Regioselective Synthesis of 6-Alkynyl-6-Deoxy and Pseudo-*C*-Disaccharides Derivatives of Mannofuranose via a 5,6-Cyclic Sulfate

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Abstract: C-6 opening of a 5,6-cyclic sulfate derivative of mannofuranoside **1** with acetylenic anion generated from oct-1-yne or phenylethyne gave corresponding 6-alkynyl-6-deoxy derivatives **2** and **3** respectively. The reaction of 5,6-cyclic sulfate **1** with lithium acetylide derived from monosaccharide led to pseudo-*C*-disaccharide **5**. A one-pot procedure was achieved using lithium acetylide in THF/HMPA, to prepare symmetric pseudo-*C*-disaccharide **7**. This method, used with a 5,6-cyclic sulfate derivative of glucofuranose **11** with the acetylide anion derived from mannofuranose **9**, gave the corresponding nonsymmetric pseudo-*C*-disaccharide **13**.

Key words: cyclic sulfate, monosaccharides, alkynes, 6-alkynyl sugars, pseudo-*C*-disaccharides

Electrophilic activation of vicinal diols towards the addition of carbon nucleophiles may be accomplished by direct conversion into a cyclic sulfate. The use of carbon nucleophiles such as phenyllithium,[1] cyanide,[2] benzylmagnesium bromide (Li_2CuCl_4 catalyzed),[3] malonate,[3] α-dithiaaryl carboxylate anions,[4] 2-dithianyllithium species,[4] (2-phenylsulfanyl)-2-dihydropyranyllithium species,[5] enolates of esters and amides,[6] α-sulfonyl, α-cyano and α-phosphonyl substituted anions,[6] dibromomethyllithium[7] allowed regiospecific ring opening of a cyclic sulfate and generated a secondary alcohol function on workup with diluted acid. Only two examples of nucleophilic displacement reactions of cyclic sulfate by acetylenic anions are described in the literature. The reaction of ethylene sulfate with phenylethynyllithium ion gave the corresponding β-substituted ethyl sulfate in quantitative yield.[1] In the first synthesis of valilactone,[8] a potent esterase inhibitor, the first step was performed by reaction of an acetylenic anion generated from 1-trimethylsilyloct-3-en-1-yne with 1,2-*O*-sulfurylheptane to give the corresponding coupled product in 63% yield.

We have previously reported the regioselective synthesis of 6-*O*-alkyl derivatives of mannofuranose and ether linked pseudo-di or trisaccharides derived from manno and glucofuranose via a 5,6-cyclic sulfate.[9,10]

Now, our interest was to synthesize methyl 6-alkynyl-6-deoxymannofuranoside and pseudo-*C*-disaccharide derivatives containing an acetylenic moiety from mannose and glucose derivatives. The *C*-oligosaccharides have been investigated as readily accessible substrates for the introduction groups with fixed distance relationship to one another. The use of these compounds as rigid frameworks in probing the spatial relationship of appendant sugars has also been described in the relationship to the generation of antiviral agents which require polydentate interactions.[11]

Most examples of alkynyl substituted *C*-disaccharides reported in the literature are synthesized by reaction of a glyconolactone with the in situ generated acetylenic anion derived from a monosaccharide.[12] For example, the synthesis of *trans*-fused dipyranyl sugars containing an acetylenic moiety at C-1 has been completed starting from D-glucose. [13]

