

CHEMISTRY

A EUROPEAN JOURNAL

Supporting Information

© Copyright Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, 2013

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

**Nathan B. Bennett, Douglas C. Duquette, Jimin Kim, Wen-Bo Liu,
Alexander N. Marziale, Douglas C. Behenna, Scott C. Virgil, and Brian M. Stoltz*^[a]**

chem_201300030_sm_miscellaneous_information.pdf

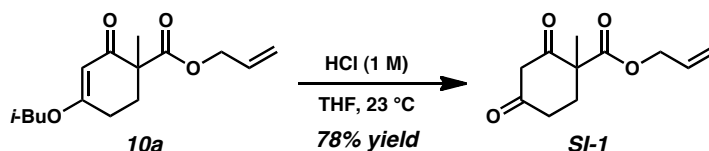
Materials and Methods. Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Reaction progress was monitored by thin-layer chromatography (TLC). Solvents were dried by passage through an activated alumina column 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*)-(CF₃)₃-*t*-BuPHOX (**8**),³ and allyl cyanofornate⁴ were prepared by known methods. Reaction temperatures were controlled by an IKA Mag 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 KMnO₄ 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. ¹H NMR spectra were recorded on a Varian Mercury 300 MHz or Varian Inova 500 MHz spectrometer and are reported relative to residual CHCl₃ (δ 7.26 ppm) or benzene-d₆ (δ 7.16 ppm). ¹³C 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 CDCl₃ (δ 77.16 ppm) or benzene-d₆ (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 ¹H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, dm = doublet of multiplets, br s = broad singlet, br d = broad doublet, app = apparent. Data for ¹³C are reported in terms of chemical shifts (δ ppm). IR spectra were obtained 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: [α]_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:

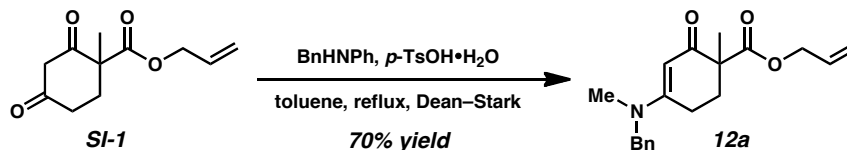
DMAP = 4-(dimethylamino)pyridine
IPA = isopropyl alcohol
LDA = lithium diisopropylamide
LiHMDS = lithium bis(trimethylsilyl)amide

Procedures for the Preparation of Compounds Related to Enaminone Screen

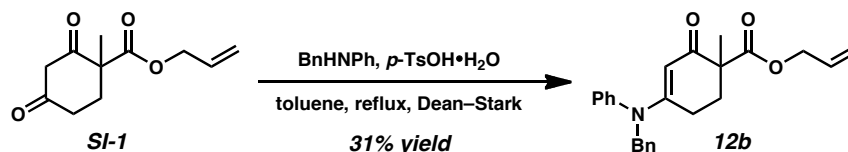
Enaminone Allylic Alkylation Precursors



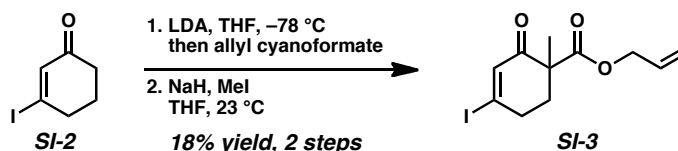
Dione SI-1. A 100 mL round-bottom flask equipped with a magnetic stir bar was charged with vinyllogous ester **10a**⁵ (3.08 g, 11.58 mmol, 1.00 equiv), THF (30 mL, 0.39 M), and aq. HCl (1 M in H₂O, 14.00 mL, 14.00 mmol, 1.21 equiv). The reaction was initially a suspension that developed into a solution 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 MgSO₄, filtered, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO₂, 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); ¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (125 MHz, CDCl₃) 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 C₁₁H₁₅O₄ [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. Na₂CO₃ solution (20 mL) and transferred to a separatory funnel where the aqueous layer was extracted four times with CH₂Cl₂. The combined organics (200 mL) were dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO₂, 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); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₉H₂₄NO₃ [M+H]⁺: 314.1751, found 314.1754.



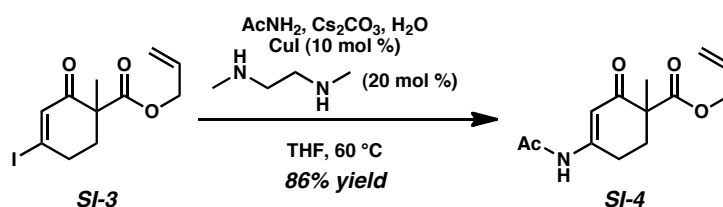
Enaminone 12b. A 50 mL round-bottom flask containing a magnetic stir bar was charged with dione **SI-1** (500.3 mg, 2.38 mmol, 1.00 equiv), toluene (24 mL, 0.10 M), benzylphenylamine (480.0 mg, 2.62 mmol, 1.10 equiv), and *p*-toluenesulfonic acid monohydrate (45.6 mg, 0.24 mmol, 10 mol %). The flask 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); $^1\text{H NMR}$ (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); $^{13}\text{C NMR}$ (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 $\text{C}_{24}\text{H}_{26}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 376.1907, found 376.1903.



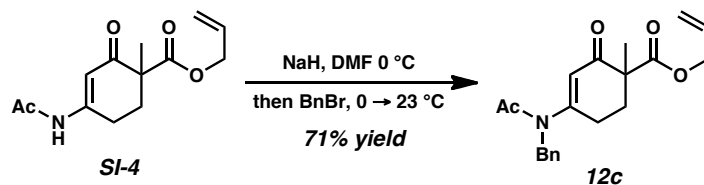
β -Iodoenone SI-3. A 200 mL round-bottom flask equipped with a magnetic stir bar was charged with diisopropyl amine (1.52 mL, 10.85 mmol, 1.19 equiv) and THF (36 mL). The flask was lowered into a 0 °C bath (ice/water) and *n*-BuLi (4.5 mL, 2.3 M in hexanes, 10.35 mmol, 1.14 equiv) was added dropwise 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

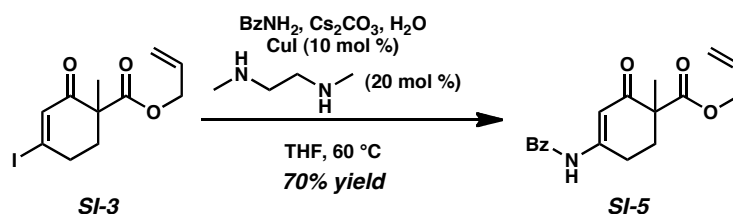
equiv). The flask was removed from the glove box, reconnected to an Ar-filled manifold, and charged with THF (6 mL). The crude orange oil from the previous step (1.61 g, 5.27 mmol, 1.00 equiv) was transferred via cannula to the flask using several THF rinses (1 x 5 mL + 3 x 2 mL, total added = 21.0 mL, 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 μ L, 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 \rightarrow 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); ^1H 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 $\text{C}_{11}\text{H}_{14}\text{O}_3\text{I}$ $[\text{M}+\text{H}]^+$: 320.9982, found 320.9981.



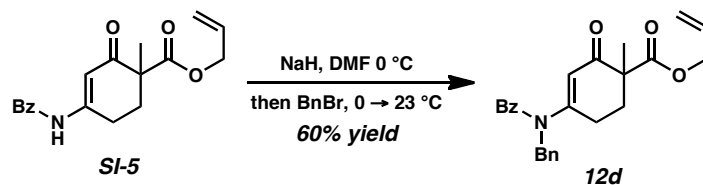
Enaminone SI-4. Adapted from procedure by Buchwald.⁷ CuI (24 mg, 0.13 mmol, 0.10 equiv), Cs_2CO_3 (624 mg, 1.92 mmol, 1.50 equiv) and acetamide (91 mg, 1.5 mmol, 1.2 equiv) were added to a 25 mL Schlenk bomb equipped with a stir bar under argon atmosphere. The Schlenk bomb was evacuated and backfilled 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 $^\circ\text{C}$ 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 \rightarrow 33 \rightarrow 50 \rightarrow 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); ^1H 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 $\text{C}_{13}\text{H}_{18}\text{NO}_4$ $[\text{M}+\text{H}]^+$: 252.1230, found 252.1219.



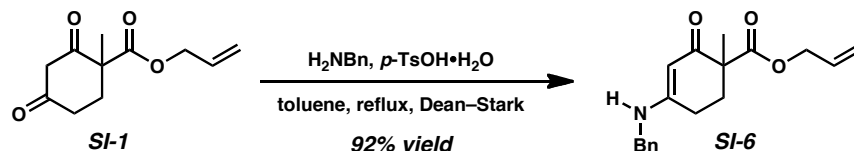
Enaminone 12c. In a 5 mL round bottom flask equipped with a stir bar under nitrogen atmosphere, enaminone **SI-4** (63 mg, 0.25 mmol, 1.0 equiv) was taken up in dry DMF (2.8 mL, 0.089 M) and cooled to 0 °C with an ice/water bath. Sodium hydride (60% suspension in mineral oil, 12 mg, 0.30 mmol, 1.2 equiv) 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 μ L, 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; ^1H 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, 119.0, 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 $\text{C}_{20}\text{H}_{24}\text{O}_4\text{N}$ $[\text{M}+\text{H}]^+$: 342.1700, found 342.1705.



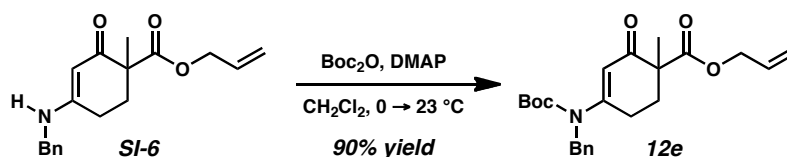
Enaminone SI-5. Adapted from procedure by Buchwald.⁷ Prepared from **SI-3** in an analogous manner to **SI-4**. Purified by flash chromatography (SiO_2 , 12 x 3 cm, 20→33→50% EtOAc in hexanes) to afford enaminone **SI-5** (220 mg, 0.702 mmol, 70% yield) as a pale yellow oil that solidified to a pale yellow amorphous solid upon standing at -20 °C; $R_f = 0.10$ (50% EtOAc in hexanes); ^1H 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 $\text{C}_{18}\text{H}_{20}\text{NO}_4$ $[\text{M}+\text{H}]^+$: 314.1387, found 314.1381.



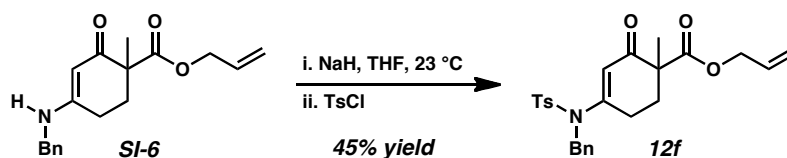
Enaminone 12d. Prepared from **SI-5** in an analogous manner to **12c**. Purified by flash chromatography (SiO_2 , 15 x 3 cm, 20% acetone in hexanes) to afford enaminone **12d** (134 mg, 0.332 mmol, 60% yield) as a yellow oil; $R_f = 0.63$ (50% EtOAc in hexanes); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 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); $^{13}\text{C NMR}$ (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 $\text{C}_{25}\text{H}_{26}\text{NO}_4$ $[\text{M}+\text{H}]^+$: 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); $^1\text{H NMR}$ (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); $^{13}\text{C NMR}$ (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 $\text{C}_{18}\text{H}_{21}\text{NO}_3$ $[\text{M}+\bullet]^+$: 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 (SiO₂, 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); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₂₃H₃₀NO₅ [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 CH₂Cl₂. The combined organics (100 mL) were dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (SiO₂, 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); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) δ 196.0, 171.9, 158.4, 144.8, 135.6, 135.3, 131.7, 130.2, 128.9, 128.1,

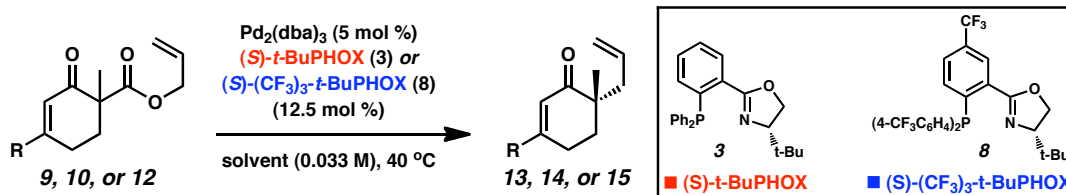
127.6, 127.5, 119.5, 118.5, 65.9, 53.0, 52.2, 32.4, 27.9, 21.8, 20.0; IR (Neat Film NaCl) 3064, 3032, 2981, 2935, 2873, 1735, 1669, 1596, 1496, 1454, 1424, 1359, 1321, 1292, 1255, 1164, 1115, 1089, 1058, 1028, 984, 910, 883, 816, 773, 743 cm^{-1} ; HRMS (MM: ESI-APCI+) m/z calc'd for $\text{C}_{25}\text{H}_{28}\text{NSO}_5$ $[\text{M}+\text{H}]^+$: 454.1683, found 454.1691.

General Procedure for Screening Reactions *Enone 9a Screen Procedure*

$\text{Pd}_2(\text{dba})_3$ (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*)-(CF₃)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 (SiO₂, ~22 x 1 cm, 2%→3% Et₂O in pentane), resuspended in Et₂O 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 ($\text{Pd}_2(\text{dba})_3$, 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.

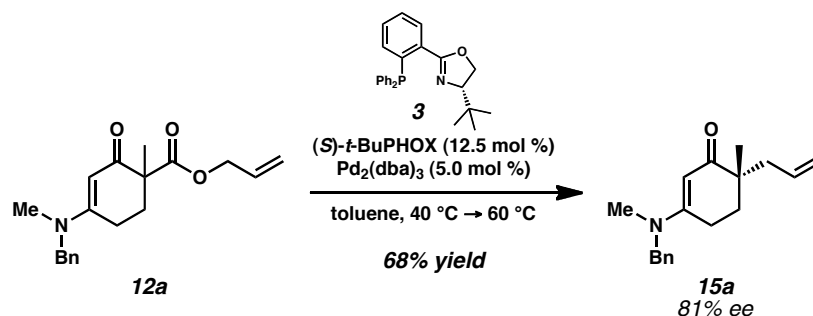
Table SI-1. Enaminone Allylic Alkylation Screen^[a]

entry	Substrate	R	Product	ligand	Enantiomeric Excess (% ee) ^[b]			
					THF	MTBE	Toluene	2:1 Hex-Tol
1	9a	H	13a	3	87	88	87	87
2				8	85	86	88	85
3	10a	<i>O</i> - <i>i</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), $\text{Pd}_2(\text{dba})_3$ (5 mol %), and (*S*)-*t*-BuPHOX (**3**) or (*S*)-(CF₃)₃-*t*-BuPHOX (**8**) (12.5 mol %) in solvent (0.033 M) at 40 °C.

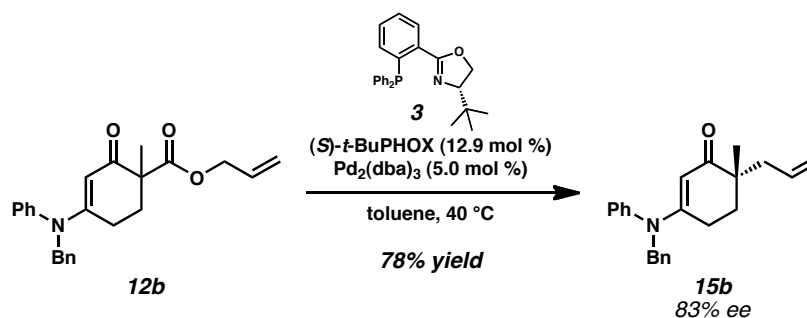
[b] Determined by chiral GC, HPLC, or SFC analysis. Red = with (*S*)-**3** as ligand and blue = with (*S*)-**8** as ligand.

Enaminone Allylic Alkylation Products



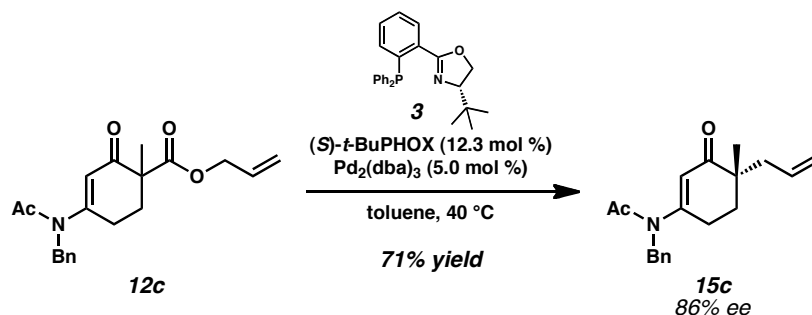
Enaminone 15a. $\text{Pd}_2(\text{dba})_3$ (14.6 mg, 0.0159 mmol, 5.0 mol %) and (*S*)-*t*-BuPHOX (**3**, 15.5 mg, 0.0400 mmol, 12.5 mol %) were added to an oven-dried scintillation vial equipped with a magnetic stir bar and the vial was cycled into a glove box. The vial was charged with toluene (2 mL) 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 (SiO₂, 27.5 x 2 cm, 100% hexanes→20%→30%→50% EtOAc in hexanes→100% EtOAc *then* SiO₂, 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); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₈H₂₃ON [M+•]⁺: 269.1780, found 269.1782; [α]_D^{25.0} -24.18 (c 1.04, CHCl₃, 81% ee); JASCO SFC conditions: 5% MeOH in CO₂, 5 mL/min, Chiralcel OD-H column, λ = 210 nm, t_R (min): major = 10.45, minor = 9.60.

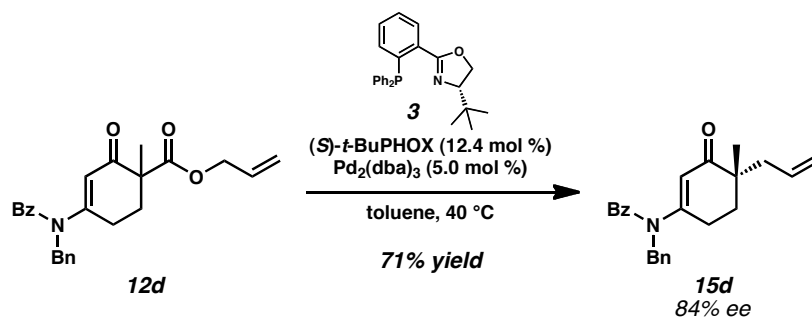


Enaminone 15b. Pd₂(dba)₃ (3.5 mg, 0.00382 mmol, 5.0 mol %) and (S)-*t*-BuPHOX (**3**, 3.8 mg, 0.00981 mmol, 12.9 mol %) were added to an oven-dried scintillation vial equipped with a magnetic stir bar and the vial was cycled into a glove box. The vial was charged with toluene (0.5 mL) and heated at 30 °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 (SiO₂, 19.5 x 1.5 cm, 100% hexanes→50% EtOAc in hexanes→100% EtOAc *then* SiO₂, 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); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₂₃H₂₆ON [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, $\lambda = 254$ nm, t_R (min): major = 8.60, minor = 6.48.

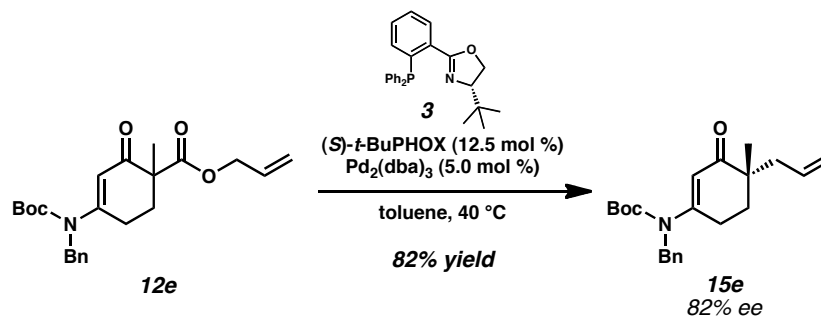


Enaminone 15c. $\text{Pd}_2(\text{dba})_3$ (2.6 mg, 0.00284 mmol, 5.0 mol %) and (S) -*t*-BuPHOX (**3**, 2.7 mg, 0.00697 mmol, 12.3 mol %) were added to an oven-dried scintillation vial equipped with a magnetic stir bar and the vial was cycled into a glove box. The vial was charged with toluene (0.51 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); ^1H 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 $\text{C}_{19}\text{H}_{24}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 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, $\lambda = 254$ nm, t_R (min): major = 8.45, minor = 10.35.



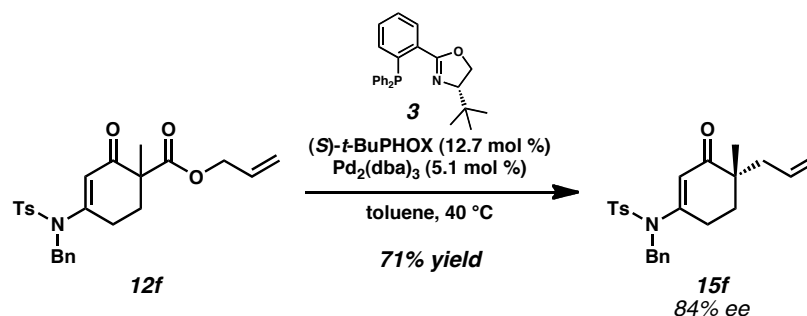
Enaminone 12d. $\text{Pd}_2(\text{dba})_3$ (4.6 mg, 0.00502 mmol, 5.0 mol %) and (S) -*t*-BuPHOX (**3**, 4.8 mg, 0.0124 mmol, 12.4 mol %) were added to an oven-dried scintillation vial equipped with a magnetic stir bar and the vial was cycled into a glove box. The vial was charged with toluene

(0.93 mL) and heated at 30 °C for 30 min, generating a red/orange solution. Enaminone **12d** (1 M in toluene, 100 μ L, 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 (SiO₂, 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); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₂₄H₂₆NO₂ [M+H]⁺: 360.1964, found 360.1956; [α]_D^{25.0} -26.61 (c 1.87, CHCl₃, 84% ee); Thar SFC conditions: 7% MeOH in CO₂, 2.5 mL/min, Chiralpak AD-H column, λ = 254 nm, t_r (min): major = 18.14, minor = 20.28.



Enaminone 15e. Pd₂(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 μ L, 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 (SiO₂, 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); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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

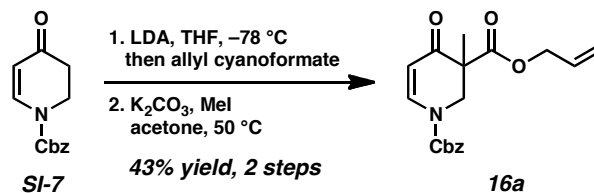
Film NaCl) 3066, 3031, 3004, 2976, 2931, 2868, 1716, 1656, 1598, 1497, 1455, 1428, 1382, 1368, 1350, 1326, 1302, 1243, 1209, 1192, 1153, 1076, 1030, 998, 946, 916, 858, 779, 767, 734 cm^{-1} ; HRMS (MM: ESI-APCI+) m/z calc'd for $\text{C}_{22}\text{H}_{30}\text{O}_3\text{N}$ $[\text{M}+\text{H}]^+$: 356.2229, found 356.2220; $[\alpha]_{\text{D}}^{25.0}$ -23.61 (c 0.92, CHCl_3 , 82% ee); JASCO SFC conditions: 7% MeOH in CO_2 , 5 mL/min, Chiralpak AD-H column, $\lambda = 210$ nm, t_{R} (min): major = 4.04, minor = 2.20.



Enaminone 15f. $\text{Pd}_2(\text{dba})_3$ (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 \rightarrow 5% \rightarrow 10% \rightarrow 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); ^1H 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 $\text{C}_{24}\text{H}_{28}\text{O}_3\text{NS}$ $[\text{M}+\text{H}]^+$: 410.1784, found 410.1792; $[\alpha]_{\text{D}}^{25.0}$ -33.05 (c 0.37, CHCl_3 , 84% ee); JASCO SFC conditions: 10% MeOH, 5 mL/min, AD-H column, $\lambda = 210$ nm, t_{R} (min): major = 5.60, minor = 4.73.

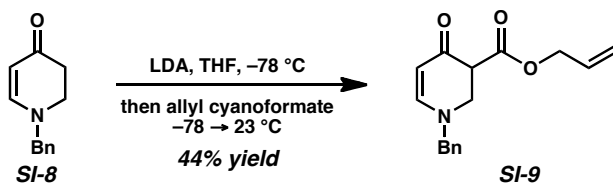
Procedures for the Preparation of 2,3-Dihydropyridin-4-ones

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

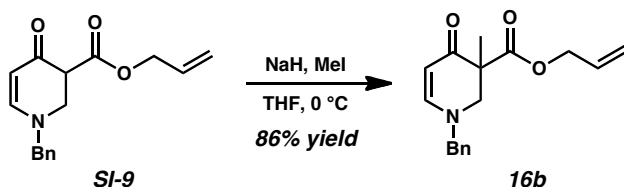


2,3-Dihydropyridin-4-one 16a. A 100 mL round-bottom flask equipped with a magnetic stir bar was charged with diisopropyl amine (442 μL , 3.01 mmol, 1.20 equiv) and THF (28 mL). The flask was cooled to $-78\text{ }^\circ\text{C}$ bath (Dry ice/IPA) and *n*-BuLi (1.30 mL, 3.01 mmol, 2.32 M in hexanes, 1.20 equiv) was added. The reaction was allowed to warm to $0\text{ }^\circ\text{C}$ over 1 h. The solution was cooled back to $-78\text{ }^\circ\text{C}$ 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 $-78\text{ }^\circ\text{C}$ 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).

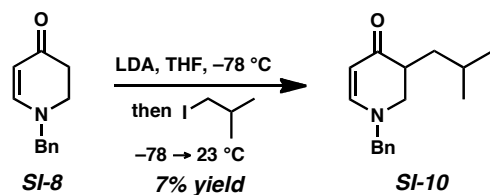
The yellow oil was transferred to an argon filled 25 mL Schlenk tube equipped with a magnetic stir bar using several acetone rinses (3 x 2 mL). K_2CO_3 (252 mg, 1.83 mmol, 2.0 equiv) and methyl iodide (115 μL , 1.84 mmol, 2.02 equiv) were added to the reaction. The resulting suspension was heated to $50\text{ }^\circ\text{C}$ 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); ^1H 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 $\text{C}_{18}\text{H}_{19}\text{NO}_5$ $[\text{M}+\text{H}]^+$: 330.1335, found 330.1335.



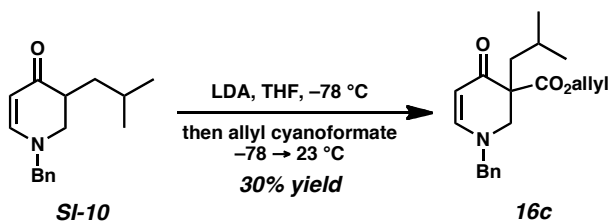
2,3-Dihydropyridin-4-one SI-9. To a flame-dried 50 mL Schlenk round-bottom flask equipped with a magnetic stir bar was added 2,3-Dihydropyridin-4-one **SI-8**¹⁰ (162.0 mg, 0.87 mmol) and THF (10 mL). The solution was cooled to $-78\text{ }^{\circ}\text{C}$ and LDA (0.1 M in THF, 9.10 mL, 0.91 mmol, 1.05 equiv) was added dropwise by syringe. After 1 h at $-78\text{ }^{\circ}\text{C}$, 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 , filtered, and concentrated under reduced pressure. The resulting crude mixture was purified by flash chromatography (SiO_2 , 10 x 2.5 cm, 30% EtOAc \rightarrow 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); ^1H 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 $\text{C}_{16}\text{H}_{18}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 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 $0\text{ }^{\circ}\text{C}$. 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 $0\text{ }^{\circ}\text{C}$ 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); ^1H 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 $\text{C}_{17}\text{H}_{20}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 286.1443, found 286.1480.

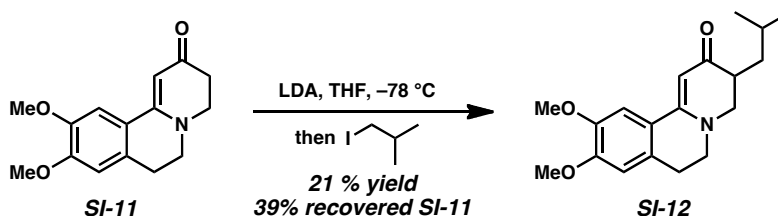


2,3-Dihydropyridin-4-one SI-10. To a flame-dried 100 mL Schlenk round-bottom flask equipped with a magnetic stir bar was added 2,3-Dihydropyridin-4-one **SI-8**¹⁰ (0.68 g, 3.63 mmol) and THF (30 mL). The solution was cooled to $-78\text{ }^\circ\text{C}$ and LDA (19.0 mL, 3.80 mmol, 1.05 equiv, 0.2 M in THF) was added dropwise by syringe. After 1 h at $-78\text{ }^\circ\text{C}$, 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 $-78\text{ }^\circ\text{C}$, 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 , filtered, 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); $^1\text{H NMR}$ (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); $^{13}\text{C NMR}$ (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 $\text{C}_{16}\text{H}_{22}\text{NO}$ $[\text{M}+\text{H}]^+$: 244.1701, found 244.1707.

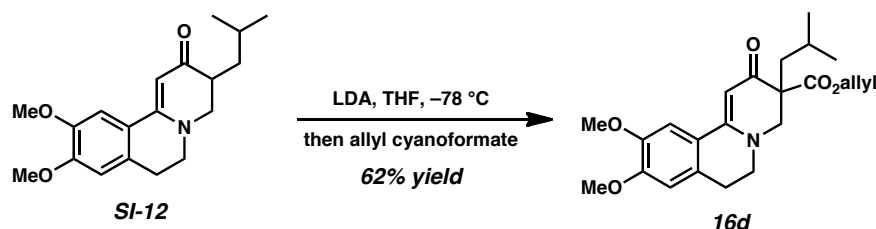


2,3-Dihydropyridin-4-one 16c. To a flame-dried 25 mL Schlenk tube equipped with a magnetic stir bar was added 2,3-Dihydropyridin-4-one **SI-10** (50.5 mg, 0.21 mmol) and THF (5 mL). After the solution was cooled to $-78\text{ }^\circ\text{C}$, LDA (2.2 mL, 0.22 mmol, 1.06 equiv, 0.1 M in THF) was added dropwise by syringe. The mixture was stirred for 1 h at $-78\text{ }^\circ\text{C}$ 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); $^1\text{H NMR}$ (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); $^{13}\text{C NMR}$ (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 $\text{C}_{20}\text{H}_{26}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 328.1913, found 328.1947.



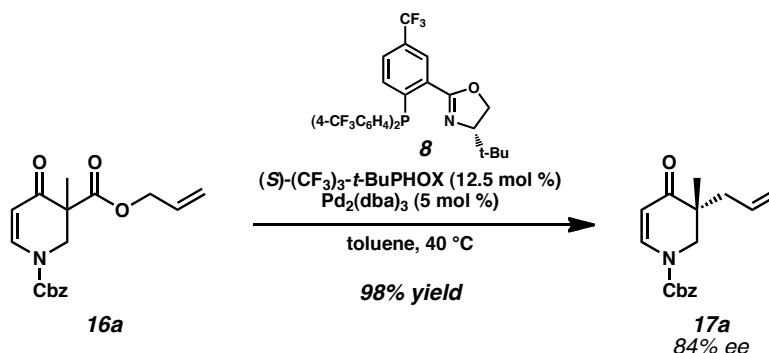
2,3-Dihydropyridin-4-one SI-12. To a cooled ($-78\text{ }^\circ\text{C}$) solution of **SI-11**¹¹ (0.67 g, 2.6 mmol, 1 equiv) in THF (25 mL) was added LDA (30 mL, 0.1 M, in THF, 30 mmol, 1.15 equiv) dropwise over 10 min. The reaction was stirred for one hour before 1-iodo-2-methylpropane (0.57 g, 3.1 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 \rightarrow 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. ^1H 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.



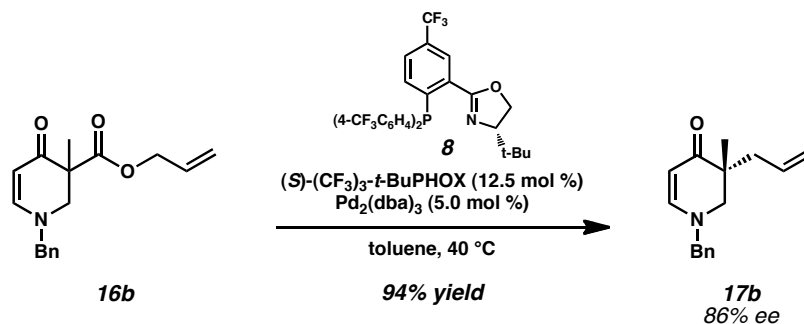
2,3-Dihydropyridin-4-one 16d. A solution of **SI-12** (149.1 mg, 0.47 mmol in 15 mol of THF) was cooled to $-78\text{ }^\circ\text{C}$ and LDA (5.2 mL, 0.1 M in THF, 0.52 mmol, 1.10 equiv) was added dropwise. The reaction was stirred for one hour before allyl cyanoformate (60.2 mg, 0.54 mmol, 1.15 equiv) 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); ^1H 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 $\text{C}_{23}\text{H}_{30}\text{NO}_5$ $[\text{M}+\text{H}]^+$: 400.2124, found 400.2110.

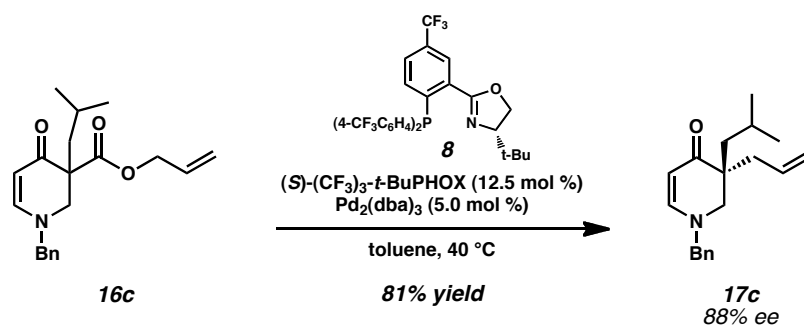
2,3-Dihydropyridin-4-one Allylic Alkylation Products



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 $(S)\text{-(CF}_3)_3\text{-t-Bu-PHOX}$ (**8**, 4.1 mg, 10.5 μmol , 0.125 equiv), $\text{Pd}_2(\text{dba})_3$ (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 $30\text{ }^\circ\text{C}$ 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 $40\text{ }^\circ\text{C}$ 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); $^1\text{H NMR}$ (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); $^{13}\text{C NMR}$ (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 $\text{C}_{17}\text{H}_{19}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 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, $\lambda = 254$ nm, t_R (min): major = 2.80, minor = 3.13.

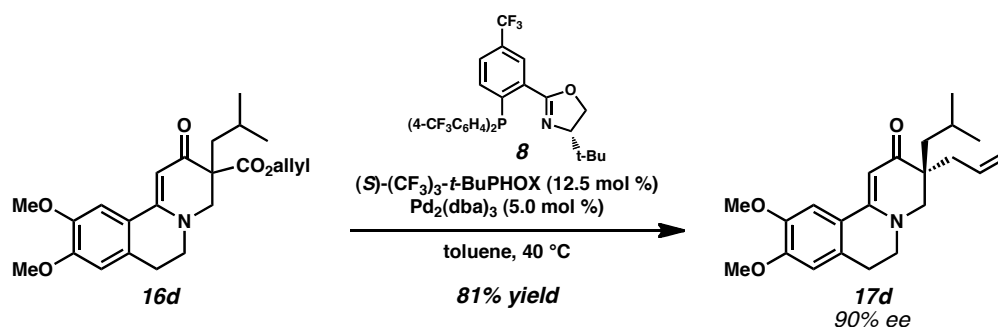


2,3-Dihydropyridin-4-one 17b. In a glove box, $\text{Pd}_2(\text{dba})_3$ (2.3 mg, 0.0025 mmol, 5.0 mol %) and $(S)\text{-(CF}_3)_3\text{-}t\text{-BuPHOX}$ (**8**, 3.7 mg, 0.00625 mmol, 12.5 mol %) were added to a scintillation vial equipped with a stir bar. The vial was charged with toluene (0.5 mL) 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); $^1\text{H NMR}$ (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); $^{13}\text{C NMR}$ (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 $\text{C}_{18}\text{H}_{20}\text{NO}$ $[\text{M}+\text{H}]^+$: 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, $\lambda = 210$ nm, t_R (min): major = 18.77, minor = 21.21.



2,3-Dihydropyridin-4-one 17c. In a glove box, $\text{Pd}_2(\text{dba})_3$ (1.4 mg, 0.0015 mmol, 5.0 mol %) and $(S)\text{-(CF}_3)_3\text{-}t\text{-BuPHOX}$ (**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; $R_f = 0.30$ (30% EtOAc in hexanes); $^1\text{H NMR}$ (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); $^{13}\text{C NMR}$ (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 $\text{C}_{18}\text{H}_{20}\text{NO}$ $[\text{M}+\text{H}]^+$: 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, $\lambda = 210$ nm, t_R (min): major = 18.77, minor = 21.21.

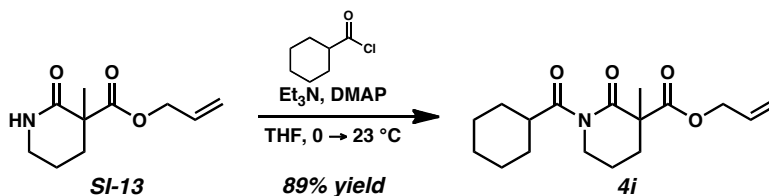
yield) as a yellow oil; $R_f = 0.40$ (30% EtOAc in hexanes); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.45–7.32 (m, 3H), 7.29–7.22 (m, 2H), 7.05 (d, $J = 7.4$ Hz, 1H), 5.62 (dddd, $J = 17.1, 10.1, 7.8, 7.0$ Hz, 1H), 5.00 (ddt, $J = 10.1, 2.1, 1.0$ Hz, 1H), 4.97–4.91 (m, 2H), 4.33 (s, 2H), 3.13 (d, $J = 3.2$ 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); $^{13}\text{C NMR}$ (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 $\text{C}_{19}\text{H}_{26}\text{NO}$ $[\text{M}+\text{H}]^+$: 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, $\lambda = 210$ nm, t_R (min): major = 11.44, minor = 14.80.



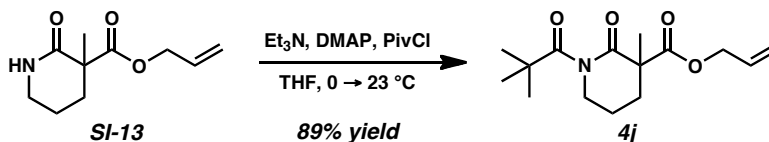
2,3-Dihydropyridin-4-one 17d. $\text{Pd}_2(\text{dba})_3$ (1.4 mg, 0.0015 mmol, 5.0 mol %) and $(S)\text{-(CF}_3)_3\text{-}t\text{-BuPHOX}$ (**8**, 2.2 mg, 0.00375 mmol, 12.5 mol %) were added to an oven-dried Schlenk tube equipped with a magnetic stir bar and the tube was cycled with vacuum/argon for 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 dihydropyridin-4-one **17d** (8.6 mg, 0.0242 mmol, 81% yield) as yellow oil; $R_f = 0.50$ (50% EtOAc in hexanes); $^1\text{H NMR}$ (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); $^{13}\text{C NMR}$ (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 $\text{C}_{22}\text{H}_{30}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 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, $\lambda = 254$ nm, t_R (min): major = 21.87, minor = 18.59.

Procedures for the Preparation of Lactams

Lactam Allylic Alkylation Precursors



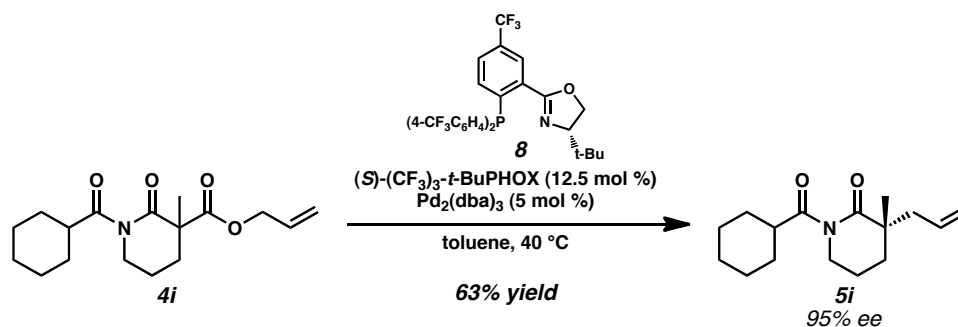
Lactam 4i. Lactam **SI-13**¹³ (117.8 mg, 0.597 mmol, 1.00 equiv) was transferred to a flame-dried 15 mL round-bottom flask using THF (4 x 0.5 mL + 1 x 0.4 mL rinses, total = 2.4 mL, 0.25 M). Et₃N (250 μ L, 1.79 mmol, 3.00 equiv) and DMAP (9.3 mg, 0.0761 mmol, 13 mol%) were added and the flask was lowered into a 0 $^\circ$ C bath (ice/water). Cyclohexanecarbonyl chloride (160 μ L, 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 Na₂SO₄, filtered, and concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography (SiO₂, 27.5 x 2 cm, 100% hexanes \rightarrow 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); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₇H₂₆O₄N [M+H]⁺: 308.1856, found 308.1871.



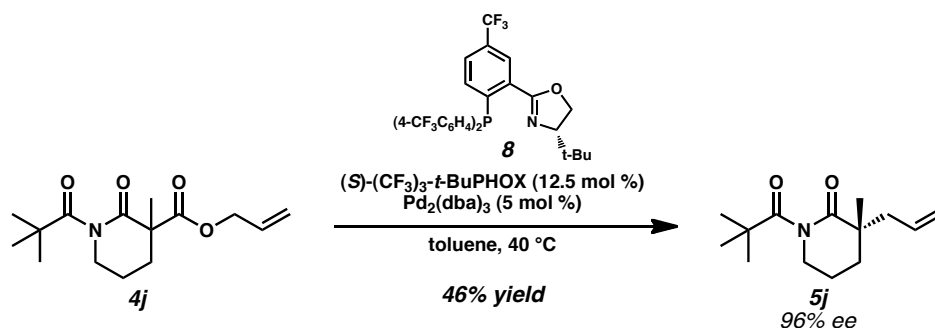
Lactam 4j. Lactam **SI-13**⁹ (480 mg, 2.4 mmol, 1.0 equiv) in a 25 mL round-bottom flask equipped with a magnetic stir bar was taken up in THF (9.6 mL, 0.25 M). Et₃N (1.0 mL, 7.2 mmol, 3.0 equiv) and DMAP (29 mg, 0.24 mmol, 0.10 equiv) were added and the flask was lowered into a 0 $^\circ$ C bath (ice/water). 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 Na₂SO₄, filtered, and concentrated under

reduced pressure. The resulting crude oil was purified by flash column chromatography (SiO₂, 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); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₅H₂₄NO₄ [M+H]⁺: 282.1700, found 282.1705.

Lactam Allylic Alkylation Products



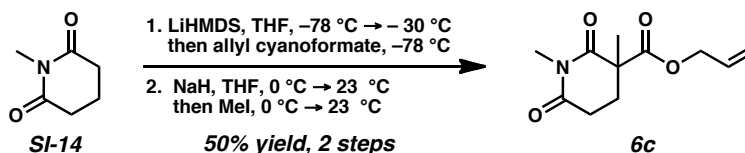
Lactam 5i. Pd₂(dba)₃ (16.4 mg, 0.0150 mmol, 5.0 mol %) and (S)-(CF₃)₃-*t*-BuPHOX (**8**, 22.1 mg, 0.0374 mmol, 12.5 mol %) were added to an oven-dried scintillation vial equipped with a magnetic stir bar and the vial was cycled into a glove box. The vial was charged with toluene (2.06 mL) and stirred 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 (SiO₂, 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); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₆H₂₆O₂N [M+H]⁺: 264.1958, found 264.1945; [α]_D^{25.0} –96.13 (c 1.06, CHCl₃, 95% ee); JASCO SFC conditions: 1% IPA in CO₂, 5 mL/min, Chiralcel OJ-H column, λ = 222 nm, *t_R* (min): major = 2.53, minor = 2.13.



Lactam 5j. $\text{Pd}_2(\text{pmdba})_3$ (27 mg, 25 μmol , 5.0 mol %) and $(S)\text{-(CF}_3)_3\text{-}t\text{-BuPHOX}$ (**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); $^1\text{H NMR}$ (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); $^{13}\text{C NMR}$ (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 $\text{C}_{14}\text{H}_{23}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 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, $\lambda = 210$ nm, t_R (min): major = 7.95, minor = 6.52.

Procedures for the Preparation of Imides

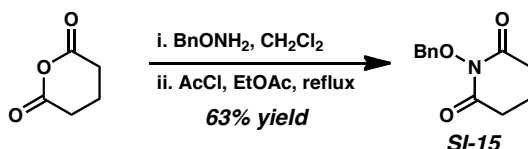
Imide Allylic Alkylation Precursors



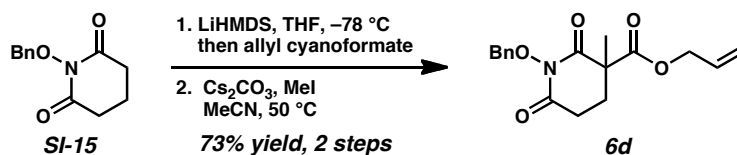
N-Methyl imide 6c. A flame-dried 200 mL round-bottom flask containing a magnetic stir bar was cycled into a glove box and loaded with LiHMDS (5.69 g, 34.0 mmol, 1.7 equiv). The flask was removed from the glove box, reconnected to a manifold, and charged with THF (100 mL, 0.2 M) and lowered into a $-78\text{ }^\circ\text{C}$ bath. Imide **SI-14**¹⁴ (2.54 g, 20.0 mmol, 1.0 equiv) was added neat. After 1 h at $-78\text{ }^\circ\text{C}$, the solution was warmed to $30\text{ }^\circ\text{C}$ and stirred for 30 min before cooling back to $-78\text{ }^\circ\text{C}$. 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 (SiO₂, 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.

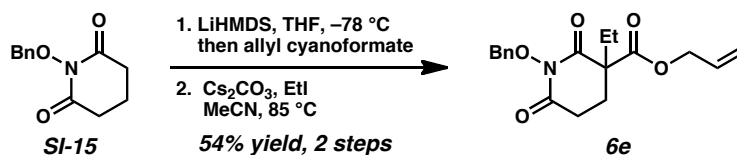
A flame-dried 200 mL flask equipped with a magnetic stir bar was charged with sodium hydride (60% in mineral oil, 312.5 mg, 7.81 mmol, 1.1 equiv) and THF (71 mL, 0.1 M) and cooled to 0 °C. A portion of the oil from the previous step (1.5 g, 7.10 mmol, 1.0 equiv) was added neat. After 1.5 h at 0 °C, the 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 Na₂S₂O₃ sol. (sat. solution half diluted) and twice with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography (SiO₂, 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); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₁H₁₇NO₄ [M+H]⁺: 226.1074, found 226.1078.



***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 K₂CO₃ (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 Na₂SO₄, 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 Na₂SO₄, filtered, and concentrated under reduced pressure. The crude solid was purified by flash column chromatography (SiO₂, 6 x 5 cm, 20% EtOAc in hexanes→50% Et₂O 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% Et₂O in methylene chloride); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₂H₁₃NO₃ [M+H]⁺: 220.0968, found 220.0971.

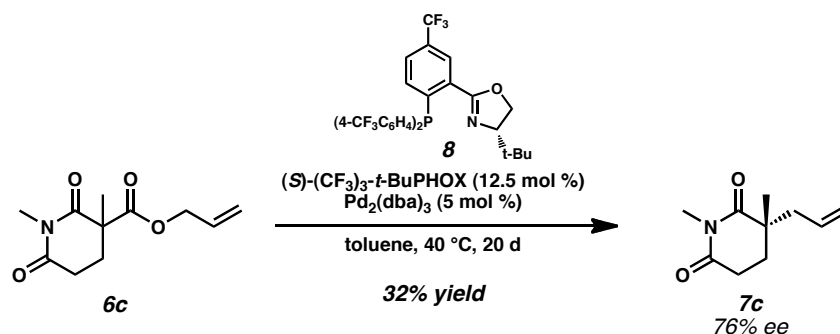


***N*-Benzyloxy imide 6d.** Acylation performed in manner analogous to *N*-methyl imide **6c** at -78 °C using *N*-benzyloxy imide **SI-15** as starting material. Alkylation performed in manner analogous to β -ketoester **18a** at 50 °C. *N*-Benzyloxy imide **6d** was isolated after flash column chromatography (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); $^1\text{H NMR}$ (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); $^{13}\text{C NMR}$ (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 $\text{C}_{17}\text{H}_{20}\text{NO}_5$ $[\text{M}+\text{H}]^+$: 318.1336, found 318.1339.

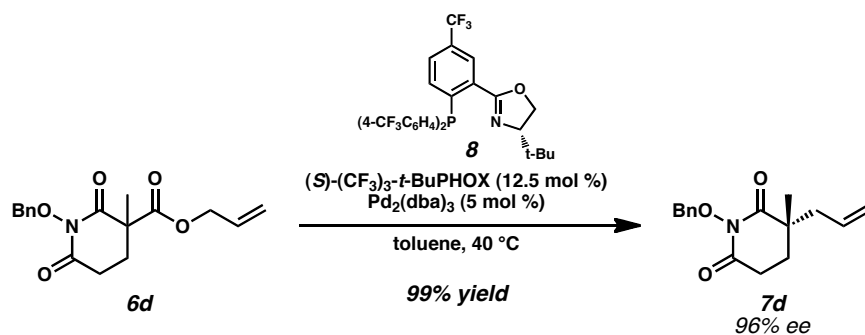


***N*-Benzyloxy imide 6e.** Acylation performed in manner analogous to *N*-methyl imide **6c** at -78 °C using *N*-benzyloxy imide **SI-15** as starting material. Alkylation performed in manner analogous to β -ketoester **18a** at 85 °C using ethyl iodide. *N*-Benzyloxy imide **6e** was isolated after 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); $^1\text{H NMR}$ (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); $^{13}\text{C NMR}$ (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 $\text{C}_{18}\text{H}_{22}\text{NO}_5$ $[\text{M}+\text{H}]^+$: 332.1492, found 332.1493.

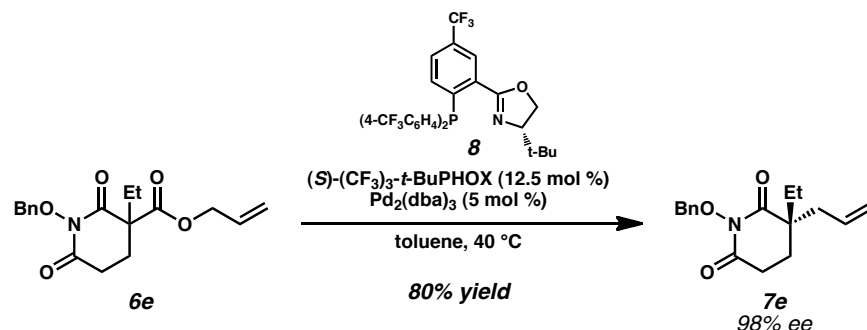
Imide Allylic Alkylation Products



***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 (SiO₂, 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); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₀H₁₆NO₂ [M+H]⁺: 182.1176, found 182.1178; [α]_D^{25.0} -54.19 (c 1.64, CHCl₃, 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.



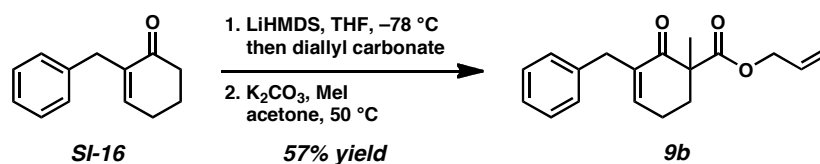
***N*-Benzyloxy imide 7d.** Prepared in a manner analogous to lactam **5h** using *N*-benzyloxy imide **6d** as starting material. *N*-Benzyloxy imide **7d** was isolated after flash column chromatography (SiO₂, 20% EtOAc in hexanes) as a colorless oil (99% yield); *R_f* = 0.29 (20% EtOAc in hexanes); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₆H₂₀NO₃ [M+H]⁺: 274.1438, found 274.1437; [α]_D^{25.0} -58.59 (c 1.26, CHCl₃, 96% ee); Thar SFC conditions: 5% MeOH in CO₂, 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); ^1H 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 $\text{C}_{17}\text{H}_{22}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 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, $\lambda = 210$ nm, t_R (min): major = 14.34, minor = 13.39.

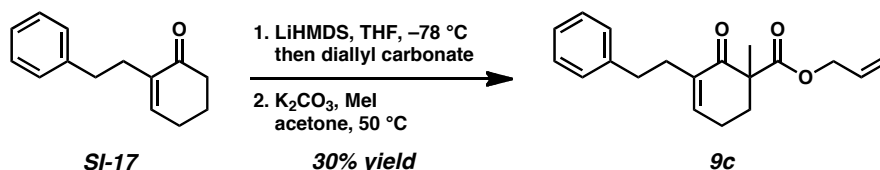
Procedures for the Preparation of Enones and Diosphenol Ethers

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 \rightarrow 5% \rightarrow 10% EtOAc in hexanes) to afford a yellow oil.

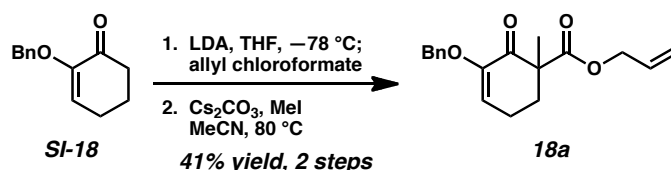
The resulting yellow oil (285.8 mg, 1.06 mmol, 1.00 equiv) was transferred to an Ar-filled 25 mL Schlenk bomb (14/20 joint off of an 8 mm Kontes valve) equipped with a magnetic stir bar using several acetone rinses (1 x 1.5 mL + 3 x 0.5 mL, total added = 3 mL, 0.35 M). K_2CO_3 (292.7 mg, 2.12 mmol, 2.00 equiv) and methyl iodide (180 μ L, 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, 1H NMR analysis indicated residual starting material, and consequently more methyl iodide (130 μ L, total added = 310 μ L, 4.98 mmol, 4.71 equiv) was added. After an additional 8.5 hours, no starting material remained by 1H 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 \rightarrow 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); 1H 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.



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 μ L, 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 \rightarrow 5% EtOAc in hexanes) to afford a yellow oil.

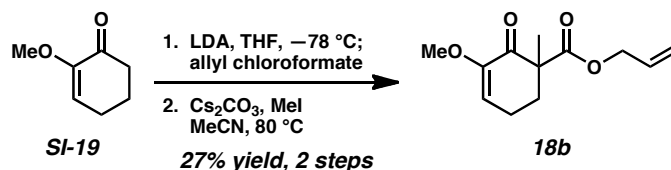
The resulting yellow oil (84.6 mg, 0.298 mmol, 1.00 equiv) was transferred to an Ar-filled 25 mL Schlenk bomb (14/20 joint off of an 8 mm Kontes valve) equipped with a magnetic stir bar using several acetone rinses (4 x 0.5 mL, total added = 2 mL, 0.15 M). K_2CO_3 (87.0 mg, 0.630 mmol, 2.12 equiv) and methyl iodide (100 μ L, 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, ¹H 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 ¹H 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 CH₂Cl₂ and concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography (SiO₂, 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); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₉H₂₃O₃ [M+H]⁺: 299.1642, found 299.1638.



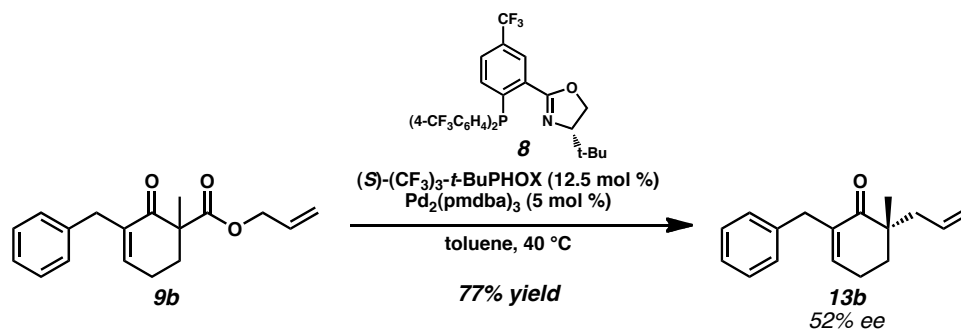
β-ketoester 18a. Diisopropylamine (390 μL, 2.78 mmol, 4.46 equiv) in a 10 mL round-bottom flask equipped with a magnetic stir bar was taken up in 2.0 mL THF and lowered into a 0 °C bath (ice/water). To the stirring solution was added *n*-butyl lithium (4.7 M solution in hexanes, 0.583 mL, 2.74 mmol, 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 NH₄Cl 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 MgSO₄, 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. Cs₂CO₃ (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 (SiO₂, 12 x 1.5 cm, 20% Et₂O 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% Et₂O in hexanes); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₈H₂₀O₄ [M+H]⁺: 301.1434, found 301.1422.

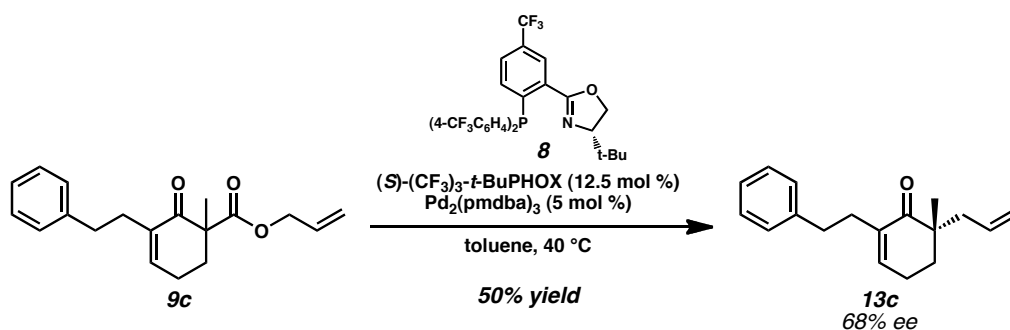


Diosphenol ether 18b. Prepared from SI-19¹⁷ in an analogous manner to 18a. Purified by flash chromatography (SiO₂, 15 x 3 cm, 20→40% Et₂O in hexanes) to afford diosphenol ether 18b (57 mg, 0.25 mmol, 27% yield over two steps) as a colorless oil; $R_f = 0.54$ (50% EtOAc in hexanes); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₂H₁₇O₄ [M+H]⁺: 225.1121, found 225.1122.

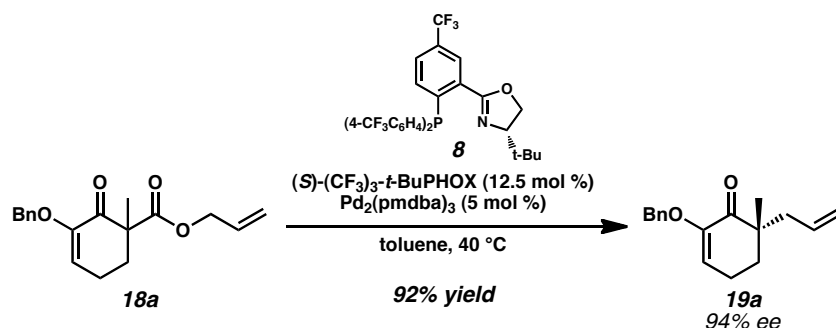
Diosphenol Ether and Enone Allylic Alkylation Products



Enone 13b. Prepared from 9b in an analogous manner to 19a. Purified by flash column chromatography (SiO₂, 12 x 2 cm, 10→20% Et₂O 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% Et₂O in hexanes); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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, CHCl₃, 52% ee); HRMS (MM: ESI-APCI+) m/z calc'd for C₁₇H₂₀O [M+H]⁺: 241.1587, found 241.1575; JASCO SFC conditions: 3% MeOH in CO₂, 5 mL/min, Chiralcel OJ-H column, λ = 210 nm, t_R (min): major = 2.40, minor = 2.11.

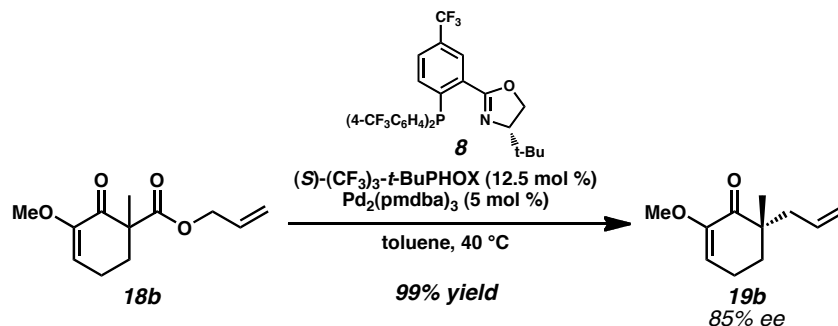


Enone 13b. Prepared from **9c** in an analogous manner to **19a**. Purified by flash column chromatography (SiO_2 , 12 x 2 cm, 10 \rightarrow 20% Et_2O in hexanes) to afford enone **13c** (17 mg, 67 μmol , 50% yield) as a colorless oil and recovered enone **9c** (8 mg, 20% recovered); $R_f = 0.73$ (40% Et_2O in hexanes); $^1\text{H NMR}$ (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); $^{13}\text{C NMR}$ (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 $\text{C}_{18}\text{H}_{22}\text{O}$ $[\text{M}+\text{H}]^+$: 255.1743, found 255.1730; JASCO SFC conditions: 3% MeOH in CO_2 , 5 mL/min, Chiralcel OJ-H column, $\lambda = 210$ nm, t_R (min): major = 2.41, minor = 2.17.



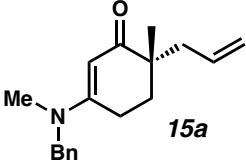
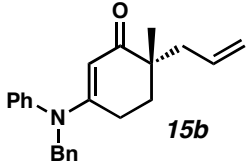
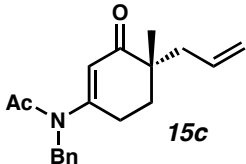
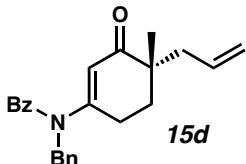
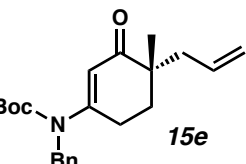
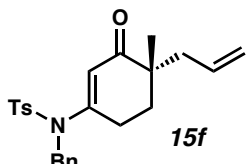
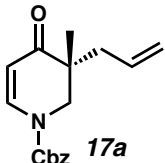
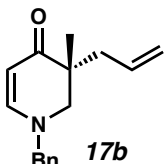
Diosphenol ether 19a. $\text{Pd}_2(\text{pmdba})_3$ (4.2 mg, 3.8 μmol , 5.0 mol %) and $(S)\text{-(CF}_3)_3\text{-}t\text{-BuPHOX}$ (**8**, 5.7 mg, 9.6 μmol , 12.5 mol %) were added to an oven-dried 2-dram vial equipped with a magnetic stir bar in a glove box. The vial was charged with toluene (1.8 mL) 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% \rightarrow 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); $^1\text{H NMR}$ (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

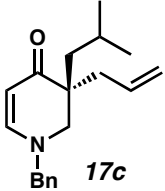
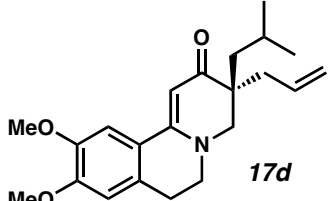
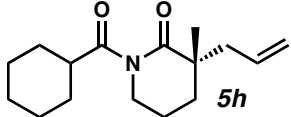
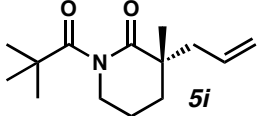
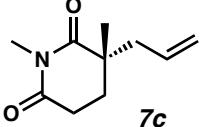
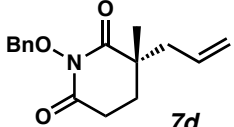
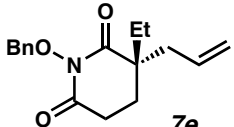
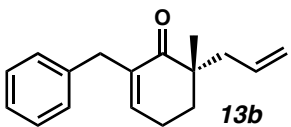
NMR (125 MHz, CDCl₃) δ 198.5, 149.0, 136.8, 134.1, 128.6, 127.9, 127.4, 118.4, 118.0, 70.0, 45.4, 41.2, 33.1, 21.9, 20.9; IR (Neat Film NaCl) 2918, 2360, 1684, 1628, 1457, 1220, 1204, 1094, 1050, 914, 736 cm⁻¹; $[\alpha]_D^{25.0}$ -12.01 (c 0.50, CHCl₃, 94% ee); HRMS (MM: ESI-APCI) m/z calc'd for C₁₇H₂₀O₂ [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.

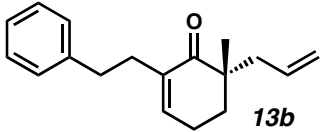
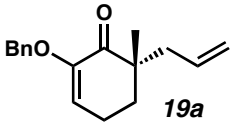
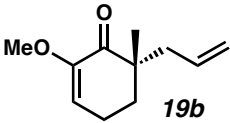


Diosphenol ether 19b. Prepared from **18b** in an analogous manner to **19a**. Purified by flash column chromatography (SiO₂, 10 x 3 cm, 5→10% Et₂O in hexanes) to afford diosphenol ether **19b** (111 mg, 0.616 mmol, 99% yield) as a colorless oil; R_f = 0.23 (40% Et₂O in hexanes); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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, CHCl₃, 85% ee); HRMS (MM: ESI-APCI+) m/z calc'd for C₁₁H₁₇O₂ [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

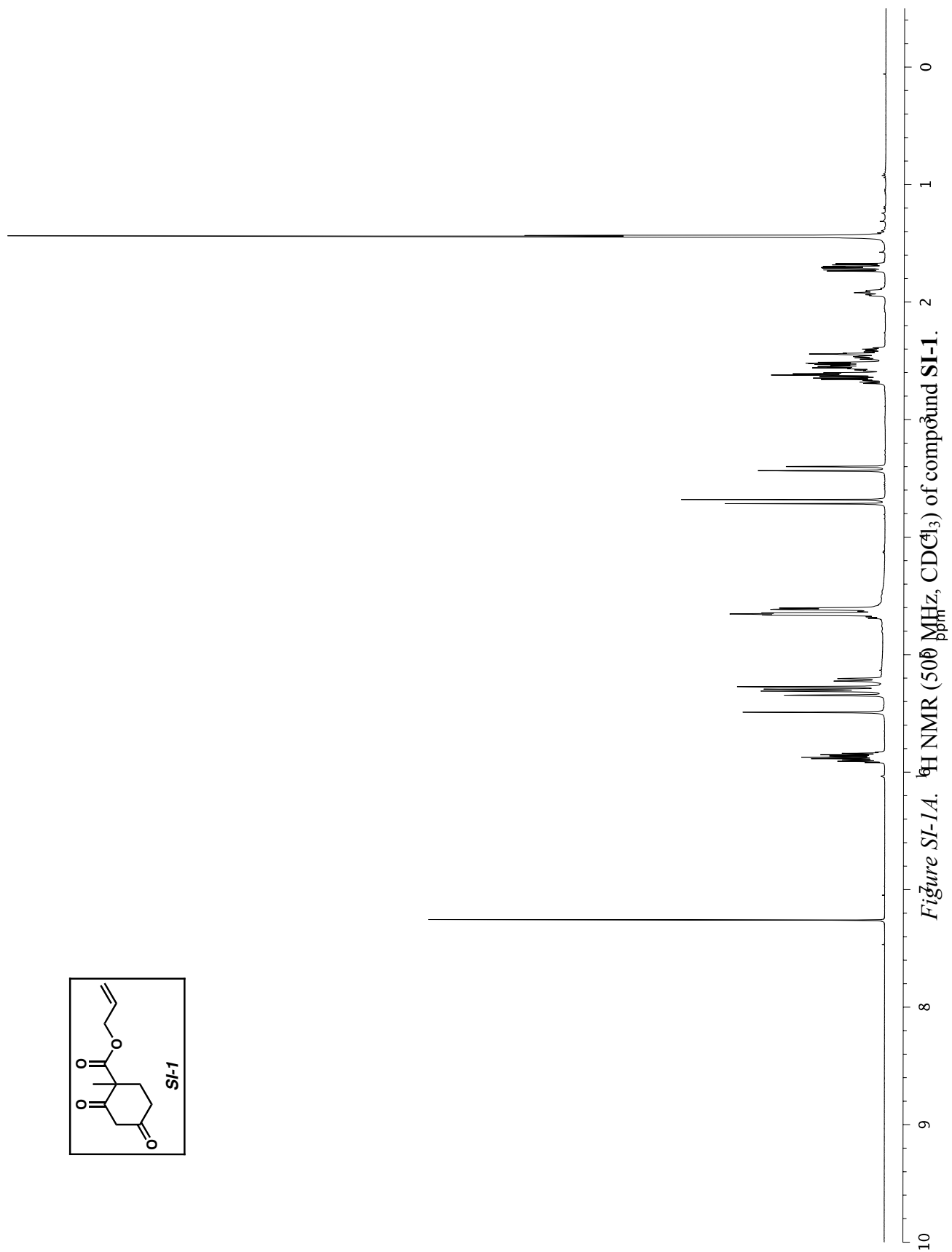
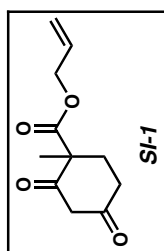
entry	product	assay conditions	retention time of major isomer (min)	retention time of minor isomer (min)	% ee
1	 15a	SFC Chiralcel OD-H 5% MeOH in CO ₂ isocratic, 5.0 mL/min 210 nm	10.45	9.60	81
2	 15b	SFC Chiralpak AS-H 5% MeOH in CO ₂ isocratic, 5.0 mL/min 254 nm	8.60	6.48	83
3	 15c	SFC Chiralpak AD-H 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

References

- [1] A. M. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen, F. J. Timmers, *Organometallics* **1996**, *15*, 1518–1520.
- [2] a) K. Tani, D. C. Behenna, R. M. McFadden, B. M. Stoltz, *Org. Lett.* **2007**, *9*, 2529–2531; b) M. R. Krout, J. T. Mohr, B. M. Stoltz, *Org. Synth.* **2009**, *86*, 181–193.
- [3] N. T. McDougal, J. Streuff, H. Mukherjee, S. C. Virgil, B. M. Stoltz, *Tetrahedron Lett.* **2010**, *51*, 5550–5554.
- [4] D. M. X. Donnelly, J.-P. Finet, B. A. Rattigan, *J. Chem. Soc. Perkin Trans. 1* **1993**, 1729–1735.
- [5] A. Y. Hong, M. R. Krout, T. Jensen, N. B. Bennett, A. M. Harned, B. M. Stoltz, *Angew. Chem. Int. Ed.* **2011**, *50*, 2756–2760.
- [6] E. Piers, J. R. Grierson, C. K. Lau, I. Nagakura, *Can. J. Chem.* **1982**, *60*, 210–223.
- [7] A. Kiapars, X. Huang, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 7421–7428.
- [8] a) D. C. Behenna, B. M. Stoltz, *J. Am. Chem. Soc.* **2004**, *126*, 15044–15045; b) J. T. Mohr, D. C. Behenna, A. M. Harned, B. M. Stoltz, *Angew. Chem. Int. Ed.* **2005**, *44*, 6924–6927.
- [9] R. Sebesta, M. G. Pizzuti, A. J. Boersma, A. J. Minnaard, B. L. Feringa, *Chem. Commun.* **2005**, 1711–1713.
- [10] P. Guerry, R. Neier, *Synthesis* **1984**, 485–488.
- [11] (a) A. C. Flick, A. Padwa, *Tetrahedron Lett.* **2008**, *49*, 5739–5741; (b) A. C. Flick, A. Padwa, *ARKIVOC* **2009**, 4–14.
- [12] B. H. Lee, M. F. Clothier and D. A. Pickering, *Tetrahedron Lett.* **1997**, *38*, 6119–6122.
- [13] D. C. Behenna, Y. Liu, T. Yurino, J. Kim, D. E. White, S. C. Virgil, B. M. Stoltz, *Nature Chem.* **2012**, *4*, 130–133.
- [14] C. M. Marson, A. Khan, R. A. Porter, *J. Org. Chem.* **2001**, *66*, 4771–4775.
- [15] E. i. Negishi, Z. Tan, S.-Y. Liou, B. Liao, *Tetrahedron* **2000**, *56*, 10197–10207.
- [16] A. A. Ponaras, Md. Y. Meah, *Tetrahedron Lett.* **1986**, *27*, 4953–4956.
- [17] G. G. Habermehl, I. Wippermann, *Zeitschrift fuer Naturforschung, B.: Chemical Sciences* **1991**, *46*, 1421–1424.



