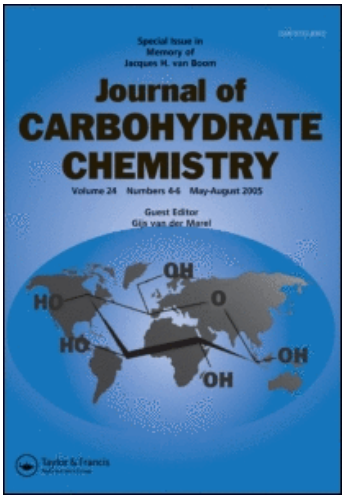

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Two Unusual Carbohydrate Reactions: Nucleophilic Ring Opening of an Anhydrosugar and Reductive Elimination with Co-occurring Hydrogenation

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Two Unusual Carbohydrate Reactions: Nucleophilic Ring Opening of an Anhydrosugar and Reductive Elimination with Co-occurring Hydrogenation

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Treatment of the 1,6-anhydrosugar epoxide **5** with a cyano-Gilman cuprate [(CuCN (6 eq.), MeLi (12 eq.)] surprisingly led to the open chain rearranged (2S,3R)-1,2-dihydroxy-3,6-dimethylheptan-4-one (**7**), structurally confirmed by conversion to the corresponding diacetate **8**. Another unusual reaction was found by hydrogenation of the 2-tosyl-1-bromosugar **11**, leading in one operation to the twofold deoxygenated chiral pyran derivative **14**. This procedure might prove to be useful in the rapid deoxygenation of sugar derivatives.

Keywords Cyano cuprates, Epoxide opening, 1,6-Anhydro sugars, Hydrogenation, Deoxygenation

INTRODUCTION

In connection with our ongoing investigation on the use of carbohydrates as building blocks for complex natural products,[1,2] we investigated further reactions of anhydrosugar derivatives. In the course of these transformations, by serendipity, we observed two unusual transformations that are mechanistically interesting and may be of general use with related substrates.

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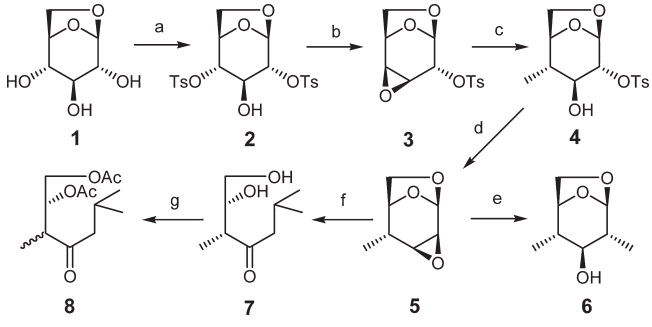
RESULTS AND DISCUSSION

Epoxide Opening

Aiming at new chiral functionalized methyl-branched stereotriads as building blocks for macrolides, the opening of sugar epoxides with methyl cuprates was one of the key reactions. Thus, in the first of the unusual reactions described here, we investigated the reaction of epoxide **5** with the cyano-Gilman cuprate or Lipshutz "higher-order" methyl cyanocuprate.[3] The epoxide **5** was prepared using a known sequence starting with levoglucosan (**1**)[4] via the bis-tosylate **2** and the galacto epoxide **3** (Sch. 1).[5,6] The opening of the epoxide **3** was achieved by reaction with methylmagnesium bromide at −44°C to 0°C, catalyzed with a small amount of CuI, to afford the methylated alcohol **4** regioselectively.[5] The key epoxide **5** was then generated nearly quantitatively by base (NaH) catalyzed ring closure.[7,8]

To arrive at the dimethyl anhydro sugar **6**, a useful macrolide building block,[8] the epoxide **5** was first reacted with the Gilman cuprate Me_2CuLi (generated from MeLi and CuI) as the methyl nucleophile and the expected methyl adduct **6** was formed stereo- and regioselectively and isolated in 67% yield.[5,8,9] In a second reaction, the conversion with the cyano-Gilman cuprate was also tested since these cuprates have been shown to have unusual reactivity toward sugar epoxides.[1,2] Surprisingly, in addition to the expected compound **6** (31%), a very polar ring opened product was also formed as the major product and identified as the ketone **7** in 67% yield (Sch. 1). In the ^{13}C NMR spectrum of **7**, the signal for a tertiary carbon atom at C-1 at 101 ppm is shifted to 48 ppm. Furthermore, a signal for a new quaternary carbon atom for C-3 at 215 ppm was typical for a carbonyl group and also signals at 51 ppm for a secondary carbon at C-2 and at 22.4 ppm and 22.5 ppm for two primary carbons at C-1 could be detected. To further



