Supporting Information

A Short, Organocatalytic Formal Synthesis of (–)-Swainsonine and Related Alkaloids

Vijay Dhand, Jason A. Draper, Jarod Moore and Robert Britton*
Department of Chemistry, Simon Fraser University
8888 University Drive, Burnaby, B.C., Canada, V5A 1S6
E-mail: rbritton@sfu.ca

General

All reactions described were performed under an atmosphere of dry argon using oven dried glassware unless otherwise specified. Flash chromatography was carried out with 230-400 mesh silica gel (E. Merck, Silica Gel 60) following the technique described by Still.[1] Concentration and removal of trace solvents was done via a Büchi rotary evaporator using dry ice/acetone condenser and vacuum from water or air aspirator. Distillation requiring Kugelrohr apparatus was accomplished with a Büchi GKR-51.

All reagents and starting materials were purchased from Sigma Aldrich, Alfa Aesar, and/or TCI America and were used without further purification. All solvents were purchased from Sigma Aldrich, EMD, Anachemia or Caledon and used without further purification. Diisopropylamine and dichloromethane was freshly distilled over calcium hydride. Tetrahydrofuran was freshly distilled over Na metal.

Nuclear magnetic resonance (NMR) spectra were recorded using deuterochloroform ($CDCl_3$, MeOD, or C_6D_6). Signal positions (δ) are given in parts per million from tetramethylsilane (δ 0) and were measured relative to the signal of the solvent ($CDCl_3$: δ 7.26, MeOD: δ 3.34, C_6D_6: δ 7.16, ^{1}H NMR; $CDCl_3$: δ 77.00, MeOD: δ 49.86, C_6D_6: δ 128.06, ^{13}C NMR). Coupling constants (*J* values) are given in Hertz (Hz) and are reported to the nearest 0.1 Hz. ^{1}H NMR spectral data are tabulated in the order: multiplicity (s, singlet; d, doublet; t, triplet; m, multiplet), number of protons, coupling constants, assignment (where possible). NMR spectra were recorded on a Bruker Avance 600 equipped with a QNP or TCI cryoprobe (600 MHz), Bruker 500 (500 MHz), or Bruker 400 (400 MHz). Assignments of ^{1}H and ^{13}C NMR spectra are based on analysis of ^{1}H-^{1}H COSY, HSQC, HMBC, TOCSY and 1D NOESY spectra.

Infrared (IR) spectra were recorded on a MB-series Bomem/Hartman & Braun Fourier transform spectrophotometer with sodium chloride plates. Only selected, characteristic absorption data are provided for each compound.

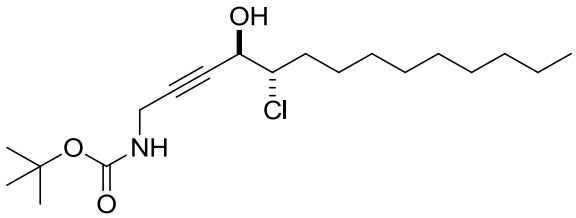
High resolution mass spectra were performed on an Agilent 6210 TOF LC/MS or Bruker micrOTOF-II LC mass spectrometer.

Optical rotation was measured on a Perkin Elmer Polarimeter 341 at 589 nm or a Rudolph Research Autopol II Polarimeter at 589 nm.

[1] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923-2925.

Experimental Procedures

Preparation of (4*R**,5*S**)-*N*-Boc-5-chloro-4-hydroxytetradec-2-yn-1-amine (9)



To a cold (0 °C), stirred solution of diisopropylamine (0.36 mL, 2.6 mmol) in tetrahydrofuran (12 mL), was added a solution of *n*-butyllithium (2.59 M in hexanes, 0.85 mL, 2.2 mmol). The mixture was stirred for 20 minutes and then cooled to -78 °C. To this solution was added protected propargylamine **8**[2] (416 mg, 1.8 mmol) in THF (1.0 mL) dropwise and the resulting mixture was stirred for 40 minutes. A solution of 2-chloroundecanal (**7**)[3] (300 mg, 1.4 mmol) in THF (1.5 mL) was added dropwise. After stirring for 20 minutes at -78 °C, a solution of tetrabutylammonium fluoride (1.0 M in THF, 1.5 mL) was added and the reaction mixture was stirred for an additional 15 minutes. After this time, the reaction was treated with a saturated aqueous solution of NH_4Cl (5 mL), and diluted with ethyl acetate (15 mL) and water (15 mL).The phases were separated, and the aqueous phase was extracted with ethyl acetate (3 x 15 mL). The combined organic phases were washed with brine (15 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude product by flash chromatography (silica gel, 4:1 hexanes:ethyl acetate) afforded (4*R**,5*S**)-*N*-Boc-5-chloro-4-hydroxytetradec-2-yn-1-amine (9) (266 mg, 53%, >14:1 diastereomeric mixture) as a colourless oil.

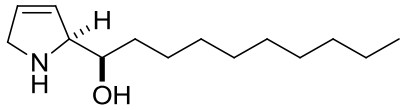
^{1}H NMR (600 MHz, CD_3OD) δ: 4.49 (m, 1H), 3.93 (m, 1H), 3.88 (s, 2H), 1.94 (m, 1H), 1.73 (m, 1H), 1.61 (m, 1H), 1.47 (s, 9H), 1.41-1.30 (m, 13H), 0.93 (t, 3H, J = 6.7 Hz).

^{13}C NMR (150 MHz, CD_3OD) δ: 158.9, 84.6, 81.9, 81.4, 68.1, 67.8, 35.3, 33.9, 31.7, 31.5, 31.5, 31.3, 31.1, 29.6, 28.4, 24.6, 15.3.

IR (neat): 3350, 2922, 2849, 1691 cm^{-1}

Exact mass calcd. for $C_{19}H_{34}{}^{35}ClNO_3$: 359.2227 (M)+; found: 359.2223 (M)+.

Preparation of hydroxyalkyl dihydropyrrole (12)



To a cold (0 °C), stirred solution of chlorohydrin **9** (100 mg, 0.27 mmol) and quinoline (4.4 μL, 0.037 mmol) in ethanol (5.0 mL) was added 5% Pd-$BaSO_4$ (30 mg, 0.014 mmol). The resulting

[2] Trost, B.M.; Lumb, J.P.; Azzarelli, J.M. *J. Am. Chem. Soc.* **2011**, *133*, 740-743.

[3] Kang, B.; Britton, R. *Org. Lett.* **2007**, *9*, 5083-5086.

mixture was stirred under an atmosphere of H_2 (balloon) at room temperature for 30 minutes and monitored by ^{1}H NMR spectroscopy. After reduction of the alkene was complete, the mixture was diluted with dichloromethane (4 mL) and filtered through a pad of Celite®, and the solvent was removed in vacuo to give the crude *cis*-alkene **10** (80 mg, 82%), which required no further purification.

^{1}H NMR (500 MHz, CD_3OD) δ: 5.62 (m, 2H), 4.54 (m, 1H), 3.94 (m, 1H), 3.81 (dd, 1H, J = 15.6, 5.6 Hz), 3.73 (dd, 1H, J = 15.6, 4.6 Hz), 1.87 (m, 1H), 1.62 (m, 1H), 1.46 (s, 9H), 1.43-1.28 (m, 14H), 0.93 (t, 3H, J = 6.9 Hz).

To a vial containing the crude *cis*-alkene **10** (20 mg, 0.055 mmol) was added ethereal HCl (2M, 0.5 mL). The reaction mixture was stirred at room temperature for 20 hours after which time the solvent was removed in vacuo. The resulting residue was dissolved in methanol (1.0 mL) and treated with aqueous solution of sodium hydroxide (2M, 1.0 mL). The reaction mixture was stirred for 3 hours after which time it was diluted with water (5 mL) and dichloromethane (5 mL). The phases were separated, and the aqueous phase was extracted with dichloromethane (3 x 5 mL). The combined organic phases were washed with brine (5 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude product by flash chromatography (silica gel, 70:30:1 dichloromethane:methanol:ammonium hydroxide) afforded hydroxyalkyl dihydropyrrole **12** (11 mg, 89%) as a colourless liquid.

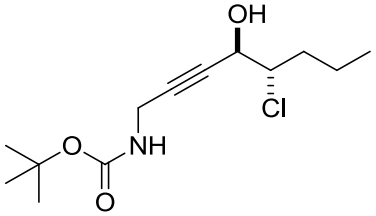
^{1}H NMR (500 MHz, CD_3OD) δ: 5.99 (m, 1H), 5.92 (m, 1H), 3.95 (m, 1H), 3.79 (m, 1H), 3.71 (m, 1H), 3.51 (m, 1H), 1.59 (m, 2H), 1.46-1.29 (m, 14H), 0.93 (t, 3H, J = 6.7 Hz).

^{13}C NMR (125 MHz, CD_3OD) δ: 131.3, 130.1, 75.4, 72.4, 55.1, 36.0, 33.9, 31.7, 31.6, 31.6, 31.3, 27.9, 24.6, 15.3.

IR (neat): 3266, 2921, 2851 cm^{-1}

Exact mass calcd for $C_{14}H_{28}NO$: 226.2293 (M+H)+; found: 226.2163 (M+H)+.

Preparation of (4*R,5*S**)-*N*-Boc-5-chloro-4-hydroxyoct-2-yn-1-amine (15a)**



To a cold (–78 °C), stirred solution of *N*-Boc-propargylamine (200 mg, 1.3 mmol) in THF (7.0 mL) was added a solution of *n*-butyllithium (2.66 M in hexanes, 1.0 mL, 2.7 mmol) dropwise. The resulting mixture was stirred at –78 °C for 1 hour. After this time, a solution of 2-chloropentanal[3] (155 mg, 1.3 mmol) in THF (0.8 mL) was added dropwise and the resulting mixture was stirred for an additional 20 minutes. The reaction mixture was then treated with a saturated aqueous solution of NH_4Cl (5 mL), and diluted with ethyl acetate (10 mL) and water (10 mL).The phases were separated, and the aqueous phase was extracted with ethyl acetate (3 x 10 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and

concentrated in vacuo. Purification of the crude product by flash chromatography (silica gel, 4:1 hexanes:ethyl acetate) afforded (4*R**,5*S**)-*N*-Boc-5-chloro-4-hydroxyoct-2-yn-1-amine (**15a**) (158 mg, 44%, 14:1 diastereomeric mixture) as a colourless oil.

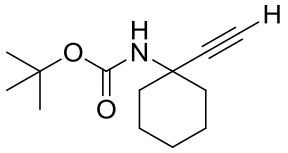
^{1}H NMR (600 MHz, CD_3OD) δ: 4.49 (m, 1H), 3.95 (dt, 1H, *J* = 10.1, 3.8 Hz), 3.88 (br s, 2H), 1.90 (m, 1H), 1.73 (m, 1H), 1.64 (m, 1H), 1.47 (s, 9H), 1.45 (m, 1H), 0.98 (t, 3H, *J* = 7.4 Hz).

^{13}C NMR (150 MHz, CD_3OD) δ: 158.9, 84.6, 81.9, 81.4, 67.8, 67.7, 37.3, 31.7, 29.6, 21.5, 14.7.

IR (neat): 3379, 2999, 2961, 1691, 1367 cm^{-1}

Exact mass calcd. for $C_{13}H_{22}{}^{35}ClNO_3$: 275.1288 (M)+; found: 275.1287 (M)+.

Preparation of *N*-Boc-1-ethynylcyclohexyl amine



To a stirred solution of 1-ethynylcyclohexylamine (0.66 mL, 4.8 mmol) in THF (40 mL) was added Di-*tert*-butyl dicarbonate (1.2 mL, 5.4 mmol) at 40 °C and the mixture was allowed to stir for 22 hours. After this time, the reaction mixture was concentrated in vacuo. Purification of the crude product by flash chromatography (silica gel, 15:1 hexanes:ethyl acetate) afforded *N*-Boc-1-ethynylcyclohexyl amine (1.1 g, 99%) as a white solid (m.p. 96-98°C).

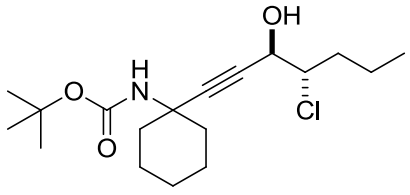
^{1}H NMR (600 MHz, $CDCl_3$) δ: 4.59 (br s, 1H), 2.36 (s, 1H), 2.07 (m, 2H), 1.71-1.54 (m, 7H), 1.45 (s, 9H), 1.26 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ: 154.0, 86.0, 79.5, 70.8, 51.1, 37.2, 28.4, 25.2, 22.3.

IR (neat): 3291, 3243, 3127, 2969, 2926, 2852, 1692 cm^{-1}

Exact mass calcd. for $C_{13}H_{22}NO_2$: 224.1672 (M+H)+; found: 224.1644 (M+H)+.

Preparation of (±)-chlorohydrin 15b



To a cold (–78 °C), stirred solution of *N*-Boc-1-ethynylcyclohexyl amine (150 mg, 0.67 mmol) in THF (4.0 mL) was added a solution of *n*-butyllithium (2.66 M in hexanes, 0.53 mL, 1.4 mmol) dropwise and the mixture was stirred for 1.5 hours. After this time, a solution of 2-chloropentanal[3] (81 mg, 0.67 mmol) in THF (0.45 mL) was added dropwise and the resulting mixture was stirred for an additional 20 minutes. The reaction mixture was then treated with a

saturated aqueous solution of NH_4Cl (3 mL), and diluted with ethyl acetate (10 mL) and water (10 mL).The phases were separated, and the aqueous phase was extracted with ethyl acetate (3 x 10 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude product by flash chromatography (silica gel, 6:1 hexanes:ethyl acetate) afforded chlorohydrin **15b** (200 mg, 87%, 10:1 diastereomeric mixture) as a colourless oil.

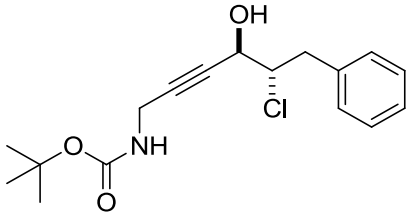
^{1}H NMR (600 MHz, CD_3OD) δ: 4.53 (d, 1H, J = 4.1 Hz), 3.98 (dt, 1H, J = 9.9, 3.7 Hz), 2.11 (br s, 2H), 1.94 (m, 1H), 1.79-1.58 (m, 10H), 1.47 (s, 9H), 1.30 (m, 1H), 0.98 (t, 3H, J = 7.4 Hz).

^{13}C NMR (150 MHz, CD_3OD) δ: 157.5, 90.1, 82.8, 80.9, 68.1, 67.9, 53.0, 39.2, 37.6, 29.7, 27.4, 24.4, 24.4, 21.6, 14.7.

IR (neat): 3356, 2995, 2926, 1692, 1367, 1275 cm^{-1}

Exact mass calcd. for $C_{18}H_{30}{}^{35}ClNO_3K$: 382.1614 (M+K)+; found: 382.1555 (M+K)+.

