Supporting Information

Intramolecular 5-Endo-trig Aminomercuration of β-Hydroxy-γ-alkenylamines:
Efficient Route to Pyrrolidine ring and its application for the Synthesis of (+)
Castanospermine and Analogues

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**General Experimental Methods.** Melting points were recorded with Thomas Hoover Capillary melting point apparatus and are uncorrected. IR spectra were recorded with FTIR as a thin film or in nujol mull or using KBr pellets and are expressed in cm\(^{-1}\); \(^1\)H (300 MHz) and \(^{13}\)C (75 MHz) NMR spectra were recorded using CDCl\(_3\) and/or D\(_2\)O as a solvent. Chemical shifts were reported in \(\delta\) unit (ppm) with reference to TMS as an internal standard and coupling constant (\(J\)) values are given in Hz. Decoupling and DEPT experiments confirmed the assignments of the signals. Elemental analyses were carried out with C, H-analyzer. Thin layer chromatography was performed on pre-coated plates (0.25 mm, silica gel). Column chromatography was carried out with silica gel (100-200 mesh). The reactions were carried out in oven-dried glassware under dry N\(_2\). Methanol, THF, diethylether, toluene, and dichloromethane were purified and dried before use. Distilled n-hexane and ethyl acetate were used for column chromatography. After decomposition of the reaction with water, the work-up involves washing of combined organic layer with water, brine, drying over anhydrous sodium sulfate and evaporation of solvent at reduced pressure.

**Procedure for 1,3-addition reaction of vinylmagnesium bromide with nitrone 2 using TMSOTf.** To a stirred solution of nitrone 2 (1.0 g, 2.61 mmol) in THF under nitrogen atmosphere was added TMSOTf (0.45 mL, 2.61 mmol) at – 10 °C and the resulting reaction mixture was stirred for 10 min. Then it was cooled to – 78 °C and vinylmagnesium bromide (1 M in diethylether, 7.8 mL, 7.83 mmol) was added dropwise over a period of 1 h. The reaction was decomposed by adding 2 M HCl (2 mL) and stirred at room temperature for additional 30 min followed by neutralization with saturated NaHCO\(_3\) (2 mL) and extracted with diethyl ether (25 mL x 3). Usual workup afforded a mixture of 3\(a/3b\) in the ratio of 87:13 calculated from \(^1\)H NMR spectrum of the crude mixture.
3-O-Benzyl-1,2-O-isopropylidene-5,6,7-trideoxy-5-(N-benzyl-N-benzyloxycarbonylamino)-\( \alpha \)-D-gluco-6-eno-hepta-1,4-furanose (5a). To a stirred solution of 4a (2.8 g, 7.06 mmol) in methanol-water (25 mL, 9:1) at 0 °C was added sodium bicarbonate (1.78 g, 21.2 mmol), benzyloxycarbonyl chloride (1.8 g, 10.6 mmol) and the reaction mixture was stirred for 3 h. The solvent was evaporated under reduced pressure and residue was extracted with chloroform (25 mL x 3). Usual work up followed by purification by column chromatography (n-hexane/ethyl acetate = 90/10) gave 5a (3.35 g, 92%) as a thick liquid; \(R_f\) 0.60 (n-hexane/ethyl acetate = 3/1); \([\alpha]_D = -35.0\) (c 0.4, CHCl₃); IR (Neat) 1697, 1602 cm\(^{-1}\); Anal. Calcd. For C\(_{32}\)H\(_{35}\)NO\(_6\): C, 72.57; H, 6.66; Found: C, 72.70; H, 6.73.

3-O-Benzyl-1,2-O-isopropylidene-5,6,7-trideoxy-5-(N-benzyl-N-benzyloxycarbonylamino)-\( \beta \)-L-ido-6-eno-hepta-1,4-furanose (5b). The reaction of 4b (3.0 g, 7.5 mmol) with sodium bicarbonate (1.9 g, 22.0 mmol) and benzyloxycarbonyl chloride (1.92 g, 11.2 mmol) was performed under the same reaction conditions as described for 5a, afforded 5b (3.5 g, 90 %) as a thick liquid; \(R_f\) 0.50 (n-hexane/ethyl acetate = 3/1); \([\alpha]_D = -19.0\) (c 1.0, CHCl₃); IR (Neat) 1693, 1612 cm\(^{-1}\); Anal. Calcd. For C\(_{32}\)H\(_{35}\)NO\(_6\): C, 72.57; H, 6.66; Found: C, 72.63; H, 6.62.