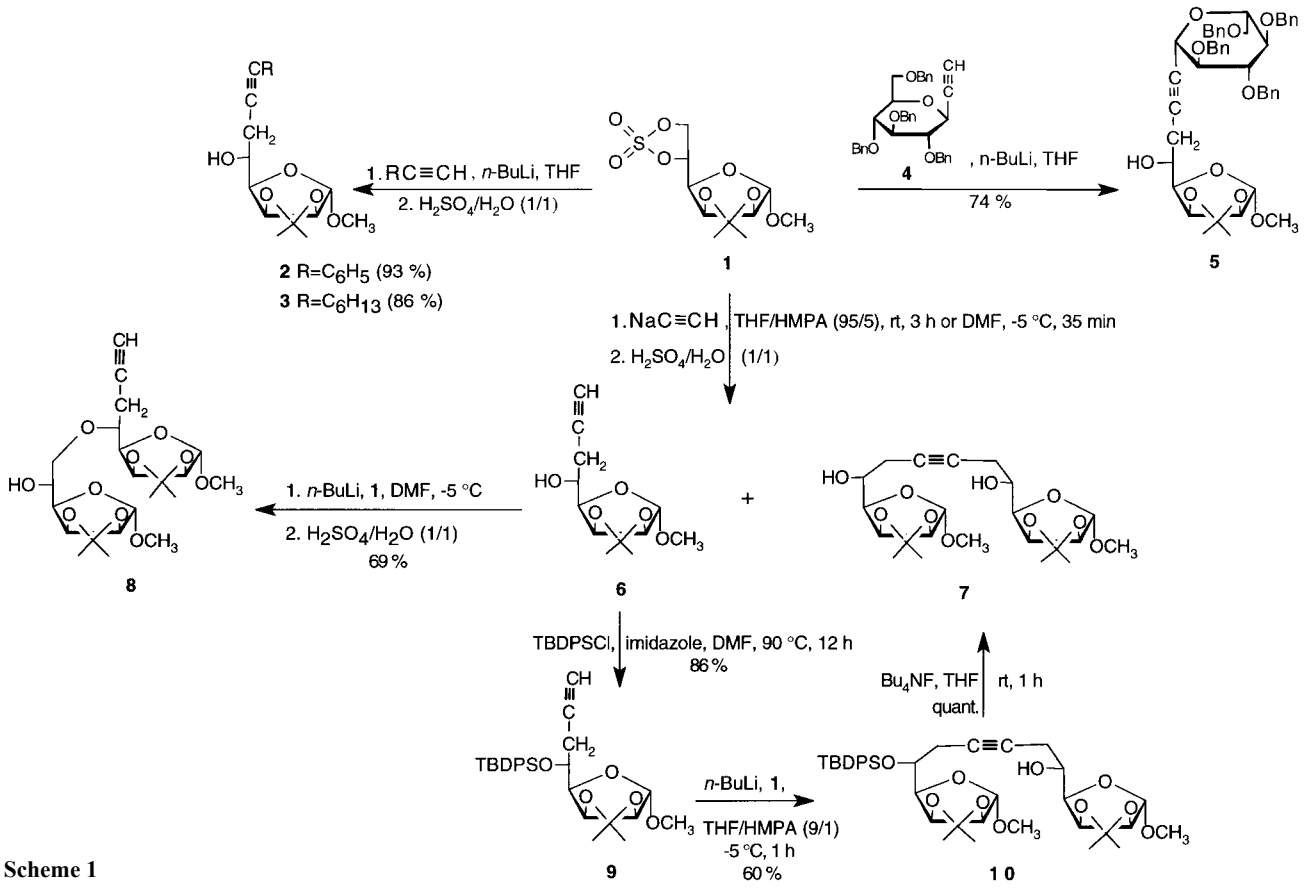
Herein we report the reaction of methyl 2,3-*O*-isopropylidene-5,6-*O*-sulfuryl-α-D-mannofuranoside (**1**) with phenylethynyl and octynyllithium, sodium acetylide and lithium acetylide of manno and glucofuranose derivatives.

5,6-Cyclic sulfate derivative **1** easily reacted with phenylacetylene and oct-1-yne in the presence of butyllithium in THF to give methyl 6,7,8-trideoxy-2,3-*O*-isopropylidene-8-phenyl-α-D-*manno*-oct-7-ynofuranoside (**2**) and methyl 6,7,8-trideoxy-8-hexyl-2,3-*O*-isopropylidene-α-D-*manno*-oct-7-ynofuranoside (**3**) in 93% and 86% yield respectively after acidic hydrolysis of the acyclic sulfate at the C-5 atom (Scheme 1).

Then, we prepared the pseudo-*C*-disaccharide **5** by reaction of the lithium acetylide derived from monosaccharide **4**[12c,14] with the 5,6-cyclic sulfate **1**, in 74% yield. To prepare a symmetric pseudo-*C*-disaccharide, our initial attempt was focused on the sequential generation of the alkylidene dianions in the reaction of sodium acetylide with 2.1 equivalents of 5,6-cyclic sulfate derivative **1** in THF/HMPA (95:5). The reaction was unsuccessful and led to a complex mixture of products.

On the other hand, the use of 3 equivalents of sodium acetylide with 5,6-cyclic sulfate **1** in DMF at –5 °C for 35 min provided the monomer **6** in 71% yield. Unexpectedly, the same reaction was achieved in THF/HMPA (95:5) at room temperature and gave a mixture of compound **6** and **7** in a 3/7 ratio in 72% yield.

The isolated compound **6** reacted with 2 equivalents of butyllithium and 5,6-cyclic sulfate **1** to only give the pseudo-disaccharide **8** connected by an ether linkage. So it was first necessary to protect the 5-OH hydroxyl group by a silyl ether (TBDPS). Then the nucleophilic opening of the 5,6-cyclic sulfate **1** by the anion derived from **9** provided pseudo-*C*-disaccharide **7** in 61% yield after deprotection of the silyl ether. The compound **7** was only obtained in



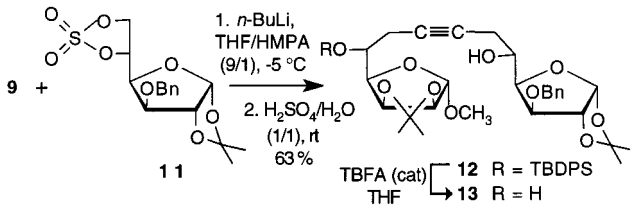
Scheme 1

32% overall yield from the cyclic sulfate **1** in four steps. Compound **7** was isolated in 50% yield from **1** following the one step reaction in THF/HMPA as described above.

