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Short Communication

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

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Cyclic acetals 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.[1a–c] Tanemura *et al.* have recently reported 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) as a catalyst for the tetrahydropyranylation of alcohols[2] and the deprotection of acetals.[3] 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 acetals of acid-sensitive carbohydrate derivatives.

Polyols **1a**–**7a** were treated with 2,2-dimethoxypropane (DMP) in various solvents in the presence of DDQ to afford the corresponding isopropylidene 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 polyols. On the other hand, in solvents like tetrahydropyran 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

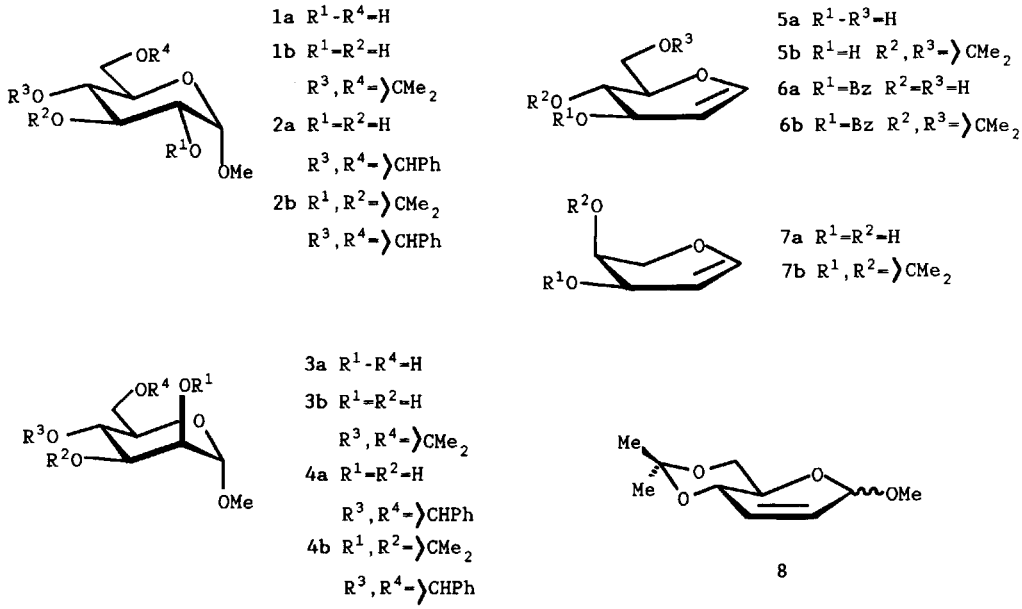

Fig. 1. Substrates and reaction products.

Table 1. Reaction conditions and yields at room temperature for the preparation of the cyclic acetals **1b–7b**.

Substrate	Solvent	DMP (equiv.)	*t*/h	Product	Yield (%)
1a	DMF	2.0	24	**1b**	89
1a	Acetone	3.0	40	**1b**	90
2a	CH_2Cl_2	5.0	48	**2b**	61[a]
3a	DMF	1.5	20	**3b**	79
4a	CH_2Cl_2	3.0	20	**4b**	95
5a	DMF	2.0	16	**5b**	48[b]
5a	Acetone	2.0	20	**5b**	52[b]
6a	CH_2Cl_2	5.0	22	**6b**	58[c]
7a	CH_2Cl_2	2.0	10	**7b**	95

[a]About 20% of **2a** was recovered. [b]In addition to some recovered starting material (ca. 15%) the hex-1-enitol **8** was obtained as a side product (10–15%). [c]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 glycals **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**,[6] **3b**,[7] **4b**,[8] **5b**[4] and **6b**.[9] The glucal **6a** was prepared by treating the respective 6-*O*-*tert*-butyldimethylsilyl 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-L-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, $[\alpha]_D - 54.7°$ (*c* 0.8, CH_2Cl_2). ^1H NMR (200 MHz, $CDCl_3$): δ 1.37 and 1.46 [2 s, 6 H, $C(CH_3)_2$], 3.60 (dd, 1 H, *J* 8.2, 11.0 Hz, H-5_{ax}), 3.99 (dd, 1 H, *J* 4.2, 11.0 Hz, H-5_{eq}), 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). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.7 and 28.9 [$C(CH_3)_2$], 65.2, 67.2 and 70.6 (C-3, C-4 and C-5), 99.8 (C-2), 108.5 [$C(CH_3)_2$], 146.7 (C-1). MS (EI): Calcd. for $C_8H_{12}O_3$: 156.0786. Obs. $M^{\cdot+} = 156.0782$. *m/z* (%) 156 (1.1), 141 (24), 81 (100), 68 (10), 59 (8), 43 (82), 28 (32).

Methyl 4,6-O-benzylidene-2,3-O-isopropylidene-α-D-*glucopyranoside* (**2b**). The substance was isolated as a syrup, $[\alpha]_D + 84.7°$ (*c* 2.2, CH_2Cl_2). ^{13}C NMR (50 MHz, $CDCl_3$): δ 27.0 and 27.4 [$C(CH_3)_2$], 55.9 (CH_3O-1), 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 (PhCH), 111.0 [$C(CH_3)_2$], 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, $[\alpha]_D - 75.5°$ (*c* 0.75, CH_2Cl_2). ^1H NMR (200 MHz, $CDCl_3$): 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). ^{13}C NMR (50 MHz, $CDCl_3$): 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 (CI): *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, $[\alpha]_D - 168.0°$ (*c* 0.5, CH_2Cl_2), m.p. 129–132°C. NMR data was in accordance with those reported in the literature.[9]

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References

1. For reviews, see (a) De Belder, A. N. *Adv. Carbohydr. Chem. Biochem. 34* (1977) 179; (b) Clode, D. M. *Chem. Rev. 79* (1979) 491; (c) Gelas, J. *Adv. Carbohydr. Chem. Biochem. 39* (1981) 71.
2. Tanemura, K., Horaguchi, T. and Suzuki, T. *Bull. Chem. Soc. Jpn. 65* (1992) 304.
3. Tanemura, K., Suzuki, T. and Horaguchi, T. *J. Chem. Soc. Chem. Commun.* (1992) 979.

4. Fraser-Reid, B., Walker, D. L., Tam, Y.-K. and Holder, N. L. *Can. J. Chem. 51* (1973) 3950.
5. Florent, J.-C. and Monneret, C. *Synthesis* (1982) 29.
6. Debost, J.-L., Gelas, J., Horton, D. and Mols, O. *Carbohydr. Res. 125* (1984) 329.
7. Evans, M. E. and Parrish, F. W. *Carbohydr. Res. 54* (1977) 105.
8. Patroni, J. J., Stick, R. V., Skelton, B. W. and White, A. H. *Aust. J. Chem. 41* (1988) 91.
9. Blackburne, I. D., Fredericks, P. M. and Guthrie, R. D. *Aust. J. Chem. 29* (1976) 381.
10. Paquette, L. A. and Oplinger, J. A. *J. Org. Chem. 53* (1988) 2953.
11. Kjølberg, O. and Neumann, K. *Acta Chem. Scand. 46* (1992) 877.

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