

Supporting Information

Total Synthesis of (-)-Secu'amamine A

Exploiting Type II Anion Relay Chemistry

Heeoon Han and Amos B. Smith, III*

Department of Chemistry,

University of Pennsylvania, Philadelphia, PA 19104, U.S.A.

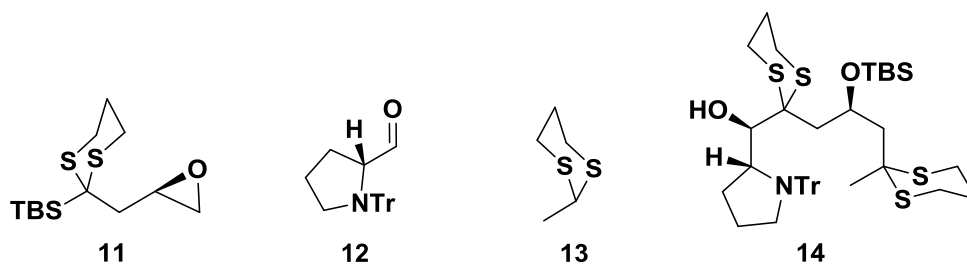
Table of Contents:

-General Methods and Experimental Procedures.....	S1-S9
- ¹ H NMR, ¹³ C NMR Spectra.....	S10-S34
- ¹ H NMR Spectra Comparison	S35
- ¹³ C NMR Spectra Comparison	S36

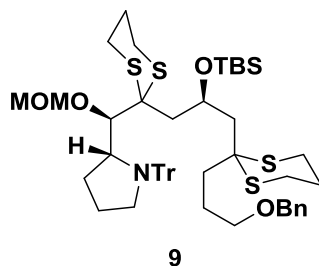
I. Materials and Methods

Reactions were carried out in oven or flame-dried glassware under an argon atmosphere, unless otherwise noted. All solvents were reagent grade. Diethyl ether and THF were obtained from a Pure SolveTM PS-400. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with 0.25 mm E. Merck precoated silica gel plates. In aqueous work-up, all organic solutions were dried over sodium sulfate or magnesium sulfate, and filtered prior to rotary evaporation at water aspirator pressure. Flash chromatography was performed with silica gel 60 (particle size 0.040 – 0.062 mm) supplied by Silicycle and Sorbent Technologies. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. ¹H and ¹³C NMR spectra were recorded on a Bruker AMX-500 spectrometer. Chemical shifts are reported as δ values relative to the internal chloroform (δ 7.26 ppm for ¹H and δ 77.16 ppm for ¹³C). Optical rotations were measured on a Jasco Perkin-Elmer model 241 polarimeter. High resolution mass spectra were measured at the University of Pennsylvania Mass Spectrometry Service Center on either a VG Micromass 70/70 H or VG ZAB-E spectrometer.

II. Experimental Procedures

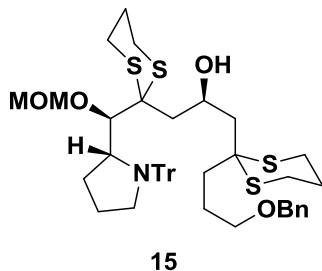


14: To a solution of **13** (0.54g, 4.0mmol) in THF (2.5mL) at -78°C was added 1.0M THF solution of t-BuOK (4.0mL, 4.0mmol) dropwise via syringe and then t-BuLi (2.4mL, 4.0mmol). The resulting solution was stirred for 30 min at -78°C , and a solution of epoxide linchpin **11** (0.98g, 3.4mmol) in THF (3.0mL) was added. The resulting solution was stirred for 30 min at -78°C and then diluted with Et₂O (25mL). To the diluted solution was added aldehyde **12** (1.0g, 3.0mmol) in THF/Et₂O (2.0mL:10mL) via cannula at -78°C . After 30 min, the reaction was quenched with a saturated aqueous NaHCO₃ solution. Then the mixture was extracted with Et₂O (50mL \times 3) and the combined organic layers were washed with brine (100mL), dried over Na₂SO₄, filtered and concentrated in vacuo. Flash chromatography on silica gel (hexane/EtOAc/triethyl amine = 8/2/0.4 to 7/3/0.2) provided **14** (1.4g, 75%) as a pale yellow oil: $[\alpha]_D^{26} = +59.2$ (c 1.60, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 7.61 (d, $J = 7.5$ Hz, 6H), 7.35 – 7.25 (m, 6H), 7.18 – 7.13 (m, 3H), 4.51 – 4.45 (m, 2H), 4.13 – 4.08 (m, 1 H), 3.55 (s, 1H), 3.37 – 3.30 (m, 1H), 3.16 – 3.05 (m, 2H), 3.01 – 2.95 (m, 1H), 2.85 – 2.73 (m, 4H), 2.67 – 2.62 (m, 1H), 2.43 – 2.38 (m, 1H), 2.33 – 2.28 (m, 1H), 2.04 – 1.92 (m, 3H), 1.81 – 1.75 (m, 1H), 1.71 (s, 3H), 1.72 – 1.63 (m, 2H), 0.96 (s, 9H), 0.32 (s, 3 H), 0.23 (s, 3 H), 0.20 – 0.11 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 130.19, 128.06, 127.69, 126.00, 78.78, 77.36, 69.62, 62.57, 56.99, 52.56, 49.77, 48.26, 43.35, 29.51, 27.85, 27.28, 26.82, 26.37, 25.97, 25.73, 25.65, 25.27, 24.98, 18.21, -3.18 , -3.35 ; HRMS (ES) m/z 766.3275 [(M+H)⁺; calcd for C₄₂H₅₉NO₂S₄Si: 766.3276].

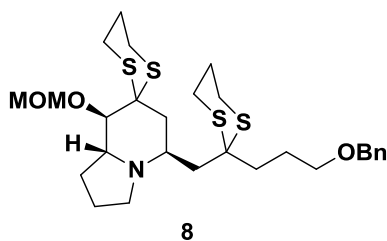


9: To a solution of **10** (1.5g, 5.6mmol) in THF (5.0mL) at -78°C was added 1.0 M THF solution of t-BuOK (0.56mL, 0.56mmol) dropwise via syringe and then 1.7M pentane solution of t-BuLi (3.3mL, 0.56mmol). The resulting solution was stirred for 30 min at -78°C , and a solution of epoxide linchpin **11** (1.3g, 4.3mmol) in THF (4.0mL) was added via cannula. The resulting solution was stirred for 30 min at -78°C and then diluted with Et₂O (60mL). To the diluted solution was added aldehyde **12** (1.9g, 0.56mmol) in THF/Et₂O (5.0mL:25mL) via cannula at -78°C . After 30 min, MOMBr (0.53mL, 6.5mmol) in THF (10mL) was added and the resulting solution was warmed to 0°C for 2h. The reaction was quenched with a saturated aqueous NaHCO₃ solution. Then the mixture was extracted with Et₂O (50mL \times 3) and the combined organic layers were washed with brine (100mL), dried over Na₂SO₄, filtered and concentrated in vacuo. Flash chromatography on silica gel (hexane/EtOAc/triethyl amine = 20/1/0.4 to 8/2/0.2) provided **2.36** (2.6g, 64%) as a pale yellow oil: $[\alpha]_D^{25} = 8.74$ (c 2.00, CH₂Cl₂); ¹H NMR (500MHz, CDCl₃) δ 7.61 (br. s., 6 H), 7.31 (d, $J = 4.6$ Hz, 4 H), 7.29 – 7.22 (m, 7H), 7.18 – 7.09 (m, 3H), 5.63 (d, $J = 5.7$ Hz, 1H), 5.12 (d, $J = 5.9$ Hz, 1H), 4.75 (s, 1 H), 4.49 (t, $J=9.51$ Hz, 1H), 4.47 (s, 2H), 4.41 (t, $J = 7.7$ Hz, 1H), 3.66 (s, 2 H), 3.51 – 3.45 (m, 1 H), 3.44 (t, $J=6.3$ Hz, 2H), 3.19 (d, $J = 14.1$ Hz, 1H), 3.16 – 3.08 (m, 1H), 3.08 – 3.02 (m, 2 H), 2.99 – 2.90 (m, 1H), 2.72 (br. s., 1H), 2.70 – 2.64 (m, 1H), 2.59 – 2.52 (m, 1H), 2.49 – 2.43 (m, 1H), 2.40 (dd, $J = 15, 2.3$ Hz, 1H), 2.08 – 1.95 (m, 3H), 1.95 – 1.85 (m, 3H), 1.85 – 1.78(m, 2H), 1.75 (dd, $J = 9.5, 15.1$ Hz, 1H), 1.72 – 1.62 (m, 2H), 1.58 – 1.52 (m, 2H), 1.52 – 1.46 (m, 1H), 1.43 (dd, $J = 9.9, 14.8$ Hz, 1H), 1.18 – 1.13 (m, 2H), 1.01 – 0.93

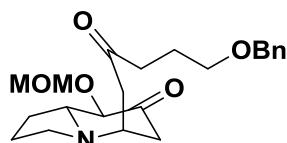
(m, 1H), 0.82 (m, 9H), 0.15 (s, 3 H), 0.09 (s, 3 H), $-0.13 - -0.25$ (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.89, 130.34, 128.39, 128.06, 127.88, 127.74, 127.45, 126.13, 98.80, 80.94, 79.10, 72.75, 70.66, 69.87, 62.78, 57.60, 55.44, 54.07, 52.57, 46.29, 43.79, 36.95, 27.51, 26.76, 26.61, 26.26, 25.77, 25.50, 25.35, 24.84, 24.69, 24.52, 18.15, -2.97 , -3.90 ; HRMS (ES) m/z 944.4267 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{53}\text{H}_{73}\text{NO}_4\text{S}_4\text{Si}$: 944.4270].



15: A solution of **9** (0.50g, 0.53mmol) in THF was treated with a 1.0 M solution of TBAF in THF (0.79mL, 0.79mmol) and stirred at reflux for 12 h. The reaction mixture was concentrated in vacuo and flash chromatography on silica gel (hexane/EtOAc/triethylamine = 20/1/0.4 to 8/2/0.2) provided alcohol **15** (0.40g, 91%) as a pale yellow oil: $[\alpha]_D^{26} = +29.0$ (c 2.00, CH_2Cl_2); ^1H NMR (500MHz, CDCl_3) δ = 7.57 (d, $J = 7.3$ Hz, 6 H), 7.35 – 7.30 (m, 4 H), 7.30 – 7.23 (m, 7 H), 7.18 – 7.12 (m, 3 H), 5.57 (d, $J = 5.5$ Hz, 1 H), 5.19 (d, $J = 5.5$ Hz, 1 H), 4.76 (d, $J = 1.4$ Hz, 1 H), 4.50 (s, 2 H), 4.43 (td, $J = 8.3, 1.8$ Hz, 1 H), 4.33 – 4.28 (m, 1 H), 3.92 (d, $J = 2.0$ Hz, 1 H), 3.64 (s, 3 H), 3.52 – 3.48 (m, 2 H), 3.14 – 3.07 (m, 1 H), 3.07 – 3.01 (m, 1 H), 2.90 – 2.75 (m, 5 H), 2.56 – 2.50 (m, 1 H), 2.12 (dd, $J = 15.5, 1.8$ Hz, 1 H), 2.17 – 2.04 (m, 4 H), 1.99 – 1.86 (m, 6 H), 1.86 – 1.80 (m, 1 H), 1.78 (dd, $J = 12.3, 8.3$ Hz, 1 H), 1.67 – 1.58 (m, 2 H), 1.44 – 1.37 (m, 1 H), 1.24 – 1.17 (m, 1 H), $-0.09 - -0.21$ (m, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.82, 130.22, 128.41, 128.03, 127.87, 127.66, 127.51, 126.16, 98.97, 83.63, 78.94, 72.68, 70.41, 65.53, 62.95, 57.59, 56.38, 52.77, 52.27, 46.24, 45.84, 35.66, 27.53, 26.36, 26.27, 25.81, 25.40, 25.31, 25.04, 24.73, 24.48; HRMS (ES) m/z 830.3406 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{47}\text{H}_{60}\text{NO}_4\text{S}_4$: 830.3405].

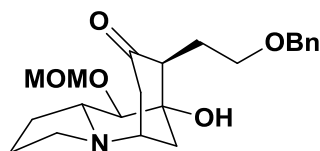


8: To a stirred solution of alcohol **15** (0.35g, 0.42mmol,) in CH₂Cl₂ (15mL) were added triethylamine (0.59mL, 4.2mmol) and methanesulfonyl chloride (0.049mL, 0.63 mmol) at room temperature. After being stirred for 0.5 h, a saturated aqueous NaHCO₃ solution (5.0mL) was added, and the resulting mixture was extracted with CH₂Cl₂ (15mL x 3). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude mesylate was dissolved in CH₂Cl₂/MeOH(10mL:1mL) and then NaHSO₄-SiO₂ (0.50g) was treated in one portion. As soon as *N*-Trityl group was removed (usually finished in 10 min), the reaction mixture was filtered and rinsed with dry CH₂Cl₂ till the concentration becomes under 0.02M. Then the filtrate was treated with excess triethylamine (1.0mL) and stirred overnight and the reaction was concentrated in vacuo. Flash chromatography (hexane/EtOAc/triethylamine = 8/2/0.2 to 5/5/0.2) afforded indolizidine **8** (0.17g, 72%) as a pale yellow oil: $[\alpha]_D^{25} = +36.9$ (c 1.00, CH₂Cl₂); ¹H NMR (500MHz, CDCl₃) δ = 7.35 – 7.31 (m, 4 H), 7.30 – 7.26 (m, 1 H), 5.16 (d, *J* = 6.7 Hz, 1 H), 4.76 (d, *J* = 6.7 Hz, 1 H), 4.50 (s, 1 H), 3.55 – 3.47 (m, 1 H), 3.43 (s, 3 H), 3.40 (d, *J* = 9.7 Hz, 3 H), 3.29 – 3.24 (m, 3 H), 3.20 (ddd, *J* = 5.3, 7.2, 9.9 Hz, 3 H), 3.14 (ddd, *J* = 3.2, 11.0, 14.2 Hz, 3 H), 3.00 – 2.95 (m, 1 H), 2.93 (td, *J* = 3.4, 6.6 Hz, 1 H), 2.91 – 2.88 (m, 1 H), 2.88 – 2.84 (m, 1 H), 2.84 – 2.80 (m, 1 H), 2.80 – 2.71 (m, 4 H), 2.71 – 2.65 (m, 1 H), 2.44 (dd, *J* = 6.6, 14.4 Hz, 1 H), 2.29 (dd, *J* = 7.1, 15.3 Hz, 1 H), 2.17 – 2.10 (m, 1 H), 2.07 (dd, *J* = 2.7, 15.6 Hz, 1 H), 2.06 – 1.99 (m, 3 H), 1.99 – 1.93 (m, 2 H), 1.93 – 1.88 (m, 1 H), 1.88 – 1.66 (m, 6 H); ¹³C NMR (125 MHz, CDCl₃) δ 138.71, 128.47, 127.69, 127.62, 97.99, 84.19, 72.89, 70.32, 56.69, 56.58, 55.28, 53.48, 52.25, 50.82, 42.73, 40.79, 36.02, 28.83, 27.65, 26.29, 26.24, 26.23, 25.61, 25.35, 25.20, 22.95; HRMS (ES) *m/z* 570.2206 [(*M*+*H*)⁺; calcd for C₂₈H₄₄NO₃S₄: 570.2204].



