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Note

New branched-chain and aminodeoxy sugars from 1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-enopyranos-2-ulose (levoglucosenone)*

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It is known that, even if the yield of the pyrolytic conversion of cellulose to 1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-enopyranos-2-ulose (**1**, levoglucosenone) is low[2], both the simplicity of the method and the availability of cellulosic materials make this compound a very attractive starting substrate for structural modifications of monosaccharides or for the synthesis of optically active, non-carbohydrate compounds. Some reactions of the enone function have already been reported: reduction[3], addition[3d,4], and Diels–Alder cycloaddition[5]. To the best of our knowledge, no mention has been made of the synthesis of a *spiro*-epoxide derived from the keto group, although this compound would play a central role for structural modifications and introduction of a quaternary centre in the molecule.

Our choice for epoxidation of levoglucosenone (**1**) has been directed to the Corey reagent prepared from reaction of sodium hydride in tetrahydrofuran on dimethylsulfoxide, followed by the addition of trimethylsulfonium iodide[6]. The addition at 0° of a solution of levoglucosenone (**1**) in methyl sulfoxide to the Corey reagent gave, after reaction, a single compound which was isolated in a 50% yield as a pure colorless syrup. The ^{1}H- and ^{13}C-n.m.r. spectra (see Experimental section) showed the persistence of both the acetal function and the double bond. The keto group had disappeared and had been replaced by a well-resolved AB system (δ 2.92 p.p.m. $J = 4.8$ Hz) corresponding to the methylene group of the epoxide ring. As this kind of addition is known to be very sensitive to steric hindrance, the hypothesis was made that epoxide **2** had been exclusively produced due to the shielding by the 1,6-anhydro bridge, preventing the attack of the bulky reagent through the *si* face of the keto group.

Alkaline hydrolysis of this epoxide by an aqueous solution of sodium hydroxide gave a diol which was isolated as a pure white crystalline material (yield 71%). Good analytical crystals were prepared and submitted to single-crystal X-ray analysis. The results have been described elsewhere[1], and they confirm the structure **3** for this diol and, by inference, the strucure **2** for the corresponding epoxide. Further characterization of

* For a preliminary report of this work, see ref. 1.

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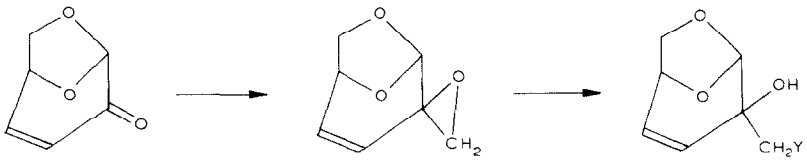

1 2

3 Y = OH
4 Y = OAc
5 Y = H
6 Y = N_3
7 Y = NH_2

Scheme 1

the diol **3** was made by acetylation with acetic anhydride in pyridine at 0° to give the monoacetate **4**. The ^{1}H-n.m.r. spectrum of **4** showed one sharp, 3-proton singlet at δ 2.10 p.p.m., which was attributed to the methyl protons of the acetyl group, and a large peak at δ 2.75 p.p.m., which is due to the hydroxyl group. This assignment was confirmed by the ^{13}C-n.m.r. spectrum.

Reduction of epoxide **2** with lithium aluminium hydride gave the 2-*C*-methyl derivative **5**. The disappearance of the AB system in the spectrum of **2** and the appearance of a singlet at δ 1.27 p.p.m. (3 protons) in the spectrum of **5** is consistent with the reductive cleavage of the epoxide ring to give a compound with a methyl group.

Azidolysis of **2** in aqueous acetone gave the crystalline azido derivative **6** whose i.r. and n.m.r. spectra were in agreement with the proposed structure. Reduction of **6** with lithium aluminium hydride afforded the crystalline amino alcohol **7**.

Thus nucleophilic ring opening of the spiro-epoxide at position 2 of levoglucosenone (**1**) was shown to occur with complete regiospecificity at the primary carbon atom according to an S_N2-type reaction. These branched-chain derivatives which contain functional groups on the side chain would be suitable for modification and elaboration of these chains into other interesting structures.

