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Note

Tritylation of secondary hydroxyl groups of sugars by triphenylmethylium salts

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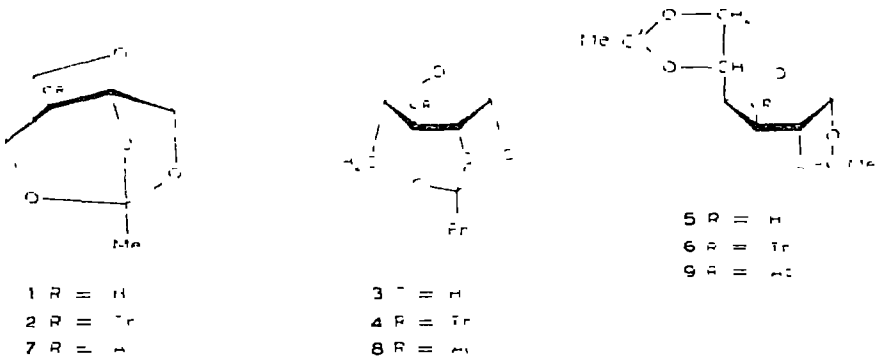
Triphenylmethyl ethers are widely used in carbohydrate chemistry[1] and are usually derived from primary hydroxyl groups; tritylation of secondary hydroxyl groups under standard conditions proceeds very slowly[2].

We now report a convenient procedure for the tritylation of secondary hydroxyl groups of carbohydrates, based on the use of triphenylmethylium perchlorate or tetrafluoroborate in combination with 2,4,6-tri-*tert*-butylpyridine (TTBP). The former salt gives the higher yields, and TTBP was selected as an acid acceptor which would be sterically hindered towards electrophilic attack of the carbonium ion at C-3. Moreover, TTBP is a crystalline, non-hygroscopic compound which is convenient to handle. The lower homologue, 2,6-di-*tert*-butylpyridine, was used as an acceptor for trifluoromethanesulphonic acid formed on methylation of sugars[3].

Preliminary experiments demonstrated the high stability of a 1:1 mixture of the triphenylmethylium salt and TTBP in dichloromethane at room temperature. Addition of a sugar derivative possessing a free secondary hydroxyl group resulted in rapid (10–15 min) and almost complete reaction, as shown by disappearance of the yellow colour and by t.l.c. One major product was formed together with traces of side products.

The tritylation procedure was applicable to acid-labile compounds such as sugar orthoesters. Thus, α-D-xylopyranose 1,2,4-orthoacetate (**1**), β-L-arabinofuranose 1,2,5-orthobenzoate (**2**), and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**5**) afforded the corresponding trityl ethers (**2**, **4**, and **6**) isolated by chromatography on alumina in high yield (68–83%).

The structures of **2**, **4**, and **6** were confirmed by p.m.r. spectroscopy, from the ratio of aromatic to non-aromatic protons. The spectrum of **2** contained a three-proton singlet for the C-Me group of the orthoacetate. The $J_{1,2}$ values for **2**, **4**, and **6** coincide with those for the acetates **7**, **8**, and **9**. For solutions of **4** and **8** in benzene coincidence of $J_{3,4}$, $J_{2,3}$, $J_{2,4}$, and $J_{5,5'}$ was observed. The anisotropy of the aromatic substituent at C-3 causes a large upfield shift of the signals for H-2,3,4. Orthoesters **2**



1 R = H
2 R = Tr
7 R = Ac

3 R = H
4 R = Tr
8 R = Ac

5 R = H
6 R = Tr
9 R = Ac

and **4** are completely hydrolysable under conditions appropriate for orthoesters, and a small amount of detritylation was also detected

The properties of **6** are very close to those reported[2] for a product isolated in 16% yield on treatment of **5** with 4-fold excess of trityl chloride for 60 h. The non-occurrence of a 5,6→3,5 migration of an isopropylidene group in the formation of **6** was established by ^{13}C-n.m.r. spectroscopy of **6** and the acetate **9** (see Table I), selective double-resonance with coherent irradiation at the frequency of H-1,2,3,4 being used for assignment of signals. Other assignments were made by analogy with other derivatives of **5**. The data in Table I clearly indicate the similarity in ring structure of **6** and **9**, and therefore establish that no acetal migration occurred during tritylation. Although the signals for C-2, C-3, and C-4 were shifted somewhat towards higher fields, an unambiguous proof of structure is provided.

TABLE I

^{13}C N.M.R. DATA FOR **6** AND **9**

	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*Me*	*Me*	*Me*	*Me*	*C'*	*C**	*Ph*	*Ac*
9	105.2	83.5	76.3	79.8	72.6	67.3	26.8	26.3	25.3	20.8	112.3	104.4		169.5
6	104.4	87.8	82.1	82.5	72.2	68.1	26.7	26.7	25.7	25.7	111.0	109.3	144.1 129.3 127.9 127.4	

The use of the new method for tritylation of secondary hydroxyl groups should be widely exploitable in carbohydrate chemistry.

