# ORTHOESTERS OF SUGARS

## COMMUNICATION 10.* STRUCTURE OF SECONDARY PRODUCTS IN GLYCOSYLATION OF ORTHOESTERS

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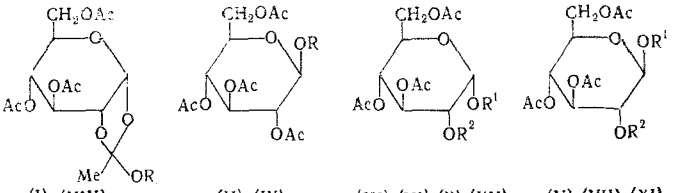
The formation of the fully acylated 1,2-trans-glycosides when the orthoesters of sugars are reacted with alcohols under the conditions of the orthoester method of glycosylation [2, 3] is at times accompanied by secondary reactions, the nature of which has not been ascertained. The consequence of such reactions are: the formation of a small amount of anomalous 1→2 linkages in the polysaccharides that are obtained by the polymerization of the inner orthoesters of arabinofuranose [4, 5] and xylopyranose [6], the probable branching and presence of 1→2 cis-glycoside linkages in the synthetic xylan [6], and also the formation of a small amount of the α-anomer in the synthesis of 3-O-β-D-glucopyranosyl-D-mannose by the orthoester method [7]. The data on the structure of the secondary products, formed in the model reaction of glycosylating the simpler alcohols with the orthoesters of α-D-glucopyranose, are given in the present paper (see [8] for prior communication).

The prior experiments on the glycosylation of methanol with 1,2-methylorthoacetyl-3,4,6-tri-O-acetyl-α-D-glucopyranose (I) in chlorobenzene in the presence of 2,6-lutidinium perchlorate at 140° revealed that, together with glucoside (II), a substance is also formed that is presumably the partially acetylated α-methyl-D-glucopyranoside derivative; the amount of this substance increases when the reaction temperature is lowered. For this reason a more detailed study was made at 84°, under conditions that lead to an accumulation of the secondary product



(I), (VIII) (II), (IX) (III), (VI), (X), (XII) (IV) (V), (VII), (XI)

R = Me (I); $C_6H_{11}$ (VIII)

R = Me (II); $C_6H_{11}$ (IX)

$R^1$ = Me, $R^2$ = H (III), $R^1$ = $R^2$ = Me (IV), $R^1$ = Me, $R^2$ = $CD_3CO$ (VI); $R^1$ = $C_6H_{11}$, $R^2$ = H (X); $R^1$ = $C_6H_{11}$, $R^2$ = Ac (XII)

$R^1$ = Me, $R^2$ = H (V); $R^1$ = Me, $R^2$ = $CD_3CO$ (VII) $R^1$ = $C_6H_{11}$, $R^2$ = H (XI)

The mixture of products obtained from the reaction of orthoester (I) with an equimolar amount of $CH_3OH$ was separated by chromatographing on silica gel ($SiO_2$) and subsequent analysis of the fractions before and after acetylation. Here the amount of the acetates of the methyl-D-glucopyranosides was determined directly, while that of the partially acetylated glucosides was determined by the increase in the amount of the full acetates of the corresponding glucosides after acetylation of the fractions. The yields of the principal reaction products were found in this way (see Table 1).

We used $CD_3OD$ to establish the structure of the products in the above described reaction. The reaction products were separated by chromatographing on $SiO_2$ and were characterized as indicated below.

*See [1] for Communication 9.

