Supplemental material for:

Synthesis of the Pentacyclic Skeleton of the Indole Alkaloid Arboflorine

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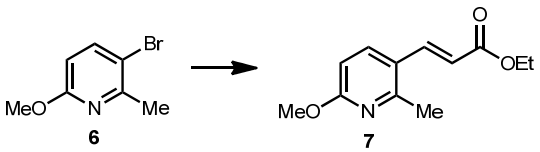
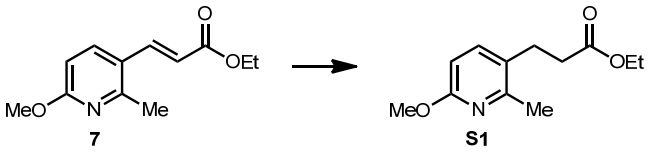
Materials and Methods

Unless stated otherwise, reactions were performed in flame-dried glassware sealed with rubber septa under a nitrogen atmosphere and the reaction mixture stirred with a Teflon-coated magnetic stir bar. Liquid reagents and solvents were transferred via syringe using standard Schlenk techniques. Tetrahydrofuran (THF), dichloromethane (DCM), diethyl ether (Et_2O), methanol (MeOH), and triethylamine (TEA) were dried by passage over a column of activated alumina; *N*,*N*-diisopropylethylamine (DIPEA) was distilled over calcium hydride. *N*,*N*-dimethylformamide (DMF) was obtained in Sure/Seal bottles from Acros. All other solvents and reagents were used as received unless otherwise noted. Reaction temperatures above 23 °C refer to oil bath temperature, which was controlled by an IKAmag temperature modulator. Reaction progress was monitored by thin layer chromatography using SiliCycle silica gel 60 F-254 precoated plates (0.25 mm) and visualized by UV irradiation (at 254 nm and 365 nm) and iodine stain. Sorbent silica gel (particle size 40-63 μm) was used for flash column chromatography (FCC). ^{1}H and ^{13}C NMR spectra were recorded on Bruker AVB-400, AVQ-400, DRX-500, AV-500, and AV-600 spectrometers. ^{1}H and ^{13}C chemical shifts (δ) are reported relative to the residual solvent signal, $CHCl_3$ (δ = 7.24 for ^{1}H NMR and δ = 77.23 for ^{13}C NMR) or DMSO-d_6 (δ = 2.50 for ^{1}H and δ = 39.51 for ^{13}C). Data are reported as follows: chemical shift (multiplicity, coupling constants where applicable, number of hydrogens). The following abbreviations are used to denote multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; m, multiplet; b, broad; app, apparent. IR spectra were recorded on a Nicolet MAGNA-IR 850 spectrometer and are reported in frequency of absorption (cm^{-1}). Only select IR peaks are reported. High resolution mass spectral data were obtained from the University of California, Berkeley Mass Spectral Facility. 6.28 M MOMCl in MeOAc was prepared according to a variation of the Belecki preparation,[1] where the reaction was run neat, in the absence of additional solvent. The resulting 6.28 M MOMCl in MeOAc solution was stored at 4 ºC and used as needed. Some of the abbreviations are defined as follows: MOM = methoxymethyl, nosyl = 2-nitrobenzenesulfonyl, (pin) = pinacolato.

Experimental Procedures



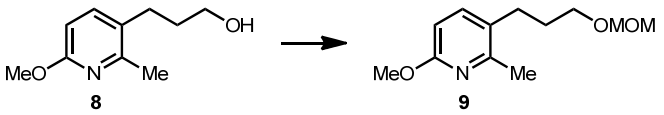
Ethyl 3-(6-methoxy-2-methylpyridin-3-yl)acrylate (**7**): A 500 mL Schlenk flask containing LiCl (12.7 g, 300 mmol, 3 equiv) was flame-dried under vacuum. 3-Bromo-6-methoxy-2-methylpyridine (**6**, 20.2 g, 100 mmol, 1 equiv), $PdCl_2(PPh_3)_2$ (1.63 g, 2.33 mmol, 2.3 mol %), TEA (42 mL, 300 mmol, 3 equiv), and DMF (100 mL) were added in single portions and the contents of the flask sparged with N_2 for 3 min under stirring. Ethyl acrylate (15 mL, 140 mmol, 1.4 equiv) was added in one portion. The flask was sealed, covered with aluminum foil, and the mixture was then stirred and heated at 100 ºC for 2 d. The reaction mixture went from bright yellow to dark yellow over the course of the reaction. The reaction mixture was partitioned between EtOAc (500 mL) and 1:1 brine:water (500 mL). The aqueous layer was back-extracted with EtOAc (200 mL). The organic fractions were combined, washed with water (2x 200 mL), brine (300 mL), dried over $MgSO_4$, filtered through Celite, evaporated under reduced pressure, dried under high vacuum, and purified by FCC (9:1 hexanes/EtOAc, wet-loaded in DCM and eluent). Fractions containing product were concentrated under reduced pressure and dried under high vacuum overnight to yield acrylate **7** (20.7 g, 93.4 mmol, 93% yield) as a slightly yellow, clear oil. $\mathbf{R_f}$ 0.55 (4:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 15.8 Hz, 1H), 7.69 (d, *J* = 8.6 Hz, 1H), 6.55 (d, *J* = 8.6 Hz, 1H), 6.21 (d, *J* = 15.9 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 3H), 2.54 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.1, 164.3, 156.4, 140.6, 136.6, 121.8, 117.7, 108.9, 60.6, 53.7, 22.4, 14.5; **IR** (thin film) ν: 3069, 2982, 1712, 1631, 1594, 1479, 1424, 1402, 1369, 1307, 1262, 1176, 1097, 1038 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ $\mathbf{C_{12}H_{16}O_3N}$: 222.1130. Found: 222.1129.



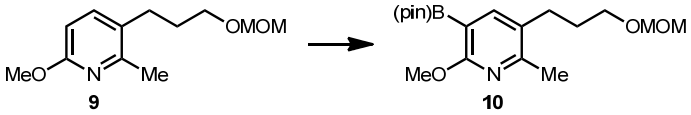
Ethyl 3-(6-methoxy-2-methylpyridin-3-yl)propanoate (**S1**): A 1 L round-bottom flask (RBF) containing acrylate **7** (20.7 g, 93.4 mmol), $Pd(OH)_2/C$ (311 mg, 20% dry basis, 1.5 wt %), and MeOH (188 mL, 0.5 M) was evacuated and backfilled with H_2 (3x), and placed under H_2 at ambient pressure. The reaction mixture was stirred vigorously for 1 d. The mixture was diluted

with 100 mL EtOAc, filtered through a plug of Celite, and the filter cake was rinsed with EtOAc. The filtrate was concentrated under reduced pressure and dried under high vacuum with heat to yield crude propanoate **S1** (20.6 g, 92.1 mmol, 99% yield) as a slightly yellow, clear oil. $\mathbf{R_f}$ 0.47 (4:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.3 Hz, 1H), 6.47 (d, *J* = 8.3 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 2.83 (t, *J* = 7.8 Hz, 2H), 2.49 (t, *J* = 7.8 Hz, 2H), 2.41 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.9, 162.2, 153.9, 139.7, 126.0, 107.5, 60.7, 53.4, 34.8, 27.2, 22.0, 14.4. **IR** (thin film) ν: 2981, 2942, 2873, 1735, 1600, 1478, 1426, 1373, 1308, 1258, 1177, 1042 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ $\mathbf{C_{12}H_{18}O_3N}$: 224.1287. Found: 224.1283.

3-(6-Methoxy-2-methylpyridin-3-yl)propan-1-ol (**8**): A 1 L RBF containing a solution of propanoate **S1** (20.6 g, 92.1 mmol, 1 equiv) in Et_2O (500 mL, 0.18 M) at 0 ºC, was charged with LAH (10.7 g, 281 mmol, 3 equiv), portionwise, over the course of 5 min. The reaction mixture was stirred at 0 ºC for an additional 2.5 h, then warmed to 23 ºC and stirred for 1.5 h. Celite (~20 mL) was added and stirred with the reaction mixture. The reaction mixture was quenched dropwise and sequentially with H_2O (10.7 mL), 15% NaOH (10.7 mL), and H_2O (32 mL) over the course of 20 min between 23 ºC and 0 ºC. Manual stirring was used when the stir bar failed during the workup. The mixture was filtered through Celite and rinsed with copious amounts of EtOAc (~500 mL). The filtrate was concentrated under reduced pressure and dried under high vacuum with heat to yield crude alcohol **8** (16.7 g, 92.3 mmol, quant.) as a faintly yellow, clear oil that was used without further purification. An analytical sample of alcohol **8** was obtained by FCC (2:1→1:1 hexanes/EtOAc) as a clear oil. $\mathbf{R_f}$ 0.40 (1:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.3 Hz, 1H), 6.48 (d, *J* = 8.3 Hz, 1H), 3.86 (s, 3H), 3.65 (t, *J* = 6.4 Hz, 2H), 2.59 (t, *J* = 7.8 Hz, 2H), 2.41 (s, 3H), 1.77 (tt, *J* = 7.8, 6.4 Hz, 2H), 1.70 (s, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.0, 153.8, 139.8, 127.3, 107.3, 62.3, 53.5, 33.2, 28.1, 22.0. **IR** (thin film) ν: 3355, 2941, 2869, 2360, 1599, 1582, 1477, 1425, 1307, 1259, 1044 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ $\mathbf{C_{10}H_{16}O_2N}$: 182.1181. Found: 182.1177.

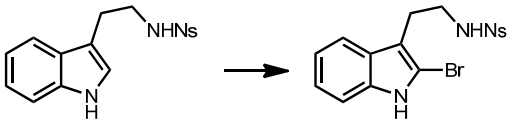


6-Methoxy-3-(3-(methoxymethoxy)propyl)-2-methylpyridine (**9**): A 1 L RBF containing a solution of crude alcohol **8** (16.7 g, 92.1 mmol, 1 equiv) in DCM (100 mL, 0.9 M) at 0 ºC, was charged with 6.28 M MOMCl in MeOAc (19 mL, 120 mmol, 1.3 equiv) followed by DIPEA (29 mL, 170 mmol, 1.8 equiv) in single portions. The reaction mixture was stirred at 0 ºC for 10 min then stirred at 23 ºC overnight. The mixture was partitioned between sat. $NaHCO_3$ (200mL) and DCM (200 mL). The aqueous layer was extracted with DCM (3x 50 mL). The organic fractions were combined, dried over $MgSO_4$, filtered, concentrated under reduced pressure, and dried under high vacuum overnight to yield crude MOM ether **9** (20.8 g) as an orange-yellow oil. The crude product was purified by FCC (1 L SiO_2, 5 in height, 8:1→6:1 hexanes/EtOAc, wet-loaded in 60 mL eluent). Fractions containing product were combined, concentrated under reduced pressure, and dried under high vacuum with heat to yield MOM ether **9** (19.6 g, 85.0 mmol, 91% yield over three steps from **20**) as a clear oil. **R_f** 0.68 (1:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.3 Hz, 1H), 6.48 (d, *J* = 8.3 Hz, 1H), 4.62 (s, 2H), 3.87 (s, 3H), 3.53 (t, *J* = 6.3 Hz, 2H), 3.36 (s, 3H), 2.60 (t, *J* = 7.8 Hz, 2H), 2.42 (s, 3H), 1.81 (tt, *J* = 7.6, 6.3 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.0, 153.9, 139.8, 127.3, 107.4, 96.7, 67.2, 55.4, 53.5, 30.4, 28.6, 22.0; **IR** (thin film) ν: 2914, 2882, 1599, 1580, 1477, 1425, 1307, 1260, 1147, 1111, 1039, 993, 919, 827 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ **$C_{12}H_{20}O_3N$**: 226.1438. Found: 226.1441.

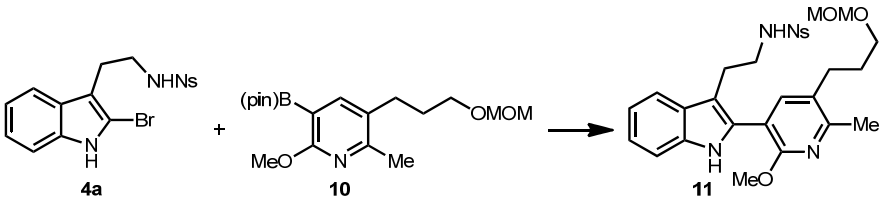


Boronic ester (**10**): A Schlenk flask containing MOM ether **9** (662 mg, 2.94 mmol, 1 equiv), [Ir(1,5-cyclooctadiene)(OMe)]$_2$ (40 mg, 0.060 mmol, 2.0 mol %), 4,4'-di-*tert*-butyl-2,2'-dipyridine (27.6 mg, 0.103 mmol, 3.5 mol %), $B_2(pin)_2$ (1.00 g, 3.94 mmol, 1.34 equiv), and THF (15 mL, 0.2 M) was evacuated and backfilled with N_2 (3x), and sealed. The reaction mixture was then stirred and heated at 80 ºC for 2 d. The mixture was loaded on Celite and excess $B_2(pin)_2$ was removed by Kugelrohr distillation (0.08 mbar, 100 ºC, 2.5 h). The Celite was filtered and rinsed with Et_2O. The filtrate was purified by FCC (4:1:1→2:1:1 hexanes/EtOAc/DCM, wet-loaded in DCM + eluent). Fractions containing product were concentrated under reduced pressure and dried under high vacuum overnight to yield boronic

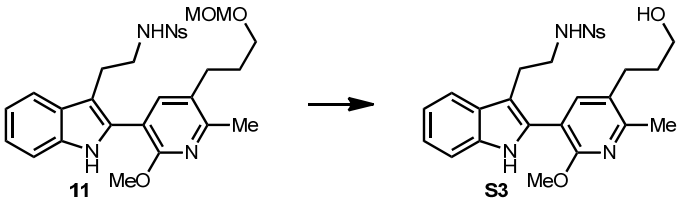
ester **10** (0.782 g, 2.21 mmol, 76% yield) as a viscous, slightly yellow oil. $\mathbf{R_f}$ 0.31 (4:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 4.61 (s, 2H), 3.90 (s, 3H), 3.51 (t, *J* = 6.3 Hz, 2H), 3.35 (s, 3H), 2.59 (t, *J* = 7.8 Hz, 2H), 2.41 (s, 3H), 1.81 (tt, *J* = 7.8, 6.4 Hz, 2H), 1.31 (s, 12H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.4, 157.2, 147.7, 126.8, 96.7, 83.7, 67.3, 55.4, 53.8, 30.5, 28.4, 25.0, 22.2. The boron-bound carbon was not detected due to quadrupolar relaxation;[2] **IR** (thin film) ν: 2978, 2947, 2930, 1599, 1566, 1460, 1396, 1373, 1328, 1283, 1145, 1111, 1058, 1038 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ **$C_{18}H_{31}O_5NB$**: 352.2290. Found: 352.2298.



2-Bromo-*N*-nosyltryptamine (**4a**): An RBF containing a solution of *N*-nosyltryptamine (**S2**, 1.01 g, 2.91 mmol, 1 equiv)[3] in 1:1 THF:$CHCl_3$ (170 mL, 0.017M) was cooled to 0 ºC in an ice bath for 15 min. Pyridinium tribromide (1.02 g, 3.19 mmol, 1.1 equiv) was added portionwise to the reaction mixture over the course of 45 min. The reaction mixture was warmed to room temperature and stirred for an additional 35 min. The mixture was quenched with sat. Na_2SO_3 (30 mL), followed by sat. $NaHCO_3$ (30 mL) one minute later. The aqueous layer was extracted with $CHCl_3$ (2 x 30 mL). The organic fractions were combined, dried over $MgSO_4$, filtered, and purified by FCC (2:1 hexanes/EtOAc, dry-loaded on SiO_2). Fractions containing product were concentrated under reduced pressure to a yellow oil. The oil was dissolved in DCM and made turbid with Et_2O and hexanes. The mixture was concentrated under reduced pressure and dried under high vacuum overnight to yield aryl bromide **4a** (0.908 g, 2.14 mmol, 73% yield) as a white powder (was also isolated as a grey or yellow powder on occasion). $\mathbf{R_f}$ 0.48 (1:1 hexanes/EtOAc); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.65 (bs, 1H), 8.22 (t, *J* = 5.8 Hz, 1H), 7.97 – 7.89 (m, 2H), 7.85 – 7.75 (m, 2H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.07 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H), 6.99 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 3.12 (dt, *J* = 7.9, 6.2 Hz, 2H), 2.81 (t, *J* = 7.7 Hz, 2H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 147.6, 136.1, 133.9, 132.9, 132.6, 129.3, 127.0, 124.4, 121.6, 119.3, 117.6, 110.8, 110.1, 109.0, 42.8, 25.4; **IR** (thin film) ν: 3376, 1538, 1449, 1415, 1337, 1164, 1124, 1073 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+Na]^+$ **$C_{16}H_{14}O_4N_3BrSNa$**: 445.9781. Found: 445.9780.