Scheme 1: a) TsCl (2.6 eq.), pyridine/acetone (1:1, 2 h, 71%); b) NaOMe (2 eq.), MeOH, 4 h, 96%; c) MeMgCl (4 eq.), CuI (kat.), THF, −44°C to 0°C 72%; d) NaH, THF, 0°C, 4 h, RT, 96%; e) CuI (5 eq), MeLi (10 eq.), Et_2O/THF, −76°C to 20°C, 12 h, 67%; f) CuCN (6 eq.), MeLi (12 eq.), Et_2O/THF, −78°C to 0°C, 2 h 20°C: **6**, 63%, **7**, 31%; g) Ac_2O, pyridine, DMAP, 71%.

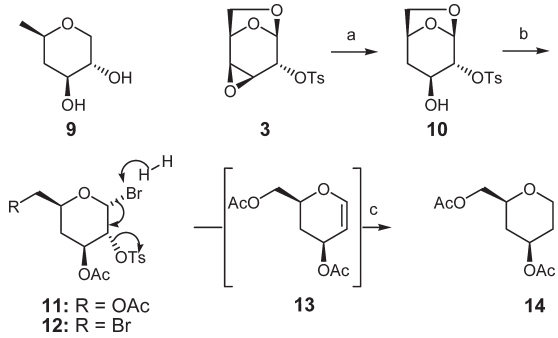
confirm the unusual structure, the diol was acetylated. However, under the action of the basic dimethylaminopyridine, the methyl group in the α-position to the carbonyl was epimerized to a 1:1 mixture of the diacetates **8**. However, the gross structure of **7** was confirmed by all spectroscopic data, in particular the mass spectra and the typical downfield shift of the signals for the acetylated hydrogens by ca. 1 ppm in the ^{1}H NMR spectrum.

The mechanism of the reaction is not entirely clear. However, reaction of the cyclic acetal, activated by the mild cuprate Lewis acid, with a methyl nucleophile may be the first step. This could be followed by rearrangement of the epoxide to a ketone, β-elimination with opening of the pyran ring to an enone, and Michael addition to the enone to yield the dimethylated product **7**.

Hydrogenative Deoxygenation

In the second part, we describe a new variation to remove two heteroatoms (originally sugar oxygen atoms) from sugar derivatives in one easily performed hydrogenative step. The reaction was found in an attempt to synthesize naturally occurring pyrans such as **9**, isolated together with a number of stereoisomers by Reátegui et al.[10] from the fungus *Ophioceras venezuelense* (Sch. 2). In our synthetic scheme, we planned to use the same intermediate **3**, which should provide the 4-deoxy sugar **10** under reductive conditions. In the remaining steps, the three oxygen functions at C-1, C-2, and C-5 had to be removed.

The first step of reduction of the epoxide in **3** was described by Černý et al., who employed sodium borohydride in dimethoxyethane and boron trifluoride catalysis.[11] This last procedure provided the deoxygenation product **10** in 92% yield. Opening of the anhydro bridge with hydrogen bromide in acetic acid gave a mixture of the bromo acetate **11** and the dibromide **12** in 45% and 34% yield, respectively.[12] We attempted several methods for the reductive



Scheme 2: a) $NaBH_4$, $BF_3{\cdot}Et_2O$, 1,2-dimethoxyethane, 50°C, 92%; b) 33% HBr in CH_3COOH, $(CH_3CO)_2O$, 24 h 20°C, 6 h reflux: **11**: 45%; **12**: 34%; c) Raney nickel, H_2, EtOH, RT, 30 min, 64%.

removal of the bromides in **11** and **12**. Whereas the dibromide reacted to form a complex mixture of different products not yet fully analyzed, the Raney nickel-catalyzed hydrogenation in ethanol of the monobromide **11** rapidly led to one single isolable product. Surprisingly, not only the anomeric bromine was reduced, but also the neighboring tosylate group. Normally, carbohydrate tosylates are not easily reduced by hydrogenation. We assume that the anomeric bromine plays an active part in this transformation. Related to the sodium iodide-mediated elimination of 1,2-bis-tosylates, the attack of hydrogen on the bromine atom may induce elimination to the intermediate olefin **13** that is hydrogenated to the pyran **14**. The process may as well proceed via radical intermediates, not shown in Scheme 2. The reaction might prove useful in the rapid and easy 1,2-deoxygenation of sugar derivatives, in particular for generation of chiral tetrahydropyran derivatives.