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TABLE 1. Yields of Reaction Products of Orthoester (I) with Methanol in Chlorobenzene in Presence of 2,6-Lutidinium Perchlorate at 84°

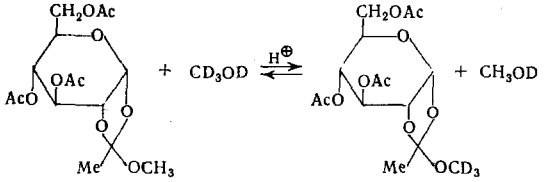
| Compound | Yield, % |
|---|---|
| Tetraacetates of methyl-D-glucopyranosides | β- 31<br>α- 1—2 |
| Partially acetylated methyl-D-glucopyranosides | β- 10<br>α- 28 |

β-Methyl-D-glucopyranoside tetraacetate (II) and β-methyl-D-glucopyranoside, obtained from (II) by deacetylation, were identified by comparison with authentic specimens [9]. The structure of the sirupy 3,4,6-tri-O-acetyl-α-methyl-D-glucopyranoside (III) was established by deacetylation and acetylation, which gave α-methyl-D-glucopyranoside and its tetraacetate, which were identified by comparison with authentic specimens [9], and by the methylation of (III) with diazomethane under conditions that excluded migration of the acetyl groups [10]. The crystalline methyl ether (IV) was obtained in nearly quantitative yield, and its constants coincide with those given in [11]. The acid hydrolysis of (IV), and subsequent reduction with $NaBD_4$ and acetylation, gave 1,3,4,5,6-penta-O-acetyl-2-O-methyl-D-sorbitol-1-D, the mass spectrum of which corresponds to the spectrum of the acetates of the 2-O-methylhexitols, which have deuterium at C-1 [12]. As a result, the partially acetylated α-methyl-D-glucopyranoside derivative has a free hydroxyl only at C-2.

The 3,4,6-tri-O-acetyl-β-methyl-D-glucopyranoside (V) that is present in the mixture of products could not be isolated in the pure state. Nevertheless, its presence and structure were proved in the following manner. Chromatographing the mixture of products on $SiO_2$ made it possible to isolate fraction A, which consisted of glucoside (V) and the tetraacetates of glucose (formed by the decomposition of the starting orthoester) and was devoid of (II) and (III) as impurities. The deacetylation of fraction A gave the crystalline β-methyl-D-glucopyranoside. The acetylation of fraction A with $(CD_3CO)_2O$ gave a mixture of the full acetates, which was subjected to chromatographic and mass-spectrometric study.

The tetraacetates of alkylhexopyranosides [13] and the penta-acetates of hexopyranose [14] are characterized by single fragmentation paths, which correspond to the decomposition of the primary ion of the acetylated glycosyl cation (m/e 331) [15]. A comparison of the described mass spectra [13, 14] with the mass spectrum obtained by us for tri-O-acetyl-mono-O-deuteroacetyl-β-methyl-D-glucopyranoside revealed that the latter has the same set of characteristic ions, in which connection a part of the peaks proved to be shifted by three mass units when compared with the described spectrum. The ions whose peaks were shifted were those that contain acetyl groups, found in the starting glucoside at C-2, C-3, C-4, and C-6 (334), C-2, C-4, and C-6 (292 and 245), at C-2, C-3, and C-4 (274), at C-2 and C-6 (203), and at C-2 and C-4 (160 and 118). Not shifted were the peaks of the ions that contain acetyl groups at C-4 and C-6 (169), and at C-3 and C-4 (211, 140). An analysis of the obtained data shows that the 2 position is the sole position of the $CD_3CO$ group in the starting glucoside. The validity of treating the mass spectra in this manner is confirmed by the fact that the mass spectrum of 2-O-trideuteroacetyl-3,4,6-tri-O-acetyl-α-methyl-D-glucopyranoside (VI), obtained from triacetate (III), coincided with the above described spectrum of the β-methyl-D-glucopyranoside derivative. As a result, the latter compound has the structure of (VII), while the starting partially acetylated glucoside contains a free hydroxyl at C-2 and has the structure of (V).