Preparation of (±)-chlorohydrin 15c



To a cold (–78 °C), stirred solution of *N*-Boc-propargylamine (700 mg, 4.5 mmol) in THF (20 mL) was added a solution of *n*-butyllithium (2.66 M in hexanes, 3.6 mL, 9.5 mmol) dropwise. The resulting mixture was stirred at –78 °C for 1 hour. After this time, a solution of 2-chlorohydrocinnamaldehyde[4] (760 mg, 4.5 mmol) in THF (3.2 mL) was added dropwise and the resulting mixture was stirred for an additional 20 minutes. The reaction mixture was then treated with a saturated aqueous solution of NH_4Cl (6 mL), and diluted with ethyl acetate (15 mL) and water (15 mL).The phases were separated, and the aqueous phase was extracted with ethyl acetate (3 x 15 mL). The combined organic phases were washed with brine (15 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude product by flash chromatography (silica gel, 4:1 hexanes:ethyl acetate) afforded (±)-chlorohydrin **15c** (669 mg, 46%, 11:1 diastereomeric mixture) as a colourless oil.

^{1}H NMR (600 MHz, CD_3OD) δ: 7.33-7.23 (m, 5H), 4.48 (m, 1H), 4.17 (m, 1H), 3.92 (br s, 2H), 3.38 (s, 1H), 3.30 (dd, 1H, J = 14.3, 5.5 Hz), 3.00 (dd, 1H, J = 14.3, 9.0 Hz), 1.47 (s, 9H).

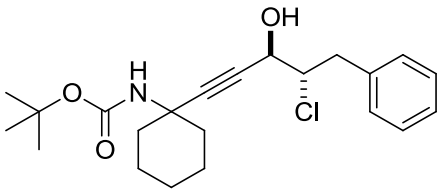
^{13}C NMR (150 MHz, CD_3OD) δ: 158.9, 139.9, 131.3, 130.3, 128.6, 85.3, 81.5, 81.5, 68.4, 67.1, 42.0, 31.7, 29.6.

IR (neat): 3368, 2977, 2930, 1691, 1396, 1366 cm^{-1}

[4] Halland, N.;Braunton, A.; Bachmann, S.; Marigo, M.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2004**, 126, 4790.

Exact mass calcd. for $C_{17}H_{22}{}^{35}ClNO_3$: 323.1388 (M)+; found: 323.1288 (M)+.

Preparation of (±)-chlorohydrin 15d



To a cold (–78 °C), stirred solution of *N*-Boc-1-ethynylcyclohexyl amine (700 mg, 3.1 mmol) in THF (18 mL) was added a solution of *n*-butyllithium (2.66 M in hexanes, 2.5 mL, 6.6 mmol) dropwise and the mixture was stirred for 1.5 hours. After this time, a solution of 2-chlorohydrocinnamaldehyde[5] (528 mg, 3.1 mmol) in THF (2.5 mL) was added dropwise and the resulting mixture was stirred for an additional 20 minutes. The reaction mixture was then treated with a saturated aqueous solution of NH_4Cl (7 mL), and diluted with ethyl acetate (15 mL) and water (15 mL).The phases were separated, and the aqueous phase was extracted with ethyl acetate (3 x 15 mL). The combined organic phases were washed with brine (15 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude product by flash chromatography (silica gel, 6:1 hexanes:ethyl acetate) afforded (±)-chlorohydrin **15d** (800 mg, 66%, 9:1 diastereomeric mixture) as a colourless oil.

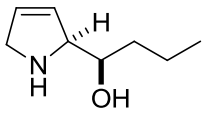
^{1}H NMR (600 MHz, CD_3OD) δ: 7.33-7.24 (m, 5H), 4.51 (d, 1H, J = 3.8 Hz), 4.19 (m, 1H), 3.37 (s, 1H), 3.36 (m, 1H), 3.03 (dd, 1H, J = 14.4, 8.8 Hz), 2.17 (m, 2H), 1.76 (m, 2H), 1.65 (m, 5H), 1.47 (s, 9H), 1.33 (m, 1H).

^{13}C NMR (150 MHz, CD_3OD) δ: 157.5, 140.0, 131.3, 130.3, 128.6, 90.8, 82.3, 81.0, 68.9, 67.2, 53.1, 42.1, 39.3, 29.7, 29.7, 27.4, 24.4, 24.4.

IR (neat): 3342, 2965, 1692, 1490 cm^{-1}

Exact mass calcd. for $C_{22}H_{30}{}^{35}ClNO_3Na$: 414.1914 (M+Na)+; found: 414.1815 (M+Na)+.

Preparation of hydroxyalkyl dihydropyrrole 16a



To a cold (0 °C), stirred solution of chlorohydrin **15a** (101 mg, 0.36 mmol) and quinoline (2.2 µL, 0.018 mmol) in ethanol (3.0 mL) was added 5% Pd-$BaSO_4$ (103 mg, 0.048 mmol). The resulting mixture was stirred under an atmosphere of H_2 (balloon) at room temperature for 30 minutes (reaction monitored by ^{1}H NMR spectroscopy). After this time the mixture was diluted with dichloromethane (4 mL) and filtered through a pad of Celite®, and the solvent was removed in vacuo to afford the crude *cis*-alkene (104 mg), which was used in the next step without further purification.

^{1}H NMR (400 MHz, CD_3OD) δ: 5.63-5.60 (m, 2H), 4.54 (m, 1H), 3.95 (m, 1H), 3.82 (dd, 1H, *J* = 15.7, 6.2 Hz), 3.72 (dd, 1H, *J* = 15.7, 4.4 Hz), 1.84 (m, 1H), 1.72-1.58 (m, 3H), 1.46 (s, 9H), 0.98 (t, 3H, *J* = 7.4 Hz).

To a vial containing the crude *cis*-alkene (104 mg, 0.37 mmol) was added ethereal HCl (2M, 0.8 mL). The reaction mixture was stirred at room temperature for 23 hours after which time the solvent was removed in vacuo. The resulting residue was dissolved in methanol (1.5 mL) and treated with aqueous solution of sodium hydroxide (2M, 1.6 mL). The reaction mixture was stirred for 4 hours after which time it was diluted with water (10 mL) and dichloromethane (10 mL). The phases were separated, and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude product by flash chromatography (silica gel, 70:30:1 dichloromethane:methanol:ammonium hydroxide) afforded hydroxyalkyl dihydropyrrole **16a** (23 mg, 45% over 3 steps) as a white solid (m.p. 101-103°C).

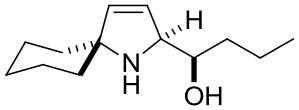
^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.95 (m, 1H), 5.75 (m, 1H), 4.13 (m, 1H), 3.84 (m, 1H), 3.75 (m, 1H), 3.49 (m, 1H), 1.56 (m, 1H), 1.47-1.36 (m, 3H), 0.94 (t, 3H, *J* = 7.4 Hz).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 130.7, 126.9, 72.9, 69.4, 53.9, 35.5, 19.5, 14.2.

IR (neat): 3351, 2956, 2923 cm^{-1}

Exact mass calcd. for $C_8H_{16}NO$: 142.1254 (M+H)+; found: 142.1232 (M+H)+.

Preparation of hydroxyalkyl dihydropyrrole 16b



To a cold (0 °C), stirred solution of chlorohydrin **15b** (183 mg, 0.53 mmol) and quinoline (3.1 μL, 0.027 mmol) in ethanol (4.0 mL) was added 5% Pd-$BaSO_4$ (150 mg, 0.071 mmol). The resulting mixture was stirred under an atmosphere of H_2 (balloon) at room temperature for 2.5 hours (reaction monitored by ^{1}H NMR spectroscopy). After this time, the mixture was diluted with dichloromethane (5 mL) and filtered through a pad of Celite®, and the solvent was removed in vacuo to afford the crude *cis*-alkene (172 mg), which was used in the next step without further purification.

^{1}H NMR (400 MHz, CD_3OD) δ: 5.66 (d, 1H, *J* = 12.1 Hz), 5.49 (dd, 1H, *J* = 12.9, 10.6 Hz), 4.85 (m, 1H), 3.92 (m, 1H), 2.02 (m, 1H), 1.94 (m, 1H), 1.83-1.48 (m, 12H), 1.46 (s, 9H), 0.96 (t, 3H, *J* = 7.1 Hz).

To a vial containing the crude *cis*-alkene (172 mg, 0.49 mmol) was added ethereal HCl (2M, 1.2 mL). The reaction mixture was stirred at room temperature for 20 hours after which time the solvent was removed in vacuo. The resulting residue was dissolved in methanol (2 mL) and treated with aqueous solution of sodium hydroxide (2M, 2.4 mL). The reaction mixture was stirred for 1 hour after which time it was diluted with water (10 mL) and dichloromethane (10 mL). The phases were separated, and the aqueous phase was extracted with dichloromethane (3 x

10 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude product by flash chromatography (silica gel, 95:5:1 dichloromethane:methanol:ammonium hydroxide) afforded hydroxyalkyl dihydropyrrole (**16b**) (85 mg, 77% over 3 steps) as a white solid (m.p. 69-71°C).

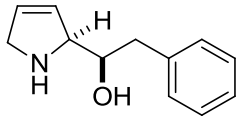
^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.90 (dd, 1H, *J* = 6.0, 2.1 Hz), 5.61 (dd, 1H, *J* = 6.0, 1.6 Hz), 4.16 (m, 1H), 3.40 (m, 1H), 1.62-1.35 (m, 14H), δ: 0.95 (t, 3H, *J* = 6.9 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.6, 124.6, 71.5, 67.6, 67.6, 40.0, 38.4, 35.4, 25.6, 23.7, 23.4, 19.6, 14.2.

IR (neat): 3394, 2926, 2848 cm^{-1}

Exact mass calcd. for $C_{13}H_{24}NO$: 210.1980 (M+H)+; found: 210.1852 (M+H)+.

Preparation of hydroxyalkyl dihydropyrrole 16c



To a cold (0 °C), stirred solution of chlorohydrin **15c** (43.5 mg, 0.13 mmol) and quinoline (2.1 µL, 0.018 mmol) in ethanol (1.0 mL) was added 5% Pd-$BaSO_4$ (14.3 mg, 0.0067 mmol) and the resulting suspension was stirred under an atmosphere of H_2 (balloon) at room temperature for 1 hour (reaction monitored by ^{1}H NMR spectroscopy). After this time, the mixture was diluted with dichloromethane (2 mL) and filtered through a pad of Celite®, and the solvent was removed in vacuo to afford the crude *cis*-alkene (45 mg), which was used in the next step without further purification.

^{1}H NMR (400 MHz, CD_3OD) δ: 7.33-7.24 (m, 5H), 5.72-5.64 (m, 2H), 4.59 (m, 1H), 4.18 (m, 1H), 3.78 (dd, 1H, *J* = 15.6, 6.1 Hz), 3.71 (dd, 1H, *J* = 15.7, 5.1 Hz), 3.26 (dd, 1H, *J* = 14.5, 4.2 Hz), 2.86 (dd, 1H, *J* = 14.5, 9.3 Hz), 1.46 (s, 9H).

To a vial containing the crude *cis*-alkene (45 mg, 0.14 mmol) was added ethereal HCl (2M, 0.9 mL). The reaction mixture was stirred at room temperature for 30 hours after which time the solvent was removed in vacuo. The resulting residue was dissolved in methanol (2 mL) and treated with aqueous solution of sodium hydroxide (2M, 1.8 mL). The reaction mixture was stirred for 3 hours after which time it was diluted with water (5 mL) and dichloromethane (5 mL). The phases were separated, and the aqueous phase was extracted with dichloromethane (3 x 5 mL). The combined organic phases were washed with brine (5 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude product by flash chromatography (silica gel, 70:30:1 dichloromethane:methanol:ammonium hydroxide) afforded hydroxyalkyl dihydropyrrole (**16c**) (12 mg, 49% over 3 steps) as a white solid (m.p. 98-100°C).

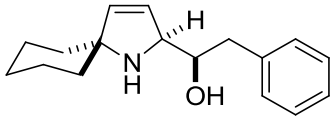
^{1}H NMR (500 MHz, CD_3OD) δ: 7.32-7.29 (m, 4H), 7.22 (m, 1H), 6.02 (m, 2H), 4.03 (m, 1H), 3.86-3.74 (m, 3H), 2.94 (dd, 1H, *J* = 13.8, 4.5 Hz), 2.73 (dd, 1H, *J* = 13.8, 8.7 Hz).

^{13}C NMR (125 MHz, CD_3OD) δ: 141.0, 131.4, 131.3, 130.2, 129.7, 128.1, 76.6, 71.9, 55.1, 42.4.

IR (neat): 3341, 3042, 2922, 1494, 1455 cm^{-1}

Exact mass calcd. for $C_{12}H_{16}NO$: 190.1254 (M+H)+; found: 190.1244 (M+H)+.

Preparation of hydroxyalkyl dihydropyrrole 16d



To a cold (0 °C), stirred solution of chlorohydrin **15d** (96.6 mg, 0.25 mmol) and quinoline (1.5 µL, 0.012 mmol) in ethanol (2.5 mL) was added 5% Pd-$BaSO_4$ (69.9 mg, 0.033 mmol) and the resulting suspension was stirred under an atmosphere of H_2 (balloon) at room temperature for 1.5 hours (reaction monitored by ^{1}H NMR spectroscopy). After this time, the mixture was diluted with dichloromethane (4 mL) and filtered through a pad of Celite®, and the solvent was removed in vacuo to afford the crude *cis*-alkene (101 mg), which was used in the next step without further purification.

^{1}H NMR (400 MHz, CD_3OD) δ: 7.31-7.22 (m, 5H), 5.73 (d, 1H, *J* = 12.0 Hz), 5.58 (dd, 1H, *J* = 12.0, 9.6 Hz), 5.00 (dd, 1H, *J* = 9.6, 3.9 Hz), 4.12 (m, 1H), 3.26 (dd, 1H, *J* = 14.5, 2.6 Hz), 2.79 (dd, 1H, *J* = 14.6, 10.9 Hz), 2.06 (m, 1H), 1.94 (m, 1H), 1.75 (m, 2H), 1.62-1.49 (m, 6H), 1.39 (s, 9H).

To a vial containing the crude *cis*-alkene (101 mg, 0.26 mmol) was added ethereal HCl (2M, 3.5 mL). The reaction mixture was stirred at room temperature for 2 days after which time the solvent was removed in vacuo. The resulting residue was dissolved in methanol (3 mL) and treated with aqueous solution of sodium hydroxide (2M, 7.0 mL). The reaction mixture was stirred for 2 hours after which time it was diluted with water (10 mL) and dichloromethane (10 mL). The phases were separated, and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude product by flash chromatography (silica gel, 95:5:1 dichloromethane:methanol:ammonium hydroxide) afforded hydroxyalkyl dihydropyrrole (**16d**) (50 mg, 78% over 3 steps, 9:1 diastereomeric mixture) as a white solid (m.p. 65-67°C).

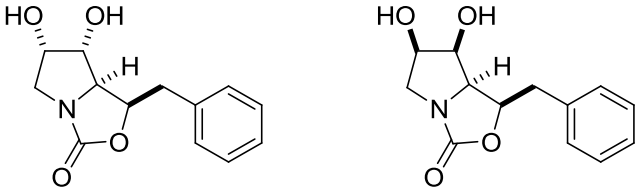
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.31-7.20 (m, 5H), 5.96 (dd, 1H, *J* = 6.1, 2.0 Hz), 5.75 (dd, 1H, *J* = 6.0, 1.6 Hz), 4.20 (m, 1H), 3.71 (m, 1H), 2.87 (dd, 1H, *J* = 13.8, 8.2 Hz), 2.76 (dd, 1H, *J* = 13.8, 5.6 Hz), 1.63-1.39 (m, 10H).

^{13}C NMR (150 MHz, $CDCl_3$) δ: 138.9, 138.7, 129.2, 128.4, 126.2, 124.5, 73.0, 67.6, 67.2, 39.7, 39.7, 38.2, 25.5, 23.7, 23.4.

