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CARBOHYDRATE RESEARCH

Note

Improved preparation of 1,6-anhydro-4-deoxy-2-*O*-*p*-toluenesulphonyl-β-D-*xylo*-hexopyranose and of its D-[4-^{2}H]*gluco*-analogue from 1,6:3,4-dianhydro-2-*O*-*p*-toluenesulphonyl-β-D-galactopyranose

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The title compound **2**, of interest for the preparation of 4-deoxyhexoses and derivatives [1–6], was previously prepared [1] by catalytic hydrogenation on Raney nickel of 1,6:3,4-dianhydro-2-*O*-*p*-toluenesulphonyl-β-D-galactopyranose **1**. Although the procedure usually gives ~ 80% yields, its reproducibility in terms of yield and reaction time depends on the quality of the catalyst which must be used in a large excess. In several cases, partial detosylation was observed. An alternative method to obtain **2** involves the hydrogenolysis of 1,6-anhydro-4-deoxy-4-iodo-2-*O*-*p*-toluenesulphonyl-β-D-glucopyranose [7,8]. In our hands, the most preferable method for a large-scale preparation of **2** is that based on a reduction of the tosylepoxide **1** with diborane generated in situ from sodium borohydride and boron trifluoride etherate in 1,2-dimethoxyethane [9,10], which gives yields > 95%. In comparison with the catalytic hydrogenation, the present method is very convenient for the preparation of deuteriated **3** using sodium borodeuteride.

The structure of **3** was confirmed by measurement of the ^{1}H and ^{13}C NMR spectra of **2** and **3** (see Table 1). Axial disposition of oxygenated substituents at C-2 and C-3, and the $^1C_4$(D) conformation of the pyranose ring followed from the small vicinal interproton coupling constants $J_{2,3}$, $J_{3,4}$, and the observation of characteristic long-range couplings $J_{1,3}$, $J_{2,4}$, and $J_{3,5}$. The presence of the hydroxyl group at C-3 was confirmed by in situ acylation by trichloroacetyl isocyanate (TAI) [11]. ^{1}H NMR spectra of trichloroacetyl carbamate (TAC)-derivatives of **2** and **3** showed a signal for one NH proton at δ 8.52, a characteristic downfield shift of H-3 (1.03

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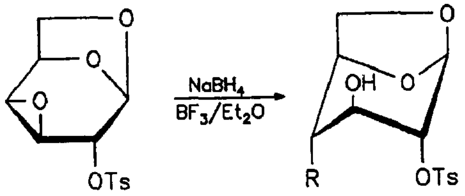
Table 1
Comparative ^{1}H and ^{13}C NMR data for **2** and **3**

