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Supporting Information

Expanding Insight into Asymmetric Palladium-Catalyzed Allylic Alkylation of N-Heterocyclic Molecules and Cyclic Ketones

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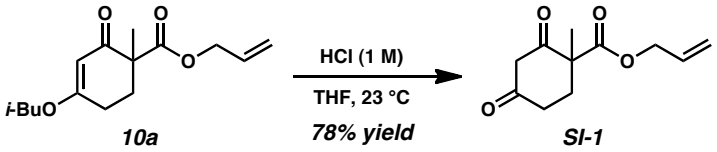
Materials and Methods. Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Reaction progress was monitored by thin-layer chromatography (TLC). Solvents were dried by passage through an activated alumina column under argon.[1] Acetone was used directly from a Sigma-Aldrich ACS reagent grade bottle. Brine solutions are saturated aqueous solutions of sodium chloride. Reagents were purchased from Sigma-Aldrich, Acros Organics, Strem, or Alfa Aesar and used as received unless otherwise stated. (*S*)-*t*-BuPHOX (**3**),[2] (*S*)-(CF_3)$_3$-*t*-BuPHOX (**8**),[3] and allyl cyanoformate[4] were prepared by known methods. Reaction temperatures were controlled by an IKAmag temperature modulator. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, *p*-anisaldehyde, or $KMnO_4$ staining. ICN silica gel (particle size 0.032-0.0653 mm) was used for flash column chromatography. Preparative HPLC purification was performed on an Agilent 1200 Series HPLC using an Agilent Prep-SIL column (5 μm, 30 x 250 mm) at ambient temperature with a flow rate of 50 mL/min. Separation was monitored by UV (λ = 254 nm) and fractions were collected at the valleys between peaks. ^{1}H NMR spectra were recorded on a Varian Mercury 300 MHz or Varian Inova 500 MHz spectrometer and are reported relative to residual $CHCl_3$ (δ 7.26 ppm) or benzene-d_6 (δ 7.16 ppm). ^{13}C NMR spectra are recorded on a Varian Mercury 300 MHz or Varian Inova 500 MHz spectrometer (75 or 125 MHz respectively) and are reported relative to $CDCl_3$ (δ 77.16 ppm) or benzene-d_6 (δ 128.06 ppm). Variable temperature NMR experiments were performed on a Varian Inova 500 MHz spectrometer and are reported relative to residual DMSO (δ 2.50 ppm). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, dm = doublet of multiplets, br s = broad singlet, br d = broad doublet, app = apparent. Data for ^{13}C are reported in terms of chemical shifts (δ ppm). IR spectra were obtained by use of a Perkin Elmer Spectrum BXII spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-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, *ee*). Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC utilizing a Chiralpak (AD, AD-H, or AS) or Chiralcel (OD-H, OJ-H, or OB-H) columns (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. Analytical chiral SFC was performed with a JASCO 2000 series instrument or a Thar SFC utilizing Chiralpak (AD-H or AS-H) or Chiralcel (OD-H, OJ-H, or OB-H) columns (4.6 mm x 25 cm), or a Chiralpak IC column (4.6 mm x 10 cm) obtained from Daicel Chemical Industries, Ltd. High resolution mass spectra (HRMS) were obtained from the Caltech Mass Spectral Facility (GC-EI+, EI+, or FAB+) or Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed ionization mode (MM: ESI-APCI+).

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

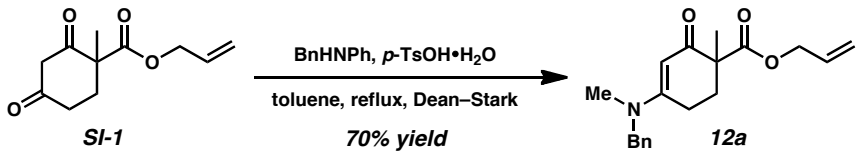
DMAP = 4-(dimethylamino)pyridine
IPA = isopropyl alcohol
LDA = lithium diisopropylamide
LiHMDS = lithium bis(trimethylsilyl)amide

Procedures for the Preparation of Compounds Related to Enaminone Screen

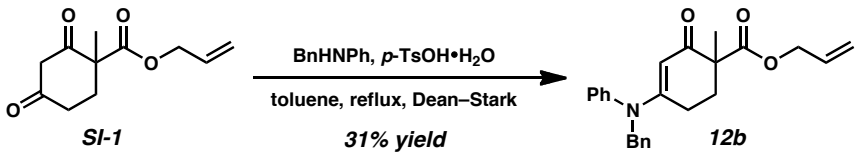
Enaminone Allylic Alkylation Precursors



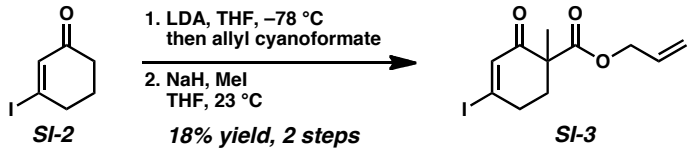
Dione SI-1. A 100 mL round-bottom flask equipped with a magnetic stir bar was charged with vinylogous ester **10a**[5] (3.08 g, 11.58 mmol, 1.00 equiv), THF (30 mL, 0.39 M), and aq. HCl (1 M in H_2O, 14.00 mL, 14.00 mmol, 1.21 equiv). The reaction was initially a suspension that developed into a solution over time. After 7 h of vigorous stirring at ambient temperature, the reaction was diluted with EtOAc (30 mL) and transferred to a separatory funnel where the aqueous layer was extracted seven times with EtOAc. The combined organics (400 mL) were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO_2, 31 x 5 cm, 100% hexanes→20%→50% EtOAc in hexanes) to afford dione **SI-1** (1.89 g, 11.58 mmol, 78% yield) as a pale yellow oil; R_f = 0.17 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) mixture of keto-enol tautomers, see spectra section; IR (Neat Film NaCl) 3500–2500 (broad stretch), 3088, 2983, 2939, 2657, 2591, 1734, 1595, 1457, 1413, 1383, 1358, 1343, 1309, 1272, 1249, 1190, 1114, 986, 932, 853 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{11}H_{15}O_4$ $[M+H]^+$: 211.0965, found 211.0966.



Enaminone 12a. A 50 mL round-bottom flask containing a magnetic stir bar was charged with dione **SI-1** (465.4 mg, 2.21 mmol, 1.00 equiv), toluene (24 mL, 0.09 M), benzylmethylamine (320 μL, 2.48 mmol, 1.12 equiv), and *p*-toluenesulfonic acid monohydrate (42.3 mg, 0.22 mmol, 10 mol %). The flask was equipped with a Dean–Stark trap and water condenser and was lowered into a preheated oil bath (135 °C). After 2 h of refluxing, the solution was removed from the oil bath and allowed to cool to room temperature. The solution was quenched with a sat. Na_2CO_3 solution (20 mL) and transferred to a separatory funnel where the aqueous layer was extracted four times with CH_2Cl_2. The combined organics (200 mL) were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO_2, 27 x 3 cm, 100% hexanes→20%→50%→60%→70% EtOAc in hexanes) to afford enaminone **12a** (484.8 mg, 1.55 mmol, 70% yield) as a yellow/orange oil; R_f = 0.24 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.33 (m, 2H), 7.32–7.27 (m, 1H), 7.09 (d, J = 7.4 Hz, 2H), 5.93–5.83 (m, 1H), 5.29 (dq, J = 17.3, 1.5 Hz, 1H), 5.26 (s, 1H), 5.18 (dq, J = 10.5, 1.4 Hz, 1H), 4.66–4.56 (m, 2H), 4.51 (s, 2H), 2.96 (s, 3H), 2.74–2.63 (m, 1H), 2.56–2.45 (m, 2H), 1.95–1.84 (m, 1H), 1.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.9, 173.7, 164.3, 132.2, 129.1, 127.8, 126.7, 118.0, 98.1, 65.6, 55.2, 51.1, 38.5, 32.6, 24.4, 21.0; IR (Neat Film NaCl) 3063, 3028, 2933, 2873, 1733, 1615, 1585, 1563, 1557, 1495, 1455, 1415, 1377, 1352, 1332, 1295, 1258, 1222, 1203, 1174, 1113, 1028, 989, 929, 821, 735 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{19}H_{24}NO_3$ $[M+H]^+$: 314.1751, found 314.1754.



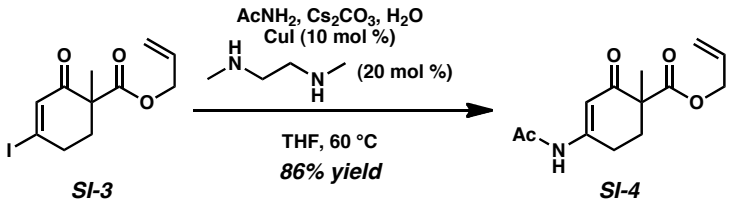
Enaminone 12b. A 50 mL round-bottom flask containing a magnetic stir bar was charged with dione **SI-1** (500.3 mg, 2.38 mmol, 1.00 equiv), toluene (24 mL, 0.10 M), benzylphenylamine (480.0 mg, 2.62 mmol, 1.10 equiv), and *p*-toluenesulfonic acid monohydrate (45.6 mg, 0.24 mmol, 10 mol %). The flask was equipped with a Dean–Stark trap and water condenser and was lowered into a preheated oil bath (135 °C). After 8 h of refluxing, the solution was removed from the oil bath and allowed to cool to room temperature. The solution was quenched with a sat. Na_2CO_3 solution (20 mL) and transferred to a separatory funnel where the aqueous layer was extracted four times with CH_2Cl_2. The combined organics (200 mL) were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was purified twice by flash column chromatography (SiO_2, 26 x 3 cm, 100% hexanes→10%→15%→20%→30%→40% EtOAc in hexanes ***then*** SiO_2, 26.5 x 3 cm, 100% hexanes→5%→10%→15%→20%→30%→ 50% EtOAc in hexanes) to afford enaminone **12b** (276.6 mg, 0.74 mmol, 31% yield) as a yellow oil; R_f = 0.50 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.33 (m, 2H), 7.33–7.24 (m, 4H), 7.21–7.18 (m, 2H), 7.13–7.10 (m, 2H), 5.90 (dddd, J = 17.2, 10.7, 5.4, 5.4 Hz, 1H), 5.39 (s, 1H), 5.31 (dq, J = 17.2, 1.6 Hz, 1H), 5.21 (dq, J = 10.5, 1.4 Hz, 1H), 4.83 (s, 2H), 4.68–4.63 (m, 1H), 4.62–4.57 (m, 1H), 2.55–2.47 (m, 1H), 2.42 (ddd, J = 13.3, 6.1, 4.9 Hz, 1H), 2.33–2.27 (m, 1H), 1.84 (ddd, J = 13.5, 8.7, 4.9 Hz, 1H), 1.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.6, 173.3, 163.9, 144.3, 136.4, 132.2, 129.9, 128.9, 128.0, 127.9, 127.7, 127.1, 118.0, 100.4, 65.6, 56.8, 51.6, 32.9, 25.9, 21.0; IR (Neat Film NaCl) 3061, 3031, 2975, 2933, 2872, 1734, 1623, 1560, 1494, 1453, 1426, 1408, 1377, 1346, 1327, 1293, 1255, 1210, 1174, 1112, 1080, 1061, 1022, 989, 929, 885, 825, 779, 733, 702 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{24}H_{26}NO_3$ $[M+H]^+$: 376.1907, found 376.1903.



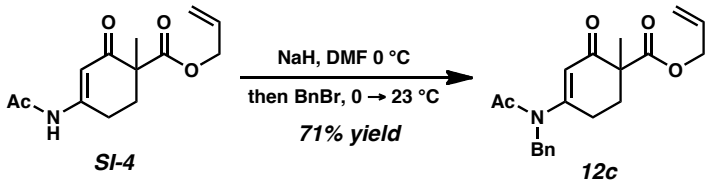
β-Iodoenone SI-3. A 200 mL round-bottom flask equipped with a magnetic stir bar was charged with diisopropyl amine (1.52 mL, 10.85 mmol, 1.19 equiv) and THF (36 mL). The flask was lowered into a 0 °C bath (ice/water) and *n*-BuLi (4.5 mL, 2.3 M in hexanes, 10.35 mmol, 1.14 equiv) was added dropwise over several minutes. The reaction was stirred for 15 min before the ice bath was removed and replaced with a –78 °C bath (dry ice/acetone). β-Iodoenone **SI-2**[6] (2.00 g, 9.09 mmol, 1.00 equiv) was transferred via cannula to the flask using several THF rinses (1 x 14 mL and 2 x 5 mL rinses, total added = 60 mL, 0.15 M), producing a yellow solution that transitioned to red over time. The reaction was stirred for one hour before allyl cyanoformate (1.12 mL, 10.38 mmol, 1.14 equiv) was added dropwise. After 2.25 hours, the reaction was quenched with sat. NH_4Cl solution and allowed to warm to room temperature. The reaction contents were transferred to a separatory funnel where the aqueous phase was extracted four times with Et_2O. The combined organics were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude oil was filtered through a short silica gel plug to afford an orange oil.

A 50 mL round-bottom flask equipped with a magnetic stir bar was cycled into a glove box (4 x 1 min cycles) and loaded with sodium hydride (161.0 mg, 95% by weight, 6.37 mmol, 1.21

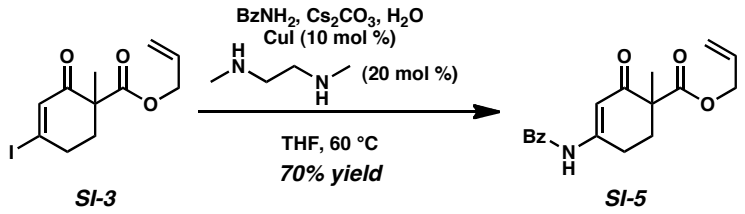
equiv). The flask was removed from the glove box, reconnected to an Ar-filled manifold, and charged with THF (6 mL). The crude orange oil from the previous step (1.61 g, 5.27 mmol, 1.00 equiv) was transferred via cannula to the flask using several THF rinses (1 x 5 mL + 3 x 2 mL, total added = 21.0 mL, 0.25 M). The grey suspension bubbled and became a yellow solution that transitioned to red over time. The reaction was stirred for 30 min before methyl iodide (400 μL, 6.43 mmol, 1.22 equiv) was added dropwise. After 3.5 hours, the reaction was quenched with water and extracted four times with dichloromethane. The combined organics were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography (SiO_2, 28.5 x 4 cm, 100% hexanes→5% EtOAc in hexanes) to afford β-Iodoenone **SI-3** (536.3 mg, 1.68 mmol, 18% yield over two steps) as a yellow oil; R_f = 0.72 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.81 (dd, J = 2.2, 1.2 Hz, 1H), 5.94–5.79 (m, 1H), 5.32–5.26 (m, 1H), 5.24 (dt, J = 10.5, 1.1 Hz, 1H), 4.67–4.56 (m, 2H), 3.05–2.96 (m, 1H), 2.93–2.85 (m, 1H), 2.43 (dt, J = 13.8, 4.9 Hz, 1H), 1.95 (ddd, J = 14.0, 9.0, 5.3 Hz, 1H), 1.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.6, 171.7, 139.6, 131.6, 125.5, 118.8, 66.1, 52.7, 38.6, 35.0, 20.3; IR (Neat Film NaCl) 3084, 2982, 2936, 2868, 1732, 1682, 1597, 1455, 1424, 1378, 1333, 1295, 1246, 1169, 1098, 1033, 986, 926, 852, 770, 737 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{11}H_{14}O_3I$ $[M+H]^+$: 320.9982, found 320.9981.



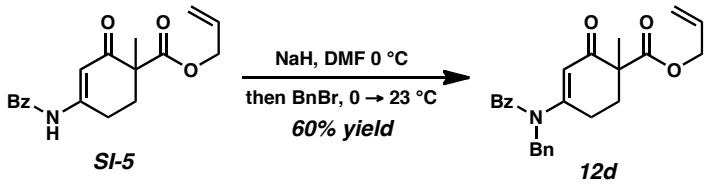
Enaminone SI-4. Adapted from procedure by Buchwald.[7] CuI (24 mg, 0.13 mmol, 0.10 equiv), Cs_2CO_3 (624 mg, 1.92 mmol, 1.50 equiv) and acetamide (91 mg, 1.5 mmol, 1.2 equiv) were added to a 25 mL Schlenck bomb equipped with a stir bar under argon atmosphere. The Schlenck bomb was evacuated and backfilled with argon three times. A solution of vinyl iodide **SI-3** (409 mg, 1.28 mmol, 1.00 equiv), *N,N*'-dimethylethylenediamine (23 mg, 0.26 mmol, 0.20 equiv) and nanopure water (23 mg, 1.3 mmol, 1.0 equiv) in THF (2.6 mL, 0.5 M) was added via syringe. The reaction flask was lowered into a 60 °C oil bath. After 12 h of stirring, TLC analysis indicated complete conversion of starting material. The reaction was subsequently diluted with 15 mL CH_2Cl_2, transferred to a separatory funnel and washed twice with 5% aqueous NH_4OH (10 mL). The combined aqueous layers were extracted twice with CH_2Cl_2 (15 mL). The combined organics were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude oil was purified by flash chromatography (SiO_2, 12 x 3 cm, 20→33→50→67% EtOAc in hexanes) to afford enaminone **SI-4** (276 mg, 1.10 mmol, 86% yield) as a pale yellow oil; R_f = 0.10 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 6.60 (s, 1H), 5.90–5.77 (m, 1H), 5.27 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.19 (dq, *J* = 10.5, 1.2 Hz, 1H), 4.58 (dq, *J* = 5.6, 1.3 Hz, 2H), 2.78 – 2.64 (m, 1H), 2.62–2.43 (m, 1H), 2.54–2.45 (m, 1H), 2.11 (s, 3H), 2.02–1.83 (m, 1H), 1.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.6 , 172.2, 169.7, 155.6, 131.5, 118.2, 109.9, 65.6, 52.1, 51.9, 31.6, 25.4, 24.8, 20.3; IR (Neat Film NaCl) 3299, 3135, 2937, 1728, 1626, 1520, 1456, 1426, 1370, 1259, 1220, 1184, 1114, 999, 939, 877 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{13}H_{18}NO_4$ $[M+H]^+$: 252.1230, found 252.1219.



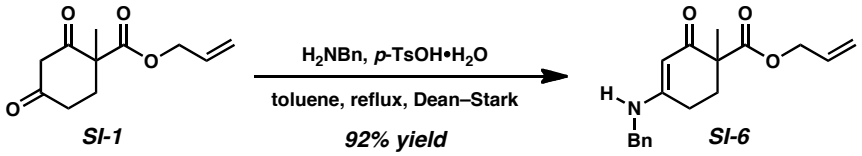
Enaminone 12c. In a 5 mL round bottom flask equipped with a stir bar under nitrogen atmosphere, enaminone **SI-4** (63 mg, 0.25 mmol, 1.0 equiv) was taken up in dry DMF (2.8 mL, 0.089 M) and cooled to 0 °C with an ice/water bath. Sodium hydride (60% suspension in mineral oil, 12 mg, 0.30 mmol, 1.2 equiv) was added to the mixture, accompanied by the formation of bubbles. The reaction was stirred for one hour before the dropwise addition of benzyl bromide (36 μL, 0.30 mmol, 1.2 equiv) by syringe. The reaction temperature was maintained at 0 °C for five hours before allowing the ice bath to gradually expire. After an additional six hours at 23 °C, TLC analysis indicated complete conversion of starting material. The reaction was subsequently diluted with EtOAc (10 mL) and sat. NH_4Cl sol. (10 mL) and transferred to a separatory funnel. The organic layer was separated from the aqueous layer, and the aqueous layer was extracted twice with EtOAc (2 x 10 mL). The combined organics were washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude oil was purified by flash chromatography (SiO_2, 15 x 3 cm, 20% acetone in hexanes) to afford enaminone **12c** (61 mg, 0.18 mmol, 71% yield) as a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.29 (m, 2H), 7.29–7.24 (m, 1H), 7.19–7.16 (m, 2H), 5.87–5.79 (m, 1H), 5.78 (s, 1H), 5.27 (dt, J = 17.2, 1.4 Hz, 1H), 5.21 (dt, J = 10.5, 1.3 Hz, 1H), 4.89–4.84 (m, 1H), 4.78–4.72 (m, 1H), 4.56 (dt, J = 5.7, 1.3 Hz, 2H), 2.58 (ddd, J = 9.3, 4.9, 1.6 Hz, 1H), 2.56–2.48 (m, 1H), 2.44 (dtd, J = 13.8, 4.8, 1.2 Hz, 1H), 2.16 (s, 3H), 1.87–1.78 (m, 1H), 1.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.2, 172.0, 170.0, 160.8, 136.5, 131.6, 129.0, 127.9, 127.5, 123.8, 1190, 66.1, 52.6, 50.8, 32.8, 27.3, 23.2, 20.2; IR (Neat Film NaCl) 3063, 3030, 2981, 2937, 2873, 1731, 1667, 1624, 1496, 1454, 1424, 1387, 1375, 1344, 1312, 1250, 1190, 1113, 1029, 986, 948, 882, 738 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{20}H_{24}O_4N$ $[M+H]^+$: 342.1700, found 342.1705.



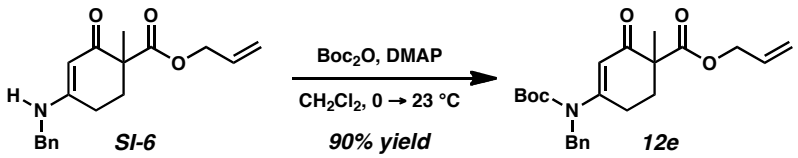
Enaminone SI-5. Adapted from procedure by Buchwald.[7] Prepared from **SI-3** in an analogous manner to **SI-4**. Purified by flash chromatography (SiO_2, 12 x 3 cm, 20→33→50% EtOAc in hexanes) to afford enaminone **SI-5** (220 mg, 0.702 mmol, 70% yield) as a pale yellow oil that solidified to a pale yellow amorphous solid upon standing at –20 °C; R_f = 0.10 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.83 – 7.74 (m, 2H), 7.56–7.47 (m, 1H), 7.47–7.40 (m, 2H), 6.70 (s, 1H), 5.88–5.75 (m, 1H), 5.25 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.17 (dq, *J* = 10.5, 1.4 Hz, 1H), 4.55 (dq, *J* = 5.5, 1.5 Hz, 2H), 2.92–2.82 (m, 1H), 2.79–2.69 (m, 1H), 2.53 (dt, *J* = 13.7, 5.4 Hz, 1H), 1.99–1.87 (m, 1H), 1.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.2, 172.5, 166.5, 155.6, 133.8, 132.7, 131.7, 128.9, 127.5, 118.4, 111.1, 65.8, 52.3, 32.0, 25.9, 20.5; IR (Neat Film NaCl) 3334, 2936, 1732, 1694, 1621, 1514, 1492, 1376, 1258, 1185, 1115, 1071, 1023, 931, 710 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{18}H_{20}NO_4$ $[M+H]^+$: 314.1387, found 314.1381.



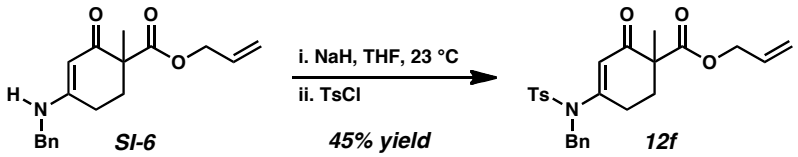
Enaminone 12d. Prepared from **SI-5** in an analogous manner to **12c**. Purified by flash chromatography (SiO_2, 15 x 3 cm, 20% acetone in hexanes) to afford enaminone **12d** (134 mg, 0.332 mmol, 60% yield) as a yellow oil; R_f = 0.63 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65–7.55 (m, 2H), 7.52–7.43 (m, 1H), 7.43–7.37 (m, 2H), 7.36–7.26 (m, 5H), 5.84 (s, 1H), 5.83–5.71 (m, 1H), 5.28–5.15 (m, 2H), 5.10–4.98 (m, 2H), 4.58–4.38 (m, 2H), 2.38–2.26 (m, 1H), 2.26–2.13 (m, 2H), 1.56 (s, 6H), 1.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.9, 171.8, 171.0, 161.8, 136.8, 136.0, 131.8, 131.6, 128.9, 128.8, 128.2, 127.9, 127.7, 121.4, 118.5, 65.9, 52.8, 52.4, 32.6, 28.8, 20.2; IR (Neat Film NaCl) 2936, 1733, 1661, 1601, 1496, 1447, 1377, 1344, 1300, 1253, 1174, 1111, 974, 794, 724 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{25}H_{26}NO_4$ $[M+H]^+$: 404.1856, found 404.1850.



Enaminone SI-6. A 250 mL round-bottom flask containing a magnetic stir bar was charged with dione **SI-1** (1.89 g, 8.98 mmol, 1.00 equiv), toluene (90 mL, 0.10 M), benzylamine (1.1 mL, 10.04 mmol, 1.12 equiv), and *p*-toluenesulfonic acid monohydrate (169.0 mg, 0.89 mmol, 10 mol %). The flask was equipped with a Dean–Stark trap and water condenser and was lowered into a preheated oil bath (135 °C). After 5.5 h of refluxing, the solution was removed from the oil bath and allowed to cool to room temperature. The solution was quenched with a sat. Na_2CO_3 solution (50 mL) and transferred to a separatory funnel where the aqueous layer was extracted once with Et_2O and three times with dichloromethane. The combined organics were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO_2, 31 x 5 cm, 100% hexanes→20%→50% EtOAc in hexanes) to afford enaminone **SI-6** (2.48 g, 8.28 mmol, 92% yield) as a yellow solid; R_f = 0.27 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.30 (m, 3H), 7.29 (s, 2H), 5.95–5.82 (m, 1H), 5.30 (dq, J = 17.2, 1.6 Hz, 1H), 5.22 (s, 1H), 5.20 (dq, J = 10.5, 1.4 Hz, 1H), 4.62 (tt, J = 5.6, 1.5 Hz, 2H), 4.56 (br s, 1H), 4.24 (d, J = 5.0 Hz, 2H), 2.59 (ddd, J = 16.5, 8.8, 4.9 Hz, 1H), 2.50 (ddd, J = 13.3, 6.2, 4.9 Hz, 1H), 2.33 (dt, J = 16.6, 5.3 Hz, 1H), 1.91 (ddd, J = 13.6, 8.8, 5.0 Hz, 1H), 1.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.4, 173.4, 162.6, 136.7, 132.2, 129.1, 128.2, 128.0, 118.0, 96.7, 65.6, 52.1, 47.5, 32.4, 26.7, 21.1; IR (Neat Film NaCl) 3260, 3064, 2978, 2933, 2868, 1730, 1576, 1545, 1452, 1427, 1375, 1359, 1297, 1253, 1218, 1199, 1172, 1107, 1028, 987, 929, 822, 735 cm^{-1}; HRMS (GC-EI+) *m/z* calc'd for $C_{18}H_{21}NO_3$ $[M+\bullet]^+$: 299.1521, found 299.1522.



Enaminone 12e. A flame-dried 25 mL round-bottom flask containing a magnetic stir bar was loaded with enaminone **SI-6** (300.1 mg, 1.00 mmol, 1.00 equiv) and 4-dimethylaminopyridine (9.5 mg, 0.078 mmol, 7.8 mol %). The flask was charged with dichloromethane (10 mL, 0.10 M) and lowered into a 0 °C bath (ice/water). Di-*tert*-butyl dicarbonate (252.7 mg, 1.16 mmol, 1.15 equiv) was added and the solution transitioned from yellow to clear. The ice bath was allowed to expire as the reaction was stirred over night. After 22 h, the stir bar was removed from the flask, the reaction contents were concentrated under reduced pressure, and the resulting crude oil was purified by flash column chromatography (SiO_2, 26.5 x 3 cm, 100% hexanes→5%→10%→15%→20% EtOAc in hexanes) to afford enaminone **12e** (360.0 mg, 0.90 mmol, 90% yield) as a pale yellow oil; R_f = 0.79 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.28 (m, 2H), 7.26–7.21 (m, 1H), 7.16–7.12 (m, 2H), 5.85 (dddd, J = 17.2, 10.5, 5.5, 5.5 Hz, 1H), 5.73 (t, J = 0.9 Hz, 1H), 5.27 (dq, J = 17.2, 1.6 Hz, 1H), 5.20 (dq, J = 10.5, 1.3 Hz, 1H), 4.80 (s, 2H), 4.58 (dddd, J = 5.6, 2.8, 1.5, 1.5 Hz, 2H), 2.92–2.77 (m, 2H), 2.45 (dt, J = 13.5, 5.3 Hz, 1H), 1.86 (ddd, J = 13.5, 7.7, 5.7 Hz, 1H), 1.42 (s, 9H), 1.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.8, 172.6, 162.2, 152.9, 137.2, 131.9, 128.8, 127.5, 126.3, 118.3, 114.8, 83.0, 65.8, 53.0, 52.5, 33.6, 28.1, 27.5, 20.4; IR (Neat Film NaCl) 3090, 3064, 3034, 2978, 2935, 2873, 1718, 1662, 1654, 1595, 1497, 1453, 1425, 1369, 1344, 1317, 1300, 1248, 1210, 1150, 1113, 1029, 989, 937, 856, 815, 769, 737 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{23}H_{30}NO_5$ $[M+H]^+$: 400.2118, found 400.2127.



Enaminone 12f. A flame-dried 25 mL round-bottom flask containing a magnetic stir bar was cycled into a glove box and loaded with sodium hydride (95% by weight, 32.6 mg, 1.29 mmol, 1.29 equiv). The flask was removed from the glove box, reconnected to an Ar-filled manifold, and charged with THF (6 mL). Enaminone **SI-6** (300.3 mg, 1.00 mmol, 1.00 equiv) was added in one portion and the grey suspension bubbled and became a yellow solution over time. The flask was rinsed with additional THF (4 mL, 10 mL total, 0.10 M). The reaction was stirred vigorously for 70 min before *p*-toluenesulfonyl chloride (287.6 mg, 1.51 mmol, 1.50 equiv) was added in one portion. After 6 h, the flask was lowered into a 0 °C bath (ice/water) and quenched with water (reaction bubbled). The mixture was transferred to a separatory funnel where the aqueous layer was extracted four times with CH_2Cl_2. The combined organics (100 mL) were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO_2, 27 x 3 cm, 100% hexanes→5%→10%→15%→ 50% EtOAc in hexanes) to afford enaminone **12f** (203.8 mg, 0.45 mmol, 45% yield) as a yellow oil; R_f = 0.68 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.33–7.25 (m, 3H), 7.23 (d, J = 6.6 Hz, 2H), 5.75 (dddd, J = 17.3, 10.8, 5.6, 5.6 Hz, 1H), 5.68 (t, J = 1.1 Hz, 1H), 5.24–5.15 (m, 2H), 4.81–4.69 (m, 2H), 4.48 (dddd, J = 13.5, 5.6, 1.4, 1.4 Hz, 1H), 4.40 (dddd, J = 13.2, 5.6, 1.4, 1.4 Hz, 1H), 2.67–2.55 (m, 2H), 2.46 (s, 3H), 2.32 (dt, J = 13.9, 5.2 Hz, 1H), 1.69 (ddd, J = 13.8, 8.0, 5.9 Hz, 1H), 1.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.0, 171.9, 158.4, 144.8, 135.6, 135.3, 131.7, 130.2, 128.9, 128.1,

127.6, 127.5, 119.5, 118.5, 65.9, 53.0, 52.2, 32.4, 27.9, 21.8, 20.0; IR (Neat Film NaCl) 3064, 3032, 2981, 2935, 2873, 1735, 1669, 1596, 1496, 1454, 1424, 1359, 1321, 1292, 1255, 1164, 1115, 1089, 1058, 1028, 984, 910, 883, 816, 773, 743 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{25}H_{28}NSO_5$ $[M+H]^+$: 454.1683, found 454.1691.

General Procedure for Screening Reactions

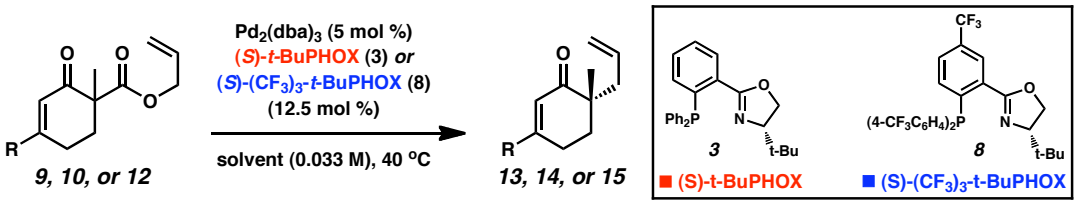
Enone 9a Screen Procedure

$Pd_2(dba)_3$ (2.4 mg, 0.00262 mmol, 0.05 equiv) and the appropriate PHOX ligand ((*S*)-*t*-BuPHOX (**3**): 2.5 mg, 0.00645 mmol, 0.125 equiv ***or*** (*S*)-$(CF_3)_3$-*t*-BuPHOX (**8**): 3.8 mg, 0.00643 mmol, 0.125 equiv) were added to an oven-dried 1 dram vial equipped with a magnetic stir bar. A separate oven-dried 1 dram vial was charged with enone **9a**[8] (10.0 mg, 0.0515 mmol, 1.00 equiv) and both vials were cycled into a nitrogen-filled glove box. The palladium/ligand vial was charged with solvent (THF, MTBE, toluene: 360 μL or 2:1 hexanes/toluene: 120 μL toluene and 340 μL hexanes) and stirred at ambient glove box temperature. After 30 min, enone **9a** was transferred to the reaction vial with several solvent rinses (THF, MTBE, toluene: 3 x 400 μL, 1.56 mL total, 0.033 M or 2:1 hexanes/toluene: 400 μL toluene and 400 μL + 300 μL hexanes, 1.56 mL solvent total, 0.033 M). The vials were tightly sealed with a teflon lined cap and electrical tape, removed from the glove box, and lowered into a heating block set to 40 °C. After 2 days, the reaction were either loaded directly onto a column (toluene and 2:1 hexanes/toluene) or filtered through a celite plug and concentrated prior to chromatography (THF and MTBE). All reactions were purified by flash column chromatography (SiO_2, ~22 x 1 cm, 2%→3% Et_2O in pentane), resuspended in Et_2O for analysis, and analyzed for enantiomeric excess with chiral GC. Characterization data for enone **13a** matches that previously reported.[8] As part of the screen, the yield was determined for enone **13a** with (*S*)-**8** in toluene (6.0 mg, 0.040 mmol, 78% yield).

Vinylogous Ester 10a and Enaminone Symyx Core Module Screen Procedure

All reagents were dispensed as solutions using a Symyx Core Module within a nitrogen-filled glovebox. Oven-dried half-dram vials were charged with a solution of the palladium source ($Pd_2(dba)_3$, 1.65 μmol, 0.05 equiv) in THF (400 μL). The palladium solutions were evaporated to dryness under reduced pressure using a Genevac centrifugal evaporator within the glovebox, and stirbars were added to the vials. The reaction vials were then charged with a solution of the PHOX ligand (4.13 μmol, 0.125 equiv) in the reaction solvent (300 μL) and stirred at 20 °C. After 30 min, a solution of vinylogous ester **10a** or the enaminone substrate (**12**, 33.0 μmol, 1.0 equiv) in the reaction solvent (700 μL) were added. The reaction vials were tightly capped and heated to the desired temperature (40 °C). The consumption of the starting material was observed by colorimetric change (from light yellow/green to red/orange) and after 5 d, the reaction mixtures were removed from the glovebox, filtered through a short silica gel plug (rinsing with EtOAc), concentrated under reduced pressure, resuspended in an appropriate solvent for analysis (HPLC: hexanes ***or*** SFC: MeOH), and analyzed for enantiomeric excess (see Methods for the Determination of Enantiomeric Excess). Characterization data for vinylogous ester **14a** matches that previously reported.[5] Experimental procedures and characterization data for enaminones **15a–f** follows.

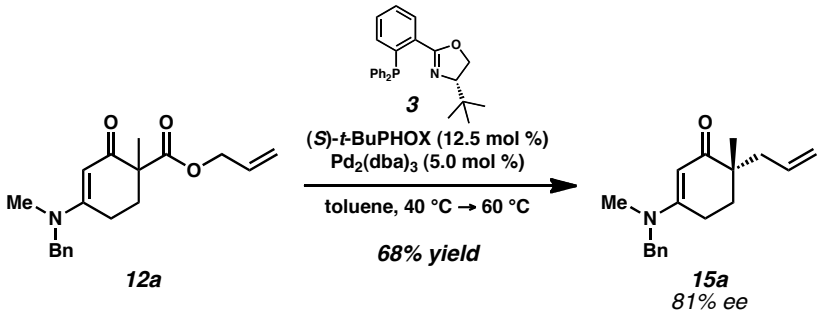
Table SI-1. Enaminone Allylic Alkylation Screen[a]



					Enantiomeric Excess (% ee)[b]			
entry	Substrate	R	Product	ligand	THF	MTBE	Toluene	2:1 Hex–Tol
1	9a	H	13a	3	87	88	87	87
2				8	85	86	88	85
3	10a	O*i*-Bu	14a	3	85	85	86	87
4				8	86	86	86	88
5	12a	NMe(Bn)	15a	3	61	60	55	52
6				8	79	78	84	83
7	12b	NPh(Bn)	15b	3	81	87	85	83
8				8	76	74	82	83
9	12c	NAc(Bn)	15c	3	89	90	88	88
10				8	83	85	88	86
11	12d	NBz(Bn)	15d	3	86	87	88	87
12				8	80	83	82	83
13	12e	NBoc(Bn)	15e	3	87	86	87	82
14				8	84	84	81	83
15	12f	NTs(Bn)	15f	3	84	83	83	82
16				8	82	83	83	83

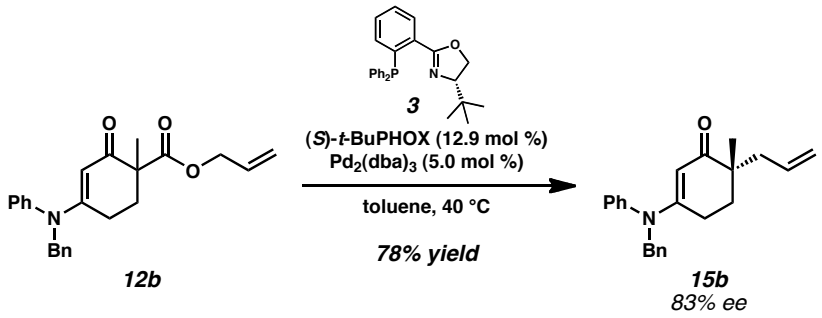
[a] Conditions: enone **9a**, vinylogous ester **10a**, or enaminone **12a–f** (1.0 equiv), $Pd_2(dba)_3$ (5 mol %), and (S)-*t*-BuPHOX (**3**) or (S)-$(CF_3)_3$-*t*-BuPHOX (**8**) (12.5 mol %) in solvent (0.033 M) at 40 °C. [b] Determined by chiral GC, HPLC, or SFC analysis. Red = with (*S*)-(**3**) as ligand and blue = with (*S*)-(**8**) as ligand.

Enaminone Allylic Alkylation Products



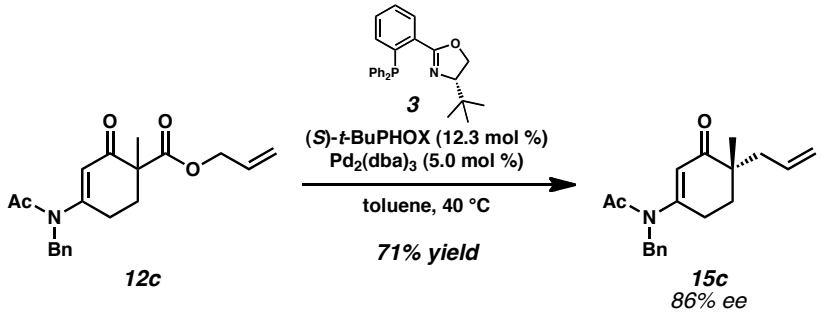
Enaminone 15a. $Pd_2(dba)_3$ (14.6 mg, 0.0159 mmol, 5.0 mol %) and (*S*)-*t*-BuPHOX (**3**, 15.5 mg, 0.0400 mmol, 12.5 mol %) were added to an oven-dried scintillation vial equipped with a magnetic stir bar and the vial was cycled into a glove box. The vial was charged with toluene (2 mL) and heated at 30 °C for 30 min, generating a red/orange solution. Enaminone **12a** (1 M in toluene, 320 μL, 0.320 mmol, 1.00 equiv) and additional toluene (7.35 mL, total added = 9.67 mL, 0.033 M) were added, producing a green solution. The vial was sealed with a Teflon-lined cap, removed from the glove box, and lowered into a heating block (40 °C). After 5 days, the

temperature was raised to 60 °C and heated for an additional day before the reaction transitioned back to a red/orange solution. The reaction was filtered through a silica gel plug, rinsed with EtOAc, and concentrated under reduced pressure. The crude oil was purified twice by flash column chromatography (SiO_2, 27.5 x 2 cm, 100% hexanes→20%→30%→50% EtOAc in hexanes→100% EtOAc ***then*** SiO_2, 26.5 x 1.5 cm, 100% hexanes→20%→30%→40% EtOAc in hexanes) to afford enaminone **15a** (58.9 mg, 0.219 mmol, 68% yield) as a pale yellow oil; R_f = 0.12 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.33 (m, 2H), 7.31–7.26 (m, 1H), 7.10 (d, J = 7.2 Hz, 2H), 5.84–5.74 (m, 1H), 5.17 (s, 1H), 5.07–5.00 (m, 2H), 4.51 (s, 2H), 2.95 (s, 3H), 2.58–2.44 (m, 2H), 2.38 (dddd, J = 13.7, 7.1, 1.2, 1.2 Hz, 1H), 2.23–2.18 (m, 1H), 1.93 (ddd, J = 13.2, 7.5, 5.5 Hz, 1H), 1.71 (ddd, J = 13.7, 6.9, 5.4 Hz, 1H), 1.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.2, 163.7, 136.9, 135.2, 129.1, 127.7, 126.3, 117.5, 98.1, 55.0, 42.1, 41.8, 38.5, 32.8, 24.0, 22.6; IR (Neat Film NaCl) 3066, 3029, 2958, 2926, 2867, 1728, 1615, 1557, 1495, 1451, 1412, 1373, 1354, 1333, 1315, 1297, 1276, 1253, 1204, 1156, 1103, 1077, 1029, 1001, 924, 823, 792, 733 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{18}H_{23}ON$ $[M+\bullet]^+$: 269.1780, found 269.1782; $[\alpha]_D^{25.0}$ –24.18 (c 1.04, $CHCl_3$, 81% ee); JASCO SFC conditions: 5% MeOH in CO_2, 5 mL/min, Chiralcel OD-H column, λ = 210 nm, t_R (min): major = 10.45, minor = 9.60.

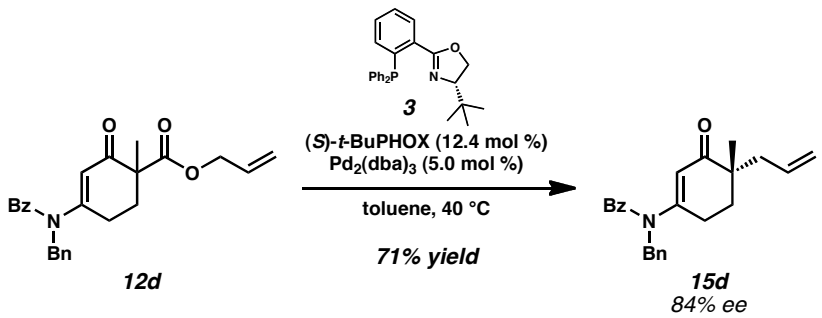


Enaminone 15b. $Pd_2(dba)_3$ (3.5 mg, 0.00382 mmol, 5.0 mol %) and (*S*)-*t*-BuPHOX (**3**, 3.8 mg, 0.00981 mmol, 12.9 mol %) were added to an oven-dried scintillation vial equipped with a magnetic stir bar and the vial was cycled into a glove box. The vial was charged with toluene (0.5 mL) and heated at 30 °C for 30 min, generating a red/orange solution. Enaminone **12b** (28.6 mg, 0.0762 mmol, 1.00 equiv) was transferred to the flask with several toluene rinses (1 x 0.81 mL + 2 x 0.5 mL, total added = 2.31 mL, 0.033 M), producing a green solution. The vial was sealed with a Teflon-lined cap, removed from the glove box, and lowered into a heating block (40 °C). After 4 days, the reaction transitioned back to an orange solution. Subsequently, the reaction was filtered through a silica gel plug, rinsed with EtOAc, and concentrated under reduced pressure. The crude oil was purified twice by flash column chromatography (SiO_2, 19.5 x 1.5 cm, 100% hexanes→50% EtOAc in hexanes→100% EtOAc ***then*** SiO_2, 23.5 x 1 cm, 100% hexanes→10%→20%→30%→40% EtOAc in hexanes) to afford enaminone **15b** (19.7 mg, 0.0594 mmol, 78% yield) as a frosty colorless oil; R_f = 0.63 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.33 (m, 2H), 7.33–7.29 (m, 2H), 7.29–7.22 (m, 2H), 7.22–7.18 (m, 2H), 7.15–7.11 (m, 2H), 5.76 (dddd, J = 15.8, 11.3, 7.8, 7.0 Hz, 1H), 5.29 (s, 1H), 5.05–5.00 (m, 2H), 4.83 (s, 2H), 2.38 (dddd, J = 13.8, 7.1, 1.3, 1.3 Hz, 1H), 2.35–2.31 (m, 2H), 2.19 (dddd, J = 13.7, 7.8, 1.1, 1.1 Hz, 1H), 1.90–1.83 (m, 1H), 1.65 (ddd, J = 13.5, 6.5, 5.6 Hz, 1H), 1.08 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.8, 163.3, 144.6, 136.7, 135.0, 129.8, 128.8, 128.0, 127.6, 127.5, 127.0, 117.6, 100.5, 56.7, 42.2, 42.0, 33.0, 25.5, 22.6; IR (Neat Film NaCl) 3063, 3031, 2959, 2926, 2863, 1622, 1563, 1494, 1453, 1426, 1404, 1374, 1351, 1329, 1275, 1204, 1156, 1078, 1060, 1028, 1002, 911, 830, 730 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{23}H_{26}ON$ $[M+H]^+$:

332.2009, found 332.1999; $[\alpha]_D^{25.0}$ –29.79 (c 1.91, $CHCl_3$, 83% ee); JASCO SFC conditions: 5% MeOH in CO_2, 5 mL/min, Chiralpak AS-H column, λ = 254 nm, t_R (min): major = 8.60, minor = 6.48.

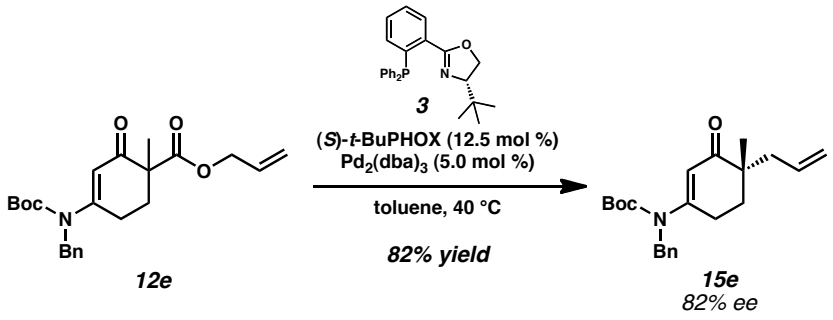


Enaminone 15c. $Pd_2(dba)_3$ (2.6 mg, 0.00284 mmol, 5.0 mol %) and (*S*)-*t*-BuPHOX (**3**, 2.7 mg, 0.00697 mmol, 12.3 mol %) were added to an oven-dried scintillation vial equipped with a magnetic stir bar and the vial was cycled into a glove box. The vial was charged with toluene (0.51 mL) and heated at 30 °C for 30 min, generating a red/orange solution. Enaminone **12c** (19.3 mg, 0.0565 mmol, 1.00 equiv) was transferred to the flask with several toluene rinses (4 x 0.3 mL, total added = 1.71 mL, 0.033 M), producing a yellow solution. The vial was sealed with a Teflon-lined cap, removed from the glove box, and lowered into a heating block (40 °C). After 2 days, the reaction transitioned back to an orange solution. Subsequently, the reaction was filtered through a silica gel plug, rinsed with EtOAc, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO_2, 19.5 x 1.5 cm, 5%→10%→20%→30% EtOAc in hexanes) to afford enaminone **15c** (12.0 mg, 0.0404 mmol, 71% yield) as a yellow oil; R_f = 0.46 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (ddt, J = 8.1, 6.7, 1.2 Hz, 2H), 7.30–7.23 (m, 1H), 7.19 (ddt, J = 7.3, 1.4, 0.7 Hz, 2H), 5.68 (t, J = 1.3 Hz, 1H), 5.66 (ddt, J = 16.9, 10.1, 7.3 Hz, 1H), 5.05 (ddt, J = 10.1, 1.9, 0.9 Hz, 1H), 4.99 (ddt, J = 17.0, 2.1, 1.4 Hz, 1H), 4.81 (s, 2H), 2.50–2.39 (m, 2H), 2.21 (ddt, J = 13.8, 7.3, 1.2 Hz, 1H), 2.17 (s, 3H), 2.10 (ddt, J = 13.8, 7.5, 1.1 Hz, 1H), 1.87 (dt, J = 13.8, 5.9 Hz, 1H), 1.69 (ddd, J = 13.8, 6.6, 5.7 Hz, 1H), 1.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.1, 169.7, 160.1, 136.6, 133.6, 128.9, 127.9, 127.7, 123.8, 118.6, 50.9, 43.6, 40.8, 32.6, 27.1, 23.2, 21.5; IR (Neat Film NaCl) 3066, 2926, 2854, 1663, 1624, 1496, 1453, 1387, 1371, 1189, 991, 916 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{19}H_{24}NO_2$ $[M+H]^+$: 298.1807, found 298.1794; $[\alpha]_D^{25.0}$ –14.12 (c 1.20, $CHCl_3$, 86% ee); Thar SFC conditions: 5% MeOH in CO_2, 3 mL/min, Chiralpak AD-H column, λ = 254 nm, t_R (min): major = 8.45, minor = 10.35.



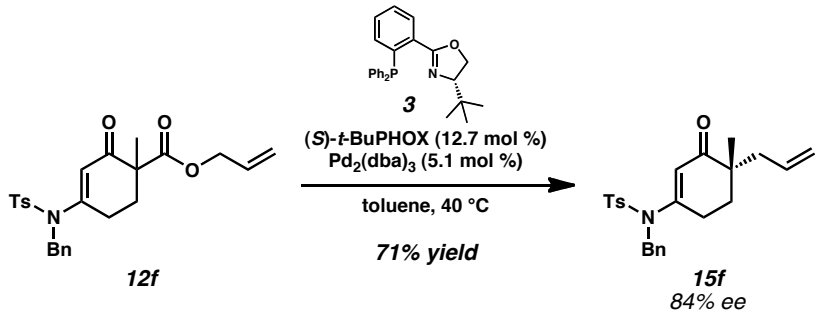
Enaminone 12d. $Pd_2(dba)_3$ (4.6 mg, 0.00502 mmol, 5.0 mol %) and (*S*)-*t*-BuPHOX (**3**, 4.8 mg, 0.0124 mmol, 12.4 mol %) were added to an oven-dried scintillation vial equipped with a magnetic stir bar and the vial was cycled into a glove box. The vial was charged with toluene

(0.93 mL) and heated at 30 °C for 30 min, generating a red/orange solution. Enaminone **12d** (1 M in toluene, 100 μL, 0.100 mmol, 1.00 equiv) was transferred to the flask with more toluene (1 mL, total added including enaminone solution = 3.03 mL, 0.033 M), producing a yellow/orange solution. The vial was sealed with a Teflon-lined cap, removed from the glove box, and lowered into a heating block (40 °C). After 2 days, the reaction transitioned back to an orange solution. Subsequently, the reaction was filtered through a silica gel plug, rinsed with EtOAc, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO_2, 19.5 x 1.5 cm, 5%→10%→15% EtOAc in hexanes) to afford enaminone **15d** (26.3 mg, 0.0713 mmol, 71% yield, 95% purity) as a yellow oil; R_f = 0.57 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63–7.59 (m, 2H), 7.50–7.43 (m, 1H), 7.39 (ddt, J = 8.2, 6.6, 1.1 Hz, 2H), 7.35–7.29 (m, 4H), 7.29–7.25 (m, 1H), 5.74 (t, J = 1.1 Hz, 1H), 5.54 (ddt, J = 17.3, 10.1, 7.4 Hz, 1H), 5.09 (d, J = 15.3 Hz, 1H), 5.00 (d, J = 15.3 Hz, 1H), 4.98 (dm, J = 9.9 Hz, 1H), 4.86 (dm, J = 17.0 Hz, 1H), 2.11–2.08 (m, 2H), 2.03 (dd, J = 14.2, 7.9 Hz, 1H), 1.95 (ddt, J = 13.8, 7.3, 1.2 Hz, 1H), 1.59 (ddd, J = 13.7, 6.5, 5.4 Hz, 1H), 1.41 (ddd, J = 13.4, 6.8, 5.3 Hz, 1H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.7, 170.8, 160.9, 136.8, 136.2, 133.6, 131.6, 128.9, 128.7, 128.1, 128.0, 127.9, 122.3, 118.4, 52.5, 43.3, 40.6, 32.4, 28.4, 21.3; IR (Neat Film NaCl) 3063, 3030, 2961, 2928, 2855, 1655, 1610, 1496, 1447, 1384, 1374, 1347, 1324, 1273, 1189, 1140, 1076, 1028, 1001, 974, 919, 792 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{24}H_{26}NO_2$ $[M+H]^+$: 360.1964, found 360.1956; $[\alpha]_D^{25.0}$ –26.61 (c 1.87, $CHCl_3$, 84% ee); Thar SFC conditions: 7% MeOH in CO_2, 2.5 mL/min, Chiralpak AD-H column, λ = 254 nm, t_R (min): major = 18.14, minor = 20.28.



Enaminone 15e. $Pd_2(dba)_3$ (11.5 mg, 0.0126 mmol, 5.0 mol %) and (*S*)-*t*-BuPHOX (**3**, 12.1 mg, 0.0312 mmol, 12.5 mol %) were added to an oven-dried scintillation vial equipped with a magnetic stir bar and the vial was cycled into a glove box. The vial was charged with toluene (2 mL) and heated at 30 °C for 30 min, generating a red/orange solution. Enaminone **12e** (1 M in toluene, 250 μL, 0.250 mmol, 1.00 equiv) and additional toluene (6.34 mL, total added = 7.59 mL, 0.033 M) were added, producing a green solution. The vial was sealed with a Teflon-lined cap, removed from the glove box, and lowered into a heating block (40 °C). After 2 days, the reaction transitioned back to an orange solution. Subsequently, the reaction was filtered through a silica gel plug, rinsed with EtOAc, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO_2, 28 x 3 cm, 100% hexanes→5%→10% EtOAc in hexanes) to afford enaminone **15e** (72.6 mg, 0.204 mmol, 82% yield) as a pale yellow oil; R_f = 0.65 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.29 (m, 2H), 7.26–7.22 (m, 1H), 7.17–7.14 (m, 2H), 5.69 (dddd, J = 16.8, 10.2, 7.4, 7.4 Hz, 1H), 5.63 (t, J = 0.9 Hz, 1H), 5.07–4.99 (m, 2H), 4.78 (s, 2H), 2.75 (tm, J = 6.1 Hz, 2H), 2.29 (dddd, J = 13.7, 7.3, 1.2, 1.2 Hz, 1H), 2.13 (dddd, J = 13.7, 7.5, 1.2, 1.2 Hz, 1H), 1.90–1.84 (m, 1H), 1.71–1.65 (m, 1H), 1.43 (s, 9H), 1.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.6, 161.6, 153.0, 137.4, 134.1, 128.8, 127.4, 126.4, 118.2, 115.4, 82.6, 52.9, 43.2, 41.2, 33.5, 28.2, 27.2, 21.9; IR (Neat

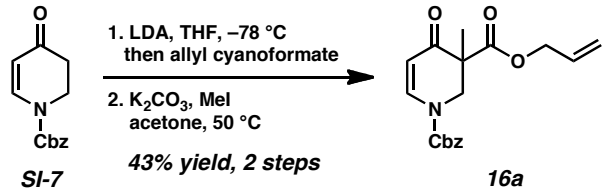
Film NaCl) 3066, 3031, 3004, 2976, 2931, 2868, 1716, 1656, 1598, 1497, 1455, 1428, 1382, 1368, 1350, 1326, 1302, 1243, 1209, 1192, 1153, 1076, 1030, 998, 946, 916, 858, 779, 767, 734 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{22}H_{30}O_3N$ $[M+H]^+$: 356.2229, found 356.2220; $[\alpha]_D^{25.0}$ –23.61 (c 0.92, $CHCl_3$, 82% ee); JASCO SFC conditions: 7% MeOH in CO_2, 5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 4.04, minor = 2.20.



Enaminone 15f. $Pd_2(dba)_3$ (10.2 mg, 0.0111 mmol, 5.1 mol %) and (*S*)-*t*-BuPHOX (**3**, 10.8 mg, 0.0279 mmol, 12.7 mol %) were added to an oven-dried scintillation vial equipped with a magnetic stir bar and the vial was cycled into a glove box. The vial was charged with toluene (2 mL) and heated at 30 °C for 30 min, generating a red/orange solution. Enaminone **12f** (1 M in toluene, 220 μL, 0.220 mmol, 1.00 equiv) and additional toluene (5.46 mL, total added = 6.68 mL, 0.033 M) were added, producing a green solution. The vial was sealed with a Teflon-lined cap, removed from the glove box, and lowered into a heating block (40 °C). After 2 days, the reaction transitioned back to an orange solution. Subsequently, the reaction was filtered through a silica gel plug, rinsed with EtOAc, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO_2, 27 x 2 cm, 100% hexanes→5%→10%→15% EtOAc in hexanes) to afford enaminone **15f** (64.1 mg, 0.157 mmol, 71% yield) as a pale yellow oil; R_f = 0.55 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dm, J = 8.3 Hz, 2H), 7.35 (dm, J = 8.6 Hz, 2H), 7.33–7.26 (m, 3H), 7.25–7.22 (m, 2H), 5.60–5.50 (m, 2H), 4.98 (dm, J = 10.2 Hz, 1H), 4.86 (dm, J = 17.0 Hz, 1H), 4.74 (d, J = 15.0 Hz, 1H), 4.66 (d, J = 15.0 Hz, 1H), 2.56–2.44 (m, 2H), 2.46 (s, 3H), 1.99–1.86 (m, 2H), 1.70 (ddd, J = 13.9, 6.6, 5.3 Hz, 1H), 1.55 (ddd, J = 13.9, 7.2, 5.5 Hz, 1H), 0.85 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.9, 157.74, 144.7, 135.4, 135.3, 133.7, 130.1, 128.9, 128.1, 127.9, 127.5, 120.7, 118.3, 53.1, 43.2, 40.6, 32.2, 27.9, 21.8, 21.3; IR (Neat Film NaCl) 3066, 3027, 2963, 2928, 2868, 1663, 1654, 1597, 1496, 1453, 1424, 1355, 1306, 1164, 1089, 1055, 1028, 1001, 912, 859, 814, 745 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{24}H_{28}O_3NS$ $[M+H]^+$: 410.1784, found 410.1792; $[\alpha]_D^{25.0}$ –33.05 (c 0.37, $CHCl_3$, 84% ee); JASCO SFC conditions: 10% MeOH, 5 mL/min, AD-H column, λ = 210 nm, t_R (min): major = 5.60, minor = 4.73.

Procedures for the Preparation of 2,3-Dihydropyridin-4-ones

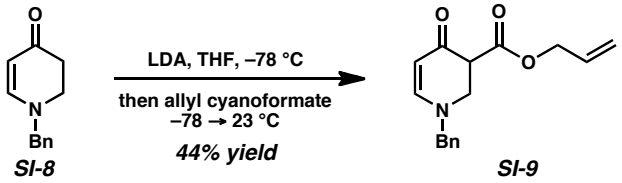
2,3-Dihydropyridin-4-one Allylic Alkylation Precursors



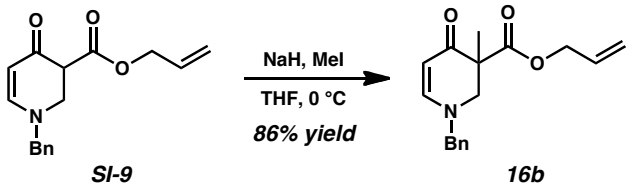
SI-7 *16a*

2,3-Dihydropyridin-4-one 16a. A 100 mL round-bottom flask equipped with a magnetic stir bar was charged with diisopropyl amine (442 μL, 3.01 mmol, 1.20 equiv) and THF (28 mL). The flask was cooled to –78 °C bath (Dry ice/IPA) and *n*-BuLi (1.30 mL, 3.01 mmol, 2.32 M in hexanes, 1.20 equiv) was added. The reaction was allowed to warm to 0 °C over 1 h. The solution was cooled back to –78 °C and was added dropwise to a solution of 2,3-Dihydropyridin-4-one **SI-7**[9] (580 mg, 2.51 mmol, 1.0 equiv) in THF (40 mL) at –78 °C using positive pressure cannulation. The reaction was stirred for 1 h at this temperature before allyl cyanoformate (300 μL, 2.88 mmol, 1.15 equiv) was added dropwise. The flask was removed from the bath and allowed to warm to room temperature slowly and stirred overnight. The reaction was quenched with water and sat. NH_4Cl solution. The phases were separated and the aqueous phase was extracted three times with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduce pressure. The resulting yellow oil was purified by flash-chromatography (2:1 Et_2O/hexanes).

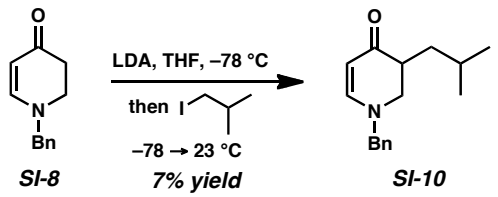
The yellow oil was transferred to an argon filled 25 mL Schlenk tube equipped with a magnetic stir bar using several acetone rinses (3 x 2 mL). K_2CO_3 (252 mg, 1.83 mmol, 2.0 equiv) and methyl iodide (115 μL, 1.84 mmol, 2.02 equiv) were added to the reaction. The resulting suspension was heated to 50 °C and vigorously stirred for 14 h. Upon completion, the reaction was allowed to cool to room temperature and filtered through a plug of celite. The resulting yellow solution was concentrated under reduced pressure and purified by flash-chromatography (1:1 Et_2O/hexanes) to afford 2,3-Dihydropyridin-4-one **16a** (210 mg, 0.64 mmol, 43% yield over two steps) as a yellow oil; R_f = 0.38 (1:1 Et_2O/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (br s, J = 22.5 Hz, 1H), 7.45–7.31 (m, 5H), 5.82 (ddt, J = 17.2, 10.4, 5.6 Hz, 1H), 5.37 (br s, 1H), 5.27 (s, 2H), 5.26 (dq, J = 17.1, 1.5 Hz, 1H), 5.20 (dq, J = 10.5, 1.3 Hz, 1H), 4.64 (dd, J = 13.5, 0.9 Hz, 1H), 4.59 (dt, J = 5.6, 1.5 Hz, 2H), 3.63 (d, J = 13.5 Hz, 1H), 1.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.9, 170.1, 152.5, 142.7, 134.8, 131.3, 128.8, 128.7, 128.4, 118.6, 106.2, 69.2, 66.1, 51.6, 50.5, 17.9; IR (Neat Film, NaCl) 3076, 3034, 2965, 2929, 2360, 2922, 1729, 1668, 1605, 1498, 1456, 1418, 1393, 1344, 1302, 1205, 1157, 1101, 1029, 966, 917, 814, 763 cm^{-1}; HRMS (MM: ESI/APCI+) *m/z* calc'd for $C_{18}H_{19}NO_5$ $[M+H]^+$: 330.1335, found 330.1335.



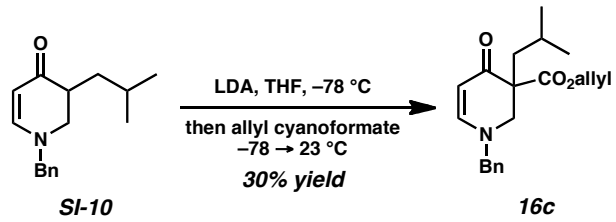
2,3-Dihydropyridin-4-one SI-9. To a flame-dried 50 mL Schlenk round-bottom flask equipped with a magnetic stir bar was added 2,3-Dihydropyridin-4-one **SI-8**[10] (162.0 mg, 0.87 mmol) and THF (10 mL). The solution was cooled to –78 °C and LDA (0.1 M in THF, 9.10 mL, 0.91 mmol, 1.05 equiv) was added dropwise by syringe. After 1 h at –78 °C, allyl cyanoformate (105.2 mg, 0.96 mmol, 1.10 equiv) was added, and the reaction mixture was stirred for another 3 h and quenched with a sat. NH_4Cl sol. The reaction was transferred to a separatory funnel where the aqueous layer was extracted with CH_2Cl_2 (4 x 30 mL). The combined organics were washed with brine, dried over $MgSO_4$, fitered, and concentrated under reduced pressure. The resulting crude mixture was purified by flash chromatography (SiO_2, 10 x 2.5 cm, 30% EtOAc → 50% EtOAc in hexanes) to afford 2,3-Dihydropyridin-4-one **SI-9** (104.8 mg, 0.38 mmol, 44% yield) as a yellow oil; R_f = 0.30 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.31 (m, 3H), 7.28–7.23 (m, 2H), 7.17 (d, *J* = 7.5 Hz, 1H), 5.87 (ddt, *J* = 17.2, 10.5, 5.7 Hz, 1H), 5.32 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.22 (dq, *J* = 10.4, 1.3 Hz, 1H), 5.06 (d, *J* = 7.5 Hz, 1H), 4.69–4.55 (m, 2H), 4.40 (d, *J* = 2.5 Hz, 2H), 3.76 (dd, *J* = 13.3, 8.7 Hz, 1H), 3.51 (dd, *J* = 13.3, 5.9 Hz, 1H), 3.40 (dd, *J* = 8.7, 5.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.2, 168.8, 153.6, 135.1, 131.6, 129.1, 128.5, 127.8, 118.6, 97.7, 66.0, 60.0, 50.5, 48.4; IR (Neat Film NaCl) 3029, 2935, 2853, 1732, 1641, 1588, 1494, 1455, 1393, 1361, 1321, 1204, 1154, 1078, 1028, 991, 967, 935, 78, 731 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{16}H_{18}NO_3$ $[M+H]^+$: 272.1287, found 272.1314.



2,3-Dihydropyridin-4-one 16b. To a flame-dried 25 mL round-bottom flask equipped with a magnetic stir bar was cycled into a glove box (4 x 1 min cycles) and loaded with sodium hydride (9.3 mg, 0.39 mmol, 1.00 equiv). The flask was removed from the glove box, reconnected to an Ar-filled manifold, charged with THF (3 mL), and cooled to 0 °C. A solution of 2,3-Dihydropyridin-4-one **SI-9** (104.2 mg, 0.39 mmol, 1.00 equiv) was added by syringe and the mixture was stirred at 0 °C for 30 min. The reaction was quenched with water, transferred to a separatory funnel, and extracted four times with CH_2Cl_2. The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was purified by flash chromatography (SiO_2, 10 x 2.5 cm, 30% EtOAc in hexanes) to afford 2,3-Dihydropyridin-4-one **16b** (95.9 mg, 0.34 mmol, 86% yield) as a colorless oil; R_f = 0.40 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43–7.30 (m, 3H), 7.25–7.20 (m, 2H), 7.13 (d, *J* = 7.4 Hz, 1H), 5.83 (ddt, *J* = 17.1, 10.8, 5.5 Hz, 1H), 5.27 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.19 (dq, *J* = 10.5, 1.3 Hz, 1H), 5.01 (d, *J* = 7.4 Hz, 1H), 4.56 (qdt, *J* = 13.4, 5.5, 1.5 Hz, 2H), 4.46–4.30 (m, 2H), 3.78 (d, *J* = 13.2 Hz, 1H), 3.15 (d, *J* = 13.3 Hz, 1H), 1.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.0, 171.6, 152.7, 135.1, 131.7, 129.0, 128.0, 118.1, 97.0, 65.8, 60.0, 55.0, 51.2, 18.5; IR (Neat Film NaCl) 3029, 2979, 2934, 2871, 1732, 1642, 1592, 1494, 1455, 1393, 1372, 1359, 1343, 1295, 1223, 1166, 1115, 1028, 975, 937, 792, 732 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{17}H_{20}NO_3$ $[M+H]^+$: 286.1443, found 286.1480.

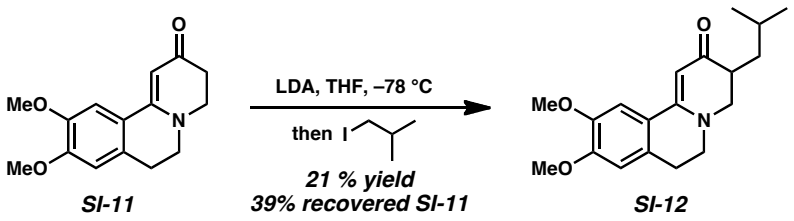


2,3-Dihydropyridin-4-one SI-10. To a flame-dried 100 mL Schlenk round-bottom flask equipped with a magnetic stir bar was added 2,3-Dihydropyridin-4-one **SI-8**[10] (0.68 g, 3.63 mmol) and THF (30 mL). The solution was cooled to –78 °C and LDA (19.0 mL, 3.80 mmol, 1.05 equiv, 0.2 M in THF) was added dropwise by syringe. After 1 h at –78 °C, 1-iodo-2-methylpropane (0.87 g, 4.73 mmol, 1.30 equiv) was added, and the reaction was stirred for another 1 h at –78 °C, brought to room temperature, and stirred overnight. The reaction was quenched with a sat. NH_4Cl sol., transferred to a separatory funnel, and extracted with CH_2Cl_2 (50 mL x 3). The combined organics were washed with brine, dried over $MgSO_4$, fitered, and concentrated. The crude mixture was purified by flash chromatography (SiO_2, 10 x 3 cm, 30% EtOAc in hexanes) to afford 2,3-Dihydropyridin-4-one **SI-10** (58.2 mg, 0.24 mmol, 7% yield) as a yellow oil; R_f = 0.50 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46–7.32 (m, 3H), 7.29–7.25 (m, 2H), 7.12 (d, J = 7.4 Hz, 1H), 4.96 (d, J = 7.4 Hz, 1H), 4.43–4.28 (m, 2H), 3.38 (dd, J = 13.0, 5.4 Hz, 1H), 3.08 (dd, J = 13.0, 7.7 Hz, 1H), 2.29 (ddt, J = 10.1, 7.6, 5.2 Hz, 1H), 1.56 (ddd, J = 14.0, 9.3, 5.0 Hz, 1H), 1.43–1.34 (m, 1H), 1.18 (ddd, J = 13.7, 9.6, 5.3 Hz, 1H), 0.82 (d, J = 6.5 Hz, 3H), 0.78 (d, J = 6.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.0, 152.8, 135.8, 128.9, 128.3, 127.8, 97.7, 60.0, 50.4, 42.0, 37.5, 25.0, 23.3, 21.4; IR (Neat Film NaCl) 3029, 2954, 2868, 1633, 1593, 1494, 1463, 1455, 1385, 1361, 1302, 1210, 1161, 1077, 778, 730 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{16}H_{22}NO$ $[M+H]^+$: 244.1701, found 244.1707.

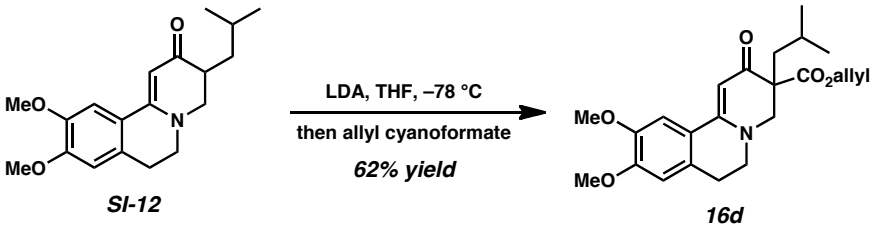


2,3-Dihydropyridin-4-one 16c. To a flame-dried 25 mL Schlenk tube equipped with a magnetic stir bar was added 2,3-Dihydropyridin-4-one **SI-10** (50.5 mg, 0.21 mmol) and THF (5 mL). After the solution was cooled to -78 °C, LDA (2.2 mL, 0.22 mmol, 1.06 equiv, 0.1 M in THF) was added dropwise by syringe. The mixtrure was stirred for 1 h at -78 °C and allyl cyanoformate (26.4 mg, 0.24 mmol, 1.20 equiv) was added. The reaction mixture was stirred for another 3 h and quenched with saturated NH_4Cl aqueous. The aqueous layer was extracted with CH_2Cl_2 (30 mL x 4) and the combined organics were washed with brine, dried over $MgSO_4$, and concentrated. The crude mixture was purified by flash chromatography (SiO_2, 10 x 1 cm, 30% EtOAc in hexanes) to afford **16c** (19.8 mg, 0.06 mmol, 30% yield) as a yellow oil; R_f = 0.30 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45_7.31 (m, 3H), 7.29_7.19 (m, 2H), 7.07 (d, *J* = 7.4 Hz, 1H), 5.86 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.32 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.20 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.96 (d, *J* = 7.3 Hz, 1H), 4.67_4.51 (m, 2H), 4.43 (s, 2H), 3.82 (d, *J* = 13.4 Hz, 1H), 3.27 (d, *J* = 13.4 Hz, 1H), 2.03 (dd, *J* = 14.2, 7.1 Hz, 1H), 1.64_1.45 (m, 2H), 0.85 (d, *J* = 6.5 Hz, 3H), 0.80 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.7, 170.9, 152.2, 135.1, 131.7, 129.0, 128.1, 118.4, 96.7, 65.8, 60.1, 54.4, 52.6, 40.4, 24.6, 24.3, 23.2; IR (Neat Film NaCl) 3029, 2957, 2870, 1729, 1644, 1593, 1455, 1360, 1267, 1215, 1159,

1132, 1077, 1029, 971, 778, 735 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{20}H_{26}NO_3$ $[M+H]^+$: 328.1913, found 328.1947.



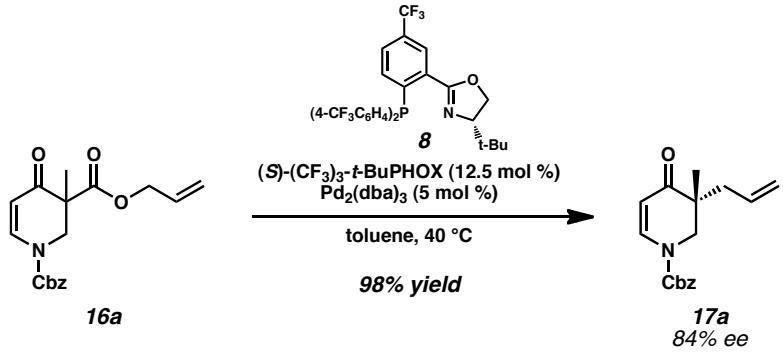
2,3-Dihydropyridin-4-one SI-12. To a cooled (–78 °C) solution of **SI-11**[11] (0.67 g, 2.6 mmol, 1 equiv) in THF (25 mL) was added LDA (30 mL, 0.1 M, in THF, 30 mmol, 1.15 equiv) dropwise over 10 min. The reaction was stirred for one hour before 1-iodo-2-methylpropane (0.57 g, 3.1 mmol, 1.20 equiv) was added dropwise. After 2 hours, the reaction mixture was brought to room temperature and stirred overnight. The reaction was quenched with sat. NH_4Cl sol. and transferred to a separatory funnel where the aqueous phase was extracted four times with CH_2Cl_2. The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude mixture purified by flash column chromatography (SiO_2, 15 x 3 cm, 50% EtOAc in hexanes→100% EtOAc) to afford recovered **SI-11** (0.26 g, 1.01 mmol, 39% recovered) **SI-12** (0.17 g, 0.54 mmol, 21% yield) as a yellow solid; R_f = 0.20 (50% EtOAc in hexanes). Spectral data matches that reported previously.[12] NMR data is included to assist the reader. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14 (s, 1H), 6.65 (s, 1H), 5.62 (s, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 3.64 (dd, J = 12.5, 5.3 Hz, 1H), 3.45–3.24 (m, 3H), 2.94 (td, J = 6.3, 3.5 Hz, 2H), 2.51–2.35 (m, 1H), 1.80–1.59 (m, 2H), 1.36–1.19 (m, 1H), 0.96 (d, J = 6.2 Hz, 3H), 0.91 (d, J = 6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.5, 156.6, 151.5, 148.1, 129.0, 120.9, 110.5, 108.4, 94.4, 56.1, 55.9, 49.2, 42.1, 37.6, 28.6, 25.6, 23.6, 21.9.



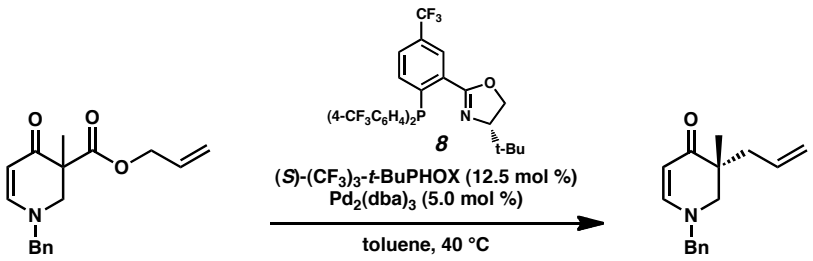
2,3-Dihydropyridin-4-one 16d. A solution of **SI-12** (149.1 mg, 0.47 mmol in 15 mol of THF) was cooled to –78 °C and LDA (5.2 mL, 0.1 M in THF, 0.52 mmol, 1.10 equiv) was added dropwise. The reaction was stirred for one hour before allyl cyanoformate (60.2 mg, 0.54 mmol, 1.15 equiv) was added dropwise. After 12 hours, the reaction was quenched with sat. NH_4Cl sol. and allowed to warm to room temperature. The reaction contents were transferred to a separatory funnel where the aqueous phase was extracted four times with CH_2Cl_2. The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude mixture was purified by flash column chromatography (SiO_2, 15 x 3 cm, 50% EtOAc in hexanes) to afford 2,3-Dihydropyridin-4-one **16d** (116.0 mg, 0.29 mmol, 62% yield) as a yellow solid; R_f = 0.40 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (s, 1H), 6.66 (s, 1H), 5.87 (ddt, J = 17.2, 10.3, 5.6 Hz, 1H), 5.59 (s, 1H), 5.30 (dq, J = 17.2, 1.6 Hz, 1H), 5.17 (dq, J = 10.4, 1.3 Hz, 1H), 4.61 (ddt, J = 5.6, 2.7, 1.4 Hz, 2H), 4.05 (d, J = 13.0 Hz, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 3.62 (d, J = 13.1 Hz, 1H), 3.55 (ddd, J = 12.1, 8.1, 5.7 Hz, 1H), 3.43 (ddd, J = 12.2, 6.9, 5.4 Hz, 1H), 3.00–2.77 (m, 2H), 2.23–2.06 (m, 1H), 1.79–1.60 (m, 2H), 0.96 (d, J = 6.2 Hz, 3H), 0.90 (d, J = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.1,

171.0, 155.7, 151.6, 148.0, 131.8, 129.0, 120.5, 118.3, 110.3, 108.4, 92.8, 65.7, 56.5, 56.0, 56.0, 54.5, 48.6, 40.4, 28.3, 25.0, 24.4, 23.5; IR (Neat Film NaCl) 2955, 1720, 1625, 1583, 1544, 1495, 1343, 1237, 1211, 1167, 11523, 1120, 1016 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{23}H_{30}NO_5$ $[M+H]^+$: 400.2124, found 400.2110.

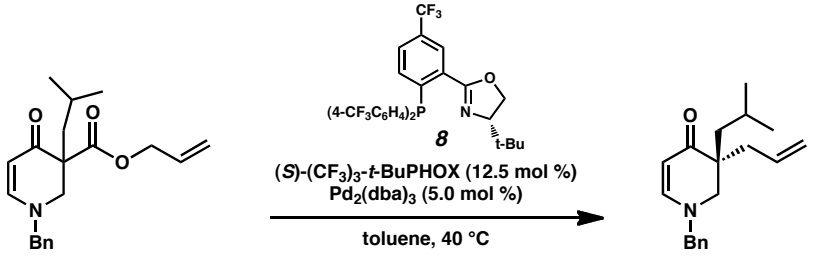
2,3-Dihydropyridin-4-one Allylic Alkylation Products



2,3-Dihydropyridin-4-one 17a. 2,3-Dihydropyridin-4-one **16a** (27.6 mg, 0.084 mmol, 1.0 equiv) was preloaded in a 1 dram vial and cycled into a glove box. A separate 1 dram vial was loaded with (S)-$(CF_3)_3$-*t*-Bu-PHOX (**8**, 4.1 mg, 10.5 μmol, 0.125 equiv), $Pd_2(dba)_3$ (3.9 mg, 4.20 μmol, 0.05 equiv), and a magnetic stir-bar. Toluene (1.6 mL) was added and the black suspension was stirred at 30 °C in a heating block for 30 min. 2,3-Dihydropyridin-4-one **16a** was dissolved in 1 mL of toluene and added to the orange catalyst solution, causing an immediate color change to olive green. The vial was capped with a Teflon screw cap and the reaction was stirred for 14 h at 40 °C in the glove box. Upon completion of the reaction the vial was allowed to cool to room temperature and removed from the glove box. The reaction was concentrated under reduced pressure and the resulting brown oil was purified by flash-chromatography (1:1 Et_2O/hexanes) to afford 2,3-Dihydropyridin-4-one **17a** (23.7 mg, 0.083 mmol, 98%) as a colorless oil; R_f = 0.73 (1:1 Et_2O/hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.42–7.36 (m, 5H), 5.69 (td, J = 17.3, 7.5 Hz, 1H), 5.27 (d, J = 2.7 Hz, 3H), 5.05 (dd, J = 29.7, 13.4 Hz, 2H), 3.91 (d, J = 13.4 Hz, 1H), 3.58 (d, J = 11.8 Hz, 1H), 2.22 (ddd, J = 46.4, 13.8, 7.5 Hz, 2H), 1.07 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.3, 152.7, 141.7, 135.0, 132.6, 128.8, 128.7, 128.4, 119.2, 106.4, 69.1, 51.4, 43.4, 39.4, 19.5; IR (Neat Film, NaCl) 2922, 1728, 1673, 1602, 1498, 1453, 1416, 1381, 1342, 1305, 1232, 1200, 1144, 1119, 1088, 956, 913, 813, 761 cm^{-1}; HRMS (MM: ESI/APCI+) *m/z* calc'd for $C_{17}H_{19}NO_3$ $[M+H]^+$: 286.1443, found 286.1438; $[\alpha]_D^{25.0}$ +9.88 (*c* 1.15, $CHCl_3$, 84% ee); Thar SFC conditions: 10% MeOH in CO_2, 3 mL/min, Chiralpak AD-H column, λ = 254 nm, t_R (min): major = 2.80, minor = 3.13.

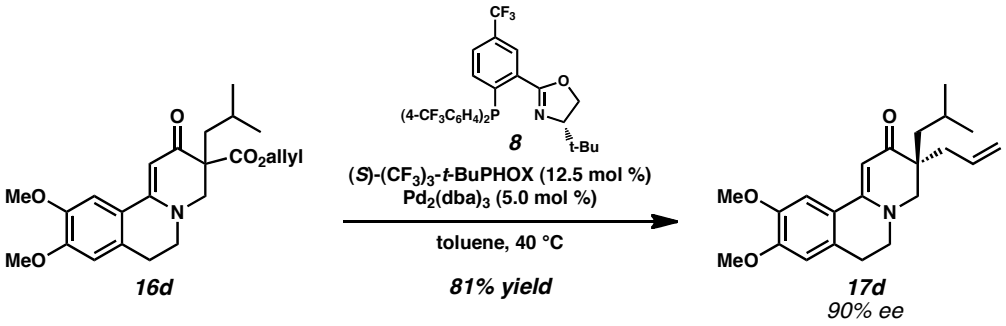


2,3-Dihydropyridin-4-one 17b. In a glove box, $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol, 5.0 mol %) and (*S*)-$(CF_3)_3$-*t*-BuPHOX (**8**, 3.7 mg, 0.00625 mmol, 12.5 mol %) were added to a scintillation vial equipped with a stir bar. The vial was charged with toluene (0.5 mL) and heated at 40 °C for 30 min. 2,3-Dihydropyridin-4-one **16b** (14.3 mg, 0.050 mmol, 1.00 equiv) and additional toluene (1.0 mL, total added = 1.5 mL, 0.033 M) were added, producing a green solution. The vial was sealed and stirred at 40 °C until the starting material was fully converted, determined by LCMS. The reaction mixture was filtered through a celite pad, rinsed with EtOAc, and concentrated under reduced pressure. The crude oil was purified by flash chromatography (SiO_2, 5 x 1 cm, 30% EtOAc in hexanes) to afford 2,3-Dihydropyridin-4-one **17b** (11.3 mg, 0.047 mmol, 94% yield) as a yellow oil; R_f = 0.30 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.25 (m, 3H), 7.24–7.14 (m, 2H), 7.03 (d, *J* = 7.4 Hz, 1H), 5.54 (ddt, *J* = 17.4, 10.1, 7.4 Hz, 1H), 4.94 (ddt, *J* = 9.9, 1.9, 0.9 Hz, 1H), 4.91–4.81 (m, 2H), 4.27 (d, *J* = 3.1 Hz, 2H), 3.07 (d, *J* = 13.0 Hz, 1H), 2.90 (d, *J* = 13.0 Hz, 1H), 2.22–1.97 (m, 2H), 0.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.5, 152.3, 135.6, 133.6, 129.0, 129.0, 129.0, 128.3, 128.0, 118.3, 96.9, 60.1, 55.9, 42.7, 39.7, 20.1, 20.0; IR (Neat Film NaCl) 3067, 3029, 2962, 2926, 1634, 1593, 1455, 1359, 1321, 1204, 1172, 1076, 1001, 916, 795 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{18}H_{20}NO$ $[M+H]^+$: 242.1545, found 242.1553; $[\alpha]_D^{25.0}$ +86.46 (c 1.16, $CHCl_3$, 86% ee); HPLC conditions: 10% IPA in hexanes, 1 mL/min, Chiralcel OJ column, λ = 210 nm, t_R (min): major = 18.77, minor = 21.21.



