Supporting Information

Design, Synthesis and Glycosidase Inhibition Studies of Novel Triazole Fused Iminocyclitol-δ-lactams

Venkatesan Santhanam, Pradeep Pant, B. Jayaram and Namakkal G Ramesh*

Department of Chemistry
Indian Institute of Technology Delhi
Hauz Khas – 110016, New Delhi, India

E-mail: ramesh@chemistry.iitd.ac.in

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(2S,3R,4R,5S)-3,4-Bis(benzyloxy)-5-(benzylxoylmethyl)-2-(tert-butylidimethyl silanyloxy methyl)-pyrrolidine 17.

A solution of compound 11 (5.0 g, 7.1 mmol) in dry THF (50 mL) was cooled to −78 °C. A solution of sodium napthalenide (prepared separately by the addition of sodium (1.56 g, 67.6 mmol) to naphthalene (9.2 g, 71.2 mmol) in dry THF) was added slowly and the reaction mixture was stirred at −78 °C for 20 minutes. The reaction mixture was brought to room temperature and quenched with aqueous sodium carbonate solution (50 mL). It was then extracted with ethyl acetate (50 mL). The organic layer was dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (3:1) as an eluent to get 17 (3.3 g, 85%) as a pale yellow viscous oil. R_f: 0.4 (hexane/ethyl acetate, 2:1); Specific rotation: [α]_D^34 = −3.6 (c 1.3, CHCl_3); IR (KBr): v = 3348, 3062, 3031, 2928, 2858, 1600, 1460, 1363, 1251, 1093, 840, 777, 739, 698 cm⁻¹; ¹H NMR (300 MHz, CDCl_3) δ 7.32–7.25 (m, 15H), 4.52–4.43 (m, 6H), 3.99 (brm, 2H), 3.78–3.65 (m, 4H), 3.57–3.45 (m, 2H), 2.06–2.02 (br m, 1H exchangeable with D_2O), 0.88 (s, 9H), 0.04 (s, 6H); ¹³C NMR (75 MHz, CDCl_3) δ 138.3 (2 x s), 138.2 (s), 128.2 (d), 127.5 (d), 127.4 (d), 127.3 (d), 82.5 (d), 82.2 (d), 73.1 (t), 72.1 (t), 72.0 (t), 69.8 (t), 61.9 (t), 60.2 (d), 57.9 (d), 25.8 (q), 18.1 (s), −5.4 (q); HRMS (ESI): m/z calcd for C_33H_46NO_4Si [M+H]^+ 548.3191 found 548.3207.

(2S,3R,4R,5S)-3,4-Bis(benzyloxy)-5-(benzylxoylmethyl)-2-(tert-butylidimethyl silanyloxy methyl)-1-N-(tert-butoxycarbonyl)-pyrrolidine 19.

To a solution of pyrrolidine 17 (2.65 g, 4.83 mmol) in dry ethyl acetate (25 mL), potassium carbonate (2.0 g, 14.47 mmol) and Boc_2O (1.35 mL, 5.87 mmol) were added and the reaction mixture was stirred at 35 °C for 16 h. The reaction mixture was then...
diluted with ethyl acetate (50 mL) and washed with water (2 x 50 mL). The organic layer was dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (9:1) as an eluent to get 19 (2.89 g, 92%) as a colourless oil. The data provided is for a mixture of rotamers in the ratio of 56:44. \( R_f: 0.8 \) (hexane/ethyl acetate, 5:1); Specific rotation: \([\alpha]_D^{30} = -19.1 \) (c 1.22, CHCl\(_3\)); IR (KBr): \( \nu = 3061, 3030, 2928, 2859, 1695, 1461, 1389, 1325, 1252, 1113, 1058, 839, 775, 737, 699 \text{ cm}^{-1}; \) \(^1\text{H} \text{ NMR (300 MHz, CDCl}_3\): \( \delta 7.56-7.46 \text{ (m, 15H), 4.98-4.55 \text{ (m, 8H), 4.29 \text{ (dd, J = 9.9, 3.0 Hz, 1H), 4.23-4.09 \text{ (m, 2H), 4.05-3.77 \text{ (m, 3H), 1.68 \text{ (s, 5H), 1.63 \text{ (s, 4H), 1.05 \text{ (s, 9H), 0.19 \text{ (s, 6H)}}; \)}^{13}\text{C NMR (75 MHz, CDCl}_3\): \( \delta 153.8 \text{ (s), 153.7 \text{ (s), 139.0 \text{ (s), 138.8 \text{ (s), 138.7 \text{ (s), 138.6 \text{ (s), 128.2 \text{ (d), 128.17 \text{ (d), 128.11 \text{ (d), 127.5 \text{ (d), 127.45 \text{ (d), 127.40 \text{ (d), 127.3 \text{ (d), 127.28 \text{ (d), 127.20 \text{ (d), 80.9 \text{ (d), 80.48 \text{ (d), 80.41 \text{ (d), 79.4 \text{ (s), 73.3 \text{ (t), 73.2 \text{ (t), 72.9 \text{ (t), 72.8 \text{ (t), 72.6 \text{ (t), 67.6 \text{ (t), 66.1 \text{ (t), 59.0 \text{ (t), 57.6 \text{ (t), 57.5 \text{ (d), 57.2 \text{ (d), 56.5 \text{ (d), 56.4 \text{ (d), 28.5 \text{ (q), 28.4 \text{ (q), 25.8 \text{ (q), 18.0 \text{ (s), } -5.5 \text{ (q), } -5.6 \text{ (q); HRMS (ESI): m/z calcd for C}_{38}H_{53}NNaO_6Si [M+Na]^+ 670.3534 found 670.3532.}

\text{(2S,3R,4R,5S)-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(hydroxymethyl)-1-N-(tert-butoxycarbonyl)-pyrrolidine 9.}

To a solution of compound 19 (2.6 g, 4.01 mmol) in dry methanol (25 mL), camphorsulfonic acid (260 mg, 10% w/w) was added and the reaction mixture was stirred at 31 °C for 16 h. Solvent was then concentrated under reduced pressure and the residue was dissolved in ethyl acetate (50 mL). It was then washed with aqueous sodium bicarbonate solution (2 x 25 mL), dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (3:1) as an eluent to get 9 (1.85 g, 86%) as a colourless oil. The data provided is for a mixture of rotamers in the ratio of 63:36. \( R_f: 0.4 \) (hexane/ethyl acetate, 4:1); Specific rotation: \([\alpha]_D^{30} = -19.3 \) (c 1.28, CHCl\(_3\)); IR (KBr): \( \nu = 3548, 3474, 3416, 3029, 2969, 2925, 2871, 1688, 1455, 1389, 1109, 1032, 738, 697, 610 \text{ cm}^{-1}; \) \(^1\text{H} \text{ NMR (300 MHz, CDCl}_3\): \( \delta 7.56-7.46 \text{ (m, 15H), 4.98-4.55 \text{ (m, 8H), 4.29 \text{ (dd, J = 9.9, 3.0 Hz, 1H), 4.23-4.09 \text{ (m, 2H), 4.05-3.77 \text{ (m, 3H), 1.68 \text{ (s, 5H), 1.63 \text{ (s, 4H), 1.05 \text{ (s, 9H), 0.19 \text{ (s, 6H)}}; \)}^{13}\text{C NMR (75 MHz, CDCl}_3\): \( \delta 153.8 \text{ (s), 153.7 \text{ (s), 139.0 \text{ (s), 138.8 \text{ (s), 138.7 \text{ (s), 138.6 \text{ (s), 128.2 \text{ (d), 128.17 \text{ (d), 128.11 \text{ (d), 127.5 \text{ (d), 127.45 \text{ (d), 127.40 \text{ (d), 127.3 \text{ (d), 127.28 \text{ (d), 127.20 \text{ (d), 80.9 \text{ (d), 80.48 \text{ (d), 80.41 \text{ (d), 79.4 \text{ (s), 73.3 \text{ (t), 73.2 \text{ (t), 72.9 \text{ (t), 72.8 \text{ (t), 72.6 \text{ (t), 67.6 \text{ (t), 66.1 \text{ (t), 59.0 \text{ (t), 57.6 \text{ (t), 57.5 \text{ (d), 57.2 \text{ (d), 56.5 \text{ (d), 56.4 \text{ (d), 28.5 \text{ (q), 28.4 \text{ (q), 25.8 \text{ (q), 18.0 \text{ (s), } -5.5 \text{ (q), } -5.6 \text{ (q); HRMS (ESI): m/z calcd for C}_{38}H_{53}NNaO_6Si [M+Na]^+ 670.3534 found 670.3532.}
7.31–7.26 (m, 15H), 4.81–4.59 (m, 4H), 4.53–4.47 (m, 3H), 4.31–4.15 (m, 1H), 4.06–3.89 (m, 3H), 3.81–3.55 (m, 1H), 3.40 (br s, 0.6H, exchangeable with D₂O), 2.54 (br s, 0.3H, exchangeable with D₂O), 1.46 (s, 4H), 1.41 (s, 5H); ¹³C NMR (75 MHz, CDCl₃): δ 155.0 (s), 153.7 (s), 138.6 (s), 138.2 (s), 138.0 (s), 137.9 (s), 137.7 (s), 128.4 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.7 (d), 127.6 (d), 127.4 (d), 127.37 (d), 127.33 (d), 127.1 (d), 81.6 (d), 81.5 (d), 81.4 (d), 80.8 (d), 80.3 (s), 80.1 (s), 73.4 (t), 73.39 (t), 73.32 (t), 73.1 (t), 72.9 (t), 66.5 (t), 65.2 (t), 62.3 (t), 61.8 (t), 58.6 (d), 57.4 (d), 56.3 (d), 55.9 (d), 28.3 (q); HRMS (ESI): m/z calcd for C₃₂H₃₉N₃NaO₆ [M+Na]⁺ 556.2670 found 556.2672.

