Supporting Information

The Structure and Stereochemistry of Gabosine K: Syntheses of

7-O-Acetyl-streptol and 7-O-Acetyl-1-epi-streptol

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Appendices

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General procedures

Melting points were measured with in Celsius degrees and were uncorrected. Optical rotations were operating at 589nm. Infrared spectra (IR) were recorded as thin film on potassium bromide discs. Nuclear magnetic resonance (NMR) spectra were measured at 300.13 MHz (1H), 400.13 MHz (1H), 75.47 MHz (13C) or at 100.13 MHz (13C). All chemical shifts were recorded in ppm relative to tetramethylsilane (δ= 0.0). Spin-spin coupling constants (J value) recorded in Hz were measured directly from the spectra. All reactions were monitored by analytical thin-layer chromatography (TLC) on aluminium-precoated plates of silica gel with detection by spraying with 5% (w/v) dodecamolybdophosphoric acid in ethanol. Silica gel 60 (230–400 mesh) was used for flash chromatography. All reagents and solvents were general reagent grade unless otherwise stated. DMF was dried by magnesium sulfate and filtered. It was then freshly distilled under reduced pressure. THF was freshly distilled from Na/benzophenone ketel under nitrogen. Dichloromethane was freshly distilled from P2O5 under nitrogen. Other reagents were purchased from commercial suppliers and were used without purification.

Experimental

7-O-acetyl-streptol (6). To a solution of the acetate 16 (79.2 mg, 0.177 mmol) in CH2Cl2 (3 mL) were added trifluoroacetic acid (TFA) (0.3 mL) and H2O (0.01 mL) and the mixture was stirred at room temperature for 24 h. The solvent was removed under reduced pressure and flash chromatography (CHCl3:MeOH, 8:1) of the residue afforded tetraol 6 (31.3 mg, 81%) as a colorless oil: [α]20D +72.1 (c 0.93, MeOH) {lit.a no optical rotation reported}; Rf 0.37 (CHCl3:MeOH, 3:1); 1H NMR (400 MHz, CD3OD) δ 2.06 (s, 3H), 3.44 (dd, J = 10.1, 4.2 Hz, 1H), 3.71 (dd, J = 10.1, 7.3 Hz, 1H), 3.94 (dd, J = 7.3, 0.7 Hz, 1H), 4.18 (t J = 4.6 Hz, 1H), 4.57 (d, J = 13.3 Hz, 1H), 4.76 (dd, J = 13.3, 0.8 Hz, 1H), 5.80–5.82 (m, 1H); 13C NMR (100 MHz, CD3OD) δ 19.2 (CH3), 63.5 (CH2), 66.0 (CH), 70.9 (CH), 71.9
Gabosine K (7). To a solution of the alkene 19 (48.1 mg, 0.108 mmol) in CH₂Cl₂ (3 mL) were added trifluoroacetic acid (TFA) (0.5 mL) and H₂O (0.05 mL) and the mixture was stirred at room temperature for 24 h. The solvent was removed under reduced pressure and flash chromatography (CHCl₃:MeOH, 8:1) of the residue afforded gabosine K (7) (20.3 mg, 86%) as a colorless oil: \([\alpha]_{D}^{20} -47.9 (c 0.52, \text{MeOH})\) \({}^{1}\)lit.\(^1\) no optical rotation reported; \(R_f\) 0.55 (t-BuOH:AcOH:H₂O 4:1:5, upper phase); \(^1\)H NMR (300 MHz, CD₃OD) \(\delta\) 2.06 (s, 3H), 3.35–3.42 (m, 2H), 4.04–4.08 (m, 2H), 4.52 (d, \(J = 13.5\) Hz, 1H), 4.72 (d, \(J = 13.2\) Hz, 1H), 5.59 (d, \(J = 1.2\) Hz, 1H); \(^1\)H NMR (400 MHz, D-Acetone) \(\delta\) 2.02 (s, 3H), 3.37 (dd, \(J = 10.1, 7.4\) Hz, 1H), 3.44 (dd, \(J = 10.1, 7.4\) Hz, 1H), 4.07 (dd, \(J = 7.4, 1.8\) Hz, 1H), 4.11 (d, \(J = 8.5\) Hz, 1H), 4.52 (d, \(J = 13.4\) Hz, 1H), 4.71 (d, \(J = 13.4\) Hz, 1H), 5.57 (d, \(J = 1.4\) Hz, 1H); \(^{13}\)C NMR (75 MHz, CD₂OD) \(\delta\) 20.7 (CH₃), 64.8 (CH₂), 73.0 (CH), 73.5 (CH), 77.1 (CH), 77.5 (CH), 128.8 (CH), 136.2 (C), 172.5 (C); MS (ESI) \(m/z\) (relative intensity) 241 ([M+Na]\(^{+}\), 100); HRMS (ESI) calcd for C₉H₁₄O₆ [M+Na]\(^{+}\) 241.0683, found 241.0675.

