Palladium-Catalyzed Enantioselective Decarboxylative Allylic Alkylation of Cyclopentanones

Robert A. Craig II, Steven A. Loskot, Justin T. Mohr, Douglas, C. Behenna, Andrew M. Harned, and Brian M. Stoltz

Warren and Katharine Schlinger Laboratory for Chemistry and Chemical Engineering, Division of Chemistry and Chemical Engineering, California Institute of Technology, MC 101-20, Pasadena, CA 91125, United States

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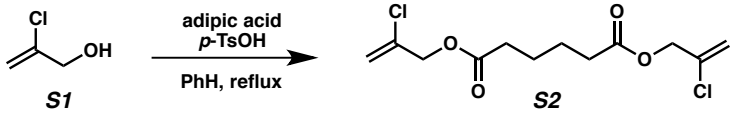
Materials and Methods

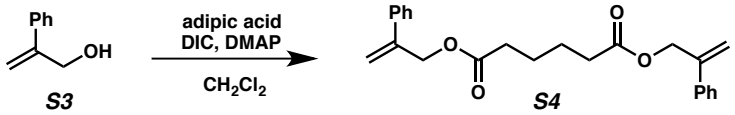
Unless stated otherwise, reactions were performed at ambient temperature (23 °C) in flame-dried or oven-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents (distilled or passed over a column of activated alumina).[1] Commercially obtained reagents were used as received with the exception of palladium acetate ($Pd(OAc)_2$), dipalladium tris(dibenzylideneacetone) ($Pd_2(dba)_3$), tetrakis(triphenylphosphine)palladium(0), and tetrabutylammonium difluorotriphenylsilicate (TBAT), which were stored in a nitrogen-filled glovebox. (*S*)-*t*-BuPHOX,[2] (*S*)-$(CF_3)_3$-*t*-BuPHOX,[3] (*R*)-$(CF_3)_3$-*i*-PrPHOX^{Me2},[4] (*S*)-$(CF_3)_2$-*i*-PrPHOX^{Ph2},[3,5] allyl 2-oxocyclopentanecarboxylate,[6] 2-phenylallyl alcohol,[7] 2-(*p*-methylbenzyl)-cyclopentanone,[8] and 2,2-dimethyl-5-oxo-cyclopenanecarboxylic acid methyl ester[9] were prepared by known methods. Reactions requiring external heat were modulated to the specified temperatures using an IKAmag temperature controller. Reaction progress was monitored by thin-layer chromatography (TLC), which was performed using E. Merck silica gel 60 F254 precoated glass plated (0.25 mm) and visualized by UV fluorescence quenching, potassium permanganate, or *p*-anisaldehyde staining. Silicycle SiliaFlash® P60 Academic Silica gel (particle size 40-63 nm) was used for column chromatography. ^1H and ^{13}C NMR spectra were recorded on a Varian Inova 500 (500 MHz and 126 MHz, respectively), Varian Mercury 300 spectrometer (300 MHz and 75 MHz, respectively), and a Bruker AV III HD spectrometer equipped with a Prodigy liquid nitrogen temperature cryoprobe (400 MHz and 101 MHz, respectively) and are reported in terms of chemical shift relative to $CHCl_3$ (δ 7.26 and δ 77.16, respectively). ^{19}F NMR spectra were recorded on a Varian Inova 500 spectrometer (470 MHz) and are reported in terms of absolute chemical shift according to IUPAC standard recommendations from $CFCl_3$.[10] 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 = septet, m = multiplet, and br s = broad singlet. Infrared (IR) spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer using thin films deposited on NaCl plates and are reported in frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm path-length cell and are reported as: $[\alpha]_D^T$ (concentration in g/100 mL, solvent). Analytical SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system utilizing Chiralpak (AD-H) or Chiracel (OD-H, OJ-H or OB-H) columns (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC utilizing chiralcel OD-H or OJ (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd., with visualization at 254 and 210 nm. High resolution mass spectra were obtained from the Caltech Mass Spectral Facility using a JEOL JMS-600H High Resolution Mass Spectrometer in fast atom bombardment (FAB+) ionization mode or a Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed (ESI/APCI) ionization mode. Julabo Presto LH45 was used to control reaction temperatures inside the nitrogen-filled glovebox.

Allyl β-Ketoester Synthesis and Characterization Data



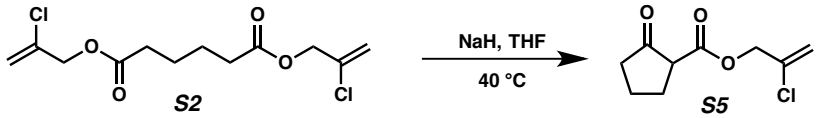
S1 *S2*

2-Chlorodiallyl adipate (S2): Esterification using alcohol **S1** was adapted from the literature.[11] Adipic acid (800 mg, 5.47 mmol, 1.00 equiv), 2-chloroallyl alcohol (**S1**, 1.30 mL, 16.4 mmol, 3.00 equiv), and *para*-toluenesulfonic acid (*p*-TsOH, 3.0 mg, 0.03 mmol, 0.03 equiv) were added to a flask and diluted in benzene (8.00 mL, 0.68 M). The flask was then fitted with a Dean-Stark trap filled with additional benzene. The reaction flask was heated to reflux with stirring for 16 h, at which time the starting material had been completely consumed (determined by TLC analysis, 9:1 Pentane:Et_2O). The reaction solution was cooled to 23 °C, washed with saturated aqueous $NaHCO_3$ (10 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude oil was purified by column chromatography (SiO_2, 10% Et_2O in pentane) to afford ester **S2** (1.62 g, >99% yield) as a pale yellow oil; R_f = 0.21 (9:1 Pentane:Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.49–5.38 (m, 4H), 4.68–4.63 (m, 4H), 2.46–2.37 (m, 4H), 1.78–1.65 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5 (C), 136.1 (C), 115.2 (CH_2), 66.1 (CH_2), 33.8 (CH_2), 24.4 (CH_2); IR (thin film, NaCl) 2943, 2873, 1740, 1637, 1419, 1374, 1134, 1077, 899, 720, 640 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{12}H_{16}Cl_2O_4$ $[M+H]^+$: 295.0504, found: 295.0516.

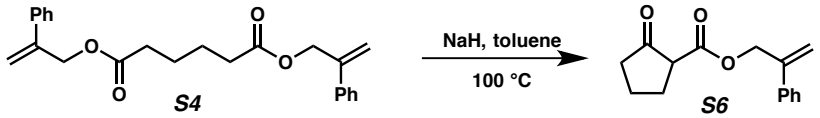


S3 *S4*

2-Phenyldiallyl adipate (S4): Esterification of **S3** was adapted from the literature.[11] A flask charged with alcohol **S3** (5.10 g, 38.0 mmol, 1.90 equiv), adipic acid (2.93 g 20.0 mmol, 1.00 equiv), and 4-(dimethylamino)-pyridine (DMAP, 1.88 g, 15.4 mmol, 0.77 equiv), was evacuated and filled with argon (3 x 5 minutes). Dichloromethane (77 mL, 0.26 M) was added and the solution was cooled to 0 °C (ice/H_2O bath) with stirring. Diisopropylcarbodiimide (DIC, 6.20 mL, 39.6 mmol, 1.98 equiv) was added dropwise and the reaction mixture was allowed to stir for 5 minutes. The cooling bath was then removed and the solution was allowed to warm to ambient temperature (ca. 23 °C). After 11 h, the consumption of starting material was complete (as determined by TLC analysis, 12:1 Hexanes:EtOAc) and the reaction was filtered through filter paper and then diluted with dichloromethane (200 mL). The solution was washed with 0.1 M aqueous HCl (200 mL), saturated aqueous $NaHCO_3$ (100 mL), and brine (100 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, 7.7% EtOAc in hexanes) to provided diallyladipate **S4** (7.06 g, 93% yield) as a pale orange oil; R_f = 0.15 (12:1 Hexanes:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.37 (m, 4H), 7.41–7.24 (m, 6H), 5.54 (d, *J* = 0.9 Hz, 2H), 5.35 (q, *J* = 1.2 Hz, 2H), 4.98 (d, *J* = 1.2 Hz, 4H), 2.36–2.23 (m, 4H), 1.61–1.56 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0 (C), 142.6 (C), 138.0 (C), 128.5 (CH), 128.1 (CH), 126.0 (CH), 115.3 (CH_2), 65.6 (CH_2), 33.9 (CH_2), 24.3 (CH_2); IR (thin film, NaCl) 2943, 1734, 1631, 1496, 1444, 1387, 1165. 1076, 1026, 910, 709, 778 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{24}H_{26}O_4$ $[M+H]^+$: 379.1904, found: 379.1908.

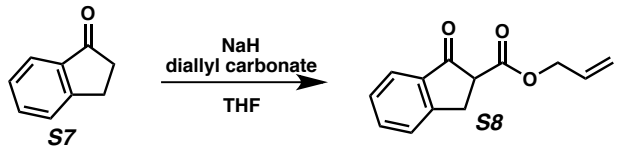


2-Chloroallyl 2-oxocyclopentanecarboxylate (S5): Dieckmann condensation was adapted from the literature.[6] A flask was charged with NaH (60% dispersion in mineral oil, 140 mg, 3.5 mmol, 1.04 equiv) and subsequently evacuated and re-filled with argon (3 x 5 minutes). THF (17 mL, 0.20 M) was added followed by 2-chlorodiallyl adipate (**S2**, 1.00 g, 3.40 mmol, 1.00 equiv). The reaction was then placed into a preheated 40 °C oil bath. After 16 h, the consumption of starting material was complete (as determined by TLC analysis, 9:1 Hexanes:EtOAc) and the reaction was removed from the heating bath and allowed to cool to ambient temperature (ca. 23 °C). After cooling, the reaction was quenched with 1.0 M aqueous HCl (20 mL). The resultant solution was extracted with EtOAc (3 x 30 mL). The combined organics were washed with brine (90 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, 10% EtOAc in hexanes) to furnish β-ketoester **S5** (502 mg, 73% yield) as a clear colorless oil; R_f = 0.27 (9:1 Hexanes:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.56 (q, *J* = 1.4 Hz, 1H), 5.44 (dd, *J* = 1.9, 0.9 Hz, 1H), 4.74 (qt, *J* = 13.9, 1.0 Hz, 2H), 3.35–3.17 (m, 1H), 2.45–2.27 (m, 4H), 2.19 (ddq, *J* = 13.2, 7.8, 5.3 Hz, 1H), 2.01–1.82 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.9 (C), 168.6 (C), 135.3 (C), 115.1 (CH_2), 66.5 (CH_2), 54.7 (CH), 38.2 (CH_2), 21.1 (CH_2); IR (thin film, NaCl) 2971, 2883, 1757, 1734, 1730, 1656, 1639, 1405, 1333, 1295, 1248, 1179, 1108, 1003, 961, 901, 833 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_9H_{12}O_3Cl$ $[M+H]^+$: 203.0475, found: 203.0470.

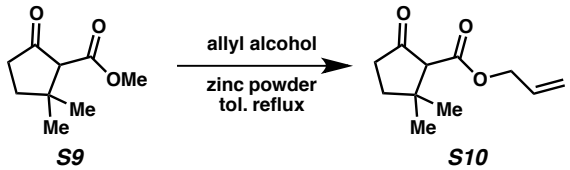


2-Phenylallyl 2-oxocyclopentanecarboxylate (S6): Dieckmann condensation was adapted from the literature.[11] A flask was charged with NaH (60% dispersion in mineral oil, 216 mg, 9.02 mmol, 1.10 equiv) and subsequently evacuated and re-filled with argon (3 x 5 minutes). Toluene (31.0 mL, 0.26 M) was added followed by 2-phenyldiallyl adipate (**S4**, 3.10 g, 8.20 mmol, 1.00 equiv). The reaction was then placed in a preheated 100 °C oil bath. After 16 h, the consumption of starting material was complete (as determined by TLC analysis, 8:2 Hexanes:EtOAc) and the reaction was removed from the heating bath and allowed to cool to ambient temperature (ca. 23 °C). After cooling, the reaction was quenched with 1 M HCl (12.5 mL) and saturated aqueous NH_4Cl (25 mL). The resultant solution was extracted with Et_2O (3 x 30 mL). The combined organics were washed with a 50:50 mixture of H_2O and brine (90 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude solution was purified by column chromatography (SiO_2, 20% EtOAc in hexanes) to afford β-ketoester **S6** (1.54 g, 77% yield) as a faint pink oil; R_f = 0.42 (8:2 Hexanes:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.40 (m, 2H), 7.39–7.28 (m, 3H), 5.56 (d, *J* = 0.9 Hz, 1H), 5.40 (q, *J* = 1.2 Hz, 1H), 5.12–4.96 (m, 2H), 3.28–3.06 (m, 1H), 2.38–2.18 (m, 4H), 2.15–1.98 (m, 1H), 1.93–1.76 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.2 (C), 169.2 (C), 142.2 (C), 138.0 (C), 128.6 (CH), 128.2 (CH), 126.2 (CH), 115.5 (CH_2), 66.6 (CH_2), 54.9 (CH), 38.2 (CH_2), 27.5 (CH_2), 21.1 (CH_2); IR (thin film, NaCl) 3467, 3083, 3056, 2962, 1725, 1574, 1496, 1450, 1400, 1341,

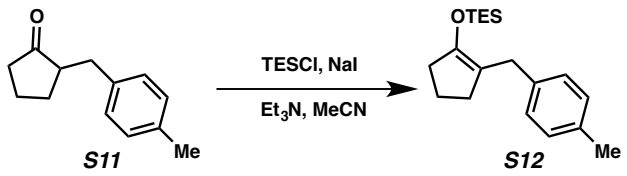
1294, 1249, 1180, 1106, 1025, 959, 914, 833, 778, 708 cm^{-1}; HRMS (APCI/ESI) m/z calc'd for $C_{15}H_{17}O_3$ $[M+H]^+$: 245.1182, found: 245.1173.



Allyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (S8): Acylation of **S7** was adapted from the literature.[11] A flask was charged with NaH (60% dispersion in mineral oil, 500 mg, 20.8 mmol, 2.50 equiv) and subsequently evacuated and re-filled with argon (3 x 5 minutes). THF (10.8 mL, 1.92 M) was added and the resultant solution was cooled to 0 °C (ice/H_2O bath). A solution of 1-indanone (**S7**, 1.10 g, 8.30 mmol, 1.00 equiv) in THF (2.6 mL, 3.20 M) was added dropwise. The solution was allowed to warm to room temperature (ca. 23 °C). After 15 minutes, diallyl carbonate (1.79 mL, 12.5 mmol, 1.50 equiv) was added dropwise. After 16 h, the consumption of starting material was complete (as determined by TLC analysis, 12:1 Hexanes:EtOAc) and the solution was quenched with saturated aqueous NH_4Cl and extracted with EtOAc (3 x 20 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, 7.7% EtOAc in hexanes) to provided β-ketoester **S8** (1.62 g, 91% yield) as a purple oil; R_f = 0.25 (12:1 Hexanes:EtOAc). β-ketoester **S8** was carried on without any further characterization.

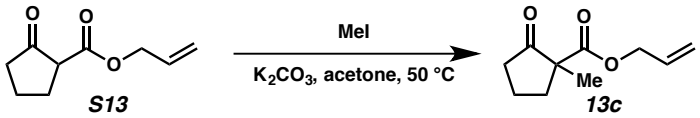


Allyl 2,2-dimethyl-5-oxocyclopentane-1-carboxylate (S9): A solution of **S9** (400 mg, 2.35 mmol, 1.00 equiv) in toluene (1.96 mL, 1.20 M) was added zinc powder (31 mg, 0.47 mmol, 0.20 equiv) and allyl alcohol (799 μL, 11.8 mmol, 5.00 equiv). The reaction mixture was allowed to stir at reflux. After 24 h the consumption of starting material was complete (as determined by TLC analysis, 9:1 Hexanes:EtOAc). The crude solution was directly purified by column chromatography (SiO_2, 10% Et_2O in hexanes) to furnish cyclopentanone **S10** (309 mg, 67% yield) as a clear colorless oil; R_f = 0.24 (9:1 Hexaes:Et_2O); ^1H NMR (400 MHz, $CDCl_3$) δ 5.91 (ddt, *J* = 17.2, 10.4, 5.8 Hz, 1H), 5.34 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.25 (dq, *J* = 10.4, 1.2 Hz, 1H), 4.62 (ddt, *J* = 5.9, 3.0, 1.4 Hz, 2H), 2.97–2.91 (m, 1H), 2.55–2.31 (m, 2H), 2.01 (ddd, *J* = 12.8, 9.1, 5.7 Hz, 1H), 1.82–1.65 (m, 1H), 1.22 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.0 (C), 168.6 (C), 131.8 (CH), 118.9 (CH_2), 65.8 (CH), 65.7 (CH_2), 41.0 (C), 36.8 (CH_2), 36.1 (CH_2), 29.1 (CH_3), 24.1 (CH_3); IR (thin film, NaCl) 2959, 2872, 1757, 1761, 1734, 1729, 1647, 1610, 1616, 1458, 1390, 1370, 1363, 1319, 1234, 1219, 1190, 1159, 1112, 1032, 991, 934, 810, 772, 736 cm^{-1}; HRMS (APCI/ESI) m/z calc'd for $C_{11}H_{16}O_3$ $[M+H]^+$: 197.1172, found 197.1169.



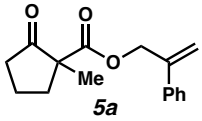
2-(*p*-methylbenzyl)-1-triethylsiloxy-1-cyclopentene (S12): To a solution of cyclopentanone **S11** (300 mg, 1.59 mmol, 1.00 equiv) and sodium iodide (310 mg, 2.00 mmol, 1.30 equiv) in acetonitrile (2.65 mL, 0.60 M) had Et_3N (357 μL, 2.54 mmol, 1.60 equiv) added dropwise. After 5 minutes of stirring, TESCl (347 μL, 2.07 mmol, 1.30 equiv) was added dropwise. After 6 hours of stirring, consumption of starting was complete (as determined by TLC analysis, 19:1 Hexanes:Et_2O). Crude solution was extracted with pentane (4 x 5 mL), the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (SiO_2, 0.5% Et_3N, 1% Et_2O in hexanes) to provide silyl enol ether **S12** (164 mg, 34%) as a pale yellow oil; R_f= 0.62 (19:1 Hexanes:Et_2O); ^{1}H NMR (400 MHz, C_6D_6) δ 7.21 (d, *J* = 7.9 Hz, 2H), 7.03 (d, *J* = 7.7 Hz, 2H), 3.52 (s, 2H), 2.30 (dddd, *J* = 8.6, 7.3, 3.4, 1.7 Hz, 2H), 2.19 (dddd, *J* = 9.5, 7.2, 3.0, 1.3 Hz, 2H), 2.13 (s, 3H), 1.72 – 1.61 (m, 2H), 1.01 (t, *J* = 7.9 Hz, 9H), 0.65 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (101 MHz, C_6D_6) δ 147.6 (C), 138.2 (C), 135.1 (C), 129.3 (CH), 129.0 (CH), 115.8 (C), 34.2 (CH_2), 33.0 (CH_2), 31.2 (CH_2), 21.1 (CH_3), 20.1 (CH_2), 7.1 (CH_3), 5.9 (CH_2); IR (thin film, NaCl) 3044, 2954, 2876, 2845, 1895, 1681, 1512, 1458, 1412, 1378, 1341, 1306, 1240, 1107, 1045, 1016, 974, 888, 859, 746, 680 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{19}H_{30}OSi$ $[M]^+$: 302.2066, found 302.2075.

α-Quaternary Cyclopentanone Synthesis and Characterization Data

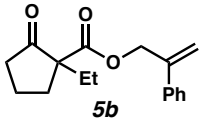


Representative Procedure: β-Ketoester Alkylation.

The alkylation β-ketoester **S13** was adapted from the literature.[11] β-ketoester **S13** (500 mg, 2.97 mmol, 1.00 equiv) was added to a suspension of anhydrous K_2CO_3 (822 mg, 5.95 mmol, 2.00 equiv) in acetone (3.00 mL, 1.00 M). To the reaction mixture was added iodomethane (0.370 mL, 5.95 mmol, 2.00 equiv). The resultant solution was placed in a preheated 50 °C oil bath. After 14 h, the consumption of starting material was complete (as determined by TLC analysis, 9:1 Pentane:Et_2O) and the reaction was removed from the heating bath and allowed to cool to ambient temperature (ca. 23 °C). After cooling, the solution was filtered with grade 4 filter paper and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, 10% Et_2O in pentane) to furnish β-ketoester **13c** (477 mg, 88% yield) as a clear colorless oil; R_f = 0.23 (9:1 Pentane:Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 (ddt, *J* = 17.3, 10.5, 5.6 Hz, 1H), 5.29 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.23 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.60 (dq, *J* = 5.6, 1.4 Hz, 2H), 2.61–2.38 (m, 2H), 2.39–2.26 (m, 1H), 2.14–1.98 (m, 1H), 2.02–1.80 (m, 2H), 1.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 215.8 (C), 172.0 (C), 131.7 (CH), 118.3 (CH_2), 65.8 (CH_2), 56.0 (C), 37.7 (CH_2), 36.2 (CH_2), 19.6 (CH_3), 19.5 (CH_2). IR (thin film, NaCl) 3462, 3086, 2973, 2886, 1752, 1731, 1648, 1457, 1406, 1375, 1316, 1273, 1153, 1064, 976, 939, 842, 814, 770 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{10}H_{15}O_3$ $[M+H]^+$: 183.1021, found 183.1022.

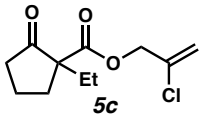


2-Phenylallyl 1-methyl)-2-oxocyclopentanecarboxylate (5a): Prepared by using the representative procedure above from 2-phenylallyl 2-oxocyclopentanecarboxylate (**S6**, 1.64 mmol) and using iodomethane as the electrophile. Purified by column chromatography (SiO_2, 10% Et_2O in pentane) to afford β-ketoester **5a** (292 mg, 69% yield) as a clear colorless oil; R_f = 0.25 (9:1 Pentane:Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.28 (m, 5H), 5.52 (q, *J* = 0.8 Hz, 1H), 5.33 (q, *J* = 1.3 Hz, 1H), 5.06 (ddd, *J* = 13.4, 1.5, 0.7 Hz, 1H), 4.96 (ddd, *J* = 13.3, 1.3, 0.7 Hz, 1H), 2.46–2.34 (m, 1H), 2.31–2.18 (m, 2H), 1.94–1.74 (m, 3H), 1.29 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 215.8 (C), 172.1 (C), 142.5 (C), 138.0 (C), 128.6 (CH), 128.2 (CH), 126.2 (CH), 115.4 (CH_2), 66.6 (CH_2), 56.1 (C), 37.7 (CH_2), 36.3 (CH_2), 19.61 (CH_3), 19.59 (CH_2); IR (thin film, NaCl) 3467, 2972, 1750, 1729, 1496, 1457, 1405, 1374, 1316, 1262, 1230, 1150, 1063, 1027, 973, 911, 840, 778, 709 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{16}H_{19}O_3$ $[M+H]^+$: 259.1334, found: 259.1347.



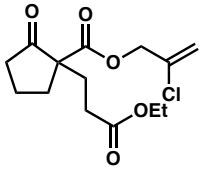
5b

2-Phenylallyl 1-ethyl)-2-oxocyclopentanecarboxylate (5b): Prepared by using the representative procedure above from 2-phenylallyl 2-oxocyclopentanecarboxylate (**S6**, 1.63 mmol) and using iodoethane as the electrophile. Purified by column chromatography (SiO_2, 10% Et_2O in pentane) to provide β-ketoester **5b** (288 mg, 65% yield) as a clear colorless oil; R_f = 0.29 (9:1 Pentane:Et_2O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.28 (m, 5H), 5.52 (d, *J* = 0.8 Hz, 1H), 5.34 (q, *J* = 1.3 Hz, 1H), 5.04 (ddd, *J* = 13.3, 1.4, 0.7 Hz, 1H), 4.99 (ddd, *J* = 13.4, 1.3, 0.6 Hz, 1H), 2.50–2.32 (m, 1H), 2.32–2.11 (m, 2H), 1.94 (dq, *J* = 14.1, 7.5 Hz, 1H), 1.89–1.78 (m, 3H), 1.62 (dq, *J* = 14.0, 7.4 Hz, 1H), 0.83 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 215.0 (C), 170.9 (C), 142.6 (C), 138.1 (C), 128.6 (CH), 128.2 (CH), 126.2 (CH), 115.5 (CH_2), 66.5 (CH_2), 61.0 (C), 38.2 (CH_2), 32.3 (CH_2), 26.9 (CH_2), 19.6 (CH_2), 9.3(CH_3); IR (thin film, NaCl) 3460, 2968, 2881, 1749, 1725, 1635, 1496, 1457, 1405, 1318, 1294, 1223, 1142, 1078, 1027, 977, 915, 824, 779, 709 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{17}H_{21}O_3$ $[M+H]^+$: 273.1491, found: 273.1480.



5c

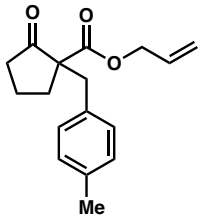
2-Chloroallyl 1-ethyl)-2-oxocyclopentanecarboxylate (5c): Prepared by using the representative procedure above from 2-chloroallyl 2-oxocyclopentanecarboxylate (**S5**, 0.99 mmol) and using iodoethane as the electrophile. Purified by column chromatography (SiO_2, 5% Et_2O in pentane) to furnish β-ketoester **5c** (228 mg, 80% yield) as a clear colorless oil; R_f = 0.3 (8:2 Pentane:Et_2O); ^1H NMR δ 5.46 (q, *J* = 1.4 Hz, 1H), 5.39 (dd, *J* = 1.8, 0.8 Hz, 1H), 4.75–4.59 (m, 2H), 2.60–2.49 (m, 1H), 2.49–2.38 (m, 1H), 2.34–2.21 (m, 1H), 2.14–1.90 (m, 4H), 1.67 (dq, *J* = 13.9, 7.4 Hz, 1H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.7 (C), 170.4 (C), 135.5 (C), 115.3 (CH_2), 66.5 (CH_2), 61.0 (C), 38.3 (CH_2), 32.3 (CH_2), 26.9 (CH_2), 19.7 (CH_2), 9.3 (CH_3); IR (thin film, NaCl) 3466, 3115, 2970, 2882, 1755, 1732, 1639, 1458, 1405, 1382, 1319, 1294, 1222, 1132, 1082, 1030, 904, 820, 797, 765, 705, 643 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{11}H_{16}O_3Cl$ $[M+H]^+$: 231.0788, found: 231.0794.



5d

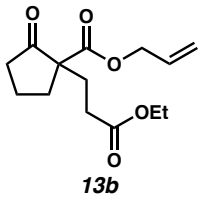
2-Chloroallyl 1-(3-ethoxy-3-oxopropyl)-2-oxocyclopentanecarboxylate (5d): Prepared by using the representative procedure above from 2-chloroallyl 2-oxocyclopentanecarboxylate (**S5**, 0.99 mmol) and using ethyl acrylate as the electrophile. Purified by column chromatography (SiO_2, 20% Et_2O in pentane) to afford β-ketoester **5d** (132 mg, 44% yield) as a clear colorless oil; R_f = 0.1 (8:2 Pentane:Et_2O); ^1H NMR δ 5.46 (dt, *J* = 2.2, 1.2 Hz, 1H), 5.43–5.39 (m, 1H), 4.75–4.61 (m, 2H), 4.12 (q, *J* = 7.1 Hz, 2H),

2.58–2.47 (m, 2H), 2.47–2.39 (m, 1H), 2.39–2.19 (m, 3H), 2.13–1.88 (m, 4H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.1 (C), 173.0 (C), 170.3 (C), 135.4 (C), 115.7 (CH_2), 66.7 (CH_2), 60.7 (CH_2), 59.4 (C), 38.1 (CH_2), 33.8 (CH_2), 29.9 (CH_2), 28.5 (CH_2), 19.8 (CH_2), 14.3 (CH_3); IR (thin film, NaCl) 3459, 2978, 1730, 1638, 1448, 1377, 1180, 1109, 1023, 905, 642 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{14}H_{20}O_5Cl$ $[M+H]^+$: 303.0999, found: 303.0986.



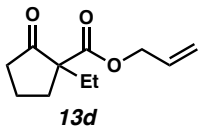
13a

Allyl 1-(4-methylbenzyl)-2-oxocyclopentanecarboxylate (13a): Prepared by using the representative procedure above from allyl 2-cyclopentanonecarboxylate (**S13**, 8.79 mmol) and using 4-methylbenzyl bromide as the electrophile. Purified by column chromatography (SiO_2, 10% Et_2O in pentane) to afford β-ketoester **13a** (2.13 g, 89% yield) as a clear colorless oil; R_f = 0.20 (9:1 Pentane:Et_2O); characterization data match known literature values.[11]



13b

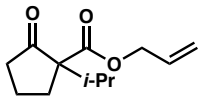
Allyl 1-(3-ethoxy-3-oxopropyl)-2-oxocyclopentanecarboxylate (13b): Prepared by using the representative procedure above from allyl 2-cyclopentanonecarboxylate (**S13**, 8.97 mmol) and using ethyl acrylate as the electrophile. Purified by column chromatography (SiO_2, 10% Et_2O in pentane) to provide β-ketoester **13b** (1.83 g, 76% yield) as a clear colorless oil; R_f = 0.20 (8:2 Pentane:Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.33–5.11 (m, 2H), 4.55 (dt, *J* = 5.6, 1.4 Hz, 2H), 4.06 (q, *J* = 7.2 Hz, 2H), 2.54–2.38 (m, 2H), 2.36 (ddd, *J* = 8.7, 6.3, 1.1 Hz, 1H), 2.32–2.12 (m, 3H), 2.08–1.77 (m, 4H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.2 (C), 172.9 (C), 170.7 (C), 131.5 (CH), 118.6 (CH_2), 65.9 (CH_2), 60.6 (CH_2), 59.3 (C), 37.9 (CH_2), 33.7 (CH_2), 29.8 (CH_2), 28.4 (CH_2), 19.6 (CH_2), 14.2 (CH_3); IR (thin film, NaCl) 3453, 3086, 2979, 1731, 1648, 1451, 1377, 1182, 1113, 1025, 985, 939, 852 cm^{-1}; HMRS (APCI) m/z calc'd for $C_{14}H_{21}O_5$ $[M+H]^+$: 269.1384, found: 269.1389.



13d

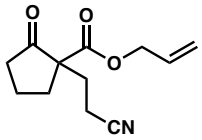
Allyl 1-ethyl-2-oxocyclopentanecarboxylate (13d): Prepared by using the representative procedure above from allyl 2-cyclopentanonecarboxylate (**S13**, 9.17 mmol) and using iodoethane as the electrophile. Purified by column chromatography

(SiO_2, 10% Et_2O in hexanes) to afford β-ketoester **13d** (1.53 g, 85% yield) as a clear colorless oil; R_f = 0.23 (9:1 Hexanes:Et_2O); characterization data match known literature values.[11]



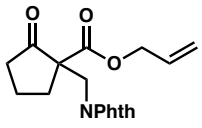
13e

Allyl 1-isopropyl-2-oxocyclopentanecarboxylate (13e): Prepared by using the representative procedure above from allyl 2-cyclopentanonecarboxylate (**S13**, 8.99 mmol) and using 2-iodopropane as the electrophile. Purified by column chromatography (SiO_2, 10% to 30% Et_2O in hexanes) to provide β-ketoester **13e** (1.55 g, 82% yield) as a clear colorless oil; R_f = 0.32 (10:1 Hexanes:EtOAc); characterization data match known literature values.[11]



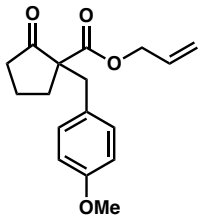
13f

Allyl 1-(cyanomethyl)-2-oxocyclopentanecarboxylate (13f): Prepared by using the representative procedure above from allyl 2-cyclopentanonecarboxylate (**S13**, 2.66 mmol) and using acrylonitrile as the electrophile. Purified by column chromatography (SiO_2, 50% Et_2O in pentane) to afford β-ketoester **13f** (589 mg, 30% yield) as a clear colorless oil; R_f = 0.20 (8:2 Pentane:Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96–5.76 (m, 1H), 5.37–5.20 (m, 2H), 4.67–4.54 (m, 2H), 2.67–2.41 (m, 4H), 2.41–2.26 (m, 1H), 2.26–2.15 (m, 1H), 2.14–1.88 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.7 (C), 170.1 (C), 131.2 (CH), 119.4 (C), 119.3 (CH_2), 66.4 (CH_2), 58.7 (C), 37.9 (CH_2), 34.1 (CH_2), 29.5 (CH_2), 19.8 (CH_2), 13.2 (CH_2); IR (thin film, NaCl) 2962, 2247, 1748, 1726, 1648, 1451, 1362, 1261, 1232, 1164, 1115, 938, 824 cm^{-1}; HMRS (ESI+) m/z calc'd for $C_{12}H_{16}O_3N$ $[M+H]^+$: 222.1125, found: 222.1127.



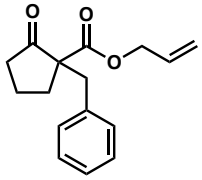
13g

Allyl 1-((1,3-dioxoisoindolin-2-yl)methyl)-2-oxocyclopentanecarboxylate (13g): Prepared by using the representative procedure above from allyl 2-cyclopentanonecarboxylate (**S13**, 8.83 mmol) and using (*N*-chloromethyl)phthalimide as the electrophile. Purified by column chromatography (SiO_2, 20% to 30% EtOAc in hexanes) to furnish β-ketoester **13g** (1.56 g, 54% yield) as a white amorphous solid; R_f = 0.27 (6:3 Hexanes:EtOAc); characterization data match known literature values.[11]



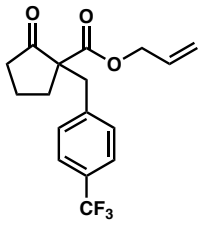
13h

Allyl 1-(4-methoxybenzyl)-2-oxocyclopentanecarboxylate (13h): Prepared by using the representative procedure above from allyl 2-cyclopentanonecarboxylate (**S13**, 8.88 mmol) and using 4-methoxybenzyl chloride as the electrophile. Purified by column chromatography (SiO_2, 9% EtOAc in hexanes) to provide β-ketoester **13h** (2.56 g, 95% yield) as a clear colorless oil; R_f = 0.17 (11:1 Hexanes:EtOAc); characterization data match known literature values.[11]



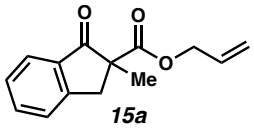
13i

Allyl 1-benzyl-2-oxocyclopentanecarboxylate (13i): Prepared by using the representative procedure above from allyl 2-cyclopentanonecarboxylate (**S13**, 8.86 mmol) and using benzyl bromide as the electrophile. Purified by column chromatography (SiO_2, 10% Et_2O in pentane) to furnish β-ketoester **13i** (824 mg, 36% yield) as a clear colorless oil; R_f = 0.17 (9:1 Pentane:Et_2O); characterization data match known literature values.[12]



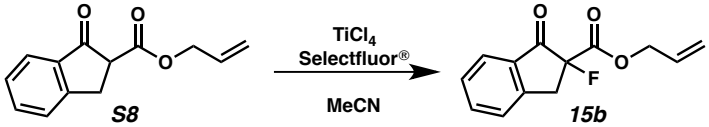
13j

Allyl 2-oxo-1-(4-(trifluoromethyl)benzyl)cyclopentanecarboxylate (13j): Prepared by using the representative procedure above from allyl 2-cyclopentanonecarboxylate (**S13**, 9.10 mmol) and using 4-trifluoromethylbenzyl bromide as the electrophile. Purified by column chromatography (SiO_2, 10% Et_2O in pentane) to furnish β-ketoester **13j** (1.93 g, 65% yield) as an amorphous solid; R_f = 0.20 (9:1 Pentane:Et_2O); characterization data match known literature values.[11]



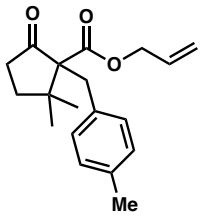
15a

Allyl 2-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (15a): Prepared by using the representative procedure above from allyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**S8**, 1.84 mmol) and using iodomethane as the electrophile. Purified by column chromatography (SiO_2, 7.7% EtOAc in hexanes) to provide β-ketoester **15a** (361 mg, 85% yield) as a pale yellow oil; R_f = 0.23 (12:1 Hexanes:EtOAc); characterization data match known literature values.[12]



S8 ***15b***

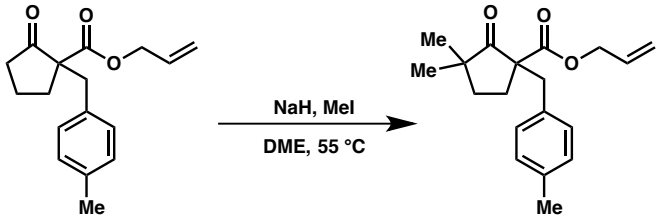
Allyl 2-fluoro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (15b): $TiCl_4$ (18 μL, 167 μmol, 0.09 equiv) was added to a solution of indanone **S8** (400 mg, 1.85 mmol, 1.00 equiv) in acetonitrile (18.5 mL, 0.10 M). After 10 minutes, Selectfluor® (786 mg, 2.22 mmol, 1.20 equiv) was added. After 3 h, the starting material had been completely consumed (determined by TLC analysis, 8:2 Pentane:Et_2O) The solution was partitioned between H_2O (100 mL) and Et_2O (25 mL), extracted with Et_2O (3 x 30 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated in vacuo. Crude product was filtered through a silica plug (Et_2O) to provide β-ketoester **15b** (421 mg, 97% yield) as an amorphous orange solid; R_f = 0.23 (8:2 Pentane:Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.70 (td, *J* = 7.5, 1.3 Hz, 1H), 7.59–7.39 (m, 2H), 5.84 (ddt, *J* = 17.2, 10.5, 5.7 Hz, 1H), 5.35–5.16 (m, 2H), 4.70 (dq, *J* = 5.7, 1.3 Hz, 2H), 3.92–3.72 (m, 1H), 3.59–3.32 (m, 1H); ^{19}F NMR (470 MHz, $CDCl_3$) –164.6 (dd, *J* =11.6, 23.2 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.2 (d, *J* = 18.2 Hz, C), 167.1 (d, *J* = 28.0 Hz, C), 150.9 (d, *J* = 3.7 Hz, C), 136.9 (CH), 133.4 (C), 130.8 (CH), 128.8 (CH), 126.7 (d, *J* = 1.5 Hz, CH), 125.8 (CH), 119.4 (CH_2), 94.7 (d, *J* = 201.8 Hz, C), 66.8 (CH_2), 38.4 (d, *J* = 23.7 Hz, CH_2); IR (thin film, NaCl) 3585, 3435, 3078, 2943, 1761, 1720, 1603, 1465, 1423, 1363, 1272, 1181, 1155, 1067, 994, 917, 806, 751, 721, 692 cm^{-1}; HRMS (ESI+) m/z calc'd for $C_{13}H_{12}FO_3$ $[M+H]^+$: 235.0765, found: 235.0768.



S14

Allyl 2,2-dimethyl-1-(4-methylbenzyl)-5-oxocyclopentane-1-carboxylate (S14): Prepared by using the representative procedure above from allyl 2,2-dimethyl-5-oxocyclopentane-1-carboxylate (**S10**, 1.48 mmol) and using 4-methylbenzyl chloride as the electrophile. Purified by column chromatography (SiO_2, 10% Et_2O in hexanes) to furnish β-ketoester **S14** (61 mg, 14% yield) as a clear colorless oil; R_f = 0.12 (9:1

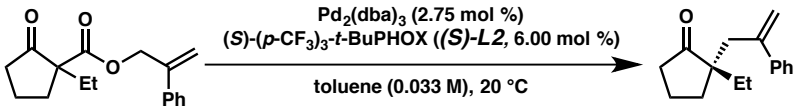
Hexanes:Et_2O); ^1H NMR δ 7.29 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 5.99 (ddt, *J* = 17.2, 10.6, 5.4 Hz, 1H), 5.35 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.19 (dq, *J* = 10.5, 1.5 Hz, 1H), 5.08 (s, 2H), 4.68 (dt, *J* = 5.4, 1.6 Hz, 2H), 2.60 (t, *J* = 7.5 Hz, 2H), 2.37 (s, 3H), 1.69 (t, *J* = 7.4 Hz, 2H), 1.24 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7 (C), 165.0 (C), 137.8 (CH), 133.9 (CH), 133.0 (CH), 129.3, 127.0, 117.3 (CH_2), 113.4 (C), 71.5 (CH_2), 64.1 (CH_2), 43.0 (C), 37.2 (CH_2), 29.1 (CH_2), 27.9 (CH_3), 21.3 (CH_3); IR (thin film, NaCl) 2948, 1685, 1617, 16517, 1457, 1370, 1356, 1283, 1224, 1170, 1087, 1047, 1020, 994, 929, 801, 788 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{19}H_{25}O_3$ $[M+H]^+$: 301.1798, found 301.1803.



13a ***S15***

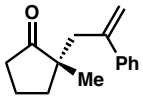
Allyl 3,3-dimethyl-1-(4-methylbenzyl)-2-oxocyclopentane-1-carboxylate (S15): The alkylation of **S15** was adapted from the literature.[13] A flask was charged with sodium hydride (60% dispersion in mineral oil, 61.7 mg, 1.54 mmol, 3.00 equiv) and subsequently evacuated and re-filled with argon (3 x 5 minutes). DME (6 mL, 0.63 M) was added followed by methyliodide (0.16 mL, 2.57 mmol, 5.00 equiv) and β-ketoester **13a** (140 mg, 0.514 mmol, 1 equiv). The heterogeneous solution was heated to 55 °C with stirring. After 2 hours, the consumption of starting was complete (as determined by TLC analysis, 9:1 Pentane:Et_2O). The solution was poured into water, and extracted with Et_2O (3 x 5 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude solution was purified by flash chromatography (SiO_2, 5% Et_2O in hexanes) to afford β-ketoester **S15** (80 mg, 52% yield) as a clear colorless oil; R_f = 0.60 (9:1 Pentane:Et_2O); ^1H NMR δ 7.05 (d, *J* = 7.9 Hz, 2H), 7.01 (d, *J* = 8.1 Hz, 2H), 5.89 (ddt, *J* = 17.2, 10.4, 5.7 Hz, 1H), 5.32 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.24 (dq, *J* = 10.4, 1.3 Hz, 1H), 4.62 (ddt, *J* = 5.6, 2.7, 1.4 Hz, 2H), 3.14 (s, 2H), 2.38–2.31 (m, 1H), 2.30 (s, 3H), 1.97 (ddd, *J* = 13.6, 8.5, 7.2 Hz, 1H), 1.78 (ddd, *J* = 12.8, 8.4, 7.2 Hz, 1H), 1.41 (ddd, *J* = 12.7, 7.2, 5.4 Hz, 1H), 1.08 (s, 3H), 0.70 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 218.5 (C), 171.3 (C), 136.6 (C), 133.5 (C), 131.7 (CH), 130.6 (CH), 129.1 (CH), 118.8 (CH_2), 66.2 (CH_2), 62.4 (C), 46.2 (C), 39.1 (CH_2), 35.5 (CH_2), 28.1 (CH_2), 25.1 (CH_3), 24.0 (CH_3), 21.2 (CH_3); IR (thin film, NaCl) 2963, 2870, 1747, 1726, 1515, 1457, 1380, 1361, 1315, 1252, 1197, 1183, 1130, 1061, 993, 977, 931, 888, 817, 775 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{19}H_{25}O_3$ $[M+H]^+$: 301.1798, found 301.1808.

