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Note

Synthesis of methyl 2-amino-2,6-dideoxy-α-D-altropyranoside and methyl 3-amino-3,6-dideoxy-α-D-glucopyranoside*

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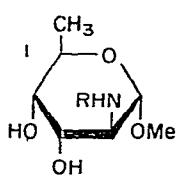
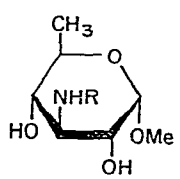
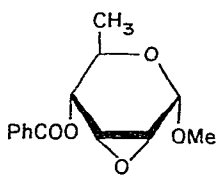
The title compounds were required for a study on the peroxyacid oxidation of amino sugars[1]. As far as we know, the 2-amino α-D-altroside **1** has not yet been described, although the 2-acetamido derivative **1a** was obtained from its 6-hydroxy analog through monotosylation, iodide exchange, and reduction[2]. The 3-amino α-D-glucoside **2** has been synthesized[3] in 24% yield by the nitromethane cyclization method, starting from methyl 6-deoxy-α-D-glucopyranoside. At the time, the best preparative procedure recorded[4] for making this starting compound from commercial methyl α-D-glucopyranoside was a multi-step operation associated with only a moderate over-all yield. More recently, however, the 6-deoxyglucoside has become available much more conveniently[5a], and the nitromethane synthesis itself has, in the meantime, been elaborated further (albeit in the L-series leading[6] to the enantiomer of **2**), rendering the described synthesis[3] of **2** even more attractive. Nevertheless, for our



1 R = H
1a R = Ac



2 R = H
2a R = Ac



3

present purpose we elected to use methyl 2,3-anhydro-4-*O*-benzoyl-6-deoxy-α-D-allopyranoside (**3**) as a point of departure, expecting that ammonolysis would furnish both **1** and **2** in a single step. Compound **3** likewise is a convenient starting material as it can be made in good over-all yield from readily available methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside[5b,7] by the Hanessian–Hullar reaction[8], which gives methyl 2,3-anhydro-4-*O*-benzoyl-6-bromo-6-deoxy-α-D-allopyranoside[5c,9] that

*Dedicated to Dr. Louis Long, Jr., in honor of his 70th birthday.

is then reductively debrominated[9]. The ammonolysis of **3** was carried out essentially as described for similar epoxides by Jarý and coworkers[2,5d,10]. It afforded the crystalline 3-amino alloside **2** as the major product (52%) and syrupy 2-amino altroside **1** as a minor product (24%). Both compounds were characterized by spectral data and their crystalline *N*-acetyl derivatives **1a** and **2a**. The observed preponderance of **2** was in accord with the rule that, in epoxide openings in flexible sugar-ring systems, the amino group tends to enter preferentially at the position more distant from the anomeric center[11].

EXPERIMENTAL

Methyl 2,3-anhydro-4-O-benzoyl-6-bromo-6-deoxy-α-D-allopyranoside. — Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside[5b,7] (1.32 g) was treated with *N*-bromosuccinimide as directed[5c,9]. However, the crude syrup obtained upon washing, drying and evaporating the ethereal product solution[5b,7] was not allowed to crystallize partially but was first purified by dissolution in benzene, treatment with activated carbon, and passage through a column of silica gel (70 g) by means of benzene–ethyl acetate (4:1). Crystallization from ether–pentane then afforded the pure product, m.p. 60° and $[\alpha]_D$ +175° (*c* 1.1, chloroform), in improved yield (1.24 g, 72%) (reported[9], m.p. 60–61°, $[\alpha]_D$ +177°). The n.m.r. data, not previously recorded, were as follows (100 MHz, in $CDCl_3$): δ 3.30–3.70 (7-proton overlapping multiplets for H-2, H-3, H-6, H-6′, and methoxyl singlet at δ 3.52), 4.28 (1-proton septet, H-5, $J_{4,5}$ 9.5 Hz, $J_{5,6}$ 6.5 Hz, $J_{5,6'}$ 3 Hz), 4.98 (1-proton doublet, H-1, $J_{1,2}$ 3 Hz), 5.28 (1-proton quartet, H-4, $J_{3,4}$ 1.5 Hz), 7.5 and 8.05 (3-proton multiplet and 2-proton quartet of benzoyl group).

Methyl 2,3-anhydro-4-O-benzoyl-6-deoxy-α-D-allopyranoside (**3**). — Hydrogenation[9] of the crystalline 6-bromo derivative (4.44 g) with 10% palladium on charcoal (4 g) gave syrupy **3** (2.94 g) containing two minor contaminants (t.l.c.). Chromatography on a 150-g silica gel column with benzene–ethyl acetate (85:15) as eluant afforded **3** (2.41 g, 71%) as a syrup that failed to crystallize although it was pure according to t.l.c. The n.m.r. data (100 MHz in $CDCl_3$) were: δ 1.20 (3-proton doublet, *C* $-CH_3$, $J_{5,6}$ 6.5 Hz), 3.46 (3-proton singlet, OCH_3), 3.6 (2-proton narrow multiplet, H-2 and H-3), 4.14 (1-proton octet, H-5, $J_{4,5}$ 9.5 Hz, $J_{5,6}$ 6.5 Hz), 4.89 (1-proton doublet, H-1, $J_{1,2}$ 3 Hz); 5.05 (1-proton quartet, H-4, $J_{3,4}$ 1.5 Hz), 7.5 and 8.07 (3-proton multiplet and 2-proton quartet of benzoyl group). The three signals recorded[9] for **3** agreed with the corresponding ones given here.

