60. J. Martel, E. Toromanoff, and C. Huynh, J. Org. Chem., 30, 1752 (1965).
61. H. Lettré and T. J. Fitzgerald, Act. Probl. Cancerol., 2, 200 (1968).
62. H. Lettré, T. J. Fitzgerald, and W. Siebs, Naturwissenschaften, 53, 132 (1966).
63. L. Velluz and G. Muller, Bull. Soc. Chim. Fr., 755 (1954).
64. C. Plotka and R. Jequer, Arch. Int. Pharmacodyn., 109, 386 (1957).
65. French Patent M2419; Chem. Abstr., 61, 12051d (1964).
66. French Patent M2418; Chem. Abstr., 61, 12051c (1964).
67. French Patent M2653; Ref. Zh. Khim., No. 9, N353 (1967).
68. French Patent M2870; Ref. Zh. Khim., No. 2, N382 (1967); French Patent CAM 77; Chem. Abstr., 64, 3626c (1966).
69. G. Muller, French Patent M2926; Ref. Zh. Khim., No. 2, N463 (1967); French Patent M2655; Ref. Zh. Khim., No. 9, N355 (1967).
70. French Patent M2994 (1967).
71. G. Muller, French Patent M2654; Ref. Zh. Khim., No. 9, N354 (1967).
72. French Patent M2731; Chem. Abstr., 62, 1699f (1965).
73. G. Muller and R. Bardoneshi, French Patent M2652; Ref. Zh. Khim., No. 9, N352 (1967).
74. G. Muller, A. B. Font, and R. Bardoneschi, Ann. Chem., 662, 105 (1963).
75. French Patent M2420; Chem. Abstr., 61, 12051e (1964).
76. E. Steinegger and A. Levan, Hereditas, 33, 385 (1947).
77. H. Corrodi and E. Hardegger, Helv. Chim. Acta, 40, 193 (1957).
78. H. Lettré, A. Mex, and E. Ruhbaum, Z. Physiol. Chem., 289, 119 (1952).
79. H. Rapoport and J. B. Lavigne, J. Am. Chem. Soc., 78, 2455 (1956).
80. S. K. Kulra and M. Fragata, FEBS Lett., 42, 112 (1974).
81. W. A. Creasey, Handbook of Experimental Pharmacology, Number 38, "Antineoplastic and Immunosuppressive Agents," Pt. 2 (1975), p. 670.
82. French Patent M2712, Ref. Zh., Khim., No. 9, N365 (1967); M2718; Chem. Abstr., 61, 15941a (1964); M2818; Chem. Abstr., 63, 14930b (1965); M3032; Chem. Abstr., 63, 440f (1965); M3180; Ref. Zh., Khim., No. 15, N381 (1967); M3375, Ref. Zh. Khim., No. 18, N295 (1967); M3787; Chem. Abstr., 67, 3287m (1967); M4245; Chem. Abstr., 68, 12774k (1968); CAM 100; Chem. Abstr., 70, 118086f (1969).

SOME FEATURES OF THE GLYCOSYLATION OF POLYCYCLIC ALCOHOLS WITH CARBOHYDRATE 1,2-ORTHOESTERS

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UDC 547.455+547.918+547.922

The majority of synthetic glycosides of triterpenoids and steroids has been obtained by the Koenigs–Knorr method or its various modifications [1, 2]. At the present time, the orthoester method has come to be used successfully for this purpose [3-7]; it is characterized by a high stereospecificity and a good reproducibility of the results. A complicating factor in the synthesis of glycosides of polycyclic alcohols by the orthoester method has been the formation of byproducts — ethers and acetates of the initial alcohols [7]. The isolation of these compounds permits us to consider the final result as the sum of three processes: glycosylation, transesterification, and the subsequent conversions of the transesterification products (Schemes 1 and 2).