EXPERIMENTAL

General. — Melting points were determined on a Büchi apparatus and are uncorrected. Specific rotations were determined with a Perkin–Elmer Model 141 polarimeter. I.r. spectra were recorded with a Perkin–Elmer Model 157 spectrometer. ^{1}H-n.m.r. spectra were recorded with a Varian T-60 spectrometer. ^{13}C-n.m.r. spectra were recorded with a JEOL FX-60 spectrometer. Tetramethylsilane (δ 0.00) was used as the internal standard. Column chromatography was performed with Kieselgel-60 (E. Merck), and t.l.c. was carried out with precoated plates (E. Merck cat. no. 5724) with detection by charring with sulfuric acid.

*1,6-Anhydro-3,4-dideoxy-β-*D-glycero-*hex-3-enopyranos-2-ulose* (*levoglucosenone*, **1**). — Cellulose (100 g) containing 1.5% by weight of phosphoric acid was pyrolyzed in two batches, at atmospheric pressure, in a round-bottomed flask equipped with a distillation apparatus and swept by a nitrogen flow, by direct heating with a

Bunsen burner. The pyrolysates were extracted with dichloromethane. Removal of the solvent left an oil which was purified by column chromatography using 7:3 petroleum ether–ethyl acetate as eluent to give levoglucosenone (**1**, 3.2 g) as a liquid: $[\alpha]_D^{20}$ −458° (*c* 0.6, chloroform) (lit. [2a] −460°); the ^{1}H-n.m.r. spectrum was identical with that reported by Broido and co-workers[2a].

Epoxidation of the levoglucosenone **1** *to oxirane* **2**. — A procedure described by Corey *et al.*[6] was followed. Sodium hydride (0.87 g of a 55% dispersion in mineral oil; 20 mmol) was washed with hexane to remove the oil. Dry methyl sulfoxide (12 mL) was added to the hydride, and the mixture was heated to 60–70°, under nitrogen, with stirring, until the evolution of hydrogen ceased. The resulting solution of methylsulfinyl carbanion was diluted with dry tetrahydrofuran (12 mL), cooled to 0°, and trimethylsulfonium iodide (4.08 g, 20 mmol), dissolved in methyl sulfoxide (20 mL), was added with stirring for 1 min. After addition of a solution of levoglucosenone (**1**, 2.2 g, 17 mmol) in methyl sulfoxide (5 mL), stirring was continued for 1 h at 0°, and then for 1 h at 20–25°. The reaction mixture was diluted with water (100 mL), and the product was extracted with dichloromethane, washed with water, and dried. Evaporation of the solvent left a syrup (1.5 g), which, after column chromatography with ethyl acetate as eluent, gave **2** (1.2 g; 50%) as an oil: $[\alpha]_D$ −143° (*c* 0.9, chloroform); ^{1}H-n.m.r. data ($CDCl_3$): δ 2.92 (2H, AB spectrum, J 4.8 Hz, methylene protons of epoxide ring), 3.78 (1 H, dd, $J_{6,6'}$ 7 Hz, $J_{6,5}$ 4 Hz, H-6 *endo*), 4.0 (1 H, d, $J_{6,6'}$ 7 Hz, H-6 *exo*), 4.80 (1 H, t, J 4.4 Hz, H-5), 5.02 (1 H, d, $J_{1,3}$ 1.8 Hz, H-1), 5.33 (1 H, dd, $J_{1,3}$ 1.8 Hz, $J_{3,4}$ 10 Hz, H-3), and 6.40 (1 H, dd, $J_{3,4}$ 10 Hz, $J_{4,5}$ 4.4 Hz, H-4); ^{13}C-n.m.r. data ($CDCl_3$): δ 52.4, 59.1, 70.8, 71.6, 102.7, 127.3, and 135.9.

