Carbohydrate Research, 83 (1980) 33–42
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

SYNTHESIS OF TRITERPENE AND STEROID GLYCOSIDES

NINA I. UVAROVA, LYUBOV N. ATOPKINA, AND GEORGI B. ELYAKOV
Pacific Institute of Bio-organic Chemistry, Far East Science Centre, Academy of Sciences of the U.S.S.R., Vladivostok-22 (U.S.S.R.)

(Received January 11th, 1979; accepted for publication, October 19th, 1979)

ABSTRACT

The glycosylation of cholesterol, β-sitosterol, 28-*O*-acetylbetulin, and betulin with acylated glycosyl halides in the presence of $Hg(OAc)_2$, $Hg(CN)_2$, $CdCO_3$, Ag_2O, Ag_2CO_3, and $HgO + HgBr_2$ usually gives acylated αβ-glycosides accompanied by acetates, ethers, and bromo and unsaturated derivatives of the initial alcohols. The use of $Hg(CN)_2$ gave mainly β anomers (40–87%), whereas α anomers preponderated when $Hg(OAc)_2$ was the catalyst. When there was a deficiency of hydrogen halide acceptor and in the presence of the acidic catalyst $HgBr_2 \cdot HBr$, the β anomer, produced initially, underwent anomerisation. Cholesteryl α-D-glucopyranoside tetra-acetate (48%) was obtained by anomerisation of the β anomer.

INTRODUCTION

We have shown[1–3] that the ortho-ester method[4–6] for glycosylating steroid and terpenoid alcohols, although stereospecific, is complicated by the formation of by-products, such as the acetates and ethers of the initial alcohols (see also ref. 7). The by-products are formed[8–10] from the ortho-ester intermediates.

Acetates, together with the desired glucosyluronic acid derivatives, were obtained[11] from estrone, 17-β-estradiol, equilin, and equilenin, and a *C*-(glucosyluronic acid) derivative was formed from equilin, cadmium carbonate being used as the hydrogen halide acceptor. Glycosylation of 3,21-dihydroxy-5β-pregnane-11,20-dione[12] in the presence of silver carbonate gave mono- and di-(glucosiduronic acids), together with the 3- and 21-acetates, ortho esters, and a 3-keto derivative.

Irrespective of the hydrogen bromide acceptor used, tetra-*O*-acetyl-α-D-glucopyranosyl bromide (α-acetobromoglucose) condensed[13] with cholesterol, in the presence of silver 4-hydroxyvalerate, to give cholesteryl β-D-glucopyranoside tetra-acetate, α-D-glucose 1,2-(cholesteryl orthoacetate), and cholesteryl α- and β-D-glucopyranoside triacetates. A comparative study of the ortho-ester and the Koenigs–Knorr reactions was performed by Evstigneeva *et al.*[14–16] in synthesising glycosylglycerols. The influence of various factors on the stereoselectivity of the Koenigs–Knorr reaction for glycosylating cyclohexanol has been reported[17]. In choosing a method for the synthesis of glycosides of rare polycyclic alcohols, it is desirable to promote

