Supporting Information

for

One-pot nucleophilic substitution–double click reactions of biazides leading to functionalized bis(1,2,3-triazole) derivatives

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Experimental procedures, spectroscopic and analytical characterization data of new compounds as well as copies of the NMR spectra
# Tables of contents

1. General information .......................................................... S2
2. Synthesis and characterization of compounds ..................... S3
3. References ................................................................. S13
4. Copies of $^1$H NMR and $^{13}$C NMR spectra ....................... S14
1. General information

Reactions were performed under argon in flame-dried flasks, if not stated otherwise. Liquid components were added by syringe. Tetrahydrofuran and dichloromethane were obtained from a solvent purification system MB-SPS-800 (M. Braun). Methanol was purchased in p. a. quality and stored under argon over molecular sieves (4 Å). Products were purified by flash chromatography on aluminum oxide. Unless otherwise stated, yields refer to analytically pure samples. $^1$H NMR [CHCl$_3$ ($\delta = 7.26$ ppm), TMS ($\delta = 0.00$ ppm), or CD$_3$OD ($\delta = 3.31$ ppm) as internal standards] and $^{13}$C NMR spectra [CDCl$_3$ ($\delta = 77.0$ ppm), or CD$_3$OD ($\delta = 49.0$ ppm) as internal standards] were recorded on Bruker AC 500, or Joel Eclipse 500 instruments in CDCl$_3$ or CD$_3$OD solution. Integrals are in accordance with assignments; coupling constants are given in Hz. IR spectra were measured with an FT-IR spectrometer Nicolet 5 SXC or with a Nexus FT-IR equipped with a Nicolet Smart Dura Sample IR ATR. HRMS analyses were performed on an Agilent ESI-TOF 6210 (4 $\mu$L/min, 1 bar, 4000 V) instrument. The elemental analyses were recorded with “Elemental-Analyzers“ (Perkin–Elmer or Carlo Erba). Melting points were measured with a Reichert apparatus (Thermovar) and are uncorrected. Optical rotations ($[\alpha]_D$) were determined with Perkin–Elmer 241 polarimeter at the temperatures given. Commercially available chemicals were used without further purification unless otherwise stated.
1-Benzyl-4-([2-(trimethylsilyl)ethoxy]methyl)-1H-1,2,3-triazole (3): A mixture of benzyl azide (1) [1] (67 mg, 0.50 mmol), alkyne 2 [2] (78 mg, 1.00 mmol), CuI (19 mg, 0.10 mmol), and triethylamine (1.45 g, 1.43 mmol) was under air atmosphere at room temperature for 16 h. Ethyl acetate (20 mL) was added, the reaction mixture was washed with aqueous ammonia solution (25%, 2 × 10 mL) and dried (Na₂SO₄). After filtration and evaporation, the residue was purified by column chromatography (aluminum oxide, hexanes/ethyl acetate, 3:1) to provide 3 (114 mg, 79%) as colorless liquid.

3,3'-Dibenzyl-5,5'-bis-([2-(trimethylsilyl)ethoxy]methyl)-3H,3'H-4,4'-bi(1,2,3-triazole) (4): A mixture of benzyl azide (1) (196 mg, 1.47 mmol), 2 (160 mg, 1.02 mmol), CuI (383 mg, 2.01 mmol), and N(iPr)₂Et (370 mg, 2.86 mmol) in acetonitrile (2 mL) was stirred at 40 °C for 19 h. Ethyl acetate (50 mL) was added, the reaction mixture was twice washed with aqueous ammonia solution (25%, 2 × 10 mL) and dried (Na₂SO₄). After filtration and evaporation, the residue was purified by column chromatography (aluminum oxide, hexanes/ethyl acetate, 3:1) to give 4 (49 mg, 17%) as colorless liquid.
C₃₀H₄₄N₆NaO₂Si₂: 599.2962; found: 599.2957; calcd for m/z [M + K]^+ C₃₀H₄₄N₆KO₂Si₂: 615.2701; found: 615.2693; Anal. calcd for C₃₀H₄₄N₆O₂Si₂ (576.9): C, 62.46; H, 7.69; N, 14.57; found: C, 61.85; H, 7.50; N, 13.98.

**One-pot synthesis of 1-benzyl-4-[(2-trimethylsilyl)ethoxy]methyl]-1H-1,2,3-triazole (3):** A mixture of sodium azide (41 mg, 0.63 mmol), benzyl bromide (5) (89 mg, 0.52 mmol), alkyne 2 (76 mg, 0.57 mmol), CuSO₄·5H₂O (13 mg, 0.052 mmol), sodium ascorbate (21 mg, 0.11 mmol), l-proline (12 mg, 0.10 mmol), and Na₂CO₃ (12 mg, 0.11 mmol) in DMF/H₂O (9:1, 1 mL) was stirred at 60 °C for 16 h. Ethyl acetate (50 mL) was added, the reaction mixture was washed with aqueous ammonia solution (25%, 2 × 10 mL) and dried (Na₂SO₄). After filtration and evaporation, the residue was purified by column chromatography (aluminum oxide, hexanes/ethyl acetate, 3:1) to give 3 (124 mg, 82%) as colorless liquid.