*1,6-Anhydro-3,4-dideoxy-2-*C*-hydroxymethyl-β-*D-threo-*hex-3-enopyranose* (**3**). — Epoxide **2** (0.5 g, 3.6 mmol) and aqueous sodium hydroxide (1N, 10 mL) were heated for 2 h at 70°. The mixture was neutralized with 30% H_2SO_4 and thoroughly extracted with chloroform. The extract was dried and evaporated to afford the solid diol **3** (0.4 g; 71%): m.p. 130–132°; $[\alpha]_D$ −117° (*c* 0.6, ethanol); ^{1}H-n.m.r. data [$(CD_3)_2SO$]: δ 3.30 (2 H, AB system, J_{gem} 12 Hz, J 6 Hz, CH_2OH), 3.52 (1 H, dd, $J_{5,6}$ 4.15 Hz, $J_{5,6'}$ 6.6 Hz, H-6 *endo*), 3.71 (1 H, d, $J_{6,6'}$ 6.6 Hz, H-6 *exo*), 4.64 (1 H, t, $J_{5,6}$ 4.15 Hz, $J_{4,5}$ 4.15 Hz, H-5), 4.75 (1 H, s, O*H*), 4.79 (1 H, X of ABX system, t, J 6 Hz, CH$_2$O*H*), 5.21 (1 H, d, $J_{1,3}$ 2 Hz, H-1), 5.35 (1 H, dd, $J_{1,3}$ 2 Hz, $J_{3,4}$ 10 Hz, H-3), and 6.03 (1 H, dd, $J_{3,4}$ 10 Hz, $J_{4,5}$ 4.15 Hz, H-4); ^{13}C-n.m.r. data [$(CD_3)_2SO$]: δ 65.8, 70.6, 71.8, 73.8, 102.2, 130.3, and 131.4.

Anal. Calc. for $C_7H_{10}O_4$: C, 53.16; H, 6.37; O, 40.47. Found: C, 53.18; H, 6.33; O, 40.30.

*2-*C*-Acetoxymethyl-1,6-anhydro-3,4-dideoxy-β-*D-threo-*hex-3-enopyranose* **4**. — A solution of crude diol **3** (0.15 g, 0.95 mmol) in pyridine (15 mL) and acetic anydride (0.5 g) was stirred at room temperature overnight. At the end of this time, the mixture was poured into water and $NaHCO_3$, and the resulting solution was extracted with dichloromethane. The extract was dried and evaporated to a solid (0.15 g, 79%), which was purified by column chromatography with 1:1 petroleum ether–ethyl acetate to yield **4**: m.p. 106–108°; $[\alpha]_D$ −95° (*c* 0.9, ethanol); ^{1}H-n.m.r. data ($CDCl_3$): δ 2.10 (3 H, s, OCOCH_3), 2.75 (1 H, s, O*H*), 3.70 (1 H, dd, $J_{5,6}$ 4 Hz, $J_{6,6'}$ 7 Hz, H-6 *endo*), 3.85 (1 H, d,

$J_{6,6'}$ 7 Hz, H-6 *exo*), 4.15 (2 H, AB system, J 11.2 Hz), 4.70 (1 H, t, J 4 Hz, H-5), 5.45 (2 H, d, $J_{1,3}$ 2.2 Hz, H-1), 5.57 (1 H, dd, $J_{1,3}$ 2.2 Hz, $J_{3,4}$ 10 Hz, H-3), and 6.18 (1 H, dd, $J_{3,4}$ 10 Hz, $J_{4,5}$ 4 Hz, H-4); ^{13}C-n.m.r. data ($CDCl_3$): δ 20.9 (q), 65.8 (t), 70.0 (t), 71.7 (d), 72.0 (s), 101.5 (d), 128.8 (d), 131.2 (d), and 170.8 (s).

Anal. Calc. for $C_9H_{12}O_5$: C, 53.99; H, 6.04; O, 39.96. Found: C, 53.95; H, 6.20; O, 39.74.

*1,6-Anhydro-3,4-dideoxy-2-*C*-methyl-β-*D-threo-*hex-3-enopyranose* (**5**). — The spiroepoxide **2** (200 mg, 1.43 mmol) in ether (5 mL) and tetrahydrofuran (5 mL) was added to a mixture of lithium aluminium hydride (500 mg, 13.2 mmol) in anhydrous ether (50 mL). The mixture was stirred for 1 h, at 30°, at the end of which time ethyl acetate and water were successively added to the mixture, and the resulting precipitate was removed by filtration and washed with ether. The combined ethereal extracts were dried and then evaporated to give colorless, syrupy **5** (100 mg, 50%), which after purification by column chromatography with 1:1 petroleum ether–ethyl acetate as eluent had $[\alpha]_D$ −76° (*c* 1.5, chloroform); ^{1}H-n.m.r. data ($CDCl_3$): δ 1.27 (3 H, s), 2.52 (1 H, s, OH) 3.70 (2 H, m, H-6), 4.61 (1 H, m, H-5), 5.20 (1 H, d, $J_{1,3}$ 2 Hz, H-1), 5.59 (1 H, dd, $J_{1,3}$ 2 Hz, $J_{3,4}$ 10 Hz, H-3), and 6.0 (1 H, dd, $J_{3,4}$ 10 Hz, $J_{4,5}$ 4.4 Hz, H-4).