EXPERIMENTAL

General

Thin-layer chromatography was performed on precoated TLC plates (silica gel). Melting points were measured with a Gallenkamp apparatus and are not corrected. NMR spectra were recorded on a Bruker Avance 500 at the following frequencies: 500.13 MHz (^{1}H) and 125.76 MHz (^{13}C). Chemical shifts of ^{1}H and ^{13}C NMR spectra are reported in ppm downfield from TMS as an internal standard. Optical rotations were measured at 25°C on a Perkin-Elmer Polarimeter 241. Mass spectra were recorded using a Finnigan MAT 8430 spectrometer in the electron-impact mode at 70 eV and chemical ionization, and are reported as m/z values and relative abundances. The infrared spectra were recorded using a FT-IR Spectrometer Nicolet 510 P.

4-Methyl-1,6:2,3-dianhydro-β-D-mannopyranose (5)

The epoxide was generated from the known hydroxy tosylate **4**[5] in a modification using sodium hydride instead of MeONa. A solution of **4** (7.00 g, 21.4 mmol) in THF (300 mL) was treated at 0°C with NaH (60% in oil, 1.7 g, 31.1 mmol) in THF (60 mL). The mixture was stirred 3 h at 20°C. For workup, an aqueous NH_4Cl solution (10 mL) was added. After stirring for 1 h, the product was extracted with diethyl ether (3 × 30 mL), the organic phase was dried ($MgSO_4$) and filtered, and the solvent was removed at reduced pressure. The epoxide was purified by chromatography on silica gel using petroleum ether/EtOAc 7:3 as the eluent to afford **5** as an oil (3.03 g, 19.5 mmol, 96%). $[\alpha]_D = -23.2^\circ$ ($c = 1.43$, $CHCl_3$), (ref. [5] -24.6° ($c = 1.57$, $CHCl_3$)). ^{1}H NMR (200 MHz, $CDCl_3$): 1.20 (d, $J_{7,4} = 7.4$ Hz, 3H, 7-H), 2.00 (m, 1H, 4-H), 2.76 (dd, $J_{3,2} = 4.0$ Hz, $J_{3,4} = 0.6$ Hz, 1H, 3-H), 3.26 (m, 1H,

2-H), 3.55–3.60 (m, 2H, 5-H, 6-H_a), 4.00 (m, 1H, 6-H_b), 5.54 (d, $J_{1,2} = 3.2$ Hz, 1H, 1-H). ^{13}C NMR (50 MHz, $CDCl_3$): 16.7 (q, C-7), 34.6 (d, C-4), 51.6 (d, C-2), 53.9 (d, C-3), 68.7 (t, C-6), 73.7 (d, C-5), 98.3 (d, C-1). MS (EI, 70eV): m/z (%) = 142 (56) [M^+], 101 (55), 98 (44), 97 (12), 83 (65), 73 (50), 71 (70), 57 (100), 55 (98), 47 (60), 43 (57), 39 (40). IR (Film): $\tilde{\nu} = 2962$ (s, C-H), 2957 (s, C-H), 2889 (s, C-H), 2360 (w, O-C-O), 1458 (s, C-H), 1381 (s, C-H), 1170 (s, C-H), 1127, (s, C-O), 1034 (s, C-O), 1003 (s, C-O), 998 (s, C-O).