The methoxyl group, contained in the principal reaction products, namely glucosides (II) and (III), could originate either from the $CD_3OD$ added to the reaction, or from the undeuterated $CH_3O$ group of the starting orthoester. The origin of the $CH_3O$ group in these products could be established from the distribution of the deuterium in them. The latter was determined from the NMR spectra of the β- and α-methyl-D-glucopyranosides, respectively obtained from (II) and (III). In both cases the ratio of the integral intensities of the signals of the protons at C-1 and the signals of the $CH_3O$ group was ~1 : 1.5. In the NMR spectrum of the synthetically prepared mixture of equimolar amounts of the two glucosides the ratio of the integral intensities of the signals of the $CH_3O$ groups of the anomers was 1 : 1. As a result, within the limits of experimental error the $CH_3O$ group in each of glucosides (II) and (III) contains 50% of $CH_3-{}^2H_3$ and 50% of $CH_3-{}^1H_3$. Apparently, this result cannot be interpreted unequivocally. However, it is most probable that the glycosylation reaction precedes the rapid, reversible transesterification, as a result of which an equalizing occurs in the amount of $CD_3O$ groups in the free $CH_3OH$ and in the orthoester

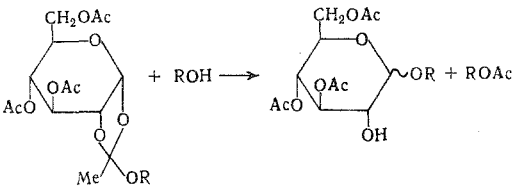


Next it was necessary to establish the generality of the reaction that leads to glycosides (III) and (V), and to ascertain the nature of the compound formed in the cleavage of the orthoester (or acetyl) group, which leads to a freeing of the hydroxyl at C-2. These problems were solved on the example of the glucosylation of cyclohexanol with 1,2-cyclohexylorthoacetyl-3,4,6-tri-O-acetyl-α-D-glucopyranose (VIII), which was synthesized* from 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide by a modification [2] of the method given in [16]. The specific rotation, the chromatographic behavior, the behavior toward hydrolysis, and the NMR spectrum of orthoester (VIII) all corresponded to its structure.

The condensation of equimolar amounts of orthoester (VIII) and cyclohexanol was run the same as described for the methyl analog. The reaction mixture was studied by chromatography and mass spectrometry before and after acetylation with $(CD_3CO)_2O$. Based on the retention time and mass spectra, cyclohexyl acetate and the tetraacetates of the β- and α-cyclohexyl-D-glucopyranosides were identified in the mixture. An analysis of the mass spectra of these glucosides, done the same as the analysis of the spectrum of the methyl analog (see above), revealed that in both cases the tetraacetates represented a mixture of the 2,3,4,6-tetra-O-acetyl- and 2-O-trideuteroacetyl-3,4,6-tri-O-acetylcyclohexyl-D-glucopyranosides, which were devoid of noticeable amounts of the isomers with the $CD_3COO$ group in other positions. As a result, the same as in the case of the methyl analog, the glycosylation of cyclohexanol with orthoester (VIII) gives the fully acetylated 1,2-trans-glucoside (IX), 3,4,6-tri-O-acetyl-α-cyclohexyl-D-glucopyranoside (X) and its β-anomer (XI), and also a small amount of the fully acetylated α-cyclohexyl-D-glucopyranoside (XII) [17]. From the ratios of the areas of the peaks of the full acetates of the anomeric cyclohexyl glucosides on the GLC were estimated the relative amounts of these compounds in the acetylation products, while the fraction of each of them, formed directly during glycosylation and arising in the deuteroacetylation of the corresponding triacetates, was estimated from the ratios of the intensities of the peaks of the deuterated and undeuterated ions in the mass spectra of these compounds. The ratio of the amount of each of the compounds in the glucosylation products was estimated on the basis of these data, and was found to be approximately (IX) : (X) : (XI) : (XII) = 35 : 20 : 8 : 3, which is close to the ratio of the yields that was found for the methyl analog (cf. with Table 1).

The assumption that the partially acetylated glucosides are the products of the secondary transformations of the principal reaction product, the fully acetylated β-D-glucopyranoside, was refuted by direct experiment. Glucoside (II) was recovered quantitatively when it was heated under the reaction conditions.