3-O-Benzyl-5-deoxy-1,2-O-isopropylidene-5-(N-benzyl-N-benzyloxycarbonylamino)-\( \alpha \)-D-gluco-hexodialdo-1,4-furanose (6a). To the solution of 5a (3.5 g, 6.6 mmol) in acetone-water (50 mL, 8:1), was added NMO (1.54 g, 13.2 mmol), catalytic amount of potassium osmate and the reaction mixture was stirred at room temperature for 12 h. Sodium sulphite (2.0 g) was added and stirred for 1 h. Acetone was removed under reduced pressure and the residue was extracted with chloroform (35 mL x 3), usual workup afforded mixture of diols (3.40 g, 92%) as a thick liquid; \(R_f\) 0.40 (n-hexane/ethyl acetate = 1/1). To a solution of diol (3.40 g, 6.0 mmol) in acetone-water (30 mL, 9:1) at 0 °C was added sodium metaperiodate (1.90 g, 9.0 mmol) and stirred for 6 h. Ethylene glycol (1.0 mL) was added and acetone was removed under reduced pressure. Extraction with chloroform (20 mL x 3) followed by usual workup and purification by column chromatography (n-hexane/ethyl acetate = 9/1) afforded
aldehyde 6a (2.90 g, 91%) as a thick liquid; $R_f$ 0.54 (n-hexane/ethyl acetate = 8/2); $[\alpha]_D = -15.5$ (c 0.38, CHCl$_3$); IR (Neat) 1703, 1699, 1608 cm$^{-1}$; Anal. Calcd. For C$_{31}$H$_{33}$NO$_7$: C, 70.04; H, 6.26; Found: C, 70.16; H, 6.38.

3-O-Benzyl-5-deoxy-5-(N-benzyl-N-benzoxy carbamylamino)-1,2-O-isopropylidene-$\beta$-L-idohexodialdo-1,4-furanose (6b). The reaction of 5b (2.90 g, 5.4 mmol) with NMO (1.3 g, 10.9 mmol) and potassium osmate was performed under the same reaction conditions as described for 6a afforded diols (2.75 g, 88%) as a thick liquid; $R_f$ 0.34 (n-hexane/ethyl acetate = 1/1). The reaction of diols (2.5 g, 4.4 mmol) with sodium-metaperiodate (1.41 g, 6.6 mmol) was performed under similar reaction conditions as described for 6a afforded aldehyde 6b (2.20 g, 93%) as a thick liquid; $R_f$ 0.55 (n-hexane/ethyl acetate = 7/3); $[\alpha]_D = +6.2$ (c 0.65, CHCl$_3$); IR (Neat) 1732, 1693, 1603 cm$^{-1}$; Anal. Calcd. For C$_{31}$H$_{33}$NO$_7$: C, 70.04; H, 6.26; Found: C, 70.0; H, 6.15.