2,4-Dimethyl-1,6-anhydro-β-D-glucopyranose (6)

A suspension of CuI (5.3 g, 28 mmol) in dry THF (25 mL) was treated at −10°C under argon with methyl lithium (40 mL, 1.6 M, 55 mmol). After stirring this mixture for 10 min at 0°C, the epoxide **5** (1.0 g, 7 mmol) in THF (10 mL) was added. After 40 min at 0°C, stirring was continued at 20°C for 12 h. The solution was diluted with diethyl ether (50 mL) and quenched by addition of a saturated aqueous solution of NH_4Cl (50 mL). The aqueous phase was extracted with diethyl ether (3 × 10 mL), the combined organic phases dried (Na_2SO_4) and filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on silica gel (elution petroleum ether/EtOAc 7:3) to afford **6** as a colorless oil (690 mg, 4.34 mmol, 67%). $[\alpha]_D = -63.3°$ ($c = 1.13$, $CHCl_3$), (ref. [5] −62.4° ($c = 0.82$, $CHCl_3$)). ^{1}H NMR (200 MHz, $CDCl_3$): 1.06 (d, $J_{8,2} = 6.1$ Hz, 3H, 8-H), 1.20 (d, $J_{7,4} = 7.6$ Hz, 3H, 7-H), 1.74 (m, 2H, 2-H, 4-H), 2.65 (brs, 1H, OH), 3.34 (s, 1H, 3-H), 3.72 (dd, $J_{6a,5} = 5.2$ Hz, $J_{6a,6b} = 6.9$ Hz, 1H, 6-H), 4.15 (d, $J_{6b,6a} = 6.9$ Hz, 1H, 6-H), 4.26 (m, 1H, 5-H), 5.23 (d, $J_{1,2} = 13.2$ Hz, 1H, 1-H). ^{13}C NMR (50 MHz, $CDCl_3$): 16.3 (q, C-8), 18.8 (q, C-7), 41.0 (d, C-4), 43.0 (d, C-2), 68.5 (t, C-6), 75.4 (d, C-3), 78.0 (d, C-5), 105.0 (d, C-1). IR (Film): $\tilde{\nu} = 3505$ (brs, O-H), 2960 (m, C-H), 2918 (m, C-H), 2898 (m, C-H), 1503 (w, C-H), 1377 (m, C-H), 1268 (s, C-H), 1170 (s, C-O), 1093 (s, C-O), 1063 (s, C-O).

(2S,3R)-1,2-Dihydroxy-3,6-dimethylheptan-4-one (7)

In a two-neck flask, CuCN (1.88 g, 21 mmol, 6 eq.) was suspended under argon in dry diethyl ether (50 mL). The mixture was cooled to −78°C and treated with methyl lithium (1.6 M in diethyl ether, 26.2 mL, 42 mmol, 12 eq.) and stirred for 15 min at 0°C. The clear solution was then cooled to −78°C and a solution of the epoxide **5** (0.50 g, 3.5 mmol) in dry THF (20 mL) was added by means of a syringe. The reaction vessel was maintained for 1 h at this temperature and then warmed to 20°C. The starting material was converted after 2 h (TLC monitoring) and the reaction was quenched by addition of water (5 mL) and aqueous NH_4Cl solution (25 mL). The mixture was extracted with diethyl ether (3 × 20 mL), the combined organic phases

dried (Na_2SO_4) and filtered, and the solvent removed under reduced pressure. The residue was separated by column chromatography on silica gel (elution with petroleum ether/EtOAc 7:3) to afford **7** (63%) as the major product together with 31% of the cyclic dimethylanhydro sugar **6** (31%), both as colorless oils.

$[\alpha]_D = -26.5^\circ$ ($c = 0.87$, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): 0.86 (d, $J_{8,6} = 6.9$ Hz, 3H, 8-H), 0.88 (d, $J_{7,6} = 6.9$ Hz, 3H, 7-H), 1.03 (d, $J_{9,3} = 15.4$ Hz, 3H, 9-H), 2.09 (m, 1H, 6-H), 2.35 (d, $J_{5,6} = 6.8$ Hz, 2H, 5-H), 2.71 (m, 1H, 3-H), 3.50 (m, 1H, 1a-H), 3.64 (m, 1H, 2-H), 3.77 (br, 1H, 1b-H). ^{13}C NMR (125 MHz, $CDCl_3$): 11.5 (q, C-9), 22.4 (q, C-8), 22.5 (q, C-7), 23.9 (d, C-6), 48.2 (d, C-3), 51.5 (t, C-5), 64.7 (t, C-1), 73.7 (d, C-2), 215.2 (s, C-4). IR (Film): $\tilde{\nu} = 3505$ (brs, O-H), 2968 (m, C-H), 2910 (m, C-H), 2897 (m, C-H), 1713 (C═O), 1376 (m, C-H), 1267 (s, C-H), 1168 (s, C-O), 1093 (s, C-O), 1063 (s, C-O), 989 (s, C-H), 860 (s, C-H). MS (EI, 70 eV): m/z (%) = 175 (7) $[M + H]^+$, 157 (42), 103 (9), 99 (13), 85 (76), 57 (87), 43 (100). MS (CI, 70 eV): m/z (%) = 175 (13) $[M + H]^+$, 157 (60), 141 (60), 57 (100), 85 (2), 57 (87), 43 (23).