(1S,5R,8S)-2-Benzyl-8-[(1-benzyl-1H-1,2,3-triazol-4-yl)methoxy]methyl]-6,6-dimethyl-3,7-dioxo-2-azabicyclo[3.3.1]nonan-9-one (7): A mixture of benzyl bromide (5) (18 mg, 0.11 mmol), alkyne 6 (3) (35 mg, 0.11 mmol), sodium azide (8 mg, 0.12 mmol), CuSO₄·5H₂O (2 mg, 0.008 mmol), sodium ascorbate (4 mg, 0.02 mmol), l-proline (3 mg, 0.026 mmol), and Na₂CO₃ (2 mg, 0.019 mmol) was stirred at 60 °C in DMF/H₂O (9:1, 1.0 mL) for 18 h. Ethyl acetate (50 mL) was added, the reaction mixture was washed with aqueous ammonia solution (25%, 2 × 10 mL) and dried (Na₂SO₄). After filtration and evaporation, the residue was purified by column chromatography (aluminum oxide, hexanes/ethyl acetate, 3:1) to give 7 (31 mg, 61%) as colorless liquid.

[α]₀²² = 57.2 (c = 0.7, MeOH); 'H NMR (CDCl₃, 500 MHz): δ = 1.16, 1.37 (2 s, 3 H each), 2.29 (s, 1 H), 3.17 (s, 1 H), 3.70–3.77, 3.83–3.90 (2 m, 1 H, 2 H), 4.02–4.07 (m, 1 H), 4.10 (d, J = 13.5 Hz, 1 H), 4.42–4.50 (m, 2 H), 4.54, 4.61 (AB system, Jₐb = 12.0 Hz, 2 H), 5.41 (s, 2 H), 7.17 (t, J = 7.0 Hz, 1 H), 7.20–7.30, 7.32–7.38 (m, 7 H, 3 H); 'C NMR (CDCl₃, 125 MHz): δ = 23.7, 26.7, 54.0, 57.9, 59.6, 64.9, 69.1, 69.2, 69.7, 74.0, 78.3, 122.2, 127.4, 128.0, 128.3, 128.68, 128.73, 129.0, 134.4, 136.1, 145.2; IR (ATR): v = 3065, 3030, 2930, 2870, 1725, 1495, 1455; HRMS (ESI-TOF): calcd for m/z [M + H]^+ C₂₆H₃₁N₄O₄: 463.2345; found: 463.2362; calcd for m/z [M + Na]^+ C₂₆H₃₀N₄NaO₄: 485.2165; found: 485.2185; calcd for m/z [M + K]^+ C₂₆H₃₀N₄KO₄: 501.1904; found: 501.1926.

1,3-Bis[[4-[(2-trimethylsilyl)ethoxy]methyl]-1H-1,2,3-triazol-1-yl]methyl]benzene (9) and 1-[3-azidomethyl]benzyl]-4-[(2-trimethylsilyl)ethoxy]methyl]-1H-1,2,3-triazole (10): A mixture of 1,3-bis(bromomethyl)benzene (8) (132 mg, 0.50 mmol), alkyne 2 (189 mg, 1.21
mmol), sodium azide (79 mg, 1.22 mmol), CuSO₄·5H₂O (25 mg, 0.10 mmol), sodium ascorbate (40 mg, 0.20 mmol), L-proline (23 mg, 0.20 mmol), and Na₂CO₃ (21 mg, 0.20 mmol) in DMF/H₂O (9:1, 0.5 mL) was stirred at 60 °C for 18 h. Ethyl acetate (50 mL) was added, the reaction mixture was washed with aqueous ammonia solution (25%, 2 × 10 mL) and dried (Na₂SO₄). After filtration and evaporation, the residue was purified by column chromatography (aluminum oxide, hexanes/ethyl acetate, 3:1) to give 9 (209 mg, 84%) and 10 (10 mg, 6%) as colorless liquids.

1H NMR (CDCl₃, 500 MHz): δ = –0.12 (s, 18 H), 0.84 (m, 4 H), 3.49 (m, 4 H), 4.46 (s, 4 H), 5.38 (s, 4 H), 7.10 (d, J = 8.0 Hz, 2 H), 7.11 (s, 1 H), 7.22 (t, J = 8.0 Hz, 1 H), 7.42 (s, 2 H); 13C NMR (CDCl₃, 125 MHz): δ = –1.5, 18.2, 53.8, 54.3, 63.8, 68.0, 122.2, 127.6, 127.9, 128.4, 129.6, 135.3, 136.5, 146.1; IR (ATR): υ = 3135, 2950, 2855, 2095, 1450 cm⁻¹; HRMS (ESI-TOF): calcd for m/z [M + H]+ C₂₄H₄₁N₆O₂Si₂: 501.2830; found: 501.2827; calcd for m/z [M + Na]+ C₂₄H₄₀N₆NaO₂Si₂: 523.2649; found: 523.2648; calcd for m/z [M + K]+ C₂₄H₄₀N₆KO₂Si₂: 539.2388; found: 539.2384.

