Supporting Information

Synthesis of Divalent Carbohydrate Mimetics by Reductive Amination with Enantiopure 1,2-Oxazines as Precursors

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Typical reductive amination procedure: The amine (1.0 equiv.) was dissolved in MeOH (16 mL/mmol) and the corresponding aldehyde (1.0 equiv.) was added. After addition of MgSO₄ (2.0 equiv.) the mixture was stirred at r.t. After complete consumption of 5 (monitored by TLC), MgSO₄ was filtered off and the filtrate was cooled to 0 °C. NaBH₄ (1.1 equiv.) was added and the mixture was stirred at r.t. during the indicated time. The reaction was quenched with H₂O and extracted with CH₂Cl₂ (3 x). The combined organic phases were washed with brine, dried with Na₂SO₄ and the solvent was removed in vacuo. The crude product was purified by flash column chromatography.

(2S,3R,4S,5S)-[3-(Benzylamino)-4-hydroxy-6,6-dimethyltetrahydro-2H-pyran-2,5-diyl]-dimethanol (10)

According to GP, aminopyran 5 (70 mg, 0.34 mmol) was dissolved in MeOH (5.5 mL), and freshly distilled benzaldehyde 7 (36 mg, 35 μL, 0.34 mmol) was added followed by addition of MgSO₄ (92 mg, 0.76 mmol). The reaction mixture was stirred for 1 h. After filtration and cooling to 0 °C, NaBH₄ (14 mg, 0.37 mmol) was added. After stirring at r.t. for 2 h, the reaction was quenched with H₂O (5.5 mL) and extracted with CH₂Cl₂ (3 x 20 mL), washed with brine, dried and concentrated. The crude product was purified by flash column chromatography (silica gel, CH₂Cl₂/ MeOH, 9:1) affording 10 (65 mg, 65%) as a colorless solid.

m.p. 125–127 °C; [α]D²² = +21.8 (c = 1.04, MeOH); ¹H NMR (500 MHz, CD₃OD): δ = 1.32, 1.41 (2 s, 3 H each, CH₃), 1.63 – 1.66 (m, 1 H, 5-H), 2.73–2.75 (m, 1 H, 3-H), 3.62 (dd, J = 3.2, 11.5 Hz, 1 H, 5-CH₂), 3.70 (d, J = 5.0 Hz, 2 H, 2-CH₂), 3.78 (A part of AB system, JₐB = 13.0 Hz, 1 H, CH₂Ph), 3.87 (dd, J = 4.3, 11.5 Hz, 1 H, 5-CH₂), 3.93 (B part of AB system, JₐB = 13.0 Hz, 1 H, CH₂Ph), 4.03 (t, J = 3.9 Hz, 1 H, 4-H), 4.05 (dt, J = 2.9, 5.0 Hz, 1 H, 2-H), 7.24–7.38 (m, 5 H, Ph) ppm; ¹³C NMR (125 MHz, CD₃OD): δ = 27.2, 28.3 (2 q, CH₃), 49.4 (d, C-5), 52.8 (t, CH₂Ph), 60.8 (d, C-3), 63.6 (t, 5-CH₂), 64.4 (t, 2-CH₂), 69.4 (d, C-2), 72.9 (d, C-4), 75.6 (s, C-6), 128.4, 129.6* (2 d, Ph), 140.2 (s, Ph) ppm. *signal with high intensity; IR (ATR): 3510-3195 (O-H, N-H), 2915 (C-H), 1460 (C=C), 1210 (C-O), 1090 (C-O-C) cm⁻¹; HRMS (ESI-TOF): m/z calcd. for C₁₆H₂₆NO₄ [M + H]⁺: 296.1856; found: 296.1863;
Elemental analysis calcd. (%) C_{16}H_{25}NO_{4} (295.4): C 65.06, H 8.53, N 4.74; found: C 65.09, H 8.42, N 4.85.