To obtain nonsymmetric pseudo-*C*-disaccharides, the acetylide anion derived from the compound **9** could react with other cyclic sulfate derivatives of monosaccharides (Scheme 2).

So, the reaction of 5,6-cyclic sulfate glucofuranose derivative **11**[15] with the anion derived from **9** afforded the pseudo-*C*-disaccharides **13** in 63% yield.

The procedure described herein constitutes a very convenient method for the synthesis of 6-*C*-alkynyl-6-deoxy-monosaccharides and symmetric or nonsymmetric pseudo-*C*-disaccharide derivatives from a 5,6-cyclic sulfate derived from manno and glucofuranose.



Scheme 2

Melting points were determined with a Buchi 535 apparatus and are uncorrected. TLC was performed on silica gel Merck 60 F_{254} plates with visualization by UV light (254 nm) and/or by charring with a vanillin–H_2SO_4 reagent. Preparative column chromatography was performed using 230–400 mesh Merck silica gel. Optical rotations were determined with a Jasco-DIP-370 electronic micropolarimeter. NMR spectra were recorded in $CDCl_3$, on a Bruker 300 WB spectrometer. Chemical shifts are expressed in ppm downfield from TMS. Coupling constants, assigned by double irradiation, are in Hz and splitting pattern abbreviations are: s, singlet; d, doublet; m, multiplet; t, triplet; q, quadruplet. Elemental analysis were performed by the "Service Central de Microanalyse du CNRS" of Vernaison (69-Rhône-France). All solvents were distilled before use. THF was distilled from $LiAlH_4$, thionyl chloride from triphenylphosphite (10 % V/V). All reactions were performed under Ar.

Methyl 6,7,8-Trideoxy-2,3-*O*-isopropylidene-8-phenyl-α-D-*manno*-oct-7-ynofuranoside (2)

To a solution of phenylacetylene (0.143 mL, 1.26 mmol) in THF (4.2 mL) cooled to –5 °C under Ar was added dropwise a solution of BuLi (0.506 mL of 2.5 M solution in THF, 1.26 mmol). After stirring at –5 °C for 2 h, compound **1** (250 mg, 0.844 mmol) was added. After 2 h at –5 °C, H_2SO_4 (40 µL) and H_2O (20 µL) were added, the mixture was stirred for 10 min at r.t. and poured into a cold molar solution of $NaHCO_3$ (10 mL). The aqueous solution was extracted with EtOAc and the combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed on silica gel (85:15 hexane–EtOAc) to yield **2** (249 mg, 93%) as a colorless syrup. *Rf* 0.40 (6:4 hexane–EtOAc); $[\alpha]_D^{27}$ +71.6 (c = 0.32, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 7.36 (m, 2H, CH(Ph)), 7.22 (m, 3H, CH(Ph)), 4.87 (s, 1H, H-1), 4.83 (dd, 1H, H-3, J_{2-3} = 5.9 Hz, J_{3-4} = 3.6 Hz), 4.53 (d, 1H, H-2), 4.12 (m, 1H, H-5), 3.96 (dd, 1H, H-4, J_{4-5} = 8.0 Hz), 3.27 (s, 3H, CH_3O), 2.85 (dd, 1H, H-6, J_{5-6} = 4.5 Hz, $J_{6-6'}$ = 17 Hz), 2.74 (dd, 1H, H-6', $J_{5-6'}$ = 6.2 Hz), 1.43, 1.27 (2s, 6H, $C(CH_3)_2$).

^{13}C NMR ($CDCl_3$): δ = 131.6, 128.1, 127.8 (CH(Ph)), 123.4 (C_{ipso}), 112.6 ($C(CH_3)_2$), 106.9 (C-1), 85.6, 82.8 (C-7, C-8), 84.9 (C-2), 80.5 (C-4), 79.8 (C-3), 68.0 (C-5), 54.3 (OCH_3), 25.9 ($C(CH_3)_2$), 25.5 (C-6), 24.6 ($C(CH_3)_2$).

