MONOSACCHARIDES

COMMUNICATION 5. BEHAVIOR OF SOME MONOSACCHARIDE DERIVATIVES IN REACTION WITH TRIPHENYL PHOSPHITE METHIODIDE

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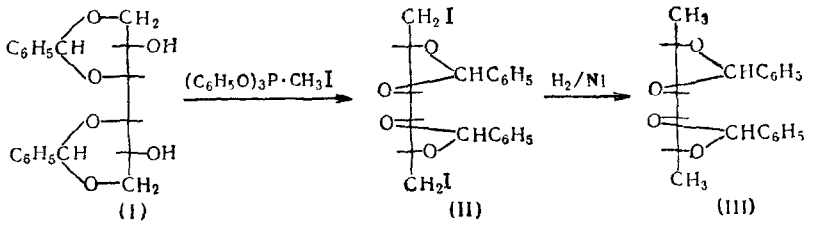
We have found previously [1-3] that the reaction of halogen or alkyl halide complexes of triphenyl phosphite with monosaccharide derivatives leads to the replacement of a free hydroxy group by a halogen atom.. It was noted that the primary alcohol grouping reacts particularly readily; the successful replacement of a secondary alcohol group in the ring is determined by the stereochemical peculiarities of the compound, namely the accessibility of the corresponding carbon atom for attack by an S_N2 mechanism.

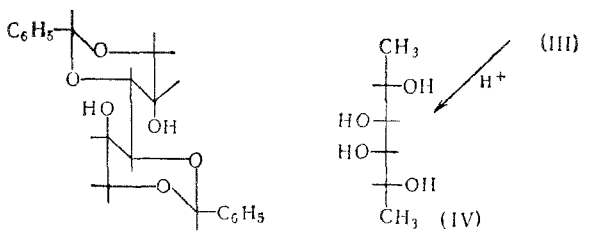
This reaction may present considerable interest as a potential route to deoxy and amino sugars However, the preparative use of the reaction is complicated by the possibility of the migration of protecting groups of the original monosaccharide derivative, as a result of which substances of different structure or complex mixtures of substances are formed. An example of such rearrangement is the formation of 6-haloglucose derivatives from 1,2 : 5,6-di-O-isopropylidene-D-glucofuranose, which we have investigated previously [1, 2].

The question of the migration of protecting groups in the course of the reaction of monosaccharide derivatives with the complexes $(C_6H_5O)_3P \cdot RX$ was made the subject of a special investigation, data on this question are presented in this paper. The most widely used method of protecting hydroxy groups in monosaccharides is the conversion of the latter into isopropylidene or benzylidene derivatives, so that the behavior of this type of acetal groupings has been studied in greatest detail.

As reagent we chose the complex formed by triphenyl phosphite with methyl iodide, which gives the best results and is the most convenient. Reactions with monosaccharide derivatives were carried out under the standard conditions that we adopted previously: in dry benzene at room temperature or with slight warming [3]. The iodo deoxy sugar formed as a result of the reaction was then usually subjected to catalytic hydrogenation to remove the iodine atom, and the deoxy derivatives so obtained were identified by comparison with known samples, or their structures were specially proved. Except in special cases, any isomerization in the course of the hydrogenation was excluded, so that the structures of the deoxy derivatives determined the structures of the iodo compounds formed in the reaction with the triphenyl phosphite complexes.