IR (neat): 3377, 2921, 2844, 1490, 1448 cm^{-1}

Exact mass calcd. for $C_{17}H_{24}NO$: 258.1980 (M+H)+; found: 258.1852 (M+H)+.

Preparation of protected aminotriols 17a and 17b



To a cold (0 °C), stirred solution of hydroxyalkyl dihydropyrrole **16c** (40 mg, 0.21 mmol) in THF (1.2 mL) was added phosgene (20% in toluene, 123 µL, 0.23 mmol) dropwise. After the mixture was stirred at 0 °C for 15 minutes, triethylamine (71 µL, 0.51 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 15 minutes, then warmed to room temperature and stirred for an additional 45 minutes. After this time, the reaction mixture was diluted with ethyl acetate (4 mL) and filtered through a pad of Celite®, and the solvent was removed in vacuo. The residue was dissolved in hexanes (4 mL) and water (4 mL), and the phases were separated. The aqueous phase was extracted with hexanes (4 x 4 mL). The combined organic phases were washed with brine (4 mL), dried (Na_2SO_4), and concentrated to give the crude carbamate (43 mg), which was used in the next step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34-7.21 (m, 5H), 5.96 (m, 1H), 5.83 (m, 1H), 4.84 (m, 1H), 4.49-4.31 (m, 3H), 2.79 (dd, 1H, *J* = 13.8, 4.1 Hz), 2.68 (dd, 1H, *J* = 13.8, 9.2 Hz).

To a cold (0 °C), stirred solution of the crude carbamate (43 mg, 0.19 mmol) in acetone (1.3 mL) and water (0.9 mL) was added a crystal of osmium tetroxide followed by 4-methylmorpholine *N*-oxide (35 mg, 0.29 mmol). The reaction mixture was allowed to warm to room temperature slowly over 24 hours. After this time, the mixture was treated with a saturated aqueous solution of sodium hydrosulfite (4 mL), and diluted with ethyl acetate (5 mL) and water (5 mL). The phases were separated, and the aqueous phase was extracted with ethyl acetate (3 x 5 mL). The combined organic phases were washed with brine (5 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude product by flash chromatography (silica gel, 1:1 hexanes:ethyl acetate) afforded protected aminotriols **17a** and **17b** (21 mg, 40% over two steps) as an inseparable 3:2 mixture of diatereomers (colorless oil).

Data for protected aminotriols **17a**

^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.34-7.24 (m, 5H), 4.97 (m, 1H), 4.34 (m, 1H), 4.02 (m, 1H), 3.99 (dd, 1H, *J* = 13.5, 5.6 Hz), 3.90 (dd, 1H, *J* = 8.9, 7.3 Hz), 3.27 (dd, 1H, *J* = 13.4 Hz, 1.2 Hz), 3.19 (dd, 1H, *J* = 15.0, 4.2 Hz), 3.11 (dd, 1H, *J* = 15.0, 9.2 Hz), 2.74 (d, 1H, *J* = 2.8 Hz), 2.71 (d, 1H, *J* = 8.1 Hz).

^{13}C NMR (150 MHz, $CDCl_3$) δ: 161.1, 136.6, 129.0, 128.8, 127.1, 76.7, 71.1, 70.5, 64.2, 53.1, 36.1.

Data for protected aminotriols **17b**

^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.34-7.24 (m, 5H), 4.93 (m, 1H), 4.43 (m, 1H), 3.98 (m, 1H), 3.60 (d, 1H, *J* = 7.3 Hz), 3.53 (dd, 1H, *J* = 14.4, 7.3 Hz), 3.49 (dd, 1H, *J* = 11.4, 8.2 Hz), 3.43

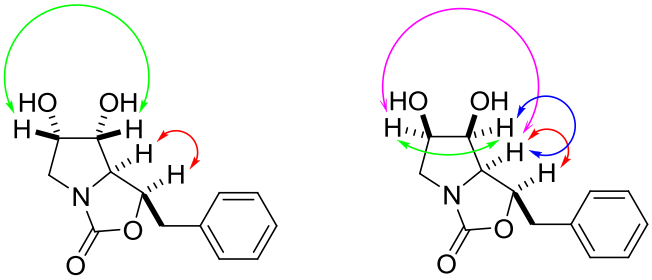
(dd, 1H, J = 11.6, 7.5 Hz), 3.31 (dd, 1H, J = 14.3, 7.3 Hz), 3.03 (d, 1H, J = 4.1 Hz), 2.79 (d, 1H, J = 5.7 Hz).

^{13}C NMR (150 MHz, $CDCl_3$) δ: 162.5, 136.6, 129.0, 128.7, 127.0, 76.9, 73.9, 71.0, 65.1, 50.1, 35.7.

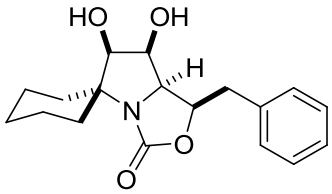
IR (neat): 3406, 3031, 2958, 2925, 1728, 1402, 1112 cm^{-1}

Exact mass calcd. for $C_{13}H_{16}NO_4$: 250.1074 $(M+H)^+$; found: 250.1068 $(M+H)^+$

Key nOe correlations for **17a** and **17b** (in $CDCl_3$):



Preparation of protected aminotriol 18



To a cold (0 °C), stirred solution of hydroxyalkyl dihydropyrrole (**16d**) (25 mg, 0.097 mmol) in THF (1.0 mL) was added phosgene (20% in toluene, 57 µL, 0.11 mmol) dropwise. After the mixture was stirred at 0 °C for 15 minutes, triethylamine (33 µL, 0.23 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 15 minutes, then warmed to room temperature and stirred for an additional 45 minutes. After this time, the reaction mixture was diluted with ethyl acetate (4 mL) and filtered through a pad of Celite®, and the solvent was removed in vacuo. The residue was diluted with hexanes (5 mL) and water (5 mL), and the phases were separated. The aqueous phase was extracted with hexanes (4 x 5 mL). The combined organic phases were washed with brine (5 mL), dried (Na_2SO_4), and concentrated to give the crude carbamate (30 mg), which was used in the next step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.31-7.20 (m, 5H), 6.34 (dd, 1H, J = 6.3, 2.3 Hz), 5.64 (dd, 1H, J = 6.3, 1.4 Hz), 5.13 (m, 1H), 4.79 (ddd, 1H, J = 8.1, 8.1, 6.0 Hz), 2.84 (dd, 1H, J = 14.3, 8.1 Hz), 2.75 (m, 1H), 2.69 (dd, 1H, J = 14.3, 6.0 Hz), 1.96-1.82 (m, 2H), 1.75-1.25 (m, 7H).

To a cold (0 °C), stirred solution of the crude carbamate (30 mg, 0.10 mmol) in acetone (1.0 mL) and water (0.7 mL) was added a crystal of osmium tetroxide followed by 4-methylmorpholine *N*-

oxide (18.6 mg, 0.16 mmol). The reaction mixture was allowed to warm to room temperature slowly over 24 hours. After this time, the mixture was treated with a saturated aqueous solution of sodium hydrosulfite (4 mL), and diluted with ethyl acetate (5 mL) and water (5 mL). The phases were separated, and the aqueous phase was extracted with ethyl acetate (3 x 5 mL). The combined organic phases were washed with brine (5 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude product by flash chromatography (silica gel, 1:1 hexanes:ethyl acetate) afforded protected aminotriol **18** (24 mg, 78% over 2 steps) as a white solid (m.p. 160-162°C).

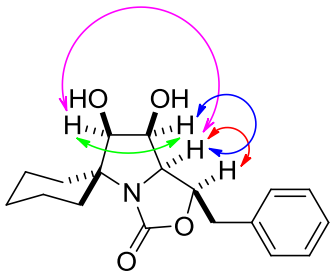
^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.33-7.24 (m, 5H), 4.86 (m, 1H), 4.09 (m, 1H), 3.93 (dd, 1H, *J* = 7.1, 4.3 Hz), 3.68 (dd, 1H, *J* = 7.8, 2.3 Hz), 3.45 (dd, 1H, *J* = 14.4, 7.3 Hz), 3.32 (dd, 1H, *J* = 14.1, 7.3 Hz), 2.76 (d, 1H, *J* = 1.9 Hz), 2.55 (m, 1H), 2.43 (d, 1H, *J* = 7.2 Hz), 1.98 (m, 1H), 1.75 (m, 2H), 1.65 (m, 2H), 1.48-1.40 (m, 4H).

^{13}C NMR (150 MHz, $CDCl_3$) δ: 157.1, 137.0, 129.0, 128.7, 126.9, 81.4, 75.1, 72.2, 64.7, 62.1, 38.8, 36.0, 27.7, 25.1, 23.3, 22.9.

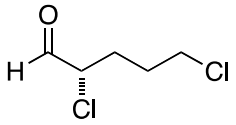
IR (neat): 3371, 2926, 2852, 1716, 1375, 1075 cm^{-1}

Exact mass calcd. for $C_{18}H_{24}NO_4$: 318.1700 $(M+H)^+$; found: 318.1692 $(M+H)^+$

Key nOe correlations (in $CDCl_3$)



Preparation of (-)-(2*S*)-2,5-dichloropentanal (21):



To a cold (–35 °C) stirred solution of (2*R*,5*S*)-2-*tert*-butyl-3,5-dimethylimidazolidin-4-one trifluoroacetic salt (471 mg, 1.66 mmol), LiCl (527 mg, 12.4 mmol), $Na_2S_2O_8$ (1.97 g, 8.29 mmol), $Cu(TFA)_2 \cdot 2H_2O$ (1.35 g, 4.15 mmol), in acetonitrile (66 mL) and H_2O (0.329mL, 18.2 mmol) was added 5-chloropentanal (**20**) (1.00 g, 8.29 mmol). After this solution was stirred for 19 days at -35 °C, the reaction mixture was quenched with water and diluted with pentane. The two phases were separated and the aqueous phase extracted with pentane (3 x 25 mL). The

combined organic layers were washed with brine (25 mL), dried (Na_2SO_4), and concentrated in vacuo. The resulting crude mixture was purified via flash chromatography (1:7 EtOAc: Hexanes) to provide (-)-(2*S*)-2,5-dichloropentanal (**21**) (797 mg, 62%) as a clear oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.55 (d, 1H, *J* = 1.9 Hz), 4.25 (ddd, 1H, *J* = 7.9, 4.9, 1.9 Hz), 3.62 (t, 2H, *J* = 6.0 Hz), 2.49 (m, 1H), 2.23 (m, 1H), 1.96-2.10 (m, 2H)

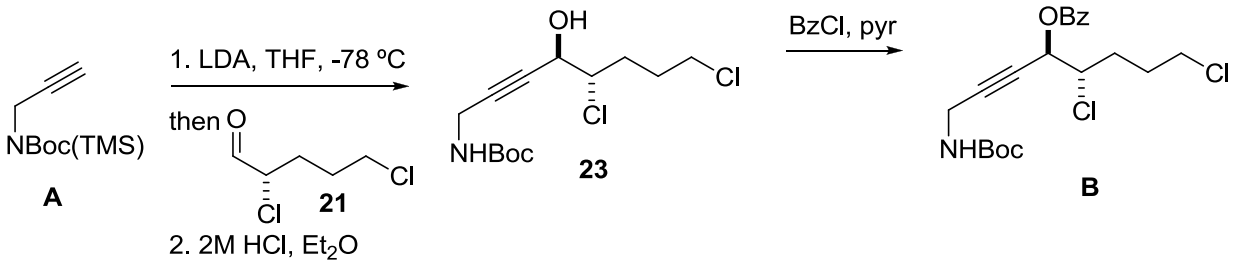
^{13}C NMR (100 MHz, $CDCl_3$) δ: 195.0, 63.0, 43.9, 29.2, 28.5

IR (neat, cm^{-1}): 2964, 1737, 1445, 1285

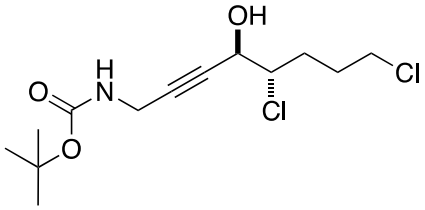
Exact mass calc'd for $C_5H_8{}^{35}Cl_2O$: 153.9952; found: 153.9948 $(M)^+$

$[\alpha]_D{}^{23}$: –24.3 (c = 1.11, $CHCl_3$)

The enantiomeric excess of 82% was determined by chiral HPLC analysis of the benzoyl ester derived from the addition of *N*-Boc-*N*-trimethylsilylpropargylamine **A** to both racemic and optically enriched **21**. Thus, to a solution of addition adduct **23** (22 mg, 0.074 mmol) in dry dichloromethane (0.75 mL) was added pyridine (60 μL, 0.74 mmol), and benzoyl chloride (90 μL, 0.74 mmol). The reaction mixture was allowed to stir overnight. After this time, the reaction was treated with saturated aqueous $NaHCO_3$ (2 mL) and diluted with dichloromethane (5 mL). The aqueous phase was extracted with dichloromethane (3 x 5 mL) and the combined organics were washed with brine (5 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by flash chromatography (1:4 EtOAc:Hexanes) to afford racemic or optically active benzoate **B**. Separation of the enantiomers was accomplished by HPLC (95:5 Hexanes:MeOH w/ 1% diethylamine, performed on an Agilent 1200 HPLC equipped with a variable wavelength UV-Vis detector and 0.46 cm x 25 cm Chiralcel OD-H chiral column). The retention times of the two enantiomers were 15.5 and 17.9 minutes. When this process was repeated with optically enriched α-chloroaldehyde **21** the ratio of the enantiomers was 9 (15.5 min):91 (17.9 min). The absolute configuration of the major enantiomer was confirmed as depicted for (-)-**23** (below) by conversion of this material into (-)-swainsonine (**1**).



Preparation of (-)-(4*R*,5*S*)-1-9*N*-*tert*-butoxycarbonyl)amino-5,8-dichloroocta-2-yn-4-ol (23):



To a cold (–78 °C), stirred solution of diisopropylamine (0.20 mL, 1.41 mmol) in dry THF (32 mL) was added was added *n*-BuLi (2.56 M, 0.47 mL, 1.2 mmol) dropwise over 3 min. After this solution was stirred for 40 minutes, *N*-*tert*-butoxycarbonyl-*N*-trimethylsilylpropargylamine (250 mg, 1.10 mmol) was added at –78 °C. After this solution was stirred for 1 hour, (–)-(2*S*)-2,5-dichloropentanal (285 mg, 1.84 mmol) was added dropwise over 5 minutes while the reaction temperature was maintained at –78 °C. The reaction mixture was stirred for 20 min then a solution of HCl in diethyl ether (2.0 M, 1.21 mL, 2.42 mmol) was added. This mixture was stirred for 5 min then treated with saturated aqueous NH_4Cl (10 mL) and EtOAc (10 mL). The resulting phases were separated and the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. The resulting crude product was purified via flash chromatography (1:4 EtOAc:Hexanes) to provide (–)-(4*R*,5*S*)-1-(*N*-*tert*-butoxycarbonyl)amino-5,8-dichloroocta-2-yn-4-ol (266 mg, 78%) as a clear oil.