3-O-Benzyl-1,2-O-isopropylidene-5,7,8-trideoxy-5-(N-benzylamino)-(5-$N$, 6(R)-O-carbonyl)-$\alpha$-D-glycero-D-gluco-7-eno-oct-1,4-furanose (7a) and 3-O-Benzyl-1,2-O-isopropylidene 5,7,8-trideoxy-5-(N-benzylamino)-(5-$N$, 6(S)-O-carbonyl)-$\alpha$-L-glycero-D-gluco-7-eno-oct-1,4-furanose (7b). Aldehyde 6a (2.7 g, 5.0 mmol) was dissolved in THF (15 mL), vinylmagnesium bromide (1M in THF, 10 mL, 10.0 mmol) was added at –50 °C and reaction mixture was stirred for 1 h. Saturated solution of NH$_4$Cl (5 mL) was added, extracted with diethylether (25 mL x 3) and solvent was removed under reduced pressure afforded inseparable mixture of Grignard products (2.4 g, 85%) as a thick liquid; $R_f$ 0.40 (n-hexane/ethyl acetate = 3/1). To the solution of Grignard products (2.2 g, 3.9 mmol) in methanol (10 mL) was added KOH (40% in H$_2$O, 3.25 mL, 23.4 mmol) and reaction mixture was refluxed at 90 °C for 10 min. Methanol was removed under reduced pressure and residue was dissolved in chloroform and the chloroform layer was washed with water (10 mL x 3). Usual workup followed by separation by column chromatography (n-hexane/ethyl acetate = 9.5/0.5) afforded 7a (1.2 g,
56%) as a white solid; mp 118–119 °C; \( R_f \) 0.43 (n-hexane/ethyl acetate = 3/1); [\( \alpha \)]\( D \) = −16.0 (c 0.37, CHCl\(_3\)); IR (KBr) 1737, 1450 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 1.27 (s, 3H), 1.39 (s, 3H), 3.83 (d, \( J = 2.3 \) Hz, 1H), 4.10 (dd, \( J = 8.0, 2.3 \) Hz, 1H), 4.20 (t, \( J = 7.7 \) Hz, 1H), 4.33 (d, \( J = 15.4 \) Hz, 1H), 4.44 (d, \( J = 11.8 \) Hz, 1H), 4.53 (d, \( J = 15.4 \) Hz, 1H), 4.58 (d, \( J = 3.6 \) Hz, 1H), 4.62 (d, \( J = 11.8 \) Hz, 1H), 4.97 (dd, \( J = 7.7, 5.2 \) Hz, 1H), 5.35 (d, \( J = 10.1 \) Hz, 1H), 5.48 (d, \( J = 17.0 \) Hz, 1H), 5.84 (d, \( J = 3.6 \) Hz, 1H), 6.02 (ddd, \( J = 16.2, 10.7, 5.2 \) Hz, 1H), 7.20-7.50 (m, 10H); \(^1\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 26.2, 26.6, 46.7, 56.1, 70.8, 76.7, 77.3, 80.8, 81.4, 103.8, 111.7, 118.1, 126.7 (s), 127.2, 127.6 (s), 127.9, 128.3 (s), 128.4 (s), 131.0, 136.4, 136.6, 158.3; Anal. Calcd. For C\(_{26}\)H\(_{29}\)NO\(_{6}\): C, 69.16; H, 6.47; Found: C, 69.23; H, 6.63. Further elution with (n-hexane/ethyl acetate = 9/1) gave \( 7b \) (0.4 g, 23%) as a white solid. mp 155–156 °C; \( R_f \) 0.33 (n-hexane/ethyl acetate = 3/1); [\( \alpha \)]\( D \) = −66.6 (c 0.75, CHCl\(_3\)); IR (KBr) 1739, 1496 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 1.30 (s, 3H), 1.42 (s, 3H), 3.62 (dd, \( J = 4.4, 3.6 \) Hz, 1H), 3.82 (d, \( J = 3.6 \) Hz, 1H), 4.14 (d, \( J = 15.7 \) Hz, 1H), 4.25 (t, \( J = 4.4 \) Hz, 1H), 4.37 (d, \( J = 11.6 \) Hz, 1H), 4.61 (d, \( J = 3.9 \) Hz, 1H), 4.62 (d, \( J = 11.6 \) Hz, 1H), 4.70 (d, \( J = 15.7 \) Hz, 1H), 5.09 (d, \( J = 10.0 \) Hz, 1H), 5.60-5.12 (m, 1H), 5.27 (d, \( J = 16.5 \) Hz, 1H), 5.65 (ddd, \( J = 16.5, 10.0, 5.2 \) Hz, 1H), 5.91 (d, \( J = 3.9 \) Hz, 1H), 7.10-7.40 (m, 10H); \(^1\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 26.2, 26.8, 46.4, 50.0, 71.4, 75.3, 78.2, 81.5, 82.1, 104.6, 111.9, 117.7, 127.2 (s), 127.6, 127.7 (s), 128.1, 128.5 (s), 128.6 (s), 134.5, 135.9, 136.3, 157.7; C\(_{26}\)H\(_{29}\)NO\(_{6}\): C, 69.16; H, 6.47; Found: C, 69.23; H, 6.63.

**3-O-Benzyl-1,2-O-isopropylidene-5,7,8-trideoxy-5-(N-benzylamino)-[5-N, 6(S)-O-carbonyl]-β-L-glycero-L-ido-7-en-oct-1,4-furanose (7c).** The reaction of aldehyde \( 6c \) (1.5 g, 2.8 mmol) in THF (10 mL) at −50 °C with vinylmagnesium bromide (1M in THF, 5.6 mL, 5.6 mmol) followed by reaction with KOH (40% in H\(_2\)O, 1.5 mL, 10.7 mmol) in methanol (7 mL) was performed under similar reaction conditions as described for \( 7a \). Purification by column chromatography (n-hexane/ethyl acetate = 80/20) afforded \( 7c \) (0.7 g, 86%) as a white solid; mp 93-94 °C; \( R_f \) 0.42 (n-hexane/ethyl acetate = 7/3); [\( \alpha \)]\( D \) = −62.0 (c 1.0, CHCl\(_3\)); IR (Nujol) 1735, 1472 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 1.32 (s, 3H), 1.41
(s, 3H), 4.01 (d, J = 3.3 Hz, 1H), 4.12 (dd, J = 9.3, 7.7 Hz, 1H), 4.19 (dd, J = 9.3, 3.3 Hz, 1H), 4.30 (d, J = 11.8 Hz, 1H), 4.55 (d, J = 14.9 Hz, 1H), 4.90 (d, J = 3.9 Hz, 1H), 4.61 (d, J = 11.8 Hz, 1H), 4.70 (t, J = 7.4 Hz, 1H), 4.75 (d, J = 14.9 Hz, 1H), 5.08 (d, J = 16.8 Hz, 1H), 5.26 (d, J = 10.5 Hz, 1H), 5.73 (ddd, J = 16.8, 10.5, 7.7 Hz, 1H), 5.97 (d, J = 3.9 Hz, 1H), 7.16-7.42 (m, 10H); 13C NMR (75 MHz, CDCl3) δ 26.3, 26.8, 47.5, 57.5, 71.1, 75.9, 80.1, 81.0, 81.9, 104.7, 111.8, 121.4, 127.3, 127.8 (s), 128.3 (s), 128.4, 128.6 (s), 131.1, 136.5, 137.0, 158.1; C26H29NO6: C, 69.16; H, 6.47; Found: C, 69.18; H, 6.53.