$C_{18}H_{22}O_5$	calcd	C	67.91	H	6.96
(318.36)	found	C	68.07	H	6.78

Methyl 6,7,8-Trideoxy-8-hexyl-2,3-*O*-isopropylidene-α-D-*manno*-oct-7-ynofuranoside (3)

Oct-1-yne (0,186 mL,1.26 mmol) was treated as described above for **2** to yield **3** (237 mg, 86%) as a colorless syrup. R_f 0.45 (6:4 hexane–EtOAc); $[\alpha]_D^{27}$ +51.1 (c = 0.23, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 4.78 (s, 1H, H-1), 4.74 (dd, 1H, H-3, J_{2-3} = 5.9 Hz, J_{3-4} = 3.5 Hz), 4.46 (d, 1H, H-2), 3.93 (m, 1H, H-5), 3.82 (dd, 1H, H-4, J_{4-5} = 8.0 Hz), 3.21 (s, 3H, CH_3O), 2.53 (dq, 1H, H-6, J_{5-6} = 4.6 Hz, $J_{6-6'}$ = 16.7 Hz, $J_{6-9,9'}$ = 2.3 Hz), 2.42 (ds, 1H, H-6', $J_{5-6'}$ = 5.9 Hz, $J_{6'-9}$ = 2.5 Hz, $J_{6'-9'}$ = 2.3 Hz), 2.06 (m, 2H, H-9, H-9'), 1.39, 1.24 (2s, 6H, $C(CH_3)_2$), 1.43–1.15 (m, 8H, $CH_{2\ 10-13}$), 0.78 (t, 3H, H-14, H-14',H-14'').

^{13}C NMR ($CDCl_3$): δ = 111.5 ($C(CH_3)_2$), 105.9 (C-1), 83.9 (C-2), 82.1 (C-7), 79.4 (C-4), 78.8 (C-3), 74.3 (C-8), 67.0 (C-5), 53.2 (OCH_3), 30.3 (C-12), 27.9, 27.5, 21.5 (C-10, C-11, C-13), 24.9 ($C(CH_3)_2$), 23.8 (C-6), 23.6 ($C(CH_3)_2$), 17.7 (C-9), 12.9 (C-14).

$C_{18}H_{30}O_5$	calcd	C	66.23	H	9.26
(326.43)	found	C	66.06	H	9.34

Methyl 6,7,8-Trideoxy-2,3-*O*-isopropylidene-8-(2,3,4,6-tetra-*O*-benzyl-6-deoxy-α-D-glucopyranos-1-yl)-α-D-*manno*-oct-7-ynofuranoside (5)

To a solution of (2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)octyne **4** (149 mg, 0.27 mmol) in THF (0.7 mL) cooled to –40 °C was added BuLi (119 μL of 2.5 M solution in THF, 0.30 mmol). After stirring at r.t. for 4 h, the mixture was cooled to –40 °C and compound **1** (96.5 mg, 0.32 mmol) and HMPA (70 μL) were added. The mixture was stirred for 2 h at –40 °C and was treated as described above for compound **2** (H_2SO_4 17 μL, H_2O 6 μL, 2 h, r.t.) chromatography on silica gel (8:2 hexane–EtOAc) gave **5** (154 mg, 74%) as a colorless syrup. R_f 0.30 (7:3 hexane–EtOAc); $[\alpha]_D^{28}$ +18.2 (c = 0.7, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 7.26 (m, 24H), 5.08–4.92 (dd, 2H, CH_2(Ph)), 4.89 (s, 1H, H-1), 4.83 (dd, 2H, CH_2(Ph)), 4.73 (dd, 1H, H-3, J_{2-3} = 5.9 Hz, J_{3-4} = 3.65 Hz), 4.53 (m, 4H, CH_2(Ph)), 4.11 (m, 2H, H-5, H-1'), 3.94 (dd, 1H, H-4, J_{4-5} = 7.7 Hz), 3.93 (m, 2H, H-6'', H-6'''), 3.62 (m, 3H, H-2', H-3', H-4'), 3.44 (m, 1H, H-5'), 3.28 (s, 3H, CH_3O), 2.75 (dq, 1H, H-6, J_{5-6} = 4.5 Hz, $J_{6-6'}$ = 16.9 Hz, J_{6-8} = 1.8 Hz), 2.62 (dq, 1H, H-6', $J_{5-6'}$ = 6.8 Hz, $J_{6'-8}$ = 1.75 Hz), 1.45, 1.30 (2s, 6H, $C(CH_3)_2$).

^{13}C NMR ($CDCl_3$): δ = 138.5, 138.2, 138.1 (4C_{ipso}), 128.4, 127.9, 128.0, 127.8 (CH(Ph)), 112.6 ($C(CH_3)_2$), 107.0 (C-1), 86.0, 82.4, 77.7 (C-2', C-3', C-4'), 82.9, 79.6 (C-7, C-7'), 80.6 (C-4), 79.8 (C-3), 78.9 (C-5'), 75.7, 75.3, 75.0, 73.5 (CH_2(Ph)), 70.1 (C-1'), 68.8 (C-6'), 68.2 (C-5), 54.5 (OCH_3), 26.0 ($C(CH_3)_2$), 25.1 (C-6), 24.6 ($C(CH_3)_2$).