Silyl ether 14. A solution of the alcohol 13 (506.3 mg, 1.53 mmol), imidazole (312 mg, 4.58 mmol) and tert-butyl dimethyl silyl chloride (TBSCl) (345 mg, 2.30 mmol) in dry DMF (5 mL) was stirred at room temperature for 24 h. The mixture was quenched with saturated NaHCO₃ solution and the aqueous phase was extracted with Et₂O (3 × 20 mL). The combined organic extracts were washed with brine, dried over anhydrous MgSO₄, and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (n-hexane:Et₂O, 1:1) to afford silyl ether 14 (648.5 mg, 95%) as a white solid: mp 83–85 °C; \([\alpha]_{D}^{20} -46.9 (c 0.79, \text{CHCl₃})\); \(R_f\) 0.5 (n-hexane:Et₂O, 1:1); IR (thin film) 2990, 2947, 1463, 1374, 1131, 836 cm⁻¹; \(^1\)H NMR (300 MHz, CDCl₃) \(\delta\) 0.07 (3H, s),
Diol 15. A solution of the silyl ether 14 (361 mg, 0.812 mmol) in 80% aqueous AcOH (5 mL) was stirred at room temperature for 1 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (n-hexane:EtOAc, 1:1) to afford diol 15 (289 mg, 88%) as a white solid: mp 123–125 °C; [α]$_{D}^{20}$ $-37.2$ (c 0.46, CHCl$_3$); $R_f$ 0.28 (n-hexane:EtOAc, 1:1); IR (thin film) 3474, 2928, 2854, 1645, 1462, 1126, 1037 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) δ 0.07 (3H, s), 0.10 (3H, s), 0.88 (9H, s), 1.28 (3H, s), 1.31 (3H, s), 2.33 (1H, brs), 2.75 (1H, brs), 3.24 (3H, s), 3.26 (3H, s), 3.43 (1H, dd, $J = 11.1$, 3.9 Hz), 4.06 (1H, dd, $J = 11.1$, 8.1 Hz), 4.18–4.28 (3H, m), 4.34 (1H, d, $J = 8.1$ Hz), 5.70 (1H, d, $J = 4.5$ Hz); $^{13}$C NMR (75 MHz, CDCl$_3$) δ $-4.2$ (CH$_3$), $-4.1$ (CH$_3$), 18.1 (CH$_3$), 18.3 (CH$_3$), 18.8 (C), 26.3 (CH$_3$), 48.2 (CH$_3$), 48.4 (CH$_3$), 64.7 (CH$_2$), 66.5 (CH), 68.4 (CH), 69.8 (CH), 72.7 (CH), 99.1 (C), 99.6 (C), 125.3 (CH), 139.8 (C); MS (ESI) m/z (relative intensity) 427 ([M+Na]$^+$, 100); HRMS (ESI) calcd for C$_{19}$H$_{36}$O$_7$Si$_1$ [M+Na]$^+$ 427.2123, found 427.2119.

