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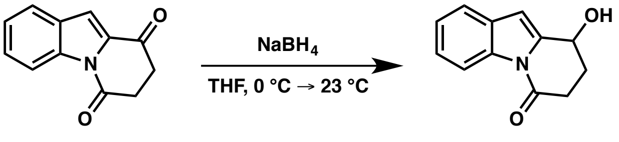
Materials and Methods

Unless stated otherwise, reactions were performed at ambient temperature (23 °C) in flame-dried glassware under an argon atmosphere using dry, deoxygentated solvents (distilled or passed over a column of activated alumina).[1] Commercially available reagents were used as received. Reactions requiring external heat were modulated to the specified temperatures using an IKAmag temperature controller. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 pre-coated plates (250 nm) and visualized by UV fluorescence quenching, potassium permanganate, or *p*-anisaldehyde staining. Silicycle SiliaFlash P60 Academic Silica gel (particle size 40-63 nm) was used for flash chromatography. Potassium (2-benzyloxy)ethyl-trifluoroborate, [2] (*S*)-(CF_3)-*t*-BuPHOX, [3] and tris(4,4'-methoxydibenzylideneacetone)dipalladium(0) [$Pd_2(pmdba)_3$][4] were prepared by known methods. NBS was purchased from Sigma Aldrich, recrystallized from H_2O, and stored in a –25 °C freezer. 2-*tert*-Butoxy-2-oxoethylzinc chloride (0.5 M in Et_2O) was purchased from Rieke Metals and used within three days. Bis(cyclopentadienyl) zirconium chloride hydride was purchased from Strem Chemicals and stored at room temperature in a N_2-filled glovebox. Hydroxylamine-*O*-sulfonic acid was purchased from Sigma Aldrich and stored at –30°C in the glovebox freezer. Triethylamine was distilled from calcium hydride immediately prior to use. MeOH was distilled from magnesium methoxide immediately prior to use. Purified water was obtained using a Barnstead NANOpure Infinity UV/UF system. ^1H and ^{13}C NMR spectra were recorded on a Varian Inova 500 (500 MHz and 126 MHz, respectively) and a Bruker AV III HD spectrometer equipped with a Prodigy liquid nitrogen temperature cryoprobe (400 MHz and 101 MHz, respectively) and are reported in terms of chemical shift relative to $CHCl_3$ (δ 7.26 and 77.16, respectively). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Infrared (IR) spectra were recorded on a Perkin Elmer Paragon 1000 Spectrometer and are reported in frequency of absorption (cm^{-1}). Analytical chiral SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system with Chiralpak AD-H column obtained from Daicel Chemical Industries, Ltd. High resolution mass spectra (HRMS) were obtained from the Caltech Mass Spectral Facility using a JEOL JMS-600H High Resolution Mass Spectrometer in fast atom bombardment (FAB+) or electron ionization (EI+) mode, or from the Caltech Center for Catalysis and Chemical Synthesis using an Agilent 6200 series TOF with an Agilent G1978A Multimode source in mixed (Multimode ESI/APCI) ionization mode. Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm.

List of Abbreviations:

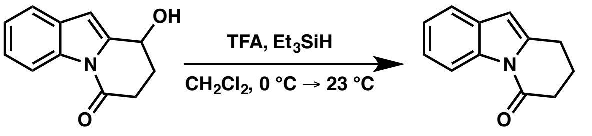
A^{ta}Phos – (di-*tert*-butyl(4-dimethylaminophenyl)phosphine), TBME – *tert*-butyl methyl ether, ee – enantiomeric excess, LHMDS – lithium bis(trimethylsilyl)amide, NBS – *N*–bromosuccinimide, SFC – supercritical fluid chromatography, TFA – trifluoroacetic acid, THF – tetrahydrofuran, TLC – thin-layer chromatography

Experimental Procedures



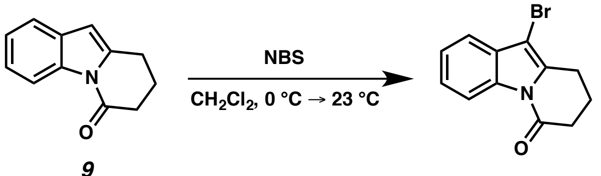
S1 *S2*

9-hydroxy-8,9-dihydropyrido[1,2-*a*]indol-6(7*H*)-one (S2): To a solution of tricycle **S1**[5] (5.92 g, 29.7 mmol, 1.00 equiv) in THF (300 mL) was added $NaBH_4$ (1.24 g, 32.8 mmol, 1.1 equiv) in two equal portions over 10 min at 0°C. The reaction mixture was allowed to warm to 23 °C over the course of 2 h at which point full consumption of starting material was observed by TLC analysis. The reaction was quenched by the addition of saturated aqueous NH_4Cl (100 mL). The biphasic mixture was poured into water (100 mL) and extracted with EtOAc (3 x 100 mL). The combined organic layers were dried over Na_2SO_4, filtered, and stripped onto silica gel. Flash column chromatography (SiO_2, 40% EtOAc in hexanes to 60% EtOAc in hexanes eluent) afforded alcohol **S2** (5.03 g, 84% yield) as a tan amorphous solid: R_f = 0.45 (1:1 EtOAc:hexanes eluent); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46 (dq, *J* = 8.2, 0.9 Hz, 1H), 7.53 (ddd, *J* = 7.7, 1.4, 0.8 Hz, 1H), 7.35 (ddd, *J* = 8.4, 7.3, 1.3 Hz, 1H), 7.30–7.26 (m, 1H), 6.60 (t, *J* = 0.8 Hz, 1H), 5.12 (t, *J* = 4.5 Hz, 1H), 3.19–3.11 (m, 1H), 2.74 (dt, *J* = 17.5, 5.1 Hz, 1H), 2.28–2.22 (m, 2H), 1.96 (br s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 139.8, 135.1, 129.2, 125.5, 124.3, 120.8, 116.8, 106.7, 62.6, 29.8, 29.6; IR (Neat Film, NaCl) 3396, 3059, 2960, 2934, 1704, 1597, 1473, 1453, 1372, 1358, 1321, 1178, 1086, 1052, 1022, 1006, 980, 942, 814, 754 cm^{-1}; HRMS (ESI/APCI) *m/z* calc'd for $C_{12}H_{12}NO_2$ $[M+H]^+$: 202.0863, found 202.0862.



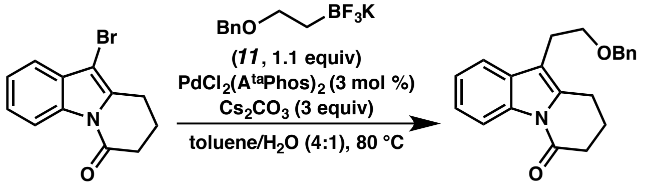
S2 *9*

8,9-dihydropyrido[1,2-*a*]indol-6(7*H*)-one (9): Two flasks were each charged with alcohol **S2** (4.38 g, 21.8 mmol, 1.00 equiv), CH_2Cl_2 (220 mL), and Et_3SiH (7.6 g, 65.4 mmol, 3.0 equiv). Each flask was then cooled to 0 °C in an ice water bath. To each flask was then added TFA (14.9 g, 130.8 mmol, 6.0 equiv) over 15 min at 0°C. The solution turned to dark purple, and was allowed to warm to 23 °C over the course of 2 h, then stirred at 23 °C for an additional 2 h. At this point, full consumption of starting material was observed by TLC analysis. The reaction was quenched by the careful addition of saturated aqueous $NaHCO_3$ at 0 °C until evolution of gas ceased. The two reaction mixtures were combined in a separatory funnel, and extracted with CH_2Cl_2 (3 x 500 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Flash column chromatography (SiO_2, 20% Et_2O in hexanes to 35% Et_2O in hexanes eluent) afforded heteroarene **9** (5.0 g, 61% yield) as a white solid: R_f = 0.25 (3:7 Et_2O:hexanes eluent); physical and spectroscopic data were consistent with those reported in the literature.[6]



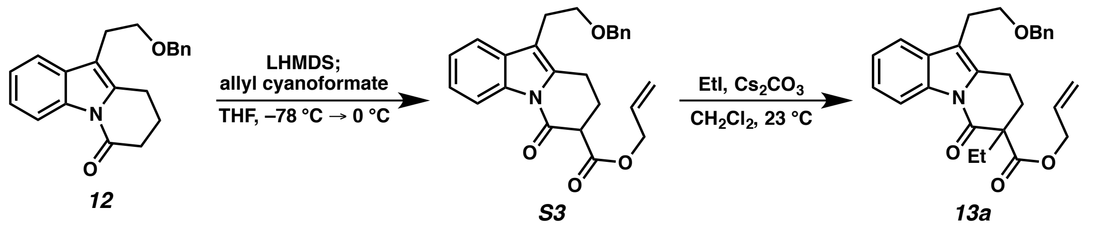
9 *10*

10-bromo-8,9-dihydropyrido[1,2-*a*]indol-6(7*H*)-one (10): To a solution of heteroarene **9** (910 mg, 4.91 mmol, 1.00 equiv) in CH_2Cl_2 (20 mL) was charged NBS (900 mg, 5.05 mmol, 1.02 equiv) in three equal portions over 15 min at 0°C. After 10 min, the cooling bath was removed and the reaction mixture was allowed to warm to 23 °C. Full consumption of starting material was complete within 20 minutes, as observed by TLC analysis. The crude reaction mixture was stripped onto silica gel and purified by flash column chromatography (SiO_2, 25% hexanes in CH_2Cl_2 eluent) to afford heteroaryl bromide **10** (1.24 g, 95% yield) as a white amorphous solid: R_f = 0.45 (3:1 CH_2Cl_2:hexanes eluent); ^1H NMR (500 MHz, $CDCl_3$) δ 8.46–8.42 (m, 1H), 7.49–7.44 (m, 1H), 7.38–7.31 (m, 2H), 2.99 (dd, *J* = 6.9, 5.8 Hz, 2H), 2.84–2.80 (m, 2H), 2.19–2.10 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.9, 135.4, 134.0, 128.9, 125.5, 124.6, 118.5, 116.5, 96.7, 34.4, 22.8, 20.9; IR (Neat Film, NaCl) 3405, 3052, 2959, 2878, 2837, 1907, 1788, 1706, 1593, 1446, 1343, 1258, 1209, 1170, 1142, 1087, 1021, 982, 928, 908, 836, 799, 746, 650, 618 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{12}H_{10}NOBr$ $[M]^+$: 262.9940, found 262.9936.



10 *12*

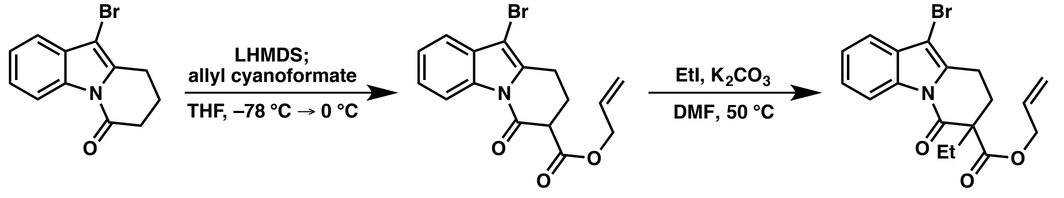
10-(2-(benzyloxy)ethyl)-8,9-dihydropyrido[1,2-*a*]indol-6(7*H*)-one (12): A 15 mL round bottom flask equipped with a magnetic stirring bar and a rubber septum was charged with heteroaryl bromide **10** (200 mg, 0.757 mmol, 1.0 equiv), potassium (2-benzyloxy)ethyltrifluoroborate (**11**) (200 mg, 0.826 mmol, 1.1 equiv), $PdCl_2(A^{ta}phos)_2$ (16 mg, 22.5 μmol, 0.03 equiv), and Cs_2CO_3 (740 mg, 2.27 mmol, 3.0 equiv). The flask was evacuated and backfilled with argon three times. Toluene (3.1 mL) and degassed water (0.7 mL) were added via syringe, and the flask was placed into a preheated 80 °C oil bath with stirring. After stirring for 2 h, the biphasic reaction mixture was cooled to 23 °C, poured into water (15 mL) and extracted with EtOAc (3 x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Flash column chromatography (25% Et_2O in hexanes) afforded heteroarene **12** (207 mg, 86% yield) as a light yellow oil: R_f = 0.3 (3:2 hexanes:Et_2O eluent); physical and spectroscopic data were consistent with those reported in the literature.[7]



allyl 10-(2-(benzyloxy)ethyl)-6-oxo-6,7,8,9-tetrahydropyrido[1,2-*a*]indole-7-carboxylate (S3): A flame-dried round bottom flask was charged with LHMDS (282 mg, 1.69 mmol, 2.0 equiv) and a magnetic stirring bar in a N_2-filled glove box. The flask was sealed, removed from the glovebox, fitted with an argon line, and suspended in a dry ice/acetone bath. THF (4.5 mL) was added slowly to the flask and allowed to stir until the LHMDS had been completely dissolved. A solution of heteroarene **12** (270 mg, 0.845 mmol, 1.0 equiv) in THF (1.1 mL) was added dropwise, and the reaction was allowed to stir for 30 min at –78 °C. Allyl cyanoformate (112 mg, 1.01 mmol, 1.2 equiv) was then added dropwise, and the reaction was allowed to warm slowly to 0 °C over 4 h. Once the cooling bath temperature reached 0 °C, 100 mL of saturated aqueous NH_4Cl was then added slowly and the mixture stirred for 20 min before being extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered and concentrated. The crude residue was purified by flash column chromatography (SiO_2, 50% Et_2O in hexanes) to give tertiary β-amidoester **S3** (256 mg, 75% yield) as a yellow oil: R_f = 0.3 (3:2 hexanes:Et_2O eluent); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48–8.41 (m, 1H), 7.47–7.41 (m, 1H), 7.34–7.25 (m, 7H), 5.93 (ddt, *J* = 17.2, 10.4, 5.7 Hz, 1H), 5.35 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.25 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.75–4.67 (m, 2H), 4.49 (s, 2H), 3.80 (dd, *J* = 8.1, 5.0 Hz, 1H), 3.68 (t, *J* = 6.9 Hz, 2H), 3.06 (ddd, *J* = 16.4, 7.9, 4.5 Hz, 1H), 2.95 (t, *J* = 6.9 Hz, 2H), 2.94–2.87 (m, 1H), 2.46 (dtd, *J* = 13.0, 8.4, 4.5 Hz, 1H), 2.29 (ddt, *J* = 13.0, 7.9, 4.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 165.0, 138.4, 134.9, 133.6, 131.6, 130.5, 128.5, 127.73, 127.65, 124.6, 124.3, 119.1, 118.1, 116.7, 114.6, 73.2, 69.5, 66.4, 51.1, 25.02, 24.98, 20.0; IR (Neat Film, NaCl) 3062, 3032, 2941, 2857, 1737, 1697, 1622, 1454, 1376, 1307, 1258, 1171, 1128, 1094, 1020, 937, 803, 746, 698 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{25}H_{26}NO_4$ $[M+H]^+$: 404.1856, found 404.1867.

allyl 10-(2-(benzyloxy)ethyl)-7-ethyl-6-oxo-6,7,8,9-tetrahydropyrido[1,2-*a*]indole-7-carboxylate (13a): To a solution of β-amidoester **S3** (210 mg, 0.52 mmol, 1.0 equiv) in 3.5 mL of CH_2Cl_2 were added Cs_2CO_3 (678 mg, 2.08 mmol, 4.0 equiv) and EtI (0.25 mL, 3.12 mmol, 6.0 equiv) at 23 °C with stirring. After 18 h, starting material was completely consumed as determined by TLC analysis. Saturated aqueous NH_4Cl (10 mL) was added, followed by extraction with EtOAc (3 x 15 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. Flash column chromatography (SiO_2, 25% Et_2O in hexanes) afforded quaternary β-amidoester **13a** (165 mg, 73% yield) as a faintly yellow oil: R_f = 0.33 (7:3 hexanes:Et_2O eluent); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54–8.45 (m, 1H), 7.48–7.40 (m, 1H), 7.35–7.22 (m, 7H), 5.82 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.22 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.16 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.64–4.59 (m, 2H), 4.50 (s, 2H), 3.67 (t, *J* = 7.0 Hz, 2H), 3.06 (dt, *J* = 16.8, 4.8 Hz, 1H), 2.99–2.81 (m, 3H), 2.46 (dt, *J* = 13.5, 4.8 Hz, 1H), 2.23–2.06 (m, 3H), 1.03 (t, *J* = 7.4 Hz, 3H); ^{13}C

NMR (126 MHz, $CDCl_3$) δ 171.4, 167.8, 138.4, 135.1, 133.9, 131.5, 130.7, 128.5, 127.7, 127.6, 124.4, 124.0, 118.8, 118.0, 116.9, 113.9, 73.2, 69.6, 66.2, 56.6, 28.9, 28.1, 24.9, 19.1, 9.4; IR (Neat Film, NaCl) 3028, 2938, 2857, 1734, 1701, 1620, 1457, 1370, 1328, 1310, 1225, 1189, 1098, 1020, 986, 935, 750, 697 cm^{-1}; HRMS (ESI/APCI) *m/z* calc'd for $C_{27}H_{30}NO_4$ $[M+H]^+$: 432.2169, found 432.2177.

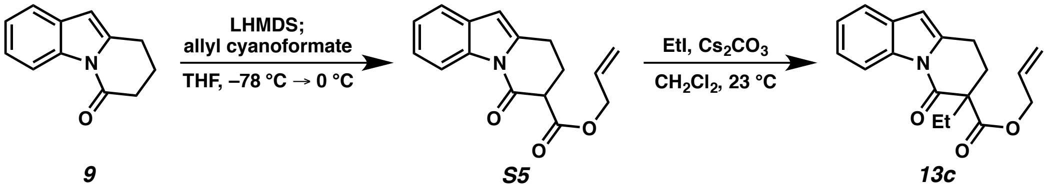


10 ***S4*** ***13b***

allyl 10-bromo-6-oxo-6,7,8,9-tetrahydropyrido[1,2-*a*]indole-7-carboxylate (S4): A flame-dried round bottom flask was charged with LHMDS (2.62 g, 1.69 mmol, 2.0 equiv) and a magnetic stirring bar in a N_2-filled glove box. The flask was sealed, removed from the glovebox, fitted with an argon line, and suspended in a dry ice/acetone bath. THF (48 mL) was added slowly to the flask and allowed to stir until the LHMDS had been completely dissolved. A solution of heteroaryl bromide **10** (2.07 g, 7.83 mmol, 1.0 equiv) in THF (4 mL) was added dropwise, and the reaction was allowed to stir for 30 min at –78 °C. Allyl cyanoformate (1.04 g, 9.36 mmol, 1.2 equiv) was then added dropwise, and the reaction was allowed to warm slowly to 0 °C over 4 h. Once the cooling bath temperature reached 0 °C, saturated aqueous NH_4Cl (200 mL) was then added slowly and the mixture stirred for 20 min before being extracted with EtOAc (3 x 250 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered and concentrated. Flash column chromatography (SiO_2, 10% EtOAc in hexanes) afforded tertiary β-amidoester **S4** (2.67 g, 98% yield) as clear colorless oil: R_f = 0.6 (3:1 hexanes:EtOAc eluent, orange by *p*-anisaldehyde stain); ^1H NMR (500 MHz, $CDCl_3$) δ 8.46–8.41 (m, 1H), 7.50–7.44 (m, 1H), 7.39–7.33 (m, 2H), 5.93 (ddt, *J* = 17.1, 10.4, 5.7 Hz, 1H), 5.35 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.27 (dq, *J* = 10.4, 1.2 Hz, 1H), 4.76–4.67 (m, 2H), 3.85 (dd, *J* = 7.7, 4.9 Hz, 1H), 3.08 (ddd, *J* = 16.9, 8.2, 4.8 Hz, 1H), 2.98 (ddd, *J* = 17.0, 7.9, 4.9 Hz, 1H), 2.59–2.50 (m, 1H), 2.37 (ddt, *J* = 13.4, 8.2, 4.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.6, 164.5, 134.3, 134.1, 131.4, 129.0, 125.8, 125.0, 119.2, 118.7, 116.6, 97.6, 66.6, 50.8, 24.5, 20.6; IR (Neat Film, NaCl) 3059, 2948, 2883, 1742, 1712, 1598, 1450, 1377, 1346, 1307, 1239, 1215, 1173, 1151, 1090, 1022, 986, 924, 753 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{16}H_{15}NO_3Br$ $[M+H]^+$: 348.0230, found 348.0220.

allyl 10-bromo-7-ethyl-6-oxo-6,7,8,9-tetrahydropyrido[1,2-*a*]indole-7-carboxylate (13b): To a solution of β-amidoester **S4** (166 mg, 0.476 mmol, 1.0 equiv) in DMF (1.6 mL) were added K_2CO_3 (263 mg, 1.9 mmol, 4.0 equiv) and EtI (80 μL, 0.95 mmol, 2.0 equiv). The reaction mixture was heated to 50 °C with stirring. After 5 h, starting material was completely consumed as determined by TLC analysis. Saturated aqueous NH_4Cl (5 mL) was added, followed by extraction with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. Flash column chromatography (SiO_2, 10% Et_2O in hexanes) afforded quaternary β-amidoester **13b** (136 mg, 76% yield) as a clear colorless oil: R_f = 0.45 (17:3

hexanes:Et_2O eluent); ^1H NMR (500 MHz, $CDCl_3$) δ 8.51–8.46 (m, 1H), 7.49–7.44 (m, 1H), 7.39–7.32 (m, 2H), 5.84 (ddt, *J* = 17.2, 10.5, 5.6 Hz, 1H), 5.25 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.20 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.69–4.60 (m, 2H), 3.12 (dt, *J* = 17.3, 4.6 Hz, 1H), 2.90 (ddd, *J* = 17.0, 11.7, 4.9 Hz, 1H), 2.53 (ddd, *J* = 13.6, 4.9, 4.3 Hz, 1H), 2.26–2.11 (m, 3H), 1.06 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 167.4, 134.5, 134.4, 131.3, 129.1, 125.6, 124.8, 119.0, 118.6, 116.7, 97.0, 66.4, 56.6, 28.5, 28.1, 19.9, 9.4; IR (Neat Film, NaCl) 3054, 2961, 2878, 1728, 1708, 1594, 1448, 1369, 1325, 1306, 1261, 1219, 1176, 1088, 1025, 920, 798, 748 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{18}H_{19}NO_3Br$ $[M+H]^+$: 376.0543, found 376.0560.

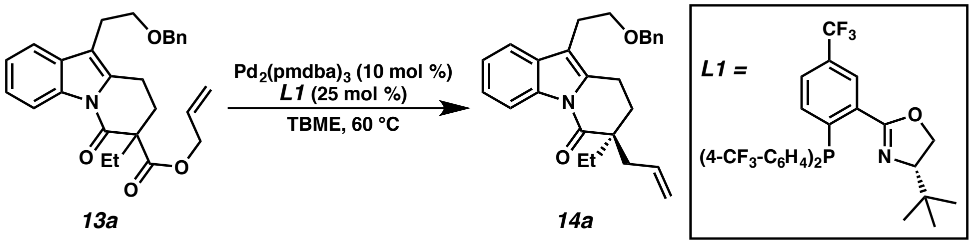


allyl 6-oxo-6,7,8,9-tetrahydropyrido[1,2-*a*]indole-7-carboxylate (S5): A flame-dried round bottom flask was charged with LHMDS (1.8 g, 10.8 mmol, 2.0 equiv) and a magnetic stirring bar in a N_2-filled glove box. The flask was sealed, removed from the glovebox, fitted with an argon line, and suspended in a dry ice/acetone bath. THF (32 mL) was added slowly to the flask and allowed to stir until the LHMDS had been completely dissolved. A solution of heteroarene **9** (1.0 g, 5.4 mmol, 1.0 equiv) in THF (4 mL) was added dropwise, and the reaction was allowed to stir for 30 min at –78 °C. Allyl cyanoformate (720 mg, 6.48 mmol, 1.2 equiv) was then added dropwise, and the reaction mixture was allowed to warm slowly to 0 °C over 4 h. Once the cooling bath temperature reached 0 °C, saturated aqueous NH_4Cl (200 mL) was then added slowly and the mixture stirred for 20 min before being extracted with EtOAc (3 x 200 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered and concentrated. Flash column chromatography (SiO_2, 15% acetone in hexanes) afforded tertiary β-amidoester **S5** (1.32 g, 91% yield) as a faintly yellow oil which solidified to an off-white amorphous solid upon storage at –30 °C: R_f = 0.35 (4:1 hexanes:acetone eluent); ^1H NMR (500 MHz, $CDCl_3$) δ 8.45–8.42 (m, 1H), 7.48–7.44 (m, 1H), 7.32–7.24 (m, 2H), 6.36 (td, *J* = 1.4, 0.7 Hz, 1H), 5.93 (ddt, *J* = 17.2, 10.5, 5.7 Hz, 1H), 5.35 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.26 (dq, *J* = 10.4, 1.2 Hz, 1H), 4.77–4.67 (m, 2H), 3.83 (dd, *J* = 8.0, 5.0 Hz, 1H), 3.11 (dddd, *J* = 16.4, 8.1, 4.5, 1.4 Hz, 1H), 2.98 (dddd, *J* = 16.4, 8.5, 4.6, 1.5 Hz, 1H), 2.55–2.46 (m, 1H), 2.38–2.29 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.0, 165.2, 137.0, 135.1, 131.5, 129.9, 124.51, 124.48, 120.0, 119.1, 116.7, 105.8, 66.5, 51.1, 25.3, 21.8; IR (Neat Film, NaCl) 3085, 3051, 2946, 2850, 1732, 1690, 1577, 1454, 1381, 1356, 1301, 1213, 1177, 1148, 1021, 977, 932, 802, 742 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{16}H_{16}NO_3$ $[M+H]^+$: 270.1130, found 270.1140.