$C_{46}H_{52}O_{10}$	calcd	C	72.23	H	6.85
(764.91)	found	C	72.06	H	6.97

Methyl 6,7,8-Trideoxy-2,3-*O*-isopropylidene-α-D-*manno*-oct-7-ynofuranoside (6)

A solution of sodium acetylide (1.1 g of 18% W solution in xylene, 2.53 mmol) was added dropwise to a solution of compound **1** (250 mg, 0.844 mmol) in DMF (2.1 mL) cooled to –5 °C under Ar. After 35 min all of starting material had disappeared to give a single spot on baseline in TLC. The mixture was concentrated under reduced pressure and the residue was diluted by 2 mL of THF. H_2SO_4 (40 μL) and H_2O (20 μL) were added dropwise and the mixture was stirred for 20 min at r.t.. A cold molar solution of $NaHCO_3$ (10 mL) was added and the mixture was treated as described above for **2** (8:2 hexane–EtOAc, silica gel chromatographed) to give **6** (14.3 mg, 70%) as a pale yellow syrup. *Rf* 0.40 (6:4 hexane–EtOAc); $[\alpha]_D^{25}$ +71.7 (c = 0.44, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 4.84 (s, 1H, H-1); 4.79 (dd, 1H, H-3, J_{2-3} = 5.9 Hz, J_{3-4} = 3.7 Hz), 4.52 (d, 1H, H-2), 4.02 (m, 1H, H-5), 3.90 (dd, 1H, H-4, J_{4-5} = 8.0 Hz), 3.26 (s, 3H, CH_3O), 2.70 (m, 1H, OH), 2.62 (dq, 1H, H-6, J_{5-6} = 4.5 Hz, $J_{6-6'}$ = 16.9 Hz, J_{6-8} = 2.7 Hz), 2.51 (dq, 1H, H-6', $J_{5-6'}$ = 6.3 Hz, $J_{6'-8}$ = 2.7 Hz), 2.01 (t, 1H, H-8), 1.41, 1.27 (2s, 6H, $C(CH_3)_2$).

^{13}C NMR ($CDCl_3$): δ = 112.6 ($C(CH_3)_2$), 106.8 (C-1), 84.8 (C-2), 80.3 (C-4), 80.2 (C-7), 79.7 (C-3), 70.7 (C-8), 67.8 (C-5), 54.4 (OCH_3), 25.9, 24.5 ($C(CH_3)_2$), 24.4 (C-6).

IR (NaCl): ν = 3287 (C C-H), 3481 cm^{-1} (O-H)

$C_{12}H_{18}O_5$	calcd	C	59.49	H	7.79
(242.27)	found	C	59.61	H	7.71

Bis(methyl 6-deoxy-2,3-*O*-isopropylidene-α-D-*manno*-furanosid-6-yl)acetylene (7)

To a solution of sodium acetylide (1.1 g of 18% W solution in xylene, 2.53 mmol) was added dropwise a solution of compound **1** (250 mg, 0.844 mmol) in THF (2.1 mL) and HMPA (0.105 mL) at r.t.. The mixture was stirred for 3 h. H_2SO_4 and H_2O (40 μL–20 μL) were added to the mixture at r.t.. After 20 min, the reaction was poured into a cold molar solution of $NaHCO_3$ (10 mL). The aqueous solution was extracted with EtOAc and the combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed on silica gel (8:2 then 6:4 hexane–EtOAc) to yield **7** (189 mg, 50%) and the monomer **6** (43 mg, 21%). R_f 0.15 (6:4 hexane–EtOAc).

^{1}H NMR ($CDCl_3$): δ = 4.84 (s, 2H, H-1, H-1'), 4.79 (dd, 2H, H-3, H-3', $J_{2-3,\ 2'-3'}$ = 5.9 Hz, $J_{3-4,\ 3'-4'}$ = 3.6 Hz), 4.51 (d, 2H, H-2, H-2'), 4.00 (m, 2H, H-5, H-5'), 3.87 (dd, 2H, H-4, H-4', $J_{4-5,\ 4'-5'}$ = 8.0 Hz), 3.26 (s, 6H, CH_3O), 2.61 (dd, 2H, H-6a, H-6a', $J_{5a-6a,\ 5a'-6a'}$ = 3.4 Hz, $J_{6a-6b,\ 6a'-6b'}$ = 14.7 Hz), 2.48 (dd, 2H, H-6b, H6b', $J_{5a-6b,\ 5a'-6b'}$ = 5.2 Hz), 1.42, 1.27 (2s, 12H, $C(CH_3)_2$).

