

Enantioselective Total Syntheses of (+)-Castanospermine, (+)-6-Epicastanospermine, (+)-Australine, and (+)-3-Epiaustraline

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SUPPORTING INFORMATION

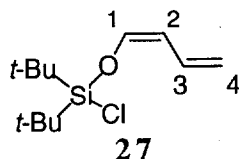
General Experimental Procedures. Boiling points (bp) refer to air bath temperatures and are uncorrected. Melting points (mp) were determined on a Thomas-Hoover capillary melting point apparatus in sealed tubes and are uncorrected. Analytical TLC was performed on Merck silica gel plates (10 cm) with QF-254 indicator. Plates were visualized using UV radiation (254 nm) in conjunction with the potassium permanganate. Column chromatography was performed using 230-400 mesh silica gel, purchased by EM Science. Cation exchange chromatography was performed on AG 50W-X8 resin purchased by Bio-Rad (100-200 mesh, H form). The column was pretreated by stirring the resin overnight in conc. NH_4OH and then washing successively with 6M HCl, H_2O , 4N NH_4OH , H_2O , 6M HCl, H_2O , 2N NH_4OH , H_2O , 3M H_2SO_4 , and H_2O . Anion exchange chromatography was performed on AG1-X8 (20-50 mesh, OH^- form). The column was pretreated by stirring the resin overnight with MeOH, 2 h with H_2O , and refluxing in H_2O overnight.

All reactions were performed on oven (140 °C) of flame-dried glassware under an inert atmosphere of dry N_2 . Solvents for extraction and chromatography were analytical grade except ethyl acetate (distilled over K_2CO_3) and methylene chloride (distilled over CaCl_2). Reaction solvents were distilled from the indicated drying agents: benzene (CaH_2), dichloromethane (P_2O_5), diethyl ether (sodium-benzophenone ketyl), methanol (Mg), tetrahydrofuran (sodium-benzophenone ketyl).

Optical rotations were obtained on a Jasco DIP-360 digital polarimeter and are reported as follows: $[\alpha]_D^{\text{temperature}}$ at 589, concentration ($c = \text{g}/100 \text{ mL}$), and solvent. Infrared spectra (IR)

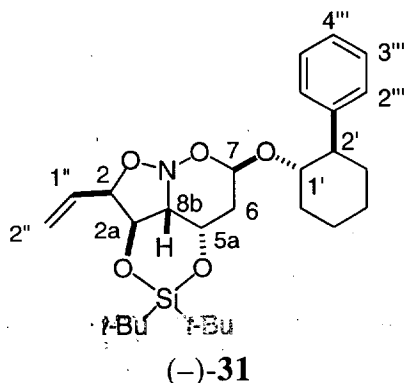
were obtained on a Mattson Galaxy 5020 spectrophotometer. Peaks are reported in cm^{-1} with the following relative intensities: s (strong, 60-100%), m (medium, 30-60%), w (weak, 0-30%). ^1H NMR and ^{13}C NMR spectra were recorded on a Varian Inova 500 (^1H 500 MHz, ^{13}C 125 MHz) or a Varian Unity 500 (^1H 500 MHz, ^{13}C 125 MHz) or a Varian Unity 400 (^1H 400 MHz, ^{13}C 100 MHz) spectrometers. Spectra were recorded in the following solvents: deuteriobenzene [$(\text{C}_6\text{D}_6$ (7.15 ppm for ^1H and 128.0 ppm for ^{13}C)] deuterium oxide [$(\text{D}_2\text{O}$ (4.63 ppm for ^1H)]]. Chemical shifts are given in ppm (δ); multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and b (broadened.) Coupling constants, J , are reported in Hertz. Mass spectra were obtained through the Mass Spectrometry Laboratory, School of Chemical Sciences, University of Illinois. Low resolution electron impact (EI) mass spectra were obtained on a Finnigan-MAT CH-5 spectrometer with typical ionization voltage of 70 eV. Low resolution chemical ionization (CI) mass spectra were obtained on a VG 70-VSE spectrometer using methane. Low resolution fast atom bombardment (FAB) spectra were obtained on a VG ZAB-SE spectrometer in magic bullet (3/1 dithioreitol/dithioerythritol) or 3-nitrobenzyl alcohol. Data are reported in the form m/z (intensity relative to base = 100). Analytical supercritical fluid chromatography (SFC) was performed on a Berger Instruments packed-column SFC with built-in photometric detector ($\lambda = 220 \text{ nm}$) using a ChiralCel OD column. Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory and represent the average of two analyses.

1-[[Di-tert-butylsilyl]oxy]-1,3-butadiene (27).



1-[[Di-tert-butylsilyl]oxy]-1,3-butadiene (27). To a solution of 2,5-dihydrofuran (4.1 mL, 54.0 mmol, 1.1 equiv) in THF (40 mL) at $-78\text{ }^{\circ}\text{C}$ was added *n*-BuLi (48.0 mL, 1.4 M solution in hexane, 67.0 mmol, 1.37 equiv) and the reaction mixture was stirred at $-23\text{ }^{\circ}\text{C}$ for 3.5 h before cooling to $-78\text{ }^{\circ}\text{C}$. Di-*t*-butylchlorosilane monotriflate **22**¹ (16.0 g, 49.0 mmol) was added dropwise, and the reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 15 min, at $0\text{ }^{\circ}\text{C}$ for 5 h, and at room temperature for 16 h. The resulting orange solution was diluted with pentane (150 mL) and washed successively with cold sat. aq. NaHCO_3 (100 mL) and NaCl (100 mL). The combined organic layers were dried (Na_2SO_4), concentrated *in vacuo*, and the residue was purified by chromatography (pentane, 600 g basic Al_2O_3 activity III) to afford 8.78 g (73%) of **27** as a clear oil. An analytical sample was obtained by diffusion pump distillation (10^{-5} Torr, room temperature). Data for **27**: IR (Nujol): 2970, 1645, 1597 (m), 1473 (m), 1253 (m), 1175 (m), 1087 (m), 1012 (w), 826 (m), 651 (w) cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 6.95 (dtd, $J_d=1.0$, 17.3, $J_t=10.7$, 1H, *H*-C3), 6.33 (ddd, $J=1.0$, 1.7, 5.9, 1H, *H*-C1), 5.20 (dd, $J=5.9$, 10.7, 1H, *H*-C2), 5.09 (dtd, $J_d=1.0$, 17.3, $J_t=1.7$, 1H, *H*-C4), 4.95 (dtd, $J_d=1.0$, 10.7, $J_t=1.7$, 1H, *H*-C4), 1.02 (s, 9H, CH_3); ^{13}C NMR (125 MHz, C_6D_6) δ 139.54 (C1), 129.70 (C2), 114.63 (C3), 112.32 (C4), 26.86 ($\text{C}(\text{CH}_3)_3$), 22.90 ($\text{C}(\text{CH}_3)_3$); MS (FAB) m/z 247.1 ($[\text{M}+1]^+$), 155.0, 137.0, 135.0, 118.9; TLC: R_f 0.72 (pentane); Anal. Calcd. for $\text{C}_{12}\text{H}_{23}\text{OClSi}$ (246.84): C, 58.39; H, 9.39; Cl, 14.36. Found: C, 58.55; H, 9.50; Cl, 14.11.

[2R-[2 α ,2a α ,5a β ,7 α (1S,2R),8b α]]-4,4-Bis(1,1-dimethylethyl)-2-ethenylhexahydro-7-[(2-phenylcyclohexyl)oxy]]-1,3,5,8-tetraoxa-8a-aza-4-silacacenaphthylene ((-)-31).

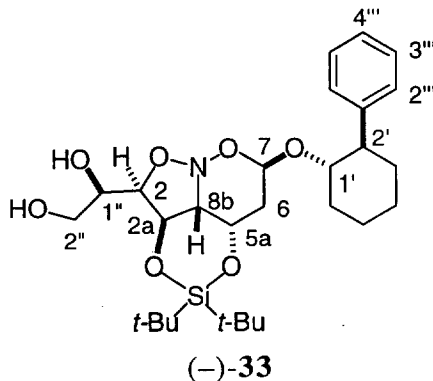


To a suspension of **21**² (210 mg, 1.65 mmol, 1.1 equiv) in CHCl_3 (5.7 mL) and CH_3CN (2.9 mL) was added **27** (370 mg, 1.5 mmol) and the yellow suspension was stirred at room temperature for 8 h. The resulting orange suspension was filtered through Celite under N_2 with a Schlenk tube and the residue was washed with Et_2O (50 mL). The filtrate was stored overnight and concentrated under high vacuum pressure to produce 401 mg (89%) of the crude **18** as a yellow oil.

To 2,6-diphenylphenol (1.92 g, 7.8 mmol, 6.0 equiv) in CH_2Cl_2 (50.0 mL) was added $\text{Al}(\text{CH}_3)_3$ (1.95 mL, 2M in toluene, 3.9 mmol, 3.0 equiv) and the resulting MAPH solution³ was stirred for 15 min at ambient temperature before being cooled to $-50\text{ }^\circ\text{C}$. Vinyl ether (+)-**23** (1.05 g, 5.2 mmol, 4.0 equiv) was added neat followed by the dropwise addition of a solution of crude **18** (0.40 g, 1.3 mmol) in CH_2Cl_2 (12.0 mL) over 15 min. The reaction mixture was stirred at $-50\text{ }^\circ\text{C}$ for 2 h, then quenched with 50% MeOH and Et_3N (50 mL) at $-50\text{ }^\circ\text{C}$, and was partitioned between Et_2O and H_2O (200 mL each). The aqueous phase was washed with Et_2O (3 x 200 mL). The combined organic layers were dried (Na_2SO_4), filtered through a pad of Celite and basic Al_2O_3 activity III (Et_2O , 100 g), and concentrated *in vacuo* but not to dryness. Benzene (150 mL) and NaHCO_3 (1.0 g) were added and the remaining Et_2O (200 mL) was removed to afford a solution of crude **29** in benzene.

To **29** was added additional benzene (200 mL) and NaHCO₃ (1.7 g) and the reaction mixture heated to reflux for 4 h. The orange suspension was filtered through Celite and concentrated *in vacuo*. The resulting brown oil was chromatographed twice (gradient from hexane/CH₂Cl₂; 1/4, 3/2, 50 g SiO₂; then hexane/Et₂O; 1/4, 20 g SiO₂) to produce 339 mg (45% based on **27**) of diastereomeric nitroso acetals in a 44:1 ratio. This material was recrystallized from hexane to produce 301 mg (40%) of nitroso acetal (–)-**31** as a white solid. This sequence of reactions could be carried out on up to a 5 mmol scale using 2 equiv of MAPH and 3 equiv. of vinyl ether. The yields ranged from 35-40% and diastereoselectivities varied between 10:1 to 20:1. Data for (–)-**31**: mp 154-155 °C; [α]_D²⁴ – 15.7 (*c* = 1.23, CHCl₃); IR (CH₂Cl₂): 2936 (s), 2904 (m), 2861 (s), 1475 (m), 1134 (s), 1105 (s), 1042 (m), 995 (m), 920 (m), 831 (s), 652 (m) cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 7.06-7.18 (m, 5H, *H*-Ph), 5.88 (ddd, *J*=5.3, 10.7, 17.1, 1H, *H*-C1"), 5.38 (d, *J* = 17.3, 1H, *H*-C2"), 5.12 (d, *J* = 10.7, 1H, *H*-C2"), 4.98 (dt, *J*_d = 10.5, *J*_t = 6.3, 1H, *H*-C5a), 4.89-4.93 (m, 2H, *H*-C2 and *H*-C2a), 4.27 (d, *J* = 3.9, 1H, *H*-C7), 3.75 (dt, *J*_d = 4.4, *J*_t = 10.5, 1H, *H*-C1'), 3.66 (dd, *J* = 6.8, 8.1, 1H, *H*-C8b), 2.76-2.79 (m, 1H, *H*-C6'), 2.46-2.51 (m, 1H, *H*-C2'), 1.90 (dd, *J* = 6.6, 12.9, 1H, *H*-C6), 1.63-1.71 (m, 2H, *H*-C4' and *H*-C5'), 1.52-1.60 (m, 1H, *H*-C6'), 1.35-1.50 (m, 3H, *H*-C3', *H*-C5', and -C6), 1.17-1.26 (m, 1H, *H*-C4'), 1.02-1.12 (m, 1H, *H*-C3'), 0.92 (s, 9H, C(CH₃)₃), 0.90 (s, 9H, C(CH₃)₃); ¹³C NMR (125 MHz, C₆D₆) δ 144.97 (C1""), 133.21 (C1"), 128.40 (C2""), 128.31 (C3""), 126.56 (C4""), 117.96 (C2"), 100.11 (C7), 82.30 (C2), 81.65 (C1'), 72.69 (C2a), 69.81 (C8b), 66.27 (C5a), 52.07 (C2'), 34.48 (C6'), 33.39 (C6), 33.02 (C5'), 27.33 (C(CH₃)₃), 27.12 (C(CH₃)₃), 26.14 (C3'), 25.41 (C4'), 21.32 (C(CH₃)₃), 20.72 (C(CH₃)₃); MS (FAB) *m/z* 502.3 ([*M*+1]⁺), 326.2, 258.1, 242.1, 239.1, 159.1, 155.0, 135.0, 118.9, 117.0; TLC: *R*_f 0.54 (CH₂Cl₂); Anal. Calcd. for C₂₈H₄₃NO₅Si (501.74): C, 67.03; H, 8.64; N, 2.79. Found: C, 67.14; H, 8.63; N, 2.59.

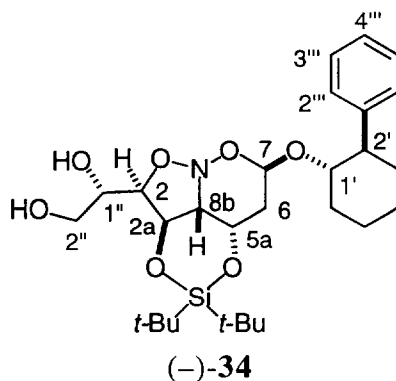
[1*R*]-[2 α (*R*),2 α ,5 α ,7 α (1*S*,2*R*),8*b* α]]-1-[[4,4-Bis(1,1-dimethylethyl)hexahydro-7-[(2-phenylcyclohexyl)oxy]]-1,3,5,8-tetraoxa-8*a*-aza-4-silaacenaphthylen-2-yl]-1,2-ethanediol ((-)-33).



