Syntheses of methyl glycosides of 6-deoxyheptoses

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Received May 20, 1993

This paper is dedicated to Professors David B. MacLean and Ian D. Spenser

GERALD O. ASPINALL, ARMANDO G. MCDONALD, and RAMESH K. SOOD. Can. J. Chem. **72**, 247 (1994).

Methyl α-D-glycopyranosides of 6-deoxy-D-*altro*-heptose, 6-deoxy-D-*manno*-heptose, and 6-deoxy-D-*talo*-heptose have been prepared. Displacements of methyl 2,3,4-tri-*O*-benzylhexopyranoside 6-trifluoromethanesulfonates with potassium cyanide, followed by reduction of the resulting heptopyranosidurononitriles with diisobutylaluminum hydride, hydrolysis of the imine, further reduction with sodium borohydride, and catalytic *O*-debenzylation, give the corresponding methyl 6-deoxyheptopyranosides. Configurational change at C-4 of methyl 6-deoxy-7-*O*-*tert*-butyldiphenylsilyl-α-D-*manno*-heptopyranoside to give the *talo* isomer was effected by oxidation followed by stereoselective reduction. ^{1}H nuclear magnetic resonance data of the glycosides, and gas chromatography of acetylated glycosides of (*R*)- and (*S*)-2-butanol serve to establish ring and enantiomeric configurations of the parent sugars when these are encountered as constituents of lipopolysaccharides or extracellular carbohydrate polymers, as in *Campylobacter* species.

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On a préparé les α-D-glycopyranosides de méthyle des 6-désoxy-α-D-*altro*-heptose, 6-désoxy-D-*manno*-heptose et 6-désoxy-D-*talo*-heptose. Les déplacements des 6-trifluorométhanesulfonates des 2,3,4-tri-*O*-benzylhexopyranosides de méthyle par le cyanure de potassium, suivis par la réduction des heptopyranosidurononitriles par l'hydrure de diisobutylaluminium, une hydrolyse de l'imine, une nouvelle réduction par le borohydrure de sodium et finalement une *O*-débenzylation catalytique conduit aux 6-désoxyheptopyranosides de méthyles correspondants. Pour effectuer un changement de configuration en C-4 du 6-désoxy-7-*O*-*tert*-butyldiphénylsilyl-α-D-*manno*-heptopyranoside de méthyle dans le but d'obtenir l'isomère *talo*, on a procédé à une oxydation suivie par une réduction sélective. On a fait appel aux données de la résonance magnétique nucléaire du ^{1}H des glycosides et à la chromatographie gazeuse des glycosides acétylés par les (*R*)- et (*S*)-2-butanol pour établir la grandeur des cycles et les configurations énantiomères des sucres parents rencontrés comme constituants des lipopolysaccharides ou comme hydrates de carbones polymériques extracellulaires, comme dans les espèces *Campylobacter*.

[Traduit par la rédaction]

Introduction

6-Deoxyheptoses are rare constituents of bacterial polysaccharides, and until very recently only two examples had been reported, 6-deoxy-D-*galacto*-heptose as a component sugar of the *Yersinia (Pasteurella) pseudotuberculosis* type II A lipopolysaccharide (LPS) (1), and 6-deoxy-D-*altro*-heptose as a constituent of the polysaccharide antigen from the Gram-positive *Eubacterium saburreum*, strain L 49 (2). In a series of investigations on the lipopolysaccharides from *Campylobacter* species further examples have been found. The O antigen chains in LPS from *C. jejuni* serotypes O:23 and O:36 have been shown to contain units of four closely related types, →3)-β-D-Glc*p*NAc-(1 → 3)-α-D-Gal*p*-(1 → 2)-α-*altro*-Hep*p*-(1-, in which the variable heptose residues differed in the presence or absence of deoxygenation at C-6 and methylation at O-3 (3), but were of unspecified enantiomeric configurations. One of the variants was 6-deoxy-α-*altro*-heptose, but of different ring size from that from the *E. saburreum* polysaccharide. From another *Campylobacter* strain, *C. coli* serotype O:30, a water-soluble extracellular antigenic polymer has been characterized as a teichoic acid-like structure with a poly(ribitol phosphate) backbone with pendant glycobiosyl units, 6-d-Hep*p*-(1 → 3)-β-D-Glc*p*NAc-(1-. As with the 6-deoxy-α-*altro*-heptose, the relative configuration of this deoxyheptose constituent was established by nmr correlation spectroscopy and shown to be β-*talo* (4), but without designation of absolute configuration. In both instances it was necessary to synthesize reference compounds of defined enantiomeric configuration from which to provide, separately, diastereomeric mixtures of (*R*)- and (*S*)-2-butyl glycoside acetates (5) for comparison with the corresponding derivatives from the polysaccharide constituents.