^{1}H NMR (400 MHz, CD_3OD) δ: 4.49 (ddd, 1H, J = 6.2, 1.8, 1.8 Hz), 3.96 (m, 1H), 3.86 (s, 2H), 3.61, (t, 2H, J = 6.2 Hz), 2.15-2.03 (m, 2H), 1.78-1.91 (m, 2H), 1.45 (s, 9H)

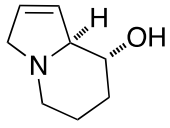
^{13}C NMR (100 MHz, CD_3OD) δ: 172.9, 83.9, 66.9, 66.4, 61.5, 45.2, 31.9, 30.8, 28.7, 20.5, 14.5

IR (neat, cm^{-1}): 3331, 2976, 1691, 1367

Exact mass calc'd for $C_{13}H_{21}{}^{35}Cl_2NO_3$: 309.0898; found: 309.0901 $(M)^+$

$[\alpha]_D{}^{23}$: –7.69 (c = 5.9, $CHCl_3$)

Preparation of indolizidine 27:



To a stirred solution of (4*R*,5*S*)-1-(*N*-*tert*-butoxycarbonyl)amino-5,8-dichloroocta-2-yn-4-ol (134 mg, 0.432 mmol) and quinoline (5 μL, 0.04 mmol) in EtOH (5 mL) was added 5% Pd-$BaSO_4$ (43

mg, 0.020 mmol) at 0 °C. The resulting suspension was allowed to warm to room temperature and stirred under an atmosphere of H_2 (balloon) for 15 min. The reaction mixture was filtered through Celite® and concentrated in vacuo to provide (2*Z*,4*R*,5*S*)-1-(*N*-*tert*-butoxycarbonyl)amino-5,8-dichloroocta-2-en-4-ol (**24**) as a clear oil which was used in the next step without further purification.

^{1}H NMR (400 MHz, CD_3OD) δ: 5.58 (m, 2H), 4.53 (m, 1H), 3.93 (m, 1H), 3.79 (dd, 1H, *J* = 15.2, 5.1), 3.70 (dd, 1H, *J* = 15.2, 3.4), 2.06 (m, 2H), 1.88 (m, 2H), 1.74 (m, 2H), 1.43 (s, 9H)

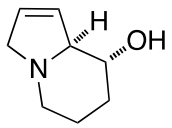
Exact mass calc'd for $C_{13}H_{23}Cl_2NO_3$: 311.1055; found: 312.1129 $(M+H)^+$

To crude (2*Z*,4*R*,5*S*)-1-(*N*-*tert*-butoxycarbonyl)amino-5,8-dichloroocta-2-en-4-ol (**24**) was added a solution of HCl in diethyl ether (2.0 M, 2.16 mL, 4.3 mmol) at room temperature. The reaction mixture was stirred for 18 h at r.t. then concentrated. The resulting oil was triturated with cold Et_2O. The remaining solid was dried in vacuo to afford crude (2*Z*,4*R*,5*S*)-(5,8-dichloro-4-hydroxyocta-2-enyl)ammonium chloride as a white solid which was used in the next step without further purification.

^{1}H NMR (400 MHz, CD_3OD) δ: 5.88 (ddd, 1H, *J* = 11.2, 7.6, 1.6 Hz), 5.70 (dddd, 1H, *J* = 15.1, 8.3, 1.2, 0.7 Hz), 4.46 (t, 1H, *J* = 6.7 Hz), 3.94 (m, 1H), 3.78 (dd, 1H, *J* = 14.6, 7.7 Hz), 3.71 (dd, 1H, *J* = 14.4, 6.1 Hz), 3.62 (t, 2H *J* = 6.1 Hz) 2.11 (m, 2H), 1.89 (m, 1H), 1.77 (m, 1H)

Exact mass calc'd for $C_8H_{16}Cl_3NO$: 247.0297; found: 212.0603 (M-Cl)

To a solution of crude (2*Z*,4*R*,5*S*)-(5,8-dichloro-4-hydroxyocta-2-enyl)ammonium chloride (**25**) in MeOH (4.3 ml) was added aqueous NaOH (2.0 M, 0.65 mL, 1.3 mmol) dropwise at room temperature over 3 hours (syringe pump). The reaction mixture was stirred for 15 hours then concentrated in vacuo. The resulting residue was dissolved in a mixture of CH_2Cl_2/MeOH/NH_4OH (aq.) (100:1:1), filtered, and concentrated in vacuo. The resulting crude mixture was purified by flash chromatography (99:1 CH_2Cl_2:MeOH w/ 1% NH_4OH, then 90:10 CH_2Cl_2:MeOH w/ 1% NH_4OH) to provide indolizidine **27** (32 mg, 54% over 3 steps) as a yellow oil.



^{1}H NMR (600 MHz, $CDCl_3$) δ: 6.17 (m, 1H), 5.95 (dddd, 1H, *J* = 6.3, 2.1, 2.1, 2.1 Hz), 3.60 (dddd, 1H, *J* = 13.3, 3.8, 2.3, 2.3 Hz), 3.38 (ddd, 1H, *J* = 10.8, 9.5, 4.5 Hz), 3.24 (dddd, 1H, *J* = 13.0, 7.4, 2.4, 1.8 Hz), 2.94 (m, 1H), 2.88 (m, 1H), 2.46 (m, 1H), 2.01 (dddd, 1H, *J* = 15.7, 7.3, 3.1, 3.1 Hz), 1.68 (m, 2H), 1.25 (m, 1H)

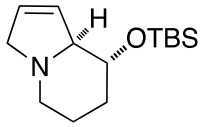
^{13}C NMR (150 MHz, $CDCl_3$) δ: 132.3, 129.7, 74.5, 71.2, 58.3 49.6, 34.2, 24.4

IR (neat, cm^{-1}): 3356, 2932

Exact mass calc'd for $C_8H_{13}NO$: 139.0997; found: 139.1003 $(M)^+$

$[\alpha]_D^{23}$: –40.4 (c = 0.82, $CHCl_3$)

Preparation of indolizidine 28:



To a solution of indolizidine **27** (21 mg, 0.15 mmol) in CH_2Cl_2 (1.5 mL) was added *tert*-butyldimethylsilyl chloride (45 mg, 0.30 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.047 mL, 0.32 mmol) at room temperature. After stirring for 2 hours the reaction mixture was treated with aqueous aq. NH_4Cl solution (1.0 mL) and diluted with CH_2Cl_2 (10 mL). The phases were separated, the aqueous phase was extracted with CH_2Cl_2 (10 mL x 3), and the combined organics were washed with brine (5 mL), dried (Na_2SO_4), and concentrated in vacuo. The resulting crude (yellow oil) was immediately purified by silica get column chromatography using 15:1 CH_2Cl_2/MeOH to provide indolizidine **28** (27 mg, 70% yield), as a colorless oil. All data were consistent with those previously reported[5].

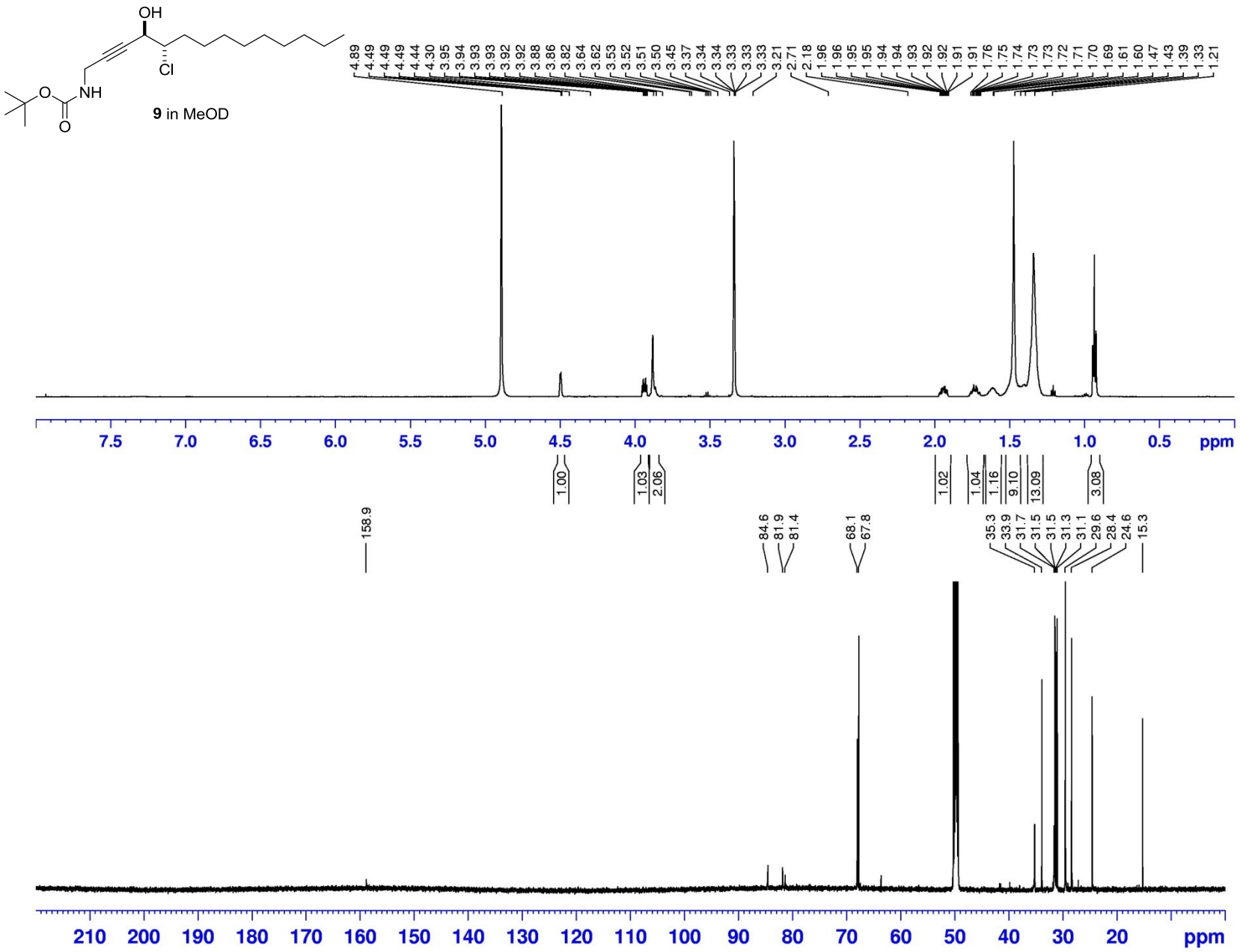
Exact mass calc'd for $C_{14}H_{28}NOSi$: 253.1862; found: 254.1957 $(M)^+$

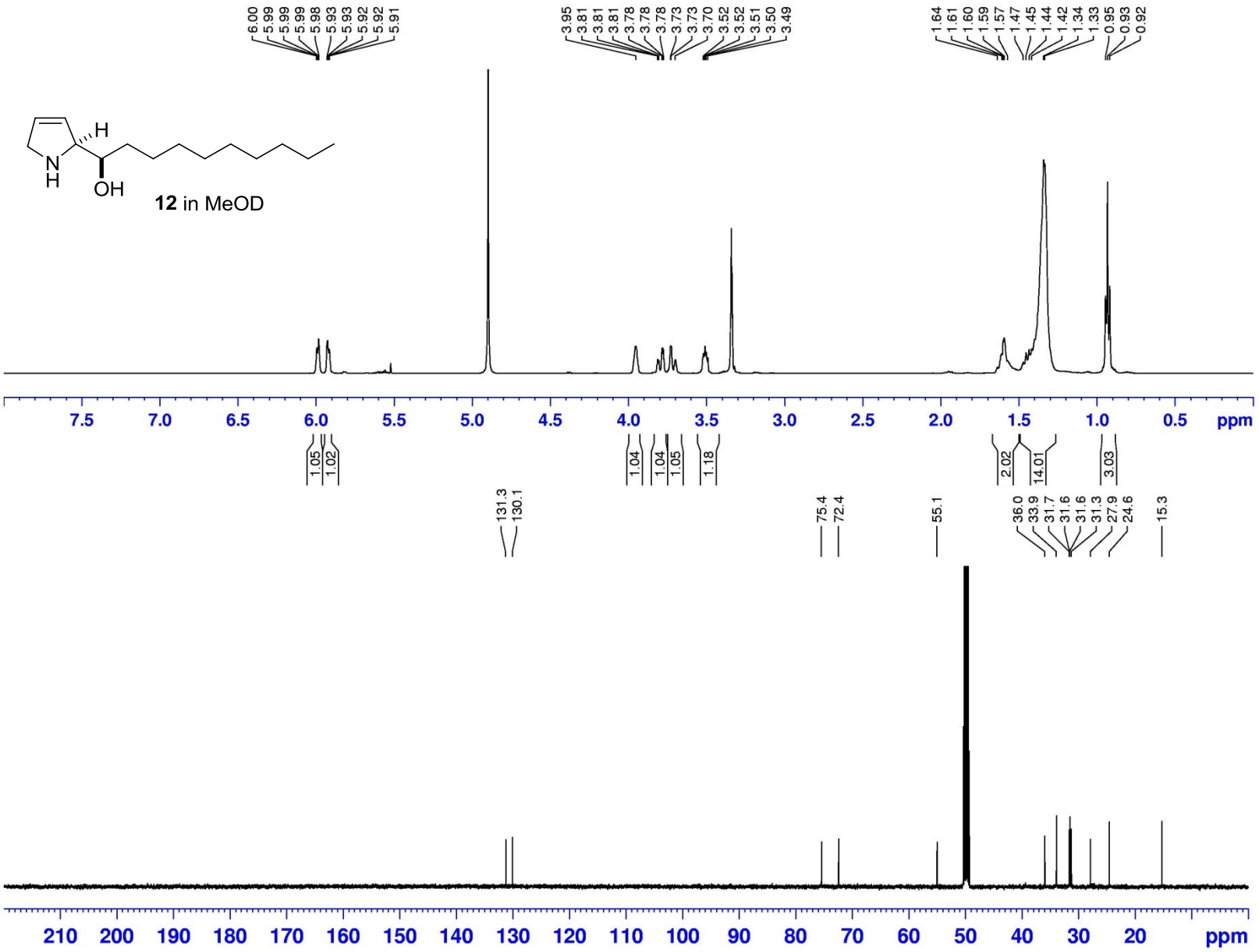
$[\alpha]_D^{23}$: –50 (c = 0.15, CH_2Cl_2) lit: $[\alpha]_D^{23}$: –59.6 (c = 1.0, CH_2Cl_2)[6]

