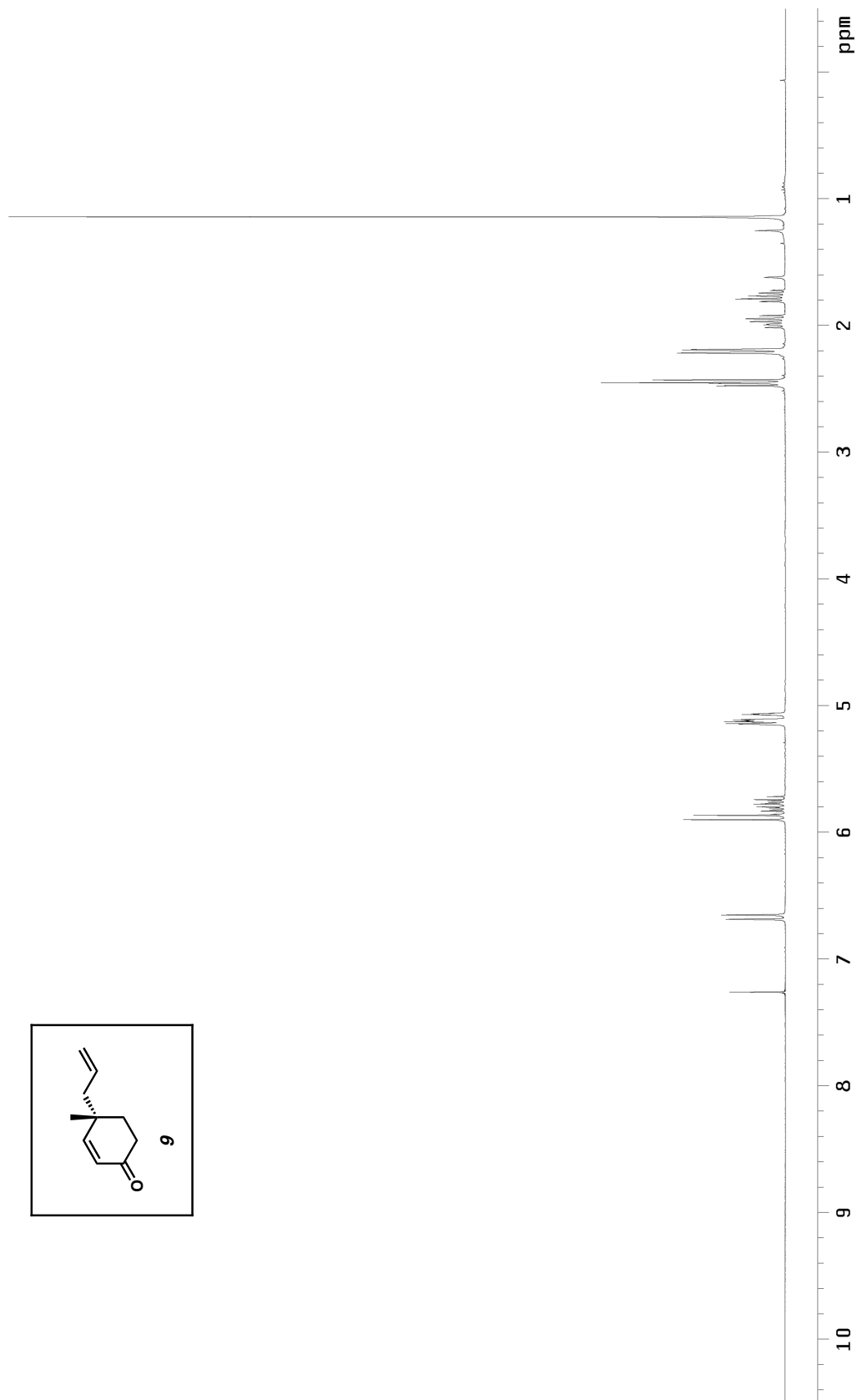


Figure SI-3A. ¹H NMR (300 MHz, CDCl₃) of compound **9**.

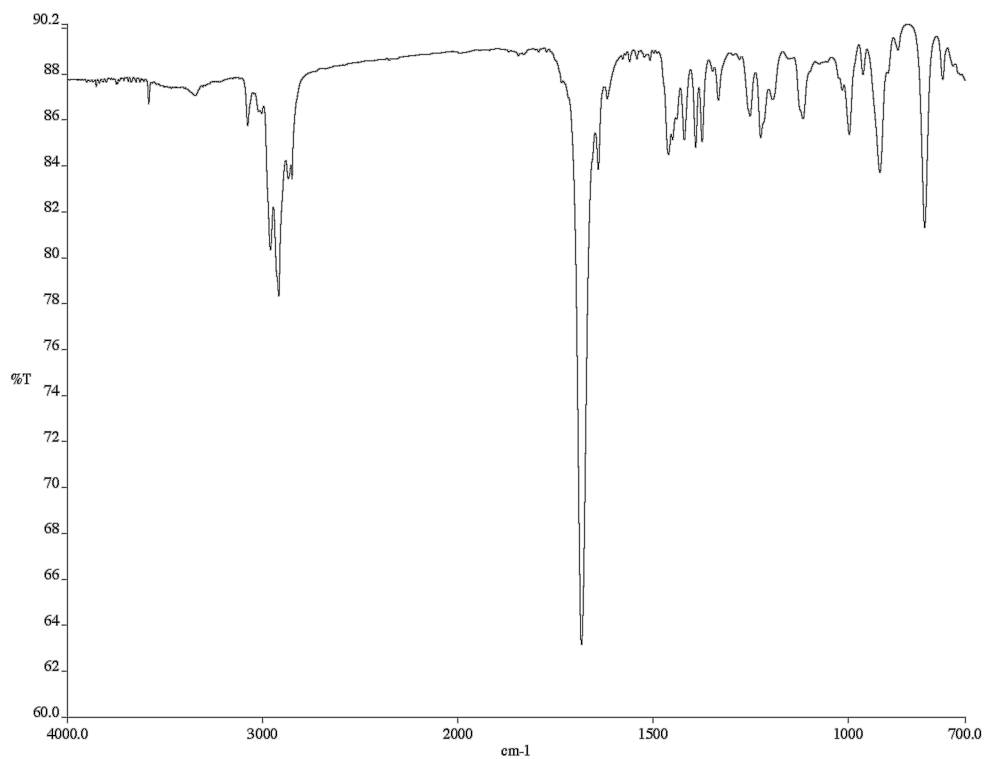


Figure SI-3B. Infrared spectrum (thin film/NaCl) of compound **9**.

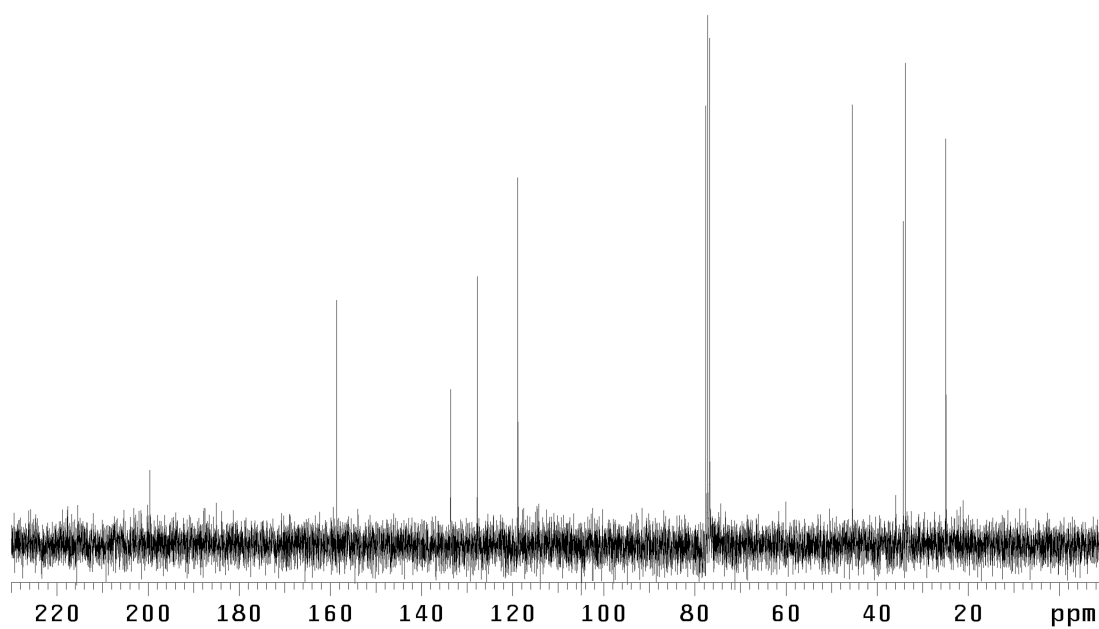


Figure SI-3C. ¹³C NMR (75 MHz, CDCl₃) of compound **9**.

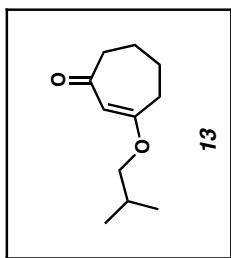
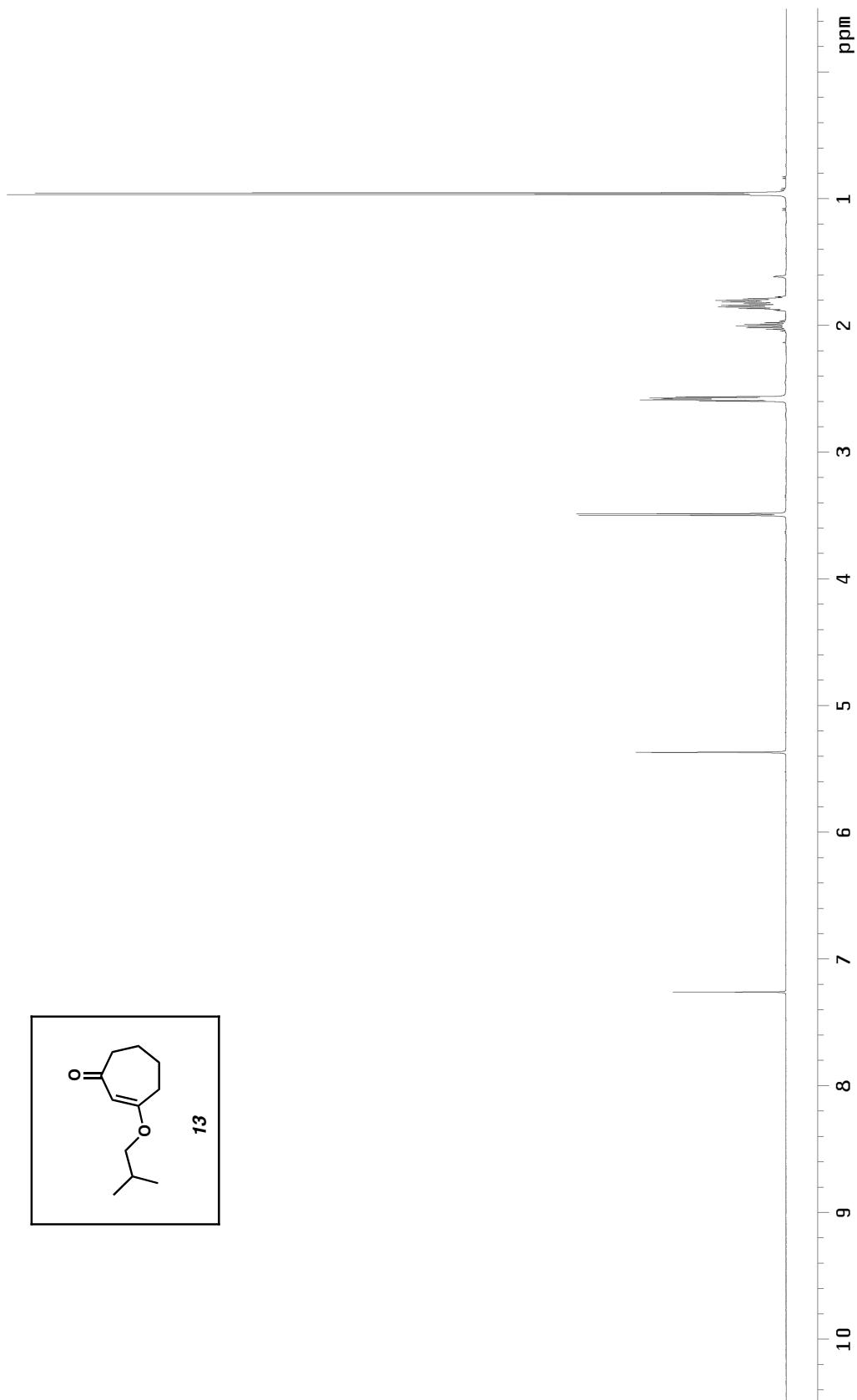


Figure SI-4A. ¹H NMR (500 MHz, CDCl₃) of compound **13**.

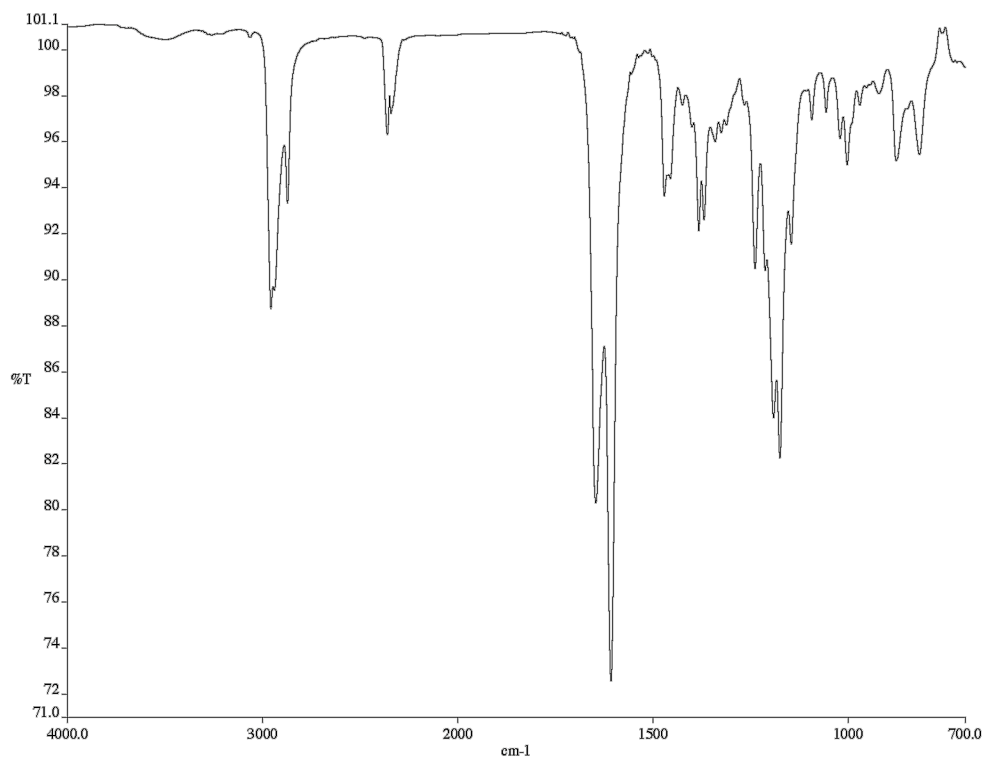


Figure SI-4B. Infrared spectrum (thin film/NaCl) of compound **13**.

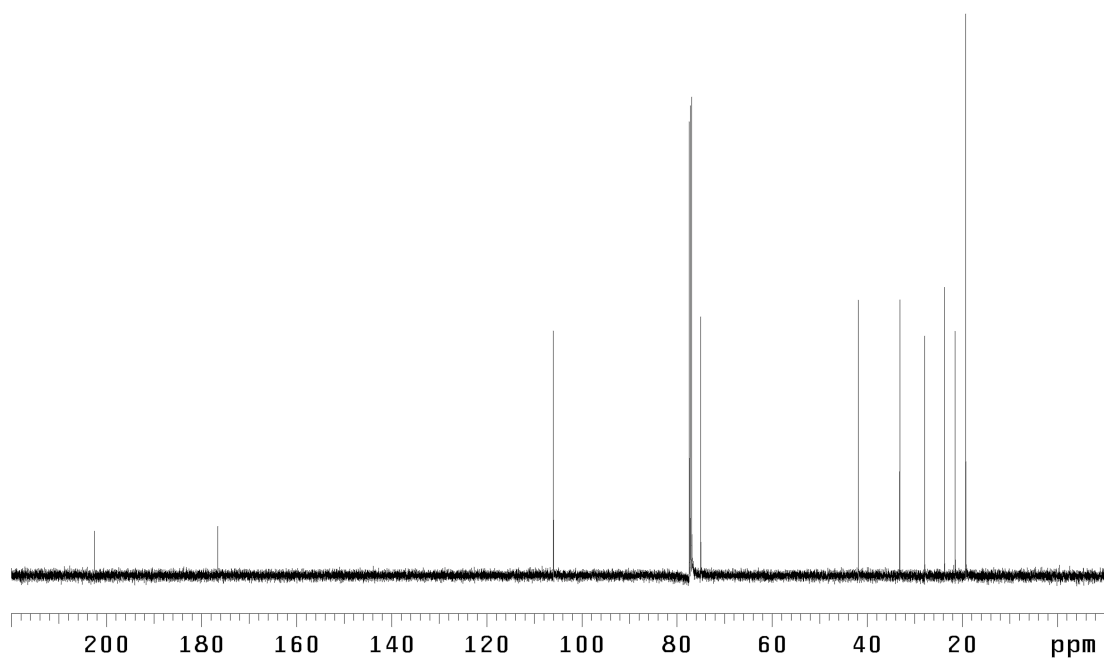


Figure SI-4C. ¹³C NMR (125 MHz, CDCl₃) of compound **13**.

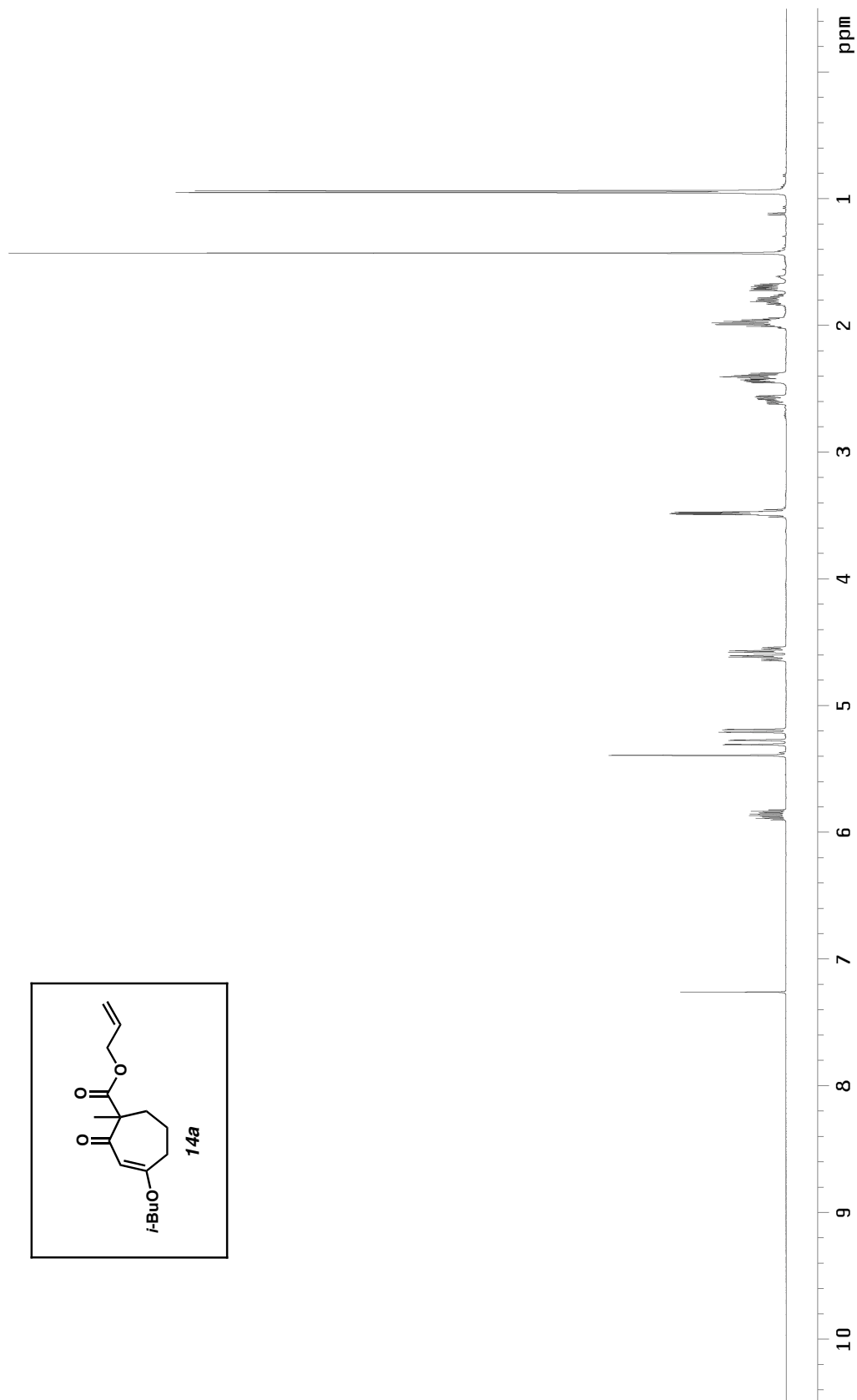


Figure SI-5A. ¹H NMR (500 MHz, CDCl₃) of compound **14a**.

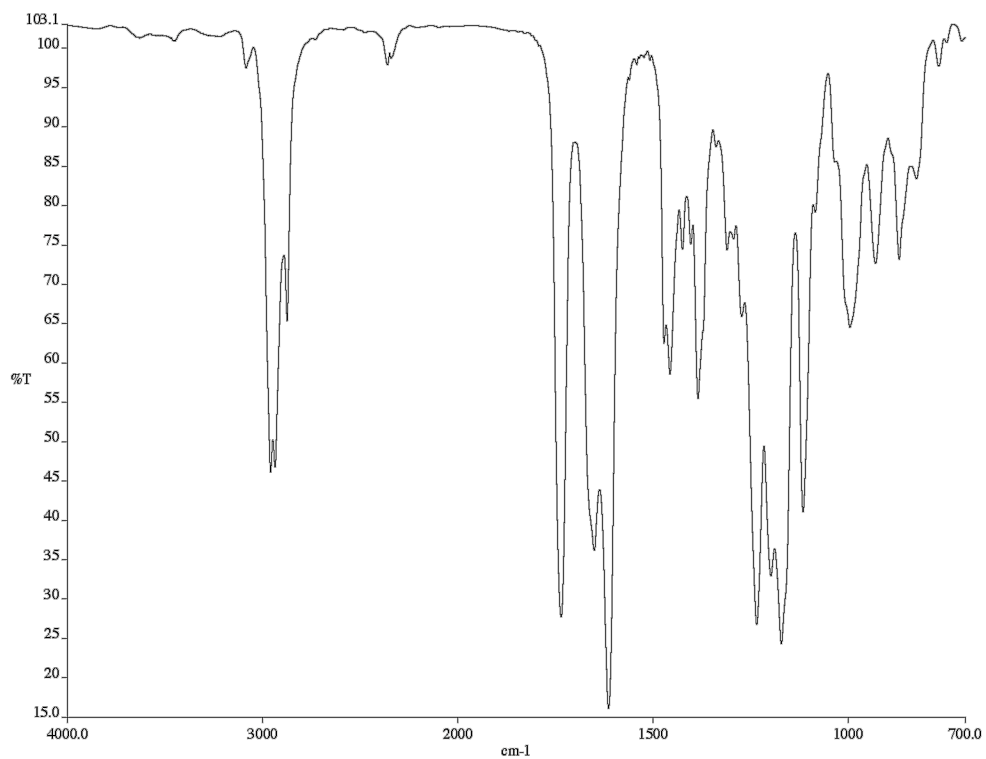


Figure SI-5B. Infrared spectrum (thin film/NaCl) of compound **14a**.

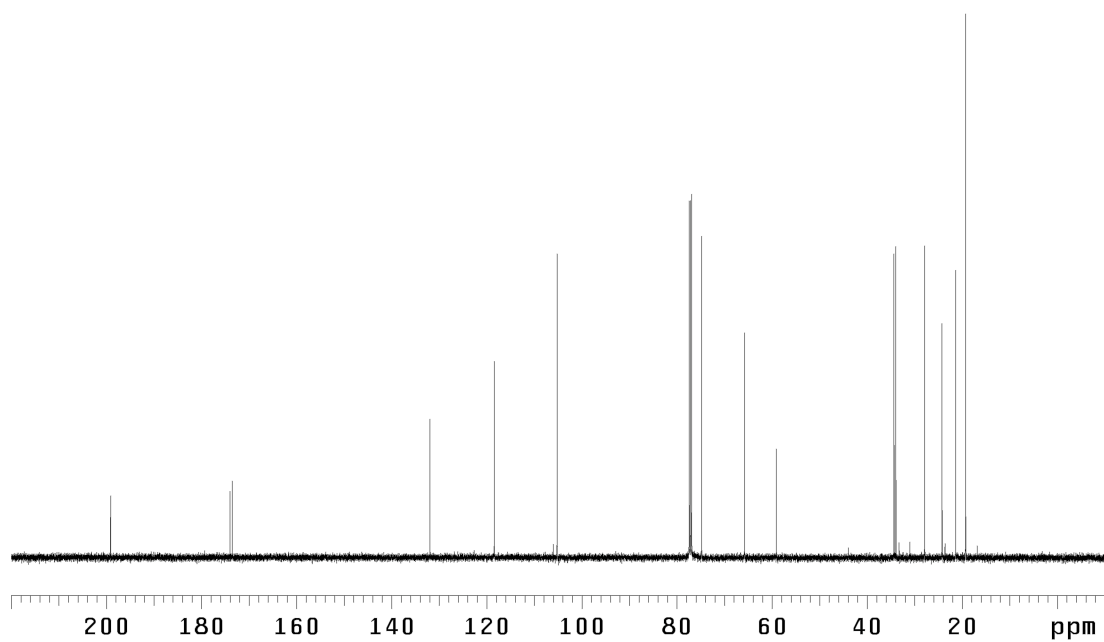


Figure SI-5C. ¹³C NMR (125 MHz, CDCl₃) of compound **14a**.

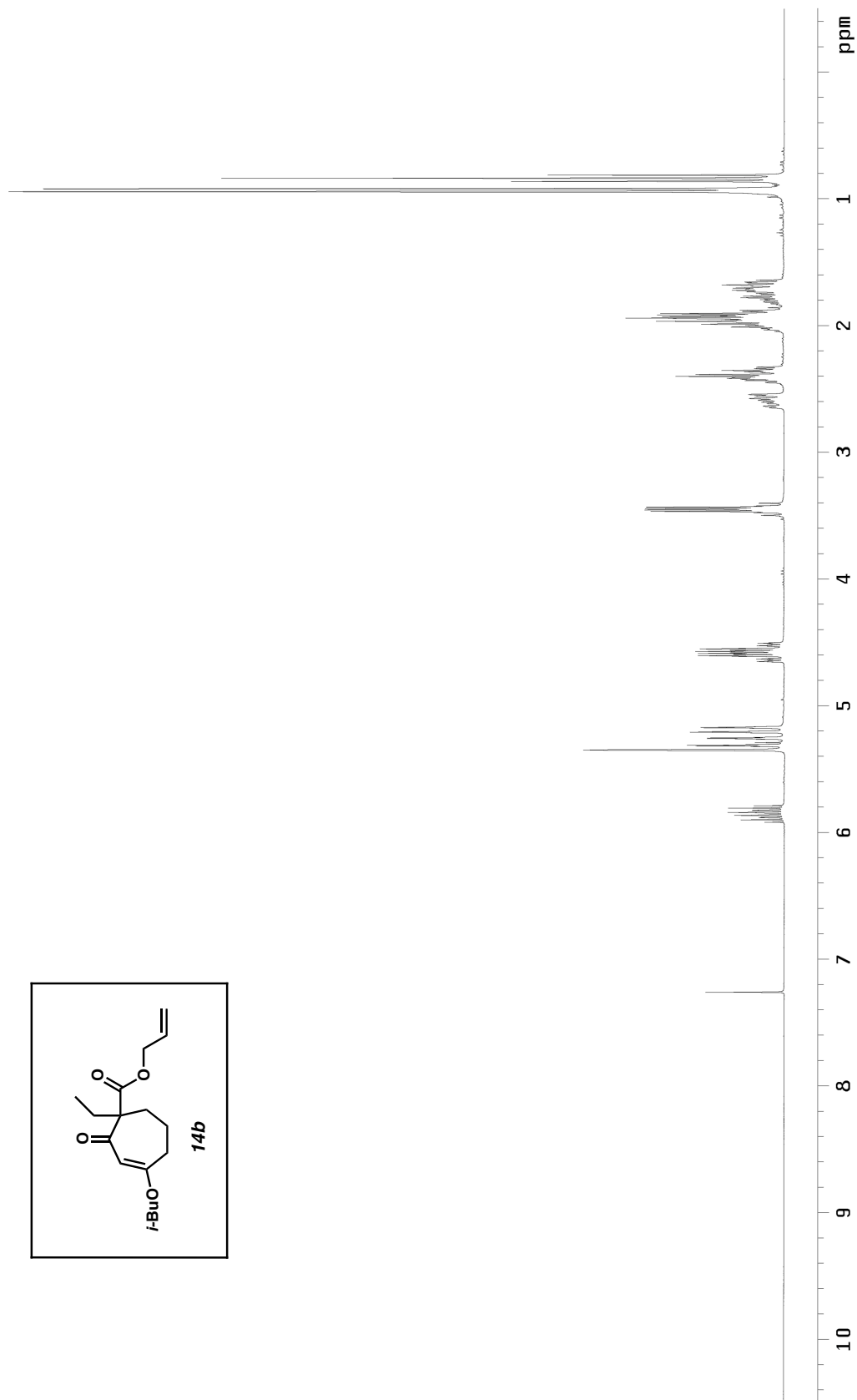


Figure SI-6A. ¹H NMR (300 MHz, CDCl₃) of compound **14b**.

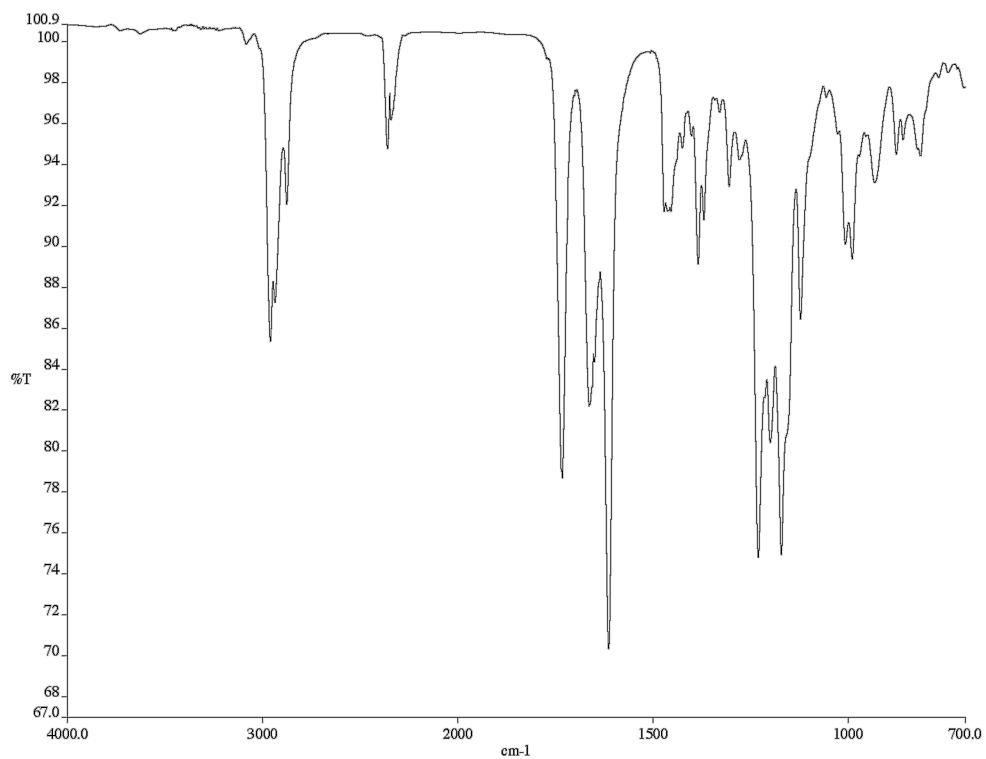


Figure SI-6B. Infrared spectrum (thin film/NaCl) of compound **14b**.

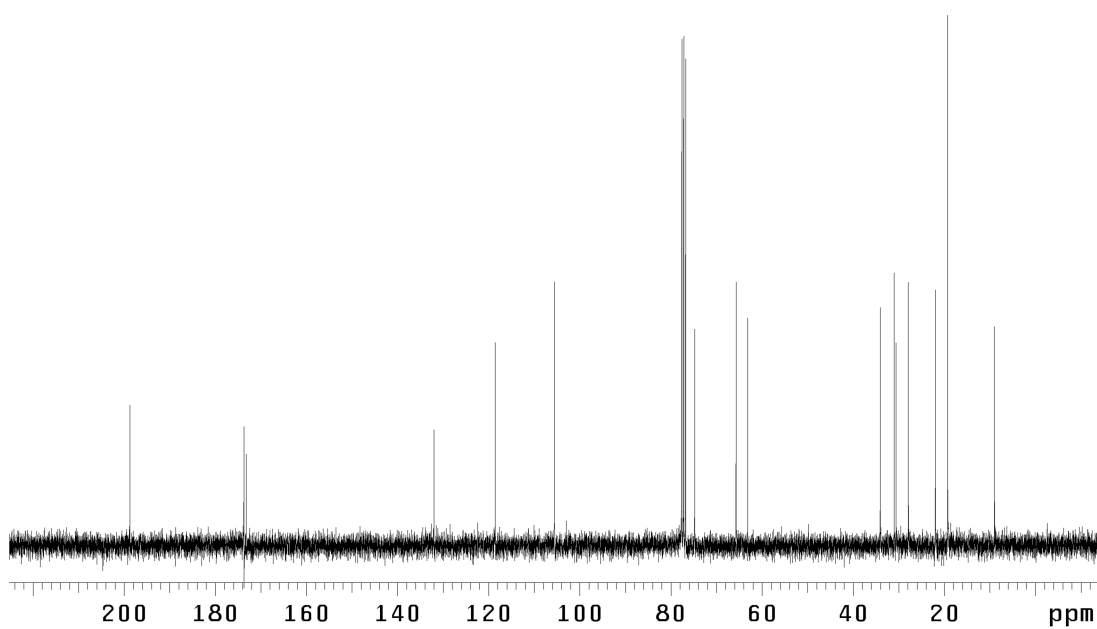


Figure SI-6C. ¹³C NMR (75 MHz, CDCl₃) of compound **14b**.

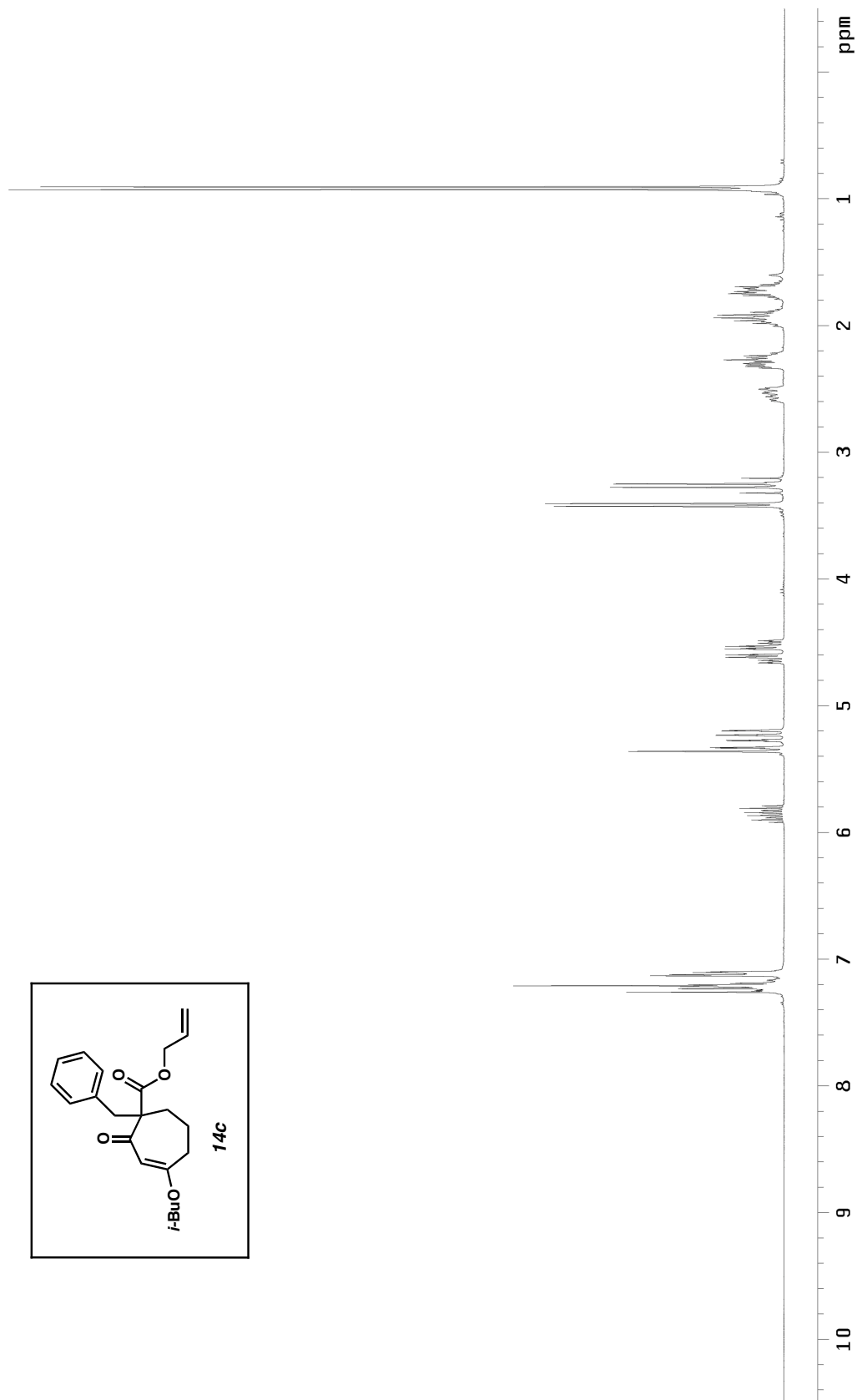


Figure SI-7A. ¹H NMR (300 MHz, CDCl₃) of compound **14c**.

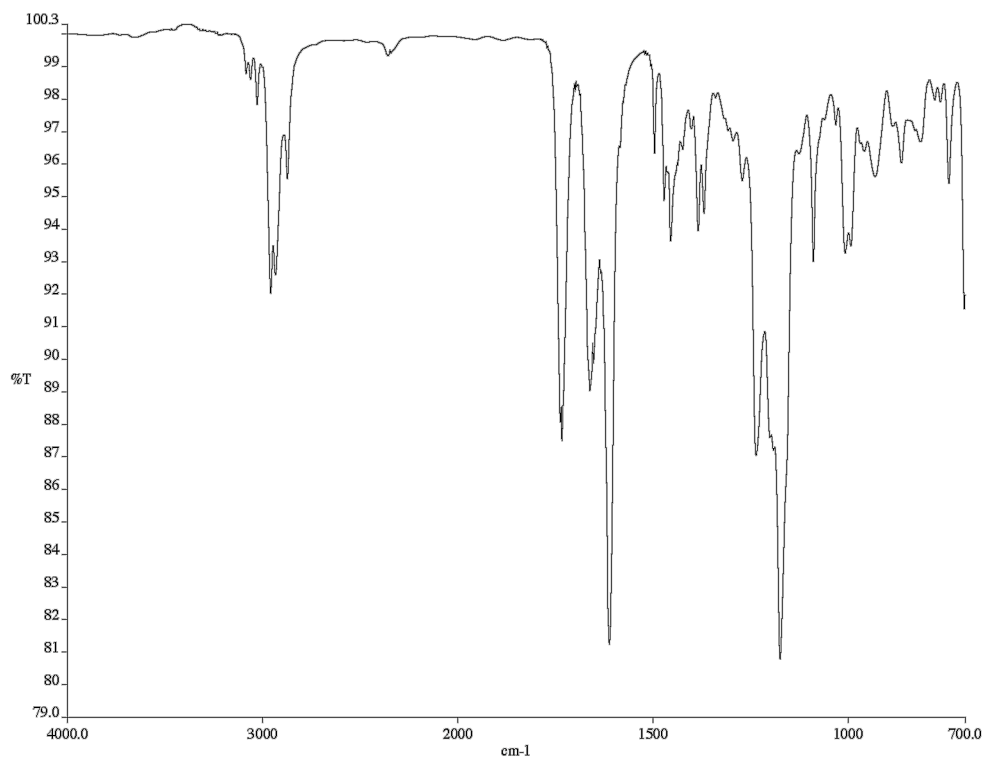


Figure SI-7B. Infrared spectrum (thin film/NaCl) of compound **14c**.

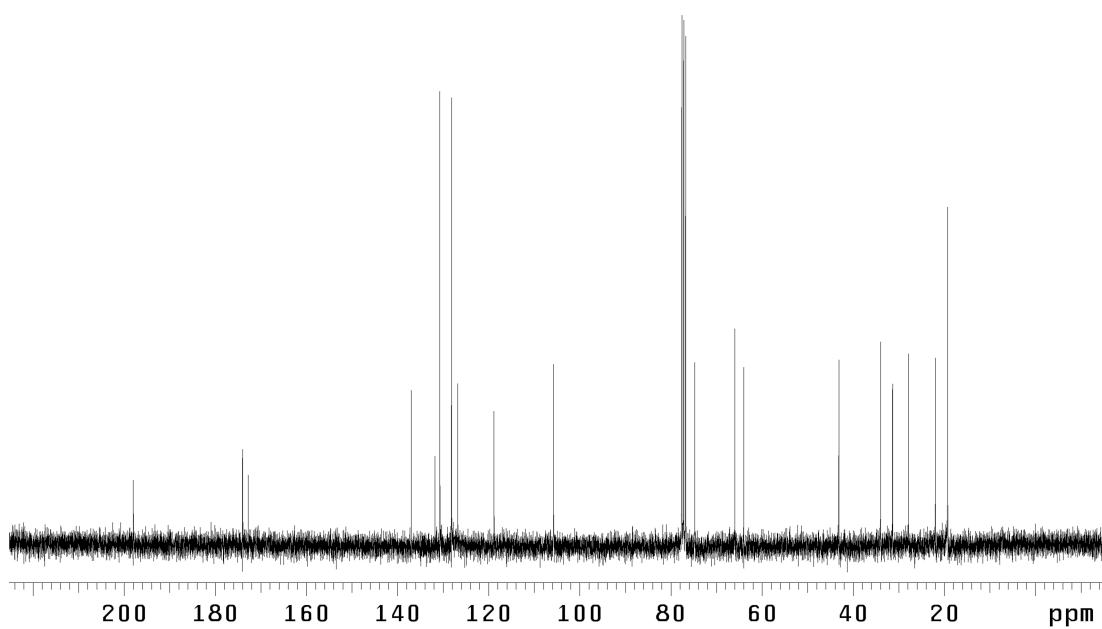


Figure SI-7C. ¹³C NMR (75 MHz, CDCl₃) of compound **14c**.

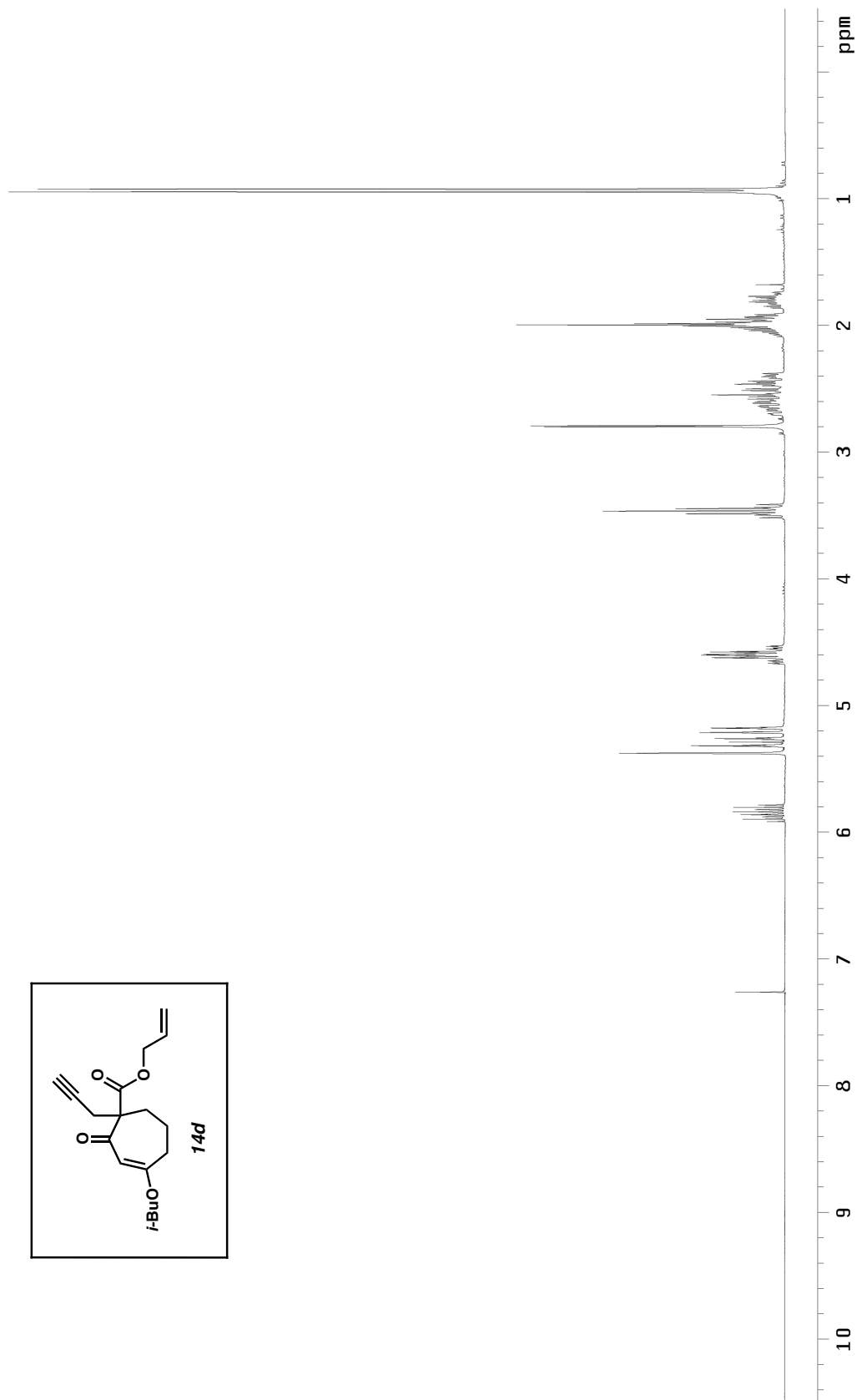


Figure SI-8A. ^1H NMR (300 MHz, CDCl_3) of compound **14d**.

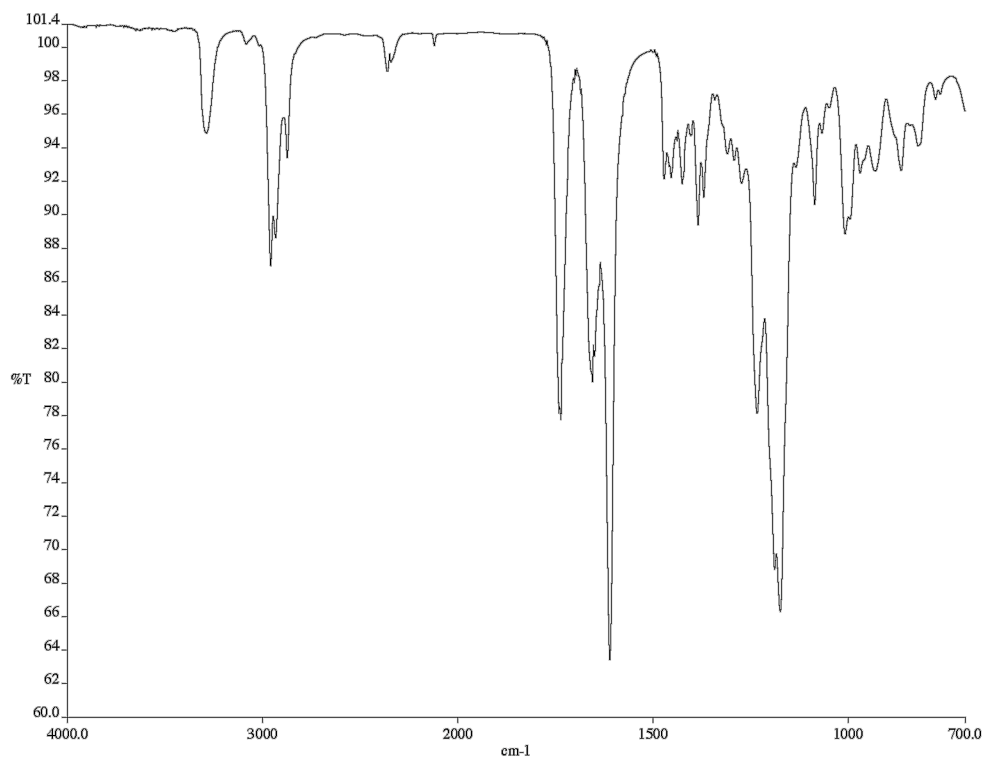


Figure SI-8B. Infrared spectrum (thin film/NaCl) of compound **14d**.

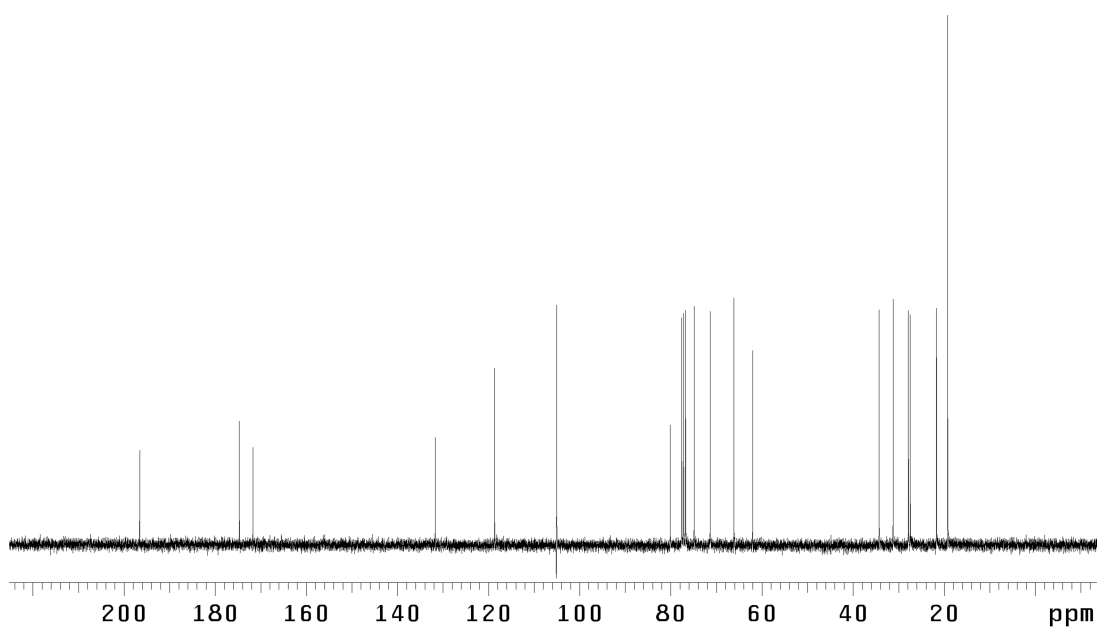


Figure SI-8C. ¹³C NMR (75 MHz, CDCl₃) of compound **14d**.

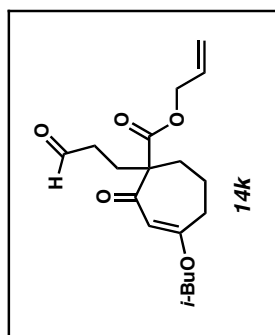
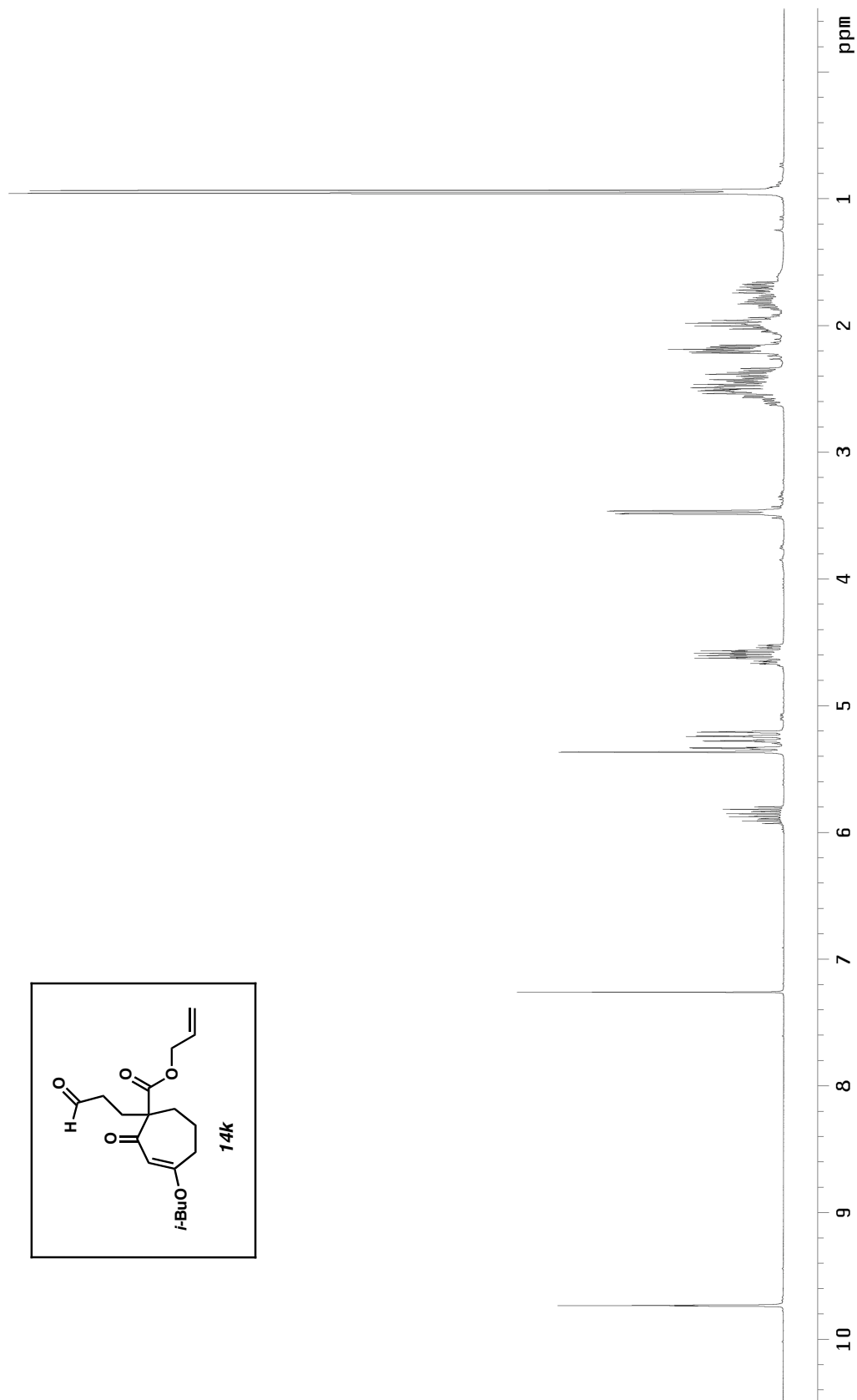


Figure SI-9A. ^1H NMR (300 MHz, CDCl_3) of compound **14k**.

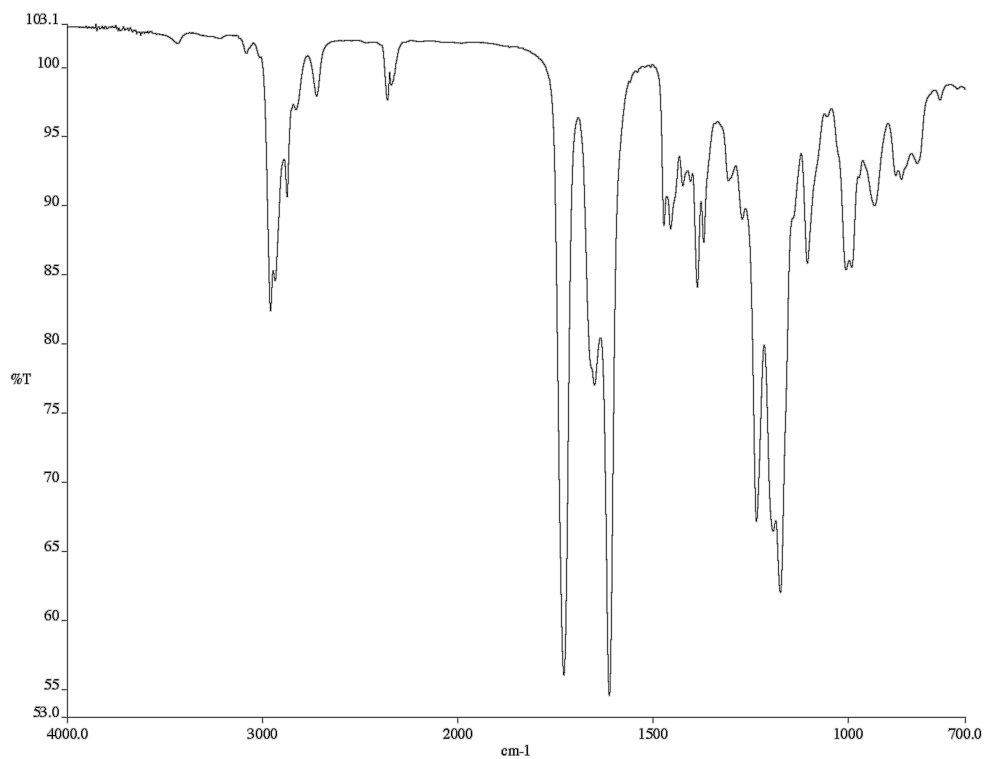


Figure SI-9B. Infrared spectrum (thin film/NaCl) of compound **14k**.

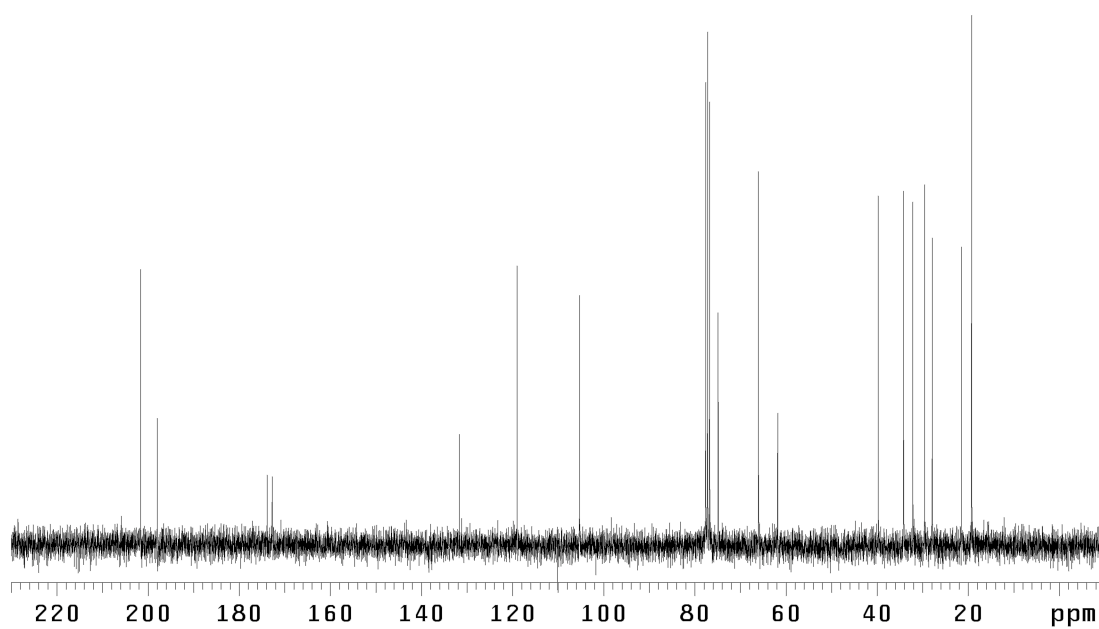


Figure SI-9C. ¹³C NMR (75 MHz, CDCl₃) of compound **14k**.

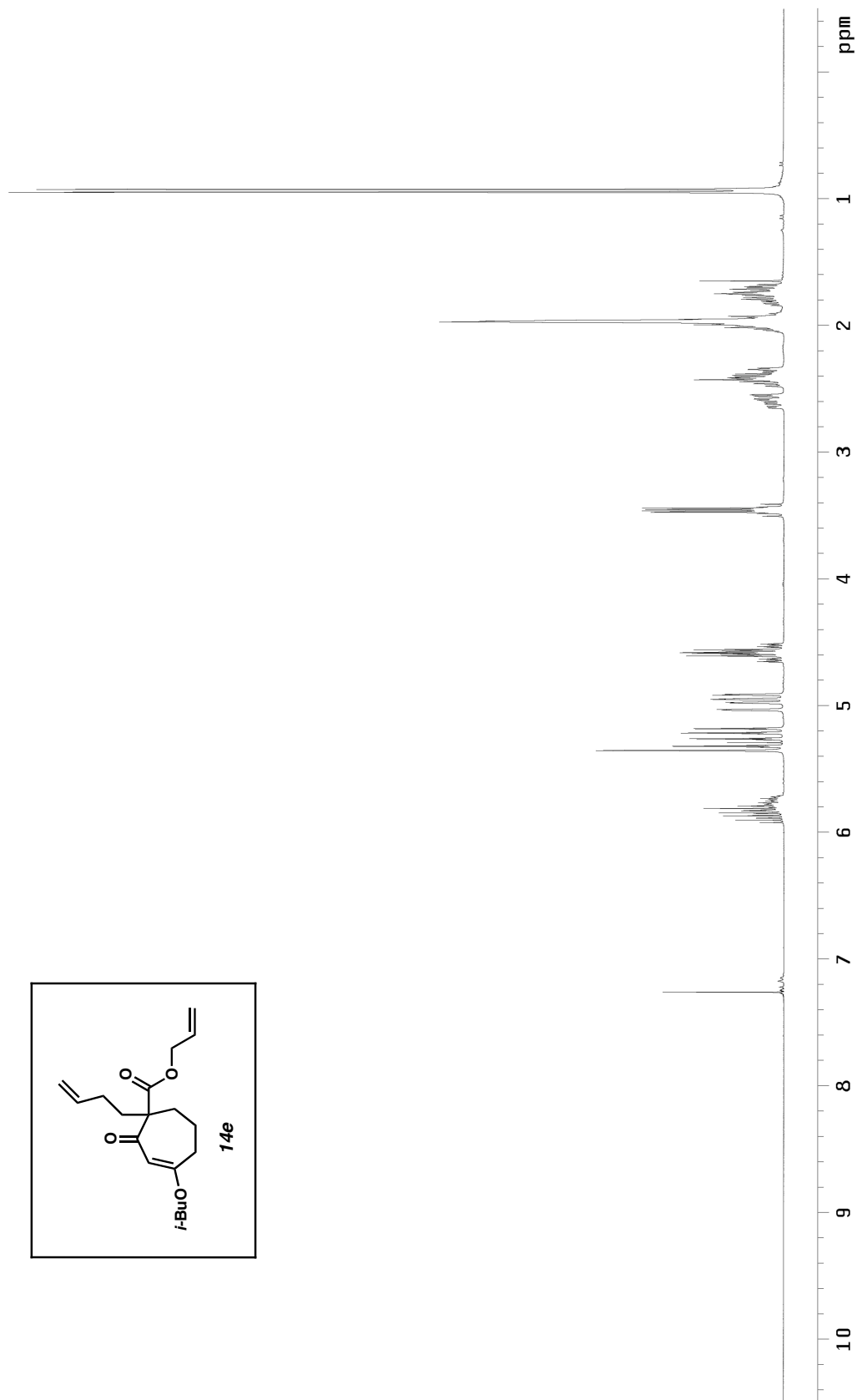


Figure SI-10A. ¹H NMR (300 MHz, CDCl₃) of compound **14e**.

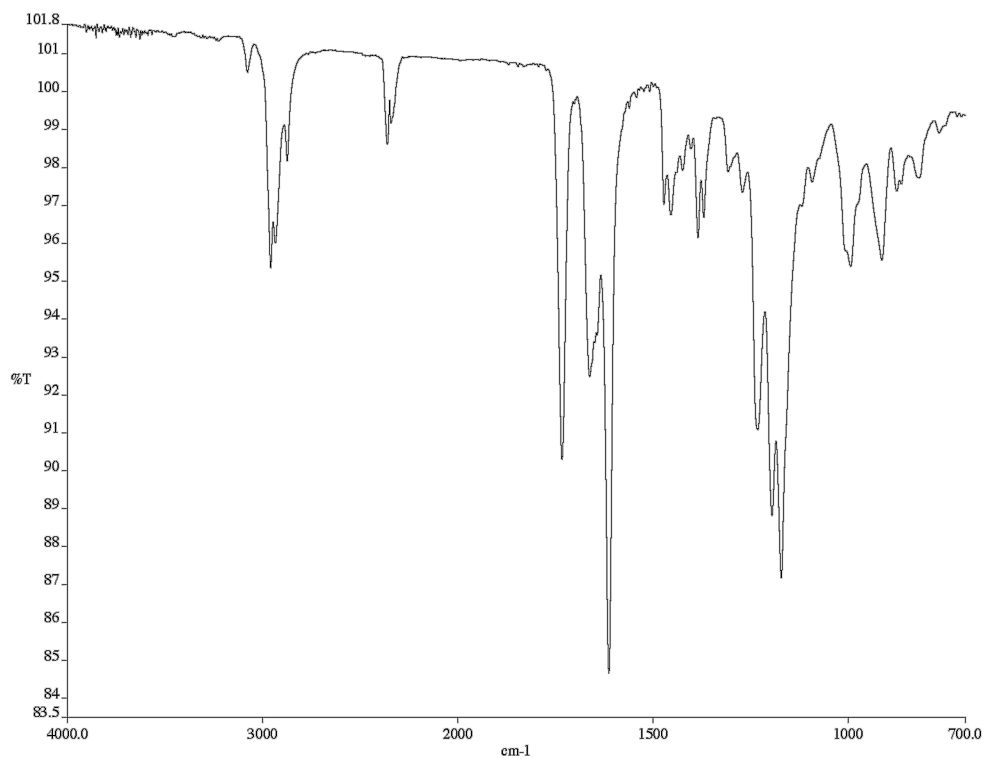


Figure SI-10B. Infrared spectrum (thin film/NaCl) of compound **14e**.

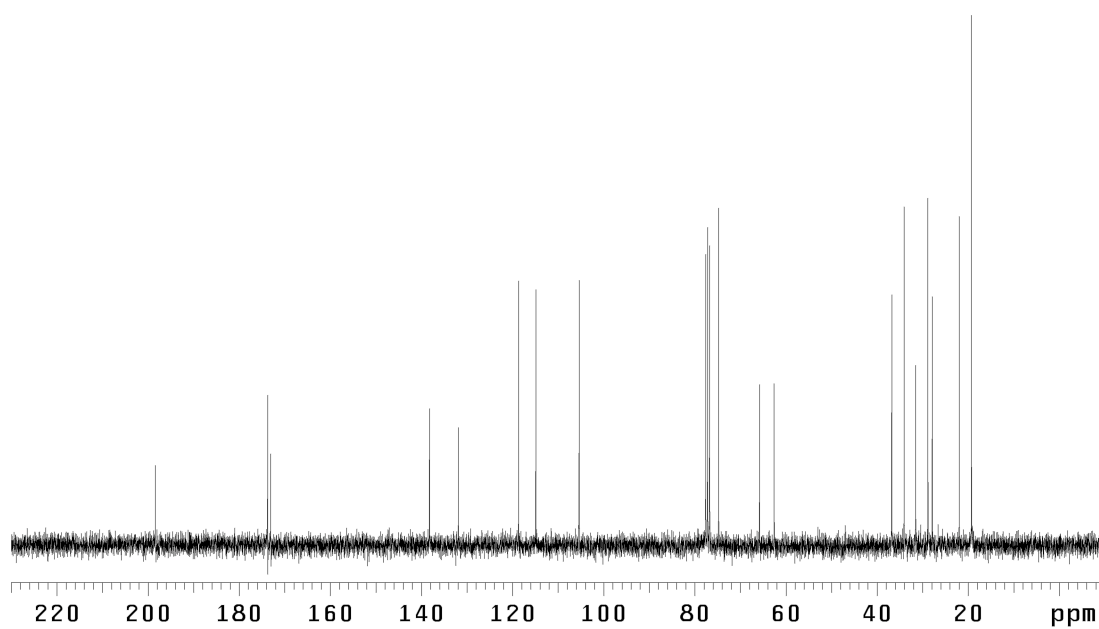


Figure SI-10C. ¹³C NMR (75 MHz, CDCl₃) of compound **14e**.

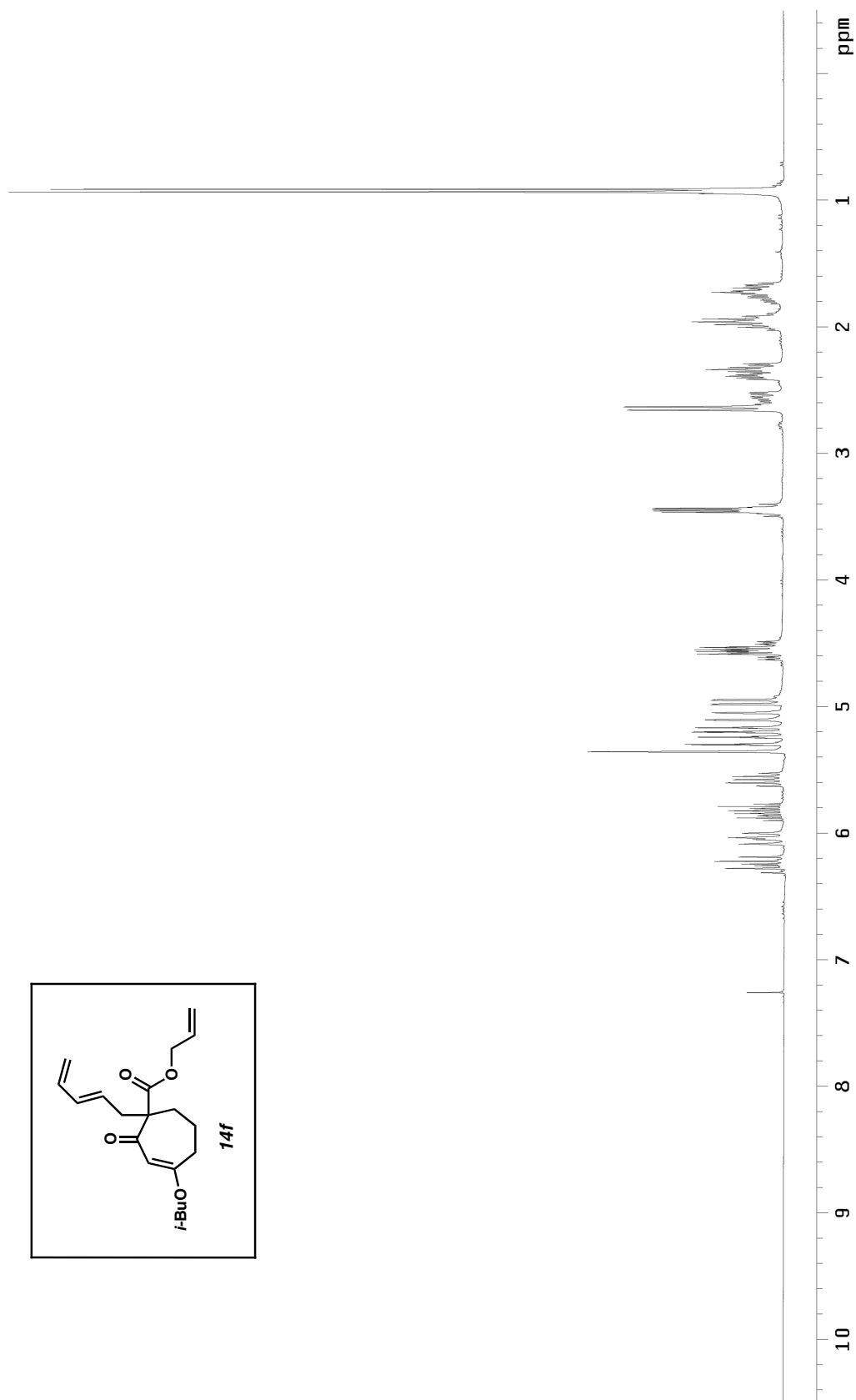


Figure SI-11A. ¹H NMR (300 MHz, CDCl₃) of compound **14f**.

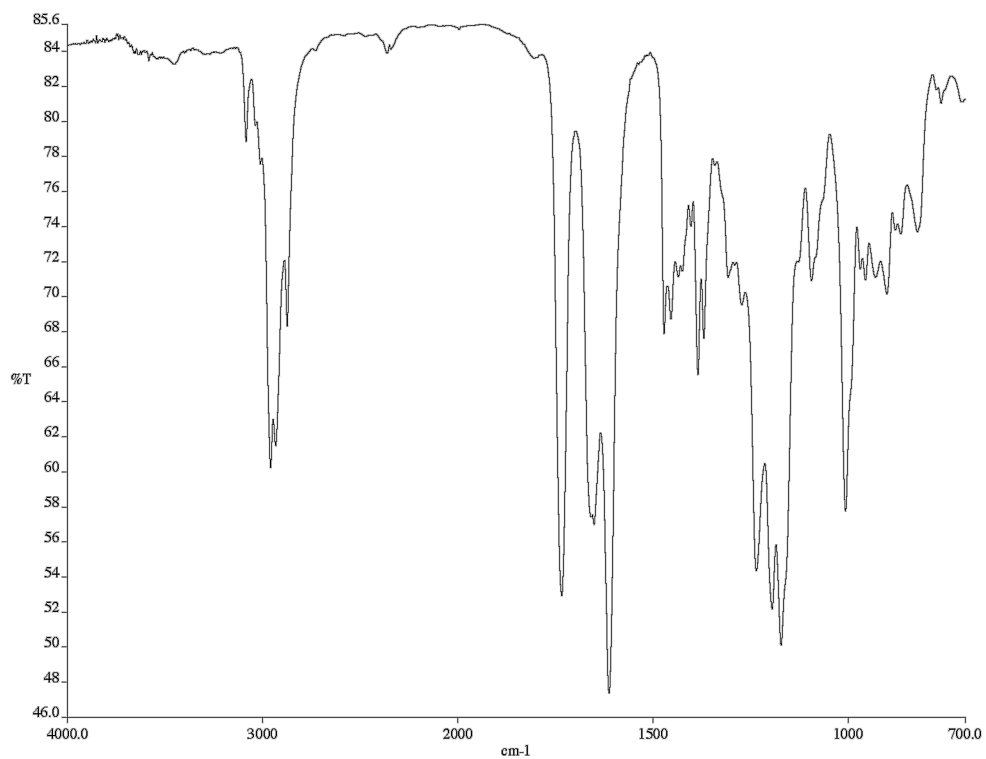


Figure SI-11B. Infrared spectrum (thin film/NaCl) of compound **14f**.

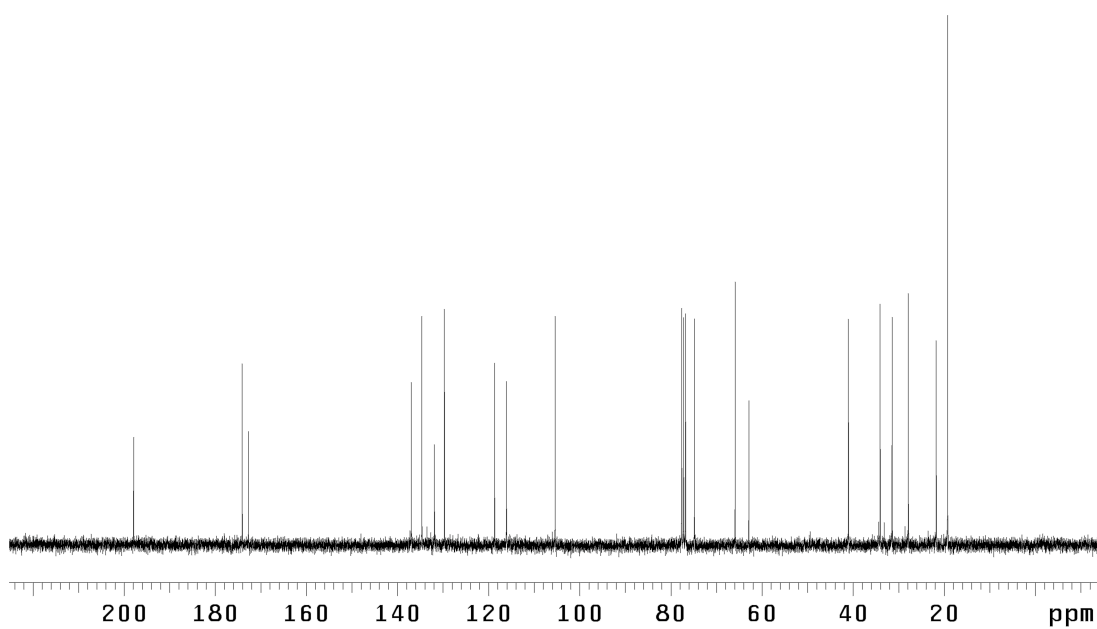


Figure SI-11C. ¹³C NMR (75 MHz, CDCl₃) of compound **14f**.