Pd(0)-Catalyzed Enantioselective Allylic Alkylation and Characterization Data:



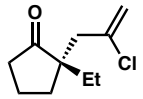
5b ***(S)-6b***

Representative Procedure: Enantioselective Allylic Alkylation.
In a nitrogen-filled glovebox, separate stock solutions of $Pd_2(dba)_3$ (2.50 mg/mL), (*S*)-$(CF_3)_3$-*t*-Bu-PHOX (**(*S*)-L2**, 10.0 mg/mL), and β-ketoester **5b** (100. mg/mL) in toluene were prepared. $Pd_2(dba)_3$ (1.92 mL, 4.8 mg, 5.20 μmol, 0.0275 equiv) and (*S*)-$(CF_3)_3$-*t*-Bu-PHOX (**(*S*)-L2**, 0.67 mL, 6.7 mg, 11.4 μmol, 0.06 equiv) were added to a 20 mL scintillation vial and placed in a pre-chilled 20 °C stirrer. After 20 minutes, the solution was diluted with toluene (2.69 mL, 20 °C) followed by β-ketoester **5b** (0.517 mL, 51.7 mg, 0.19 mmol, 1.00 equiv) in one portion (total volume 5.8 mL, 0.033 M). After 20 h, the consumption of starting material was complete (as determined by TLC analysis, 19:1 Pentane:Et_2O). The crude solution was directly purified by column chromatography (SiO_2, 100% pentane then 5% Et_2O in pentane) to furnish cyclopentanone **(*S*)-6b** (43 mg, 98% yield) as a clear colorless oil; R_f = 0.20 (19:1 Pentane:Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.26 (m, 5H), 5.26 (d, *J* = 1.7 Hz, 1H), 5.07 (dt, *J* = 1.8, 0.9 Hz, 1H), 2.77 (dd, *J* = 13.8, 1.1 Hz, 1H), 2.62 (d, *J* = 13.8 Hz, 1H), 2.17–2.04 (m, 1H), 1.99–1.84 (m, 1H), 1.82–1.66 (m, 3H), 1.66–1.60 (m, 1H), 1.51–1.31 (m, 2H), 0.79 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 223.2 (C), 146.1 (C), 142.3 (C), 128.3 (CH), 127.6 (CH), 126.8 (CH), 117.4 (CH_2), 52.8 (C), 40.0 (CH_2), 38.4 (CH_2), 31.9 (CH_2), 28.8 (CH_2), 18.8 (CH_2), 8.8 (CH_3); IR (thin film, NaCl) 3079, 3054, 2963, 2879, 1734, 1623, 1572, 1491, 1457, 1405, 1380, 1306, 1268, 1160, 1083, 1028, 902, 778, 700 cm^{-1}; HRMS (APCI/ESI) m/z calc'd for $C_{16}H_{21}O$ $[M+H]^+$: 229.1587, found 229.1589; $[\alpha]_D^{25}$ –40.78 (*c* 0.510, $CHCl_3$, 94% ee).



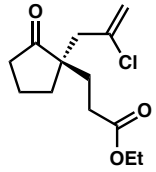
(S)-6a

2-(2-Phenyl)allyl-2-methylcyclopentanone (*(S)*-6a): Prepared by using the representative procedure above from β-ketoester **5a** (0.19 mmol), reaction time = 27.5 h. Purified by column chromatography (SiO_2, 5% Et_2O in pentane) to provide cyclopentanone **(*S*)-6a** (39 mg, 95% yield) as a clear colorless oil; R_f = 0.11 (19:1 Pentane:Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.26 (m, 5H), 5.27 (d, *J* = 1.7 Hz, 1H), 5.08 (dt, *J* = 1.8, 1.0 Hz, 1H), 2.74 (dd, *J* = 13.7, 1.1 Hz, 1H), 2.62 (d, *J* = 13.8 Hz, 1H), 2.29–2.14 (m, 1H), 2.04–1.90 (m, 1H), 1.88–1.65 (m, 3H), 1.51–1.37 (m, 1H), 0.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 223.3 (C), 146.1 (C), 142.5 (C), 128.4 (CH), 127.6 (CH), 126.8 (CH), 117.3 (CH_2), 49.0 (C), 41.8 (CH_2), 37.6 (CH_2), 35.4 (CH_2), 22.6 (CH_3), 18.8 (CH_2); IR (thin film, NaCl) 3078, 2960, 1734, 1623, 1491, 1457, 1405, 1160, 1061, 900, 778, 701 cm^{-1}; HRMS (APCI/ESI) m/z calc'd for $C_{15}H_{19}O$ $[M+H]^+$: 215.21436, found 215.21430; $[\alpha]_D^{25}$ –99.32 (*c* 0.445, $CHCl_3$, 90% ee).



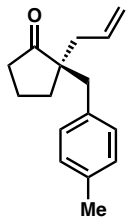
(S)-6c

2-(2-Chloro)allyl-2-ethylcyclopentanone ((*S*)-6c): Prepared by using the representative procedure above from β-ketoester **5c** (0.19 mmol), reaction time = 28.5 h. Purified by column chromatography (SiO_2, 10% Et_2O in pentane) to furnish cyclopentanone **(*S*)-6c** (26 mg, 72% yield) as a clear colorless oil; R_f = 0.71 (8:2 Pentane:Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.24 (t, *J* = 0.9 Hz, 1H), 5.15 (t, *J* = 1.1 Hz, 1H), 2.61 (dd, *J* = 14.4, 1.1 Hz, 1H), 2.49 (d, *J* = 14.4 Hz, 1H), 2.34–2.21 (m, 2H), 2.16–2.00 (m, 1H), 1.98–1.79 (m, 3H), 1.48 (qd, *J* = 7.4, 3.1 Hz, 2H), 0.84 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 222.1 (C), 139.5 (C), 116.3 (CH_2), 51.8 (C), 44.1 (CH_2), 38.2 (CH_2), 32.1 (CH_2), 28.6 (CH_2), 18.9 (CH_2), 8.6 (CH_3); IR (thin film, NaCl) 2965, 1734, 1629, 1458, 1405, 1382, 1260, 1158, 1115, 1085, 886 cm^{-1}. HRMS (FAB+) m/z calc'd for $C_{10}H_{16}ClO$ $[M+H]^+$: 187.0890, found 187.0897; $[\alpha]_D^{25}$ –38.57 (*c* 0.165, $CHCl_3$, 90% ee).



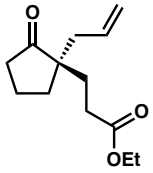
(S)-6d

2-(2-Chloro)allyl-2-(3-ethoxy-3oxopropyl)cyclopentanone ((*S*)-6d): Prepared by using the representative procedure above from β-ketoester **5d** (0.19 mmol), reaction time = 21 h. Purified by column chromatography (SiO_2, 20% Et_2O in pentane) to afford cyclopentanone **(*S*)-6d** (42 mg, 85% yield) as a clear colorless oil R_f = 0.32 (8:2 Pentane:Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33–5.23 (m, 1H), 5.18 (t, *J* = 1.2 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 2.59 (dd, *J* = 14.4, 1.1 Hz, 1H), 2.51 (d, *J* = 14.4 Hz, 1H), 2.40–2.21 (m, 4H), 2.19–2.05 (m, 1H), 2.03–1.72 (m, 5H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 221.1 (C), 173.3 (C), 138.9 (C), 116.7 (CH_2), 60.7 (CH_2), 50.7 (C), 43.9 (CH_2), 37.8 (CH_2), 33.5 (CH_2), 30.1 (CH_2), 29.1 (CH_2), 18.8 (CH_2), 14.3 (CH_3); IR (thin film, NaCl) 2962, 1734, 1629, 1375, 1304, 1267, 1191, 1025, 888 cm^{-1}; HRMS (ESI) m/z calc'd for $C_{13}H_{20}ClO_3$ $[M+H]^+$: 259.1095, found 259.1108; $[\alpha]_D^{25}$ –26.99 (*c* 0.255, $CHCl_3$, 88% ee).



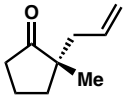
(S)-14a

2-Allyl-2-(4-methylbenzyl)cyclopentanone ((*S*)-14a): Prepared by using the representative procedure above from β-ketoester **13a** (0.19 mmol), reaction time = 13 h. Purified by column chromatography (SiO_2, 5% Et_2O in pentane) to afford cyclopentanone **(*S*)-14a** (50 mg, 93% yield) as a clear colorless oil; R_f = 0.39 (9:1 Pentane:Et_2O); $[\alpha]_D^{25}$ +12.78 (*c* 0.835, $CHCl_3$, 89% ee); characterization data match known literature values.[11]



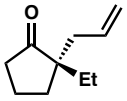
(S)-14b

2-Allyl-2-(3-ethoxy-3-oxopropyl)cyclopentanone ((*S*)-14b): Prepared by using the representative procedure above from β-ketoester **13b** (0.19 mmol), reaction time = 8 h. Purified by column chromatography (SiO_2, 20% Et_2O in pentane) to provide cyclopentanone **(*S*)-14b** (40 mg, 93% yield) as a clear colorless oil; R_f = 0.30 (8:2 Pentane:Et_2O); ^1H NMR (400 MHz, $CDCl_3$) δ 5.66 (ddt, *J* = 16.4, 10.6, 7.4 Hz, 1H), 5.11–5.01 (m, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 2.39–2.10 (m, 6H), 1.95–1.67 (m, 4H), 1.23 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 221.9 (C), 173.5 (C), 133.4 (CH), 118.7 (CH_2), 60.6 (CH_2), 50.9 (C), 39.1 (CH_2), 38.3 (CH_2), 33.3 (CH_2), 29.7 (CH_2), 29.2 (CH_2), 18.7 (CH_2), 14.3 (CH_3); IR (thin film, NaCl) 3076, 2961, 1734, 1639, 1445, 1406, 1376, 1303, 1252, 1190, 1096, 1028, 919 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{13}H_{21}O_3$ $[M+H]^+$: 225.1491, found 225.1498; $[\alpha]_D^{25}$ –18.69 (*c* 1.950, $CHCl_3$, 91% ee).



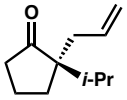
(S)-14c

2-Allyl-2-methylcyclopentanone ((*S*)-14c): Prepared by using the representative procedure above from β-ketoester **13c** (0.38 mmol), reaction time = 31 h. Purified by column chromatography (SiO_2, 5% Et_2O in pentane) to furnish cyclopentanone **(*S*)-14c** (43 mg, 81% yield) as a clear colorless oil; R_f = 0.24 (19:1 Pentane:Et_2O); $[\alpha]_D^{25}$ –72.21 (*c* 0.245, $CHCl_3$, 86% ee); characterization data match known literature values.[14]



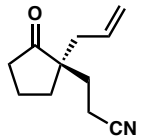
(S)-14d

2-Allyl-2-ethylcyclopentanone ((*S*)-14d): Prepared by using the representative procedure above from β-ketoester **13d** (0.38 mmol), reaction time = 31 h. Purified by column chromatography (SiO_2, 7% Et_2O in pentane) to afford cyclopentanone **(*S*)-14d** (69 mg, 79% yield) as a clear colorless oil; R_f = 0.44 (10:1 Hexanes:EtOAc); $[\alpha]_D^{25}$ –20.22 (*c* 0.340, Et_2O, 88% ee); characterization data match known literature values.[11]



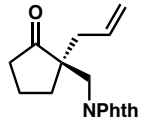
(S)-14e

2-Allyl-2-isopropylcyclopentanone ((*S*)-14e): Prepared by using the representative procedure above from β-ketoester **13e** (0.38 mmol), reaction time = 36 h. Purified by column chromatography (SiO_2, 5% Et_2O in pentane) to provide cyclopentanone **(*S*)-14e** (39 mg, 62% yield) as a clear colorless oil; R_f = 0.44 (10:1 Hexanes:EtOAc); $[\alpha]_D^{25}$ +33.57 (*c* 0.315, $CHCl_3$, 87% ee); characterization data match known literature values.[11]



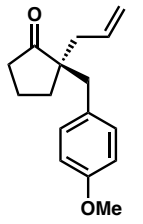
(S)-14f

2-Allyl-2-(cyanomehtyl)cyclopentanone ((*S*)-14f): Prepared by using the representative procedure above from β-ketoester **13f** (0.19 mmol), except catalyst pre-stir ran for 40 minutes (20 minutes at 30 °C followed by another 20 minutes at 0 °C) and the reaction was run at 0 °C, reaction time = 23 h. Purified by column chromatography (SiO_2, 40% Et_2O in pentane) to afford cyclopentanone **(*S*)-14f** (35 mg, 97% yield) as a clear colorless oil; R_f = 0.32 (1:1 Hexanes:Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.68 (ddt, *J* = 16.9, 10.2, 7.4 Hz, 1H), 5.26–5.07 (m, 2H), 2.52–2.21 (m, 4H), 2.18 (dt, *J* = 7.4, 1.2 Hz, 2H), 2.10–1.79 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 221.0 (C), 132.4 (CH), 119.7 (C), 119.5 (CH_2), 50.6 (C), 38.4 (CH_2), 38.0 (CH_2), 33.2 (CH_2), 30.2 (CH_2), 18.6 (CH_2), 12.3 (CH_2); IR (thin film, NaCl) 2961, 2246, 1731, 1444, 1159, 921 cm^{-1}; HRMS (EI+) m/z calc'd for $C_{11}H_{15}NO$ $[M]^+$: 177.1154, found 177.1171; $[\alpha]_D^{25}$ –13.41 (*c* 0.450, $CHCl_3$, 90% ee).



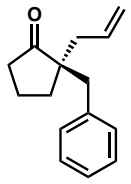
(S)-14g

2-Allyl-((1,3-dioxoisoindolin-2-yl)methyl)cyclopentanone ((*S*)-14g): Prepared by using the representative procedure above from β-ketoester **13g** (0.19 mmol), except catalyst pre-stir ran for 40 minutes (20 minutes at 30 °C followed by another 20 minutes at 0 °C) and the reaction was run at 0 °C, reaction time = 23 h. Purified by column chromatography (SiO_2, 20% Et_2O in pentane) to afford cyclopentanone **(*S*)-14g** (48 mg, 93% yield) as a white amorphous solid; R_f = 0.50 (1:1 Pentane:Et_2O); $[\alpha]_D^{25}$ –25.16 (*c* 0.305, $CHCl_3$, 92% ee); characterization data match known literature values.[11]



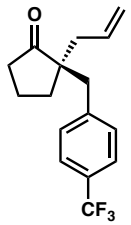
(S)-14h

2-Allyl-2-(4-methoxybenzyl)cyclopentanone ((*S*)-14h): Prepared by using the representative procedure above from β-ketoester **13h** (0.19 mmol), reaction time = 8 h. Purified by column chromatography (SiO_2, 10% Et_2O in pentane) to provide cyclopentanone **(*S*)-14h** (46 mg, >99% yield) as a clear colorless oil; R_f = 0.25 (9:1 Pentane:Et_2O); $[\alpha]_D^{25}$ +6.40 (*c* 0.275, $CHCl_3$, 92% ee); characterization data match known literature values.[11]



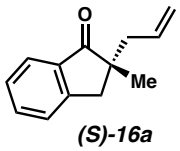
(S)-14i

2-Allyl-2-benzylcyclopentanone ((*S*)-14i): Prepared by using the representative procedure above from β-ketoester **13i** (0.19 mmol), reaction time = 13 h. Purified by column chromatography (SiO_2, 7% Et_2O in pentane) to furnish cyclopentanone **(*S*)-14i** (39 mg, 95% yield) as a clear colorless oil; R_f = 0.41 (9:1 Pentane:Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.15 (m, 3H), 7.16–7.08 (m, 2H), 5.75 (dddd, *J* = 17.0, 10.2, 7.8, 6.9 Hz, 1H), 5.18–5.05 (m, 2H), 2.94 (d, *J* = 13.3 Hz, 1H), 2.62 (d, *J* = 13.3 Hz, 1H), 2.31 (ddt, *J* = 13.8, 7.0, 1.3 Hz, 1H), 2.24–2.11 (m, 2H), 2.07–1.93 (m, 1H), 1.97–1.81 (m, 2H), 1.75 (ddq, *J* = 12.8, 8.7, 7.0 Hz, 1H), 1.56–1.41 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 223.0 (C), 137.9 (C), 133.8 (CH), 130.4 (CH), 128.3 (CH), 126.5 (CH), 118.8 (CH_2), 53.3 (C), 41.8 (CH_2), 41.0 (CH_2), 39.0 (CH_2), 31.1 (CH_2), 18.8 (CH_2); IR (thin film, NaCl) 3027, 2960, 1733, 1639, 1495, 1453, 1404, 1156, 997, 920, 757 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{15}H_{19}O$ $[M+H]^+$: 215.1436, found 215.1433; $[\alpha]_D^{25}$ +6.88 (*c* 1.950, $CHCl_3$, 88% ee).



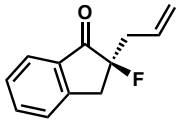
(S)-14j

2-Allyl-2-(4-(trifluoromethyl)benzyl)cylopentanone ((*S*)-14j): Prepared by using the representative procedure above from β-ketoester **13j** (0.19 mmol), reaction time = 96 h. Purified by column chromatography (SiO_2, 7% Et_2O in pentane) to furnish cyclopentanone **(*S*)-14j** (30 mg, 54% yield (83% yield based on recovered starting material **13j**) as a clear colorless oil; R_f = 0.59 (6:3 Pentane:Et_2O); $[\alpha]_D^{25}$ +10.22 (*c* 0.540, $CHCl_3$, 88% ee); characterization data match known literature values.[11]



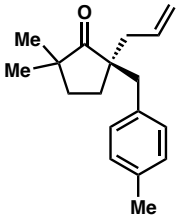
(S)-16a

2-Allyl-2-methyl-2,3-dihydro-1H-inden-1-one ((*S*)-16a): Prepared by using the representative procedure above from β-ketoester **15a** (0.19 mmol), reaction time = 4.5 h. Purified by column chromatography (SiO_2, 10% Et_2O in pentane) to afford cyclopentanone **(*S*)-16a** (33 mg, 93% yield) as a clear colorless oil; R_f = 0.36 (9:1 Hexanes:EtOAc); $[\alpha]_D^{25}$ –59.24 (*c* 0.595, $CHCl_3$, 84% ee); characterization data match known literature values.[11]



(S)-16b

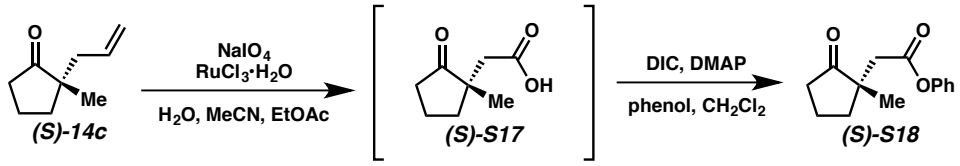
2-Allyl-2-Fluoro-2,3-dihydro-1H-inden-1-one ((*S*)-16b): Prepared by using the representative procedure above from β-ketoester **15b** (0.19 mmol), reaction time = 13 h. Purified by column chromatography (SiO_2, 5% Et_2O in pentane) to provide cyclopentanone **(*S*)-16b** (36 mg, >99% yield) as a clear colorless oil; R_f = 0.19 (19:1 Pentane:Et_2O); $[\alpha]_D^{25}$ –75.79 (*c* 0.585, $CHCl_3$, 87% ee); characterization data match known literature values.[15]



(S)-S16

(*S*)-2-allyl-5,5-dimethyl-2-(4-methylbenzyl)cyclopentan-1-one ((*S*)-S16): Prepared by using the representative procedure above from β-ketoester **S15** (0.19 mmol), reaction time = 48 h. Purified by column chromatography (SiO_2, 3% Et_2O in hexanes) to afford cyclopentanone **(*S*)-S16** (32 mg, 66% yield) as a clear colorless oil R_f = 0.24 (19:1 Hexanes:Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07–7.03 (m, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 5.73 (dddd, *J* = 17.0, 10.1, 7.8, 7.0 Hz, 1H), 5.14–5.01 (m, 2H), 2.87 (d, *J* = 13.3 Hz, 1H), 2.55 (d, *J* = 13.3 Hz, 1H), 2.30 (s, 3H), 2.26 (ddt, *J* = 13.7, 7.0, 1.3 Hz, 1H), 2.17 – 2.10 (m, 1H), 1.89–1.72 (m, 2H), 1.63 (dt, *J* = 12.8, 7.2 Hz, 1H), 1.39 (ddd, *J* = 12.8, 7.3, 6.3 Hz, 1H), 0.98 (s, 3H), 0.67 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.1 (C), 134.8 (C), 134.1 (CH), 130.6 (CH), 128.9 (CH), 118.7 (CH_2), 54.5 (C), 45.6 (C), 41.7 (CH_2), 41.6 (CH_2), 35.0 (CH_2), 27.4 (CH_2), 24.7 (CH_3), 23.9 (CH_3), 21.2 (CH_3); IR (thin film, NaCl) 2958, 2867, 1731, 1513, 1459, 1379, 1061, 997, 916, 812, 752 cm^{-1}; HRMS (ESI) m/z calc'd for $C_{18}H_{25}O$ $[M+H]^+$: 257.1900, found 275.1901; $[\alpha]_D^{25}$ +13.67 (*c* 0.58, $CHCl_3$, 73% ee).

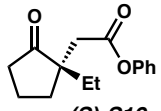
Phenyl Ester Derivative Synthesis and Characterization Data



Representative Procedure: Phenyl Ester Derivative Synthesis

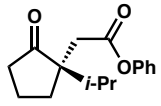
Ketone **(*S*)-14c** (34 mg, 0.25 mmol, 1.00 equiv) was diluted in H_2O (2.34 mL, 0.11 M), acetonitrile (1.50 mL, 0.160 M), and EtOAc (1.50 mL, 0.16 M). Sodium periodate ($NaIO_4$, 342 mg, 1.60 mmol, 6.40 equiv) and ruthenium(III) trichloride ($RuCl_3$, 4.7 μL, 0.1 M solution in H_2O, 0.019 equiv) were added in single portions. The reaction was allowed to stir at ambient temperature (ca. 23 °C) for 4 h, at which time consumption of starting material was complete (as determined by TLC analysis, 19:1 Pentane:Et_2O). Crude reaction mixture was filtered through a celite plug and extracted with a saturated solution of $NaHCO_3$. The aqueous solution was acidified to pH 1 with 1 M HCl. Acidified aqueous solution was extracted with dichloromethane, dried over Na_2SO_4, filtered and concentrated in vacuo. Crude solution was carried on with no further purification.

A flask charged with carboxylic acid **(*S*)-S17** (0.25 mmol, 1.00 equiv), phenol (14 mg, 0.27 mmol, 1.10 equiv), and 4-(dimethylamino)-pyridine (DMAP, 14 mg, 0.11 mol, 0.45 equiv) was evacuated and re-filled with argon (3 x 5 minutes). Dichloromethane (946 μL, 0.26 M) was added and the solution was cooled to 0 °C (ice/H_2O bath). Diisopropylcarbodiimide (DIC, 42.0 μL, 0.27 mmol, 1.10 equiv) was added dropwise and allowed to stir for 5 minutes. The cooling bath was then removed and the solution was allowed to warm to ambient temperature (ca. 23 °C). After 11 h, the consumption of starting material was complete (as determined by TLC analysis, 9:1 Hexanes:EtOAc) and the reaction was filtered through filter paper and then diluted with dichloromethane (200 mL). The solution was washed with 0.1 M aqueous HCl (200 mL), 1 M aqueous NaOH, saturated aqueous $NaHCO_3$ (100 mL), and brine (100 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, 10% hexanes in EtOAc) to provide ester **(*S*)-S18** (33 mg, 57% yield over 2 steps) as a clear colorless oil; R_f = 0.24 (9:1 Hexanes:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.31 (m, 2H), 7.22 (ddt, *J* = 7.9, 6.9, 1.2 Hz, 1H), 7.09–6.99 (m, 2H), 2.92 (d, *J* = 16.6 Hz, 1H), 2.72 (d, *J* = 16.6 Hz, 1H), 2.45–2.30 (m, 2H), 2.27–2.13 (m, 1H), 2.09–1.94 (m, 1H), 1.97–1.81 (m, 2H), 1.13 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 221.7 (C), 170.2 (C), 150.5 (C), 129.6 (CH), 126.1 (CH), 121.6 (CH), 46.5 (C), 41.6 (CH_2), 37.3 (CH_2), 35.1 (CH_2), 22.8 (CH_3), 18.9 (CH_2); IR (thin film, NaCl) 3459, 3066, 2964, 2873, 1756, 1738, 1592, 1493, 1456, 1404, 1375, 1350, 1317, 1266, 1242, 1193, 1162, 1127, 1070, 1023, 1006, 969, 925, 896, 817, 800, 772, 749, 772, 722, 698, 687 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{14}H_{17}O_3$ $[M+H]^+$: 233.1178, found 233.1176; $[\alpha]_D^{25}$ –45.05 (*c* 0.280, $CHCl_3$, 86% ee).



(S)-S19

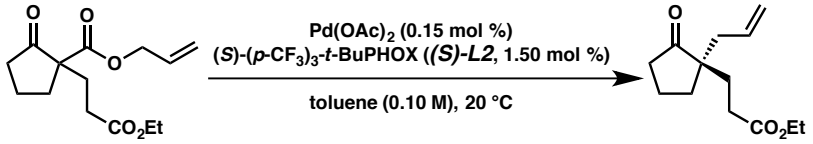
(1-Ethyl-2-oxo-cyclopentyl)-acetic acid phenyl ester ((*S*)-S19): Prepared by using the representative procedure above from cyclopentanone **(*S*)-14d** (0.25 mmol). Purified by column chromatography (SiO_2, 10% EtOAc in hexanes) to furnish ester **(*S*)-S19** (46 mg, 75% yield over 2 steps) as an amorphous solid; R_f = 0.28 (9:1 Hexanes:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.33 (m, 2H), 7.21 (tt, *J* = 7.1, 1.1 Hz, 1H), 7.07–7.02 (m, 2H), 2.90 (d, *J* = 16.7 Hz, 1H), 2.73 (d, *J* = 16.7 Hz, 1H), 2.48– 2.27 (m, 2H), 2.14 (ddd, *J* = 13.1, 10.3, 7.8 Hz, 1H), 2.06–1.94 (m, 2H), 1.95–1.80 (m, 1H), 1.53 (p, *J* = 7.4 Hz, 2H), 0.93 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 221.8 (C), 170.5 (C), 150.5 (C), 129.6 (CH), 126.0 (CH), 121.6 (CH), 50.0 (C), 39.5 (CH_2), 37.6 (CH_2), 32.4 (CH_2), 28.6 (CH_2), 18.8 (CH_2), 8.6 (CH_3); IR (thin film, NaCl) 3455, 3066, 2965, 2881, 1733, 1592, 1492, 1456, 1404, 1383, 1349, 1262, 1238, 1190, 1161, 1125, 1024, 1006, 951, 926, 895, 810, 768, 721, 688 cm^{-1}; HRMS (APCI/ESI) m/z calc'd for $C_{15}H_{19}O_3$ $[M+H]^+$: 247.1329, found 247.1327; $[\alpha]_D^{25}$ +2.45 (*c* 0.445, $CHCl_3$, 88% ee).



(S)-S20

(1-(1-Methylethyl)-2-oxo-cyclopentyl)-acetic acid phenyl ester ((S)-S20): Prepared by using the representative procedure above from cyclopentanone **(*S*)-14e** (0.20 mmol). Purified by column chromatography (SiO_2, 10% EtOAc in hexanes) to afford ester **(*S*)-S20** (27 mg, 52% yield over 2 steps) as an amorphous white solid; R_f = 0.36 (9:1 Hexanes:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 2H), 7.21 (dd, *J* = 7.0, 1.1 Hz, 1H), 7.08–7.01 (m, 2H), 2.94 (d, *J* = 16.6 Hz, 1H), 2.73 (d, *J* = 16.6 Hz, 1H), 2.56–2.42 (m, 1H), 2.33–2.20 (m, 1H), 2.20–1.80 (m, 5H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 223.1 (C), 170.8 (C), 150.5 (C), 129.6 (CH), 126.0 (CH), 121.6 (CH), 52.9 (C), 39.8 (CH_2), 38.5 (CH_2), 33.4 (CH), 29.7 (CH_2), 18.9 (CH_2), 18.4 (CH_3), 17.6 (CH_3); IR (thin film, NaCl) 2963, 1757, 1734, 1592, 1492, 1404, 1389, 1372, 1350, 1271, 1237, 1193, 1162, 1127, 1069, 1023, 932, 898, 818, 764, 719, 687 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{16}H_{21}O_3$ $[M+H]^+$: 261.1491, found 261.1495; $[\alpha]_D^{25}$ –45.05 (*c* 0.280, $CHCl_3$, 88% ee).

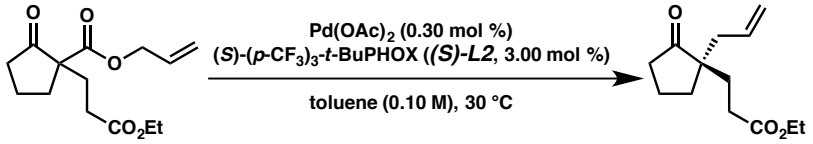
Low-Catalyst Loading, Pd(II)-Catalyzed Enantioselective Allylic Alkylation



13b *(S)-14b*

In a nitrogen-filled glovebox, stock solutions of $Pd(OAc)_2$ (1.00 mg/mL), (*S*)-$(CF_3)_3$-*t*-Bu-PHOX (**(*S*)-L2**, 10.0 mg/mL), and β-ketoester **13b** (100. mg/mL) in toluene were prepared. $Pd(OAc)_2$ (64.0 μL, 0.064 mg, 0.285 μmol, 0.0015 equiv) and (*S*)-$(CF_3)_3$-*t*-Bu-PHOX (0.17 mL, 1.69 mg, 2.85 μmol, 0.015 equiv) were added to a 20 mL scintillation vial and placed in a pre-chilled 20 °C stirrer. After 40 minutes, the solution was diluted with toluene (1.16 mL, 20 °C) followed by β-ketoester **13b** (0.51 mL, 51.0 mg, 0.19 mmol, 1.00 equiv) in one portion (total volume 1.9 mL, 0.10 M). After 28 h, the consumption of starting material was complete (as determined by TLC analysis, 19:1 Pentane:Et_2O). The crude solution was directly purified by column chromatography (SiO_2, 100% pentane then 20% Et_2O in pentane) to furnish **(*S*)-14b** (42 mg, 98% yield) as a clear colorless oil; R_f = 0.30 (8:2 Pentane:Et_2O); characterization data match those that are reported above.

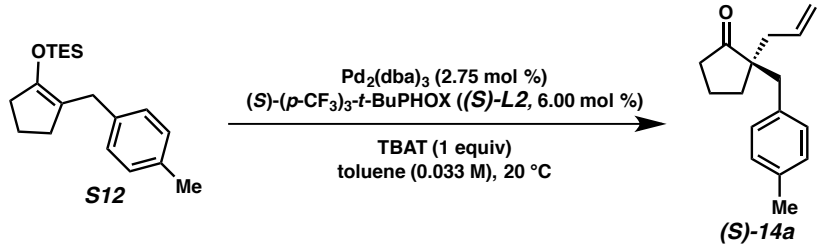
Large Scale Low-Catalyst Loading, Pd(II)-Catalyzed Enantioselective Allylic Alkylation



13b *(S)-14b*

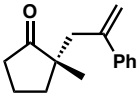
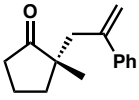
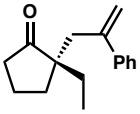
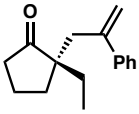
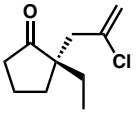
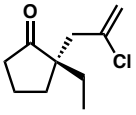
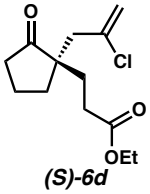
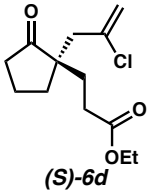
In a nitrogen filled glovebox, $Pd(OAc)_2$ (2.49 mg, 11.1 μmol, 0.003 equiv) and (*S*)-$(CF_3)_3$-*t*-Bu-PHOX (65.7 mg, 0.111 μmol, 0.03 equiv) were added to a flask and diluted with toluene (37.3 mL, 0.10M). The solution stirred in the ambient glovebox atmosphere (ca. 30 °C) for 40 minutes. β-ketoester **13b** (1.00 g, 3.73 mmol, 1.00 equiv) was then added in one portion. After 15 h, the consumption of starting material was complete (as determined by TLC analysis, 19:1 Pentane:Et_2O). The crude solution was directly purified by column chromatography (SiO_2, 100% pentante then 20% Et_2O in pentane) to furnish **(*S*)-14b** (682 mg, 82% yield, 89% ee) as a clear colorless oil; R_f = 0.30 (8:2 Pentane:Et_2O); characterization data match those that are reported above.

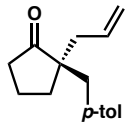
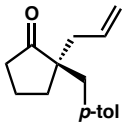
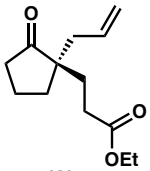
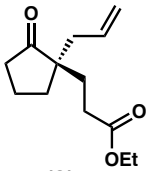
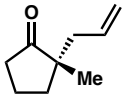
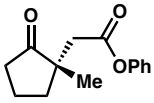
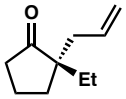
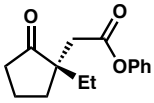
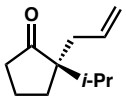
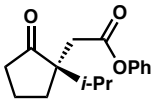
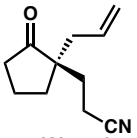
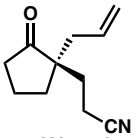
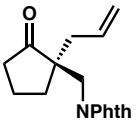
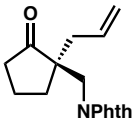
Fluoride Triggered, Pd(0)-Catalyzed Enantioselective Allylic Alkylation

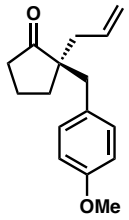
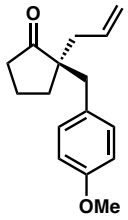
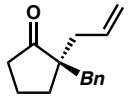
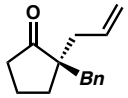
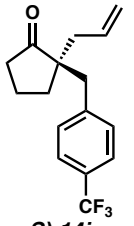
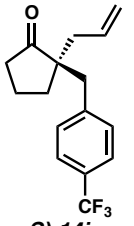
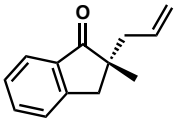
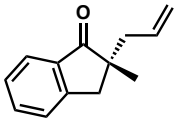
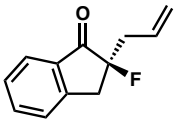
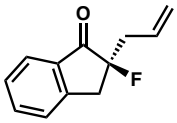
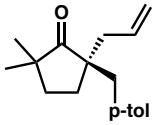
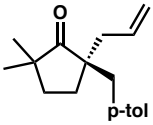


In a nitrogen-filled glovebox, separate stock solutions of $Pd_2(dba)_3$ (2.50 mg/mL), (*S*)-$(CF_3)_3$-*t*-Bu-PHOX (**(*S*)-L2**, 10.0 mg/mL), and β-ketoester **S12** (100. mg/mL) in toluene were prepared. $Pd_2(dba)_3$ (1.92 mL, 4.8 mg, 5.20 μmol, 0.0275 equiv), (*S*)-$(CF_3)_3$-*t*-Bu-PHOX (**(*S*)-L2**, 0.67 mL, 6.7 mg, 11.4 μmol, 0.06 equiv), and TBAT (103 mg, 0.19 mmol, 1.00 equiv) were added to a 20 mL scintillation vial and placed in a pre-chilled 20 °C well with stirring. After 20 minutes, the solution was diluted with toluene (2.69 mL, 20 °C) followed by the addition of diallyl carbonate (28.7 μL, 0.20 mmol, 1,05 equiv) and β-ketoester **S12** (0.574 mL, 57.4 mg, 0.19 mmol, 1.00 equiv) in one portion (total volume 5.8 mL, 0.033 M). After 48 h, the consumption of starting material appeared stalled (as determined by TLC analysis, 19:1 Pentane:Et_2O). The crude solution was directly purified by column chromatography (SiO_2, 100% hexanes then 5% Et_2O in hexanes) to furnish cyclopentanone **(*S*)-14a** (17 mg, 40% yield, 75% ee) as a clear colorless oil; characterization data match those that are reported above.

Methods for the Determination of Enantiomeric Excess (*ee*)

entry	product	compound assayed	assay conditions	retention time of major isomer (min)	retention time of minor isomer (min)	% *ee*
1	 *(S)-6a*	 *(S)-6a*	SFC Chiracel OJ-H 2% IPA isocratic 2.5 mL/min	7.11	8.59	90
2	 *(S)-6b*	 *(S)-6b*	SFC Chiracel OJ-H 1% IPA isocratic 2.5 mL/min	8.03	10.18	94
3	 *(S)-6c*	 *(S)-6c*	SFC 2 Chiralpak AD-H 3% IPA isocratic 2.5 mL/min	5.40	5.14	90
4	 *(S)-6d*	 *(S)-6d*	SFC Chiralpak AD-H 3% IPA isocratic 2.5 mL/min	5.05	6.35	88

entry	product	compound assayed	assay conditions	retention time of major isomer (min)	retention time of minor isomer (min)	% *ee*
5	 (S)-14a	 (S)-14a	HPLC Chiracel OJ 0.1% EtOH in hexanes isocratic;1 mL/min	12.90	11.43	89
6	 (S)-14*b*	 (S)-14b	SFC Chiralpak AD-H 3% IPA isocratic 2.5 mL/min	3.57	4.58	91
7	 (S)-14*c*	 (S)-18	SFC Chiracel OB-H 5% IPA isocratic 2.5 mL/min	11.37	7.36	86
8	 (S)-14*d*	 (S)-19	SFC Chiracel OB-H 3% IPA isocratic 2.5 mL/min	12.19	11.18	88
9	 (S)-14*e*	 (S)-20	SFC Chiracel OB-H 5% IPA isocratic 2.5 mL/min	7.35	6.65	88
10	 (S)-14*f*	 (S)-14*f*	SFC Chiracel OD-H 10% IPA isocratic 2.5 mL/min	2.87	2.48	90
11	 (S)-14*g*	 (S)-14*g*	HPLC Chiracel OD-H 4% IPA in hexanes isocratic; 1 mL/min	20.82	27.11	92

entry	product	compound assayed	assay conditions	retention time of major isomer (min)	retention time of minor isomer (min)	% *ee*
12	 ***(S)-14h***	 ***S)-14h***	SFC Chiracel OJ-H 1% IPA isocratic 2.5 mL/min	9.87	9.20	92
13	 ***S)-14i***	 ***S)-14i***	HPLC Chiracel OJ 0.1% EtOH in hexanes isocratic; 1 mL/min	14.61	13.26	88
14	 ***S)-14j***	 ***S)-14j***	SFC Chiralpak AD-H 1% IPA isocratic 2.5 mL/min	5.61	6.03	88
15	 ***(S)-16a***	 ***(S)-16a***	SFC Chiralpak AD-H 2% IPA isocratic 2.5 mL/min	7.17	6.30	84
16	 ***(S)-16b***	 ***(S)-16b***	SFC Chiracel OB-H 2% IPA isocratic 2.5 mL/min	7.18	4.46	87
17	 ***(S)-S16***	 ***(S)-S16***	SFC Chiralpak IC 3% IPA isocratic 2.5 mL/min	9.50	6.12	73