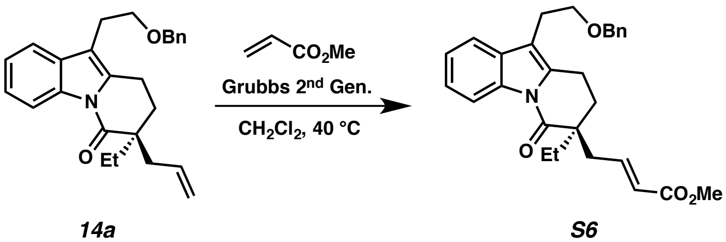
allyl 7-ethyl-6-oxo-6,7,8,9-tetrahydropyrido[1,2-*a*]indole-7-carboxylate (13c): To a solution of β-amidoester **S5** (790 mg, 2.93 mmol, 1.0 equiv) in CH_2Cl_2 (20 mL) were added Cs_2CO_3 (3.82 g, 11.73 mmol, 4.0 equiv) and EtI (1.41 mL, 17.6 mmol, 6.0 equiv) at 23 °C with stirring. After 18 h, starting material was completely consumed as determined by TLC analysis. Saturated aqueous NH_4Cl (100 mL) was added, followed by extraction with EtOAc (3 x 150 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. Flash column chromatography (SiO_2, 15% Et_2O in hexanes) afforded quaternary β-amidoester **13c** (760 mg, 87% yield) as a faintly yellow oil: R_f = 0.3 (17:3 hexanes:Et_2O eluent); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.49 (ddt, *J* = 8.0, 1.3, 0.7 Hz, 1H), 7.48–7.43 (m, 1H), 7.33–7.23 (m, 2H), 6.31 (dt, *J* = 1.8, 0.9 Hz, 1H), 5.84 (ddt, *J* = 17.2, 10.5, 5.6 Hz, 1H), 5.24 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.18 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.65 (dt, *J* = 5.6, 1.4 Hz, 2H), 3.07 (dtd, *J* = 16.8, 4.8, 1.0 Hz, 1H), 2.98 (dddd, *J* = 16.7, 11.7, 4.7, 1.9 Hz, 1H), 2.47 (dt, *J* = 13.5, 4.6 Hz, 1H), 2.26–2.10 (m, 3H), 1.05 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 168.0, 137.3, 135.3, 131.4, 130.1, 124.27, 124.25, 119.9, 118.8, 116.8, 105.2, 66.2, 56.7, 29.2, 28.2, 20.8, 9.4; IR (Neat Film, NaCl) 3395, 3051, 2964, 2880, 1704, 1597, 1446, 1353, 1260, 1101, 1021, 877, 798, 746 cm^{-1}; HRMS (ESI/APCI) *m/z* calc'd for $C_{18}H_{20}NO_3$ $[M+H]^+$: 298.1438, found 298.1435.

General Procedure A: Pd-Catalyzed Allylic Alkylation

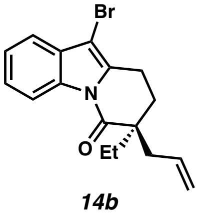
Please note that the absolute configuration of **14a** and **14c** have been inferred from previous studies.[8] The absolute configuration of **14b** was assigned by conversion to (–)-goniomitine [(–)-**1**].



(*S*)-7-allyl-10-(2-(benzyloxy)ethyl)-7-ethyl-8,9-dihydropyrido[1,2-*a*]indol-6(7*H*)-one (14a): An oven-dried 20 mL scintillation vial was charged with $Pd_2(pmdba)_3$ (14 mg, 12.7 mmol, 0.1 equiv), (*S*)-$(CF_3)_3$-*t*-BuPHOX (**L1**, 18.8 mg, 31.8 mmol, 0.25 equiv), and a magnetic stirring bar in a N_2-filled glove box. The vial was then charged with TBME (3.2 mL) and stirred at 23 °C for 30 minutes, generating a dark purple solution. To the preformed catalyst solution was added a solution of **13a** (55 mg, 0.127 mmol, 1.0 equiv) in TBME (0.64 mL). The vial was sealed, removed from the glovebox, and placed in a preheated 60 °C heating block with stirring. Full consumption of starting material was achieved after 24 h, as determined by TLC analysis. The crude reaction mixture was stripped onto silica gel, and purified by flash column chromatography (SiO_2, 5% Et_2O in hexanes) to afford α-quaternary lactam **14a** (29 mg, 59% yield) as a faintly yellow oil: R_f = 0.33 (17:3 hexanes:Et_2O eluent); 89% *ee*,[9] $[\alpha]_D^{25}$ –29.5 (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53–8.46 (m, 1H), 7.47–7.42 (m, 1H), 7.34–7.23 (m, 7H), 5.87–5.74 (m, 1H), 5.14–5.10 (m, 1H), 5.09 (s, 1H), 4.50 (s, 2H), 3.69 (t, *J* = 7.0 Hz, 2H), 3.00–2.93 (m, 4H), 2.62 (dd, *J* = 14.0, 7.0 Hz, 1H), 2.38 (dd, *J* = 13.8, 7.8 Hz, 1H), 2.00–1.93 (m, 2H), 1.84 (dq, *J* = 14.8, 7.5 Hz, 1H), 1.72 (dq, *J* = 14.5, 7.4 Hz, 1H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 138.5, 135.1, 134.4, 133.8, 130.7, 128.5, 127.71, 127.66, 124.1, 123.7, 118.8, 117.9, 116.8, 113.2, 73.2, 69.7, 46.6, 40.0, 28.6, 28.4, 24.9, 18.1, 8.5; IR (Neat Film, NaCl) 3066, 3032, 2930, 2856, 1694, 1619, 1455, 1366, 1309, 1260, 1189, 1100, 1073, 1020, 916, 801, 750, 696 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{26}H_{30}NO_2$ [M+H]$^+$: 388.2271, found 388.2269.



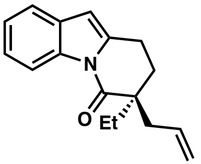
methyl (*S*,*E*)-4-(10-(2-(benzyloxy)ethyl)-7-ethyl-6-oxo-6,7,8,9-tetrahydropyrido[1,2-*a*]indol-7-yl)but-2-enoate (S6): To a solution of terminal olefin **14a** (11 mg, 28 μmol, 1.0 equiv) and methyl acrylate (25 mg, 280 μmol, 10 equiv) in CH_2Cl_2 (0.6 mL) was added Grubb's second generation catalyst (1.2 mg, 1.4 μmol, 0.05 equiv) at 23 °C. The reaction was sealed and placed in a preheated 40 °C heating block with stirring. After 3 h, complete consumption of starting material was observed by TLC analysis. Flash column chromatography (SiO_2, 35% Et_2O in hexanes) afforded α,β-unsaturated ester **S6** (3.8 mg, 30% yield) as a clear colorless oil: R_f = 0.2 (7:3 hexanes:Et_2O eluent); 89% *ee*, $[\alpha]_D^{25}$ –64.4 (*c* 0.11, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.50–8.45 (m, 1H), 7.47–7.42 (m, 1H), 7.34–7.22 (m, 7H), 6.95 (ddd, *J* = 15.5, 8.2, 7.1 Hz, 1H), 5.94–5.89 (m, 1H), 4.50 (s, 2H), 3.71 (s, 3H), 3.69 (t, *J* = 7.2 Hz, 2H), 3.00–2.92 (m, 4H), 2.79 (ddd, *J* = 14.2, 7.1, 1.6 Hz, 1H), 2.52 (ddd, *J* = 14.2, 8.3, 1.3 Hz, 1H), 1.96 (dd, *J* = 7.3, 6.0 Hz, 2H), 1.78 (qd, *J* = 7.4, 4.6 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 166.6, 144.6, 138.4, 135.0, 133.9, 130.7, 128.5, 127.73, 127.67, 124.6, 124.3, 123.9, 118.0, 116.8, 113.7, 73.2, 69.6, 51.7, 46.7, 38.0, 29.0, 28.4, 24.9, 18.1, 8.5; IR (Neat Film, NaCl) 3028, 2923, 2854, 1722, 1693, 1620, 1455, 1434, 1371, 1312, 1271, 1187, 1101, 1074, 1021, 751, 697 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{28}H_{31}NO_4$ [M]$^+$: 445.2248, found 445.2246; SFC conditions: 8% *i*-PrOH, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 40.93, minor = 44.73.



14b

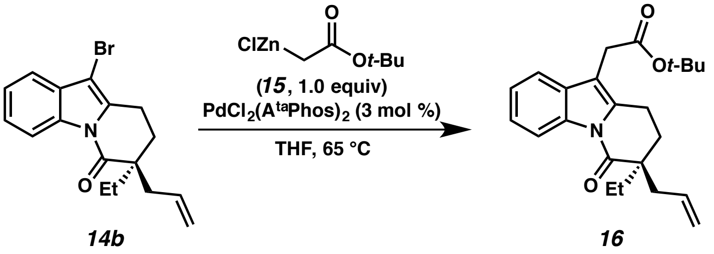
(*S*)-7-allyl-10-bromo-7-ethyl-8,9-dihydropyrido[1,2-*a*]indol-6(7*H*)-one (14b): The reaction was conducted according to general procedure A. α-Quaternary β-amidoester **13b** (386 mg, 1.02 mmol, 1.0 equiv); $Pd_2(pmdba)_3$ (56 mg, 51 μmol, 0.05 equiv); (*S*)-$(CF_3)_3$-*t*-BuPHOX (**L1**, 76 mg, 0.128 mmol, 0.125 equiv); TBME (31 mL). The reaction mixture was stirred for 8 h at 60 °C. Flash column chromatography (SiO_2, 40% CH_2Cl_2 in hexanes) afforded α-quaternary lactam **14b** (274 mg, 83% yield) as a clear colorless oil: R_f = 0.33 (2:1 hexanes:CH_2Cl_2 eluent); 96% *ee*, $[\alpha]_D^{25}$ –36.0 (*c* 1.26, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.50–8.47 (m, 1H), 7.49–7.45 (m, 1H), 7.37–7.31 (m, 2H), 5.81

(dddd, J = 16.6, 10.5, 7.7, 6.9 Hz, 1H), 5.16–5.14 (m, 1H), 5.12 (t, J = 1.2 Hz, 1H), 3.08–2.94 (m, 2H), 2.63 (ddt, J = 14.0, 7.0, 1.3 Hz, 1H), 2.40 (ddt, J = 14.0, 7.8, 1.1 Hz, 1H), 2.10–1.99 (m, 2H), 1.85 (dq, J = 14.0, 7.5 Hz, 1H), 1.81–1.69 (m, 1H), 0.97 (t, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 135.0, 134.3, 133.4, 129.2, 125.3, 124.4, 119.1, 118.4, 116.7, 96.3, 46.7, 39.8, 28.4, 28.2, 18.9, 8.5; IR (Neat Film, NaCl) 3075, 2971, 2939, 1704, 1639, 1594, 1449, 1367, 1348, 1307, 1179, 1151, 1057, 1025, 922, 751 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{17}H_{18}NOBr$ $[M]^+$: 331.0566, found 331.0566; SFC conditions: 2% MeOH, 3 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 11.87, minor = 11.11.

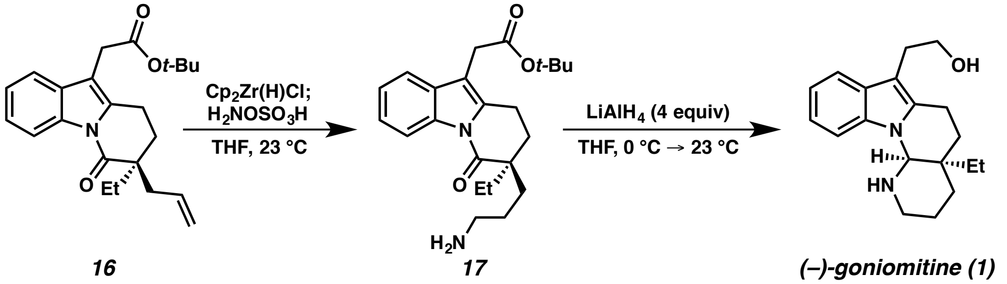


14c

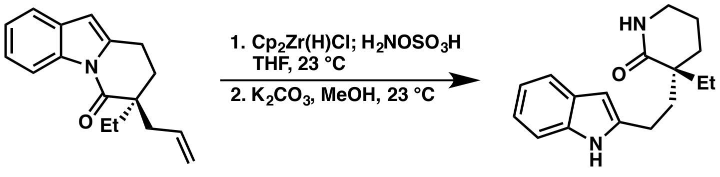
(*S*)-7-allyl-7-ethyl-8,9-dihydropyrido[1,2-*a*]indol-6(7*H*)-one (14c): The reaction was conducted according to general procedure A. α-Quaternary β-amidoester **13c** (730 mg, 2.45 mmol, 1.0 equiv); $Pd_2(pmdba)_3$ (134 mg, 0.12 mmol, 0.05 equiv); (*S*)-$(CF_3)_3$-*t*-BuPHOX (**L1**, 181 mg, 0.31 mmol, 0.125 equiv); TBME (74 mL). The reaction mixture was stirred for 24 h. Flash column chromatography (SiO_2, 5% Et_2O in hexanes) afforded α-quaternary lactam **14c** (410 mg, 71% yield) as a clear colorless oil: R_f = 0.6 (17:3 hexanes:Et_2O eluent); 94% *ee*, $[\alpha]_D^{25}$ –69.7 (*c* 2.09, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52–8.45 (m, 1H), 7.48–7.43 (m, 1H), 7.31–7.20 (m, 2H), 6.29 (td, J = 1.5, 0.8 Hz, 1H), 5.82 (dddd, J = 17.0, 10.2, 7.7, 6.9 Hz, 1H), 5.16–5.11 (m, 1H), 5.14–5.07 (m, 1H), 3.04 (tt, J = 6.3, 1.4 Hz, 2H), 2.64 (ddt, J = 14.0, 6.9, 1.3 Hz, 1H), 2.41 (ddt, J = 13.9, 7.8, 1.1 Hz, 1H), 2.08–1.95 (m, 2H), 1.87 (dq, J = 13.9, 7.5 Hz, 1H), 1.83–1.68 (m, 1H), 0.97 (t, J = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 137.9, 135.3, 133.7, 130.2, 124.0, 123.9, 119.8, 118.8, 116.7, 104.6, 46.7, 40.1, 28.9, 28.6, 19.8, 8.5; IR (Neat Film, NaCl) 3073, 2968, 2940, 2877, 1691, 1595, 1573, 1450, 1354, 1299, 1181, 1049, 1004, 911, 795, 743 cm^{-1}; HRMS (ESI/APCI) *m/z* calc'd for $C_{17}H_{20}NO$ $[M+H]^+$: 254.1539, found 254.1534; SFC conditions: 2% MeOH, 3 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 11.08, minor = 10.06.



***tert*-butyl (*S*)-2-(7-allyl-7-ethyl-6-oxo-6,7,8,9-tetrahydropyrido[1,2-*a*]indol-10-yl)acetate (16)**: To an oven-dried 20 mL scintillation vial was charged heteroaryl bromide **14b** (188 mg, 0.565 mmol, 1.0 equiv), $PdCl_2(A^{ta}Phos)_2$ (12 mg, 17 mmol, 0.03 equiv), THF (4.2 mL), and a magnetic stirring bar in a N_2-filled glovebox. A commercially available (from Rieke Metals) solution of Reformatsky reagent **15** in Et_2O (1.47 mL, 0.5 M, 0.735 mmol, 1.3 equiv) was added dropwise. The reaction was sealed and placed in a preheated 65 °C heating block with stirring. After 3 h, full consumption of starting material was observed by TLC analysis. The solution was cooled to 23 °C and MeOH (ca. 1 mL) was added to quench any excess Reformatsky reagent. The crude reaction mixture was stripped onto silica gel and purified by flash column chromatography (SiO_2, 8% Et_2O in hexanes) to afford cross-coupled product **13** (204 mg, 98% yield) as a clear colorless oil: $R_f = 0.25$ (9:1 hexanes:Et_2O eluent); $[\alpha]_D^{25}$ –39.8 (*c* 0.35, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.49–8.47 (m, 1H), 7.50–7.47 (m, 1H), 7.31–7.25 (m, 2H), 5.82 (dddd, *J* = 17.1, 10.2, 7.7, 6.9 Hz, 1H), 5.13 (ddt, *J* = 9.5, 2.0, 1.2 Hz, 1H), 5.10 (q, *J* = 1.2 Hz, 1H), 3.54 (s, 2H), 3.07–2.95 (m, 2H), 2.63 (ddt, *J* = 14.0, 7.0, 1.3 Hz, 1H), 2.41 (ddt, *J* = 14.0, 7.7, 1.1 Hz, 1H), 2.07–1.96 (m, 2H), 1.91–1.80 (m, 1H), 1.79–1.70 (m, 1H), 1.43 (s, 9H), 0.96 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 170.2, 135.03, 134.96, 133.7, 130.3, 124.3, 123.8, 118.8, 118.2, 116.7, 109.9, 81.3, 46.6, 39.9, 31.6, 28.5, 28.4, 28.2, 18.1, 8.5; IR (Neat Film, NaCl) 3073, 2972, 2933, 1729, 1698, 1618, 1456, 1366, 1311, 1259, 1141, 1075, 1022, 917, 802, 752 cm^{-1}; HRMS (ESI/APCI) *m/z* calc'd for $C_{23}H_{30}NO_3$ $[M+H]^+$: 368.2220, found 368.2210.



(–)-goniomitine (1): An oven-dried scintillation vial was charged with α-quaternary lactam **16** (137 mg, 0.37 mmol, 1.0 equiv), THF (1.5 mL), and a magnetic stirring bar in a N_2-filled glovebox. To this solution was added bis(cyclopentadienyl) zirconium chloride hydride (115 mg, 0.445 mmol, 1.2 equiv), and the mixture was stirred at 23 °C until a yellow solution was observed (ca. 45 min). An additional portion of bis(cyclopentadienyl) zirconium chloride hydride (29 mg, 0.11 mmol, 0.3 equiv) was added and the reaction mixture was stirred for an additional 30 min. Hydroxylamine-*O*-sulfonic acid (71 mg, 0.63 mmol, 1.7 equiv) was added, the vial was sealed and removed from the glovebox, and stirring was resumed at 23 °C in a fume hood for an additional 30 min. The crude reaction mixture was loaded directly onto a short plug of silica gel and eluted with 10% MeOH in CH_2Cl_2 to deliver primary amine **17** (98 mg, $R_f = 0.2$, 9:1 CH_2Cl_2:MeOH eluent) as an orange foam. Semi-crude primary amine **17** was immediately dissolved in THF (5.1 mL) and cooled to 0 °C. A solution of $LiAlH_4$ (1.02 mL, 1 M in THF, 4.0 equiv) was added dropwise, and the reaction was stirred at 0 °C for 1 h. At this point, the cooling bath was removed and the reaction was stirred for an additional 6 h. The reaction was cooled to 0 °C and quenched by the careful addition of H_2O (5 mL) and AcOH (15 mL) and stirred for 6 hours. The solution was basified with 2N NaOH until pH > 12, and then was extracted with EtOAc (3 x 100 mL), dried over Na_2SO_4, filtered and concentrated. Flash column chromatography (SiO_2, 3% MeOH in CH_2Cl_2 eluent) afforded (–)-goniomitine (**1**) (33 mg, 30% yield over two steps) as a faintly yellow oil: R_f = 0.45 (9:1 CH_2Cl_2:MeOH eluent); $[\alpha]_D^{25}$ –67.1 (*c* 0.085, $CHCl_3$ (passed through basic alumina)); ^1H NMR (500 MHz, $CDCl_3$ (passed through basic alumina)) δ 7.51 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.29 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.14 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 7.08 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 4.79 (s, 1H), 3.83 (t, *J* = 6.5 Hz, 2H), 3.08–3.00 (m, 2H), 2.98–2.90 (m, 2H), 2.88–2.76 (m, 2H), 2.52 (td, *J* = 12.9, 6.6 Hz, 1H), 1.93–1.87 (m, 1H), 1.79–1.66 (m, 3H), 1.6 (dq, *J* = 15, 7.6 Hz, 1H), 1.55–1.45 (m, 3H), 1.21 (dq, *J* = 14.7, 7.3 Hz, 1H), 0.89 (t, *J* = 7.6 Hz, 3H). (500 MHz, $CDCl_3$ (passed through basic alumina)) δ 7.51 (d, *J* = 7.8 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.15 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H), 7.08 (ddd, *J* = 7.9, 7.1, 1.1 Hz, 1H), 4.80 (s, 1H), 3.83 (td, *J* = 6.4, 1.3 Hz, 2H), 3.11 (ddd, *J* = 17.3, 6.7, 1.5 Hz, 2H), 2.93 (td, *J* = 6.5, 2.2 Hz, 2H), 2.86–2.72 (m, 2H), 2.51 (td, *J* = 12.9, 6.6 Hz, 1H), 1.91–1.85 (m, 1H), 1.75–1.65 (m, 1H), 1.57 (dt, *J* = 15.0, 7.5 Hz, 1H), 1.53–1.44 (m, 3H), 1.20 (dq, *J* = 14.7, 7.7 Hz, 1H), 0.87 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.5, 132.8, 129.2, 120.7, 119.7, 118.2, 108.4, 106.1, 71.7, 62.7, 45.8, 35.2, 34.2, 28.8, 27.8, 21.8, 21.7, 18.7, 7.2; IR (Neat Film, NaCl) 3288 (br), 3051, 2934, 2877, 2241, 1679, 1611, 1462, 1416, 1357, 1309, 1203, 1188, 1108, 1044, 1013, 908, 867, 737 cm^{-1}; HRMS (ESI/APCI) *m/z* calc'd for $C_{19}H_{27}N_2O$ $[M+H]^+$: 299.2118, found 299.2121.

