Synthesis of D-Altrose via D-Altrosan from Levoglucosenone

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(Received March 16, 1991)

Synopsis. The stereoselective reduction and *cis*-dihydroxylation of levoglucosenone (1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-enopyranos-2-ulose), gave D-altrosan (1,6-anhydro-β-D-altropyranose), which could be converted to D-altrose in high yield.

Levoglucosenone (1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-enopyranos-2-ulose, **1**)[1] is a pyrolytic product of cellulose.[2] The structure of **1** is attractive as a starting material for a variety of organic syntheses, since it includes convertible functional groups and one chiral center. We have synthesized various useful compounds from **1** to date and have demonstrated its great utility as a chiral building block.[3] In this paper, we describe a novel synthesis of D-altrose (**4**) via D-altrosan (1,6-anhydro-β-D-altropyranose, **3**)[4] from **1**. D-Altrose (**4**) is a rare sugar which cannot be obtained from natural products. Besides, the conventional syntheses of **4** are complicated due to the many steps required, or low selectivity.[5] Thus, a synthesis of **4** using fewer reaction steps with a high overall yield is required.

1,6-Anhydro-3,4-dideoxy-β-D-*threo*-hex-3-enopyranose (**2**) was synthesized by the reduction of **1**, according to the method of previous papers.[2,6,7] The *cis*-dihydroxylation of the carbon–carbon double bond of **2** stereoselectively gave D-altrosan (**3**) with catalytic osmium tetroxide in 86.0% yield, and with stoichiometric potassium permanganate in 32.7% yield. These facts arise due to an attack of osmium tetroxide and potassium permanganate on the carbon–carbon double bond from the less-hindered side, thus avoiding any steric hindrance by the 1,6-anhydro bond of the acetal ring. This observation is similar to that in the reduction of **1**. D-Altrose (**4**) was obtained by an acid hydrolysis of **3**.

In conclusion, we have developed a simple method for the preparation of D-altrose (**4**) in 3 steps in 29.1% overall yield, via D-altrosan (**3**) from levoglucosenone (**1**).

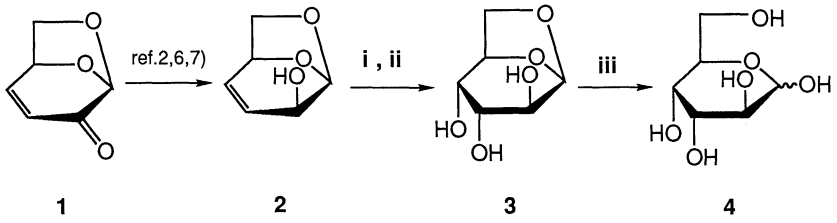
Experimental

Spectral Measurements. The IR spectra were measured with a JASCO FT/IR-5000 Spectrometer. The ^{1}H NMR spectra (300 MHz) and ^{13}C NMR spectra (75 MHz) were measured with a Bruker AM-300.

D-Altrosan (1,6-Anhydro-β-D-altropyranose, 3). *cis*-Dihydroxylation of the double bond between C-3 and C-4 of **2** was carried out by osmium tetroxide or potassium permanganate.

***cis*-Dihydroxylation by Osmium Tetroxide:** A solution (23 cm^3) of osmium tetroxide in *t*-butyl alcohol (osmium tetroxide/*t*-butyl alcohol=1/30; w/v) was added to a mixture of **2** (3.84 g, 30.0 mmol) and *N*-methylmorpholine *N*-oxide (7.03 g, 60.0 mmol) in acetone–water (150 cm^3, 8/1; v/v), and stirred for 13 h at room temperature. Na_2SO_3 (81.0 g, 643 mmol) was added to the reaction mixture with ice-cooling, and was then vigorously stirred for 10 min at room temperature. The reaction mixture was evaporated under reduced pressure. Purification of the residue by column chromatography on silica gel (eluent: dichloromethane/acetone=1/2—4; v/v) and recrystallization from 2-propanol afforded 4.19 g (86.0%) of **3** as white powder: Mp 129—130 °C; $[\alpha]_D^{25}$ −219° (*c* 1.00, H_2O) [lit,[4a,8] mp 134—135 °C; $[\alpha]_D^{20}$ −215° (*c* 1, H_2O)]; IR (KBr) 3400 (br), 1450 (br), 1137 (s), and 1073 cm^{-1} (s); ^{1}H NMR (CD_3OD, ppm from CD_3OD, 3.40 ppm) δ=3.75—3.83 (2H, m, H-6), 3.61 (1H, dd, *J*=1.7 and 8.6 Hz, H-2), 3.69 (1H, dd, *J*=4.4 and 8.6 Hz, H-3), 3.89 (1H, dd, *J*=2.5 and 4.4 Hz, H-4), 4.61 (1H, ddd, *J*=2.1, 2.5 and 4.6 Hz, H-5), 5.30 (1H, d, *J*=1.7 Hz, H-1); ^{13}C NMR (D_2O, ppm from 1,4-dioxane; 67.4 ppm) δ=102.0, 77.8, 72.9, 70.4, 70.0, 66.1. Found: C, 44.46; H, 6.26%. Calcd for $C_6H_{10}O_5$: C, 44.45; H, 6.22%.

