Multivalent Neoglycoconjugates by Regiospecific Cycloaddition of Alkynes and Azides Using Organic-Soluble Copper Catalysts

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SUPPORTING INFORMATION

General Experimental

TLC was performed on Merck Silica Gel 60 F₂₅₄ aluminium sheets. Reagent used for developing plates include ceric sulphate (1% w/v) and ammonium sulphate (2.5 % w/v) in 10 % (v/v) aqueous sulphuric acid, iodine, ethanolic sulfuric acid (10% v/v) and by UV light when applicable. Flash column chromatography was performed on Silica Gel Scharlau (230-400 mesh, ASTM). Melting points were measured on a Gallenkamp melting point apparatus and are uncorrected. Optical rotations were recorded on a Perkin-Elmer 141 polarimeter at room temperature. IR spectra were recorded on a Satellite Mattson FTIR. ¹H and ¹³C NMR spectra were recorded at room temperature on a Bruker (300-400 MHz) spectrometer. Chemical shifts are given in ppm and referenced to internal CDCl₃. *J* values are given in Hz. FAB mass spectra were recorded on a Fisons VG Autospec-Q spectrometer, using m-nitrobenzyl alcohol or thioglycerol as matrix

Starting materials

Propargyl amine, α,α' -dichloro-*m*-xylene, cyanuric chloride, and 1,2,4,5-tetrakis(bromomethyl)benzene were purchased from Aldrich. Compound **1a**,^{1,2} **1b**,³ **2a**,⁴ **6d**,⁵ **6b**,⁶ **6c**,^{6,7} and **6e**^{8,9} were obtained following the procedures described in literature. Compound **4b** was obtained following a similar procedure as described¹⁰ in 98% yield. Compound **6c** was obtained from hexakis(bromomethyl)benzene.¹¹

N-Acetyl-N-prop-2-ynyl 2,3,4,6-tetra-O-acetyl- α -D-mannopyranosylamine (**1c**).

The title compound was obtained following the procedure described for the synthesis of analogous mannopyranosylamines.¹² A mixture of mannose (2.1 g, 11.6 mmol), propargylamine (0.66 g, 12 mmol) in methanol (7 mL) was stirred at room temperature under a nitrogen

atmosphere for 2 days. Evaporation of the solvent was followed by conventional acetylation with Ac₂O-Py (15:10 mL) giving a crude product that was purified by column chromatography (ether) yielding 1g (2.53 g, 51%) as a foam: $[\alpha]_D +47^\circ$ (c 1, chloroform); IR (KBr): 3482, 3280, 1752, 1670, 1226, 1054 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 5.93 (s, 1 H, H-1), 5.48 (br s, 1 H, H-2), 5.22 (t, 1 H, J = 10.0 Hz, H-4), 5.15 (dd, 1 H, J = 10.0 and 2.9 Hz, H-3), 4.31 (br d, 1 H, J = 19.2 Hz, CH₂N), 4.26 (dd, 1 H, J = 12.3 and 5.7 Hz, H-6), 4.14 (dd, 1 H, J = 12.3 and 2.4 Hz, H-6'), 4.00 (br d, 1 H, J = 19.1, CH₂N), 3.81 (ddd, 1 H, J = 10.0, 5.8 and 2.4 Hz, H-5), 2.26 (b s, 1 H, C $\equiv$ CH), 2.25, 2.21, 2.10, 2.06, 1.96 (5 s, 15 H, 5 Ac); ¹³C NMR (CDCl₃, 75 MHz): δ 170.6, 169.9, 164.8 (5 CO), 78.3 (C-1), 75.2 (C-5), 72.1 (C $\equiv$ CH), 71.6 (C-3, C $\equiv$ CH), 70.0 (C-2), 65.6 (C-4), 62.6 (C-6), 33.6 (CH₂N), 21.9, 21.5, 20.8, 20.6 (5 Me CO).; HMRS (FAB+) C₁₉H₂₅NO₁₀Na 450.1366. Found 450.1365.