2,3-Dihydropyridin-4-one 17c. In a glove box, $Pd_2(dba)_3$ (1.4 mg, 0.0015 mmol, 5.0 mol %) and (*S*)-$(CF_3)_3$-*t*-BuPHOX (**8**, 2.2 mg, 0.00375 mmol, 12.5 mol %) were added to a scintillation vial equipped with a stir bar. The vial was charged with toluene (0.5 mL) and heated at 40 °C for 30 min. 2,3-Dihydropyridin-4-one **16c** (9.8 mg, 0.030 mmol, 1.00 equiv) and additional toluene (0.5 mL, total added = 1.0 mL, 0.030 M) were added, producing a green solution. The vial was sealed and stirred at 40 °C until the starting material was fully converted, determined by TLC. The reaction mixture was filtered through a celite pad, rinsed with EtOAc, and concentrated under reduced pressure. The crude oil was purified by flash chromatography (SiO_2, 5 x 1 cm, 30% EtOAc in hexanes) to afford 2,3-Dihydropyridin-4-one **17c** (6.9 mg, 0.024 mmol, 81%

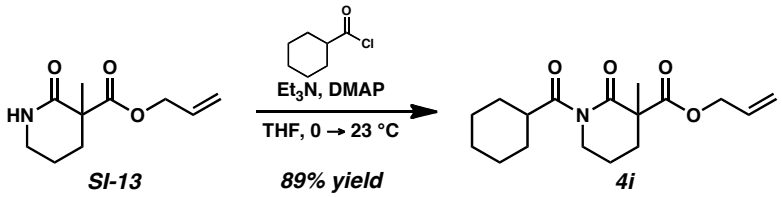
yield) as a yellow oil; R_f = 0.40 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.32 (m, 3H), 7.29–7.22 (m, 2H), 7.05 (d, *J* = 7.4 Hz, 1H), 5.62 (dddd, *J* = 17.1, 10.1, 7.8, 7.0 Hz, 1H), 5.00 (ddt, *J* = 10.1, 2.1, 1.0 Hz, 1H), 4.97–4.91 (m, 2H), 4.33 (s, 2H), 3.13 (d, *J* = 3.2 Hz, 2H), 2.34–2.24 (m, 1H), 2.16 (ddt, *J* = 14.1, 7.8, 1.1 Hz, 1H), 1.61 (qd, *J* = 6.7, 5.6 Hz, 1H), 1.47 (dd, *J* = 14.2, 6.3 Hz, 1H), 1.33 (dd, *J* = 14.2, 5.5 Hz, 1H), 0.84 (d, *J* = 6.6 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.8, 151.8, 135.6, 134.1, 128.9, 128.3, 128.1, 118.1, 98.0, 60.1, 54.6, 41.6, 38.9, 24.9, 24.4, 23.9; IR (Neat Film NaCl) 3072, 3029, 2954, 2867, 1633, 1593, 1494, 1455, 1385, 1361, 1296, 1205, 1173, 1105, 1076, 1028, 998, 793, 736 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{19}H_{26}NO$ $[M+H]^+$: 284.2014, found 284.2023; $[\alpha]_D^{25.0}$ +50.23 (c 0.65, $CHCl_3$, 88% ee); HPLC conditions: 7% IPA in hexanes, 1 mL/min, Chiralcel OJ column, λ = 210 nm, t_R (min): major = 11.44, minor = 14.80.



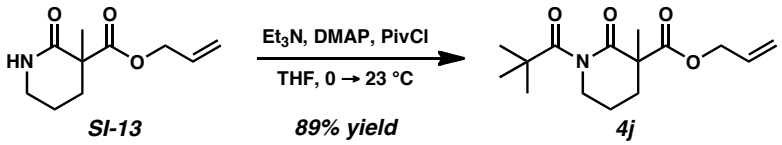
2,3-Dihydropyridin-4-one 17d. $Pd_2(dba)_3$ (1.4 mg, 0.0015 mmol, 5.0 mol %) and (*S*)-$(CF_3)_3$-*t*-BuPHOX (**8**, 2.2 mg, 0.00375 mmol, 12.5 mol %) were added to an oven-dried Schlenk tube equipped with a magnetic stir bar and the tube was cycled with vacuum/argon for 3 times. The tube was charged with toluene (1 mL) and heated at 40 °C for 30 min, generating a red/orange solution. 2,3-Dihydropyridin-4-one **16d** (11.9 mg, 0.03 mmol, 1.00 equiv) were added and the tube was lowered into a heating block (40 °C). After 3 hours, the reaction was completed, monitored by TLC. Subsequently, the reaction was filtered through a silica gel plug, rinsed with EtOAc, and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography (SiO_2, 10 x 2 cm, 50% EtOAc in hexanes) to afford dihydropyridine-4-one **17d** (8.6 mg, 0.0242 mmol, 81% yield) as yellow oil; R_f = 0.50 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (s, 1H), 6.66 (s, 1H), 5.82 (ddt, J = 17.4, 10.2, 7.4 Hz, 1H), 5.62 (s, 1H), 5.10–5.03 (m, 2H), 3.91 (s, 3H), 3.87 (s, 3H), 3.39 (s, 2H), 3.37 (td, J = 7.0, 6.5, 1.5 Hz, 2H), 2.99–2.89 (m, 2H), 2.43 (ddt, J = 13.9, 7.2, 1.3 Hz, 1H), 2.25 (ddt, J = 14.0, 7.7, 1.1 Hz, 1H), 1.74 (hd, J = 6.6, 5.0 Hz, 1H), 1.66 (dd, J = 14.1, 6.5 Hz, 1H), 1.44 (dd, J = 14.1, 5.1 Hz, 1H), 0.94 (d, J = 6.6 Hz, 3H), 0.90 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.3, 155.6, 151.4, 148.0, 134.7, 128.7, 120.8, 117.9, 110.4, 108.3, 94.3, 58.9, 56.0, 48.9, 46.1, 41.7, 39.2, 28.4, 25.1, 24.5, 24.1; IR (Neat Film NaCl) 2953, 1622, 1586, 1549, 1495, 1464, 1342, 1212, 1173, 1110, 1016, 913, 794 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{22}H_{30}NO_3$ $[M+H]^+$: 356.2147, found 356.2221; $[\alpha]_D^{25.0}$ +32.49 (c 0.71, $CHCl_3$, 90% ee); HPLC conditions: 30% IPA in hexanes, 1 mL/min, Chiralpak AD column, λ = 254 nm, t_R (min): major = 21.87, minor = 18.59.

Procedures for the Preparation of Lactams

Lactam Allylic Alkylation Precursors



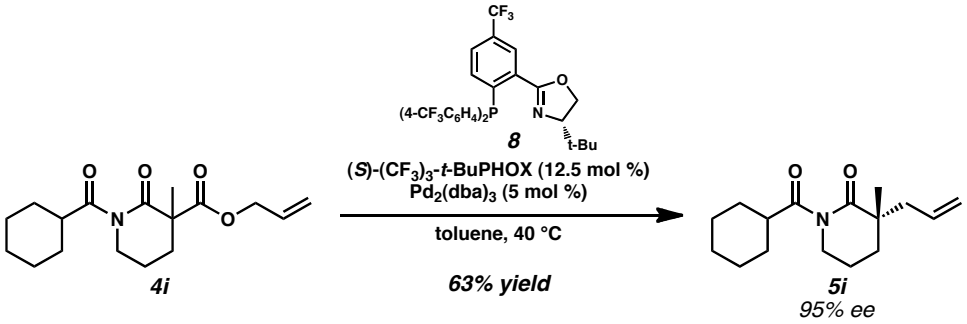
Lactam 4i. Lactam **SI-13**[13] (117.8 mg, 0.597 mmol, 1.00 equiv) was transferred to a flame-dried 15 mL round-bottom flask using THF (4 x 0.5 mL + 1 x 0.4 mL rinses, total = 2.4 mL, 0.25 M). Et_3N (250 μL, 1.79 mmol, 3.00 equiv) and DMAP (9.3 mg, 0.0761 mmol, 13 mol%) were added and the flask was lowered into a 0 °C bath (ice/water). Cyclohexanecarbonyl chloride (160 μL, 1.20 mmol, 2.00 equiv) was added dropwise and the reaction transitioned from a solution to a white slurry. The ice bath expired gradually as the reaction was stirred overnight. After 15 h of stirring, no starting material remained by TLC analysis. The reaction was subsequently quenched with brine (15 mL) and transferred to a separatory funnel where the aqueous layer was extracted four times with EtOAc. The combined organics (100 mL) were rinsed twice with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography (SiO_2, 27.5 x 2 cm, 100% hexanes→10% EtOAc in hexanes) to afford lactam **4i** (163.5 mg, 0.532 mmol, 89% yield) as a yellow oil; R_f = 0.60 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.88 (dddd, J = 17.1, 10.4, 5.8 Hz, 1H), 5.32 (dq, J = 17.2, 1.5 Hz, 1H), 5.25 (dq, J = 10.4, 1.2 Hz, 1H), 4.64 (ddt, J = 5.8, 2.5, 1.3 Hz, 2H), 3.77 (ddd, J = 13.1, 7.7, 5.1 Hz, 1H), 3.58 (dddd, J = 13.4, 7.0, 5.0, 1.1 Hz, 1H), 3.27 (tt, J = 11.4, 3.2 Hz, 1H), 2.42 (dddd, J = 13.4, 6.0, 4.9, 0.9 Hz, 1H), 1.95 (dtd, J = 10.5, 3.5, 1.8 Hz, 1H), 1.92–1.80 (m, 3H), 1.79–1.70 (m, 3H), 1.67 (dtt, J = 10.8, 3.2, 1.5 Hz, 1H), 1.52 (s, 3H), 1.47–1.34 (m, 2H), 1.34–1.16 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.3, 173.5, 172.7, 131.4, 119.2, 66.4, 53.5, 45.7, 44.6, 33.1, 30.1, 29.6, 26.1, 25.9, 25.8, 23.0, 20.3; IR (Neat Film NaCl) 3086, 2931, 2855, 1738, 1694, 1652, 1479, 1451, 1378, 1330, 1301, 1249, 1218, 1196, 1159, 1134, 1073, 1053, 1032, 981, 957, 939, 896, 887, 842, 796, 773 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{17}H_{26}O_4N$ $[M+H]^+$: 308.1856, found 308.1871.



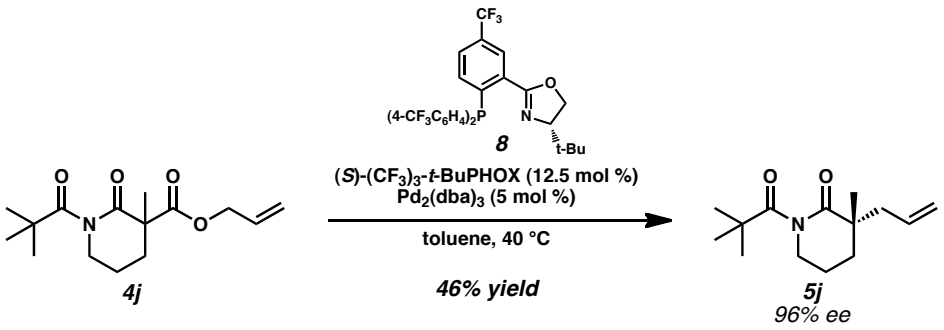
Lactam 4j. Lactam **SI-13**[9] (480 mg, 2.4 mmol, 1.0 equiv) in a 25 mL round-bottom flask equipped with a magnetic stir bar was taken up in THF (9.6 mL, 0.25 M). Et_3N (1.0 mL, 7.2 mmol, 3.0 equiv) and DMAP (29 mg, 0.24 mmol, 0.10 equiv) were added and the flask was lowered into a 0 °C bath (ice/water). Pivaloyl chloride (0.59 mL, 4.8 mmol, 2.0 equiv) was added dropwise and the reaction transitioned from a solution to a white slurry. The ice bath expired gradually as the reaction was stirred overnight. After 24 h of stirring, TLC analysis indicated that conversion had ceased at approximately 90%. The reaction was subsequently diluted with 20 mL EtOAc, quenched with brine (20 mL) and transferred to a separatory funnel where the aqueous layer was extracted three times with EtOAc (20 mL). The combined organics were washed twice with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under

reduced pressure. The resulting crude oil was purified by flash column chromatography (SiO_2, 11 x 3 cm, 20% EtOAc in hexanes) to afford lactam **4j** (612 mg, 2.18 mmol, 89% yield) as a pale yellow oil; R_f = 0.37 (20% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.90 (ddt, *J* = 17.2, 10.4, 5.9 Hz, 1H), 5.33 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.25 (dq, *J* = 10.4, 1.3 Hz, 1H), 4.70–4.59 (m, 2H), 3.62 (ddd, *J* = 12.8, 8.2, 4.9 Hz, 1H), 3.45 (dddd, *J* = 12.4, 6.2, 4.9, 1.0 Hz, 1H), 2.40 (dddd, *J* = 13.6, 7.1, 4.0, 1.0 Hz, 1H), 2.01–1.83 (m, 2H), 1.74 (ddd, *J* = 13.7, 9.5, 4.1 Hz, 1H), 1.52 (s, 3H), 1.29 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.8, 172.5, 131.7, 119.2, 66.4, 52.5, 47.9, 44.5, 33.6, 28.0, 22.8, 20.3; IR (Neat Film NaCl) 3434, 2090, 1650, 1257, 1125 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{15}H_{24}NO_4$ $[M+H]^+$: 282.1700, found 282.1705.

Lactam Allylic Alkylation Products



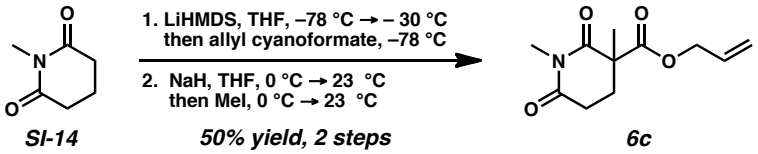
Lactam 5i. $Pd_2(dba)_3$ (16.4 mg, 0.0150 mmol, 5.0 mol %) and (*S*)-$(CF_3)_3$-*t*-BuPHOX (**8**, 22.1 mg, 0.0374 mmol, 12.5 mol %) were added to an oven-dried scintillation vial equipped with a magnetic stir bar and the vial was cycled into a glove box. The vial was charged with toluene (2.06 mL) and stirred at ambient temperature for 30 min, generating a red/orange solution. Lactam **4i** (91.9 mg, 0.299 mmol, 1.00 equiv) was transferred to the scintillation vial with toluene (3 x 2 mL + 1 x 1 mL rinses, total = 9.06 mL, 0.033 M) producing a green solution. The vial was sealed with a Teflon-lined cap, removed from the glove box, and lowered into a heating block (40 °C). After 7 days, the reaction was filtered through a silica gel plug, rinsed with EtOAc, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO_2, 27.5 x 2 cm, 100% hexanes→5%→10% EtOAc in hexanes) to afford recovered lactam **4i** (17.2 mg, 0.0560 mmol, 19% recovered) and lactam **5i** (49.8 mg, 0.189 mmol, 63% yield, 78% yield based on recovered lactam **4i**) as a yellow oil; R_f = 0.73 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74 (dddd, J = 16.6, 10.4, 7.8, 6.9 Hz, 1H), 5.13–5.06 (m, 2H), 3.76–3.67 (m, 1H), 3.57–3.49 (m, 1H), 3.18 (tt, J = 11.4, 3.3 Hz, 1H), 2.51 (ddt, J = 13.6, 6.9, 1.2 Hz, 1H), 2.27 (ddt, J = 13.6, 7.8, 1.1 Hz, 1H), 1.90 (dddd, J = 12.7, 5.5, 2.9, 1.4 Hz, 1H), 1.87–1.72 (m, 7H), 1.67 (dtt, J = 10.8, 3.5, 1.5 Hz, 1H), 1.62–1.56 (m, 1H), 1.42 (dtdd, J = 12.9, 12.0, 11.2, 3.2 Hz, 2H), 1.35–1.19 (m, 2H), 1.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.9, 179.5, 133.5, 118.9, 46.1, 45.8, 45.0, 44.5, 33.3, 30.0, 30.0, 26.1, 25.9, 25.9, 25.8, 19.8; IR (Neat Film NaCl) 3076, 2930, 2854, 1690, 1478, 1451, 1375, 1329, 1313, 1286, 1246, 1198, 1158, 1136, 1089, 1072, 1031, 996, 975, 919, 759 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{16}H_{26}O_2N$ $[M+H]^+$: 264.1958, found 264.1945; $[\alpha]_D^{25.0}$ –96.13 (c 1.06, $CHCl_3$, 95% ee); JASCO SFC conditions: 1% IPA in CO_2, 5 mL/min, Chiralcel OJ-H column, λ = 222 nm, t_R (min): major = 2.53, minor = 2.13.



Lactam 5j. $Pd_2(pmdba)_3$ (27 mg, 25 μmol, 5.0 mol %) and (*S*)-$(CF_3)_3$-*t*-BuPHOX (**8**, 37 mg, 63 μmol, 12.5 mol %) were added to an oven-dried 20 mL scintillation vial equipped with a magnetic stir bar in a glove box. The vial was charged with toluene (12 mL) and stirred at ambient temperature (28 °C) for 30 min, resulting in a deep orange solution. Lactam **4j** (140 mg, 0.50 mmol, 1.0 equiv) was transferred to the scintillation vial with toluene (2 mL, total = 15 mL, 0.033 M), producing a light green solution. The vial was sealed with a Teflon-lined cap and lowered into a heating block (40 °C). After 16 days, TLC analysis indicated that conversion had ceased at approximately 50% and the vial was removed from the glove box and the reaction was filtered through a silica gel plug, rinsed with Et_2O, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO_2, 15 x 2.5 cm, 5% EtOAc in hexanes) to afford lactam **5j** (54 mg, 0.23 mmol, 46% yield) as a colorless oil; R_f = 0.58 (20% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77 (dddd, *J* = 17.1, 10.2, 7.8, 7.0 Hz, 1H), 5.16–5.05 (m, 2H), 3.53–3.38 (m, 2H), 2.51 (ddt, *J* = 13.7, 7.0, 1.3 Hz, 1H), 2.28 (ddt, *J* = 13.7, 7.7, 1.1 Hz, 1H), 1.92–1.80 (m, 3H), 1.61–1.58 (m, 1H), 1.27 (s, 9H), 1.25 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.5, 179.0, 133.7, 118.9, 48.5, 44.2, 43.4, 43.3, 33.4, 28.1, 25.0, 19.8; IR (Neat Film NaCl) 2963, 1684, 1482, 1457, 1391, 1282, 1259, 1156, 917 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{14}H_{23}NO_2$ $[M+H]^+$: 238.1802, found 238.1809; $[\alpha]_D^{25.0}$ –7.13 (c 2.45, $CHCl_3$, 96% ee); HPLC conditions: 5% IPA in hexanes, 1 mL/min, Chiralcel OD-H column, λ = 210 nm, t_R (min): major = 7.95, minor = 6.52.

Procedures for the Preparation of Imides

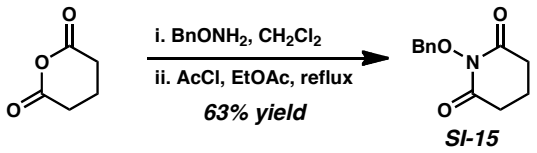
Imide Allylic Alkylation Precursors



***N*-Methyl imide 6c.** A flame-dried 200 mL round-bottom flask containing a magnetic stir bar was cycled into a glove box and loaded with LiHMDS (5.69 g, 34.0 mmol, 1.7 equiv). The flask was removed from the glove box, reconnected to a manifold, and charged with THF (100 mL, 0.2 M) and lowered into a –78 °C bath. Imide **SI-14**[14] (2.54 g, 20.0 mmol, 1.0 equiv) was added neat. After 1 h at –78 °C, the solution was warmed to 30 °C and stirred for 30 min before cooling back to –78 °C. Allyl cyanoformate (2.67 g, 24.0 mmol, 1.2 equiv) was added neat and the reaction was stirred for 1.5 h before TLC analysis indicated consumption of starting material. The reaction was subsequently quenched with brine and transferred to a separatory funnel where the aqueous layer was extracted with EtOAc (4 x 50 mL). The combined organics were rinsed twice with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The

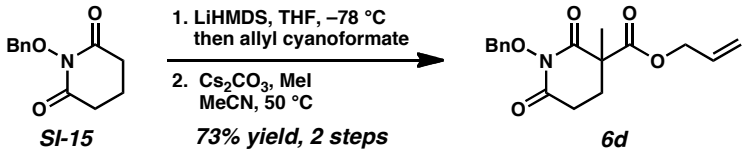
resulting crude oil was purified by flash column chromatography (SiO_2, 5 cm x 7 inches, 25%→30%→40% EtOAc in hexanes) to afford an intermediate oil (2.63 g, 0.45 mmol, 62% yield) that was moved on to the next step.

A flame-dried 200 mL flask equipped with a magnetic stir bar was charged with sodium hydride (60% in mineral oil, 312.5 mg, 7.81 mmol, 1.1 equiv) and THF (71 mL, 0.1 M) and cooled to 0 °C. A portion of the oil from the previous step (1.5 g, 7.10 mmol, 1.0 equiv) was added neat. After 1.5 h at 0 °C, the reaction was warmed to room temperature and stirred for 1 h before cooling back to 0 °C. Methyl iodide (886 μL, 14.20 mmol, 2.0 equiv) was added and the reaction was stirred for 2 h before warming to room temperature. After 15 h, the reaction was poor over a mixture of water and brine and transferred to a separatory funnel where the aqueous layer was extracted with EtOAc (4 x 50 mL). The combined organics were rinsed twice with $Na_2S_2O_3$ sol. (sat. solution half diluted) and twice with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography (SiO_2, 5 cm x 8 inches, 10% →20% EtOAc in hexanes) to afford imide **6c** (1.28 g, 5.69 mmol, 80% yield, 50% yield over two steps); R_f = 0.32 (35% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.85 (ddt, J = 17.2, 10.5, 5.7 Hz, 1H), 5.29 (dq, J = 17.2, 1.5 Hz, 1H), 5.25 (dq, J = 10.5, 1.2 Hz, 1H), 4.63 (ddt, J = 5.6, 4.1, 1.4 Hz, 2H), 3.18 (s, 3H), 2.72 (ddd, J = 18.1, 5.4, 4.4 Hz, 1H), 2.64 (ddd, J = 17.9, 11.6, 5.4 Hz, 1H), 2.35 (ddd, J = 13.9, 5.4, 4.4 Hz, 1H), 1.89 (ddd, J = 13.9, 11.6, 5.4 Hz, 1H), 1.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.0, 171.8, 171.3, 131.2, 119.3, 66.5, 50.9, 30.0, 28.7, 27.3, 21.9; IR (Neat Film NaCl) 2987, 2943, 1726, 1678, 1458, 1416, 1381, 1356, 1305, 1261, 1247, 1182, 1106, 1036, 993, 938 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{11}H_{17}NO_4$ $[M+H]^+$: 226.1074, found 226.1078.

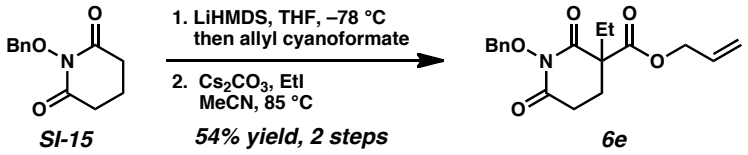


SI-15

***N*-benzyloxyimide SI-15.** Benzyloxyamine hydrochloride (3.15 g, 19.7 mmol) in a 100 mL round-bottom flask was taken up in dichloromethane (30 mL) and saturated aqueous K_2CO_3 (30 mL) and stirred for 30 min. The mixture was transferred to a separatory funnel and the phases were separated. The aqueous phase was extracted twice with dichloromethane (30 mL), the combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. A portion of the resulting crude colorless oil (1.23 g, 10.0 mmol, 1.00 equiv) was diluted with dichloromethane (10 mL, 1.0 M) in a 50 mL round-bottom flask and glutaric anhydride (1.14 g, 10.0 mmol, 1.00 equiv) was added. An exotherm was observed, and the mixture was immediately concentrated under reduced pressure. The resulting residue was taken up in EtOAc (13 mL, 0.75 M) and acetyl chloride (2.00 mL, 2.81 mmol, 2.81 equiv) was added. A water condenser was affixed and the reaction was heated to a gentle reflux (oil bath, 85 °C) for 18 h. The reaction was diluted with EtOAc (30 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude solid was purified by flash column chromatography (SiO_2, 6 x 5 cm, 20% EtOAc in hexanes→50% Et_2O in dichloromethane) to afford *N*-benzyloxyimide **SI-15** (1.37 g, 6.25 mmol, 63% yield) as a white solid; R_f = 0.64 (20% Et_2O in methylene chloride); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56–7.45 (m, 2H), 7.41–7.29 (m, 3H), 5.01 (s, 2H), 2.74–2.60 (m, 4H), 1.94–1.85 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.48 , 133.95 , 130.09 , 129.23 , 128.51 , 78.17 , 33.47 , 17.05; IR (Neat Film NaCl) 3033, 2957, 2902, 1689, 1457, 1381, 1350, 1331, 1251, 1175, 1134, 1087, 1056, 999, 968, 919, 893, 838, 759 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{12}H_{13}NO_3$ $[M+H]^+$: 220.0968, found 220.0971.

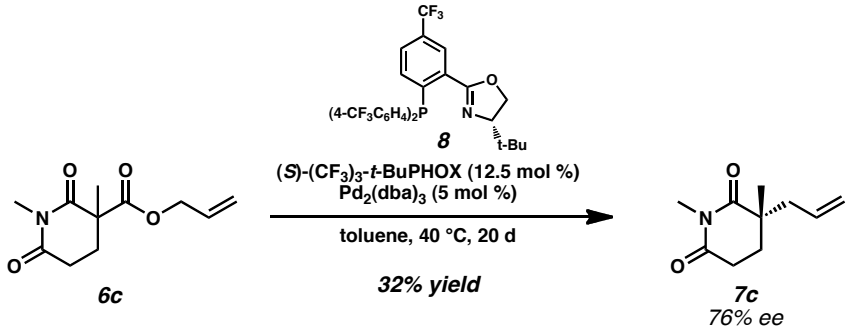


***N*-Benzyloxy imide 6d.** Acylation performed in manner analogous to *N*-methyl imide **6c** at –78 °C using *N*-benzyloxy imide **SI-15** as starting material. Alkylation performed in manner analogous to β-ketoester **18a** at 50 °C. *N*-Benzyloxy imide **6d** was isolated after flash column chromatography (SiO_2, 17 to 25% EtOAc in hexanes) as a colorless oil (73% yield over two steps); R_f = 0.20 (20% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (m, 2H), 7.37 (m, 3H), 5.87 (ddt, *J* = 17.2, 10.4, 5.9 Hz, 1H), 5.33 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.28 (dq, *J* = 10.4, 1.2 Hz, 1H), 5.01 (s, 2H), 4.66 (ddt, *J* = 13.0, 5.9, 1.3 Hz, 1H), 4.65 (ddt, *J* = 13.0, 5.9, 1.3 Hz, 1H), 2.72 (m, 2H), 2.30 (ddd, *J* = 14.1, 5.2, 4.0 Hz, 1H), 1.86 (ddd, *J* = 14.1, 11.8, 5.5 Hz, 1H), 1.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 167.9, 167.4, 133.9, 130.9, 130.1, 129.2, 128.5, 119.9, 77.9, 66.9, 52.1, 30.5, 28.5, 21.6; IR (Neat Film NaCl) 2943, 1738, 1733, 1708, 1451, 1255, 1200, 1168, 976 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{17}H_{20}NO_5$ $[M+H]^+$: 318.1336, found 318.1339.

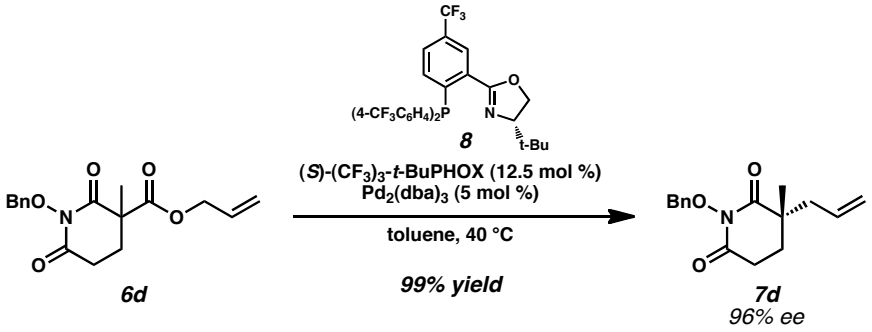


***N*-Benzyloxy imide 6e.** Acylation performed in manner analogous to *N*-methyl imide **6c** at –78 °C using *N*-benzyloxy imide **SI-15** as starting material. Alkylation performed in manner analogous to β-ketoester **18a** at 85 °C using ethyl iodide. *N*-Benzyloxy imide **6e** was isolated after flash column chromatography (SiO_2, 14 to 20% EtOAc in hexanes) as a colorless oil (54% yield over two steps); R_f = 0.24 (20% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (m, 2H), 7.37 (m, 3H), 5.87 (ddt, *J* = 17.2, 10.4, 5.9 Hz, 1H), 5.34 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.27 (dq, *J* = 10.4, 1.2 Hz, 1H), 5.0 (s, 2H), 4.66 (dt, *J* = 5.9, 1.3 Hz, 2H), 2.74 (m, 2H), 2.22 (ddd, *J* = 14.0, 5.2, 3.5 Hz, 1H), 2.05(m, 2H), 1.96 (ddd, *J* = 14.0, 12.3, 5.4 Hz, 1H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 167.5, 167.1, 134.0, 131.0, 130.1, 129.3, 128.6, 120.0, 77.9, 66.8, 56.2, 30.4, 28.3, 24.8, 9.0; IR (Neat Film NaCl) 2943, 1733, 1713, 1648, 1454, 1237, 1190, 1168, 976, 752 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{18}H_{22}NO_5$ $[M+H]^+$: 332.1492, found 332.1493.

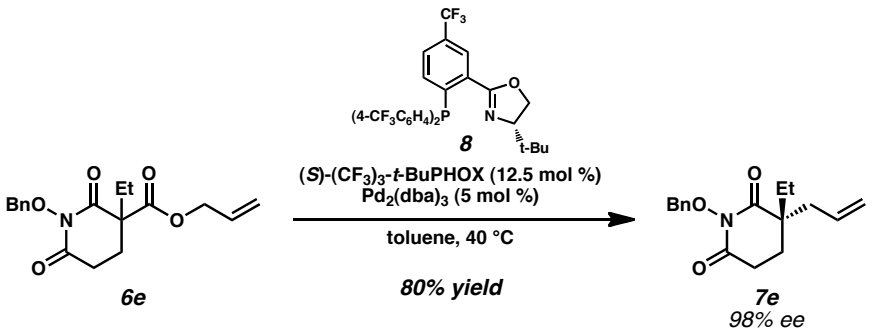
Imide Allylic Alkylation Products



***N*-Methyl imide 7c.** Prepared in a manner analogous to lactam **5h** using *N*-methyl imide **6c** as starting material. After 20 d, the reaction was filtered, concentrated, and *N*-Methyl imide **7c** was isolated following flash column chromatography (SiO_2, 3 cm x 10 inches, 5%→7%→9%→10% →12% EtOAc in hexanes) as an oil (32% yield); R_f = 0.36 (20% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.71 (dddd, J = 17.1, 10.2, 7.6, 7.1 Hz, 1H), 5.15–5.08 (m, 2H), 3.12 (s, 3H), 2.75–2.62 (m, 2H), 2.47 (ddt, J = 13.8, 7.1, 1.2 Hz, 1H), 2.29 (ddt, J = 13.8, 7.7, 1.1 Hz, 1H), 1.92 (ddd, J = 14.3, 8.6, 5.9 Hz, 1H), 1.66 (ddd, J = 14.0, 7.1, 5.8 Hz, 1H), 1.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 172.5, 132.8, 119.5, 42.6, 41.7, 29.3, 27.8, 27.0, 23.4; IR (Neat Film NaCl) 2971, 2937, 2876, 1723, 1674, 1464, 1415, 1378, 1356, 1291, 1240, 1110, 1036, 998, 919 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{10}H_{16}NO_2$ $[M+H]^+$: 182.1176, found 182.1178; $[\alpha]_D^{25.0}$ –54.19 (c 1.64, $CHCl_3$, 76% ee); HPLC conditions: 3% IPA in hexanes, 1 mL/min, Chiralpak AD column, λ = 210 nm, t_R (min): major = 11.94, minor = 17.86.



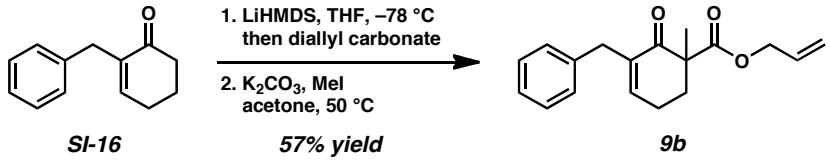
***N*-Benzyloxy imide 7d.** Prepared in a manner analogous to lactam **5h** using *N*-benzyloxy imide **6d** as starting material. *N*-Benzyloxy imide **7d** was isolated after flash column chromatography (SiO_2, 20% EtOAc in hexanes) as a colorless oil (99% yield); R_f = 0.29 (20% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.36 (m, 3H), 5.64 (dddd, *J* = 17.2, 10.2, 7.7, 7.1 Hz, 1H), 5.09–5.15 (m, 2H), 5.0 (s, 2H), 2.66–2.77 (m, 2H), 2.43 (ddt, *J* = 13.9, 7.1, 1.2 Hz, 1H), 2.26 (ddt, *J* = 13.9, 7.7, 1.2 Hz, 1H), 1.87 (ddd, *J* = 14.3, 8.5, 5.9 Hz, 1H), 1.60 (ddd, *J* = 14.3, 7.0, 5.7 Hz, 1H), 1.21 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 168.1, 133.9, 132.3, 130.3, 129.2, 128.5, 119.9, 78.0, 43.1, 42.3, 29.7, 27.6, 23.1; IR (Neat Film NaCl) 3067, 2974, 2935, 1740, 1703, 1700, 1456, 1172, 978, 748 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{16}H_{20}NO_3$ $[M+H]^+$: 274.1438, found 274.1437; $[\alpha]_D^{25.0}$ –58.59 (c 1.26, $CHCl_3$, 96% ee); Thar SFC conditions: 5% MeOH in CO_2, 3 mL/min, Chiralcel OJ-H column, λ = 210 nm, t_R (min): major = 4.03, minor = 3.64.



***N*-Benzyloxy imide 7e.** Prepared in a manner analogous to lactam **5h** using *N*-benzyloxy imide **6e** as starting material. *N*-Benzyloxy imide **7e** was isolated after flash column chromatography (SiO_2, 20% EtOAc in hexanes) as a colorless oil (80% yield); R_f = 0.20 (20% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.36 (m, 3H), 5.63 (dddd, *J* = 17.3, 10.3, 7.7, 6.9 Hz, 1H), 5.08–5.10 (m, 2H), 4.99 (s, 2H), 2.67–2.76 (m, 2H), 2.46 (ddt, *J* = 14.0, 6.9, 1.3 Hz, 1H), 2.27 (ddt, *J* = 14.0, 7.7, 1.1 Hz, 1H), 1.80 (ddd, *J* = 14.2, 7.9, 6.4 Hz, 1H), 1.76–1.71 (m, 1H), 1.70 (dq, *J* = 14.2, 7.5 Hz, 1H), 1.62 (dq, *J* = 14.2, 7.5 Hz, 1H), 0.86 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 168.0, 134.0, 132.6, 130.2, 129.2, 128.5, 119.6, 78.0, 46.5, 40.0, 29.5, 28.6, 24.7, 8.2; IR (Neat Film NaCl) 3033, 2972, 1739, 1702, 1699, 1455, 1169, 977, 751 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{17}H_{22}NO_3$ $[M+H]^+$: 288.1594, found 288.1591; $[\alpha]_D^{25.0}$ –35.98 (c 1.98, $CHCl_3$, 98% ee); Thar SFC conditions: 1% MeOH in CO_2, 2.5 mL/min, Chiralcel OB-H column, λ = 210 nm, t_R (min): major = 14.34, minor = 13.39.

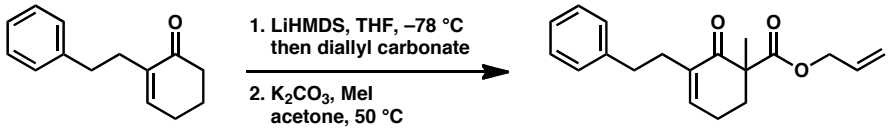
Procedures for the Preparation of Enones and Diosphenol Ethers

Enone and Diosphenol Ether Allylic Alkylation Precursors



Enone 9b. A 25 mL round-bottom flask equipped with a magnetic stir bar was cycled into a glove box, loaded with LiHMDS (527.6 mg, 3.15 mmol, 2.10 equiv), removed from the glove box, and connected to an Ar-filled manifold. The flask was charged with THF (1 mL) and lowered into a 0 °C bath (ice/water). Enone **SI-16**[15] (279.0 mg, 1.50 mmol, 1.00 equiv) was cannula transferred slowly from a scintillation vial to the flask using several THF rinses (1 x 4 mL + 2 x 0.5 mL, total added = 6 mL, 0.25 M), generating a bright red/pink solution. After the addition was complete, the 0 °C bath was removed and the reaction was allowed to warm to room temperature. After 30 min, the flask was lowered back into the 0 °C bath and diallyl carbonate (230 μL, 1.60 mmol, 1.07 equiv) was added dropwise, generating an orange solution. The bath was allowed to expire overnight. After 18 h, the reaction was quenched with sat. NH_4Cl sol. (10 mL) and transferred to a separatory funnel where the aqueous layer was extracted five times with Et_2O. The combined organics (75 mL) were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography (SiO_2, 21 x 2 cm, 100% hexanes→5%→10% EtOAc in hexanes) to afford a yellow oil.

The resulting yellow oil (285.8 mg, 1.06 mmol, 1.00 equiv) was transferred to an Ar-filled 25 mL Schlenk bomb (14/20 joint off of an 8 mm Kontes valve) equipped with a magnetic stir bar using several acetone rinses (1 x 1.5 mL + 3 x 0.5 mL, total added = 3 mL, 0.35 M). K_2CO_3 (292.7 mg, 2.12 mmol, 2.00 equiv) and methyl iodide (180 μL, 2.89 mmol, 2.73 equiv) were added to the bomb. The Kontes valve was sealed, the bomb was lowered into a preheated oil bath (50 °C), and the reaction was stirred vigorously. After 11 hours, ^{1}H NMR analysis indicated residual starting material, and consequently more methyl iodide (130 μL, total added = 310 μL, 4.98 mmol, 4.71 equiv) was added. After an additional 8.5 hours, no starting material remained by ^{1}H NMR analysis. Subsequently, the bomb was removed from the oil bath and allowed to cool to room temperature. The reaction contents were filtered through a celite plug rinsing with CH_2Cl_2 and concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography (SiO_2, 26.5 x 1.5 cm, 100% hexanes→5% EtOAc in hexanes) to afford enone **9b** (271.2 mg, 0.954 mmol, 64% yield over two steps, 90% purity) as a yellow oil. This yellow oil was diluted in EtOAc (50 mg/mL) and purified further by preparative HPLC (10% EtOAc in hexanes) to afford analytically pure enone **9b** (242.8 mg, 0.851 mmol, 57% yield over two steps) as a pale yellow oil; R_f = 0.59 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.25 (m, 2H), 7.21–7.14 (m, 3H), 6.50–6.45 (m, 1H), 5.78 (ddt, J = 17.2, 10.5, 5.6 Hz, 1H), 5.24 (dq, J = 17.2, 1.5 Hz, 1H), 5.19 (dq, J = 10.5, 1.1 Hz, 1H), 4.53 (dm, J = 5.6 Hz, 2H), 3.58 (dq, J = 15.7, 1.7 Hz, 1H), 3.51 (dq, J = 15.6, 1.7 Hz, 1H), 2.52–2.40 (m, 2H), 2.34–2.24 (m, 1H), 1.94–1.86 (m, 1H), 1.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.6, 172.6, 145.1, 139.5, 138.8, 131.8, 129.3, 128.5, 126.2, 118.4, 65.8, 53.6, 36.0, 33.7, 23.6, 20.6; IR (Neat Film NaCl) 3084, 3061, 3027, 2980, 2934, 1734, 1685, 1603, 1496, 1453, 1430, 1375, 1292, 1246, 1166, 1111, 1077, 1029, 984, 747 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{18}H_{21}O_3$ $[M+H]^+$: 285.1485, found 285.1482.

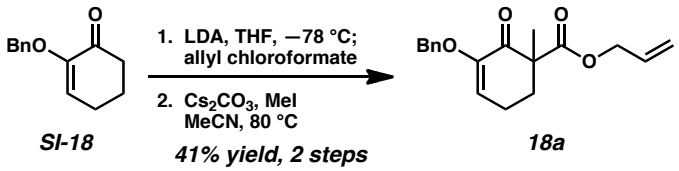


SI-17 ***30% yield*** ***9c***

Enone 9c. A 25 mL round-bottom flask equipped with a magnetic stir bar was cycled into a glove box, loaded with LiHMDS (215.6 mg, 1.29 mmol, 2.12 equiv), removed from the glove box, and connected to an Ar-filled manifold. The flask was charged with THF (0.5 mL) and lowered into a 0 °C bath (ice/water). Enone **SI-17**[15] (122.0 mg, 0.609 mmol, 1.00 equiv) was cannula transferred slowly from a scintillation vial to the flask using several THF rinses (1 x 1 mL + 2 x 0.5 mL, total added = 2.5 mL, 0.24 M), generating a bright pink solution. After the addition was complete, the 0 °C bath was removed and the reaction was allowed to warm to room temperature. After 30 min, the flask was lowered back into the 0 °C bath and diallyl carbonate (100 μL, 0.697 mmol, 1.14 equiv) was added dropwise. The bath was allowed to expire overnight. After 18 h, the reaction was quenched with sat. NH_4Cl sol. (5 mL) and transferred to a separatory funnel where the aqueous layer was extracted five times with Et_2O. The combined organics (70 mL) were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography (SiO_2, 27 x 1.5 cm, 100% hexanes→5% EtOAc in hexanes) to afford a yellow oil.

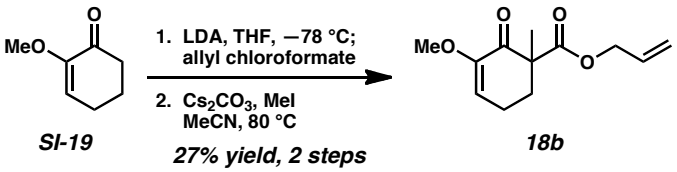
The resulting yellow oil (84.6 mg, 0.298 mmol, 1.00 equiv) was transferred to an Ar-filled 25 mL Schlenk bomb (14/20 joint off of an 8 mm Kontes valve) equipped with a magnetic stir bar using several acetone rinses (4 x 0.5 mL, total added = 2 mL, 0.15 M). K_2CO_3 (87.0 mg, 0.630 mmol, 2.12 equiv) and methyl iodide (100 μL, 1.61 mmol, 5.40 equiv) were added to the bomb.

The Kontes valve was sealed, the bomb was lowered into a preheated oil bath (50 °C), and the reaction was stirred vigorously. After 16 hours, ^{1}H NMR analysis indicated residual starting material, and consequently more Methyl iodide (130 μL, total added = 310 μL, 4.98 mmol, 4.71 equiv) was added. After an additional 8.5 hours, no starting material remained by ^{1}H NMR analysis. Subsequently, the bomb was removed from the oil bath and allowed to cool to room temperature. The reaction contents were filtered through a celite plug rinsing with CH_2Cl_2 and concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography (SiO_2, 28 x 1.5 cm, 100% hexanes→2% EtOAc in hexanes) to afford enone **9c** (75.6 mg, 0.253 mmol, 42% yield over two steps, 80% purity) as a yellow oil. This yellow oil was diluted with EtOAc (50 mg/mL) and purified further by preparative HPLC (10% EtOAc in hexanes, 50 mL/min) to afford analytically pure enone **9c** (54.1 mg, 0.181 mmol, 30% yield over two steps) as a pale yellow oil; R_f = 0.67 (30% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.24 (m, 2H), 7.20–7.15 (m, 3H), 6.53 (ddq, J = 4.6, 3.3, 1.0 Hz, 1H), 5.87 (ddt, J = 17.2, 10.5, 5.6 Hz, 1H), 5.29 (dq, J = 17.2, 1.5 Hz, 1H), 5.22 (dq, J = 10.5, 1.3 Hz, 1H), 4.65–4.57 (m, 2H), 2.74 (ddd, J = 13.4, 9.7, 6.1 Hz, 1H), 2.67 (ddd, J = 13.4, 9.3, 6.1 Hz, 1H), 2.57 (dddq, J = 13.8, 9.2, 6.4, 1.5 Hz, 1H), 2.52–2.37 (m, 2H), 2.29 (qt, J = 4.9, 1.3 Hz, 1H), 2.25 (ddt, J = 9.9, 4.8, 1.3 Hz, 1H), 1.88 (ddd, J = 13.4, 8.4, 5.3 Hz, 1H), 1.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.9, 172.7, 144.5, 142.0, 138.2, 131.8, 128.7, 128.4, 126.0, 118.5, 65.8, 53.6, 34.9, 33.6, 32.5, 23.5, 20.6; IR (Neat Film NaCl) 3026, 2930, 1733, 1683, 1603, 1495, 1456, 1377, 1244, 1167, 1109, 985, 931, 748 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{19}H_{23}O_3$ $[M+H]^+$: 299.1642, found 299.1638.



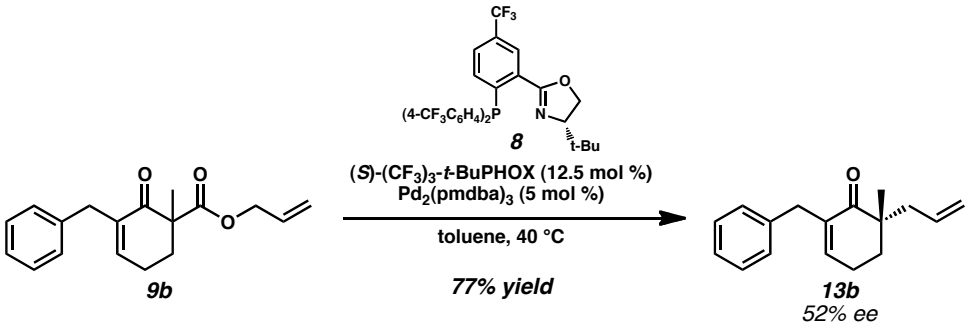
β-ketoester 18a. Diisopropylamine (390 μL, 2.78 mmol, 4.46 equiv) in a 10 mL round-bottom flask equipped with a magnetic stir bar was taken up in 2.0 mL THF and lowered into a 0 °C bath (ice/water). To the stirring solution was added *n*-butyl lithium (4.7 M solution in hexanes, 0.583 mL, 2.74 mmol, 4.40 equiv). This solution was stirred for 30 min before transferring the flask to a –78 °C bath (dry ice/acetone) and stirring the mixture for another 15 minutes. Benzyl diosphenol ether **SI-18**[16] (126 mg, 0.623 mmol, 1.00 equiv) in 1.1 mL THF (total = 3.1 mL, 0.2 M) was added dropwise by syringe and the solution was stirred for 2 h. Allyl cyanoformate (270 μL, 2.49 mmol, 4.00 equiv) was added dropwise by syringe, and the reaction was stirred for 8 h until analysis by TLC showed complete consumption of starting material. The reaction was diluted with 2 mL EtOAc and quenched with 1.5 mL each saturated aqueous NH_4Cl and water. The –78 °C bath was removed and the biphasic mixture was warmed to room temperature. The mixture was transferred to a separatory funnel and the phases were separated. The aqueous phase was extracted twice with EtOAc (5 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting crude yellow oil was taken up in acetonitrile (2.0 mL, 0.3 M) in a flame-dried 2-dram vial equipped with a magnetic stir bar. Cs_2CO_3 (264 mg, 0.810 mmol, 1.30 equiv) and methyl iodide (116 μL, 1,86 mmol, 3.00 equiv) were added and the reaction was blanketed under argon and sealed with a Teflon-lined cap. The vial was placed in a heating block (80 °C) and stirred for 8 h until analysis by TLC showed complete consumption of starting material. The reaction was diluted with 5 mL EtOAc, filtered and concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography (SiO_2, 12 x 1.5 cm, 20% Et_2O in hexanes) to afford β-ketoester **18a** (77

mg, 0.26 mmol, 41% yield over two steps) as a colorless oil; R_f = 0.34 (40% Et_2O in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.29 (m, 5H), 5.93–5.79 (m, 2H), 5.30 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.23 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.95–4.83 (m, 2H), 4.67–4.52 (m, 2H), 2.50–2.41 (m, 2H), 2.39–2.27 (m, 1H), 1.96–1.83 (m, 1H), 1.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.0, 172.3, 149.7, 136.7, 131.7, 128.6, 128.0, 127.3, 118.8, 118.5, 70.1, 65.9, 54.3, 33.7, 21.7, 20.6; IR (Neat Film NaCl) 3394, 2916, 2167, 1996, 1692, 1627, 1455, 1251, 1153, 1110, 1056 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{18}H_{20}O_4$ $[M+H]^+$: 301.1434, found 301.1422.

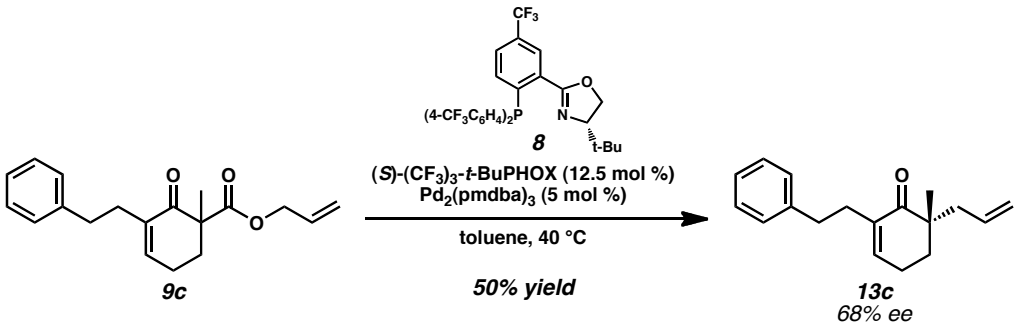


Diosphenol ether 18b. Prepared from **SI-19**[17] in an analogous manner to **18a**. Purified by flash chromatography (SiO_2, 15 x 3 cm, 20→40% Et_2O in hexanes) to afford diosphenol ether **18b** (57 mg, 0.25 mmol, 27% yield over two steps) as a colorless oil; R_f = 0.54 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.96–5.80 (m, 1H), 5.78 (d, *J* = 4.5 Hz, 1H), 5.27 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.20 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.67–4.55 (m, 2H), 3.60 (s, 3H), 2.56–2.43 (m, 2H), 2.42–2.32 (m, 1H), 1.95–1.85 (m, 1H), 1.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.0, 172.2, 150.7, 131.7, 118.4, 115.2, 65.9, 55.2, 54.3, 33.9, 21.5, 20.6; IR (Neat Film NaCl) 2936, 2839, 1734, 1696, 1631, 1455, 1378, 1365, 1252, 1231, 1174, 1110, 1081, 1064, 979, 935, 824 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{12}H_{17}O_4$ $[M+H]^+$: 225.1121, found 225.1122.

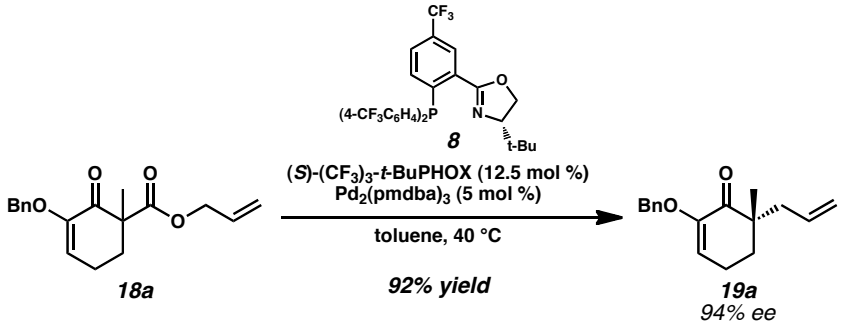
Diosphenol Ether and Enone Allylic Alkylation Products



Enone 13b. Prepared from **9b** in an analogous manner to **19a**. Purified by flash column chromatography (SiO_2, 12 x 2 cm, 10→20% Et_2O in hexanes) to afford enone **13b** (68 mg, 0.28 mmol, 77% yield) as a colorless oil and recovered enone **9b** (19 mg, 18% recovered); R_f = 0.70 (40% Et_2O in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31–7.20 (m, 2H), 7.23 – 7.10 (m, 3H), 6.46 (d, *J* = 4.0 Hz, 1H), 5.75 – 5.60 (m, 1H), 5.08 – 4.93 (m, 2H), 3.50 (dq, *J* = 3.3, 1.6 Hz, 2H), 2.41 – 2.23 (m, 3H), 2.16 (ddt, *J* = 13.7, 7.6, 1.2 Hz, 1H), 1.89 (ddd, *J* = 13.7, 6.4, 5.5 Hz, 1H), 1.74 (ddd, *J* = 13.6, 6.9, 5.5 Hz, 1H), 1.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.06 , 144.55 , 140.04 , 137.98 , 134.25 , 129.19 , 128.45 , 126.11 , 118.09 , 44.49 , 41.21 , 36.03 , 33.41 , 23.03 , 21.90; IR (Neat Film NaCl) 3063, 3027, 2964, 2924, 1668, 1640, 1495, 1453, 1430, 1376, 1174, 1077, 996, 915, 749 cm^{-1}; $[\alpha]_D^{25.0}$ –200.23 (c 3.86, $CHCl_3$, 52% ee); HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{17}H_{20}O$ $[M+H]^+$: 241.1587, found 241.1575; JASCO SFC conditions: 3% MeOH in CO_2, 5 mL/min, Chiralcel OJ-H column, λ = 210 nm, t_R (min): major = 2.40, minor = 2.11.

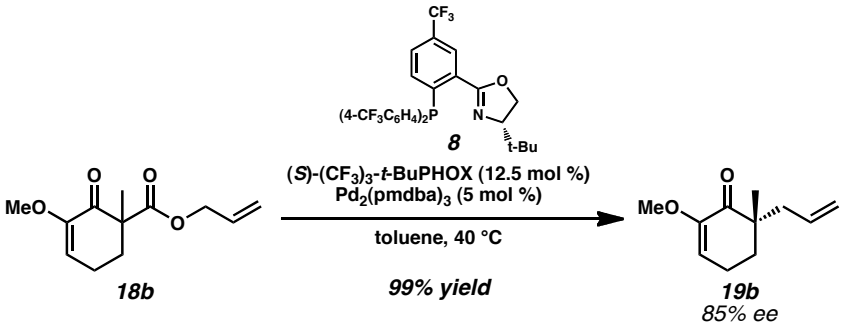


Enone 13b. Prepared from **9c** in an analogous manner to **19a**. Purified by flash column chromatography (SiO_2, 12 x 2 cm, 10→20% Et_2O in hexanes) to afford enone **13c** (17 mg, 67 μmol, 50% yield) as a colorless oil and recovered enone **9c** (8 mg, 20% recovered); R_f = 0.73 (40% Et_2O in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32–7.21 (m, 2H), 7.22–7.13 (m, 3H), 6.50 (t, *J* = 4.1 Hz, 1H), 5.74 (ddt, *J* = 16.8, 10.3, 7.4 Hz, 1H), 5.12–5.00 (m, 2H), 2.76–2.62 (m, 2H), 2.59–2.41 (m, 2H), 2.40–2.12 (m, 4H), 1.89 (ddd, *J* = 13.6, 6.7, 5.5 Hz, 1H), 1.72 (ddd, *J* = 13.6, 6.7, 5.5 Hz, 1H), 1.07 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.4, 144.2, 142.1, 137.4, 134.4, 128.7, 128.3, 125.9, 118.1, 44.4, 41.3, 35.2, 33.4, 32.4, 23.0, 22.0; IR (Neat Film NaCl) 3062, 3026, 2962, 2924, 2855, 1669, 1639, 1496, 1453, 1430, 1377, 1175, 1078, 995, 914, 747 cm^{-1}; $[\alpha]_D^{25.0}$ –32.55 (c 1.24, $CHCl_3$, 68% ee); HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{18}H_{22}O$ $[M+H]^+$: 255.1743, found 255.1730; JASCO SFC conditions: 3% MeOH in CO_2, 5 mL/min, Chiralcel OJ-H column, λ = 210 nm, t_R (min): major = 2.41, minor = 2.17.



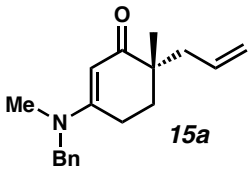
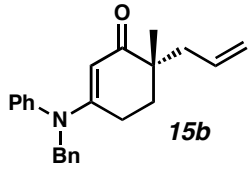
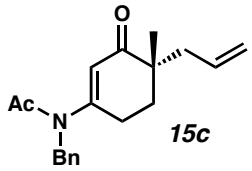
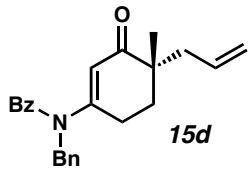
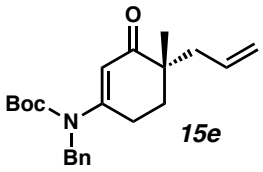
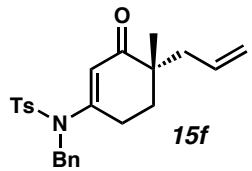
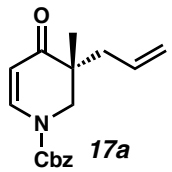
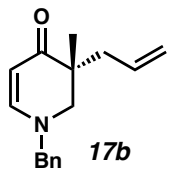
Diosphenol ether 19a. $Pd_2(pmdba)_3$ (4.2 mg, 3.8 μmol, 5.0 mol %) and (*S*)-$(CF_3)_3$-*t*-BuPHOX (**8**, 5.7 mg, 9.6 μmol, 12.5 mol %) were added to an oven-dried 2-dram vial equipped with a magnetic stir bar in a glove box. The vial was charged with toluene (1.8 mL) and stirred at ambient temperature (28 °C) for 30 min, resulting in a deep orange solution. β-ketoester **18a** (23 mg, 77 μmol, 1.0 equiv) was transferred to the scintillation vial with toluene (0.5 mL, total = 2.3 mL, 0.033 M), producing a light green solution. The vial was sealed with a Teflon-lined cap and lowered into a heating block (40 °C). After 6 days, the reaction was complete by TLC and colorimetric analysis (the reaction had reverted to an orange color) and was removed from the glove box. The reaction was filtered through a silica gel plug, rinsed with Et_2O, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO_2, 15 x 1.5 cm, 5%→10% Et_2O in hexanes) to afford diosphenol ether **19a** (18 mg, 70 μmol, 92% yield) as a colorless oil; R_f = 0.56 (40% Et_2O in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.26 (m, 5H), 5.83 (t, *J* = 4.5 Hz, 1H), 5.74 (ddt, *J* = 16.7, 10.3, 7.4 Hz, 1H), 5.12–5.03 (m, 2H), 4.85 (s, 2H), 2.42–2.33 (m, 3H), 2.21 (ddt, *J* = 13.8, 7.6, 1.2 Hz, 1H), 1.89 (ddd, *J* = 13.7, 6.7, 5.6 Hz, 1H), 1.71 (ddd, *J* = 13.7, 6.6, 5.4 Hz, 1H), 1.11 (s, 3H); ^{13}C

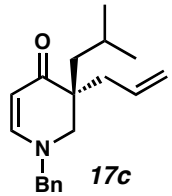
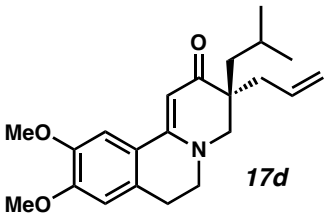
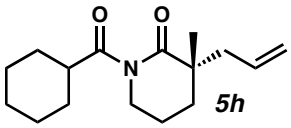
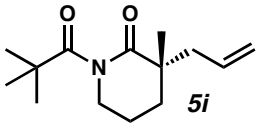
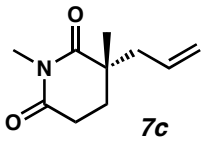
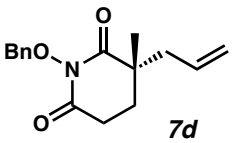
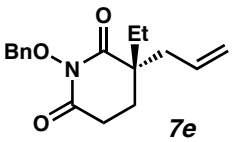
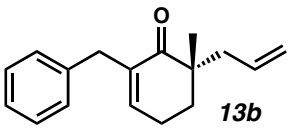
NMR (125 MHz, $CDCl_3$) δ 198.5, 149.0, 136.8, 134.1, 128.6, 127.9, 127.4, 118.4, 118.0, 70.0, 45.4, 41.2, 33.1, 21.9, 20.9; IR (Neat Film NaCl) 2918, 2360, 1684, 1628, 1457, 1220, 1204, 1094, 1050, 914, 736 cm^{-1}; $[\alpha]_D^{25.0}$ –12.01 (c 0.50, $CHCl_3$, 94% ee); HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{17}H_{20}O_2$ $[M+H]^+$: 257.1536, found 257.1529; HPLC conditions: 7% IPA in hexanes, 1 mL/min, Chiralcel OD-H column, λ = 254 nm, t_R (min): major = 7.24, minor = 8.27.

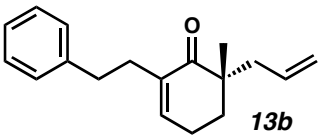
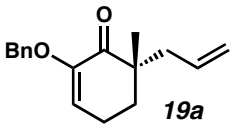
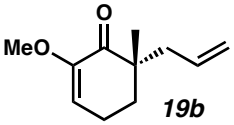


Diosphenol ether 19b. Prepared from **18b** in an analogous manner to **19a**. Purified by flash column chromatography (SiO_2, 10 x 3 cm, 5→10% Et_2O in hexanes) to afford diosphenol ether **19b** (111 mg, 0.616 mmol, 99% yield) as a colorless oil; R_f = 0.23 (40% Et_2O in hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 5.79–5.65 (m, 2H), 5.12–5.01 (m, 2H), 3.58 (s, 3H), 2.47–2.34 (m, 3H), 2.20 (ddt, *J* = 13.7, 7.6, 1.1 Hz, 1H), 1.91 (ddd, *J* = 13.7, 6.8, 5.5 Hz, 1H), 1.72 (ddd, *J* = 13.7, 6.5, 5.4 Hz, 1H), 1.11 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.6, 150.0, 134.0, 118.4, 114.5, 55.1, 45.4, 41.2, 33.2, 21.9, 20.8; IR (Neat Film NaCl) 2929, 1687, 1631, 1455, 1375, 1225, 1095, 1056, 913 cm^{-1}; $[\alpha]_D^{25.0}$ –27.47 (c 6.00, $CHCl_3$, 85% ee); HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{11}H_{17}O_2$ $[M+H]^+$: 181.1223, found 181.1222; HPLC conditions: 2% IPA in hexanes, 1 mL/min, Chiralcel OD-H column, λ = 254 nm, t_R (min): major = 13.41, minor = 12.23.

Methods for the Determination of Enantiomeric Excess

entry	product	assay conditions	retention time of major isomer (min)	retention time of minor isomer (min)	% ee
1	 *15a*	SFC Chiralcel OD-H 5% MeOH in CO_2 isocratic, 5.0 mL/min 210 nm	10.45	9.60	81
2	 *15b*	SFC Chiralpak AS-H 5% MeOH in CO_2 isocratic, 5.0 mL/min 254 nm	8.60	6.48	83
3	 *15c*	SFC Chiralpak AD-H 5% MeOH in CO_2 isocratic, 3.0 mL/min 254 nm	8.45	10.35	86
4	 *15d*	SFC Chiralpak AD-H 7% MeOH in CO_2 isocratic, 5.0 mL/min 210 nm	8.04	8.97	87
5	 *15e*	SFC Chiralpak AD-H 7% MeOH in CO_2 isocratic, 5.0 mL/min 210 nm	4.04	2.20	82
6	 *15f*	SFC Chiralpak AD-H 10% MeOH in CO_2 isocratic, 5.0 mL/min 210 nm	5.60	4.73	84
7	 *17a*	SFC Chiralpak AD-H 10% MeOH in CO_2 isocratic, 3.0 mL/min 254 nm	2.80	3.13	84
8	 *17b*	HPLC Chiralcel OJ 10% IPA in hexanes isocratic, 1.0 mL/min 210 nm	18.77	21.21	86

entry	product	assay conditions	retention time of major isomer (min)	retention time of minor isomer (min)	% ee
9	 *17c*	HPLC Chiralcel OJ 7% IPA in hexanes isocratic, 1.0 mL/min 210 nm	11.44	14.80	88
10	 *17d*	HPLC Chiralpak AD 30% IPA in hexanes isocratic, 1.0 mL/min 254 nm	21.87	18.59	90
11	 *5h*	SFC Chiralcel OJ-H 1% IPA in CO_2 isocratic, 5.0 mL/min 222 nm	2.53	2.13	95
12	 *5i*	HPLC Chiralcel OD-H 5% IPA in hexanes isocratic, 1.0 mL/min 210 nm	7.95	6.52	96
13	 *7c*	HPLC Chiralpak AD 3% IPA in hexanes isocratic, 1.0 mL/min 210 nm	11.94	17.86	76
14	 *7d*	SFC Chiralcel OJ-H 1% MeOH in CO_2 isocratic, 3.0 mL/min 210 nm	4.03	3.64	96
15	 *7e*	SFC Chiralcel OB-H 1% MeOH in CO_2 isocratic, 2.5 mL/min 210 nm	14.34	13.39	98
16	 *13b*	SFC Chiralcel OJ-H 3% MeOH in CO_2 isocratic, 5.0 mL/min 210 nm	2.40	2.11	52

entry	product	assay conditions	retention time of major isomer (min)	retention time of minor isomer (min)	% ee
17	 ***13b***	**SFC Chiralcel OJ-H 3% MeOH in CO_2 isocratic, 5.0 mL/min 210 nm**	**2.41**	**2.17**	**68**
18	 ***19a***	**HPLC Chiralcel OD-H 7% IPA in hexanes isocratic, 1.0 mL/min 254 nm**	**7.24**	**8.27**	**94**
19	 ***19b***	**HPLC Chiralcel OD-H 2% IPA in hexanes isocratic, 1.0 mL/min 254 nm**	**13.41**	**12.23**	**85**

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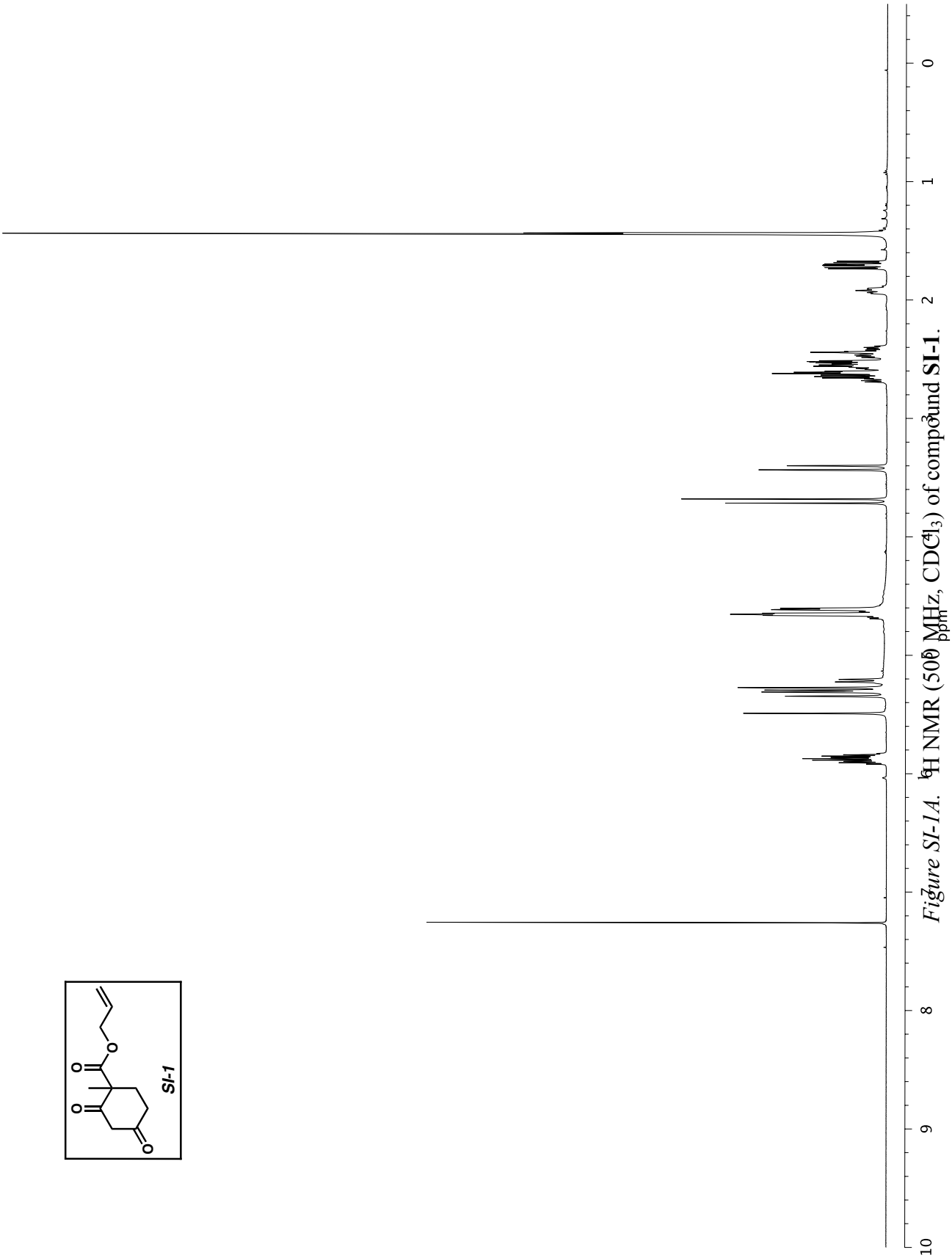


Figure SI-1A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-1**.

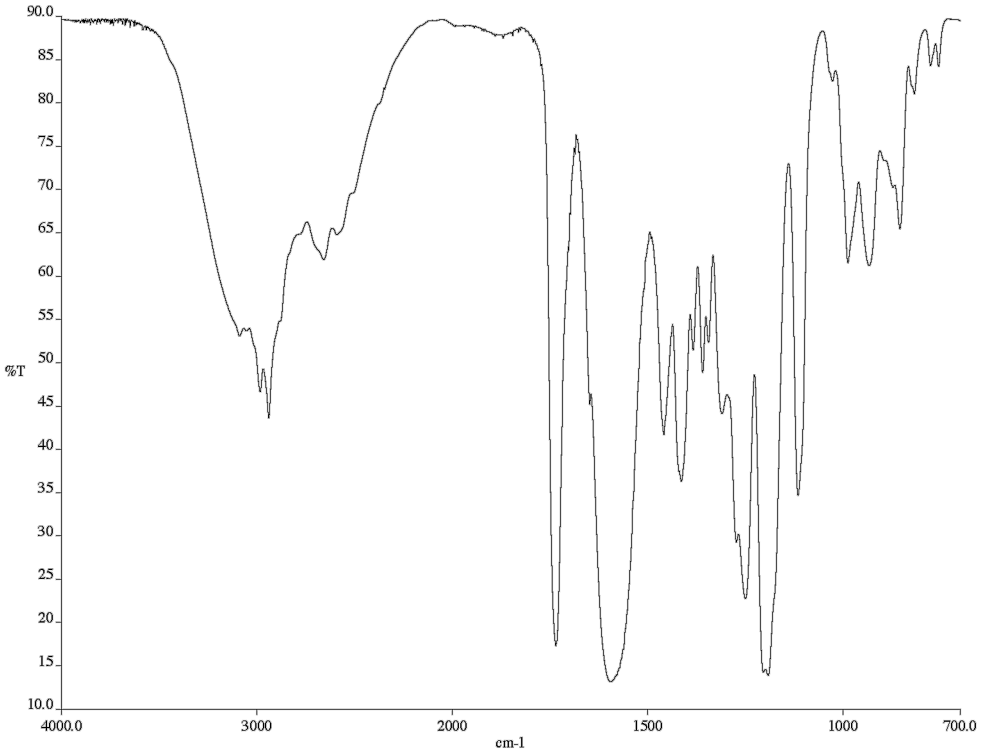


Figure SI-1B. Infrared spectrum (thin film/NaCl) of compound **SI-1**.

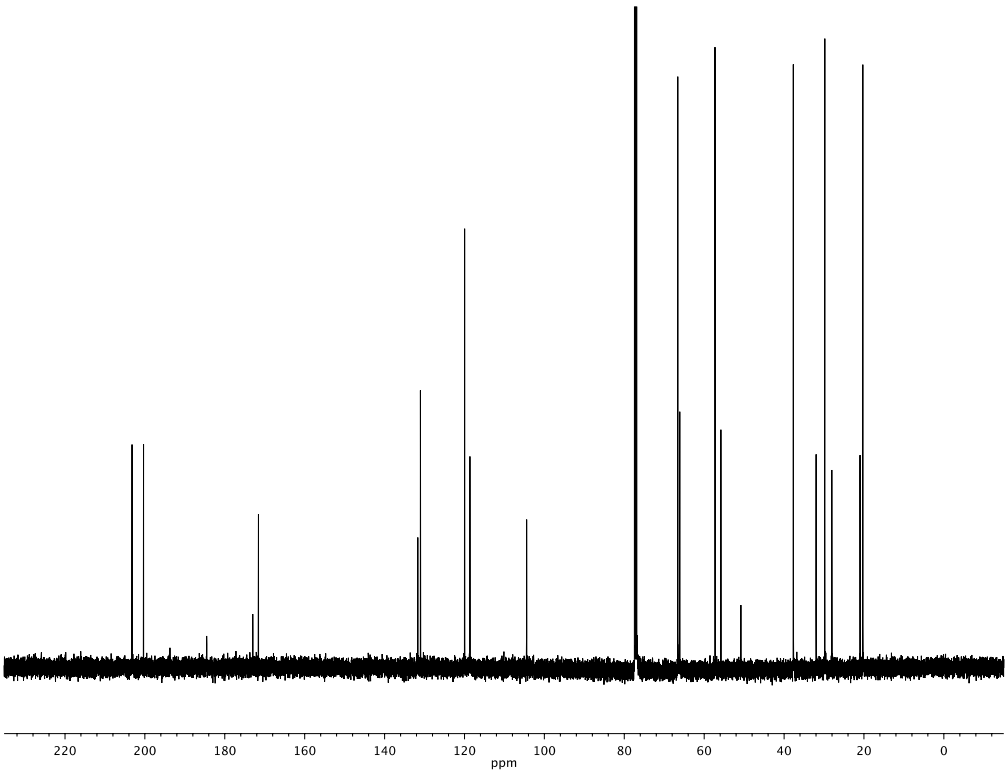


Figure SI-1C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-1**.

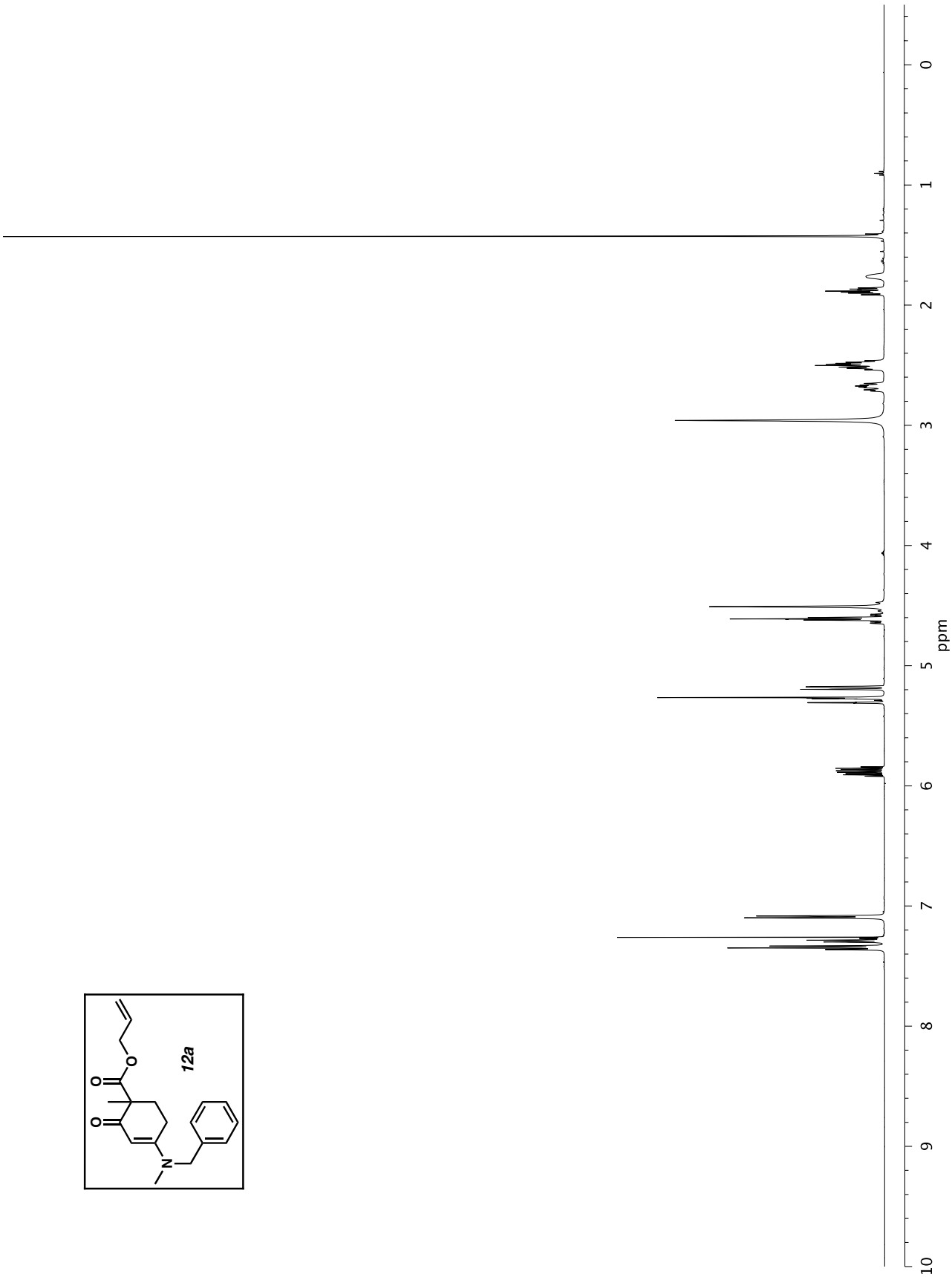


Figure SI-2A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **12a**.

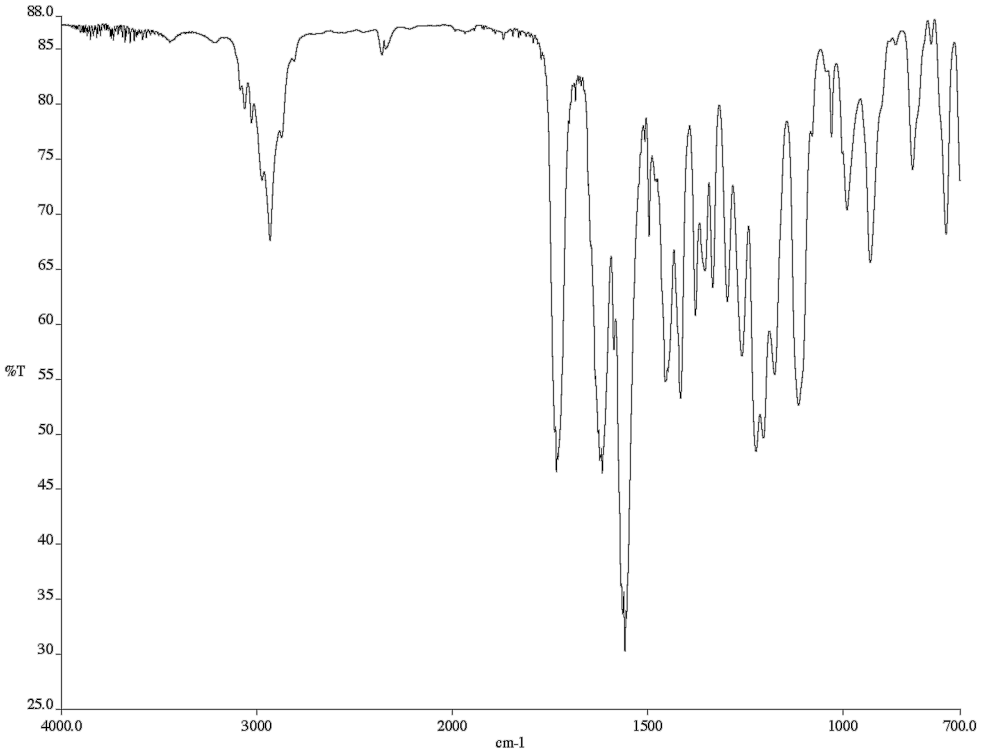


Figure SI-2B. Infrared spectrum (thin film/NaCl) of compound **12a**.

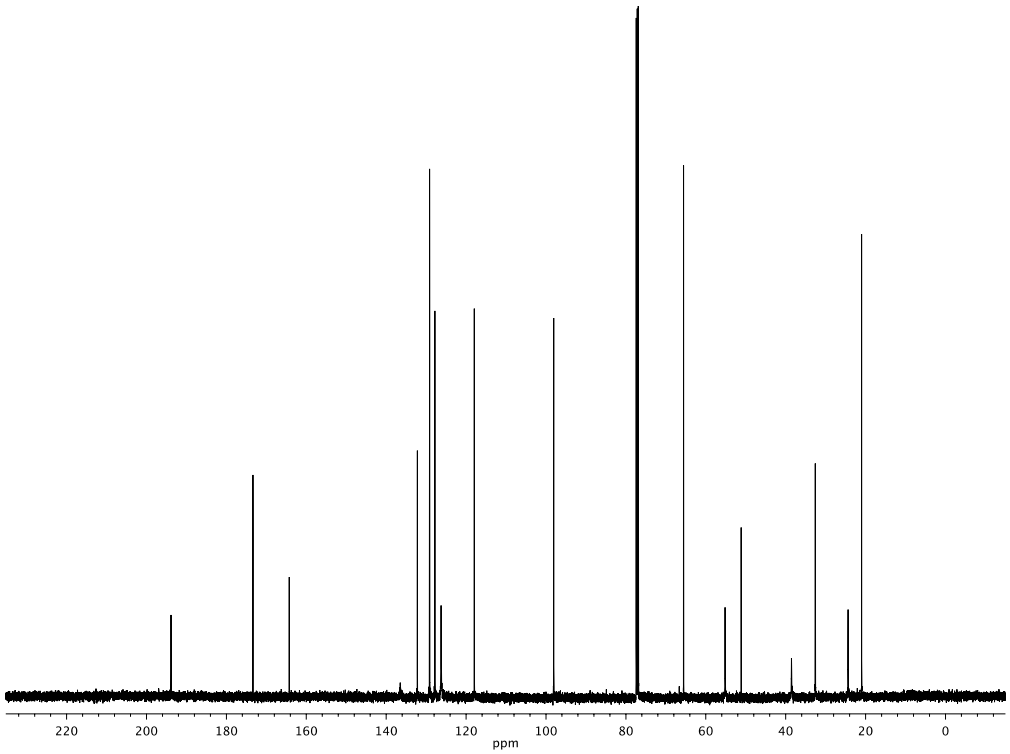


Figure SI-2C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **12a**.

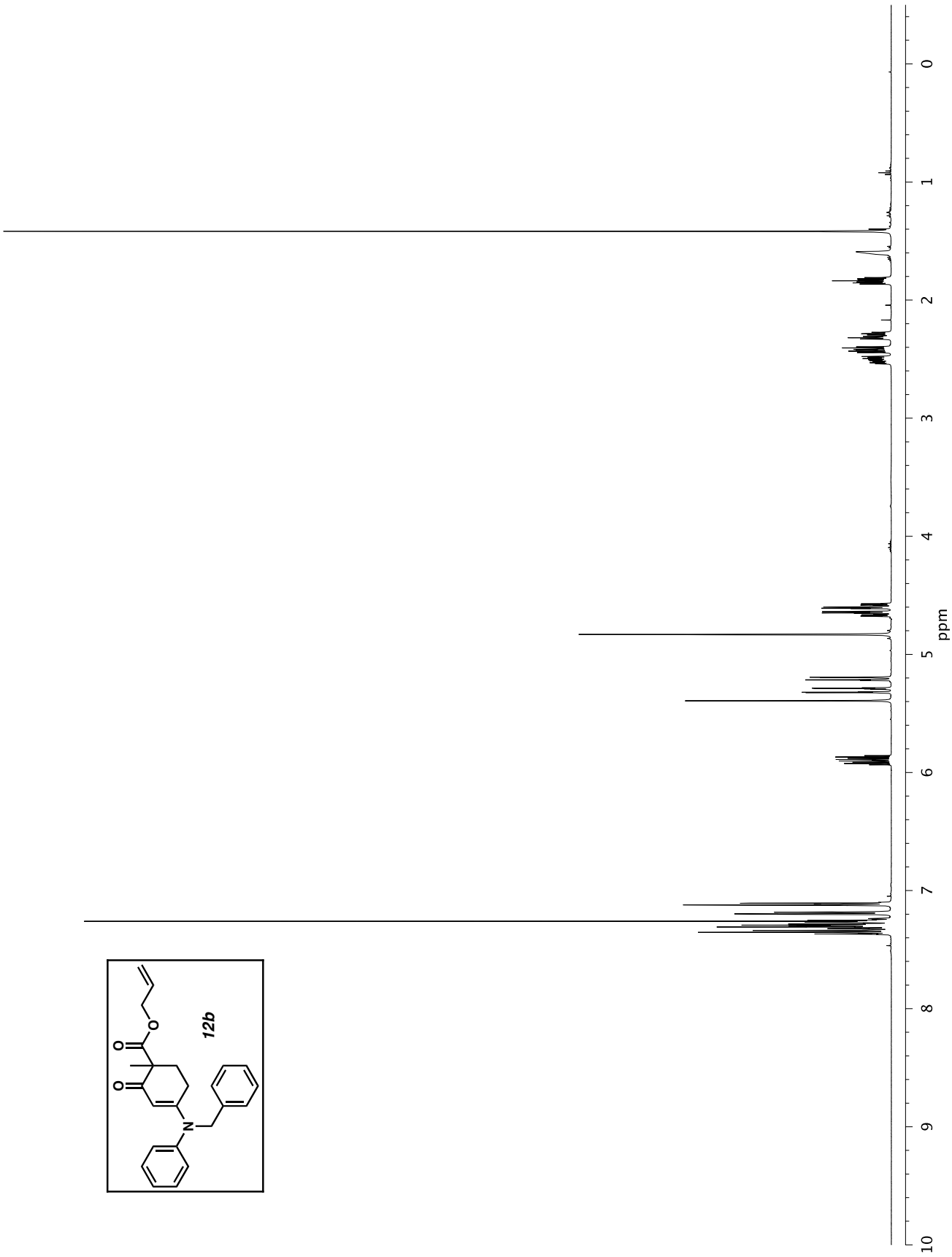


Figure SI-3A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **12b**.