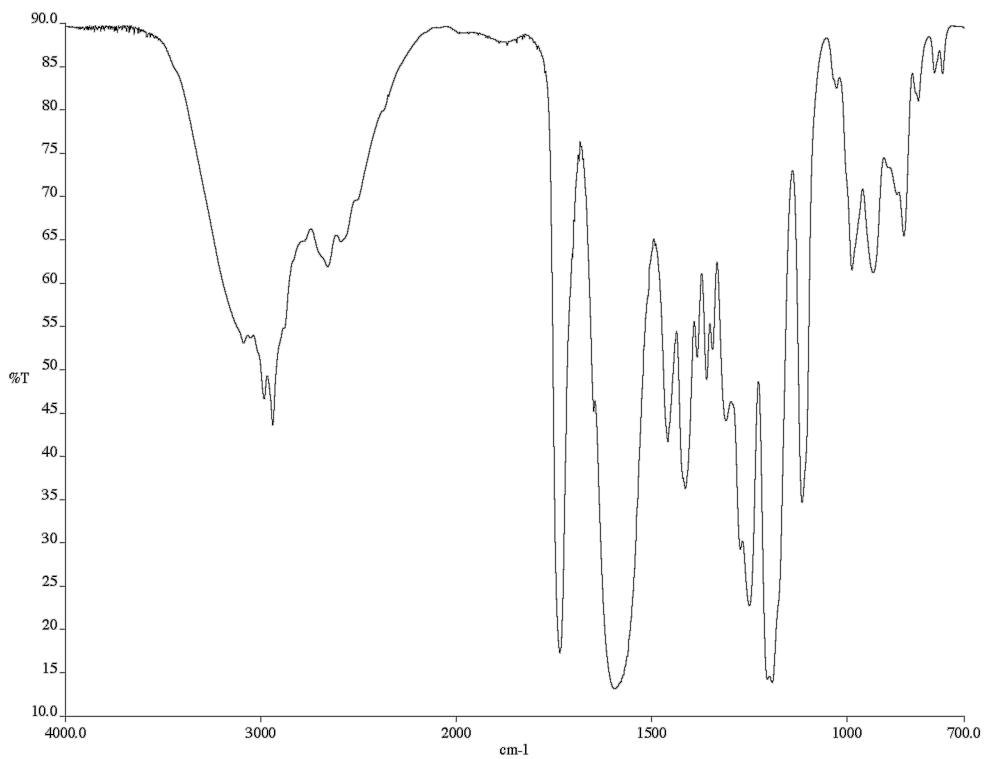


Figure SI-1B. Infrared spectrum (thin film/NaCl) of compound **SI-1**.

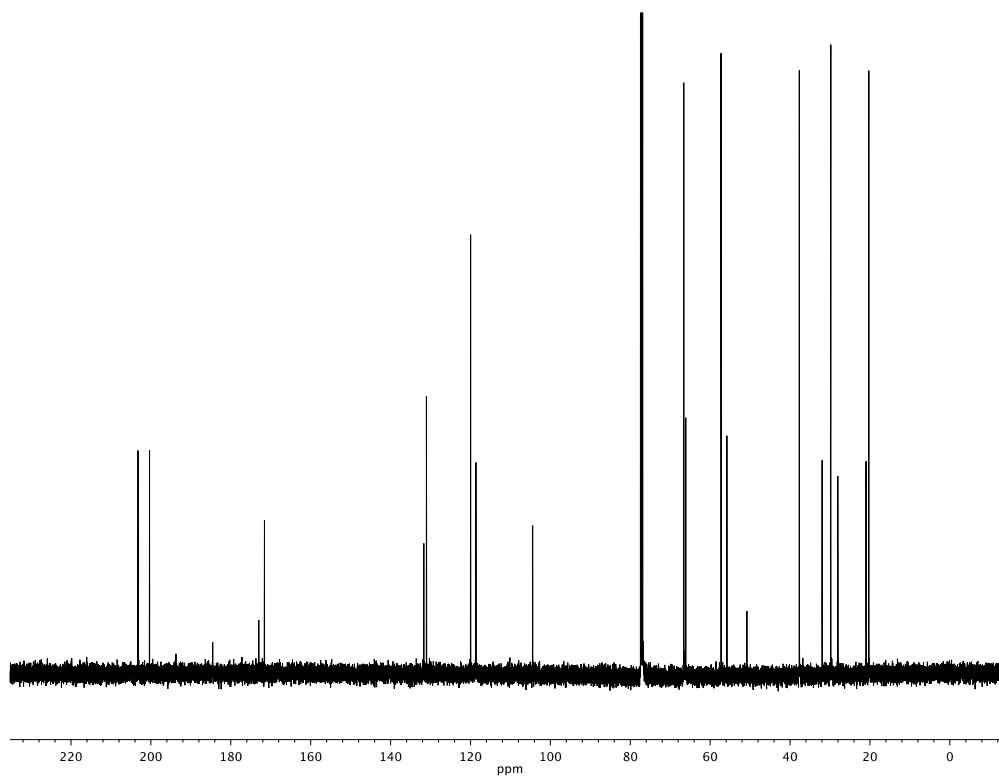


Figure SI-1C. ^{13}C NMR (125 MHz, CDCl_3) of compound **SI-1**.

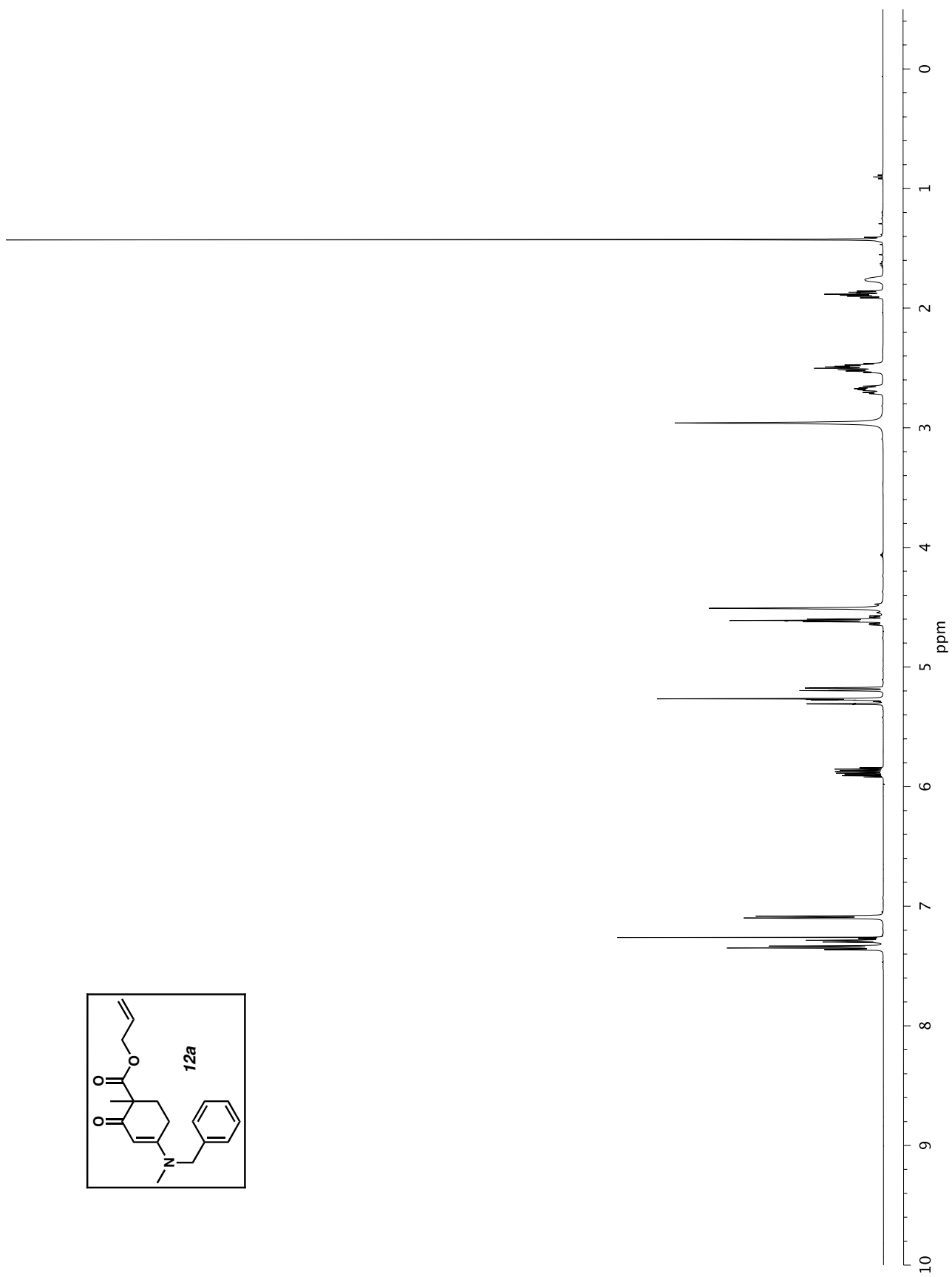
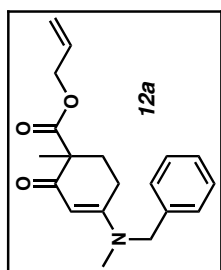


Figure SI-2A. ¹H NMR (500 MHz, CDCl₃) of compound 12a.

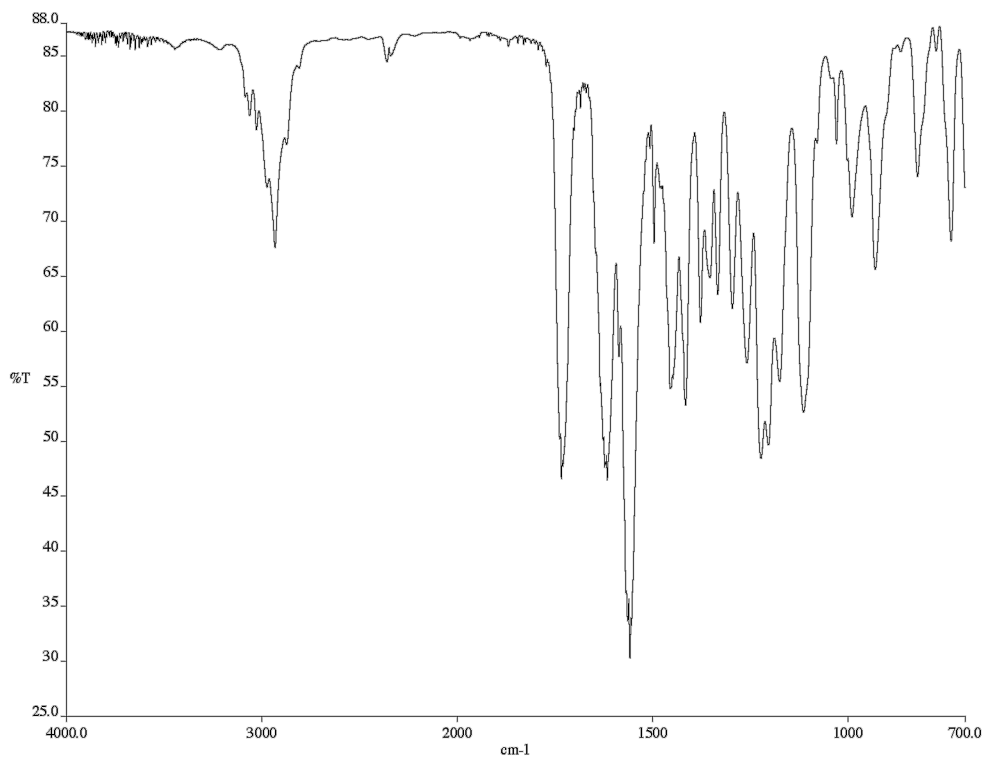


Figure SI-2B. Infrared spectrum (thin film/NaCl) of compound **12a**.

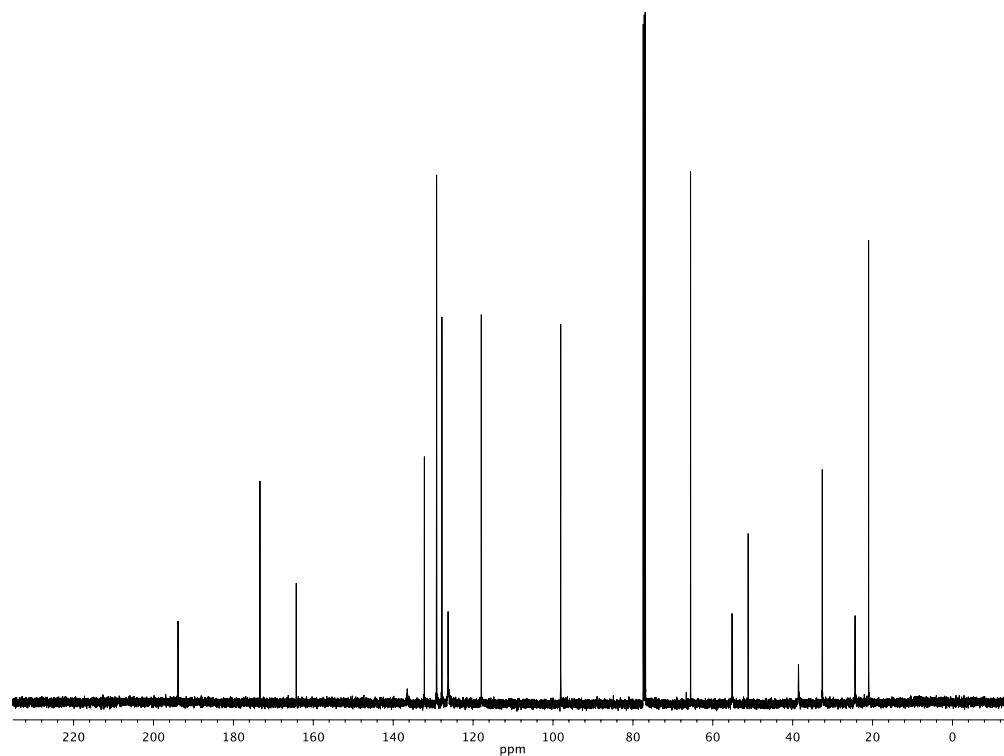


Figure SI-2C. ^{13}C NMR (125 MHz, CDCl_3) of compound **12a**.

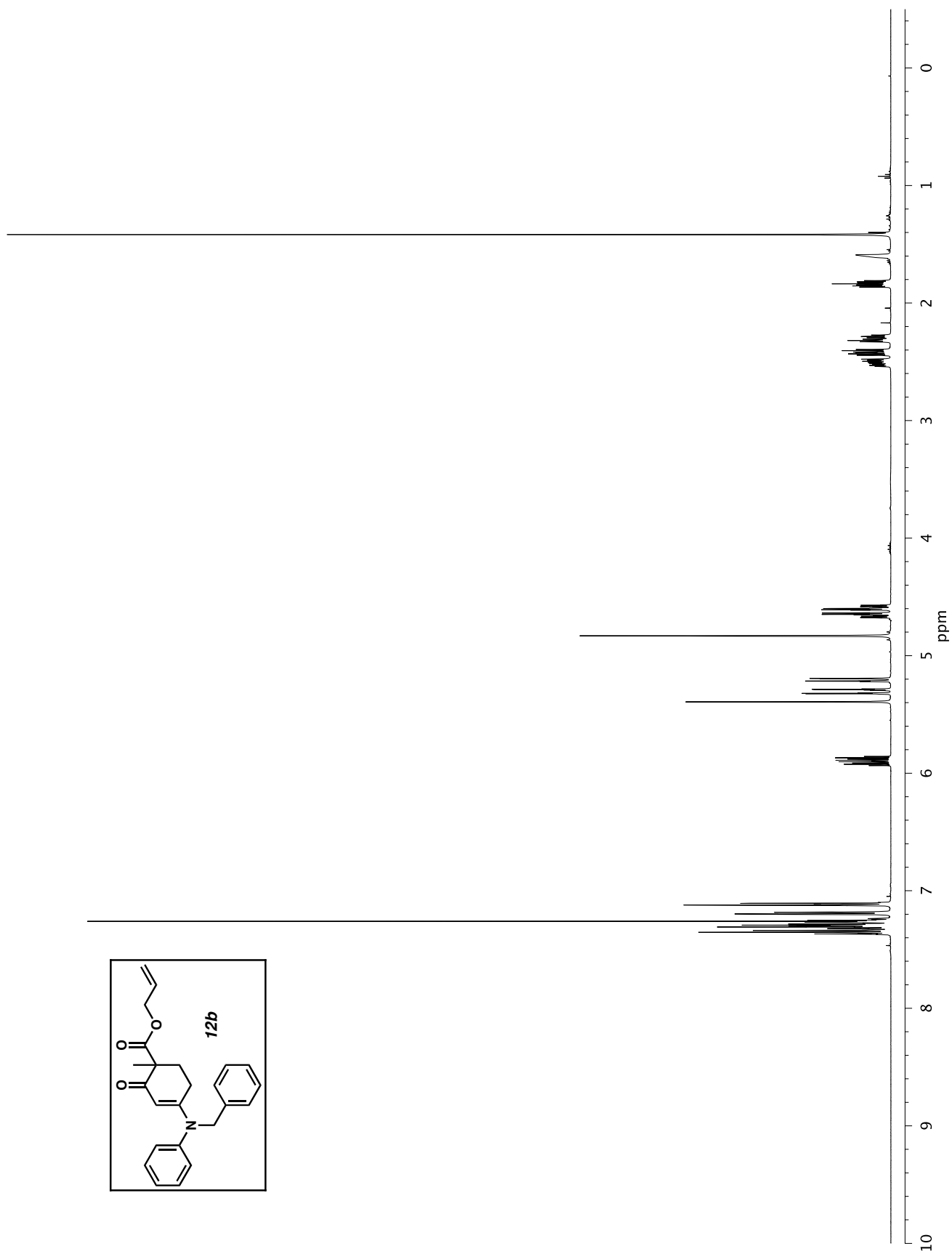


Figure SI-3A. ^1H NMR (500 MHz, CDCl_3) of compound **12b**.

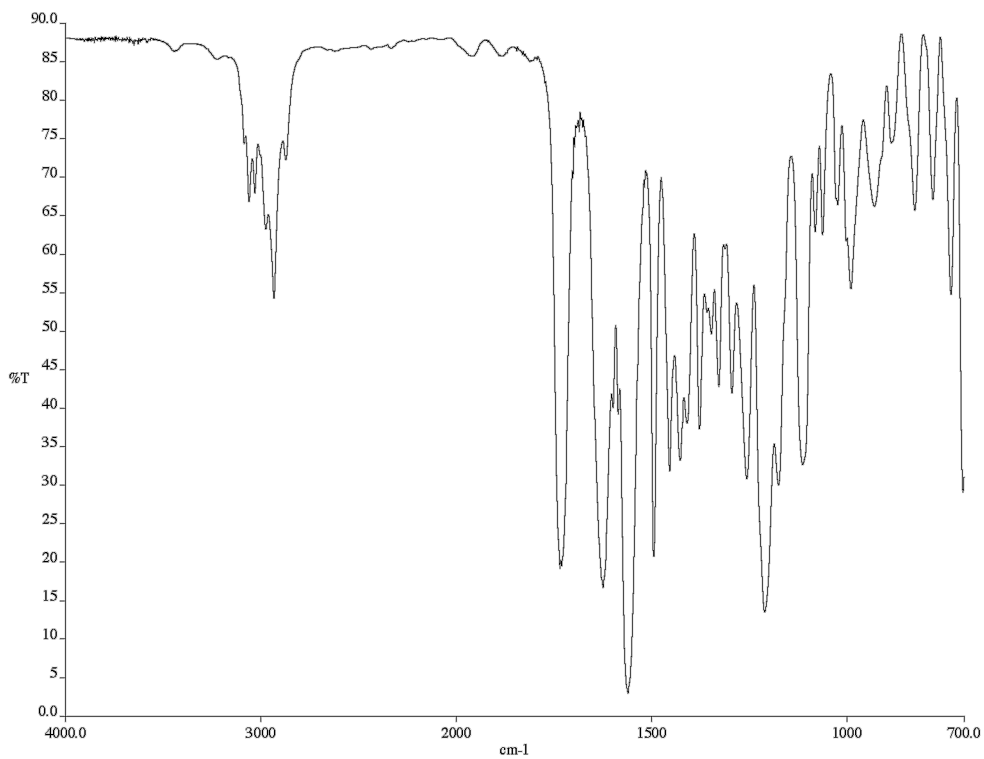


Figure SI-3B. Infrared spectrum (thin film/NaCl) of compound **12b**.

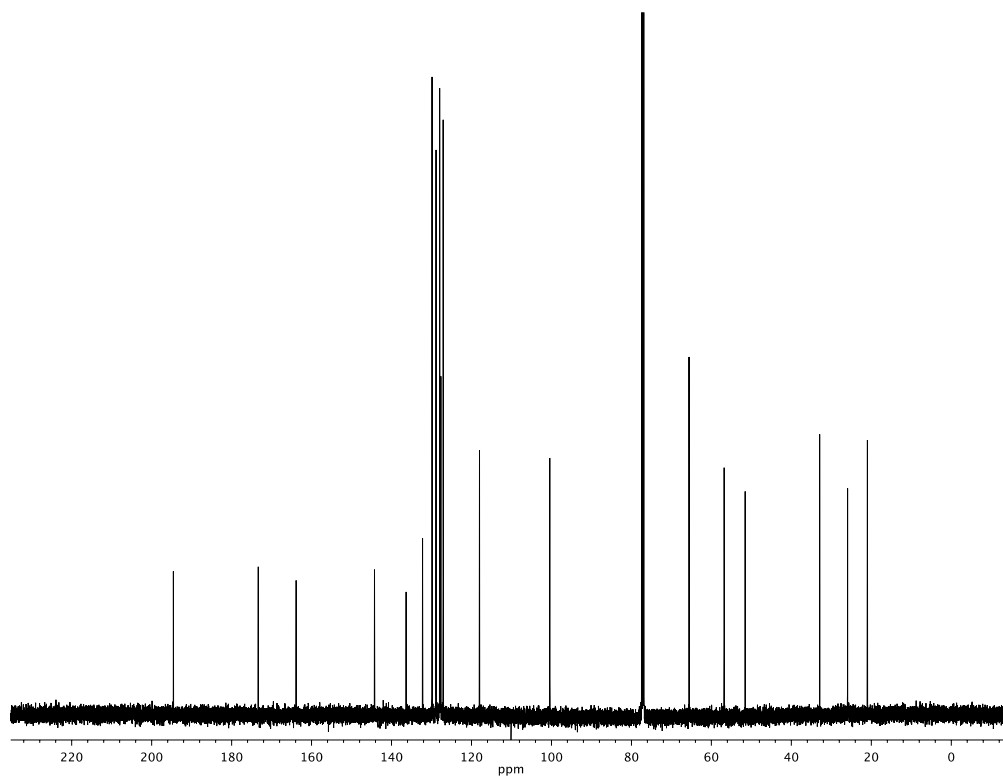


Figure SI-3C. ^{13}C NMR (125 MHz, CDCl_3) of compound **12b**.

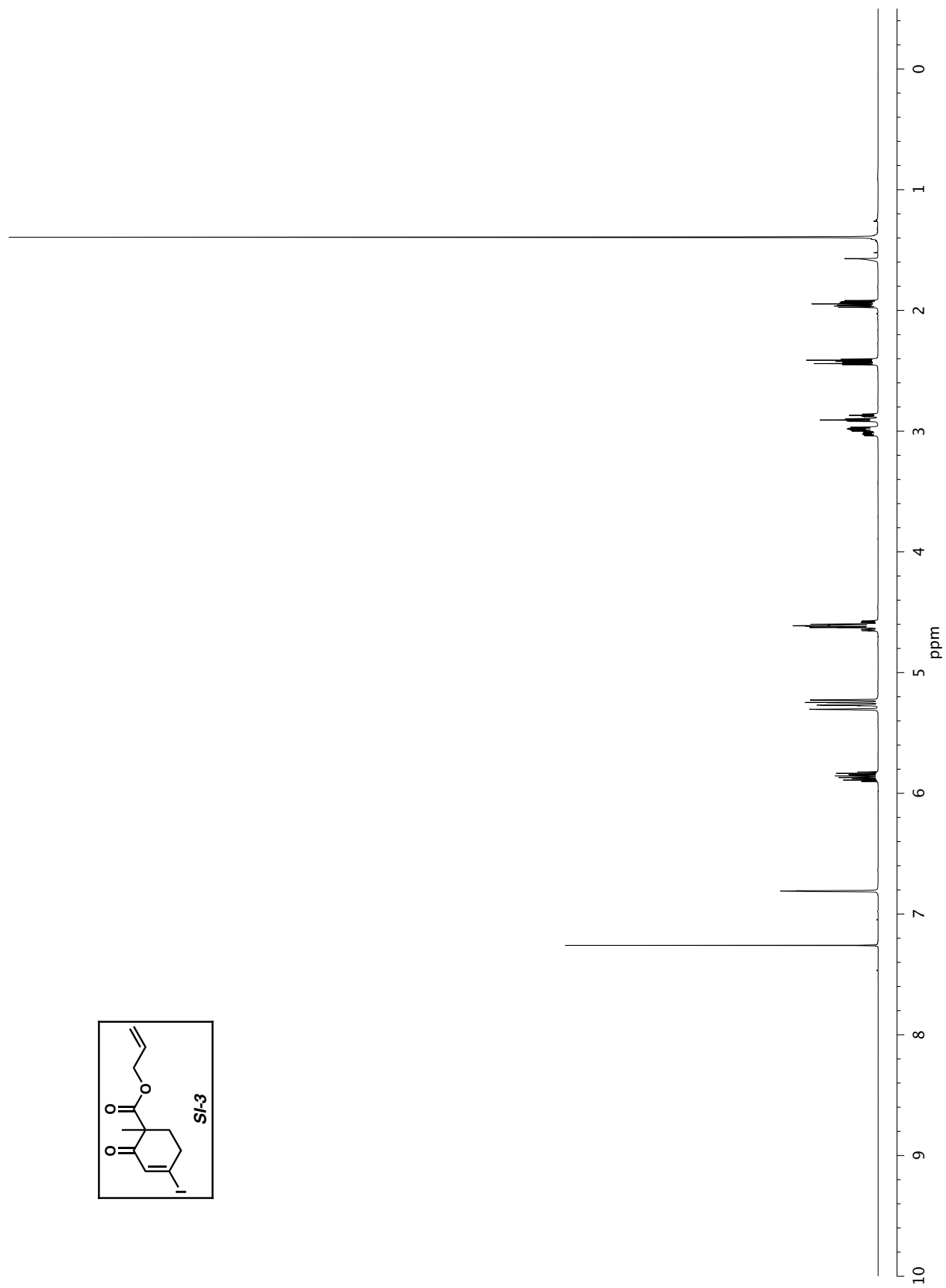


Figure SI-4A. ¹H NMR (500 MHz, CDCl₃) of compound SI-3.

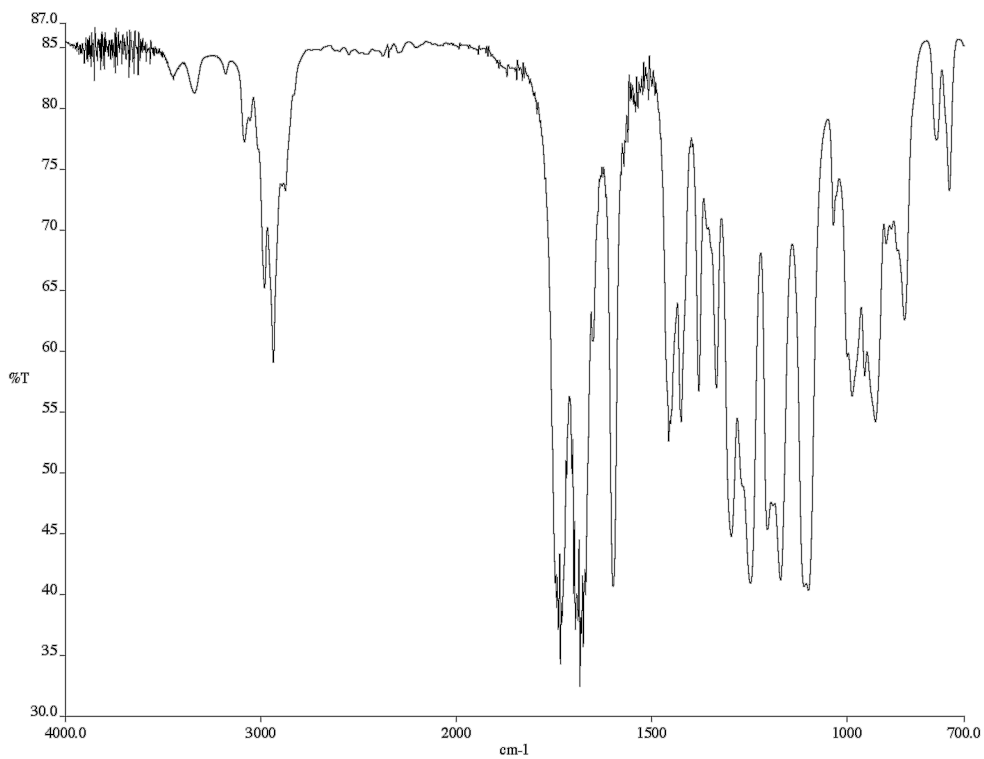


Figure SI-4B. Infrared spectrum (thin film/NaCl) of compound **SI-3**.

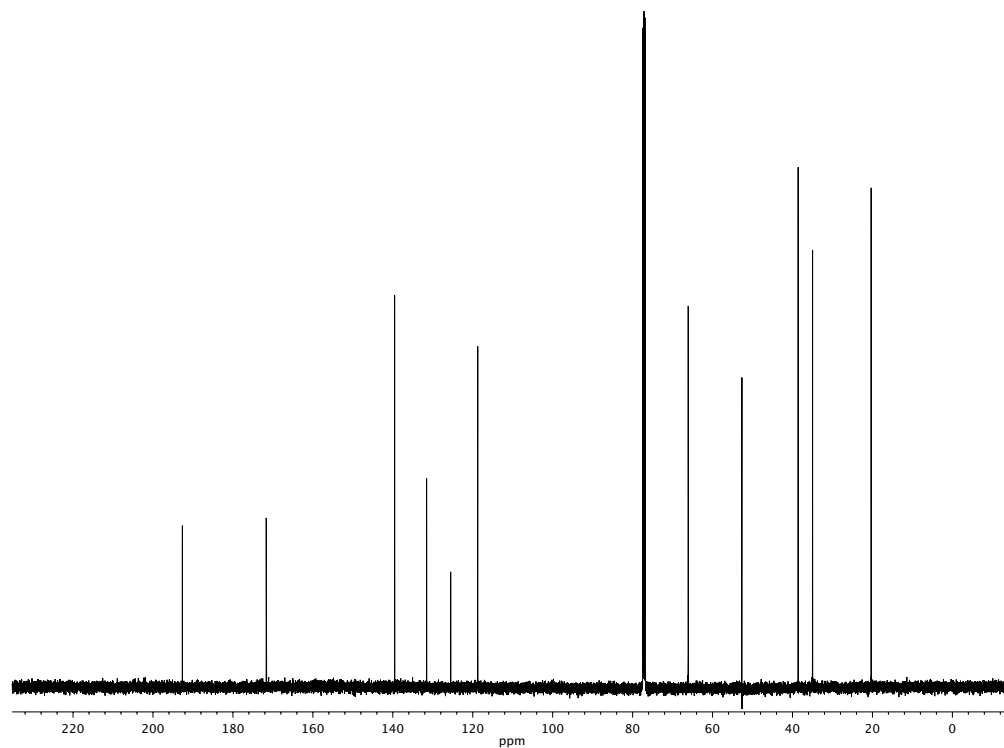


Figure SI-4C. ¹³C NMR (125 MHz, CDCl₃) of compound **SI-3**.

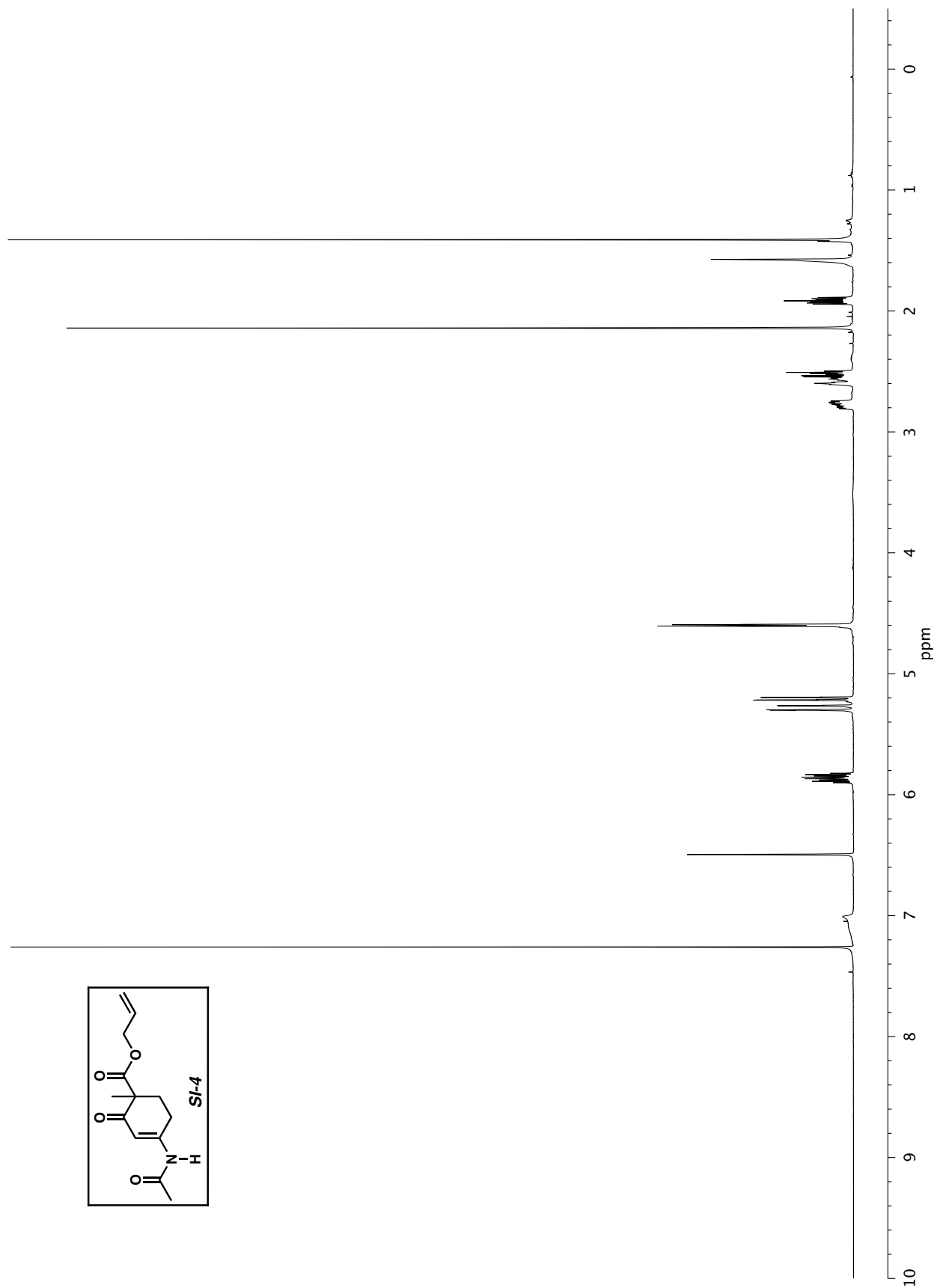


Figure SI-5A. ^1H NMR (500 MHz, CDCl_3) of compound **SI-4**.

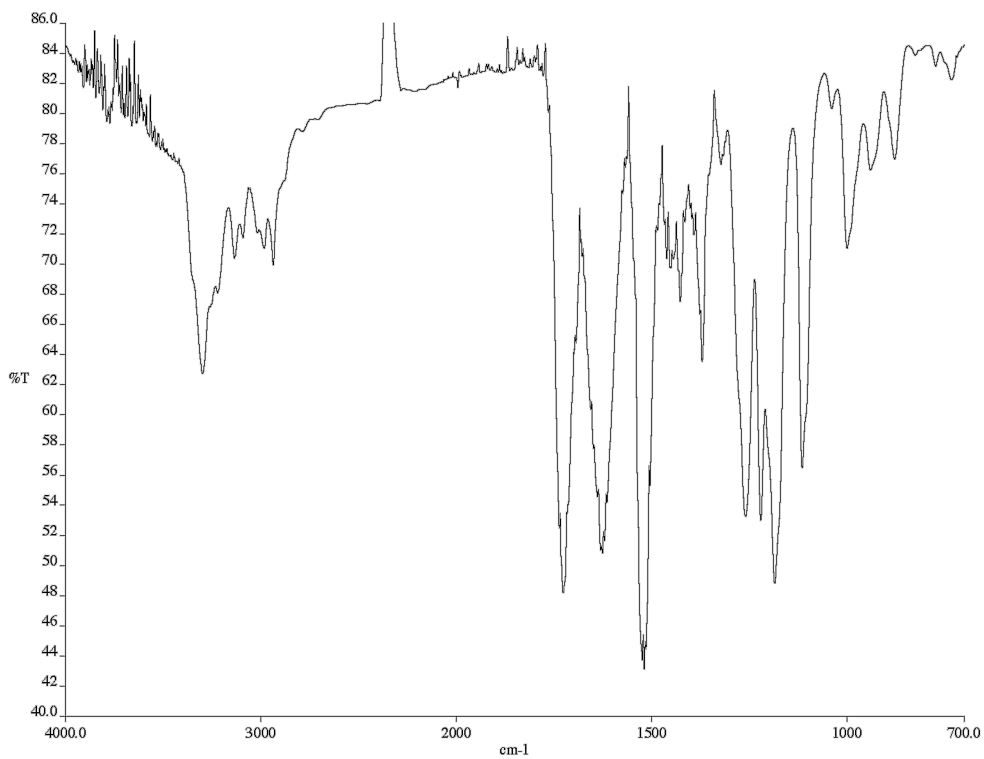


Figure SI-5B. Infrared spectrum (thin film/NaCl) of compound **SI-4**.

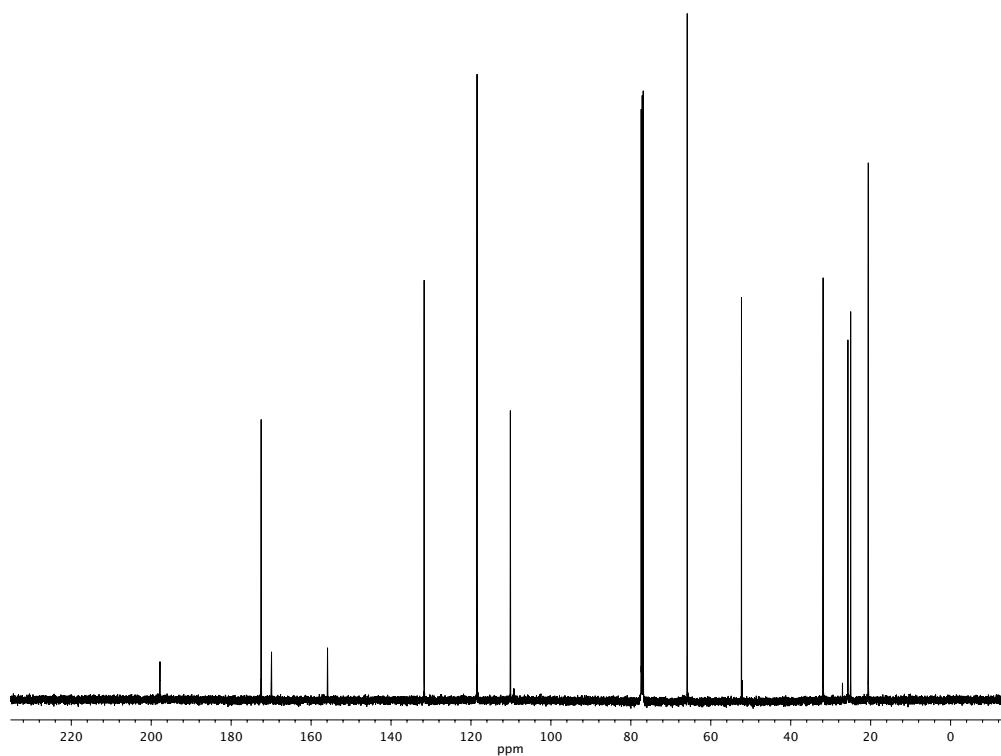


Figure SI-5C. ¹³C NMR (125 MHz, CDCl₃) of compound **SI-4**.

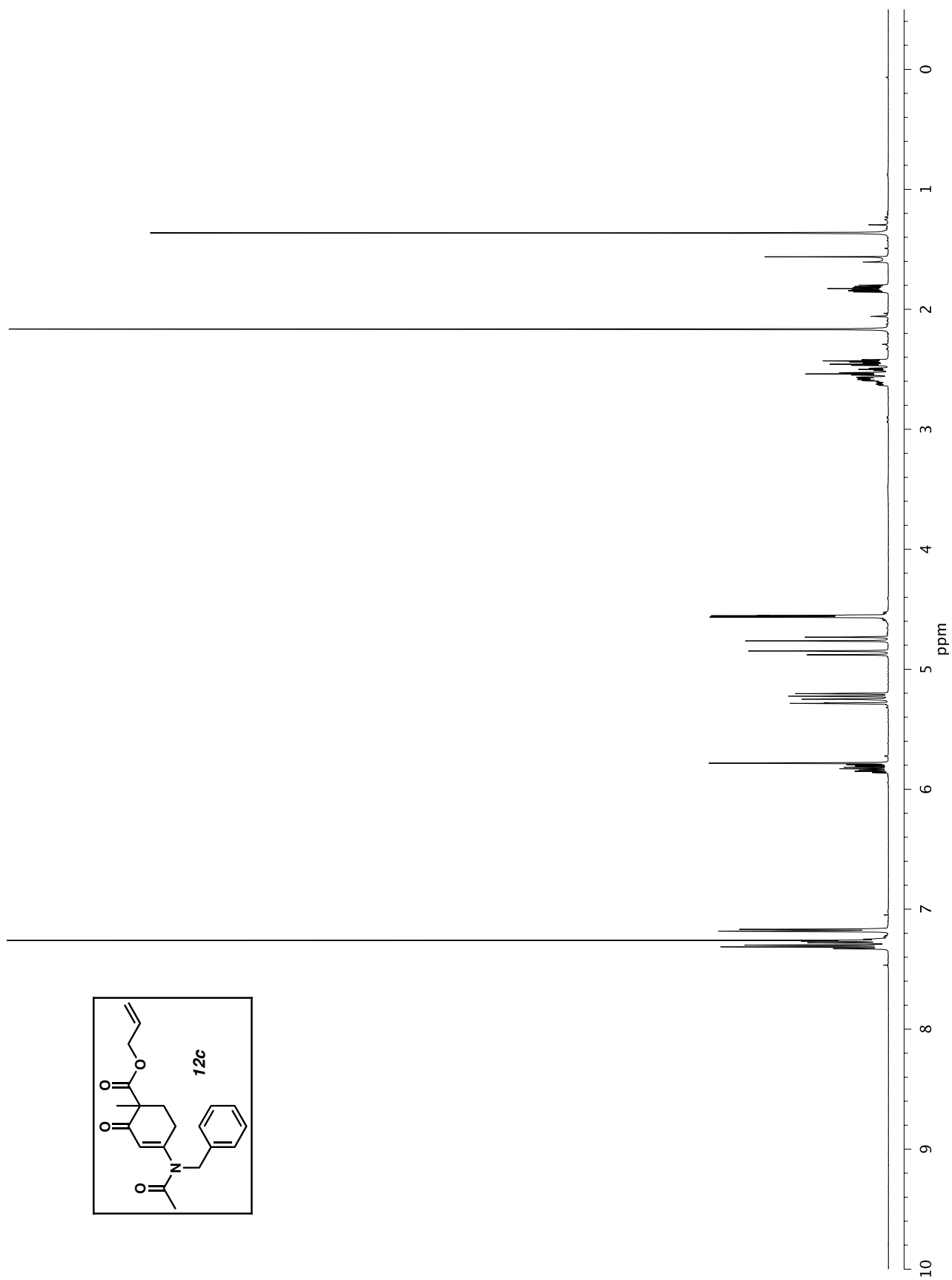


Figure SI-6A. ^1H NMR (500 MHz, CDCl_3) of compound **12c**.

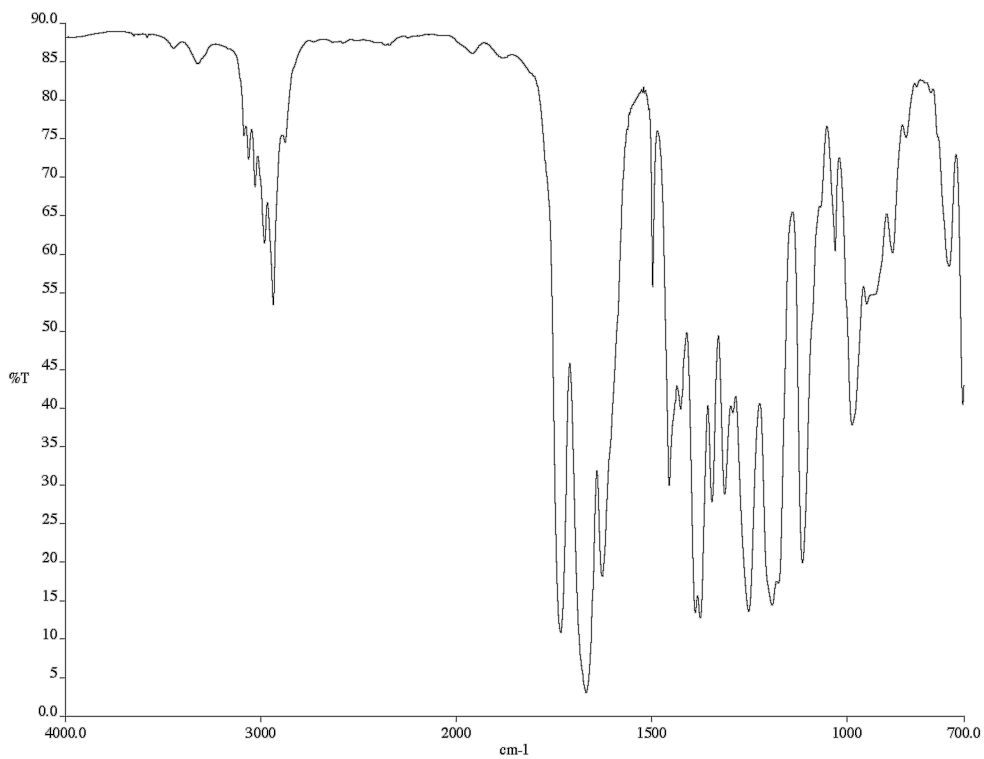


Figure SI-6B. Infrared spectrum (thin film/NaCl) of compound **12c**.

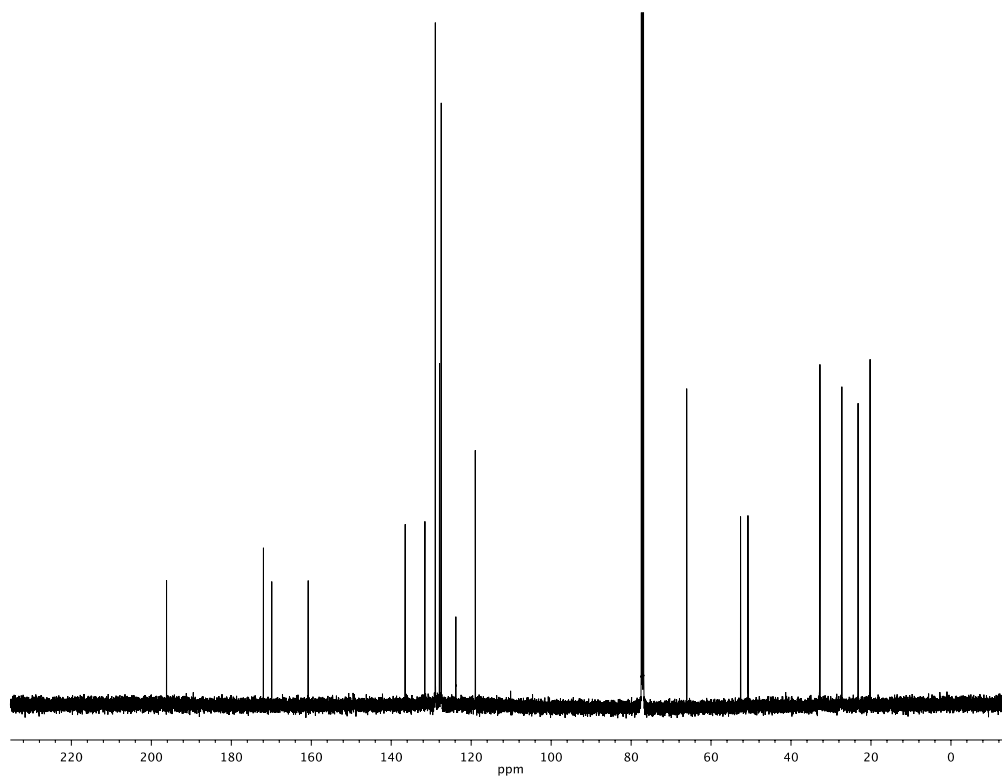


Figure SI-6C. ^{13}C NMR (125 MHz, CDCl_3) of compound **12c**.

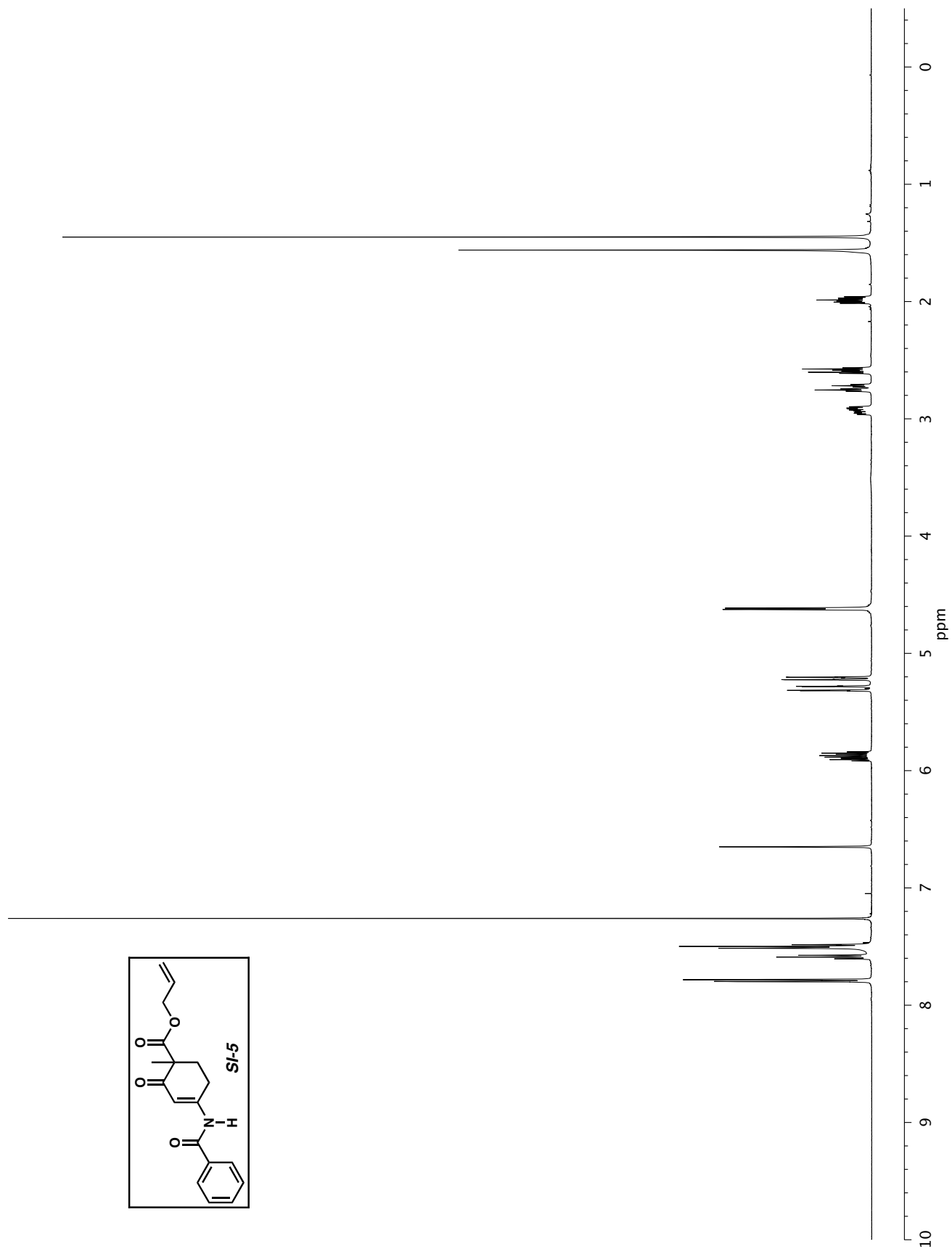


Figure SI-7A. ¹H NMR (500 MHz, CDCl₃) of compound SI-5.

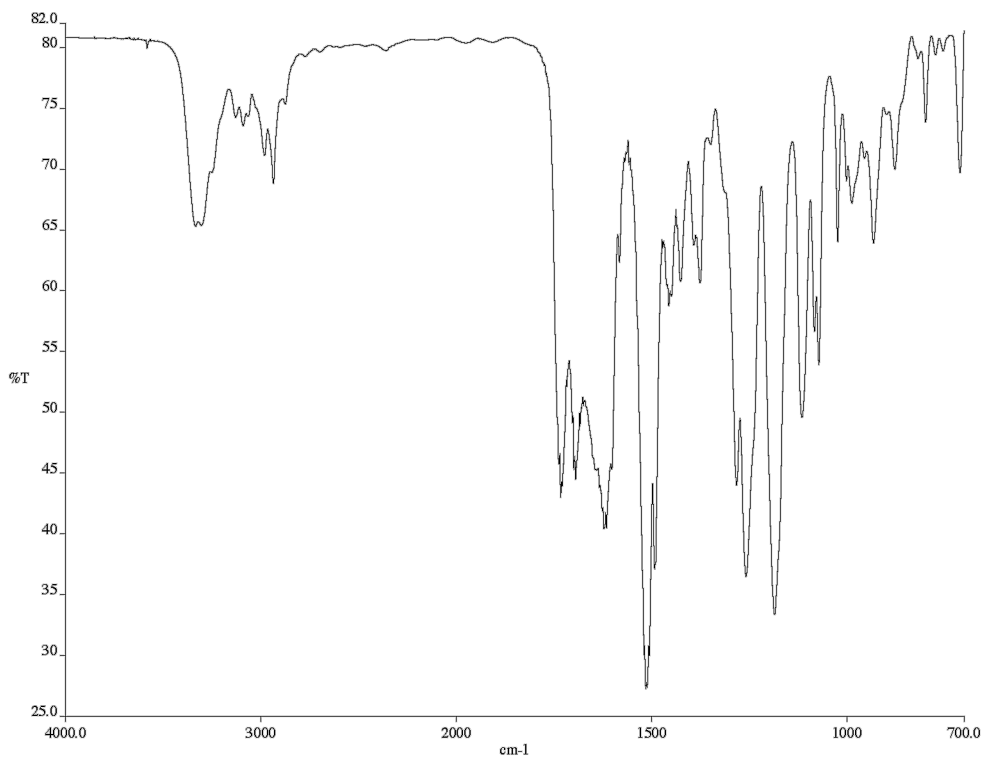


Figure SI-7B. Infrared spectrum (thin film/NaCl) of compound **SI-5**.

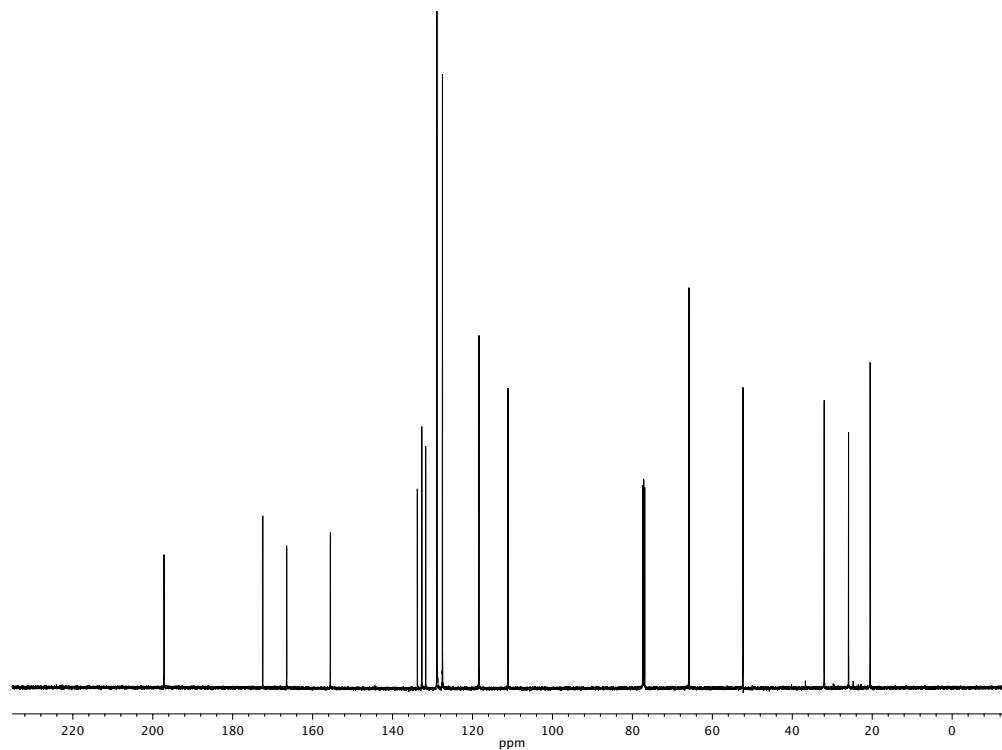


Figure SI-7C. ¹³C NMR (125 MHz, CDCl₃) of compound **SI-5**.

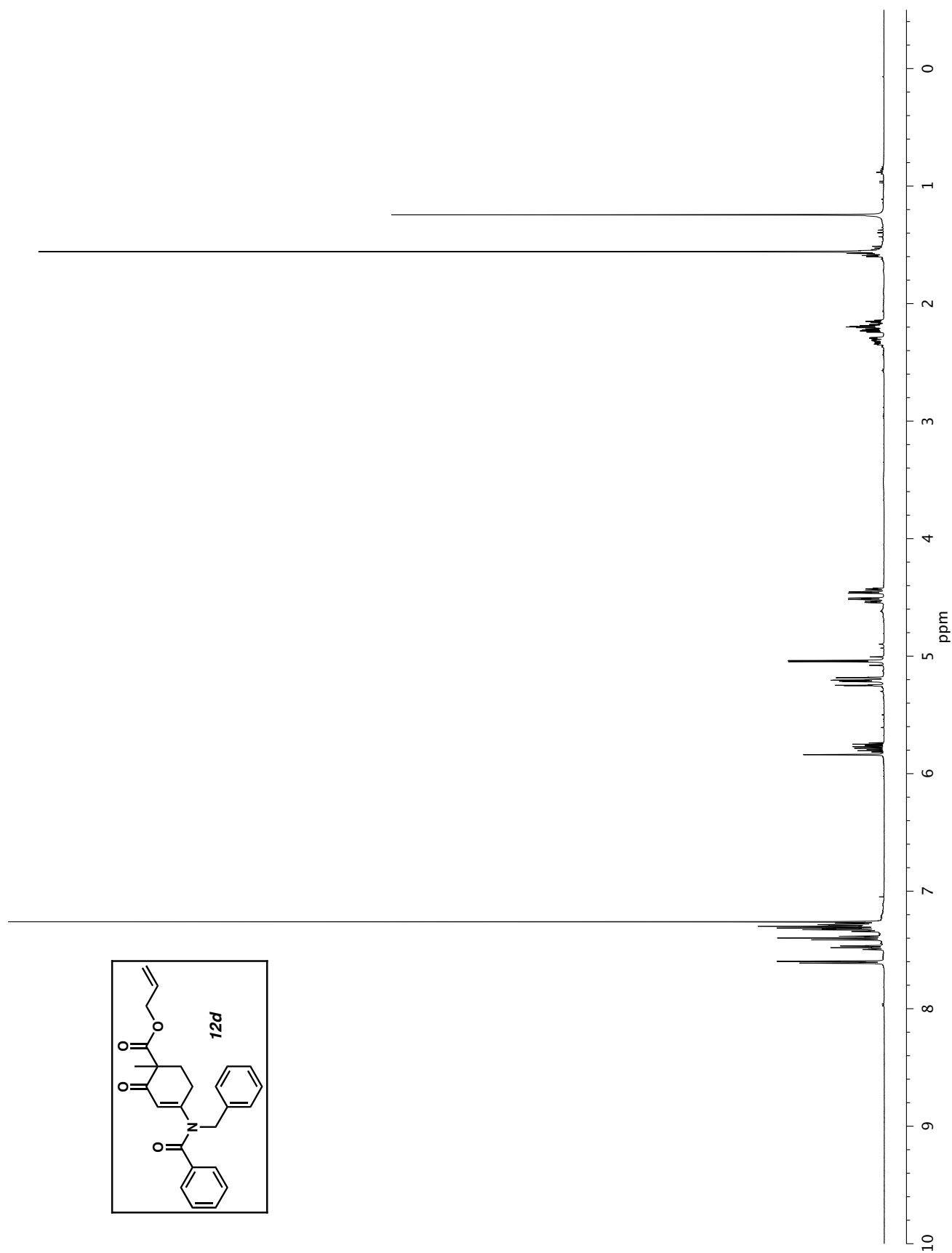


Figure SI-8A. ^1H NMR (500 MHz, CDCl_3) of compound **12d**.

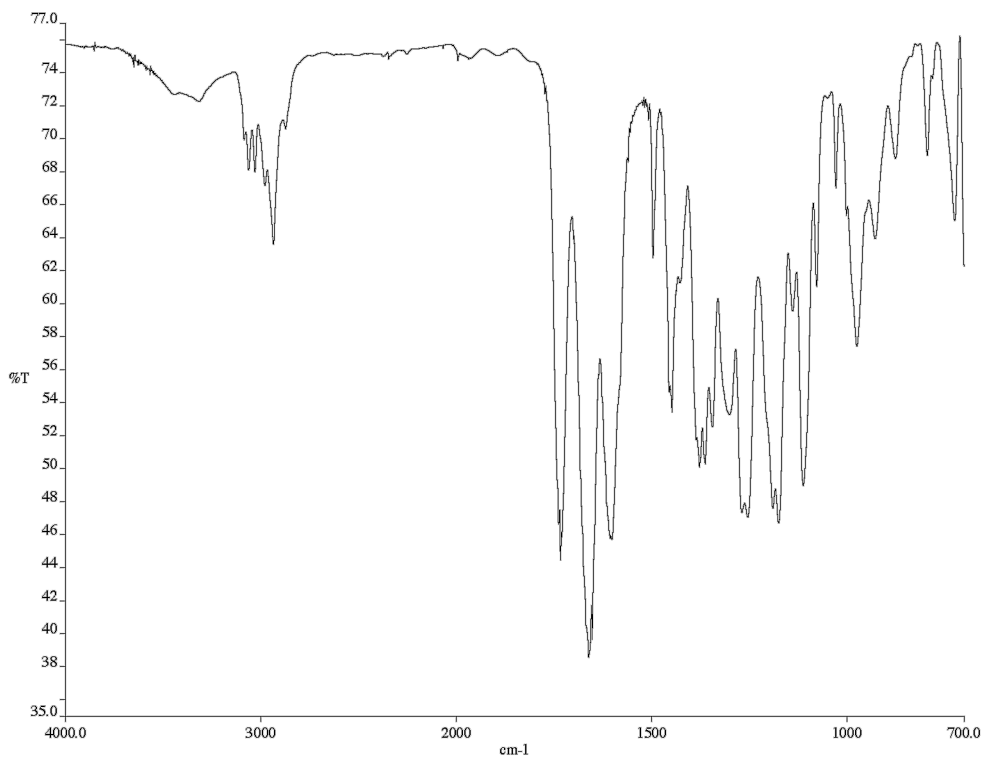


Figure SI-8B. Infrared spectrum (thin film/NaCl) of compound **12d**.

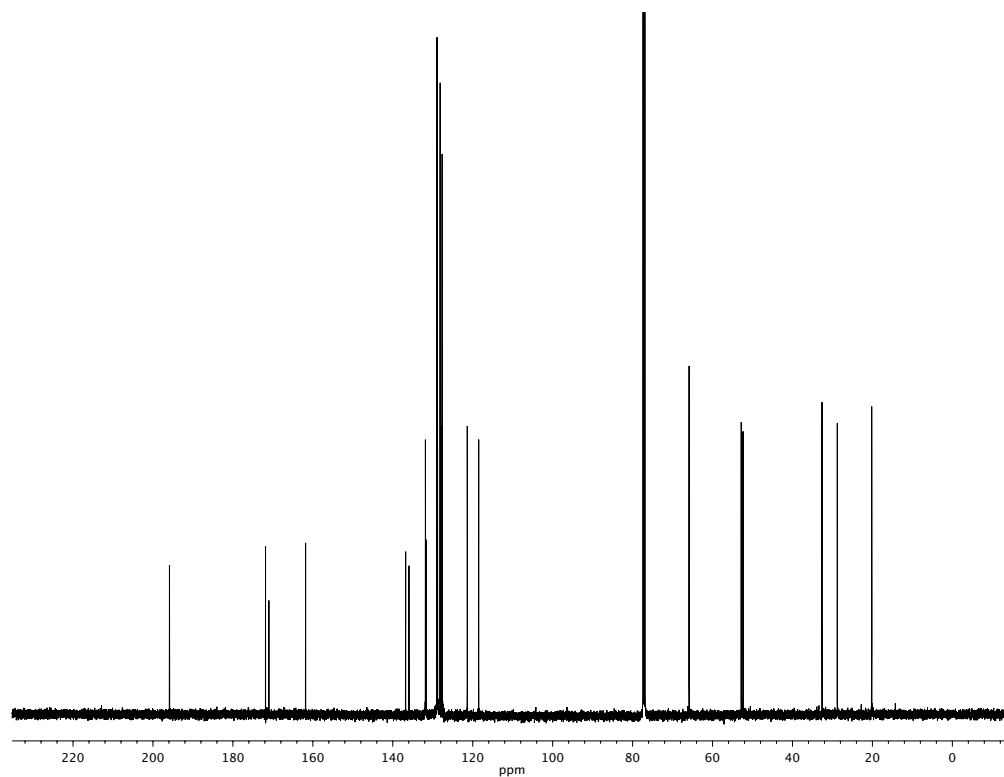
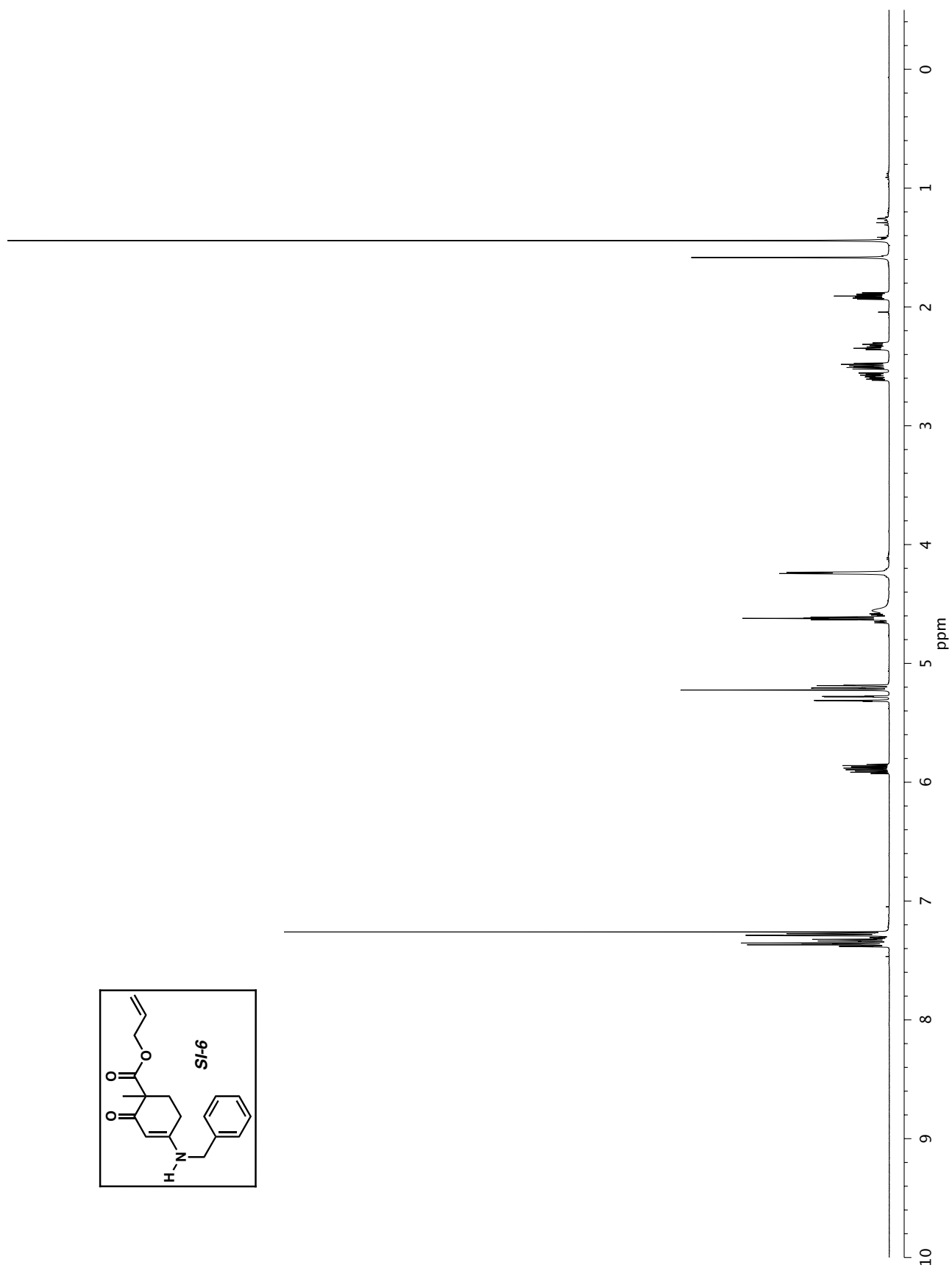


Figure SI-8C. ¹³C NMR (125 MHz, CDCl₃) of compound **12d**.