(2S,3R,4R,5S)-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(azidomethyl)-1-N-(tert-butoxycarbonyl)-pyrrolidine 7.

Compound 9 (1.0 g, 1.87 mmol) was dissolved in dry THF (10 mL), and the solution was cooled to 0 °C. Triphenylphosphine (0.74 g, 2.82 mmol) and trimethylsilyl azide (0.38 mL, 2.86 mmol) were added followed by dropwise addition of diethyl azodicarboxylate (0.74 mL, 4.68 mmol), after which the reaction mixture was warmed to 21 °C. When TLC indicated the completion of the reaction (24 h), the reaction was stopped and solvent was evaporated under vacuum. The residue was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (10:1) as an eluent to get 7 (754 mg, 72%) as a pale yellow oil. The data provided is for a mixture of rotamers in the ratio of 63:36. Rf: 0.8 (hexane/ethyl acetate, 9:1); Specific rotation: [α]D⁰³⁰–¹⁷.0 (c 0.60, CHCl₃); IR (KBr): ʋ = 3061, 3030, 2973, 2928, 2870, 2102, 1695, 1448, 1386, 1257, 1151, 1110, 1024, 742, 698 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.31–7.24 (m, 15H), 4.75–4.58 (m, 4H), 4.54–4.30 (m, 4H), 4.04–3.89 (m, 3H), 3.75–3.66 (m, 1H), 3.57 (d, J = 9.6 Hz, 1H), 3.38 (d, J = 12.0 Hz, 0.4H), 3.26 (d, J = 11.4 Hz, 0.6H), 1.46 (s, 3H), 1.41 (s, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 153.7 (s), 153.4 (s), 138.7 (s), 138.3 (s), 138.2 (s), 138.1 (s), 138.0 (s), 128.3 (d), 128.2 (d), 128.1 (d), 127.6 (d), 127.5 (d), 127.4 (d), 127.3 (d), 127.2 (d), 81.3 (d), 80.7 (d), 80.4 (d), 80.3 (s), 80.2 (s), 80.0 (d), 73.35 (t), 73.32 (t), 73.2 (t), 73.19 (t), 73.11 (t), 66.6 (t), 65.3 (t), 56.3 (d), 56.1
(d), 55.9 (d), 49.7 (t), 48.1 (t), 28.3 (q); HRMS (ESI): m/z calcd for C_{32}H_{38}Na_{5}O_{5} [M+Na]^+ 581.2734 found 581.2720.

Diethyl-1-{[(2S,3R,4R,5S)-3,4-bis(benzyloxy)-5-(benzyloxymethyl)-1-({tert-butoxy carbonyl}pyrrolidin-2-yl) methyl]1H-1',2',3'-triazole-4',5'-dicarboxylate 21.

\[
\begin{align*}
\text{BnO} & \quad \text{OBn} \\
\text{N} & \quad \text{COOEt} \\
\text{N} & \quad \text{COOEt}
\end{align*}
\]

Compound 7 (1.1 g, 1.97 mmol) was dissolved in dry toluene (12 mL) and diethyl acetylene dicarboxylate (1.6 mL, 9.97 mmol) was added. The reaction mixture was heated at 110 °C for 4 h, after which the solvent was evaporated under reduced pressure and the residue was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (4:1) as an eluent to get 21 (1.2 g, 83%) as a pale yellow oil. The data provided is for a mixture of rotamers in the ratio of 60:40. \( R_f: 0.5 \) (hexane/ethyl acetate, 4:1); Specific rotation: [\( \alpha \)]D\text{30} +13.9 \ (c 0.48, CHCl₃); IR (KBr): \( \nu = 3029, 2976, 2931, 2874, 1729, 1698, 1552, 1457, 1372, 1271, 1213, 1161, 1100, 1064, 1020, 771, 698 \) cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl₃): \( \delta = 7.29–7.20 \) (m, 15H), 5.10 (dd, \( J = 14.4, 3.9 \) Hz, 0.6H), 4.91 (dd, \( J = 13.8, 4.8 \) Hz, 0.4H), 4.75 (dd, \( J = 14.1, 4.5 \) Hz, 1H), 4.69–4.12 (m, 12H), 4.00–3.95 (m, 0.4H), 3.88–3.84 (m, 0.4H), 3.76–3.66 (m, 2H), 3.53–3.46 (m, 1H), 3.27 (t, \( J = 8.7 \) Hz, 0.6H), 1.42–1.28 (m, 15H); \(^{13}\)C NMR (75 MHz, CDCl₃): \( \delta = 160.2 \) (s), 158.7 (s), 153.9 (s), 153.3 (s), 139.6 (s), 139.4 (s), 138.5 (s), 138.2 (s), 137.7 (s), 137.4 (s), 131.5 (s), 131.1 (s), 128.38 (d), 128.31 (d), 128.2 (d), 128.1 (d), 127.8 (d), 127.7 (d), 127.59 (d), 127.54 (d), 127.4 (d), 127.3 (d), 127.1 (d), 80.7 (s), 80.3 (s), 80.2 (d), 79.9 (d), 79.8 (d), 79.5 (d), 73.2 (t), 73.1 (t), 73.0 (t), 72.9 (t), 72.8 (t), 66.2 (t), 64.4 (t), 62.4 (t), 62.2 (t), 61.58 (t), 61.51 (t), 56.1 (d), 55.4 (d), 55.0 (d), 49.2 (t), 47.7 (t), 28.3 (q), 28.1 (q), 14.1 (q), 13.7 (q); HRMS (ESI): m/z calcd for C_{40}H_{48}Na_{5}O_{9} [M+Na]^+ 751.3314 found 751.3312.
Diethyl-1-(((2S,3R,4R,5S)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)pyrrolidin-2-yl)methyl)-1H-1',2',3'-triazole-4',5'-dicarboxylate 5.

To a solution of compound 21 (1.2 g, 1.64 mmol) in dry dichloromethane (15 mL), trifluoroacetic acid (1.26 mL, 16.45 mmol) was added at 0 °C and the reaction mixture was stirred at 26 °C for 4 h. Solvent was then concentrated under reduced pressure and the residue was dissolved in ethyl acetate (25 mL). It was then washed with aqueous sodium bicarbonate solution (2 x 20 mL), dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (2:1) as an eluent to get 5 (815 mg, 79%) as a light brown oil. R\(_f\): 0.4 (hexane/ethyl acetate, 3:1); Specific rotation: [\( \alpha \)]\(_{D}^{20}\) +5.9 (c 0.9, CHCl\(_3\)); IR (KBr): \( \nu \) = 3334, 3030, 2982, 2922, 2866, 1730, 1551, 1457, 1369, 1308, 1268, 1208, 1095, 1021, 740, 699 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 7.33–7.24 (m, 15H), 4.67–4.65 (m, 2H), 4.59–4.26 (m, 10H), 4.06–4.00 (m, 2H), 3.85–3.83 (m, 1H), 3.55–3.46 (m, 3H), 1.84 (br s, 1H, exchangeable with D\(_2\)O), 1.38 (dt, \( J = 7.2, 3.0 \) Hz, 3H), 1.29 (dt, \( J = 7.2, 3.0 \) Hz, 3H); \(^13\)C NMR (75 MHz, CDCl\(_3\)): \( \delta \) 160.2 (s), 158.8 (s), 139.6 (s), 138.1 (s), 137.9 (s), 137.6 (s), 131.5 (s), 128.5 (d), 128.46 (d), 128.40 (d), 127.9 (d), 127.8 (d), 127.77 (d), 127.73 (d), 127.6 (d), 82.37 (d), 82.35 (d), 73.3 (t), 72.4 (t), 72.2 (t), 68.7 (t), 62.6 (t), 61.6 (t), 58.7 (d), 58.5 (d), 50.8 (t), 14.2 (q), 13.8 (q); HRMS (ESI): \( m/z \) calcd for C\(_{35}\)H\(_{41}\)N\(_4\)O\(_7\) [M+H]\(^+\) 629.2970 found 629.2967.