The simultaneous occurrence of glycosylation and transesterification can be explained by the dual reactivity of carbohydrate orthoesters [3, 5, 8]. Since in the glycosylation with α-D-maltose (methyl orthoacetate) (I) and with α-D-glucose 1,2-(tert-butyl orthoacetate) (II) of cholesterol, β-sitosterol, 16-dehydropregnenolone, and betulin and its mono-

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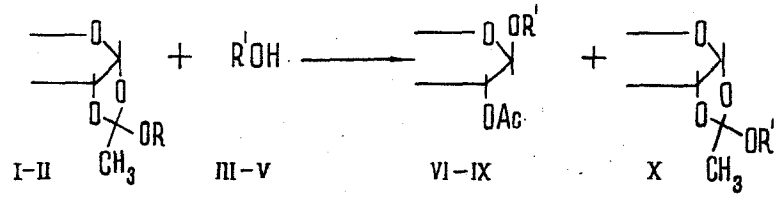
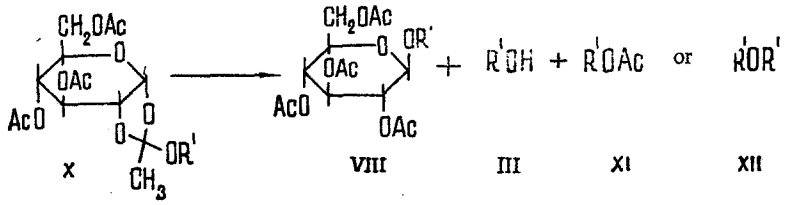


Scheme 1



Scheme 2

acetates the final mixtures contained no orthoesters of type (X) (check by the TLC method and the acid test) [7], it had to be considered that such orthoesters underwent complete conversion during the reaction, as was confirmed by subsequent experiments. Thus, heating tri-O-acetyl-α-D-glucopyranose (cholesteryl orthoacetate) (X) under the reaction conditions (azeotropic distillation and catalyst) [9] led to the complete conversion of (X) into cholesterol tetra-O-acetyl-β-D-glucopyranoside (VIII), free cholesterol (III), cholesterol acetate (XI), and dicholesteryl ether (XII) (see Scheme 2).

In addition to this, it was found that orthoesters of type (X) can easily arise in the absence of a glycosylation catalyst when polycyclic alcohols and carbohydrate 1,2-orthoesters (I, II) are heated under conditions of the azeotropic distillation of the solvent (nitromethane, chlorobenzene, and toluene) [10]. The instability of the orthoesters (type X) and the ease of their formation on heating the corresponding mixtures without a catalyst permitted the assumption that the order of mixing of the reactants in the synthesis of glycosides might be significant [3-5, 11, 12]. According to the method adopted [3-5, 11], after the addition to the solvent (nitromethane or chlorobenzene) of the orthoester (I or II) and the alcoholic component, in order to protect the mixture from traces of moisture it is necessary to distill off a portion of the solvent (5 ml) and only then to add the solution of the catalyst. However, a number of authors [10] has shown that with such a sequence at the moment of addition of the catalyst the reaction mixture already contains three substances: the initial orthoester (I or II), the alcohol, and the transesterification product.

To decrease the influence of transesterification processes on the yield of the desired glycosides it was decided first to distill off the azeotrope only from the solution of cholesterol and mercuric bromide and then to add the orthoester (II). In actual fact, this change in the sequence of performing the glycosylation reaction in the synthesis of cholesterol hepta-O-acetyl-β-D-maltoside (VI) enabled us to obtain it with a higher yield (Table 1, experiment 1) than previously (usually 42-43%) [10, 11]. The yields of dicholesteryl ether were the same in the standard method and in the modified method. Consequently, the mercuric bromide and 2,6-lutidinium perchlorate used in glycosylation do not affect the formation of orthoesters of type (X). At the same time, these substances cause the complete conversion of the transesterification products during the synthesis.

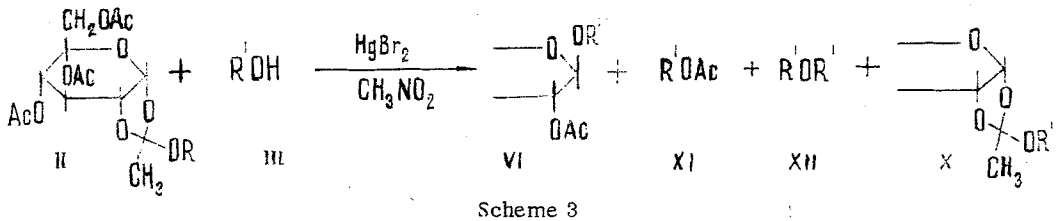
It must also be mentioned that the results of glycosylation under the conditions of the method that we are considering depend to a considerable degree on the structure of the initial alcohol. For example, in the glycosylation of cholesterol (see Table 1, experiment 1), a byproduct is dicholesteryl ether, and in the case of cholestanol it is its acetate (see Table 1, experiment 2).