A suspension of $\text{K}_2\text{Os}_2\text{O}_2(\text{OH})_4$ (29.0 mg, 0.08 mmol, 2 mol%), $\text{K}_3\text{Fe}(\text{CN})_6$ (3.90 g, 11.94 mmol, 3.0 equiv), NaHCO_3 (1.00 g, 11.94 mmol, 3.0 equiv), K_2CO_3 (1.65 g, 11.94 mmol, 3.0 equiv), and DHQ-PHN (100.0 mg, 0.20 mmol, 5 mol%) in *t*-BuOH (20 mL) and H_2O (20 mL) was stirred for 15 min. Nitroso acetal (-)-31 (2.00 g, 3.98 mmol) was added and the reaction mixture was stirred at room temperature. After 48 h, Na_2SO_3 (1.5 g) was added and stirring continued for 30 min before being partitioned between EtOAc and H_2O (500 mL each). The aqueous layers were washed with EtOAc (50 mL), and the combined organic layers were dried (Na_2SO_4), concentrated *in vacuo*, and the residue chromatographed (hexane/EtOAc, 7/3, 200 g SiO_2) to produce 2.14 g (100%) of epimeric diols in a 208:1 ratio. This material was recrystallized from hexane/ Et_2O (1/1) to produce 2.01 g (93%) of (-)-33 as a white solid. Data for (-)-33: mp 177-178 °C; $[\alpha]_{\text{D}}^{24} - 32.7$ ($c = 1.00$, CHCl_3); IR (CH_2Cl_2) 3588 (w), 3528 (w), 2936 (s), 2899 (m), 2862 (s), 1475 (m), 1450 (m), 1295 (m), 1136 (m), 1105 (s), 1070 (m), 1041 (s), 1029 (m), 1010 (m), 828 (s), 803 (m), 654 (m) cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.05-7.17 (m, 5H, *H*-Ph), 4.98 (dd, $J = 8.3, 9.8$, 1H, *H*-C2*a*), 4.91 (dt, $J_{\text{d}} = 10.2, J_{\text{t}} = 6.3$, 1H, *H*-C5*a*), 4.59 (t, $J = 8.8$, 1H, *H*-C2), 4.21 (d, $J = 3.9$, 1H, *H*-C7), 3.90-3.96 (m, 2H, *H*-C1'' and *H*-C2''), 3.80-3.85 (m, 1H, *H*-C2''), 3.72 (dt, $J_{\text{d}} = 4.4, J_{\text{t}} = 10.5$, 1H, *H*-C1'), 3.67 (dd, $J = 6.6, 8.5$, 1H, *H*-C8*b*), 3.67 (s, 1H, *HO*), 2.73-2.76 (m, 1H, *H*-C6'), 2.45-2.50 (m, 1H, *H*-C2'), 2.25 (t, $J = 6.6$, 1H,

HO), 1.83 (dd, $J = 6.6, 13.2$, 1H, $H-C6$), 1.63-1.70 (m, 2H, $H-C5'$), 1.47-1.60 (m, 2H, $H-C4'$ and $H-C6'$), 1.30-1.44 (m, 2H, $H-C3'$ and $H-C4'$), 1.23-1.29 (m, 1H, $H-C6$), 1.12-1.22 (m, 1H, $H-C3'$), 0.80 (s, 9H, $C(CH_3)_3$), 0.79 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (125 MHz, C_6D_6) δ 144.92 ($C1'''$), 128.44 ($C2'''$), 128.29 ($C3'''$), 126.60 ($C4'''$), 100.10 ($C7$), 81.83 ($C1'$), 78.58 ($C2$), 74.05 ($C2a$), 71.24 ($C1''$), 70.40 ($C8b$), 66.41 ($C5a$), 63.42 ($C2''$), 52.06 ($C2'$), 34.44 ($C6'$), 33.07 ($C6$), 33.03 ($C5'$), 27.19 ($C(CH_3)_3$), 26.93 ($C(CH_3)_3$), 26.12 ($C3'$), 25.43 ($C4'$), 21.22 ($C(CH_3)_3$), 20.56 ($C(CH_3)_3$); MS (FAB) m/z 536.3 ($[M+1]^+$), 520.3, 360.1, 282.1, 159.1, 118.9, 117.0; TLC: R_f 0.55 (hexane/EtOAc, 1:1); SFC: t_R (–)-**33** 4.32 min (99.90%); t_R (+)-**33** 4.92 min (0.10%) (ChiralCel OD, 7% MeOH in CO_2 , 150 bar, 40 °C, 3.0 mL min $^{-1}$). Anal. Calcd. for $C_{28}H_{45}NO_7Si$ (535.76): C, 62.77; H, 8.47; N, 2.61. Found: C, 62.65; H, 8.63; N, 2.50.

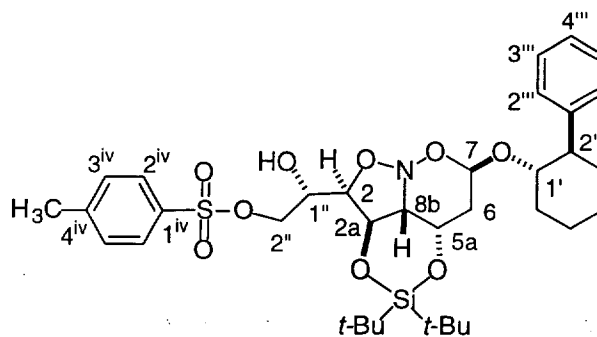
[1S-[2 α (R),2 $\alpha\alpha$,5 $\alpha\beta$,7 α (1S,2R),8 $\beta\alpha$]]-1-[[4,4-Bis(1,1-dimethylethyl)hexahydro-7-[(2-phenylcyclohexyl)oxy]]-1,3,5,8-tetraoxa-8a-aza-4-silaacenaphthylen-2-yl]-1,2-ethanediol ((–)-**34**).



A suspension of $K_2Os_2O_2(OH)_4$ (18.0 mg, 0.05 mmol, 4 mol%), $K_3Fe(CN)_6$ (1.20 g, 3.60 mmol, 3.0 equiv), $NaHCO_3$ (302.0 mg, 3.60 mmol, 3.0 equiv), K_2CO_3 (498 mg, 3.60 mmol, 3.0 equiv), and $(DHQD)_2-AQN$ (32.0 mg, 0.04 mmol, 5 mol%) in t -BuOH (6 mL) and H_2O (6 mL) was stirred for 15 min. Nitroso acetal (–)-**31** (600 mg, 1.20 mmol) was added and the reaction mixture was stirred at room temperature. After 48 h, Na_2SO_3 (1.5 g) was added and

stirring continued for 30 min before being partitioned between EtOAc and H₂O (200 mL each). The aqueous layers were washed with EtOAc (50 mL), and the combined organic layers were dried (Na₂SO₄), concentrated *in vacuo* to produce epimeric diols in a 12.0:1 ratio. The mixture was chromatographed twice (hexane/EtOAc, 7/3, 100 g SiO₂) to produce 552 mg (86%) of (–)-**34** as a white solid. Data for (–)-**34**: mp 156-158 °C; [α]_D²⁴ – 23.8 (*c* = 1.00, CHCl₃); IR (CH₂Cl₂): 3577 (w), 2936 (s), 2861 (m), 1475 (m), 1450 (m), 1136 (m), 1105 (s), 1070 (m), 1043 (s), 1029 (m), 1011 (m), 828 (s), 805 (m), 740 (m), 652 (m) cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 7.00-7.18 (m, 5H, *H*-Ph), 4.98 (dt, *J*_d = 10.3, *J*_t = 6.6, 1H, *H*-C5a), 4.89 (t, *J* = 9.5, 1H, *H*-C2a), 4.33 (dd, *J* = 3.2, 8.3, 1H, *H*-C2), 4.26 (d, *J* = 2.1, 1H, *H*-C7), 3.97 (dd, *J* = 6.3, 9.5, 1H, *H*-C8b), 3.89-3.94 (m, 1H, *H*-C1''), 3.76 (dt, *J*_d = 4.2, *J*_t = 10.5, 1H, *H*-C1'), 3.60-3.64 (m, 1H, *H*-C2''), 3.53-3.55 (m, 1H, *H*-C2''), 2.77-2.81 (m, 1H, *H*-C6'), 2.50 (ddd, *J* = 3.7, 10.5, 12.2, 1H, *H*-C2'), 2.39 (d, *J* = 5.9, 1H, *HO*), 1.88 (dd, *J* = 6.8, 13.2, 1H, *H*-C6), 1.78-1.82 (m, 1H, *HO*), 1.63-1.72 (m, 2H, *H*-C3' and *H*-C5'), 1.56-1.61 (m, 1H, *H*-C6'), 1.45-1.51 (m, 1H, *H*-C5'), 1.38-1.45 (m, 2H, *H*-C3' and *H*-C6), 1.23-1.33 (m, 1H, *H*-C4'), 1.05-1.14 (m, 1H, *H*-C4'), 0.95 (s, 9H, C(CH₃)₃), 0.93 (s, 9H, C(CH₃)₃); ¹³C NMR (125 MHz, C₆D₆) δ 144.92 (C1'''), 128.43 (C2'''), 128.30 (C3'''), 126.60 (C4'''), 100.24 (C7), 81.86 (C1'), 80.79 (C2), 72.69 (C2a), 71.20 (C8b), 69.75 (C1''), 66.50 (C5a), 64.01 (C2''), 52.04 (C2'), 34.50 (C6'), 33.05 (C6), 33.01 (C5'), 27.23 (C(CH₃)₃), 27.08 (C(CH₃)₃), 26.13 (C3'), 25.46 (C4'), 21.41 (C(CH₃)₃), 20.70 (C(CH₃)₃); MS (FAB) *m/z* 536.3 ([*M*+1]⁺), 520.3, 360.1, 282.1, 213.2, 201.2, 159.1, 119.0, 117.0; TLC: *R*_f 0.43 (hexane/EtOAc, 1:1); SFC: *t*_R (–)-**34** 4.49 min (99.98%); *t*_R (+)-**34** 5.25 min (0.02%) (ChiralCel OD, 9% MeOH in CO₂, 150 bar, 40 °C, 3.0 mL min⁻¹). Anal. Calcd. for C₂₈H₄₅NO₇Si (535.76): C, 62.77; H, 8.47; N, 2.61. Found: C, 62.48; H, 8.37; N, 2.54.

[1*R*-[2α(*R*),2αα,5αβ,7α(1*S*,2*R*),8bα]]-2-(4-Methylbenzenesulfonate)-1-[4,4-bis(1,1-dimethylethyl)octahydro-7-[(2-phenylcyclohexyl)oxy]]-1,3,5,8-tetraoxa-8a-aza-4-silaacenaphthylen-2-yl]-1,2-ethanediol (36)

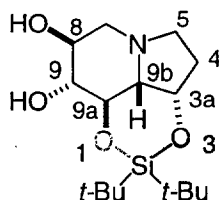


36

To a solution of (–)-**34** (540 mg, 1.0 mmol) in pyridine (15.0 mL) was added TsCl (1.15 g, 6.0 mmol, 6.0 equiv) and the reaction mixture was stirred for 3 h at room temperature before the addition of a second portion of TsCl (350 mg, 2 mmol, 2.0 equiv) to facilitate complete conversion to product. Stirring was maintained for an additional 0.5 h at room temperature before being quenched with sat. aq. NaCl (50 mL). The aqueous layers were extracted with CH₂Cl₂ (50 mL) and the combined organic layers were dried (Na₂SO₄), concentrated *in vacuo*, and the residue was chromatographed (hexane/EtOAc, 7/3, 5 g SiO₂) to produce 730 mg of the crude **36** as a white foam. Data for **36**: ¹H NMR (500 MHz, C₆D₆) δ 7.70 (d, *J* = 8.1, 2H, *H*-C2^{iv}), 7.05–7.17 (m, 5H, *H*-Ph), 6.62 (d, *J* = 8.1, 2H, *H*-C3^{iv}), 4.91 (dt, *J*_d = 10.3, *J*_t = 6.3, 1H, *H*-C5a), 4.80 (t, *J* = 9.0, 1H, *H*-C2a), 4.19–4.21 (m, 2H, *H*-C2 and *H*-C7), 4.14–4.17 (m, 1H, *H*-C2ⁱⁱ), 4.03–4.09 (m, 2H, *H*-C1ⁱ and *H*-C2ⁱⁱ), 3.84 (dd, *J* = 6.8, 9.3, 1H, *H*-C8b), 3.71 (dt, *J*_d = 4.2, *J*_t = 10.5, 1H, *H*-C1ⁱ), 2.70–2.73 (m, 1H, *H*-C6ⁱ), 2.44–2.50 (m, 1H, *H*-C2ⁱ), 2.37 (d, *J* = 5.6, 1H, HO), 1.82–1.86 (m, 1H, *H*-C6), 1.79 (s, 3H, CH₃), 1.64–1.77 (m, 2H, *H*-C3ⁱ and *H*-C5ⁱ), 1.48–1.58 (m, 2H, *H*-C4ⁱ and *H*-C6ⁱ), 1.33–1.44 (m, 2H, *H*-C6 and *H*-C5ⁱ), 1.19–1.30 (m, 1H, *H*-C3ⁱ), 1.00–1.10 (m, 1H, *H*-C4ⁱ), 0.92 (s, 9H, C(CH₃)₃), 0.87 (s, 9H, C(CH₃)₃); ¹³C NMR (125 MHz, C₆D₆) δ 144.87 (C1ⁱⁱⁱ), 144.17 (C1^{iv}), 129.79 (C3^{iv}), 128.64 (C2^{iv}), 128.43 (C2ⁱⁱⁱ), 128.28 (C3ⁱⁱⁱ), 127.49 (C4^{iv}), 126.62 (C4ⁱⁱⁱ), 100.17 (C7), 81.78 (C1ⁱ), 79.58 (C2), 72.76

(C2a), 71.31 (C8b), 70.55 (C2"), 67.68 (C1"), 66.47 (C5a), 52.02 (C2'), 34.43 (C6'), 33.00 (C6), 32.91 (C5'), 27.19 (C(CH₃)₃), 27.05 (C(CH₃)₃), 26.10 (C3'), 25.43 (C4'), 21.41 (C(CH₃)₃), 21.08 (C(CH₃)₃), 20.60 (CH₃); TLC: *R_f* 0.62 (hexane/EtOAc, 7/3).