*1,6-Anhydro-2-*C*-azidomethyl-3,4-dideoxy-β-*D-threo-*hex-3-enopyranose* (**6**). — Sodium azide (2.1 g, 32.3 mmol) and the epoxide **2** (1.3 g, 9.3 mmol) in acetone (20 mL) and water (20 mL) were boiled under reflux for 90 min, then stirred overnight at room temperature. Evaporation of the solvents gave a syrup that was extracted with chloroform. The organic solution was washed with water, dried, and concentrated to give an oil which was chromatographed. Elution with ethyl acetate and evaporation of the solvent gave a syrup (0.8 g, 47%) which crystallized after standing for several days: m.p. 63–65°; $[\alpha]_D$ −49° (*c* 0.9, chloroform); ν_{max} 3575 (OH), 2120 (N_3) cm^{-1}; ^{1}H-n.m.r. data [$(CD_3)_2SO$]: δ 3.23 (2 H, s, CH_2N_3), 3.32 (1 H, s, OH), 3.60 (1 H, dd, $J_{5,6}$ 4 Hz, $J_{6,6'}$ 7 Hz, H-6 *endo*), 3.80 (1 H, d, $J_{6,6'}$ 7 Hz, H-6 *exo*), 4.75 (1 H, t, J 4 Hz, H-5), 5.28 (1 H, d, $J_{1,3}$ 2.2 Hz, H-1), 5.50 (1 H, dd, $J_{1,3}$ 2.2 Hz, $J_{3,4}$ 9.8 Hz, H-3), and 6.12 (1 H, dd, $J_{3,4}$ 9.8 Hz, $J_{4,5}$ 4 Hz, H-4); ^{13}C-n.m.r. data ($CDCl_3$): δ 55.0 (t), 70.0 (t), 71.7 (d), 73.5 (s), 101.7 (d), 129.4 (d), and 131.0 (d).

Anal. Calc. for $C_7H_9O_3N_3$: C, 45.90; H, 4.95; O, 26.21. Found: C, 46.07; H, 5.14; O, 26.17.

*2-*C*-Aminomethyl-1,6-anhydro-3,4-dideoxy-β-*D-threo-*hex-3-enopyranose* (**7**). — To a solution of azide **6** (0.3 g, 1.64 mmol) in diethyl ether (20 mL) was added lithium aluminium hydride (0.3 g, 7.9 mmol), and the mixture was boiled under reflux for 1 h. The excess of hydride was carefully decomposed with ethyl acetate (10 mL) and water (1.5 mL), and the resulting precipitate was filtered and washed with ether. The filtrate and washings were evaporated to give **7** (0.2 g, 78%) as a white solid: m.p. 128–130°; $[\alpha]_D$ −116° (*c* 1.0, ethanol); ν_{max} 3460 cm^{-1}; ^{1}H-n.m.r. data [$(CD_3)_2CO$]: δ 2.95 (3 H, s, OH and NH_2), 3.05 (2 H, AB system, J 12.4 Hz, CH_2NH_2), 3.58 (1 H, dd, $J_{6,6'}$ 6.6 Hz, $J_{5,6}$ 4 Hz, H-6 *endo*), 3.78 (1 H, d, $J_{6,6'}$ 6.6 Hz, H-6 *exo*), 4.60 (1 H, t, J 4 Hz, H-5), 5.15 (1 H, d, $J_{1,3}$ 2 Hz, H-1), 5.50 (1 H, dd, $J_{1,3}$ 2 Hz, $J_{3,4}$ 10 Hz, H-3), and 6.05 (1 H, dd, $J_{3,4}$ 10 Hz, $J_{4,5}$ 4 Hz, H-4); ^{13}C-n.m.r. data [$(CD_3)_2CO$]: δ 55.3, 70.8, 72.1, 83.0. 104.7, 130.7, and 132.6.

Anal. Calc. for $C_7H_{11}NO_3$: C, 53.49; H, 7.05; O, 30.54. Found: C, 53.41; H, 7.00; O, 30.31.

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