0008-6215/80/0000–0000/$ 02.25,

TABLE I

COMPARATIVE DATA ON GLYCOSYLATION REACTIONS

	Starting substances (mM)			*Acylated glycosides*		*By-products (%)*[a]				*Recovered ROH (%)*
	ROH	*Glycosyl halide*[b]	*Acceptor*	*(%)*[a]	*(α,β-ratio)*	*ROAc*	*RBr*	*ROR*	*Unsaturated*	
I[c]	1 (2)	A (4.8)	2.2[e]	68	(60:40)	9	7	—	3	trace
II[c]	2 (2)	A (4.8)	2.2[e]	66	(60:40)	10	7	—	2	trace
III[c]	3 (2)	A (4.8)	2.2[e]	77	(60:40)	12	—	—	8	trace
IV[d]	1 (2)	A (4.8)	2.2[e]	40	(7:93)	13	3	—	3	32
V[c]	1 (1)	A (2.4)	1.2[e]	44	(10:90)	6	—	—	—	44
VI[c]	2 (1)	A (2.4)	1.2[e]	40	(10:90)	5	—	—	—	47
VII[c]	3 (1)	A (2.4)	1.2[e]	24	(10:90)	2	—	—	—	68
VIII[c]	1 (1)	B (1)	1[f]	87	(2:98)	—	—	8	—	trace
IX[d]	1 (1)	B (1)	1[f]	80	(β)	—	—	—	—	17
X[d]	1 (1)	A (1)	1[f]	60.3	(β)	5.6	—	3.0	—	20.1
XI[d]	1 (1)	A (1.5)	1.5[f]	77.2	(2:98)	8.4	—	3.1	—	trace
XII[d]	2 (1)	A (1.5)	1.5[f]	41.7	(3:97)	9.8	—	3.2	—	23.6
XIII[d]	3 (1)	A (1.5)	1.5[f]	79.6	(2:98)	6	—	—	—	—
XIV[d]	4 (1)	A (3)	3[f]	50% of diglucoside 36% of monoglucosides		3	—	—	—	—
XV[c]	1 (1)	A (2)	2[g]	60	(8:92)	6.6	trace	15	trace	—
XVI[c]	2 (1)	A (2)	2[g]	59	(8:92)	6.6	trace	15	trace	—
XVII[c]	3 (1)	A (2)	2[g]	69.5	(7:93)	6.7	trace	—	—	—
XVIII[c]	1 (1)	A (2.5)	1.7[h]	60	(12:88)	1	—	2	7	24
XIX[c]	1 (1)	A (2.5)	1.7[i]	51	(12:88)	2	—	1	5	33
XX[d]	1 (1)	A (2.5)	1.8[j]	55.4	(10:90)	9.5	—	—	trace	13.5

[a]Yields are given for chromatographically homogeneous substances. [b]*A*, acetobromoglucose; *B*, tetra-*O*-benzoyl-α-D-glucopyranosyl bromide. [c]At boiling point. [d]At room temperature. [e]In benzene in presence of $Hg(OAc)_2$. [f]In nitromethane in presence of $Hg(CN)_2$. [g]In toluene with $CdCO_3$ [h]In benzene with Ag_2CO_3. [i]In benzene with Ag_2O. [j]In chloroform with $HgO + HgBr_2$.

stereospecificity and impede reactions that regenerate the initial alcohol. We now report on these aspects for modifications[18-24] of the Koenigs–Knorr reaction most frequently used for glycosylation of steroid and triterpenoid alcohols.

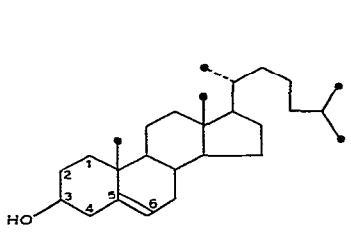
RESULTS AND DISCUSSION

Cholesterol (**1**), β-sitosterol (**2**), and 28-*O*-acetylbetulin (**3**) were condensed with α-acetobromoglucose in the presence of mercury(II) acetate under conditions used by Zemplén and Gerecs[18] for the synthesis of a gentiobiose derivative and by Lucas *et al.*[19] for the synthesis of 20-oxo-5β-pregnan-3-yl α-D-glucoside tetra-acetate (Table I, V–VI), and the modified technique used by Khorlin[20] for the synthesis of methyl oleanolate α-D-glucopyranoside tetra-acetate (yield 48%) involving a small excess of glycosyl bromide in relation to the hydrogen halide acceptor (Table I, I–IV). In I–III in Table I, acetates together with bromo and unsaturated derivatives of starting alcohols were formed in addition to αβ-glycoside tetra-acetates. The α,β-ratio was independent of the aglycon structure, and the α anomer preponderated by the end of the reaction.

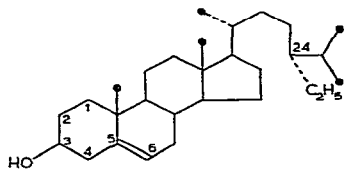
Moreover, the reaction mixtures I–IV in Table I contained partially deacetylated glucosides. After acetylation, the yield of α- and β-D-glucoside tetra-acetates was 4–6%. Condensation of **1** with acetobromoglucose at room temperature (Table I, IV) gave a lower yield of glucoside, but the total amount of by-products remained the same. The glycosylation of **1** in I in Table I gave the by-products cholesta-3,5-diene, cholesteryl bromide, and cholesteryl acetate. With β-sitosterol (**2**) and 28-*O*-acetylbetulin (**3**) (Table I, II and III), 24-(*R*)-ethylcholesta-3,5-diene, β-sitosteryl bromide, β-sitosteryl acetate, betulin diacetate, and 28-*O*-acetylbetulin-2-ene were obtained as by-products.