1H NMR (CDCl₃, 500 MHz): δ = –0.03 (s, 9 H), 0.93 (m, 2 H), 3.57 (m, 2 H), 4.33 (s, 2 H), 4.57 (s, 2 H), 5.52 (s, 2 H), 7.19–7.25 (m, 2 H), 7.29 (d, J = 8.0 Hz, 1 H), 7.38 (t, J = 8.0 Hz, 1 H), 7.45 (s, 1 H); 13C NMR (CDCl₃, 125 MHz): δ = –1.5, 18.2, 53.8, 54.3, 63.8, 68.0, 122.2, 127.6, 127.9, 128.4, 129.6, 135.3, 136.5, 146.1; IR (ATR): υ = 3135, 2950, 2855, 2095, 1450 cm⁻¹; HRMS (ESI-TOF): calcd for m/z [M + H]+ C₁₆H₂₅N₆OsSi: 345.1859; found: 345.1862; calcd for m/z [M + Na]+ C₁₆H₂₄N₆NaOsSi: 367.1679; found: 367.1679; calcd for m/z [M + K]+ C₁₆H₂₄N₆KOsSi: 383.1418; found: 383.1419; Anal. calcd for C₁₆H₂₄N₆Os (344.5): C, 55.78; H, 7.02; N, 24.40; found: C, 56.30; H, 7.12; N, 22.06.

1,2-Bis([(4-(2-trimethylsilyl)ethoxy)methyl]-1H-1,2,3-triazol-1-yl)methyl)benzene (12) and 1-[2-(azidomethyl)benzyl]-4-[(2-(trimethylsilyl)ethoxy)methyl]-1H-1,2,3-triazole (13): A mixture of 1,2-bis(bromomethyl)benzene (11) (134 mg, 0.51 mmol), alkyne 2 (187 mg, 1.20
mmol), sodium azide (78 mg, 1.20 mmol), CuSO₄·5H₂O (25 mg, 0.10 mmol), sodium ascorbate (40 mg, 0.20 mmol), L-proline (24 mg, 0.21 mmol), and Na₂CO₃ (23 mg, 0.22 mmol) in DMF/H₂O (9:1, 1.5 mL) was stirred at 60 °C for 19 h. Ethyl acetate (50 mL) was added, the mixture was washed with ammonia solution (25%, 2 x 10 mL) and dried (Na₂SO₄). After filtration and evaporation, the residue was purification by column chromatography (aluminum oxide, hexanes/ethyl acetate, 3:1) to give 12 (213 mg, 83%) as colorless solid (m.p. 71-72 °C) and 13 (12 mg, 7%) as colorless liquid.

1H NMR (CDCl₃, 500 MHz): δ = −0.10 (s, 18 H), 0.86 (m, 4 H), 3.50 (m, 4 H), 4.47 (s, 4 H), 5.52 (s, 4 H), 7.09–7.14, 7.21–7.27 (2 m, 2 H each), 7.40 (s, 2 H); 13C NMR (CDCl₃, 125 MHz): δ = −1.6, 17.9, 50.8, 51.1, 52.5, 63.8, 68.0, 122.2, 129.3, 129.4, 130.0, 133.2, 133.8, 146.0; IR (ATR): ν = 3135, 3070, 2950, 2860, 2095, 1455 cm⁻¹; HRMS (ESI-TOF): calcd for m/z [M + H]⁺ C₂₄H₄₁N₆O₂Si₂: 501.2830; found: 501.2800; calcd for m/z [M + Na]⁺ C₂₄H₄₀N₆NaO₂Si₂N: 523.2649; found: 523.2620; calcd for m/z [M + K]⁺ C₂₄H₄₀N₆KO₂Si₂N: 539.2388; found: 539.2357; Anal. calcd for C₂₄H₄₁N₆O₂Si₂ (500.9): C, 57.56; H, 8.05; N, 16.78; found: C, 57.26; H, 8.09; N, 16.69.

1H NMR (CDCl₃, 500 MHz): δ = −0.02 (s, 9 H), 0.94 (m, 2 H), 3.58 (m, 2 H), 4.42 (s, 2 H), 4.58 (s, 2 H), 5.60 (s, 2 H), 7.23 (d, J = 7.5 Hz, 1 H), 7.32–7.40 (m, 3 H), 7.44 (s, 1 H); 13C NMR (CDCl₃, 125 MHz): δ = −1.5, 18.1, 51.1, 52.5, 63.8, 68.0, 122.2, 129.3, 129.4, 130.0, 130.3, 133.2, 133.8, 146.0; IR (ATR): ν = 3135, 3070, 2950, 2860, 2095, 1455 cm⁻¹; HRMS (ESI-TOF): calcd for m/z [M + H]⁺ C₁₆H₂₅N₆O₂Si: 345.1859; found: 345.1857; calcd for m/z [M + Na]⁺ C₁₆H₂₄N₆NaOSi: 367.1679; found: 367.1677; calcd for m/z [M + K]⁺ C₁₆H₂₄N₆KO₂Si: 383.1418; found: 383.1414; Anal. calcd for C₁₆H₂₄N₆O₂Si (344.5): C, 55.78; H, 7.02; N, 24.40; found: C, 56.35; H, 7.15; N, 23.12.