As a result, it was established that, together with the principal glycosylation reaction, which leads to the fully acylated 1,2-trans-glycoside, another reaction also proceeds in the condensation of the orthoesters of sugars with alcohols in chlorobenzene in the presence of 2,6-lutidinium perchlorate, with a predominance of the α-anomer




It is evident that this reaction explains most of ten anomalies when the orthoester method is used, and specifically: the formation of 1→2 linkages and the branching in the polysaccharides that are synthesized by this method, and also the inclusion of anomeric units in the polymer chain. It should be mentioned that the indicated secondary reaction leads to the partially acetylated derivative, i.e., a compound that is quite different in its polarity and chromatographic behavior from the fully acylated 1,2-trans-glycoside. Consequently, in the synthesis of glycosides and oligosaccharides by the orthoester method the formation of secondary products cannot importantly reflect on the steric direction of the reaction, since the secondary partially acylated products can be easily separated prior to removing the protective groups. It is specifically for this reason that products of the (III) and (V) type were not detected in numerous cases of the successful application of the orthoester method [18, 19]. The sole case of detecting the anomeric disaccharide [7] is associated with the isolation method that includes prior removal of the protective groups. Here the differences in the properties of the anomeric products are counterbalanced, as a result of which the 1,2-cis-anomer accompanies the isolation of the 1,2-trans-glycoside.

Data will be presented in a following communication on the effect of the reaction conditions on the yields of the principal and secondary products, and also data on the mechanism of the observed transformations. At the present time the theory can be expressed that the anomalous reaction is associated with a

*A. V. Rodionova, student at the Moscow State University, assisted in the synthesis.

protonation of the oxygen atom at C-2 and the subsequent decomposition of the acyclic acyloxonium ion into alkyl acetate and glycosyl cation.

## EXPERIMENTAL METHOD

The purification of the solvents and $Al_2O_3$ and the preparative chromatography conditions were described in [2, 3]; the TLC on $Al_2O_3$ was run in the system: $CHCl_3$–MeCOEt, 98.5:1.5 (A), and on $SiO_2$ in the system: $CHCl_3$–MeCOEt, 85:15 (B); the GLC was run on an LCM-8MD, Model 5 instrument, using a steel column (1 m, 3% PNPGS deposited on Chromatone NA-AW-HW-HMDS, 80-100 mesh), nitrogen as the carrier gas, a flow rate of 30 ml/min, and a flame-ionization detector. The chromato-mass-spectrometry (CMS) was run on a Varian MAT III-Gnom instrument, using a steel column (1 m, 3% SE-30 deposited on Varapaste, 80-100 mesh), helium as the carrier gas, a flow rate of 15 ml/min, and an EID detector. The other mass spectra were taken on a Varian MAT, Gmb H. CH6 instrument. The compounds were analyzed by GLC and CMS, and were identified by comparison with authentic specimens. The NMR spectra were taken on a Varian DA-60-IL spectrometer relative to HMDS. The melting points were determined on a Kofler block. The solutions were evaporated in vacuo at 30-40°.

The acetylation was run with a 5 to 10-fold excess of $Ac_2O$ in pyridine (1:2 by volume) at ~20° overnight. To the mixture was added 1/5 volume of MeOH, after 30 min the mixture was diluted 10-15 times with chloroform, washed in succession with water and saturated aqueous $NaHCO_3$ solution, again several times with water, and then the organic layer was evaporated to dryness.

The deacetylation was run with 0.05-0.1 equiv. of 0.05-0.1 N NaOMe solution in absolute MeOH at ~20° for several hours. The mixture was neutralized with cationite KU-2 ($H^+$ form) and evaporated to dryness.