The alcohols **1–3** were not affected by mercury(II) acetate and mercury(II) bromide under the conditions I in Table I. However, in the presence of mercury(II) bromide and hydrogen bromide, cholesteryl bromide and β-sitosteryl bromide were formed and, to a lesser extent, cholesta-3,5-diene, 24-(*R*)-ethylcholesta-3,5-diene, and 28-*O*-acetylbetulin-2-ene. The occurrence of 3-*O*-acetyl derivatives of the starting alcohols may be explained by further conversions of the intermediate ortho esters. Thus, when a solution of 3,4,6-tri-*O*-acetyl-α-D-glucose 1,2-(cholesteryl orthoacetate) in benzene was heated in the presence of mercury(II) bromide–hydrogen bromide or mercury(II) bromide–α-acetobromoglucose for 15 min, cholesteryl β-D-glucopyranoside tetra-acetate, cholesteryl acetate, and cholesterol were formed.

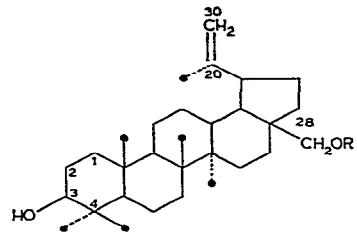
When the glycosylation of **1–3** in the presence of mercury(II) acetate (Table I, I–III) was monitored by t.l.c., it was found that, after 30 min, the glycoside formed was mainly the β anomer, whereas the glycoside in the product mixture was preponderantly the α anomer after 5 h. The occurrence of such anomerisation under the influence of $HgBr_2$ and $HHgBr_3$ has been reported by Lindberg[25]. The tetra-*O*-acetyl-β-D-glucosides of **1–3** were unchanged when solutions in benzene were heated in the presence of mercury(II) bromide, whereas β→α interconversion occurred in the



1



2



3 R = Ac
4 R = H

presence of mercury(II) bromide–hydrogen bromide or mercury(II) bromide–α-acetobromoglucose.

Quantitative data (Table II) on the anomerisation were obtained by analysing, at intervals by column chromatography, the reaction mixture obtained when cholesterol was glycosylated under the conditions I in Table I. When a solution of cholesteryl 2,3,4,6-tetra-*O*-acetyl-β-D-glucoside in benzene saturated with hydrogen bromide was boiled in the presence of mercury bromide, 48% of the α-glycoside was recovered.

Glycosylation[18,19] of **1–3** with equimolar amounts of acetobromoglucose and mercury(II) acetate (Table I, V–VII) gave αβ-mixtures of the tetra-acetates together with the acetylated alcohols as by-products.

When cholesterol (**1**) was condensed with tetra-*O*-benzoyl-α-D-glucopyranosyl bromide in the presence of mercury(II) cyanide[21] at high temperature (Table I, VIII), a high yield of the β-glycoside was obtained, together with 2% of the α anomer and dicholesteryl ether. Under these conditions, cholesterol was not affected by mercury(II) cyanide, but the yield of dicholesteryl ether was 26% in the presence of 0.5mM mercury(II) bromide. Hence, the formation of the ether in the initial experiment was due to the generation of mercury(II) bromide from the glycosyl bromide and mercury(II) cyanide.

Glycosylation of **1** with mercury(II) cyanide–tetra-*O*-benzoyl-α-D-glucopyranosyl bromide at room temperature (Table I, IX) was relatively slow, but stereospecific, yielding the β-glycoside and no by-products. When acetobromoglucose was used in a parallel experiment (Table I, X), a 60% yield of the β-glucoside was obtained together with a small proportion of by-products. When a 1.5-molar excess of glycosyl bromide was used (Table I, XI–XIII), the yield of β-glucoside was increased, as was that of the by-products, acetylated starting alcohols. Moreover, small proportions of the α anomers were also formed.

Glycosylation of betulin (**4**) (Table I, XIV) gave a satisfactory yield of the diglucoside octa-acetate (**25**) together with monoglucoside tetra-acetates.