Garegg, Lindberg, and co-workers (6, 7) have reported syntheses of 6-deoxyheptoses with the D-*manno* and D-*galacto* configurations by homologations at C-6 of the corresponding methyl 2,3,4-tri-*O*-benzyl-hexodialdo-1,5-pyranosides by reaction with methoxymethylenetriphenylphosphorane, but with rather unsatisfactory yields. We describe here an alternative approach with the cyanide displacement of 2,3,4-tri-*O*-benzyl-α-D-glycopyranoside 6-sulfonate esters used by Baer et al. (8) in the preparation of 6-deoxy-D-*gluco*-heptopyranosidurononitriles, followed by a two-step reduction involving treatment with diisobutylaluminum hydride (DIBAH), hydrolysis of the resulting imine, and further reduction with sodium borohydride. In the event this proved to be a fortunate choice for the synthesis of the *altro* derivative since, as reported in the accompanying paper (9), the attempted formation of the α-D-*altro*-hexodialdo-1,5-pyranoside by oxidation of methyl 2,3,4-tri-*O*-benzyl-α-D-altropyranoside (**1**) (10) was accompanied by configurational inversion at C-5 with the formation of the corresponding β-L-*galacto* derivative as the major product.

Results and discussion

Altrose derivative **1** was converted into the trifluoromethanesulfonate for immediate displacement by cyanide to give the 6-deoxyheptosidurononitrile **2**. Two-step reduction of **2** with DIBAH, with hydrolysis of the imine and further treatment with sodium borohydride, afforded methyl 2,3,4-tri-*O*-benzyl-6-deoxy-α-D-*altro*-heptopyranoside (**3**) in adequate yield, and

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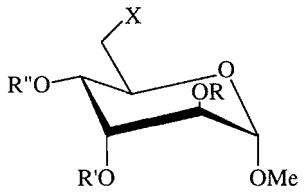
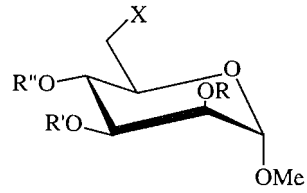
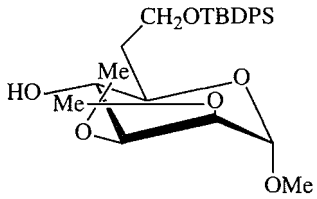


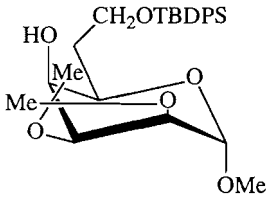
1 R = R' = R" = Bn; X = OH
2 R = R' = R" = Bn; X = CN
3 R = R' = R" = Bn; X = CH_2OH
4 R = R' = R" = H; X = CH_2OH
5 R = R' = R" = Ac; X = CH_2OAc



6 R = R' = R" = Bn; X = OH
7 R = R' = R" = Bn; X = CN
8 R = R' = R" = Bn; X = CH_2OH
9 R = R' = R" = H; X = CH_2OH
10 R = R' = R" = Ac; X = CH_2OAc
11 R = R' = R" = H; X = $CH_2OTBDPS$



12 TBDPS = *tert*-butyldiphenylsilyl



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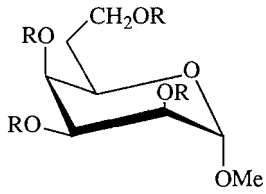

14 R = H
15 R = Ac

thence, by catalytic hydrogenolysis over palladium on carbon, methyl 6-deoxy-α-D-*altro*-heptopyranoside (**4**). For further analytical and spectroscopic characterization a portion of **4** was converted into the tetra-*O*-acetyl derivative (**5**). Hydrolysis of a sample of methyl glycoside **4** followed by reduction and acetylation furnished the 6-deoxyheptitol hexaacetate, which was indistinguishable by gas–liqud chromatography (glc) from the component in the *C. jejuni* serotypes O:23 and O:36 polysaccharide hydrolyzates (3).