(2S,3R)-1,2-Diacetoxy-3,6-dimethylheptan-4-one (8)

A solution of diol **7** in pyridine (0.5 mL) was treated with acetic anhydride (0.1 mL) and DMAP (10 mg). The solution was kept at 20°C for 2 h, quenched by addition of 2 N HCl (2 mL), and extracted with diethyl ether (3 × 20 mL). The combined organic phases were dried (Na_2SO_4) and filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on silica gel (elution petroleum ether/EtOAc 7:3) to afford the diacetate as an oil (18.3 mg, 71%). $[\alpha]_D = +22.44^\circ$ ($c = 0.18$, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.89$ (d, $J_{8,6} = 4.2$ Hz, 3H, 8-H), 0.90 (d, $J_{8,6} = 4.2$ Hz, 3H, 8-H), 0.91 (d, $J_{7,6} = 4.6$ Hz, 3H, 7-H), 0.92 (d, $J_{7,6} = 4.6$ Hz, 3H, 7-H), 1.08 (d, $J_{9,3} = 7.2$ Hz, 3H, 9-H), 1.12 (d, $J_{9,3} = 7.1$ Hz, 3H, 9-H), 2.00 (s, 3H, 10-H), 2.04 (s, 3H, 10-H), 2.05 (s, 3H, 11-H), 2.06 (s, 3H, 11-H), 2.11 (m, 1H, 6-H), 2.15 (m, 1H, 6-H), 2.35 (d, $J_{5,6} = 6.9$ Hz, 2H, 5-H), 2.36 (br, 2H, 5-H), 2.84 (m, 1H, 3-H), 2.93 (m, 1H, 3-H), 4.06 (dd, $J_{1a,1b} = 5.7$ Hz, $J_{1a,2} = 11.8$ Hz 1H, 1a-H), 4.10 (dd, $J_{1a,1b} = 5.3$ Hz, $J_{1a,2} = 11.8$ Hz 1H, 1a-H), 4.26 (dd, $J_{1b,1a} = 3.4$ Hz, $J_{1b,2} = 12.4$ Hz 1H, 1b-H), 4.37 (dd, $J_{1b,1a} = 2.8$ Hz, $J_{1b,2} = 12.4$ Hz 1H, 1b-H), 5.24 (m, 1H, 2-H), 5.33 (m, 1H, 2-H). ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 12.3$ (q, C-9), 12.3 (q, C-9), 20.6 (q, C-10), 20.8 (q, C-10), 22.4 (q, C-11), 22.4 (q, C-11), 22.5 (q, C-8), 22.5 (q, C-7), 24.0 (d, C-6), 24.1 (d, C-6), 46.7 (d, C-3), 46.9 (d, C-3), 50.9 (t, C-5), 50.9 (t, C-5), 62.7 (t, C-1), 63.5 (t, C-1), 71.6 (d, C-2), 72.2 (d, C-2), 169.8 (s, C-12), 170.1 (s, C-12), 170.4 (s, C-13), 170.5 (s, C-13), 210.2 (s, C-4), 210.4 (s, C-4). MS (EI, 70 eV): m/z (%) = 259 (3) $[M + H]^+$, 199 (6), 159 (25), 139 (33), 85 (100), 57 (92). MS (CI, 70 eV): m/z (%) = 259 (54) $[M + H]^+$, 199

(16), 157 (42), 139 (26), 97 (6), 85 (100), 57 (100), 33 (45). IR (Film): $\tilde{\nu} = 2958$ (C-H), 1747 (C=O, ester), 1461 (C-H), 1371 (C-H), 1222 (C-O).