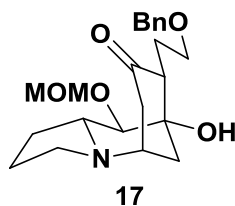
7

7: To a stirred solution of **8** (36mg, 0.063mmol) in CH₃CN:H₂O (1:1) was added trifluoroacetic acid (0.047ml, 0.63mmol) was added. Then PhI(O₂CCF₃)₂ (54mg, 0.13mmol) was added into the solution in one portion at room temperature. After 0.5 h, additional PhI(O₂CCF₃)₂ (81mg, 0.19mmol) was added. The reaction mixture was stirred for 0.5 h. The resultant mixture was extracted with hexane (5ml x 3), the aqueous layer was neutralized with solid K₂CO₃ (until to basic), and then treated with EtSH (0.5ml) followed by stirring for 5 min. The resulting solution was diluted with saturated aqueous NaHCO₃ and extracted with EtOAc (15mlx3). The combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. Flash chromatography (hexane/EtOAc/triethylamine = 5/5/0.2) afforded dione **7** (15mg, 62%) as a pale yellow oil: $[\alpha]_D^{25} = +77.5$ (c 1.00, CH₂Cl₂); ¹H NMR (500MHz, CDCl₃) δ = 7.37 – 7.26 (m, 5 H), 4.76 (d, *J* = 7.1 Hz, 1 H), 4.67 (d, *J* = 6.9 Hz, 1 H), 4.46 (s, 2 H), 3.99 (d, *J* = 9.3 Hz, 1 H), 3.97 – 3.92 (m, 1 H), 3.45 (t, *J* = 6.1 Hz, 2 H), 3.41 (s, 3 H), 2.99 – 2.94 (m, 1 H), 2.94 – 2.89 (m, 1 H), 2.84 (dd, *J* = 6.3, 13.3 Hz, 1 H), 2.71 (dt, *J* = 6.1, 8.5 Hz, 1 H), 2.58 (dd, *J* = 5.0, 16.4 Hz, 4 H), 2.55 – 2.44 (m, 2 H), 2.38 (dd, *J* = 8.5, 16.6 Hz, 1 H), 2.21 (dd, *J* = 2.0, 13.3 Hz, 1 H), 2.17 – 2.09 (m, 1 H), 2.00 – 1.92 (m, 1 H), 1.90 – 1.77 (m, 4 H); ¹³C NMR (125 MHz, CDCl₃) δ 208.74, 207.81, 138.50, 128.52, 127.79, 127.73, 96.30, 81.23, 73.02, 69.32, 62.67, 56.12, 52.98, 49.56, 43.72, 41.12, 40.67, 30.16, 23.88, 22.30; HRMS (ES) *m/z* 390.2277 [(M+H)⁺; calcd for C₂₂H₃₂NO₅: 390.2280].



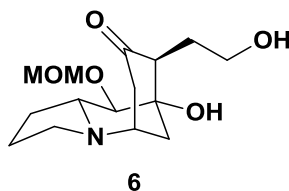
16

16: To a stirred solution of dione **7** (25mg, 0.064mmol) in MeOH (10mL) was added NaOMe (0.050mL, ca. 30% W/W in MeOH). Then the solution was stirred for 24 h and quenched with saturated aqueous NaHCO₃ and extracted with CH₂Cl₂ (20mL x 3) and the combined organic layers were dried over anhydrous Na₂SO₄. Flash chromatography (MeOH/CH₂Cl₂/triethylamine = 1/19/0.5) afforded alcohol **16** (22mg, 90%) as a pale yellow oil: $[\alpha]_D^{26} = -11.1$ (c 1.00, CH₂Cl₂); ¹H NMR (500MHz, CDCl₃) δ = 7.35 – 7.30 (m, 4 H), 7.28 – 7.24 (m, 1 H), 4.70 (d, *J* = 6.7 Hz, 1 H), 4.61 (d, *J* = 6.9 Hz, 1 H), 4.48 (s, 2 H), 4.35 (s, 1 H), 3.55 (dd, *J* = 5.4, 7.3 Hz, 3 H), 3.41 – 3.38 (m, 1 H), 3.33 (s, 3 H), 3.21 (d, *J* = 9.7 Hz, 1 H), 2.96 – 2.93 (m, 1 H), 2.84 (dt, *J* = 4.0, 8.7 Hz, 1 H), 2.68 – 2.63 (m, 1 H), 2.63 – 2.58 (m, 1 H), 2.48 – 2.40 (m, 2 H), 2.37 (dd, *J* = 5.0, 12.1 Hz, 3 H), 2.12 (dd, *J* = 2.9, 13.2 Hz, 1 H), 2.00 – 1.92 (m, 1 H), 1.87 – 1.83 (m, 2 H), 1.84 – 1.78 (m, 1 H), 1.76 – 1.68 (m, 1 H), 1.61 (ddd, *J* = 5.3, 9.5, 14.6 Hz, 1 H), 1.51 – 1.43 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 212.75, 138.38, 128.45, 127.96, 127.71, 98.86, 90.66, 73.22, 72.89, 68.60, 58.90, 56.21, 52.71, 50.56, 48.73, 38.39, 33.88, 29.29, 28.00, 21.65; HRMS (ES) *m/z* 390.2277 [(M+H)⁺; calcd for C₂₂H₃₂NO₅: 390.2280].

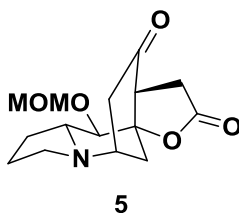


17: To a stirred solution of dione **7** (18mg, 0.046mmol) in MeOH (10mL) was added NaOMe (0.050 mL, ca. 30% W/W in MeOH). Then the solution was stirred for 6 h and quenched with saturated aqueous NaHCO₃ and concentrated in vacuo. Flash chromatography (MeOH/CH₂Cl₂/triethylamine = 1/19/0.5 to 1/9/0.5) afforded alcohol **16** (13mg, 75%) and **17** (2.5mg, 15%) as a pale yellow oil: $[\alpha]_D^{24} = -4.30$ (c 0.37, CH₂Cl₂); ¹H NMR (500MHz, CDCl₃) δ = 7.36 – 7.31 (m, 4 H), 7.31 – 7.27 (m, 1 H), 4.75 (br. s., 1 H), 4.74 (d, *J* = 6.1 Hz, 1 H), 4.54 (d, *J* = 11.9 Hz, 1 H), 4.50 (d, *J* = 6.1 Hz, 1 H), 4.49 (d, *J* = 11.9 Hz, 1 H), 3.71 (ddd, *J* = 4.3, 5.5, 9.5 Hz, 1 H), 3.46 (br. s., 1 H), 3.39 (s, 3 H), 3.38 – 3.34 (m,

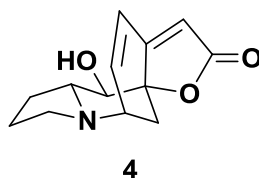
1 H), 3.29 (d, $J = 9.7$ Hz, 1 H), 2.89 – 2.83 (m, 1 H), 2.78 (d, $J = 16.2$ Hz, 1 H), 2.72 – 2.67 (m, 1 H), 2.55 (dd, $J = 3.8, 7.3$ Hz, 1 H), 2.41 – 2.34 (m, 2 H), 2.28 (dd, $J = 5.0, 12.9$ Hz, 1 H), 2.25 – 2.20 (m, 1 H), 2.19 – 2.15 (m, 1 H), 2.09 (dd, $J = 2.6, 12.9$ Hz, 1 H), 1.96 – 1.88 (m, 1 H), 1.87 – 1.80 (m, 1 H), 1.76 – 1.68 (m, 1 H), 1.54 – 1.46 (m, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 209.37, 138.32, 128.55, 128.03, 127.81, 98.86, 89.41, 74.65, 73.03, 70.59, 60.16, 59.62, 58.04, 56.22, 51.01, 48.70, 41.42, 29.85, 28.86, 24.08, 21.61; (ES) m/z 390.2277 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{22}\text{H}_{32}\text{NO}_5$: 390.2280].



6: A solution of **16** (5.0mg, 0.013mmol) in EtOH (4.0mL) was treated with Raney Ni (0.20ml slurry in H_2O) and stirred at 50°C under $\text{H}_2(\text{g})$ (1atm) for 24h. Then the mixture was filtered through celite and concentrated in vacuo. Flash chromatography ($\text{MeOH}/\text{CH}_2\text{Cl}_2/\text{triethylamine} = 1/9/0.5$) afforded diol **6** (3.5mg, 91%) as a pale yellow oil: $[\alpha]_{\text{D}}^{25} = -43.5$ (c 0.50, CH_2Cl_2); ^1H NMR (500MHz, CDCl_3) δ = 4.74 (d, $J = 6.9$ Hz, 1 H), 4.66 (d, $J = 6.9$ Hz, 1 H), 4.53 (s, 1 H), 3.73 (qd, $J = 5.5, 11.2$ Hz, 1 H), 3.65 – 3.58 (m, 1 H), 3.47 – 3.43 (m, 1 H), 3.45 (s, 3 H), 3.24 (d, $J = 9.7$ Hz, 1 H), 3.00 (dd, $J = 4.9, 9.6$ Hz, 1 H), 2.87 (dt, $J = 4.1, 8.6$ Hz, 1 H), 2.73 – 2.61 (m, 2 H), 2.46 (t, $J = 5.8$ Hz, 1 H), 2.44 – 2.39 (m, 1 H), 2.37 (dd, $J = 5.0, 17.0$ Hz, 1H), 2.34 – 2.28 (m, 1 H), 2.16 (dd, $J = 2.9, 13.4$ Hz, 1 H), 2.01 – 1.94 (m, 1 H), 1.89 (d, $J = 15.1$ Hz, 1 H), 1.88 – 1.81 (m, 1 H), 1.79 – 1.69 (m, 1 H), 1.58 (tdd, $J = 4.8, 9.7, 14.5$ Hz, 1 H), 1.54 – 1.45 (m, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 213.77, 98.92, 90.63, 72.65, 61.09, 58.95, 56.31, 53.02, 50.54, 48.74, 38.54, 33.68, 30.64, 29.12, 21.57; HRMS (ES) m/z 300.1808 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{15}\text{H}_{26}\text{NO}_5$: 300.1811].

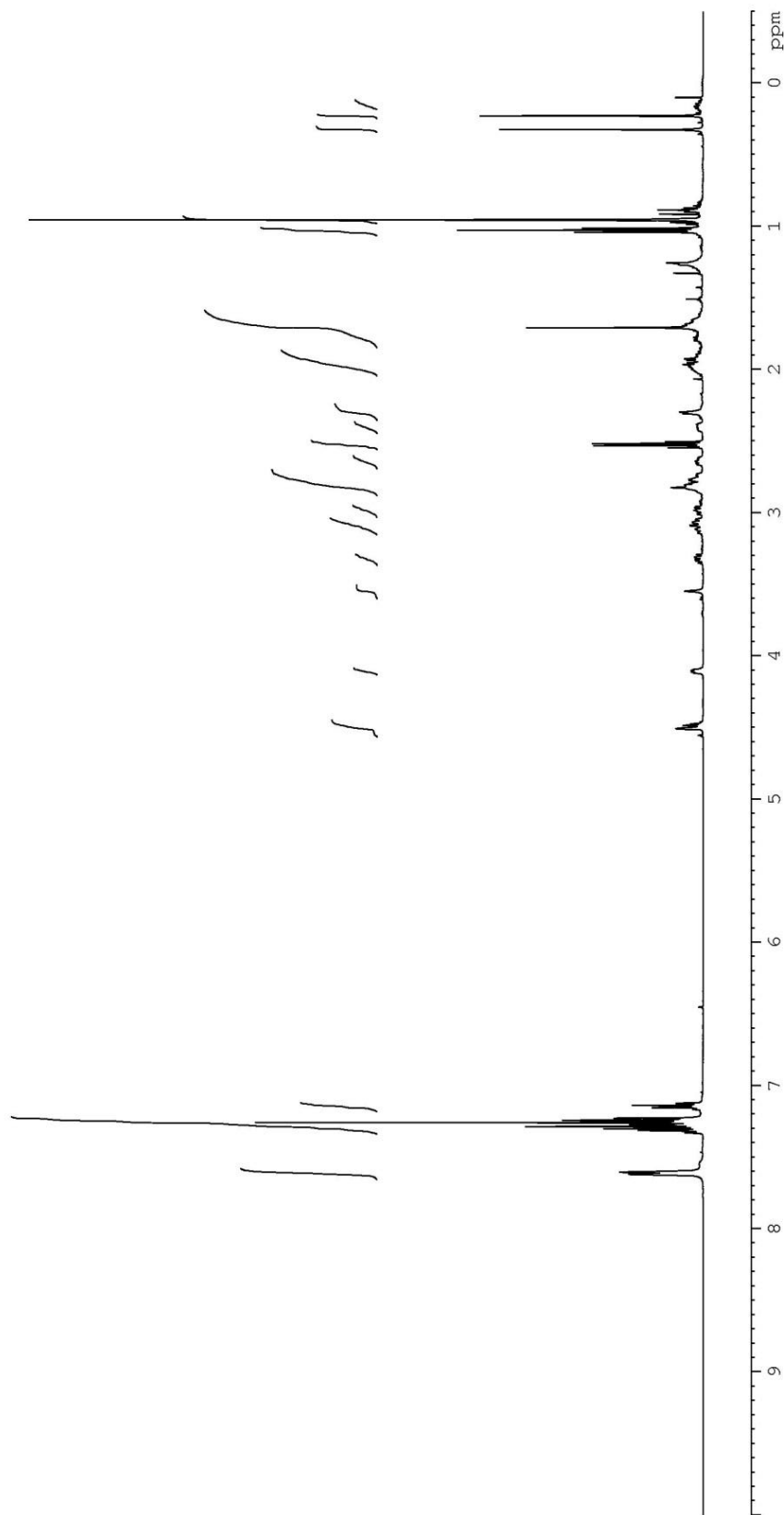
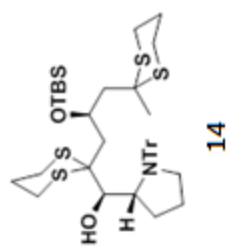


5: To a solution of **6** (4.0mg, 0.013mmol) in CH₂Cl₂ (0.50mL) were added 4 Å MS (4.0mg) and NMO (2.0mg, 0.017mmol). After 5 min, TPAP (0.47mg, 13μmol) was added to the reaction mixture. After 1 h, the reaction mixture was treated with additional NMO (1.6mg, 0.013mmol) and stirred for 1h. Then the reaction mixture was filtered through celite and concentrated in vacuo. Flash chromatography (EtOAc/hexane/triethylamine = 3/7/0.2) afforded lactone **5** (3.1mg, 75%) as a pale yellow oil: ¹H NMR (500MHz, CDCl₃) δ = 4.77 (d, *J* = 6.8 Hz, 1 H), 4.65 (d, *J* = 6.8 Hz, 1 H), 3.68 (d, *J* = 9.1Hz, 1 H), 3.60 – 3.56 (m, 1 H), 3.51 (t, *J* = 10.5 Hz, 1 H), 3.38 (s, 3 H), 2.90 (dd, *J* = 9.5, 18.5 Hz, 1 H), 2.90 – 2.87 (m, 1H), 2.78 (dd, *J* = 11.3, 18.5 Hz, 1 H), 2.58 (d, *J* = 18.5 Hz, 1 H), 2.50 – 2.43 (m, 1 H), 2.43 – 2.37 (m, 2H), 2.28 – 2.23 (m, 1H), 2.12 – 2.09 (m, 1 H), 1.96 – 1.89 (m, 1 H), 1.80 – 1.72 (m, 3 H); HRMS (ES) *m/z* 296.1510 [(M+H)⁺; calcd for C₁₅H₂₂NO₅: 296.1498].