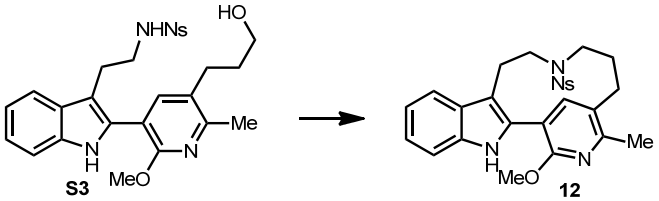


Biaryl MOM ether (**11**): A 400 mL pressure flask containing tryptamine fragment **4a** (3.30 g, 7.77 mmol, 1 equiv), pyridine fragment **10** (2.78 g, 7.92 mmol, 1.02 equiv), $Pd(PPh_3)_4$ (448 mg, 0.388 mmol, 5.0 mol %), Na_2CO_3 (2.47 g, 23.3 mmol, 3 equiv), LiCl (1.00 g, 23.6 mmol, 3 equiv), and dimethoxymethane (DMM):H_2O 9:1 (78 mL, 0.1 M) was sparged with N_2 for 4 min under stirring, sealed and then heated at 120 ºC for 3.5 h with vigorous stirring (Caution! Vessel is under high pressure! Use a blast shield and appropriate vessel for the reaction). The reaction mixture was partitioned between EtOAc (250 mL) and 1:4 sat. NH_4Cl:water (200 mL). The organic layer was washed with 1:9 sat $NaHCO_3$:water (100 mL), brine (100 mL), dried over $MgSO_4$, filtered, and purified by FCC (5:1→2:1 toluene/EtOAc). Fractions containing only product were concentrated under reduced pressure and dried under high vacuum with heat to yield biaryl compound **11** (2.24 g, 3.93 mmol, 51% yield) as an orange gum. Vigorous stirring in this biphasic reaction is necessary for high yields. $\mathbf{R_f}$ 0.30 (5:1 toluene/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.92 (dd, *J* = 5.5, 3.5 Hz, 1H), 7.60 – 7.51 (m, 3H), 7.50 (s, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.27 (d, *J* = 8.1 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.91 (t, *J* = 7.4 Hz, 1H), 5.66 (bt, *J* = 5.2 Hz, 1H), 4.65 (s, 2H), 3.98 (s, 3H), 3.58 (t, *J* = 6.2 Hz, 2H), 3.43 (td, *J* = 6.6, 5.9 Hz, 2H), 3.37 (s, 3H), 3.06 (t, *J* = 7.0 Hz, 2H), 2.69 (t, *J* = 7.6 Hz, 2H), 2.50 (s, 3H), 1.87 (tt, *J* = 7.3, 6.4 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.2, 153.9, 147.5, 140.1, 135.8, 133.3, 132.5, 131.4, 130.8, 127.80, 127.76, 125.3, 122.3, 119.6, 118.3, 112.2, 111.1, 109.1, 96.6, 67.1, 55.4, 53.6, 43.5, 30.1, 28.2, 25.4, 21.7; **IR** (thin film) ν: 3382, 2948, 1544, 1462, 1417, 1343, 1166, 1036, 914, 739 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ $\mathbf{C_{28}H_{33}O_7N_4S}$: 569.2064. Found: 569.2064.



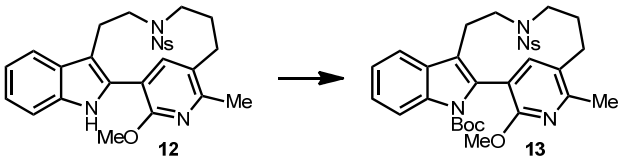
Biaryl alcohol (**S3**): A solution of MOM ether **11** (2.03 g, 3.57 mmol, 1 equiv) and 6 M HCl (3 mL, 18 mmol, 5 equiv) in MeOH (30 mL, 0.03 M) was held at reflux (65 ºC) for 1.8 h in an RBF

with a reflux condenser. The reaction mixture was cooled to 0 ºC and quenched with sat. $NaHCO_3$ (20 mL). The mixture was concentrated under reduced pressure to remove a majority of the methanol. The mixture was partitioned between EtOAc (250 mL) and 1:1 sat. $NaHCO_3$:water (250 mL). The aqueous layer was back-extracted with EtOAc (50 mL). The organic fractions were combined, washed with brine (250 mL), dried over $MgSO_4$, and purified by FCC (1:1:1 hexanes/DCM/EtOAc, dry-loaded on SiO_2). Fractions containing product were concentrated under reduced pressure and dried under high vacuum with heat to yield alcohol **S3** (390 mg, 0.74 mmol, 89% yield) as an orange gum. $\mathbf{R_f}$ 0.25 (1:1:1 hexanes/DCM/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.81 (bs, 1H), 8.01 – 7.94 (m, 1H), 7.64 – 7.52 (m, 4H), 7.36 (d, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 1H), 7.12 (ddd, *J* = 8.1, 7.1, 0.9 Hz, 1H), 6.96 (ddd, *J* = 7.9, 7.2, 0.8 Hz, 1H), 5.98 (t, *J* = 5.7 Hz, 1H), 3.98 (s, 3H), 3.67 (t, *J* = 6.1 Hz, 2H), 3.44 (td, *J* = 7.1, 6.2 Hz, 2H), 3.06 (t, *J* = 7.4 Hz, 2H), 2.70 (t, *J* = 7.4 Hz, 2H), 2.47 (s, 3H), 2.11 (bs, 1H), 1.83 (tt, *J* = 7.0, 6.5 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.1, 153.8, 147.6, 140.4, 135.7, 133.6, 133.4, 132.7, 131.4, 130.9, 127.9, 127.7, 125.4, 122.4, 119.6, 118.3, 112.1, 111.2, 109.3, 61.5, 53.8, 43.7, 32.6, 27.6, 25.9, 21.7; **IR** (thin film) ν: 3550, 3396, 2949, 2876, 1594, 1570, 1540, 1463, 1416, 1340, 1165 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ $\mathbf{C_{26}H_{29}O_6N_4S}$: 525.1802. Found: 525.1811.



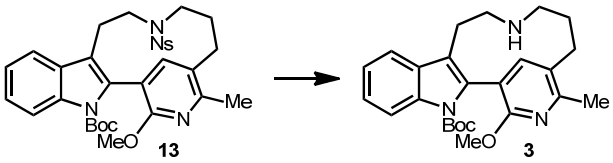
Pyridine macrocycle (**12**): A 2 L RBF containing alcohol **iv** (1.42 g, 2.70 mmol, 1 equiv) and PPh_3 (1.14 g, 4.34 mmol, 1.6 equiv) was evacuated and backfilled with N_2 (3x). THF (1.8 L, 0.0015 M, Aldrich Sure/Seal) was added via cannula, followed by the dropwise addition of diisopropyl azodicarboxylate (0.75 mL, 3.8 mmol, 1.4 equiv) over 10 min, and the reaction mixture was stirred for 1 d at 23 ºC. The flask was charged with additional PPh_3 (1.13 g, 4.31 mmol, 1.6 equiv) in one portion and diisopropyl azodicarboxylate (0.75 mL, 3.8 mmol, 1.4 equiv), dropwise, over the course of 10 min. The reaction mixture was stirred at 23 ºC for 15 h then quenched with H_2O (0.1 mL). The mixture was concentrated under reduced pressure and dried under high vacuum with heat to afford a yellow, caked solid. DCM (150 mL) was added to the crude product and mixed to form a bright yellow, opaque mixture. This mixture was vacuum filtered through a porcelain Büchner funnel with filter paper and rinsed with DCM (~50 mL).

The filtrate was concentrated under reduced pressure, made a slurry in DCM (~20 mL), and filtered in a similar manner. The residue from both filtrations were scraped and dried under high vacuum with heat to yield macrocycle **12** (1.22 g, 2.42 mmol, 89% yield) as a pale yellow solid. Compound **12** is insoluble in many common solvents. Small amounts can be dissolved in hot DCM or THF and larger amounts can be dissolved in hot DMF or DMSO. $\mathbf{R_f}$ 0.50 (1:1 hexanes/EtOAc); **^{1}H NMR** (600 MHz, DMSO-d_6) δ 11.22 (bs, 1H), 8.06 (d, *J* = 7.6 Hz, 1H), 7.99 (s, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.86 (t, *J* = 7.3 Hz, 1H), 7.80 (t, *J* = 7.4 Hz, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 7.03 (t, *J* = 7.4 Hz, 1H), 3.94 (s, 3H), 3.75 (app bs, 2H), 3.36 (app bs, 2H), 2.85 (app bs, 2H), 2.63 (bt, *J* = 5.0 Hz, 2H), 2.39 (s, 3H), 2.15 (app bp, *J* = 6.0 Hz, 2H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 156.9, 153.5, 147.7, 139.9, 135.4, 134.4, 132.4, 131.8, 131.6, 129.7, 128.2, 124.8, 124.1, 121.5, 118.8, 117.6, 111.5, 111.2, 110.5, 53.1, 47.4, 44.0, 25.6, 25.1, 22.6, 21.0; **IR** (KBr pellet) ν: 3456, 3398, 2949, 2900, 1572, 1540, 1462, 1360, 1327, 1280, 1152, 1127, 1041, 952, 853, 800, 758, 744, 585, 437 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ $\mathbf{C_{26}H_{27}O_5N_4S}$: 507.1697. Found: 507.1703; **M.P.** 183–184 ºC.

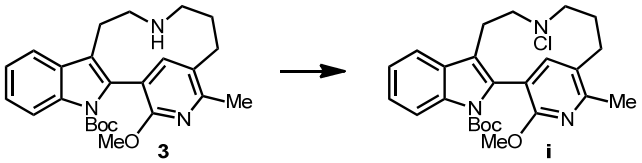


Boc-Ns-Macrocycle (**13**): A mixture of macrocycle **12** (1.02 g, 2.01 mmol, 1 equiv) in 1:1 THF/DMF (80 mL, 0.025 M) was heated and stirred in a 250 mL RBF until homogeneous, then cooled to 23 ºC. Warm di-*tert*-butyl dicarbonate (650 µL, 3.0 mmol, 1.5 equiv), 4-dimethylaminopyridine (5.0 mg, 0.41, 20 mol %), and then TEA (650 µL, 4.7 mmol, 2.3 equiv) were all added in single portions. The reaction mixture was stirred at 23 ºC for 2 d. The mixture was concentrated under reduced pressure then heated under high vacuum (0.2 mbar, 45 ºC) to remove DMF. The residue was partitioned between DCM (100 mL) and 1:1 sat. $NaHCO_3$:water (100 mL). The aqueous layer was back-extracted with DCM (20 mL). The organic fractions were combined, washed with sat. NH_4Cl (80 mL), 1:9 sat. $NaHCO_3$:water (80 mL), brine (100 mL), dried over $MgSO_4$, concentrated under reduced pressure, and dried under high vacuum with heat to yield Boc macrocycle **13** (1.18 g, 1.95 mmol, 97% yield) as an orange gum. $\mathbf{R_f}$ 0.61 (1:1 hexanes/EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.3 Hz, 1H), 8.04 – 8.00 (m, 1H), 7.73 (s, 1H), 7.66 – 7.62 (m, 2H), 7.60 – 7.56 (m, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.32 (td, *J* = 7.7,

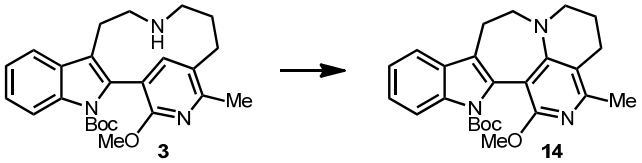
0.8 Hz, 1H), 7.25 (t, *J* = 7.4 Hz, 1H), 4.26 (dt, *J* = 13.6, 8.9 Hz, 1H), 3.87 (s, 3H), 3.73 (dt, *J* = 15.3, 8.8 Hz, 1H), 3.42 (dd, *J* = 14.5, 10.2 Hz, 1H), 2.90 – 2.76 (m, 3H), 2.50 (ddd, *J* = 17.1, 13.3, 3.8 Hz, 1H), 2.42 (s, 3H), 2.23 (dd, *J* = 13.8, 10.0 Hz, 2H), 2.09 – 1.99 (m, 1H), 1.45 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.2, 154.5, 150.1, 148.0, 138.5, 136.1, 133.9, 133.7, 133.6, 131.9, 130.7, 130.0, 124.9, 124.4, 123.8, 122.8, 119.2, 118.6, 115.4, 114.6, 83.5, 53.3, 46.7, 41.7, 27.9, 25.5, 24.4, 21.5, 21.4; **IR** (thin film) ν: 2978, 2951, 1732, 1576, 1548, 1548, 1469, 1408, 1360, 1249, 1160, 1128, 1089, 955, 910, 769, 735, 596, 578 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ **$C_{31}H_{35}O_7N_4S$**: 607.2229. Found: 607.2221.



Amine Macrocycle (**3**): A 250 mL RBF containing nosylamide **13** (1.18 g, 1.94 mmol, 1 equiv) and K_2CO_3 (538 mg, 3.89 mmol, 2 equiv) dissolved in DMF (40 mL, 0.04 M) was evacuated and backfilled with N_2 (3x). Thiophenol (0.80 mL, 7.8 mmol, 4.0 equiv) was added and the mixture was stirred for 2 d. The reaction mixture was partitioned between EtOAc (400 mL) and 1:3 sat. $NaHCO_3$:water (400 mL). The organic layer was washed with H_2O (3x 200 mL), brine (200 mL), dried over $MgSO_4$ concentrated under reduced pressure, and dried under high vacuum to a yellow powder. The crude product was purified by FCC (0.5% TEA + 1:2→1:4→1:5 hexanes/EtOAc) to yield amine **3** (754 mg, 1.79 mmol, 92% yield) as a pale yellow gum. **R_f** 0.38 (1:2 hexanes/EtOAc + 1% TEA, TLC plate pretreated with TEA); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.52 (bs, 1H), 8.22 (d, *J* = 8.3 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.29 (t, *J* = 7.7 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 3.88 (s, 3H), 3.00 (t, *J* = 4.9 Hz, 2H), 2.82 – 2.62 (m, 4H), 2.42 (s, 3H), 2.35 – 2.28 (bm, 1H), 2.23 (dt, *J* = 14.6, 6.6 Hz, 1H), 1.98 – 1.90 (bm, 1H), 1.89 – 1.82 (bm, 1H), 1.51 (bs, 1H), 1.39 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.3, 152.8, 150.1, 144.1, 136.2, 134.2, 130.4, 124.6, 124.1, 122.2, 121.3, 118.1, 115.4, 113.2, 82.7, 52.9, 47.8, 44.2, 29.7, 27.7, 27.0, 22.4, 21.1; **IR** (thin film) ν: 2977, 2932, 2842, 1728, 1578, 1558, 1459, 1412, 1360, 1329, 1303, 1240, 1159, 1129, 1118, 1064, 1024, 768, 744, 701 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ **$C_{25}H_{32}O_3N_3$**: 422.2441. Found: 422.2438.