2,4,6-Tris(2-azidoethoxy)-1,3,5-triazine (6a). To a cold solution of cyanuric chloride (1.87 g, 10 mmol) and 2-azido ethanol (5.2 g, 60 mmol) in dry acetonitrile (25 mL) was added dropwise a solution of DIPEA (7 mL) in acetonitrile (10 mL). The reaction mixture was kept at room temperature for 2 days. After evaporation the crude product was dissolved in chloroform (150 mL) and washed with water (50 mL). The organic phase was dried (Na₂SO₄), filtered and evaporated. Column chromatography (CH₂Cl₂-ether 20:1) gave **6a** (2.34 g, 70%) as a liquid. IR (film): 2105, 1554, 1329, 1294 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 4.59 (t, 1 H, J = 5.1 Hz, CH₂O), 3.68 (t, 6 H, J = 5.1 Hz, CH₂N₃); ¹³C NMR (CDCl₃, 75 MHz): δ 171.8, 67.3, 49.4.

Cycloaddition compounds

1-(2',3',4',6',-Tetra-*O*-acetyl- α -D-mannopyranosyloxyethyl)-4-(2'',3'',4'',6''-tetra-*O*-acetyl- α -D-mannopyranosyloxymethyl)-1H-[1,2,3]-triazol (3a) (Table 1, entry 1). Foam solid. $[\alpha]_D +37.5^\circ$ (c 1, chloroform); IR (film) 1750, 1436, 1369, 1234 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 7.79 (s, 1 H, H-5), 5.35-5.18 (m, 6 H, H-2',3',4',2'',3'',4''), 5.00 (s, 1 H, H-1), 4.88 (d, 1 H, J = 12.2 Hz, CH₂O), 4.71 (d, 1 H, J = 12.3 Hz, CH₂O), 4.82 (s, 1 H, H-1), 4.64 (t, 2 H, J = 5.0 Hz, CH₂N), 4.32 (dd, 1 H, J = 12.5 and 5.1 Hz, H-6), 4.21 (dd, 1 H, J = 12.2 and 5.1 Hz, H-6), 4.16-4.10 (m, 3 H, H-5,5,6), 4.06 (dd, 1 H, J = 12.4 and 2.1 Hz, H-6), 3.91 (dt, 1 H, J = 10.5 and 5.0 Hz, OCH₂CH₂N), 3.59 (m, 1 H, OCH₂CH₂N), 2.15, 2.14, 2.12, 2.10, 2.05, 2.04, 2.00, 1.97 (8 s, 24 H, 8 x Ac); ¹³C NMR (CDCl₃, 75 MHz): δ 170.5, 170.3, 169.8, 169.6, 169.5, 169.4, 143.5, 124.3, 97.2, 96.9, 69.3, 68.9, 68.6, 68.5, 66.0, 65.6, 62.2, 62.1, 60.7, 49.6, 24.8, 20.7, 20.6, 20.5; HMRS (FAB+) Calc for C₃₃H₄₅N₃O₂₀Na 826.2494. Found 826.2491.

1-(2',3',4',6',-Tetra-*O*-acetyl- α -D-mannopyranosyloxyethyl)-4-(2'',3'',4'',6''-tetra-*O*-acetyl- α -D-mannopyranosylthiomethyl)-1H-[1,2,3]-triazol (3b) (Table 1, entry 2). Solid.

M.p. 63-65 °C; $[\alpha]_D^{+96}$ (c 1.16, chloroform); IR (KBr): 1751, 1228, 1050 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz): δ 7.64 (s, 1 H, H-5), 5.38-5.16 (m, 7 H, H-1',2',3',4', 2'',3'',4''), 4.78 (d, 1 H, $J = 1.5$ Hz, H-1'), 4.59 (t, 2 H, $J = 5.3$ Hz, CH_2N), 4.40 (ddd, 1 H, $J = 9.5$, 4.9 and 2.4 Hz, H-5''), 4.31 (dd, 1 H, $J = 12.2$ and 4.9 Hz, H-6''), 4.21 (dd, 1 H, $J = 12.3$ and 5.2 Hz, H-6''), 4.15-4.02 (m, 3 H, H-6',6'', CH_2O), 3.99 (d, 1 H, $J = 14.4$ Hz, CH_2S), 3.88 (d, 1 H, $J = 14.5$ Hz, CH_2S), 3.86 (dd, 1 H, $J = 10.3$ and 5.4 Hz, CH_2O), 3.60 (ddd, 1 H, $J = 9.6$, 5.1 and 2.3 Hz, H-5'), 2.13, 2.11, 2.09, 2.05, 2.00, 1.97 (6 s, 24 H, 8 x Ac); ^{13}C NMR (CDCl_3 , 75 MHz): δ 170.0, 144.4, 123.5, 97.6 (C-1'), 81.9 (C-1''), 70.7 (C-3''), 69.6 (C-2'), 69.3 (C-5',5''), 69.2 (C-3'), 68.9 (C-2''), 66.4 (C-4''), 66.2 (CH_2O), 65.8 (C-4'), 62.4, 62.3 (C-6',6''), 49.8 (CH_2N), 24.8 (CH_2S), 20.9, 20.8, 20.7 (MeCO); HMRS (FAB+) Calc for $\text{C}_{33}\text{H}_{45}\text{N}_3\text{O}_{19}\text{SNa}$ 842.2265. Found: 842.2261.