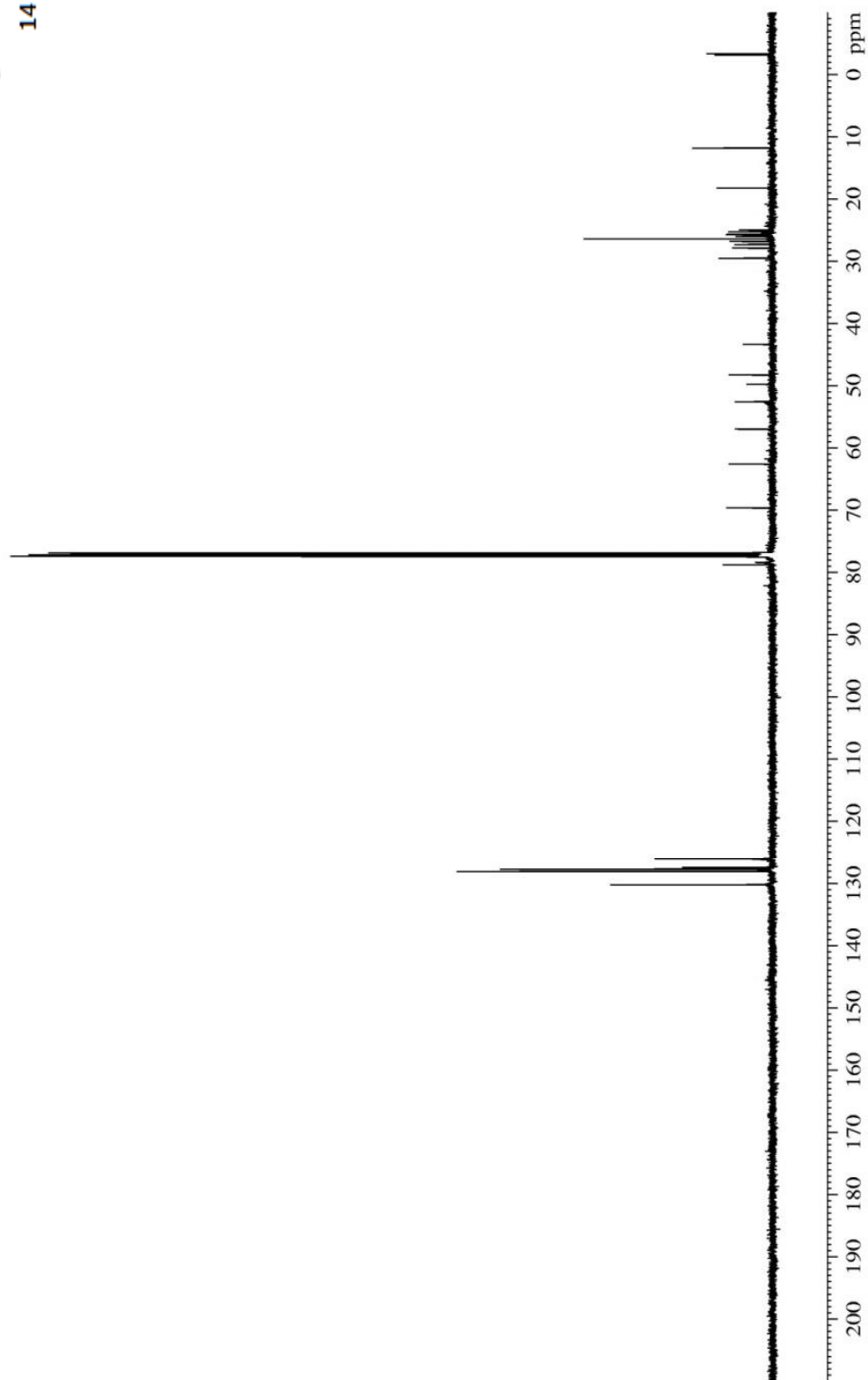
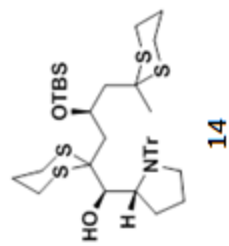


4: Following the Weinreb's five-step procedure, (–)-secu'amine A (**4**) (2.2mg) was synthesized from compound **5**: [α]_D²⁵ = –505.2 (c 0.15, CHCl₃); reported by Weinreb group [α]_D²⁵ = –511.3 (c 0.15, CHCl₃); reported by Osaki group [α]_D²⁵ = –479 (c 0.15, CHCl₃); ¹H NMR (500MHz, CDCl₃) δ = 6.79 (d, *J* = 9.6 Hz, 1 H), 6.18 (dd, *J* = 9.6 Hz, 5.4 Hz, 1H), 5.86 (s, 1H), 3.93 (brs, 1H), 3.73 (d, *J* = 8.9 Hz, 1H), 3.02 (brs, 1H), 2.60-2.55 (m, 1H), 2.55-2.50 (brs, 1H), 2.36 (d, *J* = 11.6 Hz, 1H), 2.20 (brs, 1H), 2.09-2.06 (m, 1H), 2.01 (dd, *J* = 11.6 Hz, 3.3 Hz, 1H), 1.97-1.89 (m, 1H), 1.82-1.75 (m, 1H), 1.71-1.62 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 172.21, 161.97, 133.96, 124.29, 114.07, 86.91, 74.99, 59.43, 52.12, 48.61, 36.97, 28.23, 22.19; HRMS (ES) *m/z* 234.1145 [(M+H)⁺; calcd for C₁₃H₁₅NO₃: 234.1130].

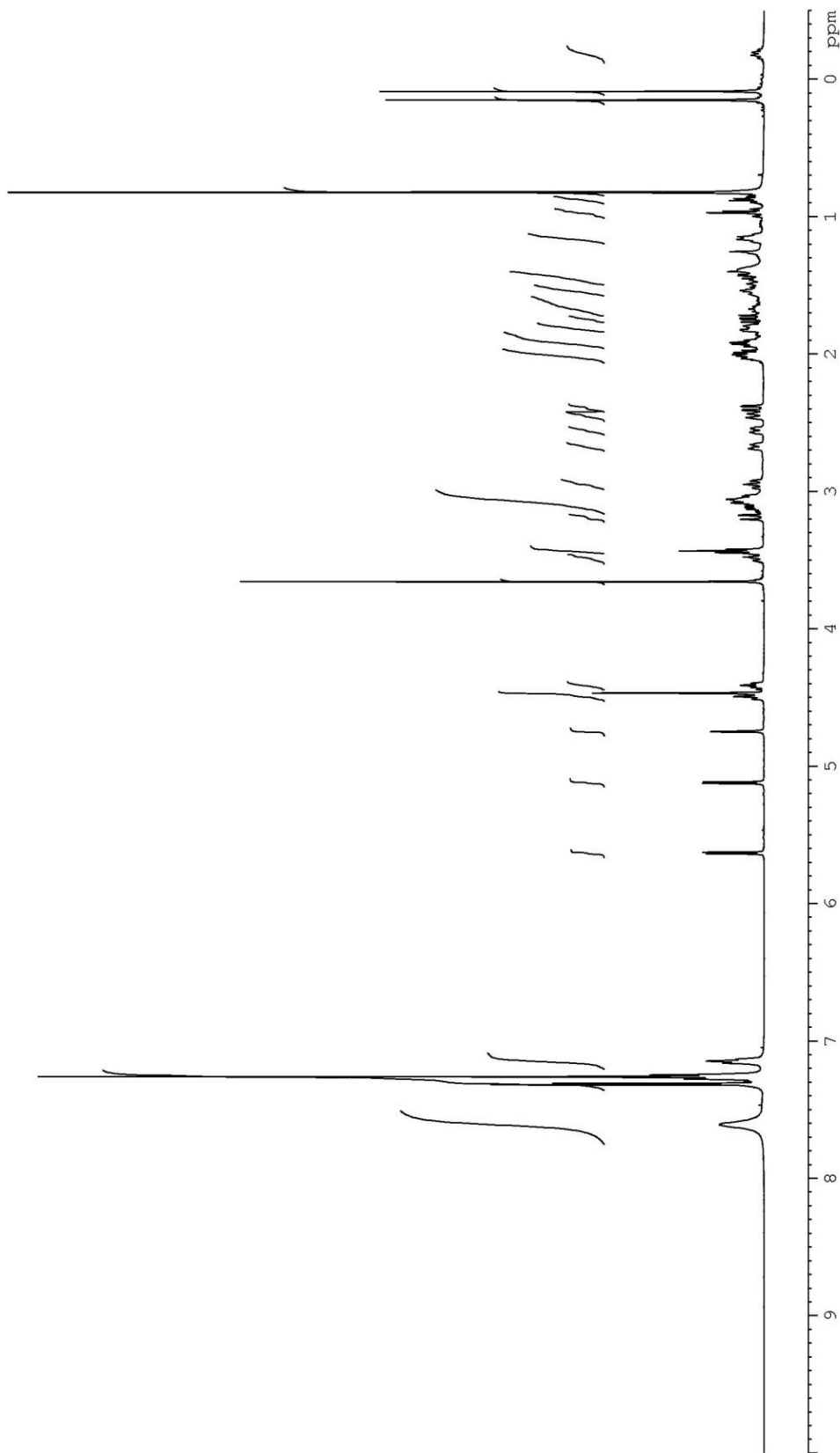
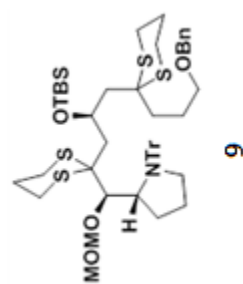
Appendix 2-1: Spectral Data



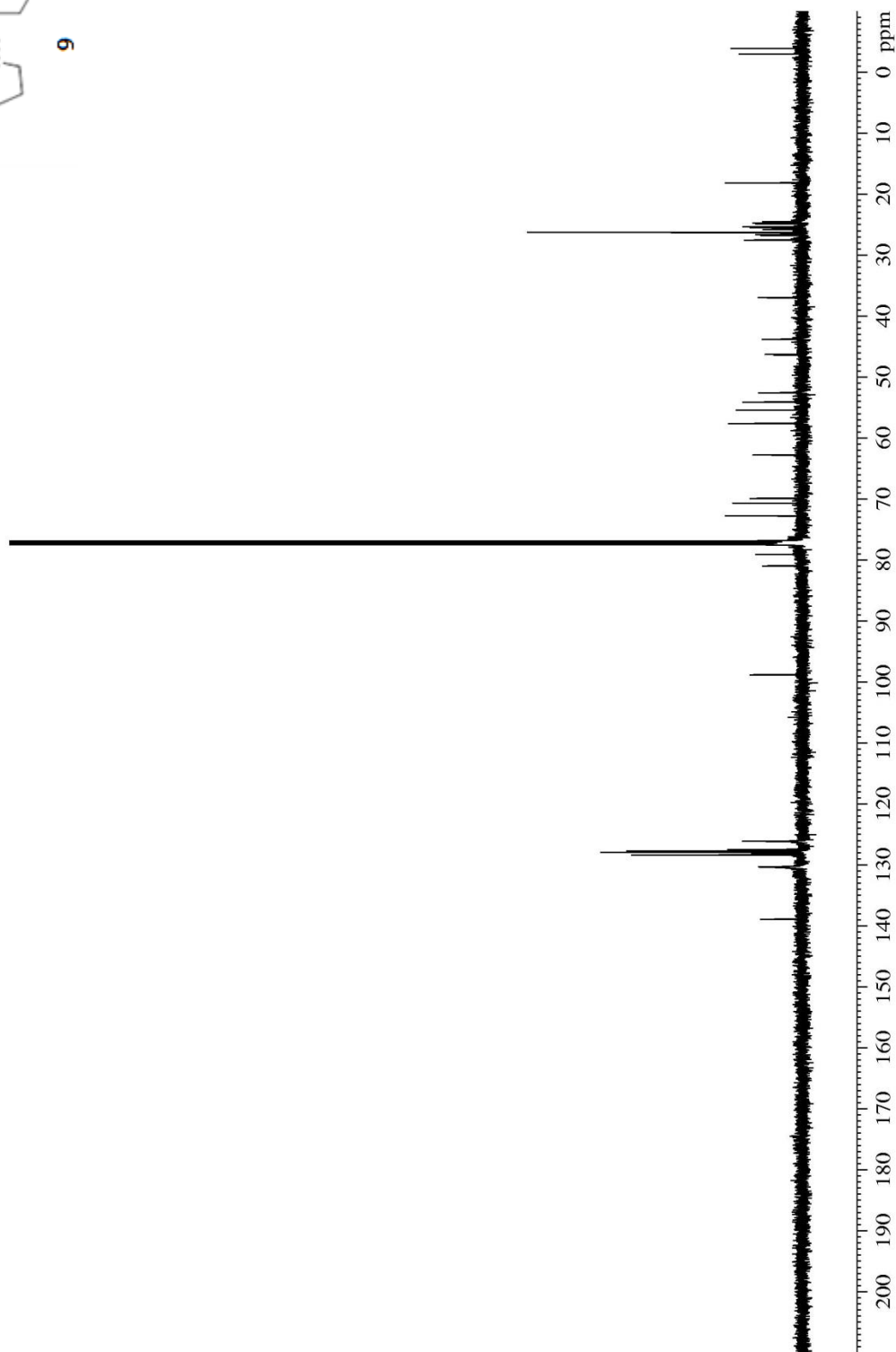
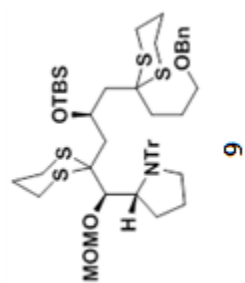
The 500 MHz ^1H NMR Spectrum of Compound **14**



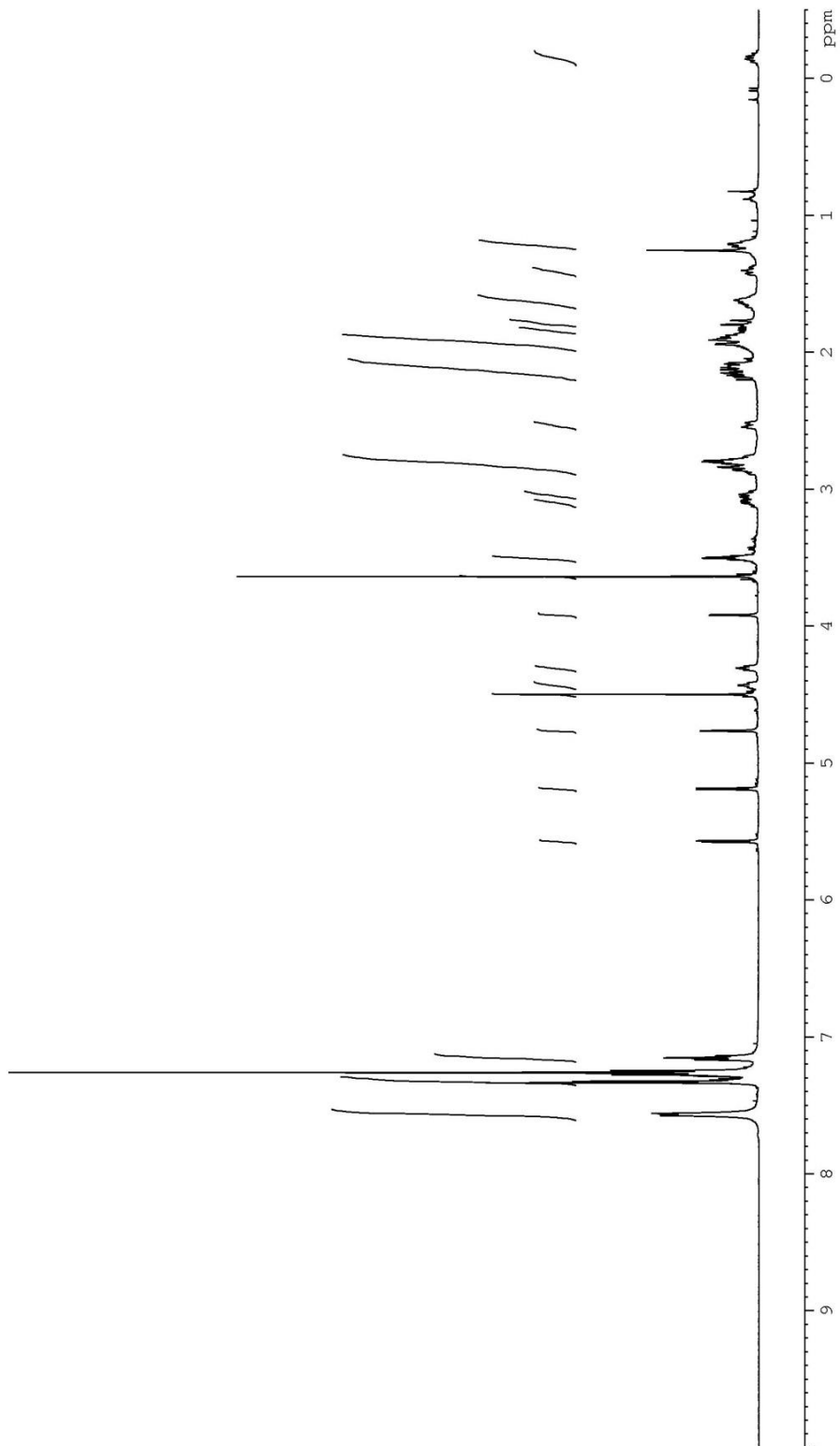
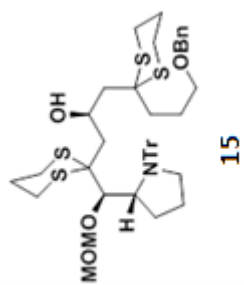
The 125 MHz ^{13}C NMR Spectrum of Compound **14**