Notes & References

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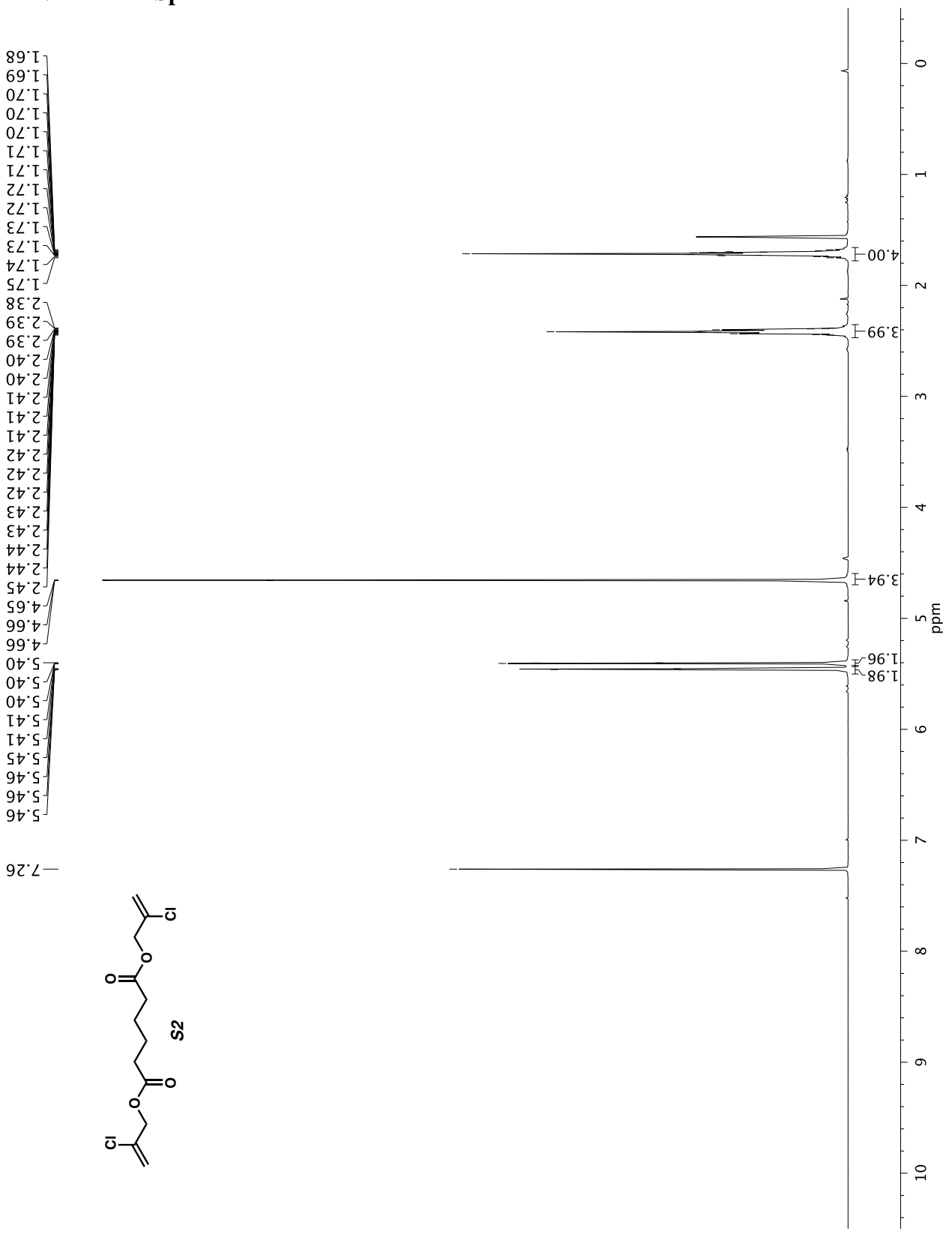
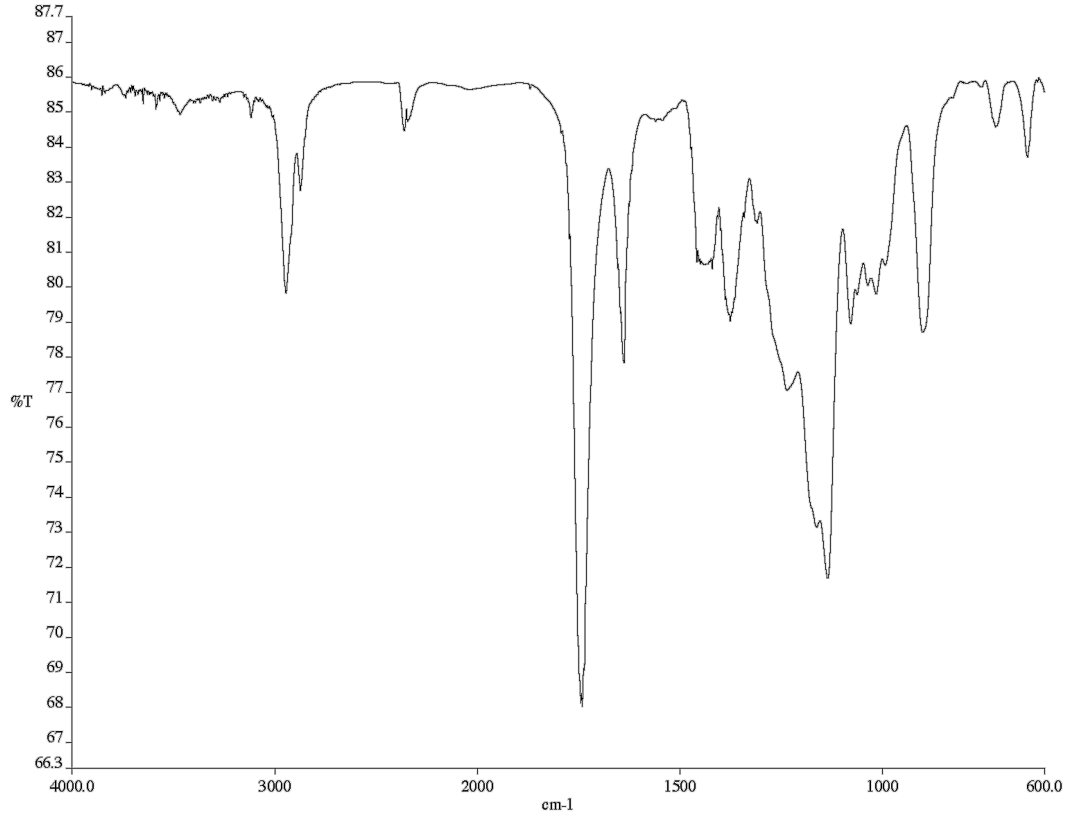
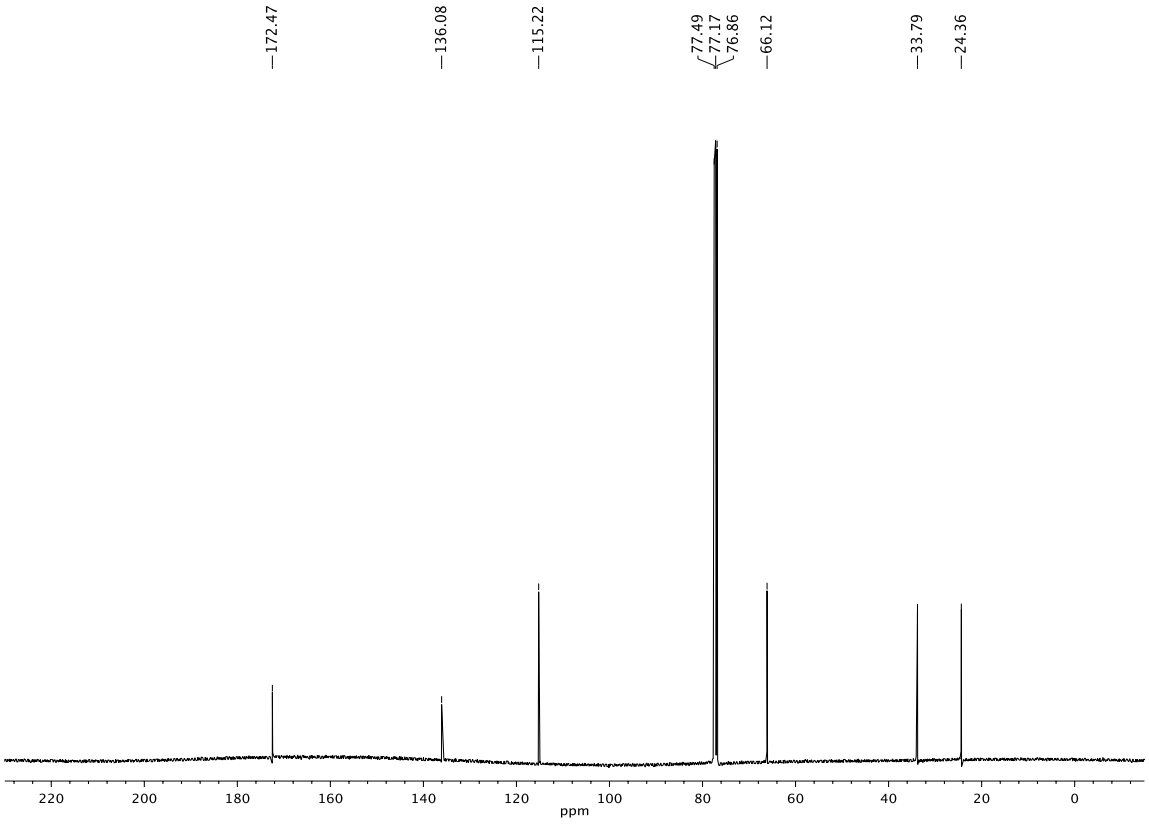
NMR & IR Spectra



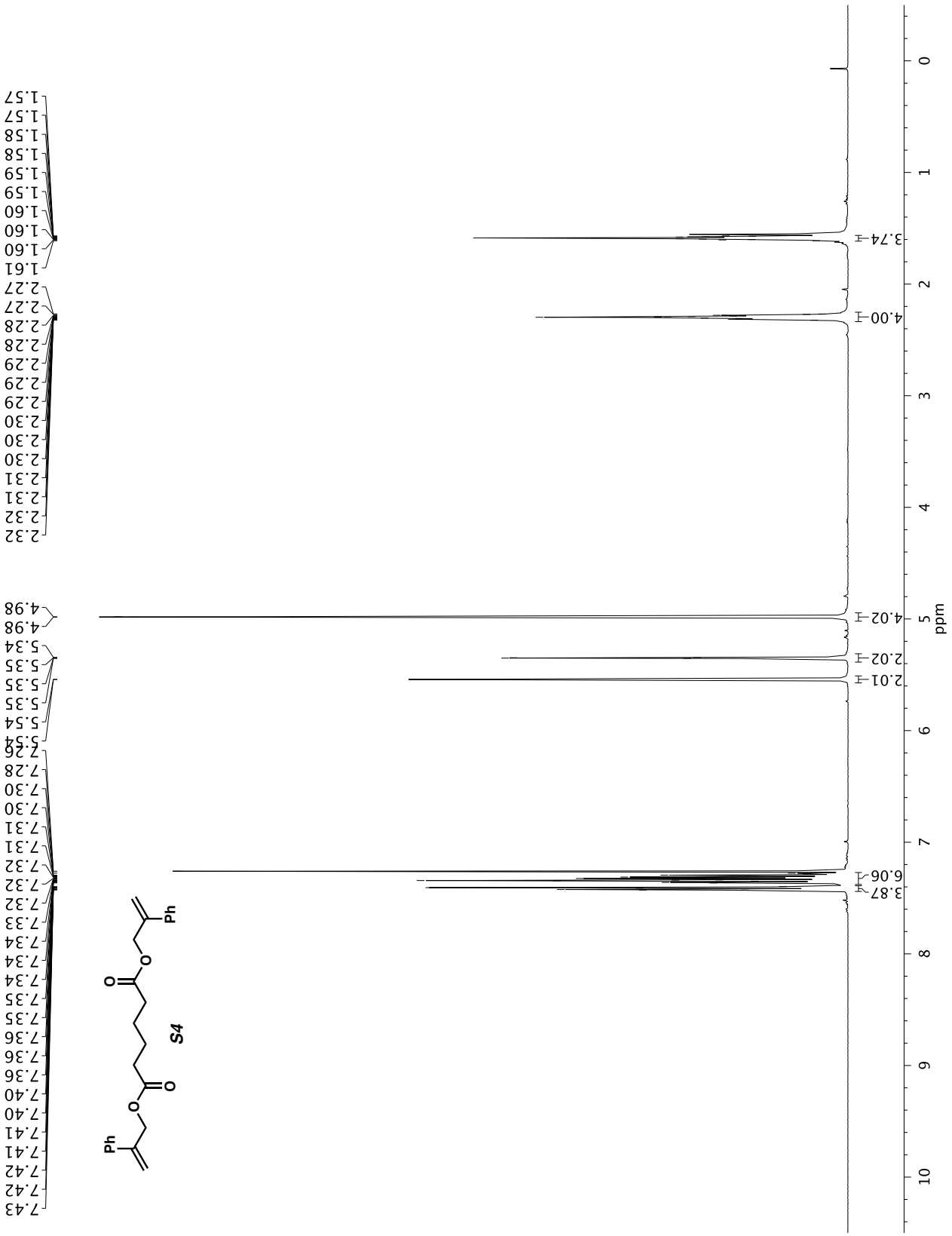
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S2**.



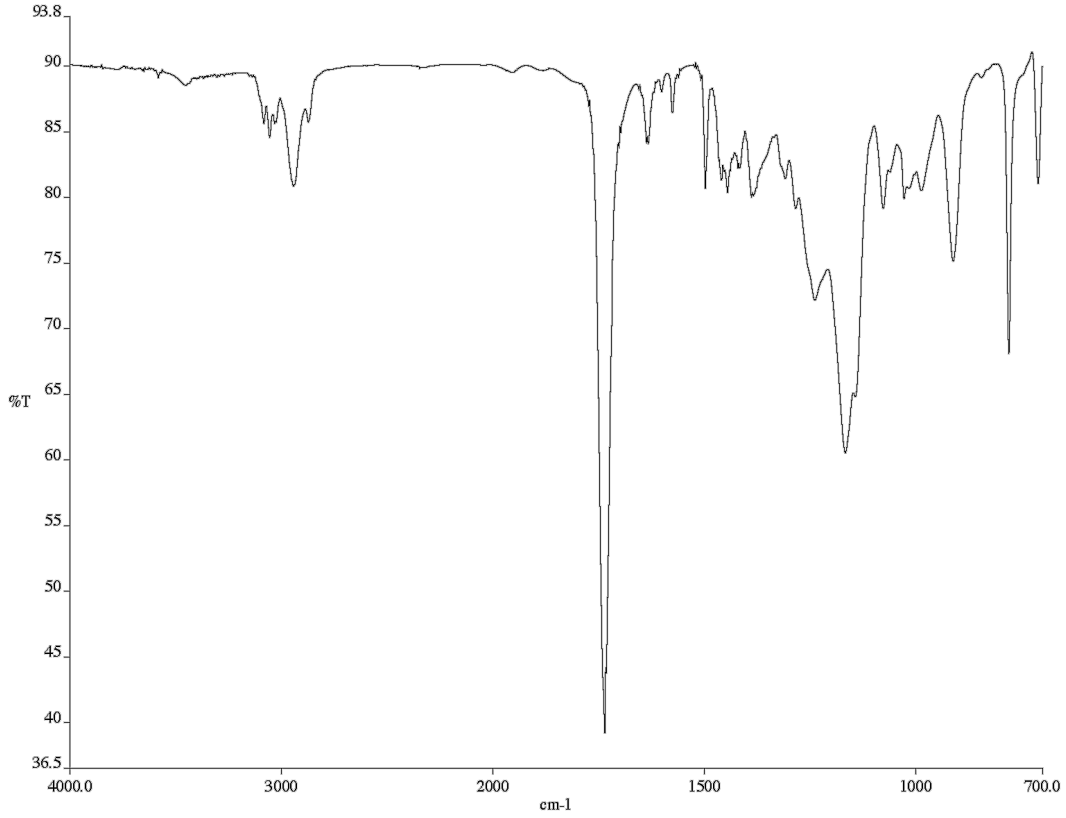
Infrared spectrum (Thin Film, NaCl) of compound **S2**.



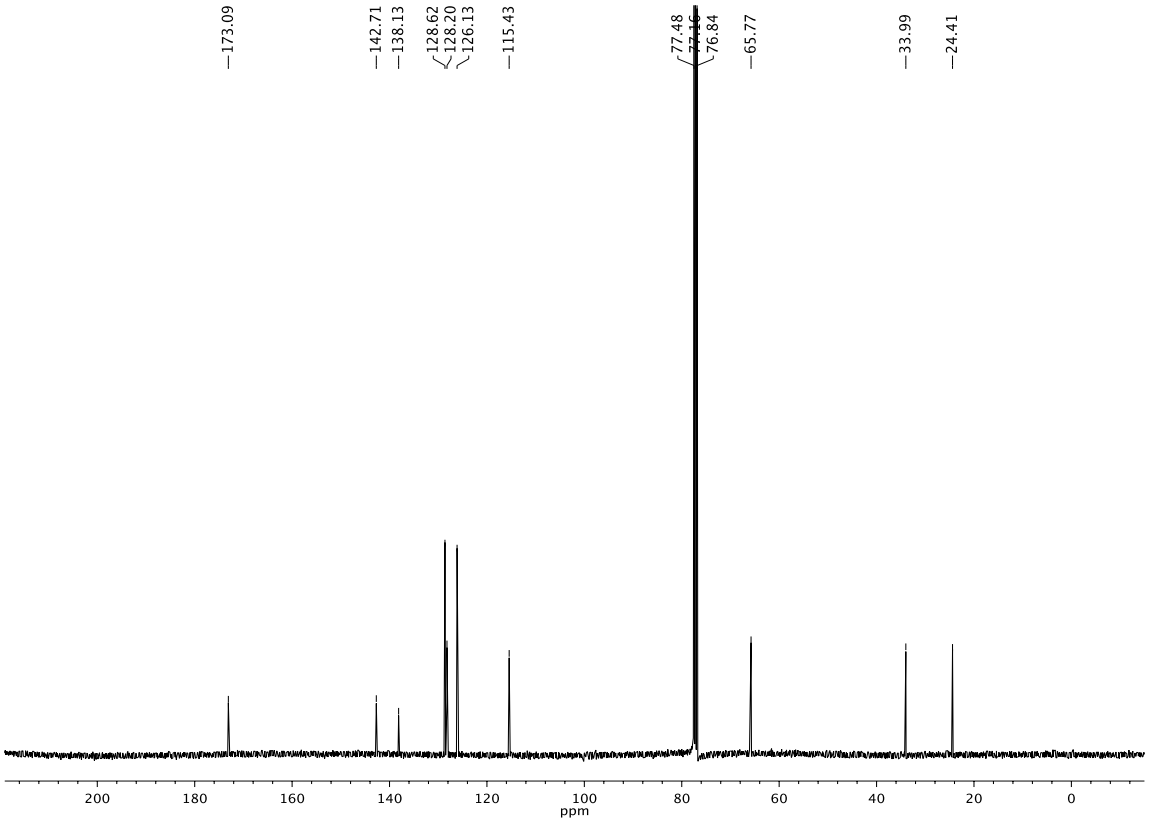
^{13}C NMR (101 MHz, $CDCl_3$) of compound **S2**.



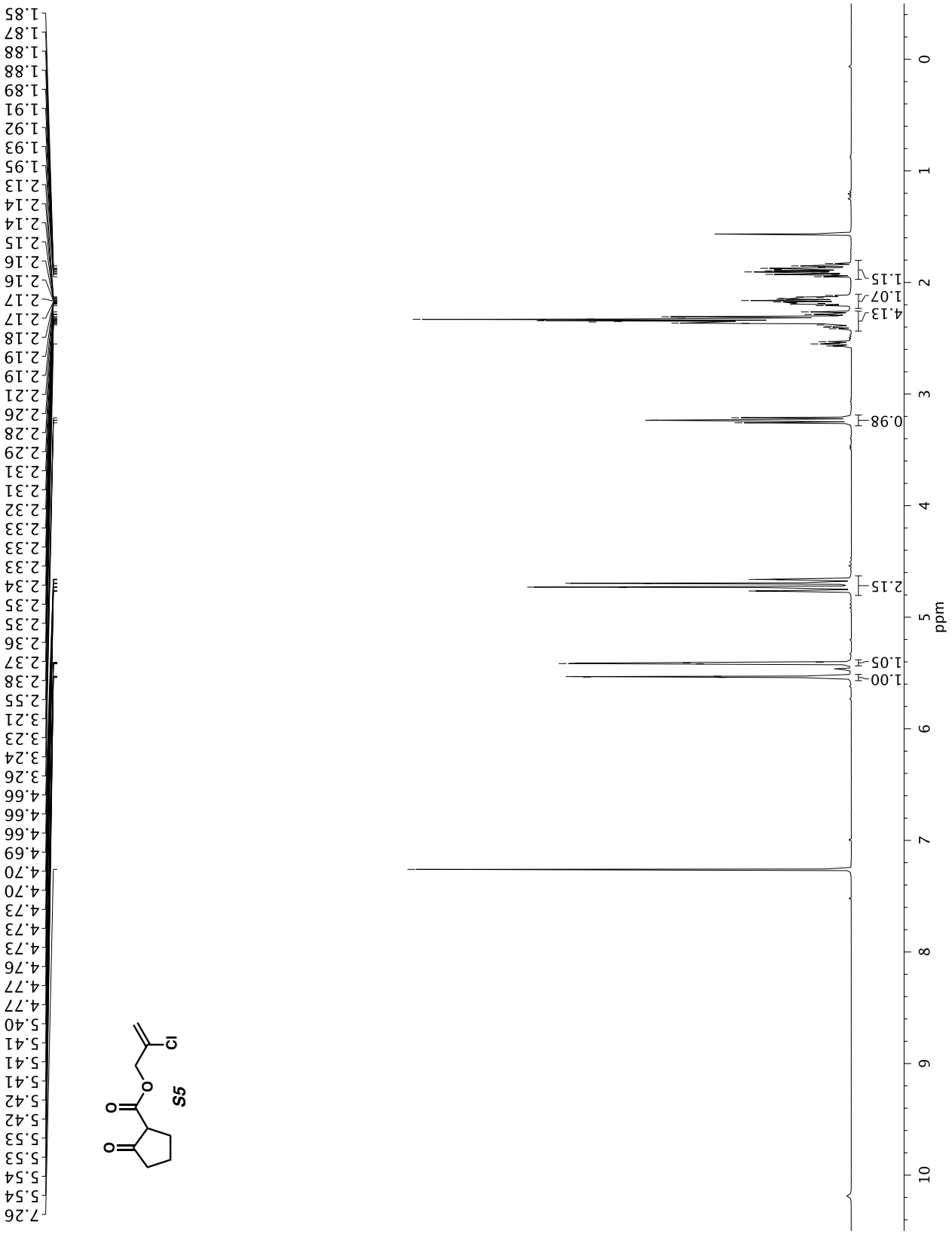
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S4**.



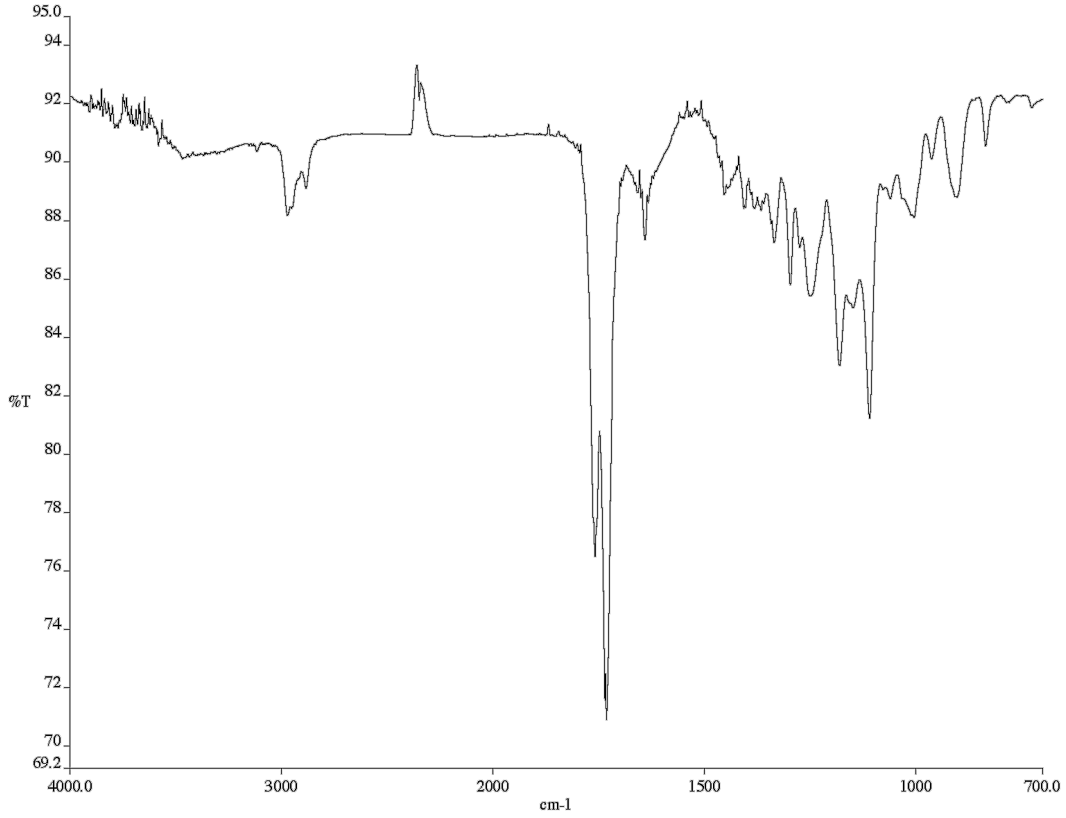
Infrared spectrum (Thin Film, NaCl) of compound **S4**.



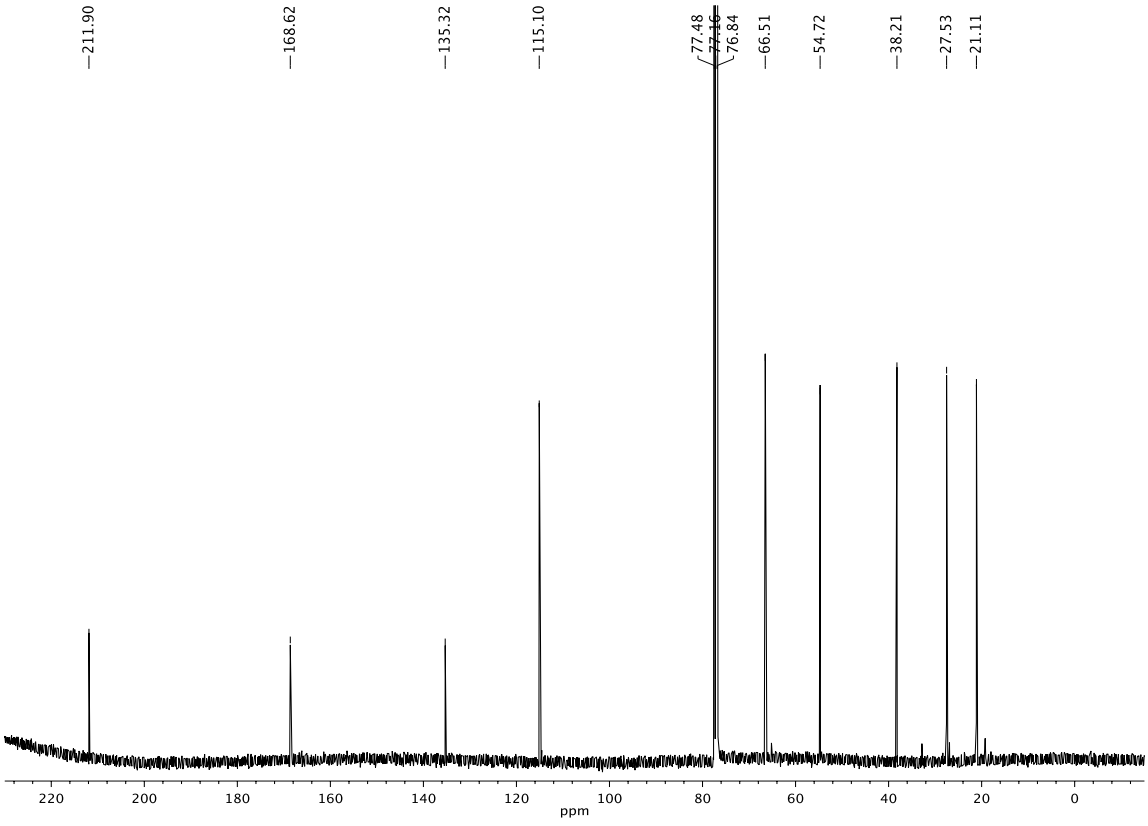
^{13}C NMR (101 MHz, $CDCl_3$) of compound **S4**.



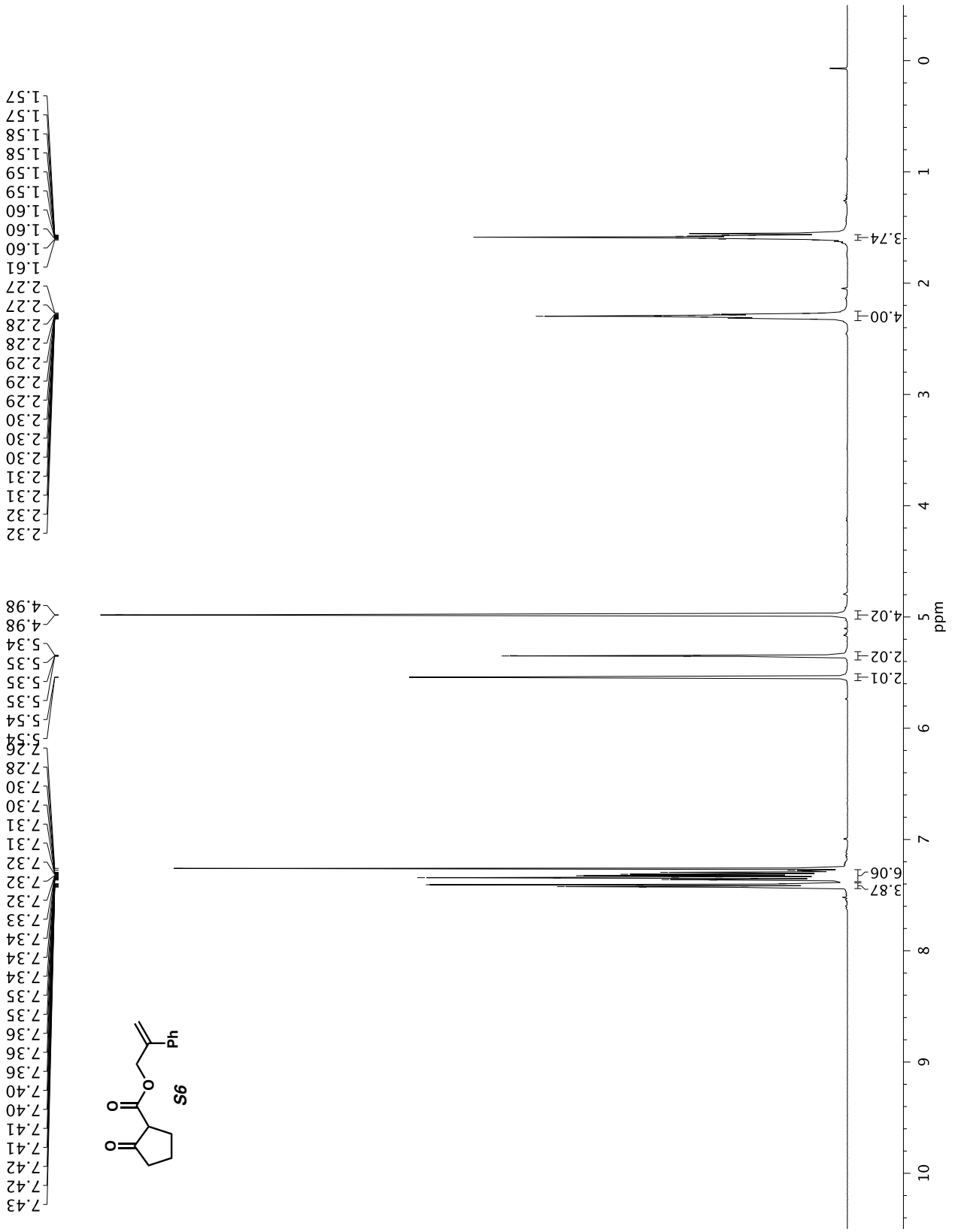
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S5**.



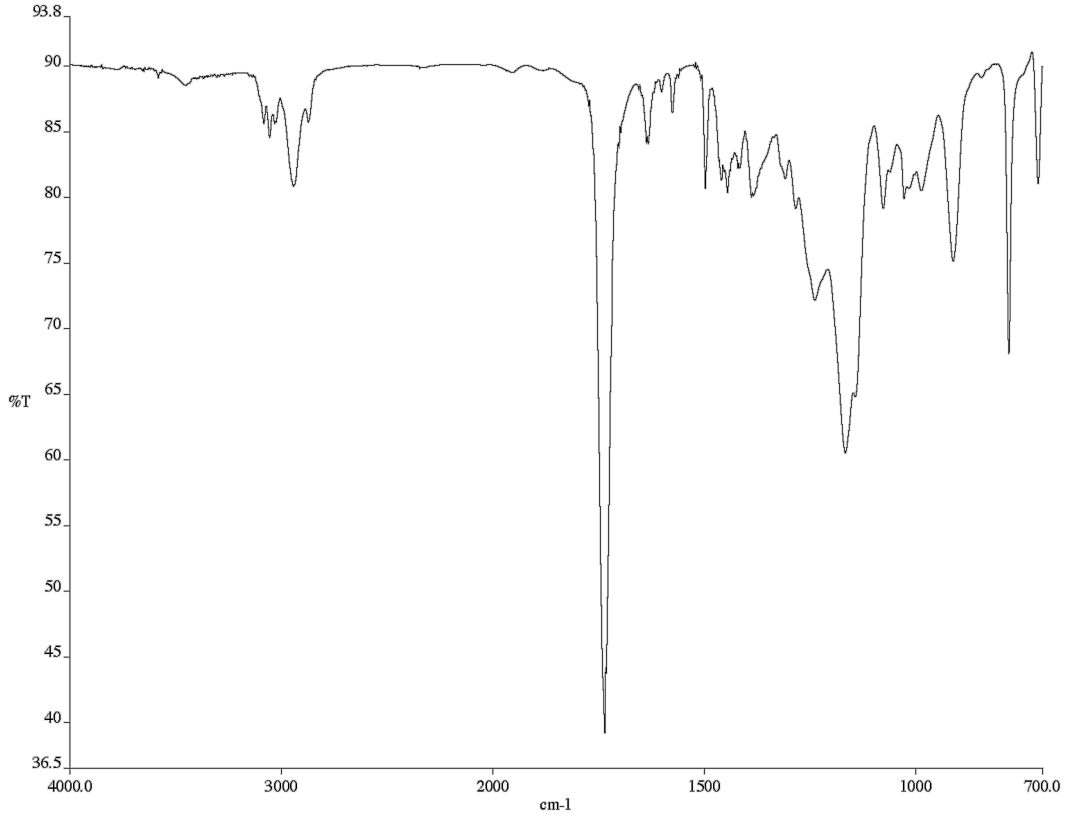
Infrared spectrum (Thin Film, NaCl) of compound **S5**.



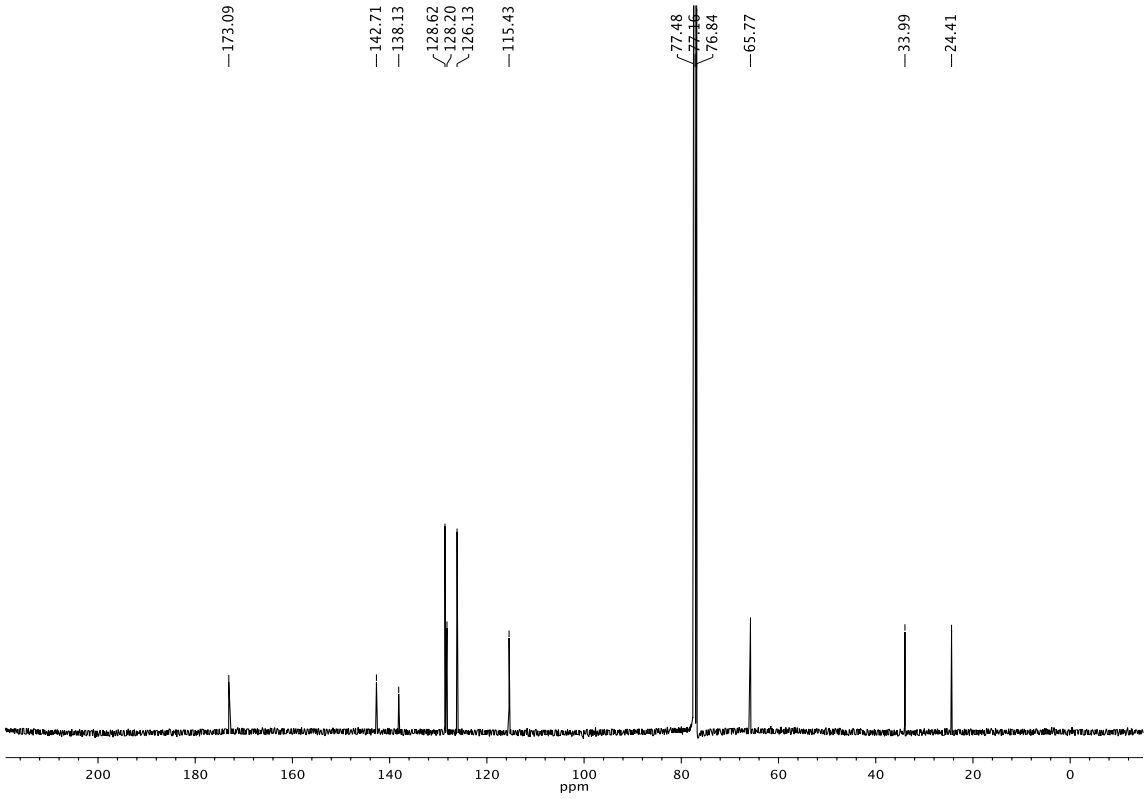
^{13}C NMR (101 MHz, $CDCl_3$) of compound **S5**.



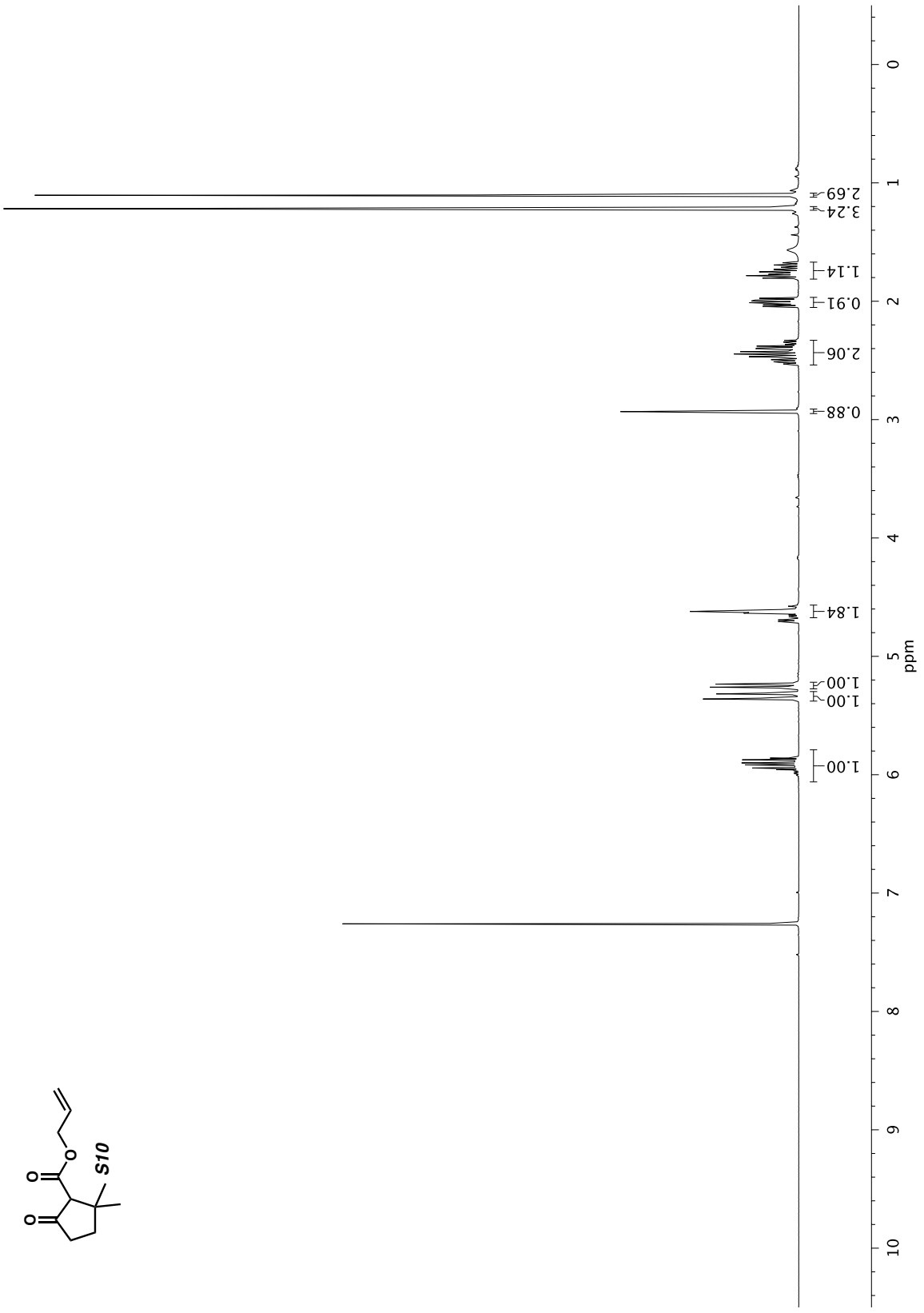
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S6**.



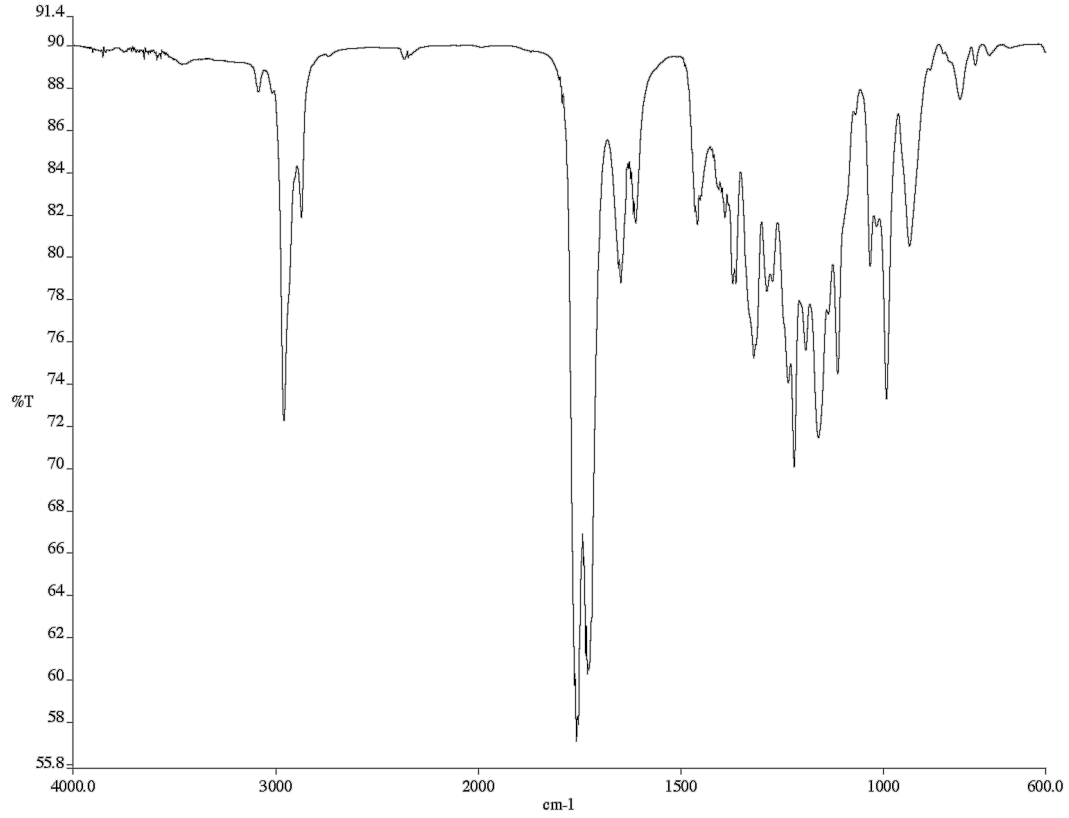
Infrared spectrum (Thin Film, NaCl) of compound **S6**.



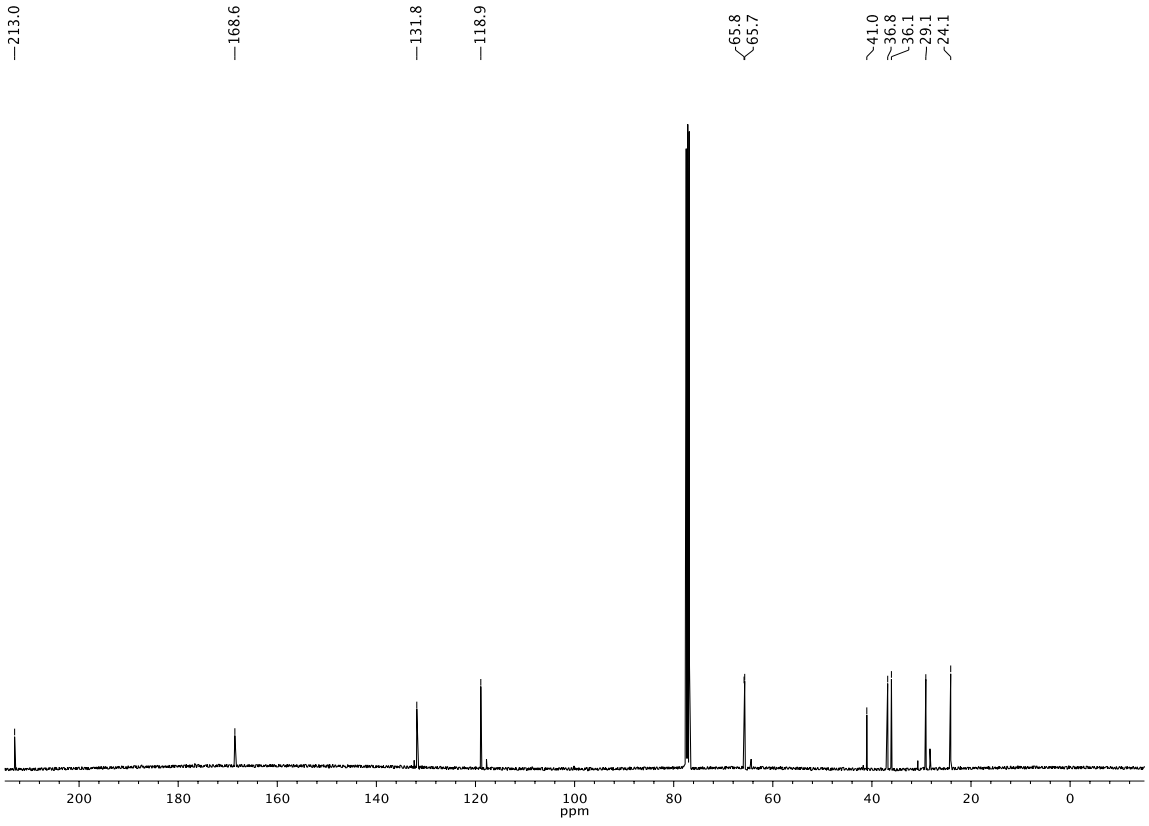
^{13}C NMR (101 MHz, $CDCl_3$) of compound **S6**.