[3a*S*-(3aα,8β,9α,9aβ,9bβ)]-2,2-Bis(1,1-dimethylethyl)octahydro-1,3-dioxo-2-silacyclohexa[hi]indolizine-8,9-diol ((-)-35).

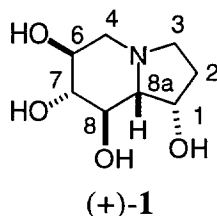


(-)-35

To Raney-nickel W-2 (\approx 10.5 g, pre-washed with H₂O (1.6 L) and MeOH (800 mL)) was added a solution of **36** (730 mg, 1.0 mmol) in MeOH (100 mL) and the reaction mixture hydrogenated in a glass lined steel autoclave under 160 psi of H₂ pressure for 36 h with stirring. The suspension was neutralized with Et₃N (5 mL) and filtered through a pad of Celite/SiO₂/Celite. The pad was washed extensively with MeOH (1L) and the filtrate concentrated to produce a yellow oil. This material was chromatographed twice (gradient from CHCl₃; CHCl₃/MeOH, 95/5; CHCl₃/MeOH/ NH₄OH, 90/9/1, 50 g SiO₂; then CHCl₃; CHCl₃/MeOH; 99/1, 90:10, 20 g SiO₂) to produce (-)-**35** as a hygroscopic silicate, and (+)-**26** (172 mg, 98%) was recovered as a white solid. The silicate was passed through a plug of basic and neutral Al₂O₃ to afford 239 mg (73%) of (-)-**35** as a white foam. Data for (-)-**35**: mp 67-68 °C; [α]_D²⁴ - 0.4 (*c* = 0.95, CHCl₃); IR (CH₂Cl₂): 3590 (m), 3586 (m), 2935 (s), 2861 (s), 1153 (s), 1046 (s), 1025 (s), 1012 (m), 827 (s), 653 (m) cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 4.64 (dt, *J_d* = 9.0, *J_t* = 6.3, 1H, *H*-C3a), 3.70-3.76 (m, 2H, *H*-C8 and *H*-C9a), 3.30 (t, *J* = 9.0, 1H, *H*-C9), 3.01 (dd, *J* = 5.4, 13.7, 1H, *H*-C7), 2.81 (dd, *J* = 6.8, 10.3, 1H, *H*-C9b), 2.74 (dd, *J* = 10.7, 13.7, 1H, *H*-C7), 2.60 (dt, *J_d* = 6.1 *J_t* = 9.0, 1H, *H*-C5), 2.57-2.62 (bs, 1H, HO), 2.49 (dt, *J_d* = 4.9 *J_t* = 8.5, 1H, *H*-C5), 2.45 (bs, 1H, HO), 2.13 (dtd, *J_d* = 6.1, 7.1 *J_t* = 8.8, 1H, *H*-C4), 1.68-1.75 (m, 1H, *H*-C4), 1.11 (s,

9H, C(CH₃)₃), 1.06 (s, 9H, C(CH₃)₃); ¹³C NMR (125 MHz, C₆D₆) δ 79.98 (C9), 74.92 (C3a), 70.36 (C8), 67.69 (C9a), 63.93 (C9b), 51.98 (C7), 48.61 (C5), 33.75 (C4), 27.52 (C(CH₃)₃), 27.38 (C(CH₃)₃), 21.57 (C(CH₃)₃), 21.18 (C(CH₃)₃); MS (FAB) *m/z* 330.2 ([*M*+1]⁺), 328.1, 155.0, 119.0; TLC: *R_f* 0.33 (CHCl₃/MeOH/NH₄OH, 90/9/1); Anal. Calcd. for C₁₆H₃₁NO₄Si (329.51): C, 58.32; H, 9.48; N, 4.25. Found: C, 58.39; H, 9.45; N, 4.28.

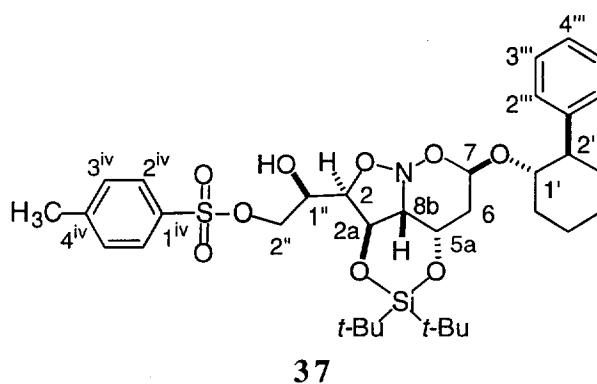
Castanospermine, [1*S*-(1*α*,6*β*,7*α*,8*β*,8*aβ*)]-Octahydro-1,6,7,8-indolizidinetetrol ((+)-1).



To a solution of (–)-**35** (350 mg, 1.1 mmol) in MeOH (40 mL) in a teflon bottle was added 46% HF (3.4 mL) and the reaction mixture was stirred at room temperature for 24 h. The mixture was concentrated *in vacuo* and the resulting purple solid was loaded onto AG1-8X ion exchange resin (20 g, pretreated) in H₂O and eluted with 2N NH₄OH (100 mL). Concentration *in vacuo* produced 177 mg (88%) of (+)-castanospermine ((+)-**1**) as a white solid. An analytical sample was obtained by recrystallization from MeOH/Et₂O. Data for (+)-**1**: mp 212 °C, dec., (lit.³¹ 210 °C dec.); [*α*]_D²⁰ + 79.7 (*c* = 1.06, H₂O, pH = 8.71), (lit.⁴ [*α*]_D + 79.9° (*c* = 0.93, H₂O)); IR (KBr): 3367 (s), 2946 (w), 2922 (m), 2858 (m), 2835 (m), 1365 (s), 1354 (w), 1258 (m), 1158 (m), 1123 (s), 1117 (s), 1092 (s), 1077 (s), 1030 (s), 1015 (s), 1010 (s), 564 (m), 531 (s) cm^{–1}; ¹H NMR (500 MHz, D₂O) δ 4.24 (ddd, *J* = 1.7, 2.9, 6.9, 1H, *H*-C1), 3.41–3.47 (m, 2H, *H*-C6 and *H*-C8), 3.15 (t, *J* = 9.0, 1H, *H*-C7), 3.01 (dd, *J* = 5.1, 10.7, 1H, *H*-C5), 2.91 (dt, *J_d* = 2.0, *J_t* = 9.0, 1H, *H*-C3), 2.17 (dddd, *J* = 2.2, 7.1, 9.5, 14.2, 1H, *H*-C2), 2.05 (q, *J* = 9.3, 1H, *H*-C3), 1.88 (q, *J* = 10.7, 1H, *H*-C5), 1.86 (dd, *J* = 4.4, 9.8, 1H, *H*-C8a), 1.54 (dtd, *J_d* = 1.7, 14.2, *J_t* = 8.8, 1H, *H*-C2); ¹³C NMR (125 MHz, D₂O) δ 78.82 (C7), 71.24 (C8a), 69.91 (C1), 69.39

(C6), 68.78 (C8), 55.20 (C5), 51.42 (C3), 32.54 (C2); MS (EI) m/z 189.1 ($[M]^+$), 171.1, 154.1, 145.1, 134.1, 127.1, 105.1, 86.1, 78.0, 77.1, 76.0, 63.0; TLC: R_f 0.47 ($\text{CHCl}_3/\text{MeOH}/\text{NH}_4\text{OH}$, 5/5/1); Anal. Calcd. for $\text{C}_8\text{H}_{15}\text{NO}_4$ (189.21): C, 50.78; H, 7.99; N, 7.40. Found: C, 50.61; H, 7.97; N, 7.26.

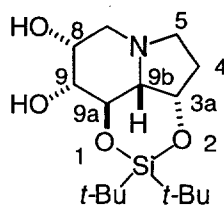
[1*S*]-[2*α*(*R*),2*αα*,5*α**β*,7*α*(1*S*,2*R*),8*bα*]-2-(4-Methylbenzenesulfonate)-1-[4,4-bis-(1,1-dimethylethyl)octahydro-7-[(2-phenylcyclohexyl)oxy]]-1,3,5,8-tetraoxa-8*a*-aza-4-silaacenaphthylen-2-yl]-1,2-ethanediol (37)**



To a solution of (–)-**33** (270 mg, 0.5 mmol) in pyridine (3.0 mL) was added TsCl (290 mg, 1.5 mmol, 3.0 equiv) and the reaction mixture stirred for 1.5 h at room temperature before the addition of more TsCl (100 mg, 0.52 mmol, 1.05 equiv) to facilitate complete conversion to product. Stirring was maintained for an additional 2.5 h at room temperature before quenching with sat. aq. NaCl (50 mL). The aqueous layers were extracted with CH_2Cl_2 (50 mL) and the combined organic layers were dried (Na_2SO_4), concentrated *in vacuo*, and the residue chromatographed (CH_2Cl_2 , 5 g SiO_2) to produce 363 mg of the crude **37** as a white foam. Data for **37**: ^1H NMR (500 MHz, C_6D_6) δ 7.81 (d, $J = 8.3$, 2H, $H\text{-C}2^{\text{iv}}$), 7.05–7.17 (m, 5H, $H\text{-Ph}$), 6.66 (d, $J = 8.1$, 2H, $H\text{-C}3^{\text{iv}}$), 4.85–4.90 (m, 2H, $H\text{-C}2\text{a}$ and $H\text{-C}5\text{a}$), 4.43 (dd, $J = 2.7$, 10.5, 1H, $H\text{-C}2''$), 4.36 (t, $J = 8.3$, 1H, $H\text{-C}2$), 4.22 (dd, $J = 5.9$, 10.5, 1H, $H\text{-C}2''$), 4.18 (d, $J = 4.2$, 1H, $H\text{-C}7$), 3.96–4.00 (m, 1H, $H\text{-C}1''$), 3.71 (dt, $J_d = 4.4$, $J_t = 10.5$, 1H, $H\text{-C}1'$), 3.60 (dd, $J = 6.3$, 8.9, 1H, $H\text{-C}8\text{b}$), 3.38 (bs, 1H, HO), 2.68–2.72 (m, 1H, $H\text{-C}6'$), 2.44–2.49 (m, 1H, $H\text{-C}6'$).

C2'), 1.79-1.83 (m, 1H, *H*-C6), 1.80 (s, 3H, CH₃), 1.64-1.70 (m, 2H, *H*-C4'), 1.43-1.58 (m, 2H, *H*-C3' and *H*-C6'), 1.36-1.42 (m, 1H, *H*-C5'), 1.21-1.32 (m, 2H, *H*-C3' and *H*-C6'), 1.14-1.19 (m, 1H, *H*-C5'), 0.78 (s, 9H, C(CH₃)₃), 0.76 (s, 9H, C(CH₃)₃); ¹³C NMR (C₆D₆) δ 144.86 (C1'''), 143.96 (C1^{iv}), 129.71 (C3^{iv}), 128.45 (C2^{iv}), 128.35 (C2'''), 128.28 (C3'''), 127.49 (C4^{iv}), 126.63 (C4'''), 100.10 (C7), 81.85 (C1'), 78.06 (C2), 73.88 (C2a), 70.42 (C2'' and C8b), 69.38 (C1''), 66.34 (C5a), 52.06 (C2'), 34.42 (C6), 33.02 (C5'), 32.94 (C6'), 27.13 (C(CH₃)₃), 26.88 (C(CH₃)₃), 26.09 (C3'), 25.41 (C4'), 21.19 (C(CH₃)₃), 21.08 (C(CH₃)₃), 20.49 (CH₃); TLC: *R_f* 0.66 (hexane/EtOAc, 1:1).

[3a*S*-(3aα,8α,9α,9aβ,9bβ)]-2,2-Bis(1,1-dimethylethyl)octahydro-1,3-dioxo-2-silacyclohexa[hi]indolizine-8,9-diol ((-)-38).

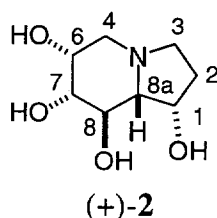


(-)-38

To Raney-Nickel (\approx 7.0 g, pre-washed with H₂O (800 mL) and MeOH (400 mL)) was added **37** (363.0 mg, 0.5 mmol) in MeOH (50.0 mL) and the reaction mixture hydrogenated in a glass lined steel autoclave under 260 psi of H₂ pressure for 36 h with stirring. The suspension was neutralized with Et₃N (5 mL) and filtered through a pad of Celite/SiO₂/Celite. The pad was washed extensively with MeOH (1L), and concentrated to produce a yellow oil. This material was chromatographed (gradient from CHCl₃; CHCl₃/MeOH, 99/1; CHCl₃/MeOH/NH₄OH, 90/9/1; 35 g SiO₂) to produce (-)-**38** as a silicate, and (+)-**26** (149 mg, 100%) was recovered as a white solid. The silicate was passed through a plug of basic and neutral Al₂O₃ to afford 131 mg (81%) of (-)-**38** as a white foam. Data for (-)-**38**: mp 67-68 °C; [α]_D²⁴ - 35.8 (*c* = 1.01, CHCl₃); IR (CH₂Cl₂): 3713 (w), 3693 (w), 3055 (s), 2987 (s), 2306 (m), 1440 (m), 1422 (m), 1270 (s), 1257 (s), 896 (m), 759 (s), 719 (s), 671 (m) cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 4.69 (dt, *J_d* =

9.0, $J_t = 6.2$, 1H, $H\text{-C3a}$), 4.27 (t, $J = 9.8$, 1H, $H\text{-C9a}$), 3.78-3.82 (m, 1H, $H\text{-C8}$), 3.56 (dt, $J_d = 6.8$, $J_t = 9.0$, 1H, $H\text{-C5}$), 3.28 (dd, $J = 3.2, 9.3$, 1H, $H\text{-C9}$), 3.04 (dd, $J = 1.7, 14.9$, 1H, $H\text{-C7}$), 2.76-2.80 (m, 2H, $H\text{-C9b}$ and $H\text{-C5}$), 2.60-2.70 (bs, 1H, HO), 2.59 (dd, $J = 2.0, 15.2$, 1H, $H\text{-C7}$), 2.45-2.55 (bs, 1H, HO), 2.18 (dtd, $J_d = 6.8, 13.2J_t = 8.8$, 1H, $H\text{-C4}$), 1.86 (ddt, $J_d = 9.8, 15.4, J_t = 4.9$, 1H, $H\text{-C4}$), 1.11 (s, 9H, $C(CH_3)_3$), 1.08 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (125 MHz, C_6D_6) δ 75.60 (C9), 75.01 (C3a), 71.80 (C8), 67.68 (C9a), 64.22 (C9b), 50.75 (C7), 50.12 (C5), 34.10 (C4), 27.54 ($C(CH_3)_3$), 27.45 ($C(CH_3)_3$), 21.57 ($C(CH_3)_3$), 21.22 ($C(CH_3)_3$); MS (FAB) m/z 330.2 ($[M+1]^+$), 328.2, 155.1, 119.0; TLC: R_f 0.57 ($CHCl_3/MeOH/NH_4OH$, 90/9/1); Anal. Calcd. for $C_{16}H_{31}NO_4Si$ (329.51): C, 58.32; H, 9.48; N, 4.25. Found: C, 58.26; H, 9.55; N, 4.20.