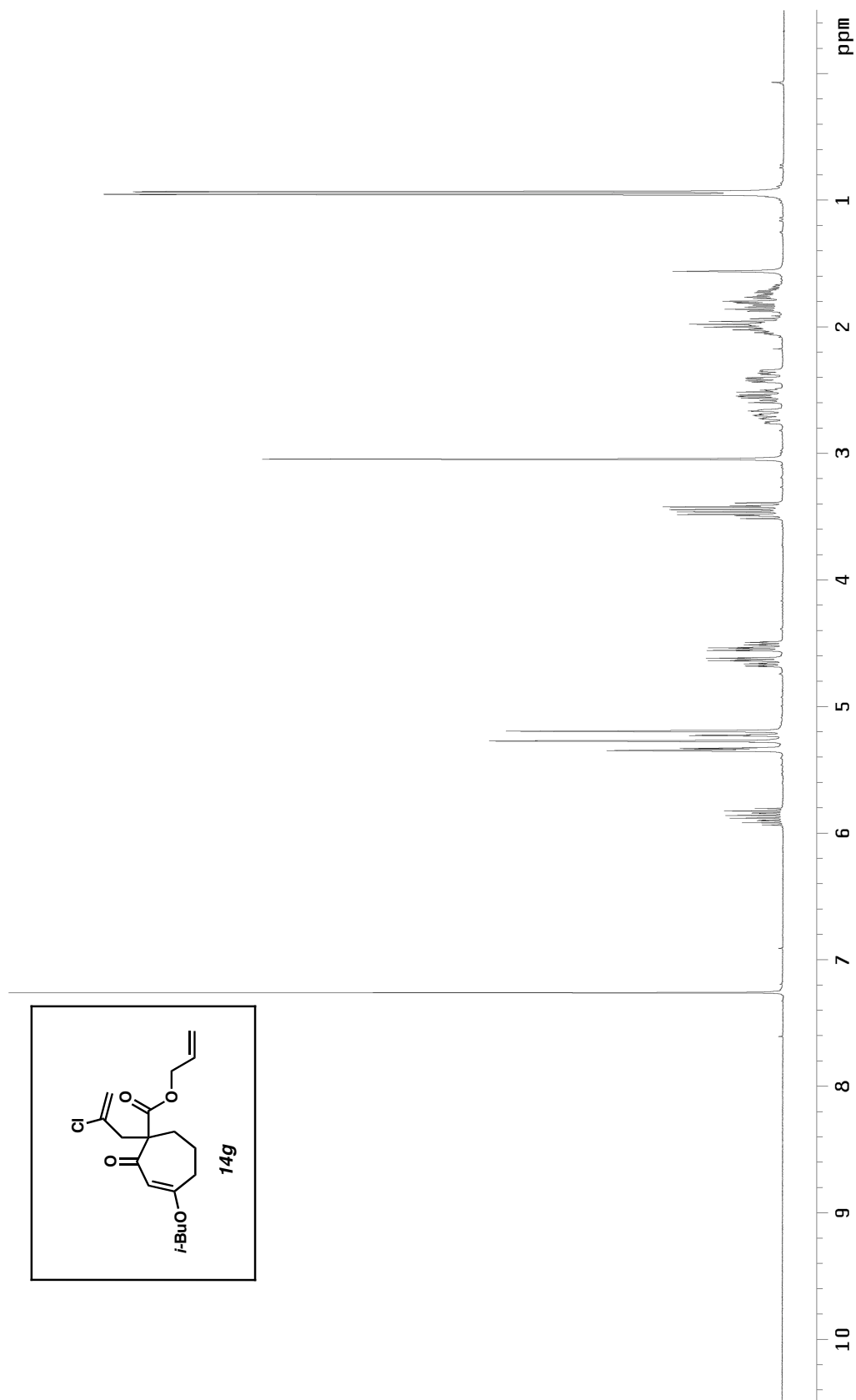


Figure SI-12A. ¹H NMR (300 MHz, CDCl₃) of compound **14g**.

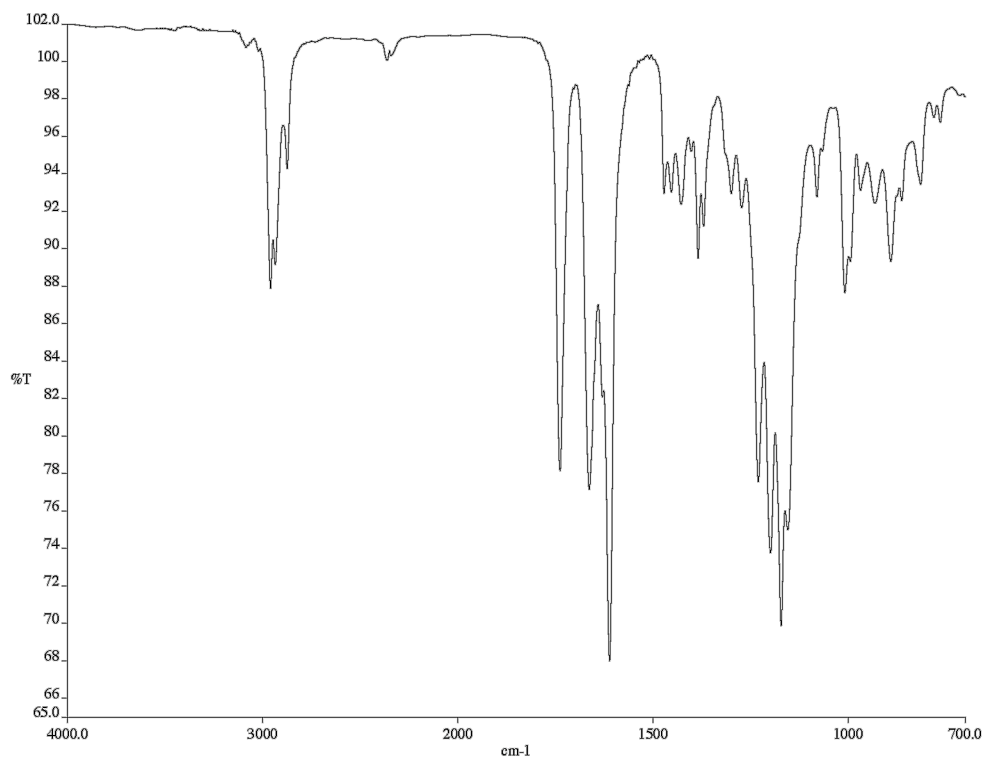


Figure SI-12B. Infrared spectrum (thin film/NaCl) of compound **14g**.

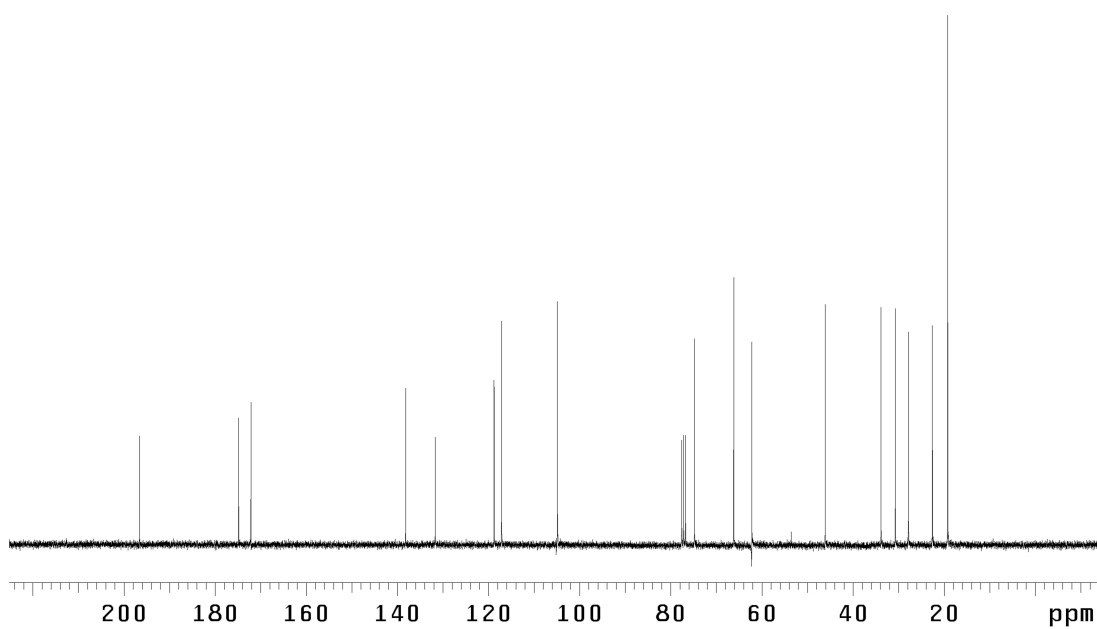


Figure SI-12C. ¹³C NMR (75 MHz, CDCl₃) of compound **14g**.

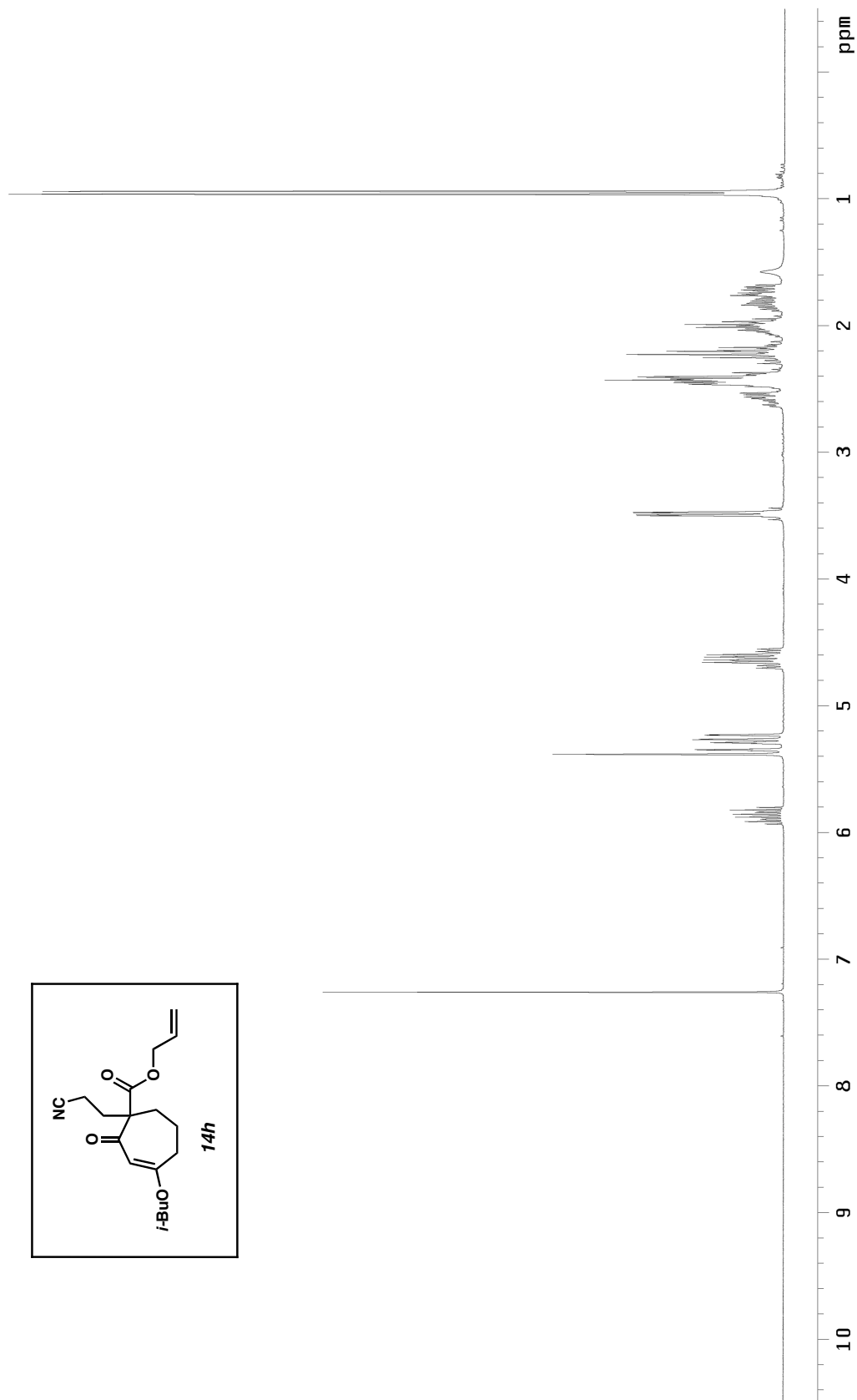


Figure SI-13A. ¹H NMR (300 MHz, CDCl₃) of compound **14h**.

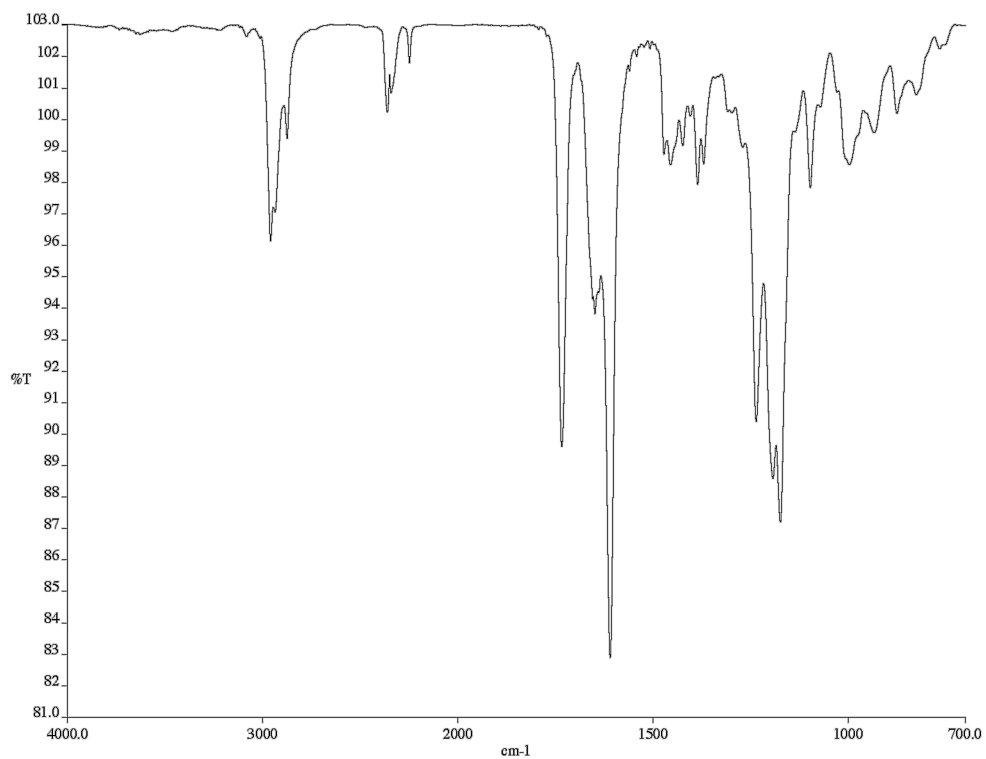


Figure SI-13B. Infrared spectrum (thin film/NaCl) of compound **14h**.

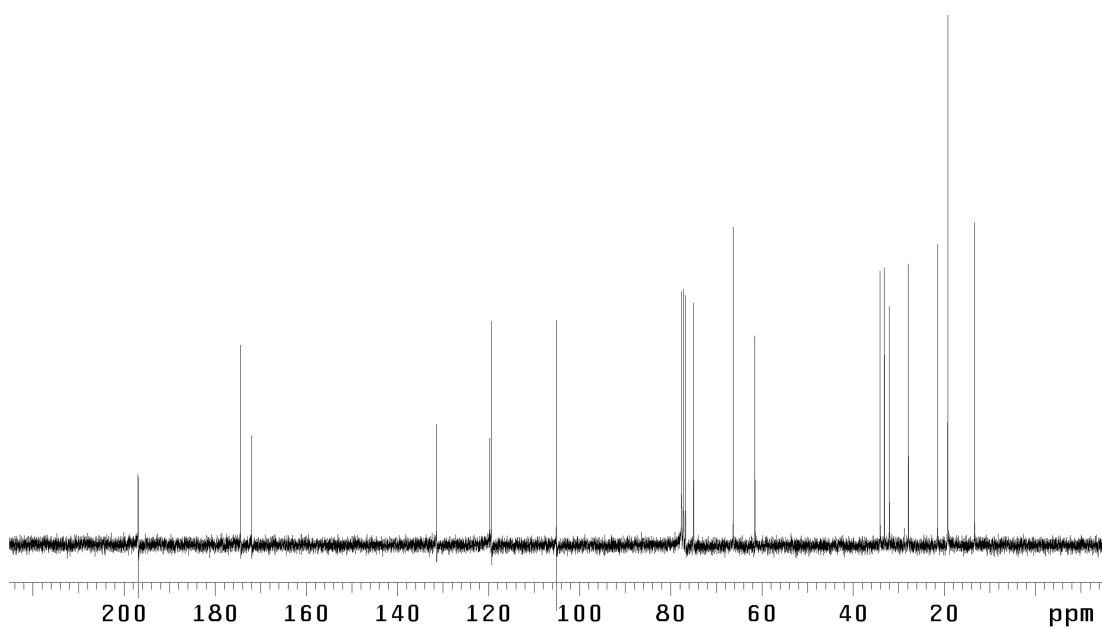


Figure SI-13C. ¹³C NMR (75 MHz, CDCl₃) of compound **14h**.

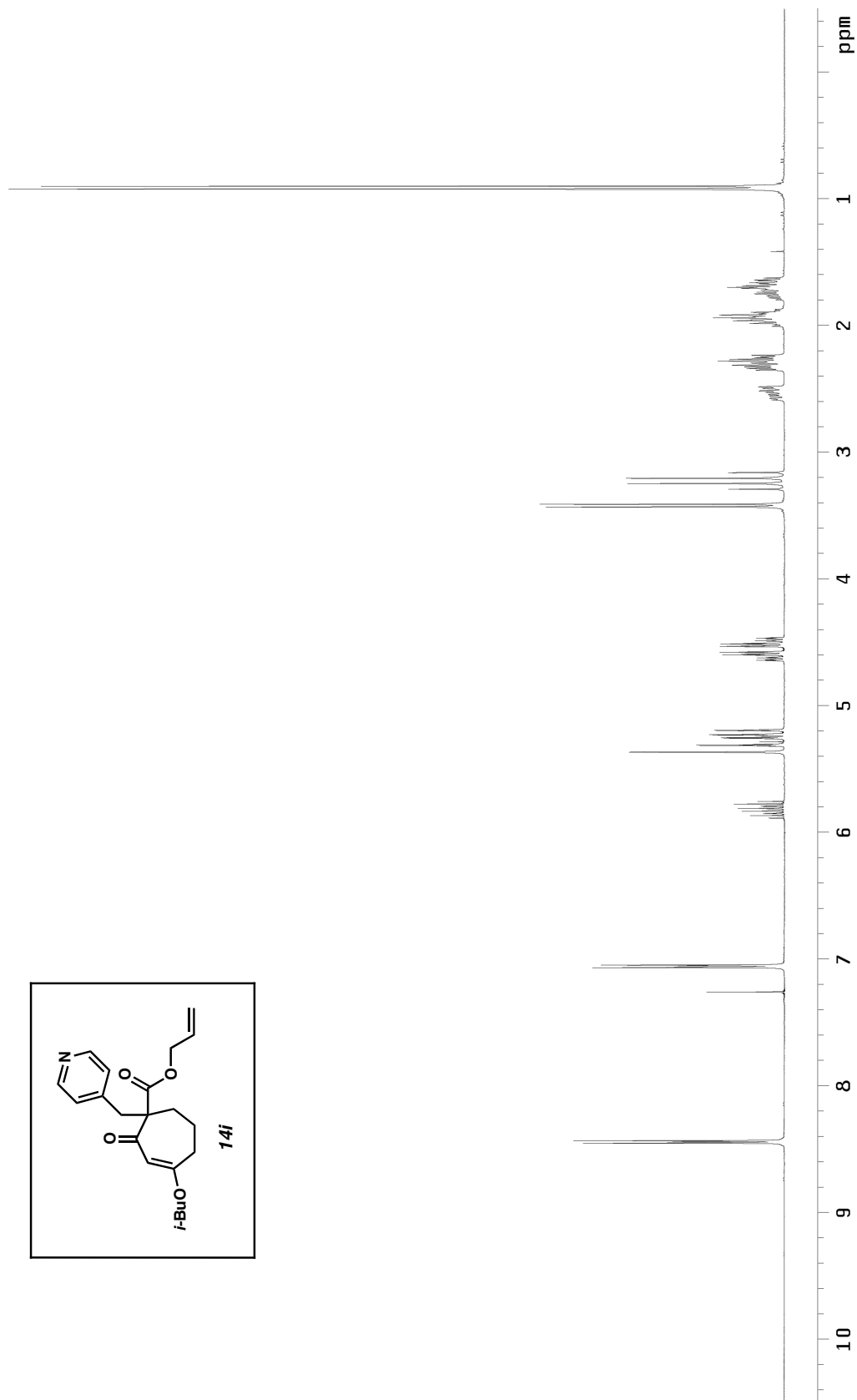


Figure SI-14A. ¹H NMR (300 MHz, CDCl₃) of compound **14i**.

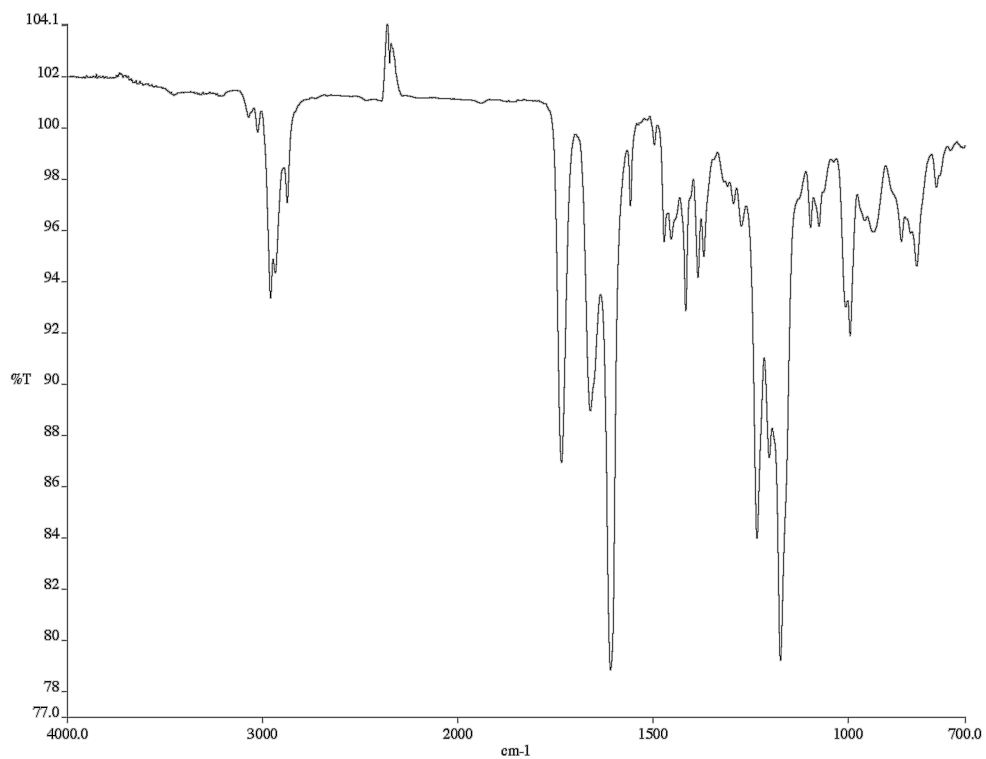


Figure SI-14B. Infrared spectrum (thin film/NaCl) of compound **14i**.

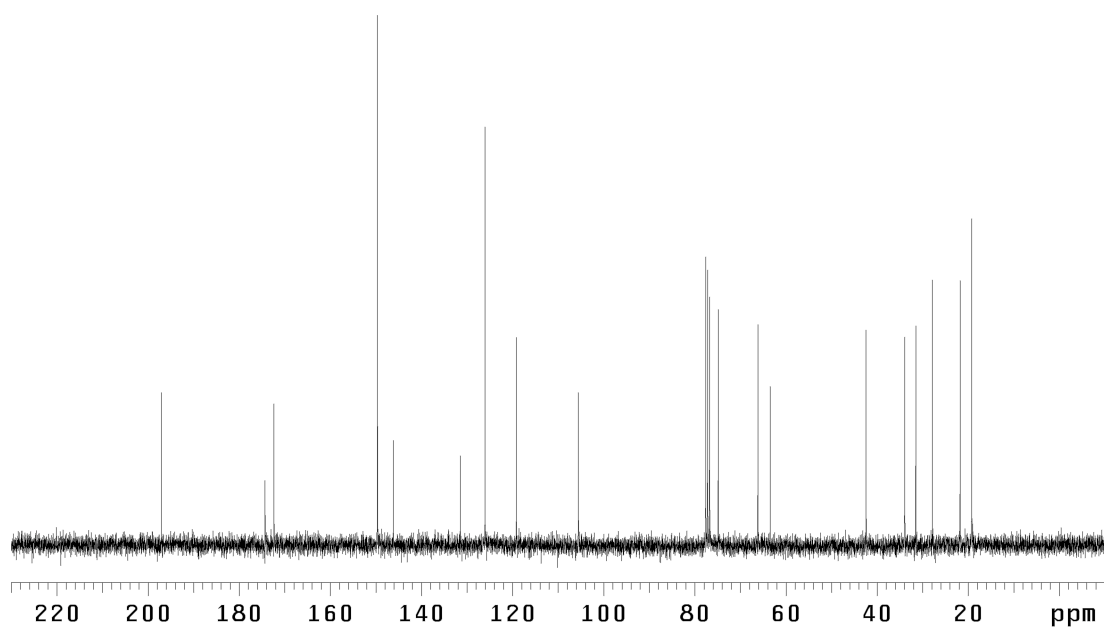


Figure SI-14C. ¹³C NMR (75 MHz, CDCl₃) of compound **14i**.

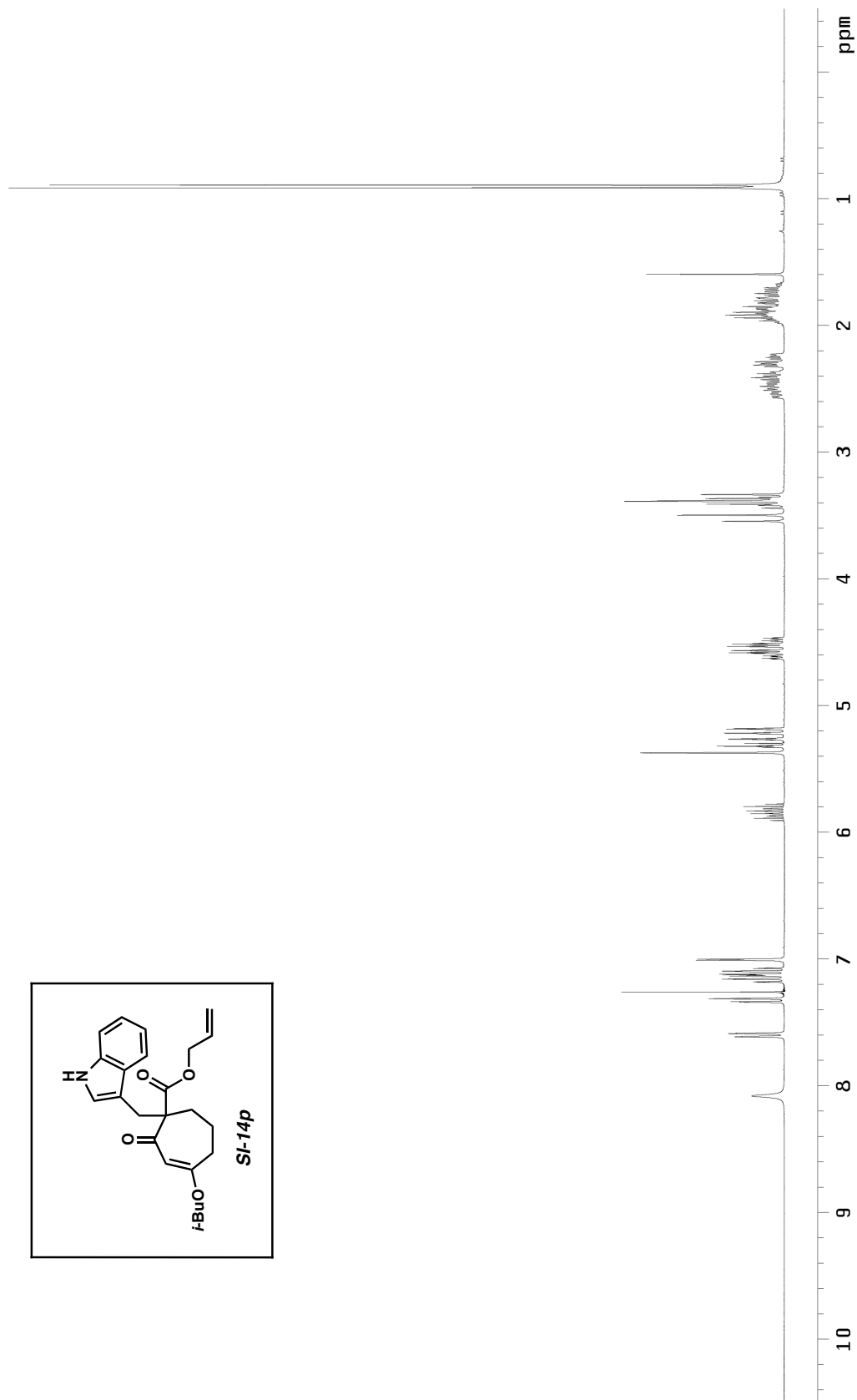


Figure SI-15A. ¹H NMR (300 MHz, CDCl₃) of compound SI-14p.

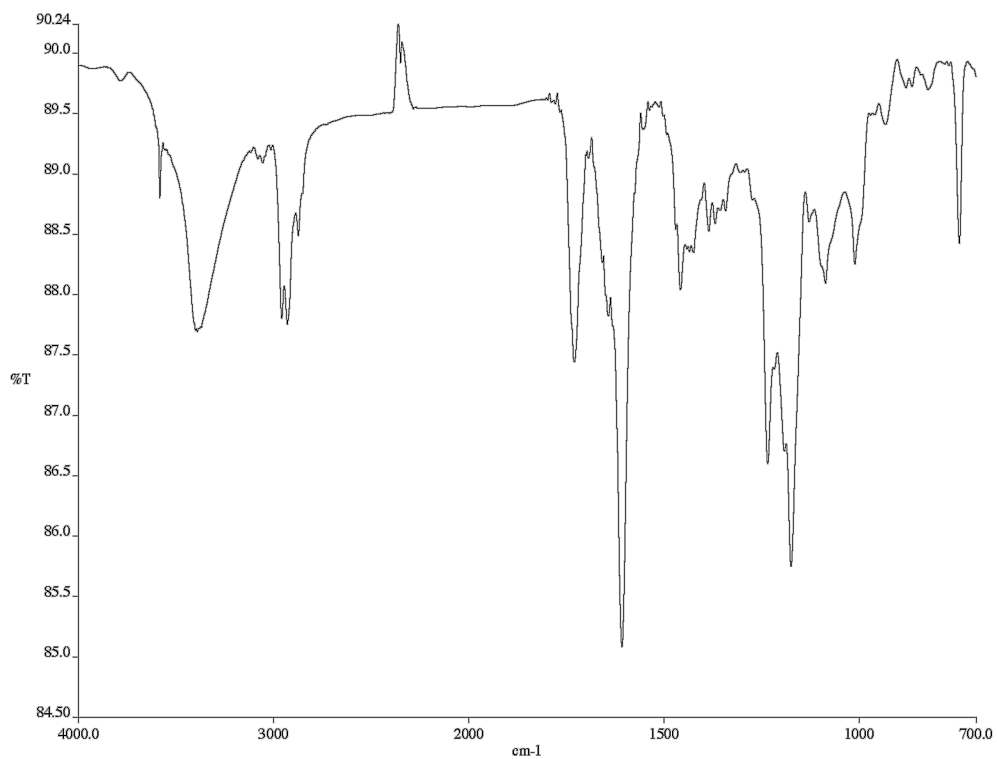


Figure SI-15B. Infrared spectrum (thin film/NaCl) of compound **SI-14p**.

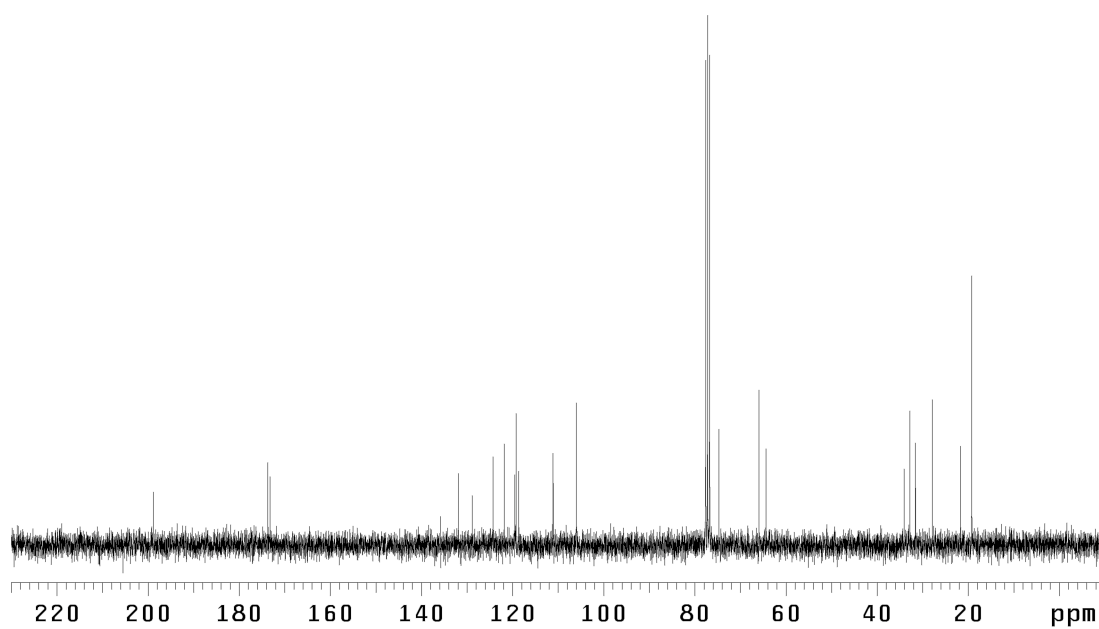


Figure SI-15C. ¹³C NMR (75 MHz, CDCl₃) of compound **SI-14p**.

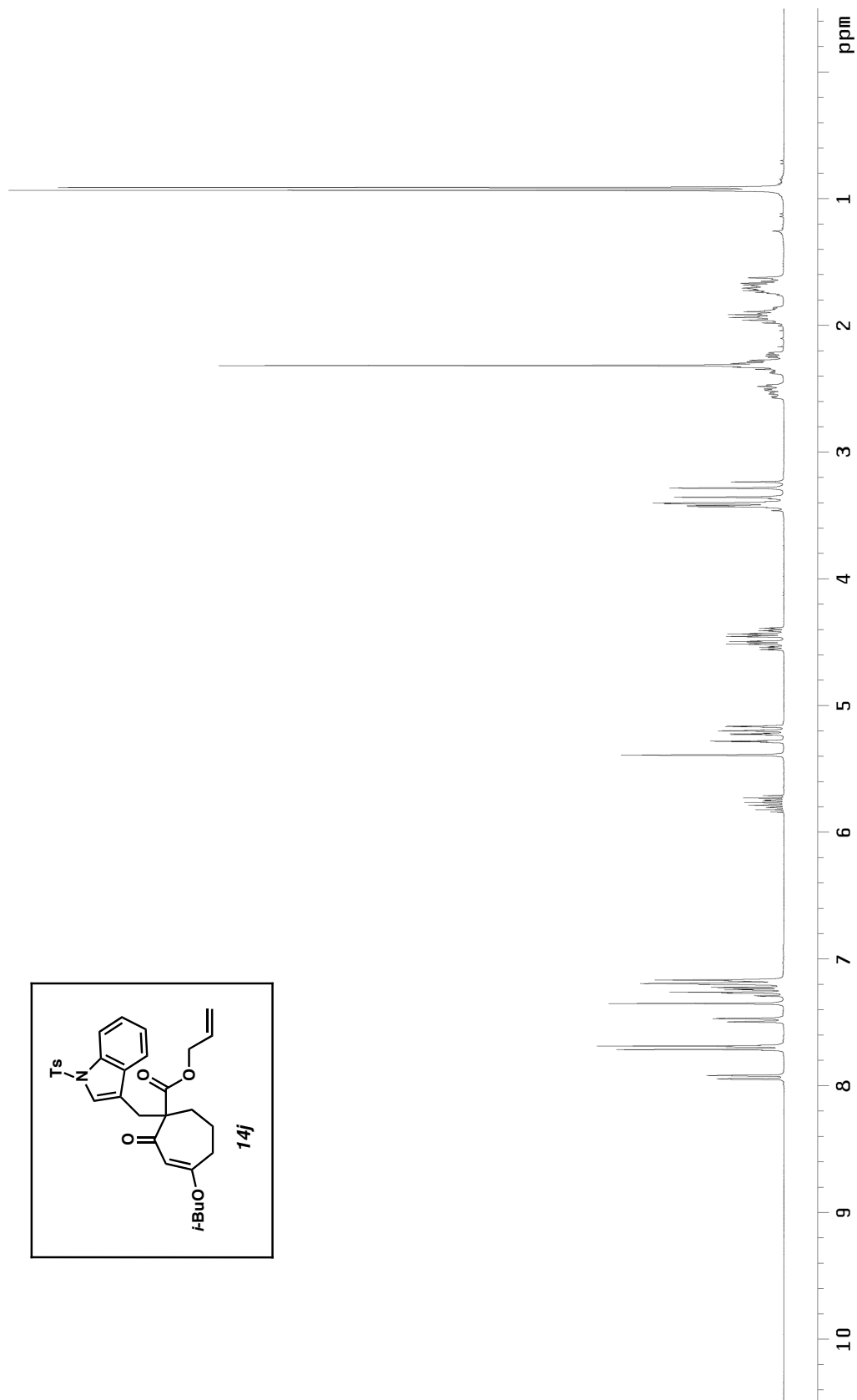


Figure SI-16A. ¹H NMR (300 MHz, CDCl₃) of compound **14j**.

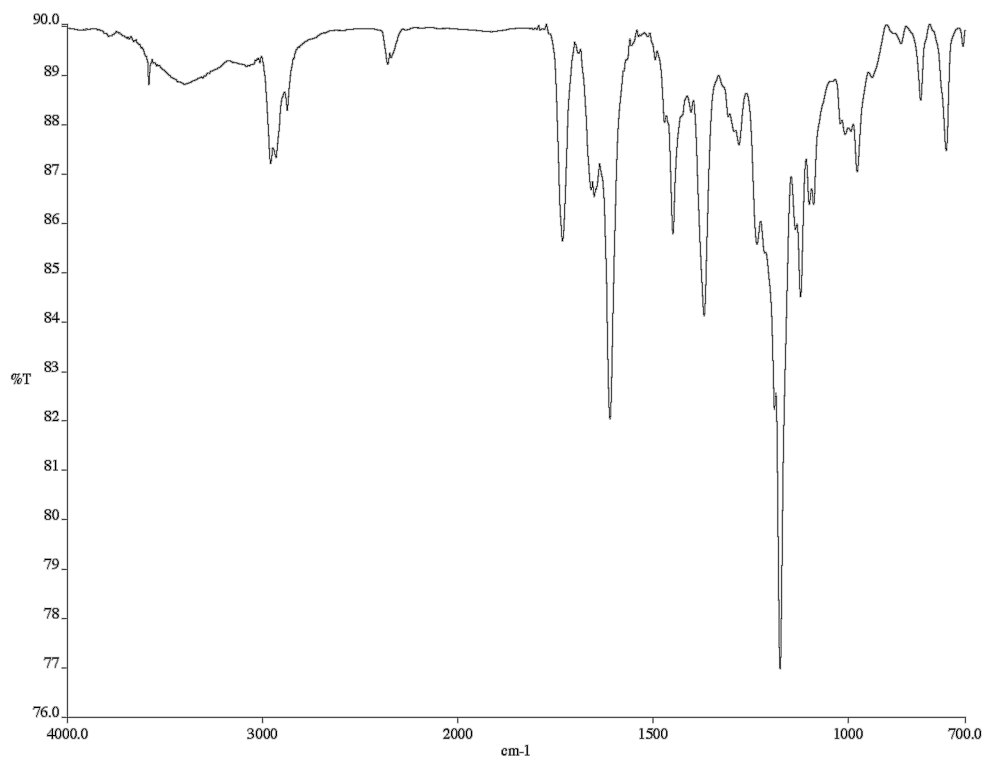


Figure SI-16B. Infrared spectrum (thin film/NaCl) of compound **14j**.

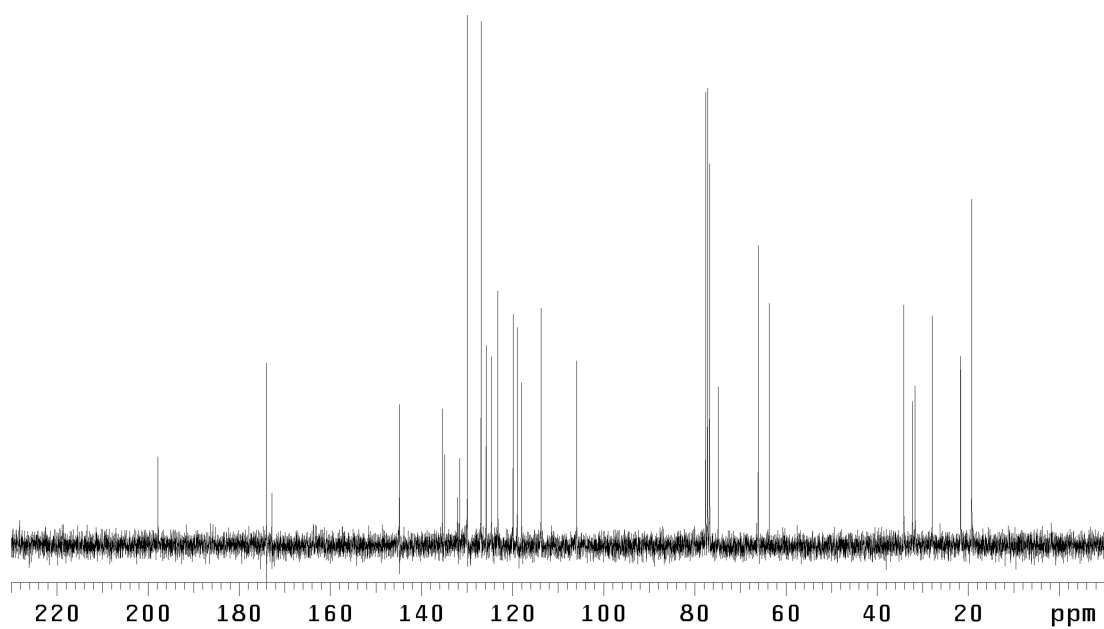


Figure SI-16C. ¹³C NMR (75 MHz, CDCl₃) of compound **14j**.

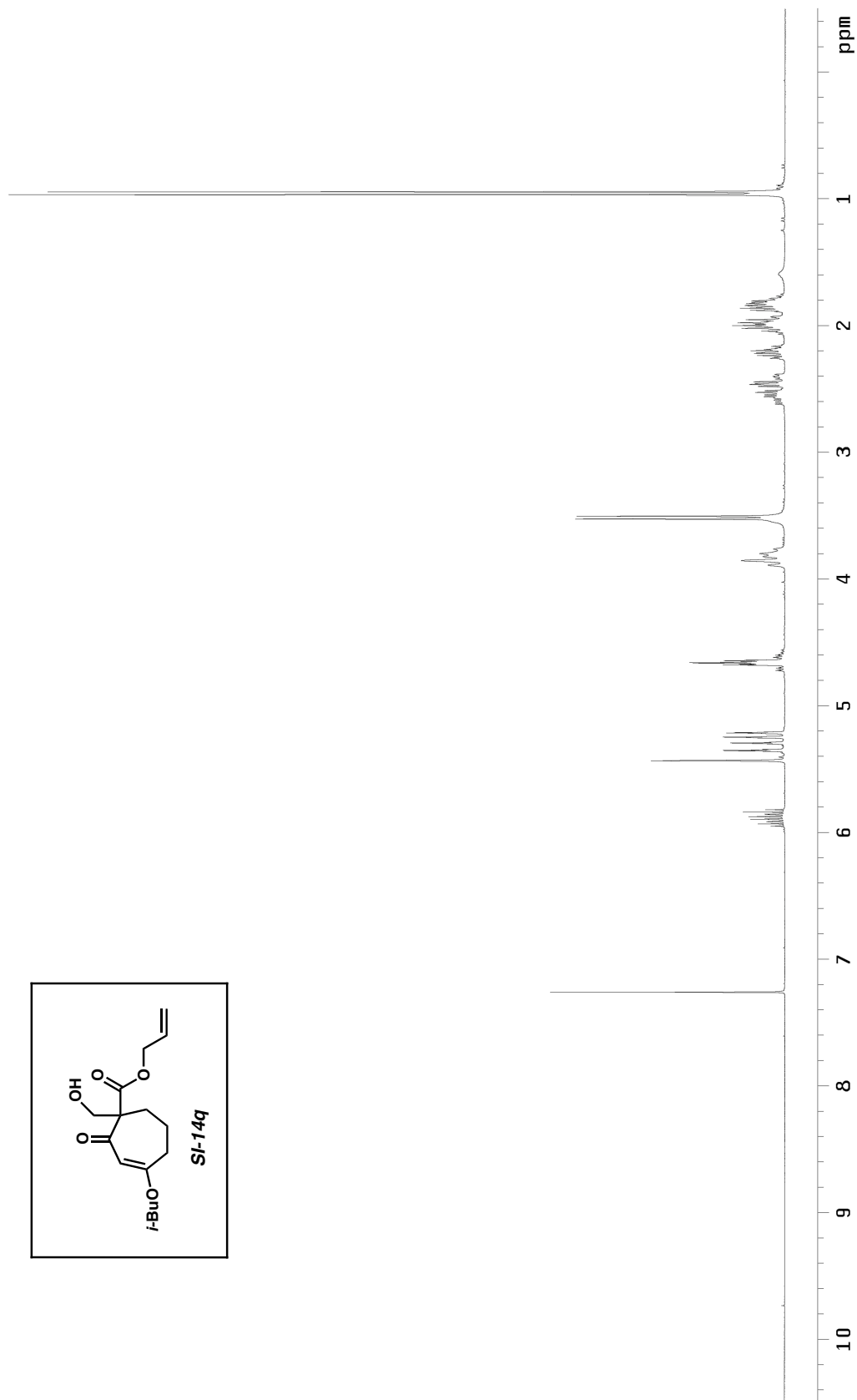


Figure SI-17A. ¹H NMR (300 MHz, CDCl₃) of compound SI-14q.

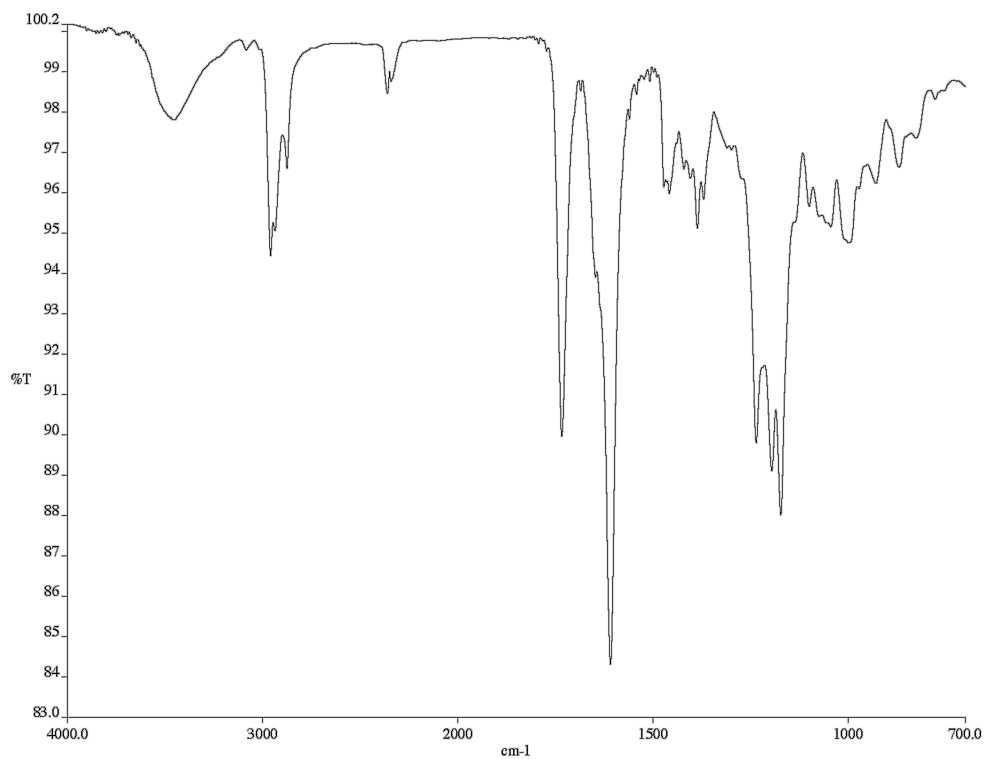


Figure SI-17B. Infrared spectrum (thin film/NaCl) of compound **SI-14q**.

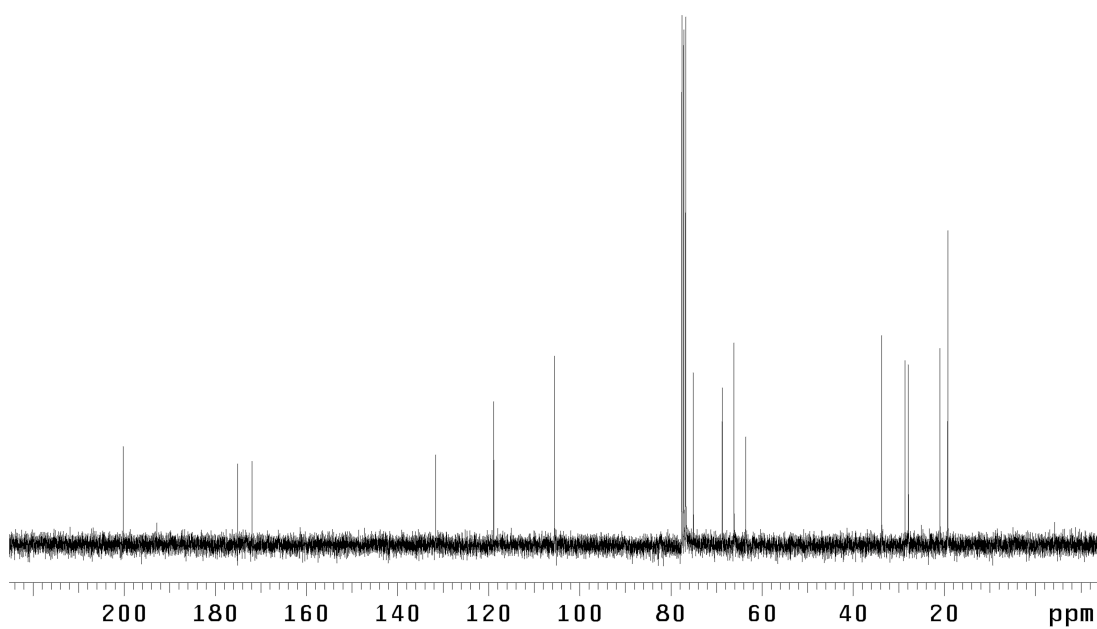


Figure SI-17C. ¹³C NMR (75 MHz, CDCl₃) of compound **SI-14q**.

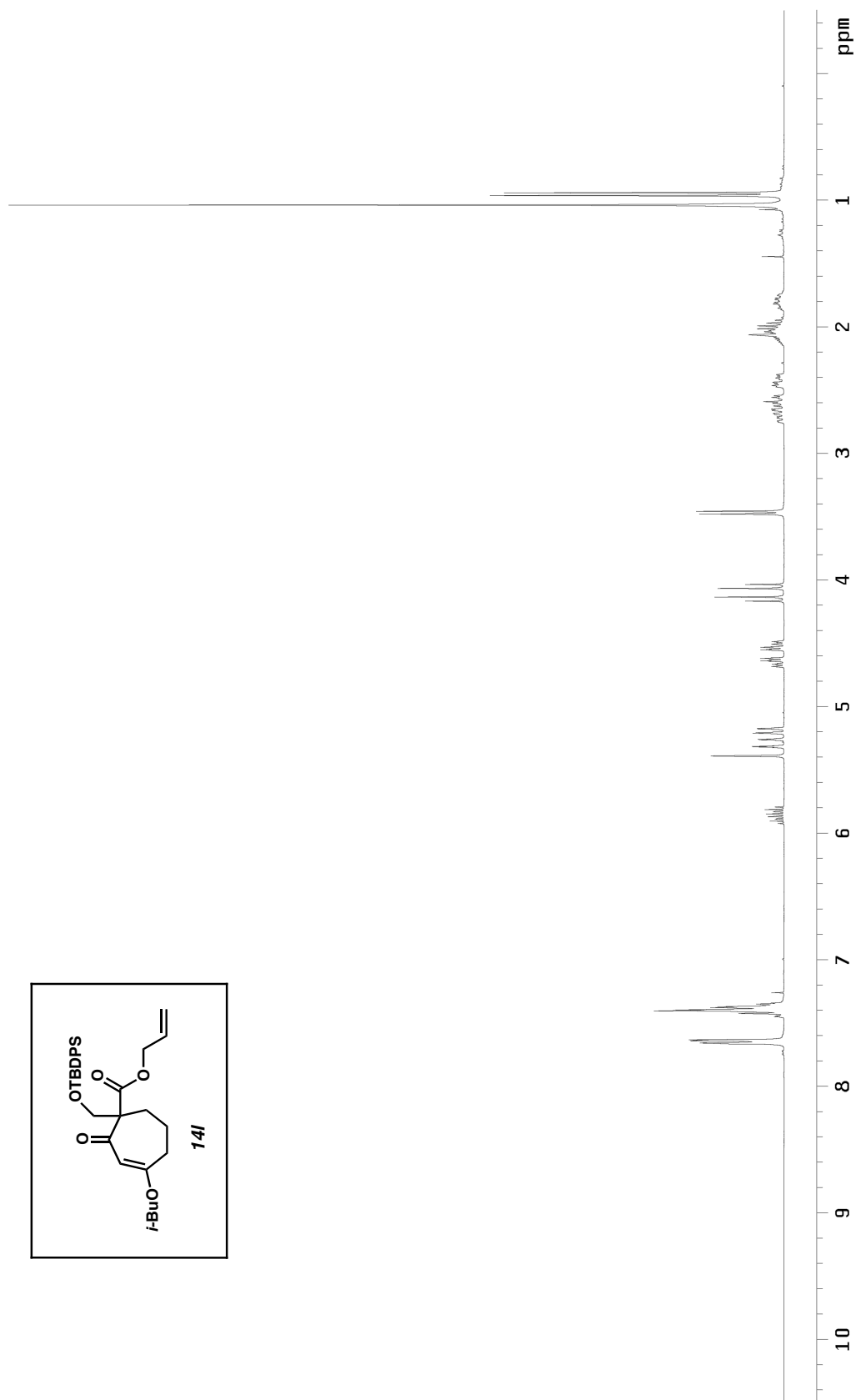


Figure SI-18A. ¹H NMR (300 MHz, CDCl₃) of compound **14I**.

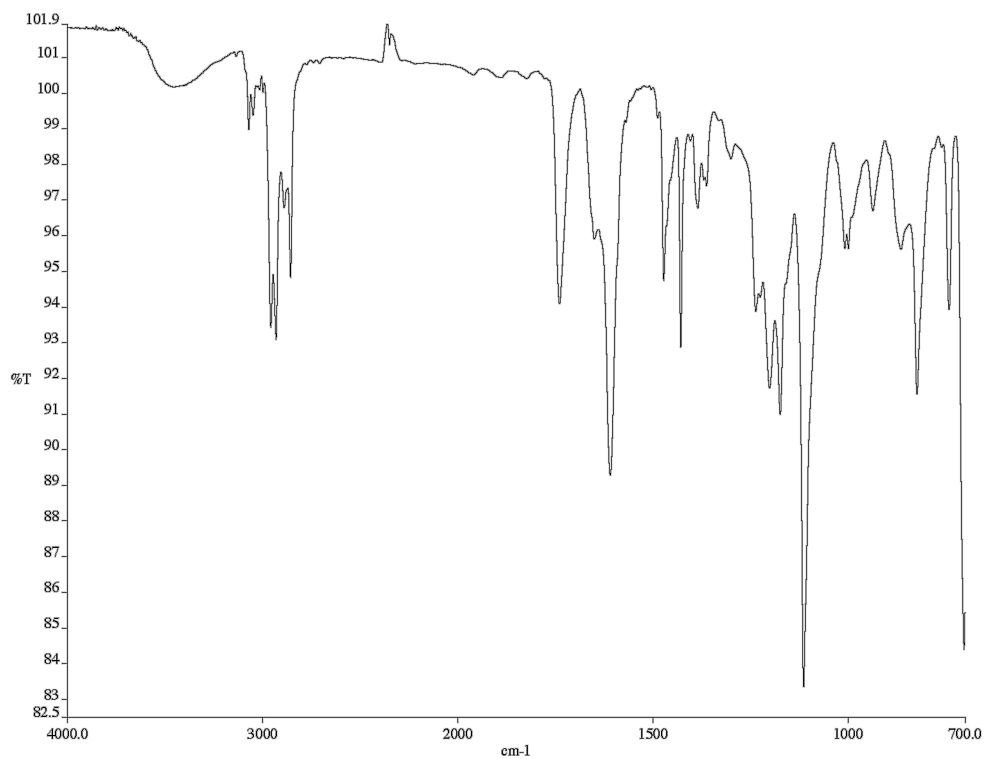


Figure SI-18B. Infrared spectrum (thin film/NaCl) of compound **14I**.

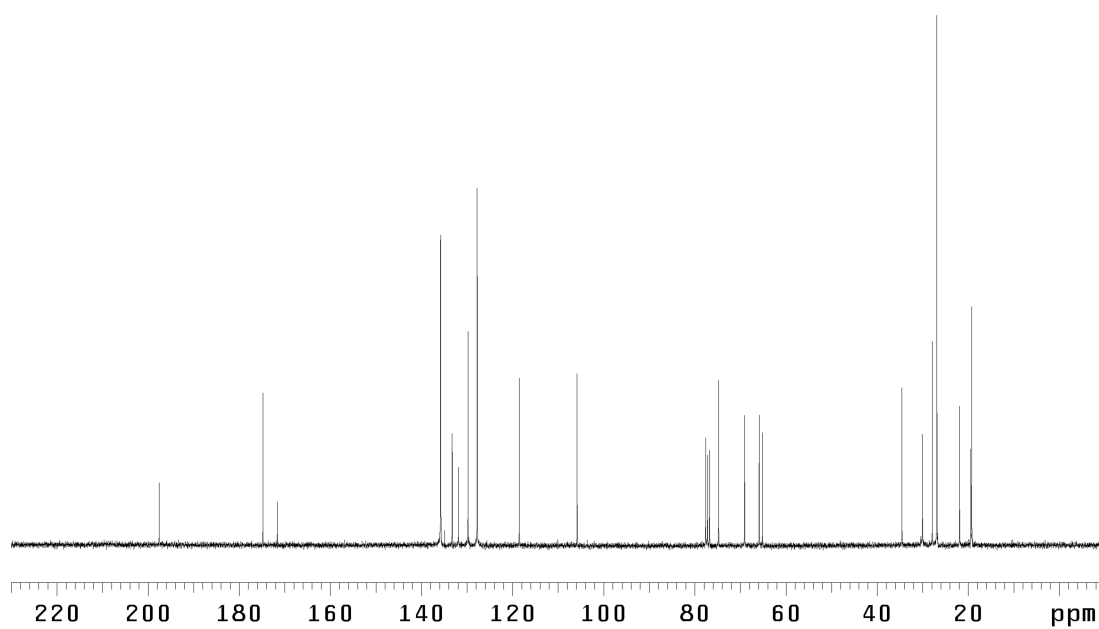


Figure SI-18C. ^{13}C NMR (75 MHz, CDCl_3) of compound **14I**.

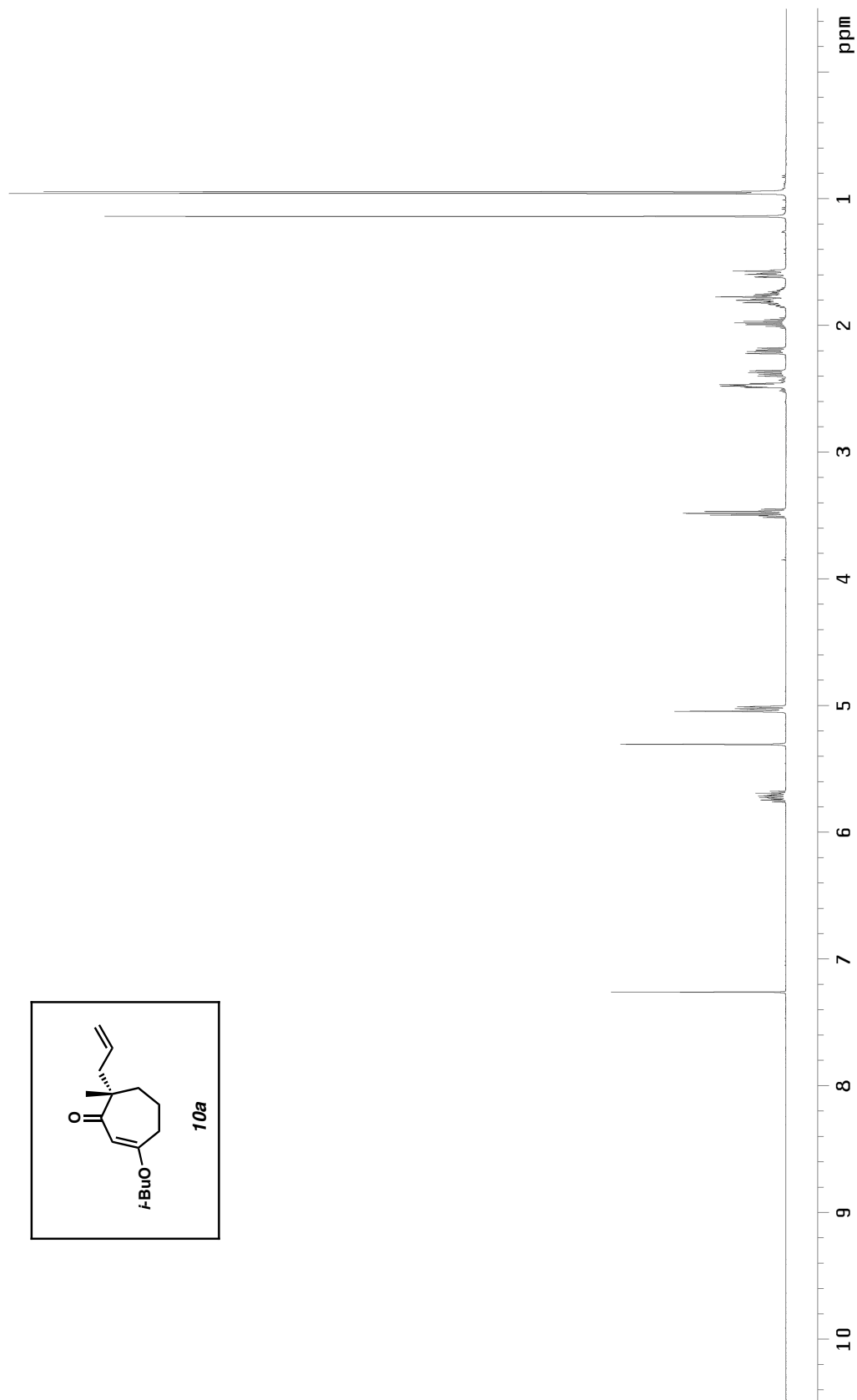


Figure SI-19A. ¹H NMR (500 MHz, CDCl₃) of compound **10a**.

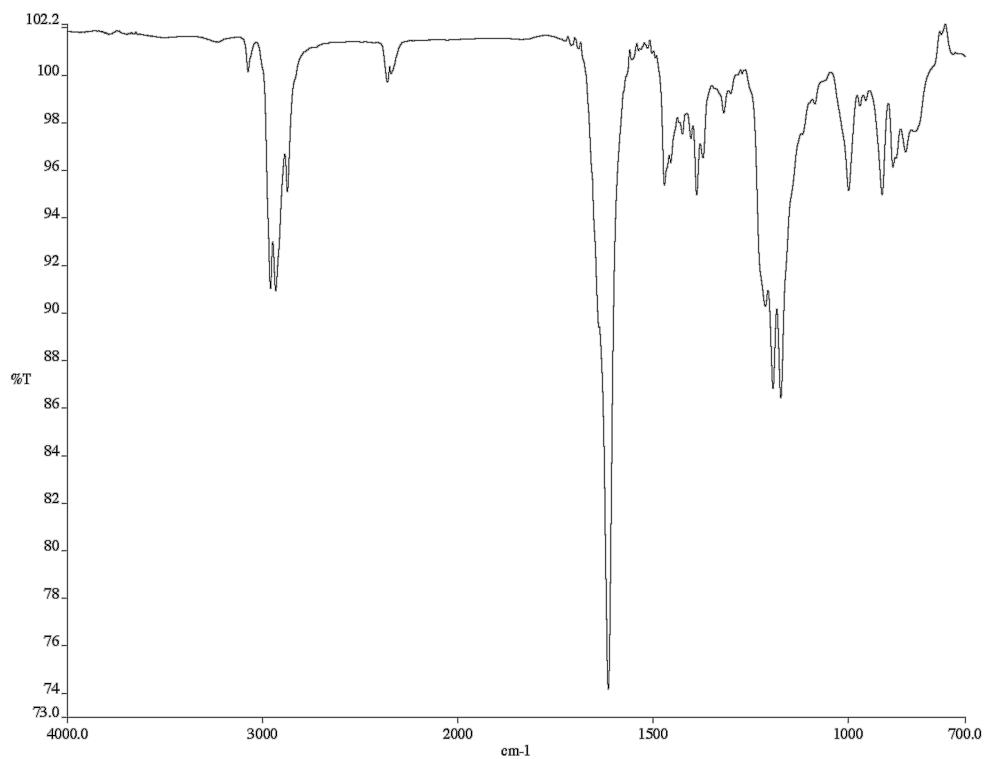


Figure SI-19B. Infrared spectrum (thin film/NaCl) of compound **10a**.

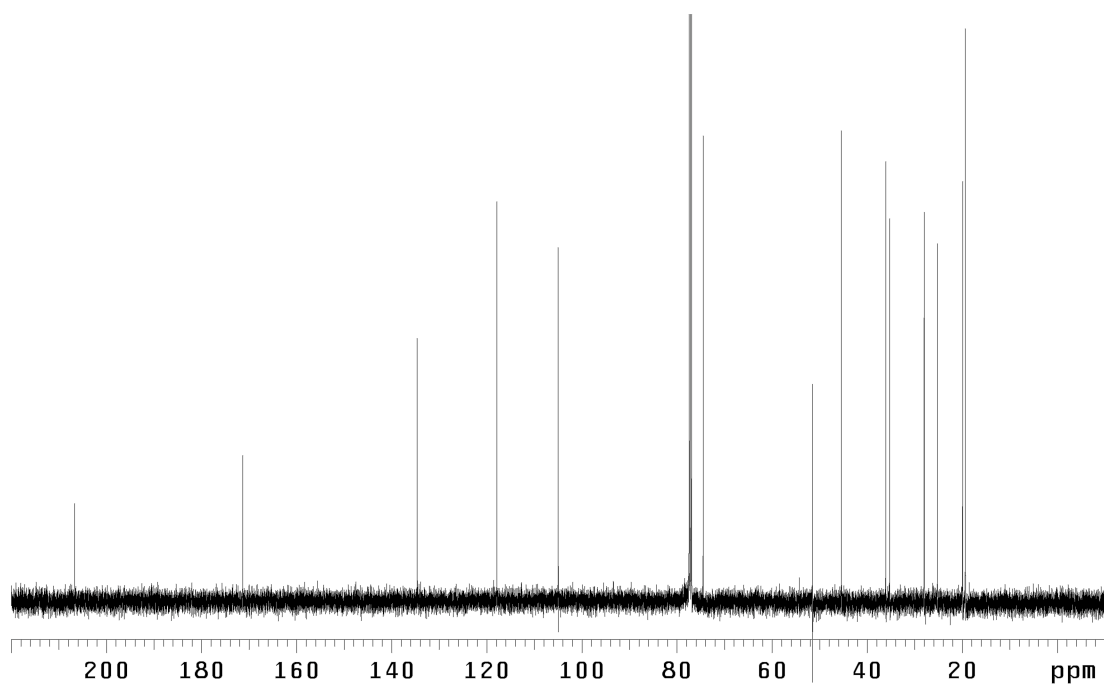


Figure SI-19C. ¹³C NMR (125 MHz, CDCl₃) of compound **10a**.

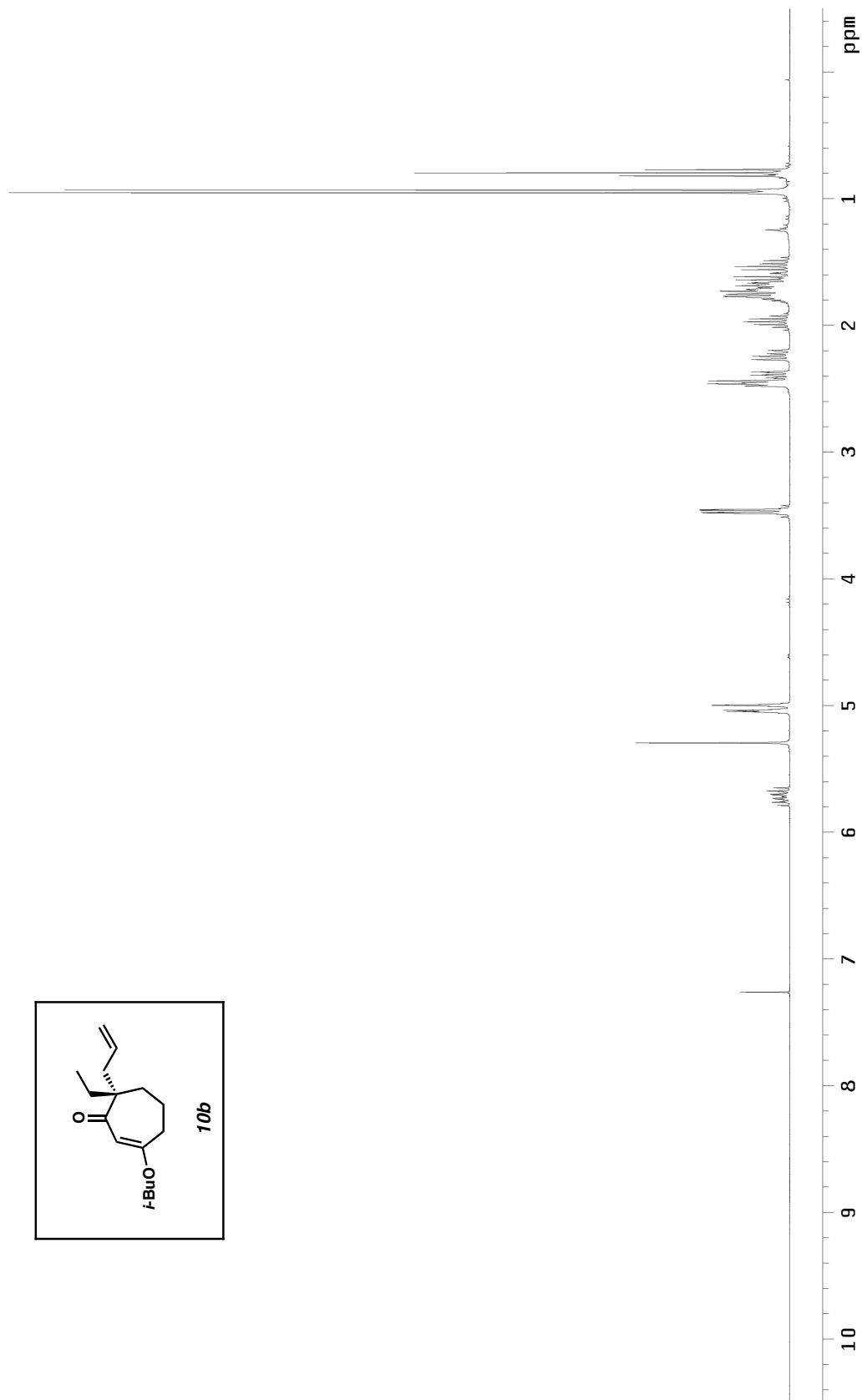


Figure SI-20A. ¹H NMR (300 MHz, CDCl₃) of compound **10b**.

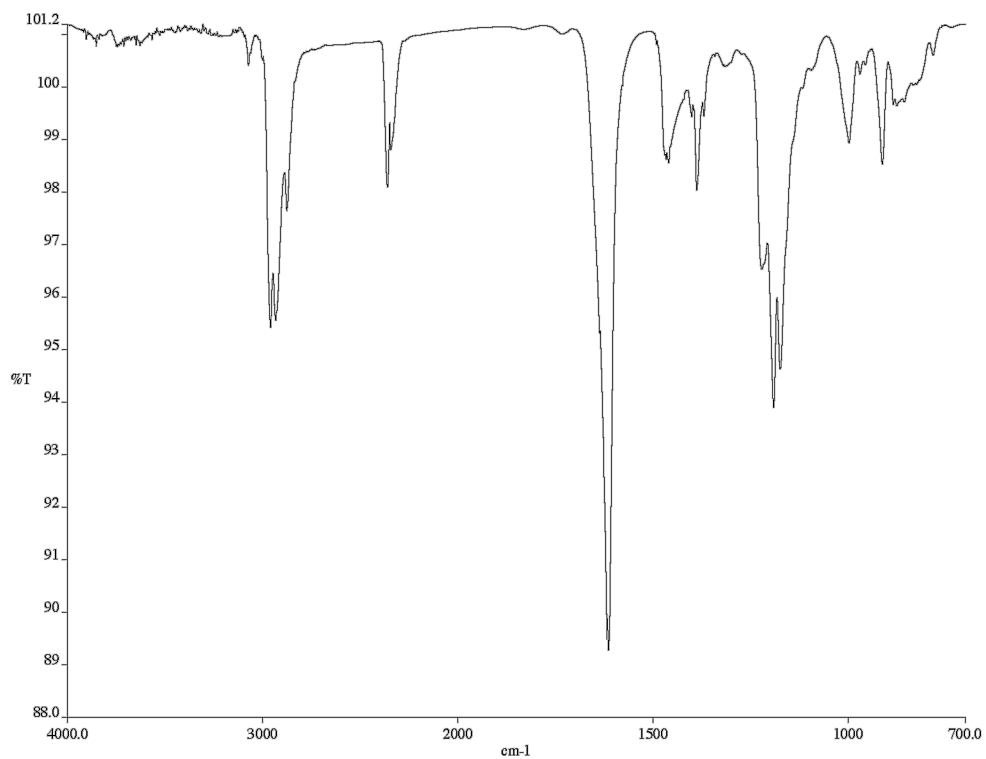


Figure SI-20B. Infrared spectrum (thin film/NaCl) of compound **10b**.

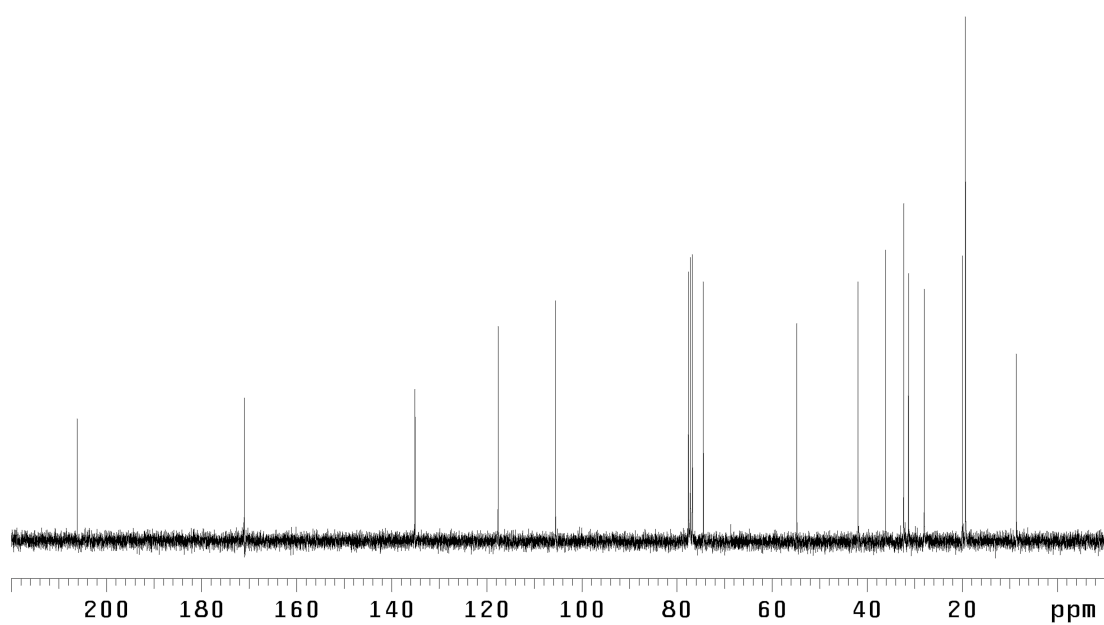


Figure SI-20C. ¹³C NMR (75 MHz, CDCl₃) of compound **10b**.

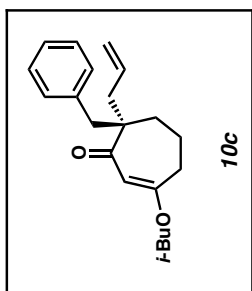
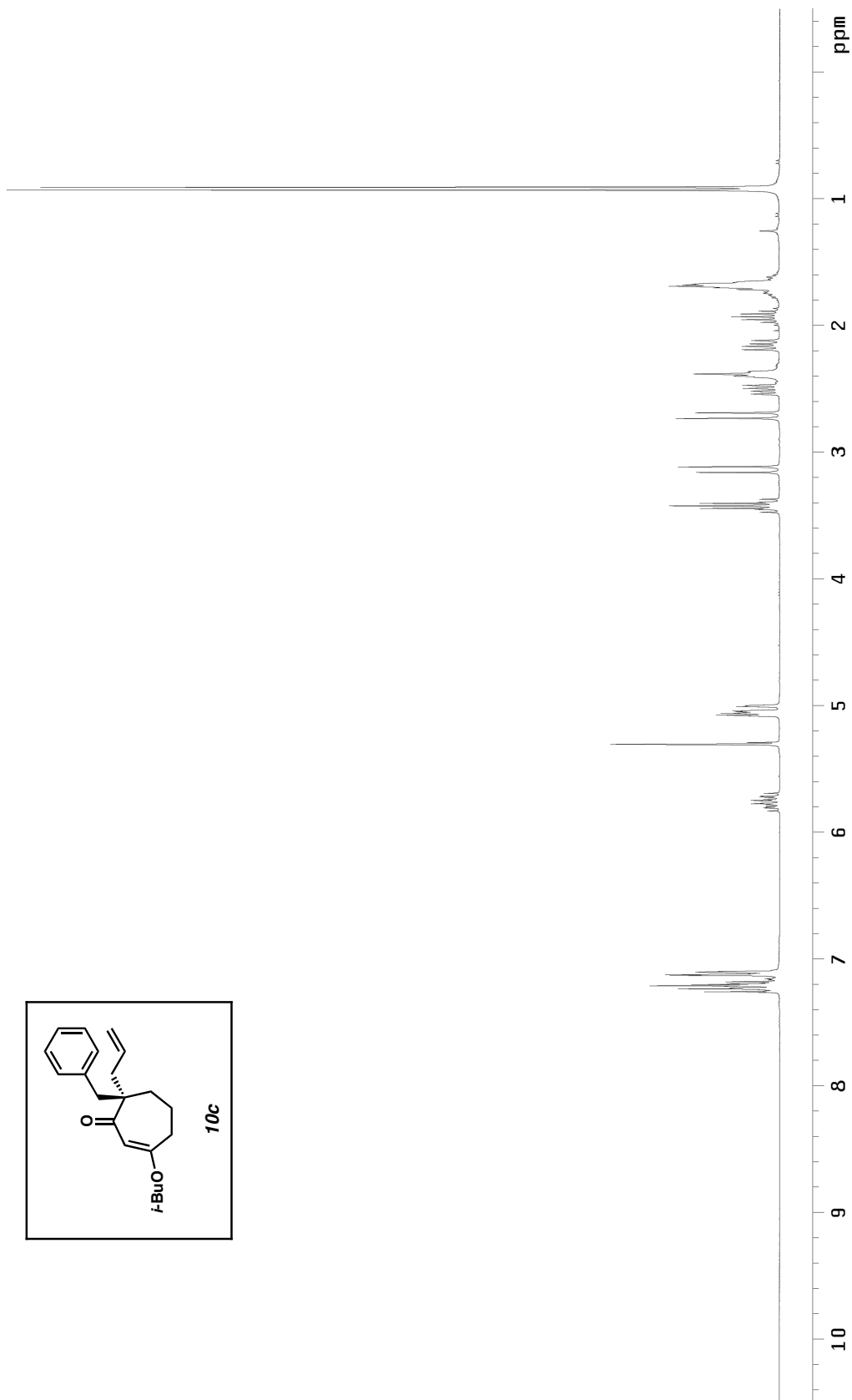


Figure SI-21A. ¹H NMR (300 MHz, CDCl₃) of compound **10c**.