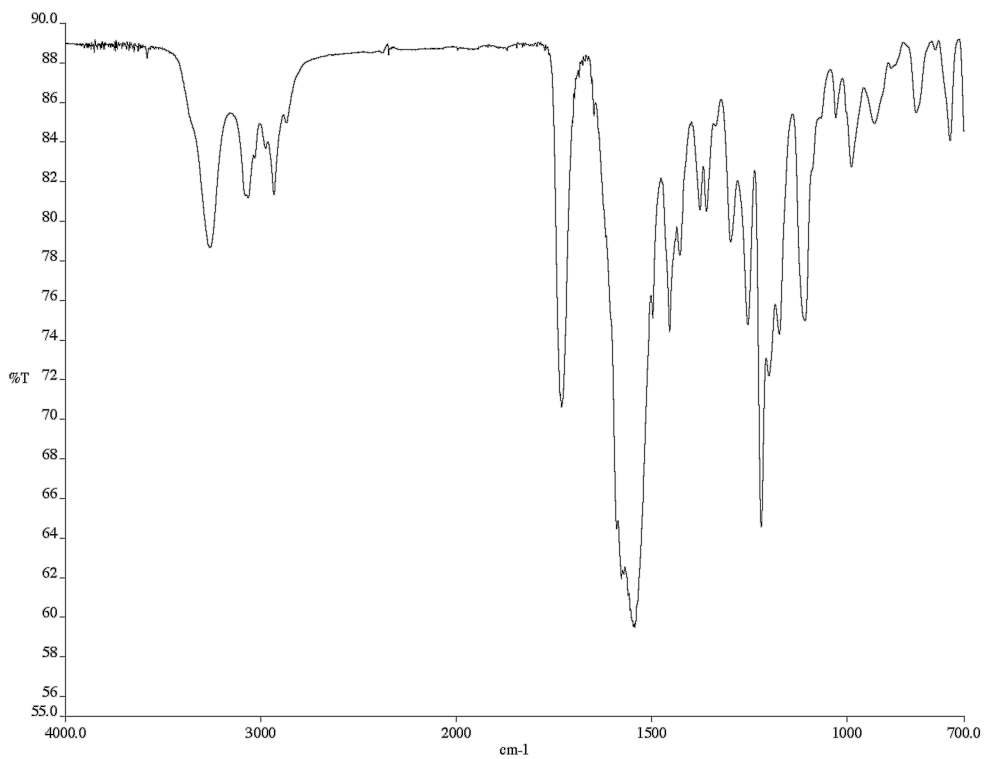


Figure SI-9B. Infrared spectrum (thin film/NaCl) of compound **SI-6**.

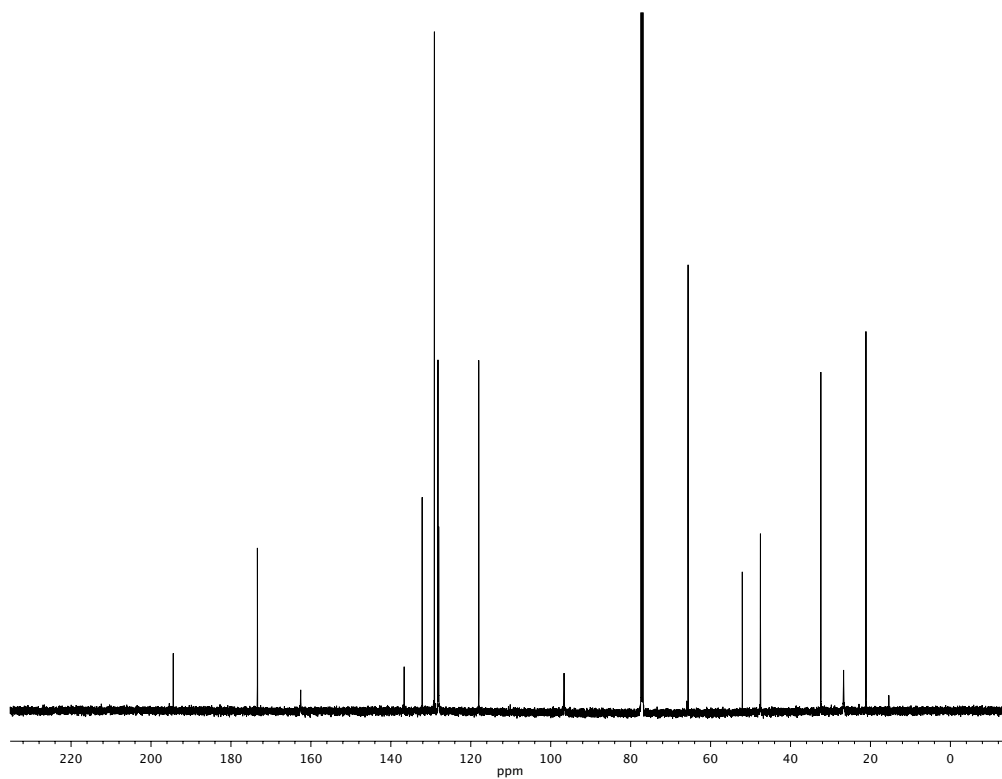


Figure SI-9C. ^{13}C NMR (125 MHz, CDCl_3) of compound **SI-6**.

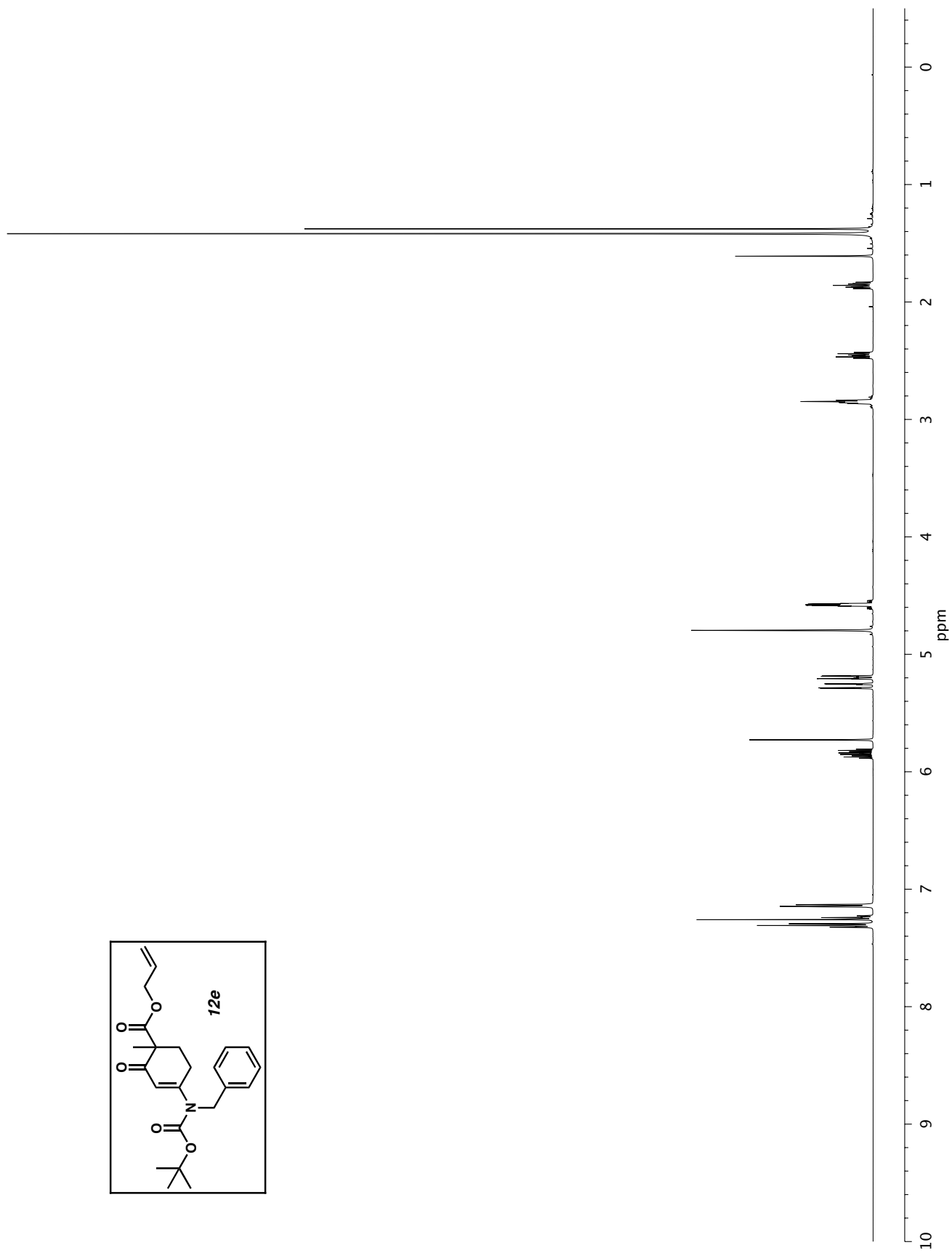


Figure SI-10A. ^1H NMR (500 MHz, CDCl_3) of compound **12e**.

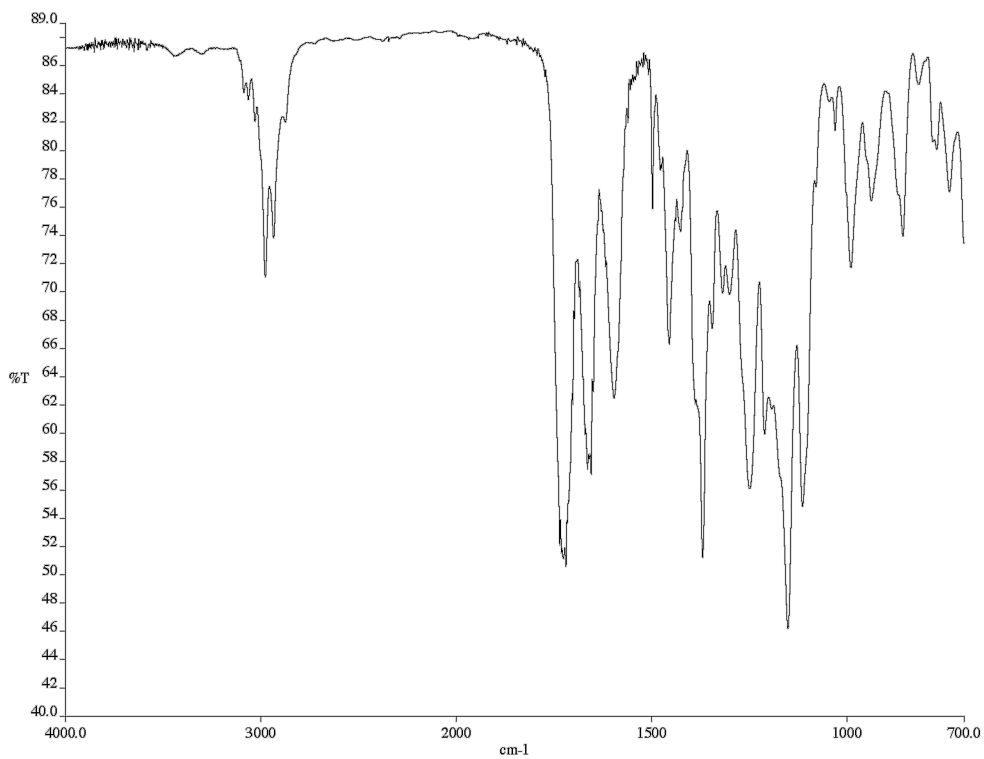


Figure SI-10B. Infrared spectrum (thin film/NaCl) of compound **12e**.

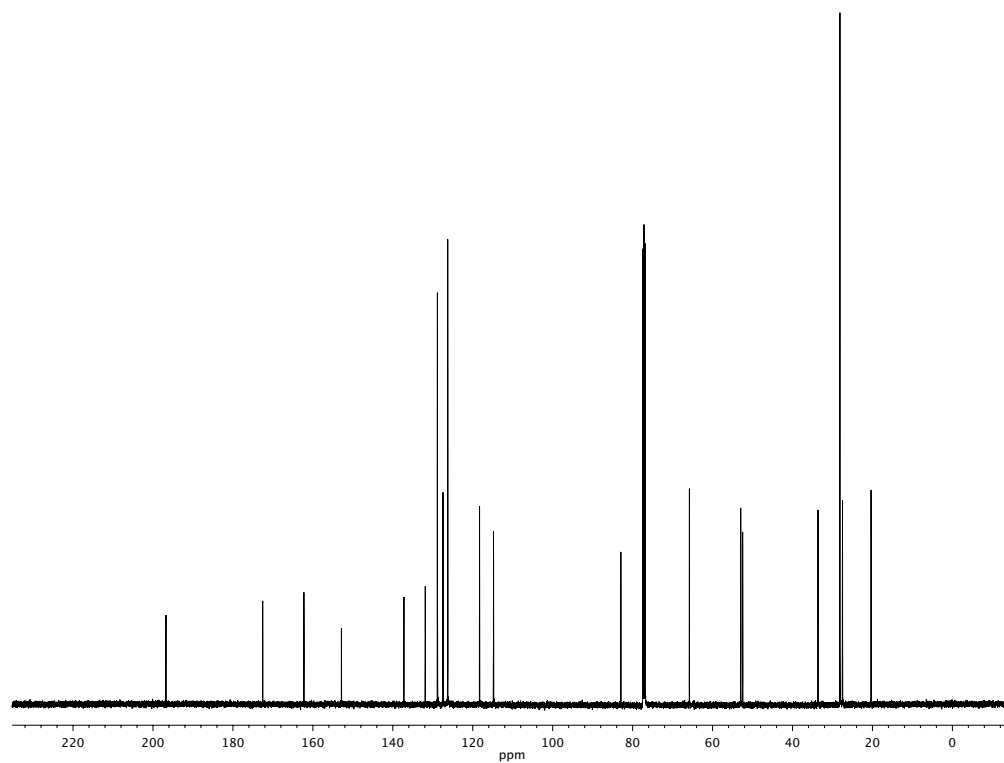
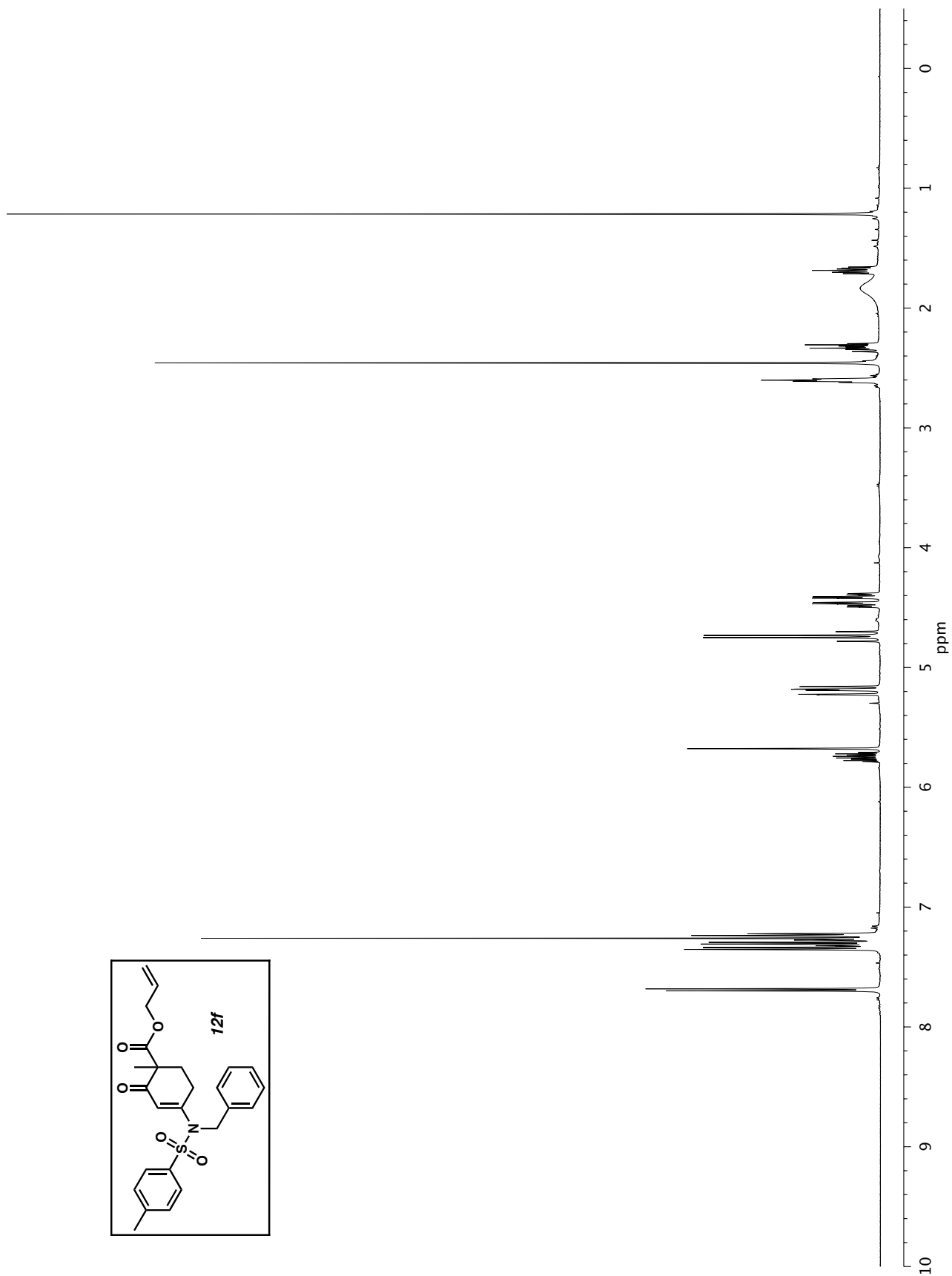


Figure SI-10C. ¹³C NMR (125 MHz, CDCl₃) of compound **12e**.

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

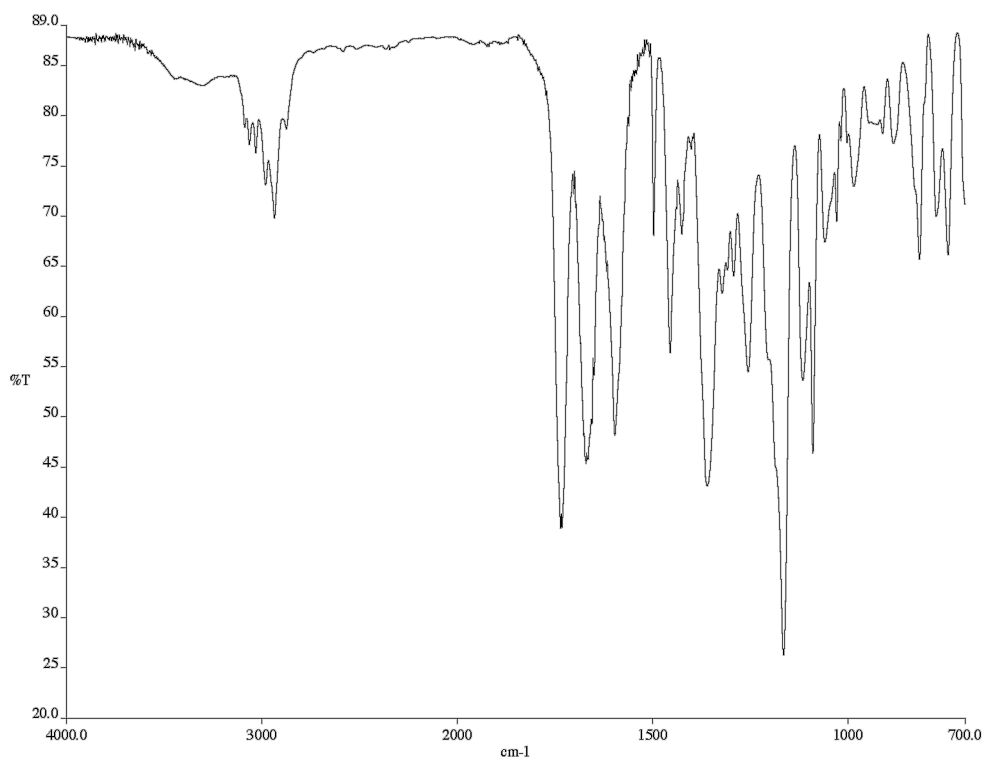


Figure SI-11B. Infrared spectrum (thin film/NaCl) of compound **12f**.

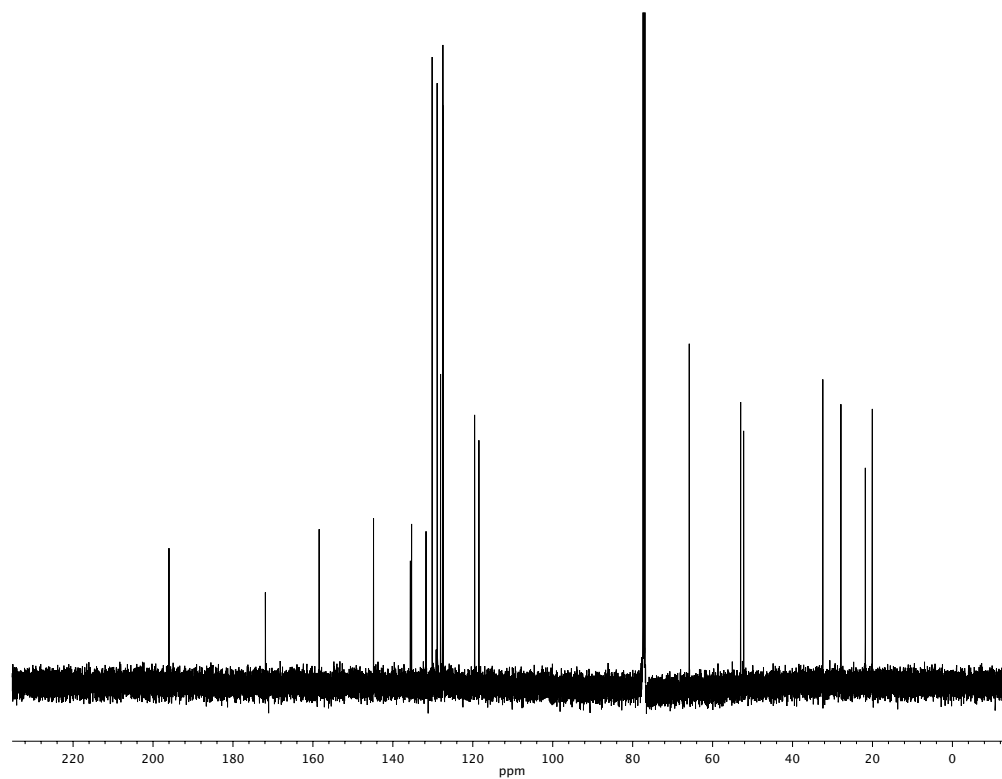


Figure SI-11C. ¹³C NMR (125 MHz, CDCl₃) of compound **12f**.

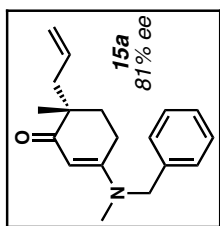
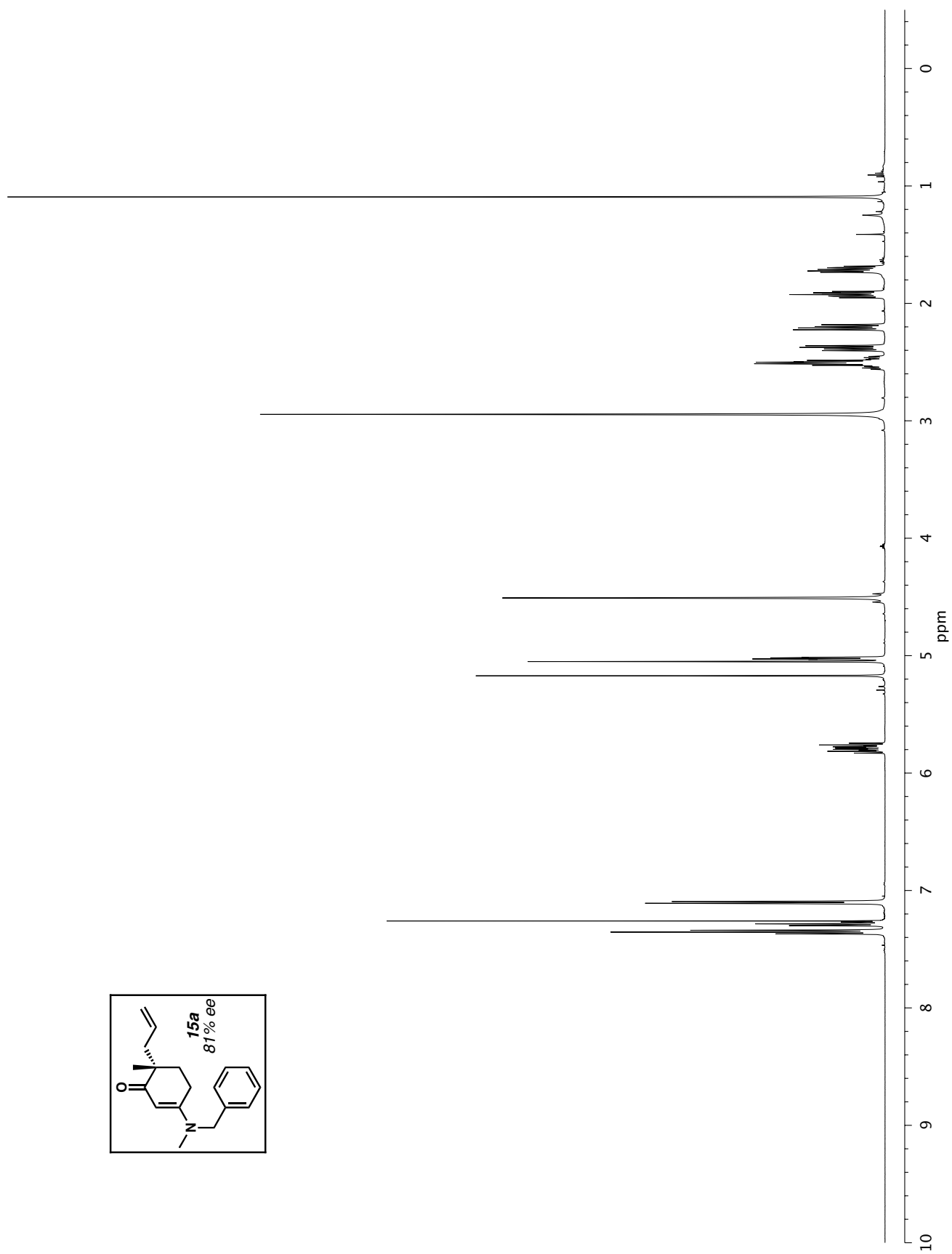


Figure SI-12A. ^1H NMR (500 MHz, CDCl_3) of compound **15a**.

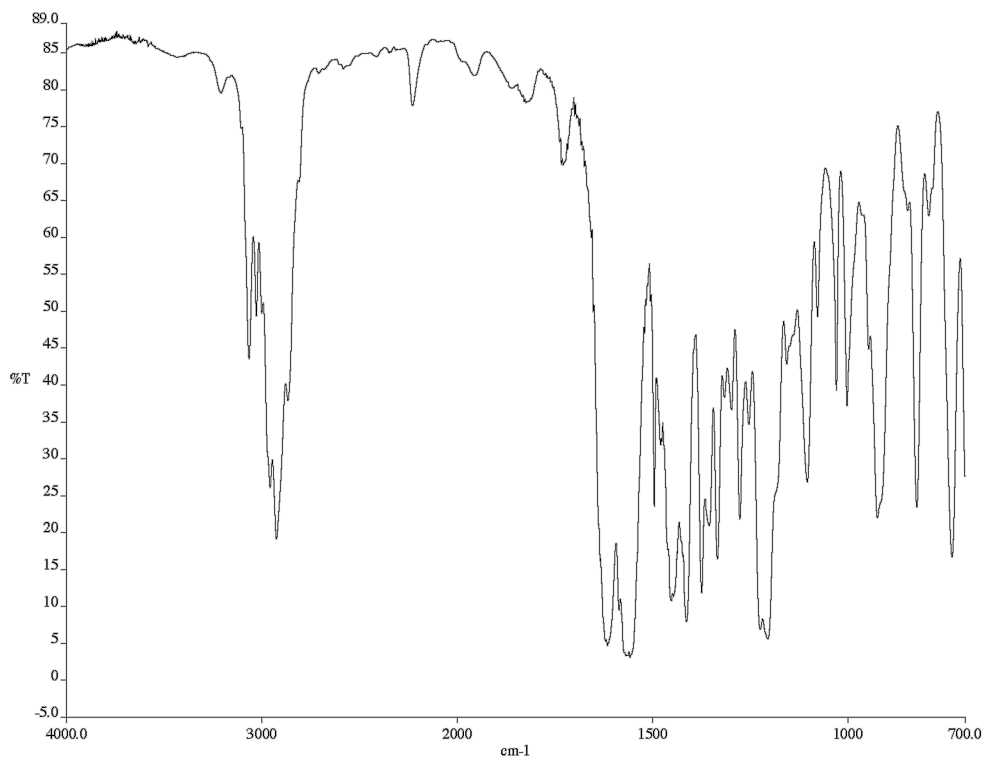


Figure SI-12B. Infrared spectrum (thin film/NaCl) of compound **15a**.

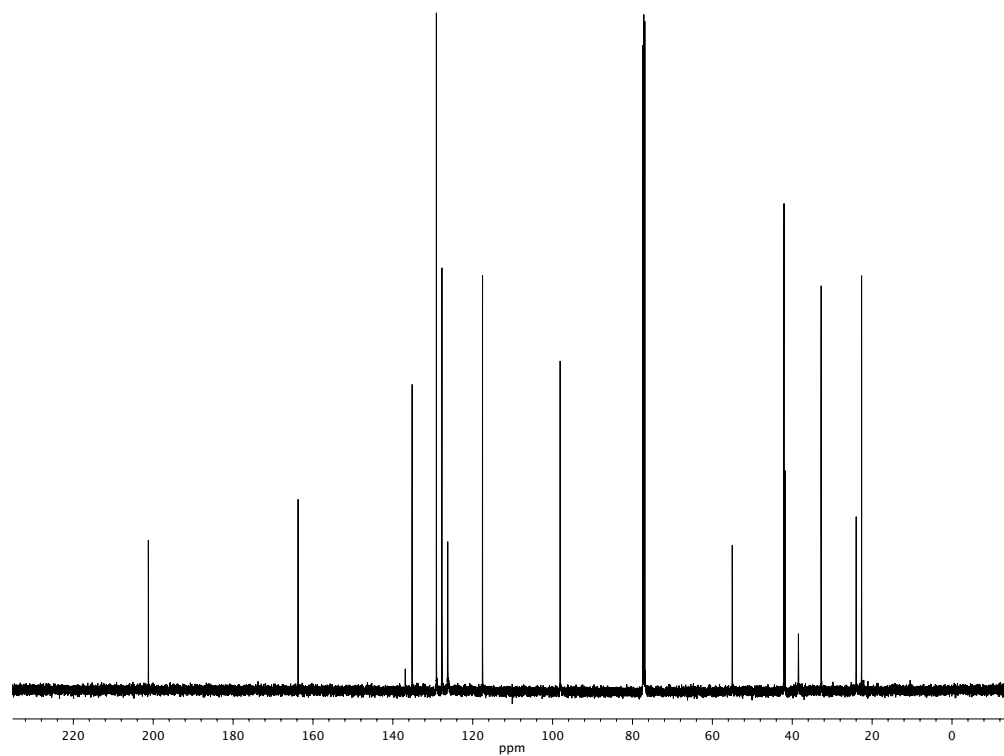
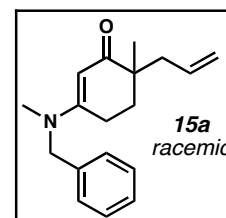


Figure SI-12C. ^{13}C NMR (125 MHz, CDCl_3) of compound **15a**.

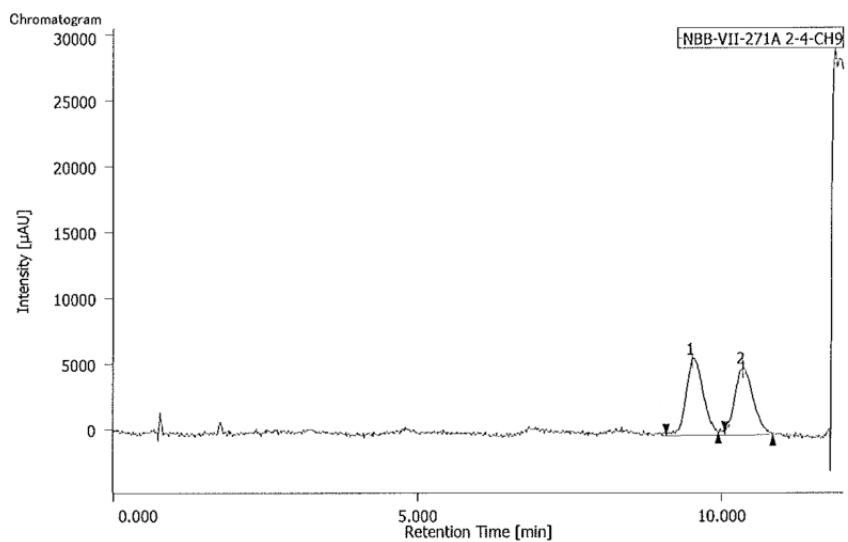
NBB-VII-271A Col 2 7MeOH-2 NBB-VII-271A 2-4 11/28/2011 2:52:51 PM

Analytical Report SFC



Chromatogram Information

User Name	User
HPLC System Name	Jasco SFC w PDA
Injection Date	11/23/2011 9:34:49 PM
Volume	5.00 [μL]
Sample #	51
Project Name	Cal Tech SFC
Executed Sequence	NBB-VII-271A Col 2 7MeOH-2
Chromatogram Name	NBB-VII-271A 2-4
Sample Name	
Acquisition Time	12.0 [min]
Acquisition Sequence	NBB-VII-271A Col 2 7MeOH-2
Control Method	Solv 1 Col 2 Isocratic 5B 5mL_min 10MPa 15min



Peak Information

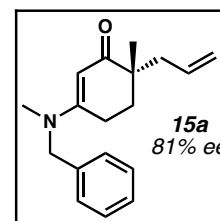
#	Peak Name	CH	tR [min]	Area [μV-sec]	Height [μV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	9	9.520	115034	5926	51.640	9.093	9.947	0.292	1.589	1.154
2	Unknown	9	10.347	107729	5211	48.360	10.053	10.640	0.322	N/A	1.233

1 / 1

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

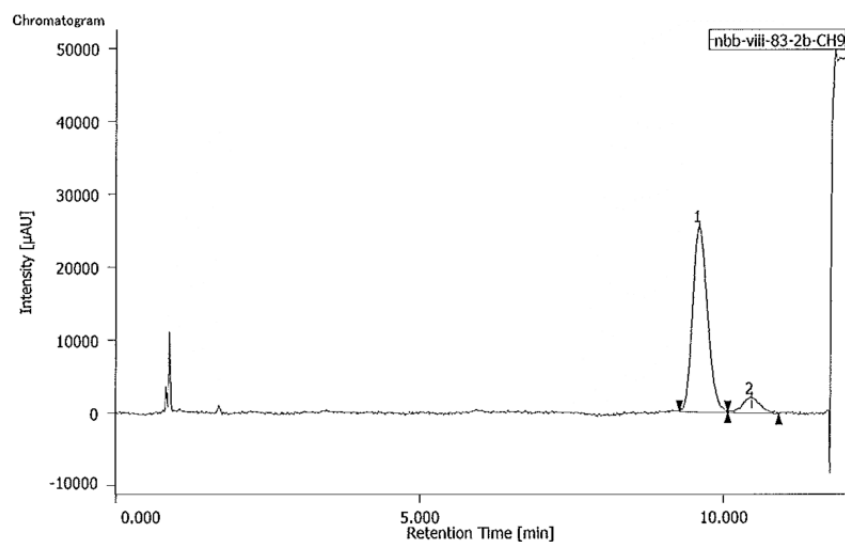
NBB-VIII-83-2B Col2 5MeOH 15min nbb-viii-83-2b 2/9/2012 12:11:21 PM

Analytical Report SFC



Chromatogram Information

User Name	User
HPLC System Name	Jasco SFC w PDA
Injection Date	2/9/2012 11:28:39 AM
Volume	5.00 [μL]
Sample #	11
Project Name	Cal Tech SFC
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

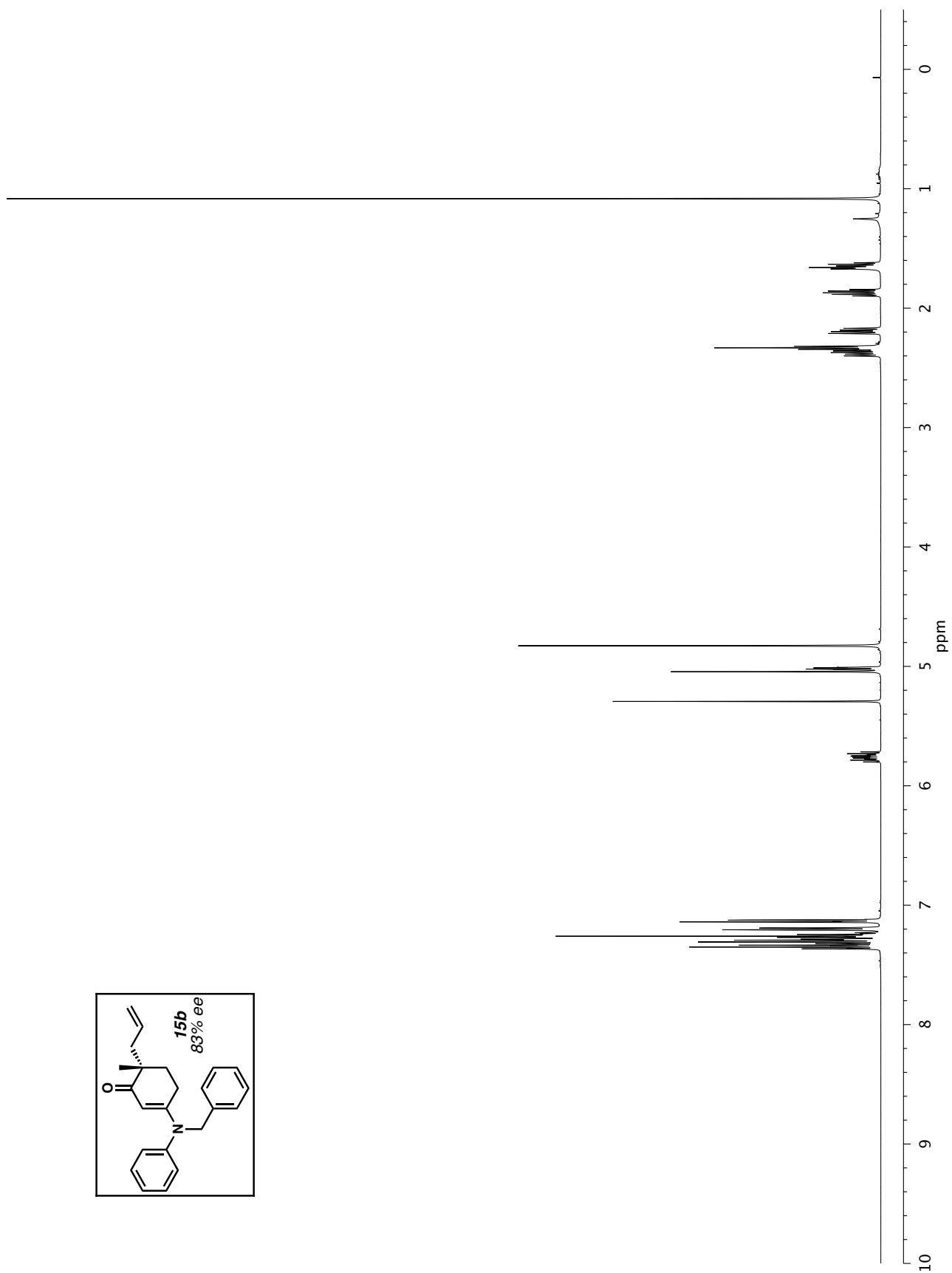


Peak Information

#	Peak Name	CH	TR [min]	Area [μV·sec]	Height [μV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	9	9.600	429906	25542	80.503	9.280	10.067	0.281	1.780	1.178
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. ¹H NMR (500 MHz, CDCl₃) of compound **15b**.

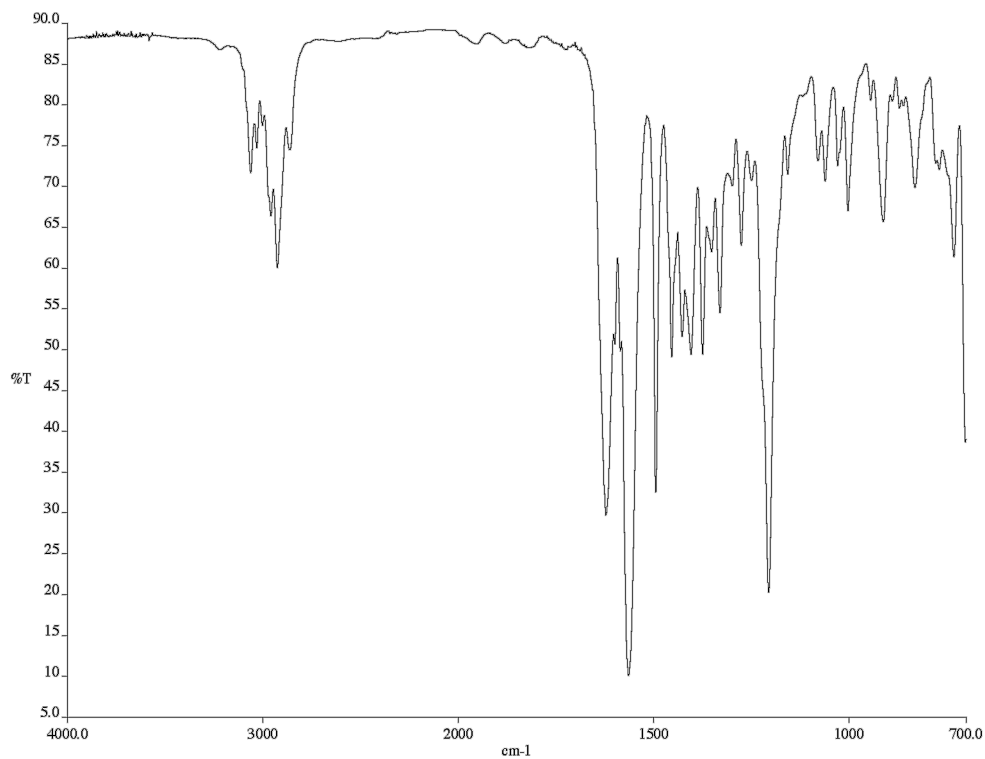


Figure SI-13B. Infrared spectrum (thin film/NaCl) of compound **15b**.

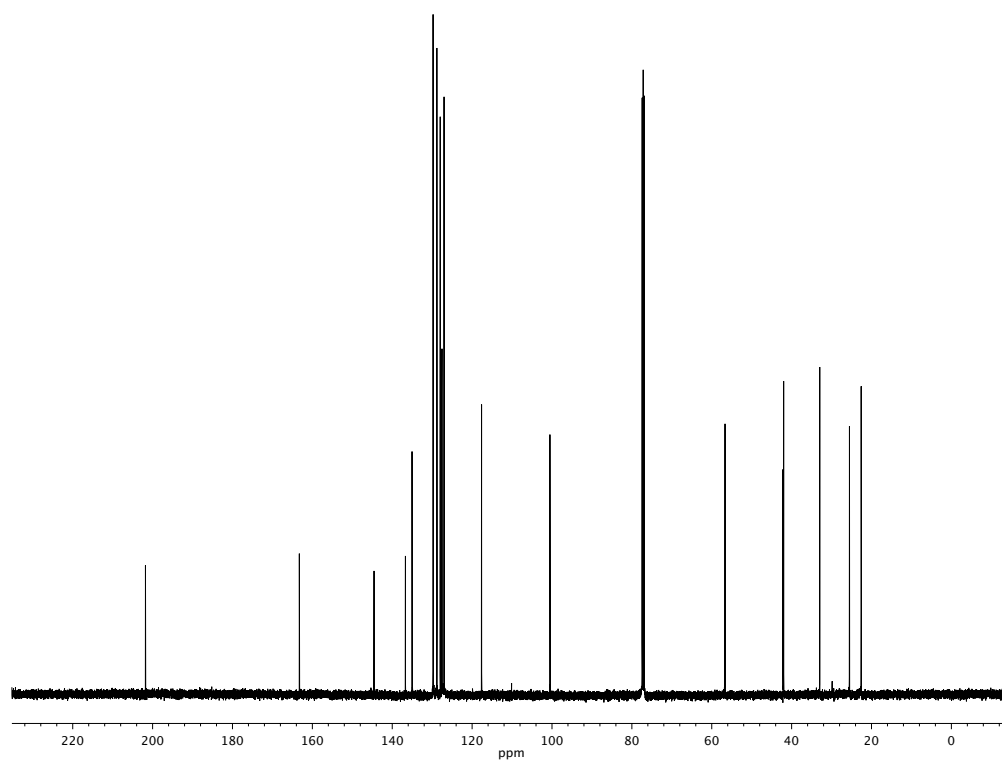
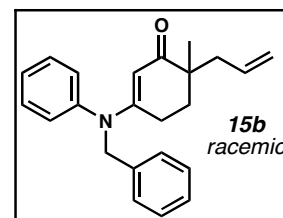


Figure SI-13C. ¹³C NMR (125 MHz, CDCl₃) of compound **15b**.

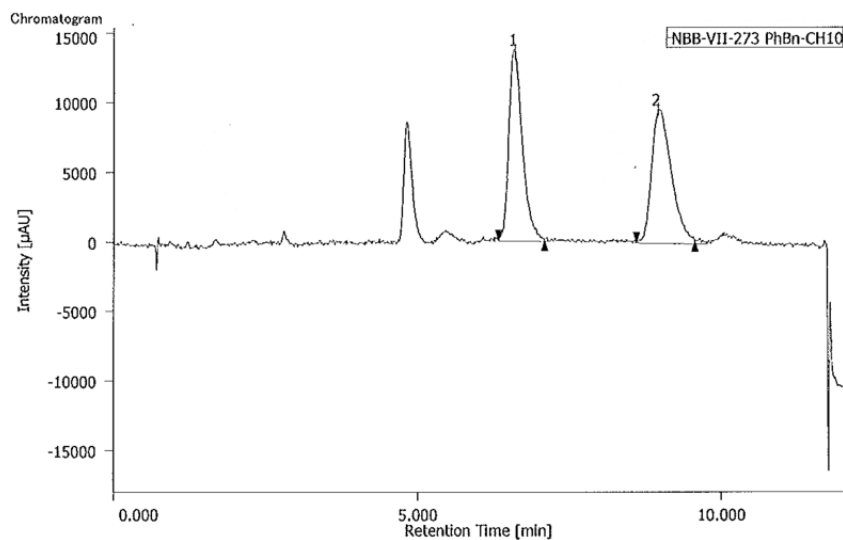
NBB-VII-273 Sub3 Col4 5MeOH-2 NBB-VII-273 PhBn 10/27/2011 4:52:15 PM

Analytical Report SFC



Chromatogram Information

User: Jasco SFC w PDA
 HPLC System Name: 10/27/2011 1:54:49 PM
 Injection Date: 5.00 [μL]
 Volume: 51
 Sample #: Cal Tech SFC
 Project Name: NBB-VII-273 Sub3 Col4 5MeOH-2
 Executed Sequence: NBB-VII-273 PhBn
 Chromatogram Name: 12.0 [min]
 Sample Name: NBB-VII-273 Sub3 Col4 5MeOH-2
 Acquisition Time: NBB-VII-273 Sub3 Col4 5MeOH-2
 Acquisition Sequence: Solv 1 Col 4 Isocratic 5B 5mL_min 10MPa 15min
 Control Method:



Peak Information

#	Peak Name	CH	TR [min]	Area [μV·sec]	Height [μV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	10	6.600	215088	13790	49.635	6.333	7.093	0.231	4.806	1.429
2	Unknown	10	8.960	218252	9641	50.365	8.600	9.560	0.348	N/A	1.695

1 / 1

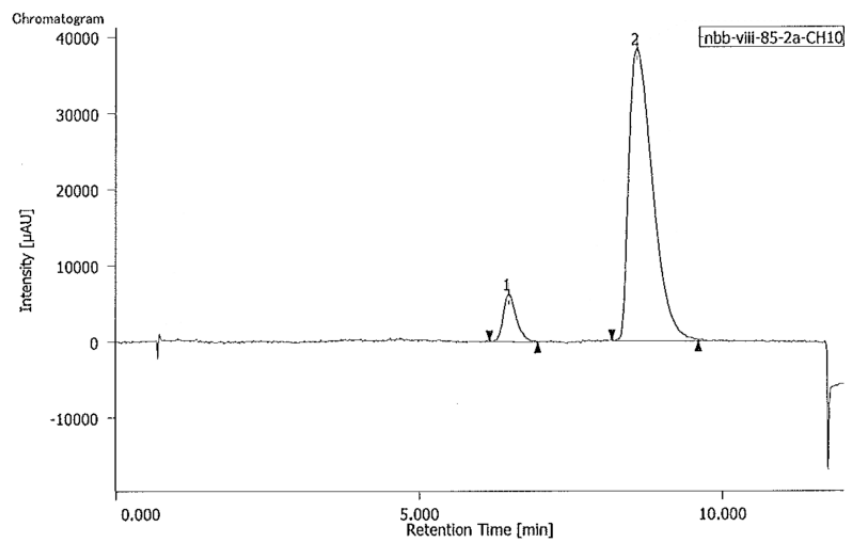
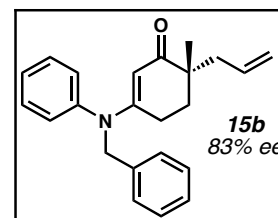
Figure SI-13D. Chiral SFC data of racemic compound **15b**.

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

Analytical Report SFC

Chromatogram Information

User: Jasco SFC w PDA
 HPLC System Name: 6/27/2012 11:12:52 AM
 Injection Date: 5.00 [μL]
 Volume: 51
 Sample #: Cal Tech SFC
 Project Name: NBB-VIII-85-2A Col4 5% MeOH 15min
 Executed Sequence: nbb-viii-85-2a
 Chromatogram Name: 12.0 [min]
 Sample Name: NBB-VIII-85-2A Col4 5% MeOH 15min
 Acquisition Time: Solv 1 Col 4 Isocratic 5B 5mL_min 10MPa 15min
 Acquisition Sequence:
 Control Method:

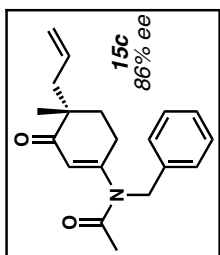
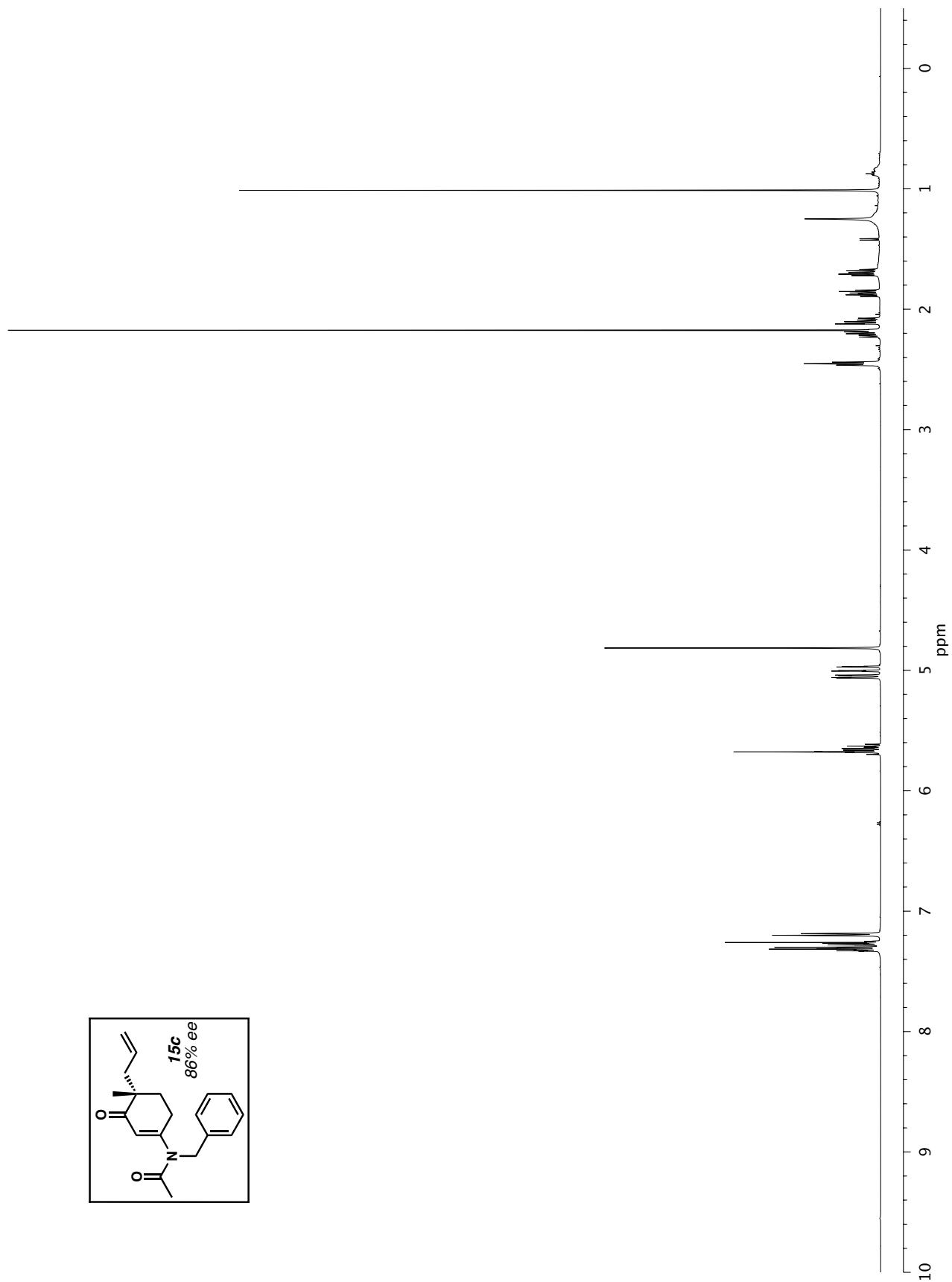


Peak Information

#	Peak Name	CH	tR [min]	Area [μV-sec]	Height [μV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	10	6.480	94763	6347	8.346	6.160	6.960	0.221	3.889	1.384
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-144. ¹H NMR (500 MHz, CDCl₃) of compound **15c**.

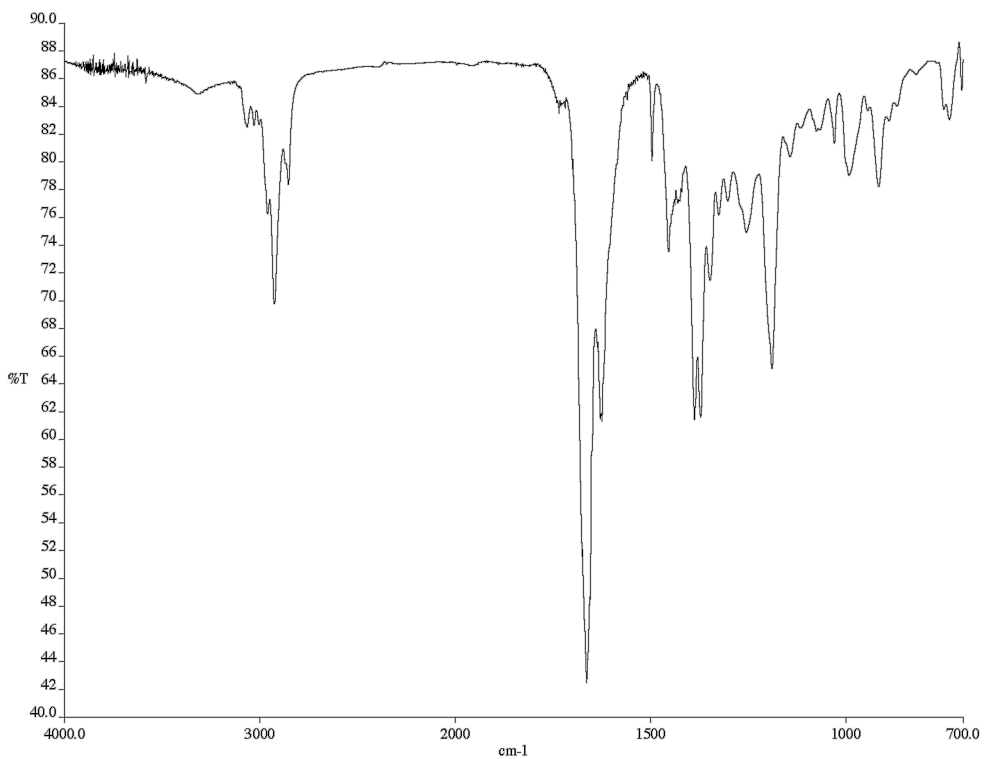


Figure SI-14B. Infrared spectrum (thin film/NaCl) of compound **15c**.

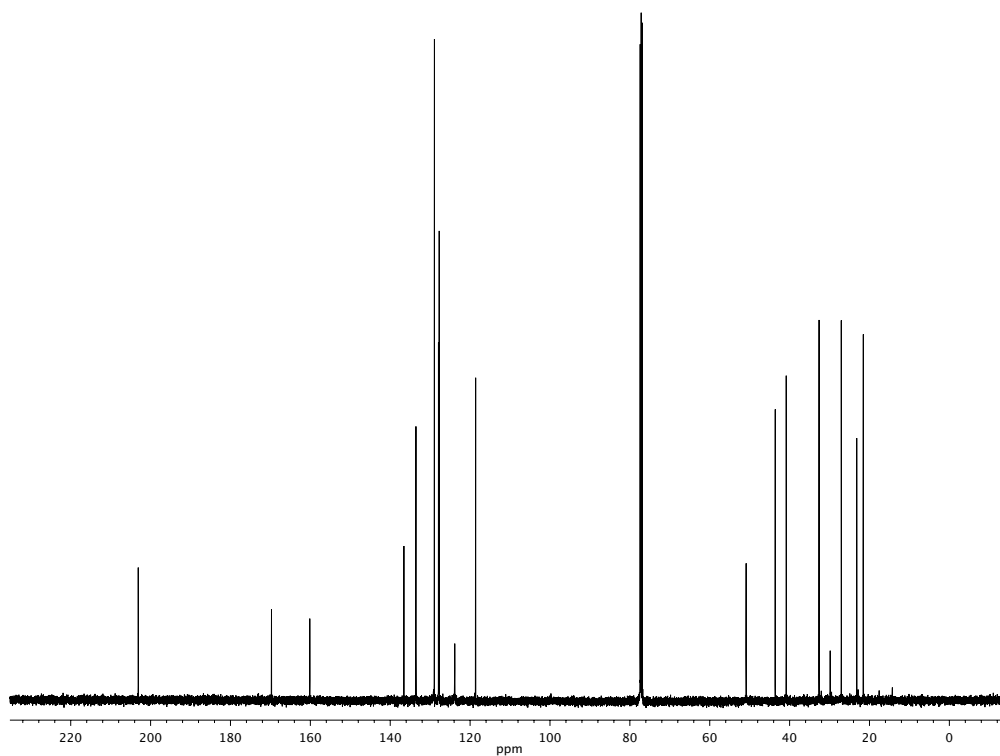
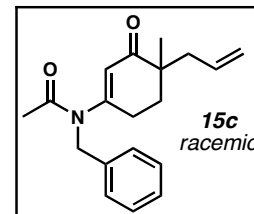


Figure SI-14C. ¹³C NMR (125 MHz, CDCl₃) of compound **15c**.

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



```
=====
Acq. Operator   : NBB                               Seq. Line :    2
Acq. Instrument : Instrument 1                       Location  : P2-C-01
Injection Date  : 10/4/2012 2:29:45 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 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)
Method Info     : S1C2 12min 5.M: 5% MeOH, AD-H 3 mL/min, 12 min
Sample Info     : NBB-IX-257 Racemic, 4-3-1
=====
```

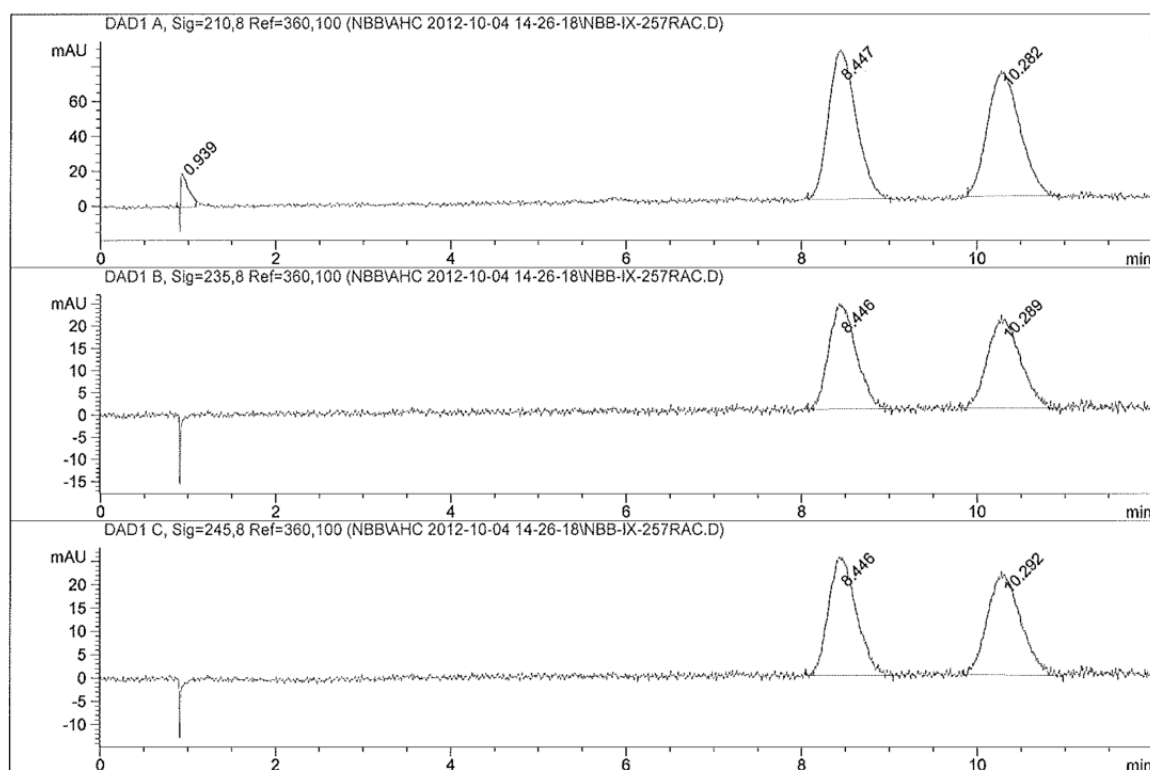
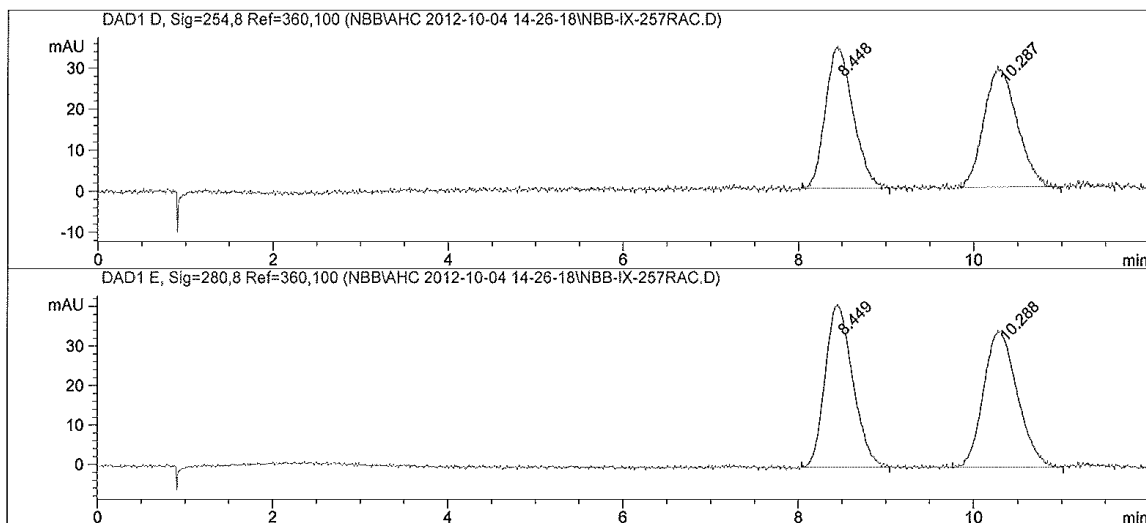


Figure SI-14D. Chiral SFC data of racemic compound **15c**.

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



=====
 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

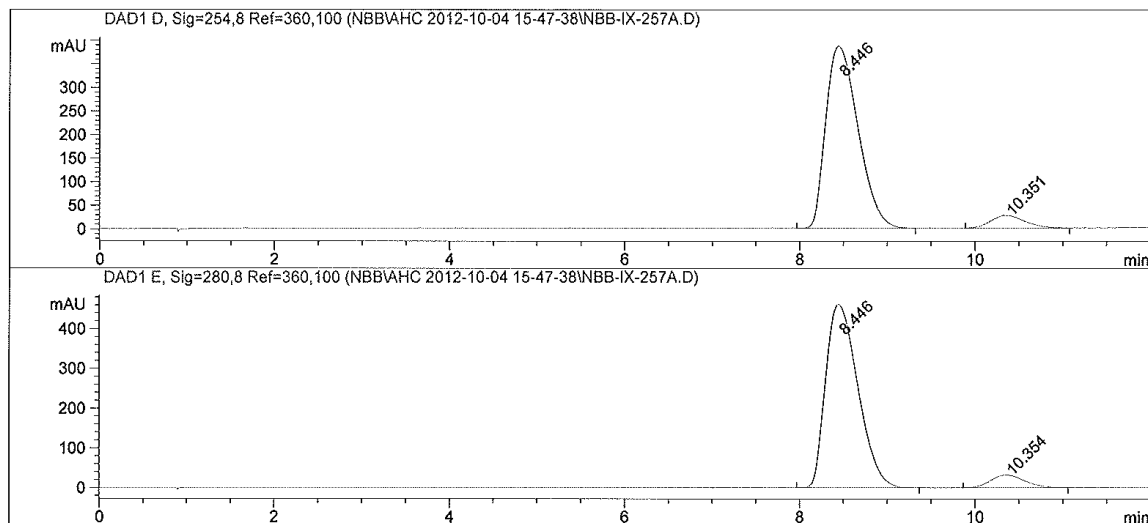
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.448	BB	0.3431	760.15375	34.23129	49.9424
2	10.287	BB	0.4083	761.90826	28.46026	50.0576
Totals :				1522.06201	62.69156	

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 ***

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

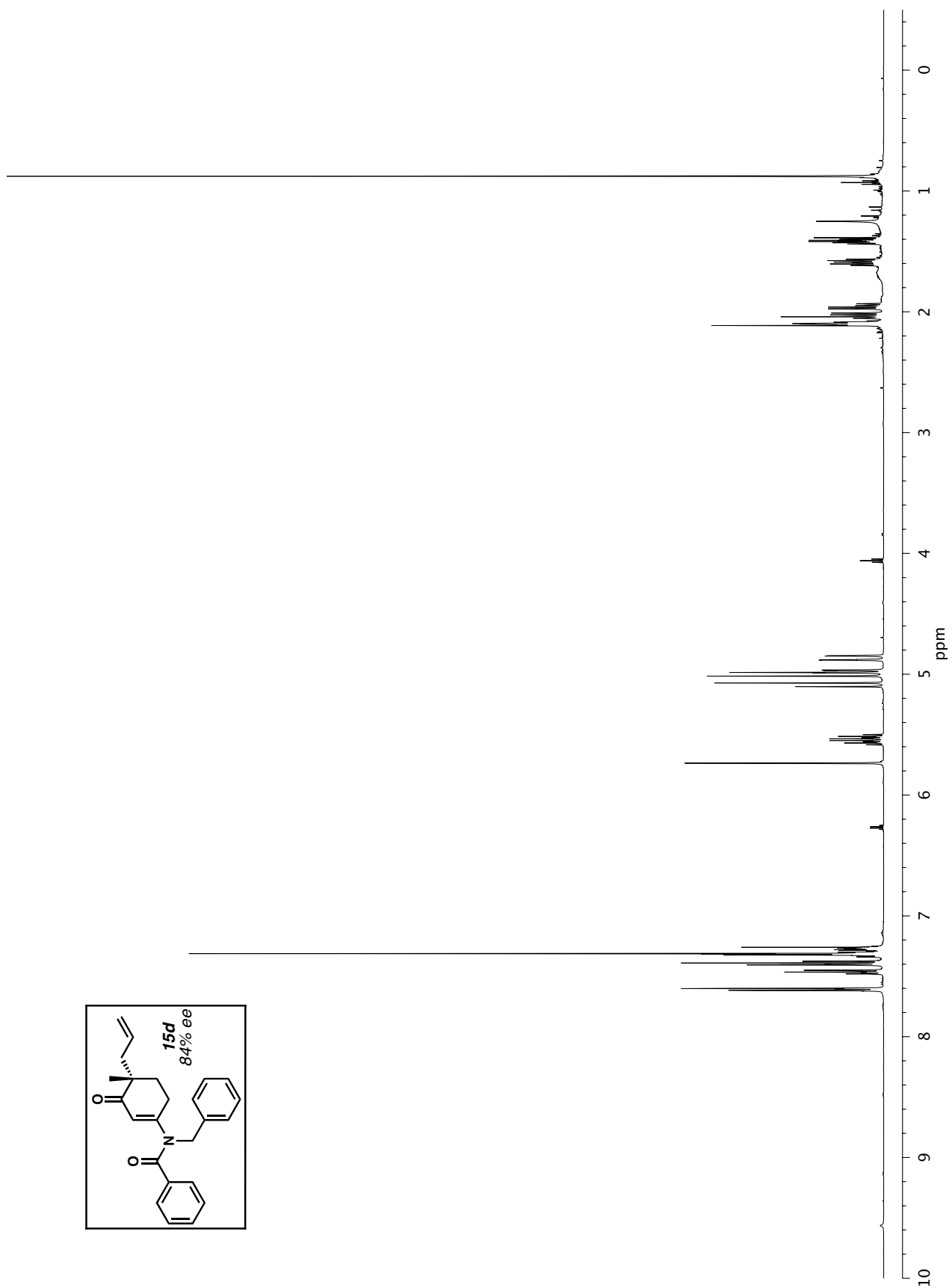
Totals : 1.06008e4 412.48260

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. $^1\text{H NMR}$ (500 MHz, CDCl_3) of compound **15d**.

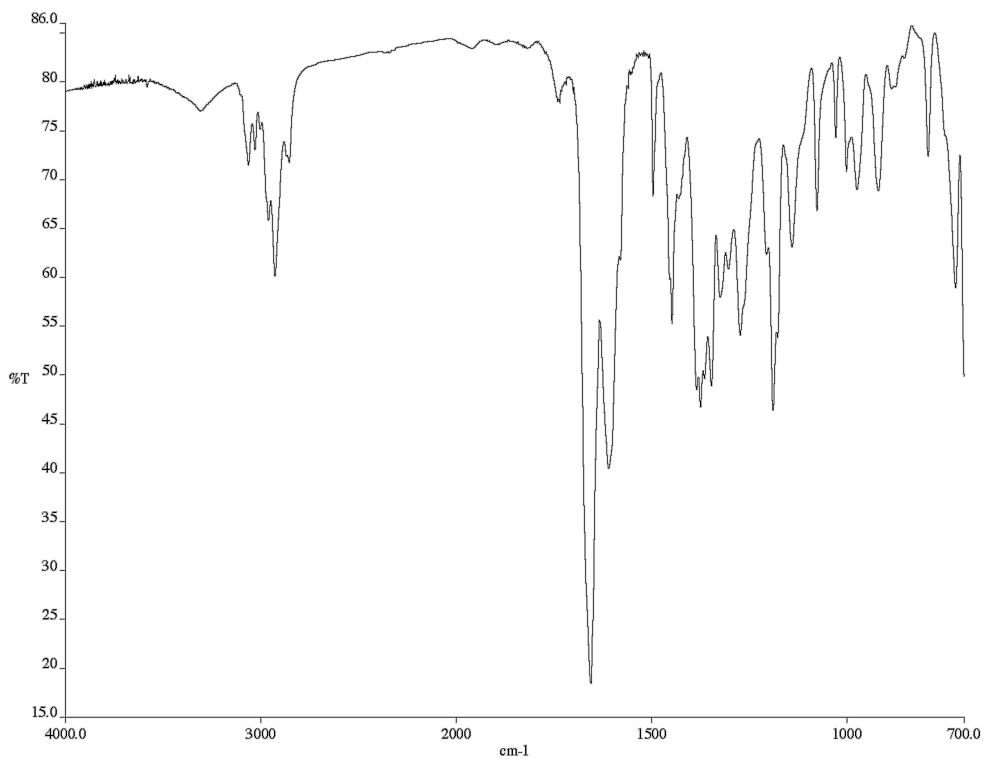


Figure SI-15B. Infrared spectrum (thin film/NaCl) of compound **15d**.