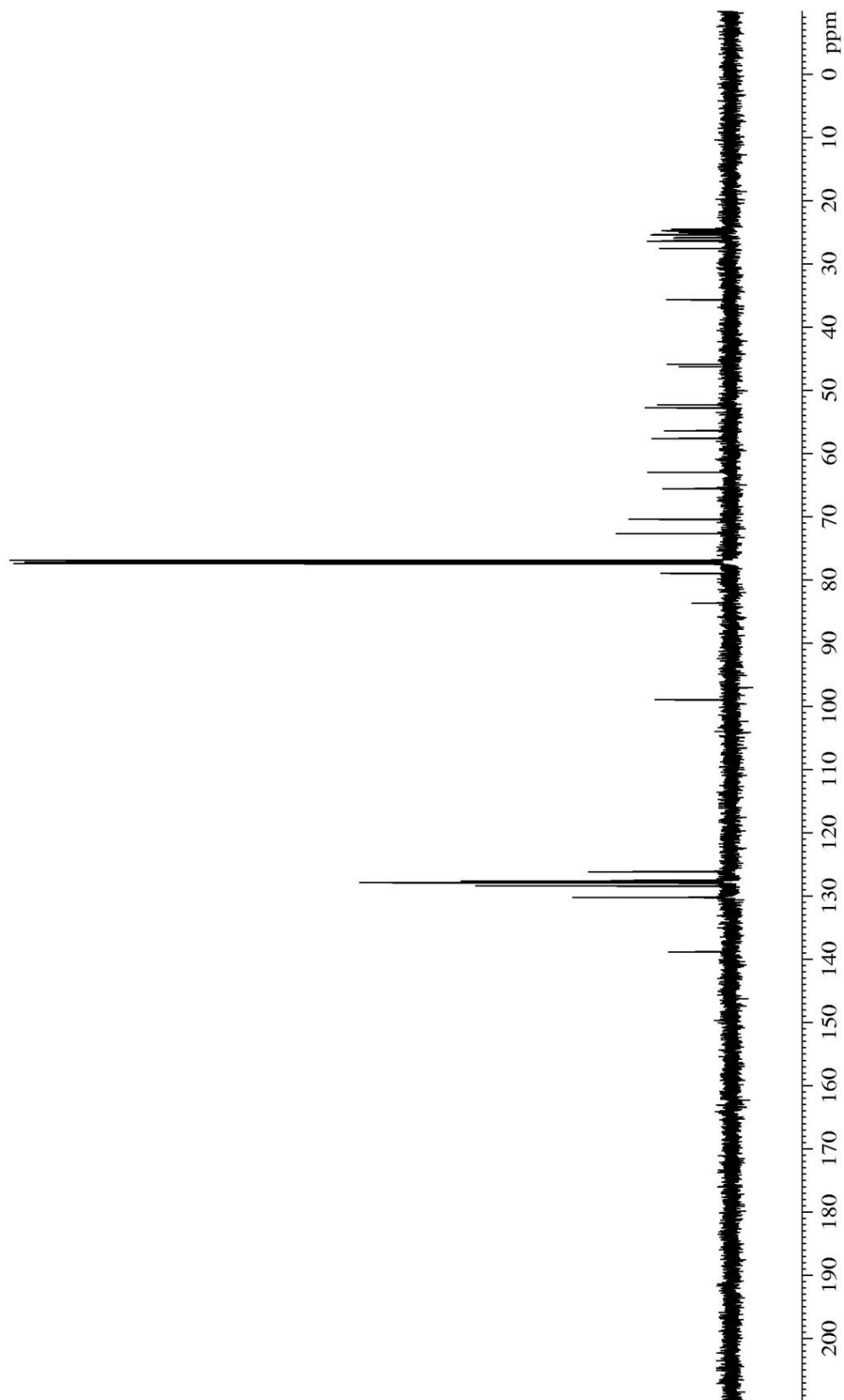
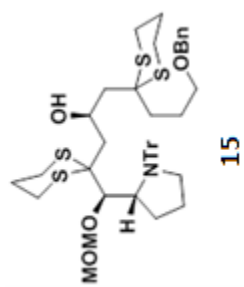
The 500 MHz ^1H NMR Spectrum of Compound **9**

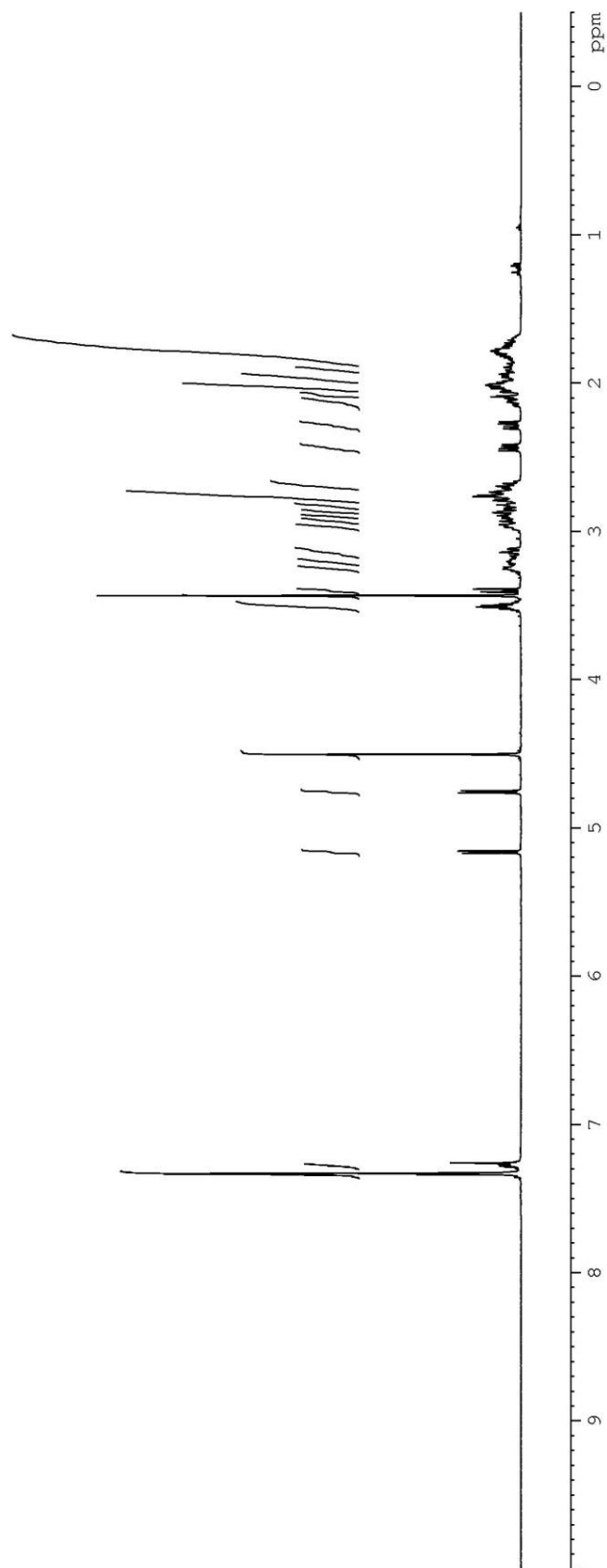
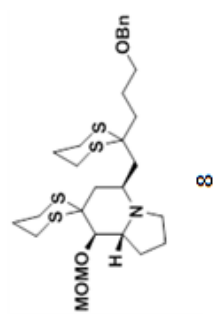


The 500 MHz ^1H -NMR Spectrum of Compound 9

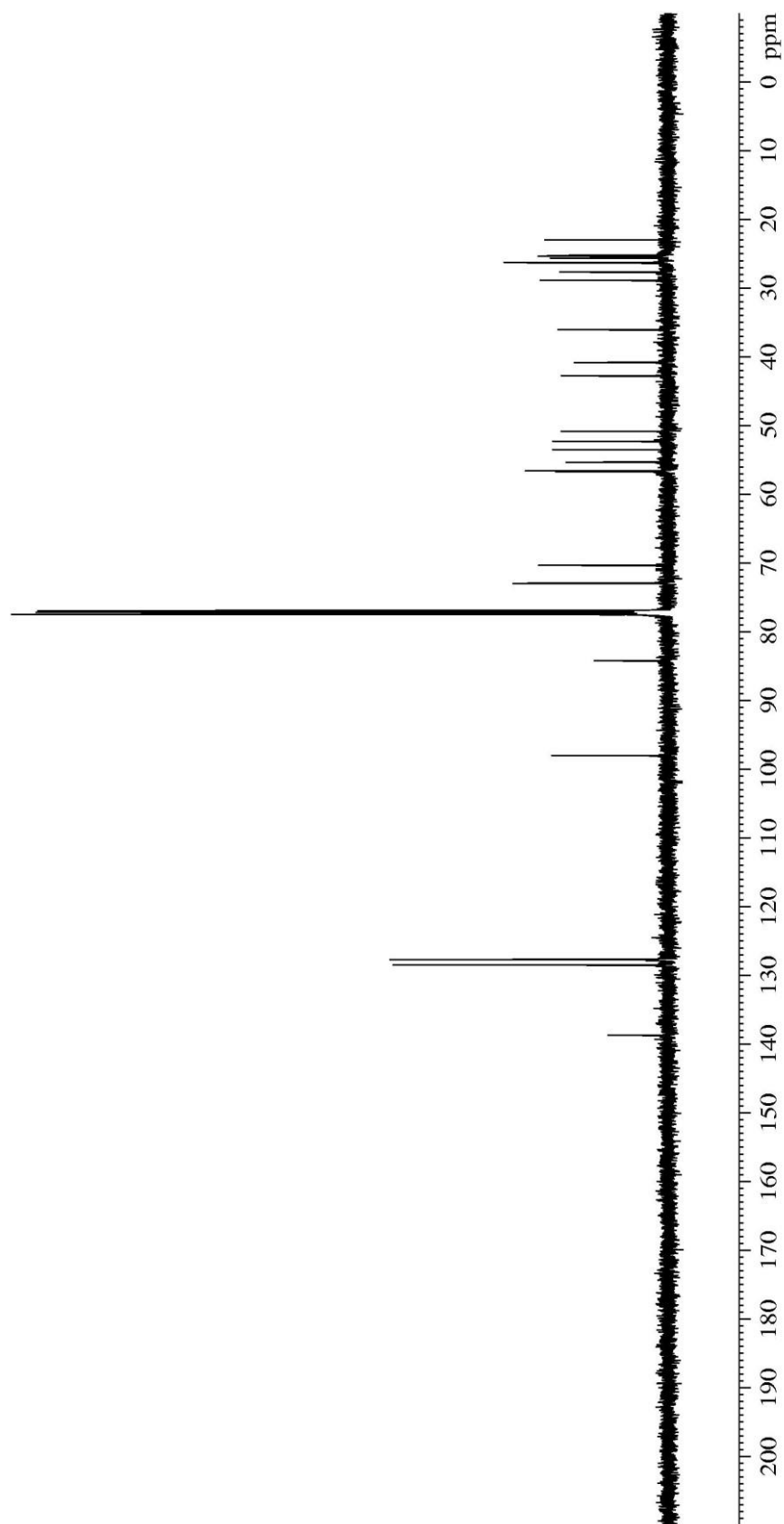
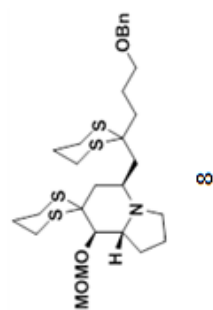


The 500 MHz ^1H -NMR Spectrum of Compound **15**

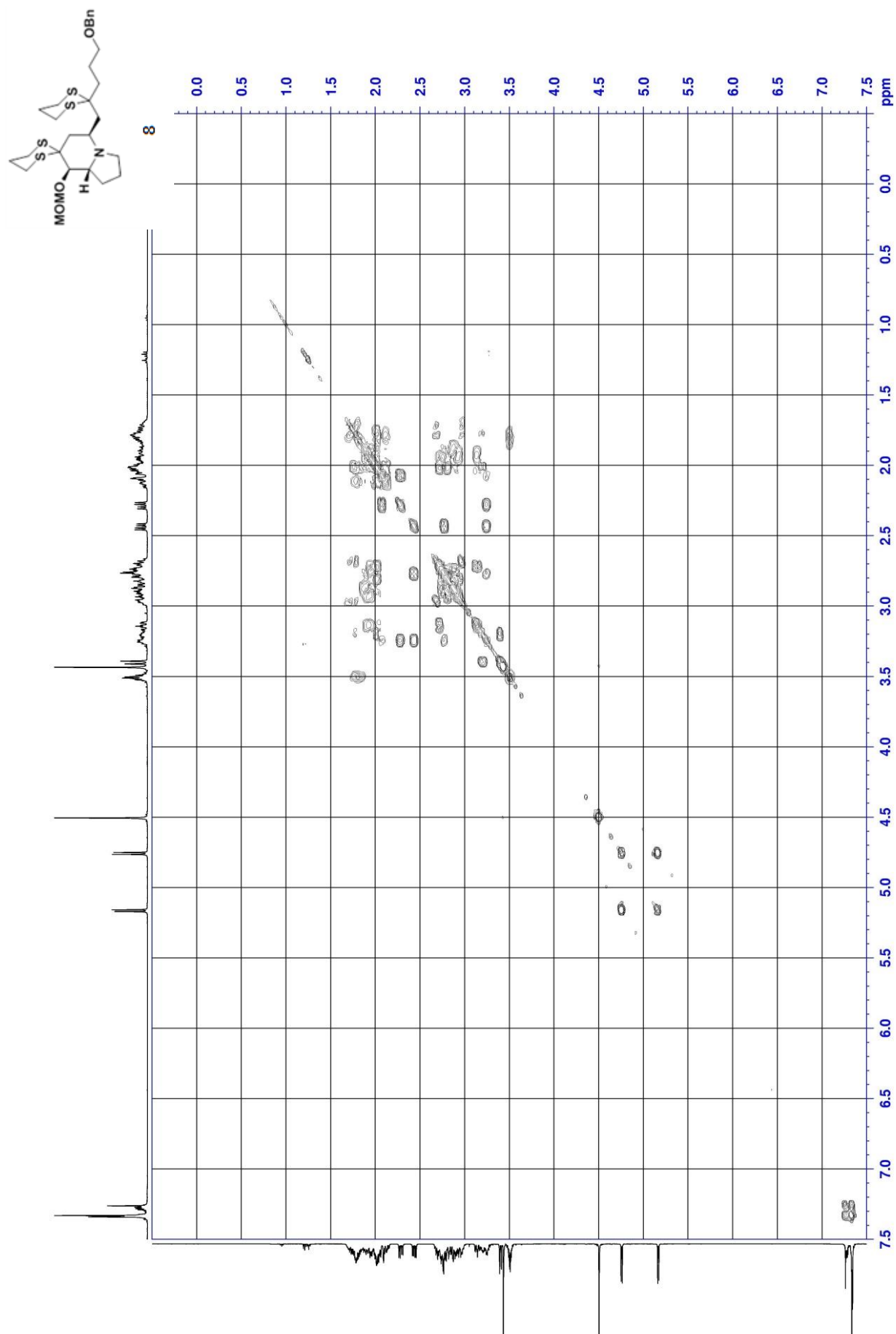




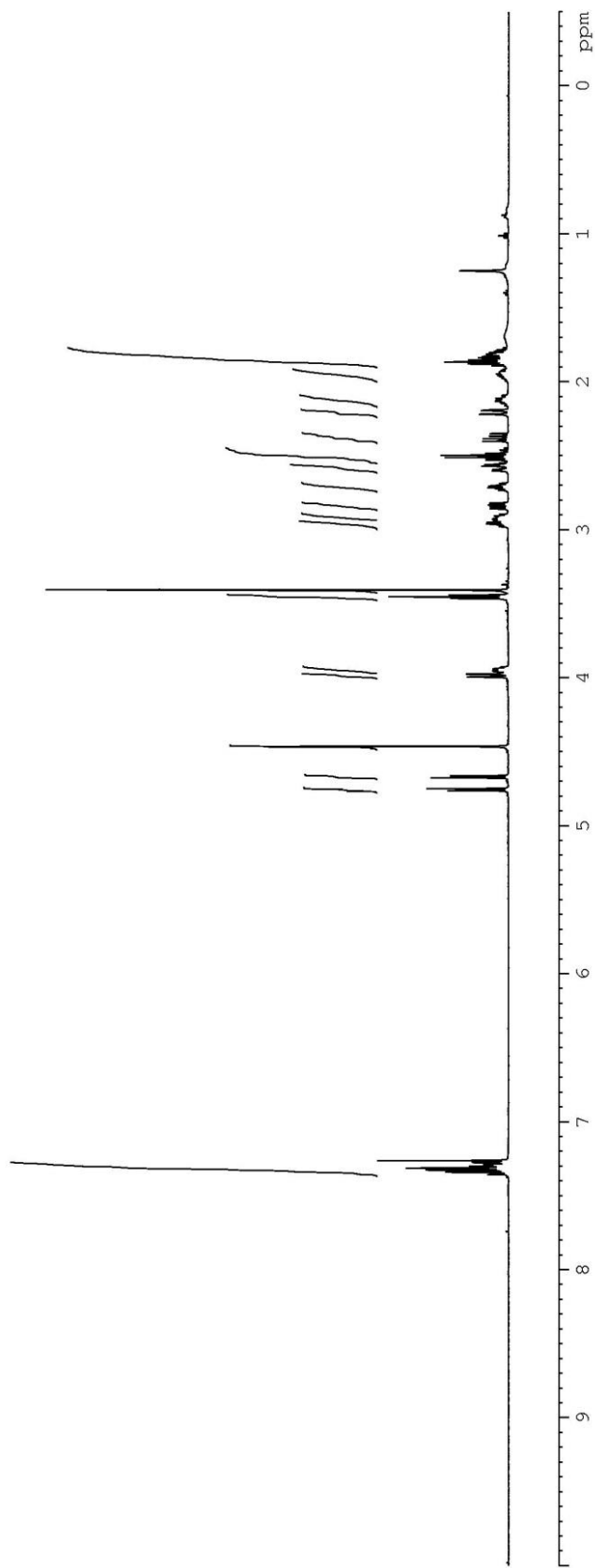
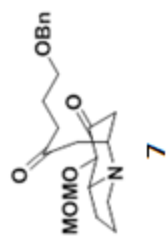
The 500 MHz ^1H -NMR Spectrum of Compound 8



