

A Non-Hallucinogenic Psychedelic Analog with Therapeutic Potential

Supplemental Material

(44 pages)

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Contents

Supplemental Methods

Spectral Data

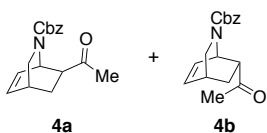
SUPPLEMENTAL METHODS

Chemistry (General). All reagents were obtained commercially unless otherwise noted. Reactions were performed using glassware that was oven dried (120°C) unless otherwise stated. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless-steel cannula. Organic solutions were concentrated under reduced pressure (~5 Torr) by rotary evaporation. Solvents were purified by passage under 12 psi N₂ through activated alumina columns. Chromatography was performed using Fisher Chemical™ Silica Gel Sorbent (230-400 Mesh, Grade 60). Compounds purified by chromatography were typically applied to the adsorbent bed using the indicated solvent conditions with a minimum amount of added dichloromethane as needed for solubility. Thin layer chromatography (TLC) was performed on Merck silica gel 60 F254 plates (250 μm). Visualization of the developed chromatogram was accomplished by fluorescence quenching or by staining with butanolic ninhydrin, aqueous potassium permanganate, ethanolic vanillin, or aqueous ceric ammonium molybdate (CAM).

Nuclear magnetic resonance (NMR) spectra were acquired on either a Bruker 400 operating at 400 and 100 MHz or a Varian-600 operating at 600 and 150 MHz for ¹H and ¹³C, respectively, and are referenced internally according to residual solvent signals. Data for ¹H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; m, multiplet), integration, and coupling constant (Hz). Data for ¹³C NMR are reported in terms of chemical shift (δ, ppm). Infrared spectra were recorded using a Thermo Scientific Nicolet iS10 spectrometer with Smart iTX Accessory (diamond ATR) and are reported in frequency of absorption. Low-resolution mass spectra were obtained using a Waters Acuity Arc LC-MS.

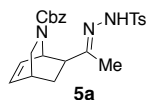
Chemistry (Synthetic Details). The specific procedures used to synthesize the compounds reported in this manuscript are detailed below along with characterization data. Spectral data (¹H and ¹³C NMR spectra) for each compound tested in biological assays is included at the end of the supporting information. All compounds tested in biological assays were confirmed to be of >95% purity based on UHPLC analysis (Waters ACQUITY Arc).

Procedure for Preparing 4a and 4b. To a solution of pyridine (10.0 g, 126.4 mmol, 1.0 equiv) and sodium borohydride (4.8 g, 126.4 mmol, 1.0 equiv) in MeOH (56 mL, 2.3 M) at -78°C was added benzylchloroformate (18.0 mL, 21.6 g, 126.4 mmol, 1.0 equiv) via slow dropwise addition. Gas evolution was observed. The mixture was stirred for 3h at -78°C, diluted with Et₂O (100 mL) and H₂O (50 mL), and warmed to room temperature. The aqueous layer was extracted with Et₂O (3 x 50 mL). The combined organic extracts were washed with brine (3 x 50 mL), dried over Na₂SO₄, and concentrated under reduced pressure to yield a clear oil. The product was passed through a short plug of silica gel using hexanes:EtOAc (95:5) as the eluent. The resulting filtrate was concentrated under reduced pressure. After purging with nitrogen, methyl vinyl ketone (10.5 mL, 126.4 mmol, 1.0 equiv) was added to the flask and the neat solution was heated to 80°C for 24 h. After cooling the mixture to room temperature, MeOH (250 mL) was added followed by 25% w/w aqueous NaOMe (2.4 mL, 8.9 mmol, 0.07 equiv). The resulting mixture was stirred for 15 min, quenched with H₂O (5 mL), then concentrated under reduced pressure. The residue was dissolved in DCM (250 mL) and then washed with H₂O (100 mL) followed by brine (50 mL). The organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The produce was purified by chromatography on silica gel (3:1 hexanes:EtOAc) to give a clear oil containing a mixture of **4a** and **4b** (26.5 g, 73% over 3 steps, ~1:1 exo:endo as a mixture of rotamers).

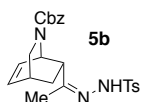


¹H NMR (CDCl₃, 400 MHz) δ 7.4–7.2 (m, 5H), 6.57–6.23 (m, 2H), 5.22–4.94 (m, 3H), 3.33 (t, 1H, *J* = 10.3 Hz), 3.18–2.58 (m, 3H), 2.35–2.05 (m, 3H), 1.91–1.66 (m, 1H), 1.64–1.23 (m, 1H) ppm; IR (Smart iTX Diamond) ν 3060, 2957, 2878, 1699, 1417, 1366, 1337, 1300, 1279, 1113, 764, 699 cm⁻¹; LC-MS (ES⁺) calcd for C₁₇H₂₀NO₃ [M + H] 286.14 found 286.22.

Procedure for Preparing 5a and 5b. To a mixture of **4a** and **4b** (4.8 g, 17.0 mmol, 1.0 equiv) in anhydrous THF (13 mL, 1.3 M) was added *p*-toluenesulfonyl hydrazide (3.16 g, 17.0 mmol, 1 equiv). The mixture was refluxed for 15–20 hour until starting material was consumed as determined by TLC. The reaction mixture was concentrated under reduced pressure, diluted with Et₂O (20 mL), and sonicated for 15 min. The white precipitate was filtered and washed with Et₂O (4 x 5 mL) to yield **5b**. The filtrate was concentrated under reduced pressure and purified by chromatography on silica gel (gradient elution: 5:1→1:1 hexanes:EtOAc) to give **5a** (75%; exo = 5.88 g, endo = 7.33 g, mixture of exo and endo = 2.62 g).

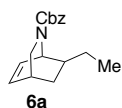


Isolated as a white solid (5.88 g, mixture of rotamers); ¹H NMR (CDCl₃, 400 MHz) δ 7.80 (dd, 2H, *J* = 20.1, 8.3 Hz), 7.43–7.26 (m, 4H), 7.25–7.11 (m, 3H), 6.49–6.36 (m, 2H), 5.10 (dd, 1H, *J* = 36.0, 12.3 Hz), 4.80–4.57 (m, 2H), 3.02 (dd, 1H, *J* = 10.0, 2.1 Hz), 2.92–2.84 (m, 1H), 2.75–2.67 (m, 1H), 2.48–2.13 (m, 5H), 1.89 (s, 2H), 1.59 (s, 1H), 1.47 (s, 1H), 1.39–1.27 (m, 1H) ppm; IR (Smart iTX Diamond) ν 3207, 2952, 2876, 1675, 1418, 1368, 1337, 1303, 1258, 1165, 1117, 1030, 917, 813, 763, 705, 667, 552 cm⁻¹; LC-MS (ES⁺) calcd for C₂₄H₂₈N₂O₄S [M + H] 454.18 found 454.33.

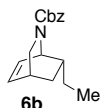


Isolated as a white solid (7.33 g, mixture of rotamers); ¹H NMR (CDCl₃, 400 MHz) δ 7.79 (t, 2H, *J* = 8.9 Hz), 7.42–7.27 (m, 6H), 7.09 (d, 1H, *J* = 8.0 Hz), 6.21 (t, 1H, *J* = 7.3 Hz), 6.08–6.00 (m, 1H), 5.23–5.05 (m, 2H), 4.93–4.82 (m, 1H), 3.33–3.23 (m, 1H), 3.06–2.96 (m, 1H), 2.96–2.86 (m, 1H), 2.81–2.71 (m, 1H), 2.41 (s, 3H), 1.93–1.46 (m, 6H) ppm; IR (Smart iTX Diamond) ν 3105, 2939, 2878, 1671, 1446, 1420, 1372, 1338, 1322, 1298, 1280, 1262, 1241, 1167, 976, 932, 818, 804, 766, 724, 670, 550 cm⁻¹; LC-MS (ES⁺) calcd for C₂₄H₂₈N₂O₄S [M + H] 454.18 found 454.33.

Procedure for Preparing 6a and 6b. To a solution of **5a** or **5b** (3.78 g, 8.35 mmol, 1.0 equiv) in THF (16.7 mL, 2 M) was added sodium cyanoborohydride (2.1 g, 33.4 mmol, 4 equiv) and *p*-toluenesulfonic acid (159 mg, 0.835 mmol, 0.1 equiv). The mixture was refluxed for 18 h, diluted with H₂O (30 mL), and extracted with cyclohexane (5 x 25 mL). The combined organic extracts were washed with H₂O (20 mL), saturated aqueous NaHCO₃ (20 mL), and brine (20 mL) before being dried over Na₂SO₄ and concentrated under reduced pressure to yield either **6a** or **6b**.



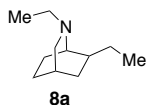
Isolated as a clear oil (2.01g, 57%, mixture of rotamers); ¹H NMR (CDCl₃, 400 MHz) δ 7.41–7.27 (m, 5H), 6.55–6.38 (m, 1H), 6.33 (q, 1H, *J* = 7.7 Hz), 5.22–5.02 (m, 2H), 4.58 (d, 1H, *J* = 6.1 Hz), 3.30–3.20 (m, 1H), 3.08–2.96 (m, 1H), 2.75–2.58 (m, 1H), 1.69–1.59 (m, 1H), 1.53–1.30 (m, 3H), 1.05–0.98 (m, 1H), 0.98–0.84 (m, 3H) ppm; IR (Smart iTX Diamond) ν 3052, 2957, 2873, 1699, 1417, 1335, 1295, 1106, 986, 764, 699 cm⁻¹; LC-MS (ES⁺) calcd for C₁₇H₂₁NO₂ [M + H] 272.17 found 272.29.



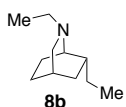
Isolated as a clear oil (2.66 g, 62%, mixture of rotamers); ¹H NMR (CDCl₃, 400 MHz) δ 7.39–7.26 (m, 5H), 6.42–6.22 (m, 2H), 5.18–5.08 (m, 2H), 4.73–4.55 (m, 1H), 3.32–3.20 (m, 1H), 3.04–2.95 (m, 1H), 2.77–2.62 (m, 1H), 2.05–1.91 (m, 1H), 1.87–1.77 (m, 1H), 1.28–1.11 (m, 1H), 1.05–0.82 (m, 5H) ppm; IR (Smart iTX Diamond) ν 3052, 2958, 2931, 2874, 1699, 1416, 1333, 1301, 1276, 1111, 977, 766, 698 cm⁻¹. LC-MS (ES⁺) calcd for C₁₇H₂₁NO₂ [M + H] 272.17 found 272.29.

Procedure for Preparing 8a and 8b. A solution of either **6a** or **6b** (132 mg, 0.95 mmol, 1.0 equiv) and 10% Pd/C was stirred in MeOH (0.2 M) under an atmosphere of N₂. The flask was then purged with H₂ gas and

stirred vigorously under an atmosphere of H₂ until the starting material had been consumed as determined by TLC. The mixture was filtered over a pad of Celite, which was washed with 50 mL of MeOH containing 1% aqueous NH₄OH. The filtrate was then dried over Na₂SO₄ and concentrated under reduced pressure to yield a clear oil. Next, a Gribble reductive amination was performed.⁴⁵ The oil was dissolved in acetic acid (0.5 mL, 1.9 M) and was heated to 55°C prior to the addition of sodium borohydride (165 mg, 4.37 mmol, 4.6 equiv). Gas evolution was observed. The mixture was stirred at 55°C for 10 h, diluted with H₂O (2 mL), cooled to 0°C and basified with solid NaOH (until pH = 14). The aqueous layer was extracted with Et₂O (4 x 10 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (100:1 DCM:MeOH with 0.5% NH₄OH) to afford product.



Isolated as a yellow oil (12 mg, 7%); ¹H NMR (CDCl₃, 400 MHz) δ 3.05–2.96 (m, 1H), 2.47 (q, 2H, *J* = 7.2 Hz), 2.37 (t, 1H, *J* = 2.4 Hz), 2.20 (dt, 1H, *J* = 9.3, 1.5 Hz), 2.00–1.89 (m, 1H), 1.73–1.64 (m, 1H), 1.64–1.58 (m, 1H), 1.56–1.36 (m, 5H), 1.32–1.23 (m, 1H), 1.19–1.11 (m, 1H), 1.00 (t, 3H, *J* = 7.2 Hz), 0.86 (t, 3H, *J* = 7.1 Hz) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 56.67, 51.92, 49.18, 40.36, 32.76, 27.15, 26.89, 25.34, 21.52, 13.64, 11.98 ppm; IR (Smart iTX Diamond) ν 2955, 2926, 2857, 2793, 1458, 1372, 1259, 1100, 1048, 799 cm⁻¹; LC-MS (ES⁺) calcd for C₁₁H₂₁N [M + H] 168.18 found 168.33.

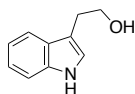
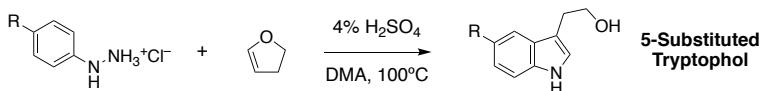


Isolated as a yellow oil (71.5 mg, 47%); ¹H NMR (CDCl₃, 400 MHz) δ 2.76 (dt, 1H, *J* = 9.8, 2.7 Hz), 2.65–2.46 (m, 3H), 2.45–2.39 (m, 1H), 1.91–1.70 (m, 3H), 1.66–1.55 (m, 3H), 1.47–1.37 (m, 1H), 1.35–1.20 (m, 2H), 1.07 (d, 3H, *J* = 14.4 Hz), 0.99 (dt, 1H, *J* = 6.3, 2.2 Hz), 0.88 (t, 3H, *J* = 7.4 Hz) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 55.71, 52.90, 49.55, 35.32, 32.94, 27.67, 26.63, 25.30, 20.02, 13.47, 12.19 ppm; IR (Smart iTX Diamond) ν 2958, 2931, 2872, 2860, 2792, 1464, 1371, 1217, 1161, 1094, 819, 756 cm⁻¹; LC-MS (ES⁺) calcd for C₁₁H₂₁N [M + H] 168.17 found 168.25.

General Procedure for Preparing Hydrazines. Most hydrazines were commercially available, however the 4-iodo and 4-benzyloxy hydrazines were synthesized in house according to the following procedure. A 0.5 M solution of 4-substituted aniline (3.99 mmol, 1 equiv) in aqueous concentrated HCl was cooled to 0°C before the addition of 2.0 M aqueous NaNO₂ (3.91 mmol, 0.98 equiv). The solution was stirred for 20 min at 0°C. Next, a solution of SnCl₂·2H₂O (10.4 mmol, 2.6 equiv) dissolved in concentrated aqueous HCl (2.4 mL) was added. The mixture was stirred for 2 h, warmed to room temperature, filtered, and rinsed with H₂O and Et₂O. The solids were dried under reduced pressure and used immediately without further purification.

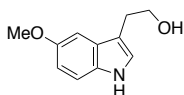
Preparation of 5-Substituted Tryptophols. All 5-substituted tryptophols were prepared from the corresponding 4-substituted hydrazines as outlined here.

General Scheme:

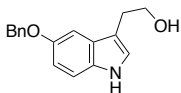


A solution of phenyl hydrazine (0.5 g, 3.46 mmol, 1 equiv) in 10 mL of a 1:1 mixture of DMA and 4% aqueous H₂SO₄ was heated to 100°C. To this solution was added 1,2-dihydrofuran (0.29 mL, 266 mg, 3.8 mmol, 1.1 equiv) via dropwise addition. The resulting mixture was stirred at 100°C until starting material was consumed as determined by TLC (~3 h). The reaction was then cooled to room temperature and diluted with EtOAc (10mL). The aqueous layer was extracted with EtOAc (5 x 10 mL). The combined organic extracts were washed with 5% aqueous LiCl (15 mL), saturated aqueous NaHCO₃ (15 mL), and H₂O (15 mL) before being dried over Na₂SO₄. The resulting product was purified by chromatography on silica gel (3:1 hexanes:EtOAc) to

yield the desired tryptophol as a brown solid (258 mg, 92%); ^1H NMR (CDCl_3 , 400 MHz) δ 8.23 (s, 1H), 7.70–7.59 (m, 1H), 7.36 (d, 1H, $J = 8.1$ Hz), 7.25–7.19 (m, 1H), 7.15 (td, 1H, $J = 7.6, 7.1, 1.0$ Hz), 7.09–7.00 (m, 1H), 3.91 (t, 2H, $J = 6.4$ Hz), 3.04 (t, 2H, $J = 6.4$ Hz), 1.86 (s, 1H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 136.47, 127.44, 122.54, 122.23, 119.49, 118.86, 112.27, 111.26, 62.64, 28.77 ppm; IR (Smart iTX Diamond) ν 3390, 3322, 3059, 2933, 2905, 2863, 1456, 1424, 1352, 1338, 1229, 1094, 1045, 1005, 738, 591 cm^{-1} ; LC-MS (ES^+) calcd for $\text{C}_{10}\text{H}_{11}\text{NO}$ [$\text{M} + \text{H}$] 162.09 found 162.21.



A solution of *p*-MeO-phenylhydrazine (2g, 11.45 mmol, 1 equiv) in 32.6 mL of a 1:1 mixture of DMA and 4% aqueous H_2SO_4 was heated to 100°C . To this solution was added 1,2-dihydrofuran (0.95 mL, 0.883 g, 12.6 mmol, 1.1 equiv) via dropwise addition. The resulting mixture was stirred at 100°C until starting material was consumed as determined by TLC (~5 h). The reaction was then cooled to room temperature and diluted with EtOAc (20 mL). The aqueous layer was extracted with EtOAc (4 x 25 mL). The combined organic extracts were washed with 5% aqueous LiCl (20 mL), saturated aqueous NaHCO_3 (20 mL), and H_2O (20 mL) before being dried over Na_2SO_4 . The resulting product was purified by chromatography on silica gel (gradient elution: 3:1→1:1 hexanes:EtOAc) to yield the desired product as a yellow oil (1.71 g, 78%); ^1H NMR (CDCl_3 , 400 MHz) δ 8.01 (s, 1H), 7.25 (s, 1H), 7.06 (d, 2H, $J = 2.5$ Hz), 6.88 (dd, 1H, $J = 8.8, 2.4$ Hz), 3.90 (t, 2H, $J = 6.4$ Hz), 3.87 (s, 3H), 3.01 (t, 2H, $J = 6.4$ Hz), 1.70 (s, 1H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 154.09, 131.70, 127.91, 123.46, 112.45, 112.09, 111.97, 100.76, 62.67, 56.06, 28.82 ppm; IR (Smart iTX Diamond) ν 3409, 2938, 2831, 1624, 1584, 1486, 1456, 1440, 1214, 1067, 1043, 922, 798 cm^{-1} ; LC-MS (ES^+) calcd for $\text{C}_{11}\text{H}_{13}\text{NO}_2$ [$\text{M} + \text{H}$] 192.10 found 192.27.

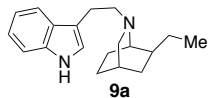


A solution of *p*-BnO-phenylhydrazine (398 mg, 1.59 mmol, 1 equiv) in 4.54 mL of a 1:1 mixture of DMA and 4% aqueous H_2SO_4 was heated to 100°C . To this solution was added 1,2-dihydrofuran (0.13 mL, 123 mg, 1.75 mmol, 1.1 equiv) via dropwise addition. The resulting mixture was stirred at 100°C until starting material was consumed as determined by TLC (~3 h). The reaction was then cooled to room temperature and diluted with EtOAc (10 mL). The aqueous layer was extracted with EtOAc (4 x 10 mL). The combined organic extracts were washed with 5% aqueous LiCl (10 mL), saturated aqueous NaHCO_3 (10 mL), and H_2O (2 x 10 mL) before being dried over Na_2SO_4 . The resulting product was purified by chromatography on silica gel (gradient elution: 3:1→1:1 hexanes:EtOAc) to yield the desired product as a brown oil (160 mg, 38%); ^1H NMR (CDCl_3 , 400 MHz) δ 7.95 (s, 1H), 7.49 (d, 2H, $J = 7.4$ Hz), 7.43–7.30 (m, 3H), 7.26 (s, 1H), 7.15 (d, 1H, $J = 2.3$ Hz), 7.06 (d, 1H, $J = 2.2$ Hz), 6.96 (dd, 1H, $J = 8.8, 2.4$ Hz), 5.12 (s, 2H), 3.89 (t, 2H, $J = 6.3$ Hz), 3.00 (t, 2H, $J = 6.3$ Hz), 1.59 (s, 1H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 153.25, 137.61, 131.79, 128.53, 127.85, 127.82, 127.63, 123.34, 113.13, 112.07, 111.93, 102.44, 71.04, 62.59, 28.77 ppm; IR (Smart iTX Diamond) ν 3419, 3062, 3032, 2929, 2878, 1624, 1582, 1483, 1454, 1381, 1293, 1219, 1194, 1064, 1043, 1025, 797, 740, 698 cm^{-1} ; LC-MS (ES^+) calcd for $\text{C}_{17}\text{H}_{18}\text{NO}_2$ [$\text{M} + \text{H}$] 268.13 found 268.24.