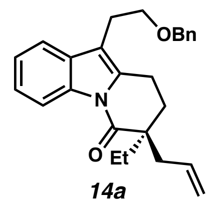
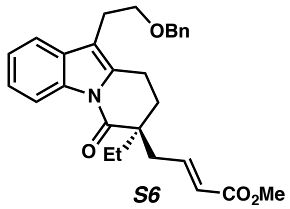
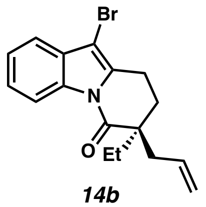
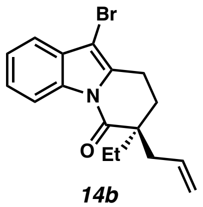
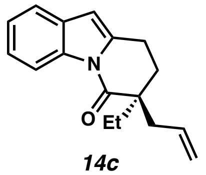
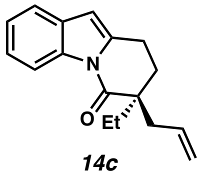


14c

18

(*R*)-3-(2-(1*H*-indol-2-yl)ethyl)-3-ethylpiperidin-2-one (18): An oven-dried 1-dram vial was charged with α-quaternary lactam **14c** (40 mg, 0.16 mmol, 1.0 equiv), THF (0.8 mL), and a magnetic stirring bar in a N_2-filled glovebox. To this solution was added bis(cyclopentadienyl) zirconium chloride hydride (49 mg, 0.19 mmol, 1.2 equiv), and the mixture was stirred at 23 °C until a light yellow solution was observed (ca. 30 min). Hydroxylamine-*O*-sulfonic acid (29 mg, 0.25 mmol, 1.6 equiv) was added, the vial was sealed and removed from the glovebox, and stirring was resumed at 23 °C in a fume hood for an additional 30 min. The crude reaction mixture was loaded directly onto a short plug of silica gel and eluted with 10% MeOH in CH_2Cl_2 to deliver the intermediate primary amine (R_f = 0.2, 9:1 CH_2Cl_2:MeOH eluent). The semi-crude primary amine was immediately dissolved in MeOH (5.2 mL), then K_2CO_3 (65 mg, 0.47 mmol, 3.0 equiv) was added. The reaction was stirred at 23 °C for 1 h, at which point complete consumption of starting material was determined by TLC analysis. Flash column chromatography (SiO_2, 40% acetone in hexanes) afforded free *N*–H lactam **18** (28 mg, 66% yield over two steps) as a white amorphous solid: R_f = 0.3 (3:2 hexanes:acetone eluent); $[\alpha]_D^{25}$ –32.7 (*c* 0.41, CH_3OH); ^1H NMR (500 MHz, $CDCl_3$) δ 8.43 (br s, 1H), 7.50 (ddt, *J* = 7.7, 1.4, 0.8 Hz, 1H), 7.29 (dq, *J* = 8.0, 1.0 Hz, 1H), 7.09 (ddd, *J* = 8.1, 7.1, 1.3 Hz, 1H), 7.07–7.02 (m, 1H), 6.21 (dd, *J* = 2.0, 0.9 Hz, 1H), 5.83 (br s, 1H), 3.32 (td, *J* = 5.7, 2.2 Hz, 2H), 2.90–2.82 (m, 1H), 2.69 (dddd, *J* = 14.7, 11.1, 4.6, 1.0 Hz, 1H), 2.13 (ddd, *J* = 13.6, 11.2, 4.5 Hz, 1H), 1.90–1.75 (m, 6H), 1.67–1.60 (m, 1H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.2, 140.0, 136.2, 128.8, 121.0, 119.8, 119.5, 110.6, 99.3, 45.3, 42.9, 37.8, 31.3, 29.2, 23.9, 19.8, 8.6; IR (Neat Film, NaCl) 3285, 3252, 2971, 2952, 2868, 1643, 1588, 1486, 1456, 1421, 1351, 1328, 1287, 1216, 1104, 1010, 795, 735 cm^{-1}; HRMS (ESI/APCI) *m/z* calc'd for $C_{17}H_{23}N_2O$ [M+H]$^+$: 271.1805, found 271.1813.

Determination of Enantiomeric Excess (Table S1)

entry	product	compound assayed	assay conditions	ee (%)
1	 ***14a***	 ***S6***	**SFC: 8% IPA, 2.5 mL/min** **Chiralpak AD-H, λ = 210 nm** **t_R (min): major 40.93, minor 44.73**	89
2	 ***14b***	 ***14b***	**SFC: 2% MeOH, 3 mL/min** **Chiralpak AD-H, λ = 210 nm** **t_R (min): major 11.87, minor 11.11**	96
3	 ***14c***	 ***14c***	**SFC: 2% MeOH, 3 mL/min** **Chiralpak AD-H, λ = 210 nm** **t_R (min): major 11.08, minor 10.06**	94

Comparison of Synthetic Material to Published Data

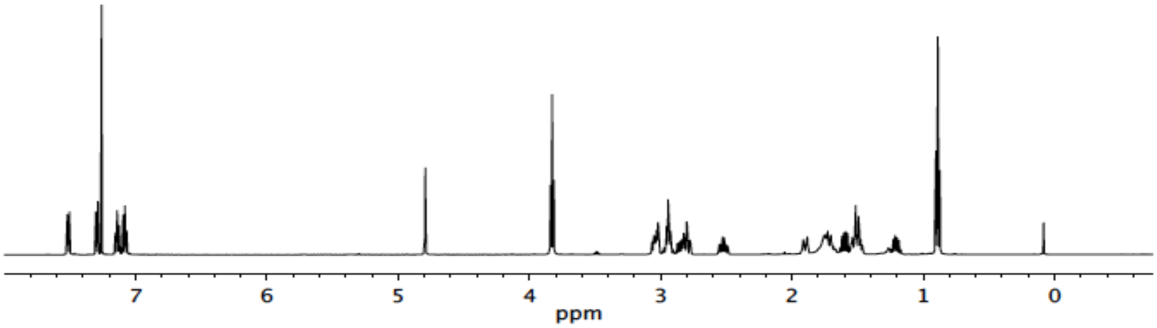
The optical rotation of our synthetic (–)-goniomitine, $[\alpha]_D^{25}$ –67.1 (*c* 0.085, $CHCl_3$ (passed through basic alumina)), differs from values previously reported in the literature: $[\alpha]_D^{25}$ –80 (*c* 0.9, $CHCl_3$),[10] $[\alpha]_D^{25}$ –87.1 (*c* 0.42, $CHCl_3$),[11] $[\alpha]_D^{25}$ –78.1 (*c* 0.14, $CHCl_3$),[12] $[\alpha]_D^{25}$ –80 (*c* 0.46, $CHCl_3$).[13] We have also noted that some ^{13}CNMR resonances of the natural product vary depending on the $CDCl_3$ used to make the sample (*vide supra*). Since we obtained SFC traces of both *rac*- and (–)-**14b**, and since the quaternary center is not susceptible to racemization, we do not believe that this discrepancy indicates erosion of enantiopurity.

Comparison of Synthetic and Natural (–)-Goniomitine (Table S2)

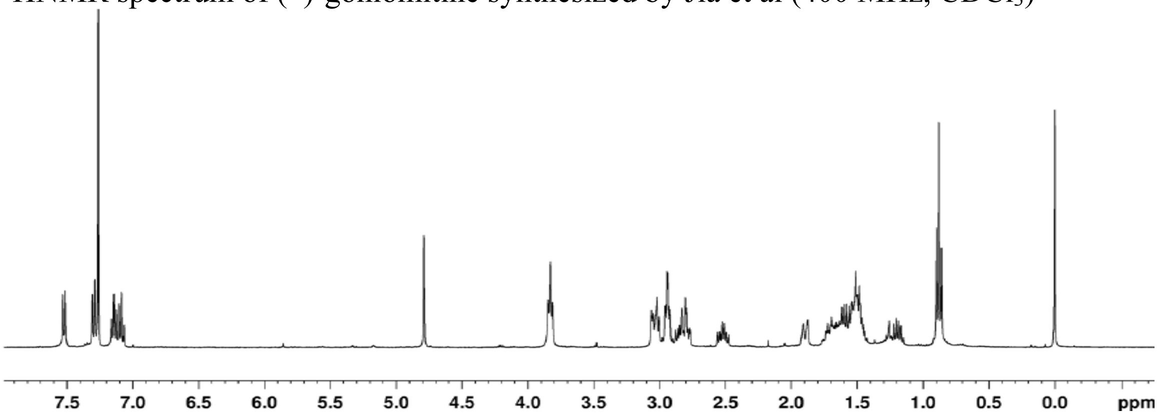
Synthetic (–)-goniomitine ($CDCl_3$ directly from bottle)	**Synthetic (–)-goniomitine** ($CDCl_3$ filtered through basic alumina)	**Natural (–)-goniomitine**[10]
^1H NMR (500 MHz, $CDCl_3$)	*^1H NMR (500 MHz, $CDCl_3$)*	*^1H NMR (400 MHz, $CDCl_3$)*
4.80 (s, 1H)	4.79 (s, 1H)	4.86 (s, 1H)
3.83 (t, J = 6.4, 2H)	3.83 (t, J = 6.5, 2H)	3.81 (t, 2H)
2.93 (td, J = 6.5, 2.2 Hz, 2H)	2.94 (td, J = 6.6, 3.3 Hz, 2H)	3.0 (t, 2H)
1.57 (dt, J = 15.0, 7.5 Hz, 1H)	1.57 (dt, J = 15.0, 7.5 Hz, 1H)	1.56 (m, J = 7 Hz, 1H)
1.20 (dq, J = 14.7, 7.7 Hz, 1H)	1.21 (dq, J = 14.7, 7.3 Hz, 1H)	1.20 (m, J = 7 Hz, 1H)
0.87 (t, J = 7.6 Hz, 3H)	0.89 (t, J = 7.6 Hz, 3H)	0.86 (t, J = 7 Hz, 3H)
^{13}C NMR (126 MHz, $CDCl_3$)	*^{13}C NMR (126 MHz, $CDCl_3$)*	*^{13}C NMR ($CDCl_3$)*
135.4	135.5	135.4
132.6	132.8	132.6
129.3	129.2	129.3
120.9	120.7	120.8
120.1	119.7	119.9
118.2	118.2	118.1
108.7	108.4	108.7
107.4	106.1	106.8
70.6	71.7	71.1
62.5	62.7	62.6
44.9	45.8	45.4
35.3	35.2	35.3
33.6	34.2	33.8
28.7	28.8	28.7
27.7	27.8	27.8
21.7	21.8	21.8
20.3	21.7	20.8
18.5	18.7	18.5
7.2	7.2	7.3

Comparison of ^{1}HNMR and ^{13}CNMR Spectra

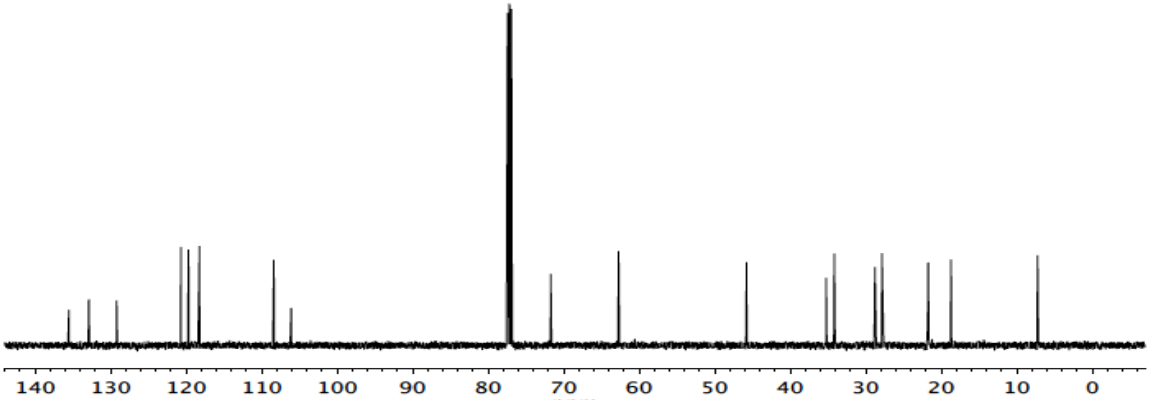
^{1}HNMR spectrum of our synthetic (–)-goniomitine (500 MHz, $CDCl_3$)



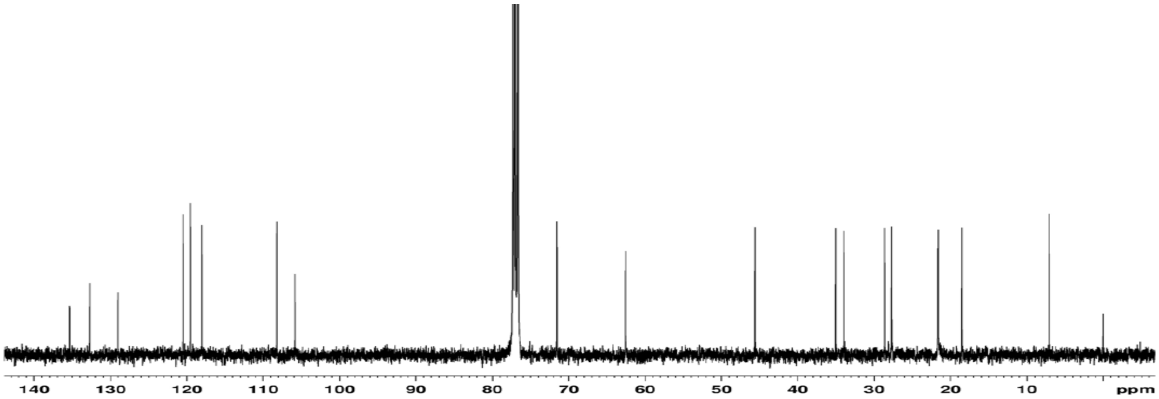
^{1}HNMR spectrum of (–)-goniomitine synthesized by Jia et al (400 MHz, $CDCl_3$)[13]



^{13}CNMR spectrum of our synthetic (–)-goniomitine (126 MHz, $CDCl_3$)



^{13}CNMR spectrum of (–)-goniomitine synthesized by Jia et al (100 MHz, $CDCl_3$)[13]



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[9] The enantiomeric excess of compound **11a** was difficult to discern using SFC analysis. Cross metathesis with methyl acrylate afforded **S6**, which enabled reliable ee determination.

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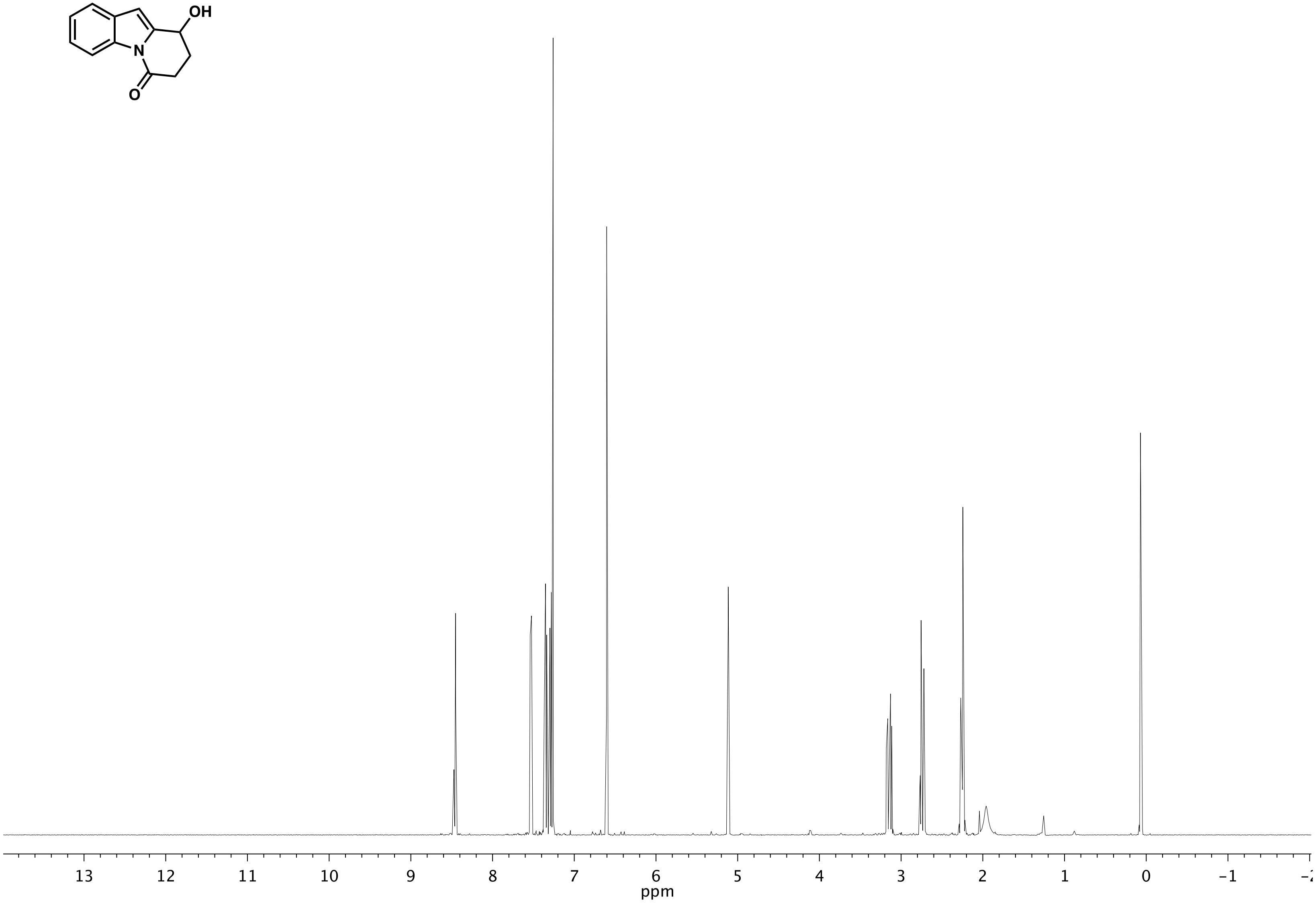
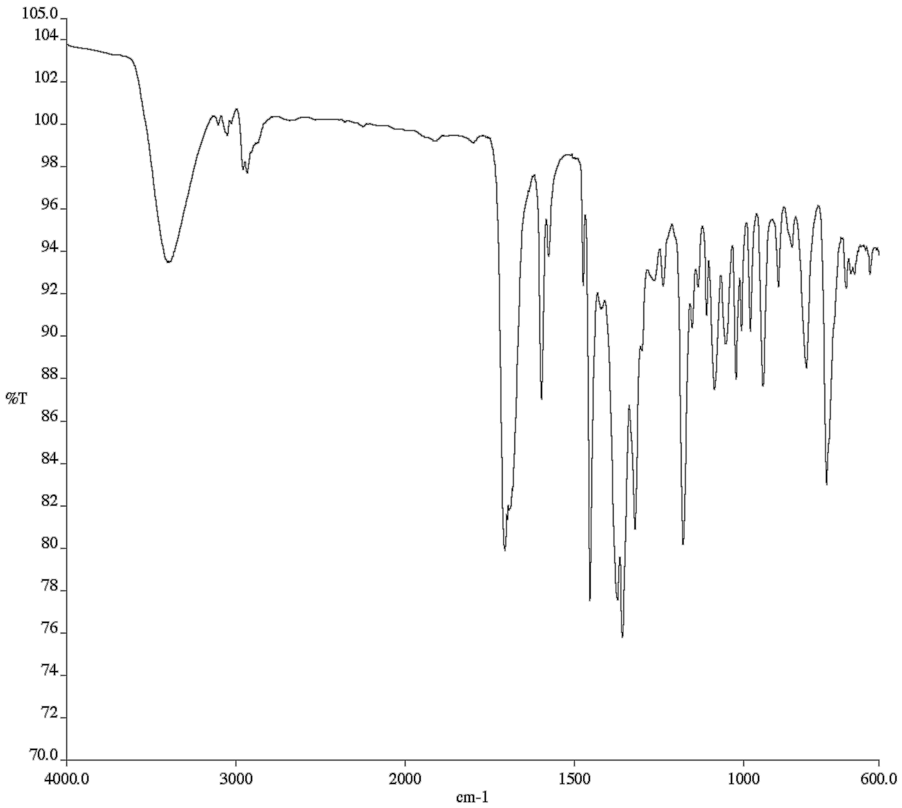
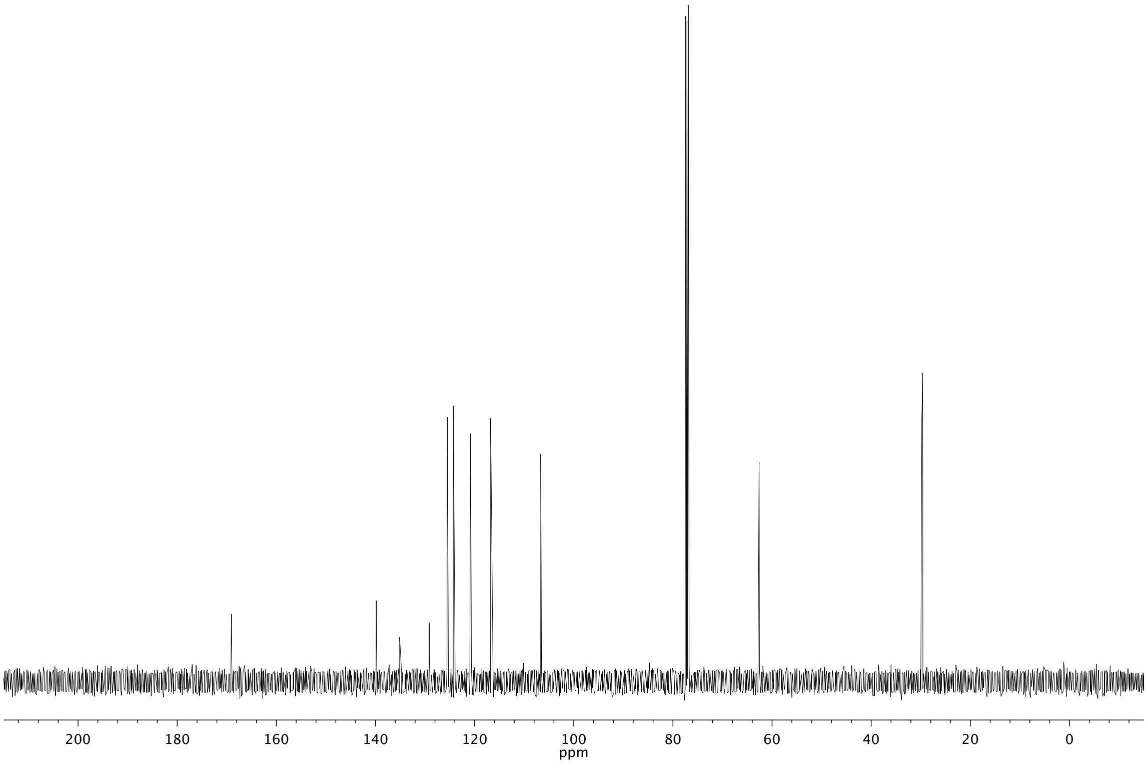


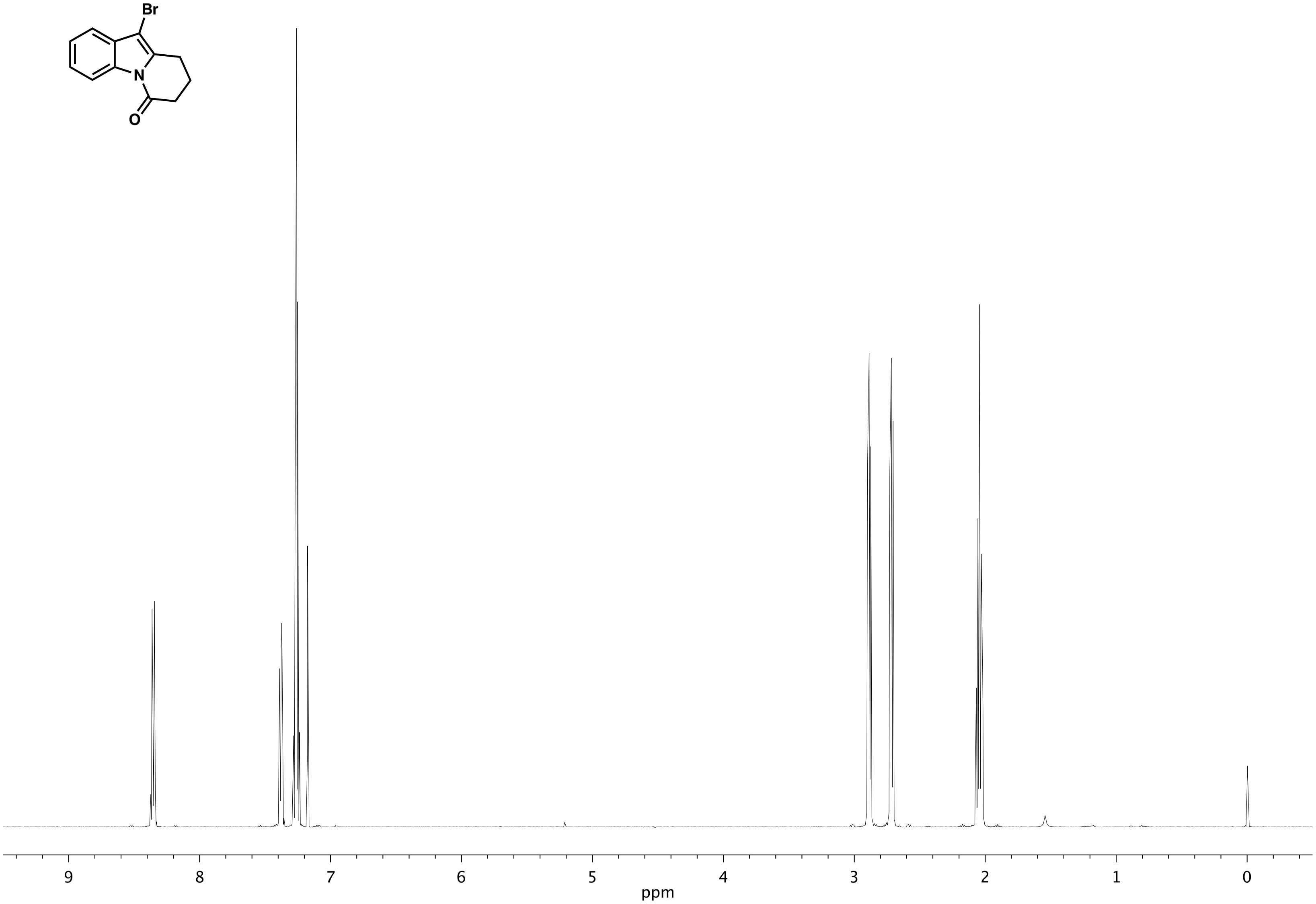
^{1}H NMR (500 MHz, CDCl$_3$) of compound **S2**.