Of a number of carbohydrate orthoesters, the highest glycosylation capacity was shown by α-D-glucose 1,2-(tert-butyl orthoacetate) (II) on condensation in chlorobenzene under the influence of 2,6-lutidinium perchlorate [7, 11, 12]. However, its use under the conditions of catalysis by mercuric bromide in nitromethane solution in the synthesis of gentiobiose

TABLE 1. Results of the Glycosylation of Polycyclic Alcohols

Initial reactant, mmole		Conditions of synthesis			Yield,* %		Recovery of the initial alcohol, %
carbohydrate 1,2-orthoester	ROH	solvent, 10 ml	catalyst, mmole	time, h	glycoside	by-product	
α-D-Maltose (methyl orthoacetate) (I), 1,0	Cholesterol† (III), 1,0	CH_3NO_2	$HgBr_2$, 0,02	2,5	VI, 49,3	Dicholesteryl ether, (XII), 18.9	19,2
I, 0,5	Cholestanol† (IV), 0,5	CH_3NO_2	$HgBr_2$, 0,01	2,5	VII, 53,8	Cholestanol acetate, 4.7	22,3
α-D-Glucose (tert-butyl orthoacetate) (II), 0.5	Cholesterol 0,5	CH_3NO_2	$HgBr_2$, 0,01	2,5	VIII, 12,5 VIIIa‡ 8,0	Cholesterol acetate, 3,7; dicholesteryl ether, 5.1	38,9
I, 1,0	β-Sitosterol (V), 1,0	C_6H_5Cl	2,6-Lutidinium perchlorate, 0.02	0,5	IX, 34,9 IXa,** 9,0	β-Sitosterol acetate, 21.5	15,2
II, 1,0	Cholesterol (III), 1,0	$C_2H_4Cl_2$	2,6-Lutidinium perchlorate, 0.02, p-toluenesulfonic acid 0.02	1,5	VIII, 26,9 VIIIb 5,6	—	51,8

*Yields given for crystalline derivatives.
†The catalyst and the alcohol were added simultaneously.
‡(VIIIa) is partially acetylated cholesterol β-D-glucoside.
**(IXa) is β-sitosterol β-D-maltoside.



Scheme 3

I. $R=CH_3$

II. $R=t-C_4H_9$

R' = residue of a polycyclic alcohol.

octaacetate showed its complete inertness [14]. In view of this, it appeared of interest to determine to what changes such a variant would lead in the case of the glycosylation of polycyclic alcohols. However, as follows from the results, the glycosylation of cholesterol by the orthoester (II) took place unsatisfactorily and led to a complex mixture of substances (see Table 1, experiment 3, and Scheme 3).

We simultaneously studied the glycosylating capacity of α-D-maltose (methyl orthoacetate) (I) [15] in the presence of 2,6-lutidinium perchlorate in chlorobenzene, since this modification had not been studied previously as applied to polycyclic alcohols. Glycosylation took place satisfactorily, and this orthoester may also be used for glycosylation under the given conditions (experiment 4). It must be mentioned that the glycosylation of steroids and terpenoids took place stereospecifically in all cases studied. Table 1 gives one of the numerous examples in which, together with the β anomer, we also isolated the α anomer of cholesterol tetra-O-acetyl-D-glucoside (VIIIb).

EXPERIMENTAL

The melting points of the substances were determined on a "Boëtius" stage, and the specific rotations on a Perkin–Elmer instrument with a cell length of 1 dm. The preparative separation of the substances was performed in columns of silica gel (KSK, 80-150 mesh) in system 1) petroleum ether–acetone (discrete gradient). TLC was performed in the petroleum ether–acetone (3:1 and 2:1) and petroleum ether–diethyl ether (95:5) systems.

