Short Communication

Isopropylideneation of Acid-Sensitive Carbohydrates Using 2,3-Dichloro-5,6-dicyano-p-benzoquinone as Catalyst

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Cyclic acetalts are used extensively as protective groups for polyhydroxy compounds and thus are of high synthetic value in carbohydrate chemistry. Their formation has been thoroughly investigated and many different catalysts and reagents have been applied for this purpose. Tanemura et al. have recently reported 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) as a catalyst for the tetrahydropyranylation of alcohols and the deprotection of acetals. They found that DDQ in dichloromethane solution was a mild and efficient catalyst under neutral conditions. In connection with some ongoing research we were interested in a mild method for the formation of cyclic acetalts of acid-sensitive carbohydrate derivatives.

Polysaccharides 1a–7a were treated with 2,2-dimethoxypropane (DMP) in various solvents in the presence of DDQ to afford the corresponding isopropylidenec acetals 1b–7b.

The results of our investigation are summarized in Table 1. The acetal formation could be accomplished in different solvents such as dichloromethane, acetone and N,N-dimethylformamide which were chosen depending on the solubility of the starting polysaccharides. On the other hand, in solvents like tetrahydrofuran and toluene the reaction proceeded very slowly (only minor conversion was observed by TLC after several days). When the methyl glycosides 1a, 3a and 4a were reacted using catalytic amounts of DDQ and an excess of DMP at room temperature, the respective isopropylidene acetals 1b, 3b and 4b could be isolated in high yields after purification by flash chromatography. Starting with derivatives 2a, 5a and 6a the reactions did not go to completion and some of the starting material (about 15–20% in all three cases) could be recovered. Use of larger

![Fig. 1. Substrates and reaction products.](image-url)
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Table 1. Reaction conditions and yields at room temperature for the preparation of the cyclic acetalts 1b–7b.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Solvent</th>
<th>DMP (equiv.)</th>
<th>t/h</th>
<th>Product Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>DMF</td>
<td>2.0</td>
<td>24</td>
<td>1b</td>
</tr>
<tr>
<td>1a</td>
<td>Acetone</td>
<td>3.0</td>
<td>40</td>
<td>1b</td>
</tr>
<tr>
<td>2a</td>
<td>CH₂Cl₂</td>
<td>5.0</td>
<td>48</td>
<td>2b</td>
</tr>
<tr>
<td>3a</td>
<td>DMF</td>
<td>1.5</td>
<td>20</td>
<td>3b</td>
</tr>
<tr>
<td>4a</td>
<td>CH₂Cl₂</td>
<td>3.0</td>
<td>20</td>
<td>4b</td>
</tr>
<tr>
<td>5a</td>
<td>DMF</td>
<td>2.0</td>
<td>16</td>
<td>5b</td>
</tr>
<tr>
<td>5a</td>
<td>Acetone</td>
<td>2.0</td>
<td>20</td>
<td>5b</td>
</tr>
<tr>
<td>6a</td>
<td>CH₂Cl₂</td>
<td>5.0</td>
<td>22</td>
<td>6b</td>
</tr>
<tr>
<td>7a</td>
<td>CH₂Cl₂</td>
<td>2.0</td>
<td>10</td>
<td>7b</td>
</tr>
</tbody>
</table>

*About 20% of 2a was recovered. *In addition to some recovered starting material (ca. 15%) the hex-1-enitol 8 was obtained as a side product (10–15%). *About 20% of the glucal 6a was recovered.

amounts of catalyst (up to 0.5 equivalents) and a greater excess of DMP (up to 10 equivalents) resulted in shorter reaction times but did not improve the yields markedly. On treatment of the unprotected glucal 5a using prolonged reaction time at room temperature and/or heating of the reaction mixture, extensive decomposition was observed. Under standard conditions 5a gave an anomeric mixture of hex-2-enitol 8 as side products (15%). A mechanism for such a conversion has been proposed by Fraser-Reid et al. 4, Florent et al. 5 have reported the complete transformation of 5a into the methyl α-glycoside of 8 on treatment 5a with DMP using p-toluenesulfonic acid (p-TsOH) as a catalyst. We found that this undesired reaction could be totally avoided by protection of the 3-OH group as the benzoyl ester. When the 3-O-benzoylated glucal 6a was allowed to react under the mild conditions reported (Table 1) only 6a and the acetal 6b were observed during the course of the reaction (TLC).