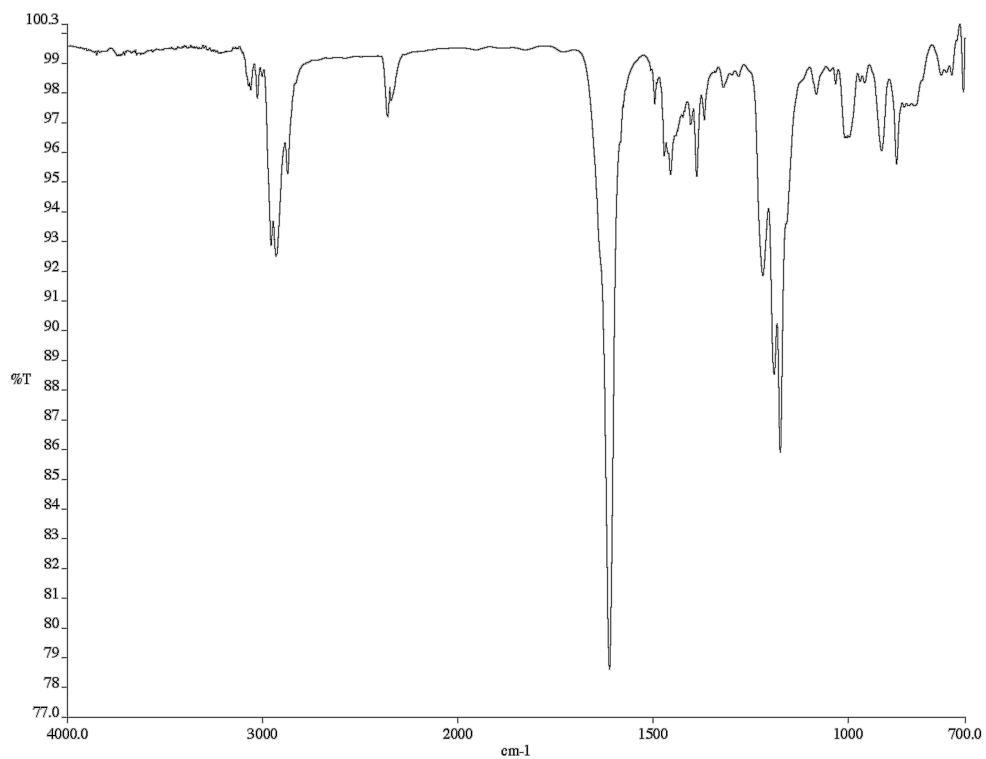


Figure SI-21B. Infrared spectrum (thin film/NaCl) of compound **10c**.

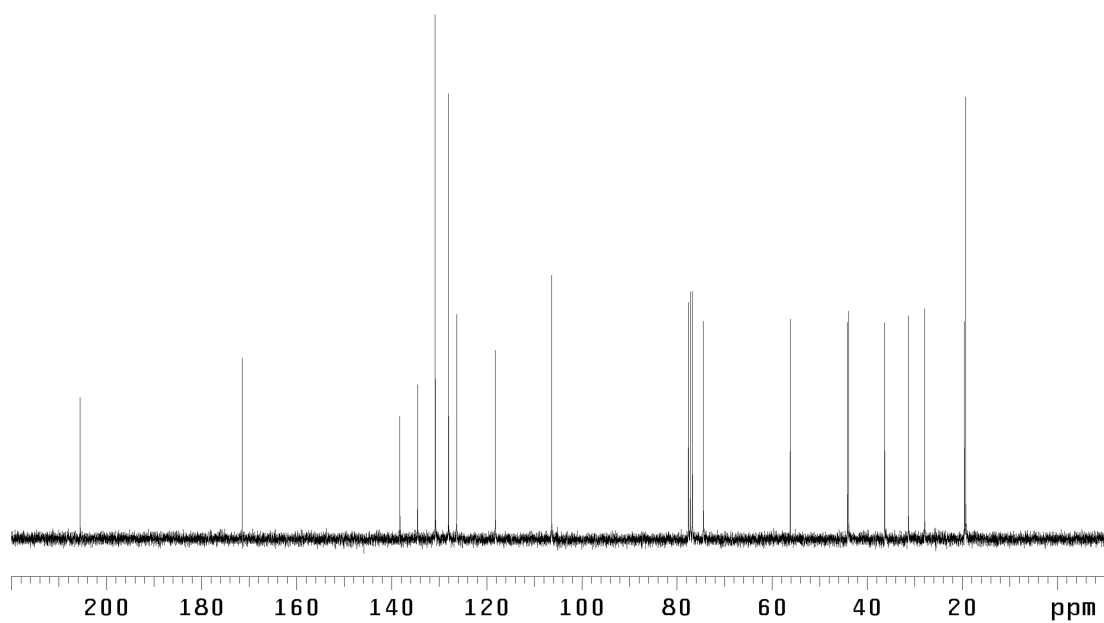


Figure SI-21C. ¹³C NMR (75 MHz, CDCl₃) of compound **10c**.

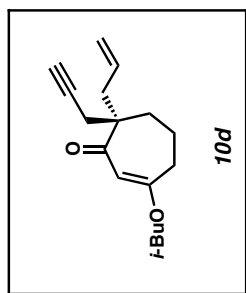
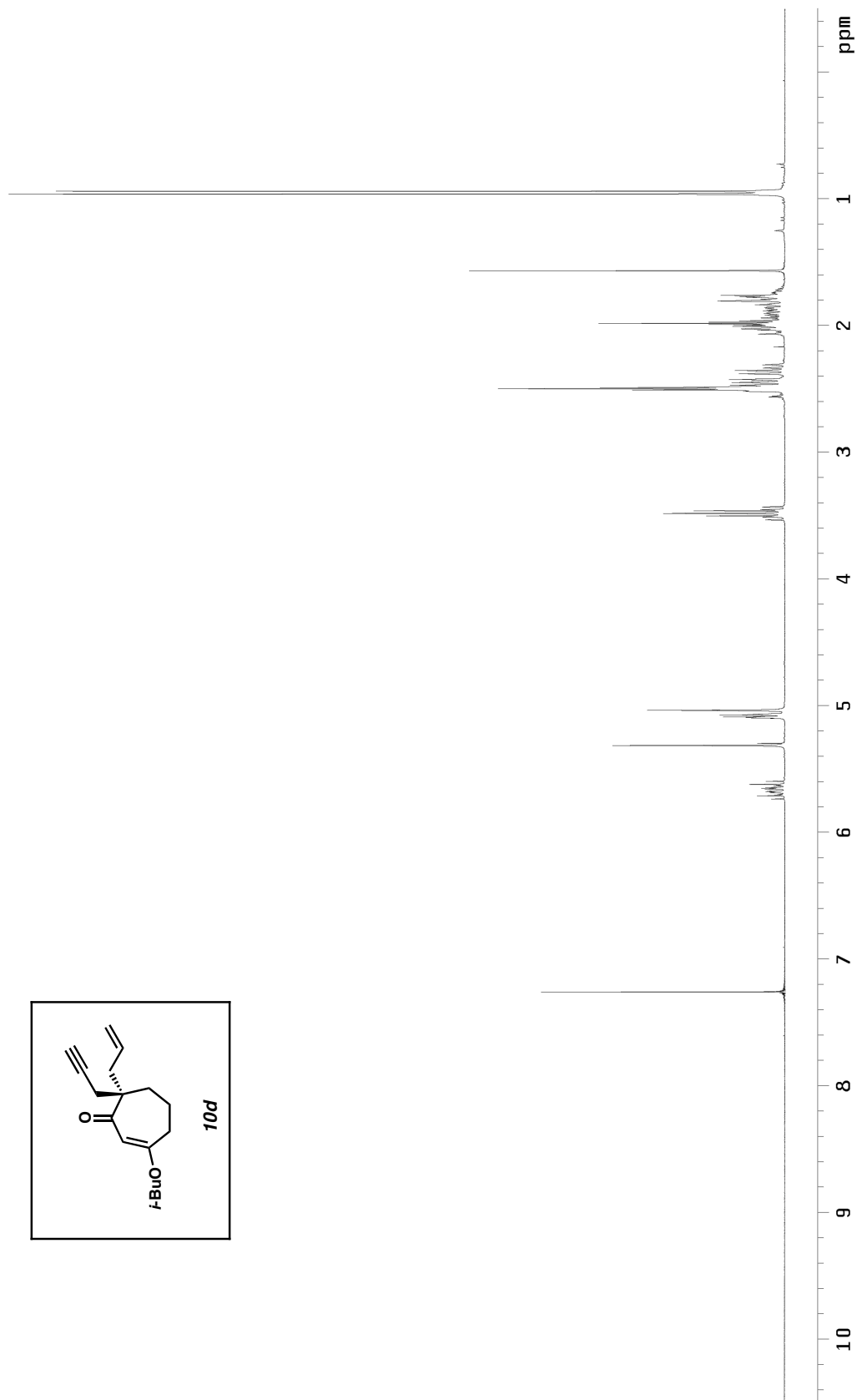


Figure SI-22A. ¹H NMR (300 MHz, CDCl₃) of compound **10d**.

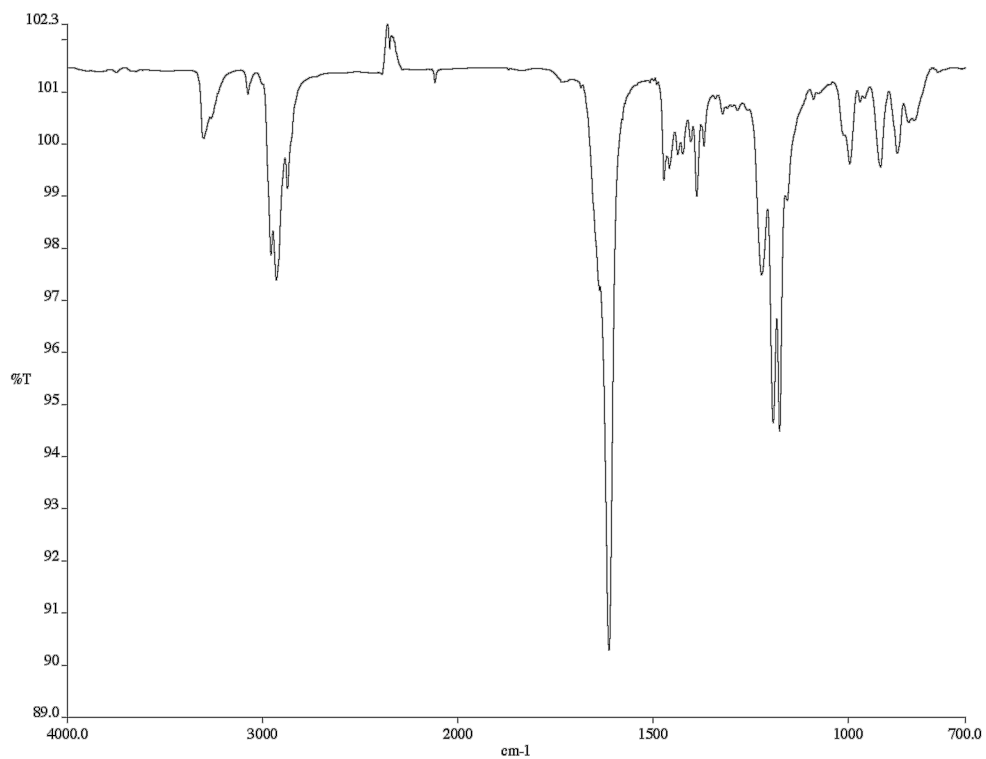


Figure SI-22B. Infrared spectrum (thin film/NaCl) of compound **10d**.

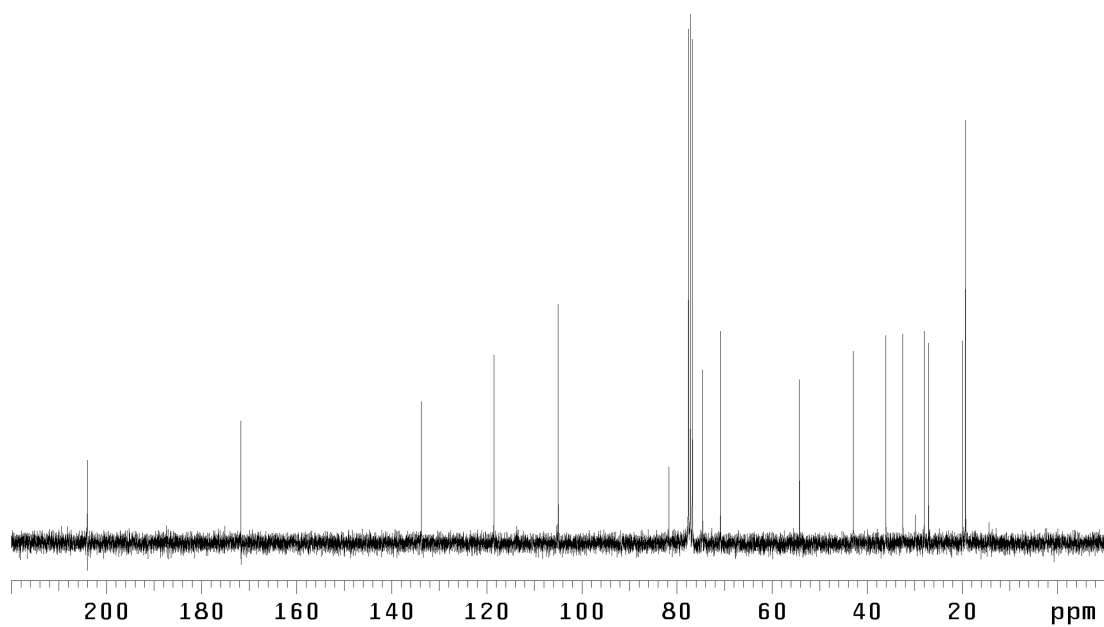


Figure SI-22C. ¹³C NMR (75 MHz, CDCl₃) of compound **10d**.

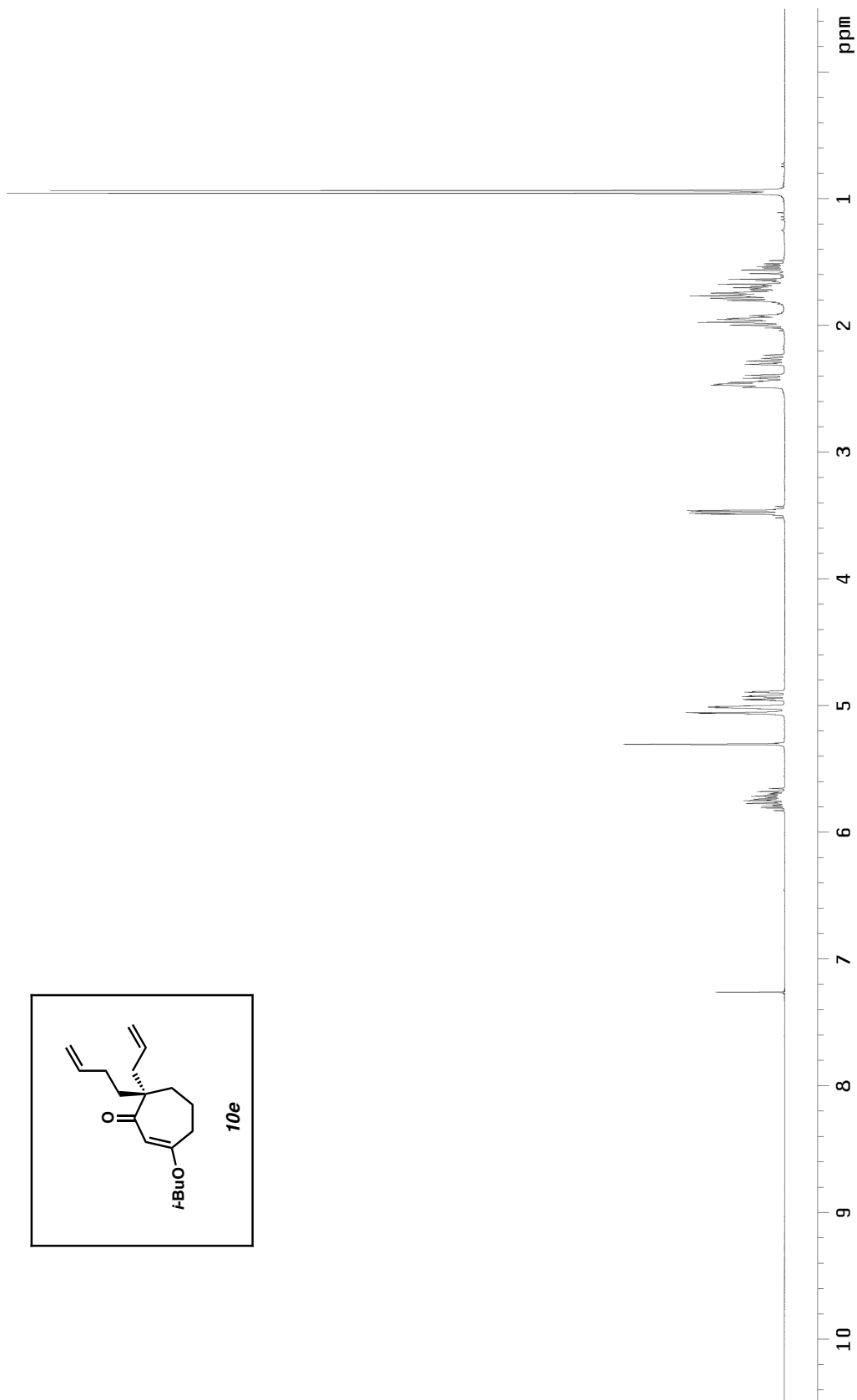


Figure SI-23A. ¹H NMR (300 MHz, CDCl₃) of compound **10e**.

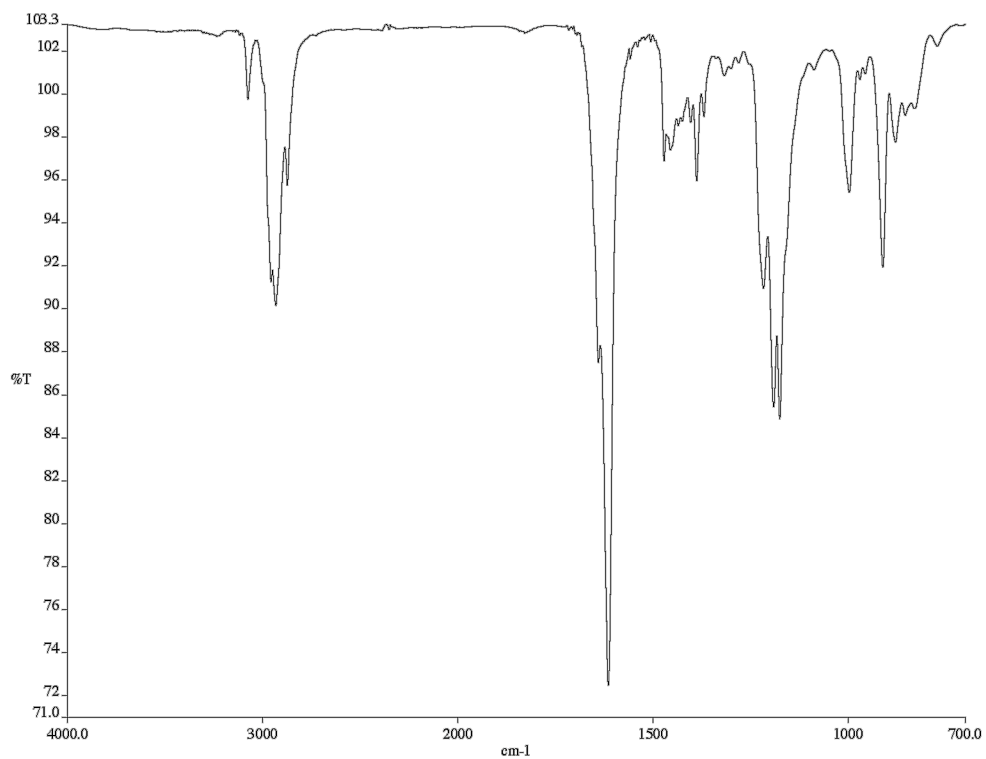


Figure SI-23B. Infrared spectrum (thin film/NaCl) of compound **10e**.

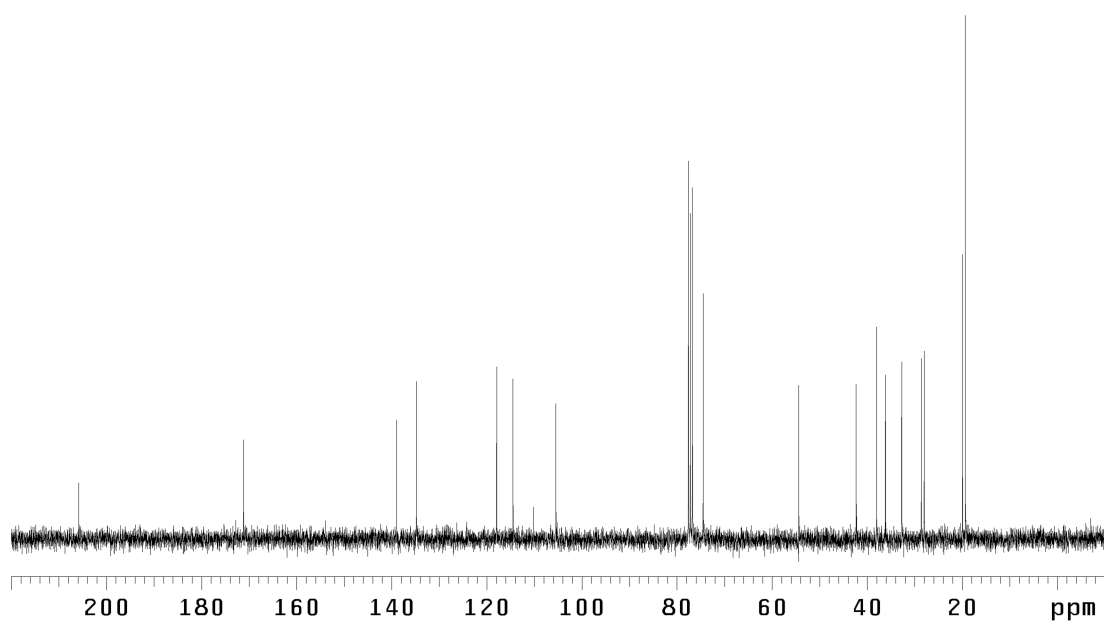


Figure SI-23C. ¹³C NMR (75 MHz, CDCl₃) of compound **10e**.

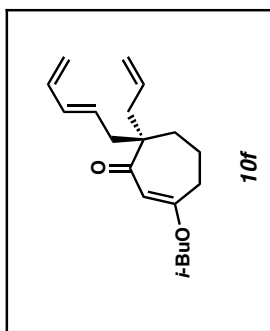
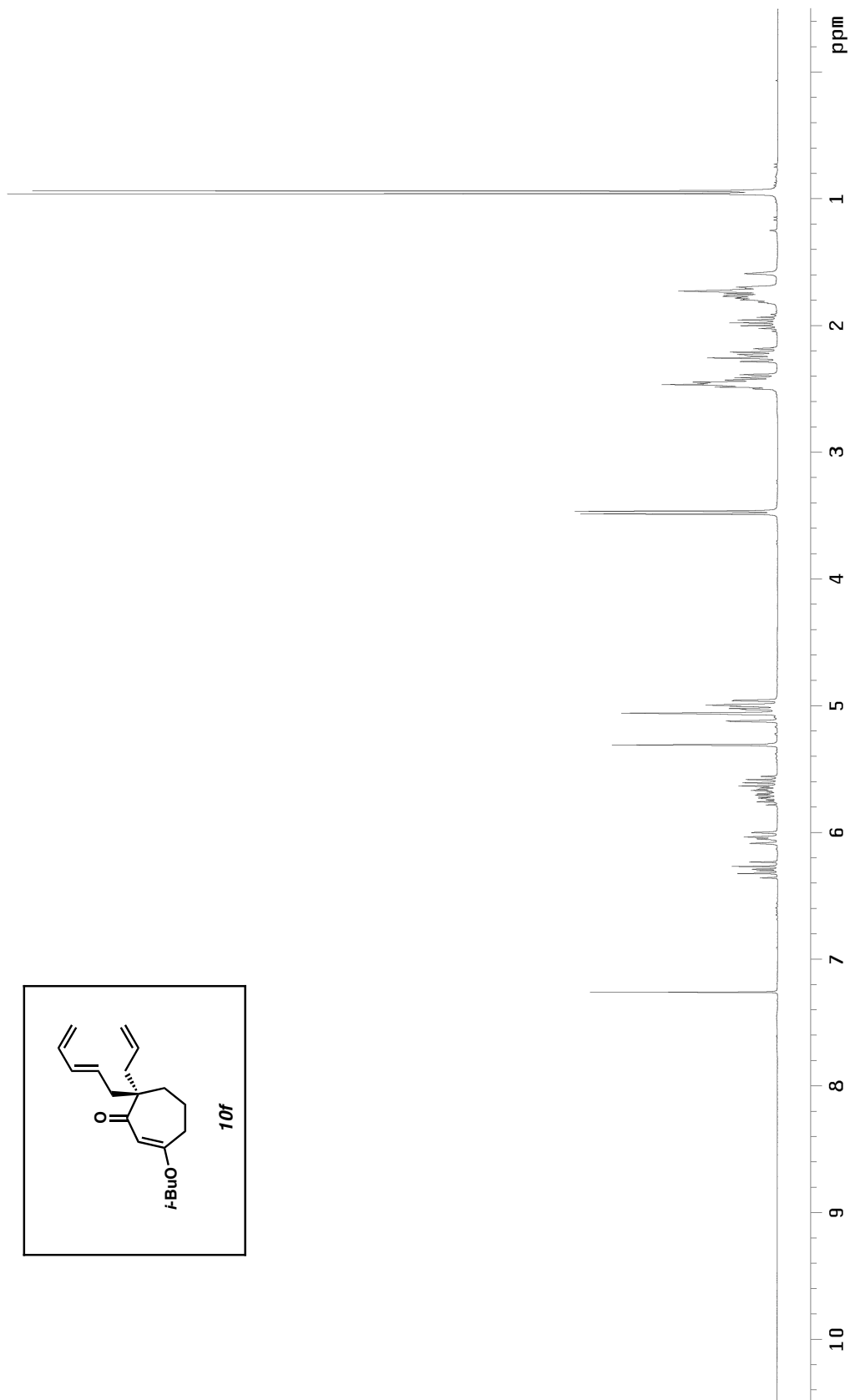


Figure SI-24A. ¹H NMR (300 MHz, CDCl₃) of compound **10f**.

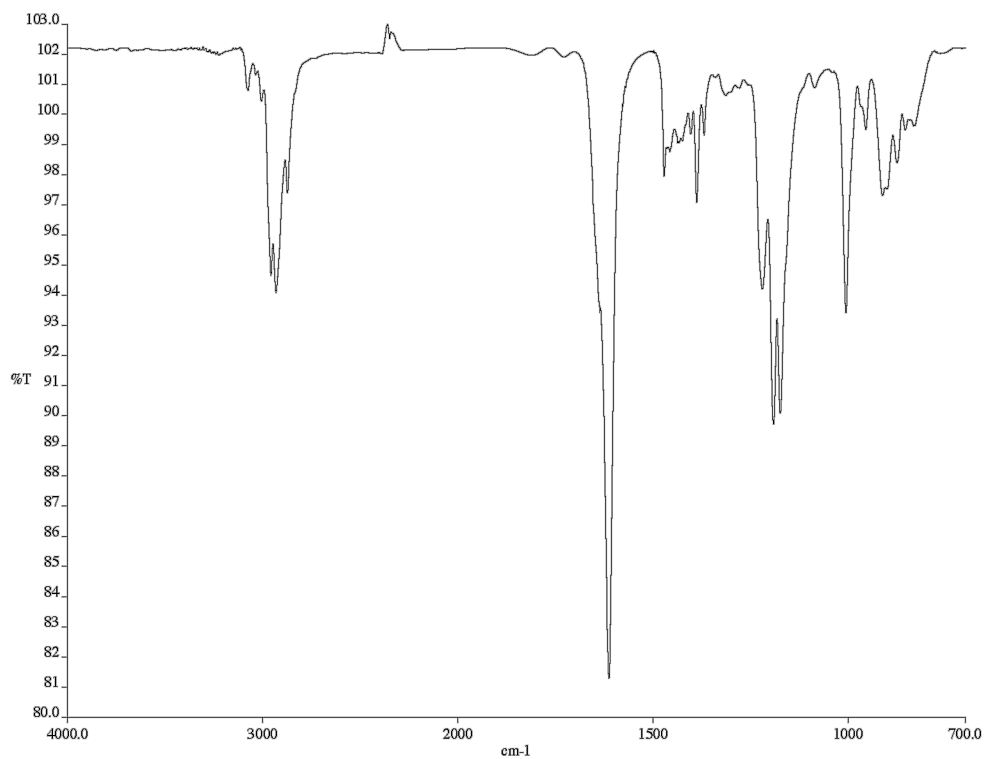


Figure SI-24B. Infrared spectrum (thin film/NaCl) of compound **10f**.

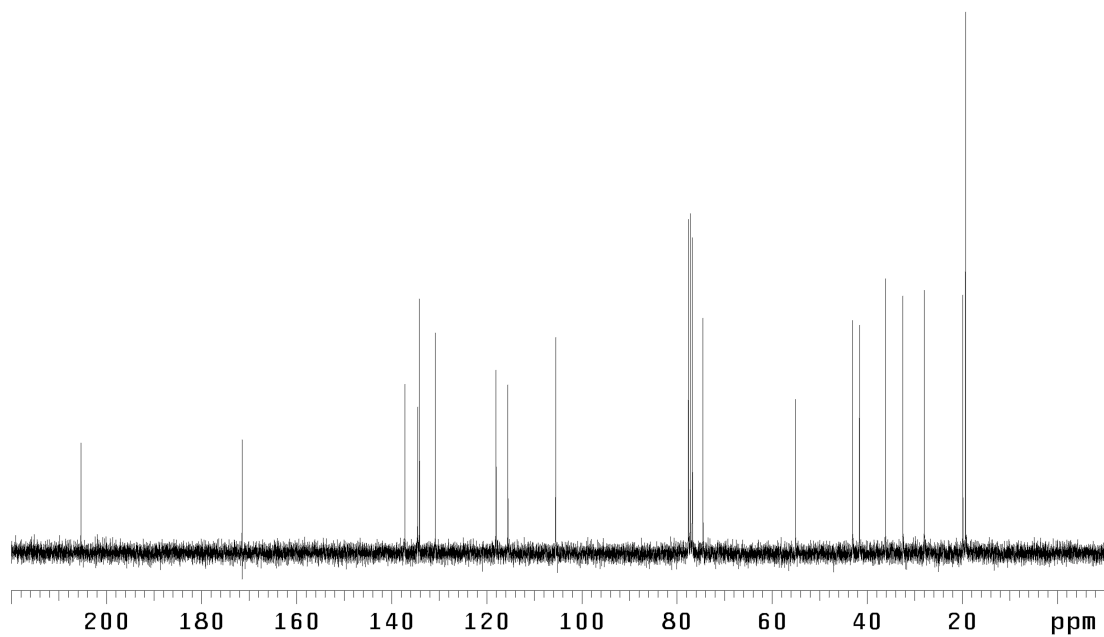


Figure SI-24C. ¹³C NMR (75 MHz, CDCl₃) of compound **10f**.

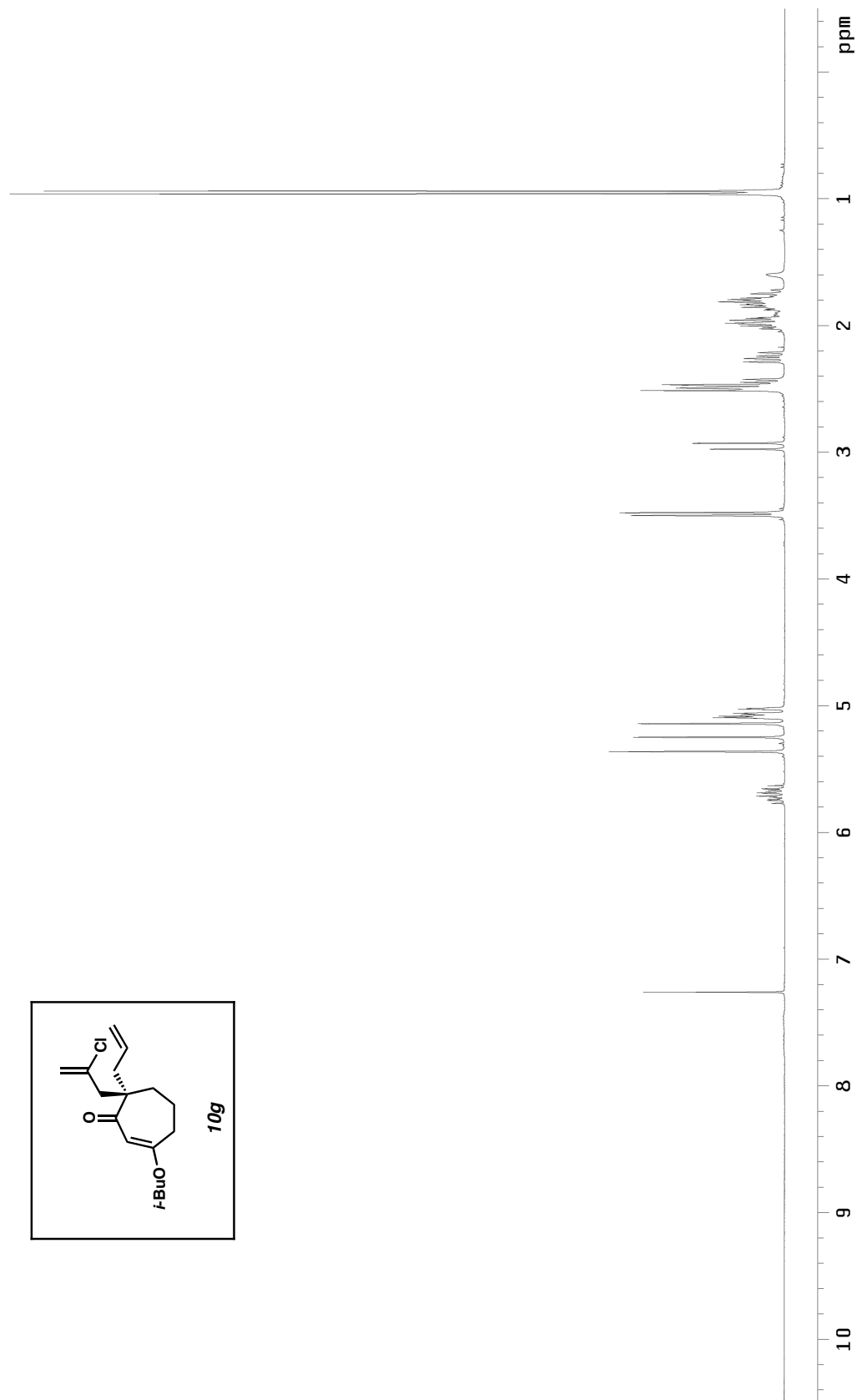


Figure SI-25A. ¹H NMR (300 MHz, CDCl₃) of compound **10g**.

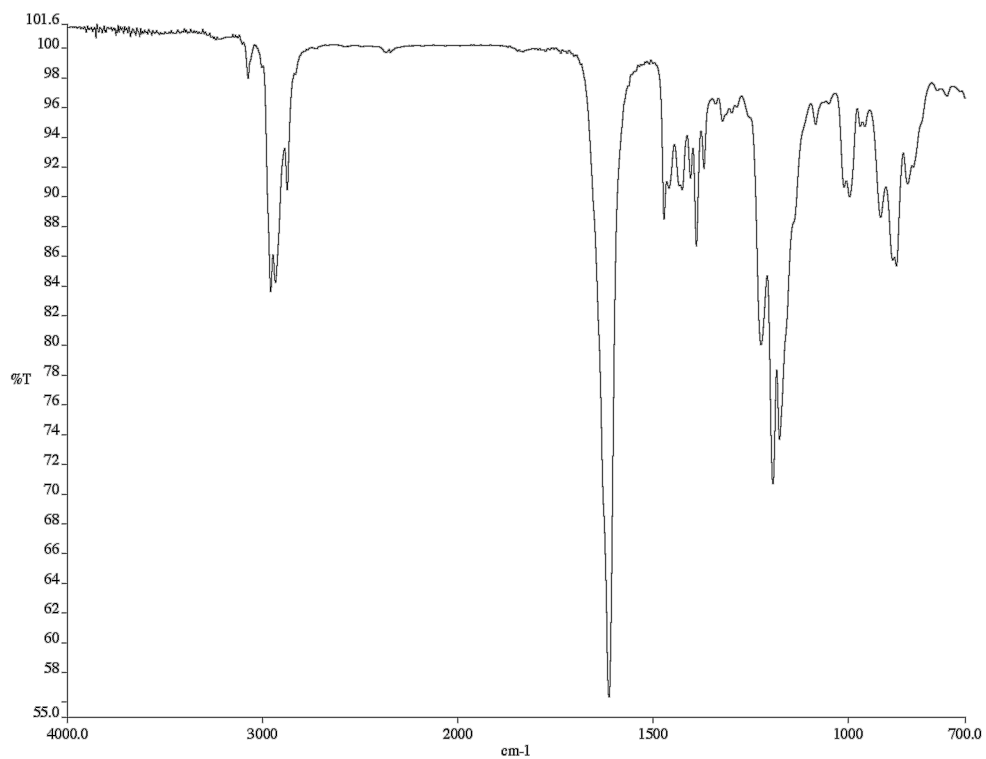


Figure SI-25B. Infrared spectrum (thin film/NaCl) of compound **10g**.

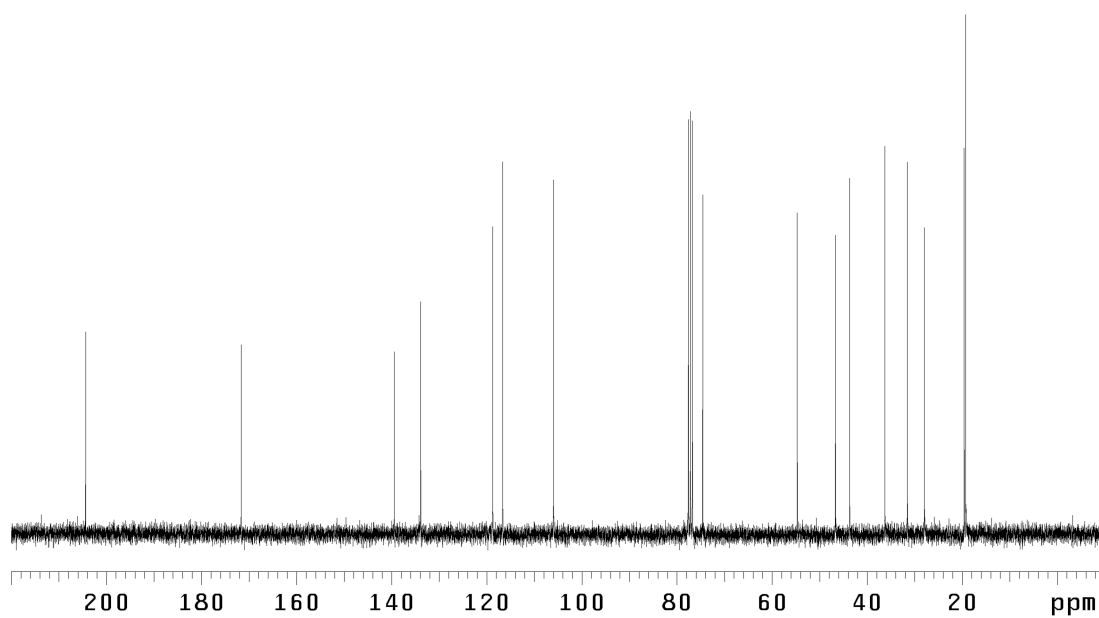


Figure SI-25C. ¹³C NMR (75 MHz, CDCl₃) of compound **10g**.

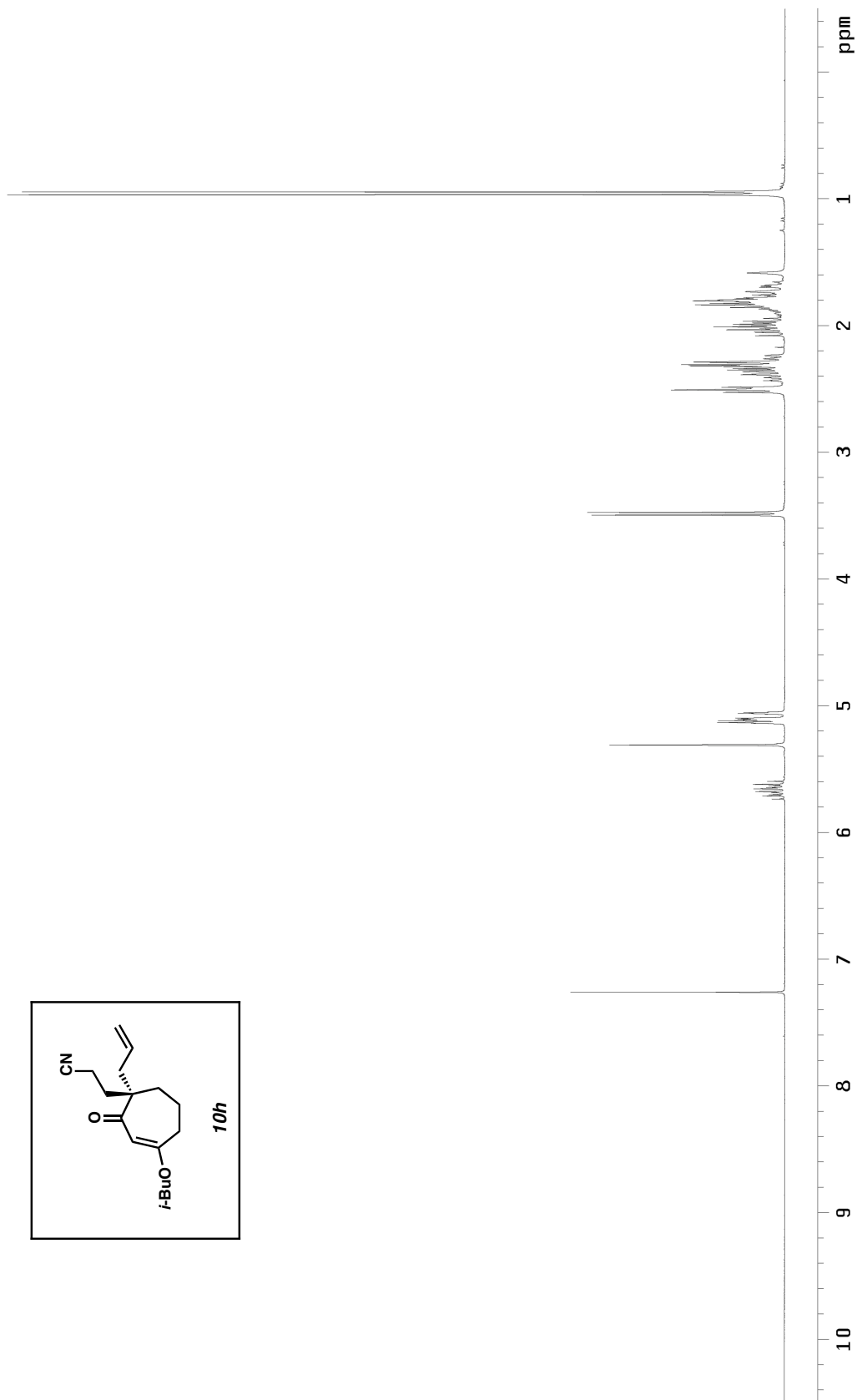


Figure SI-26A. $^1\text{H NMR}$ (300 MHz, CDCl_3) of compound **10h**.

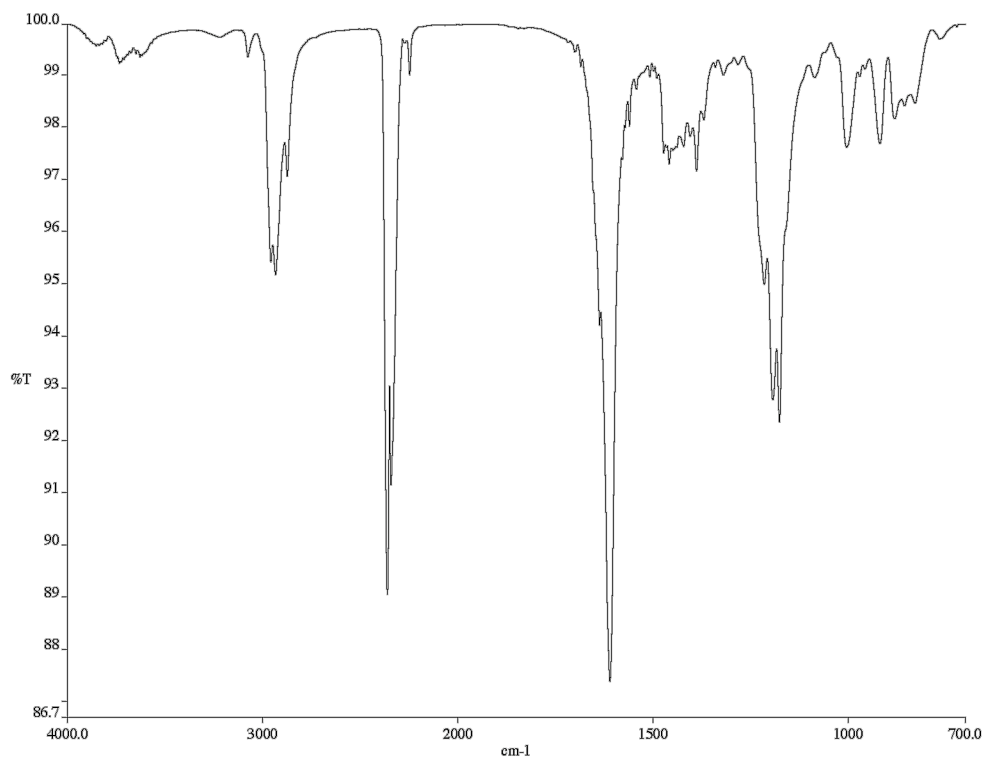


Figure SI-26B. Infrared spectrum (thin film/NaCl) of compound **10h**.

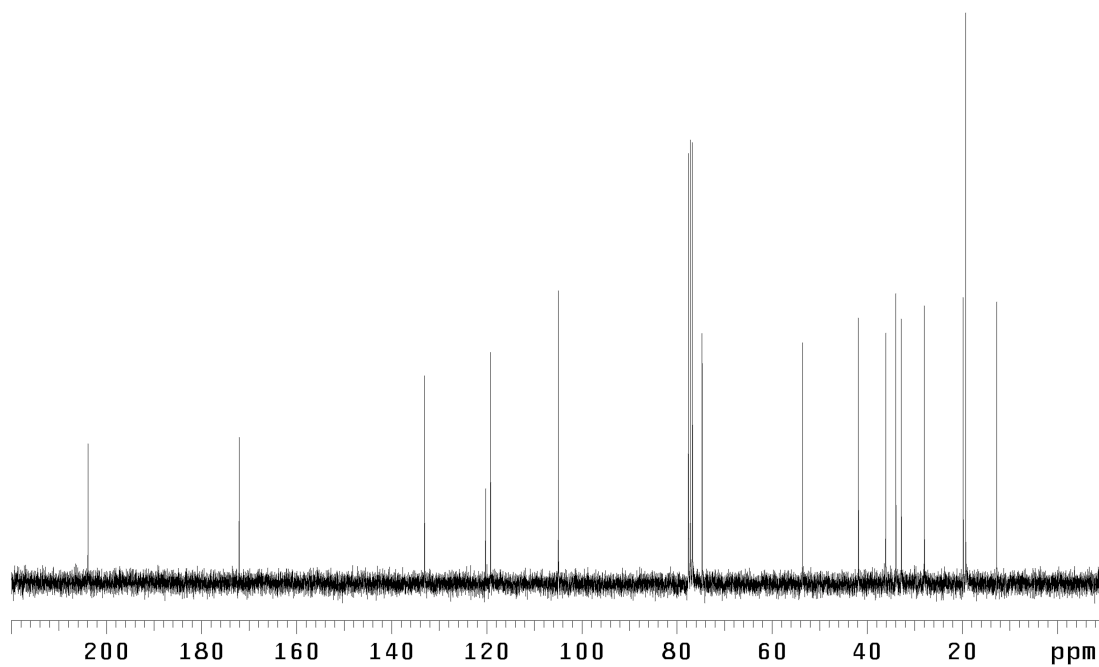


Figure SI-26C. ¹³C NMR (75 MHz, CDCl₃) of compound **10h**.

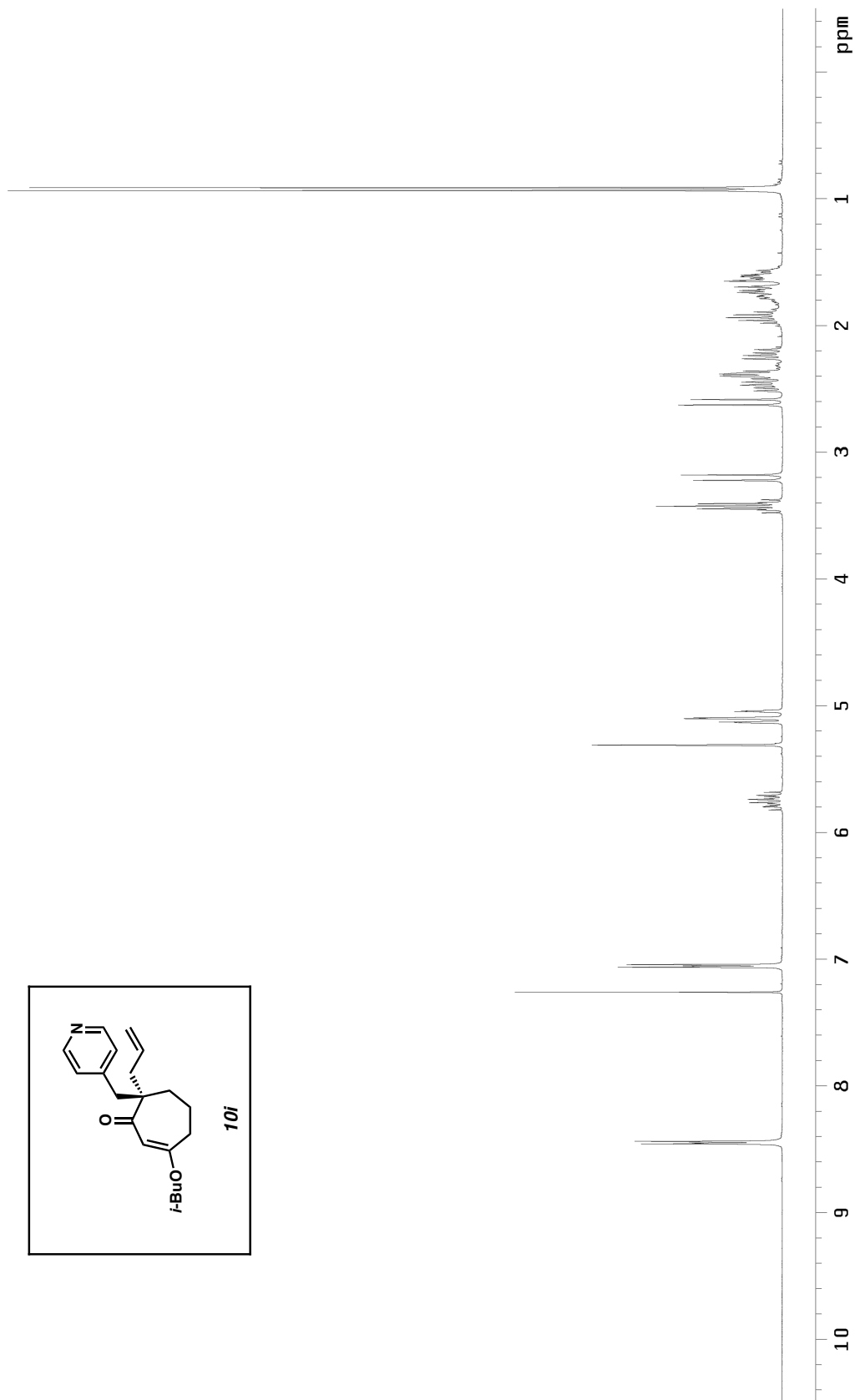


Figure SI-27A. ¹H NMR (300 MHz, CDCl₃) of compound **10i**.

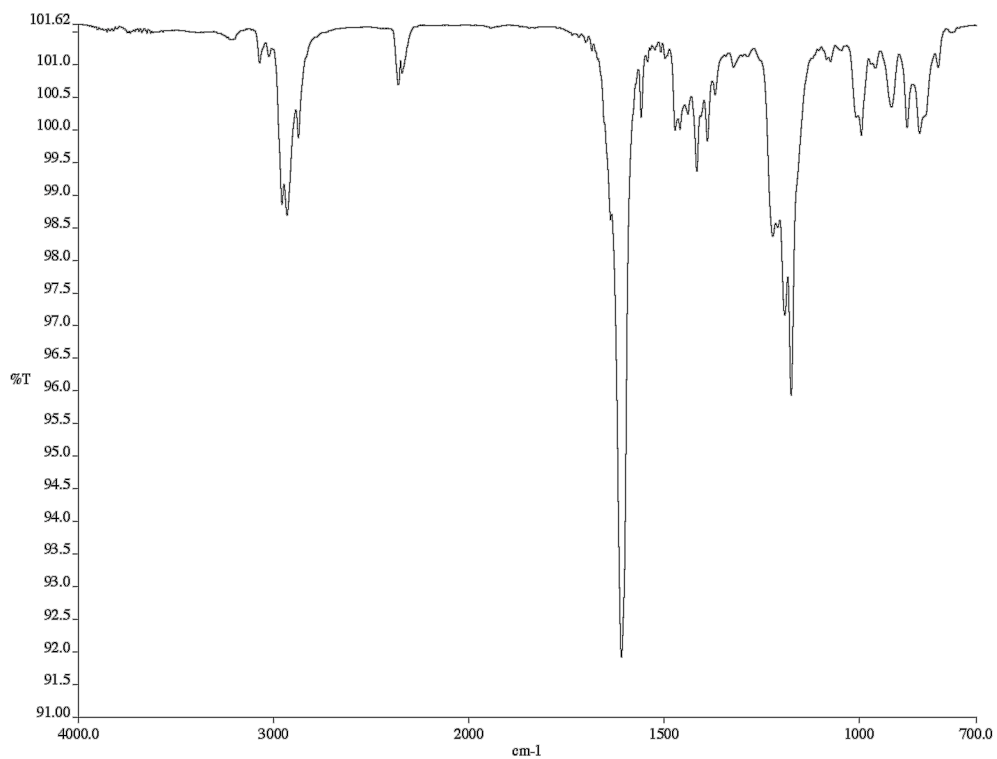


Figure SI-27B. Infrared spectrum (thin film/NaCl) of compound **10i**.

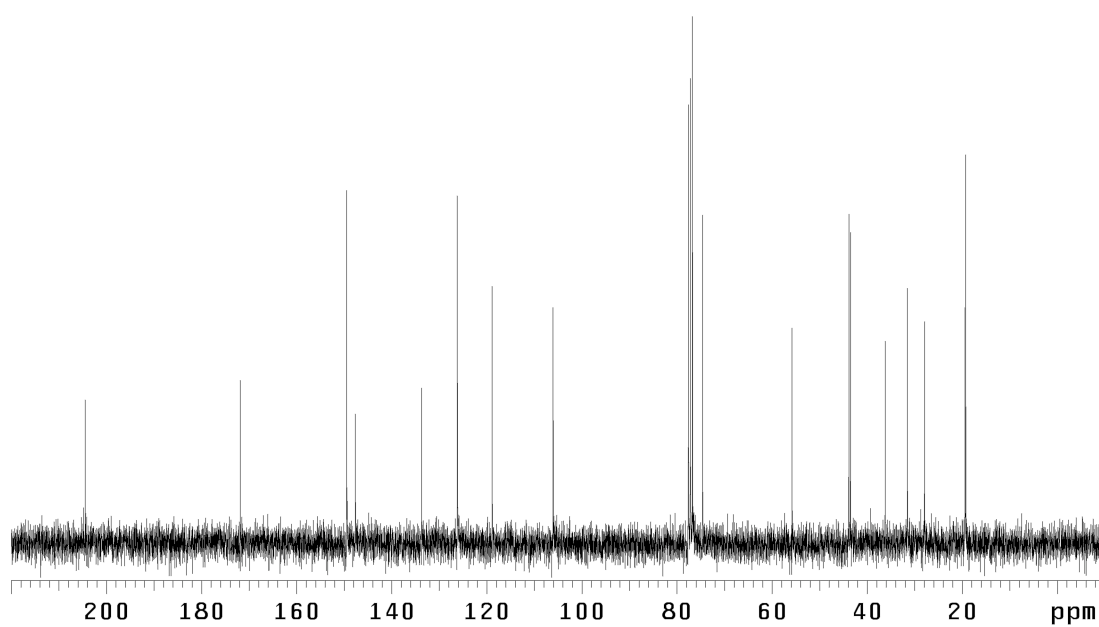


Figure SI-27C. ¹³C NMR (75 MHz, CDCl₃) of compound **10i**.

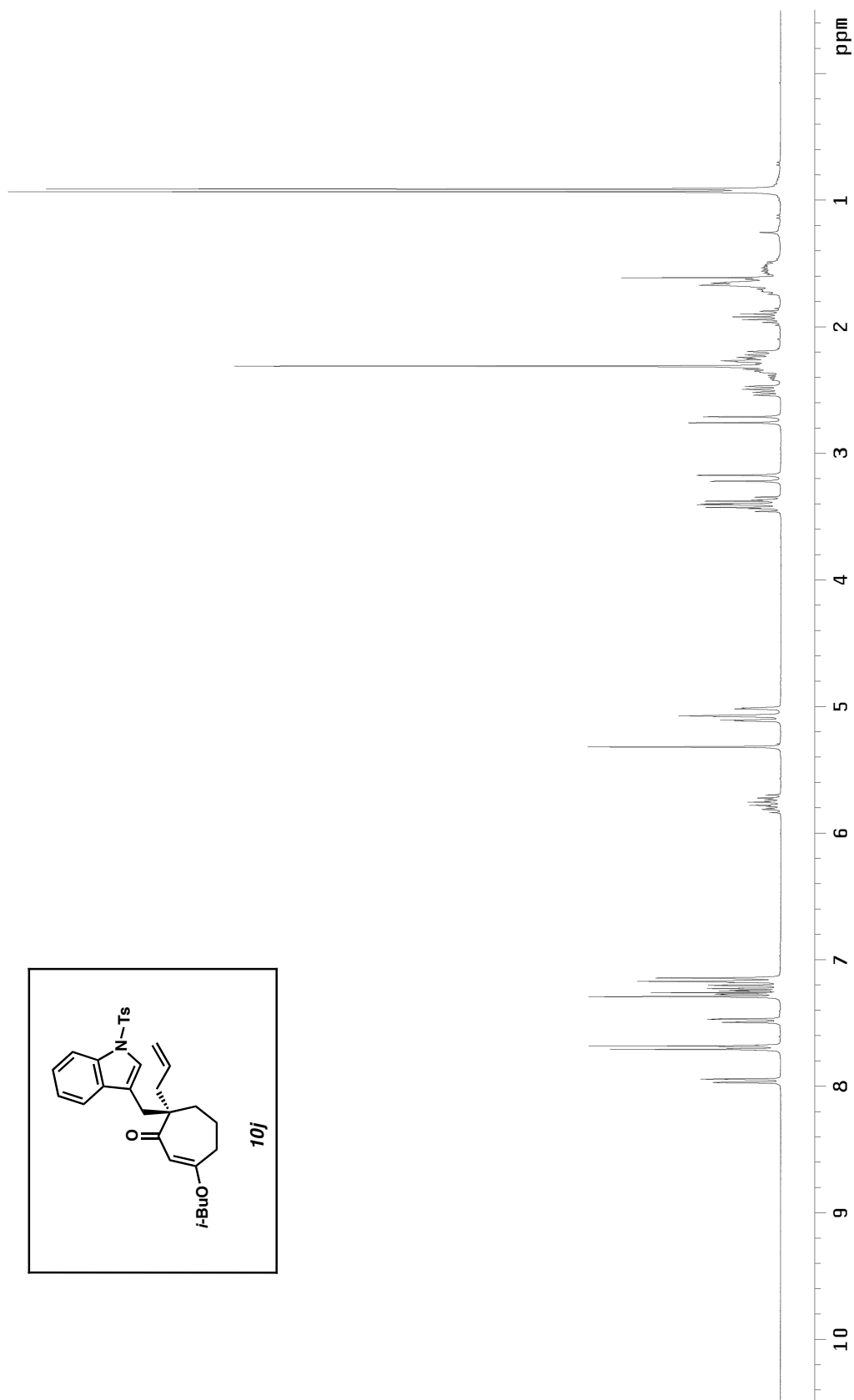


Figure SI-28A. ¹H NMR (300 MHz, CDCl₃) of compound **10j**.

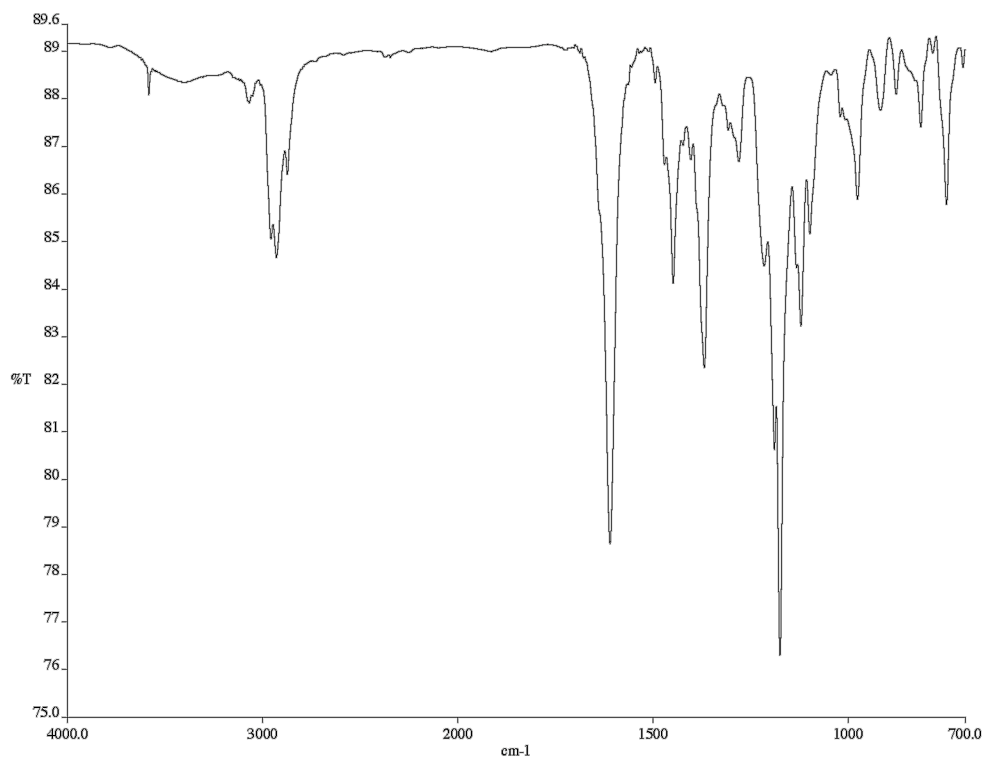


Figure SI-28B. Infrared spectrum (thin film/NaCl) of compound **10j**.

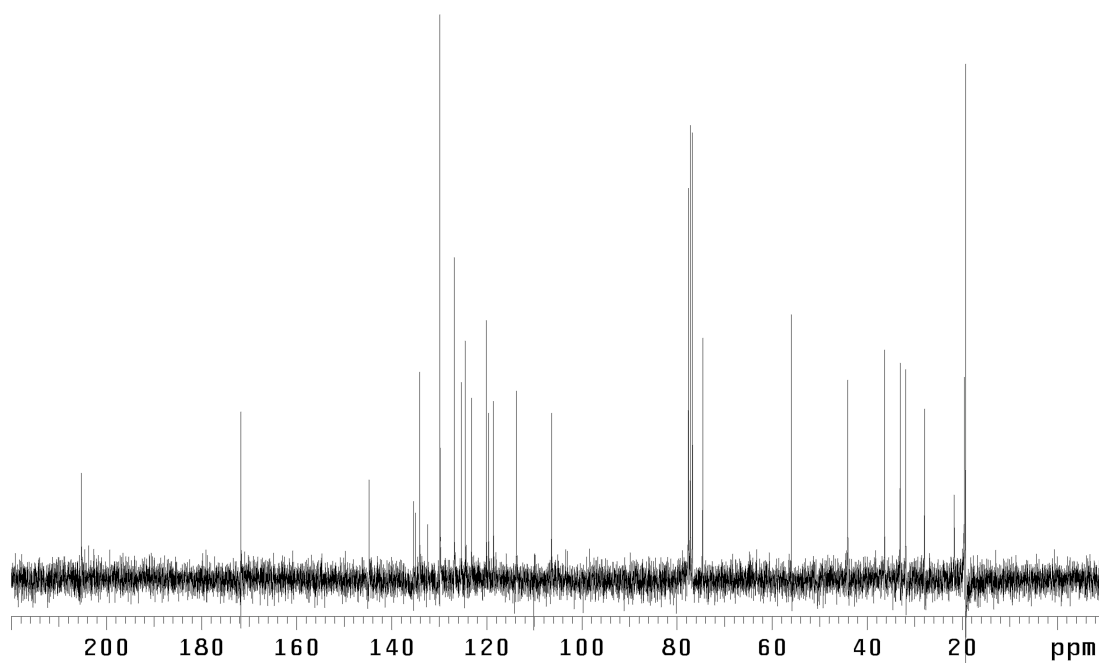


Figure SI-28C. ¹³C NMR (75 MHz, CDCl₃) of compound **10j**.

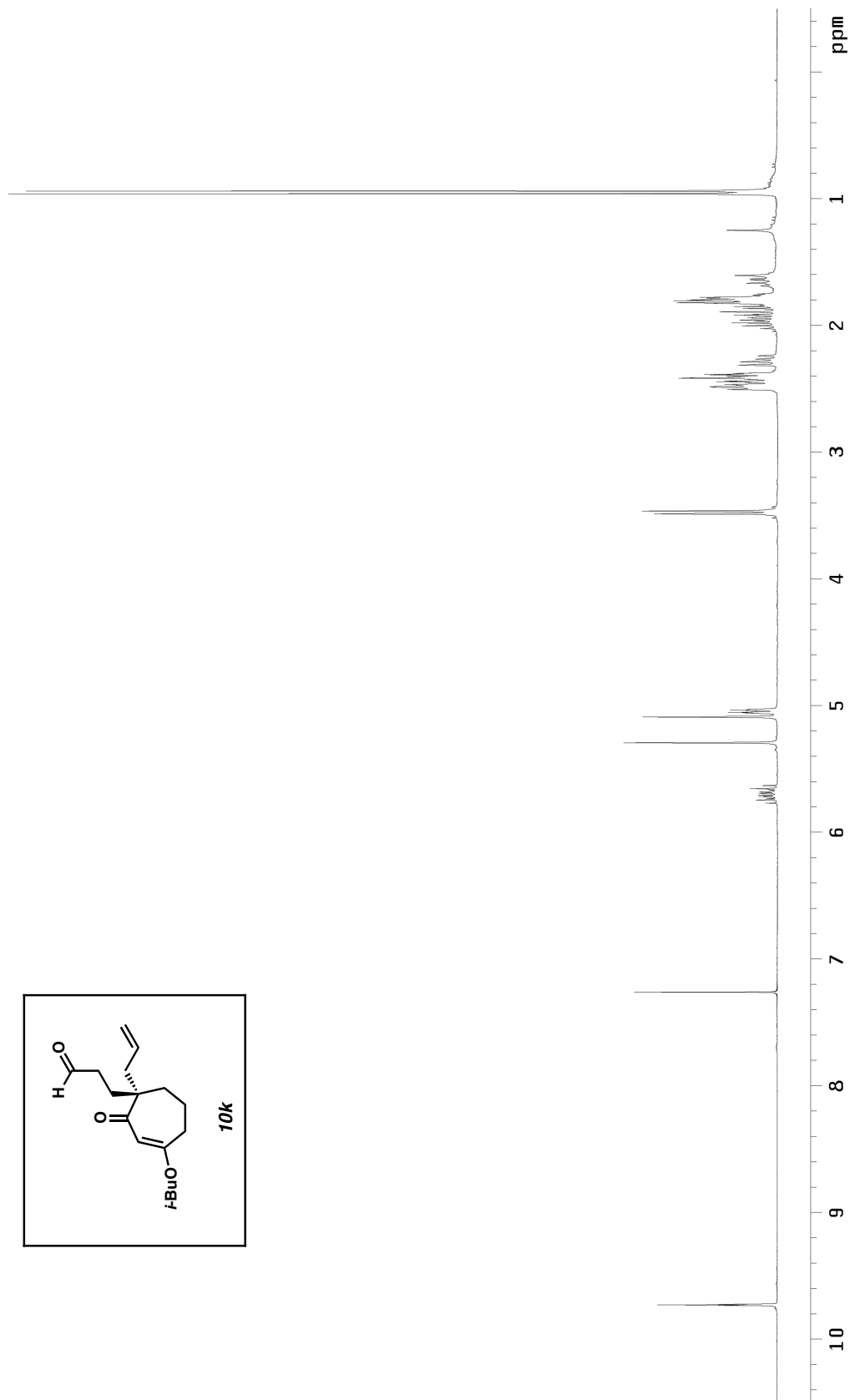


Figure SI-294. ¹H NMR (300 MHz, CDCl₃) of compound **10k**.

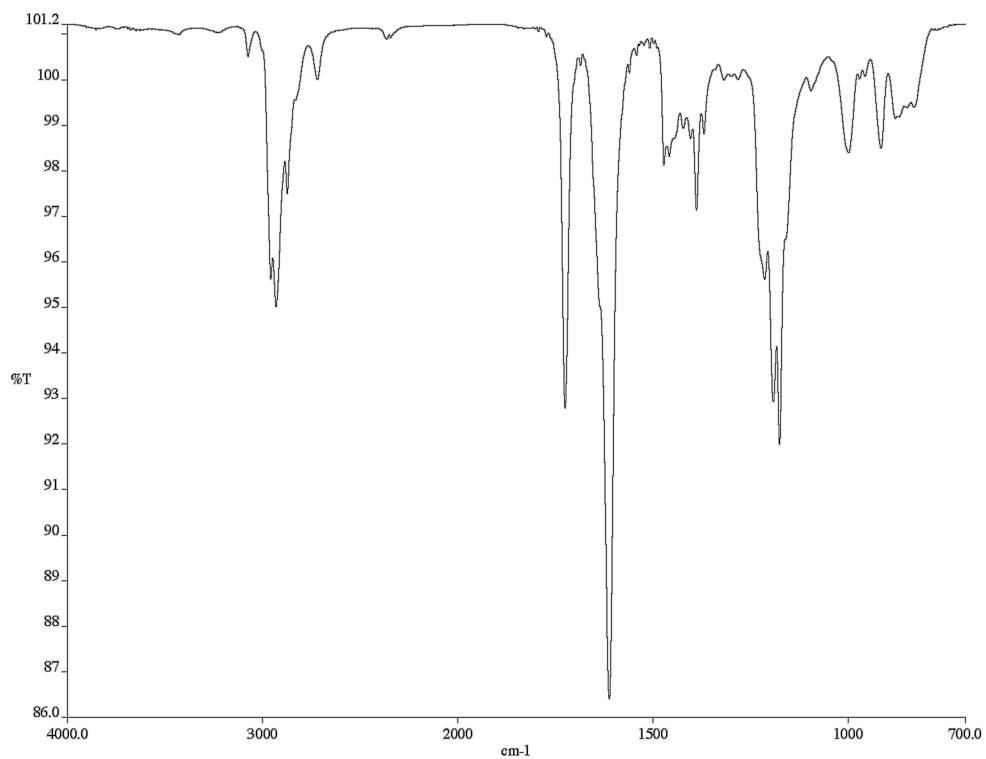


Figure SI-29B. Infrared spectrum (thin film/NaCl) of compound **10k**.

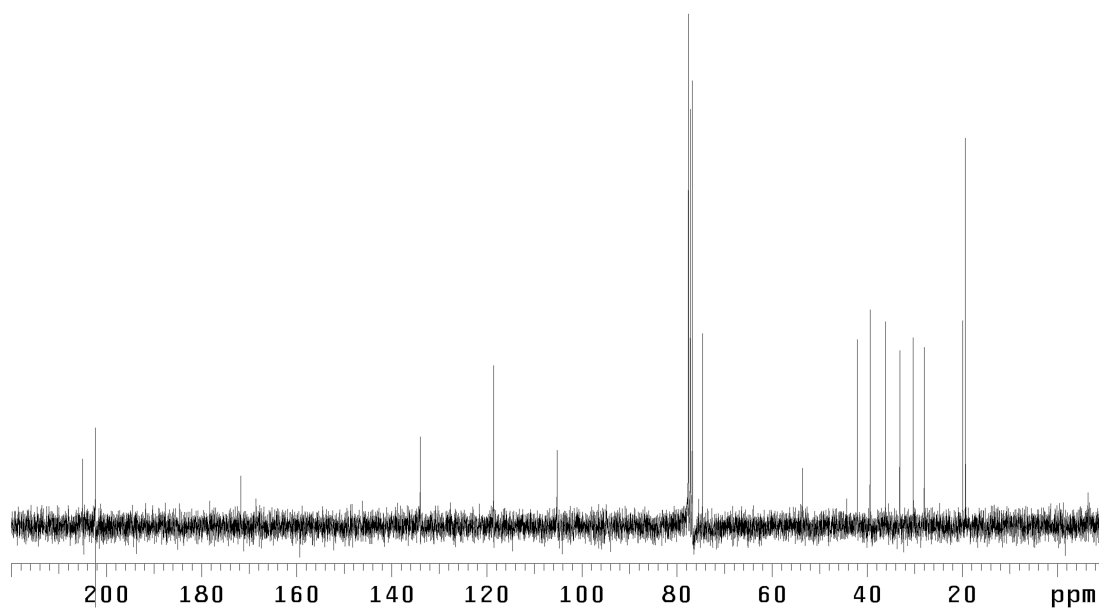


Figure SI-29C. ¹³C NMR (75 MHz, CDCl₃) of compound **10k**.

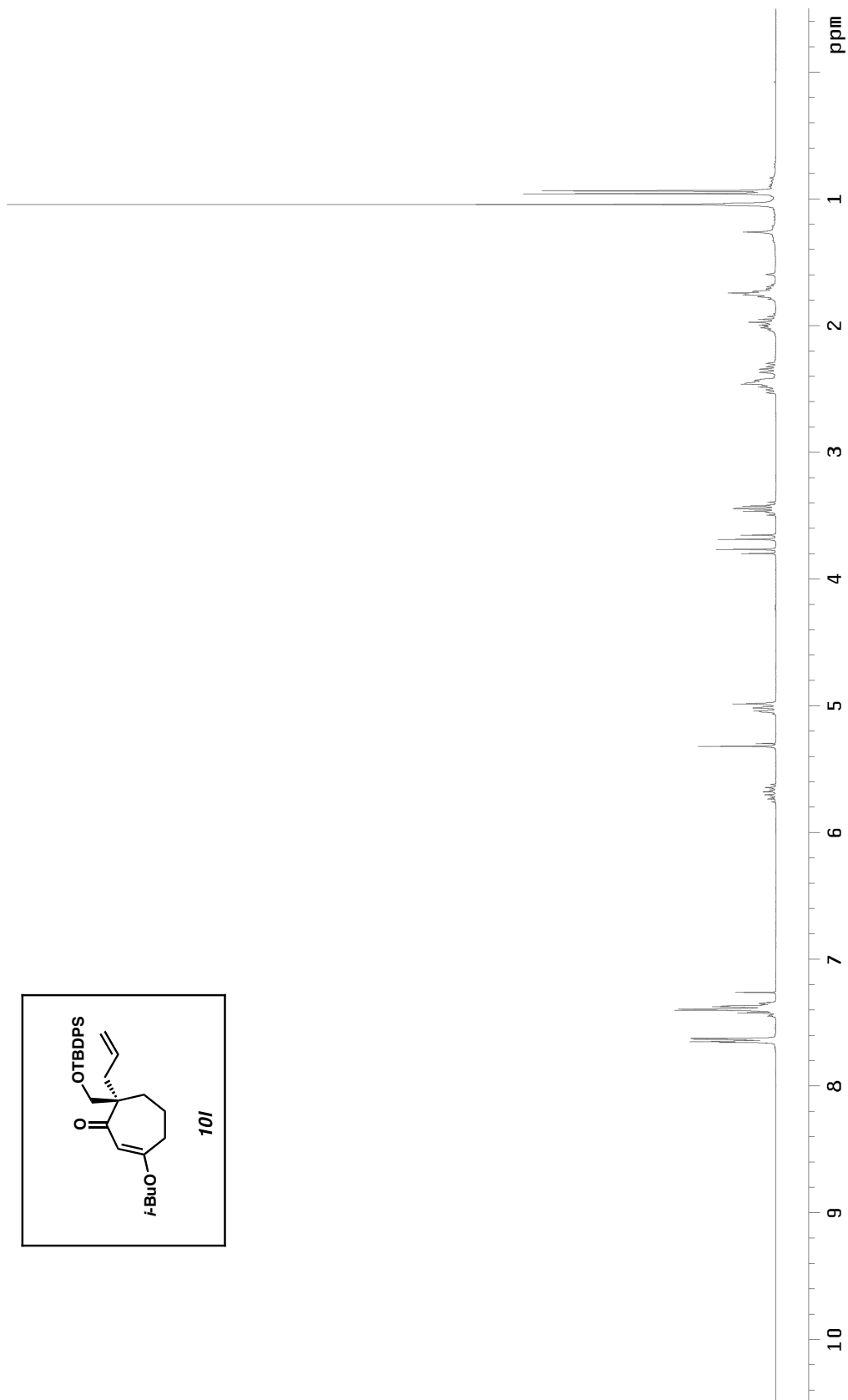


Figure SI-30A. ¹H NMR (300 MHz, CDCl₃) of compound **101**.