\((2S,3R,4S,5S)-[3-(4-Bromobenzylamino)-4-hydroxy-6,6-dimethyltetrahydro-2H-pyran-2,5-diyl]dimethanol \) \((11)\)

According to GP, aminopyran \(5\) (100 mg, 0.48 mmol) was dissolved in MeOH (7.9 mL), and 4-bromobenzaldehyde \(8\) (90 mg, 0.48 mmol) was added followed by MgSO\(_4\) (132 mg, 1.01 mmol). The reaction mixture was stirred for 1 h. After filtration and cooling to 0 °C, NaBH\(_4\) (23.9 mg, 0.63 mmol) was added. After stirring at r.t. for 2 h, the reaction was quenched with water (10 mL) and extracted with CH\(_2\)Cl\(_2\) (3x 20 mL), washed with brine, dried and concentrated. The crude product was purified by flash column chromatography (silica gel, CH\(_2\)Cl\(_2\)/MeOH, 9:1) affording \(11\) (128 mg, 71%) as a colorless solid.

m.p. 137–139 °C; \([\alpha]^{22}_D = +15.9 \) (c = 1.70, MeOH); \(^1\)H NMR (500 MHz, CD\(_3\)OD): \(\delta = 1.31, 1.40 \) (2 s, 3 H each, CH\(_3\)), 1.63–1.66 (m, 1 H, 5-H), 2.66–2.69 (m, 1 H, 3-H), 3.59–3.64 (m, 1 H, 5-CH\(_2\)), 3.69 (d, \(J = 5.1\) Hz, 2 H, 2-CH\(_2\)), 3.75 (A part of AB system, \(J_{AB} = 13.3\) Hz, 1 H, CH\(_2\)Ar), 3.83–3.89 (m, 2 H, 5-CH\(_2\), CH\(_2\)Ar), 3.99 (t, \(J = 4.0\) Hz, 1 H, 4-H), 4.04 (dt, \(J = 3.0, 5.1\) Hz, 1 H, 2-H), 7.26–7.32, 7.44–7.50 (2 m, 2 H each, Ar) ppm; \(^{13}\)C NMR (125 MHz, CD\(_3\)OD): \(\delta = 27.1, 28.2 \) (2 q, CH\(_3\)), 49.5 (d, C-5), 52.0 (t, CH\(_2\)Ar), 60.7 (d, C-3), 63.6 (t, 5-CH\(_2\)), 64.3 (t, 2-CH\(_2\)), 69.6 (d, C-2), 73.1 (d, C-4), 75.6 (s, C-6), 122.0 (s, Ar), 131.5, 132.6 (2 d, Ar), 139.9 (s, Ar) ppm; IR (ATR): 3485–3235 (O-H, N-H), 2970 (C-H), 1490 (C=C), 1160 (C-O), 1095 (C-O-C) cm\(^{-1}\); HRMS (ESI-TOF): m/z calcd. for C\(_{16}\)H\(_{24}\)BrNO\(_4\) [M + H]: 374.0961; found: 374.0965; calcd. for C\(_{16}\)H\(_{24}\)BrNaNO\(_4\) [M + Na]: 396.0781 found: 396.0779; Elemental analysis calcd. (%) for C\(_{16}\)H\(_{24}\)BrNO\(_4\) (374.3): C 51.35, H 6.46, N 3.74; found C 51.76, H 6.47, N 3.75.
(2S,3R,4S,5S)-[4-Hydroxy-6,6-dimethyl-3-(piperidin-1-yl)tetrahydro-2H-pyran-2,5-diyl]-dimethanol (13)

According to GP, aminopyran 5 (200 mg, 0.97 mmol) was dissolved in MeOH (8 mL) and 1,5-pentanediol (12) (25% in water, 0.175 mL, 0.443 mmol) was added followed by addition of MgSO\(_4\) (680 mg, 8.31 mmol). The reaction mixture was stirred overnight. After filtration and cooling to 0 °C, NaBH\(_4\) (89 mg, 2.37 mmol) was added. After stirring at r.t. for 3 h, the reaction was quenched with H\(_2\)O (10 mL), extracted with CH\(_2\)Cl\(_2\) (5 x 10 mL), washed with brine, dried and concentrated. The crude product was purified by flash column chromatography (silica gel, CH\(_2\)Cl\(_2\), CH\(_2\)Cl\(_2\)/MeOH 20:1, 10:1 to 4:1) affording the reductive amination product 13 (32 mg, 26 %) as a colorless solid.