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



^{13}C NMR (126 MHz, CDCl$_3$) of compound **S2**.



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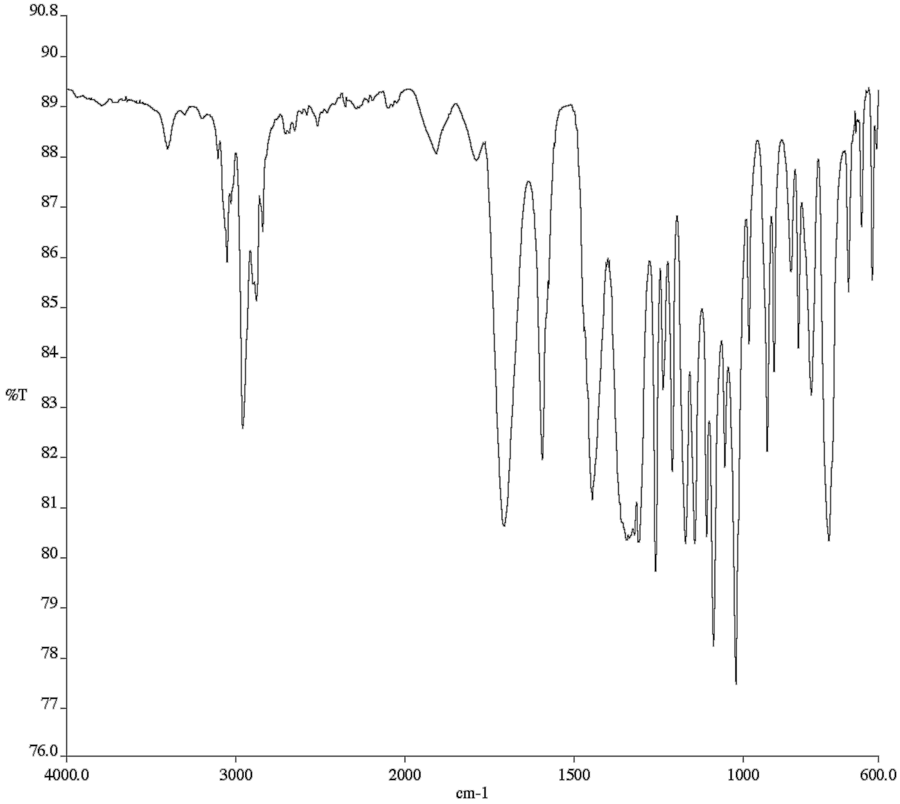
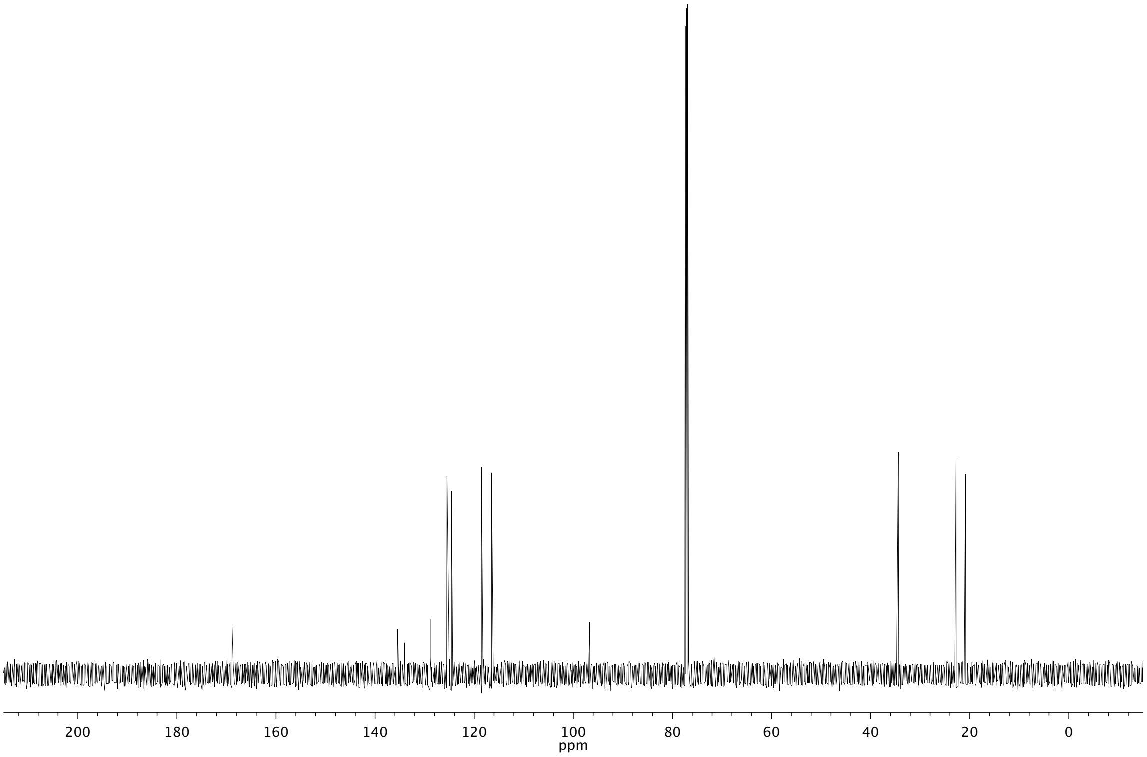
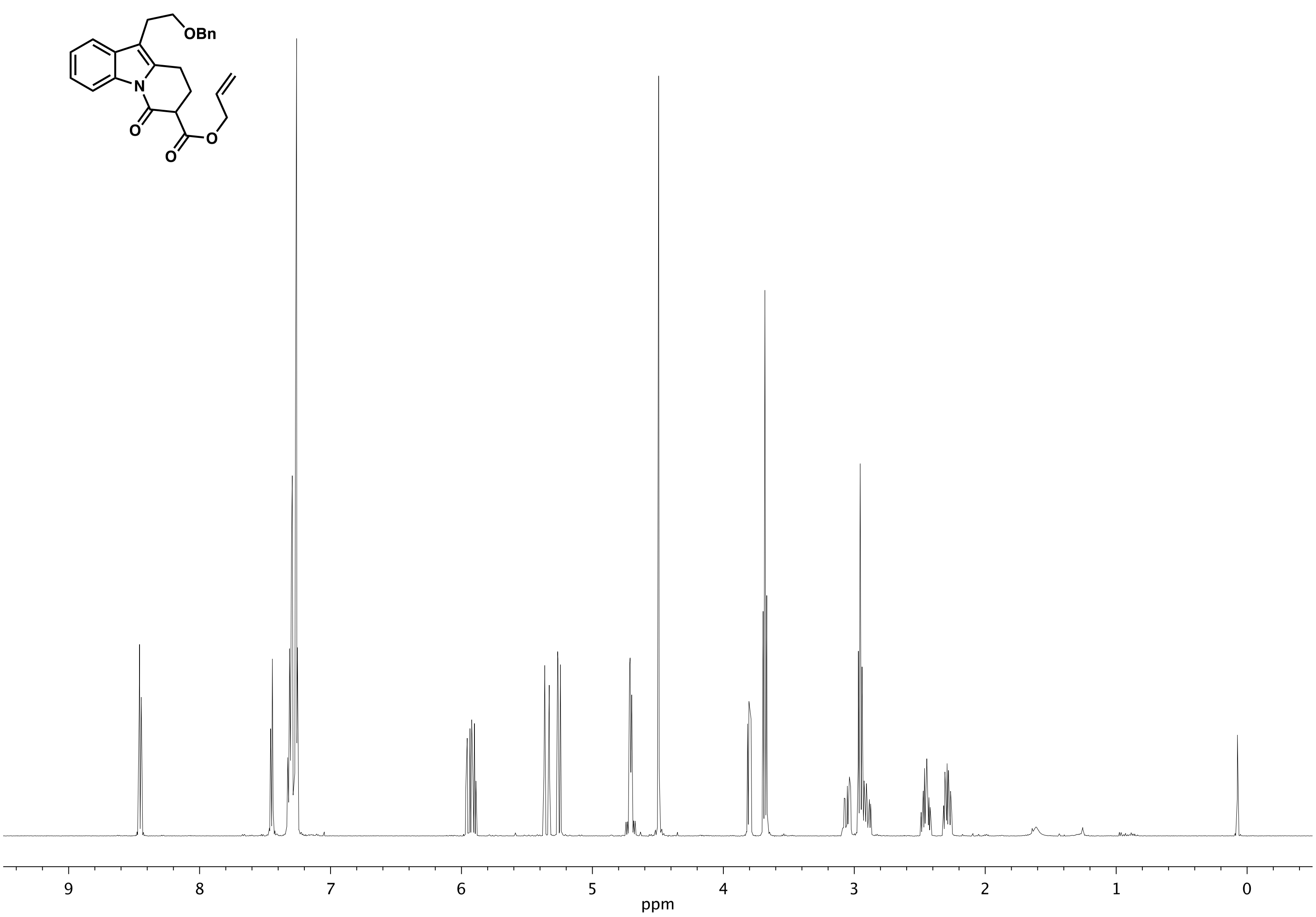


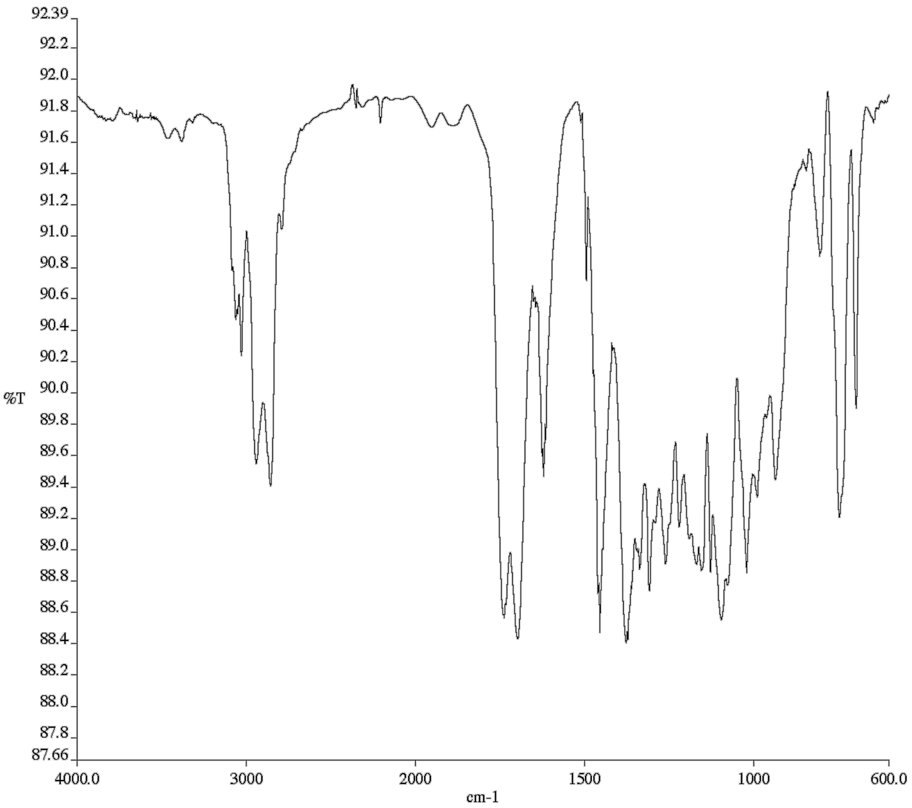
Infrared spectrum (Thin Film, NaCl) of compound **10.**



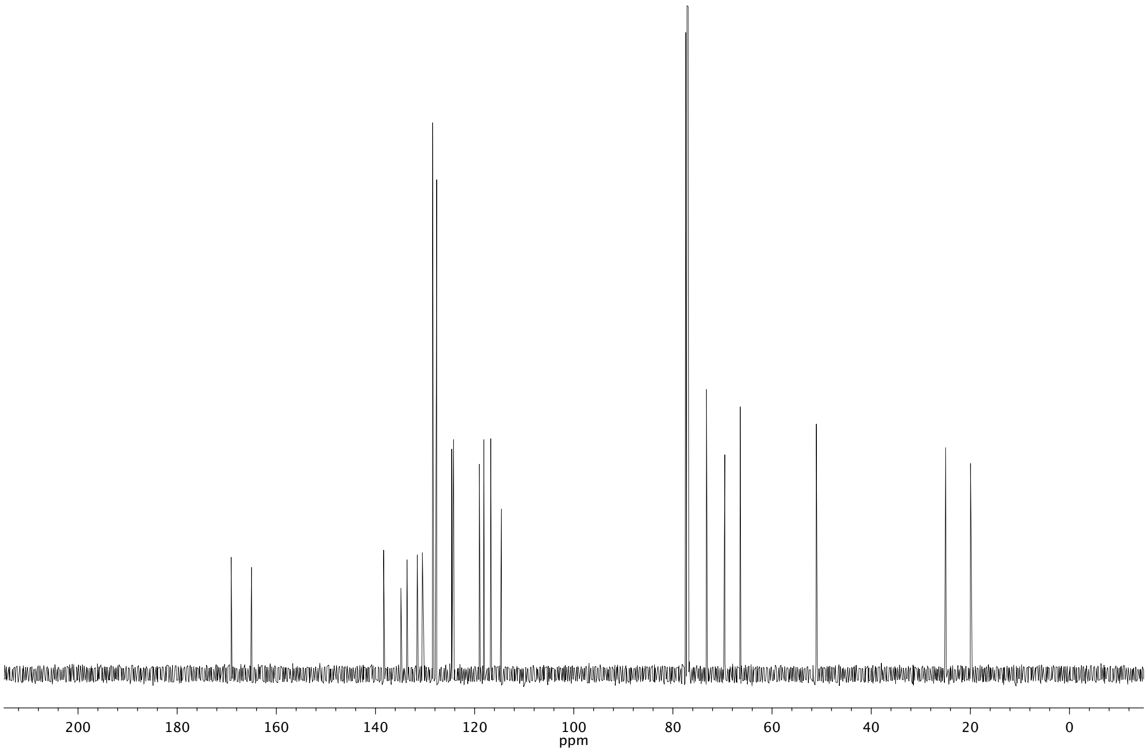
^{13}C NMR (126 MHz, $CDCl_3$) of compound **10**.



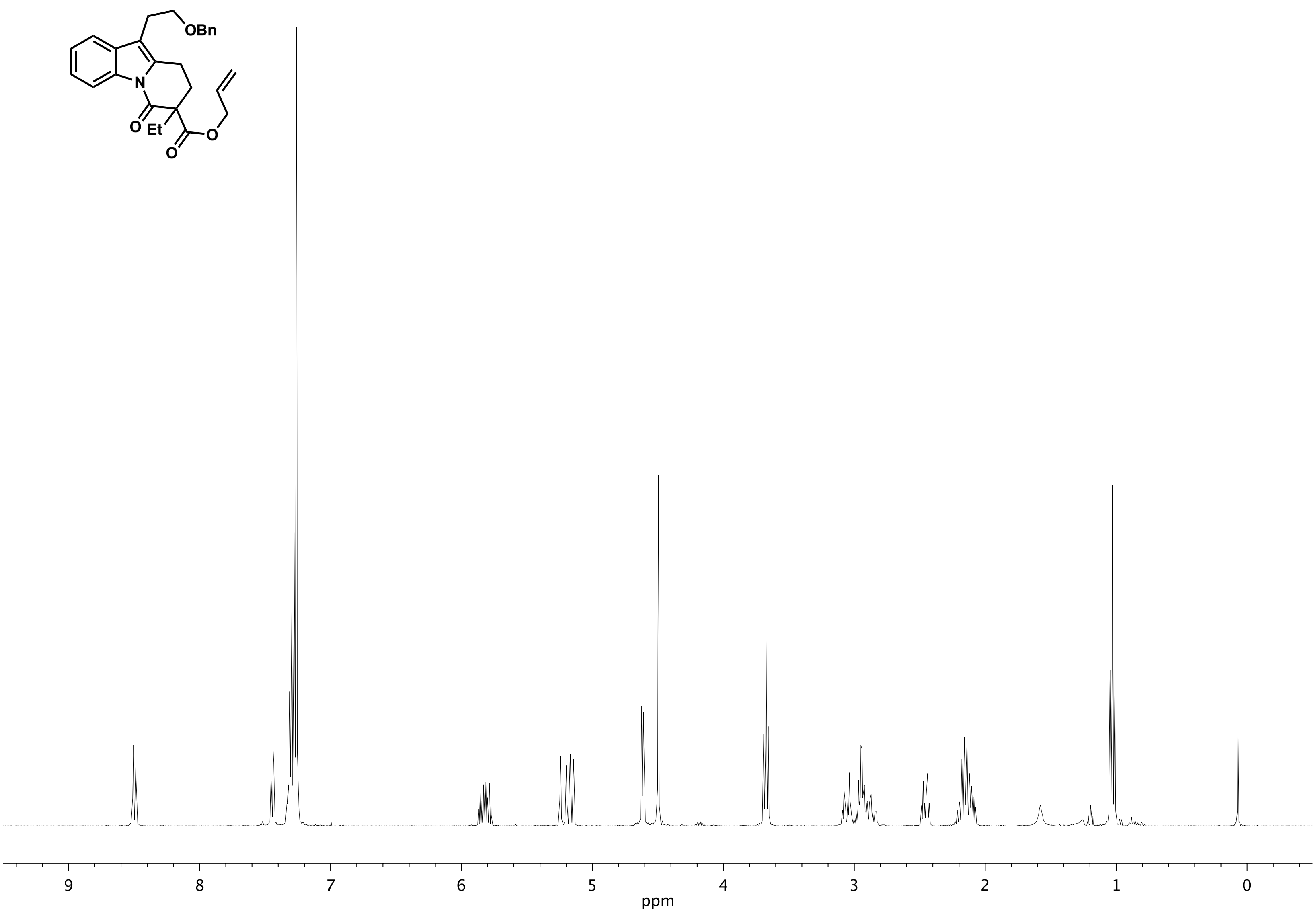
^{1}H NMR (500 MHz, $CDCl_3$) of compound **S3**.



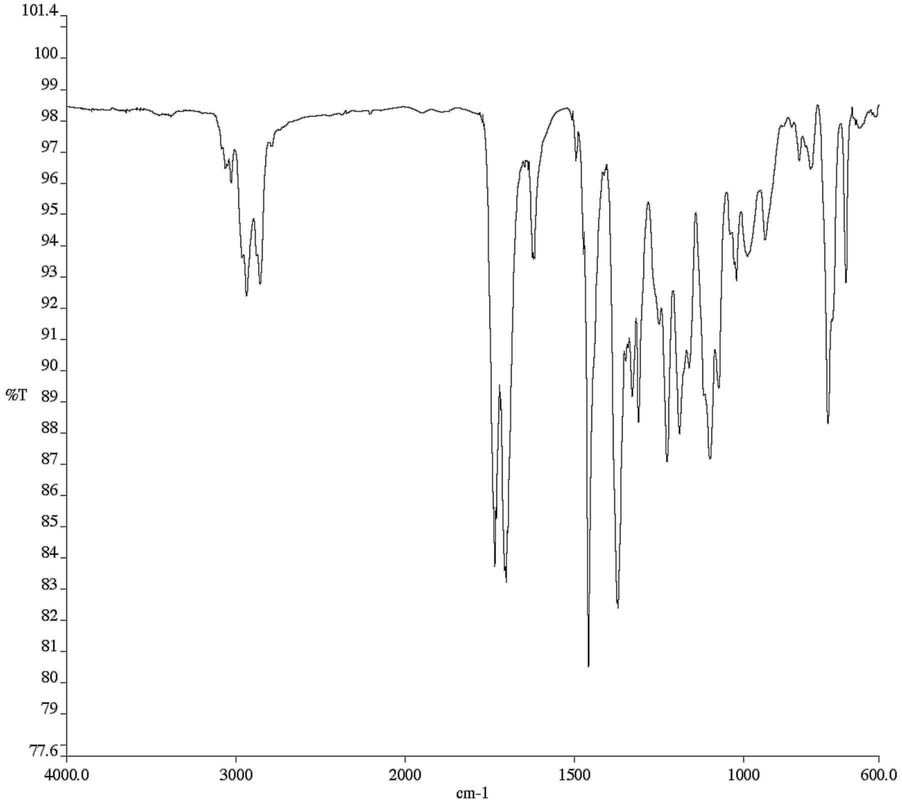
Infrared spectrum (Thin Film, NaCl) of compound **S3.**



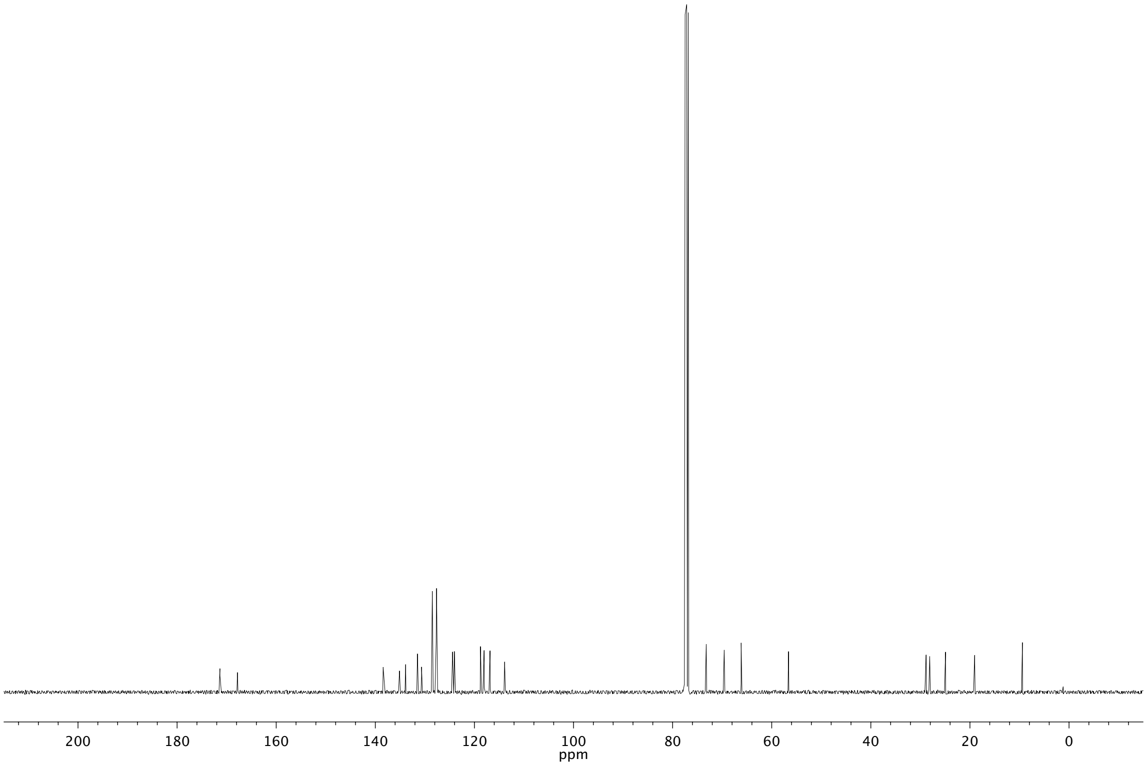
^{13}C NMR (126 MHz, CDCl$_3$) of compound **S3**.