In identical manner methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (**6**) (6) was converted successively into the 6-deoxyheptosidurononitrile (**7**), methyl 2,3,4-tri-*O*-benzyl-6-deoxy-α-D-*manno*-heptopyranoside (**8**), the parent methyl glycoside (**9**), and for further characterization the tetra-*O*-acetyl derivative (**10**) of **9**. The previously prepared (6) methyl 6-deoxy-α-D-*manno*-heptopyranoside (**8**) served as a convenient starting material for the synthesis of the C-4 epimer with the *talo* configuration. Protection of O-7 in **8** as the *tert*-butyldiphenylsilyl derivative **11** was followed by isopropylidenation with 2,2-dimethoxypropane in acetone to give methyl 6-deoxy-2,3-di-*O*-isopropylidene-7-*O*-*tert*-butyldiphenylsilyl-α-D-*manno*-heptopyranoside (**12**). The key step in the overall transformation was the Swern oxidation (dimethyl sulfoxide – oxalyl chloride) (11) from which reaction the intermediate deoxyheptosid-4-ulose was immediately treated with sodium borohydride. The reduction proceeded with high diastereoselectivity, only traces of the *manno* starting material (**12**) being detected in the reaction product, and the desired *talo* isomer (**13**) was isolated in chromatographically and spectroscopically homogeneous form in 85% yield. The configurational change at C-4 was confirmed by changes in the ^1H nmr spectrum, notably at H-4, which showed coupling constants $J_{3,4}$ = 9.2 Hz and $J_{4,5}$ = 9.4 Hz. Deprotection of **13** afforded methyl 6-deoxy-α-D-*talo*-heptopyranoside (**14**), which was further characterized as the tetra-*O*-acetate (**15**).

Hydrolysis of **14** and conversion of the reducing sugar into the 6-deoxyheptitol hexaacetate gave a derivative that was indistinguishable by glc from that formed from the 6-deoxyheptose constituent of the *C. coli* O:30 carbohydrate polymer. It was then observed that the three diastereomeric 6-deoxyheptitol hexaacetates could not be differentiated on glc columns. However, hydrolysis of the methyl glycosides **4**, **9**, and **14**, followed by glycosidation with (*R*)- and (*S*)-2-butanol and acetylation, gave in each case equilibrium mixtures of 2-butyl glycoside tetraacetates whose identities were established by chemical ionization (ci) glc-ms. These sets of derivatives served two purposes. The primary purpose was to distinguish the mixtures formed *either* from each of the enantiomeric alcohols and a given sugar anantiomer *or* from an enantiomerically pure alcohol and each sugar enantiomer (Table 1). Thus the reactions of sugars in polysaccharide hydrolyzates with a chiral 2-butanol gave the corresponding mixtures of chiral glycosides whose retention times defined the enantiomeric sugars of immediate interest as 6-deoxy-D-*altro*-heptose from *Campylobacter jejuni* serotype O:23 (3) and 6-deoxy-D-*talo*-heptose from the teichoic acid-like polymer from *C. coli* serotype O:30 (4). In addition the retention times of at least some of the components from each set of 2-butyl glycoside tetraacetates from diastereomeric sugars were sufficiently different to distinguish the parent 6-deoxyheptoses.