Melting range: 91–95 °C; \([\alpha]^{22}_D = +10.7\ (c = 0.93, \text{MeOH})\); \(^1\)H NMR (500 MHz, CD\(_3\)OD): \(\delta = 1.10, 1.25\ (2\ s, 3\ H\ each, \text{CH}_3), 1.44–1.50\ (m, 2\ H, 3’-H), 1.51–1.57\ (m, 4\ H, 2’-H), 1.81\ (td, J = 6.1, 11.9 Hz, 1 H, 5-H), 2.59–2.66\ (m, 2\ H, 1’-H), 2.71\ (t, J = 6.7 Hz, 1 H, 3-H), 2.92\ (m, 2\ H, 1’-H), 3.56–3.70\ (m, 3\ H, 2-CH\(_2\), 5-CH\(_2\)), 3.84\ (dd, J = 6.1, 11.2 Hz, 1 H, 5-CH\(_2\)), 3.95–4.01\ (m, 1 H, 2-H), 4.15\ (dd, J = 6.7, 11.9 Hz, 1 H, 4-H) ppm; \(^{13}\)C NMR (125 MHz, CD\(_3\)OD): \(\delta = 22.2\ (q, \text{CH}_3), 24.4\ (t, \text{C-3’}), 25.5\ (q, \text{CH}_3), 26.6\ (t, \text{C-2’}), 49.0\ (d, \text{C-5}), 52.4\ (t, \text{C-1’}), 61.7\ (t, 5-CH\(_2\)), 62.5\ (t, 2-CH\(_2\)), 66.4\ (d, \text{C-4}), 71.2\ (d, \text{C-2}), 71.6\ (d, \text{C-3}), 75.1\ (s, \text{C-6})\) ppm.

HRMS (ESI-TOF): m/z calcd. for C\(_{14}\)H\(_{28}\)NO\(_4\) [M + H]\(^+\): 274.2018; found: 274.2032.

Divalent amine 18

According to GP, aminopyran 5 (200 mg, 0.97 mmol) was dissolved in MeOH (17 mL), and isophthalaldehyde 14 (60 mg, 0.44 mmol) was added followed by MgSO\(_4\) (285 mg, 2.37 mmol). The reaction mixture was stirred for 21 h. After filtration and cooling to 0 °C, NaBH\(_4\) (42 mg, 1.11 mmol) was added. After stirring at r.t. for 6.5 h, the reaction was quenched with
H₂O (20 mL) and extracted with CH₂Cl₂ (3 x 20 mL), washed with brine, dried and concentrated. The crude product was purified by flash column chromatography (silica gel, CH₂Cl₂/MeOH 6:1 to 4:1) affording 18 (62 mg, 28%) as a colorless solid.

m.p. 154 °C; [α]D²² = +39.2 (c = 0.52, MeOH); ¹H NMR (500 MHz, CD₃OD): δ = 1.33, 1.42 (2 s, 6 H each, CH₃), 1.64–1.67 (m, 2 H, 5-H), 2.76 (t, J = 3.2 Hz, 2 H, 3-H), 3.63 (dd, J = 3.0, 11.4 Hz, 2 H, 5-CH₂), 3.70 (d, J = 4.8 Hz, 4 H, 2-CH₂), 3.83 (A part of AB system, J₀₂₂ = 13.0 Hz, 2 H, CH₂Ar), 3.89 (dd, J = 4.3, 11.4 Hz, 2 H, 5-CH₂), 3.98 (B part of AB system, J₀₂₂ = 13.0 Hz, 2 H, CH₂Ar), 4.05–4.07 (m, 4 H, 2-H, 4-H), 7.27–7.37 (m, 4 H, Ar) ppm; ¹³C NMR (125 MHz, CD₃OD): δ = 27.2, 28.2 (2 q, CH₃), 49.3 (d, C-5), 52.4 (t, CH₂Ar), 60.7 (d, C-3), 63.5 (t, 5-CH₂), 64.5 (t, 2-CH₂), 68.9 (d, C-2), 72.6 (d, C-4), 75.7 (s, C-6), 127.3, 128.3, 129.7 (3 d, Ar), 139.4 (s, Ar) ppm; IR (ATR): 3350 (O-H, N-H), 2975–2840 (C-H), 1475 (C=C), 1160 (C-O), 1095 (C-O-C) cm⁻¹; HRMS (ESI-TOF): m/z calcd. for C₂₆H₄₅N₂O₈ [M + H]⁺: 513.3170; found: 513.3211; Elemental analysis calcd. (%) for C₂₆H₄₄N₂O₈ (512.6): C 60.92, H 8.65, N 5.46; found: C 60.94, H 8.69, N 5.41.