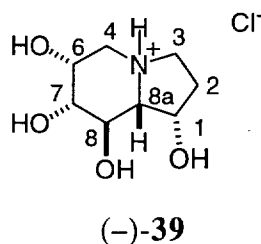
6-Epicastanospermine, [1S-(1 α ,6 α ,7 α ,8 β ,8a β)]-Octahydro-1,6,7,8-indolizidinetetrol ((+)-2)



To a solution of (–)-**38** (337 mg, 1.0 mmol) in MeOH (35 mL) in a teflon bottle was added 46% HF (3.4 mL) and the reaction mixture stirred at room temperature for 24 h. The mixture was concentrated *in vacuo* and the resulting purple solid was loaded onto AG 50W-X8 ion exchange resin (20 g, pretreated) in H_2O and eluted with 2N NH_4OH (150 mL). Concentration *in vacuo* produced 186 mg (96%) of (+)-6-epicastanospermine ((+)-**2**) as a white solid. Data for (+)-**2**: $[\alpha]_D^{24} + 1.6$ ($c = 1.00$, MeOH), (lit.⁵ $[\alpha]_D + 2.2^\circ$ ($c = 0.7$, MeOH)); 1H NMR (D_2O) δ 4.18-4.20 (m, 1H, $H\text{-C1}$), 3.78-3.82 (m, 1H, $H\text{-C6}$), 3.68 (t, $J = 9.5$, 1H, $H\text{-C8}$), 3.33 (dd, $J = 3.5, 9.5$, 1H, $H\text{-C7}$), 2.92 (dd, $J = 2.4, 12.4$, 1H, $H\text{-C5}$), 2.88 (dt, $J_d = 1.8, J_t = 9.2$, 1H, $H\text{-C3}$), 2.08-2.16 (m, 1H, $H\text{-C2}$), 2.08 (d, $J = 12.6$, 1H, $H\text{-C5}$), 1.95 (q, $J = 9.2$, 1H, $H\text{-C3}$), 1.72 (dd, $J =$

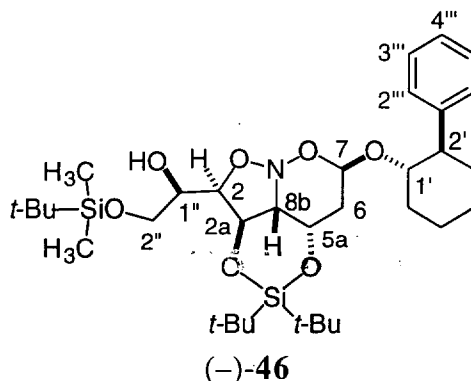
4.2, 9.7, 1H, *H*-C8a), 1.52 (dtd, $J_d = 2.2$, 14.2, $J_t = 8.8$, 1H, *H*-C2); ^{13}C NMR (100 MHz, D_2O) δ 75.14 (C7), 71.43 (C8a), 69.90 (C1), 68.66 (C6), 67.00 (C8), 55.02 (C5), 51.47 (C3), 32.46 (C2); TLC: R_f 0.41 ($\text{CHCl}_3/\text{MeOH}/\text{NH}_4\text{OH}$, 5/5/1).

6-Epicastanospermine Hydrochloride, [1S-(1 α ,6 α ,7 α ,8 β ,8a β)]-Octahydro-1,6,7,8-indolizidinetetrol Hydrochloride ((-)-39).



To (+)-2 (127 mg, 0.67 mmol) in MeOH (5 mL) was added conc. HCl (2 mL) and the reaction mixture concentrated *in vacuo* to produce a gray solid. This material was recrystallized twice from MeOH/Et₂O to afford 120 mg (80%) of (-)-6-epicastanospermine hydrochloride ((-)-39) as a gray solid. Data for (-)-39: mp 258-259 °C, dec., (lit.⁵ >250 °C dec.); $[\alpha]_D^{20} -1.39$ ($c = 1.01$, H_2O), (lit.⁶ $[\alpha]_D \sim 0$ ($c = 1.5$, H_2O)); IR (KBr): 3378 (s), 3336 (s), 3327 (s), 3097 (m), 3054 (m), 1470 (m), 1418 (m), 1380 (m), 1321 (m), 1126 (m), 1093 (m), 1073 (s), 1027 (m), 979 (m) cm^{-1} ; ^1H NMR (500 MHz, D_2O) δ 4.47 (dd, $J = 3.4$, 5.9, 1H, *H*-C1), 4.05 (m, 1H, *H*-C6), 3.93 (t, $J = 10.3$, 1H, *H*-C8), 3.58 (ddd, $J = 4.2$, 9.3, 11.5, 1H, *H*-C3), 3.55 (dd, $J = 3.2$, 9.5, 1H, *H*-C7), 3.45 (dd, $J = 3.7$, 12.9, 1H, *H*-C5), 3.06 (dd, $J = 1.0$, 12.7, 1H, *H*-C5), 2.98 (dt, $J_d = 7.6$, $J_t = 11.5$, 1H, *H*-C3), 2.93 (dd, $J = 3.7$, 10.7, 1H, *H*-C8a), 2.33-2.40 (m, 1H, *H*-C2), 1.82-1.88 (m, 1H, *H*-C2); ^{13}C NMR (125 MHz, D_2O) δ 73.24 (C7), 71.63 (C8a), 67.27 (C1), 66.79 (C6), 64.70 (C8), 54.67 (C5), 51.86 (C3), 31.40 (C2); MS (CI) m/z 225.2 ($[M]^+$), 190.1, 172.1, 119.1, 107.1, 88.0; TLC: R_f 0.39 ($\text{CHCl}_3/\text{MeOH}/\text{NH}_4\text{OH}$, 5/5/1); Anal. Calcd. for $\text{C}_8\text{H}_{16}\text{NO}_4\text{Cl}$ (225.67): C, 42.58; H, 7.15; N, 6.21; Cl, 15.71. Found: C, 42.52; H, 7.42; N, 6.10; Cl, 15.77.

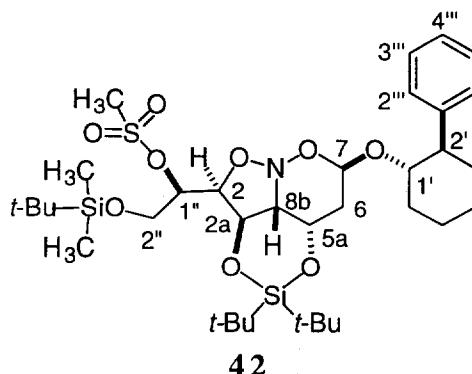
[1*R*-[2α(*R*),2αα,5αβ,7α(1*S*,2*R*),8bα]]-1-[4,4-Bis(1,1-dimethylethyl)octahydro-7-[(2-phenylcyclohexyl)oxy]]-2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,3,5,8-tetraoxa-8a-aza-4-silaacenaphthylen-2-yl]-ethanol ((-)-46).



To a solution of (-)-33 (803 mg, 1.5 mmol) in pyridine (13.0 mL) was added TBSCl (680 mg, 4.5 mmol, 3.0 equiv) and the reaction mixture stirred for 1 h at room temperature before quenching with sat. aq. NaCl (50 mL). The aqueous layers were extracted with CH₂Cl₂ (50 mL) and the combined organic layers were dried (Na₂SO₄), concentrated *in vacuo*, and the residue chromatographed (hexane/EtOAc, 4/1, 40 g SiO₂) to produce 926 g (95%) of (-)-46 as a white solid. Data for (-)-46: mp 138-140 °C; [α]_D²⁴ - 27.6 (*c* = 1.03, CHCl₃); IR (CH₂Cl₂): 3530 (w), 2935 (s), 2897 (s), 2860 (s), 1474 (s), 1151 (m), 1105 (s), 1070 (m), 1040 (s), 1029 (m), 1011 (m), 932 (m), 834 (s), 828 (s), 810 (m), 654 (m) cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 7.10-7.20 (m, 5H, *H*-Ph), 5.08 (t, *J* = 9.0, 1H, *H*-C2a), 4.97 (dt, *J*_d = 10.2, *J*_t = 6.3, 1H, *H*-C5a), 4.80 (t, *J* = 8.3, 1H, *H*-C2), 4.24 (d, *J* = 3.4, 1H, *H*-C7), 3.99-4.09 (m, 3H, *H*-C1'' and *H*-C2''), 3.73-3.80 (m, 2H, *H*-C1' and *H*-C8b), 3.53 (s, 1H, *HO*), 2.77-2.80 (m, 1H, *H*-C6'), 2.48-2.53 (m, 1H, *H*-C2'), 1.88 (dd, *J* = 6.6, 13.2, 1H, *H*-C6), 1.62-1.73 (m, 2H, *H*-C4' and *H*-C5'), 1.54-1.60 (m, 1H, *H*-C4'), 1.50-1.53 (m, 2H, *H*-C6'), 1.38-1.46 (m, 2H, *H*-C3' and *H*-C5'), 1.22-1.37 (m, 1H, *H*-C6), 1.08-1.17 (m, 1H, *H*-C3'), 1.04 (s, 9H, C(CH₃)₃, TBS), 0.85 (s, 9H, C(CH₃)₃), 0.84 (s, 9H, C(CH₃)₃), 0.20 (s, 3H, CH₃), 0.19 (s, 3H, CH₃); ¹³C NMR (125 MHz, C₆D₆) δ 144.91 (C1'''), 128.43 (C2'''), 128.29 (C3'''), 126.58 (C4'''), 100.02 (C7), 81.64

(C1'), 78.54 (C2), 73.98 (C2a), 71.72 (C1''), 70.72 (C8b), 66.45 (C5a), 64.31 (C2''), 52.08 (C2'), 34.44 (C6'), 33.03 (C6 and C5'), 27.19 (C(CH₃)₃), 26.93 (C(CH₃)₃), 26.16 (C(CH₃)₃), 26.12 (C3'), 25.41 (C4'), 21.24 (C(CH₃)₃), 20.56 (C(CH₃)₃), 18.67 (C(CH₃)₃, TBS), -5.09 (CH₃); MS (FAB) *m/z* 650.4 ([*M*]⁺), 476.3, 474.3, 309.0, 155.0, 119.0; TLC: *R_f* 0.32 (CH₂Cl₂); Anal. Calcd. for C₃₄H₅₉NO₇Si₂ (650.02): C, 62.83; H, 9.15; N, 2.15. Found: C, 62.99; H, 9.27; N, 1.99.

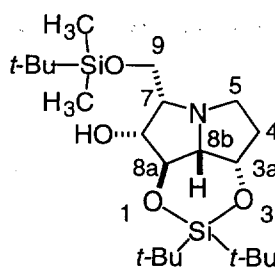
[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-[(methylsulfonyl)oxy]-ethyl]hexahydro-7-[(2-phenylcyclohexyl)oxy]]-1,3,5,8-tetraoxa-8a-aza-4-silacacenaphthylene (42)



To a solution of (–)-**46** (690 mg, 1.1 mmol) in pyridine (16.5 mL) was added Ms₂O (1.10 g, 6.4 mmol, 6.0 equiv) and the reaction mixture stirred for 1.5 h at room temperature before quenching with sat. aq. NaCl (100 mL). The aqueous layers were extracted with CH₂Cl₂ (100 mL) and the combined organic layers were dried (Na₂SO₄), concentrated *in vacuo*, and the residue chromatographed (hexane/EtOAc, 4/1, 30 g SiO₂) to produce 753 mg (98%) of the crude **42** as a white foam. Data for **42**: ¹H NMR (500 MHz, C₆D₆) δ 7.05–7.16 (m, 5H, *H*-Ph), 5.08 (dt, *J_d* = 3.9, *J_t* = 4.2, 1H, *H*-C1''), 4.96–5.03 (m, 2H, *H*-C2a and *H*-C5a), 4.86 (dd, *J* = 3.9, 8.3, 1H, *H*-C2), 4.22 (d, *J* = 4.2 1H, *H*-C7), 4.07–4.14 (m, 2H, and *H*-C2''), 3.88 (dd, *J* = 5.6, 8.3, 1H, *H*-C8b), 3.70 dt, *J_d* = 4.4, *J_t* = 10.7, 1H, *H*-C1'), 2.61–2.70 (m, 1H, *H*-C6'), 2.49 (s, 3H, CH₃), 2.44–2.49 (m, 1H, *H*-C2'), 1.85 (dd, *J* = 6.6, 13.2, 1H, *H*-C6), 1.63–1.70 (m, 2H, *H*-

C4'), 1.51-1.59 (m, 1H, *H*-C6'), 1.46-1.49 (m, 2H, *H*-C5'), 1.34-1.42 (m, 2H, *H*-C3' and *H*-C6), 1.17-1.26 (m, 1H, *H*-C3'), 1.04 (s, 9H, C(CH₃)₃, TBS), 0.93 (s, 9H, C(CH₃)₃), 0.89 (s, 9H, C(CH₃)₃), 0.02 (s, 3H, CH₃), 0.01 (s, 3H, CH₃); ¹³C NMR (125 MHz, C₆D₆) δ ; TLC: *R_f* 0.73 (hexane/EtOAc, 1:1).

[3a*R*-(3aα,4β,5β,8aβ,8bα)]-2,2-Bis(1,1-dimethylethyl)-5-[(1,1-dimethylethyl)dimethylsilyl]oxy)methyl]hexahydro-2*H*,3a*H*-1,3-dioxo-2-silacyclohexa[*gh*]-pyrrolizine-4-ol ((-)-47).