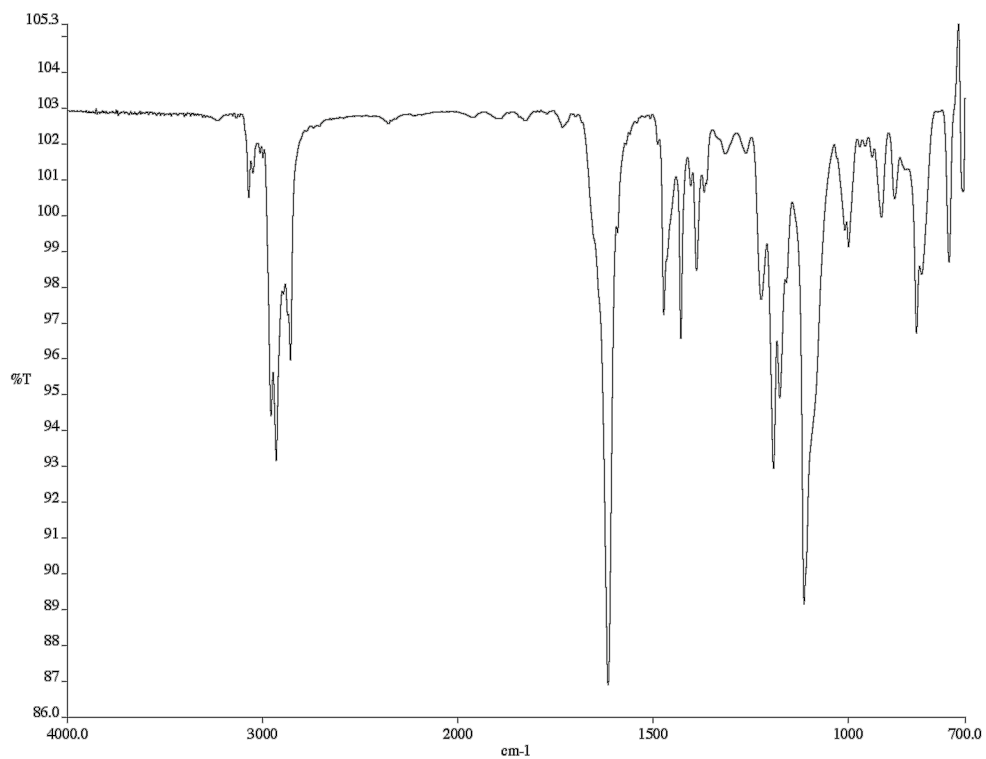


Figure SI-30B. Infrared spectrum (thin film/NaCl) of compound **101**.

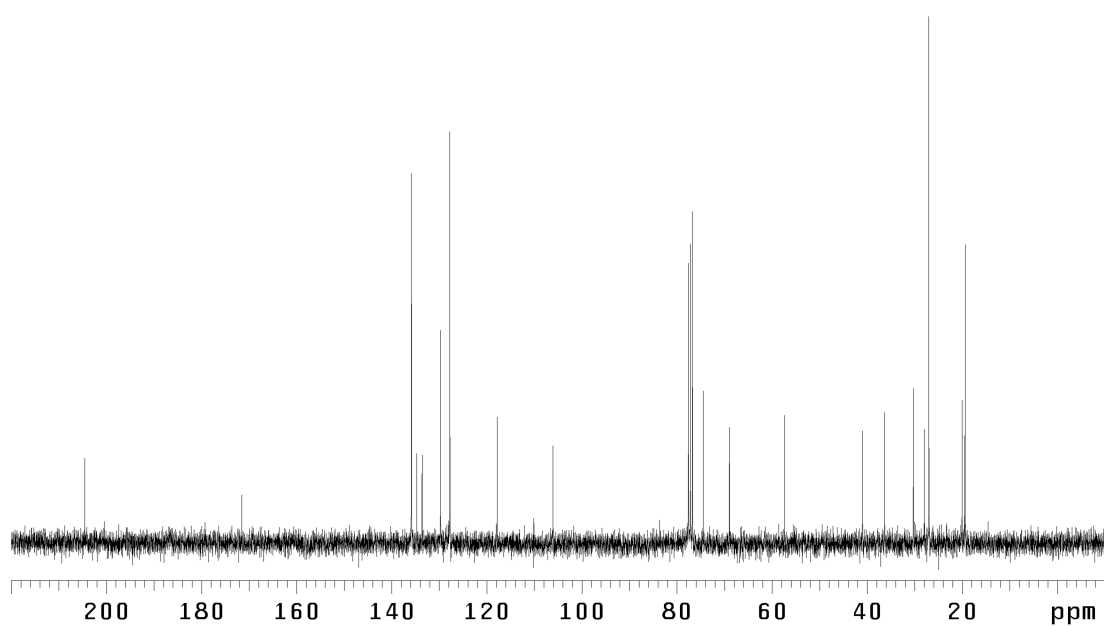


Figure SI-30C. ¹³C NMR (75 MHz, CDCl₃) of compound **101**.

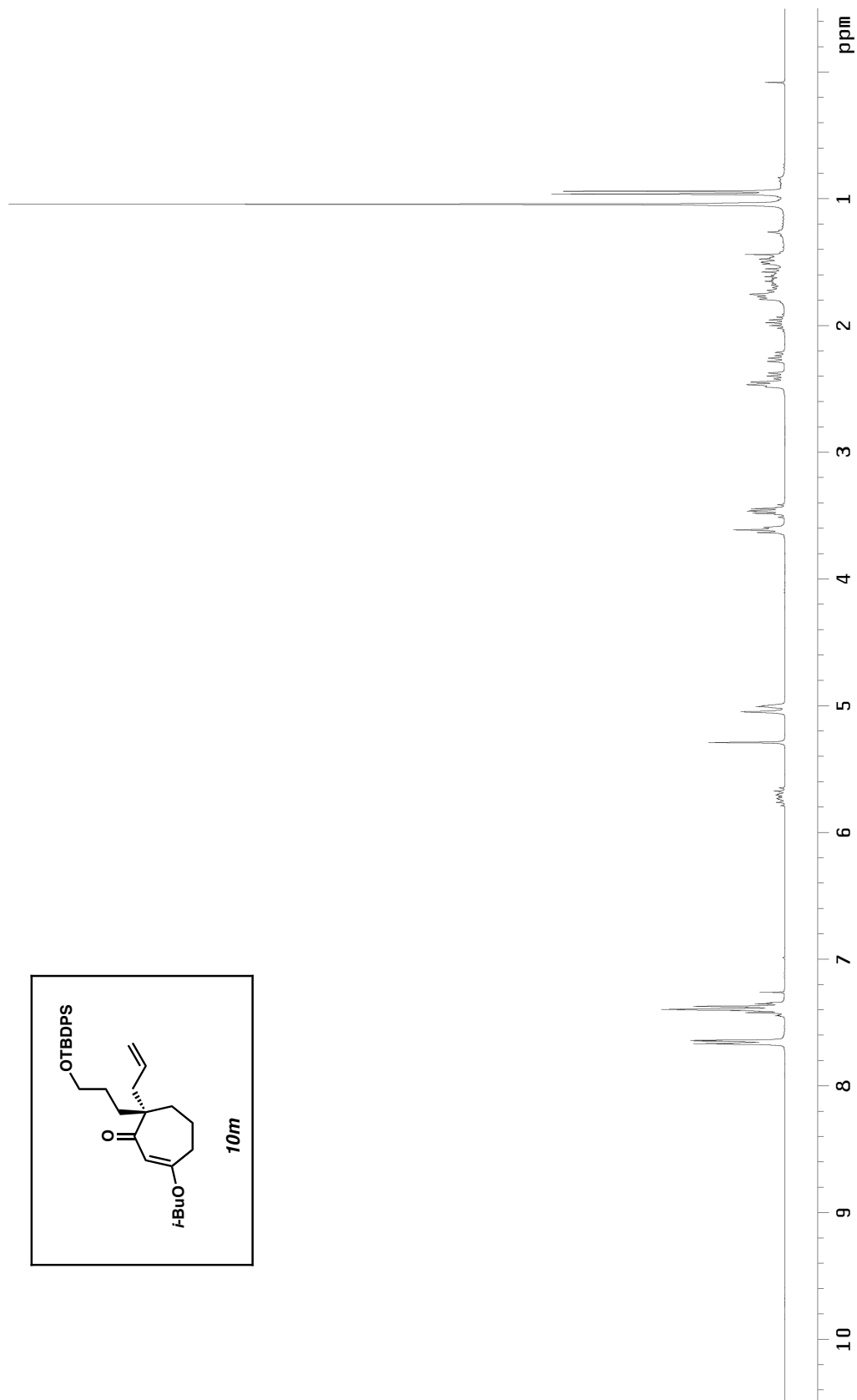


Figure SI-31A. $^1\text{H NMR}$ (300 MHz, CDCl_3) of compound **10m**.

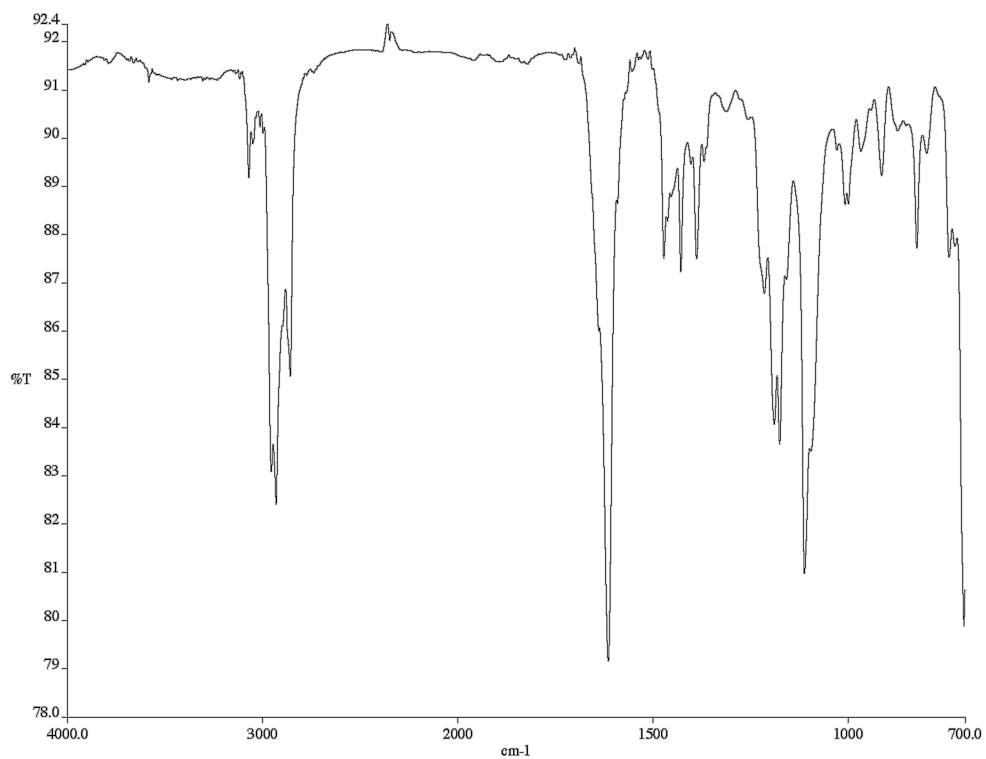


Figure SI-31B. Infrared spectrum (thin film/NaCl) of compound **10m**.

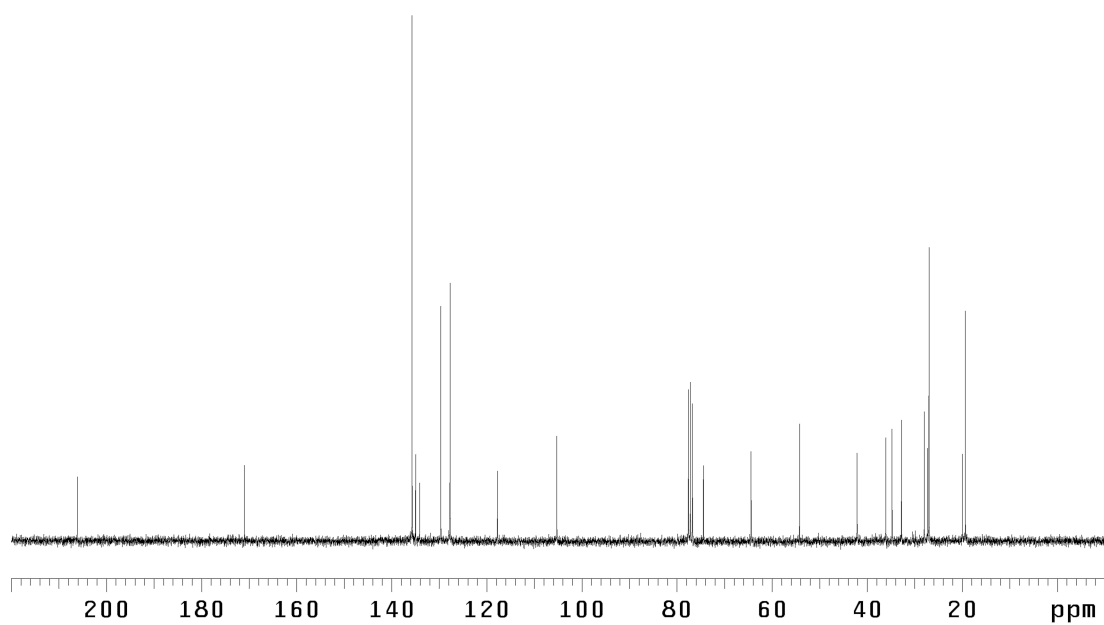


Figure SI-31C. ^{13}C NMR (75 MHz, CDCl_3) of compound **10m**.

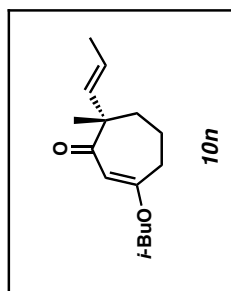
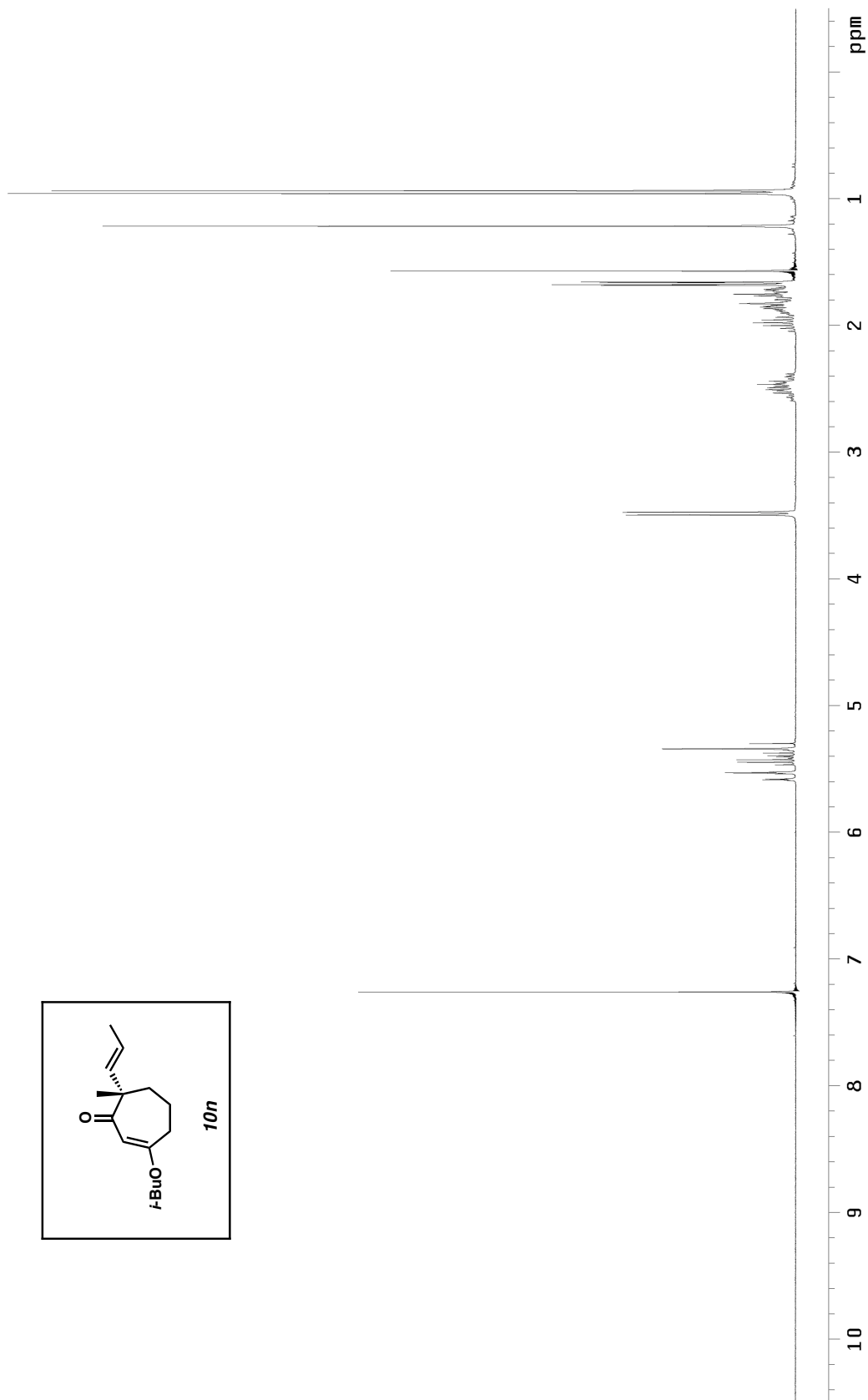


Figure SI-32A. ¹H NMR (300 MHz, CDCl₃) of compound **10n**.

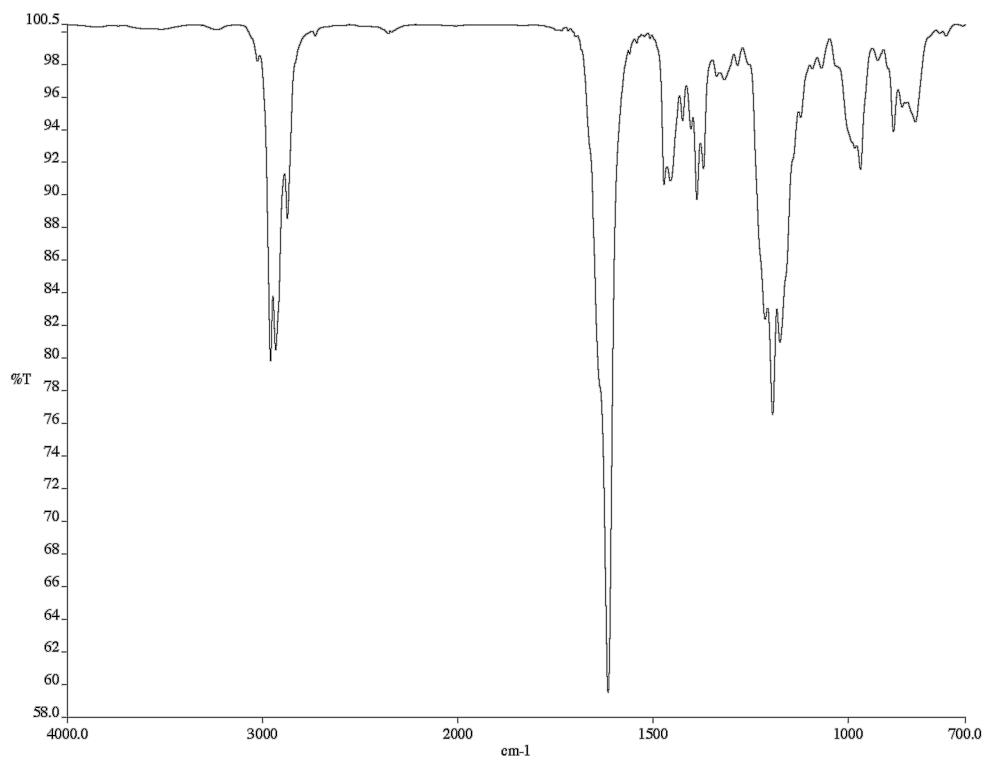


Figure SI-32B. Infrared spectrum (thin film/NaCl) of compound **10n**.

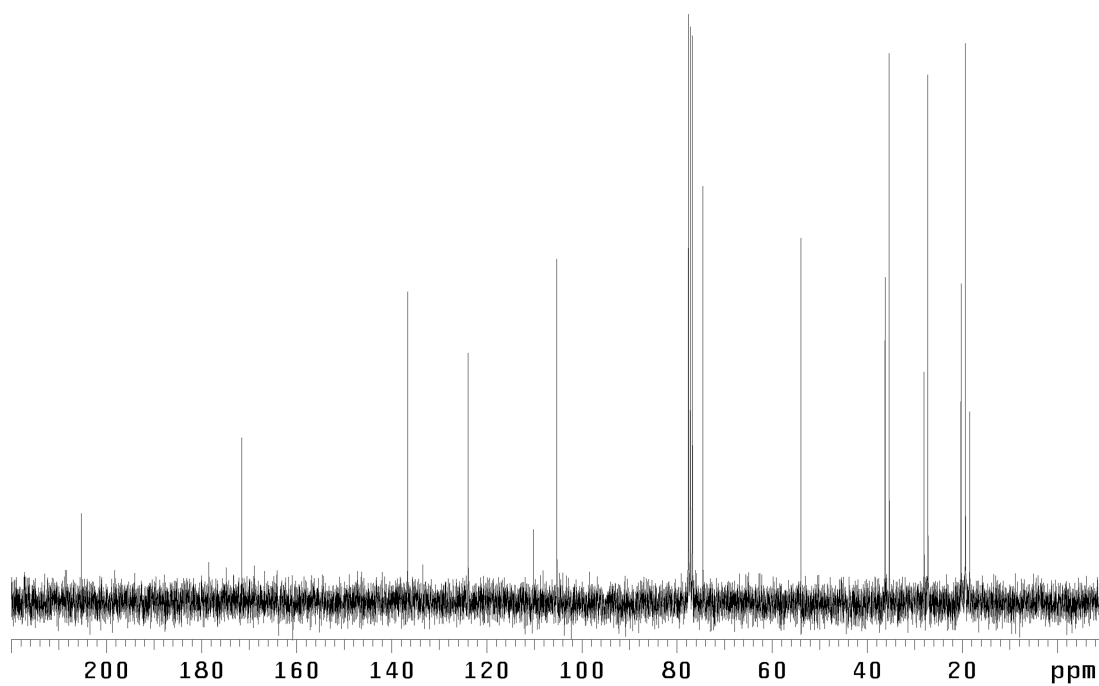


Figure SI-32C. ¹³C NMR (75 MHz, CDCl₃) of compound **10n**.

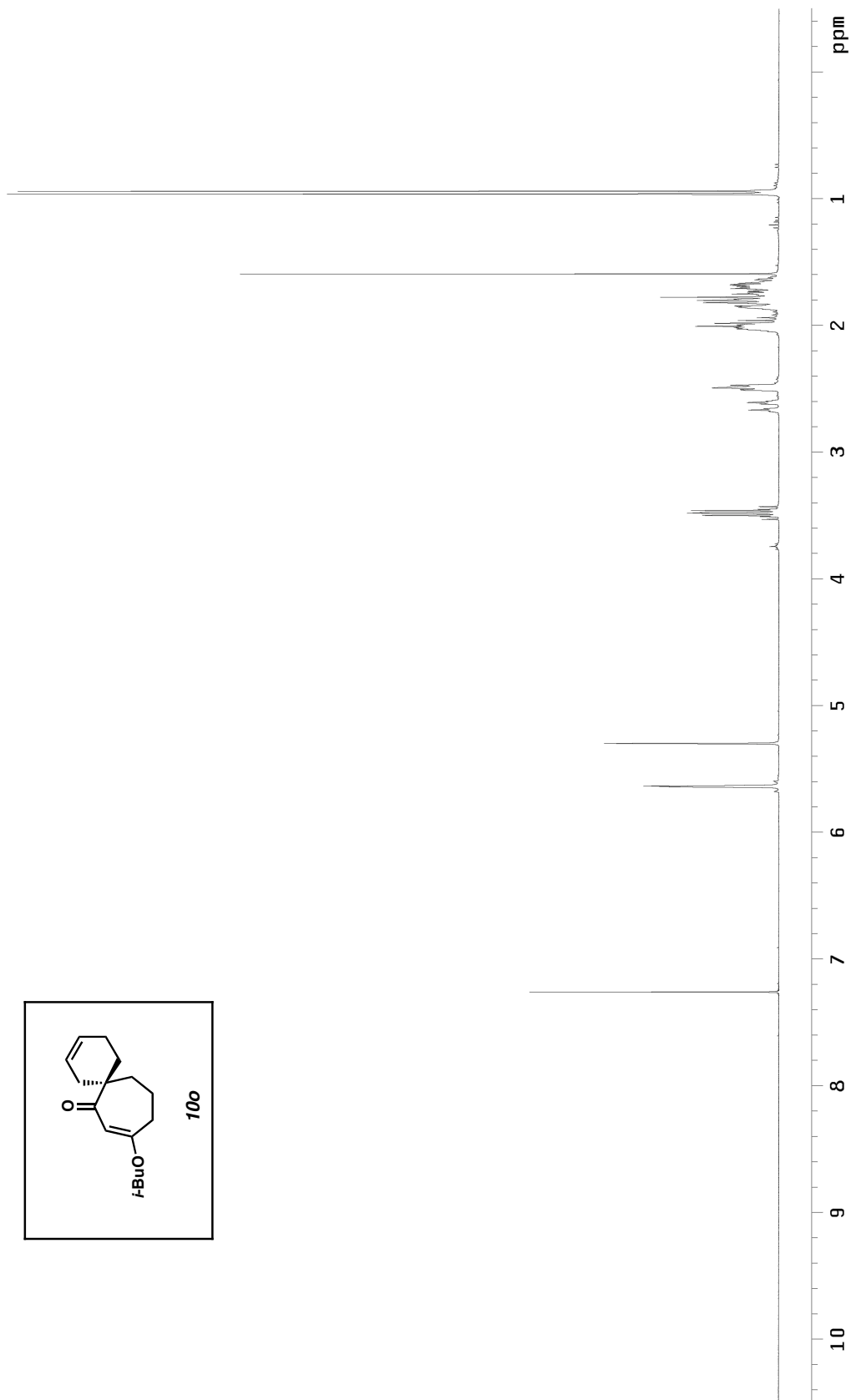


Figure SI-33A. ¹H NMR (300 MHz, CDCl₃) of compound **10o**.

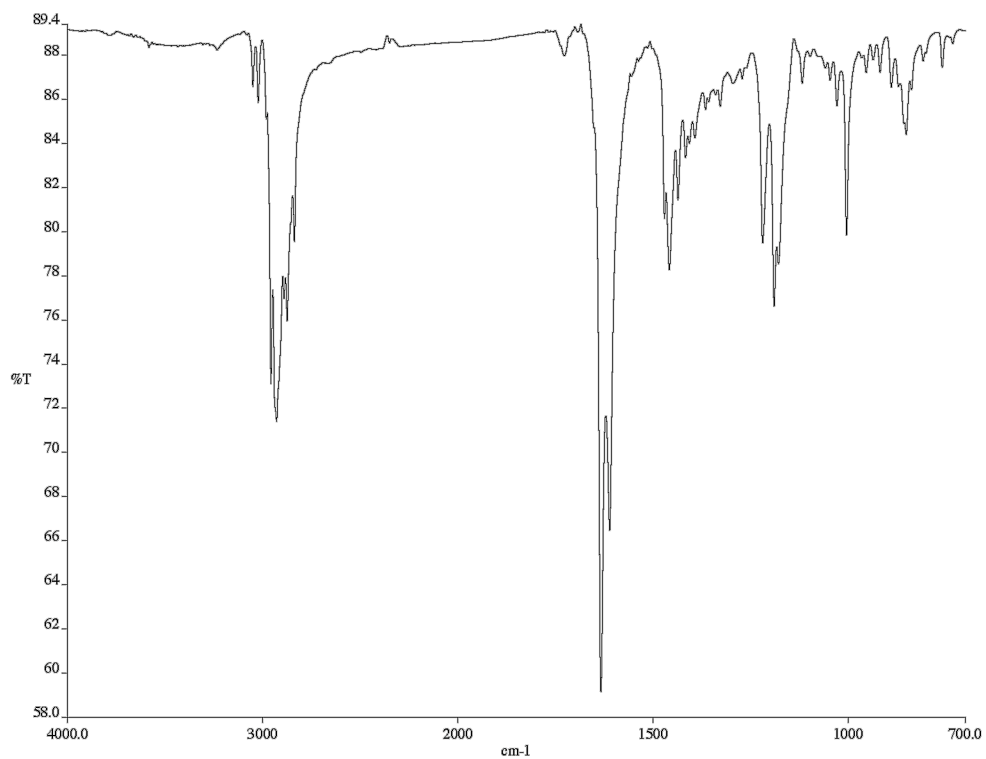


Figure SI-33B. Infrared spectrum (thin film/NaCl) of compound **10o**.

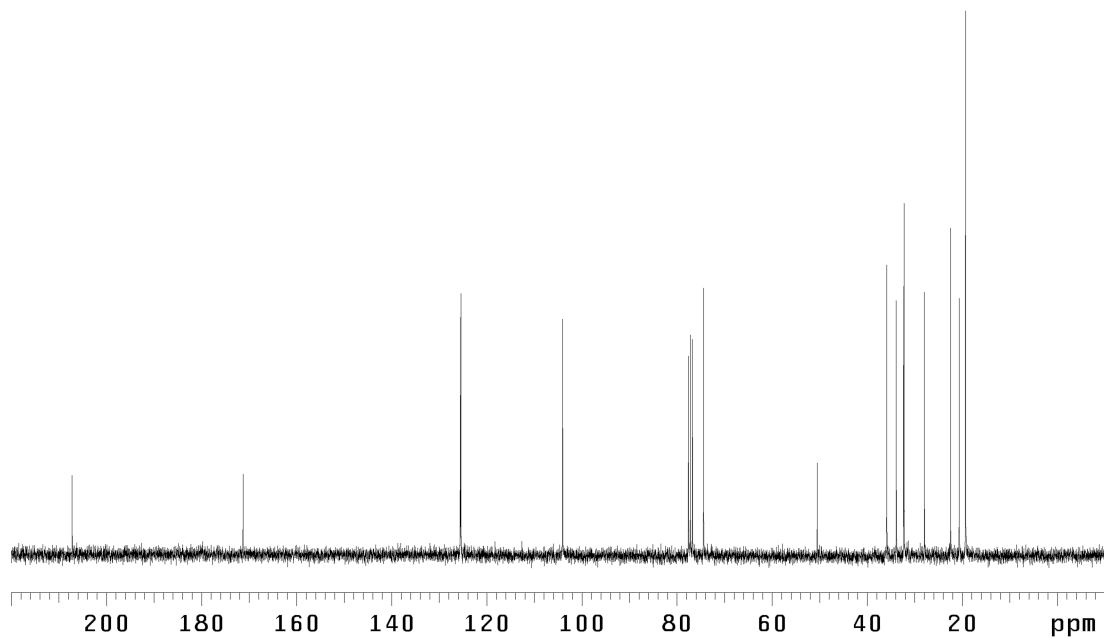


Figure SI-33C. ¹³C NMR (75 MHz, CDCl₃) of compound **10o**.

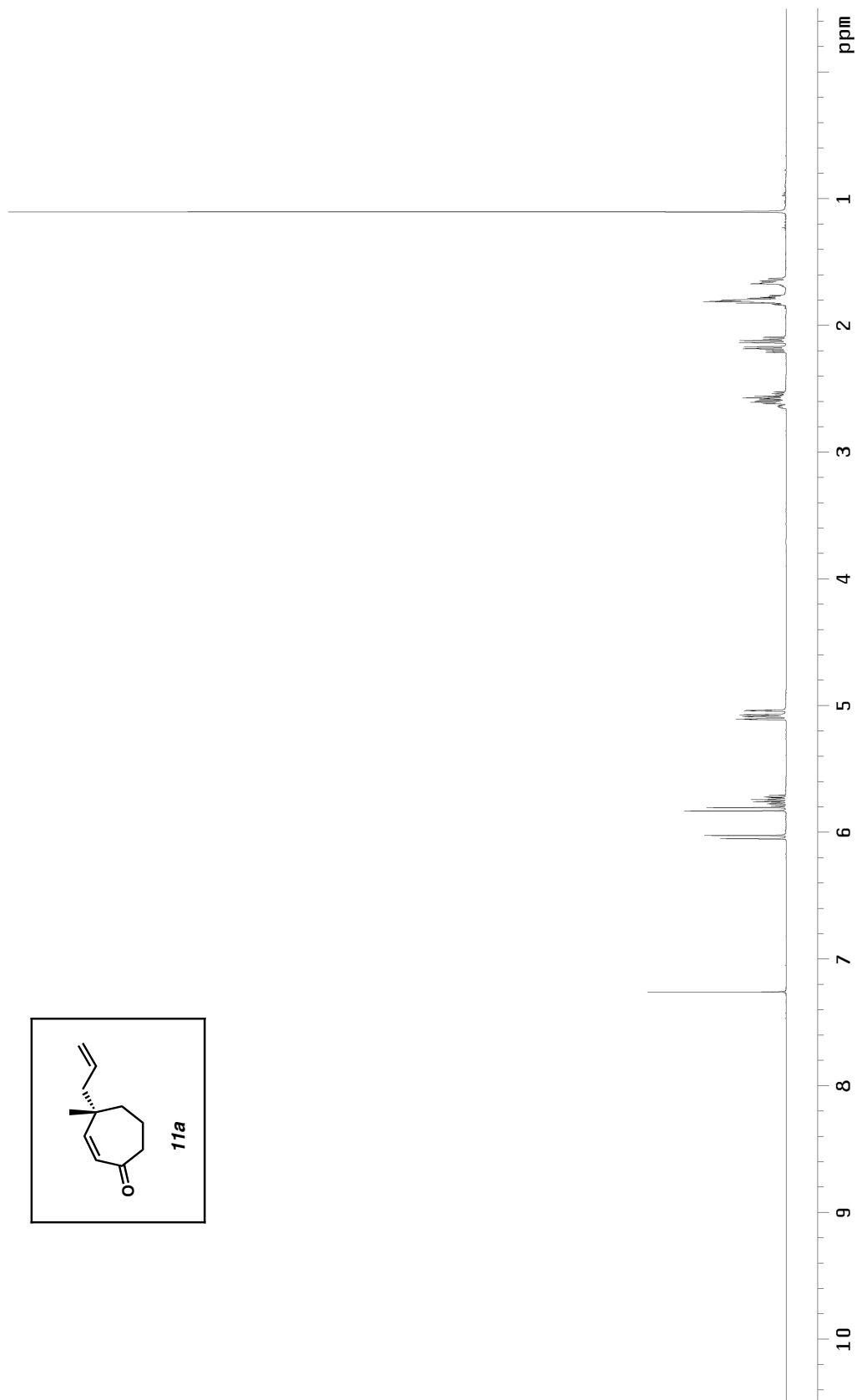


Figure SI-34A. ^1H NMR (500 MHz, CDCl_3) of compound **11a**.

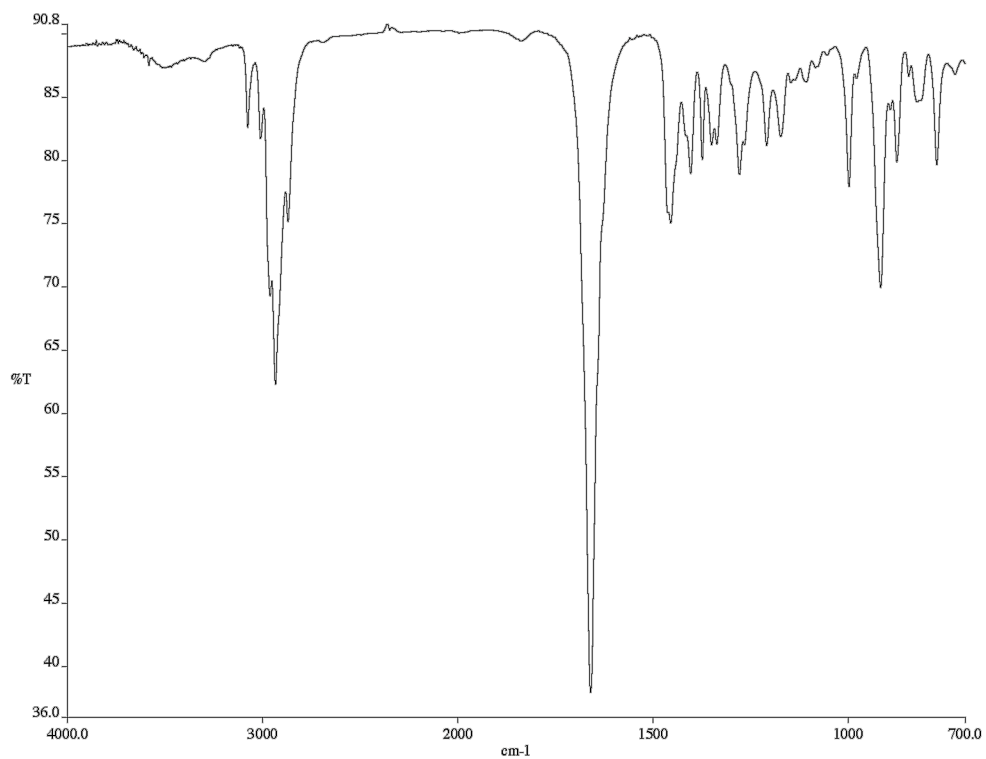


Figure SI-34B. Infrared spectrum (thin film/NaCl) of compound **11a**.

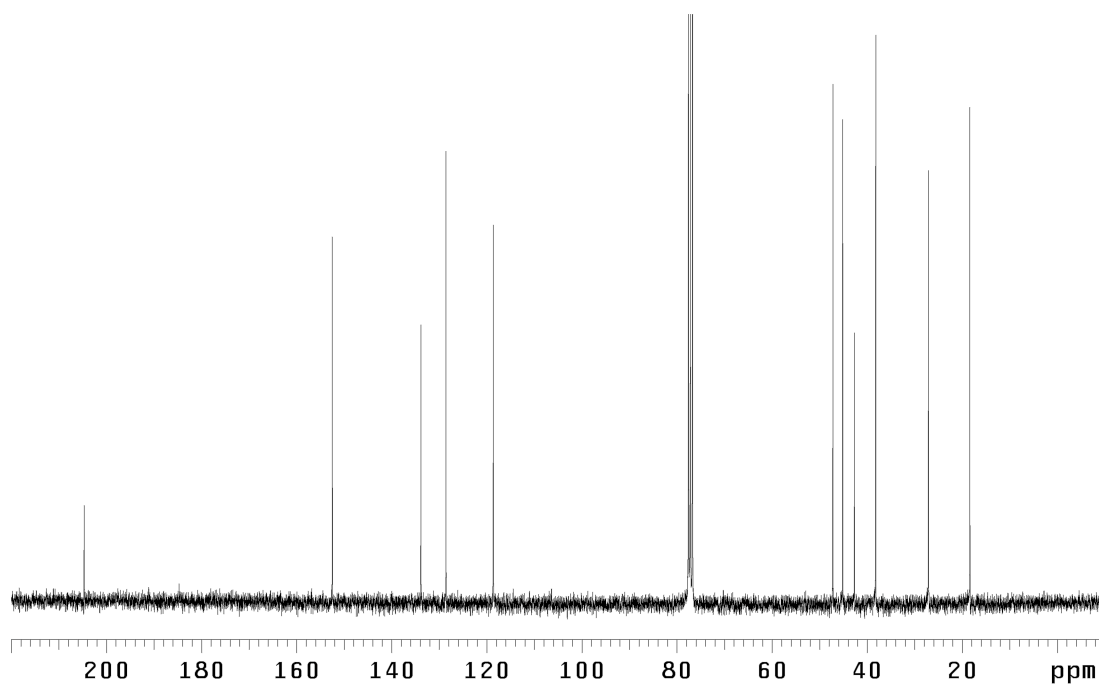


Figure SI-34C. ¹³C NMR (125 MHz, CDCl₃) of compound **11a**.

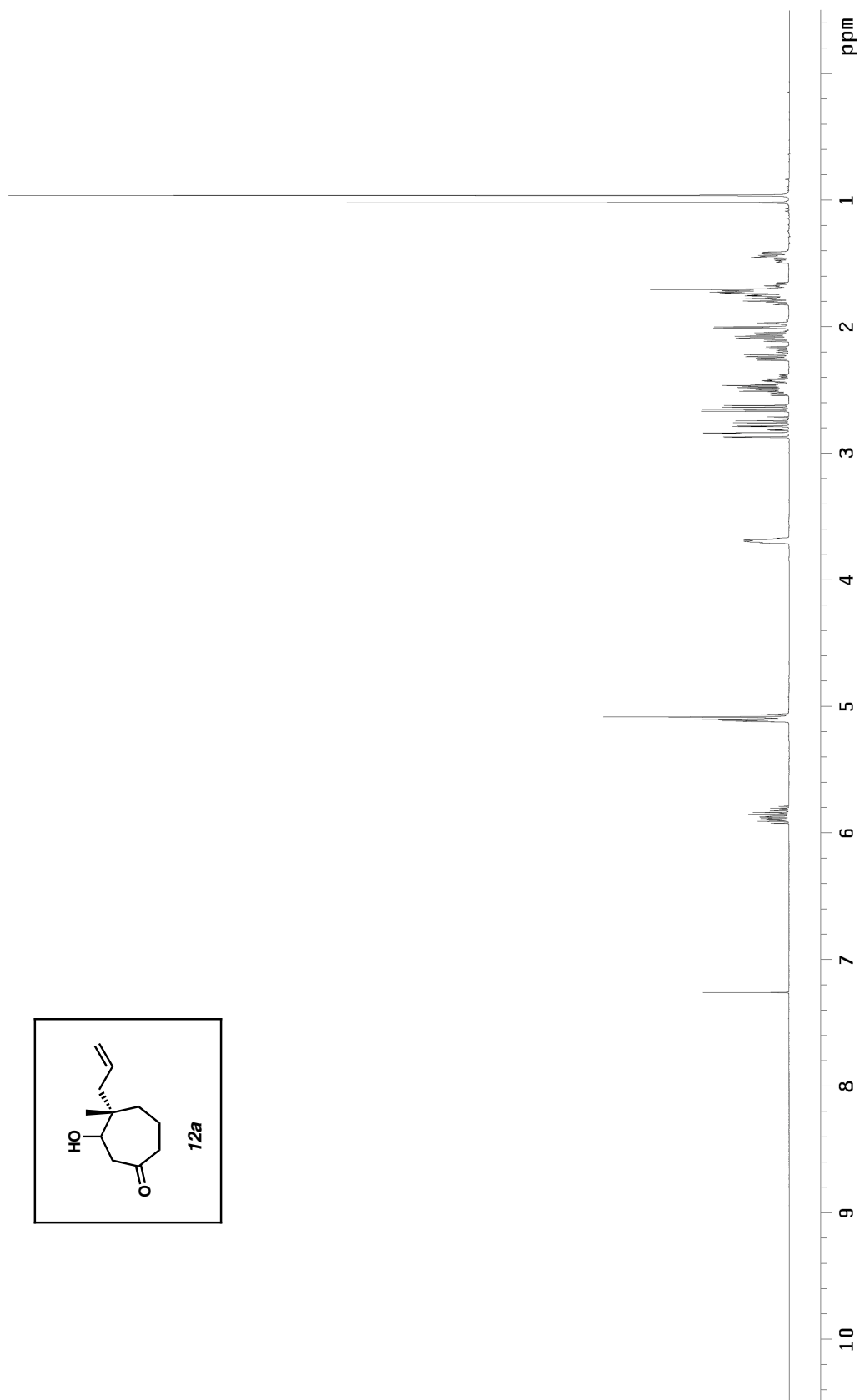


Figure SI-35A. ¹H NMR (500 MHz, CDCl₃) of compound **12a**.

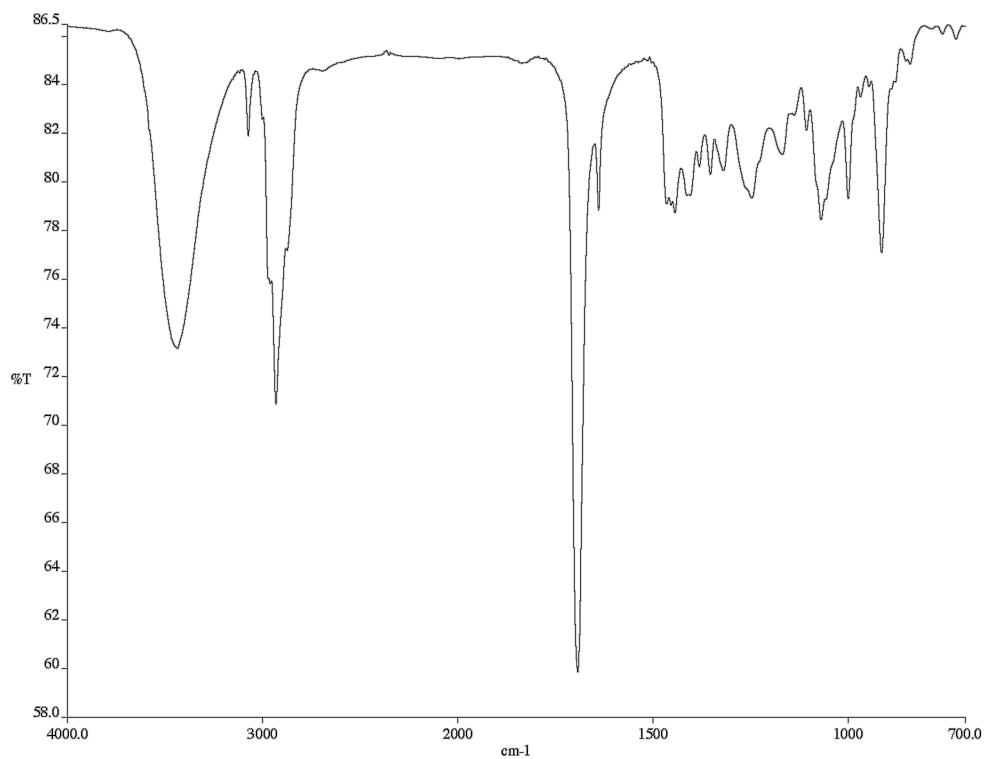


Figure SI-35B. Infrared spectrum (thin film/NaCl) of compound **12a**.

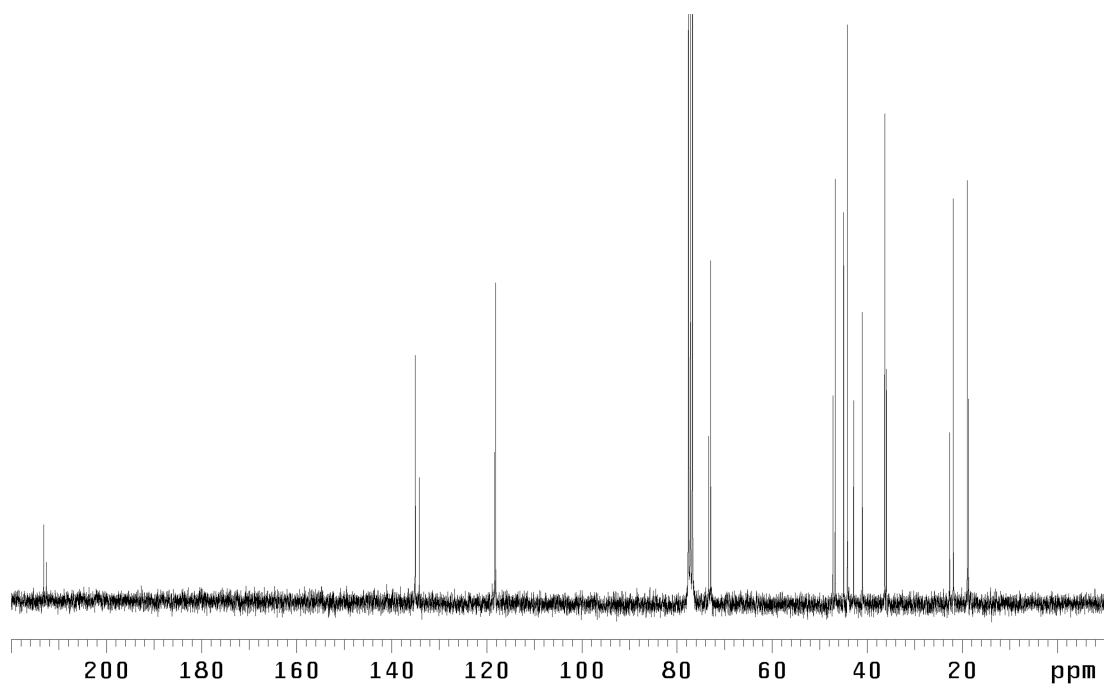


Figure SI-35C. ¹³C NMR (125 MHz, CDCl₃) of compound **12a**.

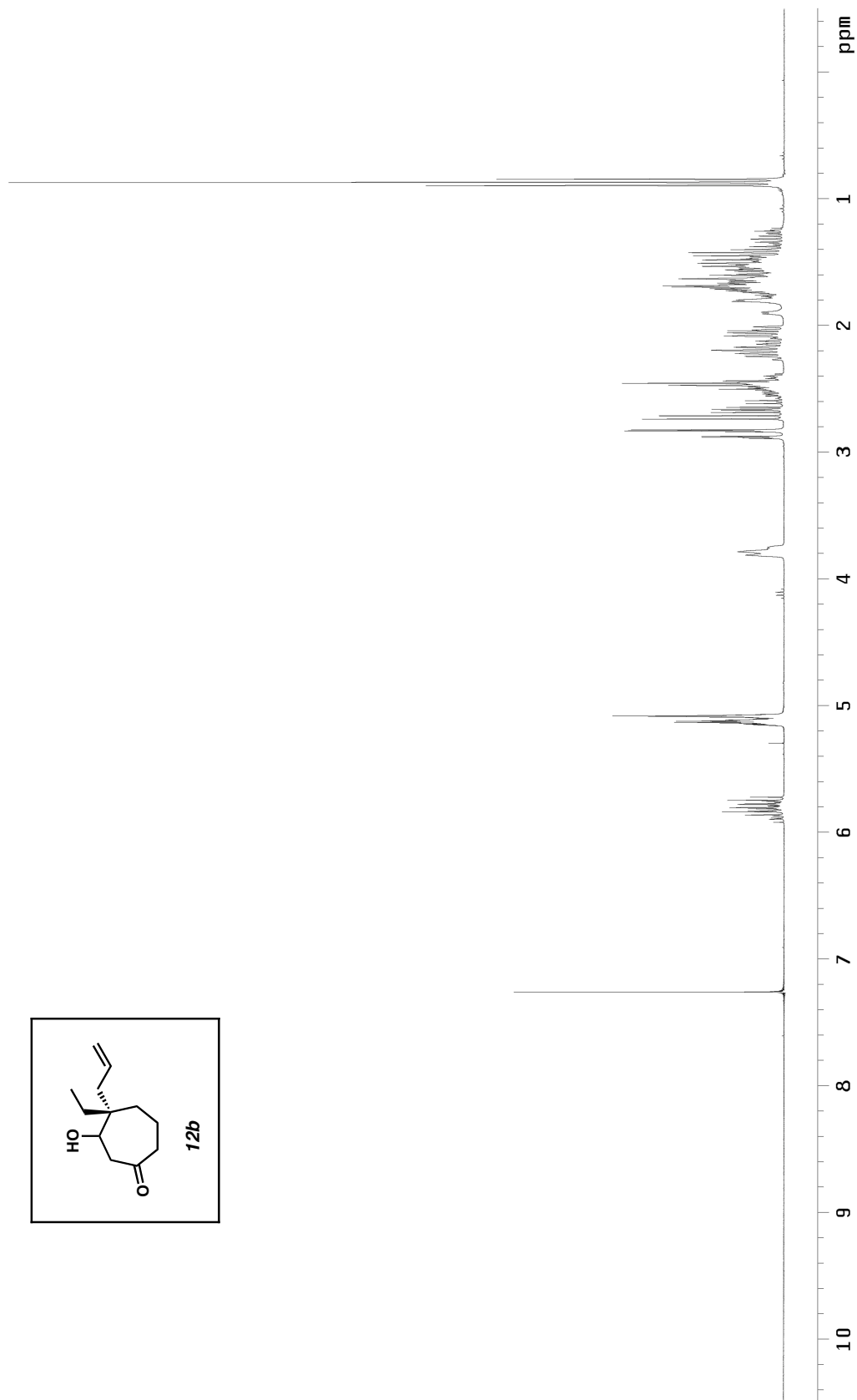


Figure SI-36A. ¹H NMR (300 MHz, CDCl₃) of compound **12b**.

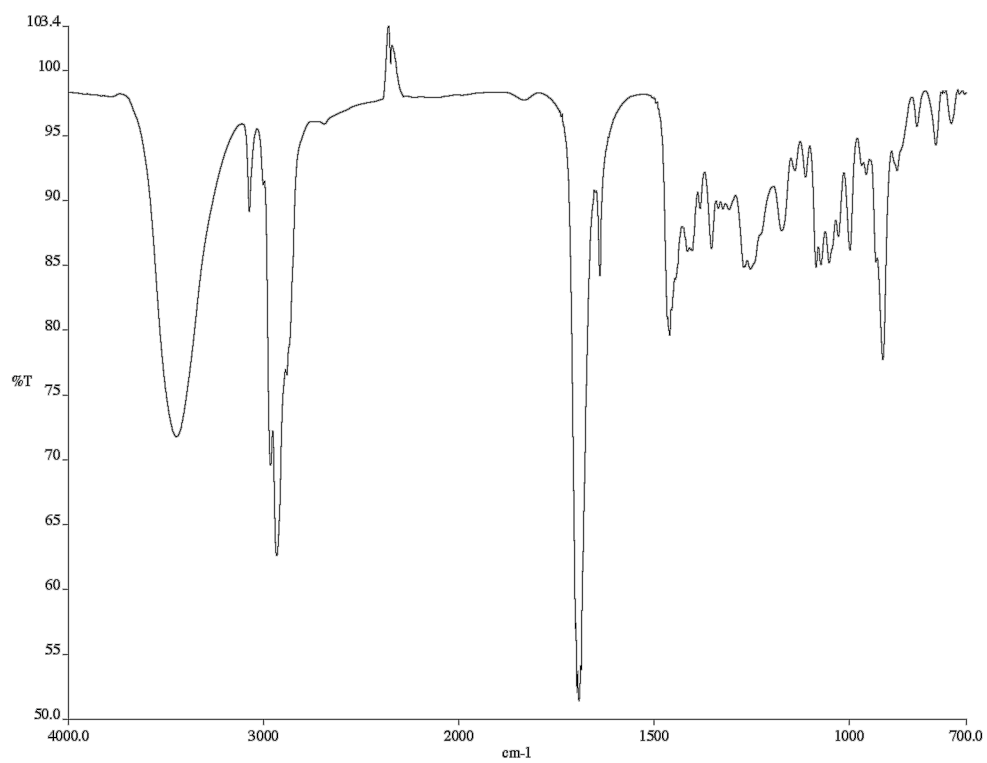


Figure SI-36B. Infrared spectrum (thin film/NaCl) of compound **12b**.

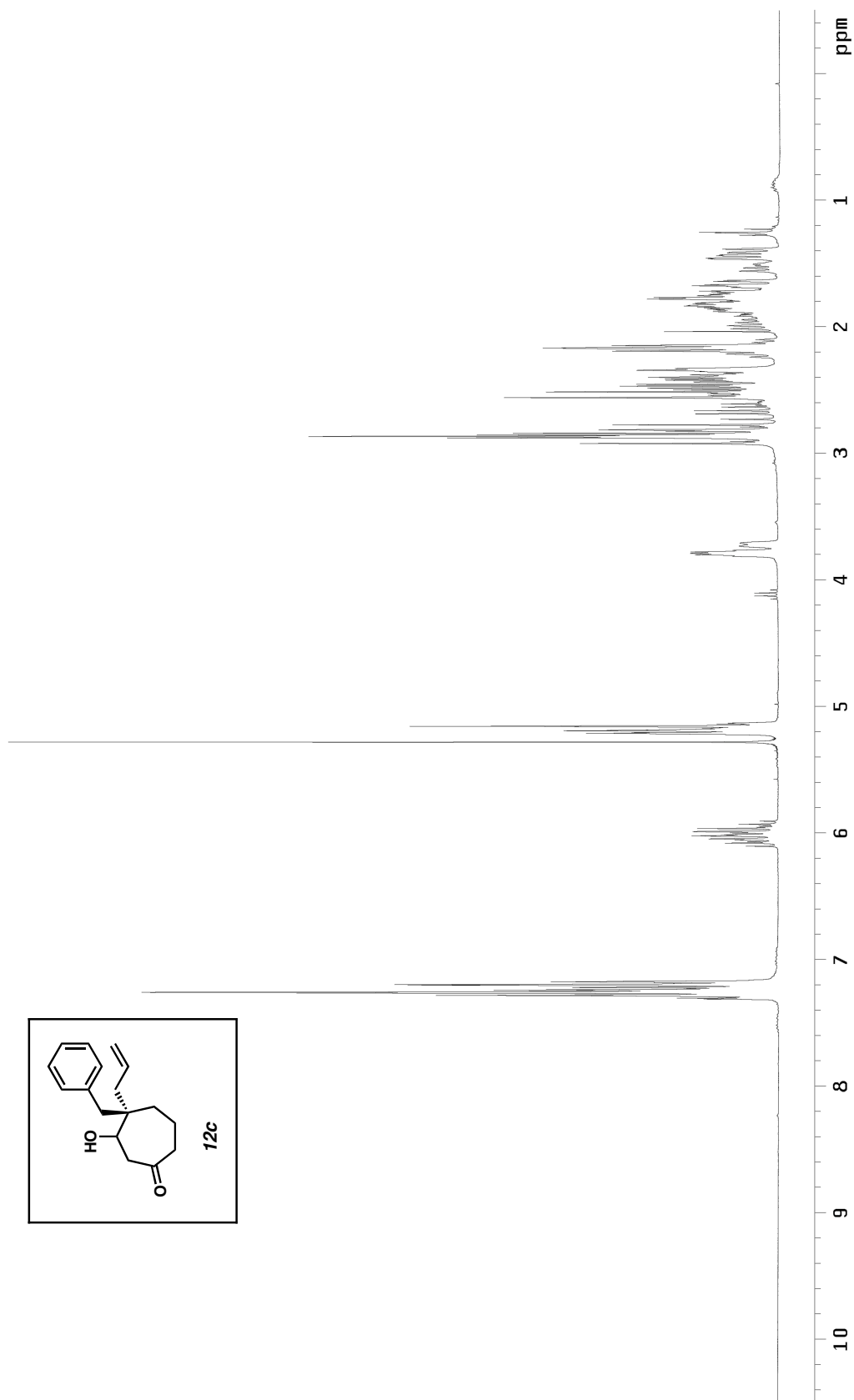


Figure SI-37A. ¹H NMR (300 MHz, CDCl₃) of compound **12c**.

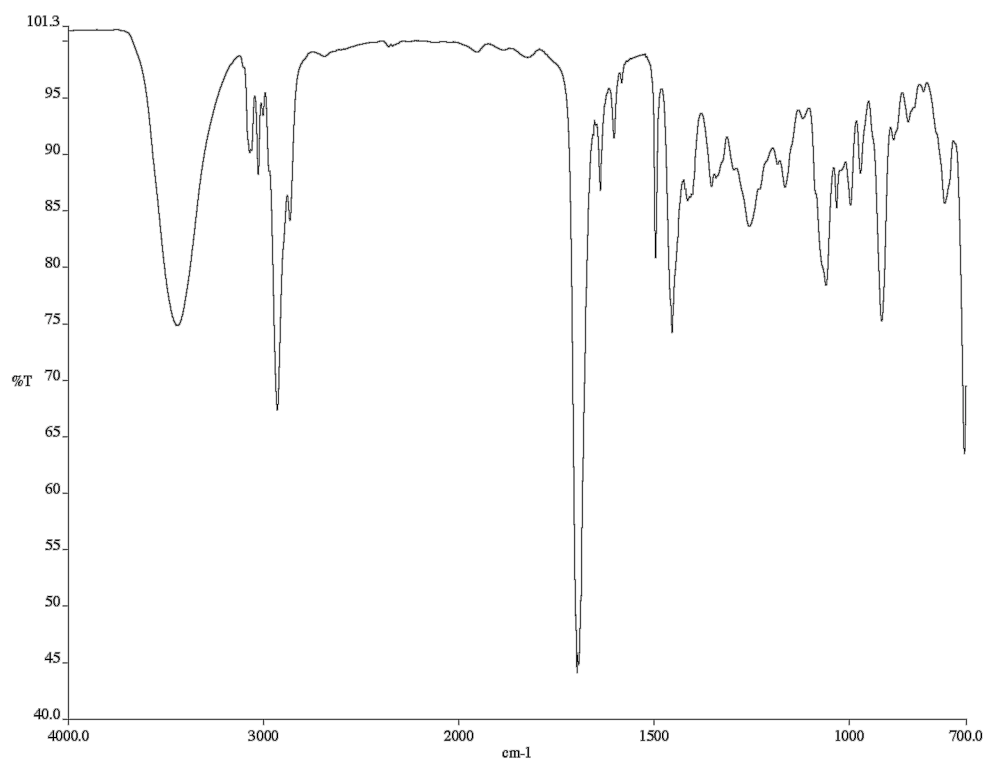


Figure SI-37B. Infrared spectrum (thin film/NaCl) of compound **12c**.

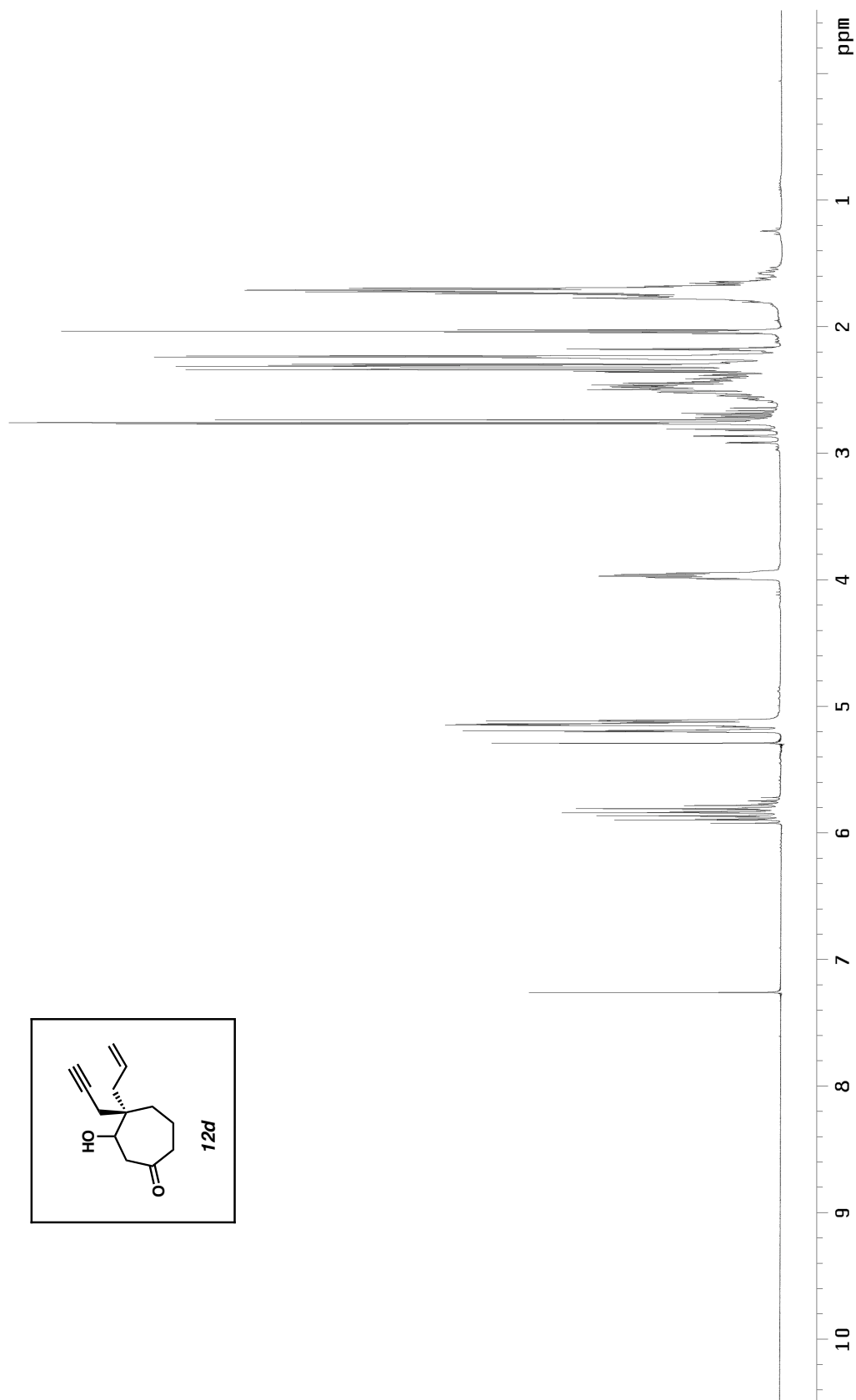


Figure SI-38A. ^1H NMR (300 MHz, CDCl_3) of compound **12d**.

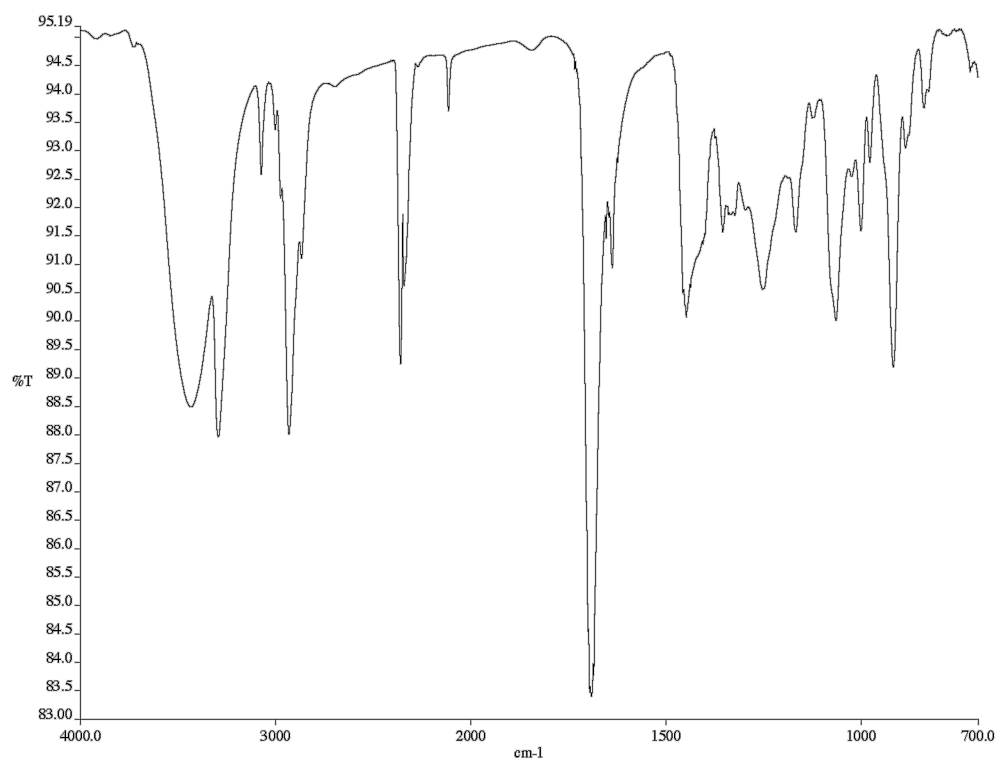


Figure SI-38B. Infrared spectrum (thin film/NaCl) of compound **12d**.

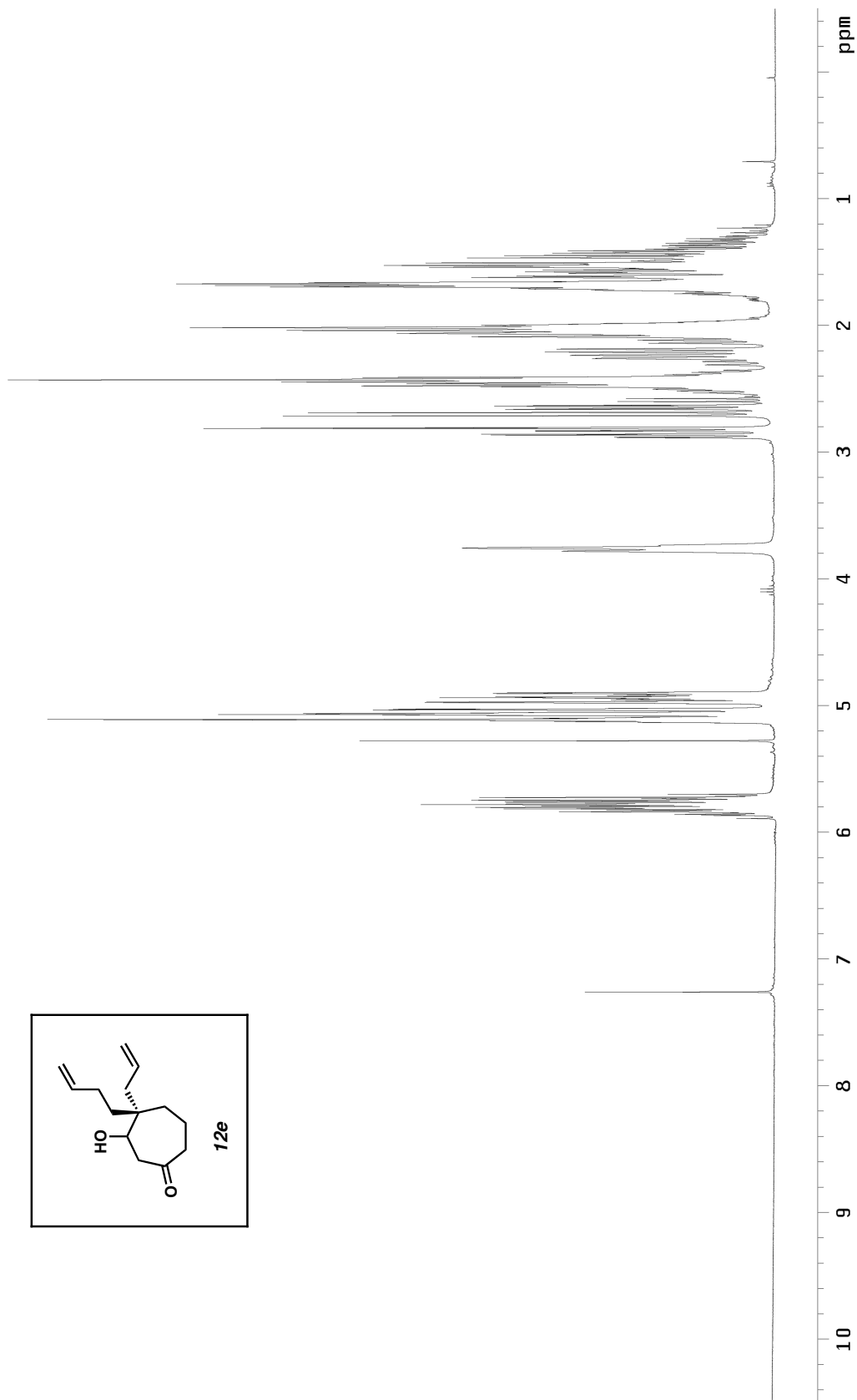


Figure SI-39A. ¹H NMR (300 MHz, CDCl₃) of compound **12e**.

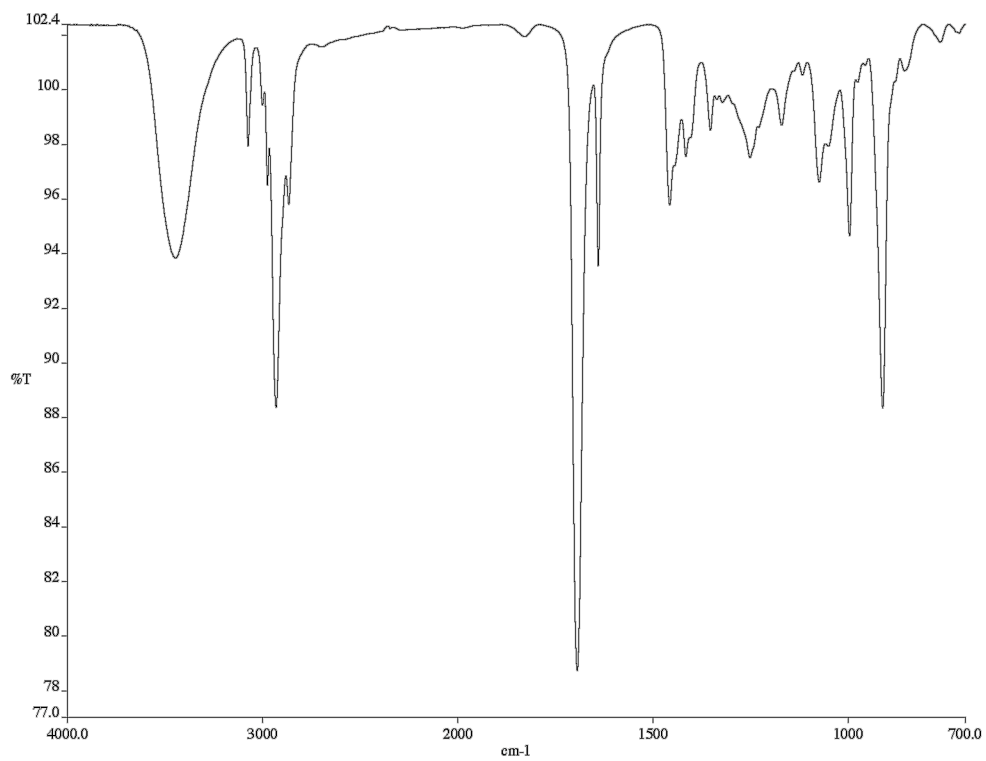


Figure SI-39B. Infrared spectrum (thin film/NaCl) of compound **12e**.

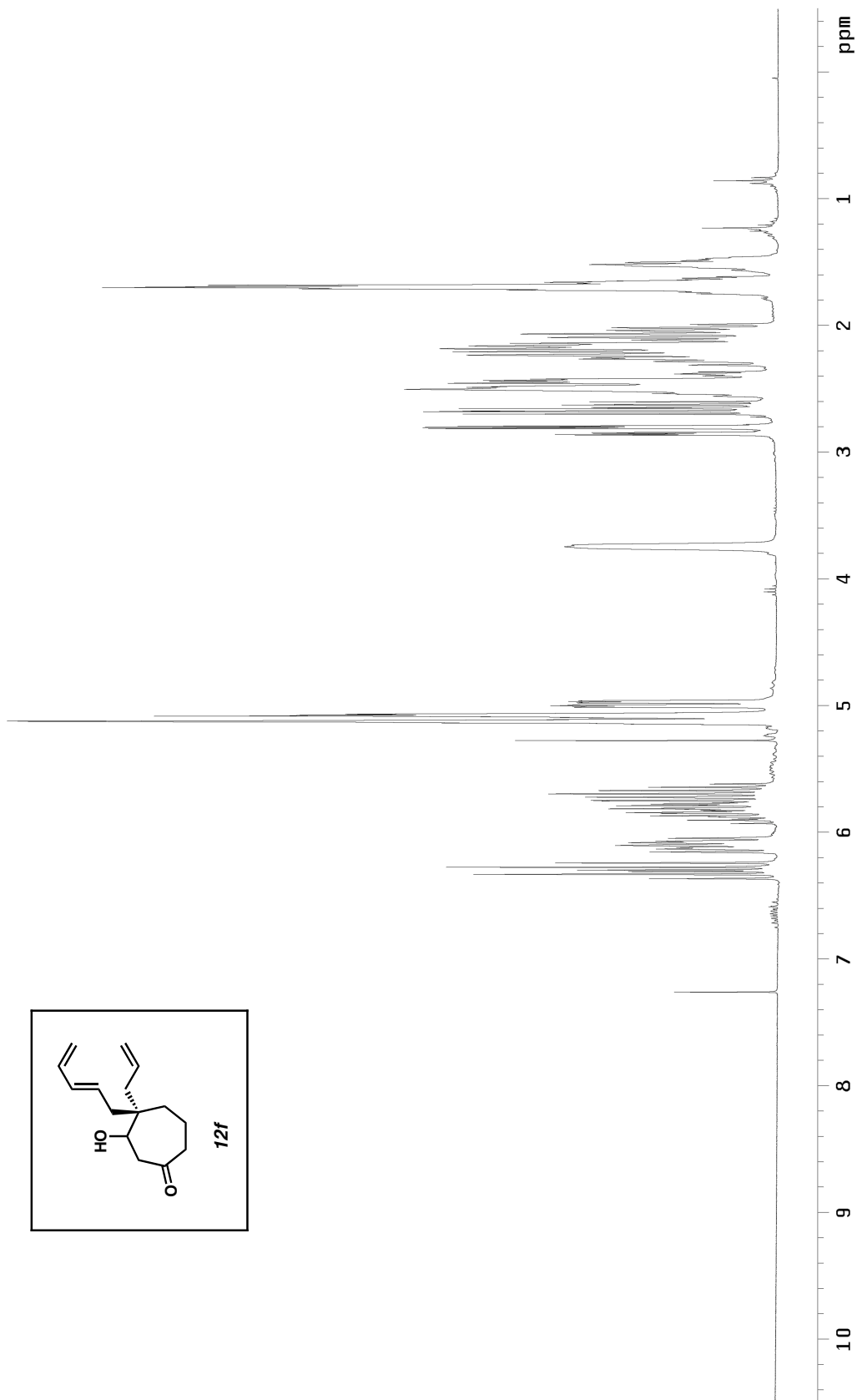


Figure SI-40A. ¹H NMR (300 MHz, CDCl₃) of compound **12f**.

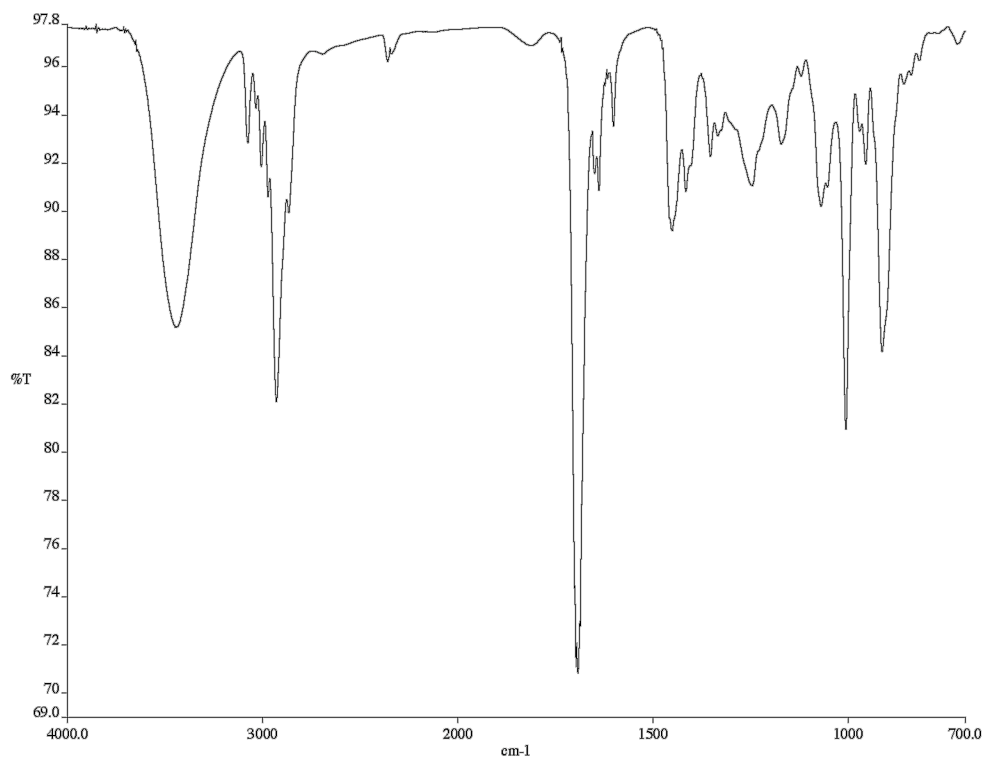


Figure SI-40B. Infrared spectrum (thin film/NaCl) of compound **12f**.