***cis*-Dihydroxylation by Potassium Permanganate:** A 0.6% aqueous sodium hydroxide (16 cm^3) was added to a solution of **2** (128 mg, 1.00 mmol) in 2 cm^3 of water. Potassium permanganate (190 mg, 1.20 mmol) was then gradually added to the ice-cooled reaction mixture. After stirring for 20 min at room temperature, the reaction mixture was neutralized by 1 mol dm^{-3} hydrochloric acid, and filtered through a Celite pad. The residue was washed with water. The filtrate was evaporated under reduced pressure. Purification of the residue by



Scheme 1. i) OsO_4, *N*-methylmorpholine *N*-oxide, acetone, H_2O, ii) Na_2SO_3, iii) 1 mol dm^{-3} HCl, 1,4-dioxane.

column chromatography on silica gel (eluent: dichloromethane/acetone=1/2—4; v/v) afforded 53 mg (32.7%) of **3** as a white powder, which was identified with the **3** obtained above by a ^{1}H NMR spectral comparison.

D-Altrose (4). A solution of **3** (1.62 g, 10.0 mmol) in 1 mol dm^{-3} hydrochloric acid (100 cm^3) and 1,4-dioxane (50 cm^3) was heated at 100 °C for 5 h. The reaction mixture was neutralized by passing it through Amberlite IRA-410 (OH^- form); the aqueous eluent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: chloroform/methanol=5—1; v/v). The first fraction, having R_f=0.4 (eluent: chloroform/methanol=4/1; v/v), was evaporated and dried under reduced pressure, and 1.09 g (6.7 mmol) of the starting material **3** was recovered. The second fraction, having R_f=0.2 (eluent: chloroform/methanol=4/1; v/v), was evaporated and dried under reduced pressure. 0.40 g of **4** was obtained.[9] The recovered **3** was hydrolyzed by the procedure described above. As a result, 0.70 g of **4** was obtained and 0.32 g of **3** was recovered (the procedures were rapeated three times). The obtained compound **4** was identified by comparing its IR spectra data and ^{13}C NMR spectra data with those of an authentic sample.[10] IR (nujol) 3300 (br) and 1065 cm^{-1} (br); ^{13}C NMR (D_2O, ppm from 1,4-dioxane; 67.4 ppm): α-Pyranose form;[11] δ=61.4 (C-6), 66.0 (C-4), 71.0 (C-3), 71.1 (C-5), 72.1 (C-2), 94.5 (C-1), β-pyranose form;[11] δ=62.4 (C-6), 65.1 (C-4), 71.4 (C-3), 71.6 (C-2), 74.9 (C-5), 92.6 (C-1), α-furanose form;[11] δ=63.2 (C-6), 72.5 (C-5), 76.7 (C-3), 82.2 (C-2), 84.1 (C-4), 102.0 (C-1), β-furanose form;[11] δ=63.2 (C-6), 73.5 (C-5), 75.9 (C-3), 77.4 (C-2), 81.9 (C-4), 96.1 (C-1).

References

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6) In Ref. 2, F. Shafizadeh and P. P. S. Chin have erroneously reported on the configurational assignments of two epimers obtained by reduction of **1** with $LiAlH_4$. The correct assignment has been reported in, J. S. Brimacombe, F. Hunedy, and L. C. N. Tucker, *Carbohydr. Res.*, **60**, C11 (1978).

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8) I. Johansson and N. K. Richtmyer, *Carbohydr. Res.*, **10**, 322 (1969).

9) **3** and **4** are equilibrated in acid solution. See Ref. 4b, and references cited therein.

10) D-Altrose (97%, mixture of anomers) purchased from Aldrich Chemical Company, Inc.

11) These assignments were based on; "Carbon-13 NMR Spectroscopy," ed by E. Breitmaier and W. Voelter, VCH, Weinheim (1987), Third completely revised edition, pp. 380—383.