Methyl 3-amino-3,6-dideoxy-α-D-glucopyranoside (**2**) *and methyl 2-amino-2,6-dideoxy-α-D-altropyranoside* (**1**). — Liquid ammonia (60 ml) was added to a cooled (−70°) solution of **3** (2.41 g) in methanol (35 ml) in a stainless-steel bomb (32 × 5 cm), and ammonolysis was allowed to proceed for 10 h at 150° and another 24 h at 130°. Subsequent evaporation of the reaction mixture gave a brown syrup to which water (20 ml) was added. Undissolved crystalline material was removed and identified as benzamide. The aqueous solution was repeatedly extracted with ether and then

evaporated to give a syrup which upon crystallization from ethanol–ethyl acetate–petroleum ether at 0° yielded a first crop (430 mg) of the α-D-*gluco* isomer **2** as colorless prisms, m.p. 172–174°, raised to 176–177° by recrystallization, $[\alpha]_D$ +144.4° (*c* 0.34, water) (reported[3], m.p. 175–177°, $[\alpha]_D$ +148°). The n.m.r. data (100 MHz in D_2O, with DOH lock signal δ 4.75) were: δ 1.25 (3-proton doublet, $J_{5,6}$ 6.5 Hz, *C*-CH_3), 2.80–3.15 (two overlapping 1-proton triplets, *J* 9.5 Hz, H-3 and H-4), 3.42 (3-proton singlet, OCH_3), 3.48 (1-proton quartet partially overlapping the OCH_3 signal, H-2, $J_{1,2}$ 3.7 Hz), 3.71 (1-proton octet, H-5, $J_{4,5}$ 9.5 Hz). The H-1 signal was not visible and was presumably obscured by the DOH peak.

The aforementioned ether extract was briefly dried ($MgSO_4$) and concentrated by partial evaporation in the open air whereby it deposited a further quantity of benzamide, which was removed. According to t.l.c. the ethereal filtrate contained both **2** and faster moving **1**, as did also the mother liquor from the foregoing first crystalline crop of **2**. The two solutions were combined and evaporated, and the residue was fractionated on a column containing 80 g of silica gel. The eluant was chloroform–methanol (7:3, v/v). Early fractions produced residual benzamide. Chromatographically homogeneous α-D-*altro* isomer **1** (290 mg) emerged after several blank fractions and was followed by mixed fractions of **1** and **2** and by fractions containing largely **2**. Crops of pure **2** totalling 375 mg (m.p. 175–178°) were obtained by crystallization. The mother liquor materials from these were rechromatographed on a second, smaller column, which furnished another 104 mg of **1** and 41 mg of **2**. The total yields, therefore, were 394 mg (24%) of **1** and 846 mg (52%) of **2**.

Syrupy but homogeneous **1** showed $[\alpha]_D$ +54° (*c* 0.4, water). It was difficult to crystallize, a low-melting powder (m.p. 45–46°) being obtained but once from a combination of solvents. The n.m.r. data (100 MHz in D_2O) were: δ 1.28 (3-proton doublet, *J* 6.5 Hz, *C*-CH_3); 3.43 (3-proton singlet, OCH_3). There were 1-proton multiplets centered at δ 3.10, 3.66, 3.89 and 4.05 attributable to H-2, H-3, H-4 and H-5 (not necessarily in that order). None of them was a triplet with large splitting (such as those seen for H-3 and H-4 in **2**), which accorded with the α-D-*altro* configuration.

A sample of **2** was acetylated by gentle warming for 3 min in an excess of acetic anhydride. Removal of the anhydride by repeated evaporation of toluene from the product gave a syrup from which the *N*-acetyl derivative **2a** was obtained in colorless crystals upon trituration with, and recrystallization from, ethyl acetate–petroleum ether with addition of a drop of ethanol; m.p. 227–228°, $[\alpha]_D$ +146° (*c* 0.8, water) (reported[3], m.p. 224° and $[\alpha]_D$ +145°). In the n.m.r. spectrum (100 MHz in D_2O) the *C*-CH_3, $NHCOCH_3$, and OCH_3 signals occurred at δ 1.28, 1.93 and 3.43, respectively. In comparison to **2** the H-3 and H-4 triplets (*J* 10 Hz) were now well separated, the former being shifted downfield to δ 4.01 and the latter, to δ 3.16. The H-2 quartet ($J_{1,2}$ 3.7 Hz, $J_{2,3}$ 10 Hz) at δ 3.62 was no longer partly obscured. The broad H-5 multiplet was centered at δ 3.79.

A sample of **1** was acetylated in a mixture of ethanol and acetic anhydride at ambient temperature to afford the crystalline *N*-acetyl derivative **1a**, which was recrys-

tallized from toluene; m.p. 135–137°, $[\alpha]_D$ +51° (*c* 0.3, water) (reported[2], m.p. 138–139°, $[\alpha]_D$ +60.4°).

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