Supplementary Materials for

Concise Total Synthesis of Herqulines B and C

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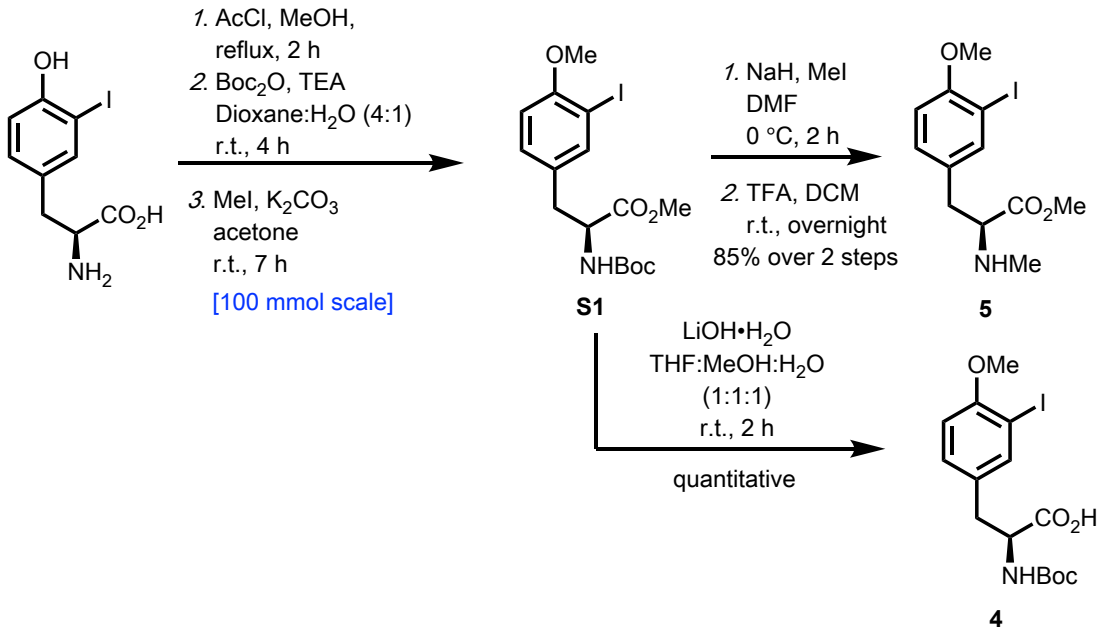
I) Experimental Section

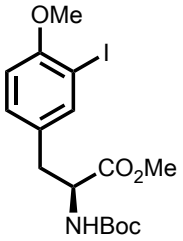
All reactions were carried out under an inert argon atmosphere with dry solvents under anhydrous conditions unless otherwise stated. Dry acetonitrile (MeCN), dichloromethane (DCM), diethyl ether (Et_2O), tetrahydrofuran (THF), toluene (PhMe), dimethylformamide (DMF), benzene, and triethylamine (TEA) were obtained by passing the previously degassed solvents through activated alumina columns. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous material, unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm E. Merck silica plates (60F-254), using UV light as the visualizing agent and/or phosphomolybdic acid and heat as a developing agent. Flash silica gel chromatography was performed using E. Merck silica gel (60, particle size 0.043 – 0.063 mm). NMR spectra were recorded on Bruker DRX-600 and AMX-400 instruments and were calibrated using residual undeuterated solvent as an internal reference (chloroform-*d*: ^{1}H NMR δ = 7.26 ppm, ^{13}C NMR δ = 77.16 ppm). The following abbreviations were used to explain NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer by electrospray ionization time-of-flight (ESI-TOF) reflectron experiments.

Experimental Procedures and Characterization Data for Synthesis of Herqulines B and C



Scheme S1. Synthesis of **4** and **5**

Compound S1



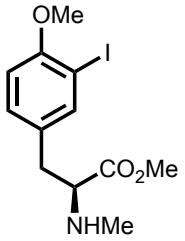
Procedure: To a solution of 3-iodo-*L*-tyrosine (30.7 g, 100 mmol, 1 equiv) in MeOH (100 mL) was added acyl chloride (14.2 mL, 200 mmol, 2 equiv) dropwise at 0 ºC. The mixture was then heated to reflux for 2 h before all solvent was removed *in vacuo*. The resulting hydrochloride salt was used in the next step directly without further purification.

The salt was re-dissolved in dioxane/H_2O (4:1) (100 mL, 1 M). Triethylamine (TEA, 41.5 mL, 300 mmol, 3.0 equiv) and Boc_2O (24 mL, 105 mmol, 1.05 equiv) were added at room temperature and the mixture was stirred for 4 h. The reaction mixture was concentrated to remove dioxane and transferred to a separatory funnel containing water and 50 mL 1N HCl. The mixture was extracted with EtOAc (100 mL × 3) and combined organic layers

were washed with brine, dried over Na_2SO_4, concentrated to give the Boc-protected amine which was directly used in the next step.

The Boc-protected amine was dissolved in acetone (200 mL, 0.5 M) and K_2CO_3 (27.6 g, 200 mmol, 2 equiv) was added in one portion. The mixture was stirred at room temperature for 15 min before adding iodomethane (12.5 mL, 200 mmol, 2 equiv). The reaction was kept at room temperature for 7 h. The mixture was filtered and washed with acetone to remove the salts. The resulting solution was concentrated *in vacuo* and the residue was re-dissolved in EtOAc (200 mL) and washed with brine (200 mL). The organic layer was dried over Na_2SO_4, concentrated to give the crude product which was purified by flash chromatography (EtOAc/Hexanes = 1:3) to give product **S1** as white solid (43.5 g, 100 mmol) in quantitative yield over 3 steps. Spectroscopic data matched reported literature data. [1]

Compound 5



Procedure: To a solution of **S1** (28.8 g, 66 mmol, 1 equiv) and iodomethane (6.2 mL, 99 mmol, 1.5 equiv) in DMF (130 mL, 0.5 M) was added NaH (60% in mineral oil, 2.7 g, 68 mmol, 1.03 equiv) at 0 ºC portionwise. After 2 h, the reaction was quenched by adding H_2O (300 mL) and extracted with EtOAc (300 mL x 4). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated to give the methylation product which was directly used in the next step.

The methylation product was dissolved in a mixture of TFA/DCM (1:5, 120 mL) and stirred at room temperature overnight. The reaction was quenched by adding KOH (1N aq.) and $NaHCO_3$ (sat. aq.) at 0 ºC until pH = 8. The mixture was extracted with DCM (150 mL x 3) and combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated to give a yellow oil. The crude product was purified by flash chromatography (EtOAc/Hexanes = 1:3) to give product **5** (20.0 g, 57.4 mmol) as pale yellow oil in 87% yield over 2 steps.

Physical State: pale yellow oil;

TLC: R_f = 0.6 (MeOH/EtOAc = 1:20);

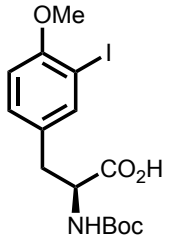
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20.0}}$ = +16.7 (*c* = 1.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.57 (d, *J* = 2.2 Hz, 1H), 7.14 – 7.03 (m, 1H), 6.72 (d, *J* = 8.4 Hz, 1H), 3.83 (s, 3H), 3.67 (s, 3H), 3.37 (t, *J* = 6.7 Hz, 1H), 2.83 (dd, *J* = 6.7, 3.4 Hz, 2H), 2.35 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 174.7, 157.1, 140.0, 131.4, 130.3, 110.8, 86.0, 64.7, 56.4, 51.8, 38.1, 34.8;

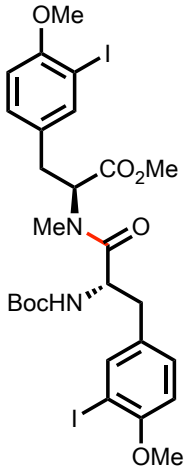
HRMS (m/z): calculated for $C_{12}H_{17}INO_3$ $[M+H]^+$ 350.0248, found 350.0253.

Compound 4



Procedure: To a solution of **S1** (26.8 g, 61.6 mmol, 1 equiv) in THF/MeOH/H_2O (1:1:1, 120 mL, 0.5 M) was added LiOH•H_2O (5.18 g, 123 mmol, 2 equiv) at room temperature. After 2 h, the reaction mixture was concentrated to remove MeOH and THF and the crude product was diluted with H_2O and EtOAc. The organic layer was discarded, and the aqueous layer was acidified to pH 2 with 1N HCl. The precipitated white solid was re-dissolved in EtOAc (200 mL), washed with brine and dried over Na_2SO_4, concentrated to give the product **4** (25.9 g, 61.6 mmol, quantitative yield) as a mixture of rotamers. Spectroscopic data matched reported literature data. [2] The material was used directly for the next step without further purification.

Compound 6



Procedure: To a solution of acid **4** (25.9 g, 61.6 mmol, 1 equiv) in DMF (80 mL) was added DIPEA (16.1 mL, 93 mmol, 1.5 equiv) and HATU (28.1 g, 73.9 mmol, 1.2 equiv) at 0 ºC. The mixture was warmed to room temperature and stirred for 15 min before adding a solution of amine **5** (23 g, 66 mmol, 1.07 equiv) in DMF (50 mL). The reaction was stirred at room temperature overnight. DMF was removed under reduced pressure and the residue was dissolved in EtOAc and brine. The mixture was extracted with EtOAc (100 mL x 3) and dried over Na_2SO_4, concentrated to give a pale yellow foam. The crude product was purified by flash chromatography (EtOAc/Hexanes = 1:2) to give product **6** (37.5 g, 49.7 mmol) as white foam in 81% yield.

Physical State: white foam;

TLC: R_f = 0.25 (Hexanes/EtOAc = 2:1);

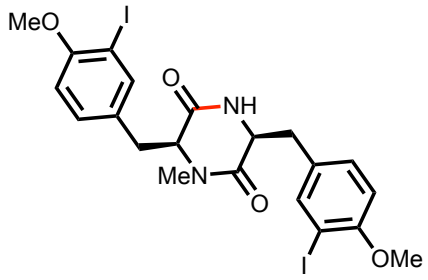
$[\alpha]_D^{20.0}$ = -26.9 (*c* = 1.0, $CHCl_3$);

^{1}H NMR (600 MHz, $CDCl_3$) (major rotomer) δ (ppm) 7.60 (d, *J* = 2.2 Hz, 1H), 7.57 (d, *J* = 2.2 Hz, 1H), 7.12 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.98 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.70 (d, *J* = 8.4 Hz, 1H), 6.66 (d, *J* = 8.4 Hz, 1H), 5.11 (d, *J* = 8.8 Hz, 1H), 5.07 (dd, *J* = 9.5, 6.0 Hz, 1H), 4.79 – 4.62 (m, 1H), 3.82 (s, 3H), 3.82 (s, 3H), 3.70 (s, 3H), 3.28 – 3.18 (m, 1H), 2.94 (dd, *J* = 13.7, 7.1 Hz, 1H), 2.85 (dd, *J* = 14.6, 9.5 Hz, 1H), 2.80 (s, 3H), 2.76 (dd, *J* = 13.7, 6.0 Hz, 1H), 1.39 (s, 9H);

^{13}C NMR (151 MHz, $CDCl_3$) (major rotomer) δ (ppm) 171.8, 170.6, 157.1 (2 C), 155.0, 140.4, 139.8, 131.0, 130.8, 130.5, 130.0, 110.8 (2 C), 85.9, 85.8, 79.9 (2 C), 59.1, 56.4, 52.6, 51.6, 37.5, 33.3, 33.2, 28.4 (3 C);

HRMS (m/z): calculated for $C_{27}H_{35}I_2N_2O_7$ $[M+H]^+$ 753.0528, found 753.0538.

Compound 7



Procedure: Dipeptide **6** (30.2 g, 40.1 mmol, 1 equiv) was dissolved in formic acid (150 mL) and stirred at room temperature overnight. The solvent was removed *in vacuo*. The residual formic acid was removed by azeotropic distillation with toluene (50 mL x 2). The obtained yellow solid was suspended in *sec*-butanol/toluene (4:1, 200 mL, 0.2 M). The suspension was heated to 105 ºC to give a pale yellow clear solution. After 5 h, the solvent was removed and the resulting solid was purified by flash chromatography (MeOH/EtOAc = 1:30) to give product **7** (21.4 g, 34.5 mmol) as white solid in 86% yield.

Physical State: white solid;

TLC: R_f = 0.5 (MeOH/EtOAc = 1:20);

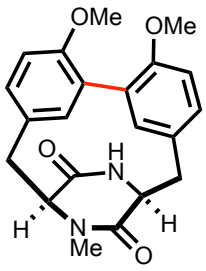
$[\alpha]_D^{20.0}$ = -128.0 (*c* = 1.0, $CHCl_3$);

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.60 (d, *J* = 2.2 Hz, 1H), 7.39 (d, *J* = 2.2 Hz, 1H), 7.06 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.88 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 1H), 6.74 (d, *J* = 8.3 Hz, 1H), 5.83 (d, *J* = 2.7 Hz, 1H), 4.14 (t, *J* = 4.1 Hz, 1H), 3.89 – 3.84 (m, 1H), 3.83 (s, 3H), 3.83 (s, 3H), 3.14 (dd, *J* = 14.3, 3.7 Hz, 1H), 3.08 (s, 3H), 3.03 (dd, *J* = 14.3, 4.5 Hz, 1H), 2.89 (dd, *J* = 13.6, 3.1 Hz, 1H), 0.93 (dd, *J* = 13.7, 11.2 Hz, 1H);

^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) 165.6, 165.2, 158.0, 157.5, 141.0, 139.9, 131.5, 130.8, 130.1, 129.2, 111.3, 111.2, 86.7 (2 C), 63.1, 56.8, 56.7, 56.6, 39.8, 35.4, 33.3;

HRMS (m/z): calculated for $C_{21}H_{23}I_2N_2O_4$ $[M+H]^+$ 620.9742, found 620.9747.

Compound 8



Procedure: To a solution of compound **7** (4.6 g, 7.4 mmol, 1 equiv) in DMSO/H_2O (100:1, 372 mL, 0.02 M) was added $Pd(dppf)_2Cl_2•CH_2Cl_2$ (1.20 g, 1.5 mmol, 0.2 equiv), B_2Pin_2 (7.55 g, 29.7 mmol, 4 equiv) and K_2CO_3 (6.16 g, 44.6 mmol, 6 equiv). The solution was degassed through an argon balloon for 10 min, then moved to a 90 °C oil bath. After stirring for 60 min, 60 mL of *air* was added to the mixture *via* syringe and stirred at same temperature overnight. After cooling to room temperature, the reaction was poured into an ice bath and 1 N HCl (aq., 500 mL) was added. The mixture was extracted with EtOAc (300 mL x 4). The combined organic layers were washed with brine (500 mL x 3) and dried over Na_2SO_4, concentrated to give a yellow foam. The crude product was purified by flash chromatography (EtOAc to EtOAc/MeOH = 30:1) to give product **8** (1.63 g, 4.4 mmol) as white foam in 60% yield.[2]

Physical State: white foam;

TLC: R_f = 0.3 (MeOH/EtOAc = 1:20);

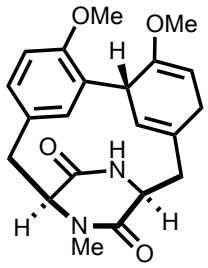
$[\alpha]_D^{20.0}$ = +32.8 (*c* = 1.0, $CHCl_3$);

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.03 (dd, *J* = 8.2, 2.6 Hz, 1H), 6.98 – 6.93 (m, 1H), 6.76 (d, *J* = 8.3 Hz, 1H), 6.70 (d, *J* = 8.4 Hz, 1H), 6.49 (dd, *J* = 2.6, 0.9 Hz, 1H), 6.43 – 6.41 (m, 1H), 5.94 (s, 1H), 4.46 (d, *J* = 6.3 Hz, 1H), 4.31 (d, *J* = 6.6 Hz, 1H), 4.07 – 3.96 (m, 2H), 3.91 (s, 3H), 3.86 (s, 3H), 2.94 (dd, *J* = 15.9, 6.7 Hz, 1H), 2.76 (s, 3H), 2.63 (dd, *J* = 15.9, 6.3 Hz, 1H);

^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) 167.9, 166.9, 155.8, 155.6, 142.0, 141.7, 130.0, 129.8, 129.6, 129.2, 125.5, 125.3, 112.3, 111.9, 62.3, 56.4, 56.2 (2 C), 34.9, 34.2, 31.8;

HRMS (m/z): calculated for $C_{21}H_{23}N_2O_4$ $[M+H]^+$ 367.1652, found 367.1662.

Compound 9



Procedure: To a flame dried 100 mL round bottom flask was condensed liquid NH_3 (20 mL) at -78 ºC under Ar atmosphere, after which lithium metal (172 mg, 24.6 mmol, 15 equiv) was added. The solution turned to dark blue and kept stirring for 10 min before adding a solution of **8** (600 mg, 1.64 mmol, 1 equiv) and trifluoroethanol (0.96 ml, 13.1 mmol, 8 equiv) in THF (15 mL). The resulting solution was stirred at -78 ºC for 60 min and quenched by adding excess trifluoroethanol (1.5 mL) and the blue color disappeared immediately. Following evaporation of all NH_3, the residue was dissolved in EtOAc and brine. The mixture was extracted with EtOAc (50 mL x 3), dried over Na_2SO_4, and concentrated to give a pale yellow foam. The crude product was purified by flash chromatography (EtOAc/MeOH = 50:1) to give product **9** (464 mg, 1.26 mmol) as white foam in 77% yield.