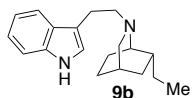
Procedure for Preparing 9a, 9b, 10a, and 10b. First, the hydroxyl groups of the tryptophols shown above were converted to the iodides. To accomplish this transformation, a solution of iodine (251 mg, 0.99 mmol, 1.4 equiv) and triphenyl phosphine (260 mg, 0.99 mmol, 1.4 equiv) in DCM (2.75 mL, 0.25 M) was cooled to 0°C . Next, a tryptophol (0.71 mmol, 1.0 equiv) was added dropwise. The solution was stirred until starting material had been consumed as determined by TLC (~5 h). The reaction mixture was concentrated under reduced pressure to afford the alkyl iodide, which was used immediately without further purification.

In a separate flask, a mixture of **6a** or **6b** (271 mg, 1.0 mmol, 1.0 equiv) and 10% Pd/C (85 mg, 0.08 mmol, 0.08 equiv) was stirred in MeOH (5 mL, 0.2 M) under an atmosphere of N_2 . The flask was then purged with H_2 gas and stirred vigorously under an atmosphere of H_2 until the starting material had been consumed as determined by TLC (~3 h). The mixture was filtered over a pad of Celite, which was washed with 50 mL of MeOH containing 1% aqueous NH_4OH . The filtrate was then dried over Na_2SO_4 and concentrated under reduced pressure to yield a clear oil. The oil was immediately dissolved in DMF (2.5 mL, 0.4 M) and added to a flask containing the unpurified alkyl iodide (271 mg, 1.0 mmol, 1.0 equiv, generated as described above) and

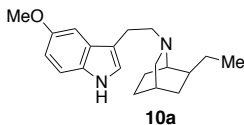
solid NaHCO₃ (168 mg, 2 mmol, 2 equiv.). The mixture was heated at 80°C for 20h before being cooled to room temperature and diluted with 1M aqueous Na₂CO₃ (15 mL) and EtOAc (15 mL). The aqueous layer was extracted with EtOAc (3 x X 10 mL). The combined organic extracts were washed with H₂O (10 mL), 5% aqueous LiCl (10 mL), and brine (10 mL) before being dried over Na₂SO₄ and concentrated under reduced pressure. The product was purified by chromatography on silica gel (100:1 DCM:MeOH with 0.5% NH₄OH)



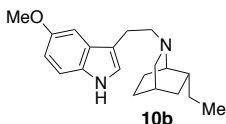
Isolated as a tan solid (30 mg, 24%, 2 steps); ¹H NMR (CDCl₃, 400 MHz) δ 7.95 (s, 1H), 7.64 (d, 1H, *J* = 7.8 Hz), 7.35 (d, 1H, *J* = 8.0 Hz), 7.24–7.16 (m, 1H), 7.16–7.10 (m, 1H), 7.05 (d, 1H, *J* = 1.8 Hz), 3.19–3.12 (m, 1H), 2.96–2.72 (m, 4H), 2.49 (s, 1H), 2.36 (d, 1H, *J* = 9.2 Hz), 2.09–1.99 (m, 1H), 1.79–1.71 (m, 1H), 1.71–1.65 (m, 1H), 1.63–1.42 (m, 5H), 1.40–1.31 (m, 1H), 1.24–1.16 (m, 1H), 0.90 (t, 3H, *J* = 7.1 Hz) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 136.29, 127.83, 121.84, 121.65, 119.13, 119.04, 115.21, 111.15, 56.89, 56.82, 53.30, 40.62, 32.87, 27.44, 26.95, 25.35, 24.40, 21.97, 12.04 ppm; IR (Smart iTX Diamond) ν 3418, 3170, 3055, 2930, 2860, 2798, 1456, 1357, 1228, 1147, 1092, 740 cm⁻¹; LC-MS (ES⁺) calcd for C₁₉H₂₆N₂ [M + H] 283.22 found 283.35.



Isolated as a tan solid (66 mg, 23%, 2 steps); ¹H NMR (CDCl₃, 400 MHz) δ 8.07 (s, 1H), 7.65 (d, 1H, *J* = 7.8 Hz), 7.35 (d, 1H, *J* = 8.0 Hz), 7.19 (t, 1H, *J* = 7.4 Hz), 7.12 (t, 1H, *J* = 7.4 Hz), 7.07–7.03 (m, 1H), 3.01–2.91 (m, 3H), 2.91–2.83 (m, 2H), 2.77–2.70 (m, 1H), 2.55–2.50 (m, 1H), 1.97–1.78 (m, 3H), 1.73–1.56 (m, 3H), 1.52–1.41 (m, 1H), 1.36–1.26 (m, 2H), 1.08–1.00 (m, 1H), 0.89 (t, 3H, *J* = 7.4 Hz) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 136.37, 127.73, 122.03, 121.65, 119.30, 119.10, 114.97, 111.21, 57.30, 56.20, 53.91, 35.48, 32.92, 27.68, 26.67, 25.26, 24.39, 20.15, 12.19 ppm; IR (Smart iTX Diamond) ν 3416, 3139, 3055, 2926, 2858, 2823, 1456, 1354, 1231, 1112, 1088, 738 cm⁻¹; LC-MS (ES⁺) calcd for C₁₉H₂₆N₂ [M + H] 283.22 found 283.35.

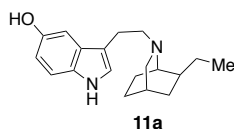


Isolated as an amorphous brown solid (71.2 mg, 44%, 2 steps); ¹H NMR (CDCl₃, 400 MHz) δ 8.05 (s, 1H), 7.23 (d, 1H, *J* = 8.7 Hz), 7.09 (d, 1H, *J* = 2.0 Hz), 7.04–6.98 (m, 1H), 6.86 (dd, 1H, *J* = 8.8, 2.3 Hz), 3.88 (s, 3H), 3.27–3.12 (m, 1H), 2.96–2.76 (m, 4H), 2.54 (s, 1H), 2.37 (d, 1H, *J* = 9.3 Hz), 2.11–1.98 (m, 1H), 1.81–1.72 (m, 1H), 1.72–1.65 (m, 1H), 1.65–1.43 (m, 5H), 1.42–1.33 (m, 1H), 1.28–1.16 (m, 1H), 0.91 (t, 3H, *J* = 7.1 Hz) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 153.91, 131.50, 128.16, 122.60, 114.58, 111.97, 111.87, 101.05, 56.85, 56.57, 56.13, 53.35, 40.43, 32.66, 27.38, 26.78, 25.15, 24.20, 21.90, 12.03 ppm; IR (Smart iTX Diamond) ν 3415, 3045, 2931, 2860, 2828, 1624, 1585, 1485, 1456, 1215, 1172, 1064, 1032, 796 cm⁻¹; LC-MS (ES⁺) calcd for C₂₀H₂₉N₂O [M + H] 313.23 found 313.34.

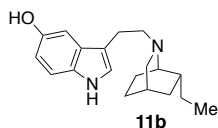


Isolated as an amorphous brown solid (56 mg, 18%, 2 steps); ¹H NMR (CDCl₃, 400 MHz) δ 8.67 (s, 1H), 7.23 (d, 1H, *J* = 8.8 Hz), 7.08 (d, 1H, *J* = 2.3 Hz), 7.00 (d, 1H, *J* = 1.9 Hz), 6.86 (dd, 1H, *J* = 8.8, 2.4 Hz), 3.85 (s, 3H), 3.02–2.93 (m, 3H), 2.93–2.86 (m, 2H), 2.80–2.73 (m, 1H), 2.63–2.56 (m, 1H), 2.02–1.83 (m, 3H), 1.75–1.59 (m, 3H), 1.55–1.44 (m, 1H), 1.40–1.29 (m, 2H), 1.07 (m, 1H), 0.92 (t, 3H, *J* = 7.4 Hz) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 153.77, 131.57, 127.99, 122.66, 114.24, 114.21, 111.94, 100.83, 57.10, 56.10, 55.99, 53.63, 35.34, 32.87, 27.58, 26.60, 25.23, 24.32, 20.10, 12.14 ppm; IR (Smart iTX Diamond) ν 3412, 3041, 2930, 2871, 2827, 1625, 1586, 1486, 1456, 1216, 1173, 1064, 1032, 795 cm⁻¹; LC-MS (ES⁺) calcd for C₂₀H₂₉N₂O [M + H] 313.23 found 313.34.

Procedure for Preparing 11a and 11b. First, the 5-benzyloxy-isoquinuclidine was synthesized as described above. Next, this starting material (100 mg, 0.26 mmol, 1.0 equiv) was dissolved MeOH (1.3 mL, 0.2 M) containing 10% Pd/C (22 mg, 0.02 mmol, 0.08 equiv) under a N₂ atmosphere. The flask was then purged with H₂ gas and stirred vigorously under an atmosphere of H₂ until the starting material had been consumed as determined by TLC (~24 h). The mixture was filtered over a pad of Celite, which was washed with 50 mL of MeOH containing 1% aqueous NH₄OH. The filtrate was then dried over Na₂SO₄ and concentrated under reduced pressure to yield a brown oil. The product was purified by chromatography on silica gel (30:1 DCM:MeOH with 1% NH₄OH)



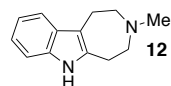
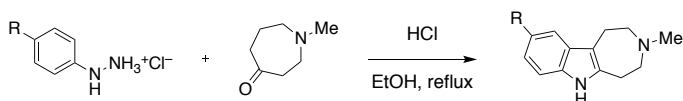
Isolated as a tan foam (32 mg, 41%, 3 steps); ¹H NMR (CDCl₃, 400 MHz) δ 7.96 (s, 1H), 7.14 (d, 1H, *J* = 8.6 Hz), 6.94 (s, 1H), 6.83 (d, 1H, *J* = 1.8 Hz), 6.80–6.72 (dd, 1H, *J* = 8.6, 1.8 Hz), 5.74 (bs, 1H), 3.13 (dt, 1H, *J* = 9.2, 2.9 Hz), 2.93–2.71 (m, 4H), 2.56–2.49 (m, 1H), 2.35 (d, 1H, *J* = 9.5 Hz), 2.08–1.95 (m, 1H), 1.80–1.71 (m, 1H), 1.70–1.64 (m, 1H), 1.63–1.40 (m, 5H), 1.39–1.17 (m, 2H), 0.88 (t, 3H, *J* = 7.1 Hz) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 149.82, 131.40, 128.36, 122.85, 114.05, 112.26, 111.91, 103.71, 56.99, 56.59, 53.67, 40.64, 32.59, 27.43, 26.66, 25.01, 23.95, 22.08, 12.17 ppm; IR (Smart iTX Diamond) ν 3400, 3278, 2929, 2860, 1625, 1581, 1456, 1362, 1186, 1092, 936, 796, 754 cm⁻¹; LC-MS (ES⁺) calcd for C₁₉H₂₇N₂O [M + H] 299.21 found 299.34.



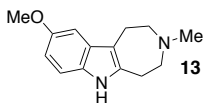
Isolated as a tan foam (20 mg, 15%, 3 steps); ¹H NMR (CDCl₃, 600 MHz) δ 7.98 (s, 1H), 7.16 (d, 1H, *J* = 8.6 Hz), 6.94 (s, 1H), 6.88 (d, 1H, *J* = 2.0 Hz), 6.78 (dd, 1H, *J* = 8.6, 2.2 Hz), 3.03–2.92 (m, 4H), 2.76–2.71 (m, 1H), 2.62–2.57 (m, 1H), 2.01–1.82 (m, 3H), 1.69 (s, 1H), 1.67–1.57 (m, 2H), 1.48–1.41 (m, 1H), 1.35–1.19 (m, 3H), 1.05–0.99 (m, 1H), 0.83 (t, 3H, *J* = 7.4 Hz) ppm; ¹³C NMR (CDCl₃, 150 MHz) δ 150.66, 131.34, 128.18, 122.68, 113.51, 113.03, 112.03, 103.77, 57.33, 55.57, 54.52, 34.85, 32.65, 27.52, 26.35, 24.90, 24.01, 19.49, 12.09 ppm; IR (Smart iTX Diamond) ν 3402, 3286, 2924, 2857, 1625, 1581, 1456, 1377, 1208, 1080, 936, 795, 751 cm⁻¹; LC-MS (ES⁺) calcd for C₁₉H₂₇N₂O [M + H] 299.21 found 299.34.

Procedure for Preparing 12, 13, 14, 15, 16, and 17. To a solution of 4-substituted phenyl hydrazine hydrochloride (1.0 mmol) in EtOH (0.1 M) was added 1-methylazepan-4-one hydrochloride (164 mg, 1.0 mmol, 1.0 equiv) followed by concentrated aqueous HCl (0.5 mL, 6.0 mmol, 6.0 equiv). The mixture was refluxed for 24 h and then concentrated under reduced pressure. The oily residue was dissolved in DCM (~25 mL) and basified with 1M aqueous NaOH (~20mL). The aqueous layer was extracted with DCM (3 x 20 mL). The combined organic extracts were dried over Na₂SO₄ and concentrated under reduced pressure to yield an oil that was purified by chromatography on silica gel (20:1 DCM:MeOH with 0.5% NH₄OH).

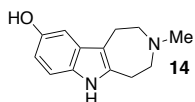
General Scheme:



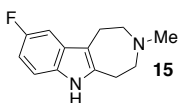
Isolated as a brown solid (127 mg, 64%); ¹H NMR (CDCl₃, 400 MHz) δ 7.78 (s, 1H), 7.50–7.43 (m, 1H), 7.28 (d, 1H, *J* = 1.6 Hz), 7.15–7.05 (m, 2H), 3.01–2.92 (m, 4H), 2.92–2.82 (m, 4H), 2.53 (s, 3H) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 136.10, 134.68, 129.05, 121.12, 119.36, 117.74, 112.89, 110.44, 58.05, 56.30, 46.16, 28.59, 23.95 ppm; IR (Smart iTX Diamond) ν 3140, 3055, 3032, 2904, 2829, 2756, 1451, 1337, 739 cm⁻¹; LC-MS (ES⁺) calcd for C₁₃H₁₇N₂ [M + H] 201.14 found 201.33.



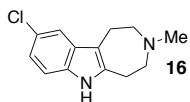
Isolated as a light brown solid (146 mg, 63%); ^1H NMR (CDCl_3 , 400 MHz) δ 7.74 (s, 1H), 7.15 (d, 1H, $J = 8.7$ Hz), 6.92 (d, 1H, $J = 2.4$ Hz), 6.77 (dd, 1H, $J = 8.7, 2.4$ Hz), 3.85 (s, 3H), 2.98–2.82 (m, 8H), 2.53 (s, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 154.13, 137.12, 129.79, 129.40, 112.70, 111.15, 110.91, 100.13, 58.04, 56.29, 56.11, 46.15, 28.61, 24.00 ppm. IR (Smart iTX Diamond) ν 3136, 3035, 2924, 2882, 2822, 1594, 1451, 1215, 1107, 1035, 837, 791 cm^{-1} ; LC-MS (ES^+) calcd for $\text{C}_{14}\text{H}_{19}\text{N}_2\text{O}$ [$\text{M} + \text{H}$] 231.15 found 231.32.



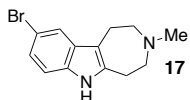
Synthesized from the *p*-benzyloxyhydrazine followed by hydrogenolysis of the benzyl group. Following Fischer indole cyclization, the benzyloxy indole was added to a mixture of 10% Pd/C (0.08 equiv) in MeOH (4.6 mL) under an atmosphere of N_2 . The slurry was stirred at room temperature for 12 hours, filtered over a small pad of Celite, and rinsed with 50 mL of methanol and 1% ammonium hydroxide. The filtrates were concentrated under reduced pressure to a brown oil. The desired product was purified by chromatography on silica gel (30:1 DCM:MeOH with 0.5% NH_4OH) to yield a white crystalline solid (80 mg, 40%, two steps). ^1H NMR ($\text{DMSO-}d_6$, 400 MHz) δ 10.32 (s, 1H), 8.46 (s, 1H), 6.99 (d, 1H, $J = 8.5$ Hz), 6.65 (d, 1H, $J = 2.2$ Hz), 6.47 (dd, 1H, $J = 8.5, 2.2$ Hz), 2.87–2.79 (m, 2H), 2.70–2.68 (m, 6H), 2.39 (s, 3H) ppm; ^{13}C NMR ($\text{DMSO-}d_6$, 100 MHz) δ 150.18, 137.63, 129.39, 129.05, 111.02, 110.58, 110.00, 101.62, 57.95, 56.14, 45.80, 27.76, 23.70 ppm; IR (Smart iTX Diamond) ν 3391, 3273, 3047, 2927, 1590, 1455, 1200, 1111, 928, 840, 797, 735 cm^{-1} . LC-MS (ES^+) calcd for $\text{C}_{13}\text{H}_{17}\text{N}_2\text{O}$ [$\text{M} + \text{H}$] 217.13 found 217.32.



Isolated as a yellow solid (97 mg, 88%); ^1H NMR (CDCl_3 , 400 MHz) δ 7.79 (s, 1H), 7.16 (dd, 1H, $J = 8.8, 4.4$ Hz), 7.09 (dd, 1H, $J = 9.77, 2.37$ Hz), 6.84 (td, 1H, $J = 9.0, 2.4$ Hz), 3.01–2.92 (m, 2H), 2.91–2.80 (m, 6H), 2.52 (s, 3H) ppm. ^{13}C NMR (CDCl_3 , 100 MHz) δ 158.01 (d, $J = 233.9$ Hz), 138.24, 131.12, 129.50 (d, $J = 9.5$ Hz), 113.23 (d, $J = 4.6$ Hz), 110.90 (d, $J = 9.7$ Hz), 109.11 (d, $J = 26.3$ Hz), 102.86 (d, $J = 23.4$ Hz), 57.95, 56.19, 46.21, 28.77, 24.09 ppm. IR (Smart iTX Diamond) ν 3146, 3103, 3040, 2929, 2880, 2809, 2753, 1584, 1453, 1169, 1103, 932, 855, 794, 767, 749 cm^{-1} . LC-MS (ES^+) calcd for $\text{C}_{13}\text{H}_{16}\text{FN}_2$ [$\text{M} + \text{H}$] 219.13 found 219.31.



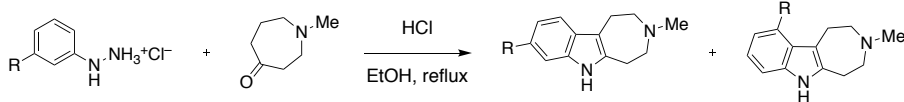
Isolated as a yellow solid (89 mg, 62%); ^1H NMR (CDCl_3 , 400 MHz) δ 7.99 (s, 1H), 7.41 (d, 1H, $J = 1.7$ Hz), 7.14 (d, 1H, $J = 8.5$ Hz), 7.04 (dd, 1H, $J = 8.5, 1.9$ Hz), 2.98–2.79 (m, 8H), 2.52 (s, 3H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 137.82, 133.01, 130.16, 125.00, 121.13, 117.33, 112.68, 111.37, 57.84, 56.08, 46.04, 28.55, 23.85 ppm; IR (Smart iTX Diamond) ν 3128, 3085, 3020, 2922, 2849, 2736, 2694, 1446, 1361, 1316, 1052, 917, 851, 783, 718, 601 cm^{-1} . LC-MS (ES^+) calcd for $\text{C}_{13}\text{H}_{16}\text{ClN}_2$ [$\text{M} + \text{H}$] 235.10 found 235.30.



Isolated as a brown solid (161 mg, 65%); ^1H NMR (CDCl_3 , 400 MHz) δ 7.93 (s, 1H), 7.57 (d, 1H, $J = 1.24$ Hz), 7.17 (dd, 1H, $J = 8.5, 1.5$ Hz), 7.10 (d, 1H, $J = 8.5$ Hz), 2.99–2.77 (m, 8H), 2.52 (s, 3H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 137.66, 133.27, 130.84, 123.71, 120.45, 112.66, 112.58, 111.82, 57.86, 56.11, 46.12, 28.62, 23.91 ppm; IR (Smart iTX Diamond) ν 3126, 3082, 3020, 2922, 2848, 2733, 1575, 1450, 1316, 1113, 1046, 914, 852, 781, 739, 594 cm^{-1} . LC-MS (ES^+) calcd for $\text{C}_{13}\text{H}_{16}\text{BrN}_2$ [$\text{M} + \text{H}$] 279.05 found 279.22

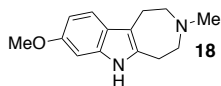
Procedure for Preparing 18. Compound 18 (TBG), was prepared analogously to compounds 12–17 with slight modifications.