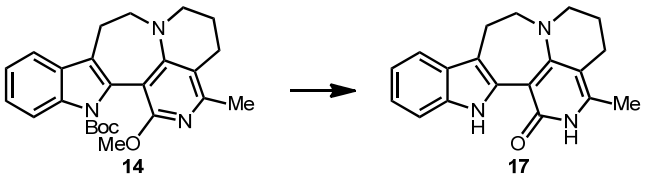


N-Chloro Macrocycle (**i**): A 25 mL RBF, wrapped in aluminum foil, containing a solution of macrocyclic amine **3** (80 mg, 0.19 mmol, 1 equiv) in DCM (4 mL, 0.05 M) was charged with NCS (41 mg, 0.31 mmol, 1.5 equiv) in one portion. The reaction mixture was stirred at 23 ºC for 3 h, concentrated, and purified by FCC (6:1 Hexanes/EtOAc + 1% TEA, wet-loaded in eluent). Fractions containing product were combined, repeatedly co-evaporated with DCM, and dried under high-vacuum to yield chloramine **i** (80 mg, 0.18 mmol, 93% yield) as a white foam. $\mathbf{R_f}$ 0.57 (2:1 hexanes/EtOAc + 1% TEA, TLC plate pretreated with TEA); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.3 Hz, 1H), 8.22 (bs, 1H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.32 (ddd, *J* = 8.2, 7.2, 1.0 Hz, 1H), 7.23 (ddd, *J* = 7.8, 7.1, 0.7 Hz, 1H), 3.87 (s, 3H), 3.57 (t, *J* = 11.6 Hz, 1H), 3.19 (app d, *J* = 7.0 Hz, 1H), 2.89 – 2.80 (m, 1H), 2.80 – 2.64 (m, 3H), 2.58 (d, *J* = 12.7 Hz, 1H), 2.43 (s, 3H), 2.19 (t, *J* = 12.7 Hz, 2H), 1.95 – 1.86 (m, 1H), 1.38 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.7, 153.2, 150.2, 146.1, 136.3, 134.6, 130.2, 124.6, 123.9, 122.6, 120.0, 118.1, 115.8, 113.2, 83.2, 64.0, 57.1, 53.2, 28.1, 27.9, 25.2, 24.1, 21.3; **IR** (thin film) ν: 2978, 2948, 2840, 1731, 1578, 1558, 1459, 1406, 1361, 1329, 1304, 1245, 1210, 1158, 1130, 1059, 1020, 996, 909, 768, 734 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ $\mathbf{C_{25}H_{31}O_3N_3Cl}$: 456.2048. Found: 456.2046.



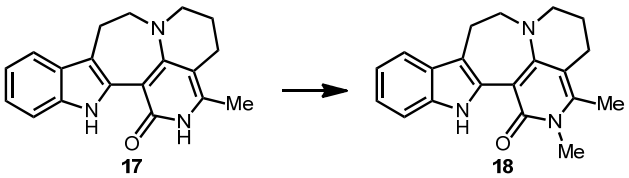
Pentacycle (**14**): A solution of amine **3** (650 mg, 154 mmol, 0.257 mmol/tube, 1 equiv) in THF (45 mL, 0.034 M) was dosed among six 10 mL quartz tubes wrapped in aluminum foil. Each tube was charged with NIS (116 mg, 0.516 mmol, 2 equiv), the contents sparged with N_2 for 1 min, and the reaction mixture was stirred for 30 min. The reaction solution turned orange during this time. The tubes were removed from the aluminum foil and irradiated with a medium pressure mercury lamp for 20 min. The reaction mixture turned opaque brown/black upon irradiation. Each tube was charged with TEA (0.20 mL, 0.43 mmol, 5.6 equiv). The reaction mixture turned a transparent, clear orange upon addition of TEA. The reaction mixture was irradiated for an additional 5 h. All six reaction mixtures were combined (reaction vessels rinsed with DCM), concentrated under reduced pressure to a brown powder, and purified by FCC (8:1:1

Hex/DCM/EtOAc, wet-loaded in DCM + eluent). Fractions containing product were concentrated under reduced pressure and dried under high vacuum with heat to yield pentacycle **14** (525 mg, 1.25 mmol, 81% yield) as a yellow gum. $\mathbf{R_f}$ 0.59 (2:1 hexanes/EtOAc + 1% TEA, TLC plate pretreated with TEA, fluorescent under 365 nm UV); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 7.7 Hz, 1H), 7.26 (t, *J* = 7.8 Hz, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 3.85 (s, 3H), 3.71 (td, *J* = 11.1, 4.7 Hz, 1H), 3.59 (dt, *J* = 10.7, 3.8 Hz, 1H), 3.11 (t, *J* = 10.4 Hz, 1H), 3.05 – 2.97 (m, 2H), 2.74 (ddd, *J* = 15.7, 11.0, 4.8 Hz, 1H), 2.67 – 2.58 (m, 2H), 2.36 (s, 3H), 1.97 (tdd, *J* = 9.2, 8.8, 3.8 Hz, 1H), 1.78 (dd, *J* = 11.2, 5.2 Hz, 1H), 1.43 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.8, 152.5, 151.8, 150.6, 136.9, 131.5, 128.4, 124.2, 122.2, 120.9, 117.5, 116.0, 115.0, 104.7, 82.9, 62.3, 53.3, 51.4, 28.05, 25.1, 22.4, 22.2, 19.7; **IR** (thin film) ν: 2974, 2944, 2860, 1731, 1581, 1560, 1456, 1378, 1367, 1324, 1251, 1230, 1145, 1077, 733 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ $\mathbf{C_{25}H_{30}O_3N_3}$: 420.2286. Found: 420.2282.

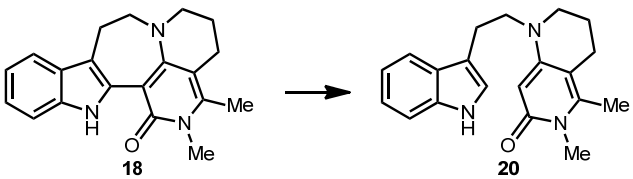


Pyridone Pentacycle (**17**): Two 20 mL vials containing a solution of pyridine **14** (520 mg, 124 mmol, 1 equiv) and ethanethiol (1.8 mL, 25 mmol, 20 equiv) in DMF (24.5 mL, 0.05 M) were charged with NaH (60% suspension in mineral oil, 300 mg, 12.5 mmol, 10 equiv). A slight exotherm was observed and the mixture was stirred until bubbling subsided. N_2 was gently blown over the vials, which were then sealed with Teflon caps, and the mixtures were heated and stirred at 140 ºC for 4 h. The reaction mixtures were diluted with water (200 mL), vacuum filtered through a porcelain Büchner funnel with filter paper, and then rinsed with water (~50 mL) and hexanes (~3 mL). The residue was dissolved in DCM and acetone, concentrated under reduced pressure, and dried under high vacuum with heat to yield crude pyridone pentacycle **17** (370 mg, 1.21 mmol, 98% yield) as a pale yellow-tan powder. $\mathbf{R_f}$ 0.25 (5% MeOH in DCM, fluorescent under 365 nm UV); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 12.41 (s, 1H), 11.32 (s, 1H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 7.9 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.05 (t, *J* = 7.3 Hz, 1H), 3.46 (t, *J* = 4.6 Hz, 2H), 3.42 (t, *J* = 5.8 Hz, 2H), 3.17 (t, *J* = 4.4 Hz, 2H), 2.53 (t, *J* = 5.9 Hz, 2H), 2.29 (s, 3H), 1.91 (app p, *J* = 5.9 Hz, 2H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 163.2, 155.0, 136.0, 133.0, 132.9, 127.8, 120.2, 117.9, 116.8, 110.4, 109.2, 106.5, 97.2, 53.3, 51.7, 25.8, 22.7,

22.0, 15.6; **IR** (thin film) ν: 2921, 2881, 1626, 1600, 1493, 1468, 1431, 1360, 1328, 1169 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ $\mathbf{C_{19}H_{20}O_1N_3}$: 306.1609. Found: 306.1601.



N-Me Pyridone Pentacycle (**18**): A 250 mL RBF containing a mixture of pyridone **17** (370 mg, 1.21 mmol, 1 equiv) in DMF (24 mL, 0.05 M) was heated until homogeneous then cooled to 23 ºC. The flask was charged with K_2CO_3 (336 mg, 2.4 mmol, 2 equiv), then MeI (130 µL, 2.1 mmol, 1.7 equiv), and the reaction mixture was then heated and stirred at 45 ºC for 12 h. The flask was again charged with MeI (0.50 mL, 8.0 mmol, 6.6 equiv), K_2CO_3 (480 mg, 3.47 mmol, 2.9 equiv), and DMF (6 mL, 0.04 M) then the reaction mixture was heated and stirred at 45 ºC for 16 h. The mixture was diluted with water (200 mL), vacuum filtered through a porcelain Büchner funnel with filter paper, and rinsed with water (~50 mL) and hexanes (~3 mL). The residue was purified by FCC (1.5%→2.5% MeOH in DCM, wet-loaded in DCM). Fractions containing product were combined, concentrated under reduced pressure, and dried under high vacuum with heat to yield *N*-Me pyridone **18** (264 mg, 0.827 mmol, 67% yield over two steps from pyridine **14**) as a tan-yellow solid. $\mathbf{R_f}$ 0.80 (10% MeOH in DCM); $^{\mathbf{1}}$**H NMR** (600 MHz, $CDCl_3$) δ 12.45 (s, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.11 (ddd, *J* = 7.9, 7.1, 0.8 Hz, 1H), 7.05 (ddd, *J* = 7.7, 7.1, 0.6 Hz, 1H), 3.55 (s, 3H), 3.36 (t, *J* = 4.7 Hz, 2H), 3.31 (t, *J* = 5.9 Hz, 2H), 3.12 (t, *J* = 4.7 Hz, 2H), 2.50 (t, *J* = 6.0 Hz, 2H), 2.20 (s, 3H), 1.83 (app p, *J* = 6.0 Hz, 2H); $^{\mathbf{13}}$**C NMR** (151 MHz, $CDCl_3$) δ 163.6, 154.1, 137.1, 133.8, 132.9, 128.2, 120.9, 118.3, 117.3, 110.7, 110.4, 108.4, 99.0, 53.8, 51.9, 31.6, 26.3, 25.0, 22.7, 16.2; **IR** (thin film) ν: 3255, 3051, 2926, 2838, 1629, 1554, 1519, 1493, 1466, 1429, 1360, 1335, 1236, 1196, 1169, 1095, 1010, 909, 780, 734, 645 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ $\mathbf{C_{20}H_{22}ON_3}$: 320.1757. Found: 320.1756.



Reduced Product (**20**): A solution of *N*-Me pyridone **18** (15 mg, 0.047 mmol, 1 equiv) in MeOH (4 mL, 0.01 M) and 37% $HCl_{(aq)}$ (0.70 mL, 8.5 mmol, 180 equiv) in a 20 mL vial was charged

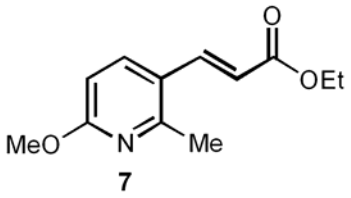
with Zn dust (350 mg, 5.35 mmol, 114 equiv), and heated and stirred at 70 ºC under a condenser with vial adapter for 2 min, then 23 ºC for 2 min. The reaction mixture was filtered through filtered paper and rinsed with EtOAc (20 mL) followed by water (20 mL). The filtrate was cooled to 0 ºC, basified to a pH >13 with cold, sat. $NaOH_{(aq)}$ (10 mL). The white precipitate was filtered through a glass frit Büchner funnel. The organic layer was separated, washed with brine (20 mL), dried over Na_2SO_4, concentrated under reduced pressure, and dried over high vacuum with heat to afford crude **20** (12.6 mg) as a light yellow powder. The crude product was purified by FCC (5%→7.5% MeOH in DCM, wet-loaded in DCM) to yield **20** as a white foam (9.6 mg, 0.30 mmol, 64% yield) $\mathbf{R_f}$ 0.18 (5% MeOH in DCM); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.64 (bs, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.07 (t, *J* = 7.4 Hz, 1H), 7.00 (d, *J* = 1.3 Hz, 1H), 5.74 (s, 1H), 3.50 (t, *J* = 7.6 Hz, 2H), 3.49 (s, 3H), 3.09 (t, *J* = 5.6 Hz, 2H), 3.00 (t, *J* = 7.5 Hz, 2H), 2.44 (t, *J* = 6.4 Hz, 2H), 2.20 (s, 3H), 1.74 (tt, *J* = 6.3, 5.8 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.8, 152.7, 141.4, 136.6, 127.6, 122.5, 122.1, 119.4, 118.7, 113.0, 111.6, 104.7, 90.2, 52.6, 49.5, 31.0, 24.5, 22.3, 21.8, 16.5; **IR** (thin film) ν: 3272, 2925, 2856, 1634, 1558, 1534, 1496, 1458, 1352, 1330, 1198, 909, 804, 735 cm^{-1}; **HRMS** (**ESI**) *m*/*z* calcd for $[M+H]^+$ $\mathbf{C_{20}H_{24}ON_3}$: 322.1914. Found: 322.1913.

References

(1) Berliner, M. A.; Belecki, K. *J. Org. Chem.* **2005**, *70*, 9618–9621.

(2) Ohmura, T.; Kijima, A.; Suginome, M. *J. Am. Chem. Soc.* **2009**, *131*, 6070–6071.

(3) Matsuda, Y.; Kitajima, M.; Takayama, H. *Org. Lett.* **2008**, *10*, 125–128.


O
OEt
MeO
N
Me

7

^{1}H NMR

0.97
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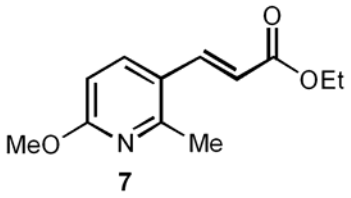
0.04
0.99
0.97
0.04
2.06
3.00
2.91
3.08
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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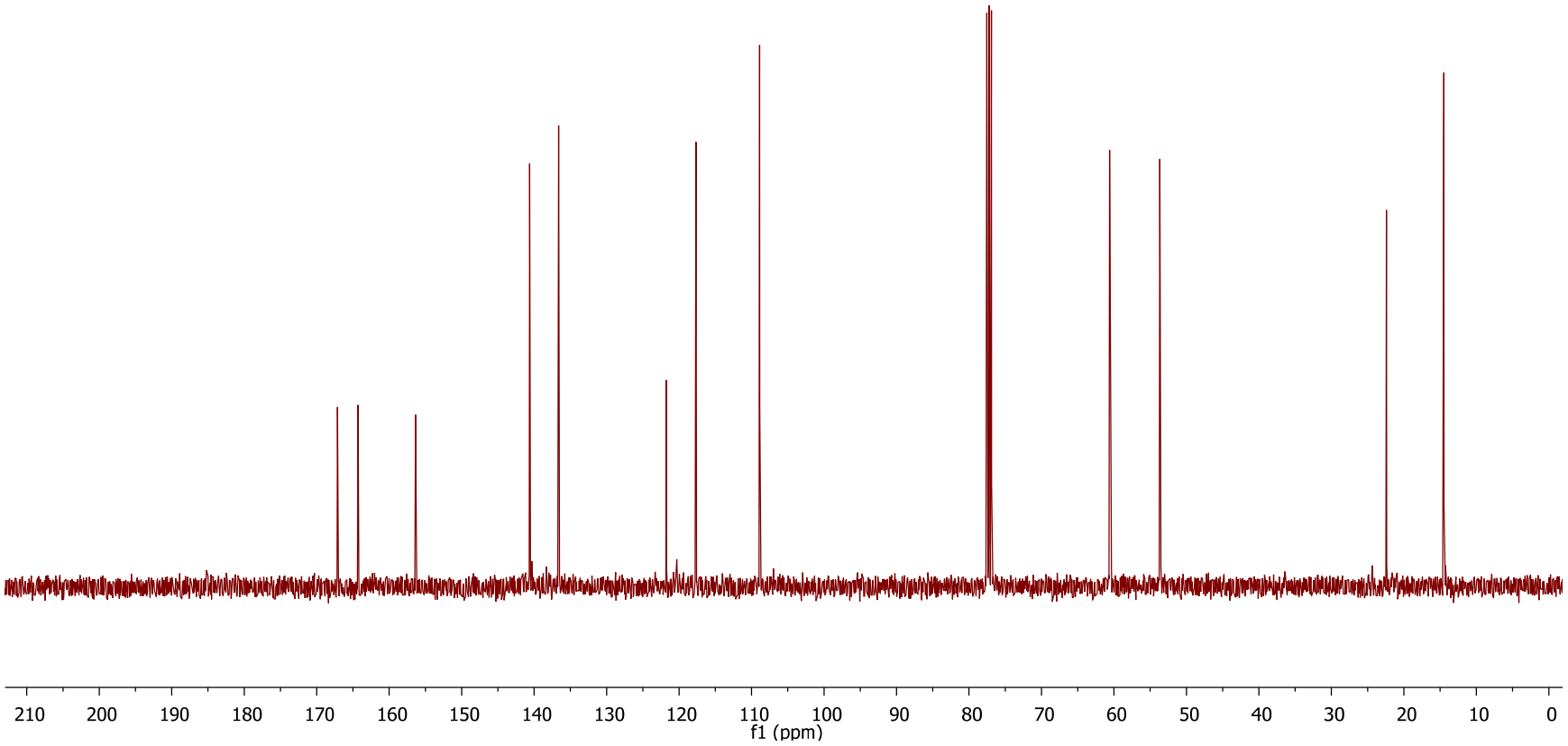
N
Me