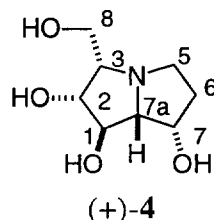


(-)-47

To Raney-Nickel (≈ 10.5 g, pre-washed with H₂O (1.6 L) and MeOH (800 mL)) was added **42** (753 mg, 1.0 mmol) in MeOH (120.0 mL) and the reaction mixture hydrogenated in a glass lined steel autoclave under 160 psi of H₂ pressure for 48 h with stirring. The suspension was neutralized with Et₃N (5 mL) and filtered through a pad of Celite/SiO₂/Celite. The pad was washed extensively with MeOH (2L), and concentrated to produce a yellow oil. This material was chromatographed (gradient from CHCl₃; CHCl₃/MeOH; 99/1, 95/5, 80 g SiO₂) to produce (-)-**47** as a silicate, and (+)-**26** (216 mg, 100%) was recovered as a white solid. The silicate was passed through a plug of basic and neutral Al₂O₃ to afford 345 mg (78%) of (-)-**47** as a white foam. Data for (-)-**47**: mp 137-138 °C; [α]_D²⁴ - 60.8 (*c* = 1.01, CHCl₃); IR (CH₂Cl₂): 3526 (w), 2950 (s), 2935 (s), 2860 (s), 1465 (m), 1136 (m), 1080 (s), 1059 (s), 840 (s), 828 (s) cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 4.74 (q, *J* = 7.1, 1H, *H*-C3a), 4.28-4.33 (m, 2H, *H*-C8a and *H*-C8), 3.81 (dd, *J* = 4.0, 11.2, *H*-C9), 3.78 (dd, *J* = 4.4, 11.2, *H*-C9), 3.57-3.59 (m, 1H, *H*-C7), 3.18-3.26 (m, 2H, *H*-C5 and *H*-C8b), 2.96 (bs, 1H, HO), 2.85 (dt, *J_d* = 10.5, *J_t* = 7.5, 1H, *H*-C5), 1.98-2.08

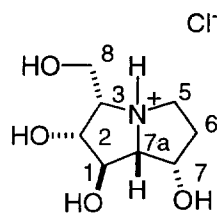
(m, 2H, *H*-C5), 1.21 (s, 9H, C(CH₃)₃), 1.13 (s, 9H, C(CH₃)₃), 0.89 (s, 9H, C(CH₃)₃, TBS), -8.73 (s, 3H, CH₃), -9.96 (s, 3H, CH₃); ¹³C NMR (C₆D₆) δ 74.54 (C8), 77.51 (C8a), 75.15 (C3a), 65.67 (C8b), 63.47 (C7), 60.44 (C9), 46.31 (C5), 33.01 (C4), 27.33 (C(CH₃)₃), 27.12 (C(CH₃)₃), 25.59 (C(CH₃)₃, TBS), 21.47 (C(CH₃)₃), 20.88 (C(CH₃)₃), 17.90 (C(CH₃)₃, TBS), -5.98 (CH₃), -6.06 (CH₃); MS (FAB) *m/z* 444.2 ([*M*]⁺), 442.2, 428.2, 386.1, 330.1, 298.1; TLC: *R_f* 0.15 (CHCl₃/MeOH, 95/5); Anal. Calcd. for C₂₂H₄₅NO₄Si₂ (443.78): C, 59.54; H, 10.22; N, 3.16. Found: C, 59.29; H, 10.18; N, 3.14.

3-Epiaustraline, [1*R*-(1α,2β,3β,7β,7aβ)]-Hexahydro-3-hydroxymethyl-1*H*-pyrrolizidine-1,2,7-triol ((+)-4)



To a solution of (-)-47 (450 mg, 1.01 mmol) in MeOH (35 mL) in a teflon bottle was added 48% aqueous HF (3.4 mL) and the reaction mixture stirred at room temperature for 24 h. The reaction mixture was concentrated *in vacuo* and the resulting purple oil loaded onto AG 50W-X8 ion exchange resin (20 g, pretreated) in H₂O and eluted with 2N NH₄OH (300 mL). Concentration *in vacuo* afforded 183 mg (96%) of (+)-3-epiaustraline ((+)-4) as a hygroscopic white foam. Data for (+)-4: [α]_D²⁴ + 6.2 (*c* = 1.00, MeOH); ¹H NMR (500 MHz, D₂O) δ 4.19 (dt, *J_d* = 1.5, *J_t* = 4.4, 1H, *H*-C7), 4.09 (t, *J* = 3.2, 1H, *H*-C1), 3.93 (dd, *J* = 3.4, 4.4, 1H, *H*-C2), 3.82 (AB_x, dd, *J* = 5.8, 12.0, 1H, *H*-C8), 3.73 (AB_x, dd, *J* = 6.3, 12.0, 1H, *H*-C8), 3.19 (dd, *J* = 3.6, 3.9, 1H, *H*-C7a), 3.09 (dt, *J_d* = 4.4, *J_t* = 5.8, 1H, *H*-C3), 2.94 (ddd, *J* = 5.9, 9.0, 12.2, 1H, *H*-C5), 2.67-2.71 (m, 1H, *H*-C5), 1.65-1.78 (m, 2H, *H*-C6); ¹³C NMR (100 MHz, D₂O) δ 78.29 (C2), 74.61 (C7a), 74.03 (C1), 69.51 (C7), 63.12 (C3), 57.03 (C8), 44.50 (C5), 34.84 (C6); TLC: *R_f* 0.23 (CHCl₃/MeOH/NH₄OH, 5/5/1).

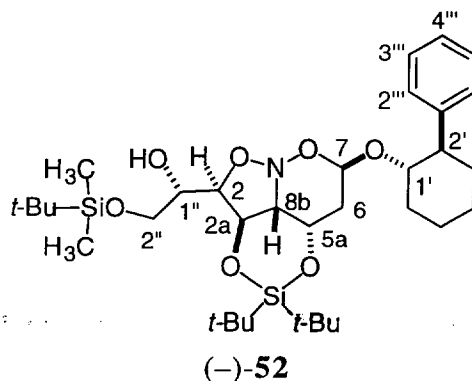
3-Epiaustraline Hydrochloride, [1*R*-(1 α ,2 β ,3 β ,7 β ,7*a* β)]-Hexahydro-3-hydroxymethyl-1*H*-pyrrolizidine-1,2,7-triol Hydrochloride ((-)-48).



(-)-48

To a solution of (+)-4 (177 mg, 0.92 mmol) in MeOH (10 mL) was added conc. HCl (2 mL) and the reaction mixture concentrated *in vacuo* to produce a pink solid. This material could be recrystallized from either MeOH or MeOH/Et₂O to afford 185.0 mg (89%) of (-)-3-epiaustraline hydrochloride ((-)-48) as a cream crystals. Data for (-)-48: mp 159-160 °C dec., (lit.⁷ 148-152 °C dec. (recrystallization from methanolic HCl)); [α]_D²⁵ - 6.1 (*c* = 1.01, H₂O), (lit.⁷ [α]_D - 3.5 (*c* = 1.35, H₂O)). IR (KBr): 3392 (s), 3297 (s), 2921 (m), 2802 (m), 2604 (m), 2563 (m), 1384 (m), 1084 (s), 1065 (s), 1053 (m), 1007 (m), 892 (m), 643 (m) cm⁻¹; ¹H NMR (500 MHz, D₂O) δ 4.48 (t, *J* = 4.9, 1H, *H*-C7), 4.38 (s, 1H, *H*-C1), 4.07 (d, *J* = 3.4, 1H, *H*-C2), 4.02 (d, *J* = 5.9, 1H, *H*-C7a), 3.77-3.90 (m, 3H, *H*-C3 and *H*-C8), 3.38-3.49 (m, 2H, *H*-C5), 2.01 (dd, *J* = 5.4, 14.2, 1H, *H*-C6), 1.86-1.94 (m, 1H, *H*-C6); ¹³C NMR (125 MHz, D₂O) δ 78.66 (C7a), 76.70 (C2), 73.49 (C1), 68.59 (C7), 66.41 (C8), 55.42 (C3), 46.76 (C5), 34.37 (C6); MS (CI) *m/z* 225.2 (*M*⁺), 190.1, 172.1, 158.1, 119.1; TLC: *R*_f 0.20 (CHCl₃/MeOH/ NH₄OH, 5/5/1); Anal. Calcd. for C₈H₁₆NO₄Cl (225.67): C, 42.58; H, 7.15; N, 6.21; Cl, 15.71. Found: C, 42.54; H, 7.15; N, 6.24; Cl, 15.60.

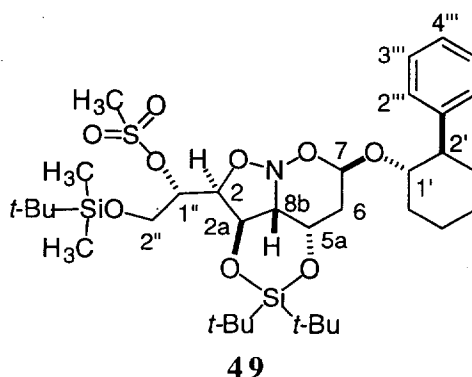
[1*S*-[2α(*R*),2α,5αβ,7α(1*S*,2*R*),8bα]]-1-[4,4-bis(1,1-dimethylethyl)octahydro-7-[(2-phenylcyclohexyl)oxy]]-1,3,5,8-tetroxa-8a-aza-4-silaacenaphthylen-2-yl]-2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethanol ((-)-52).



To a solution of (-)-34 (945 mg, 1.76 mmol) in pyridine (22.0 mL) was added TBSCl (928 mg, 6.16 mmol, 3.5 equiv) and the reaction mixture stirred for 4 h at room temperature before quenching with sat. aq. NaCl (100 mL). The aqueous layers were extracted with CH₂Cl₂ (100 mL) and the combined organic layers were dried (Na₂SO₄), concentrated *in vacuo*, and the residue chromatographed (hexane/EtOAc, 4/1, 40 g SiO₂) to produce 1.06 g (93%) of (-)-52 as white needles. Data for (-)-52: mp 140-141 °C; [α]_D²⁴ - 22.0 (*c* = 1.02, CHCl₃); IR (CH₂Cl₂): 3567 (w), 2935 (s), 2898 (m), 2860 (s), 1475 (s), 1135 (s), 1105 (s), 1070 (m), 1043 (s), 1029 (m), 838 (s), 804 (m), 780 (m), 751 (m), 743 (m), 652 (m) cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 7.06-7.16 (m, 5H, *H*-Ph), 4.99-5.04 (m, 2H, *H*-C2a and *H*-C5a), 4.64 (dd, *J* = 1.2, 8.3, 1H, *H*-C2), 4.26 (d, *J* = 3.7, 1H, *H*-C7), 4.10-4.16 (m, 2H, *H*-C1'' and *H*-C8b), 3.73-4.09 (m, 2H, *H*-C1'' and *H*-C2''), 3.67 (dd, *J* = 6.4, 9.5, 1H, *H*-C2''), 2.79-2.82 (m, 1H, *H*-C6'), 2.46-2.51 (m, 1H, *H*-C2'), 2.26 (d, *J* = 6.1, 1H, *HO*), 1.90 (dd, *J* = 6.6, 12.9, 1H, *H*-C6), 1.59-1.70 (m, 2H, *H*-C3' and *H*-C5'), 1.53-1.58 (m, 1H, *H*-C6'), 1.35-1.49 (m, 3H, *H*-C3', *H*-C4' and *H*-C6), 1.20-1.28 (m, 1H, *H*-C5'), 1.01-1.13 (m, 1H, *H*-C4'), 0.97 (s, 9H, C(CH₃)₃, TBS), 0.93 (s, 9H, C(CH₃)₃), 0.90 (s, 9H, C(CH₃)₃), 0.005 (s, 3H, CH₃), - 0.002 (s, 3H, CH₃); ¹³C NMR (125 MHz, C₆D₆) δ 144.97 (C1'''), 128.40 (C2'''), 127.48 (C3'''), 126.55 (C4'''), 100.11 (C7), 81.59 (C1'), 79.94 (C2), 72.75 (C2a), 71.24 (C1''), 69.64 (C8b), 66.61 (C5a), 64.39 (C2''),

52.06 (C2'), 34.48 (C6), 33.05 (C6'), 33.01 (C5'), 27.24 (C(CH₃)₃), 27.09 (C(CH₃)₃), 26.13 (C3'), 26.00 (C(CH₃)₃, TBS), 25.43 (C4'), 21.45 (C(CH₃)₃), 20.73 (C(CH₃)₃), 18.41 (C(CH₃)₃, TBS), -5.40 (CH₃); MS (FAB) *m/z* 650.4 ([*M*]⁺), 474.3, 460.3, 402.3, 357.2, 213.2, 159.2, 135.0, 118.9; TLC: *R_f* 0.22 (CH₂Cl₂); Anal. Calcd. for C₃₄H₅₉NO₇Si (650.02): C, 62.83; H, 9.15; N, 2.15. Found: C, 62.86; H, 9.25; N, 2.42.