Acetate 16. To a solution of the diol 15 (87.6 mg, 0.216 mmol) and 2,4,6-collidine (0.086 mL, 0.649 mmol) in dry CH$_2$Cl$_2$ (3 mL) at −78 °C was added acetyl chloride (AcCl) (0.018 mL, 0.253 mmol) slowly. The reaction mixture was stirred for 18 h at −78 °C and quenched with water (3 mL). The resultant solution was allowed to warm to room temperature. The aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic extracts were then washed with cold 1N HCl (2 × 5 mL),
cold deionized water (5 mL) and cold diluted NaHCO₃ (5 mL). The organic layer was washed with brine (2 × 5 mL), dried (MgSO₄), and filtered. Concentration of the filtrate followed by flash chromatography (n-hexane:Et₂O, 1:1) gave acetate 16 (90.4 mg, 94%) as a colorless oil: [α]²⁰ₒD −44.2 (c 0.71, CHCl₃); Rₚ 0.66 (n-hexane:EtOAc, 1:1); IR (thin film) 3486, 2948, 2892, 1742, 1130, 835 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.06 (3H, s), 0.09 (3H, s), 0.87 (9H, s), 1.28 (3H, s), 1.31 (3H, s), 2.06 (3H, s), 2.76 (1H, brs), 3.24 (3H, s), 3.26 (3H, s), 3.46 (1H, dd, J = 10.8, 3.6 Hz), 4.06 (1H, dd, J = 10.8, 8.1 Hz), 4.17–4.20 (2H, m), 4.48 (1H, d, J = 12.9 Hz), 4.90 (1H, d, J = 12.6 Hz), 5.77 (1H, d, J = 5.1 Hz); ¹³C NMR (75 MHz, CDCl₃) δ −4.3 (CH₃), −4.2 (CH₃), 18.1 (CH₃), 18.3 (CH₃), 18.8 (C), 21.4 (CH₃), 26.2 (CH₃), 48.1 (CH₃), 48.4 (CH₃), 64.6 (CH₂), 66.3 (CH), 68.3 (CH), 69.7 (CH), 70.7 (CH), 99.1 (C), 99.6 (C), 127.9 (CH), 136.6 (C), 171.6 (C); MS (ESI) m/z (relative intensity) 469 ([M+Na]⁺, 100); HRMS (ESI) calcd for C₂₁H₃₈O₈Si₁ [M+Na]⁺ 469.2228, found 469.2230.

**Silyl ether 17.** A solution of the alcohol 12 (567.7 mg, 1.72 mmol), imidazole (351 mg, 5.16 mmol) and tert-butyl dimethyl silyl chloride (TBSCl) (388 mg, 2.57 mmol) in dry DMF (5 mL) was stirred at room temperature for 2 h. The mixture was quenched with saturated NaHCO₃ and the aqueous phase was extracted with Et₂O. The combined organic extracts were washed with brine, dried over anhydrous MgSO₄, and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (n-hexane:Et₂O, 1:1) to afford firstly silyl ether 17 (783.5 mg, 100%) as a colorless oil: [α]²⁰ₒD −239 (c 0.89, CHCl₃); Rₚ 0.66 (n-hexane:Et₂O, 1:1); IR (thin film) 2954, 2931, 1472, 1372, 1141, 838 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.10 (s, 3H), 0.11 (s, 3H), 0.89 (s, 9H), 1.28 (s, 3H), 1.31 (s, 3H), 1.38 (s, 3H), 1.50 (s, 3H), 3.27 (s, 6H), 3.59 (dd, J = 11.1, 7.8 Hz, 1H), 3.75 (dd, J = 11.1, 7.8 Hz, 1H), 4.06 (d, J = 13.5 Hz, 1H), 4.32–4.35 (m, 1H), 4.47 (dd, J = 13.5, 1.5 Hz, 1H), 4.53 (dd, J = 7.8, 0.9 Hz, 1H), 5.28 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ −4.3 (CH₃), −4.0 (CH₃), 18.0 (CH₃), 18.1 (CH₃), 18.7 (C), 20.1 (CH₃), 26.1 (CH₃), 29.1 (CH₃), 48.2 (CH₃), 48.3 (CH₃), 63.6
Diol 18. A solution of the silyl ether 17 (744 mg, 1.67 mmol) in 80% aqueous AcOH (7.5 mL) was stirred at room temperature for 1 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (n-hexane:EtOAc, 1:1) to afford diol 18 (571.1 mg, 84%) as a colorless oil: \([\alpha]_{D}^{20} -138 (c 0.99, \text{CHCl}_3); \ R_f 0.28 \) (n-hexane:EtOAc, 1:1); IR (thin film) 3400, 2953, 1637, 1463, 1376, 1126, 837 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 0.10\) (s, 3H), 0.11 (s, 3H), 0.89 (s, 9H), 1.29 (s, 3H), 1.32 (s, 3H), 2.55 (brs, 2H), 3.26 (s, 3H), 3.28 (s, 3H), 3.58 (dd, \(J = 10.8\) Hz, 1H), 3.67 (dd, \(J = 10.8\), 8.1 Hz, 1H), 4.15 (d, \(J = 12.9\) Hz, 1H), 4.23 (d, \(J = 12.9\) Hz, 1H), 4.34 (d, \(J = 7.5\) Hz, 1H), 4.49 (d, \(J = 7.8\) Hz, 1H), 5.47 (s, 1H, s); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta -4.3\) (CH\(_3\)), \(\delta -4.0\) (CH\(_3\)), 18.0 (CH\(_3\)), 18.1 (CH\(_3\)), 18.6 (C), 26.2 (CH\(_3\)), 48.3 (CH\(_3\)), 48.4 (CH\(_3\)), 64.8 (CH\(_2\)), 70.8 (CH), 71.9 (CH), 72.5 (CH), 72.7 (CH), 99.2 (C), 99.4 (C), 128.5 (CH), 137.4 (C); MS (ESI) \(m/z\) (relative intensity) 427 ([M+Na]\(^+\), 100); HRMS (ESI) calcd for C\(_{19}\)H\(_{36}\)O\(_7\)Si\(_1\) [M+Na]\(^+\) 427.2123, found 427.2128.