7

^{13}C NMR


210
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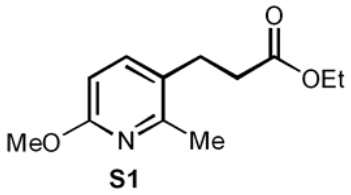
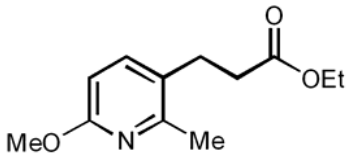
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
OEt
MeO
N
Me

S1

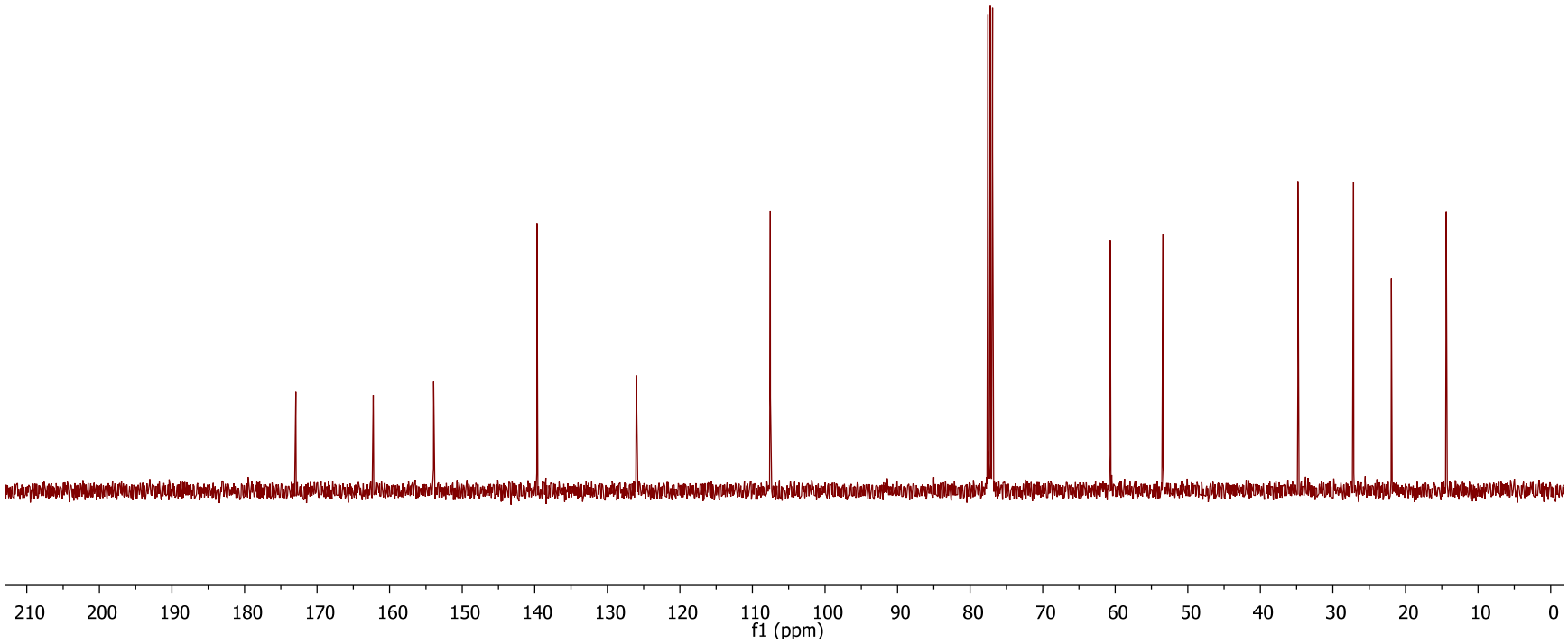
^{1}H NMR

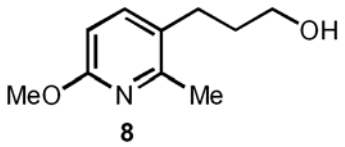
0.96
0.95
2.04
2.87
2.01
1.99
2.86
3.27
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


O
OEt
MeO
N
Me

S1

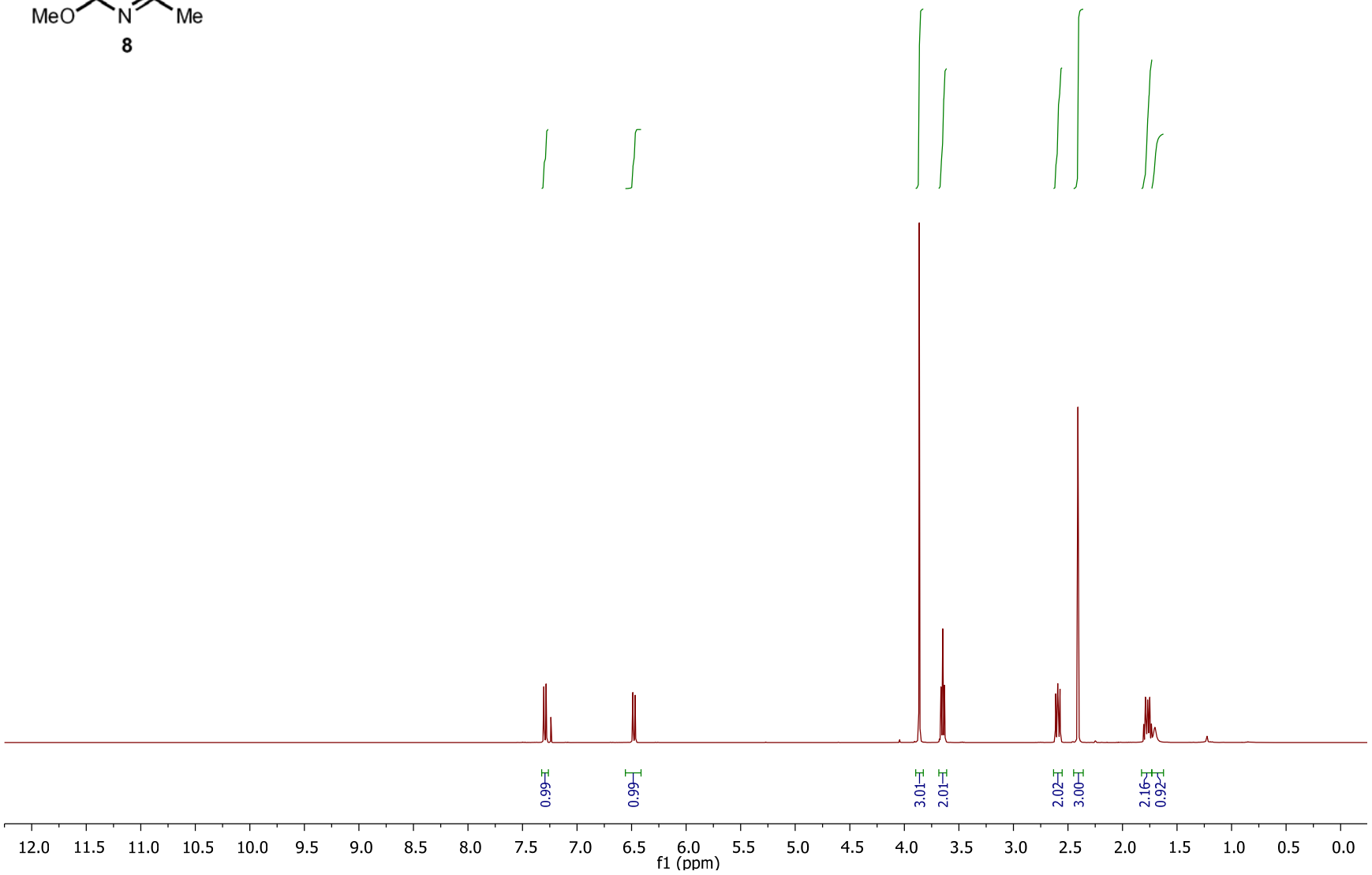
^{13}C NMR

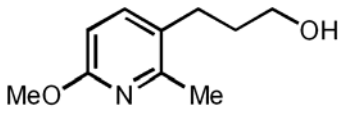

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


OH
MeO
N
Me

8

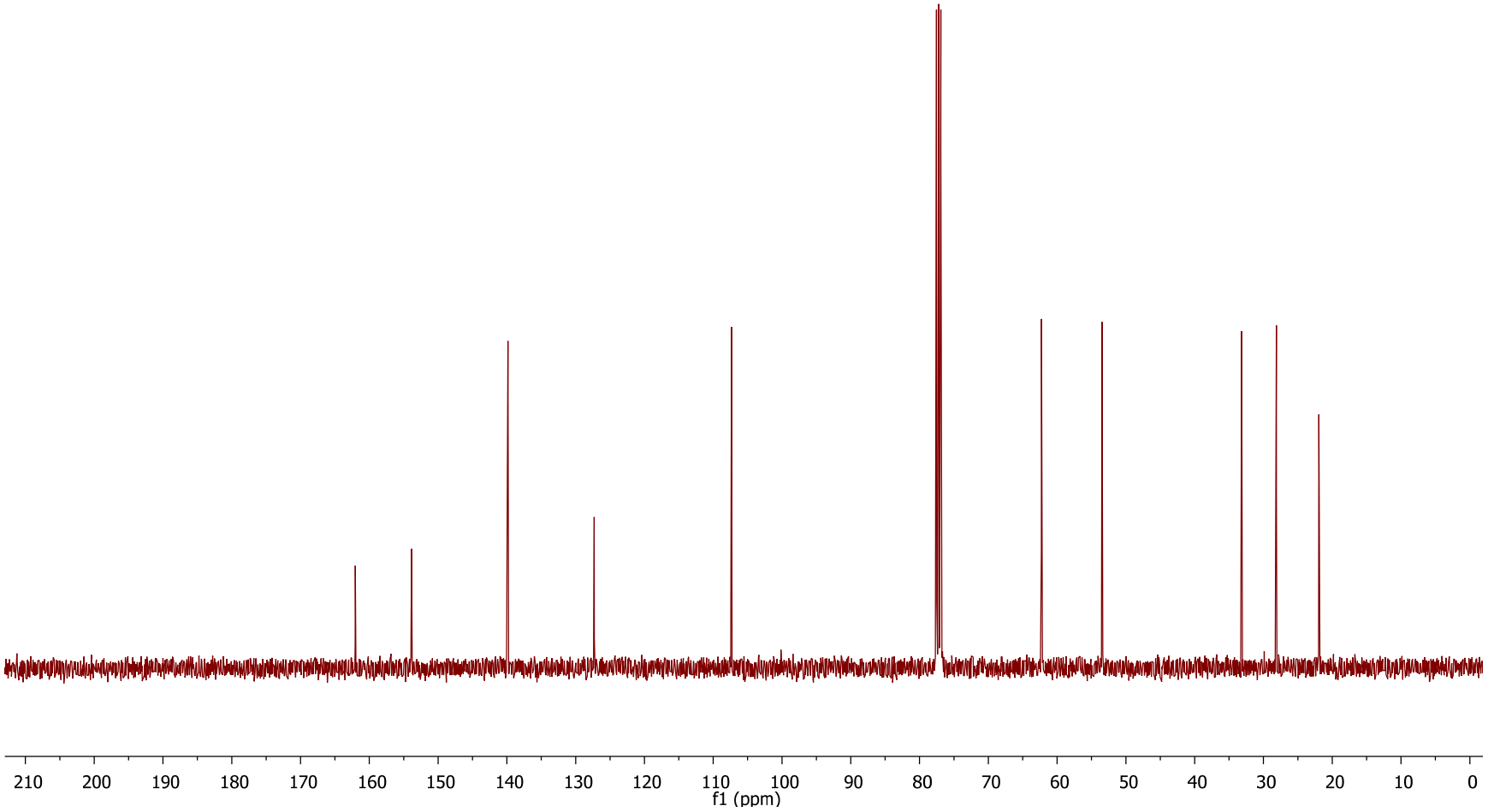
^{1}H NMR

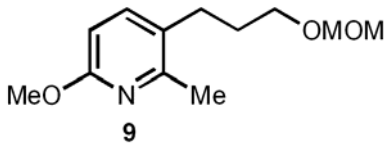

0.99
0.99
3.01
2.01
2.02
3.00
2.16
0.92
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


OH
MeO
N
Me

8

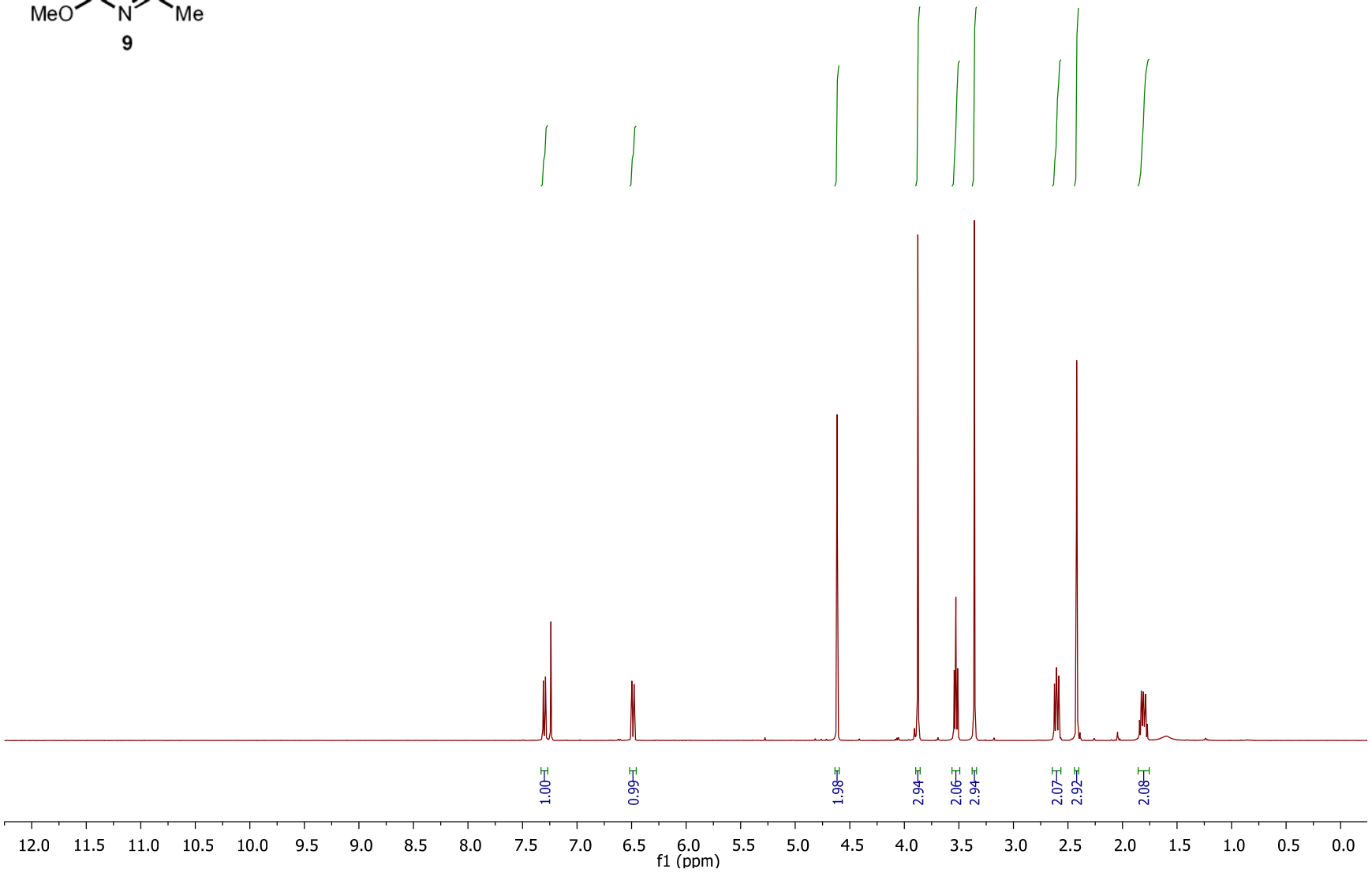
^{13}C NMR

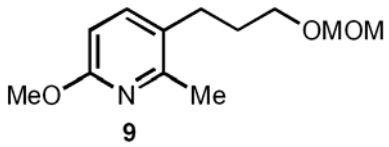

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


OMOM
MeO
N
Me

9

^{1}H NMR

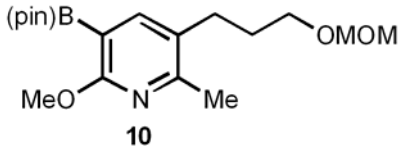

1.00
0.99
1.98
2.94
2.06
2.94
2.07
2.92
2.08
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


