

SUPPLEMENTARY MATERIAL

Synthesis of Glycophanes (12) and (13)

Glycophane (12)

To a stirred solution of azido-alkyne **10** (2.45 g, 4.8 mmol) in toluene (0.8 L) at rt were successively added DBU (14.4 mL, 20 eq) and commercially available CuI (Aldrich, ref. 215554, 1.12 g, 1.2 eq) in one portion. The colourless mixture that turned to grey-blue was stirred for 48 h at rt (TLC-monitoring: SiO₂, CH₂Cl₂/MeOH, 9:1, R_f 0.81) and finally filtered through a small pad of Celite. The solvent was evaporated under reduced pressure, the residue dissolved in CH₂Cl₂ (150 mL), washed by sat. aqueous NH₄Cl (3 × 20 mL) and water (20 mL). The organic phase was isolated, dried over MgSO₄, concentrated under reduced pressure, and the residue purified by gradient chromatography (SiO₂, EtOAc/*n*-hexane, 1:1 to 3:1) to yield glycophane **12** (1.74 g, 71%) as a colourless foam: mp 108-110°C; [α]_D +1.3 (c 1.3 CHCl₃); FTIR (neat film) 3057, 3927, 2873, 1640 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.59-6.93 (m, 32H, 2 *H*-triazole, 30 Tr*H*), 6.01 (d, *J* = 10.2 Hz, 2H, 2 H-2), 5.67 (m, 2H, 2 H-3), 5.04 (bs, 2H, 2 H-1), 4.73-4.47 (m, 6H, 2 H-4, 2 H-9, 2 H-9'), 4.41 (d, *J* = 11.9 Hz, 2H, 2 H-7), 4.26 (d, *J* = 9.0 Hz, 2H, 2 H-5), 4.13 (ddd, *J* = 7.0 Hz, *J* = 3.0 Hz, 2H, 2 H-8), 3.90 (m, 2H, 2 H-8'), 3.52 (m, 2H, 2 H-7'), 3.25 (d, *J* = 10.3 Hz, 2H, 2 H-6), 3.00 (dd, *J* = 4.0 Hz, 2H, 2 H-6'); ¹³C NMR (62.9 MHz, CDCl₃) δ 146.0 (C-1 Tr), 143.9 (C-4 triazole), 131.2 (C-3), 128.7 (C-5 triazole), 127.9 (C-3 Tr), 127.1 (C-2 Tr), 125.9 (C-2), 95.9 (C-1), 86.5 (CPh₃), 71.4 (C-5), 70.3 (C-4), 67.4 (C-9), 64.4 (C-7), 62.2 (C-6), 50.9 (C-8); ESI-HRMS *m/z* 991.4389 [C₆₀H₅₉N₆O₈ requires 991.4394], 1013.4208 [C₆₀H₅₈N₆NaO₈ requires 1013.4214], 1029.3948 [C₆₀H₅₈N₆KO₈ requires 1029.3953].

Glycophanes (13a) and (13b)

The same procedure was used as for the synthesis of **12**. From azido-alkyne **11** (2.05 g, 4.02 mmol) was obtained firstly after column purification glycophane **13a** (1.23 g, 60%) as a white foam: mp 88-90°C; [α]_D +23.6 (c 0.8, CHCl₃); FTIR (neat film) 3051, 2927, 2867 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.71-7.29 (m, 32H, 30 Tr*H*, 2 *H*-triazole), 6.14 (d, *J* = 10.4 Hz, 2H, 2 H-2), 5.90 (m, 2H, 2 H-3), 5.20 (bs, 2H, 2 H-1), 4.76 (d, *J* = 12.4 Hz, 2H, 2 H-4), 4.63-4.46 (m, 6H, 2 H-10', 2 H-10, 2 H-5), 4.30 (d, *J* = 9.0 Hz, 2H, 2 H-6'), 4.18-3.99 (m, 4H, 2 H-9, 2 H-9'), 3.70 (m, 2H, 2 H-7'), 3.57 (d, *J* = 9.7 Hz, 2H, 2 H-7), 3.38 (dd, *J* = 10.1, *J* = 5.2 Hz, 2H, 2 H-6), 2.33 (m, 4H, 2 H-8, 2 H-8'); ¹³C NMR (62.9 MHz, CDCl₃) δ 145.2 (C-1 Tr), 144.0 (C-4 triazole), 131.1 (C-3), 128.8 (C-3 Tr), 127.9 (C-2 Tr), 127.2 (C-2), 126.5 (C-5 triazole), 122.7 (C-4 Tr), 94.7 (C-1), 86.6 (CPh₃), 71.4 (C-5), 70.0 (C-4), 64.9 (C-10), 63.7 (C-7), 63.2 (C-6), 47.7 (C-9), 30.7 (C-8); ESI-HRMS *m/z* 1041.4521 [C₆₂H₆₂N₆NaO₈ requires 1041.4526], 1057.4261 [C₆₂H₆₂N₆KO₈ requires 1057.4266]; MALDI-HRMS *m/z* 1041.45214 [C₆₂H₆₂N₆NaO₈ requires 1041.45213], 1019.47019 [C₆₂H₆₃N₆O₈ requires 1019.47019].