^{1}H NMR (400 MHz, $CDCl_3$) of compound **S10**.



Infrared spectrum (Thin Film, NaCl) of compound **S10**.



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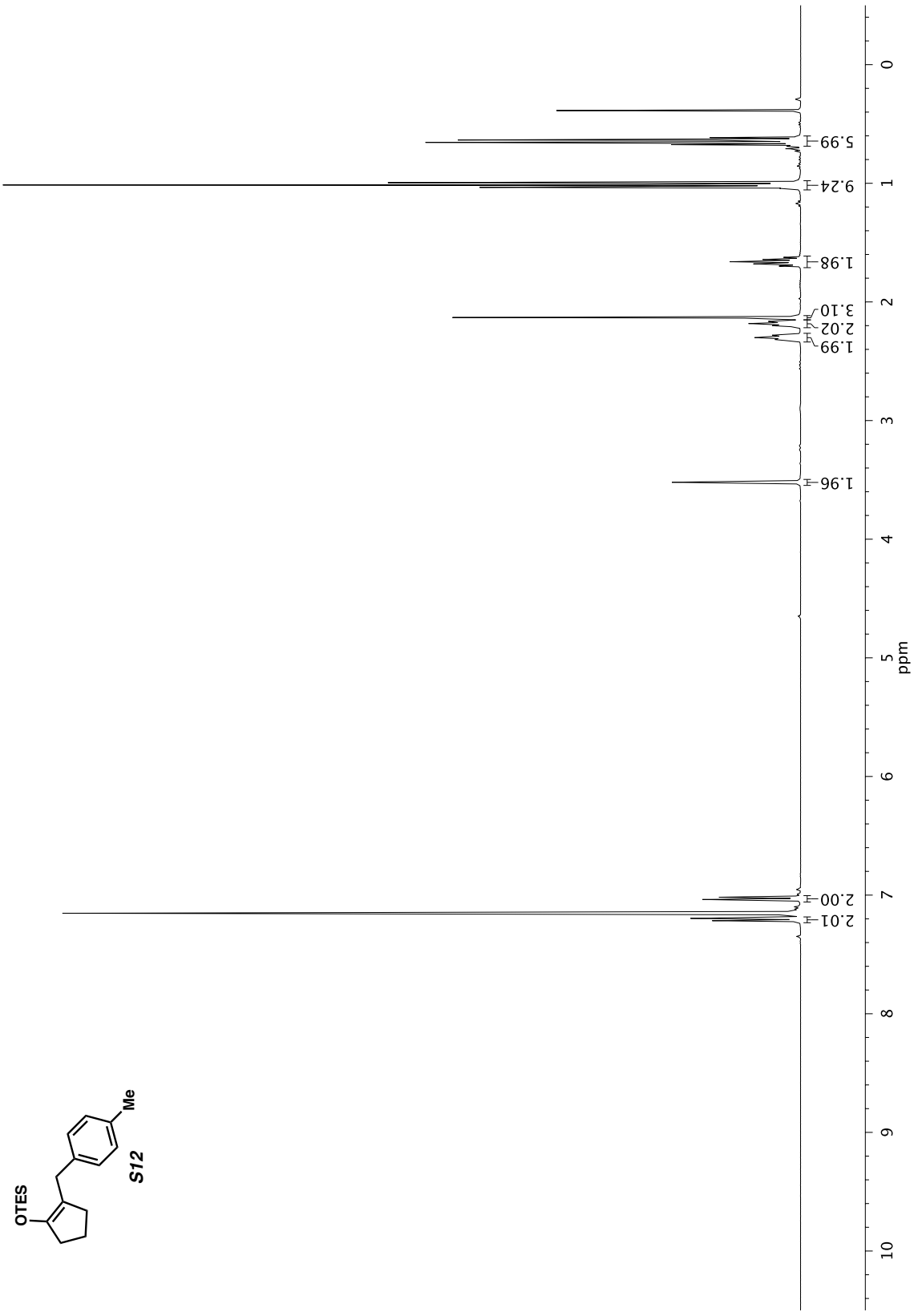
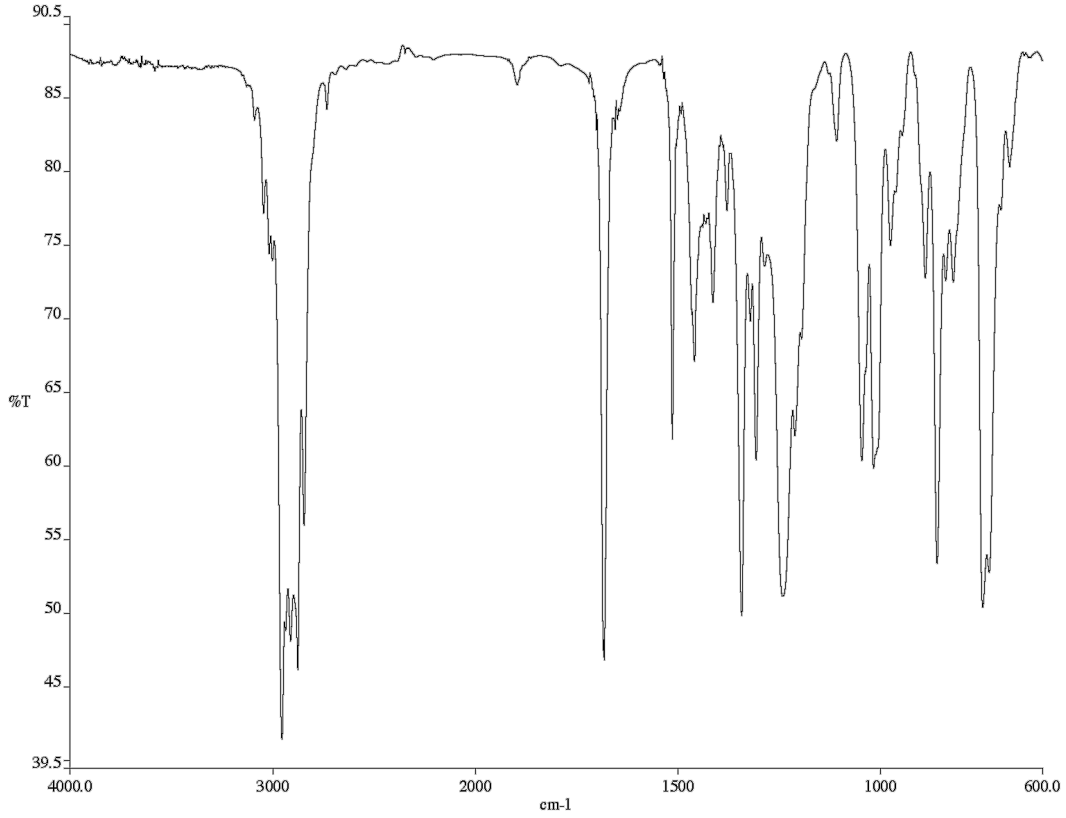
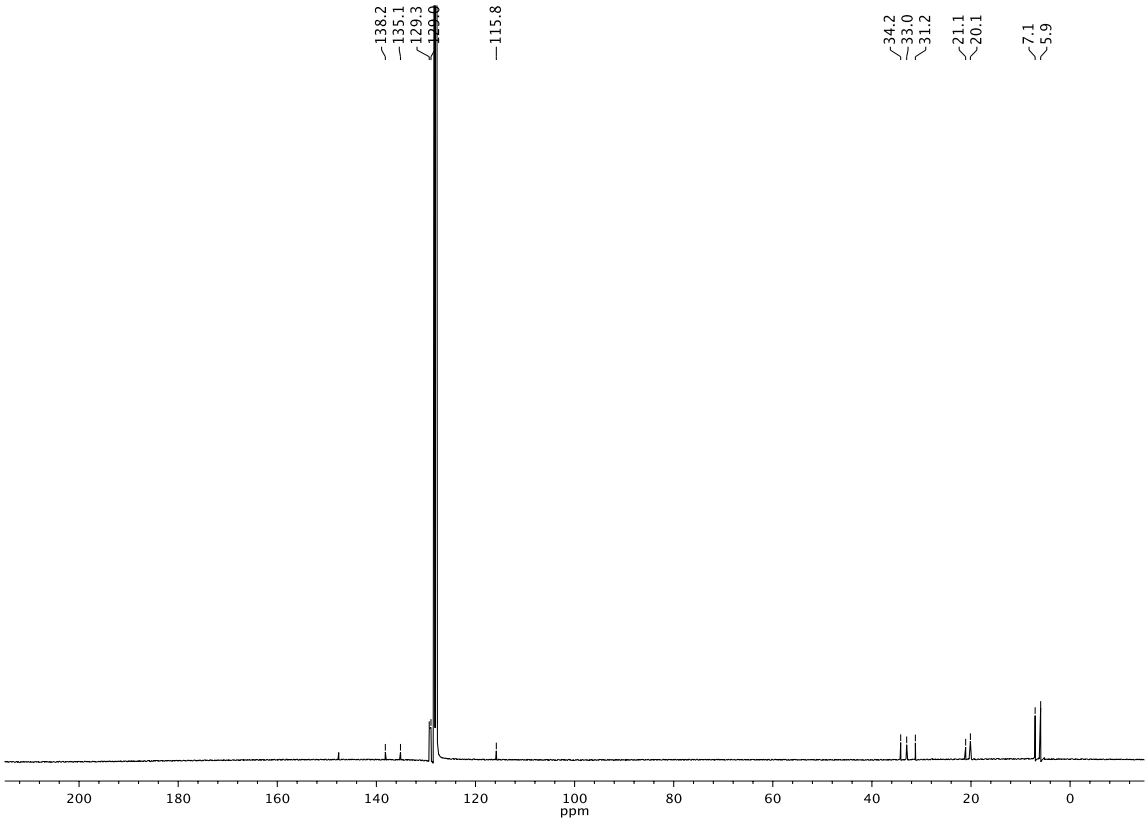


^{1}H NMR (400 MHz, C_6D_6) of compound **S12**.



Infrared spectrum (Thin Film, NaCl) of compound **S12**.



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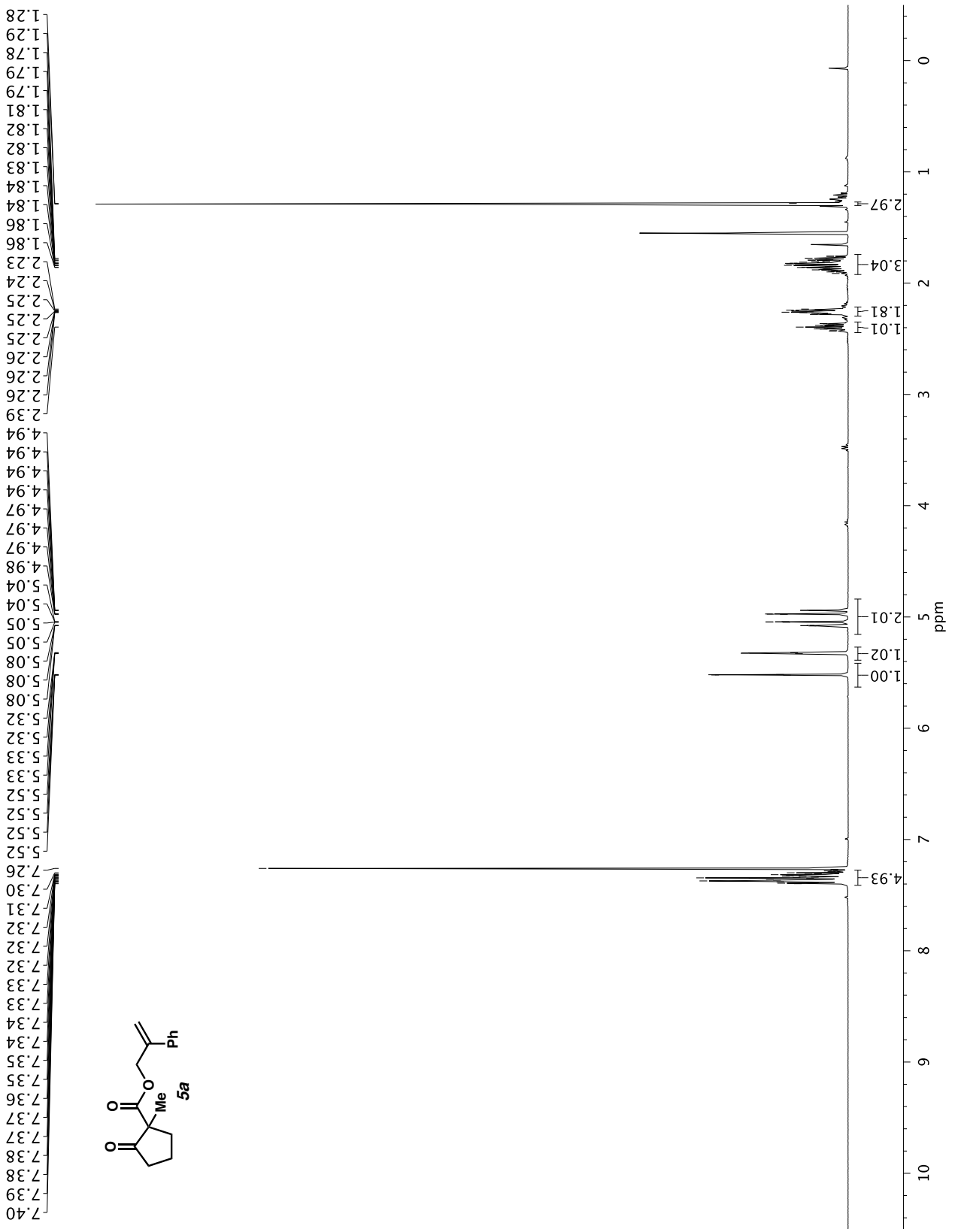
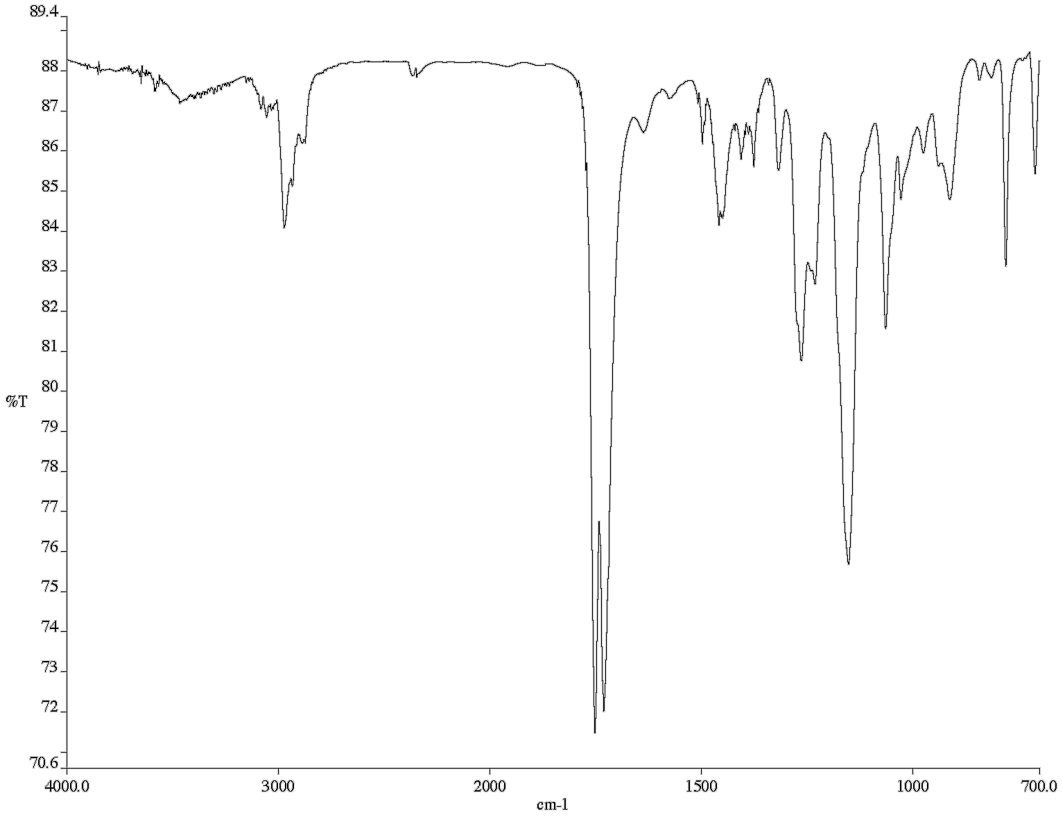
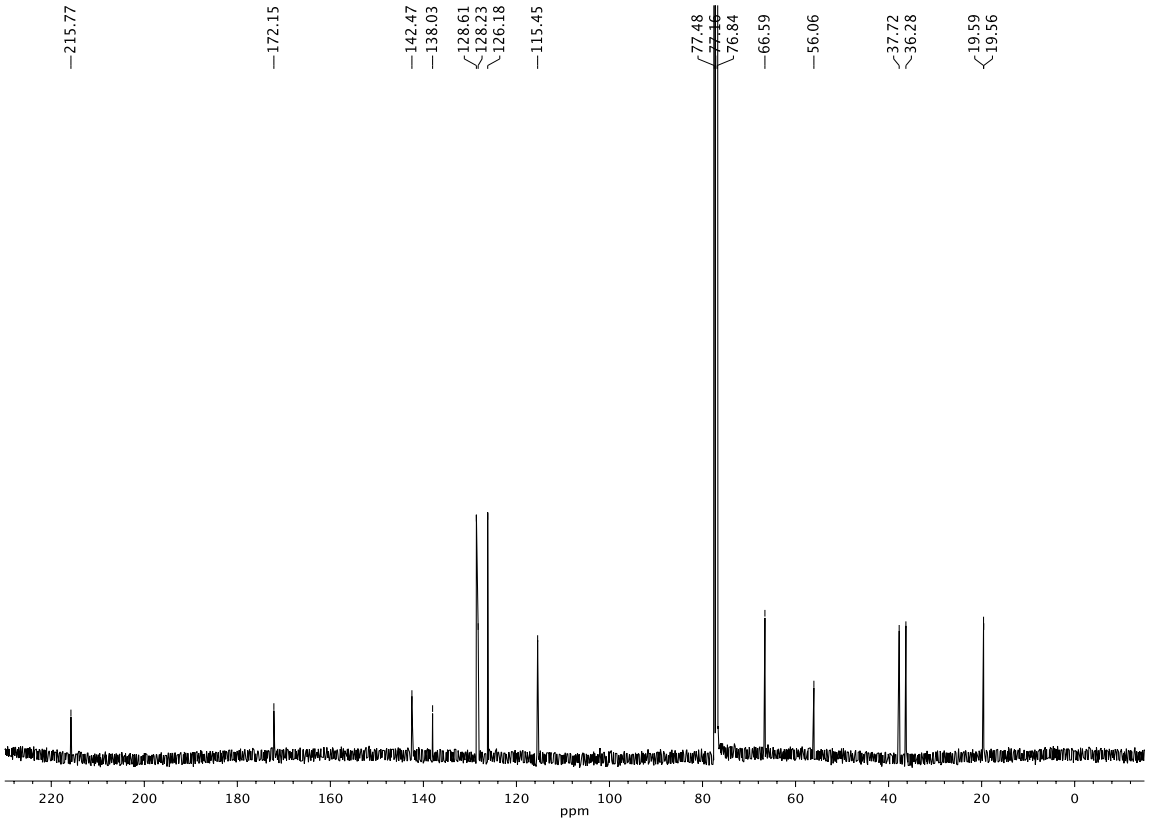


^{1}H NMR (400 MHz, $CDCl_3$) of compound **5a**.



Infrared spectrum (Thin Film, NaCl) of compound **5a**.



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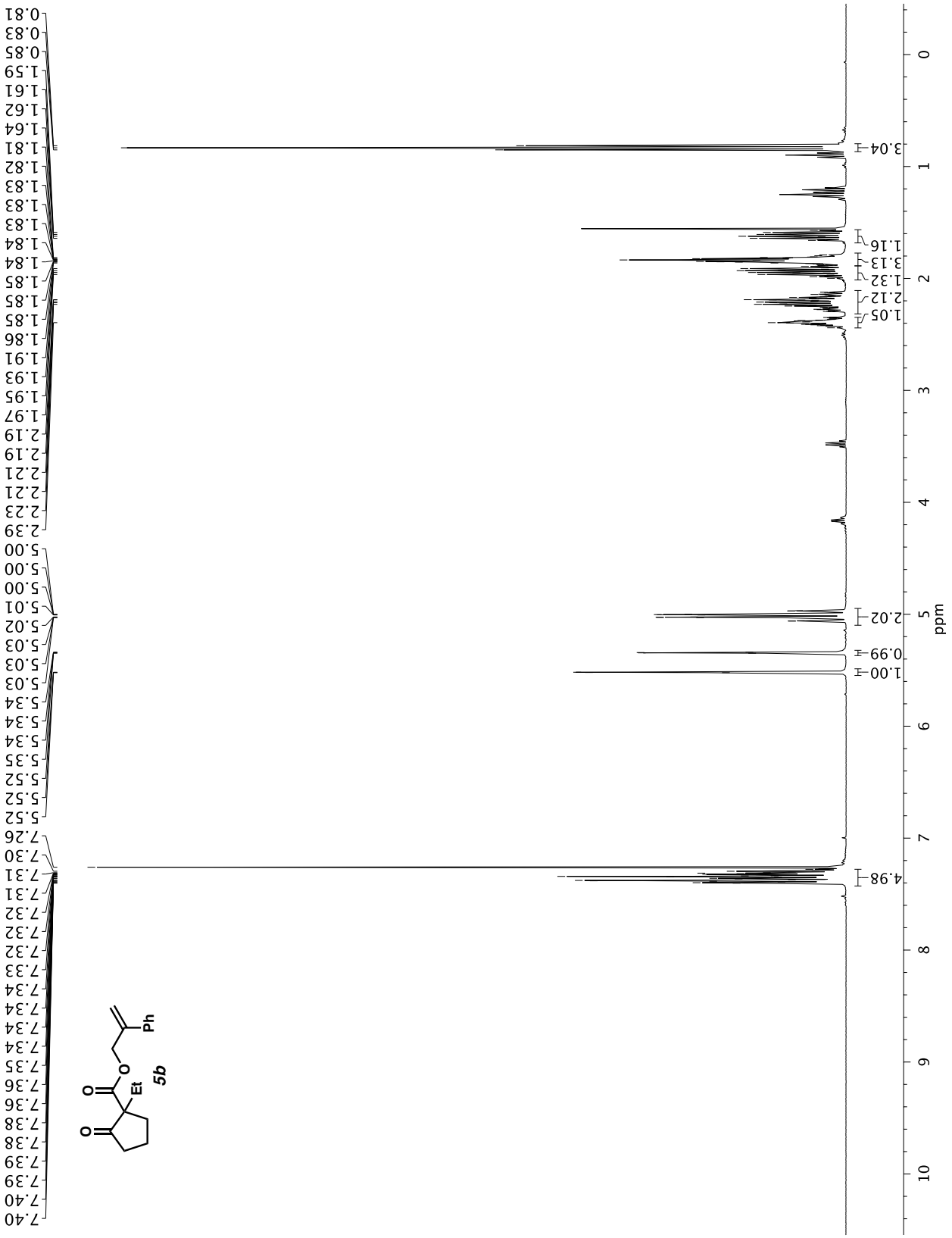
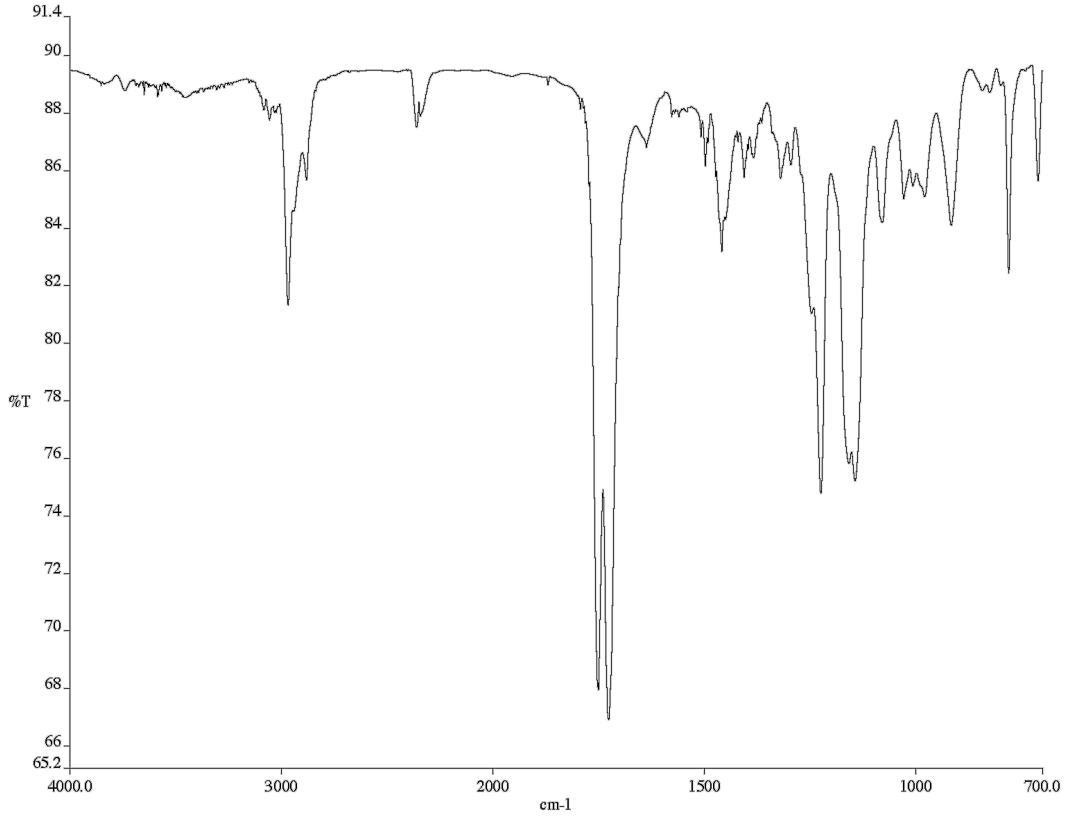
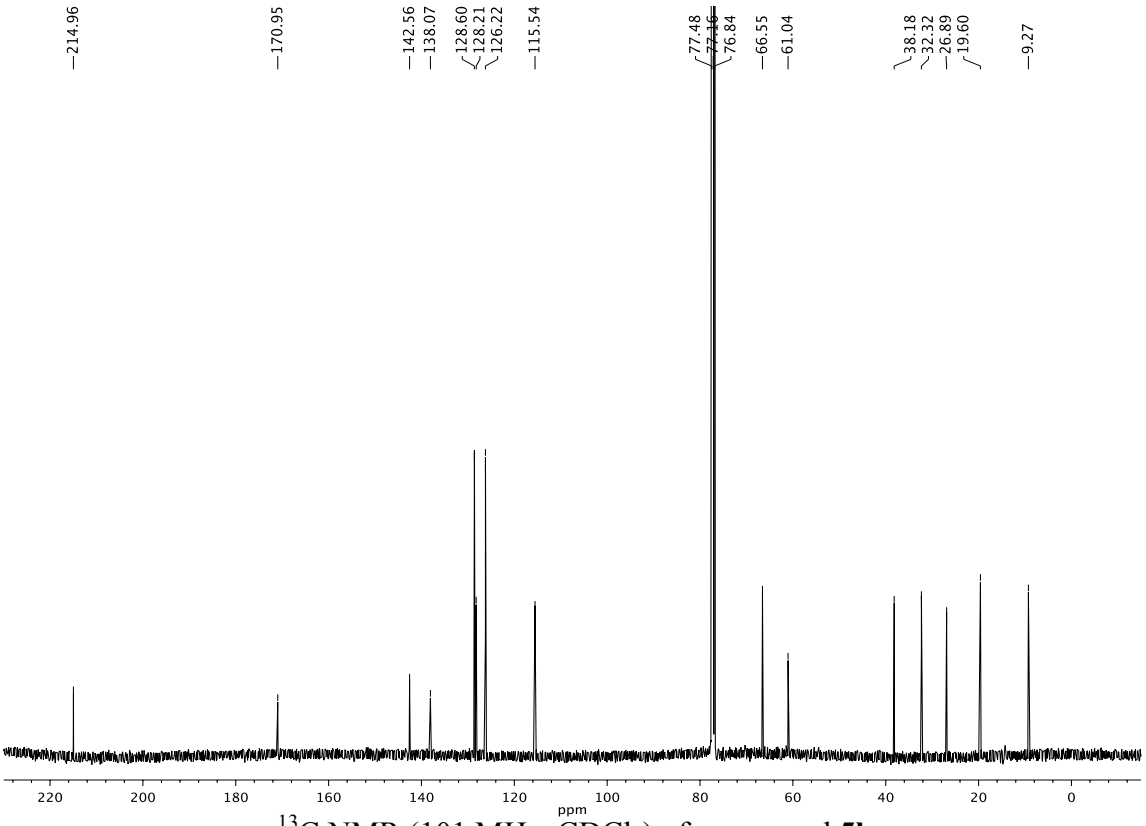


^{1}H NMR (400 MHz, $CDCl_3$) of compound **5b**.



Infrared spectrum (Thin Film, NaCl) of compound **5b**



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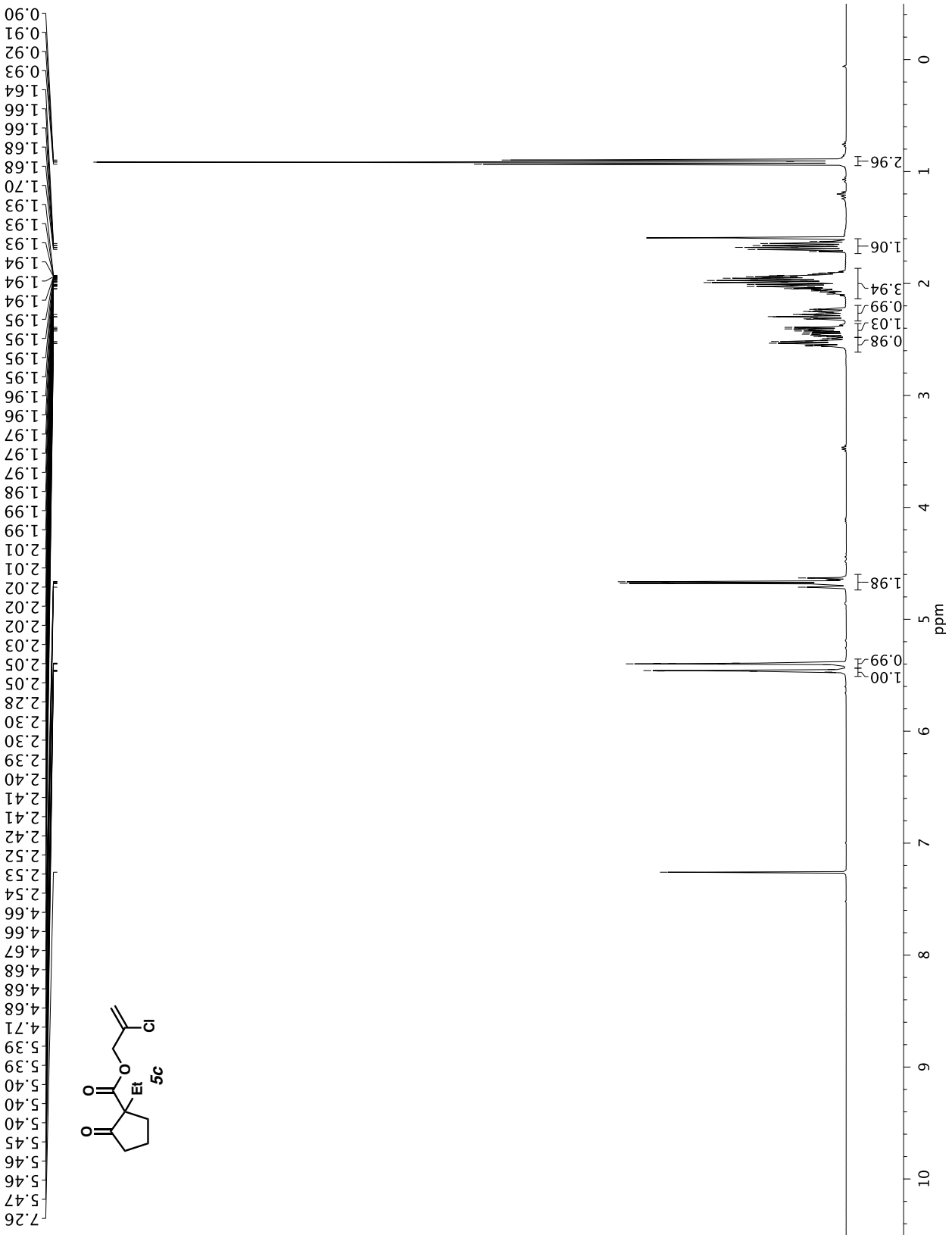
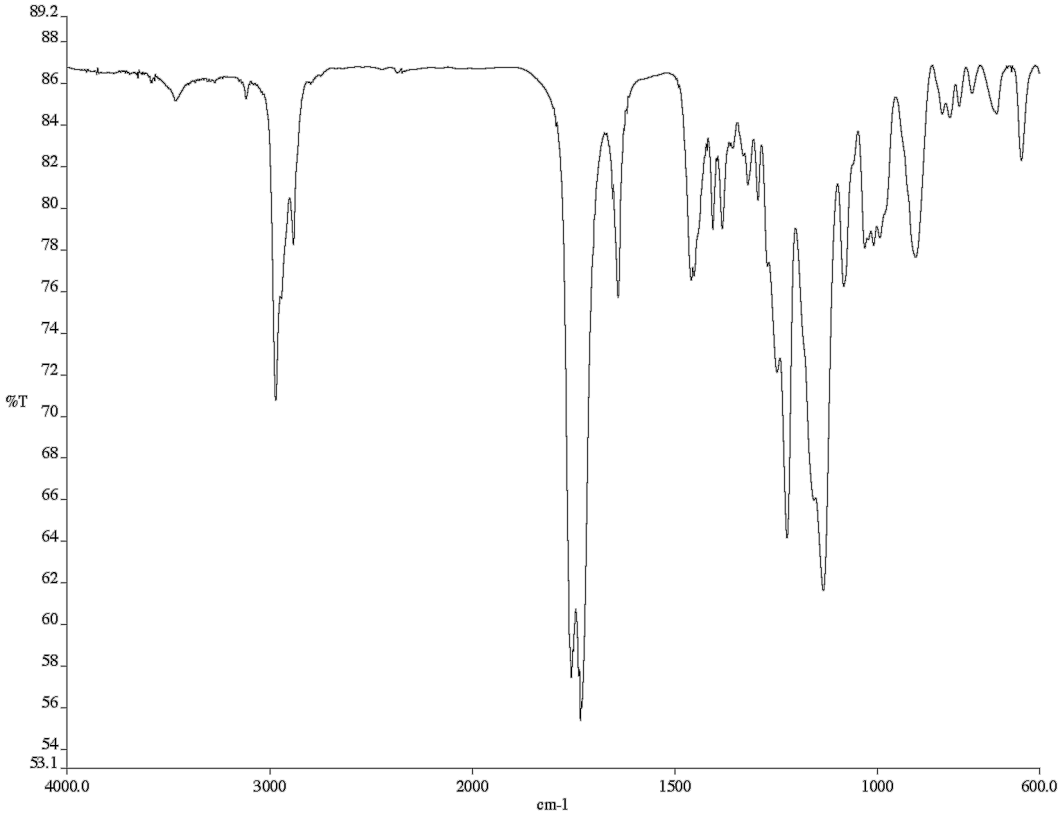
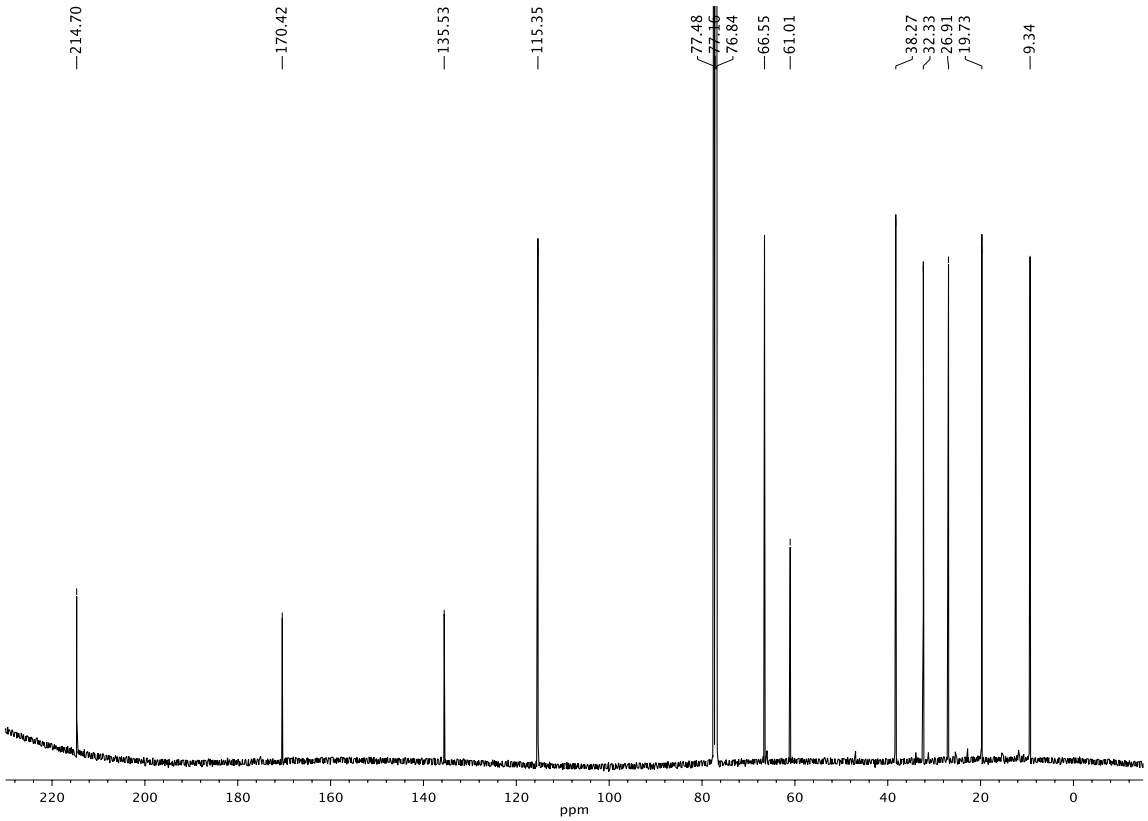


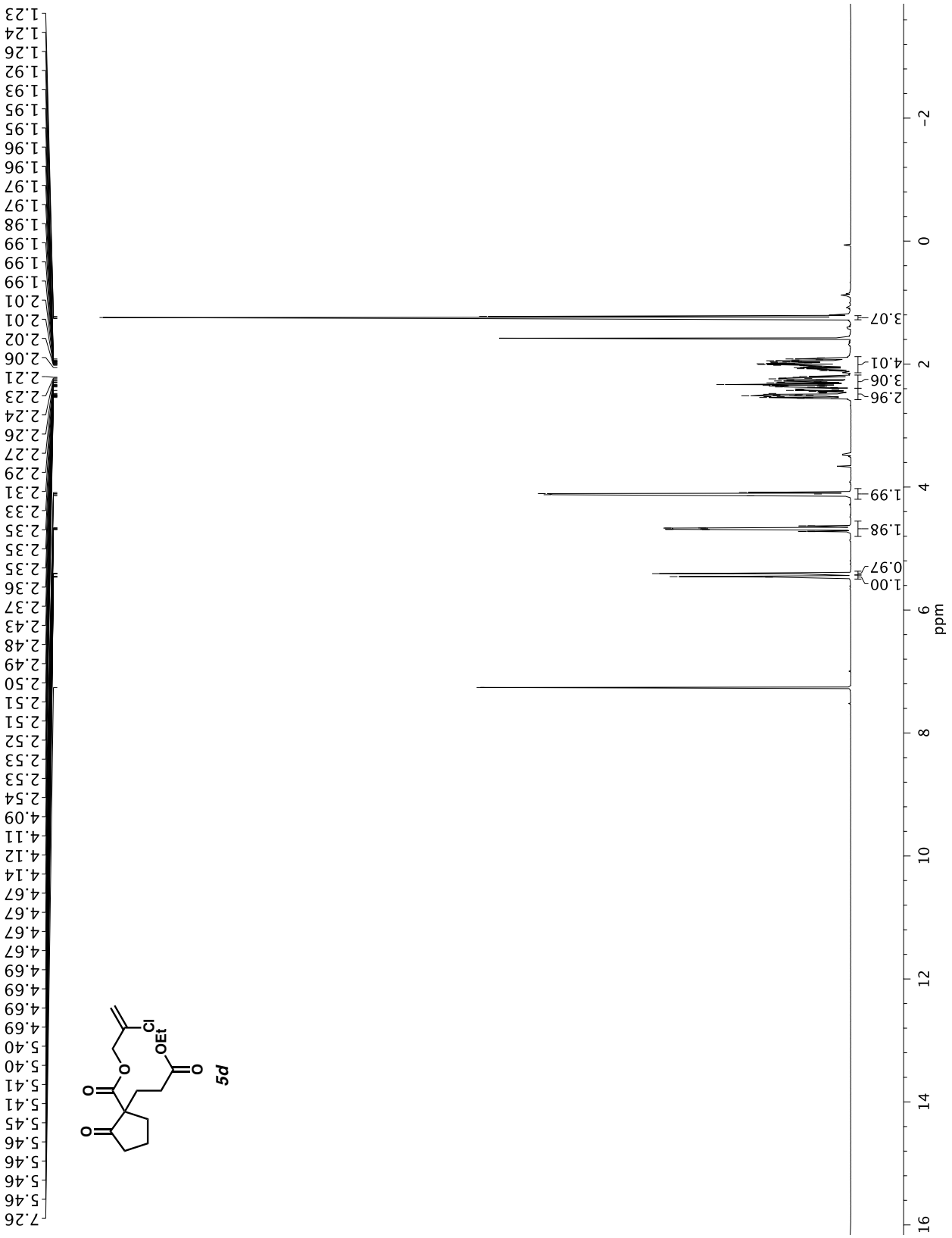
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5c**.