Representative procedure (RP) for the synthesis of divalent compounds by click-reactions in the presence of TBTA, synthesis of bis(1,2,3-triazole) 12: A mixture of 1,2-
bis(bromomethyl)benzene (11) (67 mg, 0.25 mmol), alkyne 2 (86 mg, 0.55 mmol), sodium azide (40 mg, 0.62 mmol), CuSO₄·5H₂O (13 mg, 0.05 mmol), sodium ascorbate (20 mg, 0.10 mmol), tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amine (TBTA) [4] (27 mg, 0.05 mmol), L-proline (12 mg, 0.10 mmol), and Na₂CO₃ (11 mg, 0.10 mmol) in CH₃CN/H₂O (4:1, 0.5 mL) was stirred at 40 °C for 23 h. Ethyl acetate (50 mL) was added, the reaction mixture was washed with aqueous ammonia solution (25%, 2 × 10 mL) and dried (Na₂SO₄). After filtration and evaporation, the residue was purified by column chromatography (aluminum oxide, hexanes/ethyl acetate, 3:1) to give 12 (117 mg, 94%) as colorless solid.

1,3-Bis(1,2,3-triazole) 14 and azidomethyl(1,2,3)-triazole 15: A mixture of 1,3-bis(bromomethyl)benzene (8) (26 mg, 0.099 mmol), alkyne 6 (80 mg, 0.24 mmol), sodium azide (16 mg, 0.25 mmol), CuSO₄·5H₂O (5 mg, 0.020 mmol), sodium ascorbate (8 mg, 0.040

\([\alpha]_{D}^{22} = 54.4 \; (c = 0.7, \text{MeOH})\); \(^1\)H NMR (CDCl₃, 500 MHz): \(\delta = 1.17, 1.38 \; (2 \; s, \; 6 \; H), 2.29 \; (s, \; 2 \; H), 3.17 \; (s, \; 2 \; H), 3.71–3.78 \; (m, \; 2 \; H), 3.83–3.91 \; (m, \; 4 \; H), 4.06 \; (t, \; J = 7.0 \; Hz, \; 2 \; H), 4.11 \; (d, \; J = 14.0 \; Hz, \; 2 \; H), 4.44–4.50 \; (m, \; 4 \; H), 4.55, 4.63 \; (AB \; system, \; J_{AB} = 12.0 \; Hz, \; 4 \; H), 5.36, 5.40 \; (AB \; system, \; J_{AB} = 15.0 \; Hz, \; 4 \; H), 7.11 \; (s, \; 2 \; H), 7.14–7.20, 7.22–7.30 \; (2 \; m, \; 4 \; H, \; 9 \; H), 7.33 \; (t, \; J = 7.5 \; Hz, \; 1 \; H); \(^{13}\)C NMR (CDCl₃, 125 MHz): \(\delta = 23.8, 26.7, 53.5, 58.0, 59.6, 64.8, 69.1, 69.4, 69.8, 74.1, 78.3, 122.4, 127.4, 127.5, 128.2, 128.3, 128.8, 129.9, 135.7, 136.1, 145.4, 208.2; \) IR (ATR): \(\nu = 2925, 2870, 1725, 1495, 1455 \; \text{cm}^{-1}; \) HRMS (ESI-TOF): calcd for \(m/z \; [M + H]^+ \; C_{46}H_{55}N_{8}O_{8}: 847.4143; \) found: 847.3999; calcd for \(m/z \; [M + Na]^+ \; C_{46}H_{54}Na_{8}NaO_{8}: 869.3963; \) found: 869.3920; calcd for \(m/z \; [M + Na]^+ \; C_{46}H_{54}NaNaO_{8}: 885.3702; \) found: 885.3816. 

1,3-Bis(1,2,3-triazole) 14 and azidomethyl(1,2,3)-triazole 15: A mixture of 1,3-bis(bromomethyl)benzene (8) (26 mg, 0.099 mmol), alkyne 6 (80 mg, 0.24 mmol), sodium azide (16 mg, 0.25 mmol), CuSO₄·5H₂O (5 mg, 0.020 mmol), sodium ascorbate (8 mg, 0.040
mmol), L-proline (5 mg, 0.043 mmol), and Na₂CO₃ (4 mg, 0.038 mmol) in DMF/H₂O (9:1, 0.5 mL) was stirred at 60 °C 17 h. Ethyl acetate (50 mL) was added, the mixture was washed with aqueous ammonia solution (25%, 2 × 10 mL) and dried (Na₂SO₄). After filtration and evaporation, the residue was purified by column chromatography (aluminum oxide, hexanes/ethyl acetate, 3:1) to give 14 (34 mg, 40%) and 15 (19 mg, 37%) as colorless liquids.

Data of 14, see above.