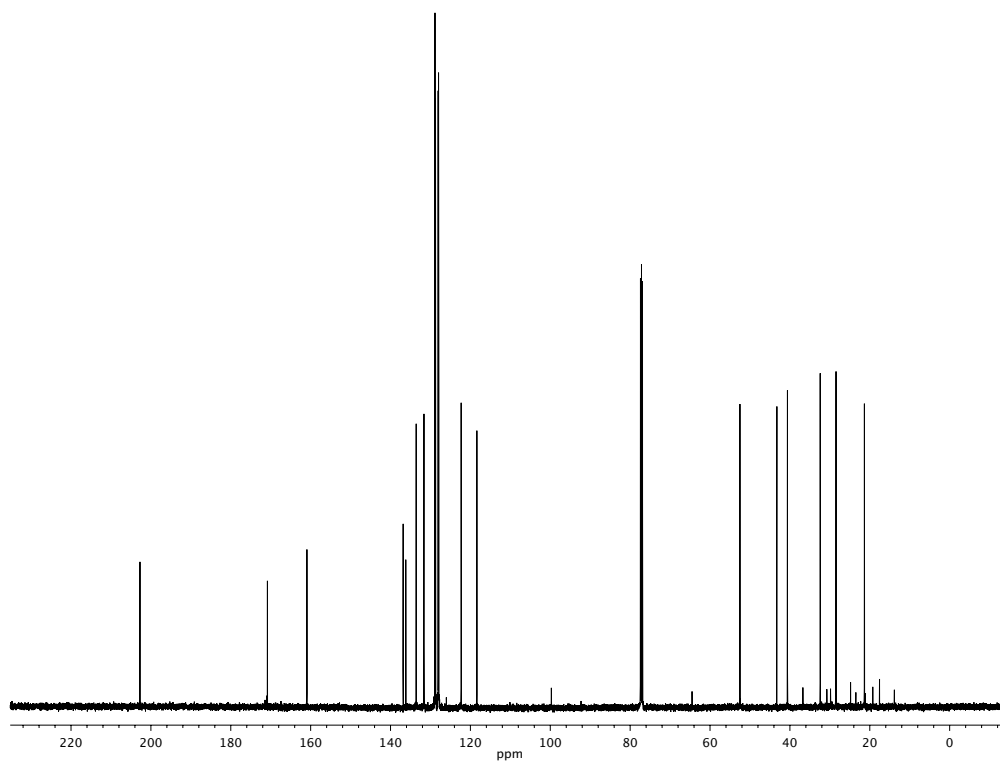
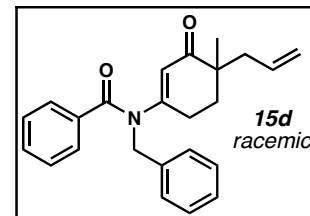


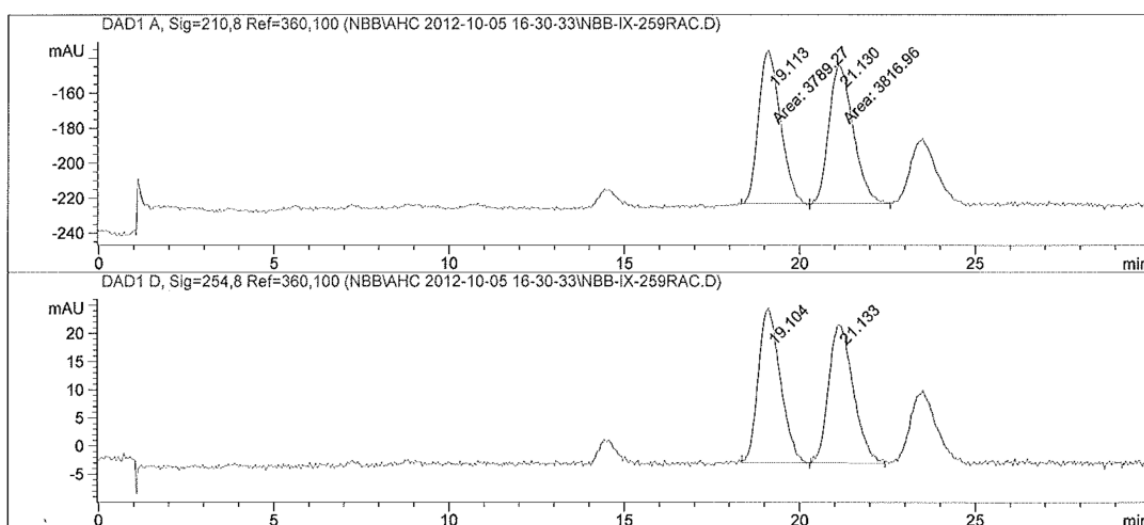
Figure SI-15C. ¹³C NMR (125 MHz, CDCl₃) of compound **15d**.

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



```

=====
Acq. Operator   : NBB                               Seq. Line :    4
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
  
```



=====
 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	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

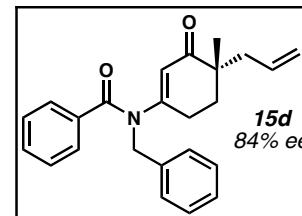
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.104	BB	0.6731	1203.76782	27.37041	49.9413
2	21.133	BB	0.7281	1206.59875	24.43527	50.0587

Totals : 2410.36658 51.80568

=====

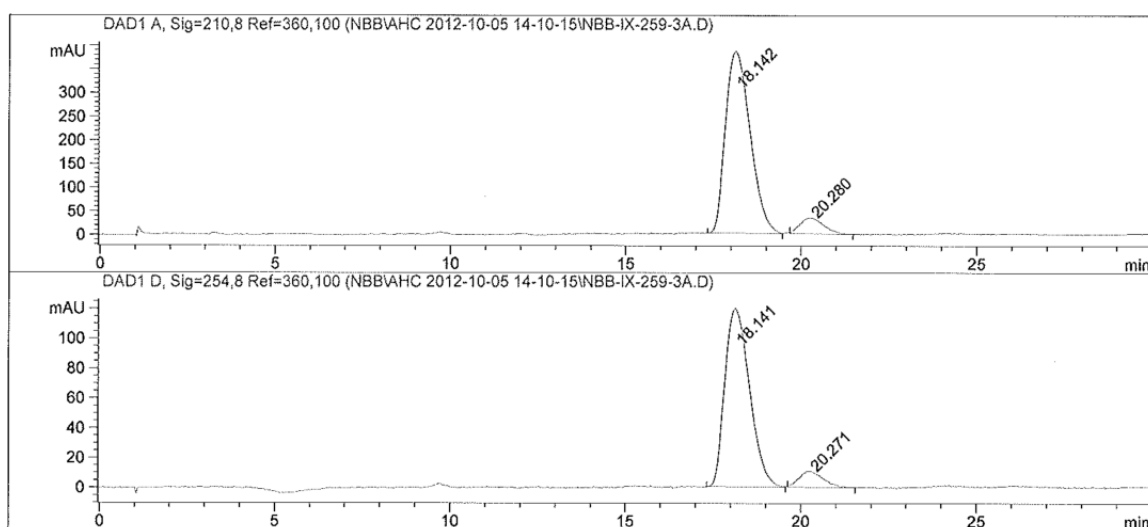
*** End of Report ***

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



```

=====
Acq. Operator   : NBB                               Seq. Line :    5
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
  
```



=====
 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	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**.

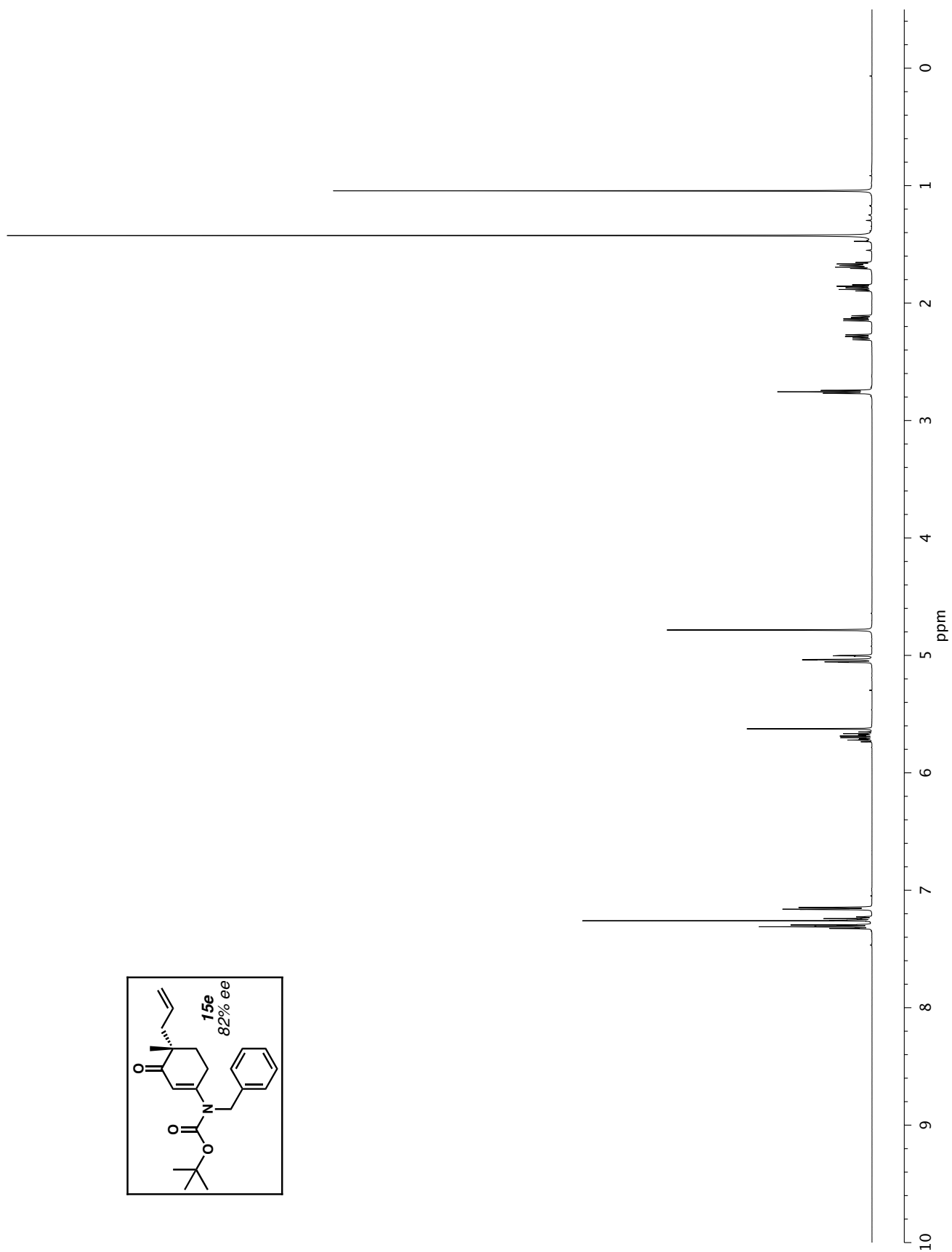
Data File C:\CHEM32\1\DATA\NBB\AHC 2012-10-05 14-10-15\NBB-IX-259-3A.D
Sample Name: NBB-IX-259-3A

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. ^1H NMR (500 MHz, CDCl_3) of compound **15e**.

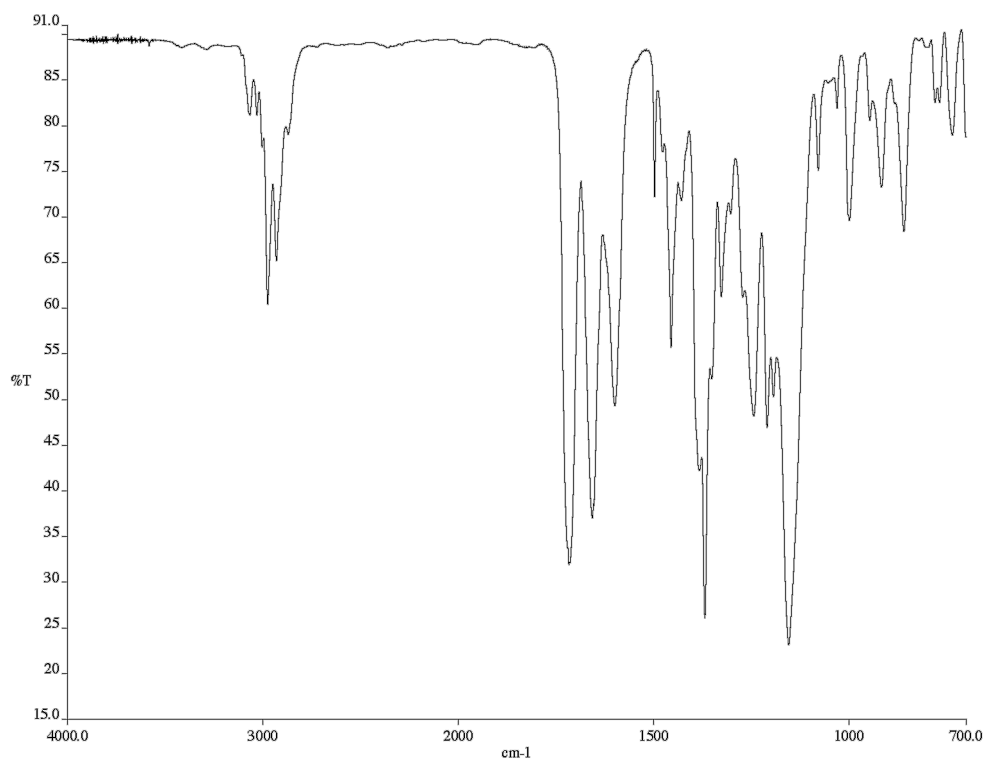


Figure SI-16B. Infrared spectrum (thin film/NaCl) of compound **15e**.

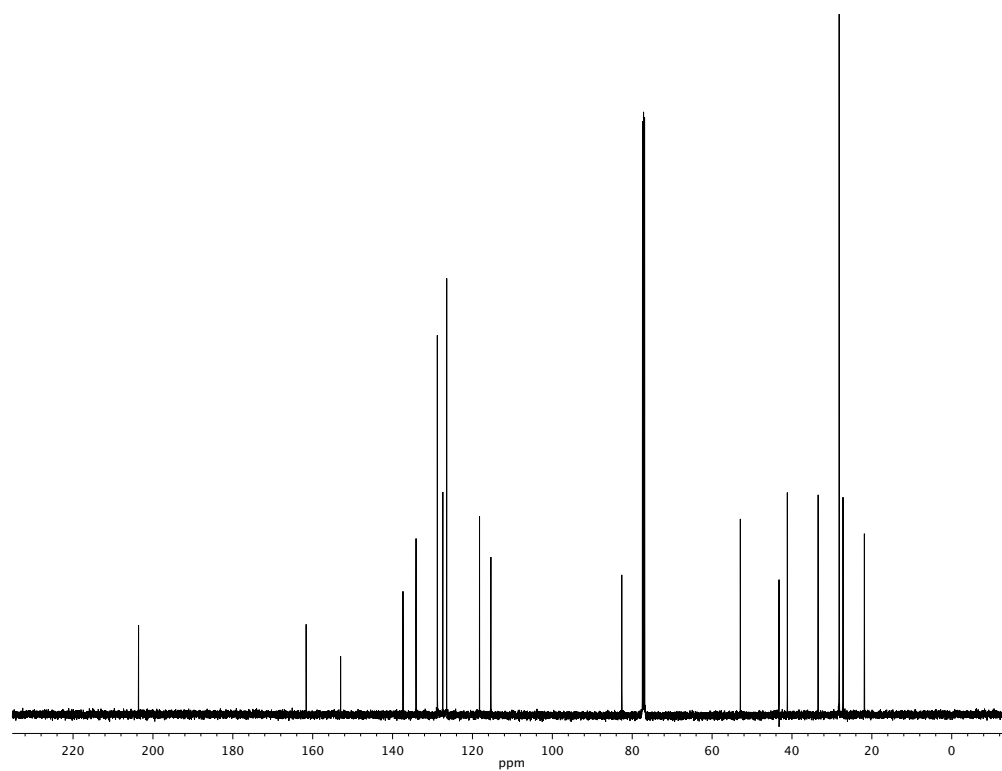


Figure SI-16C. ¹³C NMR (125 MHz, CDCl₃) of compound **15e**.

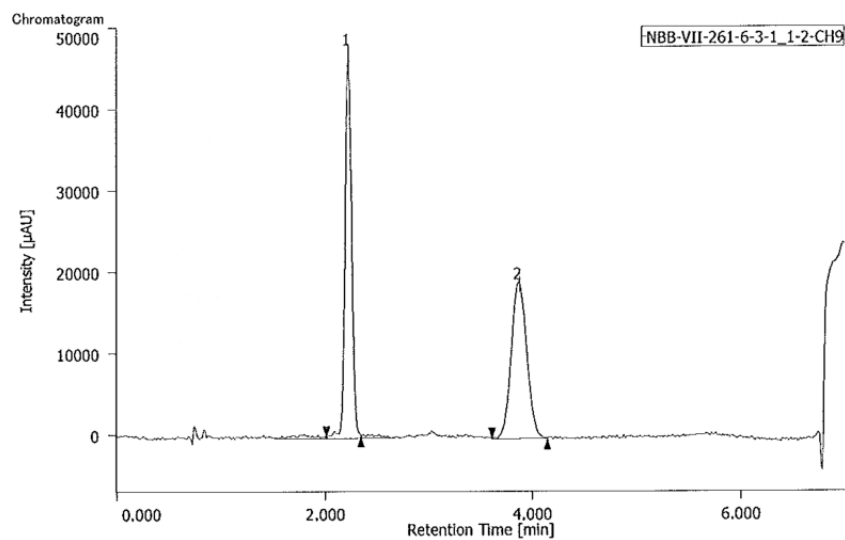
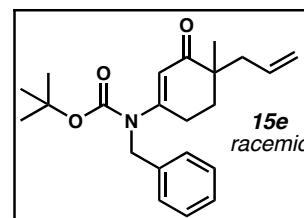
NBB-VII-261_Sub46Col1 NBB-VII-261-6-3-1_1-2 10/22/2011 11:00:54 AM

Analytical Report SFC

Chromatogram Information

User
 HPLC System Name
 Injection Date
 Volume
 Sample #
 Project Name
 Executed Sequence
 Chromatogram Name
 Sample Name
 Acquisition Time
 Acquisition Sequence
 Control Method

User
 Jasco SFC w/ PDA
 10/21/2011 12:55:32 PM
 5.00 [μL]
 51
 Cal Tech SFC
 NBB-VII-261_Sub46Col1
 NBB-VII-261-6-3-1_1-2
 7.0 [min]
 NBB-VII-261_Sub46Col1
 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	8.516	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**.

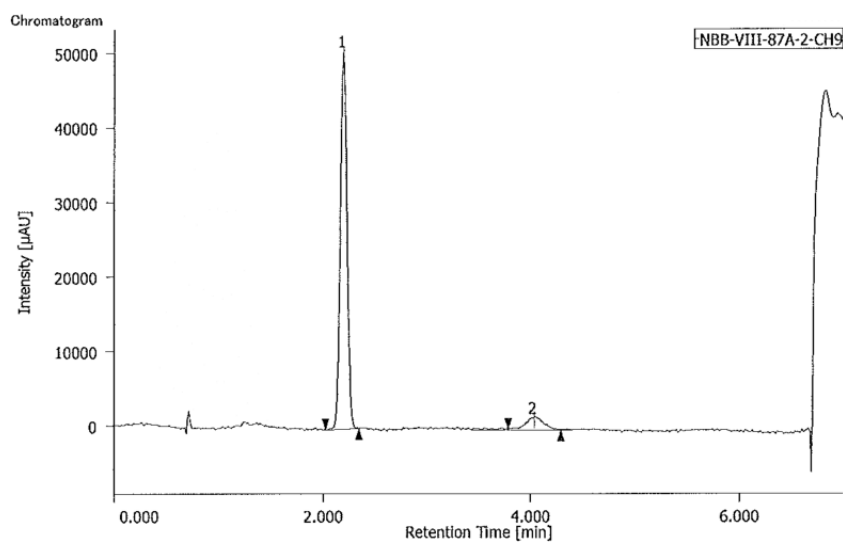
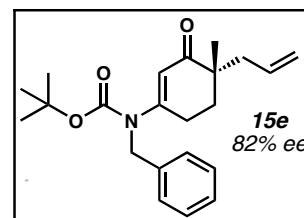
NBB-VIII-87A Col1 7 MeOH NBB-VIII-87A-2 12/16/2011 10:44:03 AM

Analytical Report SFC

Chromatogram Information

User
 HPLC System Name
 Injection Date
 Volume
 Sample #
 Project Name
 Executed Sequence
 Chromatogram Name
 Sample Name
 Acquisition Time
 Acquisition Sequence
 Control Method

User
 Jasco SFC w PDA
 12/16/2011 10:34:12 AM
 5.00 [μL]
 51
 Cal Tech SFC
 NBB-VIII-87A Col1 7 MeOH
 NBB-VIII-87A-2
 7.0 [min]
 NBB-VIII-87A Col1 7 MeOH
 Solv 1 Col 1 Isocratic 7B 5mL_min 10MPa 10min

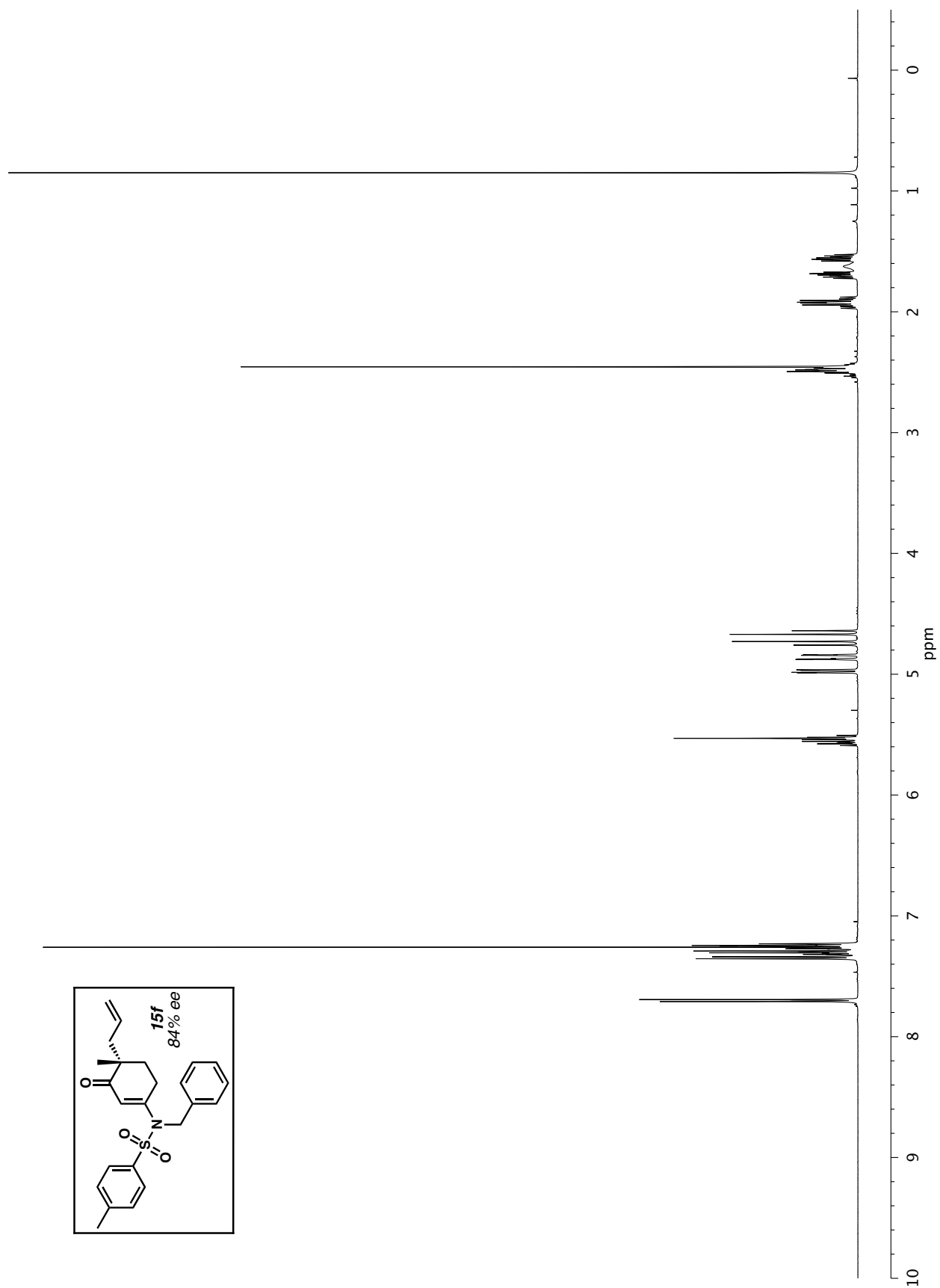


Peak Information

#	Peak Name	CH	tR [min]	Area [μV-sec]	Height [μV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	9	2.200	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	0.176	N/A	N/A

1 / 1

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

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

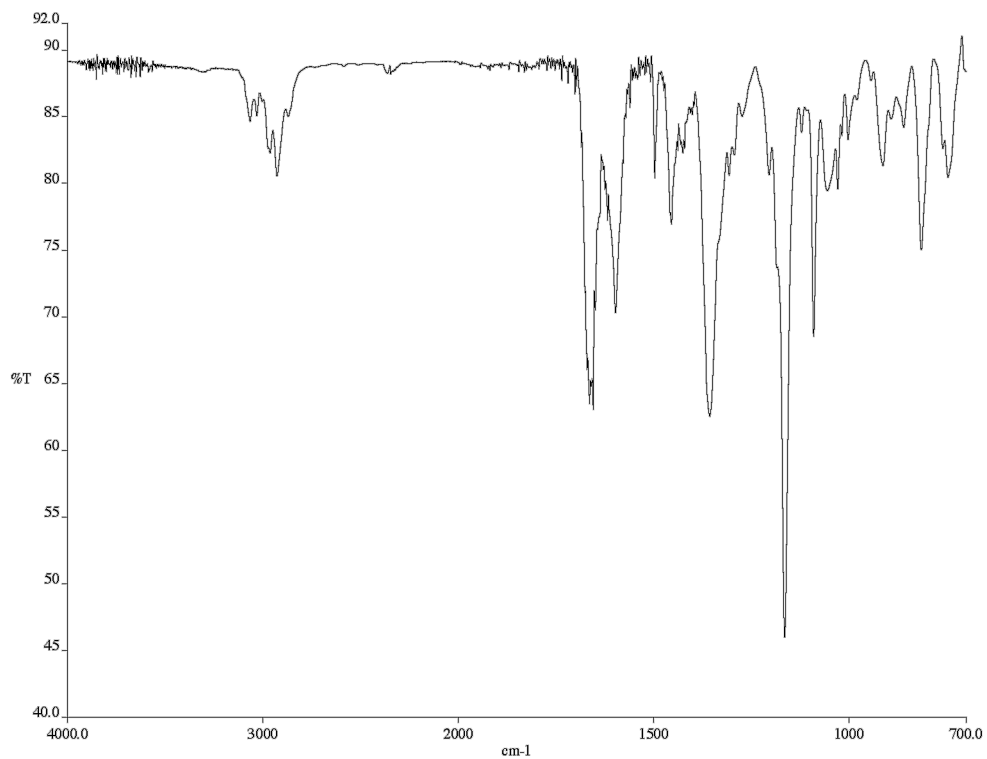


Figure SI-17B. Infrared spectrum (thin film/NaCl) of compound **15f**.

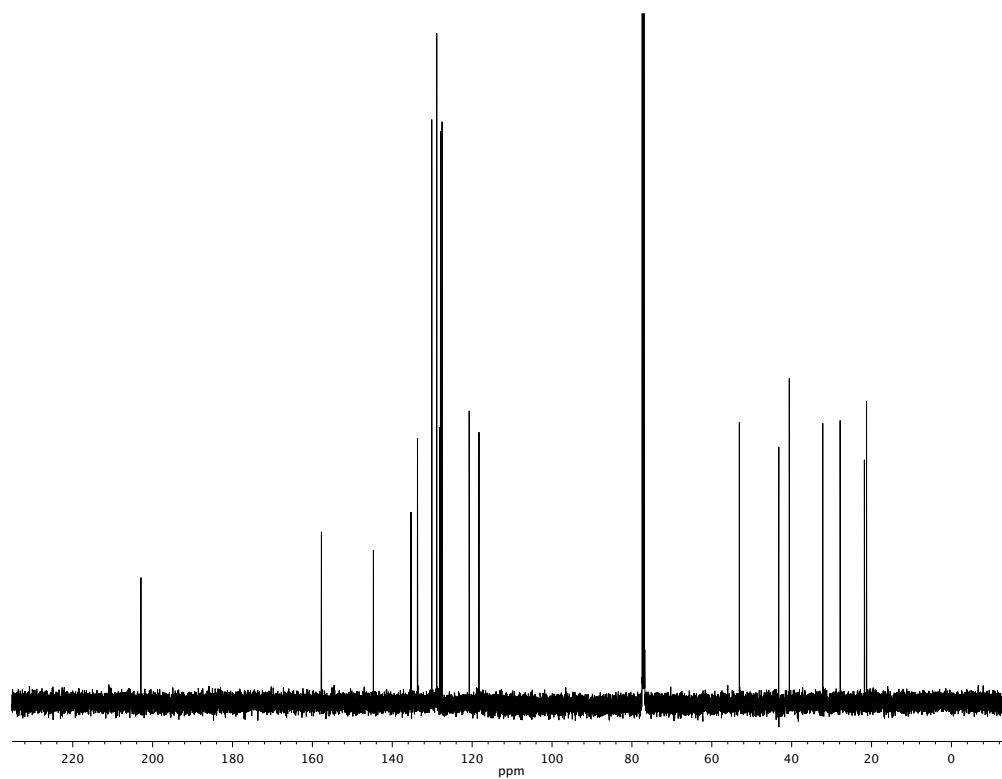


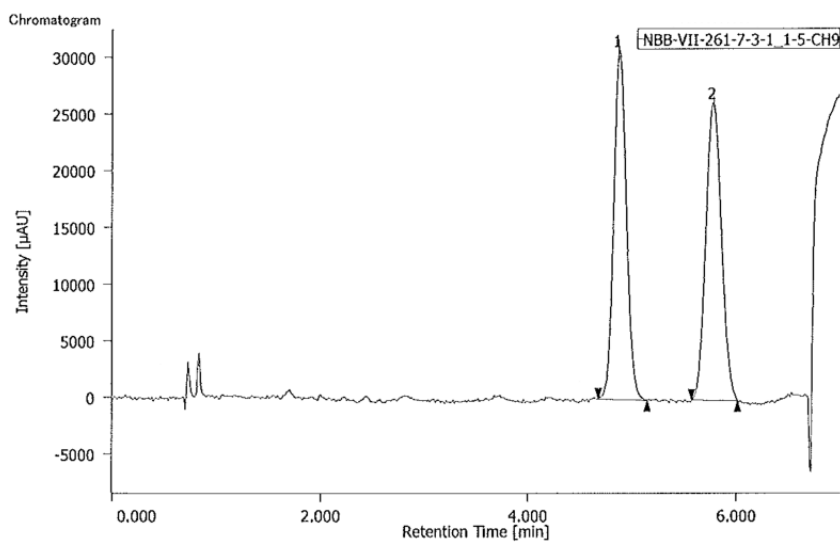
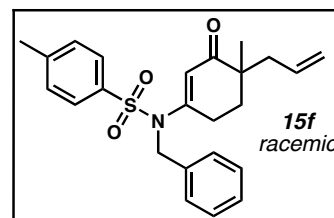
Figure SI-17C. ¹³C NMR (125 MHz, CDCl₃) of compound **15f**.

NBB_VII_261 NBB-VII-261-7-3-1_1-5 10/20/2011 11:38:40 AM

Analytical Report SFC

Chromatogram Information

User: Jasco SFC w PDA
 HPLC System Name: NBB_VII_261
 Injection Date: 10/20/2011 11:20:35 AM
 Volume: 5.00 [μL]
 Sample #: 76
 Project Name: Cal Tech SFC
 Executed Sequence: NBB_VII_261
 Chromatogram Name: NBB-VII-261-7-3-1_1-5
 Sample Name:
 Acquisition Time: 7.0 [min]
 Acquisition Sequence: NBB_VII_261
 Control Method: Solv 1 Col 1 Isocratic 10B 5mL_min 10MPa 10min
 Meth



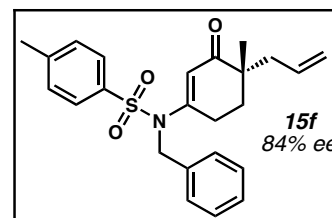
Peak Information

#	Peak Name	CH	tR [min]	Area [μV-sec]	Height [μV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	9	4.880	260592	30824	48.700	4.680	5.147	0.130	3.634	1.138
2	Unknown	9	5.787	274504	26280	51.300	5.573	6.013	0.164	N/A	1.041

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

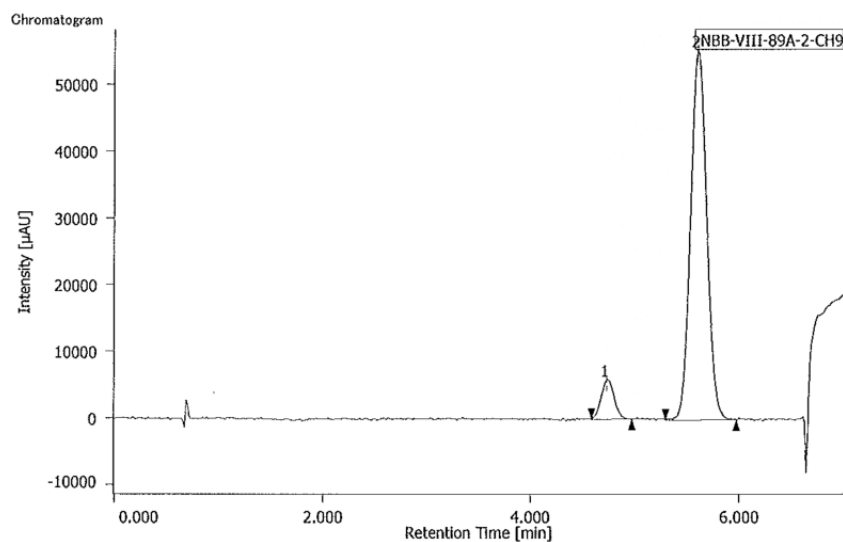
NBB-VIII-89A Col1 10 MeOH-3 NBB-VIII-89A-2 12/17/2011 12:59:35 PM

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]
Acquisition Sequence	NBB-VIII-89A Col1 10 MeOH-3
Control Method	Solv 1 Col 1 Isocratic 10B 5mL_min 10MPa 10min

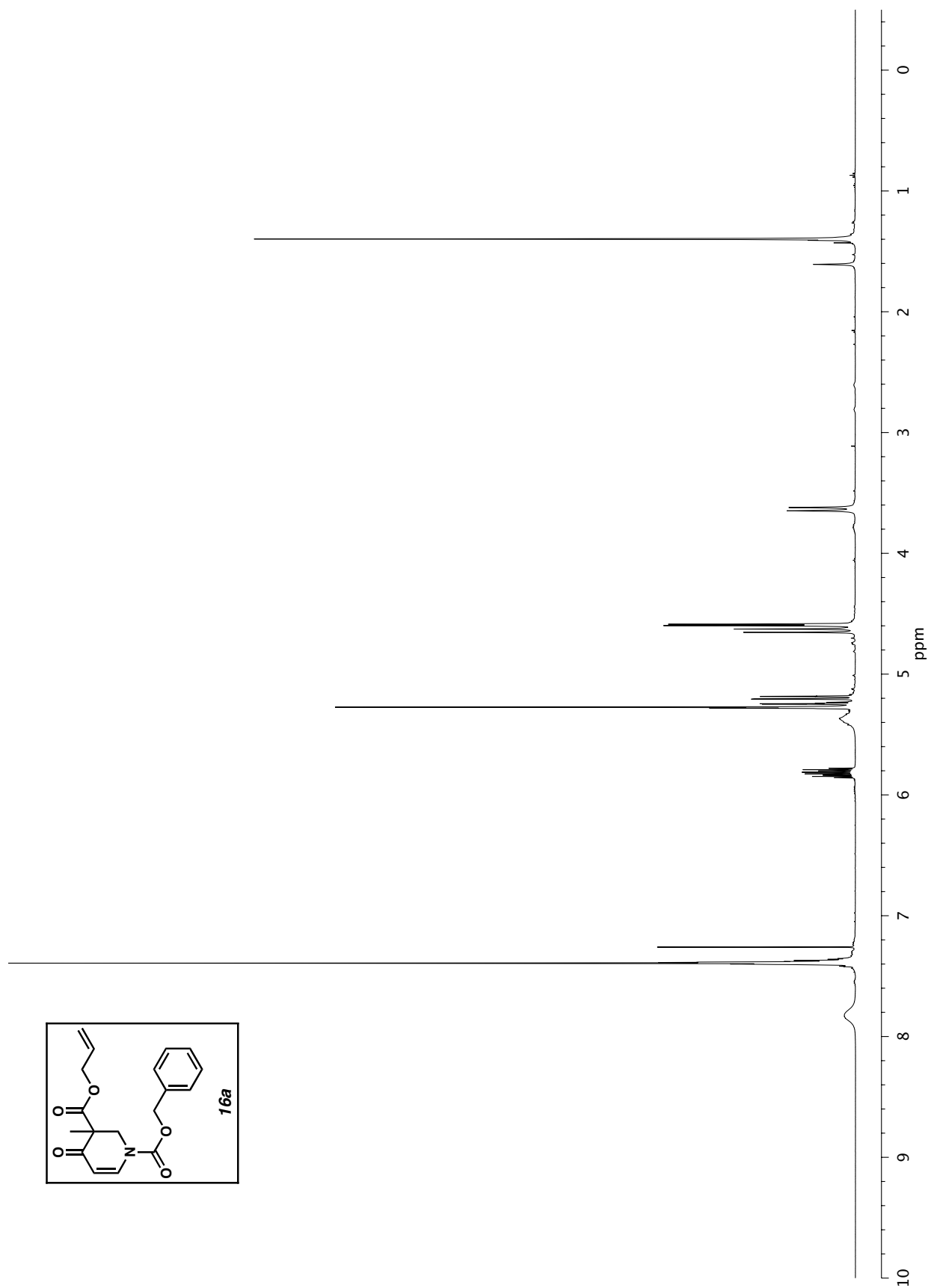


Peak Information

#	Peak Name	CH	tR [min]	Area [μV-sec]	Height [μV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	9	4.733	51755	5932	8.031	4.587	4.973	0.136	3.386	1.126
2	Unknown	9	5.600	592694	65307	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. ^1H NMR (500 MHz, CDCl_3) of compound **16a**.

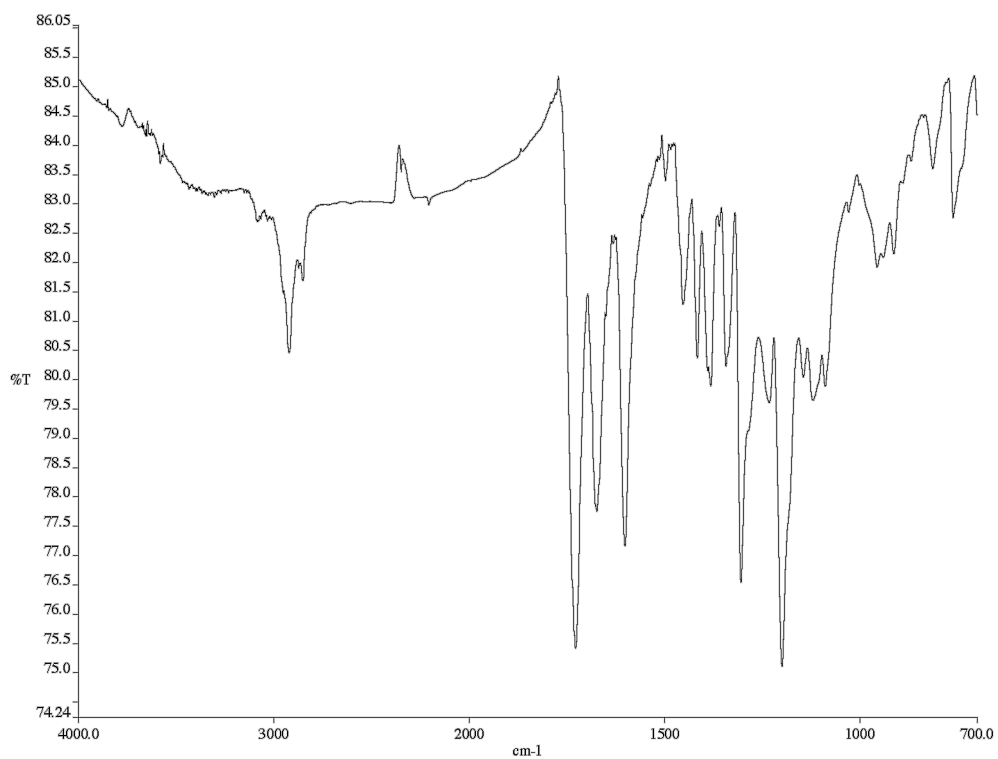


Figure SI-18B. Infrared spectrum (thin film/NaCl) of compound **16a**.

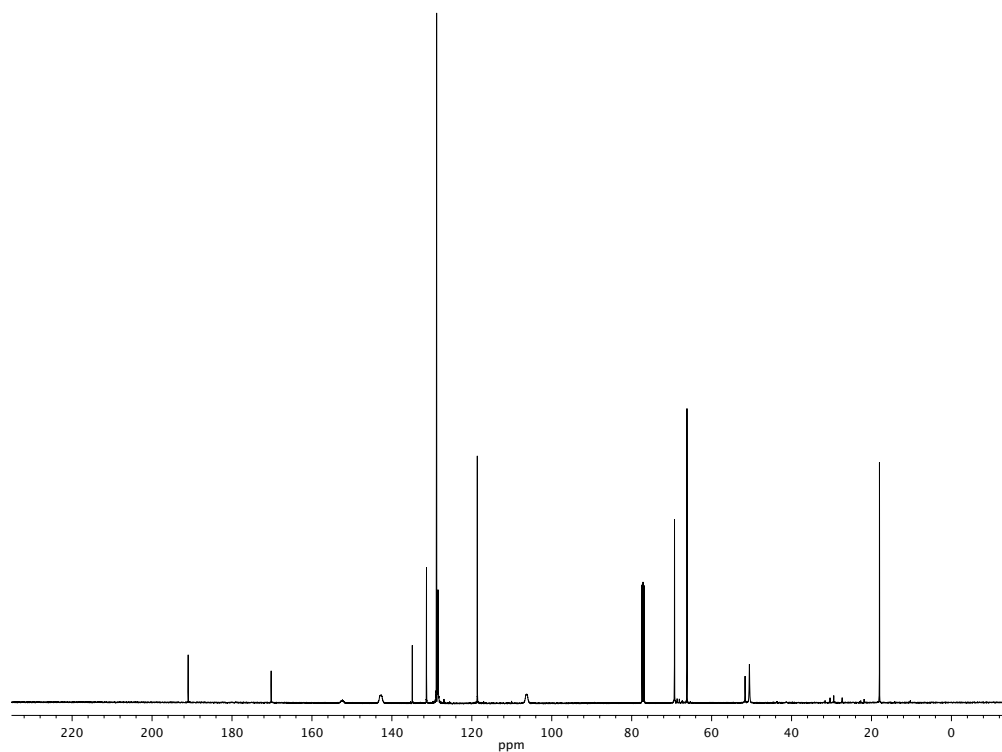
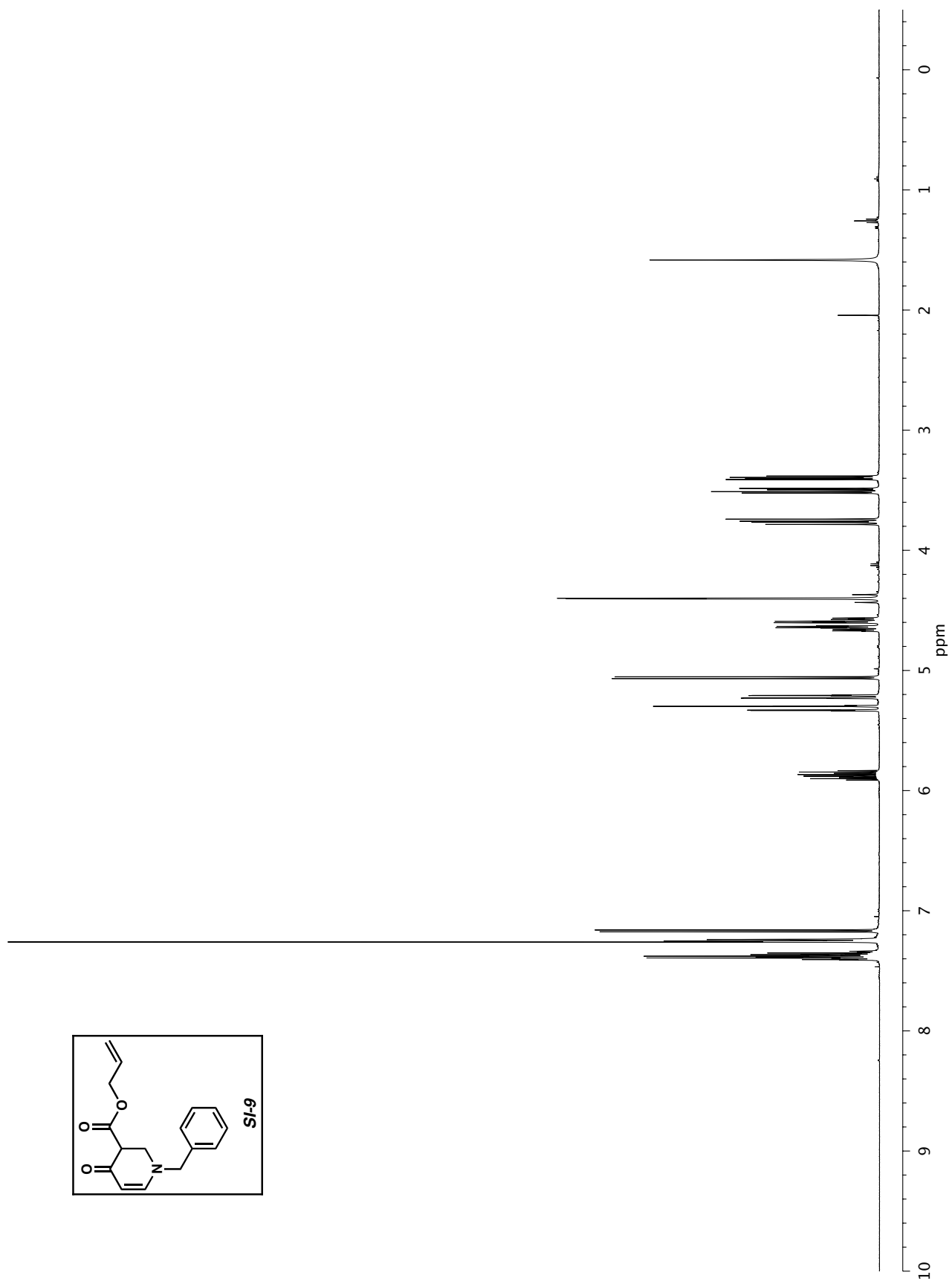


Figure SI-18C. ¹³C NMR (125 MHz, CDCl₃) of compound **16a**.

Figure SI-19A. $^1\text{H NMR}$ (500 MHz, CDCl_3) of compound SI-9.

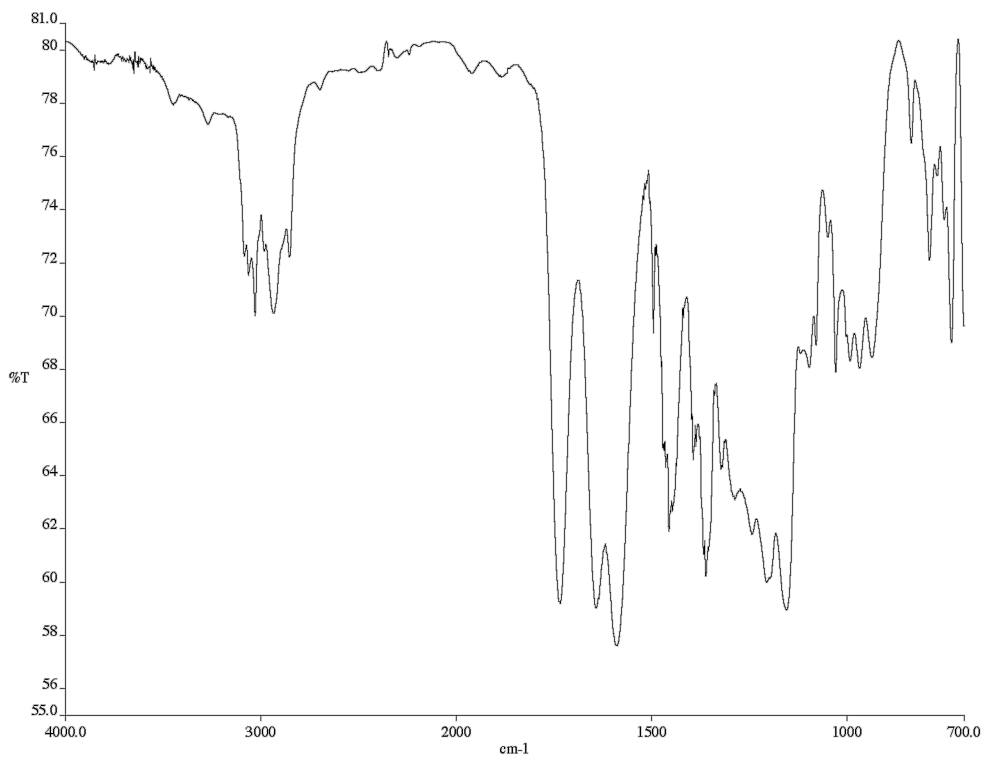


Figure SI-19B. Infrared spectrum (thin film/NaCl) of compound **SI-9**.

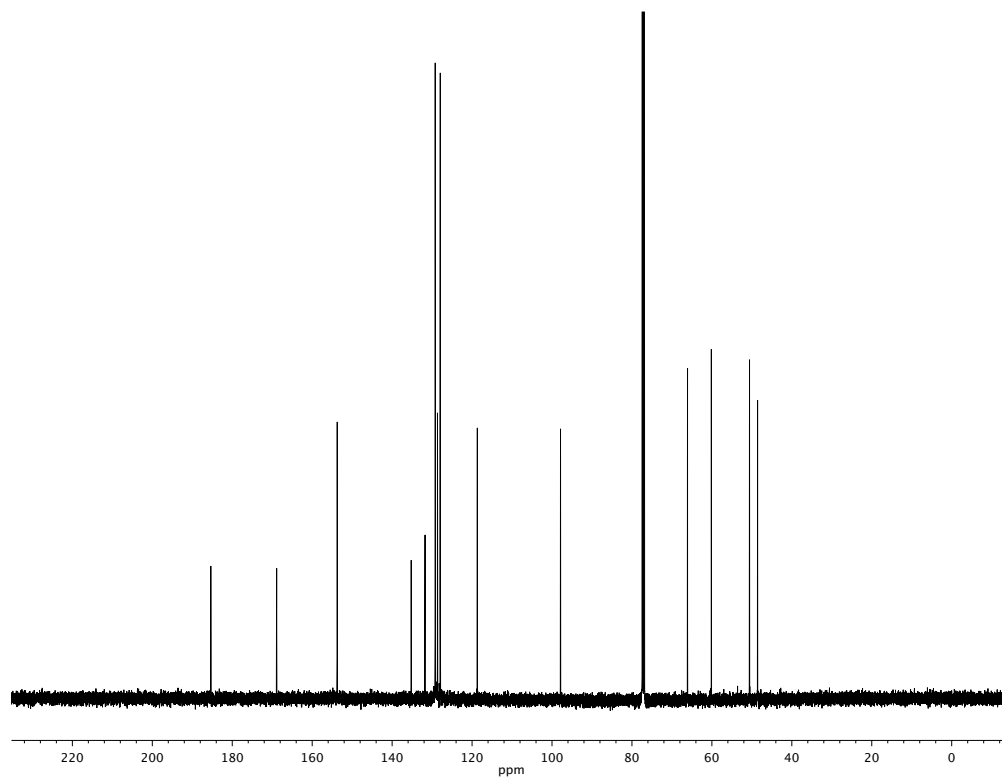


Figure SI-19C. ^{13}C NMR (125 MHz, CDCl_3) of compound **SI-9**.

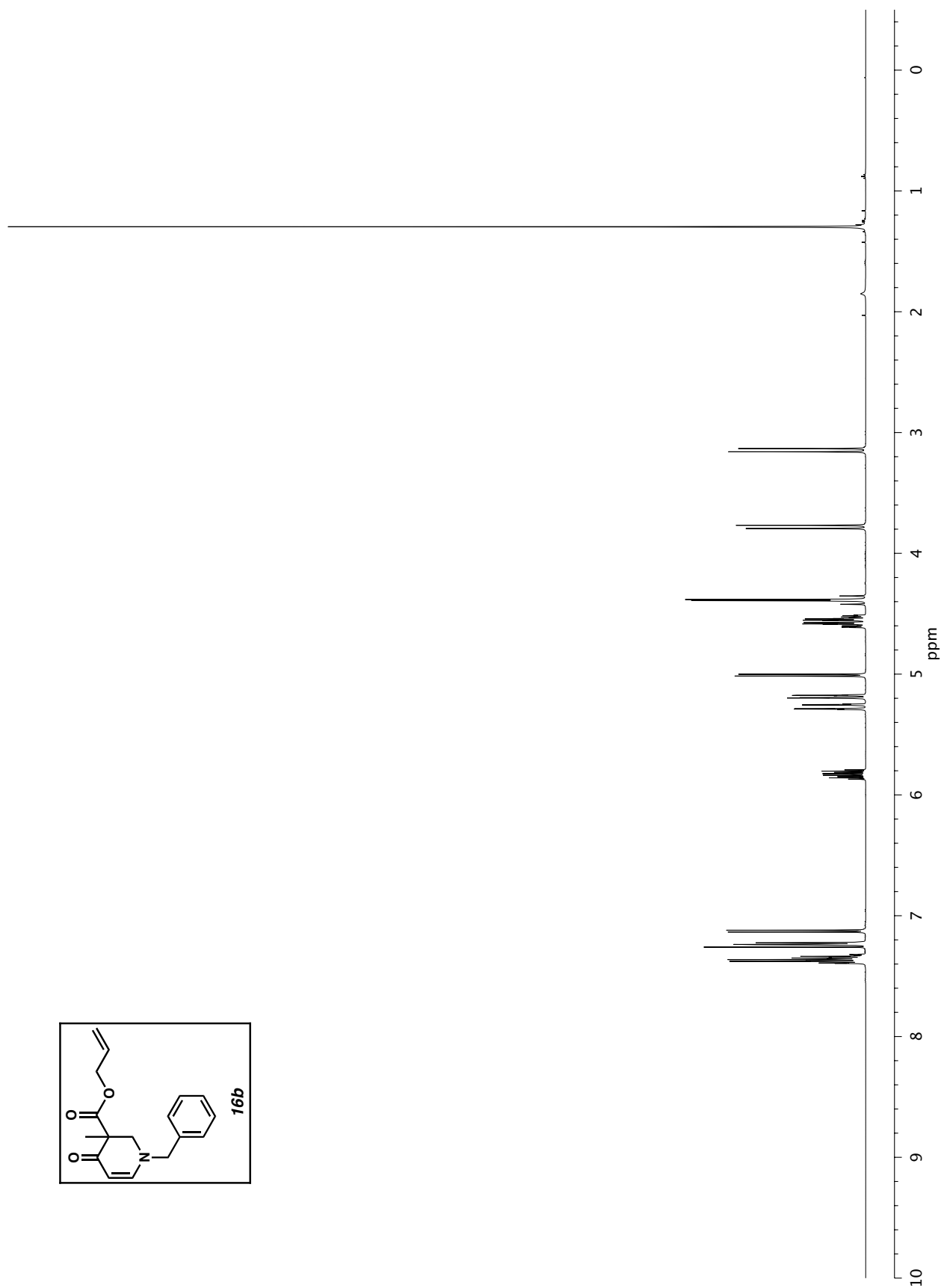


Figure SI-20A. ¹H NMR (500 MHz, CDCl₃) of compound **16b**.

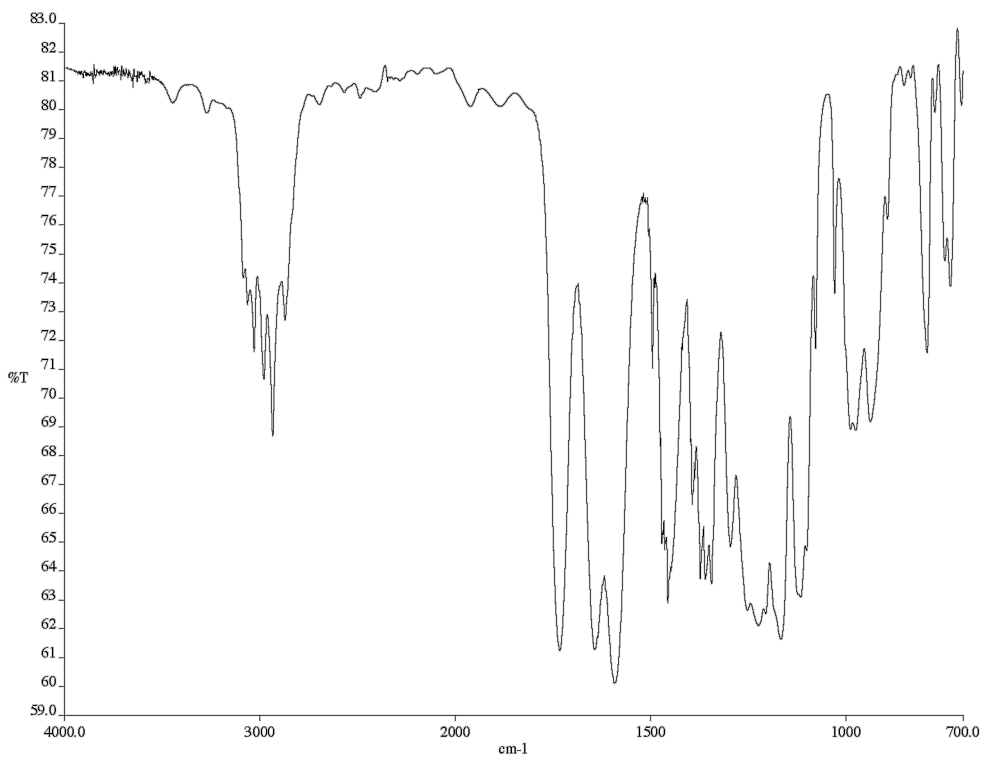


Figure SI-20B. Infrared spectrum (thin film/NaCl) of compound **16b**.

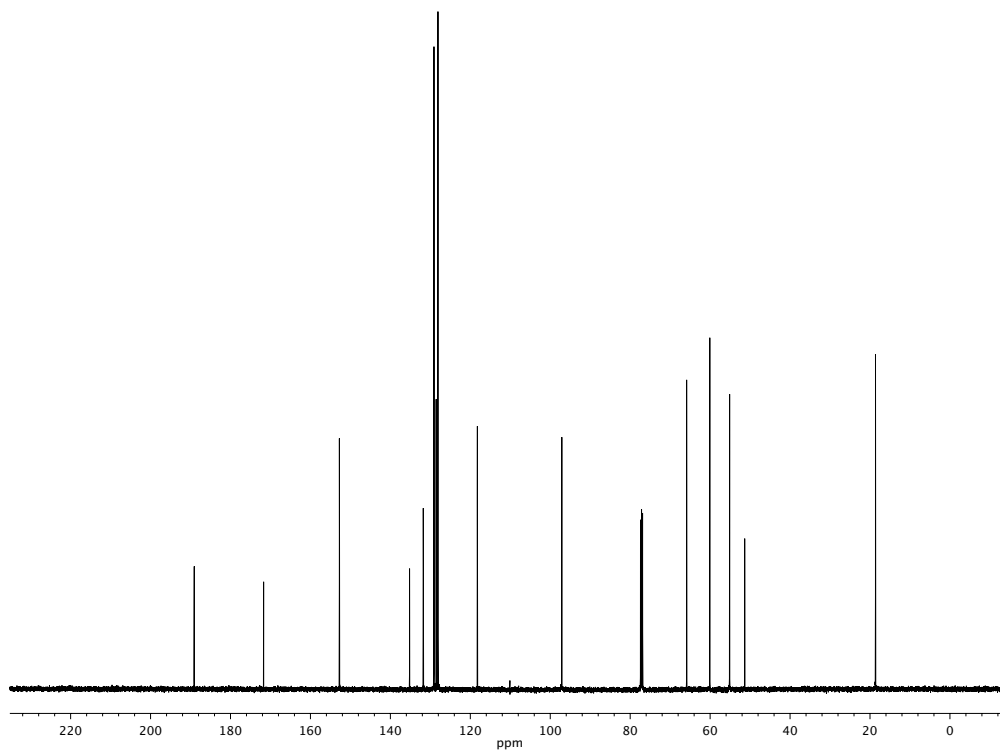


Figure SI-20C. ¹³C NMR (125 MHz, CDCl₃) of compound **16b**.

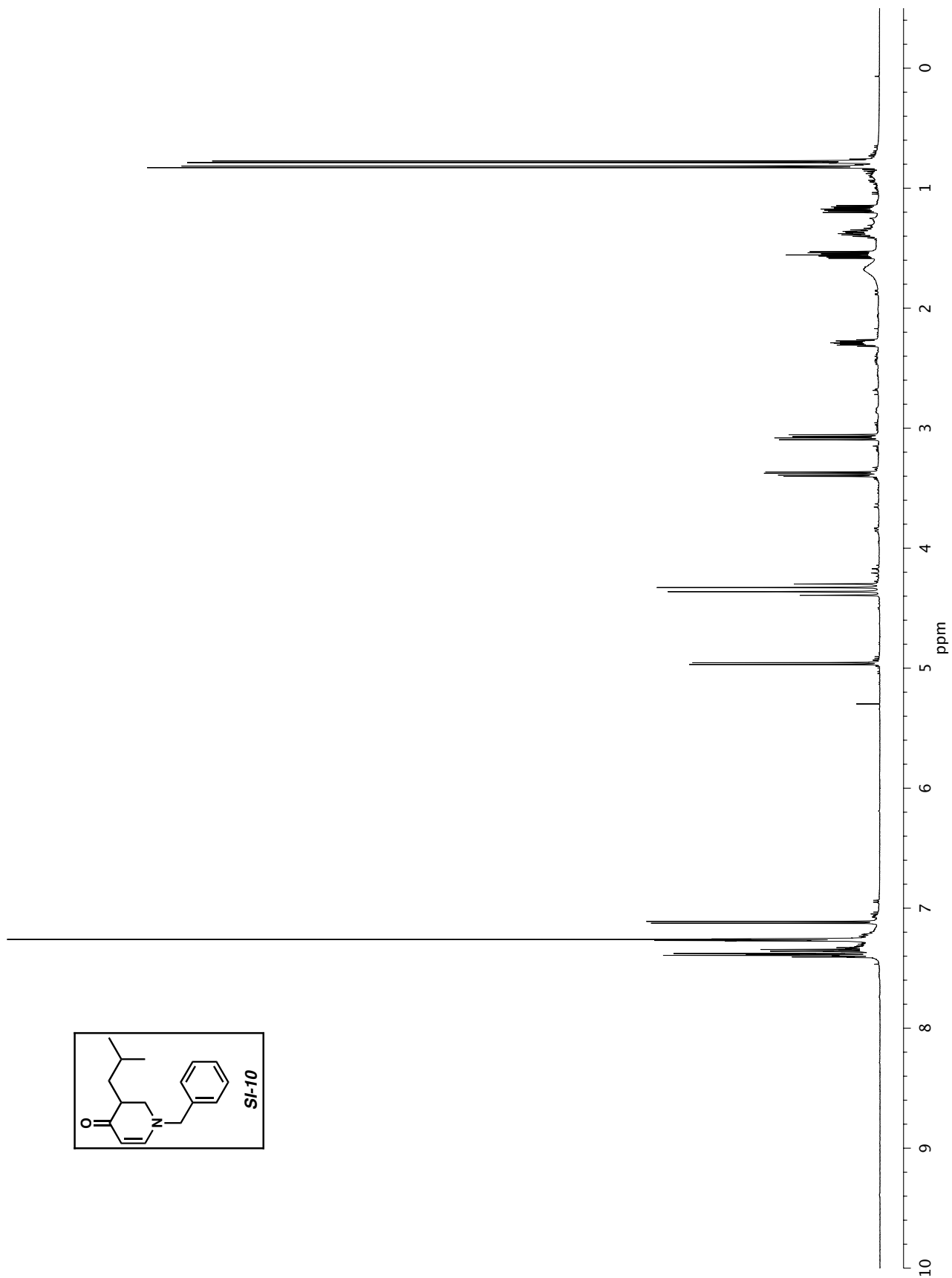


Figure SI-21A. ^1H NMR (500 MHz, CDCl_3) of compound SI-10.

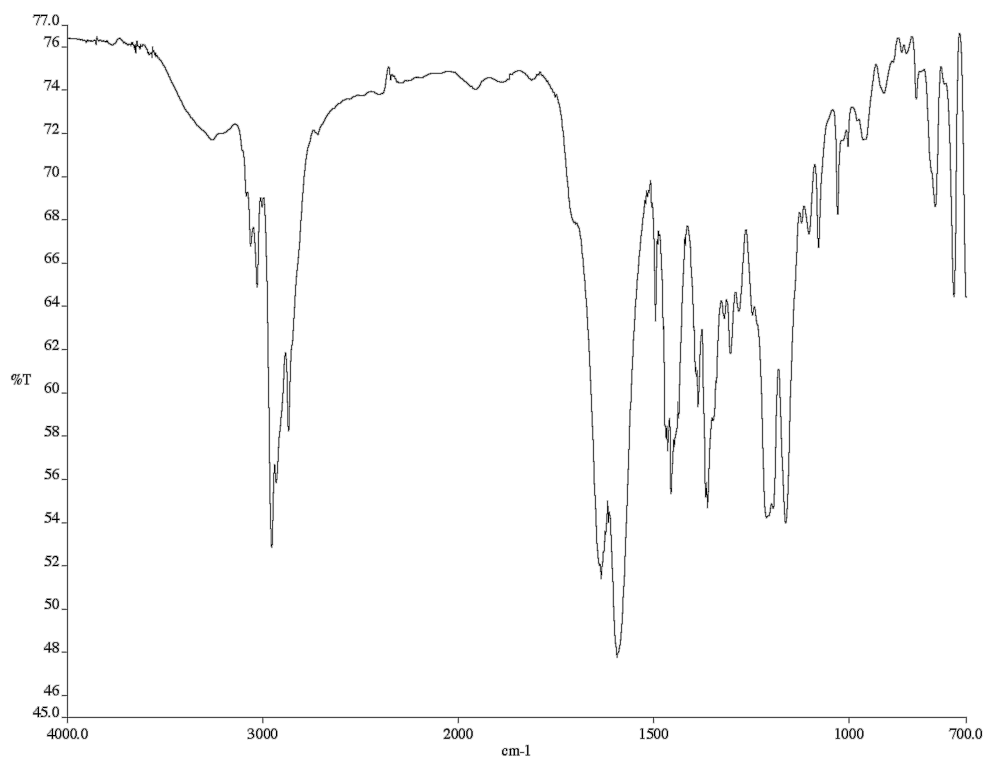


Figure SI-21B. Infrared spectrum (thin film/NaCl) of compound **SI-10**.

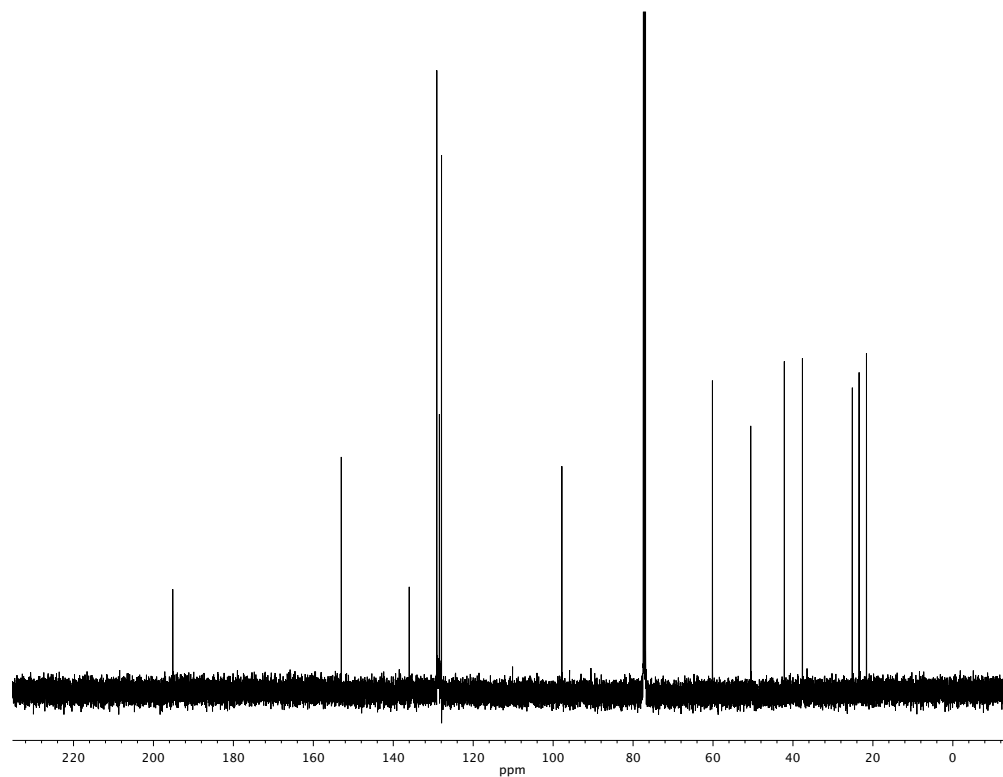
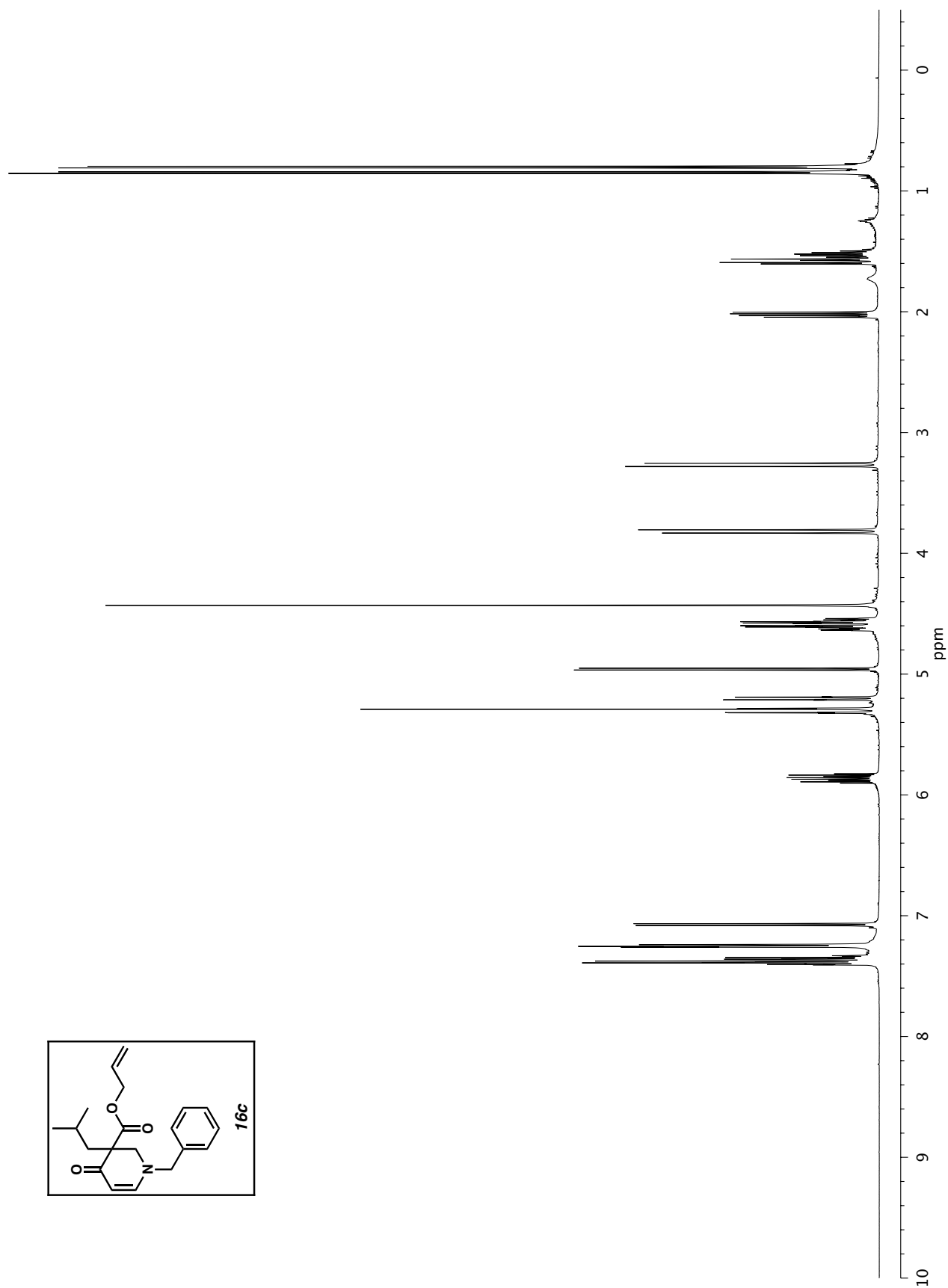


Figure SI-21C. ¹³C NMR (125 MHz, CDCl₃) of compound **SI-10**.