The ^1H nmr data were obtained from 1D spectra and, with the aid of ^1H COSY correlations, resonances were assigned for individual carbon-bound protons for the methyl glycosides **4**, **9**, and **14** (Table 2), and the corresponding tetraacetates **5**, **10**, and **15** (Table 2). The vicinal coupling constants $J_{n,n+1}$ were in accord with all glycoside derivatives in the $^4C_1$ conformation. A long-range W coupling between H-2 and H-4 was detected in the COSY spectra of **15**. The observation of such a coupling had been a key factor in the assignment of the *talo* configuration for the 6-deoxyheptose constituent of *C. coli* polymer (4).

Experimental

General procedures

Unless otherwise stated, experimental methods and spectroscopic analyses were performed as described in the previous paper (9).

Derivatives of 6-deoxyheptoses for glc and glc–ms analysis

(*a*) Methyl 6-deoxyheptopyranosides were hydrolyzed in 1 M trifluoroacetic acid for 4 h at 100°C, and the hydrolyzates were concen-

TABLE 1. The glc retention times of (*R*)- and (*S*)-2-butyl glycoside tetra-*O*-acetates of 6-deoxyheptoses

Parent sugar configuration	Retention times (min)[a]							
	(*R*)-2-Butyl glycosides				(*S*)-2-Butyl glycosides			
6-Deoxy-D-*altro*-	18.57	20.25	20.37	21.68	18.38	20.34	20.65	21.96
6-Deoxy-D-*manno*-	17.59	19.85	19.95	21.54	17.19	19.69	20.23	
6-Deoxy-D-*talo*-	18.73	20.22	22.74		19.29	19.94	22.62	

[a]Gas–liquid chromatography was performed on a narrow bore DB-23 (30 m × 0.25 mm) column, 200°C (10 min), 200° → 240°C at 2°/min.

TABLE 2. The ^{1}H nmr chemical shift data (ppm) and vicinal coupling constants (Hz) for methyl 6-deoxy-α-D-heptopyranosides **4**, **9**, and **14**, and their respective 2,3,4,7-tetra-*O*-acetyl derivatives **5**, **10**, and **15**[a]

Sugar ring configuration	H-1 ($J_{1,2}$)	H-2 ($J_{2,3}$)	H-3 ($J_{3,4}$)	H-4 ($J_{4,5}$)	H-5	H-6 ($J_{5,6}$)	H-6′ ($J_{5,6'}$)	H-7
altro (**4**)	4.54 (2.9)	3.73 (2.4)	3.85 (3.1)	3.67 (8.4)	3.96	1.95 (2.9)	1.75 (10.3)	3.74
manno (**8**)	4.65 (1.5)	3.87 (3.4)	3.67 (9.5)	3.45 (9.7)	3.60	2.06 (2.4)	1.67 (7.8)	3.57
talo (**14**)	4.77 (bs)	3.78 (~1)	3.79 (3.3)	3.72 (~1)	3.91	1.93 (9.9)	1.75 (4.2)	3.67
altro (**5**)	4.58 (~1)	4.94 (3.9)	5.21 (3.5)	5.00 (9.5)	4.17	1.97 (3.0)	1.78 (7.5)	4.27
manno (**10**)	4.65 (1.5)	5.24 (3.4)	5.31 (10.0)	5.12 (9.9)	3.87	1.90 (2.9)	1.83	4.23
talo (**15**)	4.77 (1.1)	5.10 (2.5)	5.29 (3.5)	5.21 (<2)	4.13	2.01 (12.2)	1.78 (3.2)	4.22

[a]Resonances of methyl glycoside and *O*-acetyl protons are omitted.

trated and converted into 6-deoxyheptitol hexaacetates for glc analysis (12).

(*b*) Hydrolyzates were converted in chiral 2-butyl glycoside tetraacetates as described by Gerwig et al. (5) for glc analysis. The identities of the desired chiral glycosides were confirmed by ci glc–ms.

*Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-*α*-D-*altro*-heptopyranosyluronononitrile 2*

Triflic anhydride (0.79 mL, 4.68 mmol) was added to a solution of 2,6-di-*tert*-butylpyridine (1.16 mL, 5.1 mmol) in dry dichloromethane at −15°C and, after stirring for 10 min, a solution of **1** (1.08 g) in dry dichloromethane was added dropwise and the mixture was stirred at −15°C for 1 h. The solution was poured into aqueous 5% sodium hydrogen carbonate, the organic layer was separated, dried, and concentrated. The residual syrup in acetonitrile:water (9:1, 30 mL) was treated with potassium cyanide (0.24 g, 3.68 mmol) for 2.5 h at room temperature, the solution was concentrated, and the residue was dissolved in ethyl acetate, washed successively with 1 M HCl, aqueous saturated $NaHCO_3$, and water, dried, and concentrated. The residual syrup was chromatographed on silica gel (light petroleum – ethyl acetate, 3.5:1) to give compound **2** (0.9 g, 82%), $[\alpha]_D$ +85 (*c* 1.35); ir ν_{max}: 2250 (C≡N) cm^{-1}; ^{1}H nmr δ: 4.68–4.26 (m, 8H, H-1, H-5, 3 × CH_2Ph), 3.81 (t, 1H, H-2), 3.71 (d, 1H, H-3), 3.61 (3.61 (dd, 1H, $J_{3,4}$ 3.0 Hz, $J_{4,5}$ 9.66 Hz), 3.42 (s, 3H, OMe), 2.80 (dd, 1H, $J_{5,6}$ 3.08 Hz, $J_{6,6'}$ 16.7 Hz, H-6), and 2.5 (dd, 1H, $J_{5,6'}$ 8.3 Hz, H-6′). Anal. calcd. for $C_{29}H_{31}NO_5$: C 73.55, H 6.59, N 2.95; found: C 73.83, H 6.45, N 2.93.

*Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-*α*-D-*altro*-heptopyranoside 3*

DIBAH (1 M in hexane, 0.73 mL) was added to a solution of **2** (0.314 g, 0.66 mmol) in dry toluene (5 mL) at 0°C; after 30 min a further quantity of DIBAH solution (0.2 mL) was added and reaction was terminated after 10 min by the addition of methanol (0.5 mL) followed by aqueous 2 M HCl (0.5 mL). The mixture was stirred for 45 min and filtered, the aqueous layer in the filtrate was extracted with ether, and the combined organic layers were washed with 2 M HCl, aqueous saturated $NaHCO_3$, and water, dried, and concentrated. Sodium borohydride (10 mg) was added to the residual syrup in methanol (5 mL); the solution was stirred at room temperature for 30 min before excess of hydride was destroyed by the addition of acetone, evaporated to dryness, and then evaporated again (×3) with methanol. The residue in ethyl acetate was washed successively with aqueous 2 M HCl, saturated $NaHCO_3$, and water, dried, and concentrated to a syrup that was chromatographed on silica gel (light petroleum – ethyl acetate, 2:1) to give **3** (0.168 g, 53%), $[\alpha]_D$ +87 (*c* 0.8); ^{1}H nmr δ: 4.67–4.26 (m, 8H, H-1, H-5, and 3 × CH_2Ph), 3.83–3.69 (m, 4H, H-2,3,7,7′), 3.56 (dd, 1H, $J_{3,4}$ 3.1 Hz, $J_{4,5}$ 9.2 Hz, H-4), 3.39 (s, 3H, OMe), 3.17 (t, 1H, exchanged with D_2O, OH), 2.13–2.05 (m, 1H, H-6), and 1.79 (m, 1H, H-6′). Anal. calcd. for $C_{29}H_{34}O_6$: C 72.78, H 7.16; found: C 72.68, H 7.21.