Mild glycosylation conditions that have a sufficiently high degree of stereospecificity are valuable for glycosylating labile, not readily-available alcohols containing several hydroxyl groups.

Cadmium carbonate has been used to remove acid generated during the glycosylation of polycyclic alcohols[11,23,24]. The reactions of **1–3** with acetobromoglucose

TABLE II

GLYCOSYLATION OF CHOLESTEROL WITH α-ACETOBROMOGLUCOSE IN BENZENE IN THE PRESENCE OF MERCURY ACETATE

Reaction time (h)	*Yield of acetylated glycoside (%)*[a]			*Cholesterol (%)*
	Total	*α*	*β*	
15 min	41.5	1	40.5	50.5
30 min	53	3	50	31.3
1	60.3	8.3	52	11.3
2	63.3	17.7	45.6	4
5	68	41	27	traces

[a]Yields given for chromatographically homogeneous substances.

in toluene in the presence of cadmium carbonate (Table I, XV–XVII) gave good yields of β-glucosides together with small proportions of the α anomers. However, the formation of by-products could not be prevented. Moreover, the high reaction-temperature restricted the application of the method to non-labile alcohols.

Glycosylation of cholesterol in the presence of silver carbonate[22] and silver oxide[22] (Table I, XVIII and XIX) gave mainly β-glycoside, together with some α anomer and by-products. Neither silver oxide nor silver carbonate had any effect on cholesterol. Glycosylation of **1** in the presence of $HgO + HgBr_2$ in chloroform gave similar results, and deacetylation of the products was extensive. After re-acetylation, 15% of cholesteryl αβ-D-glucopyranoside tetra-acetate was obtained.

Thus, in most of the conditions examined, condensation of polycyclic alcohols with acylated glycosyl halides gives a mixture of acylated αβ-glucosides and, like the ortho-ester glycosylation method, also yields a number of by-products.

EXPERIMENTAL

Solvents were purified as described by Kochetkov *et al.*[4]. I.r. spectra were recorded for solutions in $CHCl_3$ with a UR-20 spectrophotometer. N.m.r. spectra were recorded at 25° for solutions in $CDCl_3$ (internal Me_4Si) with a Bruker HX90E spectrometer. Mass spectra were recorded with an LKB 9000 instrument.

Optical rotations were determined with a Perkin–Elmer 141 polarimeter at 25°. T.l.c. was performed on KCK silica gel with *A*, light petroleum–acetone (3:1); *B*, light petroleum–ether (95:5); and *C*, hexane, and detection by charring with sulphuric acid. Column chromatography was performed on KCK silica gel (80–120 mesh).

Condensations in the presence of mercury(II) acetate. — (I)* A mixture of aceto-bromoglucose (2 g), mercury(II) acetate (0.7 g), cholesterol (0.77 g), and benzene

*The roman numerals used for the following sections correspond with those in Table I.

(32 ml) was heated at 120° for 5 h and monitored by t.l.c. (solvents *A* and *B*) every 30 min. The mixture was cooled, diluted with benzene, washed with water, dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with a light petroleum–acetone gradient (acetone 0→20%). The fractionation, which was monitored by t.l.c. (solvents *A* and *B*), gave the following fractions (see Table I).

(*1*) A mixture (0.08 g) of cholesta-3,5-diene and cholesteryl bromide. P.l.c. (solvent *C*) gave cholesta-3,5-diene (0.02 g), m.p. 78–79° (from acetone), $[\alpha]_D^{20}$ −114° (*c* 0.4, chloroform); mass spectrum: *m/e* 368 (M^+); ^{13}C-n.m.r. data: δ 124.6 (C-3), 129.2 (C-4), 141.3 (C-5), and 123.0 (C-6); and cholesteryl bromide (0.06 g), m.p. and mixture m.p. 98–100°.

(*2*) Cholesteryl acetate (0.07 g), m.p. and mixture m.p. 113–114°.

(*3*) Cholesteryl α-D-glucopyranoside tetra-acetate[27] (0.26 g), m.p. 193–195° (from ethanol), $[\alpha]_D^{20}$ +92° (*c* 1, chloroform); lit.[27] m.p. 195°, $[\alpha]_D^{20}$ +88°.