General Scheme:



To an ice-cold solution of aqueous 6 M HCl (15 mL) was added 3-methoxyaniline (2.2 ml, 20.0 mmol, 1.0 equiv) dropwise. Next, NaNO₂ (1.520 g, 22.0 mmol, 1.1 equiv) was dissolved in H₂O (15 mL) and added to the solution slowly. After stirring at 0 °C for 15 minutes, SnCl₂ (11.4 g, 60.0 mmol, 3.0 equiv) dissolved in concentrated aqueous HCl (15 mL) was added to the solution dropwise. After stirring at 0 °C for 2.5 h, the reaction mixture was filtered, washed with hexanes, and dried under reduced pressure to yield the product as a light yellow solid that was used without further purification.

To a solution of 3-methoxyphenylhydrazine hydrochloride (1.566 g, 9.0 mmol, 3.0 equiv) in 0.1 M EtOH (30 mL) was added 1-methylazepan-4-one hydrochloride (489 mg, 3.0 mmol, 1.0 equiv) followed by concentrated aqueous HCl (1.0 mL, 12.0 mmol, 4.0 equiv). The mixture was refluxed for 12 h and then concentrated under reduced pressure. The oily residue was dissolved in DCM (~25mL) and basified with 1M aqueous NaOH (~20mL). The aqueous layer was extracted with DCM (3 x 20 mL). The combined organic extracts were dried over Na₂SO₄ and concentrated under reduced pressure to yield a mixture of the 6- and 4-substituted indoles. The 6-substituted indole was purified by chromatography on silica gel (10:1 DCM:MeOH with 0.5% NH₄OH).



Isolated as light yellow solid (379 mg, 55%); ¹H NMR (CDCl₃, 400 MHz) δ 7.67 (br s, 1H), 7.32 (d, 1H, *J* = 8.5 Hz), 6.80 – 6.73 (m, 2H), 3.83 (s, 3H), 2.98 – 2.83 (m, 8H), 2.53 (s, 3H) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 155.93, 135.33, 134.68, 123.59, 118.29, 112.53, 108.80, 94.66, 57.98, 56.34, 55.95, 45.93, 28.36, 23.91 ppm; IR (Smart iTX Diamond) ν 3153, 3121, 3073, 2940, 2879, 1628, 1458, 1197, 1033, 910, 834, 799 cm⁻¹; LC-MS (ES⁺) calcd for C₁₄H₁₉N₂O [M+H] 231.15 found 231.36.

Procedure for Preparing 13 • ½ fumarate. Fumaric acid (116 mg, 1.0 mmol, 0.8 equiv) was added to a sealed tube containing acetone (12 mL). The solution was carefully heated until all of the fumaric acid dissolved. After cooling the solution to room temperature, a solution of **13** free base (288 mg, 1.25 mmol, 1.0 equiv) in acetone (1 mL) was added, and the mixture was cooled in the freezer overnight. The solid was filtered, washed with acetone, and dried under reduced pressure to yield **13** • fumarate as the 2:1 salt (220 mg, 61%); ¹H NMR (CD₃OD, 400 MHz) δ 7.15 (d, 1H, *J* = 8.7 Hz), 6.92 (s, 1H), 6.72 (d, 1H, *J* = 8.7 Hz), 6.68 (s, 1H), 3.80 (s, 3H), 3.42–3.34 (m, 4H), 3.18 (t, 2H, *J* = 5.5 Hz), 3.10 (t, 2H, *J* = 5.5 Hz), 2.91 (s, 3H) ppm; ¹³C NMR (CD₃OD, 100 MHz) δ 171.76, 155.37, 136.32, 135.55, 131.75, 129.59, 112.49, 112.31, 110.58, 100.58, 58.77, 56.70, 56.27, 44.77, 25.09, 21.55 ppm. IR (Smart iTX Diamond) ν 3384, 2979, 2924, 2297, 2822, 1695, 1551, 1353 1167, 982, 912, 802 cm⁻¹; LC-MS (ES⁺) calcd for C₁₄H₁₉N₂O [M+H] 231.15 found 231.36.

Procedure for Preparing 18 • fumarate. Fumaric acid (77 mg, 0.66 mmol, 0.8 equiv) was added to a sealed tube containing acetone (8 mL). The solution was carefully heated until all of the fumaric acid dissolved. After cooling the solution to room temperature, a solution of **18** free base (193 mg, 0.84 mmol, 1.0 equiv) in acetone (1 mL) was added, and the mixture was cooled in the freezer overnight. The solid was filtered, washed with acetone, and dried under reduced pressure to yield **18** • fumarate as the 1:1 salt (187 mg, 64%); ¹H NMR (CD₃OD, 400 MHz) δ 7.28 (d, 1H, *J* = 8.7 Hz), 6.82 (s, 1H), 6.71 (s, 2H), 6.68 (d, 1H, *J* = 8.7 Hz), 3.79 (s, 3H), 3.54–3.45 (m, 4H), 3.22 (t, 2H, *J* = 5.3 Hz), 3.13 (t, 2H, *J* = 5.3 Hz), 3.00 (s, 3H) ppm; ¹³C NMR (CD₃OD, 100 MHz) δ 170.71, 157.57, 137.23, 135.99, 133.23, 123.71, 118.86, 110.47, 110.10, 95.31, 58.62, 56.68, 55.99, 44.48, 24.77, 21.35 ppm; IR (Smart iTX Diamond) ν 3375, 3008, 2899, 2505, 1694, 1556, 1337, 1162, 1034, 967, 814, 775 cm⁻¹; LC-MS (ES⁺) calcd for C₁₄H₁₉N₂O [M+H] 231.15 found 231.36.

Procedure for the Large-Scale Preparation of 18 • fumarate. To an ice-cold solution of aqueous 6 M HCl (30 mL) was added 3-methoxyaniline (4.4 ml, 40.0 mmol, 1.0 equiv) dropwise. Next, NaNO₂ (3.040 g, 44.0 mmol, 1.1 equiv) was dissolved in H₂O (30 mL) and added to the solution slowly. After stirring at 0 °C for 15 minutes, SnCl₂ (22.8 g, 120.0 mmol, 3.0 equiv) dissolved in concentrated aqueous HCl (30 mL) was added to

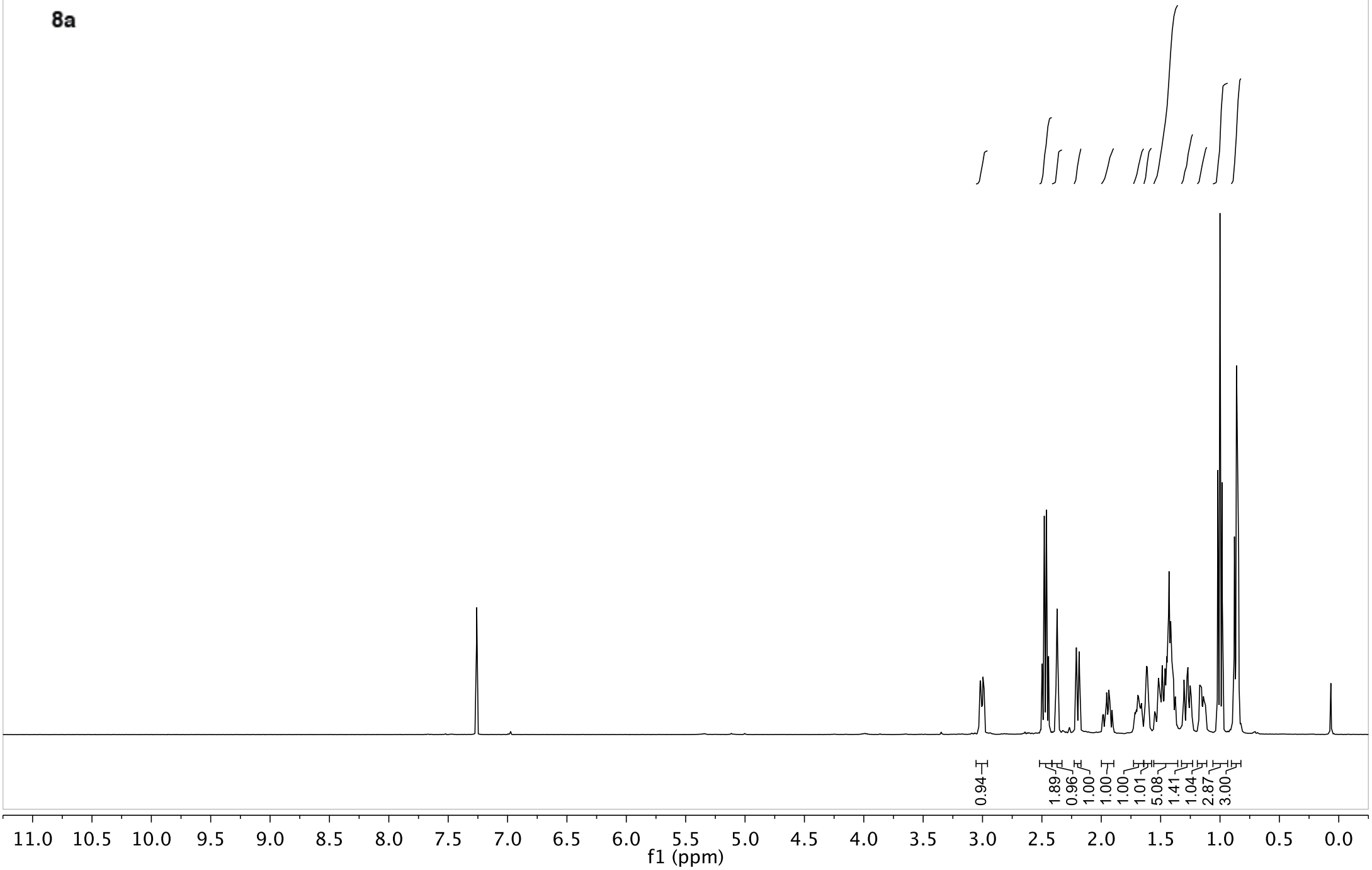
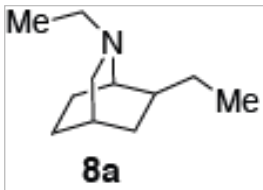
the solution dropwise. After stirring at 0 °C for 2.5 h, the reaction mixture was filtered, washed with hexanes, and dried under reduced pressure to yield 3-methoxyphenylhydrazine hydrochloride as a light yellow solid (5.4 g, 78%) that was used without further purification.

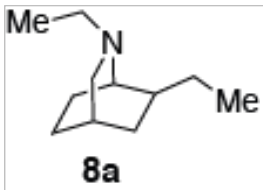
To a solution of 3-methoxyphenylhydrazine hydrochloride (4.802 g, 27.6 mmol, 3.0 equiv) in 0.15 M EtOH (60 mL) was added 1-methylazepan-4-one hydrochloride (1.5 g, 9.2 mmol, 1.0 equiv) followed by concentrated aqueous HCl (3.1 mL, 36.8 mmol, 4.0 equiv). The mixture was refluxed for 12 h and then concentrated under reduced pressure. The oily residue was dissolved in DCM (~50 mL) and basified with 1M aqueous NaOH (~50 mL). The aqueous layer was extracted with DCM (3 x 30 mL). The combined organic extracts were dried over Na₂SO₄ and concentrated under reduced pressure to yield a mixture of the 6- and 4-substituted indoles. Addition of EtOAc to the unpurified product mixture resulted in precipitation of the 6-substituted isomer, which was isolated via filtration. The mother liquor was concentrated, and this procedure was repeated six times until a total of 1.028 g of tabernanthalog free base (49%) was collected.

Next, fumaric acid (408 mg, 3.5 mmol, 0.8 equiv) was added to a sealed tube containing acetone (20 mL). The solution was carefully heated until all of the fumaric acid dissolved. After cooling the solution to room temperature, a solution of **18** free base (1.028 mg, 4.4 mmol, 1.0 equiv) in acetone (5 mL) was added dropwise, and the mixture was cooled in the freezer overnight. The solid was filtered, washed with acetone, and dried under reduced pressure to yield **18** • fumarate as the 1:1 salt (1.055 g, 69%).

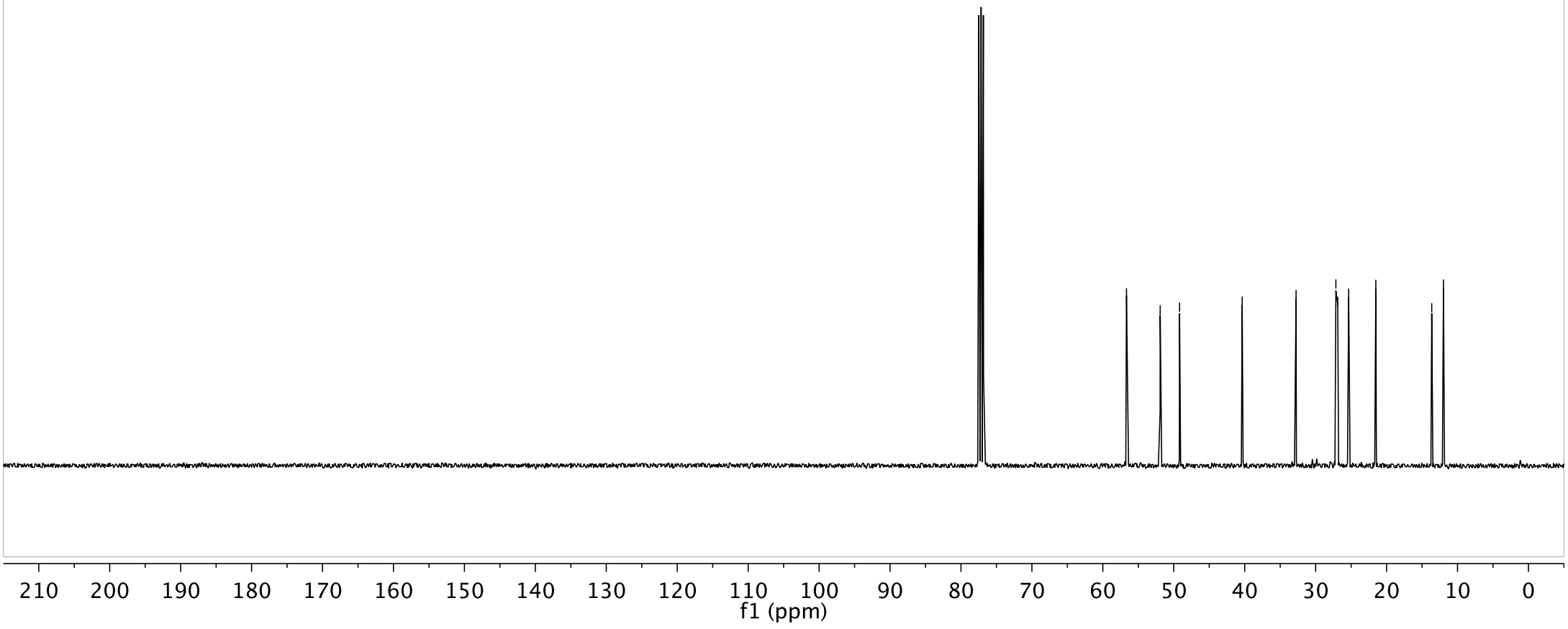
SUPPLEMENTAL REFERENCES

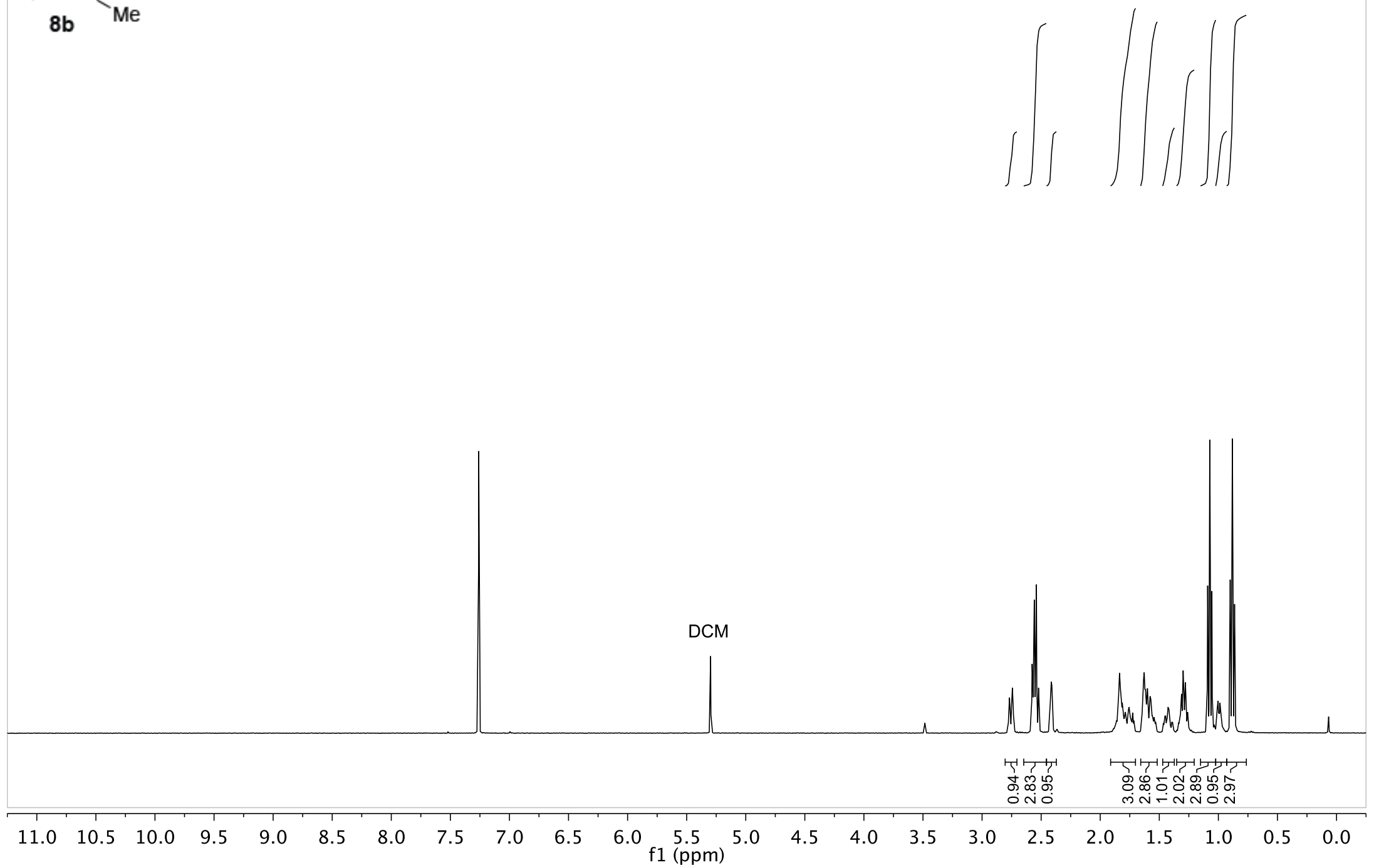
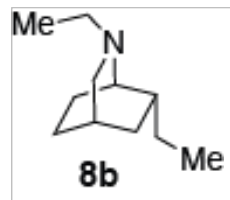
45. Gribble, G. W.; Jasinski, J. M.; Pellicone, J. T.; Panetta, J. A. Reactions of Sodium Borohydride in Acidic Media. VIII. N-Alkylation of Aliphatic Secondary Amines with Carboxylic Acids. *Synthesis*, 1978, 10, 766–768.