<table>
<tr><th>^{1}H</th><th colspan="3">Chemical shifts (ppm)</th><th>H,H</th><th colspan="2">Coupling constants (Hz)</th></tr>
<tr><th></th><th>2</th><th>3</th><th>+TAI [a]</th><th></th><th>2</th><th>3</th></tr>
<tr><td>H-1</td><td colspan="2">5.28</td><td>[0.10]</td><td>1,2</td><td colspan="2">2.0</td></tr>
<tr><td>H-2</td><td colspan="2">4.23</td><td>[0.14]</td><td>1,3</td><td colspan="2">1.5</td></tr>
<tr><td>H-3</td><td colspan="2">3.94</td><td>[1.03]</td><td>2,3</td><td colspan="2">1.5</td></tr>
<tr><td>H-4α</td><td>2.32</td><td></td><td>[0.14]</td><td>2,4β</td><td colspan="2">1.5</td></tr>
<tr><td>H-4β</td><td colspan="2">1.71</td><td>[0.13]</td><td>3,4α</td><td>5.8</td><td></td></tr>
<tr><td>H-5</td><td colspan="2">4.54</td><td>[0.03]</td><td>3,4β</td><td colspan="2">3.0</td></tr>
<tr><td>H-6en</td><td colspan="2">4.14</td><td>[0.08]</td><td>3,OH</td><td colspan="2">6.0</td></tr>
<tr><td>H-6ex</td><td colspan="2">3.68</td><td>[0.07]</td><td>3,5</td><td colspan="2">1.5</td></tr>
<tr><td>OH</td><td colspan="2">2.68</td><td></td><td>4α,4β</td><td>15.1</td><td></td></tr>
<tr><td>OTs:</td><td></td><td></td><td></td><td>4α,5</td><td>4.4</td><td></td></tr>
<tr><td>H-2′,6′</td><td colspan="2">7.82</td><td>[0.01]</td><td>4α,6ex</td><td>1.5</td><td></td></tr>
<tr><td>H-3′,5′</td><td colspan="2">7.37</td><td>[0.00]</td><td>4β,5</td><td colspan="2">1.9</td></tr>
<tr><td>CH_3</td><td colspan="2">2.46</td><td>[0.00]</td><td>5,6en</td><td colspan="2">0.8</td></tr>
<tr><td></td><td></td><td></td><td></td><td>5,6ex</td><td colspan="2">5.0</td></tr>
<tr><td></td><td></td><td></td><td></td><td>6en,6ex</td><td colspan="2">7.1</td></tr>
<tr><th>^{13}C</th><th colspan="2">Chemical shifts (ppm)</th><th></th><th>C,H</th><th colspan="2">Coupling constants (Hz)</th></tr>
<tr><th></th><th>2</th><th>3</th><th></th><th></th><th>2</th><th>3</th></tr>
<tr><td>C-1</td><td colspan="2">99.24</td><td></td><td>C-1,H-1</td><td colspan="2">176</td></tr>
<tr><td>C-2</td><td colspan="2">76.76</td><td></td><td>C-2,H-2</td><td colspan="2">151</td></tr>
<tr><td>C-3</td><td>66.42</td><td>66.36</td><td></td><td>C-3,H-3</td><td colspan="2">151</td></tr>
<tr><td>C-4</td><td>32.50</td><td>32.18</td><td></td><td>C-4,H-4α</td><td>128</td><td>[b]</td></tr>
<tr><td>C-5</td><td>71.41</td><td>71.34</td><td></td><td>C-4,H-4β</td><td colspan="2">128</td></tr>
<tr><td>C-6</td><td colspan="2">67.65</td><td></td><td>C-5,H-5</td><td colspan="2">156</td></tr>
<tr><td></td><td></td><td></td><td></td><td>C-6,H-6en</td><td colspan="2">151</td></tr>
<tr><td>OTs:</td><td></td><td></td><td></td><td>C-6,H-6ex</td><td colspan="2">151</td></tr>
<tr><td>C-1′</td><td colspan="2">133.13</td><td></td><td>C-2′,H-2′</td><td colspan="2">165</td></tr>
<tr><td>C-2′,6′</td><td colspan="2">127.85</td><td></td><td>C-6′,H-6′</td><td colspan="2">165</td></tr>
<tr><td>C-3′,5′</td><td colspan="2">130.06</td><td></td><td>C-3′,H-3′</td><td colspan="2">162</td></tr>
<tr><td>C-4′</td><td colspan="2">145.36</td><td></td><td>C-5′,H-5′</td><td colspan="2">162</td></tr>
<tr><td>CH_3</td><td colspan="2">21.66</td><td></td><td>CH_3</td><td colspan="2">126</td></tr>
</table>

[a] Trichloroacetyl isocyanate (TAI) - induced acylation shifts for **2** are given in square brackets.
[b] $J_{\text{C-4},\,^{2}\text{H-4}\alpha}$.

ppm) and smaller induced shifts of protons in neighbouring positions. The presence of deuterium at C-4 in **3** was evidenced in the proton decoupled ^{13}C NMR spectrum by the characteristic splitting of the C-4 signal by deuterium (triplet with one-bond coupling $J_{\text{C,D}}$ 20 Hz) and the isotopic upfield shifts of carbon signals in the α- and β-positions [12] (0.32, 0.06, and 0.07 ppm for C-4, C-3, and C-5, respectively). The axial orientation of deuterium at C-4 followed from the comparison of the ^{1}H NMR spectra of **2** and **3**, where the latter one showed the absence of signal H-4*ax* as well as corresponding coupling constants. Proton-coupled, ^{13}C NMR spectra of **3** differed from **2** in the shape of the C-4 signal [basic splitting to doublet of triplets due to one-bond coupling $J_{\text{C-4,H-4}\beta}$ 128 and $J_{\text{C-4},^{2}\text{H}-4\alpha}$ 20 Hz] and in the simplification of the fine splitting of signals C-2, C-3, C-5, and C-6 by



1

2 R = H

3 R = ^{2}H

the absence of two- and/or three-bond couplings with H-4β. The observed values of $J_{C,H}$ reflect the known effects of the hybridization and substitution of individual carbon atoms. The rate of deuterium incorporation in 3 was estimated as ~ 92% from comparison of the relative intensities of signals for C-4 in ^{13}C NMR spectra and H-4 in ^{1}H NMR spectroscopy for 2 and 3, as well as of ions at m/z 145/146 in EIMS.