(*4*) Cholesteryl β-D-glucopyranoside tetra-acetate[7] (0.19 g), m.p. and mixture m.p. 157–159°, $[\alpha]_D^{20}$ −26° (*c* 1, chloroform).

(*5*) A mixture (0.52 g) of the foregoing glycosides.

(II) β-Sitosterol (0.83 g), acetobromoglucose (2 g), and mercury(II) acetate (0.7 g) were treated in benzene as in (I) and the resulting mixture was worked-up in the same way, to give the following fractions.

(*1*) A mixture (85 mg) of 24-(*R*)-ethylcholesta-3,5-diene and β-sitosteryl bromide, which was fractionated by p.l.c. (solvent *C*) to give 24-(*R*)-ethylcholesta-3,5-diene, m.p. 66–67° (from acetone), $[\alpha]_D^{20}$ −110° (*c* 0.1, chloroform); and cholesteryl bromide, m.p. and mixture m.p. 78–79° (from acetone).

(*2*) β-Sitosteryl acetate[28] (90 mg), m.p. and mixture m.p. 123–124°, $[\alpha]_D^{20}$ −36° (chloroform); lit.[28] m.p. 130–132°, $[\alpha]_D^{20}$ −42°.

(*3*) β-Sitosteryl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside, m.p. 190–192° (from ethanol), $[\alpha]_D^{20}$ +96° (*c* 1, chloroform); p.m.r. data: δ 5.22 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1). (Found: C, 69.44; H, 9.56. $C_{43}H_{68}O_{10}$ calc.: C, 69.32; H, 9.20%.)

(*4*) β-Sitosteryl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside, m.p. 167–168° (from ethanol), $[\alpha]_D^{20}$ −21° (*c* 1, chloroform); lit.[28] m.p. 167.5–168.5°, $[\alpha]_D^{20}$ −24° (chloroform).

(*5*) A mixture (0.26 g) of the glycosides in (*3*) and (*4*).

(III) 28-*O*-Acetylbetulin (0.97 g), acetobromoglucose (2 g), and mercury(II) acetate (0.7 g) were treated in benzene as in (I), and the resulting mixture was worked-up to give the following fractions.

(*1*) 28-*O*-Acetylbetulin-2-ene (70 mg), m.p. 58–60°, $[\alpha]_D^{20}$ +27° (*c* 0.5, chloroform); $\nu_{max}^{CHCl_3}$ 1740 (COOR), 890, 1640, and 3080 cm^{-1} (C=CH_2); mass spectrum: *m/e* 466 (M^+); ^{13}C-n.m.r. data: δ 136.3 (C-2), 140.0 (C-3), 150.2 (C-20), and 109.8 (C-30). (Found: C, 81.23; H, 10.63. $C_{32}H_{50}O_2 \cdot 0.5\,CH_3OH$ calc.: C, 80.86; H, 10.85%.)

(*2*) 3,28-Di-*O*-acetylbetulin (0.12 g), m.p. and mixture m.p. 217–219°, $[\alpha]_D^{20}$ +23.5° (*c* 1, chloroform); lit.[29] m.p. 217–219°, $[\alpha]_D^{20}$ +23° (chloroform).

(*3*) Betulin-3-yl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (0.5 g), m.p. 111–

114° (from aqueous ethanol), $[\alpha]_D^{20}$ +95° (*c* 1, chloroform); $\nu_{max}^{CHCl_3}$ 1740 (COOR), 890, 1640, and 3080 cm^{-1} (C=CH_2); p.m.r. data: δ 5.2 (d, 1 H, $J_{1,2}$ 4.2 Hz, H-1). (Found: C, 67.79; H, 8.77. $C_{46}H_{70}O_{12}$ calc.: C, 67.78; H, 8.67%.)

(*4*) A mixture (0.75 g) of the glycoside in (*3*) and its β anomer.

(IV) Acetobromoglucose (2 g) and mercury(II) acetate (0.7 g) were added to a solution of cholesterol (0.77 g) in benzene (32 ml). The mixture was stirred for 5 h at room temperature and worked-up, as described in (I), to give cholesta-3,5-diene (0.02 g), cholesteryl bromide (0.03 g), cholesteryl acetate (0.11 g), cholesterol (0.25 g), cholesteryl 2,3,4,6-tetra-*O*-acetyl-α- (30 mg), -β- (0.53 g), and -$\alpha\beta$-D-glucopyranoside (20 mg).