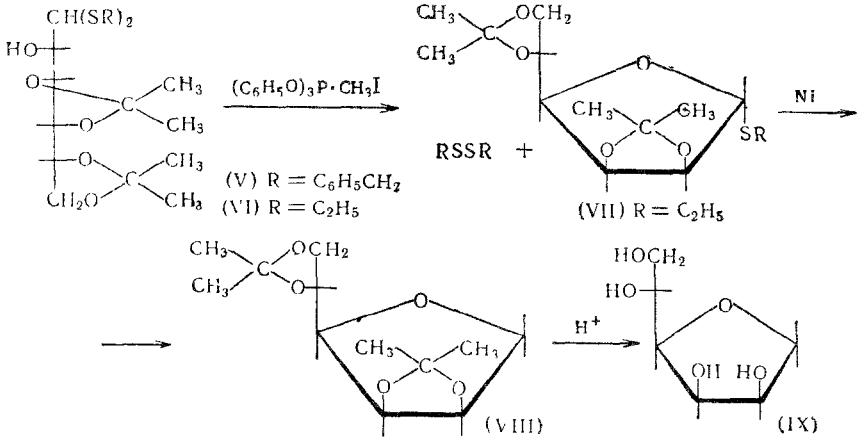
We showed that in the reaction of $(C_6H_5O)_3P \cdot CH_3I$ with 1,3:4,6-di-O-benzylidenedulcitol (I), 1,6-diiodo-1,6-dideoxy-2,3:4,5-di-O-benzylidenedulcitol (II) (one of the two known isomers, m.p. 127-128° [4]) was formed. The structure of (II) was confirmed by its hydrogenolysis over nickel, which led to the dideoxy derivative (III), which by acid hydrolysis gave 1,6-dideoxydulcitol (IV) [5]. Hence, the reaction of 1,3:4,6-di-O-benzylidenedulcitol with $(C_6H_5O)_3P \cdot CH_3I$ is accompanied by the migration of the benzylidene groups into the 2,3- and 4,5-positions, as a result of which the primary hydroxyl becomes replaced.





This fact is rather unexpected, for it is known that 1,3-O-benzylideneglycerol reacts with $(C_6H_5O)_3P$ CH_3I with formation of O-benzylidene-2-iodo-2-deoxyglycerol [6]. The difference in reactivity between 1,3-O-benzylideneglycerol and 1,3:4,6-di-O-benzylidenedulcitol is possibly associated with the difference in the spatial disposition of the hydroxyl In the glycerol derivative there is conformational equilibrium between forms in which the hydroxyl is equatorial and axial, respectively, whereas the conformations of both 1,3-dioxane rings of 1,3·4,6-di-O-benzylidenedulcitol are stabilized by the presence of two heavy substituents, as a result of which the free hydroxy group must preferentially take up the axial position. It is possible that the axial position of the hydroxy group in the 1,3-dioxane ring makes its replacement by an S_N2 mechanism difficult and favors the displacement of the benzylidene group.

Migrations of acetal groupings may occur also in the course of attempts to replace a hydroxy group of the open chain of an acyclic derivative of a carbohydrate by halogen. We found that the reactions of the mercaptals (V) and (VI) of 3,4.5,6-di-O-isopropylidene-D-mannose with $(C_6H_5O)_3P \cdot CH_3I$ are fairly complex. From the products of the reaction of 3,4·5,6-di-O-isopropylidene-D-mannose dibenzyl mercaptal (V) we isolated only dibenzyl disulfide in the pure state, in the reaction of 3,4:5,6-di-O-idopropylidene-D-mannose diethyl mercaptal (VI) we isolated crystalline ethyl 2,3:5,6-di-O-isopropylidene-1-thio-D-mannofuranoside (VII), which, judging from the magnitude of its specific rotation must be assigned the α-configuration. The reaction mixture contained some other substances, one of which appeared to be diethyl disulfide, and another, which contained halogen, could be isolated only in extremely low yield: it is possible that the halogen derivative was unstable and decomposed in the course of its isolation.

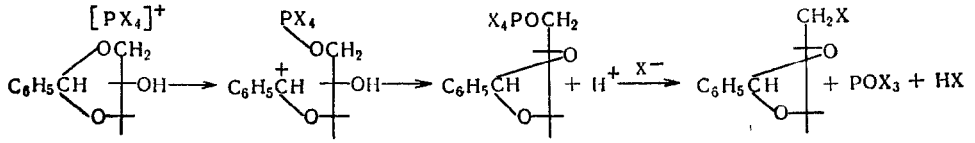


To prove its structure, the ethyl 2,3:5,6-di-O-isopropylidene-1-thio-α-D-mannofuranoside (VII) obtained from 3,4:5,6-di-O-isopropylidene-D-mannose diethyl mercaptal (VI) was boiled with Raney nickel in alcohol, subsequent hydrolysis of the isopropylidene groups led to crystalline 1,4-anhydro-D-mannitol (mannitan) (IX), identical to the compound described previously [7, 8].