Methyl 6-deoxy-α-D-altro-heptopyranoside 4 and the tetra-O-acetyl derivative 5

Compound **3** (75 mg, 0.15 mmol) in ethanol (5 mL) was hydrogenolyzed over palladium 5% on carbon for 72 h. Filtration of the mixture and concentration of the filtrate afforded **4** (30 mg), $[\alpha]_D$ +100 (*c* 1.98, water); ^{13}C nmr (D_2O) δ_C: 100.6 ($^1J_{C,H}$ 166.9 Hz, C-1), 58.3 (C-7), 55.7 (OMe), 32.7 (C-6). Acetylation of a sample of **4** followed by chromatography on silica gel (light petroleum – ethyl acetate, 2.5:1) furnished tetraacetate **5**, which gave a single peak on glc (program A, isothermal at 200°C), $R_{[Me\ Ac_4\ \alpha\text{-D-}Manp]}$ 1.33, $[\alpha]_D$ +77 (*c* 1.01); ^{13}C nmr δ_C: 170.8, 169.9, 169.6, 169.2 (4 × CH_3CO), 98.5 ($^1J_{C,H}$ 167.3 Hz, C-1), 60.3 (C-7), 55.4 (OMe), 30.2 (C-6), 20.8, 20.75, 20.7, 20.6 (4 ×

CH_3CO). Anal. calcd. for $C_{16}H_{24}O_{10}$: C 51.05, H 6.42; found: C 51.13, H 6.41.

Methyl 2,3,4-tri-O-benzyl-6-deoxy-α-D-manno-heptopyranosyluruononitrile 7

Conversion of compound **6** (4.03 g, 8.68 mmol) into the triflate ester, and thence by reaction with potassium cyanide, as described for **2**, yielded **7** (2.43 g, 59%), $[\alpha]_D$ +44 (*c* 1.35); ir ν_{max}: 2240 (C≡N) cm^{-1}; ^1H nmr δ: 4.70 (s, 1H, H-1), 3.87 (dd, 1H, $J_{3,4}$ 8.9 Hz, H-3), 3.79 (dd, 1H, $J_{2,3}$ 2.8 Hz, H-2), 3.76 (dd, 1H, $J_{4,5}$ 9.1 Hz, H-4), 3.74 (dd, 1H, $J_{5,6}$ 5.5 Hz, $J_{5,6'}$ 2.9 Hz, H-5), 3.34 (s, 3H, OMe), 2.74 (dd, 1H, $J_{6,6'}$ 16.4 Hz, H-6), and 2.5 (m, 1H, H-6′). Anal. calcd. for $C_{29}H_{31}NO_5$: C 73.55, H 2.95, N 2.95; found: C 73.21, H 6.53, N 2.81.

*Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-α-D-manno-heptopyranoside 8*

Reduction of **7** (1.8 g, 3.8 mmol) with DIBAH, as described for the preparation of **3**, yielded **8** (0.91 g, 50%), $[\alpha]_D$ +31 (*c* 1.8) (lit. (6) $[\alpha]_D$ +39); ^1H nmr δ: 4.66 (d, $J_{1,2}$ 1.8 Hz, H-1), 3.86 (dd, 1H, $J_{3,4}$ 9.0 Hz, H-3), 3.79 (dd, 1H, $J_{2,3}$ 2.8 Hz, H-2), 3.76 (m, 2H, H-5, H-7), 3.75 (dd, 1H, $J_{4,5}$ 8.8 Hz, H-4), 3.30 (s, 3H, OMe), 2.10 (m, 1H, H-6), and 1.84 (m, 1H, H-6′). Anal. calcd. for $C_{29}H_{34}O_6$: C 72.78, H 7.16; found: C 72.42, H 7.13.

*Methyl 6-deoxy-α-D-manno-heptopyranoside 9 and the tetra-*O*-acetyl derivative 10*

Hydrogenolysis of **8** (0.91 g, 1.90 mmol), as described for the conversion of **3** into **4**, afforded **9** (0.33 g, 84%); ^{13}C nmr (D_2O) δ_C: 100.9 ($^1J_{C,H}$ 170.2 Hz, C-1), 58.4 (C-7), 54.8 (OMe), 33.4 (C-6). Acetylation of a sample of **9** followed by chromatography on silica gel (light petroleum – ethyl acetate, 2.5:1) furnished tetraacetate **10**, which gave a single peak on glc (program A, isothermal at 200°C), $R_{[Me\ Ac_4\ \alpha\text{-D-Man}p]}$ 1.29, $[\alpha]_D$ +59 (*c* 1.65) (lit. (6) $[\alpha]_D$ +62); ^{13}C nmr δ_C: 170.8, 169.9, 169.85, 169.8 (4 × CH_3CO), 98.4 ($^1J_{C,H}$ 172.4 Hz, C-1), 60.2 (C-7), 55.0 (OMe), 30.4 (C-6), 20.8 (2C), 20.7, 20.6 (4 × CH_3CO). Anal. calcd. for $C_{16}H_{24}O_{10}$: C 51.05, H 6.42; found: C 51.30, H 6.33.