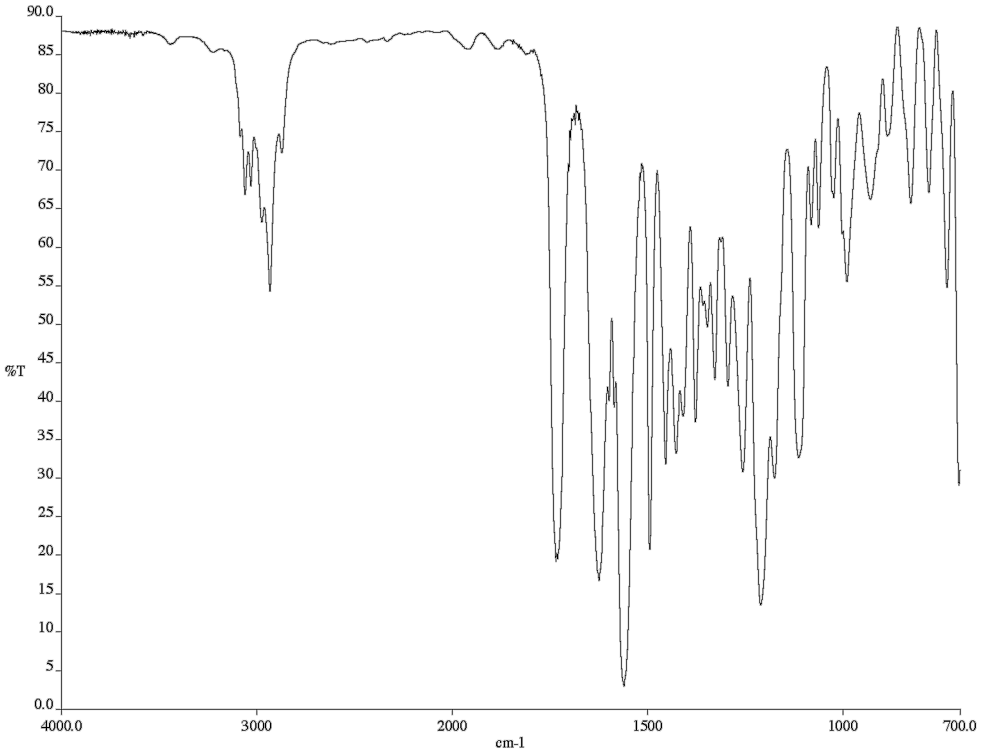


Figure SI-3B. Infrared spectrum (thin film/NaCl) of compound **12b**.

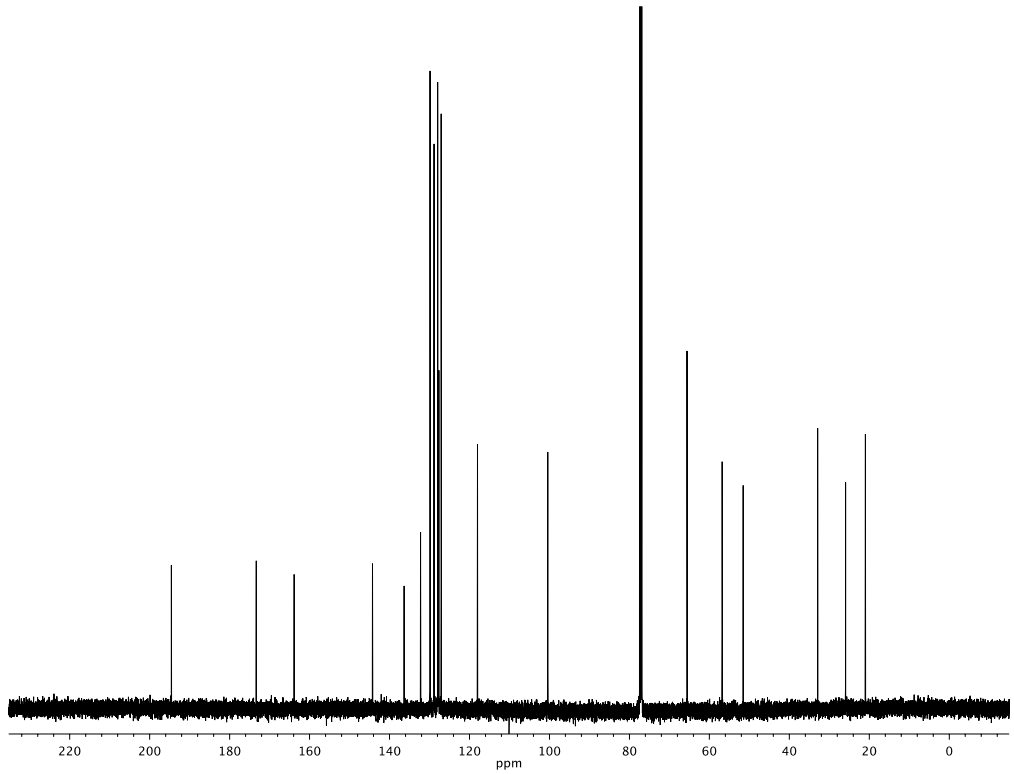


Figure SI-3C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **12b**.

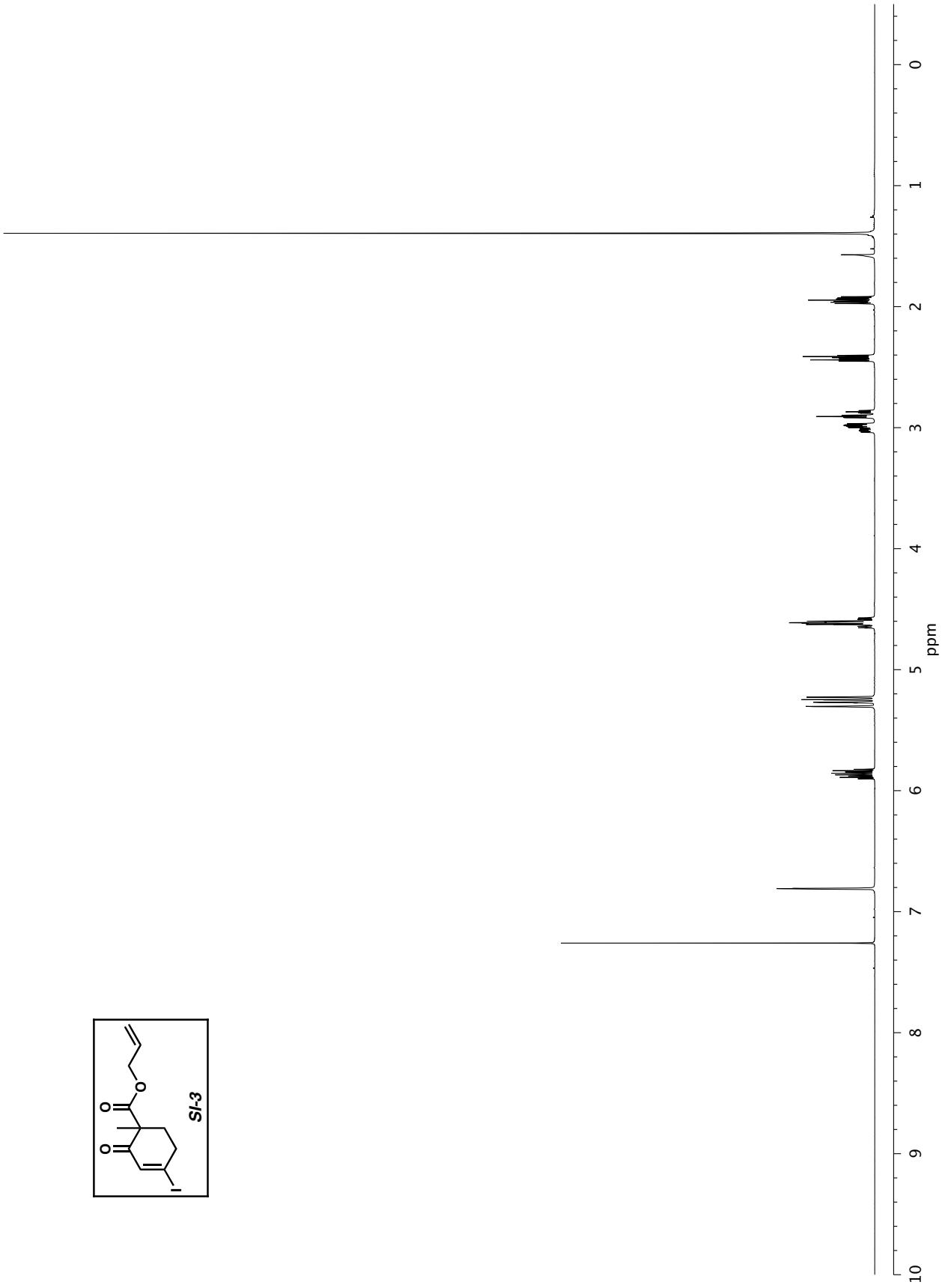


Figure SI-4A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-3**.

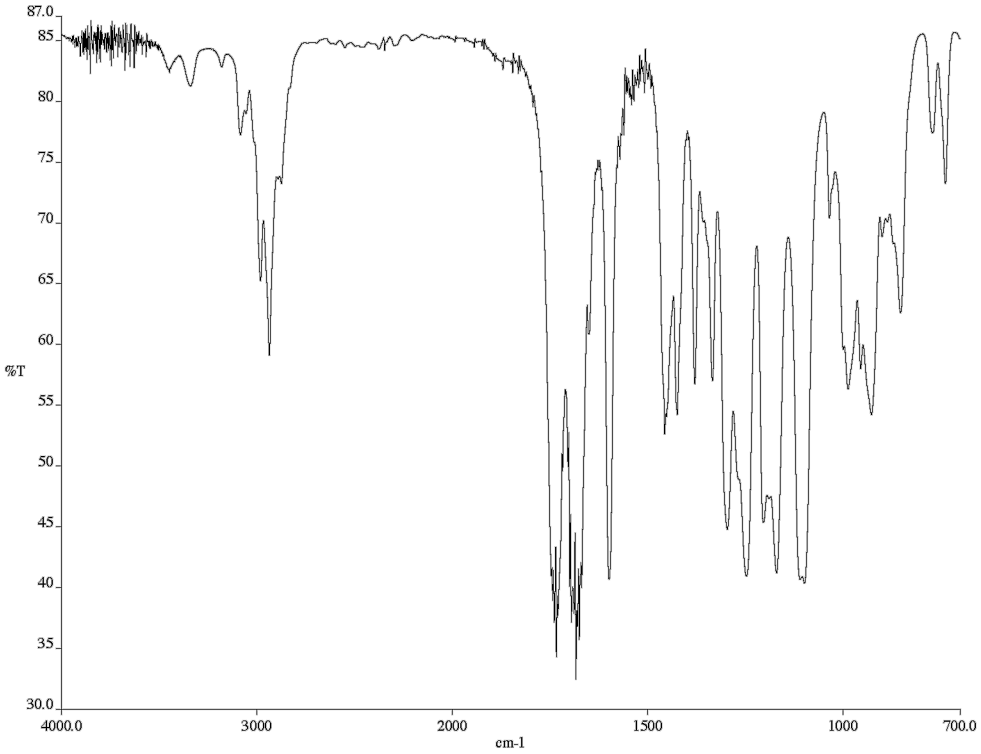


Figure SI-4B. Infrared spectrum (thin film/NaCl) of compound **SI-3**.

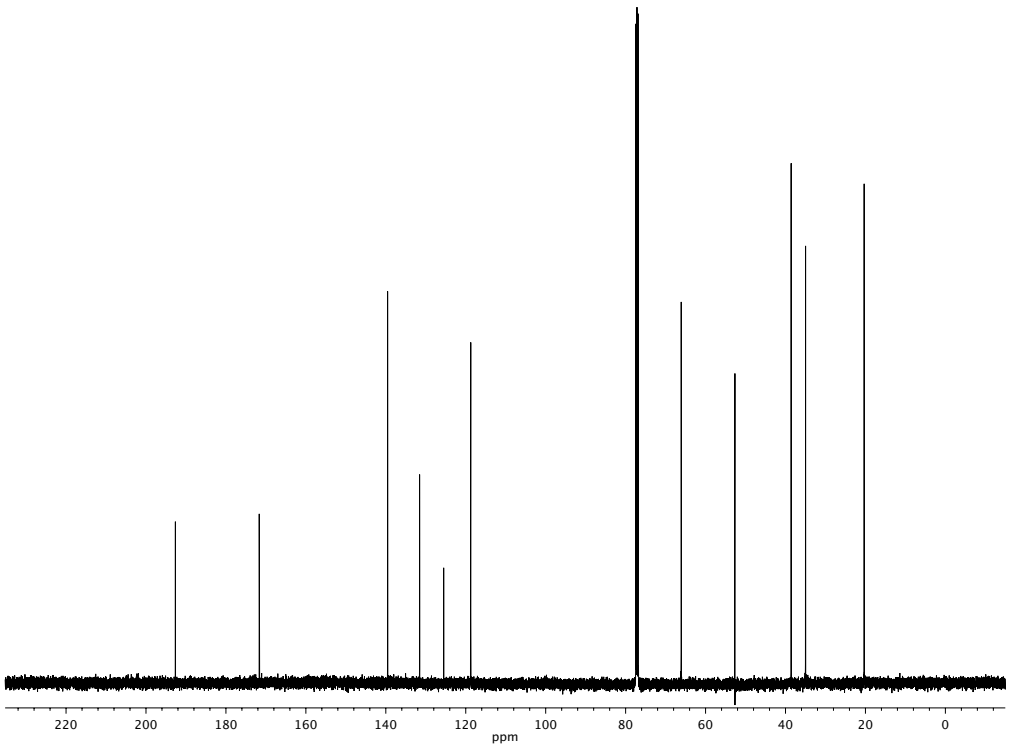


Figure SI-4C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-3**.

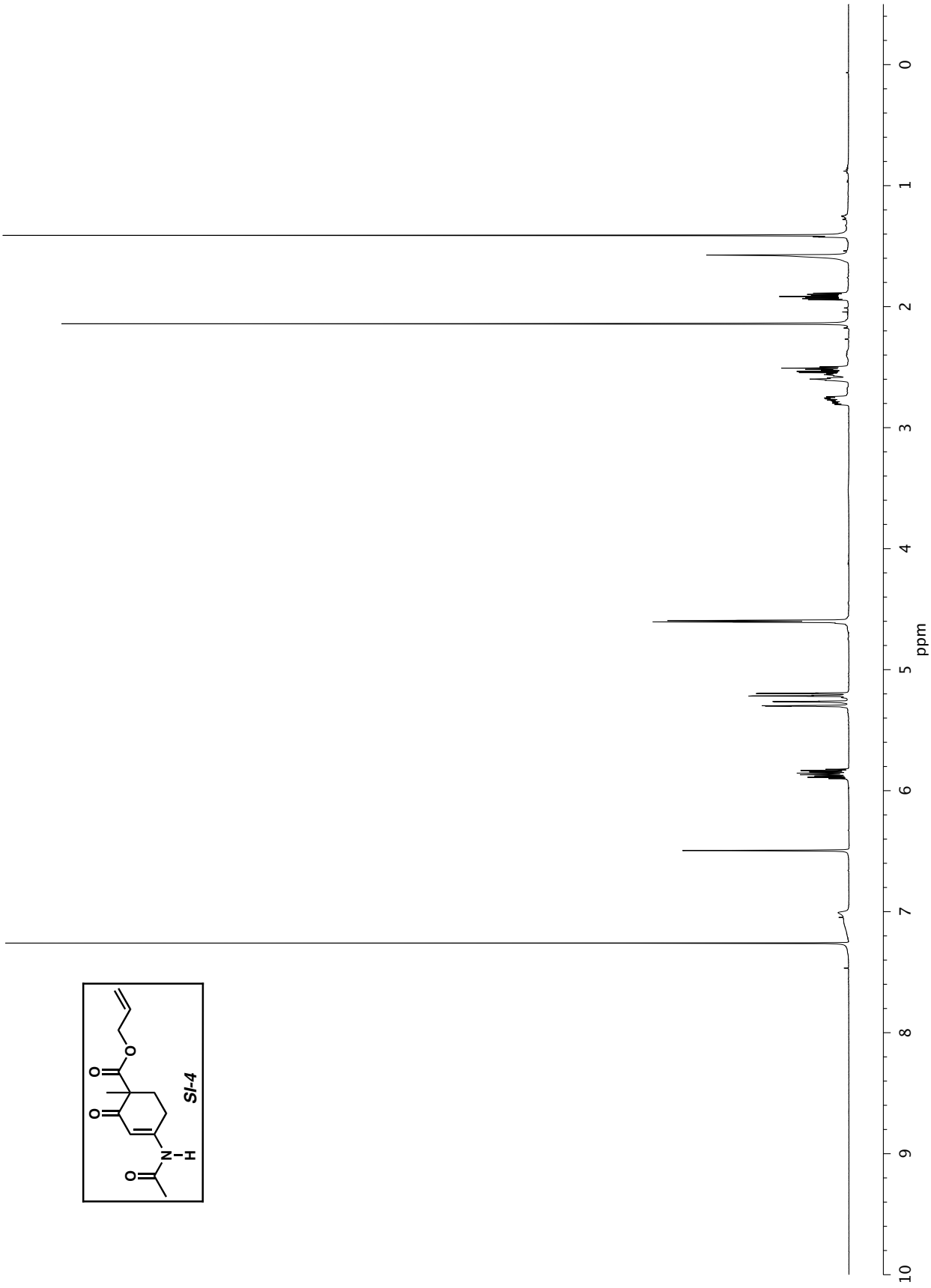


Figure SI-5A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-4**.

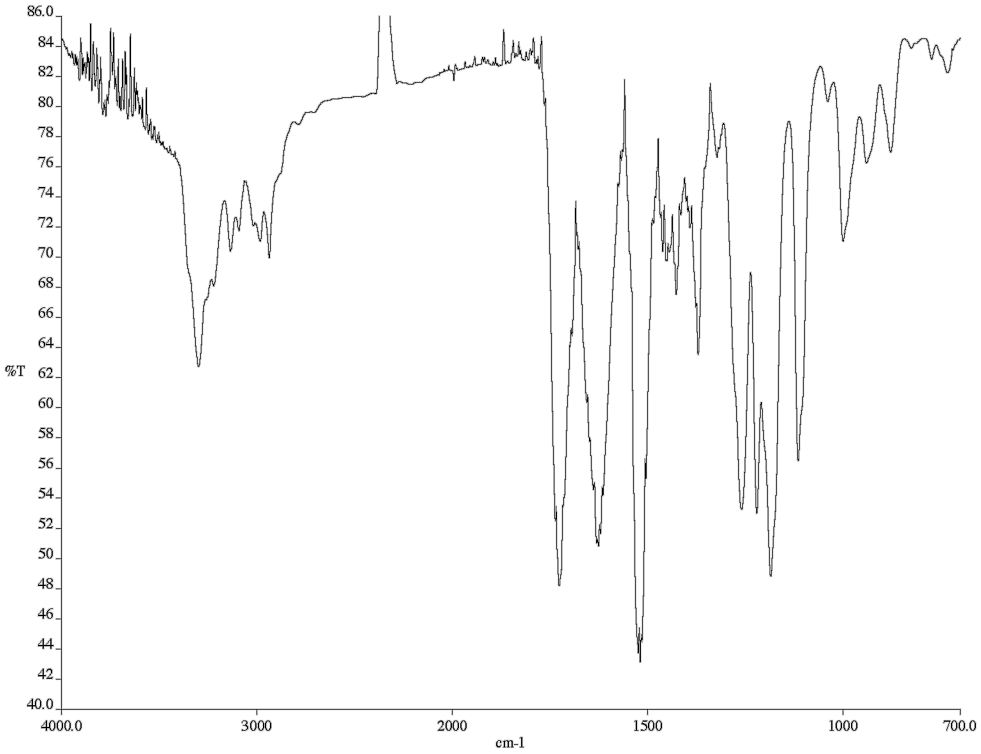


Figure SI-5B. Infrared spectrum (thin film/NaCl) of compound **SI-4**.

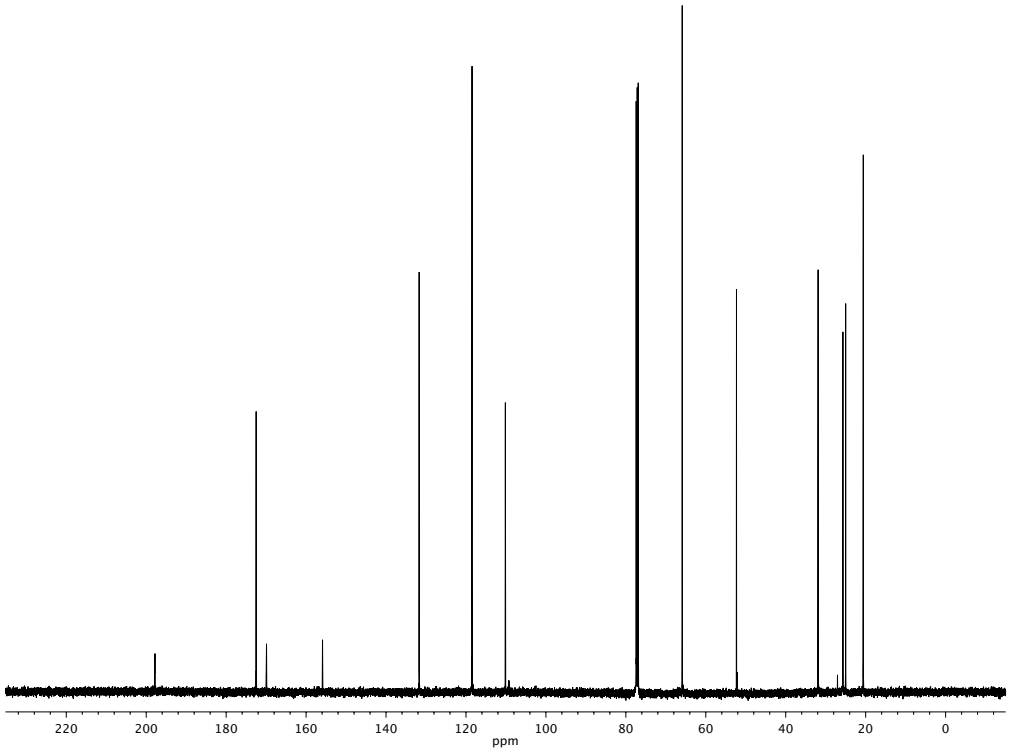


Figure SI-5C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-4**.

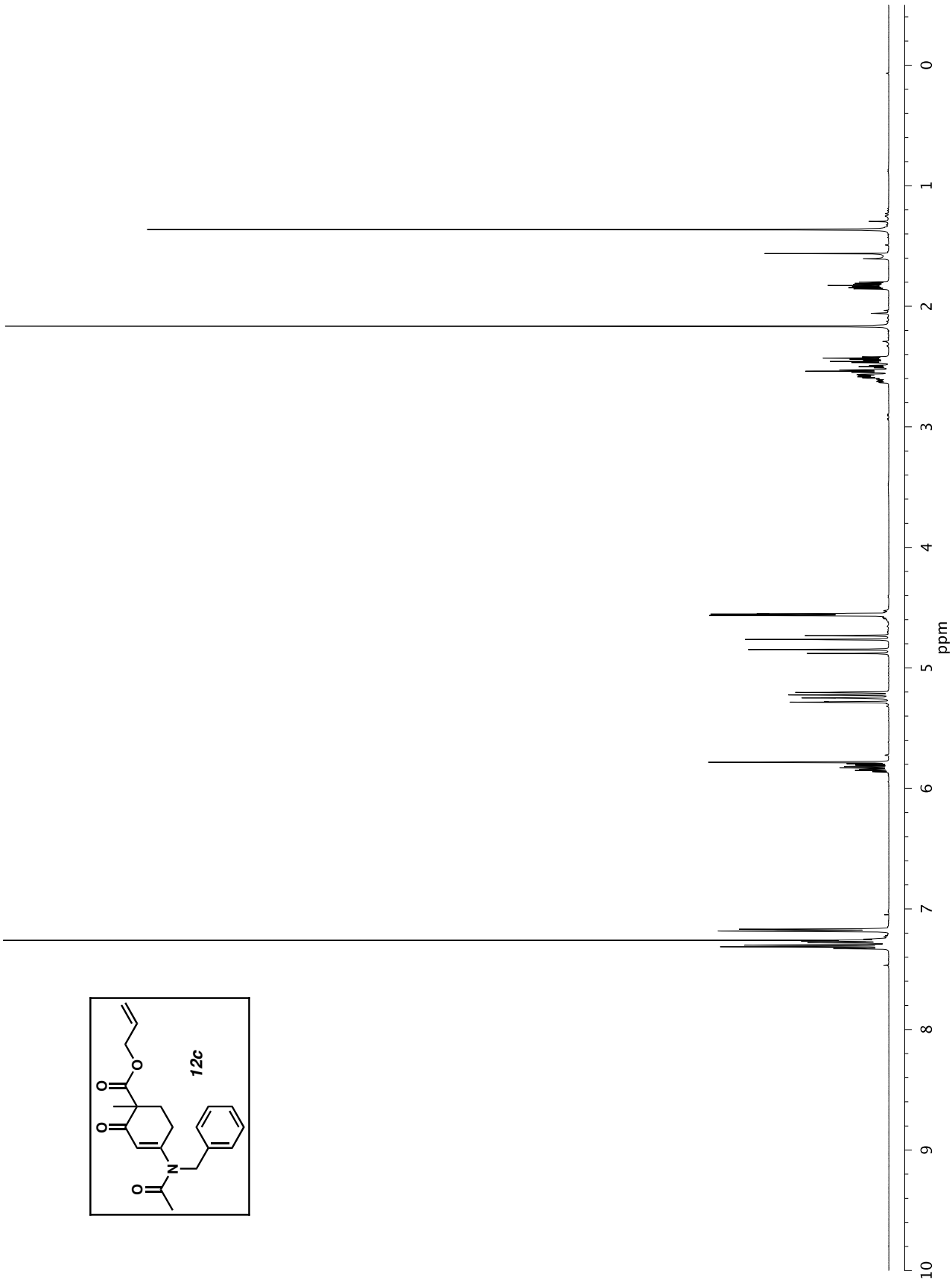


Figure SI-64. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **12c**.

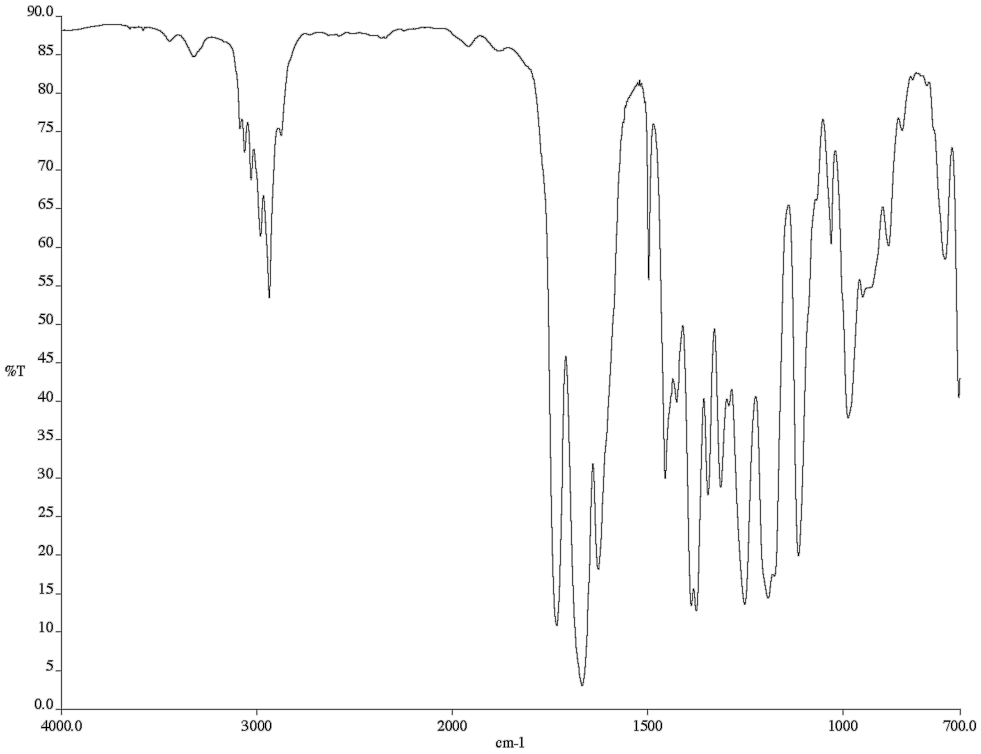


Figure SI-6B. Infrared spectrum (thin film/NaCl) of compound **12c**.

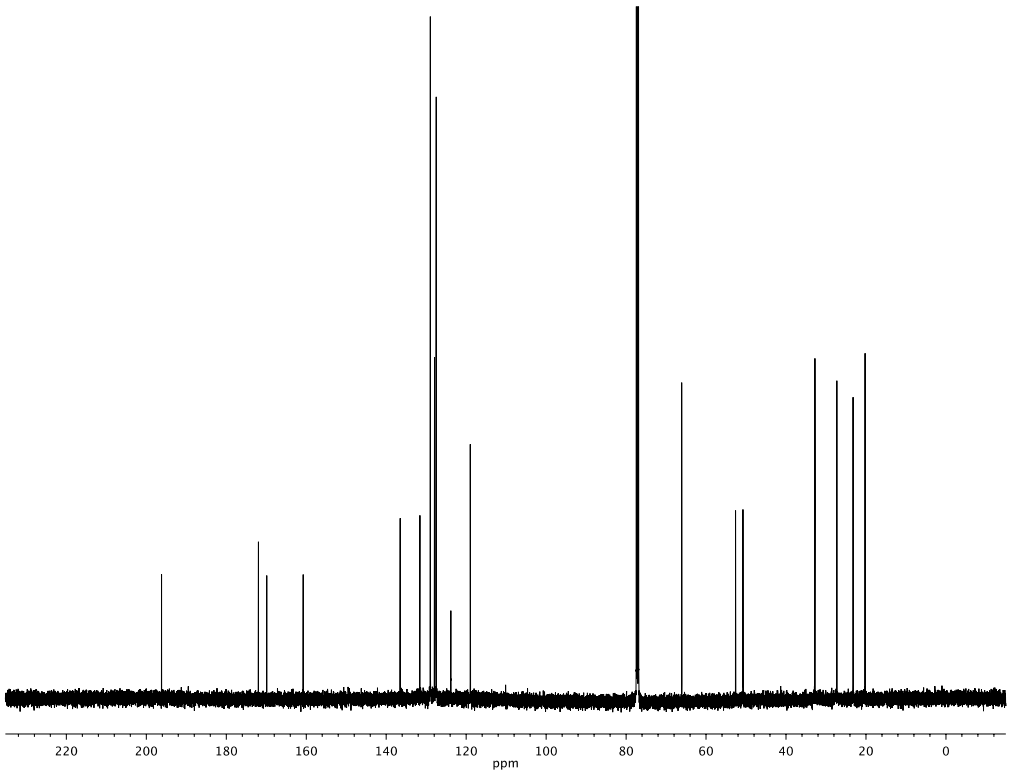


Figure SI-6C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **12c**.

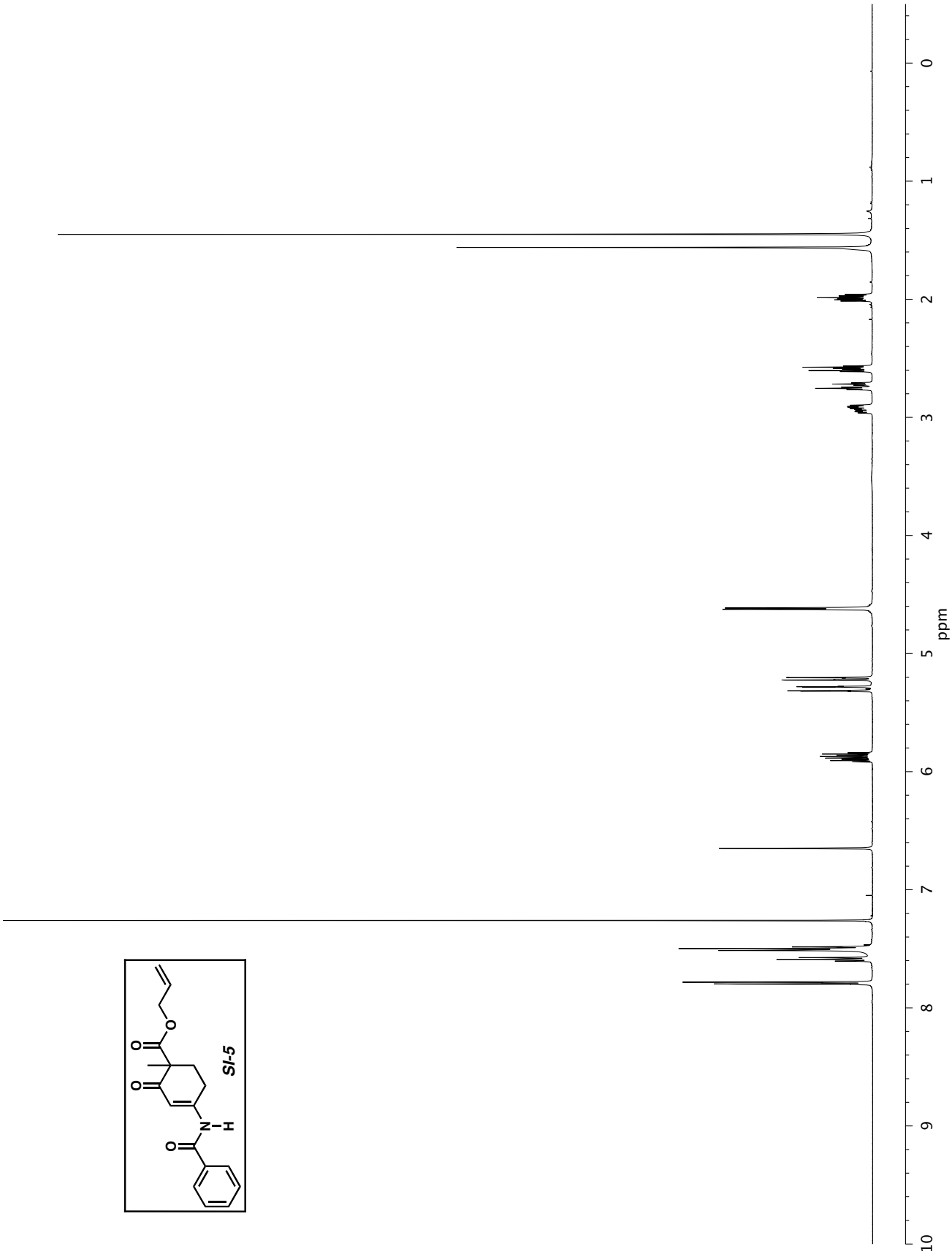


Figure SI-7A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-5**.

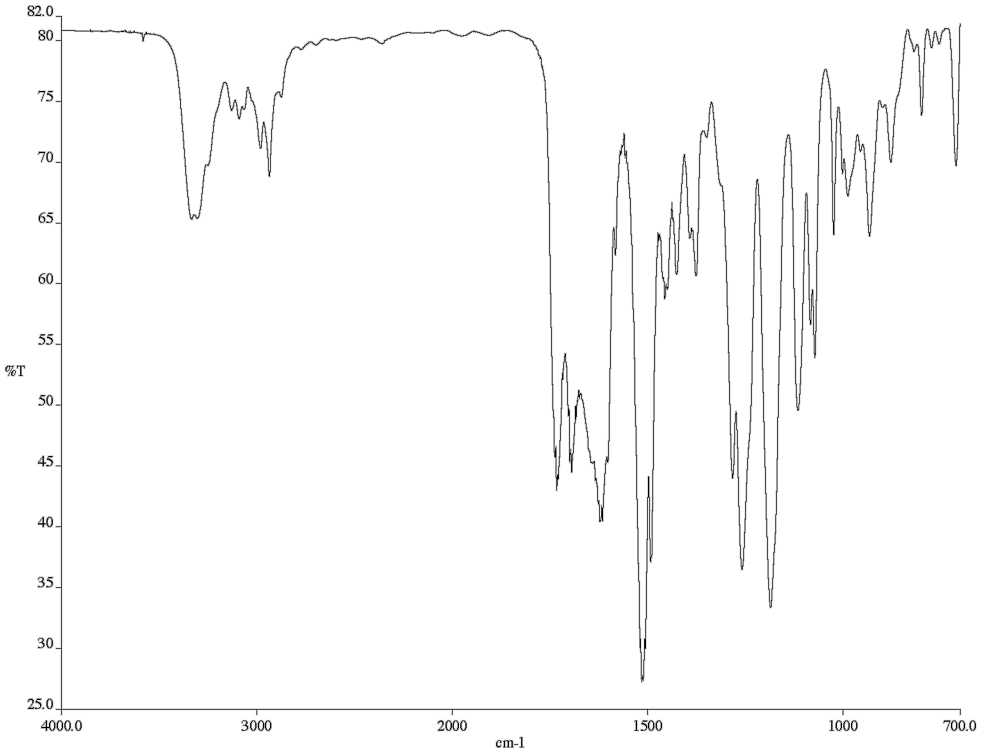


Figure SI-7B. Infrared spectrum (thin film/NaCl) of compound **SI-5**.

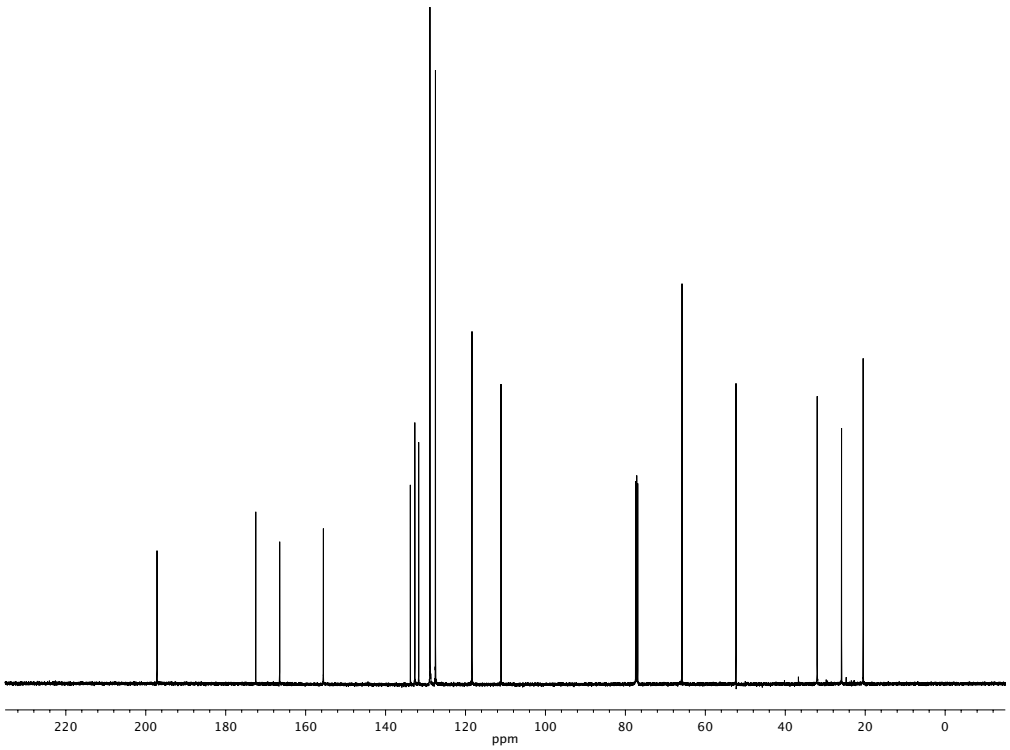


Figure SI-7C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-5**.

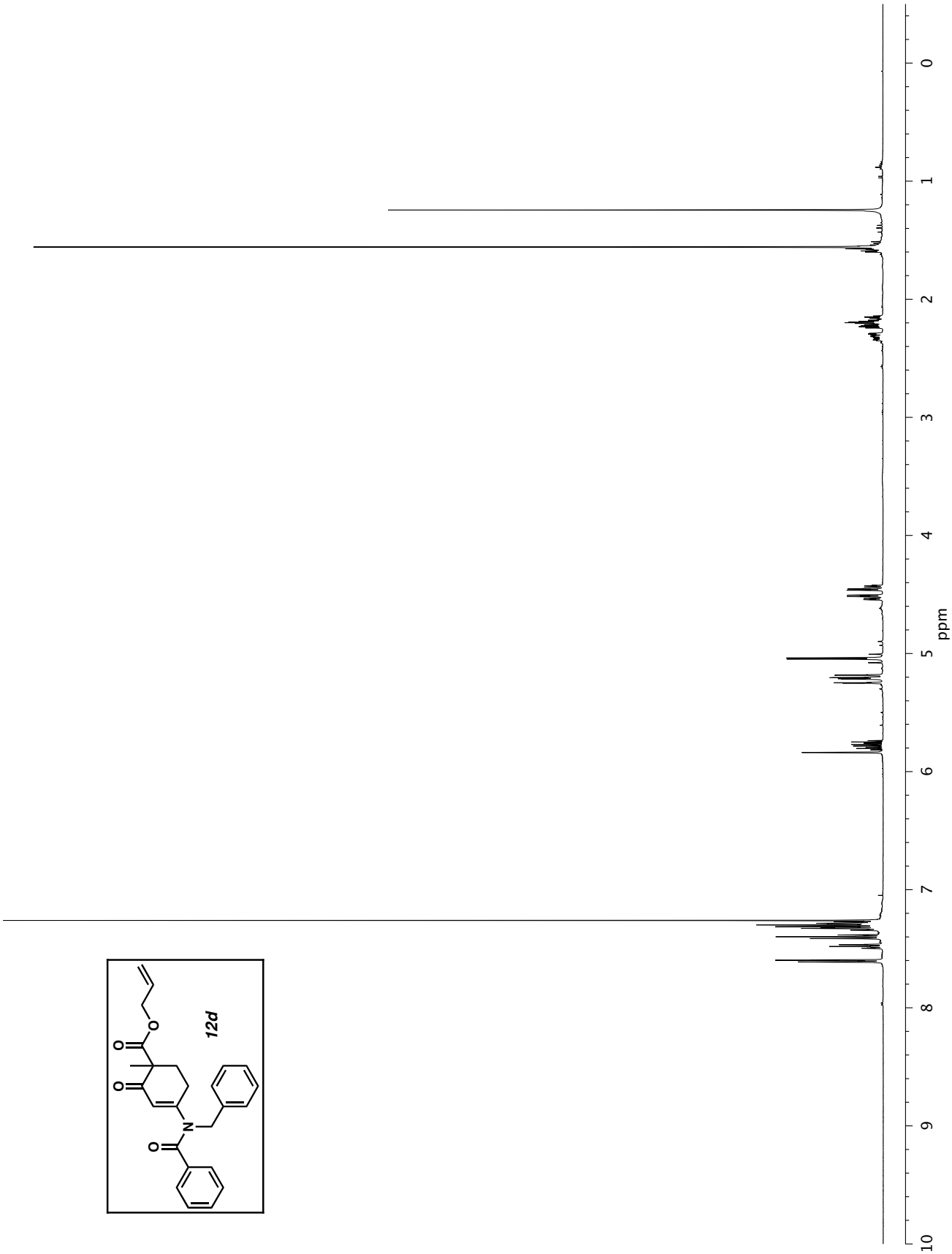


Figure SI-8A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **12d**.

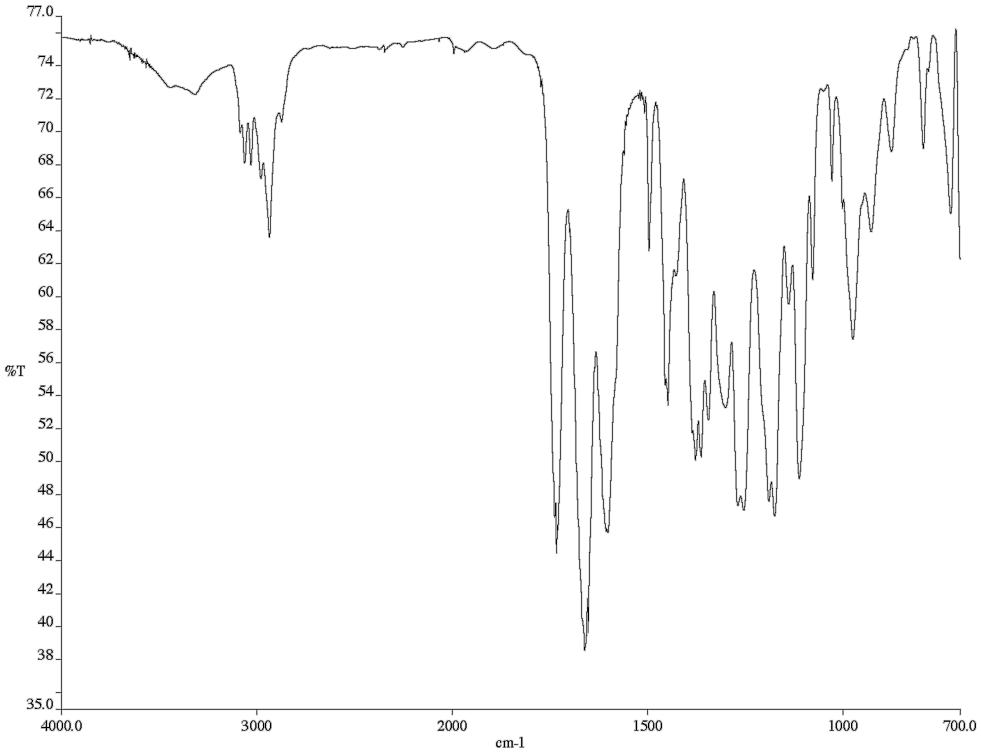


Figure SI-8B. Infrared spectrum (thin film/NaCl) of compound **12d**.

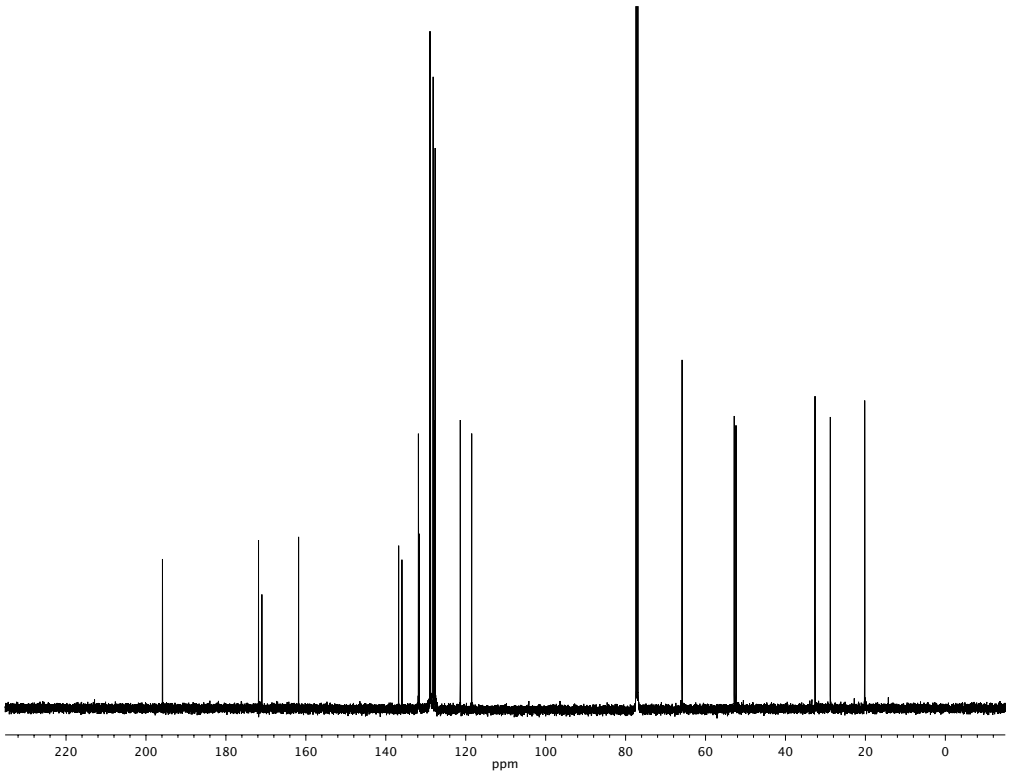


Figure SI-8C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **12d**.

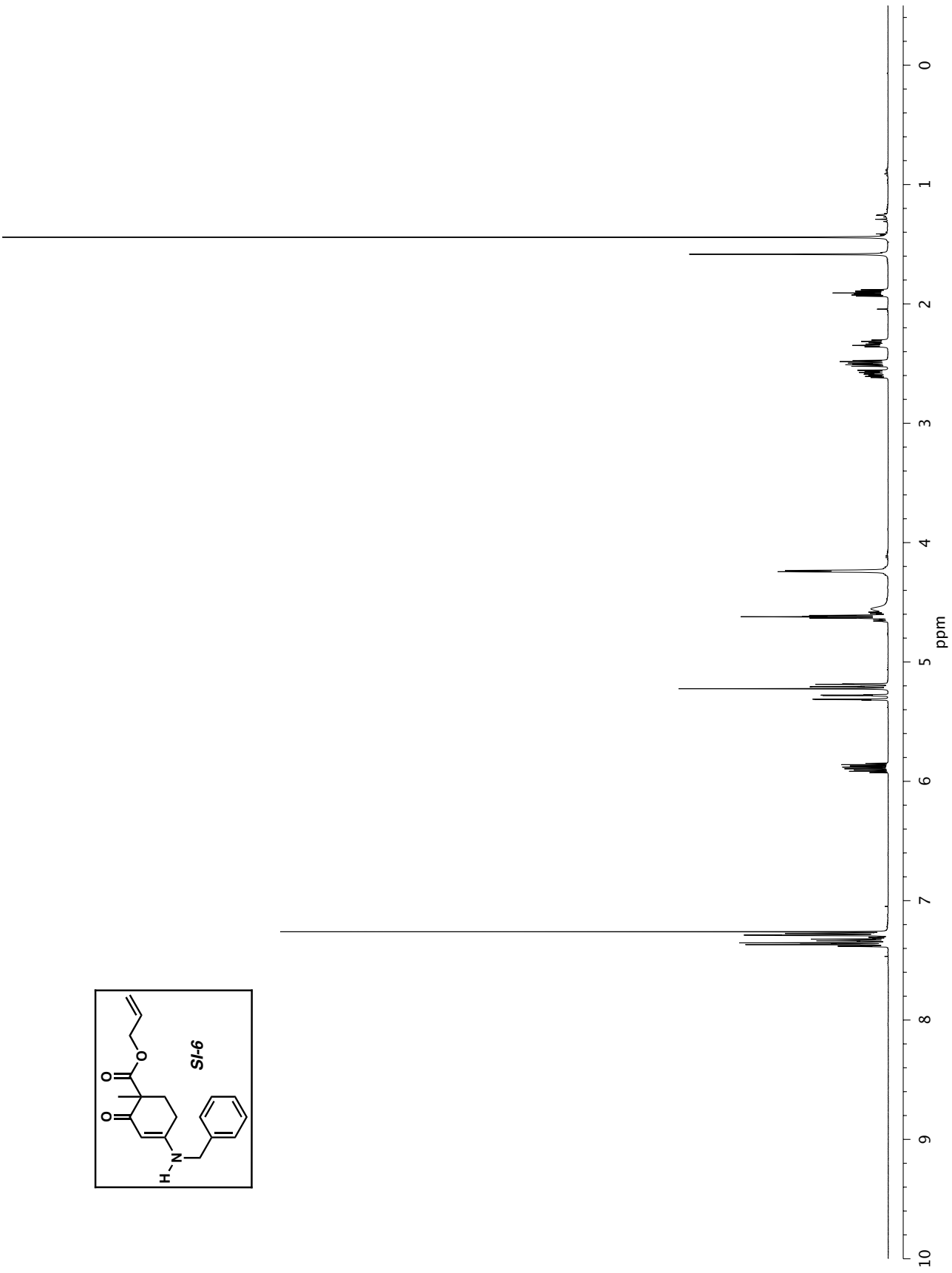


Figure SI-9A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-6**.

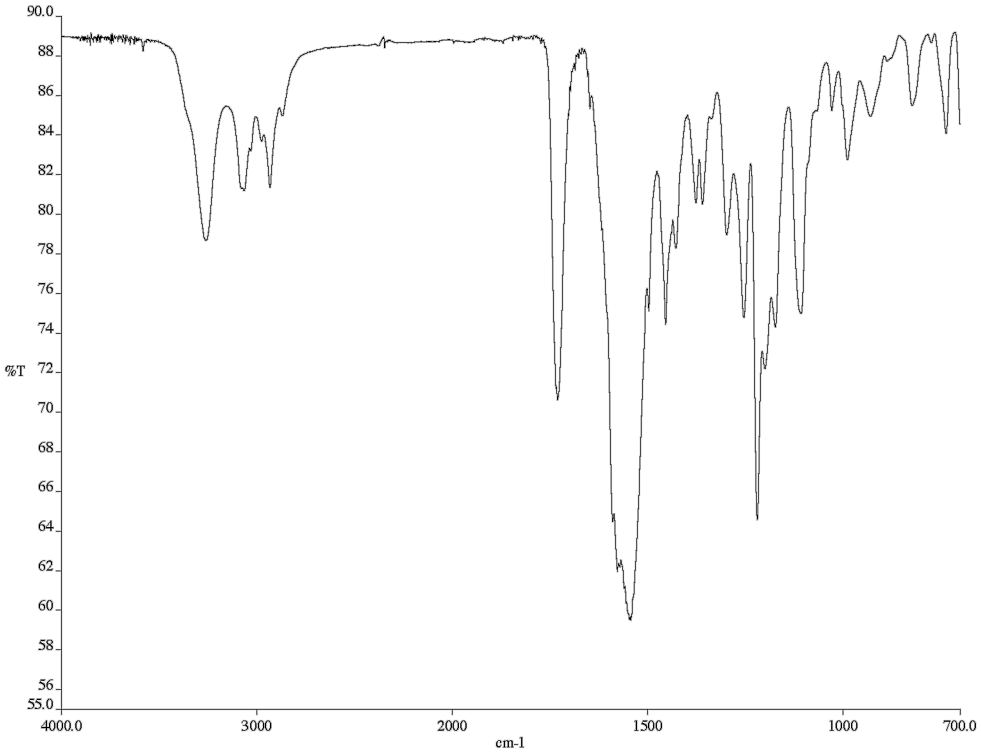


Figure SI-9B. Infrared spectrum (thin film/NaCl) of compound **SI-6**.

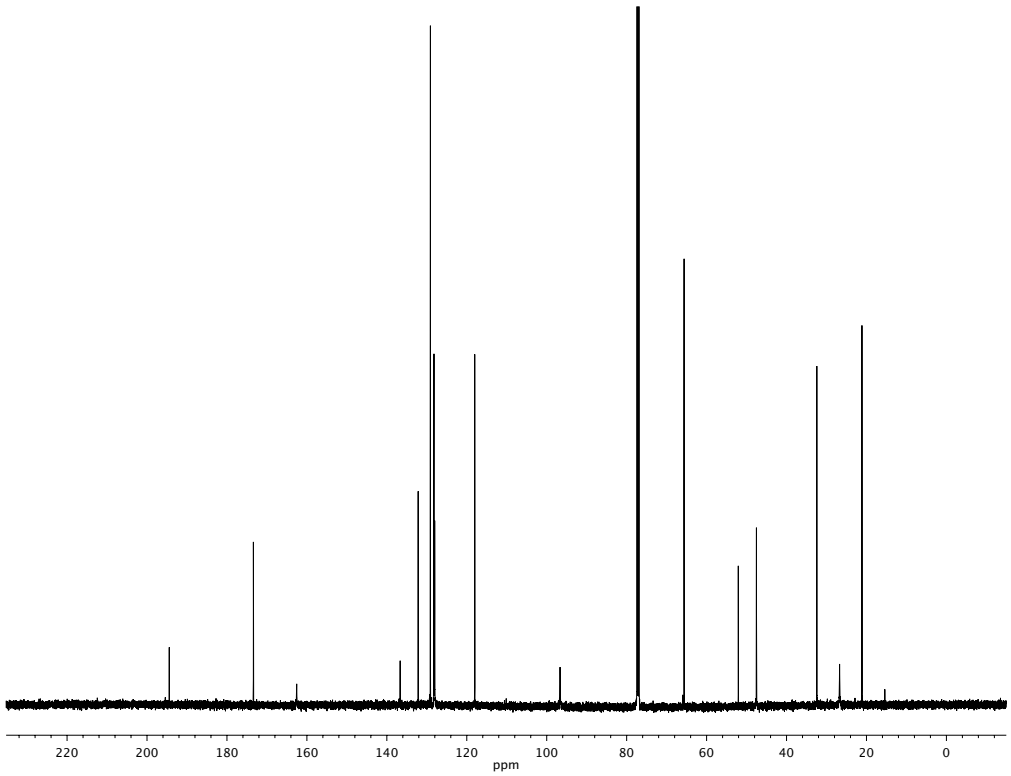


Figure SI-9C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-6**.

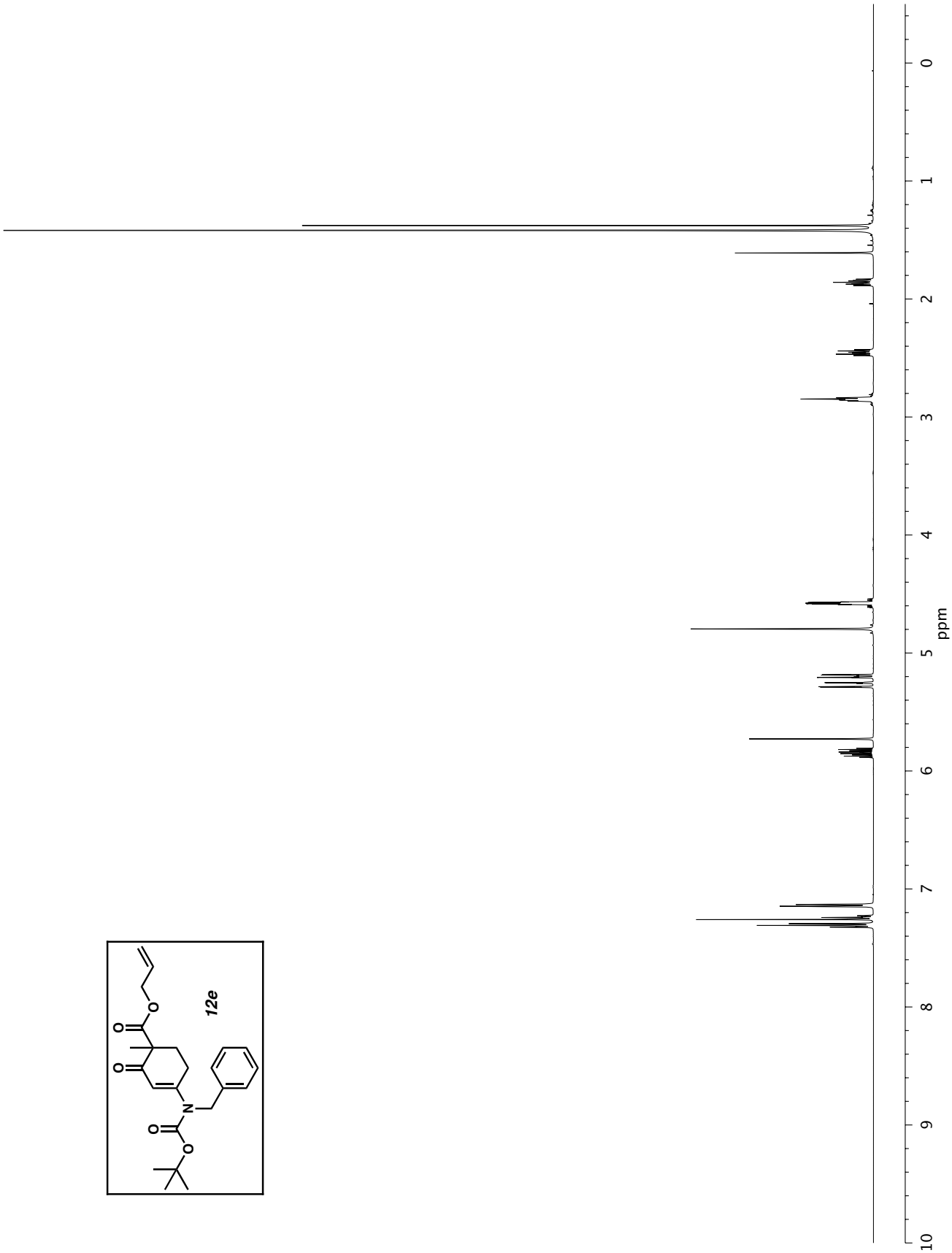


Figure SI-10A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **12e**.

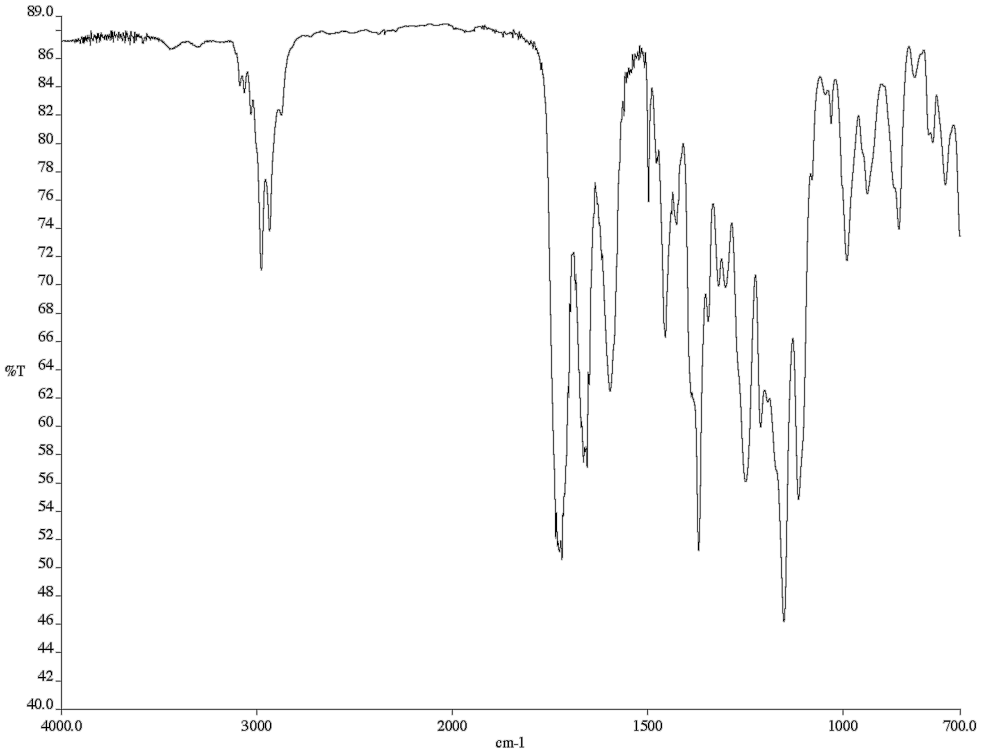


Figure SI-10B. Infrared spectrum (thin film/NaCl) of compound **12e**.

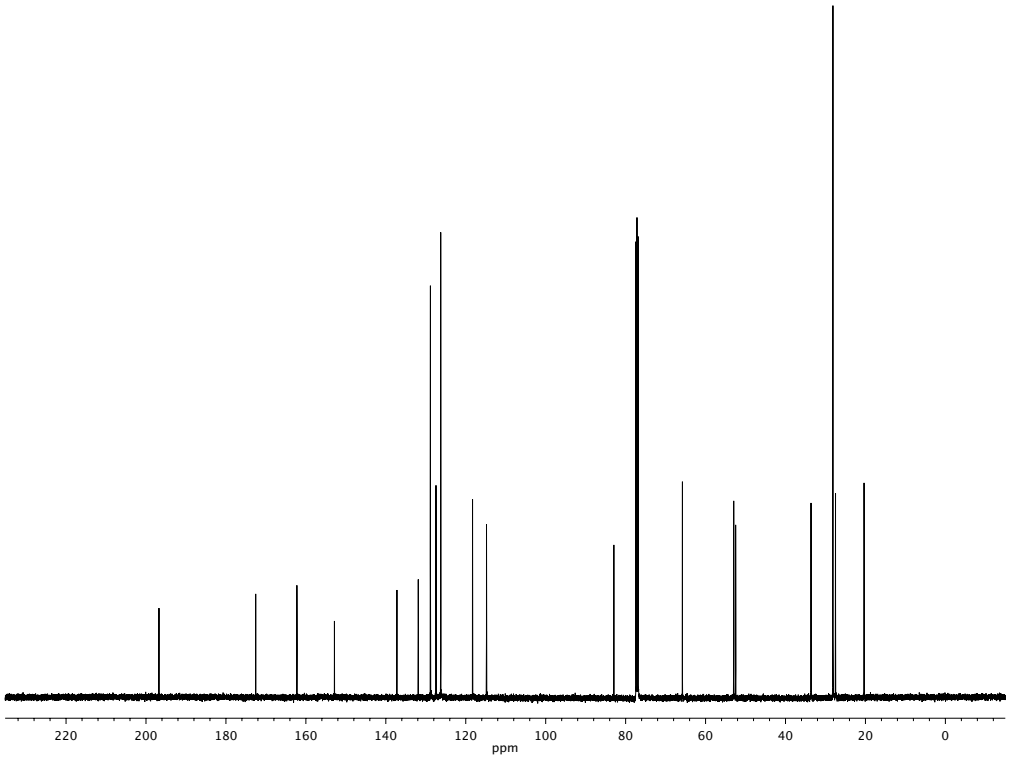


Figure SI-10C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **12e**.

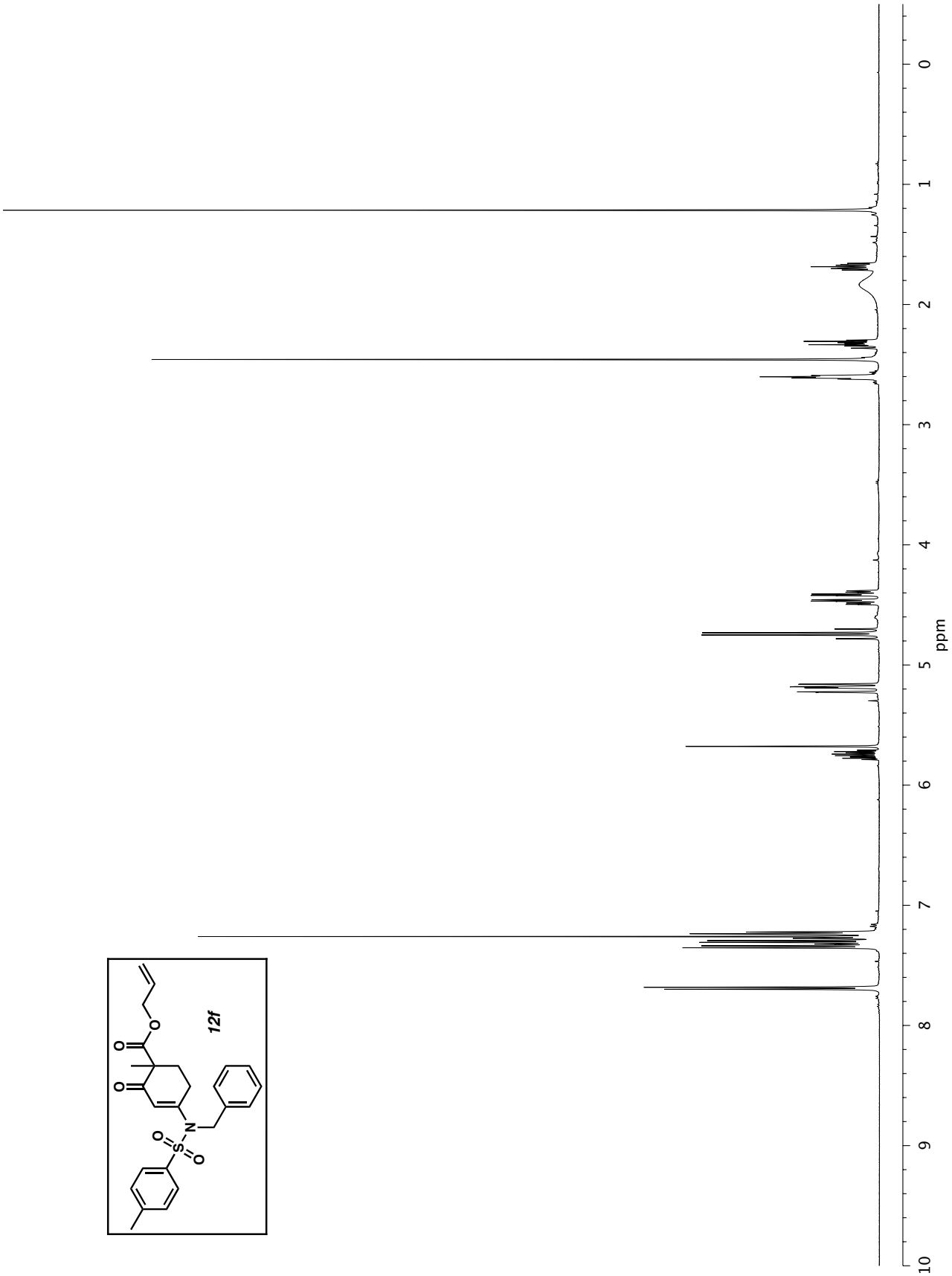


Figure SI-11A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **12f**.

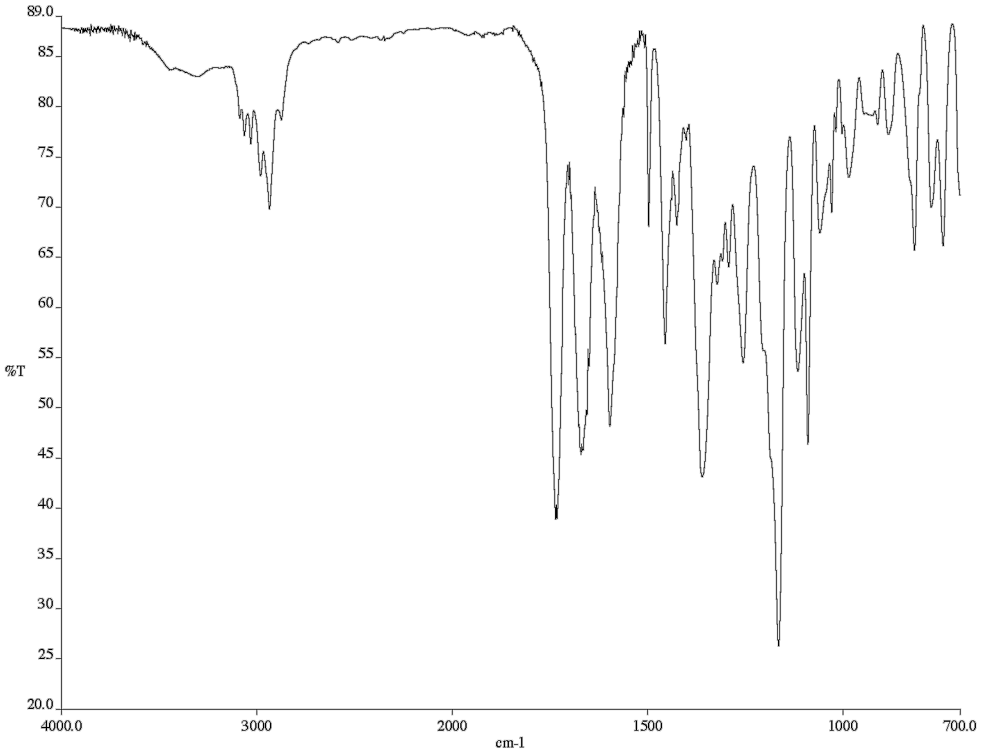


Figure SI-11B. Infrared spectrum (thin film/NaCl) of compound **12f**.

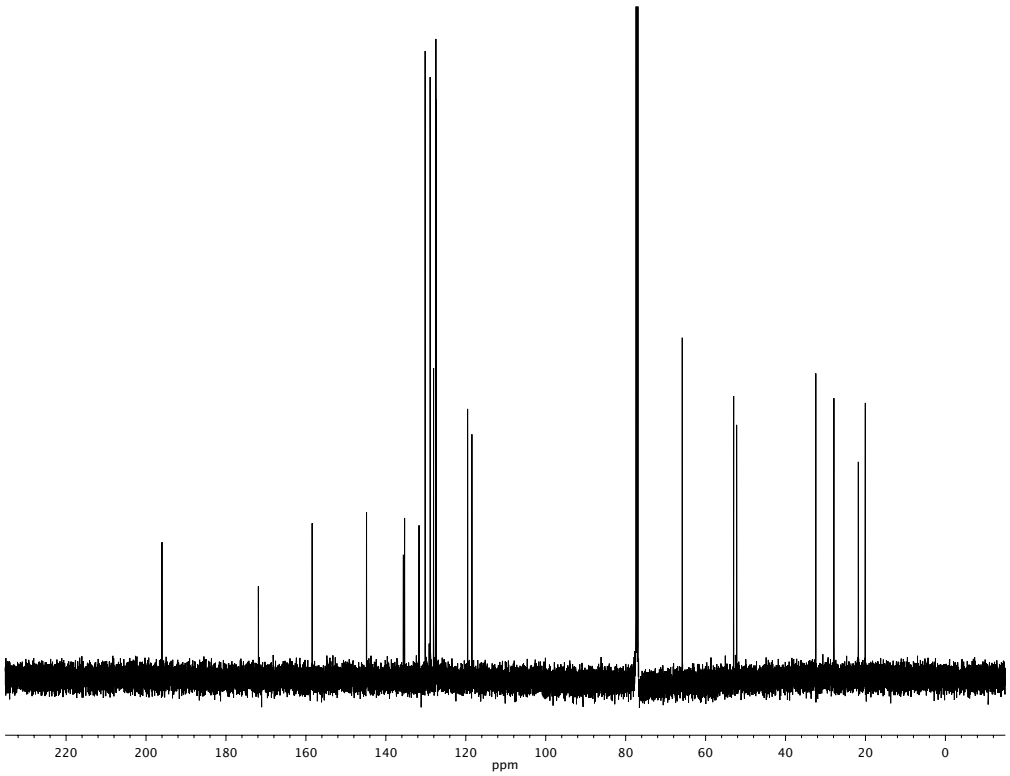


Figure SI-11C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **12f**.

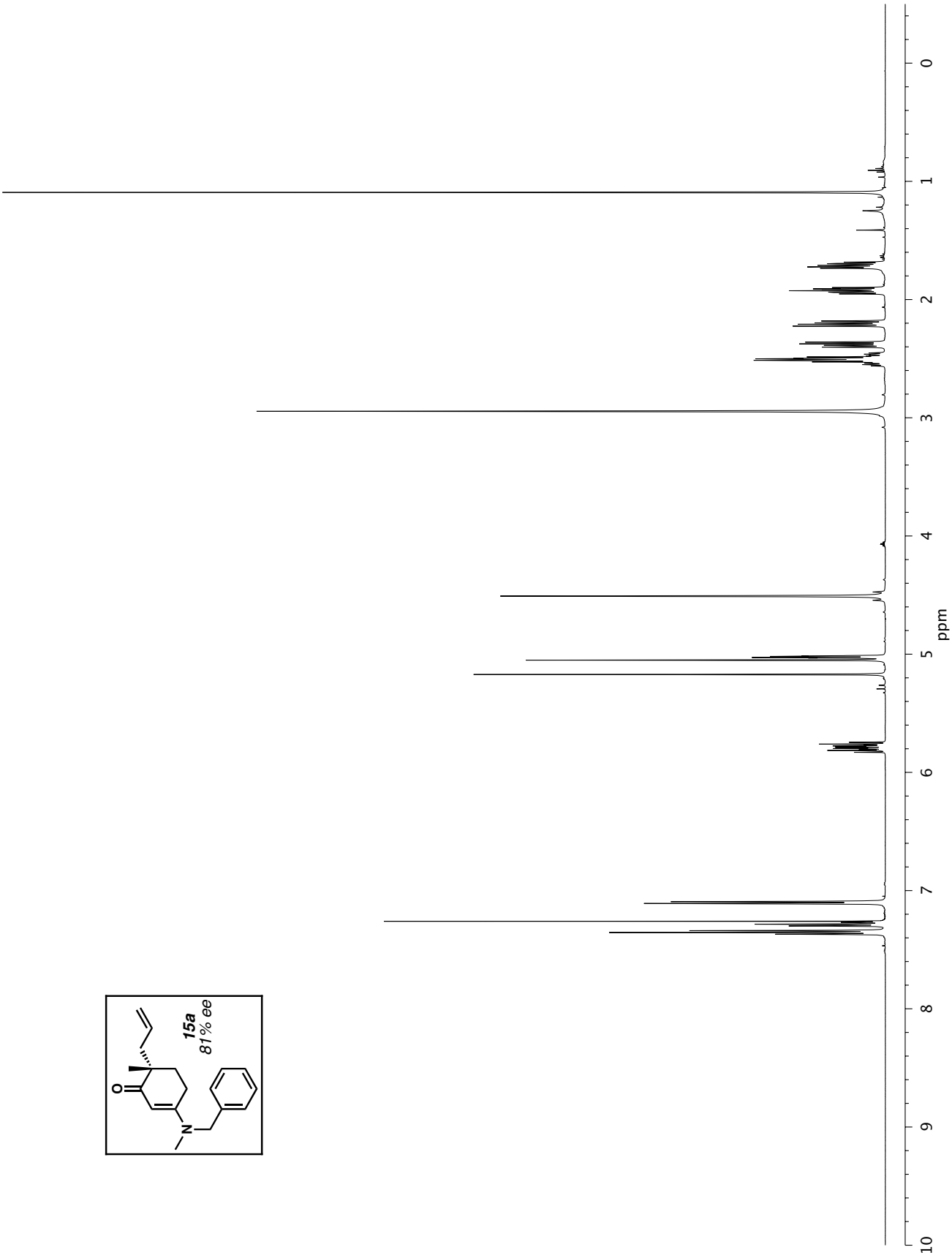


Figure SI-12A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **15a**.

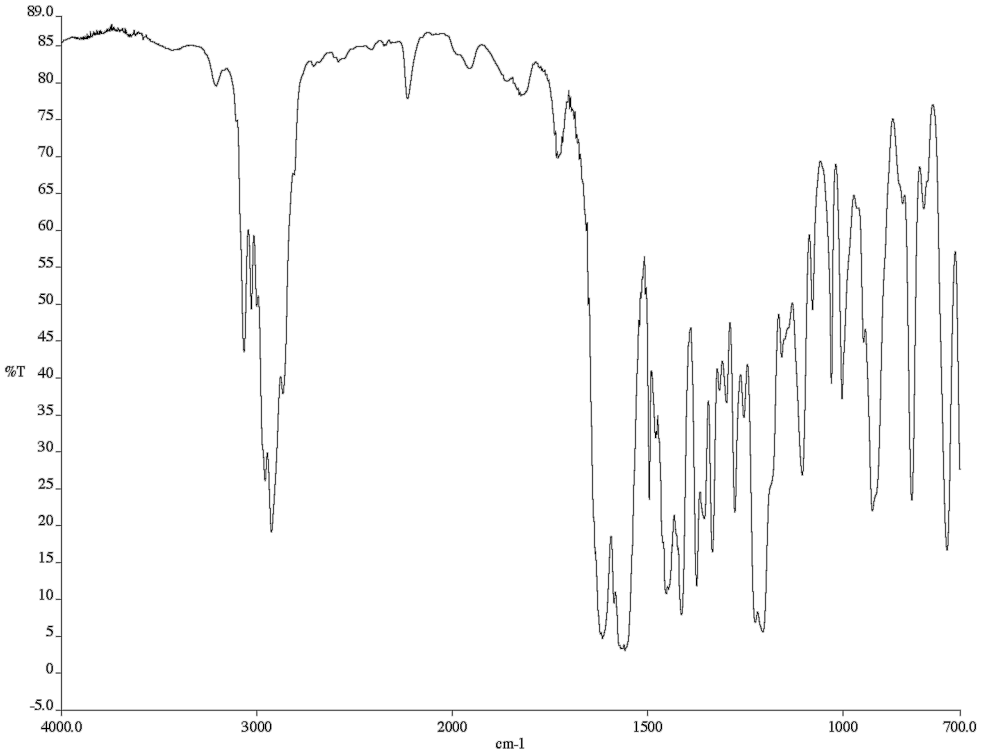


Figure SI-12B. Infrared spectrum (thin film/NaCl) of compound **15a**.

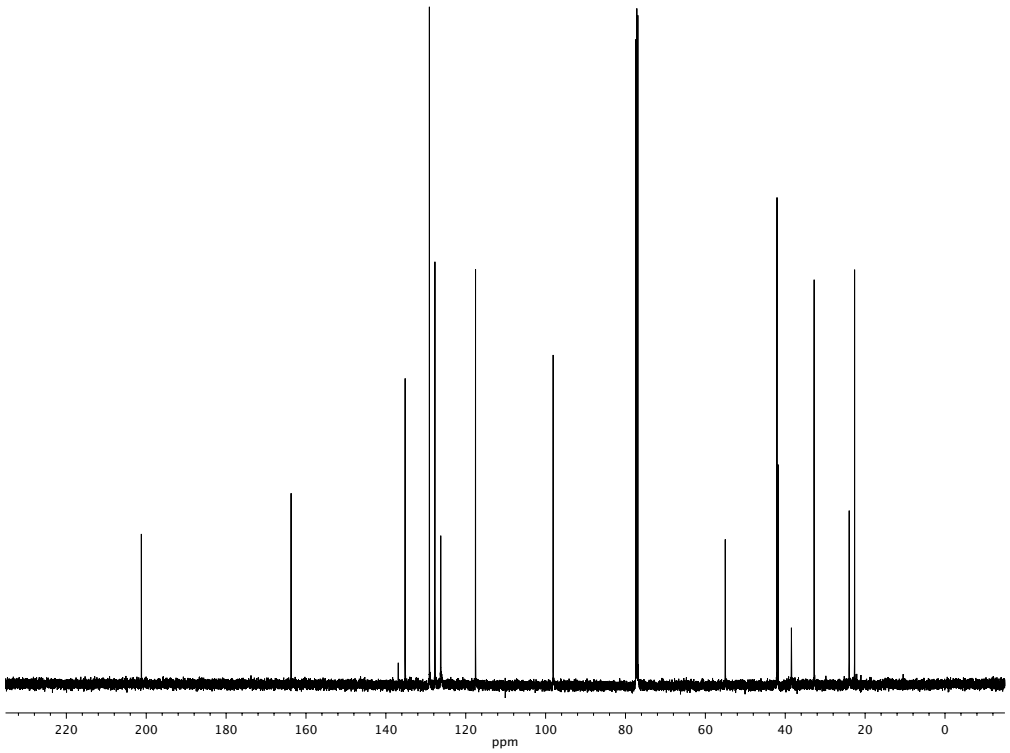
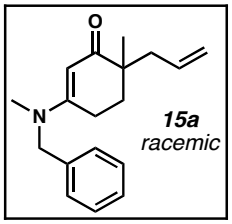


Figure SI-12C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **15a**.

NBB-VII-271A Col 2 7MeOH-2 NBB-VII-271A 2-4 11/28/2011 2:52:51 PM

Analytical Report SFC



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Chromatogram Name	NBB-VII-271A 2-4
Sample Name	
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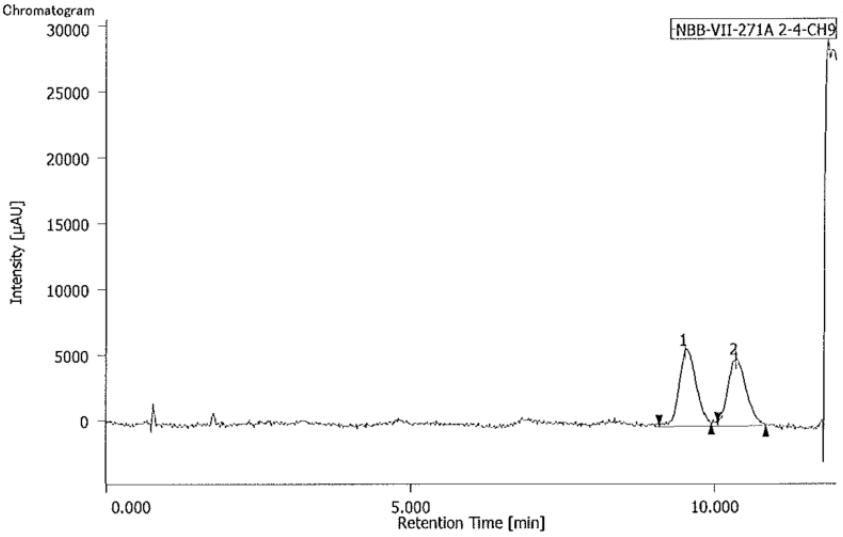
Acquisition Sequence	NBB-VII-271A Col 2 7MeOH-2
Control Method	Solv 1 Col 2 Isocratic 5B 5mL_min 10MPa 15min

Chromatogram



Peak Information

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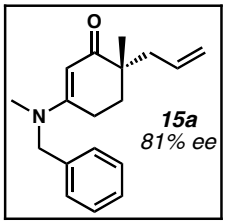
2	Unknown	9	10.347	107729	5211	48.360	10.053	10.840	0.322	N/A	1.233

1 / 1

Figure SI-12D. Chiral SFC data of racemic compound **15a**.