As we have pointed out earlier [3], 2,3:4,5-di-O-isopropylidene-D-galactose mercaptals react normally with $(C_6H_5O)_3P \cdot CH_3I$, and the mercaptal grouping takes no part in the reaction. However, the example that we have just described shows that, when a hydroxy group that can be replaced is on the carbon atom adjacent to the mercaptal grouping, the normal course of the substitution reaction is disturbed and it is again accompanied by the migration of protecting groups. It must be added that an attempt to carry out the reaction with mercaptals of 2,3:5,6-di-O-isopropylidene- and 3,4:5,6-di-O-isopropylidene-D-glucoses showed that in this case reaction is very complex and leads to mixtures of substances of various kinds. The available data do not yet permit us to establish the cause of these complications They are probably associated with the participation of the mercaptal grouping in the substitution

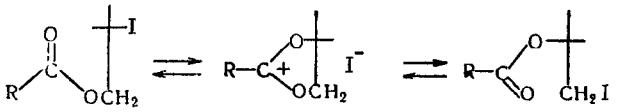
process. In this case a deciding factor is the mutual spatial disposition of the mercaptal grouping and the atoms suffering the direct attack of the reagent or drawn into the reaction. As there are at present no data on the conformation of the multifunctional aliphatic chain of mercaptals, any conclusions on this question would be premature.

The migration of the acetal protecting grouping in both the cases cited above is clearly a process that is directly connected with the actual replacement of the hydroxy group. It is of interest to examine the possible mechanism of the whole process, though a final conclusion on this question demands a special complicated investigation. The structure of the products shows that in both cases displacement of the acetal grouping occurs with preservation of the configuration of the unprotected hydroxyl. A reaction mechanism analogous to the mechanism proposed by Smith [9] for the reaction of 1,2:5,6-di-O-isopropylidene- D-glucofuranose with phosphorus pentachloride (formation of a substituted phosphoric ester at the free hydroxy group, and the further cleavage of this with formation of a carbonium cation) is therefore not very probable. As the complexes formed by triphenyl phosphite with halogens and alkyl halides have an ionic structure of the type $(PX_4)^+ (PX_6)^-$ or $[PX_4]^+ X^-$ [10], the mechanism of the migration probably consists in primary attack of the oxygen atom of the acetal grouping by the cation; it is most likely that further reaction proceeds in accordance with a continuous "push-pull" scheme, which may be broken down conventionally into the stages portrayed in the equations; in all probability these stages (formation of a phosphoric ester at the primary alcohol group and its attack by the anion) are not kinetically independent, but are effected in a single reaction complex.