Glycophane (13b), by-product (R = I)

White foam (0.54 g, 23.4 %); mp 108-110°C; [α]_D +37.7 (c 1.2 CHCl₃); FTIR (neat film) 3057, 2933, 2873 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.71-7.29 (m, 31H, 30 Tr*H*, 1 *H*-triazole), 6.14 (d, *J* = 10.4 Hz, 2H, 2 H-2), 5.90 (m, 2H, 2 H-3), 5.20 (bs, 2H, 2 H-1), 4.76 (d, *J* = 12.4 Hz, 2H, 2 H-4), 4.63-4.46 (m, 6H, 2 H-10', 2 H-10, 2 H-5), 4.30 (d, *J* = 9.0 Hz, 2H, 2 H-6'), 4.18-3.99 (m, 4H, 2 H-9, 2 H-9'), 3.70 (m, 2H, 2 H-7'), 3.57 (d, *J* = 9.7 Hz, 2H, 2 H-7), 3.38 (dd, *J* = 10.1 Hz, *J* = 5.2 Hz, 2H, 2 H-6), 2.46-2.21 (m, 4H, 2 H-8, 2 H-8'); ¹³C NMR (62.9 MHz, CDCl₃) δ 145.6 (C-1 Tr), 144.0 (C-4 triazole), 131.6 (C-5' triazole), 131.1 (C-3), 129.1 (C-5' triazole), 128.8 (C-4' triazole), 127.9 (C-3 Tr), 127.1 (C-2 Tr), 126.4 (C-2), 123.3 (C-4 Tr), 94.5 (C-1), 86.5 (CPh₃), 71.7 (C-5), 70.4 (C-4), 65.3 (C-10'), 64.4 (C-10), 63.0 (C-7), 62.8 (C-7'), 49.7 (C-9), 48.1 (C-9'), 30.7 (C-8'), 29.9 (C-8); ESI-HRMS *m/z* 1167.3488 [C₆₂H₆₁N₆NaO₈ requires 1167.3493], 1183.3227 [C₆₂H₆₁N₆KO₈ requires 1183.3232].

Synthesis of Glycophane (19)

The same procedure of macrocyclization was used as for **12** (TLC-monitoring: SiO₂, CH₂Cl₂/MeOH, 19:1, R_f 0.66). From azido-alkyne **18** (2.02 g, 3.741 mmol), 0.854 g (1.2 eq.) of CuI and 11.5 mL (20 eq.) of DBU were obtained after chromatography 1.221 g (60 %) of macrocycle **19** as a white foam: mp 108-109°C; [α]_D +43.2 (c 0.8, CHCl₃); FTIR (neat film) 3078, 3057, 3024, 2927, 2873 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.73 (s, 2H, 2 *H*-triazole), 7.57-7.11 (m, 30H, 30 Tr*H*), 5.90 (d, *J* = 10.5 Hz, 2H, 2 H-2), 5.78 (m, 2H, 2 H-3), 5.21 (bs, 2H, 2 H-1), 4.72-4.90 (m, *J* = 12.7 Hz, 6H, 2 H-4, 2 H-7, 2 H-7'), 4.57-4.24 (m, 6H, 2 H-12', 2 H-12, 2 H-11'), 3.99-4.31 (m, *J* = 12.4 Hz, *J* = 5.4 Hz, 4H, 2 H-11, 2 H-13'), 3.88 (m, 2H, 2 H-6'), 3.71 (m, 2H, 2 H-13), 3.46-3.28 (m, 6H, 2 H-5, 2 H-10, 2 H-10'), 3.21 (dd, *J* = 10.1 Hz, *J* = 4.4 Hz, 2H, 2 H-6); ¹³C NMR (100.6 MHz, CDCl₃) δ 145.4 (C-1 Tr), 144.1 (C-4 triazole), 131.8 (C-3), 128.9 (C-3 Tr), 127.9 (C-5 triazole), 127.2 (C-2 Tr), 127.1 (C-2), 127.0 (C-4 Tr), 93.8 (C-1), 86.4 (CPh₃), 71.7 (C-4), 70.6 (C-5), 69.7 (C-11), 69.3 (C-10), 68.6 (C-12), 62.9 (C-7), 61.47 (C-6), 50.23 (C-13); MALDI-HRMS *m/z* 1079.49132 [C₆₄H₆₇N₆O₁₀ requires 1079.49187], *m/z* 1101.47327 [C₆₄H₆₆N₆O₁₀Na requires 1101.47326], *m/z* 1117.44720 [C₆₄H₆₆N₆O₁₀K requires 1117.44720]; ESI-HRMS *m/z* 1101.4733 [C₆₄H₆₆N₆NaO₁₀ requires 1101.4738], *m/z* 1117.4472 [C₆₄H₆₆N₆KO₁₀ requires 1117.4477].