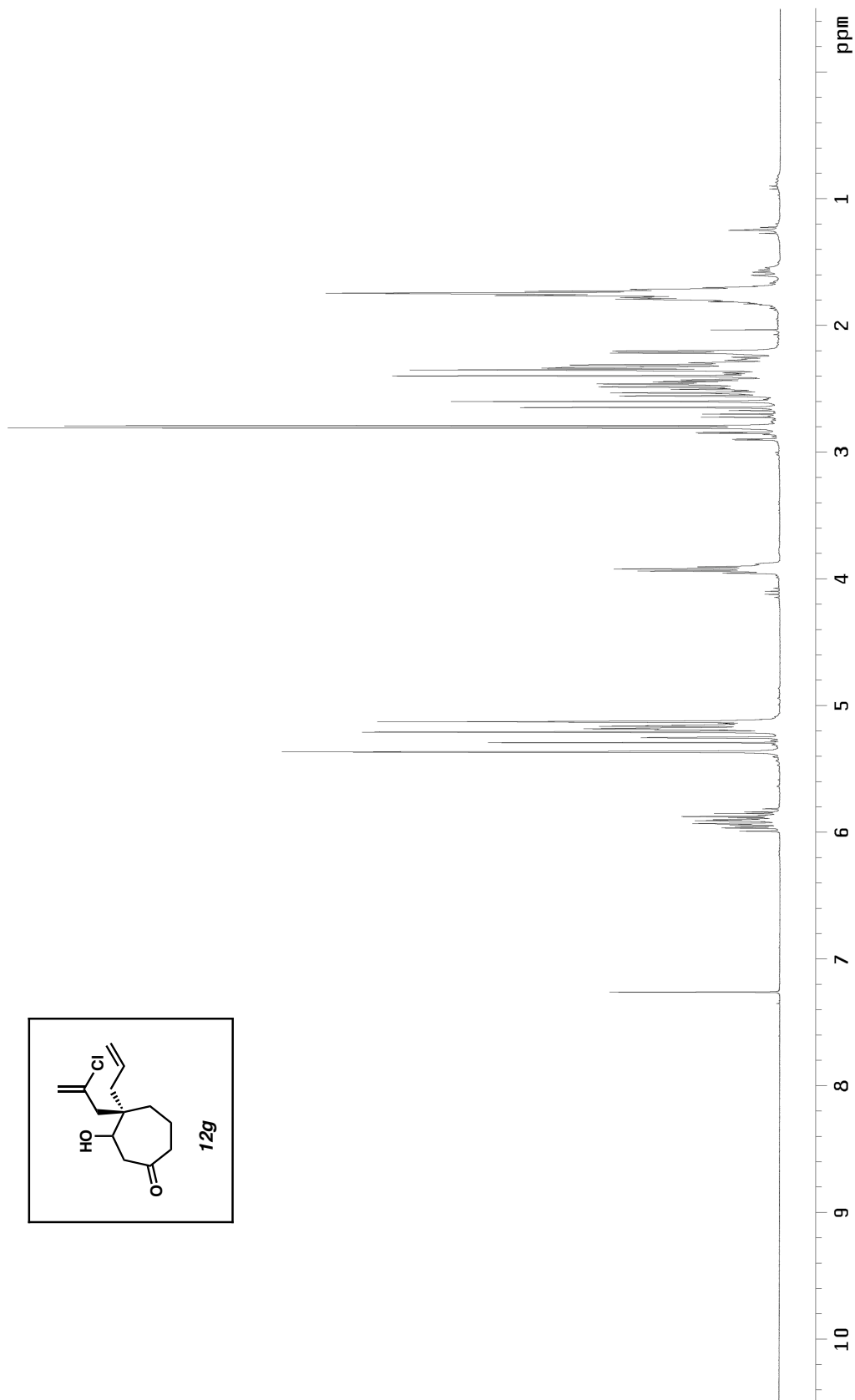


Figure SI-41A. ¹H NMR (300 MHz, CDCl₃) of compound **12g**.

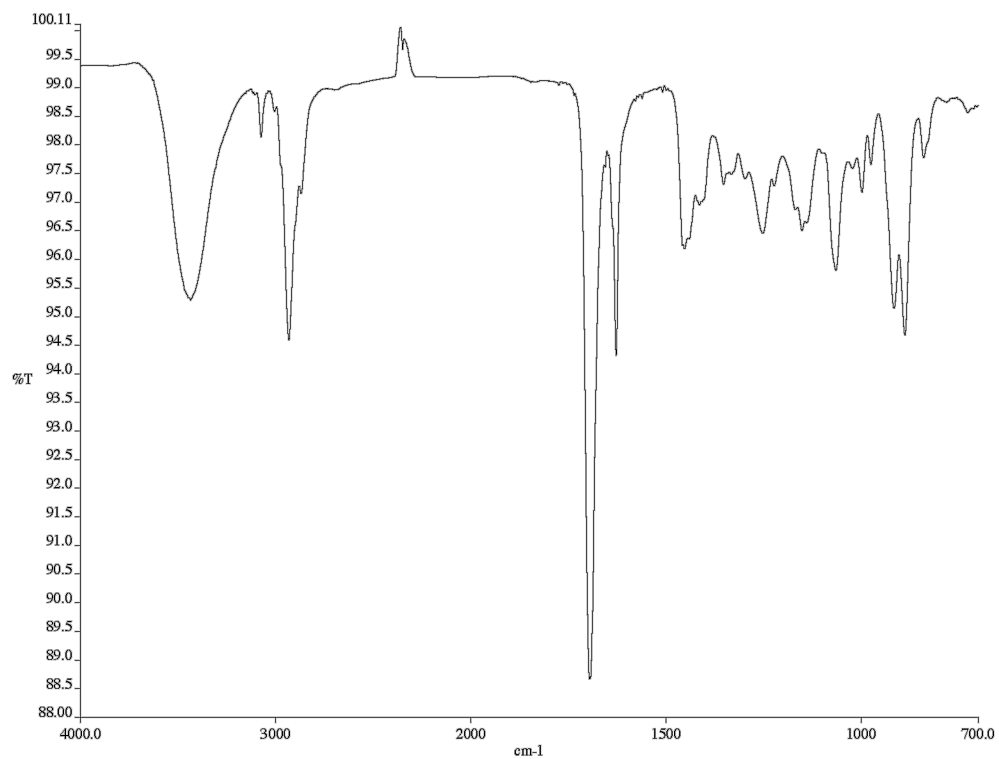


Figure SI-41B. Infrared spectrum (thin film/NaCl) of compound **12g**.

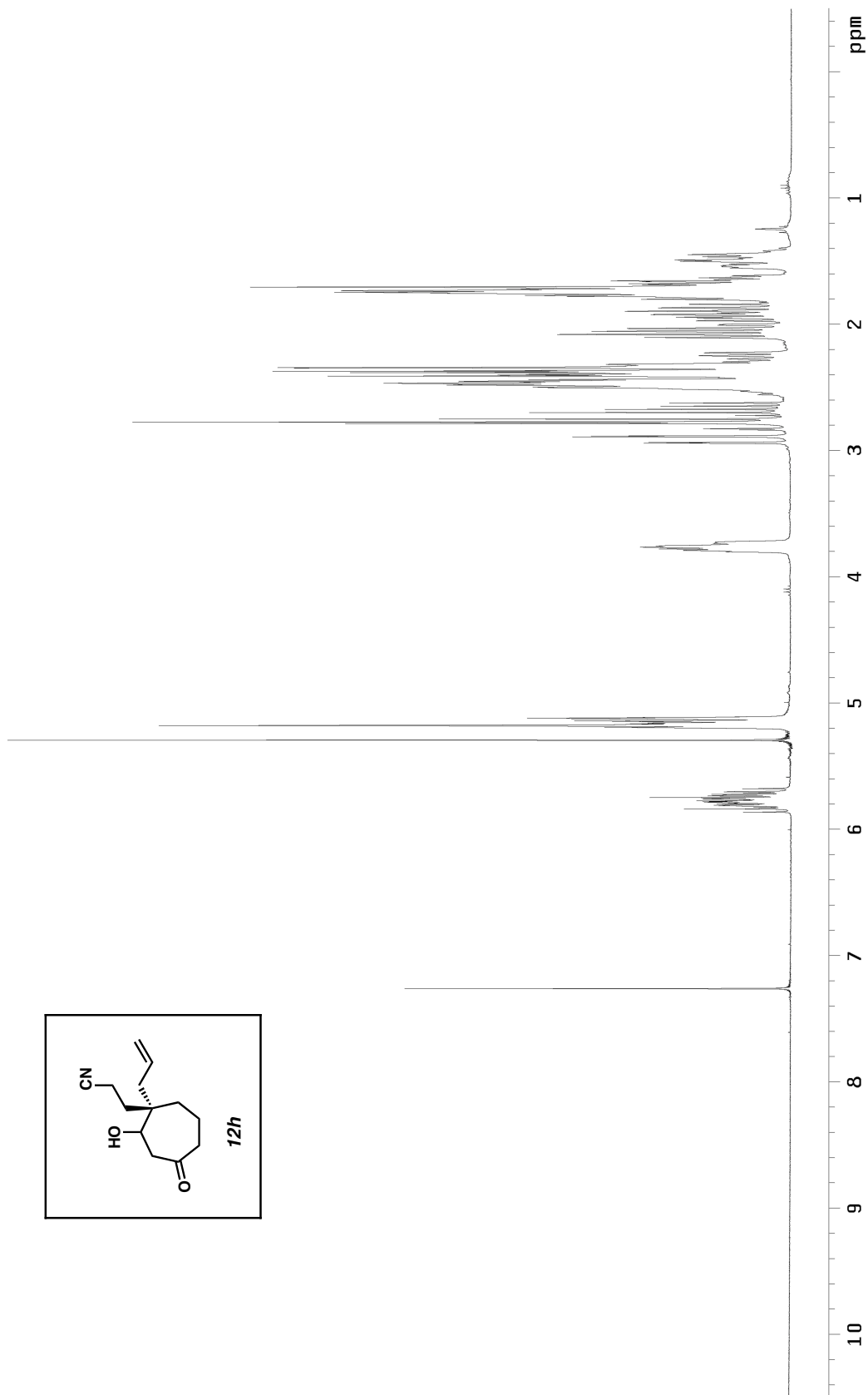


Figure SI-42A. ¹H NMR (300 MHz, CDCl₃) of compound **12h**.

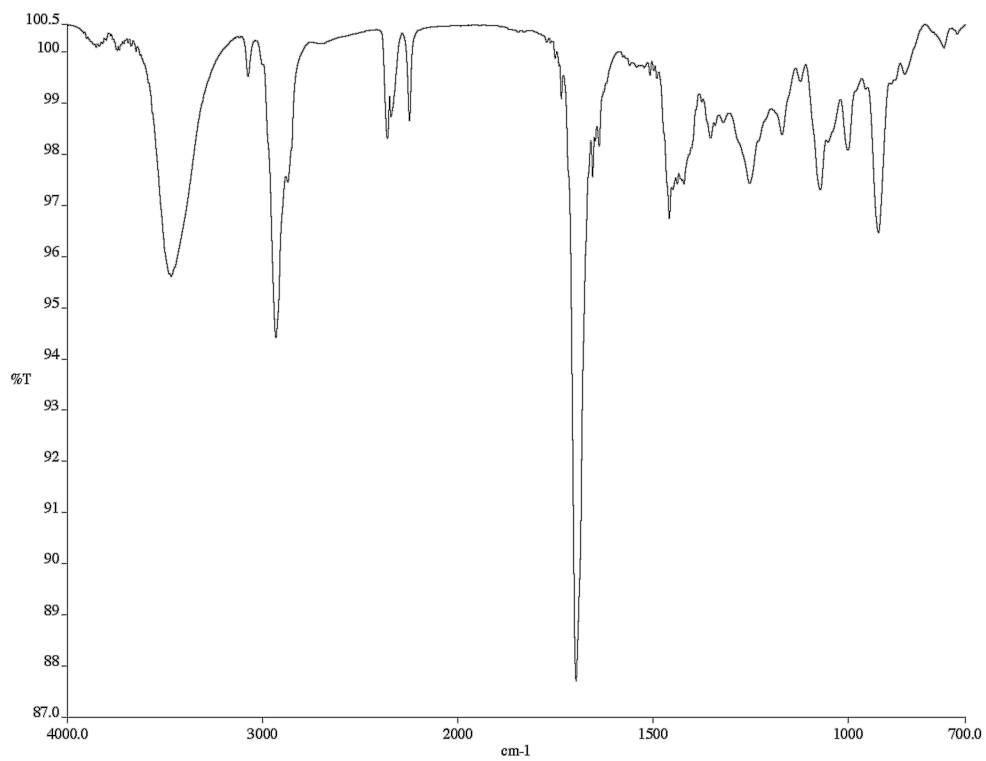


Figure SI-42B. Infrared spectrum (thin film/NaCl) of compound **12h**.

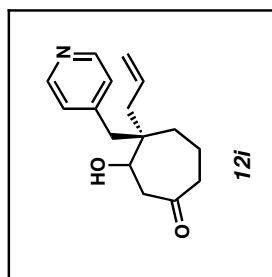
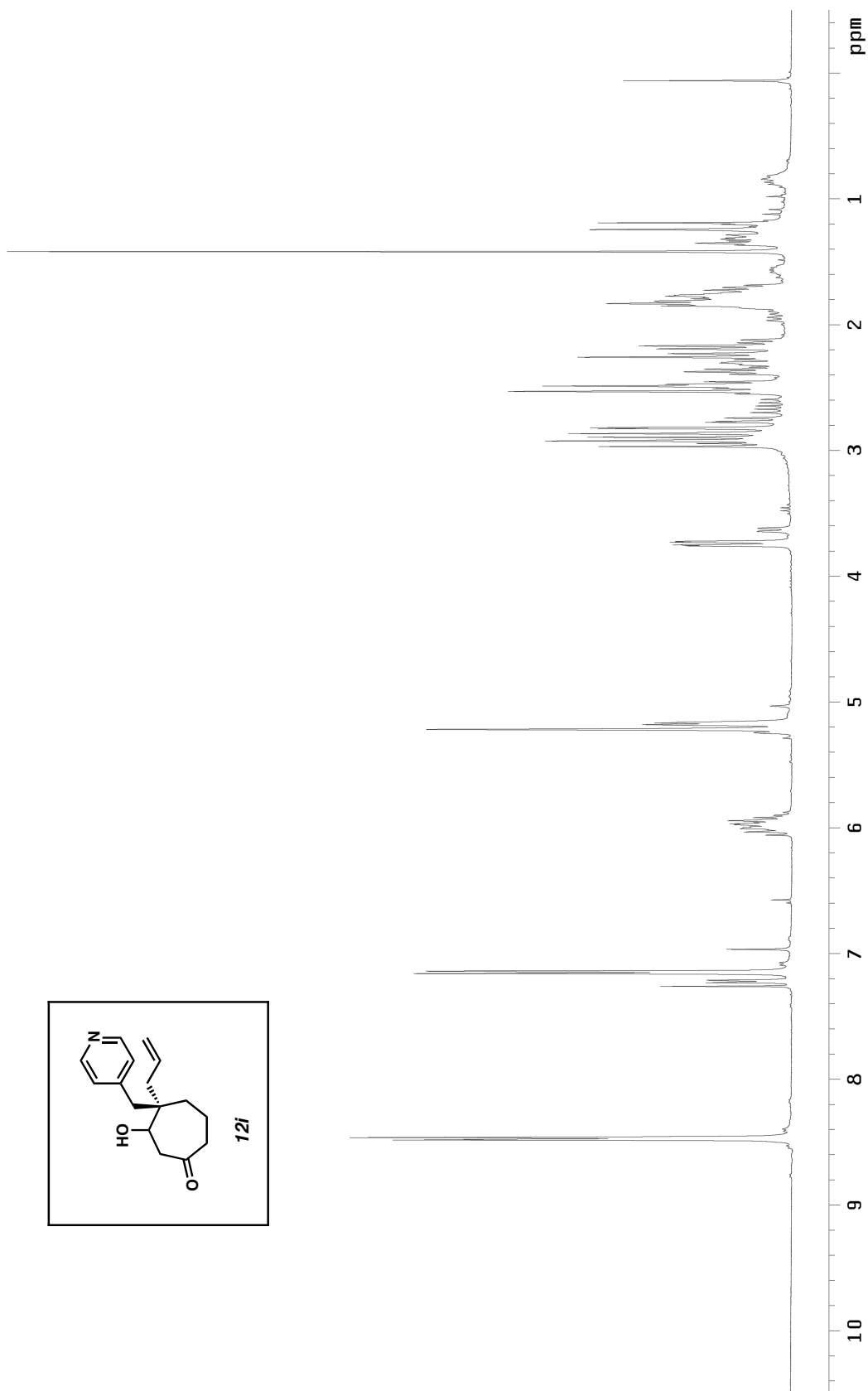


Figure SI-43A. ¹H NMR (300 MHz, CDCl₃) of compound **12i**.

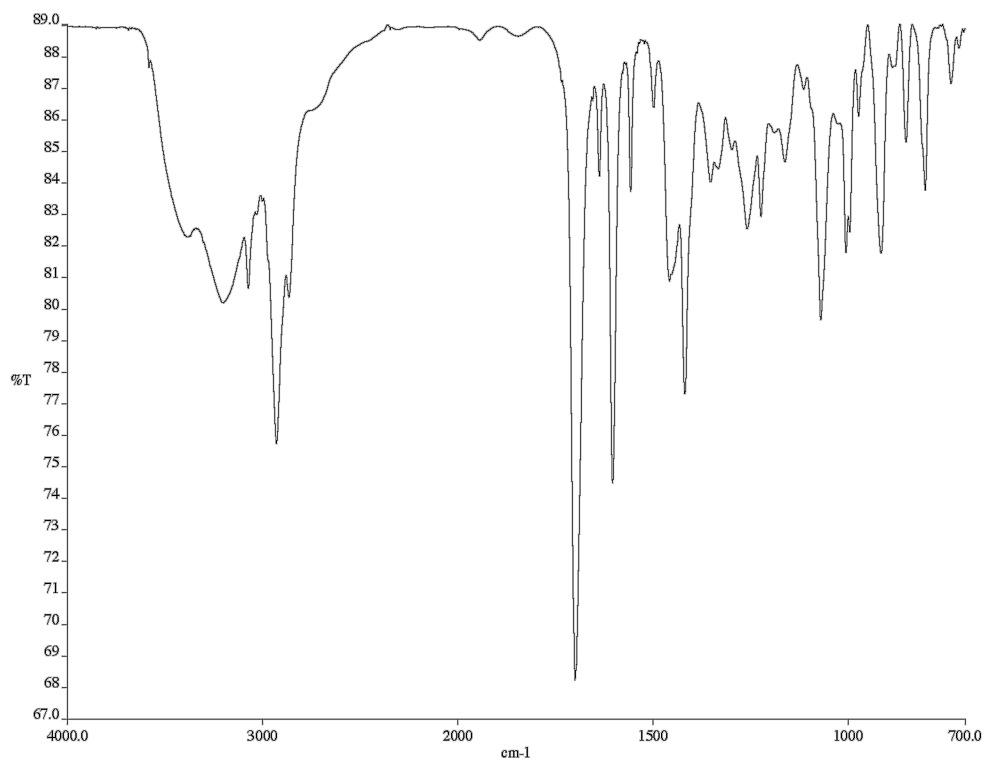


Figure SI-43B. Infrared spectrum (thin film/NaCl) of compound **12i**.

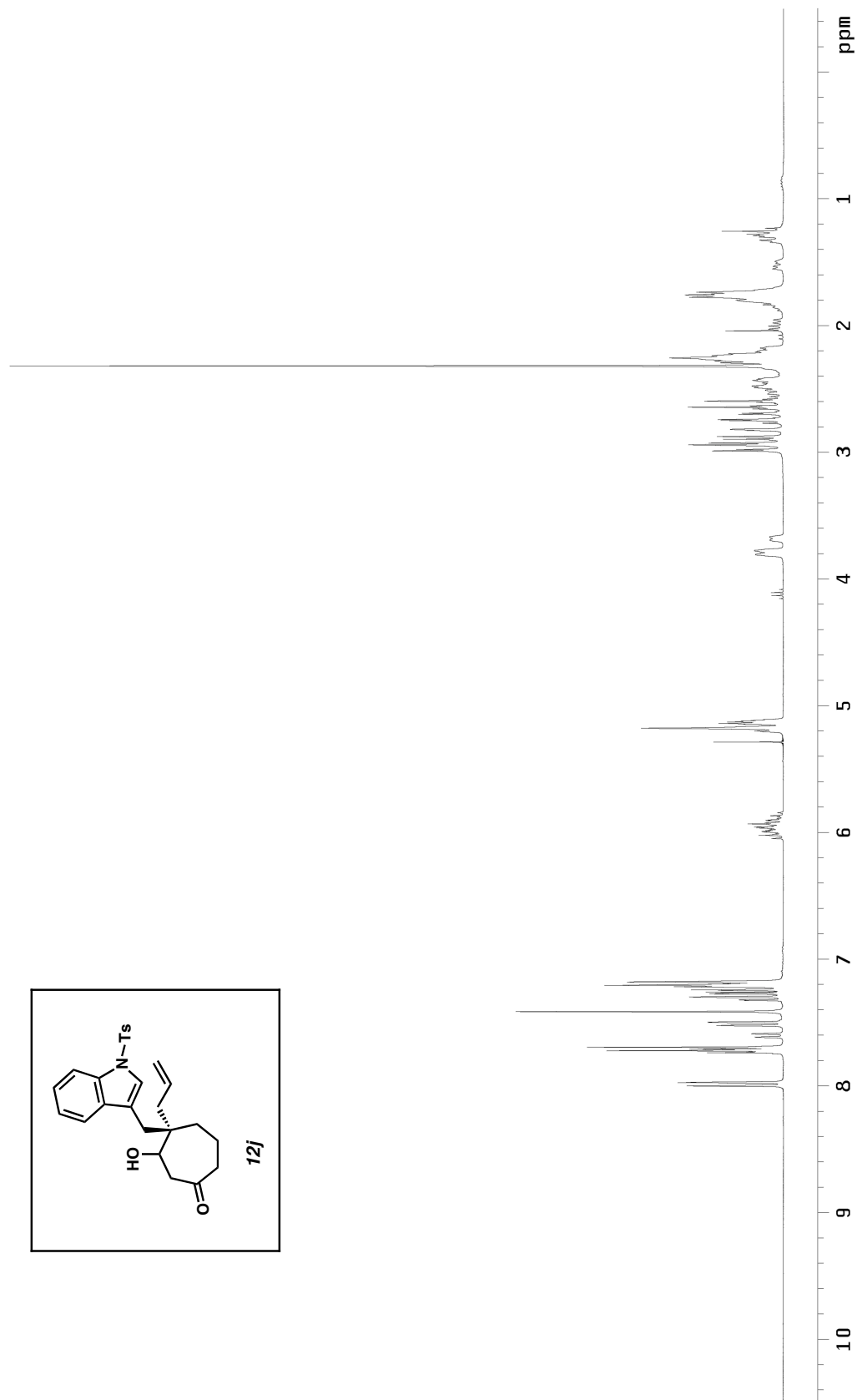


Figure SI-44A. ¹H NMR (300 MHz, CDCl₃) of compound **12j**.

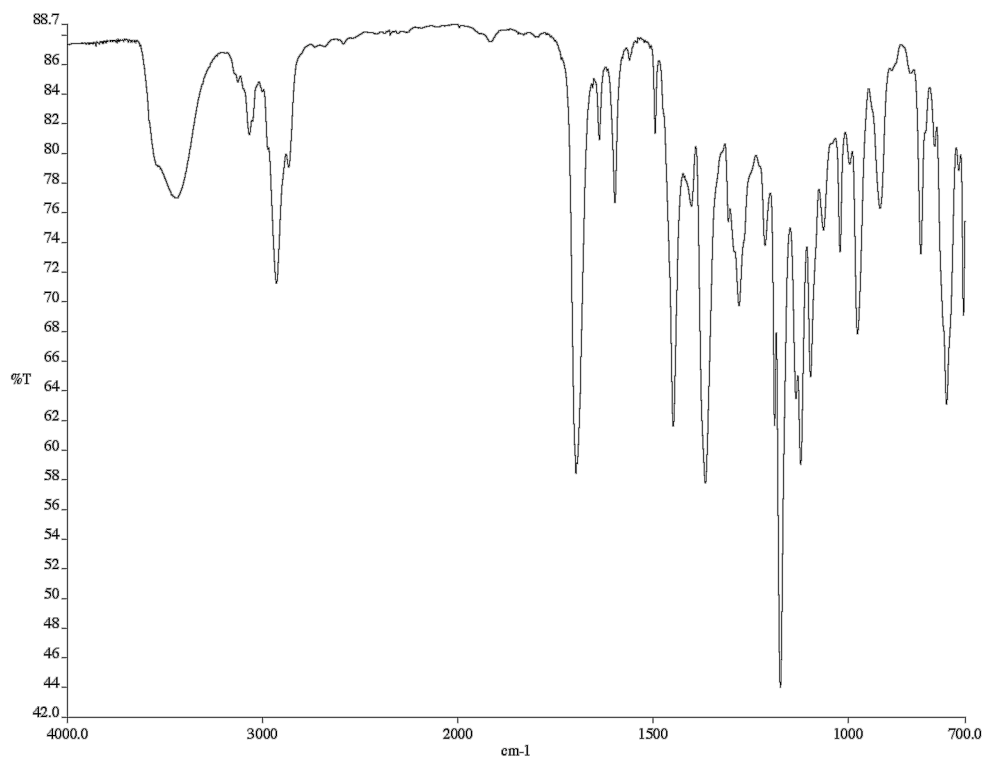


Figure SI-44B. Infrared spectrum (thin film/NaCl) of compound **12j**.

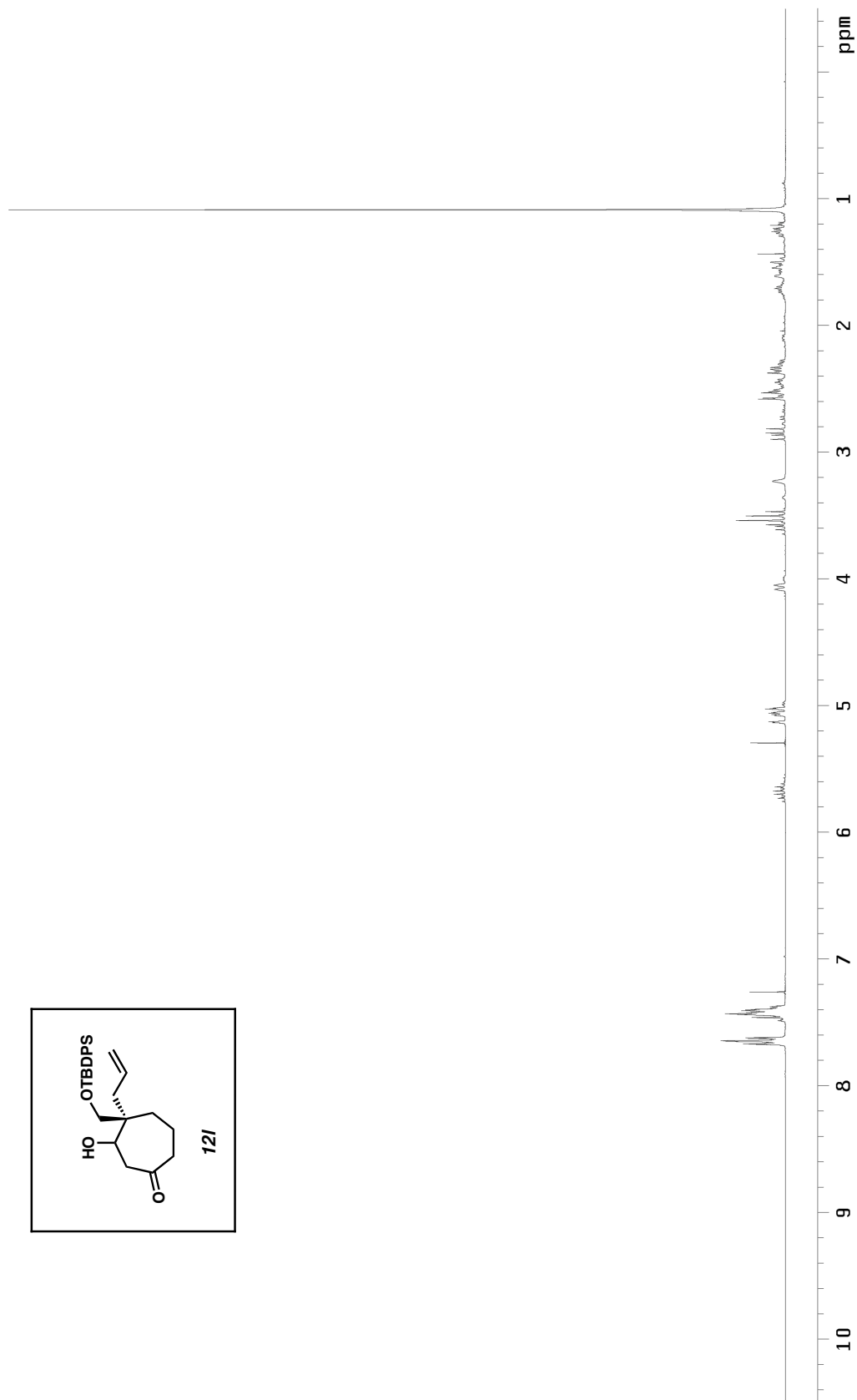


Figure SI-45A. ¹H NMR (300 MHz, CDCl₃) of compound **12l**.

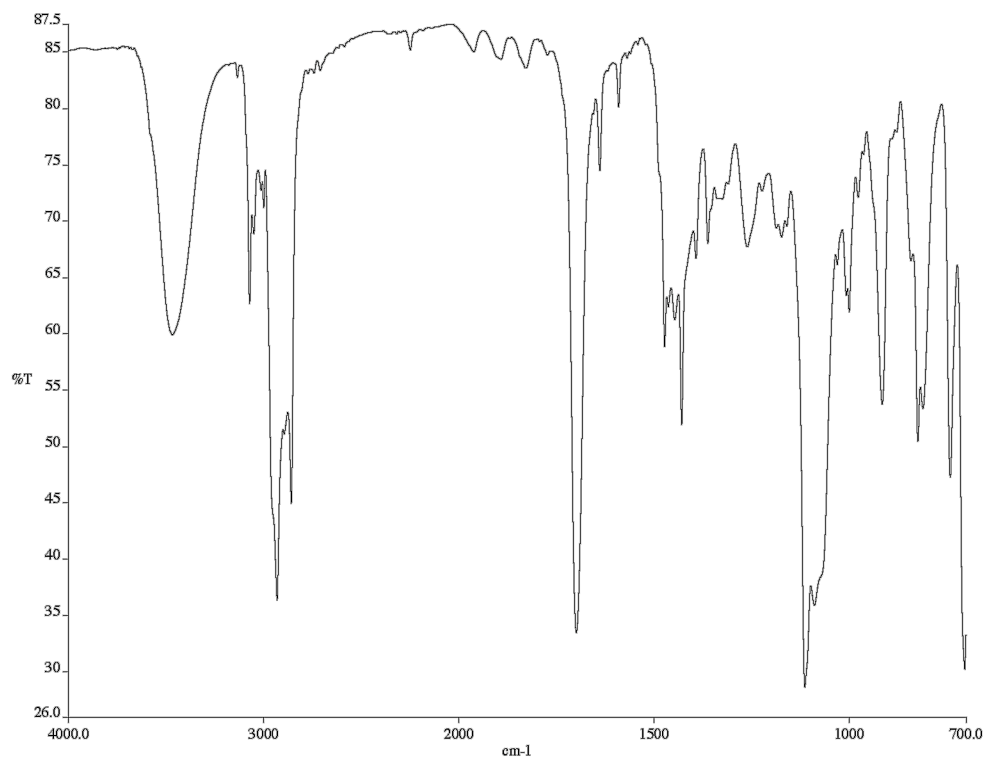


Figure SI-45B. Infrared spectrum (thin film/NaCl) of compound **121**.

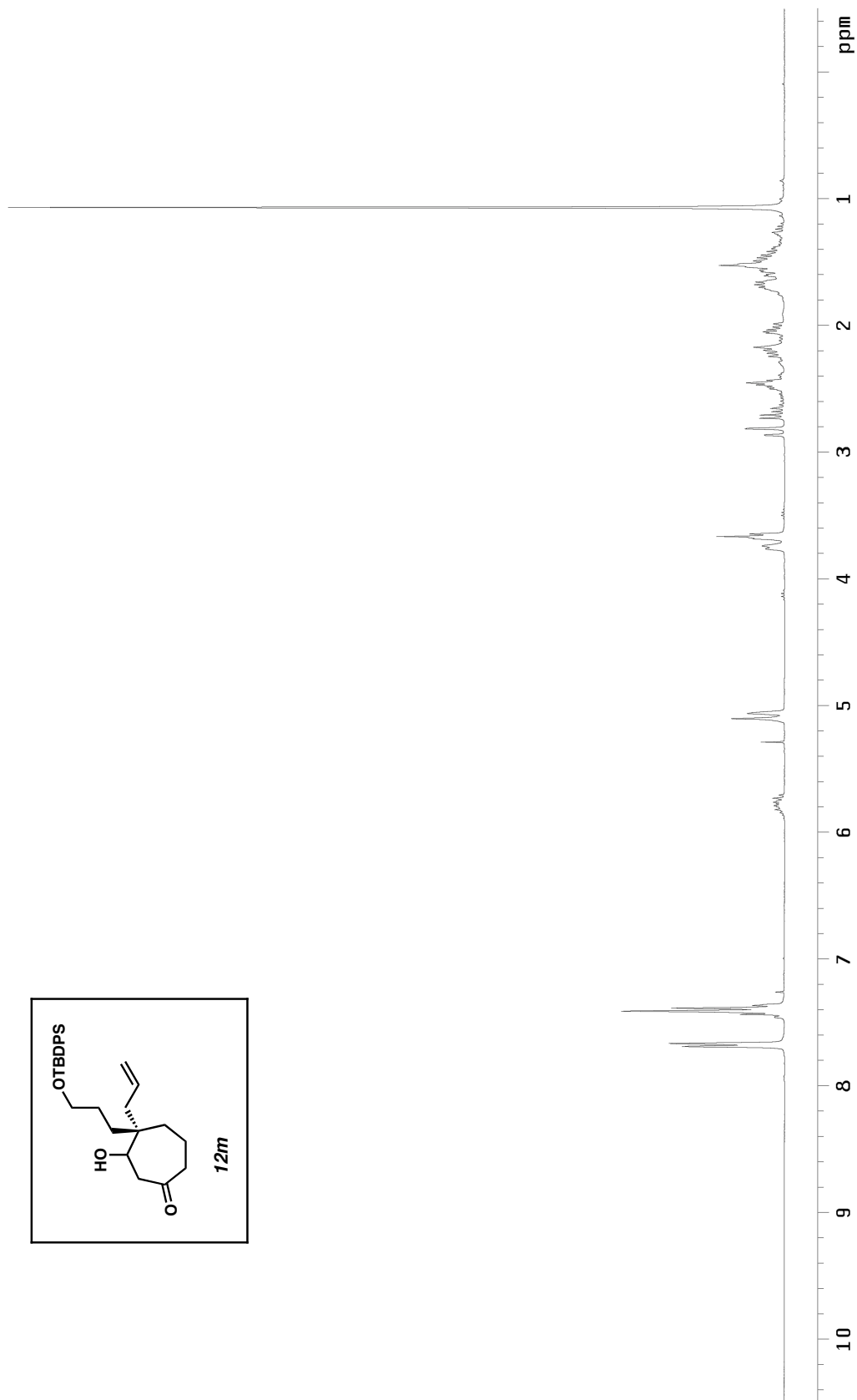


Figure SI-46A. ^1H NMR (300 MHz, CDCl_3) of compound **12m**.

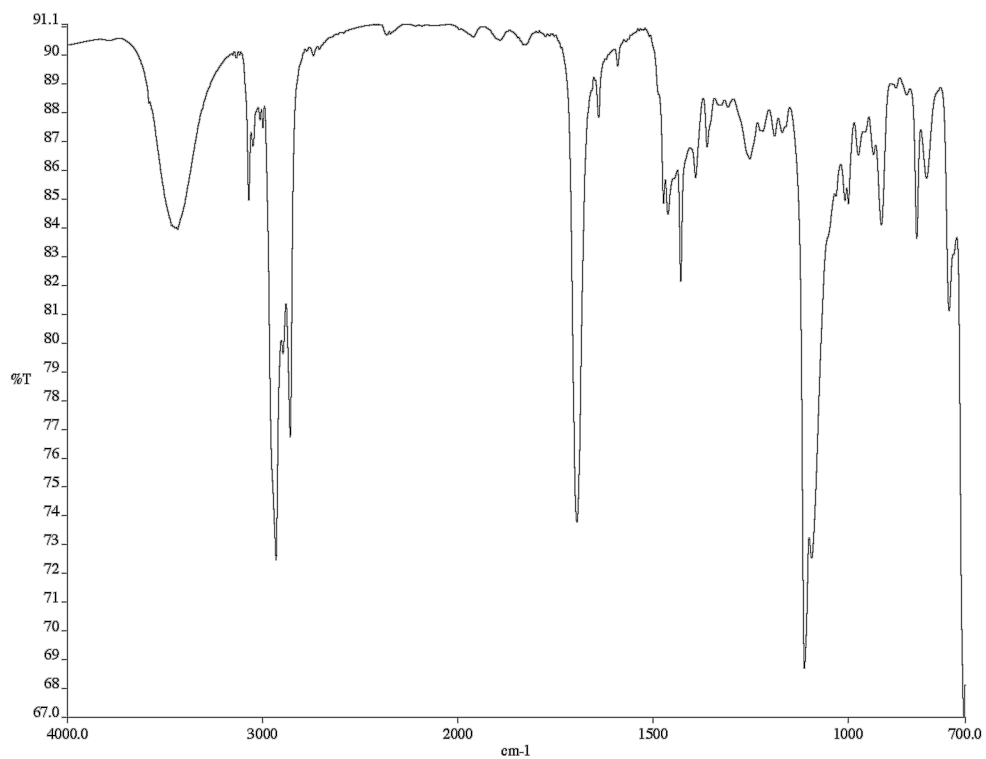


Figure SI-46B. Infrared spectrum (thin film/NaCl) of compound **12m**.

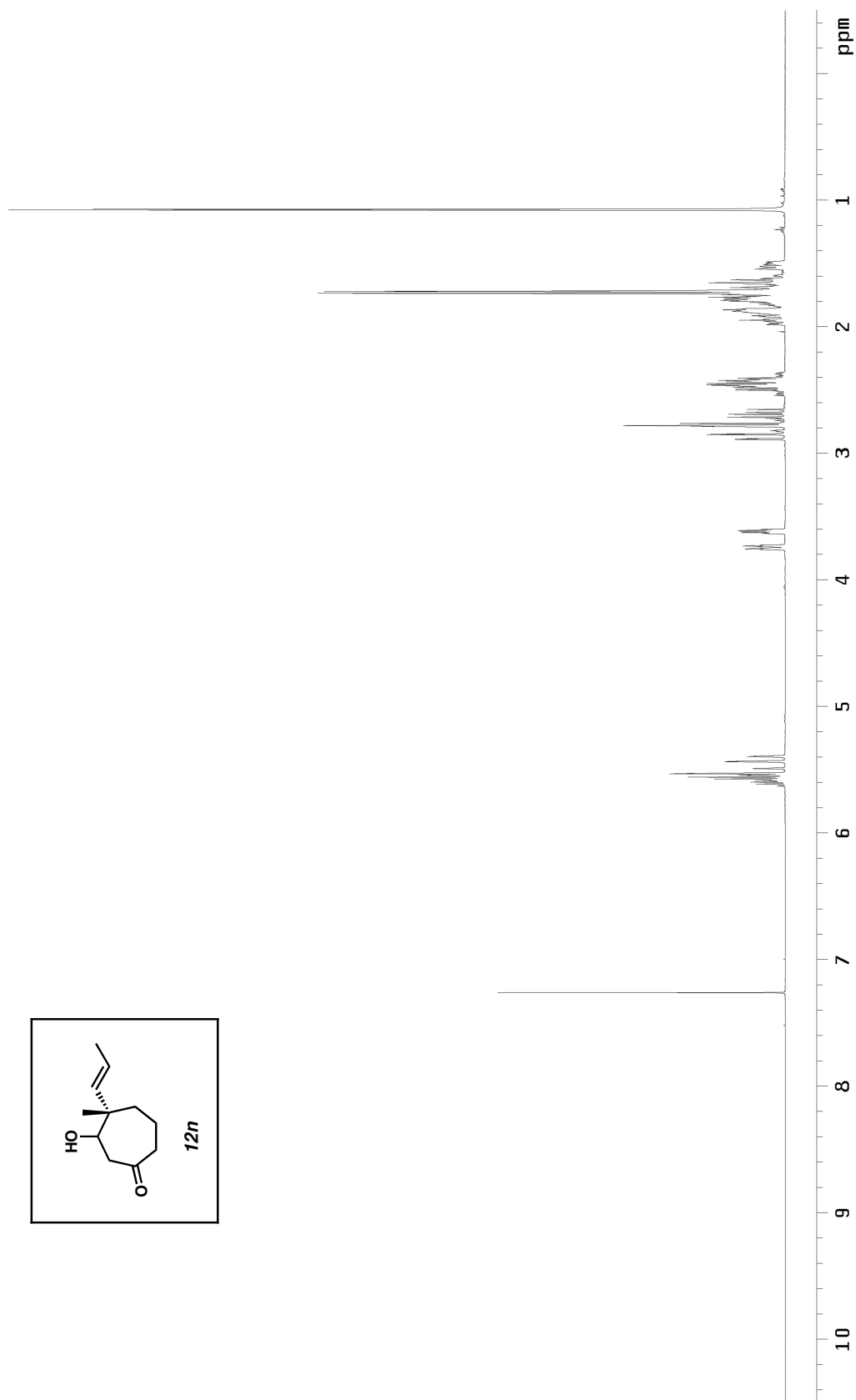


Figure SI-47A. ¹H NMR (400 MHz, CDCl₃) of compound **12n**.

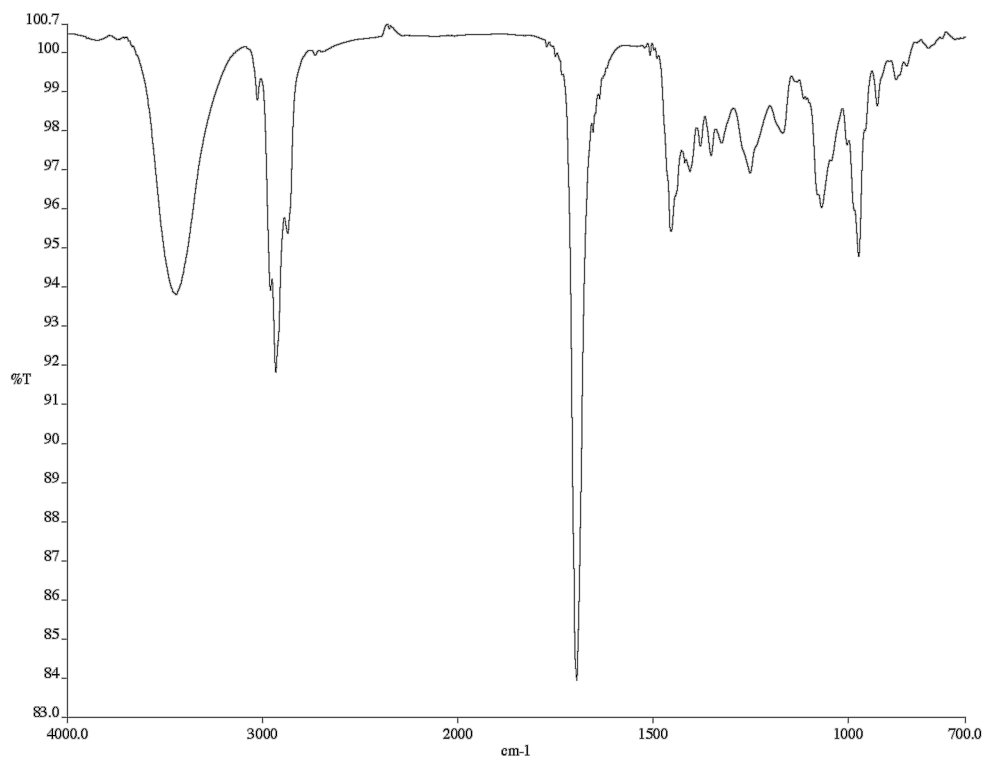


Figure SI-47B. Infrared spectrum (thin film/NaCl) of compound **12n**.

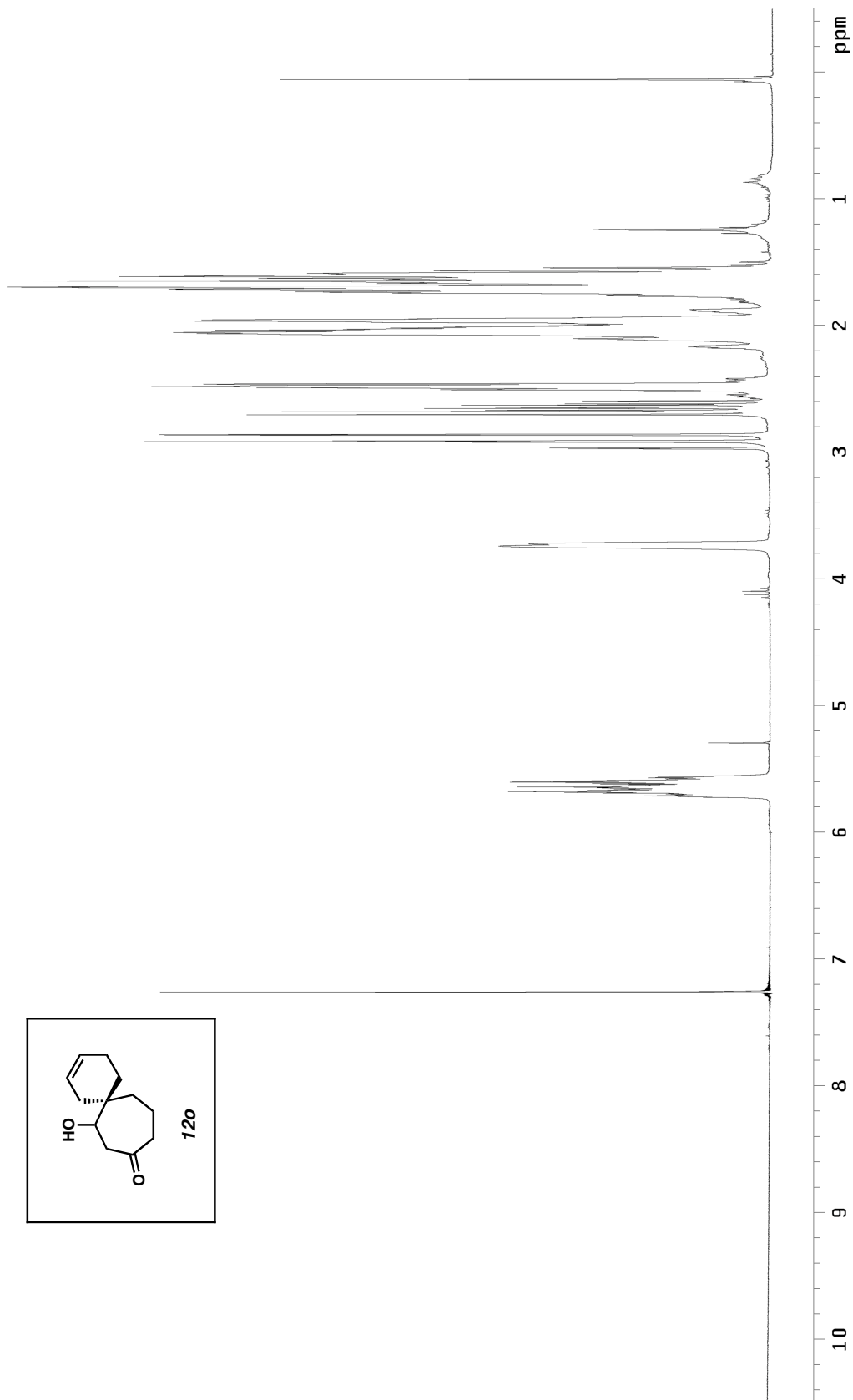


Figure SI-48A. ¹H NMR (300 MHz, CDCl₃) of compound **12o**.

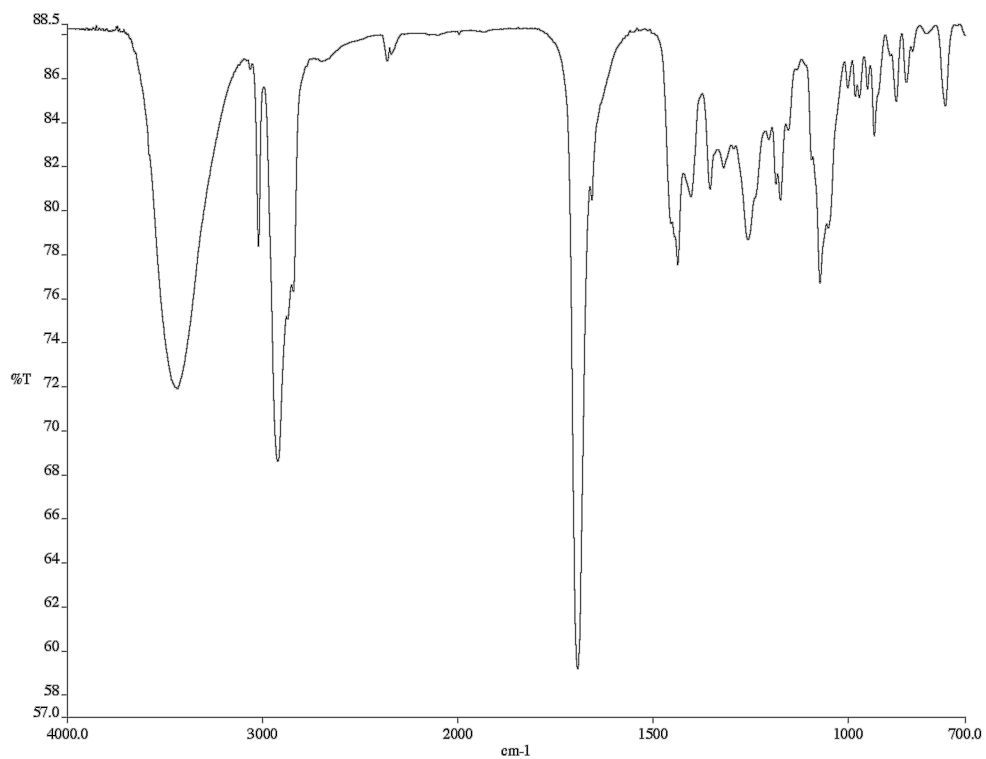


Figure SI-48B. Infrared spectrum (thin film/NaCl) of compound **12o**.

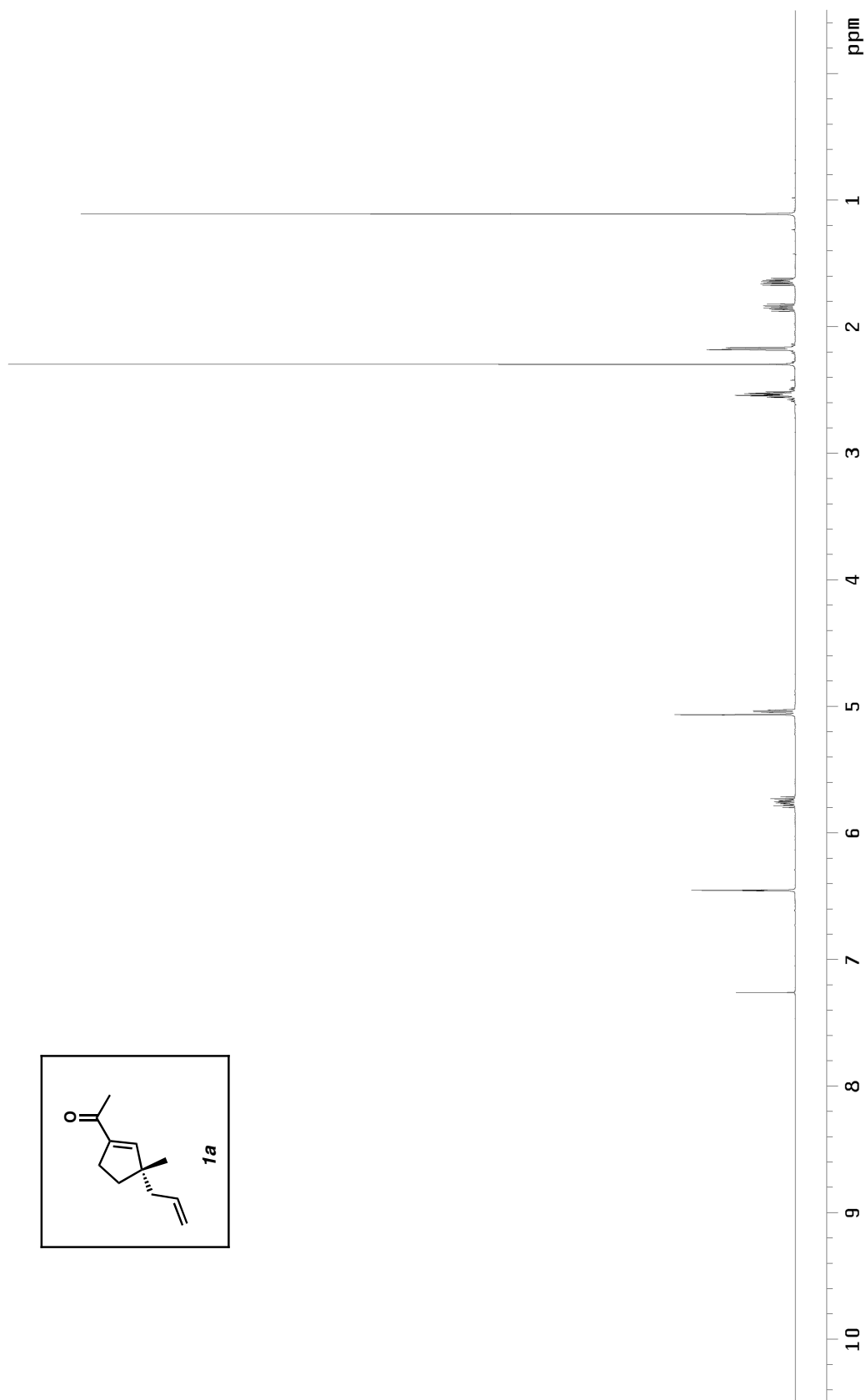


Figure SI-49A. ¹H NMR (500 MHz, CDCl₃) of compound **1a**.

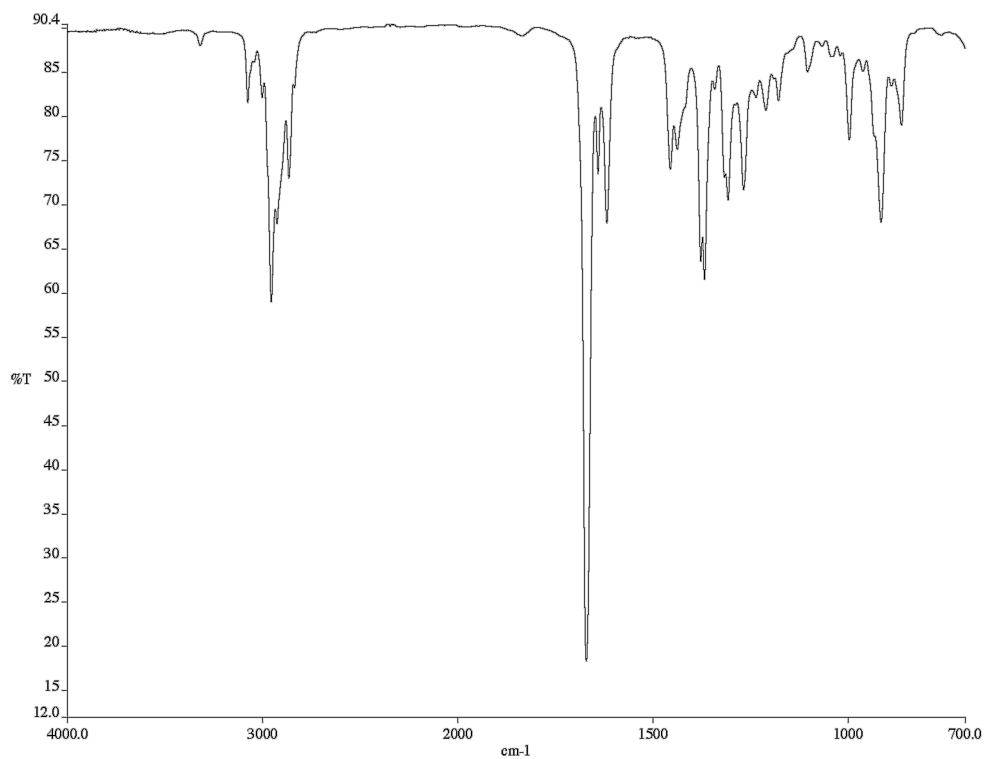


Figure SI-49B. Infrared spectrum (thin film/NaCl) of compound **1a**.

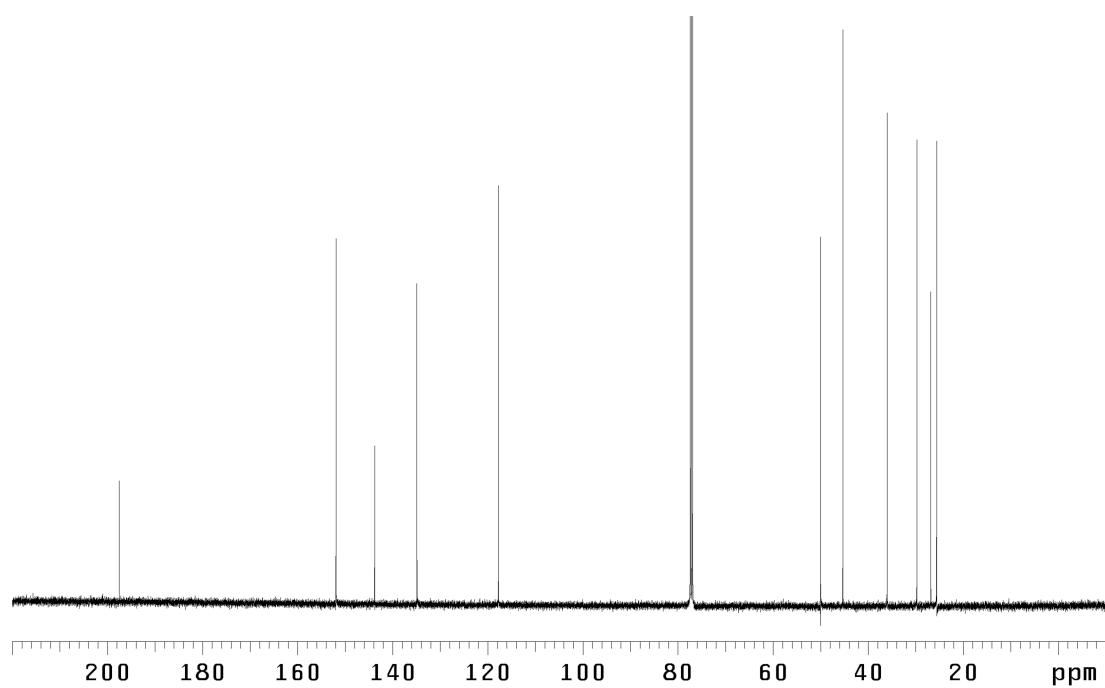


Figure SI-49C. ¹³C NMR (125 MHz, CDCl₃) of compound **1a**.

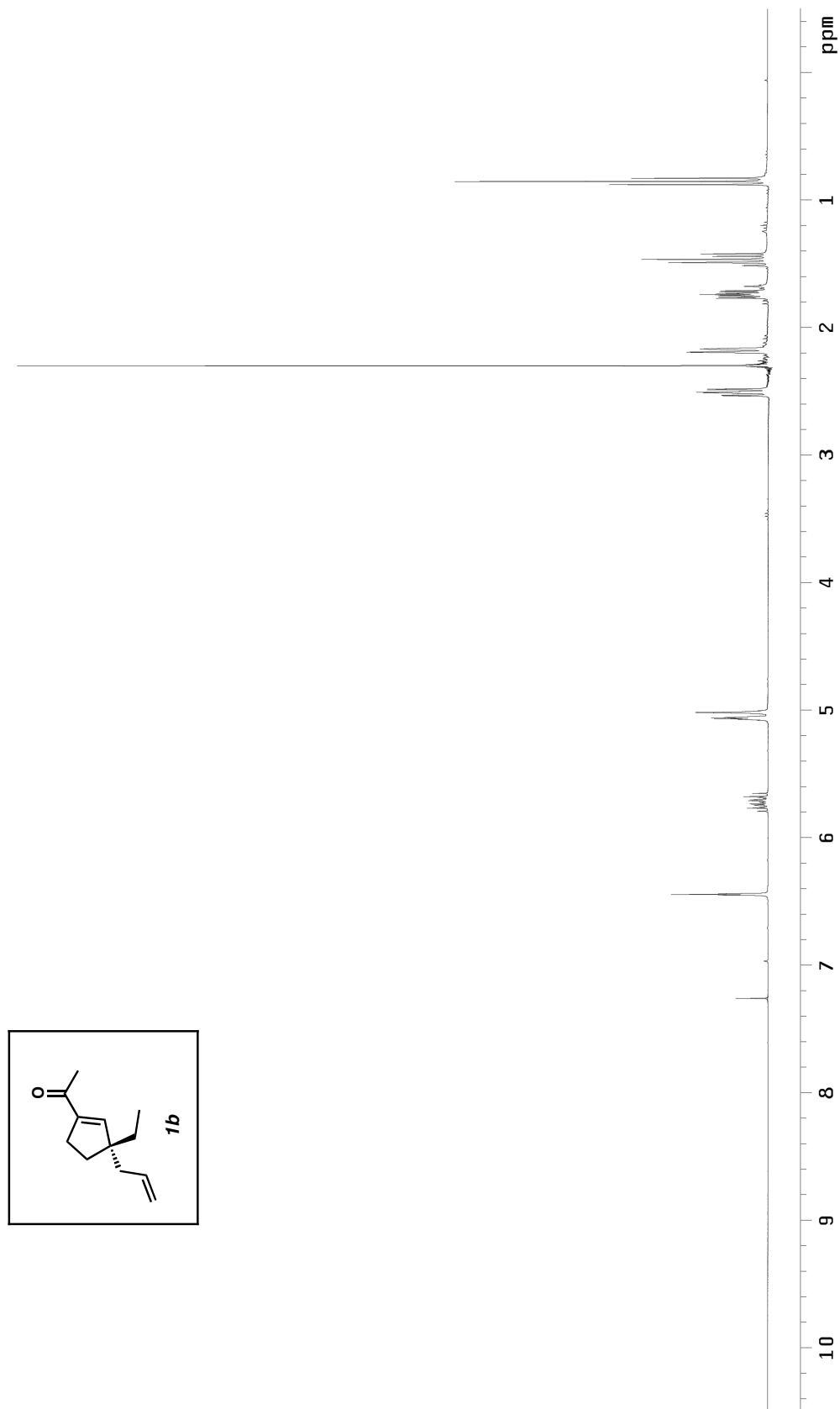


Figure SI-50A. ¹H NMR (300 MHz, CDCl₃) of compound **1b**.

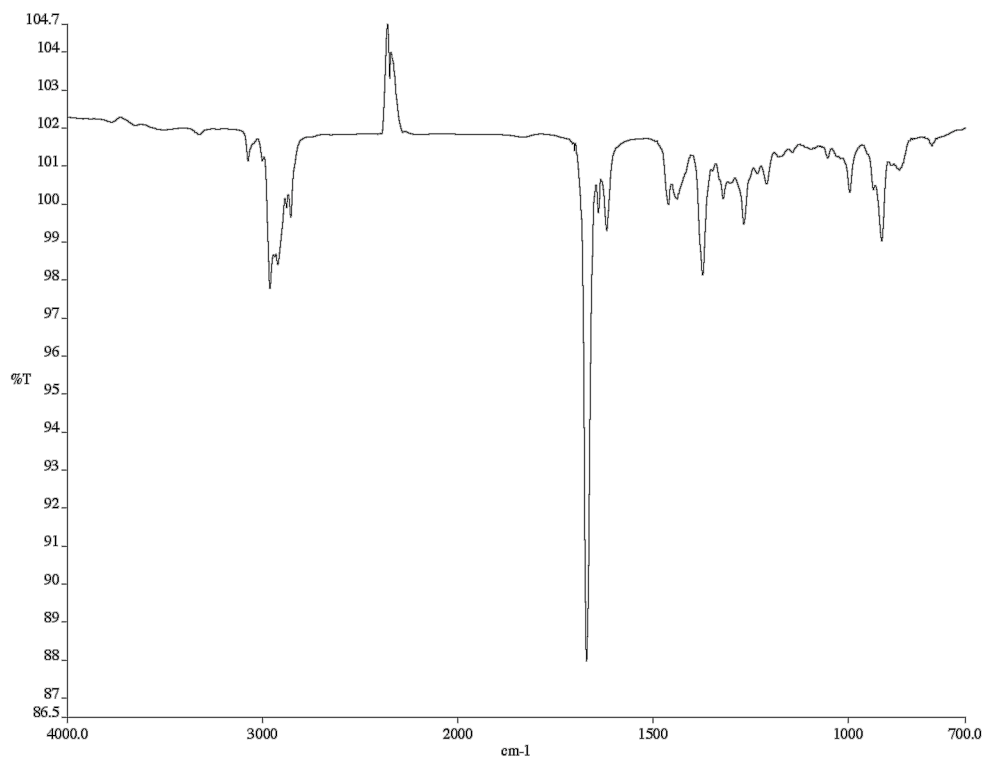


Figure SI-50B. Infrared spectrum (thin film/NaCl) of compound **1b**.

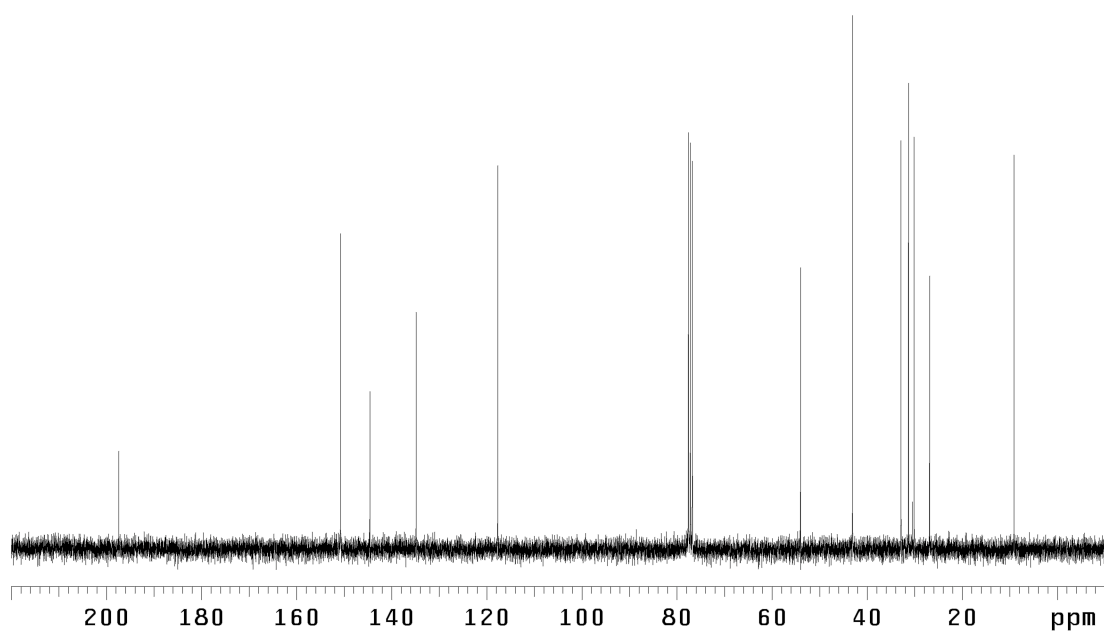


Figure SI-50C. ¹³C NMR (75 MHz, CDCl₃) of compound **1b**.

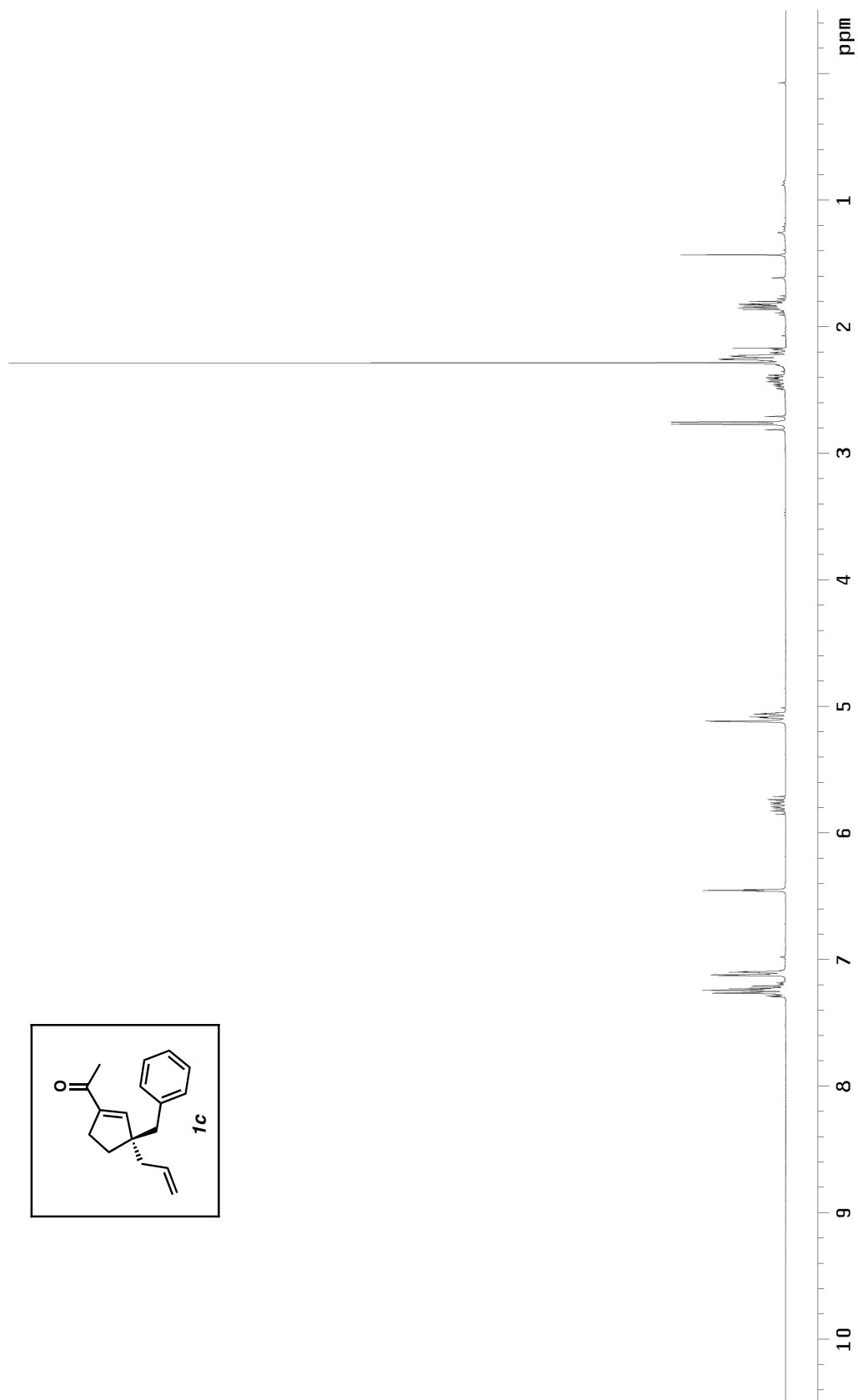


Figure SI-51A. ¹H NMR (300 MHz, CDCl₃) of compound **1c**.

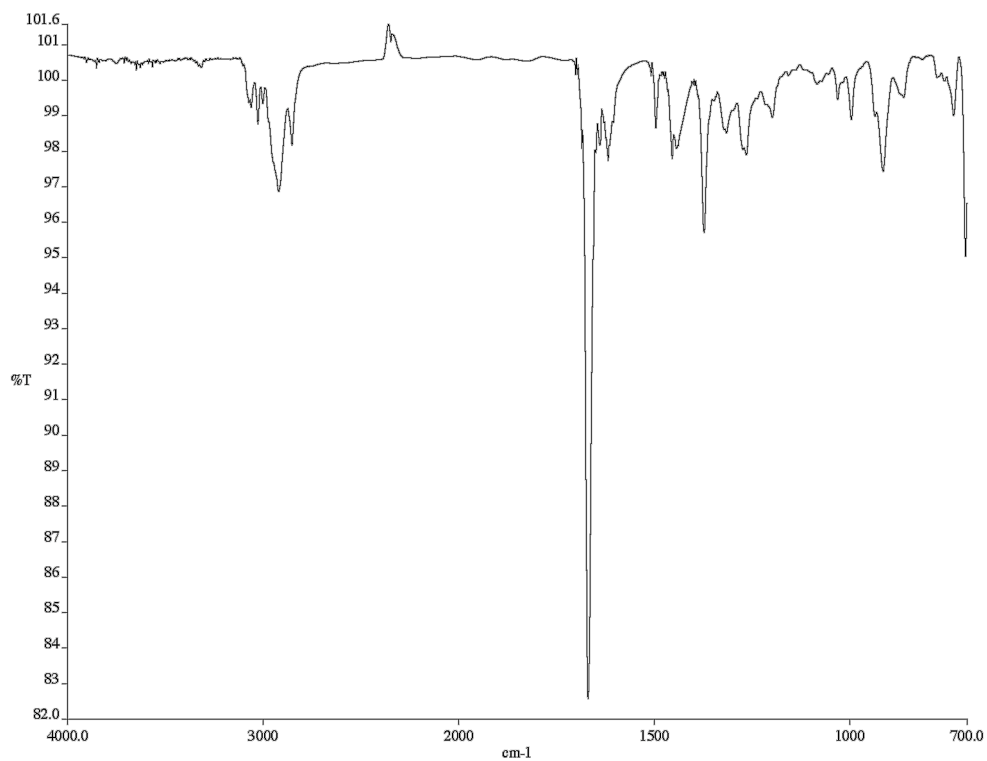


Figure SI-51B. Infrared spectrum (thin film/NaCl) of compound **1c**.

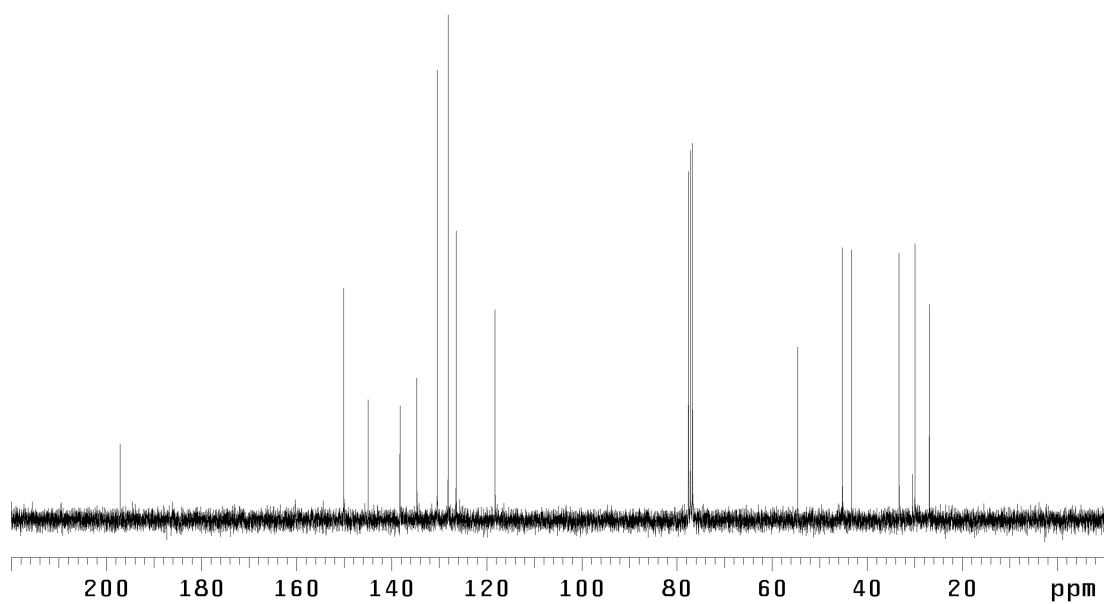


Figure SI-51C. ¹³C NMR (75 MHz, CDCl₃) of compound **1c**.

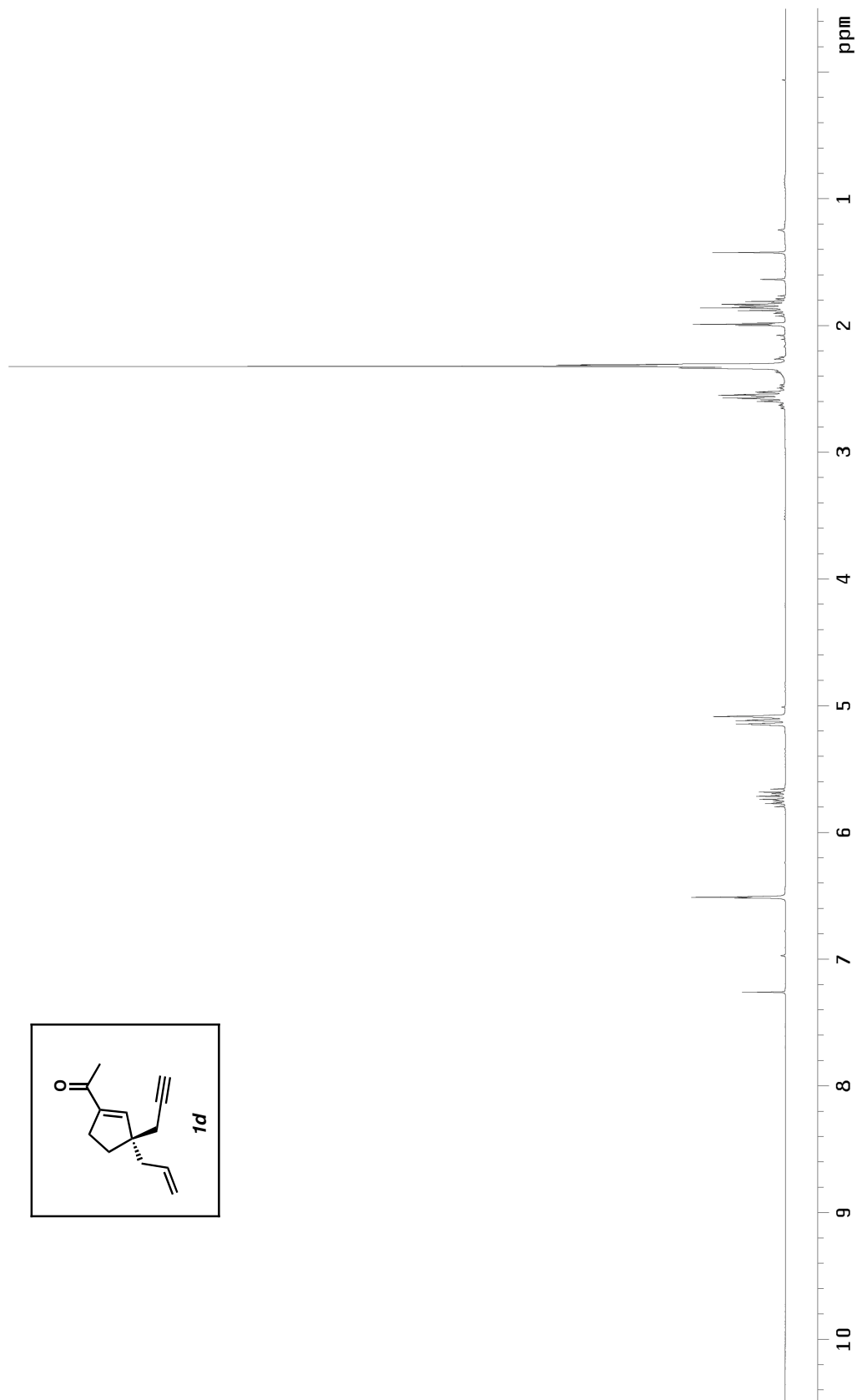


Figure SI-52A. ¹H NMR (300 MHz, CDCl₃) of compound **1d**.