OMOM
MeO
N
Me

9

^{13}C NMR

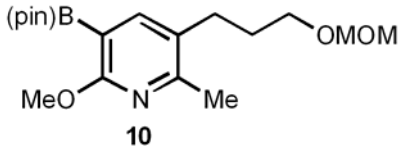
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


(pin)B
OMOM
MeO
N
Me

10

^{1}H NMR

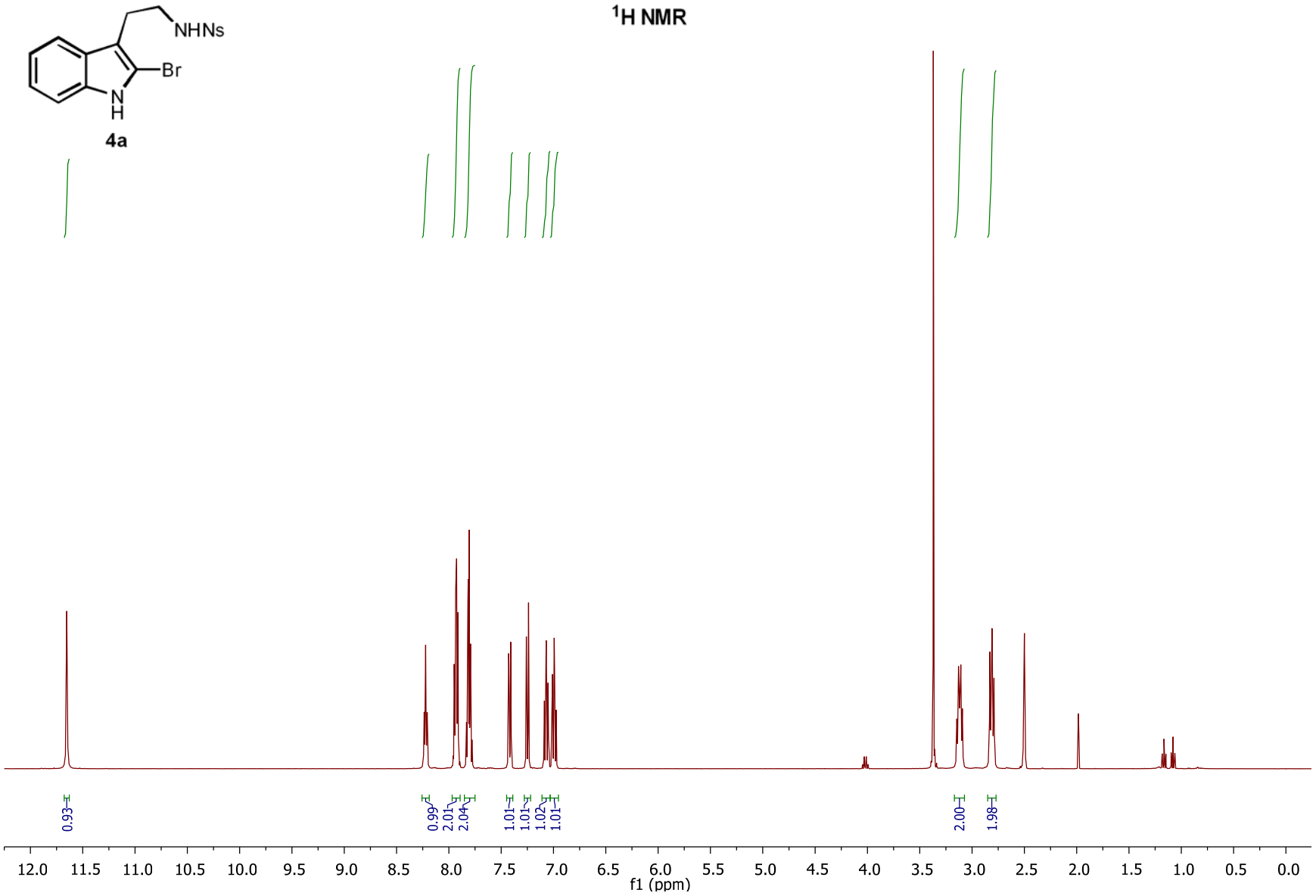
0.97
2.00
2.98
2.04
3.00
2.04
2.99
2.23
12.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

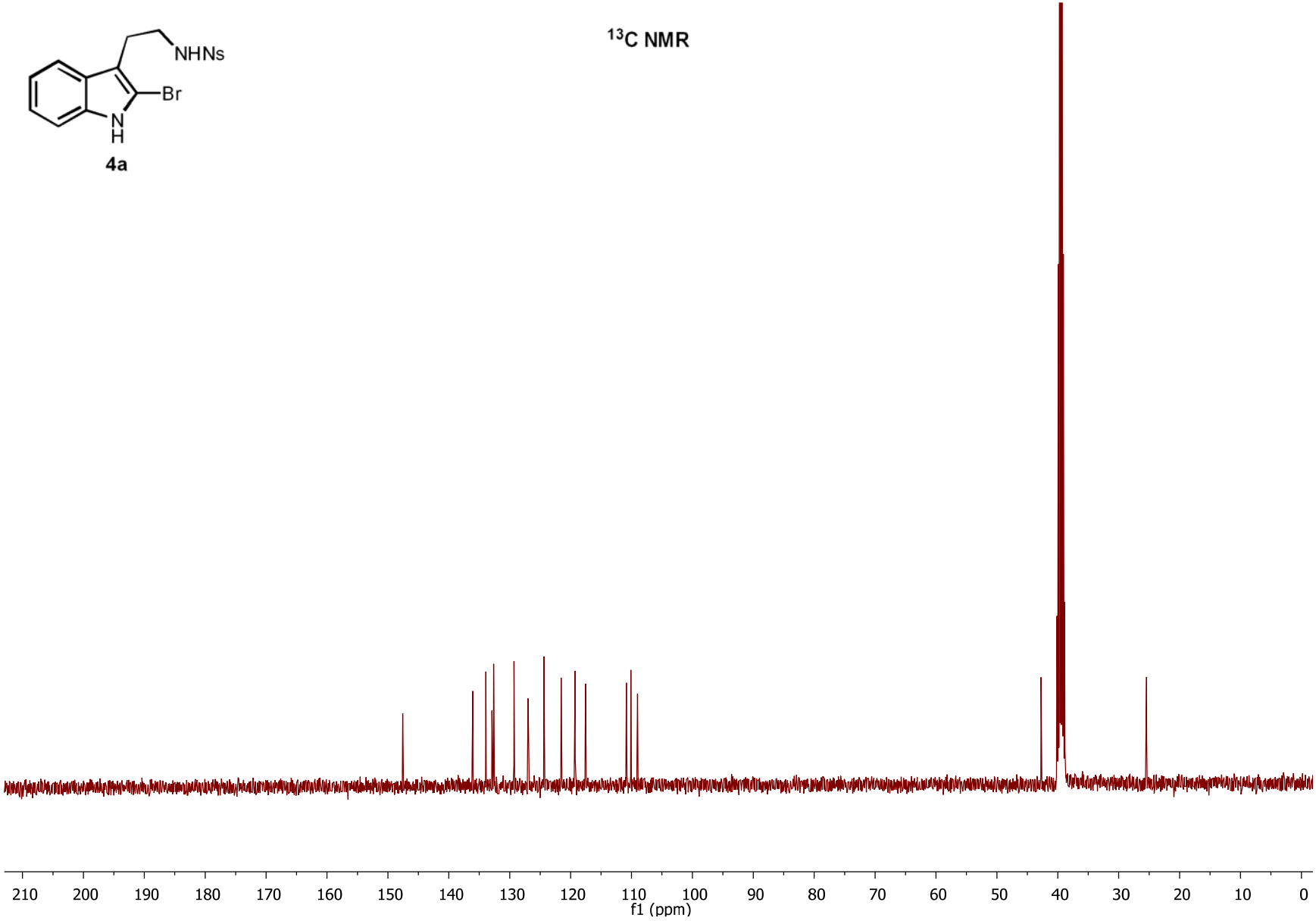

(pin)B
OMOM
MeO
N
Me

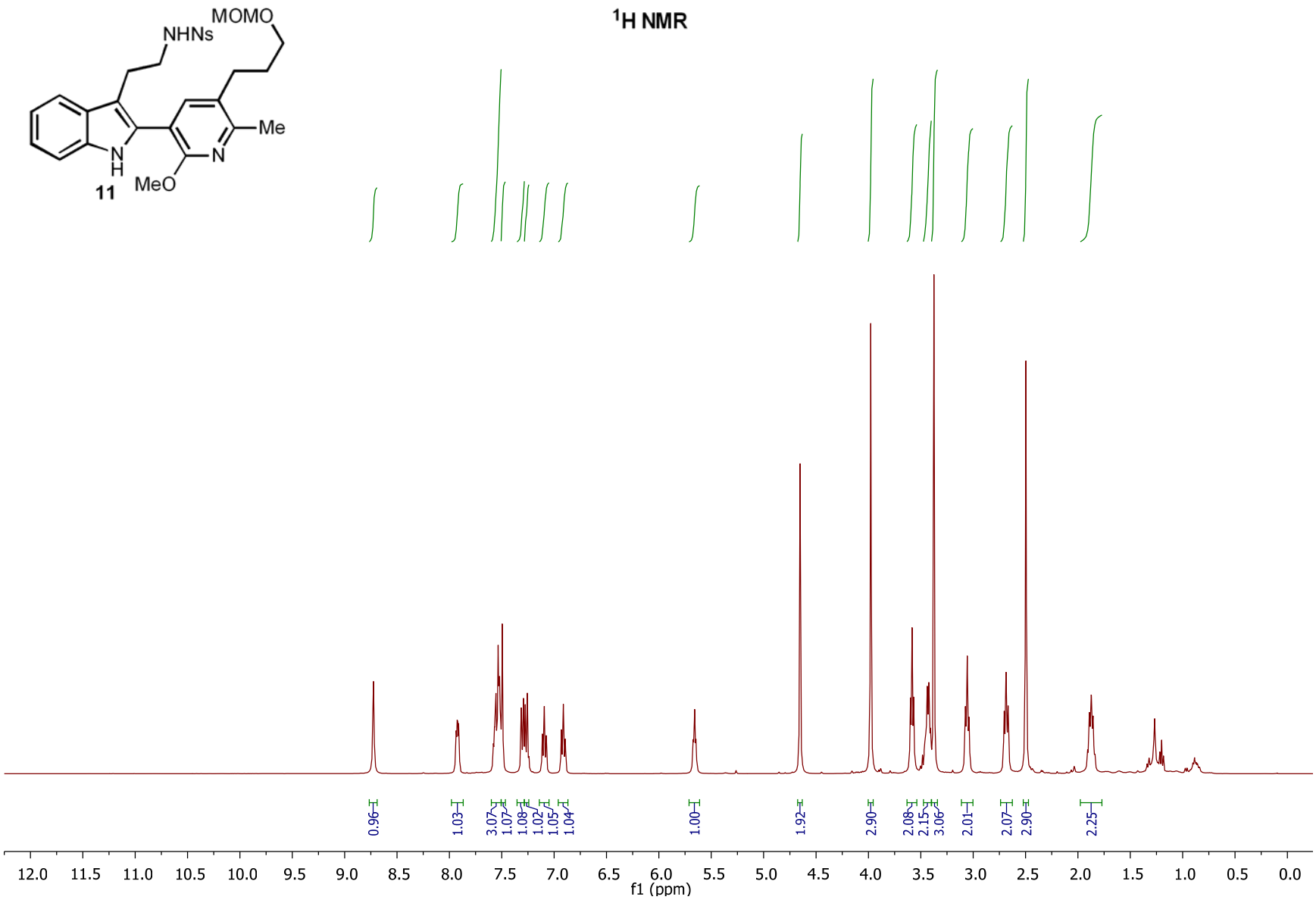
10

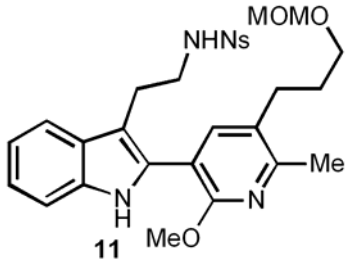
^{13}C NMR

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


NHNs
Br
N
H
4a
^{1}H NMR
0.93
0.99
2.01
2.04
1.01
1.01
1.02
1.01
2.00
1.98
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