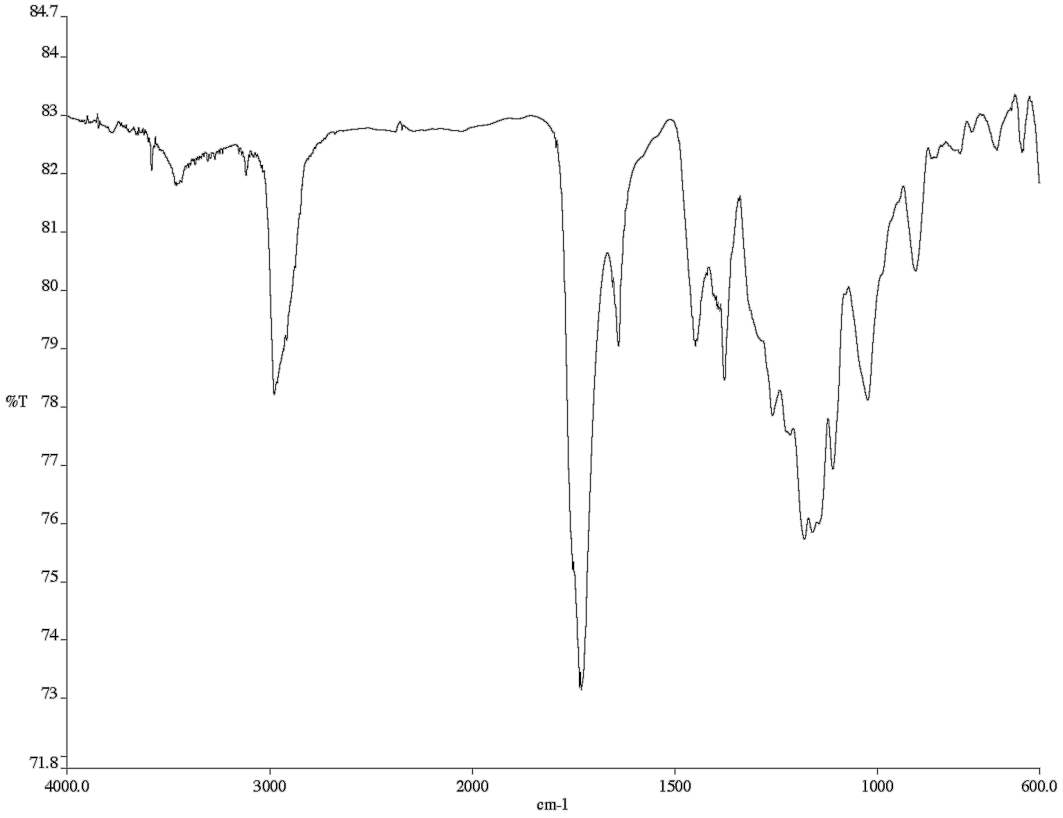
Infrared spectrum (Thin Film, NaCl) of compound **5c**.



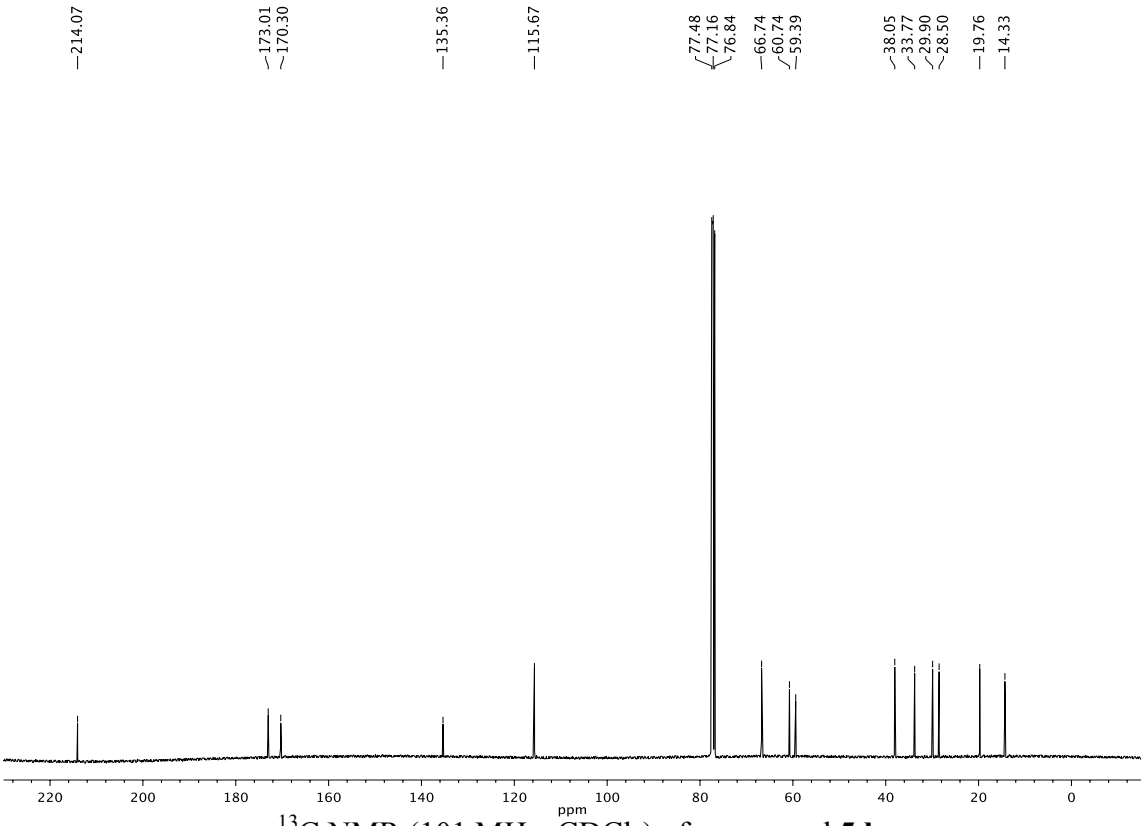
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5c**.



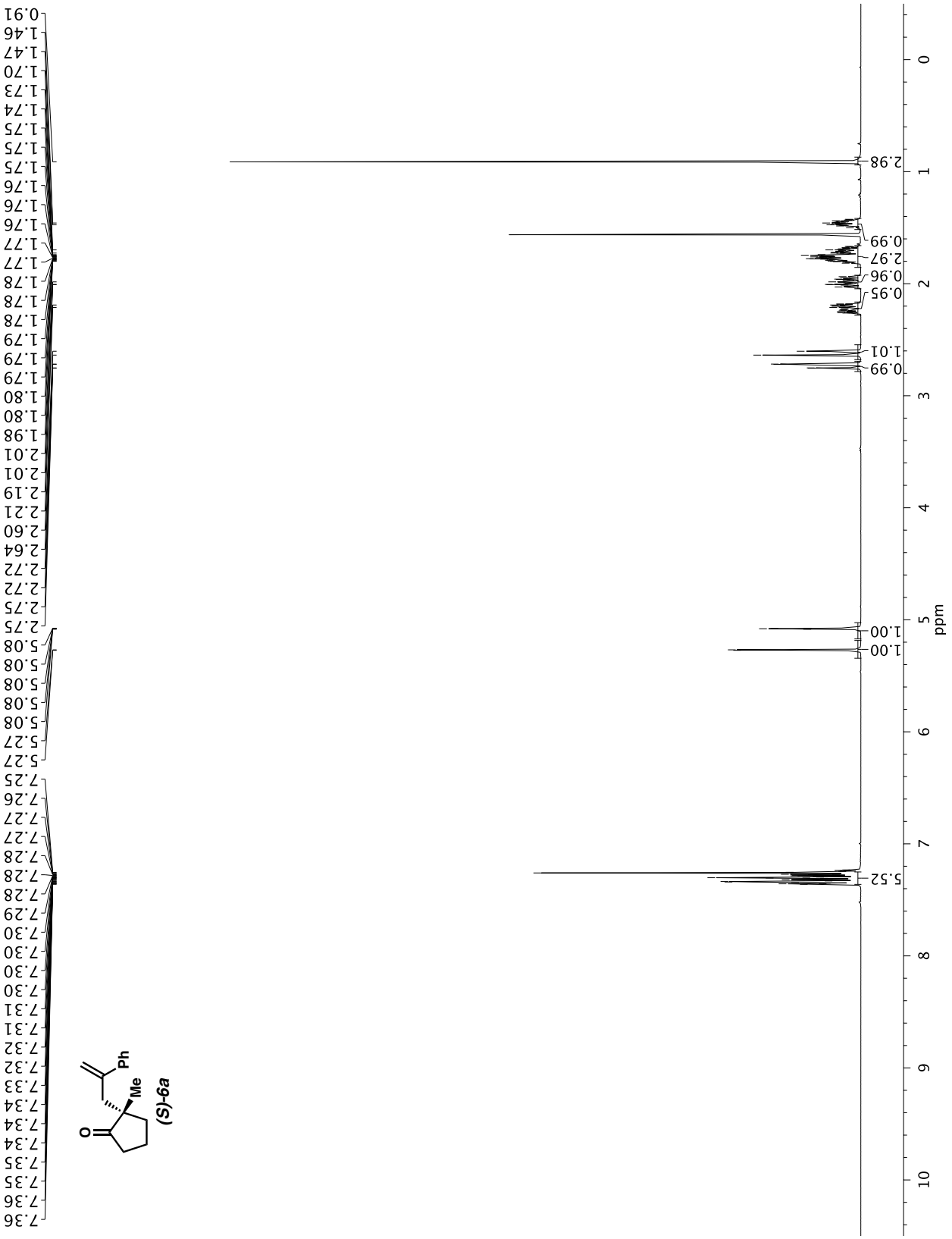
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5d**.



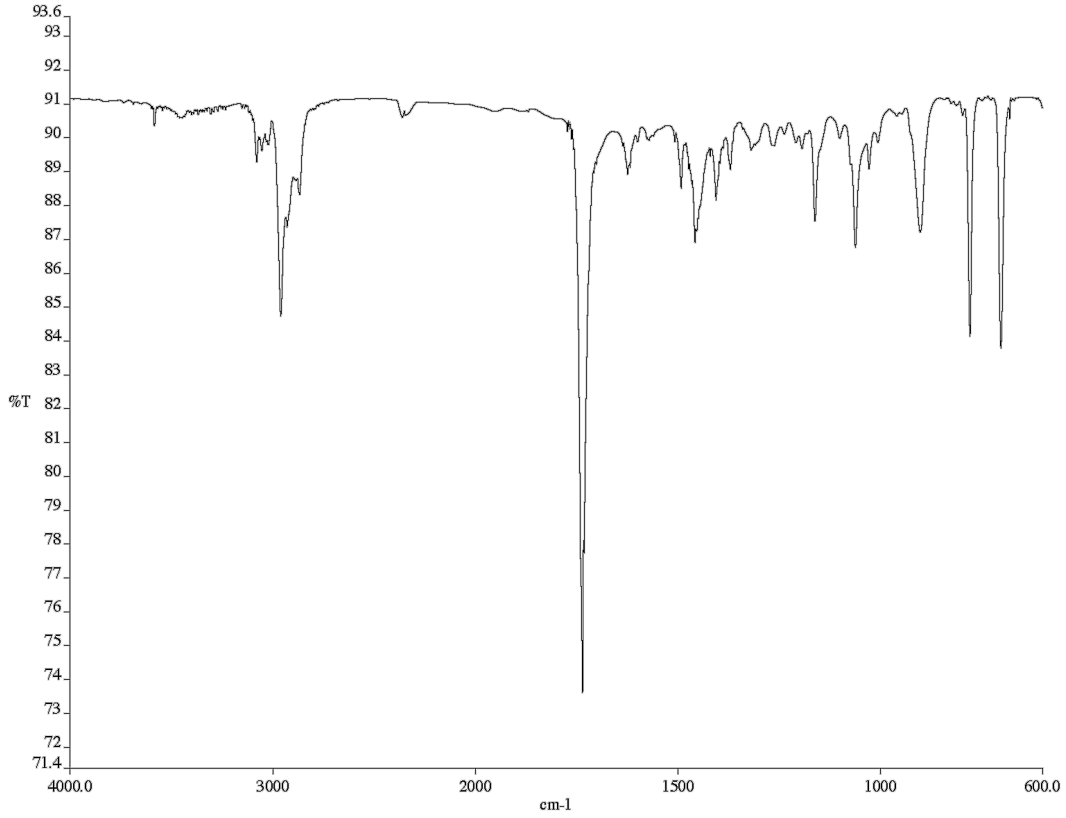
Infrared spectrum (Thin Film, NaCl) of compound **5d**.



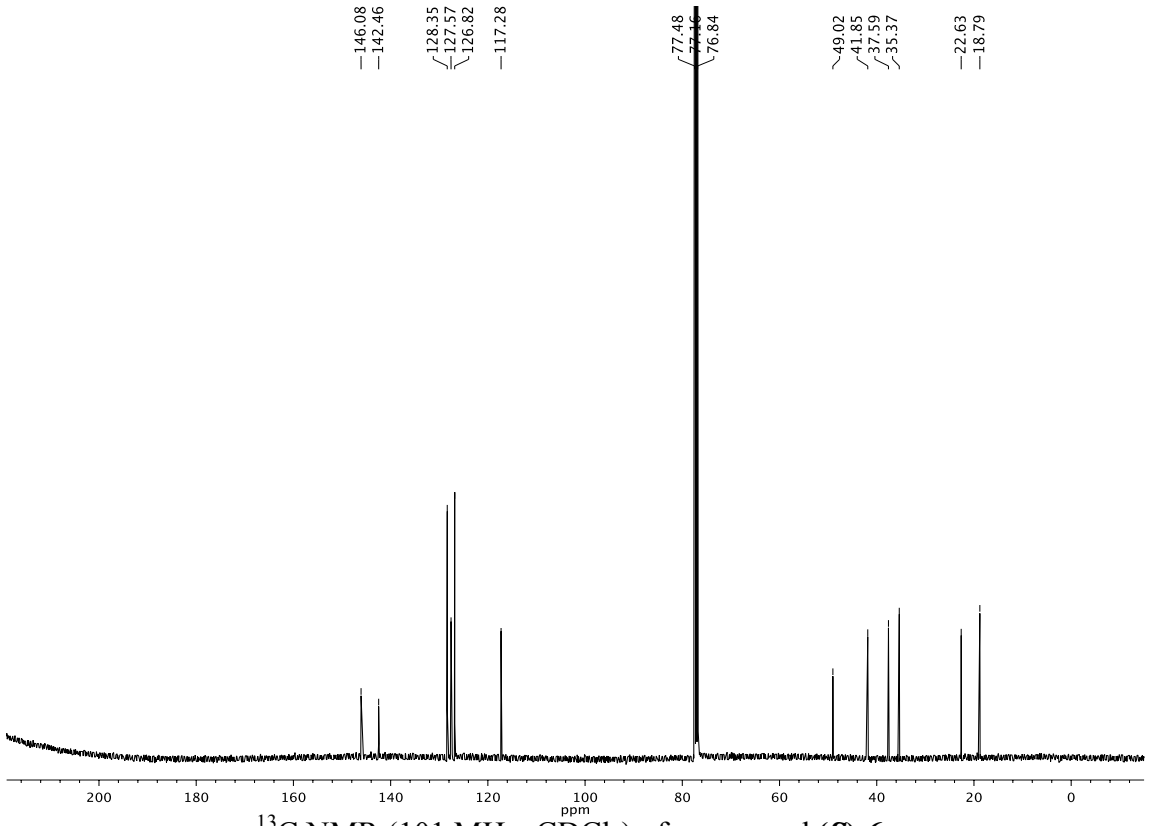
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5d**.



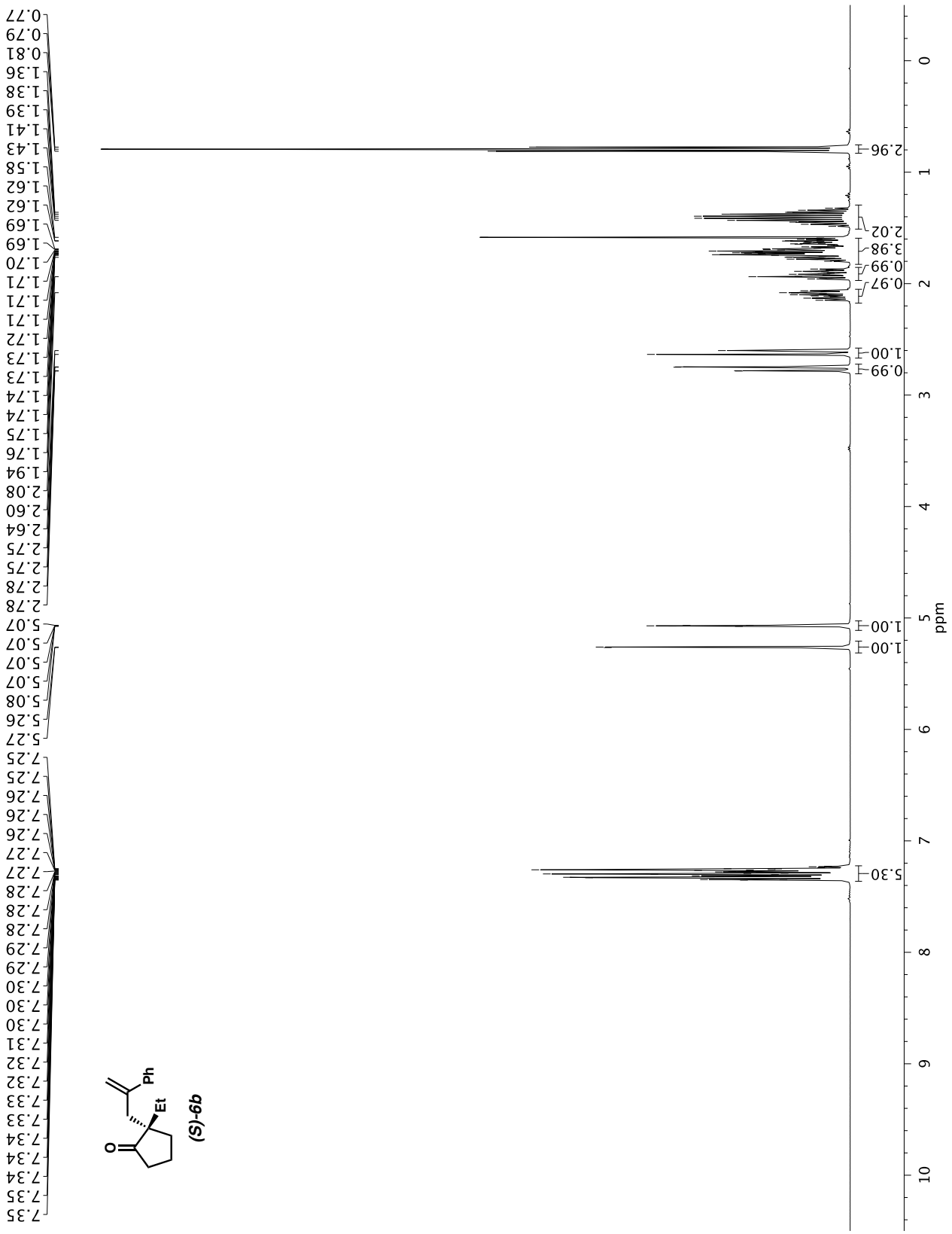
^{1}H NMR (400 MHz, $CDCl_3$) of compound **(*S*)-6a**.



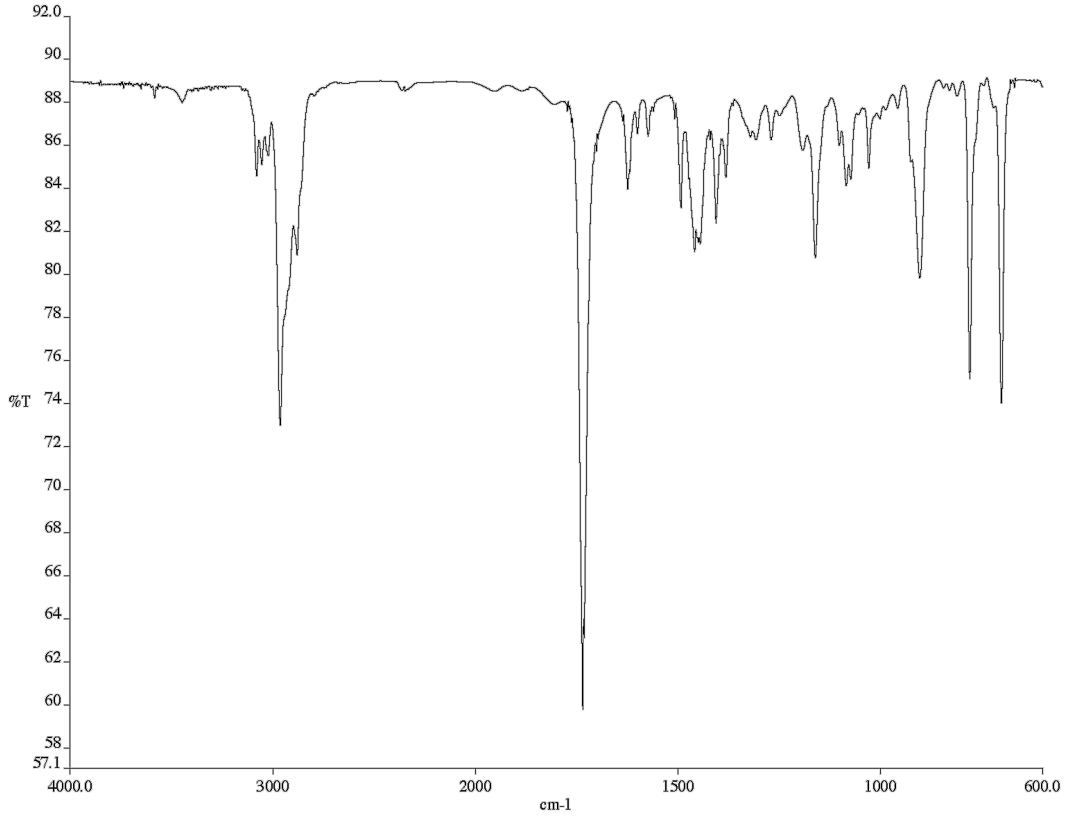
Infrared spectrum (Thin Film, NaCl) of compound **(*S*)-6a**.



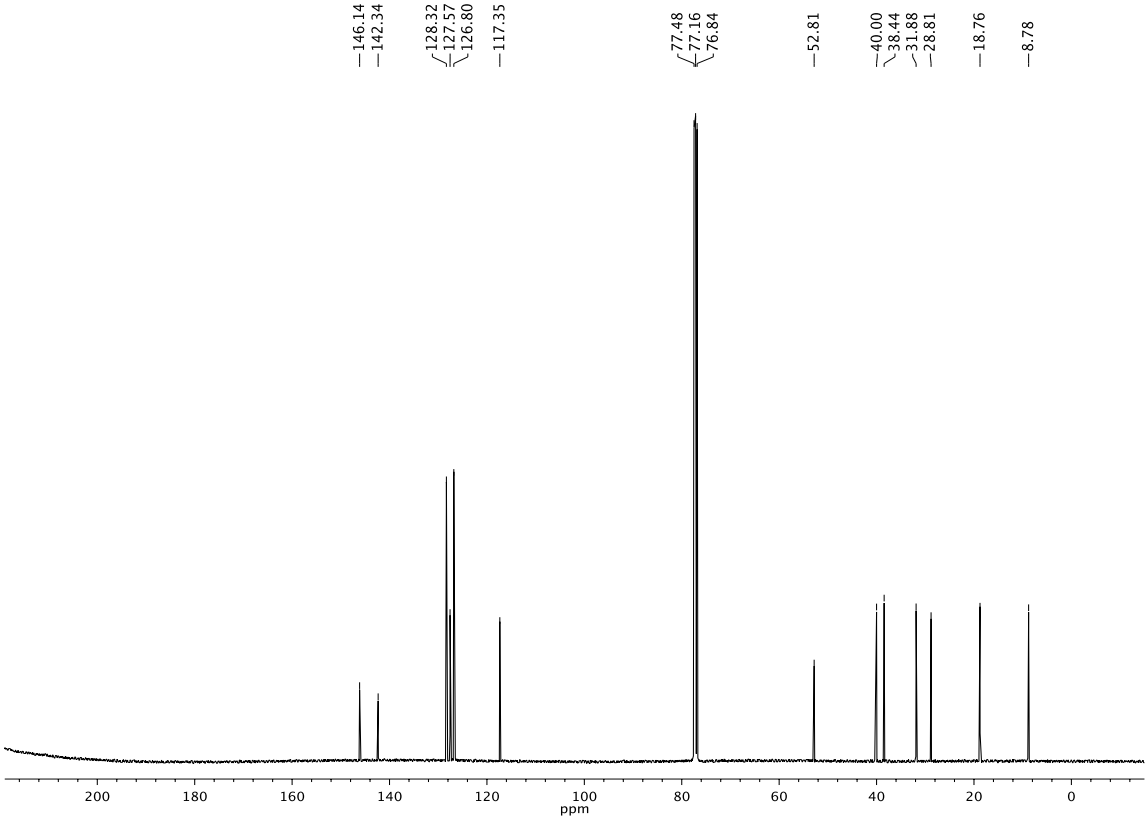
^{13}C NMR (101 MHz, $CDCl_3$) of compound **(*S*)-6a**.



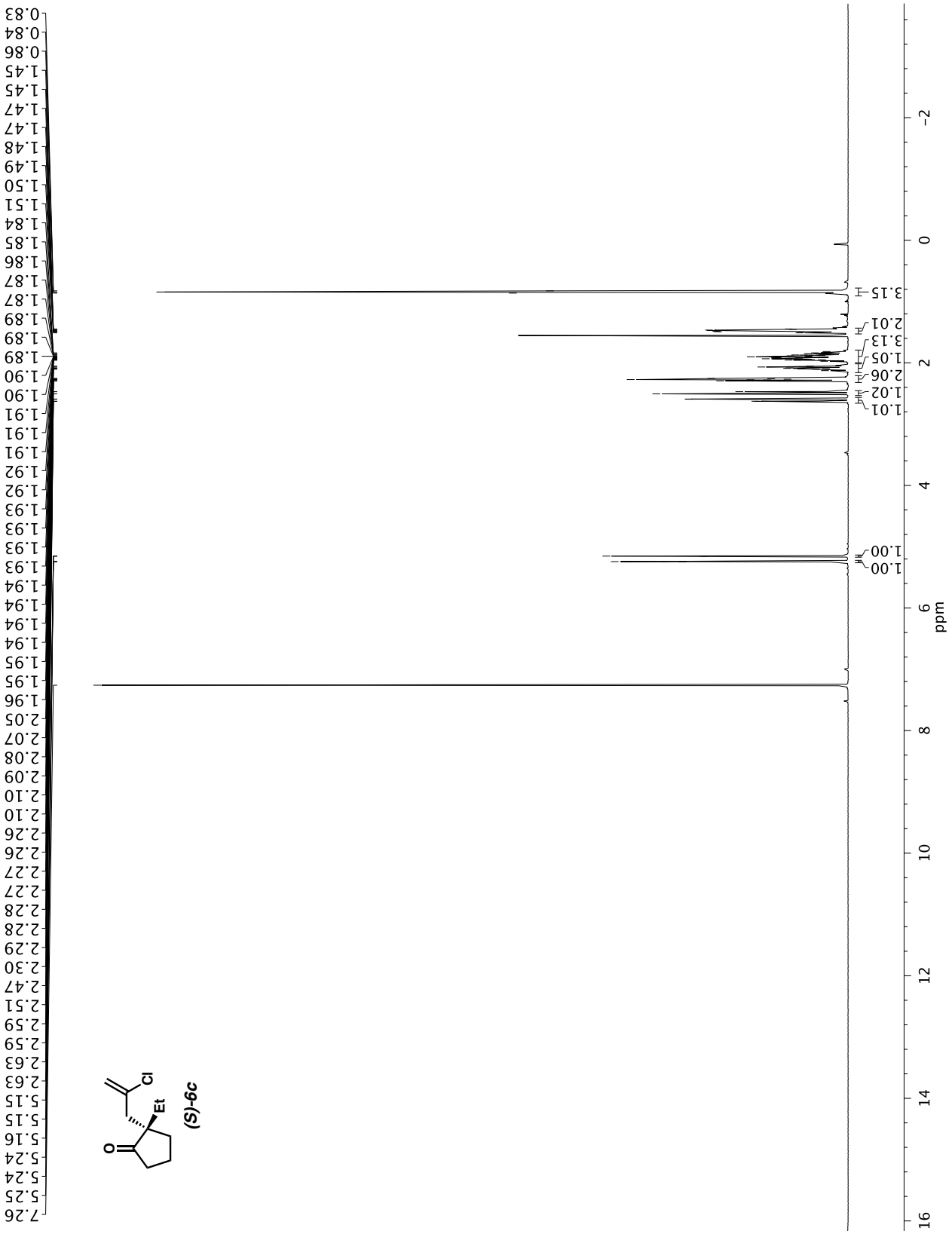
^{1}H NMR (400 MHz, $CDCl_3$) of compound **(*S*)-6b**.



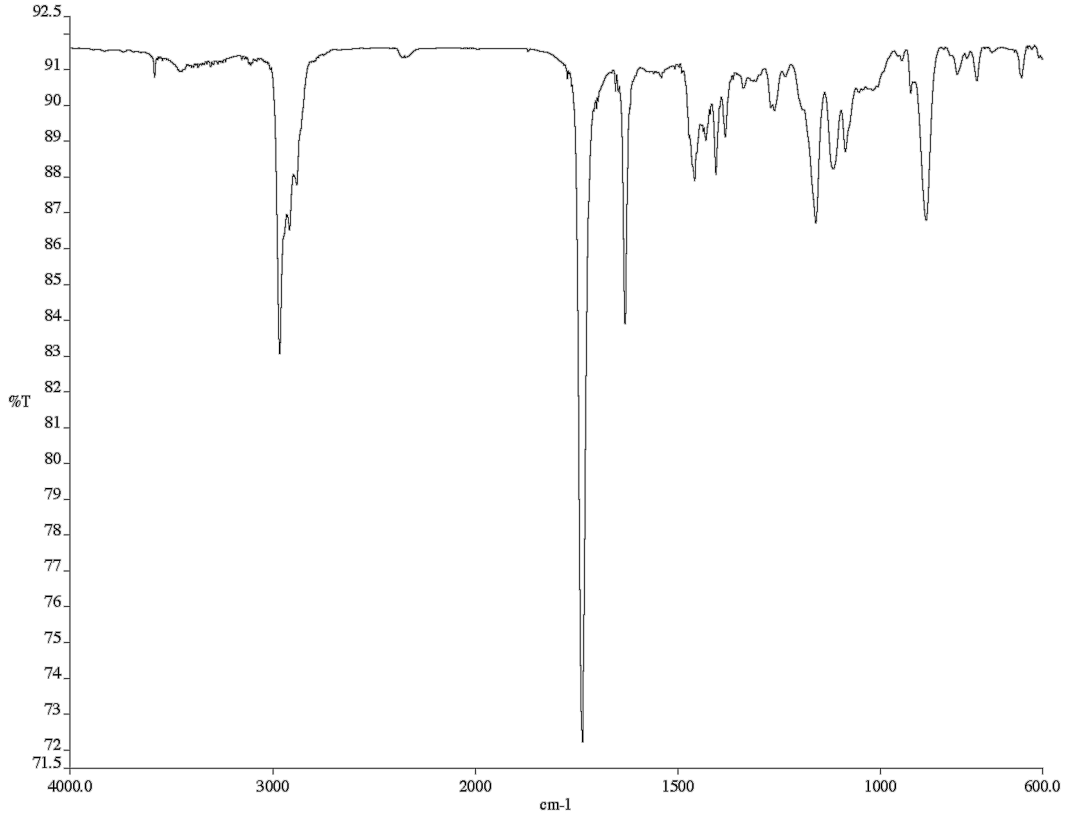
Infrared spectrum (Thin Film, NaCl) of compound **(*S*)-6b**.



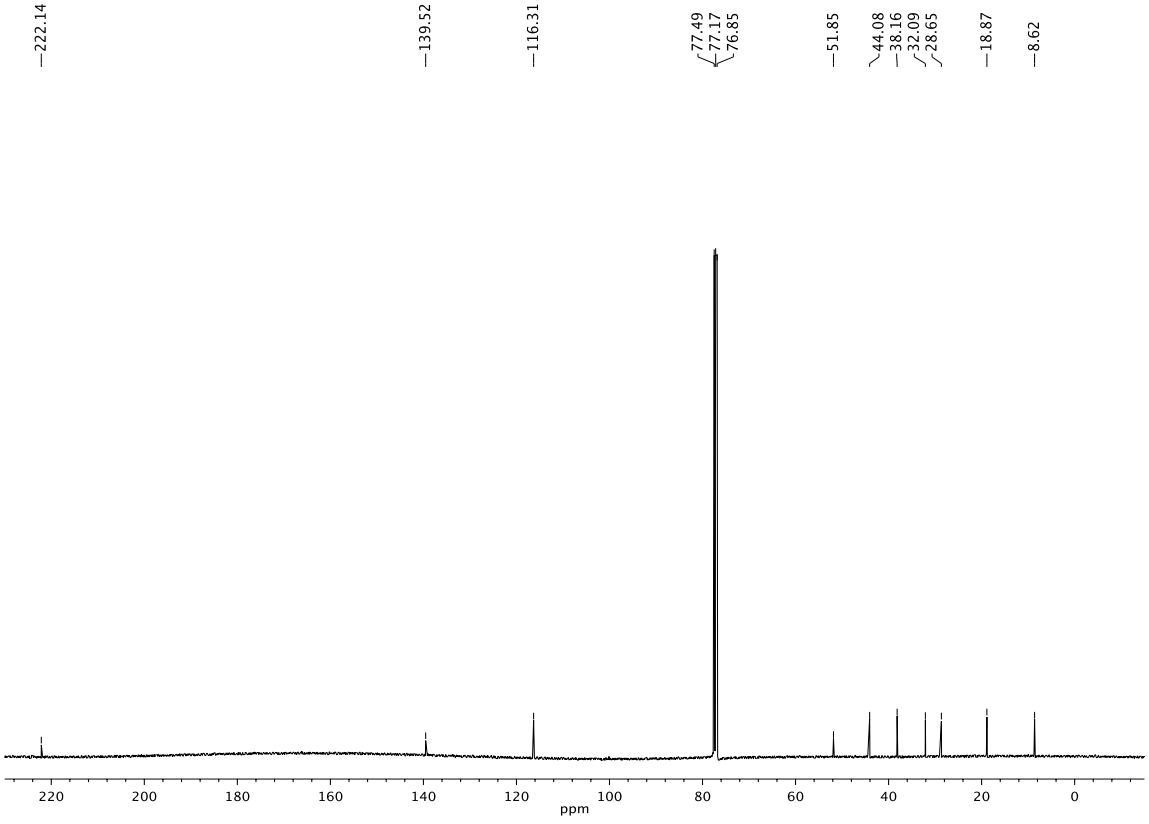
^{13}C NMR (101 MHz, $CDCl_3$) of compound **(*S*)-6b**.



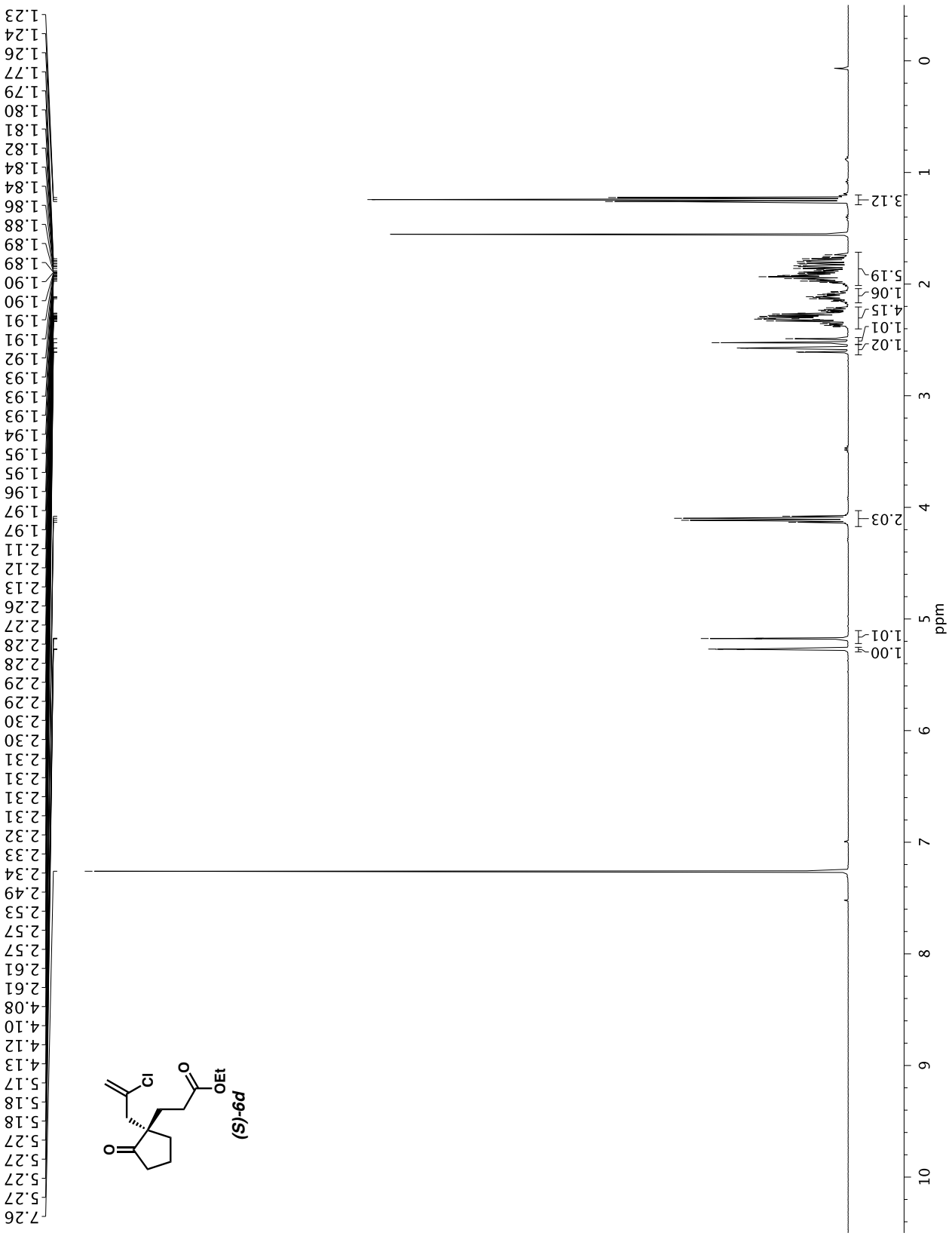
^{1}H NMR (400 MHz, $CDCl_3$) of compound **(*S*)-6c**.



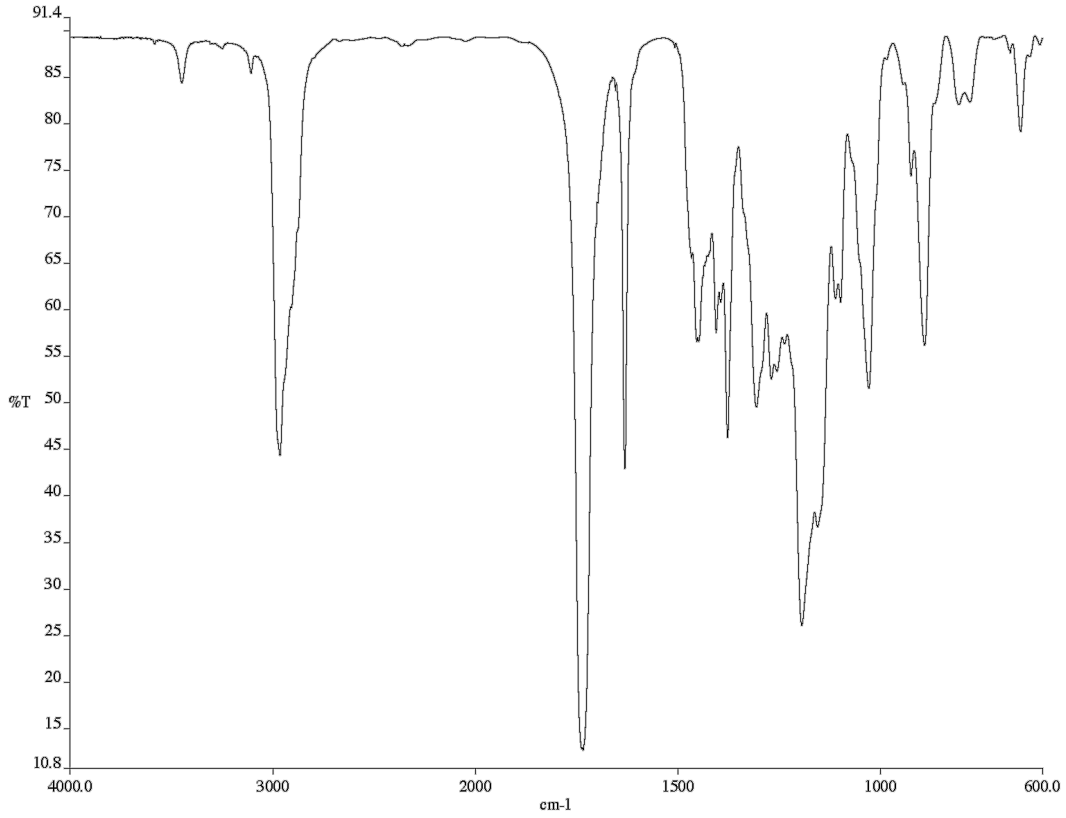
Infrared spectrum (Thin Film, NaCl) of compound **(*S*)-6c**.



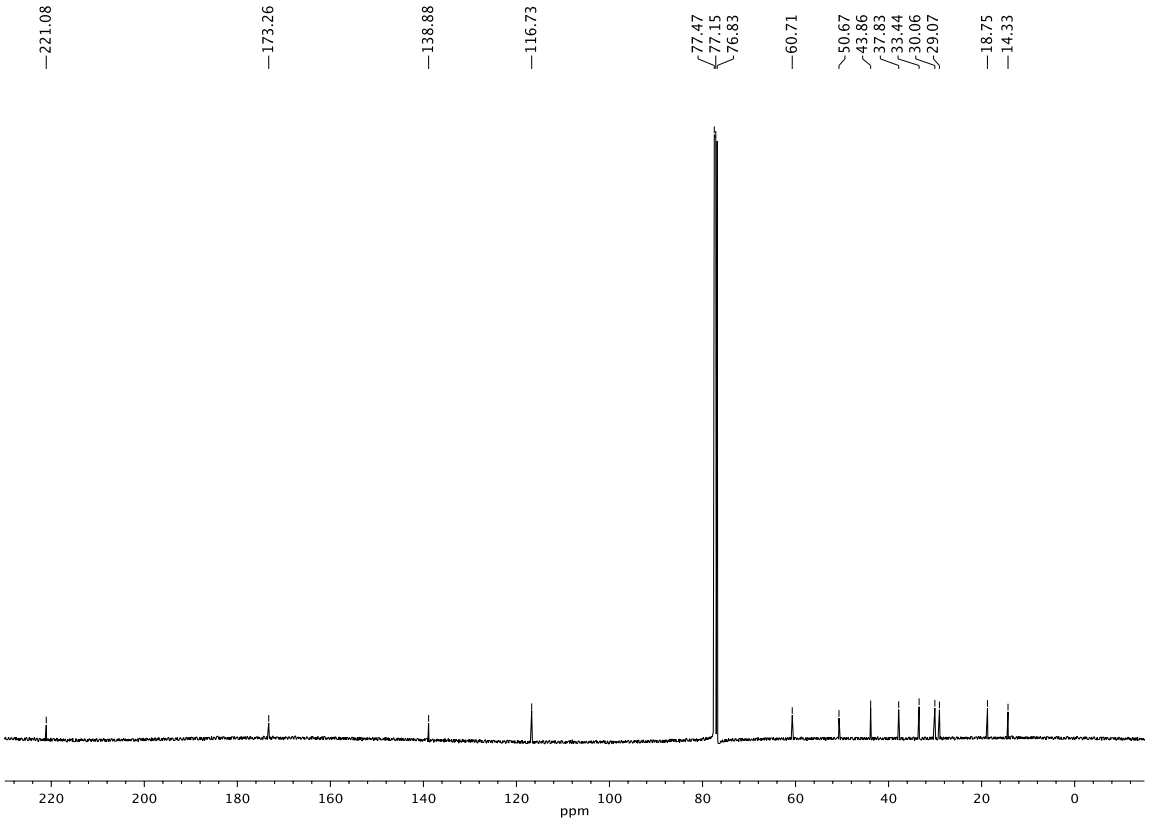
^{13}C NMR (101 MHz, $CDCl_3$) of compound **(*S*)-6c**.