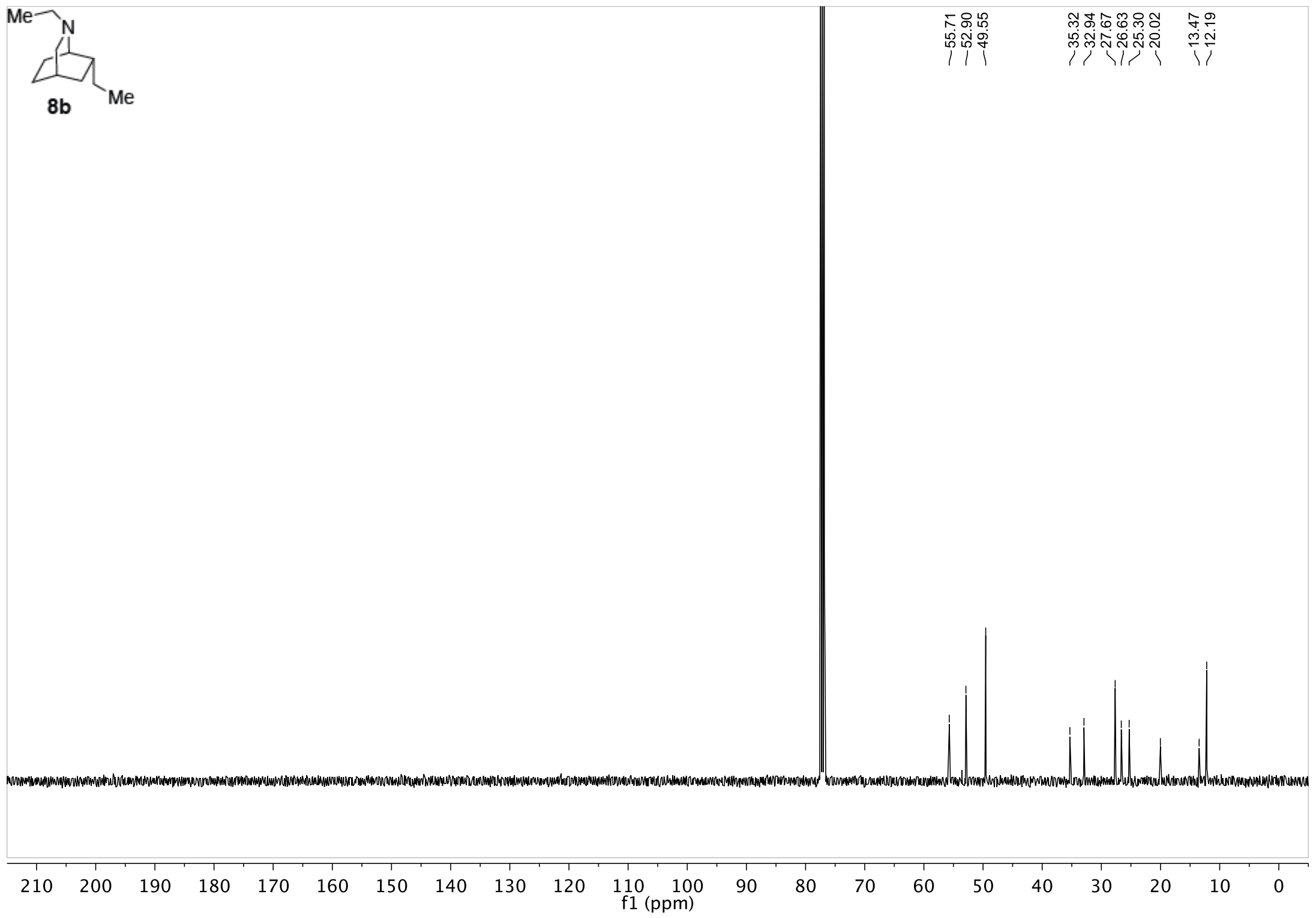
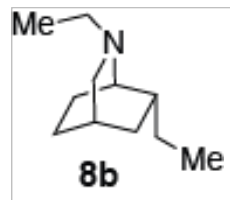


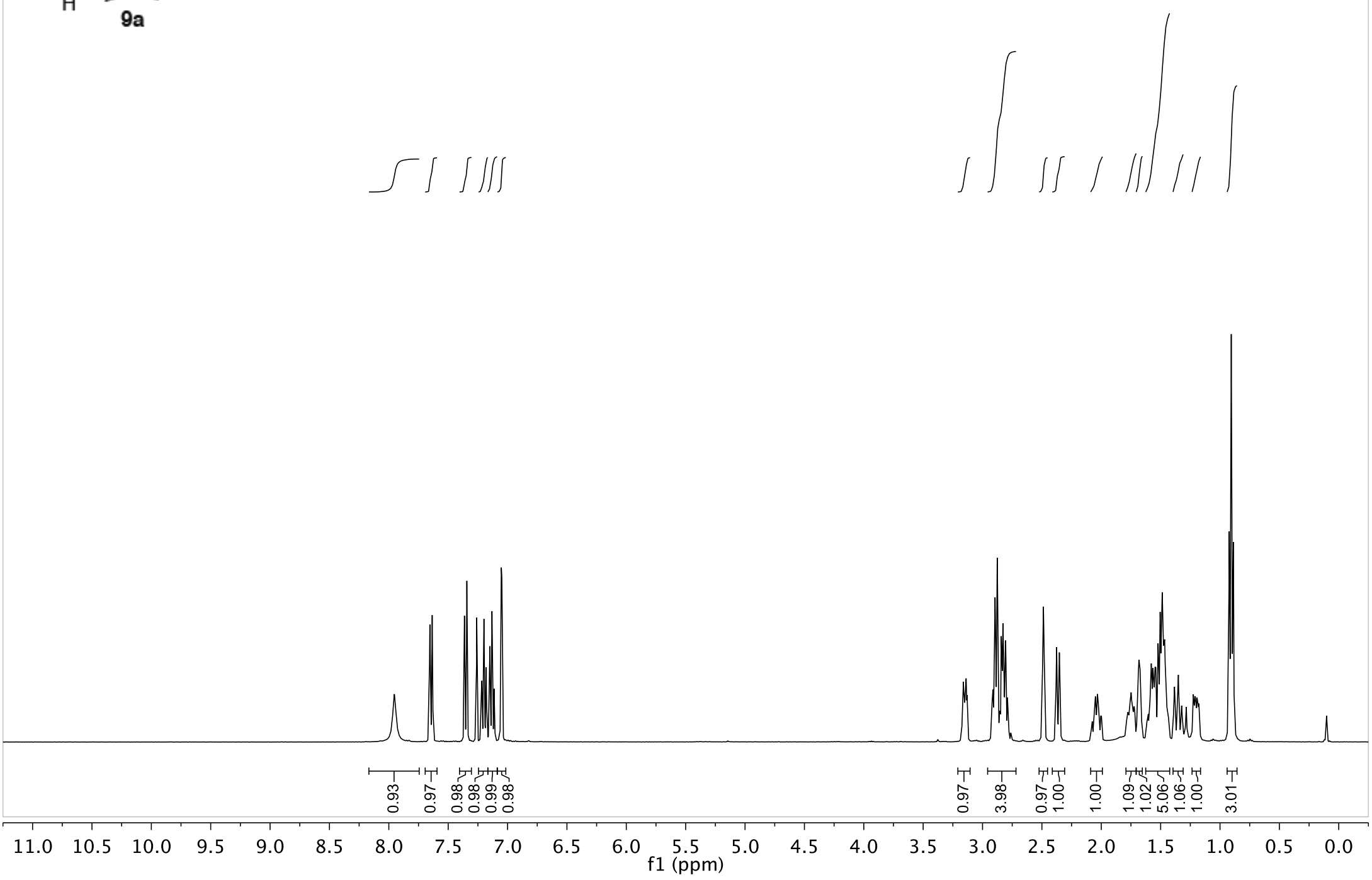
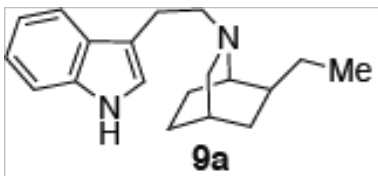


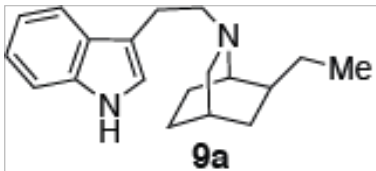
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40.36
32.76
27.15
26.89
25.34
21.52
13.64
11.98









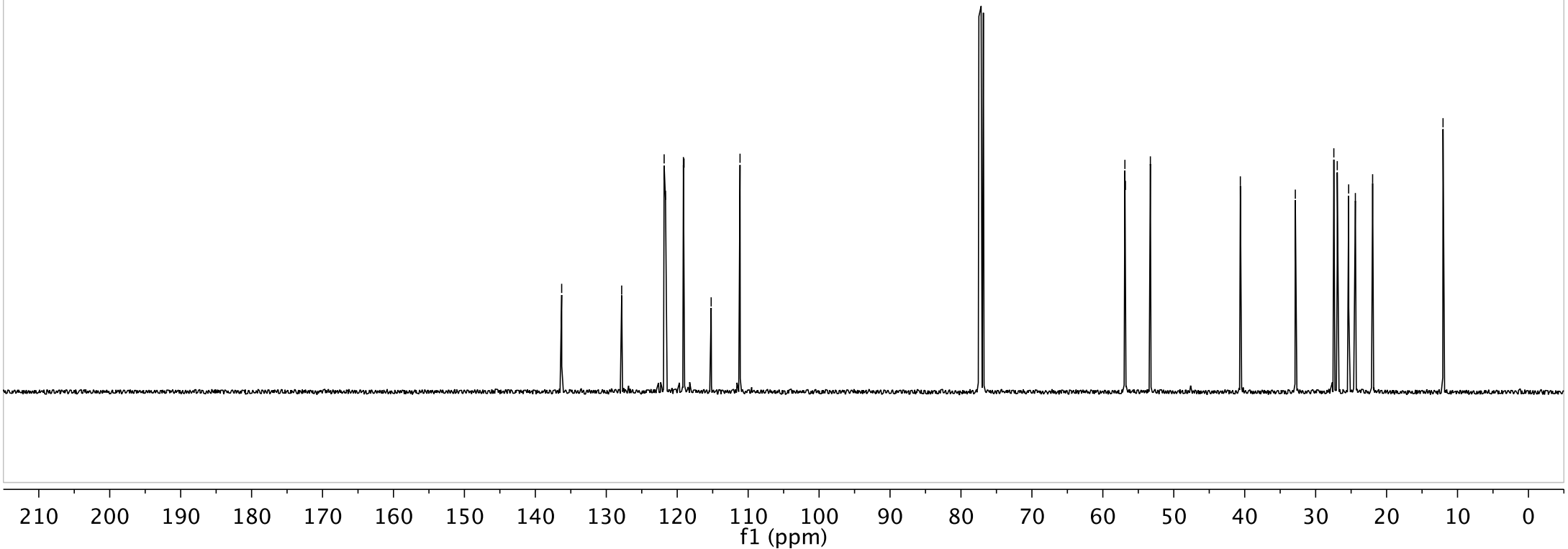


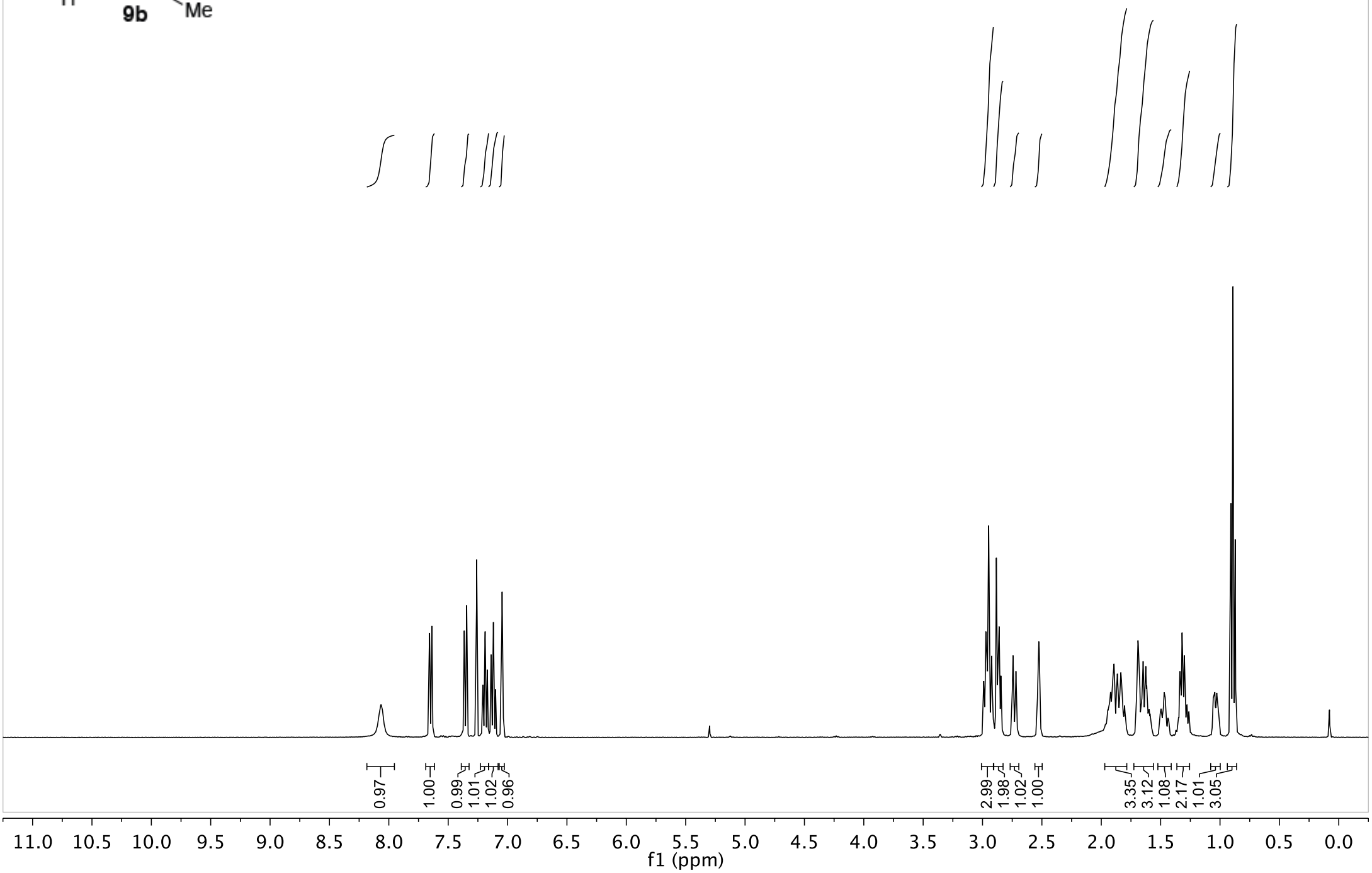
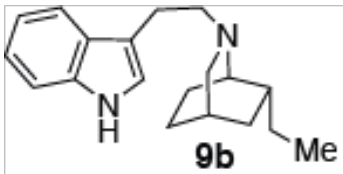
— 136.29
— 127.83
{ 121.84
{ 121.65
{ 119.13
{ 119.04
{ 115.21
{ 111.15

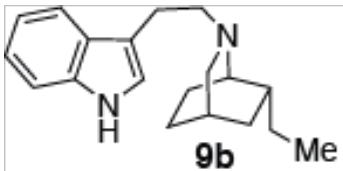
{ 56.89
{ 56.82
{ 53.30

— 40.62
{ 32.87
{ 27.44
{ 26.95
{ 25.35
{ 24.40
{ 21.97

— 12.04





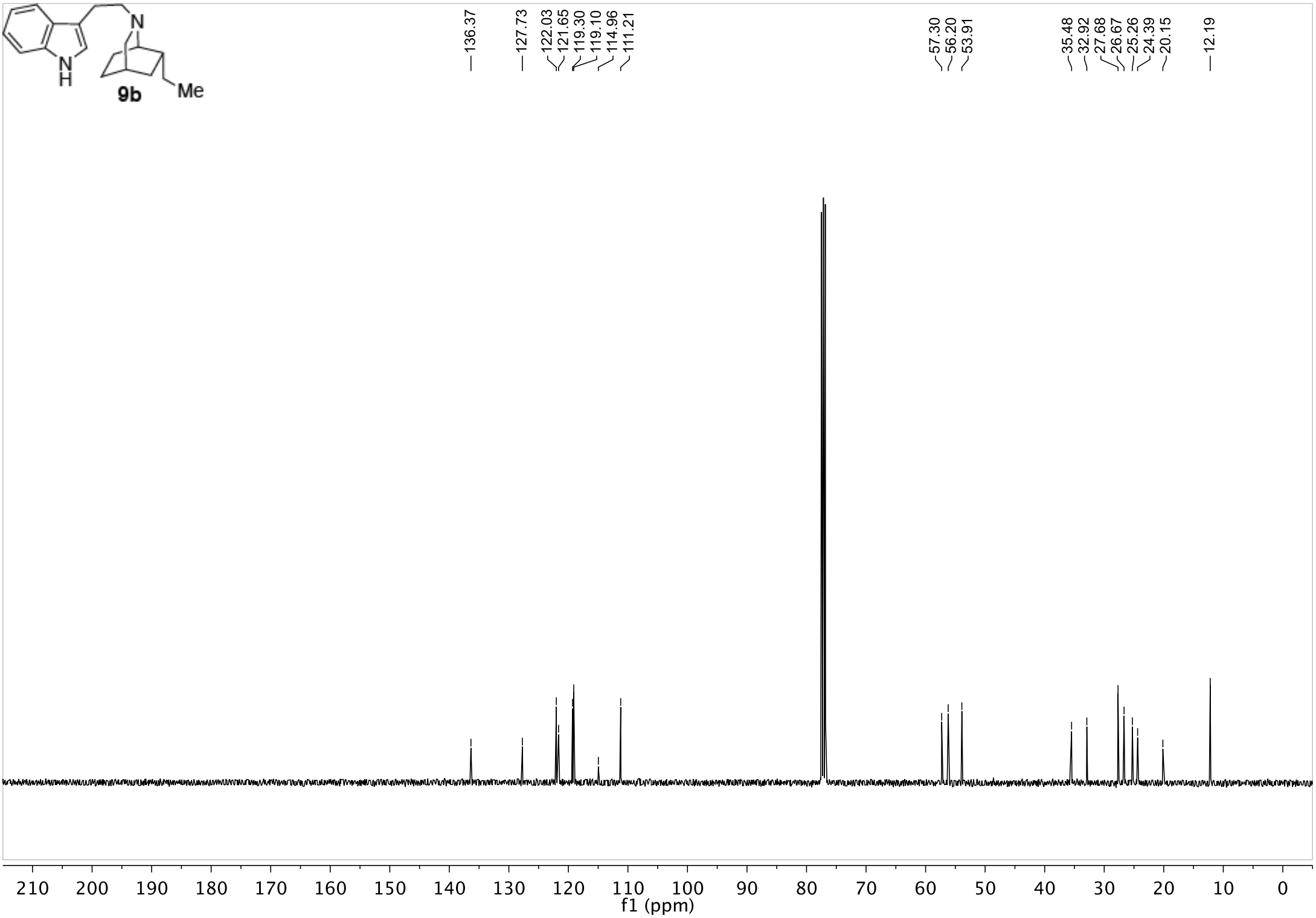


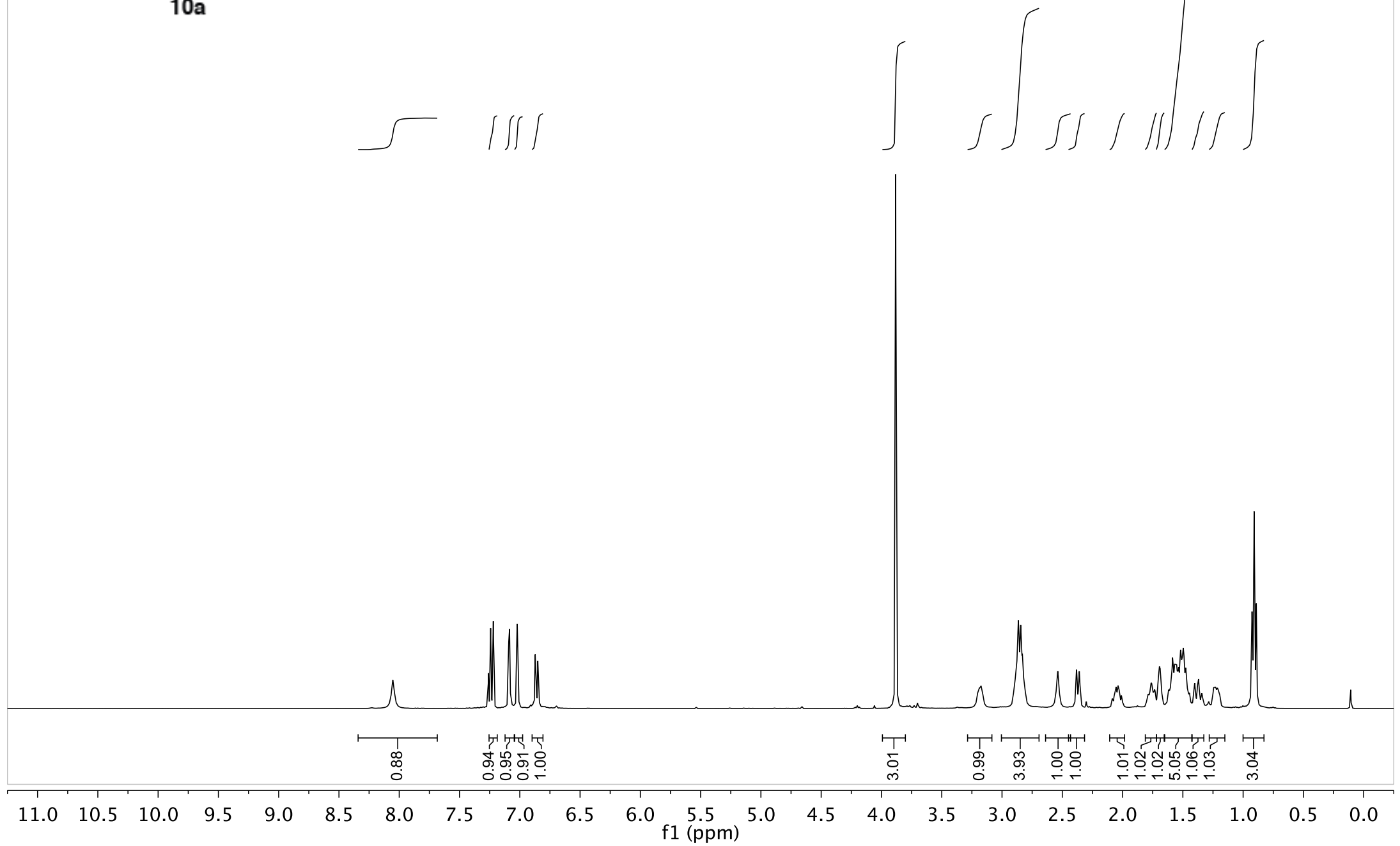
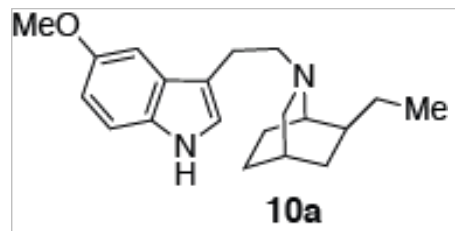
— 136.37
— 127.73
122.03
121.65
119.30
119.10
114.96
111.21