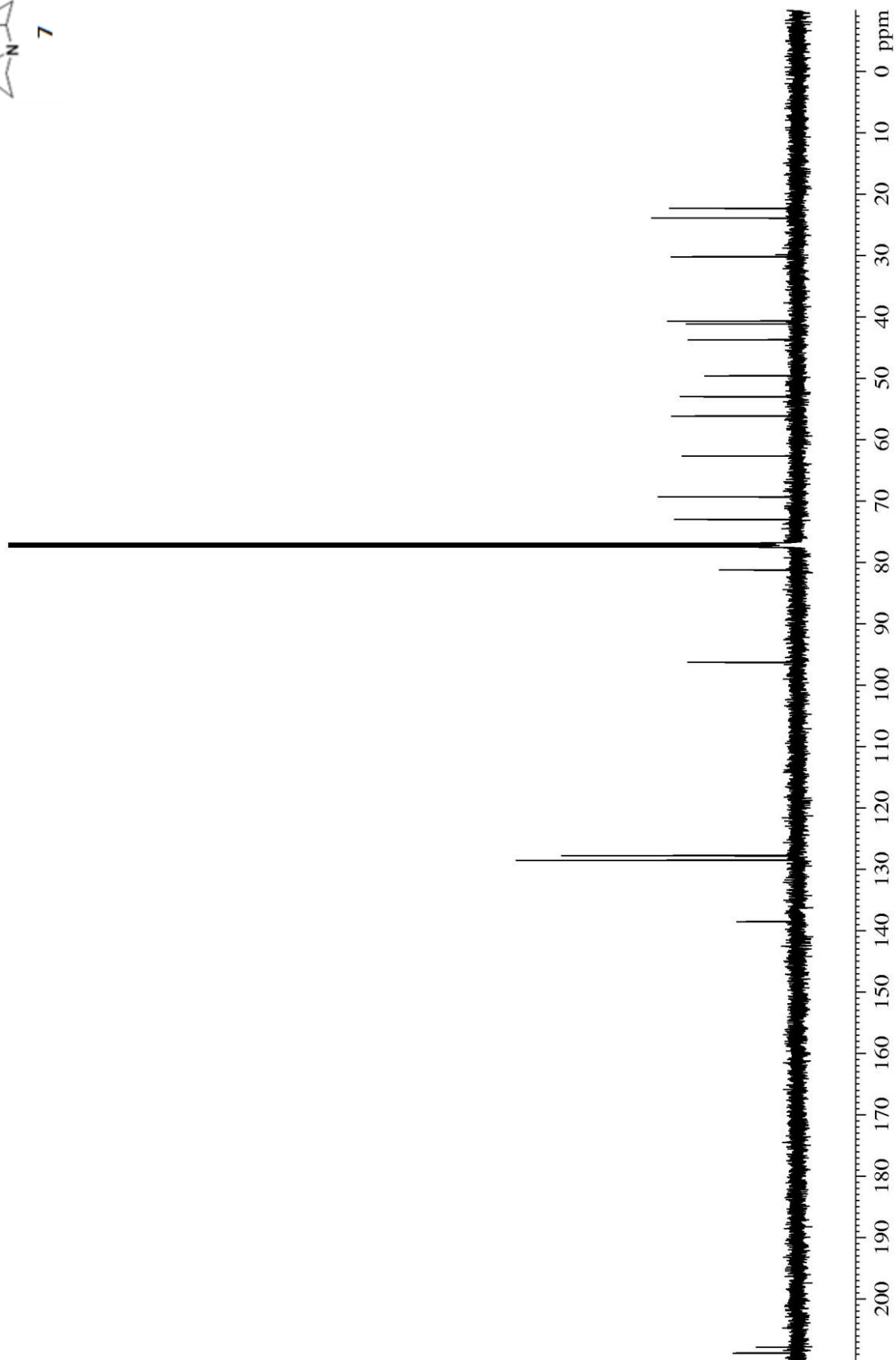
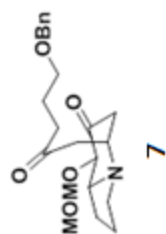
The 125 MHz ^{13}C NMR Spectrum of Compound 8



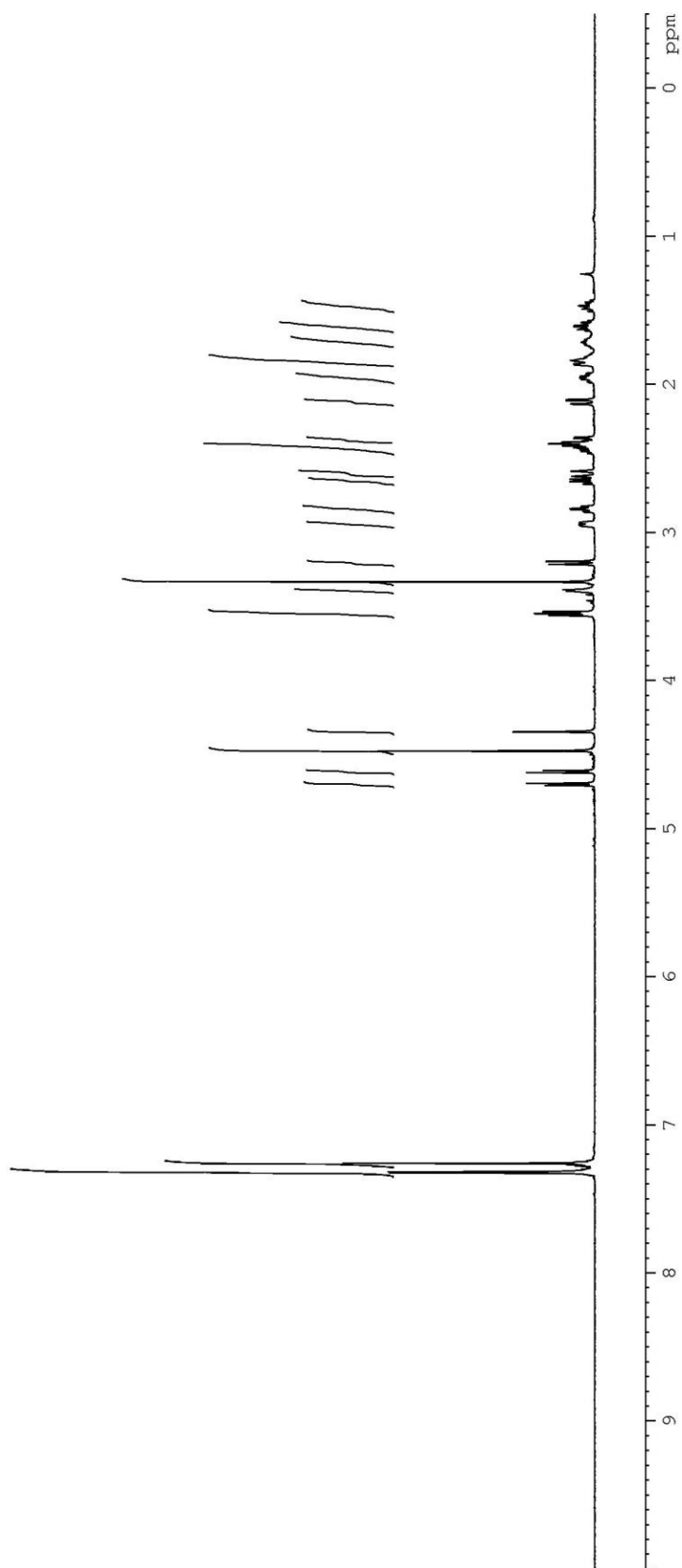
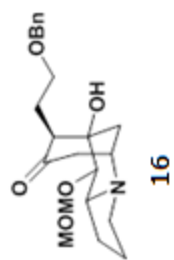
The COSY Spectrum of Compound 8



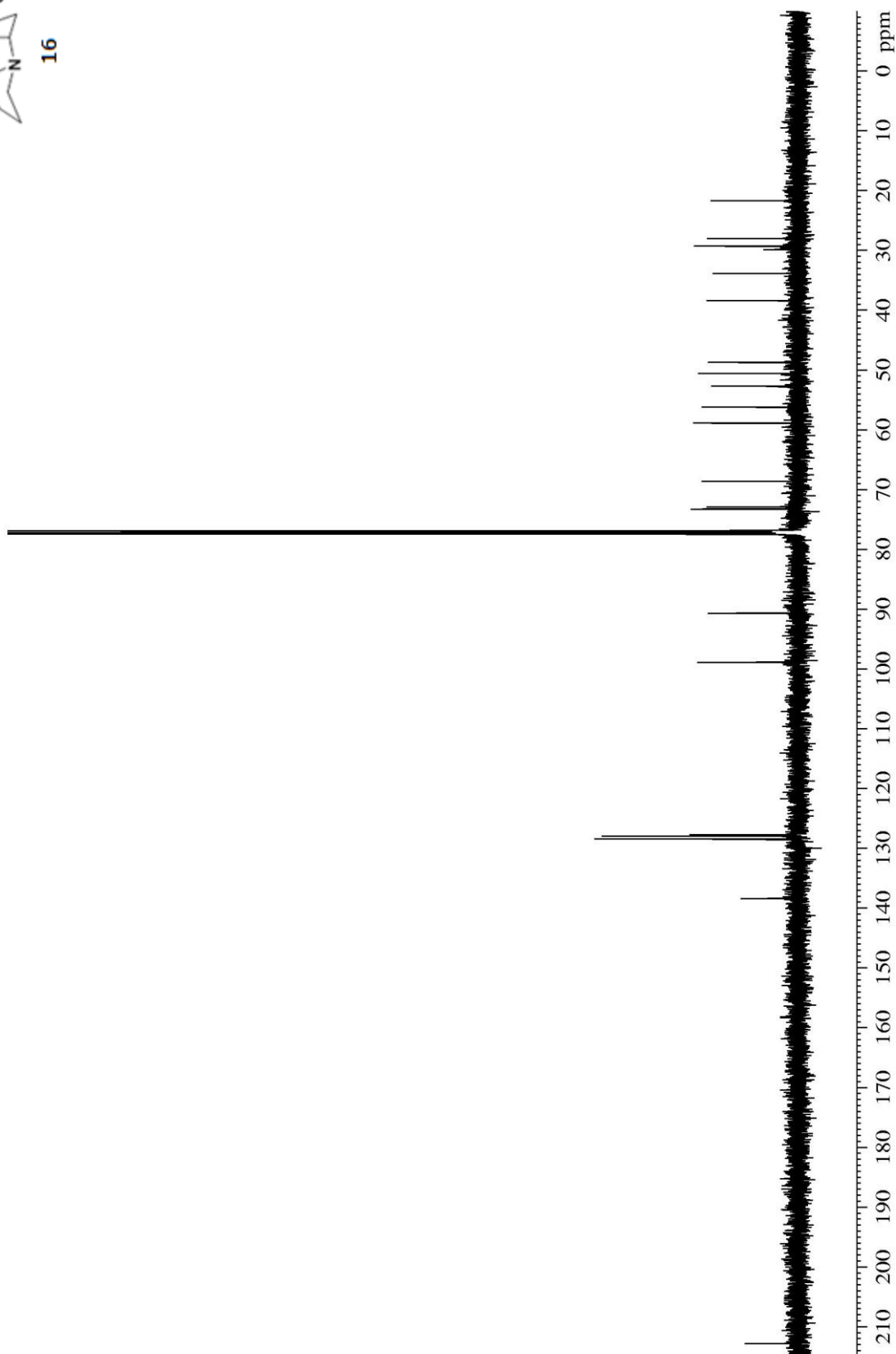
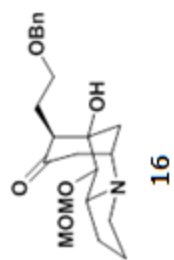
The 500 MHz ^1H NMR Spectrum of Compound 7



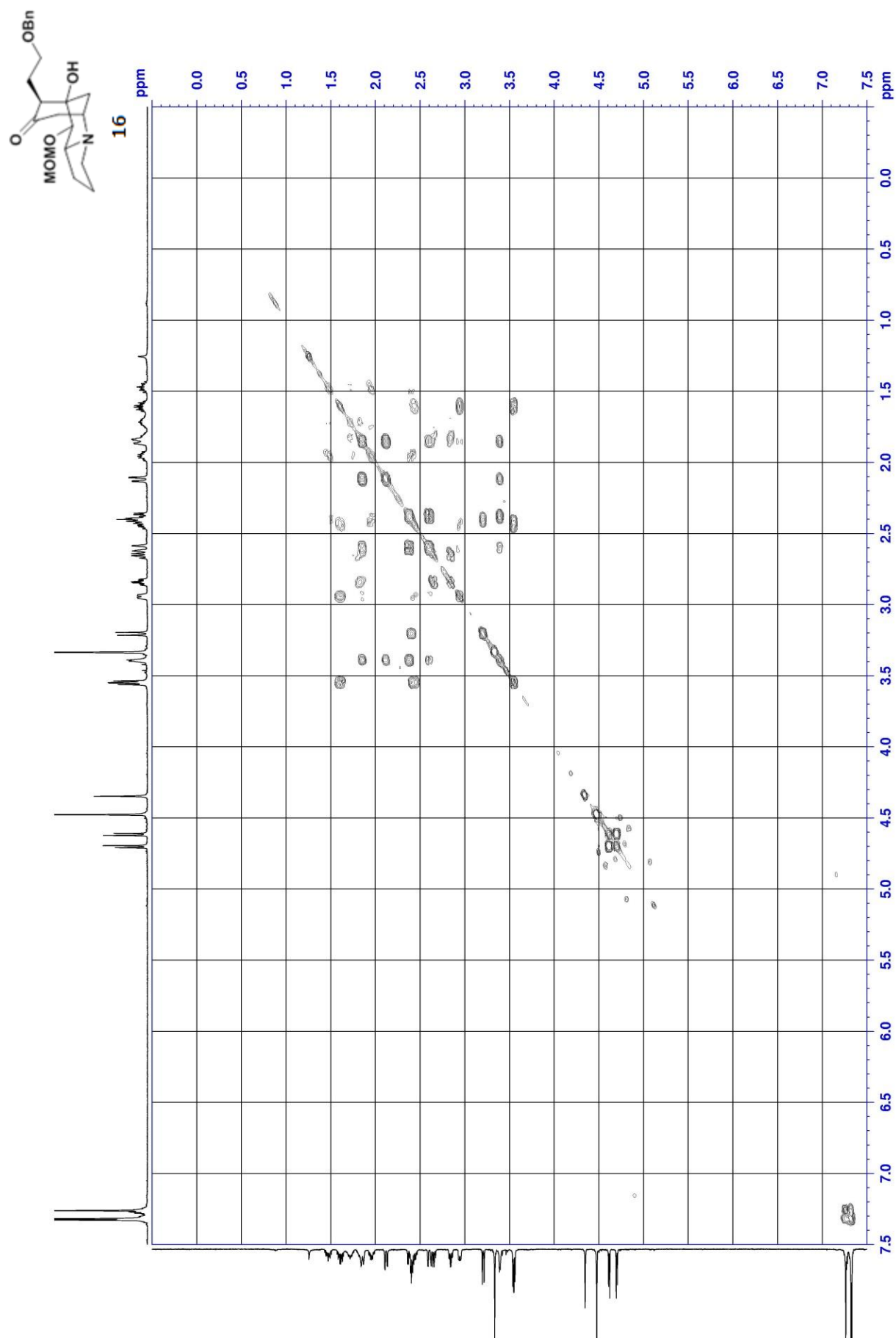
The 125 MHz ^{13}C NMR Spectrum of Compound 7