3-O-Benzyl-1,2-O-isopropylidene-5,7,8-trideoxy-5-(N-benzylamino)-6(R)-hydroxy-α-D-glycero-D-gluco-7-eno-oct-1,4-furanose (8a). The reaction of carbamate 7a (0.4 g, 0.88 mmol), with KOH (40% in H2O, 0.62 mL, 4.42 mmol) in methanol (3.0 mL) at 90 °C for 48 h followed by workup as described for synthesis of 7a and purification by column chromatography (n-hexane/ethyl acetate = 80/20) afforded 8a (0.37 g, 98%) as a thick liquid; Rf 0.56 (n-hexane/ethyl acetate = 7/3); [α]D = −32.0 (c 0.25, CHCl3); IR (Neat) 3550-3150, 1647 cm⁻¹; 1H NMR (300 MHz, CDCl3) δ 1.32 (s, 3H), 1.48 (s, 3H), 1.80 (bs, exchanges with D2O, 2H), 3.34 (dd, J = 8.0, 4.4 Hz, 1H), 3.81 (s, 2H), 4.05 (dd, J = 7.7, 3.0 Hz, 1H), 4.10 (d, J = 3.0 Hz, 1H), 4.37-4.47 (m, 1H), 4.53 (d, J = 11.3 Hz, 1H), 4.62 (d, J = 3.9 Hz, 1H), 4.67 (d, J = 11.3 Hz, 1H), 5.20 (d, J = 10.2 Hz, 1H), 5.37 (d, J = 17.0 Hz, 1H), 5.90 (d, J = 3.9 Hz, 1H), 5.91 (ddd, J = 17.0, 10.2, 4.5 Hz, 1H), 7.18-7.40 (m, 10H); 13C NMR (75 MHz, CDCl3) δ 26.3, 26.8, 52.7, 59.3, 71.6, 72.0, 80.6, 81.3, 82.2, 104.3, 111.5, 116.2, 126.8, 127.5 (s), 127.8 (s), 128.2 (s), 128.4 (s), 136.8, 136.9, 140.2; Anal. Calcd. For C25H31NO5: C, 70.57; H, 7.34; Found: C, 70.65; H, 7.41.

3-O-Benzyl-1,2-O-isopropylidene-5,7,8-trideoxy-5-(N-benzylamino)-6(S)-hydroxy-α-L-glycero-D-gluco-7-eno-oct-1,4-furanose (8b). The reaction of 7b (0.79 g, 1.9 mmol) with KOH (40% in H2O, 1.3 mL, 9.5 mmol) was performed under similar reaction conditions as described for 8a, followed by purification by column chromatography (n-hexane/ethyl acetate = 8/2) afforded 8b (0.75 g, 94%) as a
thick liquid; \( R_f \) 0.56 (n-hexane/ethyl acetate = 7/3); \([\alpha]_D = -40 \) (c 0.65, CHCl₃); IR (Neat) 3550-3200, 1638 cm⁻¹; \(^1^H\) NMR (300 MHz, CDCl₃ + D₂O) \( \delta \) 1.34 (s, 3H), 1.48 (s, 3H), 3.51 (dd, \( J = 7.2, 6.0 \) Hz, 1H), 3.83 (d, \( J = 12.9 \) Hz, 1H), 3.96 (d, \( J = 12.9 \) Hz, 1H), 4.06 (d, \( J = 3.3 \) Hz, 1H), 4.06 (d, \( J = 3.3 \) Hz, 1H), 4.07 (t, \( J = 6.0 \) Hz, 1H), 4.19 (dd, \( J = 7.2, 3.3 \) Hz, 1H), 4.48 (d, \( J = 11.6 \) Hz, 1H), 4.61 (d, \( J = 3.9 \) Hz, 1H), 4.66 (d, \( J = 11.6 \) Hz, 1H), 5.17 (dd, \( J = 10.2, 1.1 \) Hz, 1H), 5.23 (dd, \( J = 16.8, 1.1 \) Hz, 1H), 5.88 (ddd, \( J = 16.8, 10.2, 6.0 \) Hz, 1H), 5.96 (d, \( J = 3.9 \) Hz, 1H), 7.10-7.40 (m, 10H); \(^1^C\) NMR (75 MHz, CDCl₃) \( \delta \) 26.2, 26.7, 53.7, 60.0, 71.7, 71.9, 80.2, 80.4, 82.2, 104.5, 111.5, 116.4, 126.7, 127.7 (s), 127.9 (s), 128.1 (s), 128.3 (s), 136.7, 138.4, 140.4; Anal. Calcd. For C₂₅H₃₁NO₅: C, 70.57; H, 7.34; Found: C, 70.68; H, 7.35.

