

Efficient Multistep Asymmetric Synthesis of an Azasugar in Water

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SUPPLEMENTARY INFORMATION

General remarks

¹H and ¹³C NMR spectra were recorded on Bruker DRX 300 MHz using the residual peaks of CHCl₃ (δ 7.26) in CDCl₃, of MeOH (δ 3.30) in CD₃OD, or that of H₂O (δ 4.80) in D₂O as reference. Optical rotations, $[\alpha]_D$, were measured on a Perkin-Elmer 341 polarimeter at the sodium D line and at ambient temperature. High resolution mass spectra were recorded on a JEOL SX-102 spectrometer. Analytical thin layer chromatography was performed on Merck silica gel 60 F₂₅₄ plates, and the plates were visualized with UV light and the phosphomolybdic acid/cerium sulphate staining reagent (purchased from Aldrich as a 20 wt% solution in ethanol but diluted to ca 5 wt% before use). Reverse solid phase extraction was performed on Sep-Pak columns purchased from Waters. Distilled water was used in all reactions and commercial reagents were used as received from the supplier.

Experimental procedure and analytical data for compound **3** can be found elsewhere.¹

(2*E*,4*S*,5*R*)-6-Bromo-hex-2-en-1,4,5-triol (**4**):

Dibromide **2** (70 mg, 0.255 mmol) was stirred in water (4 mL) for 3 h at 50 °C. The acidic solution was then neutralized with solid NaHCO₃ (21 mg, 0.255 mmol). Filtration through a C18 reverse phase plug (5g) using water then methanol as eluent afforded 90-95% pure **4** (53 mg, 98%), after concentration of appropriate fractions, and was used as such in the subsequent step. A pure sample was obtained by flash column chromatography on silica gel (ethyl acetate/methanol 95/5). M.p: 77-78 °C; $[\alpha]_D$ -34.1 (c=5.3 in MeOH); ¹H NMR (CDCl₃, 300 MHz): δ 6.05 (ddt, J = 15.7, 5.0, 1.0 Hz, 1H), 5.80 (ddt, J = 15.6, 6.6, 1.6 Hz, 1H), 4.27 (t, J = 5.7 Hz, 1H), 4.23 (d, 4.8 Hz, 2H), 3.75 (m, 1H), 3.60 (dd, J = 10.6, 4.3 Hz, 1H), 3.47 (dd, J = 10.6, 6.6 Hz, 1H), 2.72 (br s, 1H), 2.42 (br s, 1H); ¹³C NMR (CDCl₃, 75 MHz): δ 133.3, 129.0, 73.6, 73.1, 62.6, 35.3. HRMS (ES⁺) found 232.9822, calcd for C₆H₁₁O₃BrNa (M+Na) 232.9792.

4,5-Anhydro-1-bromo-1-deoxy-L-idoitol (5):

To a stirred solution of **4** (50 mg, 0.237 mmol) in water (1.5 mL) was added $K_2[W_2O_3(O_2)_4(H_2O)_2]$ (2.4 mg, 0.0047 mmol). After 8 h at room temperature, the reaction mixture was eluted through a C18 reverse phase plug (5 g) using water then methanol as eluent. After concentration of appropriate fractions, epoxy alcohol **5** (53 mg, 99%) was obtained in 84% *de*,² as a colorless oil. ¹H NMR (300 MHz, CD₃OD, mixture of isomers): δ 3.86-3.75 (m, 2H), 3.64-3.50 (m, 3H), 3.43 (dd, *J* = 10.4, 6.9 Hz, 1H), 3.15-3.01 (m, 2H); ¹³C NMR (75 MHz, CD₃OD, major isomer): δ 76.8, 75.8, 65.1, 60.2, 59.5, 37.6. HRMS (ES+) found 248.9760, calcd for C₆H₁₁O₄BrNa (M+Na) 248.9738.

(2S,3S,4S)-2-[(1R)-1,2-dihydroxyethyl]pyrrolidine-3,4-diol (1):

To a 5 mL round-bottomed flask containing epoxy alcohol **5** (51 mg, 0.225 mmol) was added a solution of 10% aq. NH₃ (2 mL). After stirring at room temperature for 3 h, K₂CO₃ (62 mg, 0.450 mmol) was added and the solution then heated at 70 °C for 1 h. The reaction mixture was then concentrated and the residue subjected to flash column chromatography eluting with ethanol/methanol/25% aq. NH₃ (10/10/1) to give enantiomerically pure **1** (32 mg, 88%). M.p: 133-135 °C, Lit.³ 134-135 °C; $[\alpha]_D +3.6$ (*c* = 0.8, H₂O), Lit.³ +2.8 (*c*=2.0); ¹H NMR (300 MHz, D₂O): δ 4.13 (m, 1H), 4.06 (m, 1H), 3.79-3.68 (m, 2H), 3.58 (dd, *J* = 11.7, 4.8 Hz, 1H), 3.10 (dd, *J* = 12.3, 5.0 Hz, 1H), 2.98-2.86 (m, 2H); ¹³C NMR (75 MHz, D₂O): δ 80.8, 79.7, 74.2, 73.9, 68.2, 65.9, 53.2. HRMS (FAB+) found 164.0925, calcd for C₆H₁₄NO₄ 164.0923.

References and Footnotes

- (1) O. Hidestål, R. Ding, A. Almesåker, U. M. Lindström, *Green Chemistry*, **7**, 2005, in press.
- (2) The diastereomeric ratio was determined by integrating the peaks in the ¹³C NMR spectrum. The peaks from the two diastereomers in the ¹H NMR spectrum were overlapping.
- (3) R. C. Bernotas, *Tetrahedron Lett.*, 1990, **31**, 469.