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Note

Synthesis of 1,2-orthoesters of D-glucose and polycyclic alcohols *via* glycosyl nitrates

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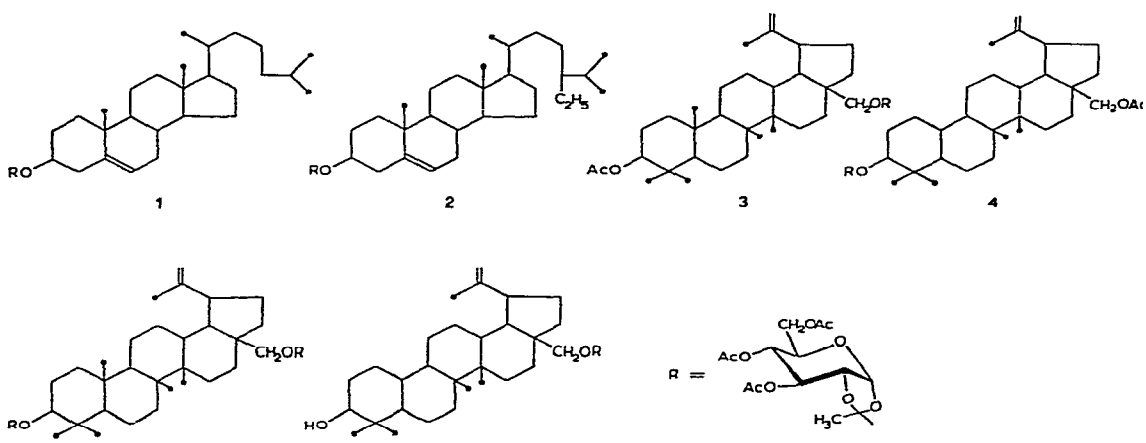
In studies of the glycosylation of polycyclic alcohols with carbohydrate 1,2-orthoesters[1–4], we have examined the properties of orthoesters in which the alkoxyl residues have steroid or triterpenoid structures. Such orthoesters may be the source of the by-products[2–5] (acetates and ethers) of glycosylation by this route. By analogy with the results of Kochetkov *et al.*[6], we think that these orthoesters can be used to obtain isomeric β-D-glycosides.

When this work was started, there were two effective methods for synthesizing carbohydrate 1,2-orthoesters with polycyclic alcohols[7,8]. The procedure of Wulff and Krüger[7] involved the condensation of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide with a polycyclic alcohol or partially substituted carbohydrate in tetrahydrofuran in the presence of silver salicylate. Thus, on using cholesterol, the orthoester **1** was the main product (t.l.c.), but attempted isolation[7] afforded cholesterol and cholesterol acetate. The orthoesters **1–6** were synthesised by the method of Zurabyan *et al.*[8], which involves the interaction of glycosyl halides having



cis-1,2-substituents with derivatives of partially substituted carbohydrates in the presence of silver nitrate and 2,4,6-trimethylpyridine (collidine) in dry acetonitrile. The reaction takes place[8] *via* acetylated glycosyl nitrates with *trans*-1,2-substituents. The orthoesters **1–6** were synthesized in a tetrahydrofuran medium because of the limited solubility of steroids and triterpenoids in acetonitrile[9].

Depending on the structure of the alcohol, the reaction time varied from 18 to 60 hours. Betulin gave **5** in addition to the orthoester **6**, which gave **3** on acetylation.

The orthoester **1** was obtained in two crystalline modifications (m.p. 99–101° and 134–136°); the low-melting form changed into the high-melting one on storage (1.5–2 months) and recrystallization.

The structures **1** (for both crystalline modifications) and **2–6** were confirmed by analytical data, hydrolysis, and n.m.r. data. The singlets at δ 1.60–1.61 indicate an *endo*-configuration of Me-2 in the dioxolane ring[10,11].

The orthoesters **1–6**, when synthesized *via* intermediary glycosyl nitrates, were obtained in yields of 36–80%; **2–6** were hitherto unknown.

EXPERIMENTAL

Column chromatography was performed on Silica Gel KCK (150–180 mesh) prepared by the procedure of Wulff and Krüger[7]. T.l.c. was performed on Silica Gel L 5-40 (Lachema, Czechoslovakia), using light petroleum–acetone (2:1) (*A*) and detection with conc. sulphuric acid–methanol (1:10) at 100–200°. Evaporations were carried out *in vacuo* at 35–40°. N.m.r. spectra were recorded on Bruker and ZKR-60 instruments for solutions in $CDCl_3$ or CCl_4, using hexamethyldisilazane as internal standard. Specific rotations were determined with a Perkin–Elmer 141 instrument, using a 1-dm tube. Melting points were obtained by using a Boetius hot-stage, without subsequent correction.

Compounds **2–6** were fully hydrolysed with 5mM sulphuric acid in 90% aqueous acetone at 20° for 30 min (monitoring by t.l.c.).