NBB-VIII-83-2B Col2 5MeOH 15min nbb-viii-83-2b 2/9/2012 12:11:21 PM

Analytical Report SFC



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Injection Date	2/9/2012 11:28:39 AM
Volume	5.00 [µL]
Sample #	11
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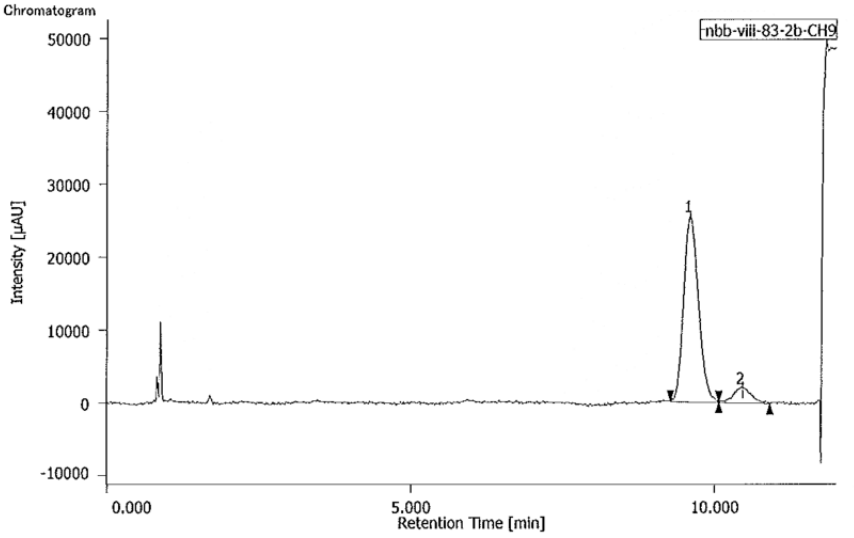
Executed Sequence	NBB-VIII-83-2B Col2 5MeOH 15min
Chromatogram Name	nbb-viii-83-2b
Sample Name	
Acquisition Time	12.0 [min]
Acquisition Sequence	NBB-VIII-83-2B Col2 5MeOH 15min
Control Method	Solv 1 Col 2 Isocratic 5B 5mL_min 10MPa 15min

Chromatogram



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
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2	Unknown	9	10.453	45114	2182	9.497	10.067	10.907	0.305	N/A	1.075

1 / 1

Figure SI-12E. Chiral SFC data enantioenriched of compound **15a**.

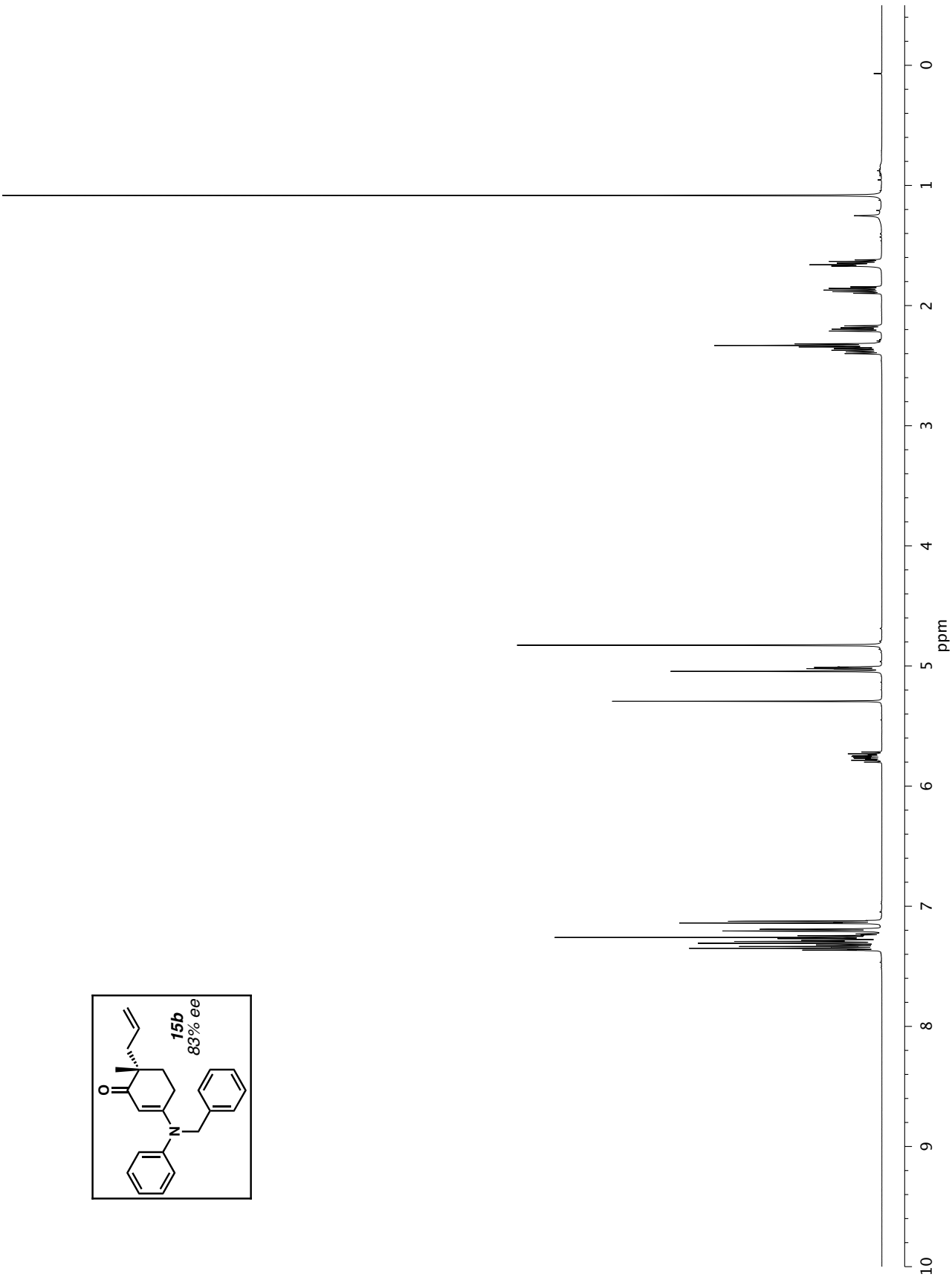


Figure SI-13A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **15b**.

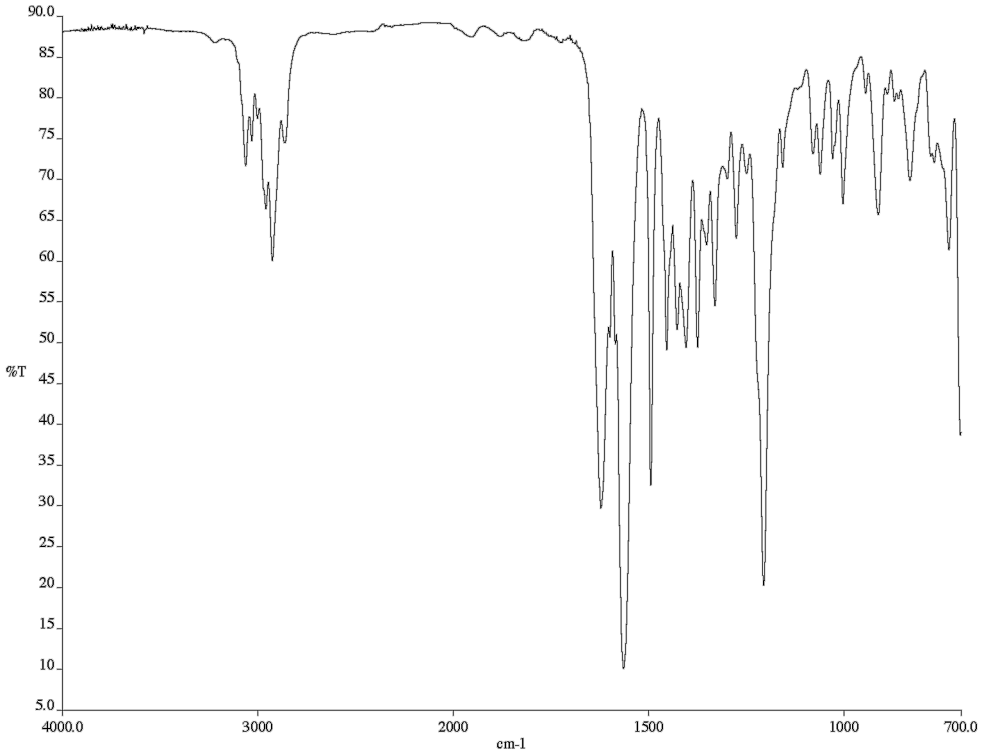


Figure SI-13B. Infrared spectrum (thin film/NaCl) of compound **15b**.

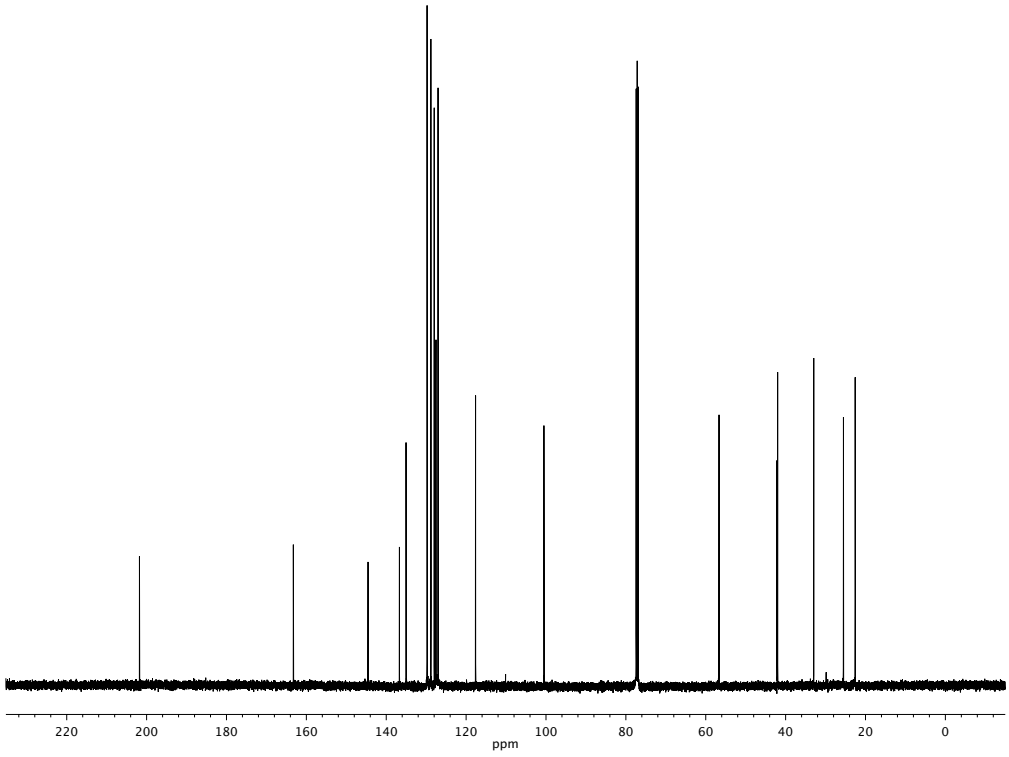
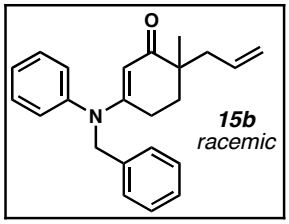


Figure SI-13C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **15b**.

NBB-VII-273 Sub3 Col4 5MeOH-2 NBB-VII-273 PhBn 10/27/2011 4:52:15 PM

Analytical Report SFC



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Sample #	51
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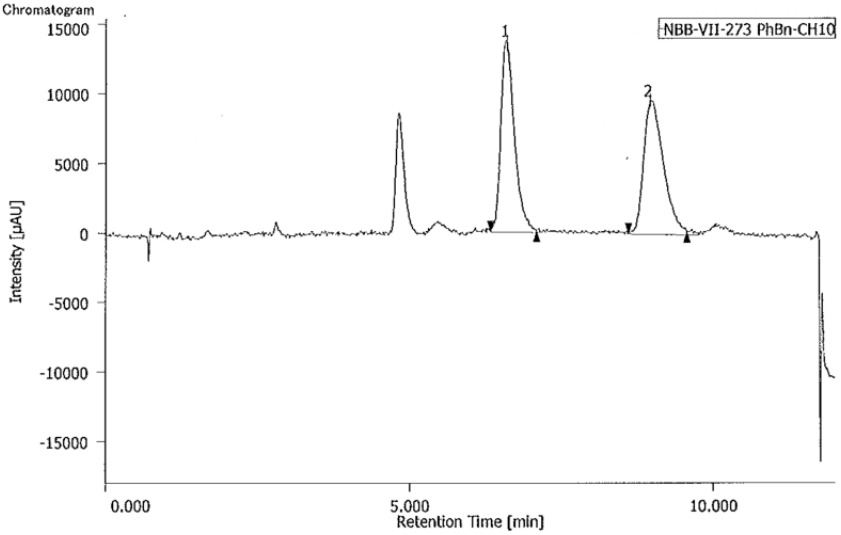
Acquisition Time	12.0 [min]
Acquisition Sequence	NBB-VII-273 Sub3 Col4 5MeOH-2
Control Method	Solv 1 Col 4 Isocratic 5B 5mL_min 10MPa 15min



Peak Information

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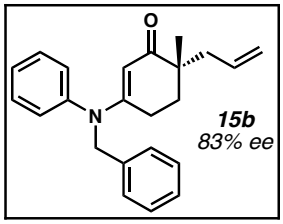
2	Unknown	10	8.960	218252	9641	50.365	8.600	9.560	0.348	N/A	1.695

1 / 1

Figure SI-13D. Chiral SFC data of racemic compound **15b**.

NBB-VIII-85-2A Col4 5% MeOH 15min nbb-viii-85-2a 6/27/2012 11:39:10 AM

Analytical Report SFC



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Sample #	51
Project Name	Cal Tech SFC
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Chromatogram Name	nbb-viii-85-2a
Sample Name	
Acquisition Time	12.0 [min]
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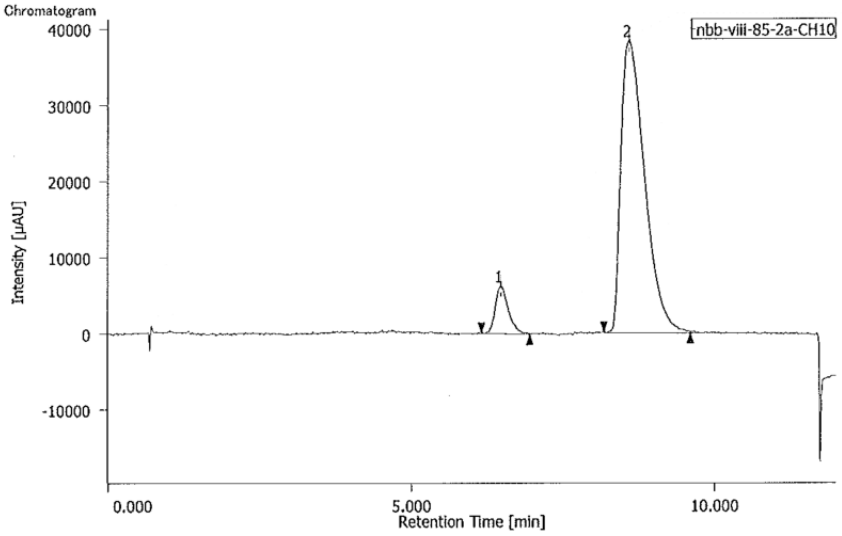
Control Method	Solv 1 Col 4 Isocratic 5B 5mL_min 10MPa 15min

Chromatogram



Peak Information

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2	Unknown	10	8.600	1040639	38422	91.654	8.187	9.600	0.422	N/A	1.835

1 / 1

Figure SI-13E. Chiral SFC data of enantioenriched compound **15b**.

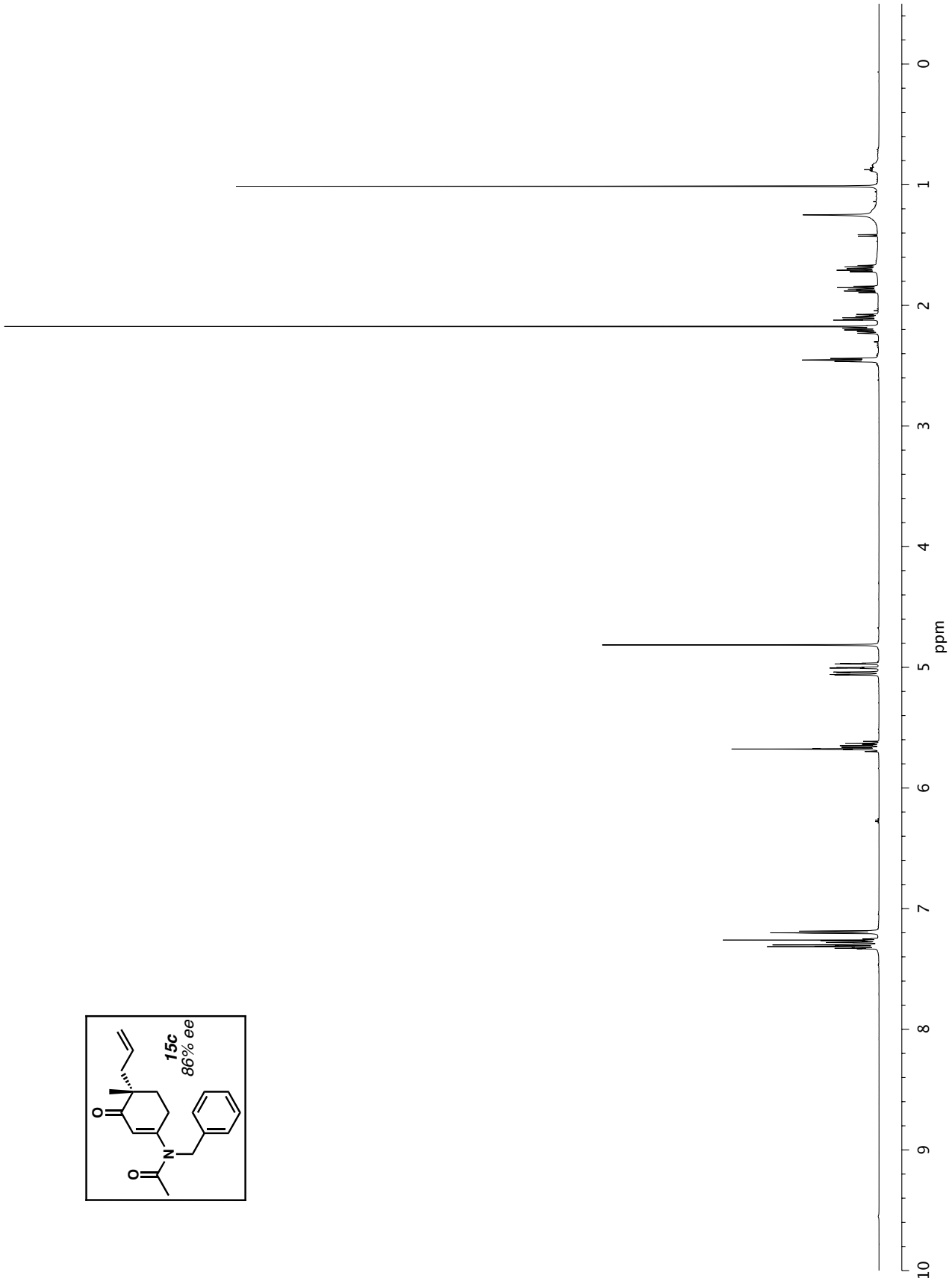


Figure SI-14A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **15c**.

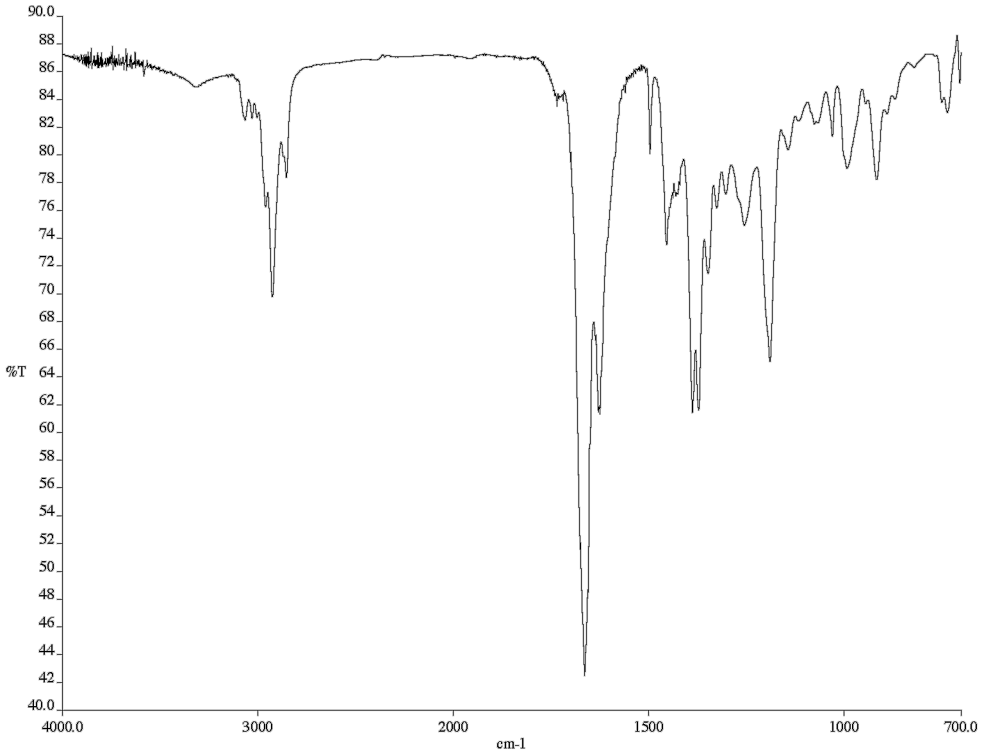


Figure SI-14B. Infrared spectrum (thin film/NaCl) of compound **15c**.

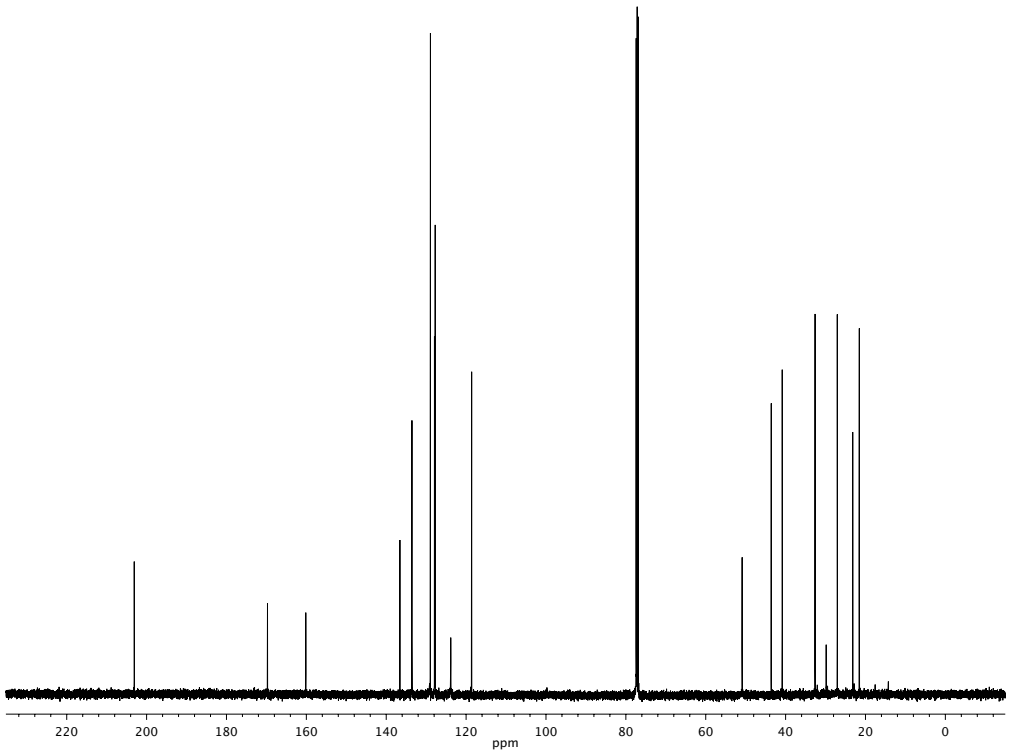
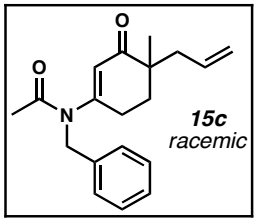


Figure SI-14C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **15c**.

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                                                      Inj Volume : 5 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 10 µl
    Acq. Method     : C:\Chem32\1\DATA\NBB\AHC 2012-10-04 14-26-18\S1C2 12MIN 5.M
    Last changed    : 5/19/2011 9:00:59 PM by DCB
    Analysis Method : C:\CHEM32\1\DATA\NBB\AHC 2012-10-04 14-26-18\NBB-IX-257RAC.D\DA.M (S1C2
                      12MIN 5.M)
    Last changed    : 10/4/2012 2:52:53 PM by JNI
                      (modified after loading)
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    Sample Info     : NBB-IX-257 Racemic, 4-3-1
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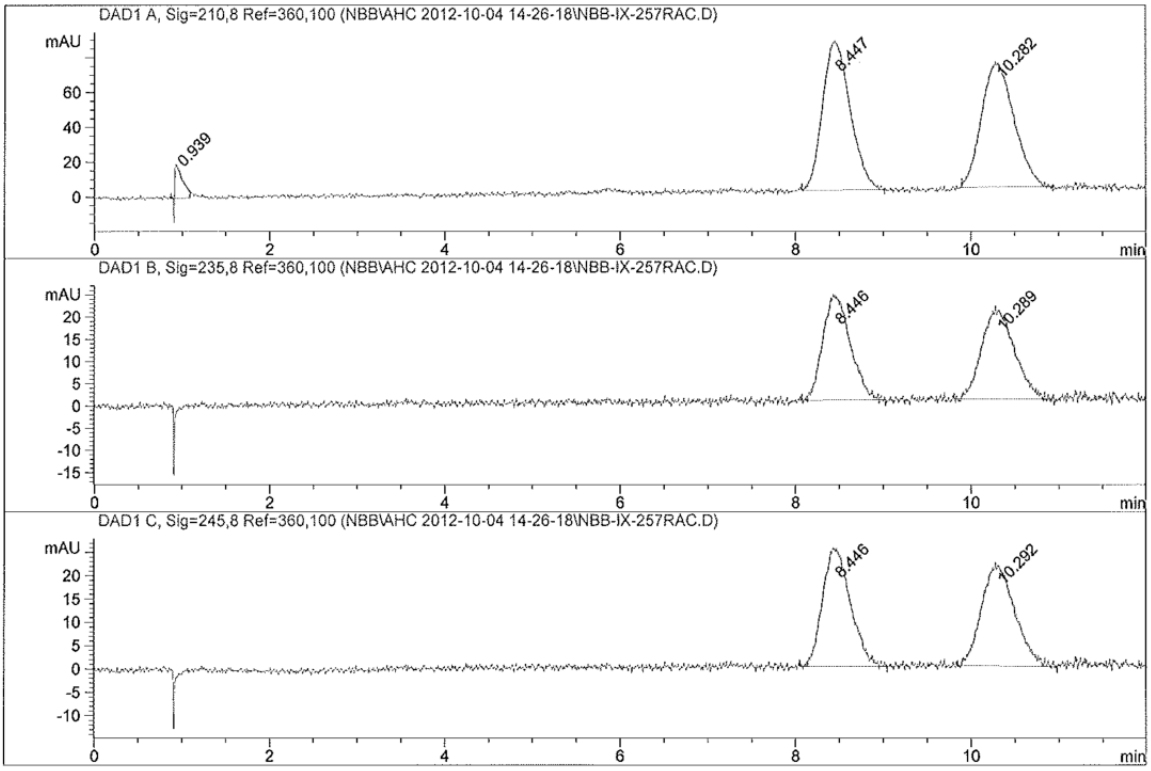
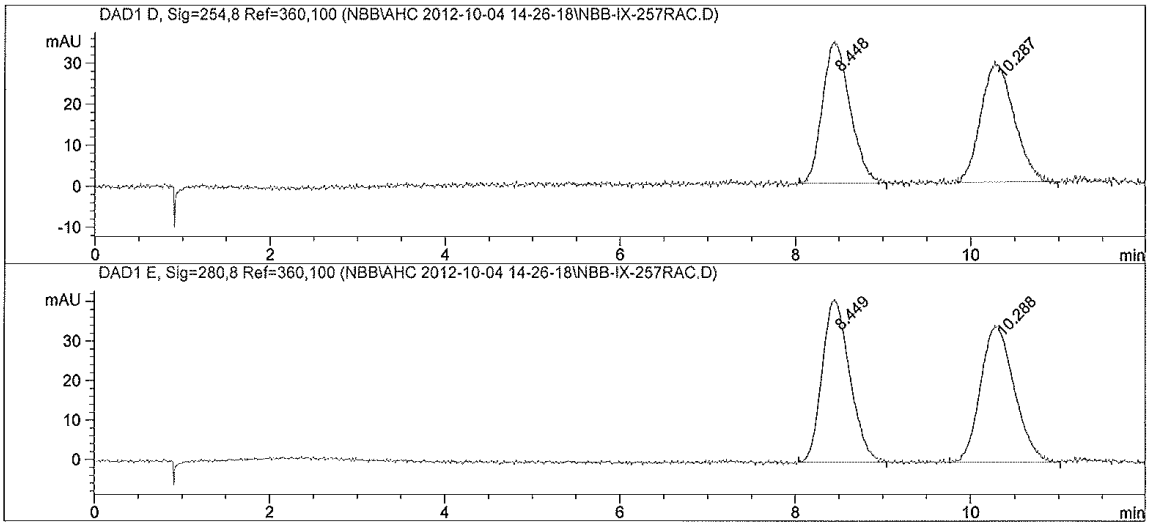


Figure SI-14D. Chiral SFC data of racemic compound **15c**.

Data File C:\CHEM32\1\DATA\NBB\AHC 2012-10-04 14-26-18\NBB-IX-257RAC.D
Sample Name: NBB-IX-257rac



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Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.939	BB	0.0949	113.87008	18.23328	2.9604
2	8.447	BB	0.3010	1879.52710	85.33506	48.8635
3	10.282	BB	0.3308	1853.08533	70.93210	48.1761
Totals :				3846.48251	174.50044	

Signal 2: DAD1 B, Sig=235,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.446	BB	0.3360	517.12830	23.56898	49.5066
2	10.289	BB	0.4053	527.43506	19.89780	50.4934
Totals :				1044.56335	43.46678	

Data File C:\CHEM32\1\DATA\NBB\AHC 2012-10-04 14-26-18\NBB-IX-257RAC.D
Sample Name: NBB-IX-257rac

Signal 3: DAD1 C, Sig=245,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.446	BB	0.3447	560.93591	25.10540	49.4459
2	10.292	BB	0.3865	573.50763	21.00747	50.5541
Totals :				1134.44354	46.11286	

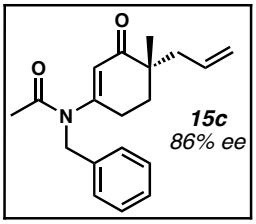
Signal 4: DAD1 D, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.448	BB	0.3431	760.15375	34.23129	49.9424
2	10.287	BB	0.4083	761.90826	28.46026	50.0576
Totals :				1522.06201	62.69156	

Signal 5: DAD1 E, Sig=280,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.449	BB	0.3437	912.00861	40.97363	49.7294
2	10.288	BB	0.4101	921.93524	34.23816	50.2706
Totals :				1833.94385	75.21178	

*** End of Report ***

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Data File C:\CHEM32\1\DATA\NBB\AHC 2012-10-04 15-47-38\NBB-IX-257A.D
Sample Name: NBB-IX-257A

    ======================================================================
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    Acq. Instrument : Instrument 1                  Location : P2-C-01
    Injection Date  : 10/4/2012 3:51:04 PM             Inj :   1
                                                   Inj Volume : 5 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 10 µl
    Acq. Method     : C:\Chem32\1\DATA\NBB\AHC 2012-10-04 15-47-38\S1C2 12MIN 5.M
    Last changed    : 5/19/2011 9:00:59 PM by DCB
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                      12MIN 5.M)
    Last changed    : 10/4/2012 4:07:59 PM by JNI
                      (modified after loading)
    Method Info     : S1C2 12min 5.M: 5% MeOH, AD-H 3 mL/min, 12 min

    Sample Info     : NBB-IX-257A, Enantioenriched
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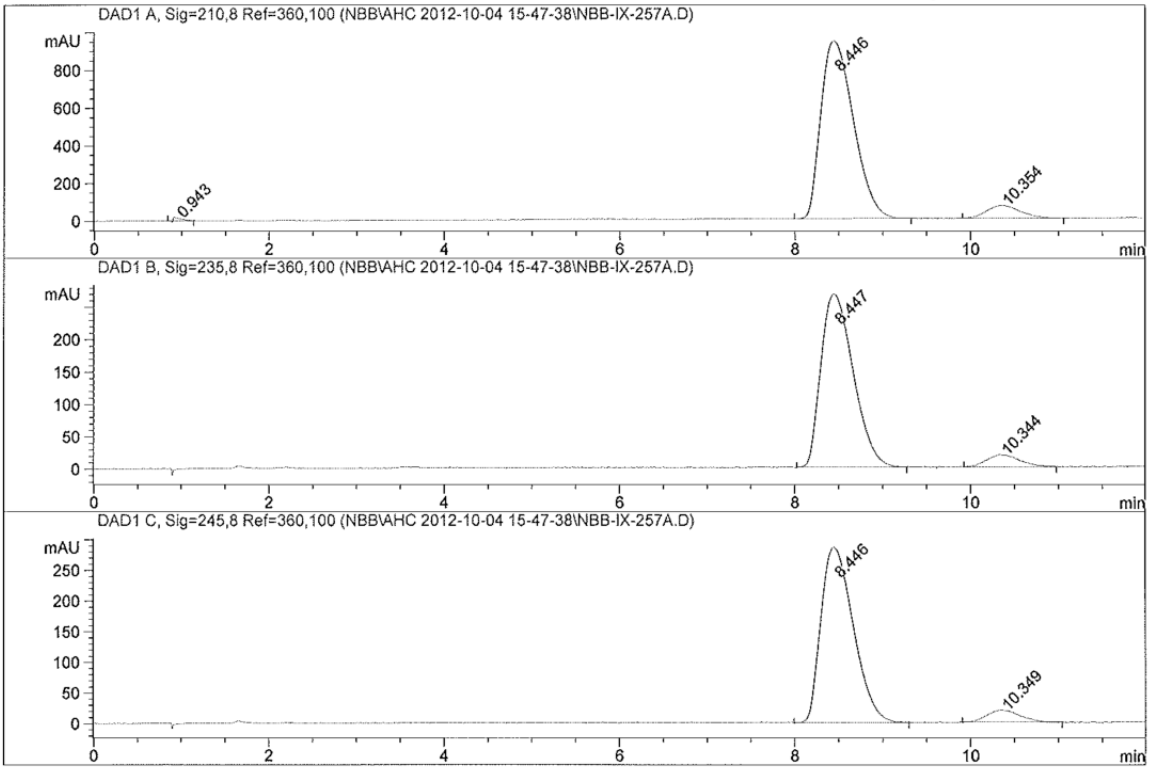
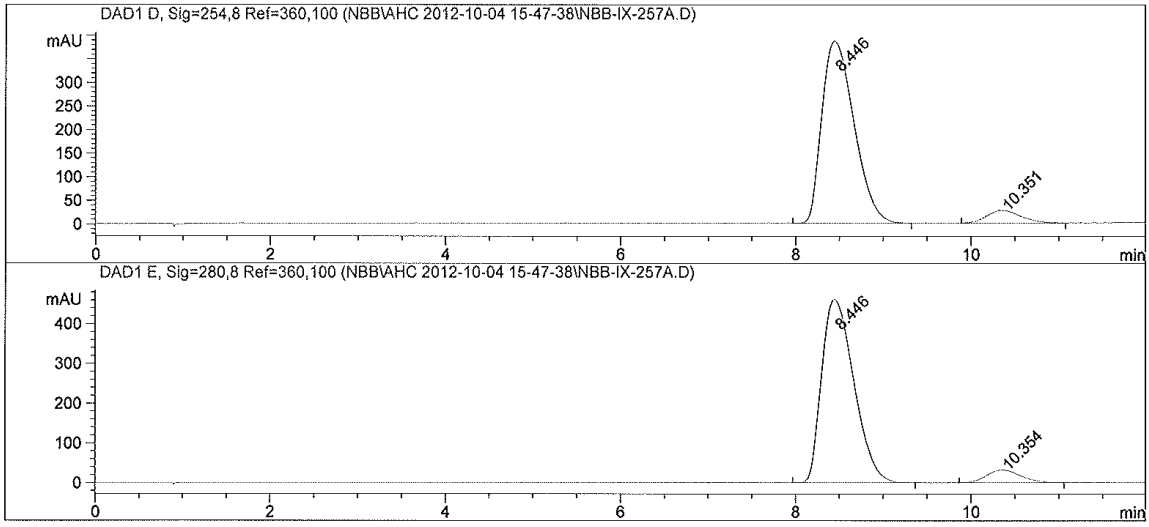


Figure SI-14E. Chiral SFC data of enantioenriched compound **15c**.

Data File C:\CHEM32\1\DATA\NBB\AHC 2012-10-04 15-47-38\NBB-IX-257A.D
Sample Name: NBB-IX-257A



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.943	BB	0.1079	128.53369	17.05869	0.4895
2	8.446	BB	0.4090	2.43412e4	943.31750	92.6927
3	10.354	BB	0.4117	1790.38196	67.02154	6.8179
Totals :				2.62601e4	1027.39774	

Signal 2: DAD1 B, Sig=235,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.447	BB	0.4024	6847.52051	267.69025	93.1500
2	10.344	BB	0.3904	503.54898	18.68495	6.8500
Totals :				7351.06949	286.37520	

Data File C:\CHEM32\1\DATA\NBB\AHC 2012-10-04 15-47-38\NBB-IX-257A.D
Sample Name: NBB-IX-257A

Signal 3: DAD1 C, Sig=245,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.446	BB	0.4026	7314.68262	285.79251	93.2437
2	10.349	BB	0.3876	530.01166	19.84396	6.7563
Totals :				7844.69427	305.63647	

Signal 4: DAD1 D, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.446	BB	0.4107	9876.51074	385.71722	93.1672
2	10.351	BB	0.4197	724.33203	26.76538	6.8328
Totals :				1.06008e4	412.48260	

Signal 5: DAD1 E, Sig=280,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.446	BB	0.4065	1.17996e4	461.17719	93.2482
2	10.354	BB	0.4160	854.37073	31.95074	6.7518
Totals :				1.26540e4	493.12793	

*** End of Report ***

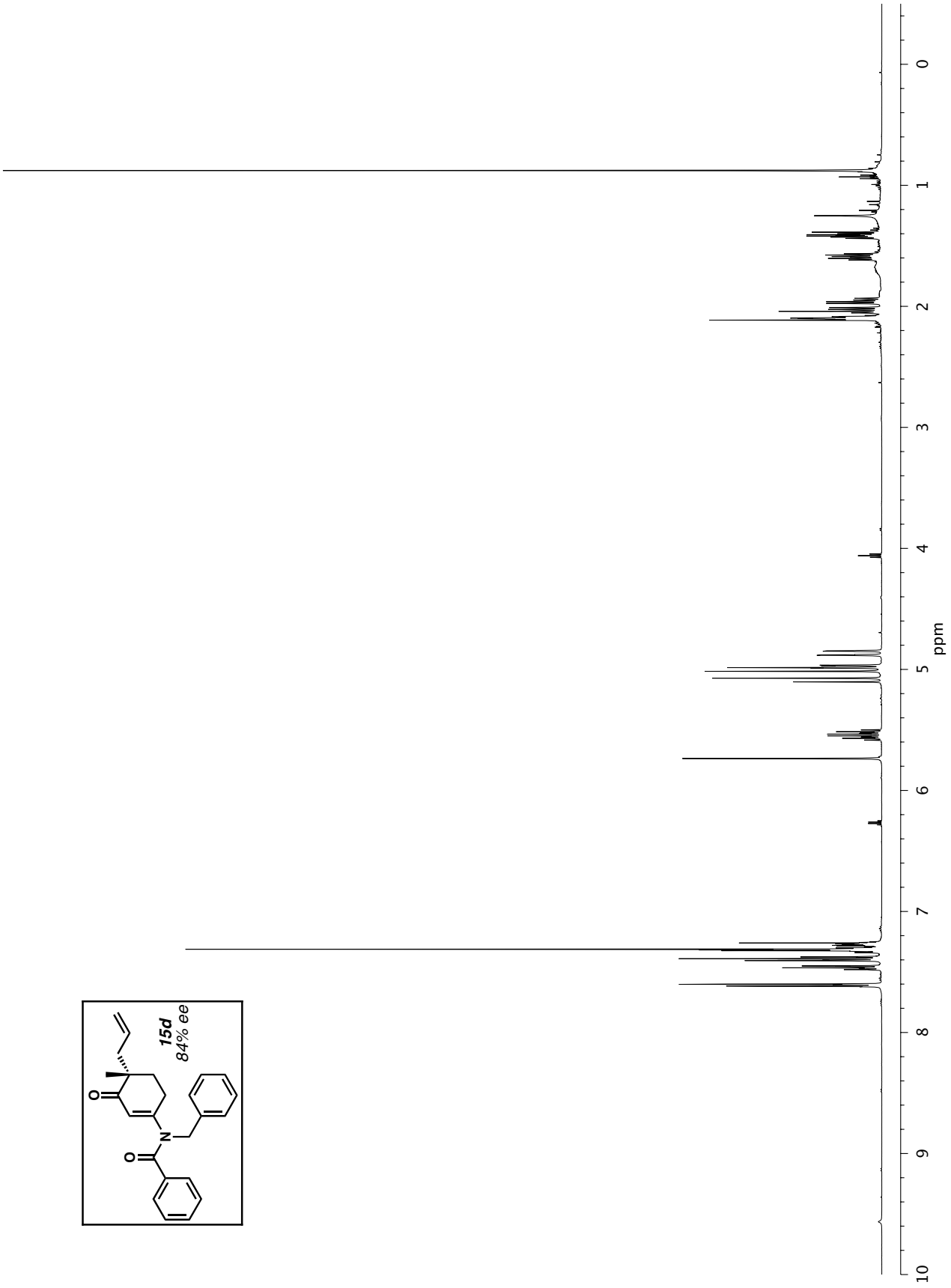


Figure SI-15A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **15d**.

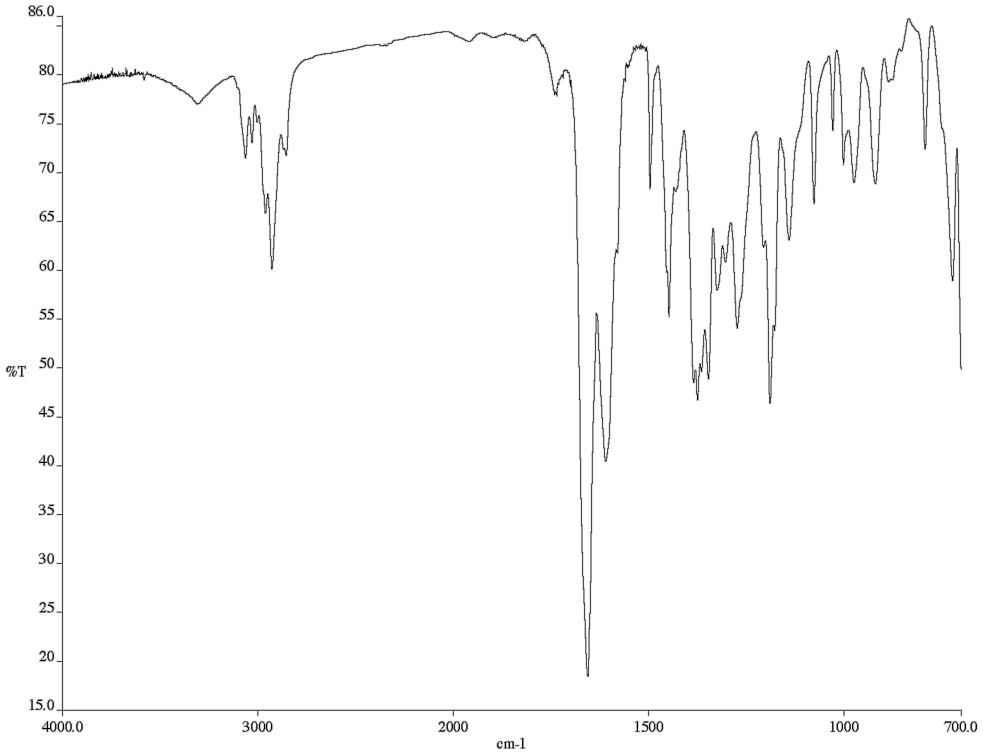


Figure SI-15B. Infrared spectrum (thin film/NaCl) of compound **15d**.

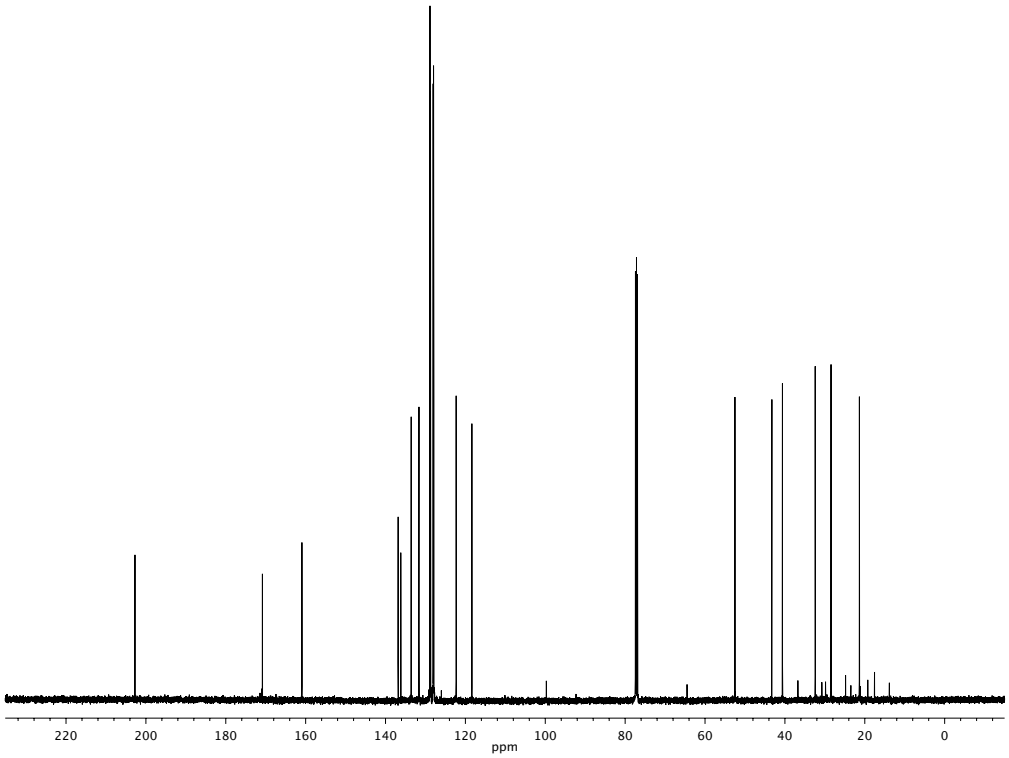
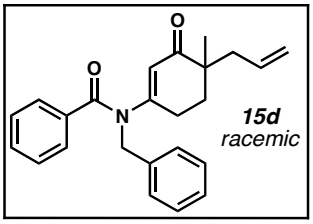


Figure SI-15C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **15d**.

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Data File C:\CHEM32\1\DATA\NBB\AHC 2012-10-05 16-30-33\NBB-IX-259RAC.D
Sample Name: NBB-IX-259rac

    ========================================================================
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    Acq. Instrument : Instrument 1                      Location : P2-C-02
    Injection Date  : 10/5/2012 4:39:27 PM                  Inj :   1
                                                      Inj Volume : 5 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 10 µl
    Acq. Method     : C:\Chem32\1\DATA\NBB\AHC 2012-10-05 16-30-33\S1C2 20MIN 7-2.M
    Last changed    : 10/5/2012 2:09:16 PM by JNI
    Analysis Method : C:\CHEM32\1\DATA\NBB\AHC 2012-10-05 16-30-33\NBB-IX-259RAC.D\DA.M (S1C2
                      20MIN 7-2.M)
    Last changed    : 10/5/2012 5:12:31 PM by JNI
                      (modified after loading)
    Method Info     : S1C2 30min10.M: 7% IPA, AD-H 2.5 mL/min, 30 min

    Sample Info     : NBB-IX-259 Racemic, 5-3-1
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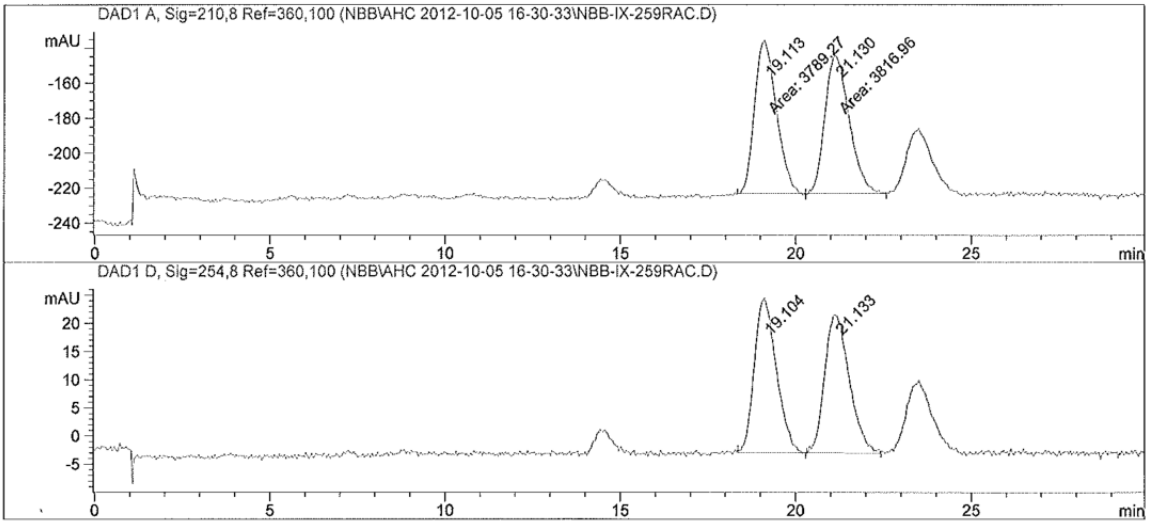


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    ========================================================================
                              Area Percent Report
    ========================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=210,8 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  19.113 MM    0.7220 3789.26807   87.47143  49.8180
       2  21.130 MM    0.8097 3816.95605   78.56348  50.1820

    Totals :                  7606.22412  166.03491

Instrument 1 10/5/2012 5:13:05 PM JNI                          Page   1 of 2
```

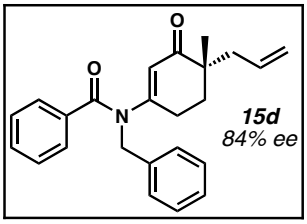
Figure SI-15D. Chiral SFC data of racemic compound **15d**.

Data File C:\CHEM32\1\DATA\NBB\AHC 2012-10-05 16-30-33\NBB-IX-259RAC.D
Sample Name: NBB-IX-259rac

Signal 2: DAD1 D, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.104	BB	0.6731	1203.76782	27.37041	49.9413
2	21.133	BB	0.7281	1206.59875	24.43527	50.0587
Totals :				2410.36658	51.80568	

*** End of Report ***

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Data File C:\CHEM32\1\DATA\NBB\AHC 2012-10-05 14-10-15\NBB-IX-259-3A.D
Sample Name: NBB-IX-259-3A

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    Acq. Instrument : Instrument 1                  Location : P2-C-03
    Injection Date  : 10/5/2012 2:50:04 PM             Inj :   1
                                                   Inj Volume : 5 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 7 µl
    Acq. Method     : C:\Chem32\1\DATA\NBB\AHC 2012-10-05 14-10-15\S1C2 20MIN 7-2.M
    Last changed    : 10/5/2012 2:09:16 PM by JNI
    Analysis Method : C:\CHEM32\1\DATA\NBB\AHC 2012-10-05 14-10-15\NBB-IX-259-3A.D\DA.M (S1C2
                      20MIN 7-2.M)
    Last changed    : 10/5/2012 4:21:35 PM by JNI
                      (modified after loading)
    Method Info     : S1C2 30min10.M: 7% IPA, AD-H 2.5 mL/min, 30 min

    Sample Info     : NBB-IX-259-3A, Enantioenriched
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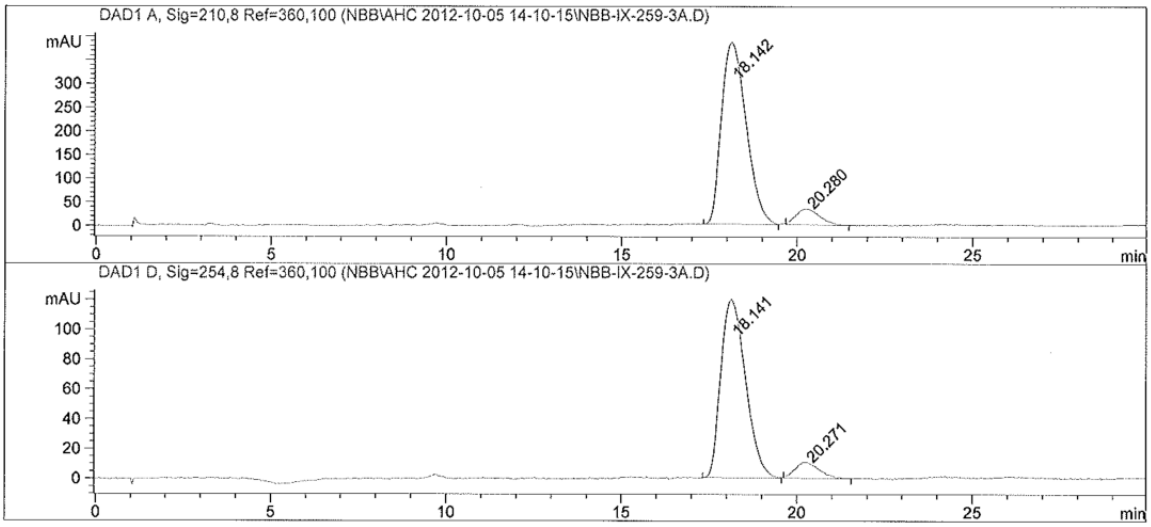


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    ==========================================================================
                              Area Percent Report
    ==========================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=210,8 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  18.142 BB    0.7288 1.89158e4   383.96072  92.0466
       2  20.280 BB    0.5815 1634.45569   34.08136   7.9534

    Totals :                  2.05503e4   418.04209

Instrument 1 10/5/2012 4:22:01 PM JNI                          Page   1 of 2
```

Figure SI-15E. Chiral SFC data of enantioenriched compound **15d**.

Data File C:\CHEM32\1\DATA\NBB\AHC 2012-10-05 14-10-15\NBB-IX-259-3A.D
Sample Name: NBB-IX-259-3A

Signal 2: DAD1 D, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.141	BB	0.7748	5890.54053	119.55161	91.8569
2	20.271	BB	0.6096	522.19653	10.69611	8.1431
Totals :				6412.73706	130.24772	

*** End of Report ***

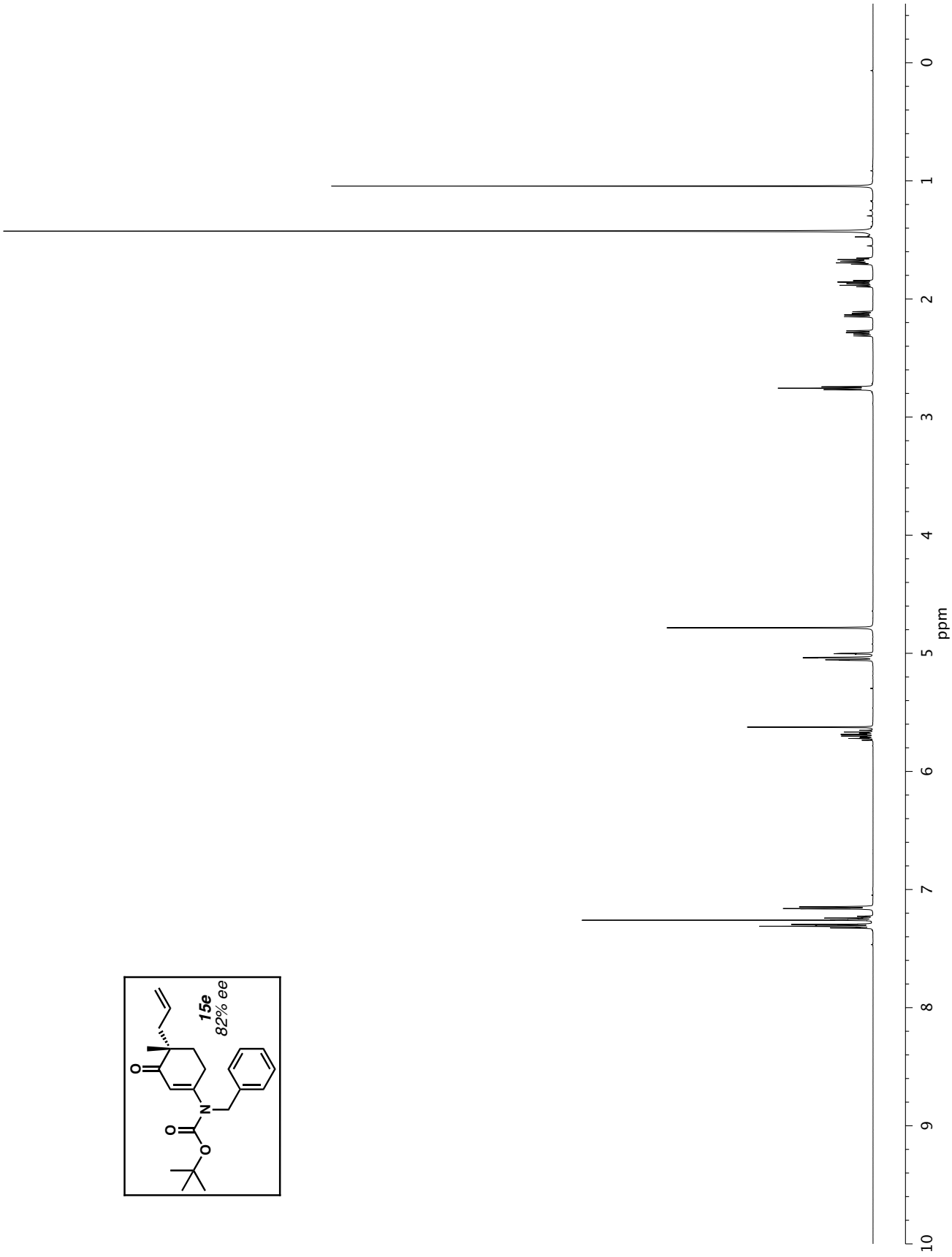


Figure SI-16A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **15e**.

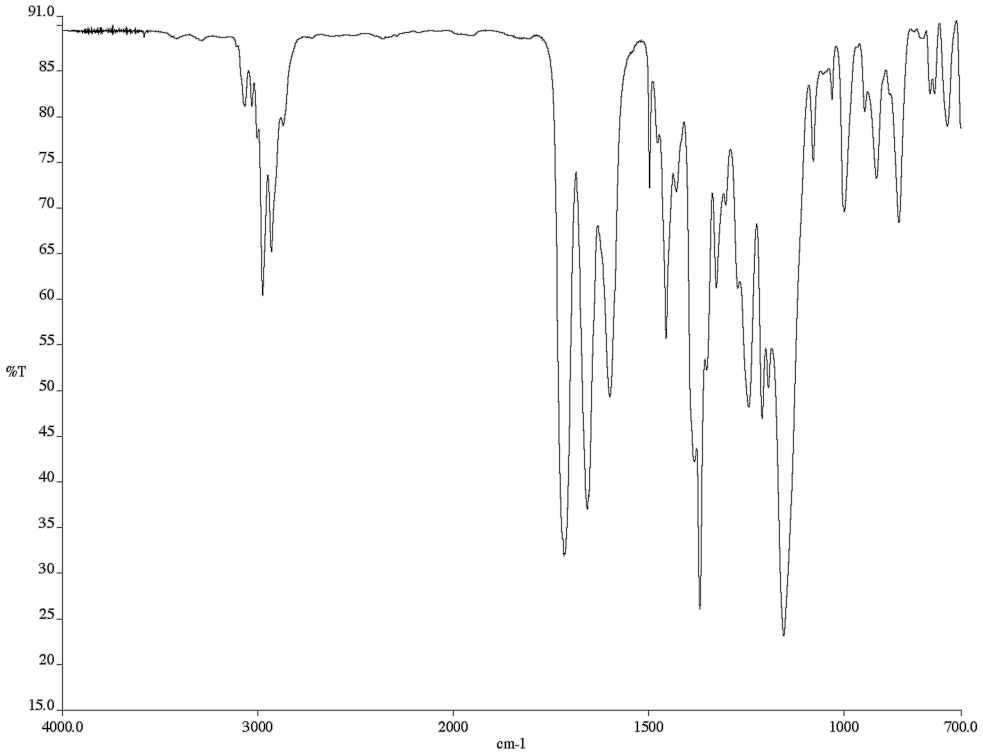


Figure SI-16B. Infrared spectrum (thin film/NaCl) of compound **15e**.

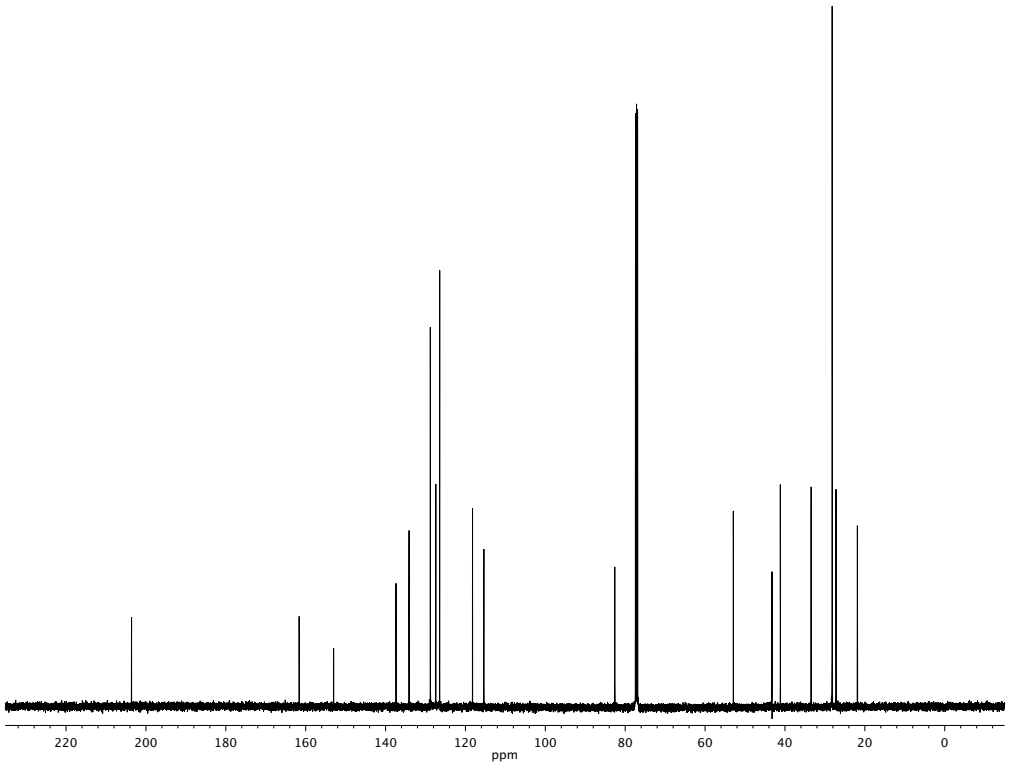
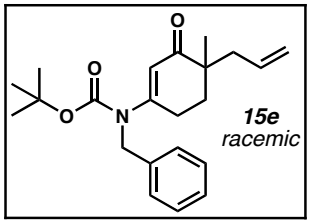


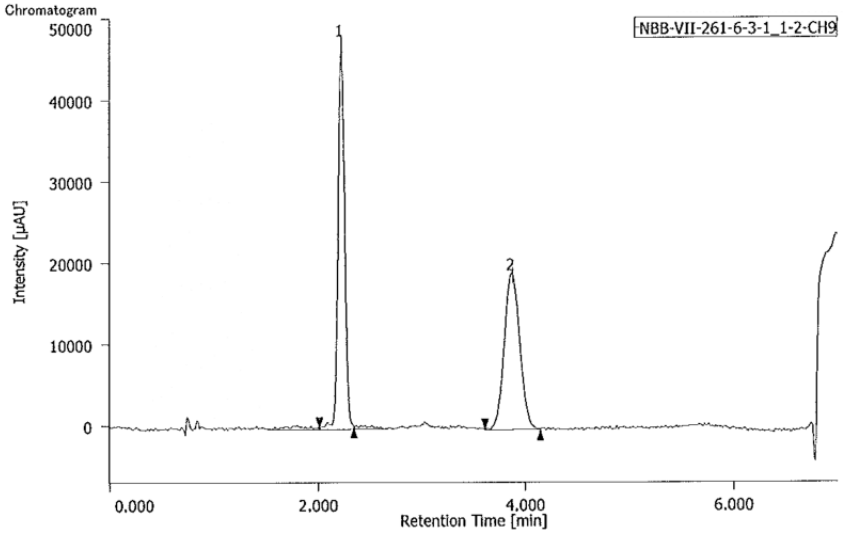
Figure SI-16C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **15e**.

NBB-VII-261_Sub46Col1 NBB-VII-261-6-3-1_1-2 10/22/2011 11:00:54 AM

Analytical Report SFC



Chromatogram Information	
User Name	User
HPLC System Name	Jasco SFC w PDA
Injection Date	10/21/2011 12:55:32 PM
Volume	5.00 [µL]
Sample #	51
Project Name	Cal Tech SFC
Executed Sequence	NBB-VII-261_Sub46Col1
Chromatogram Name	NBB-VII-261-6-3-1_1-2
Sample Name	
Acquisition Time	7.0 [min]
Acquisition Sequence	NBB-VII-261_Sub46Col1
Control Method	Solv 1 Col 1 Isocratic 7B 5mL_min 10MPa 10min



Peak Information

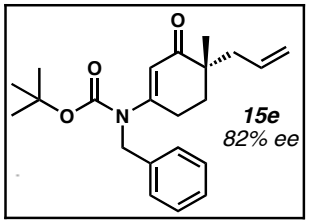
#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	9	2.227	207330	47860	50.806	2.013	2.347	0.066	8.519	1.041
2	Unknown	9	3.880	200750	19212	49.194	3.613	4.147	0.163	N/A	0.999

1 / 1

Figure SI-16D. Chiral SFC data of racemic compound **15e**.

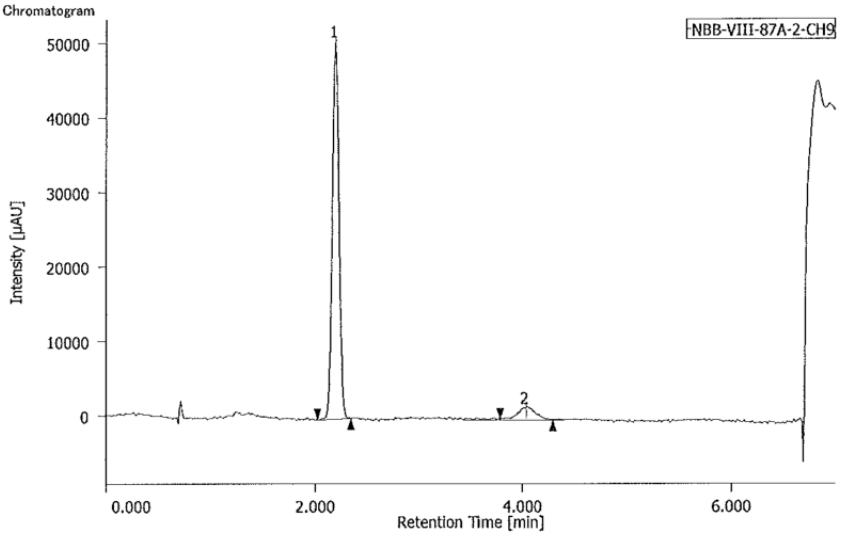
NBB-VIII-87A Col1 7 MeOH NBB-VIII-87A-2 12/16/2011 10:44:03 AM

Analytical Report SFC



Chromatogram Information	
User Name	User
HPLC System Name	Jasco SFC w PDA
Injection Date	12/16/2011 10:34:12 AM
Volume	5.00 [µL]
Sample #	51
Project Name	Cal Tech SFC
Executed Sequence	NBB-VIII-87A Col1 7 MeOH
Chromatogram Name	NBB-VIII-87A-2
Sample Name	
Acquisition Time	7.0 [min]
Acquisition Sequence	NBB-VIII-87A Col1 7 MeOH
Control Method	Solv 1 Col 1 Isocratic 7B 5mL_min 10MPa 10min

Chromatogram



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	9	2.200	226470	50772	91.066	2.027	2.347	0.070	8.868	1.001
2	Unknown	9	4.040	22218	1792	8.934	3.787	4.293	0.175	N/A	N/A

1 / 1

Figure SI-16E. Chiral SFC data of enantioenriched compound **15e**.

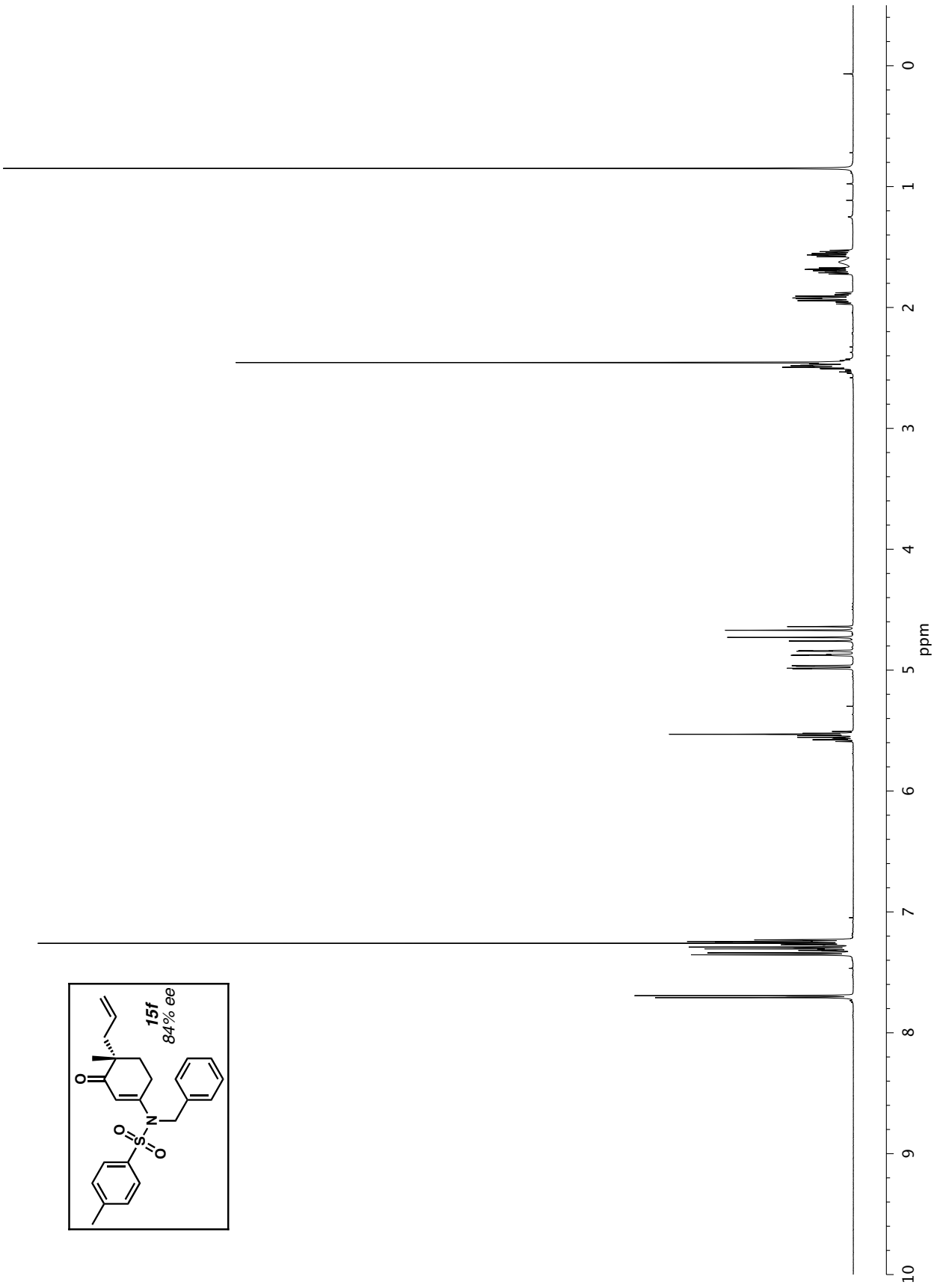


Figure SI-17A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **15f**.

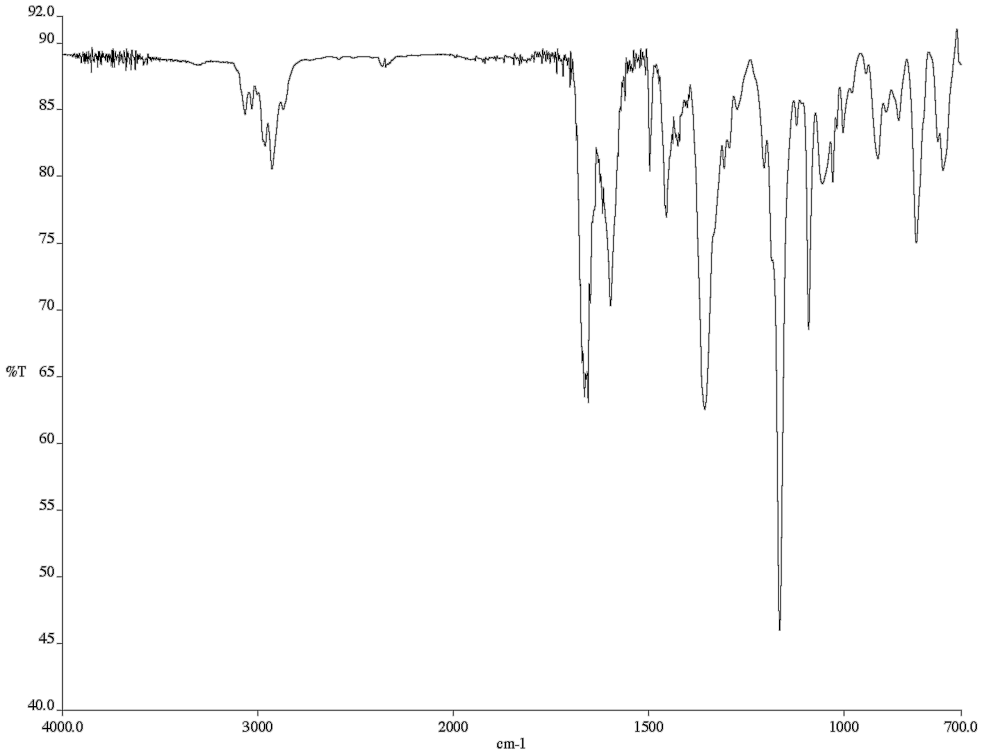


Figure SI-17B. Infrared spectrum (thin film/NaCl) of compound **15f**.

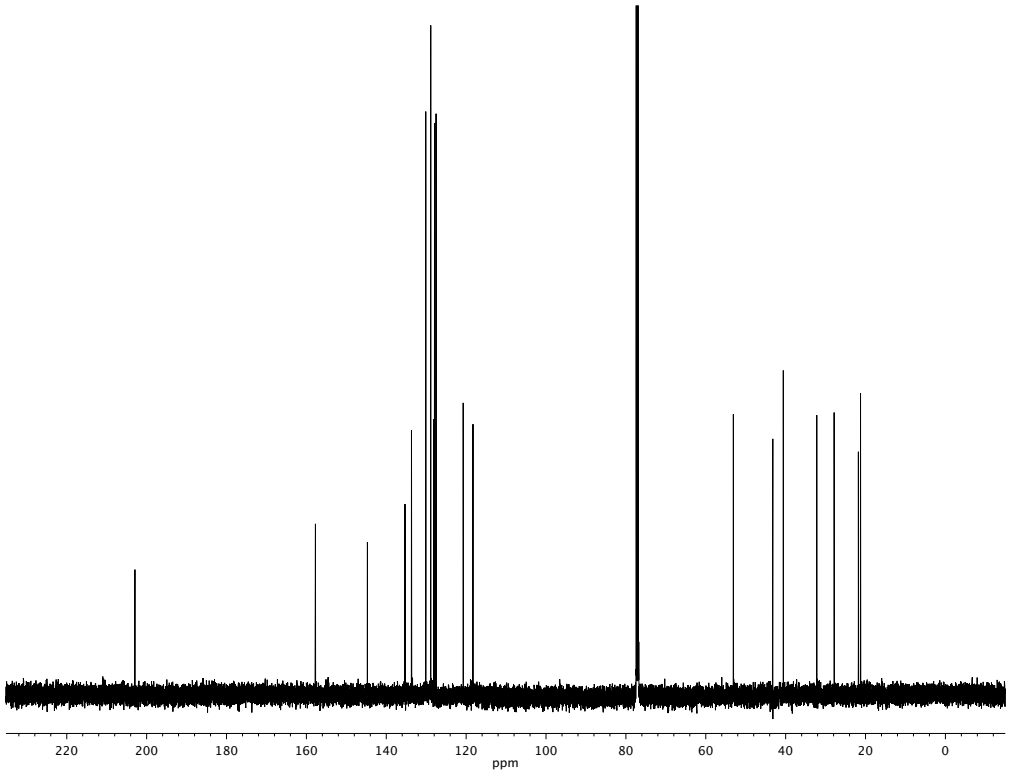


Figure SI-17C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **15f**.

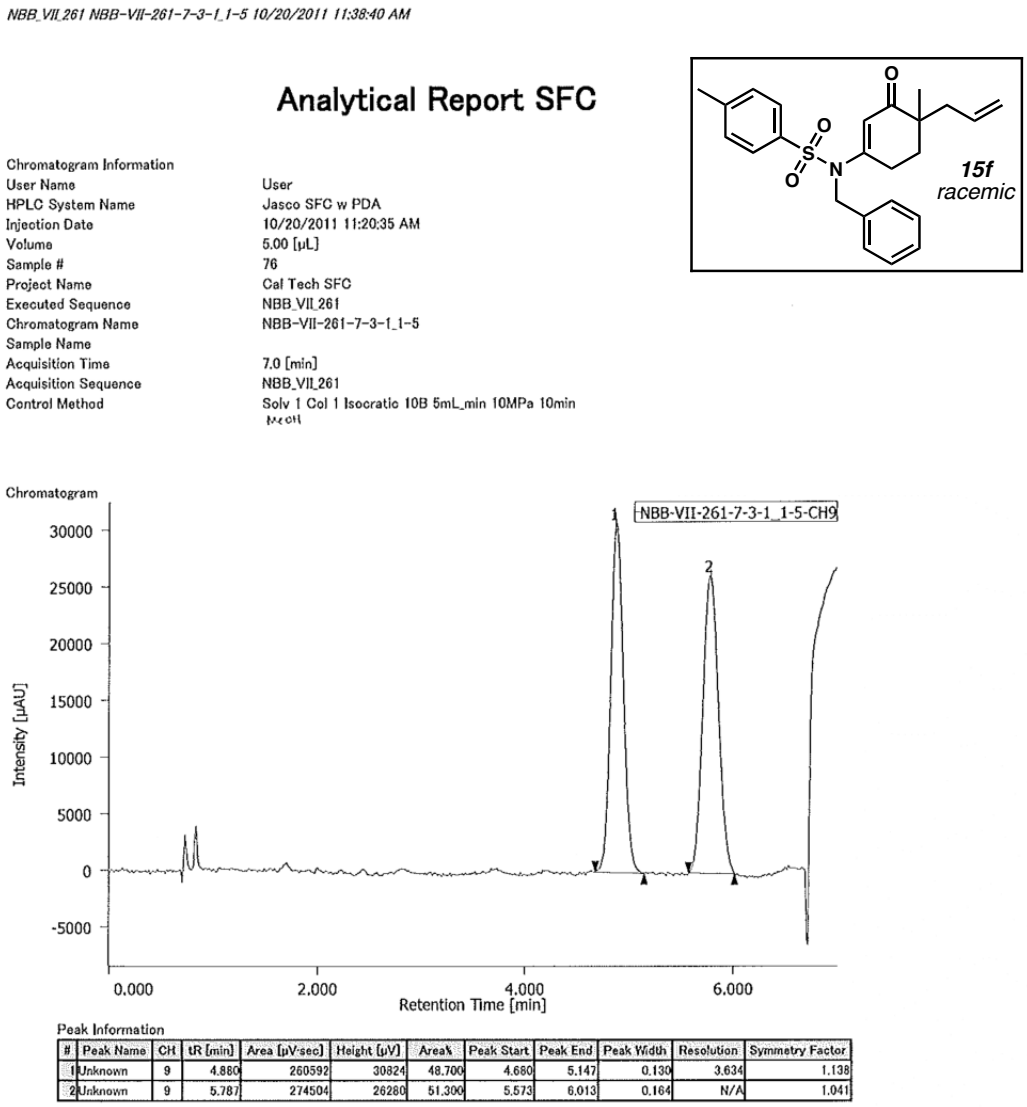
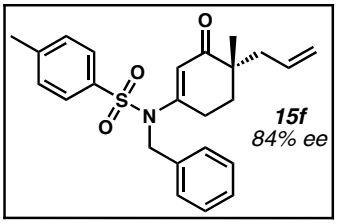


Figure SI-17D. Chiral SFC data of racemic compound **15f**.

NBB-VIII-89A Col1 10 MeOH-3 NBB-VIII-89A-2 12/17/2011 12:59:35 PM

Analytical Report SFC



Chromatogram Information	
User Name	User
HPLC System Name	Jasco SFC w PDA
Injection Date	12/17/2011 10:12:13 AM
Volume	5.00 [µL]
Sample #	51
Project Name	Cal Tech SFC
Executed Sequence	NBB-VIII-89A Col1 10 MeOH-3
Chromatogram Name	NBB-VIII-89A-2
Sample Name	
Acquisition Time	7.0 [min]
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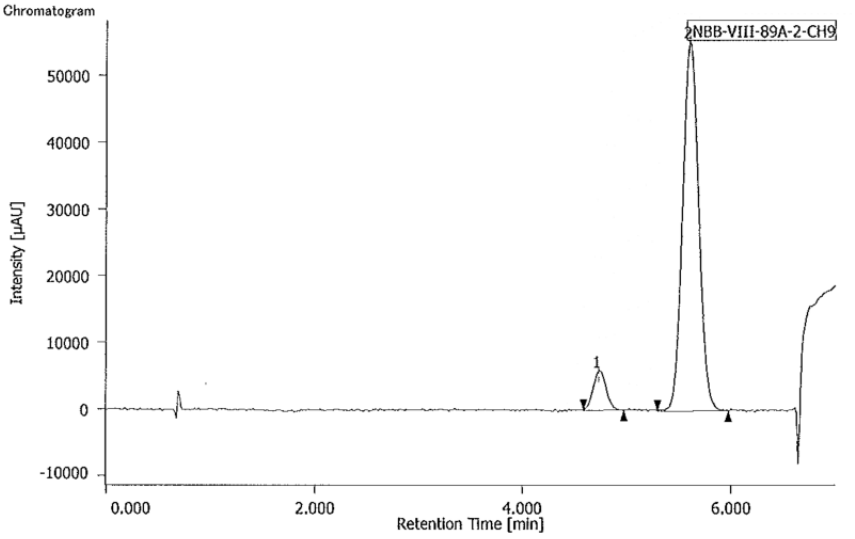
Control Method	Solv 1 Col 1 Isocratic 10B 5mL_min 10MPa 10min

Chromatogram



Peak Information

#	Peak Name	CH	tR (min)	Area (µV·sec)	Height (µV)	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
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2	Unknown	9	5.600	592694	55307	91.969	5.293	5.973	0.166	N/A	1.117

1 / 1

Figure SI-17E. Chiral SFC data of enantioenriched compound **15f**.