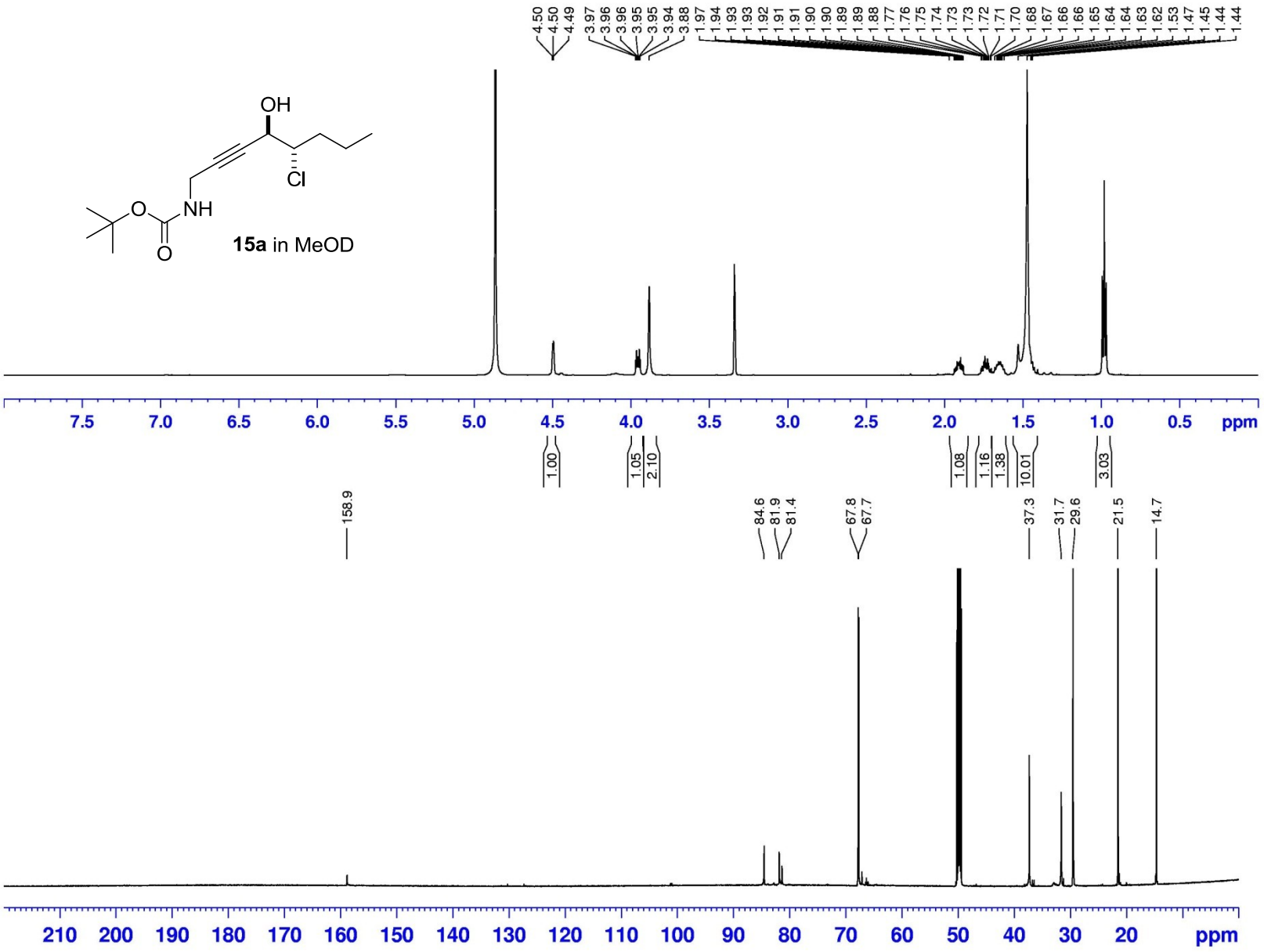
See ^{1}H NMR spectral data in table form on page 33.

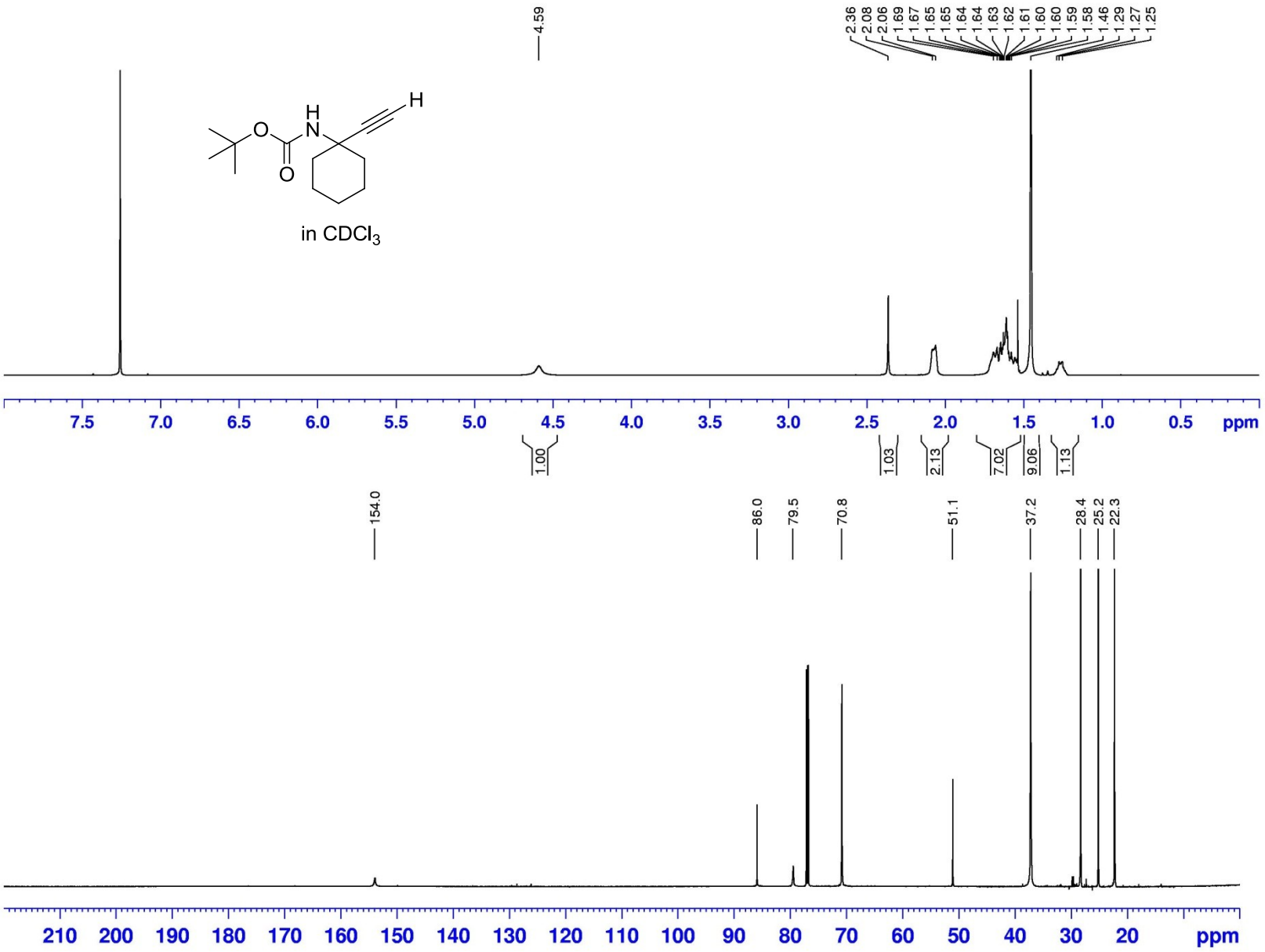
[5] C. W. G. Au, S. G. Pyne, *J. Org. Chem*. **2006**, *71*, 7097.

[6] R. W. Bates, M. R. Dewey, *Org. Lett.* **2009**, *11*, 3706.


OH
Cl
NH
O
O
9 in MeOD
4.89 4.49 4.49 4.49 4.44 4.30 3.95 3.94 3.93 3.93 3.92 3.92 3.88 3.86 3.82 3.64 3.62 3.53 3.52 3.51 3.50 3.45 3.37 3.34 3.34 3.33 3.33 3.33 3.21 2.71 2.18 1.96 1.96 1.95 1.95 1.94 1.94 1.93 1.92 1.92 1.91 1.91 1.76 1.75 1.74 1.73 1.73 1.72 1.71 1.70 1.69 1.61 1.60 1.47 1.43 1.39 1.33 1.21
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00 1.03 2.06 1.02 1.04 1.16 9.10 13.09 3.08
158.9
84.6 81.9 81.4 68.1 67.8
35.3 33.9 31.7 31.5 31.5 31.3 31.1 29.6 28.4 24.6 15.3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


6.00
5.99
5.99
5.99
5.98
5.93
5.93
5.92
5.92
5.91
3.95
3.81
3.81
3.81
3.78
3.78
3.78
3.73
3.73
3.70
3.52
3.52
3.51
3.50
3.49
1.64
1.61
1.60
1.59
1.57
1.47
1.45
1.44
1.42
1.34
1.33
0.95
0.93
0.92
H
N
H
OH
12 in MeOD
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.05
1.02
1.04
1.04
1.05
1.18
2.02
14.01
3.03
131.3
130.1
75.4
72.4
55.1
36.0
33.9
31.7
31.6
31.6
31.3
27.9
24.6
15.3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


OH
Cl
NH
O
O
15a in MeOD
4.50
4.50
4.49
3.97
3.96
3.96
3.95
3.95
3.94
3.88
1.97
1.94
1.93
1.93
1.92
1.91
1.91
1.90
1.90
1.89
1.89
1.88
1.77
1.76
1.75
1.74
1.73
1.73
1.72
1.71
1.70
1.68
1.67
1.66
1.66
1.65
1.64
1.64
1.63
1.62
1.53
1.47
1.45
1.44
1.44
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.05
2.10
1.08
1.16
1.38
10.01
3.03
158.9
84.6
81.9
81.4
67.8
67.7
37.3
31.7
29.6
21.5
14.7
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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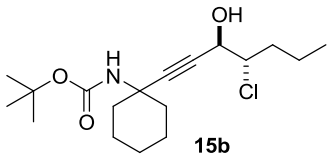
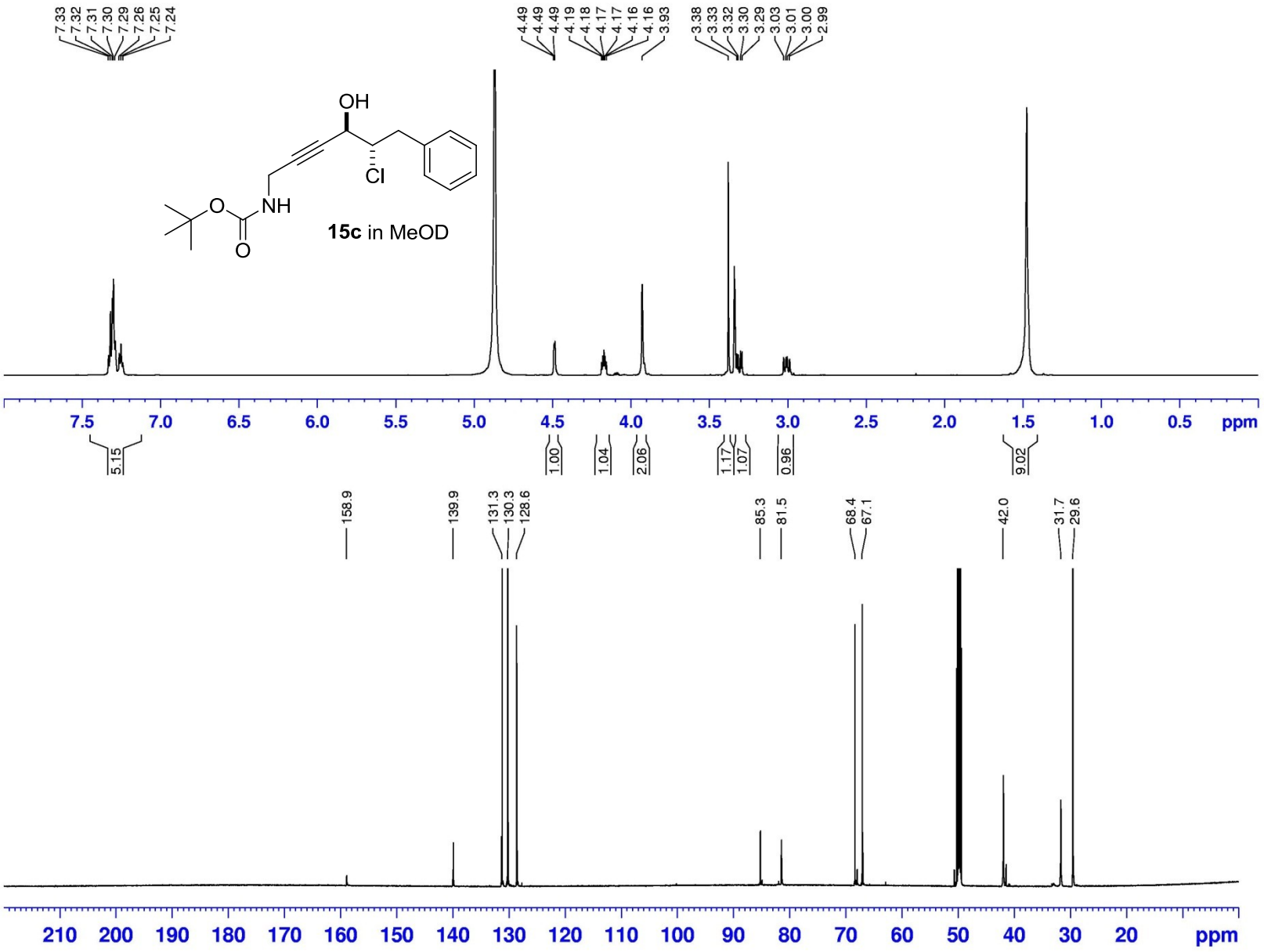
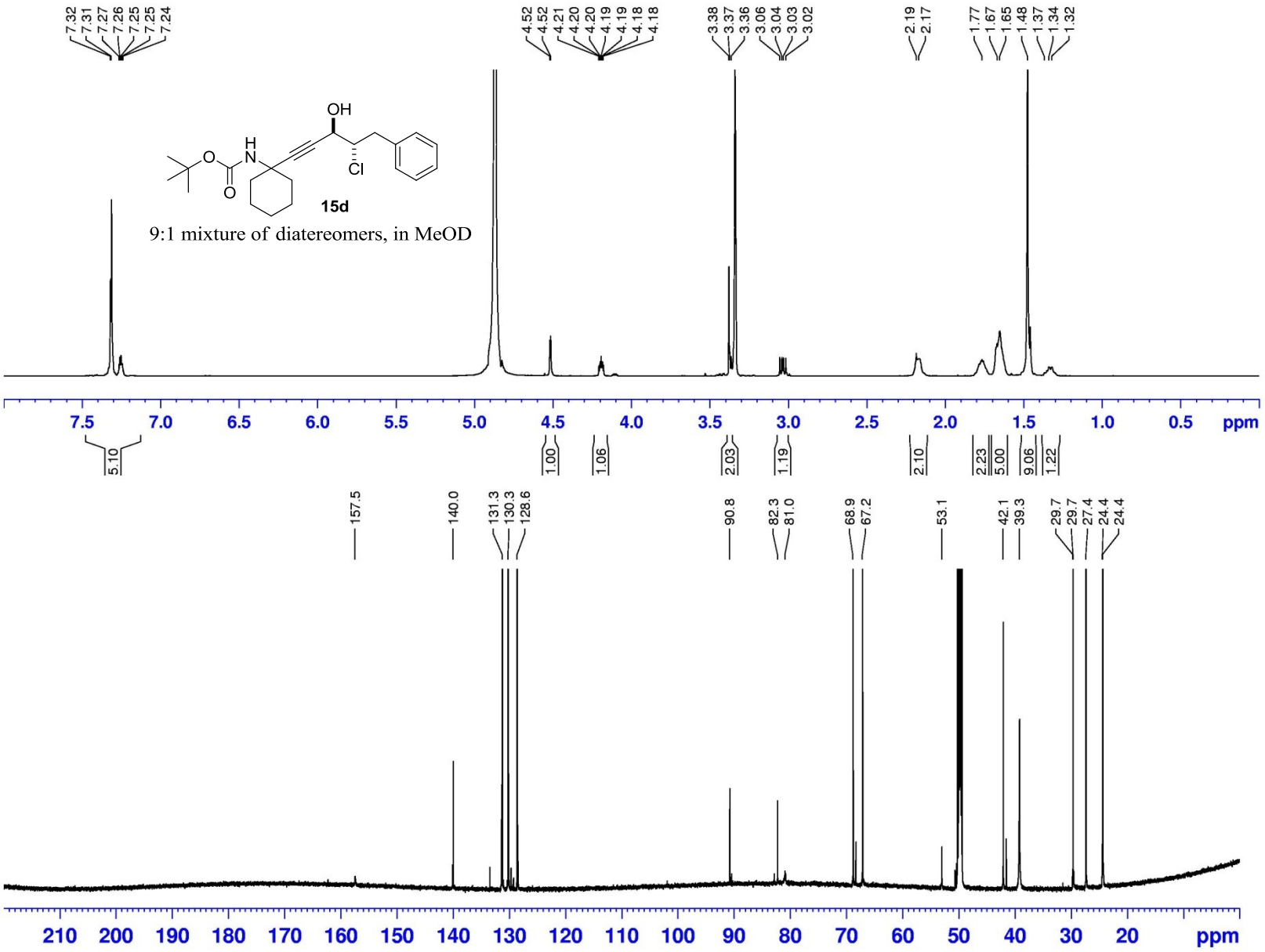
2.36
2.08
2.06
1.69
1.67
1.65
1.65
1.64
1.64
1.63
1.62
1.61
1.60
1.60
1.59
1.58
1.46
1.29
1.27
1.25
H
H
N
O
O
in CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.03
2.13
7.02
9.06
1.13
154.0
86.0
79.5
70.8
51.1
37.2
28.4
25.2
22.3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