Experiment 1. Cholesterol Hepta-O-acetyl-β-D-maltoside (VI). A solution of 1 mmole (0.386 g) of cholesterol (III) and 0.02 mmole of $HgBr_2$ in 10 ml of nitromethane was distilled until 3 ml of the solvent had passed over, and then 1 mmole (0.650 g) of α-D-maltose (methyl acetate) (I) was added. The mixture was boiled with the azeotropic distillation of the solvent for 2.5 h. Then the nitromethane was evaporated off, two to three drops of pyridine was added, and the mixture was evaporated to dryness. The residue was chromatographed on a column in system 1 (40:1→35:1). After crystallization from solvents we obtained 0.07 g (18.9%) of dicholesteryl ether (XII), mp 200-201°C; 0.074 g (19.2%) of (III); and 0.50 g (49.3%) of (VI), mp 179-182.5°C.

Experiment 2. Cholestanol Hepta-O-acetyl-β-D-maltoside (VII). The glycosylation of 0.05 mmole of (IV) was performed under the conditions of experiment 1 with 0.5 mmole of (I) and 0.01 mmole of $HgBr_2$, giving: 0.011 g (4.7%) of cholestanol acetate; 0.044 g (22.3%) of (IV), and 0.408 g (53.8%) of (VII), mp 170-171°C (ethanol); $[\alpha]_D^{20}$ +42.5° (c 1.43; $CHCl_3$). Literature data [16]: mp 171-172°C; $[\alpha]_D^{20}$ +52.7° (c 1.15).

Experiment 3. A mixture of 0.5 mmole of (III), 0.5 mmole of (II), and 0.01 mmole of $HgBr_2$ was treated under the conditions of experiment 1. Chromatography on a column of silica gel in system 1 led to the isolation of 0.010 g (5.1%) of (XII); 0.008 g (3.7%) of (XI); 0.074 g (38.9%) of (III); 0.042 g (12.5%) of (VIII); and 0.025 g (8%) of (VIIIa).

Experiment 4. A solution of 1 mmole (0.411 g) of (V) and 1 mmole (0.650 g) of (I) in 10 ml of chlorobenzene was distilled until 3 ml of solvent had passed over, and then 0.02 mmole of 2,6-lutidinium perchlorate in dichloroethane solution was added. The mixture was then boiled for 30 minutes and evaporated. The residue was chromatographed on silica gel in system 1 (30:1-17:1), which yielded 0.099 g (21.5%) of β-sitosterol acetate; 0.063 g (15.2%) of (V); 0.09 g (9.0%) of (IXa); and 0.36 g (34.9%) of (IX).

Experiment 5. To a flask containing 10 ml of dichloroethane was added 1 mmole of (III) and 1 mmole of (II), 2 ml of the solvent was distilled off, and 0.02 mmole of pyridinium perchlorate and 0.2 mole of p-toluenesulfonic acid were added and the mixture was boiled with azeotropic distillation of the solvent for 1.5 h. Separation on a column yielded 0.20 g (26.9%) of (VIII); 0.202 g (51.8%) of (III); and 0.049 g of (VIIIb), mp 192.5-194°C.

SUMMARY

1. The results of the glycosylation of polycyclic alcohols by the orthoester method depend to a considerable degree on the structure of the initial alcohols.

2. It has been shown that a change in the order of addition of the components increases the yield of glycosides but does not suppress the formation of byproducts.

LITERATURE CITED

1. N. K. Kochetkov et al., Carbohydrate Chemistry [in Russian], Moscow (1967), p. 216.
2. G. Wulff and G. Röhle, Angew. Chem., Internat. Edit., 13, 157 (1974).
3. A. Ya. Khorlin, A. F. Bochkov, and N. K. Kochetkov, Khim. Prirodn. Soedin., 6 (1966).
4. N. K. Kochetkov, A. Ya. Khorlin, A. F. Bochkov, and G. L. Kretsu, Izv. Akad. Nauk SSSR, Ser. Khim., 2028 (1966).
5. N. K. Kochetkov, A. Ia. Khorlin, and A. F. Bochkov, Tetrahedron, 23, 693 (1967).
6. V. G. Bukharov and S. P. Shcherbak, Khim. Prirodn. Soedin., 373 (1975).
7. N. I. Uvarova, G. I. Oshitok, and G. B. Elyakov, Carbohydrate Res., 27, 79 (1973).
8. V. V. Mezheritskii, E. P. Olekhnovich, and G. N. Dorofeenko, Usp. Khim., 42, 896 (1973).
9. N. I. Uvarova, G. I. Oshitok, N. F. Samoshina, and G. B. Elyakov, Khim. Prirodn. Soedin., 460 (1974).
10. N. I. Uvarova, N. F. Samoshina, L. E. Novikova, and G. B. Elyakov, Carbohydrate Res., 42, 165 (1975).