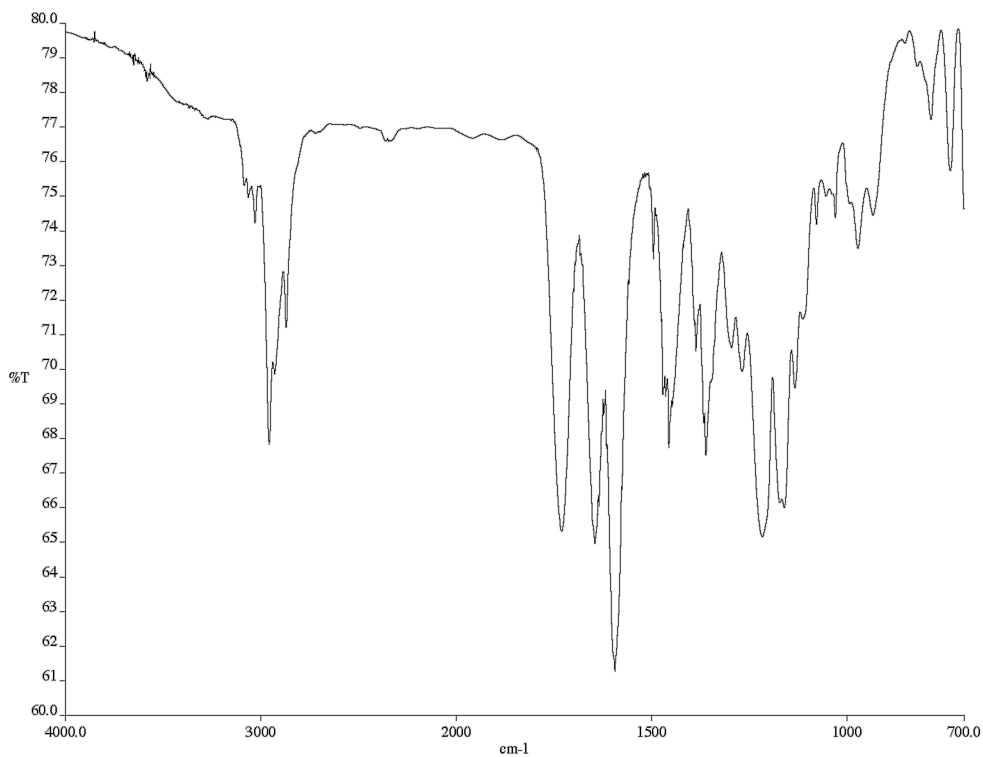


Figure SI-22B. Infrared spectrum (thin film/NaCl) of compound **16c**.

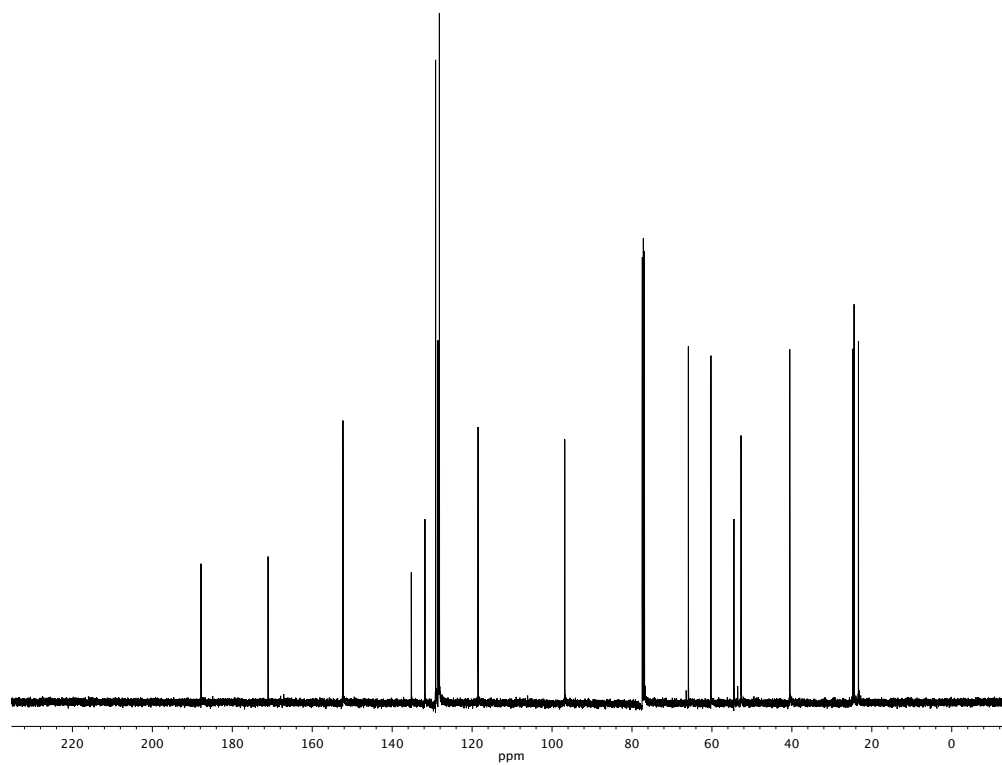


Figure SI-22C. ¹³C NMR (125 MHz, CDCl₃) of compound **16c**.

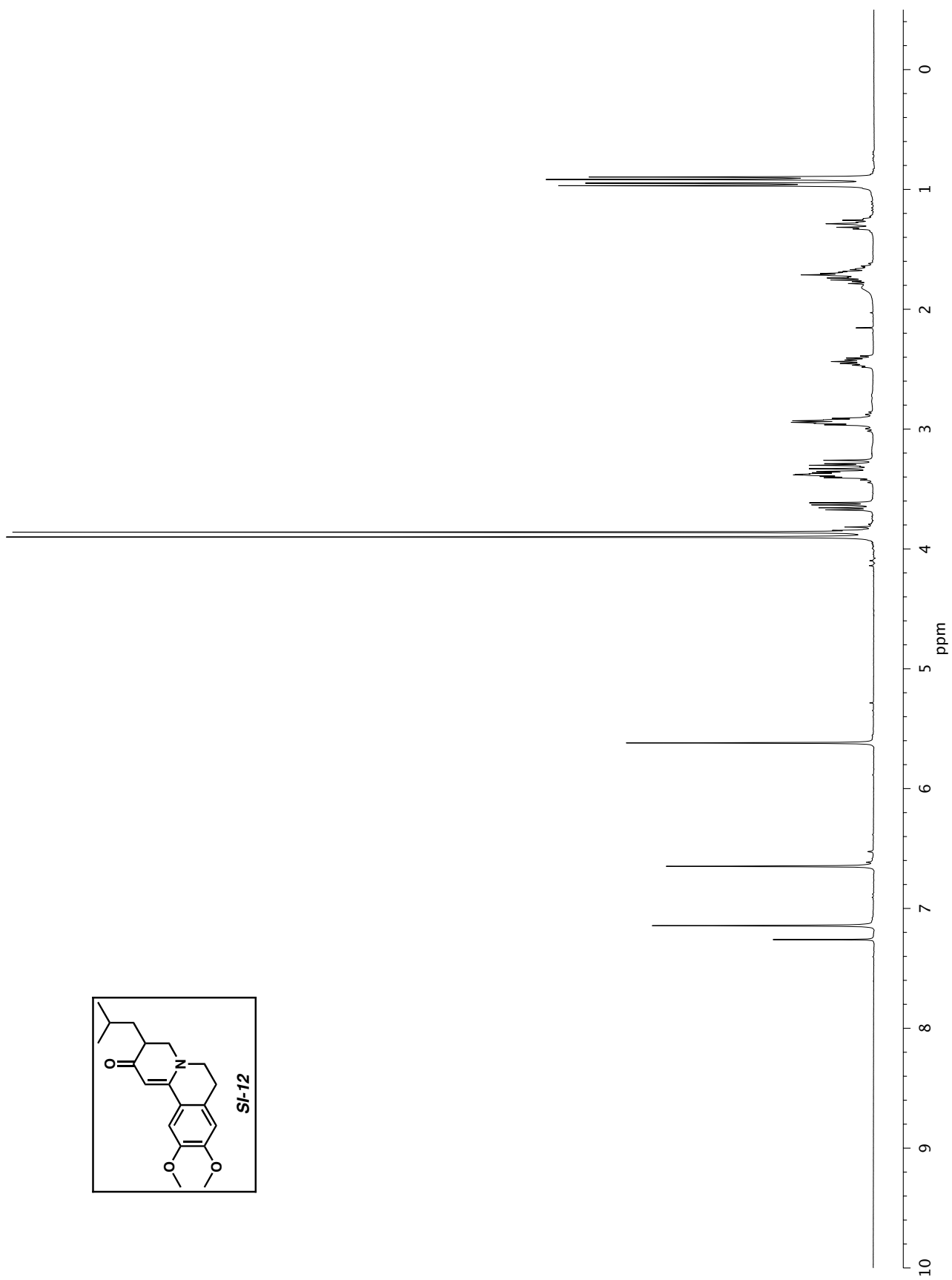


Figure SI-23A. ^1H NMR (500 MHz, CDCl_3) of compound SI-12.

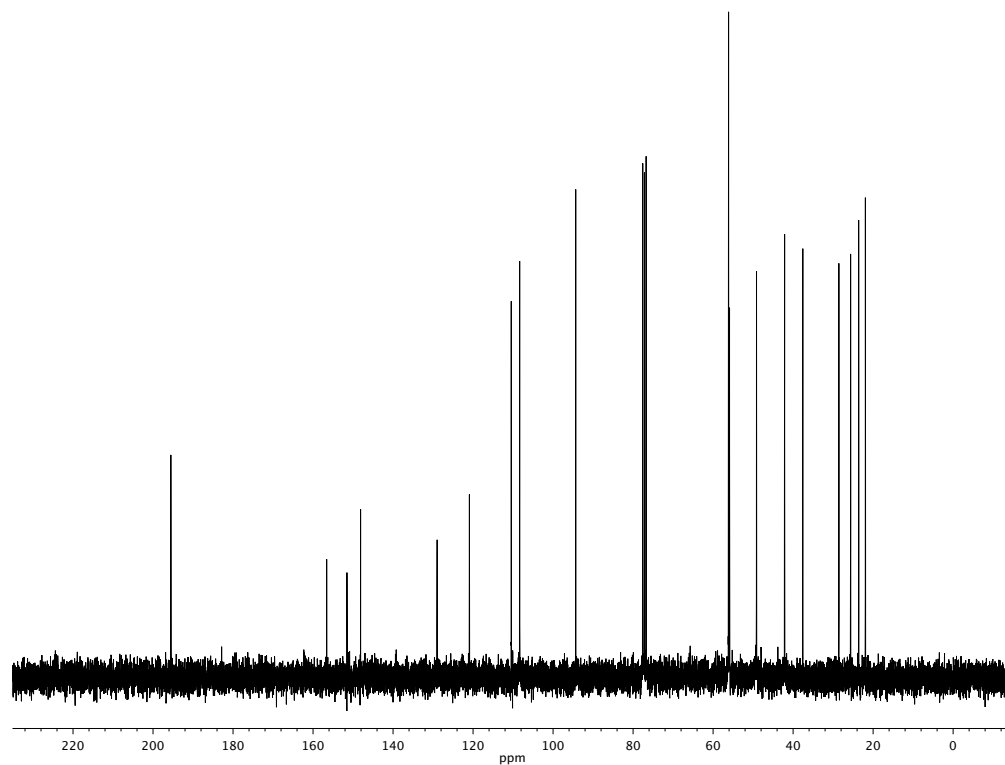
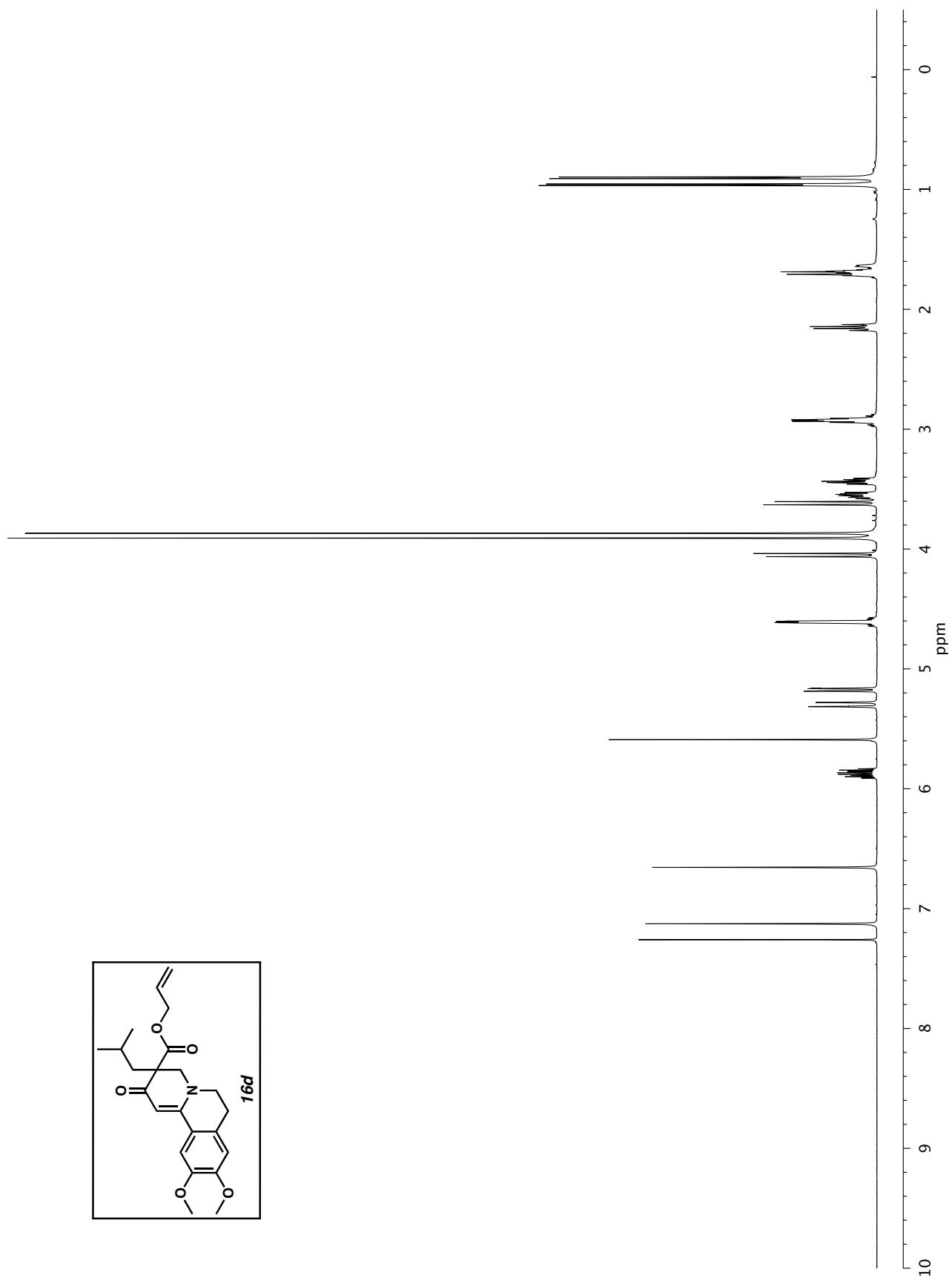


Figure SI-23B. ^{13}C NMR (125 MHz, CDCl_3) of compound SI-12.

Figure SI-244. ^1H NMR (500 MHz, CDCl_3) of compound **16d**.

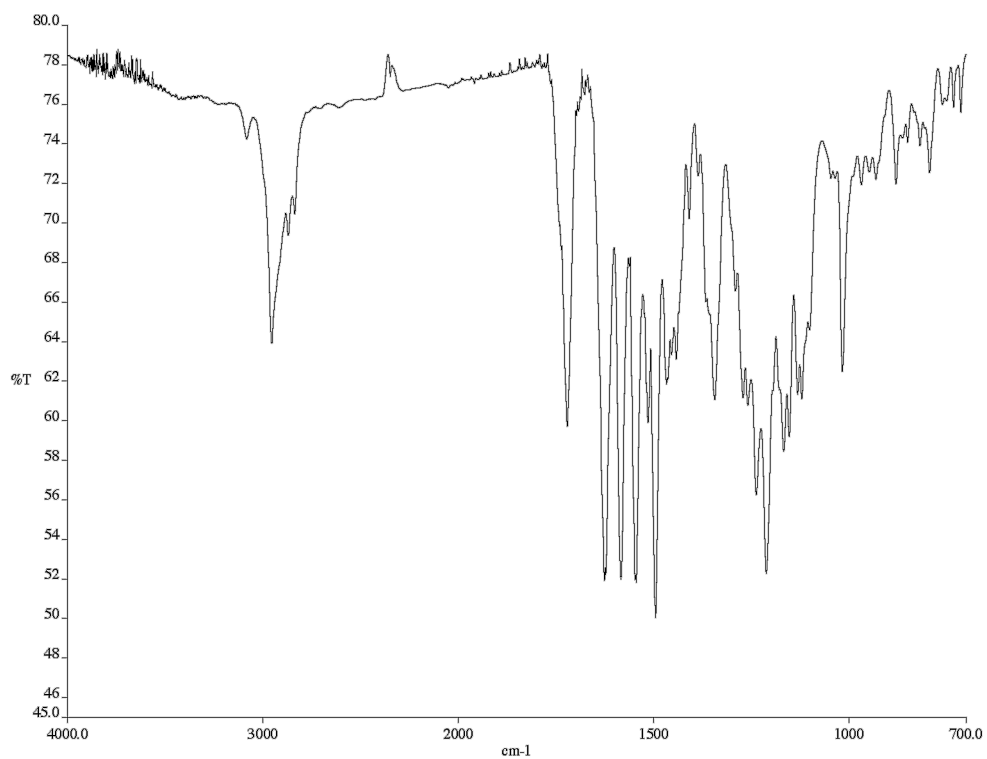


Figure SI-24B. Infrared spectrum (thin film/NaCl) of compound **16d**.

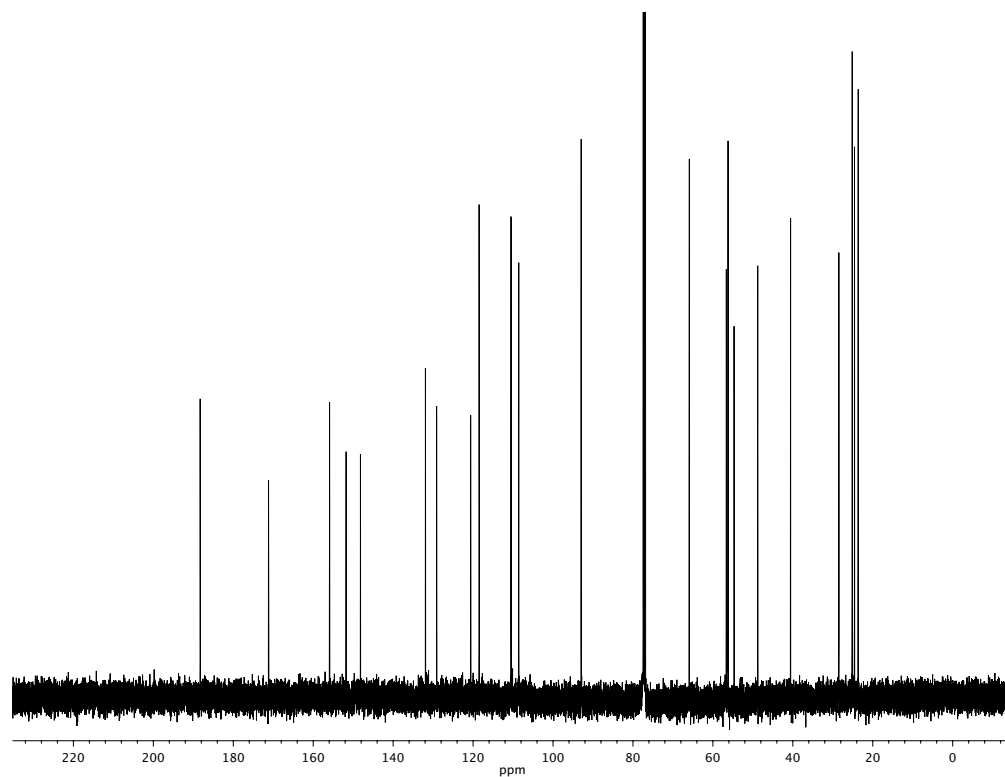
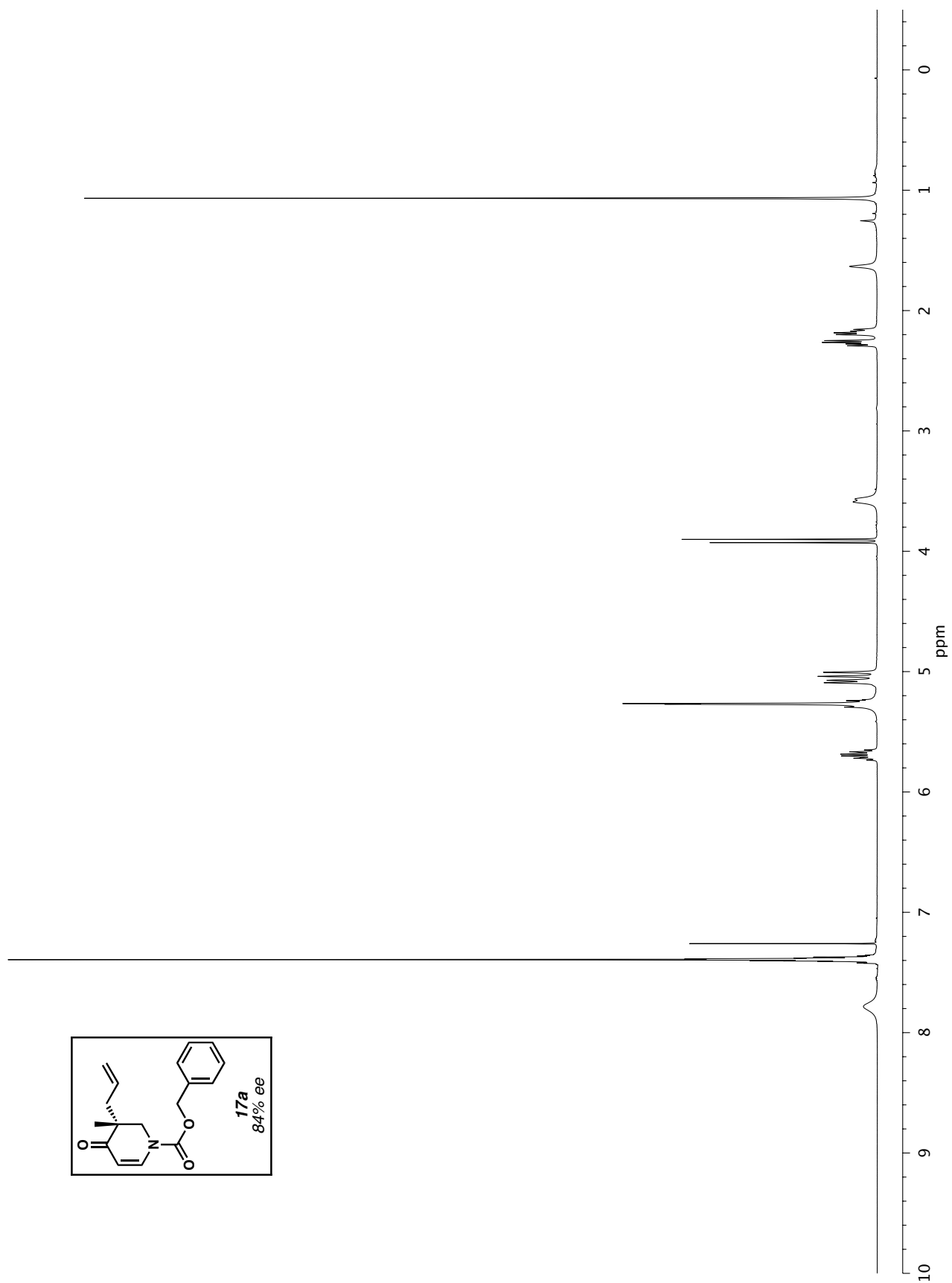


Figure SI-24C. ¹³C NMR (125 MHz, CDCl₃) of compound **16d**.

Figure SI-25A. ¹H NMR (500 MHz, CDCl₃) of compound **17a**.

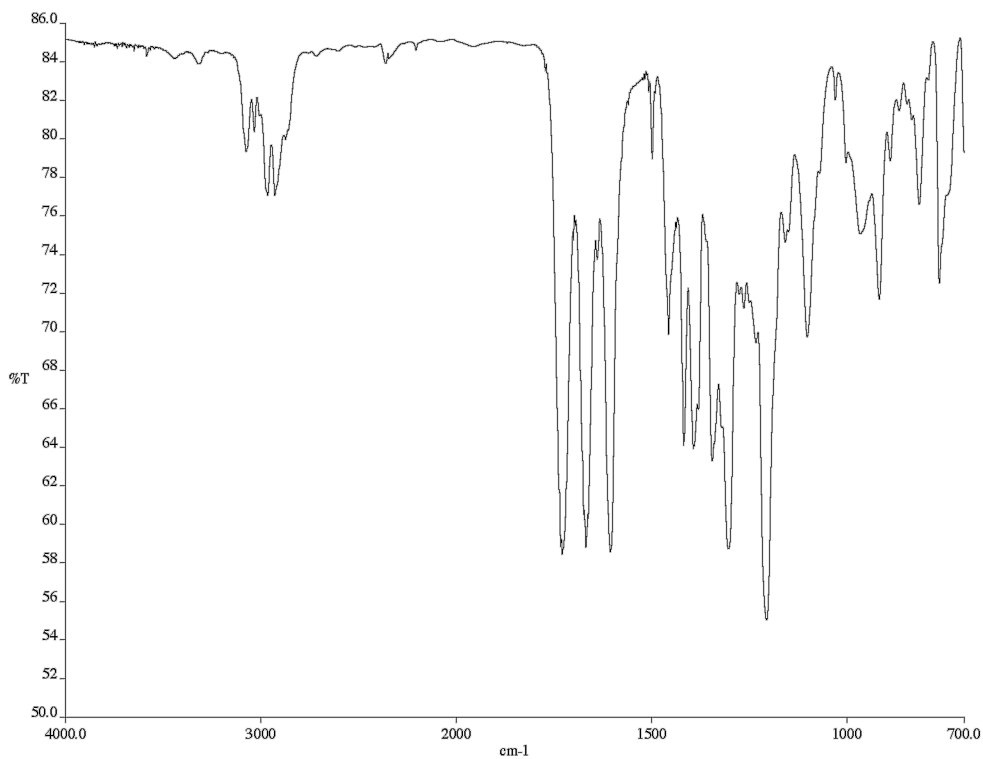


Figure SI-25B. Infrared spectrum (thin film/NaCl) of compound **17a**.

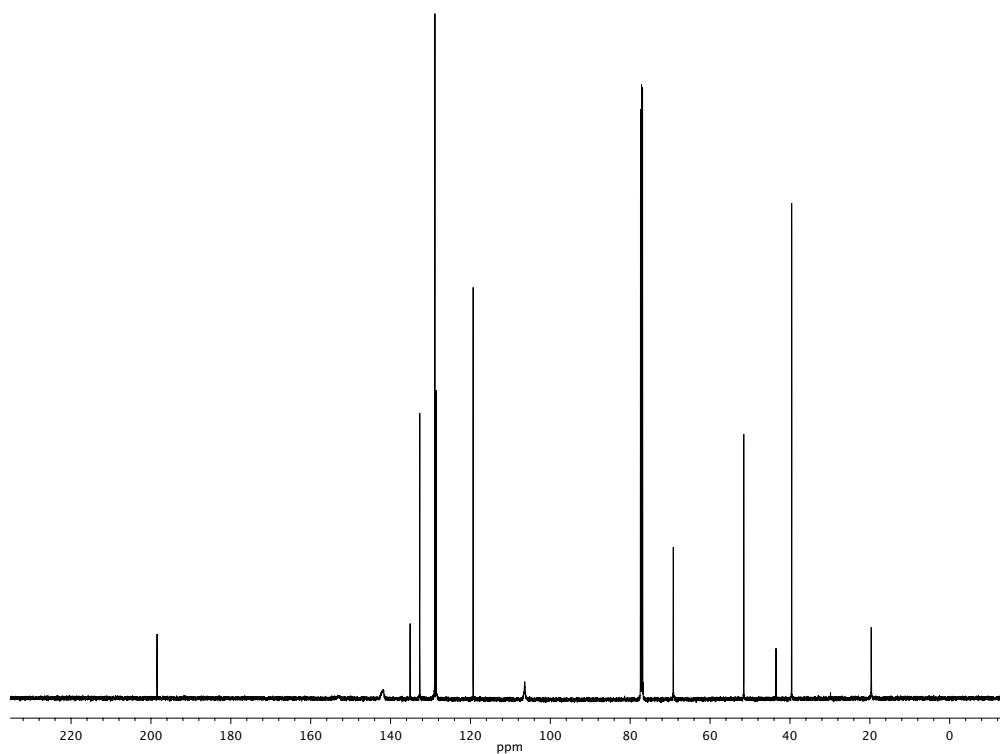


Figure SI-25C. ^{13}C NMR (125 MHz, CDCl_3) of compound **17a**.

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

=====

Acq. Operator	: ANM	Seq. Line	: 2
Acq. Instrument	: Instrument 1	Location	: P4-F-01
Injection Date	: 9/18/2012 12:40:04 PM	Inj	: 1
		Inj Volume	: 5 µl
Acq. Method	: C:\Chem32\1\DATA\ANM\AM_109_110_111_19_09_2012 2012-09-18 12-35-04\S1C2 12MIN 5.M		
Last changed	: 5/19/2011 9:00:59 PM by DCB		
Analysis Method	: C:\CHEM32\1\DATA\ANM\AM_109_110_111_19_09_2012 2012-09-18 12-35-04\AM-I- 109_RAC_1.D\DA.M (S1C2 12MIN 5.M)		
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		

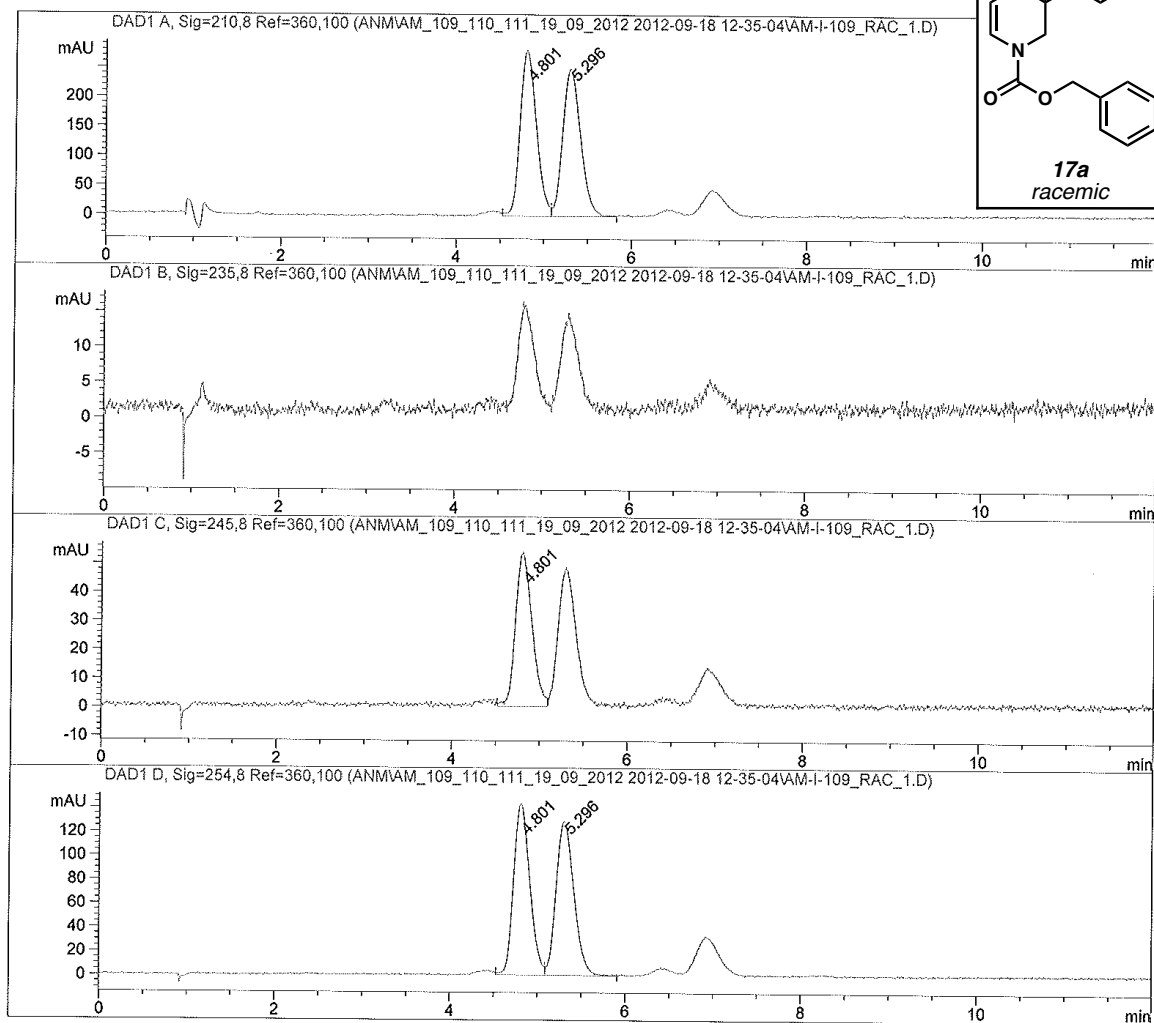
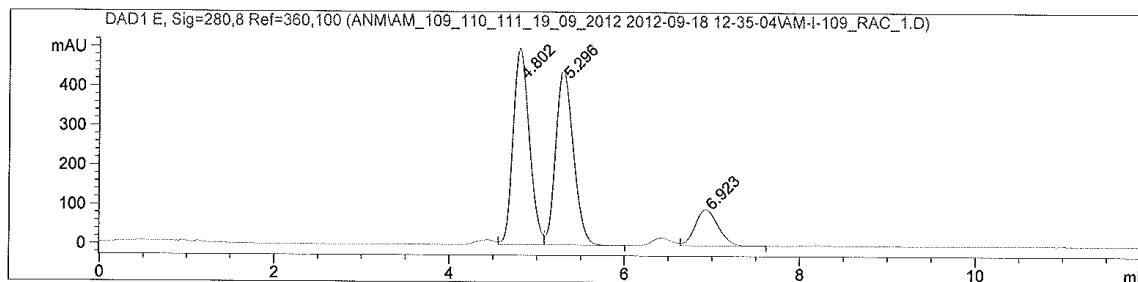


Figure SI-25D. Chiral SFC data of racemic compound **17a**.

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



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

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Sample Amount : 5.00000 [ng/ul] (not used in calc.)
 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

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

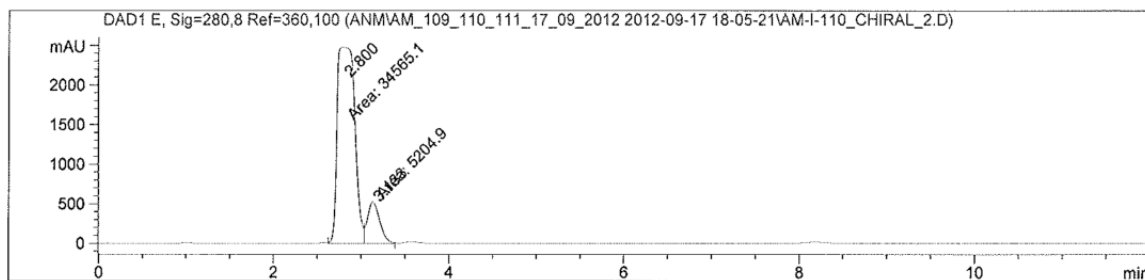
Signal 5: DAD1 E, Sig=280,8 Ref=360,100

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

Totals : 1.44314e4 1032.54185

=====
*** End of Report ***

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



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

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Sample Amount : 5.00000 [ng/ul] (not used in calc.)
 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	2.794	MF	0.2034	2.44176e4	2000.59717	89.3508
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 [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.795	MF	0.1592	1.51950e4	1591.19885	92.1743
2	3.133	FM	0.1579	1290.07031	136.13354	7.8257

Totals : 1.64851e4 1727.33240

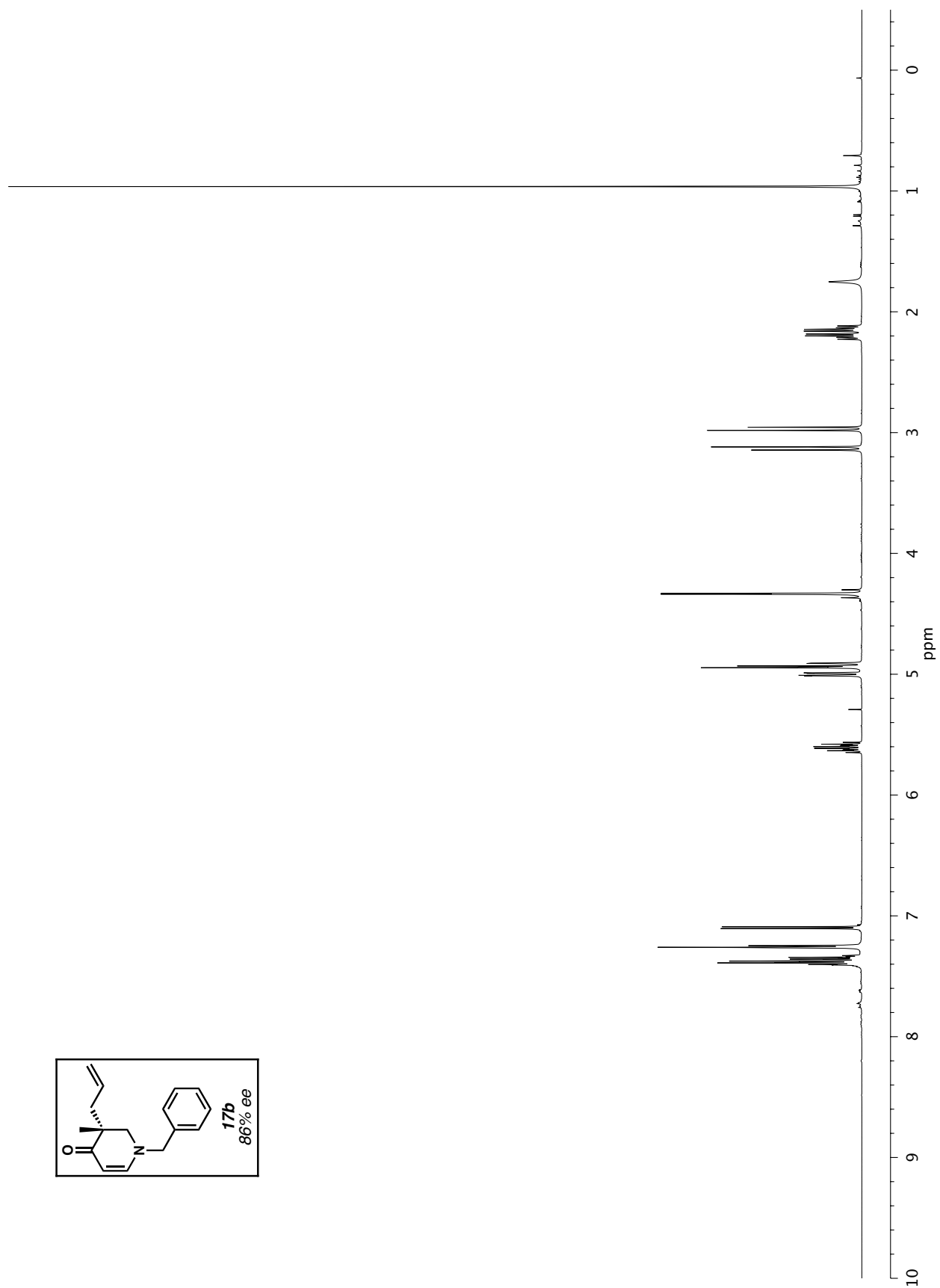
Data File C:\CHEM32\...\M\AM_109_110_111_17_09_2012 2012-09-17 18-05-21\AM-I-110_CHIRAL_2.D
Sample Name: AM-i-110_chiral_2

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
2	3.133	FM	0.1635	5204.90234	530.56769	13.0875

Totals : 3.97700e4 3013.52911

=====
*** End of Report ***

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

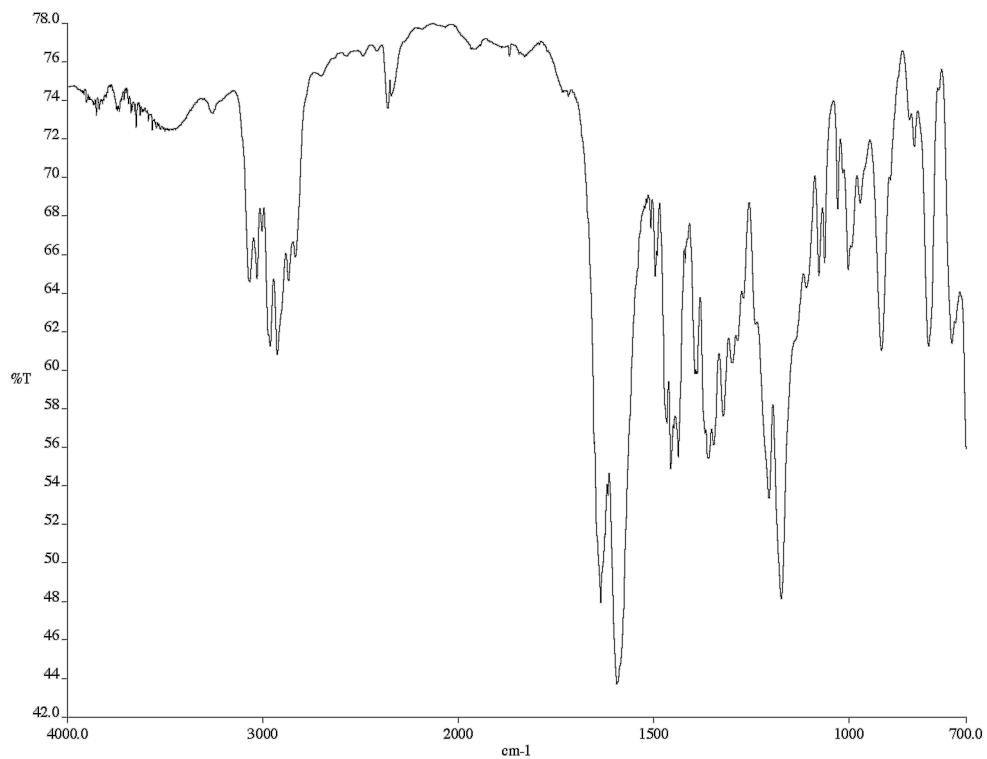


Figure SI-26B. Infrared spectrum (thin film/NaCl) of compound **17b**.

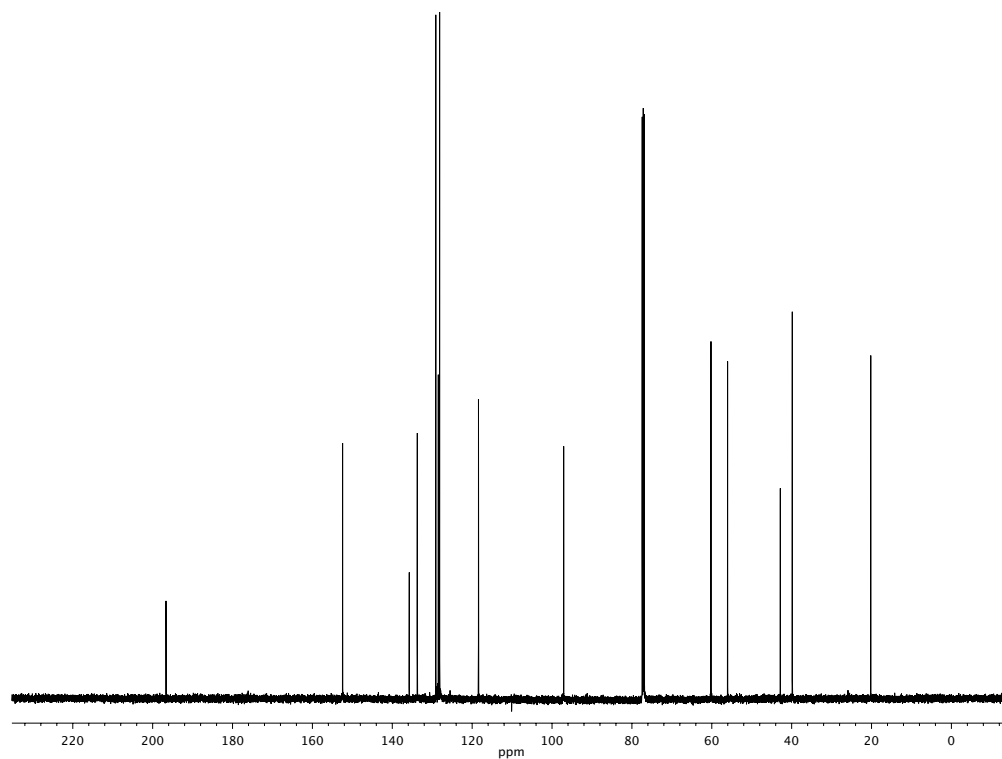
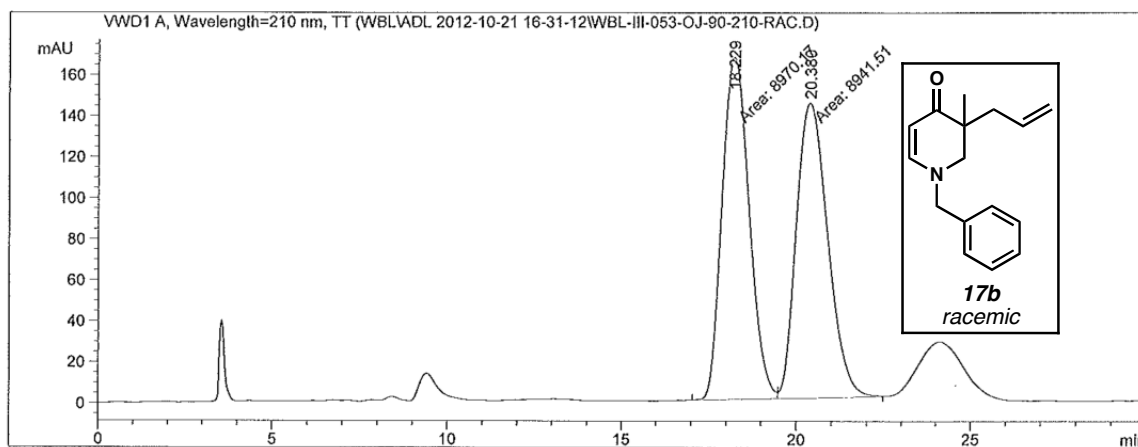


Figure SI-26C. ^{13}C NMR (125 MHz, CDCl_3) of compound **17b**.

Data File C:\CHEM32\2\DATA\WBL\ADL 2012-10-21 16-31-12\WBL-III-053-OJ-90-210-RAC.D
 Sample Name: wbl-III-053-oj-90-210-rac

```
=====
Acq. Operator   : wbl                               Seq. Line : 13
Acq. Instrument : HPLC 2                             Location  : Vial 73
Injection Date  : 10/21/2012 8:44:23 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 16-31-12\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 [min]	Type	Width [min]	Area mAU*s	Height [mAU]	Area %
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

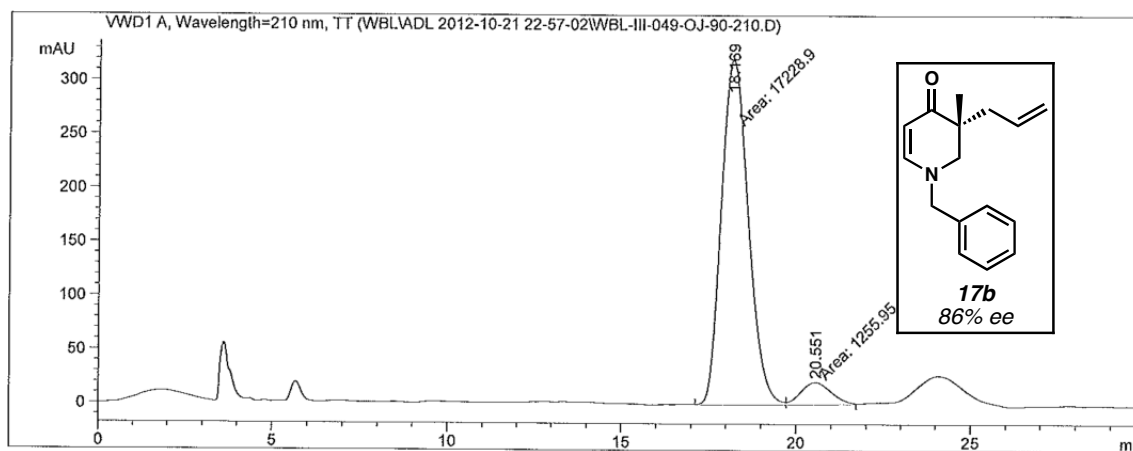
=====
 Summed Peaks Report
 =====

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

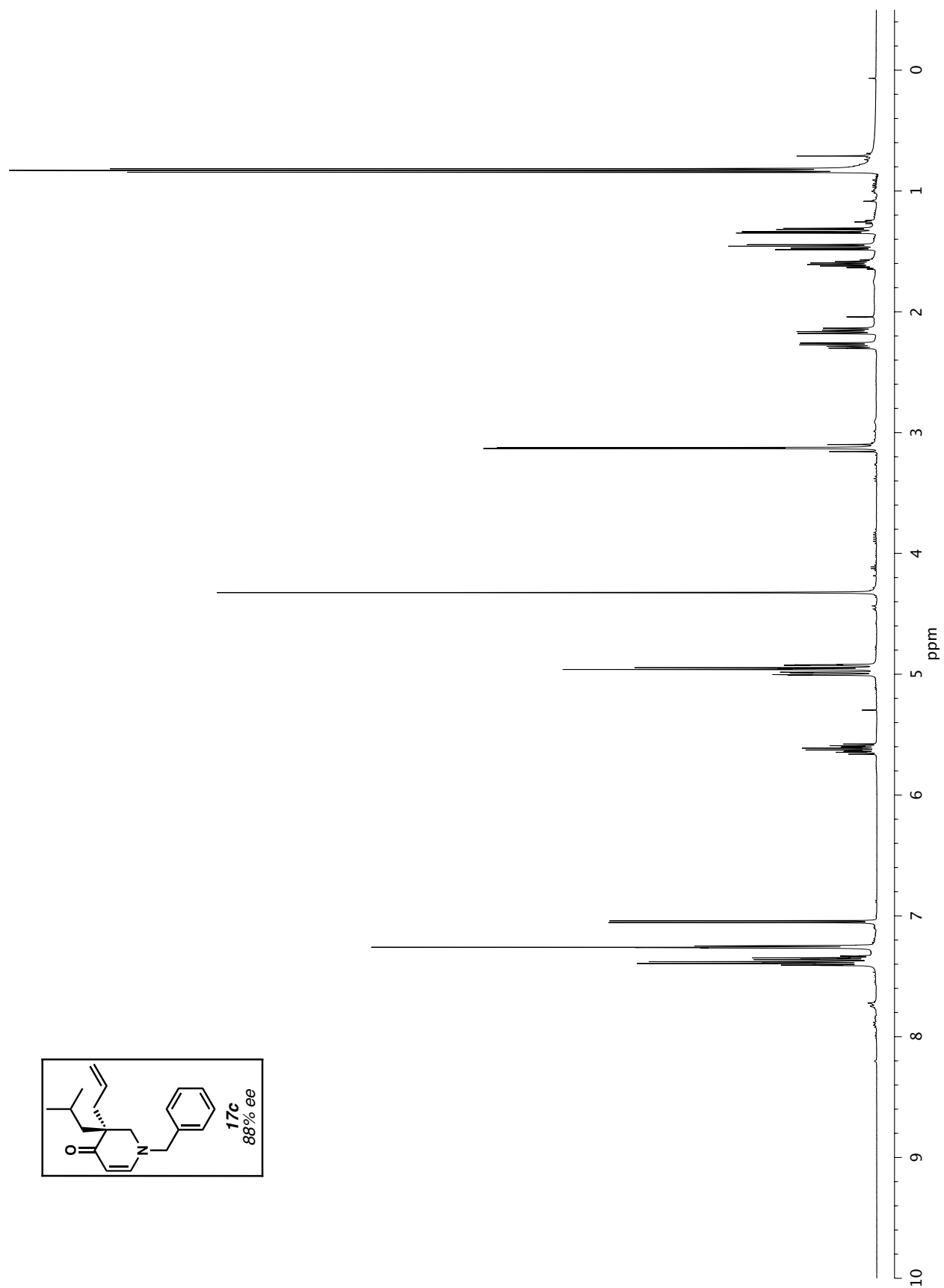
Signal 1: VWD1 A, Wavelength=210 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
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
 =====

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



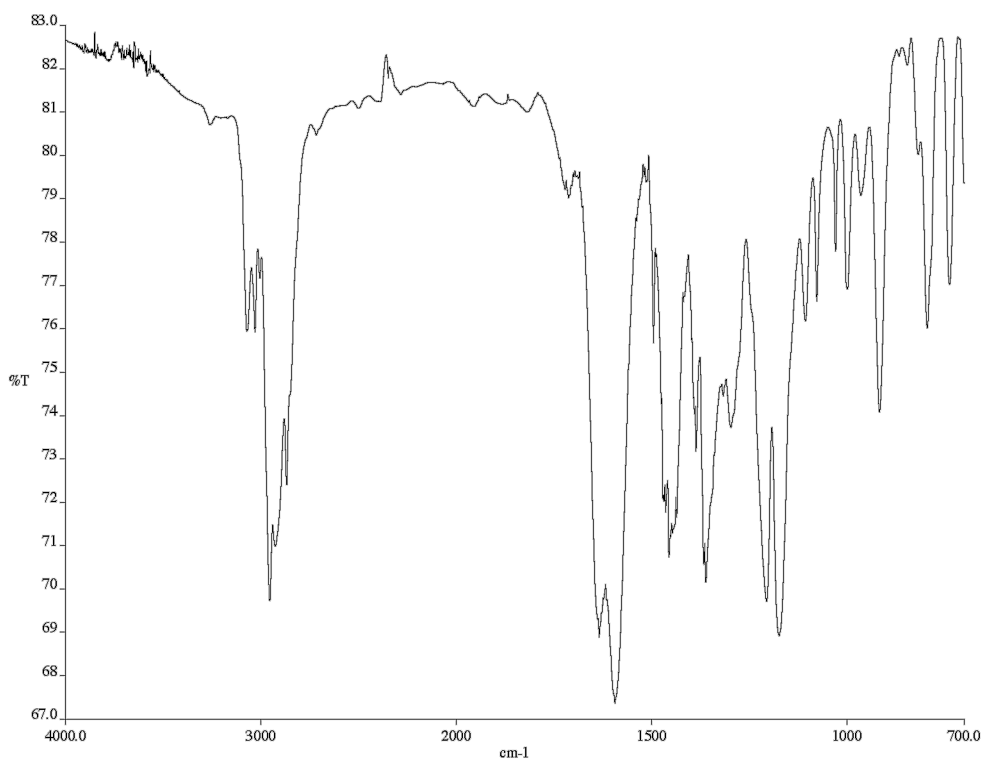


Figure SI-27B. Infrared spectrum (thin film/NaCl) of compound **17c**.

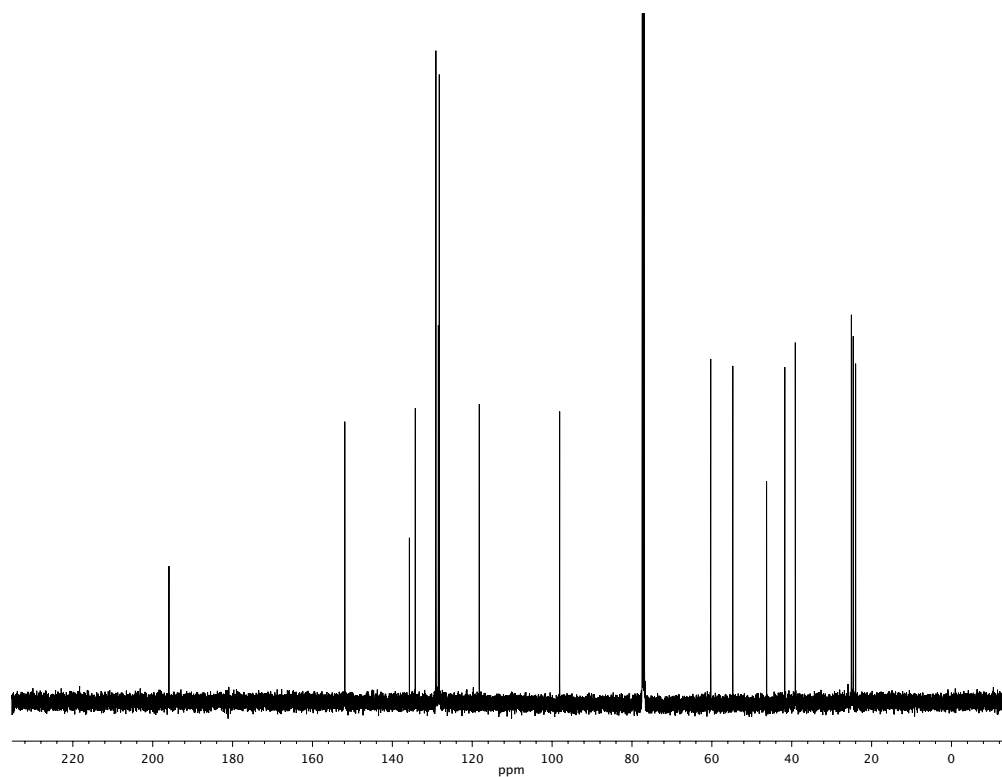
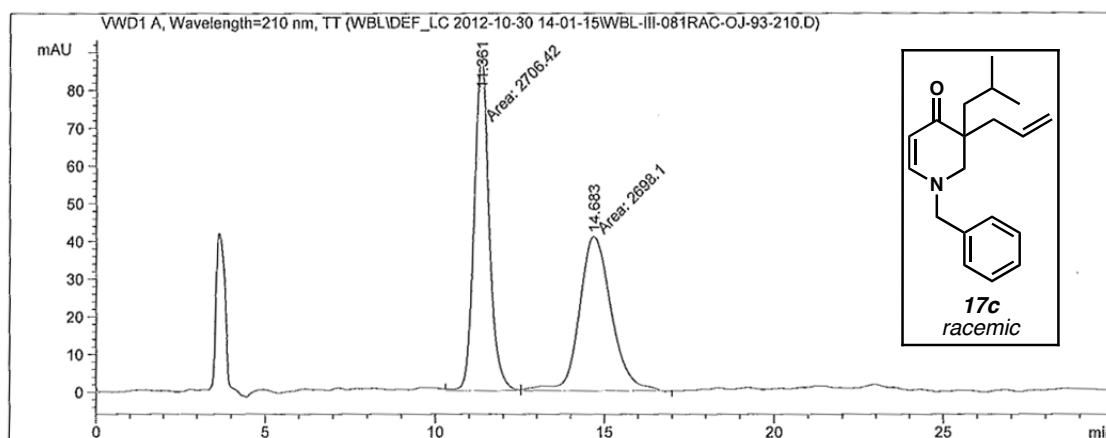


Figure SI-27C. ¹³C NMR (125 MHz, CDCl₃) of compound **17c**.

a File C:\CHEM32\2\DATA\WBL\DEF_LC 2012-10-30 14-01-15\WBL-III-081RAC-OJ-93-210.D
 Sample 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 [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
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
 =====

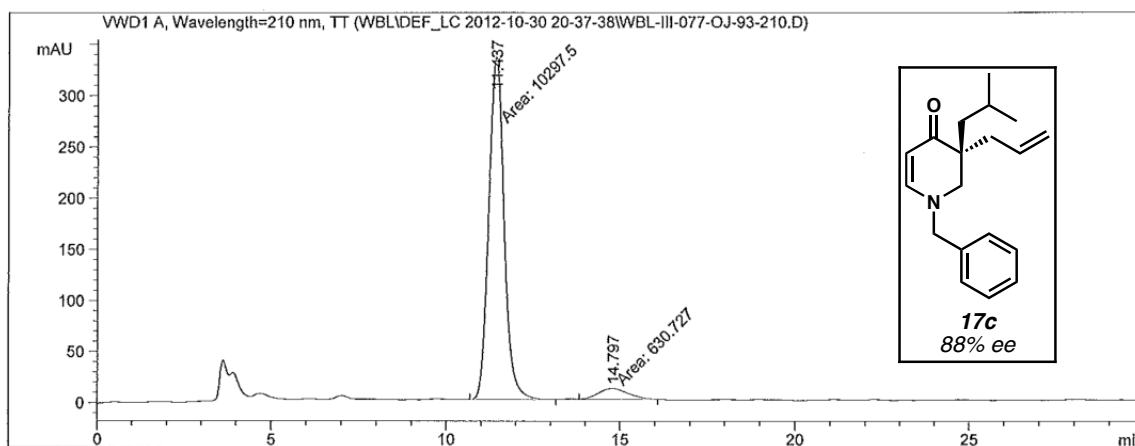
Figure SI-27D. Chiral SFC data of racemic compound 17c.

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

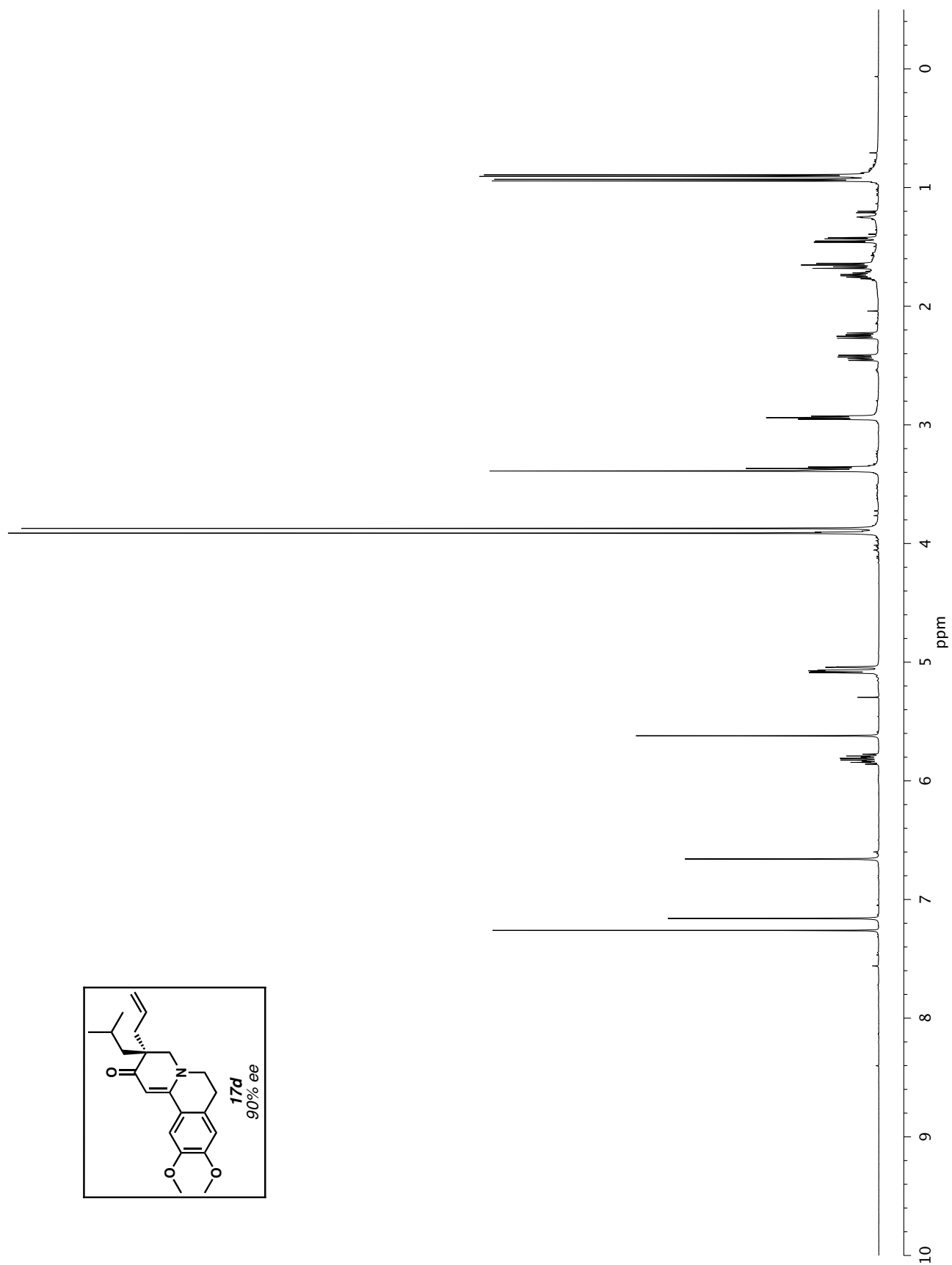
```
Totals :                1.09283e4  344.85762
```