3-\( O\)-Benzyl-1,2-\( O\)-isopropylidene-5,7,8-trideoxy-5-(\( N\)-benzylamino)-6(\( R\))-hydroxy-\( \beta \)-L-glycero-L-idooct-1,4-furanose (8c). The reaction of 7c (0.4 g, 0.88 mmol) with KOH (40% in H₂O, 0.62 mL, 4.42 mmol) was performed under similar reaction conditions as described for 8a. Purification by column chromatography (n-hexane/ethyl acetate = 80/20) afforded 8c (0.37 g, 98%) as a thick liquid; \( R_f \) 0.56 (n-hexane/ethyl acetate = 7/3); \([\alpha]_D = -35.0 \) (c 0.40, CHCl₃); IR (Neat) 3600-3150, 1642 cm⁻¹; \(^1^H\) NMR (300 MHz, CDCl₃) \( \delta \) 1.31 (s, 3H), 1.46 (s, 3H), 2.00 (bs, exchanges with D₂O, 2H), 3.25 (dd, \( J = 8.8, 3.9 \) Hz, 1H), 3.83 (d, \( J = 12.7 \) Hz, 1H), 3.89 (d, \( J = 3.3 \) Hz, 1H), 3.97 (d, \( J = 12.7 \) Hz, 1H), 4.11 (dd, \( J = 8.8, 3.3 \) Hz, 1H), 4.04-4.18 (m, 1H), 4.43 (d, \( J = 11.0 \) Hz, 1H), 4.62 (d, \( J = 3.9 \) Hz, 1H), 4.65 (d, \( J = 11.0 \) Hz, 1H), 5.10 (d, \( J = 10.5 \) Hz, 1H), 5.22 (d, \( J = 17.1 \) Hz, 1H), 5.69 (ddd, \( J = 17.1, 10.5, 5.5 \) Hz, 1H), 5.90 (d, \( J = 3.9 \) Hz, 1H), 7.10-7.44 (m, 10H); \(^1^C\) NMR (75 MHz, CDCl₃) \( \delta \) 26.3, 26.7, 52.6, 59.7, 69.7, 71.3, 79.9, 81.7, 81.9, 104.0, 111.5, 115.8, 126.9, 127.8 (s), 128.0, 128.2 (s), 128.3 (s), 128.5 (s), 136.6, 136.8, 140.0; Anal. Calcd. For C₂₅H₃₁NO₅: C, 70.57; H, 7.34; Found: C, 70.59; H, 7.47.

1,2-\( O\)-Isopropylidene-5,7,8-trideoxy-5,8-(\( N\)-benzoxycarbonylamino)-6(\( R\))-hydroxy-\( \alpha \)-D-glycero-D-gluco-oct-1,4-furanose (10a). To a solution of 9a (0.10 g, 0.23 mmol) in methanol (4 mL)
was added ammonium formate (0.09 g, 1.40 mmol) and 10% Pd/C (0.03 g). The reaction mixture was heated at 80 °C for 1 h, filtered through celite and the filtrate was evaporated to give thick oil. To a solution of amino alcohol (0.057 g, 0.23 mmol), in methanol-water (8 mL, 9:1) was added sodium bicarbonate (0.058 g, 0.70 mmol) and benzylchloroformate (0.06 g, 0.35 mmol) at 0 °C and stirred for 3 h. Methanol was removed under reduced pressure and residue was extracted with chloroform (10 mL x 3). Purification by column chromatography (n-hexane/ethyl acetate = 3/2) afforded 10a (0.068 g, 76%, overall) as a thick liquid; $R_f$ 0.36 (n-hexane/ethyl acetate = 1/1); $[\alpha]_D = -53$ (c 0.23, CHCl$_3$); IR (Neat) 3550-3130, 1690 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.31 (s, 3H), 1.46 (s, 3H), 1.90-2.18 (m, 2H), 2.24 (bs, exchanges with D$_2$O, 1H), 3.47 (ddd, $J = 10.6, 8.8, 2.2$ Hz, 1H), 3.65 (dd, $J = 8.3, 2.1$ Hz, 1H), 3.71 (dq, $J = 10.6, 7.4$ Hz, 1H), 3.98 (d, $J = 10.5$ Hz, 1H), 4.06 (d, $J = 2.1$ Hz, 1H), 4.58 (d, $J = 3.6$ Hz, 1H), 4.60-4.66 (m, 1H), 5.13 (q, $J = 12.4$ Hz, 2H), 5.59 (bs, exchanges with D$_2$O, 1H), 5.91 (d, $J = 3.6$ Hz, 1H), 7.22-7.42 (m, 5H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 26.1, 26.9, 31.1, 45.3, 64.2, 67.8, 73.1, 73.8, 81.1, 84.2, 104.7, 111.4, 127.8 (s), 128.1, 128.5 (s), 135.9, 157.2; Anal. Calcd. For C$_{19}$H$_{25}$NO$_7$: C, 60.15; H, 6.64; Found: C, 60.24; H, 6.73.