(6S,7R,8R,8aS)-Ethyl-7,8-bis(benzyloxy)-6-((benzyloxy)methyl)-4-oxo-4,6,7,8,8a,9-hexahydropyrrolo[1,2\(a\)] [1',2',3']triazolo[1',5'-d]pyrazine-3-carboxylate 23.
Compound 5 (400 mg, 0.636 mmol) was dissolved in dry toluene (4 mL) and camphorsulfonic acid monohydrate (32 mg, 0.127 mmol) was added. The reaction mixture was heated at 110 °C for 9 h, after which the solvent was evaporated under reduced pressure and the residue was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (2:1) as an eluent to get 23 (311 mg, 84%) as a light brown oil. Rf: 0.6 (hexane/ethyl acetate, 1:1); Specific rotation: [α]D28 –60.9 (c 0.34, CHCl3); IR (KBr): ν =3060, 3029, 2927, 2867, 1734, 1676, 1448, 1411, 1361, 1206, 1096, 1021, 743, 698 cm⁻¹; ¹H NMR (300 MHz, CDCl3): δ 7.36–7.21 (m, 15H), 4.68 (d, J = 11.7 Hz, 2H), 4.61–4.58 (m, 2H), 4.51–4.34 (m, 9H), 4.25–4.21 (m, 1H), 4.04 (dd, J = 9.3, 1.8 Hz, 1H), 3.87 (dd, J = 9.3, 5.4 Hz, 1H), 1.42 (t, J = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl3): δ 159.6 (s), 152.8 (s), 139.1 (s), 137.8 (s), 137.1 (s), 136.9 (s), 129.9 (s), 128.6 (d), 128.5 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.8 (d), 127.7 (d), 127.5 (d), 81.1 (d), 80.1 (d), 73.5 (t), 73.3 (t), 72.9 (t), 66.2 (t), 61.8 (t), 57.1 (d), 56.9 (d), 46.7 (t), 14.1 (q); HRMS (ESI): m/z calcd for C33H34NaNO6 [M+Na]+ 605.2370 found 605.2366.

(65,7R,8R,8aS)-7,8-Bis(benzyloxy)-6-((benzyloxy)methyl)-7,8,8a,9-tetrahydro pyrrolo[1,2-a][1',2',3' triazolo[1',5'd] pyrazin-4(6H)-one 29.

Compound 23 (500 mg, 0.86 mmol) was dissolved in dry methanol (5 mL) and potassium carbonate (356 mg, 2.57 mmol) was added. The reaction mixture was stirred at 25 °C for 6 h, after which the solvent was evaporated under reduced pressure. To the resulting milky white residue, a mixture of ethyl acetate and water (20 mL, 1:1) was added. Conc. HCl was then added to the mixture until a clear solution was obtained. The organic layer was then separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure. The residue contains 27 was dissolved in glacial acetic acid (5 mL) and heated at 120 °C for 24 h. The reaction mixture was then quenched with aqueous sodium bicarbonate solution (20 mL) and extracted with ethyl acetate (2 x 10 mL). The organic layer was then dried over anhydrous sodium sulphate and concentrated under reduced pressure. The residue
was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (2:1) as an eluent to get 29 (250 mg, 57% over two steps) as a pale yellow oil. \(R_f\): 0.6 (hexane/ethyl acetate, 1:1); Specific rotation: \([\alpha]_D^{28}\)–29.8 (c 1.75, CHCl\(_3\)); IR (KBr): \(\bar{\nu} = 3060, 3029, 2926, 2865, 1664, 1551, 1450, 1360, 1204, 1095, 1025, 739, 697\) cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 8.09\) (s, 1H), 7.39–7.24 (m, 15H), 4.67 (d, \(J = 11.7\) Hz, 2H), 4.61–4.45 (m, 7H), 4.42–4.29 (m, 2H), 4.24 (dd, \(J = 6.6, 5.1\) Hz, 1H), 4.02 (dd, \(J = 9.3, 2.4\) Hz, 1H), 3.85 (dd, \(J = 9.3, 5.1\) Hz, 1H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta = 154.7\) (s), 137.8 (s), 137.2 (s), 137.0 (s), 134.1 (d), 129.6 (s), 128.6 (d), 128.5 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.86 (d), 127.80 (d), 127.7 (d), 127.6 (d), 81.5 (d), 80.4 (d), 73.6 (t), 73.3 (t), 72.9 (t), 66.3 (t), 57.5 (d), 56.7 (d), 46.1 (t); HRMS (ESI): \(m/z\) calcd for C\(_{30}\)H\(_{30}\)N\(_4\)NaO\(_4\) [M+Na]\(^+\) 533.2159 found 533.2152.

\(65,7R,8R,8aS\)-7,8-Dihydroxy-6-(hydroxymethyl)-7,8a,9-tetrahydropyrrolo[1,2-a][1,2,3]triazolo[1,5-d]pyrazin-4(6H)-one 1.

![Chemical structure](image-url)

Compound 29 (250 mg, 0.49 mmol) was dissolved in dry methanol (5 mL). 10\% Pd/C (250 mg, 100\% w/w) was added. Hydrogen gas was bubbled into the reaction mixture continuously while stirring at 22 °C for 24 h. The reaction mixture was then filtered through a celite pad and solvent was concentrated under reduced pressure and the crude residue was purified by column chromatography over silica gel using a mixture of acetonitrile and ammonium hydroxide solution (10:1) as an eluent to get 1 as colourless oil (102 mg, 87\%). \(R_f\): 0.3 (acetonitrile/NH\(_4\)OH, 9:1); Specific rotation: \([\alpha]_D^{29}\)–46.1 (c 0.41, CH\(_3\)OH); IR (KBr): \(\bar{\nu} = 3338, 3198, 1661, 1403, 1205, 1112, 1075, 756, 570\) cm\(^{-1}\); \(^1\)H NMR (400 MHz, D\(_2\)O): \(\delta = 8.20\) (s, 1H), 4.99 (dd, \(J = 13.2, 5.2\) Hz, 1H), 4.72–4.66 (m, 1H), 4.53 (d, \(J = 13.2\) Hz, 1H), 4.49–4.45 (m, 2H), 4.32 (q, \(J = 4.8\) Hz, 1H), 4.07 (dd, \(J = 12.0, 4.4\) Hz, 1H), 4.03 (dd, \(J = 12.0, 4.8\) Hz, 1H); \(^{13}\)C NMR (100 MHz, D\(_2\)O): \(\delta = 156.7\) (s), 133.7 (d), 129.8 (s), 75.3 (d), 73.5 (d), 60.9 (d), 58.9 (d), 58.2 (t), 45.0 (t); HRMS (ESI): \(m/z\) calcd for C\(_9\)H\(_{12}\)N\(_4\)NaO\(_4\) [M+Na]\(^+\) 263.0751 found 263.0751.
(6S,7R,8R,8aS)-7,8-Bis(benzyloxy)-6-((benzyloxy)methyl)-3-(hydroxymethyl)-7,8,8a,9-tetrahydropyrrolo[1,2α][1,2,3]triazolo[1,5-d]pyrazin-4(6H)-one 25.

Compound 23 (430 mg, 0.74 mmol) was dissolved in dry THF (5 mL) and lithium borohydride (16 mg, 0.74 mmol) was added. The reaction mixture was stirred at 21 °C for 2 h, after which the solvent was evaporated under reduced pressure and the residue was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (1:1) as an eluent to get 25 (281 mg, 70%) as a pale yellow oil. Rf: 0.4 (hexane/ethyl acetate, 1:1); Specific rotation: [α]D^29 –26.4 (c 0.47, CHCl₃); IR (KBr): υ = 3471, 2922, 2857, 1647, 1453, 1365, 1267, 1200, 1029, 751, 698 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.37–7.22 (m, 15H), 4.92 (d, J = 6.3 Hz, 2H), 4.67 (d, J = 11.7 Hz, 2H), 4.62–4.58 (m, 2H, 1H exchangeable with D₂O), 4.53–4.41 (m, 6H), 4.39–4.33 (m, 2H), 4.24 (t, J = 6.0 Hz, 1H), 4.04 (dd, J = 9.6, 2.4 Hz, 1H), 3.85 (dd, J = 9.3, 5.4 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 156.2 (s), 150.2 (s), 137.7 (s), 137.1 (s), 136.9 (s), 128.69 (d), 128.64 (d), 128.4 (d), 128.3 (d), 128.2 (d), 127.9 (d), 127.8 (d), 127.7 (d), 127.6 (d), 126.3 (s), 81.4 (d), 80.2 (d), 73.7 (t), 73.4 (t), 72.9 (t), 66.1 (t), 57.8 (d), 57.2 (t), 57.1 (d), 46.1 (t); HRMS (ESI): m/z calcd for C₃₁H₃₂KN₄O₅ [M+K]^⁺ 579.2004 found 579.2011.