Physical State: white foam;

TLC: R_f = 0.6 (MeOH/EtOAc = 1:20);

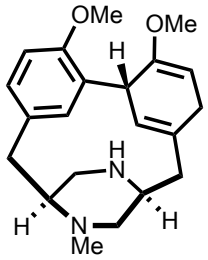
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20.0}}$ = +35.5 (*c* = 0.6, $CHCl_3$);

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.88 (d, *J* = 3.2 Hz, 1H), 6.95 (d, *J* = 2.5 Hz, 1H), 6.86 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.65 (d, *J* = 8.3 Hz, 1H), 5.41 – 5.36 (m, 1H), 4.68 (dd, *J* = 4.3, 2.9 Hz, 1H), 4.30 (d, *J* = 4.5 Hz, 1H), 4.24 (dt, *J* = 5.7, 2.8 Hz, 1H), 3.81 (s, 3H), 3.71 – 3.63 (m, 1H), 3.48 (s, 3H), 3.43 (d, *J* = 16.2 Hz, 1H), 3.37 – 3.32 (m, 1H), 3.23 – 3.14 (m, 1H), 2.87 (d, *J* = 16.2 Hz, 1H), 2.83 – 2.74 (m, 1H), 2.55 (dd, *J* = 13.4, 5.8 Hz, 1H), 2.45 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) 168.8, 161.1, 155.9, 155.4, 133.0, 132.1, 131.1, 130.2, 128.6, 126.4, 110.8, 91.0, 84.8, 62.8, 56.2, 54.5, 41.5, 37.3, 36.7, 32.6, 26.2;

HRMS (m/z): calculated for $C_{21}H_{25}N_2O_4$ $[M+H]^+$ 369.1809, found 369.1815.

Compound 10



Procedure: To a solution of **9** (320 mg, 0.87 mmol, 1 equiv) in toluene (15 mL) was added $[Ir(COE)_2Cl]_2$ (156 mg, 0.17 mmol, 0.2 equiv) and Et_2SiH_2 (0.71 mL, 8.7 mmol, 10 equiv). The mixture was sealed under argon and heated at 120 ºC for 2 h. After cooling to room temperature, the solvent was removed *in vacuo*. The residue was directly purified by flash chromatography (EtOAc/MeOH = 40:1) to give product **10** (254 mg, 0.75 mmol) as white foam in 86% yield. [3]

Physical State: white foam;

TLC: R_f = 0.25 (MeOH/$CHCl_3$ = 1:10);

$[\alpha]_D^{20.0}$ = +56.2 (*c* = 0.29, $CHCl_3$);

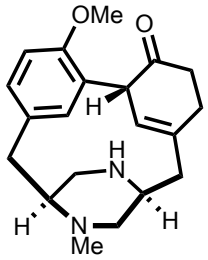
^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 8.59 (d, *J* = 2.3 Hz, 1H), 6.94 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.65 (d, *J* = 8.2 Hz, 1H), 5.22 (dd, *J* = 3.7, 2.0 Hz, 1H), 4.78 (t, *J* = 3.5 Hz, 1H), 4.45 (q, *J* = 4.3 Hz, 1H), 3.84 (s, 3H), 3.55 (s, 3H), 3.37 – 3.25 (m, 3H), 3.24 – 3.18 (m, 2H), 3.14 – 3.06 (m, 2H), 2.94 – 2.86 (m, 1H), 2.83 (t, *J* = 11.3 Hz, 1H), 2.36 (s, 3H), 2.24 (dd, *J* = 14.0, 5.8 Hz, 1H), 2.06 (d, *J* = 13.9 Hz, 1H), 2.00 (br, 1 H);

^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) 155.2, 154.3, 138.9, 132.4, 129.6 (2 C), 129.5, 109.6, 90.5, 55.7, 55.1, 54.3, 53.9, 52.9, 50.1, 41.1, 38.4, 37.4, 37.2, 34.0;

*Note: One aromatic carbon was missing in ^{13}C NMR. A similar result was observed for compound **11,** whose structure was unambiguously assigned using X-ray crystallography.*

HRMS (m/z): calculated for $C_{21}H_{29}N_2O_2$ $[M+H]^+$ 341.2224, found 341.2231.

Compound 11



Procedure: To a solution of **10** (35 mg, 0.10 mmol, 1 equiv) in MeOH/H_2O (2 mL) was added oxalic acid (18 mg, 0.20 mmol, 2 equiv). The mixture was stirred at room temperature for 2 h and the solvent was removed *in vacuo*. The residue was dissolved in EtOAc and saturated aqueous $NaHCO_3$ (5 ml). The mixture was extracted with EtOAc (5 mL x 3) and dried over Na_2SO_4, concentrated to give a pale yellow foam. The crude product was purified by flash chromatography (EtOAc/MeOH = 40:1) to give product **11** (31 mg, 0.095 mmol) as white solid in 95% yield.

Physical State: white solid;

TLC: R_f = 0.25 (MeOH/$CHCl_3$ = 1:10);

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20.0}}$ = +71.7 (*c* = 0.53, $CHCl_3$);

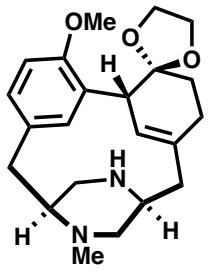
^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 8.70 (d, *J* = 2.3 Hz, 1H), 6.96 (dd, *J* = 8.3, 2.3 Hz, 1H), 6.66 (d, *J* = 8.2 Hz, 1H), 5.41 (m, 1H), 4.59 (dd, *J* = 3.8, 1.5 Hz, 1H), 3.82 (s, 3H), 3.38 – 3.31 (m, 2H), 3.24 (m, 1H), 3.16 (dd, *J* = 11.4, 1.6 Hz, 1H), 3.12 – 3.06 (m, 2H), 3.03 (d, *J* = 15.7 Hz, 1H), 2.93 (t, *J* = 11.3 Hz, 1H), 2.72 – 2.64 (m, 2H), 2.48 (m, 1H), 2.35 (s, 3H), 2.33 (d, *J* = 5.7 Hz, 1H), 2.23 (d, *J* = 14.0 Hz, 1H), 2.08 (d, *J* = 10.6 Hz, 1H);

^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) 212.0, 155.7, 138.9, 135.5, 131.2, 130.2, 128.8, 110.5, 56.1, 55.6, 54.4, 52.9, 50.9, 47.7, 41.7, 40.0, 39.4, 38.9, 33.3;

Note: One aromatic carbon was missing in ^{13}C NMR. X-ray crystallography assigned the structure.

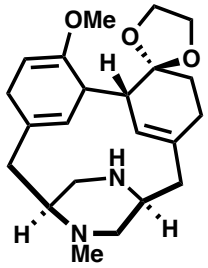
HRMS (m/z): calculated for $C_{20}H_{27}N_2O_2$ $[M+H]^+$ 327.2067, found 327.2070.

Compound 12



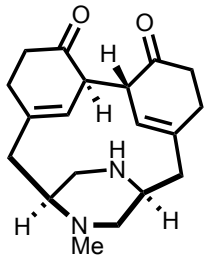
Procedure: To a solution of **10** (20 mg, 0.054 mmol, 1 equiv) in benzene (6 mL) was added ethylene glycol (45 μL, 0.81 mmol, 15 equiv) and *p*-toluenesulfonic acid (5 mg, 0.027 mmol, 0.5 equiv) was added. The resulting suspension was placed in an 110 ºC oil bath and water was removed by Dean Stark Trap. The solution was stirred for 0.5 h at which time LC/MS analysis indicated complete conversion to desired mass (M+/Z = 371). After cooling to room temperature, suspension was dilutied with EtOAc and saturated aqueous $NaHCO_3$ was added and the layers that formed were separated. The aqueous phase was then extracted with EtOAc (15 mL x 3) and the pooled organic fractions were dried over Na_2SO_4. The solvent was removed under reduced pressure to give a pale yellow oil that was used without further purification in the next step.

Compound 13



Procedure: To a flame dried 100 mL round bottom flask was condensed liquid NH_3 (10 mL) at -78 ºC under Ar atmosphere, after which lithium metal (12 mg, 1.62 mmol, 30 equiv) and *tert*-butanol (0.5 mL) were added. The solution turned to dark blue and kept stirring for 10 min before adding a solution of crude **12** from the previous step in THF (5 mL). The resulting solution was stirred at -78 ºC for 2 h and quenched by adding excess solid NH_4Cl and the blue color disappeared immediately. Following evaporation of all NH_3, the residue was dissolved in EtOAc and brine. The mixture was extracted with EtOAc (15 mL x 3) dried over Na_2SO_4, and concentrated to give a pale yellow foam **13** which was used in the next step without further purification.

Herquline C (14)



Procedure: To a solution of **13** in 1:1 THF/MeOH (1.5 mL) was added 1N HCl (0.5 mL). The pale yellow cloudy solution stirred at 65 ºC under argon for 30 min at which time the solution had become clear and homogeneous. Solvents were then removed under reduced pressure and the residue was redissolved in MeOH. The resulting solution was passed through a plug of basic alumina and concentrated. Purification using preparative TLC (10% MeOH in $CHCl_3$, 1% *i*$PrNH_2$) afforded a 1:5 mixture of herqulines B (**3**) and C (**14**) as a white solid (5.0 mg, 0.016 mmol, 28 % over 3 steps).

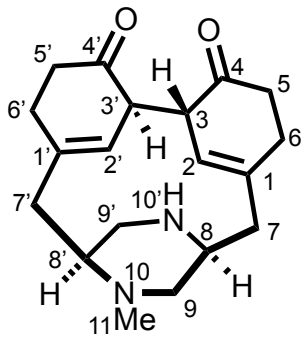
Physical State: white solid;

TLC: R_f = 0.25 (10% MeOH in $CHCl_3$, 1% *i*$PrNH_2$);

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 5.25 (m, 1H), 5.14 (m, 1H), 3.98 (s, 1H), 3.83 (s, 1H), 3.18 (dd, *J* = 13.5, 7.5 Hz, 1H), 3.16 – 3.12 (m, 1H), 2.87 – 2.75 (m, 3H), 2.72 – 2.55 (m, 4H), 2.52 – 2.43 (m, 5H), 2.42 – 2.35 (m, 2H), 2.34 (s, 3H), 2.25 – 2.20 (m, 1H), 2.14 (dd, *J* = 11.5, 4.5 Hz, 1H), 2.10 (d, *J* = 14.1 Hz, 1H);

^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) 212.2, 211.0, 139.7, 138.6, 125.7, 125.4, 58.6, 58.2, 50.8, 50.5, 49.0, 46.7, 44.6, 40.6, 40.2, 39.4, 39.0, 34.2, 33.3;

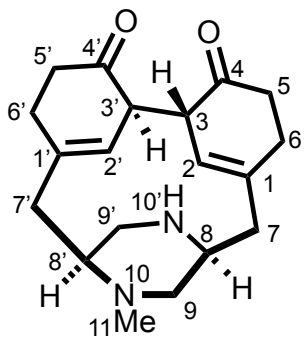
HRMS (m/z): calculated for $C_{19}H_{27}N_2O_2$ $[M+H]^+$ 315.2067, found 315.2071.



Herquline C (**14**)
(Reported by Tang)

Tabulated data for Natural (Tang[4]) and Synthetic Herquline C
^{1}H NMR (600 MHz, $CDCl_3$)

	Natural Herquline C	Synthetic Herquline C	Delta ppm
H2’	5.26, m	5.25, m	0.01
H2	5.14, m	5.14, m	–
H3	3.99, br, s	3.98, br, s	0.01
H3’	3.83 br, s	3.83 br, s	–
H9’	3.17, dd 2.65, overlaps	3.18, dd 2.65, overlaps	0.01 –
H8	3.13, m	3.14, m	0.01
H6’	2.83, m 2.40, m	2.83, m 2.40, m	– –
H9	2.81, m 2.15, m	2.81, m 2.14, m	– 0.01
H6	2.76, m 2.46, m	2.76, m 2.46, m	– –
H5	2.68, m 2.48, overlaps	2.68, m 2.48, overlaps	– –
H5’	2.62, m 2.51, m	2.62, m 2.51, m	– –
H7’	2.48, overlaps 2.11, m br, d	2.48, overlaps 2.10, m br, d	– 0.01
H7	2.38, m overlaps 2.22, m br, d	2.38, m overlaps 2.22, m br, d	– –
11-Me	2.35, s	2.34, s	0.01
H8’	2.32, m	2.32, m	–

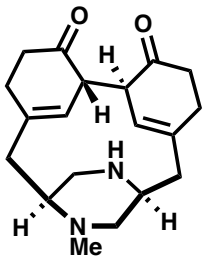


Herquline C (**14**)
(Reported by Tang)

Tabulated data for Natural (Tang[4]) and Synthetic Herquline C
^{13}C NMR (151 MHz, $CDCl_3$)

	Natural Herquline C	Synthetic Herquline C	Delta ppm
C4’	212.2	212.2	–
C4	211.0	211.0	–
C1’	139.8	139.7	0.1
C1	138.7	138.6	0.1
C2	125.5	125.7	0.2
C2’	125.4	125.4	–
C8’	58.6	58.6	–
C9	58.1	58.2	0.1
C3	50.8	50.8	–
C8	50.5	50.5	–
C3’	49.0	49.0	–
C9’	46.9	46.7	0.2
11-Me	44.6	44.6	–
C7	40.6	40.6	–
C5’	40.2	40.2	–
C5	39.4	39.4	–
C7’	39.1	39.0	0.1
C6	34.2	34.2	–
C6’	33.3	33.3	–

Herquline B (3)



Procedure: The mixture of herqulines B & C obtained from the previous step was taken up in toluene (2.0 mL) and sealed under argon atmosphere. DBU (5.0 uL, 0.032 mmol, 2 equiv) was added and the mixture stirred at room temperature for 0.5 h. Solvent was then removed under reduced pressure and the crude residue was directly subjected to preparative TLC (10% MeOH in $CHCl_3$, 1% *i*$PrNH_2$) to give the title compound **3** as a white solid (5.0 mg, quantitative yield).

Physical State: white solid;

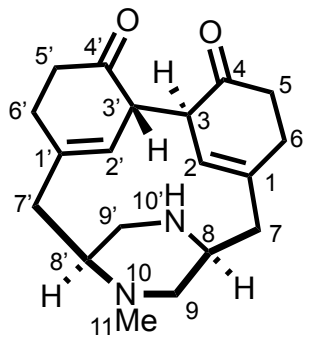
TLC: R_f = 0.25 (10% MeOH in $CHCl_3$, 1% *i*$PrNH_2$);

$[\alpha]_D^{20.0}$ = –98 (*c* = 0.05, $CHCl_3$); –82 (*c* = 0.05, MeOH);

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 5.30 (d, *J* = 3.1 Hz, 1H), 5.26 (s, 1H), 3.95 (s, 1H), 3.83 (s, 1H), 3.14 (m, 1H), 3.01 – 2.93 (m, 1H), 2.89 (dd, *J* = 13.9, 6.0 Hz, 1H), 2.73 (d, *J* = 13.9 Hz, 1H), 2.70 – 2.60 (m, 4H), 2.58 (m, 1H), 2.56 – 2.46 (m, 5H), 2.40 (m, 1H), 2.33 (m, 1H), 2.26 (s, 3H), 2.23 (m, 1H), 1.78 (dd, *J* = 14.3, 4.5 Hz, 1H);

^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) 212.0, 209.9, 138.3, 136.2, 126.7, 124.0, 59.4, 53.2, 52.0, 50.8, 48.8, 45.7, 42.9, 42.2, 39.6, 39.3, 37.3, 32.9, 30.7;

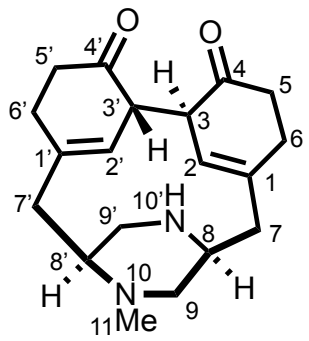
HRMS (m/z): calculated for $C_{19}H_{27}N_2O_2$ $[M+H]^+$ 315.2067, found 315.2081.