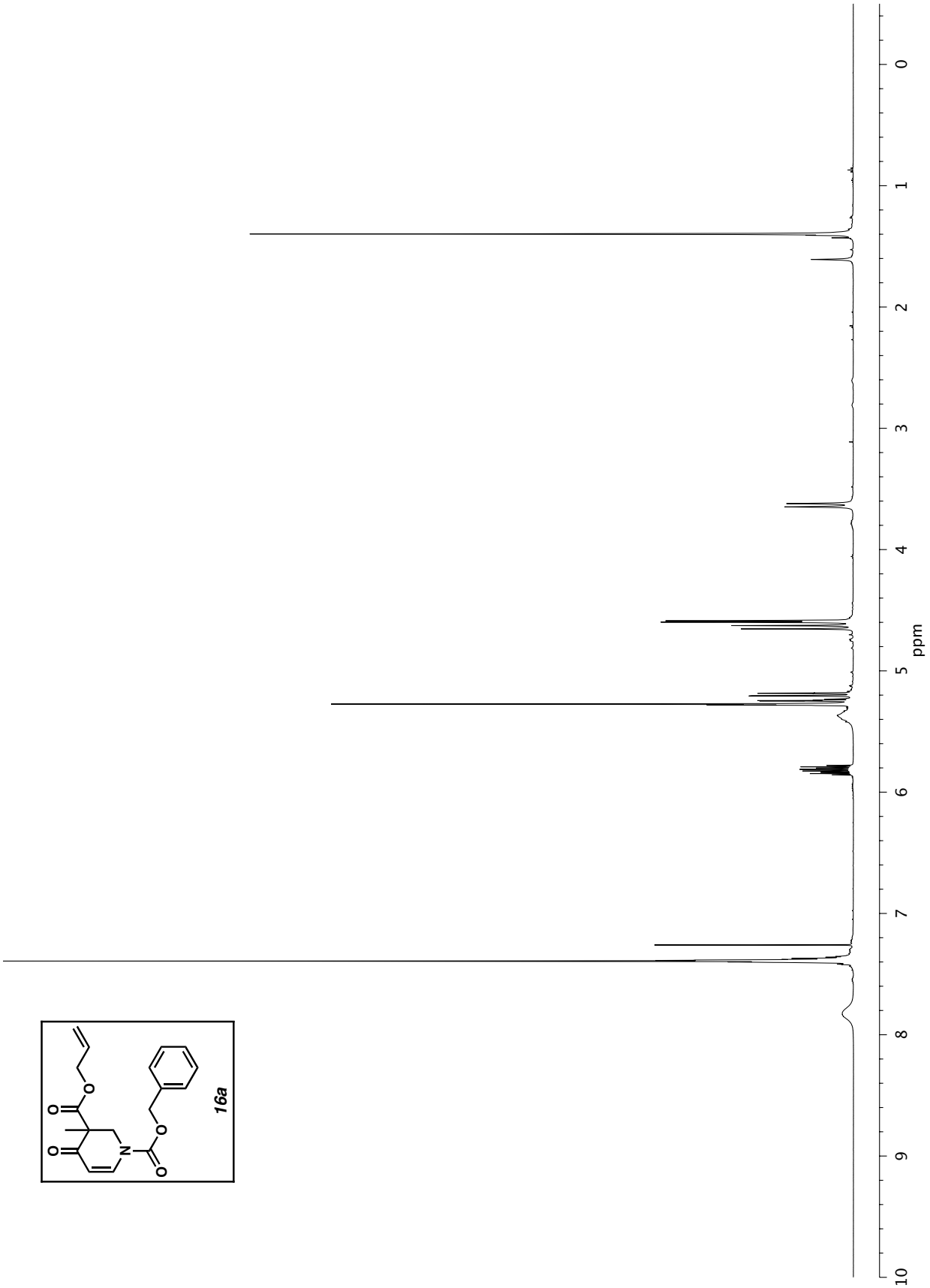

Figure SI-18A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **16a**.

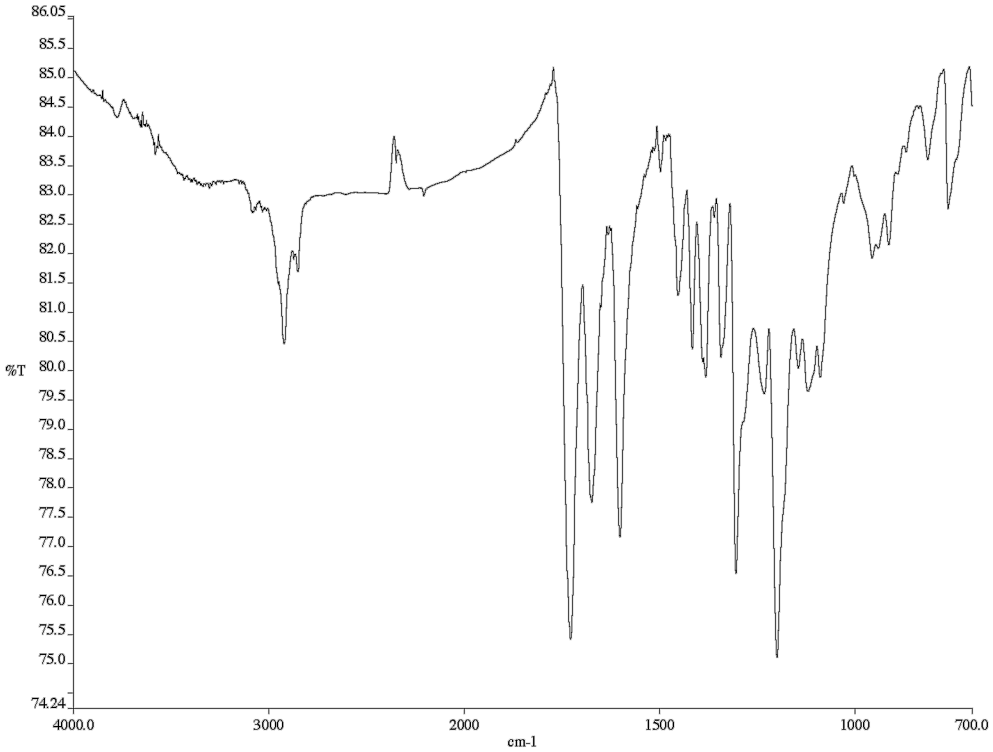

Figure SI-18B. Infrared spectrum (thin film/NaCl) of compound **16a**.

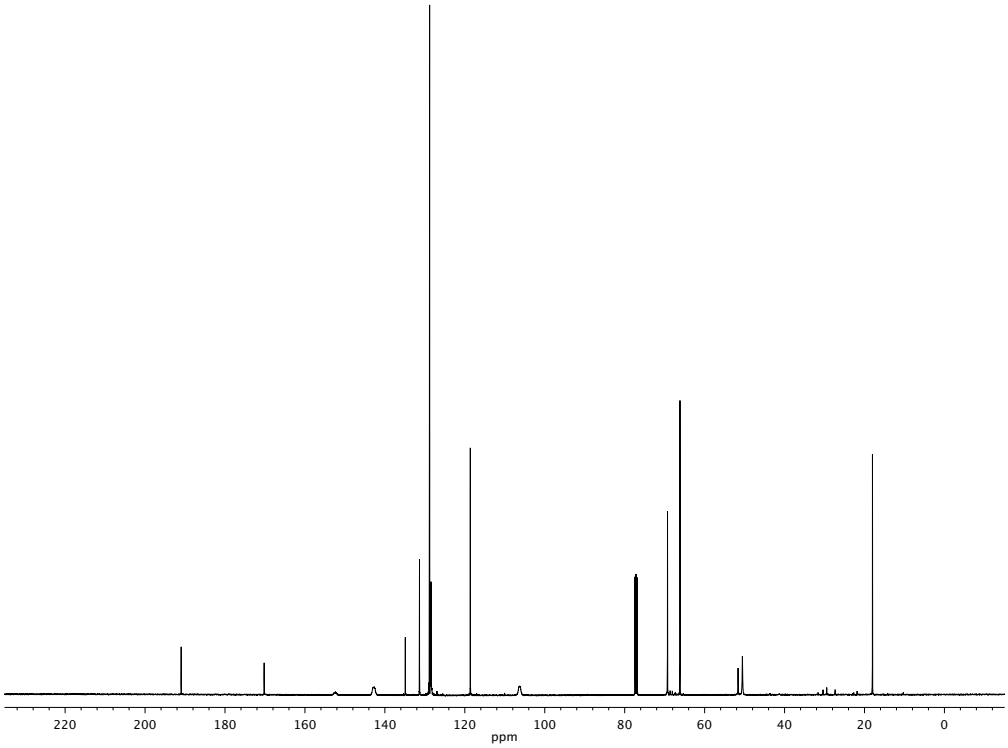

Figure SI-18C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **16a**.

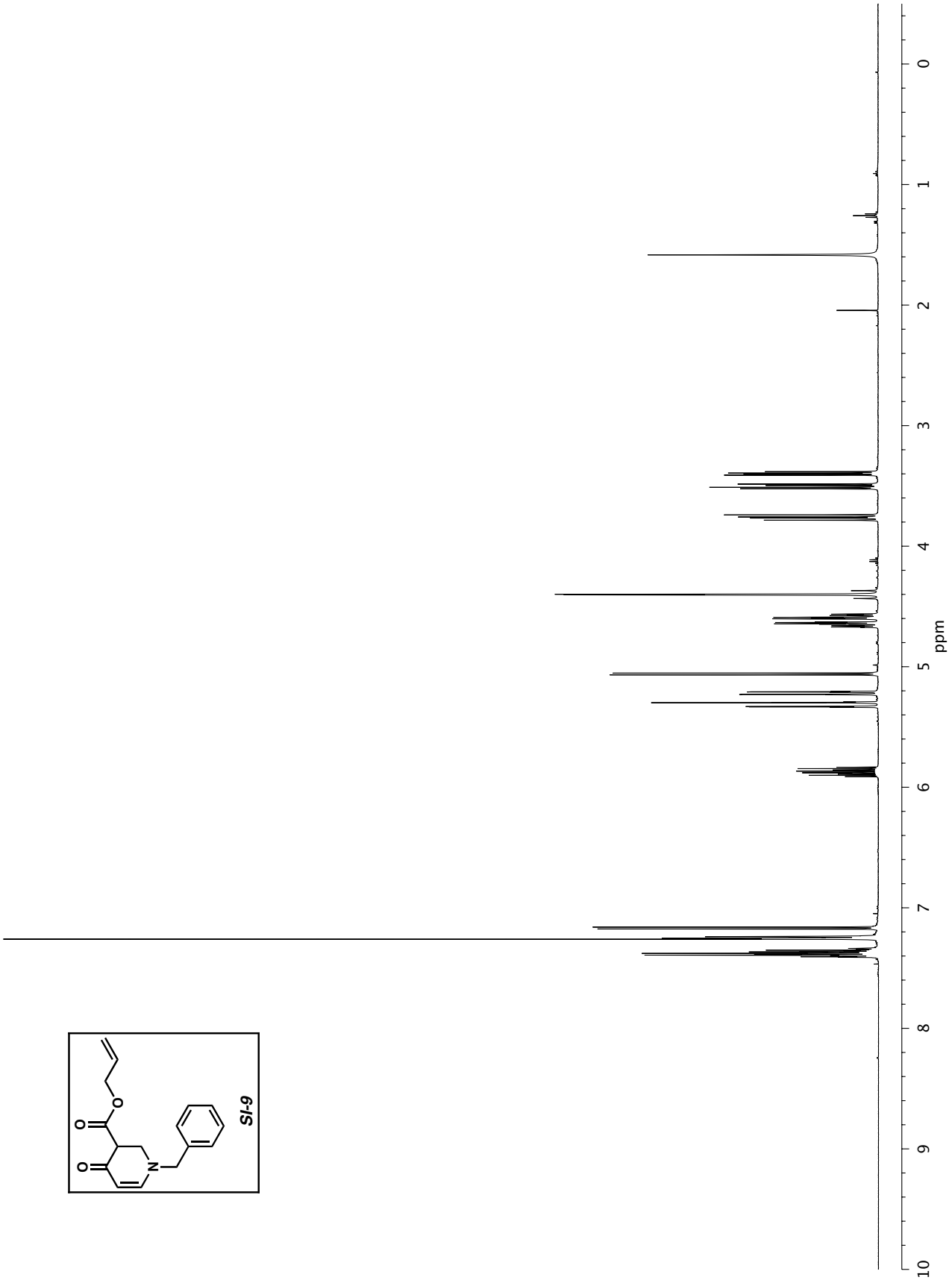

Figure SI-194. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-9**.

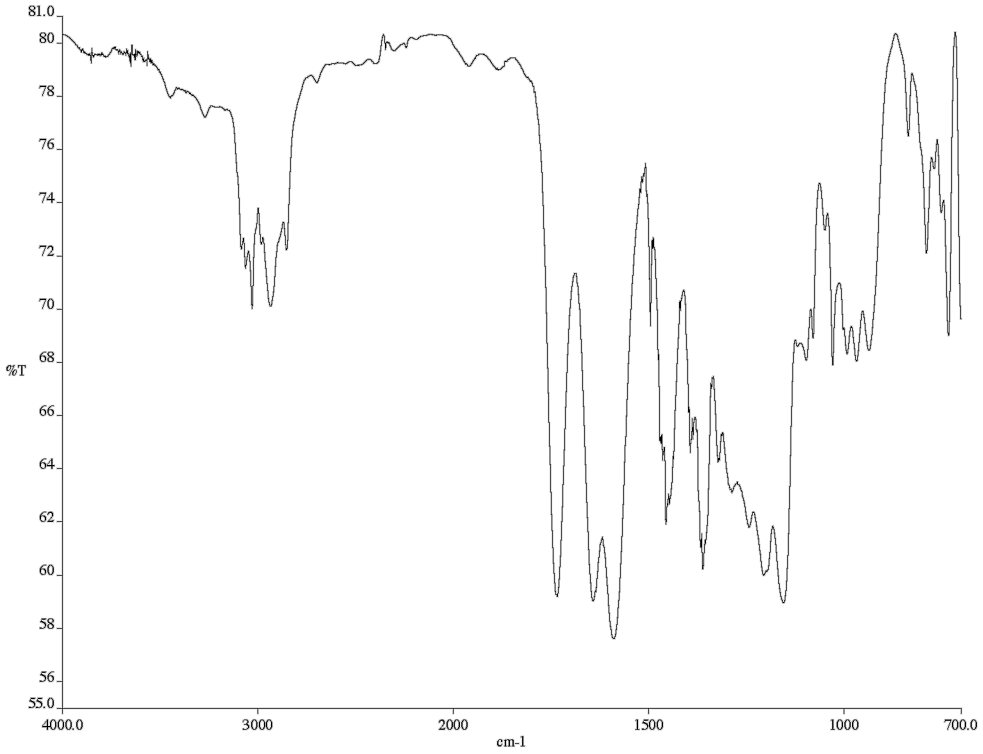

Figure SI-19B. Infrared spectrum (thin film/NaCl) of compound **SI-9**.

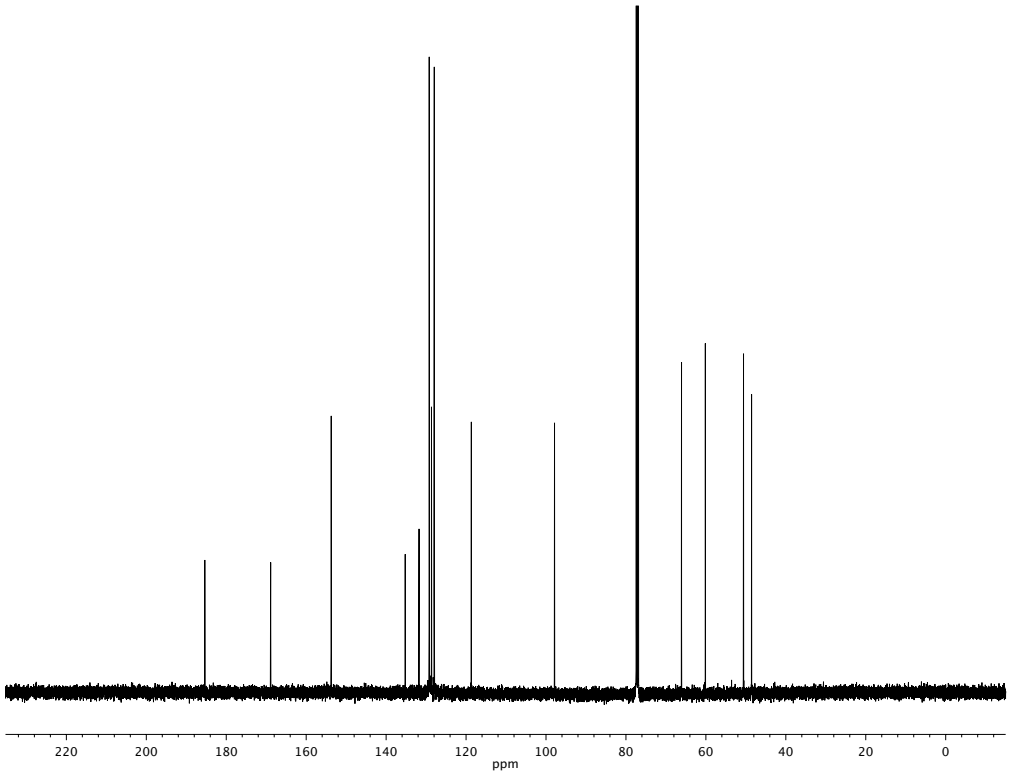

Figure SI-19C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-9**.

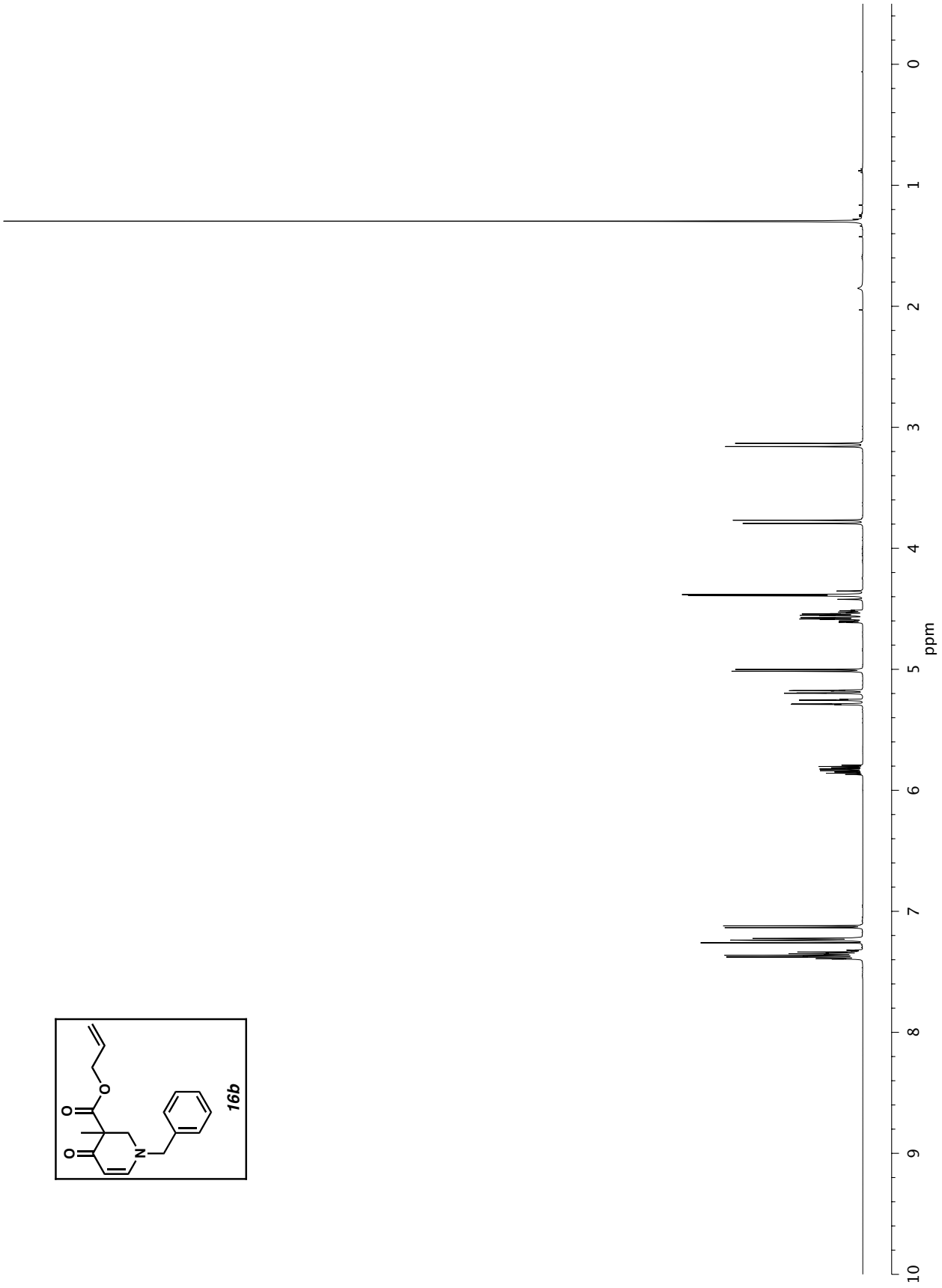

Figure SI-20A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **16b**.

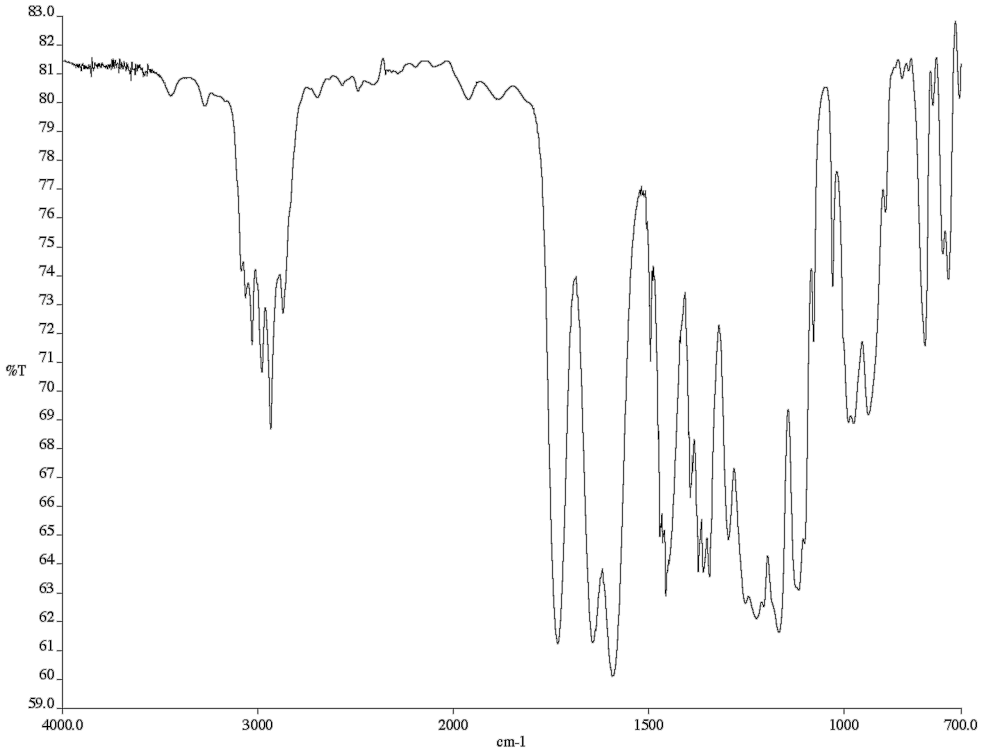

Figure SI-20B. Infrared spectrum (thin film/NaCl) of compound **16b**.

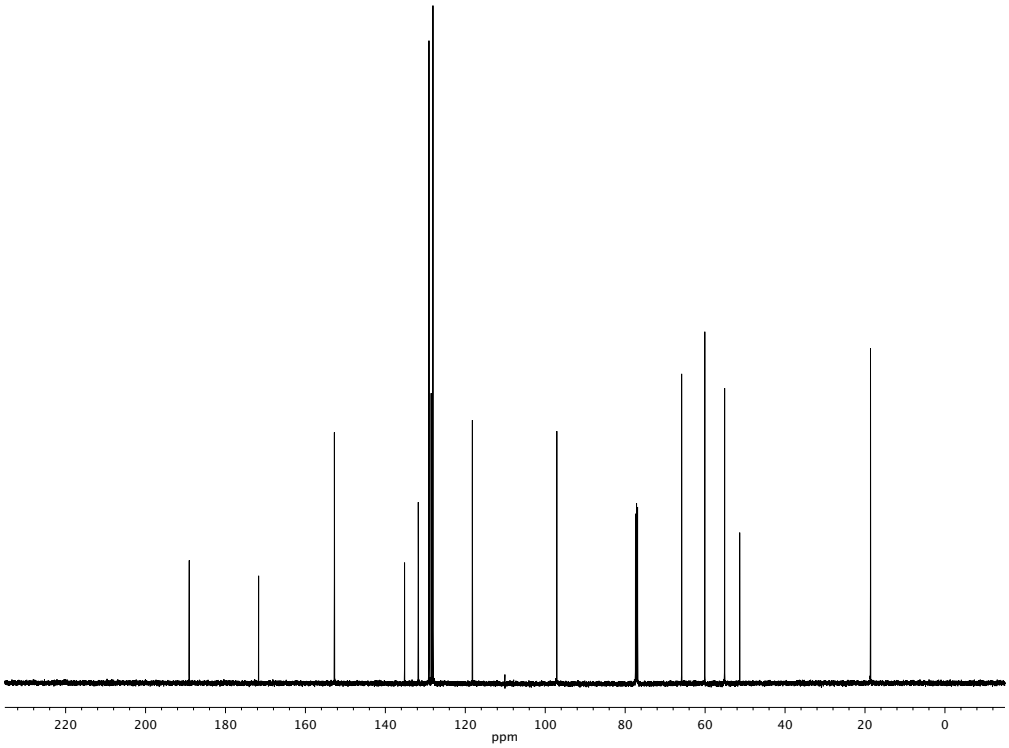

Figure SI-20C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **16b**.

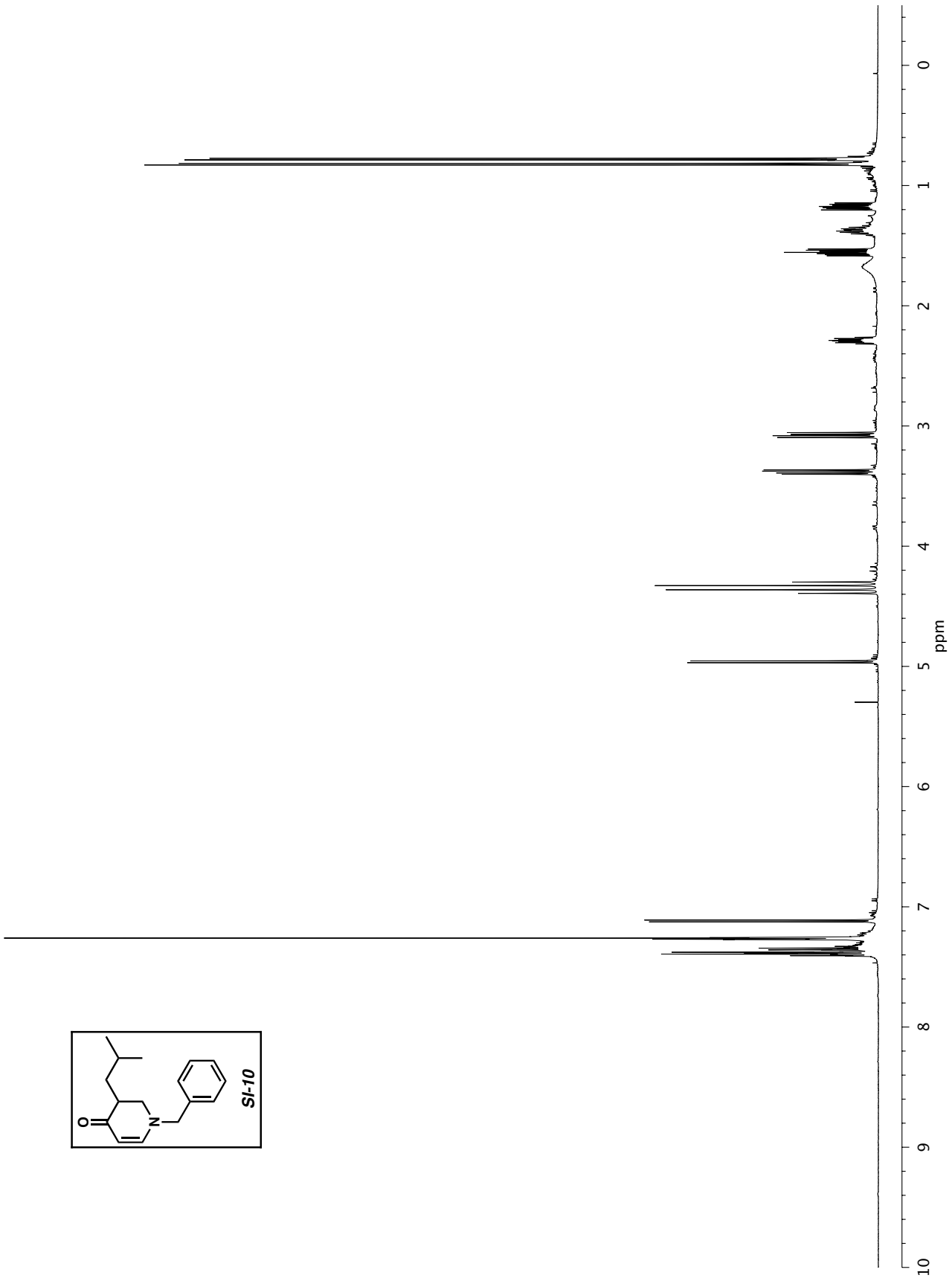

Figure SI-21A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-10**.

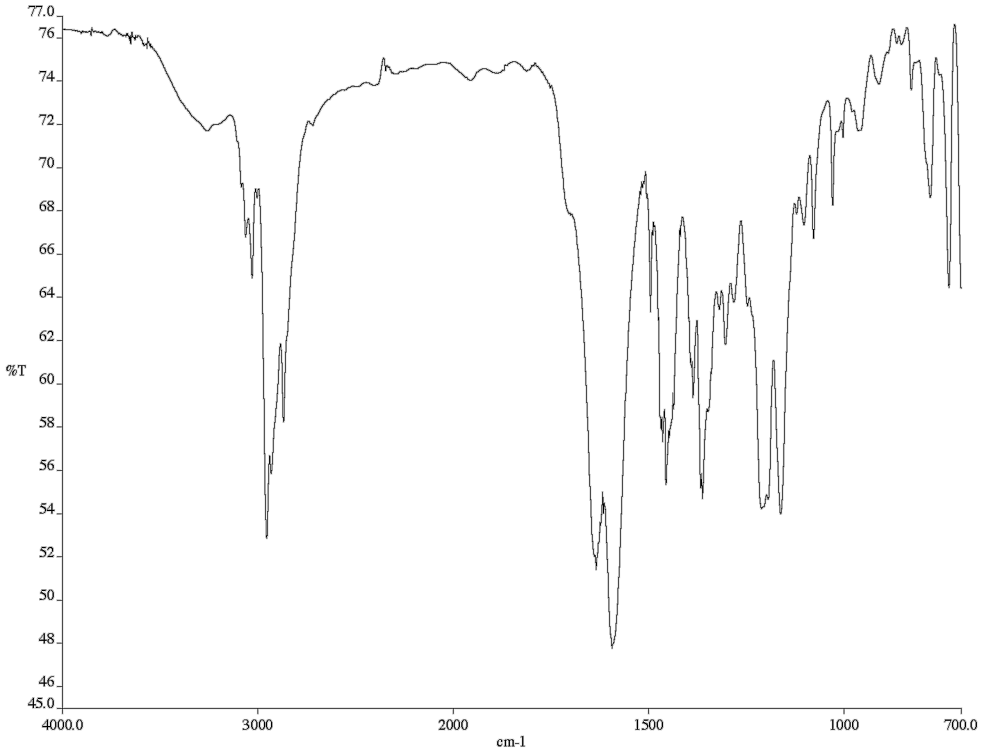

Figure SI-21B. Infrared spectrum (thin film/NaCl) of compound **SI-10**.

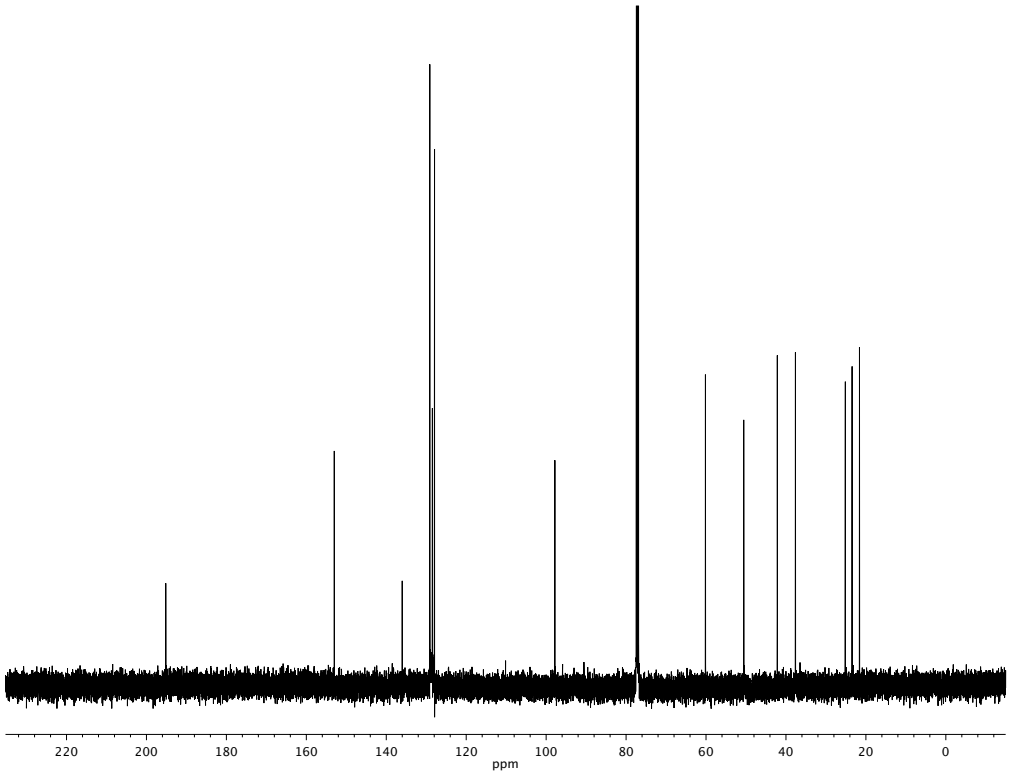

Figure SI-21C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-10**.

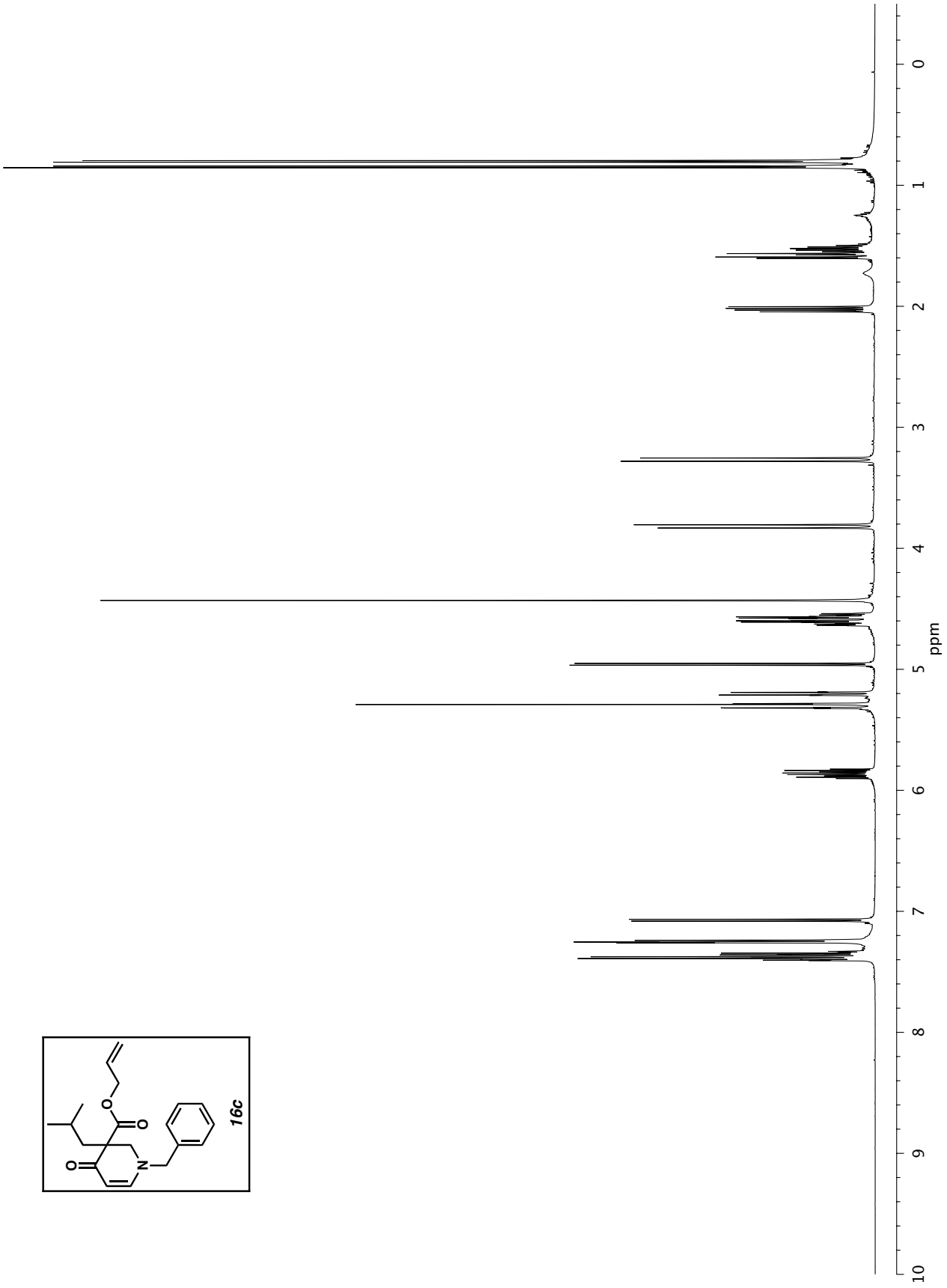

Figure SI-22A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **16c**.

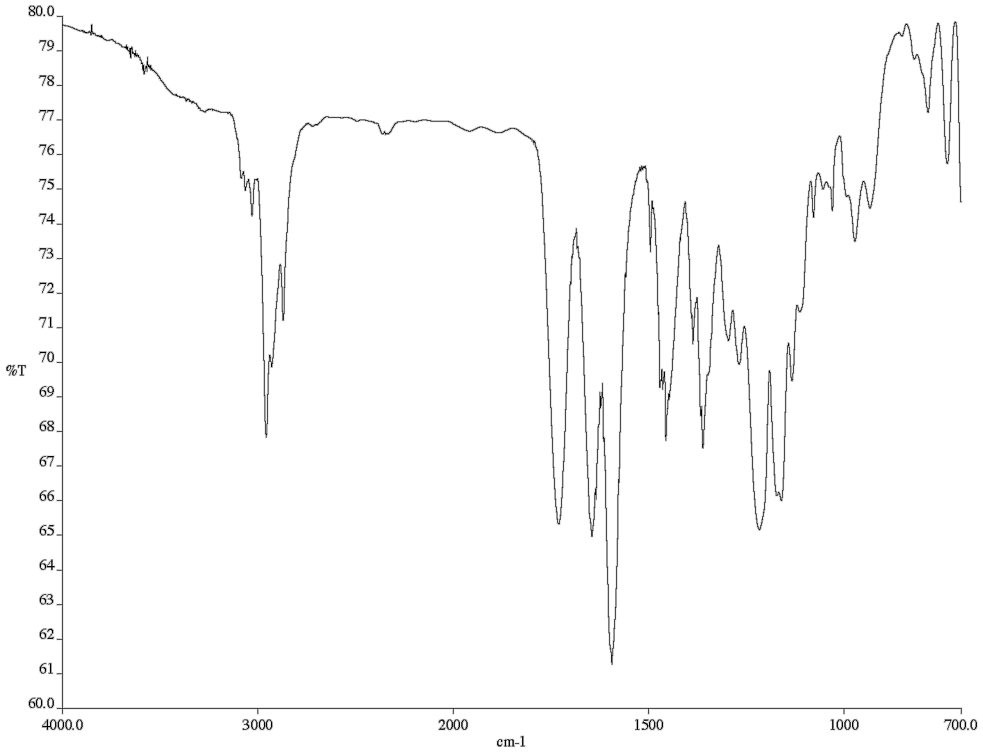

Figure SI-22B. Infrared spectrum (thin film/NaCl) of compound **16c**.

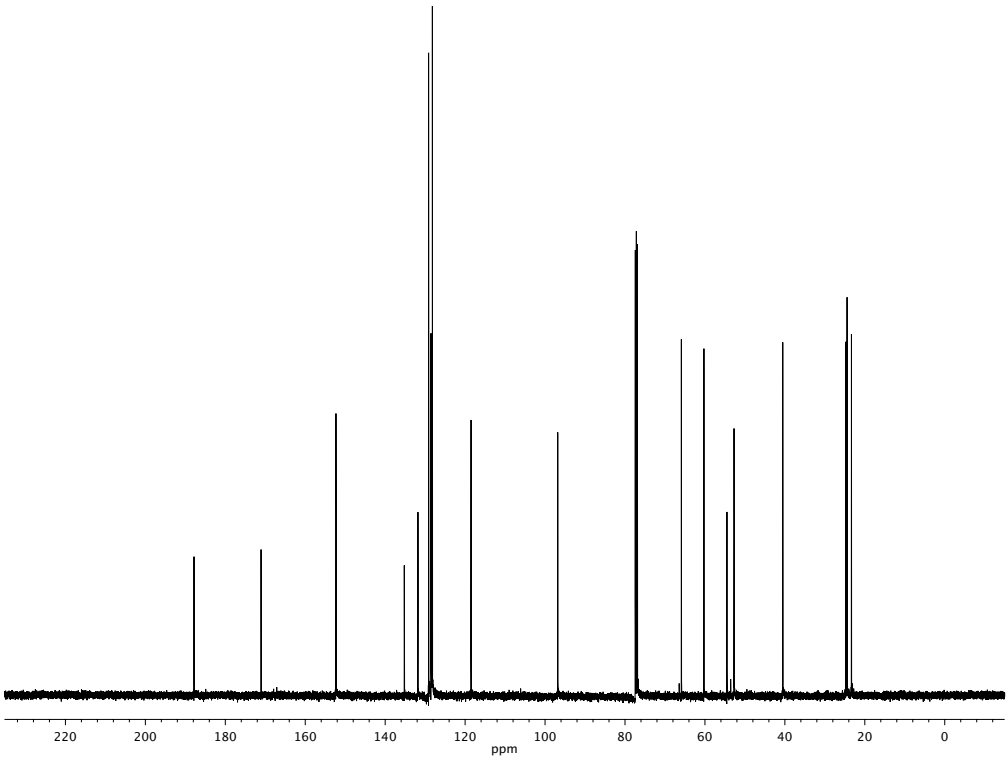

Figure SI-22C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **16c**.

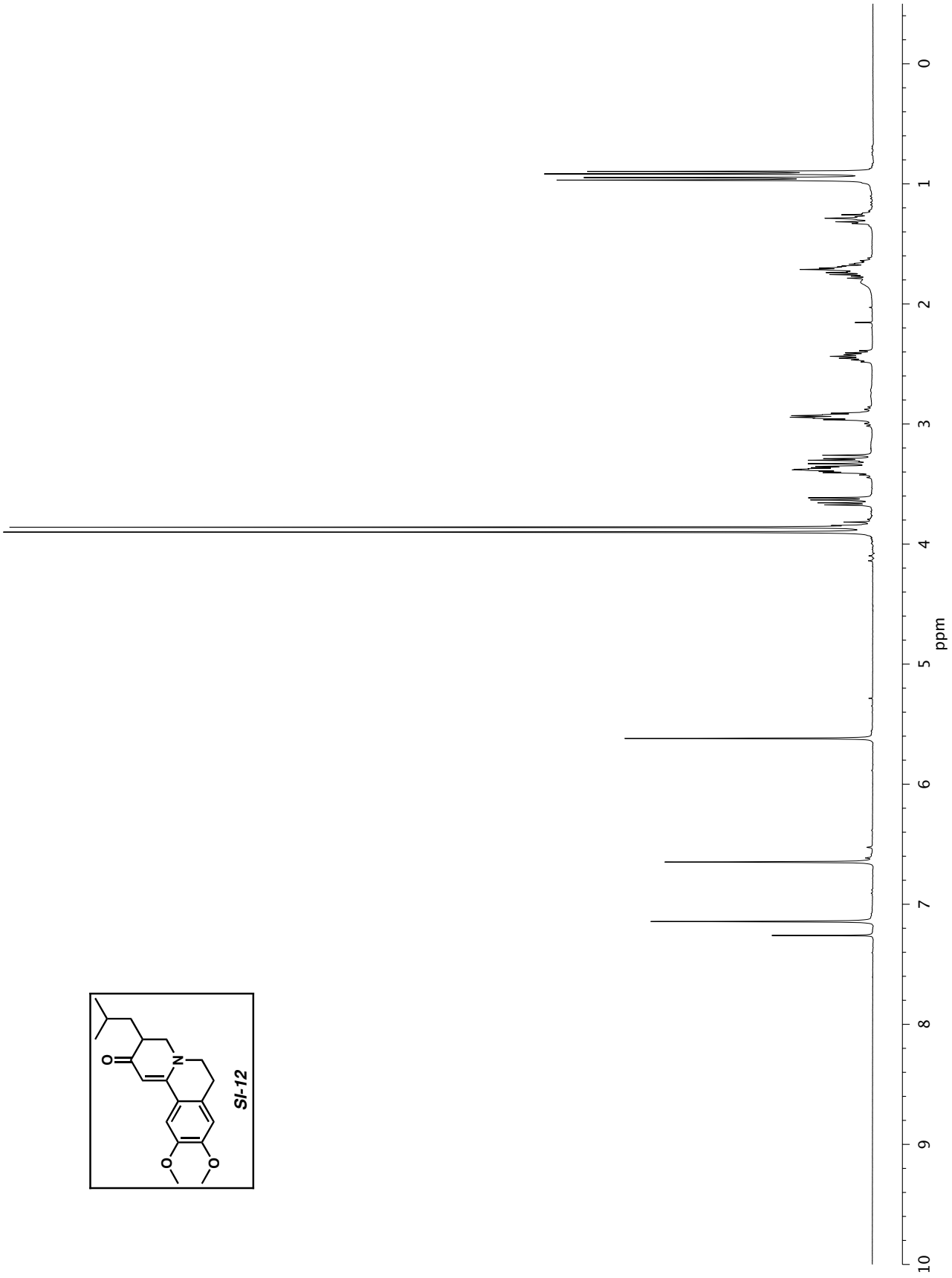

Figure SI-23A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-12**.

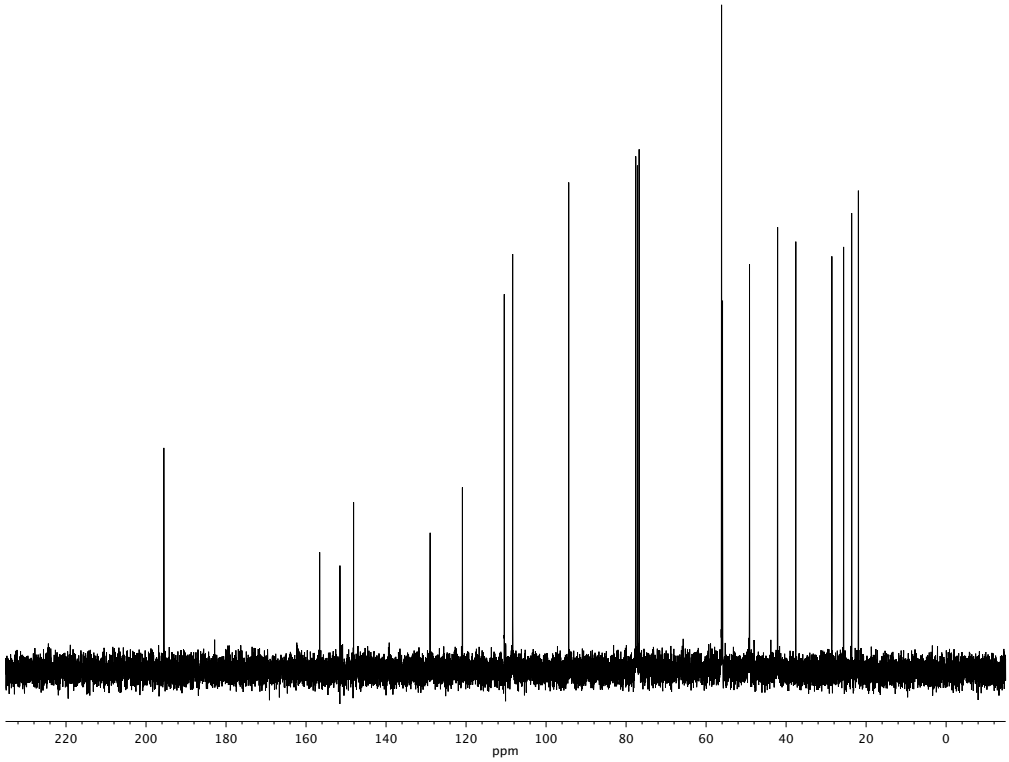

Figure SI-23B. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-12**.

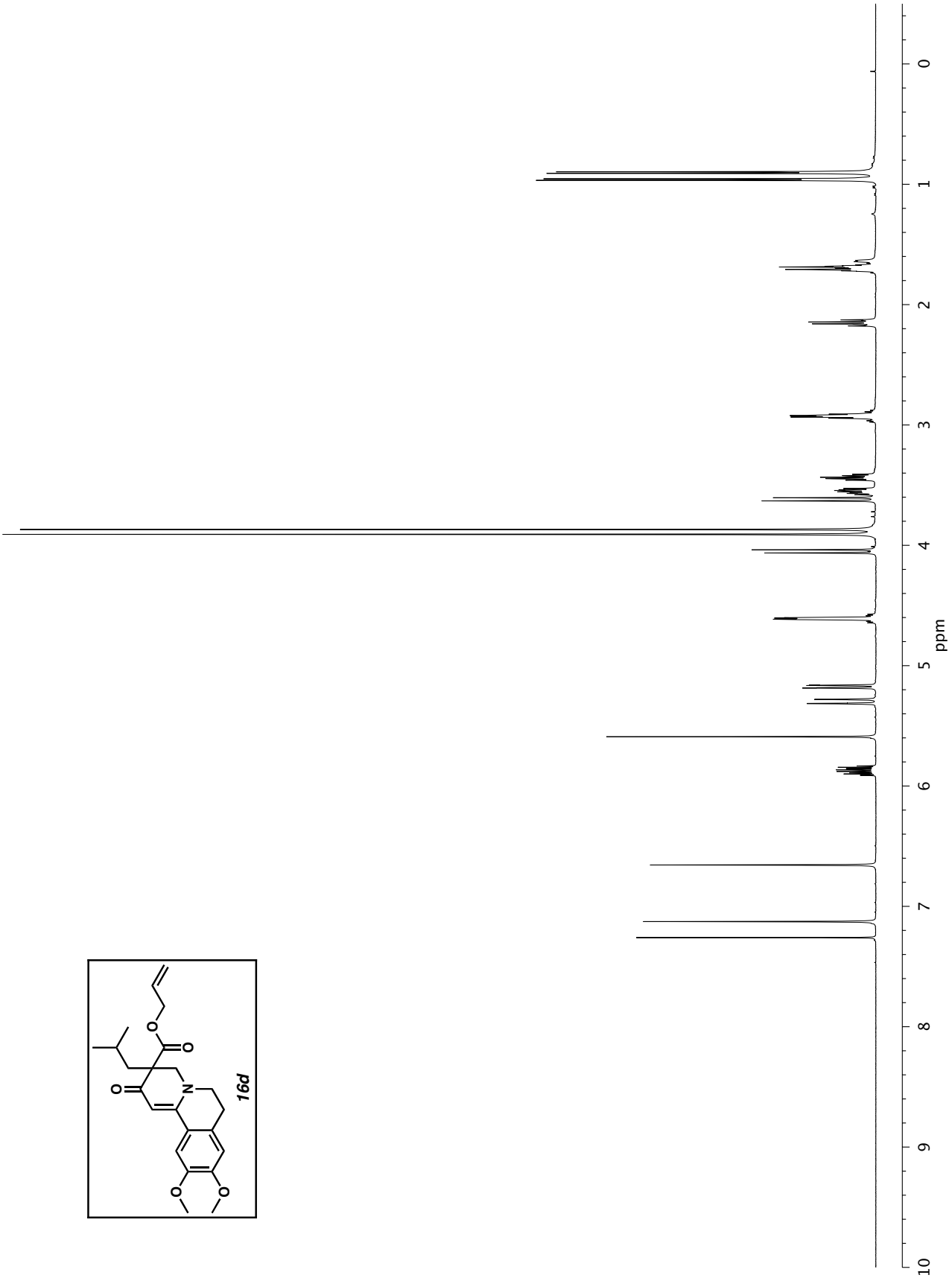

Figure SI-24A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **16d**.

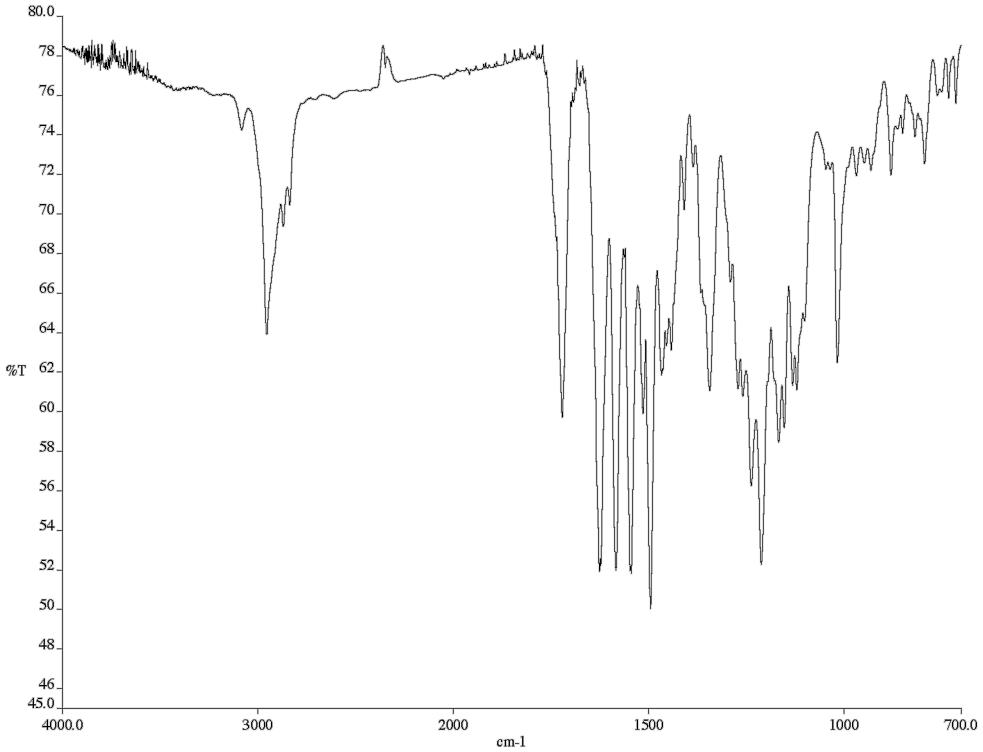

Figure SI-24B. Infrared spectrum (thin film/NaCl) of compound **16d**.

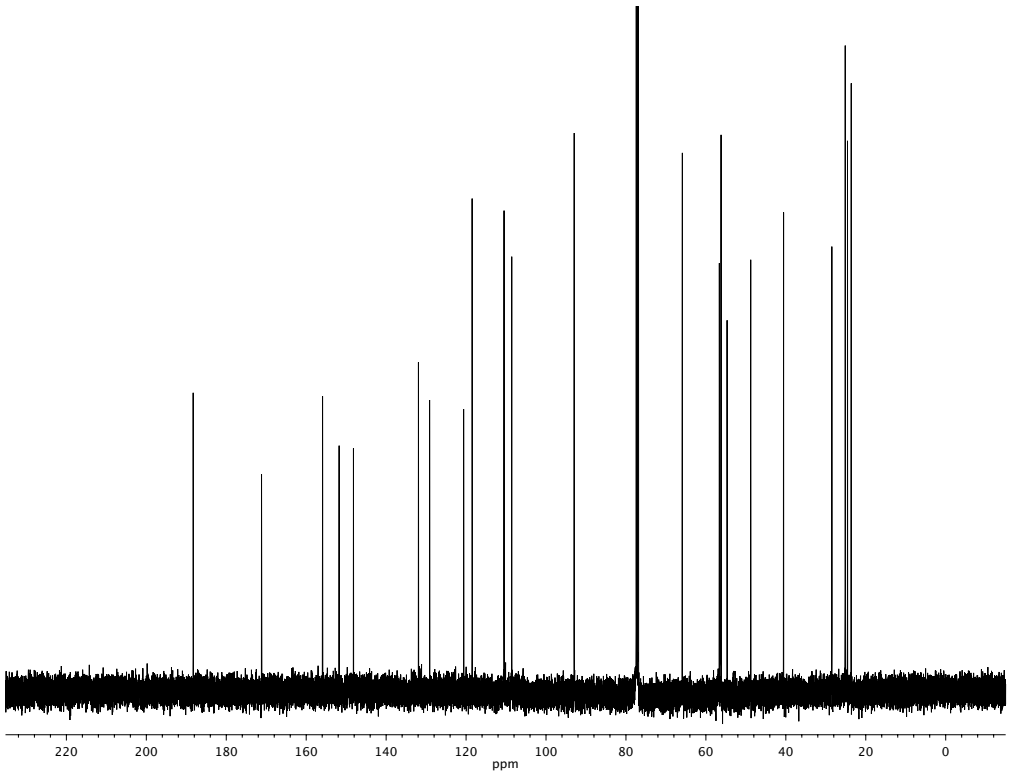

Figure SI-24C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **16d**.

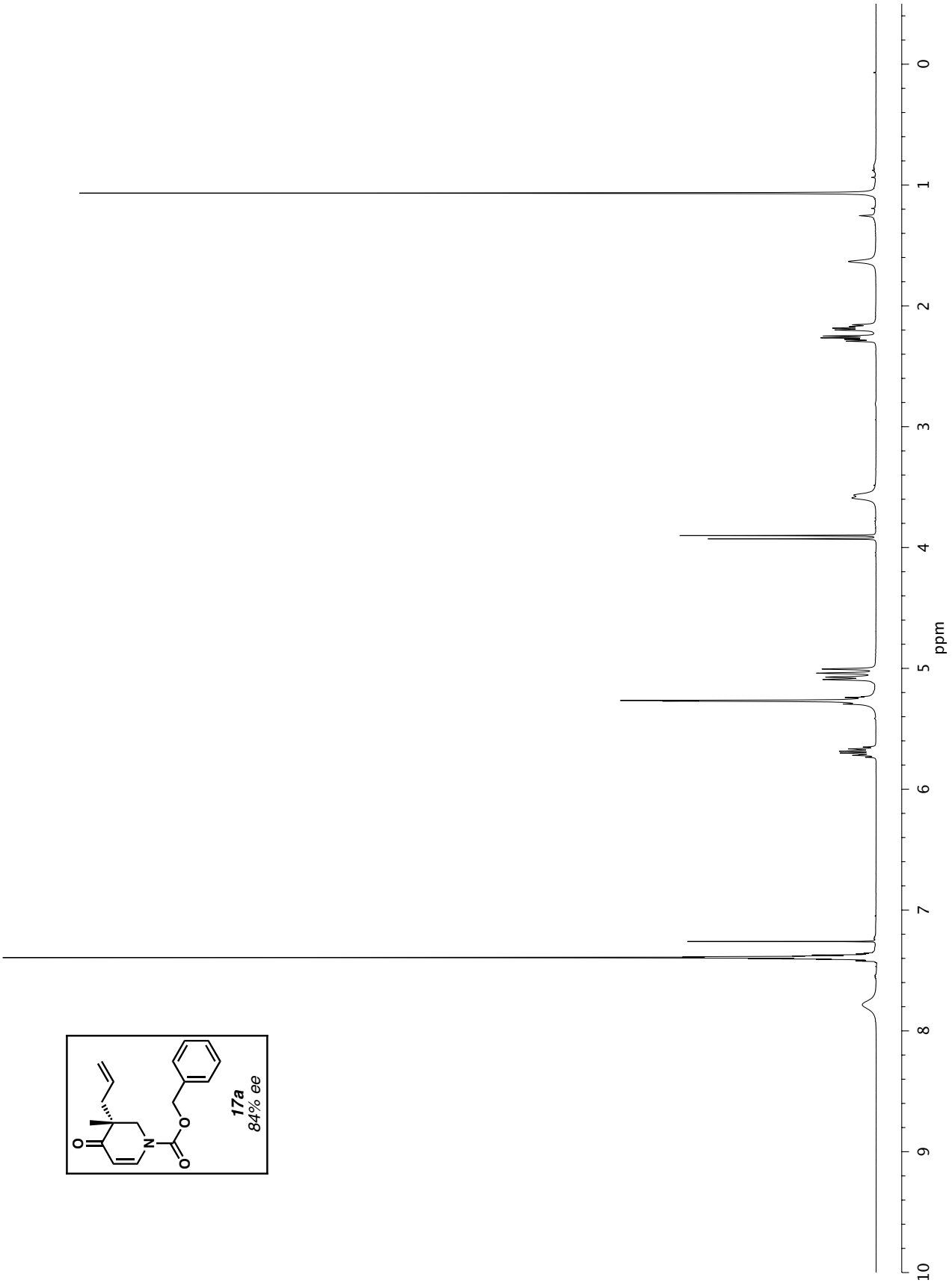

Figure SI-25A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **17a**.

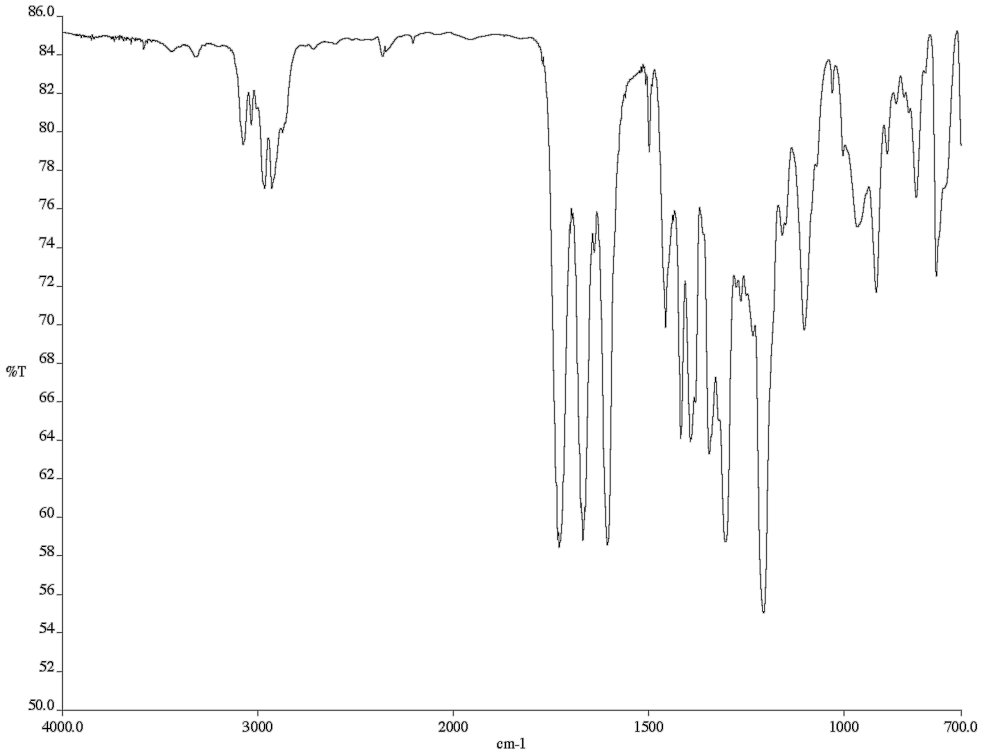

Figure SI-25B. Infrared spectrum (thin film/NaCl) of compound **17a**.

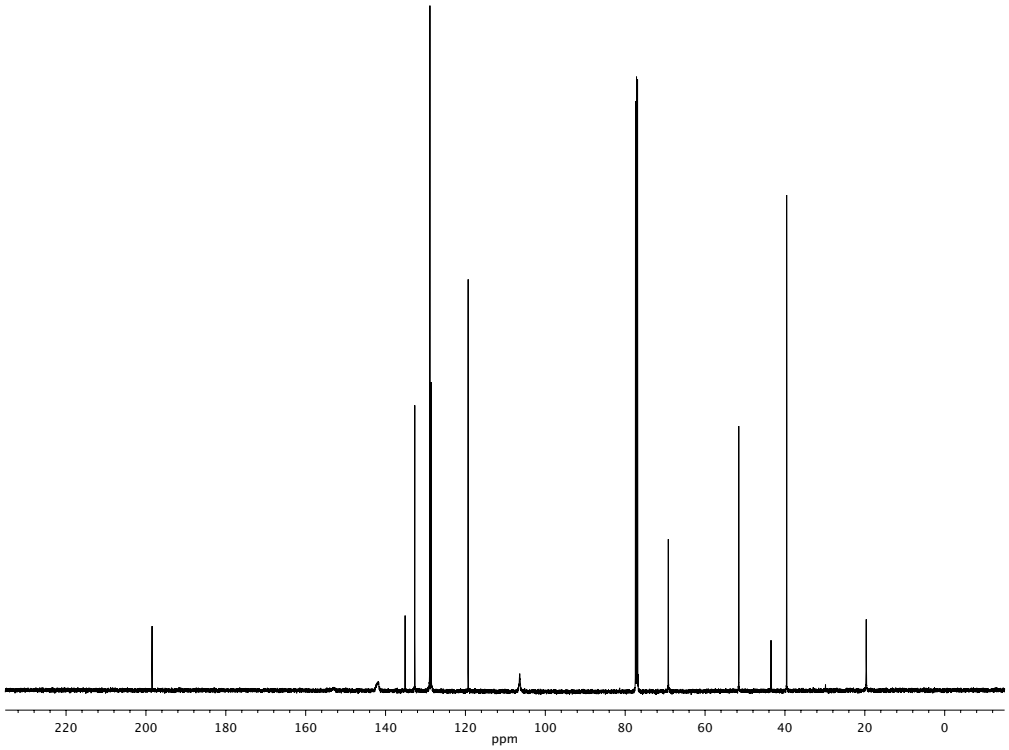

Figure SI-25C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **17a**.

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                                                   Inj Volume : 5 µl
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                  12MIN 5.M
Last changed    : 5/19/2011 9:00:59 PM by DCB
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Last changed    : 5/19/2011 9:00:59 PM by DCB
Method Info     : S1C2 12min 5.M: 5% MeOH, AD-H 3 mL/min, 12 min
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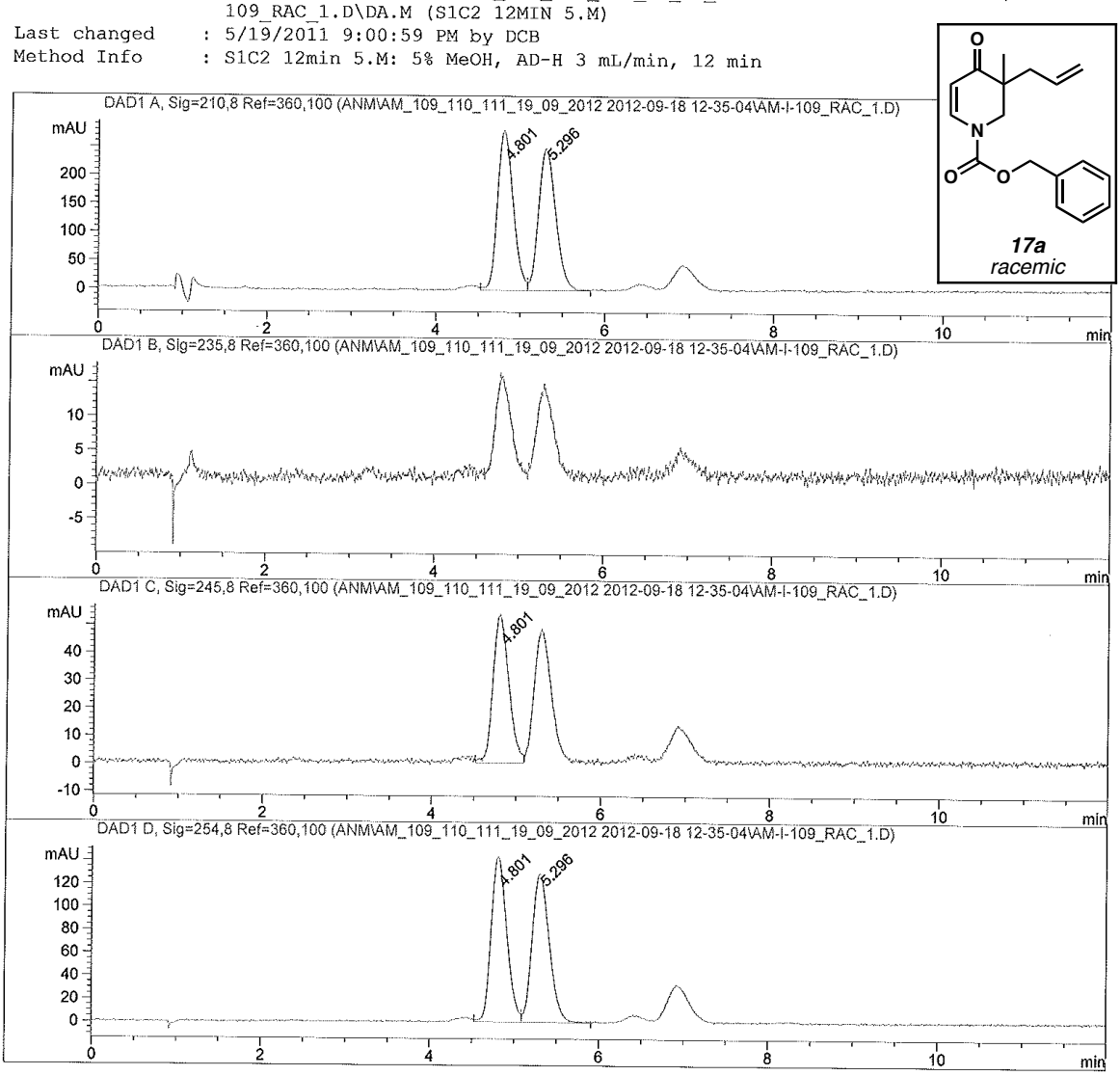


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Instrument 1 9/18/2012 3:04:12 PM JNI                    Page   1 of 3
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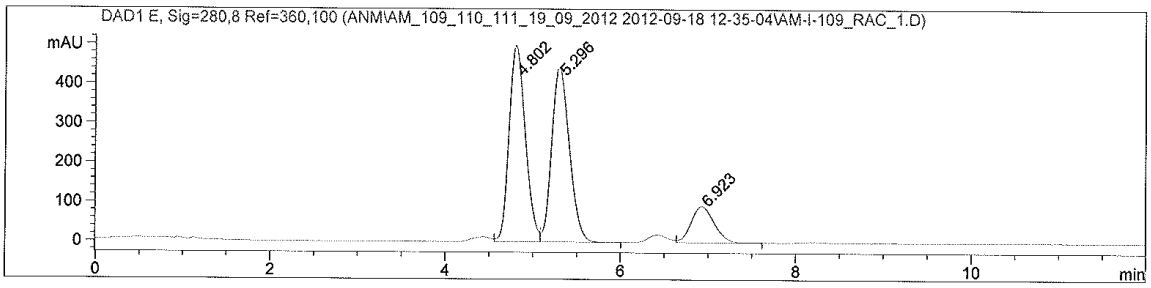
Figure SI-25D. Chiral SFC data of racemic compound **17a**.

Data File C:\CHEM32\...\ANM\AM_109_110_111_19_09_2012 2012-09-18 12-35-04\AM-I-109_RAC_1.D
Sample Name: AM-i-109_rac_1



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Area Percent Report

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Dilution : 1.0000
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.801	VV	0.2045	3664.44873	280.39090	50.7811
2	5.296	VV	0.2183	3551.72461	249.17192	49.2189
Totals :				7216.17334	529.56282	

Signal 2: DAD1 B, Sig=235,8 Ref=360,100

Signal 3: DAD1 C, Sig=245,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.801	VV	0.2018	702.84430	53.31551	100.0000
Totals :				702.84430	53.31551	

Signal 4: DAD1 D, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.801	VV	0.2038	1863.76855	143.27269	50.4753
2	5.296	VB	0.2218	1828.66467	128.65884	49.5247
Totals :				3692.43323	271.93153	

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Sample Name: AM-i-109_rac_1

Signal 5: DAD1 E, Sig=280,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.802	VV	0.2032	6442.83447	496.96964	44.6444
2	5.296	VB	0.2214	6284.14746	443.22113	43.5448
3	6.923	VB	0.2833	1704.45483	92.35108	11.8107
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Different Inj Volume from Sequence !     Actual Inj Volume : 10 µl
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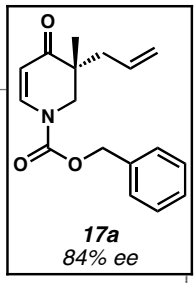


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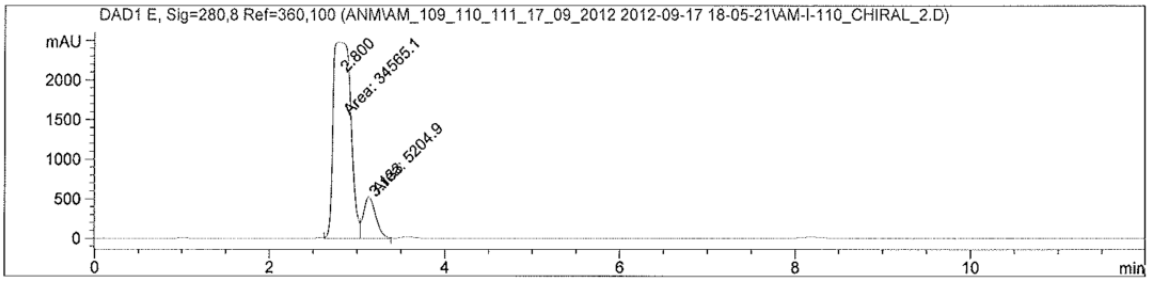
Figure SI-25E. Chiral SFC data of enantioenriched compound **17a**.

Data File C:\CHEM32\...M\AM_109_110_111_17_09_2012 2012-09-17 18-05-21\AM-I-110_CHIRAL_2.D
Sample Name: AM-i-110_chiral_2

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Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,8 Ref=360,100

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   2   3.132 FM    0.1621 2910.19556  299.30103  10.6492

Totals :                  2.73278e4  2299.89819


Signal 2: DAD1 B, Sig=235,8 Ref=360,100


Signal 3: DAD1 C, Sig=245,8 Ref=360,100


Signal 4: DAD1 D, Sig=254,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
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   2   3.133 FM    0.1579 1290.07031  136.13354   7.8257

Totals :                  1.64851e4  1727.33240
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Data File C:\CHEM32\...M\AM_109_110_111_17_09_2012 2012-09-17 18-05-21\AM-I-110_CHIRAL_2.D
Sample Name: AM-i-110_chiral_2

Signal 5: DAD1 E, Sig=280,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.800	MF	0.2320	3.45651e4	2482.96143	86.9125
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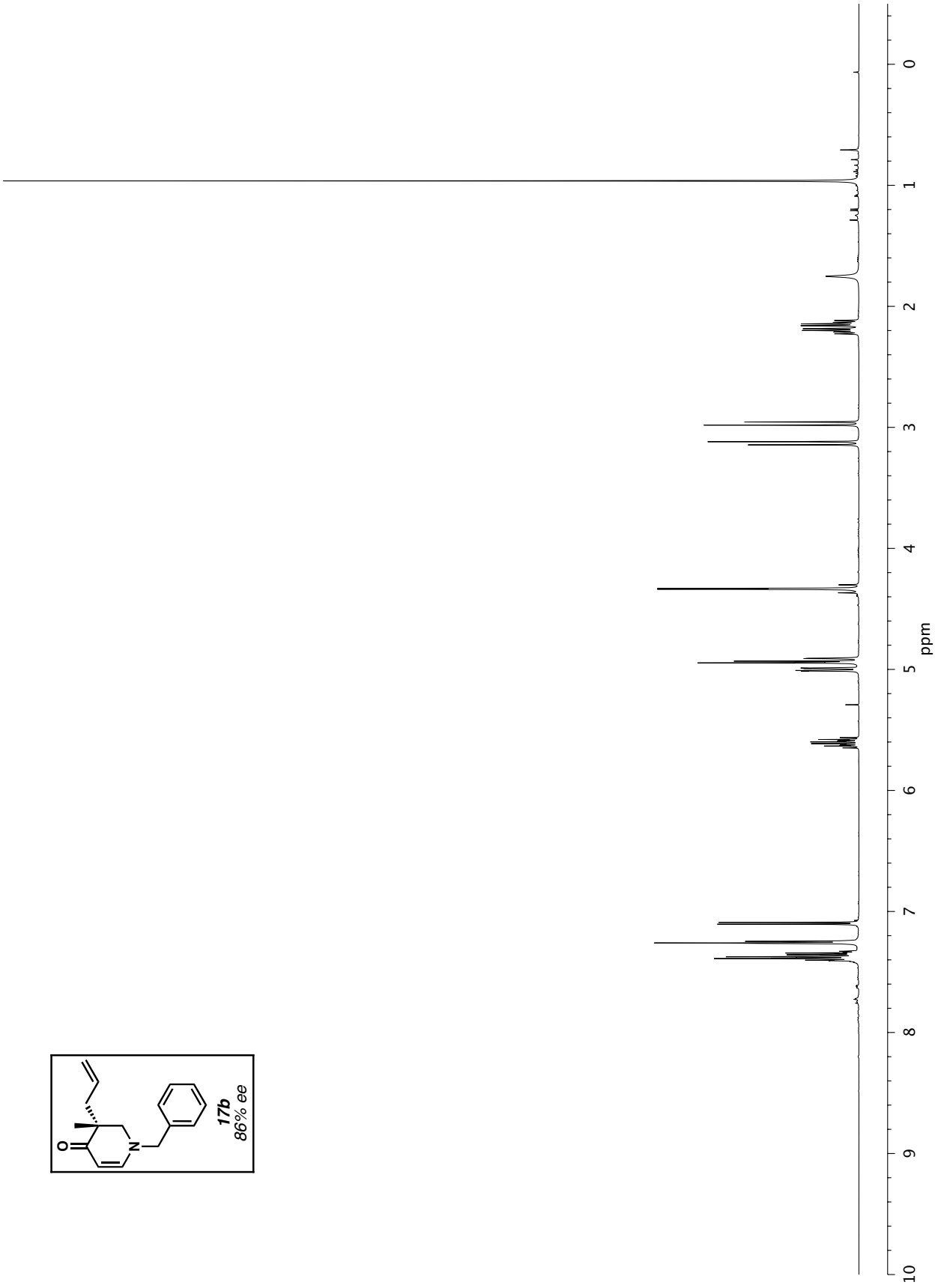

Figure SI-26A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **17b**.

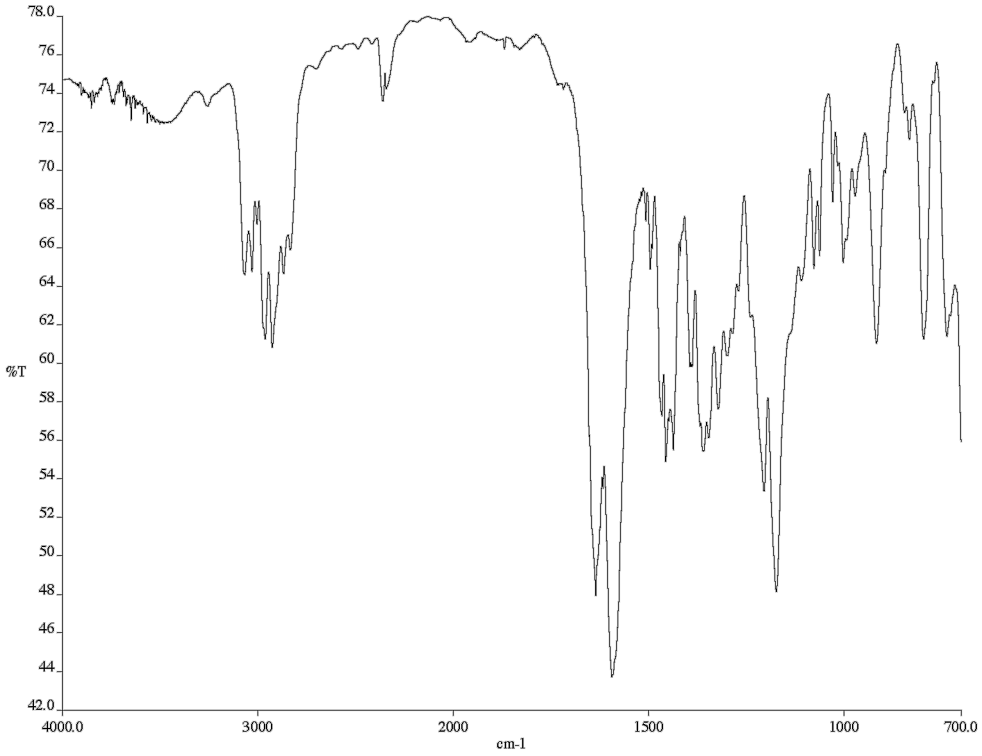

Figure SI-26B. Infrared spectrum (thin film/NaCl) of compound **17b**.

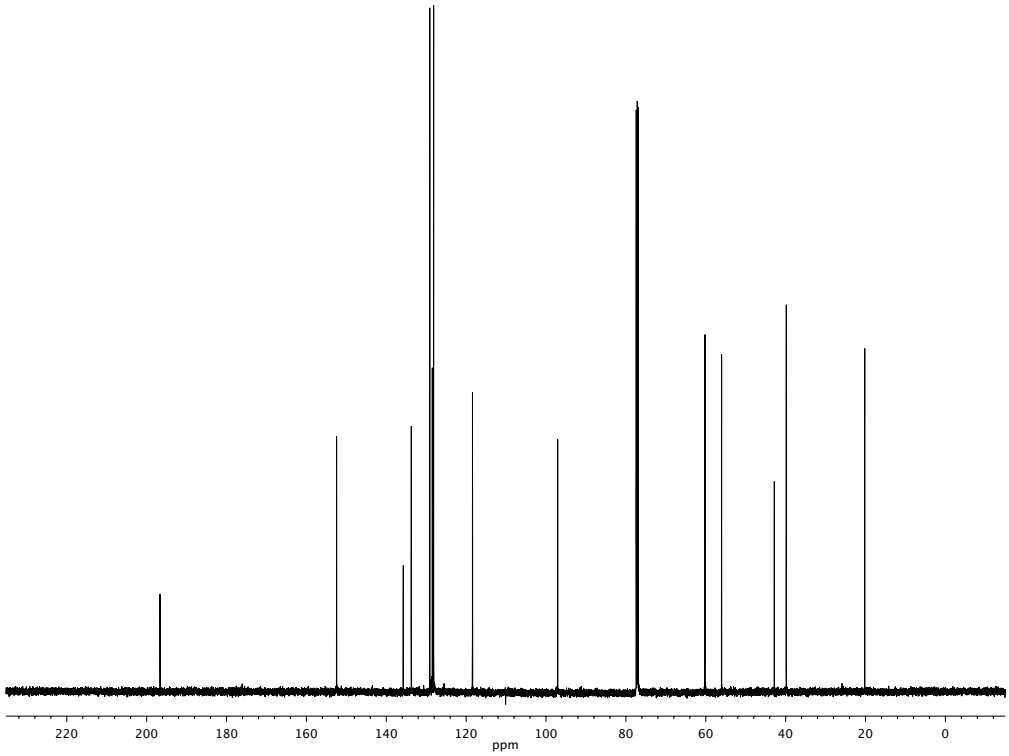

Figure SI-26C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **17b**.

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    Acq. Instrument : HPLC 2                          Location : Vial 73
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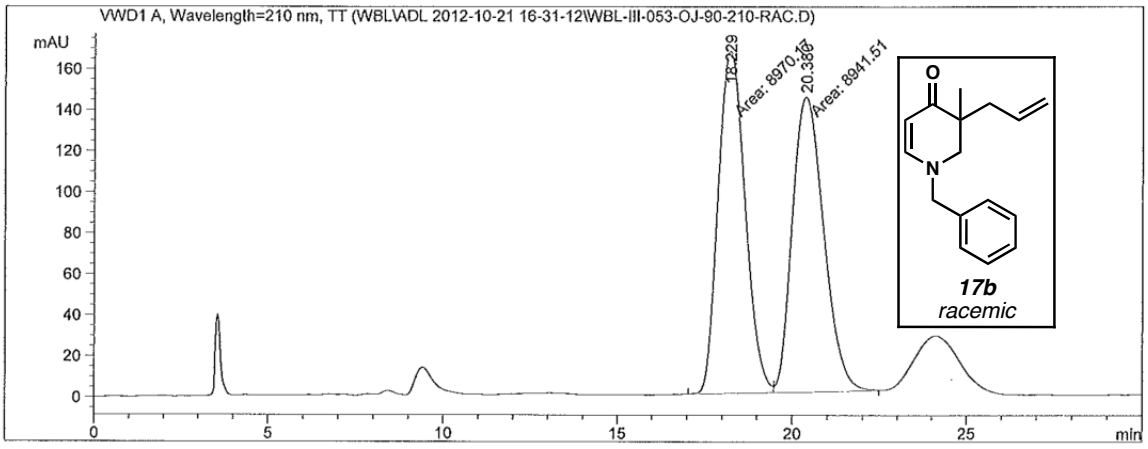


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    Dilution:                     :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=210 nm, TT

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  18.229 MF    0.8969 8970.16992  166.69754  50.0800
       2  20.380 FM    1.0367 8941.51465  143.75609  49.9200

    Totals :                  1.79117e4   310.45363

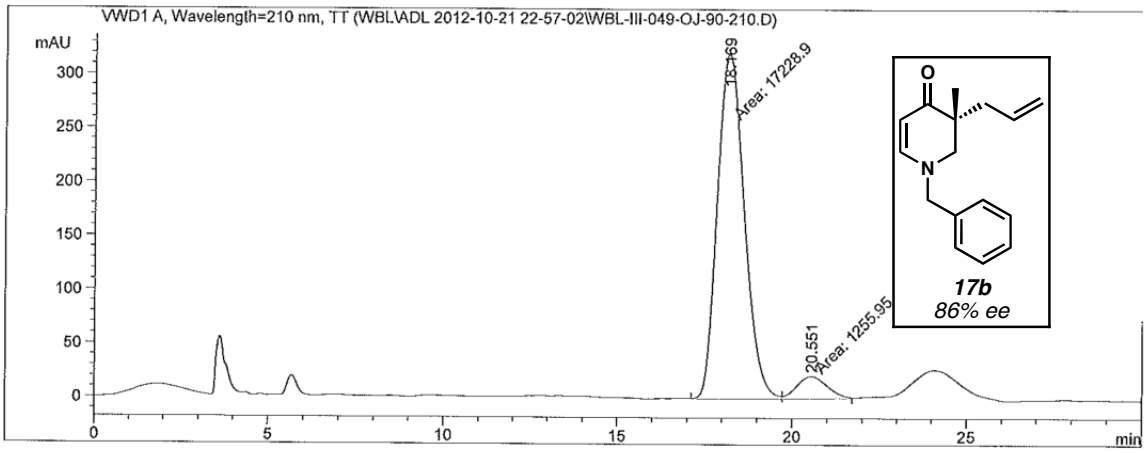
    ==========================================================================
                              Summed Peaks Report
    ==========================================================================

HPLC 2 10/31/2012 5:22:26 PM wbl                          Page   1 of 2
```

Figure SI-26D. Chiral SFC data of racemic compound **17b**.