\[ \sigma^0_{D_{22}} = 19.3 \ (c = 0.9, \ \text{MeOH}) \]; \( ^1H \text{ NMR} (\text{CDCl}_3, 500 \text{ MHz}) \): \( \delta = 1.17, 1.38 \ (2 \text{ s, } 3 \text{ H each}), \ 2.29 \ (\text{s, } 1 \text{ H}), \ 3.18 \ (\text{s, } 1 \text{ H}), \ 3.72–3.78, \ 3.84–3.91 \ (2 \text{ m, } 1 \text{ H, } 2 \text{ H}), \ 4.05 \ (\text{dt, } J = 2.0, 7.0 \text{ Hz, } 1 \text{ H}), \ 4.11 \ (\text{d, } J = 13.5 \text{ Hz, } 1 \text{ H}), \ 4.32 \ (\text{s, } 2 \text{ H}), \ 4.42–4.52 \ (\text{m, } 2 \text{ H}), \ 4.55, \ 4.63 \ (2 \text{ d, } J = 12.0 \text{ Hz, } 1 \text{ H each}), \ 5.41, \ 5.45 \ (\text{AB system, } J_{AB} = 15.0 \text{ Hz, } 2 \text{ H}), \ 7.15–7.21, \ 7.22–7.38 \ (2 \text{ m, } 3 \text{ H, } 6 \text{ H}), \ 7.38 \ (\text{t, } J = 8.0 \text{ Hz, } 1 \text{ H}); \ ^{13}C \text{ NMR} (\text{CDCl}_3, 125 \text{ MHz}) \): \( \delta = 23.8, \ 26.7, \ 53.8, \ 54.3, \ 58.0, \ 59.6, \ 64.9, \ 69.1, \ 69.4, \ 69.9, \ 74.1, \ 78.3, \ 122.2, \ 127.5, \ 127.6, \ 127.9, \ 128.4, \ 128.8, \ 129.7, \ 135.3, \ 136.2, \ 136.5, \ 145.4, \ 208.2; \ IR \ (\text{ATR}) \): \( \nu = 3065, \ 3030, \ 2925, \ 2870, \ 2095, \ 1725, \ 1495, \ 1455 \text{ cm}^{-1} \); \ HRMS (ESI-TOF): calcd for \( m/z [M + \text{Na}]^+ \) C_{27}H_{31}N_{7}NaO_{4}: 540.2335; found: 540.2294.

1,4-Bis(1,2,3-triazole) 17 and azidomethyl(1,2,3-triazole) 18: Following the RP, a mixture of 1,4-bis(bromomethyl)benzene (16) (26 mg, 0.099 mmol), alkyne 6 (80 mg, 0.24 mmol), sodium azide (17 mg, 0.26 mmol), CuSO₄·5H₂O (5 mg, 0.02 mmol), sodium ascorbate (8 mg, 0.04 mmol), TBTA (11 mg, 0.021 mmol), L-proline (5 mg, 0.043 mmol), and Na₂CO₃ (4 mg, 0.038 mmol) in CH₃CN/H₂O (4:1, 0.5 mL) was stirred at 40 °C for 14 h. Standard work-up and purification by column chromatography (aluminum oxide, hexanes/ethyl acetate, 3:1) gave 17 (70 mg, 82%) and 18 (3 mg, 6%) as colorless liquids.

\[ \sigma^0_{D_{22}} = 52.8 \ (c = 0.8, \ \text{MeOH}) \]; \( ^1H \text{ NMR} (\text{CDCl}_3, 500 \text{ MHz}) \): \( \delta = 1.15, 1.36 \ (2 \text{ s, } 6 \text{ H each}), \ 2.28 \ (\text{t,
J = 2.0 Hz, 2 H), 3.15 (s, 2 H), 3.70–3.76, 3.83–3.90 (2 m, 2 H, 4 H), 4.01–4.05 (m, 2 H), 4.09 (d, J = 14.0 Hz, 2 H), 4.44–4.49 (m, 4 H), 4.52, 4.60 (2 d, J = 12.0 Hz, 2 H each), 5.36–5.40 (m, 4 H), 7.14–7.19, 7.20–7.30 (2 m, 6 H, 10 H); 13C NMR (CDCl3, 125 MHz): δ = 23.7, 26.6, 53.4, 57.9, 59.6, 64.8, 69.0, 69.3, 69.8, 74.0, 78.3, 122.2, 127.4, 128.2, 128.6, 128.7, 135.7, 136.1, 145.3, 208.1; IR (ATR): ν = 3065, 3030, 2925, 2870, 1725, 1495, 1455 cm⁻¹; HRMS (ESI-TOF): calcd for m/z [M + Na]⁺ C46H54N8NaO6: 869.3963; found: 869.3962; calcd for m/z [M + K]⁺ C46H54N8KO6: 885.3702; found: 885.3697.

[α]D²² = 66.0 (c = 0.15, MeOH); ¹H NMR (CDCl3, 500 MHz): δ = 1.17, 1.38 (s, 3 H each), 2.30 (t, J = 2.0 Hz, 1 H), 3.18 (s, 1 H), 3.73–3.79, 3.85–3.92, 4.04–4.08 (3 m, 1 H, 2 H, 1 H), 4.12 (d, J = 13.5 Hz, 1 H), 4.34 (s, 2 H), 4.45–4.53 (m, 2 H), 4.55, 4.63 (2 d, J = 12.0 Hz, 1 H each), 5.40–5.45 (m, 2 H), 7.14–7.19 (m, 10 H); 13C NMR (CDCl3, 125 MHz): δ = 23.8, 26.7, 53.7, 54.3, 58.0, 64.9, 69.2, 69.4, 74.2, 78.4, 122.2, 127.5, 128.4, 128.5, 128.81, 128.85, 134.6, 136.1, 136.2, 145.6, the C=O signal could not be detected; IR (ATR): ν = 3060, 3030, 2925, 2870, 2095, 1725, 1495, 1455 cm⁻¹; HRMS (ESI-TOF): calcd for m/z [M + Na]⁺ C27H33N7NaO4: 540.2335; found: 540.2331; calcd for m/z [M + K]⁺ C27H33N7KO4: 556.2075; found: 556.2072.