1-[2'-(2'',3'',4'',6''-Tetra-*O*-acetyl- α -D-mannopyranosyloxy)-ethyl]-4-[N-acetyl-N-(2'',3'',4'',6''-tetra-*O*-acetyl- α -D-mannopyranosyl)-aminomethyl]-1H-[1,2,3]-triazol (3c) (Table 1, entry 3). Solid: M.p. 89-91 °C; $[\alpha]_D^{+20}$ (c 1, chloroform); IR (KBr): 1750, 1656, 1372, 1228, 1051 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz): δ 7.64 (s, 1 H, H-5), 5.96 (s, 1 H, H-1'''), 5.52 (s, 1 H, H-2'''), 5.31-5.09 (m, 5 H, H-2'',3'',4'',3''',4'''), 4.79 (d, 1 H, $J = 16.5$ Hz, CH_2N), 4.78 (s, 1 H, H-1''), 4.65 (d, 1 H, $J = 17.0$ Hz, CH_2N), 4.57 (m, 2 H, $\text{OCH}_2\text{CH}_2\text{N}$), 4.38 (d, 1 H, $J = 13.6$ Hz, H-6), 4.27-4.10 (m, 3 H, H-5'', H-6'' or H-6'''), 4.06 (d, 1 H, $J = 12.2$ and 2.2 Hz, H-6'' or H-6'''), 3.90 (m, 2 H, CH_2O), 3.73 (m, 1 H, H-5'''), 2.14, 2.10, 2.09, 2.07, 12.00, 1.96, 1.56 (7 s, 27 H, 9 Ac); ^{13}C NMR (CDCl_3 , 75 MHz): δ 171.3, 169.9, 169.8, 169.7, 142.5, 124.1, 97.7, 79.6, 75.3, 71.1, 70.0, 69.1, 68.9, 66.3, 65.7, 65.5, 62.4, 62.2, 49.8, 40.1, 22.0, 20.8, 20.7, 20.5; HMRS (FAB+) Calc for $\text{C}_{35}\text{H}_{48}\text{N}_4\text{O}_{20}\text{Na}$ 867.2760. Found 267.2759.

1,2-Bis{4'-(2'',3'',4'',6''-tetra-*O*-acetyl- α -D-mannopyranosyloxymethyl)-1'H-[1',2',3']-triazol-1'-yl}-ethane (5a) (Table 1, entry 5). Solid. M.p. 59-61 °C; $[\alpha]_D^{+37}$ (c 2, chloroform); IR (KBr) 3144, 1746, 1372, 1230, 1135, 1048 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz): δ 7.43 (s, 2 H, H-5 triazol), 5.30-5.25 (m, 4 H, H-3'',4''), 5.19 (s, 2 H, H-2''), 4.96 (s, 4 H, CH_2N), 4.94 (s, 2 H, H-1''), 4.80 (d, 2 H, $J = 12.3$ Hz, CH_2O), 4.65 (d, 2 H, $J = 12.3$ Hz, CH_2O), 4.29 (dd, 2 H, $J = 12.2$ and 5.0 Hz, H-6''), 4.11 (dd, 2 H, $J = 12.3$ and 2.4 Hz, H-6''), 4.06 (m, 2 H, H-5''), 2.15, 2.12, 2.04, 1.98 (4 s, 24 H, 8 x Ac); ^{13}C NMR (CDCl_3 , 75 MHz): δ 170.7, 170.1, 170.0, 169.8, 144.0, 124.3, 96.9, 69.5, 69.1, 68.8, 66.2, 62.5, 60.7, 49.6, 20.9, 20.8, 20.7, 20.7; HMRS (FAB+) Calcd. for $\text{C}_{36}\text{H}_{48}\text{N}_6\text{O}_{20}\text{Na}$ 907.2821. Found 907.2824.