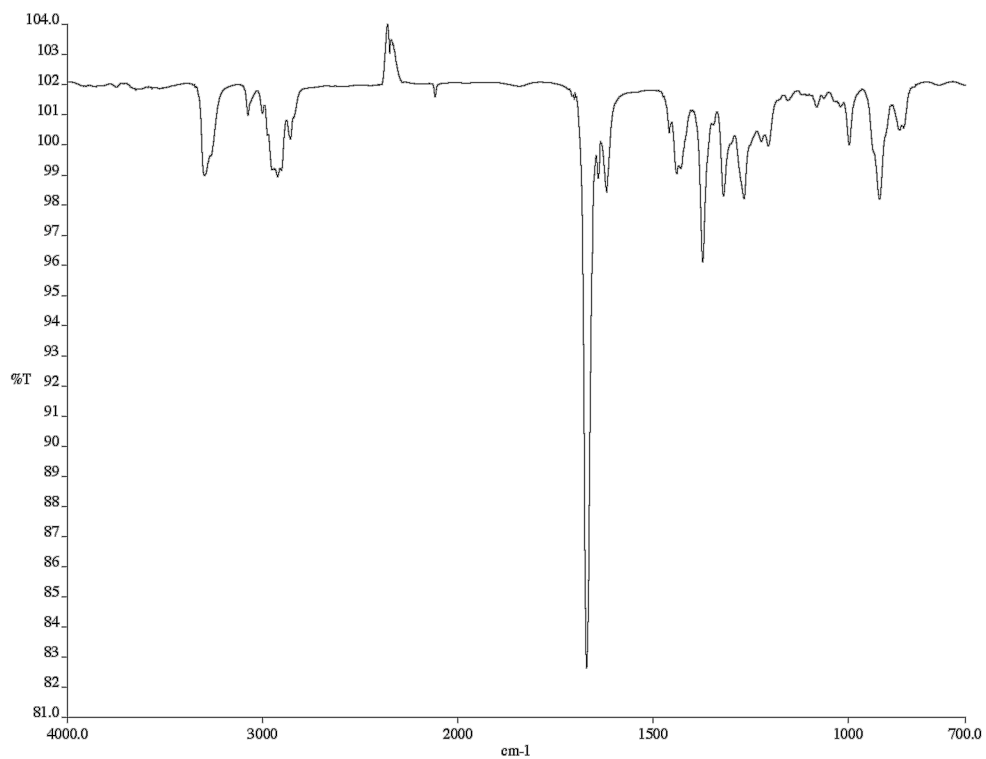


Figure SI-52B. Infrared spectrum (thin film/NaCl) of compound **1d**.

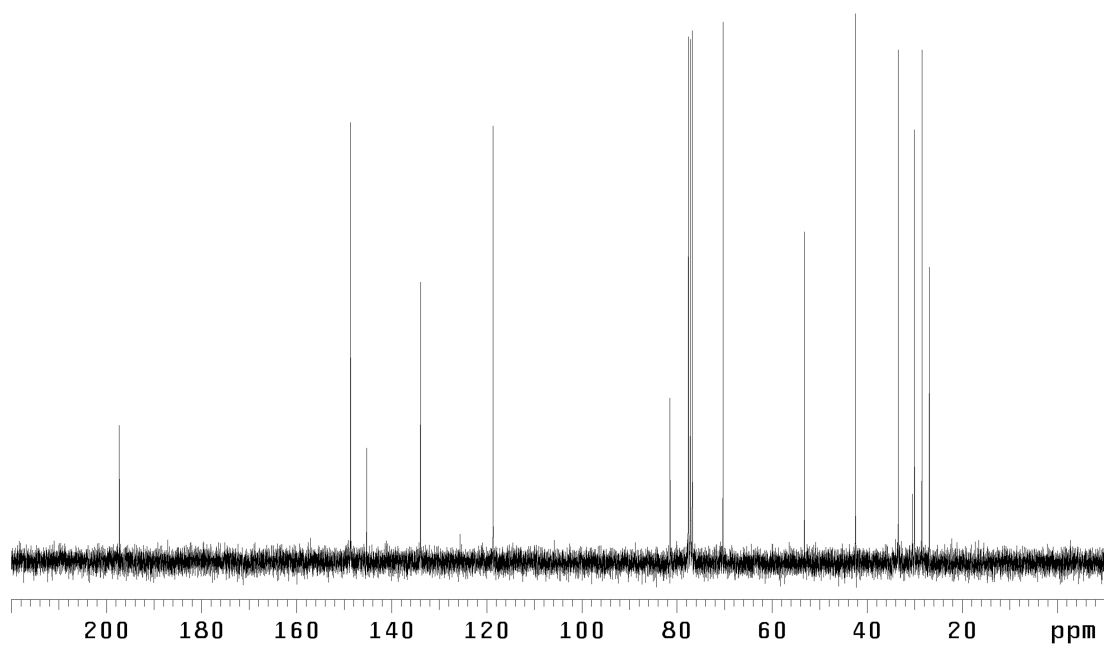


Figure SI-52C. ¹³C NMR (75 MHz, CDCl₃) of compound **1d**.

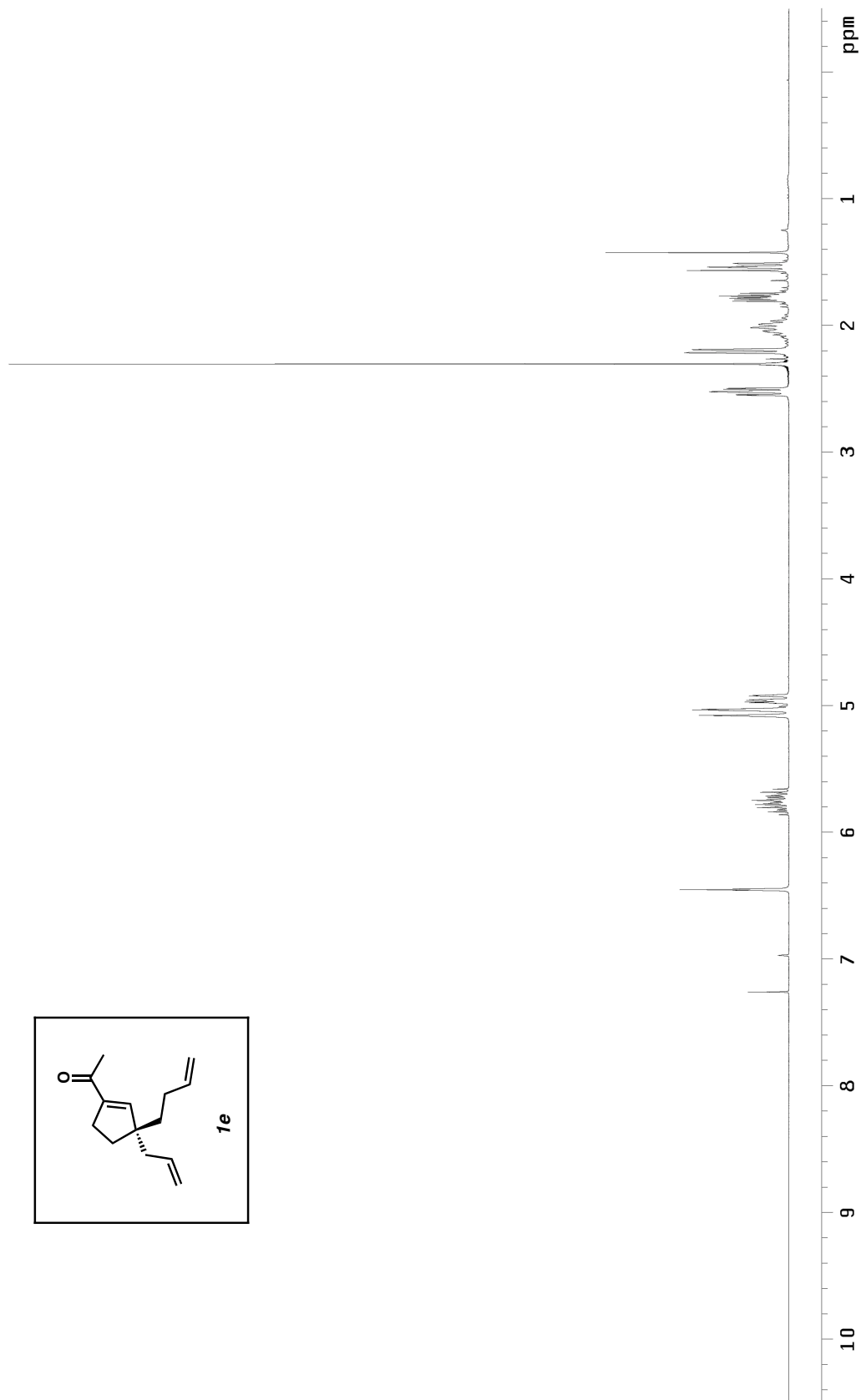


Figure SI-53A. ¹H NMR (300 MHz, CDCl₃) of compound **1e**.

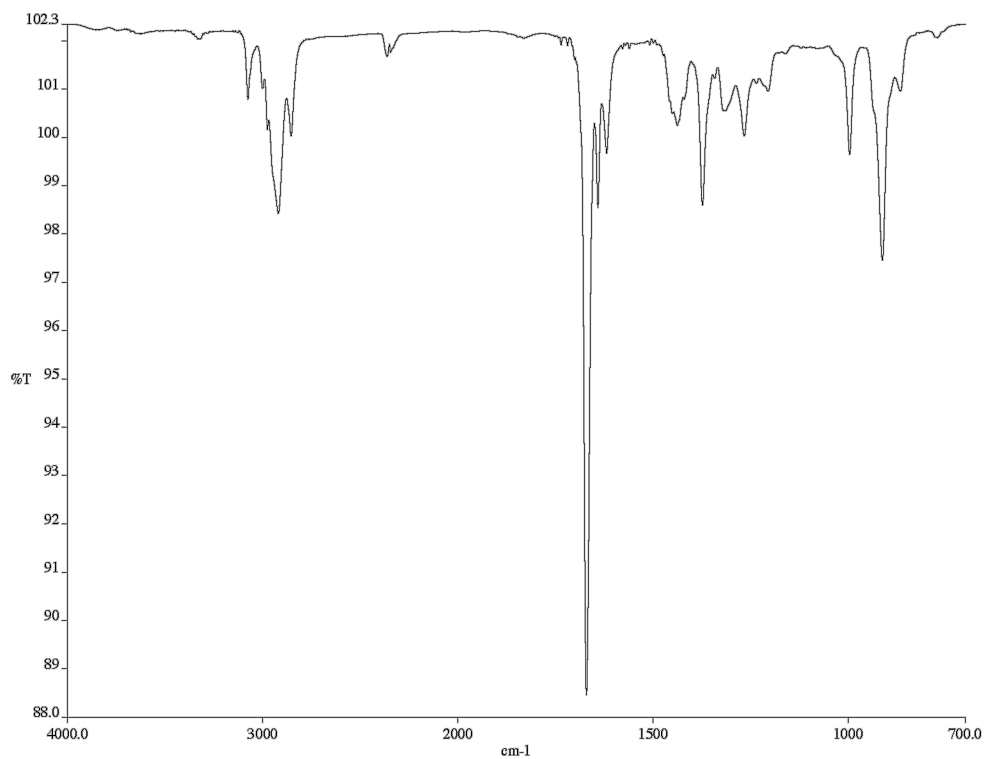


Figure SI-53B. Infrared spectrum (thin film/NaCl) of compound **1e**.

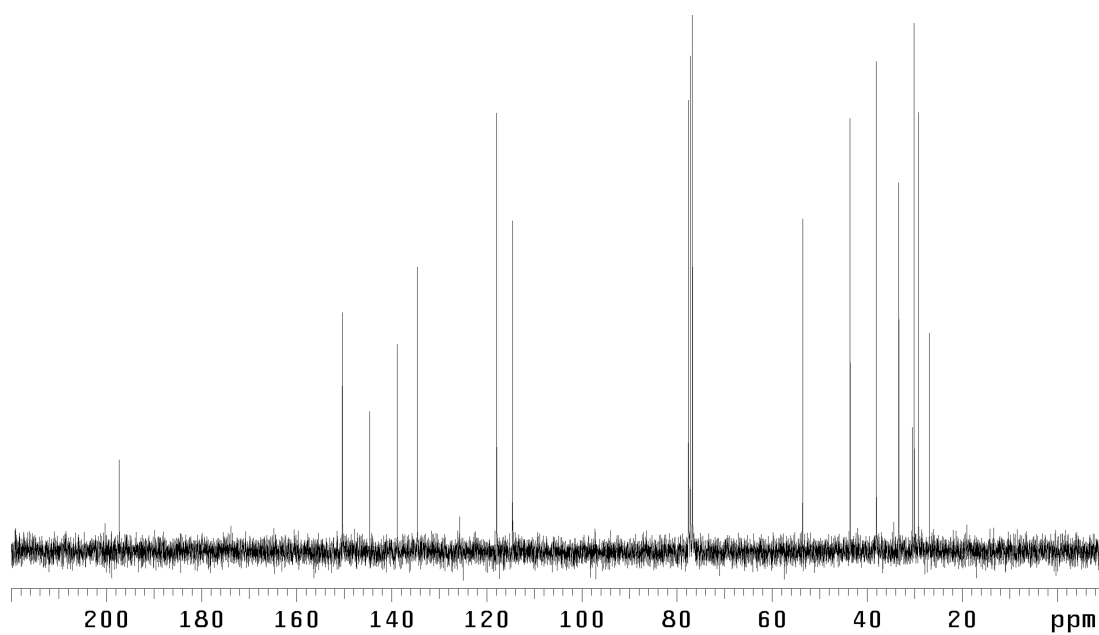


Figure SI-53C. ¹³C NMR (75 MHz, CDCl₃) of compound **1e**.

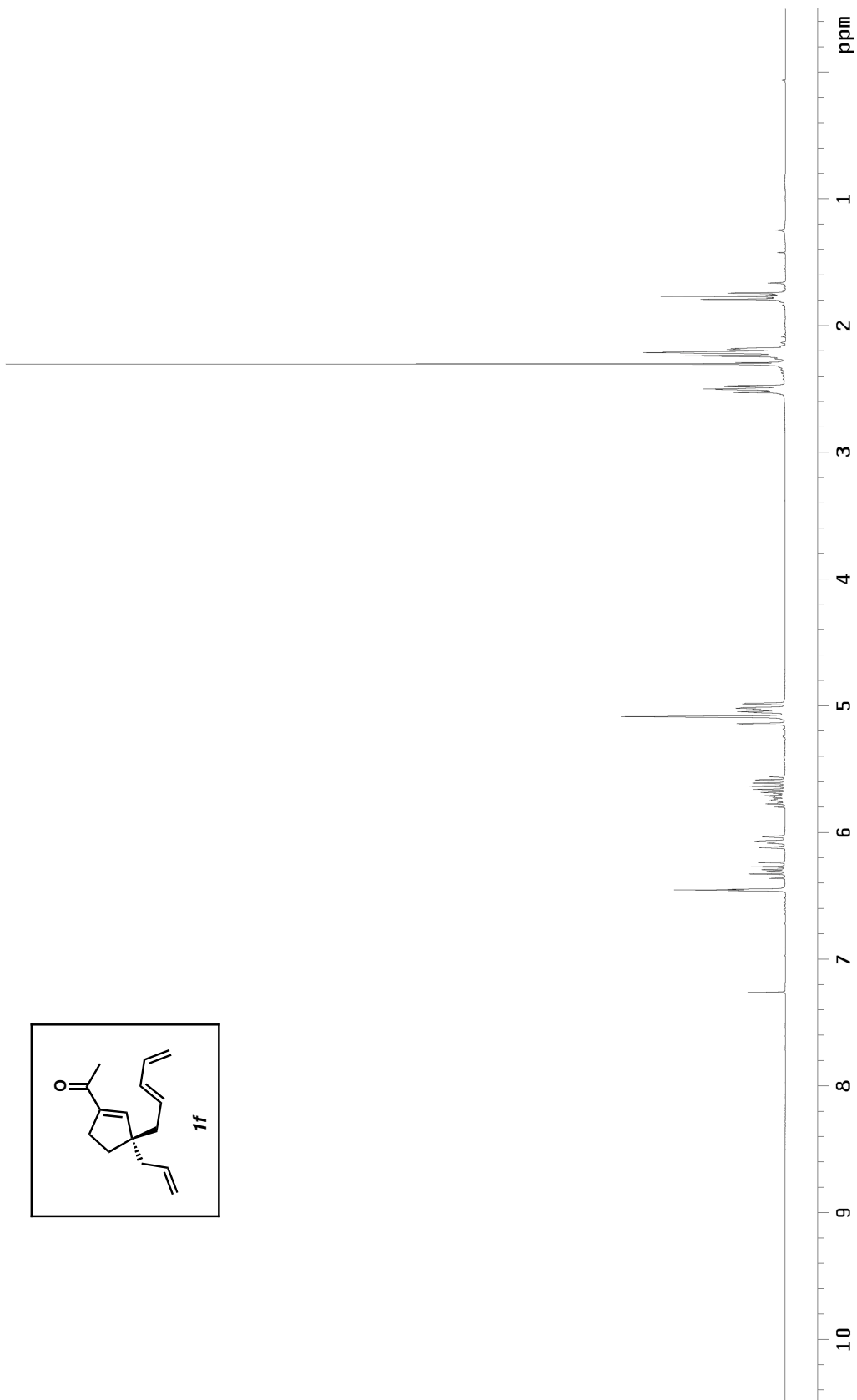


Figure SI-54A. ¹H NMR (300 MHz, CDCl₃) of compound **1f**.

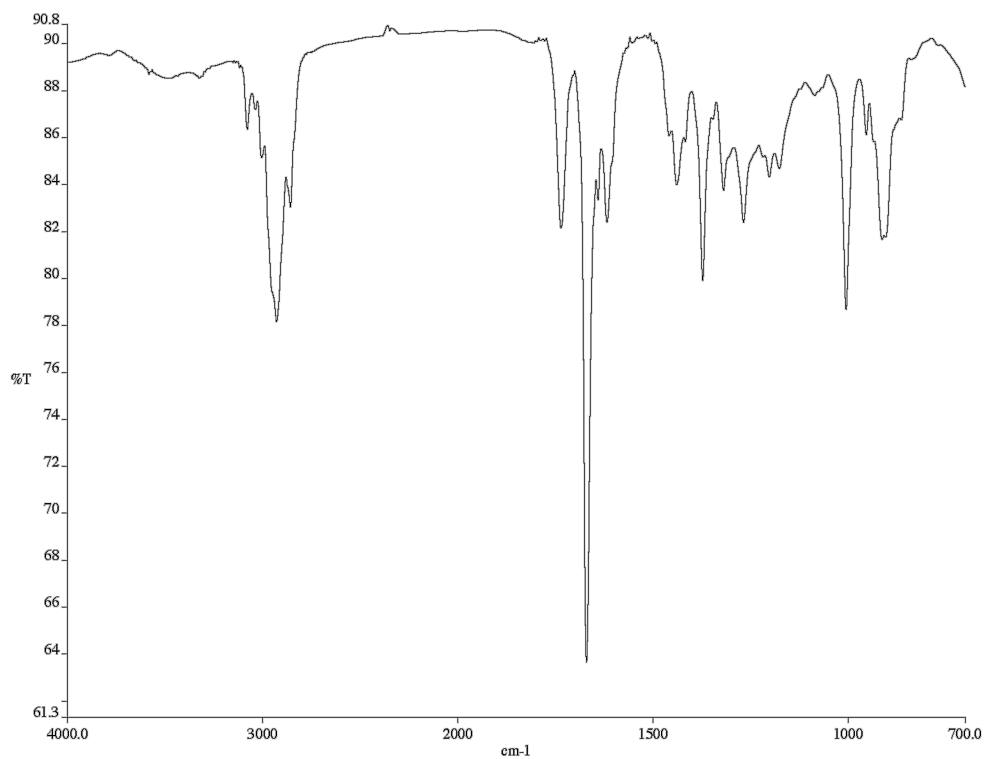


Figure SI-54B. Infrared spectrum (thin film/NaCl) of compound **1f**.

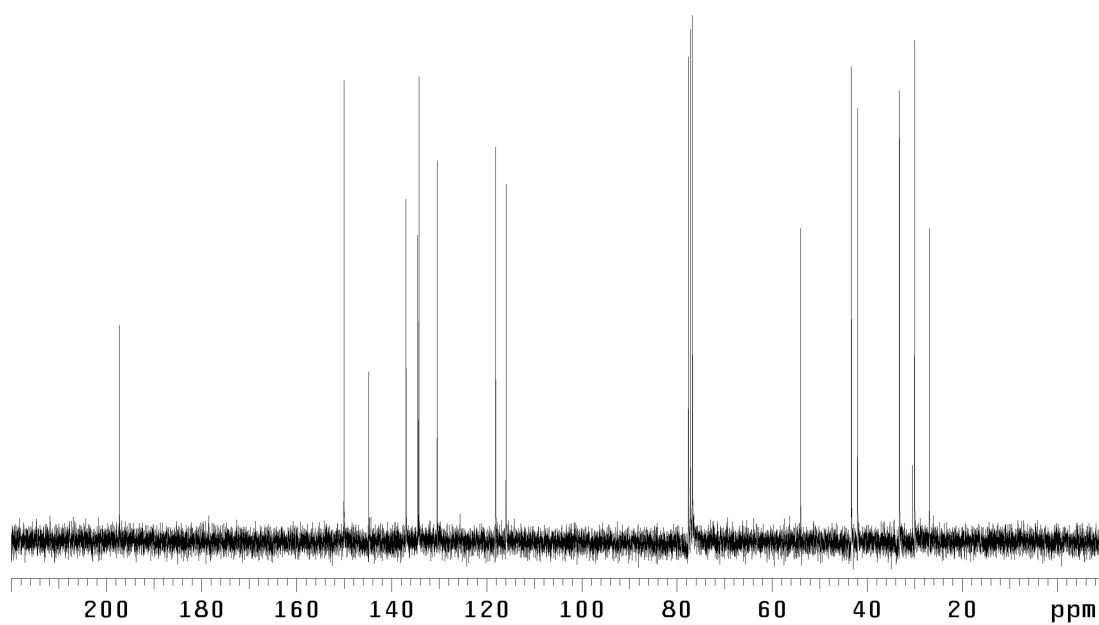


Figure SI-54C. ¹³C NMR (75 MHz, CDCl₃) of compound **1f**.

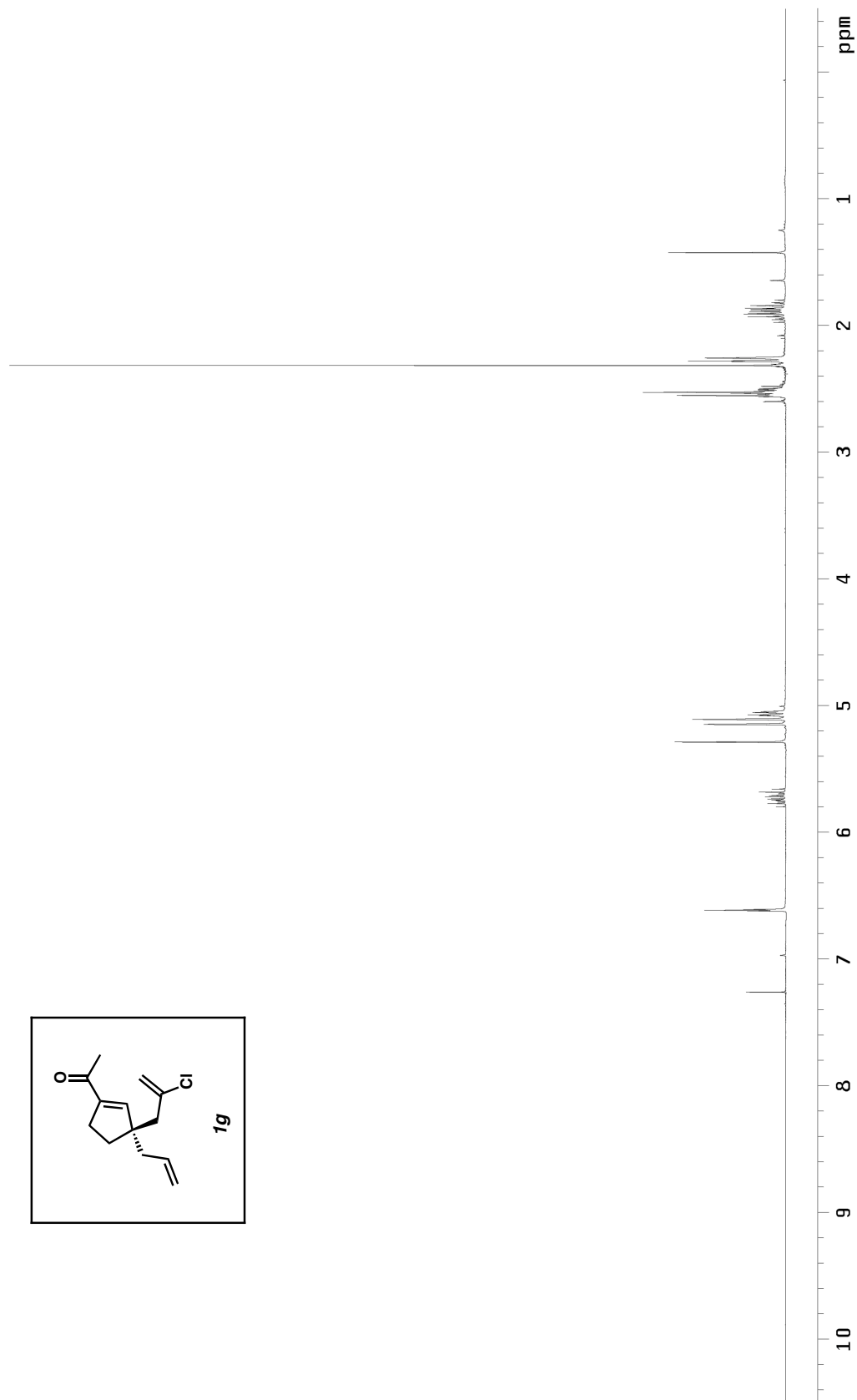


Figure SI-55A. ¹H NMR (300 MHz, CDCl₃) of compound **1g**.

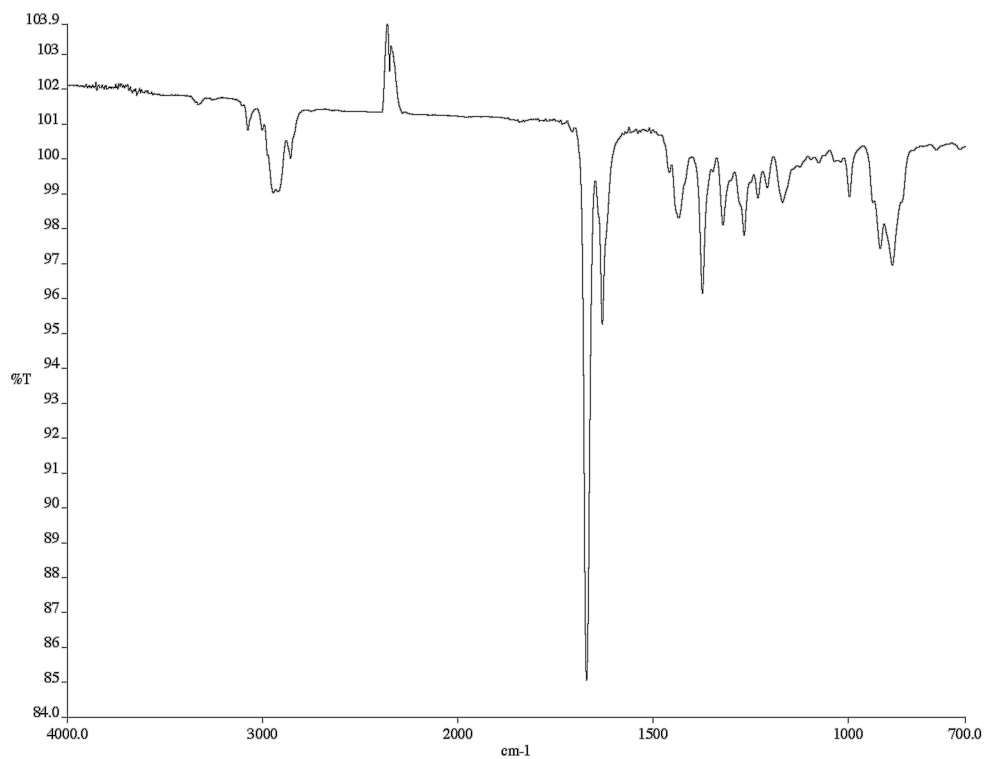


Figure SI-55B. Infrared spectrum (thin film/NaCl) of compound **1g**.

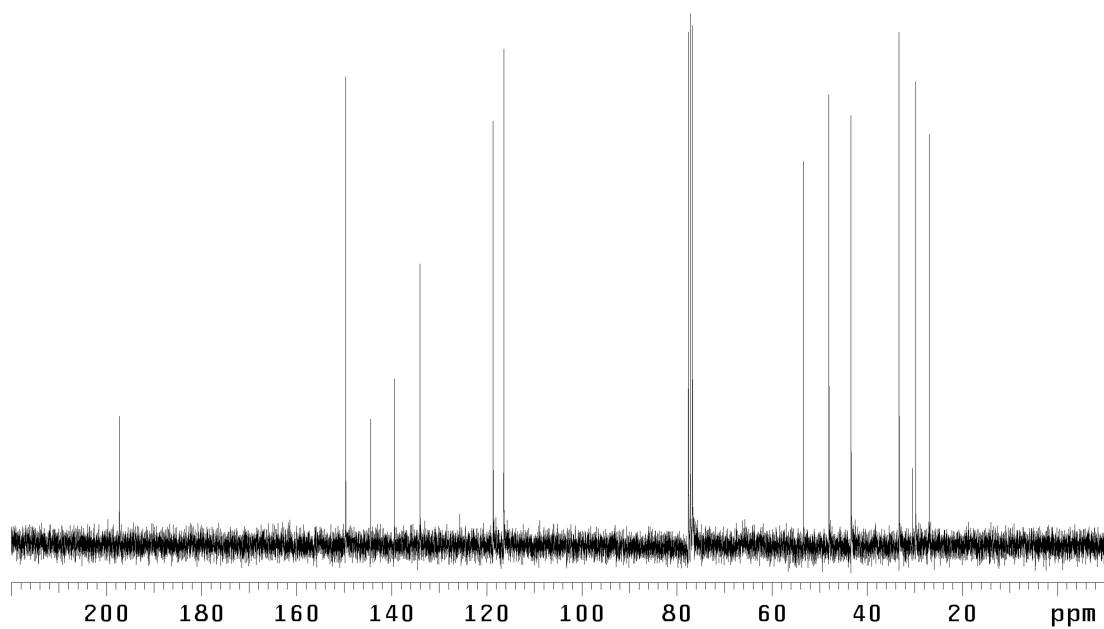


Figure SI-55C. ¹³C NMR (75 MHz, CDCl₃) of compound **1g**.

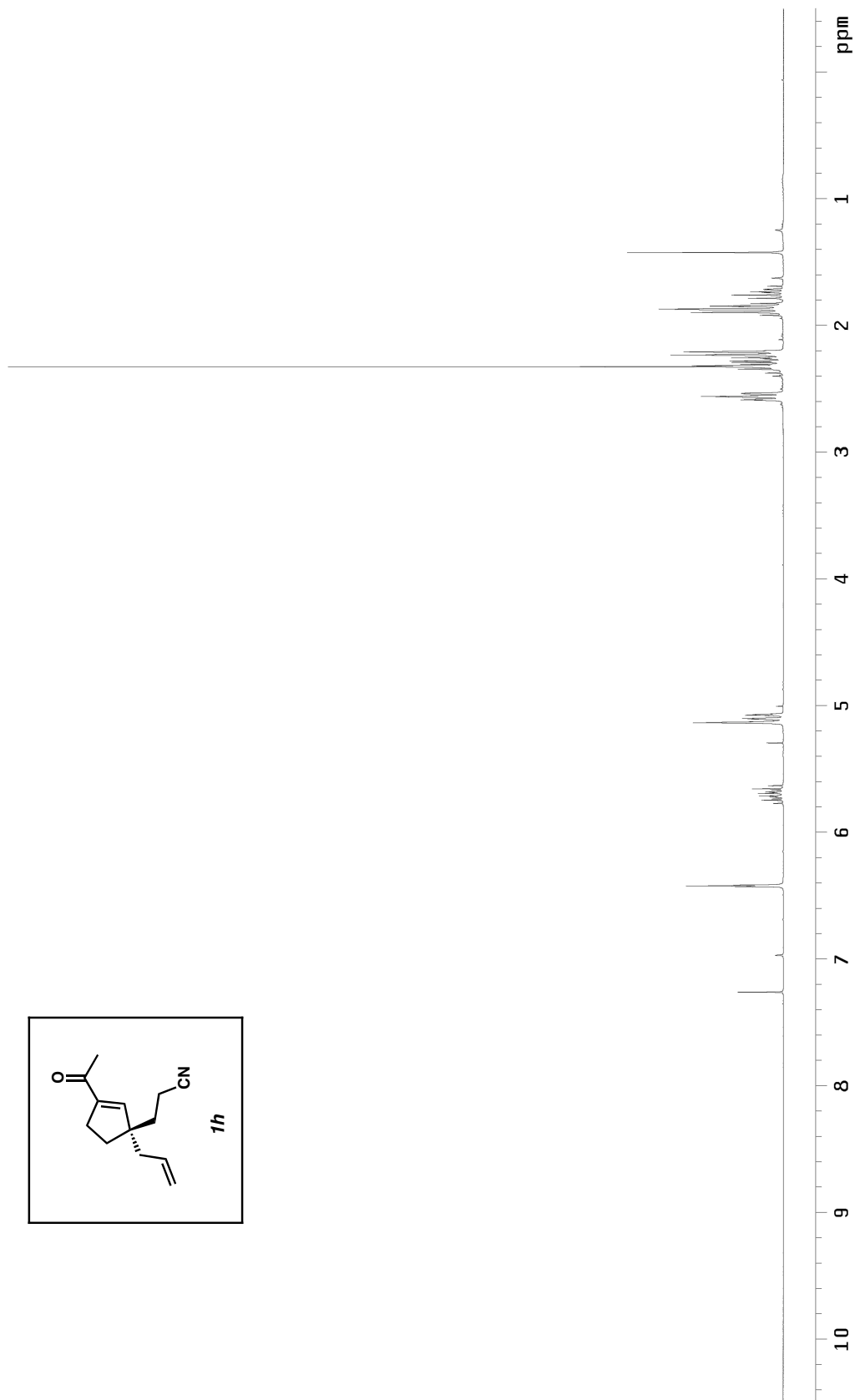


Figure SI-56A. ¹H NMR (300 MHz, CDCl₃) of compound **1h**.

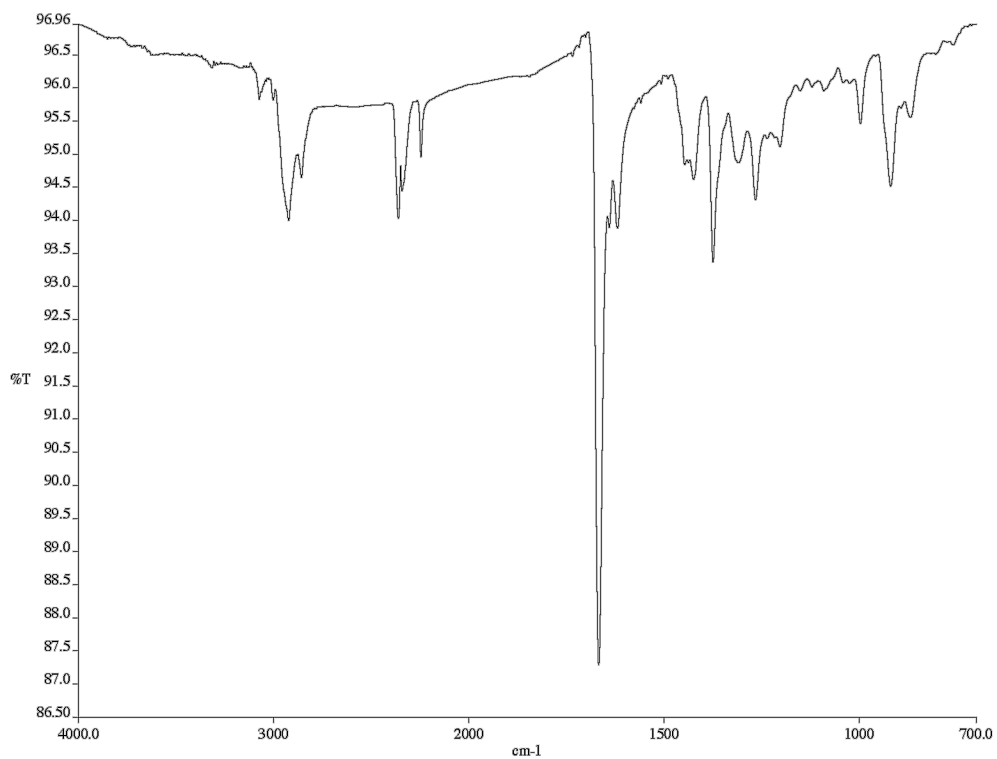


Figure SI-56B. Infrared spectrum (thin film/NaCl) of compound **1h**.

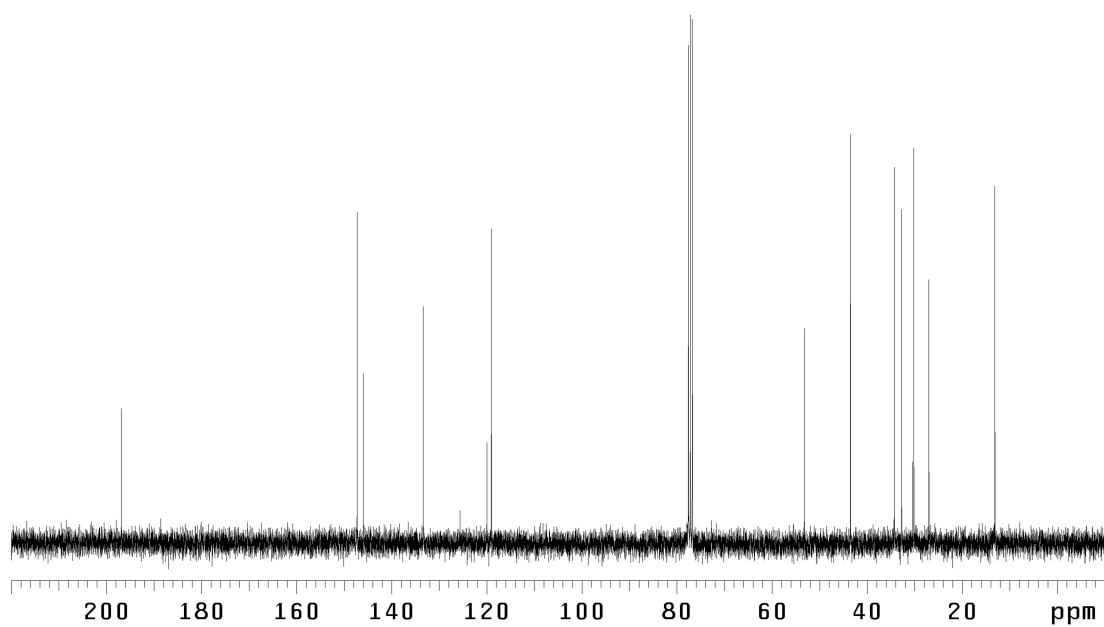


Figure SI-56C. ¹³C NMR (75 MHz, CDCl₃) of compound **1h**.

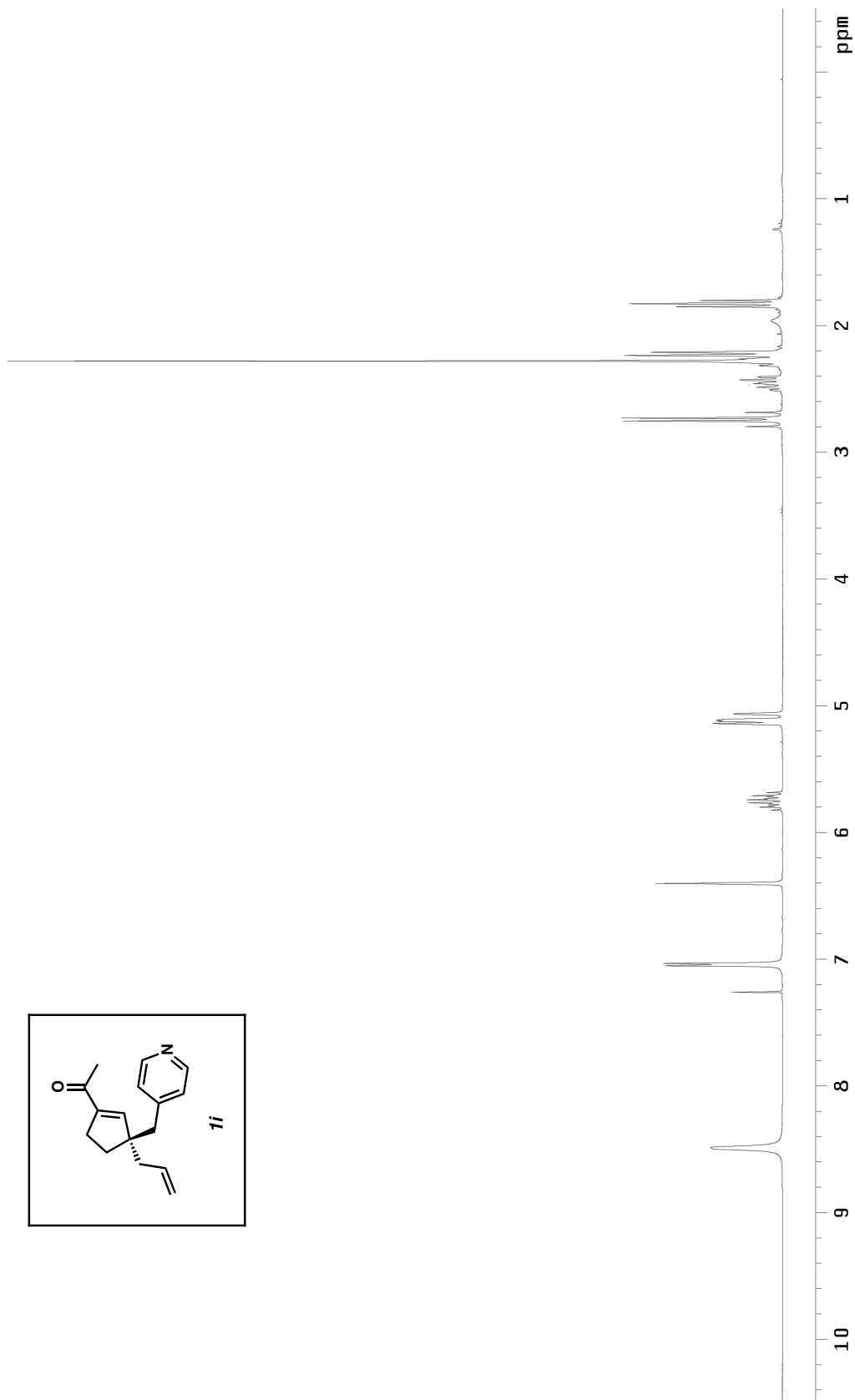


Figure SI-57A. ¹H NMR (300 MHz, CDCl₃) of compound **1i**.

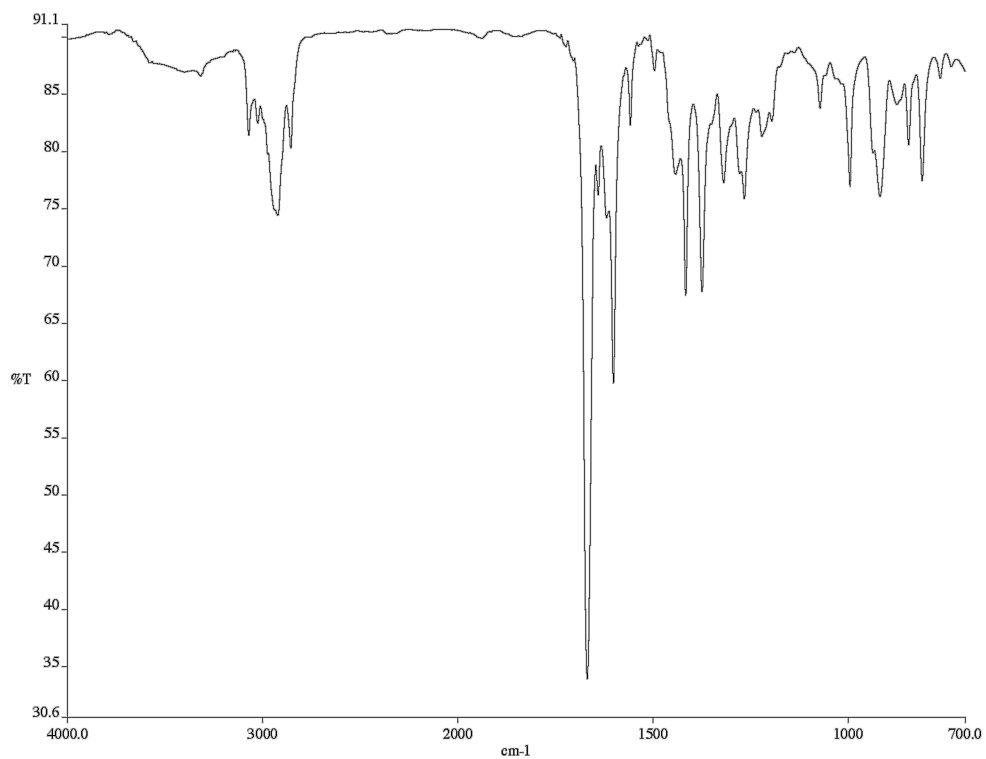


Figure SI-57B. Infrared spectrum (thin film/NaCl) of compound **1i**.

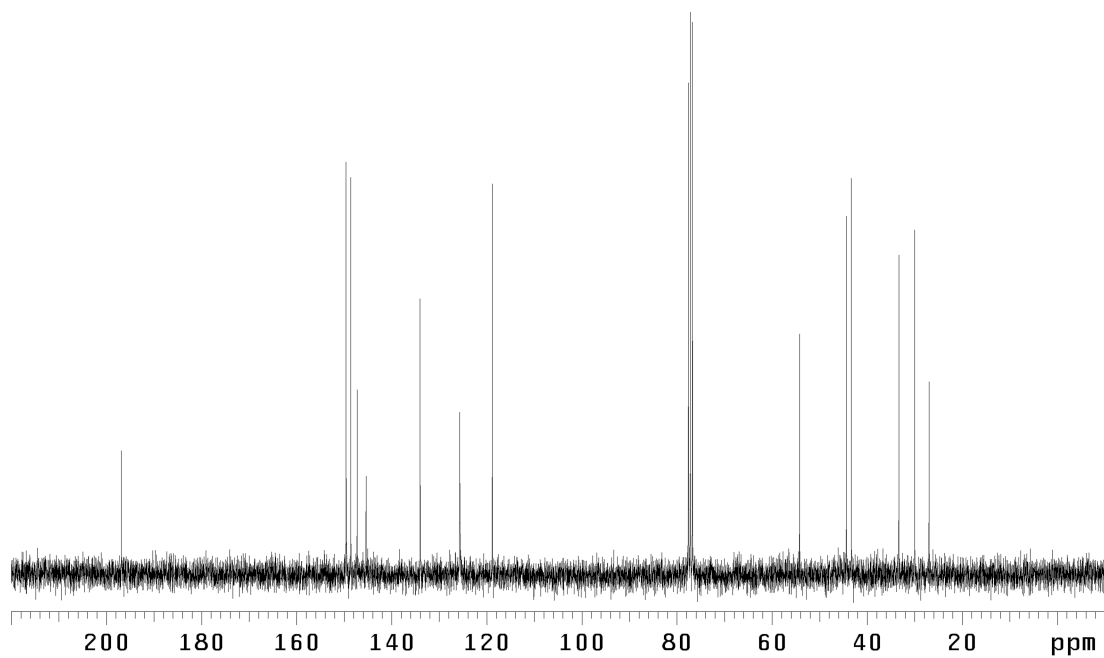


Figure SI-57C. ^{13}C NMR (75 MHz, CDCl_3) of compound **1i**.

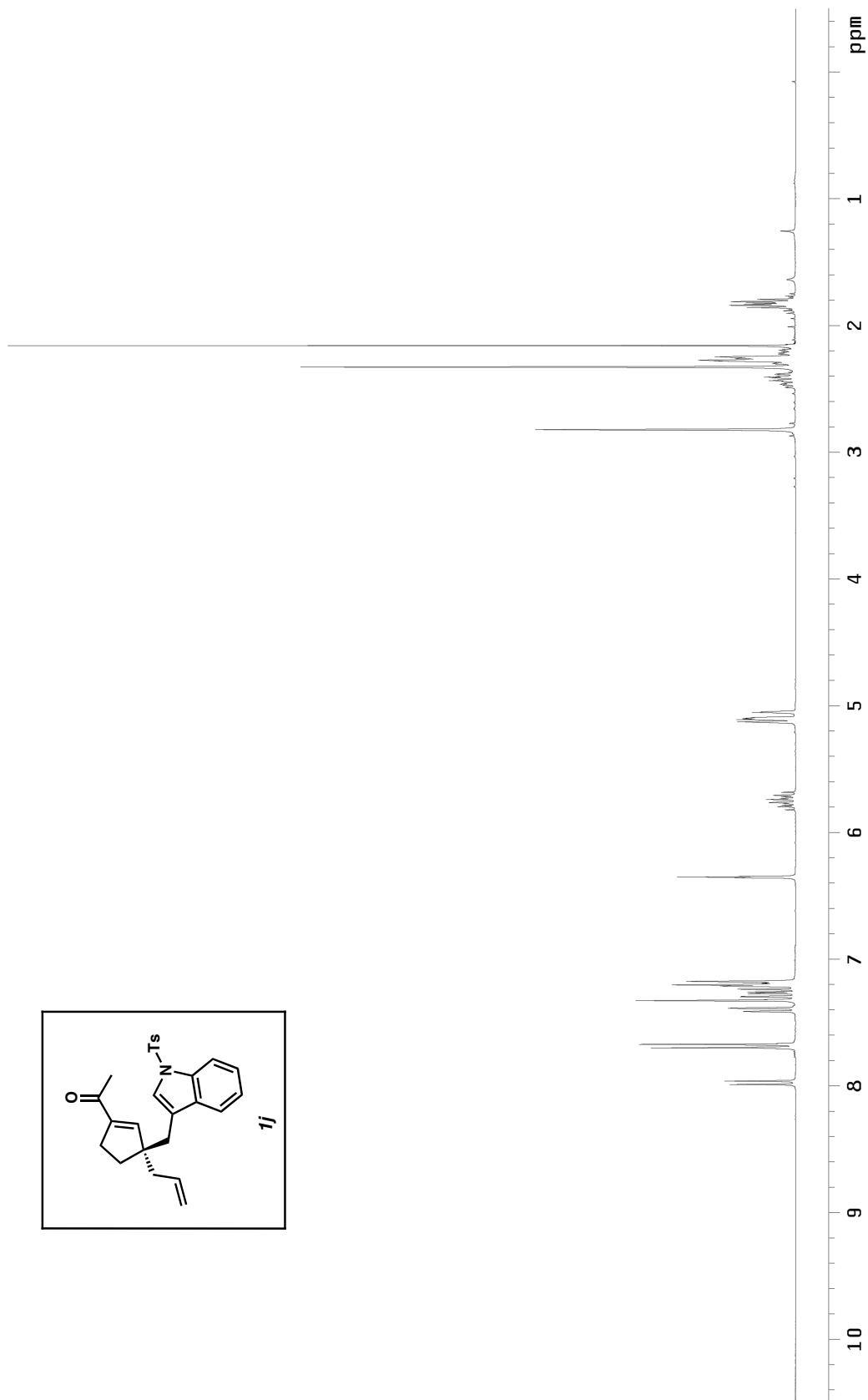


Figure SI-58A. ¹H NMR (300 MHz, CDCl₃) of compound **1j**.

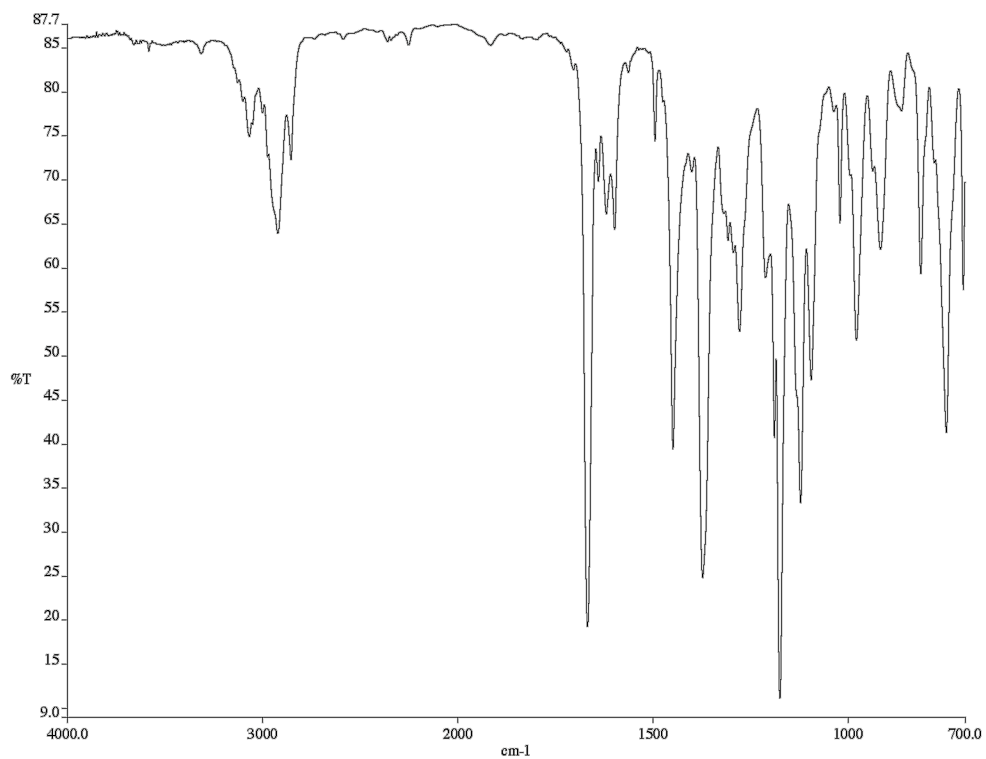


Figure SI-58B. Infrared spectrum (thin film/NaCl) of compound **1j**.

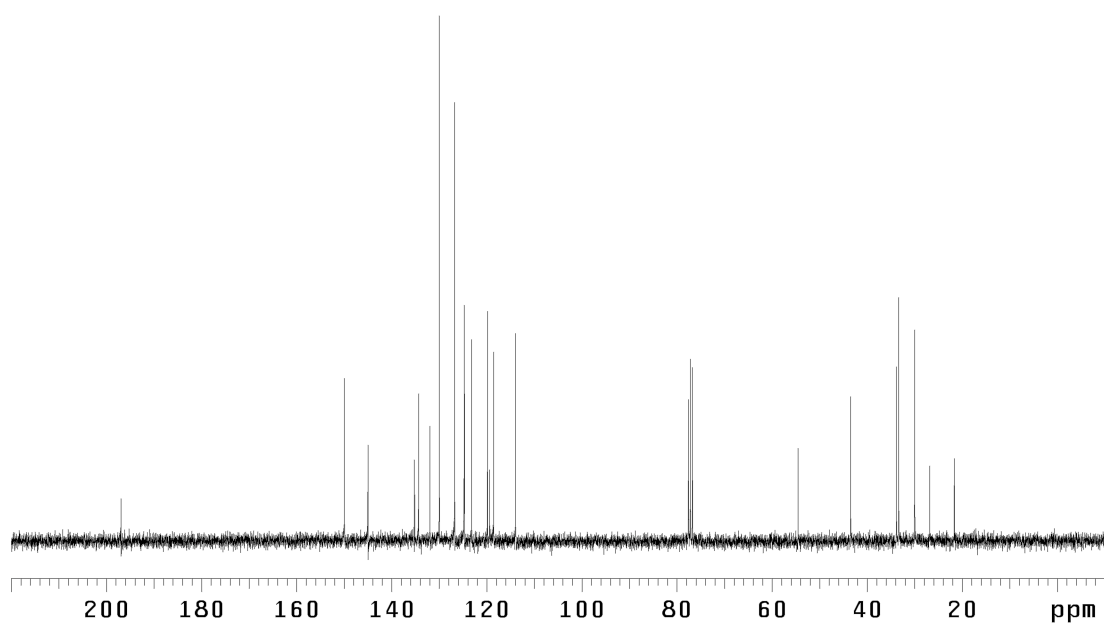


Figure SI-58C. ¹³C NMR (75 MHz, CDCl₃) of compound **1j**.

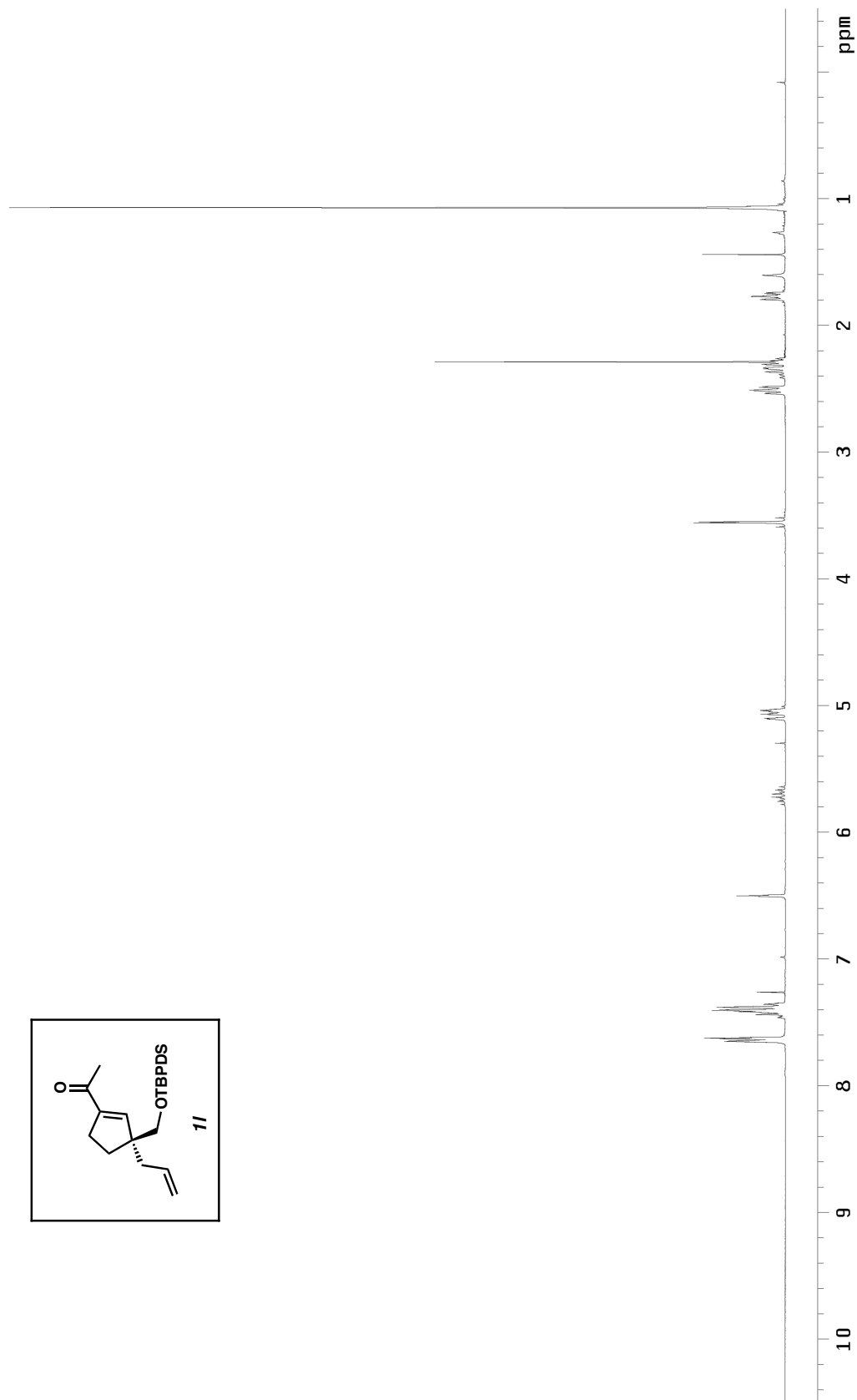


Figure SI-59A. ^1H NMR (300 MHz, CDCl_3) of compound **11**.

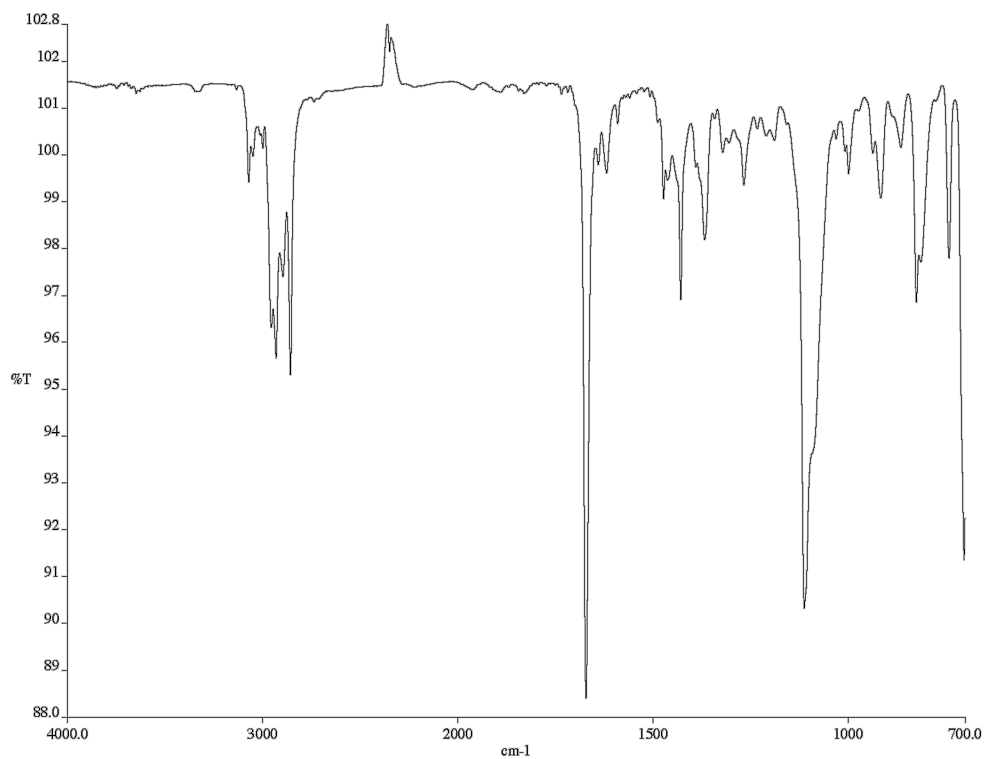


Figure SI-59B. Infrared spectrum (thin film/NaCl) of compound **11**.

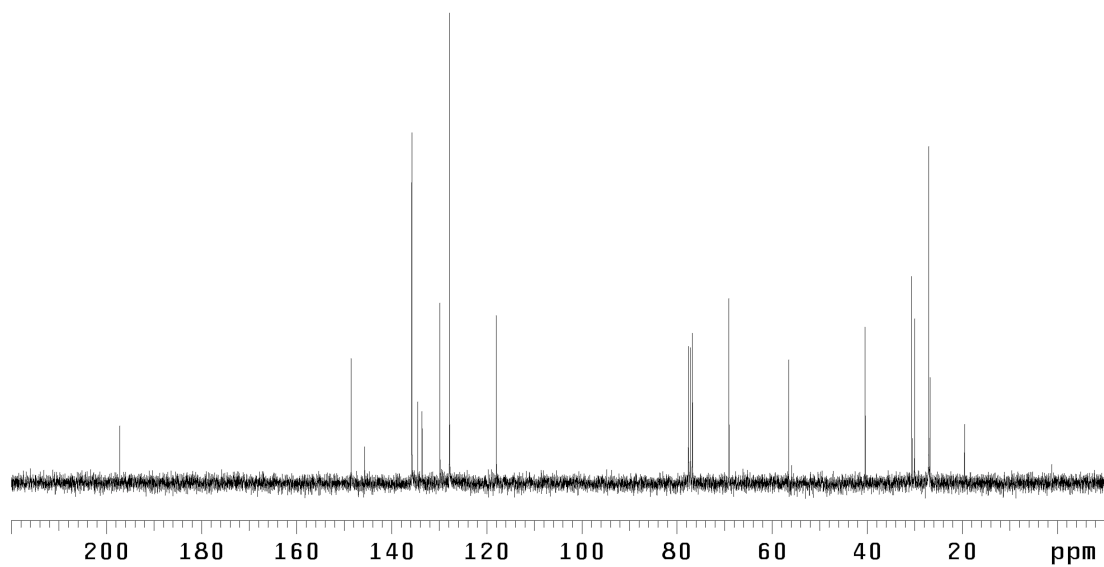


Figure SI-59C. ¹³C NMR (75 MHz, CDCl₃) of compound **11**.

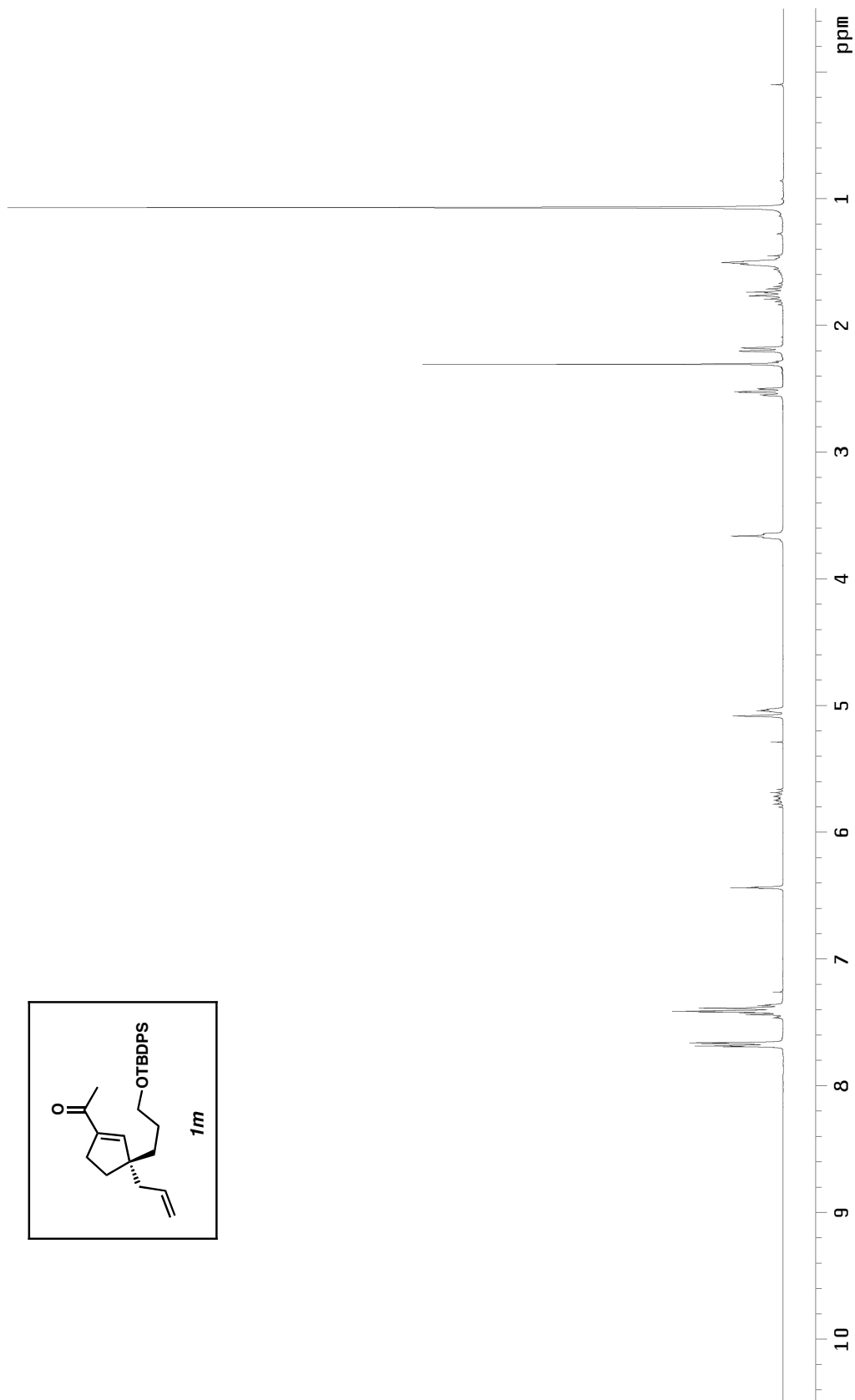


Figure SI-60A. ^1H NMR (300 MHz, CDCl_3) of compound **1m**.

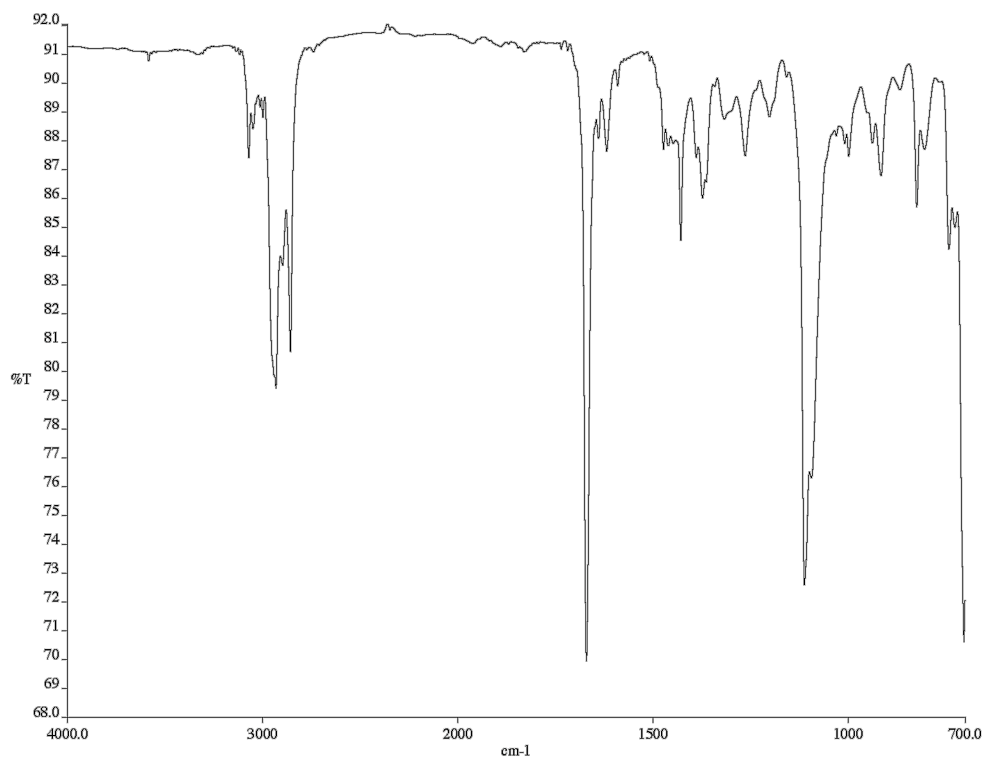


Figure SI-60B. Infrared spectrum (thin film/NaCl) of compound **1m**.

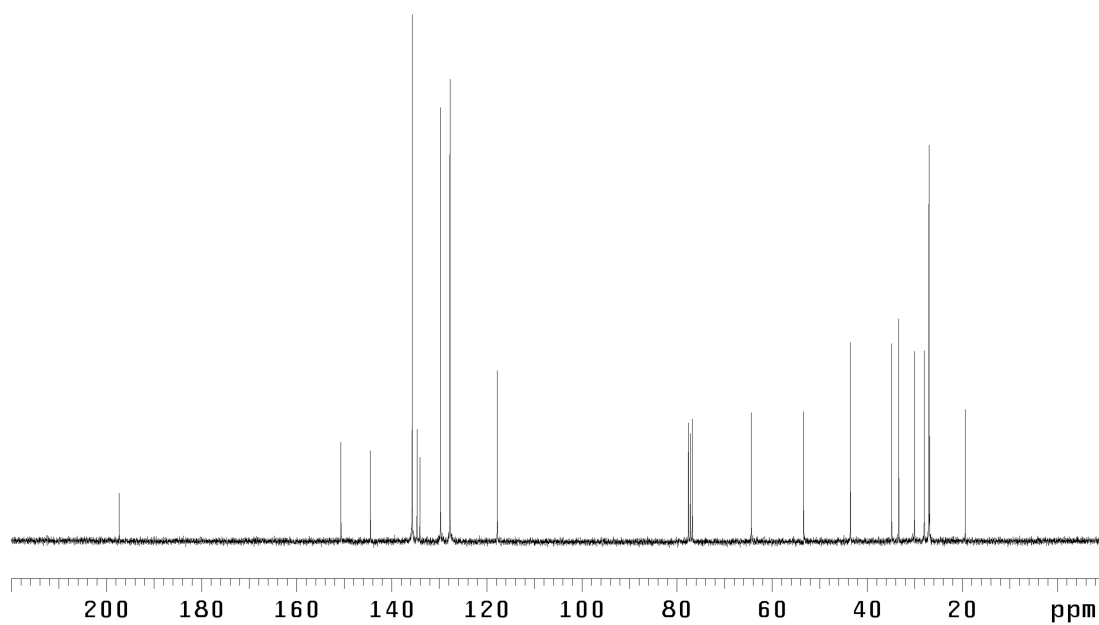


Figure SI-60C. ^{13}C NMR (75 MHz, CDCl_3) of compound **1m**.

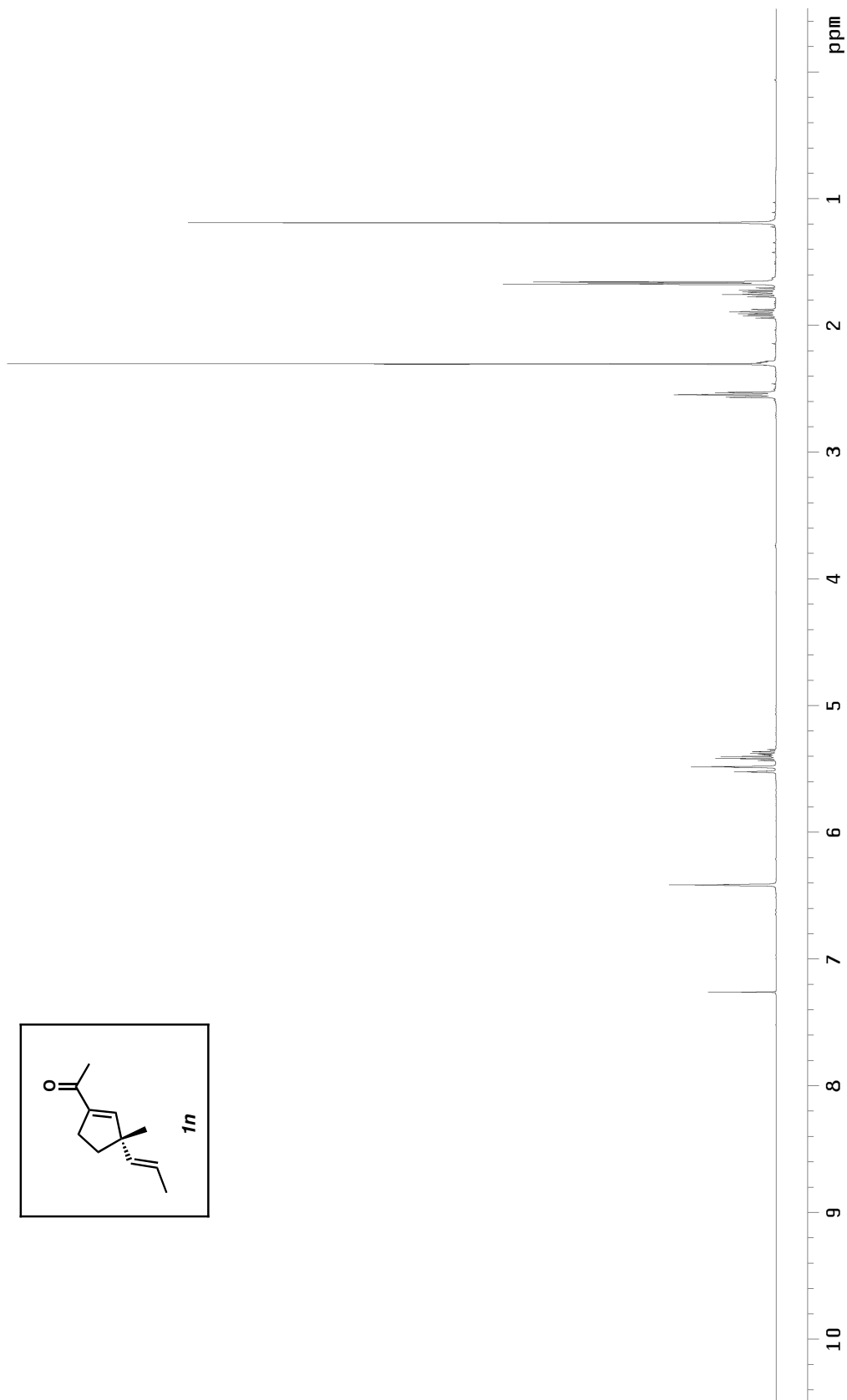


Figure SI-61A. ¹H NMR (400 MHz, CDCl₃) of compound **1n**.