1,3-Bis(1,2,3-triazole) 20: Following the RP, a mixture of 1,3-bis(bromomethyl)benzene (8) (26 mg, 0.099 mmol), compound 19 [3] (80 mg, 0.24 mmol), sodium azide (16 mg, 0.25 mmol), CuSO₄·5H₂O (5 mg, 0.02 mmol), sodium ascorbate (8 mg, 0.04 mmol), TBTA (11 mg, 0.022 mmol), L-proline (5 mg, 0.043 mmol), and Na₂CO₃ (4 mg, 0.038 mmol) in CH₂CN/H₂O (4:1, 0.5 mL) was stirred at 40 °C for 14 h. Standard work-up and purification by column chromatography (aluminum oxide, CH₂Cl₂/MeOH, 25:1) provided 20 (42 mg, 50%) as colorless liquid.
[α]D = 24.5 (c = 1.5, MeOH); 1H NMR (CDCl3, 500 MHz): δ = 1.29, 1.52 (s, 6 H each), 1.59 (s, 2 H), 2.73 (s, 2 H), 3.67-3.73, 3.81-3.87, 3.98-4.07 (3 m, 2 H, 2 H, 4 H), 4.13 (d, J = 11.5 Hz, 2 H), 4.26 (d, J = 13.5 Hz, 2 H), 4.43 (t, J = 7.0 Hz, 2 H), 4.47, 4.61 (2 d, J = 12.0 Hz, 2 H each), 4.69 (t, J = 3.0 Hz, 2 H), 5.28, 5.34 (AB system, J = 15.5 Hz, 4 H), 5.66 (s, 1 H), 6.69 (s, 1 H), 7.05 (m, 2 H), 7.09–7.17, 7.20–7.28 (2 m, 4 H, 9 H), 7.34 (m, 1 H, Ar); 13C NMR (CDCl3, 125 MHz): δ = 26.5, 29.5, 42.3, 53.5, 57.3, 57.5, 64.3, 64.5, 66.6, 66.8, 70.8, 73.4, 122.5, 126.3, 127.0, 128.0, 128.2, 128.5, 129.7, 135.9, 138.0, 145.9; IR (ATR): ν = 3395, 2920, 2850, 1495, 1465, 1455 cm⁻¹; HRMS (ESI-TOF): calcd for m/z [M + Na]+ C46H58N8O8: 873.4275; found: 873.4311; calcd for m/z [M + K]+ C46H58N8KO8: 889.4041; found: 889.4054.

1,4-Bis(1,2,3-triazole) 21: Following the RP, a mixture of 1,4-bis(bromomethyl)benzene (16) (42 mg, 0.16 mmol), 19 (130 mg, 0.39 mmol), sodium azide (27 mg, 0.41 mmol), CuSO4·5H2O (8 mg, 0.032 mmol), sodium ascorbate (13 mg, 0.066 mg), TBTA (17 mg, 0.032 mmol), L-proline (7 mg, 0.061 mmol), and Na2CO3 (7 mg, 0.066 mg) in CH3CN/H2O (4:1, 0.5 mL) was stirred at 40 °C for 21 h. Standard work-up and purification column chromatography (aluminum oxide, CH2Cl2/MeOH, 25:1) afforded 21 (109 mg, 80%) as colorless solid (m.p. 108–110 °C).

[α]D = 74.5 (c = 1.0 MeOH); 1H NMR (CDCl3, 500 MHz): δ = 1.26, 1.46 (s, 6 H each), 1.53 (s, 2 H), 2.64 (s, 2 H), 3.55 (s, 2 H), 3.67–3.80, 3.92–4.02 (2 m, 4 H, 4 H), 4.08 (d, J = 11.5 Hz, 2 H), 4.23 (d, J = 13.5 Hz, 2 H), 4.37 (t, J = 6.0 Hz, 2 H), 4.51, 4.57 (2 d, J = 12.0 Hz, 2 H each), 4.62 (s, 2 H), 5.36 (s, 4 H), 7.10–7.16, 7.18–7.22, 7.25–7.29 (3 m, 6 H, 4 H, 2 H); 13C NMR (CDCl3, 125 MHz): δ = 26.5, 29.5, 42.5, 53.5, 57.2, 57.8, 64.2, 64.6, 66.2, 67.2, 71.4, 73.3, 122.6, 127.1, 128.2, 128.5, 128.7, 135.2, 137.8, 145.7; IR (ATR): ν = 3365, 3065, 3030, 2920, 2855, 1495, 1455 cm⁻¹; HRMS (ESI-TOF): calcd for m/z [M + H]+ C46H58N8O8: 851.4416; found: 851.4475; calcd for m/z [M + Na]+ C46H58N8NaO8: 873.4275; found: 873.4301.