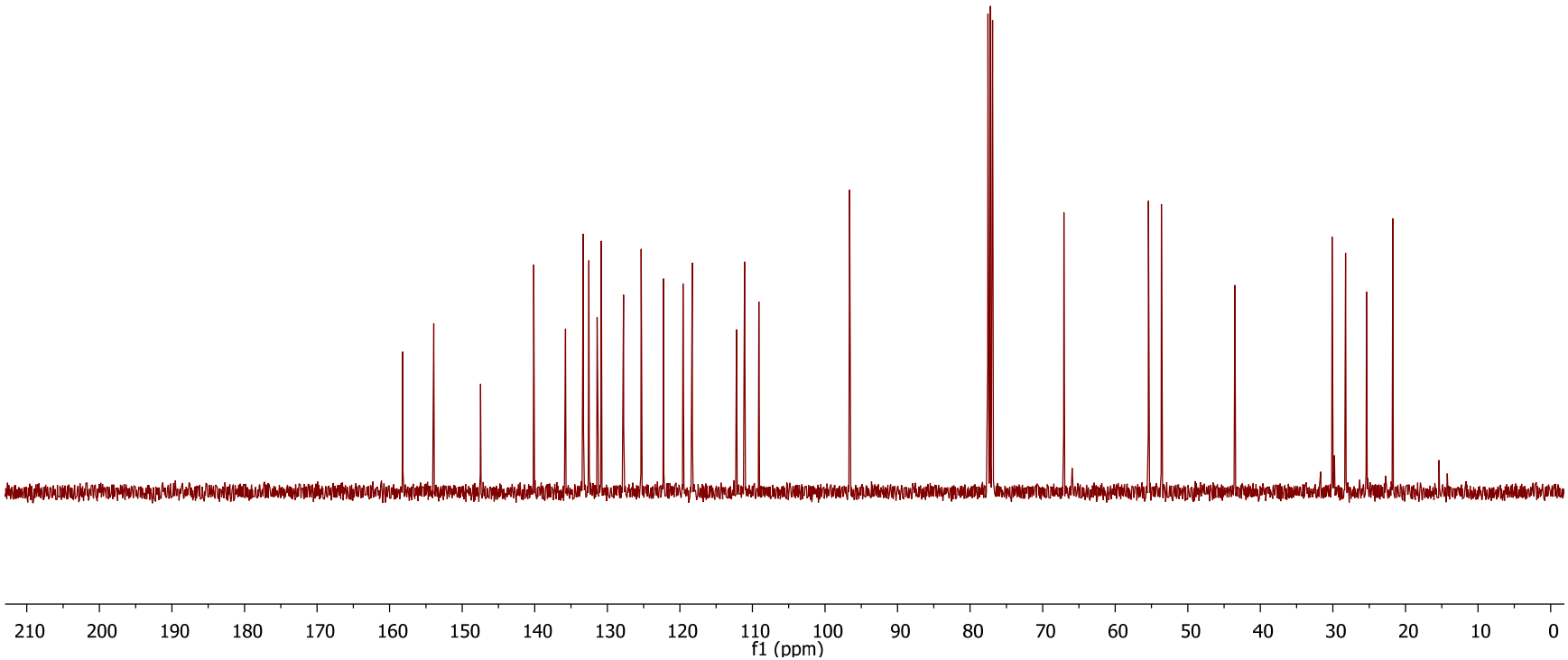

NHNs
Br
N
H
4a
^{13}C NMR
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

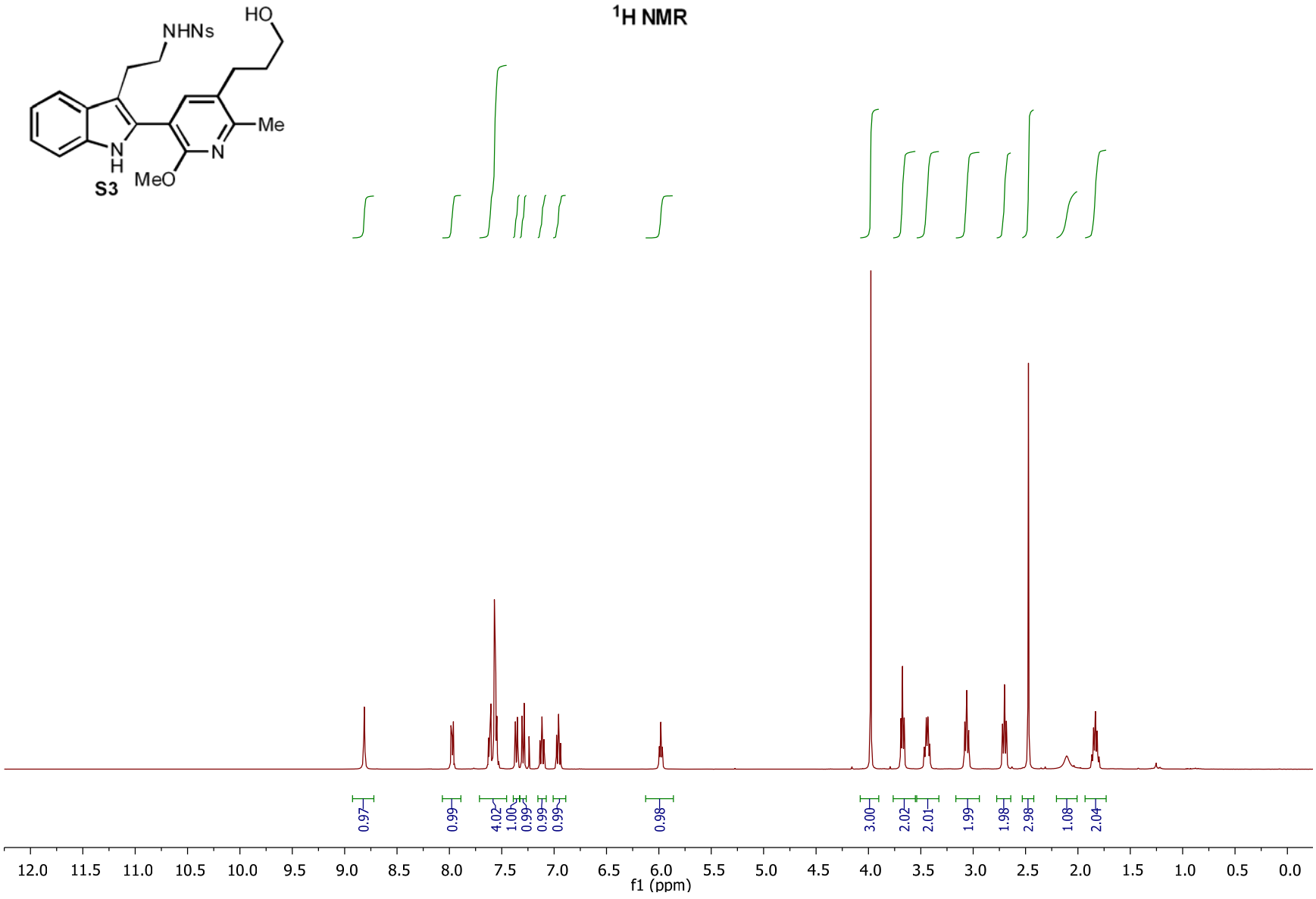

MOMO
NHNs
Me
N
H
N
MeO
11
^{1}H NMR
0.96
1.03
3.07
1.07
1.08
1.02
1.05
1.04
1.00
1.92
2.90
2.08
2.15
3.06
2.01
2.07
2.90
2.25
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

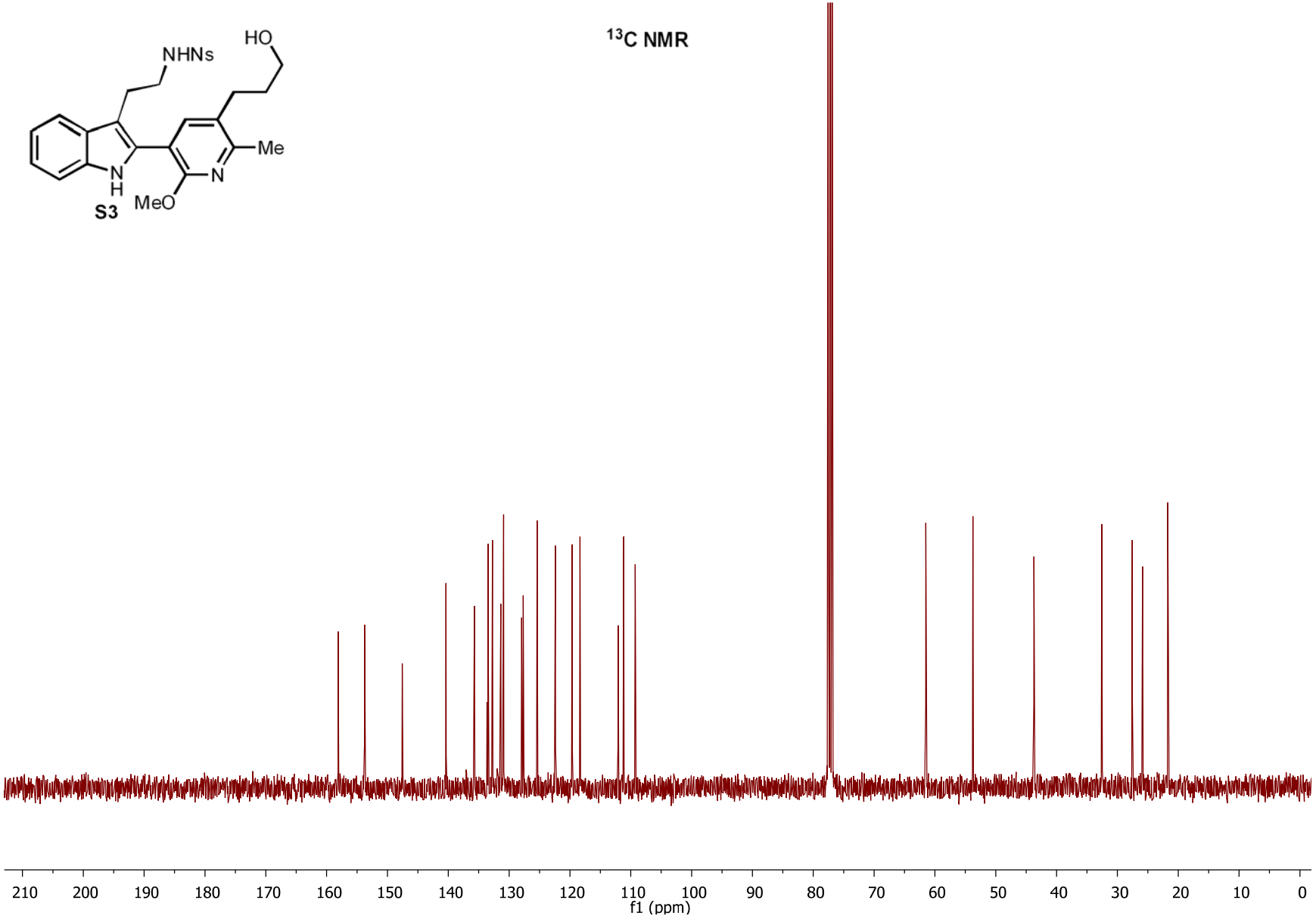

MOMO
NHNs
Me
N
H
N
MeO

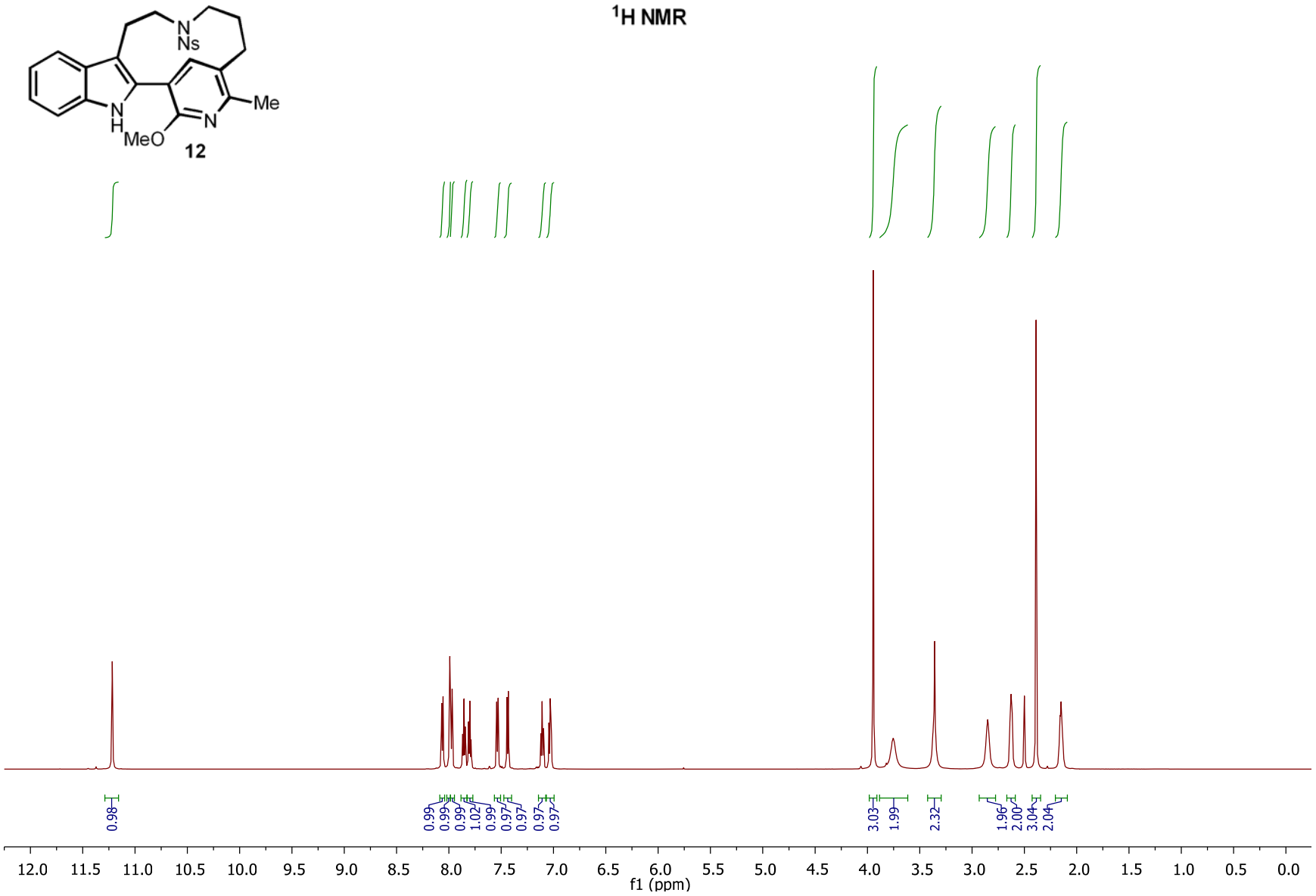
11

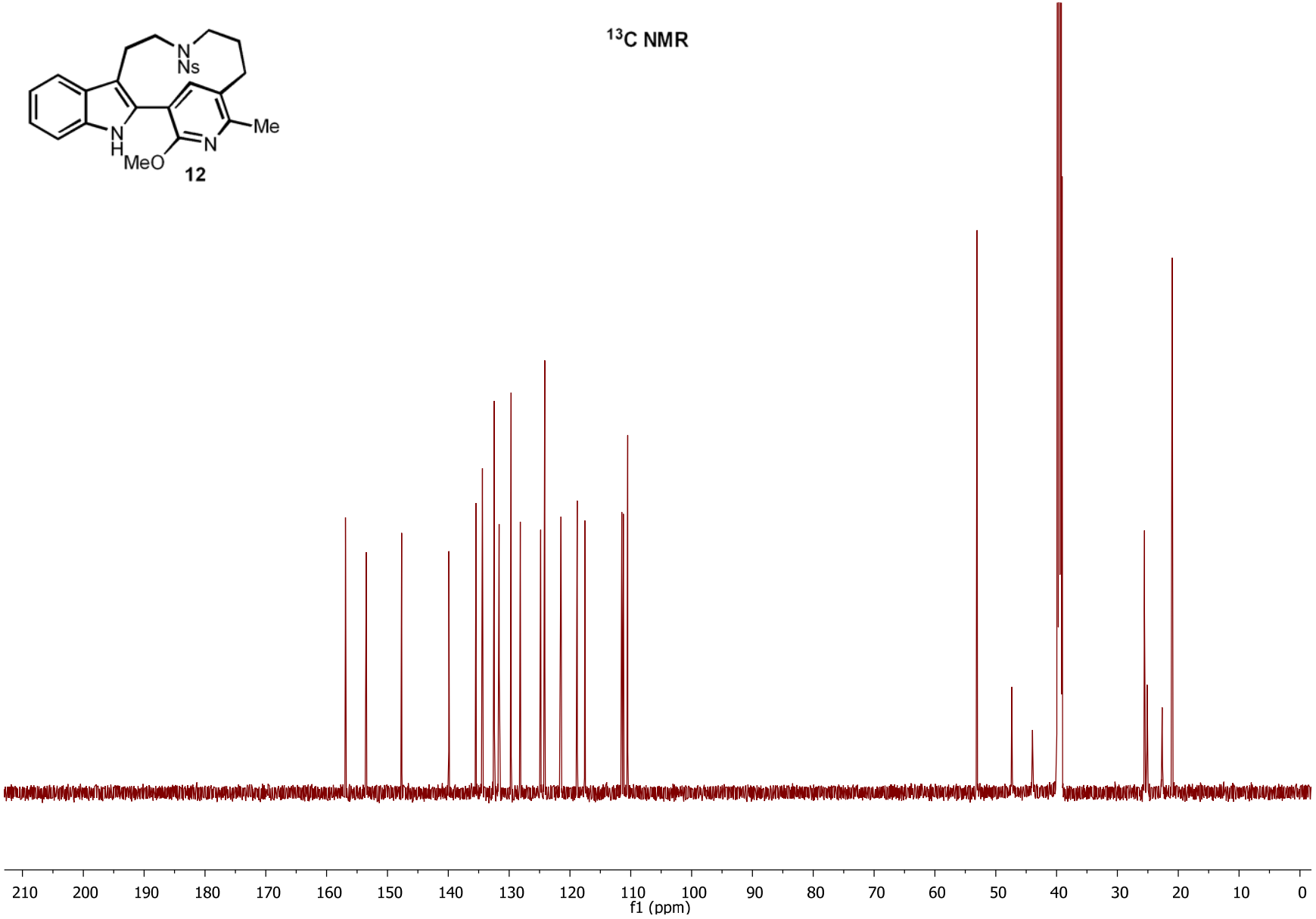
^{13}C NMR

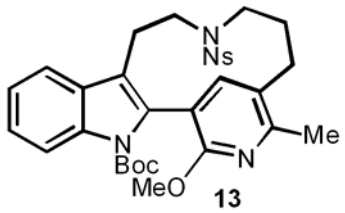

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


HO
NHNs
Me
N
N
H
MeO
S3
^{1}H NMR
0.97
0.99
4.02
1.00
0.99
0.99
0.99
0.98
3.00
2.02
2.01
1.99
1.98
2.98
1.08
2.04
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


HO
NHNs
Me
N
H
MeO
S3
^{13}C NMR
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


^{1}H NMR
N
Ns
N
H
MeO
N
Me
12
0.98
0.99
0.99
0.99
1.02
0.99
0.97
0.97
0.97
3.03
1.99
2.32
1.96
2.00
3.04
2.04
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