Deprotection of glycophanes (12) and (19)

To a solution of the trityl ether in a 1:1-mixture of MeOH/CH₂Cl₂ (50 mL) were added a few crystals of CSA and the mixture stirred at rt until starting material disappeared completely [16b]. The solution was quenched by NEt₃ (ca 10 μL) and concentrated under reduced pressure. The crude residue was dissolved in CH₂Cl₂ (50 mL), washed with water (2 × 5 mL), the isolated organic phase dried over MgSO₄, concentrated under vacuum and purified by gradient chromatography (SiO₂, CH₂Cl₂/CH₃OH, 95:5 to 4:1).

Glycophane (20)

Yield: 0.575 g (95 %) of diol **20** from 1.185 g (1.19 mmol) of trityl ether **12** as a colourless gum: $[\alpha]_D +51.1$ (*c* 1.1, MeOH); $^1\text{H NMR}$ (400 MHz, CD_3OD) δ 7.99 (s, 2H, 2H triazole), 6.01 (d, $J = 10.2$ Hz, 2H, 2 H-2), 5.76 (m, 2H, 2 H-3), 5.03 (bs, 2H, 2 H-1), 4.76-4.47 (m, 6H, 2 H-4, 2 H-9, 2 H-9'), 4.41 (d, $J = 11.9$ Hz, 2H, 2 H-7), 4.26 (d, $J = 9.0$ Hz, 2H, 2 H-5), 4.13 (dt, $J = 7.0$ Hz, $J = 3.0$ Hz, 2H, 2 H-8), 3.90 (m, 2H, 2 H-8'), 3.52 (m, 2H, 2 H-7'), 3.25 (d, $J = 10.3$ Hz, 2H, 2 H-6), 3.00 (dd, $J = 4.0$ Hz, 2H, 2 H-6'); $^{13}\text{C NMR}$ (62.9 MHz, CD_3OD) δ 144.2 (C-4 triazole), 131.2 (C-3), 128.7 (C-5 triazole), 125.9 (C-2), 95.9 (C-1), 71.4 (C-5), 70.3 (C-4), 67.4 (C-7), 64.4 (C-9), 62.2 (C-6), 50.9 (C-8); ESI-HRMS m/z 507.2198 [$\text{C}_{22}\text{H}_{31}\text{NO}_8$ requires 507.2203], m/z 529.2017 [$\text{C}_{22}\text{H}_{30}\text{N}_6\text{NaO}_8$ requires 529.2023].

Glycophane (21)

Yield: 0.310 g (85 %) of diol **21** from 0.660 g (0.612 mmol) of trityl ether **19** as a colourless gum: $[\alpha]_D +19.0$ (*c* 1.2, MeOH); $^1\text{H NMR}$ (400 MHz, CD_3OD) δ 7.73 (s, 2H, 2 H triazole), 6.05 (d, $J = 10.5$ Hz, 2H, 2 H-2), 5.75 (m, 2H, 2 H-3), 4.90 (bs, 2H, 2 H-1), 4.91-4.65 (m, 6H, $J = 12.7$ Hz, 2 H-4, 2 H-7, 2 H-7'), 4.57-4.24 (m, 6H, 2 H-12', 2 H-12, 2 H-11'), 4.25-3.90 (dd, $J = 12.4$ Hz, $J = 5.4$ Hz, 4H, 2 H-11, 2 H-9'), 3.88 (m, 2H, 2 H-6'), 3.71 (m, 2H, 2 H-9), 3.46-3.28 (m, 6H, 2 H-5, 2 H-10, 2 H-10'), 3.21 (dd, $J = 10.1$ Hz, $J = 4.4$ Hz, 2H, 2 H-6); $^{13}\text{C NMR}$ (100.6 MHz, CD_3OD) δ 144.1 (C-4 triazole), 131.8 (C-3), 127.9 (C-5 triazole), 127.1 (C-2), 93.8 (C-1), 71.7 (C-4), 70.6 (C-5), 69.7 (C-11), 69.3 (C-10), 68.6 (C-12), 62.9 (C-7), 61.5 (C-6), 50.2 (C-13); ESI-HRMS m/z 595.2722 [$\text{C}_{26}\text{H}_{39}\text{N}_6\text{O}_{10}$ requires 595.2728], m/z 617.2542 [$\text{C}_{26}\text{H}_{38}\text{N}_6\text{NaO}_{10}$ requires 617.2547].