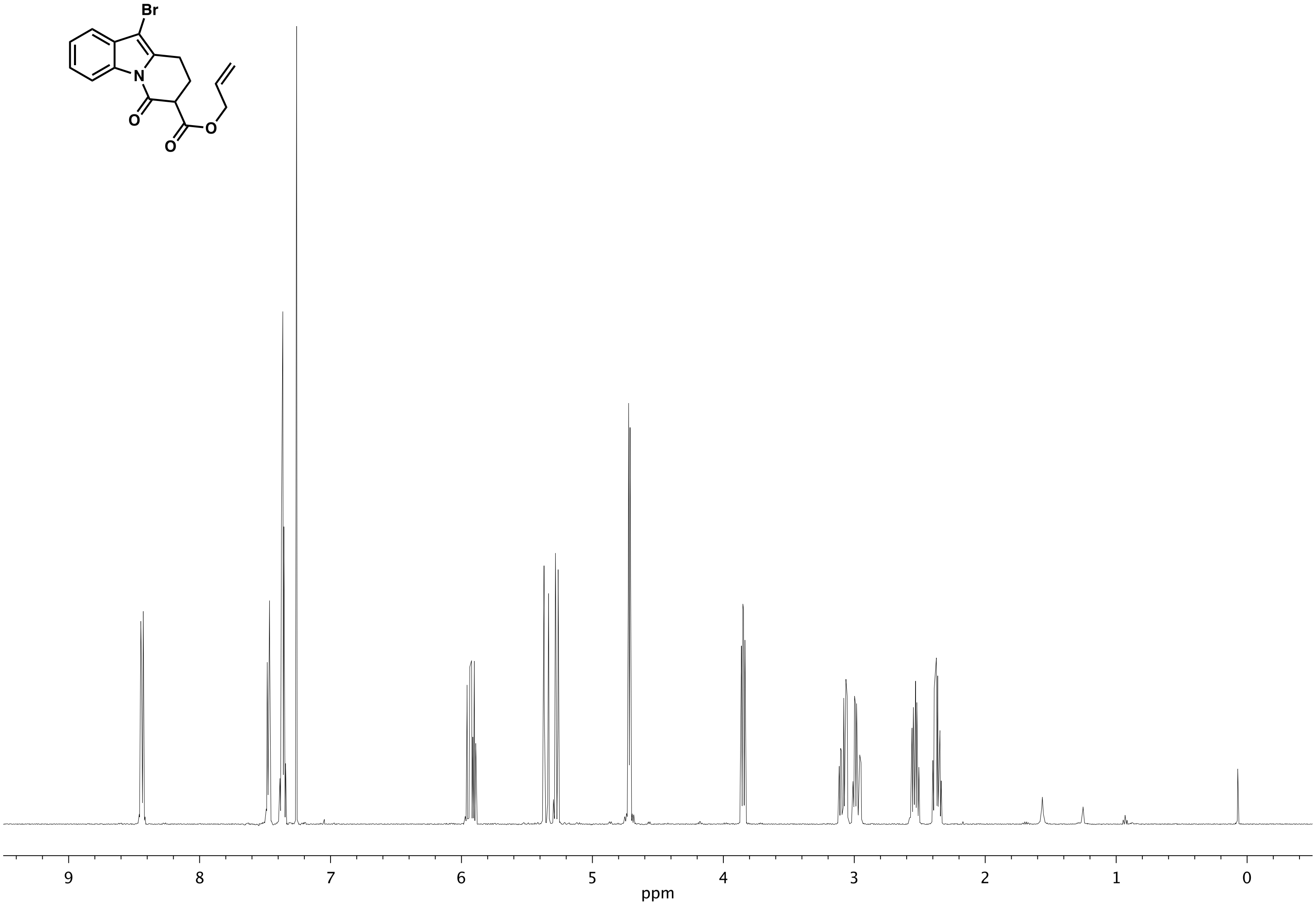
^{1}H NMR (400 MHz, CDCl$_3$) of compound **13a**.



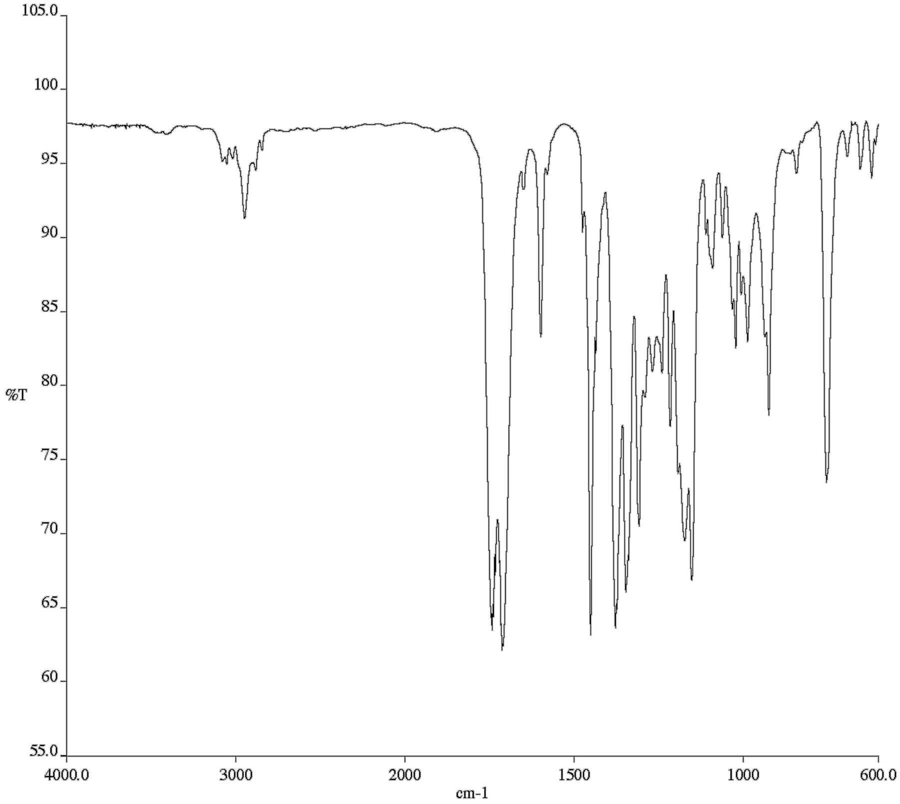
Infrared spectrum (Thin Film, NaCl) of compound **13a.**



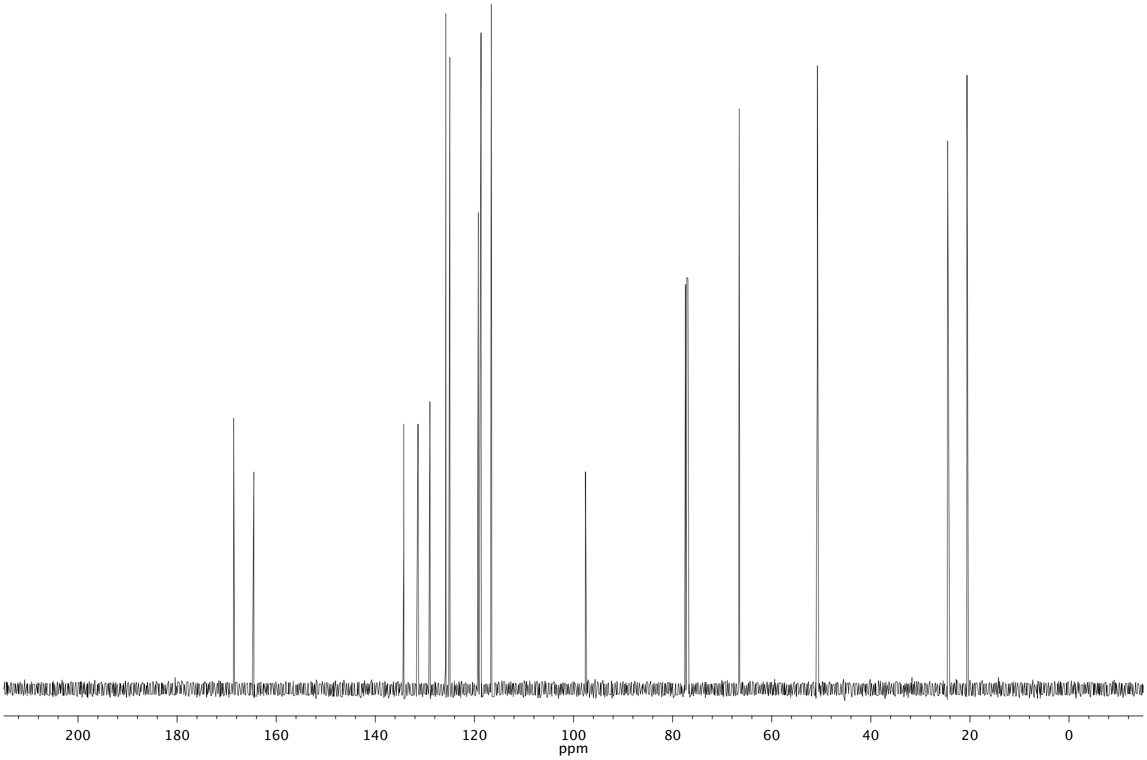
^{13}C NMR (101 MHz, $CDCl_3$) of compound **13a**.



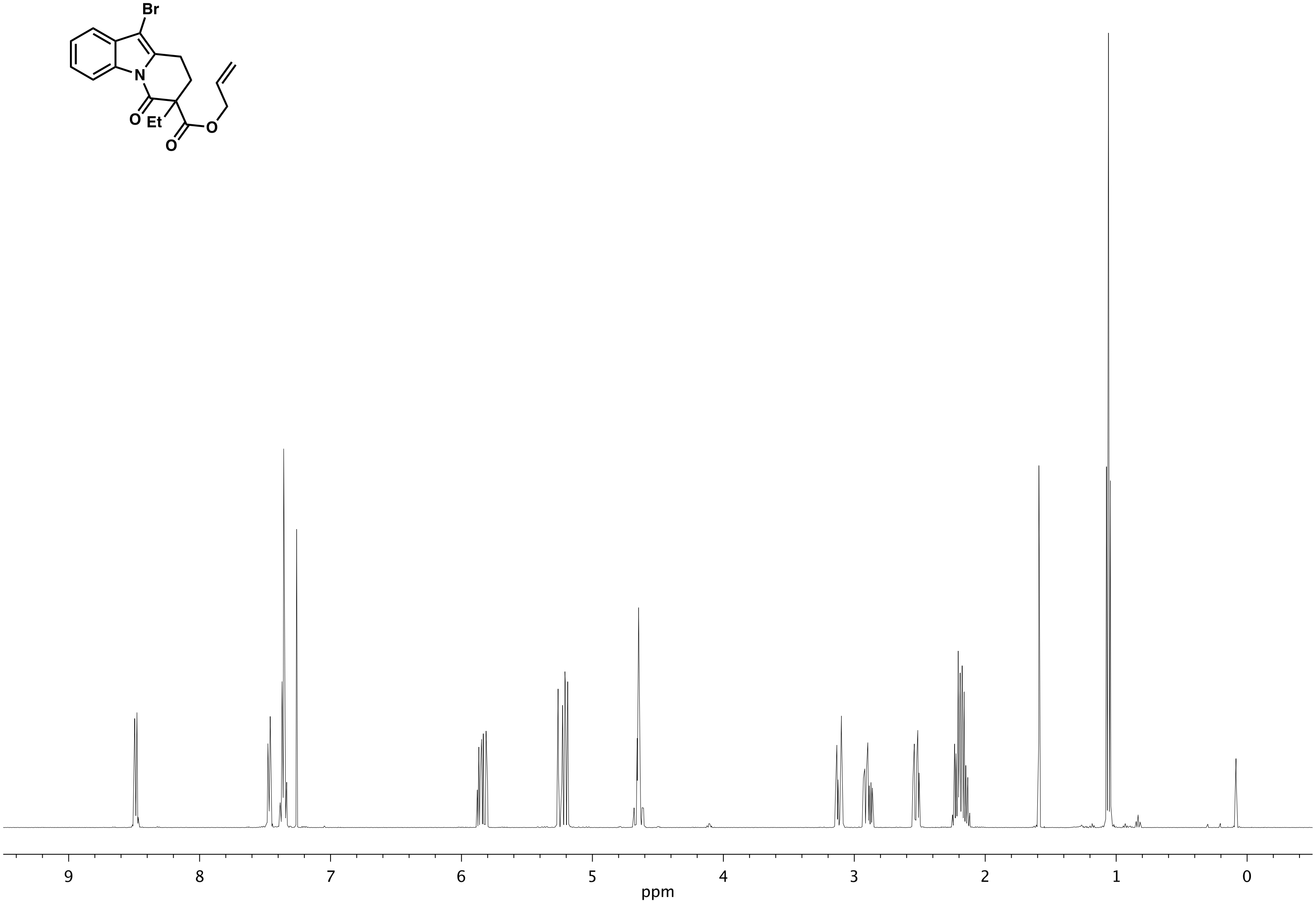
^{1}H NMR (500 MHz, $CDCl_3$) of compound **S4**.



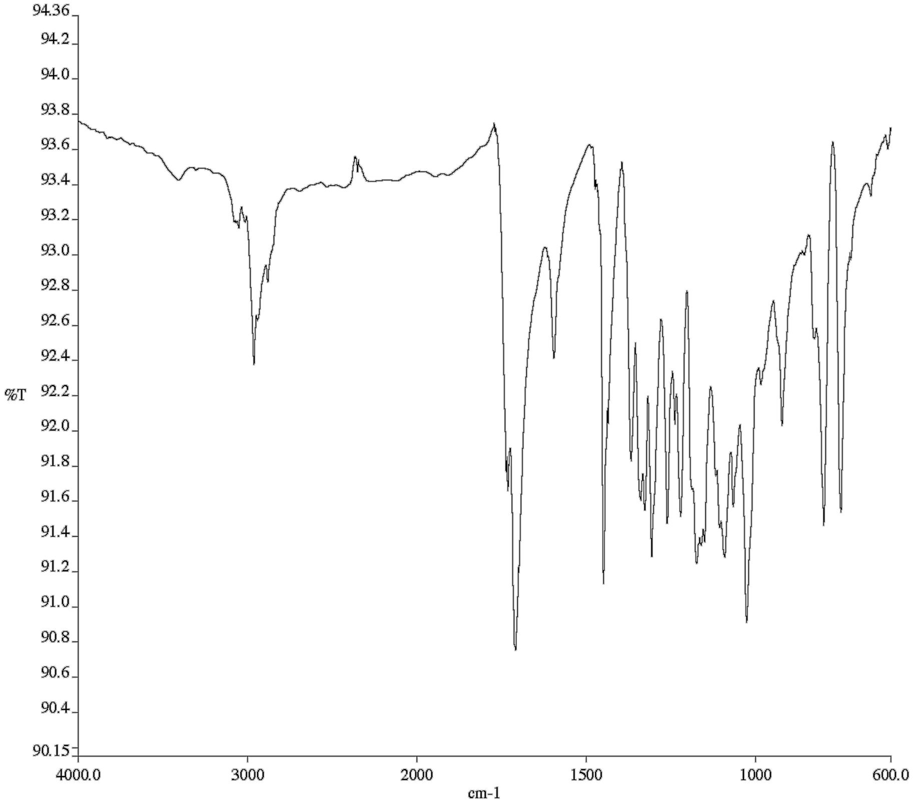
Infrared spectrum (Thin Film, NaCl) of compound **S4.**



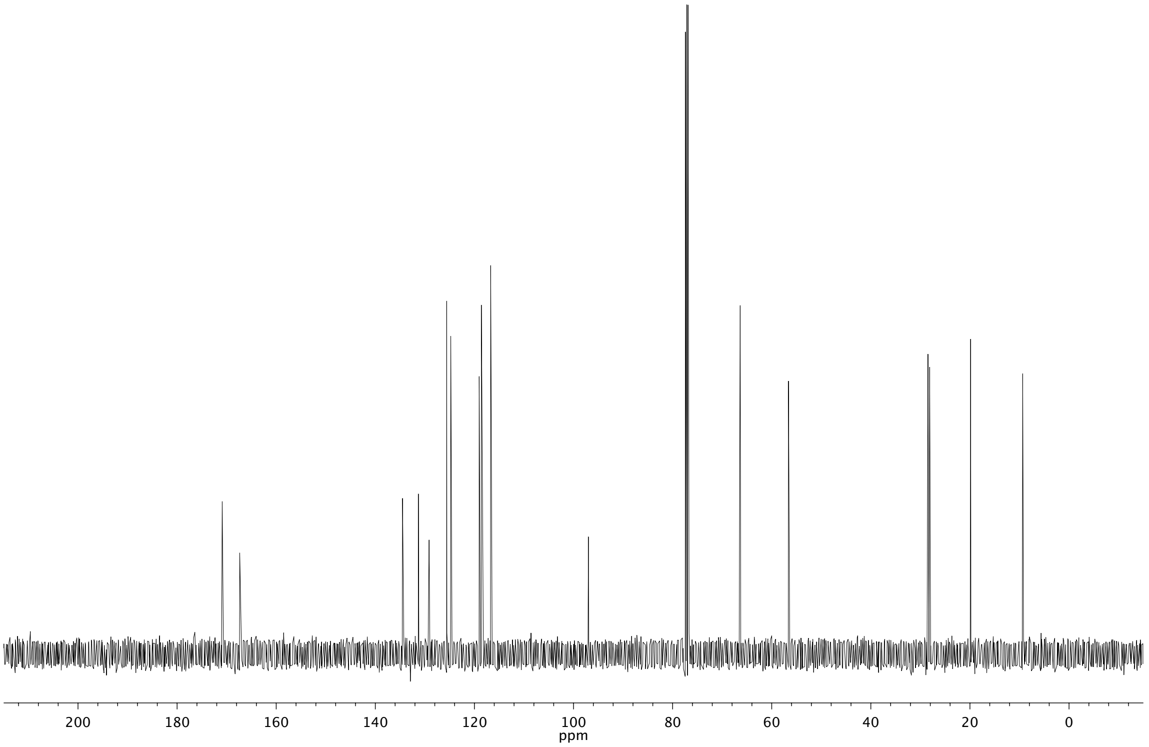
^{13}C NMR (126 MHz, CDCl$_3$) of compound **S4**.



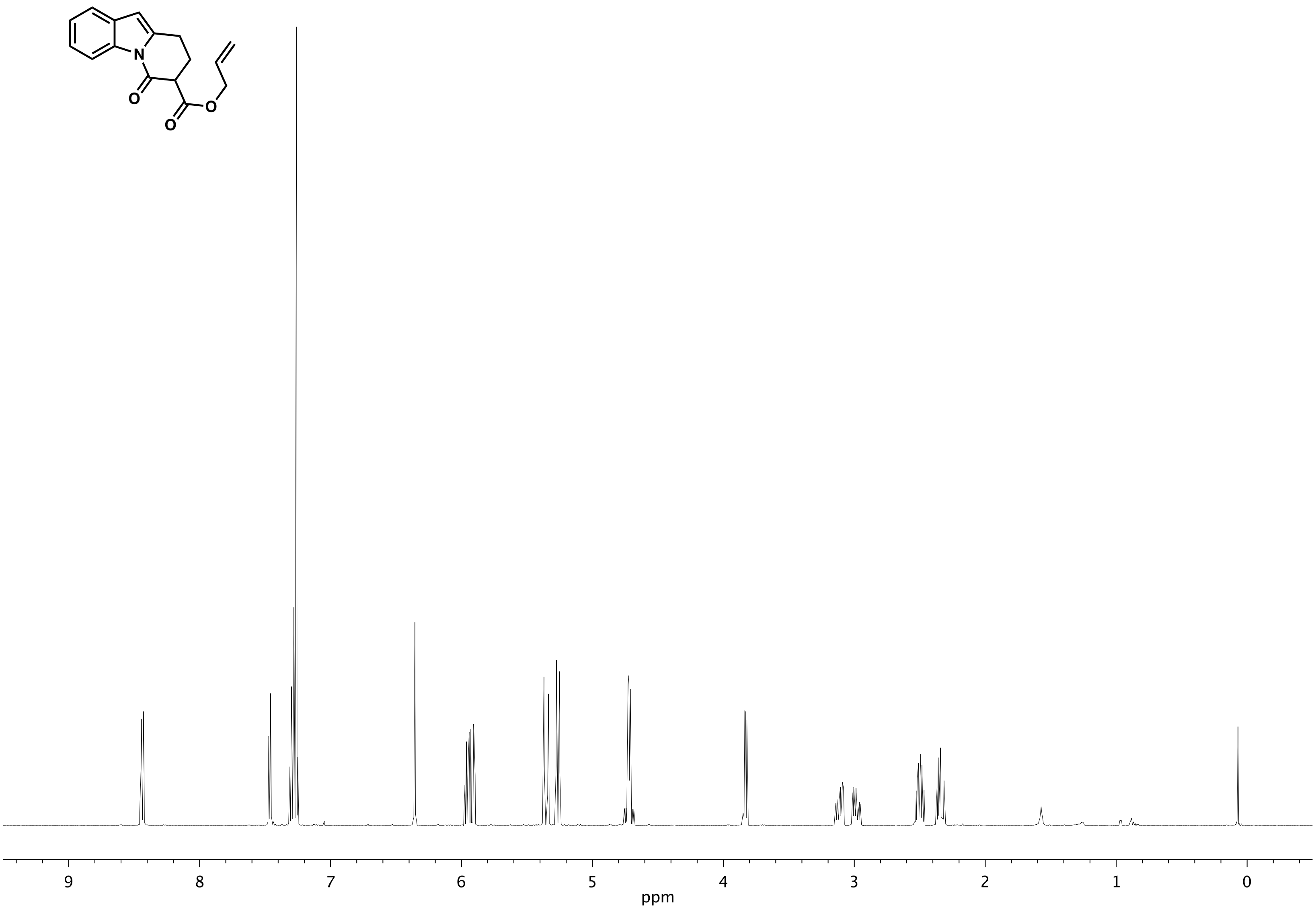
^{1}H NMR (500 MHz, $CDCl_3$) of compound **13b**.



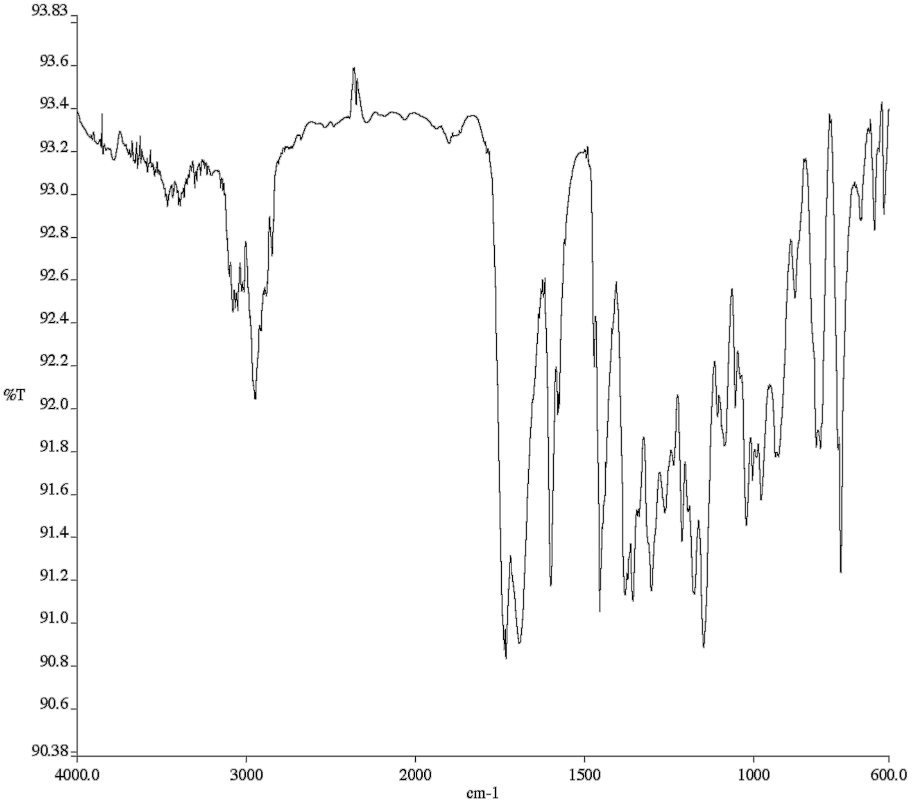
Infrared spectrum (Thin Film, NaCl) of compound **13b.**



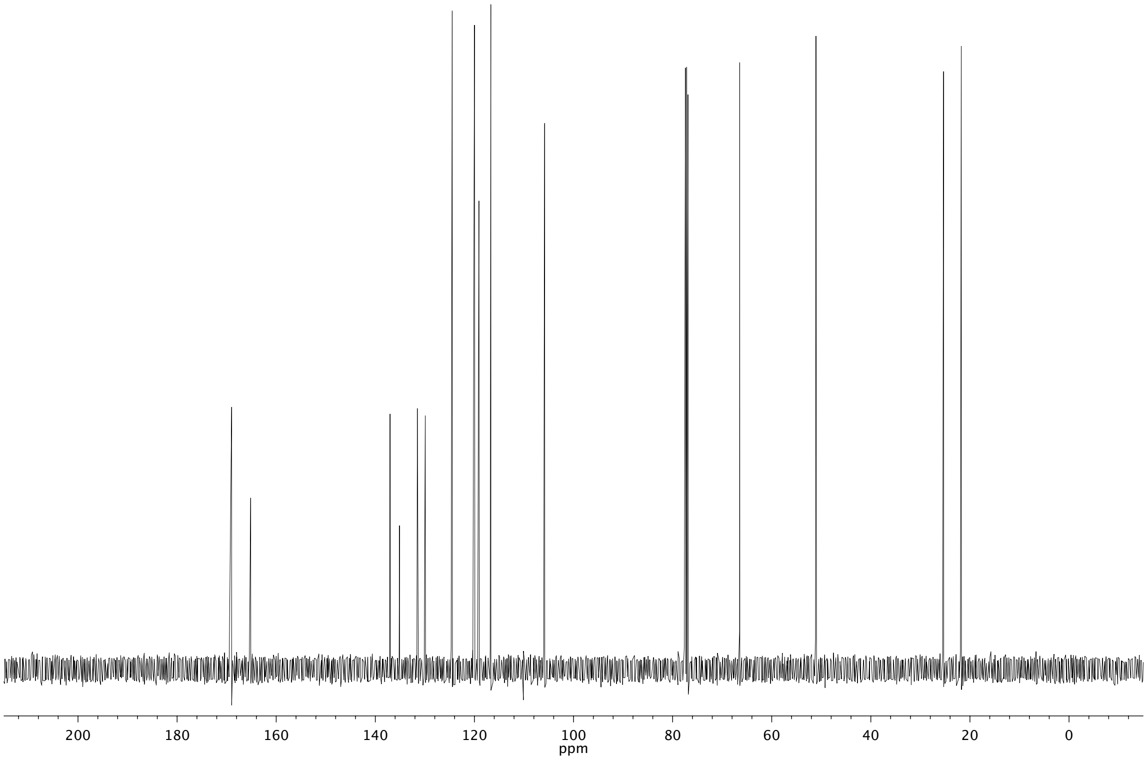
^{13}C NMR (126 MHz, CDCl$_3$) of compound **13b**.