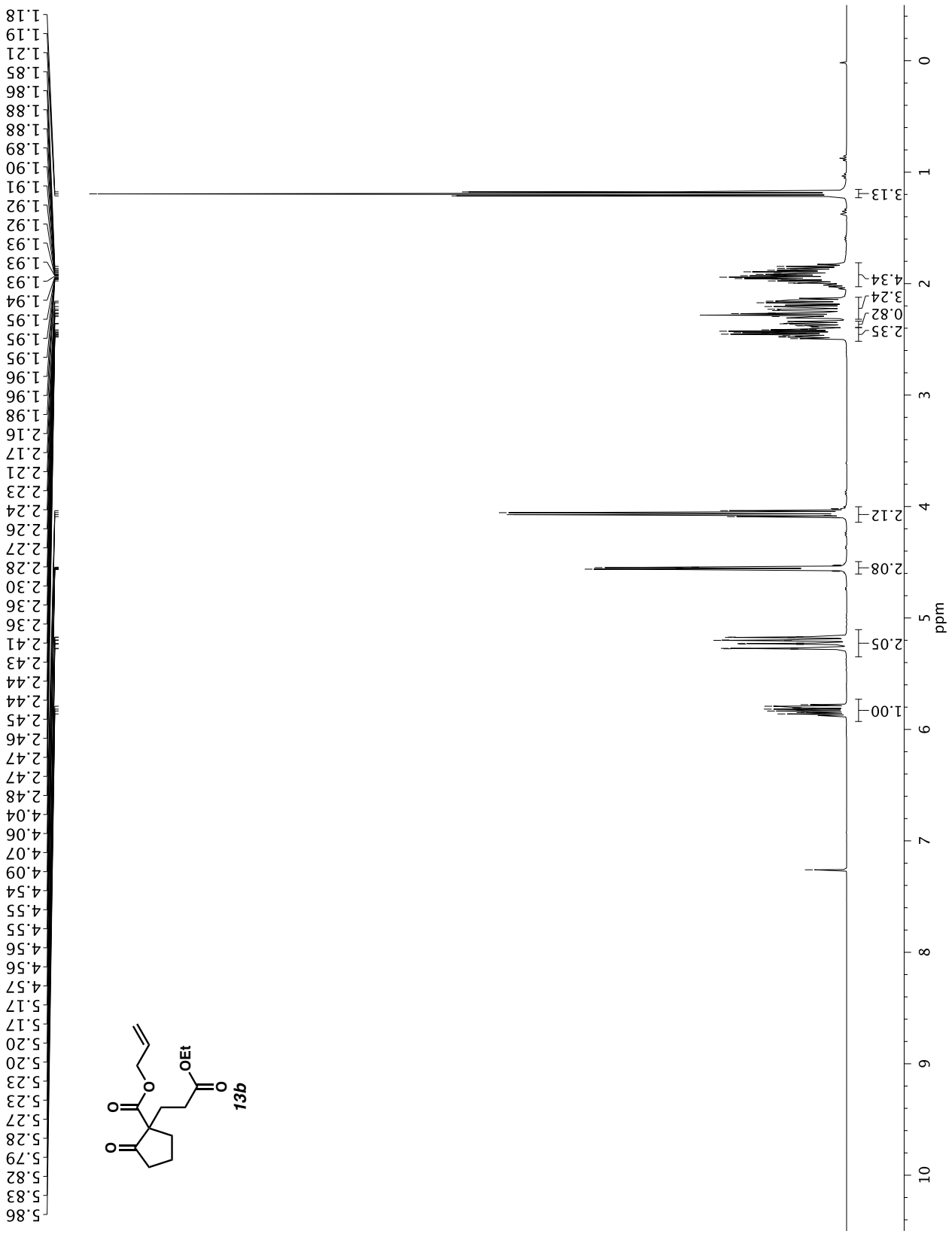
^{1}H NMR (400 MHz, $CDCl_3$) of compound **(*S*)-6d**.



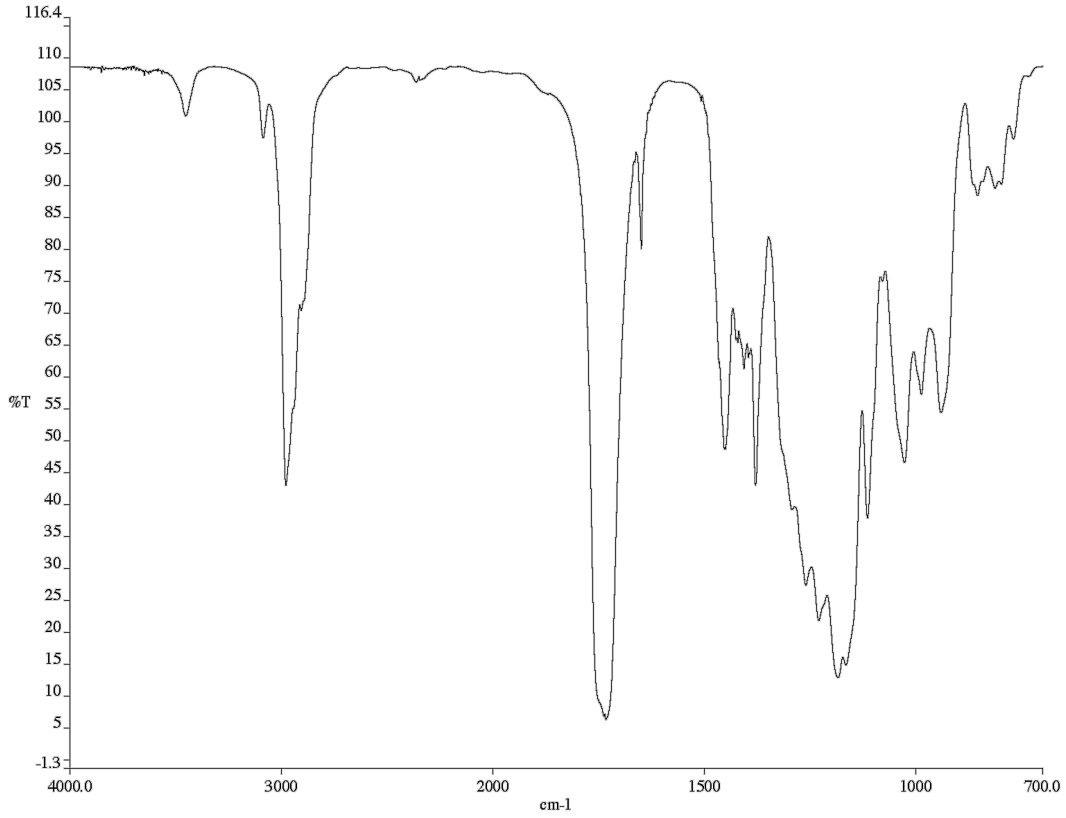
Infrared spectrum (Thin Film, NaCl) of compound **(*S*)-6d**.



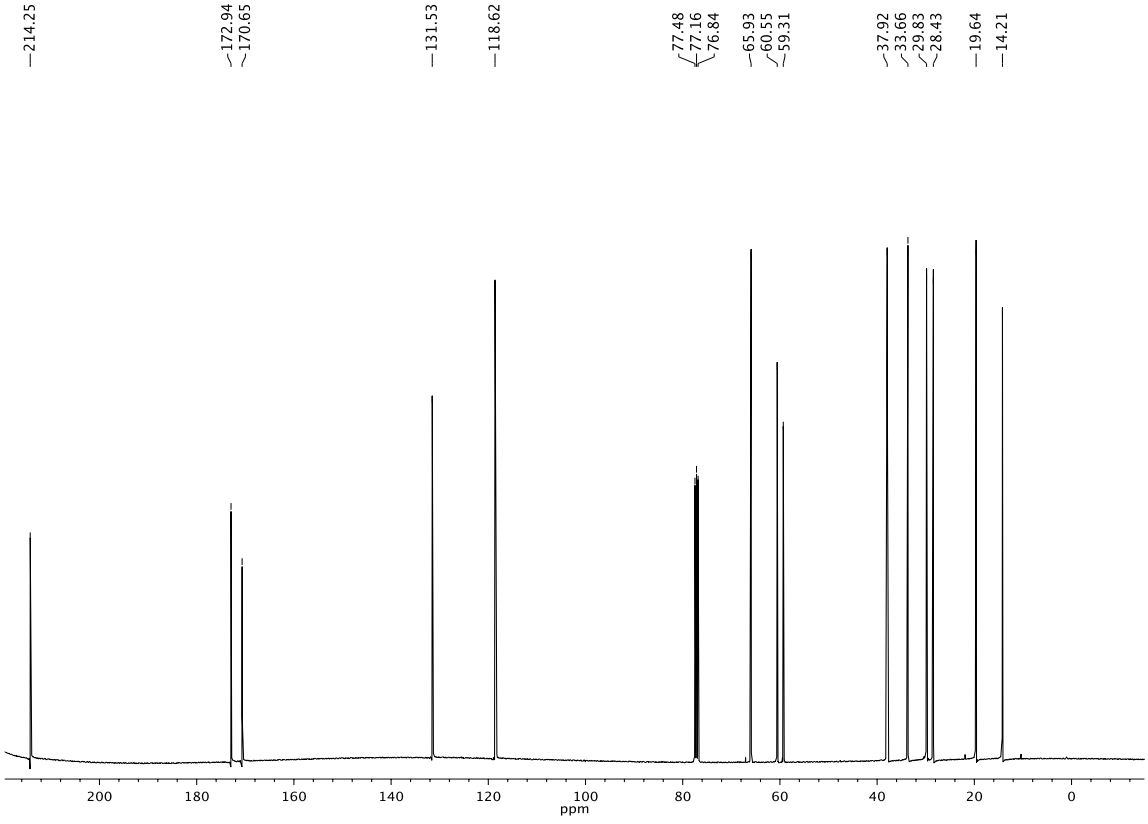
^{13}C NMR (101 MHz, $CDCl_3$) of compound **(*S*)-6d**.



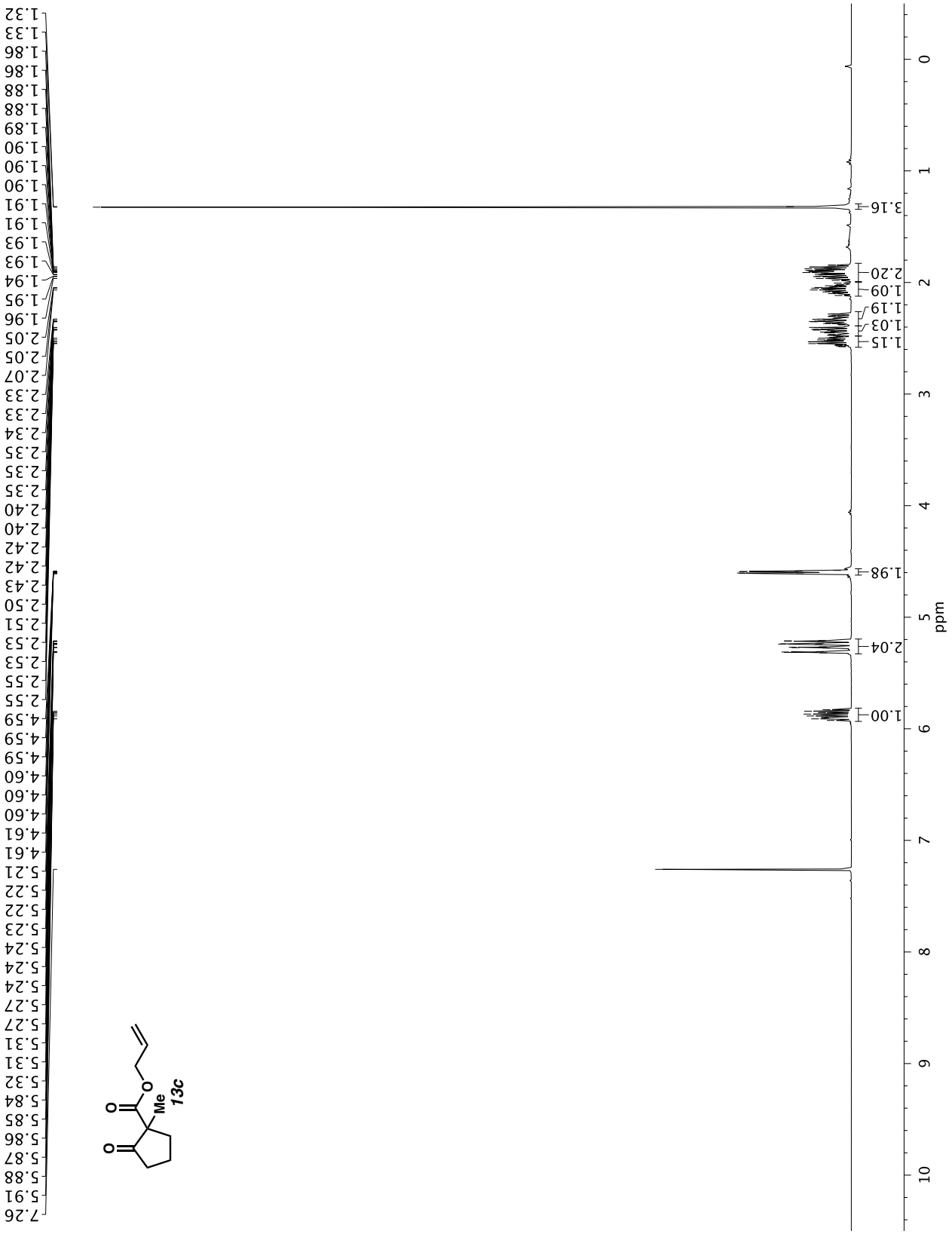
^{1}H NMR (400 MHz, $CDCl_3$) of compound **13b**.



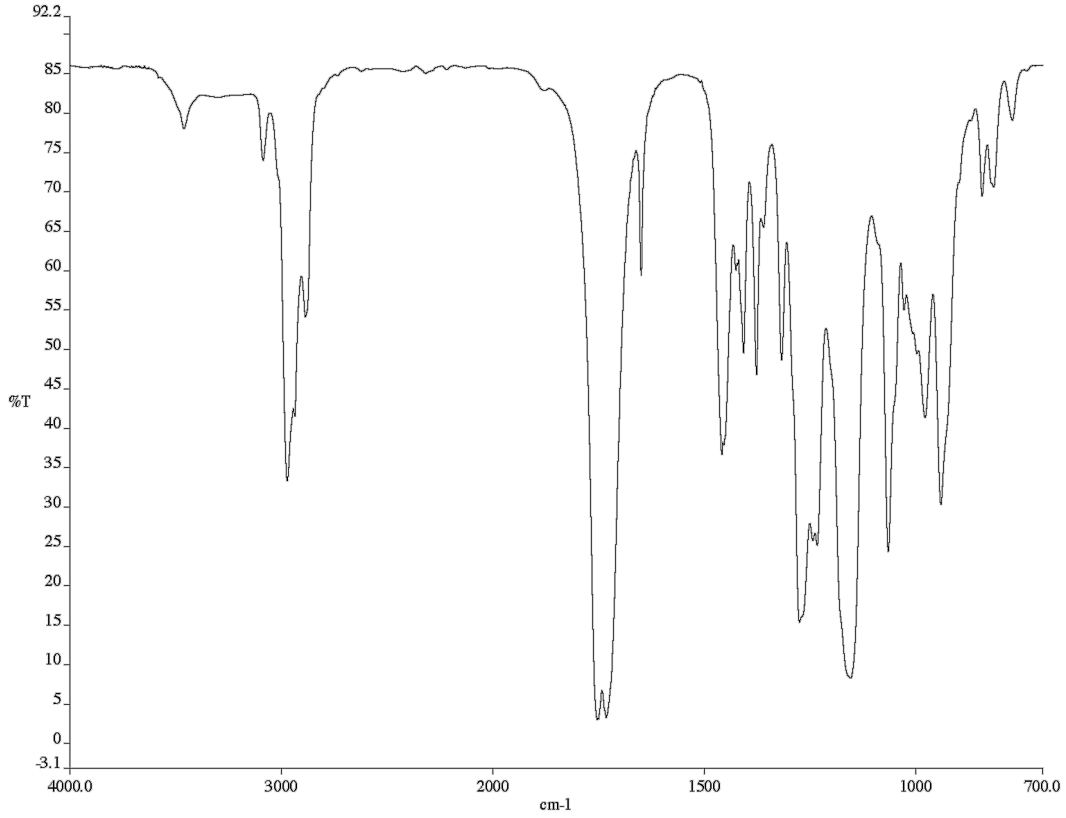
Infrared spectrum (Thin Film, NaCl) of compound **13b**.



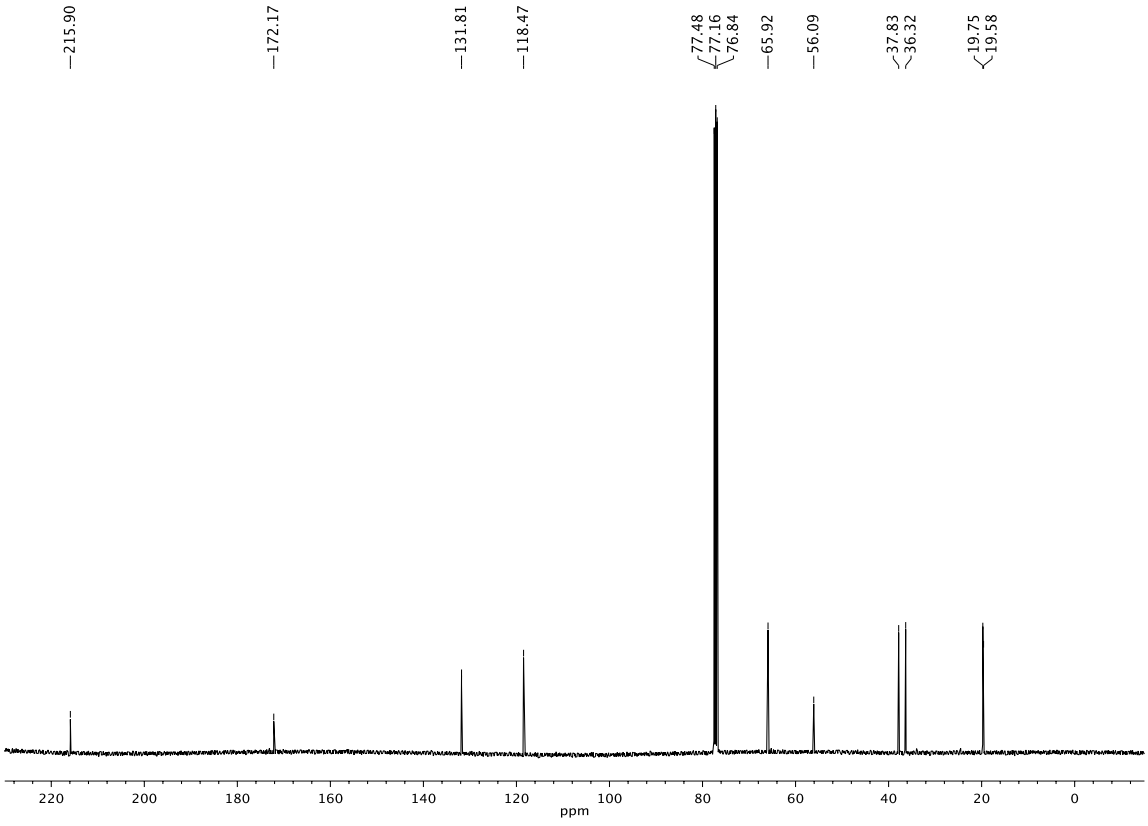
^{13}C NMR (101 MHz, $CDCl_3$) of compound **13b**.



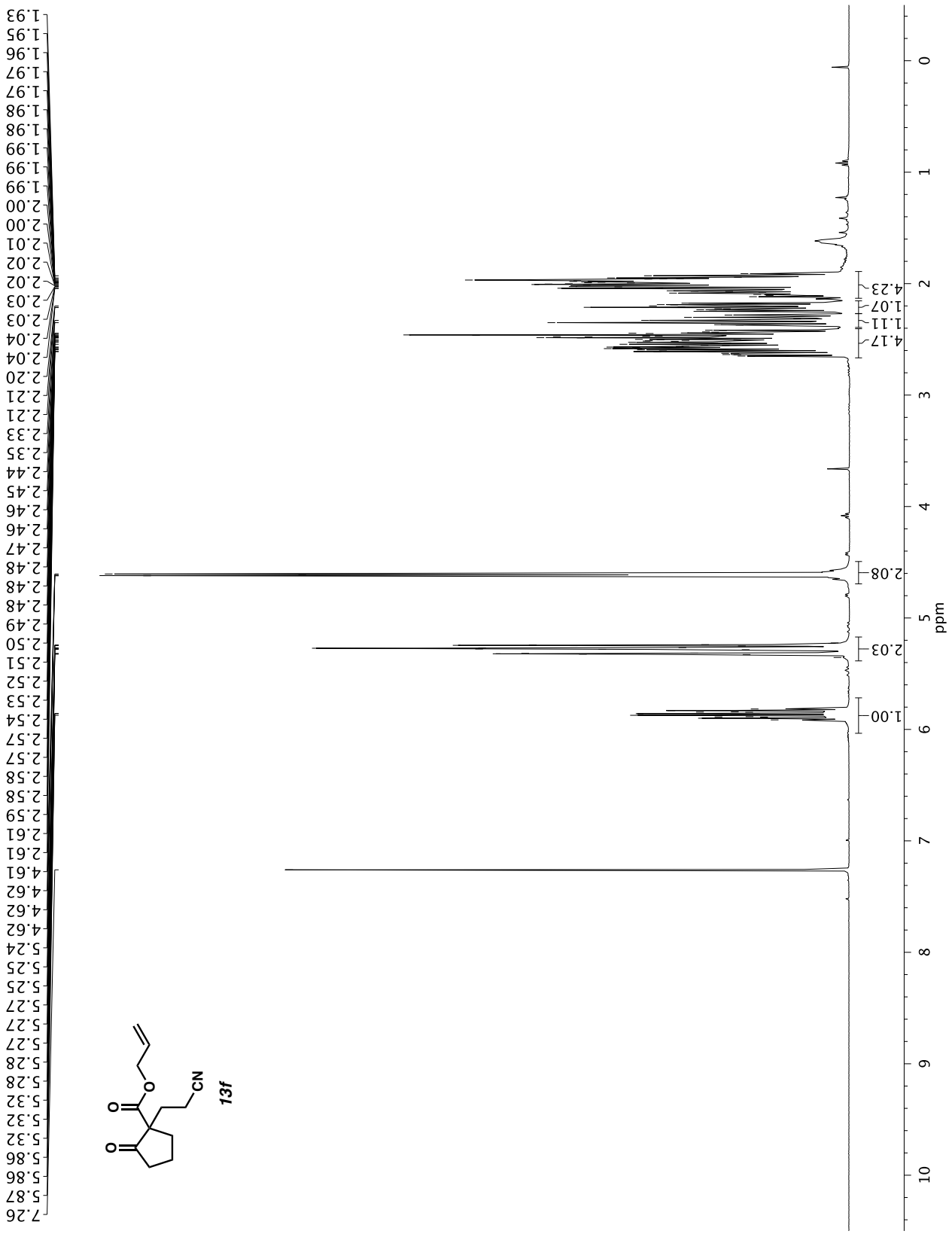
^{1}H NMR (400 MHz, $CDCl_3$) of compound **13c**.



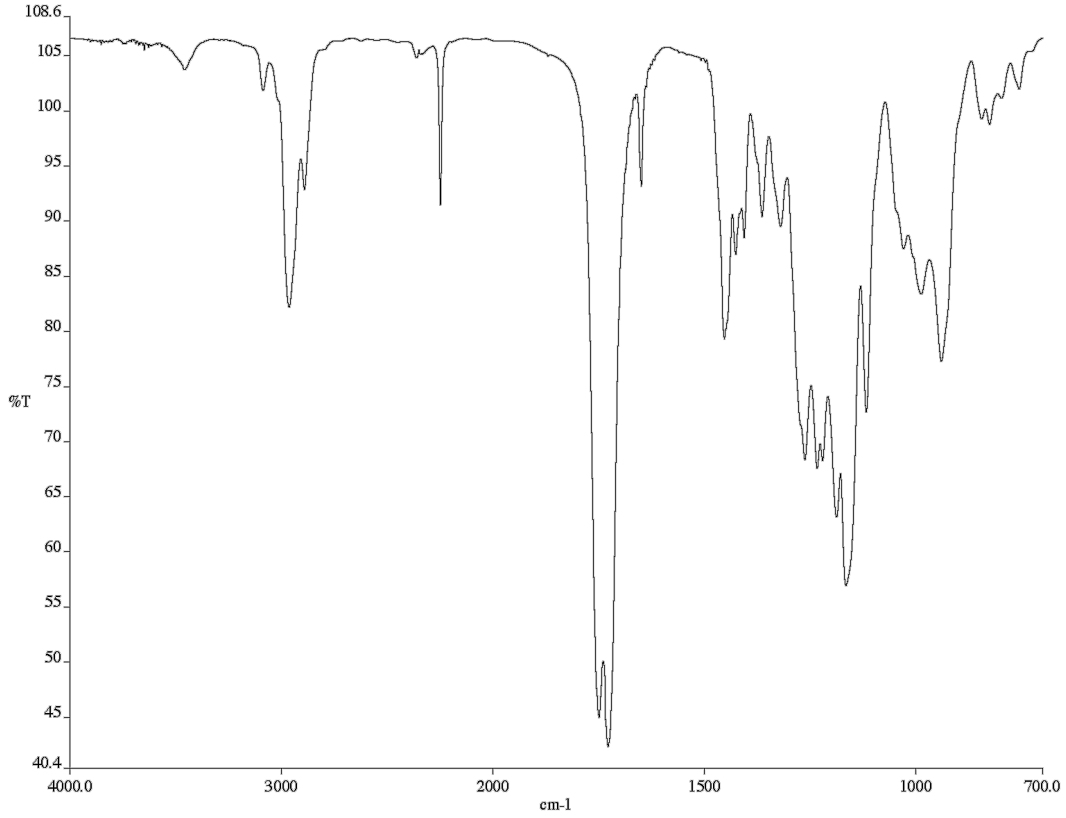
Infrared spectrum (Thin Film, NaCl) of compound **13c**.



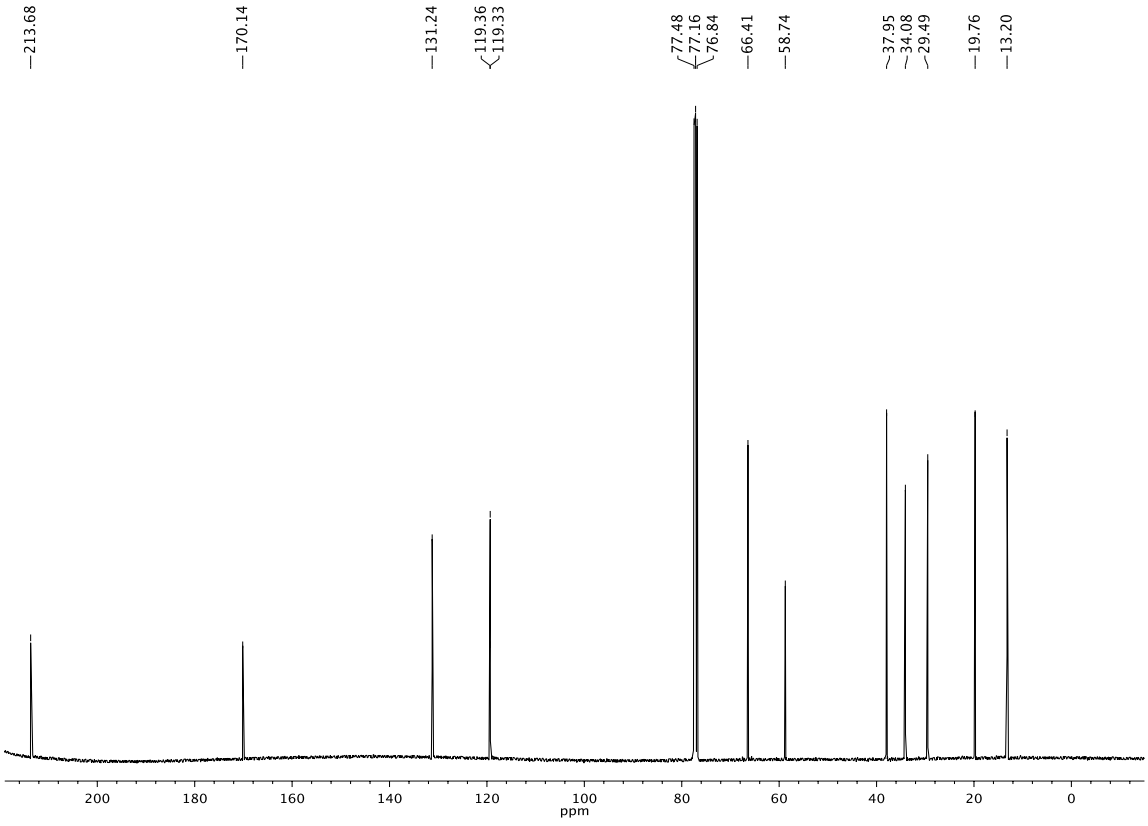
^{13}C NMR (101 MHz, $CDCl_3$) of compound **13c**.



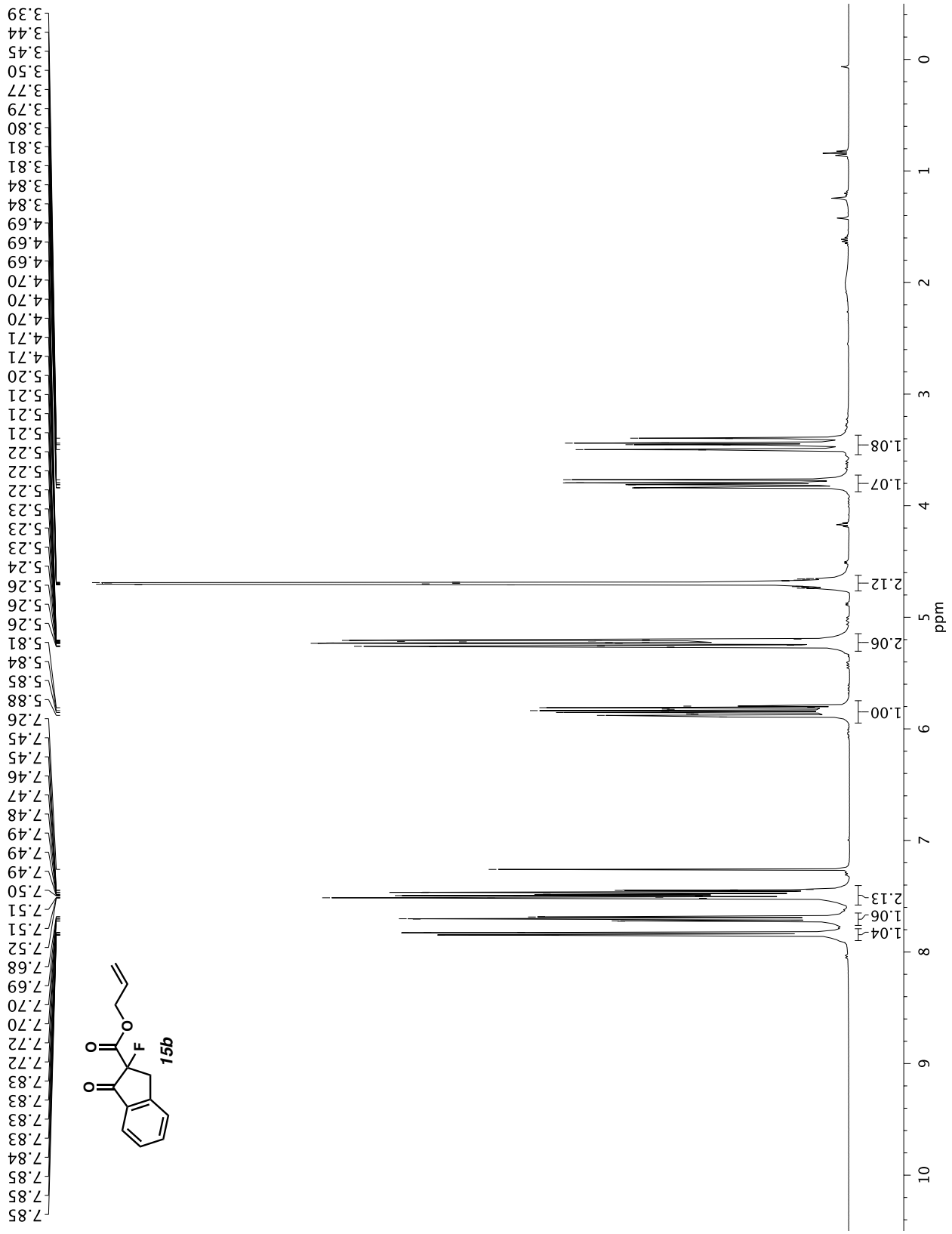
^{1}H NMR (400 MHz, $CDCl_3$) of compound **13f**.



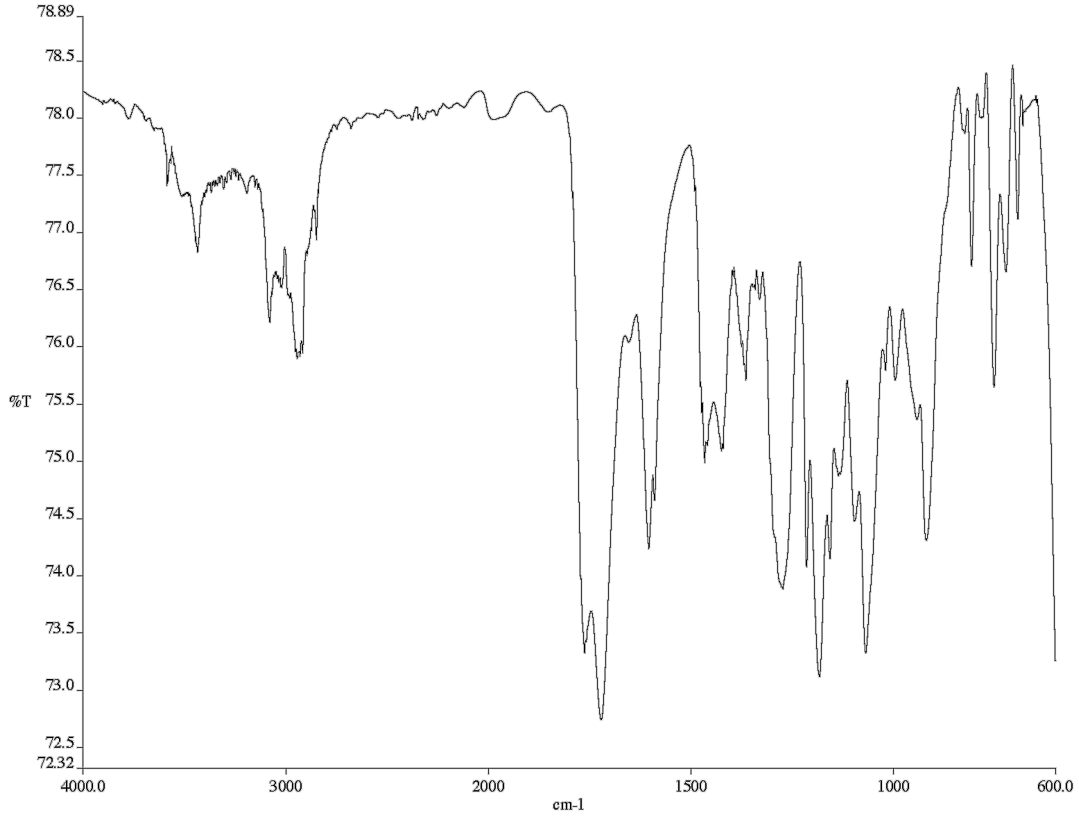
Infrared spectrum (Thin Film, NaCl) of compound **13f**.



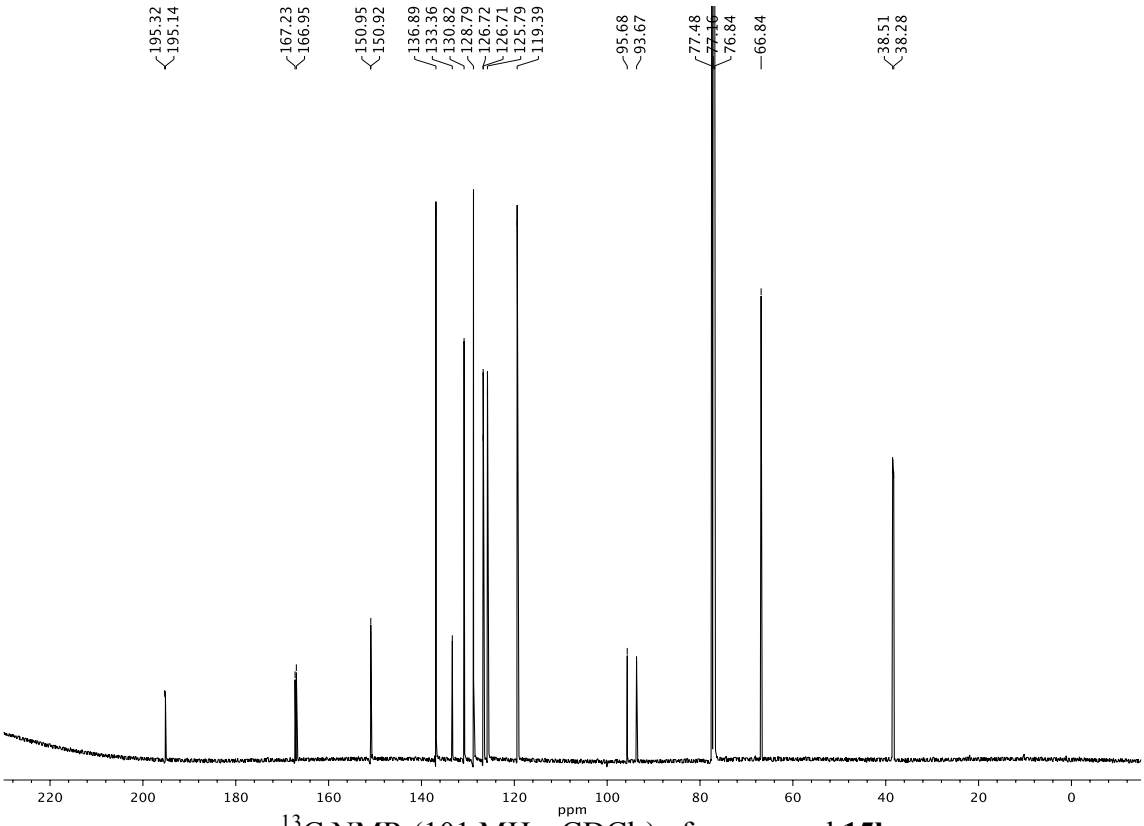
^{13}C NMR (101 MHz, $CDCl_3$) of compound **13f**.



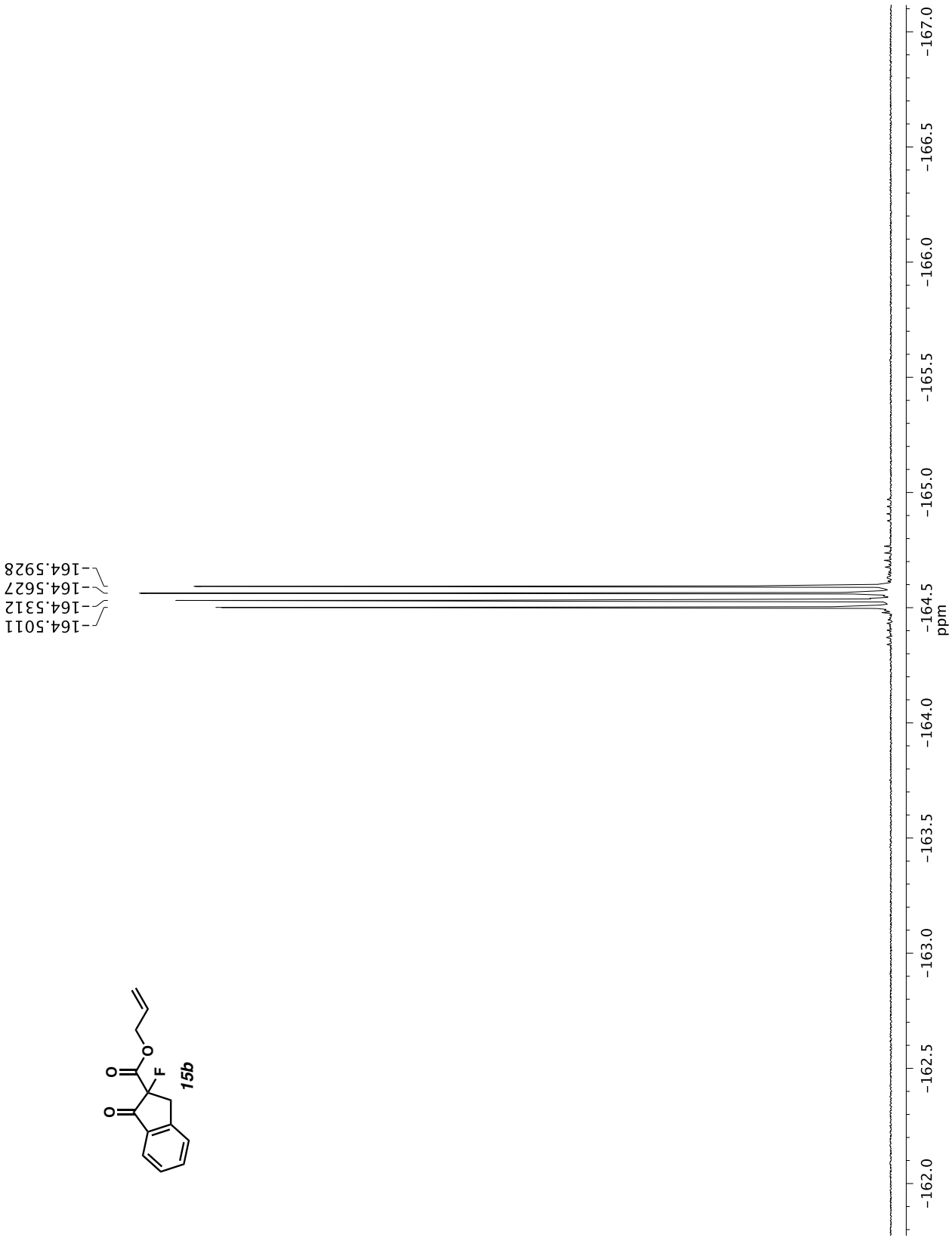
^{1}H NMR (400 MHz, $CDCl_3$) of compound **15b**.