1,3-Bis{4'-(2'',3'',4'',6''-tetra-*O*-acetyl- α -D-mannopyranosyloxymethyl)-1'H-[1',2',3']-triazol-1'-methyl}-benzene (5b) (Table 1, entry 5). Solid. M.p. 81-83 °C; $[\alpha]_D^{+16}$ (c 1, methanol); IR (KBr): 1746, 1457, 1371, 1227, 1135, 1048 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz): δ 7.55 (s, 2 H, H-5 triazol), 7.41 (t, 1 H, $J = 7.5$ Hz, C_6H_4), 7.30-7.22 (m, 3 H, C_6H_4),

5.60 (s, 4 H, CH₂N), 5.31-5.26 (m, 4 H, H-3'',4''), 5.21 (br d, 2 H, $J = 1.7$ Hz, H-2''), 4.94 (d, 2 H, $J = 1.7$ Hz, H-1''), 4.84 (d, 2 H, $J = 12.4$ Hz, CH₂O), 4.67 (d, 2 H, $J = 12.4$ Hz, CH₂O), 4.28 (dd, 2 H, $J = 12.2$ and 5.1 Hz, H-6''), 4.12-4.00 (m, 4 H, H-5'',6''), 2.14, 2.10, 2.03, 1.99 (4 s, 24 H, 8 x Ac); ¹³C NMR (CDCl₃, 75 MHz): δ 170.8, 170.1, 169.8, 144.0, 135.7, 130.2, 128.5, 127.6, 123.1, 97.0, 69.6, 69.1, 68.8, 66.2, 62.4, 61.2, 53.9, 20.9, 20.8, 20.7; HMRS (FAB+) Calc for C₄₂H₅₂N₆O₂₀Na 983.3134. Found 983.3136.

1,3-Bis{4'-(2'',3'',4'',6''-tetra-*O*-acetyl- α -D-mannopyranosylthiomethyl)-1'H-[1',2',3']-triazol-1'-methyl}-benzene (5c) (Table 1, entry 6). Solid. M.p. 87-88 °C; [α]_D +112° (*c* 1, chloroform); IR (KBr): 1749, 1371, 1228, 1050 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 7.48 (s, 2 H, H-5 triazol), 7.25, 7.22 (br s, 4 H, C₆H₄), 5.51 (s, 4 H, CH₂N), 5.36-5.21 (m, 8 H, H-1'',2'',3'',4''), 4.36 (ddd, 2 H, $J = 9.8, 5.0$ and 2.4 Hz, H-5''), 4.28 (dd, 2 H, $J = 12.1$ and 5.1 , H-6''), 4.04 (dd, 2 H, $J = 12.1$ and 2.1 Hz, H-6''), 3.95 (d, 2 H, $J = 14.6$ Hz, CH₂S), 3.84 (d, 2 H, $J = 14.6$ Hz, CH₂S), 2.14, 2.09, 2.05, 1.98 (4 s, 24 H, 8 x Ac); ¹³C NMR (CDCl₃, 75 MHz): δ 170.6, 169.9, 169.8, 169.6, 144.6, 135.7, 132.1, 130.0, 128.5, 127.5, 122.1, 81.7, 70.7, 69.5, 69.3, 66.2, 62.2, 53.7, 24.8, 20.8, 20.7, 20.6; HMRS (FAB+) Calc for C₄₂H₅₂N₆O₁₈S₂Na 1015.2677. Found 1015.2670.