^{13}C NMR ($CDCl_3$): δ = 112.6 ($C(CH_3)_2$), 106.9 (C-1, C-1'), 84.8 (C-2, C-2'), 80.5 (C-4, C-4'), 79.8 (C-3, C-3'), 78.5 (C-7, C-7'), 68.1 (C-5, C-5'), 54.4 (OCH_3), 25.9 ($C(CH_3)_2$), 24.8 (C-6, C-6'), 24.6 ($C(CH_3)_2$).

$C_{22}H_{34}O_{10}$	calcd	C	57.63	H	7.47
(458.50)	found	C	57.73	H	7.37

Methyl 6,7,8-Trideoxy-2,3-*O*-isopropylidene-5-*O*-(methyl 6-deoxy-2,3-*O*-isopropylidene-α-D-*manno*-furanosid-6-yl)-α-D-*manno*-oct-7-ynofuranoside (8)

Compound **6** (72.4 mg, 0.3 mmol) was treated by two equivalents of BuLi (0.245 mL of 2.5 M solution in THF, 0.614 mmol) in DMF (2 mL) cooled to –5 °C under Ar for 2 h. Compound **1** (136.8 mg, 0.48 mmol) was added at –5 °C and the mixture stirred to r.t.. After 15 min TLC show the total conversion of all starting material in a single spot on base line. After concentration under reduced pressure, the residue was dissolved in THF (3 mL) and treated as described above for **2** to yield **8** (95 mg, 69%) as a colorless syrup. R_f 0.8 (1:1 hexane–EtOAc); $[\alpha]_D^{25}$+ 55.1 (c = 0.85, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 4.76 (m, 3H, H-1, H-1', H-3), 4.72 (dd, 1H, H-3', $J_{2'-3'}$ = 5.9 Hz, $J_{3'-4'}$ = 3.8 Hz), 4.45 (m, 2H, H-2, H-2'), 4.10 (m, 2H, H-5, H-5'), 3.95 (dd, 1H, H-4, J_{3-4} = 3.6 Hz, J_{4-5} = 9.1 Hz), 3.71 (m, 2H, H-4', H-6''), 3.43 (dd, 1H, H-6''', $J_{6''-6'''}$ = 10.5 Hz, $J_{6'''-5'}$ = 8.1 Hz), 3.20, 3.19 (2s, 6H, CH_3O), 2.71 (dt, 1H, H-6, J_{5-6} =

5.8 Hz, $J_{6-6'}$ = 17.3 Hz, J_{6-8} = 2.7 Hz), 2.46 (dq, 1H, H-6', $J_{5-6'}$ = 4.6 Hz, $J_{6'-8}$ = 2.7 Hz), 1.93 (t, 1H, H-8), 1.36, 1.35, 1.23, 1.21 (4s, 12H, $C(CH_3)_2$).

^{13}C NMR ($CDCl_3$): δ = 112.4 ($2C(CH_3)_2$), 107.2, 106.6 (C-1, C-1'), 84.6, 84.5 (C-2, C-2'), 80.2 (C-7), 79.8 (C-4), 79.5 (C-3'), 79.2 (C-3, C-4'), 75.9 (C-5), 72.9 (C-6'), 70.3 (C-8), 68.4 (C-5'), 54.3, 54.2 (OCH_3), 25.8, 25.6, 24.7, 24.6 ($C(CH_3)_2$), 21.3 (C-6').

IR (NaCl): ν = 3280 cm^{-1} (C≡C-H), 3477 cm^{-1} (O-H)

$C_{22}H_{34}O_{10}$	calcd	C	57.63	H	7.47
(458.50)	found	C	57.54	H	7.42

Methyl 5-*O*-*tert*-Butyldiphenylsilyl-6,7,8-trideoxy-2,3-*O*-isopropylidene-α-D-*manno*-oct-7-ynofuranoside (9)

To a solution of **6** (112.5 g, 0.46 mmol) in DMF (4 mL) was added at r.t., imidazole (158 mg, 2.32 mmol) and TBDPSCl (302 μL, 1.16 mmol). The mixture was heated to 90 °C overnight. The mixture was concentrated under reduced pressure and the residue was dissolved in H_2O (15 mL) and extracted with EtOAc (3 × 15 mL). The combined organic layers were dried (Na_2SO_4), concentrated under reduced pressure and the residue was chromatographed on silica gel (98:2 hexane–EtOAc) to yield **9** (155 mg, 86 %) as a colorless syrup: R_f 0.68 (1:9 EtOAc–hexane); $[\alpha]_D^{25}$ +32.4 (*c* = 0.8, CH_2Cl_2).