(6S,7R,8R,8aS)-7,8-Dihydroxy-3,6-bis(hydroxymethyl)-7,8,8a,9-tetrahydropyrrolo[1,2-α][1,2,3]triazolo[1,5-d]pyrazin-4(6H)-one 2.

Compound 25 (340 mg, 0.63 mmol) was dissolved in dry methanol (5 mL). 10% Pd/C (340 mg, 100% w/w) was added. Hydrogen gas was bubbled into the reaction mixture continuously while stirring at 24 °C for 24 h. The reaction mixture was then filtered through a celite pad and solvent was concentrated under reduced pressure.
and the crude residue was purified by column chromatography over silica gel using a mixture of acetonitrile and ammonium hydroxide solution (6:1) as an eluent to get 2 as colourless oil (120 mg, 70%). \( R_f \): 0.3 (acetonitrile/NH\(_4\)OH, 4:1); Specific rotation: \([\alpha]_D^{28} -14.9 \) (c 0.78, CH\(_3\)OH); IR (KBr): \( \tilde{\nu} = 3343, 2942, 1646, 1588, 1448, 1373, 1332, 1199, 1112, 1074, 1026, 751, 623 \text{ cm}^{-1} \); \( ^1\text{H NMR} \) (300 MHz, DMSO-\( d_6 \)): \( \delta \) 5.70 (d, \( J = 4.5 \) Hz, 1H exchangeable with D\(_2\)O), 5.54 (d, \( J = 4.2 \) Hz, 1H exchangeable with D\(_2\)O), 5.22 (t, \( J = 4.2 \) Hz, 1H exchangeable with D\(_2\)O), 4.86–4.82 (m, 2H, 1H exchangeable with D\(_2\)O), 4.71 (dd, \( J = 12.6, 6.0 \) Hz, 1H), 4.62 (dd, \( J = 12.6, 5.4 \) Hz, 1H), 4.47–4.30 (m, 2H), 4.17–4.10 (m, 2H), 3.99–3.95 (m, 2H), 3.77–3.70 (m, 1H); \( ^{13}\text{C NMR} \) (75 MHz, DMSO-\( d_6 \)): \( \delta \) 155.8 (s), 147.6 (s), 125.7 (s), 74.9 (d), 73.4 (d), 61.9 (d), 59.2 (d), 58.0 (t), 53.8 (t), 44.9 (t); HRMS (ESI): \( m/z \) calcld for C\(_{10}\)H\(_{14}\)N\(_4\)NaO\(_5\) [M+Na]\(^+\) 293.0856 found 293.0859.

Compound 15:

![Compound 15](image)

To a solution of compound 14 (4.2 g, 5.83 mmol) in dry dichloromethane (45 mL), Dess-Martin periodinane (4.95 g, 11.67 mmol) was added at 0 °C and the reaction mixture was stirred at room temperature for 5 h. Then the reaction mixture was diluted with dichloromethane (50 mL), washed with aqueous sodium thiosulfate solution (50 mL x 2) followed by water (50 mL). The organic layer was dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (9:1) as an eluent to get 15 (3.57 g, 85%) as a colourless oil in a diastereomeric ratio of 3:1. Data for the mixture of diastereomers: \( R_f \): 0.8 (hexane/ethyl acetate, 4:1); Specific rotation: \([\alpha]_D^{31} -18.59 \) (c 0.57, CHCl\(_3\)); IR (KBr): \( \tilde{\nu} = 3476, 3034, 2937, 2867, 1602, 1457, 1346, 1253, 1147, 1101, 837, 742, 697, 670, 564 \text{ cm}^{-1} \); \( ^1\text{H NMR} \) (300 MHz, CDCl\(_3\)) (mixture of diastereomers) \( \delta \) 7.84 (d, \( J = 6.6 \) Hz, 2H), 7.77 (d, \( J = 6.6 \) Hz, 0.5H), 7.68 (d, \( J = 7.8 \) Hz, 0.2H), 7.32–7.20 (m, 23H), 7.14 (m, 0.5H), 7.10–7.09 (m, 3H), 4.83–4.76 (m, 0.6H), 4.70–4.51 (m, 8H), 4.42–4.30 (m, 2H), 4.26–4.17 (m, 2H), 4.09–3.95 (m, 3H, 1H exchangeable with D\(_2\)O), 3.89–3.67 (m, 5H), 3.56–3.53 (m, 1H), 3.42–3.36 (m, 0.15H), 3.31–3.26 (m, 0.12H), 2.39 (s, 3H), 2.31
(s, 0.7H), 0.89 (s, 9H), 0.80 (s, 2H), 0.79 (s, 1H), 0.25 (s, 6H), (−0.05)−(−0.077) (m, 2H), (−0.086)−(−0.11) (m, 0.75H); $^{13}$C NMR (75 MHz, CDCl$_3$) (mixture of diastereomers) $\delta$

143.0 (s), 138.3 (s), 138.0 (s), 137.7 (s), 137.5 (s), 129.6 (d), 129.2 (d), 129.0 (d), 128.5 (d), 128.4 (d), 128.29 (d), 128.26 (d), 128.24 (d), 128.21 (d), 128.15 (d), 128.07 (d), 127.9 (d), 127.8 (d), 127.7 (d), 127.6 (d), 127.5 (d), 127.4 (d), 127.3 (d), 127.2 (d), 127.1 (d), 92.6 (s), 88.9 (s), 83.8 (d), 80.2 (d), 78.2 (d), 75.1 (t), 73.7 (t), 73.3 (t), 72.8 (t), 72.7 (t), 62.3 (t), 59.8 (d), 59.3 (d), 25.9 (q), 25.8 (q), 25.7 (q), 21.4 (q), 18.3 (s), −5.5 (q); HRMS (ESI): $m/z$ calcd for C$_{40}$H$_{51}$NNaO$_7$Si [M+Na]$^+$ 740.3048 found 740.3041.

1-O-(tert-Butyldimethylsilyl)-3,4,6-tri-O-benzyl-2-deoxy-2-(p-toluenesulfonamido)-L-iditol 16:

To a solution of compound 15 (3.4 g, 4.73 mmol) in dry MeOH (35 mL), CeCl$_3$.7H$_2$O (2.12 g, 5.68 mmol) was added at −78 °C and stirred for 1 h. Sodium borohydride (720 mg, 18.97 mmol) was added in portions and the reaction mixture was stirred at −78 °C for 4 h. It was brought to room temperature and the solvent was concentrated under reduced pressure. The resulting residue was dissolved in ethyl acetate (20 mL) and washed with water (20 mL). The organic layer was dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (9:1) as an eluent to get 16 (1.89 g, 56%) as an off-white solid, along with compound 14 (1.02 g, 30%) as an off white solid. Data for compound 16: M.P: 72–75 °C; $R_f$: 0.5 (hexane/ethyl acetate, 4:1); Specific rotation: $[\alpha]$_D$^{29}$+4.58 (c 1.92, CHCl$_3$); IR (KBr): $\tilde{\nu}$ = 3546, 3475, 3416, 3150, 3030, 2931, 2861, 1620, 1462, 1330, 1156, 1100, 1052, 837, 772, 745, 697 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.78 (d, $J$ = 7.5 Hz, 2H), 7.38–7.24 (m, 17H), 5.02 (d, $J$ = 7.2 Hz, 1H, exchangeable with D$_2$O), 4.87 (d, $J$ = 11.1 Hz, 1H), 4.79 (d, $J$ = 11.1 Hz, 1H), 4.60 (d, $J$ = 11.1 Hz, 1H), 4.52 (m, 2H), 4.47 (d, $J$ = 11.1 Hz, 1H), 4.24 (d, $J$ = 8.7 Hz, 1H), 3.82 (br m, 1H), 3.58 (d, $J$ = 9.0 Hz, 1H), 3.51–3.43 (m, 4H), 3.23 (dd, $J$ = 9.3 Hz, 4.2 Hz, 1H), 2.41 (s, 3H), 2.33 (br s, 1H, exchangeable with D$_2$O), 0.87 (s, 9H), 0.00 (s, 3H), −0.013 (s, 3H); $^{13}$C NMR (75 MHz,
CDCl$_3$ $\delta$ 143.3 (s), 138.3 (s), 138.2 (s), 137.98 (s), 137.96 (s), 129.6 (d), 128.38 (d), 128.30 (d), 128.2 (d), 127.84 (d), 127.80 (d), 127.7 (d), 127.6 (d), 126.9 (d), 79.0 (d), 76.9 (d), 75.5 (t), 75.0 (t), 73.3 (t), 71.8 (t), 69.3 (d), 61.9 (t), 54.9 (d), 25.7 (q), 21.4 (q), 18.0 (s), −5.5 (q), −5.6 (q); HRMS (ESI): $m/z$ calcd for C$_{40}$H$_{53}$NNaO$_7$Si $[M+Na]^+$ 742.3204 found 742.3222.