The use of DDQ as a catalyst allowed us to synthesize the carbohydrate derivatives 1b–7b in good yields. Especially useful is the application of this reaction to highly acid-sensitive carbohydrates such as the glycols 5a–7a allowing the synthesis of the isopropylidene compounds 5b–7b under extremely mild conditions. Further investigations on the mechanism of the reaction are in progress.

Experimental

Physical data of all the products were in accordance with the assigned structures and the published data for 1b, 6b, 7b, 4b, 5b and 6b. 8 The glucal 6a was prepared by treating the respective 6-O-tert-butylidemethylsilyl ether 10 with tetrabutylammonium fluoride at 0°C in a THF solution. Mass spectra were recorded under electron impact conditions at 70 eV (EI). Methane was used for chemical ionization (CI). For further experimental details see elsewhere. 11

Typical procedure: 1,5-anhydro-2-deoxy-3,4-O-isopropylidene-1-erythro-pent-1-enitol (7b). To a solution of 7a (281 mg) in 15 ml of dry dichloromethane were added DDQ (54 mg) and DMP (499 mg). The solution was kept at room temperature for 10 h, evaporated in vacuo and the residue was submitted to flash chromatography with dichloromethane as the eluant to yield 361 mg (95%) of 7b as a syrup, [α]D - 54.7° (c 0.8, CH₂Cl₂). 1H NMR (200 MHz, CDCl₃): δ 1.37 and 1.46 [2 s, 6 H, C(CH₃)₂], 3.60 (dd, 1 H, J 8.2, 11.0 Hz, H-₅₆), 3.99 (dd, 1 H, J 4.2, 11.0 Hz, H-₅₄), 4.17 (ddd, 1 H, J 4.2, 5.6, 8.2 Hz, H-₄), 4.46 (dd, 1 H, J 4.0, 5.6 Hz, H-₃), 5.00 (dd, 1 H, J 4.0, 6.2 Hz, H-₂), 6.52 (d, 1 H, J 6.2 Hz, H-₁). 13C NMR (50 MHz, CDCl₃): δ 26.7 and 28.9 [C(CH₃)₂], 65.2, 67.2 and 70.6 (C-3, C-4 and C-5), 99.8 (C-2), 108.5 [C(CH₃)₂], 146.7 (C-1). MS (EI): Calcd. for C₈H₁₅O₃: 156.0786. Obsd. M⁺ = 156.0782. m/z (%): 156 (1.1), 141 (24), 81 (100), 68 (10), 59 (8), 43 (82), 28 (32).

Methyl 4,6-O-benzylidene-2,3,4-isopropylidene-a-D-glucopyranoside (2b). The substance was isolated as a syrup, [α]D + 84.7° (c 2.2, CH₂Cl₂). 13C NMR (50 MHz, CDCl₃): δ 27.0 and 27.4 [C(CH₃)₂], 55.9 (CH₂-O), 64.2 and 68.9 (C-5 and C-6), 73.5, 76.8 and 81.2 (C-2, C-3 and C-4), 98.5 (C-1), 101.3 (PhCH₃), 111.0 [C(CH₃)₂], 125.7–136.2 (Ar).

1,5-Anhydro-3-O-benzoyl-2-deoxy-D-arabino-hex-1-enitol (6a). The substance was isolated as a syrup, [α]D - 75.5° (c 0.75, CH₂Cl₂). 1H NMR (200 MHz, CDCl₃): δ 2.44 (br s, 1 H), 3.92–3.97 (m, 3 H), 4.07–4.12 (m, 2 H), 4.83 (dd, 1 H, J 2.4, 6.0 Hz, H-2), 5.54 (ddd, 1 H, J 1.6, 2.4, 6.8 Hz, H-₃), 6.50 (dd, 1 H, J 1.6, 6.0 Hz, H-₁), 7.40–8.06 (3 m, 5 H, ArH). 13C NMR (50 MHz, CDCl₃): δ 62.0 and 68.4 (C-5 and C-6), 74.3 and 78.1 (C-3 and C-4), 99.0 (C-2), 127.8–132.8 (Ar), 145.5 (C-1), 166.9 (C=O). MS (EI): m/z (%): 251 (33, M–H), 233 (48), 202 (14), 201 (82), 129 (100), 111 (76), 105 (26), 97 (16), 85 (9), 81 (33), 29 (16).

1,5-Anhydro-3-O-benzoyl-2-deoxy-4,6-O-isopropylidene-D-arabino-hex-1-enitol (6b). Colourless crystals. [α]D - 168.0° (c 0.5, CH₂Cl₂), m.p. 129–132°C. NMR data was in accordance with those reported in the literature. 9

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References

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