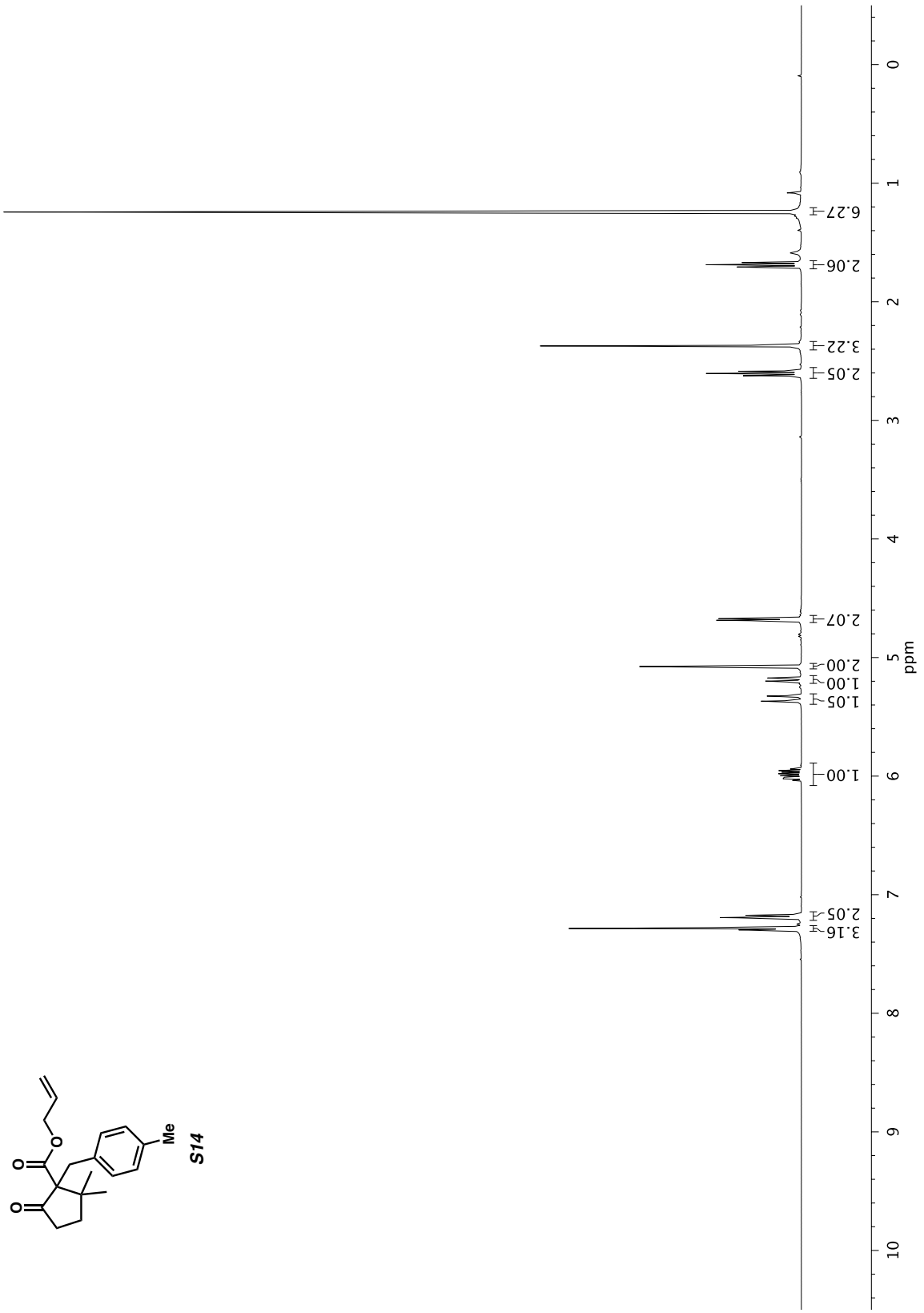
Infrared spectrum (Thin Film, NaCl) of compound **15b**.



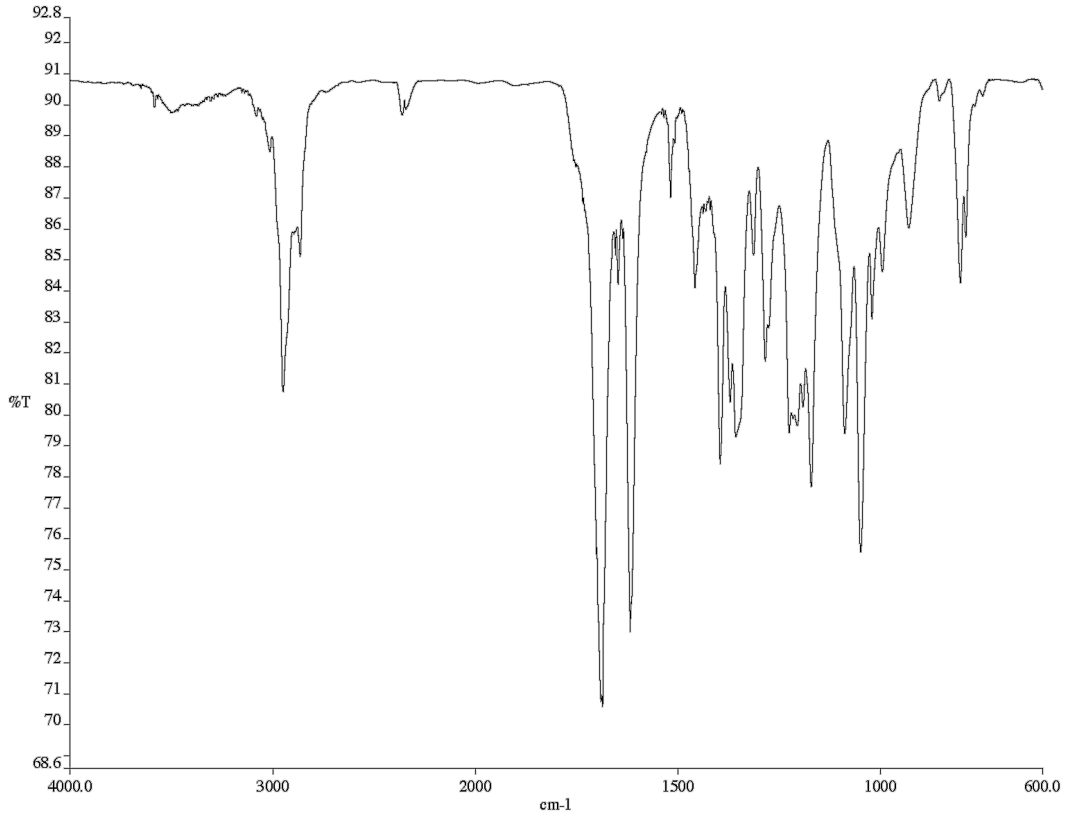
^{13}C NMR (101 MHz, $CDCl_3$) of compound **15b**.



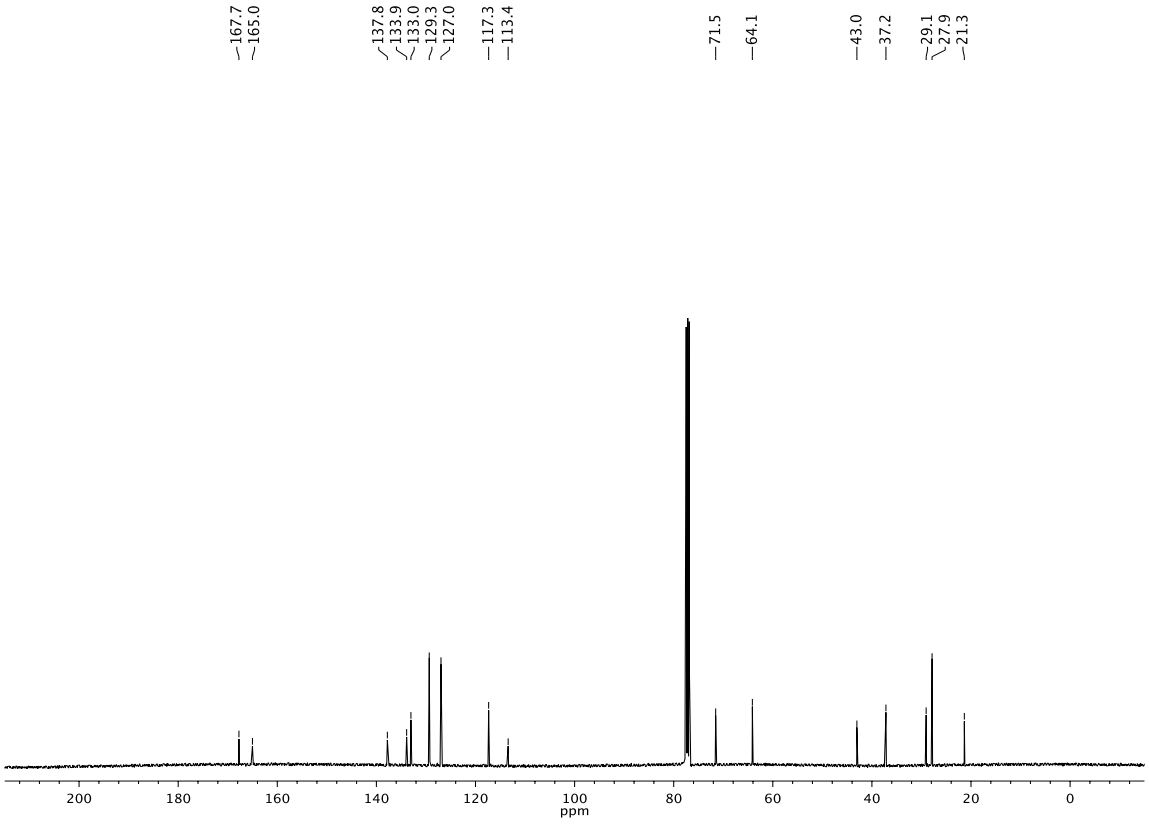
^{19}F NMR (470 MHz, $CDCl_3$) of compound **15b**.



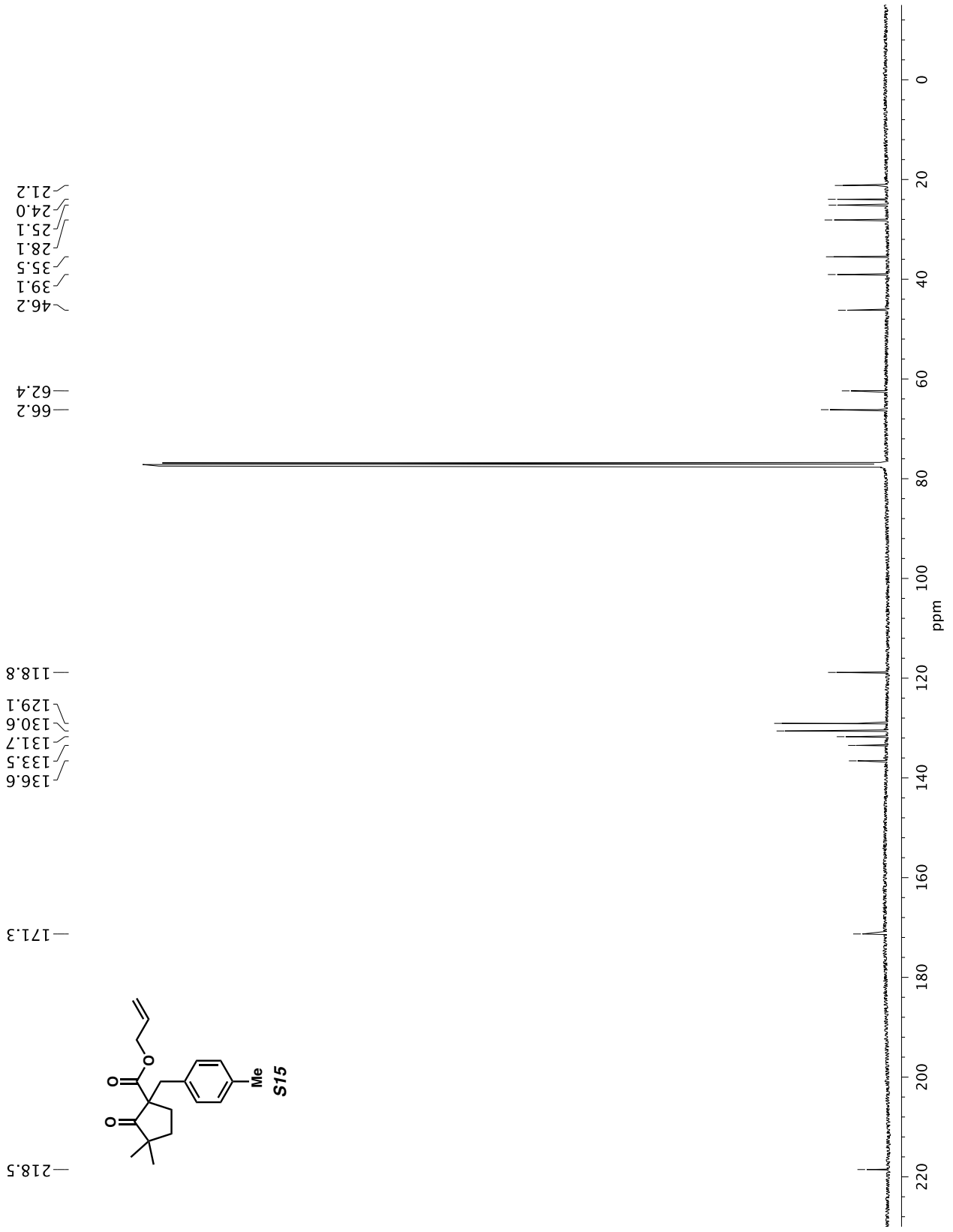
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S14**.



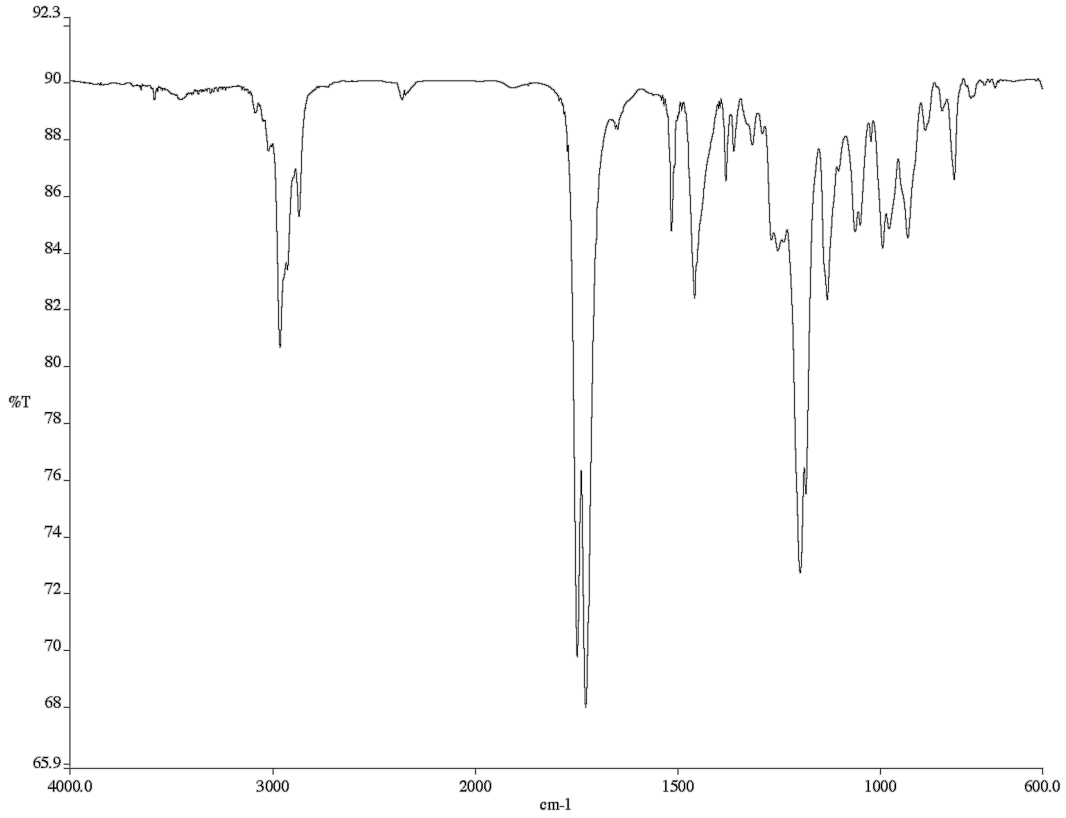
Infrared spectrum (Thin Film, NaCl) of compound **S14**.



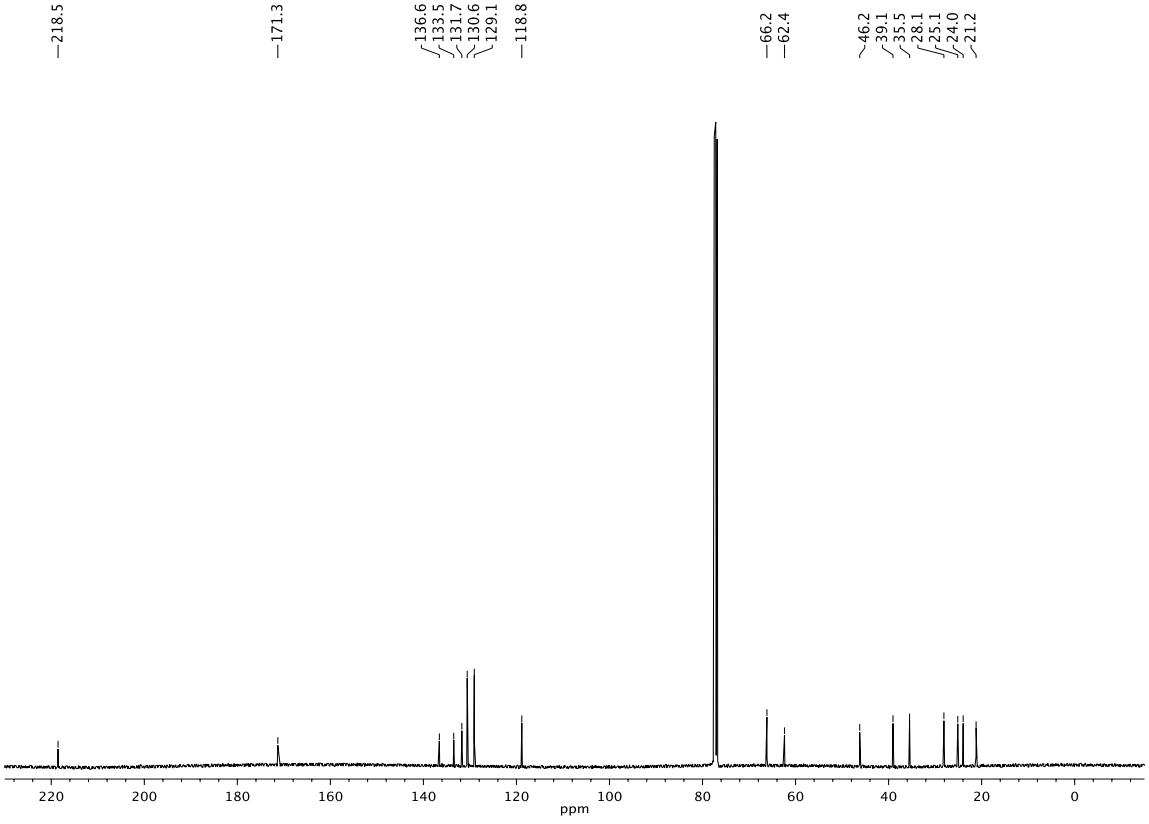
^{13}C NMR (101 MHz, $CDCl_3$) of compound **S14**.



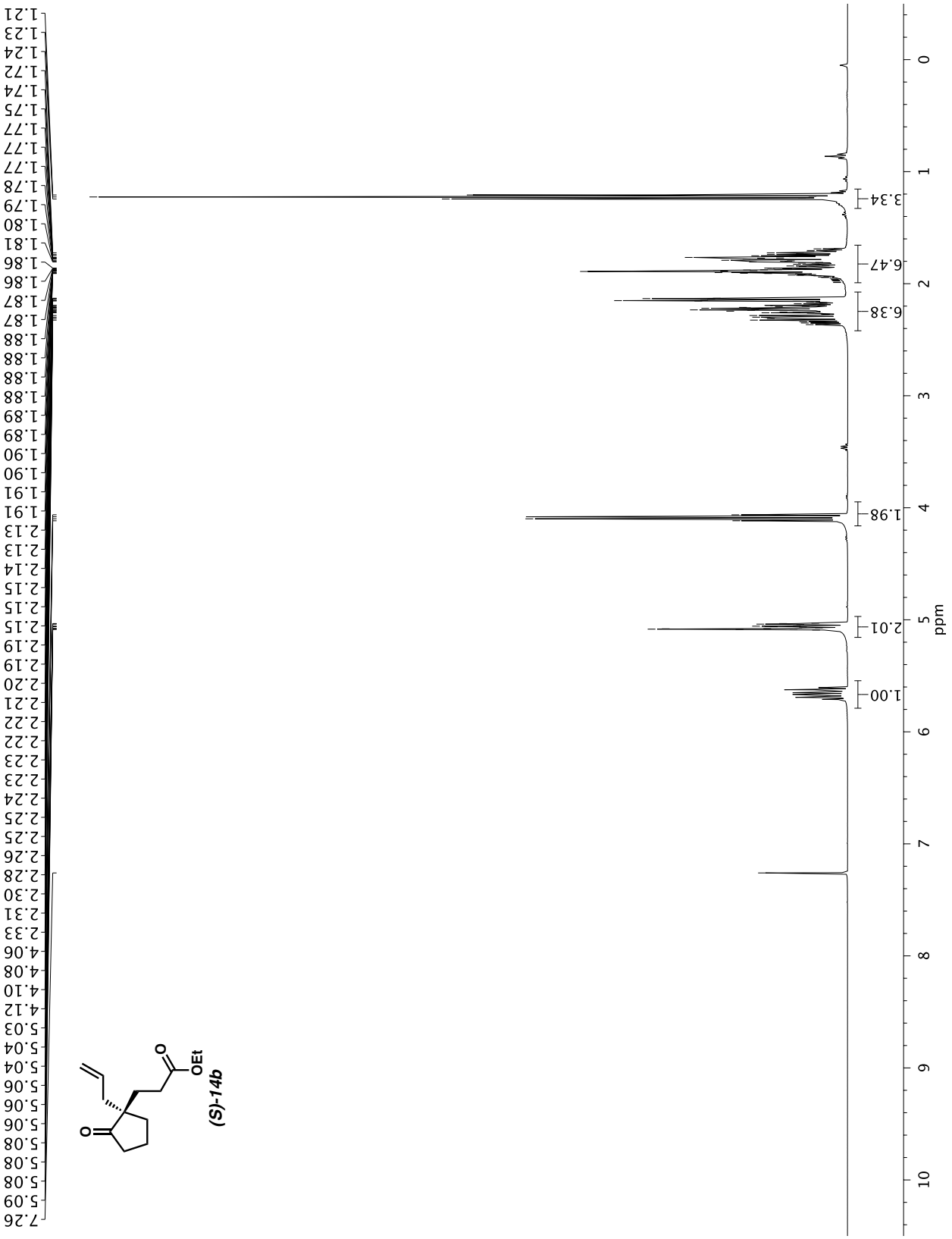
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S15**.



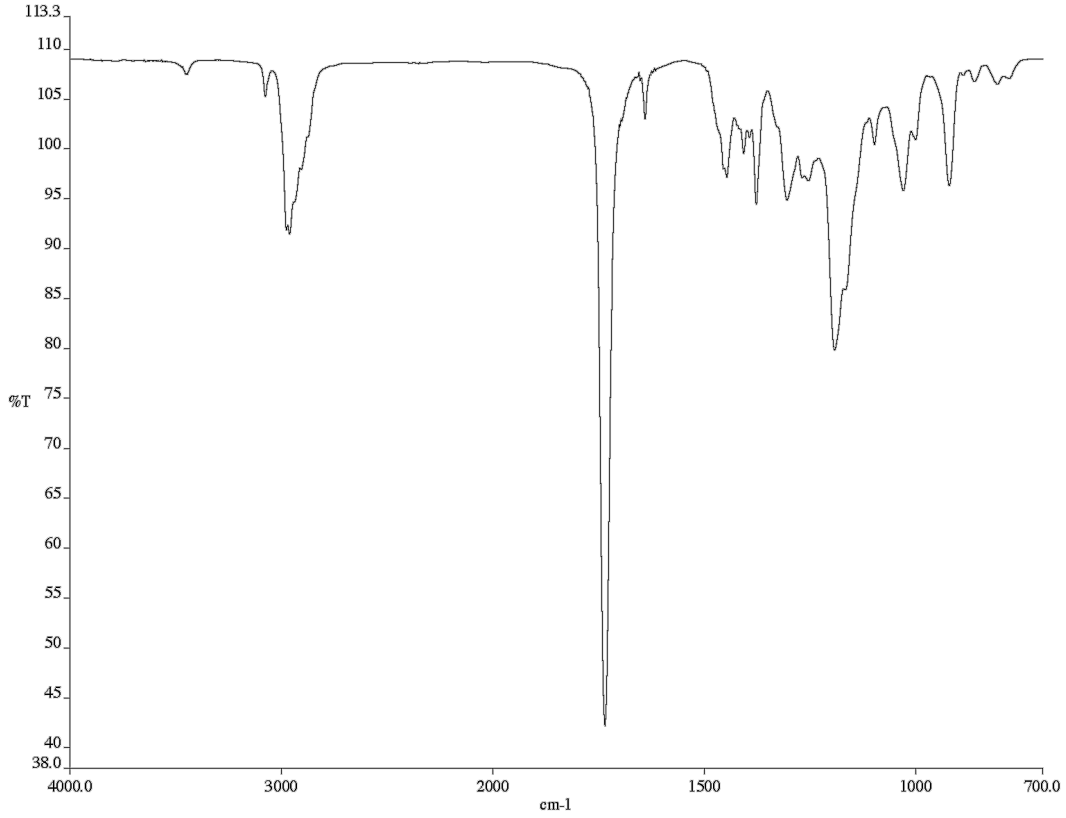
Infrared spectrum (Thin Film, NaCl) of compound **S15**.



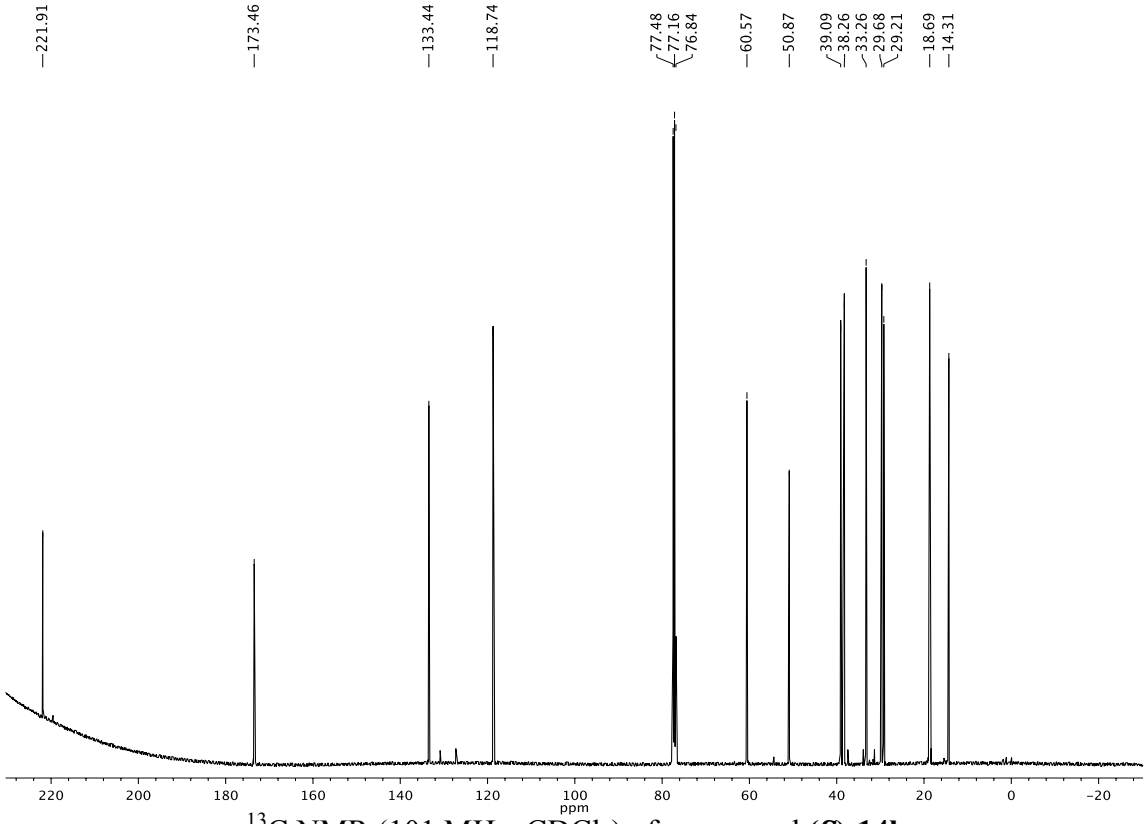
^{13}C NMR (101 MHz, $CDCl_3$) of compound **S15**.



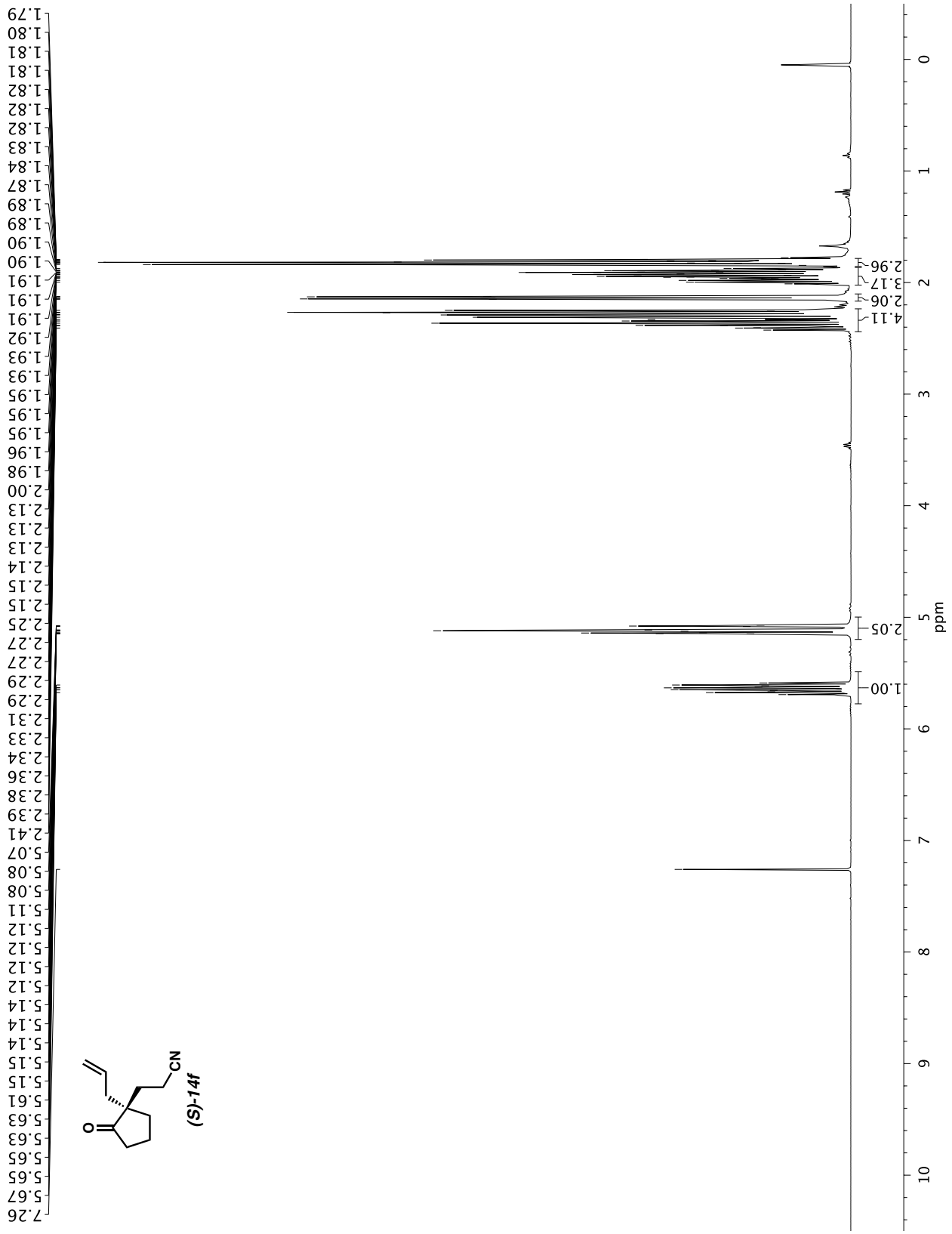
^{1}H NMR (400 MHz, $CDCl_3$) of compound **(*S*)-14b**.



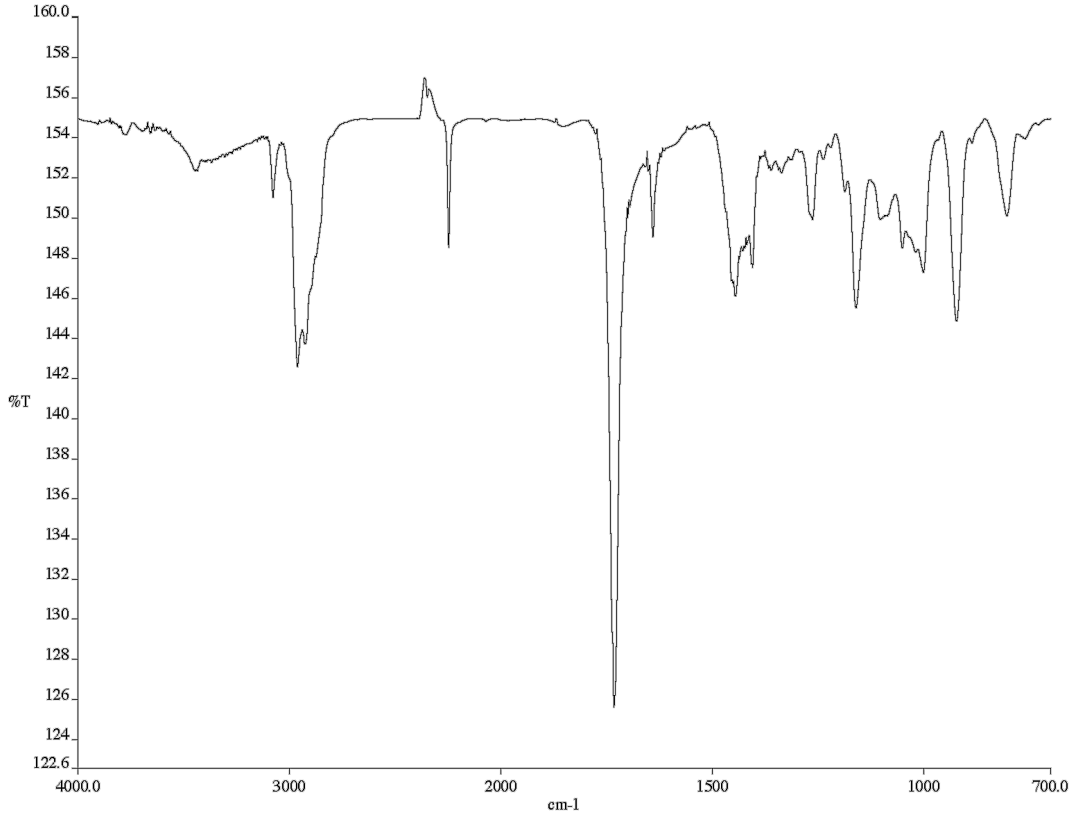
Infrared spectrum (Thin Film, NaCl) of compound **(*S*)-14b**.



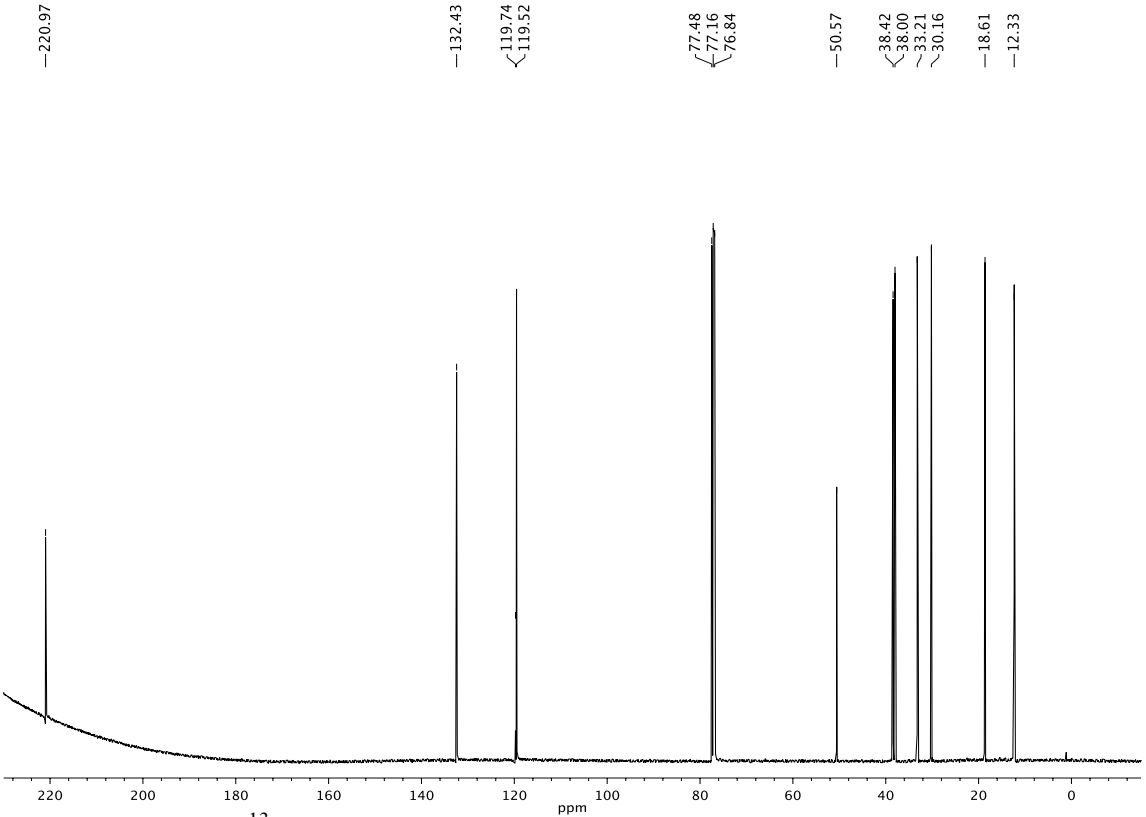
^{13}C NMR (101 MHz, $CDCl_3$) of compound **(*S*)-14b**.



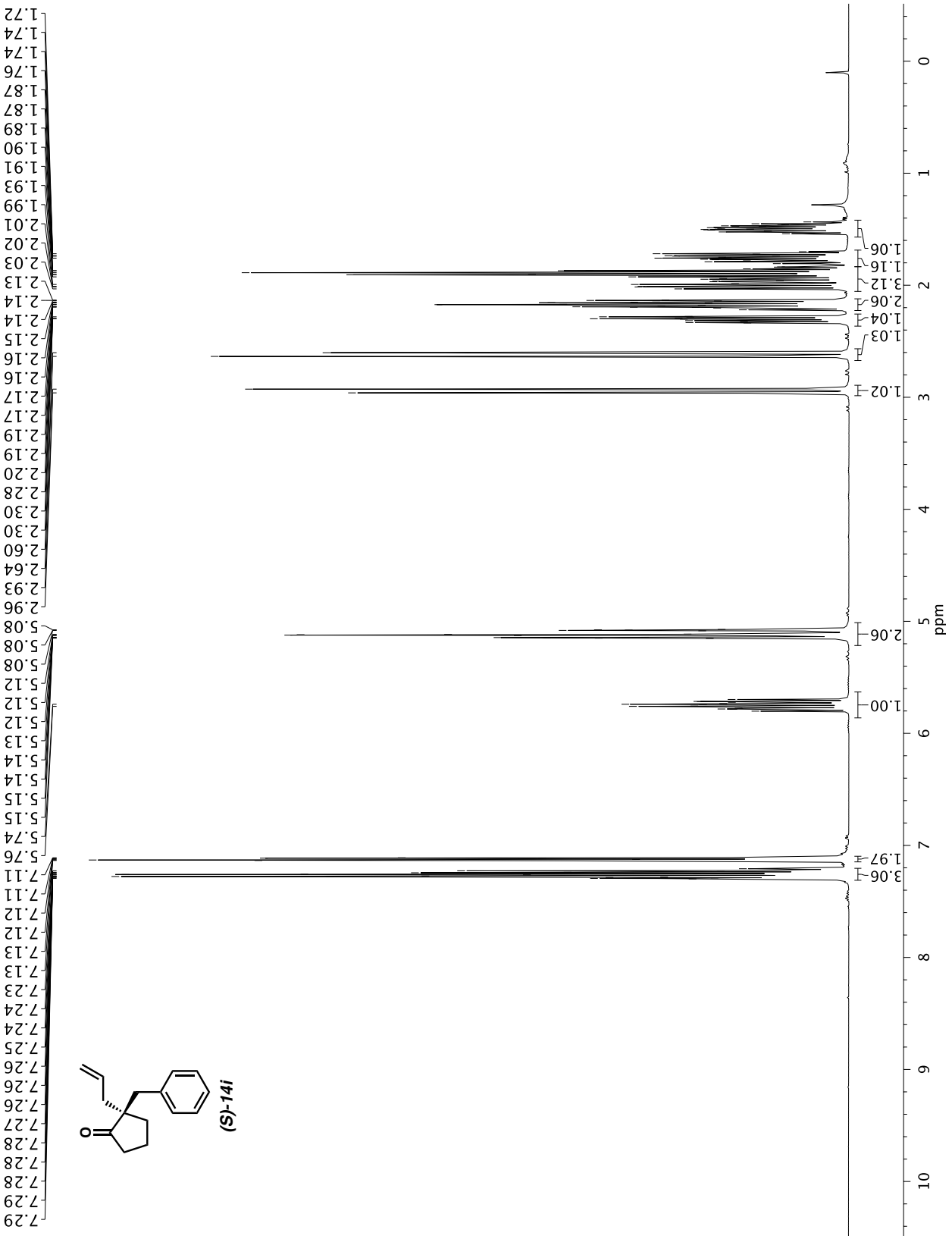
^{1}H NMR (400 MHz, $CDCl_3$) of compound **(*S*)-14f**.



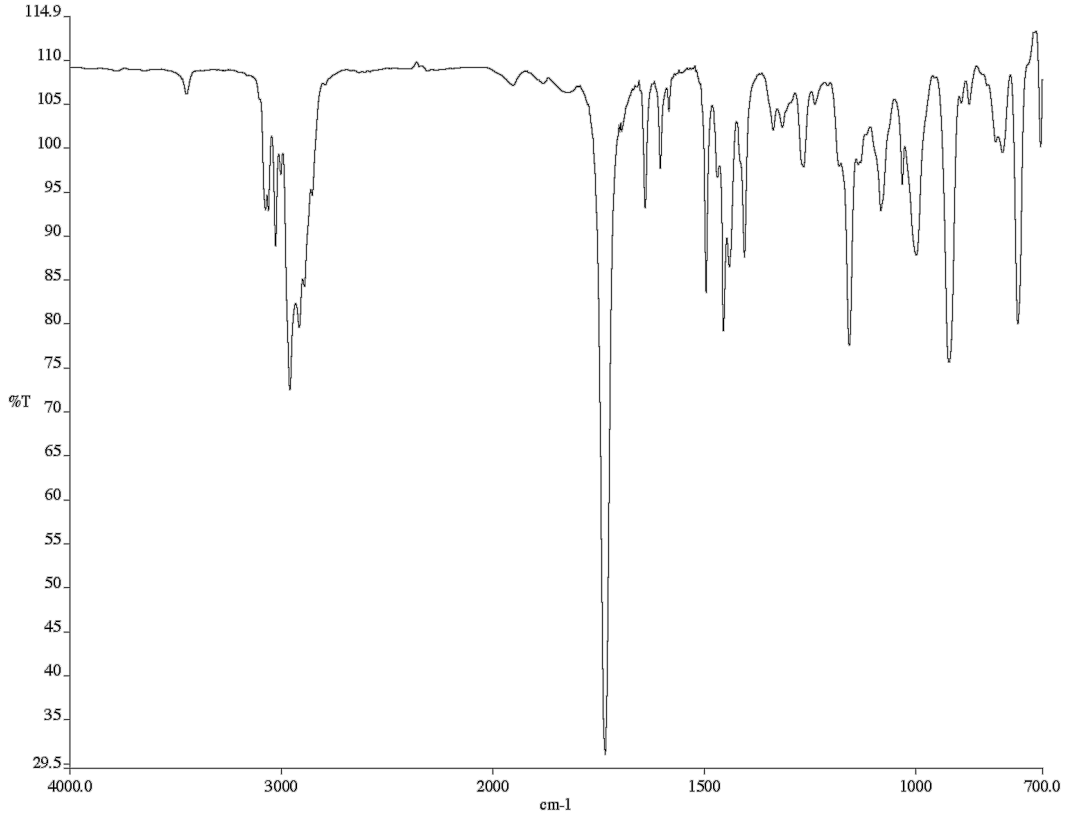
Infrared spectrum (Thin Film, NaCl) of compound **(*S*)-14f**.