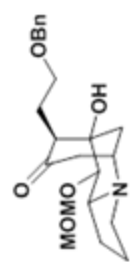
The 500 MHz ^1H NMR Spectrum of Compound **16**



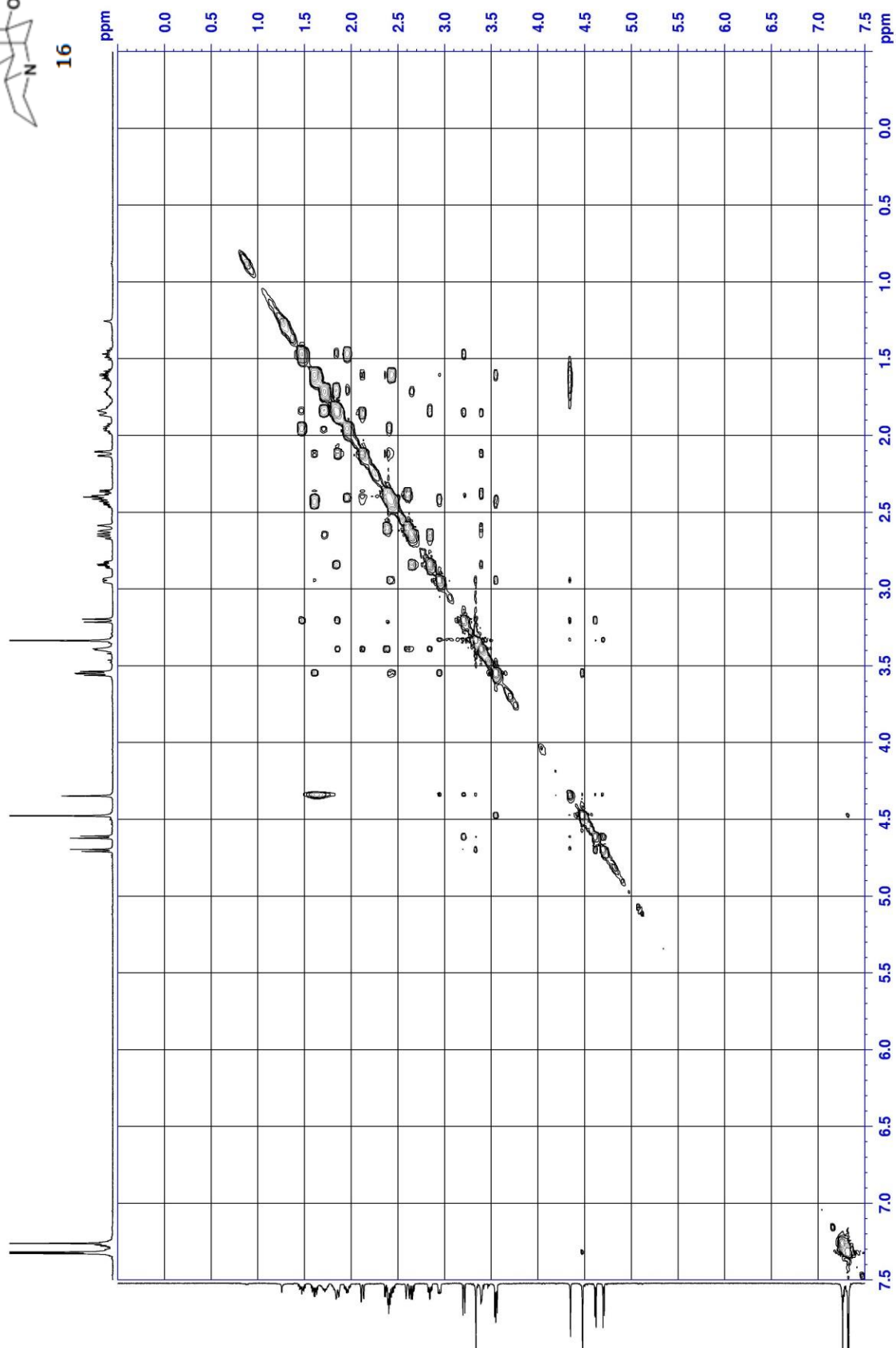
The 125 MHz ^{13}C NMR Spectrum of Compound **16**



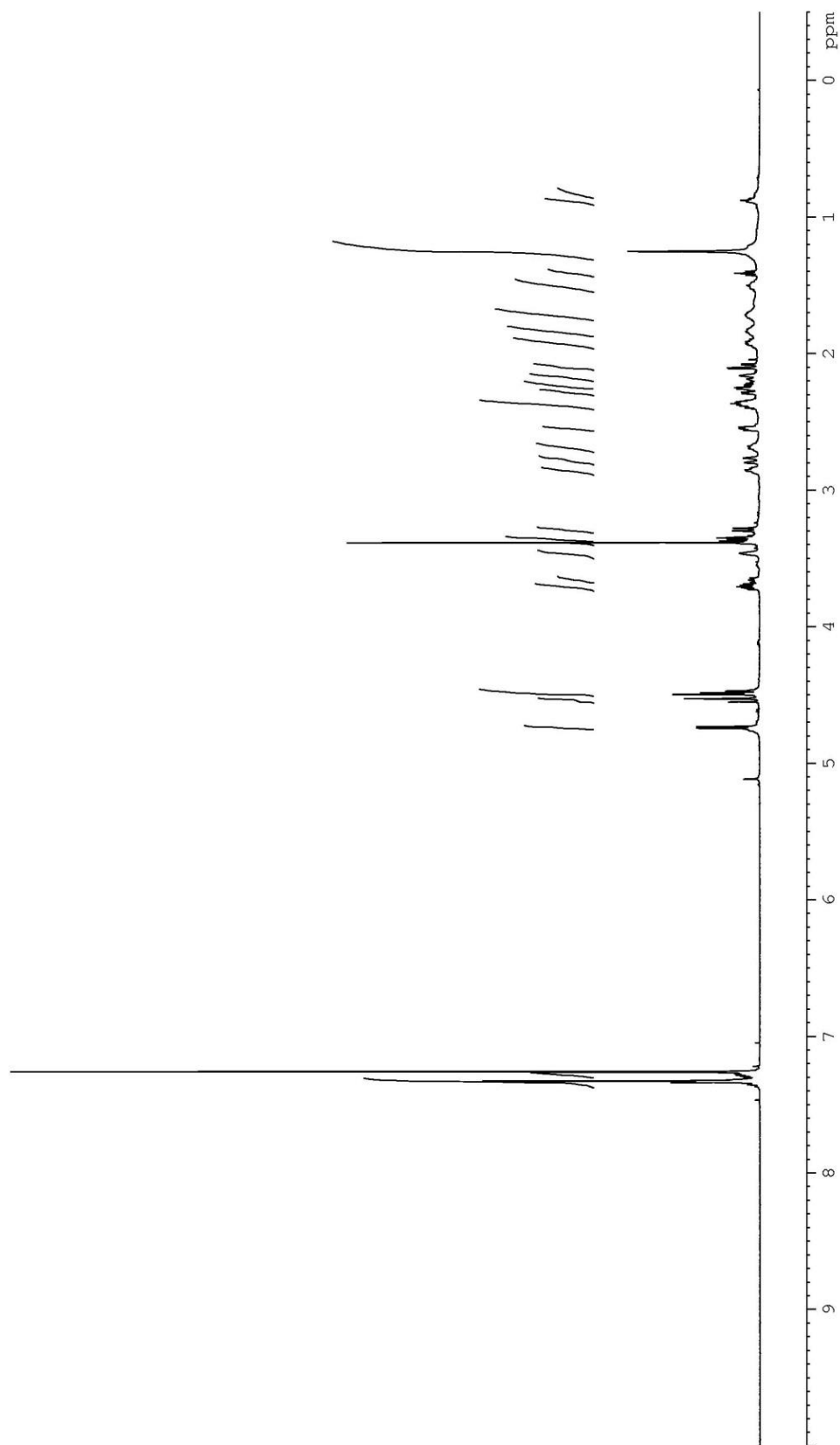
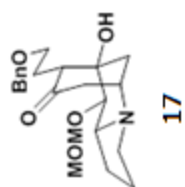
The COSY Spectrum of Compound **16**



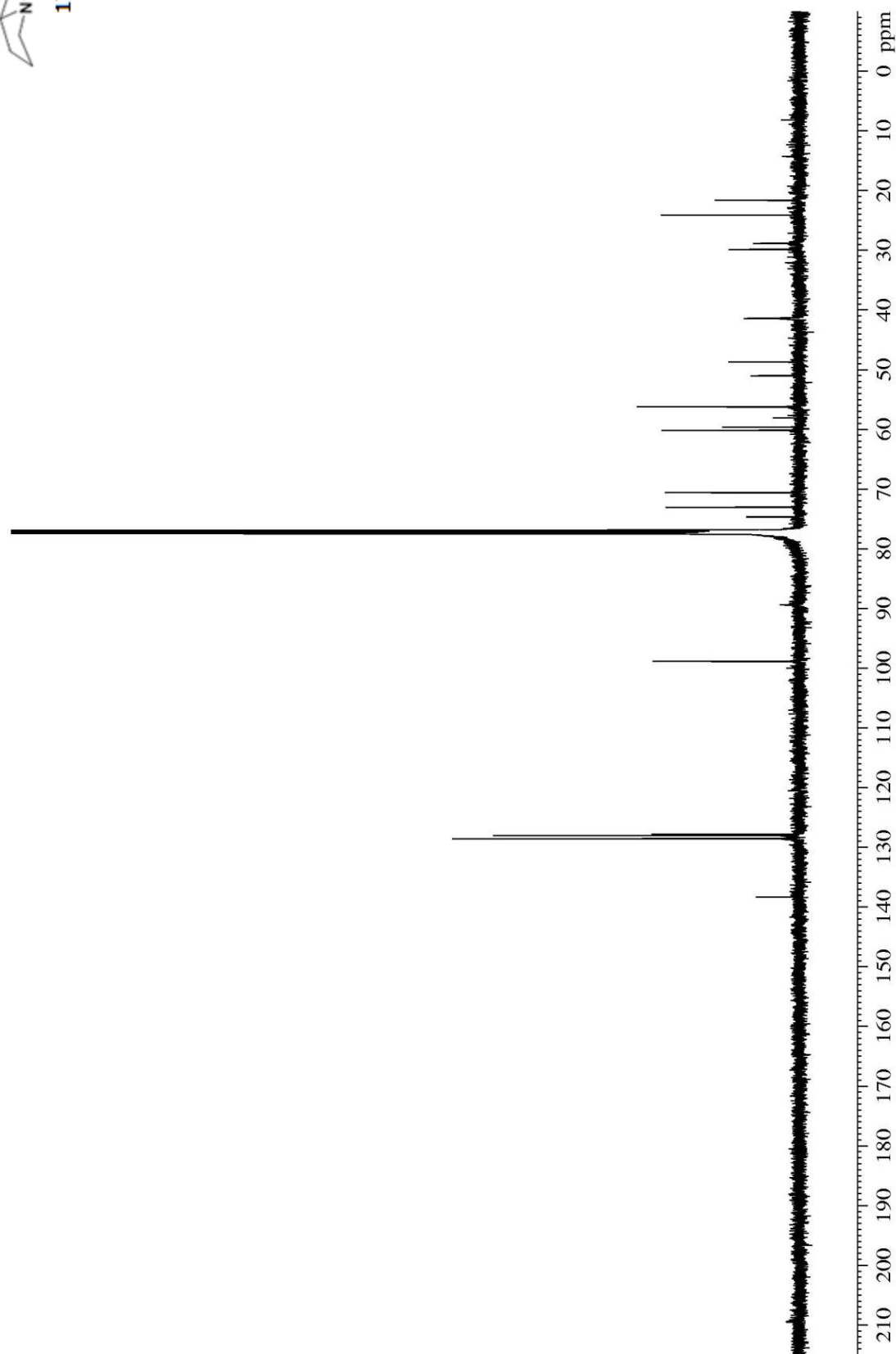
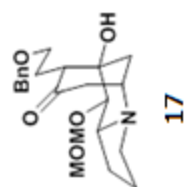
16