Condensation of 1,2-Methylorthoacetyl-3,4,6-tri-O-acetyl-α-D-glucopyranose (I) with Methanol. A solution of 800 mg (2.20 mmole) of (I) [2] in 11 ml of chlorobenzene was distilled at atmospheric pressure until 3 ml had been removed and then the mixture was cooled to 30°. To 0.20 ml (0.011 mmole) of an 0.055 M solution of 2,6-lutidinium perchlorate [3] in $MeNO_2$ was added 4 ml of chlorobenzene and the mixture was evaporated at atmospheric pressure to 1.5 ml. The obtained solution was transferred hot to an ampul, immediately mixed with the orthoester solution and with 1.10 ml (2.20 mmole) of a 2.0 M solution of absolute MeOH in chlorobenzene, after which the ampul was sealed immediately, with careful protection from moisture, and heated at 84° for 9 h. To the ampul was added 2 drops of pyridine, the solution was evaporated to dryness, and the residue was treated with 10 ml of 95% AcOH. The solution was kept at 20° for 10 min, after which toluene was added and the mixture was evaporated to dryness. The residue was repeatedly evaporated with toluene and dried in vacuo. The obtained sirup (780 mg) contains a substance with $R_f$ 0.7, which is identical with glucoside (II), 0.3, and then a "tail" up to the starting line (system B). The mixture was chromatographed on $SiO_2$, collecting the fractions: a) 200 mg of a substance with $R_f$ 0.7; b) 85 mg of a substance with $R_f$ 0.7 and 0.3; and c) 500 mg of a substance with $R_f$ ranging from 0.3 to 0.0 (column balance 100%). The tetraacetates of the α- and β-methyl-D-glucopyranosides in a 3:56 ratio were identified in fraction a) by GLC analysis, starting with 185° and heating at a rate of 2 deg/min. Acetylation of sample a) and subsequent chromatographing gave a mixture with the same ratio of the anomers. Only glucoside (II) was detected in fraction b) by the same method (the sensitivity of detecting the α-anomer, determined via a control experiment, is better than 0.5%), while the tetraacetates of the α- and β-methyl-D-glucopyranosides in a 1:2 ratio were detected after acetylation. Using the same method, the tetraacetates of the methyl-D-glucosides were not detected in fraction c), while after acetylation the tetraacetates of the α- and β-methyl-D-glucopyranosides and a mixture of the pentaacetates of glucopyranose (with a predominance of the α-anomer) were found in a ratio of 5:2:8 (the calculation constants were found from the areas of the peaks in a standard equimolar mixture of the authentic compounds). The yields of the products, given in Table 1, were determined from the found ratios and yields of the fractions.

Condensation of Orthoester (I) with Tetradeuteromethanol. In a similar manner we condensed 8 g (22.1 mmole) of (I) with 1.10 ml (24.0 mmole) of $CD_3OD$ in 30 ml of chlorobenzene in the presence of 0.11 mmole of 2,6-lutidinium perchlorate. The reaction mixture was worked up and chromatographed. The fractions, containing the substance with $R_f$ 0.7, were combined as fraction a) ((3.11 g), and all of the others were combined as b). The recrystallization of a) from 20 ml of a 3:2 ether–pentane mixture gave 2.08 g (26%) of glucoside (II), mp 104-105° (the mixed melting point with an authentic specimen was not depressed), $[\alpha]_D$ –18.0° (C 3.2; $CHCl_3$). Based on the TLC in system A and the GLC the substance is identical with an authentic specimen [9].

Fraction b) was combined with the mother liquor from the recrystallization of (II), and the mixture was repeatedly chromatographed on $SiO_2$. Here we obtained a fraction of the pure triacetate (III) (1.48 g, 18.5%, $R_f$ 0.3) and 2.42 g of a mixture of triacetates (III) and (V) and the tetraacetates of glucose ($R_f$ 0.1-0.25) (fraction c).

β-Methyl-D-glucopyranoside. The deacetylation of 362 mg of glucoside (II) and subsequent recrystallization from MeOH–ether (1:5) gave 180 mg (93% yield) of β-methyl-D-glucopyranoside, mp 110°, the mixed melting point of which with an authentic specimen was not depressed $[\alpha]_D$ −32.0° (C 1.3, $H_2O$); see [9]. The NMR spectrum is deuteropyridine contains the signals (δ, ppm): 3.43 s (1.5 H, $OCH_3$), 4.52 d (1H), $J_{1,2}$ 7.5 Hz, H-1).

α-Methyl-D-glucopyranoside. The deacetylation of 530 mg of (III) gave 310 mg (98% yield) of α-methyl-D-glucopyranoside, mp 165-166° (the mixed melting point with an authentic specimen was not depressed), $[\alpha]_D$ +156° (C 1.4; $H_2O$); see [9]. The NMR spectrum in deuteropyridine contains the signals (δ, ppm): 3.26 s (1.5 H, $OCH_3$), 4.94 d (1H), $J_{1,2}$ 3.5 Hz, H-1).