Herquline B (**3**)
(Reported by Ōmura)

Tabulated data for Natural (Ōmura[5]) and Synthetic Herquline B
^{1}H NMR (600 MHz, $CDCl_3$)

	Natural Herquline B	Synthetic Herquline B	Delta ppm
H2	5.31, m	5.30, m	0.01
H2’	5.25, m	5.26, m	0.01
H3’	3.95, br, s	3.95, br, s	–
H3	3.80 br, s	3.83 br, s	0.03
H8	3.25, m	3.14, m	0.11
H9’	3.01, dd 2.92, dd	3.01, dd 2.89, dd	– 0.03
H7’	2.73, dd 1.78, dd	2.73, dd 1.78, dd	– –
H5’	2.68, m 2.48, m	2.68, m 2.48, m	– –
H5	2.68, m 2.48, m	2.68, m 2.48, m	– –
H6’	2.67, m 2.48, m	2.67, m 2.48, m	– –
H6	2.61, m 2.32, m	2.61, m 2.33, m	– 0.01
H9	2.58, m	2.58, m	–
H7	2.56, m 2.28, m	2.56, m 2.23, m	– 0.05
H8’	2.41, m	2.40, m	0.01
11-Me	2.26, s	2.26, s	–



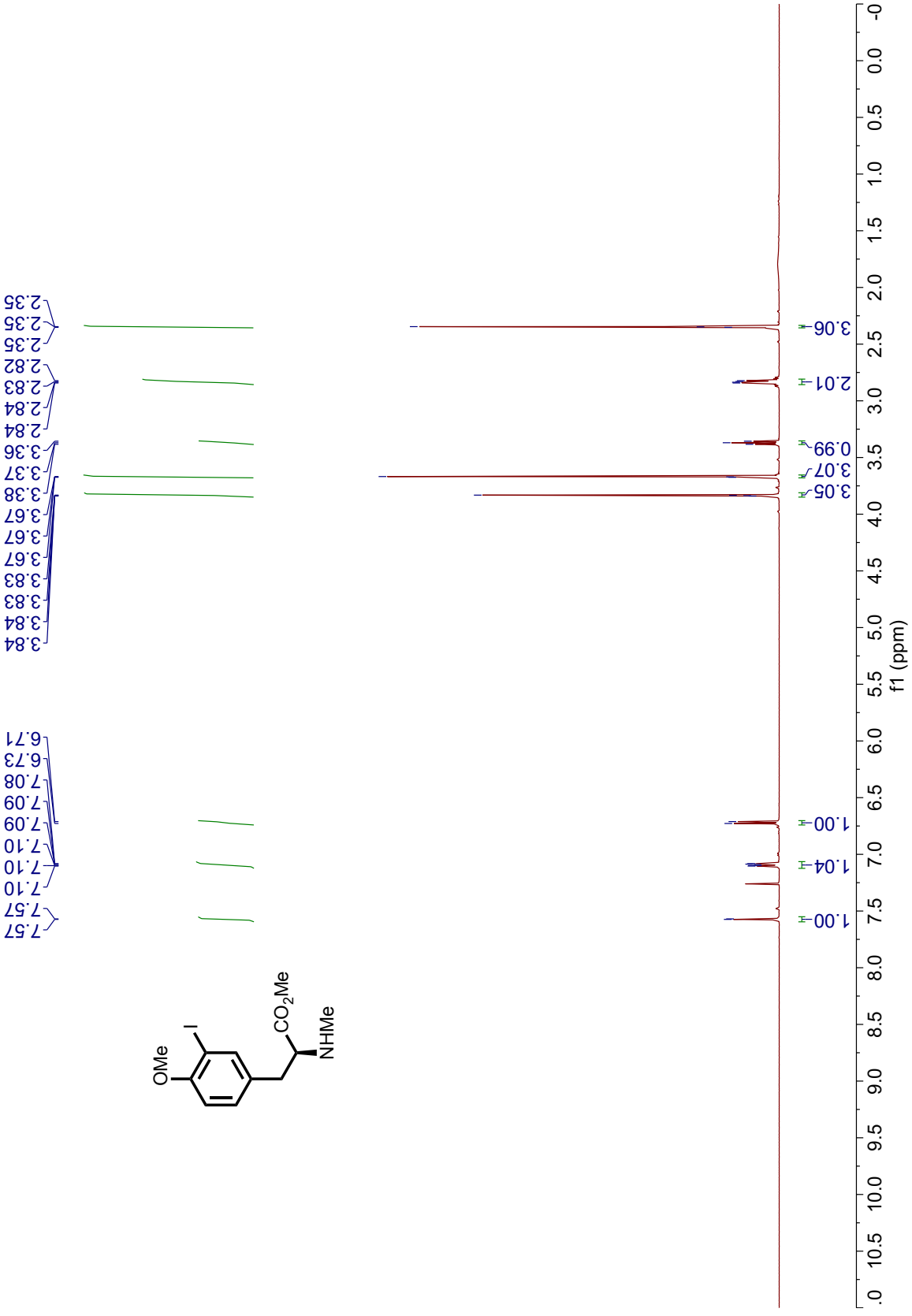
Herquline B (**3**)
(Reported by Ōmura)

Tabulated data for Natural (Ōmura[5]) and Synthetic Herquline B
^{13}C NMR (151 MHz, $CDCl_3$)

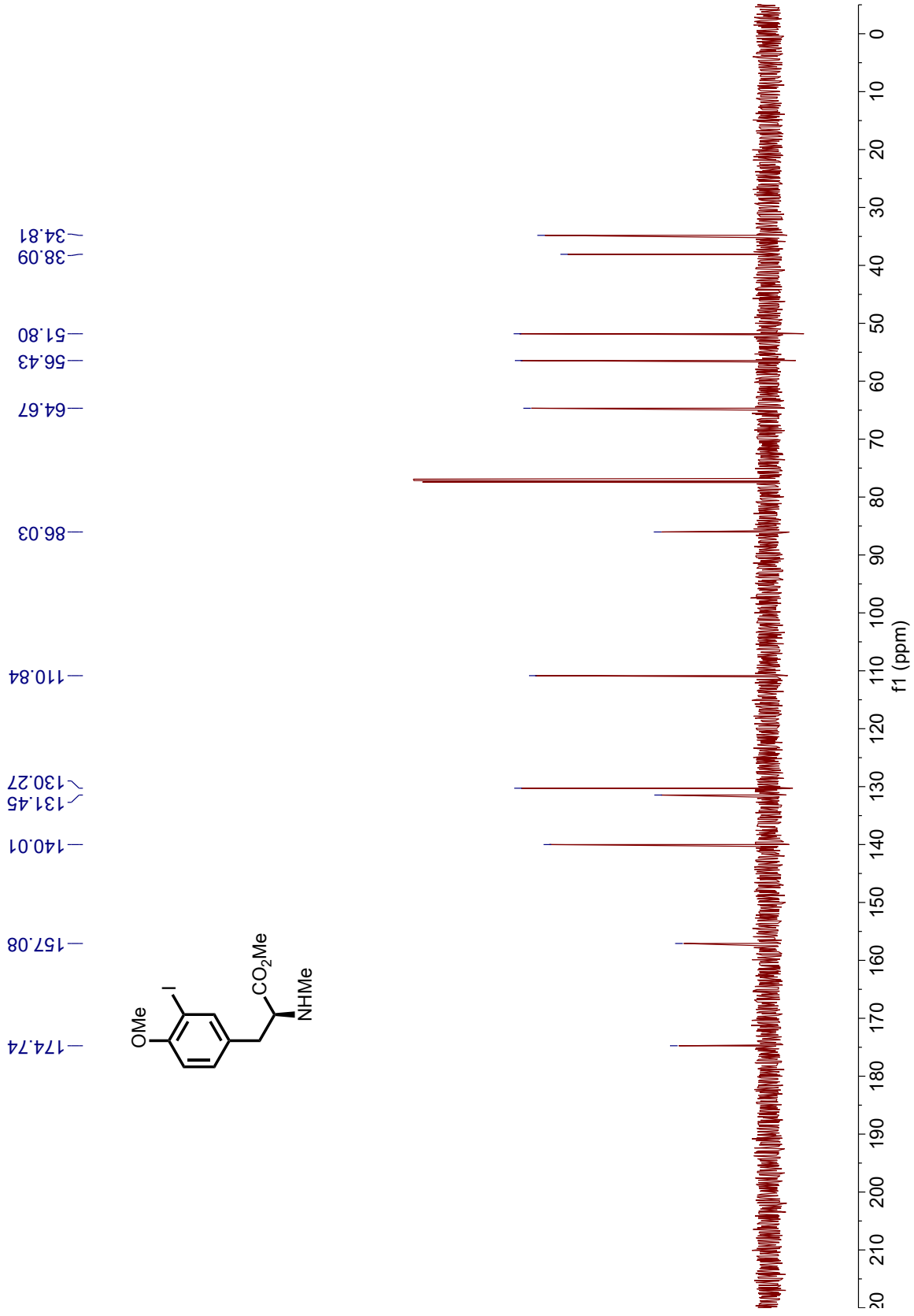
	Natural Herquline B	Synthetic Herquline B	Delta ppm
C4	211.9	212.0	0.1
C4’	209.8	209.9	0.1
C1	138.4	138.3	0.1
C1’	135.7	136.2	0.5
C2’	127.2	126.7	0.5
C2	124.8	124.0	0.8
C8’	59.1	59.4	0.3
C9	53.2	53.2	–
C8	51.6	52.0	0.4
C3’	50.9	50.8	0.1
C3	48.9	48.8	0.1
C9’	44.8	45.7	0.9
11-Me	42.9	42.9	–
C7	41.7	42.2	0.5
C5	39.7	39.6	0.1
C5’	39.4	39.3	0.1
C7’	37.0	37.3	0.3
C6’	33.2	32.9	0.3
C6	30.8	30.7	0.1

II) ^{1}H- and ^{13}C-NMR Spectra

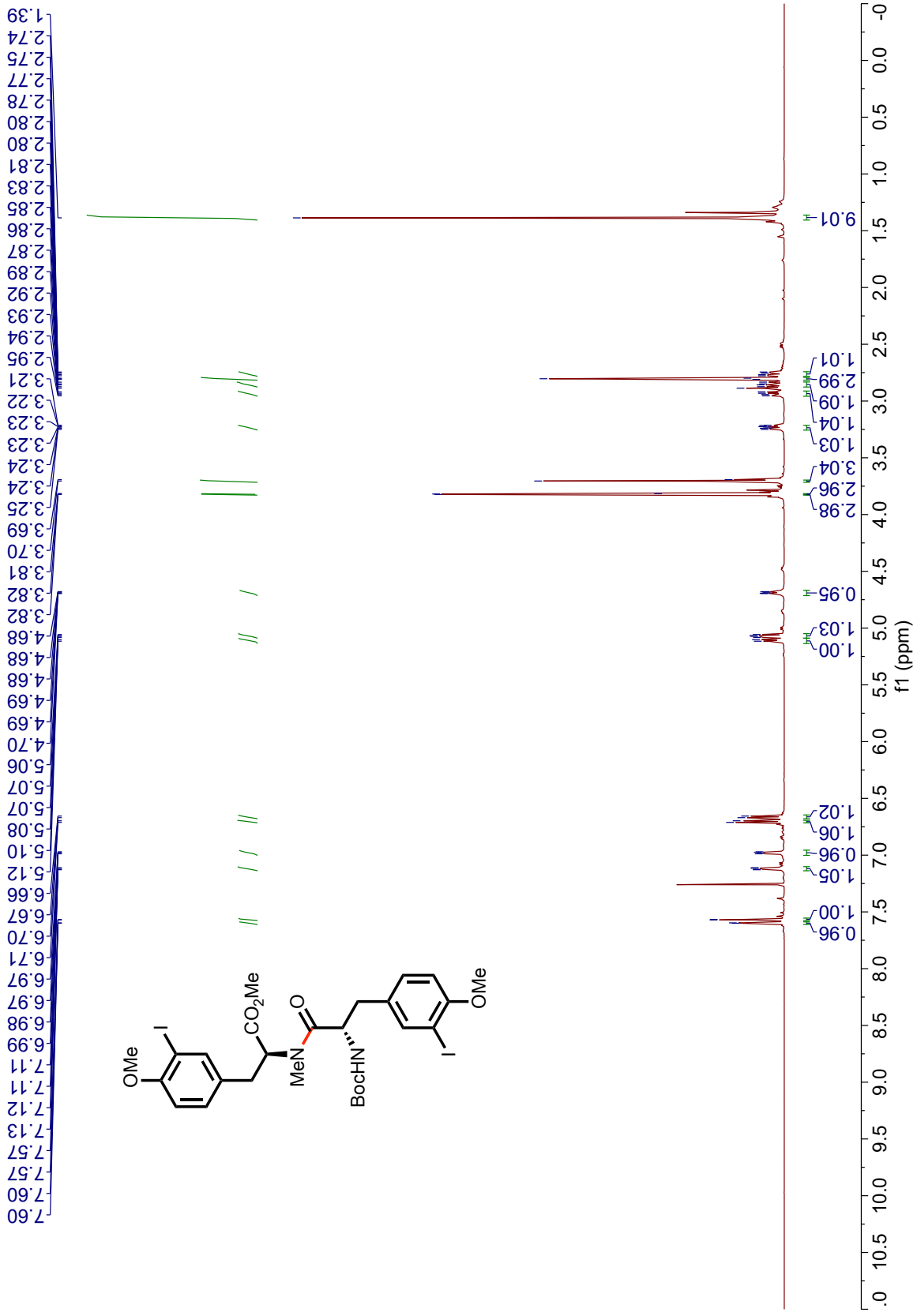
^{1}H NMR of **5**


2.35
2.35
2.35
2.82
2.83
2.84
2.84
3.36
3.37
3.38
3.67
3.67
3.67
3.83
3.83
3.84
3.84
6.71
6.73
7.08
7.09
7.09
7.10
7.10
7.10
7.57
7.57
3.06
2.01
0.99
3.07
3.05
1.00
1.04
1.00
f1 (ppm)
OMe
I
CO2Me
NHMe

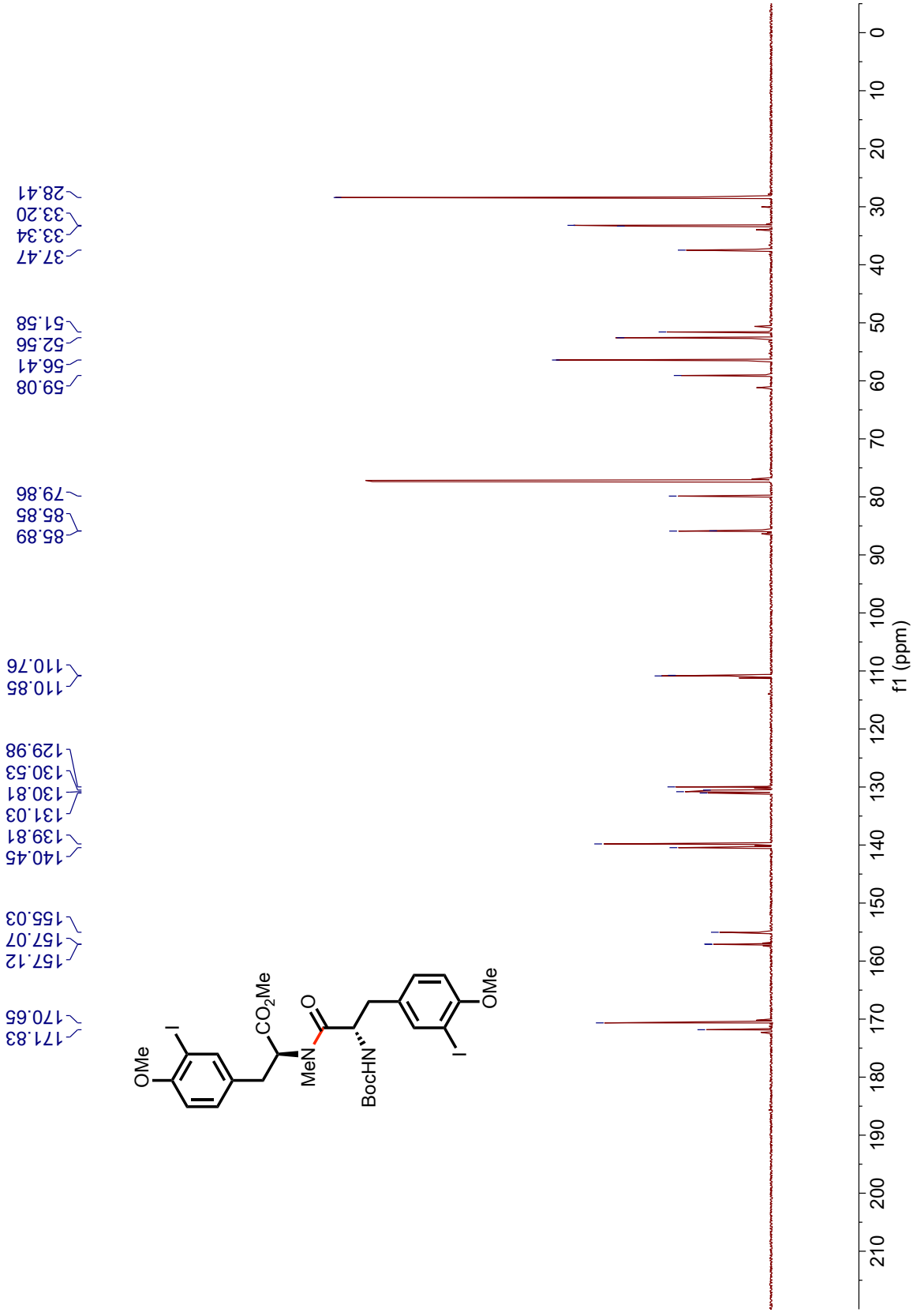
^{13}C NMR of **5**


34.81
38.09
51.80
56.43
64.67
86.03
110.84
130.27
131.45
140.01
157.08
174.74
OMe
I
CO2Me
NHMe
f1 (ppm)