(3S,4S,5R,6S)-5-Amino-3-(hydroxymethyl)-2,2-dimethyl-6-(propoxymethyl)tetrahydro-2H-pyran-4-ol (22): A stirred suspension of palladium on carbon (10%, 100 mg) in dry methanol (5 mL) was saturated with hydrogen for 30 min. Compound 19 (97 mg, 0.29 mmol) was added and the mixture was stirred under an atmosphere of hydrogen at room temperature for 17 h.
After filtration, the solution was concentrated under vacuum to give 22 (59 mg, 81%) as colorless liquid.

\[ \text{22} \]

\(^1\)H NMR (CDCl\(_3\), 500 MHz): \( \delta = 0.88 \) (t, \( J = 7.0 \) Hz, 3 H), 1.11, 1.28 (2 s, 3 H each), 1.55 (m, 2 H), 1.75 (t, \( J = 12.0 \) Hz, 1 H), 2.98 (t, \( J = 5.0 \) Hz, 1 H), 3.35–3.41 (m, 2 H), 3.50–3.54 (m, 2 H), 3.56–3.60 (m, 1 H), 3.70–3.77 (m, 2 H), 4.02–4.06 (m, 1 H), 4.14 (s, 4 H);

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \( \delta = 10.5, 22.7, 24.4, 26.5, 48.4, 56.9, 62.9, 68.2, 70.2, 73.4, 74.9, 75.0 \);

HRMS (ESI-TOF): calcd for \( \text{m/z} \ [M + H]^+ \text{C}_{12}\text{H}_{26}\text{NO}_4 \): 248.1862; found: 248.1858.

\((1R,5S,8S,9S)-2-\text{Benzyl}-8-\{[(1-\text{benzyl}-1H-1,2,3-triazol-4-yl)methoxy]methyl\}-6,6-\text{dimethyl}-3,7-\text{dioxo}-2-\text{azabicyclo}[3.3.1]\text{nonan-9-ol} (23): To a solution of 7 (40 mg, 0.09 mmol) in 3 mL of ethanol was added NaBH\(_4\) (7 mg, 0.18) at 0 °C. The mixture was stirred for 3 h at room temperature. After removal of ethanol, water was added to the residue and the mixture was extracted with dichloromethane (3 \( \times \) 20 mL). The combined organic phases were dried (Na\(_2\)SO\(_4\)), filtered and concentrated. Purification by column chromatography (aluminum oxide, hexanes/ethyl acetate, 5:1) gave 23 (40 mg, 99%) as colorless liquid.

\[ \text{23} \]

\[^{[a]}\text{D}\text{22} = 49.0 \) (c = 1.5, MeOH); \(^1\)H NMR (CDCl\(_3\), 500 MHz): \( \delta = 1.28, 1.48 \) (2 s, 3 H each), 1.57 (s, 1 H), 2.68 (s, 1 H), 3.14 (s, 1 H), 3.70–3.74, 3.78–3.82 (2 m, 1 H each), 4.00–4.07 (m, 2 H), 4.09–4.14 (m, 1 H), 4.25 (d, \( J = 13.5 \) Hz, 1 H), 4.40 (dt, \( J = 2.0, 6.0 \) Hz, 1 H), 4.52, 4.59 (AB system, \( J_{AB} = 12.0 \) Hz, 2 H), 4.65 (s, 1 H), 5.38–5.42 (m, 2 H), 7.12 (t, \( J = 7.5 \) Hz, 1 H), 7.17–7.36 (m, 10 H);

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \( \delta = 26.5, 29.6, 42.5, 54.0, 57.3, 57.7, 64.5, 64.6, 66.4, 67.2, 71.3, 73.2, 122.4, 127.1, 128.0, 128.2, 128.5, 128.7, 129.0, 134.5, 137.8, 145.6; IR (ATR): \( \nu = 3365, 3065, 3030, 2920, 2870, 1495, 1455 \text{ cm}^{-1}; \) HRMS (ESI-TOF): calcd for \( \text{m/z} \ [M + H]^+ \text{C}_{26}\text{H}_{33}\text{NaO}_4 \): 465.2502; found: 465.2468; calcd for \( \text{m/z} \ [M + Na]^+ \text{C}_{26}\text{H}_{32}\text{NaO}_4 \): 487.2321; found: 487.2288; calcd for \( \text{m/z} \ [M + K]^+ \text{C}_{26}\text{H}_{32}\text{K}^+ \text{NaO}_4 \): 503.2061; found: 503.2028.

\((3S,4S,5R,6S)-5-\text{Amino-6-\{[(1-\text{benzyl}-1H-1,2,3-triazol-4-yl)methoxy]methyl\}-3-(hydroxymethyl)}-2,2-\text{dimethyltetrahydro-2H-pyran-4-ol} (24): A stirred suspension of
palladium on carbon (10%, 50 mg) in methanol (4 mL) was saturated with hydrogen for 30 min. Compound 23 (12 mg, 0.026 mmol) was added and the mixture was stirred under an atmosphere of hydrogen at room temperature for 21 h. After filtration, the solution was concentrated under vacuum to give 24 (9 mg, 92%, estimated purity ca. 80%) as colorless liquid.