2,3,4,6-Tetra-O-acetyl-α-methyl-D-glucopyranoside. The acetylation of 250 mg of glucoside (III) gave 2,3,4,6-tetra-O-acetyl-α-methyl-D-glucopyranoside, the recrystallization of which from a 1:1 ether–pentane mixture gave 250 mg (89% yield) of product with mp 100-101° (the mixed melting point with an authentic specimen was not depressed), $[\alpha]_D$ +130° (C 1.75; $CHCl_3$). Based on the TLC (system A) and GLC the compound is identical with an authentic specimen [9].

2-O-Trideuteroacetyl-3,4,6-tri-O-acetyl-α-methyl-D-glucopyranoside (VI). Glucoside (III) (25 mg) was acetylated with $(CD_3CO)_2O$, and based on the CMS the product was identified as being the tetraacetate of α-methyl-D-glucopyranoside; the mass spectrum contains peaks with the m/e (the intensities in percent of the intensity of the peak with m/e 98 are given in parentheses): 334 (5), 292 (1), 274 (1), 245 (42), 242 (8), 211 (3), 203 (30), 200 (9), 169 (30), 160 (70), 157 (28), 140 (40), 118 (40), 115 (70), 112 (80), 81 (62), 46 (140).

2-O-Methyl-3,4,6-tri-O-acetyl-α-methyl-D-glucopyranoside (IV). Glucoside (III) (200 mg) was methylated as described in [10]. The crystalline reaction product (200 mg, 96%) was recrystallized from 2 ml of ether at −10° to give 150 mg (72%) of methyl ether (IV) [11], mp 119-120°, $[\alpha]_D$ +148° (C 1.31; $CHCl_3$). Based on the GLC and TLC (system A), the compound and mother liquor were identical.

1,3,4,5,6-Penta-O-acetyl-2-O-methyl-D-sorbitol-1-$^2H_1$. A mixture of 20 mg of (IV) and 2 ml of 1 N $H_2SO_4$ solution was heated in a sealed ampul at 105° for 4 h, neutralized with Amberlite IRA-410 ($HCO_3^-$), and evaporated to dryness. The residue was treated with 10 mg of $NaBD_4$ and 0.9 ml of MeOH, allowed to stand overnight, 0.1 ml of AcOH was added, and the whole was evaporated to dryness. The residue was evaporated twice with absolute MeOH, dried in vacuo, and acetylated. Based on the TLC in system A, the reaction product is homogeneous. The mass spectrum contains peaks with the m/e (the intensities in percent of the intensity of the peak with m/e 43 are given in parentheses): 333 (15), 183 (10), 172 (15), 139 (40), 129 (52), 118 (75), 117 (35), 87 (62), 79 (52), 74 (63), 73 (15), 52 (40); based on the data given in [13], the mass spectrum of 2-O-methylhexitol acetate contains characteristic peaks with m/e 139, 117, and 73.

Identification of Glucoside (V) in Fraction c). Mixture c) (1.5 g) was chromatographed on $SiO_2$, checking the composition of the fractions by acetylation and GLC analysis. We obtained 150 mg of a mixture, which contained only the partially acetylated derivatives of β-methyl-D-glucopyranoside and glucose (d). A part of the obtained mixture (20 mg) was deuteroacetylated. Based on the CMS, the tetraacetate of β-methyl-D-glucopyranoside was identified in the products, the mass spectrum of which contains peaks with the m/e (the intensities in percent of the peak with m/e 98 are given in parentheses): 334 (8), 292 (3), 274 (2), 245 (50), 242 (10), 211 (7), 203 (40), 200 (10), 169 (45), 160 (80), 157 (25), 140 (50), 118 (45), 115 (80), 81 (50), 46 (170). The main portion of fraction d) was deacetylated. A methanol solution of the reaction product was filtered through powderlike cellulose (2 × 2 cm), the filtrate was evaporated, and the residue was recrystallized from MeOH–ether to give 80 mg of β-methyl-D-glucopyranoside with mp 110° (the mixed melting point with an authentic specimen was not depressed), $[\alpha]_D$ −32.5° (C 1.5; $H_2O$).