1,2-O-Isopropylidene-5,7,8-trideoxy-5,8-(N-benzoxy carbonylamino)-6(S)-hydroxy-$\alpha$-L-glycero-D-gluco-oct-1,4-furanose (10b). The reaction of 9b (0.16 g, 0.30 mmol) with ammonium formate (0.156 g, 2.5 mmol) and 10% Pd/C (0.10 g) followed by reaction of amino alcohol (0.076 g, 0.30 mmol) with sodium bicarbonate (0.078 g, 0.90 mmol) and benzylchloroformate (0.08 g, 0.46 mmol) was performed under similar reaction conditions as described for the synthesis of 10a. Usual workup followed by purification by column chromatography (n-hexane/ethyl acetate = 3/2) afforded 10b (0.09 g, 77%, overall) as a white solid; mp 83-84 °C; $R_f$ 0.40 (n-hexane/ethyl acetate = 1/1); $[\alpha]_D = +33$ (c 0.55, CHCl$_3$); IR (Nujol) 3550-3200, 1688 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.31 (s, 3H), 1.47 (s, 3H), 1.86-2.40 (m, 2H), 3.22 (bs, exchanges with D$_2$O, 1H), 3.46 (ddd, $J = 11.0, 9.1, 6.6$ Hz, 1H), 4.07 (dd, $J = 10.2, 5.0$ Hz, 1H), 4.11-4.19 (m, 2H), 4.56 (dd, $J = 9.1, 5.0$ Hz, 1H), 4.59 (d, $J = 3.6$ Hz, 1H),
5.11 (q, J = 12.0 Hz, 2H), 5.25 (bs, exchanges with D₂O, 1H), 5.91 (d, J = 3.6 Hz, 1H), 7.15-7.24 (m, 5H); ¹³C NMR (75 MHz, CDCl₃) δ 26.3, 27.0, 32.9, 45.7, 58.5, 67.8, 72.3, 74.4, 80.1, 84.3, 104.6, 111.8, 127.9 (s), 128.2, 128.5, 135.8, 156.7; Anal. Calcd. For C₁₉H₂₅NO₇: C, 60.15; H, 6.64; Found: C, 60.29; H, 6.68.

1,2-O-Isopropylidene-5,7,8-trideoxy-5,8-(N-benzoxy carbonylamino)-6(S)-hydroxy-α-L-glycero-L-ido-oct-1,4-furanose (10c). The reaction of compound 9c (0.09 g, 0.21 mmol) with 10% Pd/C (0.03 g) and ammonium formate (0.08 g, 1.27 mmol), in methanol (3 mL) followed by reaction of amino alcohol (0.052 g, 0.21 mmol) with sodium bicarbonate (0.053 g, 0.63 mmol) and benzylchloroformate (0.054 g, 0.32 mmol) was performed under similar reaction conditions as described for 10a. Purification by column chromatography (n-hexane/ethyl acetate = 1/1) afforded 10c (0.06 g, 75%, overall) as a white solid; mp = 154-155 °C, Rf 0.52 (ethyl acetate); [α]D = −74 (c 0.27, CHCl₃); IR (Nujol) 3550-3150, 1694 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 1.30 (s, 3H), 1.47 (s, 3H), 1.90 (dd, J = 12.6, 8.1 Hz, 1H), 2.22-2.40 (m, 1H), 3.52 (t, J = 9.5 Hz), 3.74 (q, J = 9.5 Hz, 1H), 3.95-4.30 (m, 1H), 4.16 (d, J = 2.7 Hz, 1H), 4.21 (d, J = 4.1 Hz, 1H), 4.28-4.37 (m, 1H), 4.48 (d, J = 3.9 Hz, 1H), 5.87 (d, J = 3.9 Hz, 1H), 7.20-7.40 (m, 5H); ¹³C NMR (75 MHz, CDCl₃) δ 26.1, 26.8, 32.0, 45.4, 64.7, 67.7, 75.5, 77.2, 80.6, 85.0, 104.5, 111.3, 127.7 (s), 128.0, 128.4 (s), 136.1, 157.5; Anal. Calcd. For C₁₉H₂₅NO₇: C, 60.15; H, 6.64; Found: C, 60.21; H, 6.76.