1,6-Anhydro-4-deoxy-2-*O*-tosyl-β-D-xylohexopyranose (10)

A solution of 2-*O*-tosyl-1,6:3,4-dianhydro-*β*-D-galactopyranose (**3**)[5,6] (11.00 g, 37 mmol) and sodium borohydride (5.50 g, 145 mmol) in 1,2-dimethoxyethane (110 mL) was treated dropwise at 20°C over 1 h with boron trifluoride diethyl etherate (11 mL). The mixture was stirred for 20 h (TLC monitoring) and then adjusted to pH = 7 by addition of 5% HCl. The solvents were completely removed at reduced pressure and the residue was diluted with cold water (200 mL) and extracted with CH_2Cl_2 (5 × 100 mL). The combined organic phases were dried ($CaCl_2$) and filtered, the solvent evaporated, and the residue crystallized from CH_2Cl_2/Et_2O/PE to yield **3** (10.20 g, 35.1 mmol, 92%) as a colorless solid. m.p. = 89–90°C (ref. [11] m.p. 89–91°C). $[\alpha]_D = -42^\circ$ ($c = 1.1$, $CHCl_3$), (ref. [11] -40° ($c = 1.0$, $CHCl_3$)). ^{1}H NMR (200 MHz, $CDCl_3$): 1.61 (d, $J_{4a,4b} = 15$ Hz 1H, 4a-H), 2.20 (dd, $J_{4b,3} = 1.3$ Hz, $J_{4b,4a} = 15.3$ Hz, 4b-H), 2.35 (s, 3H, Ar-CH_3), 3.15 (brs, 1H, OH), 3.57 (m, 1H, 3-H), 2.38 (m, 1H, 4-H), 3.85 (m, 1H, 6b-H), 4.08 (d, $J_{6a,6b} = 6.9$ Hz, 1H, 6a-H), 4.17 (d, $J_{2,1} = 4.5$ Hz, 1H, 2-H), 4.44 (m, 1H, 5-H), 5.18 (d, $J_{1,2} = 4.5$ Hz 1H, 1-H), 7.29 (d, $J_{Ar,Ar} = 8.1$ Hz, 2H, Ar-H), 7.74 (d, $J_{Ar,Ar} = 8.3$ Hz, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$): 21.6 (q, Ar-CH_3) 32.5 (t, C-4), 64.8 (d, C-3), 67.6 (t, C-6), 72.1 (d, C-5), 76.9 (d, C-2), 99.0 (d, C-1), 127.8 (d, C-Ar), 127.9 (d, C-Ar), 130.0 (d, C-Ar), 130.1 (d, C-Ar), 133.1 (s, C-Ar), 145.3 (s, C-Ar). MS (EI, 70 eV): m/z (%) = 300 [M^+], 188 (10), 155 (38), 145 (80), 99 (100), 91 (80), 71 (64), 69 (88), 65 (30), 58 (30), 44 (41), 41 (66), 31 (20). HREIMS: Calc. for $C_7H_{12}O_3$ 300.3275. Found 300.0775.

3,6-*O*-Diacetyl-4-desoxy-2-*O*-tosyl-D-xyloyranosylbromide (11)

A solution of tosylate (**3**) (1.000 g, 3.33 mmol) in acetic acid anhydride (6.5 mL) was treated with a 33% solution of HBr in acetic acid (14.5 mL). The mixture was initially stirred for 24 h at 20°C and then heated for 6 h at 70°C (TLC monitoring). The solvent was completely removed at reduced pressure, and the residue treated with a saturated solution of $NaHCO_3$ and then extracted with CH_2Cl_2 (2 × 100 mL). The organic phase was washed with water (2 × 30 mL) and dried (Na_2SO_4), and the solvent removed at reduced pressure. The residue was separated by flash chromatography on silica gel (petroleum ether/EtOAc 1:5) to afford the monobromide **11** (696 mg, 1.5 mmol, 45%) and the dibromide **12** (542 mg, 34%), both as unstable oils. ^{1}H NMR (200 MHz, $CDCl_3$): 1.61 (m, 1H, 4a-H), 1.87 (s, 3H, Ac-CH_3), 2.04 (s, 3H, Ac-CH_3), 2.20 (m, 1H, 4b-H), 2.42 (s, 3H, Ar-CH_3), 4.11 (m, 2H, 6a-H, 6b-H),