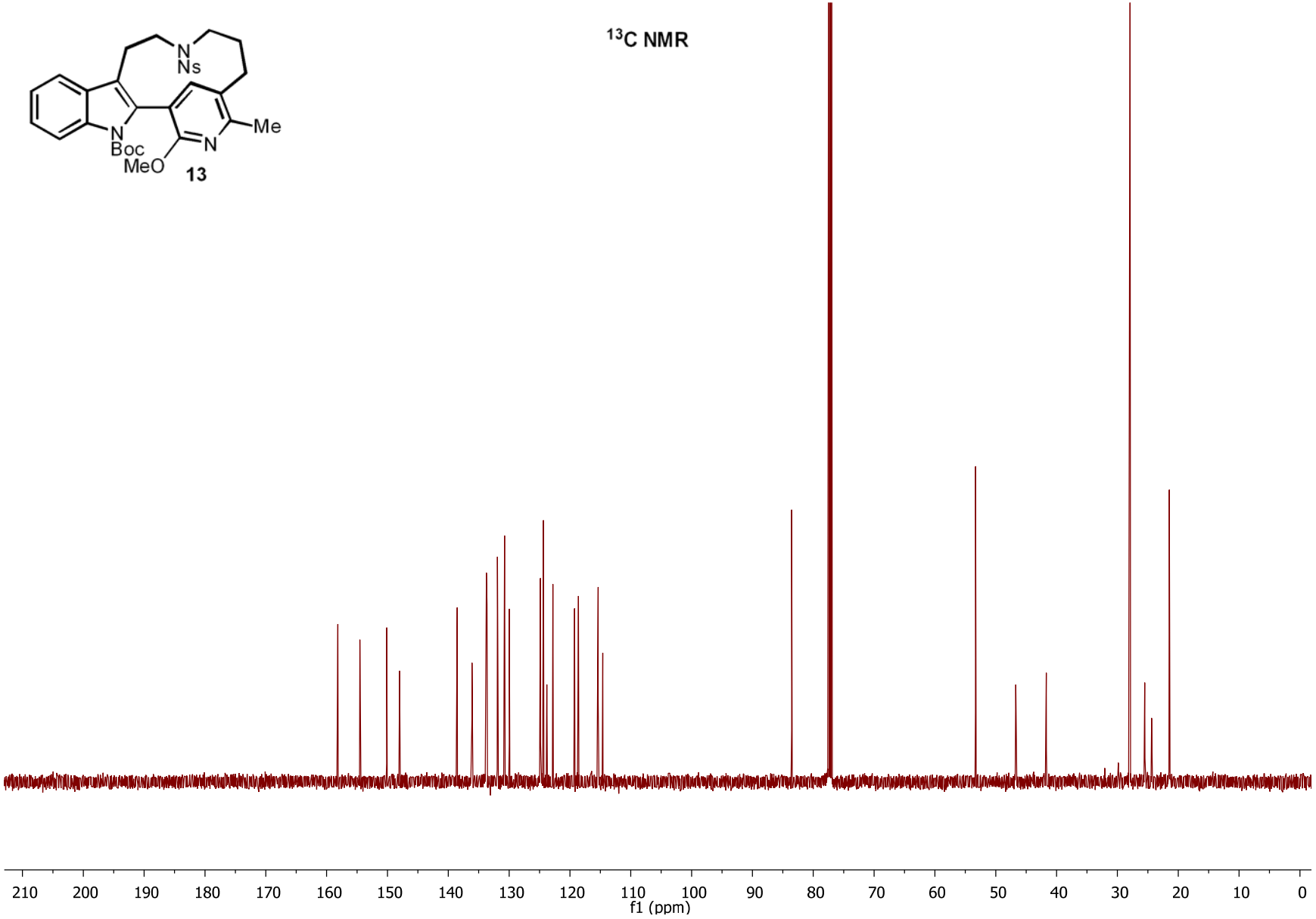

^{13}C NMR
N
Ns
N
H
MeO
N
Me
12
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

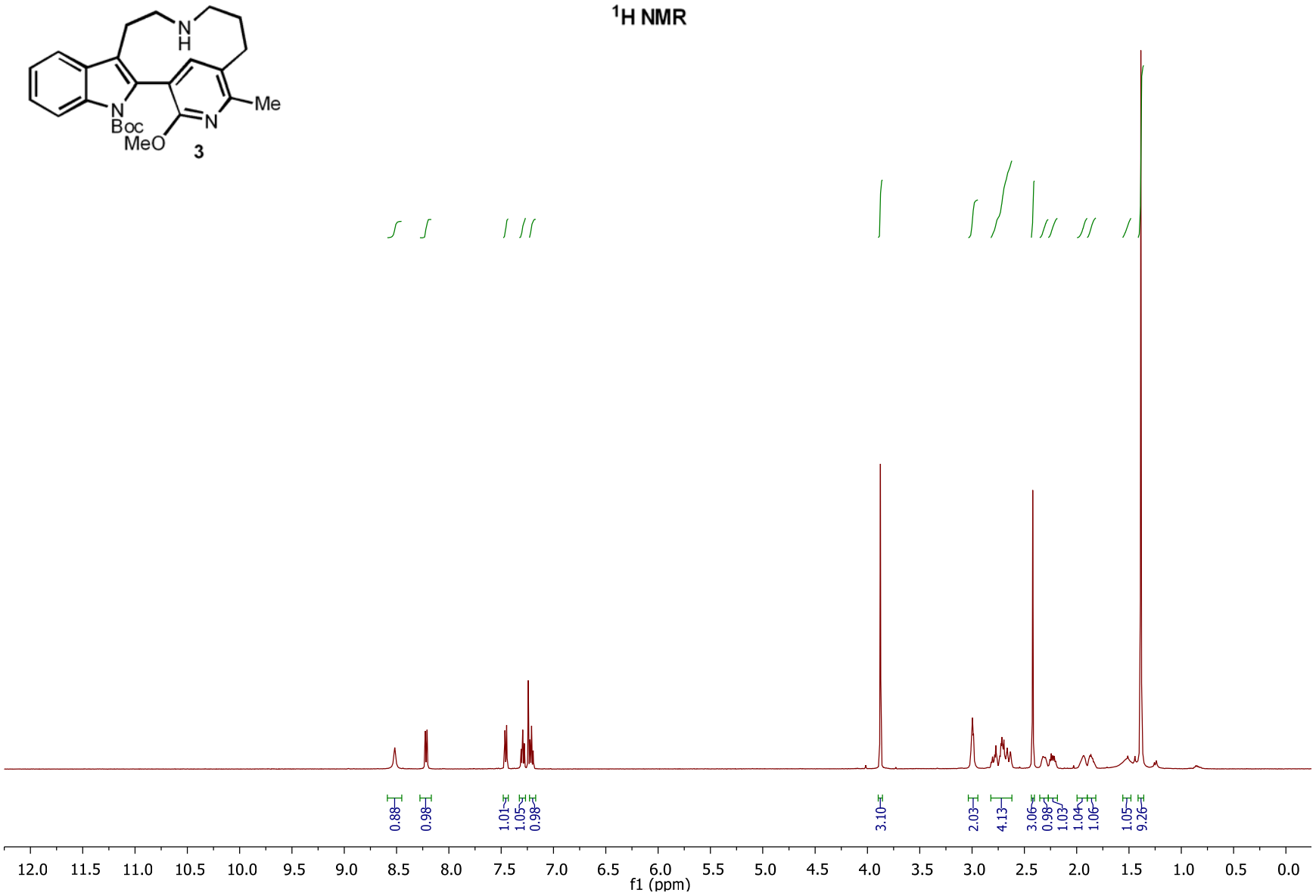

N
Ns
N
Boc
MeO
N
Me

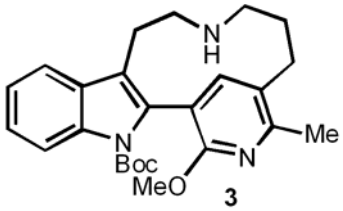
13

^{1}H NMR

0.97
0.98
1.00
2.00
0.98
1.04
0.99
1.09
0.93
3.00
1.00
0.99
2.99
1.02
2.97
2.02
1.03
9.03
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

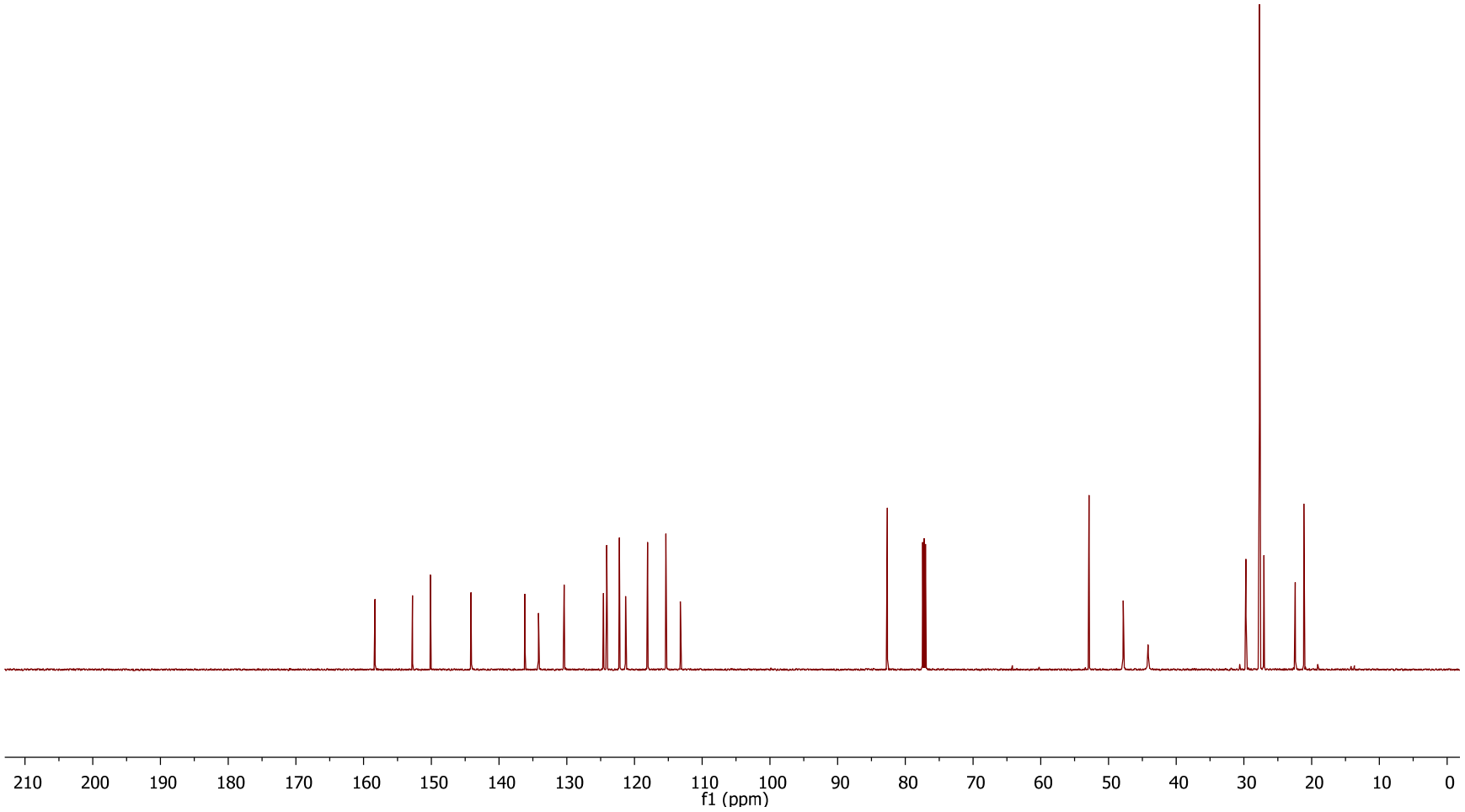

^{13}C NMR
N
Ns
N
Boc
MeO
Me
N
13
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

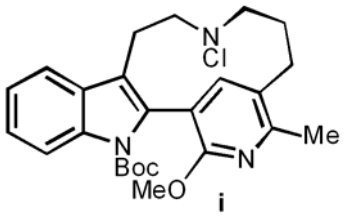

^{1}H NMR
N
H
N
Boc
MeO
N
Me
3
0.88
0.98
1.01
1.05
0.98
3.10
2.03
4.13
3.06
0.98
1.03
1.04
1.06
1.05
9.26
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


N
H
N
Boc
MeO
N
Me

3

^{13}C NMR

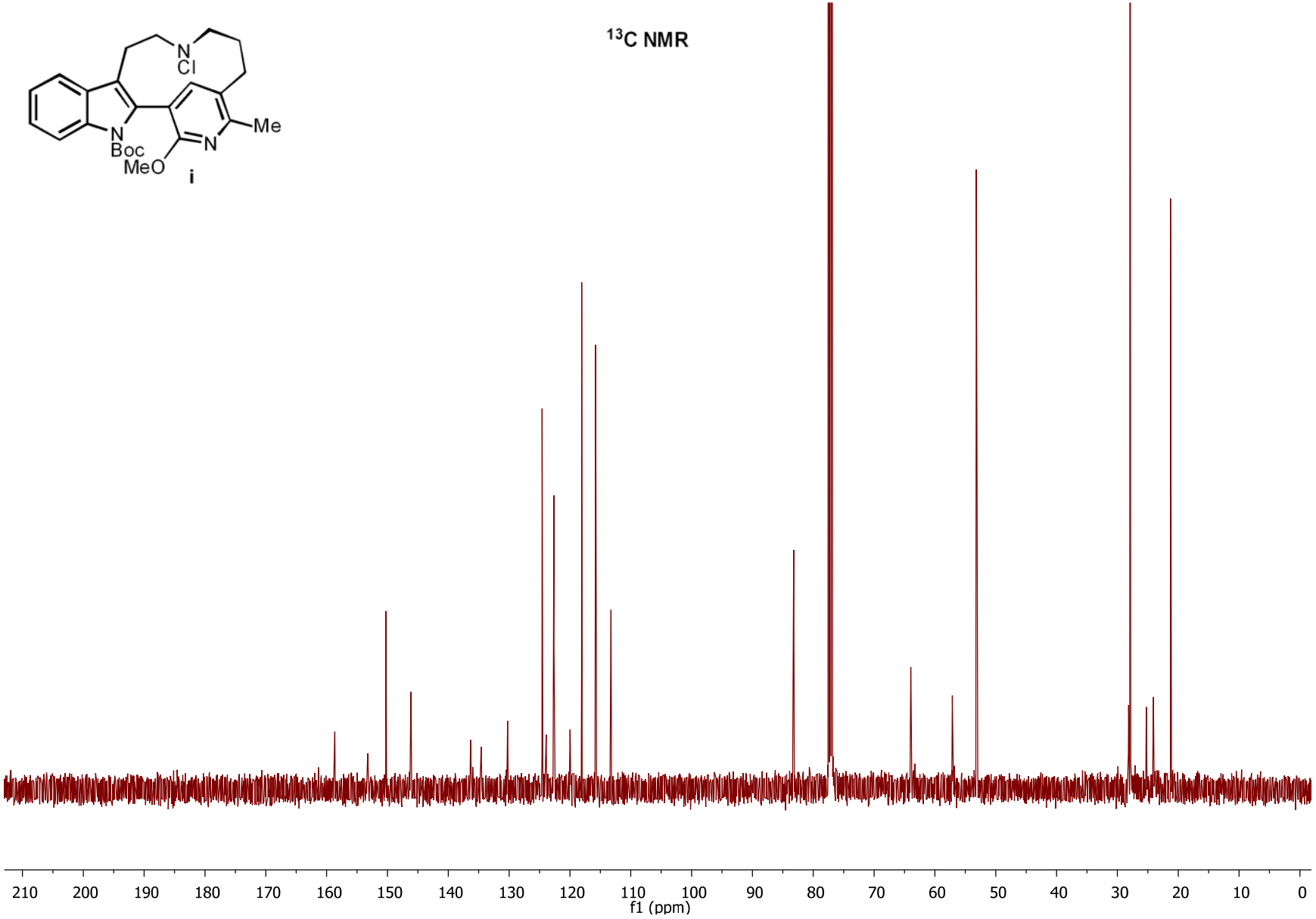

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

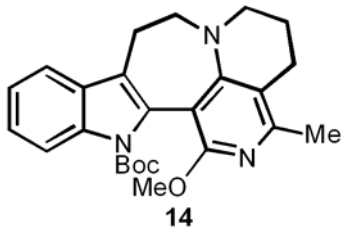

N
Cl
N
Boc
MeO
Me
N

i

^{1}H NMR

1.90
1.03
1.04
1.20
3.08
0.91
1.03
1.05
3.03
1.02
3.12
1.95
1.05
9.17
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

