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Note

Interaction of orthoesters of sugars with steroid and triterpenoid alcohols

NINA I. UVAROVA, NADEZHDA F. SAMOSHINA, LARISA E. NOVIKOVA, AND GEORGI B. ELYAKOV

Pacific Institute of Bioorganic Chemistry, Far East Science Centre, Academy of Sciences of the U.S.S.R., Vladivostok-22 (U.S.S.R.)

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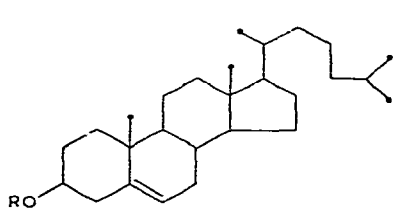
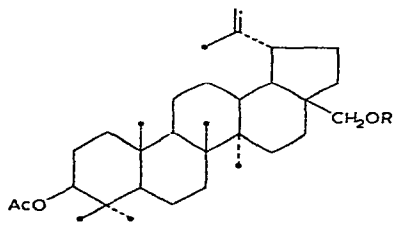
In our previous communications[1–5] on the synthesis of glycosides of steroid and triterpenoid alcohols by the orthoester method, we noted the formation of by-products. It was assumed[2,5] that orthoesters, isomeric with the glycoside acetates, may be the source of the by-products, even though the presence of such orthoesters was not detected in the reaction mixtures. Furthermore, 1 mmole of 3,4,6-tri-*O*-acetyl-α-D-glucopyranose 1,2-(cholesteryl orthoacetate) (**1**) in the presence[6] of 0.04 mmole of $HgBr_2$ in nitromethane, with azeotropic distillation for 2.5 h, gave cholesteryl β-D-glucopyranoside tetra-acetate (17.8%), dicholesteryl ether (10.5%), cholesteryl acetate (11.1%), and cholesterol (55.0%).

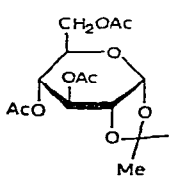
We now report on the behaviour of sugar orthoesters in the glycosylation of polycyclic alcohols, using various solvents but no catalyst. It was established that 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-*tert*-butyloxyethylidene)-α-D-glucopyranose (**4**) and 3,6-



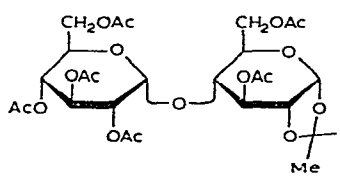
1 R = R′
2 R = R″



3 R = R″



= R′



= R″

di-*O*-acetyl-1,2-*O*-(1-methoxyethylidene)-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-α-D-glucopyranose (**5**) undergo transesterification with cholesterol, yielding **1** and **2** respectively. The orthoester **5** is transesterified by betulin monoacetate at C-3, to give **3**. The formation of **1–3** takes place in toluene and solvents used in the synthesis of glycosides by the orthoester method[7–9].

TABLE I

Expt.	*Carbohydrate portion of orthoester (mmol, g)*	*ROH (mmol, g)*	*Solvent (10 ml)*	*Time (h)*	*Orthoester yield (%)*[a]
1	**5** (0.5, 0.323)	Cholesterol (0.5, 0.194)	Nitromethane	2.5	**2** 51.7
2	**5** (0.5, 0.323)	Cholesterol (0.5, 0.194)	Chlorobenzene	0.5	**2** 37.1
3	**5** (0.5, 0.323)	Cholesterol (0.5, 0.194)	Toluene	2.5	**2** 65.8
4	**5** (1, 0.650)	Cholesterol (0.5, 0.193)	Toluene	2.0	**2** 75.3
5	**4** (1, 0.370)	Cholesterol (0.5, 0.194)	Toluene	1.5	**1** 89.7
6	**4** (1, 0.370)	Cholesterol (0.5, 0.194)	Dichloroethane	1.5	**1** 18.7
7	**5** (0.5, 0.325)	3-*O*-Acetylbetulin (0.5, 0.243)	Nitromethane	2.5	**3** 75.0
8	**5** (1, 0.650)	3-*O*-Acetylbetulin (0.5, 0.243)	Toluene	1.5	**3** 88.0

[a]In Expts. 1–6, the orthoester yields are given for crystalline products, and in 7–8, for chromatographically homogeneous material.

The results of experiments 1–8, shown in Table I, indicate that the formation of orthoesters of the types **1–3** may occur in parallel with the formation of polycyclic alcohol glycosides. The conditions (Expts. 4 and 8), under which transesterification of **4** and **5** by cholesterol and of **5** by betulin acetate at C-3 takes place in toluene, may be used for preparation of steroid and triterpenoid orthoesters in addition to other methods described previously[10,11]. The structures of **1–3** were confirmed by analytical data, hydrolysis[7], and n.m.r. data. Singlets at δ 1.74–1.75 indicate an *endo*-configuration for Me-2 in the dioxolane ring[10–12]. The reaction mixtures (Expts. 1–8) were concentrated to dryness and the residues were chromatographed[10] on a column of Silica Gel KCK (150–180 mesh), using light petroleum–acetone (30:1–13.5:1). T.l.c. on Silica Gel (5–40 μm, Czechoslovakia, La Chema), using light petroleum–acetone (2:1), gave the following compounds: **1**, m.p. 101–102°, $[\alpha]_D^{20}$ +2° (*c* 0.63, chloroform); lit.[7,10], m.p. 98–100°, $[\alpha]_D^{20}$ +2° (chloroform); **2**, m.p. 162–164° (from methanol), $[\alpha]_D^{20}$ +50° (*c* 0.45, chloroform) (Found: C, 63.67;

H, 8.14. $C_{53}H_{80}O_{18}$ calc.: C, 63.33; H, 8.02%); **3**, m.p. 190–192° (from methanol), $[\alpha]_D^{20}$ +65° (*c* 0.91, chloroform) (Found: C, 63.04; H, 8.03. $C_{58}H_{86}O_{20}$ calc.: C, 63.14; H, 7.85%).

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