(V) A solution of cholesterol (0.39 g) in benzene (16 ml) was treated with acetobromoglucose (1 g) and mercury(II) acetate (0.4 g), as described in (I), to give cholesteryl acetate (24 mg), cholesterol (0.17 g), and cholesteryl 2,3,4,6-tetra-*O*-acetyl-α- (20 mg), -β- (0.26 g), and -$\alpha\beta$-D-glucopyranoside (30 mg).

(VI) A solution of β-sitosterol (0.42 g) in benzene (16 ml) was treated with acetobromoglucose (1 g) and mercury(II) acetate (0.4 g), as described in (V), to give β-sitosteryl acetate (25 mg), β-sitosterol (0.2 g), β-sitosteryl 2,3,4,6-tetra-*O*-acetyl-α- (20 mg), -β- (0.26 g), and -$\alpha\beta$-D-glucopyranoside (20 mg).

(VII) A mixture of 28-*O*-acetylbetulin (0.43 g), acetobromoglucose (1 g), and mercury(II) acetate (0.4 g) in benzene (16 ml) was treated as described in (V), to give 3,28-di-*O*-acetylbetulin (12 mg), 28-*O*-acetylbetulin (0.29 g), and 28-*O*-acetylbetulin-3-yl 2,3,4,6-tetra-*O*-acetyl-$\alpha\beta$-D-glucopyranoside (0.174 g).

Condensations in the presence of mercury cyanide. — (VIII) A mixture of cholesterol (0.39 g), tetra-*O*-benzoyl-α-D-glucopyranosyl bromide (0.66 g), and mercury(II) cyanide (0.25 g) in nitromethane (10 ml) was heated at 140° for 2 h, until t.l.c. revealed the disappearance of cholesterol. The mixture was worked-up as described above, to give the following fractions.

(*1*) Dicholesteryl ether (30 mg), m.p. and mixture m.p. 200–202° (from methanol–chloroform), $[\alpha]_D^{20}$ −45° (*c* 1.76, chloroform).

(*2*) Cholesteryl 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranoside (20 mg), m.p. 228–230° (from methanol–chloroform), $[\alpha]_D^{20}$ +52.5° (*c* 0.4, chloroform); p.m.r. data: δ 5.2 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1). (Found: C, 74.86; H, 7.41. $C_{61}H_{72}O_{10} \cdot CH_3OH$ calc.: C, 74.56; H, 7.58%.)

(*3*) The β anomer (0.82 g) of (*2*), m.p. 214–216° (from methanol–chloroform), $[\alpha]_D^{20}$ +15° (*c* 0.9, chloroform); p.m.r. data: δ 4.95 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1). (Found: C, 75.92; H, 7.29. $C_{61}H_{72}O_{10}$ calc.: C, 75.93; H, 7.51%.)

(IX) When the mixture in (VIII) was agitated for 48 h at room temperature, the products were cholesterol (0.07 g) and the β-glycoside tetrabenzoate (0.77 g).

(X) A mixture of cholesterol (0.39 g), acetobromoglucose (0.41 g), mercury(II) cyanide (0.25 g), and nitromethane (10 ml) was agitated for 24 h at room temperature. The products were dicholesteryl ether (7 mg), cholesteryl acetate (24 mg), cholesterol (77 mg), and the β-glycoside tetra-acetate (0.43 g).

(XI) The mixture in (X) was agitated at room temperature for 4 h. More

acetobromoglucose (0.2 g) and mercury(II) cyanide (0.125 g) were added, and the mixture was agitated for another 20 h and then worked-up as described above, to give dicholesteryl ether (12 mg), cholesteryl acetate (44 mg), and the α- (10 mg) and β-glycoside tetra-acetates (0.54 g).

(XII) When β-sitosterol (0.42 g) was glycosylated as described in (XI), the products were β-sitosteryl acetate (22 mg), β-sitosterol (0.1 g), the α- (11 mg) and β-glycoside tetra-acetates (0.3 g), and di-β-sitosteryl ether (4 mg).