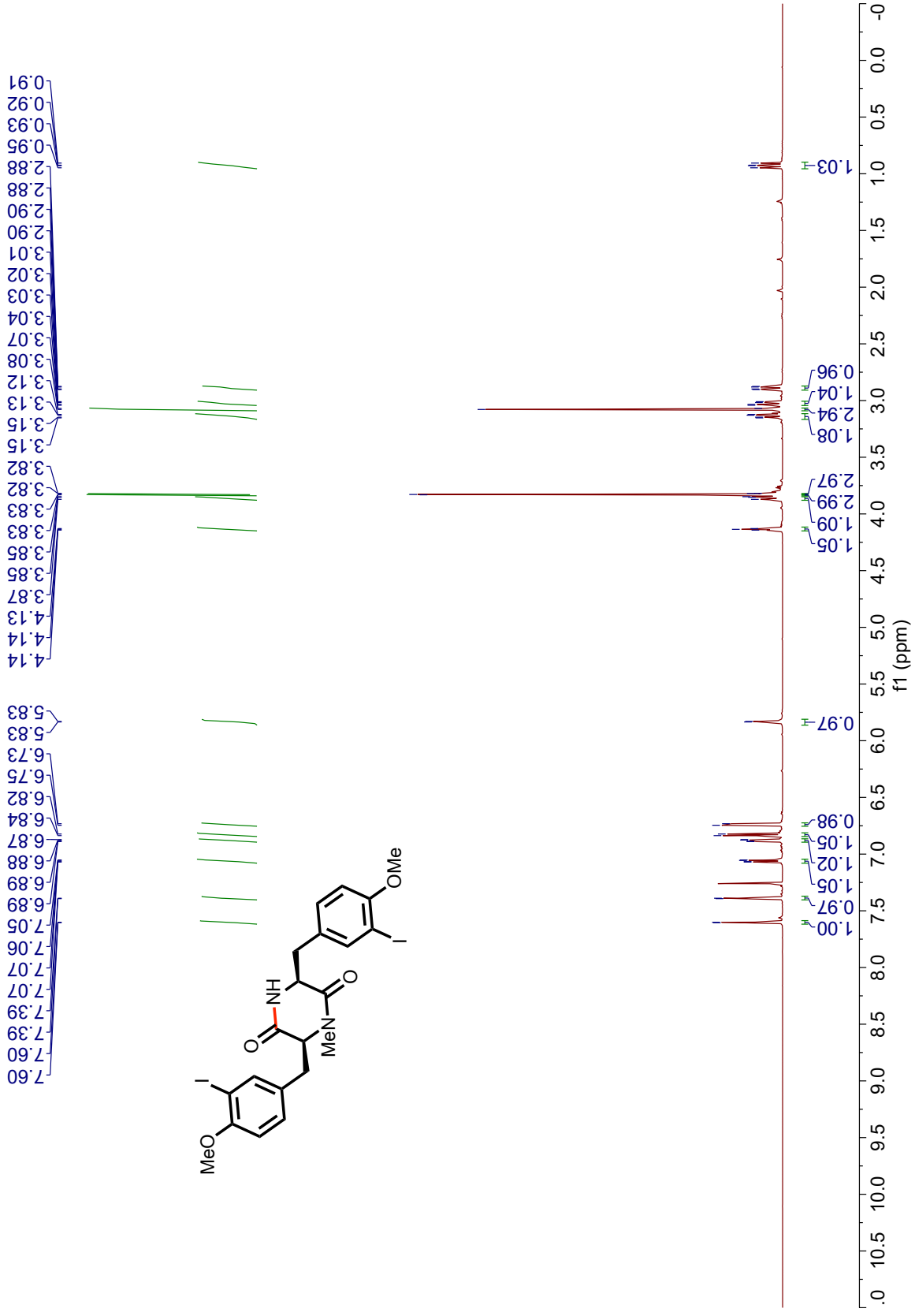
^{1}H NMR of **6**



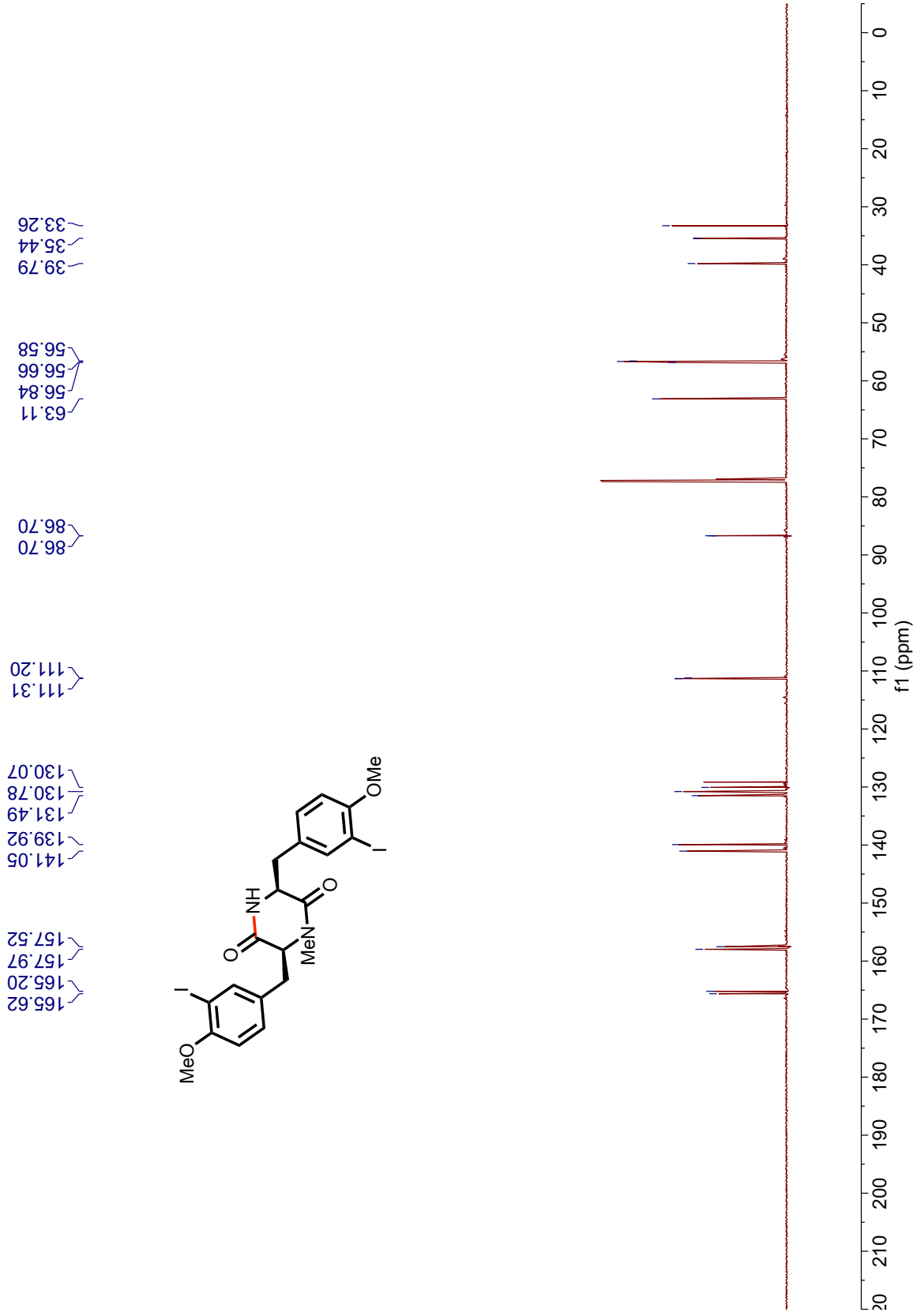
^{13}C NMR of **6**


28.41
33.20
33.34
37.47
51.58
52.56
56.41
59.08
79.86
85.85
85.89
110.76
110.85
129.98
130.53
130.81
131.03
139.81
140.45
155.03
157.07
157.12
170.65
171.83
OMe
I
CO2Me
MeN
O
BocHN
OMe
I
f1 (ppm)

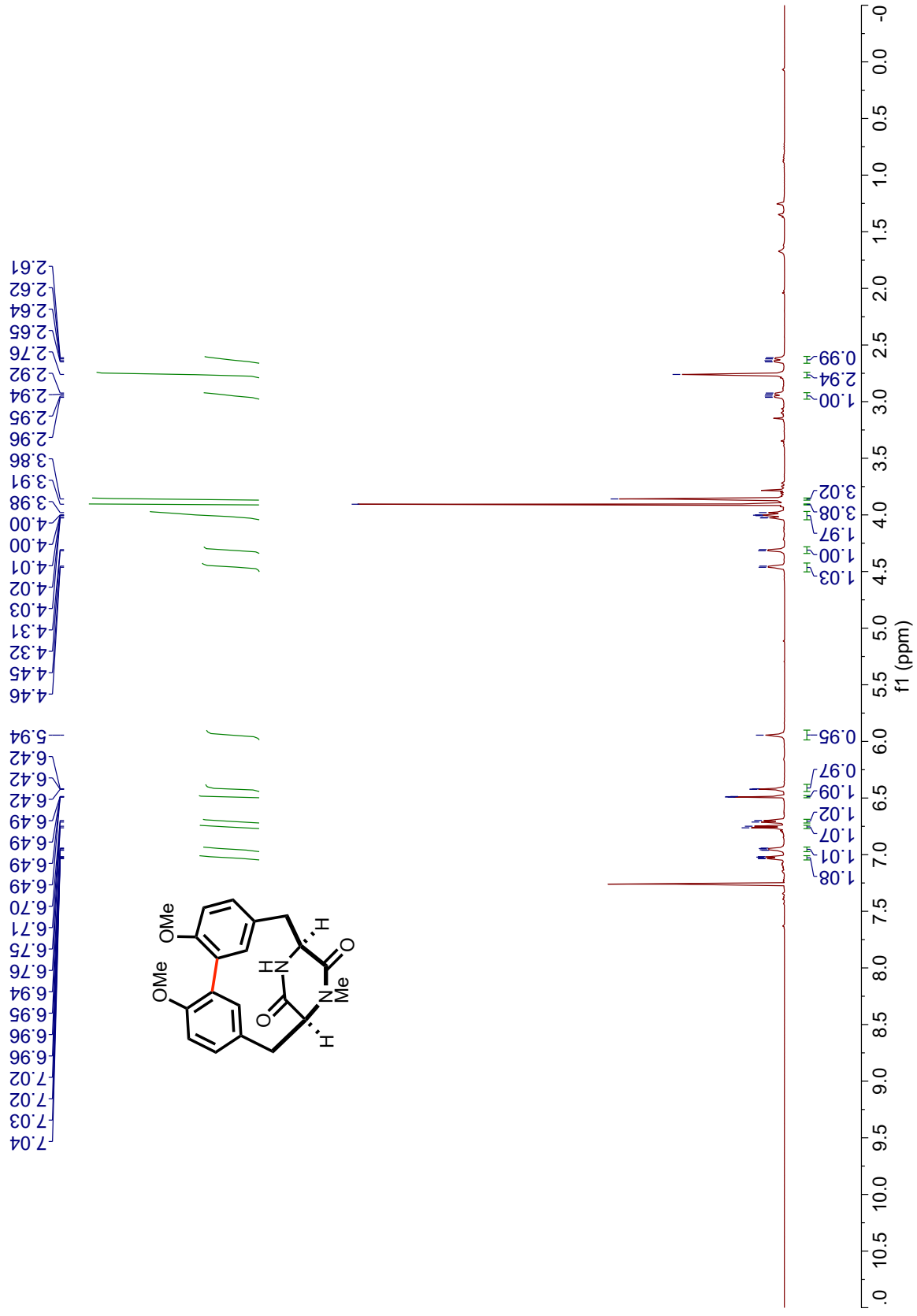
^{1}H NMR of **7**



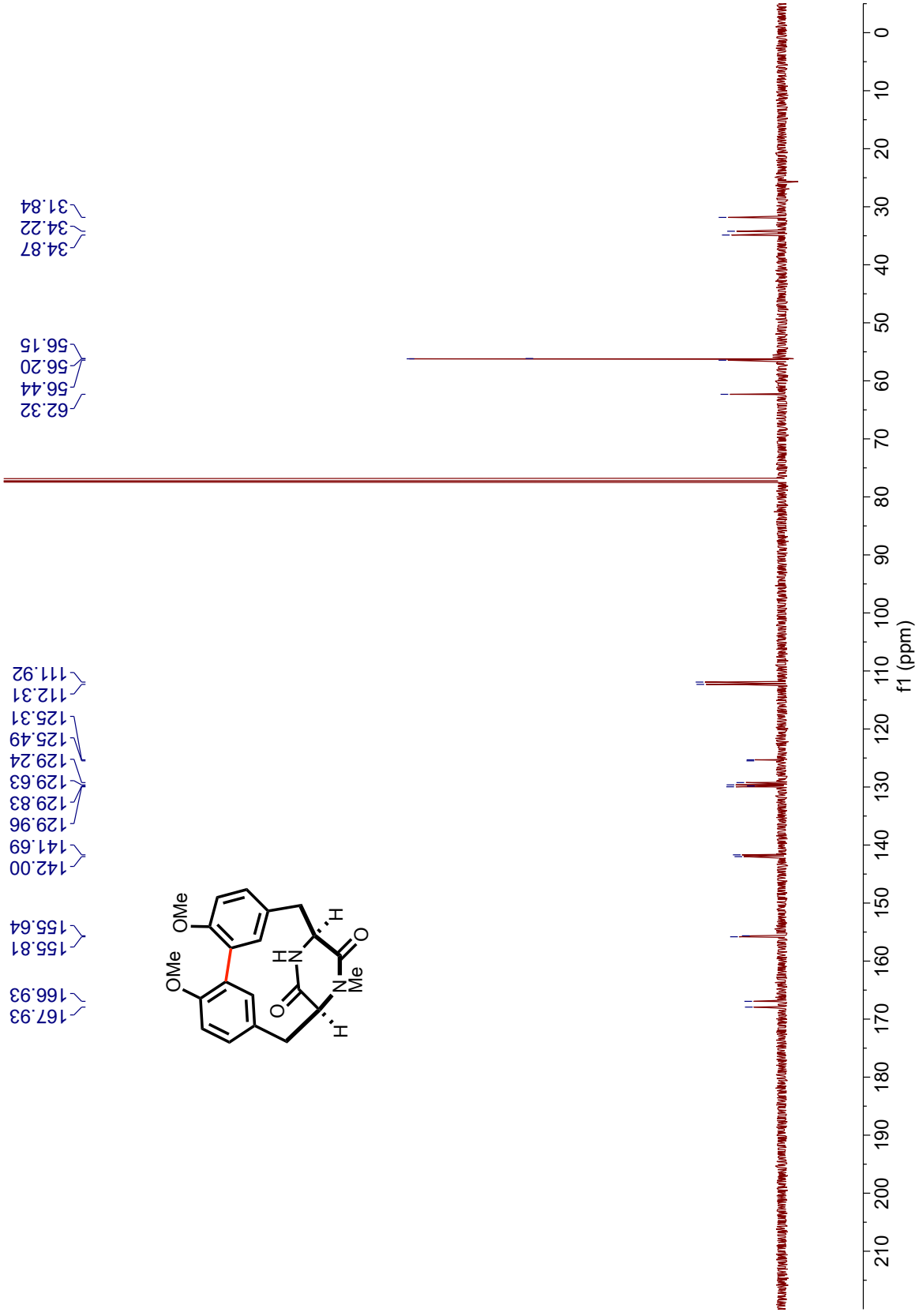
^{13}C NMR of **7**


33.26
35.44
39.79
56.58
56.66
56.84
63.11
86.70
86.70
111.20
111.31
130.07
130.78
131.49
139.92
141.05
157.52
157.97
165.20
165.62
MeO
I
MeN
NH
O
O
OMe
I
f1 (ppm)