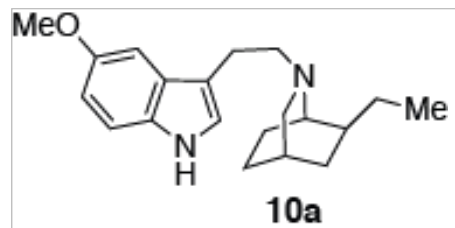
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56.20
53.91

35.48
32.92
27.68
26.67
25.26
24.39
20.15

— 12.19







— 153.91

— 131.50

— 128.16

— 122.60

114.58

111.97

111.87

— 101.05

77.48

77.48

77.36

77.16

76.84

56.85

56.57

56.13

53.35

— 40.43

32.66

27.38

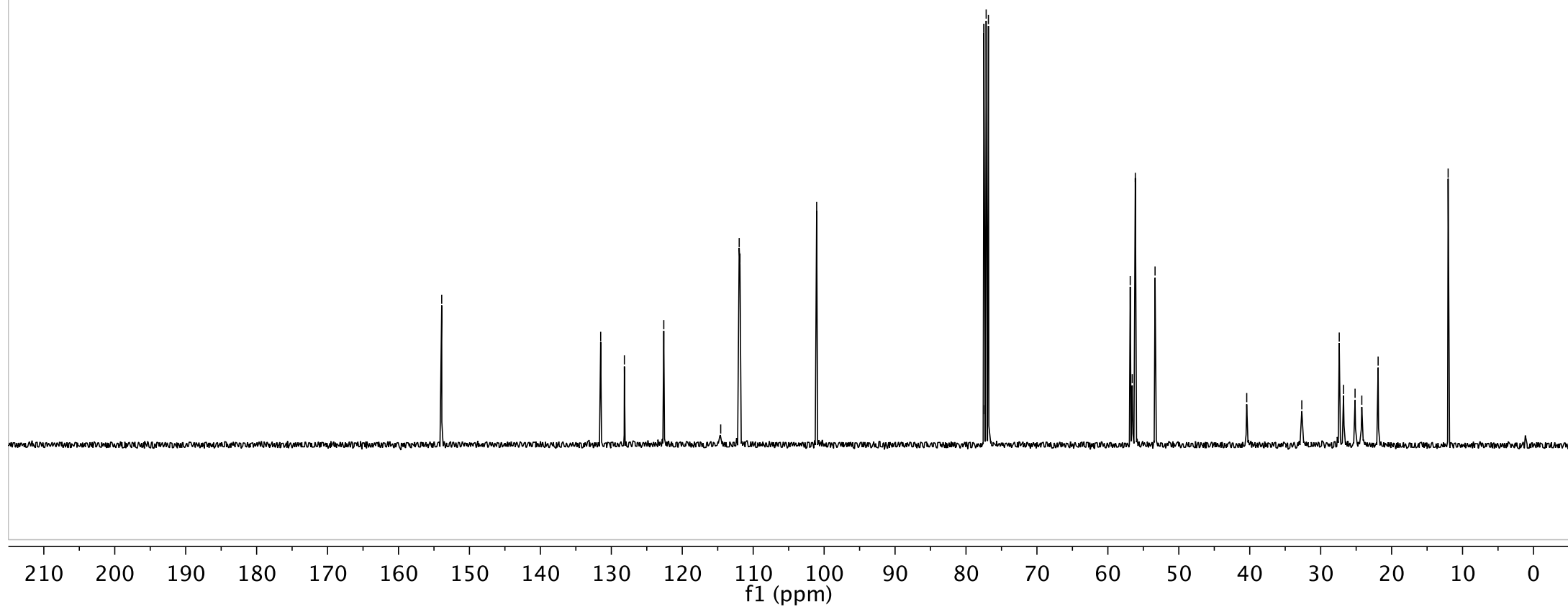
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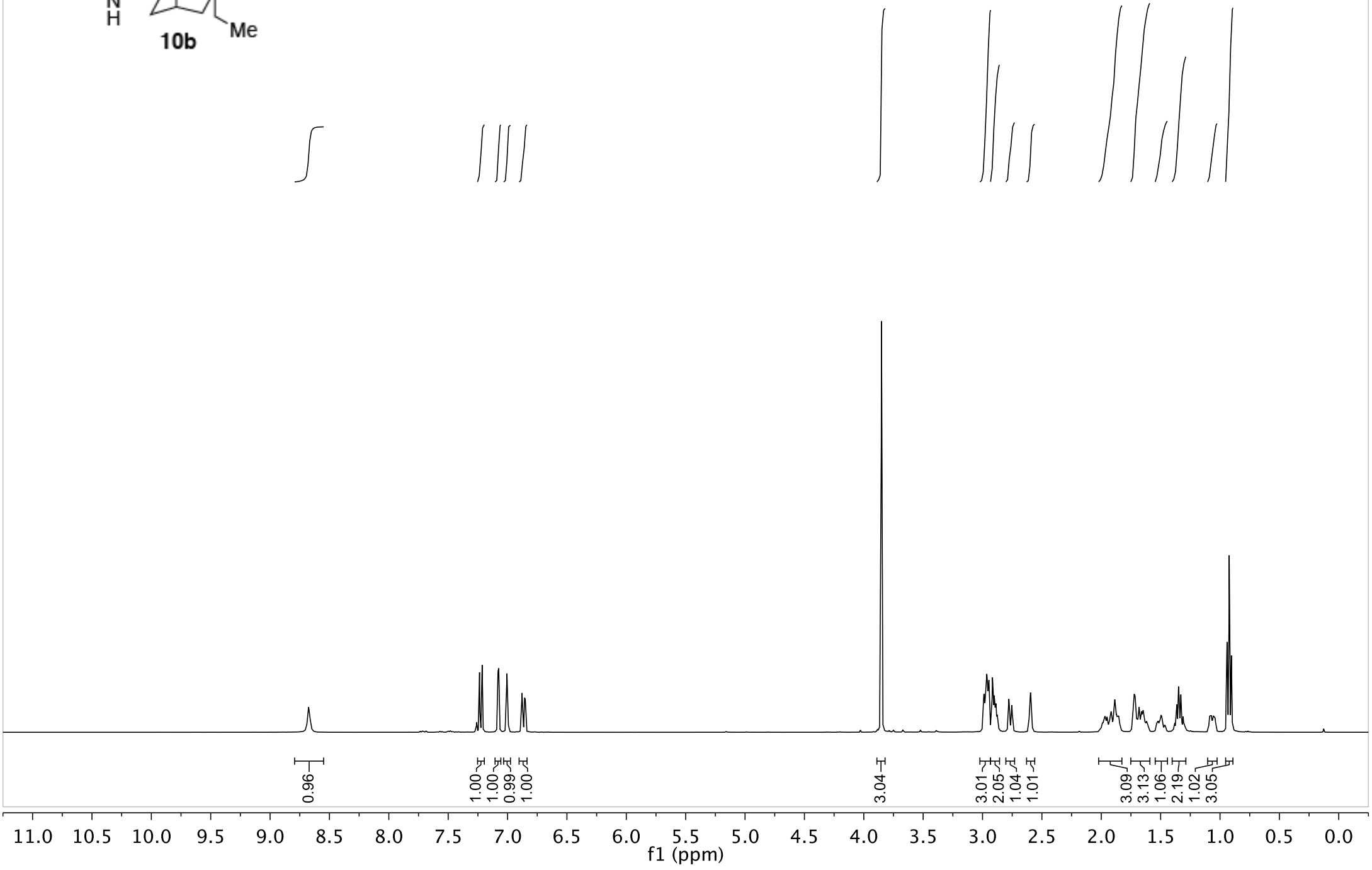
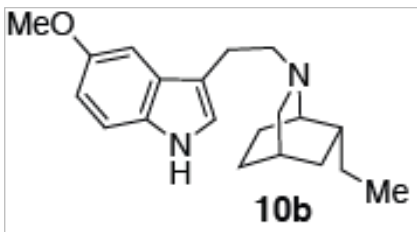
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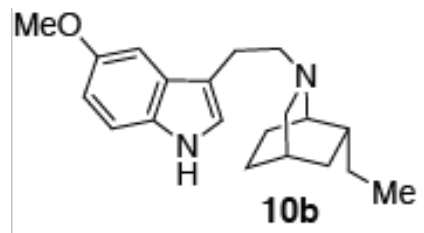
24.20

21.90

— 12.03







— 153.7

~ 131.5

~ 127.9

~ 122.6

~ 114.2

~ 114.2

~ 111.9

— 100.8

~ 57.10

~ 56.10

~ 55.99

~ 53.63

~ 35.34

~ 32.87

~ 27.58

~ 26.60

~ 25.23

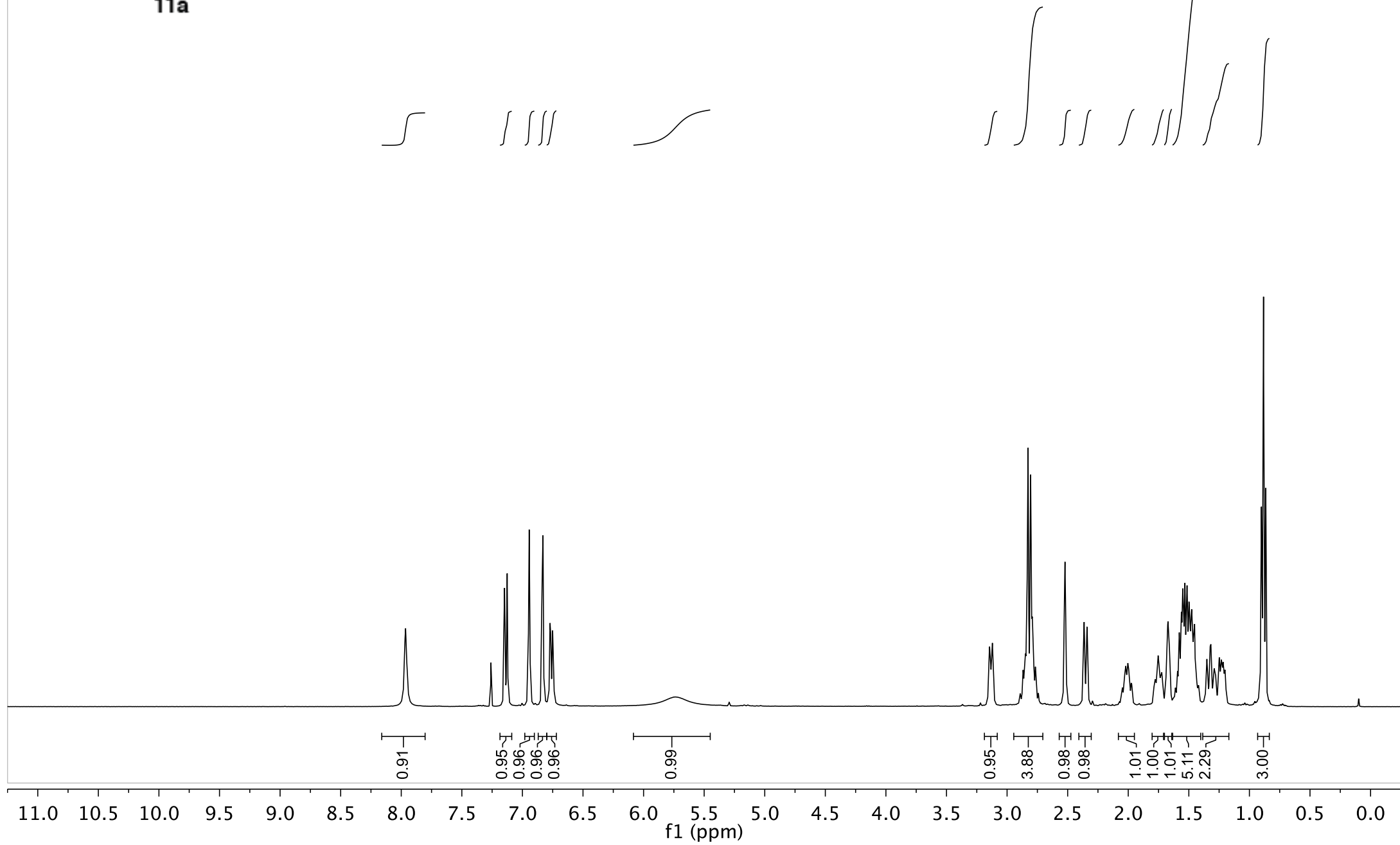
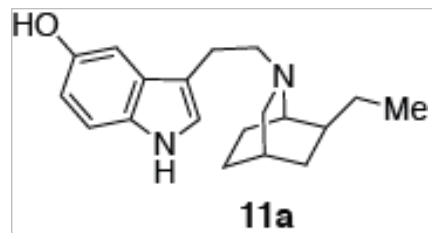
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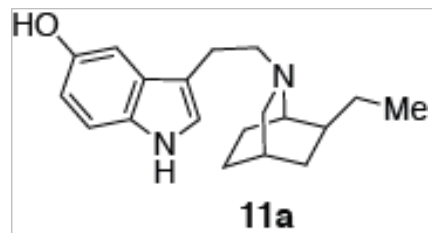
~ 20.10

— 12.14

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

f1 (ppm)





—149.82

—131.40

—128.36

—122.85

∩114.05

∩112.26

∩111.91

—103.71

∩56.99

∩56.59

∩53.67

—40.64

∩32.59

∩27.43

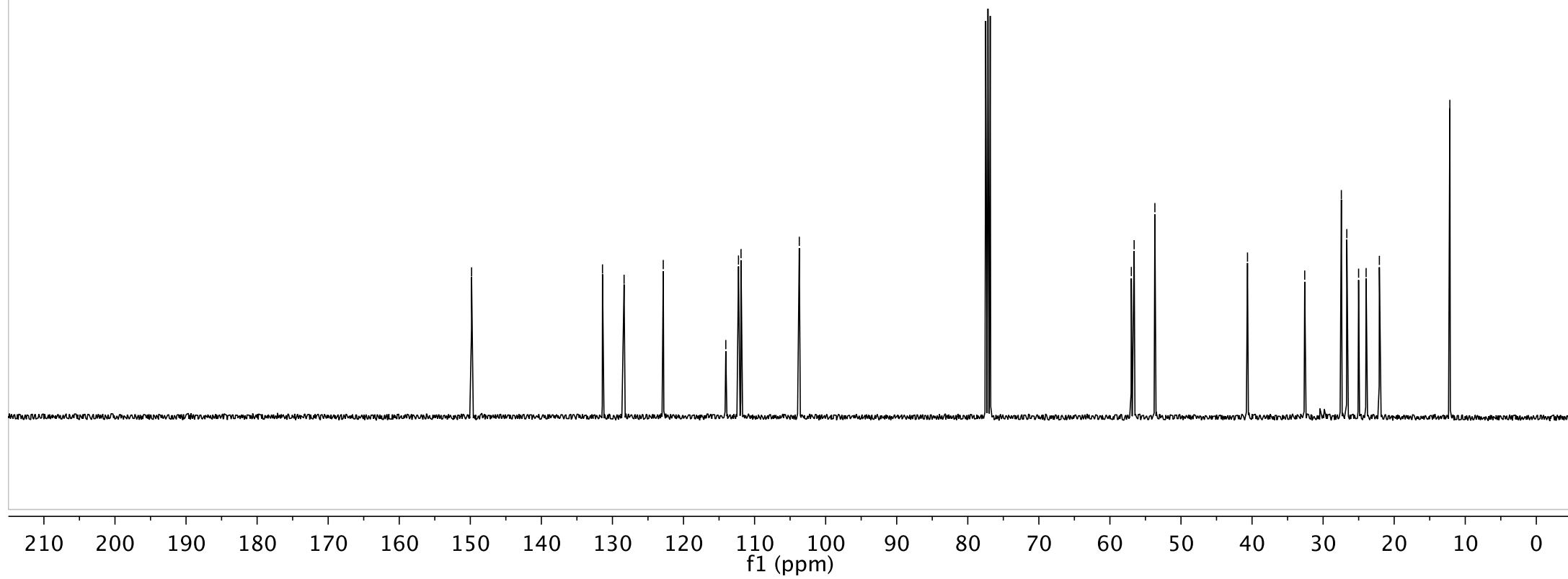
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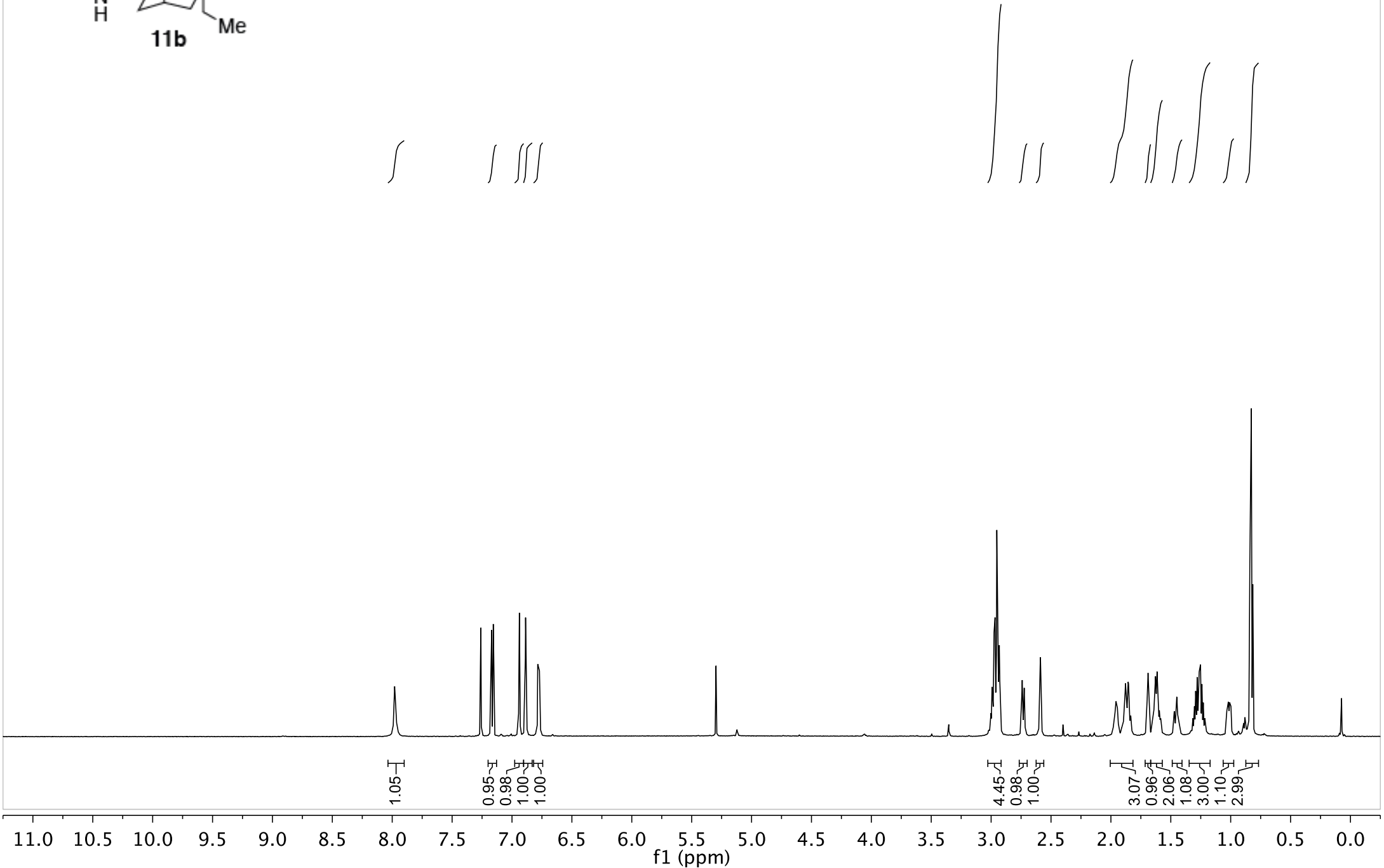
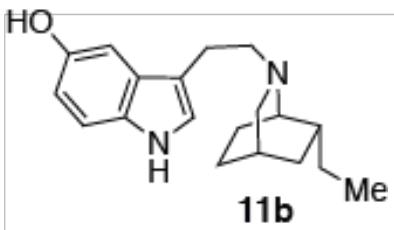
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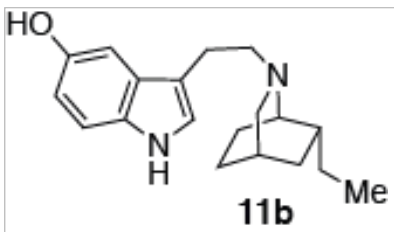
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∩22.08