2,4,6-Tris{2-[4'-(2'',3'',4'',6''-tetra-*O*-acetyl- α -D-mannopyranosyloxymethyl)-1'H-[1',2',3']triazol-1'-yl]-ethoxy}-1,3,5-triazine (7a) (Table 2, entry 1). Solid. M.p. 72-73 °C; [α]_D +32° (*c* 1, chloroform); IR (KBr): 1755, 1561, 1234, 1134, 1048 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 7.81 (s, 3 H, H-5'), 5.32-5.29 (m, 6 H, H-3'',4''), 5.23 (s, 3 H, H-2''), 4.97 (s, 3 H, H-1''), 4.86-4.80 (m, 15 H, CH₂N, CH₂O, CH₂O), 4.68 (d, 3 H, $J = 12.2$ Hz, CH₂O), 4.30 (dd, 3 H, $J = 12.2$ and 5.0 Hz, H-6''), 4.20-4.00 (m, 6 H, H-5'',6''), 2.15, 2.12, 2.04, 1.98 (4 s, 36 H, MeCO); ¹³C NMR (CDCl₃, 75 MHz): δ 171.5 (C-2,4,6), 170.6, 169.9, 169.8, 169.6 (CO), 142.0 (C-4'), 124.1 (C-5'), 96.9 (C-1''), 69.3 (C-2''), 69.0 (C-3''), 68.7 (C-5''), 67.0 (OCH₂CH₂), 66.0 (C-4''), 62.3 (C-6''), 60.8 (CH₂O), 48.8 (CH₂N), 20.9, 20.7, 20.7, 20.6 (*MeCO*); HMRS (FAB+) Calc for C₂₈H₂₆N₈O₂Na 529.2076. Found 529.2081.

1,2,4,5-Tetrakis{4'-(2'',3'',4'',6''-tetra-*O*-acetyl- α -D-mannopyranosyloxymethyl)-1'H-[1',2',3']-triazol-1'-methyl}-benzene (7b) (Table 2, entry 2). Solid. M.p. 109-111 °C; [α]_D +54° (*c* 1, chloroform); IR (KBr): ν 3143, 1750, 1438, 1372, 1239, 1134, 1049 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 7.70 (s, 4 H, H-5 triazol), 7.15 (s, 2 H, Ar), 5.68 (s, 8 H, CH₂N), 5.35-5.25 (m, 8 H, H-3'',4''), 5.20 (s, 4 H, H-2''), 4.98 (s, 4 H, H-1''), 4.83 (d, 4 H, $J = 12.3$ Hz, CH₂O), 4.68 (d, 4 H, $J = 12.3$ Hz, CH₂O), 4.29 (dd, 4 H, $J = 12.2$ and 4.9 Hz, H-6''), 4.15-4.00 (m, 8 H, H-5'',6''), 2.14, 2.11, 2.04, 1.98 (4 s, 48 H, 16 Ac); ¹³C NMR (CDCl₃, 75 MHz): δ

170.6, 169.9, 169.8, 169.6, 144.0, 134.9, 132.0, 123.6, 96.7, 69.3, 68.9, 68.6, 65.9, 62.2, 60.6, 50.5, 20.7, 20.6, 20.5; HMRS (FAB+) Calc for $C_{78}H_{98}N_{12}O_{40}Na$ 1865.5901. Found 1865.5856.

1,2,3,4,5,6-Hexakis-[4-(2'',3'',4'',6'')-tetra-*O*-acetyl- α -D-mannopyranosyloxymethyl)-1'H-[1',2',3']-1'-methyl]benzene (7c) (Table 2, entry 3). Solid. M.p. 162-164 °C; IR (KBr): 1749, 1371, 1228, 1135, 1080, 1048 cm^{-1} ; 1H NMR ($CDCl_3$, 300 MHz): δ 7.56 (s, 1 H, H-5), 5.85 (s, 2 H, CH_2N), 5.27 (m, 2 H, H-3',4'), 5.16 (s, 1 H, H-2'), 4.90 (s, 1 H, H-1'), 4.72 (d, 1 H, $J = 12.5$ Hz, CH_2O), 4.59 (d, 1 H, $J = 12.5$, CH_2O), 4.25 (dd, 1 H, $J = 11.9$ and 4.1 Hz, H-6'), 4.05 (m, 2 H, H-5',6'), 2.13, 2.10, 2.05, 1.98 (4 s, 12 H, 4 x Ac); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.8, 170.1, 170.0, 169.7, 144.2, 137.5, 123.7, 96.9, 69.5, 69.0, 68.7, 66.1, 62.3, 60.7, 48.2, 20.9, 20.8, 20.7, 20.6; HMRS (FAB+) Calc for $C_{114}H_{144}N_{18}O_{60}Na$ 2748.870. Found 2748.860.