```
Data File C:\CHEM32\2\DATA\WBL\ADL 2012-10-21 22-57-02\WBL-III-049-OJ-90-210.D
Sample Name: wbl-III-049-oj-90-210
    ==========================================================================
    Acq. Operator   : wbl                              Seq. Line :   5
    Acq. Instrument : HPLC 2                          Location : Vial 75
    Injection Date  : 10/21/2012 11:52:16 PM              Inj :   1
                                                     Inj Volume : 5.0 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 30.0 µl
    Acq. Method     : C:\CHEM32\2\DATA\WBL\ADL 2012-10-21 22-57-02\10IPA30_210.M
    Last changed    : 4/28/2010 2:57:04 PM by DCB
    Analysis Method : C:\CHEM32\2\METHODS\10IPA.M
    Last changed    : 10/31/2012 3:00:46 PM by wbl
                      (modified after loading)
    Method Info     : 10% IPA   10 min   Equil   1 mL/min

    ==========================================================================
```




```
    ==========================================================================
                              Area Percent Report
    ==========================================================================

    Sorted By             :      Signal
    Multiplier:                   :      1.0000
    Dilution:                     :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=210 nm, TT

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|--------|----------|----------|--------|
       1  18.169 MF    0.8968 1.72289e4   320.17657  93.2055
       2  20.551 FM    1.0040 1255.94946   20.84948   6.7945

    Totals :                  1.84849e4   341.02606

    ==========================================================================
                              Summed Peaks Report
    ==========================================================================

HPLC 2 10/31/2012 5:14:16 PM wbl                          Page   1 of 2
```

Figure SI-26E. Chiral SFC data of enantioenriched compound **17b**.

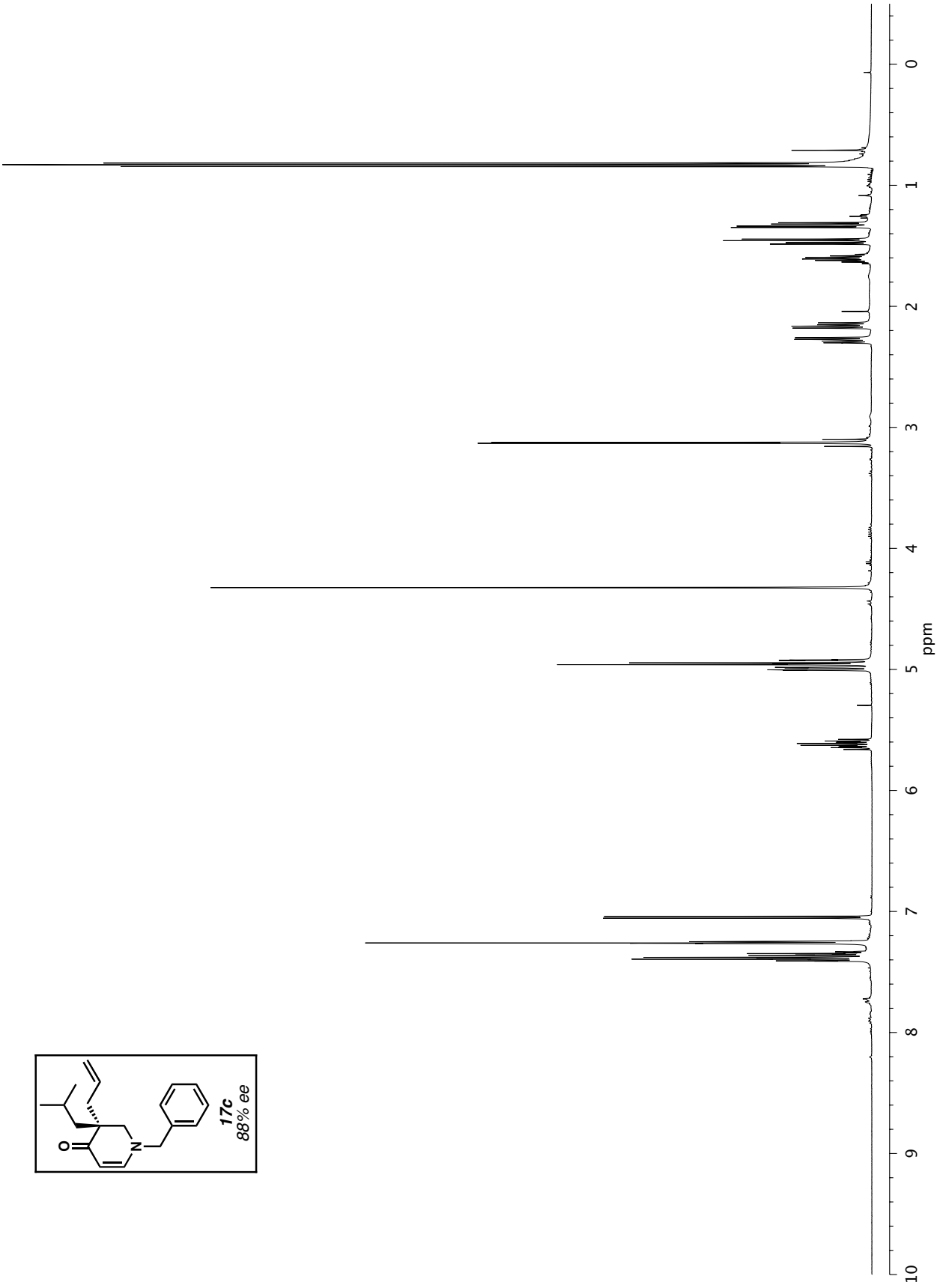


Figure SI-27A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **17c**.

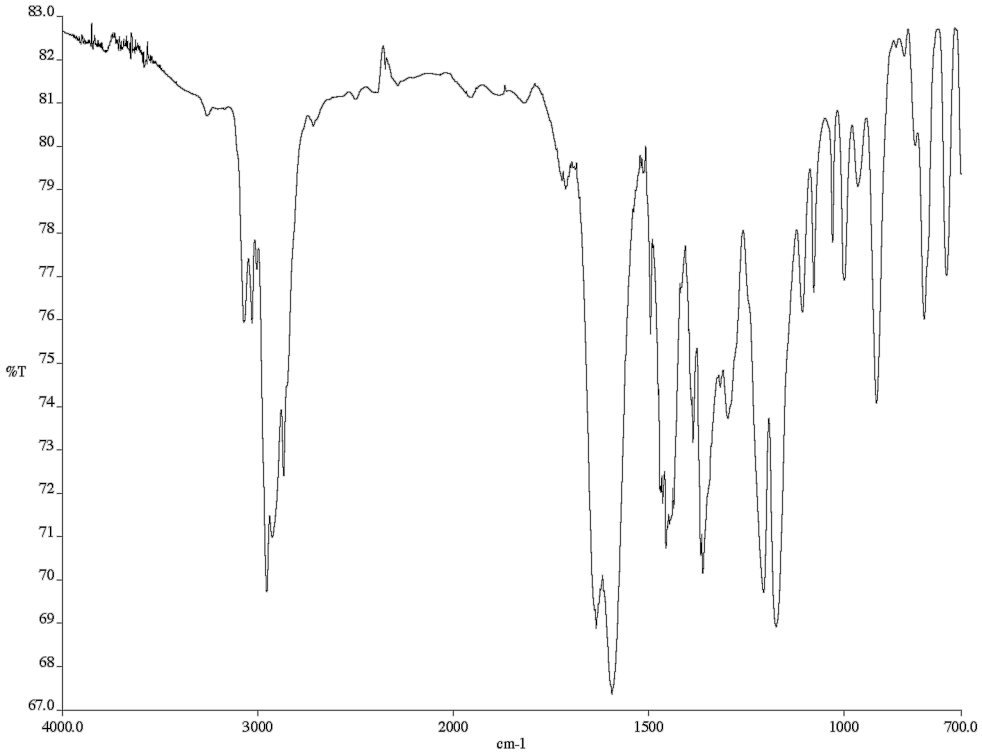


Figure SI-27B. Infrared spectrum (thin film/NaCl) of compound **17c**.

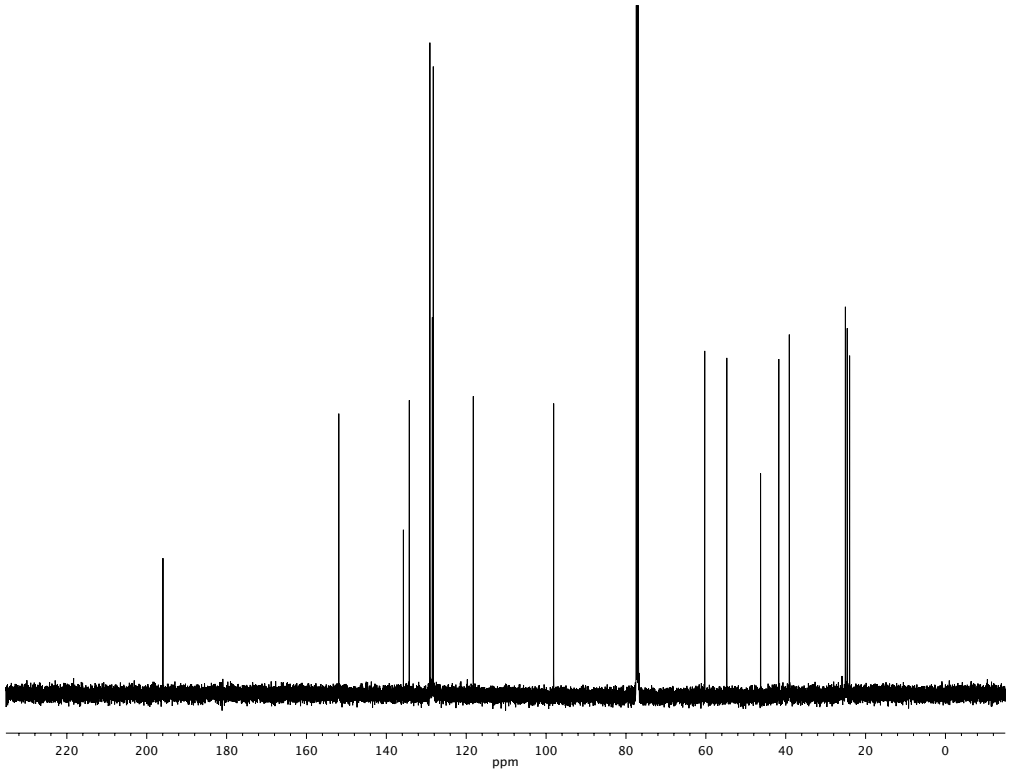
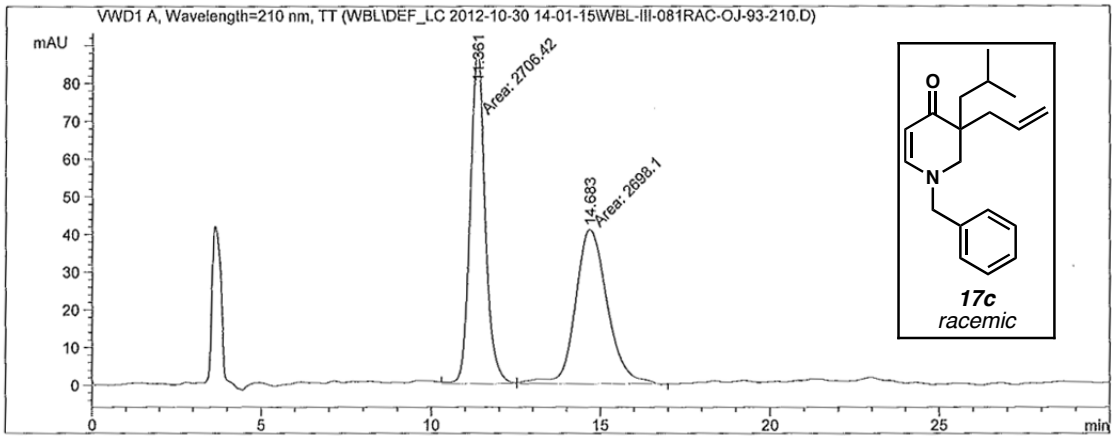


Figure SI-27C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **17c**.

```
:a File C:\CHEM32\2\DATA\WBL\DEF_LC 2012-10-30 14-01-15\WBL-III-081RAC-OJ-93-210
\ple Name: wbl-III-081rac-OJ-93-210
================================================================================
Acq. Operator   : wbl                          Seq. Line :   7
Acq. Instrument : HPLC 2                        Location : Vial 76
Injection Date  : 10/30/2012 3:16:37 PM             Inj :   1
                                               Inj Volume : 5.0 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 20.0 µl
Acq. Method     : C:\CHEM32\2\DATA\WBL\DEF_LC 2012-10-30 14-01-15\7IPA30_210.M
Last changed    : 8/1/2010 3:49:01 PM by ksp
Analysis Method : C:\CHEM32\2\METHODS\10IPA.M
Last changed    : 10/31/2012 3:00:46 PM by wbl
                  (modified after loading)
Method Info     : 10% IPA   10 min   Equil   1 mL/min

================================================================================
```




```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=210 nm, TT

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  11.361 MF    0.5093 2706.41626   88.56285  50.0769
   2  14.683 FM    1.0990 2698.10400   40.91831  49.9231

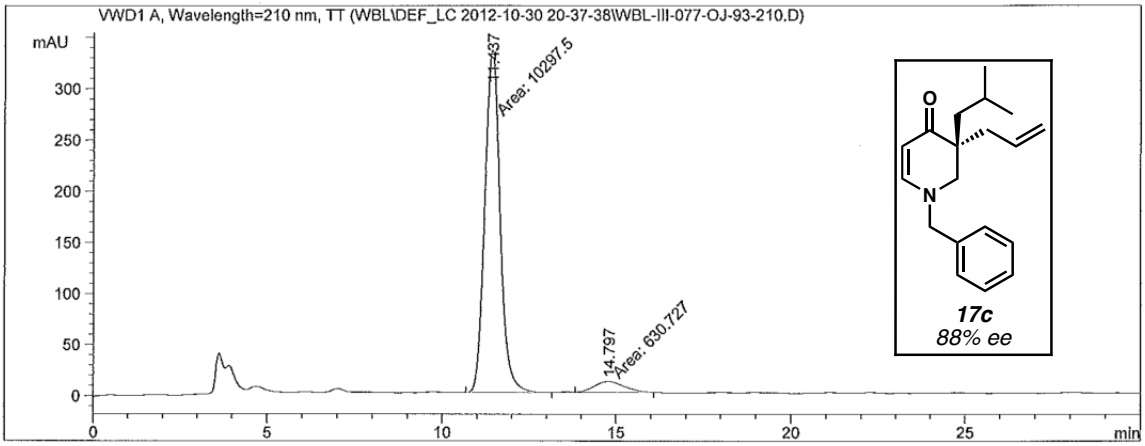
Totals :                  5404.52026  129.48116

================================================================================
                          Summed Peaks Report
================================================================================
```


Figure SI-27D. Chiral SFC data of racemic compound **17c**.

```
Sample Name: wbl-III-077-OJ-93-210
================================================================================
Acq. Operator   : wbl                                Seq. Line :   4
Acq. Instrument : HPLC 2                             Location : Vial 77
Injection Date  : 10/30/2012 9:00:26 PM                   Inj :   1
                                                    Inj Volume : 5.0 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 20.0 µl
Acq. Method     : C:\CHEM32\2\DATA\WBL\DEF_LC 2012-10-30 20-37-38\7IPA30_210.M
Last changed    : 8/1/2010 3:49:01 PM by ksp
Analysis Method : C:\CHEM32\2\METHODS\10IPA.M
Last changed    : 9/7/2012 11:51:51 AM by wbl
                  (modified after loading)
Method Info     : 10% IPA   10 min   Equil   1 mL/min

================================================================================
```




```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=210 nm, TT

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|---------|--------|
   1  11.437 MM    0.5135 1.02975e4   334.25787  94.2285
   2  14.797 MM    0.9917  630.72687   10.59974   5.7715

Totals :                  1.09283e4   344.85762

================================================================================
                          Summed Peaks Report
================================================================================

HPLC 2 10/30/2012 9:56:40 PM wbl                          Page   1 of 2
```

Figure SI-27E. Chiral SFC data of enantioenriched compound **17c**.

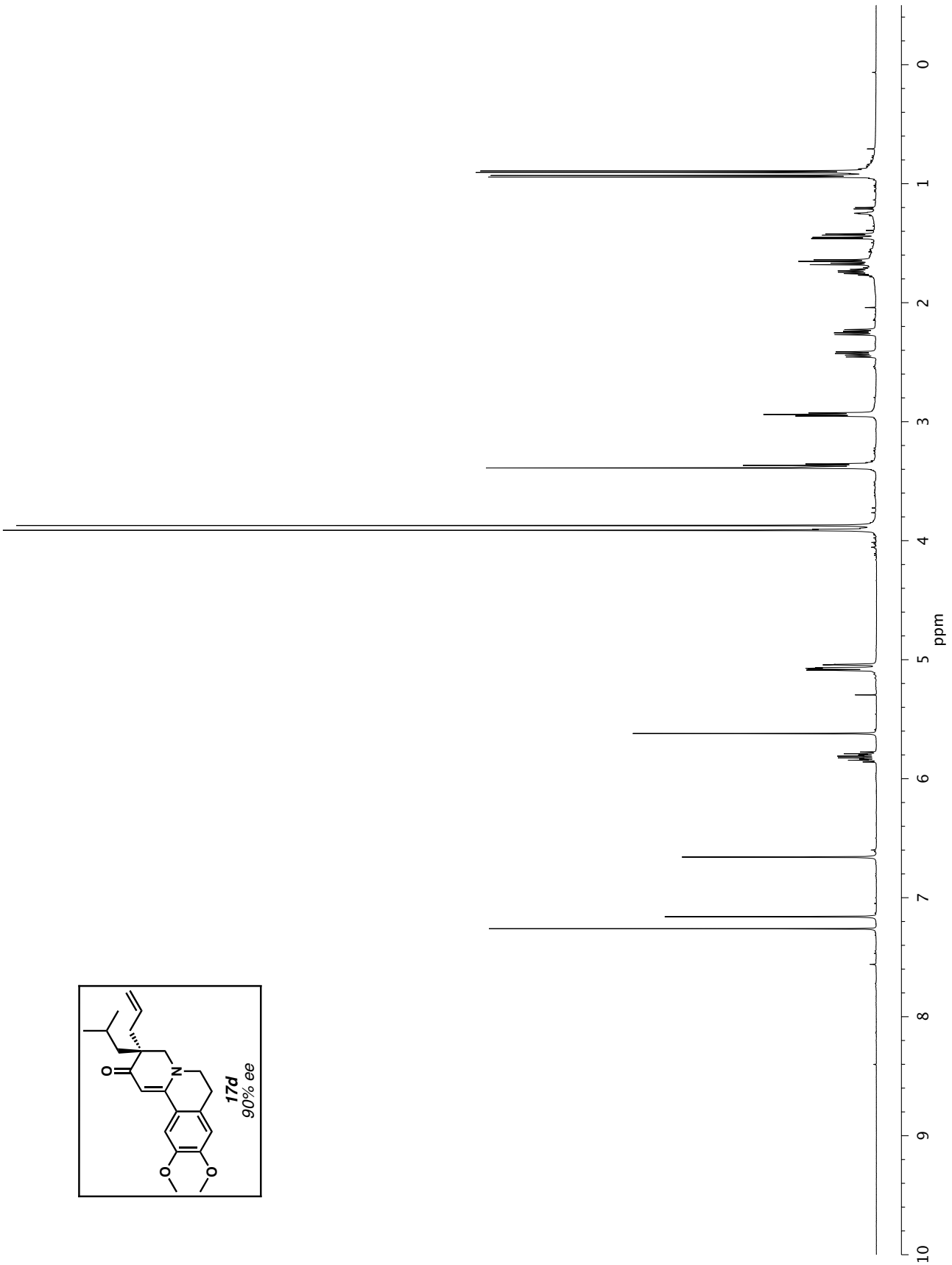


Figure SI-28A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **17d**.

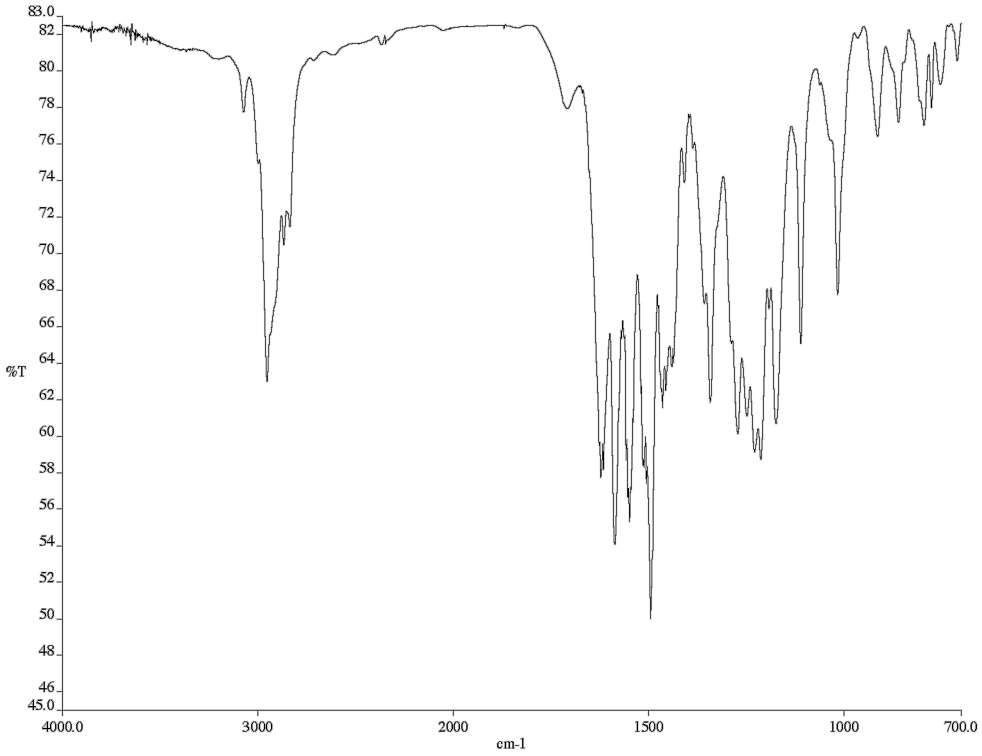


Figure SI-28B. Infrared spectrum (thin film/NaCl) of compound **17d**.

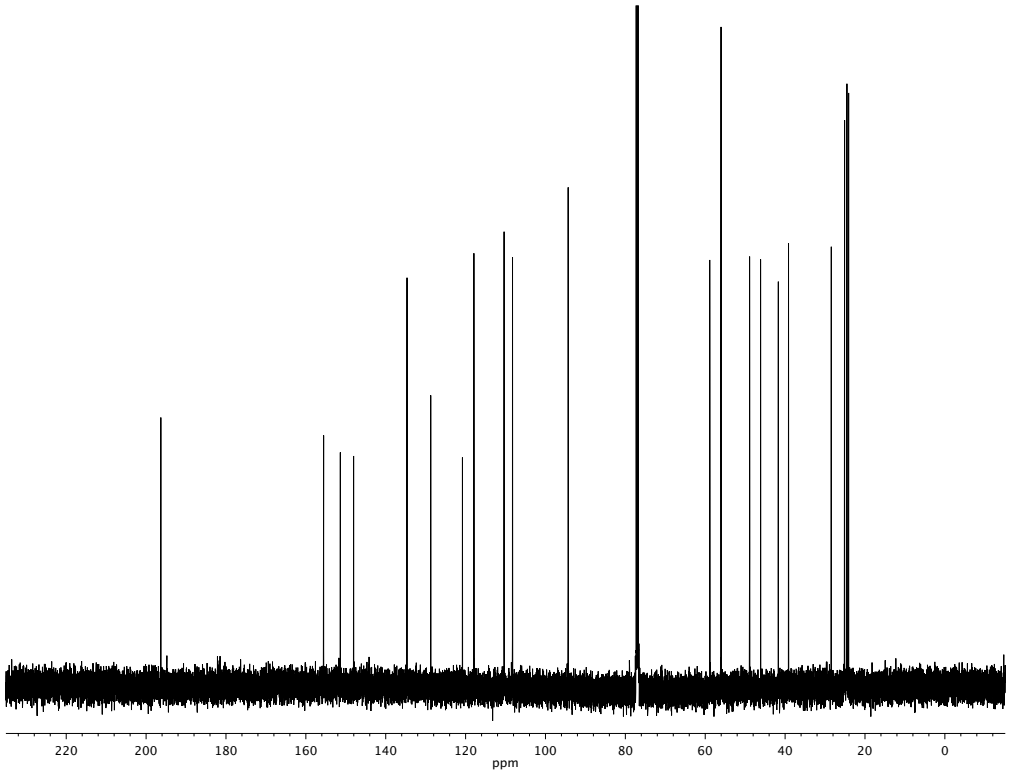
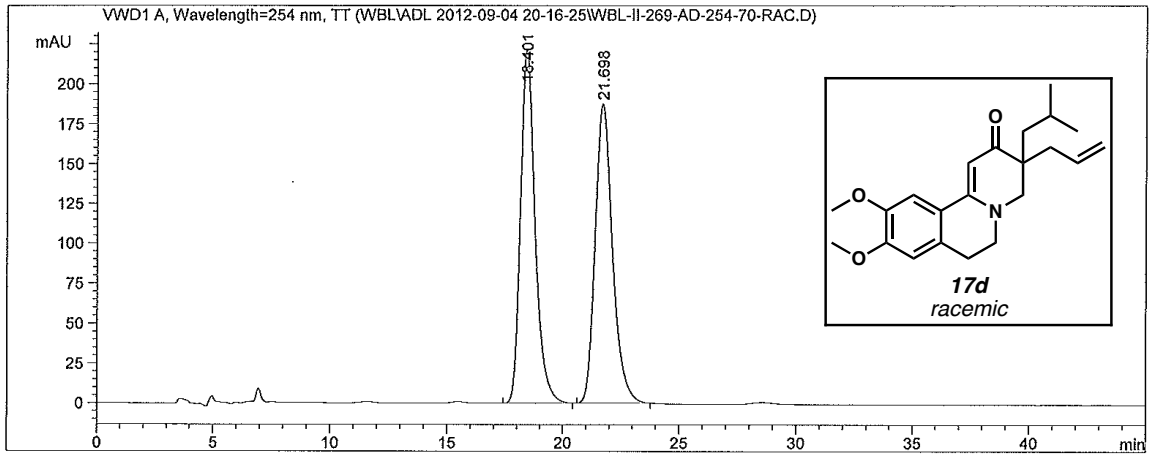


Figure SI-28C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **17d**.

```
Data File C:\CHEM32\2\DATA\WBL\ADL 2012-09-04 20-16-25\WBL-II-269-AD-254-70-RAC.D
Sample Name: wbl-II-269-AD-254-70-rac
    ==========================================================================
    Acq. Operator   : wbl                              Seq. Line :   4
    Acq. Instrument : HPLC 2                          Location : Vial 2
    Injection Date  : 9/4/2012 8:39:02 PM                  Inj :   1
                                                     Inj Volume : 5.0 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 20.0 µl
    Acq. Method     : C:\CHEM32\2\DATA\WBL\ADL 2012-09-04 20-16-25\30IPA45_254.M
    Last changed    : 4/26/2010 10:48:49 PM
    Analysis Method : C:\CHEM32\2\METHODS\10IPA.M
    Last changed    : 4/26/2010 11:07:08 PM
    Method Info     : 10% IPA   10 min   Equil   1 mL/min

    ==========================================================================
```




```
    ==========================================================================
                                Area Percent Report
    ==========================================================================

    Sorted By             :      Signal
    Multiplier:                   :      1.0000
    Dilution:                     :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=254 nm, TT

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  18.401 BB    0.6646 9816.01563  220.97881  50.0911
       2  21.698 BB    0.7905 9780.31738  187.30730  49.9089

    Totals :                  1.95963e4   408.28610


    ==========================================================================
                                Summed Peaks Report
    ==========================================================================

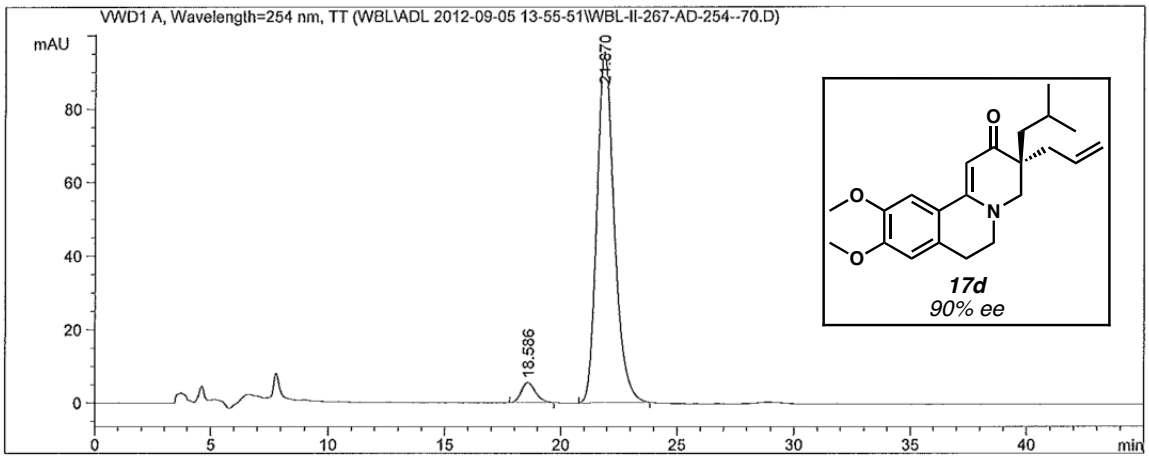
    Signal 1: VWD1 A, Wavelength=254 nm, TT

HPLC 2 9/5/2012 4:02:06 PM JAC                          Page   1 of 2
```

Figure SI-28D. Chiral HPLC data of racemic compound **17d**.

```
Data File C:\CHEM32\2\DATA\WBL\ADL 2012-09-05 13-55-51\WBL-II-267-AD-254--70.D
Sample Name: wbl-II-267-AD-254--70
    ==========================================================================
    Acq. Operator   : wbl                              Seq. Line :   5
    Acq. Instrument : HPLC 2                           Location : Vial 2
    Injection Date  : 9/5/2012 3:04:40 PM                   Inj :   1
                                                      Inj Volume : 5.0 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 20.0 µl
    Acq. Method     : C:\CHEM32\2\DATA\WBL\ADL 2012-09-05 13-55-51\30IPA45_254.M
    Last changed    : 4/26/2010 10:48:49 PM
    Analysis Method : C:\CHEM32\2\METHODS\10IPA.M
    Last changed    : 4/26/2010 11:07:08 PM
    Method Info     : 10% IPA   10 min   Equil   1 mL/min

    ==========================================================================
```




```
    ==========================================================================
                              Area Percent Report
    ==========================================================================

    Sorted By             :      Signal
    Multiplier:                   :      1.0000
    Dilution:                     :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=254 nm, TT

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  18.586 BB    0.5086  235.34474    5.50853   4.4942
       2  21.870 BB    0.7687 5001.31982   95.41990  95.5058

    Totals :                  5236.66457  100.92843


    ==========================================================================
                              Summed Peaks Report
    ==========================================================================

    Signal 1: VWD1 A, Wavelength=254 nm, TT

HPLC 2 9/5/2012 4:01:44 PM JAC                              Page   1 of 2
```

Figure SI-28E. Chiral HPLC data of enantioenriched compound **17d**.

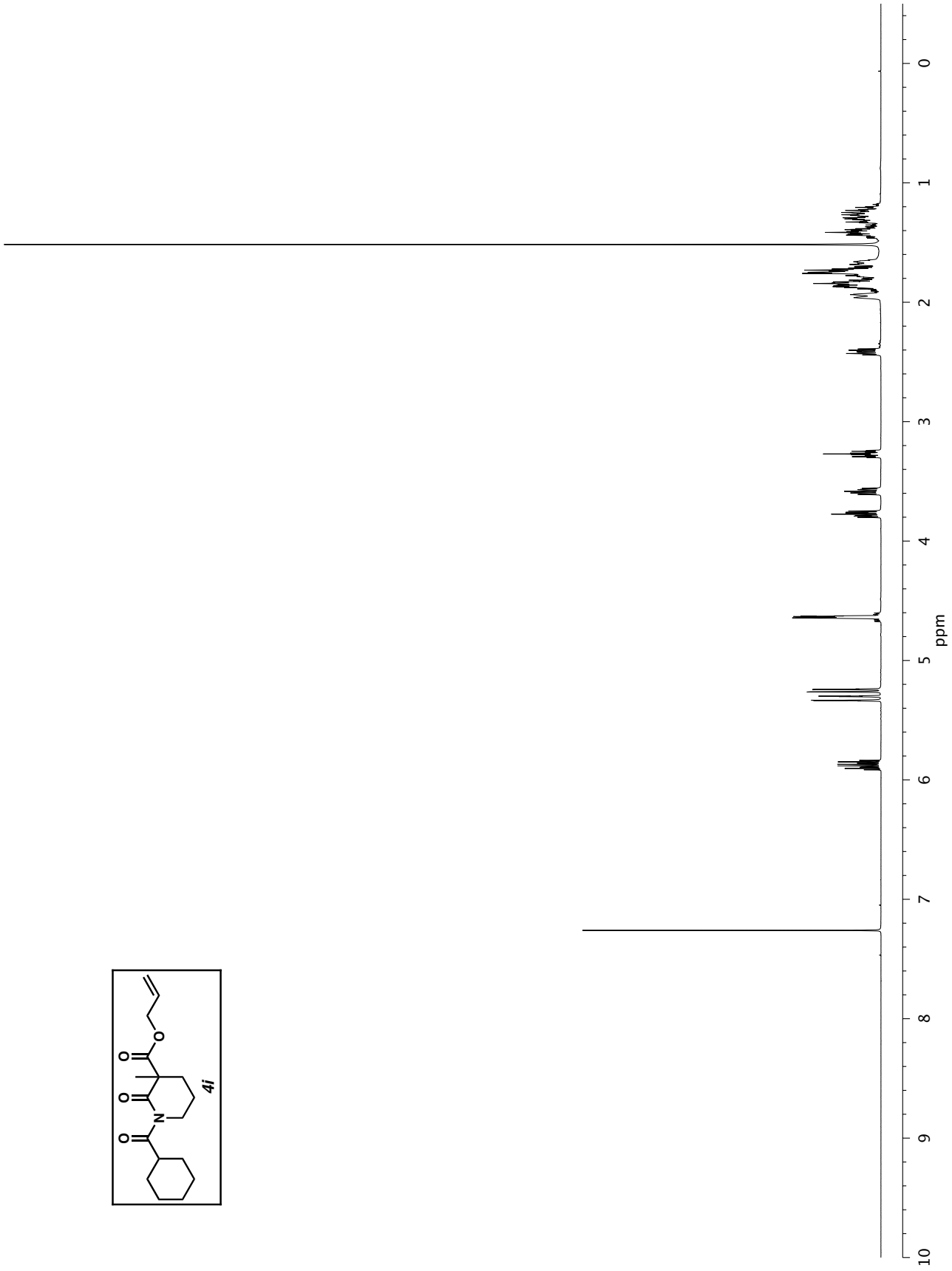


Figure SI-29A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **4i**.

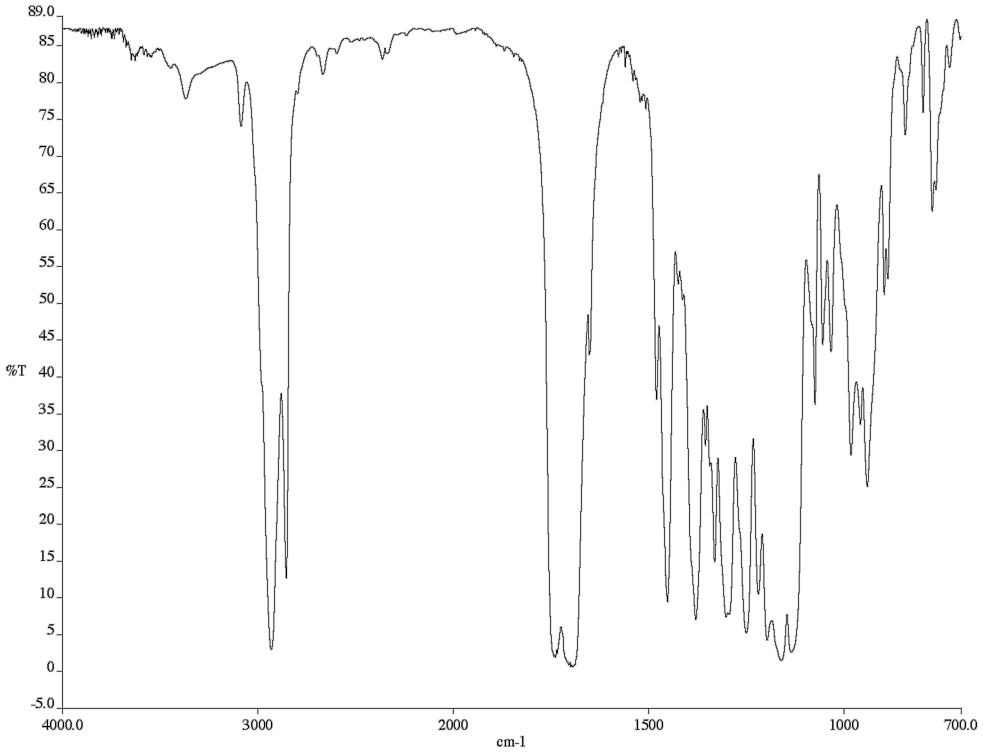


Figure SI-29B. Infrared spectrum (thin film/NaCl) of compound **4i**.

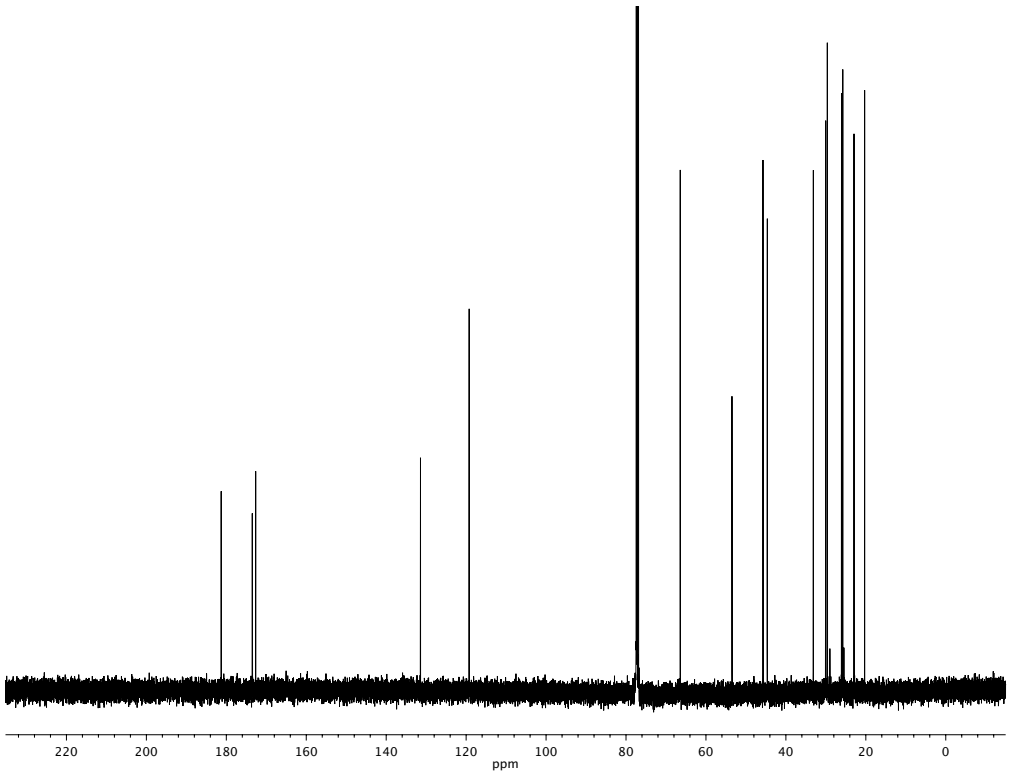


Figure SI-29C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **4i**.

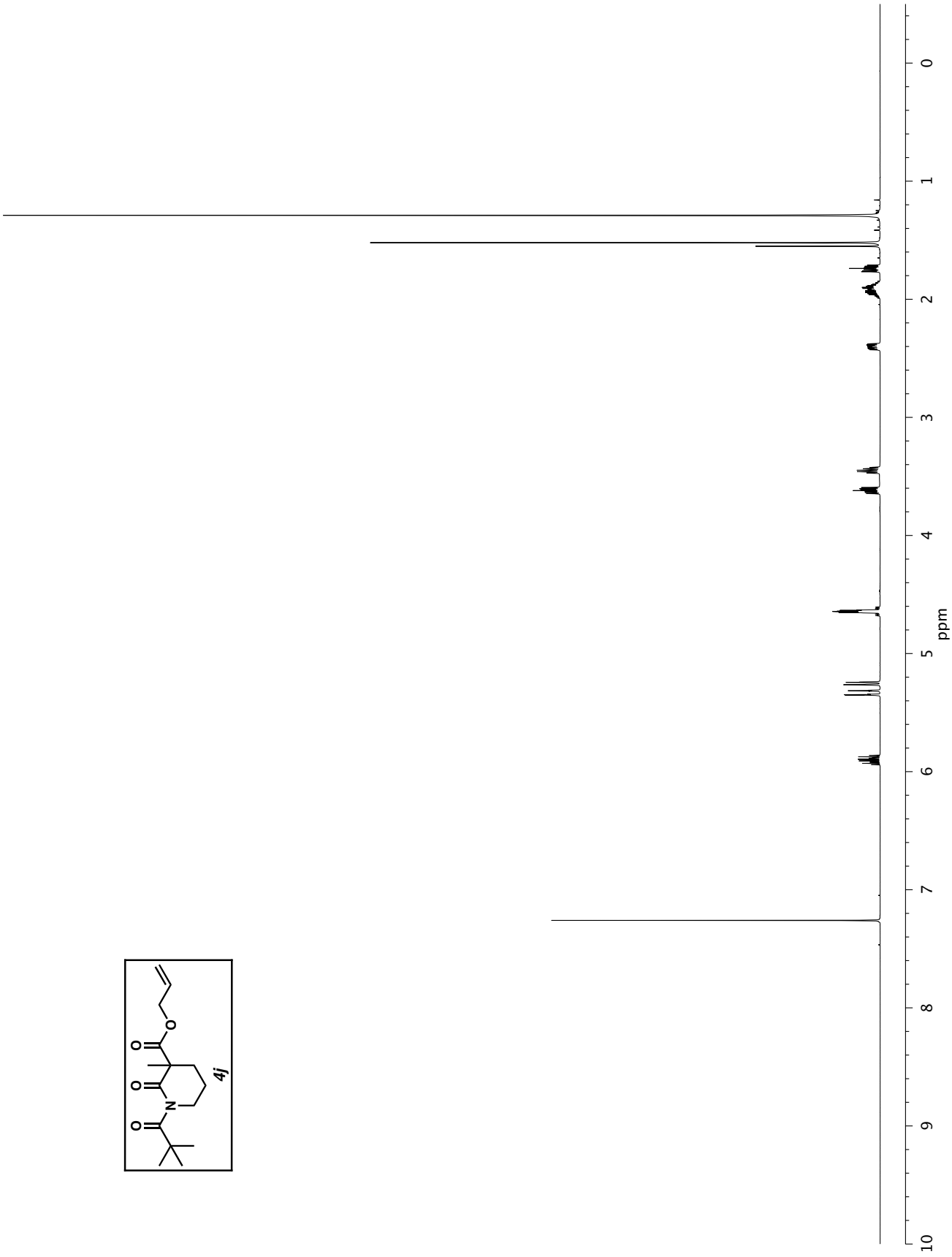


Figure SI-30A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **4j**.

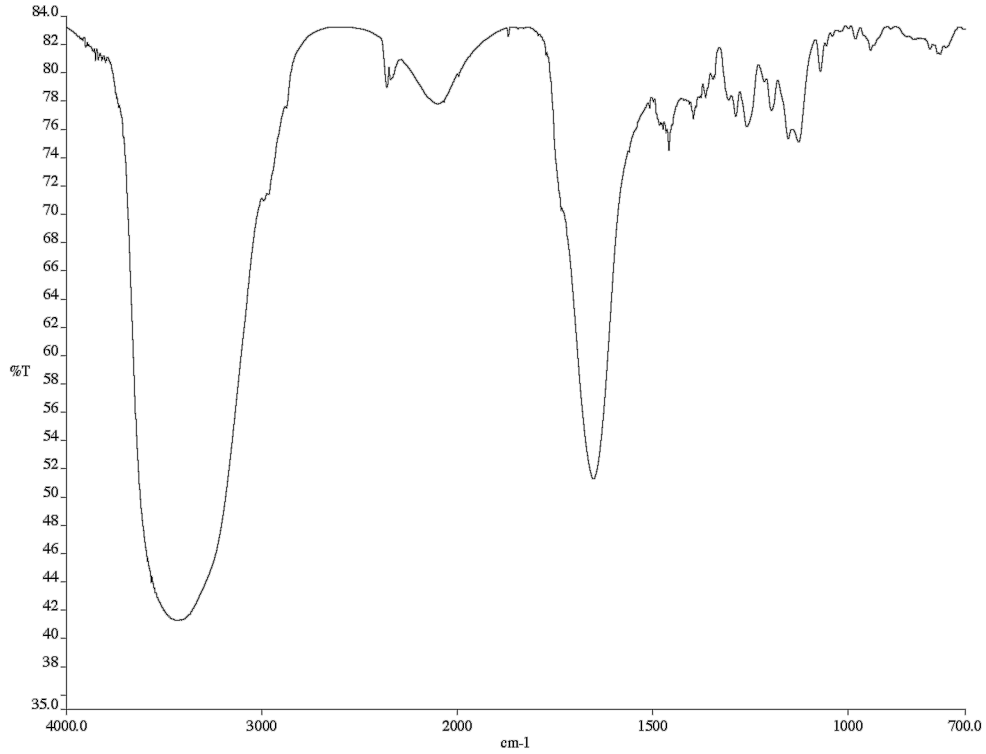


Figure SI-30B. Infrared spectrum (thin film/NaCl) of compound **4j**.

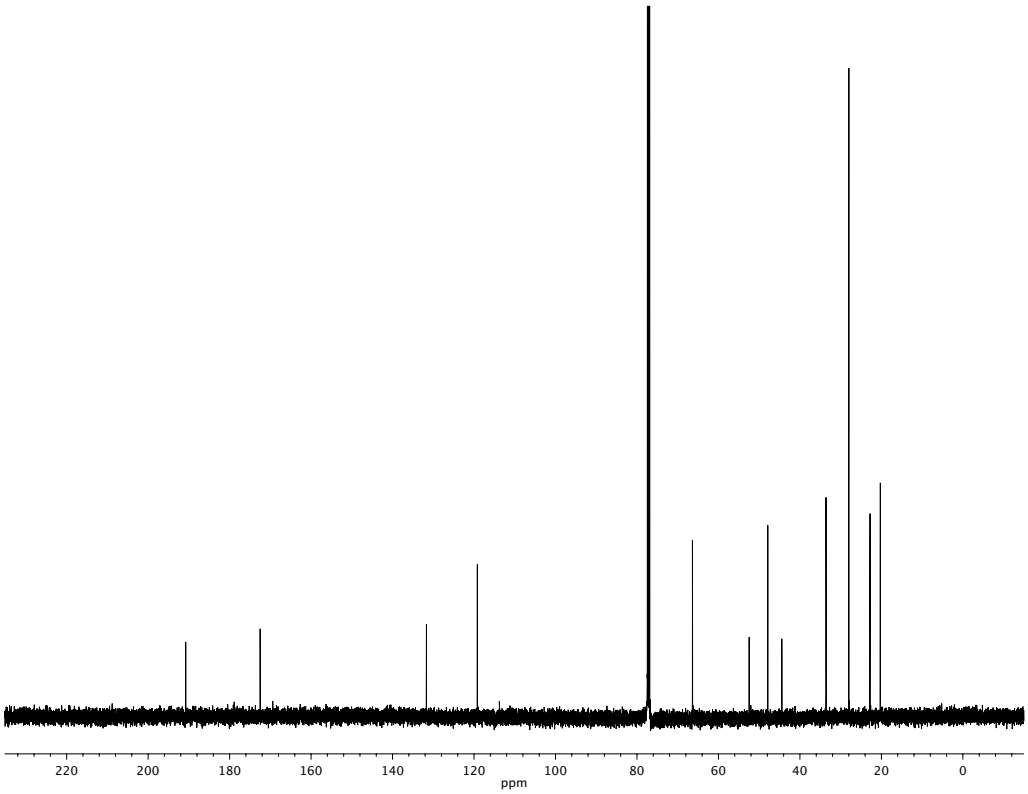


Figure SI-30C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **4j**.

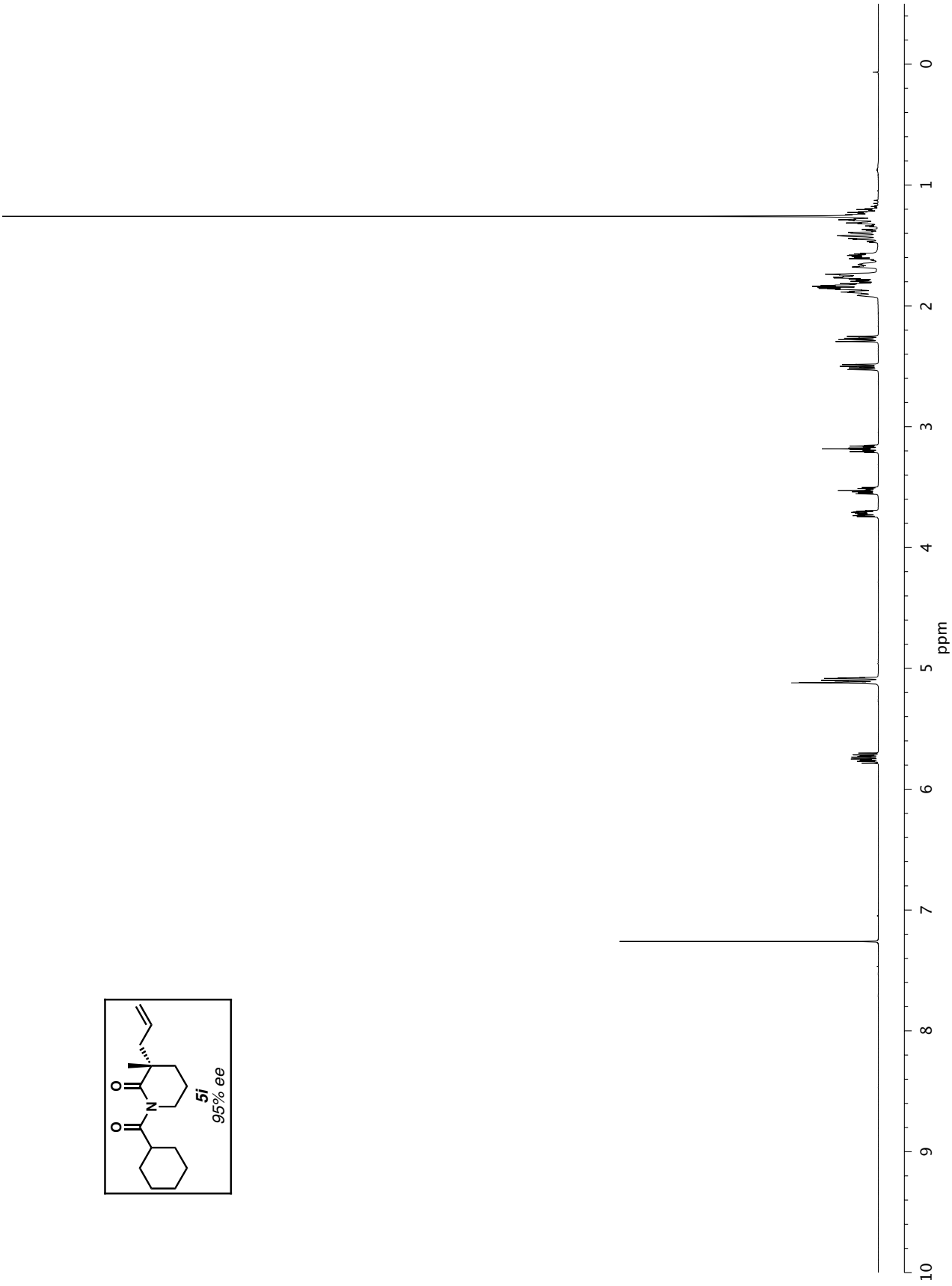


Figure SI-314. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **5i**.

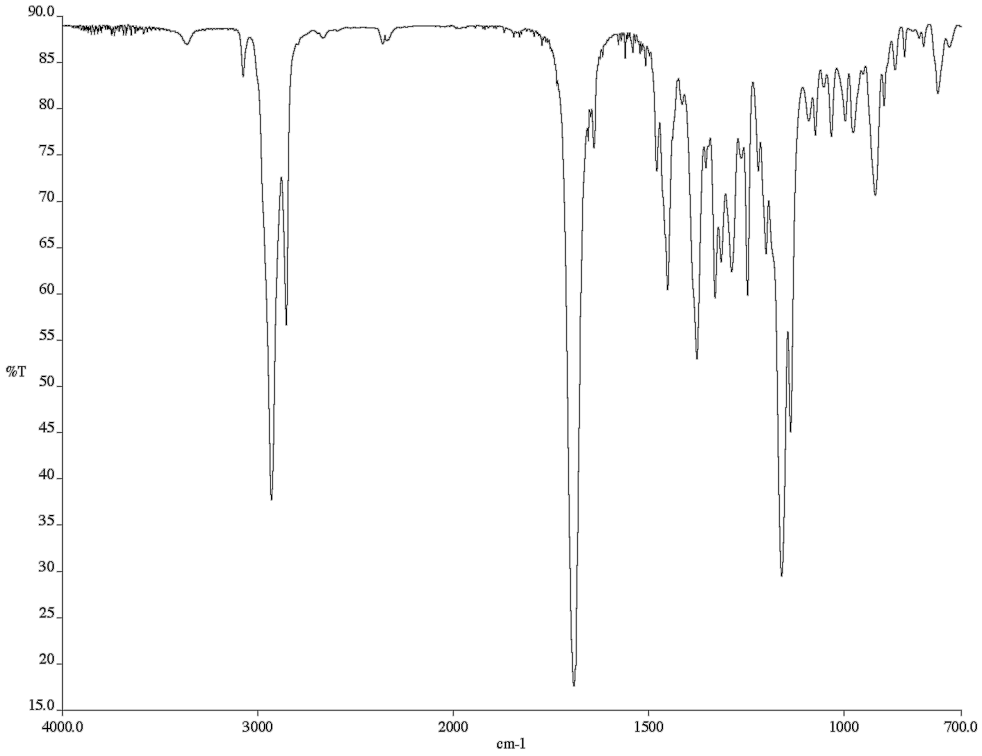


Figure SI-31B. Infrared spectrum (thin film/NaCl) of compound **5i**.

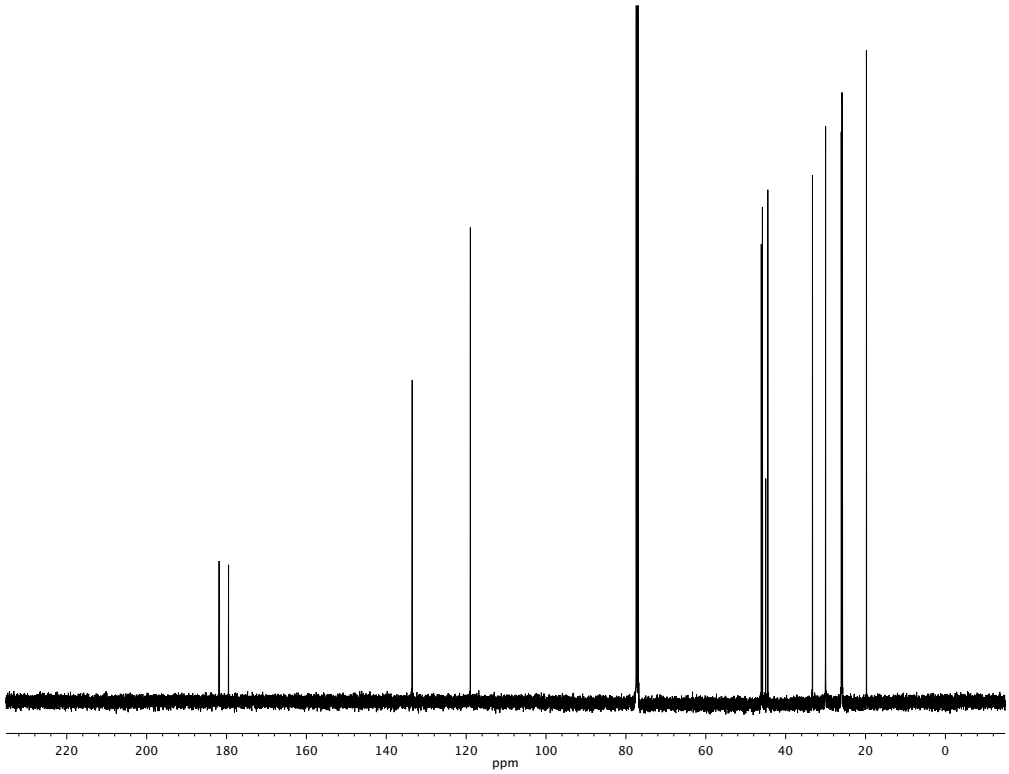
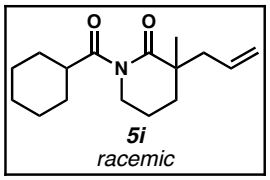


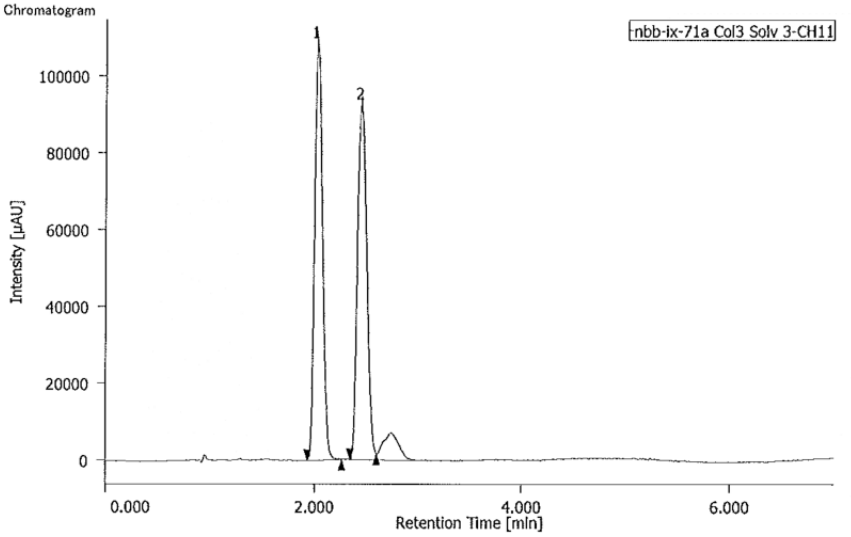
Figure SI-31C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **5i**.

NBB-IX-71A Col3 Sol3 nbb-ix-71a Col3 Solv 3 6/27/2012 4:36:10 PM

Analytical Report SFC



Chromatogram Information	
User Name	User
HPLC System Name	Jasco SFC w PDA
Injection Date	6/27/2012 4:19:18 PM
Volume	5.00 [µL]
Sample #	51
Project Name	Cal Tech SFC
Executed Sequence	NBB-IX-71A Col3 Sol3
Chromatogram Name	nbb-ix-71a Col3 Solv 3
Sample Name	
Acquisition Time	7.0 [min]
Acquisition Sequence	NBB-IX-71A Col3 Sol3
Control Method	Solv 3 Col 3 Isocratic 1B 5mL_min 10MPa 10min



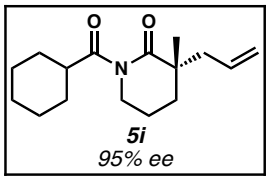
Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	11	2.027	582758	109067	49.989	1.933	2.267	0.085	2.713	1.370
2	Unknown	11	2.453	583015	93030	50.011	2.347	2.600	0.100	N/A	1.264

Figure SI-31D. Chiral SFC data of racemic compound **5i**.

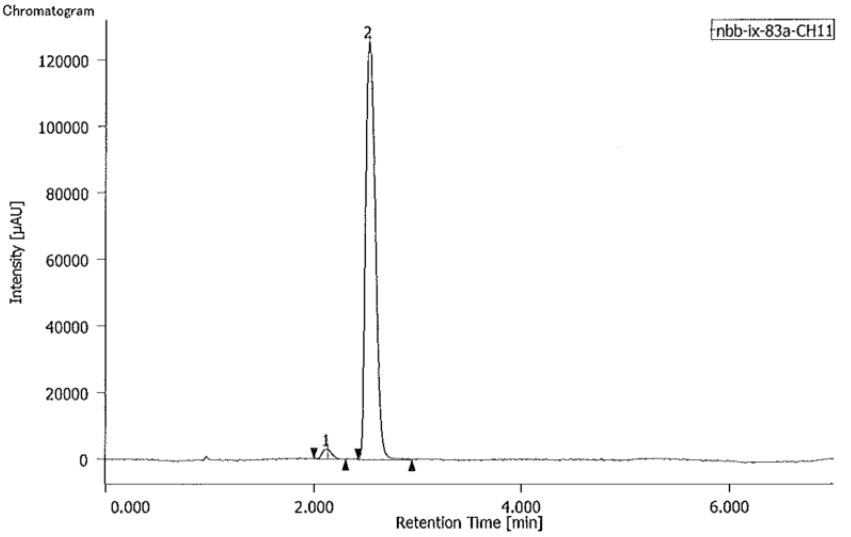
NBB-IX-83A Col3 Sol3 nbb-ix-83a 6/27/2012 4:54:07 PM

Analytical Report SFC



Chromatogram Information	
User Name	User
HPLC System Name	Jasco SFC w PDA
Injection Date	6/27/2012 4:44:41 PM
Volume	5.00 [µL]
Sample #	6
Project Name	Cal Tech SFC
Executed Sequence	NBB-IX-83A Col3 Sol3
Chromatogram Name	nbb-ix-83a
Sample Name	
Acquisition Time	7.0 [min]
Acquisition Sequence	NBB-IX-83A Col3 Sol3
Control Method	Solv 3 Col 3 Isocratic 1B 5mL_min 10MPa 10min

Chromatogram



Peak Information

#	Peak Name	CH	tR [min]	Area [µV*sec]	Height [µV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	11	2.133	20281	2998	2.414	2.000	2.307	0.102	2.287	0.955
2	Unknown	11	2.533	819906	125753	97.586	2.427	2.947	0.104	N/A	1.386

1 / 1

Figure SI-31E. Chiral SFC data of enantioenriched compound **5i**.

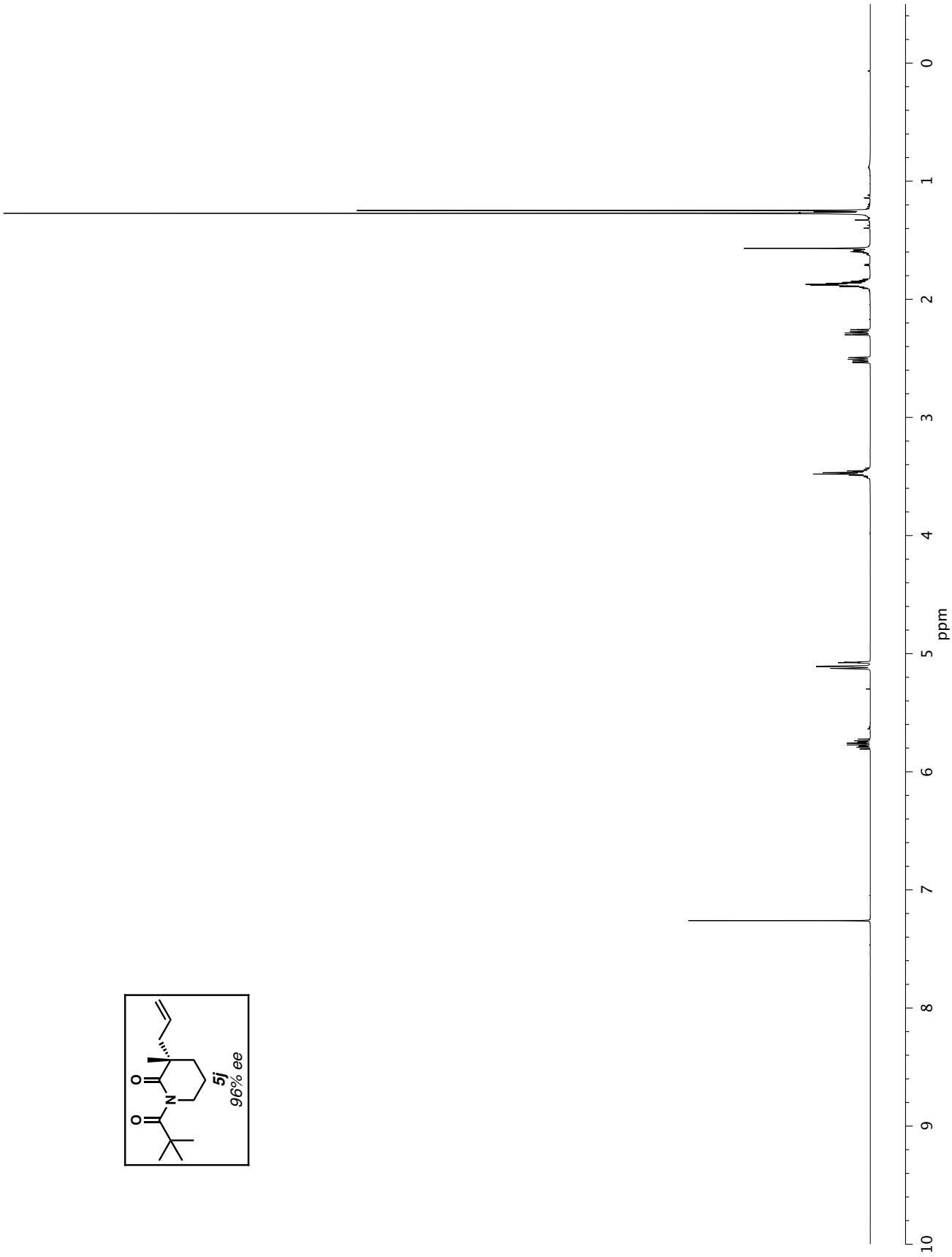


Figure SI-32A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **5j**.

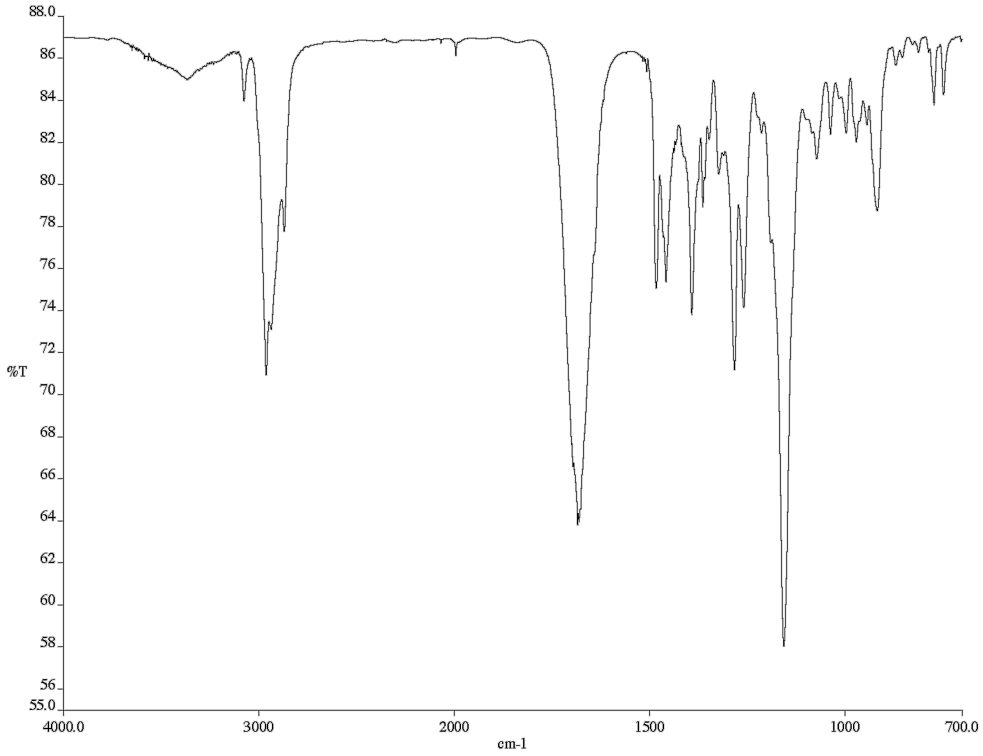


Figure SI-32B. Infrared spectrum (thin film/NaCl) of compound **5j**.

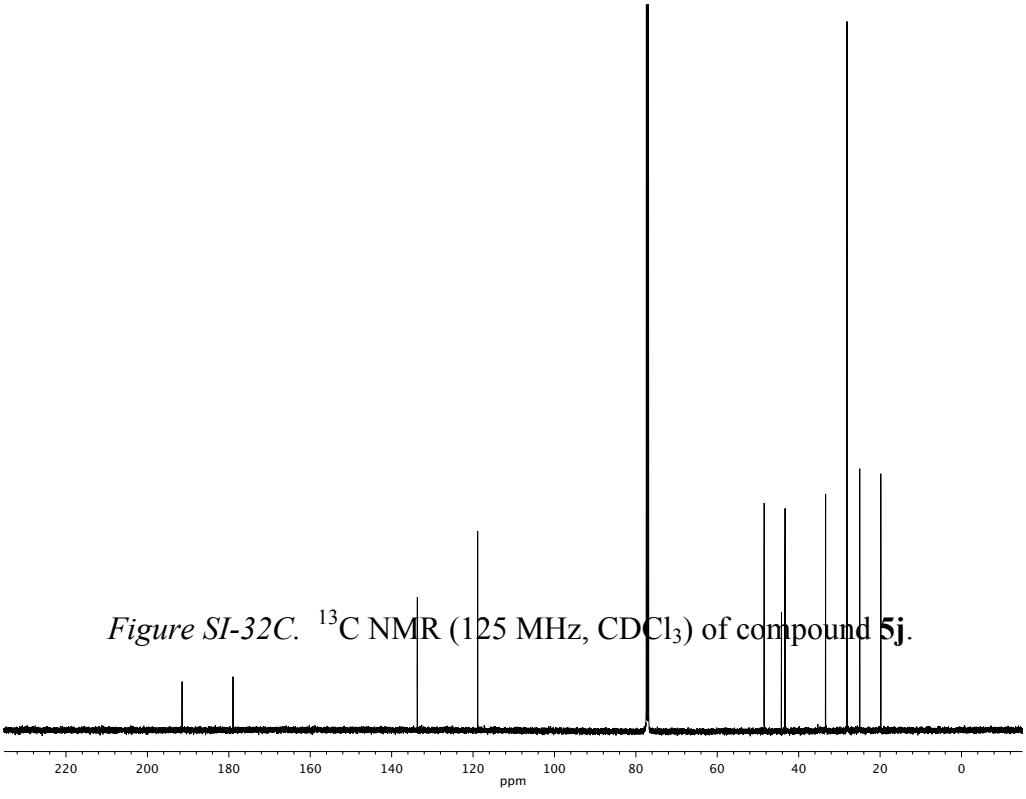
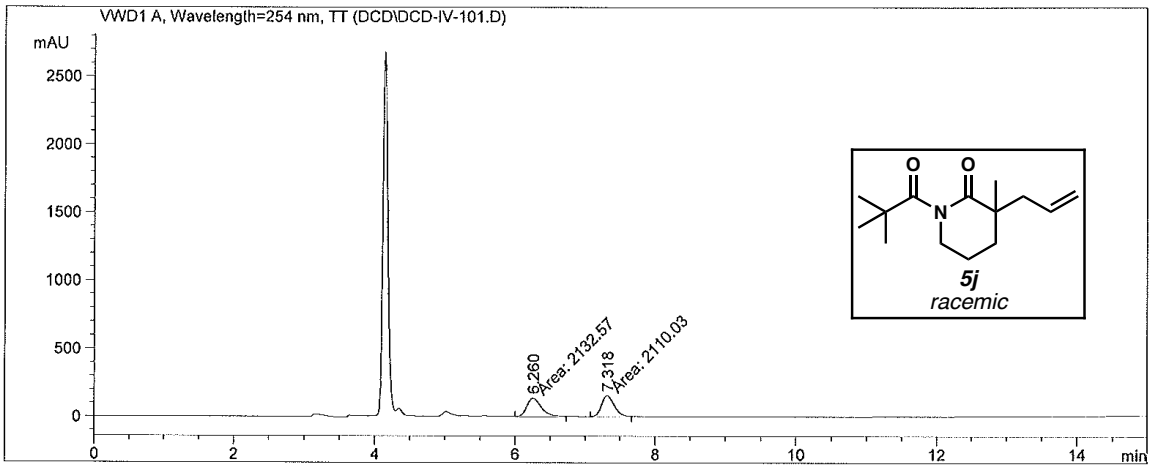


Figure SI-32C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **5j**.

```
Data File C:\CHEM32\1\DATA\DCD\DCD-IV-101.D
Sample Name: DCD-IV-101
    ==========================================================================
    Acq. Operator   : DCD                              Seq. Line :   3
    Acq. Instrument : HPLC 1                          Location : Vial 31
    Injection Date  : 7/31/2012 3:42:30 PM                 Inj :   1
                                                    Inj Volume : 5.0 µl
    Acq. Method     : C:\CHEM32\1\METHODS\5IPA15_254.M
    Last changed    : 5/28/2010 3:34:42 PM by AYH
    Analysis Method : C:\CHEM32\1\METHODS\2IPA_EQUIL.M
    Last changed    : 4/26/2010 10:02:39 PM
    Method Info     : 2% IPA    10 min  equil   1 mL/min

    ==========================================================================
```




```
    ==========================================================================
                              Area Percent Report
    ==========================================================================

    Sorted By             :      Signal
    Multiplier:                   :      1.0000
    Dilution:                     :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=254 nm, TT

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|-----|-------|----------|----------|--------|
       1   6.260 MM    0.2537 2132.57080  140.07813  50.2656
       2   7.318 MM    0.2203 2110.03296  159.66458  49.7344

    Totals :                  4242.60376  299.74271


    ==========================================================================
                              Summed Peaks Report
    ==========================================================================

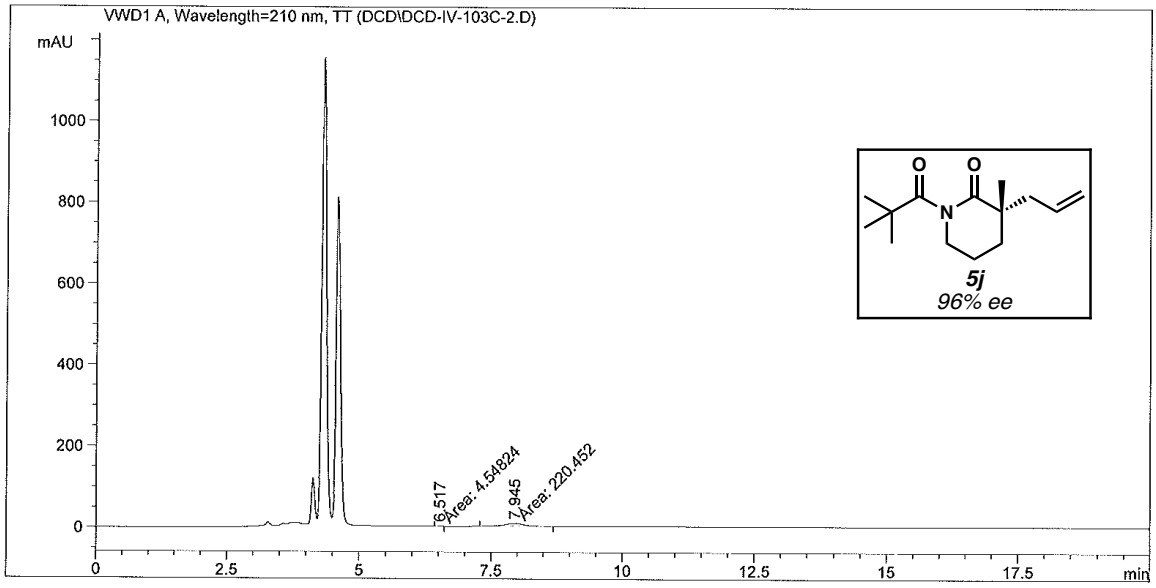
    Signal 1: VWD1 A, Wavelength=254 nm, TT

HPLC 1 7/31/2012 4:07:59 PM ANM                          Page   1 of 2
```

Figure SI-32D. Chiral HPLC data of racemic compound **5j**.