1,2-O-Isopropylidene-5,7,8-trideoxy-5,8-(N-benzylamino)-α-D-gluco-oct-1,4-furan-6-ulose (11). To a solution of oxalyl chloride (0.09 g, 0.7 mmol) in CH₂Cl₂ (3 mL) at -78 °C was added DMSO (0.1 g, 1.3 mmol) and the mixture was stirred for 15 min, solution of alcohol 9a (0.25 g, 0.58 mmol) in CH₂Cl₂ (5 mL) was added, and the mixture was stirred at -78 °C for additional 1 h. Triethyl amine (0.30 g, 0.30 mmol) was added, and the mixture was allowed to warm to room temperature. Usual workup followed by purification by column chromatography (n-hexane/ethyl acetate = 90/10) afforded 11 (0.21 g, 85%) as thick liquid; Rf 0.64 (n-hexane/ethyl acetate = 5/5); [α]D = −20 (c 0.40, CHCl₃); IR (Neat)

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1745, 1643 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 1.31 (s, 3H), 1.48 (s, 3H), 2.20-2.45 (m, 3H), 3.12-3.22 (m, 1H), 3.31 (d, J = 8.5 Hz, 1H), 3.50 (d, J = 13.0 Hz, 1H), 4.27 (dd, J = 8.5, 3.0 Hz, 1H), 4.35 (d, J = 3.0 Hz, 1H), 4.54 (d, J = 13.0 Hz, 1H), 4.55 (d, J = 3.9 Hz, 1H), 4.65 (q, J = 11.3 Hz, 2H), 5.97 (d, J = 3.9 Hz, 1H), 7.18-7.40 (m, 10 H); ¹³C NMR (75 MHz, CDCl₃); δ 26.2, 26.7, 37.2, 49.0, 59.8, 66.9, 71.9, 81.4 (s), 82.3, 104.5, 111.4, 126.9, 127.4 (s), 127.5, 128.0 (s), 128.1 (s), 129.2 (s), 137.5, 212.4; Anal. Calcd. For C₂₅H₂₉NO₅ C, 70.90; H, 6.90; Found: C, 71.02; H, 6.82.

Reduction of ketone (11). To a solution of ketone 11 (0.25 g, 0.59 mmol) in methanol-water (9:1, 8 mL) at – 50 °C, sodium borohydride (0.11 g, 0.30 mmol) was added and stirred for 1 h. Methanol was evaporated under reduced pressure and residue was extracted with chloroform (10 mL x 3). Usual workup afforded the mixture of alcohols (0.23 g, 92%) in the ratio of 1:10 as indicated by ¹H NMR analysis of crude mixture. The mixture was further converted to 10a and 10b as described in synthesis of 10a.

(1S,6S,7R,8R,8aR)-2,6,7,8-Tetrahydroxy-indolizidine [(+)-castanospermine] (1a). Compound 10b (0.08 g, 0.21 mmol) was treated with TFA-H₂O (2 mL, 2:1) at 25 °C for 2.5 h. Trifluoroacetic acid was co-evaporated with benzene to furnish thick liquid. To a solution of above product in dry methanol (4 mL) was added 10% Pd/C (0.04 g) and the solution was hydrogenated at 80 psi for 12 h. The catalyst was filtered, washed with methanol and the filtrate concentrated to afforded thick liquid. Purification by column chromatography (chloroform/methanol = 7/3) afforded 1a (0.032 g, 80%) as a white solid; mp 211 °C, (Lit¹ 212 °C); Rf 0.50 (methanol); [α]D = + 78.9 (c 0.30, H₂O), [Lit² [α]D = + 78.6 (c 0.25, H₂O)]; IR (Nujol) 3600-3200 cm⁻¹; ¹H NMR (300 MHz, D₂O) δ 1.79 (ddd, J = 14.1, 8.7, 1.9 Hz, 1H), 2.10 (dd, J = 9.9, 4.5 Hz, 1H), 2.13 (t, J = 10.8 Hz, 1H), 2.28 (q, J = 9.3 Hz, 1H), 2.33 (ddd, J = 14.1, 7.4, 2.4 Hz, 1H), 3.08 (dt, J = 9.1, 2.4 Hz, 1H), 3.18 (dd, J = 10.8, 5.0 Hz, 1H), 3.40 (t, J = 9.1 Hz, 1H), 3.68 (m, 1H), 3.67 (t, J = 9.1 Hz, 1H), 4.48 (ddd, J = 6.7, 4.5, 1.8 Hz, 1H); ¹³C NMR (75 MHz, D₂O) δ 34.8, 54.0, 56.9, 70.4, 71.2, 71.7, 73.7, 80.6; Anal. Calcd. For C₈H₁₅NO₄ C, 50.78; H, 7.99; Found: C, 50.80; H, 8.07.