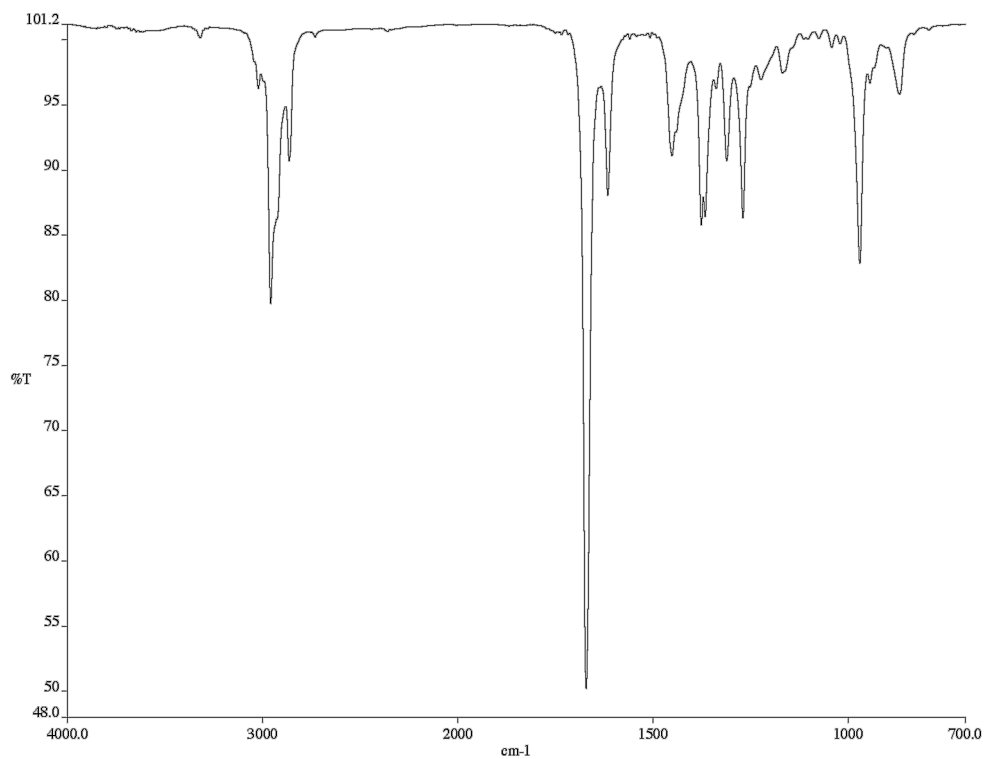


Figure SI-61B. Infrared spectrum (thin film/NaCl) of compound **1n**.

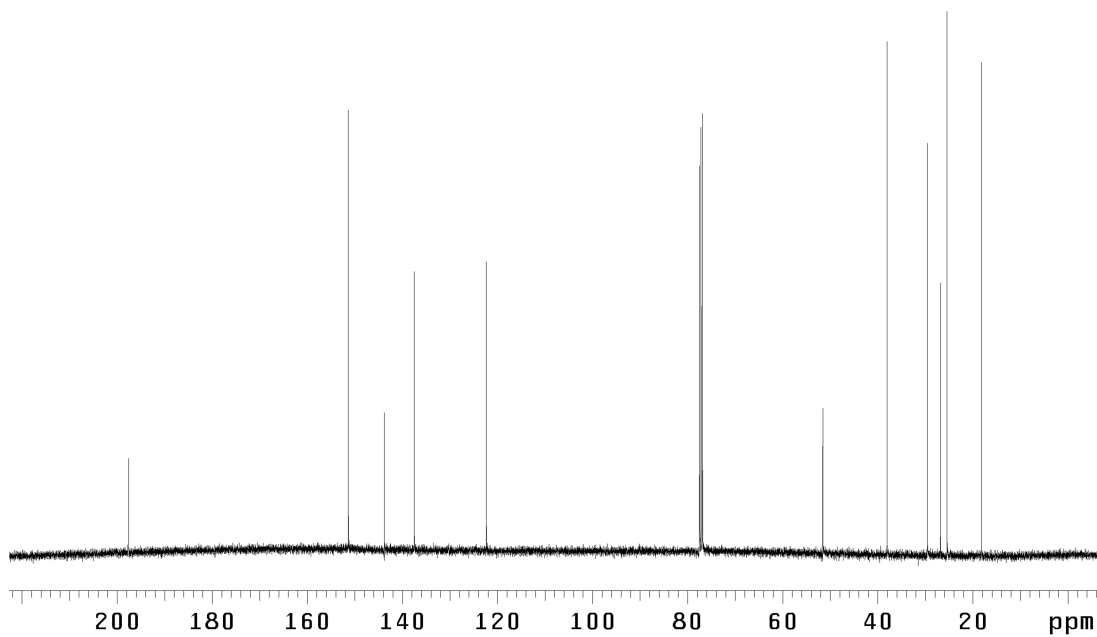


Figure SI-61C. ¹³C NMR (100 MHz, CDCl₃) of compound **1n**.

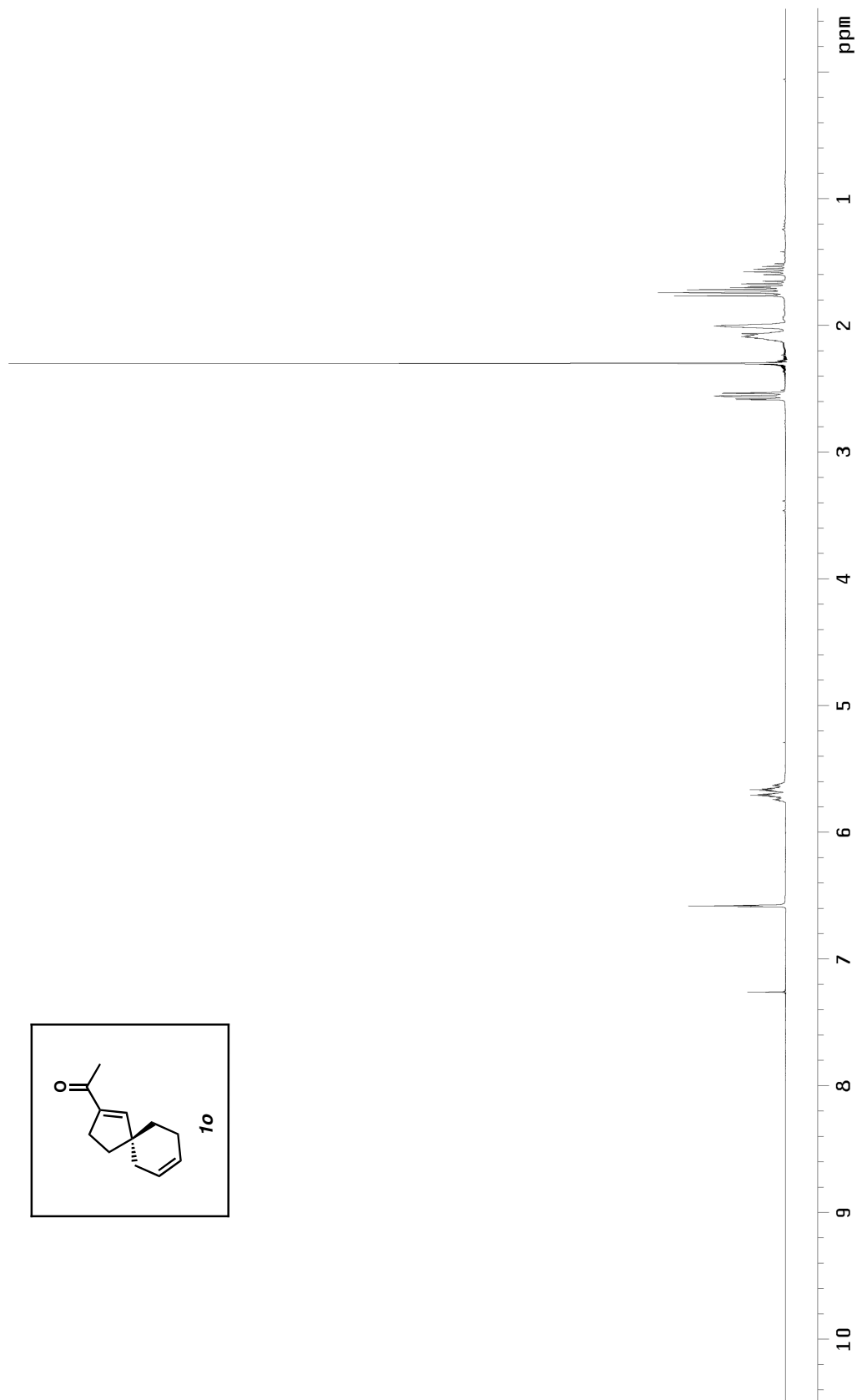


Figure SI-62A. ¹H NMR (300 MHz, CDCl₃) of compound **1o**.

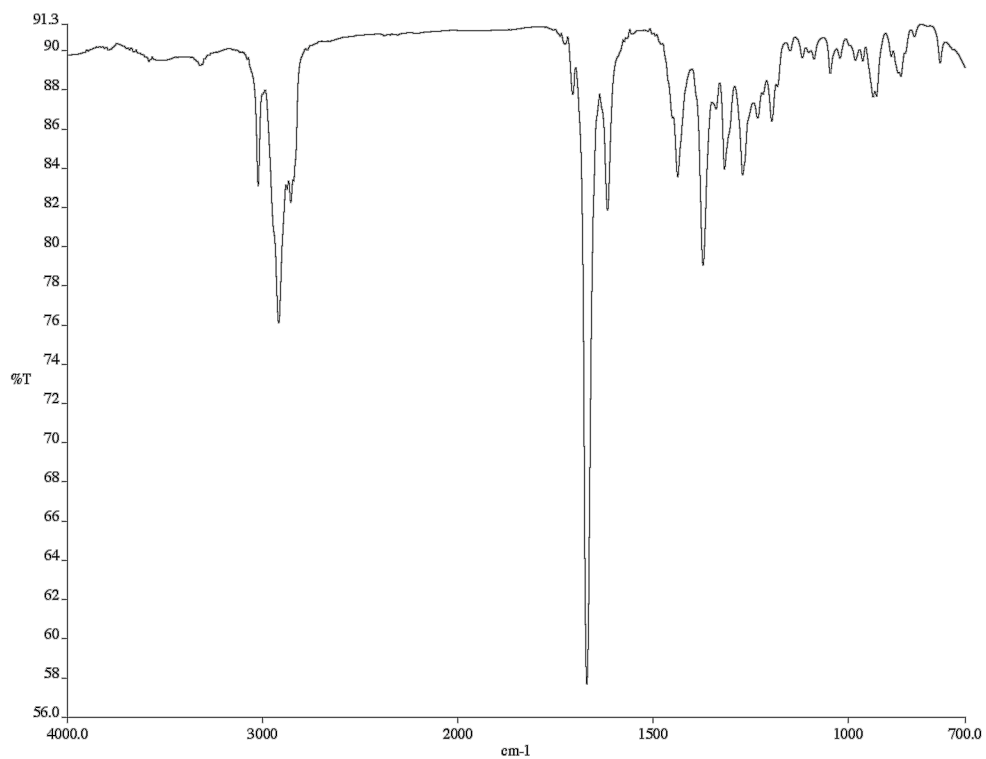


Figure SI-62B. Infrared spectrum (thin film/NaCl) of compound **1o**.

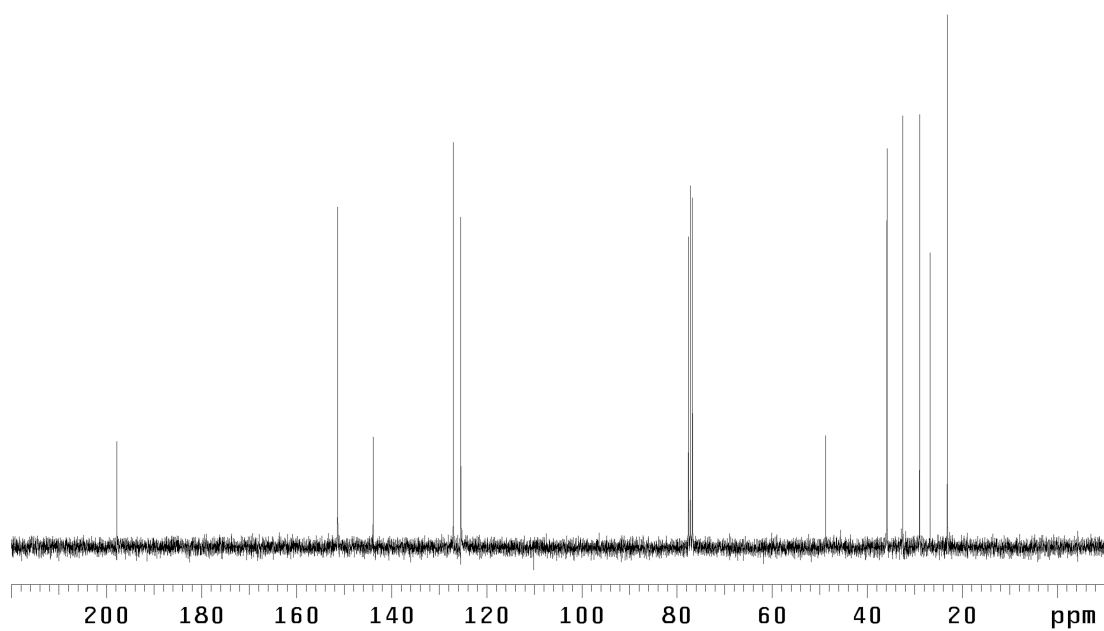


Figure SI-62C. ¹³C NMR (75 MHz, CDCl₃) of compound **1o**.

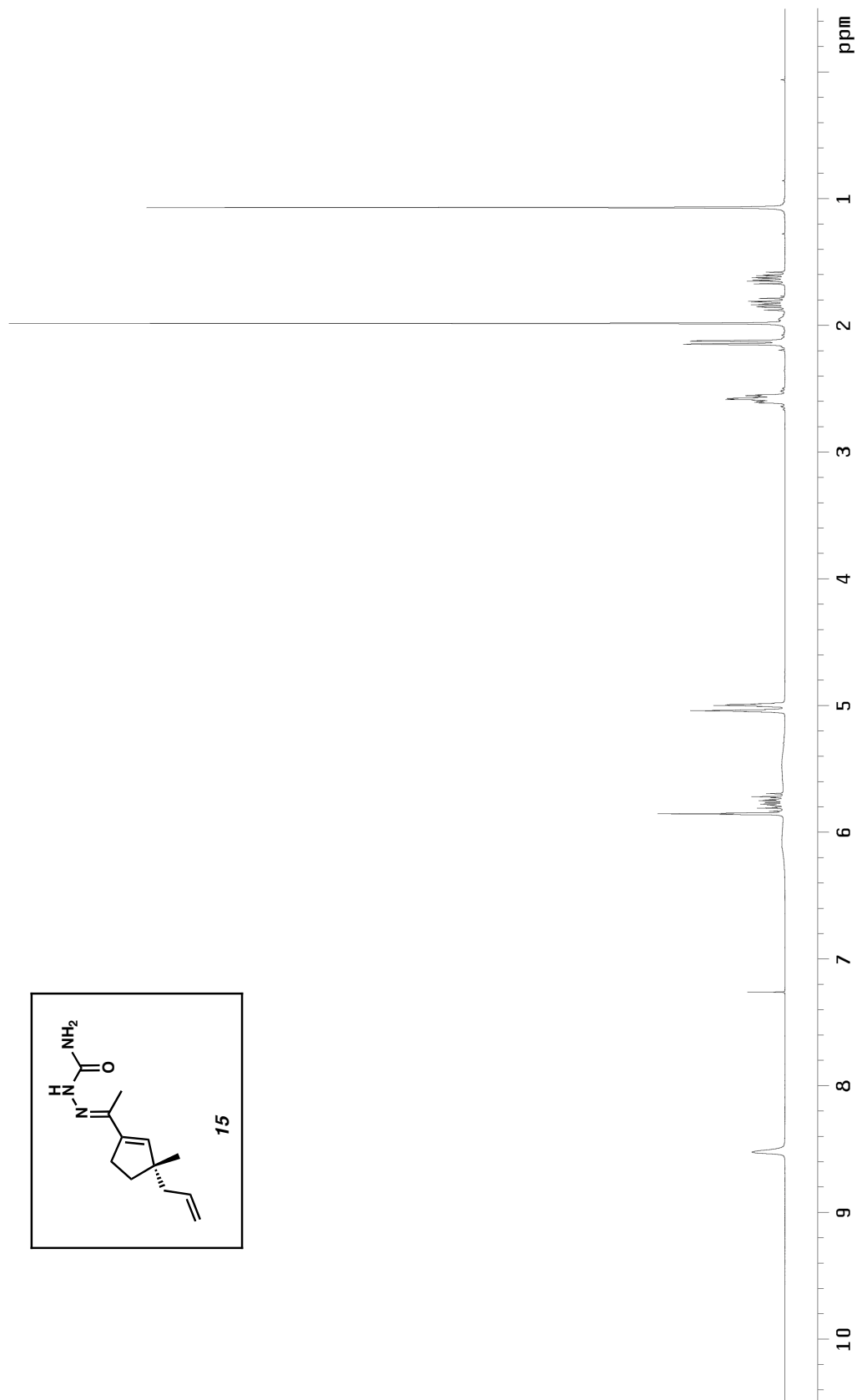


Figure SI-63A. ¹H NMR (300 MHz, CDCl₃) of compound **15**.

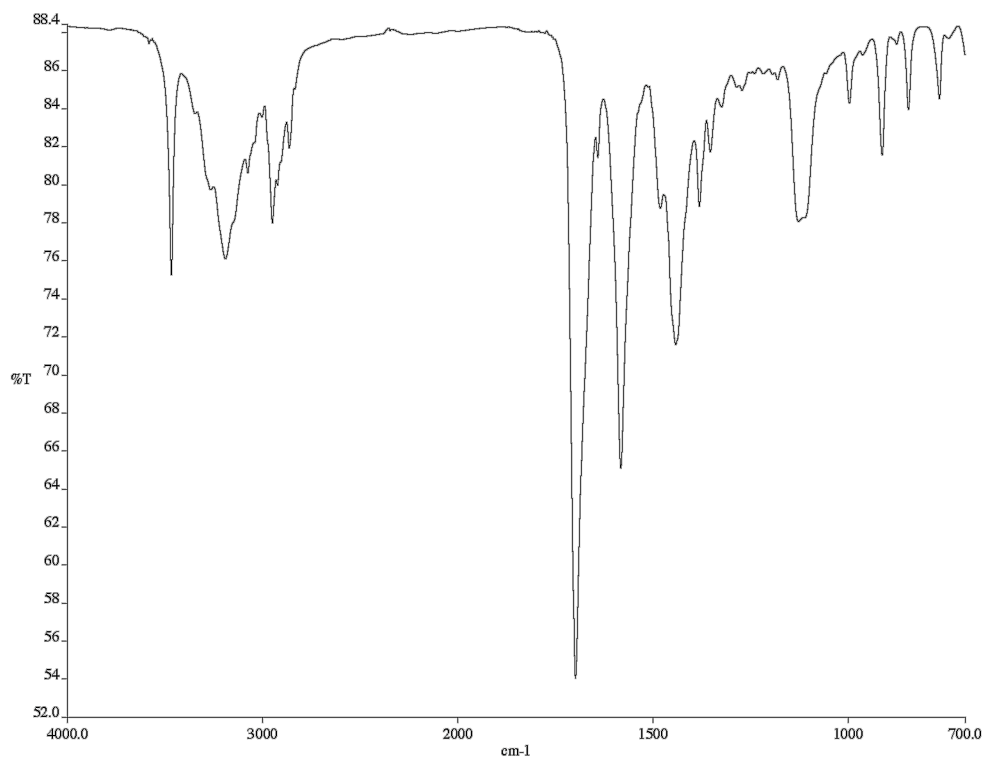


Figure SI-63B. Infrared spectrum (thin film/NaCl) of compound **15**.

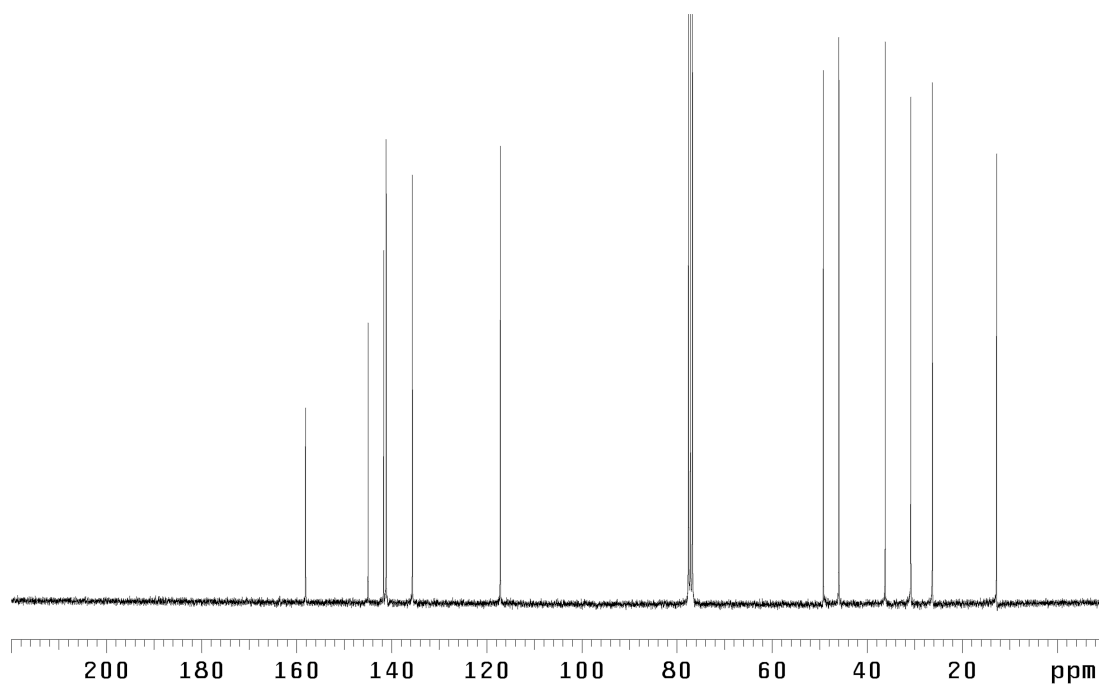


Figure SI-63C. ¹³C NMR (75 MHz, CDCl₃) of compound **15**.

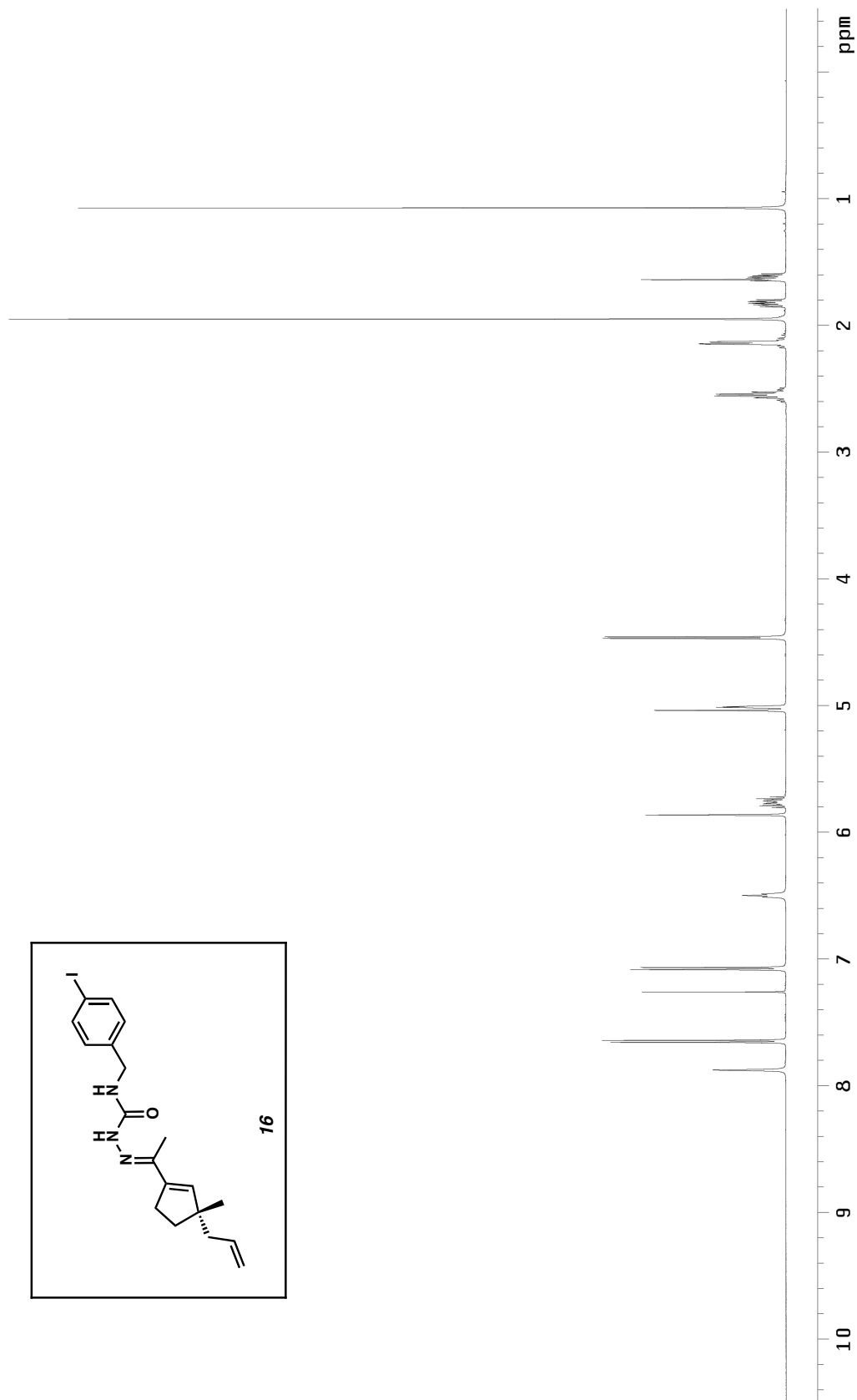


Figure SI-64A. ¹H NMR (500 MHz, CDCl₃) of compound **16**.

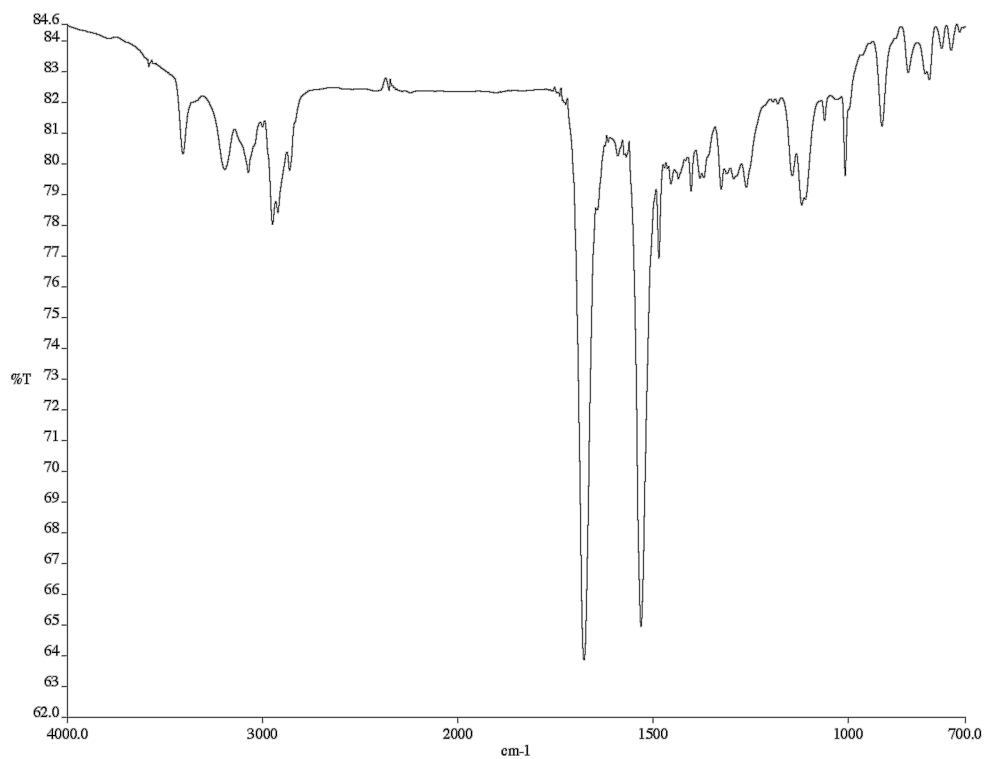


Figure SI-64B. Infrared spectrum (thin film/NaCl) of compound **16**.

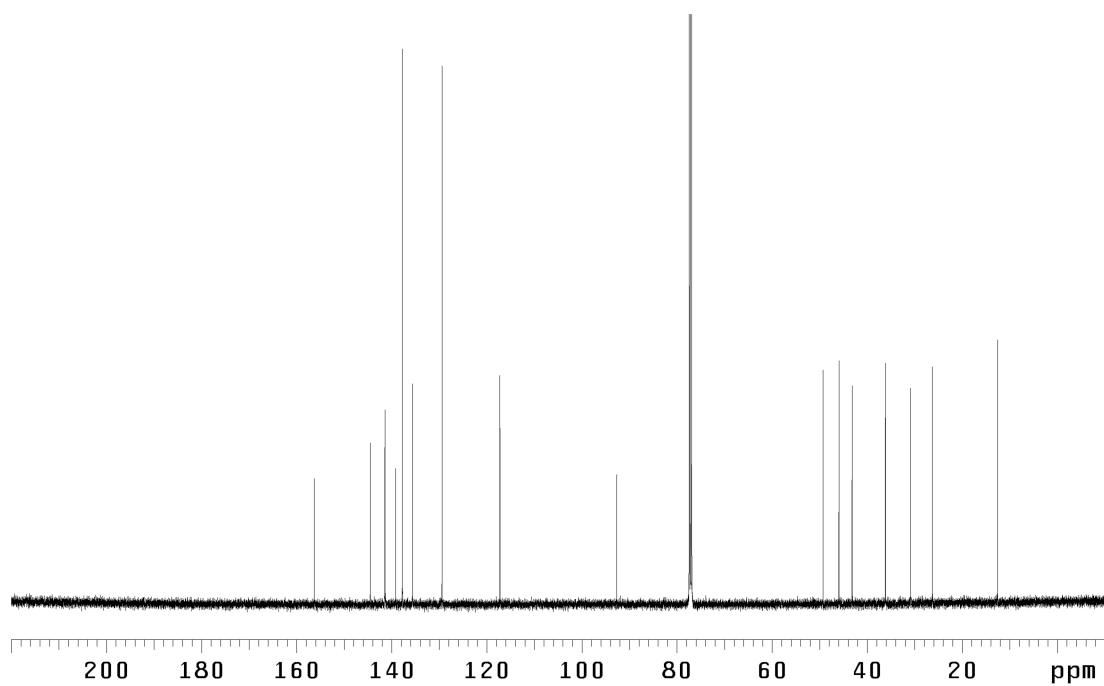


Figure SI-64C. ¹³C NMR (125 MHz, CDCl₃) of compound **16**.

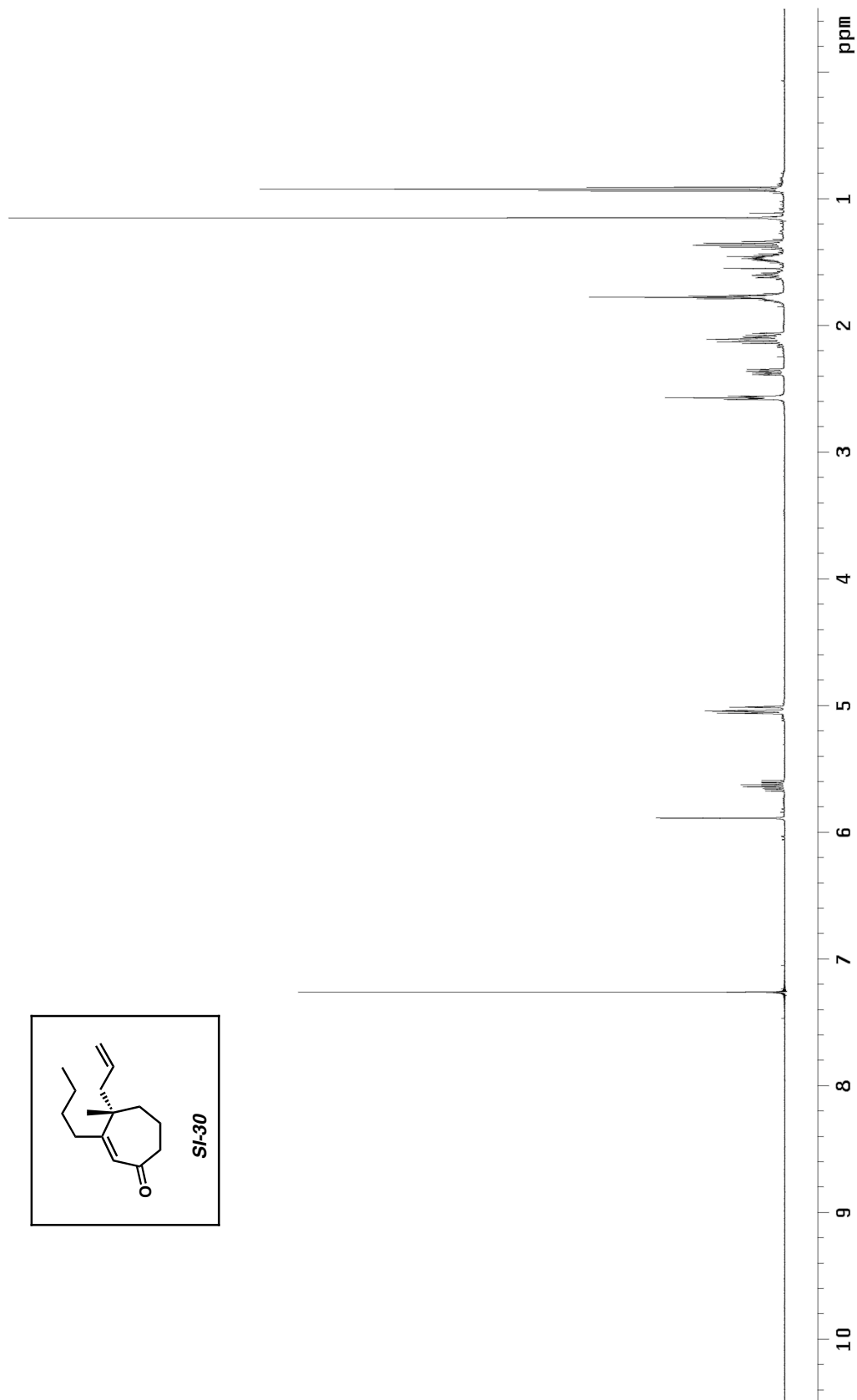


Figure SI-65A. ¹H NMR (500 MHz, CDCl₃) of compound SI-30.

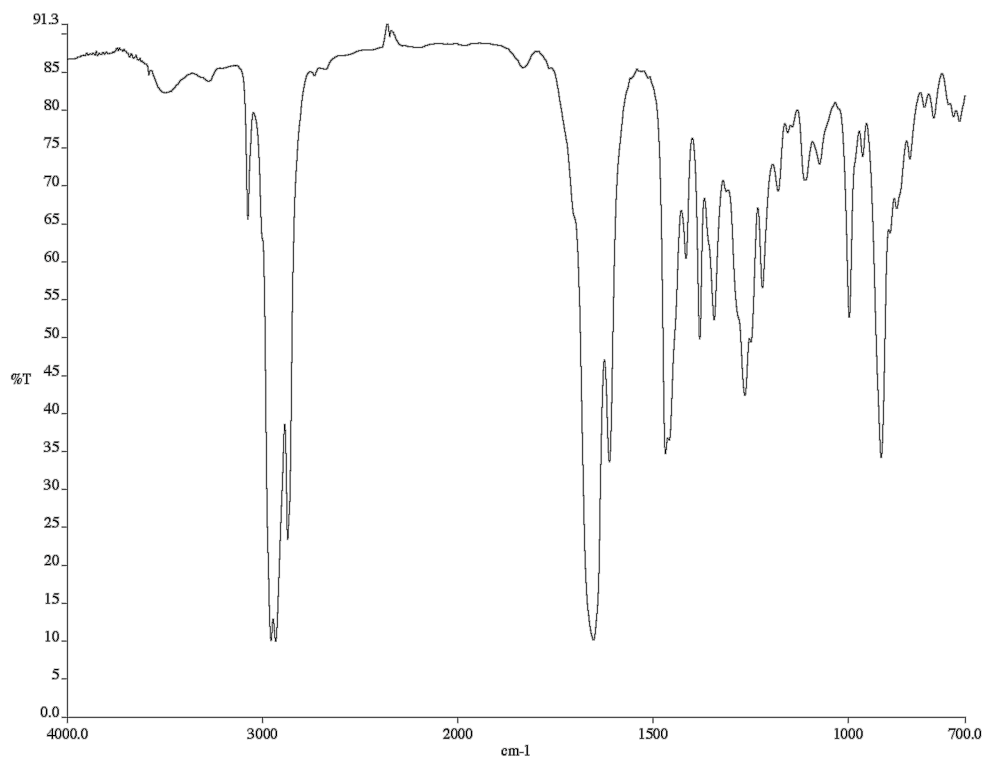


Figure SI-65B. Infrared spectrum (thin film/NaCl) of compound **SI-30**.

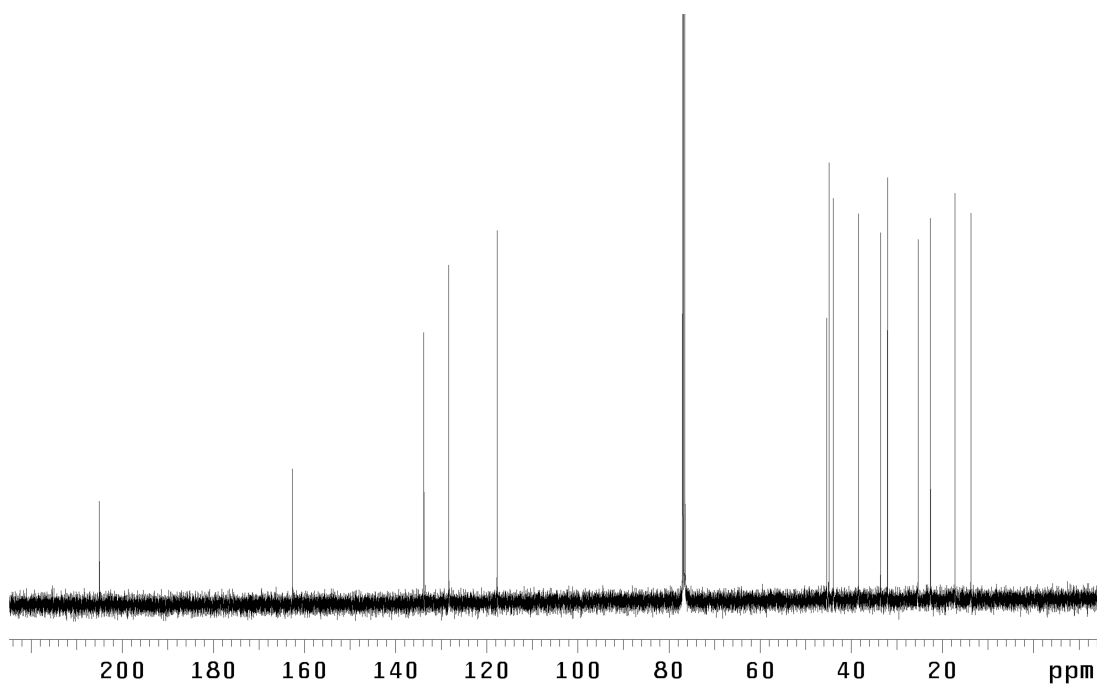


Figure SI-65C. ¹³C NMR (125 MHz, CDCl₃) of compound **SI-30**.

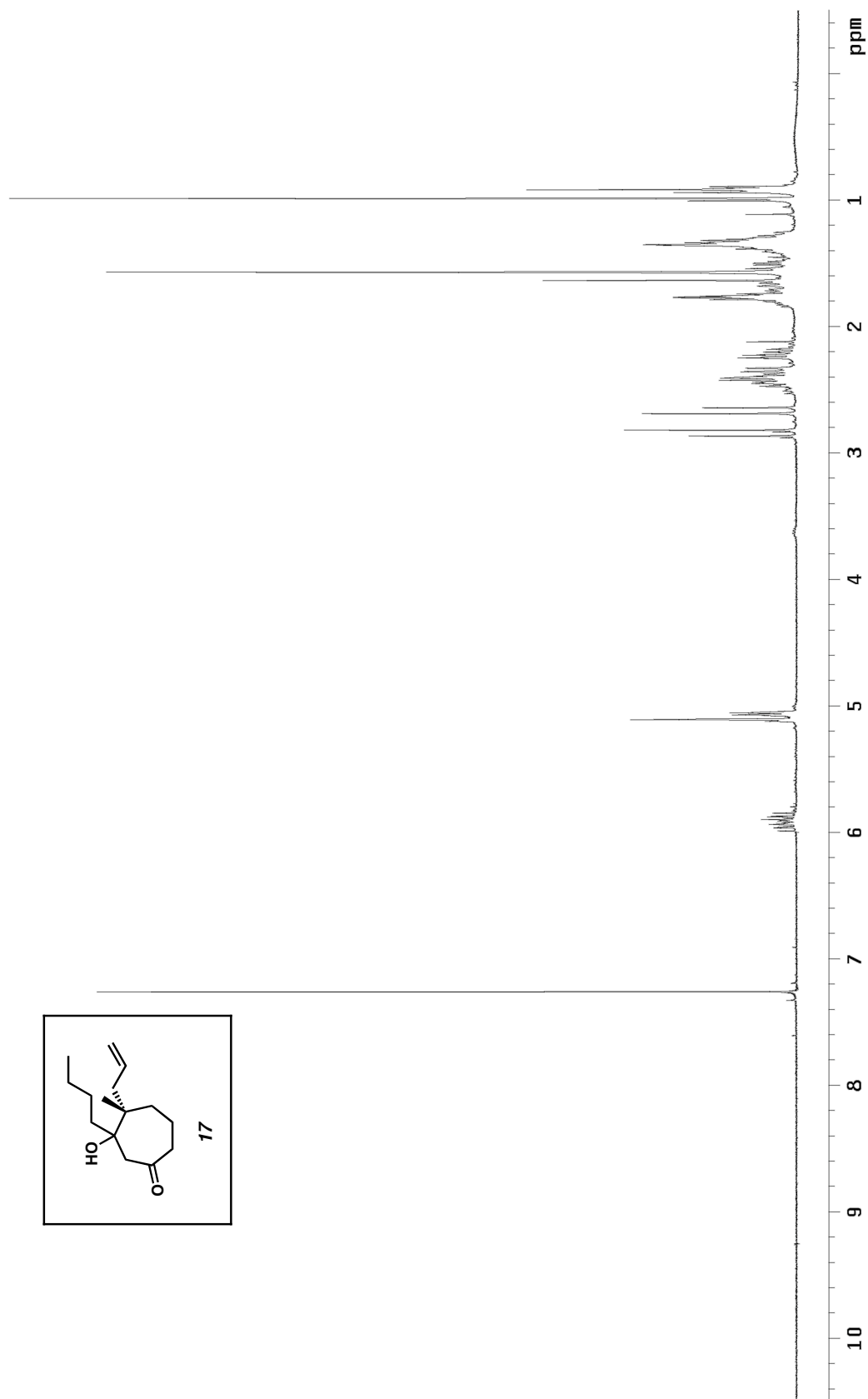


Figure SI-66A. ¹H NMR (500 MHz, CDCl₃) of compound 17.

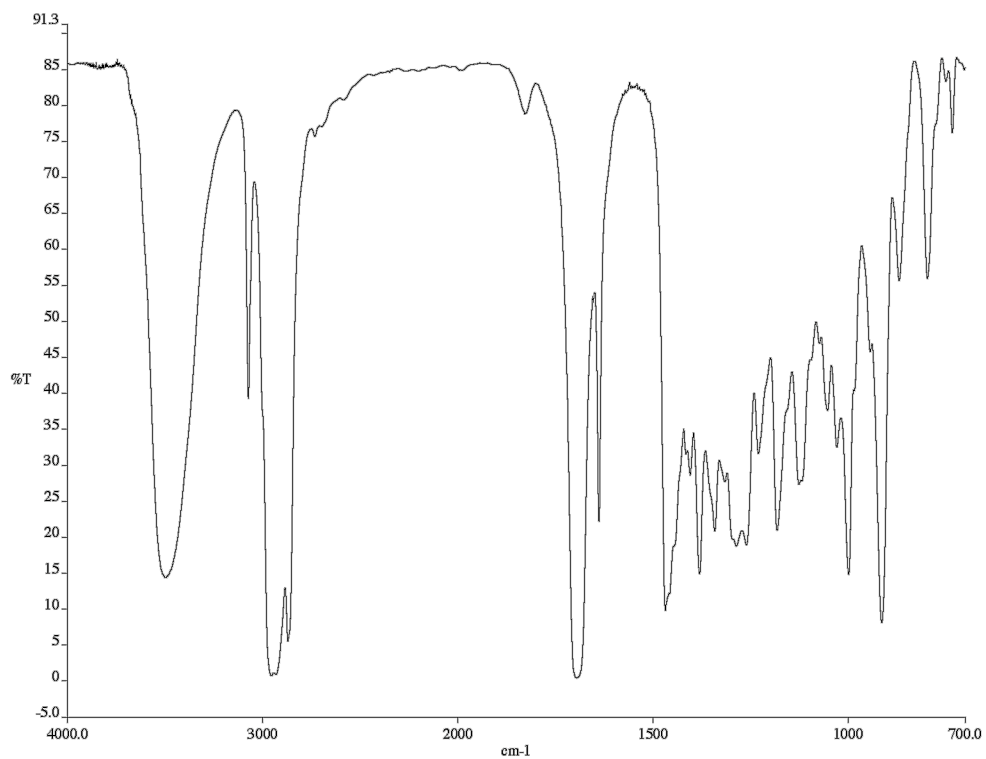


Figure SI-66B. Infrared spectrum (thin film/NaCl) of compound **17**.

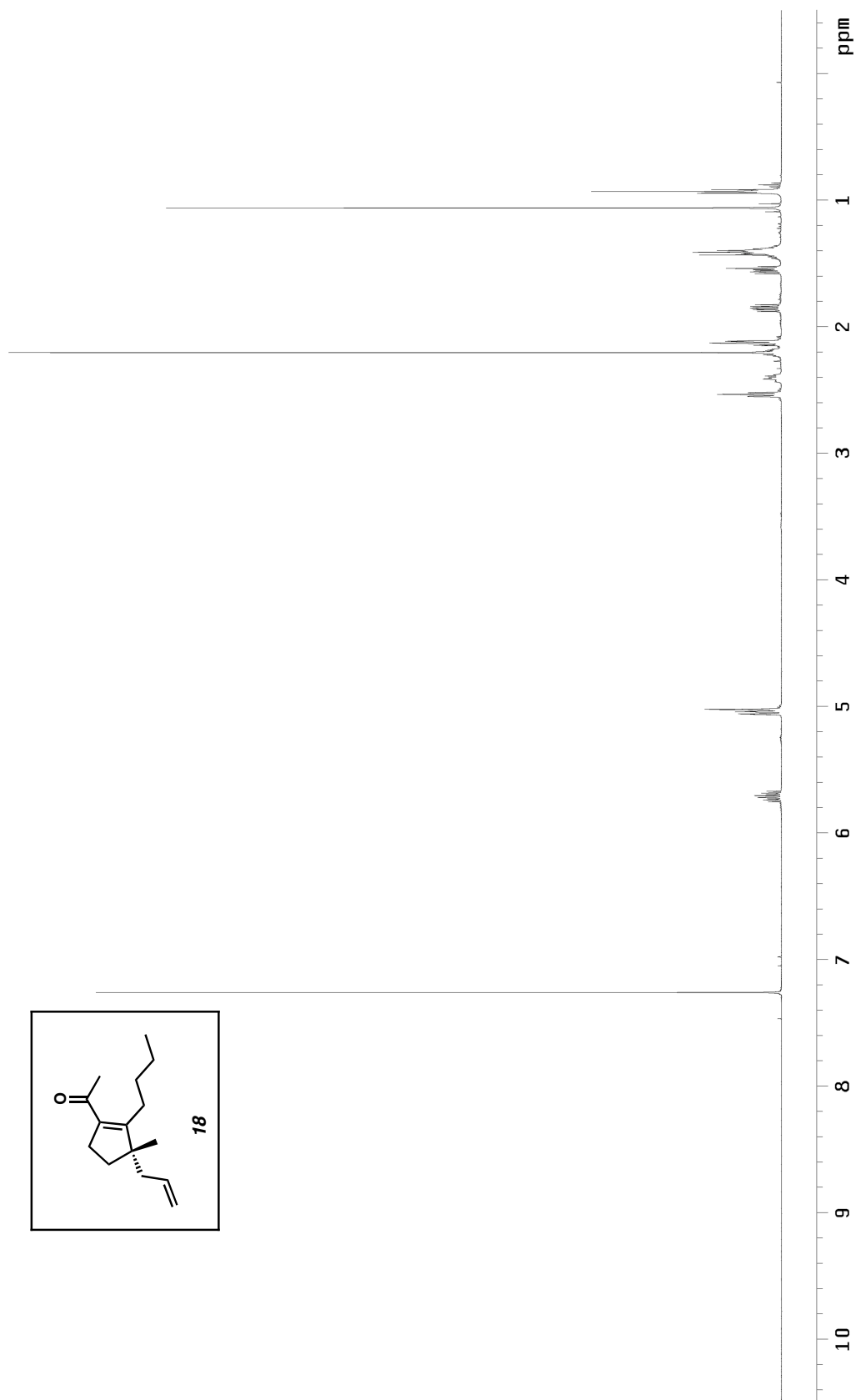


Figure SI-67A. ¹H NMR (500 MHz, CDCl₃) of compound **18**.

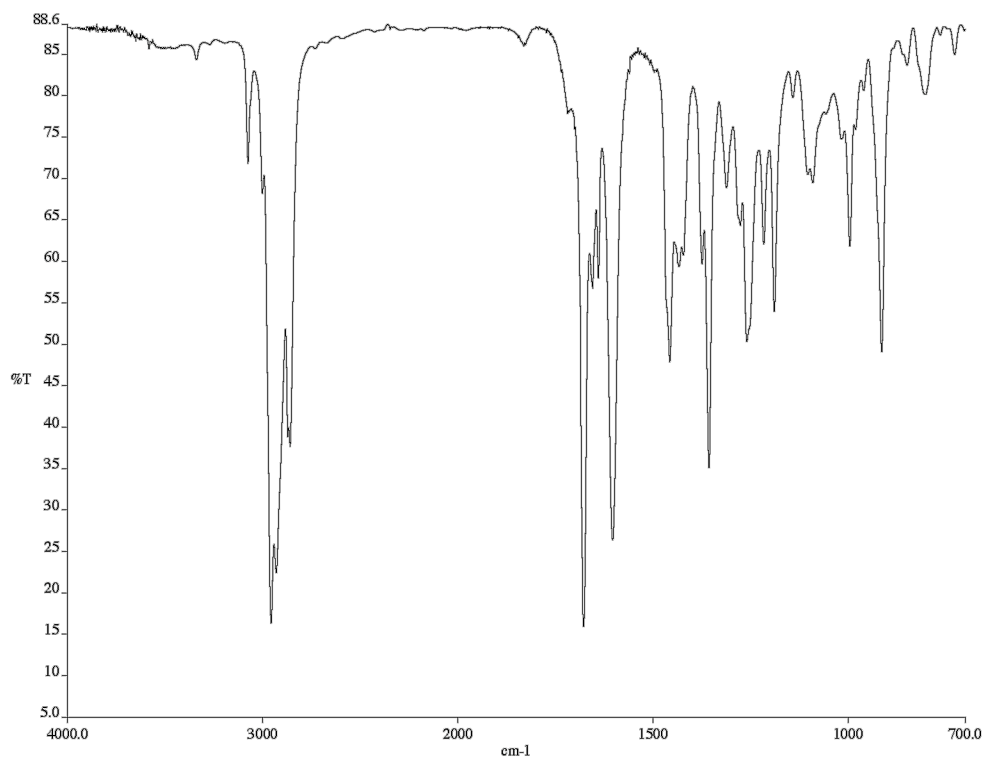


Figure SI-67B. Infrared spectrum (thin film/NaCl) of compound **18**.

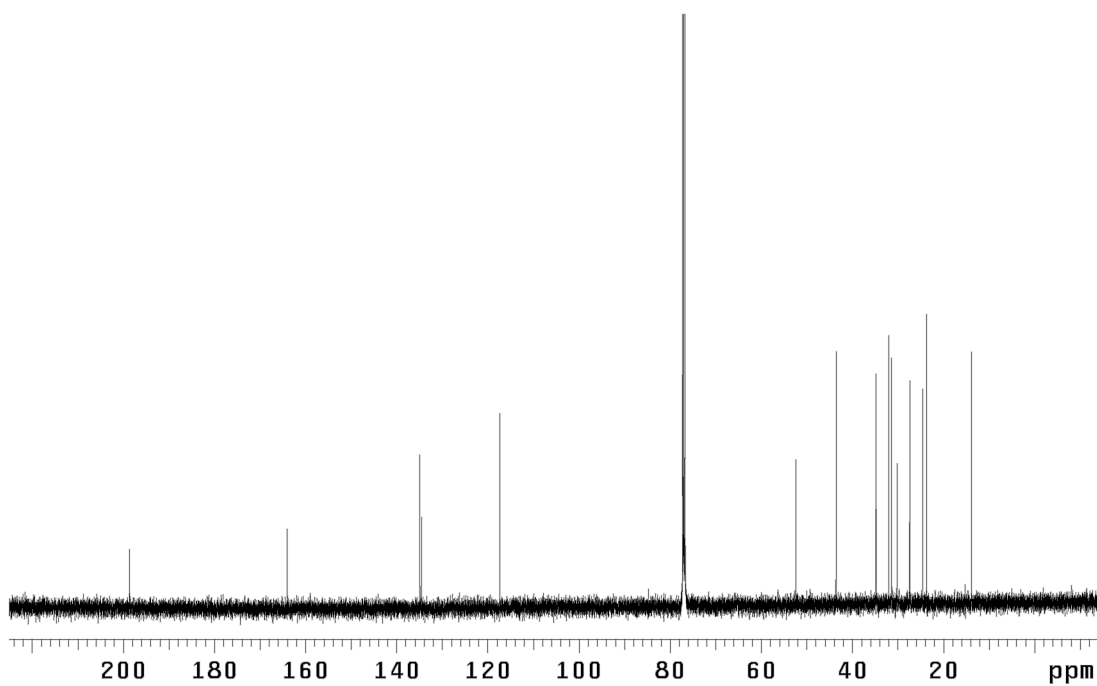


Figure SI-67C. ¹³C NMR (125 MHz, CDCl₃) of compound **18**.

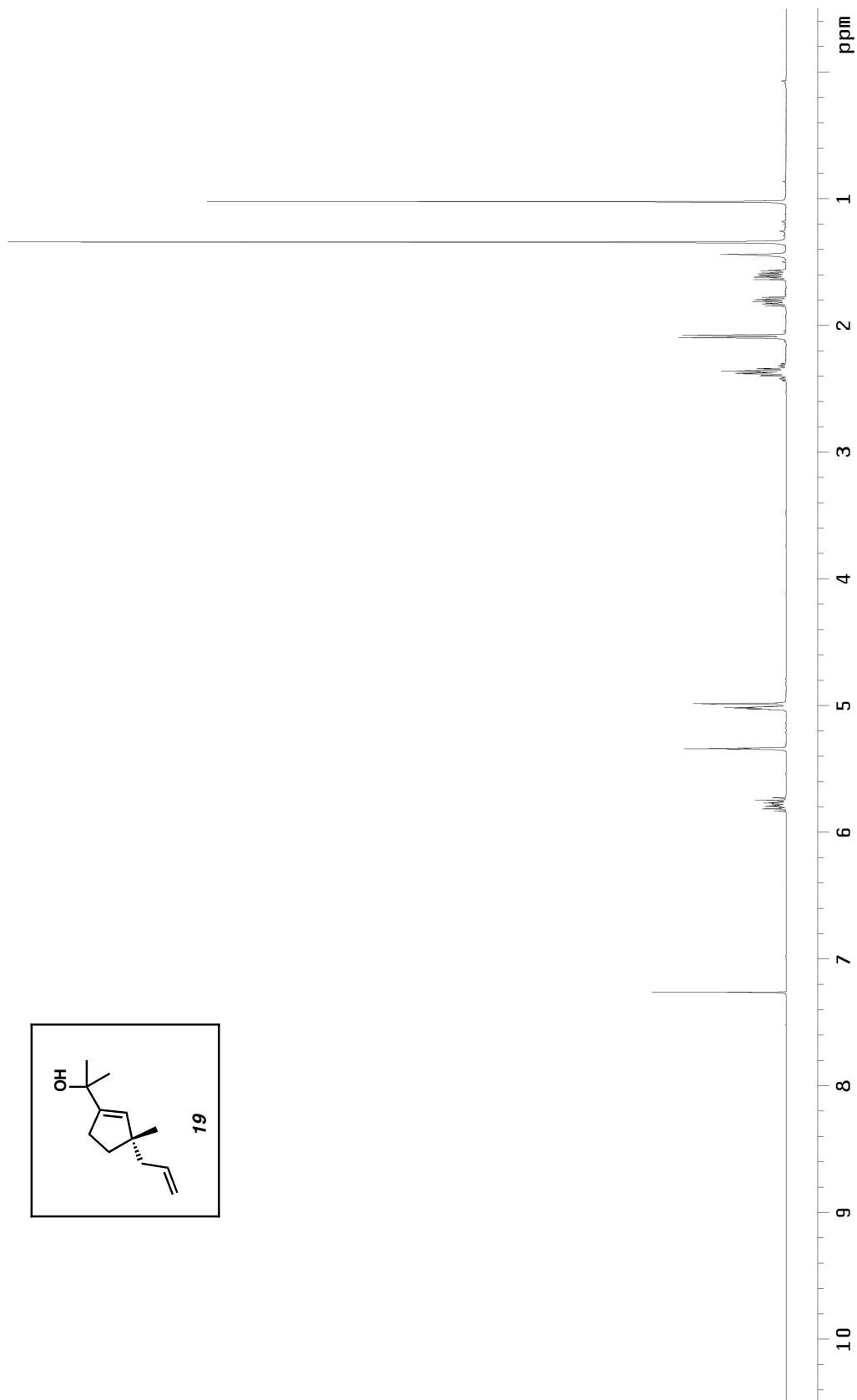


Figure SI-68A. ¹H NMR (400 MHz, CDCl₃) of compound **19**.

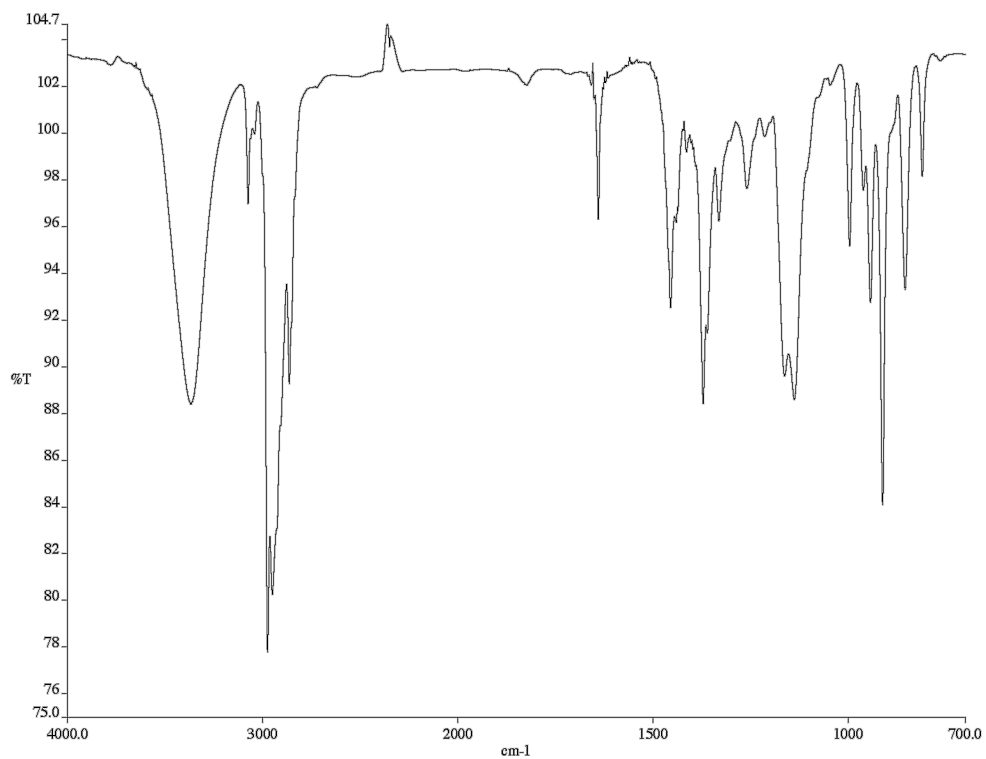


Figure SI-68B. Infrared spectrum (thin film/NaCl) of compound **19**.

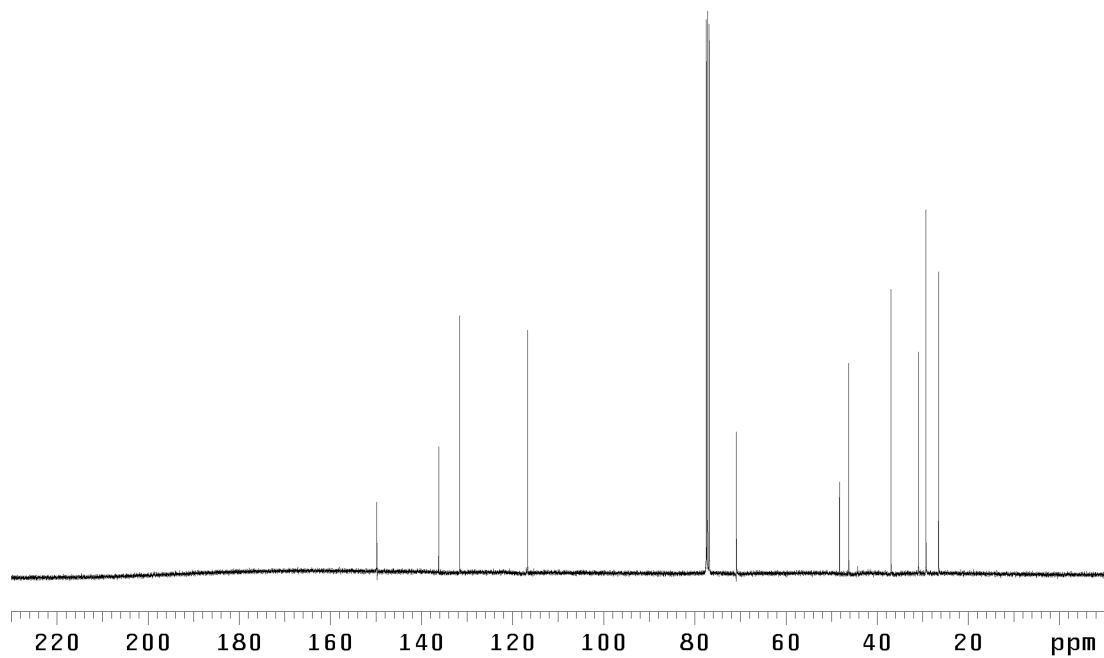


Figure SI-68C. ¹³C NMR (100 MHz, CDCl₃) of compound **19**.

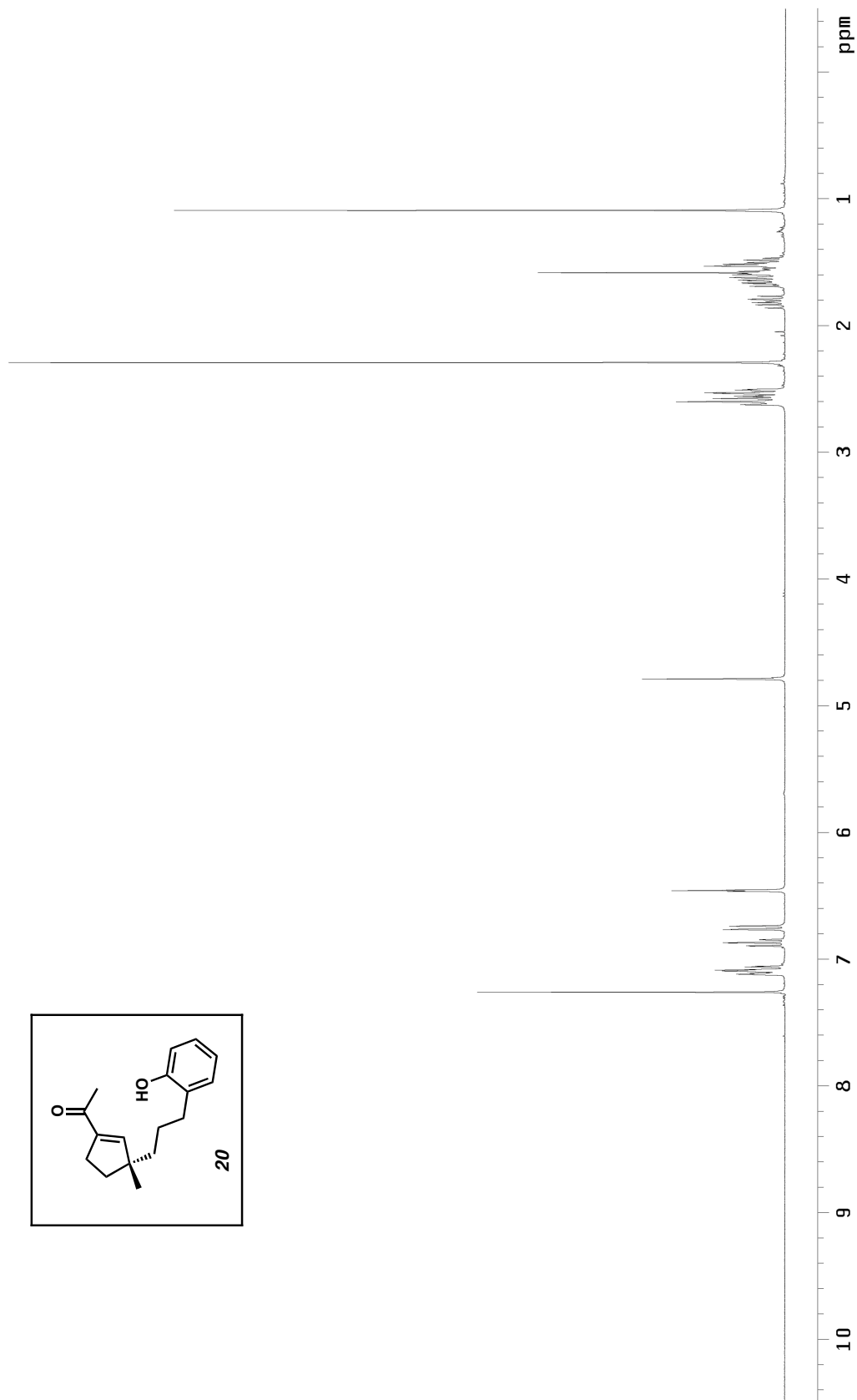


Figure SI-69A. ¹H NMR (300 MHz, CDCl₃) of compound **20**.

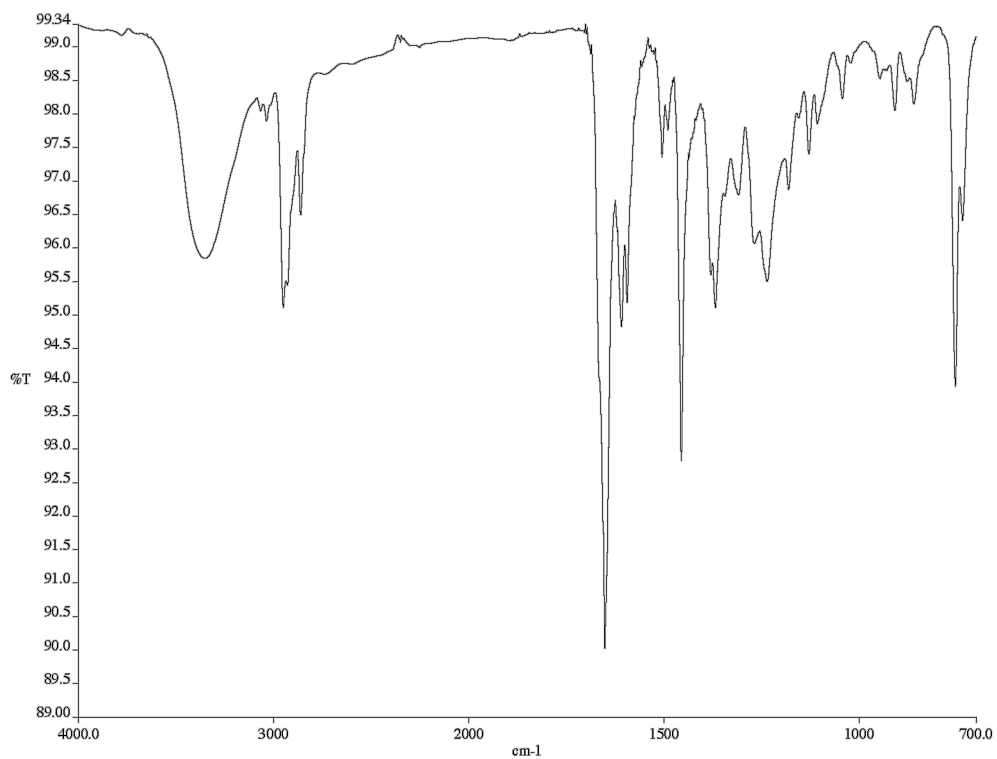


Figure SI-69B. Infrared spectrum (thin film/NaCl) of compound **20**.

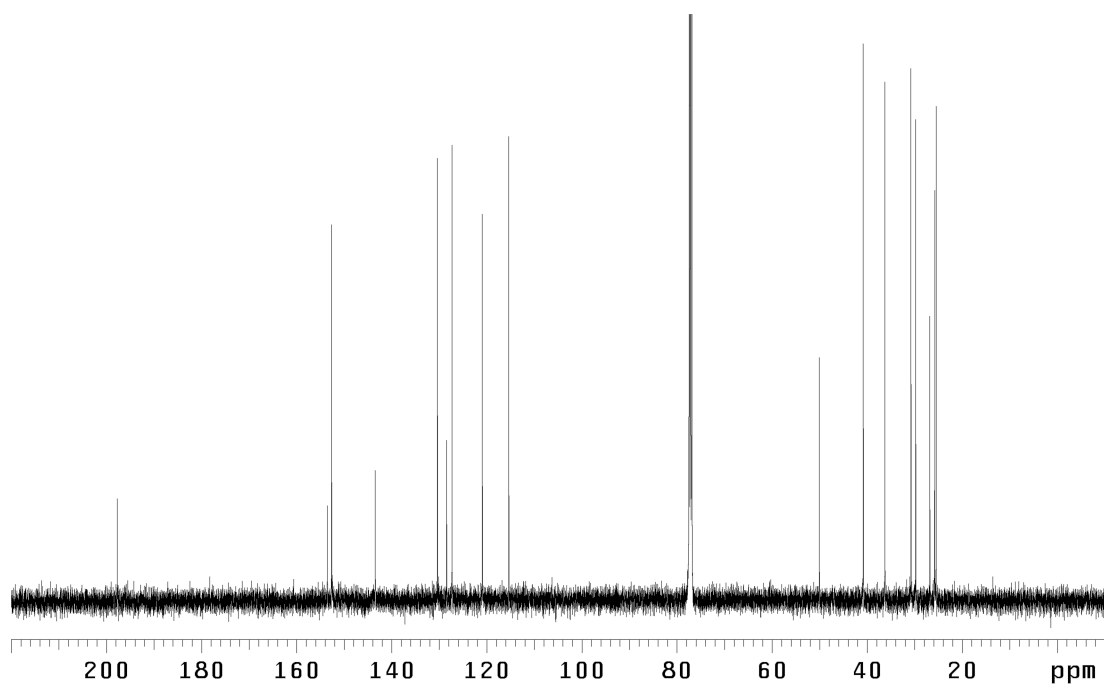


Figure SI-69C. ¹³C NMR (125 MHz, CDCl₃) of compound **20**.

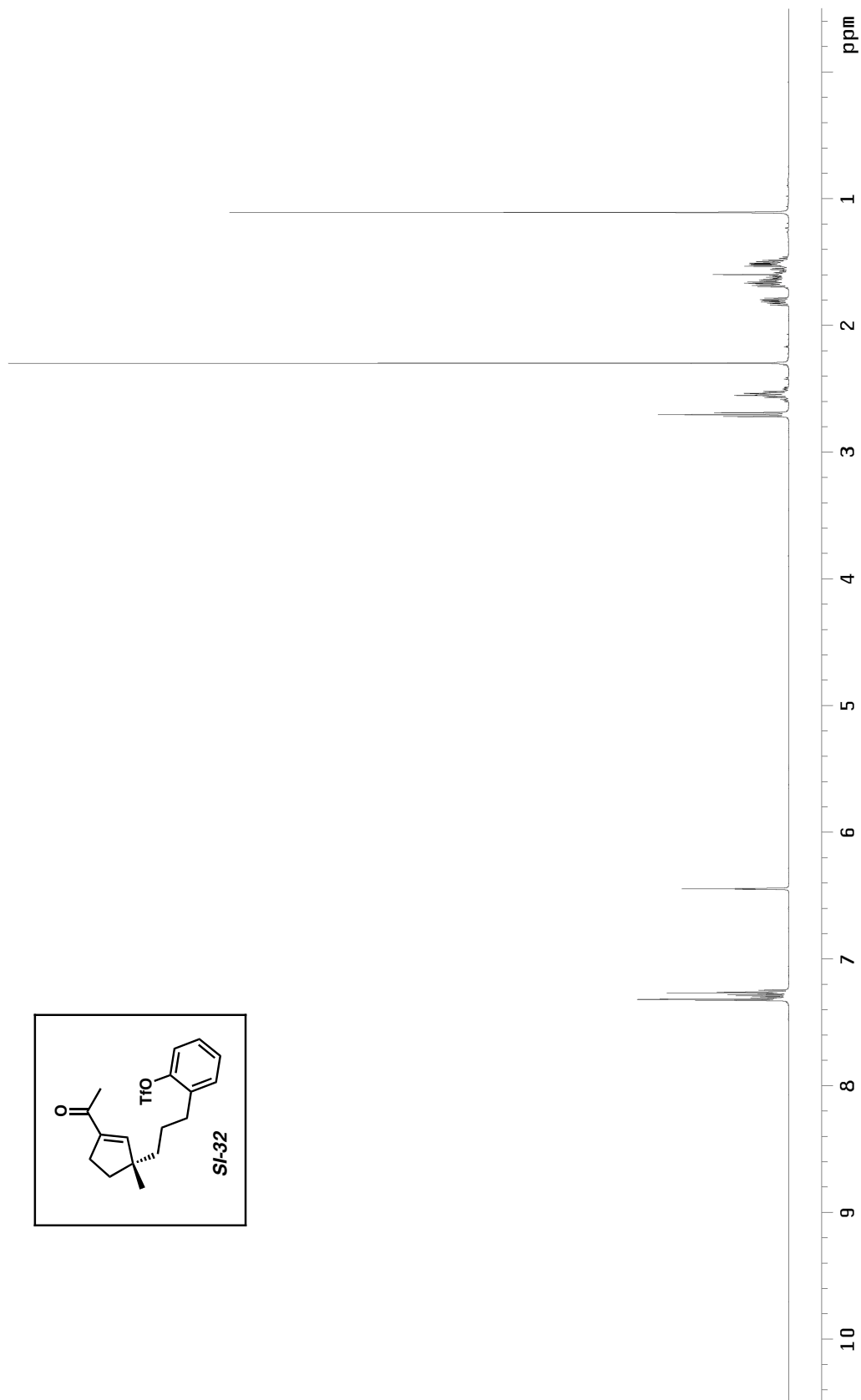


Figure SI-70A. ^1H NMR (500 MHz, CDCl_3) of compound **SI-32**.

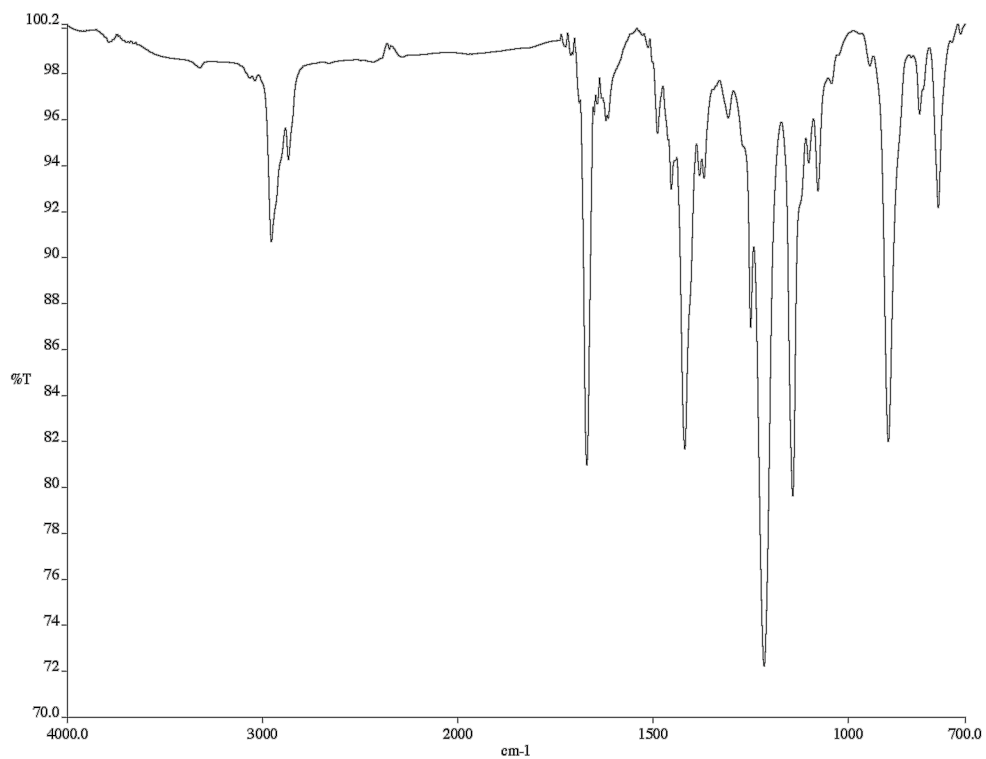


Figure SI-70B. Infrared spectrum (thin film/NaCl) of compound **SI-32**.

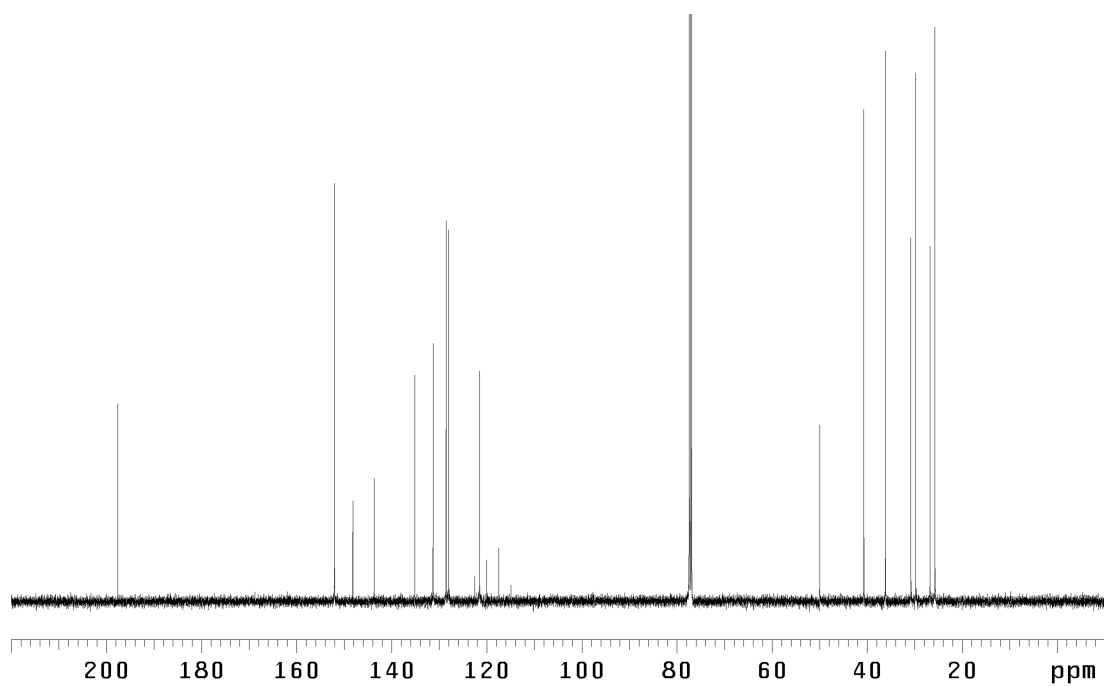


Figure SI-70C. ¹³C NMR (125 MHz, CDCl₃) of compound **SI-32**.