1. Experimental

General.—Melting points were determined on a Boëtius micro melting-point apparatus and are uncorrected. Optical rotations were measured in CHCl$_3$ at 20°C with a Bendix–Ericsson ETL 143 A polarimeter. TLC was performed on Silica Gel sheets (Alufolien E. Merck, Art. 5554) in 10:1 benzene–acetone and detection by charring with 10% H$_2$SO$_4$. NMR spectra were recorded with a Varian Unity 500 spectrometer (^{1}H at 500 MHz and ^{13}C at 125.7 MHz frequency) in CDCl$_3$; internal references (Me)$_4$Si and CDCl$_3$, for ^{1}H and ^{13}C, respectively. Mass spectra (EI) were measured with a Jeol MS D 100 spectrometer (70 eV, direct inlet t 100–120°C). NaB^{2}H$_4$ (98.1%) was purchased from the Institute of Nuclear Research, Řež, Czech Republic.

*1,6-Anhydro-4-deoxy-2-*O*-*p*-toluenesulphonyl-β-*D-xylo*-hexopyranose* (**2**).—To a suspension of finely ground tosylepoxide **1** (110 g, 0.37 mol) and NaBH$_4$ (55 g, 1.45 mol) in 1.1 L of 1,2-dimethoxyethane was added dropwise (under a hood) BF$_3$ etherate (110 mL) during 1 h. The mixture was stirred and cooled with water; the temperature should not exceed 30°C. After addition of BF$_3$ etherate, the solution was left standing overnight for ~ 20 h at room temperature. TLC revealed a spot identified as **2** (R_f 0.2) and traces of **1** (R_f 0.5). Then the mixture was adjusted to pH 7 with 5% HCl, concentrated under diminished pressure (water pump) at < 40°C, and poured into 3 L of ice–water. Several extractions with CHCl$_3$ (total volume 2 L), drying of the organic phase with anhyd CaCl$_2$, and evaporation gave syrupy **2** which crystallized on addition of a small amount of ether yielding practically pure **2** (106.6 g, 96%); mp 89–91°C, $[\alpha]_D$ −40° (c 1.0, CHCl$_3$). Recrystallization from EtOH–H$_2$O or CHCl$_3$–Et$_2$O–petroleum ether gave **2**; mp

92–93°C, $[\alpha_D]$ $-40°$ (*c* 1.2, $CHCl_3$); Lit. [1], mp 93–95°C, $[\alpha]_D$ $-42°$ (*c* 1.7, $CHCl_3$); Lit. [8], mp 92–94°C, $[\alpha]_D$ $-40°$ (*c* 2.0, $CHCl_3$); EIMS: *m/z* 300 (0.5, $M^{\cdot +}$?), 172 (11.5), 155 (17.5, $[C_7H_7O_2S]^+$), 145 (19.7, $[C_6H_9O_4]^+$, 99 (100, $[C_5H_7O_2]^+$), 91 (71), 71 (36), 70 (6.5), 69 (70.6). ^1H and ^{13}C NMR ($CDCl_3$) in Table 1.

*1,6-Anhydro-4-deoxy-2-*O*-*p*-toluenesulphonyl-β-*D*-[4-^{2}H]glucopyranose* (**3**).—A similar procedure as described above was used for the preparation of 1.0 g of **3**. 1,2-Dimethoxyethane was dried with NaH and distilled before use. Air humidity was excluded. Yield 95%, mp 89–91°C, $[\alpha]_D$ $-38°$ (*c* 1.0, $CHCl_3$); ^1H and ^{13}C NMR ($CDCl_3$) in Table 1. EIMS: *m/z* 172 (9.5), 155 (17, $[C_7H_7O_2S]^+$), 146 (18.5, $[C_6H_8{}^2HO_4]^+$), 99 (100, $[C_5H_7O_2]^+$), 91 (75), 72 (30), 71 (16), 70 (51), 69 (29).

Acknowledgments

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