Divalent amine 19

According to GP, aminopyran 5 (100 mg, 0.48 mmol) was dissolved in MeOH (8.5 mL), and terephthalaldehyde 15 (32 mg, 0.24 mmol) was added followed by MgSO₄ (143 mg, 1.19 mmol). The reaction mixture was stirred for 24 h. After filtration and cooling to 0 °C, NaBH₄ (20 mg, 0.52 mmol) was added. After stirring at r.t. for 3 h, the reaction was quenched with H₂O (10 mL) and extracted with CH₂Cl₂ (3 x 10 mL), washed with brine, dried and concentrated. The crude product was purified by flash column chromatography (silica gel, CH₂Cl₂/MeOH 6:1 to 4:1) affording 19 (60 mg, 50%) as a colorless solid.

Melting range: 143–146 °C; [α]D²² = +22.5 (c = 1.32, MeOH); ¹H NMR (500 MHz, CD₃OD): δ = 1.32, 1.41 (2 s, 6 H each, CH₃), 1.64 (m, 2 H, 5-H), 2.70–2.72 (m, 2 H, 3-H), 3.61 (dd, J = 3.1, 11.5 Hz, 2 H, 5-CH₂), 3.66, 3.69 (AB part of ABX system, J₀₂₂ = 11.7 Hz, Jₐₓₓ = J₉ₓₓ = 5.1 Hz, 2 H each, 2-CH₂), 3.76 (A part of AB system, J₀₂₂ = 13.0 Hz, 2 H, CH₂Ar), 3.86 (dd, J = 4.5, 11.5 Hz, 2 H, 5-CH₂), 3.90 (B part of AB system, J₀₂₂ = 13.0 Hz, 2 H, CH₂Ar), 4.00 (t, 5\...
\[ J = 3.9 \text{ Hz}, 2 \text{ H}, 4\text{-H}, \] 4.04 (dt, \( J = 2.9, 5.1 \text{ Hz}, 2 \text{ H}, 2\text{-H}, \) 7.39 (s, 4 H, Ar) ppm; \) \[ ^{13}C\text{ NMR (125 MHz, CD}_{3}\text{OD): } \delta = 27.2, 28.3 (2 \text{ q, CH}_{3}), 49.4 (\text{ d, C-5}), 52.5 (\text{ t, CH}_{2}\text{Ar}), 60.7 (\text{ d, C-3}), 63.6 (\text{ t, 5-CH}_{2}), 64.3 (\text{ t, 2-CH}_{2}), 69.5 (\text{ d, C-2}), 73.0 (\text{ d, C-4}), 75.7 (\text{ s, C-6}), 129.8 (\text{ d, Ar}), 139.6 (\text{ s, Ar}) \text{ ppm; IR (ATR): } 3350 (\text{ O-H, N-H}), 2980-2830 (\text{ C-H}), 1470 (\text{ C=C}), 1215 (\text{ C-O}), 1090 (\text{ C-O-C}) \text{ cm}^{-1}; \) HRMS (ESI-TOF): m/z calcd. For \( \text{C}_{26}\text{H}_{44}\text{N}_{2}\text{NaO}_{8} \) [M + Na]\(^{+}\): 535.2990; found: 535.3017.