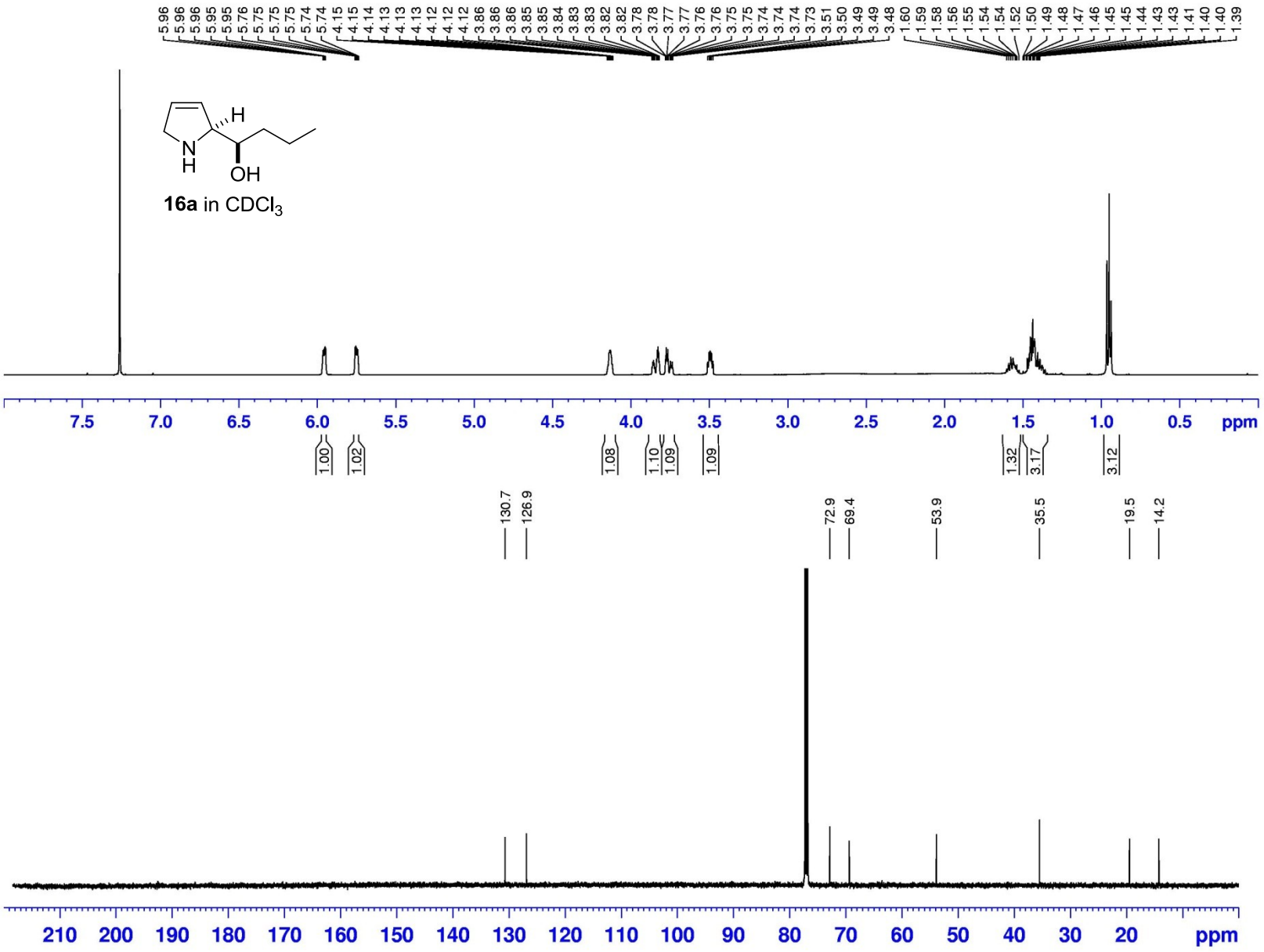


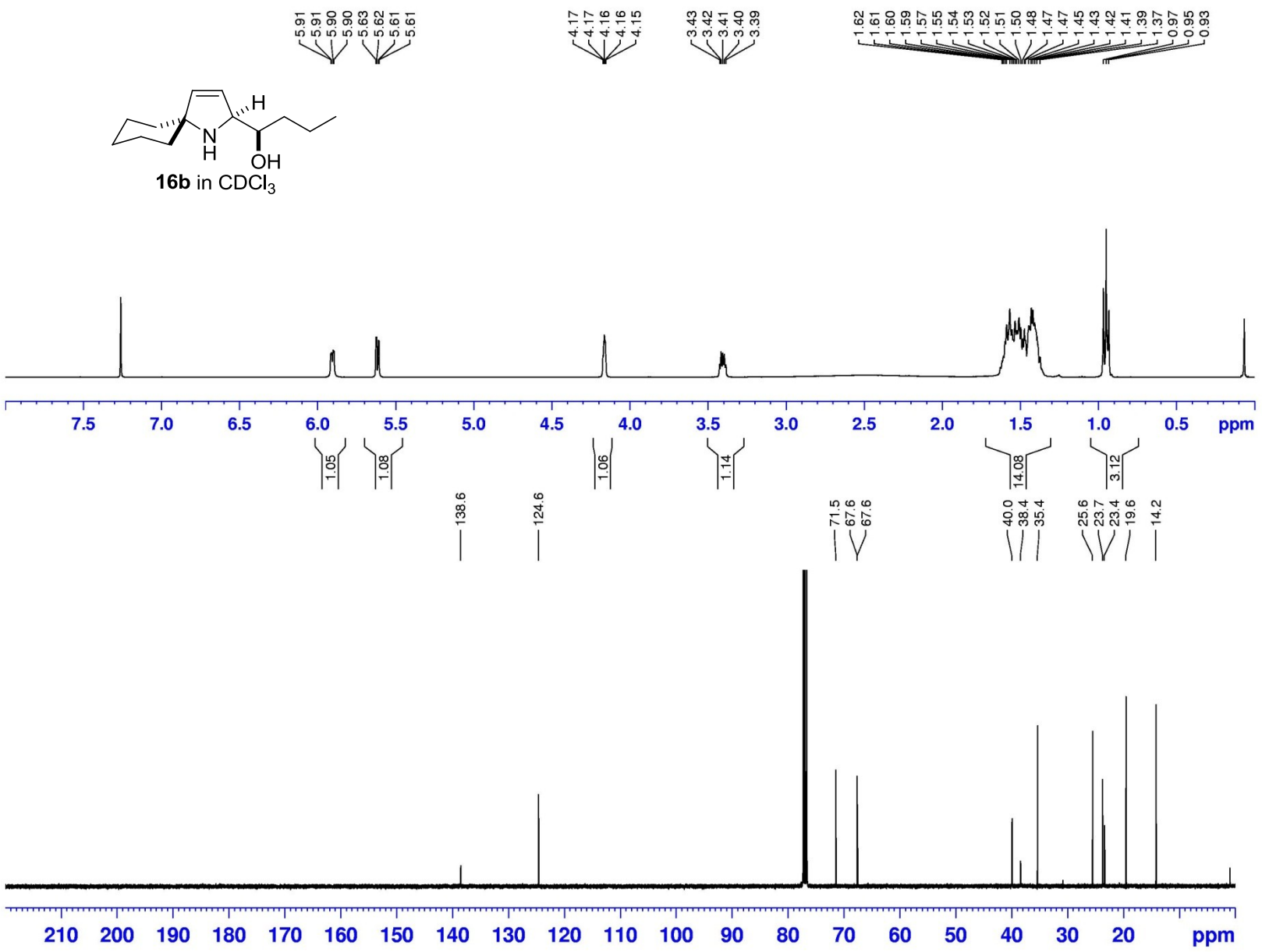
15b

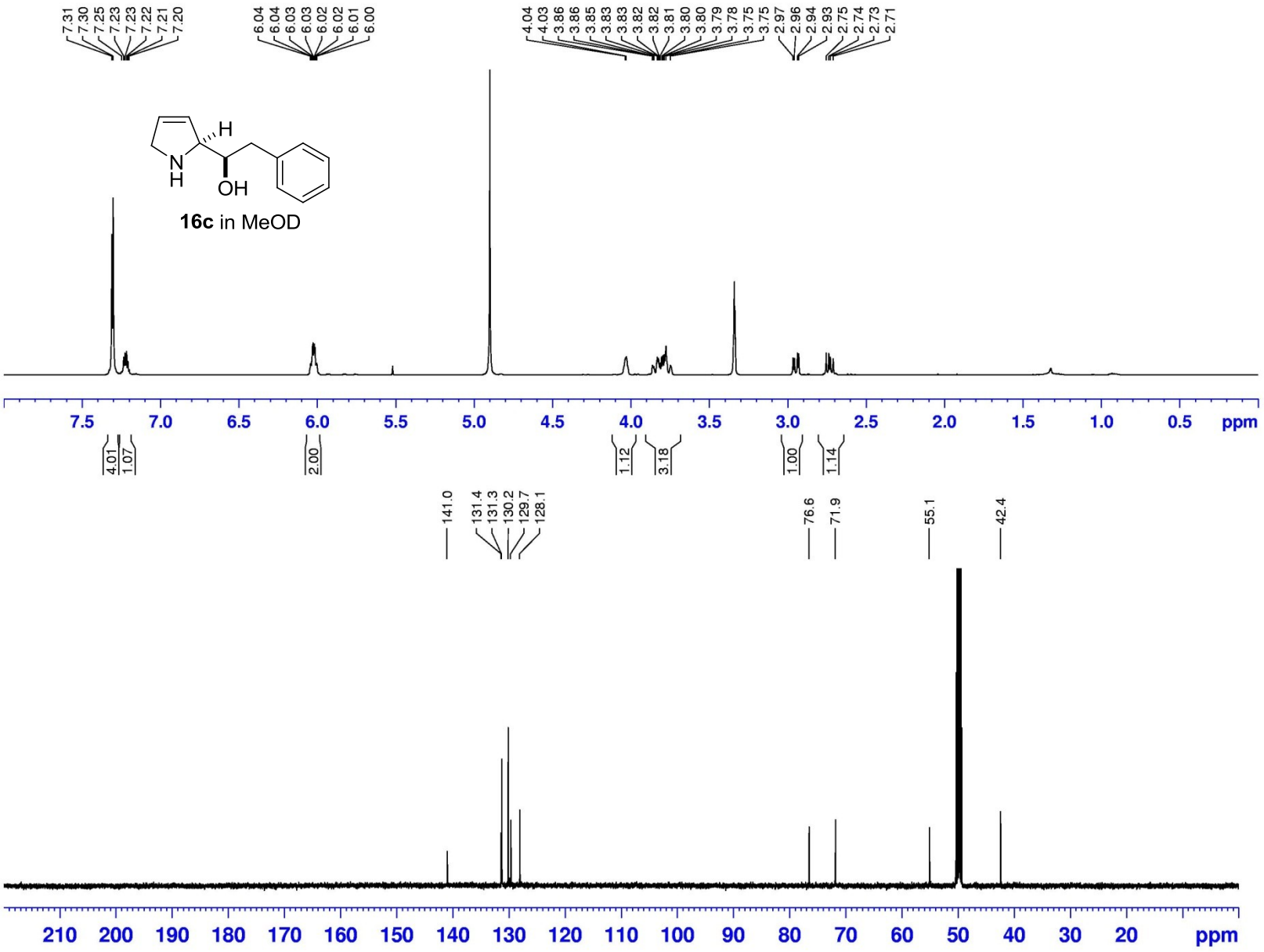
10:1 mixture of diastereomers, in MeOD

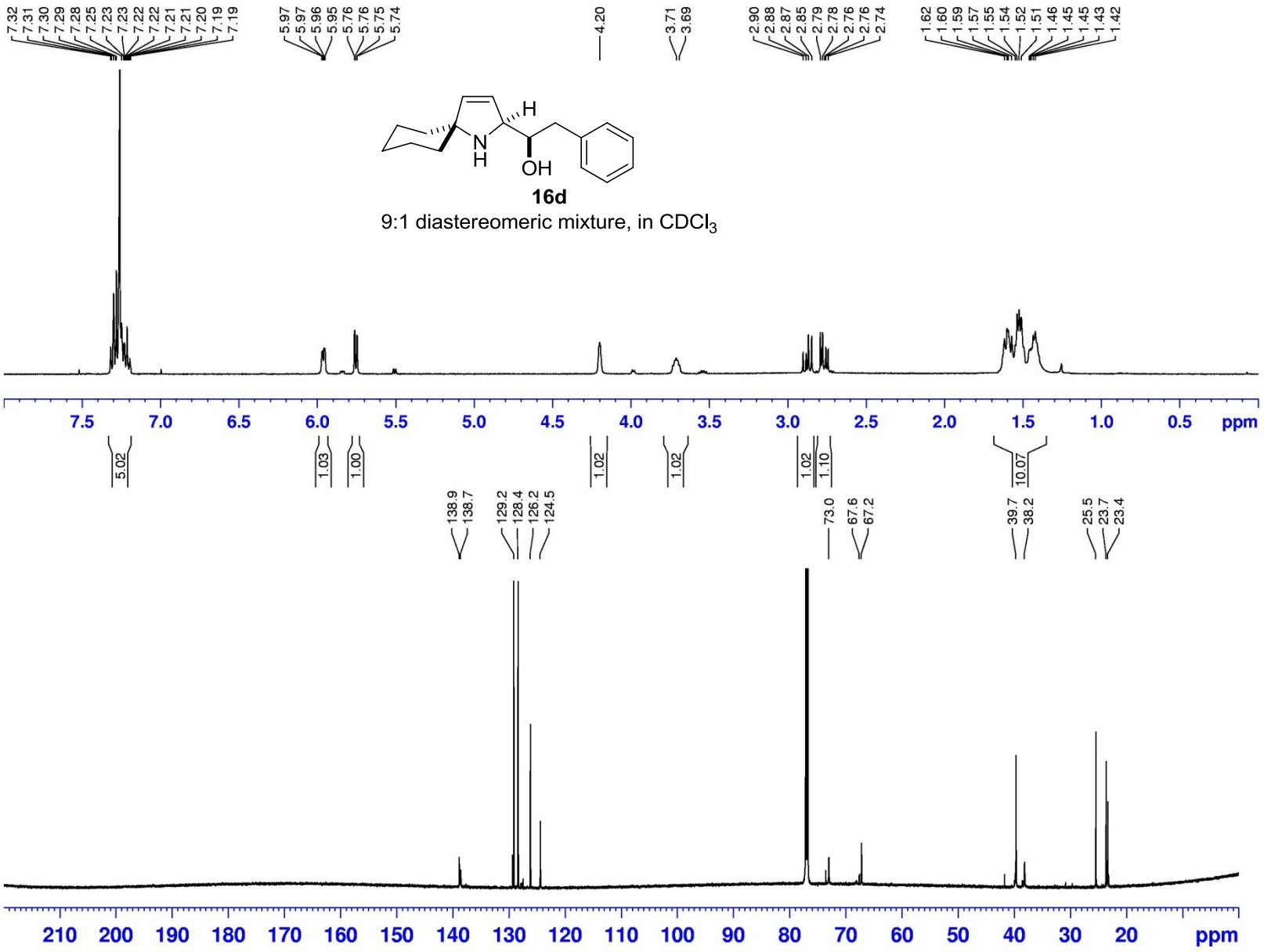

7.33
7.32
7.31
7.30
7.29
7.26
7.25
7.24
4.49
4.49
4.49
4.19
4.18
4.17
4.17
4.16
4.16
3.93
3.38
3.33
3.32
3.30
3.29
3.03
3.01
3.00
2.99
OH
Cl
NH
O
O
15c in MeOD
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
5.15
1.00
1.04
2.06
1.17
1.07
0.96
9.02
158.9
139.9
131.3
130.3
128.6
85.3
81.5
68.4
67.1
42.0
31.7
29.6
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