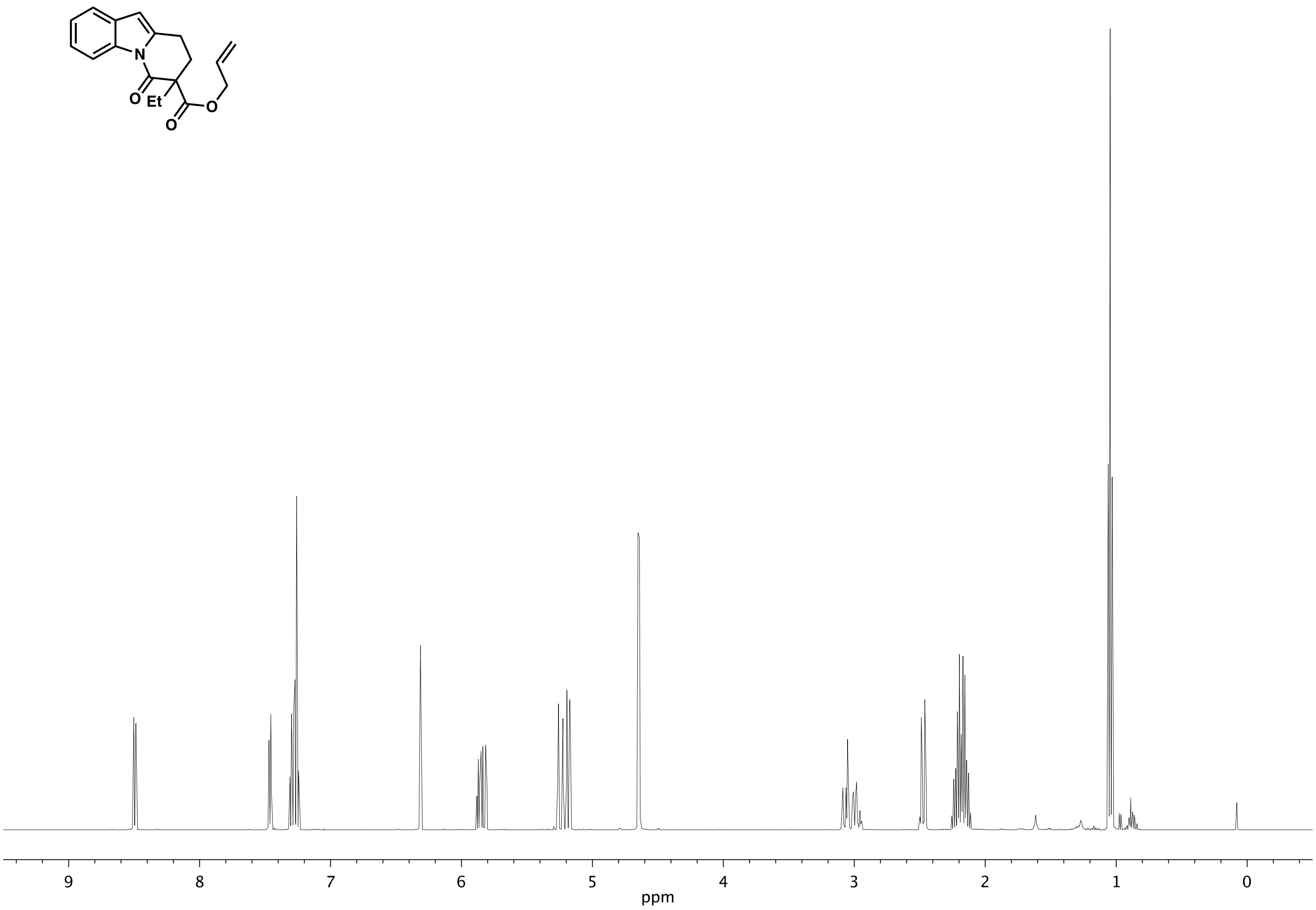
^{1}H NMR (500 MHz, $CDCl_3$) of compound **S5**.



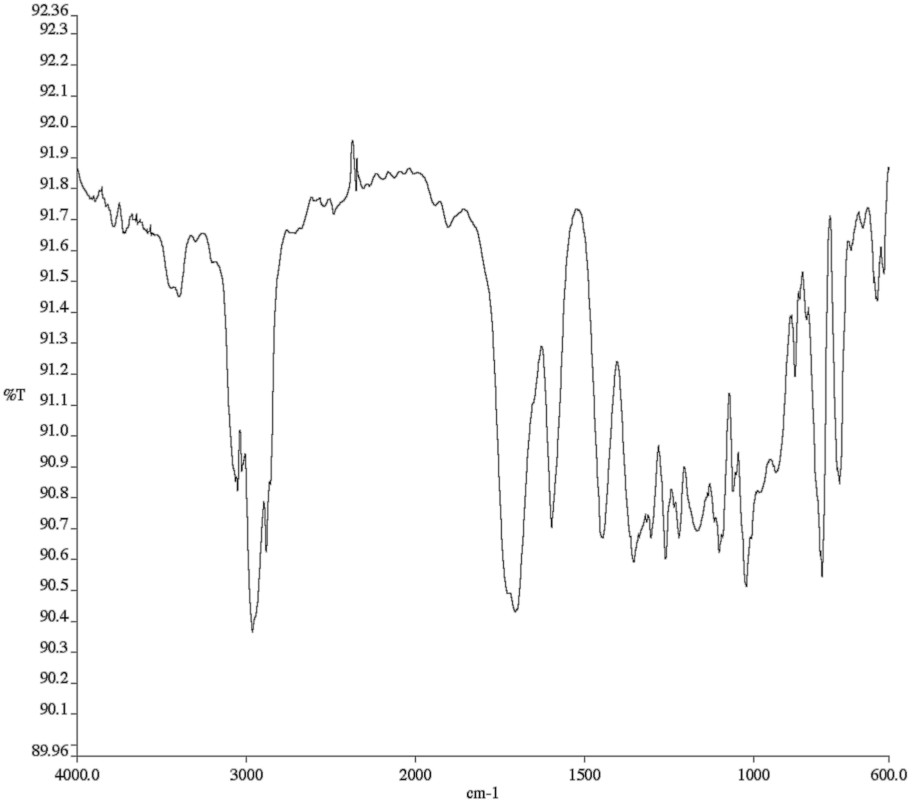
Infrared spectrum (Thin Film, NaCl) of compound **S5.**



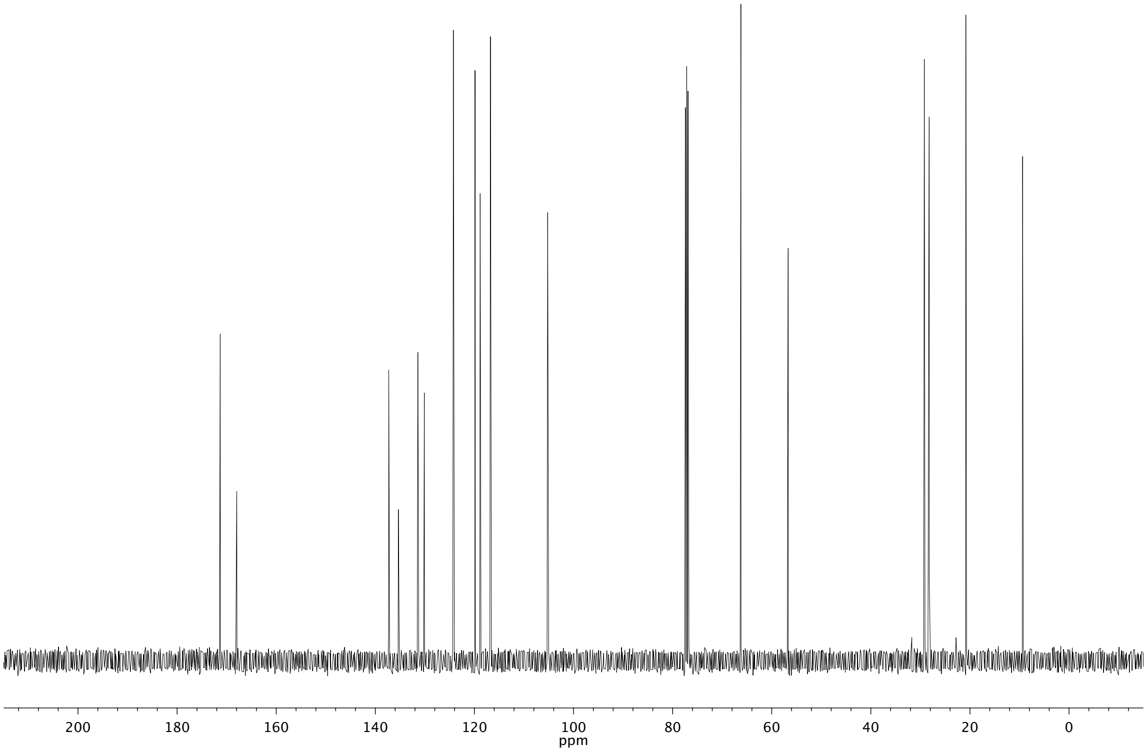
^{13}C NMR (126 MHz, CDCl$_3$) of compound **S5**.



^{1}H NMR (500 MHz, $CDCl_3$) of compound **13c**.



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



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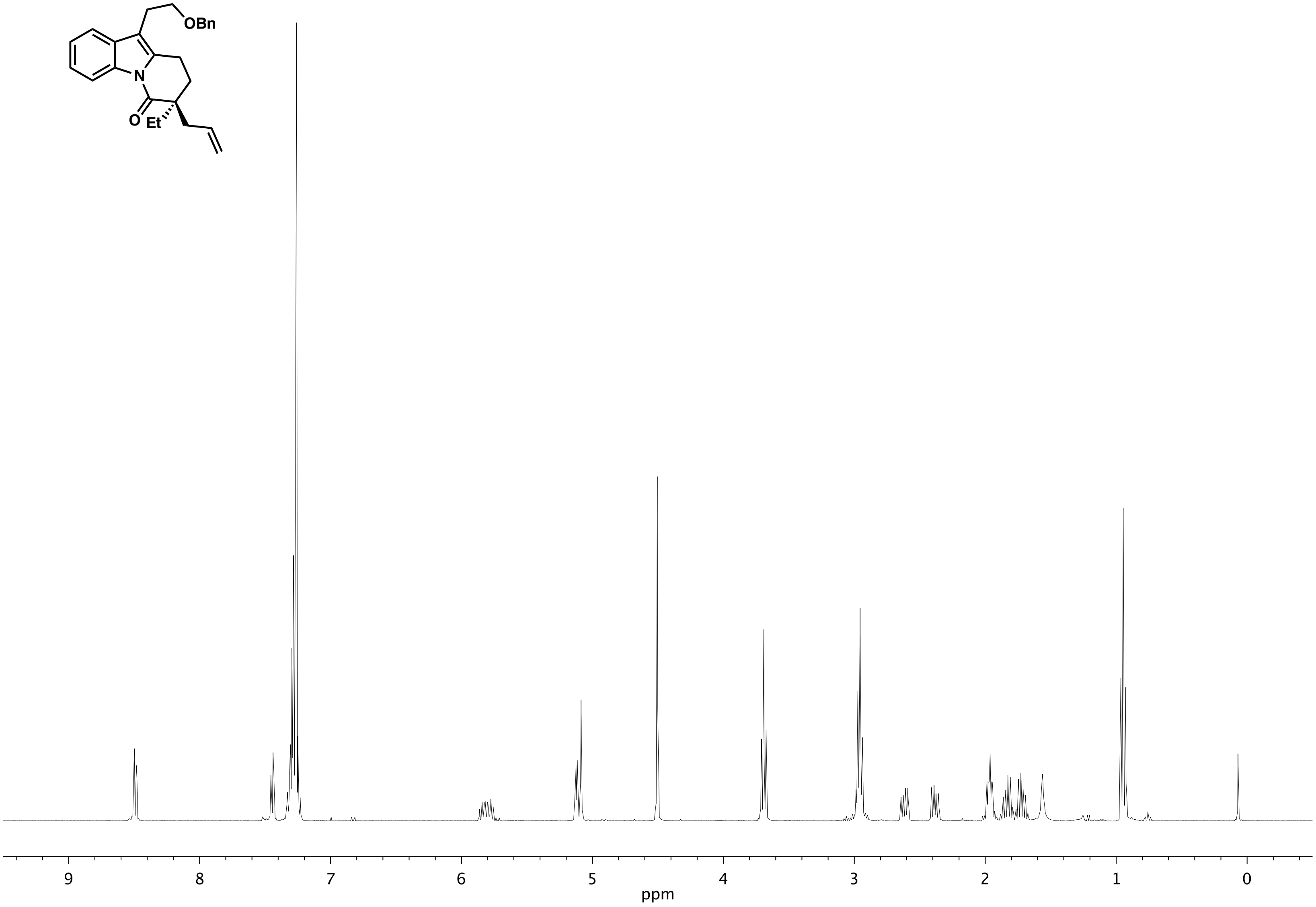
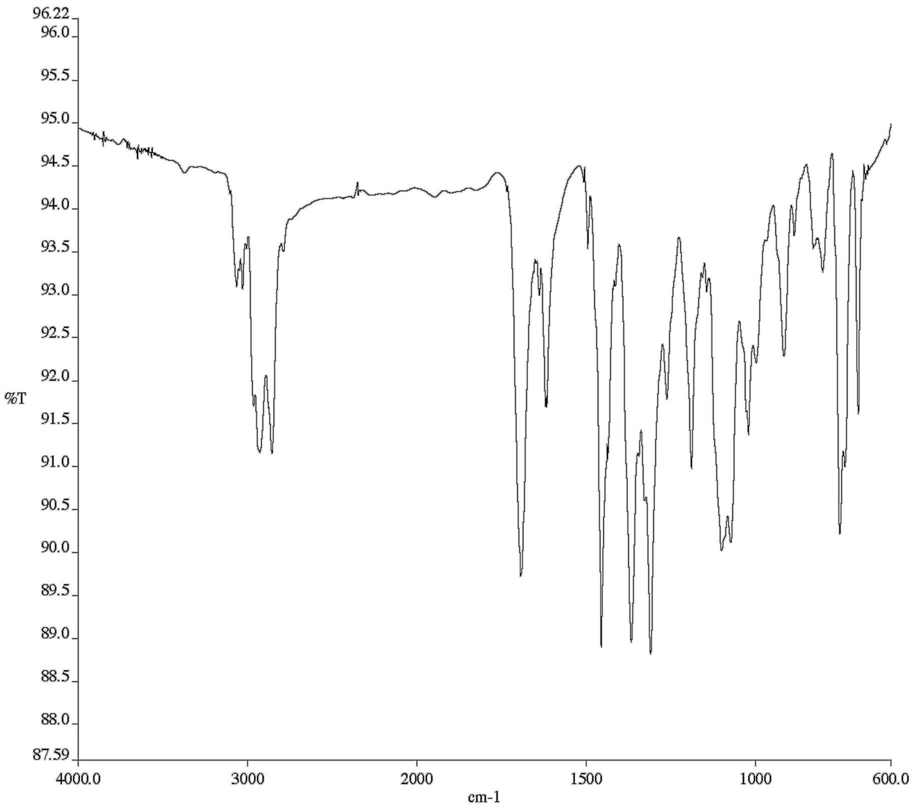
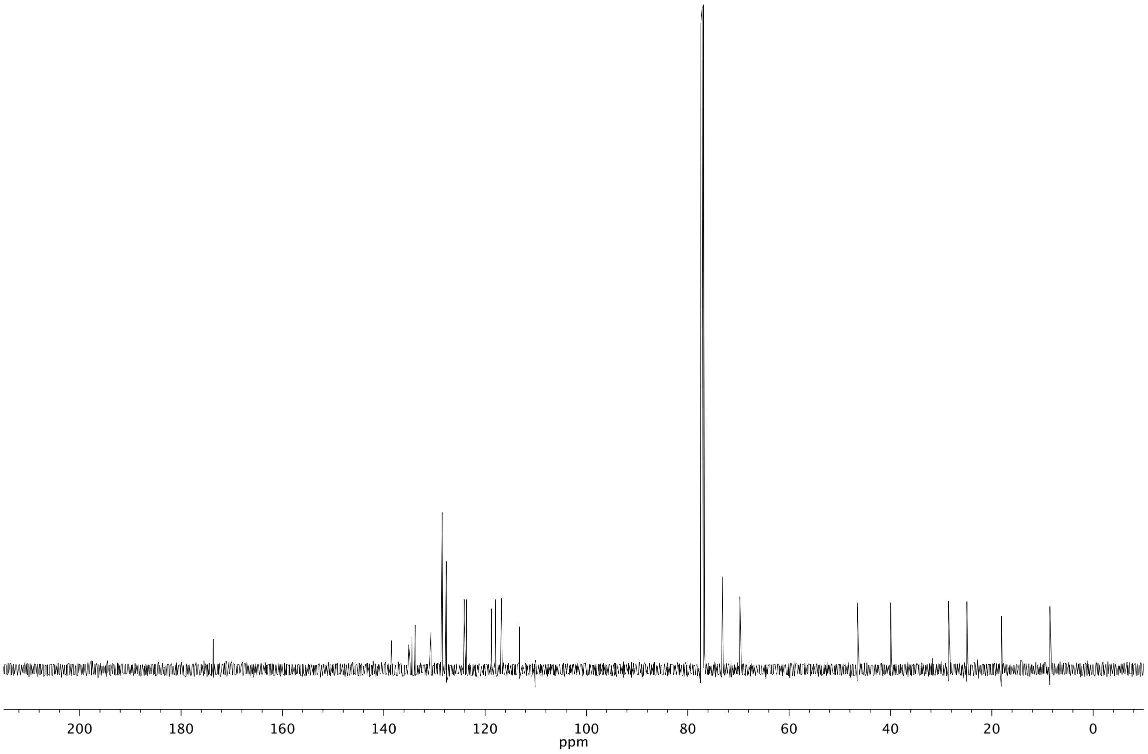


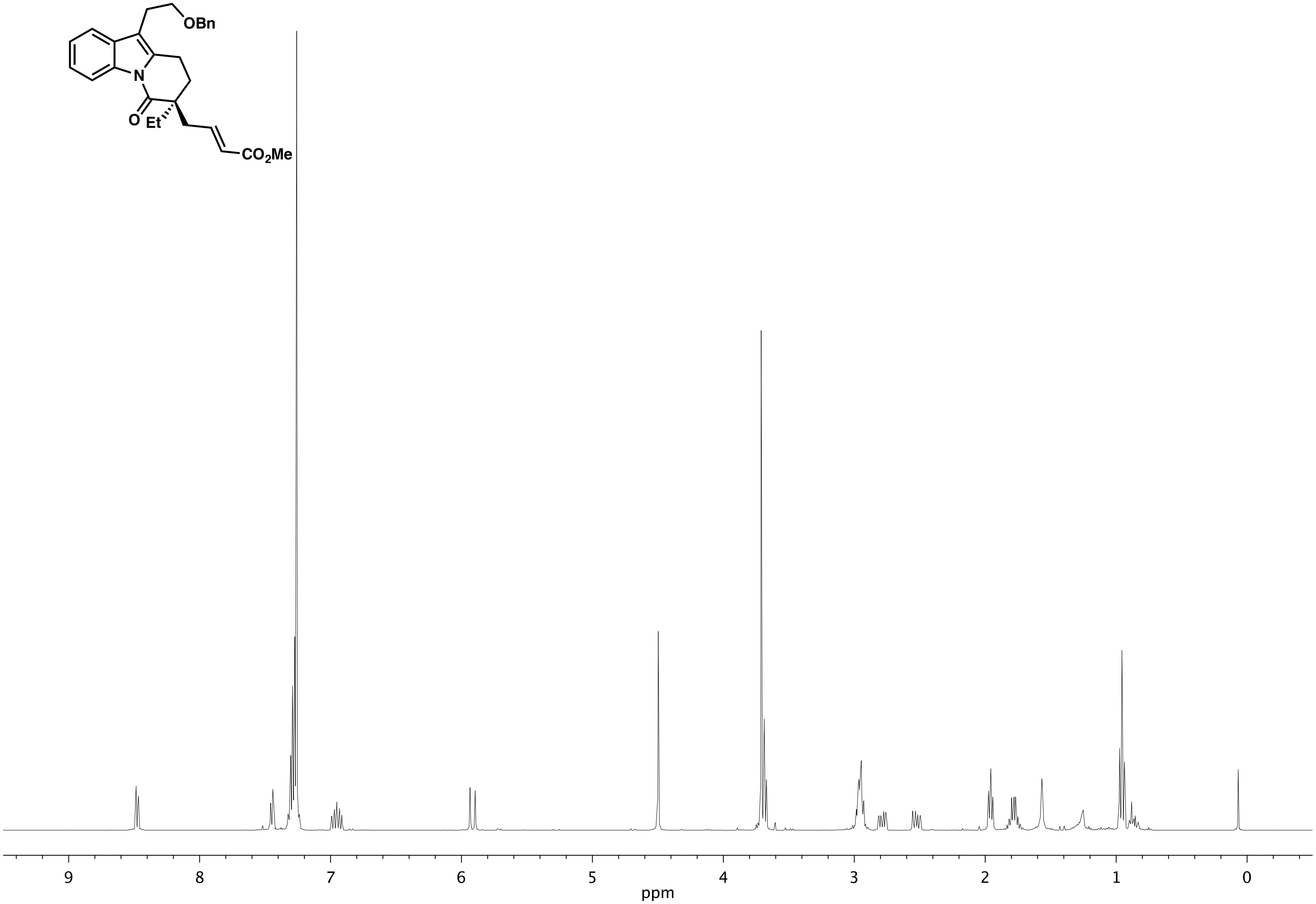
^{1}H NMR (400 MHz, CDCl$_3$) of compound **14a**.