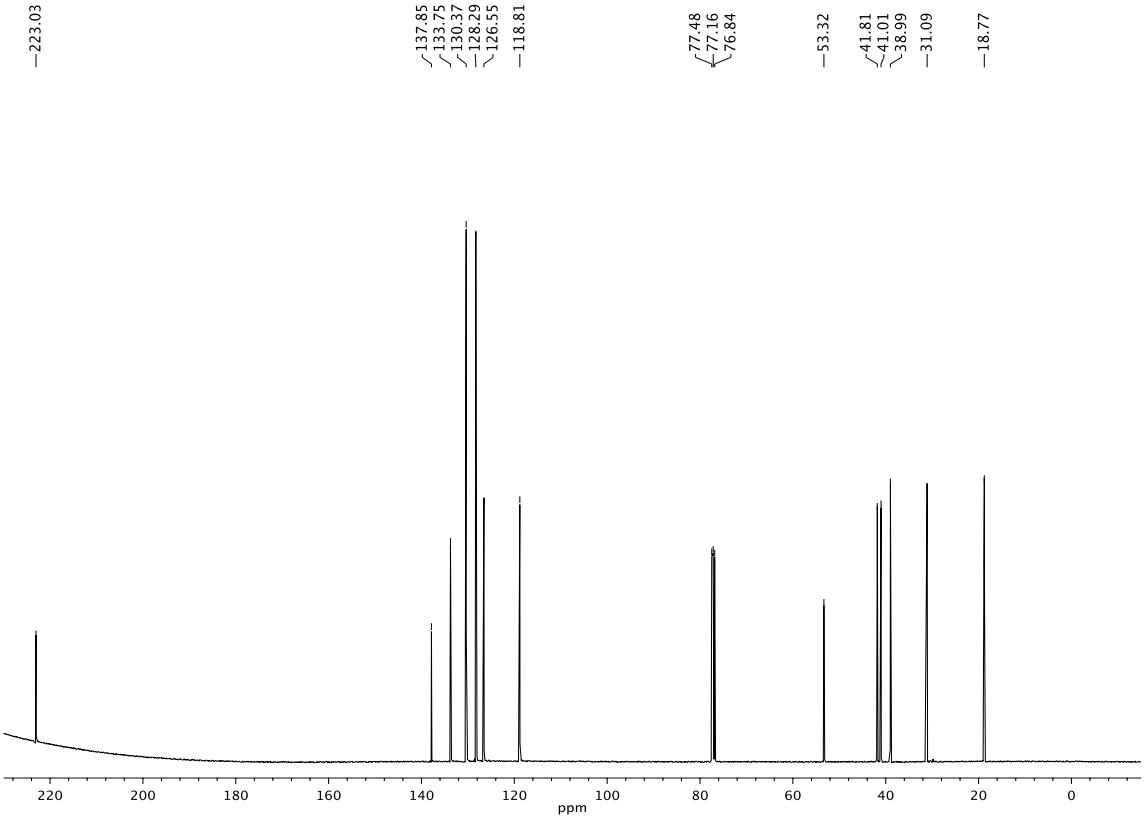
^{13}C NMR (101 MHz, $CDCl_3$) of compound **(*S*)-14f**.



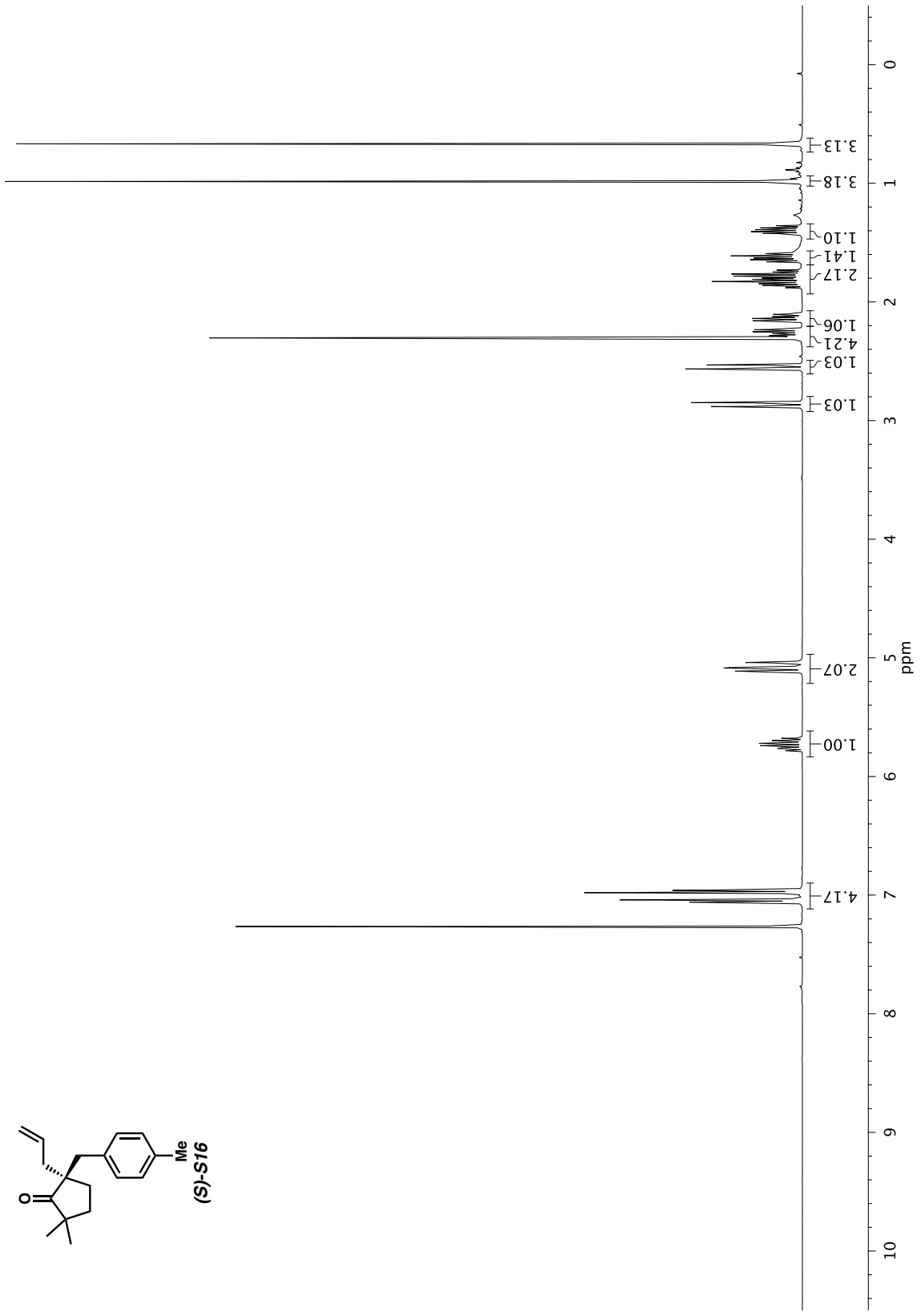
^{1}H NMR (400 MHz, $CDCl_3$) of compound **(*S*)-14i**.



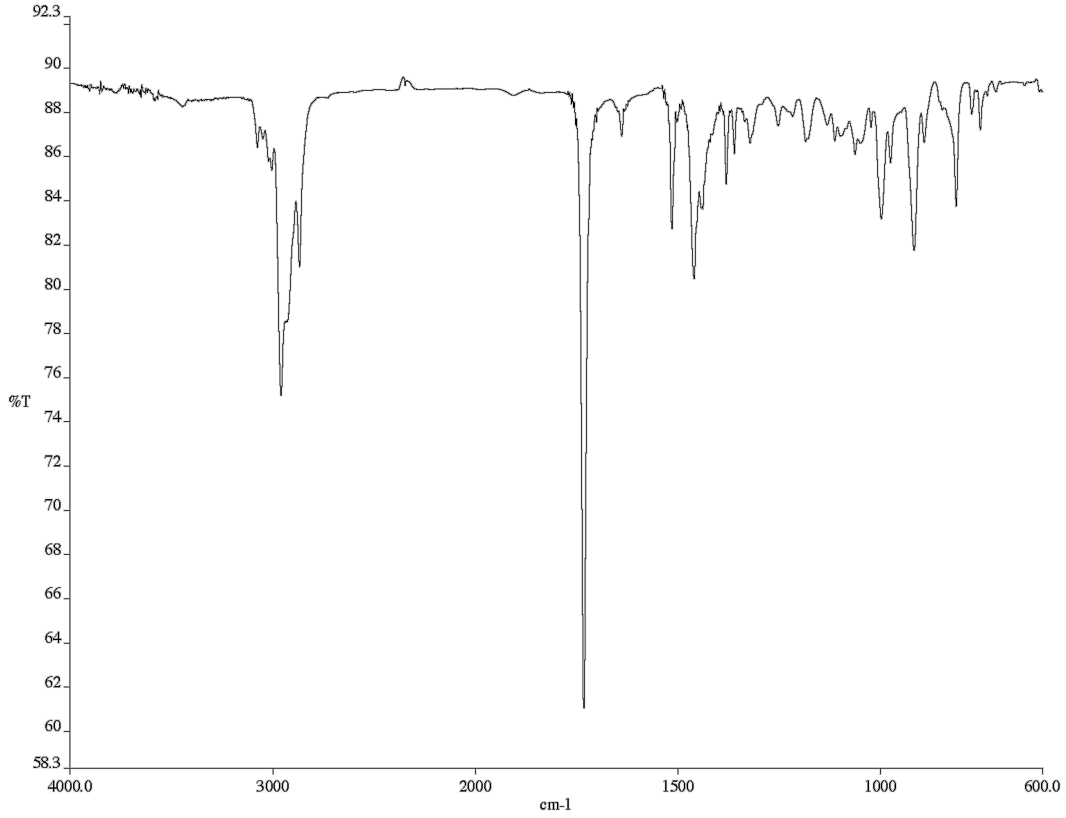
Infrared spectrum (Thin Film, NaCl) of compound **(*S*)-14i**.



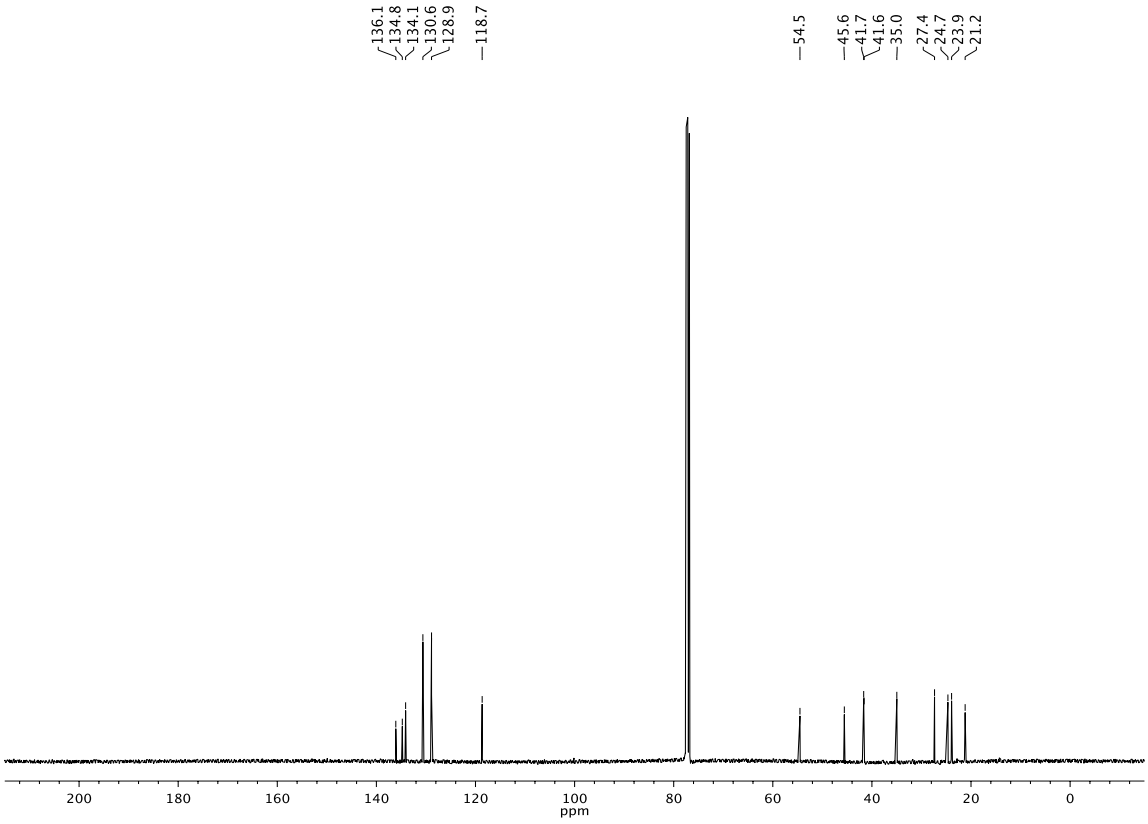
^{13}C NMR (101 MHz, $CDCl_3$) of compound **(*S*)-14i**.



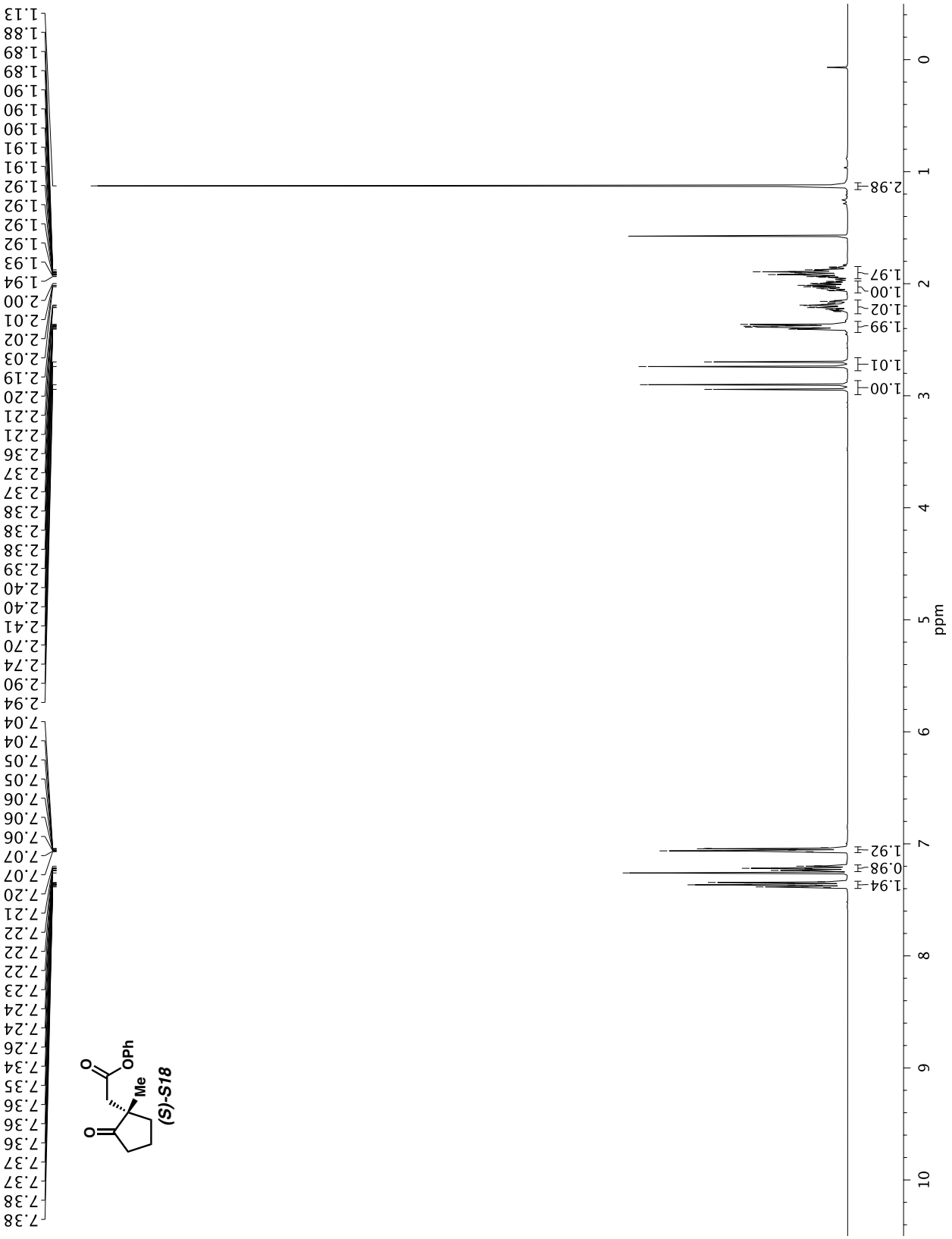
^{1}H NMR (400 MHz, $CDCl_3$) of compound **(*S*)-S16**.



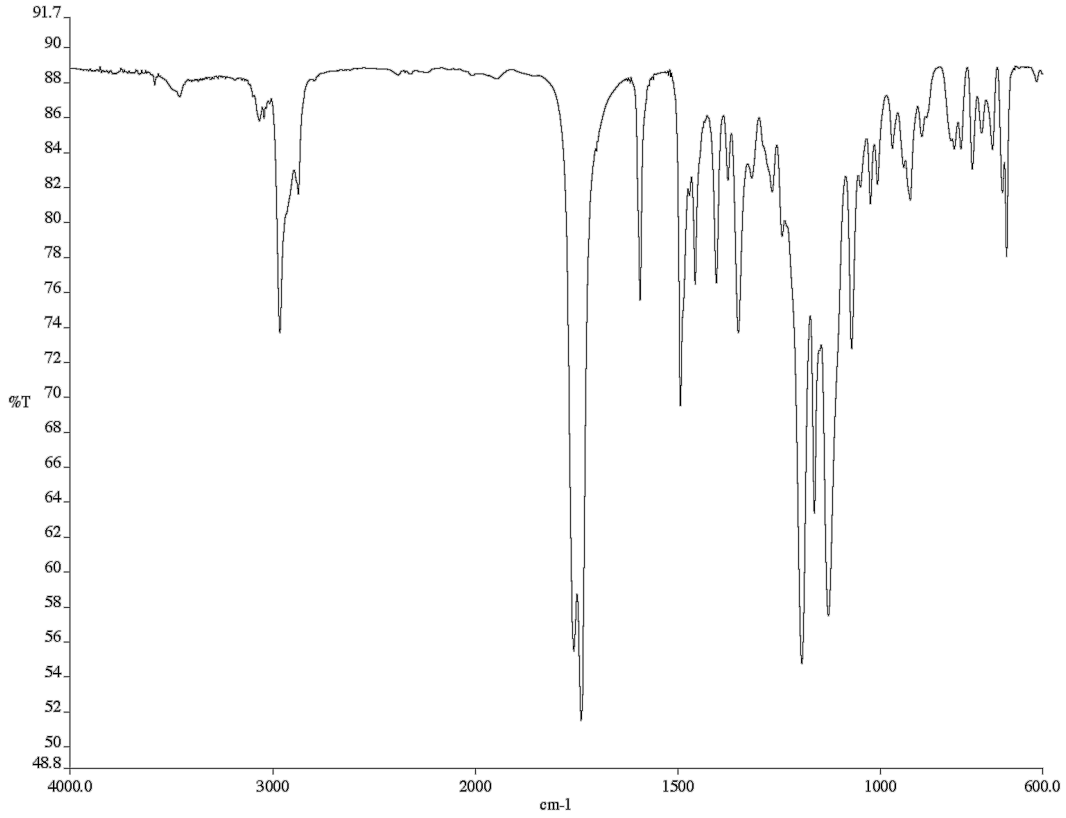
Infrared spectrum (Thin Film, NaCl) of compound **(*S*)-S16**.



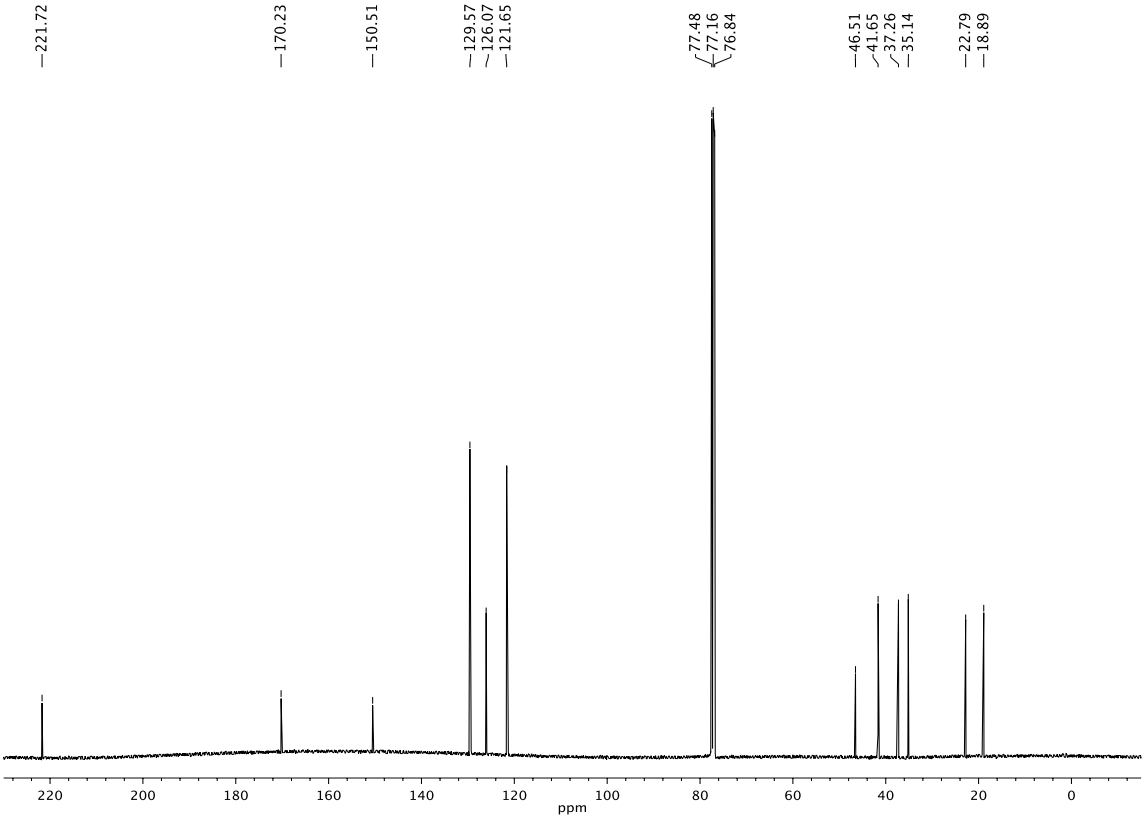
^{13}C NMR (101 MHz, $CDCl_3$) of compound **(*S*)-S16**.



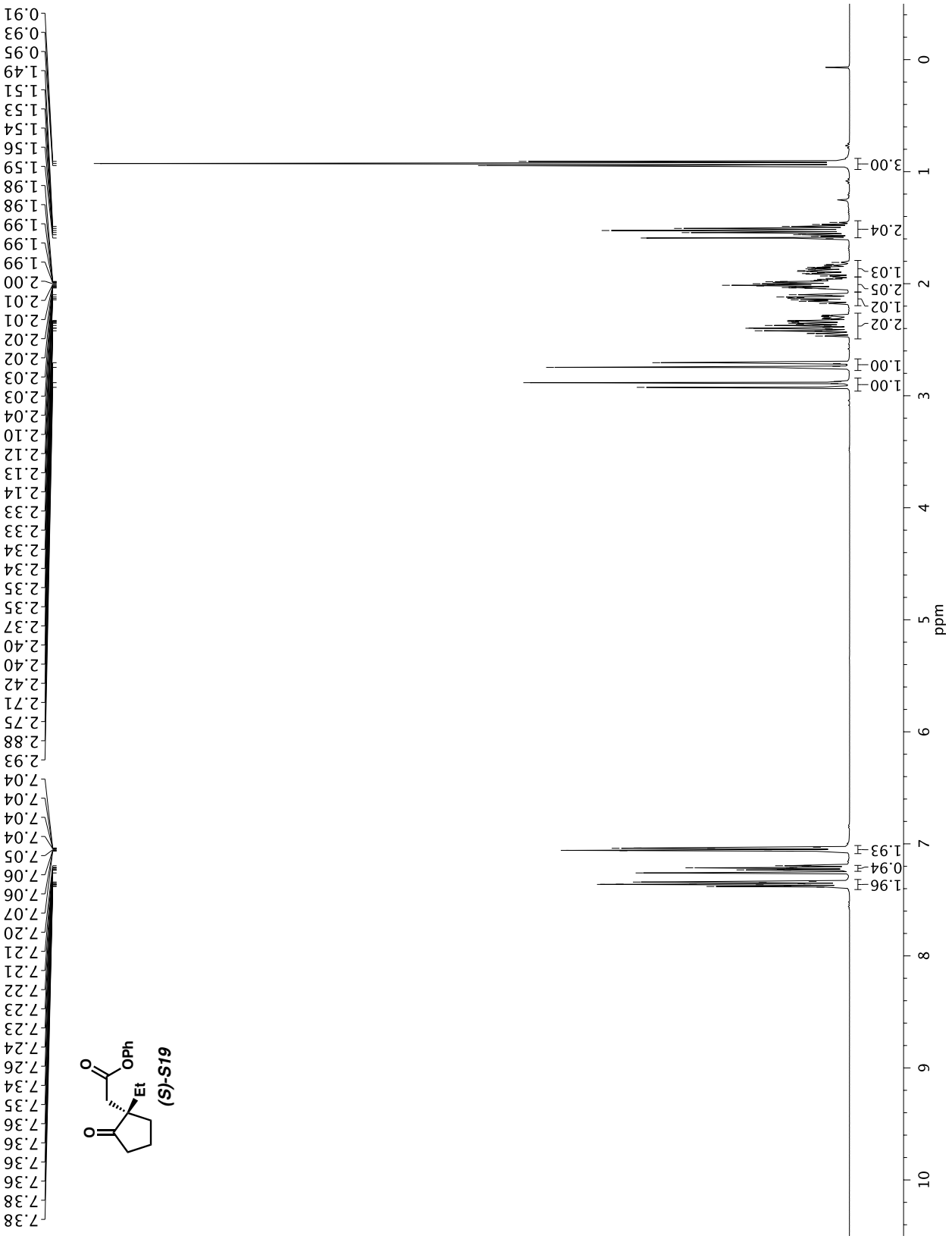
^{1}H NMR (400 MHz, $CDCl_3$) of compound **(*S*)-S18**.



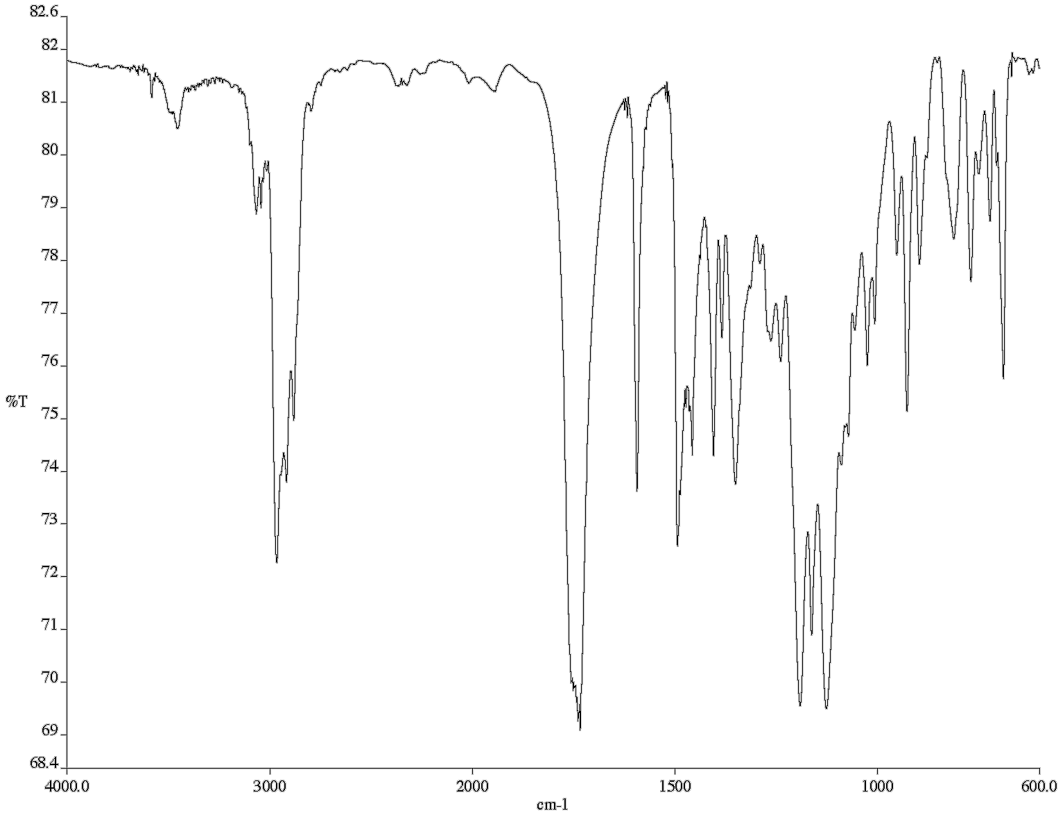
Infrared spectrum (Thin Film, NaCl) of compound **(*S*)-S18**.



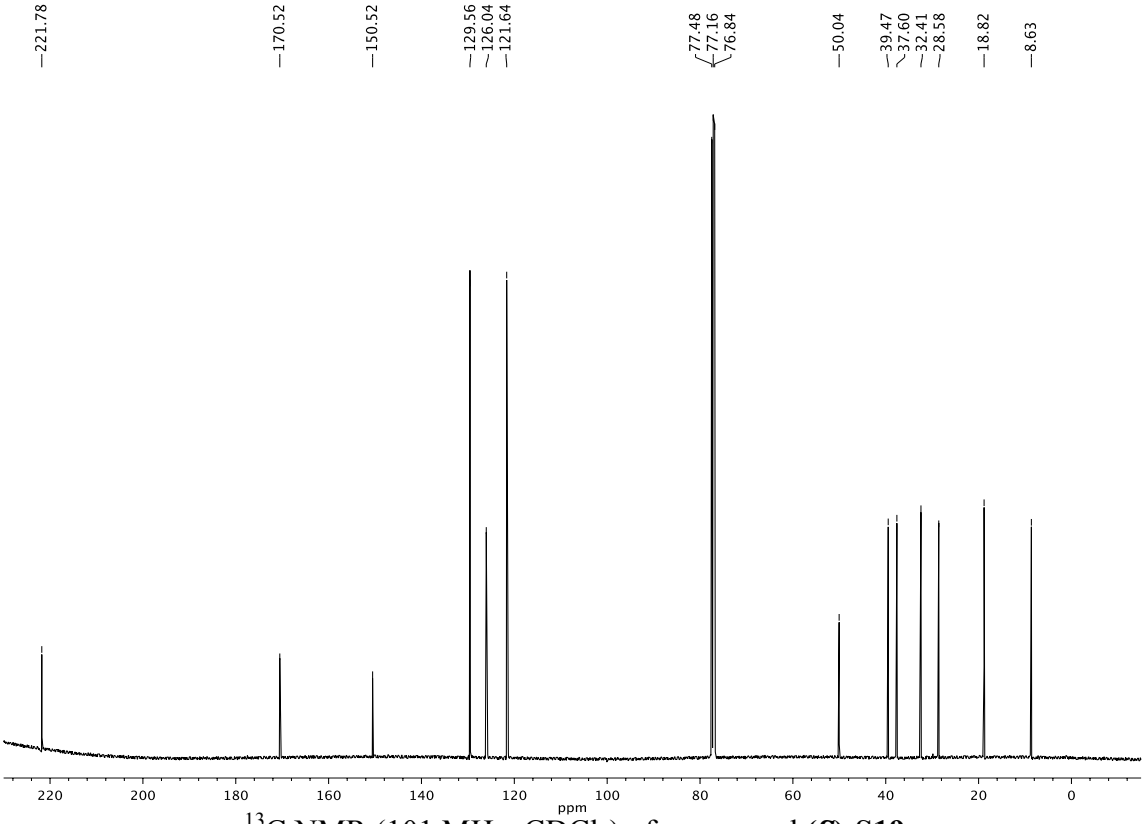
^{13}C NMR (101 MHz, $CDCl_3$) of compound **(*S*)-S18**.



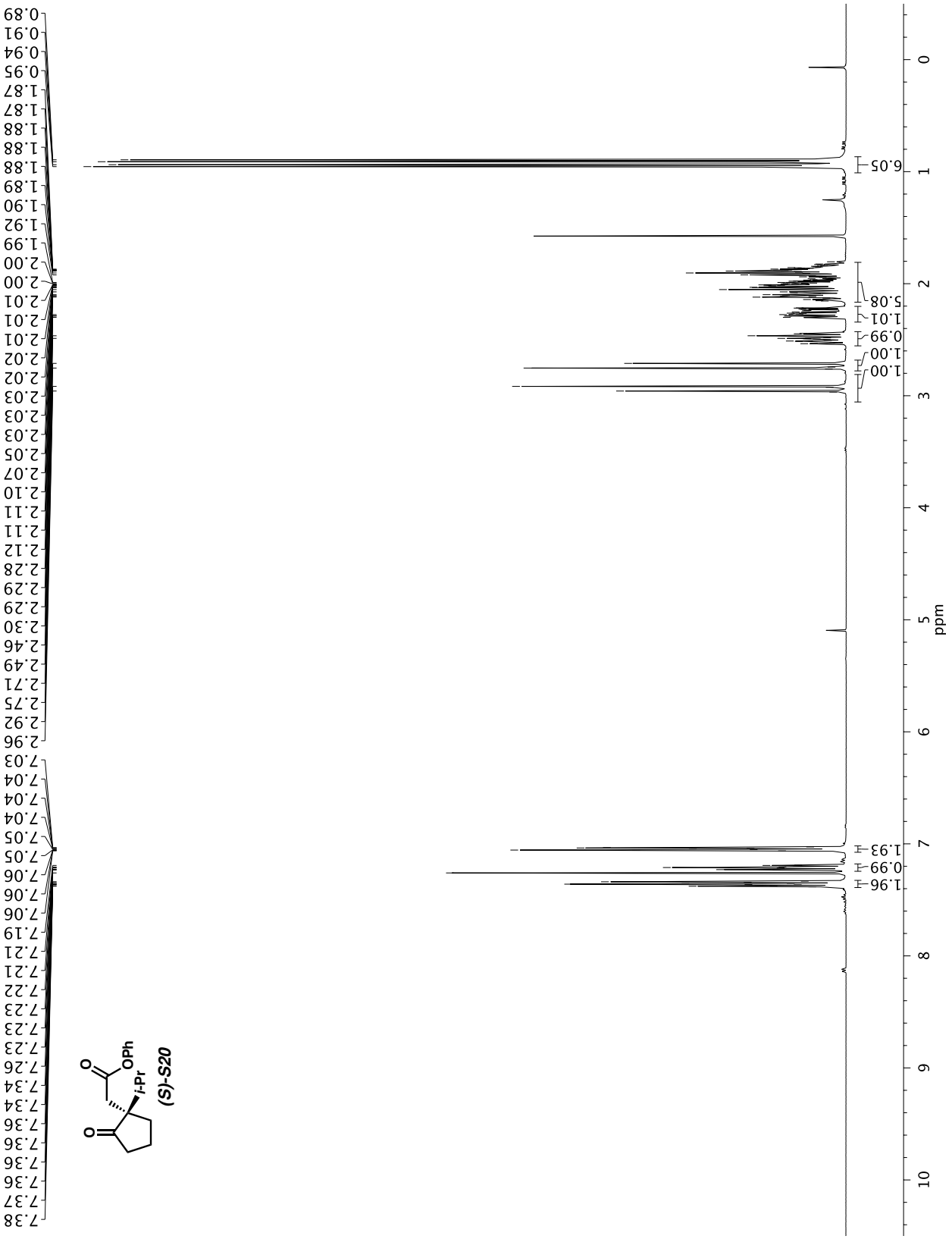
^{1}H NMR (400 MHz, $CDCl_3$) of compound **(*S*)-S19**.



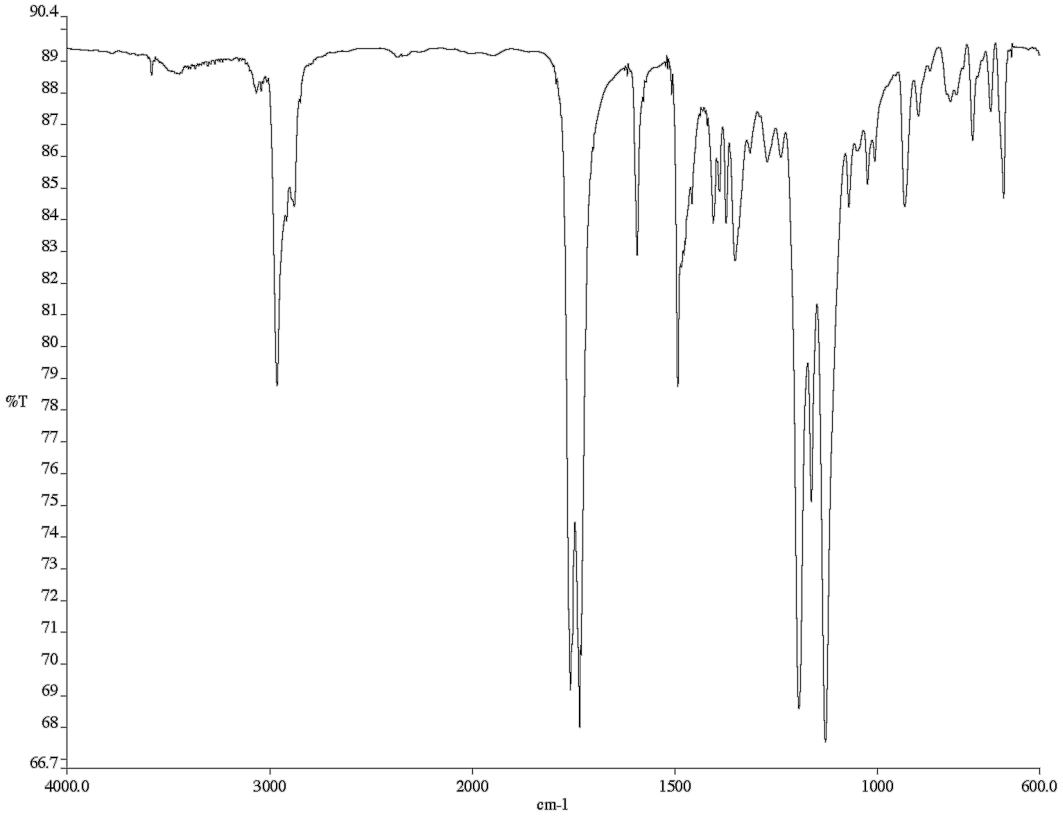
Infrared spectrum (Thin Film, NaCl) of compound **(*S*)-S19**.



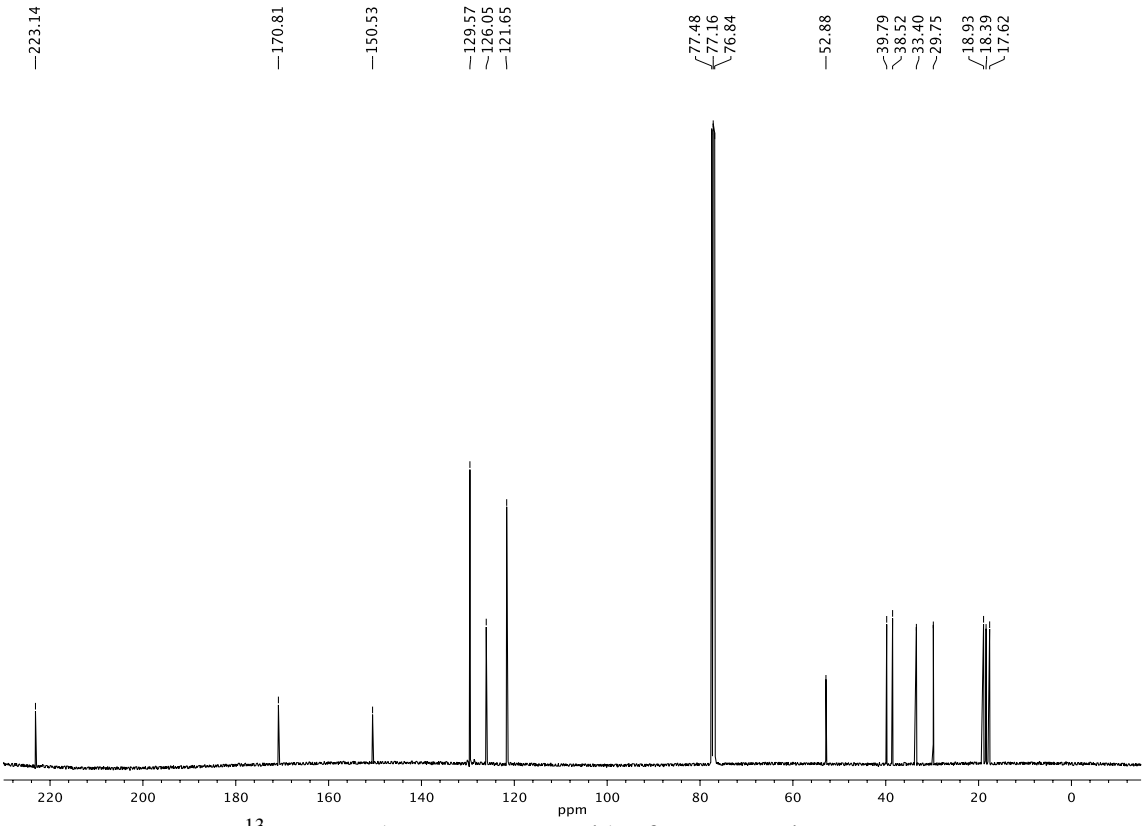
^{13}C NMR (101 MHz, $CDCl_3$) of compound **(*S*)-S19**.



^{1}H NMR (400 MHz, $CDCl_3$) of compound **(*S*)-S20**.



Infrared spectrum (Thin Film, NaCl) of compound **(*S*)-S20**.



^{13}C NMR (101 MHz, $CDCl_3$) of compound **(*S*)-S20**.