4.29–4.43 (m, 2H, 2-H, 3-H), 5.29 (m, 1H, 5-H), 6.42 (d, $J_{1,2} = 3.9$ Hz, 1H, 1-H), 7.32 (d, $J_{Ar,Ar} = 8.1$ Hz, 2H, Ar-H), 7.78 (d, $J_{Ar,Ar} = 7.8$ Hz, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$): 21.0 (q, Ac-CH_3), 21.1 (q, Ac-CH_3), 22.1 (q, Ar-CH_3) 32.3 (t, C-4), 64.7 (d, C-3), 67.6 (t, C-6), 70.7 (d, C-5), 76.6 (d, C-2), 88.4 (d, C-1), 128.3 (d, 2 × C-Ar), 130.2 (d, C-Ar), 130.3 (d, C-Ar), 133.5 (s, C-Ar), 145.9 (s, C-Ar), 170.0 (s, Ac-C═O), 170.9 (s, Ac-C═O).

Data for 3-*O*-Acetyl-6-bromo-2-*O*-tosyl-4,6-desoxy-D-glucopyranosyl bromide (12)

^{1}H NMR (200 MHz, $CDCl_3$): 1.62 (m, 1H, 4a-H), 1.87 (s, 3H, Ac-CH3), 2.18 (m, 1H, 4b-H), 2.39 (s, 3H, Ar-CH3), 3.43–3.51 (m, 2H, 6a-H, 6b-H), 4.29–4.43 (m, 2H, 2-H, 3-H), 5.17 (m, 1H, 5-H), 6.34 (d, $J_{1,2} = 3.7$ Hz 1H, 1-H), 7.37 (d, $J_{Ar,Ar} = 8.1$ Hz, 2H, Ar-H), 7.72 (d, $J_{Ar,Ar} = 7.8$ Hz, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$): 21.0 (q, Ac-CH3), 22.2 (q, Ar-CH_3) 30.3 (t, C-6), 32.1 (t, C-4), 64.8 (d, C-3), 71.2 (d, C-5), 76.5 (d, C-2), 88.2 (d, C-1), 128.4 (d, 2 × C-Ar), 130.1 (d, C-Ar), 130.4 (d, C-Ar), 133.3 (s, C-Ar), 145.9 (s, C-Ar), 170.1 (s, Ac-C═O).

3,6-Di-*O*-acetyl-1,5-anhydro-2,4-dideoxy-D-threitol (14)

A solution of monobromide **11** (500 mg, 1.07 mmol) in ethanol (9 mL) was treated with Et_3N (0.7 mL) and Raney nickel (600 mg) and the suspension was stirred under hydrogen at 20°C for 2 h. The mixture was filtered, the solvent removed at reduced pressure, and the residue purified by chromatography on silica gel (petroleum ether/EtOAc) to afford **14** (148 mg, 0.69 mmol, 64%) as an oil. $[\alpha]_D = +1.5^\circ$ (*c* 0.9, MeOH). ^{1}H NMR (200 MHz, $CDCl_3$): 1.32 (m, 1H, 2a-H), 1.61 (m, 1H, 4a-H), 1.85–1.94 (m, 2H, 2b-H, 4b-H), 1.97 (s, 3H, Ac-CH_3), 2.01 (s, 3H, Ac-CH_3), 3.38–3.45 (m, 1H, 1a-H), 3.51–3.61 (m, 1H, 1b-H), 3.91–4.96 (m, 3H, 6a-H, 6b-H, 3-H), 4.80–4.91 (m, 1H, 5-H). ^{13}C NMR (50 MHz, $CDCl_3$): 21.1 (q, Ac-CH_3), 21.5 (q, Ac-CH_3), 31.9 (t, C-4), 34.0 (t, C-2), 66.1 (t, C-1), 67.0 (t, C-6), 70.1 (d, C-3), 74.1 (d, C-5), 170.6 (s, Ac-C═O), 171.1 (s, Ac-C═O). MS (EI, 70 eV): *m/z* (%) = 216 [M^+], 172 (14), 172 (13), 145 (3), 101 (18), 99 (10), 91 (25), 86 (100), 58 (33), 44 (22), 30 (34). HREIMS: Calc. $C_7H_{12}O_3$ (216.2310). Found 216.0997.

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