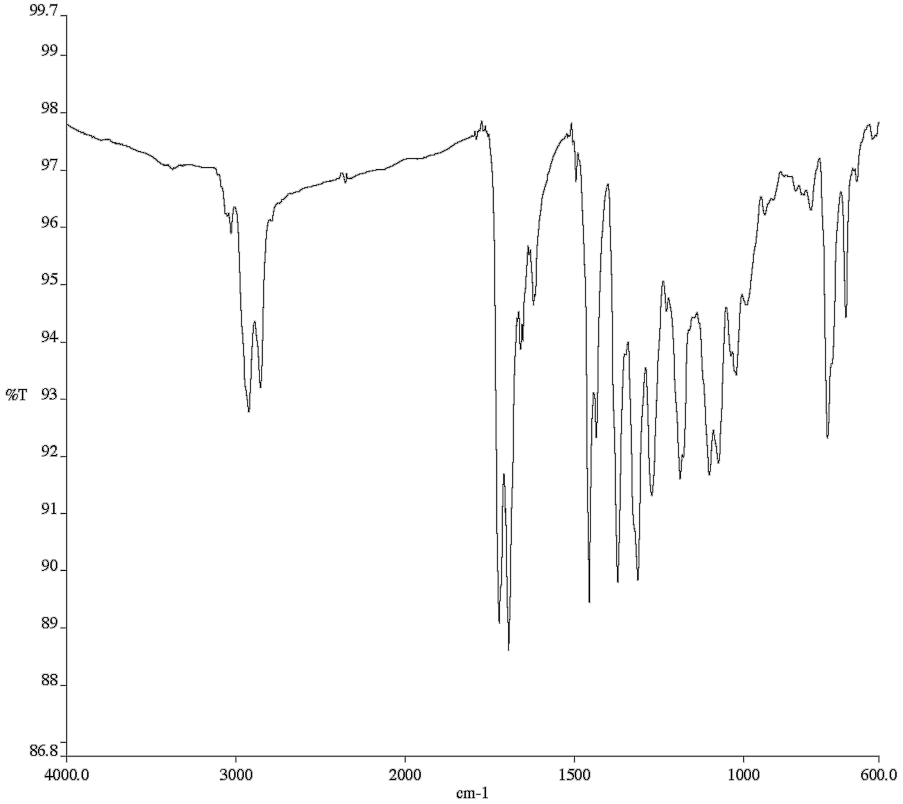
Infrared spectrum (Thin Film, NaCl) of compound **14a.**



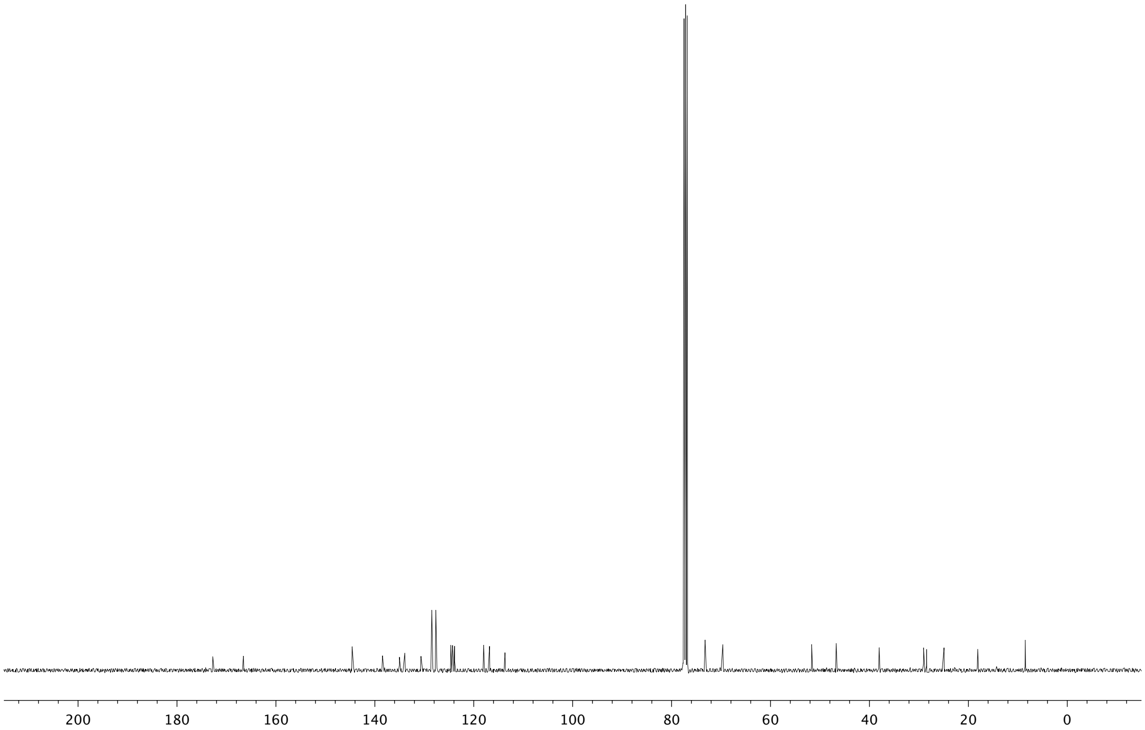
^{13}C NMR (126 MHz, $CDCl_3$) of compound **14a**.



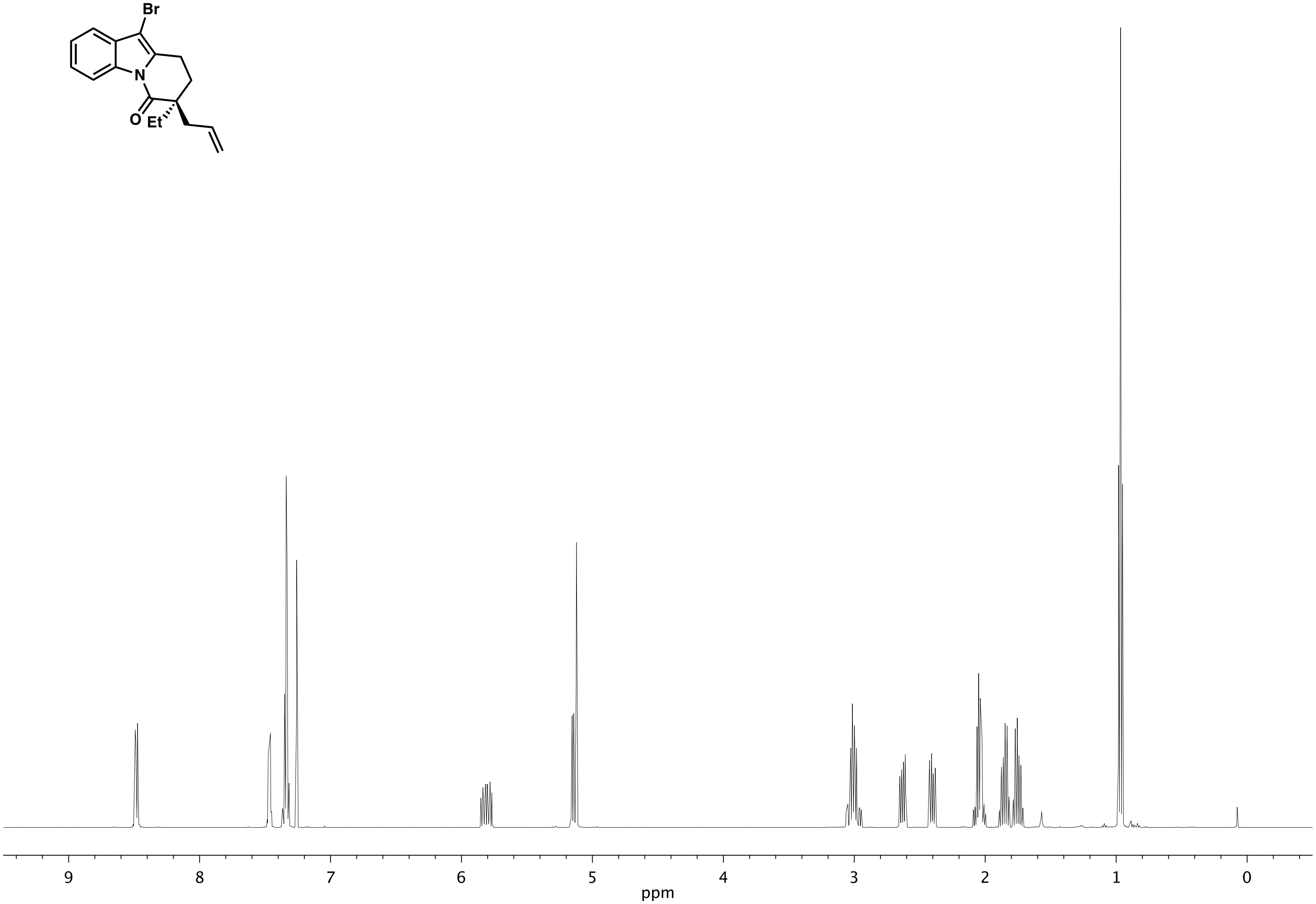
^{1}H NMR (400 MHz, CDCl$_3$) of compound **S6**.



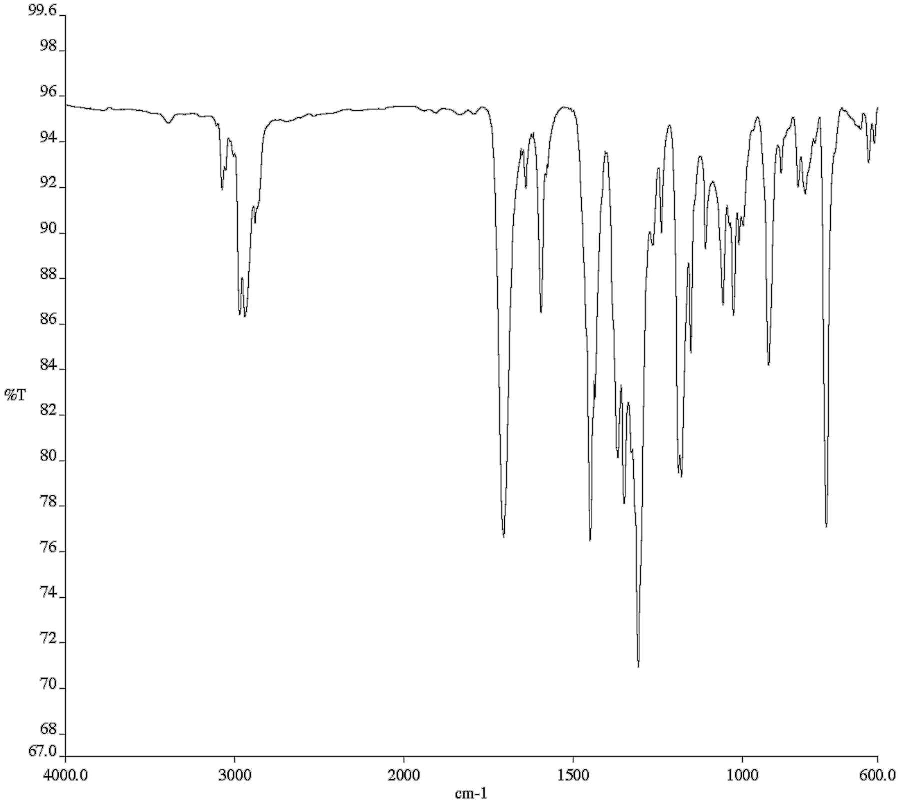
Infrared spectrum (Thin Film, NaCl) of compound **S6.**



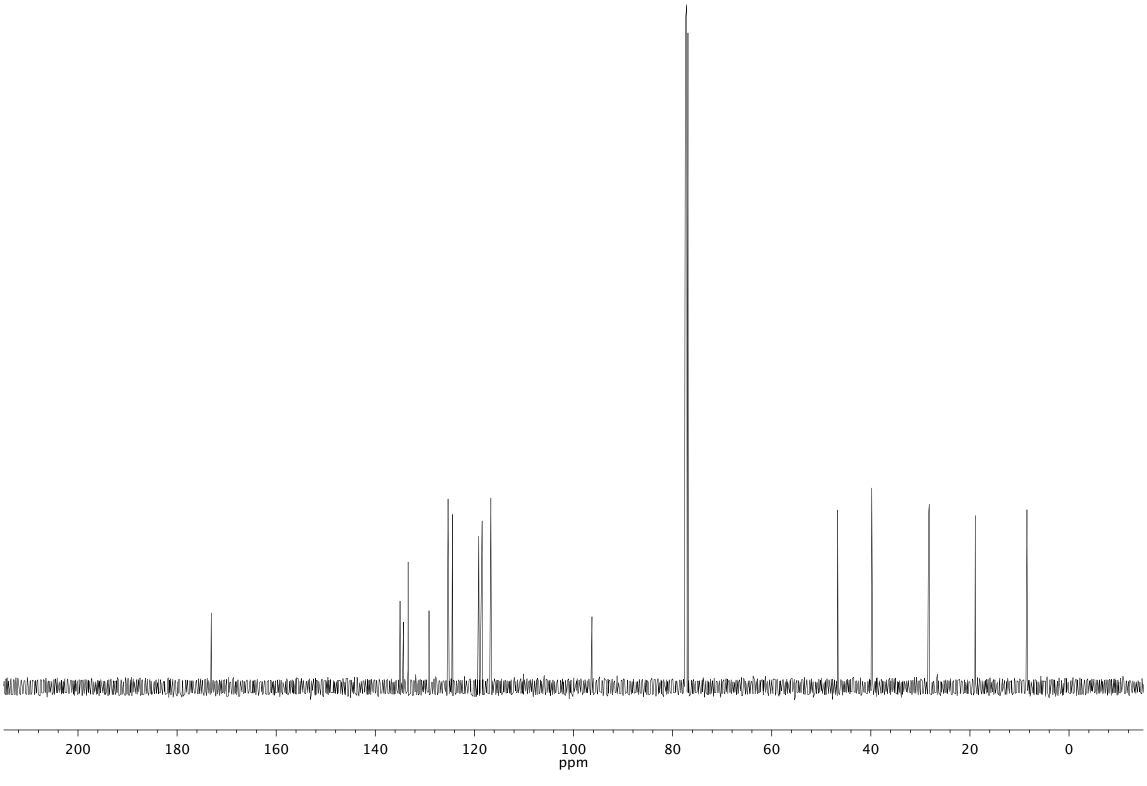
^{13}C NMR (101 MHz, $CDCl_3$) of compound **S6**.



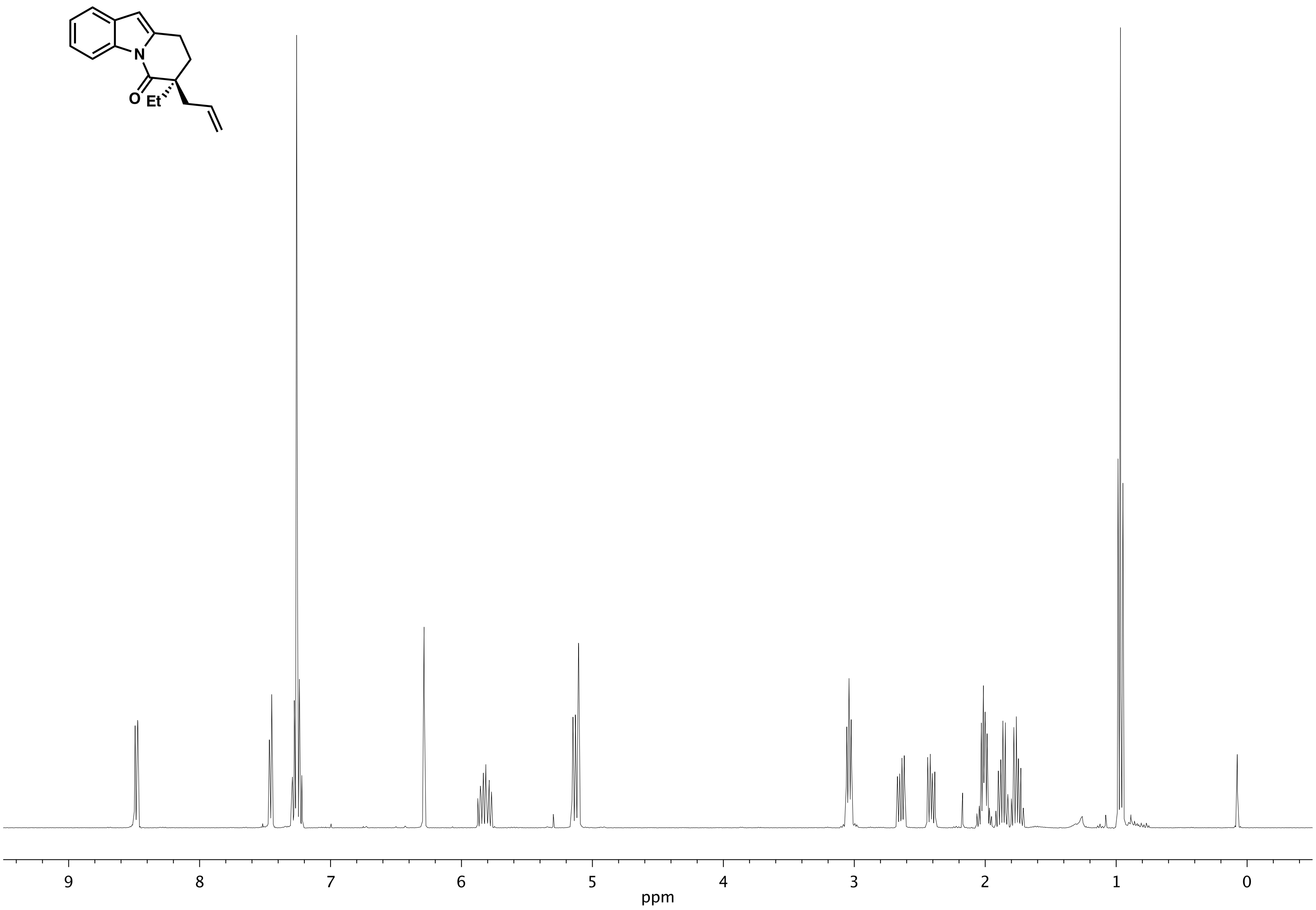
^{1}H NMR (500 MHz, $CDCl_3$) of compound **14b**.



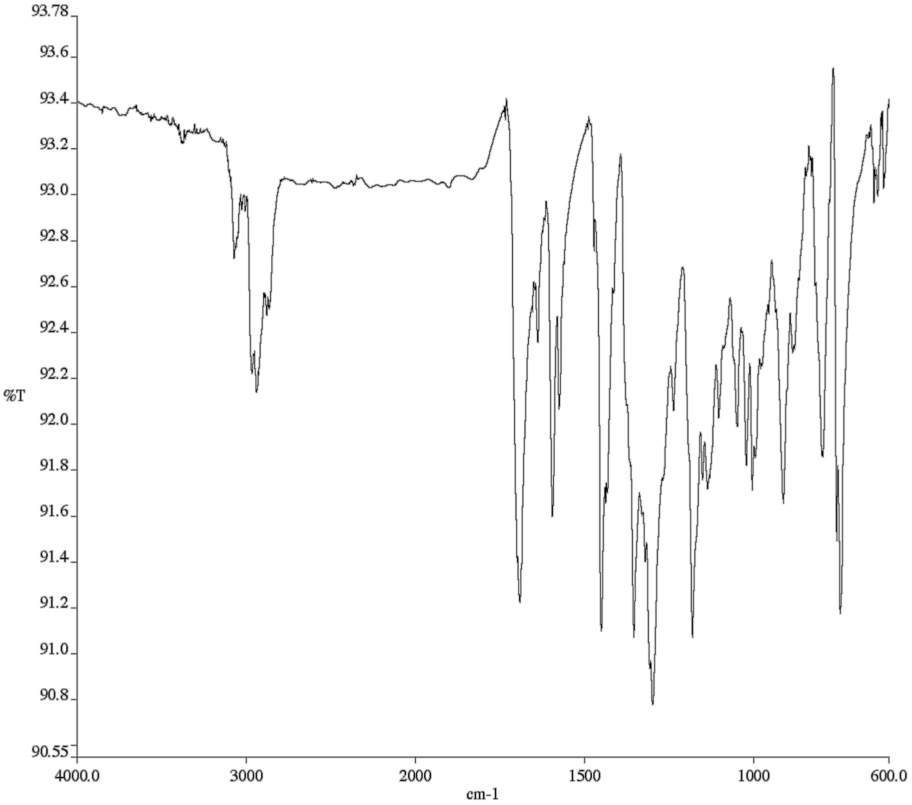
Infrared spectrum (Thin Film, NaCl) of compound **14b.**



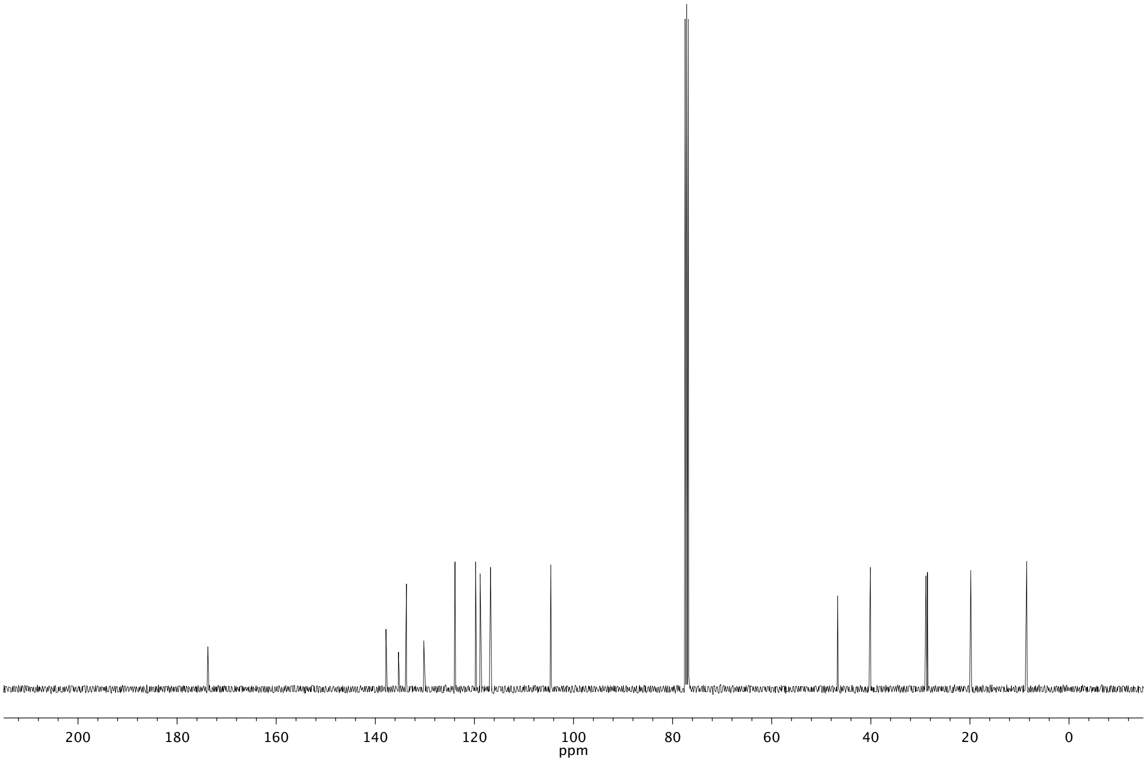
^{13}C NMR (126 MHz, $CDCl_3$) of compound **14b**.



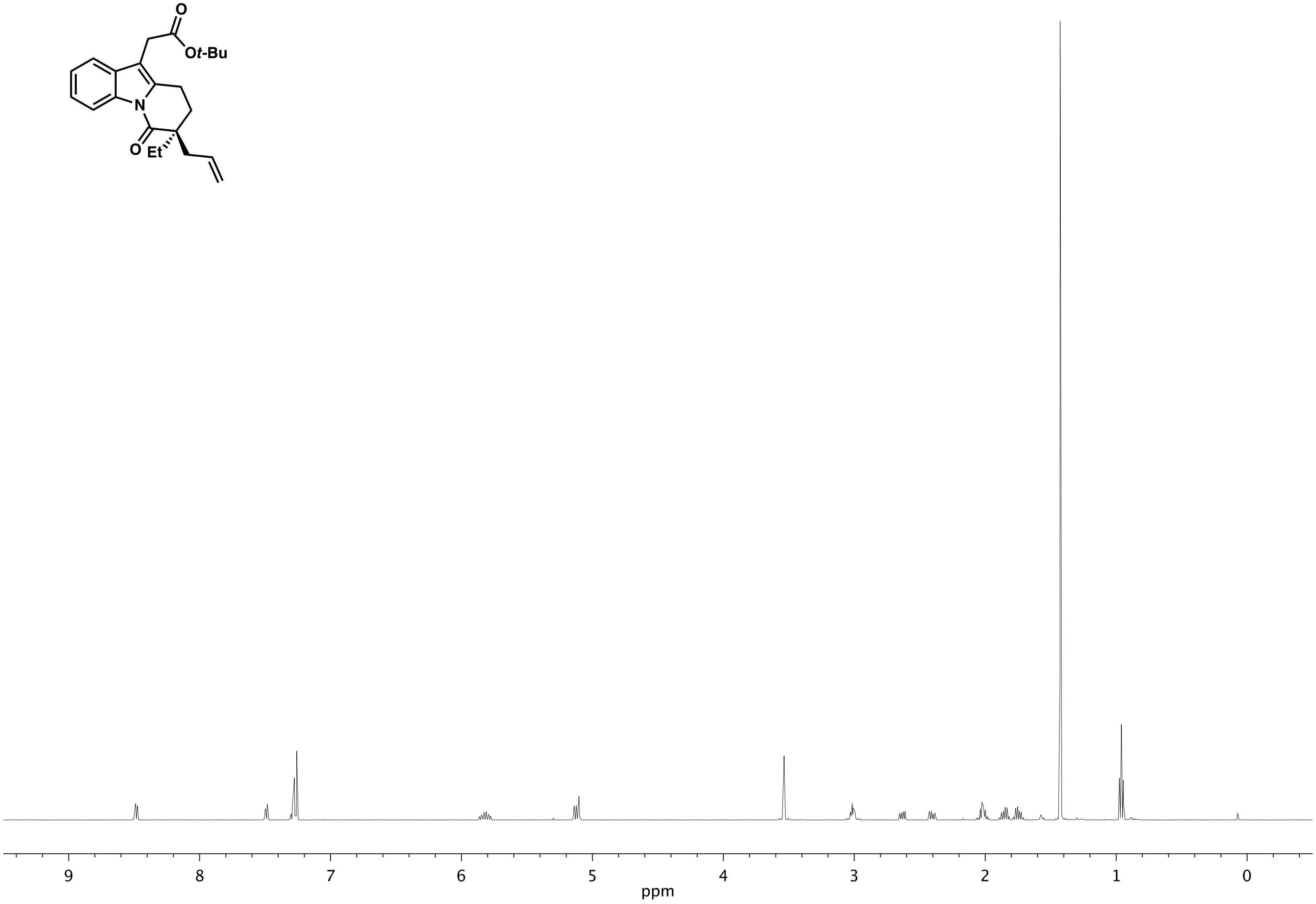
^{1}H NMR (400 MHz, $CDCl_3$) of compound **14c**.