Acetate 19. To a solution of the diol 18 (551.2 mg, 1.36 mmol) and 2,4,6-collidine (0.54 mL, 4.08 mmol) in dry CH\(_2\)Cl\(_2\) (10 mL) at \(-78^\circ\)C was added acetyl chloride (AcCl) (0.14 mL, 1.97 mmol) slowly. The reaction mixture was stirred for 18 h at \(-78^\circ\)C and quenched with water (5 mL). The resultant solution was allowed to warm to room temperature. The aqueous phase was extracted with EtOAc. The combined organic extracts were then washed with cold 1N HCl, cold D.I. water and cold diluted NaHCO\(_3\). The organic layer was washed with brine, dried (MgSO\(_4\)), and filtered. Concentration of the filtrate followed by flash chromatography (n-hexane:Et\(_2\)O, 1:1) gave acetate 19 (559.6 mg, 92%) as
a colorless oil: $\left[\alpha\right]^{20}_{D} -183 \ (c \ 0.86, \ \text{CHCl}_3)\); $R_f$ 0.24 ($n$-hexane:Et$_2$O, 1:1); IR (thin film) 3491, 2953, 1745, 1462, 1372, 1251, 1127, 837 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 0.11 (s, 6H), 0.89 (s, 9H), 1.29 (s, 3H), 1.32 (s, 3H), 2.07 (s, 3H), 2.33 (brs, 1H), 3.26 (s, 3H), 3.29 (s, 3H), 3.59 (dd, $J = 10.2, 7.8$ Hz, 1H), 3.67 (dd, $J = 11.1, 7.8$ Hz, 1H), 4.31–4.34 (m, 2H), 4.43 (d, $J = 12.9$ Hz, 1H), 4.87 (d, $J = 12.9$ Hz, 1H), 5.52 (s, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ $-4.3$ (CH$_3$), $-4.0$ (CH$_3$), 18.0 (CH$_3$), 18.1 (CH$_3$), 18.6 (C), 21.4 (CH$_3$), 26.2 (CH$_3$), 48.3 (CH$_3$), 48.4 (CH$_3$), 64.2 (CH$_2$), 69.8 (CH), 70.6 (CH), 72.3 (CH), 72.6 (CH), 99.2 (C), 99.4 (C), 130.7 (CH), 134.1 (C), 171.6 (C); MS (ESI) $m/z$ (relative intensity) 469 ([M+Na]$^+$, 100); HRMS (ESI) calcd for C$_{21}$H$_{38}$O$_8$Si$_1$ [M+Na]$^+$ 469.2228, found 469.2233.
(-)-Gadobenate

HO:  HO

HO:  HO

AcO

Solvent: CD$_3$OD