\[
\text{[\alpha]}_{D}^{22} = 10.2 \ (c = 0.35 \text{ MeOH}); \ H NMR (CD}_{3}OD, 500 MHz): \delta = 1.27, 1.48 (2 s, 3 H each, 1.60 (m, 1 H), 2.65 (m, 1 H), 3.67 (dd, J = 6.1, 9.3 Hz, 1 H), 3.75 (dd, J = 6.3, 9.3 Hz, 1 H), 4.05 (dd, J = 1.8, 12.4 Hz, 1 H), 4.08 (d, J = 13.4 Hz, 1 H), 4.24 (dd, J = 1.8, 12.4 Hz, 1 H), 4.28 (d, J = 13.4 Hz, 1 H), 4.35 (dt, J = 1.9, 6.2 Hz, 1 H), 4.51, 4.58 (AB system, J_{AB} = 12.3 Hz, 2 H), 4.64 (t, J = 3.5 Hz, 1 H, 4-H), 7.13–7.24, 7.29–7.38 (2 m, 2 H, 3 H), 7.79 (s, 2 H); 13C NMR (CD}_{3}OD, 100 MHz):
\]

\[
\delta = 26.2, 29.2, 54.3, 53.2, 57.5, 58.3, 64.0, 64.5, 66.4, 68.1, 71.7, 74.3, 124.7, 127.6, 128.5, 128.6, 129.0, 129.3, 129.4, 136.1, 138.6, 145.9.
\]

Reduction of 1,4-Bis(1,2,3-triazole) 21 to compound 25: Analogously to the reduction of compound 23, palladium on carbon (10%, 21 mg) in dry methanol (1 mL) and compound 21 (22 mg, 0.026 mmol) gave after 5 d at room temperature, work-up and purification by column chromatography (aluminum oxide, CH}_{2}Cl_{2}/MeOH, 5:1 to 1:3) provided 25 (7 mg, 40%, estimated purity ca. 80%) as colorless liquid.

\[
\text{[\alpha]}_{D}^{22} = 10.2 \ (c = 0.35 \text{ MeOH}); \ H NMR (CD}_{3}OD, 500 MHz): \delta = 1.21, 1.29 (2 s, 6 H each, 1.78–1.85 (m, 2 H), 2.67 (t, J = 5.5 Hz, 2 H), 3.49 (dd, J = 8.5, 11.0 Hz, 2 H), 3.64–3.72 (m, 4 H), 3.81 (dd, J = 5.0, 11.0 Hz, 4.00–4.07 (m, 4 H), 4.59, 4.65 (AB system, J_{AB} = 11.0 Hz, 4 H), 5.59 (s, 4 H), 7.34 (s, 4 H), 7.94 (s, 2 H); 13C NMR (CD}_{3}OD, 125 MHz): \delta = 23.0, 26.5, 42.7, 49.4, 53.8, 62.5, 64.4, 66.4, 66.5, 70.7, 71.3, 71.7, 75.8, 124.4, 128.7, 129.1, 129.5, 136.6, 146.1 (s, C-4').
\]

Samarium diiodide-promoted reduction of 1,4-bis(1,2,3-triazole) 24 to compound 26: 1,2-Diiodoethane (178 mg, 0.63 mmol) and samarium (103 mg, 0.69 mmol) were transferred into a dried flask under argon. THF (4 mL) was added under argon and the resulting solution was
stirred under argon [5]. After the solution turned blue, the mixture was stirred for further 2 h. To 2 mL of the solution was added 21 (40 mg, 0.047 mmol). The mixture stirred for 5 h at room temperature, then quenched with aqueous NaHCO₃ solution. After extraction of the mixture with dichloromethane, the organic phases were combined and dried (Na₂SO₄). After filtration and removal of solvent, the residue was purified by column chromatography (aluminum oxide, CH₂Cl₂/MeOH, 10:1) to give 26 (20 mg, 50%, estimated purity ca. 90%) as colorless liquid.

\[
\begin{align*}
\text{\textsuperscript{1}H NMR (CD₃OD, 500 MHz): } & \delta = 1.30, 1.40 \text{ (2 s, 6 H each), 1.68–1.70 (m, 2 H), 3.02 (s, 2 H), 3.62–3.66 (m, 4 H), 3.70–3.75, 3.76–3.82 (2 m, 2 H each), 3.93 (dd, } J = 4.0, 11.0 \text{ Hz, 2 H), 4.03, 4.15 (2 d, } J = 13.0 \text{ Hz, 2 H each), 4.13–4.19 (m, 4 H), 4.23 \text{ (m, 2 H), 4.59, 4.60 (AB system, } J = 12.1 \text{ Hz), 5.57 (s, 4 H), 7.22–7.27, 7.28–7.35 (2 m, 5 H, 9 H), 7.88 (s, 2 H)}; \\
\text{\textsuperscript{13}C NMR (CD₃OD, 125 MHz): } & \delta = 25.9, 26.8, 50.2, 53.2, 58.7, 61.8, 64.2, 65.3, 66.0, 69.9, 71.4, 75.0, 123.9, 128.3, 128.6, 128.7, 129.0, 135.4, 135.8, 144.2; \text{ HRMS (ESI-TOF): calcd for } m/z [M + H]^+ \text{ C}_{46}H_{63}N_{8}O_{8}: 855.4769; \text{ found: 855.4778}; \text{ calcd. for } m/z [M + Na]^+ \text{ C}_{46}H_{62}N_{8}NaO_{8}: 877.4588; \text{ found: 877.4603.}
\end{align*}
\]

3. References


4. Copies of NMR spectra