^1H NMR ($CDCl_3$): δ = 7.81, 7.37 (m, 10H, CH(Ph)), 4.82 (dd, 1H, H-3, J_{2-3} = 5.8 Hz, J_{3-4} = 3.3 Hz), 4.79 (s, 1H, H-1), 4.54 (d, 1H, H-2), 4.27 (dd, 1H, H-4, J_{4-5} = 8.9 Hz), 4.09 (m, 1H, H-5), 3.32 (s, 3H, CH_3O), 2.46 (dt, 1H, H-6, J_{5-6} = 5.9 Hz, $J_{6-6'}$ = 17.1 Hz, J_{6-8} = 2.5 Hz), 2.31 (dt, 1H, H-6', $J_{5-6'}$ = 6.1 Hz, $J_{6'-8}$ = 2.5 Hz), 2.02 (t, 1H, H-8), 1.26; 1.21 (2s, 6H, $C(CH_3)_2$), 1.10 (s, 9H, $C(CH_3)_3$).

^{13}C NMR ($CDCl_3$): δ = 136.2, 136.1 (CH(Ph)), 134.1, 133.2 (C_{ipso}), 129.5, 127.5 (CH(Ph)), 111.9 ($C(CH_3)_2$), 106.8 (C-1), 85.0 (C-2), 80.8 (C-7), 80.2 (C-4), 79.4 (C-3), 70.6 (C-8), 68.1 (C-5), 54.1 (OCH_3), 26.9 ($C(CH_3)_3$), 25.9, 24.6 ($C(CH_3)_2$), 24.5 (C-6), 19.4 ($C(CH_3)_3$).

IR (NaCl): ν = 3303 cm^{-1} (C≡C-H)

$C_{28}H_{36}O_5Si$	calcd	C	69.97	H	7.55
(480.67)	found	C	70.12	H	7.42

Methyl 6,7,8-Trideoxy-2,3-*O*-isopropylidene-8-(methyl 5-*O*-*tert*-butyldiphenylsilyl-6-deoxy-2,3-*O*-isopropylidene-α-D-*manno*-furanosid-6-yl)-α-D-*manno*-oct-7-ynofuranoside (10)

To a solution of **9** (155.2 mg, 0.323 mmol) in THF (0.8 mL)/HMPA (0.08mL) cooled to –5 °C was added under Ar a solution of BuLi (129 μL of 2.5 M solution in THF, 0.323 mmol). The mixture was stirred for 1 h at r.t. and then cooled to –5 °C. Compound **1** (0.105 g, 0.35 mmol) was added and the mixture was stirred at –5 °C overnight and then mixture was treated as described above for **2**, flash chromatography on silica gel (9:1 hexane–EtOAc) to yield **10** (136 mg, 60.5%) as a colorless syrup. Desilylation with TBFA (cat.) in THF (5mL) at r.t. yielded quantitatively **7** in 2 h. R_f 0.82 (6:4 hexane–EtOAc); $[\alpha]_D^{25}$ +43.2 (*c* = 0.4, CH_2Cl_2).

^1H NMR ($CDCl_3$): δ = 7.77, 7.28 (m, 10H, CH(Ph)), 4.83 (s, 1H, H-1), 4.76 (dd, 1H, H-3, J_{2-3} = 5.9 Hz, J_{3-4} = 3.5 Hz), 4.72 (dd, 1H, H-3', $J_{2'-3'}$ = 5.8 Hz, $J_{3'-4'}$ = 3.2 Hz), 4.69 (s, 1H, H-1'), 4.49 (d, 1H, H-2), 4.44 (d, 1H, H-2'), 4.10 (dd, 1H, H-4', $J_{4'-5'}$ = 8.9 Hz), 3.99 (m, 2H, H-5, H-5'), 3.88 (dd, 1H, H-4, J_{4-5} = 7.7 Hz), 3.23, 3.22 (2s, 6H, CH_3O), 2.61–2.17 (m, 4H, H-6, H-6', H-6", H-6'"), 1.40, 1.25, 1.16, 1.12 (4s, 12H, $C(CH_3)_2$), 0.98 (s, 9H, $C(CH_3)_3$).

^{13}C NMR ($CDCl_3$): δ = 136.1, 136.0 (CH(Ph)), 134.2, 133.1 (C_{ipso}), 129.5, 127.2 (CH(Ph)), 112.5, 111.9 ($C(CH_3)_2$), 107.0 (C-1, C-1'), 84.9 (C-2, C-2'), 80.6 (C-4'), 80.4 (C-4), 79.9 (C-3), 79.5 (C-7), 79.4 (C-3'), 77.7 (C-7'), 68.6, 68.2 (C-5, C-5'), 54.4, 54.1 (OCH_3), 26.8 ($C(CH_3)_3$), 25.9, 25.8 ($C(CH_3)_2$), 25.0, 24.9 (C-6, C-6'), 24.6 (2 $C(CH_3)_2$), 19.3 ($C(CH_3)_3$).