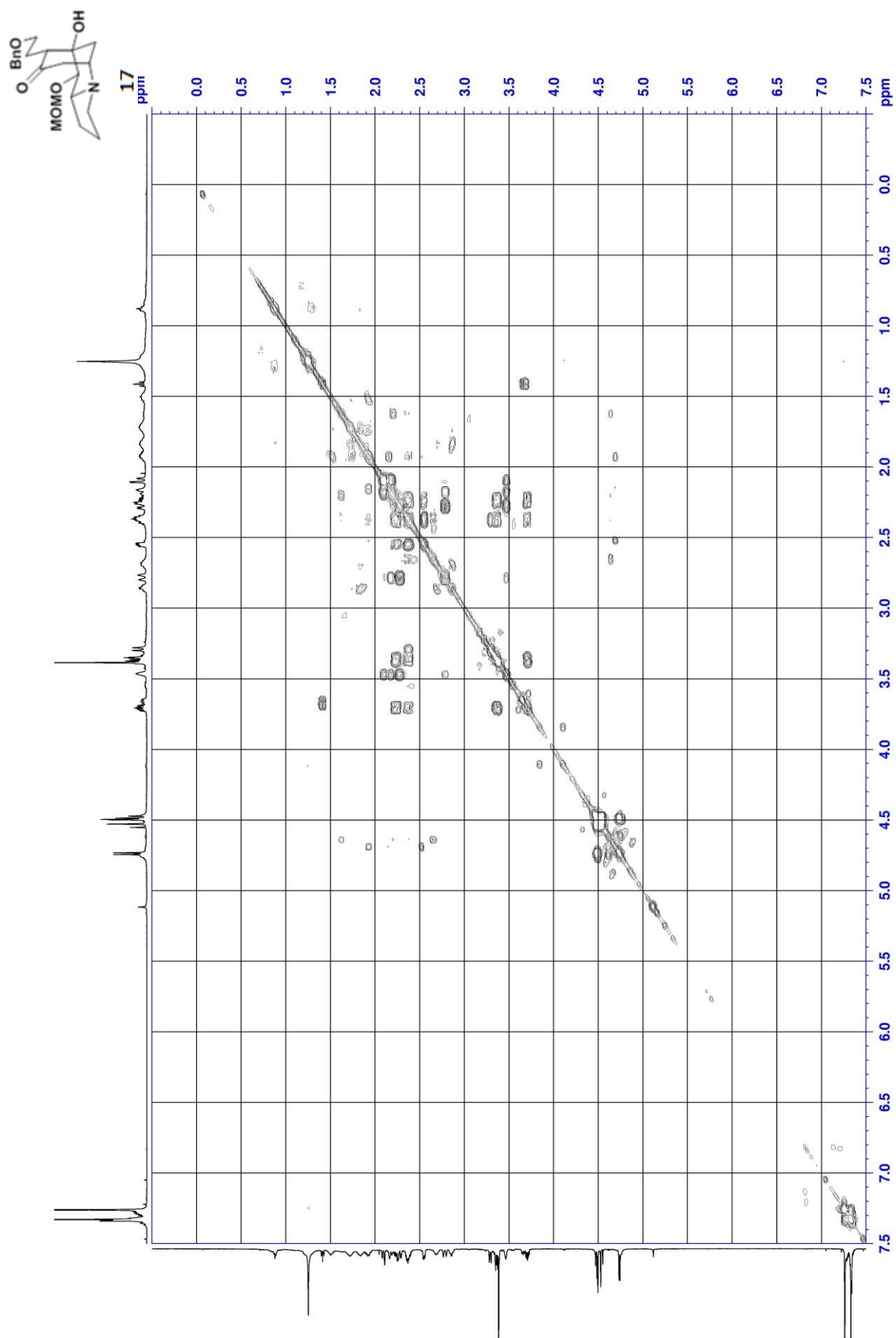
The NOESY Spectrum of Compound 16



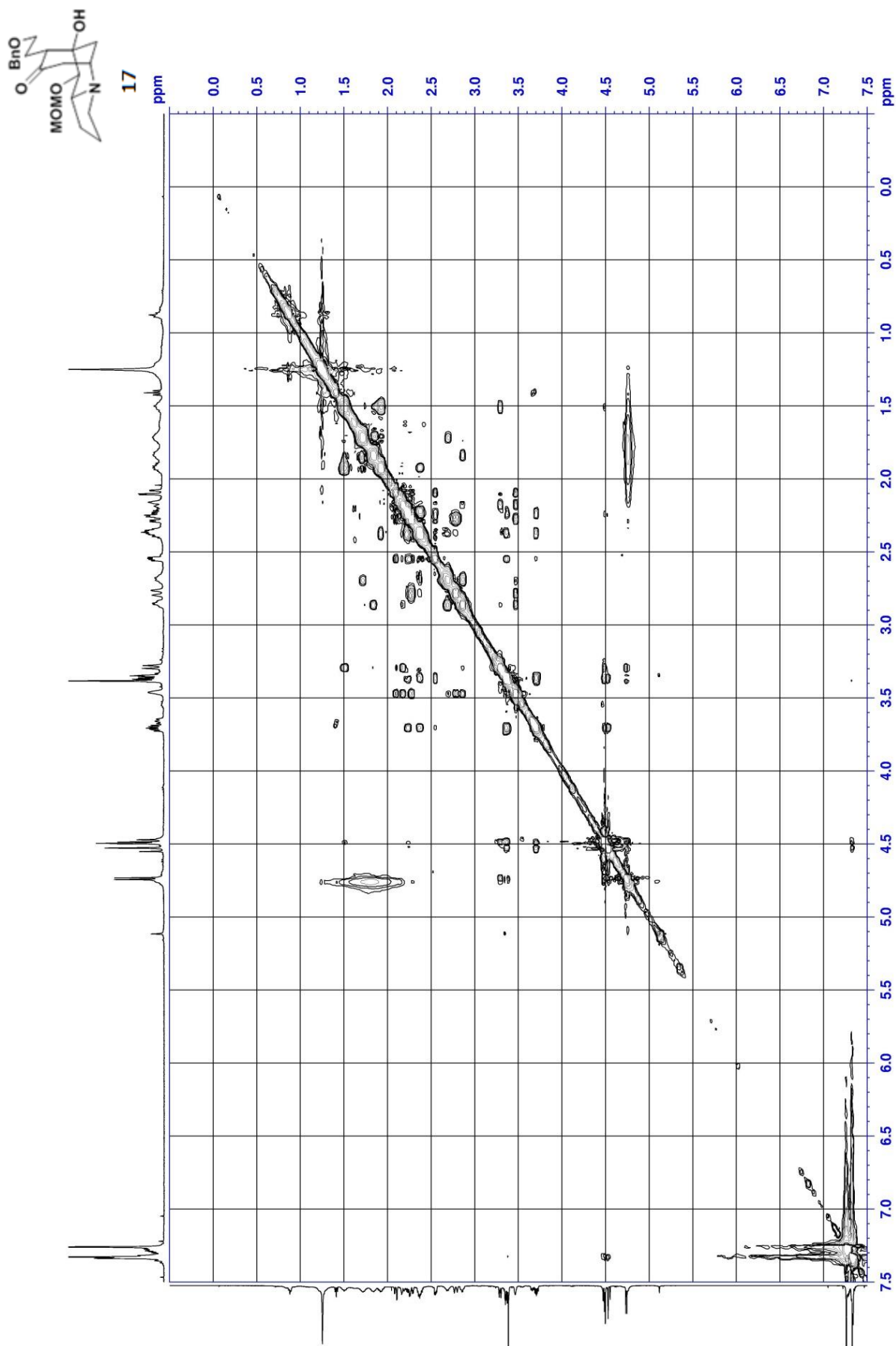
The 500 MHz ^1H NMR Spectrum of Compound **17**



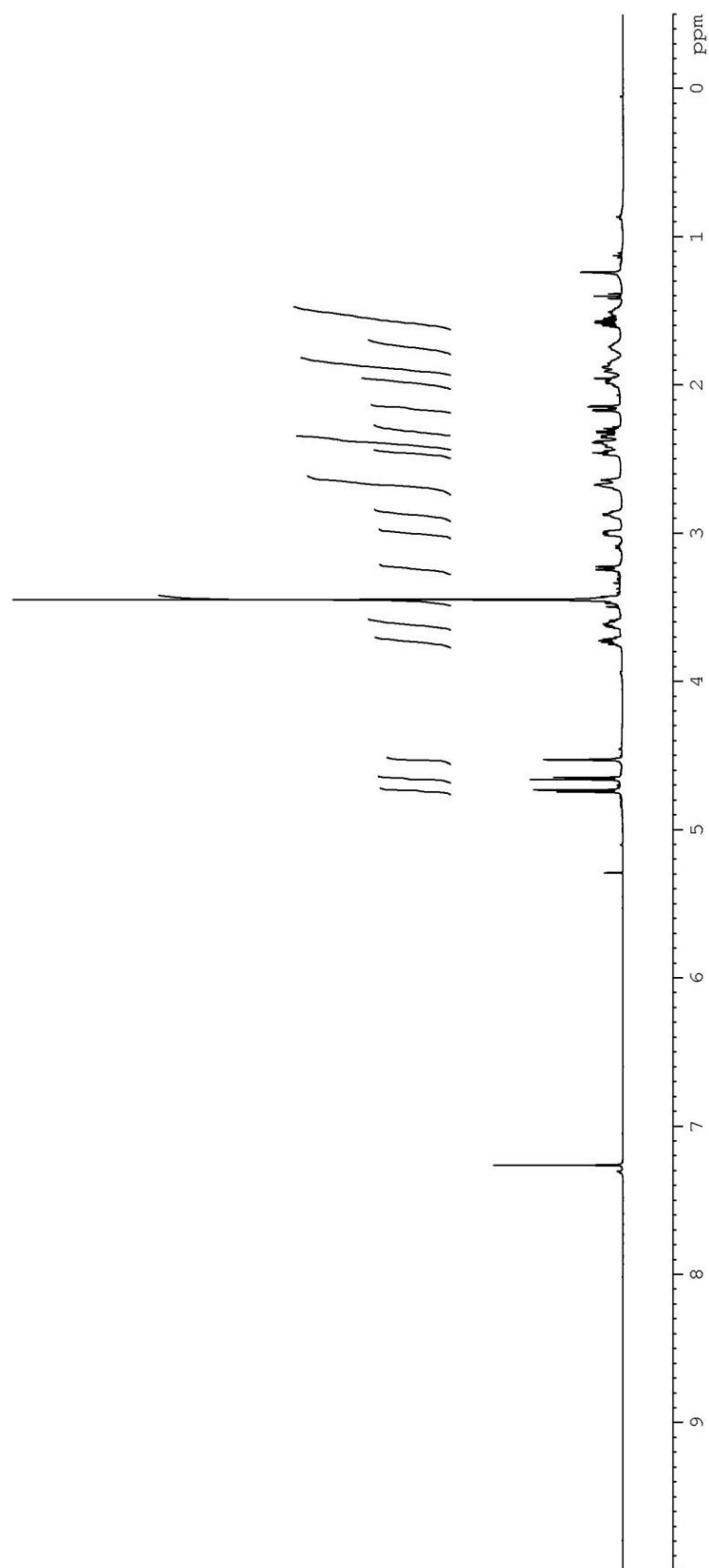
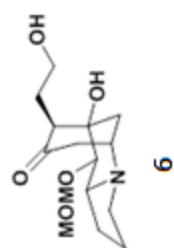
The 125 MHz ^{13}C NMR Spectrum of Compound **17**



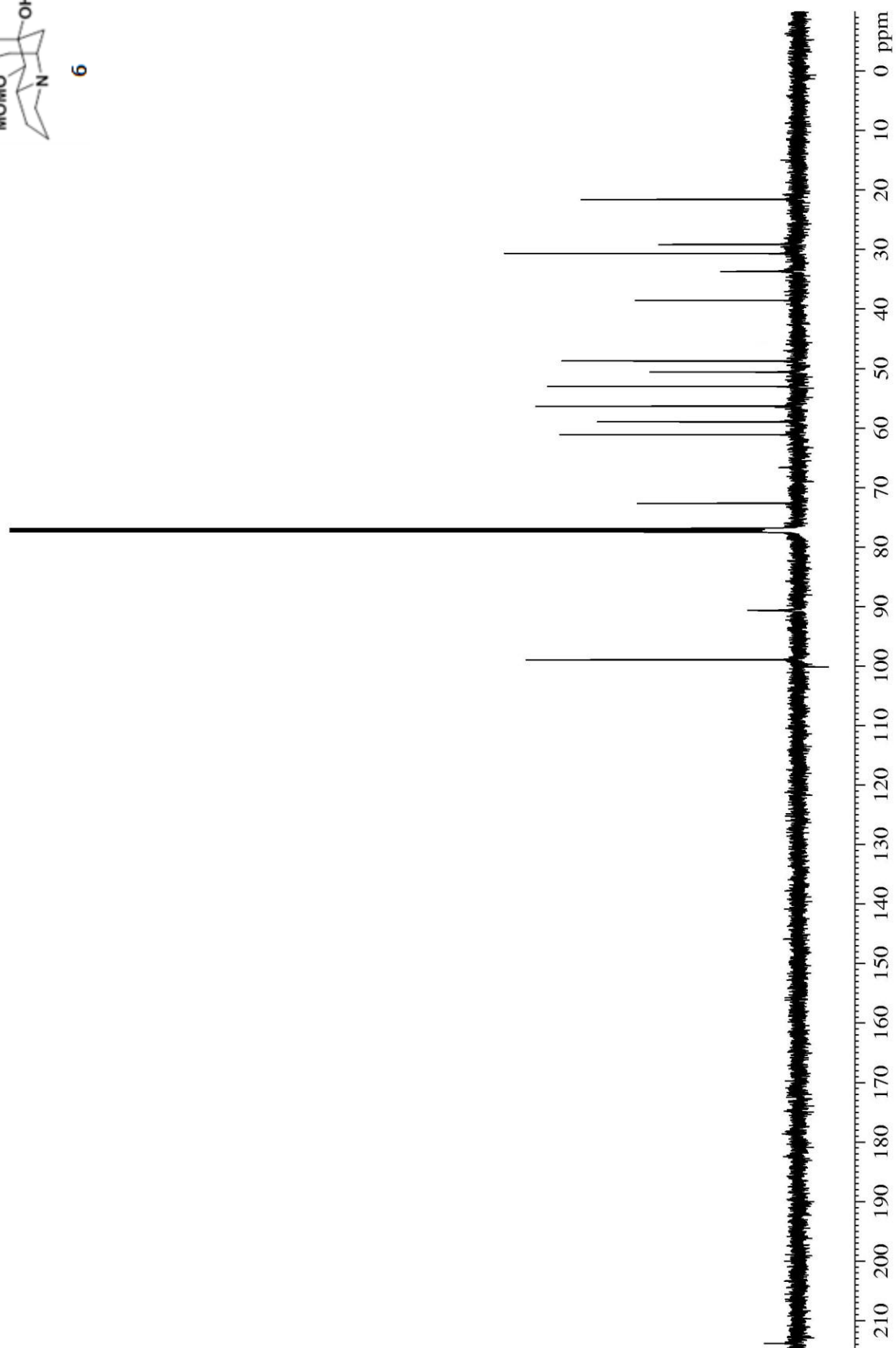
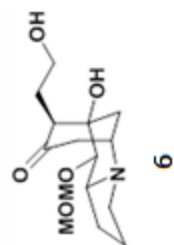
The COSY Spectrum of Compound 17



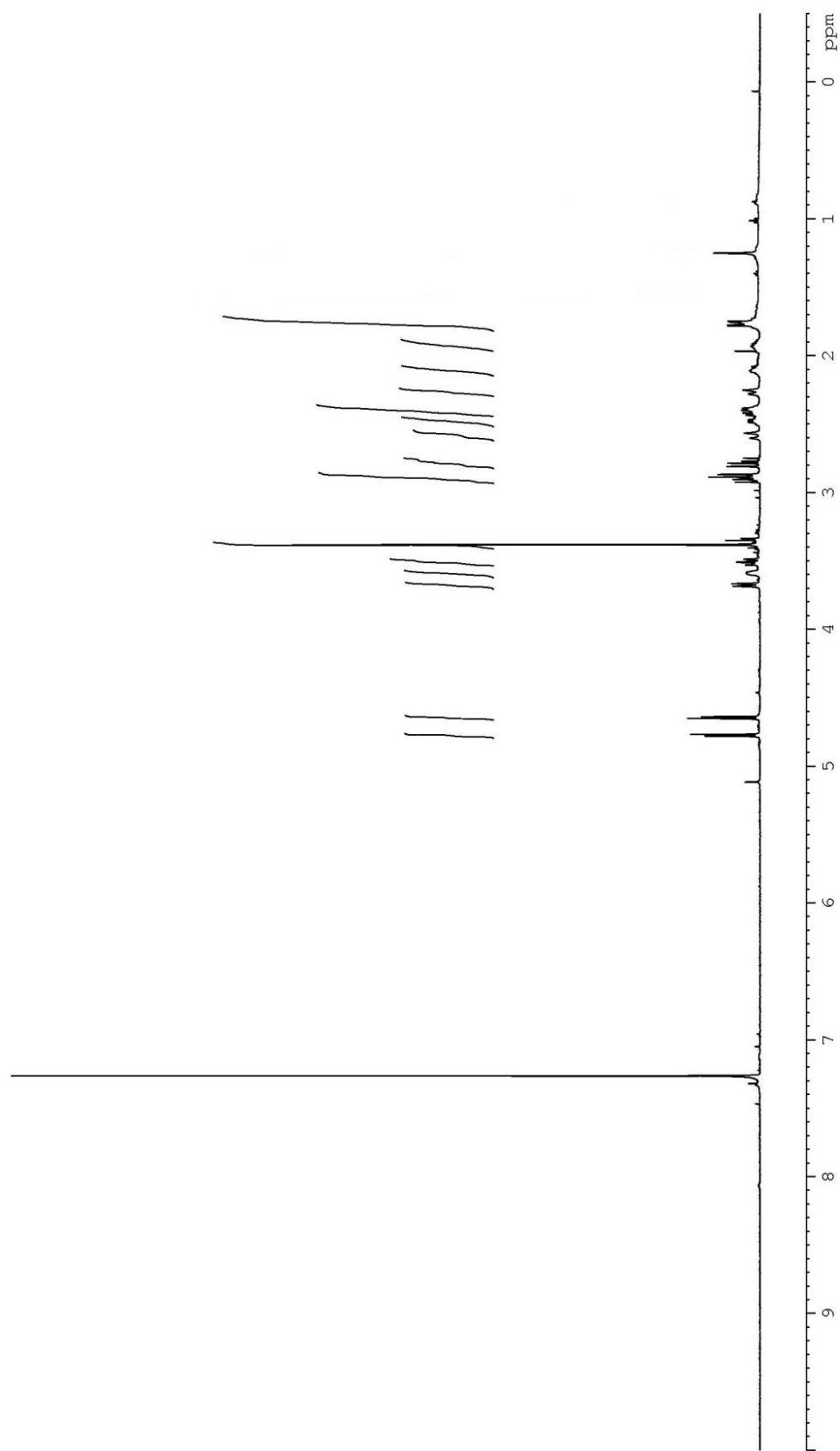
The NOESY Spectrum of Compound 17



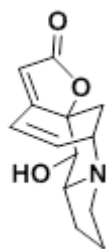
The 500 MHz ^1H NMR Spectrum of Compound **6**