Mono{(2¹,3¹-di-*O*-acetyl)-6¹-[4'-(2'',3'',4'',6'')-tetra-*O*-acetyl- α -D-mannopyranosyloxymethyl)-1'H-[1',2',3']triazol-1-yl]-6¹-deoxy}hexakis(2,3,6-tri-*O*-acetyl)cyclomaltoheptaose (7d) (Table 2, entry 4). Solid: M.p. 157-158 °C; $[\alpha]_D +109^\circ$ (c 1, chloroform); IR (KBr): 1751, 1438, 1372, 1237, 1047 cm^{-1} ; 1H NMR ($CDCl_3$, 300 MHz): δ 7.70 (s, 1 H, H-5' triazol), 5.62 (d, 1 H, $J = 3.7$ Hz, H-1 of unit I CD), 5.4-5.16 (m, 10 H, H-3 of CD, H-2'',3'',4''), 5.14 (d, 1 H, $J = 4.0$ Hz, H-1 CD), 5.1 (d, 1 H, $J = 4.0$ Hz, H-1 CD), 5.08 (d, 1 H, $J = 4.0$ Hz, H-1 CD), 5.07 (d, 1 H, $J = 4.0$ Hz, H-1 CD), 5.03 (d, 1 H, $J = 3.6$ Hz, H-1 CD), 4.98 (br s, 1 H, H-1''), 4.96 (dd, 1 H, $J = 8.6$ and 3.9 Hz, H-2 of unit I CD), 4.90-4.48, 4.36-4.06 (2 m, 30 H, 6 x H-2 CD, 7 x H-5 CD, 14 x H-6 CD, H-5'',6'',6''), 3.80-3.60 (m, 7 H, 7 x H-4 CD), 2.15-1.96 (10 s, 72 H, Ac); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.2-169.3 (13 signals), 143.2 (C-4' triazol), 126.1(C-5' triazol), 97.1, 96.8, 96.8, 96.7, 96.6, 96.5, 96.4 (7 C-1'), 77.3, 77.2, 77.0, 76.8, 76.7, 76.4, 75.8, 71.5, 71.4, 71.2, 71.0, 70.9, 70.8, 70.4, 70.2, 70.1, 69.9, 69.6, 69.5, 69.5, 69.4, 69.3, 69.1, 68.6, 66.1, 62.7, 62.6, 62.5, 62.4, 62.3, 62.2, 60.9, 49.2, 20.8, 20.8, 20.7, 20.6; HMRS (FAB+) Calc for $C_{99}H_{131}N_3O_{64}Na$ 2509.702. Found 2409.744.

Heptakis{2,3-di-*O*-acetyl-6-deoxy-6-[4'-(2'',3'',4'',6'')-tetra-*O*-acetyl- α -D-mannopyranosyloxymethyl)-1'H-[1',2',3']triazol-1-yl]}cyclomaltoheptaose (7e) (Table 2, entry 5). Solid. M.p. 198-200 °C; $[\alpha]_D + 58^\circ$ (c 1, chloroform); IR (KBr): 1751, 1773, 1229, 1048 cm^{-1} ; 1H NMR ($CDCl_3$, 300 MHz): δ 7.87 (s, 7 H, H-5' triazol), 5.55 (d, 7 H, $J = 3.7$ Hz, H-1), 5.41-5.18 (m, 28 H, H-3,2'',3'',4''), 4.98 (br s, 7 H, H-1''), 4.80 (dd, 7 H, $J = 9.6$ and 3.5 Hz, H-2), 4.76 (d, 7 H, $J = 12.5$ Hz, CH_2O), 4.06 (d, 7 H, $J = 7.4$ Hz, CH_2O), 5.02-4.52 (m, 21 H, H-5,6,6), 4.30 (dd, 7 H, $J = 12.5$ and 4.5 Hz, H-6''), 4.10 (m, 14 H, H-5'',6''), 3.58 (t, 7 H, $J = 9.0$ Hz, H-4), 2.09, 2.08, 2.03, 1.92, 1.78 (5 s, 126 H, Ac); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.6,

170.3, 169.9, 169.6, 169.5, 143.32, 126.2, 96.9, 96.6, 67.2, 69.3, 69.0, 68.6, 65.2, 62.3, 60.7, 50.2, 20.7, 20.6. HMRS (FAB+) Calc for $C_{189}H_{245}N_{21}O_{112}Na$ 4625.408. Found 4625.405.