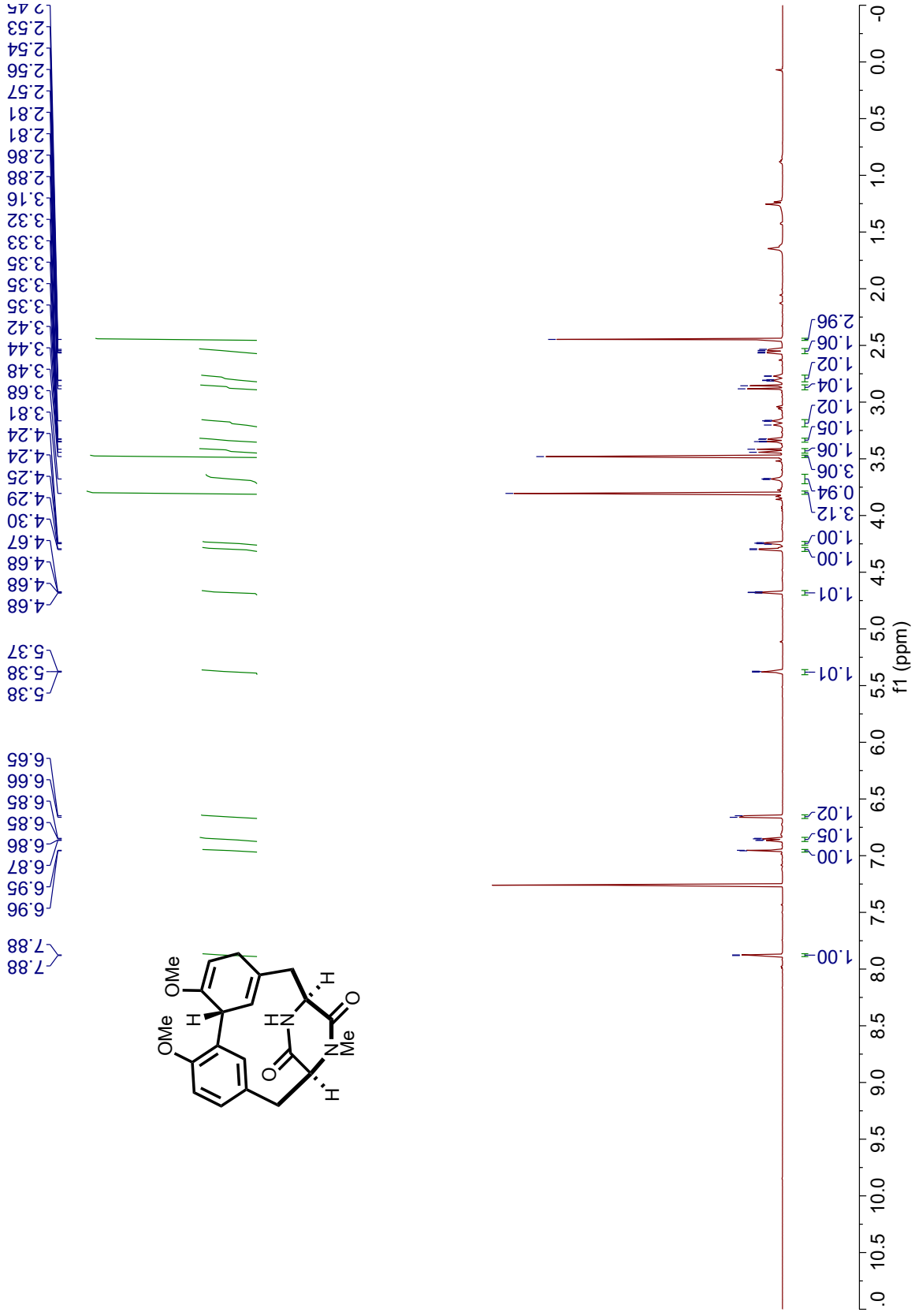
^{1}H NMR of **8**



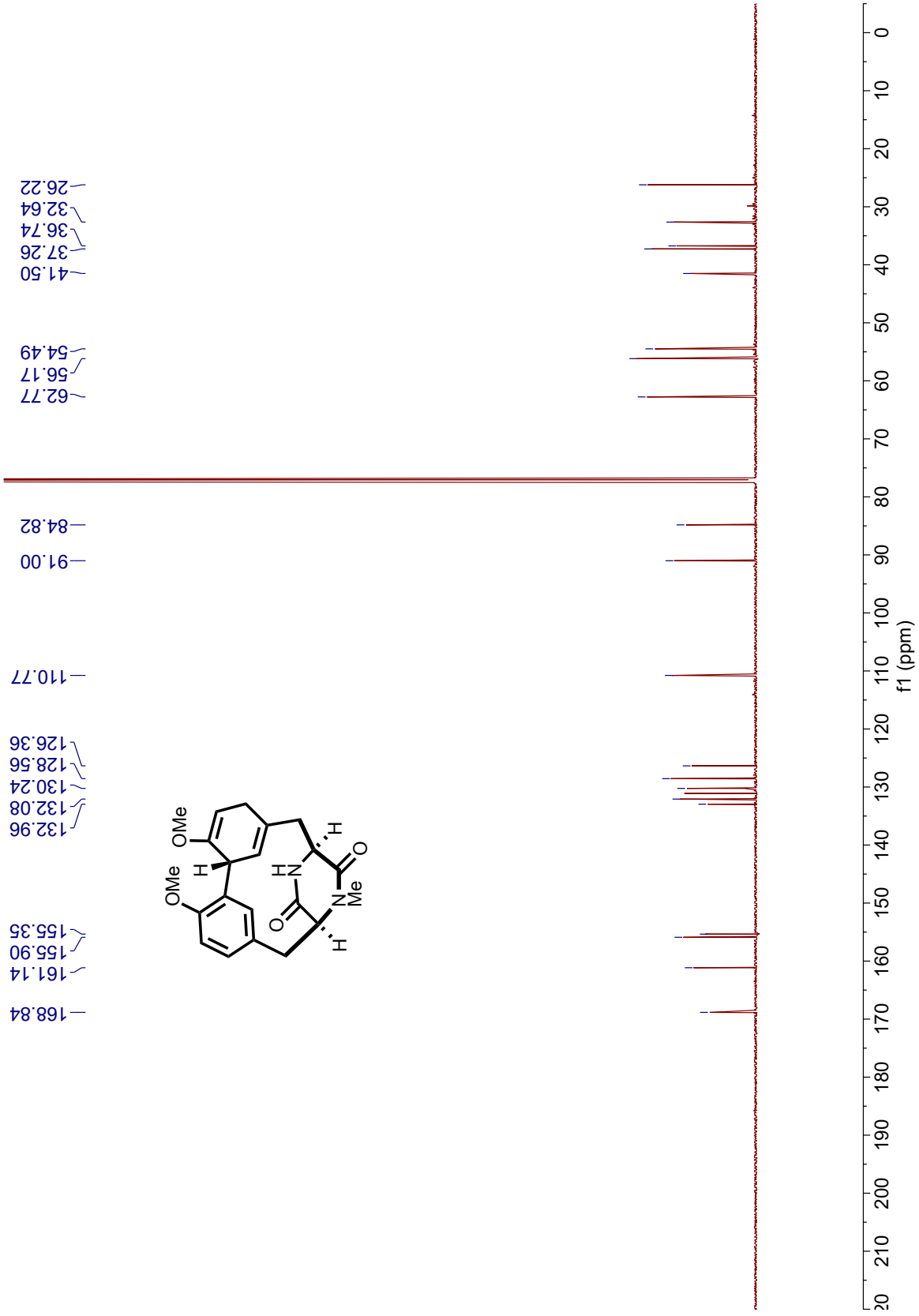
^{13}C NMR of **8**


31.84
34.22
34.87
56.15
56.20
56.44
62.32
111.92
112.31
125.31
125.49
129.24
129.63
129.83
129.96
141.69
142.00
155.64
155.81
166.93
167.93
OMe
OMe
H
O
N
H
O
N
Me
H
f1 (ppm)

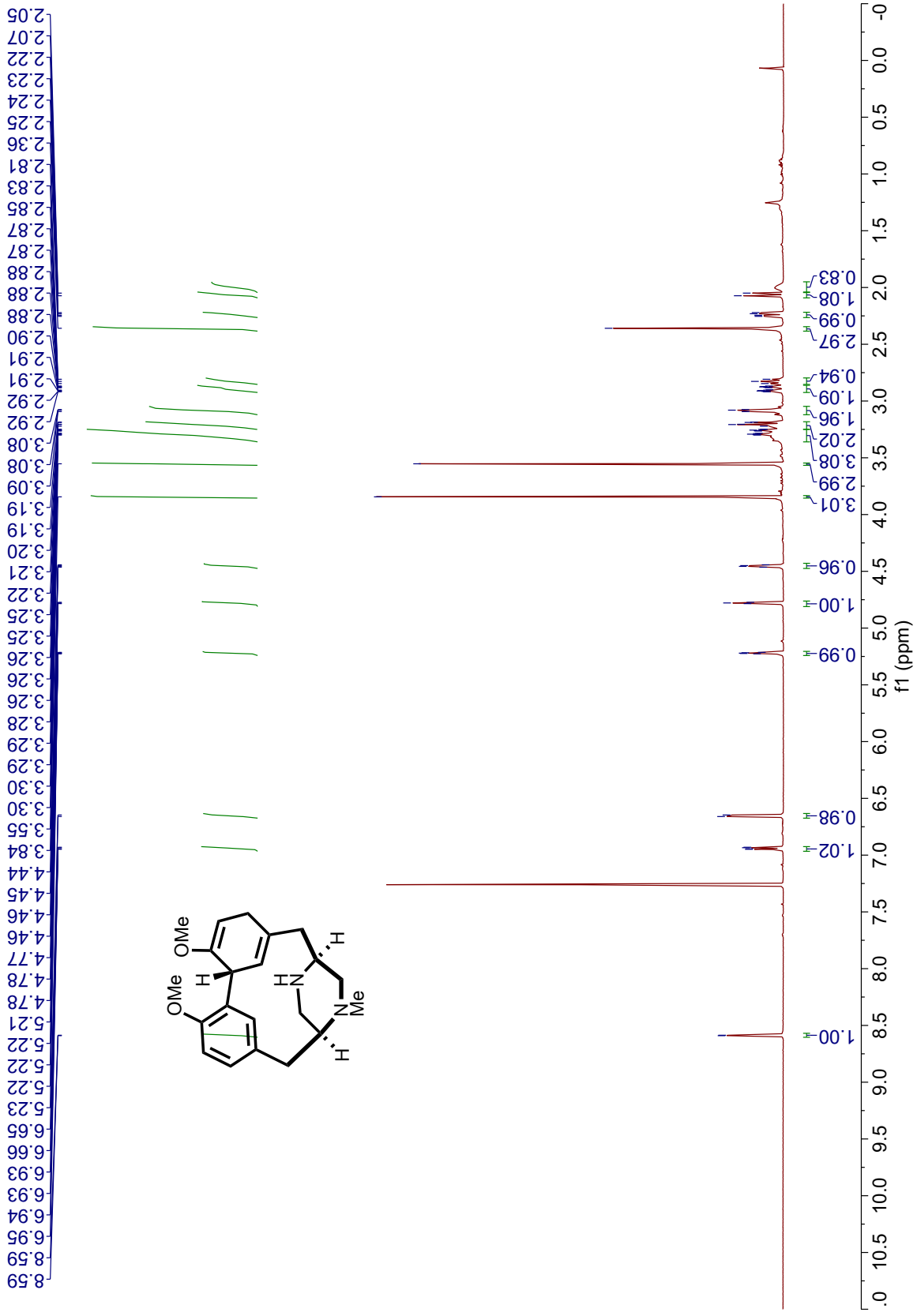
^{1}H NMR of **9**


2.45
2.53
2.54
2.56
2.57
2.81
2.81
2.86
2.88
3.16
3.32
3.33
3.35
3.35
3.35
3.42
3.44
3.48
3.68
3.81
4.24
4.24
4.25
4.29
4.30
4.67
4.68
4.68
4.68
5.37
5.38
5.38
6.65
6.66
6.85
6.85
6.86
6.87
6.95
6.96
7.88
7.88
OMe
OMe
H
H
N
N
Me
O
O
H
H
2.96
1.06
1.02
1.04
1.02
1.05
1.06
3.06
0.94
3.12
1.00
1.00
1.01
1.01
1.02
1.05
1.00
1.00
f1 (ppm)

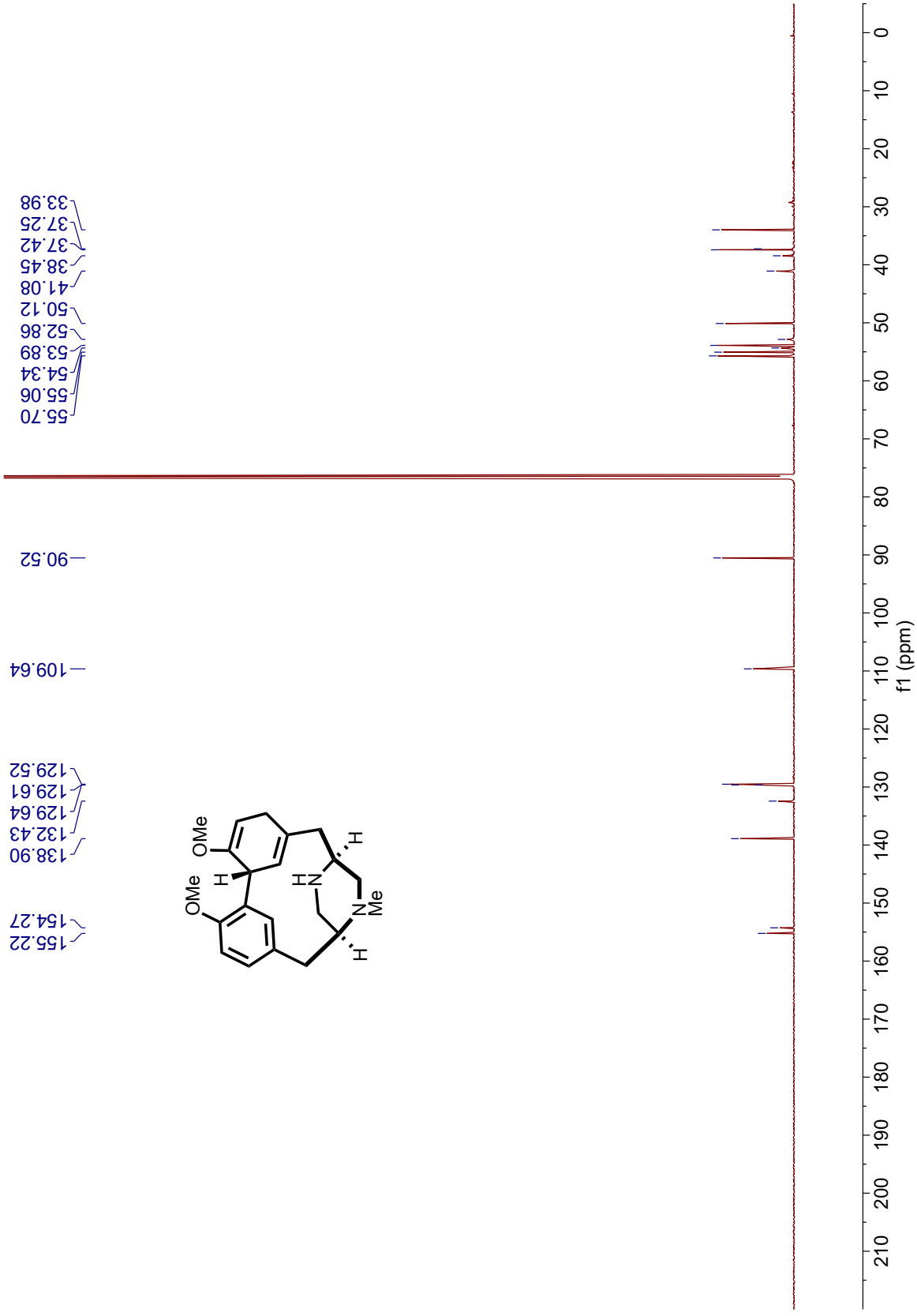
^{13}C NMR of **9**


26.22
32.64
36.74
37.26
41.50
54.49
56.17
62.77
84.82
91.00
110.77
126.36
128.56
130.24
132.08
132.96
155.35
155.90
161.14
168.84
OMe
OMe
H
H
N
N
Me
O
O
H
H
f1 (ppm)