EXPERIMENTAL

Dichloromethane was distilled from calcium hydride before use and triphenylmethylium salts were obtained by the method of Dauben *et al.*[4]. T.l.c. was performed

on silica gel with chloroform–acetone (50 1) Melting points were determined with a Kofler apparatus and optical rotations with a Perkin–Elmer 141 polarimeter N.m r spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with Varian DA-60-IL (^1H) and WP-60 (^{13}C) spectrometers Stabilisation of the resonance conditions was performed by using the deuterium nucleus of the solvent

3-O-Trityl-α-D-xylopyranose 1,2,4-orthoacetate (**2**) — Orthoester **1**[5] (156 mg, 0 90 mmol) was added to a mixture of TTBP[6] [223 mg, 0 902 mmol, m p 71° (from methanol)] and triphenylmethylium perchlorate (308 mg, 0 90 mmol) in dichloromethane (5 ml) The mixture gradually became homogeneous and the yellow colour disappeared After storage at room temperature for 30 min, 1:1 methanol–pyridine (0 1 ml) was added followed by chloroform (10 ml) Salts were removed, the filtrate was concentrated, and the residue was eluted from alumina with pentane to yield **2** (310 mg, 83%), m p 125–126°, $[\alpha]_D$ +19° (*c* 4, chloroform) N m r data (CCl_4) δ 7 10–7 57 (m, 15 H Tr), 5 51 (d, 1 H, $J_{1,2}$ 4 9 Hz, H-1), 4 00 (m, 2 H), 3.54 (m, 1 H), 3 18 (m, 1 H), 1 40 (s, 3 H, C-Me), 1 31 (d, 1 H)

Anal. Calc for $C_{26}H_{24}O_5$ C, 74 5, H, 5 77. Found: C, 74 66; H, 5 93

3-O-Trityl β-L-arabinofuranose 1,2,5-orthobenzoate (**4**) — Orthoester **3**[7] (47 2 mg, 0 20 mmol) was added to a mixture of triphenylmethylium perchlorate (68 4 mg, 0 20 mmol) and TTBP (50 1 mg, 0 202 mmol) in dichloromethane (0 8 ml) The triphenylmethylium perchlorate rapidly dissolved, and the yellow colour of the reaction mixture faded within 10 min After 20 min, the mixture was concentrated, the residue was extracted with benzene (0.5 ml), the extract was concentrated, and the residue was eluted from alumina with benzene to yield **4** (79 mg, 82%), R_F 0 60, containing trace amount of side products with R_F 0 80 and 0 44 Crystallization from benzene–pentane afforded pure **4** (54 6 mg), m p 159–160°, $[\alpha]_D$ +0 3° (*c* 3 4, chloroform) N m r data (CCl_4): δ 7 03–7 50 (m, 20 H, 4 Ph), 5 82 (d, 1 H, $J_{1,2}$ 3 9 Hz, H-1), 4 28 (dd, 1 H, H-2), 4 17 (s, 1 H, H-3), 3.49 (m, 3 H)

Anal Calc for $C_{31}H_{26}O_5$ C, 77 83, H, 5 44 Found C, 78 02, H, 5 69

Tritylation of **3** with triphenylmethylium tetrafluoroborate, under conditions similar to those described above, afforded 33% of **4**

1,2:5,6-Di-O-isopropylidene-3-O-trityl-α-D-glucofuranose (**6**) — To a mixture of TTBP (125 mg, 0 505 mmol), triphenylmethylium perchlorate (172 mg, 0 50 mmol), and 1,2.5,6-di-*O*-isopropylidene-α-D-glucofuranose (130 mg, 0 50 mmol), dichloromethane (2 ml) was added After 30 min, the mixture was concentrated and the residue was extracted with pentane (3 ml) The extract was concentrated and the residue was eluted from alumina with a gradient pentane→ether, to give components (42 mg) having R_F 0 56 and 0 68, and **6** (143 mg) Crystallization of **6** from methanol–ethanol (1:1) gave material (137 mg, 68%) having m p 120–122°, R_F 0 56, $[\alpha]_D$ −19 5° (*c* 1, chloroform) lit[2] m.p 115°, $[\alpha]_D$ −24 1° (chloroform) N m r data (CCl_4). δ 7 10–7 50 (m, 15 H, 3 Ph), 5 39 (d, 1 H, $J_{1,2}$ 3 8 Hz, H-1), 4.51 (m, 1 H), 3.94 (m, 4 H), 3 08 (d, 1 H, H-2), 1 37 (s, 6 H, 2 C-Me), 1 27 (s, 3 H, C-Me), 0 88 (s, 3 H, C-Me)

Anal. Calc for $C_{31}H_{34}O_6$: C, 74 20, H, 6 78 Found: C, 74 30, H, 6 94.

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