7.32
7.31
7.27
7.26
7.25
7.25
7.24
4.52
4.52
4.21
4.20
4.20
4.19
4.19
4.18
4.18
3.38
3.37
3.36
3.06
3.04
3.03
3.02
2.19
2.17
1.77
1.67
1.65
1.48
1.37
1.34
1.32
OH
H
N
O
O
Cl
15d
9:1 mixture of diatereomers, in MeOD
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
5.10
1.00
1.06
2.03
1.19
2.10
2.23
5.00
9.06
1.22
157.5
140.0
131.3
130.3
128.6
90.8
82.3
81.0
68.9
67.2
53.1
42.1
39.3
29.7
29.7
27.4
24.4
24.4
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


5.96 5.96 5.96 5.95 5.95 5.76 5.75 5.75 5.75 5.74 5.74 4.15 4.15 4.14 4.13 4.13 4.13 4.12 4.12 4.12 3.86 3.86 3.86 3.85 3.85 3.84 3.83 3.83 3.82 3.82 3.78 3.78 3.77 3.77 3.76 3.76 3.75 3.75 3.74 3.74 3.74 3.73 3.51 3.50 3.49 3.49 3.48 1.60 1.59 1.58 1.56 1.55 1.54 1.54 1.52 1.50 1.49 1.48 1.47 1.46 1.45 1.45 1.44 1.43 1.43 1.41 1.40 1.40 1.39
H
N
H
OH
16a in CDCl3
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00 1.02 1.08 1.10 1.09 1.09 1.32 3.17 3.12
130.7 126.9 72.9 69.4 53.9 35.5 19.5 14.2
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

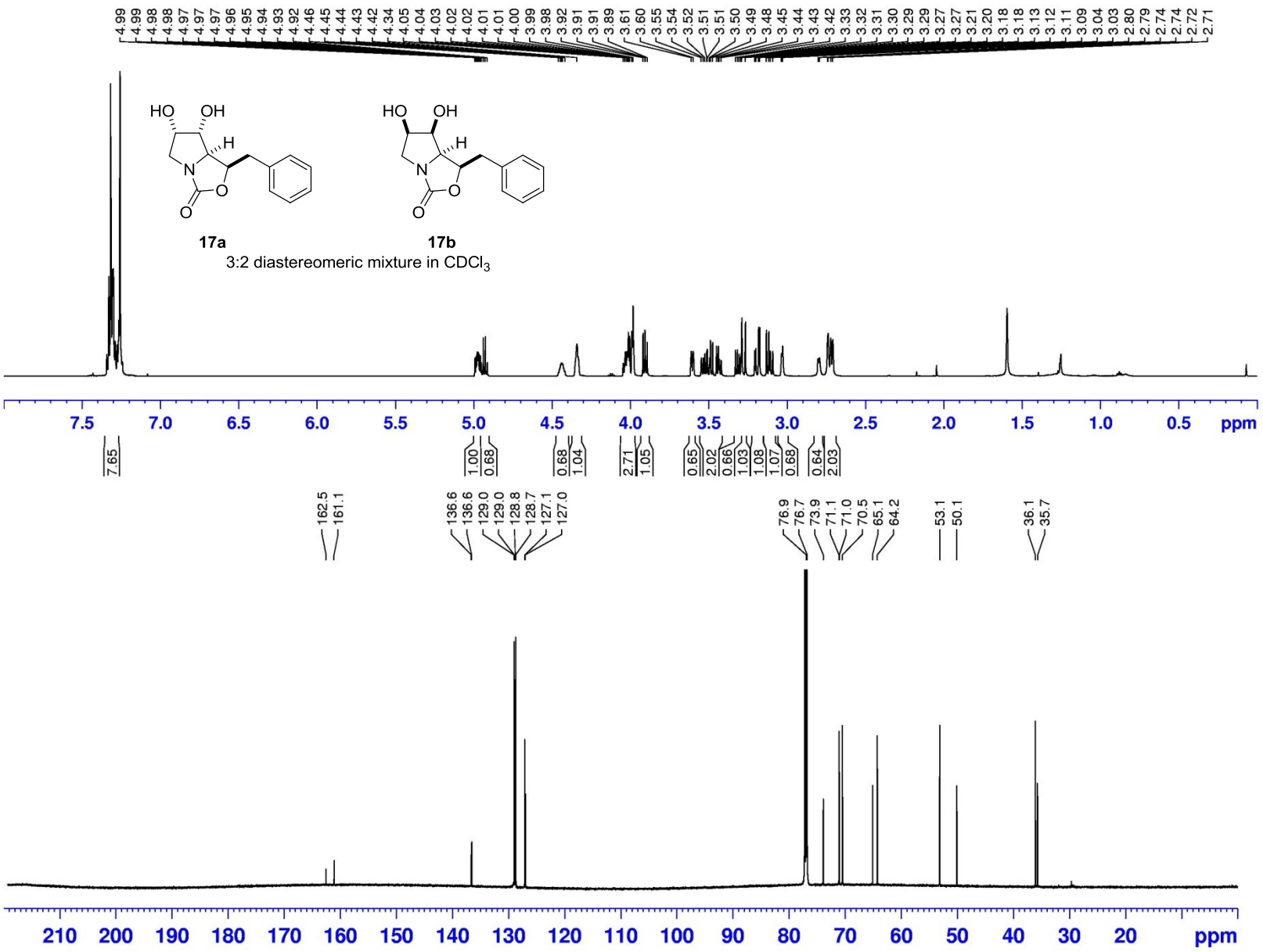

5.91
5.91
5.90
5.90
5.63
5.62
5.61
5.61
4.17
4.17
4.16
4.16
4.15
3.43
3.42
3.41
3.40
3.39
1.62
1.61
1.60
1.59
1.57
1.55
1.54
1.53
1.52
1.51
1.50
1.48
1.47
1.47
1.45
1.43
1.42
1.41
1.39
1.37
0.97
0.95
0.93
H
N
H
OH
16b in CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.05
1.08
1.06
1.14
14.08
3.12
138.6
124.6
71.5
67.6
67.6
40.0
38.4
35.4
25.6
23.7
23.4
19.6
14.2
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

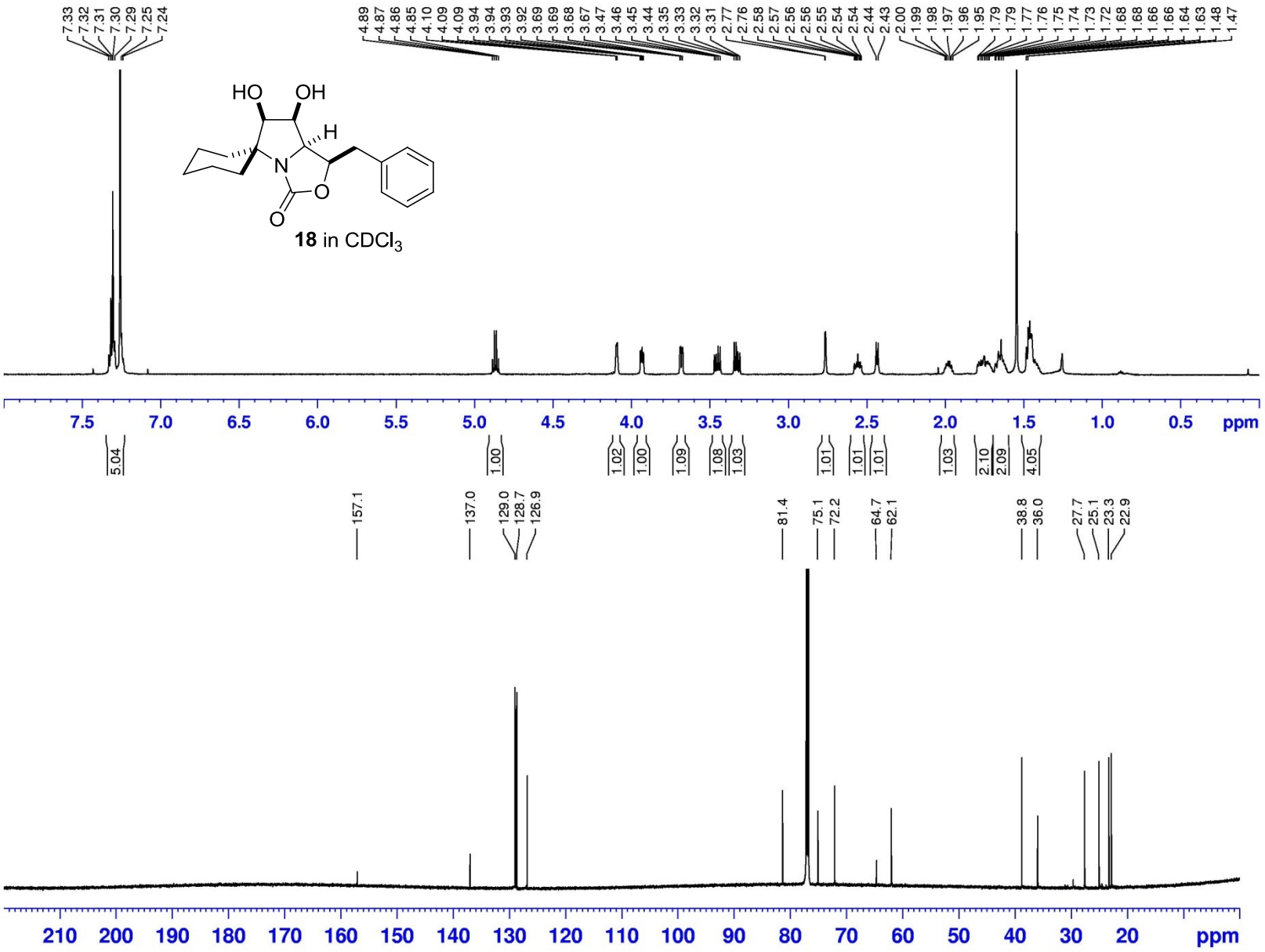

7.31
7.30
7.25
7.23
7.23
7.22
7.21
7.20
6.04
6.04
6.03
6.03
6.02
6.02
6.01
6.00
4.04
4.03
3.86
3.86
3.85
3.83
3.83
3.82
3.82
3.81
3.80
3.80
3.79
3.78
3.75
3.75
2.97
2.96
2.94
2.93
2.75
2.74
2.73
2.71
H
N
H
OH
16c in MeOD
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.01
1.07
2.00
1.12
3.18
1.00
1.14
141.0
131.4
131.3
130.2
129.7
128.1
76.6
71.9
55.1
42.4
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