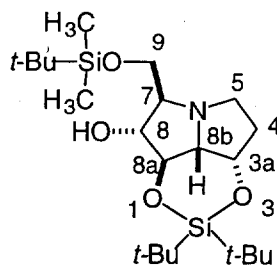
[2*R*]-[2α(1*S*),2α,5αβ,7α(1*S*,2*R*),8bα]-4,4-Bis(1,1-dimethylethyl)-2-[2-[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-[(methylsulfonyl)oxy]-ethyl]hexahydro-7-[(2-phenylcyclohexyl)oxy]-1,3,5,8-tetraoxa-8a-aza-4-silaacenaphthylene (49)



To a solution of (–)-**52** (600 mg, 1.0 mmol) in pyridine (16.0 mL) was added Ms₂O (1.75 g, 10.0 mmol) and the reaction mixture stirred for 0.5 h at room temperature before quenching with sat. aq. NaCl (100 mL). The aqueous layers were extracted with CH₂Cl₂ (2 x 100 mL) and the combined organic layers were dried (Na₂SO₄), concentrated *in vacuo*, and the residue chromatographed (hexane/EtOAc, 4/1, 30 g SiO₂) to produce 657 mg (90%) of crude **49** as a white foam. Data for **49**: ¹H NMR (500 MHz, C₆D₆) δ 7.07–7.18 (m, 5H, *H*-Ph), 5.16 (dt, *J_d* = 9.8, *J_t* = 3.4, 1H, *H*-C1''), 4.93–4.98 (m, 2H, *H*-C2a and *H*-C5a), 4.82 (dd, *J* = 8.3, 9.5, 1H, *H*-C2), 4.24 (d, *J* = 4.2, 1H, *H*-C7), 4.04 (d, *J* = 3.4, 1H, *H*-C2''), 3.87 (dd, *J* = 6.1, 8.8, 1H, *H*-C8b), 3.74 (dt, *J_d* = 4.6, *J_t* = 10.7, 1H, *H*-C1'), 2.70–2.73 (m, 1H, *H*-C6'), 2.63 (s, 3H, CH₃), 2.50 (ddd, *J* = 3.7, 9.8, 12.9, 1H, *H*-C2'), 1.87 (dd, *J* = 6.8, 13.2, 1H, *H*-C6), 1.61–

1.73 (m, 2H, *H*-C3' and *H*-C5'), 1.56-1.61 (m, 1H, *H*-C6'), 1.49-1.52 (m, 1H, *H*-C5'), 1.34-1.46 (m, 2H, *H*-C4' and *H*-C6), 1.20-1.30 (m, 1H, *H*-C3'), 1.02-1.14 (m, 1H, *H*-C4'), 0.95 (s, 9H, C(CH₃)₃, TBS), 0.903 (s, 9H, C(CH₃)₃), 0.900 (s, 9H, C(CH₃)₃), 0.11 (s, 3H, CH₃), 0.10 (s, 3H, CH₃); ¹³C NMR (125 MHz, C₆D₆) δ 144.81 (C1'''), 128.46 (C2'''), 128.26 (C3'''), 126.64 (C4'''), 100.32 (C7), 82.15 (C1'), 81.16 (C1''), 77.46 (C2), 72.55 (C2a), 71.90 (C8b), 66.22 (C5a), 63.28 (C2''), 52.03 (C2'), 38.63 (CH₃), 34.42 (C6'), 33.07 (C6), 32.98 (C5'), 27.22 (C(CH₃)₃), 27.00 (C(CH₃)₃), 26.06 (C3'), 25.98 (C(CH₃)₃, TBS), 25.42 (C4'), 21.33 (C(CH₃)₃), 20.60 (C(CH₃)₃), 18.48 (C(CH₃)₃, TBS), -5.33 (CH₃), -5.51 (CH₃); TLC: *R_f* 0.75 (hexane/EtOAc, 7/3).

[3a*R*-(3aα,4β,5β,8aβ,8bα)]-2,2-Bis(1,1-dimethylethyl)-5-[(1,1-dimethylethyl)dimethylsilyl]oxy)methyl]hexahydro-2*H*,3a*H*-1,3-dioxo-2-silacyclohexa[*gh*]-pyrrolizine-4-ol ((-)-51).

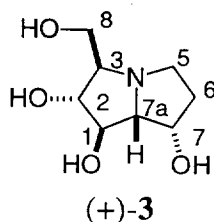


(-)-51

To Raney-nickel (\approx 10.5 g, pre-washed with H₂O (1.6 L) and MeOH (800 mL)) was added **49** (657 mg, 1.0 mmol) in MeOH (100.0 mL) and the reaction mixture hydrogenated in a glass lined steel autoclave under 260 psi of H₂ pressure for 36 h with stirring. The suspension was filtered through a pad of Celite/SiO₂/Celite and the pad was washed extensively with MeOH (2L). The filtrate was concentrated to produce a yellow oil. This material was chromatographed (gradient from CHCl₃/MeOH, 99/1; CHCl₃/MeOH, 95/5; 25 g SiO₂) to produce 397 mg (82%) of the crude **50** as a clear oil, and (+)-**26** (164 mg, 93%) was recovered as a white solid. Mesylate **50** (397 mg) was heated to reflux in CH₃CN (1L) for 16 h. The cooled reaction mixture was quenched with

Et₃N (5 mL), concentrated *in vacuo*, and the residue chromatographed three times (gradient from CHCl₃; CHCl₃/MeOH, 99/1; 50 g SiO₂, then hexane/Et₂O, 7/3; 50 g SiO₂, then gradient from CHCl₃; CHCl₃/MeOH, 99/1; 50 g SiO₂) to afford (–)-**51** as a silicate. The silicate was passed through a plug of basic and neutral Al₂O₃ to afford 280 mg (70% from (–)-**52**) of (–)-**51** as a yellow solid. Data for (–)-**51**: mp 114–115 °C; [α]_D²⁰ – 68.2 (*c* = 0.64, CHCl₃); IR (CH₂Cl₂): 3592 (w), 3586 (w), 2950 (s), 2934 (s), 2860 (s), 1475 (m), 1464 (m), 1145 (m), 1077 (s), 828 (s), 814 (m) cm^{–1}; ¹H NMR (500 MHz, C₆D₆) δ 4.59 (q, *J* = 7.6, 1H, *H*-C3a), 4.17 (dd, *J* = 9.0, 10.5, 1H, *H*-C8a), 4.04 (dd, *J* = 7.3, 8.8, 1H, *H*-C8), 3.70 (dd, *J* = 9.9, 6.0, 1H, *H*-C9), 3.68 (dd, *J* = 9.9, 5.5, 1H, *H*-C9), 3.27 (dd, *J* = 6.8, 10.5, 1H, *H*-C8b), 3.01 (ddd, *J* = 7.3, 10.0, 14.2, 1H, *H*-C5), 2.76 (q, *J* = 5.9, 1H, *H*-C7), 2.53 (ddd, *J* = 3.2, 9.0, 11.2, 1H, *H*-C5), 2.48 (bs, 1H, *HO*), 1.82–1.94 (m, 2H, *H*-C4), 1.18 (s, 9H, C(CH₃)₃), 1.10 (s, 9H, C(CH₃)₃), 0.97 (s, 9H, C(CH₃)₃, TBS), 0.064 (s, 3H, CH₃), 0.056 (s, 3H, CH₃); ¹³C NMR (125 MHz, C₆D₆) δ 77.47 (C8), 77.08 (C8a), 76.13 (C3a), 74.31 (C7), 66.67 (C9), 66.27 (C8b), 55.04 (C5), 32.01 (C4), 27.58 (C(CH₃)₃), 27.34 (C(CH₃)₃), 26.04 (C(CH₃)₃, TBS), 21.73 (C(CH₃)₃), 21.11 (C(CH₃)₃), 18.42 (C(CH₃)₃, TBS), –5.27 (CH₃), –5.34 (CH₃); MS (FAB) *m/z* 444.2 ([*M*]⁺), 443.3, 442.3, 428.3, 386.2, 330.1, 298.2; TLC: *R*_f 0.69 (CHCl₃/MeOH, 98/2); Anal. Calcd. for C₂₂H₄₅NO₄Si₂ (443.78): C, 59.54; H, 10.22; N, 3.16. Found: C, 59.53; H, 10.08; N, 3.22.

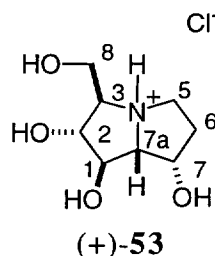
Australine, [1*R*-(1α,2β,3α,7β,7aβ)]-Hexahydro-3-hydroxymethyl-1*H*-pyrrolizidine-1,2,7-triol ((+)-**3**).



To a solution of (–)-**51** (440 mg, 0.99 mmol) in MeOH (35 mL) in a teflon bottle was added 48% aqueous HF (3.4 mL) and the reaction mixture stirred at room temperature for 24 h. The

reaction mixture was concentrated *in vacuo* and the resulting purple oil loaded onto AG 50W-X8 ion exchange resin (20 g, pretreated) in H₂O and eluted with 2N NH₄OH (300 mL). Concentration *in vacuo* afforded 169 mg (90%) of (+)-australine ((+)-3) as a yellow oil. Data for (+)-3: $[\alpha]_{\text{D}}^{20} + 18.6$ ($c = 2.51$, MeOH), (lit.⁸ $[\alpha]_{\text{D}}^{26} + 19.3$ ($c = 2.09$, MeOH); ¹H NMR (500 MHz, D₂O) δ 4.19 (dt, $J_{\text{d}} = 2.2$, $J_{\text{t}} = 4.2$, 1H, *H*-C7), 4.04 (t, $J = 7.8$, 1H, *H*-C1), 3.71 (dd, $J = 8.3$, 9.5, 1H, *H*-C2), 3.60 (AB_x, dd, $J = 3.7$, 12.0, 1H, *H*-C8), 3.43 (AB_x, dd, $J = 6.6$, 12.0, 1H, *H*-C8), 3.02 (dd, $J = 4.4$, 7.6, 1H, *H*-C7a), 2.98 (ddd, $J = 2.2$, 7.6, 9.8, 1H, *H*-C5), 2.52-2.58 (m, 2H, *H*-C3 and *H*-C5), 1.82-1.87 (m, 1H, *H*-C6), 1.71-1.79 (m, 2H, *H*-C6); ¹³C NMR (100 MHz, D₂O) δ 78.43 (C2), 72.69 (C1), 70.47 (C7a), 70.22 (C3), 69.09 (C7), 62.19 (C8), 51.58 (C5), 34.90 (C6); TLC: R_{f} 0.29 (CHCl₃/MeOH/NH₄OH, 5/5/1).

Australine Hydrochloride, [1*R*-(1 α ,2 β ,3 α ,7 β ,7*a* β)]-Hexahydro-3-hydroxymethyl-1*H*-pyrrolizidine-1,2,7-triol Hydrochloride ((+)-53).



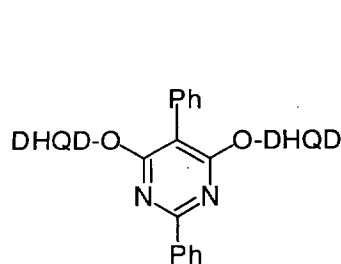
To a solution of (+)-3 (30.0 mg, 0.16 mmol) in MeOH (5 mL) was added conc. HCl (1 mL) and the reaction mixture concentrated *in vacuo* to produce 35.2 mg (98%) of australine hydrochloride ((+)-53) as a brown oil. Data for (+)-53: $[\alpha]_{\text{D}}^{25} + 22.2$ ($c = 0.50$, H₂O), (lit.⁹ $[\alpha]_{\text{D}} + 23.1$ ($c = 1$, H₂O); IR (nujol): 3335 (s), 3068 (s), 2359 (m), 1384 (m), 1635 (m), 1428 (m), 1067 (m), 1047 (m), 1010 (m); ¹H NMR (500 MHz, D₂O) δ 4.49 (dd, $J = 3.4$, 3.9, 1H, *H*-C7), 4.30 (dt, $J_{\text{d}} = 0.5$, $J_{\text{t}} = 7.8$, 1H, *H*-C1), 3.97 (dd, $J = 8.1$, 10.5, 1H, *H*-C2), 3.80 (dd, AB_x, $J = 2.7$, 13.2, 1H, *H*-C8), 3.74-3.69 (m, 2H, *H*-C7a and *H*-C8), 3.62 (ddd, 1H, $J = 2.4$, 7.8, 11.0, *H*-C5), 3.17-3.24 (m, 2H, *H*-C3 and *H*-C5), 2.11-2.15 (m, 1H, *H*-C6), 2.00-2.08 (m, 1H, *H*-C6); ¹³C NMR (125 MHz, D₂O) δ 75.41 (C2), 72.57 (C7a), 71.44 (C1), 70.64 (C3),

68.06 (C7), 55.73 (C8), 52.14 (C5), 34.33 (C6); MS (CI) m/z 190.1 ($[M-Cl]^+$), 188.1, 172.1, 158.1, 112.1, 87.1; TLC: R_f 0.28 ($CHCl_3/MeOH/NH_4OH$, 5/5/1); HRMS Calcd. for $C_8H_{16}NO_4$: 190.1079. Found: 190.1076.

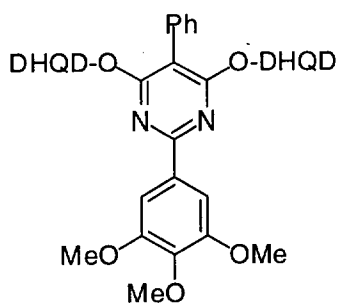
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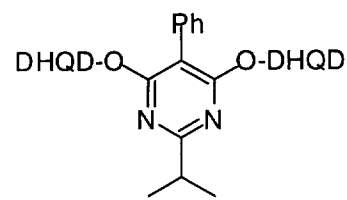
Chiral Ligands: DHQD-derived



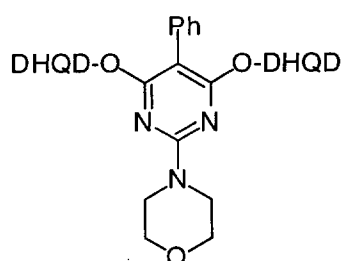
(DHQD)₂-PYR



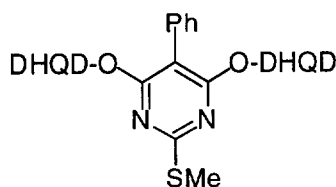
(DHQD)₂-PYR(OMe)₃



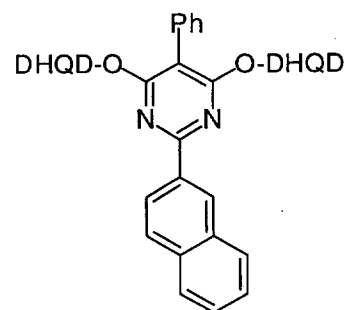
(DHQD)₂-PYR(*i*Pr)



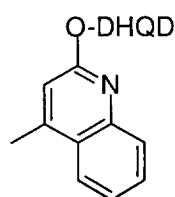
(DHQD)₂-PYR(*N*-Morpholino)



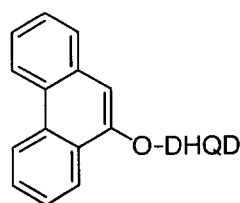
(DHQD)₂-PYR(SMe)



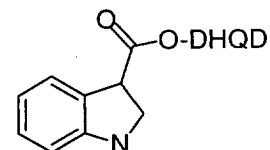
(DHQD)₂-PYR(Naphthyl)