```
Data File C:\CHEM32\1\DATA\DCD\DCD-IV-103C-2.D
Sample Name: DCD-IV-103c-2

================================================================================
Acq. Operator   : DCD                                 Seq. Line :   3
Acq. Instrument : HPLC 1                              Location : Vial 95
Injection Date  : 9/7/2012 1:48:27 PM                     Inj :   1
                                                   Inj Volume : 5.0 µl
Acq. Method     : C:\CHEM32\1\METHODS\5IPA20_210.M
Last changed    : 7/5/2012 5:09:36 PM by DCD
Analysis Method : C:\CHEM32\1\METHODS\5IPA60_280.M
Last changed    : 9/7/2012 2:25:21 PM by ANM
                  (modified after loading)
Method Info     : 5% IPA    60 min   280 nm   1 mL/min
```




```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=210 nm, TT

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   6.517 MM    0.1193    4.54824 6.35558e-1   2.0214
   2   7.945 MM    0.4770  220.45190    7.70195  97.9786

Totals :                  225.00014    8.33751

================================================================================

HPLC 1 9/7/2012 2:25:57 PM ANM                          Page   1 of 1
```

Figure SI-32E. Chiral HPLC data of enantioenriched compound **5j**.

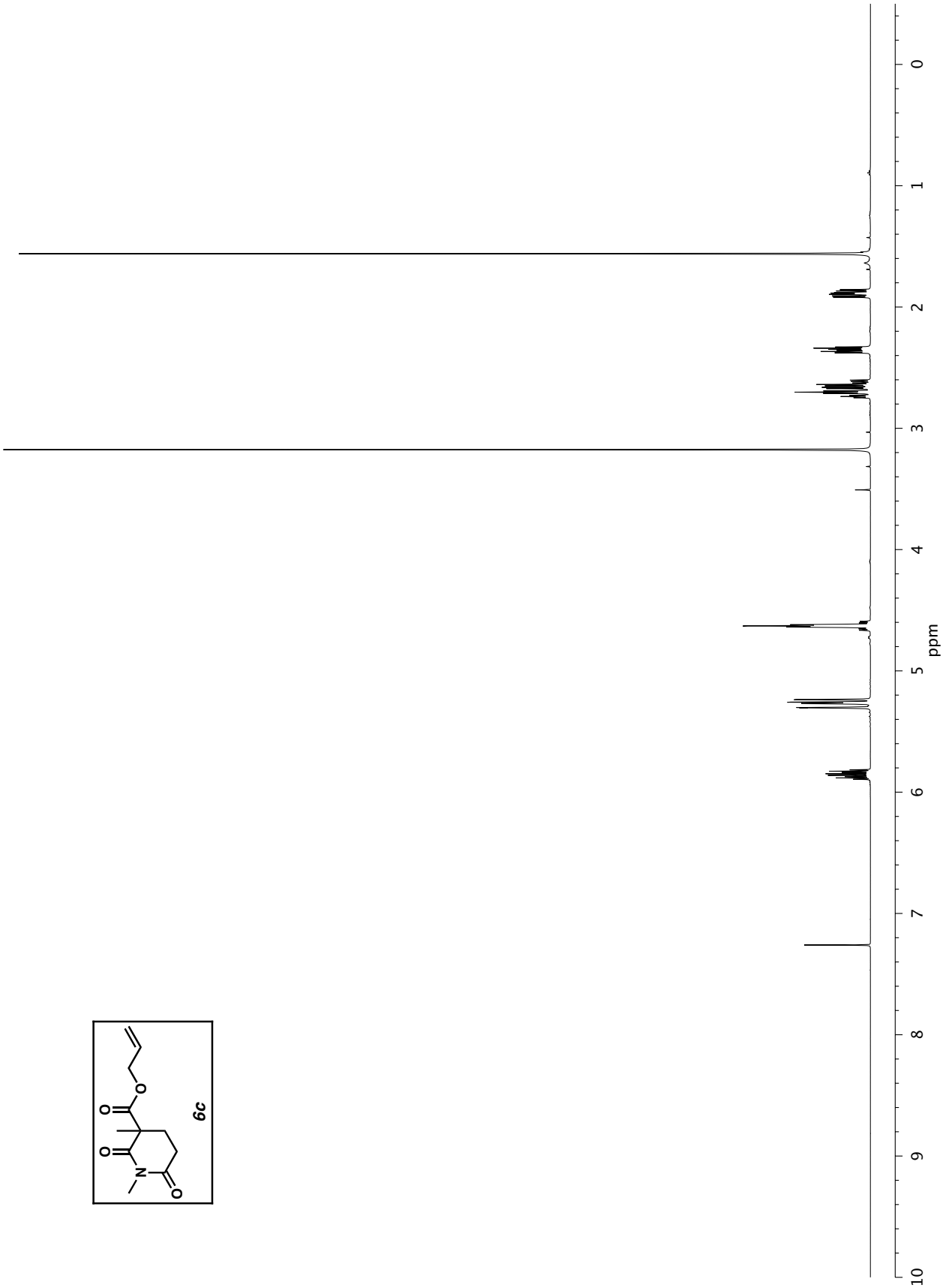


Figure SI-334. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **6c**.

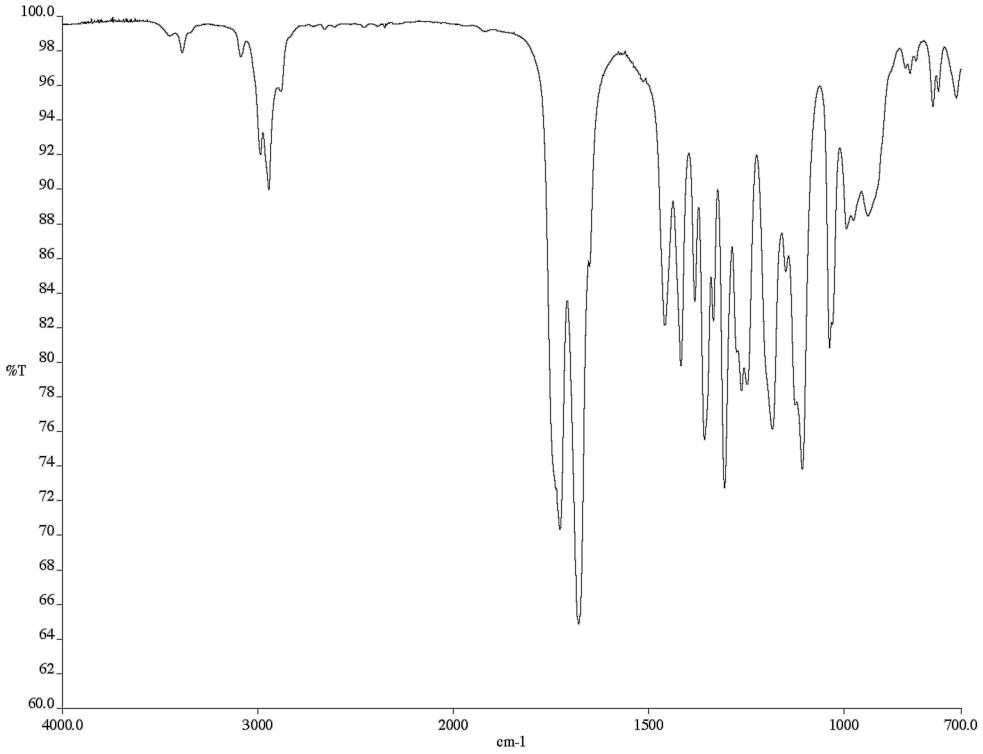


Figure SI-33B. Infrared spectrum (thin film/NaCl) of compound **6c**.

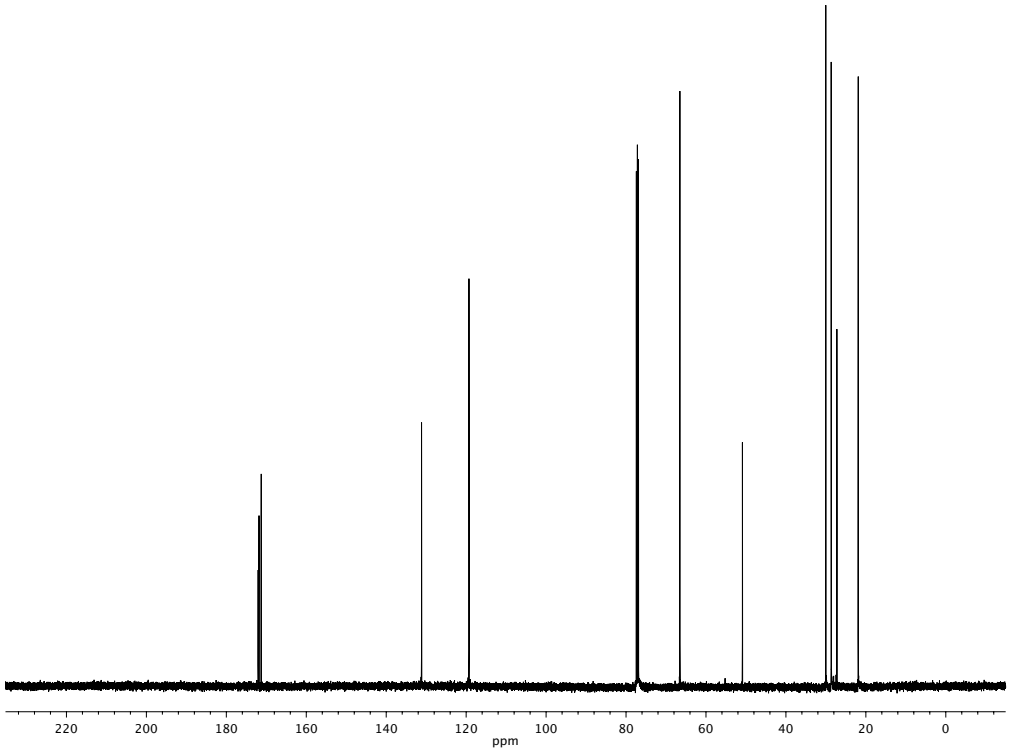


Figure SI-33C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **6c**.

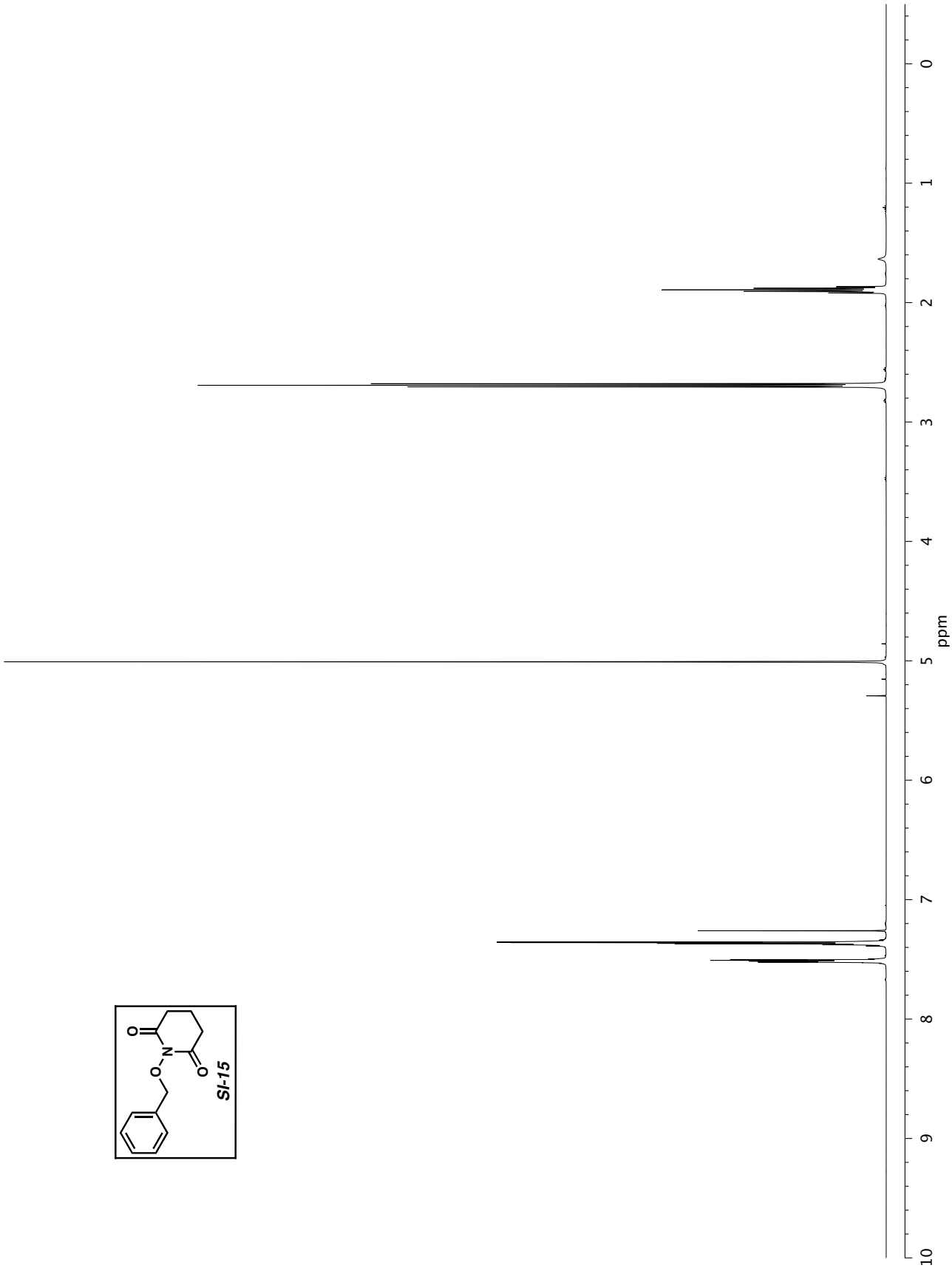


Figure SI-34A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-15**.

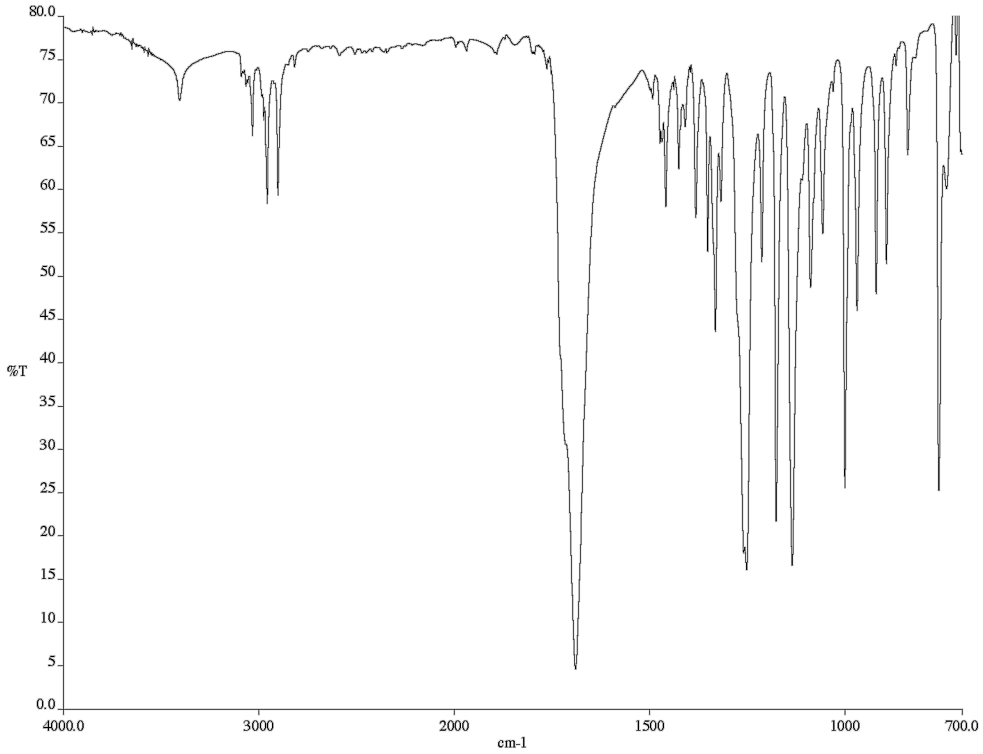


Figure SI-34B. Infrared spectrum (thin film/NaCl) of compound **SI-15**.

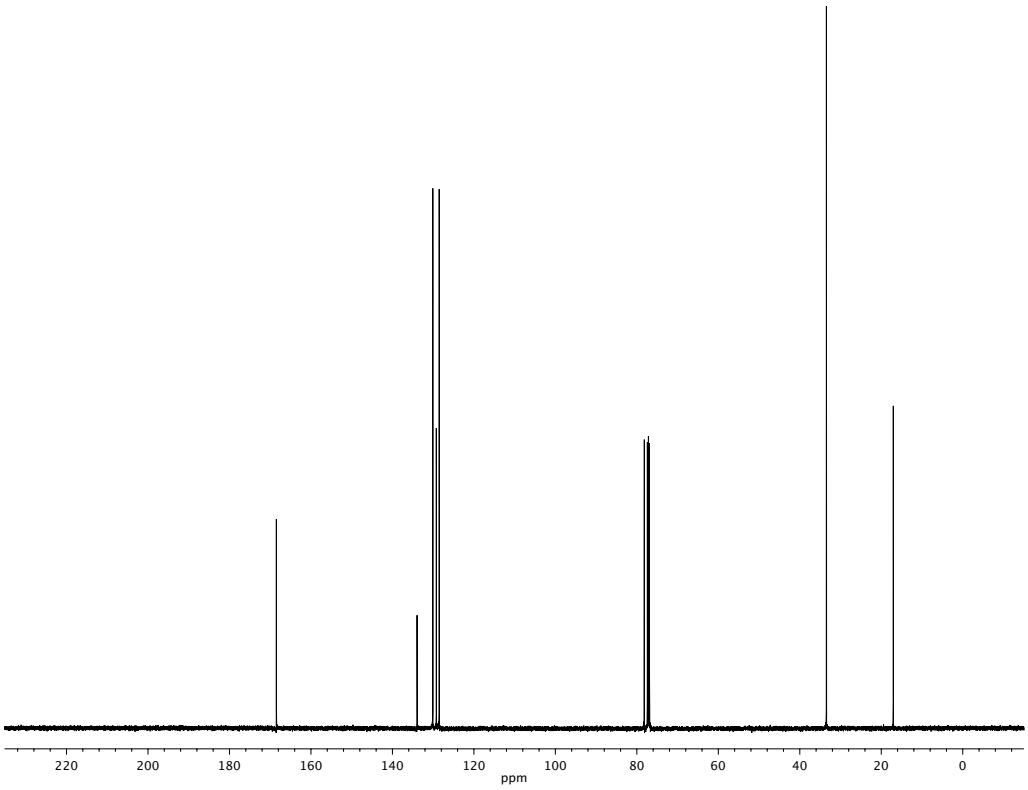


Figure SI-34C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-15**.

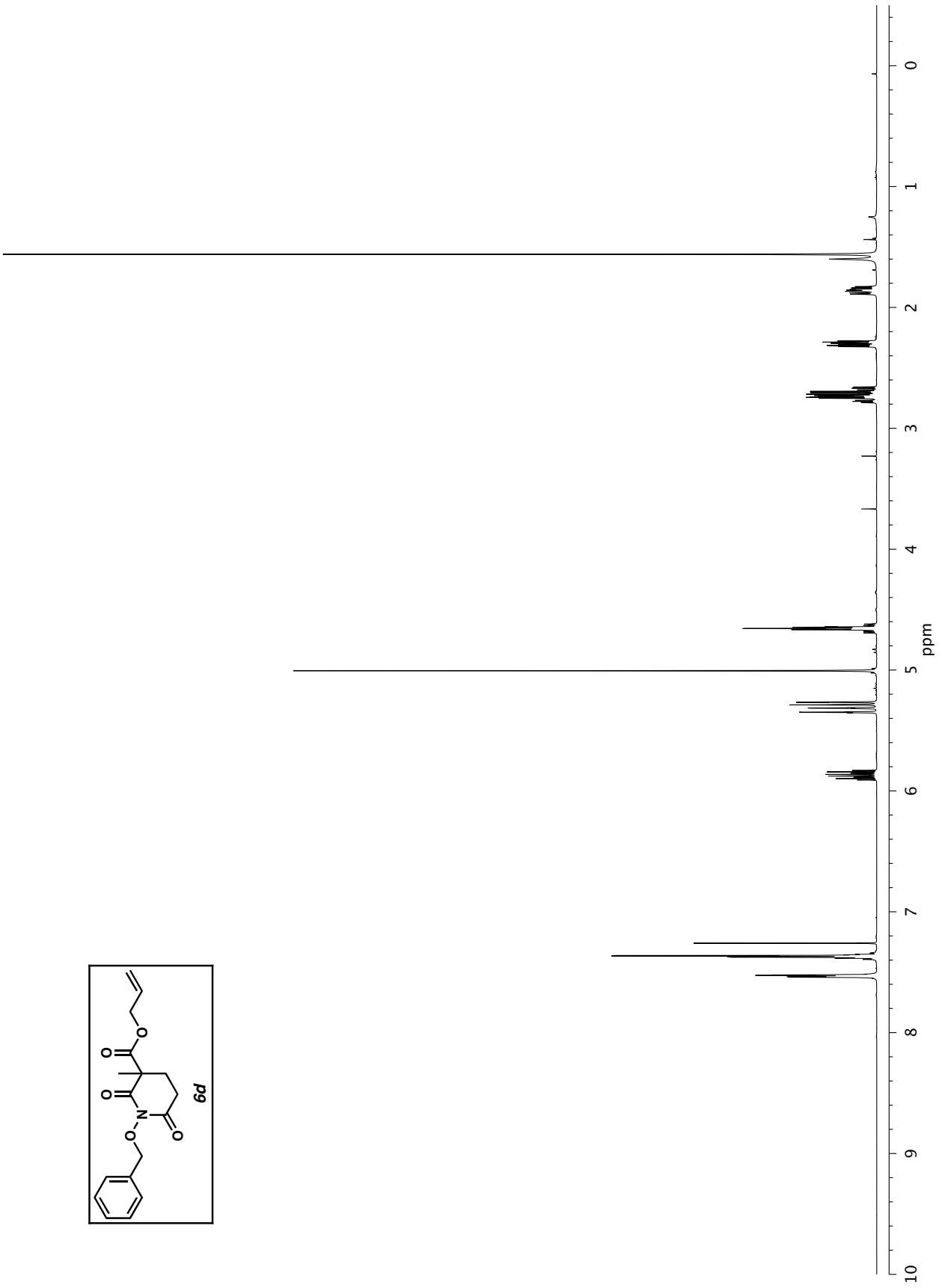


Figure SI-354. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **6d**.

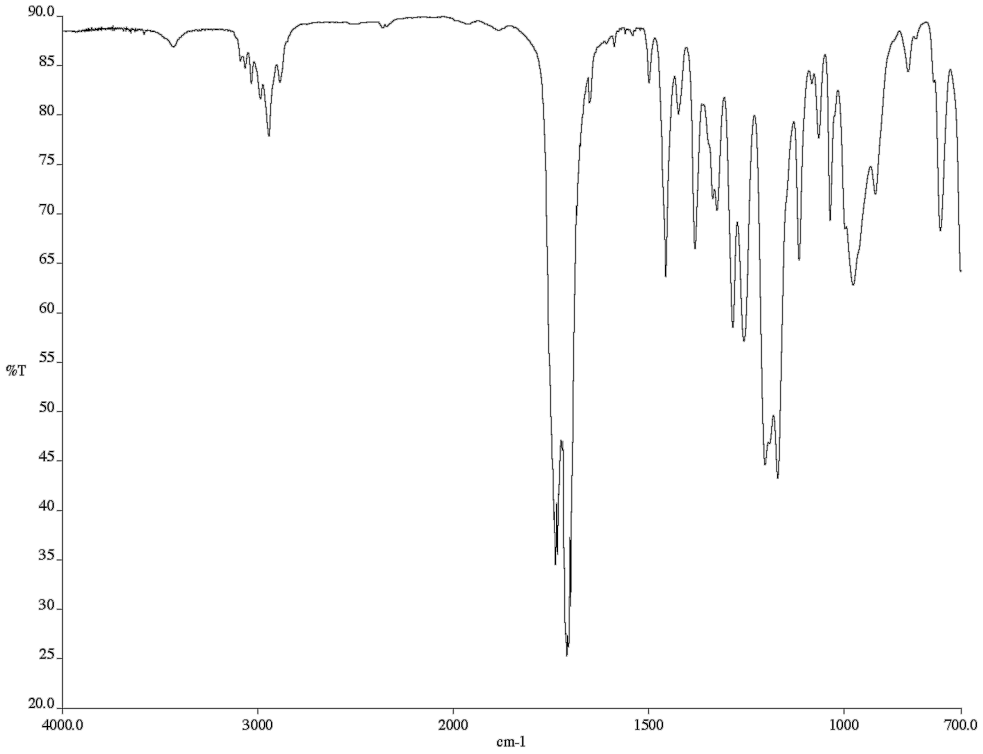


Figure SI-35B. Infrared spectrum (thin film/NaCl) of compound **6d**.

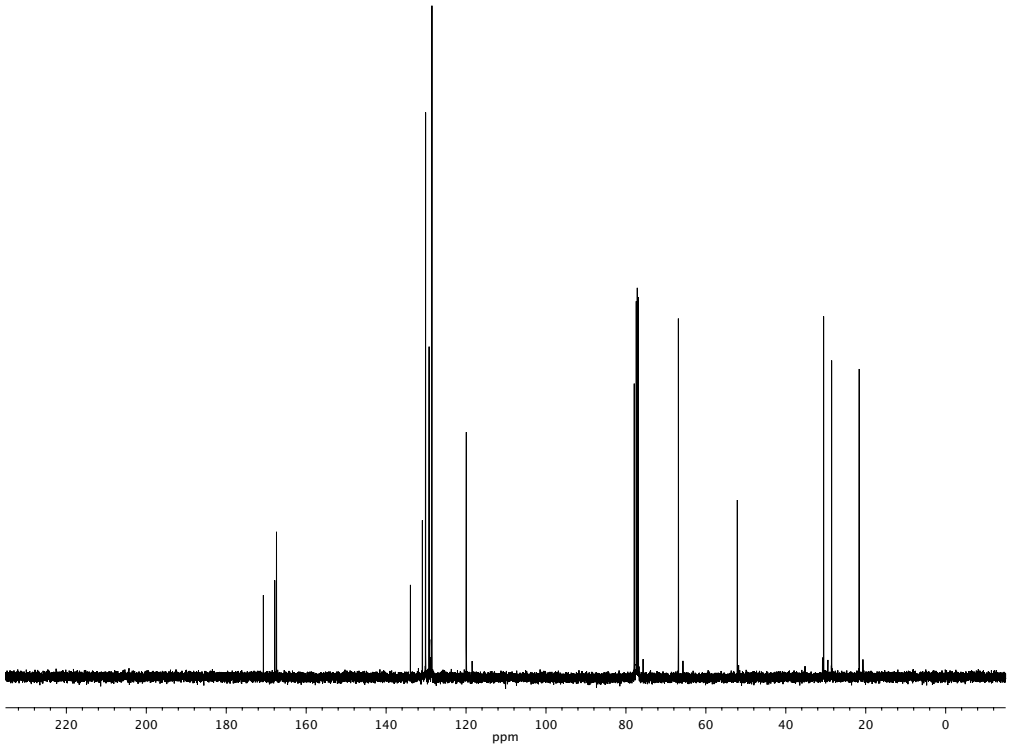


Figure SI-35C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **6d**.

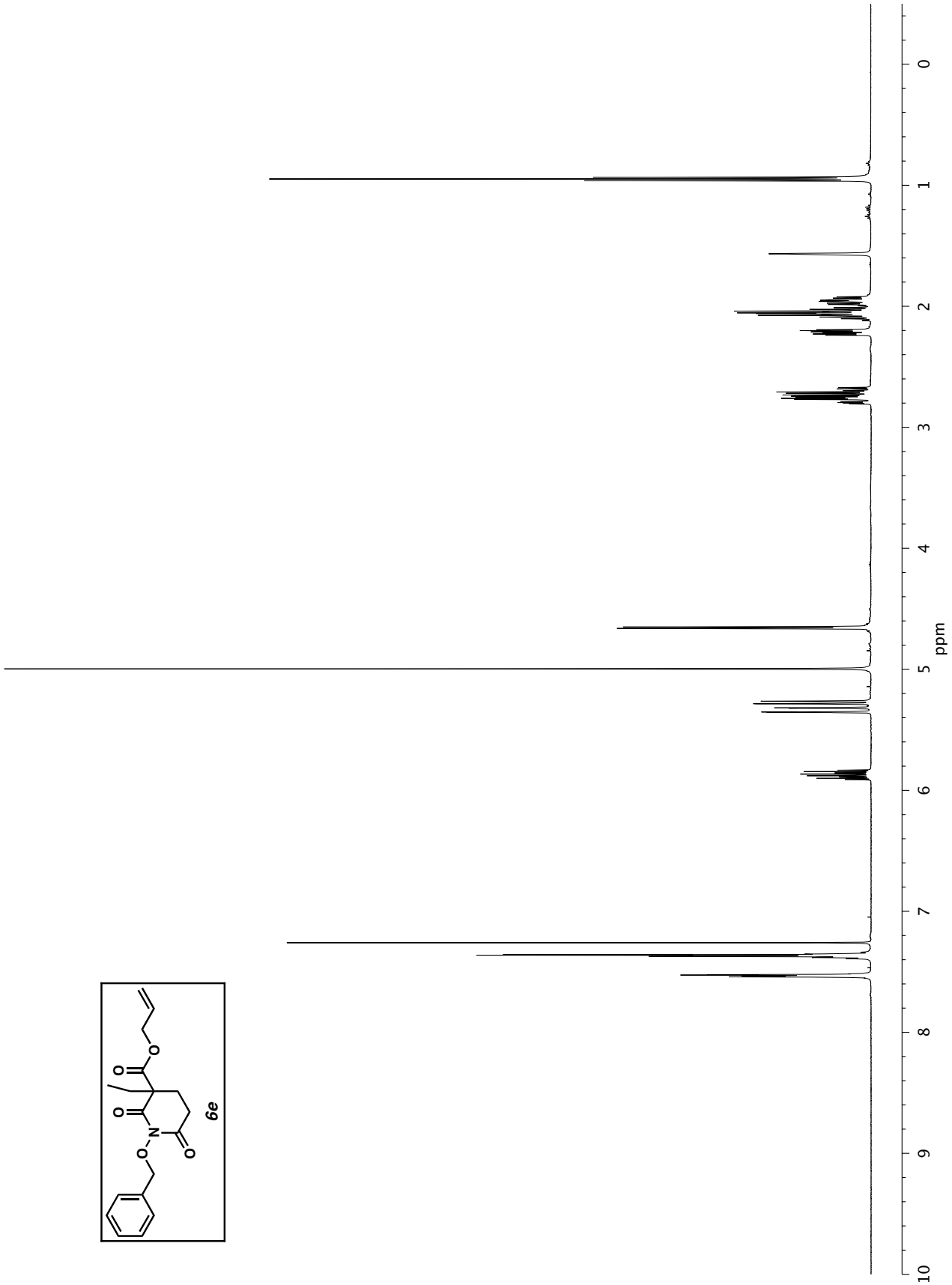


Figure SI-364. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **6e**.

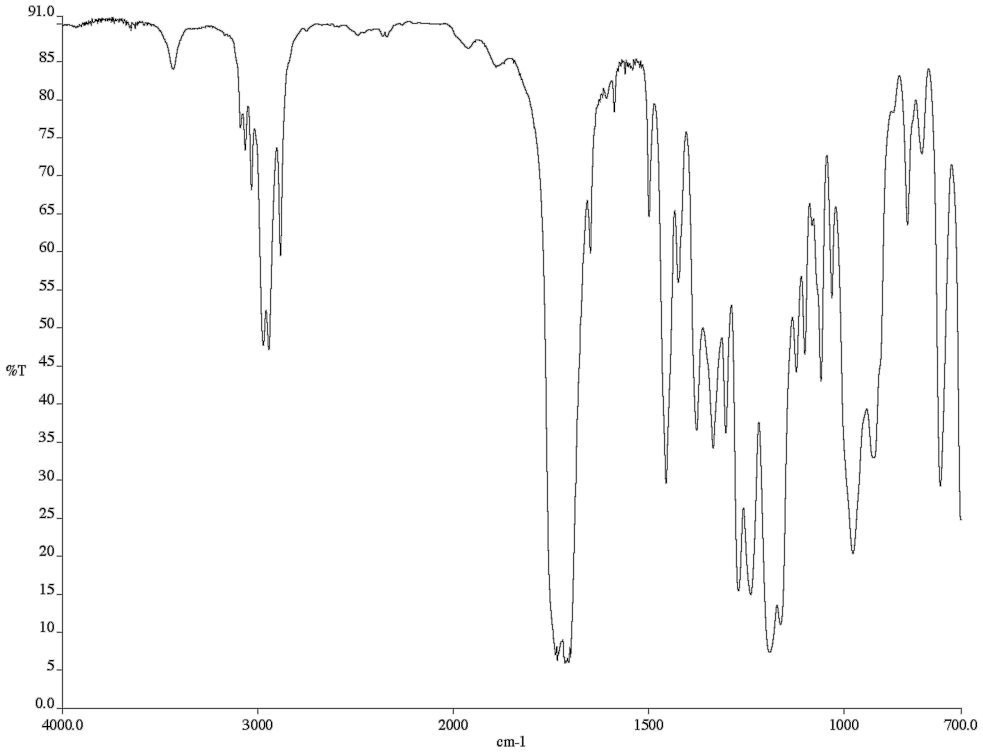


Figure SI-36B. Infrared spectrum (thin film/NaCl) of compound **6e**.

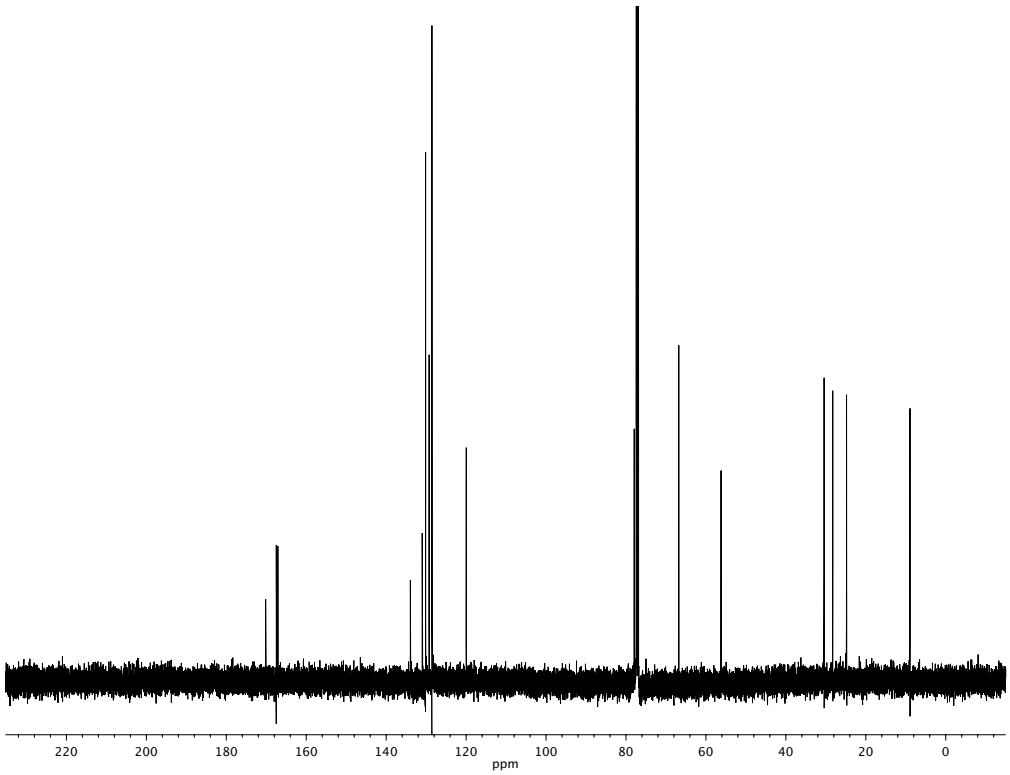


Figure SI-36C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **6e**.

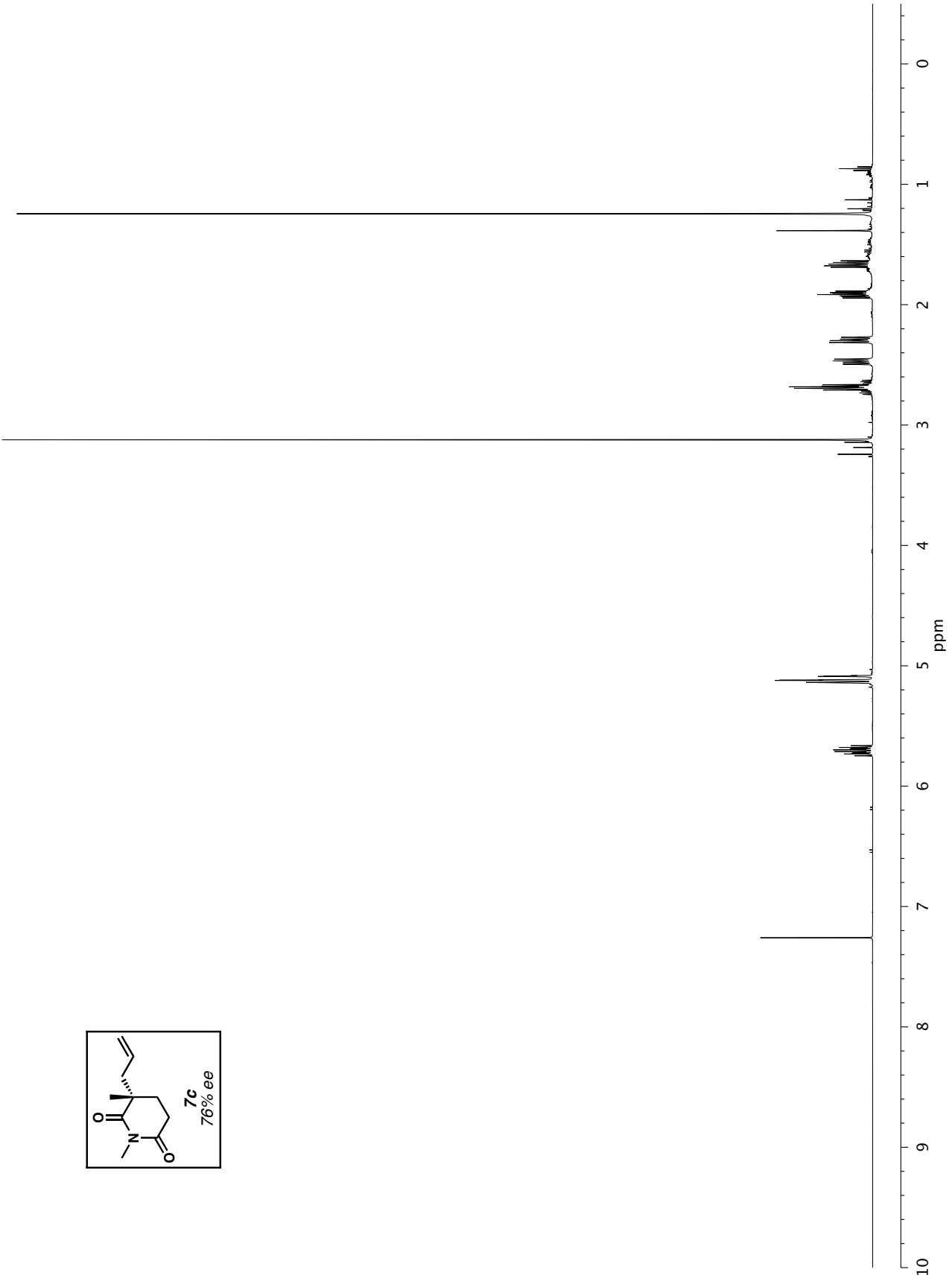


Figure SI-37A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **7c**.

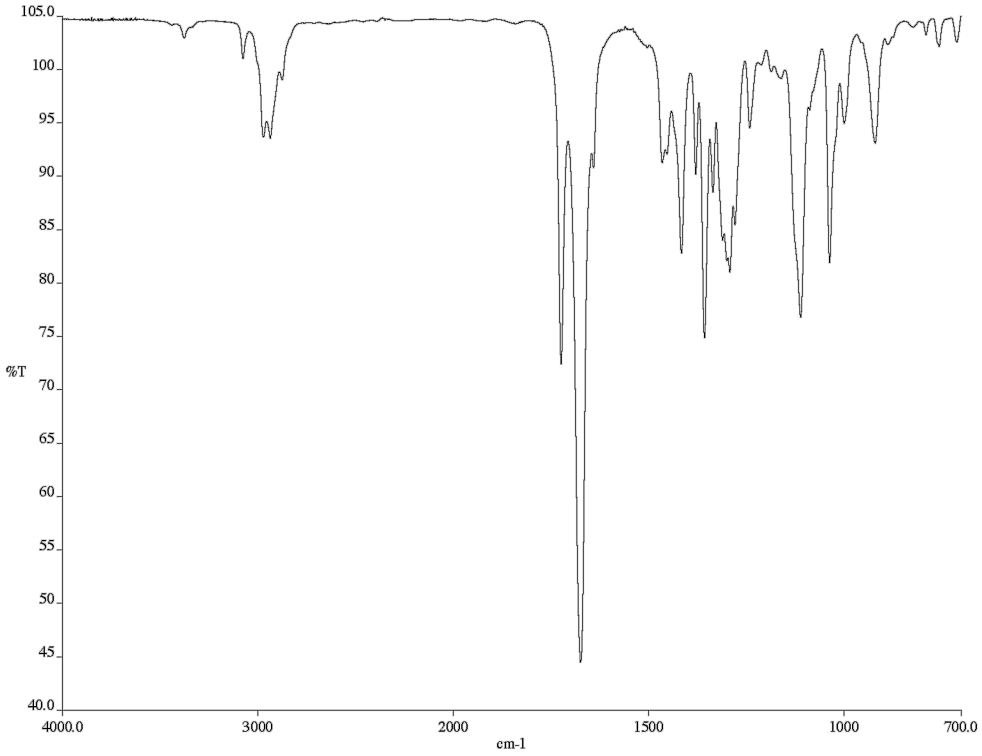


Figure SI-37B. Infrared spectrum (thin film/NaCl) of compound **7c**.

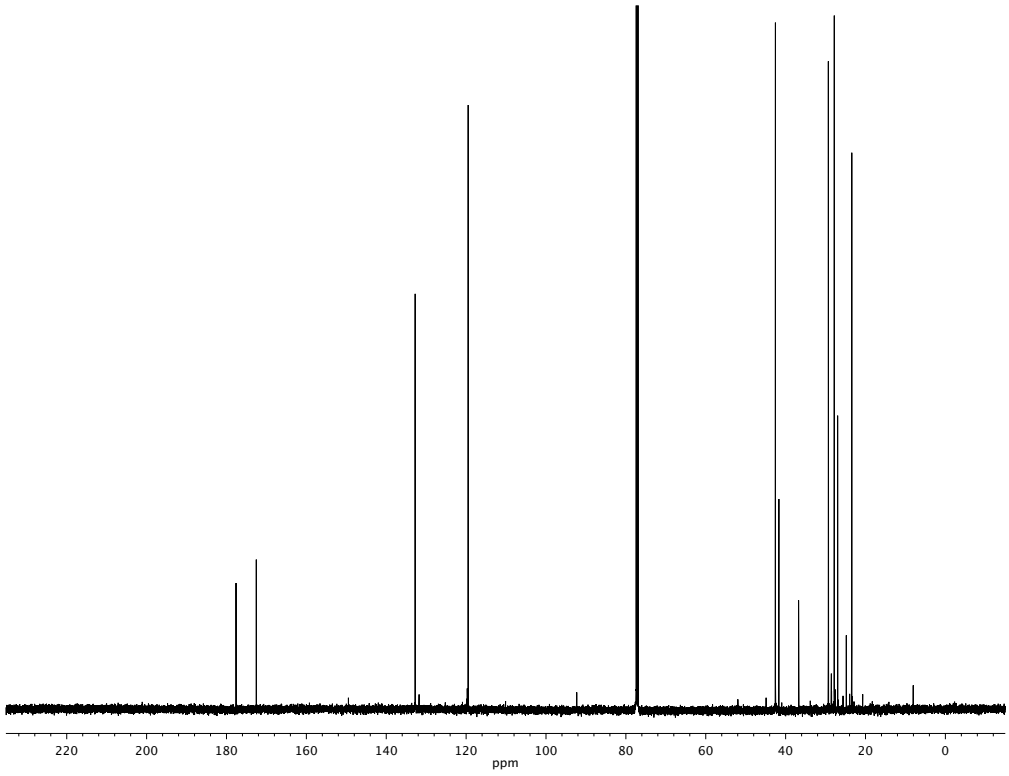
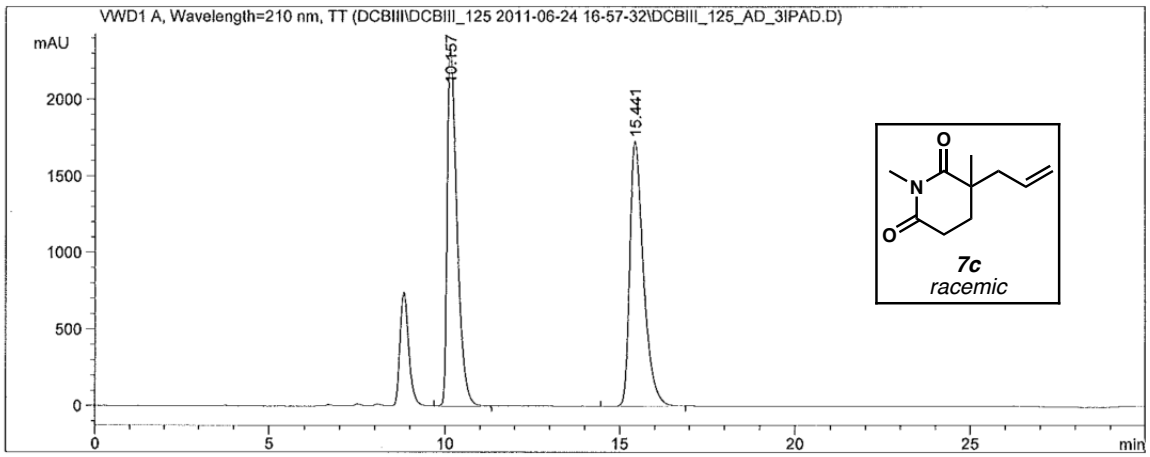


Figure SI-37C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **7c**.

```
Data File C:\CHEM32\2\DATA\DCBIII\DCBIII_125 2011-06-24 16-57-32\DCBIII_125_AD_3IPAD.D
Sample Name: DCBIII_125
    ======================================================================
    Acq. Operator   : DCB                              Seq. Line :  82
    Acq. Instrument : HPLC 2                          Location : Vial 61
    Injection Date  : 6/25/2011 4:25:18 PM                Inj :   1
                                                     Inj Volume : 5.0 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 2.0 µl
    Acq. Method     : C:\CHEM32\2\DATA\DCBIII\DCBIII_125 2011-06-24 16-57-32\3IPA30_210.M
    Last changed    : 5/25/2010 1:18:17 PM by AYH
    Analysis Method : C:\CHEM32\2\METHODS\2_5IPA30_254.M
    Last changed    : 6/16/2011 8:10:28 PM by MBL
    Method Info     : 2_5% IPA    30 min   254 nm   1 mL/min

    ======================================================================
```




```
    ======================================================================
                            Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier:                   :      1.0000
    Dilution:                     :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=210 nm, TT

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|-----|-------|----------|----------|--------|
       1  10.157 VV    0.3006 4.59450e4  2315.91797  49.3261
       2  15.441 VB    0.4091 4.72005e4  1727.09167  50.6739

    Totals :                  9.31455e4  4043.00964


    ======================================================================
                            Summed Peaks Report
    ======================================================================

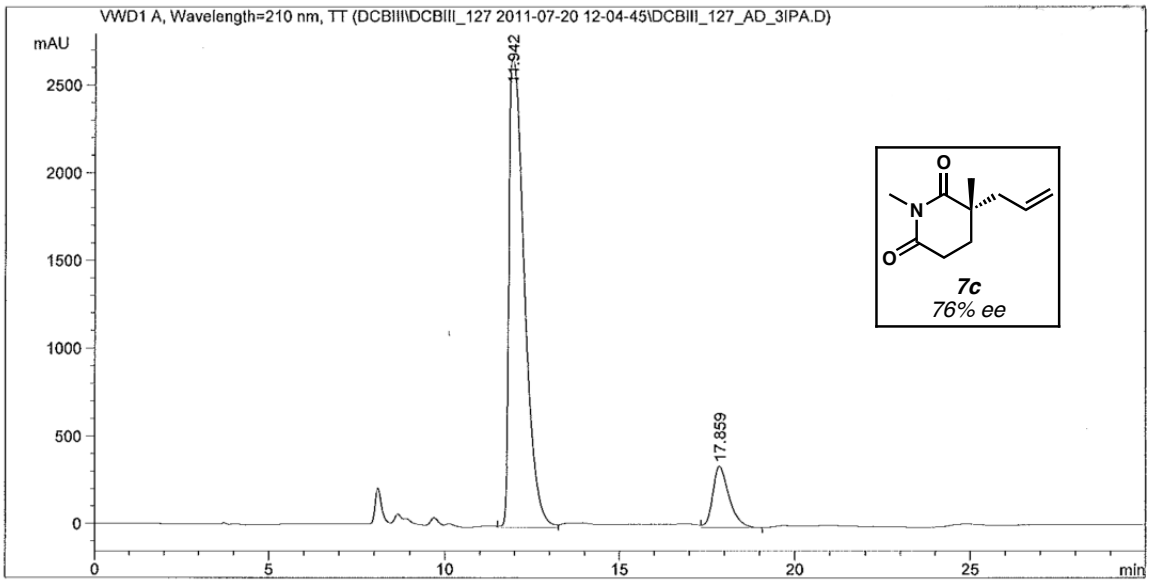
    Signal 1: VWD1 A, Wavelength=210 nm, TT

HPLC 2 6/26/2011 8:42:30 PM MBL                              Page   1 of 2
```

Figure SI-37D. Chiral HPLC data of racemic compound **7c**.

```
Data File C:\CHEM32\2\DATA\DCBIII\DCBIII_127 2011-07-20 12-04-45\DCBIII_127_AD_3IPA.D
Sample Name: DCBIII_127

    ======================================================================
    Acq. Operator   : DCB                          Seq. Line :   7
    Acq. Instrument : HPLC 2                        Location : Vial 62
    Injection Date  : 7/20/2011 1:19:33 PM             Inj :   1
                                                   Inj Volume : 5.0 µl
    Acq. Method     : C:\CHEM32\2\DATA\DCBIII\DCBIII_127 2011-07-20 12-04-45\3IPA30 210.M
    Last changed    : 5/25/2010 1:18:17 PM by AYH
    Analysis Method : C:\CHEM32\2\METHODS\POS2.M
    Last changed    : 7/20/2011 1:15:46 PM by JK
                      (modified after loading)
    Method Info     : POSITION #2 METHOD : Valve to Position # 2 (Column # 1).
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier:                   :      1.0000
    Dilution:                     :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=210 nm, TT

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  11.942 VV    0.4660 8.26292e4  2679.66138  87.9644
       2  17.859 VV    0.4847 1.13056e4   349.93817  12.0356

    Totals :                  9.39348e4  3029.59955

    ======================================================================

HPLC 2 7/20/2011 2:04:32 PM JK                                Page   1 of 1
```

Figure SI-37E. Chiral HPLC data of enantioenriched compound **7c**.

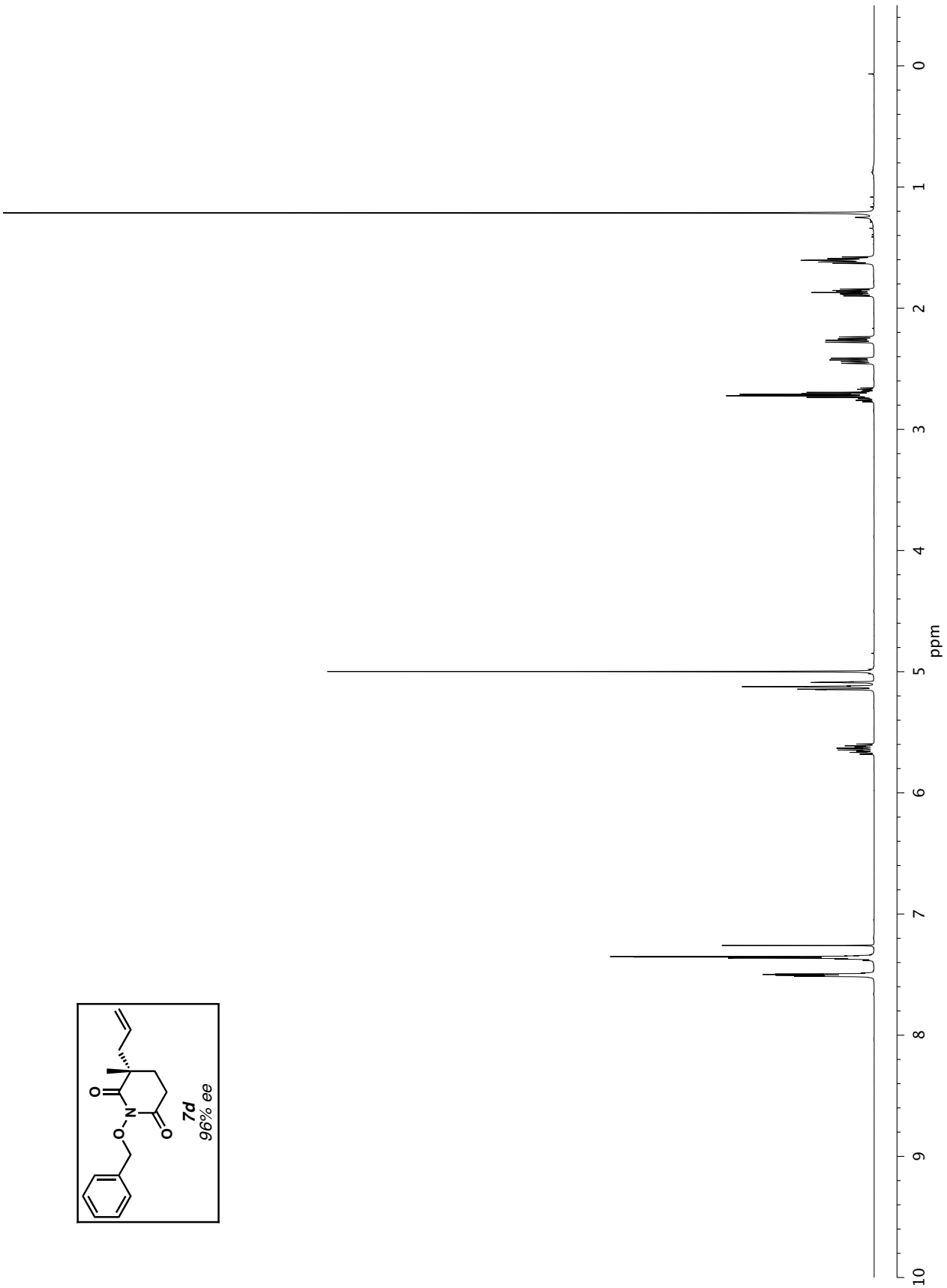


Figure SI-384. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **7d**.

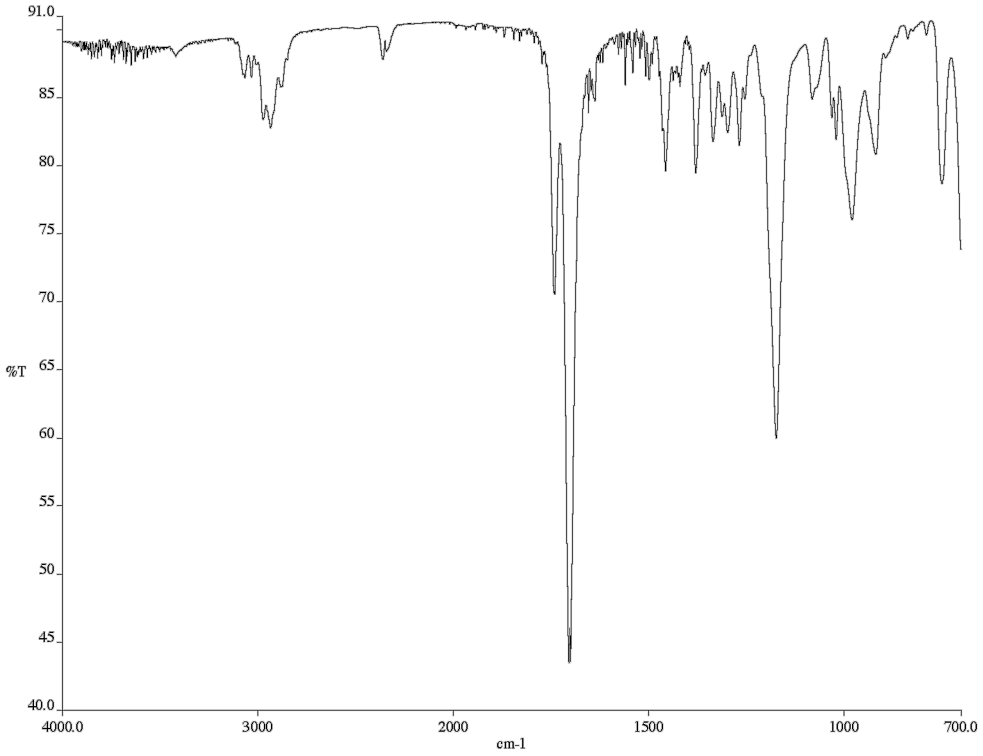


Figure SI-38B. Infrared spectrum (thin film/NaCl) of compound **7d**.

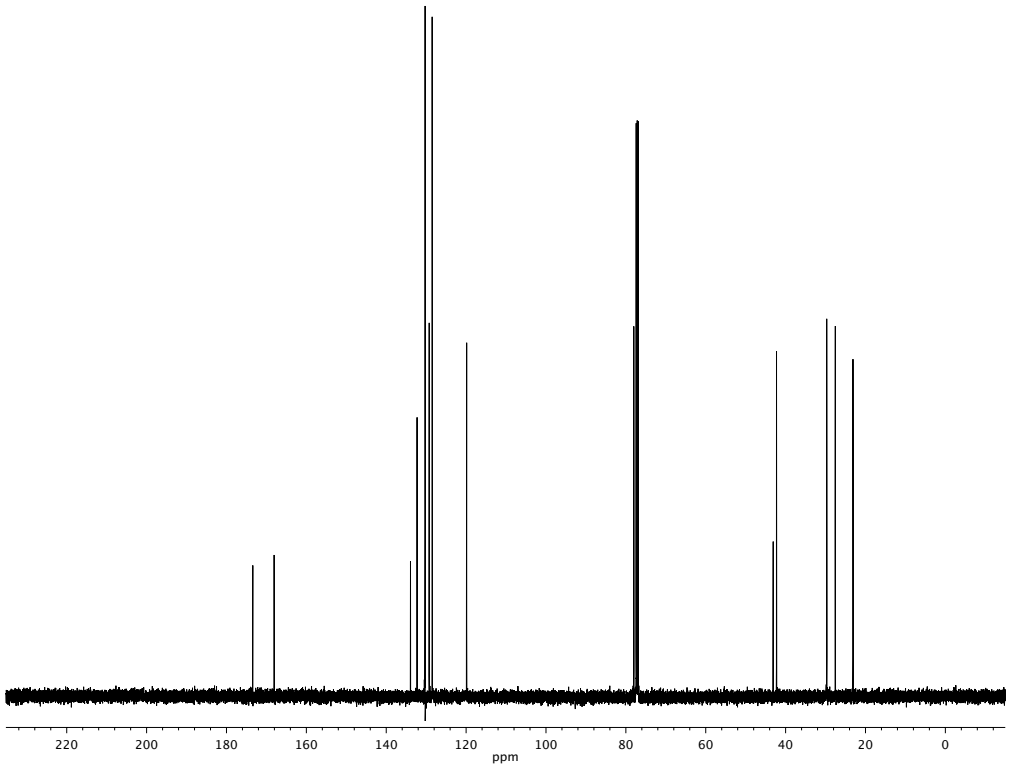
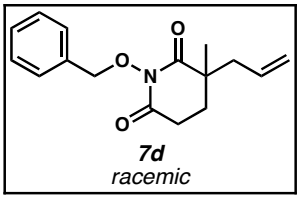


Figure SI-38C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **7d**.




```
Data File C:\CHEM32\1\DATA\JK\AHC 2012-01-12 16-17-40\JK-V-83-R.D
Sample Name: JK-V-83-r

==========================================================================
Acq. Operator   : JK                              Seq. Line :   3
Acq. Instrument : Instrument 1                    Location : P1-F-06
Injection Date  : 1/12/2012 4:26:00 PM                Inj :   1
                                                  Inj Volume : 5 µl
Acq. Method     : C:\Chem32\1\DATA\JK\AHC 2012-01-12 16-17-40\S1C4 12MIN 5.M
Last changed    : 5/19/2011 8:57:55 PM by DCB
Analysis Method : C:\CHEM32\1\DATA\JK\AHC 2012-01-12 16-17-40\JK-V-83-R.D\DA.M (S1C4 12MIN
                  5.M)
Last changed    : 5/19/2011 8:57:55 PM by DCB
Method Info     : S1C4 12min 5.M: 5% MeOH, OJ-H 3 mL/min, 12 min
```

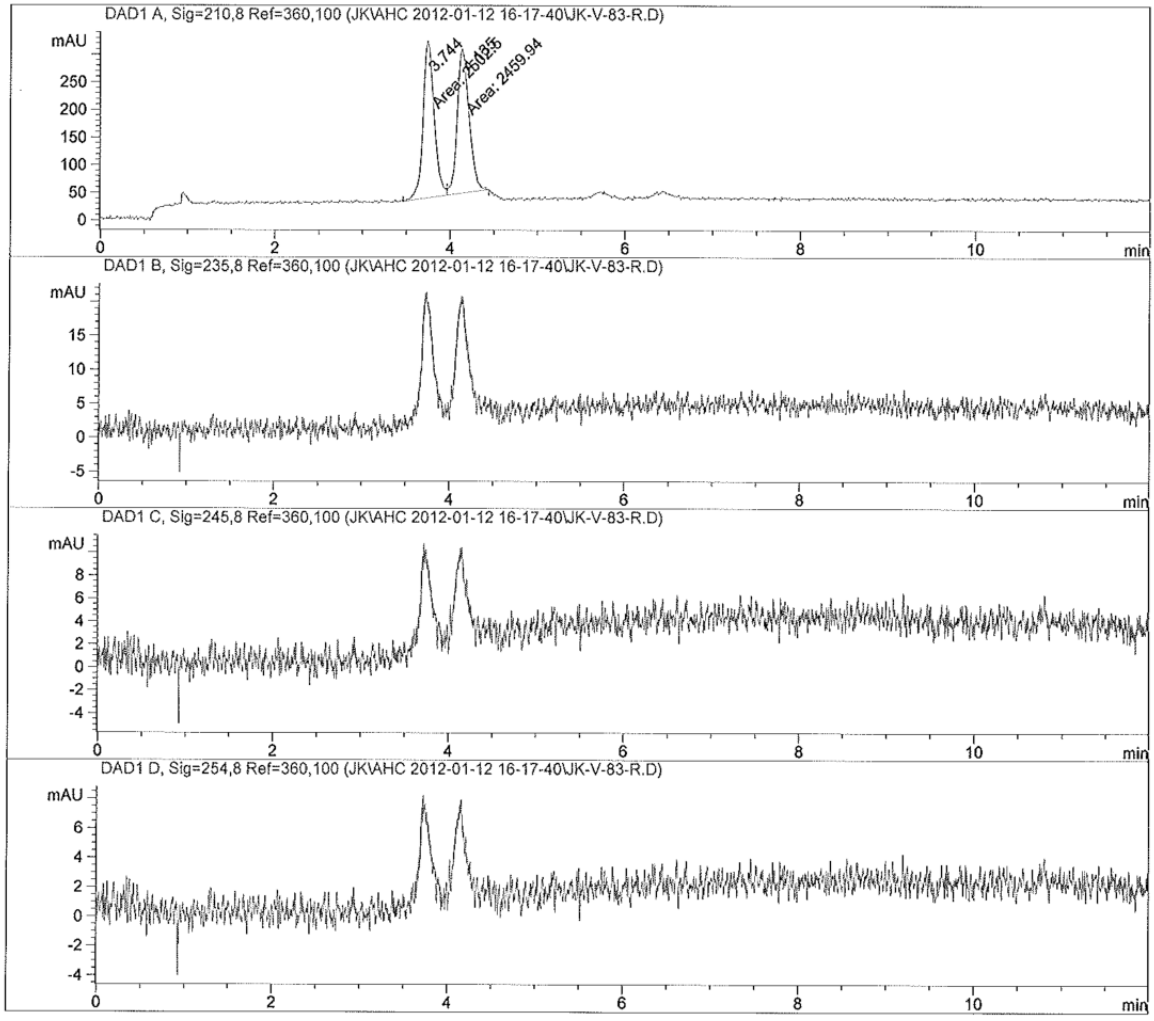
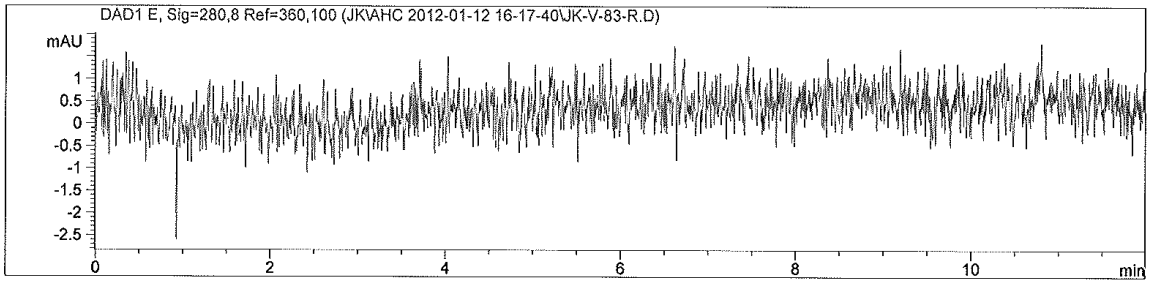


Figure SI-38D. Chiral SFC data of racemic compound **7d**.

Data File C:\CHEM32\1\DATA\JK\AHC 2012-01-12 16-17-40\JK-V-83-R.D
Sample Name: JK-V-83-r



==========

Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.744	MF	0.1469	2502.50342	283.92230	50.4289
2	4.135	FM	0.1584	2459.94043	258.85748	49.5711
Totals :				4962.44385	542.77979	

Signal 2: DAD1 B, Sig=235,8 Ref=360,100

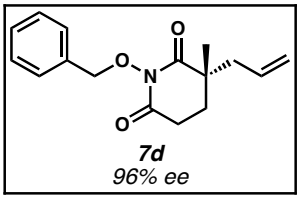
Signal 3: DAD1 C, Sig=245,8 Ref=360,100

Signal 4: DAD1 D, Sig=254,8 Ref=360,100

Signal 5: DAD1 E, Sig=280,8 Ref=360,100

==========

*** End of Report ***




```
Data File C:\CHEM32\1\DATA\JK\AHC 2012-01-12 16-17-40\JK-V-83-C.D
Sample Name: JK-V-83-c

==========================================================================
Acq. Operator   : JK                              Seq. Line :   5
Acq. Instrument : Instrument 1                    Location : P1-F-07
Injection Date  : 1/12/2012 4:42:28 PM                Inj :   1
                                                Inj Volume : 5 µl
Acq. Method     : C:\Chem32\1\DATA\JK\AHC 2012-01-12 16-17-40\S1C4 12MIN 5.M
Last changed    : 5/19/2011 8:57:55 PM by DCB
Analysis Method : C:\CHEM32\1\DATA\JK\AHC 2012-01-12 16-17-40\JK-V-83-C.D\DA.M (S1C4 12MIN
                  5.M)
Last changed    : 1/12/2012 4:59:04 PM by AHC
                  (modified after loading)
Method Info     : S1C4 12min 5.M: 5% MeOH, OJ-H 3 mL/min, 12 min
```

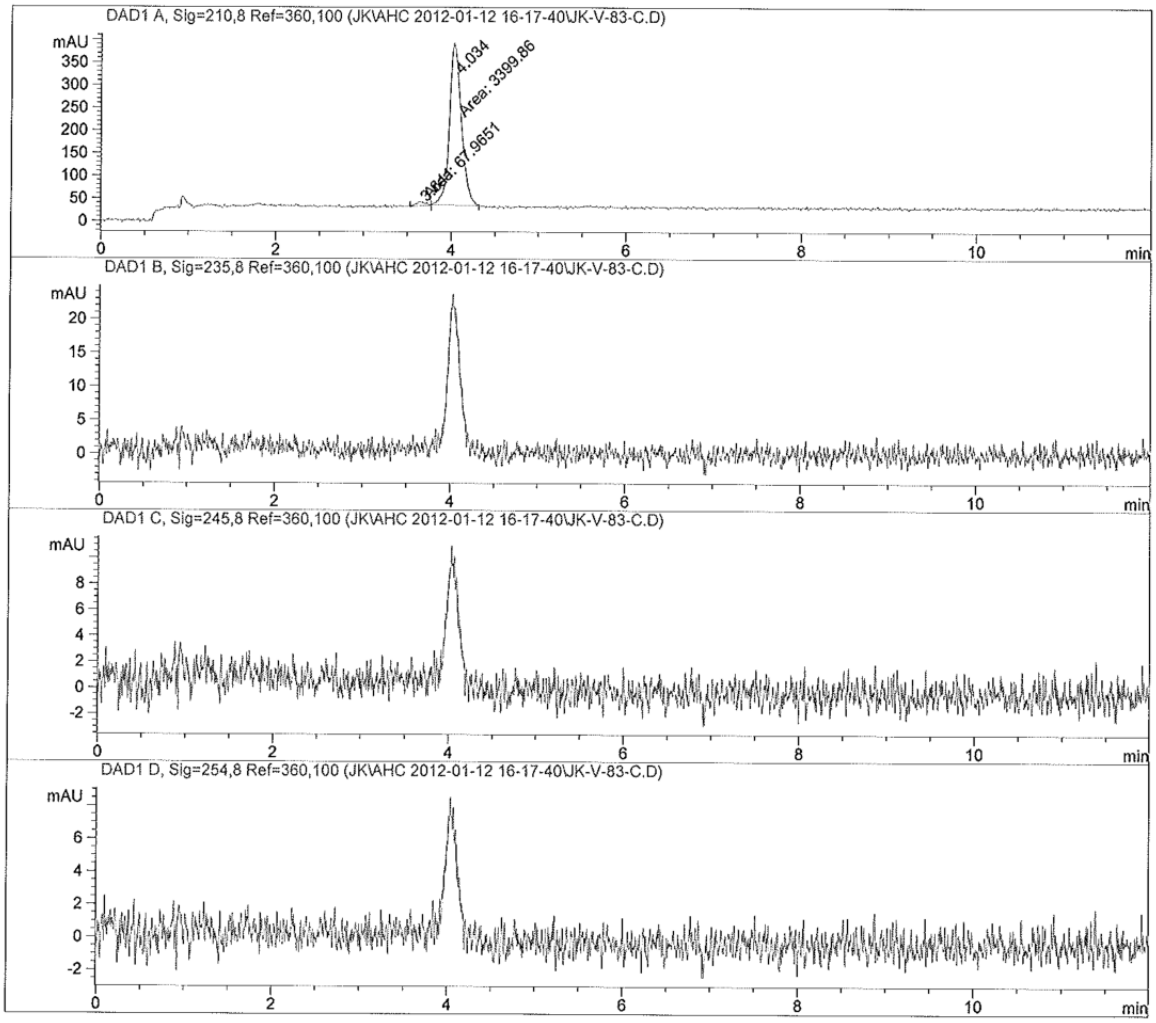
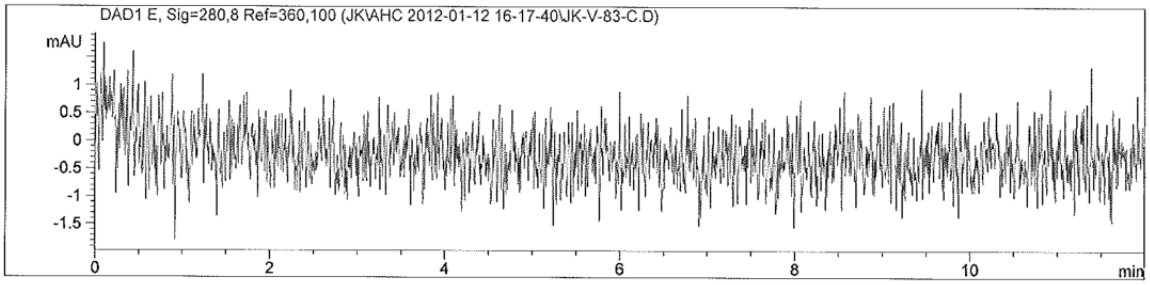


Figure SI-38E. Chiral SFC data of enantioenriched compound **7d**.

Data File C:\CHEM32\1\DATA\JK\AHC 2012-01-12 16-17-40\JK-V-83-C.D
Sample Name: JK-V-83-c



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.641	MM	0.1183	67.96515	9.57130	1.9599
2	4.034	MM	0.1586	3399.85913	357.17441	98.0401
Totals :				3467.82428	366.74571	

Signal 2: DAD1 B, Sig=235,8 Ref=360,100

Signal 3: DAD1 C, Sig=245,8 Ref=360,100

Signal 4: DAD1 D, Sig=254,8 Ref=360,100

Signal 5: DAD1 E, Sig=280,8 Ref=360,100

*** End of Report ***

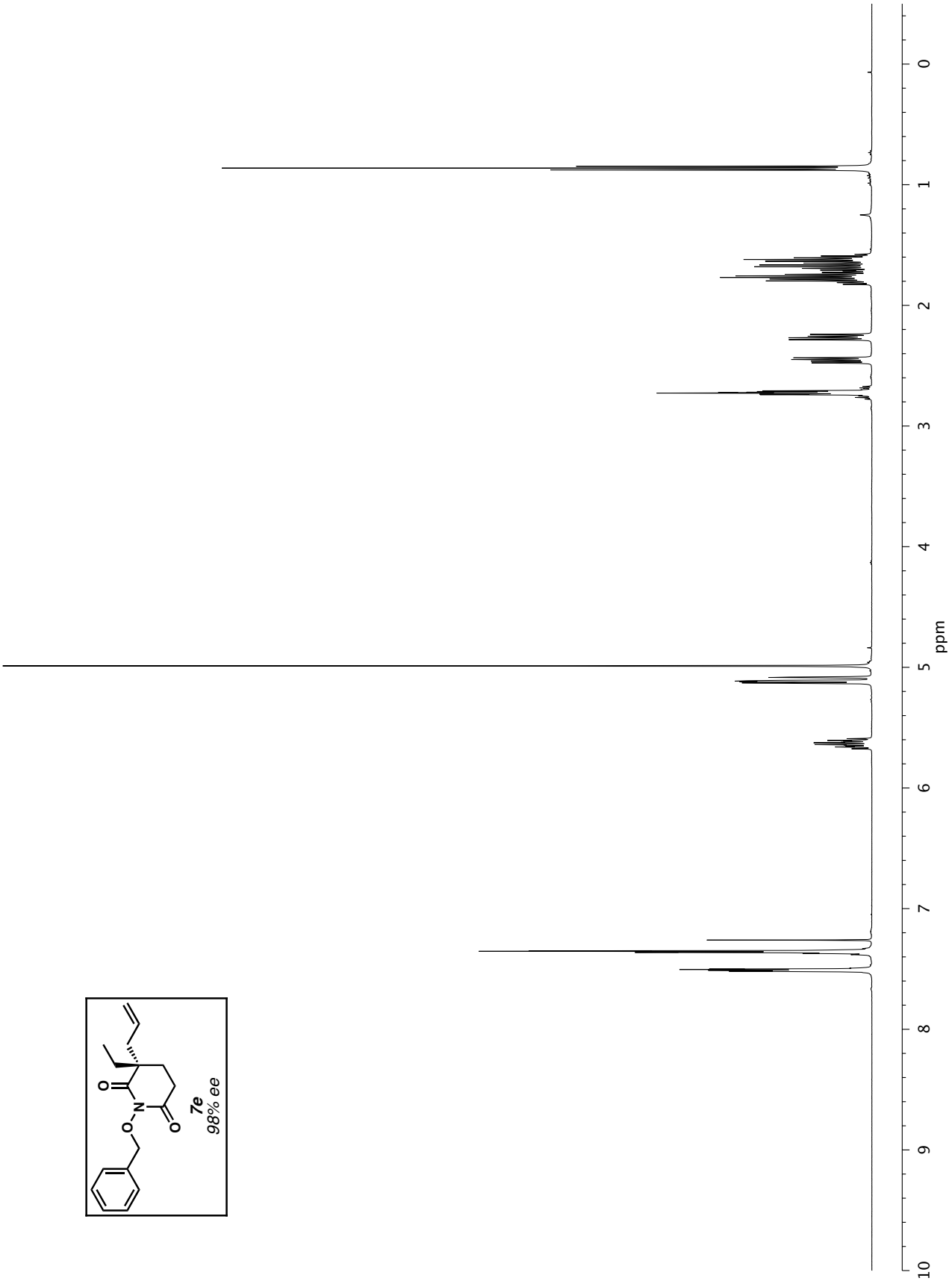


Figure SI-394. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **7e**.

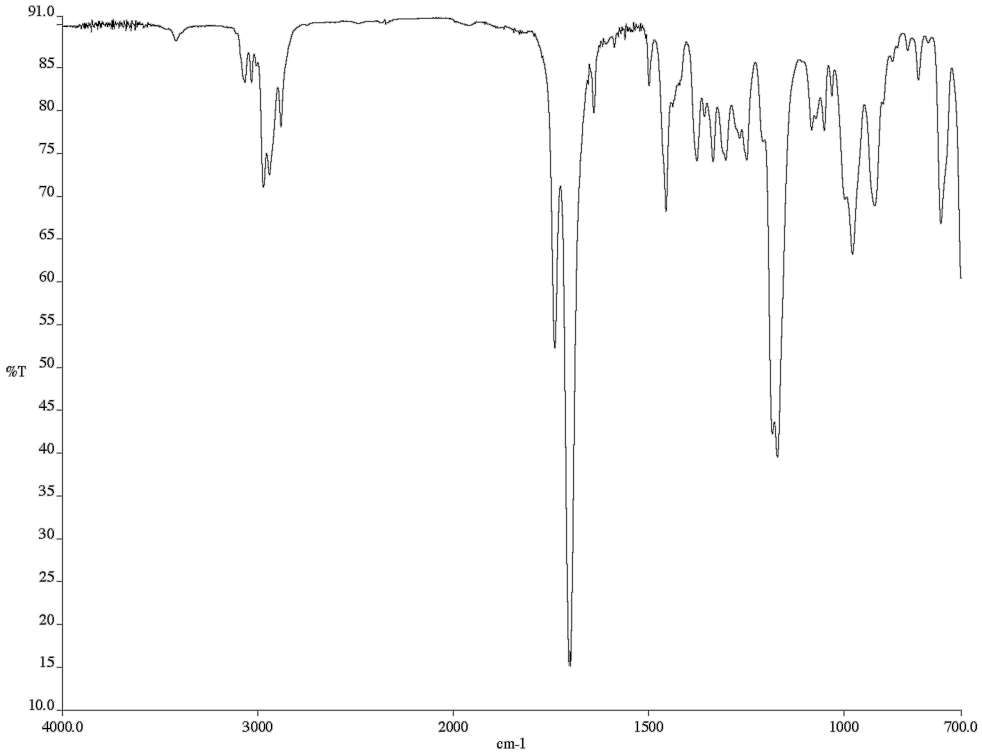


Figure SI-39B. Infrared spectrum (thin film/NaCl) of compound **7e**.

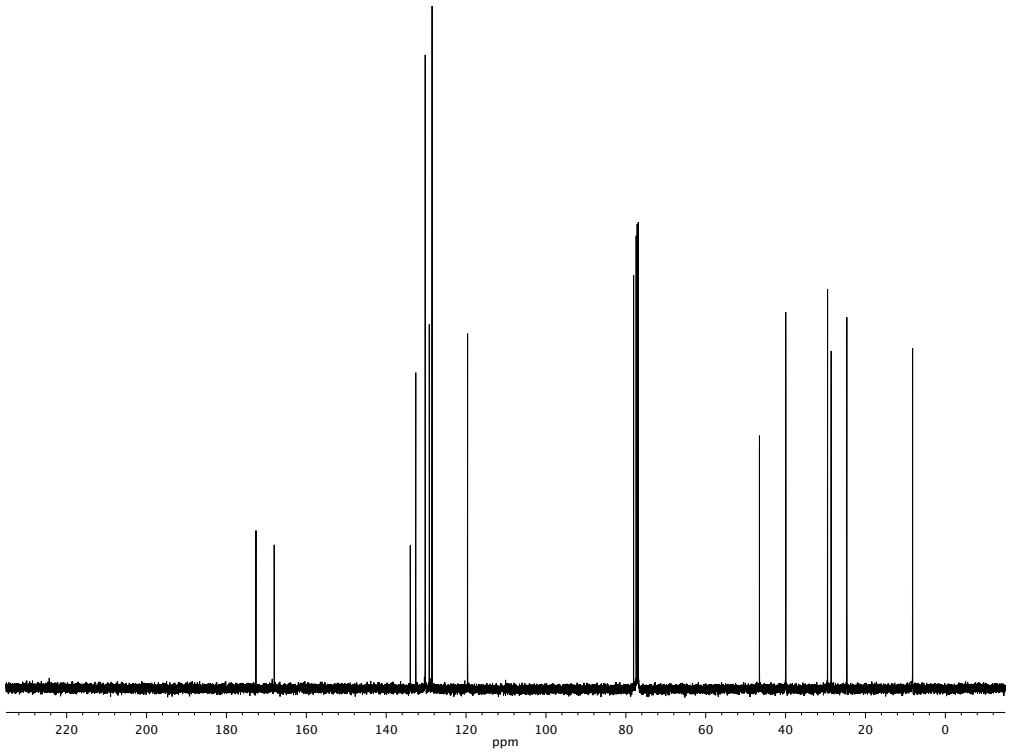
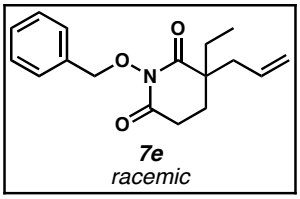


Figure SI-39C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **7e**.




```
Data File C:\CHEM32\1\DATA\JK\ADL 2012-01-13 17-32-43\JK-V-93-RACEMIC.D
Sample Name: JK-V-93-racemic

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Acq. Instrument : Instrument 1                     Location : P1-B-01
Injection Date  : 1/13/2012 5:36:44 PM                 Inj :   1
                                                  Inj Volume : 5 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 10 µl
Acq. Method     : C:\Chem32\1\DATA\JK\ADL 2012-01-13 17-32-43\S1C6 20MIN1.M
Last changed    : 1/13/2012 4:24:23 PM by JK
Analysis Method : C:\CHEM32\1\DATA\JK\ADL 2012-01-13 17-32-43\JK-V-93-RACEMIC.D\DA.M (S1C6
                  20MIN1.M)
Last changed    : 1/15/2012 10:45:33 AM by JK
Method Info     : S1C6 20min1.M: 1% MeOH, OB-H 2.5 mL/min, 20 min
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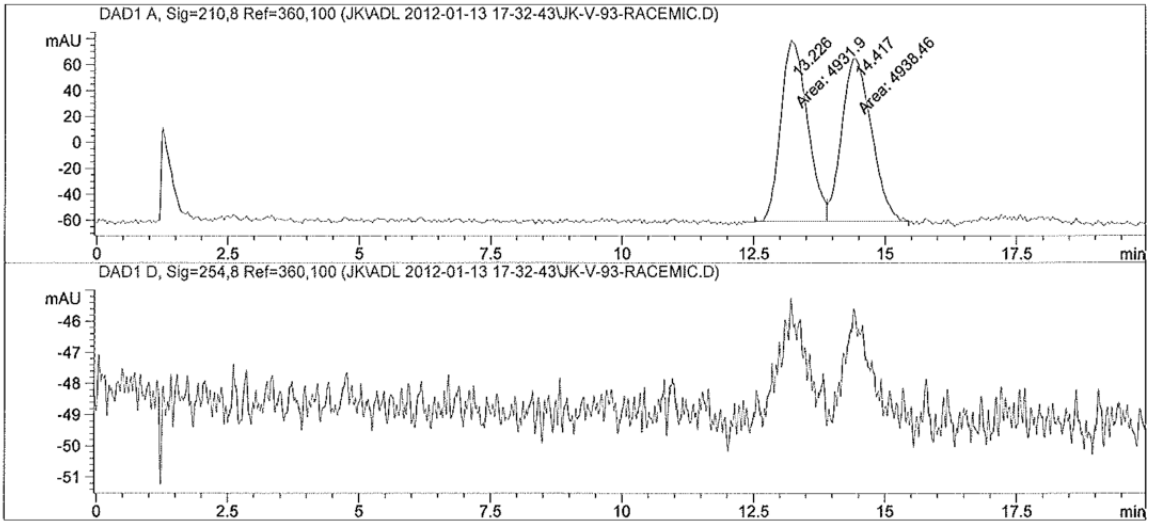


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=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|--------|----|-------|----------|----------|--------|
   1  13.226 MF    0.5903 4931.90381  139.24123  49.9668
   2  14.417 FM    0.6560 4938.46289  125.45995  50.0332

Totals :                  9870.36670  264.70118


Instrument 1 1/15/2012 10:46:47 AM JK                    Page   1 of 2
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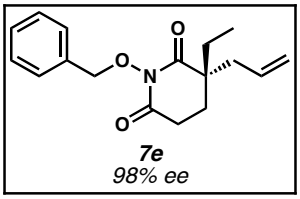
Figure SI-39D. Chiral SFC data of racemic compound **7e**.