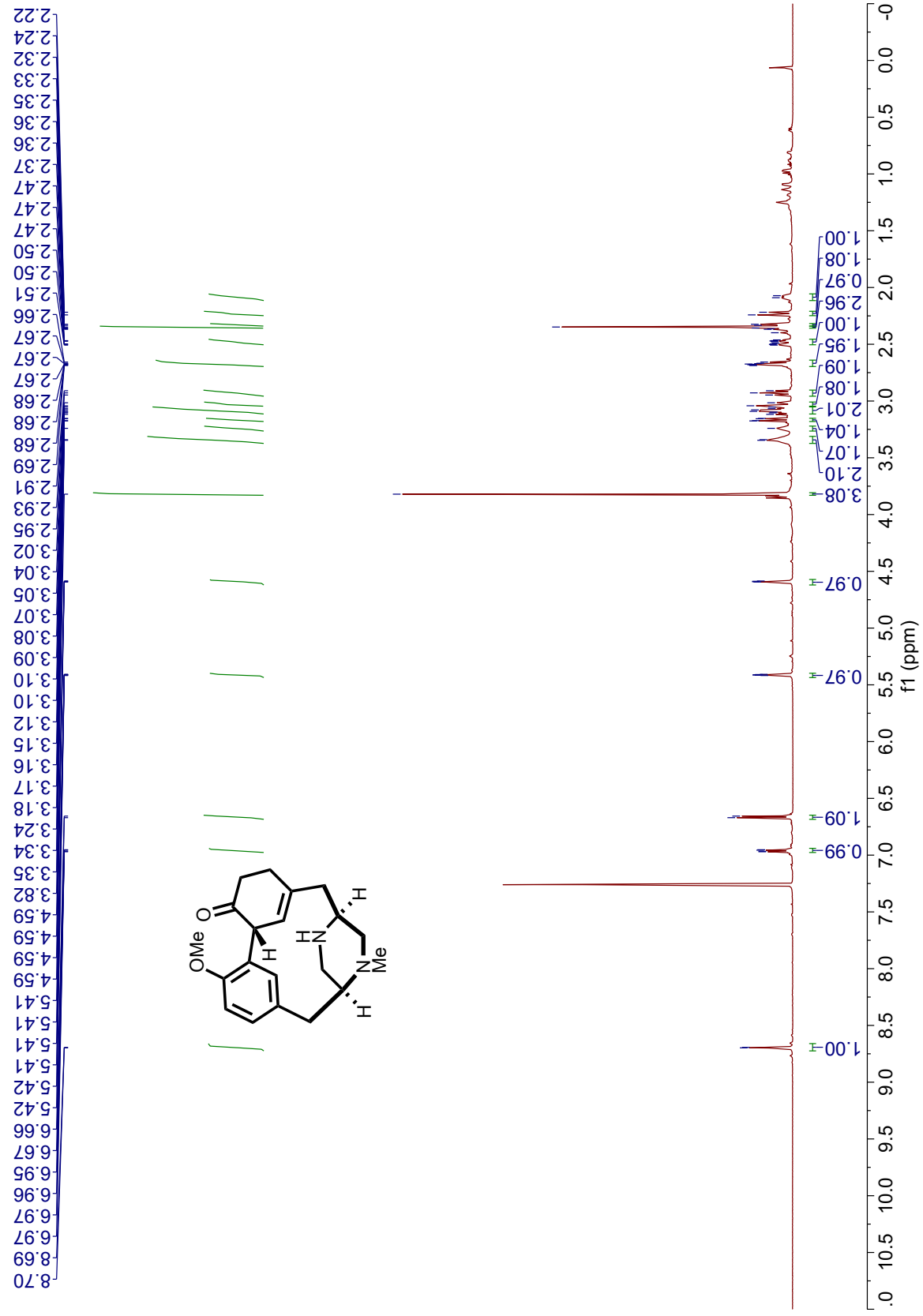
^{1}H NMR of **10**



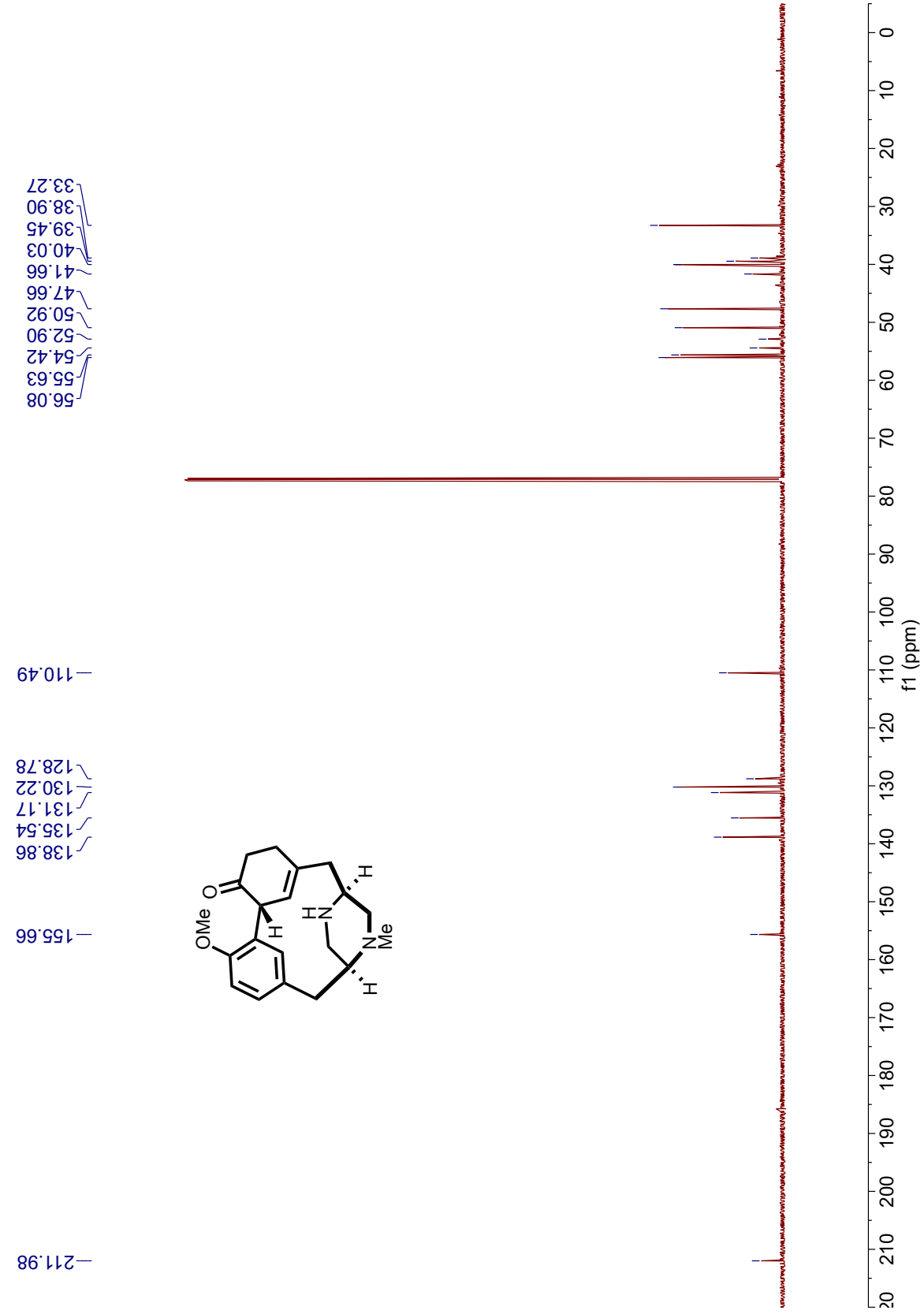
^{13}C NMR of **10**


33.98
37.25
37.42
38.45
41.08
50.12
52.86
53.89
54.34
55.06
55.70
90.52
109.64
129.52
129.61
129.64
132.43
138.90
154.27
155.22
OMe
OMe
H
H
N
Me
H
H
f1 (ppm)

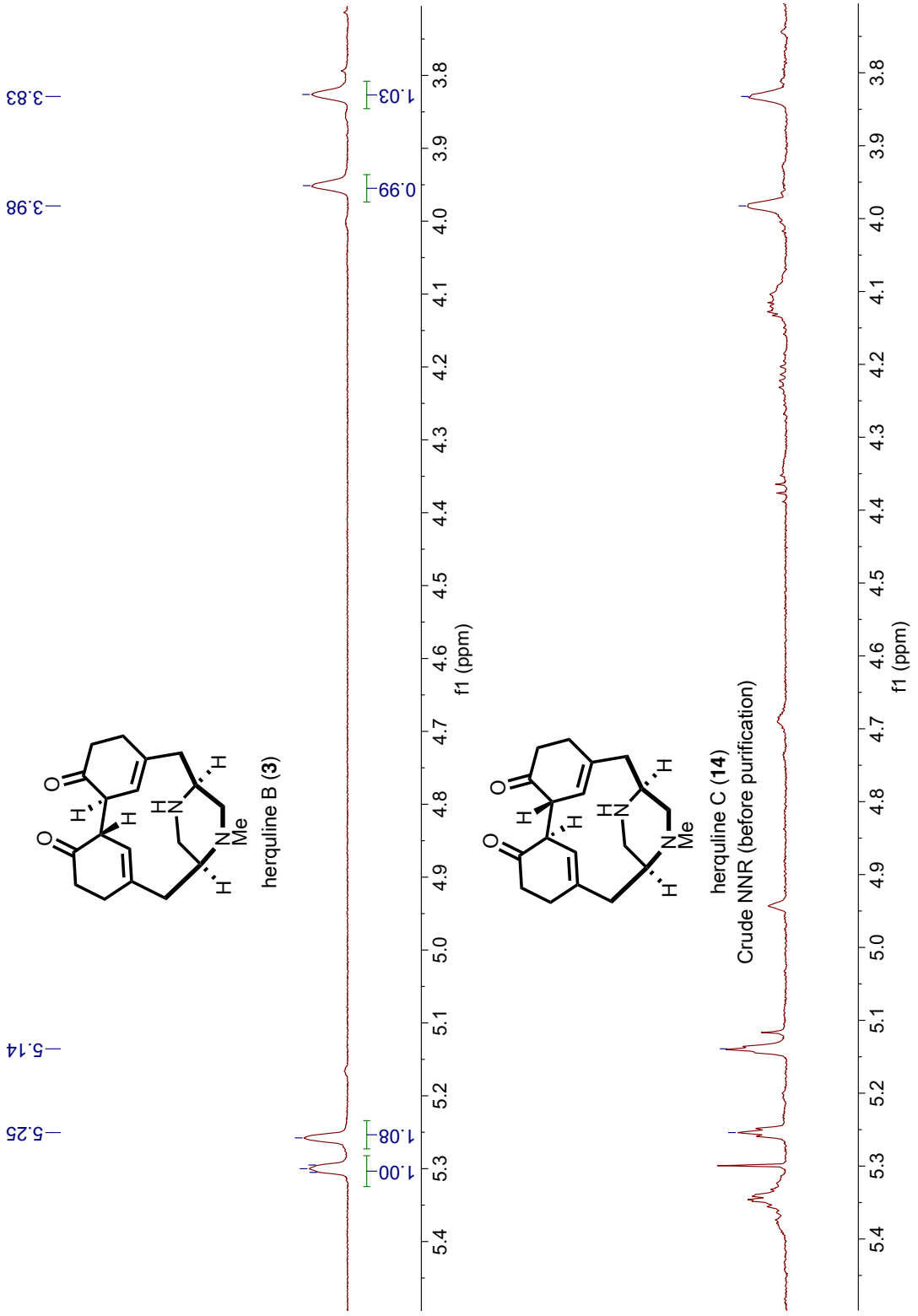
^{1}H NMR of **11**



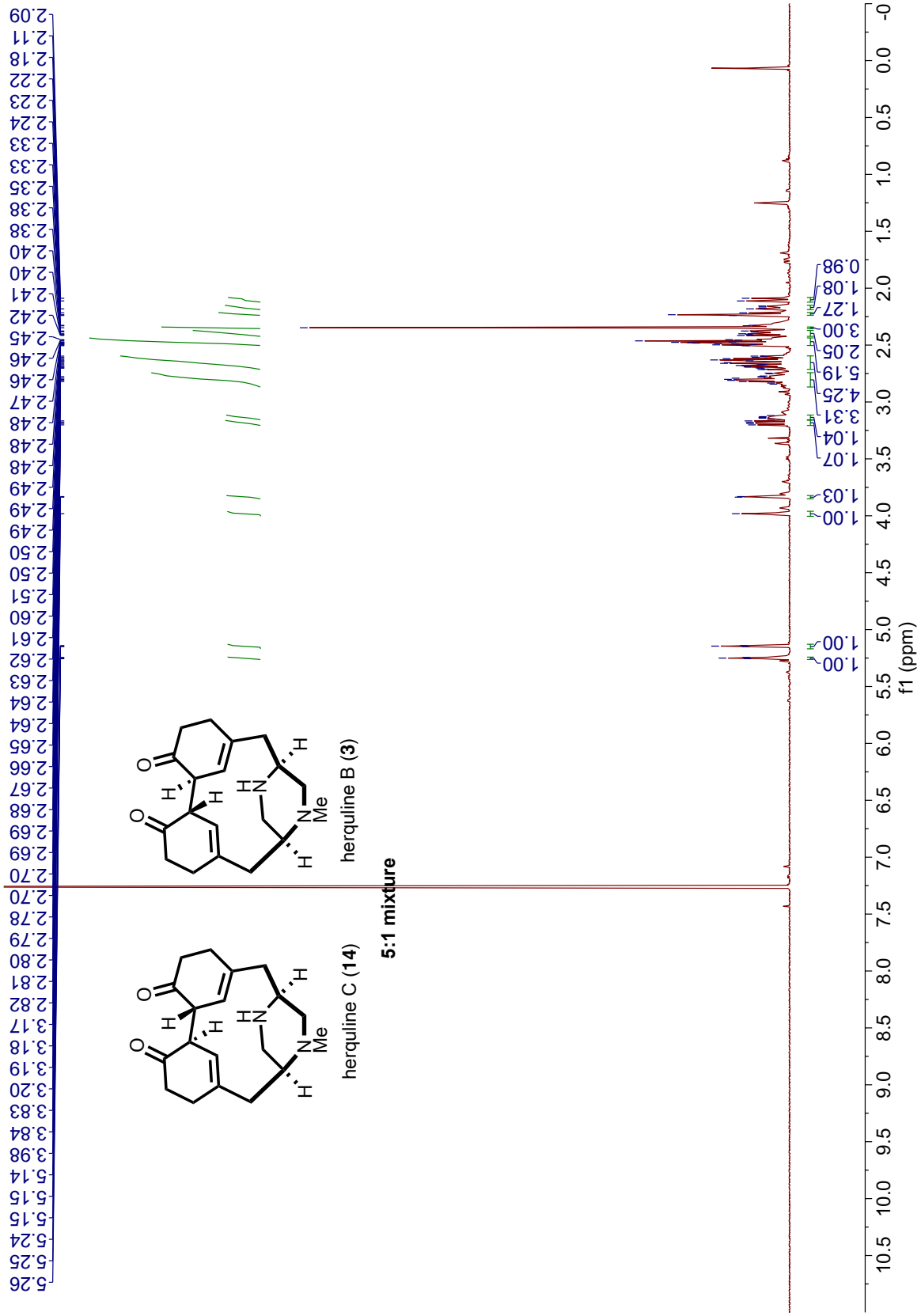
^{13}C NMR of **11**


211.98
155.66
138.86
135.54
131.17
130.22
128.78
110.49
56.08
55.63
54.42
52.90
50.92
47.66
41.66
40.03
39.45
38.90
33.27
OMe
O
H
N
H
N
Me
H
f1 (ppm)

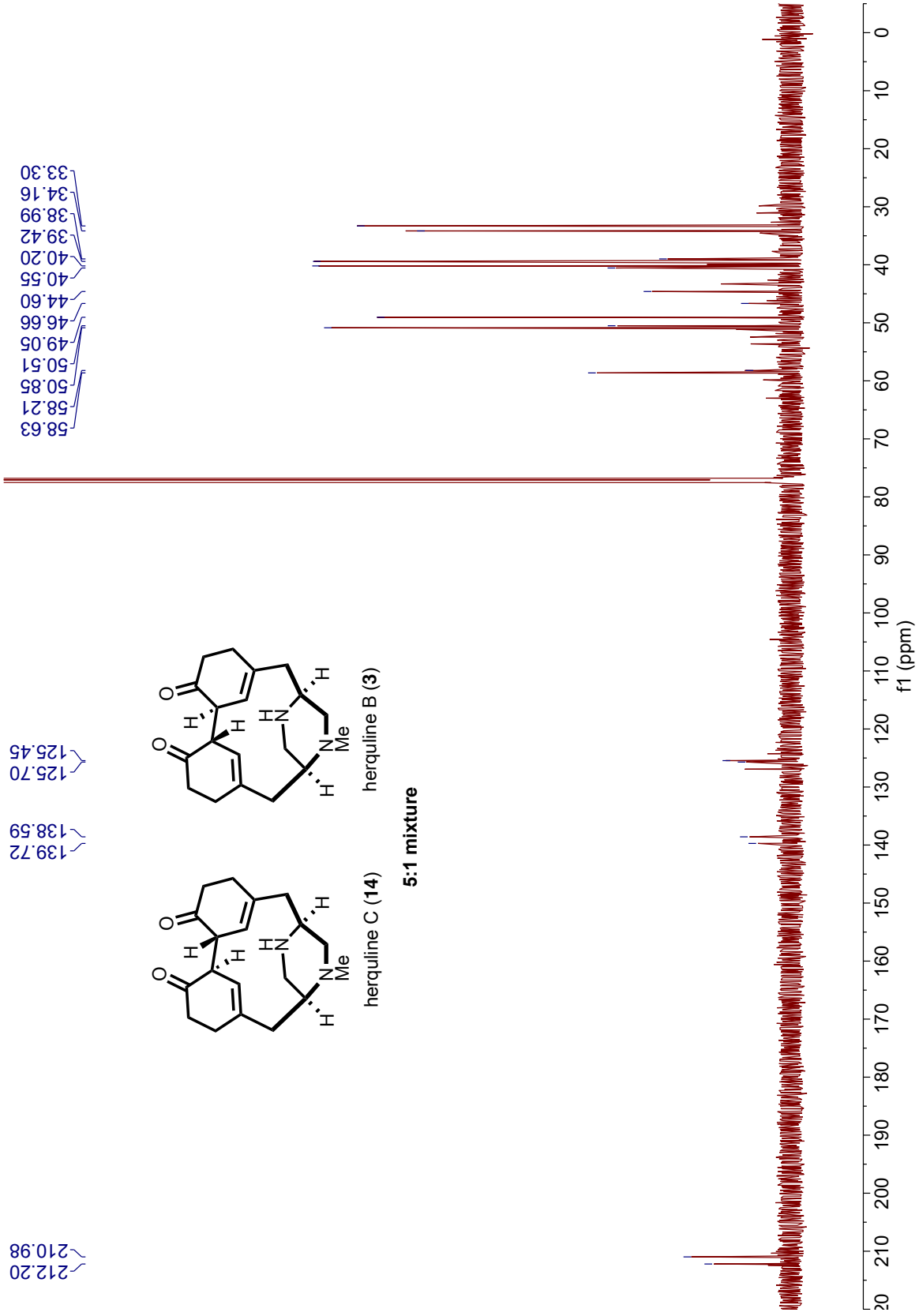
Comparing Herqulin B (**3**) and Crude Herquline C (**14**) from reaction mixture (before purification)