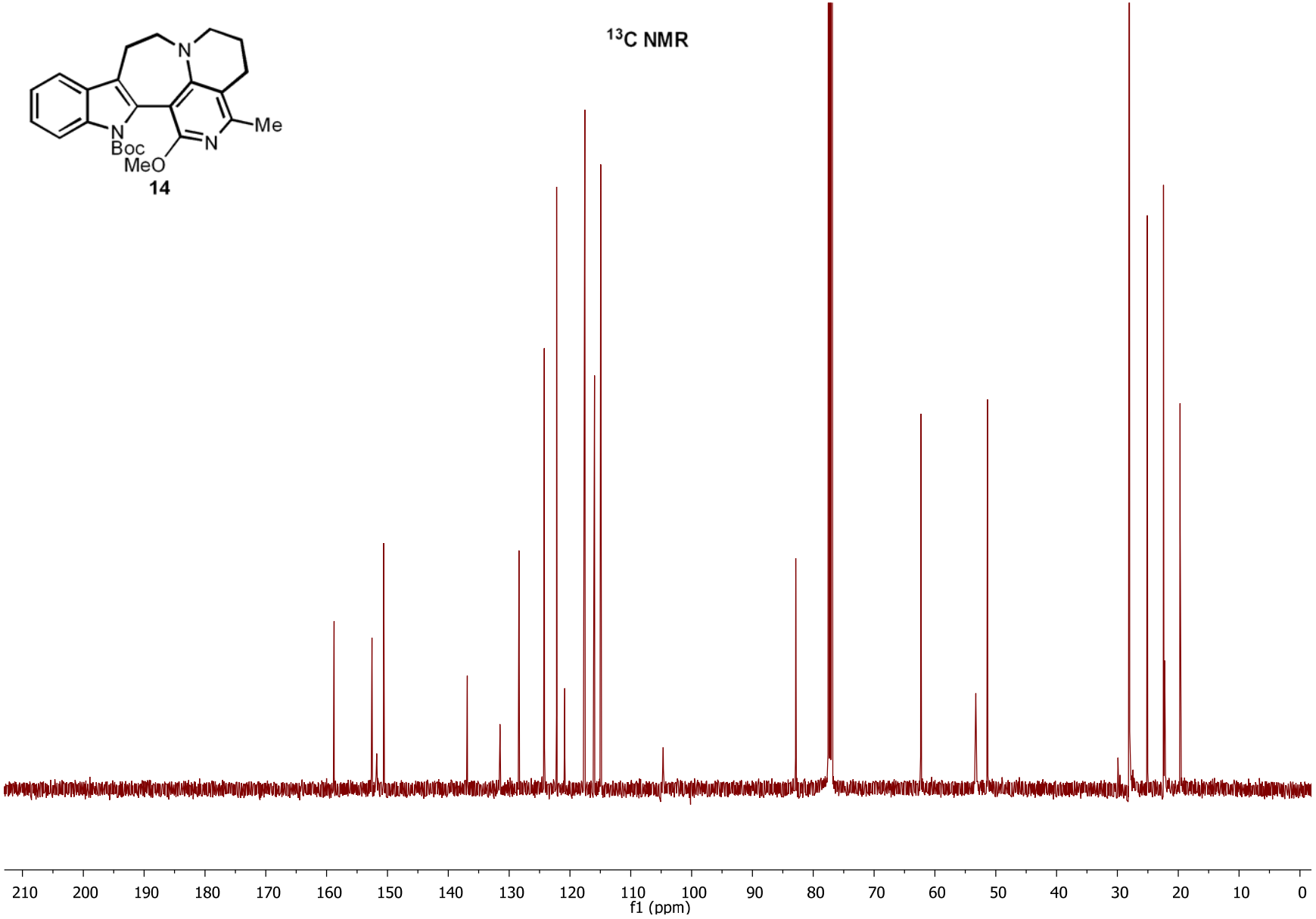

^{13}C NMR
N
Cl
N
Boc
MeO
N
Me
i
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

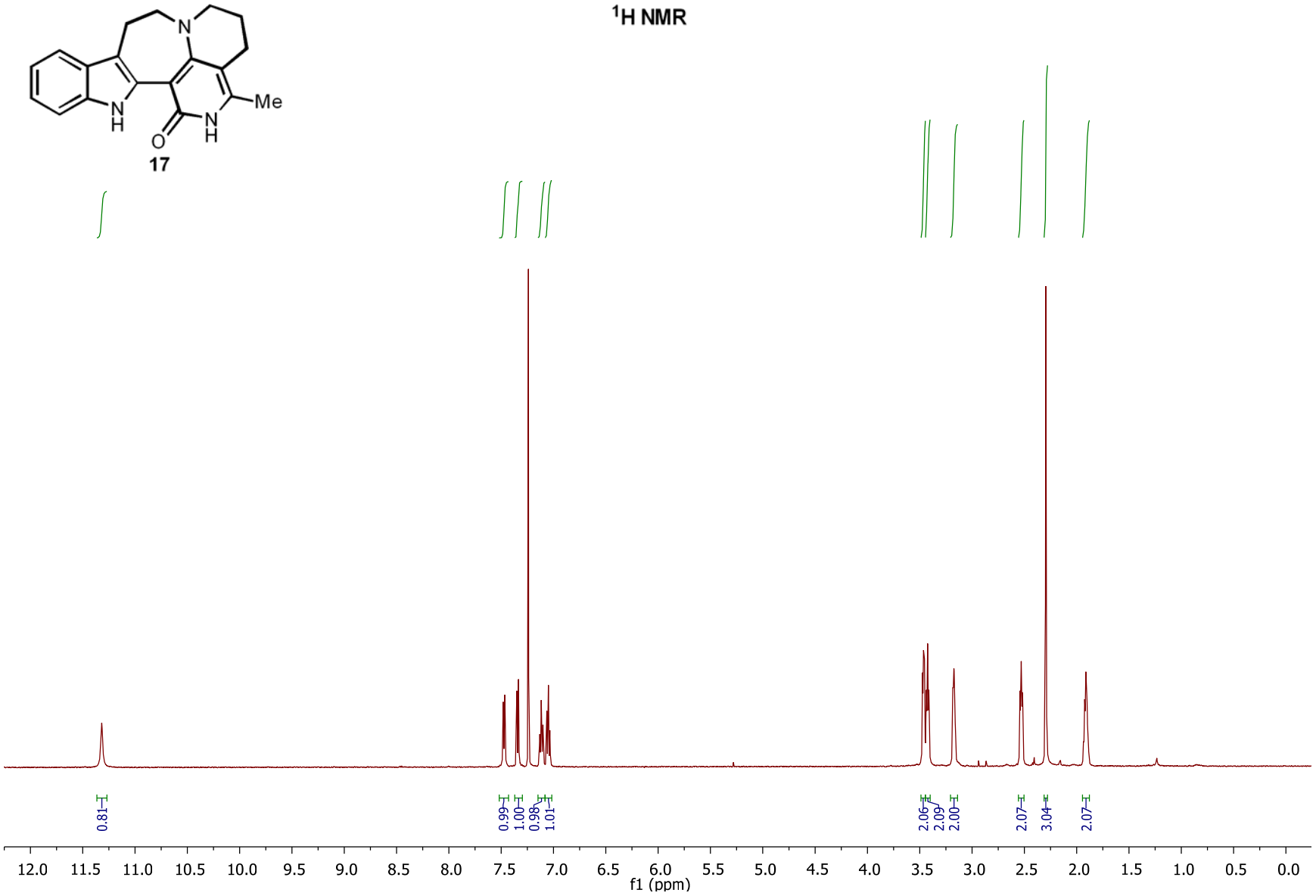

N
N
Boc
MeO
N
Me

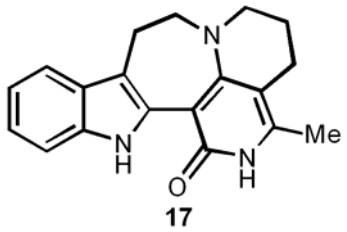
14

^{1}H NMR

0.94
0.97
1.00
0.97
2.97
1.03
1.00
1.03
2.02
1.02
2.05
2.94
1.05
1.04
8.98
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


^{13}C NMR
N
N
Boc
MeO
Me
14
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

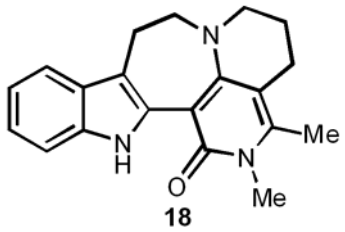

17
^{1}H NMR
0.81
0.99
1.00
0.98
1.01
2.06
2.09
2.00
2.07
3.04
2.07
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


N
N
H
Me
N
H
O

17

^{13}C NMR

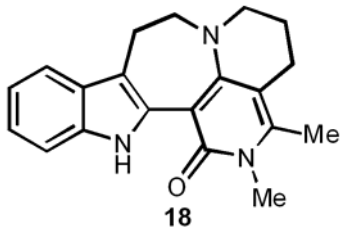
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
N
H
O
N
Me
Me

18

^{1}H NMR

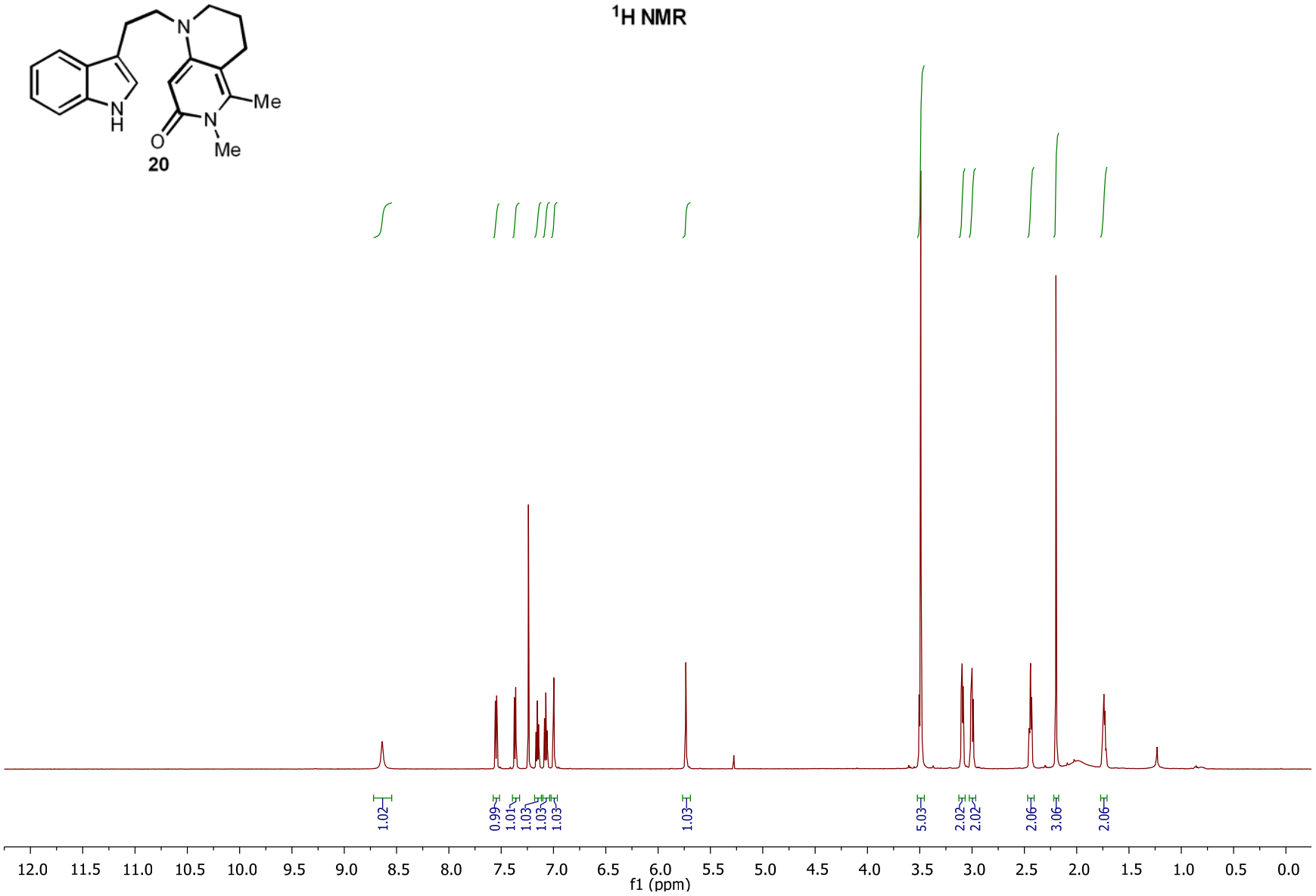
0.98
1.00
0.99
0.99
1.01
3.04
2.03
2.04
2.02
2.02
3.02
2.03
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

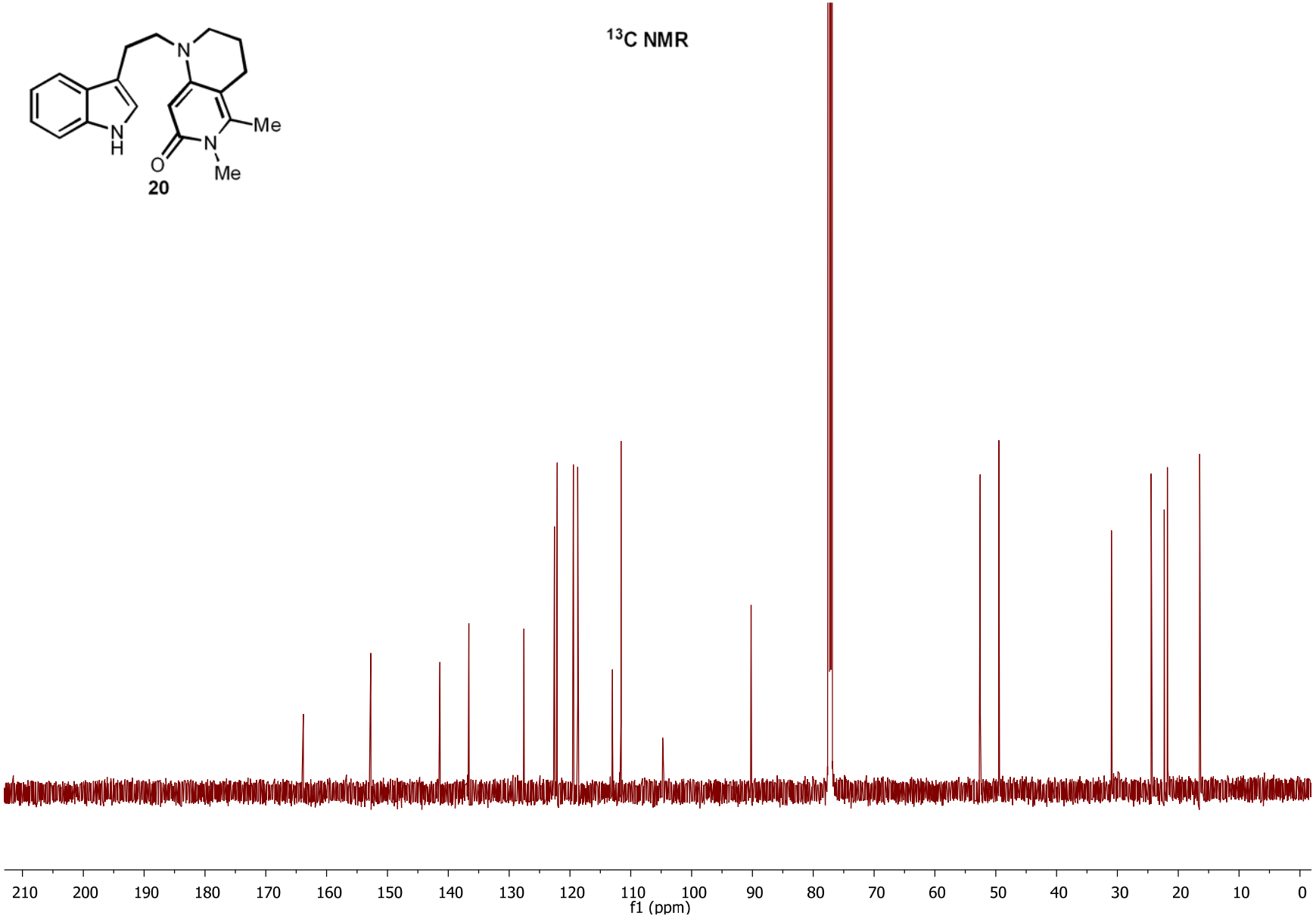

N
N
H
O
N
Me
Me

18

^{13}C NMR

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


^{1}H NMR
N
N
H
O
N
Me
Me
20
1.02
0.99
1.01
1.03
1.03
1.03
1.03
5.03
2.02
2.02
2.06
3.06
2.06
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


^{13}C NMR
N
H
O
N
Me
Me
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)