($2S,3R,4R,5R$)-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(tert-butyldimethyl silanyloxymethyl)-1-$N$-(p-tolylsulfonfyl)pyrrolidine 12.

![Chemical Structure](attachment:structure.png)

Compound 16 (3.0 g, 4.16 mmol) was dissolved in dry THF (30 mL), and the solution was cooled to 0 °C. Triphenylphosphine (2.73 g, 10.4 mmol) was added followed by dropwise addition of diethyl azodicarboxylate (1.65 mL, 10.4 mmol), after which the reaction mixture was warmed to room temperature. When TLC indicated the completion of the reaction (3 h), the reaction was stopped and solvent was evaporated under vacuum. The residue was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (10:1) as an eluent to get 12 (2.45 g, 84%) as a pale yellow oil. $R_f$: 0.8 (hexane/ethyl acetate, 4:1); Specific rotation: $[\alpha]_D^{29} = -14.9$ (c 0.53, CHCl$_3$); IR (KBr): $\tilde{\nu}$ = 3031, 2932, 2859, 1620, 1458, 1349, 1253, 1161, 1089, 838, 776, 740, 698, 666 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.62 (d, $J = 8.1$ Hz, 2H), 7.21–7.11 (m, 15H), 6.88 (d, $J = 3.6$ Hz, 2H), 4.48–4.32 (m, 4H), 4.09–4.05 (m, 3H), 3.92–3.83 (m, 2H), 3.75–3.67 (m, 4H), 3.55–3.51 (m, 1H), 2.24 (s, 3H), 0.82 (s, 9H), 0.0 (s, 3H), −0.017 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 143.5 (s), 138.3 (s), 137.8 (s), 137.6 (s), 133.7 (s), 129.4 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.9 (d), 127.67 (d), 127.61 (d), 127.5 (d), 127.4 (d), 127.3 (d), 81.7 (d), 80.8 (d), 73.2 (t), 72.8 (t), 71.2 (t), 70.7 (t), 64.6 (d), 63.7 (d), 61.4 (t), 25.9 (q), 21.4 (q), 18.2 (s), −5.3 (q), −5.4 (q); HRMS (ESI): $m/z$ calcd for C$_{40}$H$_{53}$NNaO$_6$Si $[M+Na]^+$ 724.3099 found 724.3073.
(2S,3R,4R,5R)-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(tert-butyldimethylsilanyl oxymethyl)pyrrolidine 18:

A solution of compound 12 (2.45 g, 3.49 mmol) in dry THF (25 mL) was cooled to −78 °C. A solution of sodium napthalenide {prepared separately by the addition of sodium (765 mg, 33.26 mmol) to naphthalene (4.5 g, 35.12 mmol) in dry THF} was added slowly and the reaction mixture was stirred at −78 °C for 20 minutes. The reaction mixture was brought to room temperature, quenched with aqueous sodium carbonate solution (25 mL) and extracted with ethyl acetate (25 mL). The organic layer was dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (3:1) as an eluent to get 18 (1.55 g, 81%) as a pale yellow viscous oil. Rf: 0.4 (hexane/ethyl acetate, 2:1); Specific rotation: [α]D$^29$+6.9 (c 3.8, CHCl$_3$); IR (KBr): $\tilde{\nu}$ =3436, 3030, 2929, 2859, 1640, 1457, 1363, 1253, 1097, 839, 776, 739, 698 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) δ 7.29–7.19 (m, 15H), 4.51–4.41 (m, 6H), 3.89–3.88 (m, 1H), 3.82–3.74 (m, 2H), 3.68 (dd, J = 9.6 Hz, 6.0 Hz, 1H), 3.54 (dd, J = 9.0 Hz, 5.7 Hz, 1H), 3.46 (dd, J = 9.0 Hz, 6.0 Hz, 1H), 3.34–3.23 (m, 2H), 2.08 (br s, 1H exchangeable with D$_2$O), 0.84 (s, 9H), 0.00 (s, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 138.4 (s), 138.28 (s), 138.21 (s), 128.3 (d), 128.28 (d), 128.25 (d), 127.6 (d), 127.5 (d), 127.4 (d), 85.0 (d), 82.9 (d), 73.1 (t), 71.8 (t), 71.59 (t), 71.56 (t), 63.2 (d), 62.8 (d), 61.9 (t), 25.9 (q), 18.2 (s), −5.3 (q), −5.4 (q); HRMS (ESI): m/z calcd for C$_{33}$H$_{46}$NO$_4$Si [M+H]$^+$ 548.3191 found 548.3192.

(2S,3R,4R,5R)-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(tert-butyldimethylsilanyl oxymethyl)-1-N-(tert-butoxycarbonyl)-pyrrolidine 20.

To a solution of pyrrolidine 18 (4.2 g, 7.66 mmol) in dry ethyl acetate (50 mL), sodium carbonate (2.5 g, 23.59 mmol) and Boc$_2$O (2.0 mL, 8.70 mmol) were added and...
the reaction mixture was stirred at 25 °C for 16 h. The reaction mixture was then diluted with ethyl acetate (20 mL) and washed with water (2 x 20 mL). The organic layer was dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (9:1) as an eluent to get 20 (4.1 g, 83%) as a colourless oil. The data provided is for a mixture of rotamers: $R_f$: 0.8 (hexane/ethyl acetate, 5:1); Specific rotation: $[\alpha]_{D}^{23}$–9.7 (c 0.3, CHCl$_3$); IR (KBr): $\tilde{\nu}$ = 3029, 2931, 2865, 1696, 1605, 1461, 1379, 1252, 1172, 1097, 842, 742, 699 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.27–7.21 (m, 15H), 4.63–4.47 (m, 6H), 4.18–4.06 (m, 3H), 3.85–3.60 (m, 5H), 1.41 (br s, 9H), 0.84 (s, 9H), 0.00 (s, 3H), –0.014 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 154.8 (s), 138.4 (s), 138.3 (s), 138.2 (s), 128.2 (d), 127.7 (d), 127.5 (d), 127.49 (d), 127.42 (d), 83.7 (d), 82.8 (d), 82.2 (d), 79.8 (s), 73.0 (t), 72.7 (t), 71.8 (t), 70.3 (t), 69.5 (t), 61.7 (d), 60.9 (t), 59.9 (d), 28.3 (q), 25.9 (q), 18.2 (s), –5.3 (q), –5.4 (q); HRMS (ESI): $m/z$ calcd for C$_{38}$H$_{53}$KNO$_6$Si [M+K]$^+$ 686.3274 found 686.3238.

$(2S,3R,4R,5R)$-3,4-Bis(benzyloxy)-5-(benzyloxymethyl)-2-(hydroxymethyl)-1-$N$-(tert-butoxycarbonyl)-pyrrolidine 10.