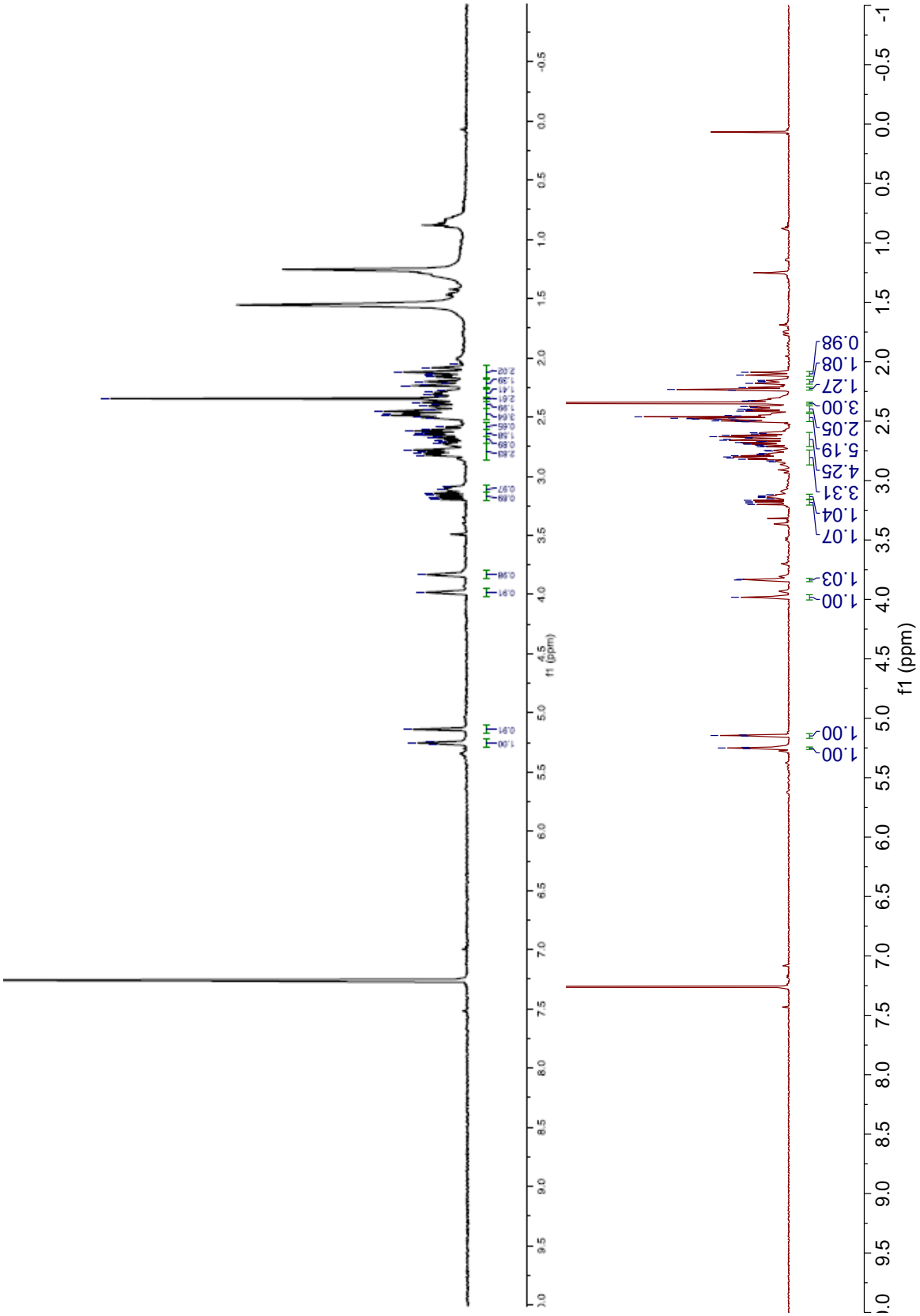
^{1}H NMR of herqulines B (**3**) and C (**14**) (1:5 mixture)



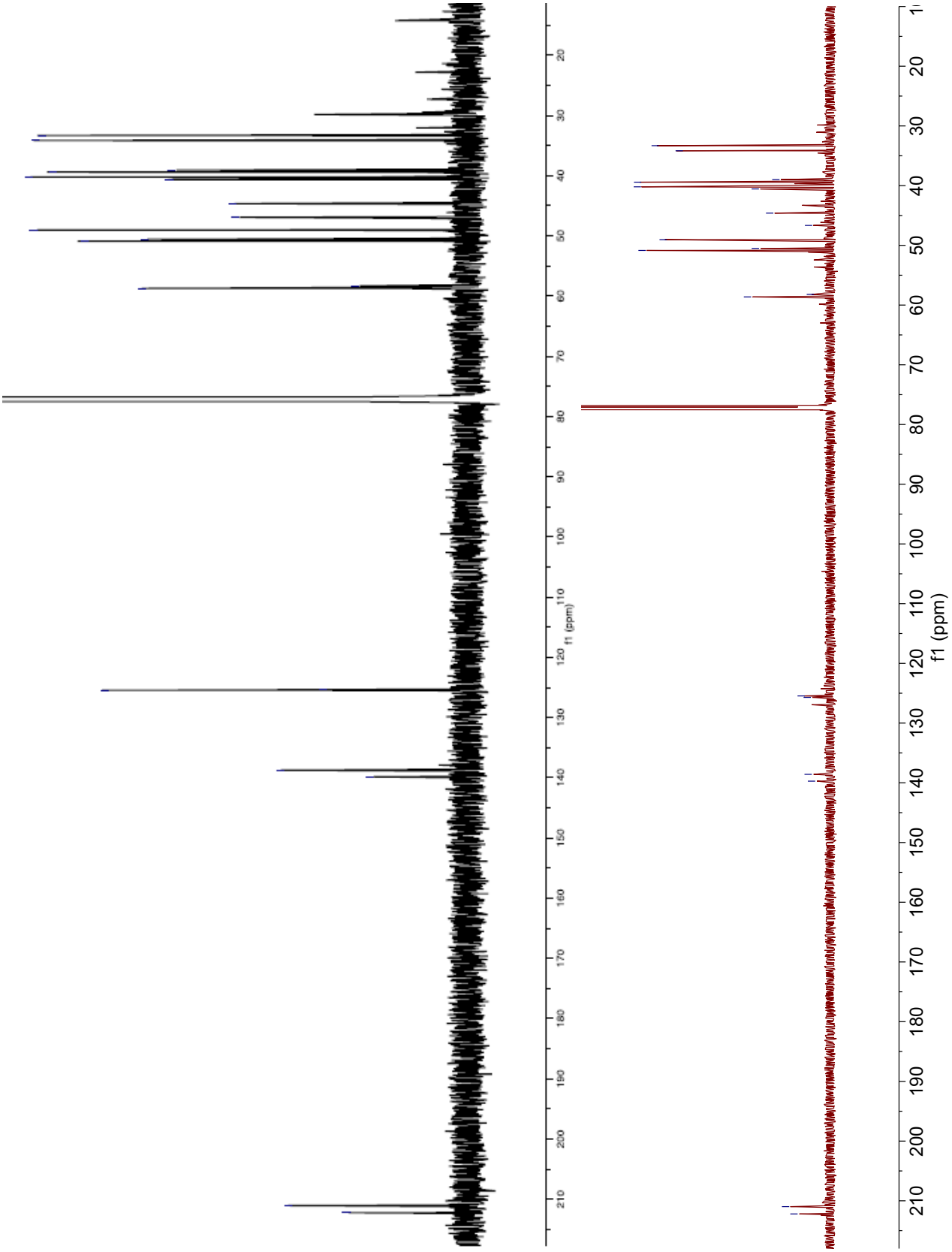
^{13}C NMR of herqulines B (**3**) and C (**14**) (5:1 mixture)



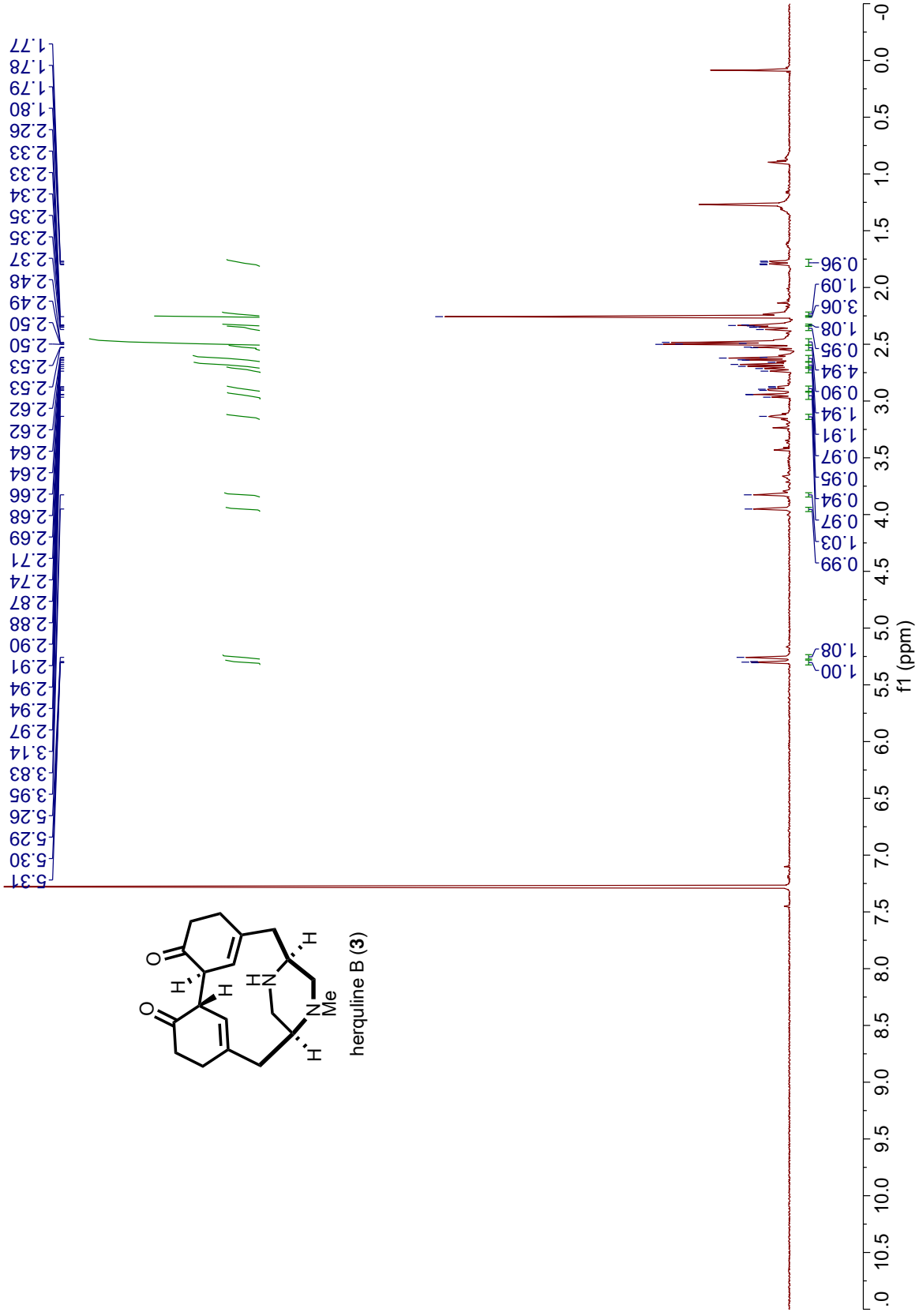
Comparing Synthetic Herquline C (**14**) (Wood[6] and Baran) (^{1}H NMR, 600 MHz, $CDCl_3$)



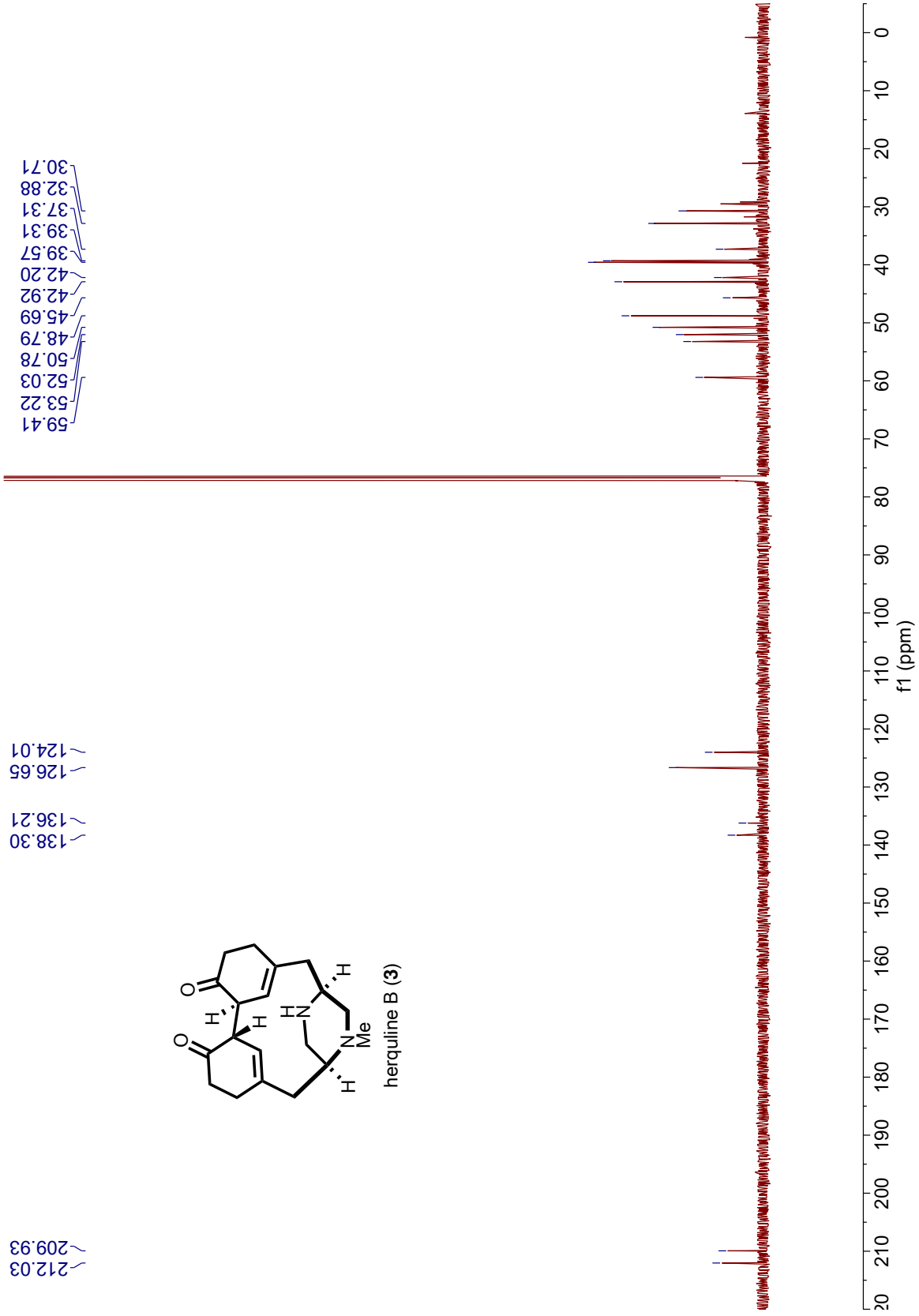
Comparing Synthetic Herquline C (**14**) (Wood[6] and Baran) (^{13}C NMR, 151 MHz, $CDCl_3$)