**Divalent amine 20**

According to **GP**, aminopyran 5 (200 mg, 0.97 mmol) was dissolved in MeOH (17 mL), and 4,4'-biphenyldicarbaldehyde 16 (97 mg, 0.46 mmol) was added followed by MgSO\(_4\) (285 mg, 2.37 mmol). The reaction mixture was stirred for 2.5 h. After filtration and cooling to 0 °C, NaBH\(_4\) (38 mg, 1.01 mmol) was added. After stirring at r.t. for 2 h, the reaction was quenched with H\(_2\)O (20 mL) and extracted with CH\(_2\)Cl\(_2\) (3 x 20 mL), washed with brine, dried and concentrated. The crude product was purified by flash column chromatography (silica gel, CH\(_2\)Cl\(_2\)/MeOH 9:1 to 4:1) affording 20 (103 mg, 40%) as a colorless solid.

m.p. 118–120 °C; [\( \alpha \)]\(_{D}^{22}\) = +28.8 (c = 0.69, MeOH); \(^{1}H\text{ NMR (700 MHz, CD}_{3}\text{OD): } \delta = 1.33, 1.42 (2 \text{ s, 6 H each, CH}_{3}), 1.67 (\text{ q, J \approx 3.9 Hz, 2 H, 5-H}), 2.83–2.85 (\text{ m, 2 H, 3-H}), 3.65 (\text{ dd, J = 3.1, 11.4 Hz, 2 H, 5-CH}_{2}), 3.74 (\text{ d, J = 4.8 Hz, 4 H, 2-CH}_{2}), 3.90–3.92 (\text{ m, 4 H, CH}_{2}\text{Ar, 5-CH}_{2}), 4.03 (\text{ B part of AB system, J}_{AB} = 13.1 \text{ Hz, 2 H, CH}_{2}\text{Ar}), 4.06–4.09 (\text{ m, 4 H, 4-H, 2-H}), 7.45–7.47, 7.60–7.63 (2 \text{ m, 4 H each, Ar}) \text{ ppm; } ^{13}C\text{ NMR (175 MHz, CD}_{3}\text{OD): } \delta = 27.2, 28.2 (2 \text{ q, CH}_{3}), 49.9 (\text{ d, C-5}), 52.1 (\text{ t, CH}_{2}\text{Ar}), 60.8 (\text{ d, C-3}), 63.5 (\text{ t, 5-CH}_{2}), 64.6 (\text{ t, 2-CH}_{2}), 68.9 (\text{ d, C-2}), 72.6 (\text{ d, C-4}), 75.8 (\text{ s, C-6}), 128.2, 130.3 (2 \text{ d, Ar}), 138.5, 141.4 (2 \text{ s, Ar}) \text{ ppm; IR (ATR): } 3360–3290 (\text{ O-H, N-H}), 2970–2880 (\text{ C-H}), 1470 (\text{ C=C}), 1230 (\text{ C-O}), 1090 (\text{ C-O-C}) \text{ cm}^{-1}; \text{ HRMS (ESI-TOF): } m/z \text{ calcd. for } \text{C}_{32}\text{H}_{49}\text{N}_{2}\text{O}_{8} \) [M + H]\(^{+}\): 589.3463 found: 589.3478; calcd. for \( \text{C}_{32}\text{H}_{48}\text{N}_{2}\text{NaO}_{8} \) [M + Na]\(^{+}\): 611.3303; found: 611.3294; Elemental analysis calcd. (%) for \( \text{C}_{32}\text{H}_{48}\text{N}_{2}\text{O}_{8} (588.7): C 65.28, H 8.22, N 4.76; \) found: C 64.63, H 8.04, N 4.76.
Divalent amine 23

According to G P, serinol 22 (200 mg, 2.20 mmol) was dissolved in MeOH (34 mL), and isophthalaldehyde 14 (134 mg, 1.00 mmol) was added followed by MgSO₄ (645 mg, 5.36 mmol). The reaction mixture was stirred for 21 h. After filtration and cooling to 0 °C, NaBH₄ (83.2 mg, 2.20 mmol) was added. After stirring at r.t. for 3 h, the reaction mixture was quenched with H₂O (20 mL) and extracted with CH₂Cl₂ (3 x 40 mL), washed with brine, dried and concentrated. The crude product was purified by flash column chromatography (silica gel, CH₂Cl₂/MeOH, 9:1) affording 23 (72 mg, 25%) as a colorless oil.