To a solution of compound 20 (4.0 g, 6.17 mmol) in dry methanol (40 mL), camphorsulfonic acid monohydrate (400 mg, 10% w/w) was added and the reaction mixture was stirred at 25 °C for 16 h. Solvent was then concentrated under reduced pressure and the residue was dissolved in ethyl acetate (40 mL). It was then washed with aqueous sodium bicarbonate solution (2 x 20 mL), dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (3:1) as an eluent to get 10 (2.7 g, 82%) as a colourless oil. The data provided is for a mixture of rotamers in a ratio of 2:1. $R_f$: 0.4 (hexane/ethyl acetate, 4:1); Specific rotation: $[\alpha]_{D}^{23}$–10.6 (c 0.7, CHCl$_3$); IR (KBr): $\tilde{\nu}$ = 3438, 3061, 3030, 2970, 2927, 2869, 1691, 1605, 1454, 1395, 1315, 1256, 1171, 1100, 1033, 914, 854, 743, 700, 606 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.30–7.23 (m, 15H), 4.66–4.41 (m, 6H), 4.31–
3.89 (m, 4H), 3.85–3.68 (m, 4H), 3.55–3.52 (m, 1H), 3.33 (br s, 0.3H exchangeable with D₂O, for –OH signal of one rotamer), 1.44 (s, 3H), 1.39 (s, 6H); ³¹C NMR (75 MHz, CDCl₃): δ 155.7 (s), 154.2 (s), 137.9 (s), 137.6 (s), 137.3 (s), 129.8 (d), 128.8 (d), 128.4 (d), 128.35 (d), 128.32 (d), 128.2 (d), 128.18 (d), 128.11 (d), 128.0 (d), 127.8 (d), 127.79 (d), 127.77 (d), 127.73 (d), 127.5 (d), 127.3 (d), 126.8 (d), 126.7 (d), 82.9 (d), 82.2 (d), 81.2 (d), 80.6 (s), 80.2 (s), 73.1 (t), 72.5 (t), 72.2 (t), 72.0 (t), 68.4 (t), 67.7 (t), 62.4 (t), 61.8 (d), 61.2 (d), 60.6 (d), 59.5 (d), 28.2 (q); HRMS (ESI): m/z calcd for C₃₂H₃₉NNaO₆ [M+Na]⁺ 556.2670 found 556.2673.

(2S,3R,4R,5R)-3,4-Bis(benzyloxy)-5-(benzyloxyethyl)-2-(azidomethyl)-1-N-(tert-butoxycarbonyl)-pyrrolidine 8.

Compound 10 (460 mg, 0.86 mmol) was dissolved in dry THF (5 mL), and the solution was cooled to 0 °C. Triphenylphosphine (452 mg, 1.72 mmol) and trimethylsilyl azide (0.28 mL, 2.15 mmol) were added followed by dropwise addition of diethyl azodicarboxylate (0.4 mL, 2.58 mmol), after which the reaction mixture was warmed to 24 °C. When TLC indicated the completion of the reaction (24 h), the reaction was stopped and solvent was evaporated under vacuum. The residue was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (10:1) as an eluent to get 8 (274 mg, 57%) as a colourless oil. The data provided is for a mixture of rotamers: Rf: 0.8 (hexane/ethyl acetate, 9:1); Specific rotation: [α]D²³–9.4 (c 0.82, CHCl₃); IR (KBr): ν = 3062, 3031, 2973, 2926, 2866, 2099, 1696, 1453, 1386, 1289, 1171, 1098, 1030, 911, 856, 741, 699 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.29–7.23 (m, 15H), 4.59–4.47 (m, 6H), 4.26–4.23 (m, 2H), 4.10–4.06 (m, 1H), 4.00 (m, 0.4H), 3.85 (m, 0.6H), 3.66–3.55 (m, 3H), 3.35 (dd, J = 11.7, 6.6 Hz, 1H), 1.44 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ 154.7 (s), 138.1 (s), 137.9 (s), 137.3 (s), 128.4 (d), 128.36 (d), 128.31 (d), 127.9 (d), 127.8 (d), 127.77 (d), 127.72 (d), 127.6 (d), 82.3 (d), 81.8 (d), 80.8 (d), 80.4 (s), 73.0 (t), 72.5 (t), 72.0 (t), 68.8 (t), 61.8 (d), 58.1 (d), 49.6 (t), 28.3 (q); HRMS (ESI): m/z calcd for C₃₂H₃₈N₄NaO₅ [M+Na]⁺ 581.2734 found 581.2734.
Diethyl-1-(((2S,3R,4R,5R)-3,4-bis(benzyloxy)-5-(benzyloxymethyl)-1-(tert-butoxycarbonyl)pyrrolidin-2-yl)methyl)-1H-1',2',3'-triazole-4',5'-dicarboxylate 22.

Compound 8 (0.52 g, 0.93 mmol) was dissolved in dry toluene (6 mL) and diethylacetylene dicarboxylate (0.75 mL, 4.67 mmol) was added. The reaction mixture was heated at 110 °C for 4 h, after which the solvent was evaporated under reduced pressure and the residue was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (4:1) as an eluent to get 22 (515 mg, 76%) as a pale yellow oil. The data provided is for a mixture of rotamers: Rf: 0.5 (hexane/ethyl acetate, 4:1); Specific rotation: [α]D23 = -52.9 (c 0.61, CHCl3); IR (KBr): υ =3063, 3030, 2979, 2930, 2873, 1730, 1555, 1471, 1454, 1391, 1272, 1208, 1171, 1100, 1015, 854, 739, 698 cm⁻¹; 1H NMR (300 MHz, CDCl3): δ 7.33–7.25 (m, 15H), 4.86–4.39 (m, 14H), 4.19–4.18 (m, 1H), 4.00 (br m, 0.5H, due to one rotamer), 3.83 (br m, 1H), 3.70–3.63 (m, 1.5H), 1.42–1.22 (m, 15H); 13C NMR (75 MHz, CDCl3): δ 160.4 (s), 158.6 (s), 154.3 (s), 153.8 (s), 140.2 (s), 139.9 (s), 138.1 (s), 137.9 (s), 137.1 (s), 130.1 (s), 129.7 (s), 128.4 (d), 128.3 (d), 128.2 (d), 127.9 (d), 127.7 (d), 127.6 (d), 127.4 (d), 82.7 (d), 81.8 (d), 81.5 (d), 80.5 (s), 73.2 (t), 72.4 (t), 72.2 (t), 69.2 (t), 68.7 (t), 62.5 (t), 61.8 (d), 61.6 (t), 61.3 (d), 57.4 (d), 57.1 (d), 50.3 (t), 49.7 (t), 28.1 (q), 27.8 (q), 14.1 (q), 13.7 (q); HRMS (ESI): m/z calcd for C40H48KN4O9 [M+K]+ 767.3053 found 767.3049.

Diethyl-1-(((2S,3R,4R,5R)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)pyrrolidin-2-yl)methyl)-1H-1',2',3'-triazole-4',5'-dicarboxylate 6.

To a solution of compound 22 (650 mg, 0.89 mmol) in dry dichloromethane (7 mL), trifluoroacetic acid (0.7 mL, 9.14 mmol) was added at 0 °C and the reaction mixture was stirred at 26 °C for 4 h. Solvent was then concentrated under reduced
pressure and the residue was dissolved in ethyl acetate (25 mL). It was then washed with aqueous sodium bicarbonate solution (2 x 20 mL), dried over anhydrous sodium sulphate and filtered. Evaporation of the solvent under vacuum gave a residue, which was passed through column chromatography over silica gel using a mixture of hexane and ethyl acetate (2:1) as an eluent to get 6 as pale yellow oil (430 mg, 77%) and proceeded without any further purification.

\((6S,7R,8R,8aR)-\text{Ethyl-7,8-bis(benzyloxy)-6-((benzyloxy)methyl)-4-oxo-4,6,7,8,8a,9-hexahydropyrrolo[1,2-a][1',2',3']triazolo[1',5'-d]pyrazine-3-carboxylate 24.}\)