```

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

```

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

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

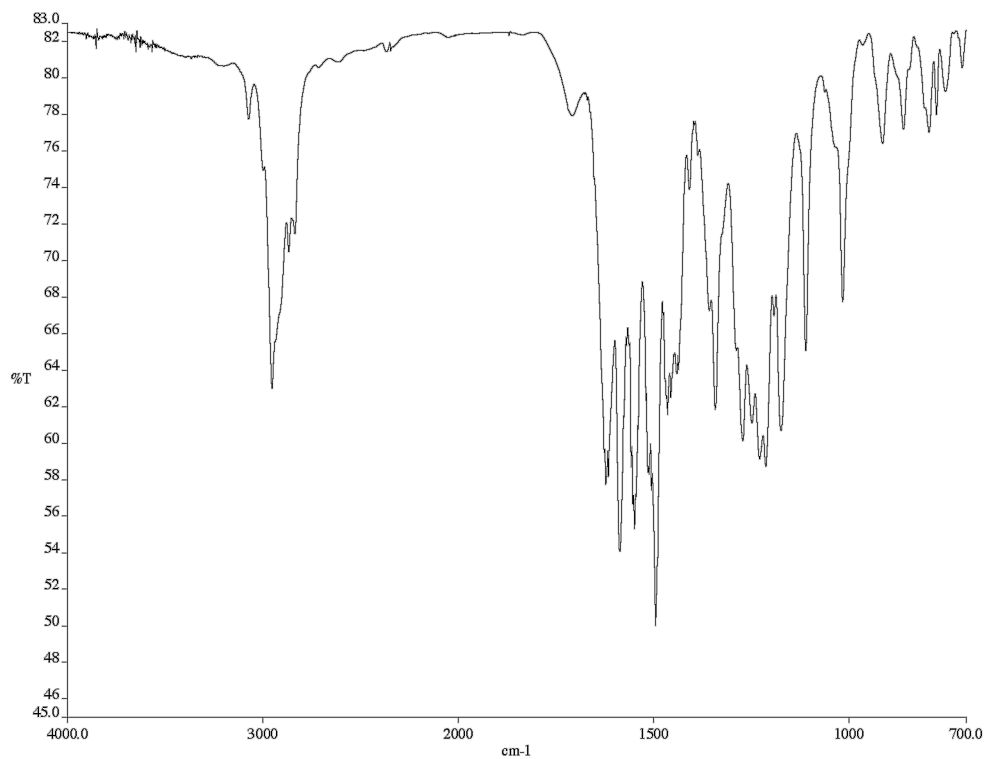


Figure SI-28B. Infrared spectrum (thin film/NaCl) of compound **17d**.

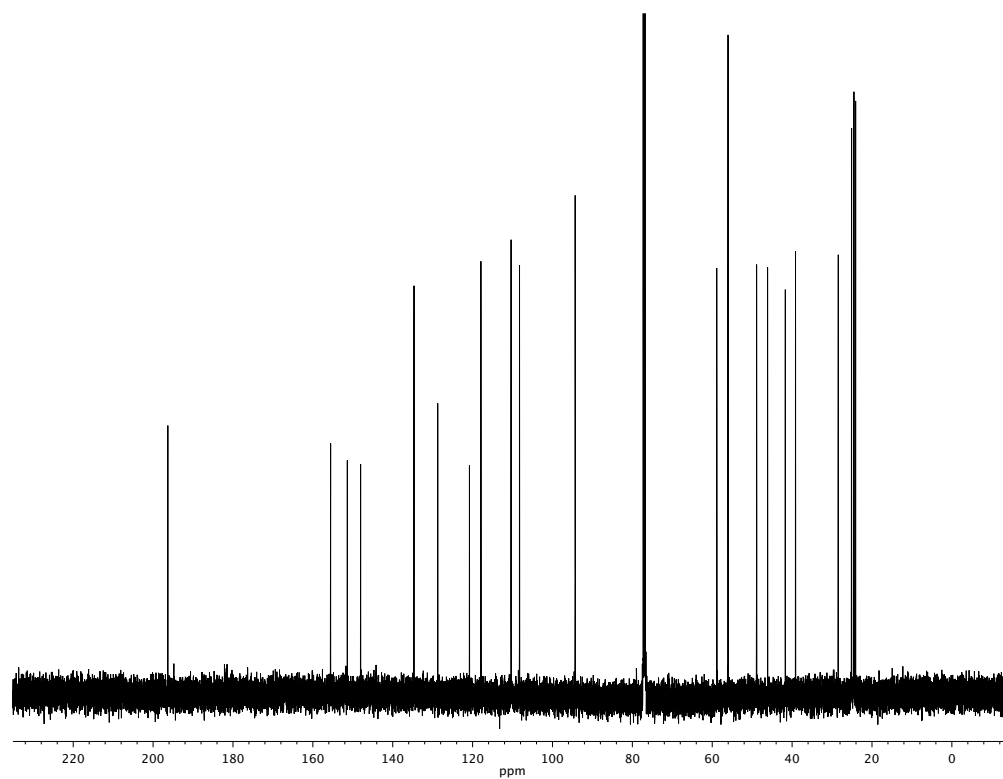
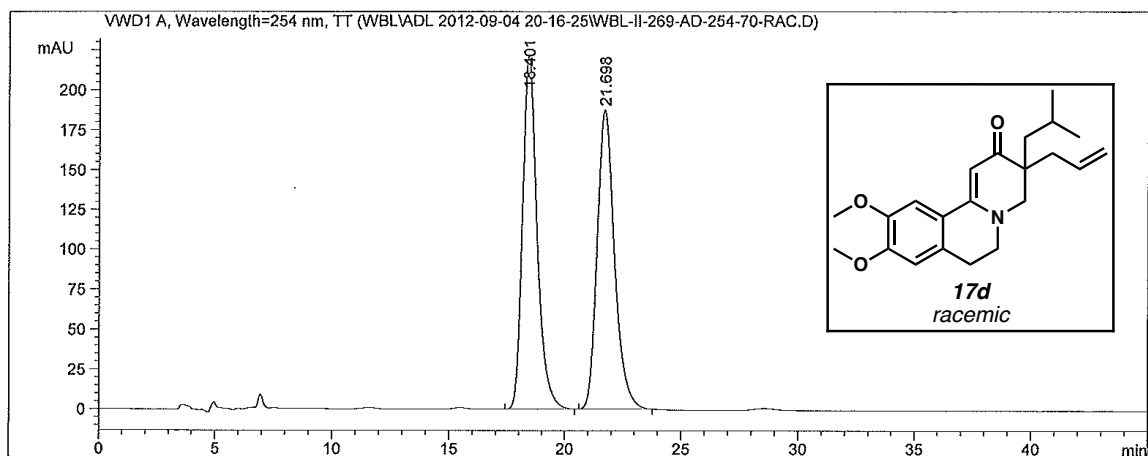


Figure SI-28C. ¹³C NMR (125 MHz, CDCl₃) of compound **17d**.

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 [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
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

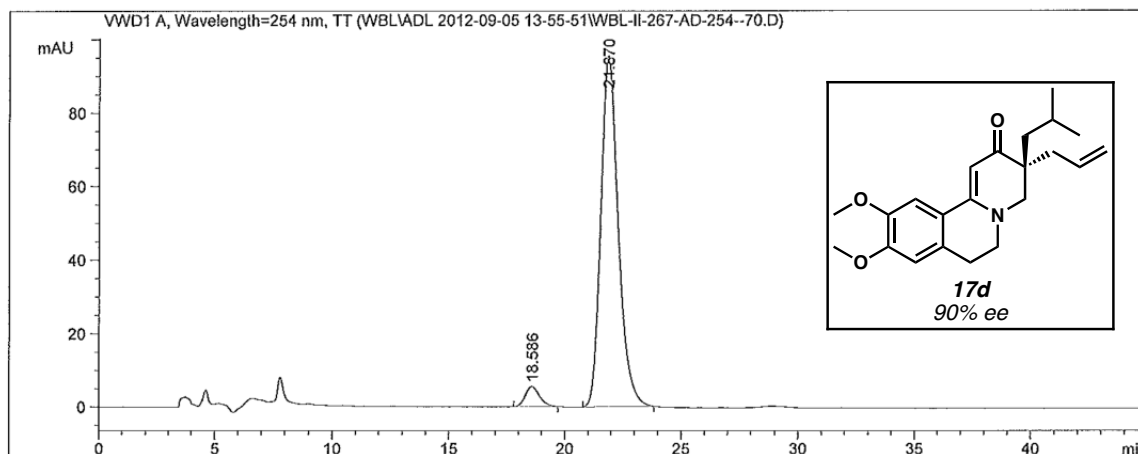
=====
 Summed Peaks Report
 =====

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

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 [min]	Type	Width [min]	Area mAU*s	Height [mAU]	Area %
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

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

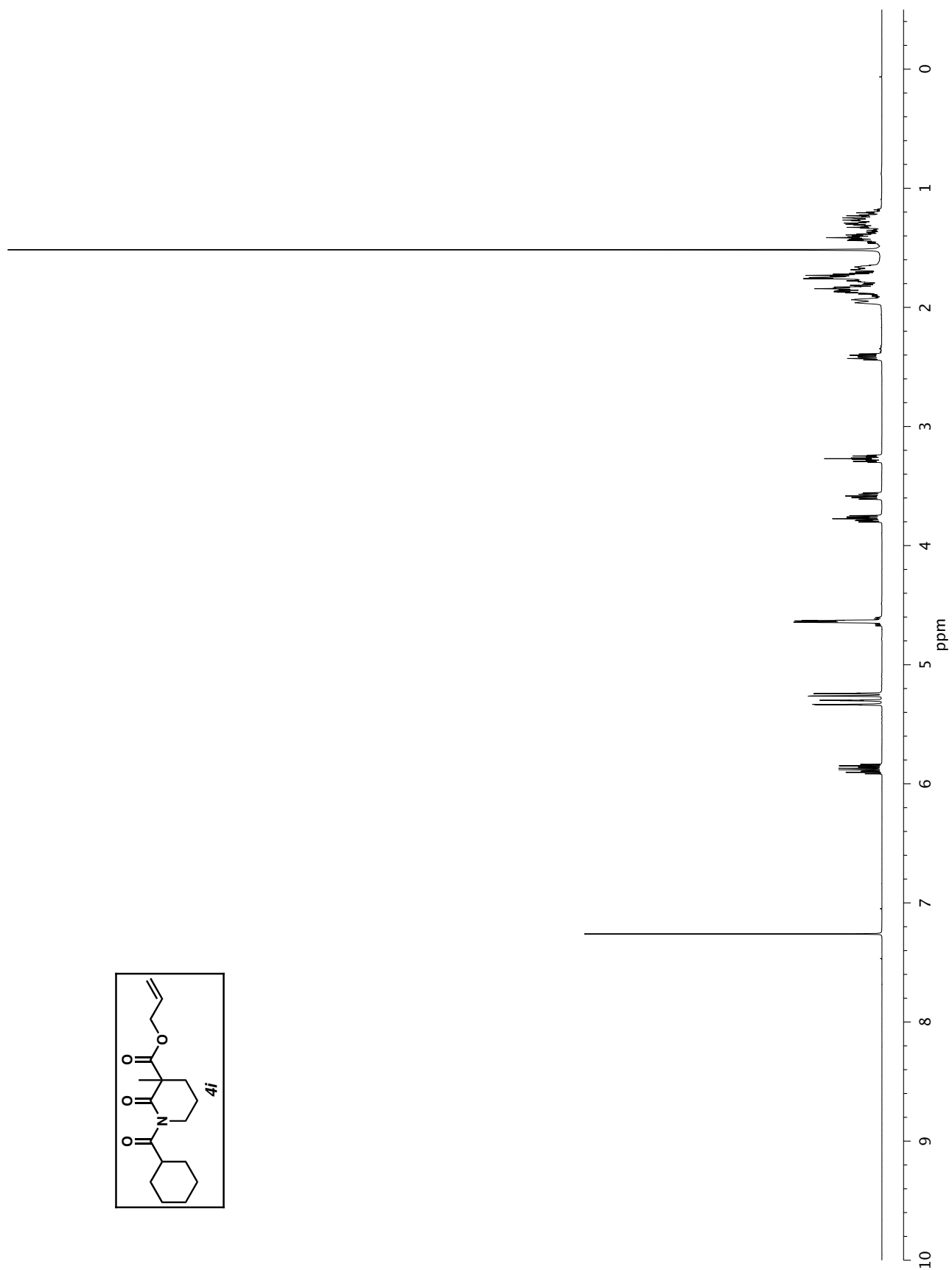
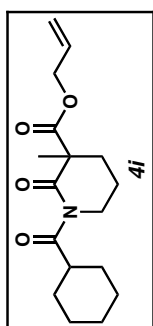


Figure SI-29A. ¹H NMR (500 MHz, CDCl₃) of compound **4i**.

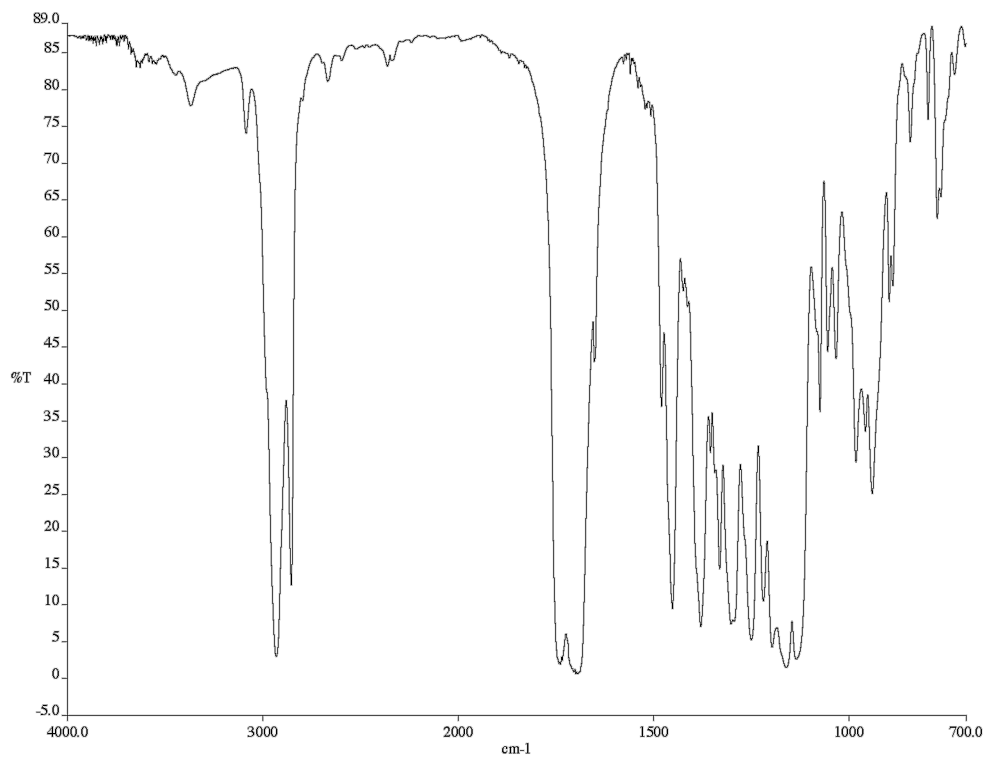


Figure SI-29B. Infrared spectrum (thin film/NaCl) of compound **4i**.

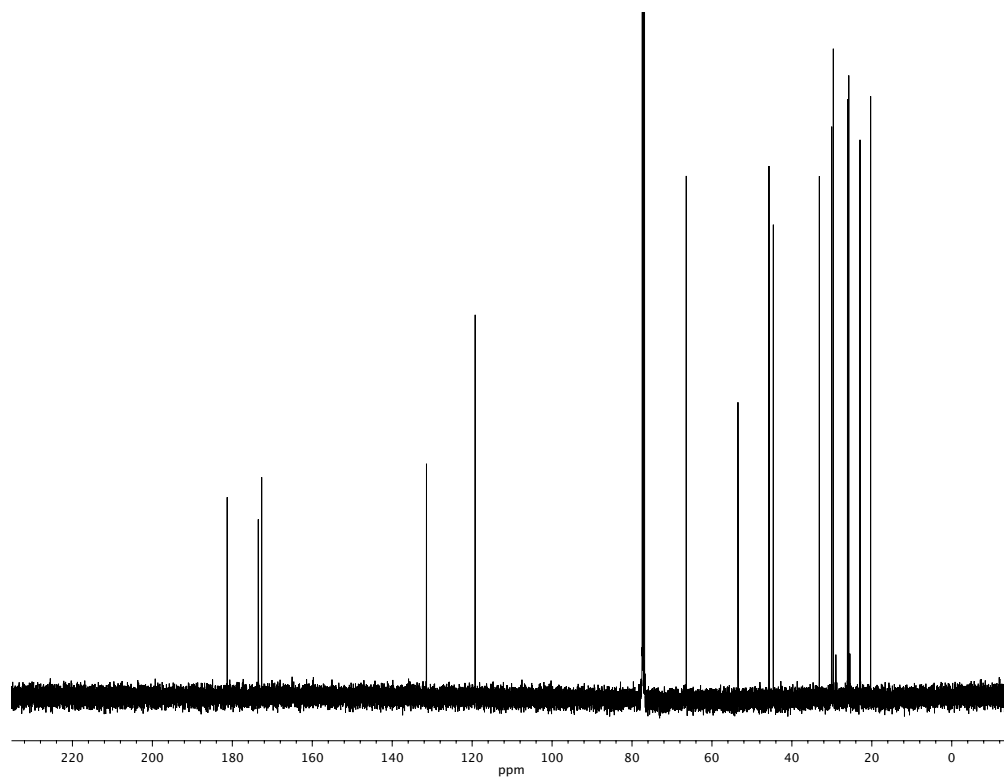
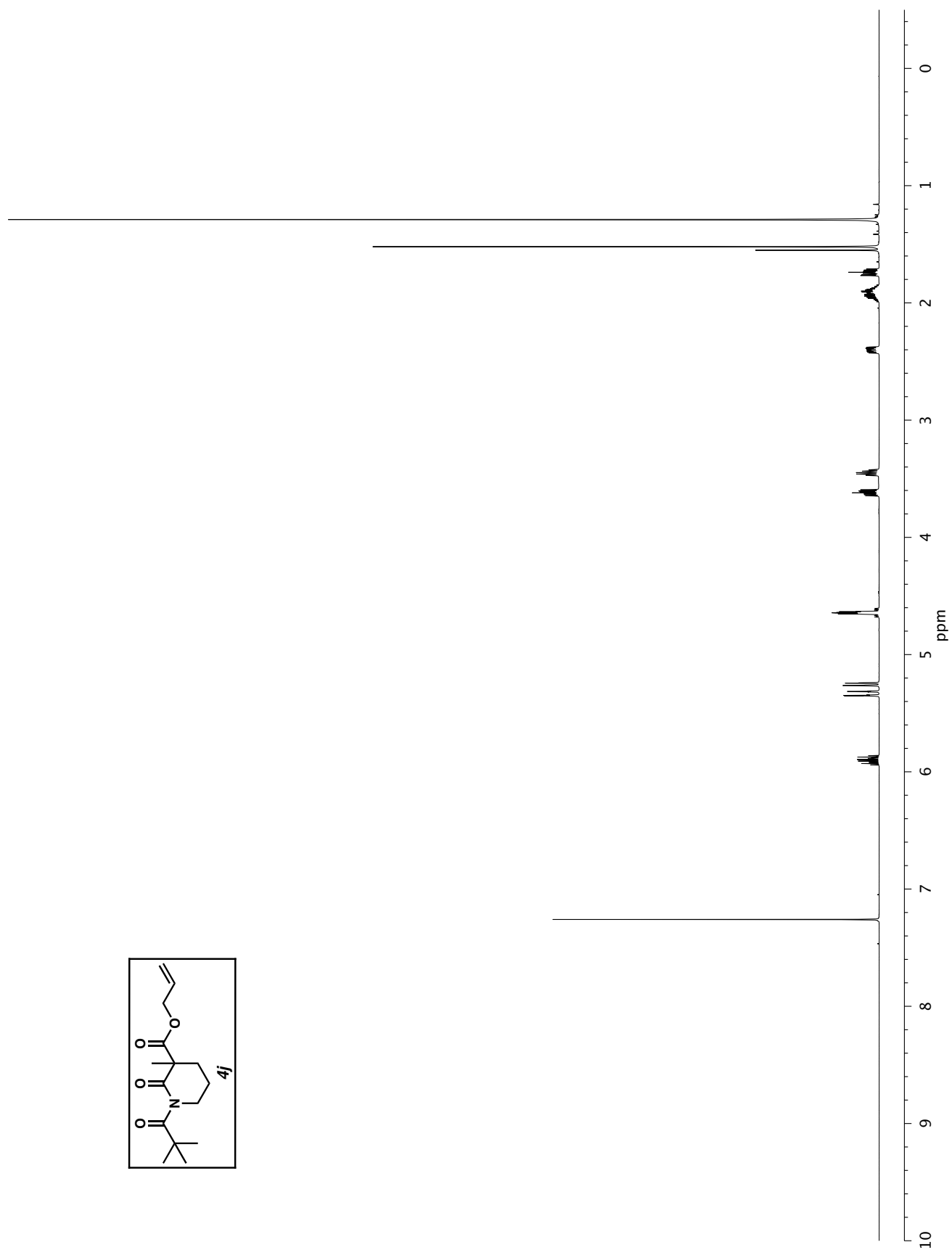


Figure SI-29C. ¹³C NMR (125 MHz, CDCl₃) of compound **4i**.

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

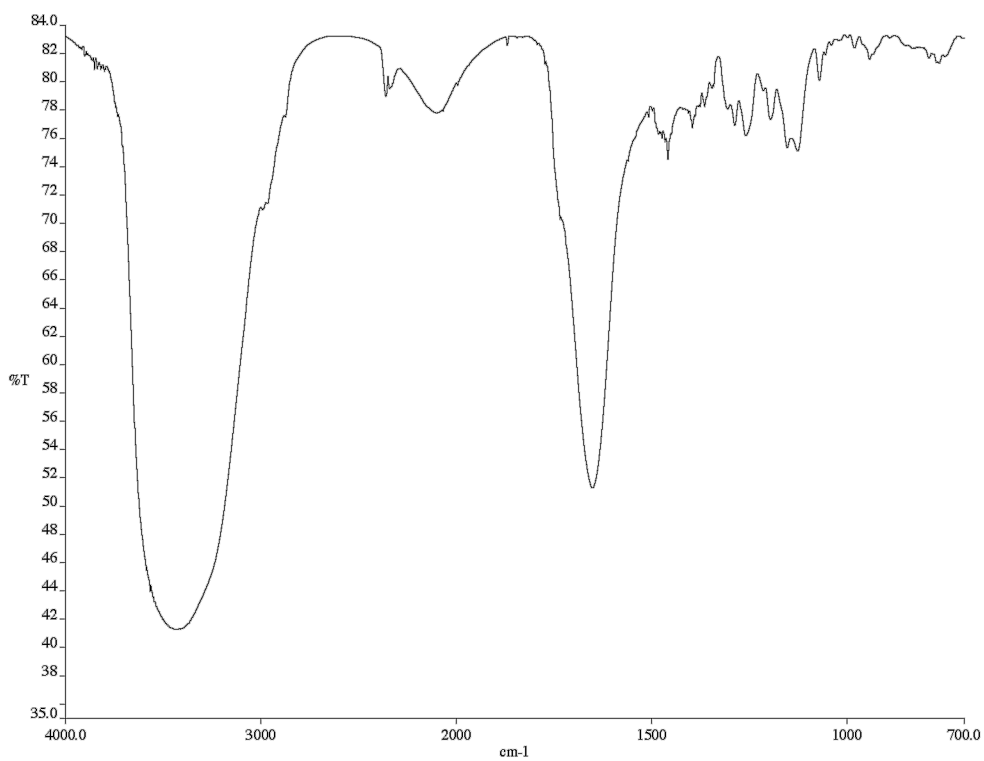


Figure SI-30B. Infrared spectrum (thin film/NaCl) of compound **4j**.

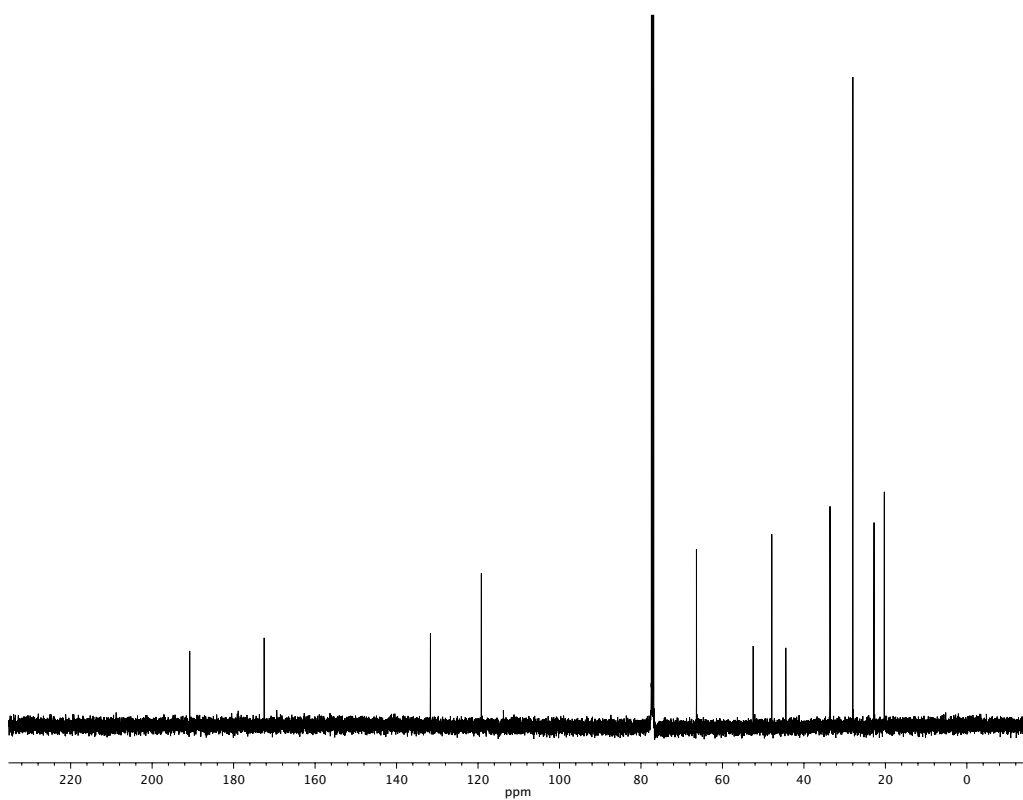


Figure SI-30C. ¹³C NMR (125 MHz, CDCl₃) of compound **4j**.

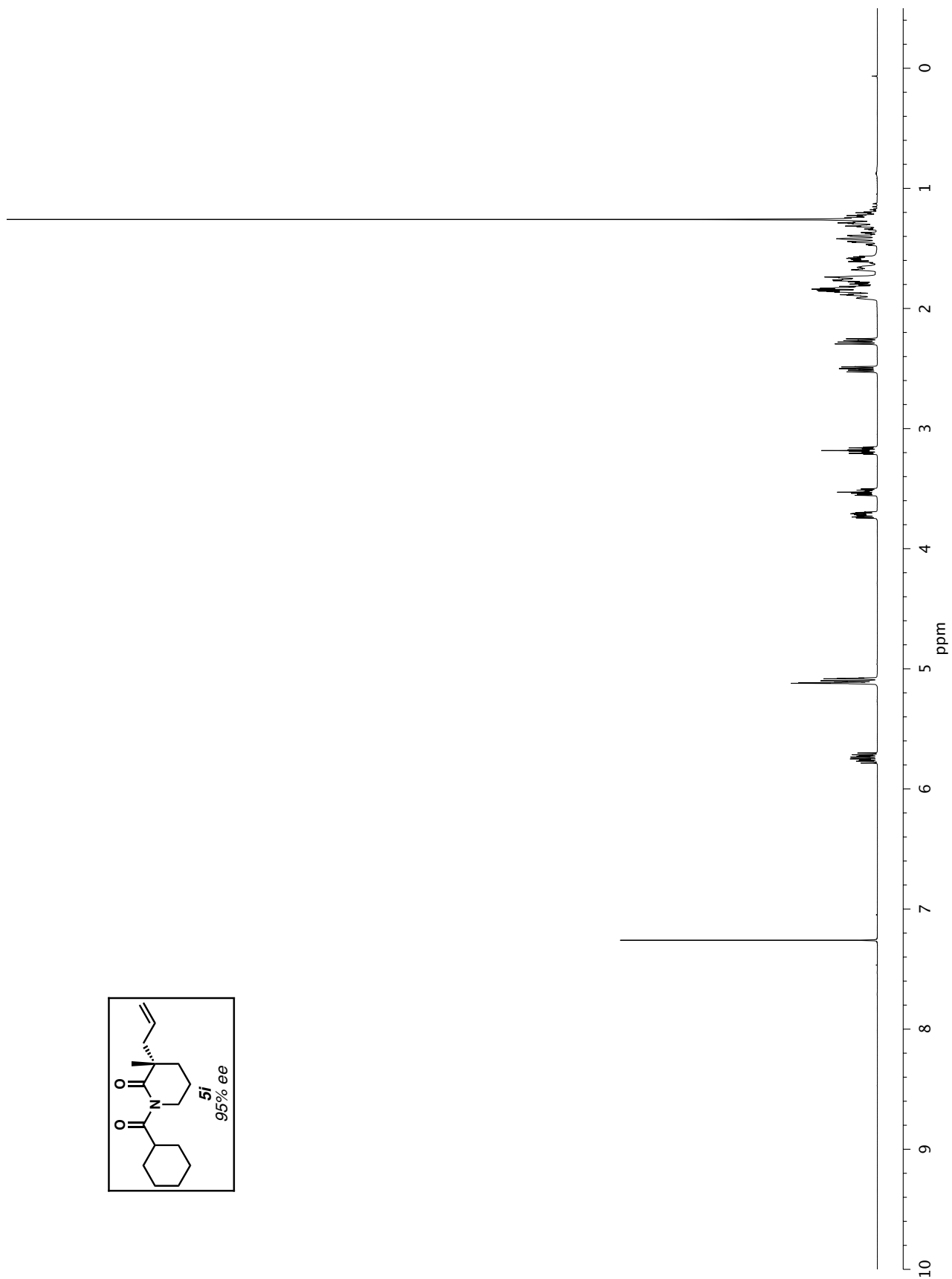
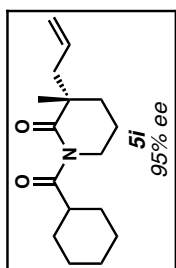


Figure SI-31A. $^1\text{H NMR}$ (500 MHz, CDCl_3) of compound **5i**.

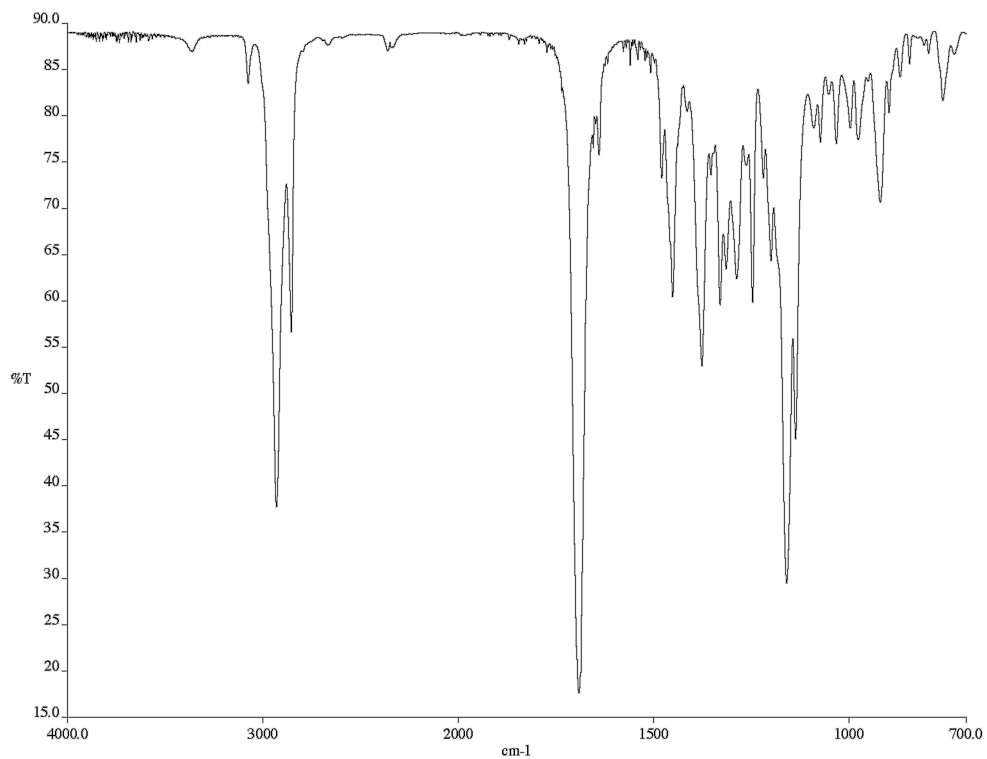


Figure SI-31B. Infrared spectrum (thin film/NaCl) of compound **5i**.

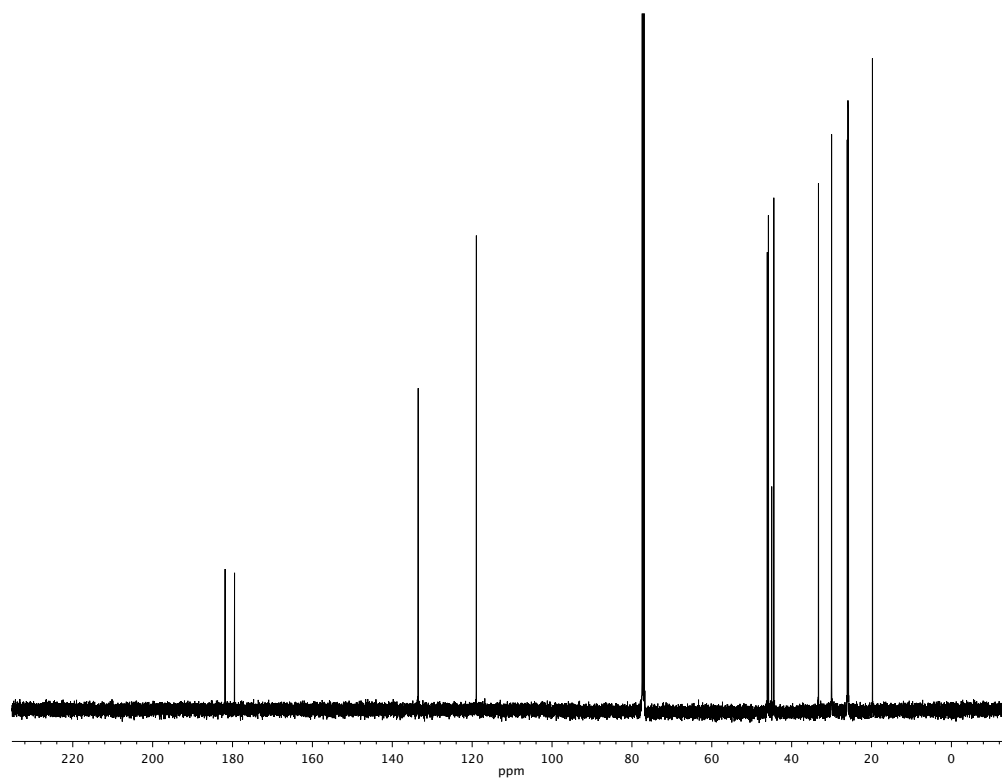
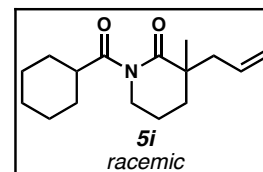


Figure SI-31C. ^{13}C NMR (125 MHz, CDCl_3) of compound **5i**.

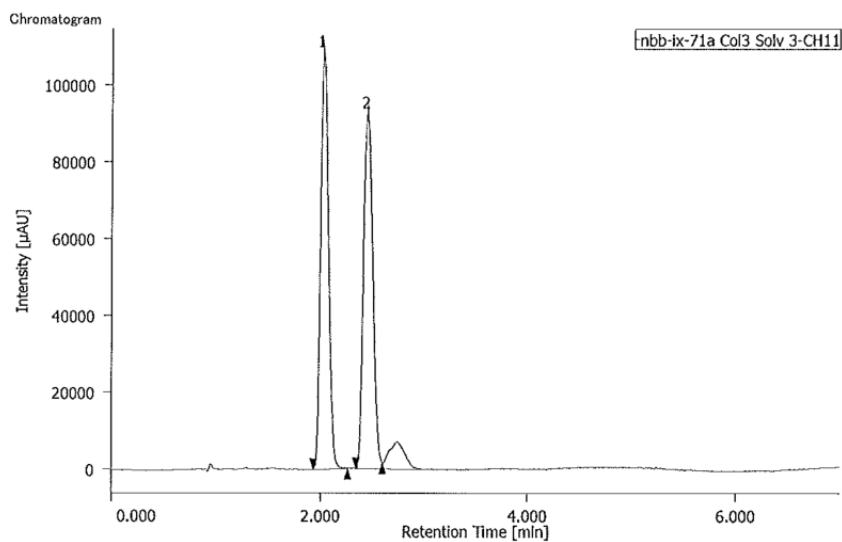
NBB-IX-71A Col3 Sol3 nbb-ix-71a Col3 Solv 3 6/27/2012 4:36:10 PM

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

1 / 1

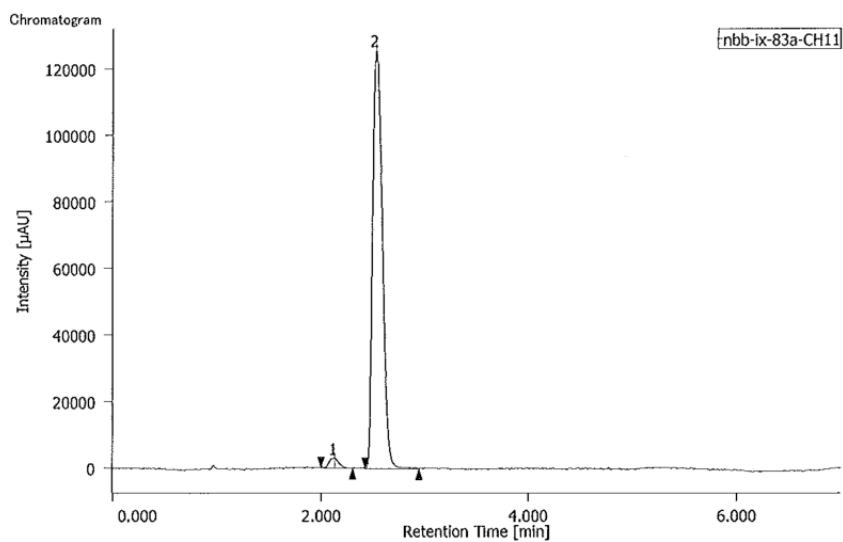
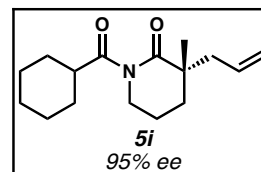
Figure SI-31D. Chiral SFC data of racemic compound **5i**.

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

Analytical Report SFC

Chromatogram Information

User: Jasoo SFC w PDA
 HPLC System Name: NBB-IX-83A Col3 Sol3
 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

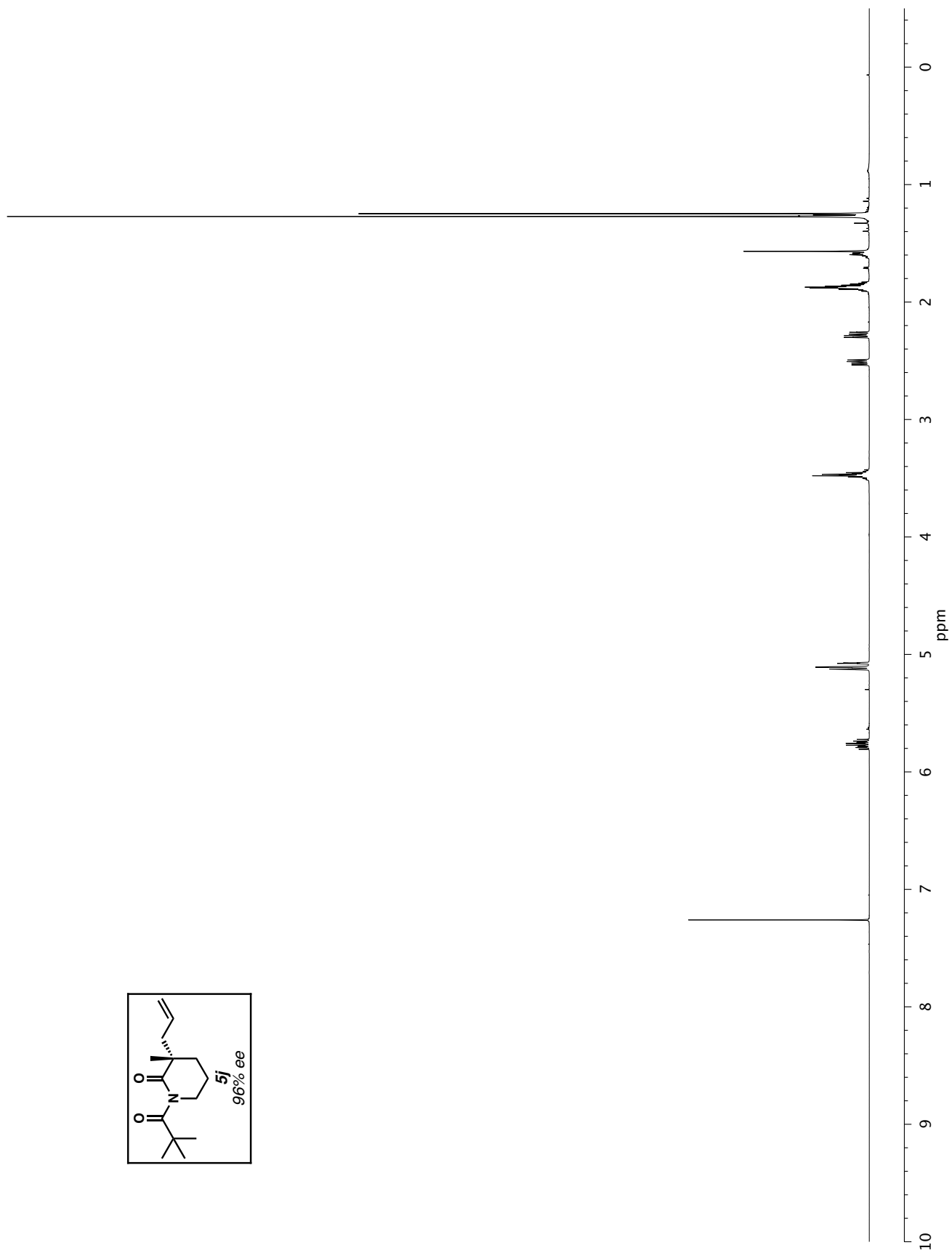


Peak Information

#	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. $^1\text{H NMR}$ (500 MHz, CDCl_3) of compound **5j**.

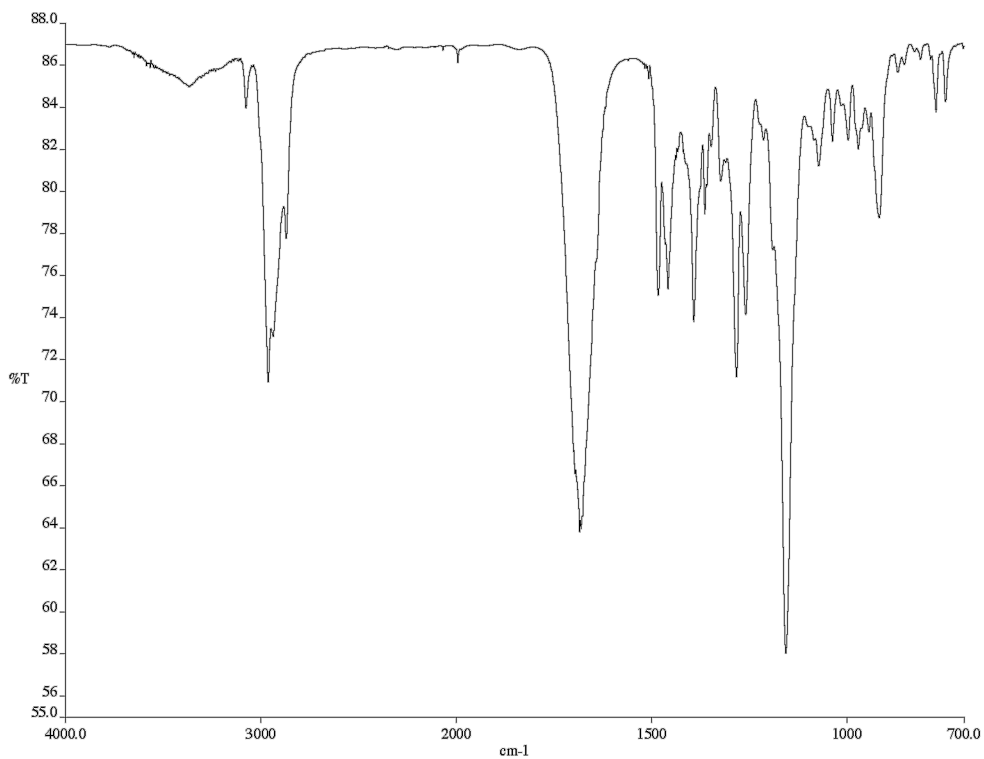


Figure SI-32B. Infrared spectrum (thin film/NaCl) of compound **5j**.

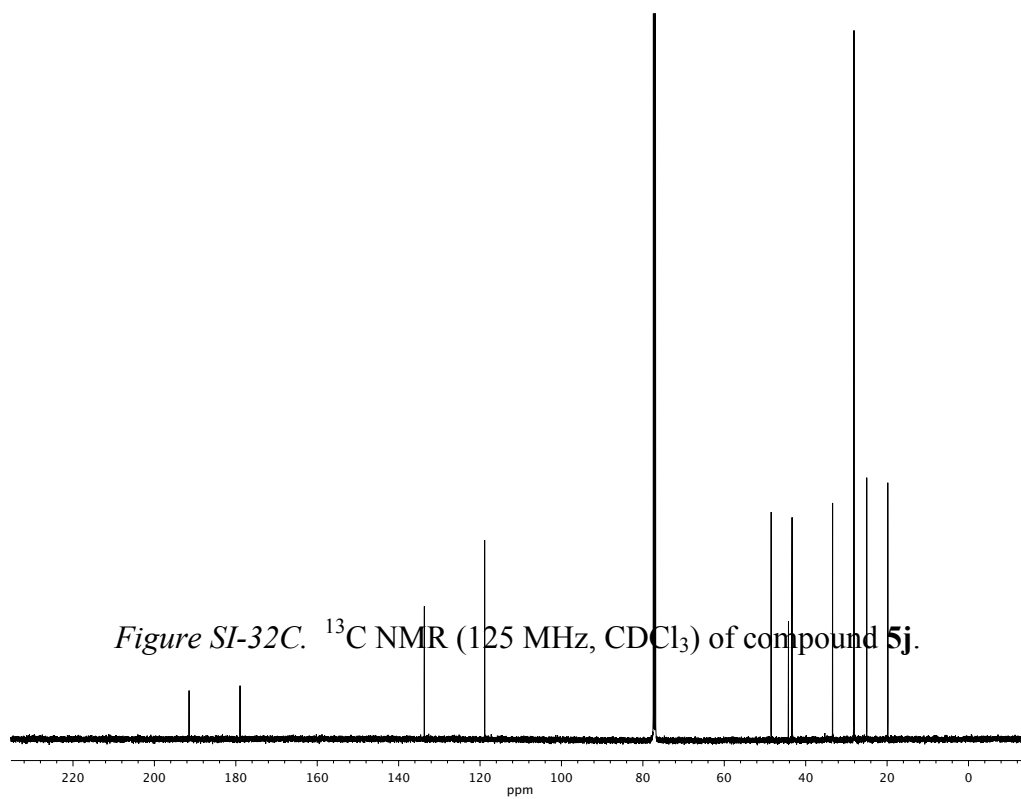


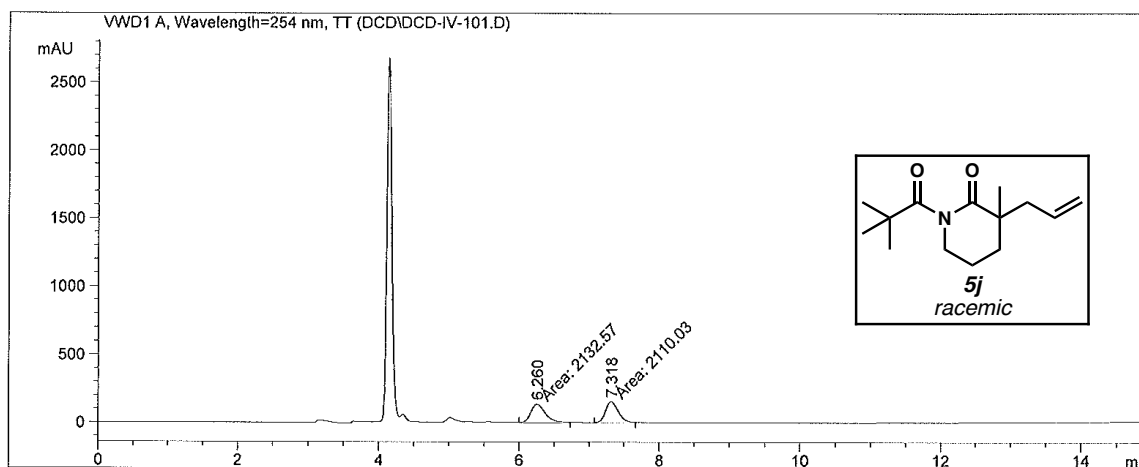
Figure SI-32C. ¹³C NMR (125 MHz, CDCl₃) of compound **5j**.

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 [min]	Type	Width [min]	Area mAU*s	Height [mAU]	Area %
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

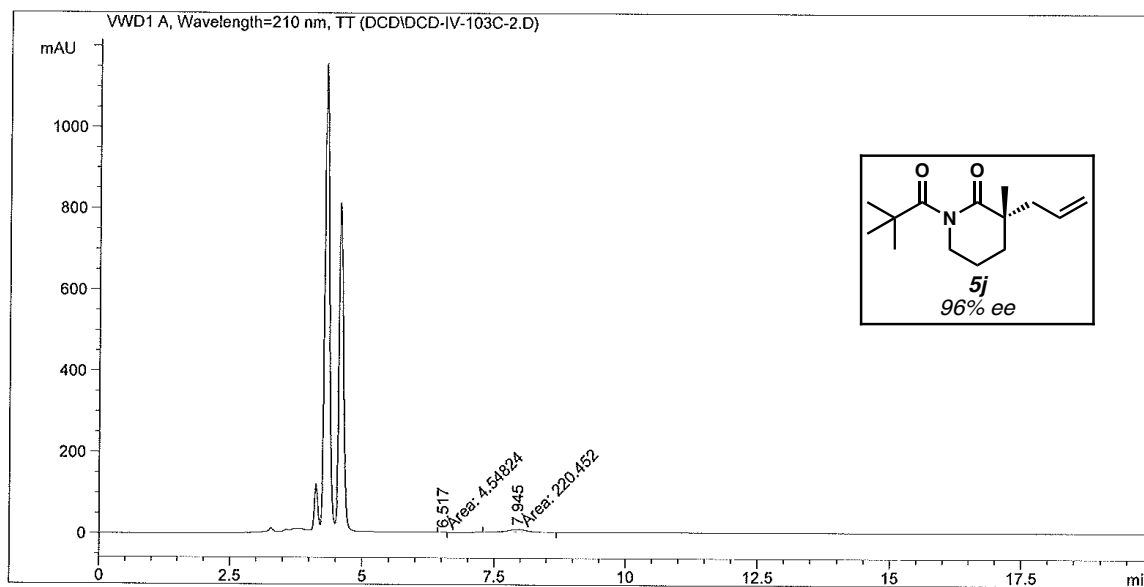
Figure SI-32D. Chiral HPLC data of racemic compound **5j**.

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 [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
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

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

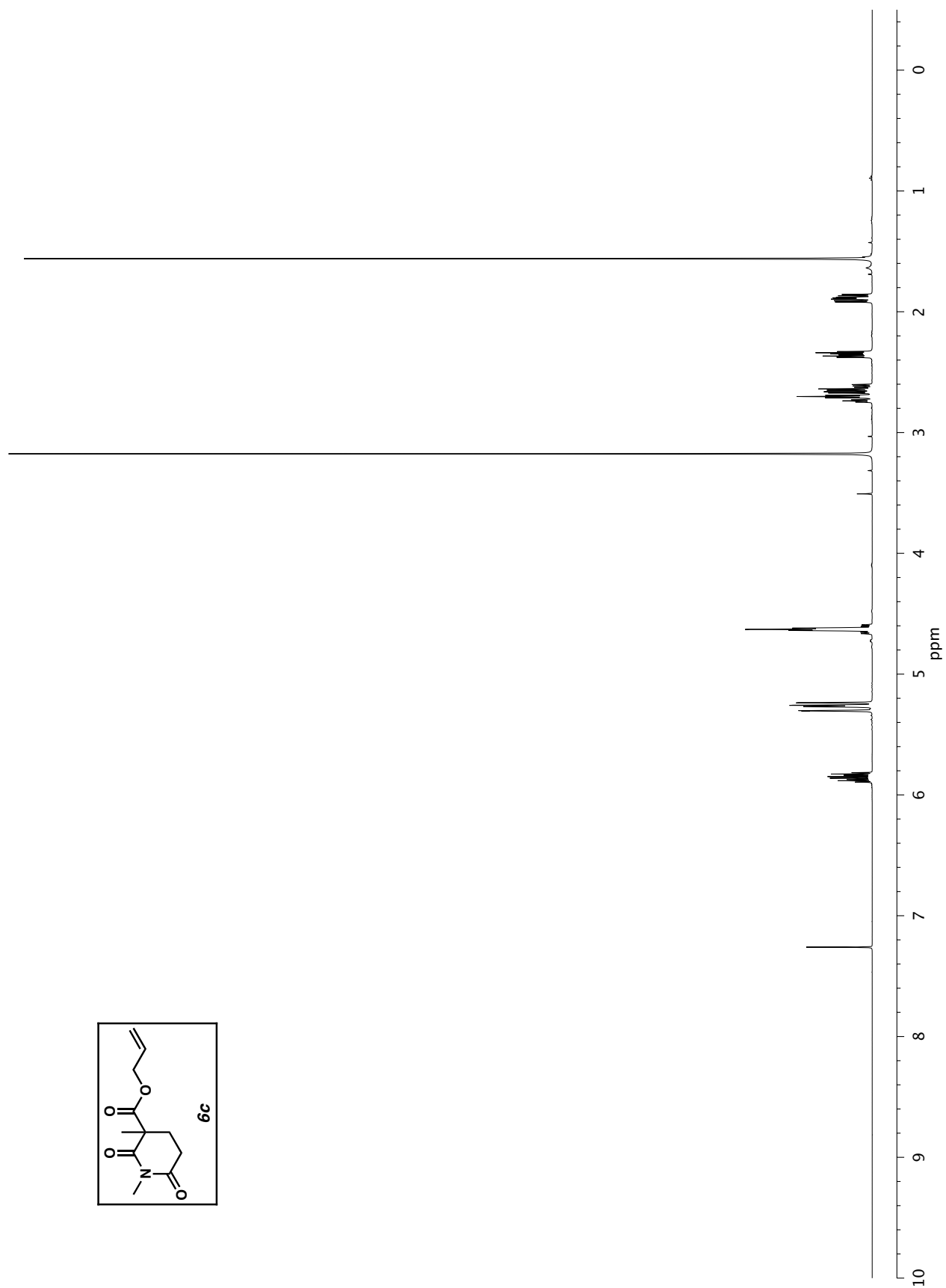


Figure SI-33A. ¹H NMR (500 MHz, CDCl₃) of compound **6c**.

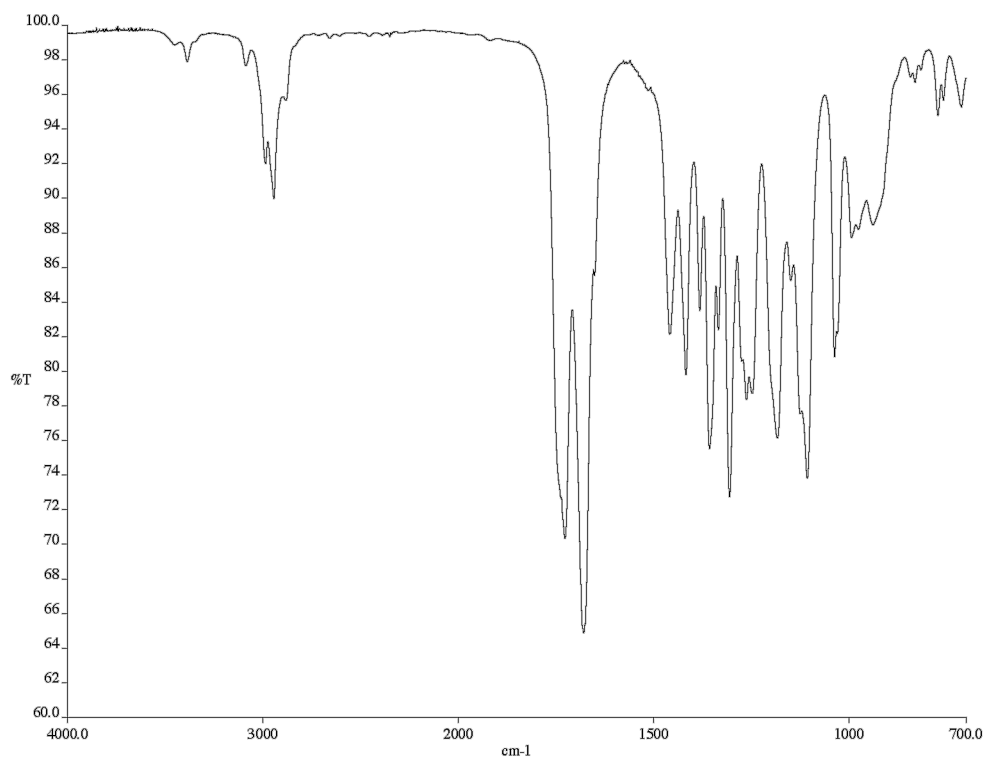


Figure SI-33B. Infrared spectrum (thin film/NaCl) of compound **6c**.

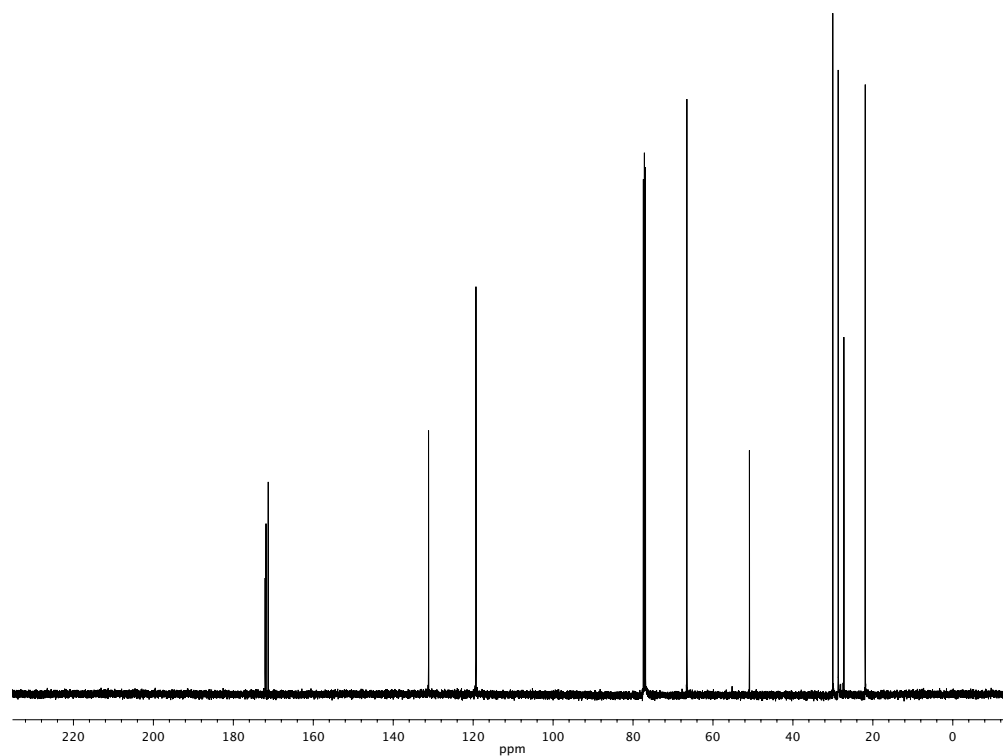


Figure SI-33C. ¹³C NMR (125 MHz, CDCl₃) of compound **6c**.

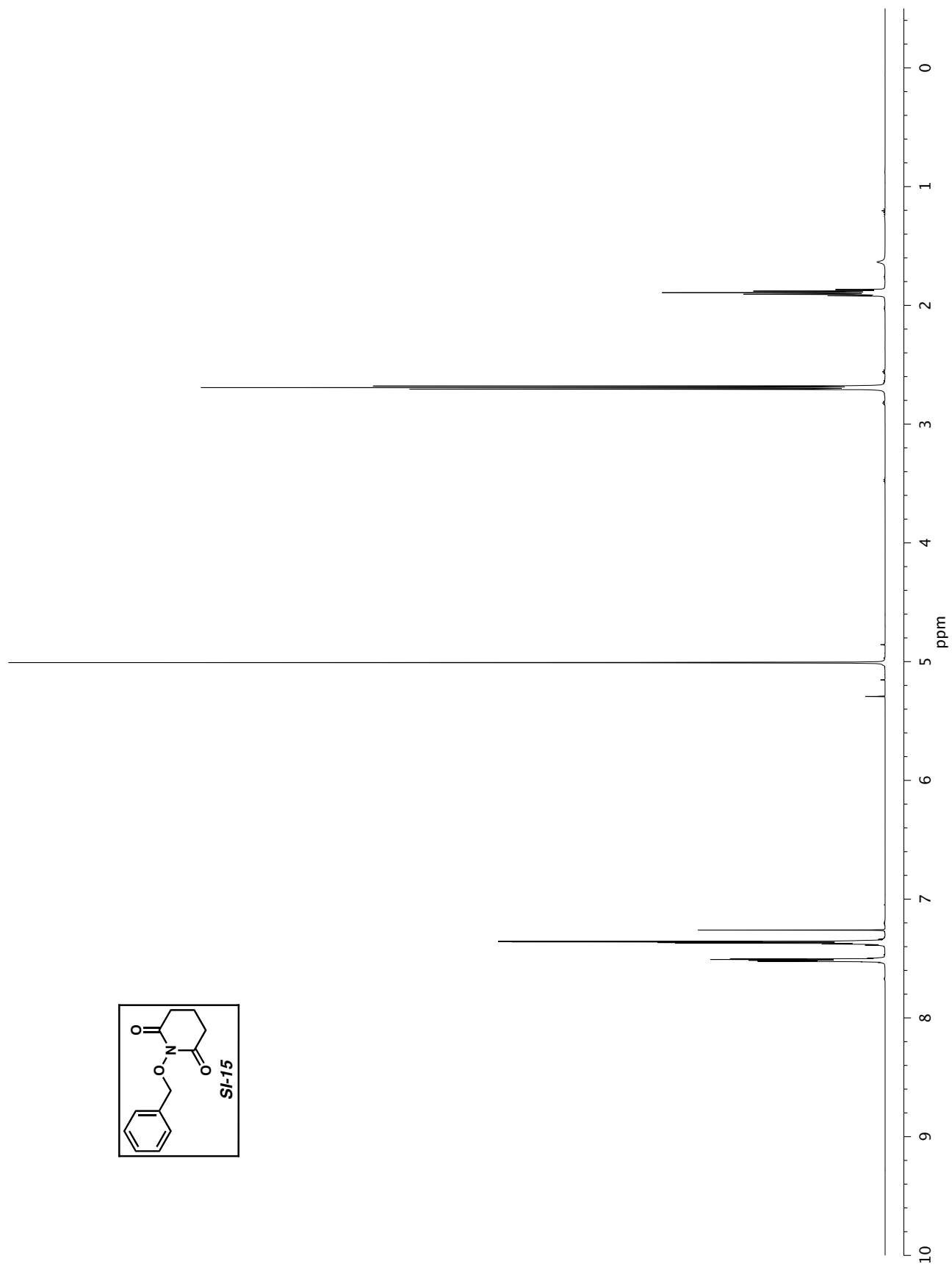


Figure SI-34A. ^1H NMR (500 MHz, CDCl_3) of compound SI-15.

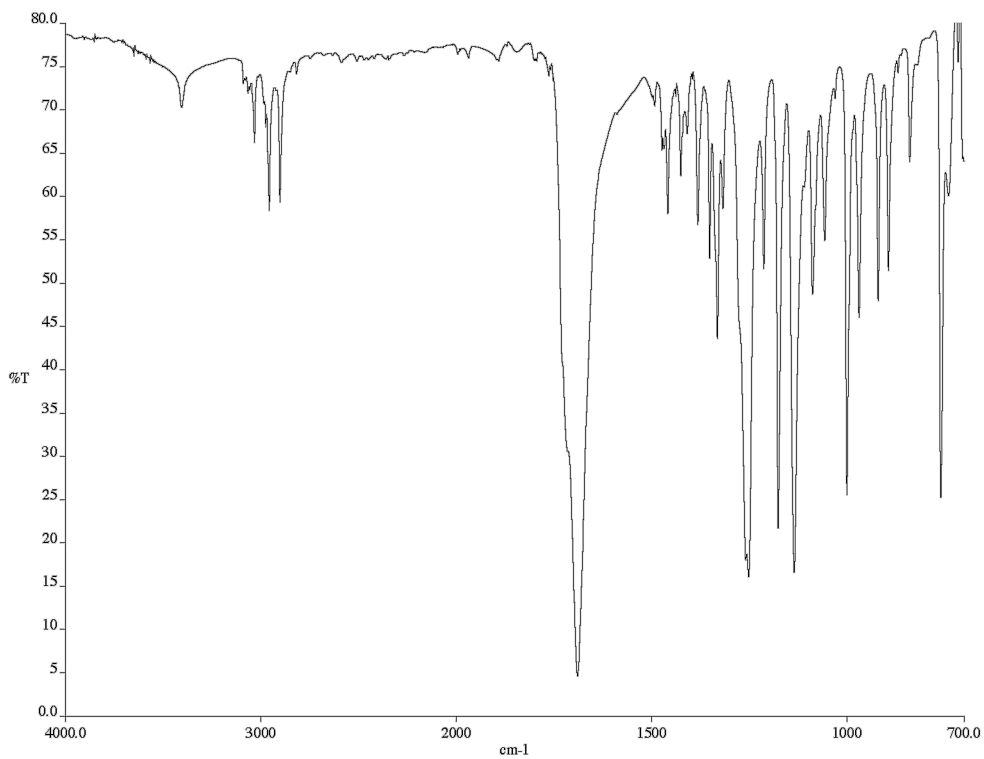


Figure SI-34B. Infrared spectrum (thin film/NaCl) of compound **SI-15**.

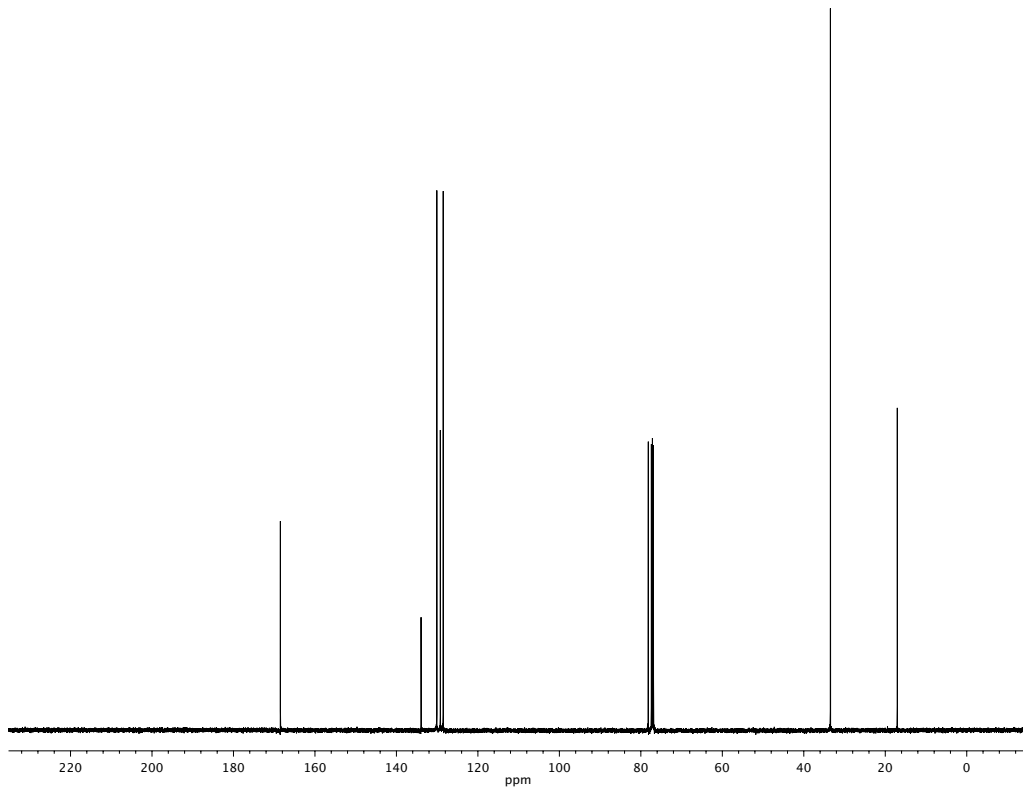
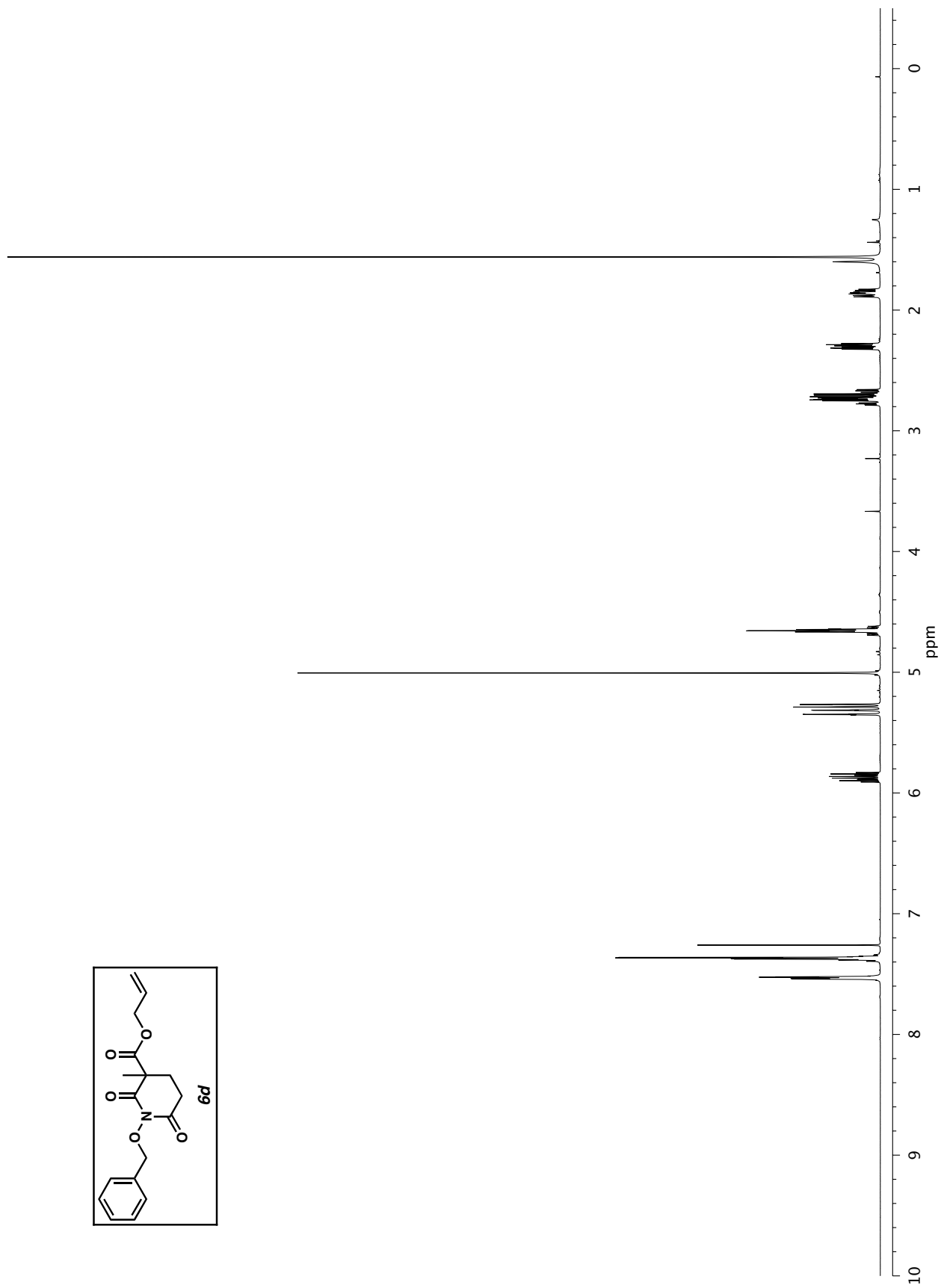


Figure SI-34C. ¹³C NMR (125 MHz, CDCl₃) of compound **SI-15**.

Figure SI-35A. ^1H NMR (500 MHz, CDCl_3) of compound **6d**.

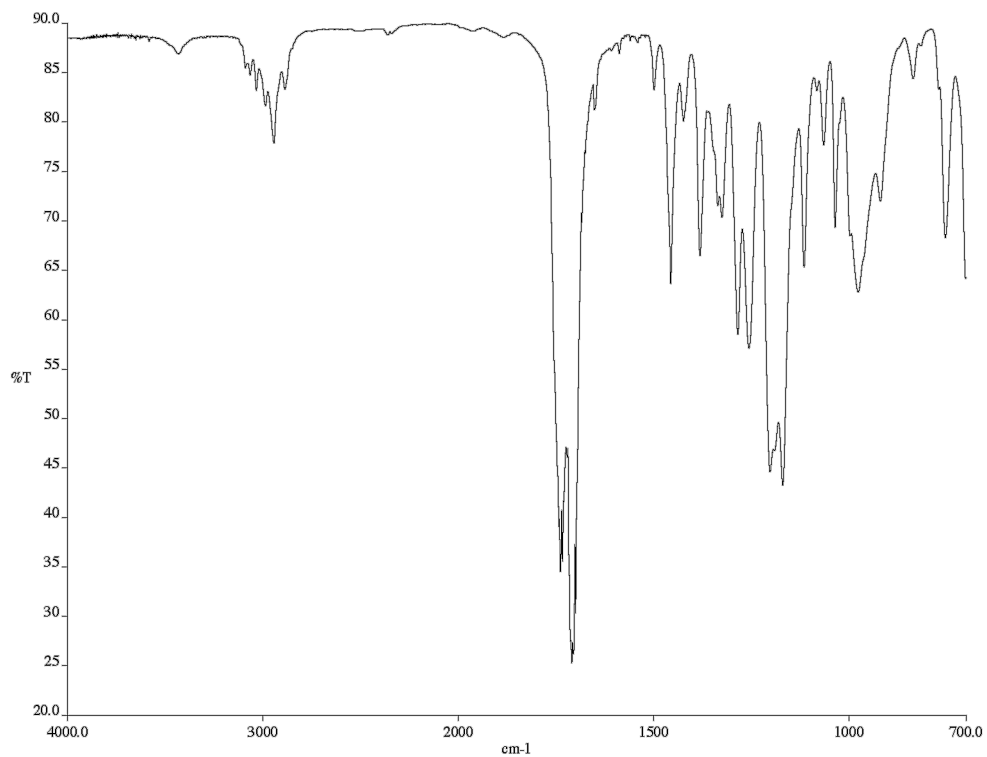


Figure SI-35B. Infrared spectrum (thin film/NaCl) of compound **6d**.

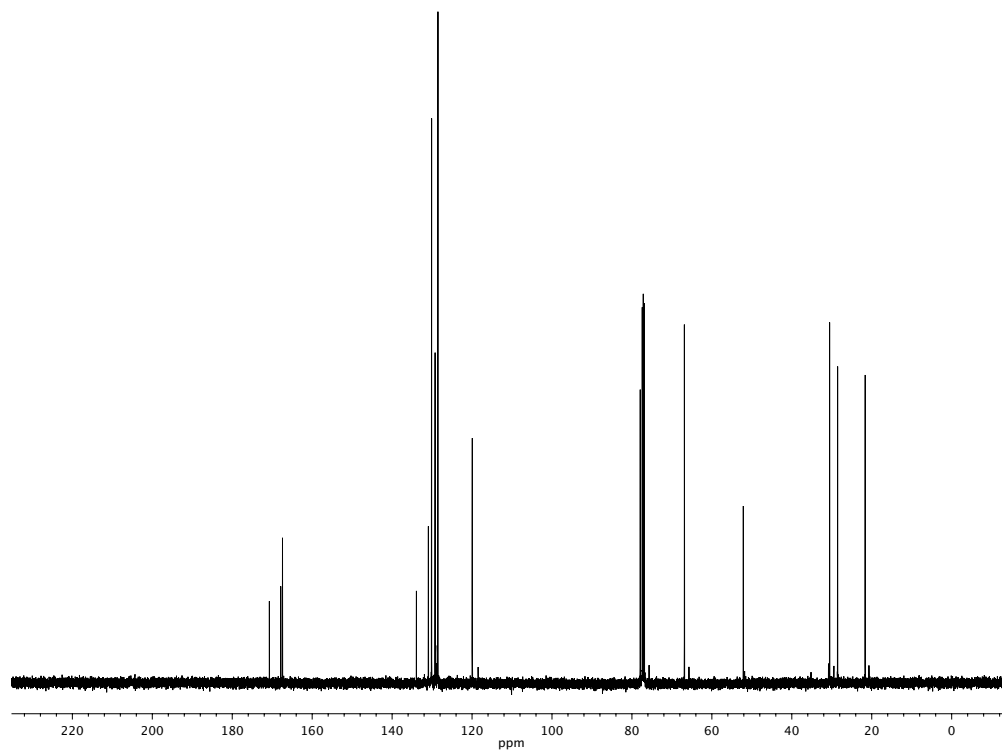


Figure SI-35C. ¹³C NMR (125 MHz, CDCl₃) of compound **6d**.

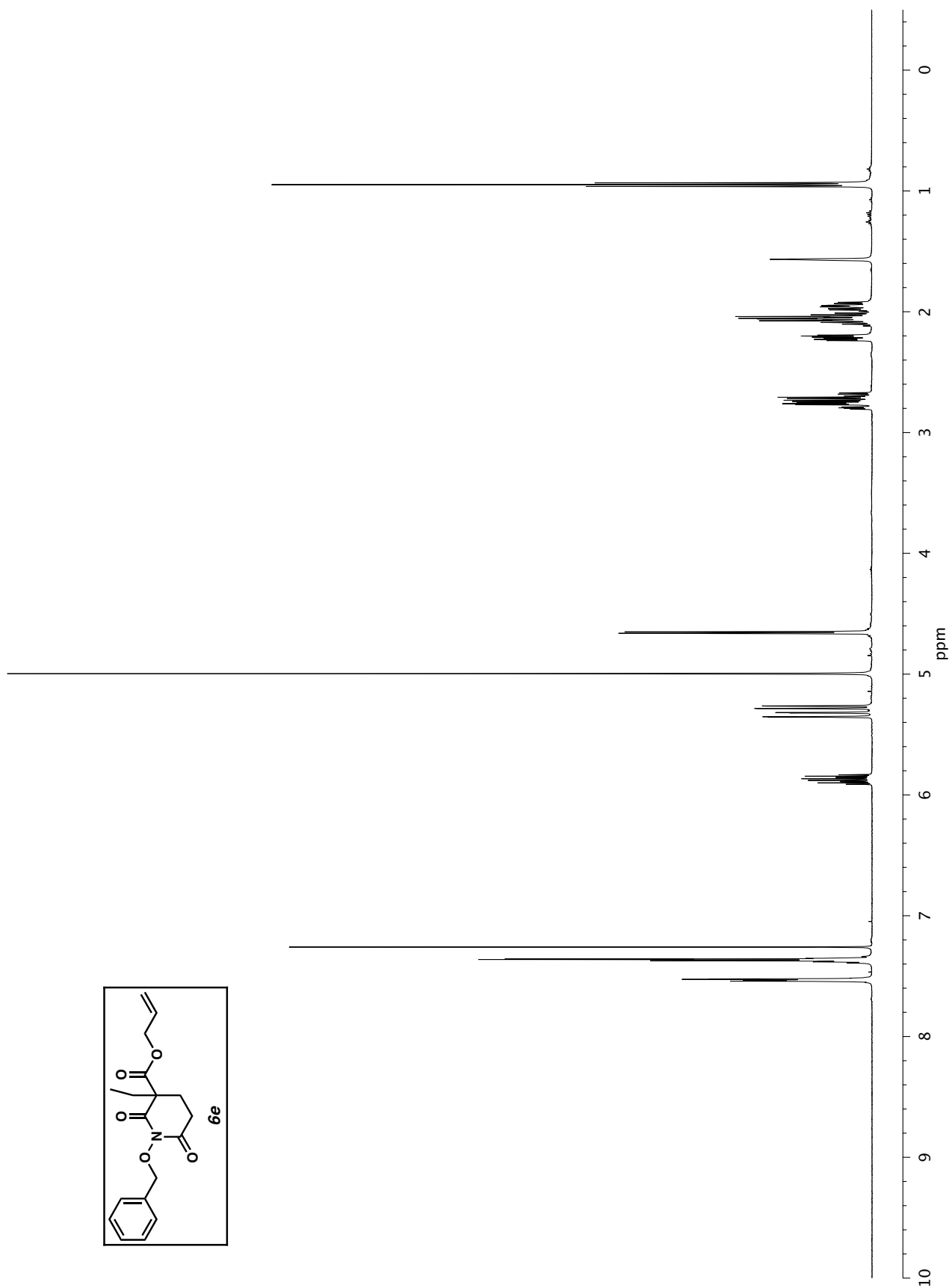


Figure SI-36A. ¹H NMR (500 MHz, CDCl₃) of compound **6e**.

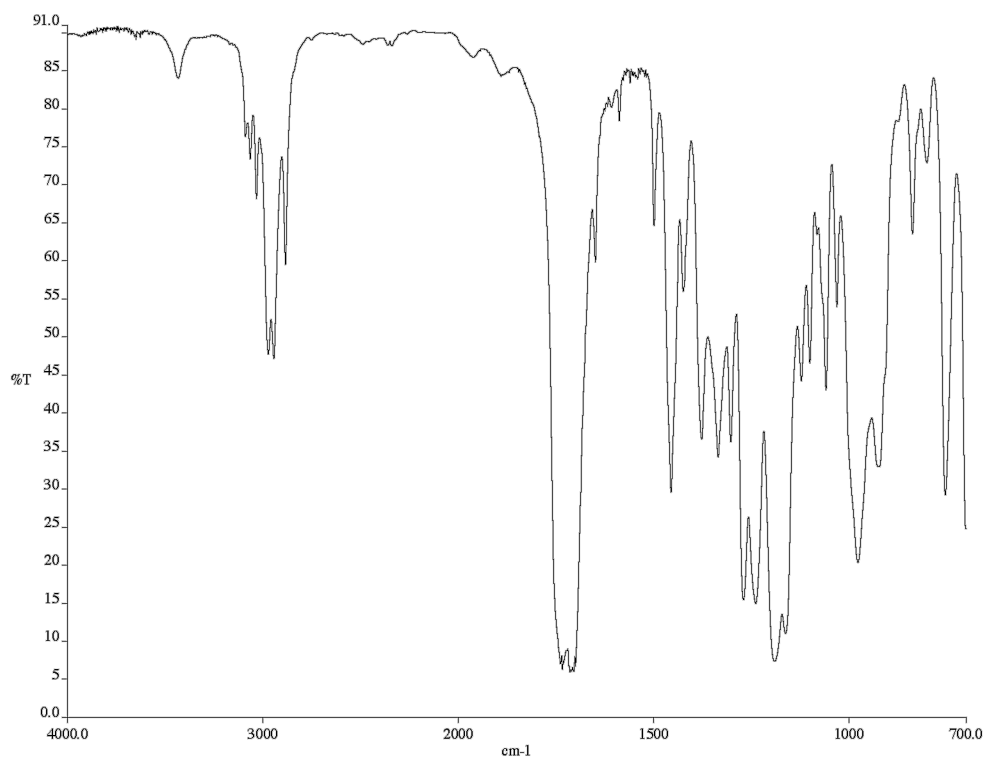


Figure SI-36B. Infrared spectrum (thin film/NaCl) of compound **6e**.

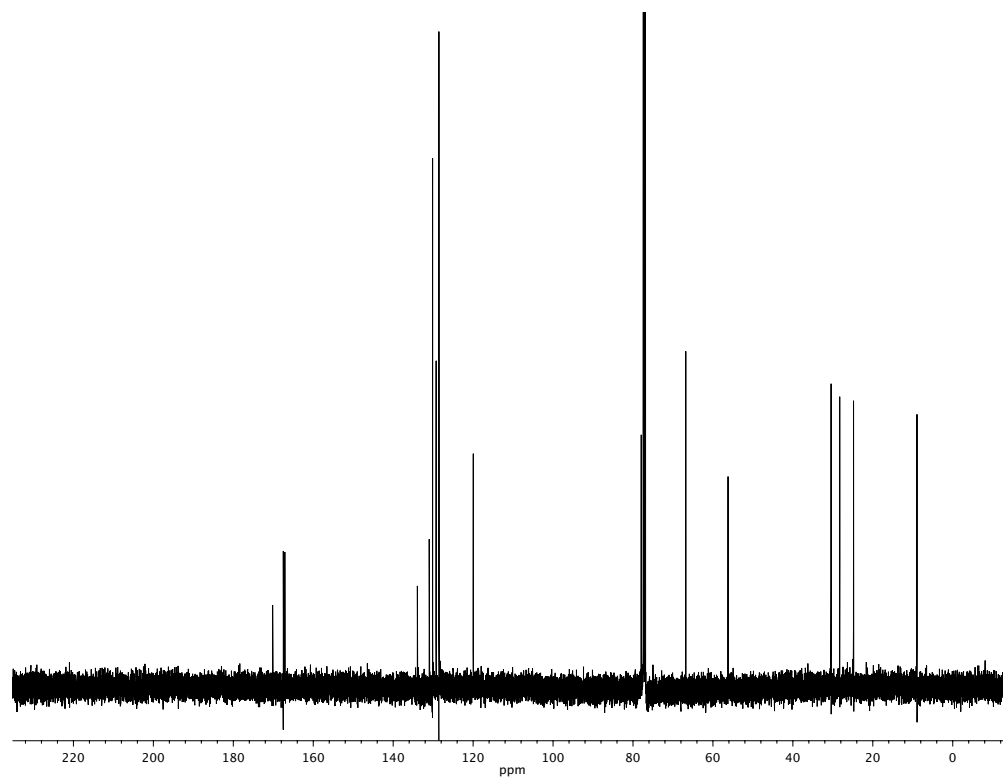
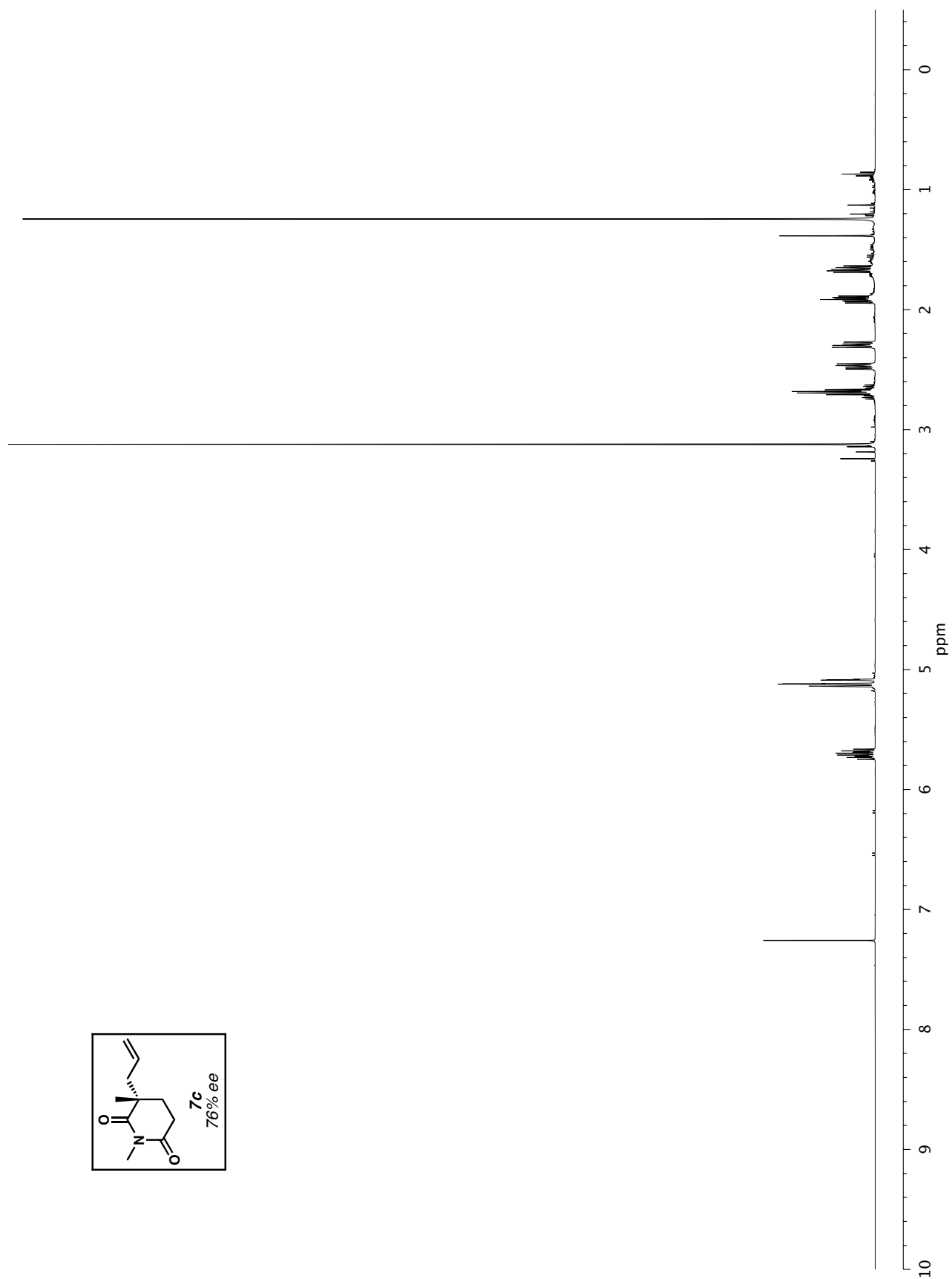


Figure SI-36C. ^{13}C NMR (125 MHz, CDCl_3) of compound **6e**.

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

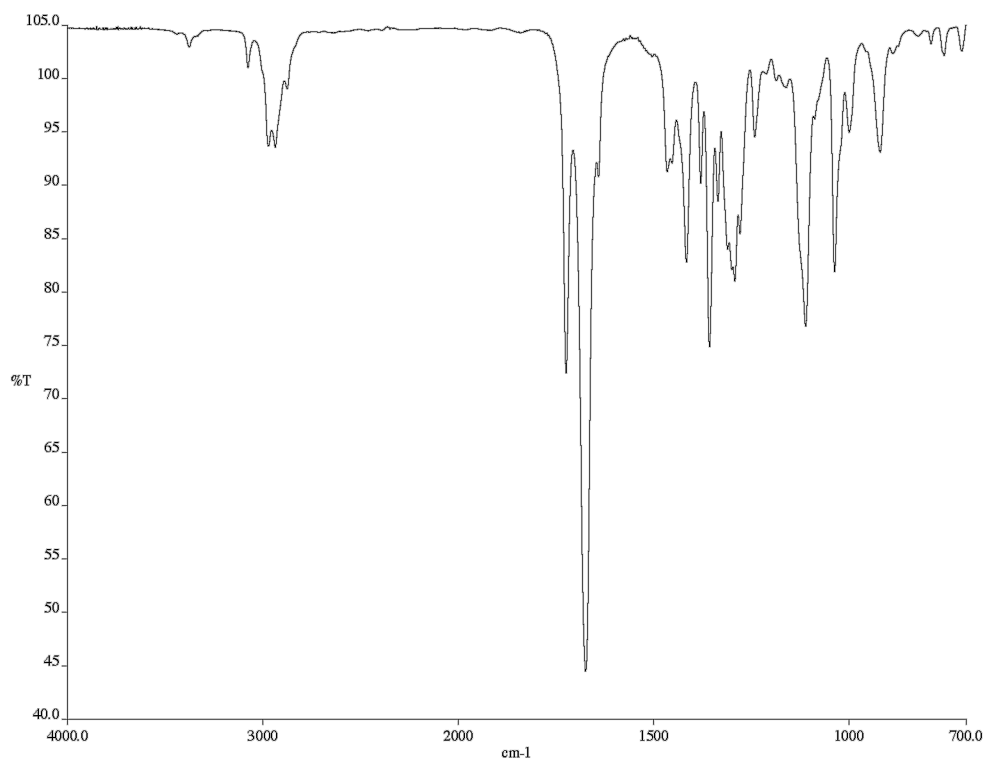


Figure SI-37B. Infrared spectrum (thin film/NaCl) of compound **7c**.

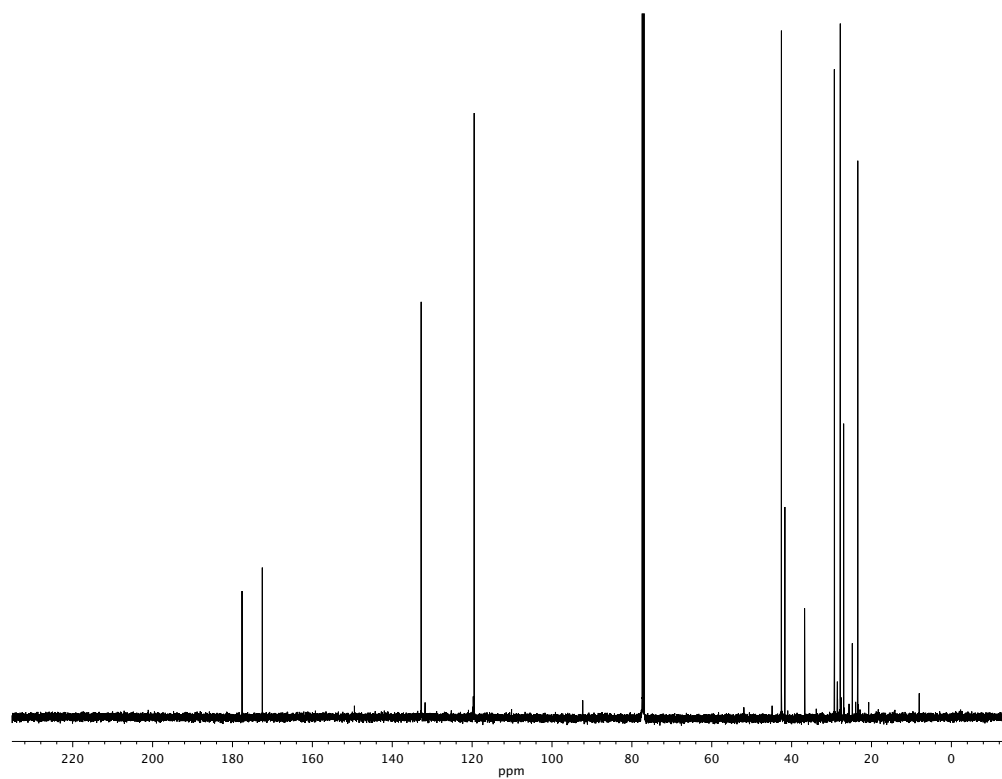
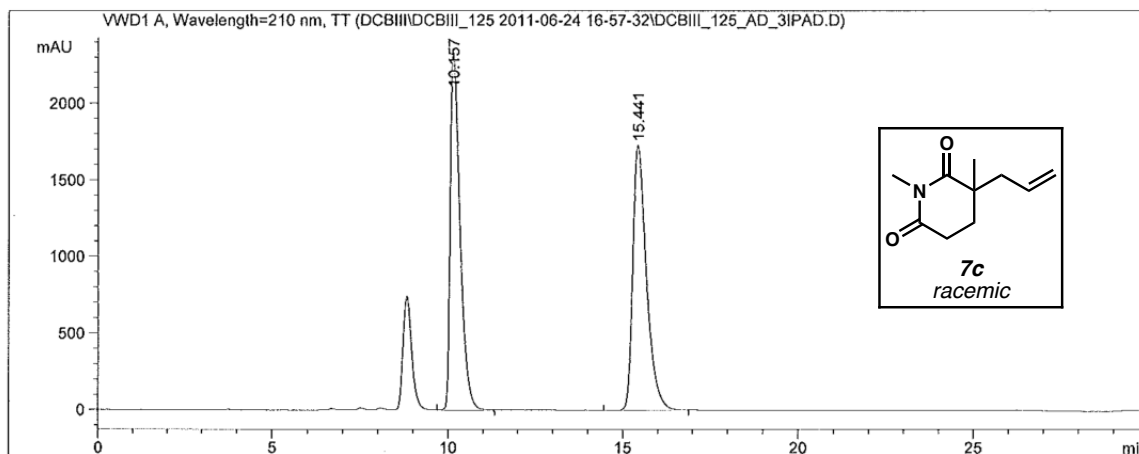


Figure SI-37C. ¹³C NMR (125 MHz, CDCl₃) of compound **7c**.

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 [min]	Type	Width [min]	Area mAU*s	Height [mAU]	Area %
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

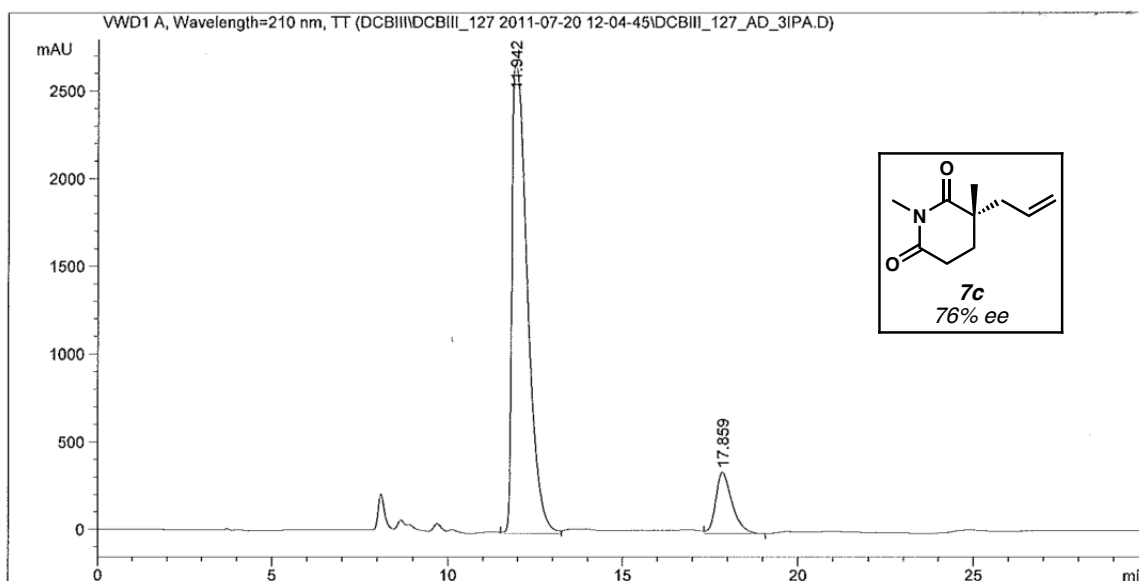
Figure SI-37D. Chiral HPLC data of racemic compound **7c**.

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
 =====

