Carbohydrate Research, 85 (1980) 298–301.
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

Note

A simple method for detritylation of carbohydrate derivatives

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(Received September 28th, 1979; accepted for publication, February 18th, 1980)

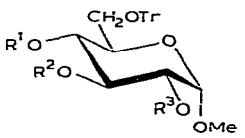
Trityl ethers are widely used in the selective protection of primary hydroxyl groups[1], and several methods[2–9] have been suggested for their cleavage. However, the simultaneous removal of other protecting groups, such as benzyl[10], benzylidene[10], toluene-*p*-sulphonyl[11], and acetyl[8], has often been observed, as has acetyl and benzyl migration[12,13].

We now report on the use of metal ions for the selective removal of trityl groups under conditions that avoid hydrolysis or migration of other groups[14].

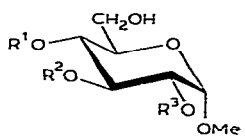
When a solution of methyl 6-*O*-trityl-α-D-glucopyranoside (**1**) and each of its partially acetylated derivatives (**2**–**8**) in an aprotic solvent was boiled under reflux for 5 h in the presence of an anhydrous, bivalent-metallic (Cu^{2+}, Ni^{2+}, Fe^{2+}, Co^{2+},

TABLE I

DETRITYLATION OF **1**–**8** WITH ANHYDROUS CUPRIC SULPHATE–BENZENE (REFLUX FOR 5 h)



1—8



9—16

Substrate	*Product*	R^1	R^2	R^3	*Yield (%)*
1	**9**	H	H	H	100
2	**10**	H	H	Ac	90
3	**11**	H	Ac	H	95
4	**12**	Ac	H	H	98
5	**13**	Ac	Ac	H	90
6	**14**	Ac	H	Ac	91
7	**15**	H	Ac	Ac	85
8	**16**	Ac	Ac	Ac	89

Zn^{2+}) sulphate, the corresponding detritylated compounds (**9–16**) were formed in high yield.

Several hydrolytic reactions are catalysed by metal ions and particularly by copper[17–21]. The results shown in Table I demonstrate that cupric sulphate, under the conditions described in the Experimental, is an effective catalyst for detritylating **2–8** without causing acetyl migration (readily established by p.m.r. spectroscopy). Other metal ions have been tested, but cupric ions, being the most acidic, seem to be the most active[16].

The reaction probably involves a Cu(II)–O(ethereal oxygen) complex which promotes cleavage of the trityl ether C–O–C bonds. When $CuSO_4 \cdot 5H_2O$ was used, no reaction occurred during 24 h.

The yields of detritylated products seem to be related to the boiling temperature of the reaction mixture, although some catalyst inactivation due to the oxygenated solvents cannot be ruled out. Benzene is the solvent of choice, since the use of toluene and xylene, as the higher-boiling homologues, cause partial isomerisation, and, in some cases, hydrolysis of the acetyl groups.

The combination cupric sulphate–benzene provides a simple and convenient procedure for the selective removal of trityl groups under conditions that avoid such acetyl migration as that from secondary to primary positions[22].

EXPERIMENTAL

General. — Unless otherwise stated, solutions were concentrated *in vacuo* at $<50°$. Sulphate salts were dried according to standard procedures. Optical rotations were measured for solutions in $CHCl_3$ with a Perkin–Elmer 141 polarimeter. U.v. spectra were recorded for solutions in CH_3CN with a Cary 118 spectrophotometer, and i.r. spectra for solutions in $CHCl_3$ or mulls in Nujol with a Perkin–Elmer 157 spectrophotometer. Mass spectra were obtained with an MS-902 AEI mass spectrometer. P.m.r. spectra (internal Me_4Si) were recorded with a Perkin–Elmer 90-MHz spectrometer. All melting points are uncorrected. T.l.c. was performed on silica gel F_{254} (Merck) with *A*, ethyl acetate–hexane (1:1); *B*, chloroform–acetone (3:1); *C*, chloroform–acetone–methanol (30:5:2); and *D*, chloroform–2-propanol (9:1); and detection by charring with sulphuric acid.

Acetyl derivatives were converted into **1** on hydrolysis with methanolic sodium hydroxide, and into methyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside on treatment with acetic anhydride and pyridine.

Compounds **1–8** were prepared as previously described[14].

Detritylation. — Typically, a solution of 0.1 mmol of each of the substrates **1–8** in benzene (20 ml, analytical grade) was boiled under reflux for 5 h in the presence of anhydrous $CuSO_4$ (1.5 g), and then cooled and poured into a column (2.5 × 10 cm) of dry silica gel. The column was eluted with benzene (100 ml) and then with a linear gradient of benzene–ethyl acetate (200 ml). The eluate was monitored by t.l.c.

Fractions containing the detritylated product were collected. The structures were confirmed by mass and i.r. spectra.

Methyl 2-*O*-acetyl-α-D-glucopyranoside (**10**), obtained from **2**, had $[\alpha]_D^{20}$ +81° (*c* 0.78) and was a chromatographically homogeneous, amorphous solid, m.p. 61–64° [from light petroleum (b.p. 40–70°)–ether]; lit.[23] m.p. 110–111°, $[\alpha]_{578}^{22}$ +156° (*c* 1, water).

Methyl 3-*O*-acetyl-α-D-glucopyranoside (**11**), obtained from **3**, had m.p. 146° (from ether–carbon tetrachloride), $[\alpha]_D^{20}$ +107° (*c* 0.89); lit.[23] m.p. 150–151°, $[\alpha]_{578}^{22}$ +164° (*c* 1, water).

Methyl 4-*O*-acetyl-α-D-glucopyranoside (**12**), obtained from **4**, had m.p. 132–133° (from ethyl acetate–carbon tetrachloride), $[\alpha]_D^{20}$ +86° (*c* 1.03); lit.[23] m.p. 127–129°, $[\alpha]_{578}^{22}$ +166° (*c* 0.4, water).

Methyl 2,3-di-*O*-acetyl-α-D-glucopyranoside (**15**), obtained from **7**, was a chromatographically homogeneous oil, $[\alpha]_D^{22}$ +75° (*c* 0.72); lit.[24] $[\alpha]_D^{25}$ +112.4° (*c* 1, water).

Methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (**16**), obtained from **8**, had m.p. 110°, $[\alpha]_D^{22}$ +147° (*c* 0.8); lit.[7] m.p. 110°, $[\alpha]_D^{26}$ +148°.

Methyl 3,4-di-*O*-acetyl-α-D-glucopyranoside (**13**), obtained from **5**, had m.p. 91–92° (from acetone–light petroleum), $[\alpha]_D^{22}$ +129° (*c* 0.92). P.m.r. data ($CDCl_3$): δ 4.6 (d, *J* 3.5 Hz, H-1), 3.55 (H-2), and 5.50–5.10 (m, H-3,4). The signal due to H-1 was decoupled on irradiation at δ 3.55, and therefore HO-2 is not acetylated.

Methyl 2,4-di-*O*-acetyl-α-D-glucopyranoside (**14**), obtained from **6**, had m.p. 141–142° (from ethanol–benzene), $[\alpha]_D^{22}$ +102° (*c* 0.9). P.m.r. data (acetone-d_6): δ 5.02–4.82 (m, 2 H, H-2,4), 4.75–4.60 (H-1), 3.91 (dd, *J* 9 and 10 Hz, H-3), 3.73 (m, H-5), and 3.61 (d, H-6,6′). On irradiation at δ 3.73, the signals at 5.02–4.82 (H-2,4) simplified. The same effect occurred on irradiation at δ 3.91.

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