¹H NMR (500 MHz, CD₃OD): δ = 2.76 (quint., J ≈ 5.6 Hz, 2 H, 1-H), 3.56, 3.64 (AB part of ABX system, J⁴ = 11.1 Hz, J⁴ = 5.5 Hz, J⁴ = 5.8 Hz, 4 H each, 2-H), 3.86 (s, 4 H, CH₂Ar), 7.25–7.33 (m, 3 H, Ar), 7.39 (s, 1 H, Ar) ppm; ¹³C NMR (125 MHz, CD₃OD): δ = 52.1 (t, CH₂Ar), 61.2 (d, C-1), 62.4 (t, C-2), 128.4, 129.6, 129.7 (3 d, Ar), 141.1 (s, Ar) ppm; IR (ATR): 3325 (O-H, N-H), 2955–2855 (C-H), 1465 (C=C), 1155 (C-O) cm⁻¹; HRMS (ESI-TOF): m/z calcd. for C₁₄H₂₅N₂O₄ [M + H]⁺: 285.1809; found: 285.1801; calcd. for C₁₄H₂₄N₂NaO₄ [M + Na]⁺: 307.1628; found: 307.1618; Elemental analysis calcd. (%) for C₁₄H₂₄N₂O₄ (284.3): C 59.13, H 8.51, N 9.85; found: C 59.19, H 8.76, N 9.79.

Divalent amine 24

According to G P, serinol 22 (200 mg, 2.20 mmol) was dissolved in MeOH (38 mL), and biphenyl-4,4′-dicarbaldehyde 16 (220 mg, 1.04 mmol) was added followed by MgSO₄ (645 mg, 5.36 mmol). The reaction mixture was stirred for 3 h. After filtration and cooling to 0 °C, NaBH₄ (89 mg, 2.35 mmol) was added. After stirring at r.t. for 2 h, the reaction was quenched with H₂O (20 mL) and extracted with CH₂Cl₂ (3 x 40 mL), washed with brine, dried and concentrated. The crude product was purified by flash column chromatography (silica gel, CH₂Cl₂/MeOH, 9:1) affording 24 (123 mg, 33%) as a colorless oil.
$^1$H NMR (500 MHz, DMF-d$_7$): $\delta = 2.69$–2.78 (m, 2 H, 1-H), 3.55, 3.62 (AB part of ABX system, $J_{AB} = 10.7$ Hz, $J_{AX} = J_{BX} = 5.5$ Hz, 4 H each, 2-H), 3.90 (s, 4 H, CH$_2$Ar), 4.49 (bs, 4 H, OH), 7.49, 7.66 (2 d, $J = 8.0$ Hz, 4 H each, Ar) ppm; $^{13}$C NMR (125 MHz, DMF-d$_7$): $\delta = 51.2$ (t, CH$_2$Ar), 61.2 (d, C-1), 62.0 (t, C-2), 126.7, 128.8 (2 d, Ar), 139.2, 141.0 (2 s, Ar) ppm; IR (ATR): 3365–3280 (O-H, N-H), 2970-2850 (C-H), 1450 (C=C), 1120 (C-O) cm$^{-1}$; HRMS (ESI-TOF): m/z calcd. for C$_{20}$H$_{29}$N$_2$O$_4$ [M + H]$^+$: 361.2122; found: 361.2135 Elemental analysis calcd. (%) for C$_{20}$H$_{28}$N$_2$O$_4$ (360.4): C 66.64, H 7.83, N 7.77; found: C 66.57, H 7.79, N 7.77.
$^1$H NMR (500 MHz, CD$_3$OD):

$^{13}$C NMR (125 MHz, CD$_3$OD):
$^1$H NMR (500 MHz, CD$_3$OD):

$^{13}$C NMR (125 MHz, CD$_3$OD):
$^1$H NMR (500 MHz, CD$_3$OD):

11

$^{13}$C NMR (125 MHz, CD$_3$OD):

11
$^1$H NMR (500 MHz, CD$_2$OD):

$^{13}$C NMR (125 MHz, CD$_2$OD):
$^1$H NMR (500 MHz, CD$_3$OD):

$^{13}$C NMR (125 MHz, CD$_3$OD):
$^1$H NMR (700 MHz, CD$_3$OD):

$^{13}$C NMR (175 MHz, CD$_3$OD):
$^1$H NMR (500 MHz, DMF-d$_7$):

$^{13}$C NMR (125 MHz, DMF-d$_7$):