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Note

A simple synthesis of 6-deoxy-D-(6-^{2}H)glucopyranose

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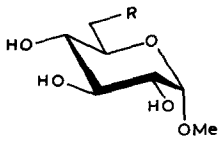
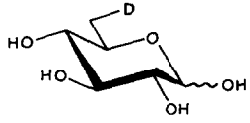
Deoxy sugars can function as analogues of natural sugars and be of value for the elucidation of the pathways of biosynthesis of natural products. Deoxy sugars can be obtained by reduction of sulphonates with borohydride in dipolar aprotic solvents[1], reduction of a deoxyiodo sugar by chromous acetate in the presence of a thiol[2], radical-mediated deoxygenation of a hydroxyl function[3,4], or catalytic hydrogenation of a bromodeoxy sugar[5].

These syntheses are not always applicable easily for the synthesis of deuterium-labelled deoxy sugars. For example, catalytic hydrogenation with deuterium gas is expensive when carried out on a large scale. Therefore, we sought, a simple, low-cost route for the synthesis of deuterium-labelled deoxy sugars, using sodium (^{2}H)borohydride and/or D_2O. The method reported[6] for the incorporation of deuterium into aromatic compounds by the reduction of aryl bromides by sodium (^{2}H)borohydride in the presence of a palladium catalyst has now been applied to the synthesis of the title compound.



1 R = Br
2 R = D



3

When a solution in D_2O of methyl 6-bromo-6-deoxy-α-D-glucopyranoside (**1**), prepared by debenzoylation of methyl 4-*O*-benzoyl-6-bromo-6-deoxy-α-D-glucopyranoside[7] with ammonia, was stirred in the presence of sodium (^{2}H)borohydride and palladium(II) chloride, methyl-6-deoxy-α-D-(6-^{2}H)glucopyranoside (**2**) was ob-

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tained with an incorporation of ~ 100% deuterium. However, reduction of **1** with sodium borohydride–palladium(II) chloride in D_2O gave **2** with ~ 50% incorporation of deuterium (mass spectrometry). There was ~ 40% incorporation of deuterium when a solution of **1** in H_2O was stirred with sodium (^{2}H)borohydride–palladium(II) chloride.

^{2}H NMR spectroscopy of **2** obtained from the sodium (^{2}H)borohydride–D_2O reaction showed a single peak at 1.13 ppm that confirmed the presence of the deuterium at C-6. Compound **2** was not purified but treated with acid to give 6-deoxy-D-(6-^{2}H)glucopyranose with a 91% incorporation of deuterium. Thus, when (^{2}H)borohydride is used as reducing agent in D_2O, a higher incorporation of deuterium into the product is found than when either borohydride–D_2O or (^{2}H)borohydride–H_2O is used. Presumably, in the first case, in situ catalytic reduction with D_2 takes place whereas, in the borohydride–D_2O and (^{2}H)borohydride–H_2O experiments, HD is formed, resulting in a deuterium incorporation of ~ 50% that of the first experiment.

EXPERIMENTAL

^{1}H NMR spectra (250 MHz) were recorded on solutions in D_2O with the HDO peak (δ 4.75) as internal reference, using a Bruker ACF 250 spectrometer unless otherwise stated. ^{2}H NMR spectra (38.398 MHz) were recorded on solutions in H_2O with the H_2O peak as internal reference. CI (ammonia)-mass spectra were obtained with a Kratos MS 80 mass spectrometer.

Methyl 6-deoxy-α-D-(6-^{2}H)glucopyranoside (**2**).—Methyl 6-bromo-6-deoxy-α-D-glucopyranoside (**1**; 1.5 g, 5.9 mmol) was added to a suspension of palladium(II) chloride (2.1 g, 11.8 mmol) in H_2O or D_2O (30 mL). Sodium (^{2}H)borohydride (or borohydride) (1.75 g, 45 mmol) was added in small portions with stirring during 1 h at room temperature, the mixture was stirred for a further 30 min, then filtered through Celite, and concentrated to give crude **2** that was purified further by batchwise treatment with Amberlite MB-3 resin (100 mL). The product did not crystallise but was used in this form in the next synthetic step. NMR data: ^{1}H, δ 1.1 (d, 3 H, H-6,6,6), 2.9–3.8 (m, 4 H, H-2/5), 3.25 (s, 3 H, OMe) 4.6 (d, 1 H, H-1); ^{2}H, δ 1.13 (s, H-6).

CI-mass spectra of **2** prepared using (*a*) $NaB(^2H)_4$–$(^2H)_2O$, *m/z* 197 [$(M + 19)^+$, 100%], 196 (10), 165 (75), 164 (7), 147 (10), 124 (20) (Calcd for $[C_7{}^1H_{14}{}^2HO_5 + NH_4]^+$: *m/z* 197); (*b*) $NaBH_4$–$(^2H)_2O$, *m/z* 197 [$(M + 19)^+$, 100%], 196 (87), 183 (18), 165 (100), 164 (70), 146 (12), 128 (15); (*c*) $NaB(^2H)_4$–H_2O, *m/z* 197 [$(M + 19)^+$ 70%], 196 (100), 165 (50), 164 (70), 146 (5).

6-Deoxy-D-(6-^{2}H)glucose (**3**).—The crude product from the $NaB(^2H)_4$–$(^2H)_2O$ reaction was treated with M HCl (20 mL) at 45°C for 12 h. The aqueous solution was deionised with Amberlite MB-3 resin, then concentrated to yield **3** (0.84 g, 79%), α,β ratio 1:2. ^{1}H NMR data: δ 1.15 (m, ~ 2 H, H-6α,β), 3.0–4.9 (m, 4 H, H-2/5α,β), 4.5 (d, 1 H, $J_{1,2}$ 8 Hz, H-1β), 5.0 (d, 1 H, $J_{1,2}$ 3 Hz, H-1α).

CI-mass spectra and deuterium incorporation in **3** prepared using (*a*) $NaB(^2H)_4$–$(^2H)_2O$, *m/z* 183 [$(M + 19)^+$, 100%], 182 (10), 165 (75), 164 (7), 147 (18), 124 (34); D incorporation, 90.7% (Calcd for $[C_6{}^1H_{12}{}^2HO_5 + NH_4]^+$: *m/z* = 183); (*b*) $NaBH_4$–$(^2H)_2O$, *m/z* 183 [$(M + 19)^+$, 100%], 182 (85), 165 (100), 164 (70), 146 (14), 128 (16); D incorporation, 51.1%; (*c*) $NaB(^2H)_4$–H_2O, *m/z* 183 [$(M + 19)^+$, 70%], 182 (100), 165 (48), 164 (65), 146 (9); D incorporation, 39.1%.

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