$C_{38}H_{52}O_{10}Si$	calcd	C	65.50	H	7.52
(696.90)	found	C	65.68	H	7.59

6,7,8-Trideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-8-(methyl 5-*O*-*tert*-butyldiphenylsilyl-6-deoxy-2,3-*O*-isopropylidene-α-D-*manno*-furanosid-6-yl)-α-D-*gluco*-oct-7-ynofuranoside (12)

9 was treated as described above for **6** with 3-*O*-benzyl-1,2-*O*-isopropylidene-5,6-*O*-sulfuryl-α-D-glucofuranose (**11**) (125 mg, 0.336 mmol) to yield **12** (174 mg, 63%) as a yellow syrup. R_f 0.31 (7:3 hexane–EtOAc); $[\alpha]^{27}_D$ –27.9 (*c* = 1.2; CH_2Cl_2).

^1H NMR ($CDCl_3$): δ = 7.77, 7.31 (2m, 15H, CH(Ph)), 5.91 (d, 1H, H-1', J_{1-2} = 3.7 Hz), 4.76 (s, 1H, H-1), 4.66 (dd, 2H, CH_2(Ph)), 4.60 (d, 1H, H-2'), 4.50 (d, 1H, H-2), 4.19 (dd, 1H, H-4, J_{4-5} = 8.9 Hz), 4.15–4.06 (m, 4H, H-3', H-4', H-5', H-5), 3.27 (s, 3H, CH_3O), 2.49–2.33 (m, 4H, H-6, H-6', H-6", H-6'"), 1.46, 1.30, 1.25, 1.21 (4s, 12H, $C(CH_3)_2$), 1.06 (s, 9H, $C(CH_3)_3$).

^{13}C NMR ($CDCl_3$): δ = 137.4 (C_{ipso}), 136.2, 136.0 (CH(Ph)), 134.2, 133.1 (C_{ipso}), 129.6, 128.5, 128.0, 127.5, 127.3 (CH(Ph)), 111.9, 111.7 ($C(CH_3)_2$), 106.9 (C-1), 105.1 (C-1'), 84.9 (C-2), 82.5 (C-2'), 81.7 (C-4', C-3'), 80.7 (C-4), 79.8 (C-7), 79.4 (C-3), 77.9 (C-7'), 72.3 CH_2(Ph), 68.7, 67.2 (C-5, C-5'), 54.1 (OCH_3), 26.9 ($C(CH_3)_3$), 26.3, 25.9 ($C(CH_3)_2$), 25.3, 25.0 (C-6, C-6'), 24.6 (2 $C(CH_3)_2$), 19.3 ($C(CH_3)_3$).

$C_{44}H_{56}O_{10}Si$	calcd	C	68.37	H	7.30
(773.00)	found	C	68.29	H	7.47

6,7,8-Trideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-8-(methyl 6-deoxy-2,3-*O*-isopropylidene-α-D-*manno*-furanosid-6-yl)-α-D-*gluco*-oct-7-ynofuranose (13)

Compound **13** was obtained quantitatively by treatment of **12** in THF (7 mL) by TBAF (cat.). **13** as a colorless syrup. R_f 0.18 (7:3 hexane-EtOAc); $[\alpha]^{27}_D$ –1.5° (*c* = 0.4; CH_2Cl_2).

^1H NMR ($CDCl_3$): δ = 7.28 (m, 5H, CH(Ph)), 5.87 (d, 1H, H-1', J_{1-2} = 3.7 Hz), 4.84 (s, 1H, H-1), 4.80 (dd, 1H, H-3, J_{2-3} = 5.85 Hz, J_{3-4} = 3.6 Hz), 4.69 (d, 1H, CH_2(Ph)), 4.55 (2d, 2H, H-2', CH_2(Ph)), 4.52 (d, 1H, H-2), 4.11–3.95 (m, 4H, H-3', H-4', H-5', H-5), 3.88 (dd, 1H, H-4, J_{4-5} = 7.95 Hz), 3.26 (s, 3H, CH_3O), 2.64–2.43 (m, 4H, H-6, H-6', H-6", H-6'"), 1.44, 1.42, 1.25(2) (3s, 12H, $C(CH_3)_2$).

^{13}C NMR ($CDCl_3$): δ = 137.2 (C_{ipso}), 128.5, 128.0, 127.7 (CH(Ph)), 112.9, 111.7 ($C(CH_3)_2$), 106.9 (C-1), 105.0 (C-1'), 84.8 (C-2), 82.3 (C-2'), 81.7, 81.4 (C-4', C-3'), 80.5 (C-4), 79.8 (C-3), 78.6, 78.5 (C-7, C-7'), 72.2 CH_2(Ph), 68.2, 67.2 (C-5, C-5'), 54.4 (OCH_3), 26.8, 26.3, 25.9 ($C(CH_3)_2$), 25.0, 24.8 (C-6, C-6'), 24.6 (2 $C(CH_3)_2$).

$C_{28}H_{38}O_{10}$	calcd	C	62.91	H	7.16
(534.60)	found	C	62.81	H	7.01

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