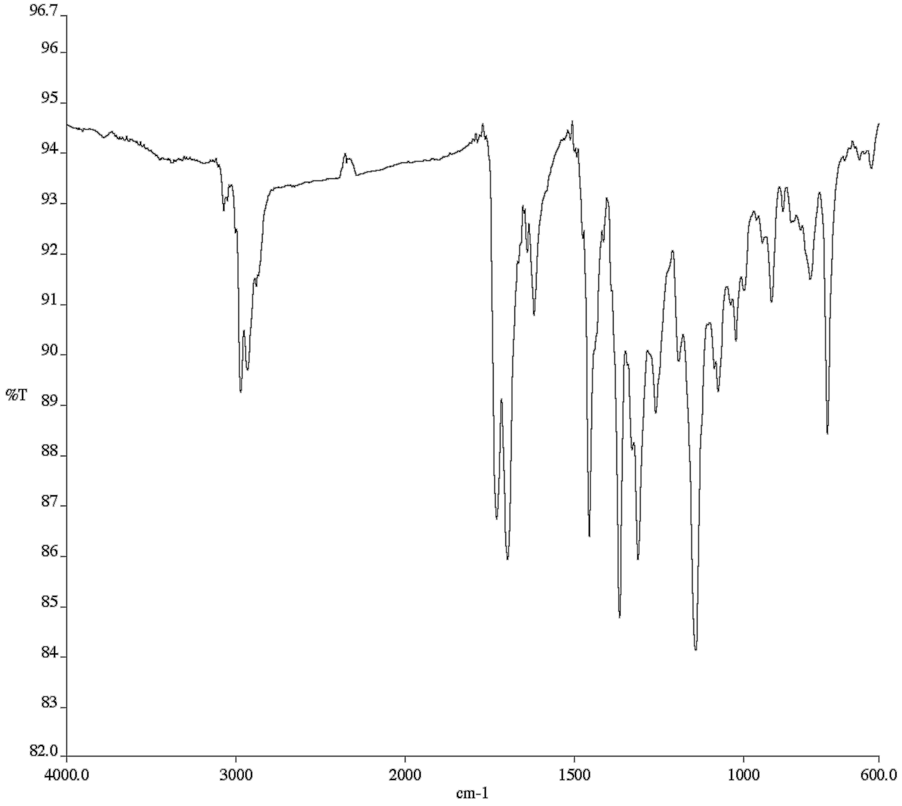
Infrared spectrum (Thin Film, NaCl) of compound **14c.**



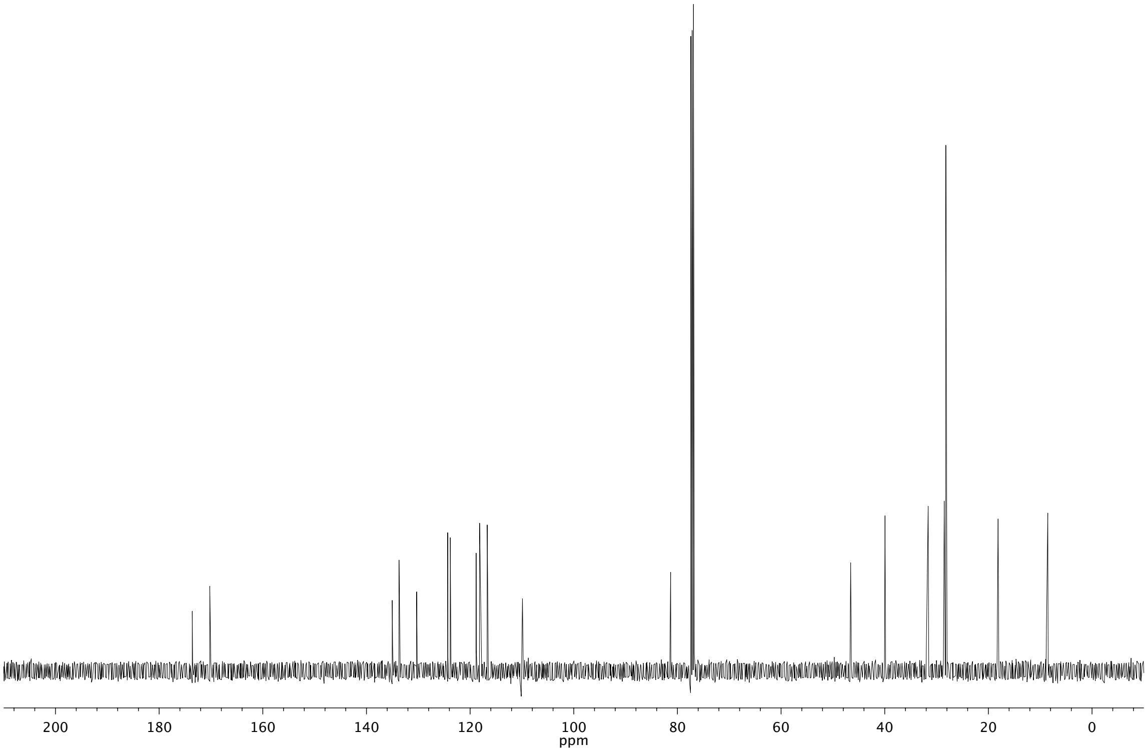
^{13}C NMR (101 MHz, $CDCl_3$) of compound **14c**.



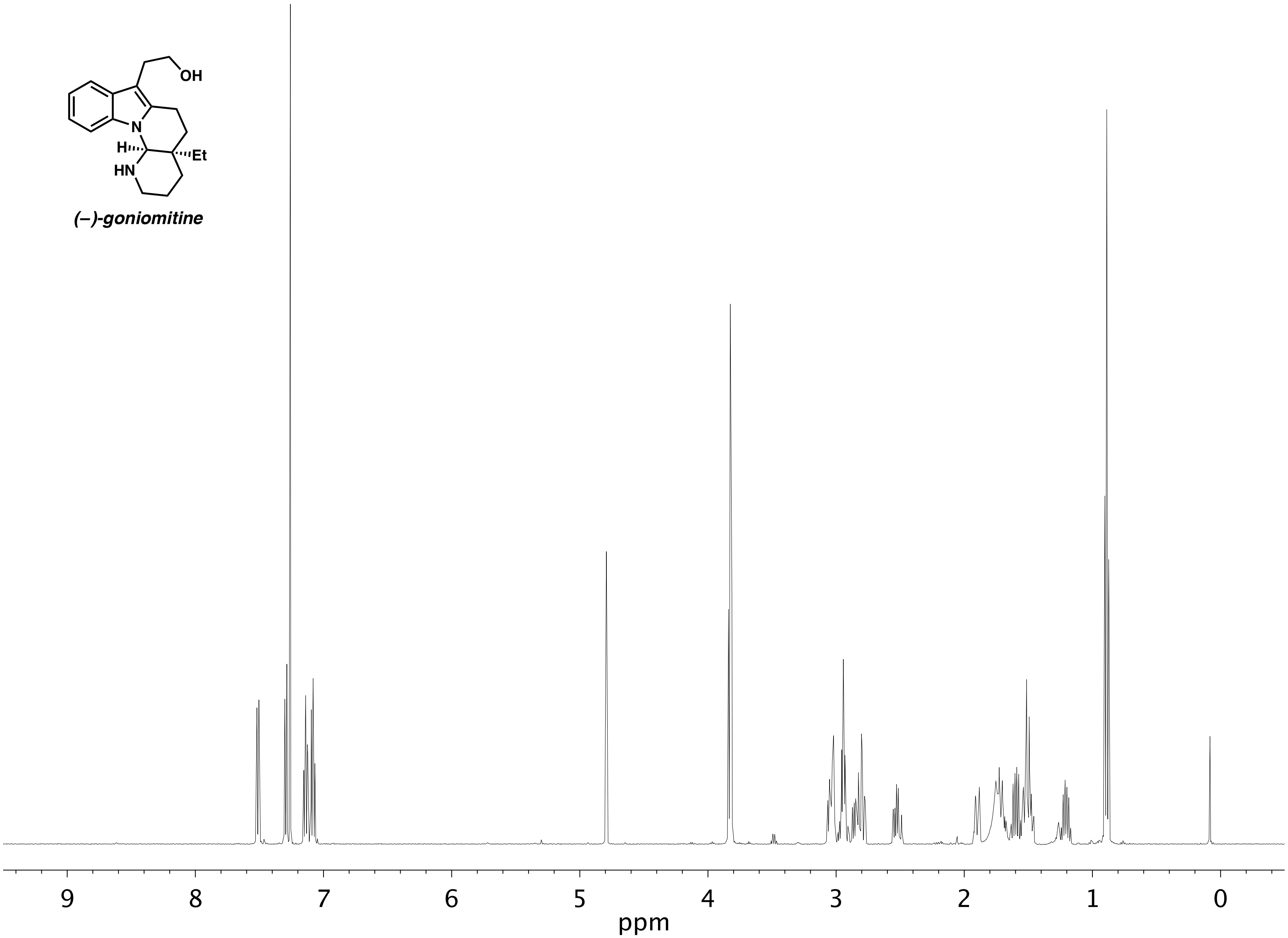
^{1}H NMR (500 MHz, CDCl$_3$) of compound **16**.



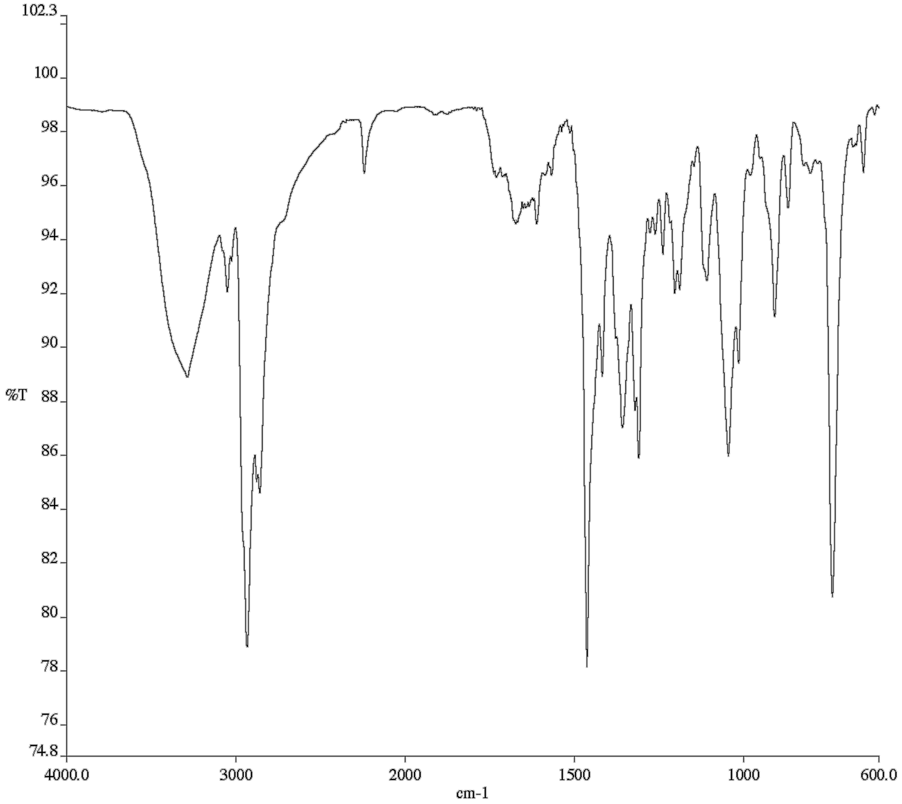
Infrared spectrum (Thin Film, NaCl) of compound **16.**



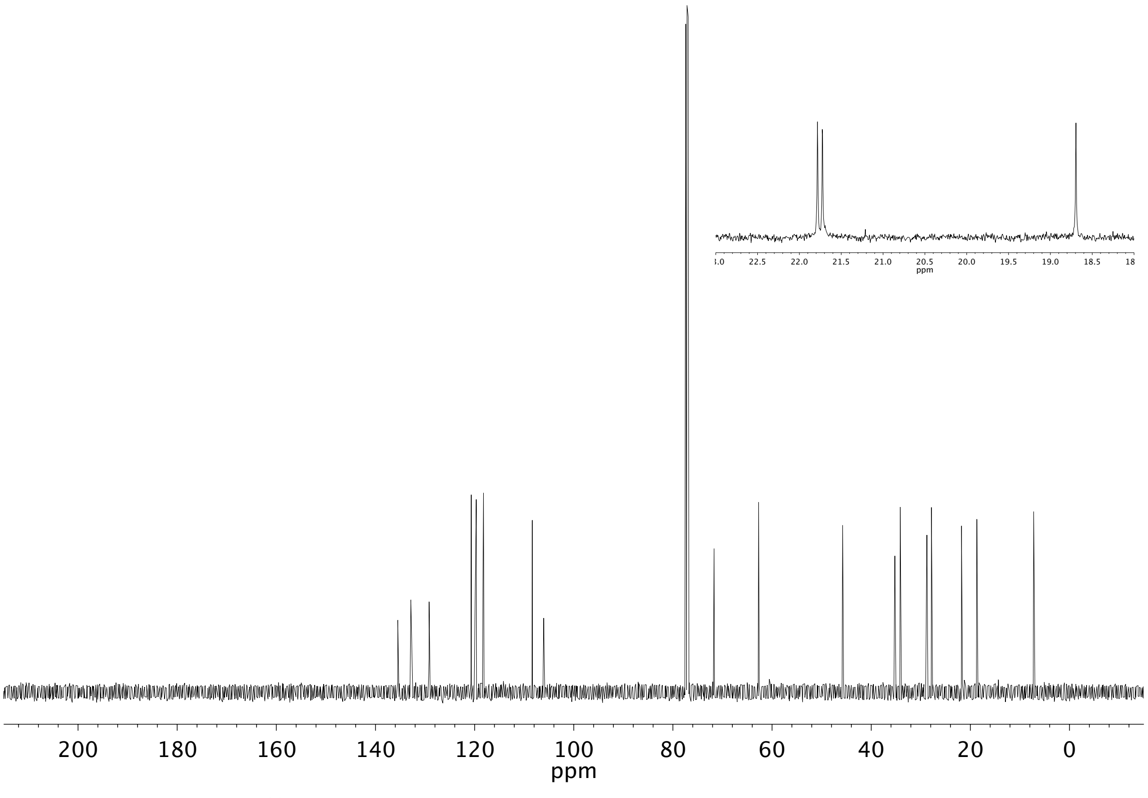
^{13}C NMR (126 MHz, CDCl$_3$) of compound **16**.



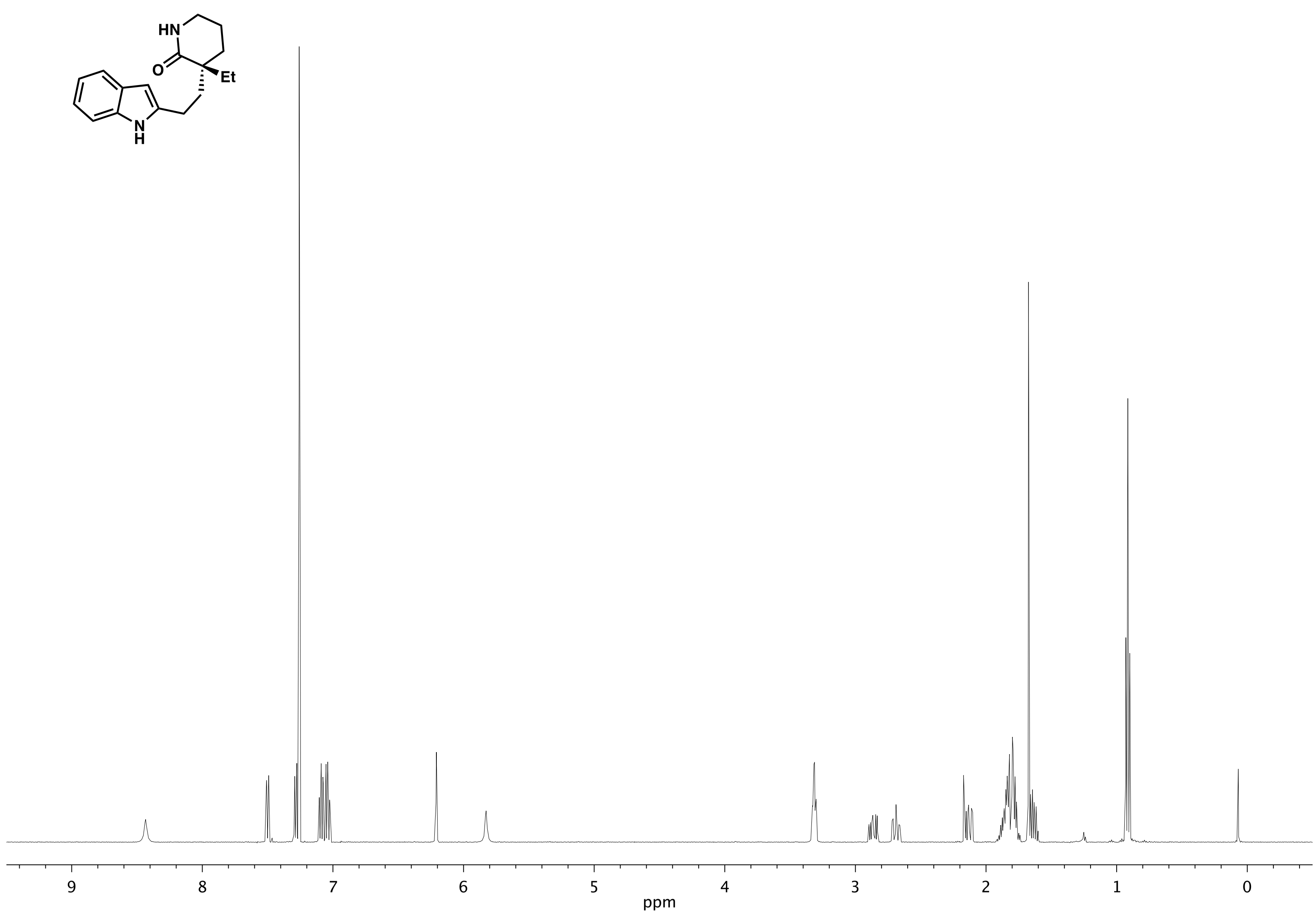
^{1}H NMR (500 MHz, $CDCl_3$) of (–)-goniomitine (**1**).



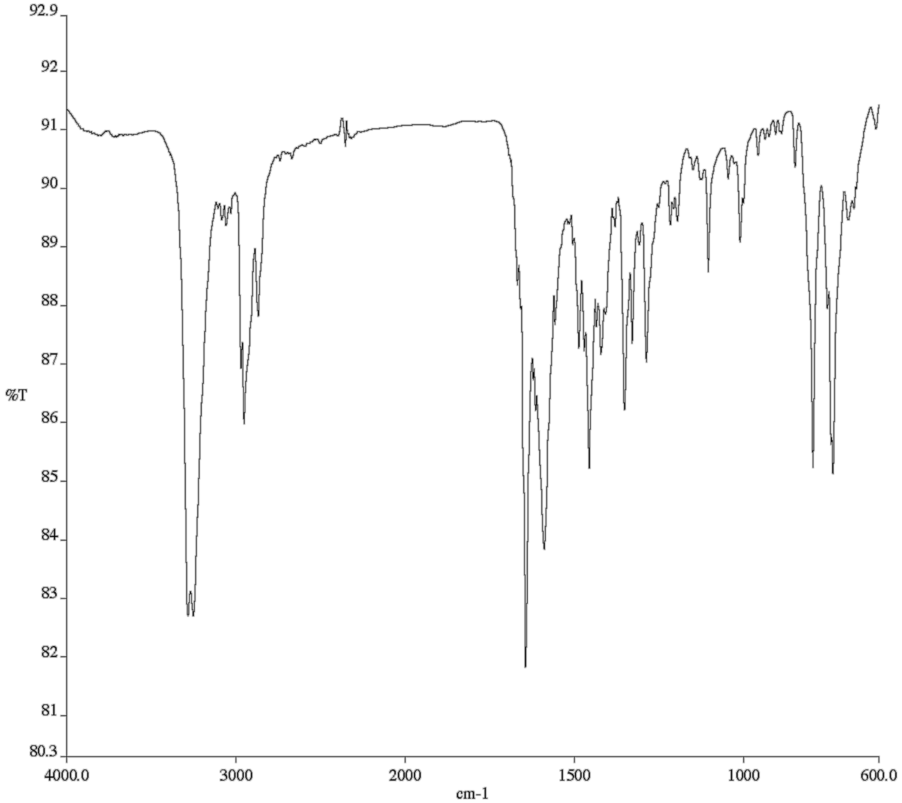
Infrared spectrum (Thin Film, NaCl) of (–)-goniomitine (**1**).



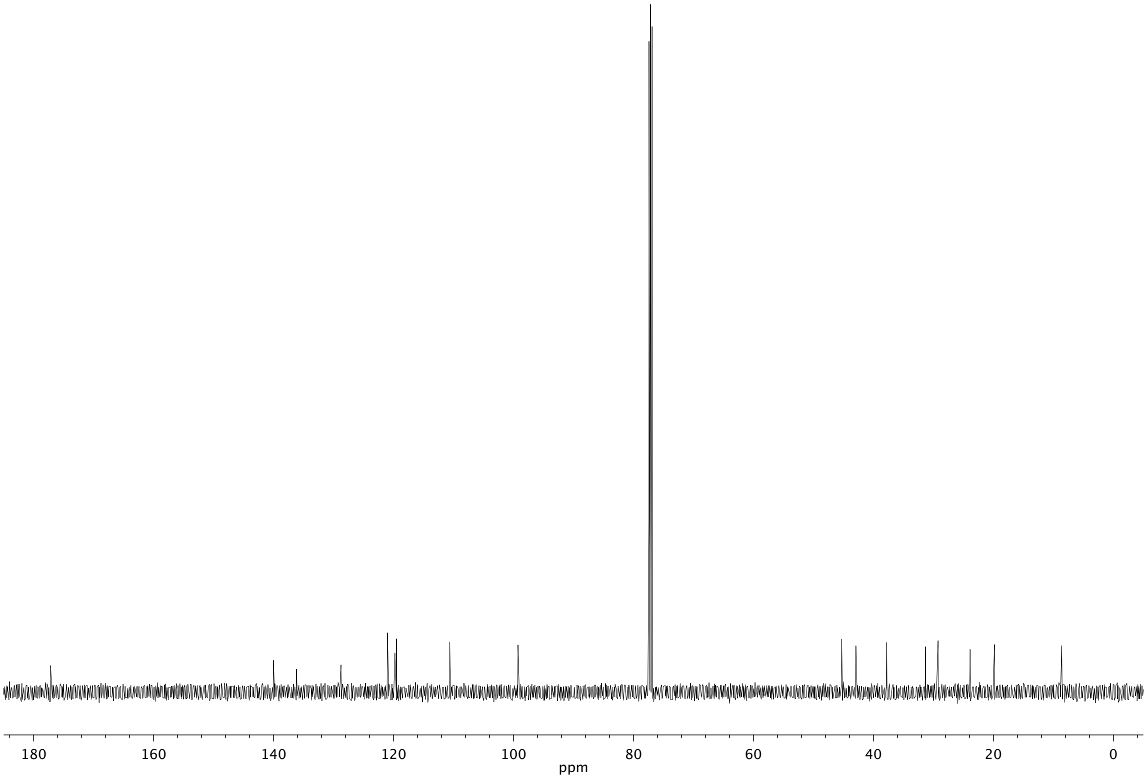
^{13}C NMR (126 MHz, $CDCl_3$) of (–)-goniomitine (**1**).



^{1}H NMR (500 MHz, CDCl$_3$) of compounds **18**.



Infrared spectrum (Thin Film, NaCl) of compound **18.**



^{13}C NMR (126 MHz, CDCl$_3$) of compound **18**.