1,2-Cyclohexylorthoacetyl-3,4,6-tri-O-acetyl-α-D-glucopyranose (VIII). The condensation of 43.00 g (0.104 mole) of 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide with 24.0 ml (0.228 mole) of cyclohexanol in nitromethane was run the same as described in [2] (in working up the reaction mixture the organic layer was additionally washed with 10% NaCl solution). The reaction product was evaporated with aqueous EtOH and then recrystallized from 200 ml of a 1:1 EtOH–MeOH mixture. We obtained 19.6 g (44%) of orthoester (VIII), mp 83°, $[\alpha]_D$ +25.0° (C 2.3; $CHCl_3$); when tested under hydrolytic conditions the substance is cleaved completely to orthoesters [2]. The NMR spectrum in $CDCl_3$ contains the signals (δ, ppm):

1.65 s (3H, C–$CH_3$), 1.98-2.02 (9H, $CH_3COO$–) and 5.10 d (1H, $J_{1,2}$ 4.5 Hz, H-1). Found: C 55.82; H 7.54%. $C_{20}H_{30}O_{10}$. Calculated: C 55.92, H 7.07%.

Condensation of Orthoester (VIII) with Cyclohexanol. The condensation of 43 mg (0.10 mmole) of orthoester (VIII) with 0.10 mmole of cyclohexanol was run the same as described above. A sample a) (~0.01 ml) was removed from the reaction mixture, while the main portion was worked up as described above and the product was deuteroacetylated. Mixture b) was obtained. Both mixtures were studied by CMS. Cyclohexyl acetate was identified in a); the mass spectrum contains peaks with the m/e (the intensities in percent of the peak with m/e 54 are given in parentheses): 143 (5), 100 (25), 99 (23), 83 (47), 82 (100), 81 (43), 67 (100), 61 (46), 58 (38). The tetraacetates of the α- and β-cyclohexyl-D-glucopyranosides in a 1:2 ratio (based on the areas of the peaks) were identified in mixture b). Their mass spectra contain peaks with the m/e (the intensities in percent relative to the peak with m/e 98 are given in parentheses): α-glucoside – 334 (4), 245 (13), 242 (7), 203 (22), 200 (11), 169 (44), 160 (37), 157 (29), 140 (55), 118 (29), 115 (63), 98 (100), 81 (59), 46 (96); β-glucoside – 331 (3), 289 (1), 271 (1), 245 (4), 242 (17), 215 (5), 211 (2), 203 (5), 200 (33), 182 (15), 169 (25), 160 (5), 157 (73), 140 (65), 118 (5); 115 (98), 81 (46), 46 (10).

Behavior of 2,3,4,6-Tetra-O-acetyl-β-methyl-D-glucopyranoside (II) under Glycosylation Conditions. A mixture of 0.01 mmole of glucoside (II), 0.1 mmole of methanol and 0.001 mmole of 2,6-lutidinium perchlorate was heated in chlorobenzene. The mixture was worked up as described above and separated into two portions, one of which was studied directly by TLC and GLC, while the other portion was studied after acetylation. Nothing except the starting glucoside (II) was detected in either case (the sensitivity of detecting the α-anomer and glucose pentaacetates is better than 0.5% of the main compound).

## CONCLUSIONS

1. On the example of the methyl- and cyclohexylorthoacetates of glucopyranose it was shown that the glycosylation of alcohols with the orthoesters of sugars is accompanied by a side reaction that leads to the formation of the anomeric glycosides with a free hydroxyl at C-2 and a predominance of the α-anomer. In this reaction the orthoester group is removed as the alkyl acetate.

2. Data were obtained which indicate that the glycosylation of the alcohol by the orthoester precedes the rapid reversible transesterification step, with exchange of the alkoxyl moieties between the alcohol and the orthoester.

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