(XIII) When 28-*O*-acetylbetulin (0.484 g) was glycosylated as described in (XI), the products were 3,28-di-*O*-acetylbetulin (35 mg), and the α- (20 mg) and β-glycoside tetra-acetates (0.63 g).

(XIV) When betulin (0.44 g) was glycosylated as described in (XI), the products were 3,28-di-*O*-acetylbetulin (20 mg); betulin-28-yl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside[3] (50 mg), m.p. and mixture m.p. 140–143° (from ethanol); 28-*O*-acetylbetulin-3-yl β-D-glucoside tetra-acetate (0.24 g), and 3,28-di-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)betulin[3] (0.5 g), m.p. and mixture m.p. 230–231° (from ethanol).

Condensations in the presence of cadmium carbonate. — (XV) A mixture of cholesterol (0.39 g) and cadmium carbonate (0.34 g) in toluene (20 ml) was kept at 140° and solvent (5 ml) was distilled off. A solution of acetobromoglucose (0.82 g) in toluene (20 ml) was then added dropwise during 1 h, under conditions of azeotropic distillation, which was continued for another 30 min. The cooled mixture was filtered and concentrated *in vacuo*. The residue was fractionated on a column of silica gel, to yield dicholesteryl ether (60 mg), cholesteryl acetate (30 mg), and the α- (30 mg) and β-glycoside tetra-acetates (0.39 g).

(XVI) Glycosylation of β-sitosterol (0.42 g), as in (XV), gave di-β-sitosteryl ether (60 mg), β-sitosteryl acetate (30 mg), and the α- (26 mg) and β-glycoside tetra-acetates (0.43 g).

(XVII) Glycosylation of 28-*O*-acetylbetulin (0.484 g), as in (XV), gave 3,28-di-*O*-acetylbetulin (40 mg), and the α- (45 mg) and β-glycoside tetra-acetates (0.55 g).

Condensations in the presence of silver carbonate. — (XVIII) A mixture of cholesterol (0.39 g), benzene (10 ml), and freshly prepared silver carbonate (0.47 g) was heated under conditions of azeotropic distillation, whilst adding dropwise, during 1 h, a solution of acetobromoglucose (1 g) in benzene (10 ml). The mixture was then heated for another 30 min, cooled, filtered, and concentrated *in vacuo*. The residue was subjected to column chromatography, to yield cholest-3,5-diene (25 mg), a mixture (10 mg) of cholesteryl acetate and dicholesteryl ether, cholesterol (90 mg), and the α- (50 mg) and β-glycoside tetra-acetates (0.38 g).

Condensation in the presence of silver oxide. — (XIX) Cholesterol (0.39 g) was treated with a solution of acetobromoglucose (1 g) in benzene in the presence of silver oxide (0.39 g), as described in (XVIII), to give cholest-3,5-diene (18 mg), cholesteryl acetate (10 mg), dicholesteryl ether (5 mg), cholesterol (0.17 g), and the α- (40 mg) and β-glycoside tetra-acetates (0.32 g).

Condensation in the presence of HgO + $HgBr_2$. — A mixture of Drierite (1.2 g),

yellow mercury(II) oxide (0.4 g), mercury(II) bromide (25 mg), cholesterol (0.39 g), and chloroform (7.5 ml) was agitated at room temperature for 30 min. More acetobromoglucose (1 g) was added and agitation was continued for 24 h. The mixture was filtered and concentrated, and the residue was subjected to chromatography on a column of silica gel, to give cholesteryl acetate (40 mg), cholesterol (50 mg), and the α- (10 mg) and β-glycoside tetra-acetates (0.29 g). The fraction containing deacetylated αβ-glycoside was treated with acetic anhydride in pyridine and refractionated, to yield a 1:2 αβ-mixture (0.11 g) of glycoside tetra-acetates.

*Anomerisation of cholesteryl 2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranoside.* — A solution of the glycoside (0.71 g) and $HgBr_2$ (0.36 g) in benzene (32 ml) was saturated with dry hydrogen bromide at 0°, and then boiled under reflux for 3 h. The cooled mixture was washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was crystallised from ethanol, to give the anomer (0.25 g). The mother liquor was concentrated, and the residue was subjected to chromatography on a column of silica gel, to give more α anomer (0.1 g); total yield, 0.35 g (48%).