```

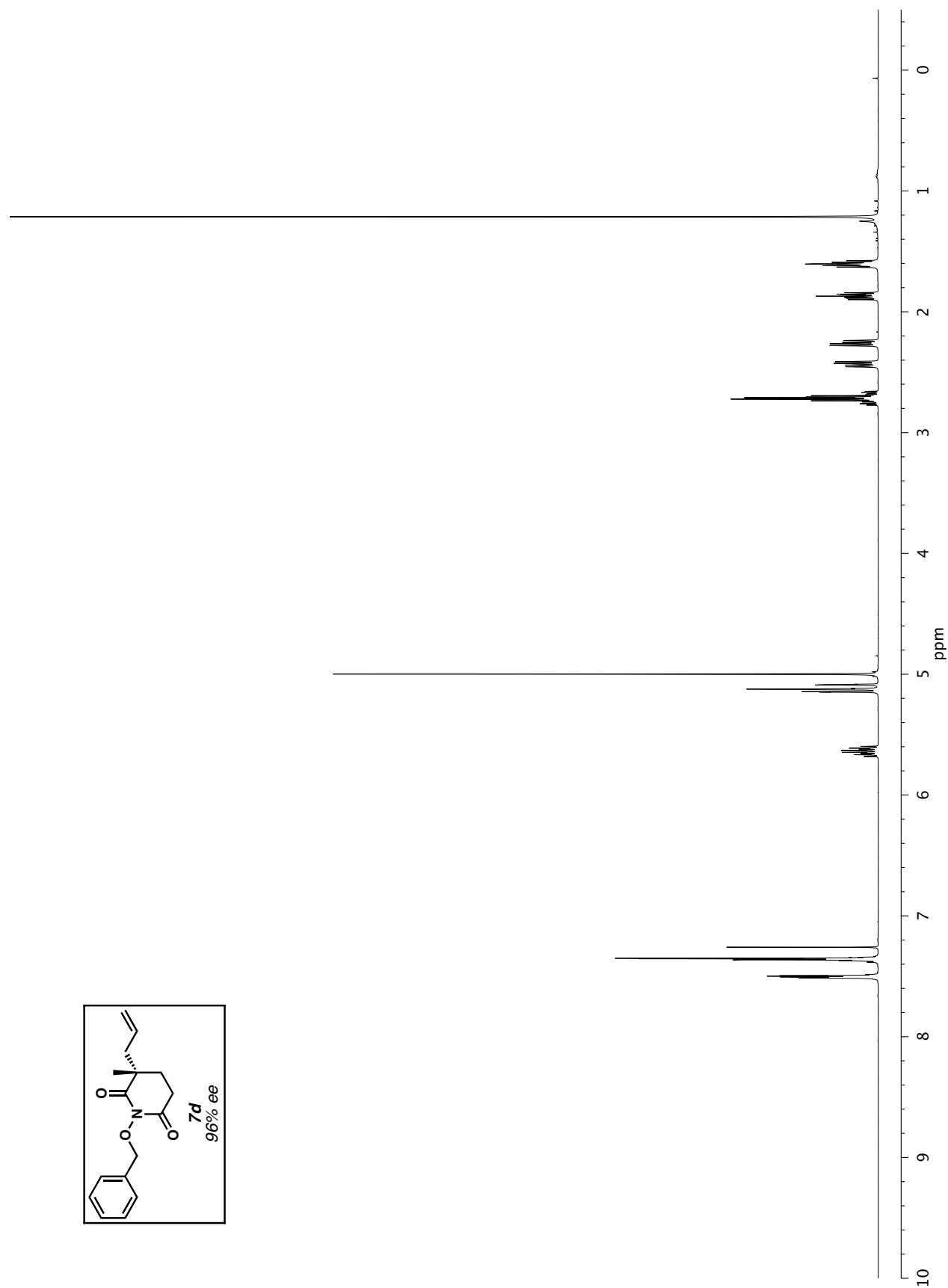
Sorted By      :      Signal
Multiplier:    :      1.0000
Dilution:      :      1.0000
Use Multiplier & Dilution Factor with ISTDs
  
```

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

Peak #	RetTime [min]	Type	Width [min]	Area mAU*s	Height [mAU]	Area %
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

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

Figure SI-38A. ^1H NMR (500 MHz, CDCl_3) of compound **7d**.

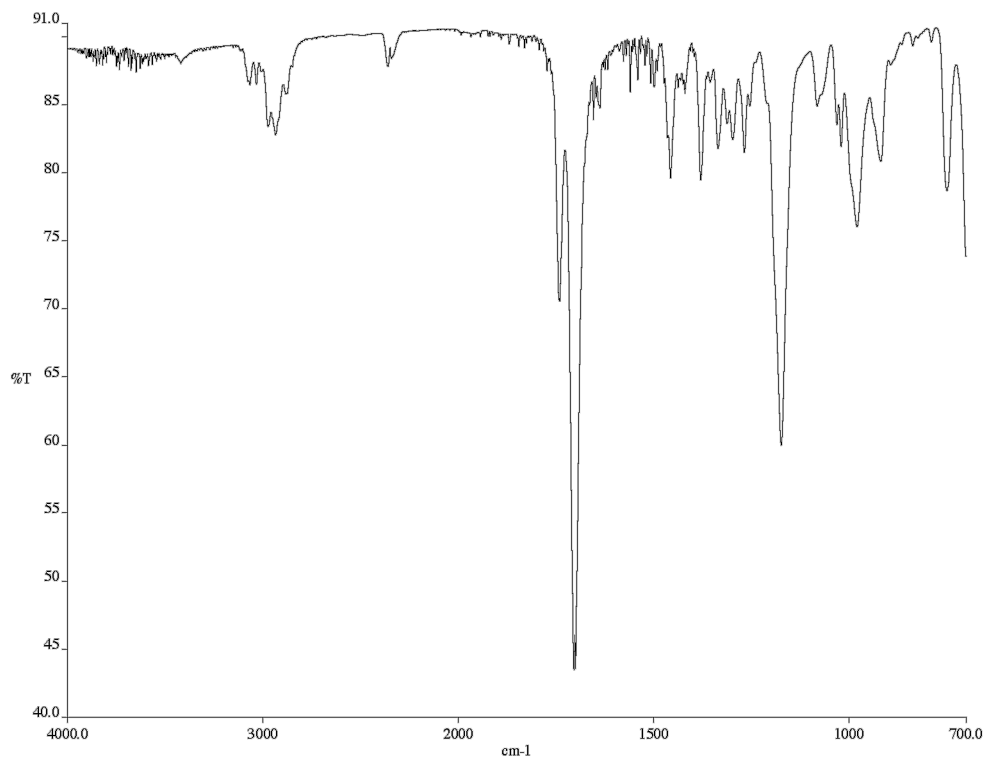


Figure SI-38B. Infrared spectrum (thin film/NaCl) of compound **7d**.

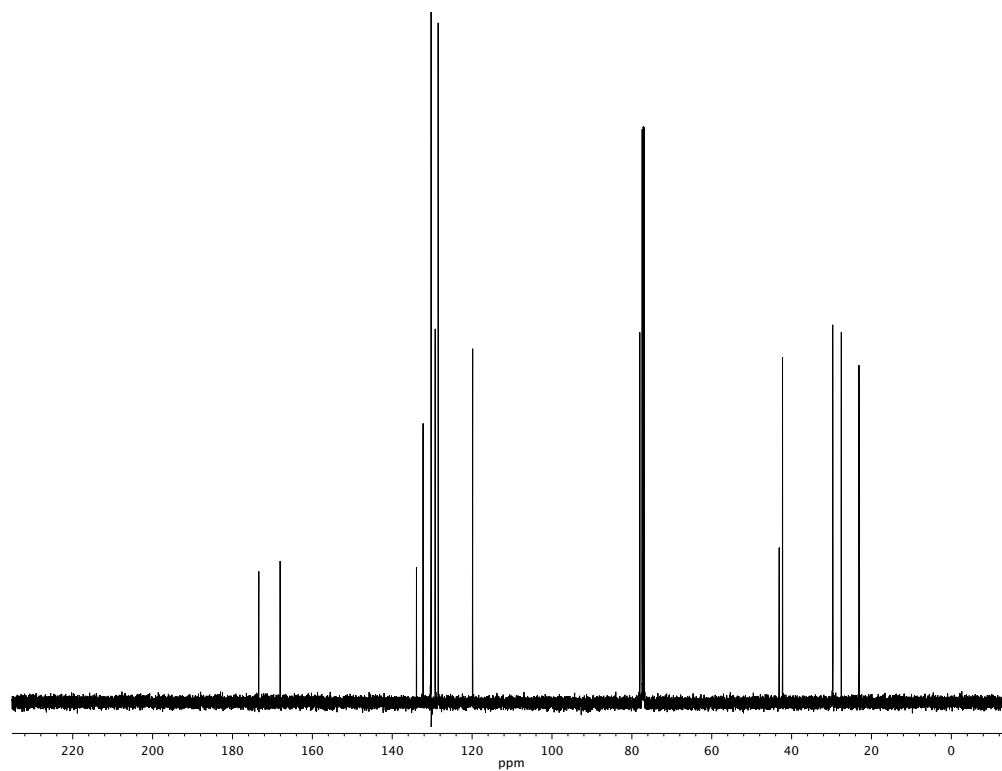
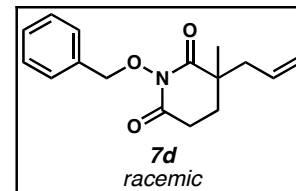


Figure SI-38C. ^{13}C NMR (125 MHz, CDCl_3) of compound **7d**.

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	

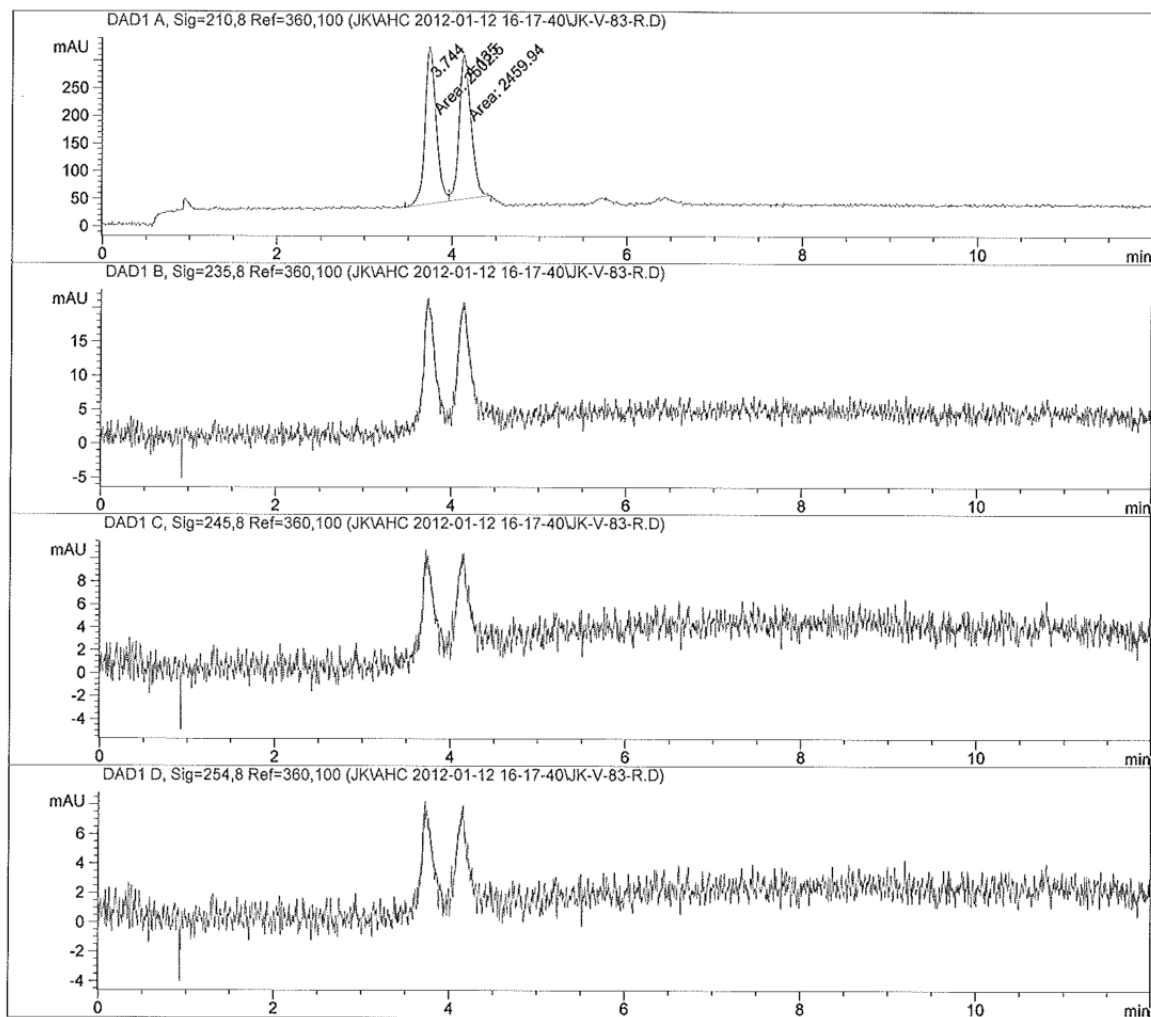
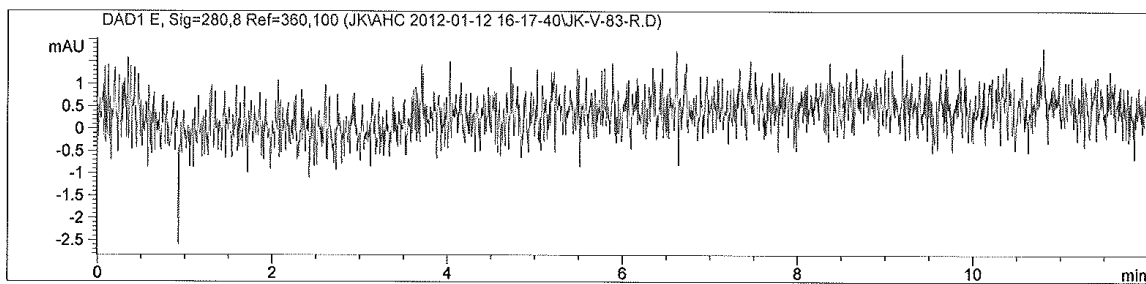


Figure SI-38D. Chiral SFC data of racemic compound **7d**.

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

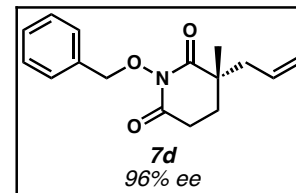
Signal 3: DAD1 C, Sig=245,8 Ref=360,100

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
  
```

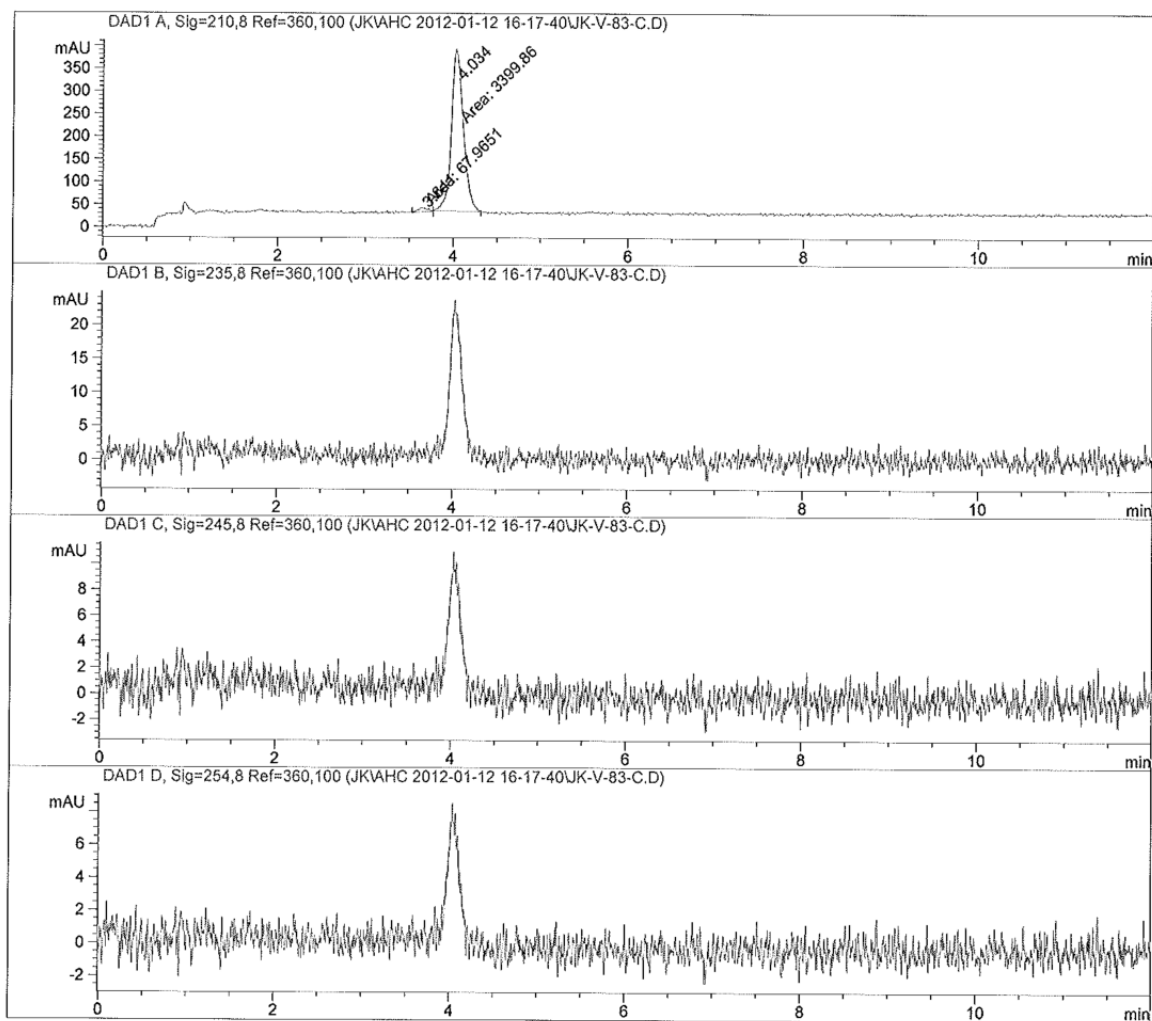
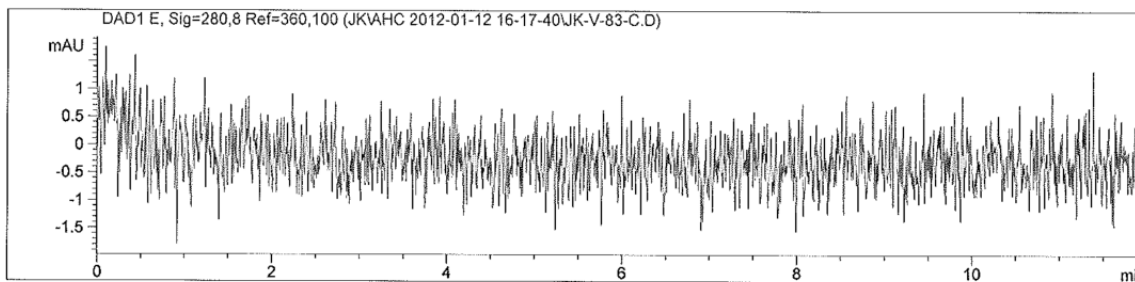


Figure SI-38E. Chiral SFC data of enantioenriched compound **7d**.

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

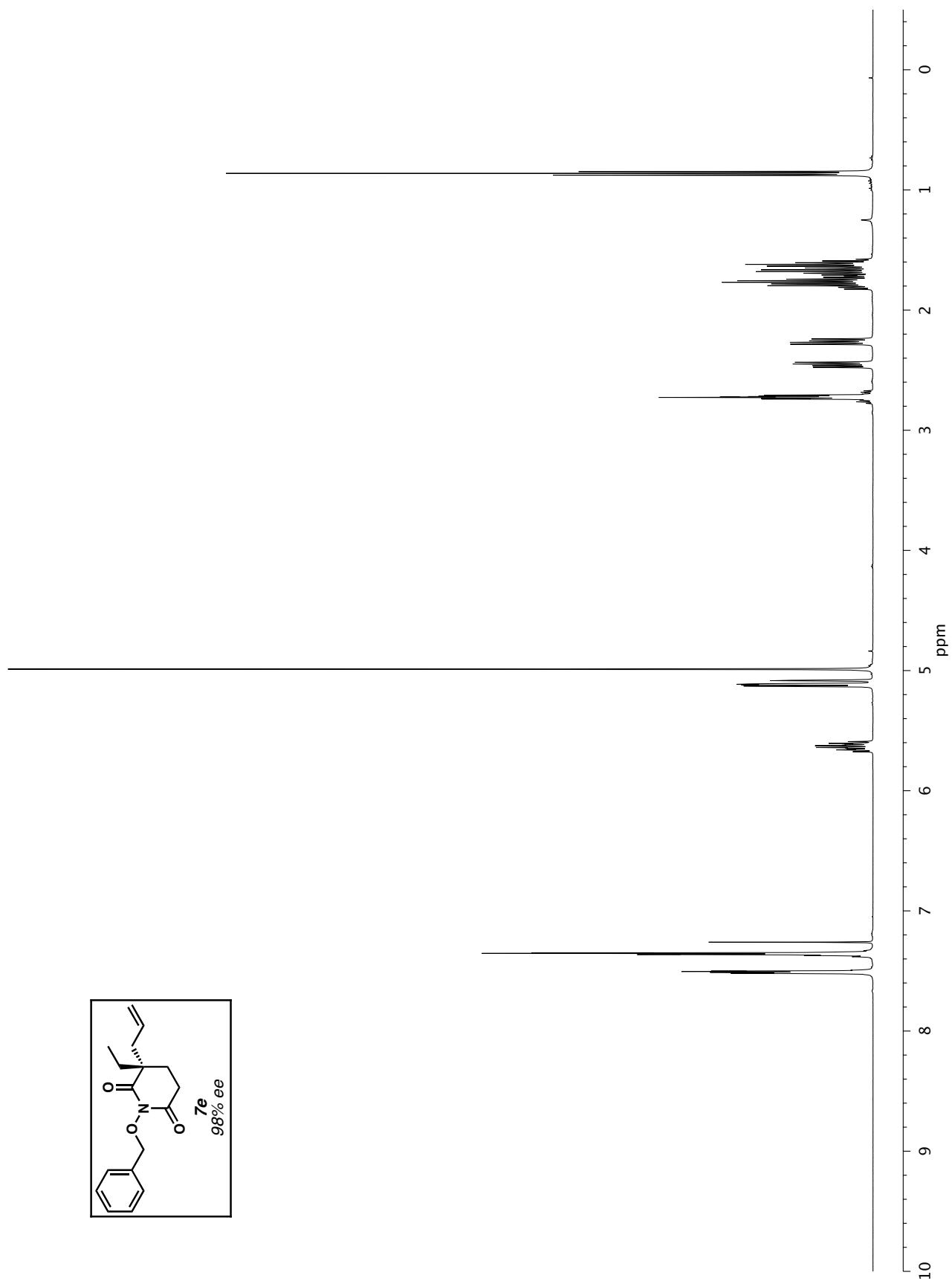
Signal 2: DAD1 B, Sig=235,8 Ref=360,100

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-39A. ^1H NMR (500 MHz, CDCl_3) of compound **7e**.

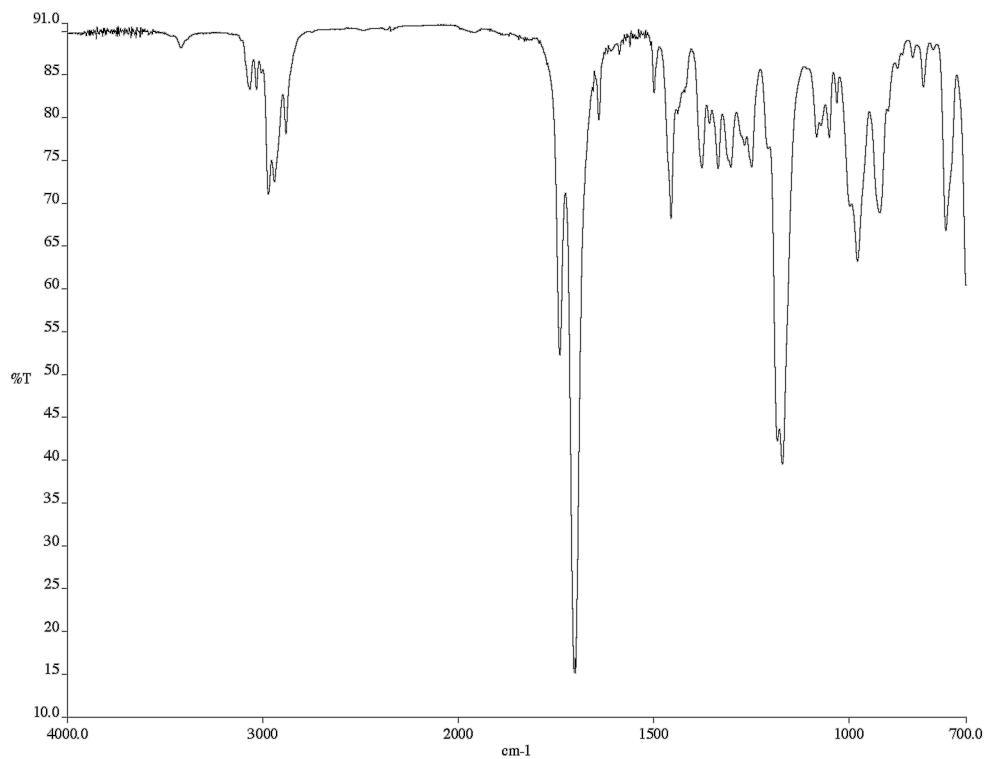


Figure SI-39B. Infrared spectrum (thin film/NaCl) of compound **7e**.

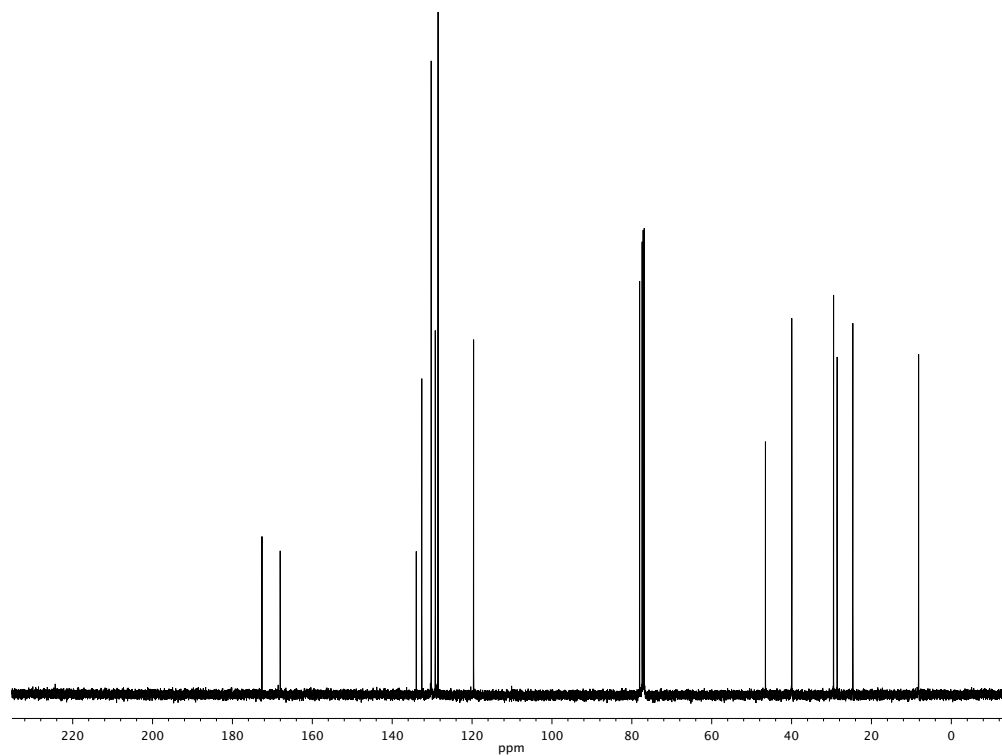
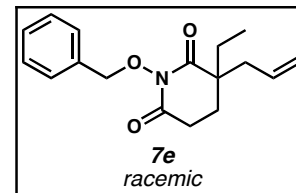


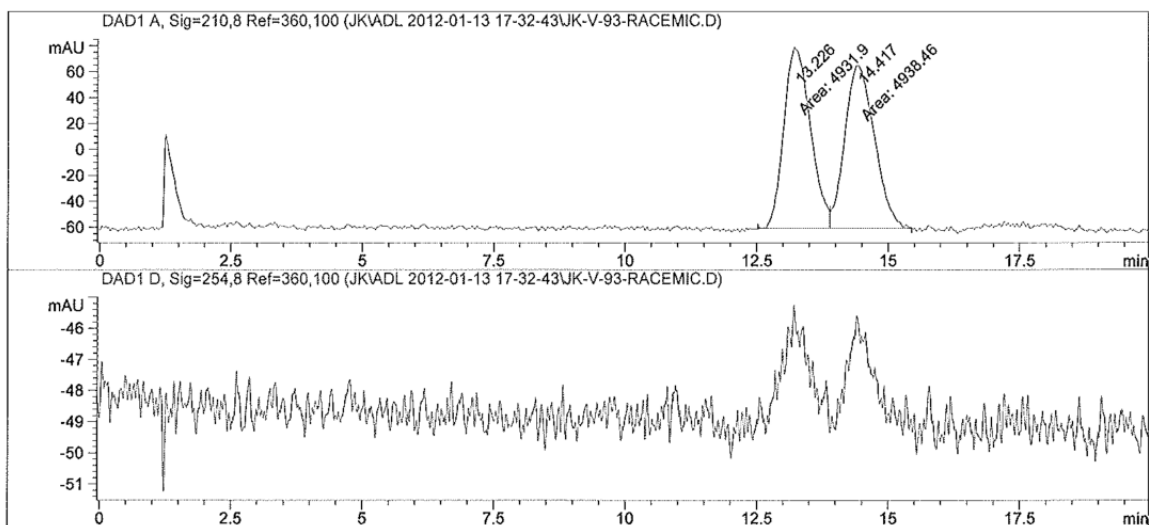
Figure SI-39C. ¹³C NMR (125 MHz, CDCl₃) of compound **7e**.

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



```

=====
Acq. Operator   : JK                               Seq. Line :    2
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
=====
  
```



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

```

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

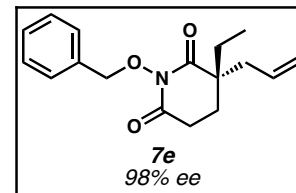
Signal 1: DAD1 A, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	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

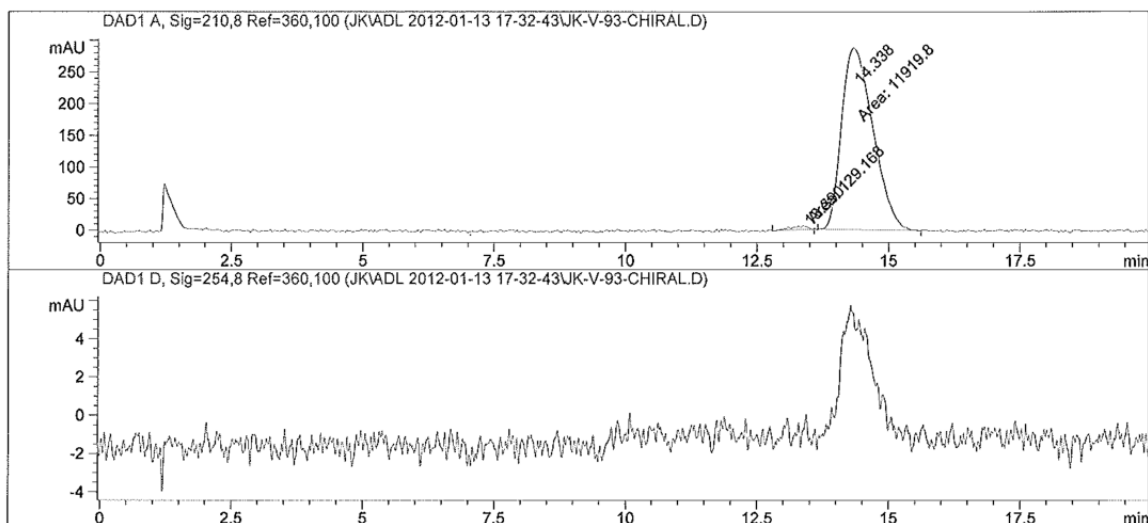
Figure SI-39D. Chiral SFC data of racemic compound 7e.

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