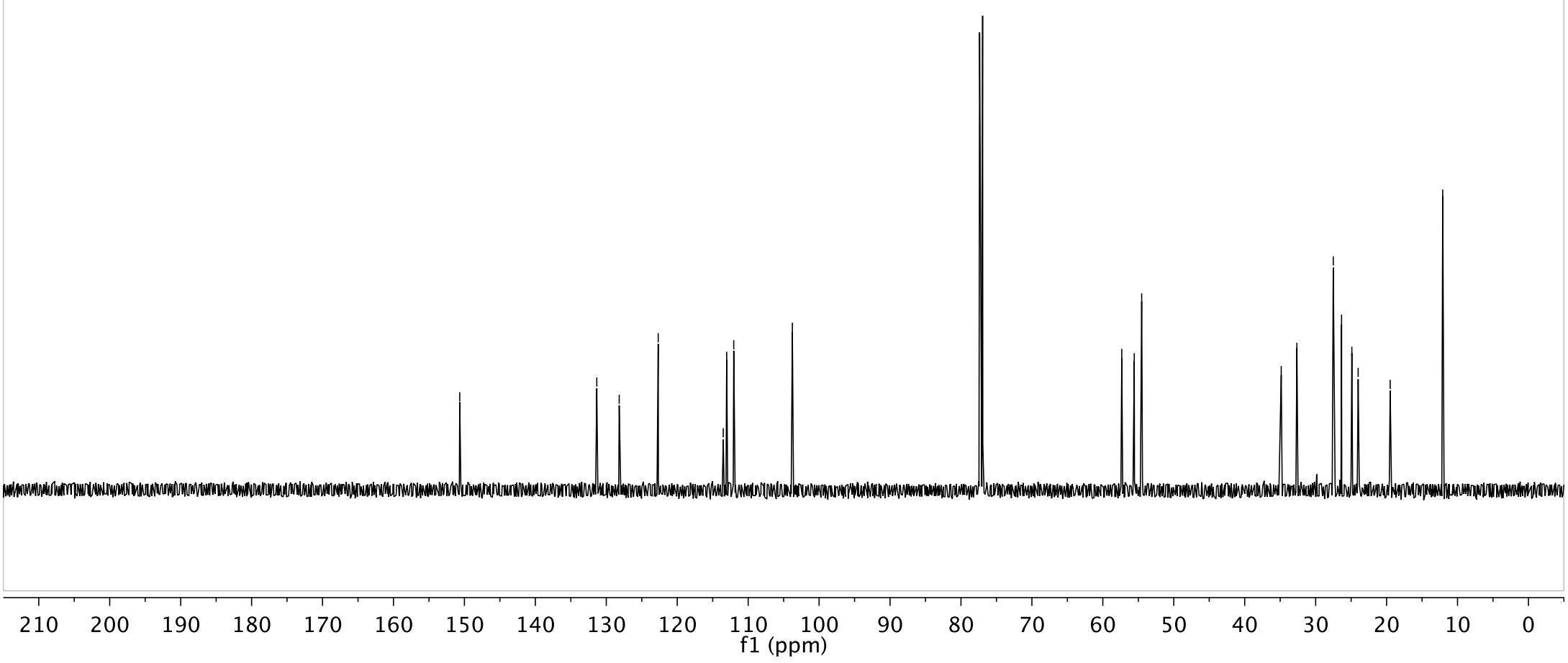
—12.17

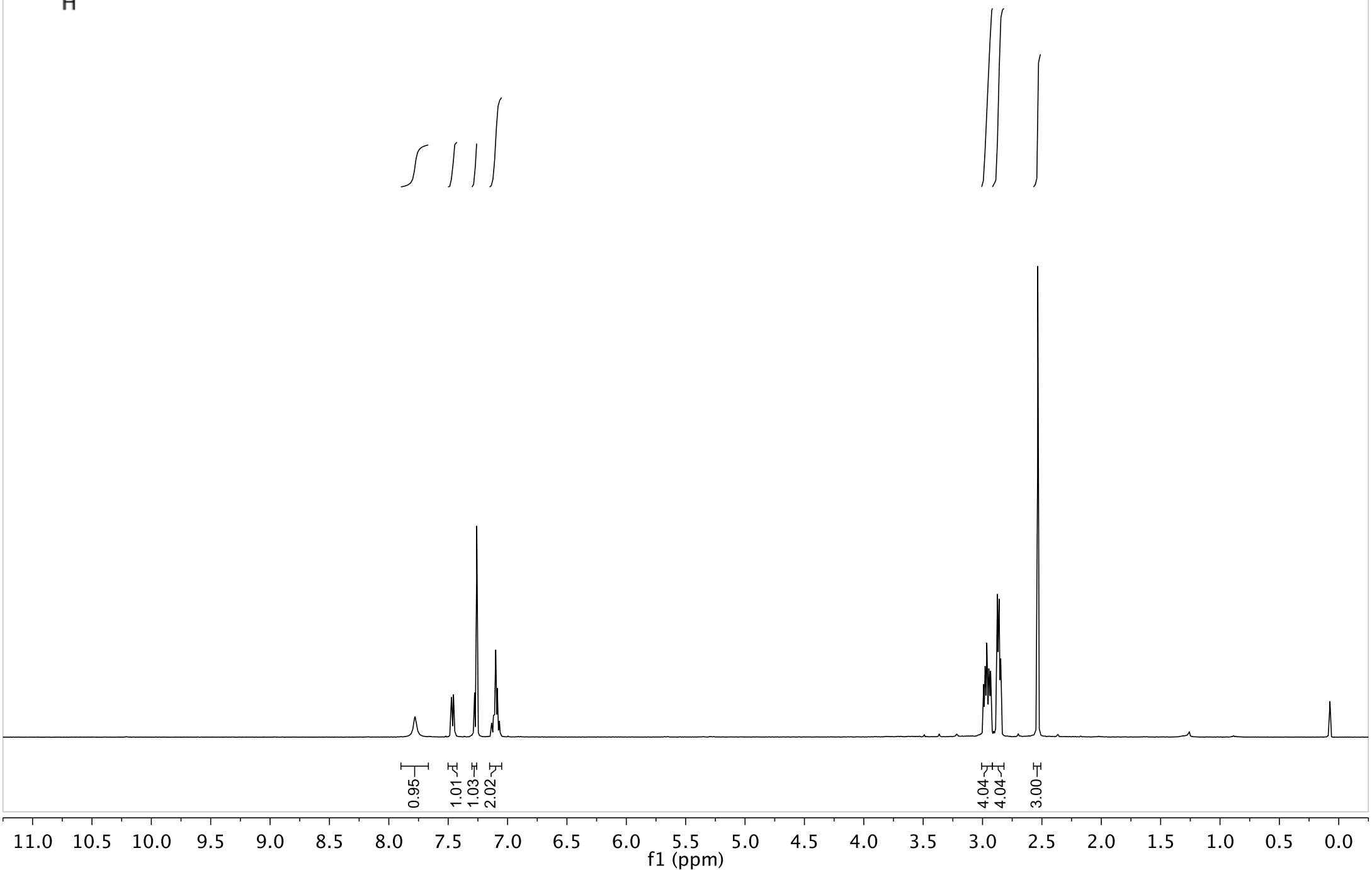
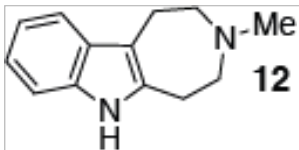


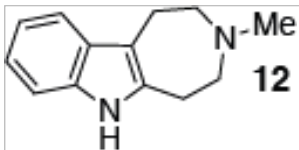




- 150.66
- 131.34
- 128.18
- 122.68
- 113.51
- 113.03
- 112.03
- 103.77
- 57.33
- 55.57
- 54.52
- 34.85
- 32.65
- 27.52
- 26.35
- 24.90
- 24.01
- 19.49
- 12.09

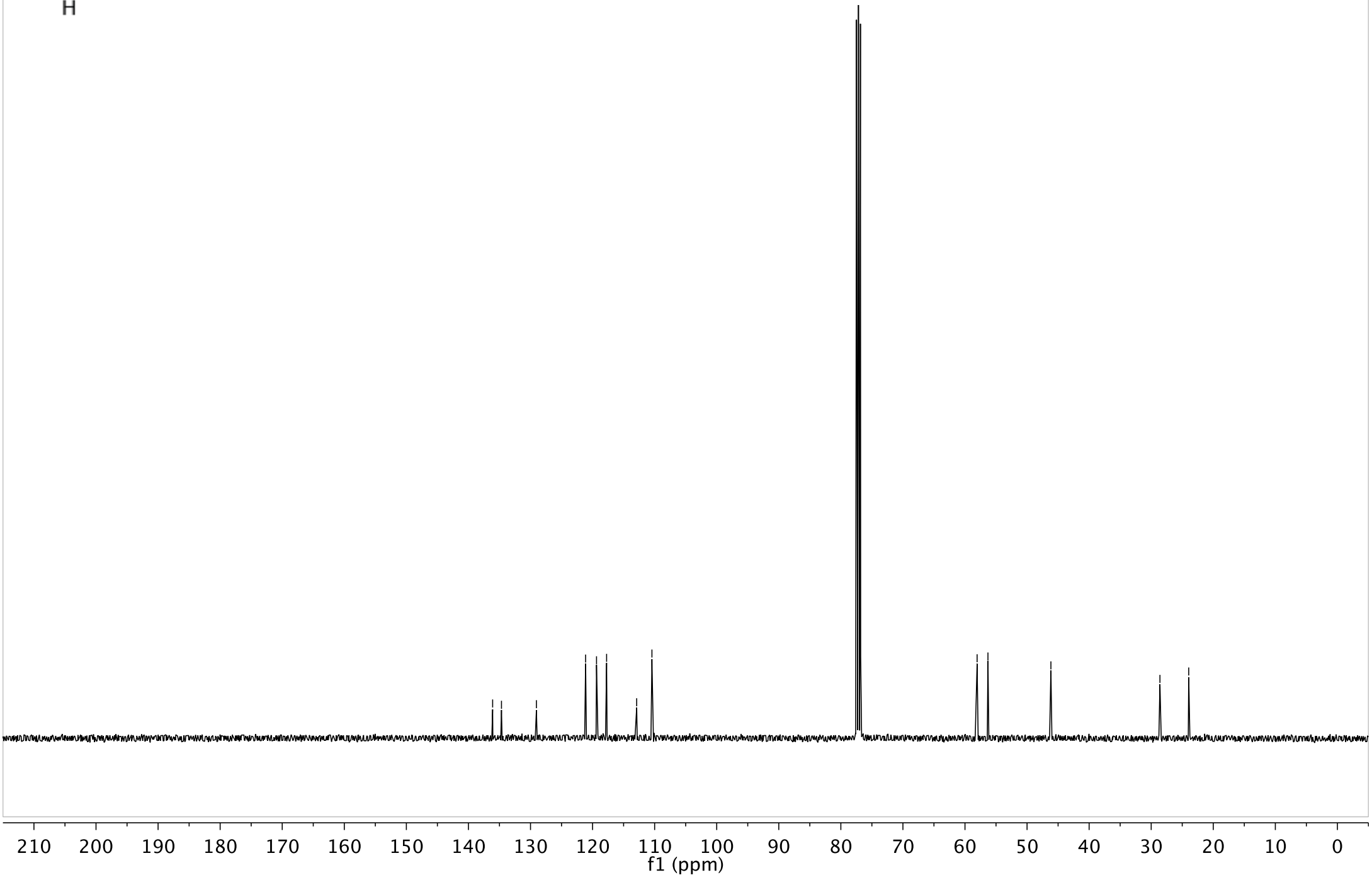


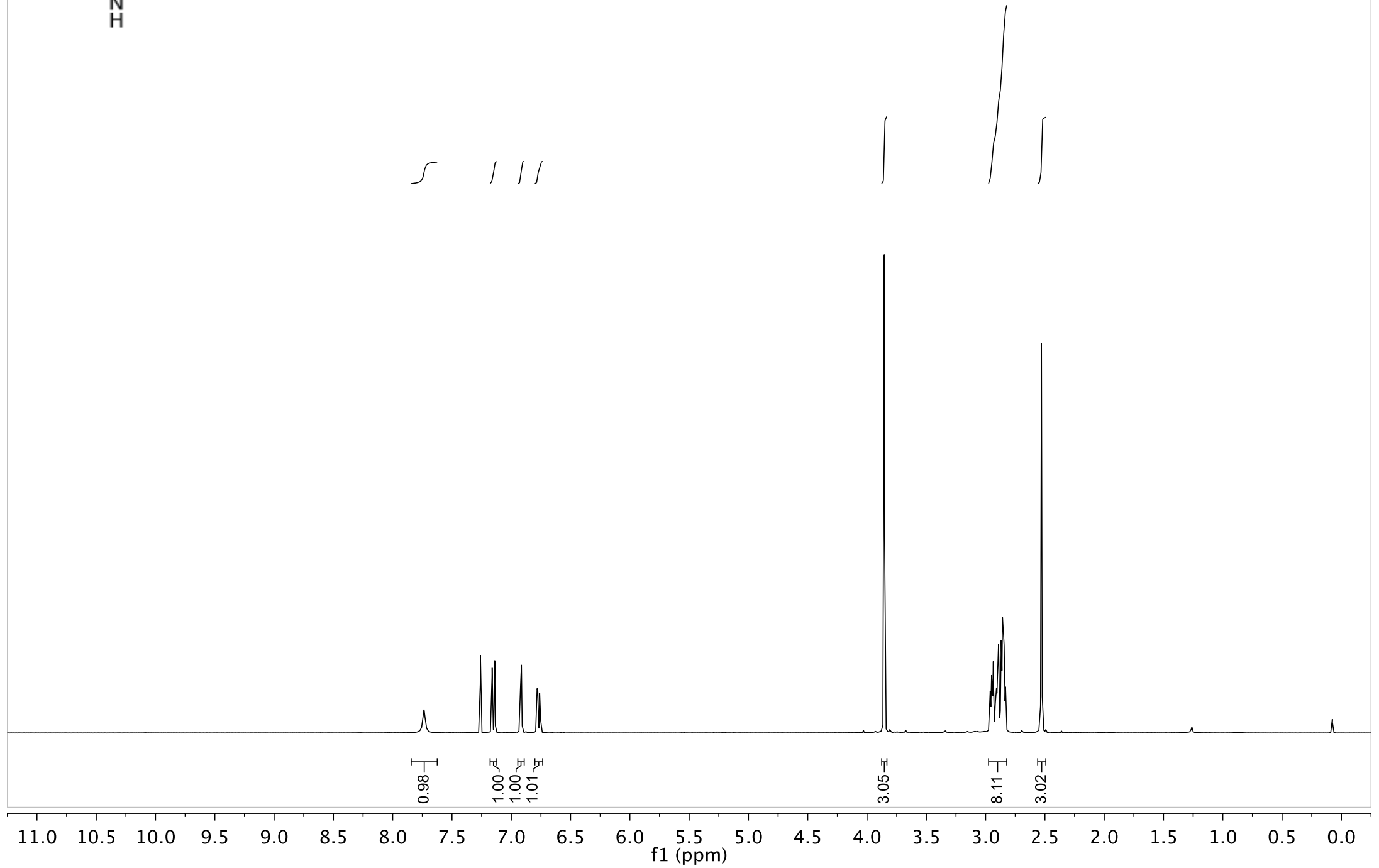
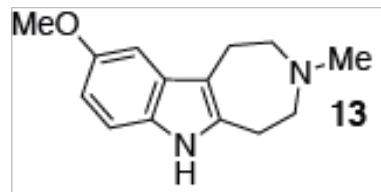


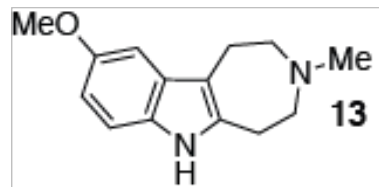


~ 136.10
~ 134.68
— 129.05
~ 121.12
~ 119.36
~ 117.74
~ 112.89
~ 110.44

~ 58.05
~ 56.30
— 46.16
— 28.59
— 23.95







— 154.13

— 137.12

129.79

129.40

112.70

111.15

110.91

— 100.13

58.04

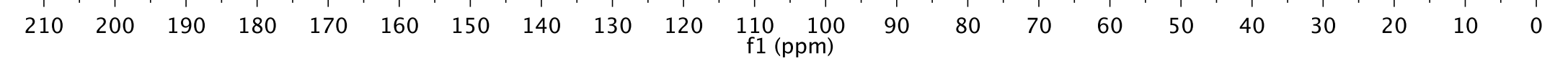
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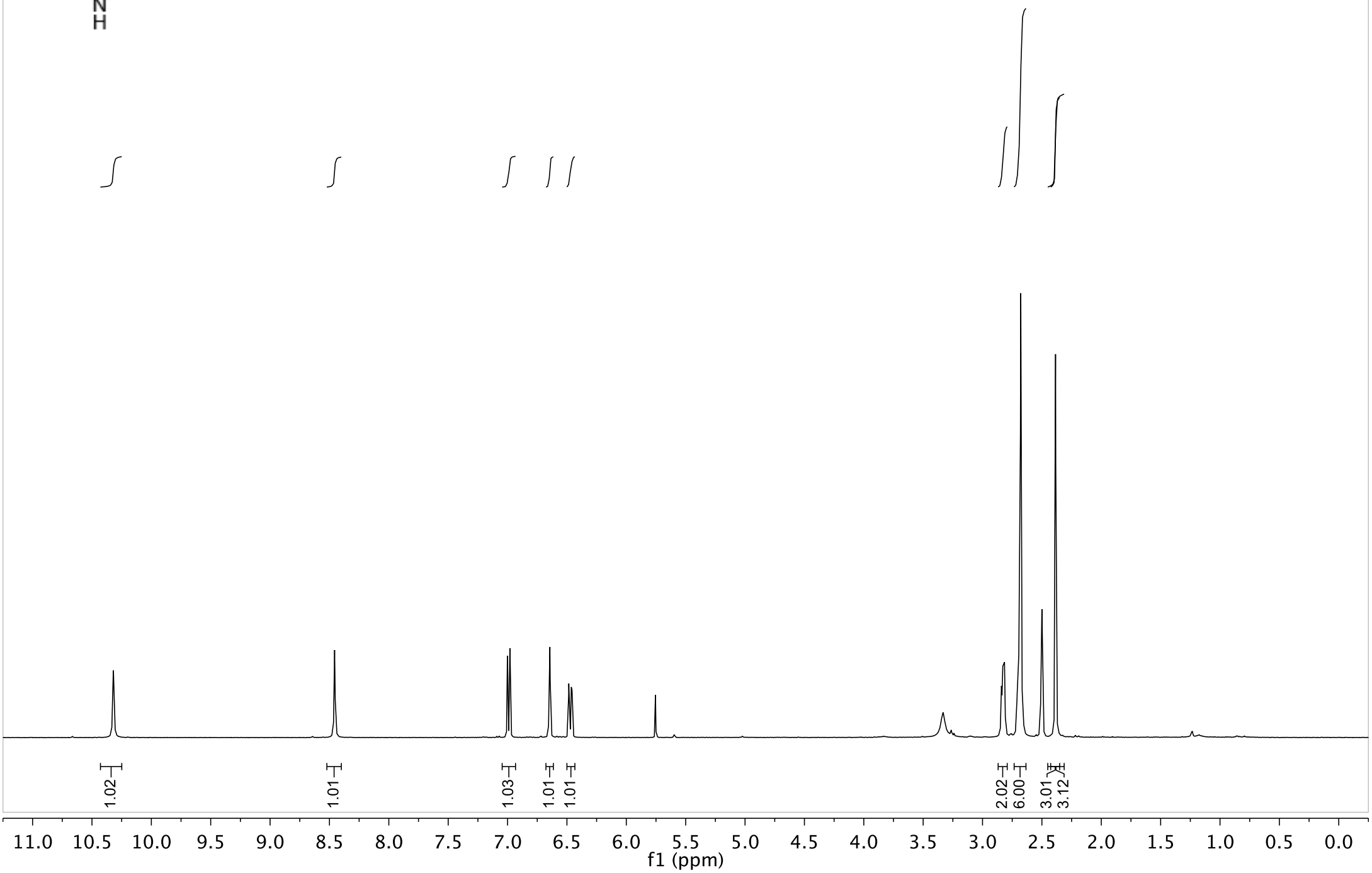
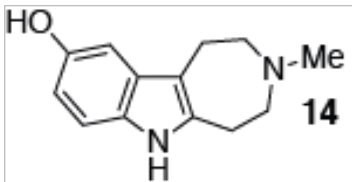
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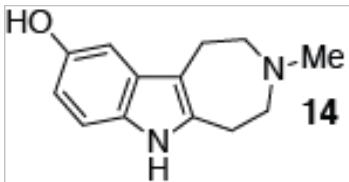
— 46.15