REFERENCES

1 G. B. Elyakov, N. I. Uvarova, I. V. Dardymov, O. E. Mislitskaya, and L. M. Antonik, *Khim.-Farm. Zh.*, (1969) 5–8.
2 G. B. Elyakov, N. I. Uvarova, and G. I. Oshitok, *Khim.-Farm. Zh.*, (1971) 7–9.
3 N. I. Uvarova, G. I. Oshitok, and G. B. Elyakov, *Carbohydr. Res.*, 27 (1973) 79–87.
4 N. K. Kochetkov, A. Ya. Khorlin, and A. F. Bochkov, *Tetrahedron*, 23 (1967) 693–707.
5 N. K. Kochetkov, A. F. Bochkov, T. A. Sokolovskaya, and V. I. Snyatkova, *Carbohydr. Res.*, 16 (1971) 17–27.
6 A. Ya. Khorlin, A. F. Bochkov, and N. K. Kochetkov, *Khim. Prir. Soedin.*, (1966) 6–12.
7 G. Wulff and G. Röhle, *Angew. Chem.*, 13 (1974) 157–168.
8 N. I. Uvarova, G. I. Oshitok, N. F. Samoshina, and G. B. Elyakov, *Khim. Prir. Soedin.*, (1974) 460–463.
9 N. I. Uvarova, N. F. Samoshina, L. E. Novikova, and G. B. Elyakov, *Carbohydr. Res.*, 42 (1975) 165–167.
10 N. I. Uvarova, N. F. Samoshina, L. E. Novikova, and G. B. Elyakov, *Tezisy Dokl. XI Mendeleevsk. S'ezd po Obshch. i Prikl. Khim.*, Nauka, 1975, p. 115.
11 R. B. Conrow and S. Bernstein, *J. Org. Chem.*, 36 (1971) 863–869.
12 V. R. Mattox and W. A. Vrieze, *J. Org. Chem.*, 37 (1972) 3990–3996.
13 G. Wulff, G. Röhle, and N. Krüger, *Chem. Ber.*, 105 (1972) 1097–1110, 1111–1121, 1121–1132.
14 A. P. Kaplun, V. E. Kalugin, V. I. Shvets, and R. P. Evstigneeva, *Bioorg. Khim.*, 1 (1975) 1675–1676.
15 A. P. Kaplun, V. I. Shvets, and R. P. Evstigneeva, *Zh. Org. Khim.*, 13 (1977) 1606–1612.
16 A. P. Kaplun, V. I. Shvets, and R. P. Evstigneeva, *Bioorg. Khim.*, 3 (1977) 222–231.
17 J. E. Wallace and L. R. Schroeder, *J. Chem. Soc., Perkin Trans. 1*, (1976) 1938–1941.
18 G. Zemplén and A. Gerecs, *Ber.*, 64 (1931) 1545–1554.
19 R. A. Lucas, D. F. Dickel, R. L. Dziemian, M. I. Ceglowski, B. H. Hensle, and H. B. MacPhillamy, *J. Am. Chem. Soc.*, 82 (1960) 5688–5693.
20 N. K. Kochetkov, A. Ya. Khorlin, and V. I. Snyatkova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, (1964) 2028–2036.
21 B. Helferich and K. Weis, *Chem. Ber.*, 89 (1956) 314–321.
22 Ch. Meystre and K. Miescher, *Helv. Chim. Acta*, 27 (1944) 231–236.
23 I. Kitagawa, K. Sik Im, and Y. Fujimoto, *Chem. Pharm. Bull.*, 25 (1977) 800–808.
24 P. Kocovsky, K. K. Kosoev, and Z. Prochazka, *Collect. Czech. Chem. Commun.*, 38 (1973) 3273–3278.

25 B. LINDBERG, *Acta Chem. Scand.*, 1 (1947) 710–716.
26 I. BROOME, B. R. BROWN, AND G. H. SUMMERS, *J. Chem. Soc.*, (1957) 2071–2075.
27 E. HARDEGGER AND I. PASCUAL, *Helv. Chim. Acta*, 31 (1948) 281–286.
28 C. A. KIND AND V. D. CELENTANO, *J. Org. Chem.*, 18 (1953) 1473–1477.
29 L. G. MATYUKHINA, *Zh. Obshch. Khim.*, 34 (1964) 2796–2798.