\[
\begin{align*}
\text{Compound 6 (320 mg, 0.509 mmol) was dissolved in dry toluene (4 mL) and camphorsulfonic acid monohydrate (26 mg, 0.104 mmol) was added. The reaction mixture was heated at 110 °C for 9 h, after which the solvent was evaporated under reduced pressure and the residue was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (2:1) as an eluent to get 24 (240 mg, 81%) as a light brown oil.} \\
R_f: 0.6 \text{ (hexane/ethyl acetate, 1:1); Specific rotation: } [\alpha]_{D}^{23} -127.3 (c \text{ 0.15, CHCl}_3); \text{ IR (KBr): } \tilde{\nu} = 3060, 3030, 2924, 2859, 1735, 1679, 1564, 1446, 1410, 1364, 1213, 1179, 1080, 1023, 744, 700 \text{ cm}^{-1}; \text{ }^1\text{H NMR (400 MHz, CDCl}_3\text{): } \delta 7.37 - 7.26 (m, 13H), 7.15 - 7.12 (m, 2H), 4.72 (dd, } J = 13.2, 4.0 \text{ Hz, 1H), 4.67 - 4.62 (m, 2H), 4.60 - 4.54 (m, 1H), 4.51 - 4.39 (m, 7H), 4.35 (s, 1H) 4.24 (d, } J = 11.6 \text{ Hz, 1H), 4.13 (dd, } J = 9.2, 4.8 \text{ Hz, 1H), 4.05 (d, } J = 4.0 \text{ Hz, 1H), 3.45 (dd, } J = 10.4, 8.8 \text{ Hz, 1H), 1.43 (t, } J = 7.2 \text{ Hz, 3H); }^{13}\text{C NMR (100 MHz, CDCl}_3\text{): } \delta 159.7 \text{ (s), 153.6 \text{ (s), 139.4 \text{ (s), 137.9 \text{ (s), 136.9 \text{ (s),} } 136.2 \text{ (s), 129.9 \text{ (s), 128.7 \text{ (d), 128.5 \text{ (d), 128.46 \text{ (d), 128.40 \text{ (d), 128.1 \text{ (d), 127.9 \text{ (d), 127.88 \text{ (d), 127.81 \text{ (d), 127.7 \text{ (d), 79.9 \text{ (d), 78.9 \text{ (d), 73.2 \text{ (t), 71.5 \text{ (t), 71.1 \text{ (t), 66.9 \text{ (t), 61.9 \text{ (t), 61.5 \text{ (d), 59.4 \text{ (d), 46.4 \text{ (t), 14.1 \text{ (q); HRMS (ESI): }} m/z \text{ calcd for C}_{33}\text{H}_{34}\text{Na}_{4}\text{NaO}_6 \text{[M+Na]}^{+} 605.2371 \text{ found 605.2348.}}}
\end{align*}
\]
Compound 24 (220 mg, 0.378 mmol) was dissolved in dry methanol (3 mL) and potassium carbonate (157 mg, 1.13 mmol) was added. The reaction mixture was stirred at 26 °C for 6 h, after which the solvent was evaporated under reduced pressure. To the resulting milky white residue, a mixture of ethyl acetate and water (20 mL, 1:1) was added. Conc. HCl was then added to the mixture until a clear solution was obtained. The organic layer was then separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure. The residue contains 28 was dissolved in glacial acetic acid (3 mL) and heated at 120 °C for 24 h. The reaction mixture was then quenched with aqueous sodium bicarbonate solution (20 mL) and extracted with ethyl acetate (2 x 10 mL). The organic layer was then dried over anhydrous sodium sulphate and concentrated under reduced pressure. The residue was purified column chromatography over silica gel using a mixture of hexane and ethyl acetate (2:1) as an eluent to get 30 (156 mg, 80% over two steps) as a pale yellow oil. Rf: 0.6 (hexane/ethyl acetate, 1:1); Specific rotation: $[\alpha]_D^{23} = -60.4$ (c 0.22, CHCl$_3$); IR (KBr): $\tilde{\nu}$ = 3062, 3030, 2925, 2868, 1667, 1553, 1495, 1453, 1416, 1363, 1256, 1204, 1110, 1091, 1027, 983, 742, 698, 606 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.14 (s, 1H), 7.34–7.25 (m, 13H), 7.14–7.04 (m, 2H), 4.73–4.67 (m, 2H), 4.64–4.63 (m, 1H), 4.59–4.33 (m, 7H), 4.23 (d, $J$ = 12.0 Hz, 1H), 4.10–4.03 (m, 2H), 3.45–3.39 (m, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 155.5 (s), 137.8 (s), 136.9 (s), 136.3 (s), 134.2 (d), 129.9 (s), 128.6 (d), 128.5 (d), 128.3 (d), 128.0 (d), 127.9 (d), 127.8 (d), 127.7 (d), 79.8 (d), 79.0 (d), 73.1 (t), 71.4 (t), 71.0 (t), 67.0 (t), 61.1 (d), 59.7 (d), 45.7 (t); HRMS (ESI): m/z calcld for C$_{30}$H$_{31}$N$_4$O$_4$ [M+H]$^+$ 511.2340 found 511.2338.
(6S,7R,8R,8aR)-7,8-Dihydroxy-6-(hydroxymethyl)-7,8,8a,9-tetrahydropyrrolo[1,2-a][1,2,3]triazolo[1,5-d]pyrazin-4 (6H)-one 3.

Compound 30 (140 mg, 0.27 mmol) was dissolved in dry methanol (5 mL). 10% Pd/C (140 mg, 100% w/w) was added. Hydrogen gas was bubbled into the reaction mixture continuously while stirring at 26 °C for 24 h. The reaction mixture was then filtered through a celite pad and solvent was concentrated under reduced pressure and the crude residue was purified by column chromatography over silica gel using a mixture of acetonitrile and ammonium hydroxide solution (10:1) as an eluent to get 3 as colourless oil (53 mg, 80%). $R_f$: 0.3 (acetonitrile/NH$_4$OH, 9:1); Specific rotation: $[\alpha]_D^{23}$–67.2 (c 0.19, CH$_3$OH); IR (KBr): $\tilde{\nu}$ =3390, 2927, 2849, 1655, 1558, 1425, 1370, 1200, 1109, 1079, 1052, 1031, 758, 611 cm$^{-1}$; $^1$H NMR (400 MHz, D$_2$O): $\delta$ 8.21 (s, 1H), 5.04 (dd, $J = 11.2, 2.4$ Hz, 1H), 4.66–4.55 (m, 2H), 4.42 (m, 1H), 4.34 (d, $J = 3.2$ Hz, 1H), 4.13–4.10 (m, 1H), 3.98–3.91 (m, 2H); $^{13}$C NMR (100 MHz, D$_2$O): $\delta$ 157.3 (s), 133.7 (d), 129.9 (s), 77.2 (d), 74.1 (d), 66.0 (d), 60.6 (d), 58.9 (t), 45.6 (t); HRMS (ESI): $m/z$ calcld for C$_9$H$_{12}$N$_4$NaO$_4$ [M+Na]$^+$ 263.0751 found 263.0750.

(6S,7R,8R,8aR)-7,8-Bis(benzyloxy)-6-((benzyloxy)methyl)-3-(hydroxymethyl)-7,8,8a,9-tetrahydropyrrolo[1,2-a][1,2,3]triazolo[1,5-d]pyrazin-4(6H)-one 26.

Compound 24 (120 mg, 0.21 mmol) was dissolved in dry THF (2 mL) and lithium borohydride (4.5 mg, 0.21 mmol) was added. The reaction mixture was stirred at 26 °C for 2 h, after which the solvent was evaporated under reduced pressure and the residue was passed through column chromatography over silica gel using a mixture of hexane and ethyl acetate (1:1) as an eluent to get 26 (82 mg, 74%) as a pale yellow oil and the product was proceeded without further purification.
(6S,7R,8R,8aR)-7,8-Dihydroxy-3,6-bis(hydroxymethyl)-7,8,8a,9-tetrahydropyrrolo[1,2-a][1,2,3]triazolo[1,5-d]pyrazin-4(6H)-one 4.

Compound 26 (82 mg, 0.152 mmol) was dissolved in dry methanol (5 mL). 10% Pd/C (80 mg, 100% w/w) was added. Hydrogen gas was bubbled into the reaction mixture continuously while stirring at 29 °C for 24 h. The reaction mixture was then filtered through a celite pad and solvent was concentrated under reduced pressure and the crude residue was purified by column chromatography over silica gel using a mixture of acetonitrile and ammonium hydroxide solution (6:1) as an eluent to get 4 as colourless oil (35 mg, 85%). $R_f$: 0.3 (acetonitrile/NH$_4$OH, 4:1); Specific rotation: $[\alpha]_D^{23} = -21.1$ (c 0.09, CH$_3$OH); IR (KBr): $\tilde{\nu}$ = 3433, 2951, 2843, 1649, 1560, 1453, 1427, 1402, 1111, 1018, 613 cm$^{-1}$; $^1$H NMR (400 MHz, D$_2$O): $\delta$ 5.03 (dd, $J$ = 10.8, 2.0 Hz, 1H), 4.92 (d, $J$ = 13.6 Hz, 1H), 4.88 (d, $J$ = 13.2 Hz, 1H), 4.64–4.59 (m, 2H), 4.44 (m, 1H), 4.36 (d, $J$ = 2.8 Hz, 1H), 4.15–4.13 (m, 1H), 3.98–3.96 (m, 2H); $^{13}$C NMR (100 MHz, D$_2$O): $\delta$ 157.4 (s), 147.0 (s), 126.3 (s), 77.3 (d), 74.1 (d), 65.9 (d), 60.6 (d), 59.0 (t), 54.0 (t), 45.6 (t); HRMS (ESI): $m/z$ calcd for C$_{10}$H$_{14}$N$_4$NaO$_5$ [M+Na]$^+$ 293.0856 found 293.0854.
\(^1\)H–NMR spectrum of compound 17

\[^{13}\text{C}\]–NMR spectrum of compound 17
DEPT-135 spectrum of compound 17

(75 MHz, CDCl₃)
$^1$H–NMR spectrum of compound 19

(300 MHz, CDCl$_3$)
(mixture of rotamers)