*Methyl 6-deoxy-7-*O*-tert-butyldiphenylsilyl-α-D-manno-heptopyranoside 11*

Imidazole (0.26 g, 2.4 equiv.) and *tert*-butyldiphenylsilyl chloride (0.523 g, 1.2 equiv.) were added successively to compound **10** (0.33 g, 1.59 mmol) in *N,N*-dimethylformamide (5 mL) and the mixture was stirred at 25°C for 16 h. Dichloromethane was added to the mixture, and the solution was washed with water, dried, concentrated, and chromatographed on silica gel (light petroleum – ethyl acetate, 1:4) to give **11** (0.446 g, 63%), $[\alpha]_D$ +43 (*c* 1.5); ^1H nmr δ: 7.66, 7.44–7.25 (m, 10H, aromatic), 4.64 (d, 1H, $J_{1,2}$ 0.9 Hz, H-1), 3.92 (dd, 1H, $J_{2,3}$ 3.3 Hz, H-2), 3.84 (m, 2H, H-7), 3.80 (dd, 1H, $J_{3,4}$ 8.8 Hz, H-3), 3.70 (dd, 1H, $J_{5,6}$ 4.2 Hz, H-5), 3.60 (dd, 1H, $J_{4,5}$ 9.4 Hz, H-4), 3.27 (s, 3H, OMe), 2.11 (m, 1H, H-6), 1.75 (m, 1H, H-6′), and 1.04 (s, 9H, *tert*-butyl). Exact Mass calcd. for $C_{24}H_{34}O_6Si$ + H: 447.2203; found: 447.2182.

*Methyl 6-deoxy-2,3-*O*-isopropylidene-7-*O*-tert-butyldiphenylsilyl-α-D-manno-heptopyranoside 12*

A solution of compound **11** (0.411 g, 9.21 mmol) in acetone (5 mL) containing 2,3-dimethoxypropane (0.4 mL) and *p*-toluenesulfonic acid (5 mg) was stirred at 25°C for 1 h. The reaction was quenched by the addition of $NaHCO_3$ (20 mg), the mixture was concentrated, and the residue in dichloromethane was washed successively with aqueous $NaHCO_3$ and water, dried, and concentrated. The residue was chromatographed on silica gel (light petroleum – ethyl acetate, 4:1) to give **12** (0.391 g, 87%), $[\alpha]_D$ +22 (*c* 1.05); ^1H nmr δ: 7.66, 7.45–7.26 (m, 10H, aromatic), 4.85 (s, 1H, H-1), 4.13 (dd, 1H, $J_{3,4}$ 9.2 Hz, H-3), 4.12 (dd, 1H, $J_{2,3}$ ~3 Hz, H-2), 3.85 (m, 2H, H-7), 3.73 (m, 1H, H-5), 3.60 (t, 1H, $J_{4,5}$ 9.4 Hz, H-4), 3.33 (s, 3H, OMe), 2.03 (m, 1H, H-6), 1.83 (m, 1H, H-6′), 1.53, 1.36 (2s, each 3H, $C(CH_3)_2$), 1.06 (s, 9H, *tert*-butyl). Exact Mass calcd. for $C_{27}H_{38}O_6Si$ + H: 487.2516; found: 487.2490. Anal. calcd. for $C_{27}H_{38}O_6Si$: C, 66.69, H 7.88; found: C 66.86, H 7.86.