*3,4,6-Tri-*O*-acetyl-α-*D*-glucopyranose 1,2-(cholesteryl orthoacetate)* (**1**). — A mixture of cholesterol (0.387 g), 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**7**, 1.027 g), silver nitrate (0.424 g), and collidine (0.35 ml) was stirred in 10 ml of tetrahydrofuran at room temperature for 36 h. Silver bromide was filtered off, the filtrate was concentrated, the residue was dissolved in chloroform, and the solution was washed free of collidine nitrate with water. The solution was concentrated and the residue was eluted from silica gel with benzene–acetone (40:1). Combination of the appropriate fractions and crystallization of the residue from methanol gave **1** (0.53 g, 74%), m.p. 100–101°, $[\alpha]_D^{20}$ +2° (*c* 0.63, chloroform), R_F 0.56 (solvent *A*); lit.[12] m.p. 98–100°. N.m.r. data: δ 1.6 (CMe), 5.50–5.57 (d, $J_{1,2}$ 5 Hz, H-1).

*3,4,6-Tri-*O*-acetyl-α-*D*-glucopyranose 1,2-(β-sitosteryl orthoacetate)* (**2**). — A mixture of β-sitosterol (0.207 g), **7** (0.616 g), silver nitrate (0.254 g), and collidine (0.2 ml) was stirred in tetrahydrofuran (5 ml) for 48 h. The reaction mixture was treated as described above, and the crude product was eluted from silica gel with light

petroleum–acetone (32:1) to give β-sitosterol (18.3%) and **2** (0.257 g, 80%) which, after crystallization from light petroleum, had m.p. 124–125°, $[\alpha]_D^{20}$ +3° (*c* 0.4, chloroform), R_F 0.56 (solvent *A*). N.m.r. data: δ 1.6 (CMe), 5.5–5.6 (d, $J_{1,2}$ 5 Hz, H-1).

Anal. Calc. for $C_{43}H_{68}O_{10}$: C, 69.42; H, 9.08. Found: C, 69.44; H, 9.33.

*3,4,6-Tri-*O*-acetyl-α-*D*-glucopyranose 1,2-(3-*O*-acetylbetulin-28-yl orthoacetate)* (**3**). — A mixture of betulin 3-acetate (0.244 g), **7** (0.616 g), silver nitrate (0.254 g), and collidine (0.2 ml) was stirred in tetrahydrofuran (5 ml) for 18 h and then processed as described above. The crude product was eluted from silica gel with light petroleum–acetone (30:1) to give betulin 3-acetate (20.05%) and amorphous **3** (75.5%), $[\alpha]_D^{20}$ +26° (*c* 0.4, chloroform), R_F 0.51 (solvent *A*). N.m.r. data: δ 1.6 (CMe), 5.47–5.52 (d, $J_{1,2}$ 5 Hz, H-1).

Anal. Calc. for $C_{46}H_{70}O_{12}$: C, 67.78; H, 8.67. Found: C, 68.46; H, 9.14.

*3,4,6-Tri-*O*-acetyl-α-*D*-glucopyranose 1,2-(28-*O*-acetylbetulin-3-yl orthoacetate)* (**4**). — A mixture of betulin 28-acetate (0.242 g), **7** (0.616 g), silver nitrate (0.254 g), and collidine (0.2 ml) was stirred in tetrahydrofuran (5 ml) for 48 h. The reaction mixture was processed as described above for **3** to give unreacted 28-acetate (52.8%) and **4** (0.14 g, 37.3%), m.p. 186–190° (from methanol), $[\alpha]_D^{20}$ +11° (*c* 0.4, chloroform), R_F 0.51 (solvent *A*). N.m.r. data: δ 1.6 (CMe), 5.53–5.61 (d, $J_{1,2}$ 5 Hz, H-1).

Anal. Calc. for $C_{46}H_{70}O_{12}$: C, 67.78; H, 8.67. Found: C, 67.56; H, 8.82.

*Bis[3,4,6-tri-*O*-acetyl-α-*D*-glucopyranose (1,2-]betulin-3,28-diyl diorthoacetate)* (**5**). — A mixture of betulin (0.442 g), **7** (2.465 g), silver nitrate (1.018 g), and collidine (0.8 ml) was stirred in tetrahydrofuran (10 ml) for 60 h. The reaction mixture was processed as described above, and the crude product was eluted from silica gel with light petroleum–acetone (30:1, 28:1, 26:1) to yield **5** (0.546 g, 49.5%), m.p. 144–145° (from light petroleum), $[\alpha]_D^{20}$ +23° (*c* 0.69, chloroform), R_F 0.36 (solvent *A*). N.m.r. data: δ 1.6 (CMe), 5.49–5.55 (d, $J_{1,2}$ 4.8 Hz, H-1).

Anal. Calc. for $C_{58}H_{86}O_{20}$: C, 63.14; H, 7.85. Found: C, 63.28; H, 8.05.

3,4,6-Tri-*O*-acetyl-α-D-glucopyranose 1,2-(betulin-28-yl orthoacetate) (**6**) was also obtained as an amorphous solid (0.268 g, 36.1%), R_F 0.42 (solvent *A*), ν_{max} 3620 (hydroxyl), 890, 1643, and 3080 cm^{-1} (*exo*-methylene double bond).

Anal. Calc. for $C_{44}H_{68}O_{11}$: C, 68.36; H, 8.87. Found: C, 68.74; H, 9.18.

Acetylation of **6** gave **3**.

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