$^{13}$C–NMR spectrum of compound 19

(75 MHz, CDCl$_3$)
(mixture of rotamers)
\[ ^{13}\text{C}-\text{NMR spectrum of compound } 19 \text{ (expanded)} \]

*indicates signals due to rotamers
DEPT-135 spectrum of compound 19

(75 MHz, CDCl₃)
(mixture of rotamers)
$^{1}H$–NMR spectrum of compound 9

$^{13}C$–NMR spectrum of compound 9
$^{13}$C-NMR spectrum of compound 9 (expanded)

*indicates signals due to rotamers
DEPT-135 spectrum of compound 9

(75 MHz, CDCl₃) (mixture of rotamers)
$^1$H–NMR spectrum of compound 7

(300 MHz, CDCl$_3$)

(mixture of rotamers)

$^{13}$C–NMR spectrum of compound 7

(75 MHz, CDCl$_3$)

(mixture of rotamers)
$^{13}$C-NMR spectrum of compound 7 (expanded)

*indicates signals due to rotamers
DEPT-135 spectrum of compound 7

(75 MHz, CDCl₃)
(mixture of rotamers)
$^1$H–NMR spectrum of compound 21

(300 MHz, CDCl$_3$)
(mixture of rotamers)

$^{13}$C–NMR spectrum of compound 21

(75 MHz, CDCl$_3$)
(mixture of rotamers)
$^{13}$C-NMR spectrum of compound 21 (expanded)

* indicates signals due to rotamers
DEPT-135 spectrum of compound 21

(75 MHz, CDCl₃)
(mixture of rotamers)
$^{1}H$–NMR spectrum of compound 5

(300 MHz, CDCl$_3$)

$^{13}C$–NMR spectrum of compound 5

(75 MHz, CDCl$_3$)
DEPT-135 spectrum of compound 5

![DEPT-135 spectrum of compound 5](image)
$^1$H–NMR spectrum of compound 23

$^{13}$C–NMR spectrum of compound 23
DEPT-135 spectrum of compound 23
$^{1}$H–NMR spectrum of compound 29

$^{13}$C–NMR spectrum of compound 29
DEPT-135 spectrum of compound 29

![Chemical structure and spectrum image]
$\text{H–NMR spectrum of compound 1}$

$\text{C–NMR spectrum of compound 1}$
DEPT-135 spectrum of compound 1

(100 MHz, D₂O)
$^1$H–NMR spectrum of compound 25

$^{13}$C–NMR spectrum of compound 25
DEPT-135 spectrum of compound 25

(75 MHz, CDCl₃)
$^1$H–NMR spectrum of compound 2

(300 MHz, DMSO-$d_6$)

$^{13}$C–NMR spectrum of compound 2

(75 MHz, DMSO-$d_6$)
DEPT-135 spectrum of compound 2
$^1$H–NMR spectrum of compound 15

(300MHz, CDCl$_3$) (mixture of diastereomers)

$^{13}$C–NMR spectrum of compound 15

(75MHz, CDCl$_3$) (mixture of diastereomers)
$^{13}$C-NMR spectrum of compound 15 (expanded)

*indicates signals due to diastereomers
DEPT-135 spectrum of compound 15

(75MHz, CDCl₃)

(mixture of diastereomers)
$^{1}$H–NMR spectrum of compound 16

$^{13}$C–NMR spectrum of compound 16
DEPT-135 spectrum of compound 16
$^1$H–NMR spectrum of compound 12

(300 MHz, CDCl$_3$)

$^{13}$C–NMR spectrum of compound 12

(75 MHz, CDCl$_3$)
DEPT-135 spectrum of compound 12
$^1\text{H}-\text{NMR}$ spectrum of compound 18

$^{13}\text{C}-\text{NMR}$ spectrum of compound 18
DEPT-135 spectrum of compound 18
$^1$H–NMR spectrum of compound 20

(300 MHz, CDCl$_3$) (mixture of rotamers)

$^{13}$C–NMR spectrum of compound 20

(75 MHz, CDCl$_3$) (mixture of rotamers)
\(^{13}\)C-NMR spectrum of compound 20 (expanded)

*indicates signals due to rotamers

DEPT-135 spectrum of compound 20

(mixture of rotamers)
$^1$H–NMR spectrum of compound 10

$^1$H–NMR spectrum of compound 10

$^13$C–NMR spectrum of compound 10

Current Data Parameters
NMRD vendor centered 5500 MHz
PDUCD 1

Current Data Parameters
NMRD vendor centered 5500 MHz
PDUCD 1
$^{13}$C-NMR spectrum of compound 10 (expanded)

*indicates signals due to rotamers
DEPT-135 spectrum of compound 10

(75 MHz, CDCl₃) (mixture of rotamers)
$^1$H–NMR spectrum of compound 8

(300 MHz, CDCl$_3$) (mixture of rotamers)

$^{13}$C–NMR spectrum of compound 8

(75 MHz, CDCl$_3$) (mixture of rotamers)
$^{13}$C-NMR spectrum of compound 8 (expanded)

*indicates signals due to rotamers

DEPT-135 spectrum of compound 8

(75 MHz, CDCl$_3$) (mixture of rotamers)
$^{1}H$–NMR spectrum of compound 22

$^{13}C$–NMR spectrum of compound 22
$^{13}$C-NMR spectrum of compound 22 (expanded)

*indicates signals due to rotamers
DEPT-135 spectrum of compound 22

(75 MHz, CDCl₃) (mixture of rotamers)
$^{13}$C–NMR spectrum of compound 24

Current Data Parameters
NAME  Vegeta400ALL  
EIRFQ  159  
PUSH/PUSH  1  

P1 – Acquisition Parameters
Data:  20170205  
Type:  2D  
SPECTRUM:  2DMULT
FIDRES:  50000,180
PULPROG:  600,100
TD:  400.00
TE:  0.20
T1:  0.10
T2:  1.0000
SPP1:  400.124789 MHz
MVO1:  10
P1:  0.00
PLIM:  13.0000

P1 – Processing parameters
SI:  45
SF:  400.130059 MHz
PC:  0
LP:  0
GD:  9
PC:  3.00

$^{1}$$\text{H}$–NMR spectrum of compound 24

Current Data Parameters
NAME  Vegeta400ALL  
EIRFQ  159  
PUSH/PUSH  1  

P1 – Acquisition Parameters
Data:  20170205  
Type:  2D  
SPECTRUM:  2DMULT
FIDRES:  50000,180
PULPROG:  600,100
TD:  400.00
TE:  0.20
T1:  0.10
T2:  1.0000
SPP1:  400.124789 MHz
MVO1:  10
P1:  0.00
PLIM:  13.0000

P1 – Processing parameters
SI:  45
SF:  400.130059 MHz
PC:  0
LP:  0
GD:  9
PC:  3.00

$^{13}$C–NMR spectrum of compound 24

Current Data Parameters
NAME  Vegeta400ALL  
EIRFQ  159  
PUSH/PUSH  1  

P1 – Acquisition Parameters
Data:  20170205  
Type:  2D  
SPECTRUM:  2DMULT
FIDRES:  50000,180
PULPROG:  600,100
TD:  400.00
TE:  0.20
T1:  0.10
T2:  1.0000
SPP1:  400.124789 MHz
MVO1:  10
P1:  0.00
PLIM:  13.0000

P1 – Processing parameters
SI:  45
SF:  400.130059 MHz
PC:  0
LP:  0
GD:  9
PC:  3.00

$^{13}$C–NMR spectrum of compound 24

Current Data Parameters
NAME  Vegeta400ALL  
EIRFQ  159  
PUSH/PUSH  1  

P1 – Acquisition Parameters
Data:  20170205  
Type:  2D  
SPECTRUM:  2DMULT
FIDRES:  50000,180
PULPROG:  600,100
TD:  400.00
TE:  0.20
T1:  0.10
T2:  1.0000
SPP1:  400.124789 MHz
MVO1:  10
P1:  0.00
PLIM:  13.0000

P1 – Processing parameters
SI:  45
SF:  400.130059 MHz
PC:  0
LP:  0
GD:  9
PC:  3.00
DEPT-135 spectrum of compound 24

(100 MHz, CDCl₃)
$^1$H–NMR spectrum of compound 30

$^{13}$C–NMR spectrum of compound 30
DEPT-135 spectrum of compound 30
$^{1} \text{H-NMR}$ spectrum of compound 3

$^{13} \text{C-NMR}$ spectrum of compound 3
DEPT-135 spectrum of compound 3

(100 MHz, D$_2$O)
$^1$H–NMR spectrum of compound 4

(400 MHz, D$_2$O)

$^{13}$C–NMR spectrum of compound 4

(100 MHz, D$_2$O)
DEPT-135 spectrum of compound 4

(100 MHz, D₂O)