— 28.61

— 24.00







— 150.18

— 137.63

— 129.39
— 129.05

— 111.02
— 110.58
— 110.00

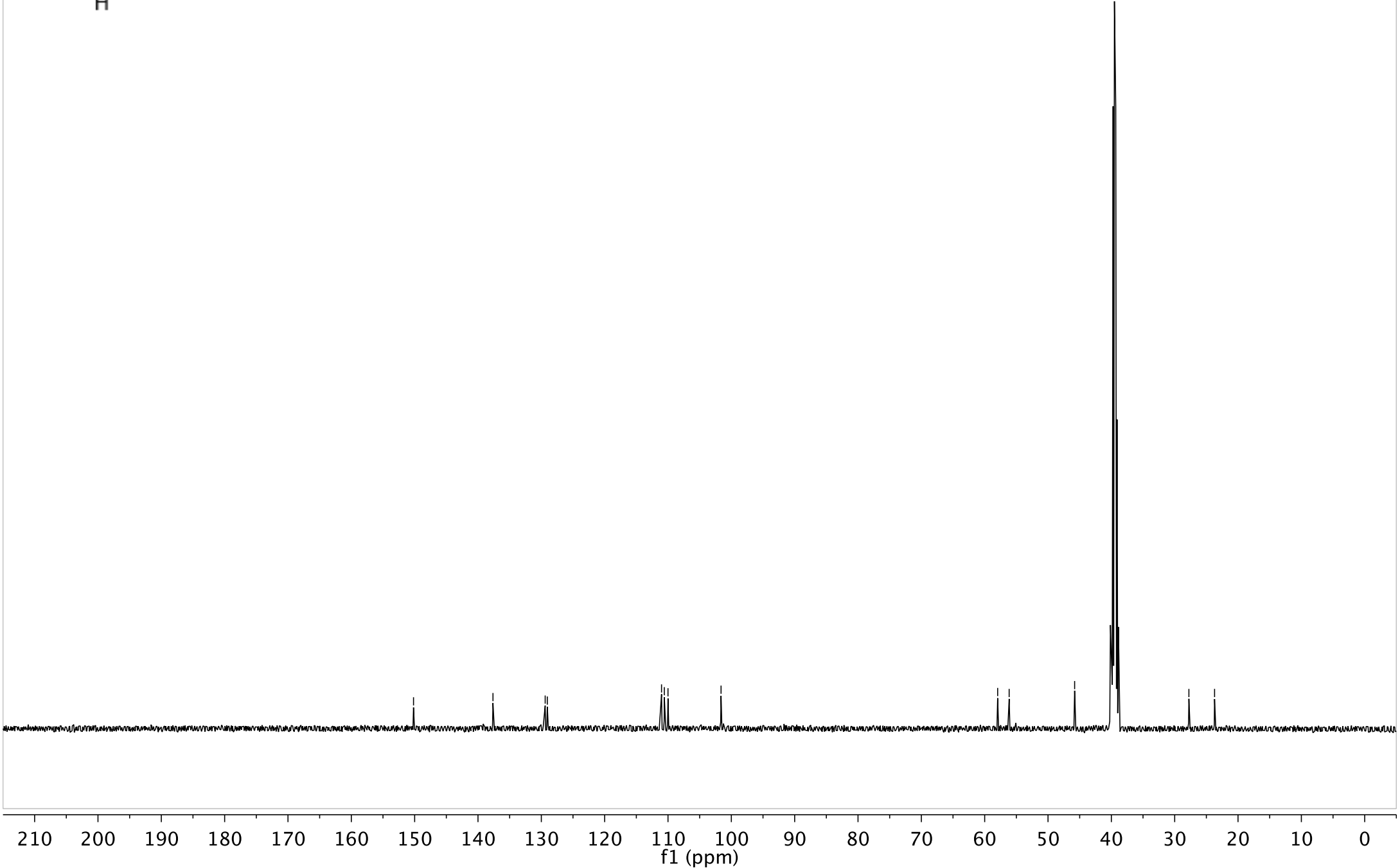
— 101.62

— 57.95
— 56.14

— 45.80

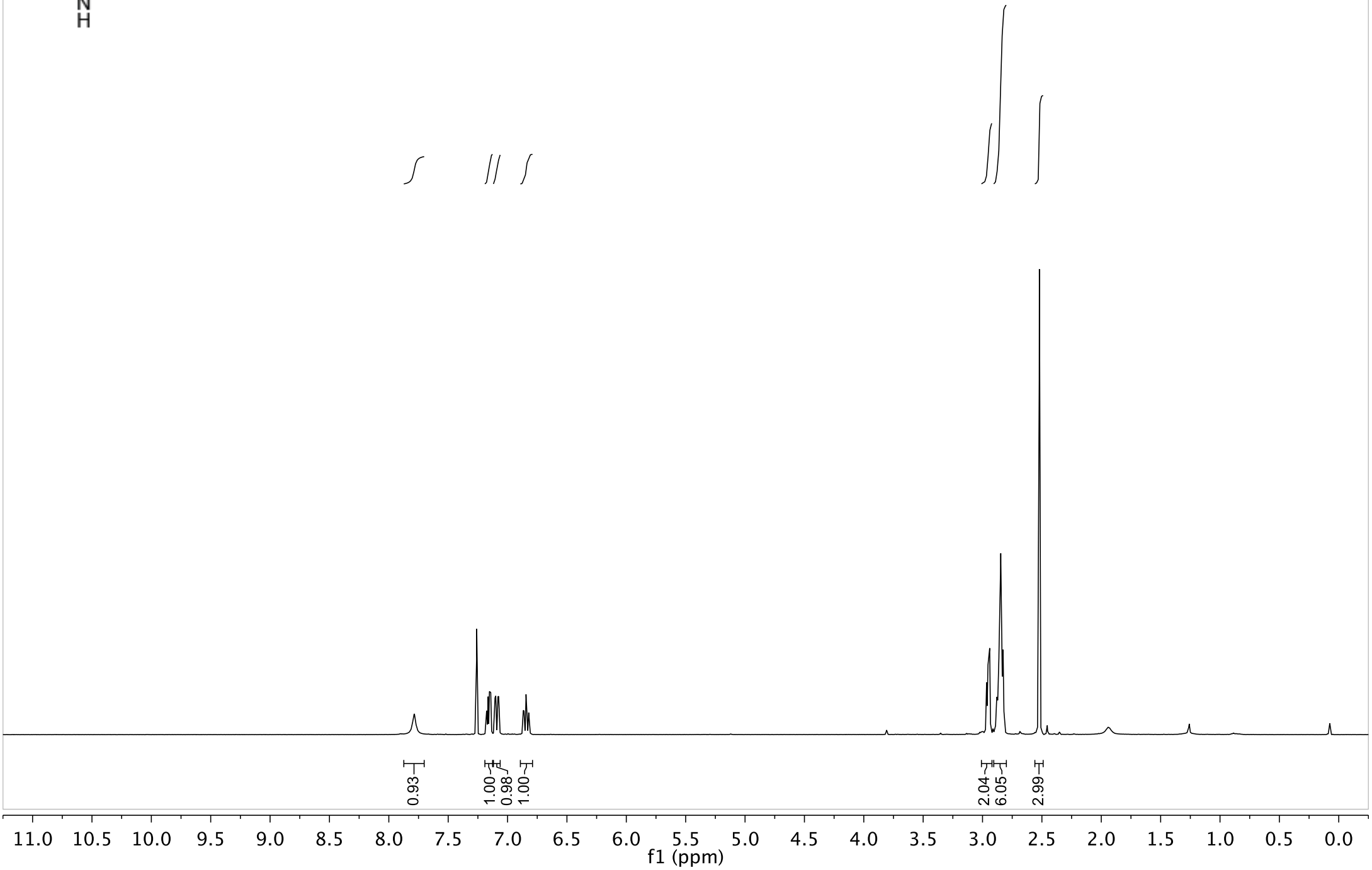
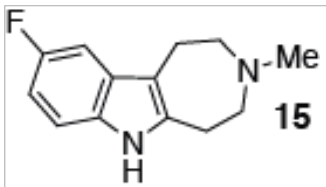
— 27.76

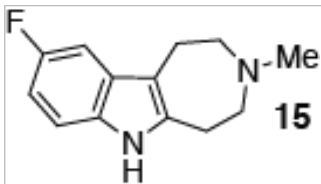
— 23.70



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f1 (ppm)





159.17
156.85

138.24

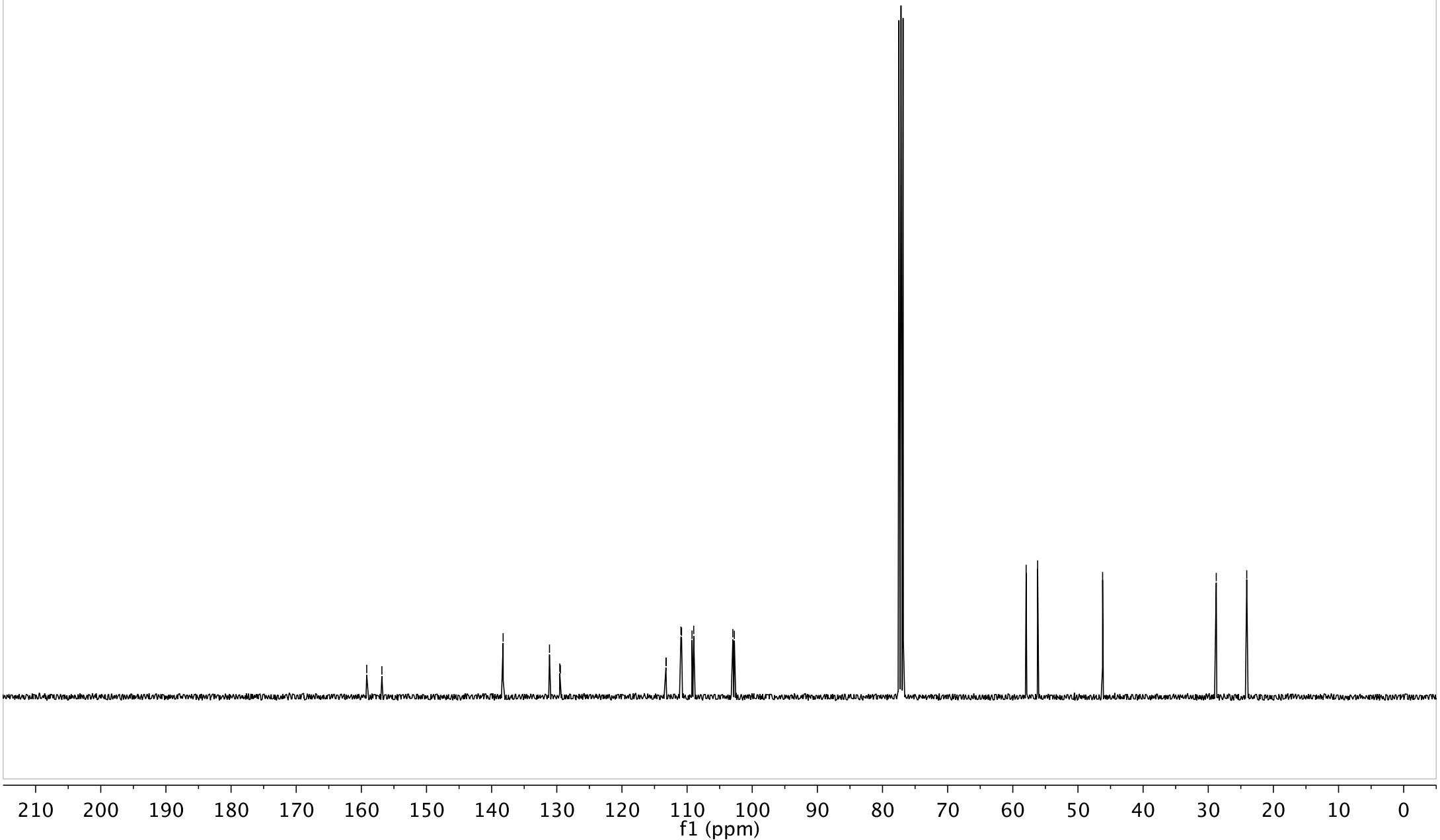
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129.54
129.45

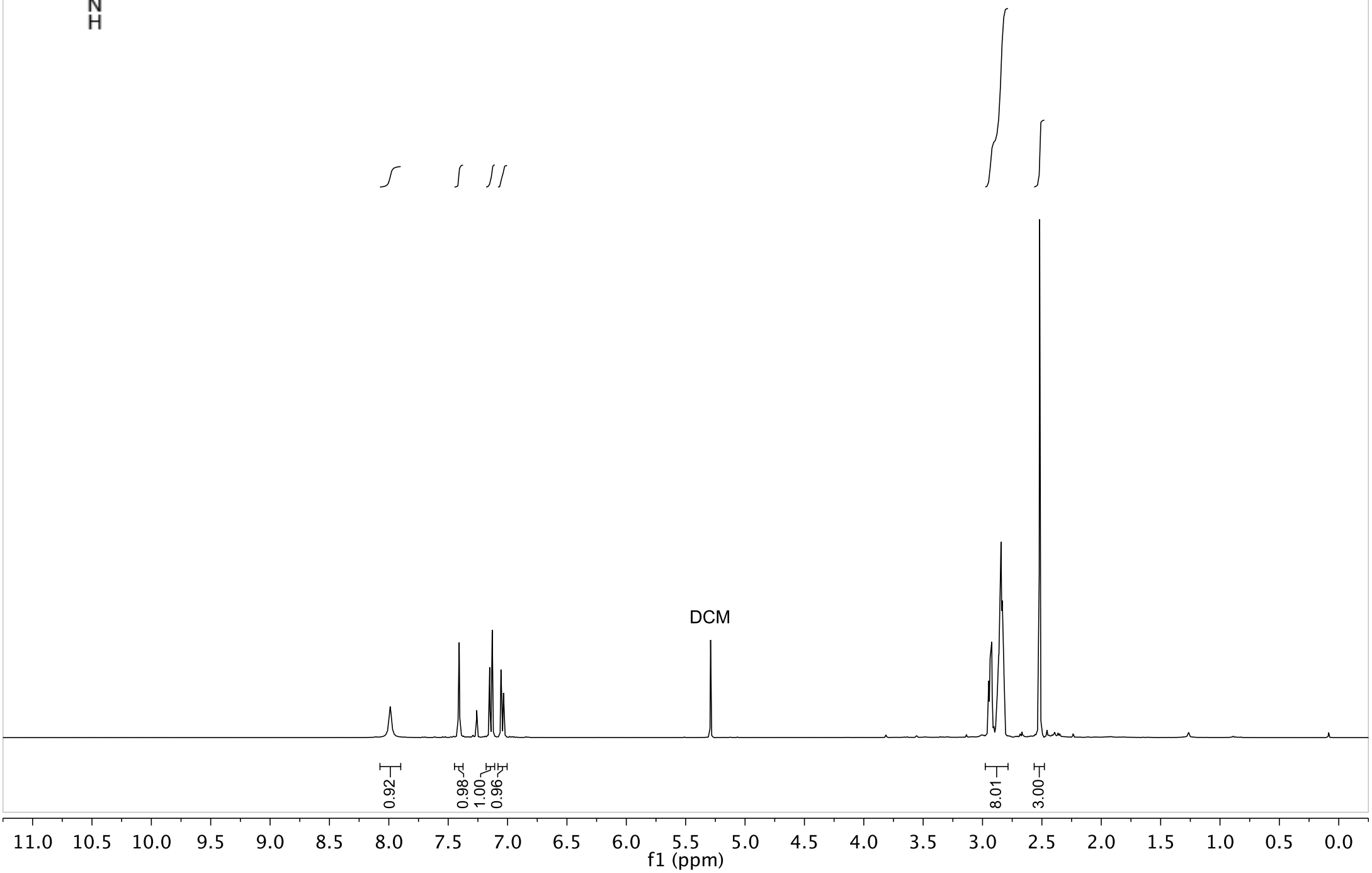
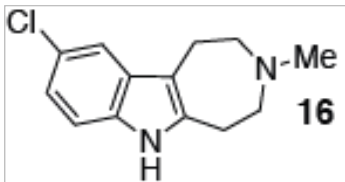
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113.20
110.95
110.85
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108.98
102.98
102.74

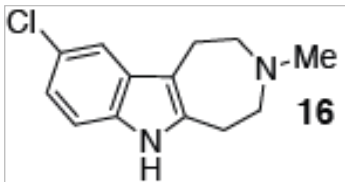
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56.19

46.21

28.77
24.09







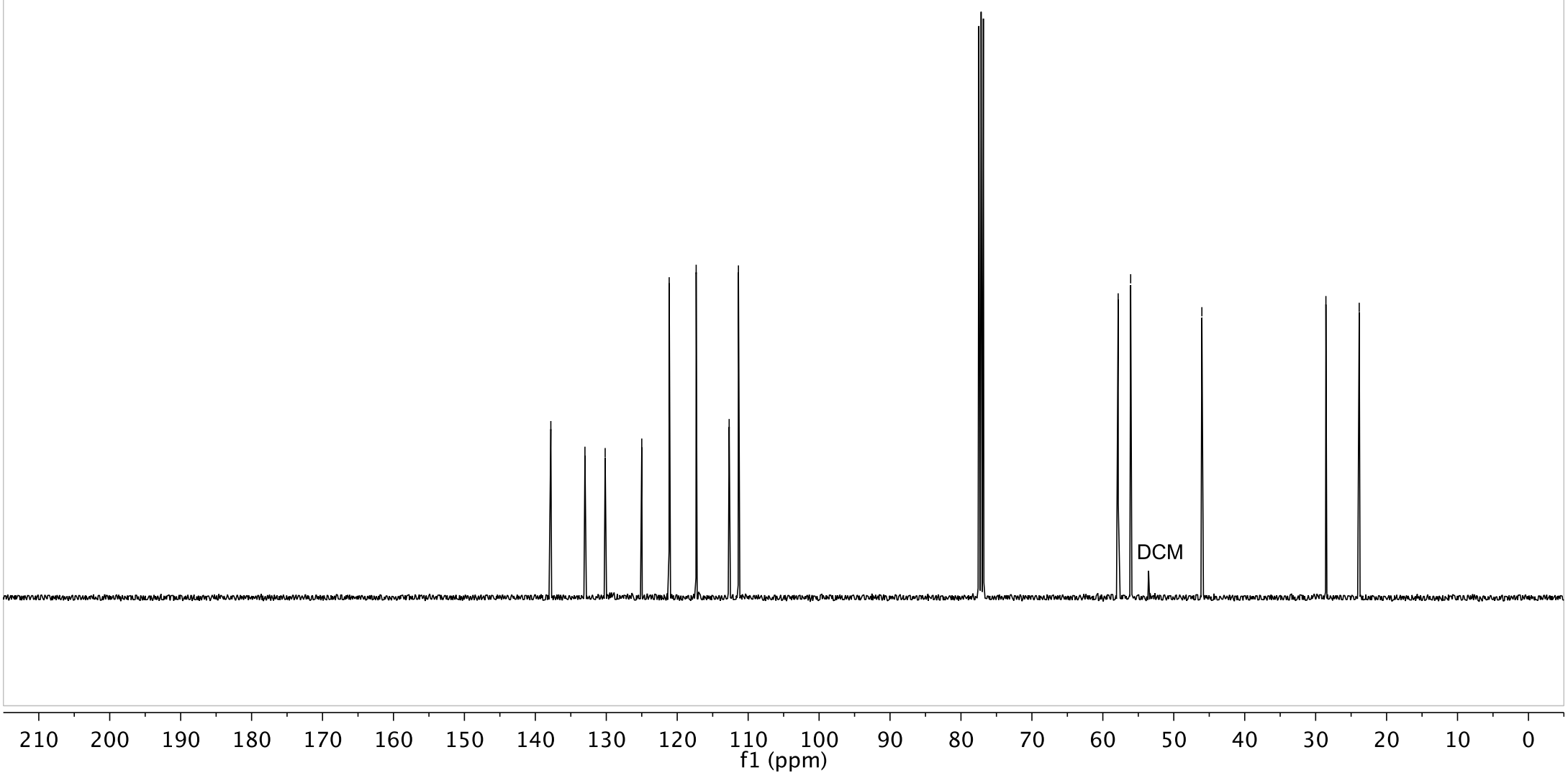
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133.01
130.16
125.00
121.13
117.33
112.68
111.37