```

=====
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
  
```



=====
 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	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

Figure SI-39E. Chiral SFC data of enantioenriched compound 7e.

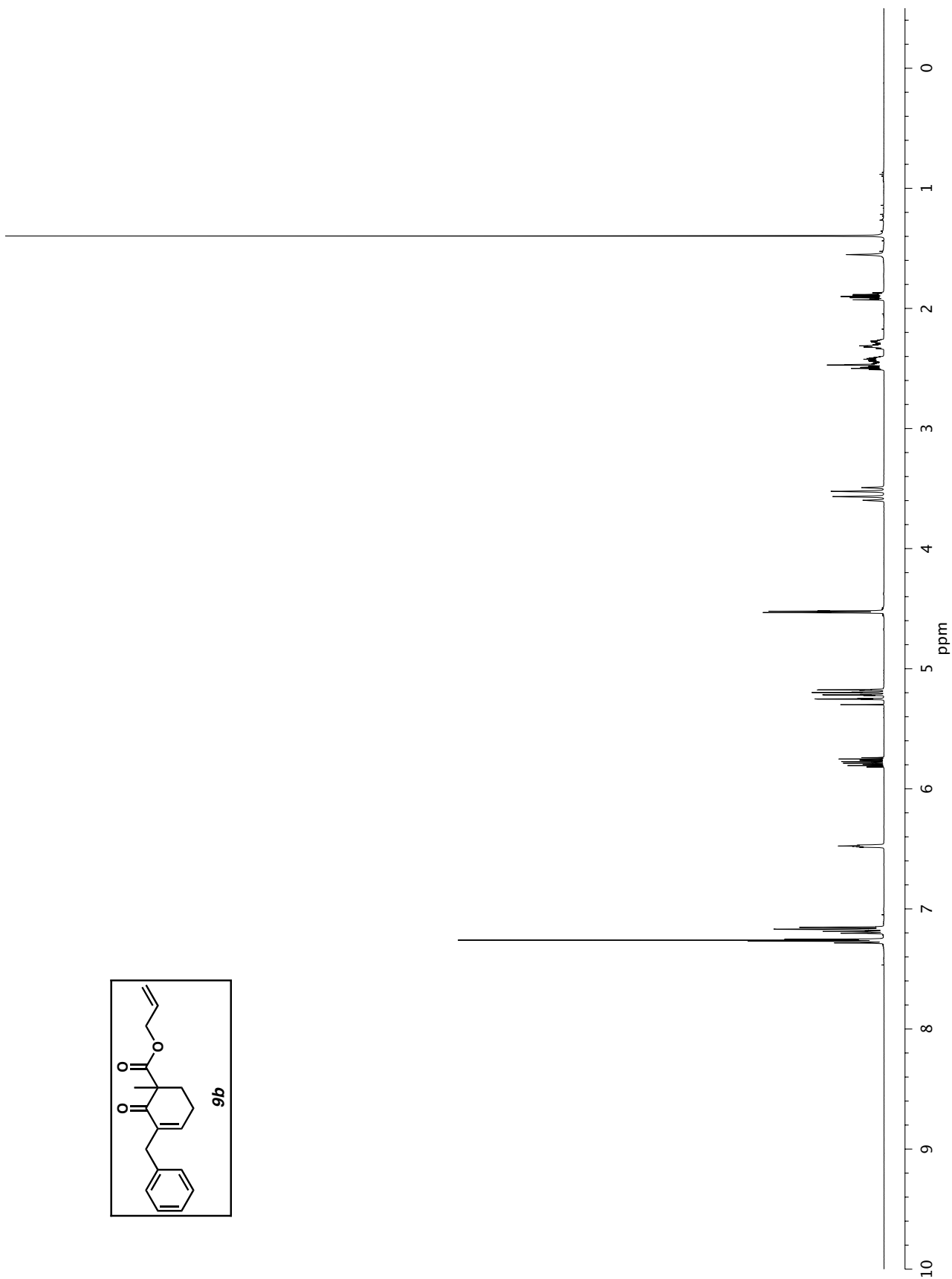


Figure SI-40A. ^1H NMR (500 MHz, CDCl_3) of compound **9b**.

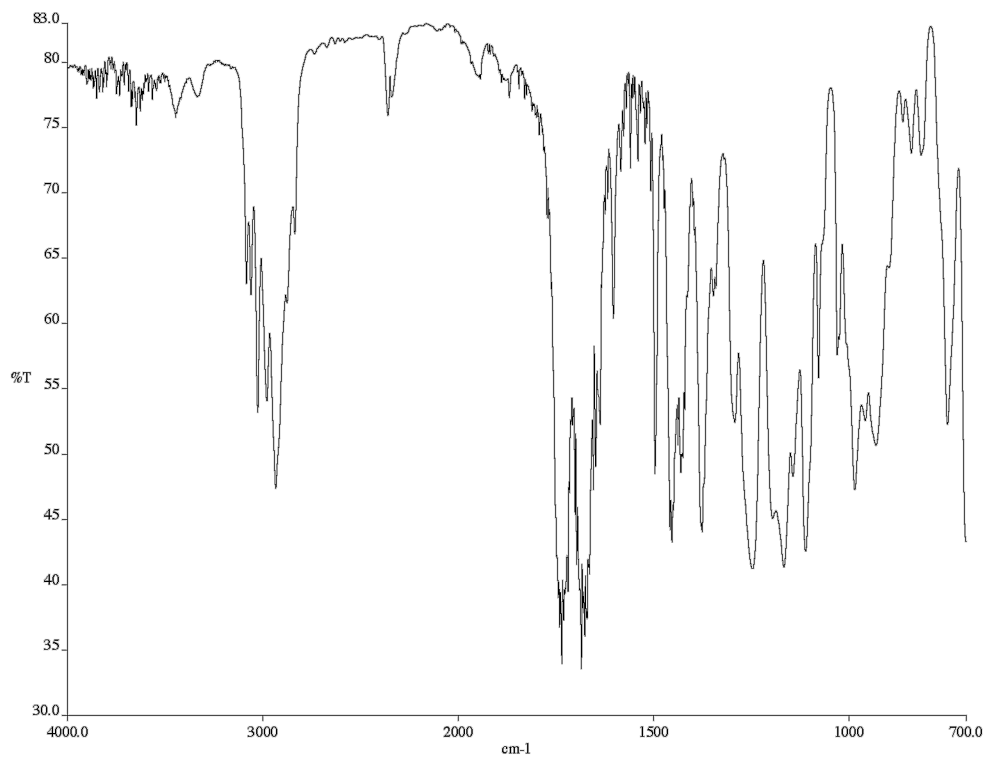


Figure SI-40B. Infrared spectrum (thin film/NaCl) of compound **9b**.

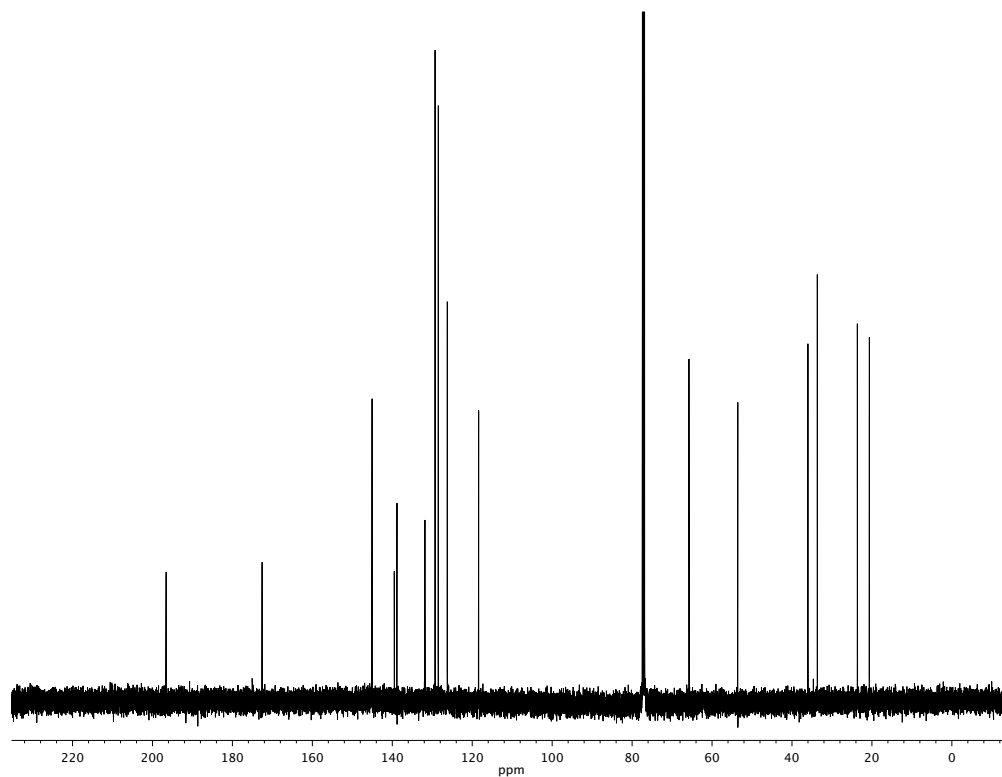


Figure SI-40C. ¹³C NMR (125 MHz, CDCl₃) of compound **9b**.

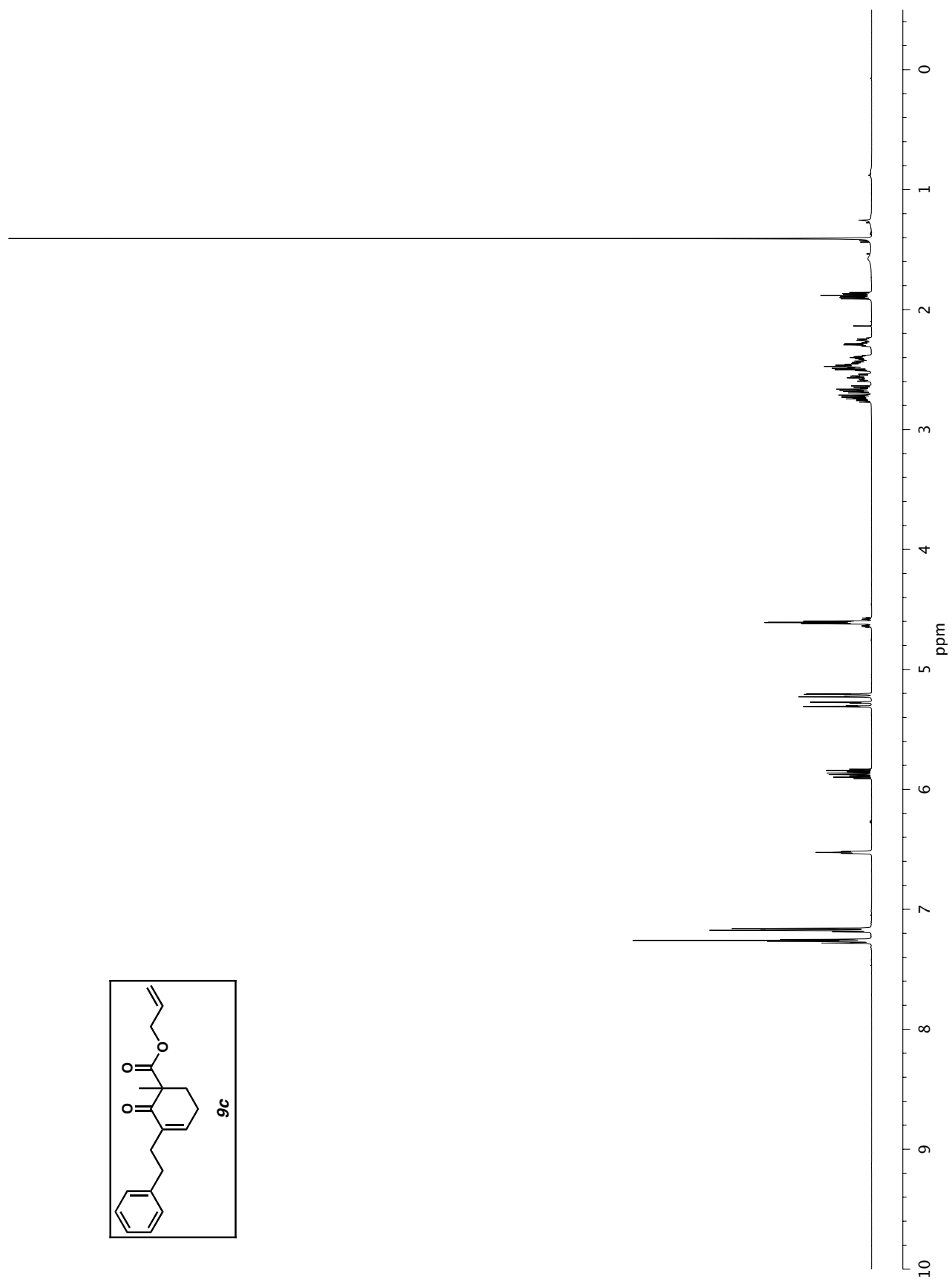


Figure SI-41A. $^1\text{H NMR}$ (500 MHz, CDCl_3) of compound **9c**.

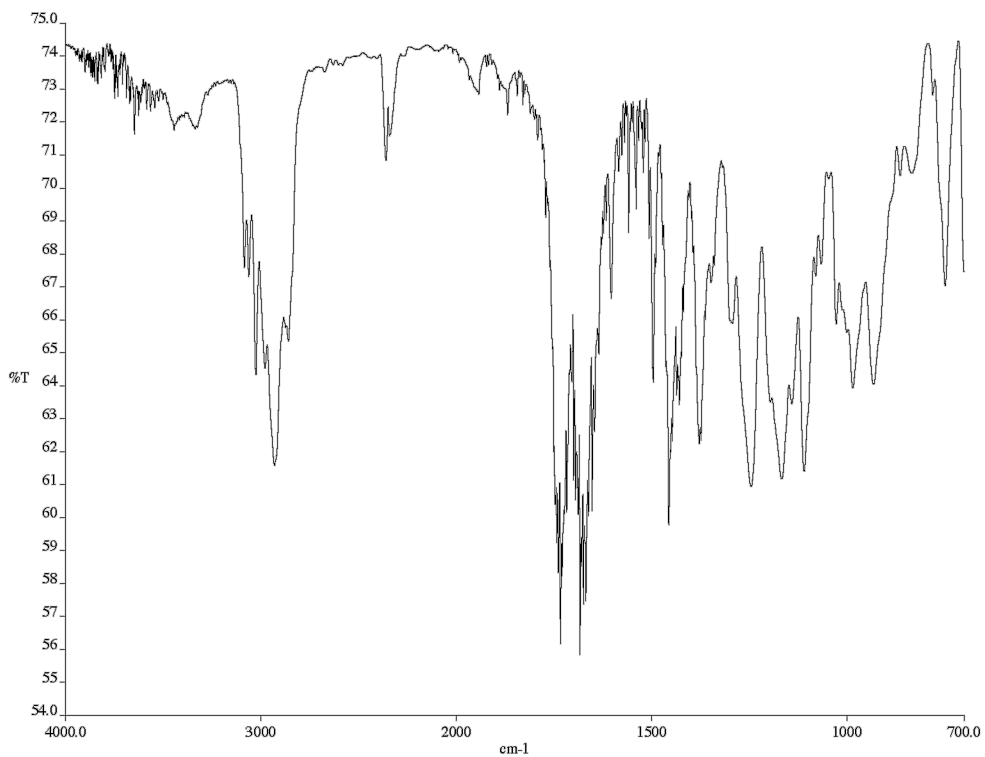


Figure SI-41B. Infrared spectrum (thin film/NaCl) of compound **9c**.

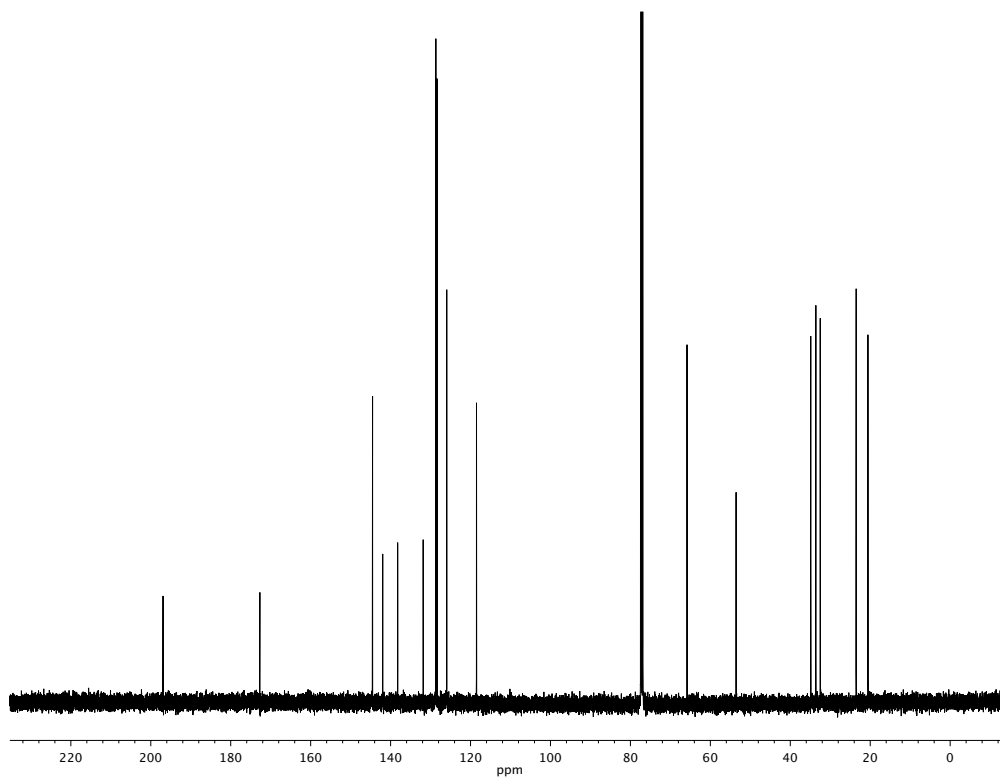
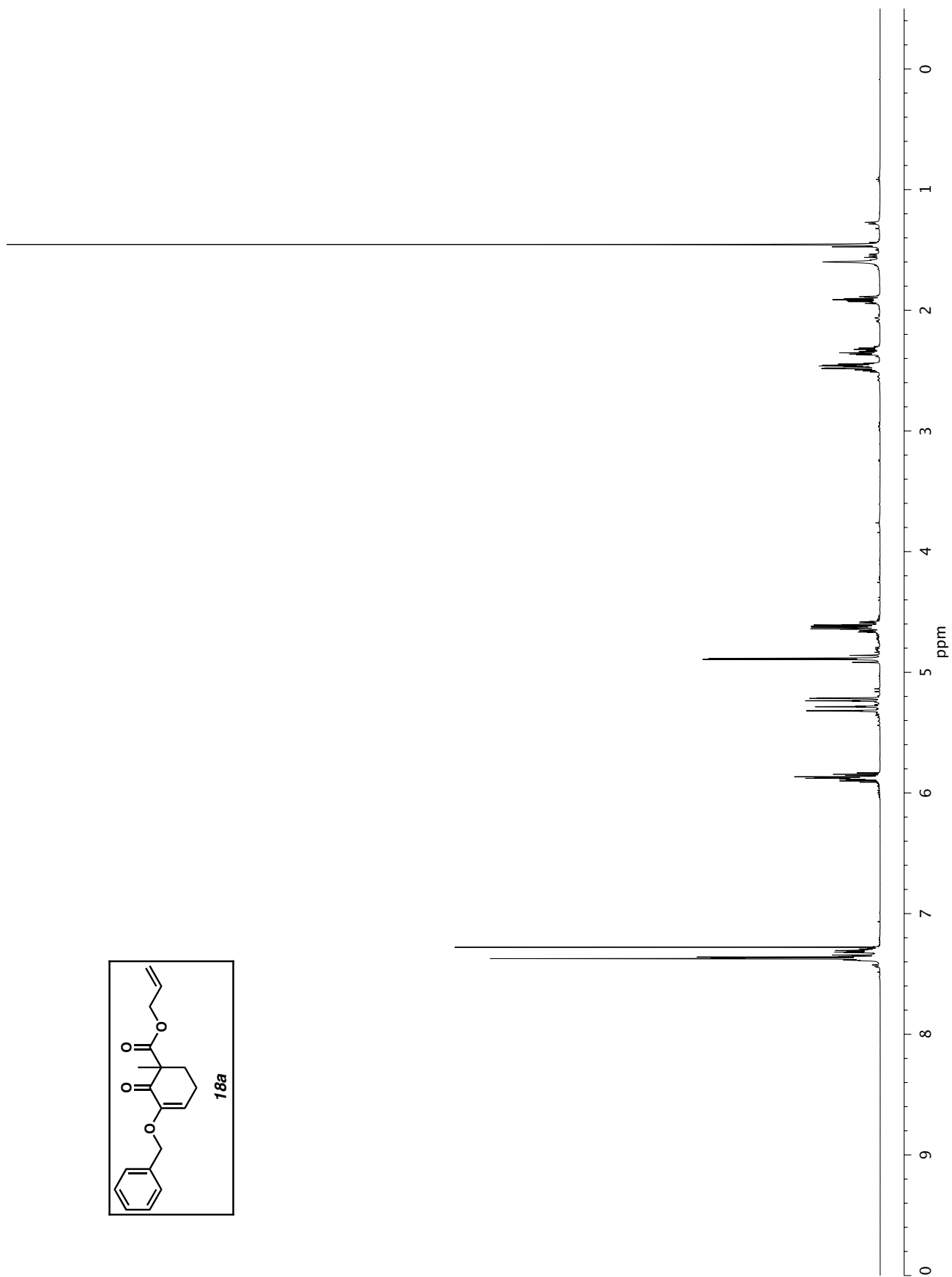


Figure SI-41C. ¹³C NMR (125 MHz, CDCl₃) of compound **9c**.



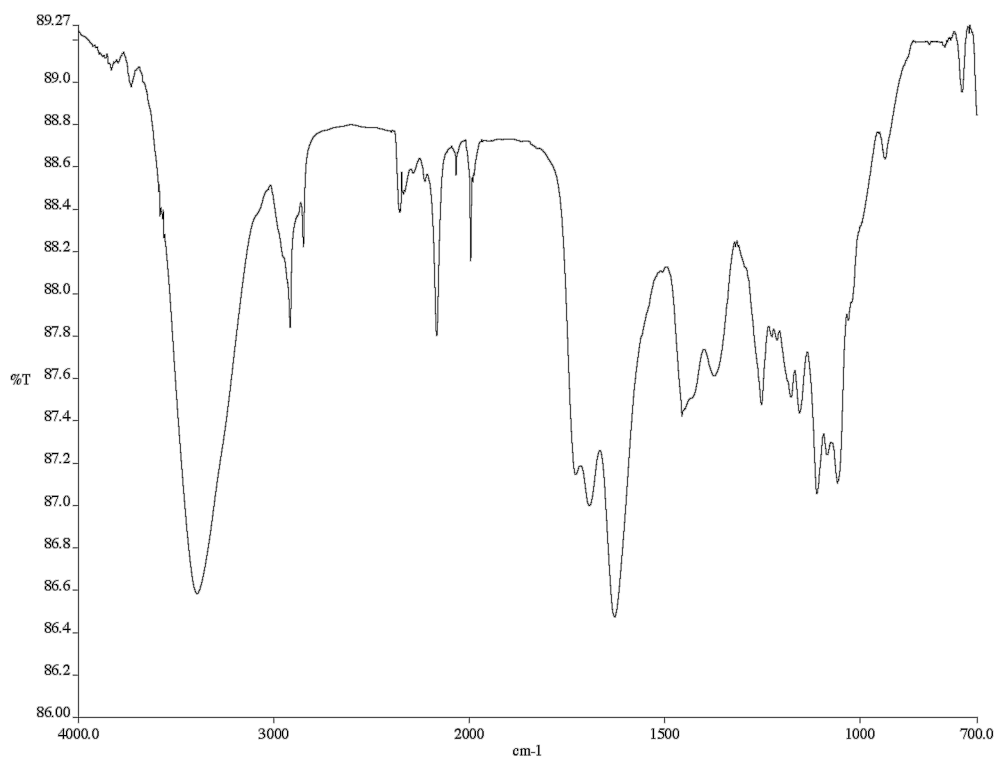


Figure SI-42B. Infrared spectrum (thin film/NaCl) of compound **18a**.

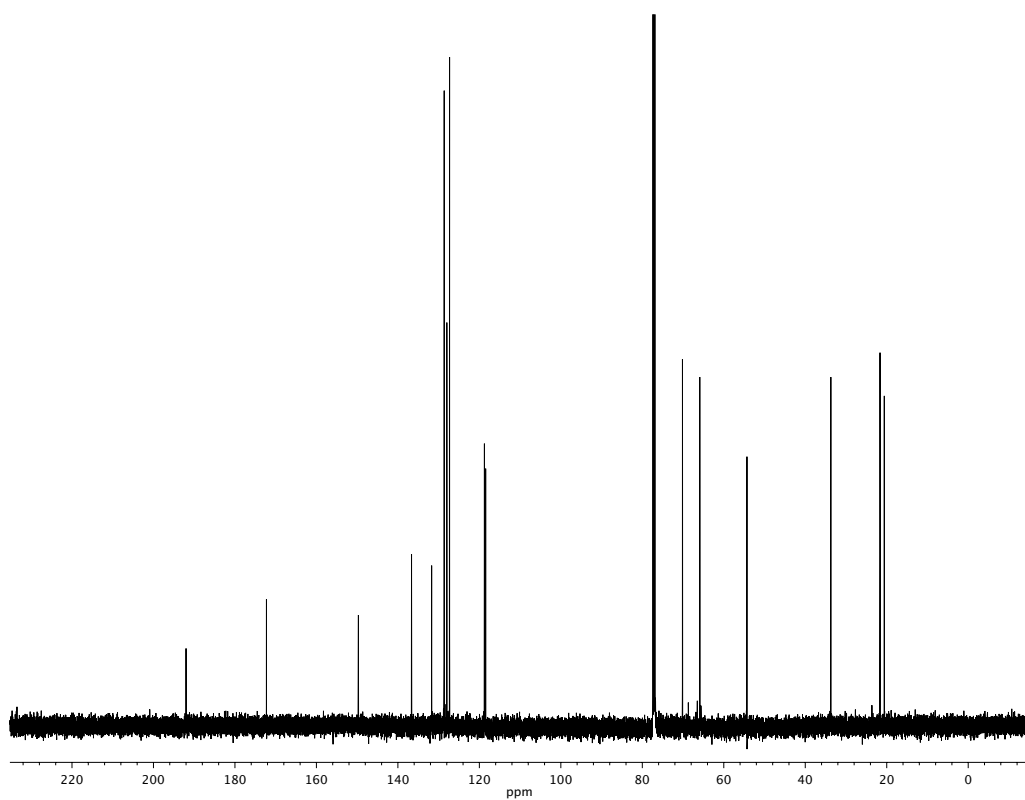


Figure SI-42C. ¹³C NMR (125 MHz, CDCl₃) of compound **18a**.

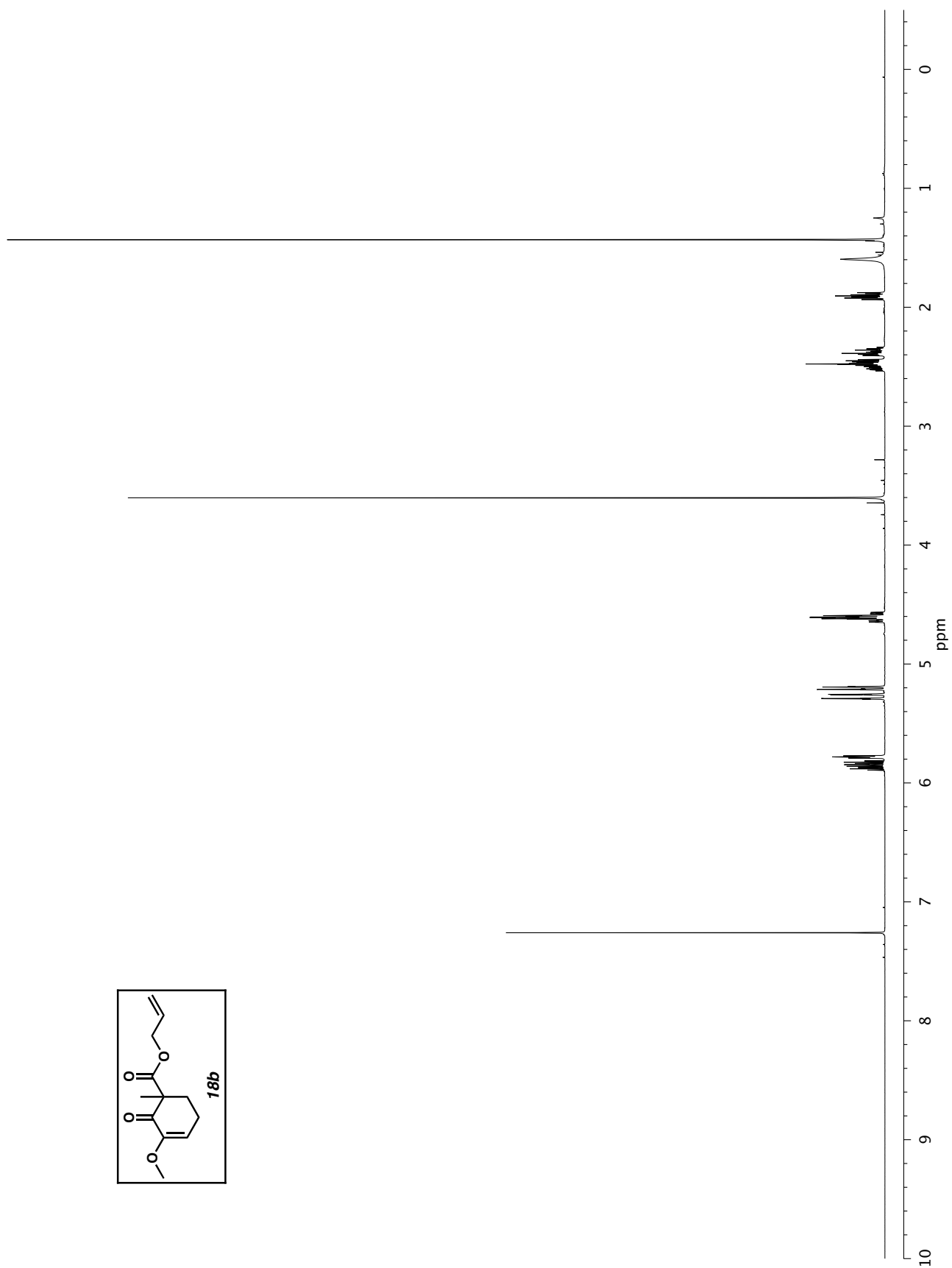


Figure SI-43A. ^1H NMR (500 MHz, CDCl_3) of compound **18b**.

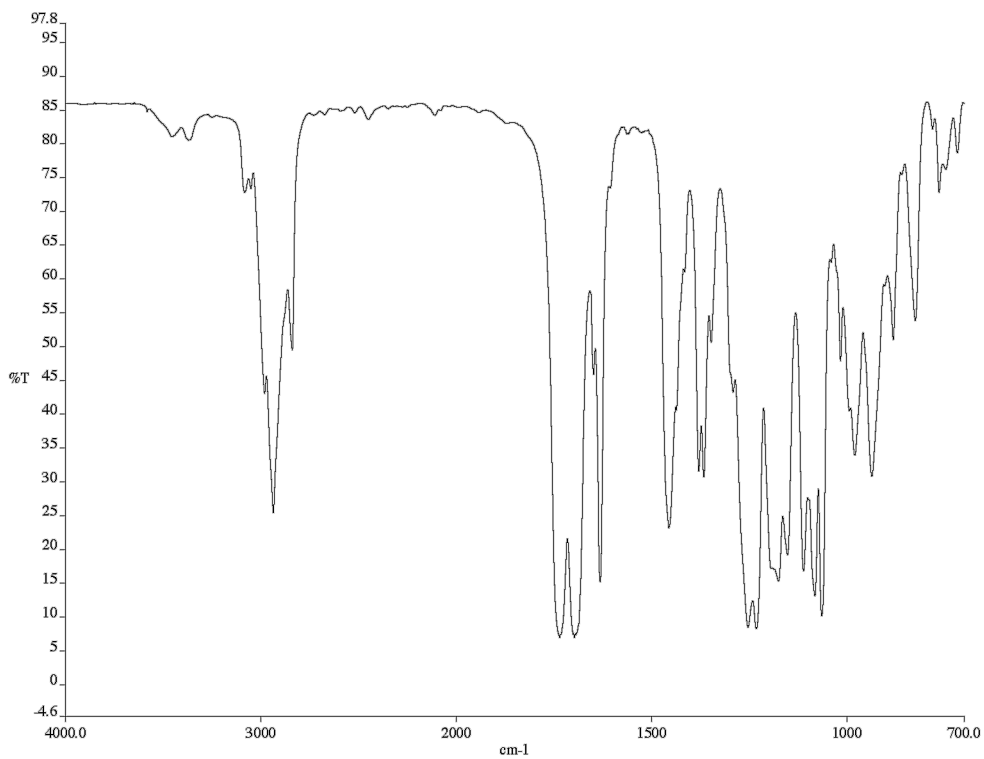


Figure SI-43B. Infrared spectrum (thin film/NaCl) of compound **18b**.

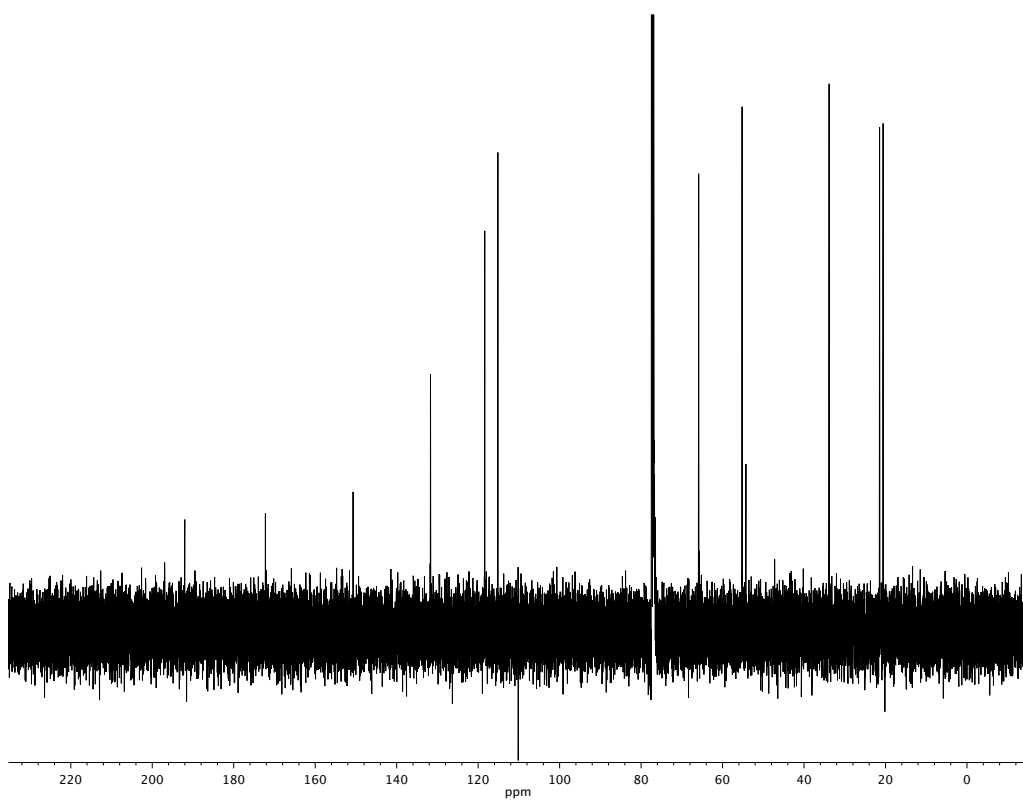
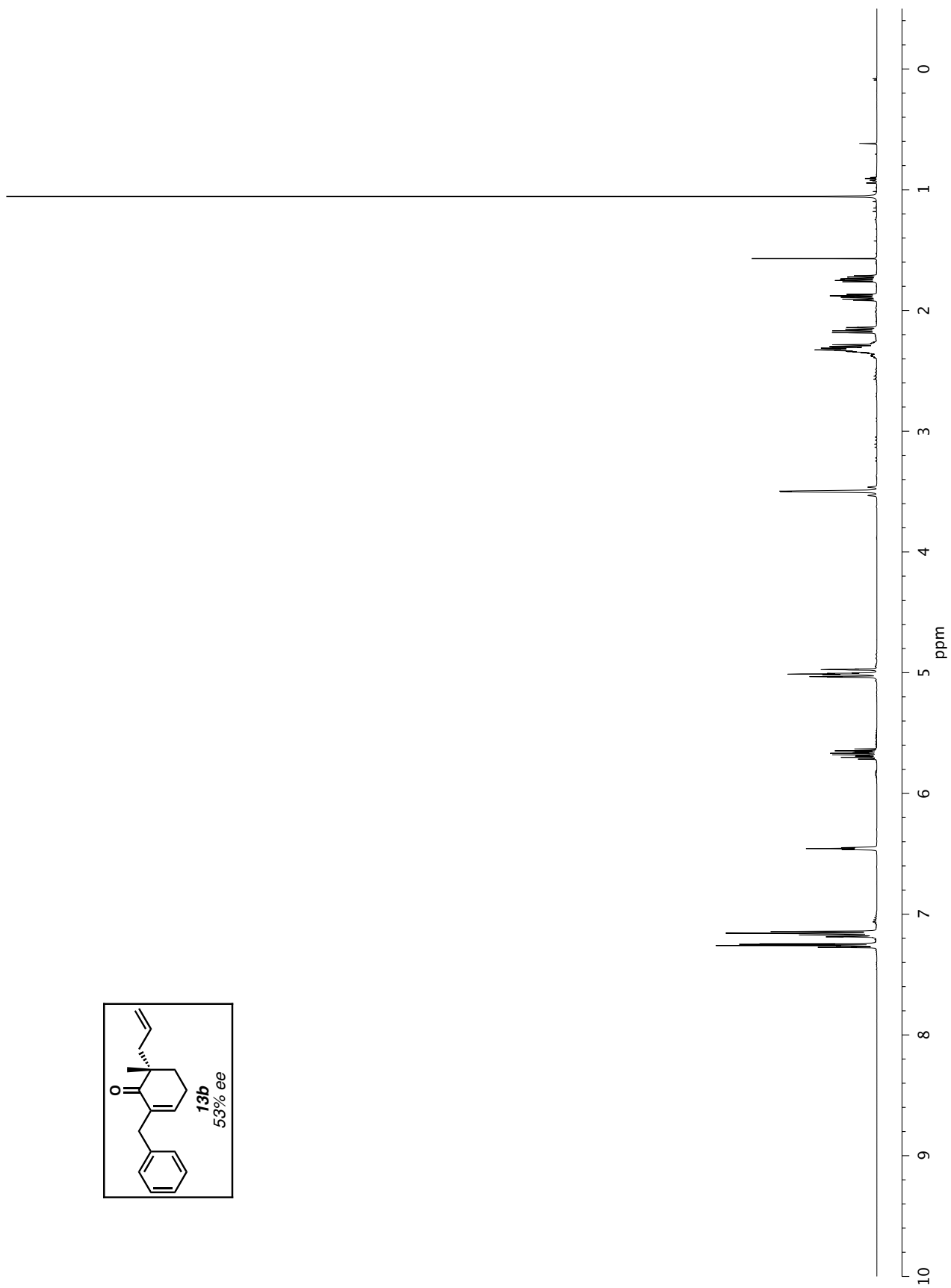


Figure SI-43C. ¹³C NMR (125 MHz, CDCl₃) of compound **18b**.

Figure SI-444. ¹H NMR (500 MHz, CDCl₃) of compound **13b**.

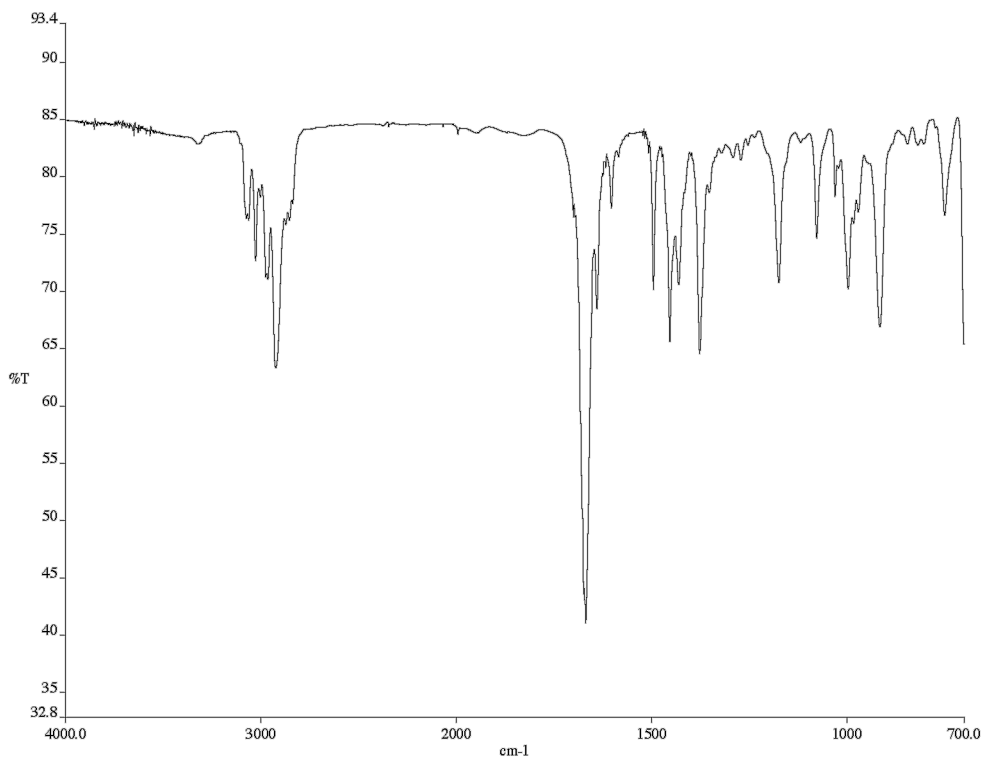


Figure SI-44B. Infrared spectrum (thin film/NaCl) of compound **13b**.

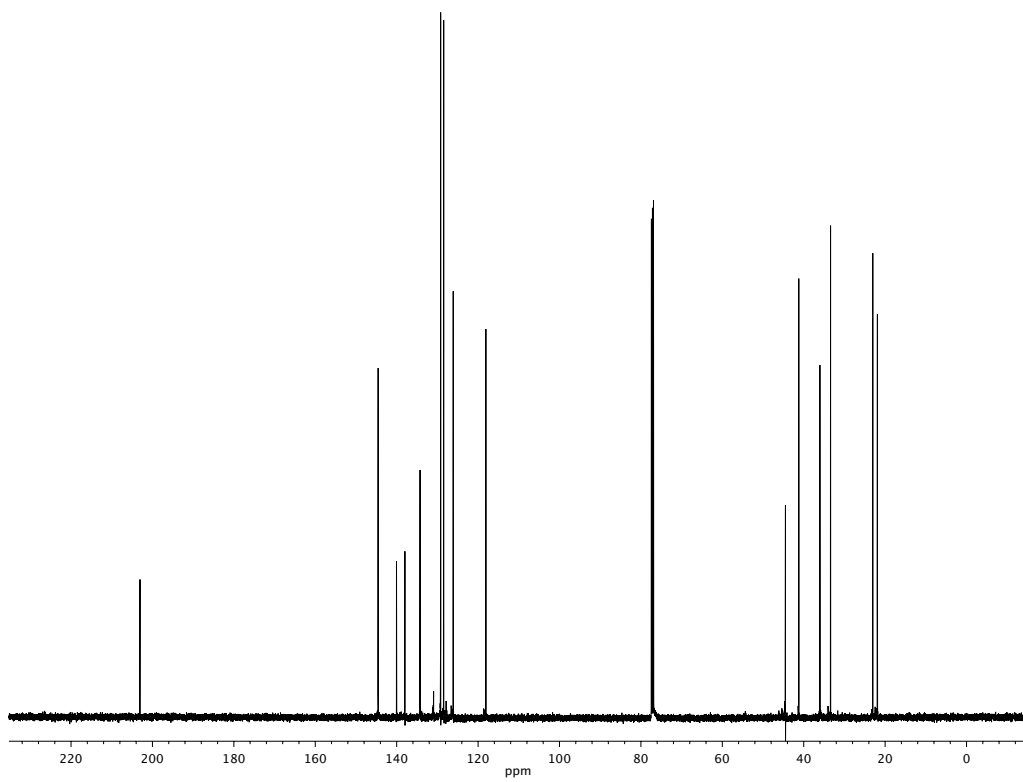


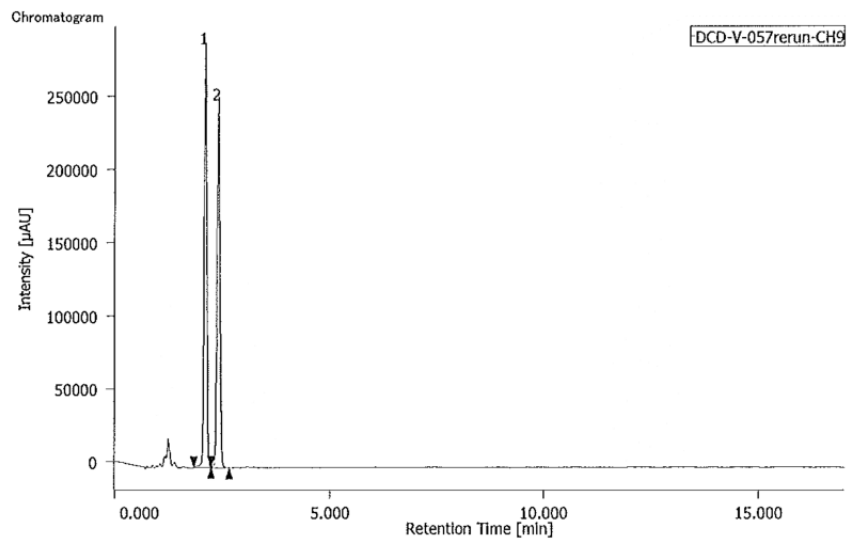
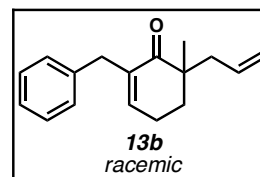
Figure SI-44C. ¹³C NMR (125 MHz, CDCl₃) of compound **13b**.

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

Analytical Report SFC

Chromatogram Information

User Name User
 HPLC System Name Jasco SFC w PDA
 Injection Date 10/29/2012 7:48:40 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



Peak Information

#	Peak Name	CH	IR [min]	Area [μV·sec]	Height [μV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	9	2.107	1166667	287168	49.986	1.853	2.253	0.062	2.716	1.191
2	Unknown	9	2.413	1167308	249093	50.014	2.253	2.667	0.071	N/A	1.102

1/1

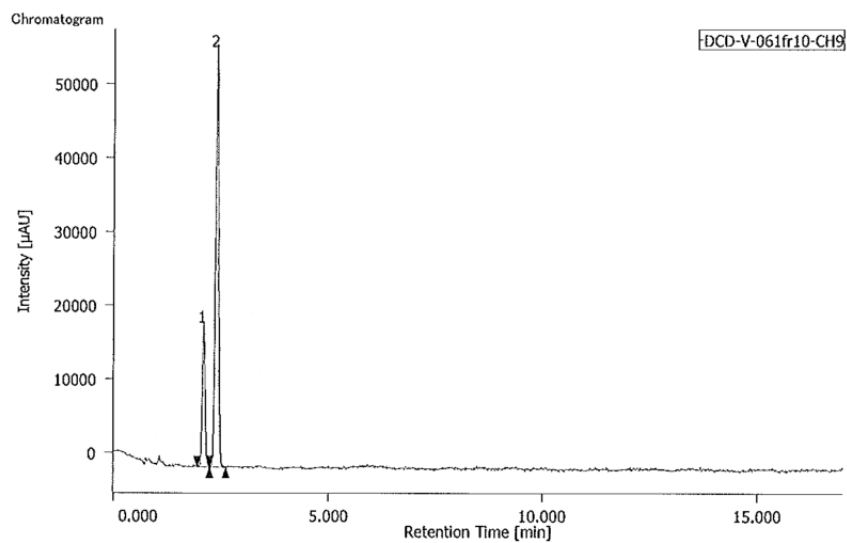
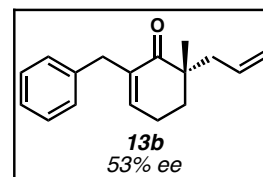
Figure SI-44D. Chiral SFC data of racemic compound **13b**.

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

Analytical Report SFC

Chromatogram Information

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

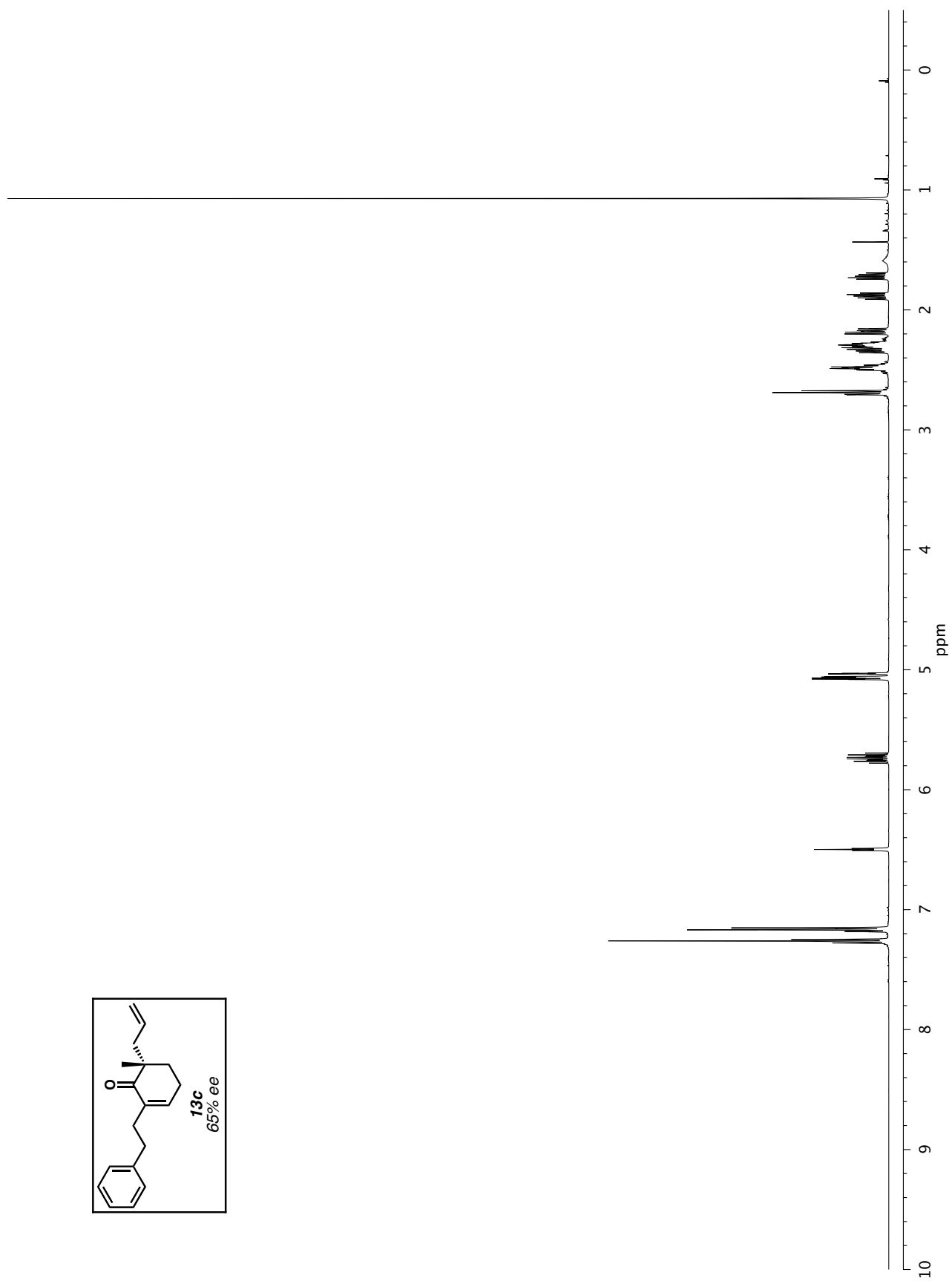


Peak Information

#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	9	2.107	86755	19212	23.374	1.960	2.253	0.069	2.367	1.089
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. ^1H NMR (500 MHz, CDCl_3) of compound **13c**.

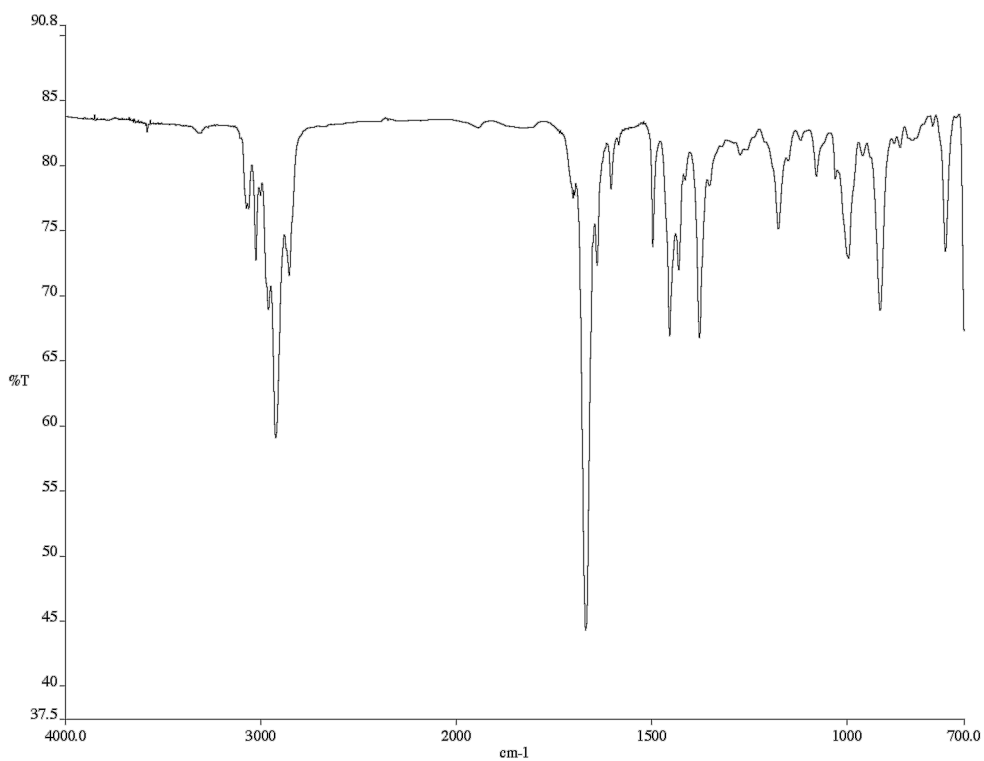


Figure SI-45B. Infrared spectrum (thin film/NaCl) of compound **13c**.

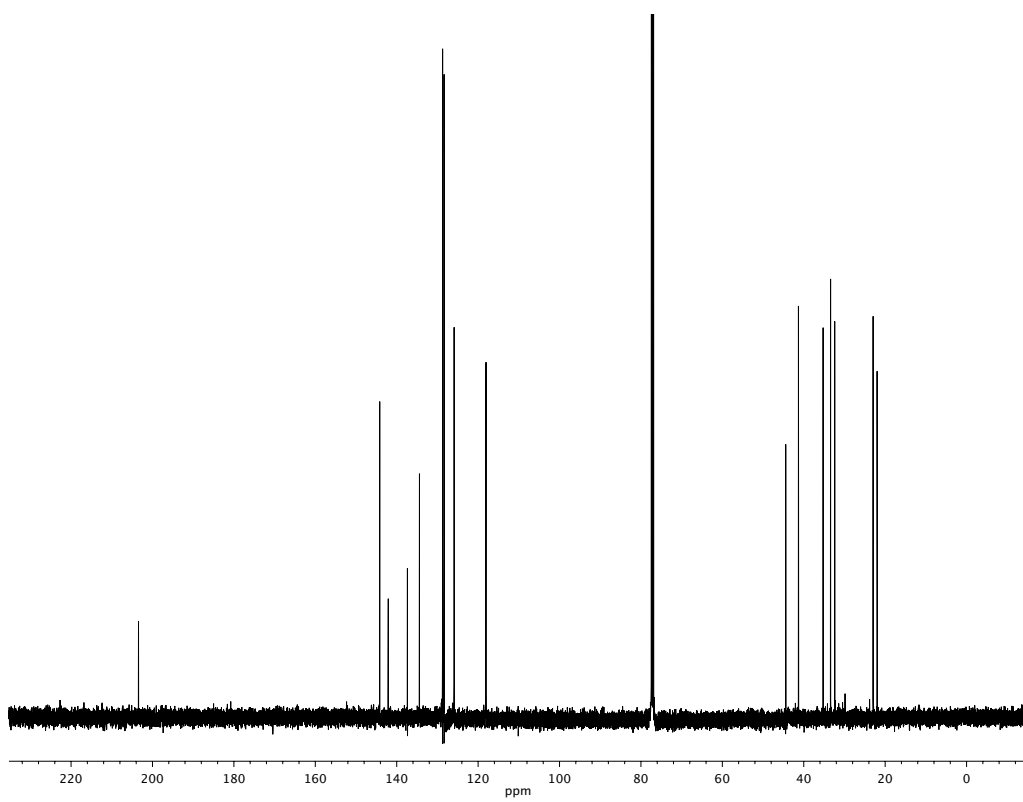


Figure SI-45C. ¹³C NMR (125 MHz, CDCl₃) of compound **13c**.

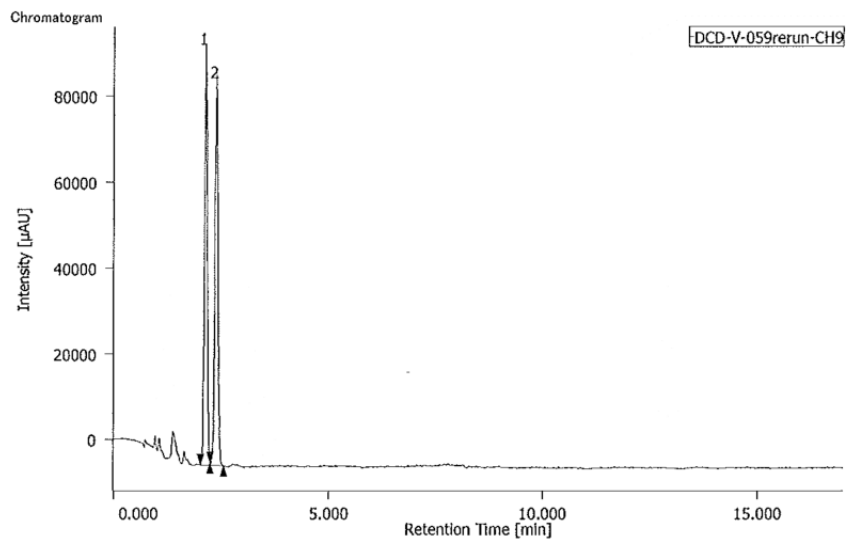
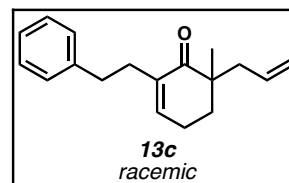
DCD-V-059rerun DCD-V-059rerun 11/8/2012 4:32:48 PM

Analytical Report SFC

Chromatogram Information

User
 HPLC System Name
 Injection Date
 Volume
 Sample #
 Project Name
 Executed Sequence
 Chromatogram Name
 Sample Name
 Acquisition Time
 Acquisition Sequence
 Control Method

User
 Jasco SFC w PDA
 10/29/2012 10:09:51 PM
 5.00 [μL]
 12
 Cal Tech SFC
 DCD-V-059rerun
 DCD-V-059rerun
 17.0 [min]
 DCD-V-059rerun
 Solv 1 Col 3 Isocratic 3B 5ml_min 10MPa 20min



Peak Information

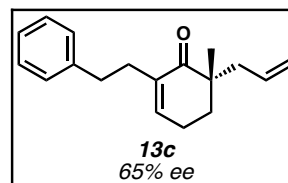
#	Peak Name	CH	TR [min]	Area [μV·sec]	Height [μV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	9	2.133	432536	97121	50.091	2.027	2.253	0.088	2.102	1.223
2	Unknown	9	2.387	430969	89423	49.909	2.253	2.560	0.074	N/A	1.082

1 / 1

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

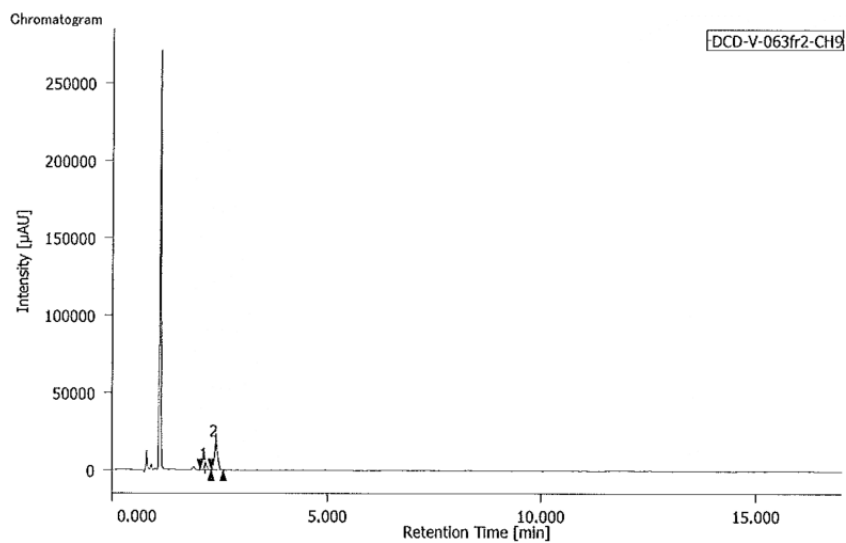
DCD-V-063 DCD-V-063fr2 11/8/2012 4:33:34 PM

Analytical Report SFC



Chromatogram Information

User: Jasco SFC w PDA
 HPLC System Name: 10/28/2012 5:02:04 PM
 Injection Date: 5.00 [μL]
 Volume: 48
 Sample #: Cal Tech SFC
 Project Name: DCD-V-063
 Executed Sequence: DCD-V-063fr2
 Chromatogram Name: Sample Name
 Acquisition Time: 17.0 [min]
 Acquisition Sequence: DCD-V-063
 Control Method: Solv 1 Col 3 Isocratic 3B 5mL_min 10MPa 20min

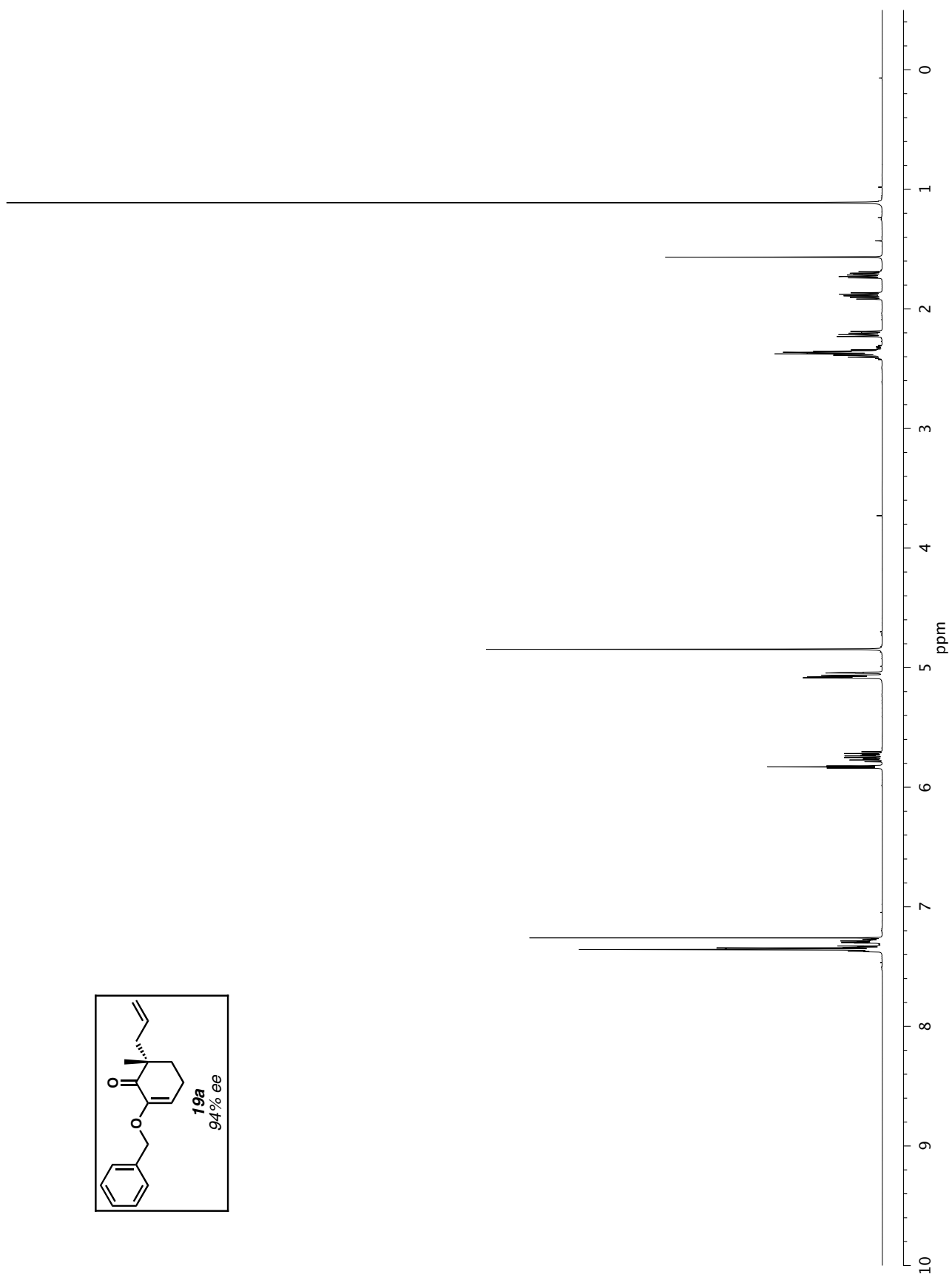


Peak Information

#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Peak Start	Peak End	Peak Width	Resolution	Symmetry Factor
1	Unknown	9	2.173	19981	4792	17.391	2.053	2.307	0.067	2.003	1.284
2	Unknown	9	2.413	94820	19501	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. ¹H NMR (500 MHz, CDCl₃) of compound **19a**.

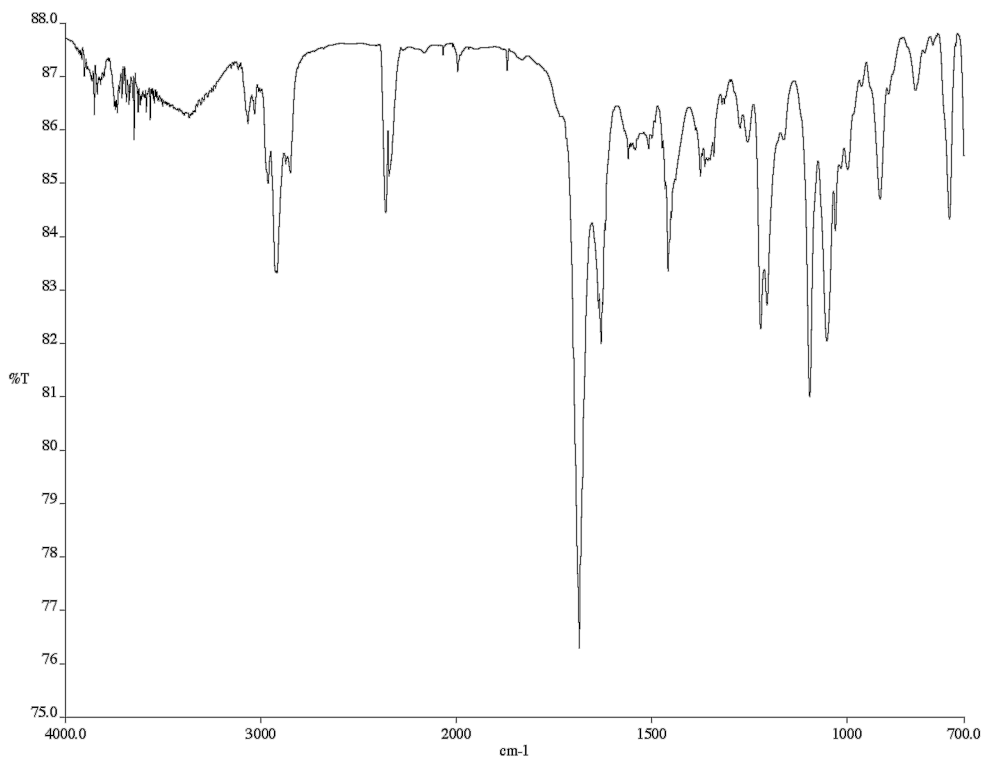


Figure SI-46B. Infrared spectrum (thin film/NaCl) of compound **19a**.

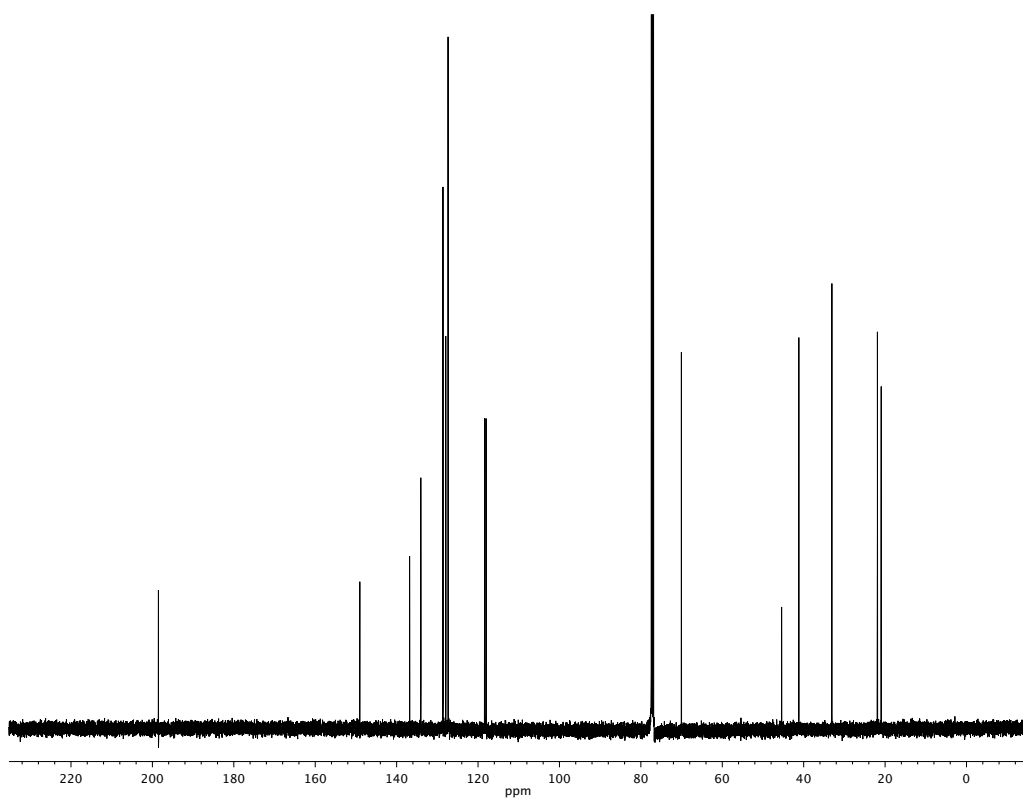
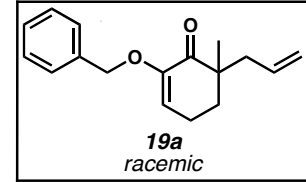


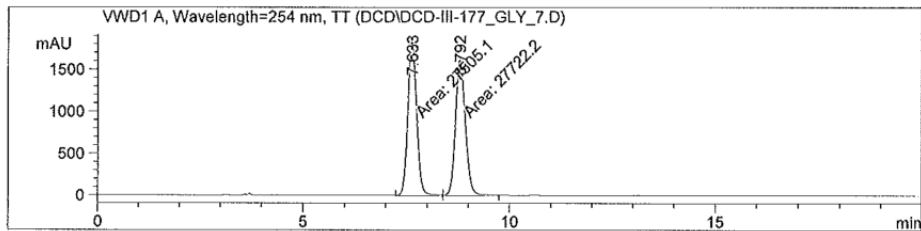
Figure SI-46C. ¹³C NMR (125 MHz, CDCl₃) of compound **19a**.

Data File C:\CHEM32\1\DATA\DCD\DCD-III-177_GLY_7.D
 Sample Name: DCD-III-177_Gly_7



```
=====
Acq. Operator   : DCD                      Seq. Line :    3
Acq. Instrument : HPLC 1                   Location  : Vial 81
Injection Date  : 2/13/2012 5:09:54 PM     Inj       :    1
                                           Inj Volume: 5.0 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\15IPA20_225.M
Last changed   : 2/8/2012 2:32:24 PM by JCH
                (modified after loading)
Method Info    : 15% IPA   20 min  225 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 [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
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
 =====

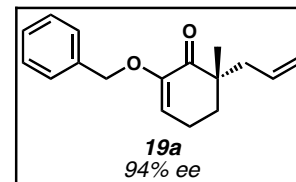
Signal 1: VWD1 A, Wavelength=254 nm, TT

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

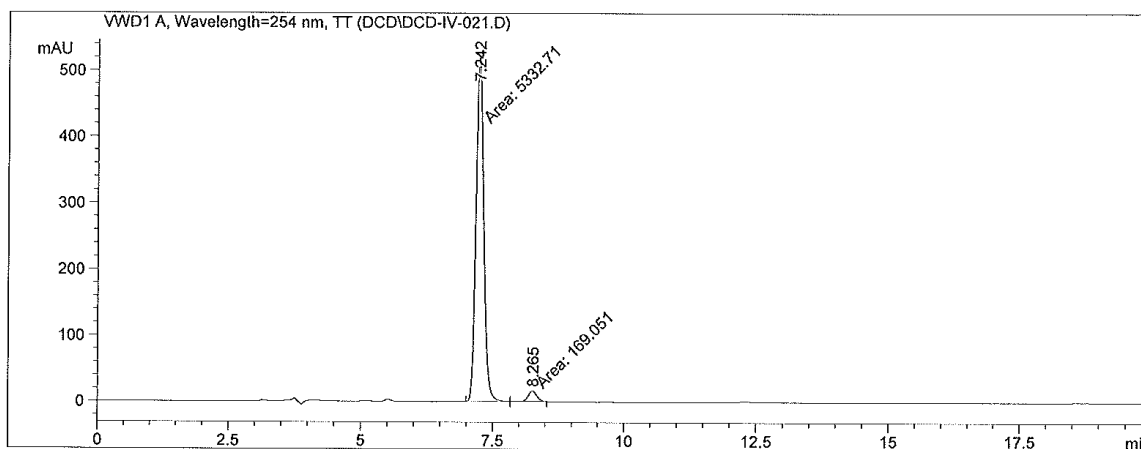
Signal 1: VWD1 A, Wavelength=254 nm, TT

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 [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
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
 =====

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

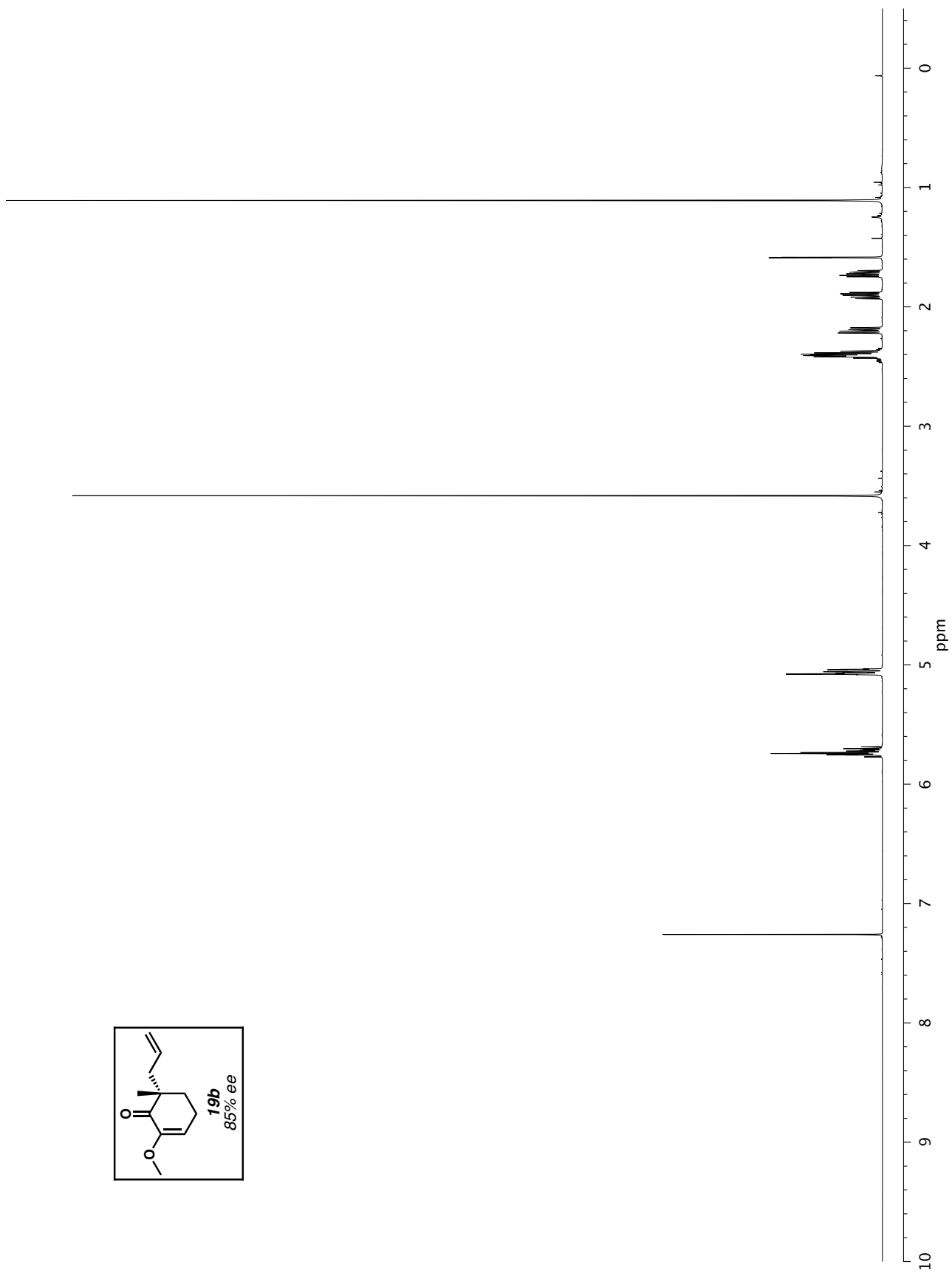


Figure SI-47A. ^1H NMR (500 MHz, CDCl_3) of compound **19b**.

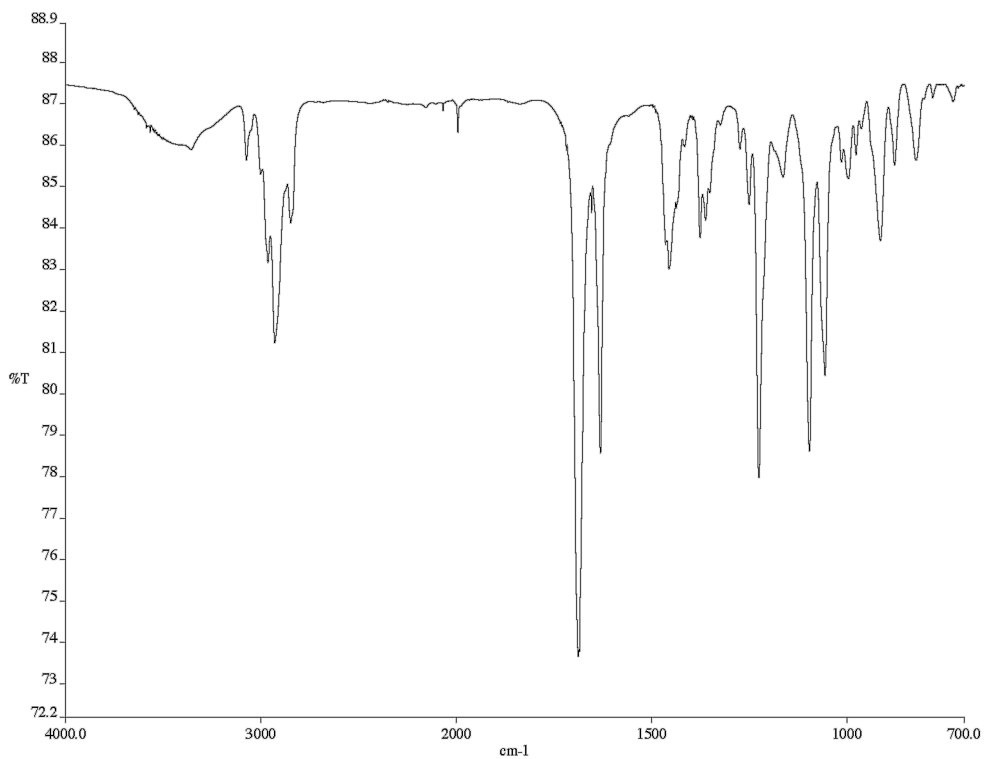


Figure SI-47B. Infrared spectrum (thin film/NaCl) of compound **19b**.

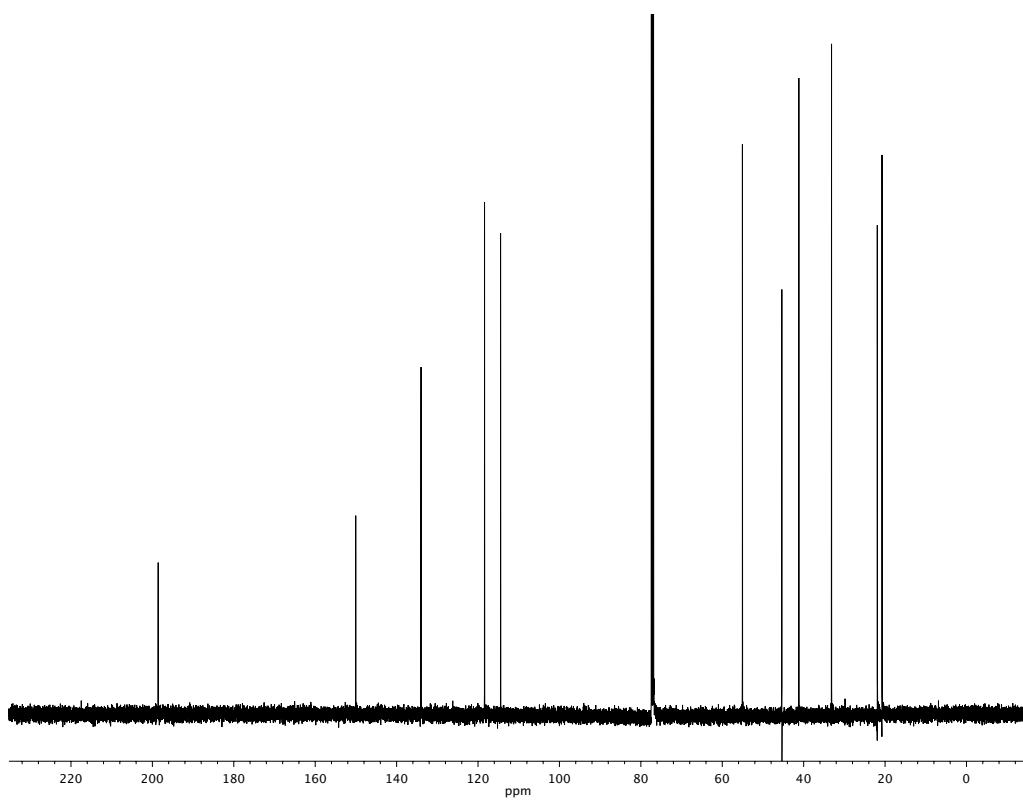
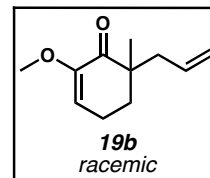


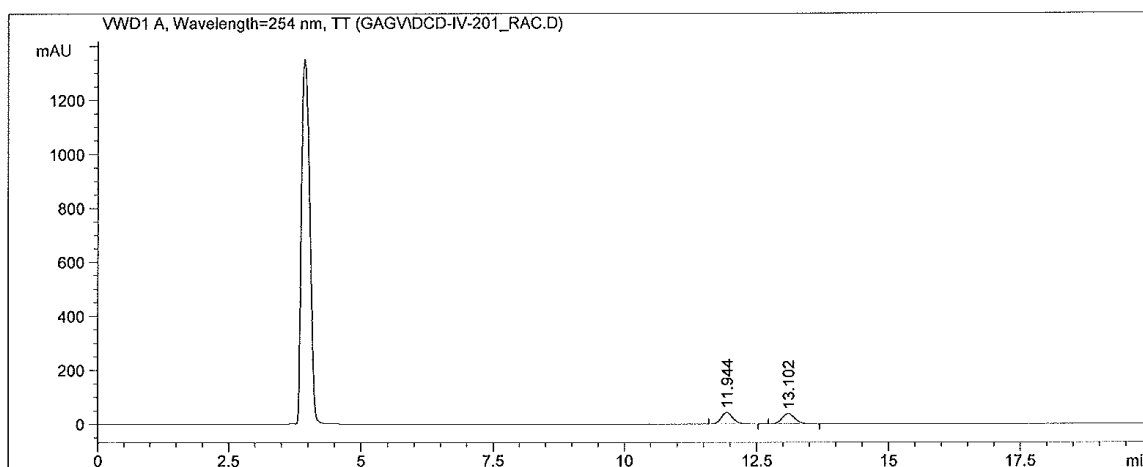
Figure SI-47C. ¹³C NMR (125 MHz, CDCl₃) of compound **19b**.

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

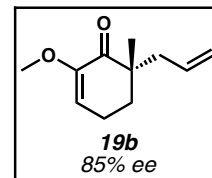
Totals : 1272.20862 80.24419

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

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

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

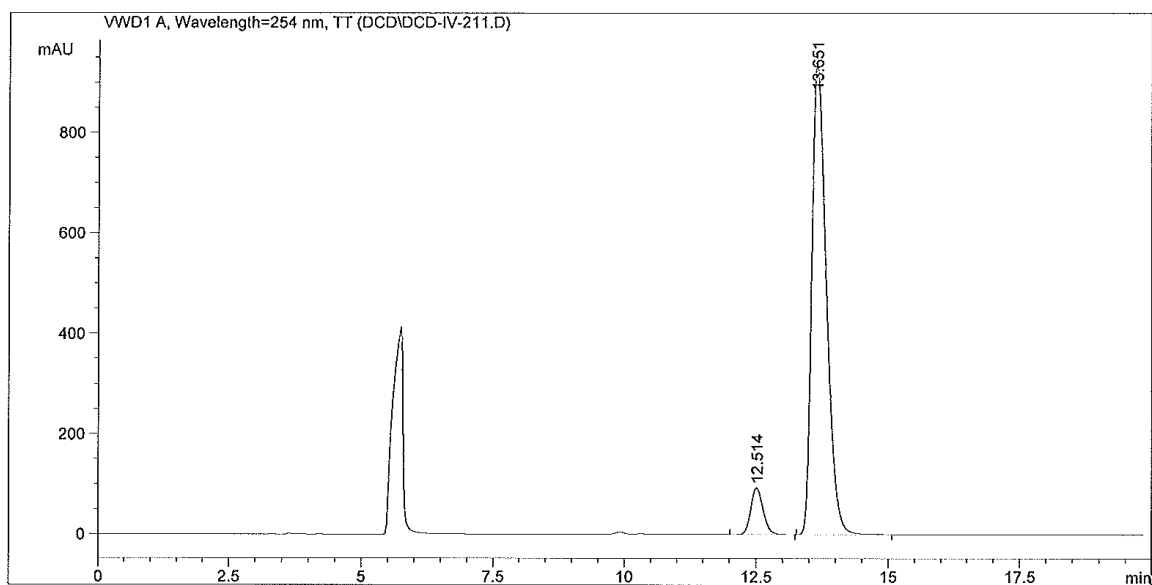
Data File C:\CHEM32\1\DATA\DCD\DCD-IV-211.D
 Sample Name: DCD-IV-211



```

=====
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 [min]	Type	Width [min]	Area mAU*s	Height [mAU]	Area %
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**.