*Methyl 6-deoxy-2,3-*O*-isopropylidene-7-*O*-tert-butyldiphenylsilyl-α-D-talo-heptopyranoside 13*

A solution of **12** (0.361 g, 0.74 mmol) in dichloromethane (5 mL) was added dropwise to a stirred mixture of Me_2SO (0.23 mL, 3.24 mmol) in dichloromethane (4 mL) and oxalyl chloride (1.2 mL, 0.24 mmol) in dichloromethane (10 mL) at −78°C, at which temperature the mixture was kept for 45 min. The reaction was quenched by the addition of triethylamine (2 mL) in dichloromethane (5 mL); it was stirred for 30 min at −78°C and then brought slowly to 20°C. The solution was diluted with dichloromethane (20 mL) and washed three times with water, dried, and concentrated. The residual 4-ulose was reduced by stirring with sodium borohydride (56 mg, 2 equiv.) in methanol (10 mL) at 25°C for 90 min. Excess of hydride was destroyed by the addition of acetone, the mixture was concentrated, evaporated with methanol (×3), and the residue was chromatographed on silica gel (light petroleum – ethyl acetate, 4:1) to give **13** (0.306 g, 85%), $[\alpha]_D$ +27 (*c* 0.82); ^1H nmr δ: 7.68–7.62, 7.46–7.26 (m, 10H, aromatic), 4.94 (s, 1H, H-1), 4.22 (dd, 1H, $J_{3,4}$ 5.1 Hz, H-3), 4.05 (dd, 1H, $J_{2,3}$ 6.7 Hz, H-2), 4.01 (t, 1H, $J_{4,5}$ 4.9 Hz, H-4), 3.88 (m, H, H-7), 3.79 (m, 1H, H-7′), 3.57 (d, 1H, $J_{5,6}$ <2 Hz, H-5), 3.38 (s, 3H, OMe), 2.04 (m, 1H, H-6), 1.81 (m, 1H, H-6′), 1.58, 1.38 (2s, each 3H, $C(CH_3)_2$), and 1.05 (s, 9H, *tert*-butyl). Exact Mass calcd. for $C_{27}H_{38}O_6Si$ + H: 487.2516; found: 487.2534. Anal. calcd. for $C_{27}H_{38}O_6Si$: C, 66.69, H 7.88; found: C 66.46, H 7.74.

Methyl 6-deoxy-α-D-talo-heptopyranoside 14

A solution of **13** (0.246 g, 5.06 mmol) in oxolane (5 mL) was treated with 1 M tetrabutylammonium fluoride in oxolane (1.4 mL) at 25°C for 30 min and concentrated. The residue was treated with aqueous saturated $NaHCO_3$ (20 mL), the mixture was extracted with ethyl acetate, and the extract was dried and concentrated. The residual product was heated in aqueous 2 M acetic acid (5 mL) at 80°C for 2 h, and the solution was concentrated. A solution of the residue in water was extracted with dichloromethane, and the aqueous layer was concentrated to a syrup that was chromatographed on silica gel (methanol–dichloromethane, 1:9) to give **14** (90 mg, 86%), $[\alpha]_D$ +84 (*c* 3.0, water); ^{13}C nmr (D_2O) δ_C: 101.6 ($^1J_{C,H}$ 171.3 Hz, C-1), 58.3 (C-7), 55.0 (OMe), 33.0 (C-6). Acetylation of a sample of **9** followed by chromatography on silica gel (light petroleum – ethyl acetate, 2.5:1) furnished tetraacetate **15**, which gave a single peak on glc (program A, isothermal at 200°C); $R_{[Me\ Ac_4\ \alpha\text{-D-Man}p]}$ 2.25, $[\alpha]_D$ +81 (*c* 1.02); ^{13}C nmr δ_C: 170.7, 170.3, 169.9, 169.5 (4 × CH_3CO), 99.4 ($^1J_{C,H}$ 172.2 Hz, C-1), 60.4 (C-7), 55.1 (OMe), 29.9 (C-6), 20.8, 20.7, 20.6, 20.5 (4 × CH_3CO). Anal. calcd. for $C_{16}H_{24}O_{10}$: C 51.05, H 6.42; found: C 50.87, H 6.28.

Acknowledgements

We thank the Natural Sciences and Engineering Research Council of Canada for financial support through its strategic and research grants programs. We thank Dr. Henrianna Pang and her associates for accurate mass determinations and for the ci glc–ms experiments.

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