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Data File C:\CHEM32\1\DATA\JK\ADL 2012-01-13 17-32-43\JK-V-93-CHIRAL.D
Sample Name: JK-V-93-chiral

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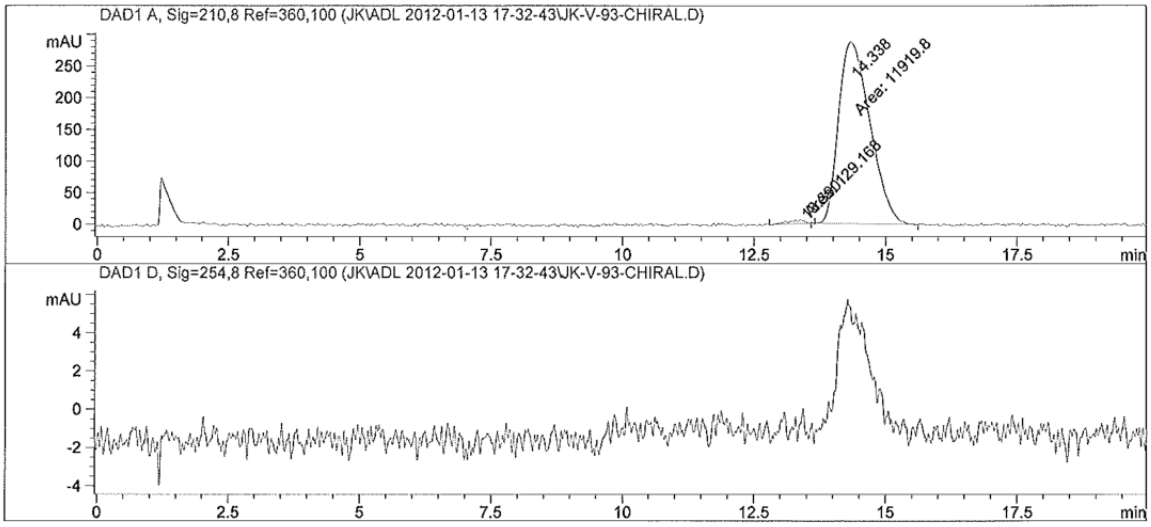
Acq. Operator   : JK                                Seq. Line :   5
Acq. Instrument : Instrument 1                       Location : P1-C-01
Injection Date  : 1/13/2012 6:03:35 PM                   Inj :   1
                                                   Inj Volume : 5 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 10 µl
Acq. Method     : C:\Chem32\1\DATA\JK\ADL 2012-01-13 17-32-43\S1C6 20MIN1.M
Last changed    : 1/13/2012 4:24:23 PM by JK
Analysis Method : C:\CHEM32\1\DATA\JK\ADL 2012-01-13 17-32-43\JK-V-93-CHIRAL.D\DA.M (S1C6
                  20MIN1.M)
Last changed    : 1/15/2012 10:53:04 AM by JK
                  (modified after loading)
Method Info     : S1C6 20min1.M: 1% MeOH, OB-H 2.5 mL/min, 20 min
```

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================================================================================
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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  13.390 MM    0.3785  129.16808    5.68712   1.0720
   2  14.338 MM    0.6926 1.19198e4   286.81857  98.9280

Totals :                  1.20490e4   292.50569


Instrument 1 1/15/2012 10:55:25 AM JK                        Page   1 of 2
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Figure SI-39E. Chiral SFC data of enantioenriched compound **7e**.

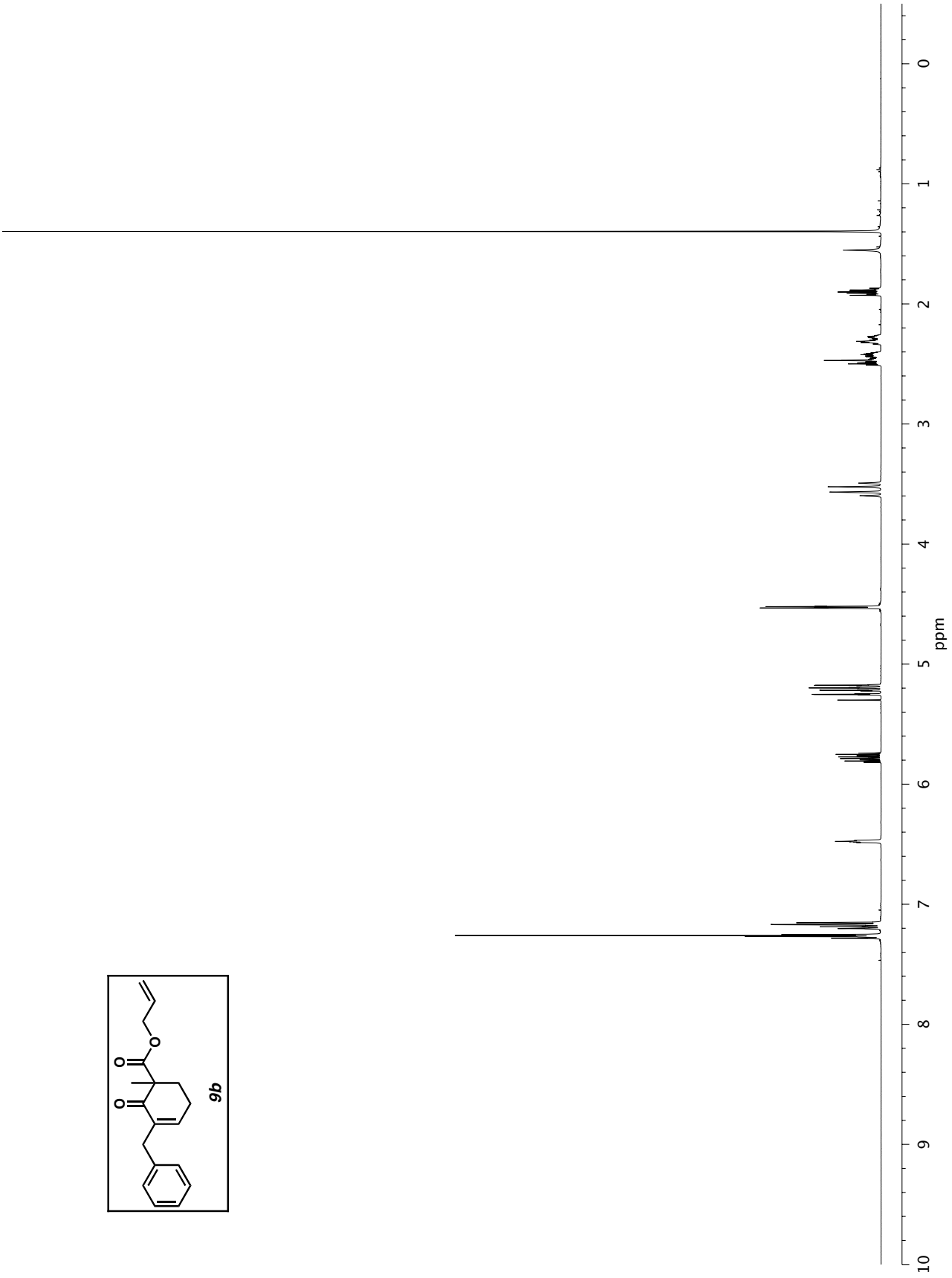


Figure SI-404. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **9b**.

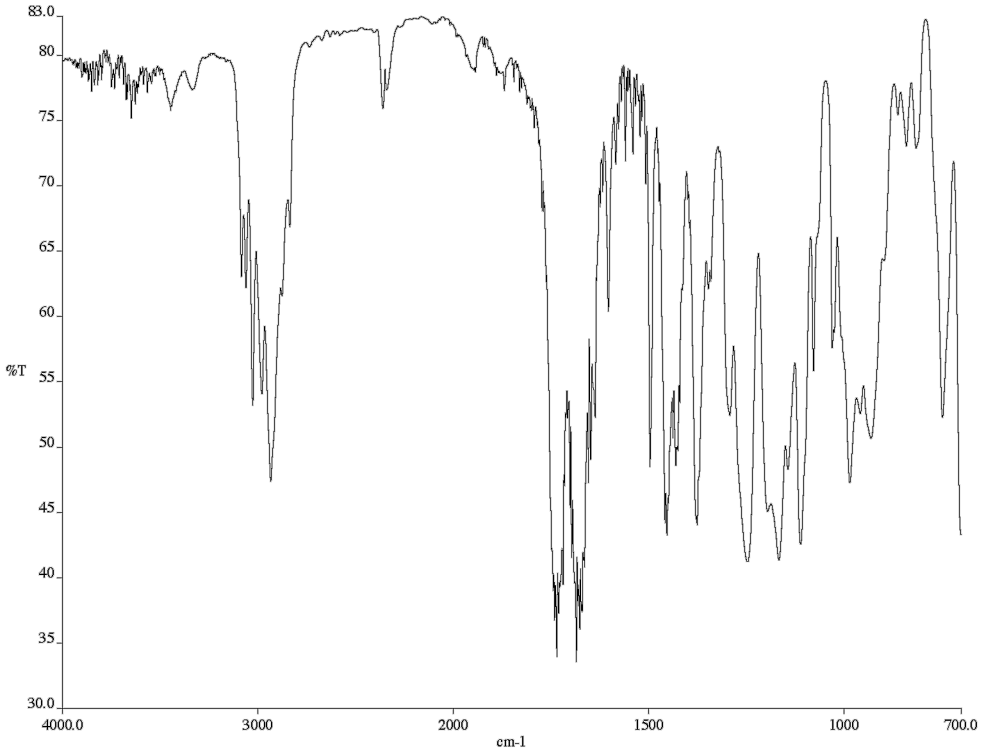


Figure SI-40B. Infrared spectrum (thin film/NaCl) of compound **9b**.

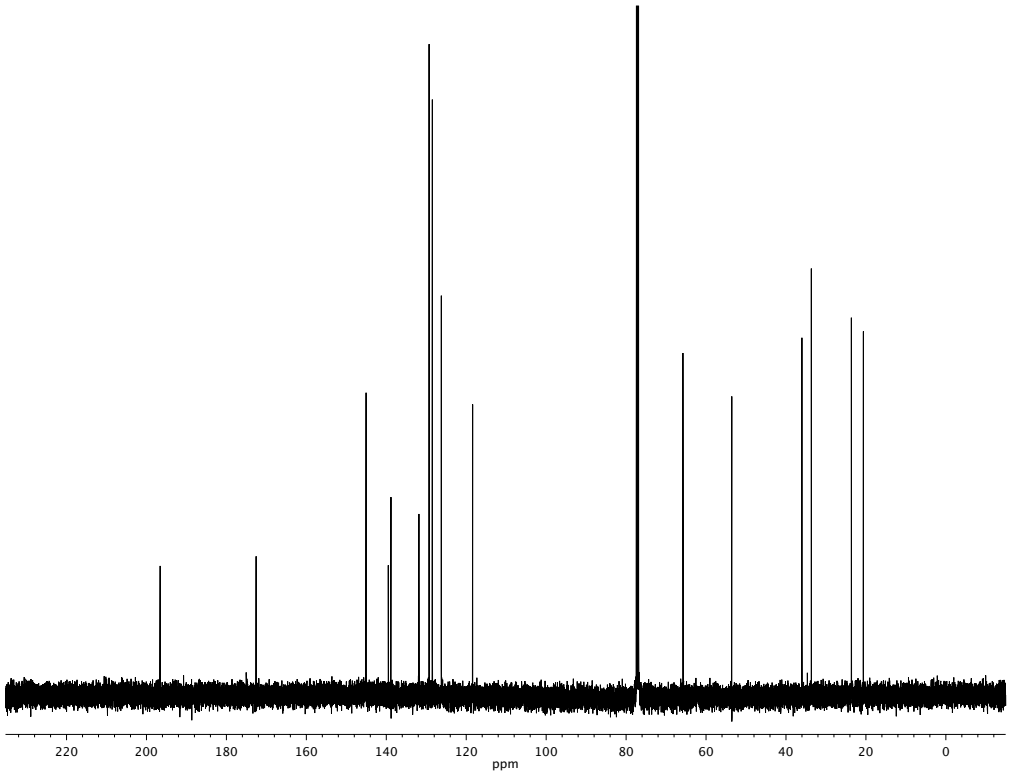


Figure SI-40C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **9b**.

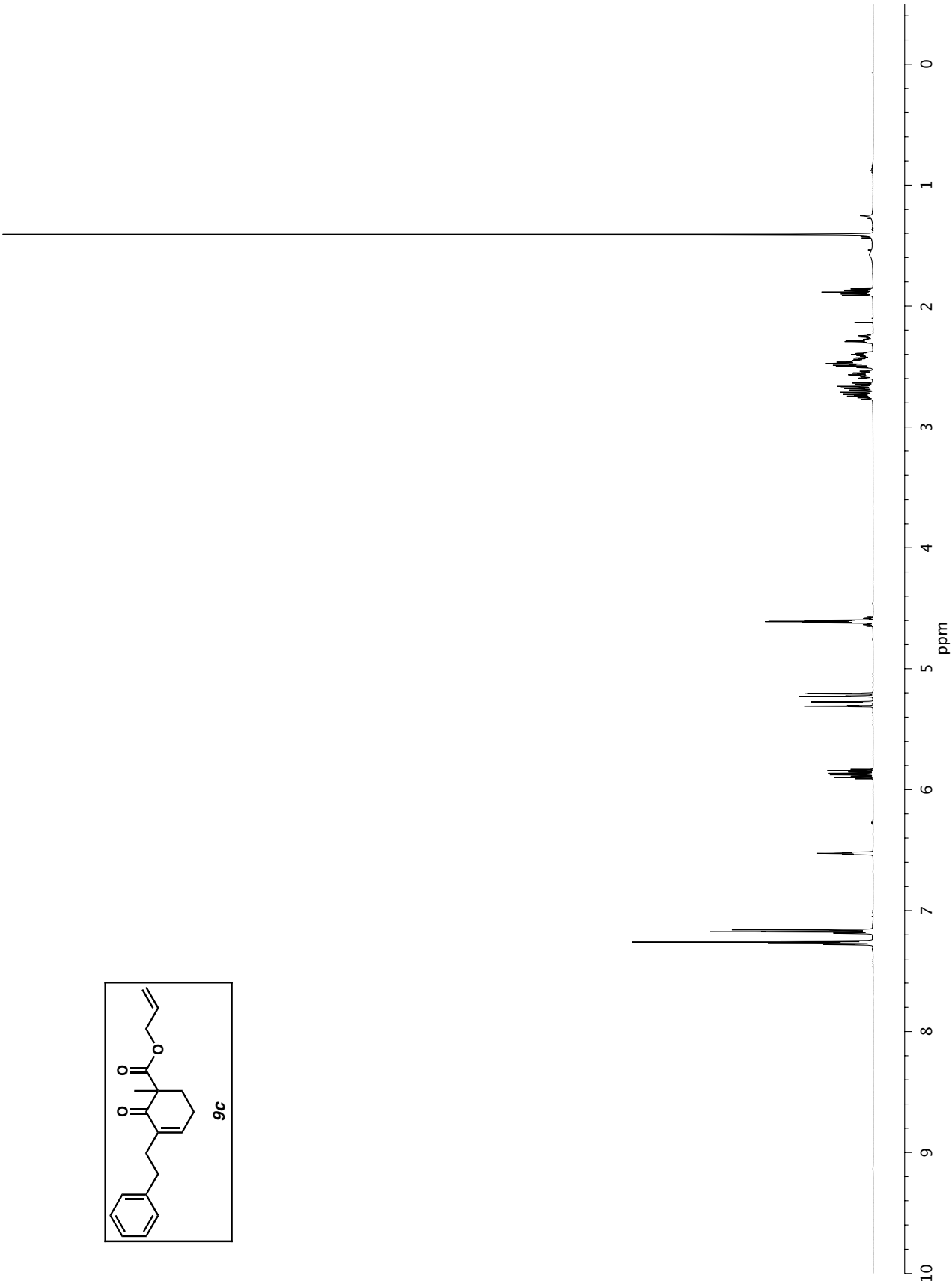


Figure SI-414. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **9c**.

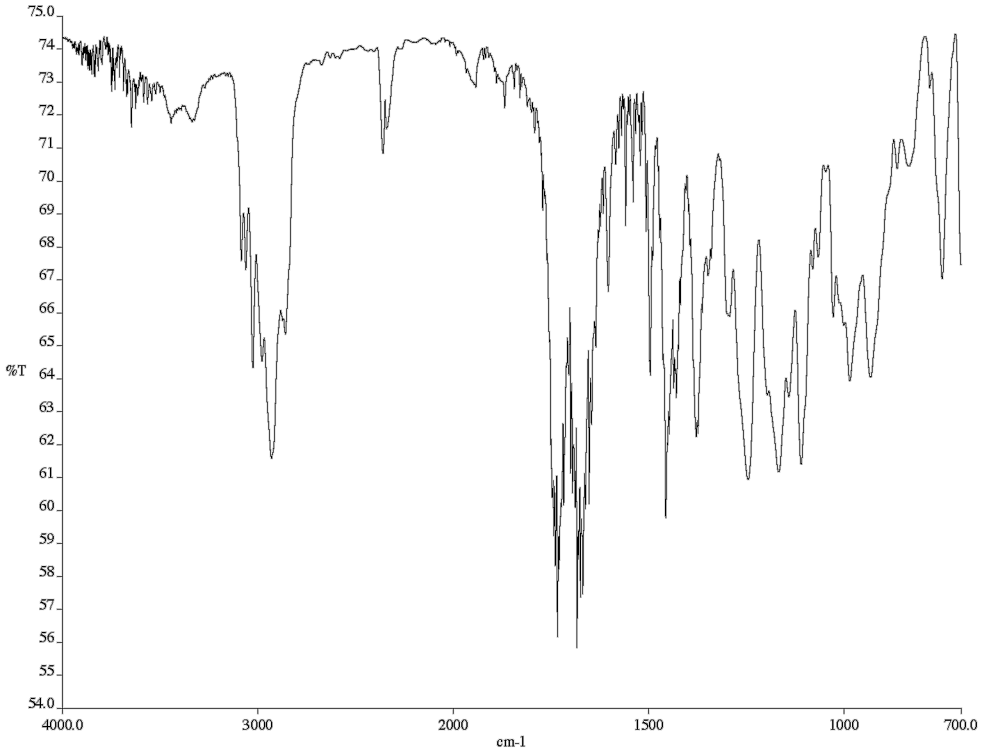


Figure SI-41B. Infrared spectrum (thin film/NaCl) of compound **9c**.

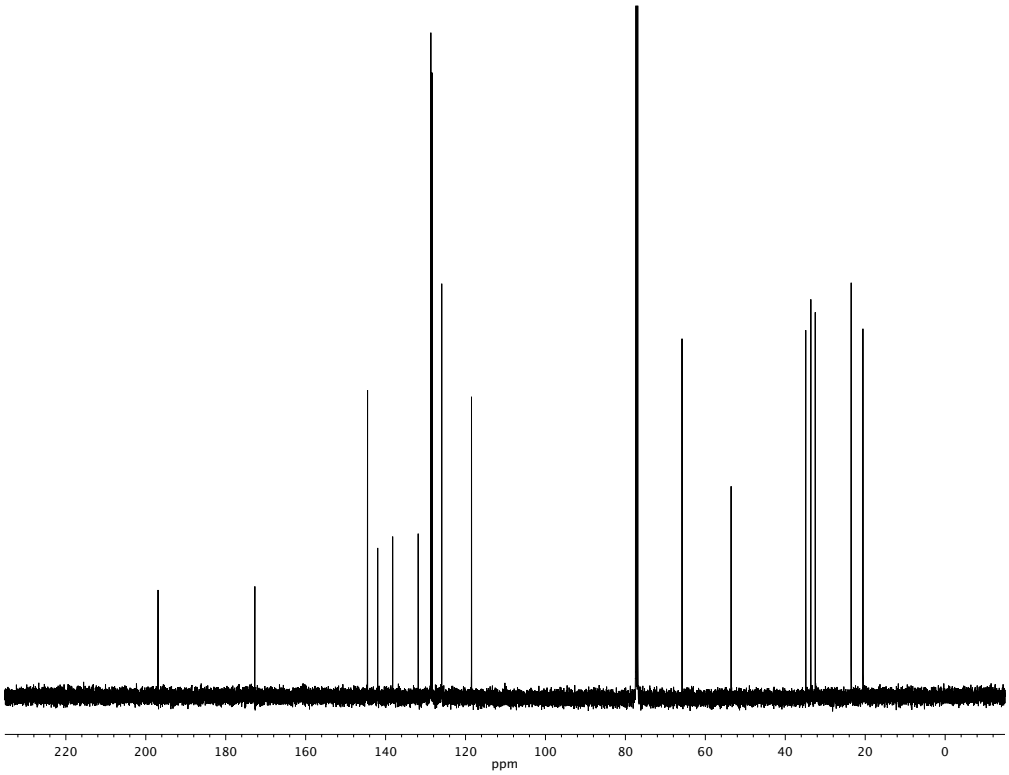


Figure SI-41C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **9c**.

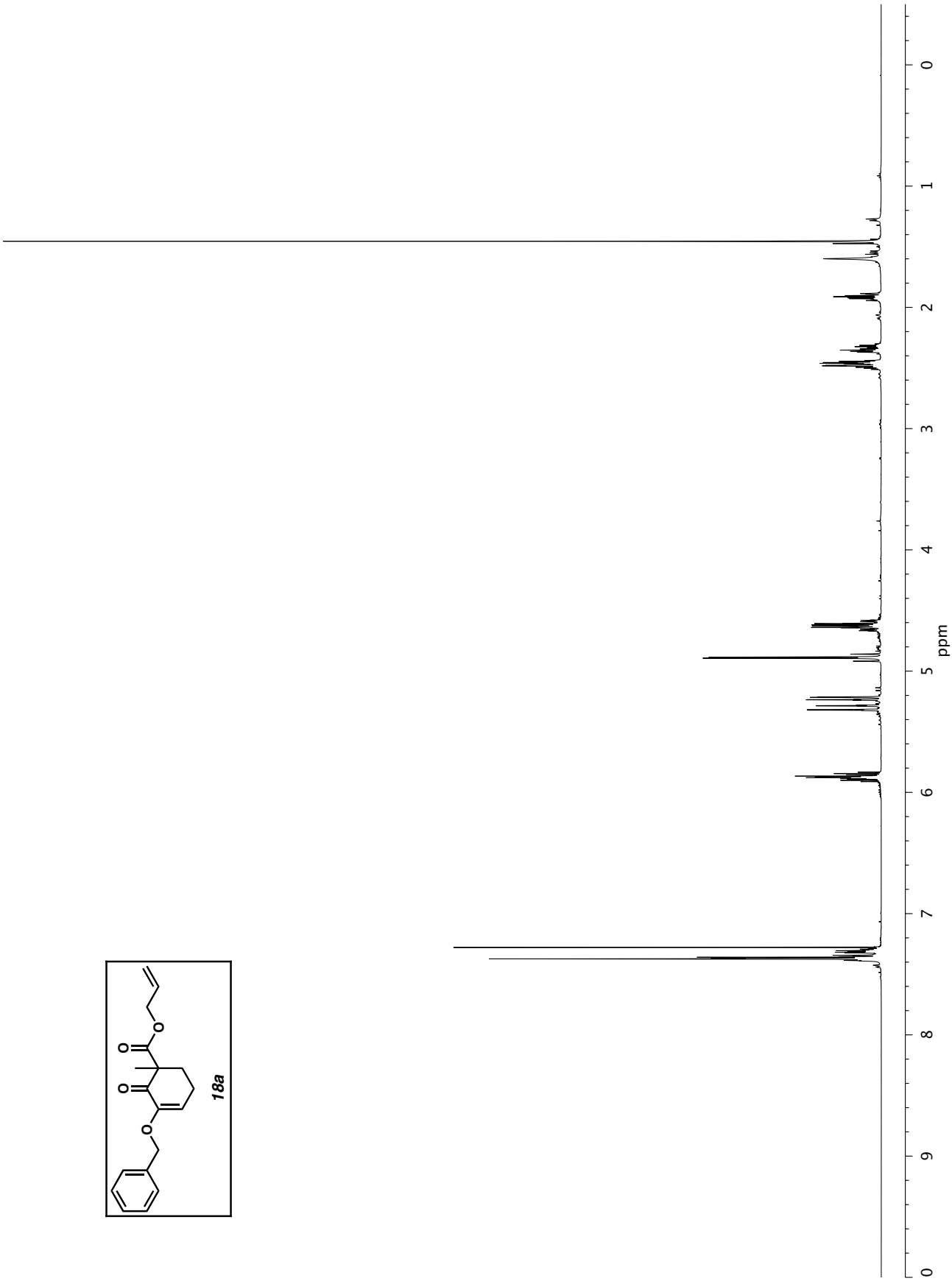


Figure SI-42A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **18a**.

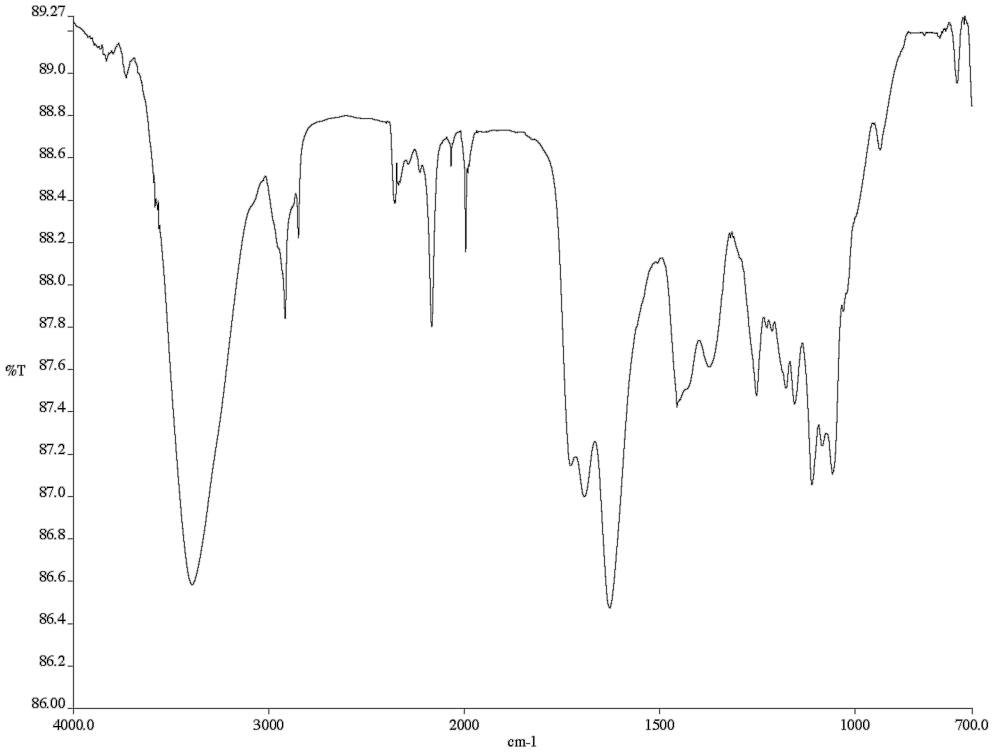


Figure SI-42B. Infrared spectrum (thin film/NaCl) of compound **18a**.

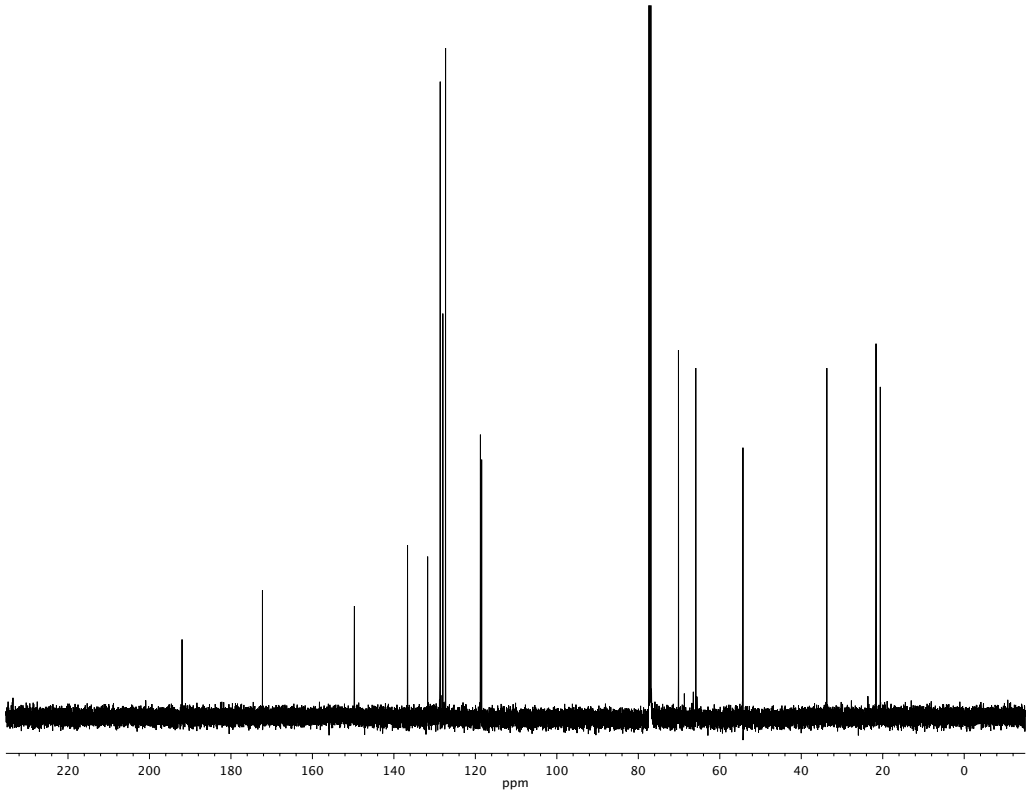


Figure SI-42C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **18a**.

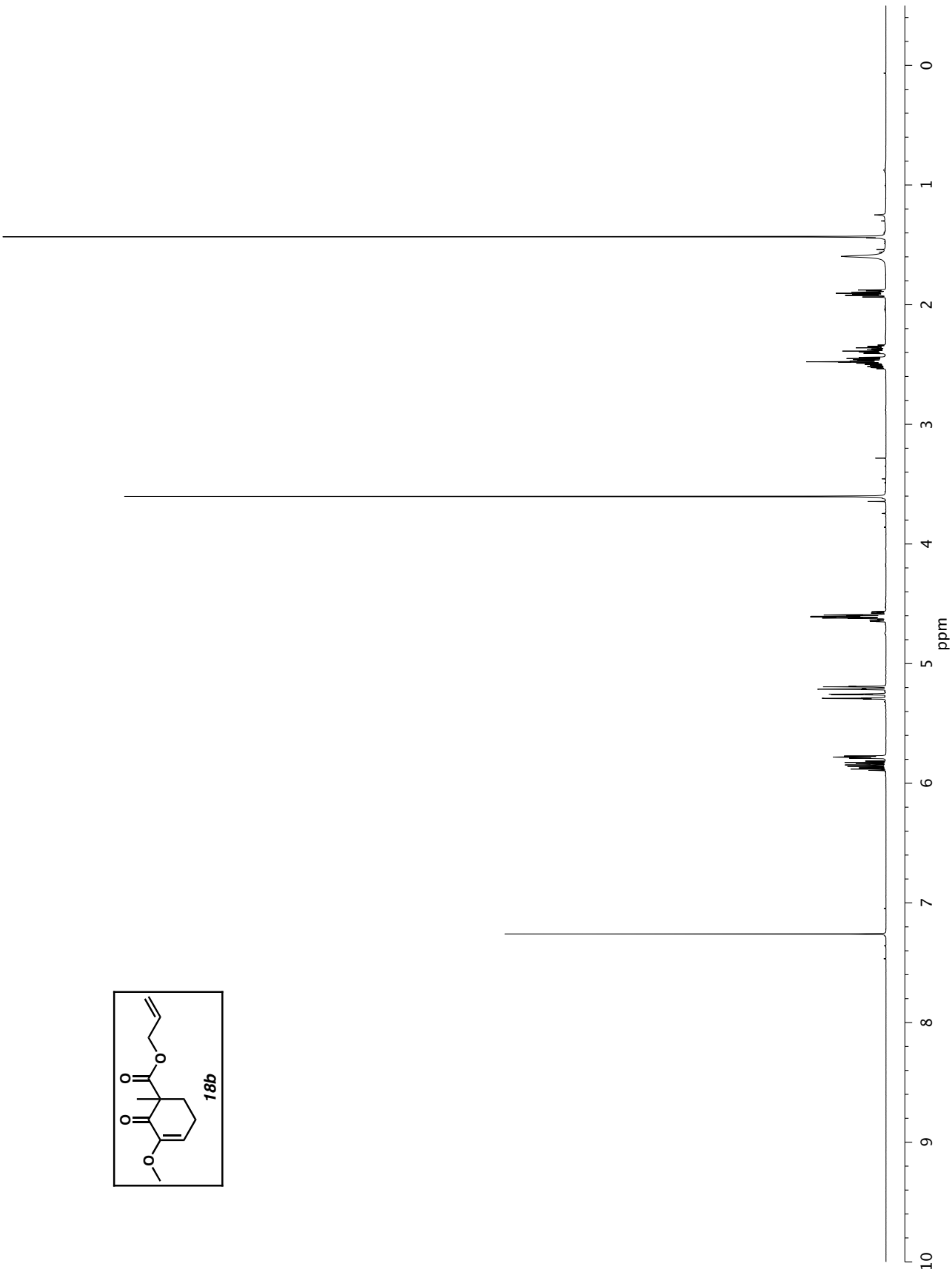


Figure SI-43A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **18b**.

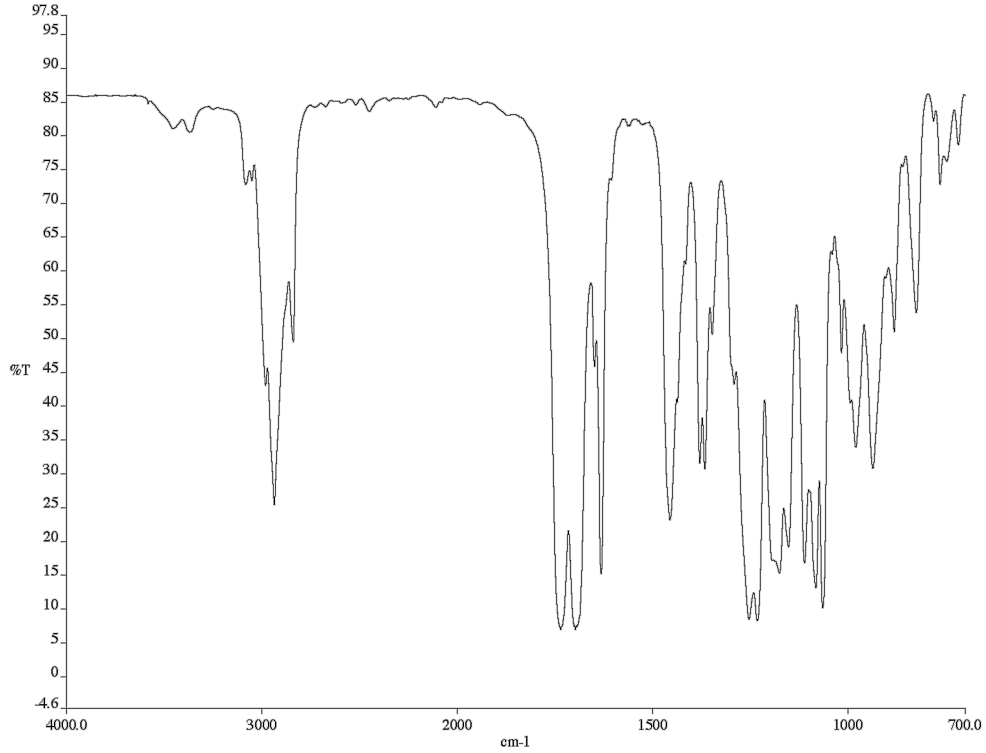


Figure SI-43B. Infrared spectrum (thin film/NaCl) of compound **18b**.

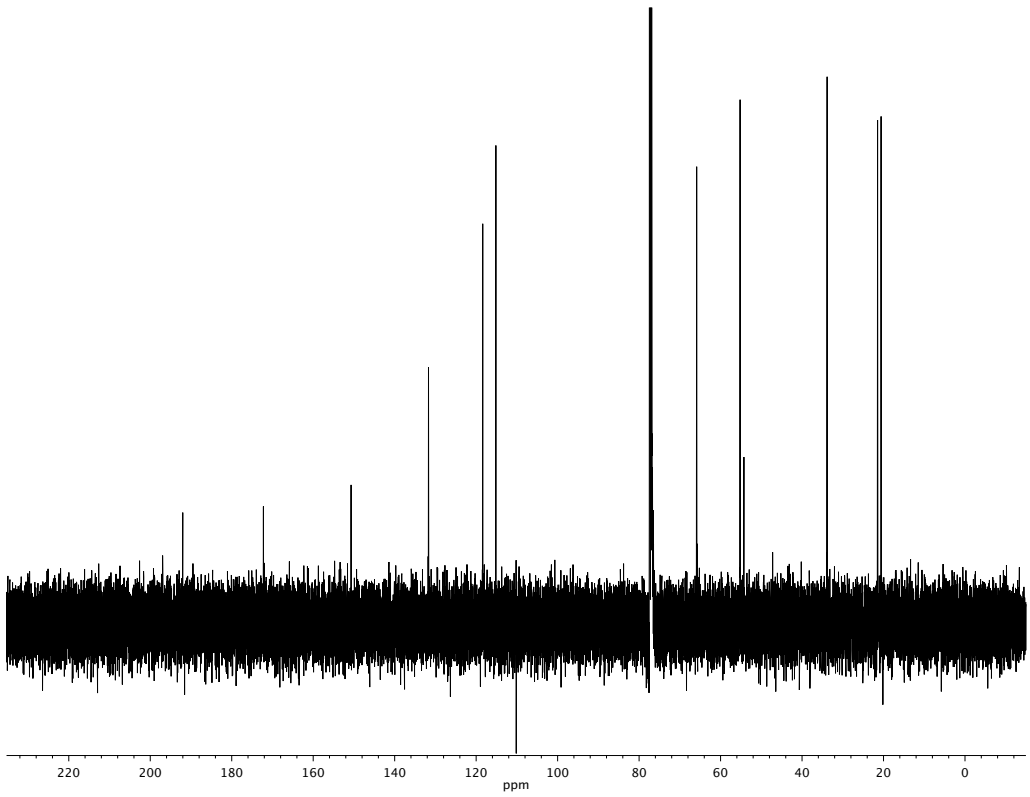


Figure SI-43C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **18b**.

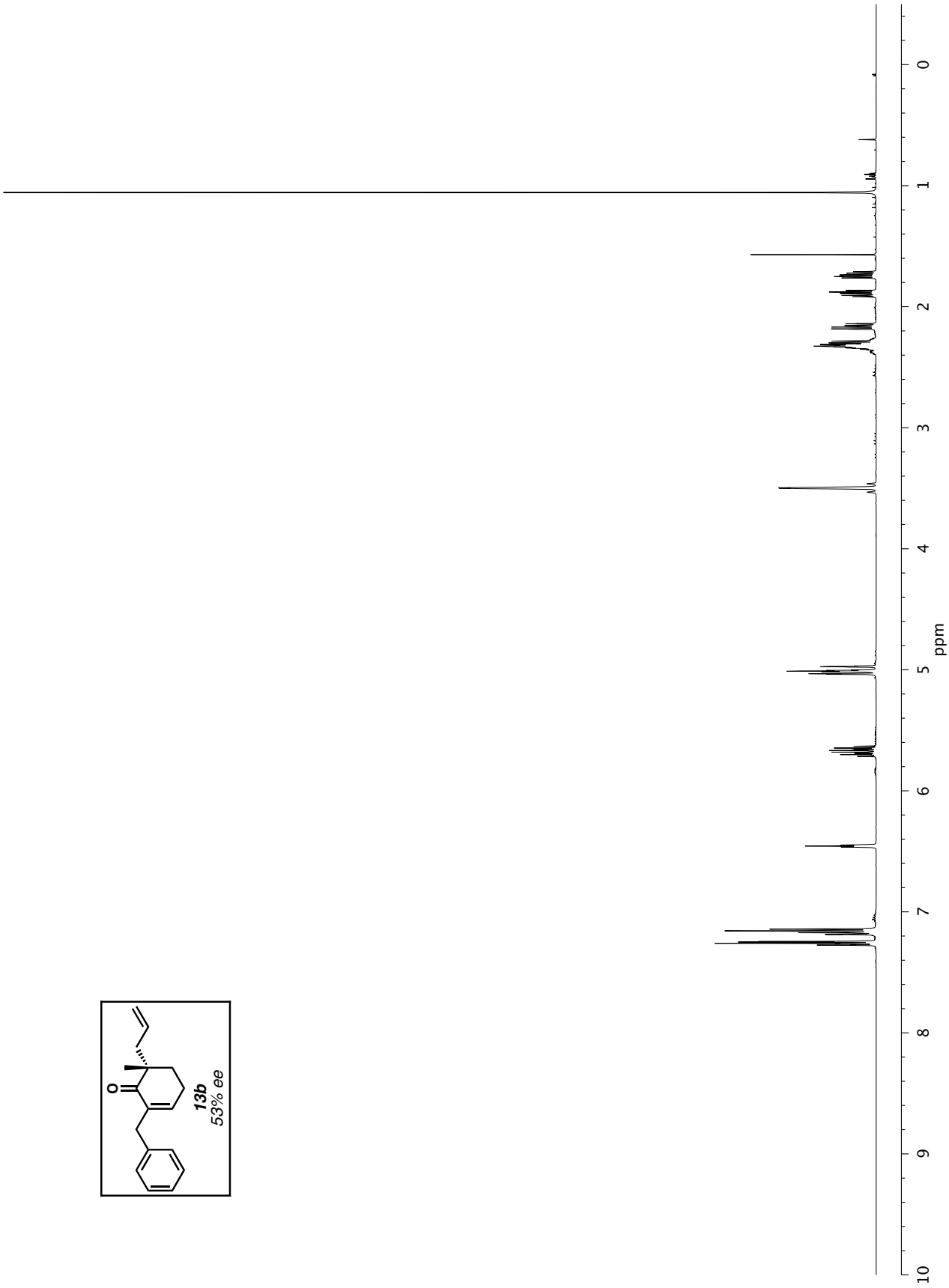


Figure SI-44A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **13b**.

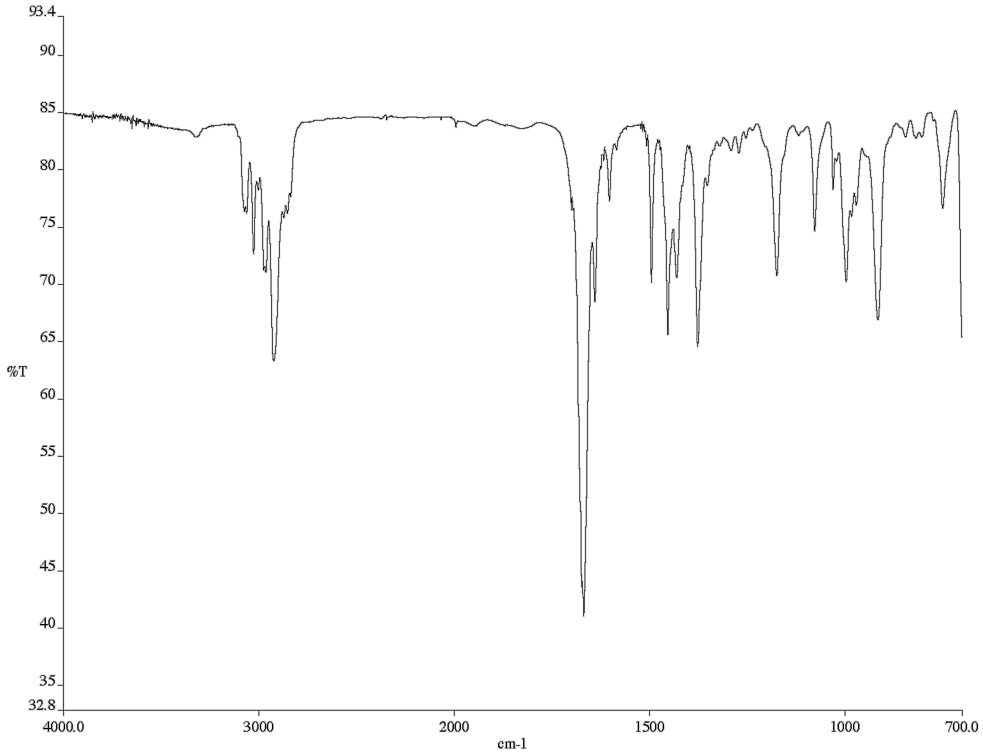


Figure SI-44B. Infrared spectrum (thin film/NaCl) of compound **13b**.

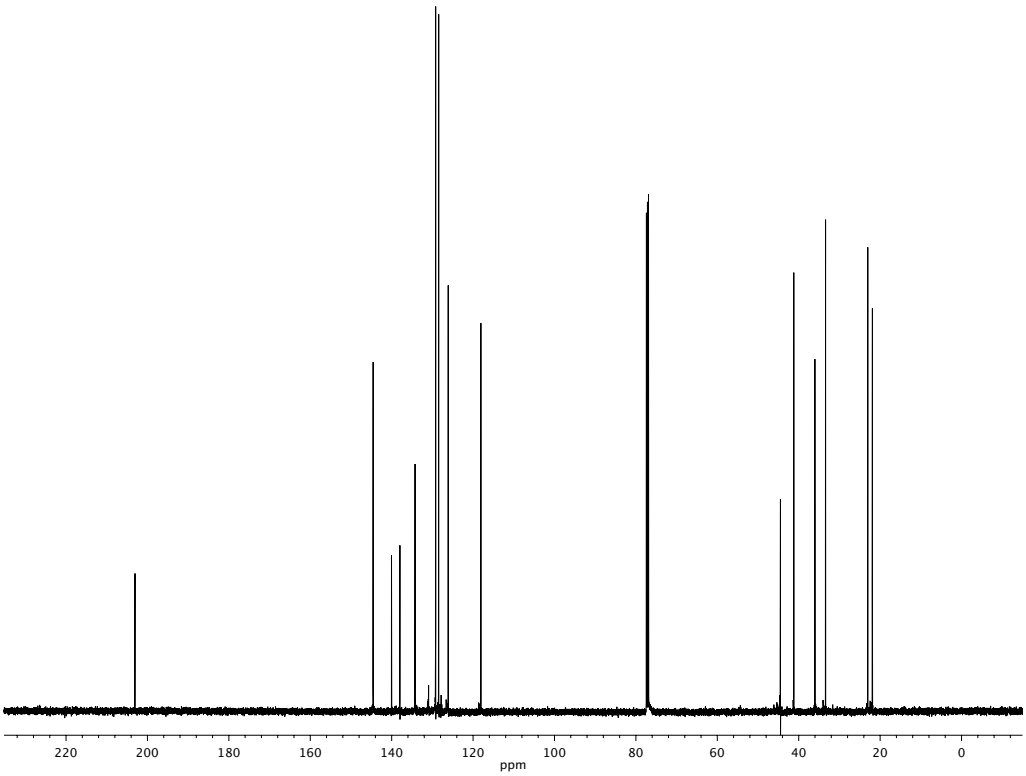
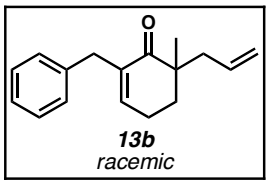


Figure SI-44C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **13b**.

DCD-V-057rerun DCD-V-057rerun 11/8/2012 4:34:57 PM

Analytical Report SFC



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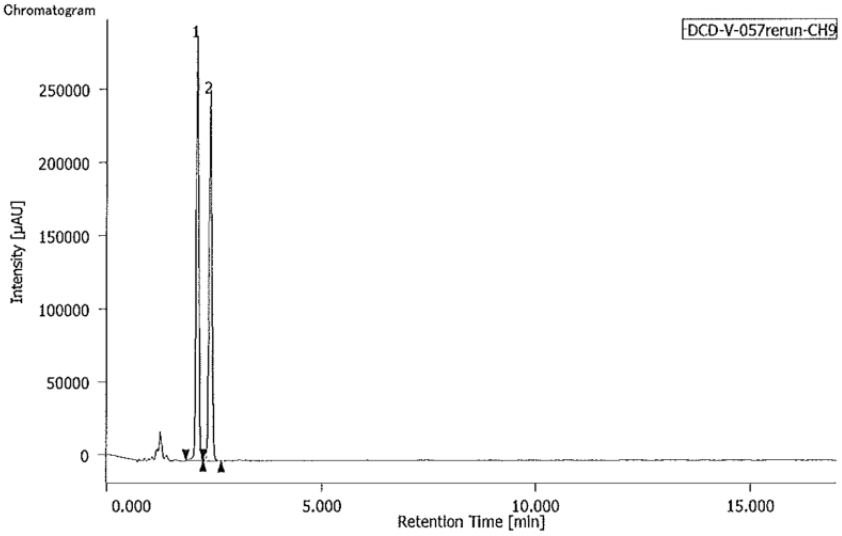
Injection Date	10/29/2012 7:46:40 PM
Volume	5.00 [µL]
Sample #	11
Project Name	Cal Tech SFC
Executed Sequence	DCD-V-057rerun
Chromatogram Name	DCD-V-057rerun
Sample Name	
Acquisition Time	17.0 [min]
Acquisition Sequence	DCD-V-057rerun
Control Method	Solv 1 Col 3 Isocratic 3B 5ml_min 10MPa 20min

Chromatogram



Peak Information

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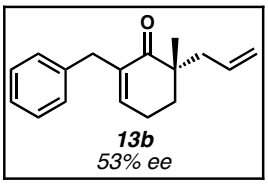
2	Unknown	9	2.413	1167308	249093	50.014	2.253	2.667	0.071	N/A	1.102

1 / 1

Figure SI-44D. Chiral SFC data of racemic compound **13b**.

DCD-V-061_063 DCD-V-061fr10 11/8/2012 4:35:32 PM

Analytical Report SFC



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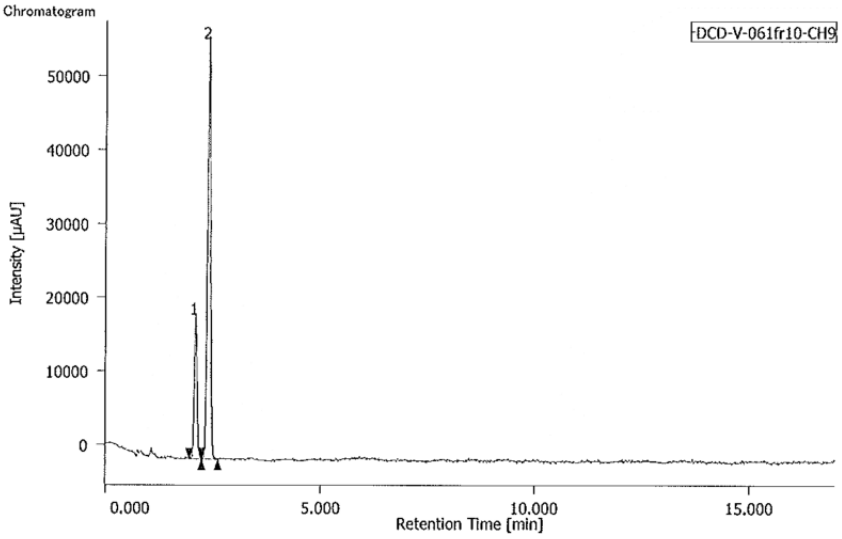
User Name	User
HPLC System Name	Jasco SFC w PDA
Injection Date	10/28/2012 10:34:49 PM
Volume	3.00 [µL]
Sample #	53
Project Name	Cal Tech SFC
Executed Sequence	DCD-V-061_063
Chromatogram Name	DCD-V-061fr10
Sample Name	
Acquisition Time	17.0 [min]
Acquisition Sequence	DCD-V-061_063
Control Method	Solv 1 Col 3 Isocratic 3B 5ml_min 10MPa 20min



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
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2	Unknown	9	2.400	284406	56497	76.626	2.253	2.627	0.077	N/A	1.131

1 / 1

Figure SI-44E. Chiral SFC data of enantioenriched compound **13b**.

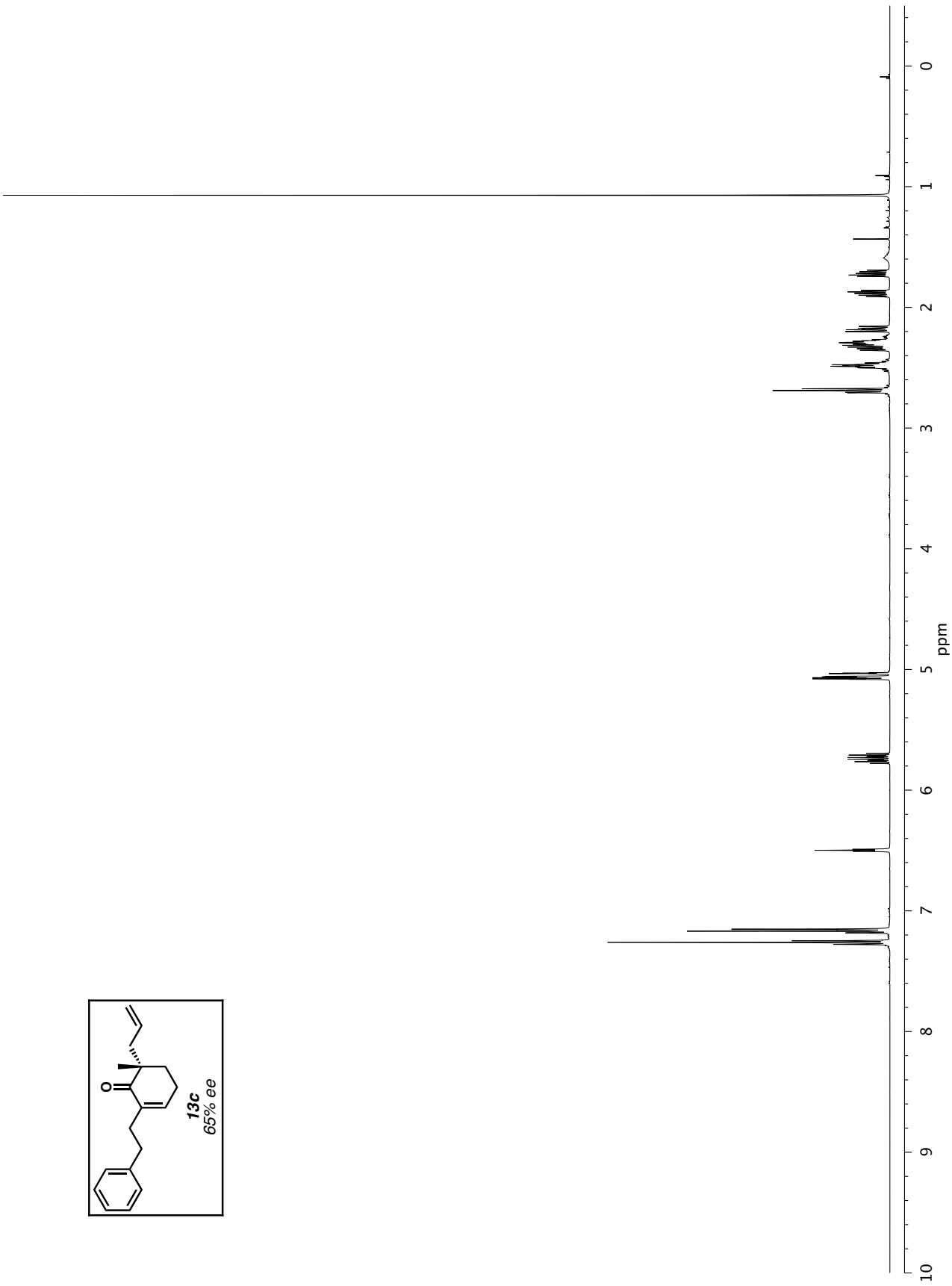


Figure SI-45A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **13c**.

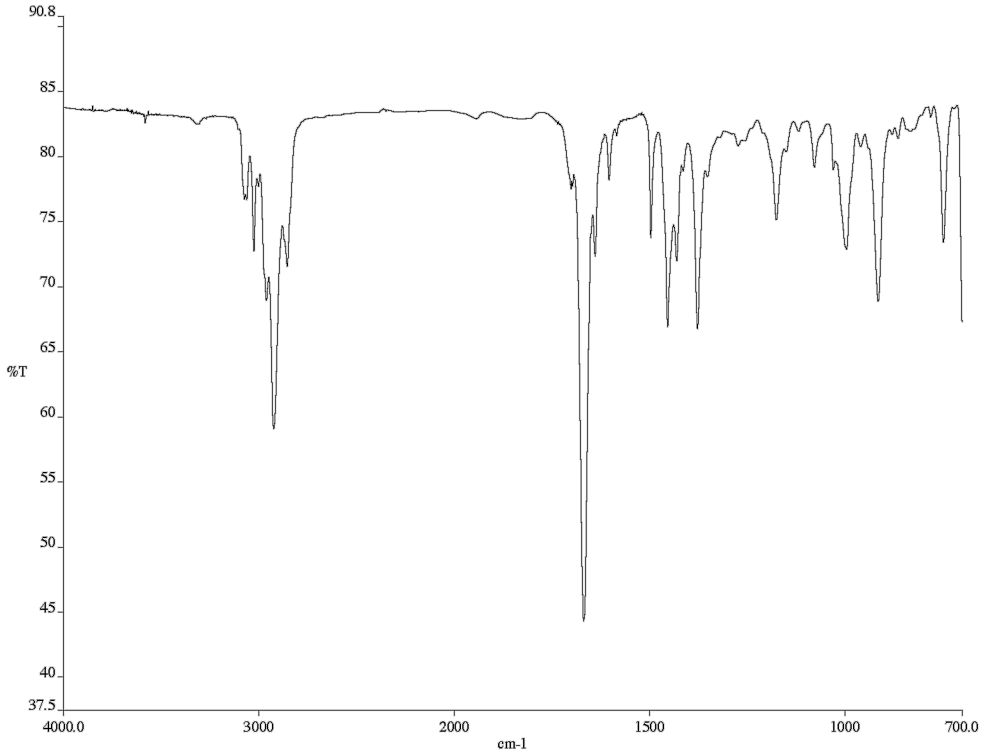


Figure SI-45B. Infrared spectrum (thin film/NaCl) of compound **13c**.

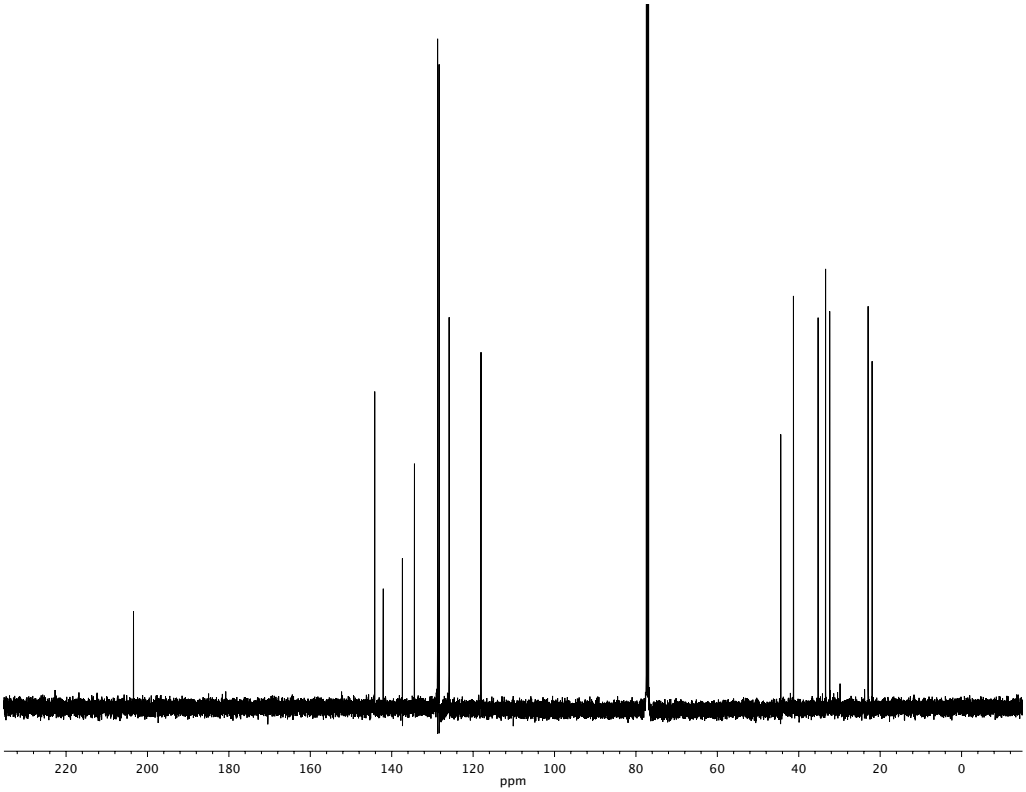
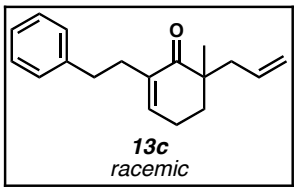


Figure SI-45C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **13c**.

DCD-V-059rerun DCD-V-059rerun 11/8/2012 4:32:48 PM

Analytical Report SFC



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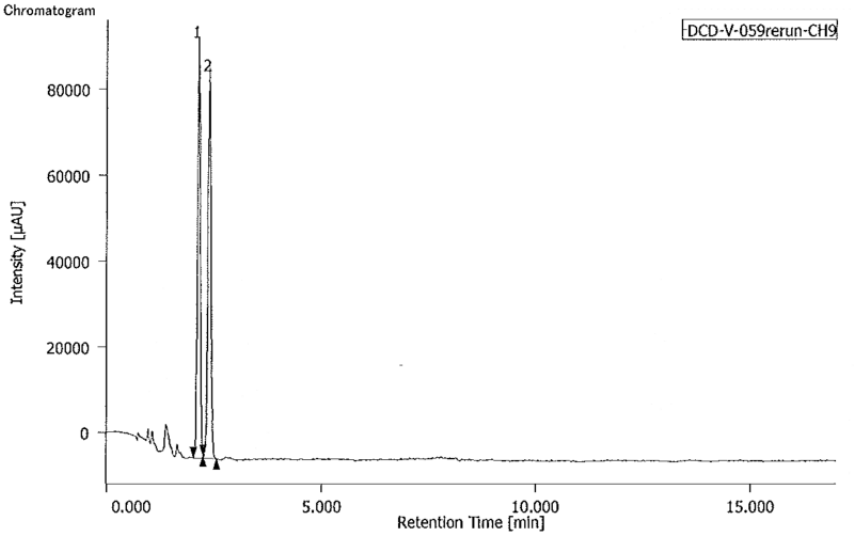
Volume	5.00 [µL]
Sample #	12
Project Name	Cal Tech SFC
Executed Sequence	DCD-V-059rerun
Chromatogram Name	DCD-V-059rerun
Sample Name	
Acquisition Time	17.0 [min]
Acquisition Sequence	DCD-V-059rerun
Control Method	Solv 1 Col 3 Isocratic 3B 5ml_min 10MPa 20min

Chromatogram



Peak Information

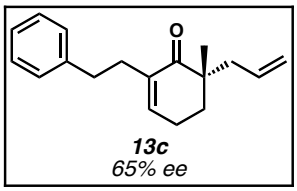
#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	9	2.133	432536	97121	50.091	2.027	2.253	0.068	2.102	1.223
2	Unknown	9	2.387	430969	89423	49.909	2.253	2.560	0.074	N/A	1.082

1 / 1

Figure SI-45D. Chiral SFC data of racemic compound **13c**.

DCD-V-063 DCD-V-063fr2 11/8/2012 4:33:34 PM

Analytical Report SFC



Chromatogram Information

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Injection Date	10/28/2012 5:02:04 PM
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Chromatogram Name	DCD-V-063fr2
Sample Name	
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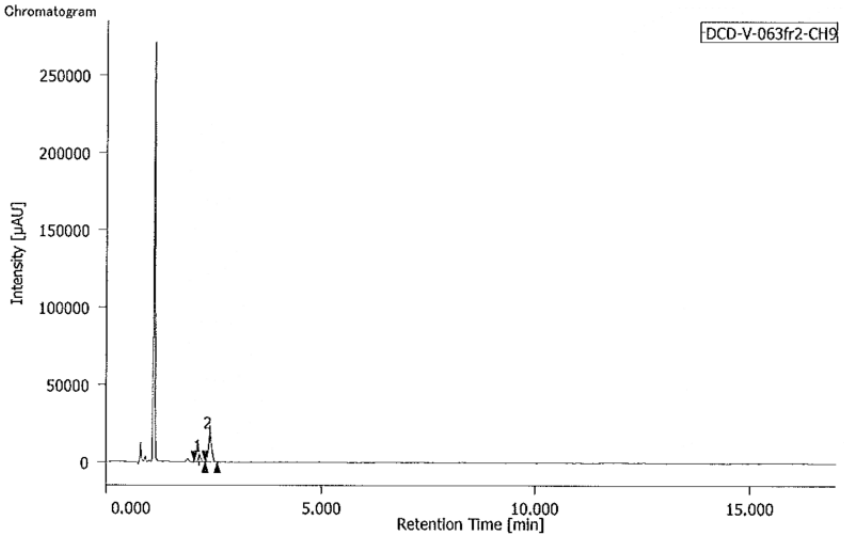
Acquisition Sequence	DCD-V-063
Control Method	Solv 1 Col 3 Isocratic 3B 5ml_min 10MPa 20min

Chromatogram



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
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2	Unknown	9	2.413	94820	19601	82.609	2.307	2.587	0.074	N/A	1.359

1 / 1

Figure SI-45E. Chiral SFC data of enantioenriched compound **13c**.

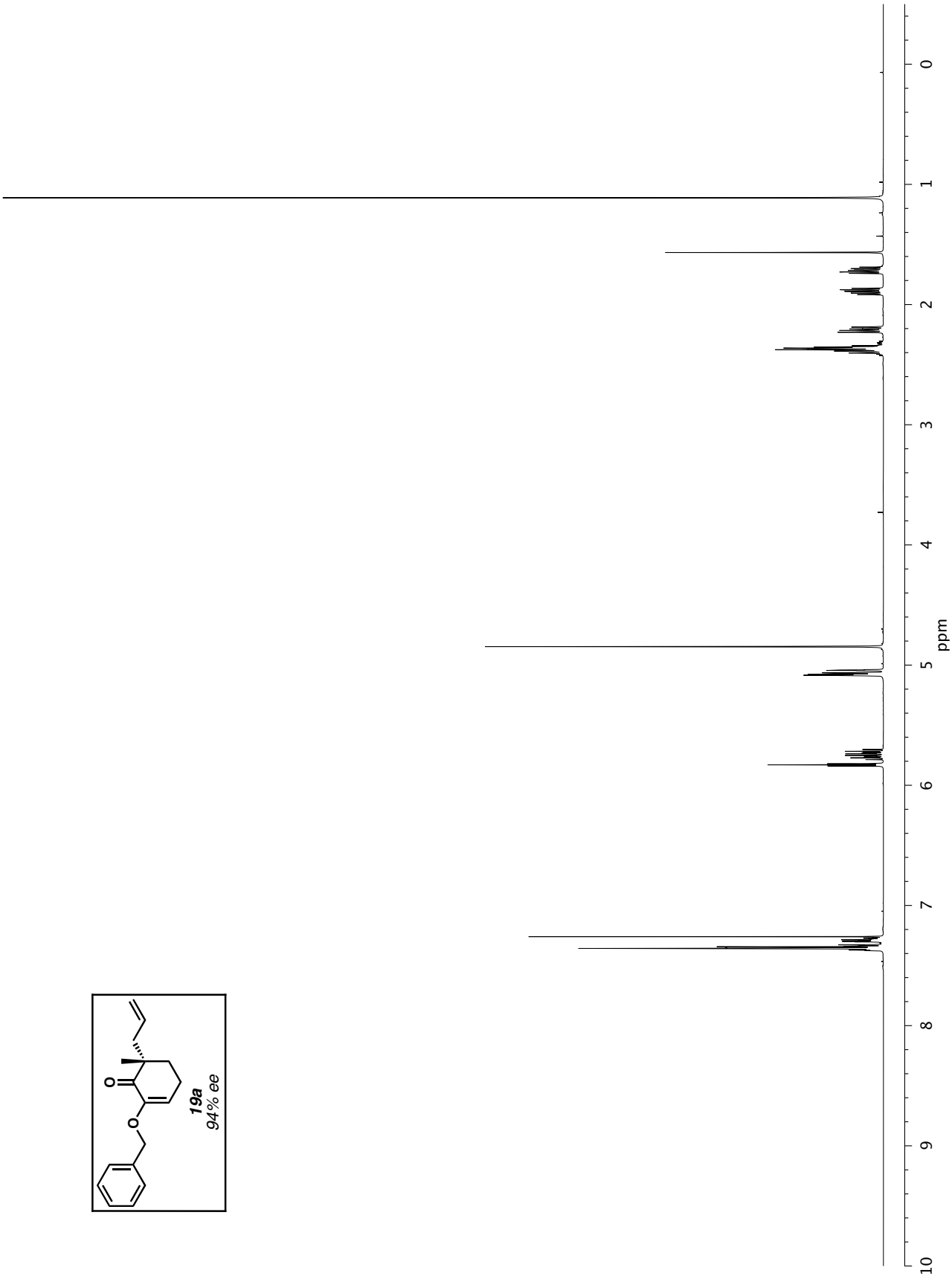


Figure SI-46A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **19a**.

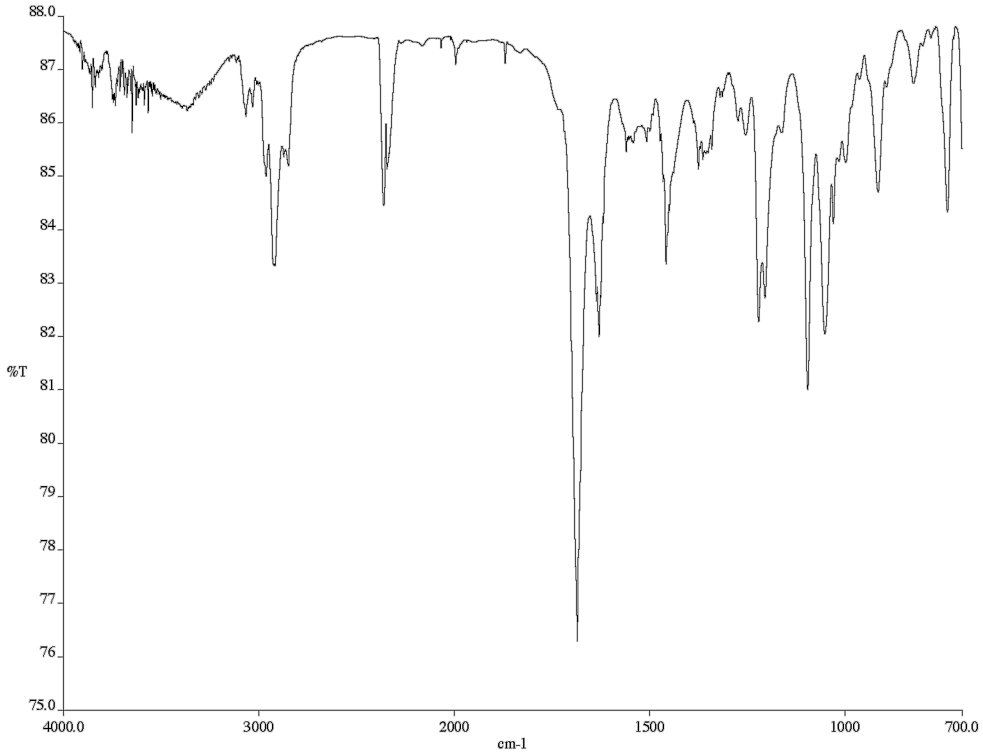


Figure SI-46B. Infrared spectrum (thin film/NaCl) of compound **19a**.

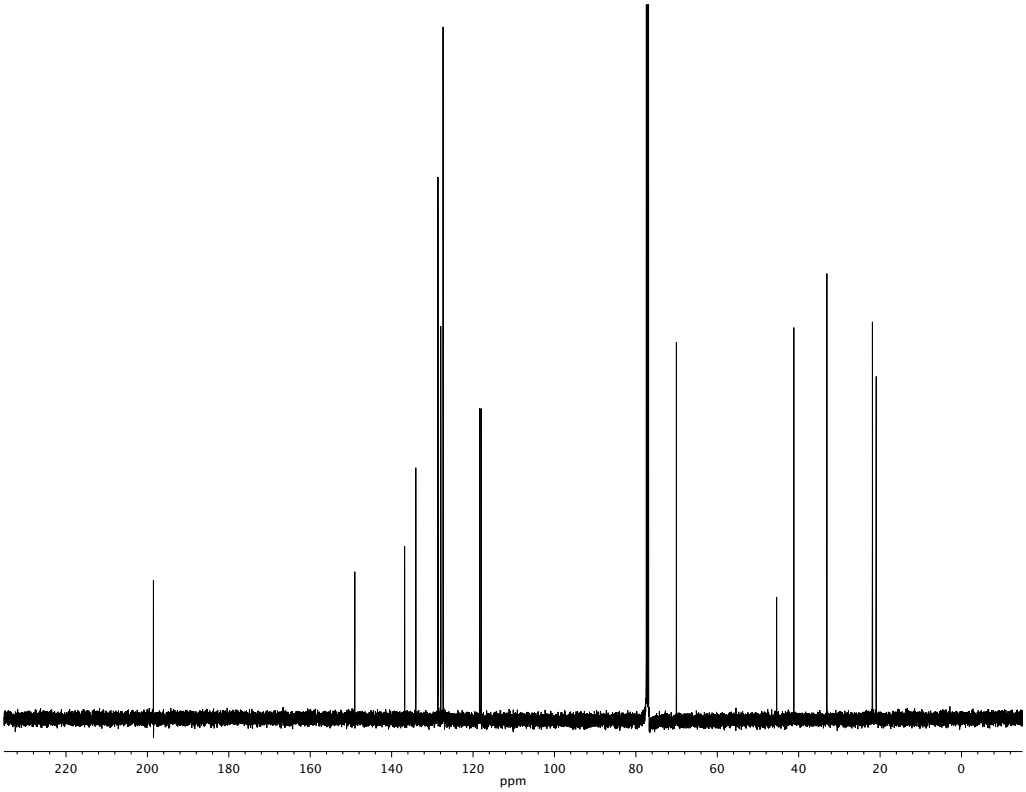
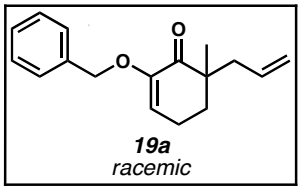


Figure SI-46C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **19a**.

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                                                     Inj Volume : 5.0 µl
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    Last changed    : 4/26/2010 9:51:26 PM
    Analysis Method : C:\CHEM32\1\METHODS\15IPA20_225.M
    Last changed    : 2/8/2012 2:32:24 PM by JCH
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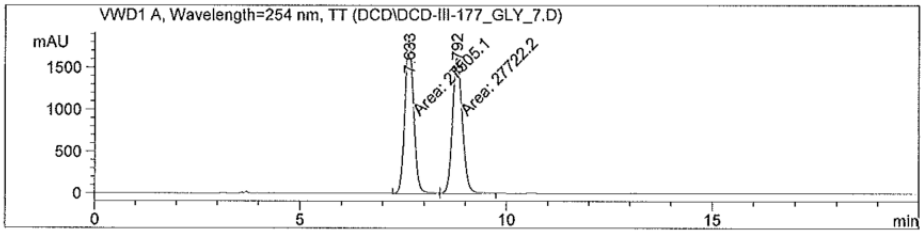


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    Dilution:                     :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=254 nm, TT

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1   7.633 MM    0.2506 2.75051e4  1829.12830  49.8034
       2   8.792 MM    0.2865 2.77222e4  1612.60437  50.1966

    Totals :                  5.52272e4  3441.73267


    ==========================================================================
                              Summed Peaks Report
    ==========================================================================

    Signal 1: VWD1 A, Wavelength=254 nm, TT
    ==========================================================================
                            Final Summed Peaks Report
    ==========================================================================

    Signal 1: VWD1 A, Wavelength=254 nm, TT
```
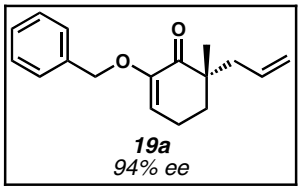
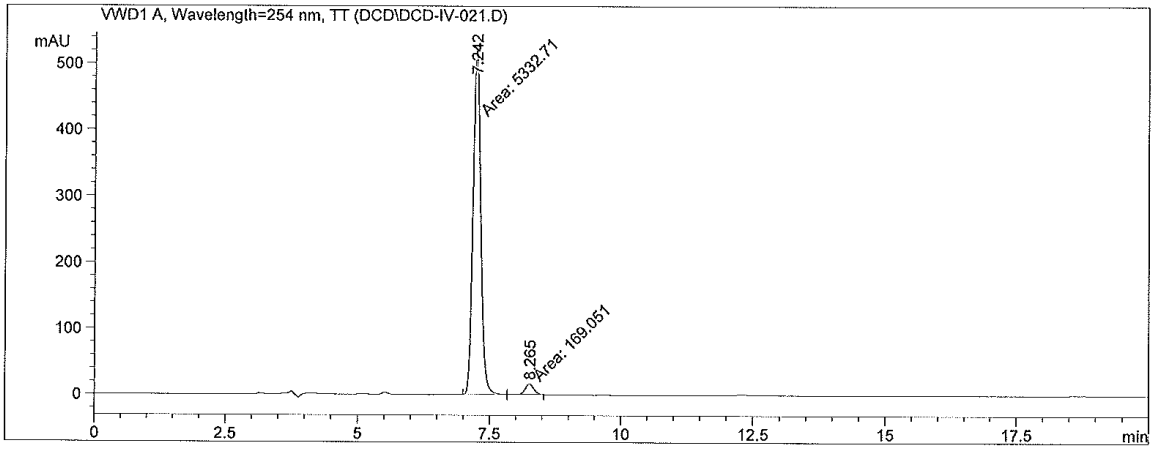


Figure SI-46D. Chiral HPLC data of racemic compound **19a**.




```
Data File C:\CHEM32\1\DATA\DCD\DCD-IV-021.D
Sample Name: DCD-IV-021
    ==========================================================================
    Acq. Operator   : DCD                                  Seq. Line :   3
    Acq. Instrument : HPLC 1                               Location : Vial 42
    Injection Date  : 6/26/2012 1:04:32 PM                     Inj :   1
                                                          Inj Volume : 5.0 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 1.0 µl
    Acq. Method     : C:\CHEM32\1\METHODS\7IPA20_254.M
    Last changed    : 4/26/2010 9:51:26 PM
    Analysis Method : C:\CHEM32\1\METHODS\1IPA15_210.M
    Last changed    : 6/22/2012 5:19:03 PM by ANM
                      (modified after loading)
    Method Info     : 1% IPA    15 min   210 nm   1 mL/min

    ==========================================================================
```




```
    ==========================================================================
                              Area Percent Report
    ==========================================================================

    Sorted By             :      Signal
    Multiplier:                   :      1.0000
    Dilution:                     :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=254 nm, TT

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1   7.242 MF    0.1711 5332.71240  519.53253  96.9273
       2   8.265 FM    0.1804  169.05138   15.61860   3.0727

    Totals :                  5501.76378  535.15113

    ==========================================================================
                              Summed Peaks Report
    ==========================================================================

HPLC 1 6/26/2012 3:40:25 PM ANM                          Page   1 of 2
```

Figure SI-46E. Chiral HPLC data of enantioenriched compound **19a**.

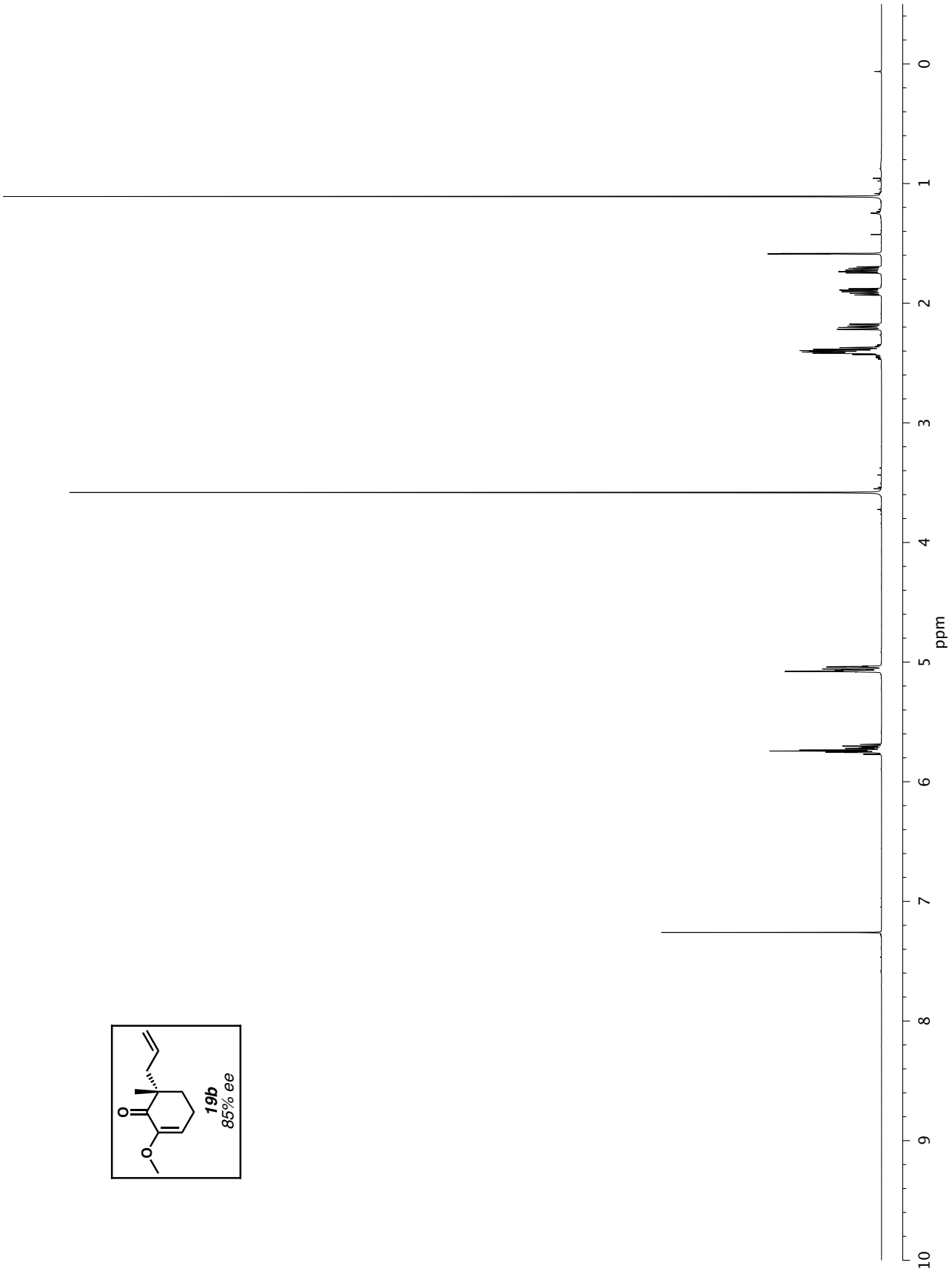


Figure SI-47A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **19b**.

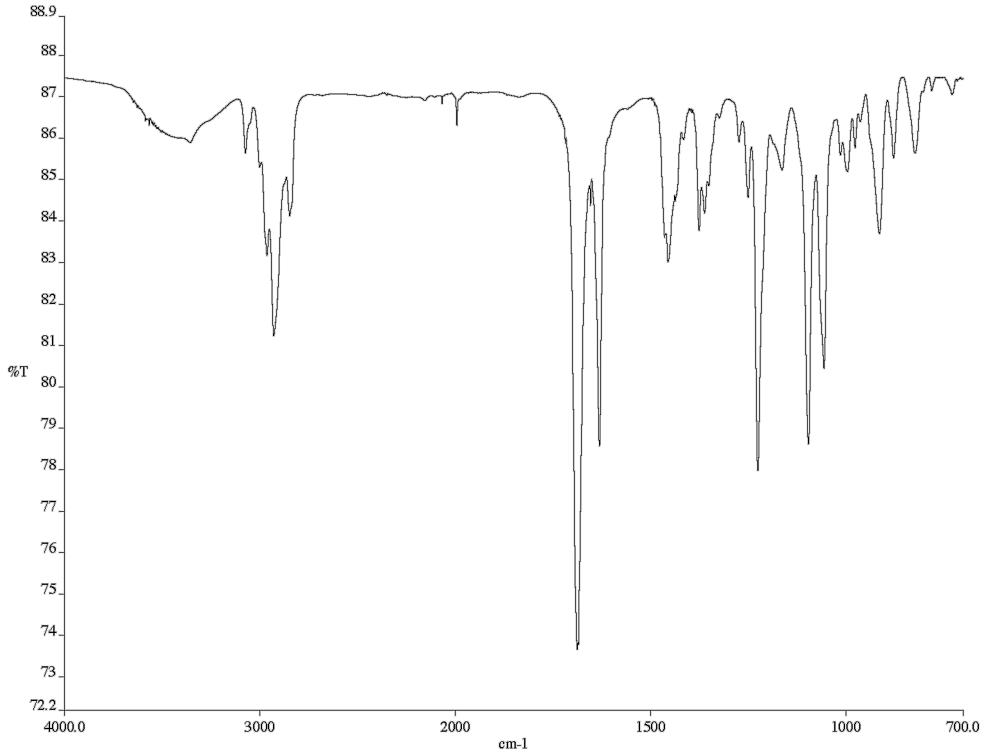


Figure SI-47B. Infrared spectrum (thin film/NaCl) of compound **19b**.

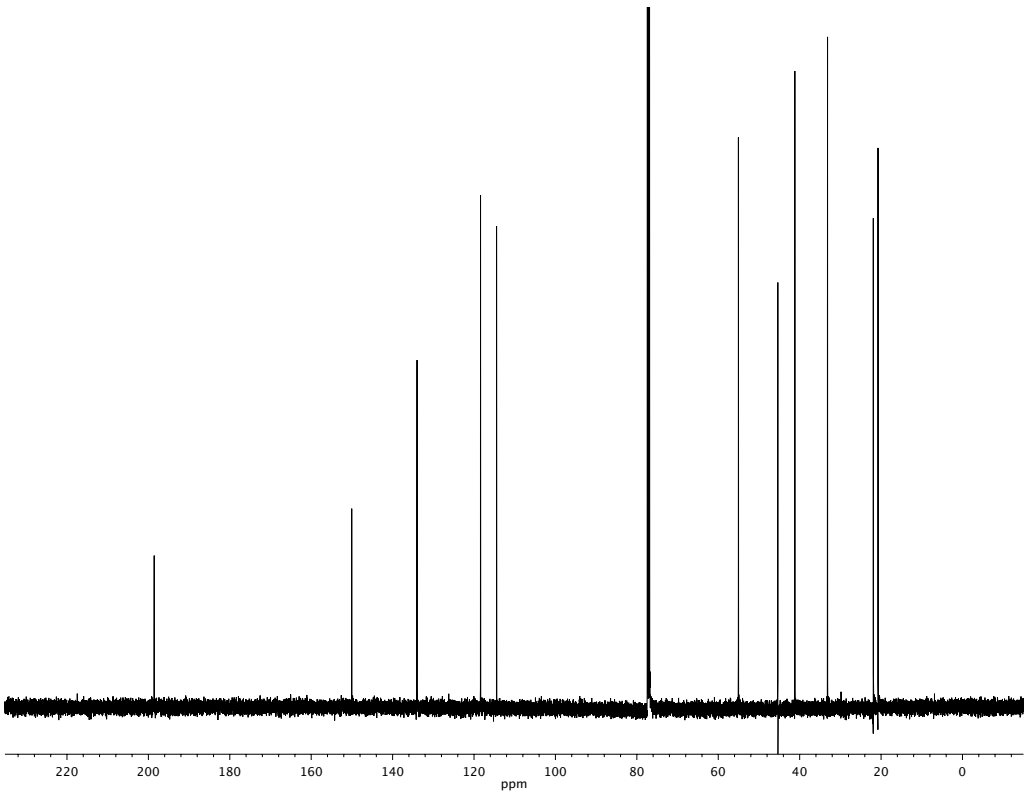
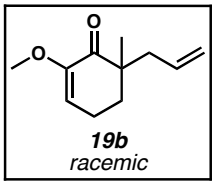
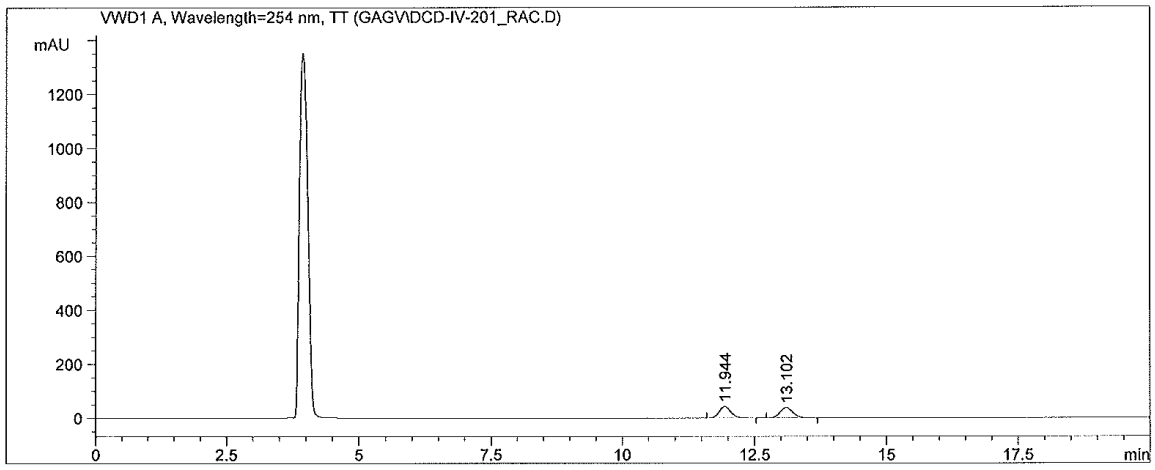


Figure SI-47C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **19b**.

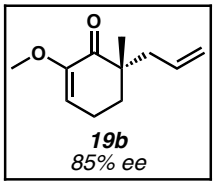



```
Data File C:\CHEM32\1\DATA\GAGV\DCD-IV-201_RAC.D
Sample Name: DCD-IV-201_rac
    ==========================================================================
    Acq. Operator   : GAGV                              Seq. Line :  12
    Acq. Instrument : HPLC 1                           Location : Vial 73
    Injection Date  : 8/23/2012 8:20:38 PM                  Inj :   1
                                                      Inj Volume : 5.0 µl
    Acq. Method     : C:\CHEM32\1\METHODS\2IPA20_254.M
    Last changed    : 4/26/2010 9:48:36 PM
    Analysis Method : C:\CHEM32\1\METHODS\025IPA30_254MG.M
    Last changed    : 8/21/2012 6:18:46 PM by JCH
    Method Info     : 0.25% IPA   30 min   254 nm   1 mL/min

    ==========================================================================
```

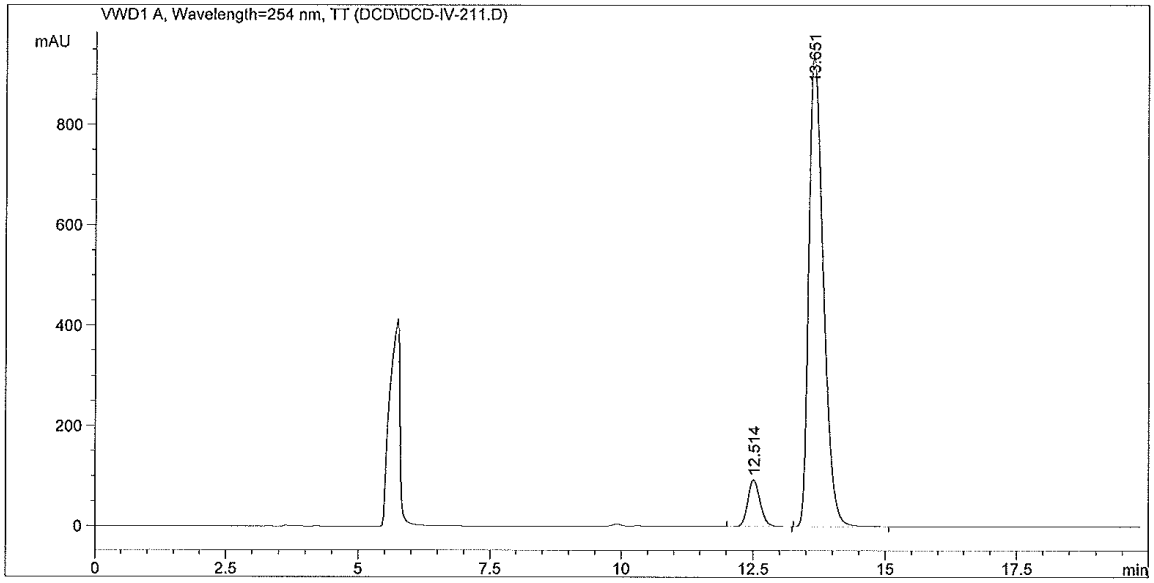



```
    ==========================================================================
                              Area Percent Report
    ==========================================================================

    Sorted By             :      Signal
    Multiplier:                   :      1.0000
    Dilution:                     :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=254 nm, TT

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  11.944 BB    0.2333  636.77869   42.08311  50.0530
       2  13.102 BB    0.2569  635.42993   38.16108  49.9470

    Totals :                  1272.20862   80.24419

    ==========================================================================
                              Summed Peaks Report
    ==========================================================================

    Signal 1: VWD1 A, Wavelength=254 nm, TT

HPLC 1 8/23/2012 8:47:06 PM JCH                          Page   1 of 2
```

Figure SI-47D. Chiral SFC data of racemic compound **19b**.




```
Data File C:\CHEM32\1\DATA\DCD\DCD-IV-211.D
Sample Name: DCD-IV-211

==========================================================================
Acq. Operator   : DCD                              Seq. Line :   3
Acq. Instrument : HPLC 1                          Location : Vial 52
Injection Date  : 9/20/2012 3:54:06 PM                Inj :   1
                                                  Inj Volume : 5.0 µl
Acq. Method     : C:\CHEM32\1\METHODS\2IPA20_254.M
Last changed    : 4/26/2010 9:48:36 PM
Analysis Method : C:\CHEM32\1\METHODS\5IPA60_280.M
Last changed    : 9/20/2012 4:17:39 PM by ANM
                  (modified after loading)
Method Info     : 5% IPA    60 min   280 nm   1 mL/min
```




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|--------|----|-------|----------|----------|--------|
   1  12.514 VB    0.2516 1518.20447   93.34123   7.7886
   2  13.651 BB    0.2950 1.79745e4   937.44110  92.2114

Totals :                  1.94927e4  1030.78233

==========================================================================
```


Figure SI-47E. Chiral SFC data of enantioenriched compound **19b**.