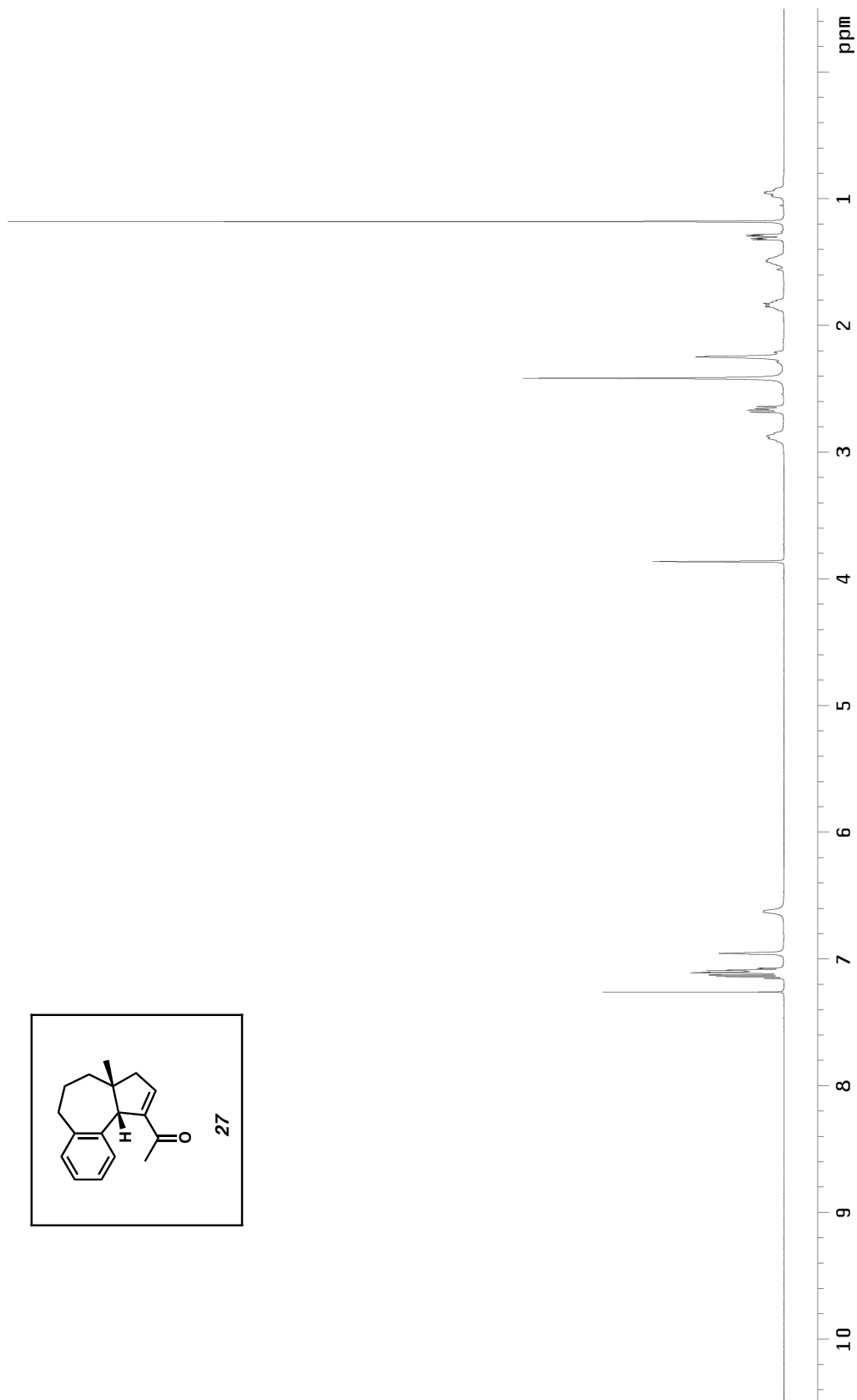


Figure SI-71A. ¹H NMR (500 MHz, CDCl₃) of compound 27.

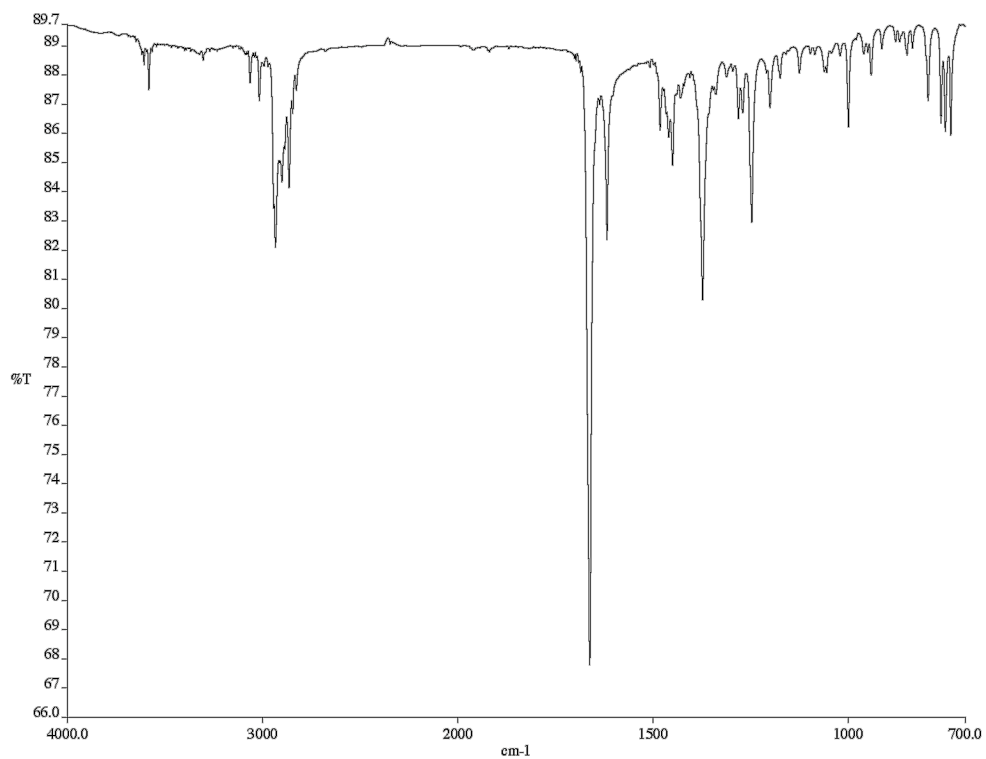


Figure SI-71B. Infrared spectrum (thin film/NaCl) of compound **27**.

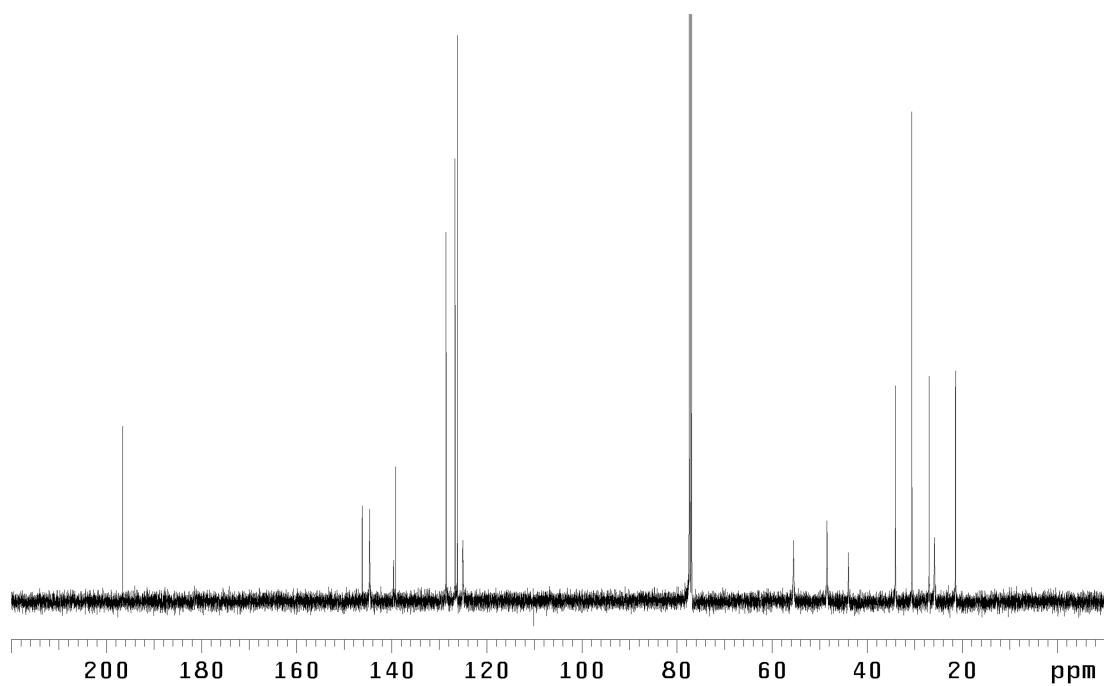


Figure SI-71C. ¹³C NMR (125 MHz, CDCl₃) of compound **27**.

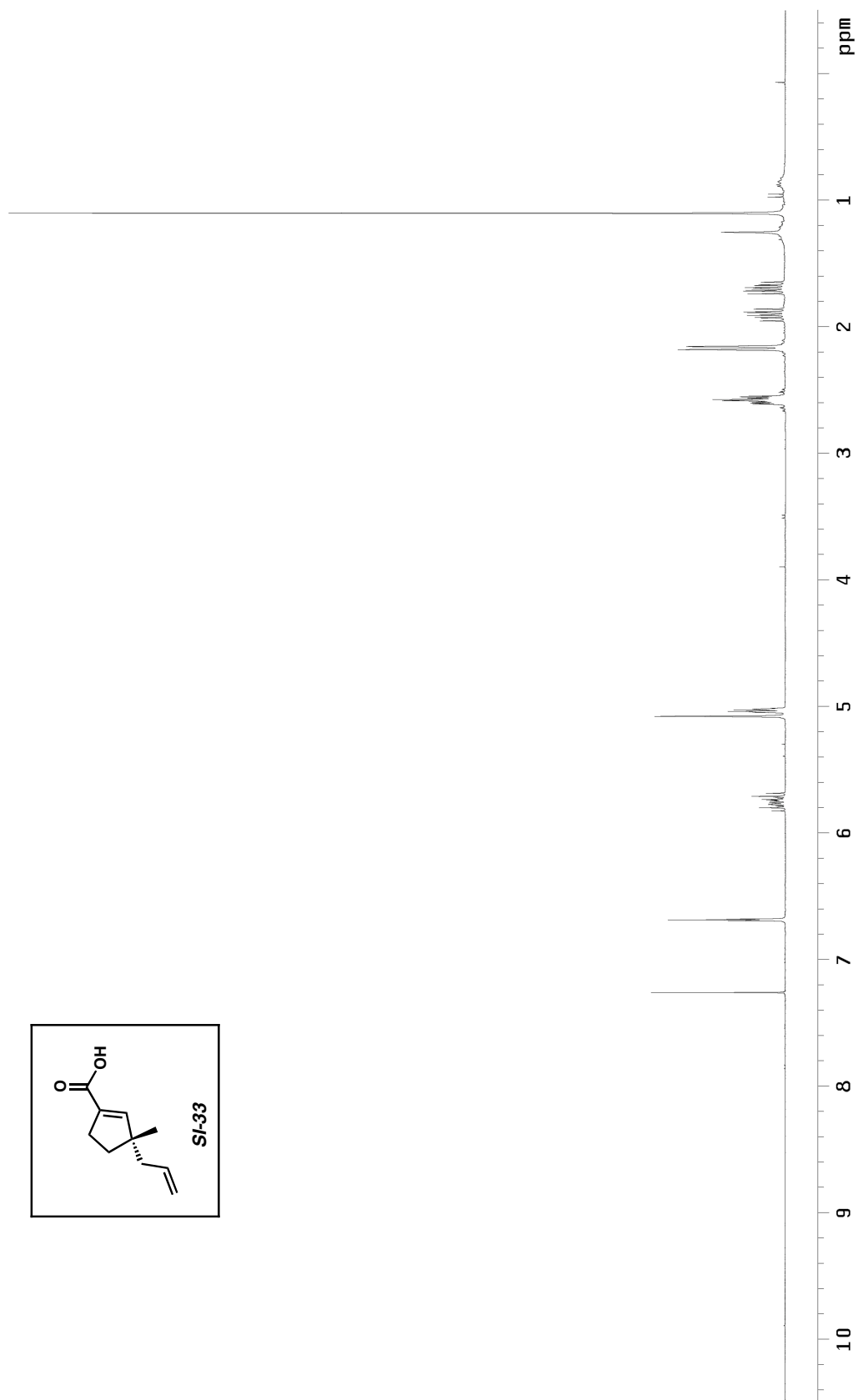


Figure SI-72A. ¹H NMR (300 MHz, CDCl₃) of compound **SI-33**.

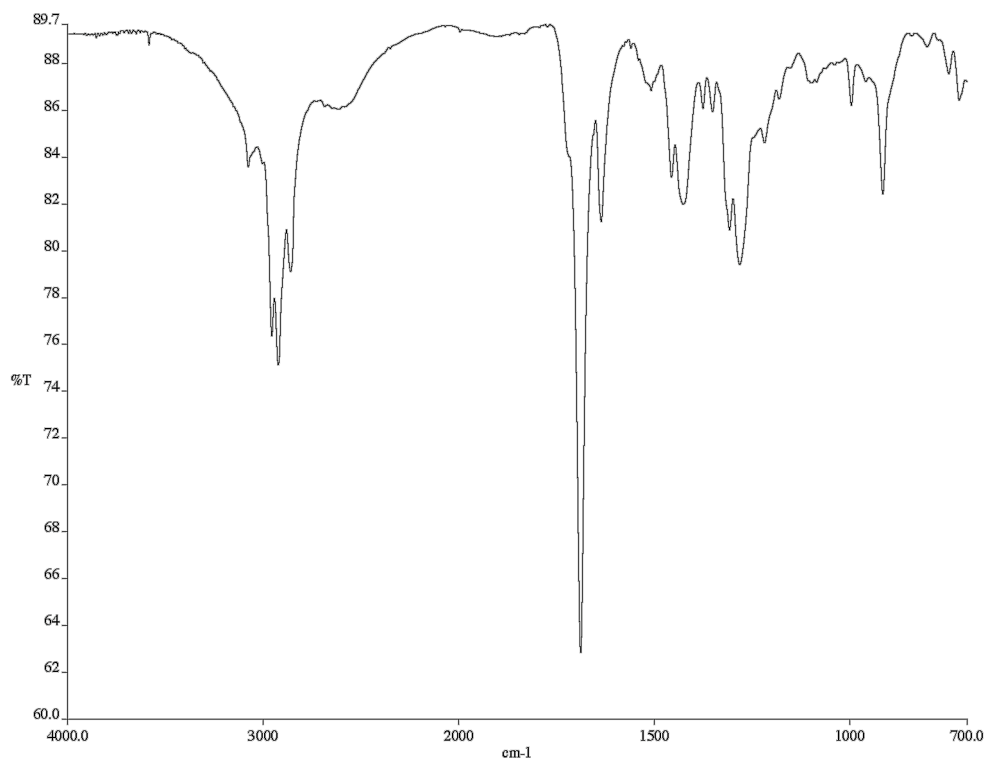


Figure SI-72B. Infrared spectrum (thin film/NaCl) of compound **SI-33**.

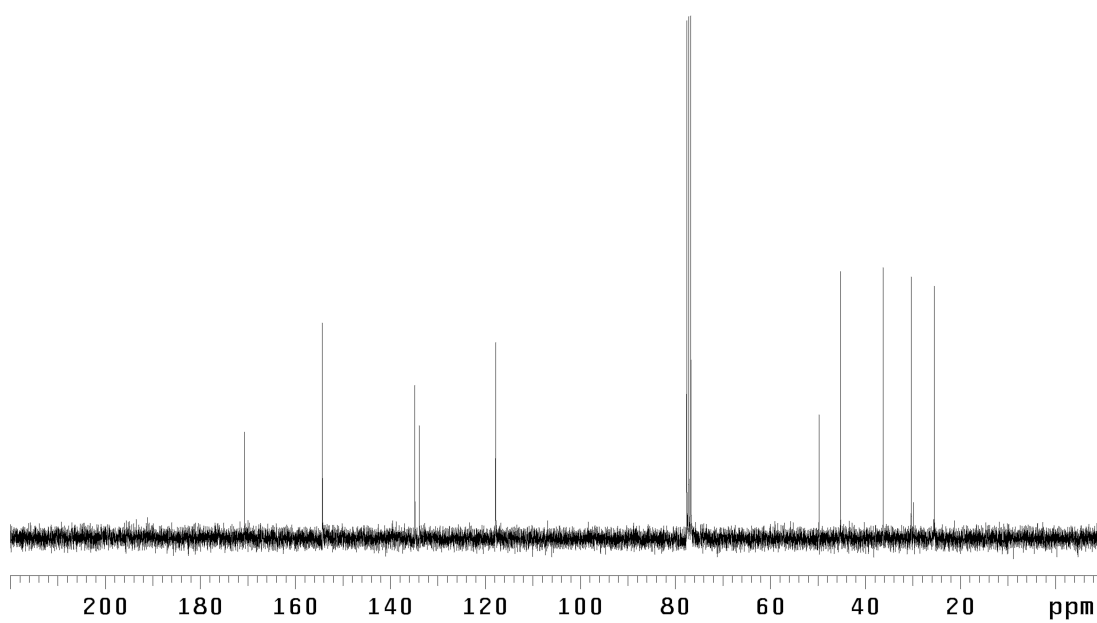


Figure SI-72C. ¹³C NMR (75 MHz, CDCl₃) of compound **SI-33**.

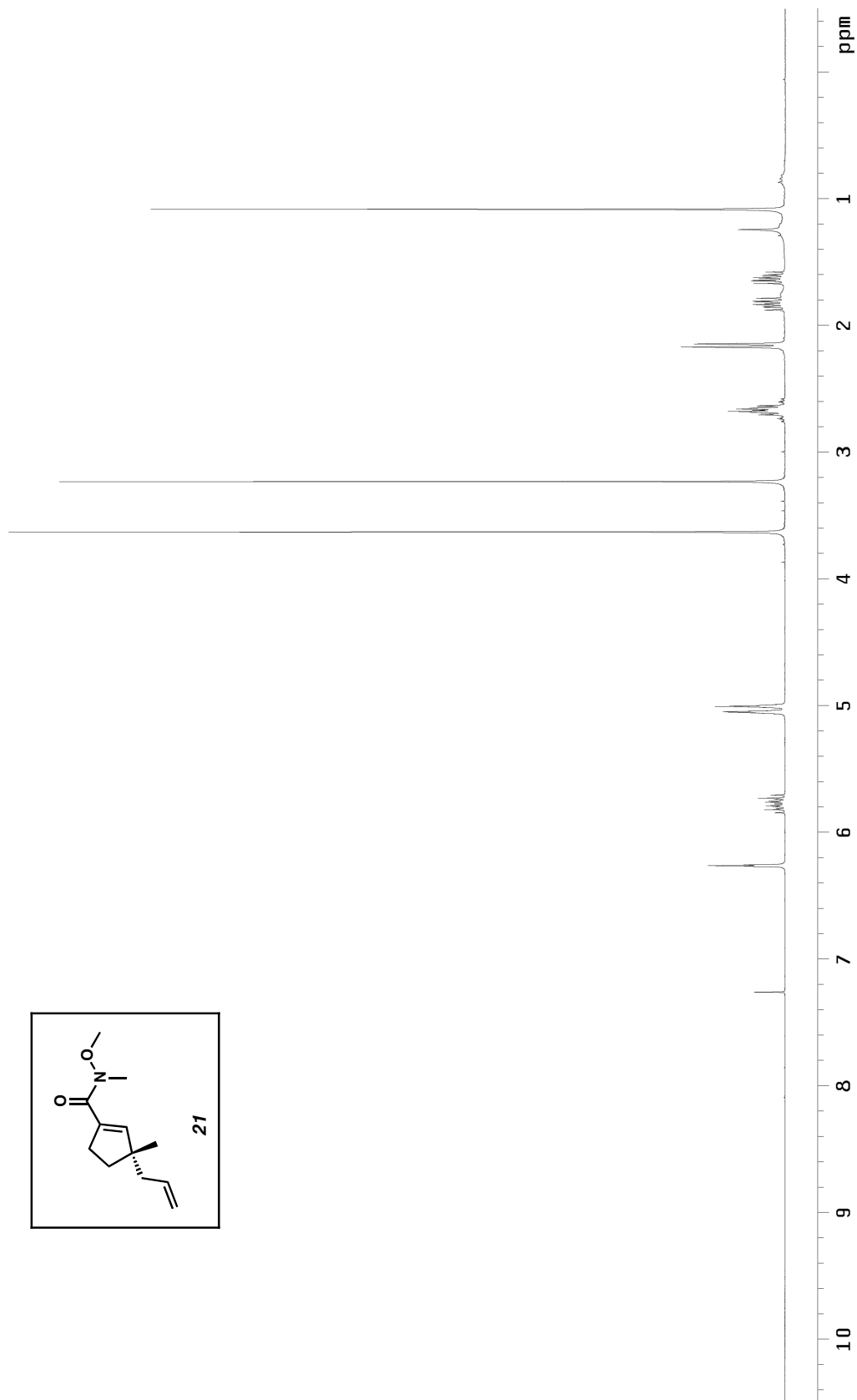


Figure SI-73A. ¹H NMR (300 MHz, CDCl₃) of compound 21.

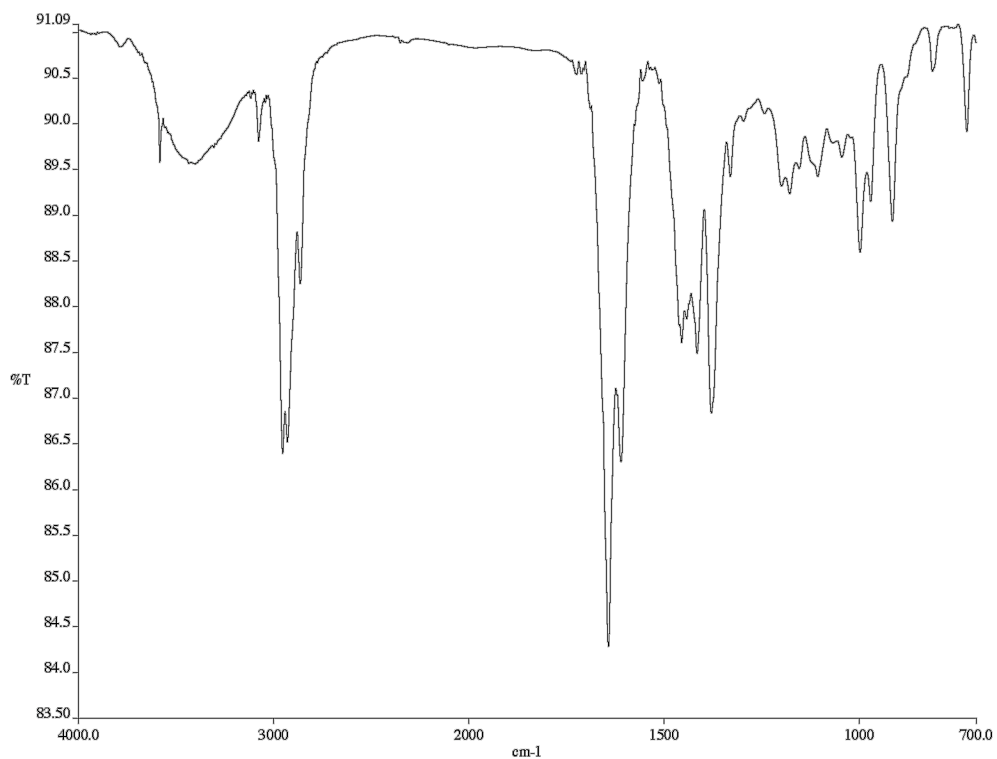


Figure SI-73B. Infrared spectrum (thin film/NaCl) of compound **21**.

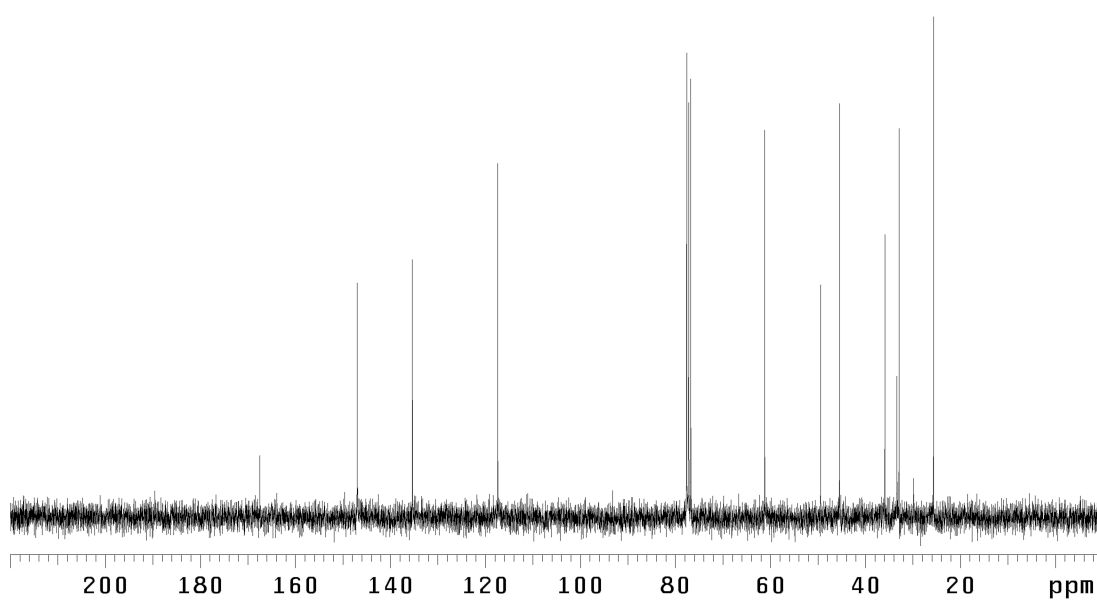


Figure SI-73C. ¹³C NMR (75 MHz, CDCl₃) of compound **21**.

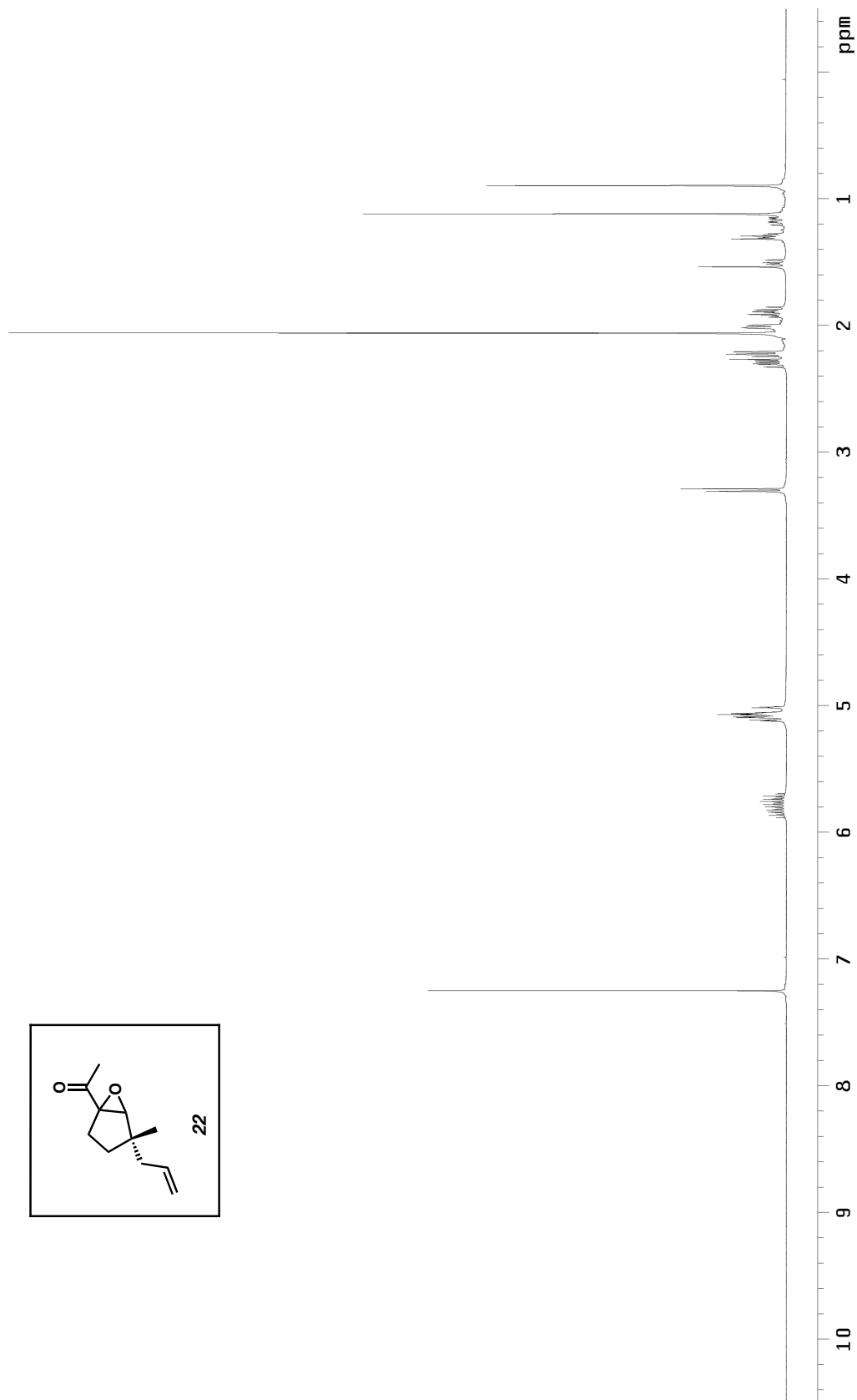


Figure SI-74A. ¹H NMR (400 MHz, CDCl₃) of compound 22.

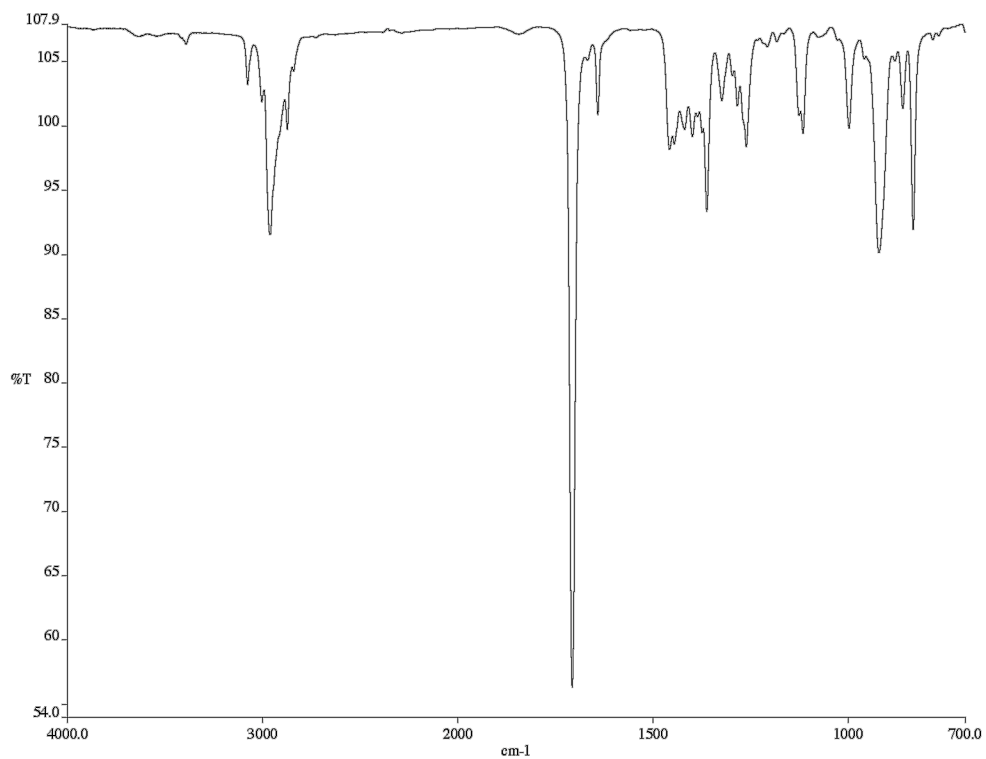


Figure SI-74B. Infrared spectrum (thin film/NaCl) of compound **22**.

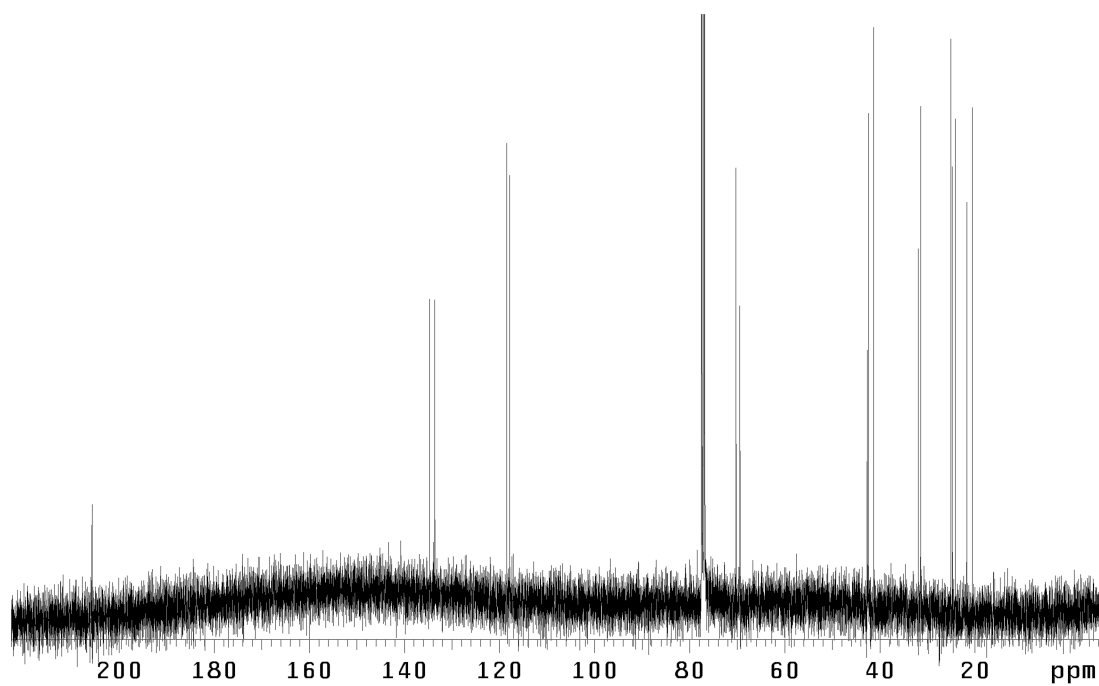


Figure SI-74C. ¹³C NMR (100 MHz, CDCl₃) of compound **22**.

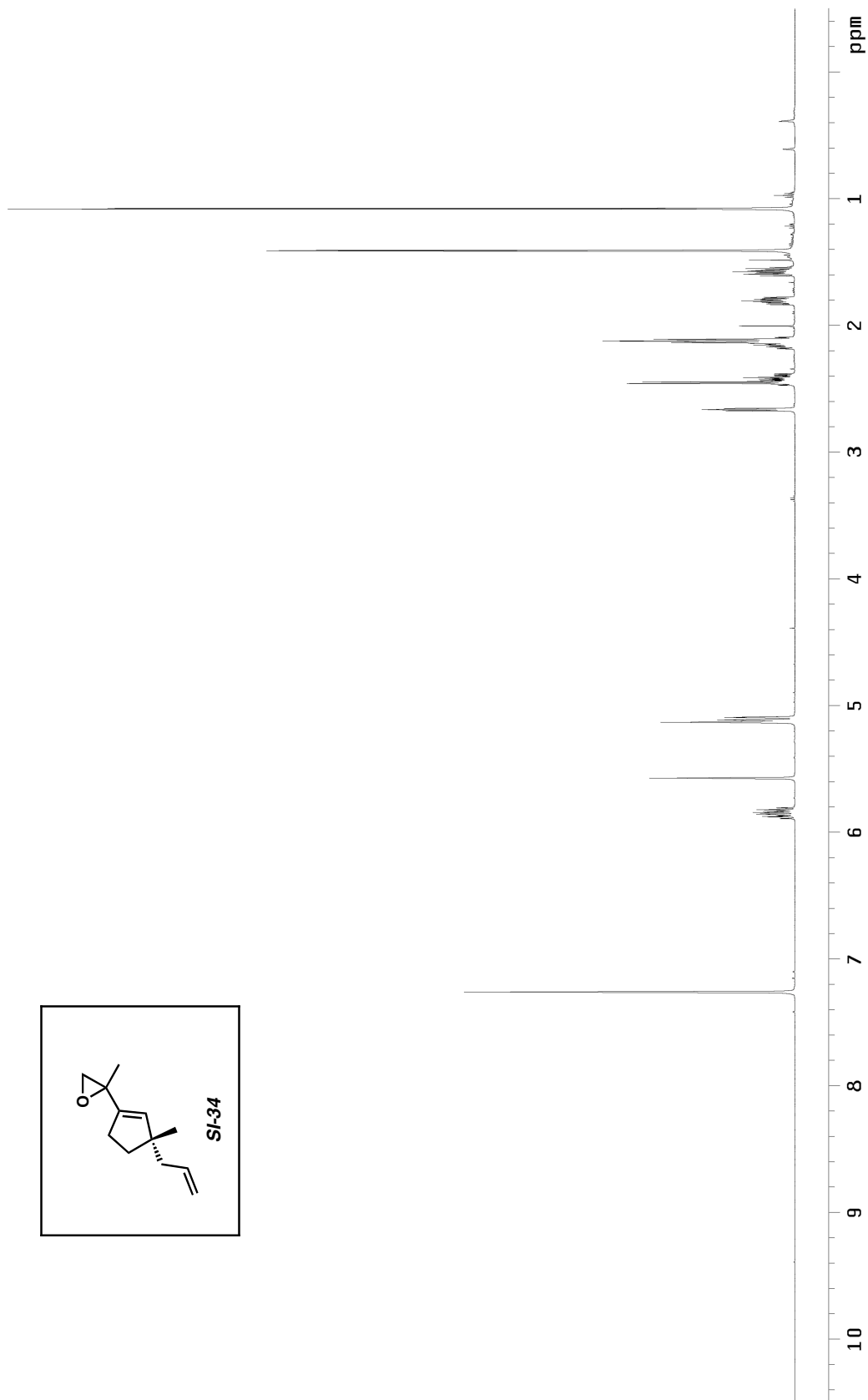


Figure SI-75A. ¹H NMR (500 MHz, CDCl₃) of compound SI-34.

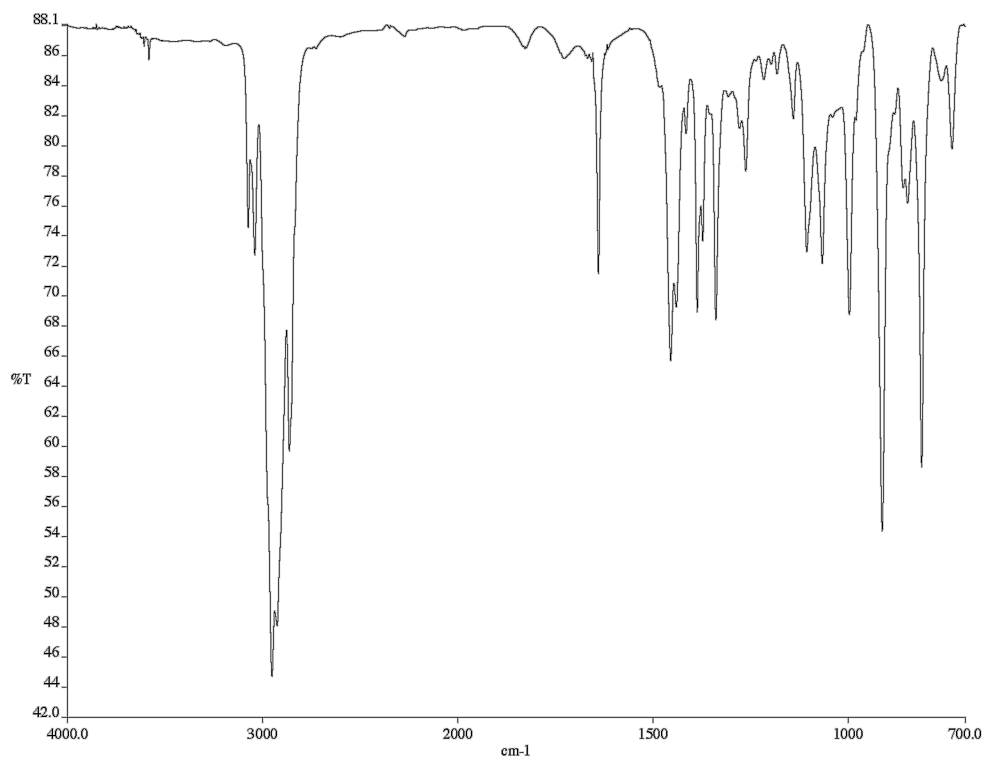


Figure SI-75B. Infrared spectrum (thin film/NaCl) of compound **SI-34**.

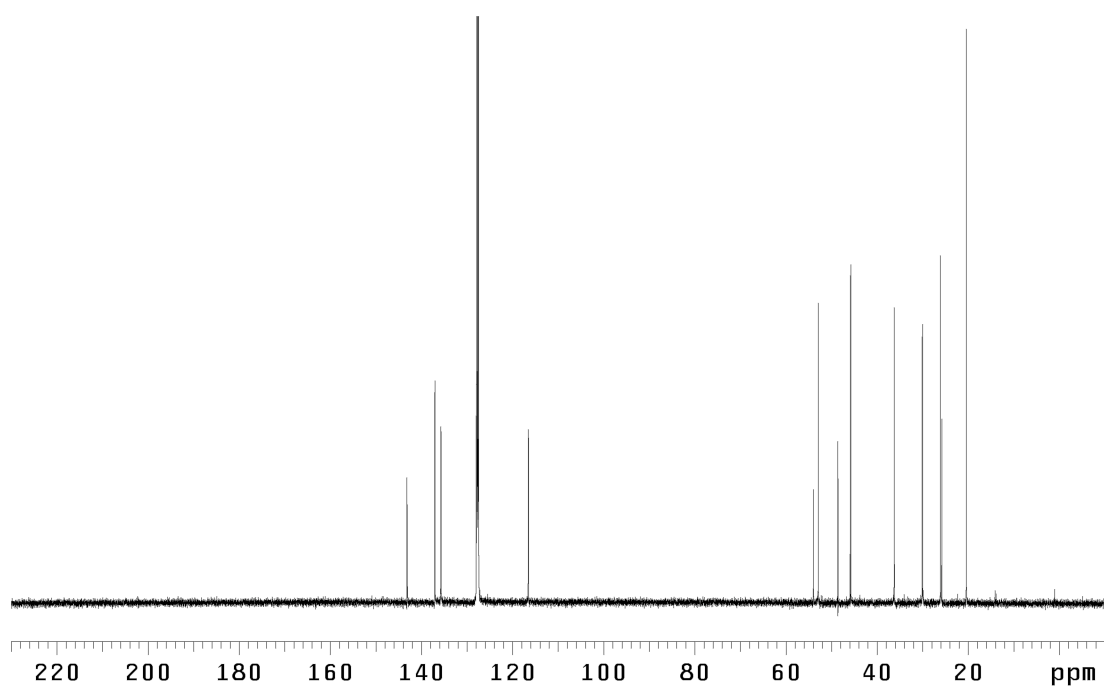


Figure SI-75C. ¹³C NMR (125 MHz, CDCl₃) of compound **SI-34**.

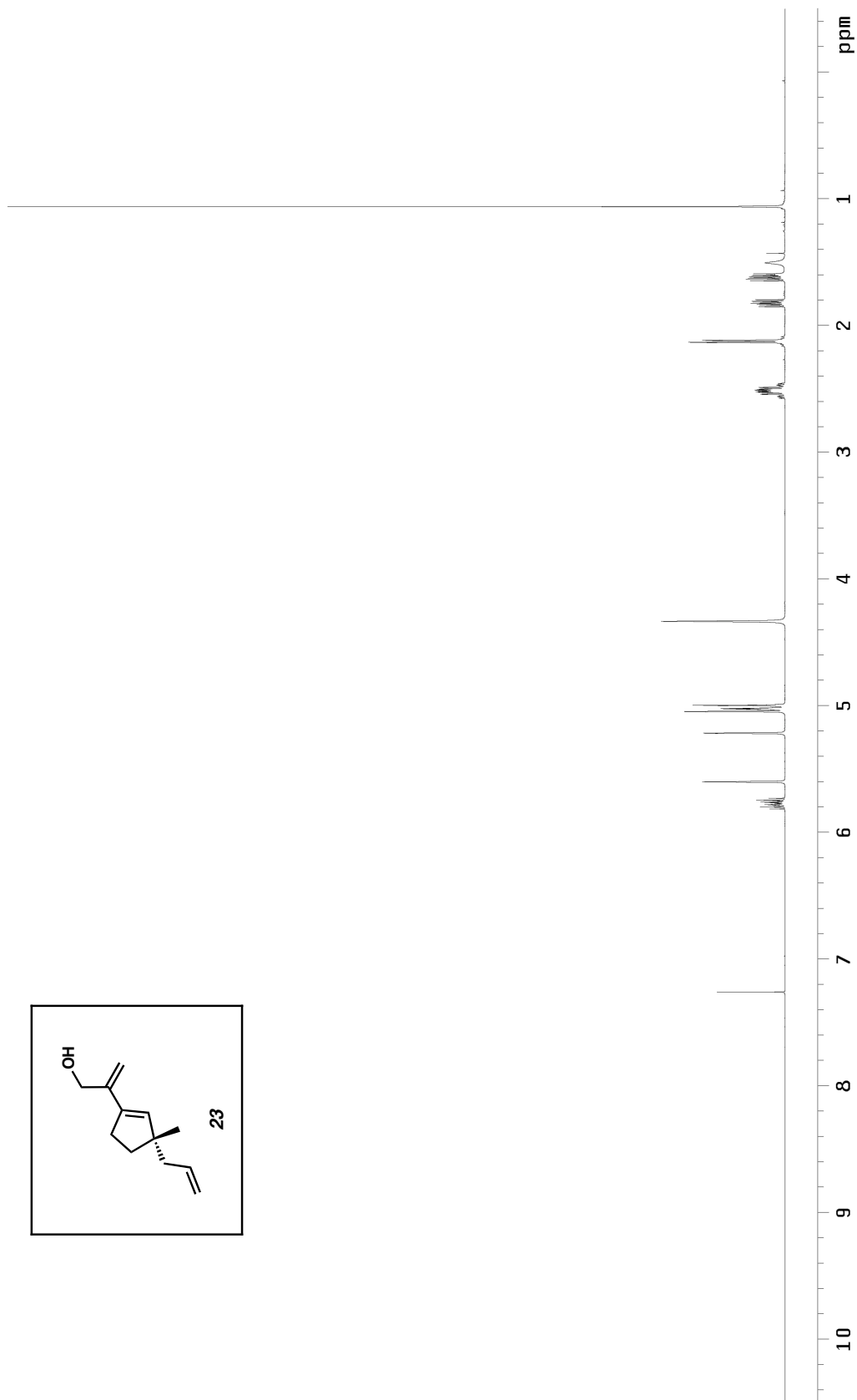


Figure SI-76A. ¹H NMR (500 MHz, CDCl₃) of compound **23**.

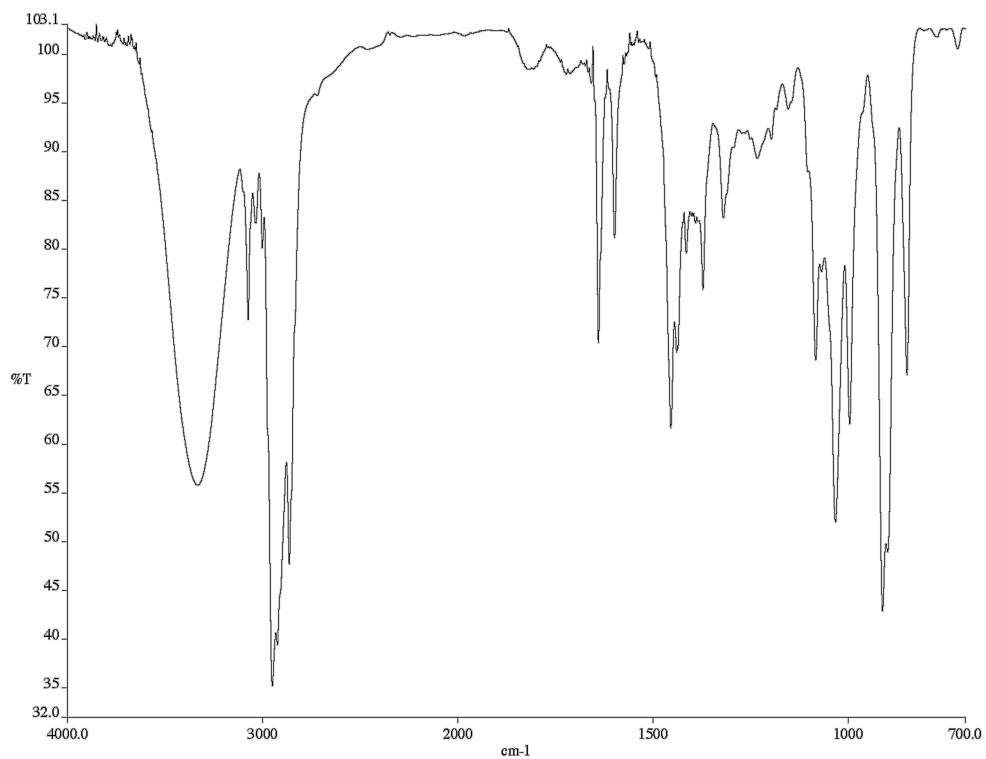


Figure SI-76B. Infrared spectrum (thin film/NaCl) of compound **23**.

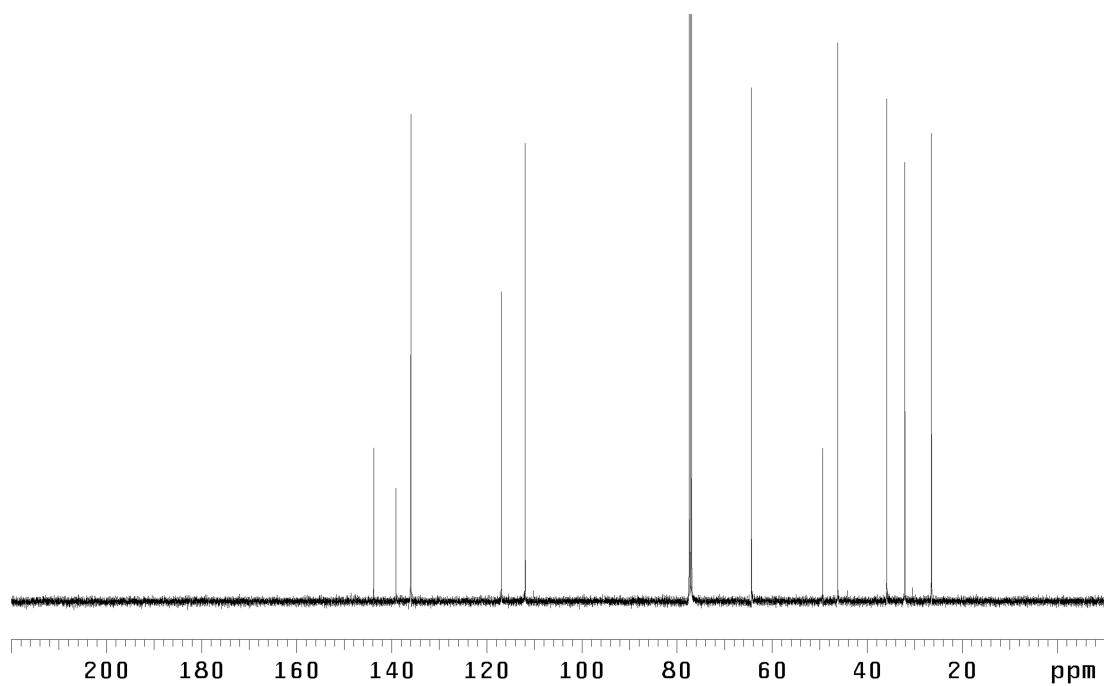


Figure SI-76C. ^{13}C NMR (125 MHz, CDCl_3) of compound **23**.

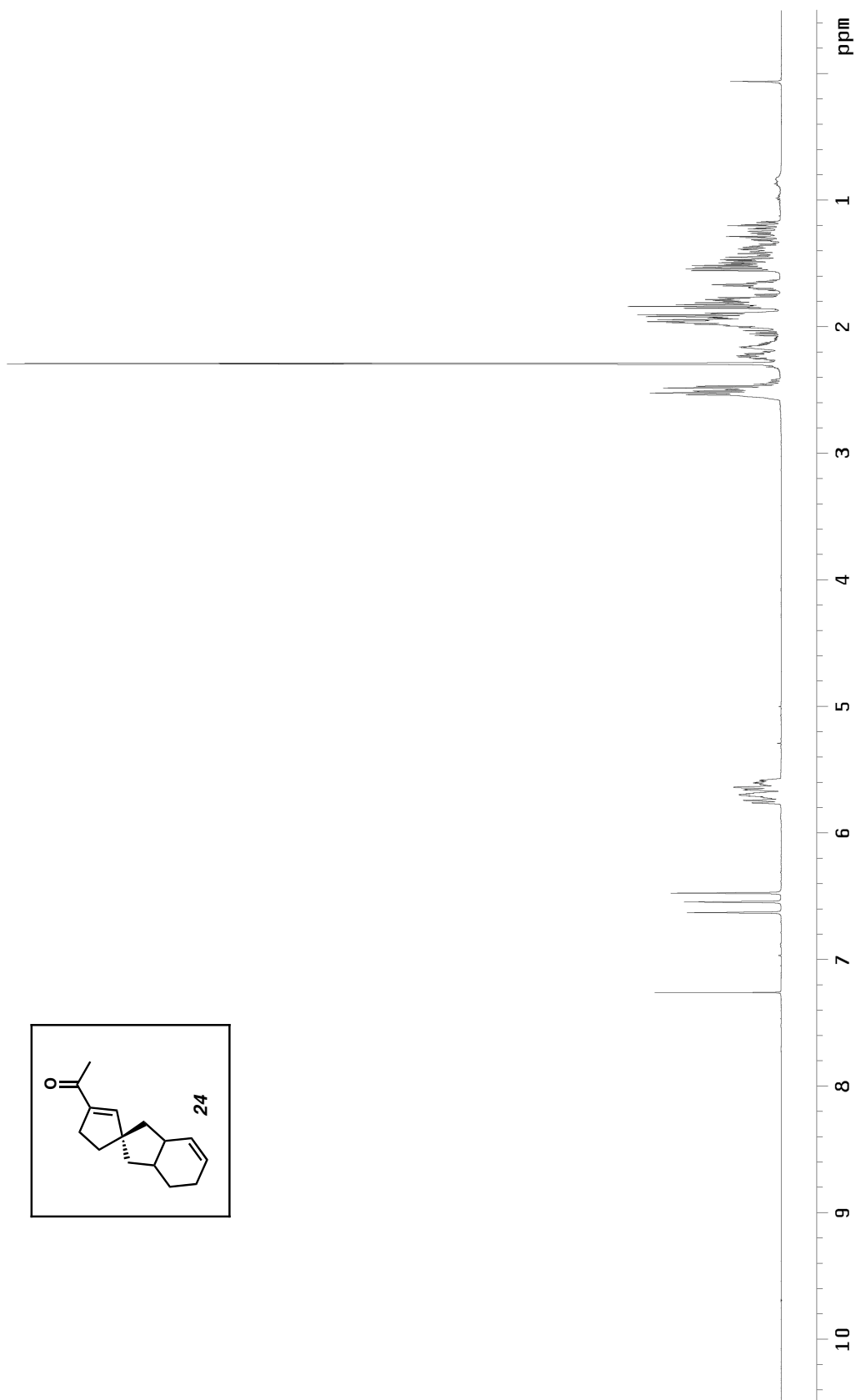


Figure SI-77A. $^1\text{H NMR}$ (500 MHz, CDCl_3) of compound **24**.

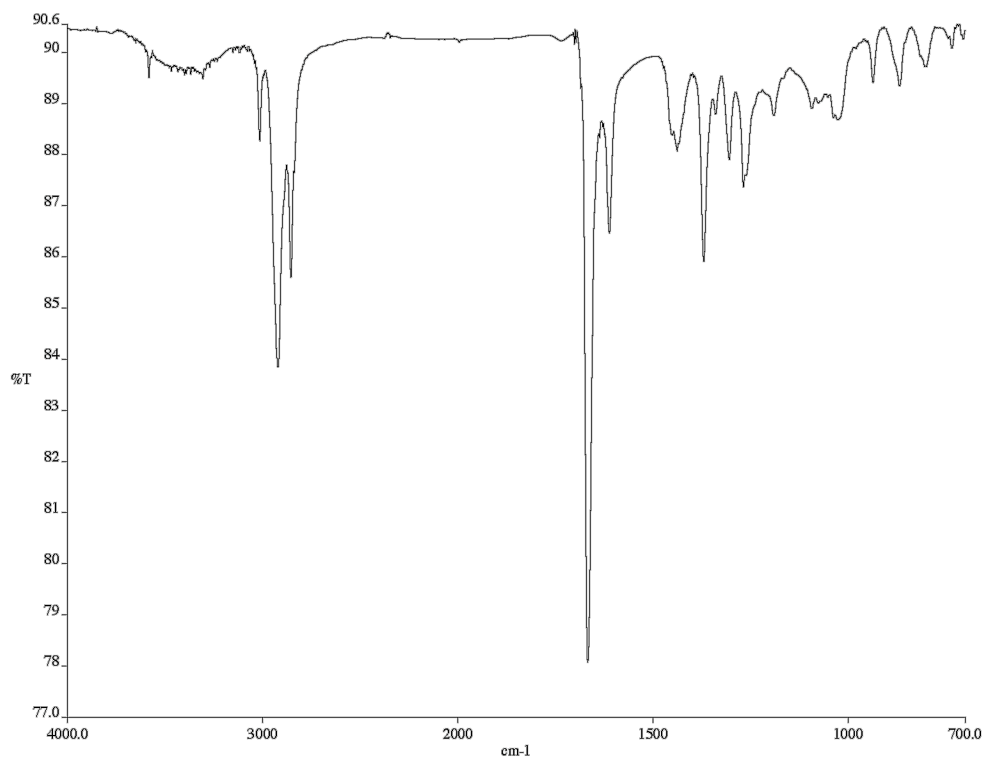


Figure SI-77B. Infrared spectrum (thin film/NaCl) of compound **24**.

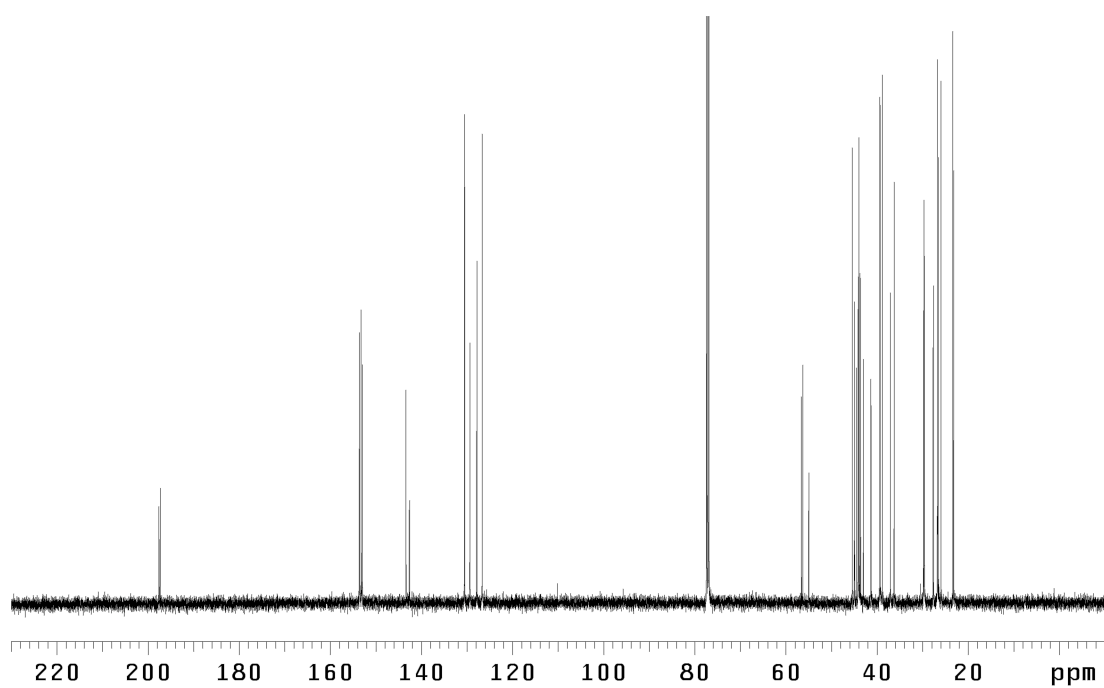


Figure SI-77C. ¹³C NMR (125 MHz, CDCl₃) of compound **24**.

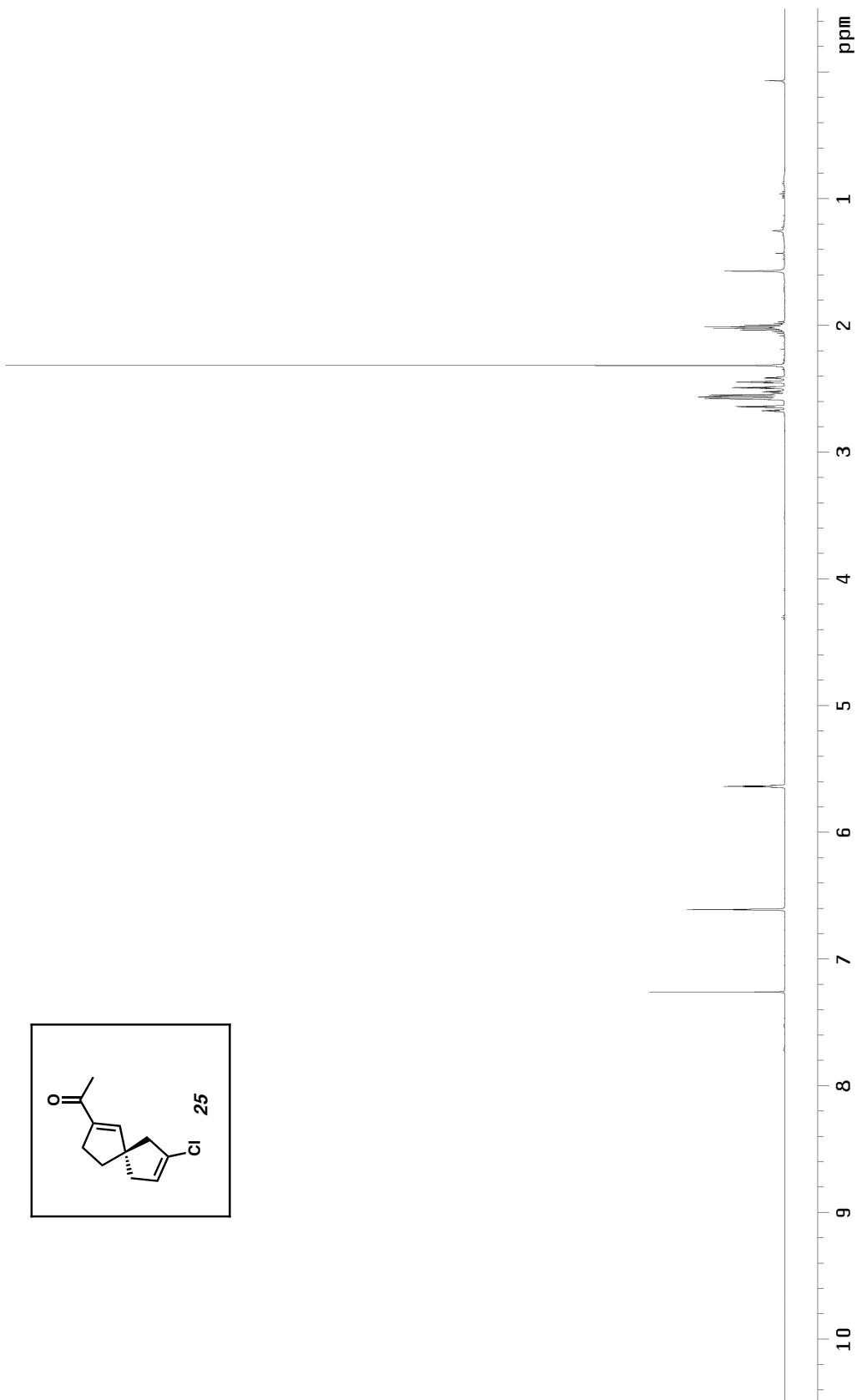


Figure SI-78A. ¹H NMR (500 MHz, CDCl₃) of compound 25.

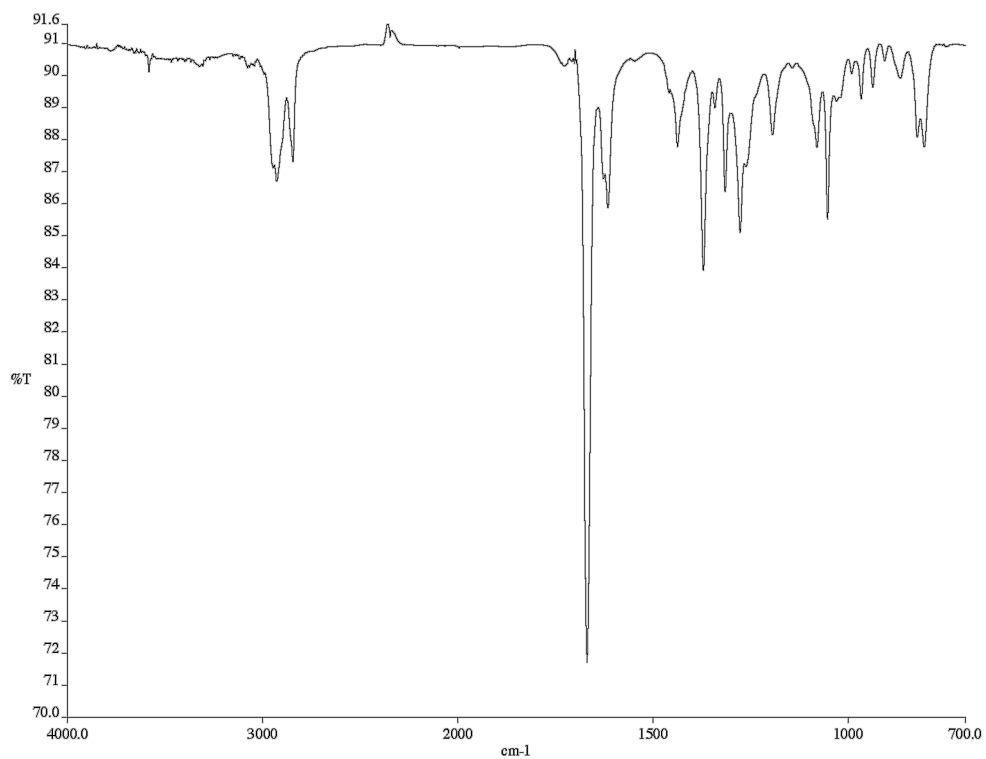


Figure SI-78B. Infrared spectrum (thin film/NaCl) of compound **25**.

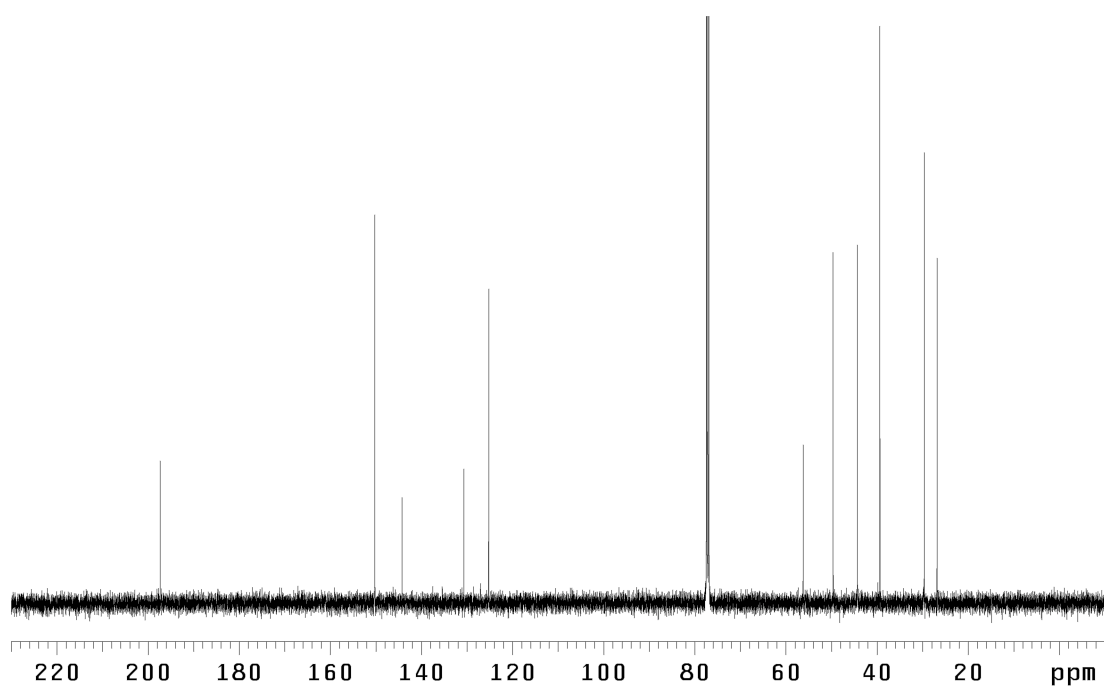


Figure SI-78C. ¹³C NMR (125 MHz, CDCl₃) of compound **25**.

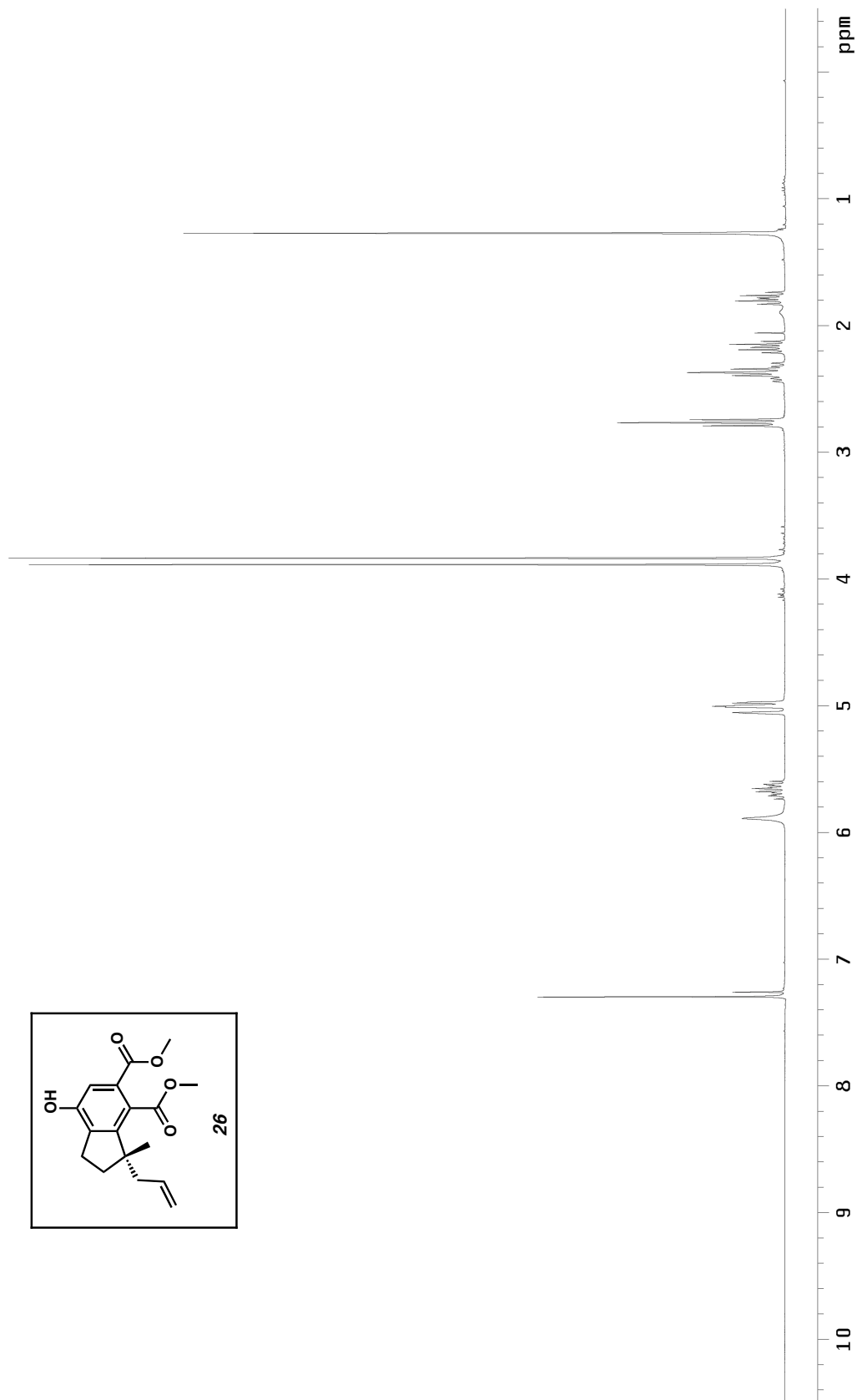


Figure SI-79A. ¹H NMR (300 MHz, CDCl₃) of compound 26.

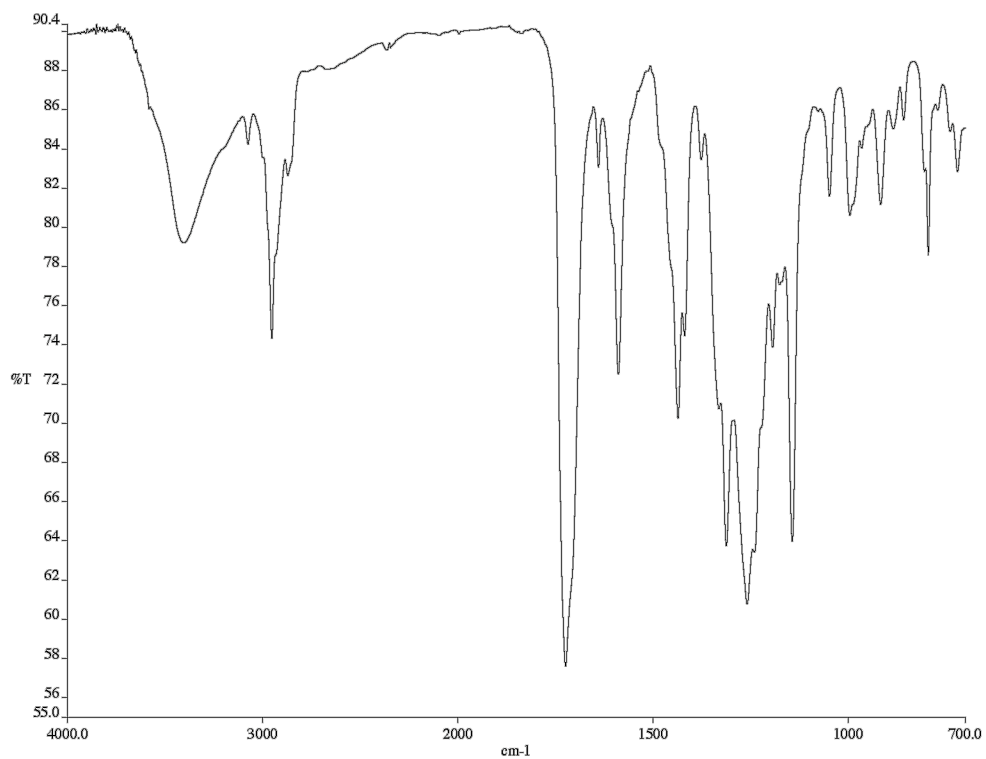


Figure SI-79B. Infrared spectrum (thin film/NaCl) of compound **26**.

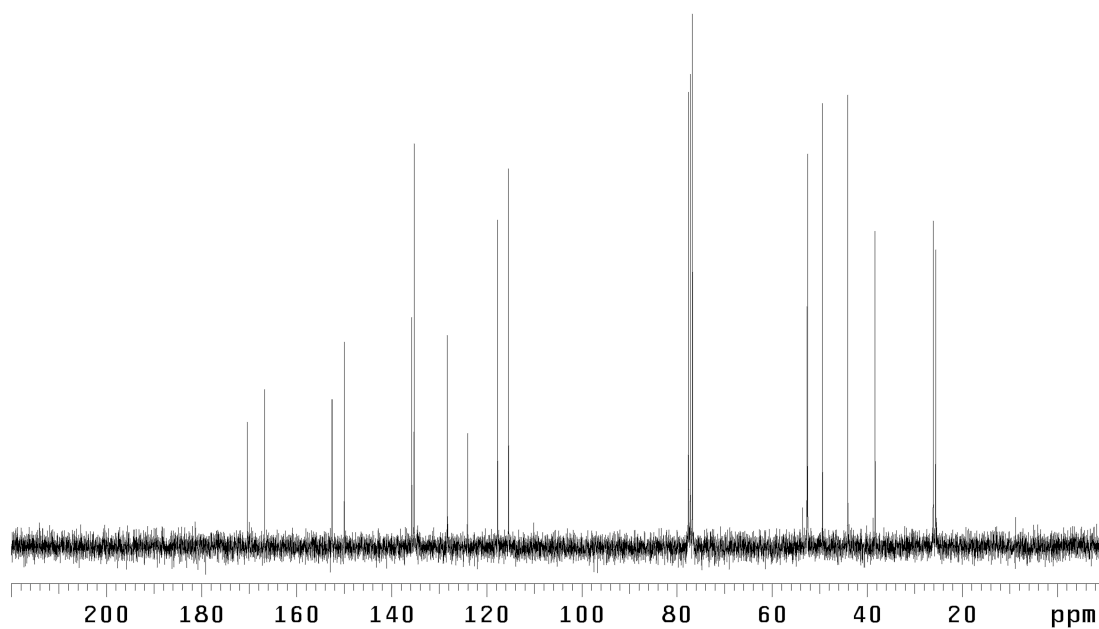


Figure SI-79C. ¹³C NMR (75 MHz, CDCl₃) of compound **26**.