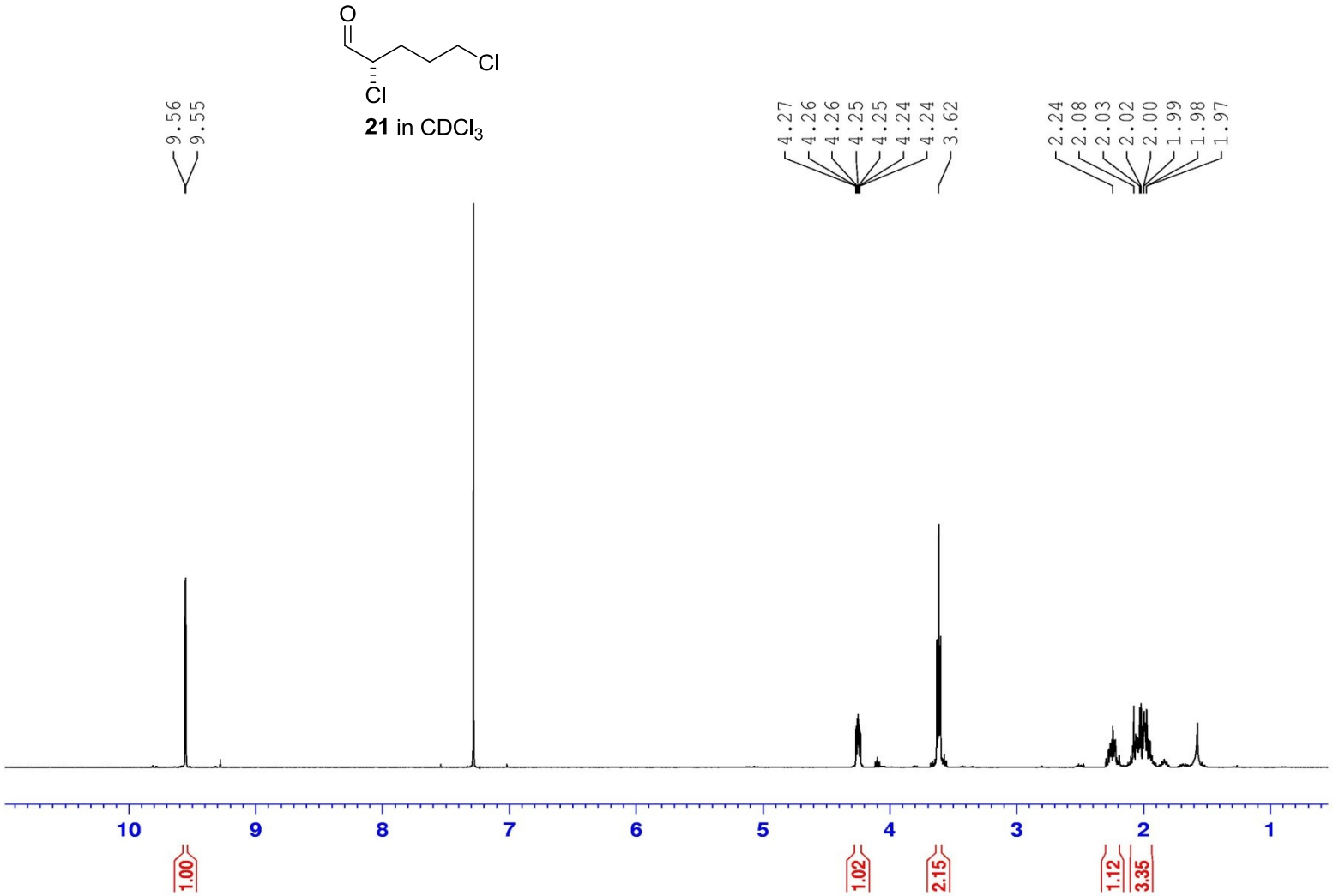


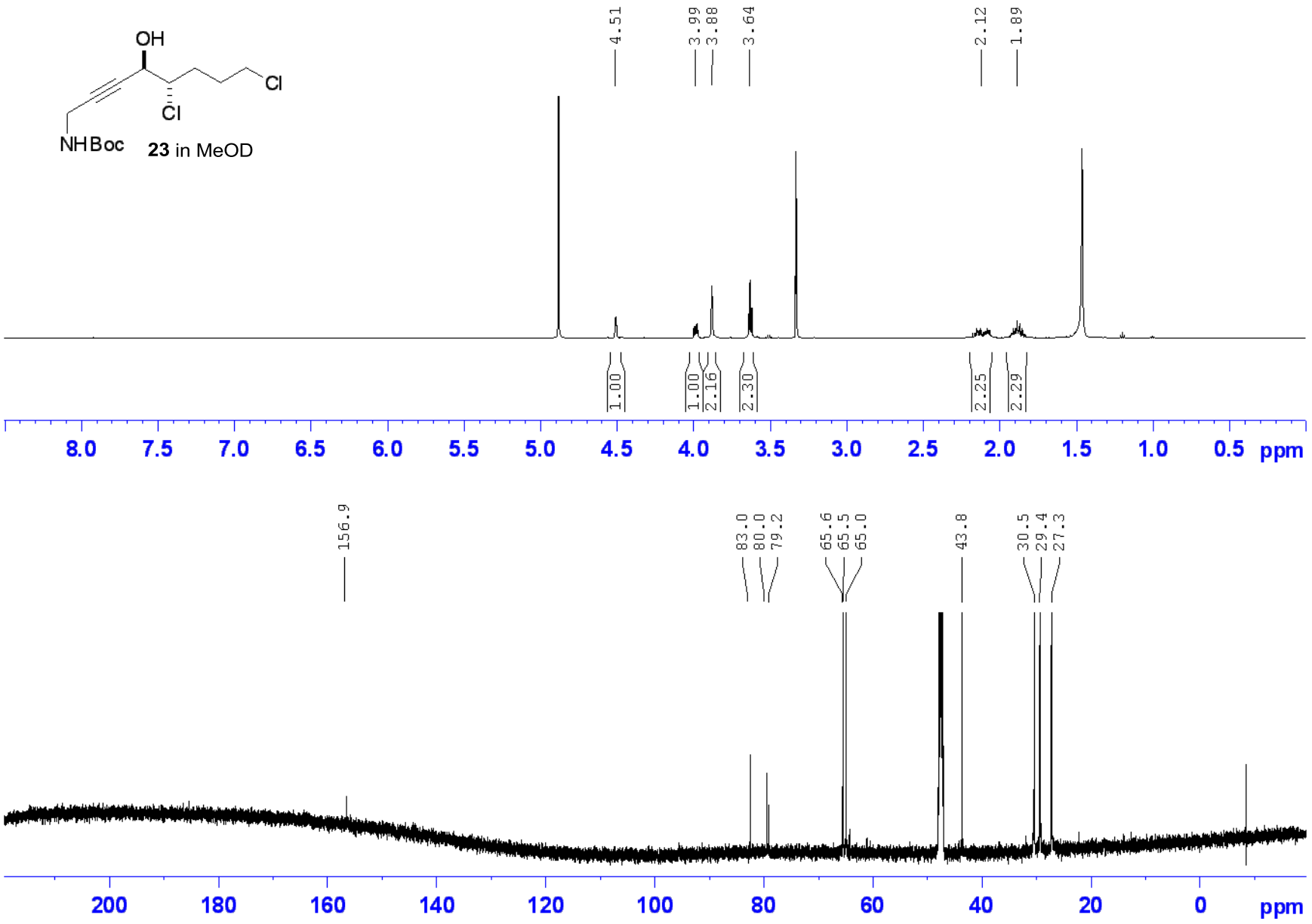
16d

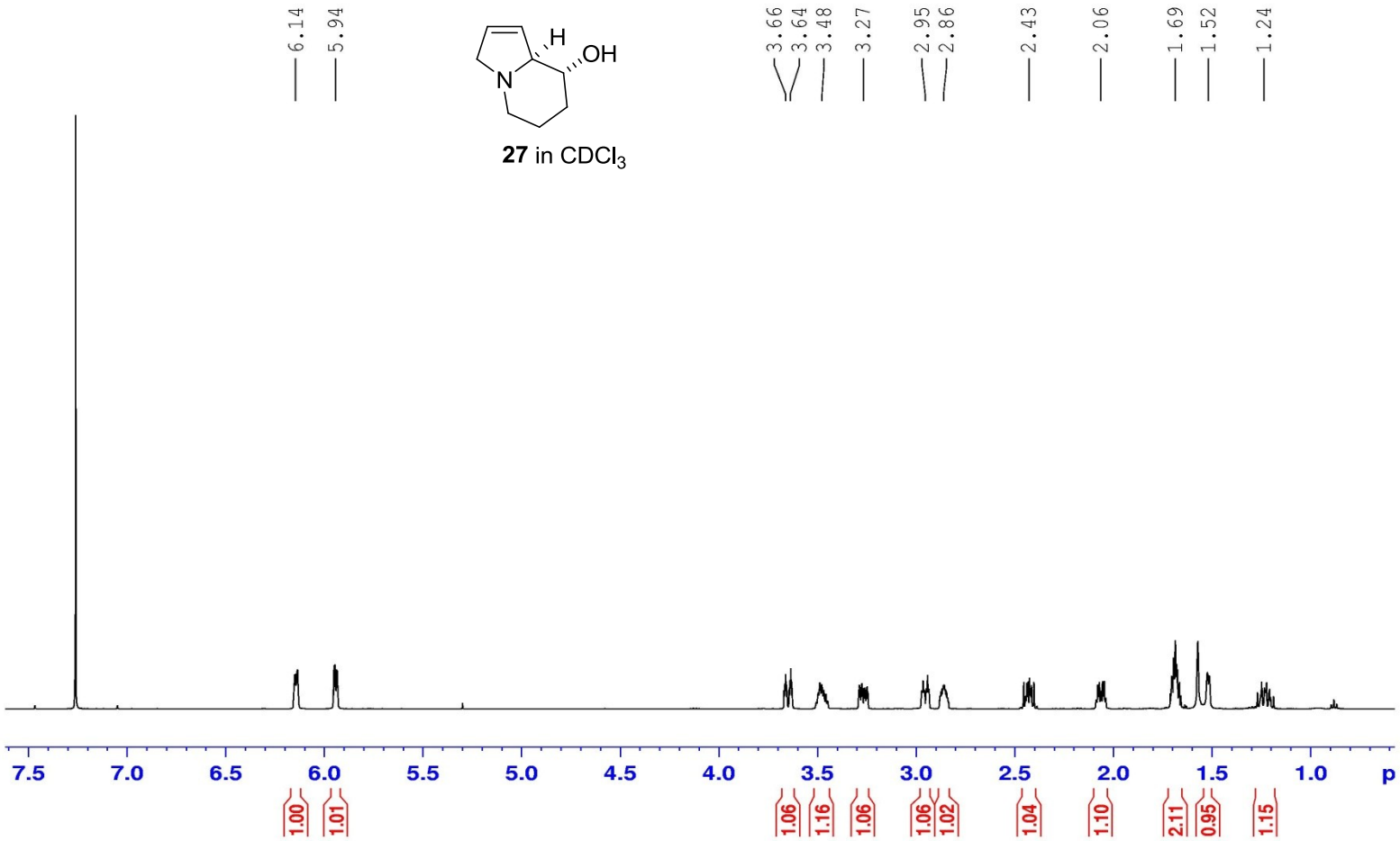
9:1 diastereomeric mixture, in $CDCl_3$


4.99 4.99 4.98 4.98 4.97 4.97 4.97 4.96 4.95 4.94 4.93 4.92 4.46 4.45 4.44 4.43 4.42 4.34 4.05 4.04 4.03 4.02 4.02 4.01 4.01 4.00 3.99 3.98 3.92 3.91 3.91 3.89 3.61 3.60 3.55 3.54 3.52 3.51 3.51 3.50 3.49 3.48 3.45 3.44 3.43 3.42 3.33 3.32 3.31 3.30 3.29 3.29 3.27 3.27 3.21 3.20 3.18 3.18 3.13 3.12 3.11 3.09 3.04 3.03 2.80 2.79 2.74 2.74 2.72 2.71
HO OH H N O O
HO OH H N O O
17a
17b
3:2 diastereomeric mixture in CDCl3
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
7.65 1.00 0.68 0.68 1.04 2.71 1.05 0.65 2.02 0.66 1.03 1.08 1.07 0.68 0.64 2.03
162.5 161.1 136.6 136.6 129.0 129.0 128.8 128.7 127.1 127.0 76.9 76.7 73.9 71.1 71.0 70.5 65.1 64.2 53.1 50.1 36.1 35.7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


HO
OH
H
N
O
O
18 in CDCl3
7.33
7.32
7.31
7.30
7.29
7.25
7.24
4.89
4.87
4.86
4.85
4.10
4.09
4.09
3.94
3.94
3.93
3.92
3.69
3.69
3.68
3.67
3.47
3.46
3.45
3.44
3.35
3.33
3.32
3.31
2.77
2.76
2.58
2.57
2.56
2.56
2.55
2.54
2.54
2.44
2.43
2.00
1.99
1.98
1.97
1.96
1.95
1.79
1.79
1.77
1.76
1.75
1.74
1.73
1.72
1.68
1.68
1.66
1.66
1.64
1.63
1.48
1.47
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
5.04
1.00
1.02
1.00
1.09
1.08
1.03
1.01
1.01
1.01
1.03
2.10
2.09
4.05
157.1
137.0
129.0
128.7
126.9
81.4
75.1
72.2
64.7
62.1
38.8
36.0
27.7
25.1
23.3
22.9
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


O
Cl
Cl
21 in CDCl3
9.56
9.55
4.27
4.26
4.26
4.25
4.25
4.24
4.24
3.62
2.24
2.08
2.03
2.02
2.00
1.99
1.98
1.97
10
9
8
7
6
5
4
3
2
1
1.00
1.02
2.15
1.12
3.35


OH
Cl
Cl
NHBoc
23 in MeOD
4.51
3.99
3.88
3.64
2.12
1.89
1.00
1.00
2.16
2.30
2.25
2.29
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
156.9
83.0
80.0
79.2
65.6
65.5
65.0
43.8
30.5
29.4
27.3
200
180
160
140
120
100
80
60
40
20
0
ppm


6.14
5.94
3.66
3.64
3.48
3.27
2.95
2.86
2.43
2.06
1.69
1.52
1.24
H
OH
N
27 in CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
p
1.00
1.01
1.06
1.16
1.06
1.06
1.02
1.04
1.10
2.11
0.95
1.15

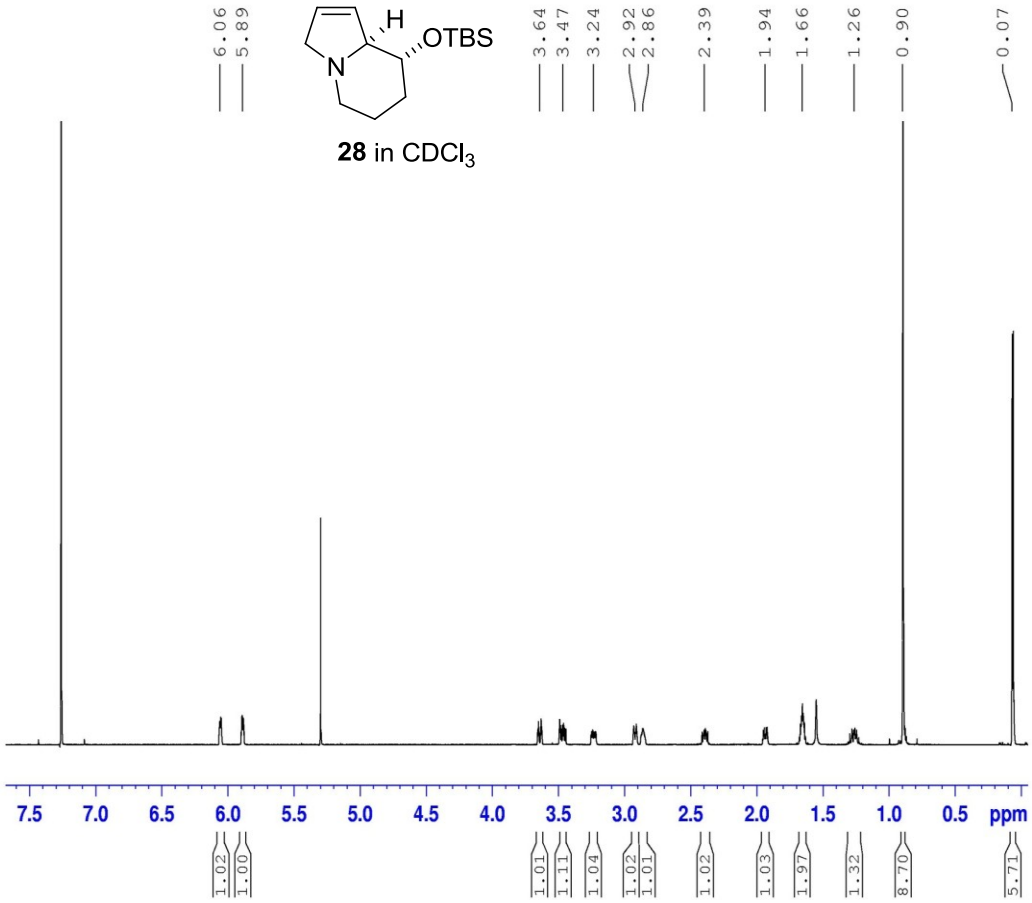


Table 1. Comparison of ^{1}H NMR spectral data of indolizidine **28**

	Pyne[5]	*J*	observed	*J*
	6.05	1.4, 6.4	6.06	1.4, 6.3
	5.88		5.89	
	3.63	1.4, 2.3, 2.3, 13.3	3.64	1.5, 2.3, 3.7, 12.9
	3.46	4.6, 9.2, 13.7	3.47	4.6, 9.2, 13.5
	3.23	2.3, 2.3, 8.7, 13.3	3.24	1.7, 2.4, 6.3, 13.1
	2.91	3.6, 11.4	2.92	3.5, 11.2
	2.86		2.86	
	2.39	6.4, 8.7, 11.4	2.39	6.9, 9.3, 11.2
	1.93	4.1, 7.8, 11.9	1.94	3.9, 7.4, 12.1
	1.68-1.62		1.68-1.62	
	1.32-1.19		1.26	
	0.89		0.9	
	0.06		0.07	
	0.05		0.06	