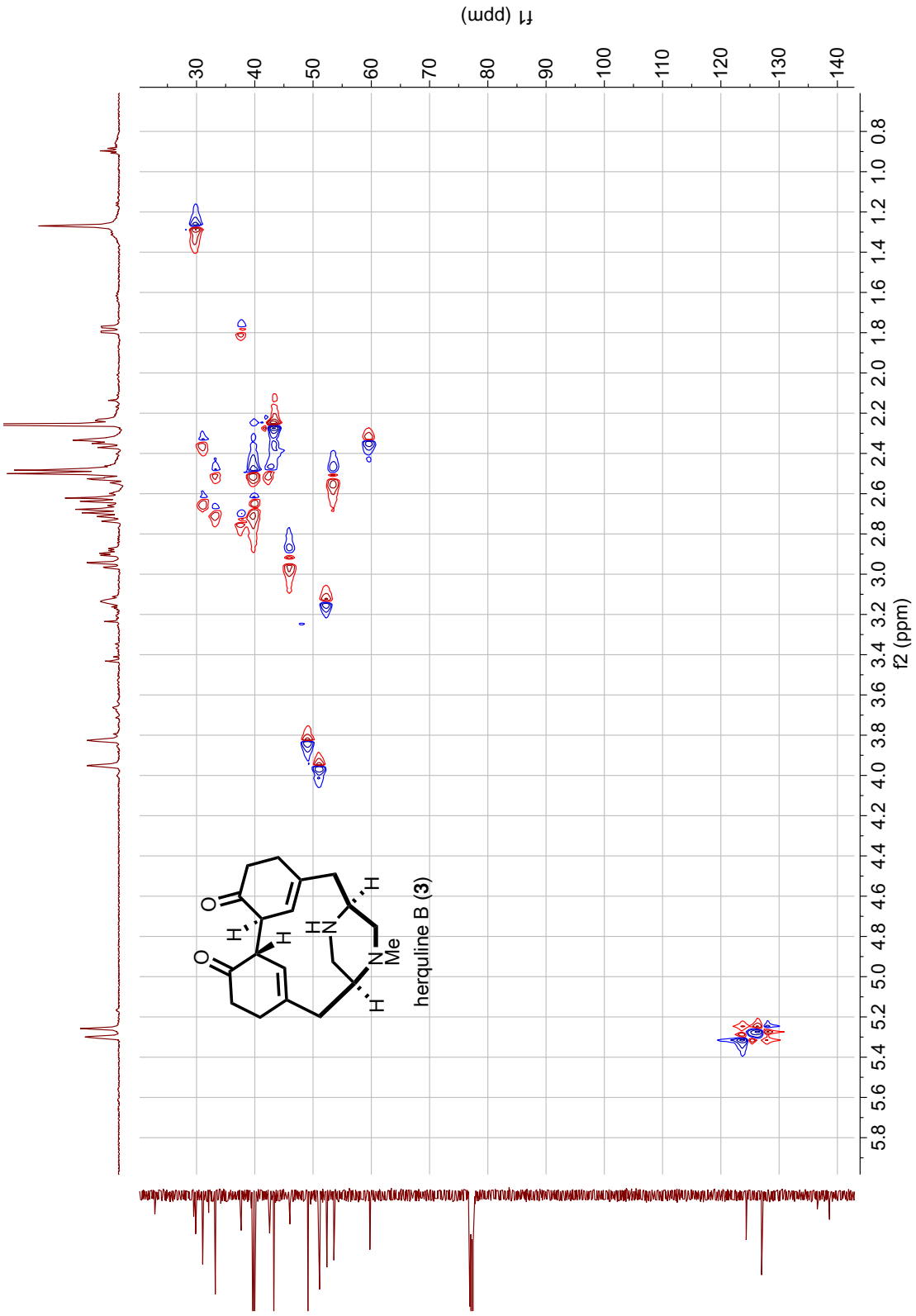
^{1}H NMR of herquline B (**3**)



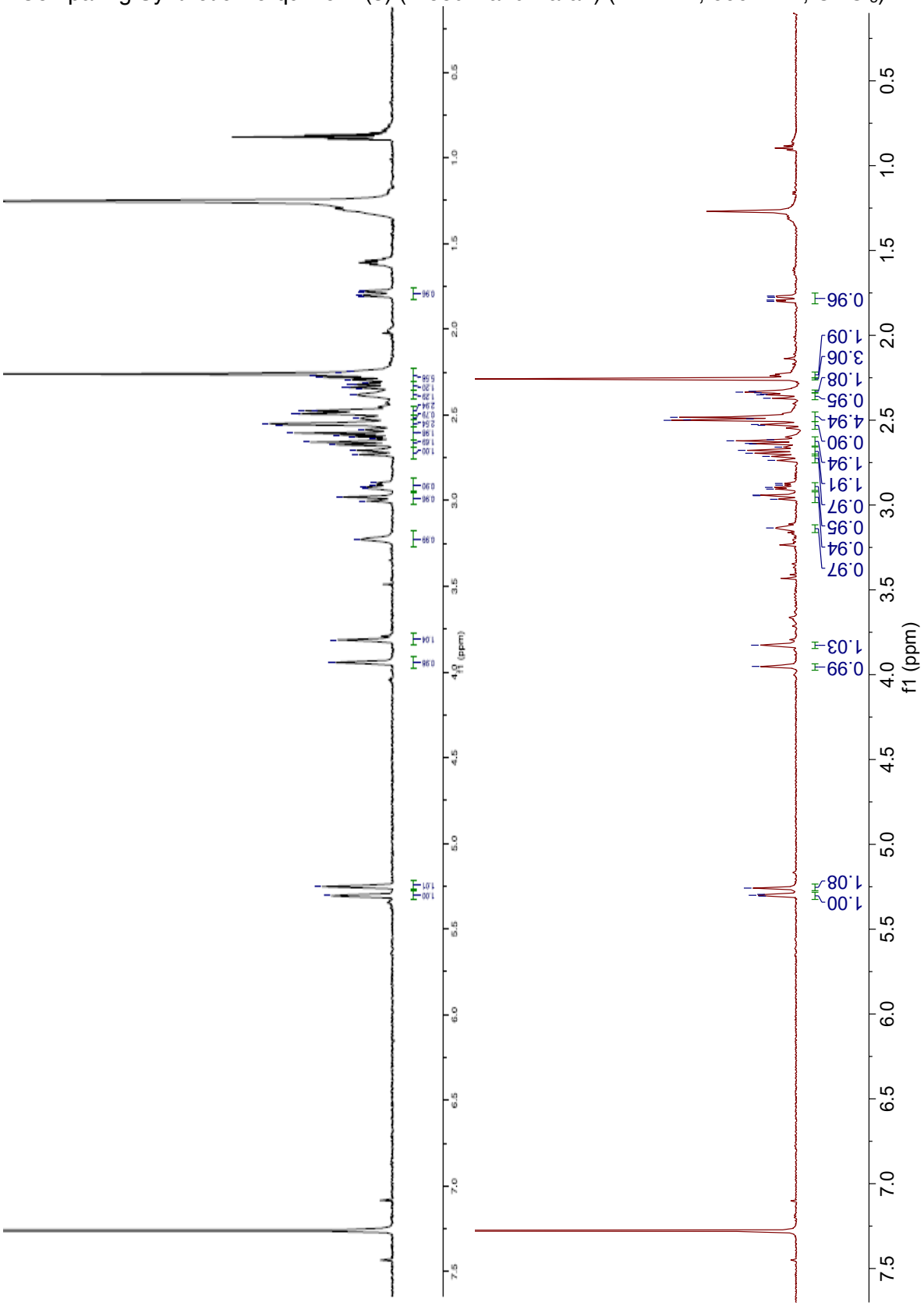
^{13}C NMR of herquline B (**3**)



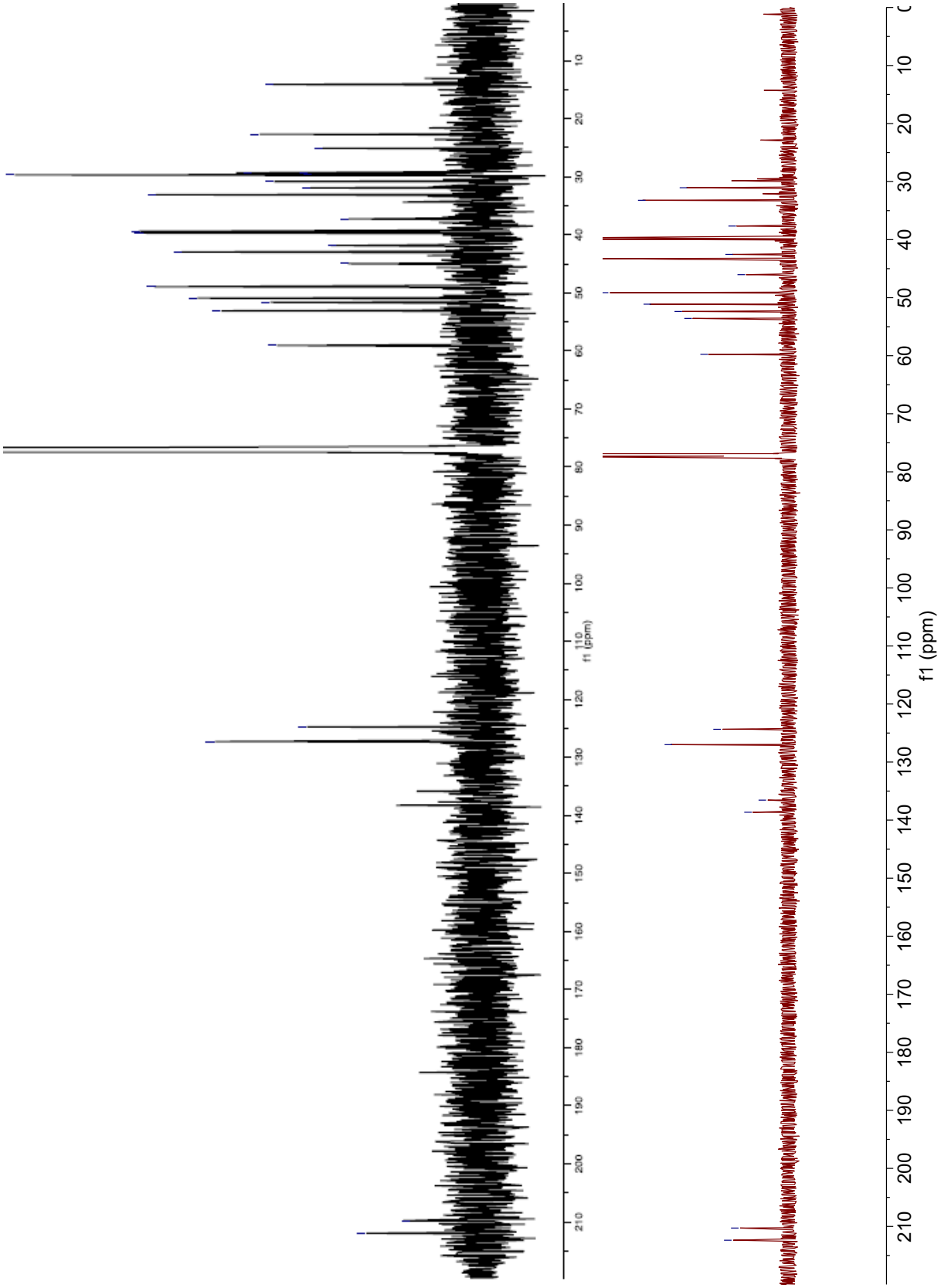
HSQC of herquline B (**3**)



Comparing Synthetic Herquline B (**3**) (Wood[6] and Baran) (^{1}H NMR, 600 MHz, $CDCl_3$)



Comparing Synthetic Herquline B (**3**) (Wood[6] and Baran) (^{13}C NMR, 600 MHz, $CDCl_3$)



III) X-Ray Crystallography Data (compound 11)

The single crystal X-ray diffraction studies were carried out on a Bruker SMART APEX II CCD diffractometer equipped with Cu K_α radiation (λ =1.54178 Å).

Crystals of the subject compound were used as received (grown from CH_2Cl_2 and hexanes).
A 0.240 x 0.040 x 0.040 mm piece of a colorless crystal was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using ϕ and ϖ scans. Crystal-to-detector distance was 40 mm and exposure time was 2, 4 and 8s seconds (depending on the 2θ range) per frame using a scan width of 1.25°. Data collection was 100.0% complete to 67.679° in θ. A total of 29527 reflections were collected covering the indices, -22<=h<=23, -23<=k<=23, -10<=l<=10. 3598 reflections were found to be symmetry independent, with a R_{int} of 0.0326. Indexing and unit cell refinement indicated a **Primitive**, **Hexagonal** lattice. The space group was found to be ***P*6$_5$**. The data were integrated using the Bruker SAINT Software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All carbon bonded hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Crystallographic data are summarized in Table 1.

Notes: Excellent data and refinement

Absolute structure parameter 0.04(6) conclusive

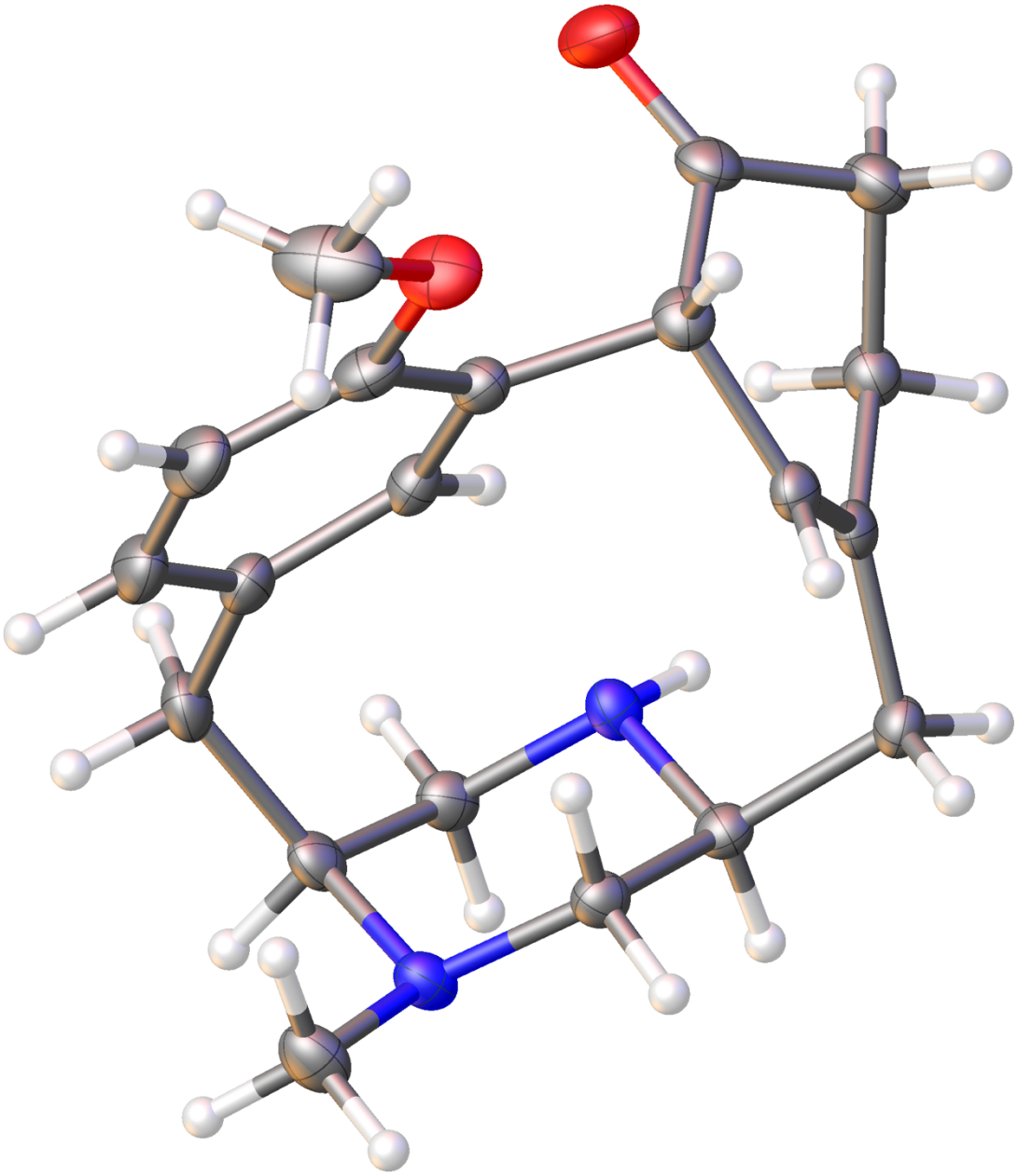


Figure S1. X-ray structure of **11**

Table S1. Crystal data and structure refinement for **11**.

Report date	2018-11-29	
Identification code	baran708_sq	
Empirical formula	C20 H26 N2 O2	
Molecular formula	C20 H26 N2 O2	
Formula weight	326.43	
Temperature	100.0 K	
Wavelength	1.54178 Å	
Crystal system	Hexagonal	
Space group	$P6_5$	
Unit cell dimensions	a = 19.5192(4) Å	α= 90°.
	b = 19.5192(4) Å	β= 90°.
	c = 8.5136(2) Å	γ = 120°.
Volume	2809.10(13) $Å^3$	
Z	6	
Density (calculated)	1.158 Mg/m^3	
Absorption coefficient	0.591 mm^{-1}	
F(000)	1056	
Crystal size	0.24 x 0.04 x 0.04 mm^3	
Crystal color, habit	colorless plank	
Theta range for data collection	2.614 to 71.208°.	
Index ranges	-22<=h<=23, -23<=k<=23, -10<=l<=10	
Reflections collected	29527	
Independent reflections	3598 [R(int) = 0.0326]	
Completeness to theta = 67.679°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7534 and 0.6607	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3598 / 1 / 222	
Goodness-of-fit on F^2	1.036	
Final R indices [I>2sigma(I)]	R1 = 0.0272, wR2 = 0.0716	
R indices (all data)	R1 = 0.0283, wR2 = 0.0726	
Absolute structure parameter	0.04(6)	
Largest diff. peak and hole	0.259 and -0.112 $e.Å^{-3}$	

IV) References:

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