11. A. F. Bochkov, V. I. Snyatkova, and N. K. Kochetkov, Izv. Akad. Nauk SSSR, Ser. Khim., 2684 (1967).
12. N. K. Kochetkov, A. F. Bochkov, T. A. Sokolovskaya, and B. I. Snyatkova, Carbohydrate Res., 16, 17 (1971).
13. N. K. Kochetkov, A. F. Bochkov, and T. A. Sokolovskaya, Dokl. Akad. Nauk SSSR, 187, 96 (1969).
14. A. F. Bochkov and T. A. Sokolovskaya, Izv. Akad. Nauk SSSR, Ser. Khim., 2793 (1971).
15. N. K. Kochetkov, A. Ya. Khorlin, A. F. Bochkov, L. B. Demushkina, and I. O. Zolotukhin, Zh. Obshch. Khim., 37, 1272 (1967).
16. A. Plattner and A. Uffer, Helv. Chim. Acta, 28, 1049 (1945).

OILS OF THE SEEDS OF NINE SPECIES OF THE GENUS *Crambe*

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UDC 547.915+665.3

Of the 18 species of *Crambe* (colewort) growing in the territory of the USSR [1], *Crambe abyssinica* (Abyssinian colewort) has been intensively studied and introduced into cultivation, since it gives a fatty oil valuable for food purposes [2]. At the present time, Abyssinian colewort is grown as an oil crop in the southern regions of Povolzh'e and the central zone of Russian [3]. The fatty oil of this plant contains about 60% of erucic acid, which is used to prepare polyamide resins, polyesters, surface-active agents, etc. [4, 5]. Other species of colewort also contain large amounts of fatty oil [6-8].

We have investigated the oil of the seeds of nine species of colewort: *Crambe abyssinica* Hochst., *C. amabilis* Butk. et Majlum, *C. cordifolia* Stev., *C. koktebelica* (Junge) N. Busch., *C. kitschyana* Boiss., *C. orientalis* L., *C. pinnatifida* R. Br., *C. steveniana* Rupr., and *C. tataria* Sebeók.

The species of the genus *Crambe* are close phylogenetically and therefore the oils from their seeds differed little in their physicochemical properties. The seeds of the species studied had a high oil content — 29.42-38.73%, the highest being found in the seeds of the Abyssinian colewort — 38.73%. Some physicochemical indices of the oils are also characterized by the following facts: refractive index — 1.4715-1.4748; relative viscosity, $^{\circ}E_{20}$ — 10.86-11.42; acid No., mg KOH/g — 1.78-3.56; saponification No., mg KOH/g — 170.34-178.54; iodine No., % iodine — 100.18-110.82; thiocyanogen No., % iodine — 74.88-78.13; Reichert—Meissl No., % — 0.62-0.87; Polenske No., % — 0.24-0.58.

When the oil was saponified with alcoholic alkali, fatty acids were isolated having the following characteristics: iodine No. — 105.64-116.71; cyanogen No. — 78.03-81.34; neutralization No. — 178.28-185.50 mg KOH/g; mean molecular weight — 302.48-314.73.

It can be seen from the facts given that the iodine numbers of the oils are considerably lower than those of many species of the family Cruciferae and coincide with the iodine numbers of other species of colewort such as common colewort (*Crambe maritima*) (111.5) [7], and *Crambe pontica* (109.60) [8].

The qualitative and quantitative compositions of the fatty acids of the oils were determined by gas—liquid chromatography with the characteristics given previously [8]. The methyl esters of total fatty acids, and also of the saturated and unsaturated fatty acids separately, their separation being performed by the acetone method, were subjected to gas-chromatographic determination. The acids were identified by the internal-standard method

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