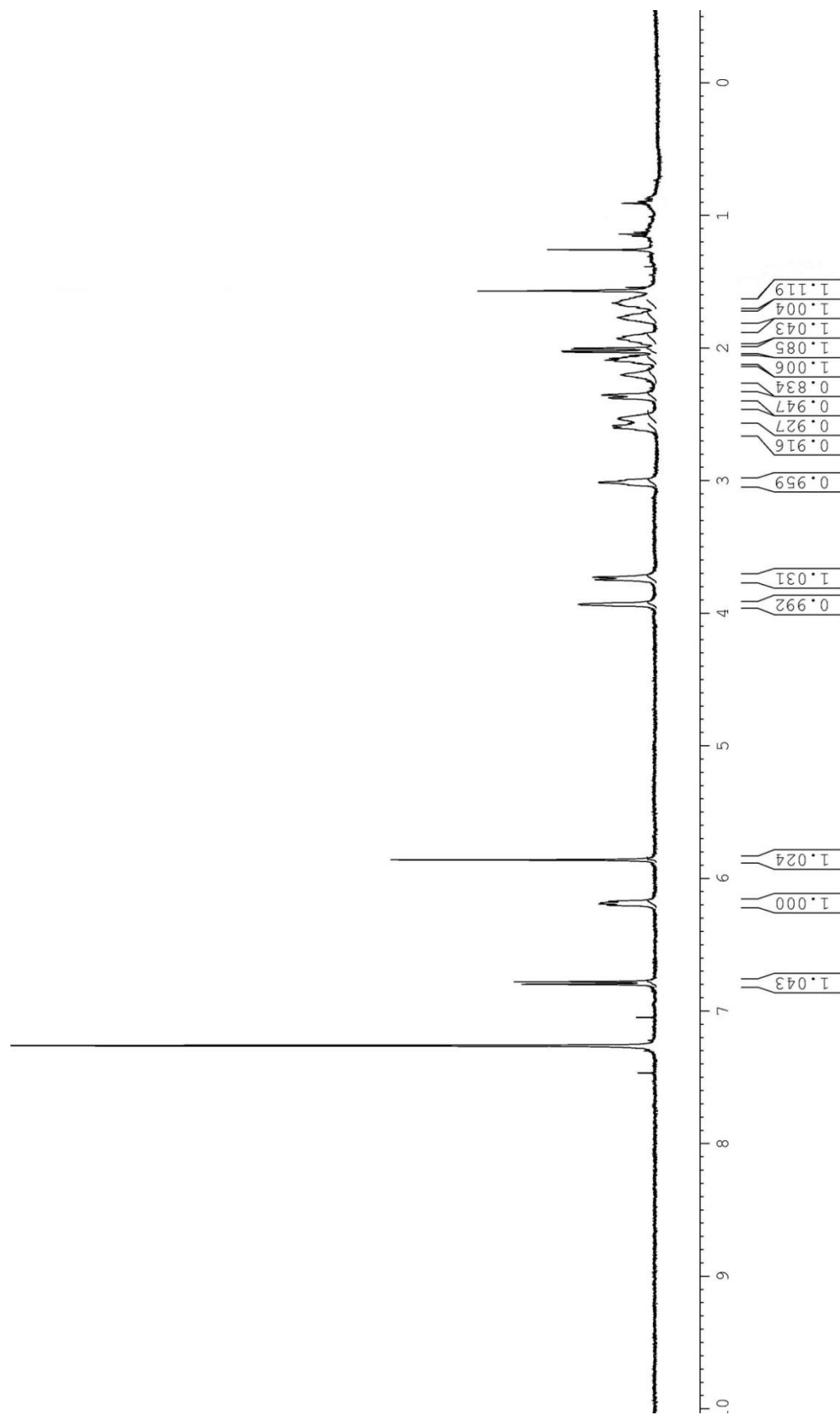
The 125 MHz ^{13}C NMR Spectrum of Compound **6**



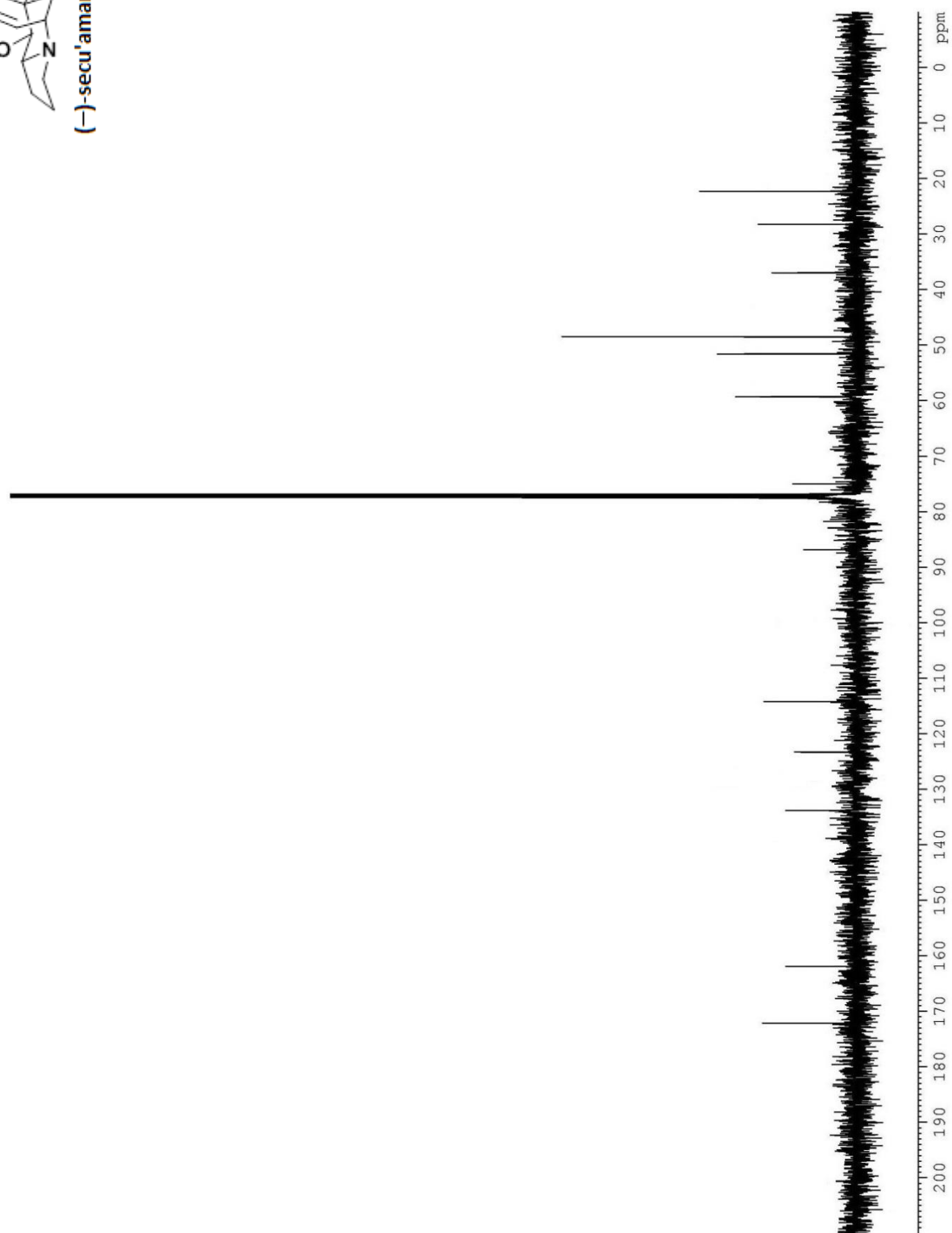
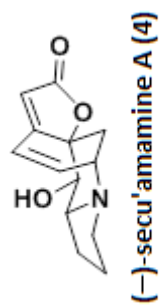
The 500 MHz ¹H NMR Spectrum of Compound **5**



(-)-secu'amine A (4)

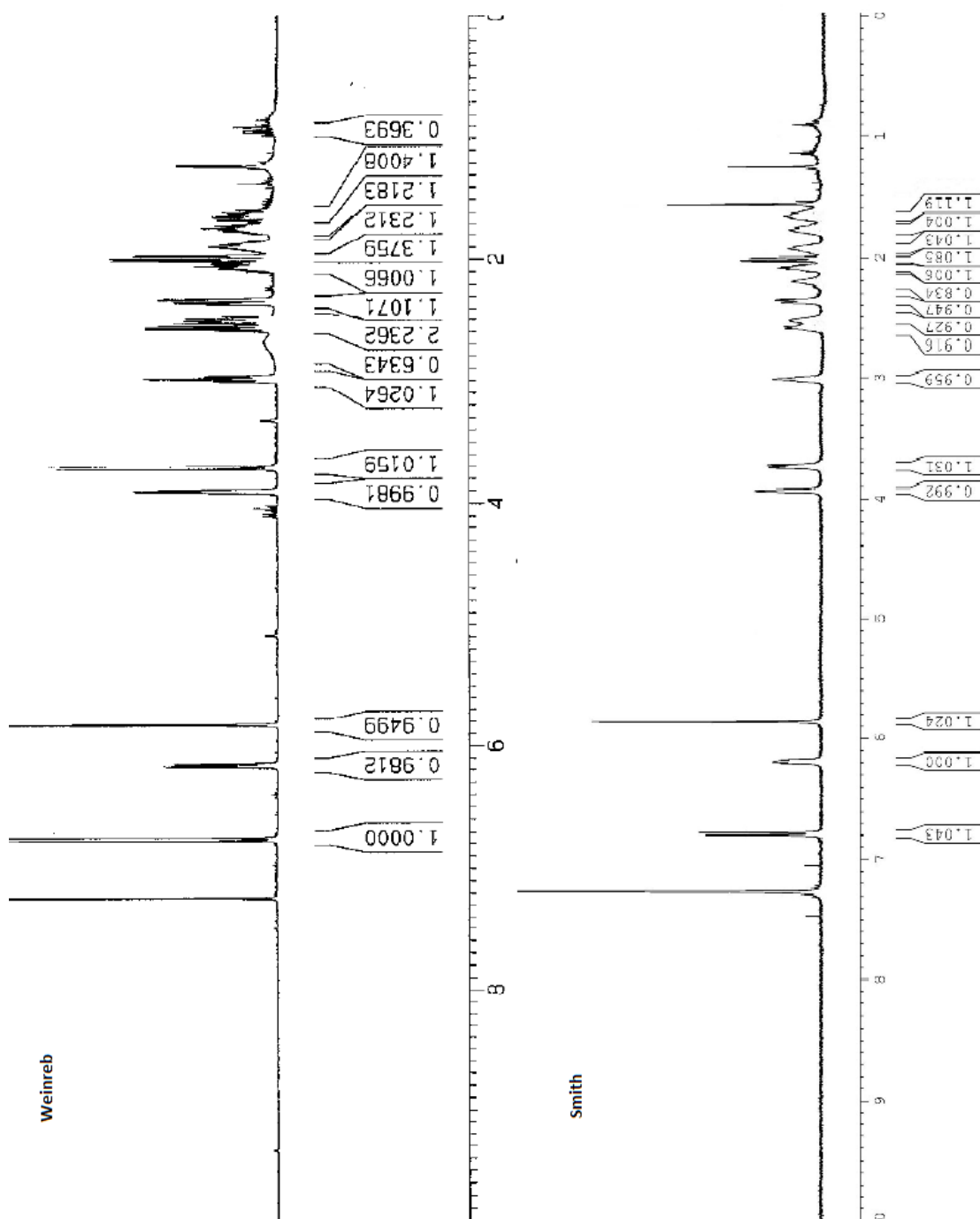


The 500 MHz ^1H NMR Spectrum of Compound **(-)-secu'amine A**



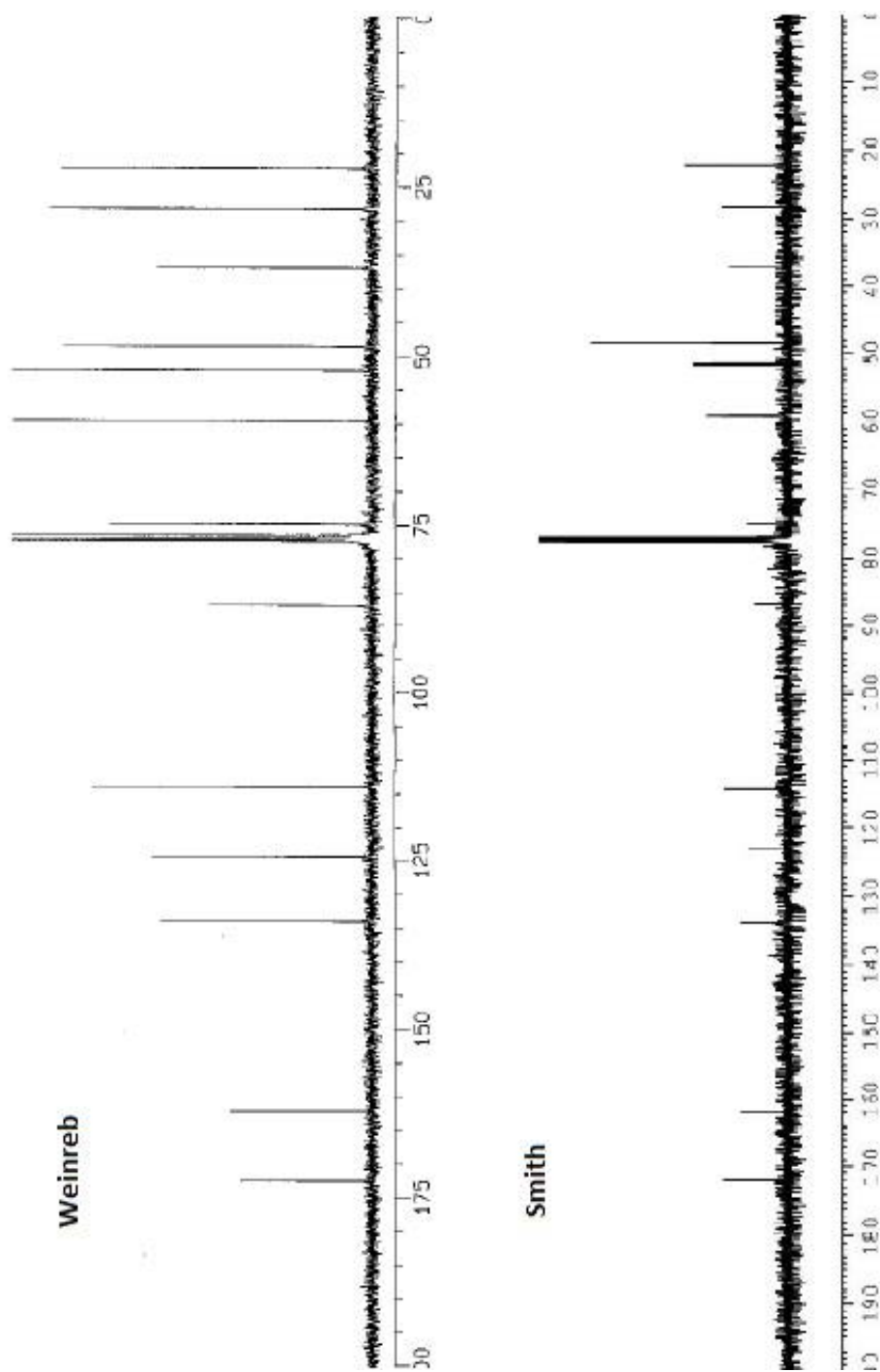
The 125 MHz ^{13}C NMR Spectrum of Compound (-)-secu'amine A

¹H NMR Data comparison of secu'amamine A- between Smith's lab and Weinreb's lab.



Smith	Weinreb	O-H
6.79	6.76	
6.18	6.16	
5.86	5.83	
3.63	3.9	
3.73	3.7	
3.02	2.98	
2.60-2.55	2.60-2.47	
2.55-2.50		
2.36	2.34	
2.2	2.68	
2.09-2.06	2.09-2.03	
2.01	1.98	
1.97-1.89	1.94-1.86	
1.82-1.75	1.78-1.72	
1.71-1.62	1.68-1.60	

¹³C NMR Data comparison of secu'amamine A- between Smith's lab and Weinreb's lab.



Smith	Weinreb
172.21	172.42
161.97	162.08
133.96	133.99
124.29	124.34
114.07	114.06
86.91	87.05
74.99	74.8
59.43	59.53
52.12	52.12
48.61	48.6
36.97	36.88
28.23	28.24
22.19	22.19