Heptakis{2,3-di-*O*-acetyl-6-deoxy-6-[4'-(2'',3'',4'',6''-tetra-*O*-acetyl- α -D-mannopyranosylthiomethyl)-1'H-[1',2',3']-triazol-1-yl]}cyclomaltoheptaose (7f) (Table 2, entry 6). Solid. M.p. 200-202 °C; $[\alpha]_D^{25} + 122^\circ$ (c 1, chloroform); IR (KBr): 1751, 1229, 1049 cm^{-1} ; 1H NMR ($CDCl_3$, 300 MHz): δ 7.75 (s, 7 H, H-5 triazol), 5.51 (b s, 7 H, H-1), 5.42 (s, 7 H, H-1''), 5.35 (t, 7 H, J = 9.5 Hz, H-3), 5.33 (t, 7 H, J = 9.9 Hz, H-4''), 5-27 (b s, 7 H, H-2''), 5.18 (dd, 7 H, J = 9.8 and 3.0 Hz, H-3''), 4.88 (br d, 7 H, J = 14.2 Hz, H-6), 4.75 (m, 14 H, H-2,6), 4.48 (m, 7 H, H-5), 4.35 (m, 7 H, H-5''), 4.31 (dd, 7 H, J = 12.1 and 4.1, H-6''), 4.35 (m, 7 H, H-5''), 4.31 (dd, 7 H, J = 12.1 and 4.1 Hz, H-6''), 4.12 (d, 7 H, J = 12.0 Hz, H-6''), 3.89 (d, 7 H, J = 14.2 Hz, CH_2S), 3.79 (d, 7 H, J = 14.2 Hz, CH_2S), 3.54 (t, 7 H, J = 8.7 Hz, H-4), 2.12, 2.09, 2.05, 2.02, 1.95, 1.78 (6 s, 126 H, CH_3CO); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.7, 170.4, 169.9, 169.7, 144.0, 125.2, 96.7, 81.9, 76.8, 70.7, 69.7-69.3 (6 signals), 66.2, 62.3, 50.1, 24.8, 20.9, 20.8, 20.7, 20.6. HMRS (FAB+) Calc for $C_{189}H_{245}N_{21}O_{105}S_7Na$ 4738.25 Found 4738.19.

References

- (1) H. B. Mereyala, S. R. Gurralla, *Carbohydr. Res.* **1998**, 307, 351.
- (2) R. J. Kaufman, R. S. Sidhu, *J. Org. Chem.* **1982**, 47, 4941.
- (3) Z. H. Gan, R. Roy, *Tetrahedron Lett.* **2000**, 41, 1155.
- (4) A. Y. Chernyak, G. V. M. Sharma, L. O. Kononov, P. R. Krishna, A. B. Levinsky, N. K. Kochetkov, A. V. R. Rao, *Carbohydr. Res.* **1992**, 223, 303.
- (5) L. F. Zhang, Y. C. Wong, L. Chen, C. B. Ching, S. C. Ng, *Tetrahedron Lett.* **1999**, 40, 1815.
- (6) Gilbert, E. E. Patent N° US-138, **1984** USA (CA: 106:158921).
- (7) G. Van Wuytswinkel, B. Verheyde, F. Compennolle, S. Toppet, W. Dehaen, *J. Chem. Soc. Perkin I* **2000**, 9, 1337.
- (8) J. Boger, R. J. Corcoran, J. M. Lehn, *Helv. Chim. Acta* **1978**, 6, 2190.
- (9) C. RoehriStoeckel, O. Dangles, R. Brouillard, *Tetrahedron Lett.* **1997**, 38, 1551.
- (10) A. B. Theocharis, N. E. Alexandrou, A. Terzis, *J. Heterocycl. Chem.* **1990**, 27 1741.
- (11) J. Zavada, M. Pankova, P. Holy, M. Tichy, *Synthesis* 1994, 1132.
- (12) W. Hayes, H. M. I. Osborn, S. D. Osborne, R. A. Rastall, B. Romagnoli, *Tetrahedron Lett.* **2002**, 43 7683.