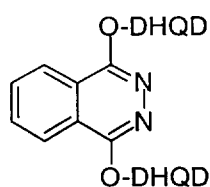
(DHQD)₂-MEQ



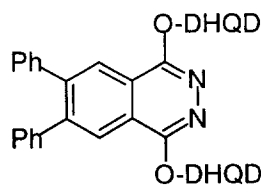
DHQD-PHN



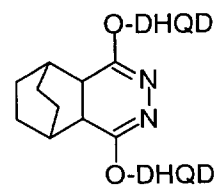
DHQD-IND



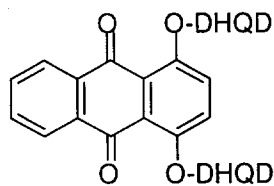
(DHQD)₂-PHAL



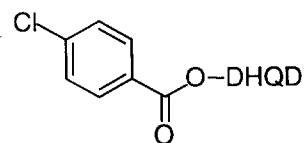
(DHQD)₂-DP-PHAL



(DHQD)₂-2.2.2-bicyclo-PHAL



(DHQD)₂-AQN



DHQD-CLB

**Table. Asymmetric Dihydroxylation of (-)-31:
DHQD-Derived Chiral Ligands.**

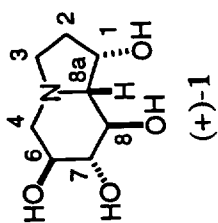
entry	ligand	(-)-33:(-)-34 ^a
1	none	2.0:1
2	(DHQD) ₂ -PYR	2.0:1
3	(DHQD) ₂ -PYR(OMe) ₃	2.3:1
4	(DHQD) ₂ -PYR(<i>i</i> -Pr)	1.8:1
5	(DHQD) ₂ -PYR(<i>N</i> -Morpholino)	1.2:1
6	(DHQD) ₂ -PYR(SMe)	1.5:1
7	(DHQD) ₂ -PYR(Naphthyl)	1.5:1
8	DHQD-MEQ	2.4:1
9	DHQD-PHN	6.0:1
10	DHQD-IND	1:1.2
11	(DHQD) ₂ -PHAL	1:1.8
12	(DHQD) ₂ -DP-PHAL	1:1.9
13	(DHQD) ₂ -2.2.2-bicyclo-PHAL	1:2.0
14	(DHQD) ₂ -AQN	1:12.0

^a Conversions ranged between 70-100%. Diastereomeric ratios was determined by 500 MHz ¹H NMR analysis.

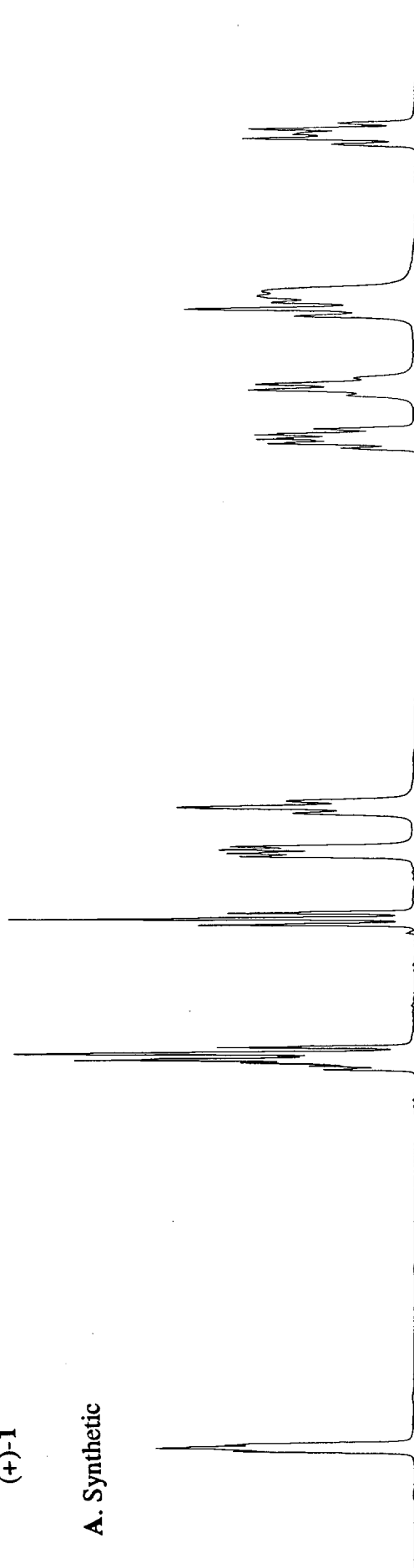
**750 MHz ^1H NMR of
(+)-castanospermine ((+)-1)**

A. Synthetic

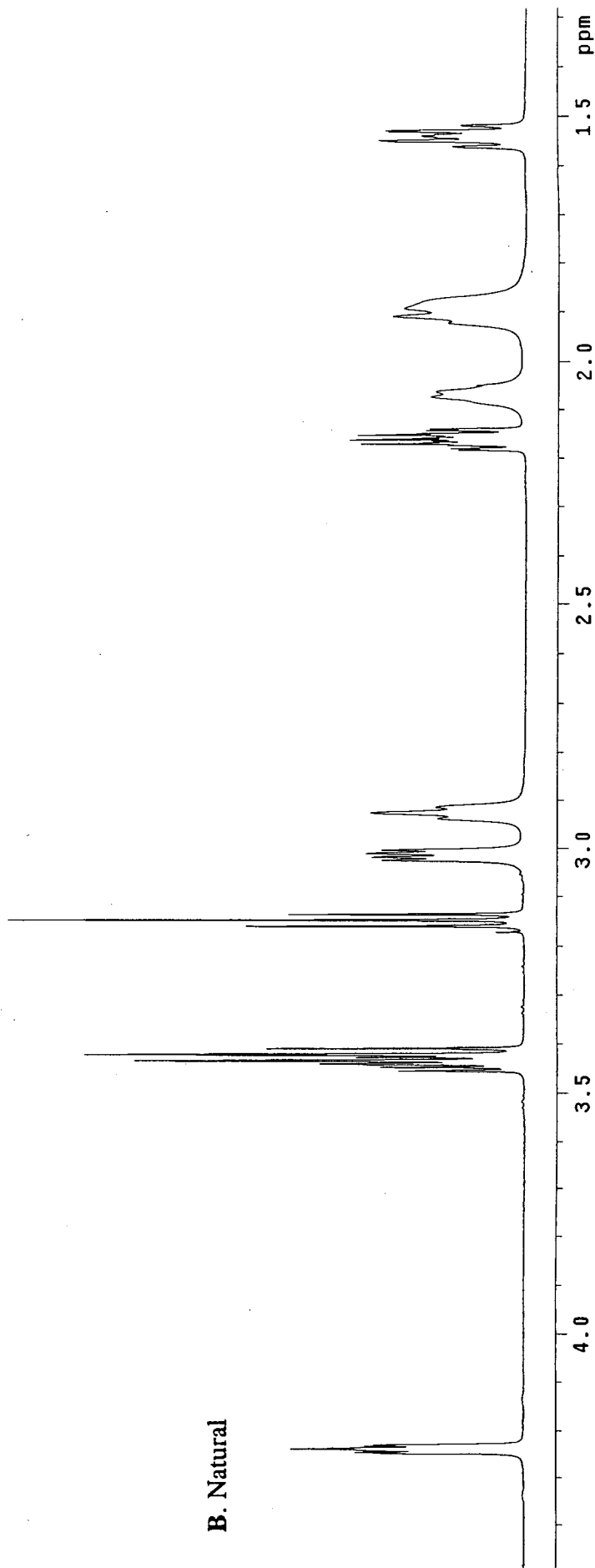
B. Natural



A. Synthetic



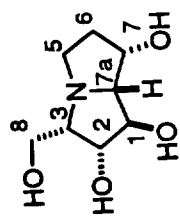
B. Natural



**750 MHz ^1H NMR of
(+)-3-epiaustraline ((+)-4)**

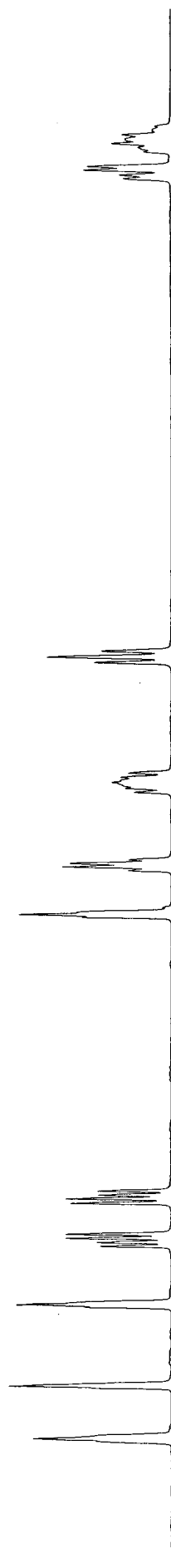
A. Synthetic

B. Natural

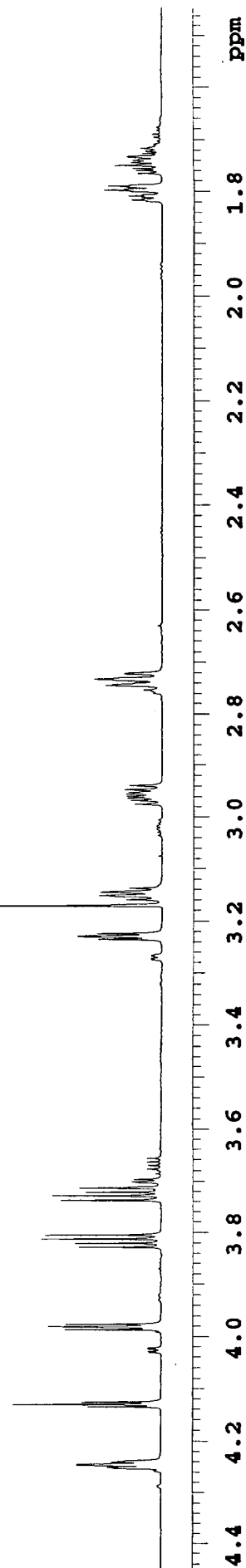


(+)-4

A. Synthetic



B. Natural

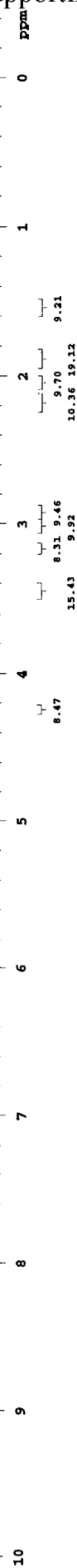
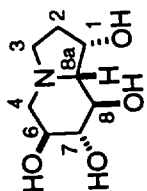


**¹H NMR, ¹³C NMR, COSY, and HETCOR for
(+)-castanospermine ((+)-1)**

STANDARD PROTON PARAMETERS

exp1 s2pul

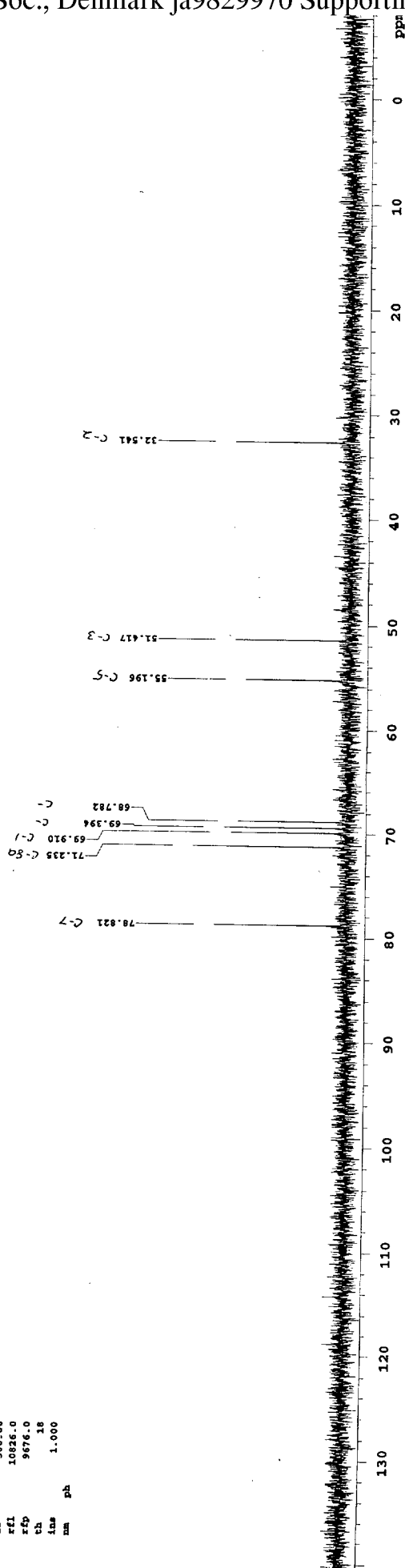
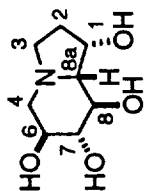
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 file 18
 ACQUISITION
 exp dpr 0
 dof 0
 nnn
 sfrq 500.085 dm
 H1 dm c
 tn 200
 at 4.096 dmf
 65336 dseq
 np 8000.0 dres 1.0
 sw 4000 homo n
 fb 16
 bs 55 dfrq2
 DEC2
 tpr 7.1 daz 0
 pw 0 dpr2 1
 dt 0 dfr2 0
 tof 32 dm1 n
 nt 32 dm2 c
 ct 200
 alock gain not used dseq2 1.0
 FLMS
 il n homo2 n
 in n
 dp y lb PROCESSING
 bs nm wtfile 0.30
 DISPLAY
 sp -250.1 fn proc ft
 wp 5500.9 math not used f
 vr 216
 ac 0 werr
 wc 400 wexp
 hnm 13.75 wbs
 ls 5702.68 wnt
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 rfp 2315.4
 th 7
 lns 100.000
 na ph

