## Preliminary communication

# Stereospecific synthesis of ethyl (2-acetamido-2-deoxy- $\alpha$ -D-glucopyranosyl)-acetate

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C-Glucopyranosides are a class of compounds that are of interest as chiral intermediates and enzyme inhibitors<sup>1-3</sup>. The synthesis of the  $\beta$  derivatives of C-glucopyranosides may be effected easily with a high degree of stereospecificity<sup>3-6</sup>, whereas few examples of stereospecific synthesis of  $\alpha$  derivatives have been reported<sup>7,8</sup>. No synthesis of C-glycosyl derivatives of 2-acetamido-2-deoxy-D-glucose has been reported hitherto, although such compounds could be useful as enzyme inhibitors.

We now report the first example of stereospecific synthesis of an  $\alpha$ -C-glycosyl derivative of 2-acetamido-2-deoxy-D-glucose, namely ethyl (2-acetamido-4,6-O-benzyl-idene-2-deoxy- $\alpha$ -D-glucopyranosyl)acetate (2).

The synthesis was based on the finding<sup>9</sup> that 2-O-acetyl-D-glucopyranoses reacted with (ethoxycarbonylmethylene)triphenylphosphorane to afford an  $\alpha_{\beta}$ -mixture of C-D-glucopyranosyl derivatives. A solution of 2-acetamido-4,6-O-benzylidene-2-deoxy-D-glucopyranose<sup>10</sup> (1) in acetonitrile containing 2 equiv. of (ethoxycarbonylmethylene)triphenylphosphorane was boiled for 30 h. Flash chromatography of the crude product gave a C-glycosidic fraction (50%) which was shown to be ethyl (2-acetamido-4,6-O-benzylidene-2-deoxy- $\alpha$ -D-glucopyranosyl)acetate (2), m.p. 213--214° (from methanol),  $[\alpha]_D$  +33° (c 0.7 methanol) (Calc. for C<sub>19</sub>H<sub>25</sub>NO<sub>7</sub>: C, 60.77; H, 6.64; N, 3.69. Found: C, 60.50; H, 6.48; N, 3.82). N.m.r. data: <sup>1</sup>H (200 MHz, CDCl<sub>3</sub>),  $\delta$  1.23 (t, 3 H, J 7 Hz, Me), 1.95 (s, 3 H, NAc), 2.48 (dd, 1 H,  $J_{1'a,1'b}$  15,  $J_{1'a,1}$  6 Hz, H-1'a), 2.66 (dd, 1 H,  $J_{1'b,1'a}$  15,  $J_{1'b,1}$  10 Hz, H-1'b), 3.3-4.3 (m, 9 H), 4.73 (dt, 1 H,  $J_{1,1'b}$  10,  $J_{1,1'a}$  6,  $J_{1,2}$  6 Hz, H-1), 5.43 (s, 1 H, OCHO), 6.68 (d, J 7 Hz, NH), 7.2-7.5 (m, 5 H, Ph); <sup>13</sup>C (25.2 MHz, C<sub>5</sub>D<sub>5</sub>N), 14.3 (q, CH<sub>3</sub>CH<sub>2</sub>O), 22.9 (q, COCH<sub>3</sub>), 33.8 (t, C-1'), 54.9 (d), 60.7 (t, C-6), 65.1 (d), 68.2 (d), 69.4 (t, OCH<sub>2</sub>CH<sub>3</sub>), 73.4 (d), 84.2 (d), 102.1 (d, OCHO), 127.0, 128.3, 129.1 and 138.4 (Ar), 171.1 and 171.2 p.p.m. (s, C=O).

Comparison of the values of  $J_{1,2}$ ,  $\delta$  H-1',  $\delta$  H-1, and  $\delta$  C-1' with those for compounds of similar structure (see Table I) clearly indicates the  $\alpha$  configuration of 2. The chemical shifts of the signals for C-1' are at higher field (33-34 p.p.m.) in the  $\alpha$  isomers and at lower field (37-38 p.p.m.) in the  $\beta$  isomers. This difference is useful for assigning the configuration of C-glucopyranosides.

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TABLE I

N.M.R. DATA FOR SOME C-D-GL	<b>UCOPYRANOSIDES</b>
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Compound	Config.	J <sub>1,2</sub> b (Hz)	δ H-1'	δ H-1	C·1' (p.p.m.)
2	α	6	2.48, 2.66	4.73	33.84
3°	α	6	2.58, 2.72	4.64	33.20
4 <sup><i>a</i></sup>	α	6	2.56, 2.72	4.64	33.74
5°	β	10	2.47	3.90	37.27
6 <sup><i>a</i></sup>	β	10	2.44, 2.56	3.83	37.61

<sup>*a*</sup> Compounds 4 and 6 were obtained<sup>11</sup> by reaction of 2-O-acetyl-3,4,6-tri-O-benzyl-D-glucopyranose with (ethoxycarbonylmethylene)triphenylphosphorane and isolated by preparative t.l.c. Compound 4 was an oil,  $[\alpha]_D + 36.2^\circ$  (c 1.4, chloroform). Compound 6 was an oil,  $[\alpha]_D + 10.8^\circ$  (c 1.4, chloroform). <sup>*b*</sup> Values of 5.8 and 9.6 Hz, respectively, have been reported<sup>8</sup> for  $\alpha$ - and  $\beta$ -allyl derivatives.



These results give further support to the hypothesis<sup>9</sup> that the presence of a participating group at C-2 in the starting sugar facilitates the cyclisation of the Wittig products. Also, the reaction employed has previously led to  $\alpha,\beta$ -mixtures<sup>9</sup> or to the thermo-dynamically more-favored  $\beta$  isomer<sup>6</sup>.

Catalytic hydrogenolysis of 2 (H<sub>2</sub>-Pd/C) afforded pure ethyl (2-acetamido-2-deoxy- $\alpha$ -D-glucopyranosyl)acetate (7), m.p. 163–165° (from methanol-ethyl ether),  $[\alpha]_{D}$  +61.2° (c 1, methanol) (Calc. for C<sub>12</sub>H<sub>21</sub>NO<sub>7</sub>: C, 49.48; H, 7.27; N, 4.81. Found C, 49.24; H, 7.09; N, 4.33). <sup>1</sup>H-N.m.r. data (200 MHz, CD<sub>3</sub>OD):  $\delta$  1.25 (t, 3 H, J 7 Hz, Me), 1.97 (s, 3 H, NAc), 2.51 (dd, 1 H,  $J_{1'a,1'b}$  15,  $J_{1'a,1}$  5 Hz, H-1'a), 2.71 (dd, 1 H,  $J_{1'b,1'a}$  15,  $J_{1'b,1}$  10 Hz, H-1'b), 3.3–3.8 (5 H), 3.97 (dd, 1 H,  $J_{1,2}$  5,  $J_{2,3}$  10 Hz, H-2), 4.14 (q, 2 H, J 7 Hz, OCH<sub>2</sub>CH<sub>3</sub>), and 4.56 (dt, 1 H,  $J_{1,1'a}$  5,  $J_{1,1'b}$  10,  $J_{1,2}$  5 Hz, H-1).

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