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(1R,6S,7R,8R,8aR)-2,6,7,8-Tetrahydroxy-indolizidine [(+)-1-epi-castanospermine] (1b). The reaction of 10a (0.04 g, 0.10 mmol) with TFA-H2O (1.0 mL, 2:1), 10% Pd/C (0.02 g) was performed as described for 1a. Purification by column chromatography (chloroform/methanol = 8/2) afforded 1b (0.016 g, 80%) as a thick liquid; Rf 0.55 (methanol); [α]D = + 7.0 (c 0.5, MeOH), [Lit2] [α]D = + 6.2 (c 0.15, MeOH); IR (Neat) 3600-3200 cm−1; 1H NMR (300 MHz, D2O) δ 1.70-1.85 (m, 1H), 2.38 (ddd, J = 18.0, 14.3, 9.1 Hz, 1H), 2.40-2.58 (m, 2H), 2.87 (q, J = 9.0 Hz, 1H), 3.09 (ddd, J = 11.8, 9.6, 2.5 Hz, 1H), 3.28 (dd, J = 11.3, 5.0 Hz, 1H), 3.38 (dd, J = 9.0, 7.2 Hz, 1H), 3.43 (t, J = 9.0 Hz, 1H), 3.63-3.78 (m, 1H), 4.34 (ddd, J = 8.5, 5.5, 3.3 Hz, 1H); 13C NMR (75 MHz, D2O) δ 32.2, 51.1, 53.7, 68.9, 72.2, 72.5, 73.3, 78.1; Anal. Calcd. For C8H15NO4 C, 50.78; H, 7.99; Found: C, 50.76; H, 8.11.

(1S,6S,7R,8R,8aS)-2,6,7,8-Tetrahydroxy-indolizidine [(+)-8a-epi-castanospermine] (1c). The reaction of 10c (0.05 g, 0.13 mmol) with TFA-H2O (1.0 mL, 2:1), 10% Pd/C (0.03 g) was performed using similar reaction conditions as described for 1a. Purification by column chromatography (chloroform/methanol = 7/3) afforded 1c (0.021 g, 84%) as a thick liquid; Rf 0.45 (methanol); [α]D = + 30 (c 0.4, MeOH), [Lit3] [α]D = + 28 (c 0.3, MeOH); IR (Neat) 3600-3200 cm−1; 1H NMR (300 MHz, D2O) δ 1.62-1.77 (m, 1H), 2.31 (ddd, J = 17.8, 13.5, 9.1 Hz, 1H), 2.53 (dd, J = 8.0, 2.0 Hz, 1H), 2.58-2.77 (m, 2H), 2.92-3.10 (m, 2H), 3.82-3.92 (m, 1H), 3.96 (t, J = 3.6 Hz, 1H), 3.98-4.08 (m, 1H), 4.42 (ddd, J = 9.4, 8.0, 4.1 Hz, 1H); 13C NMR (75 MHz, D2O) δ 32.5, 54.9, 55.8, 70.3, 70.6, 71.2, 71.3, 71.5. Anal. Calcd. For C8H15NO4 C, 50.78; H, 7.99; Found: C, 50.91; H, 8.11.

References:


Figure 1: $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 7a
Figure 3: $^1$H NMR (600 MHz, CDCl$_3$) spectrum of compound 7b.
Figure 4: $^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of compound 7b
Figure 5: $^1$H NMR (300 MHz, CDCl$_3$) spectrum of compound 7c
Figure S: $^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of compound 8a
Figure 9: $^1$H NMR (500 MHz, CDCl$_3$ + D$_2$O) spectrum of compound Sb
Figure 10: $^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of compound 8b
Figure 11: $^1$H NMR (300 MHz, CDCl$_3$) spectrum of compound 8c
Figure 12: $^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of compound 8c
Figure 17: $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 9c
Figure 18: $^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of compound 9c
Figure 19: $^1$H NMR (300 MHz, CDCl$_3$) spectrum of compound 10a
Figure 21: $^1$H NMR (300 MHz, CD$_2$Cl$_2$) spectrum of compound 10b
Figure 23: $^1$H NMR (300 MHz, CDCl$_3$) spectrum of compound 10c

$^{10c}$
Figure 24: $^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of compound 10c
Figure 26: $^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of compound 11
Figure 27: $^1$H NMR (300 MHz, D$_2$O) spectrum of compound 1a.
Figure 30: $^{13}$C NMR (75 MHz, D$_2$O) spectrum of compound 1b
Figure 31: $^1$H NMR (300 MHz, D$_2$O) spectrum of compound 1c
Figure 32: $^{13}$C NMR (75 MHz, D$_2$O) spectrum of compound 1c