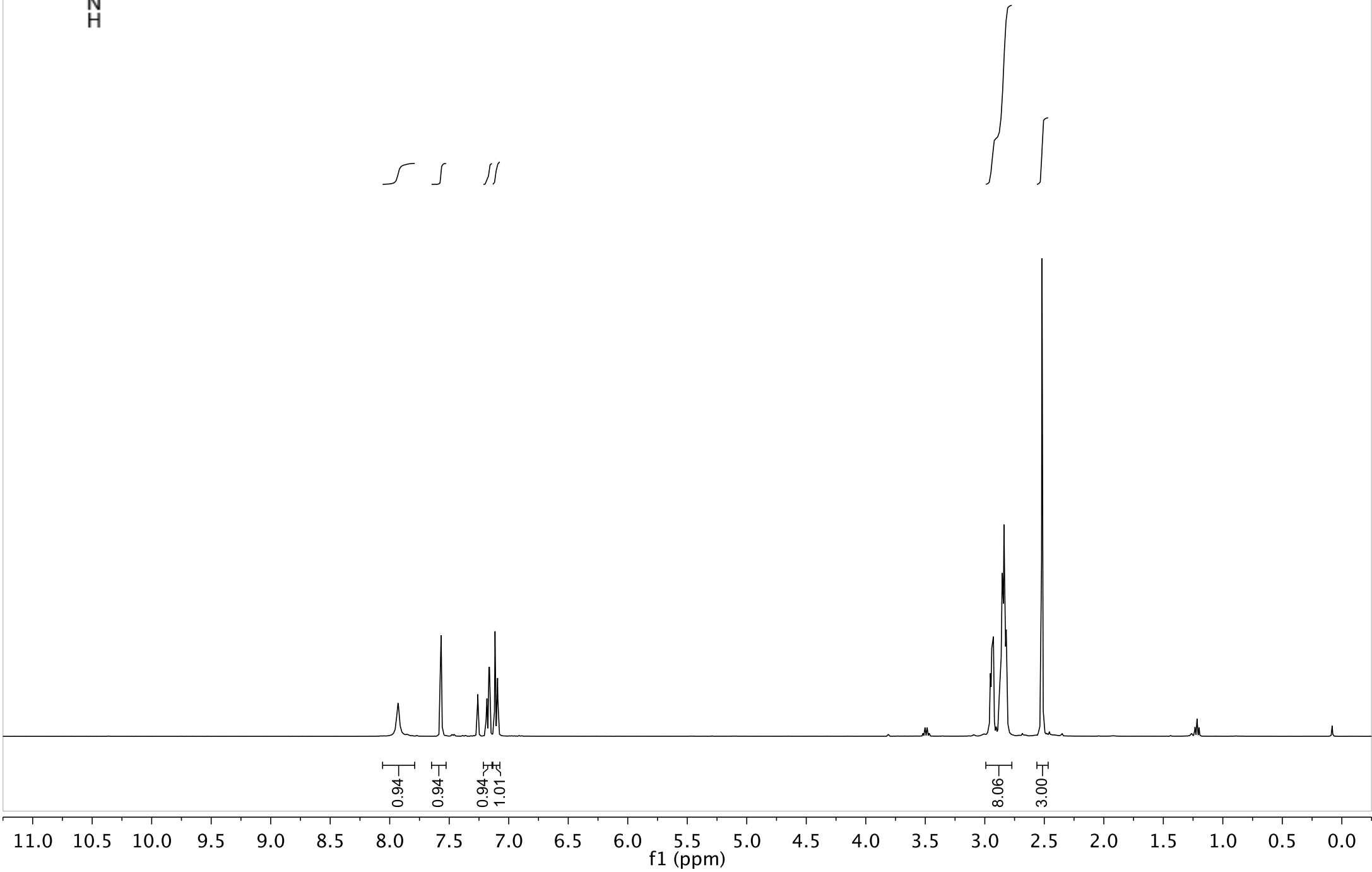
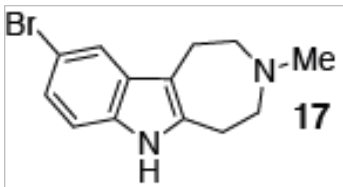
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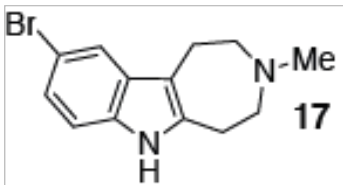
46.04

28.55

23.86







137.66
133.27
130.84
123.71
120.45
112.66
112.58
111.82

77.48
77.16
76.84

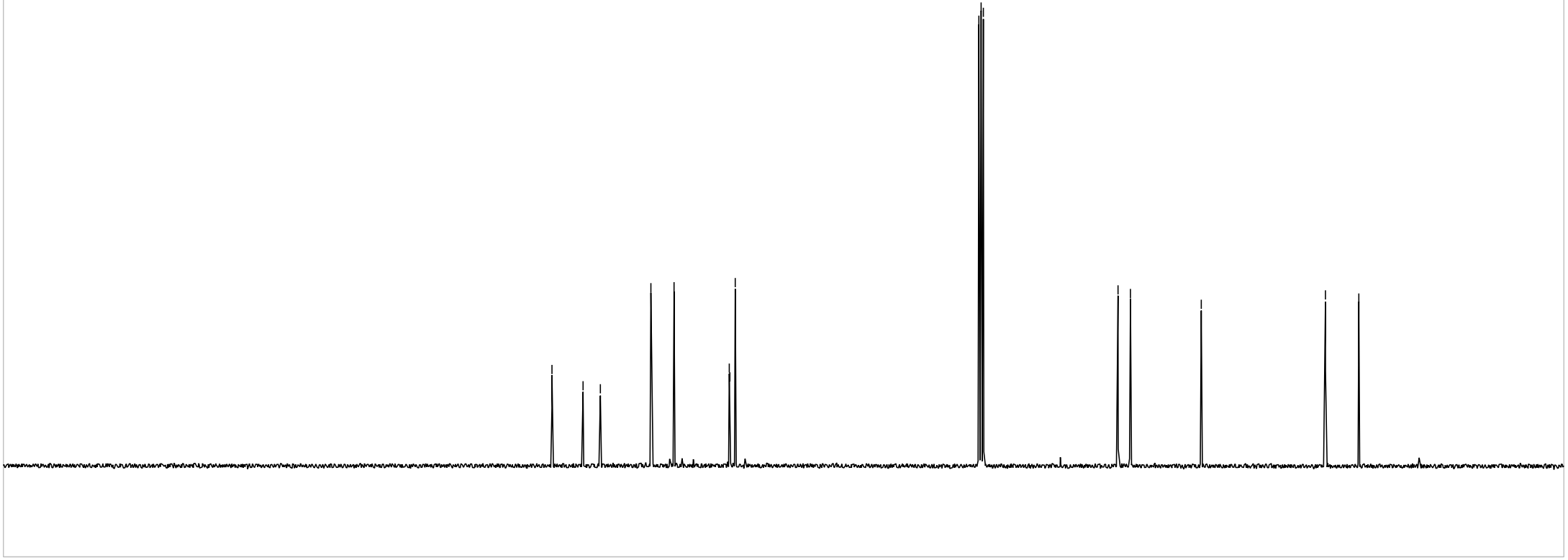
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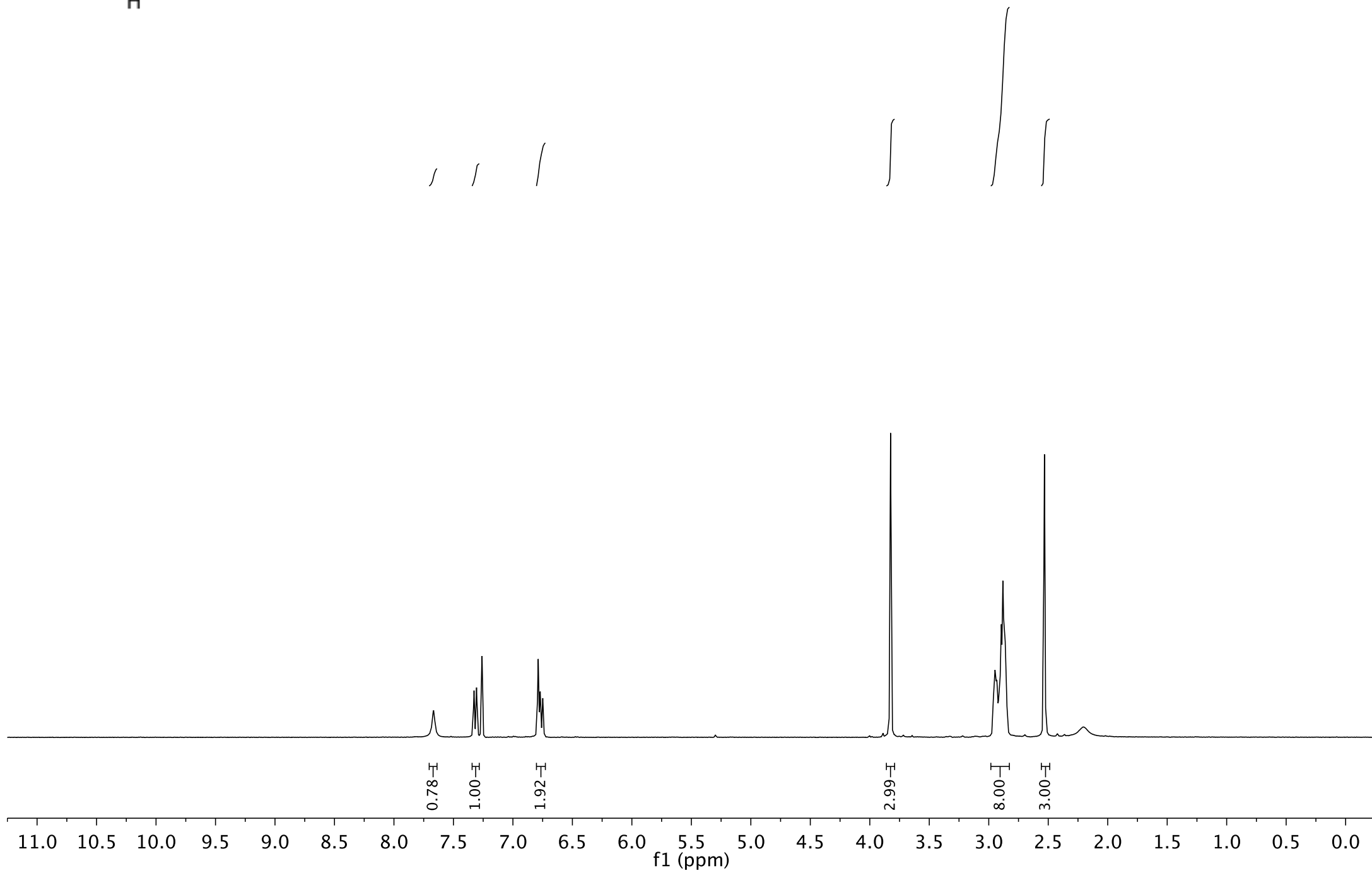
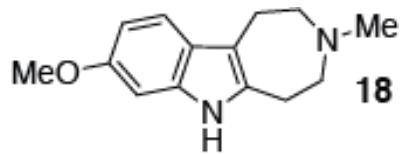
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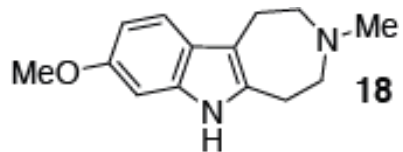
28.62
23.91

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

f1 (ppm)







— 155.93

∩ 135.33
∩ 134.68

— 123.59

— 118.29

— 112.53

— 108.80

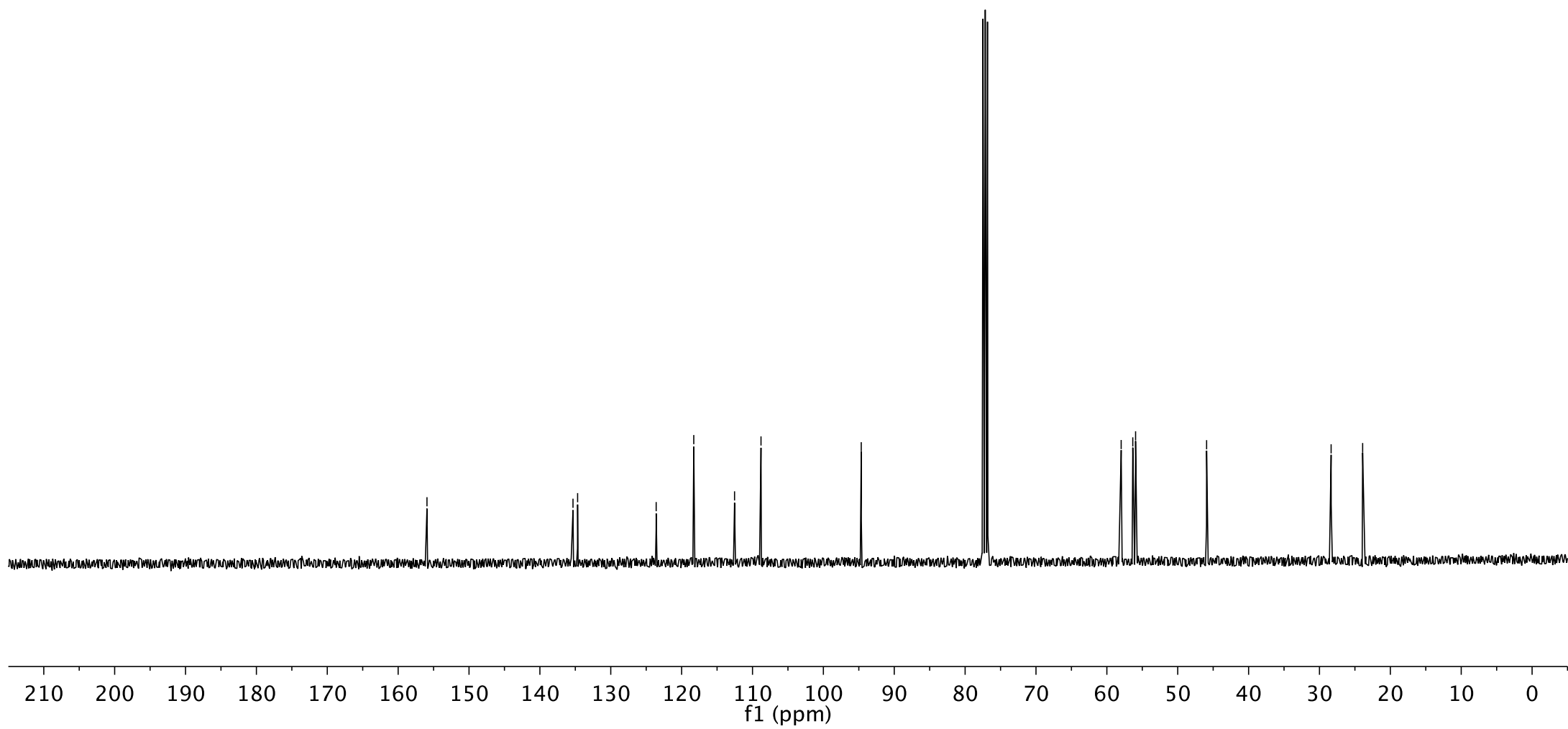
— 94.66

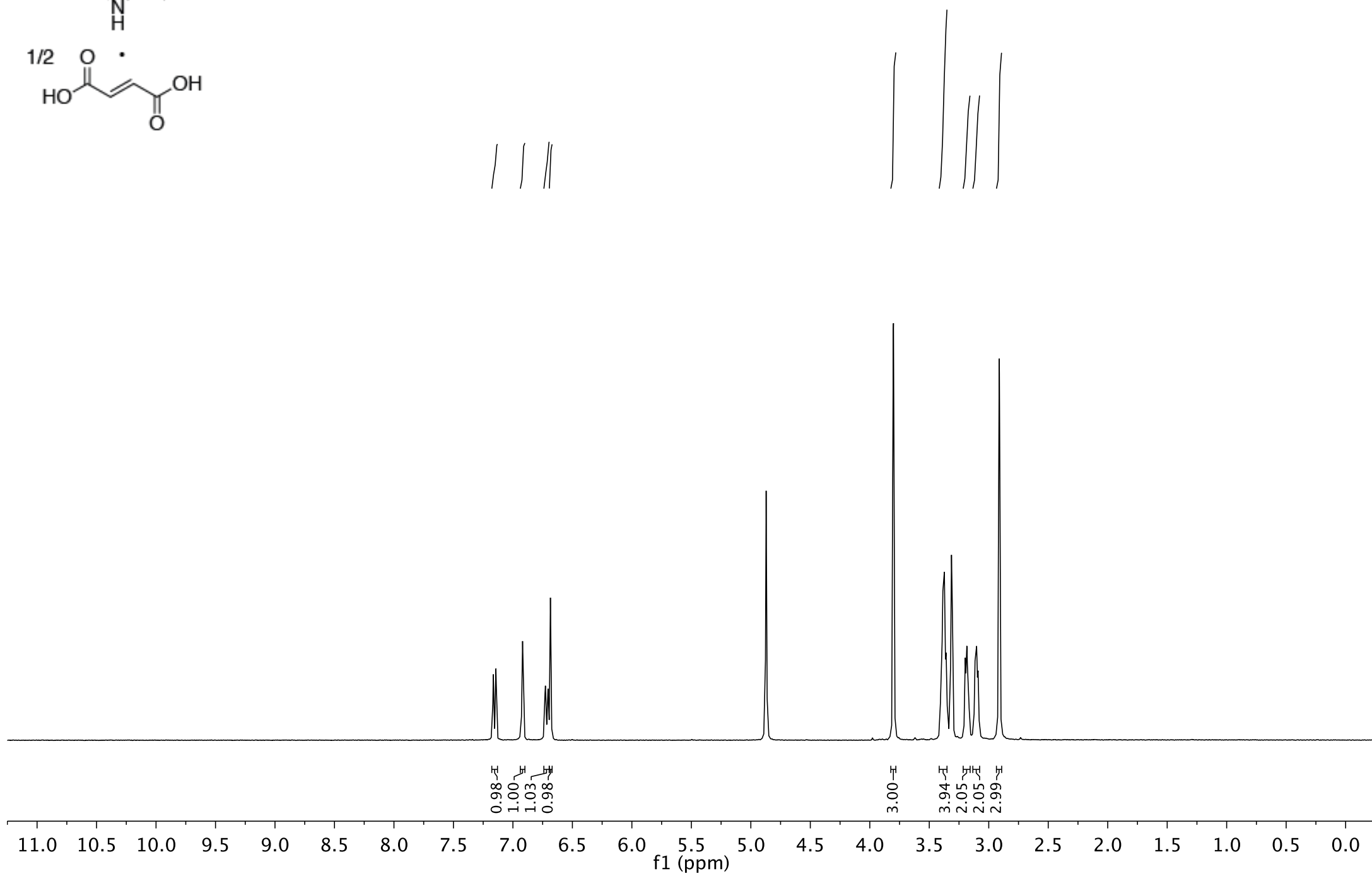
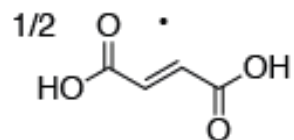
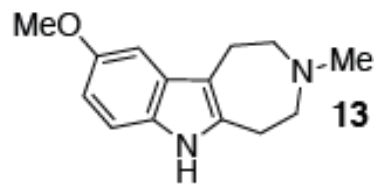
∩ 57.98
∩ 56.34
∩ 55.95

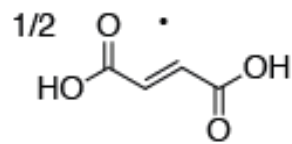
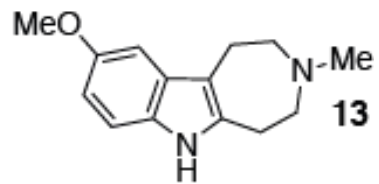
— 45.93

— 28.36

— 23.91







—171.76

—155.37

—136.32

—135.55

—131.75

—129.59

—112.49

—112.31

—110.53

—100.58

—58.77

—56.70

—56.27

—44.77

—25.09

—21.55