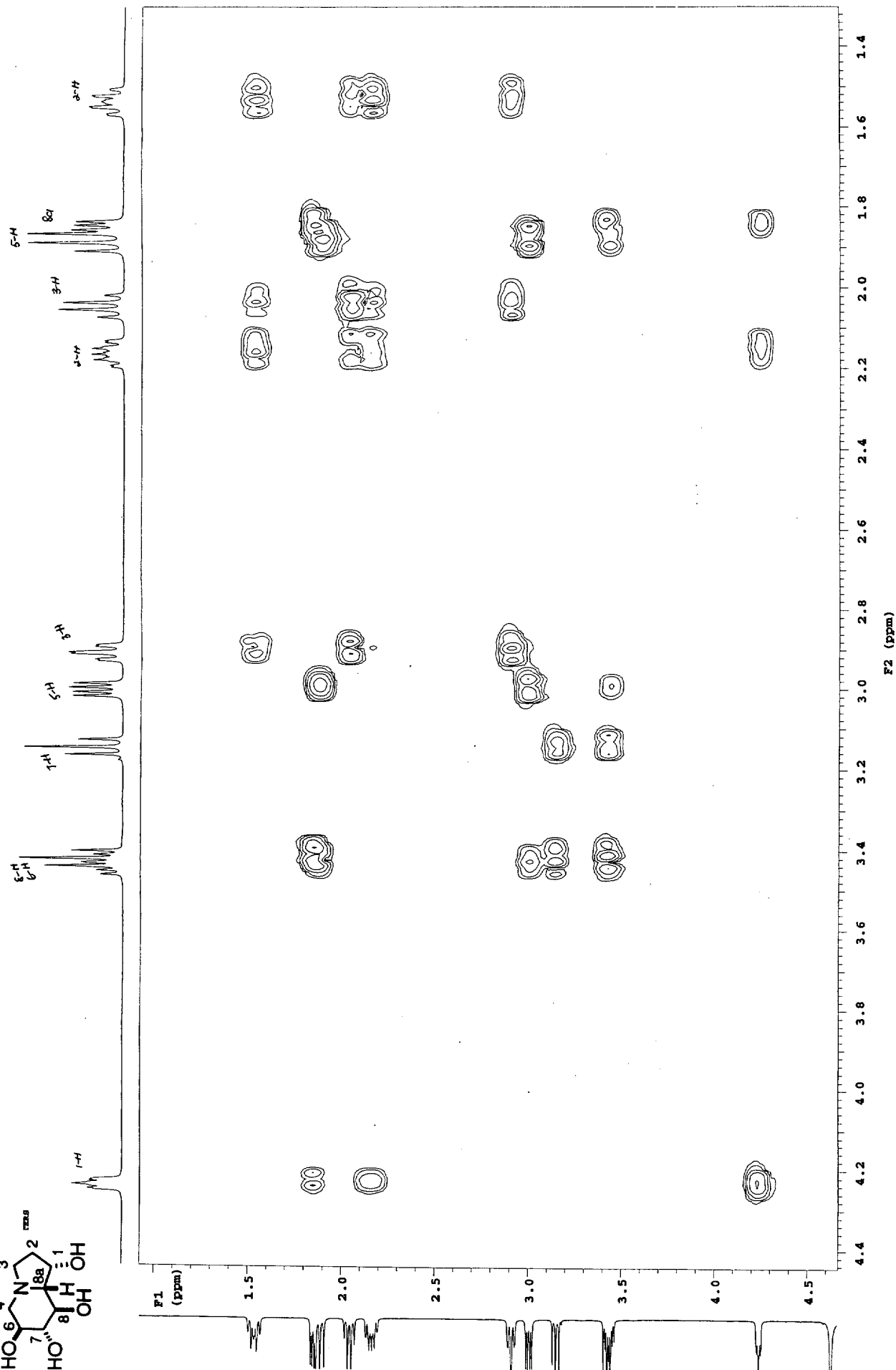
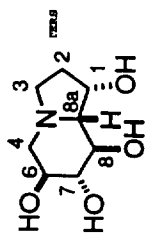


STANDARD CARBON PARAMETERS

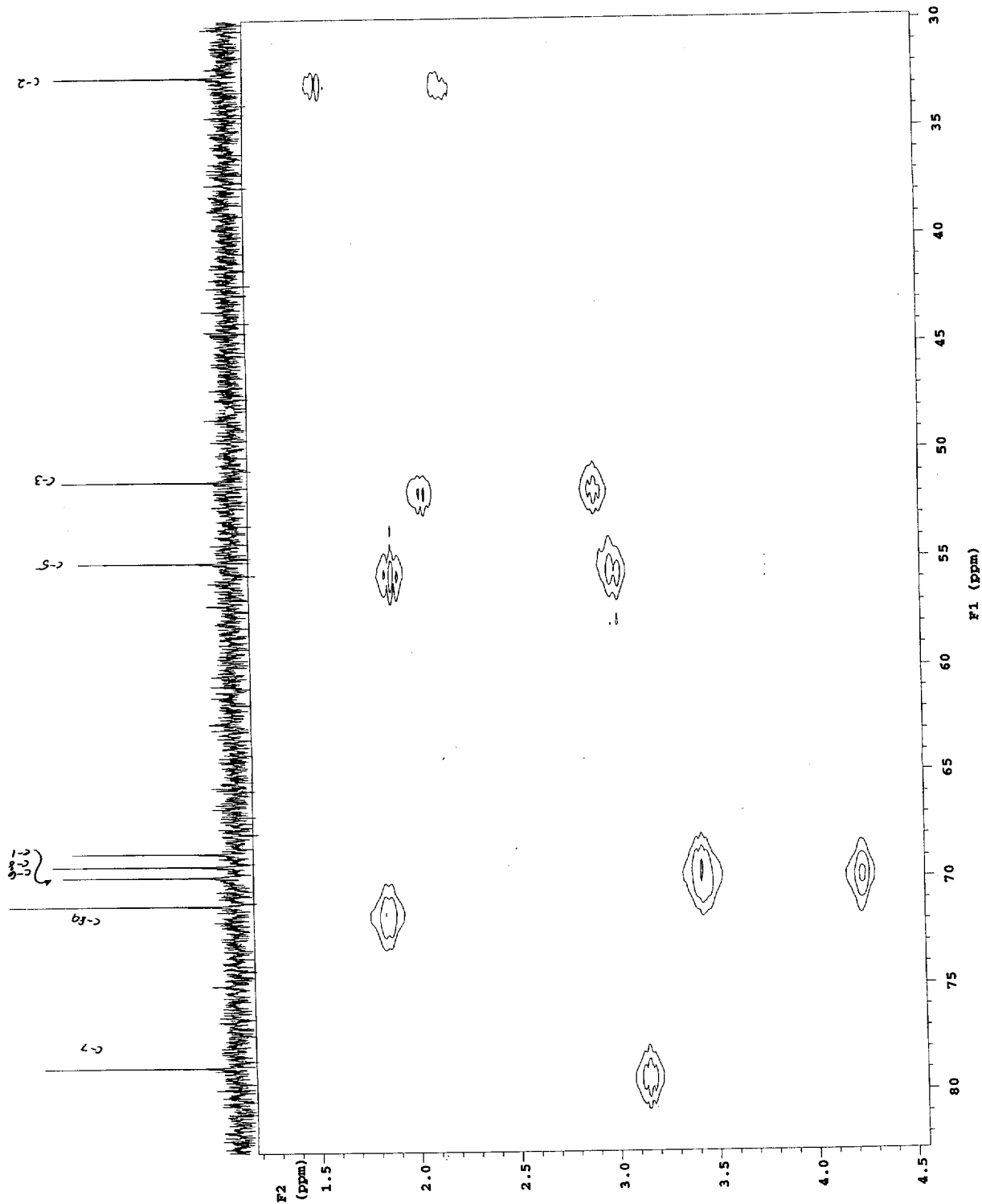
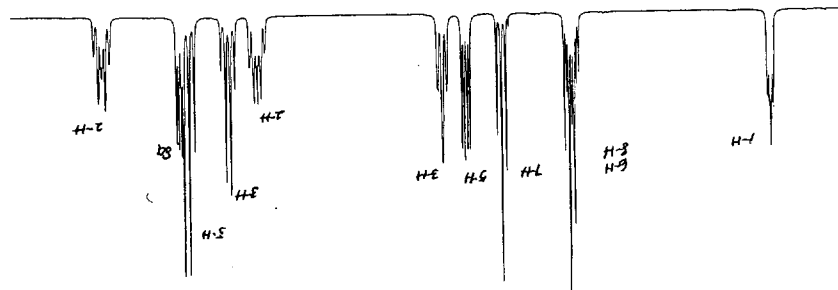
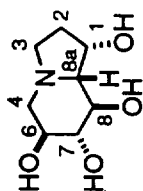
exp2 s3pul

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 solvent D2O dn H1
 file /export/home/- dpr 43
 data/v500/martinbo- dof -829.0
 rough/eam.04.46.13- dn yyy
 C-1 dm w
 ACQUISITION dm 11053
 sfrq 125.657 dm 11053
 tn C13 dm 1.0
 at 1.087 homo n
 NO 40896 PROCESSING
 sw 18814.7 lb 1.00
 fb 10400 wfile
 bs 16 proc ft
 ss 1 fn not used f
 tprz 54 math
 pw 10.0
 dl 1.000 warr
 tof -3654.5 warr
 nt 10000 wha
 ct 2998 wnt
 alock n
 gain not used
 FLAGS
 fl n
 in n
 op y
 hs mn
 DISPLAY
 sp -1150.0
 wp 18814.7
 vs 40
 sc 0
 wc 400
 hnm 75.26
 ls 500.00
 rfl 10826.0
 rfp 9876.0
 th 18
 lns 1.000
 mn ph





STANDARD PROTON PARAMETERS

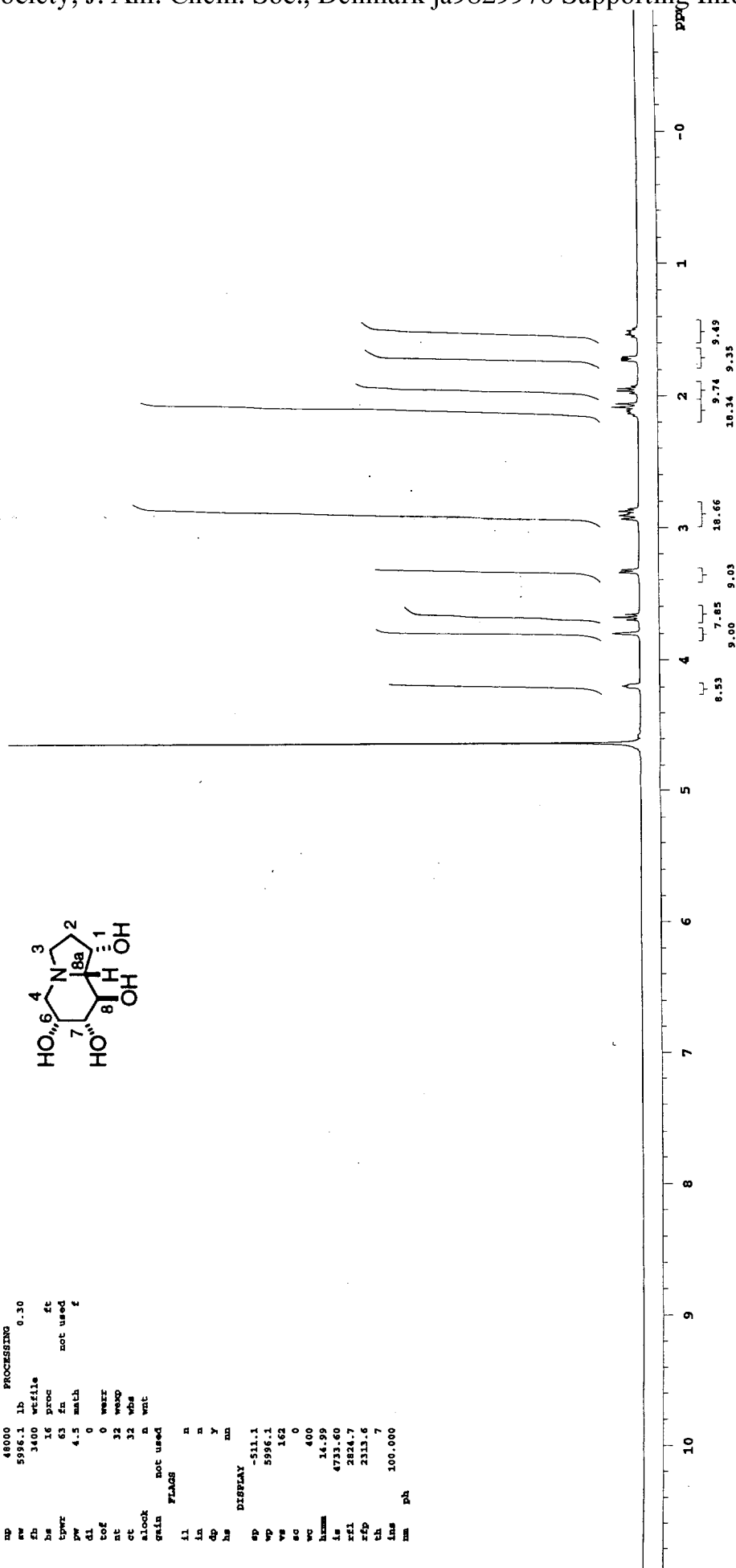
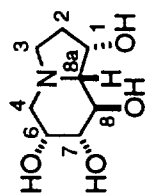


**^1H NMR, ^{13}C NMR, COSY, and HETCOR for
(+)-6-epicastanospermine ((+)-2)**

STANDARD PROTON PARAMETERS

exp1 #2bul

SAMPLE DEC. & VT
 date Apr 10 98 dfreq 499.700
 solvent D2O dm H1
 file /export/home/- dprv 20
 data/us00/martinbo-dof 0
 rough/restore data- dm
 /sam.04.13.10m01r dm
 ACQUISITION dm 200
 sfreq 499.700 dnoq
 tn H1 dres 1.0
 at 4.003 homo n
 up 48000 PROCESSING
 aw 5996.1 lb 0.30
 fb 3400 wfile
 bs 16 proc ft
 tprv 63 fn not used
 pw 4.5 mth f
 dl 0
 tof 0 vwr
 nt 32 wvop
 ct 32 wba
 alook n wnt
 gain not used
 FLAG
 il n
 in n
 qp y
 hs nm
 DISPLAY
 sp -511.1
 wp 5996.1
 vs 162
 ac 0
 vc 400
 hnum 14.99
 ls 4733.60
 xfl 2824.7
 xfp 2313.6
 th 7
 ins 100.000
 nm ph



exp1 std13c

Chemical structure of 8a, a bicyclic compound with a piperidine ring fused to a pyrrolidine ring. The piperidine ring has hydroxyl groups at positions 2, 6, and 7. The pyrrolidine ring has a hydroxyl group at position 1. The bridgehead carbon is labeled 8a.