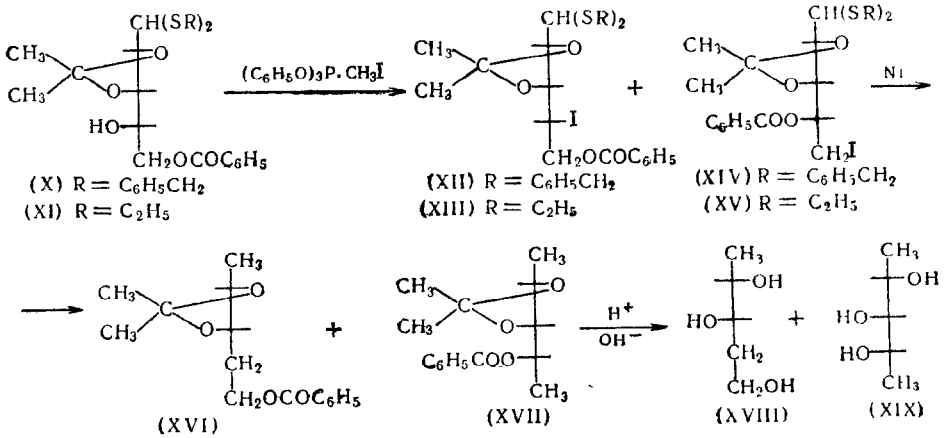


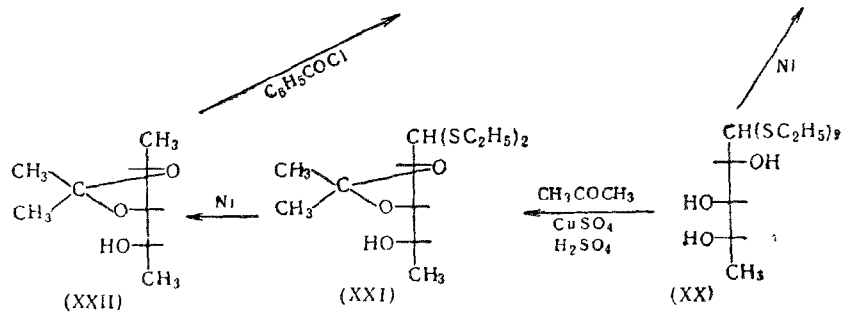
The results presented show that the use of acetal protection in the substitution of hydroxyls of monosaccharide derivatives by halogen has certain limitations.

Some difficulties are met also when protecting groupings of the ester type are used in these reactions. In this case a neighboring-group phenomenon is observed: an intramolecular exchange reaction between the halogen and the adjacent ester grouping is observed; moreover, for an optically active halogen derivative isomerization is always accompanied by inversion of configuration.



It is known that such rearrangements are observed in the course of thermal treatments, and the position of the equilibrium depends on the nature of the acid [11], the formation of intermediate acyl-oxonium cations accompanies numerous reactions of esters of polyalcohols containing halogen (see, e.g , 12, 13] We found that the 2,3-O-isopropylidene-5-O-benzoyl-L-arabinose mercaptal (X) or (XI) reacts with $(C_6H_5O)_3P \cdot CH_3I$ with formation of two substances: the 4-iodo-4-deoxy derivative (XII) or (XIII), which is the main component of the mixture, and the isomeric rearrangement product (XIV) or (XV), in which the halogen is at C_5





It is possible that in this case the actual replacement of hydroxyl by halogen proceeds normally and the rearrangement occurs only in the course of the isolation It is impossible altogether to exclude the possibility that part of the compound might rearrange also in the reduction process used for proof of structure. Thus, rearrangement during hydrogenation probably explains the formation of the three reduction products from 1,6-di-O-benzoyl-2,5-diiodo-2,5-dideoxy-3,4-O-isopropylidene-L-iditol described in our previous communication [3].

The mixture of iodo compounds (XII) and (XIV) or (XIII) and (XV) obtained as a result of the reaction of the diethyl or dibenzyl mercaptal of 2,3-O-isopropylidene- 5-O-benzoyl-L-arabinose with $(C_6H_5O)_3P \cdot CH_3I$ was converted by boiling with Raney nickel in alcohol into the mixture of deoxy derivatives (XVI) and (XVII); further, after acid and alkaline hydrolysis, we obtained a mixture of 1,4-dideoxy-D-xylitol (XVIII) and 1,5-dideoxy-L-arabitol (XIX). In the periodate oxidation of this mixture 1.25 moles of oxidant was used per mole of dideoxypentitol, which corresponds to a 3 : 1 ratio of (XVIII) and (XIX) in the mixture.

The original suggestion about the structure of the rearrangement product and the dideoxy derivatives formed by its reduction and subsequent hydrolysis was made on the basis of the fact that these compounds have higher chromatographic mobilities than normal substitution products. To obtain rigorous proof of structure, 1,5-dideoxy-2,3-O-isopropylidene-4-O-benzoyl-L-arabitol was isolated from its mixture with 1,4-dideoxy-2,3-O-isopropylidene-5-O-benzoyl-D-xylitol in the pure state, it was found to be identical to a synthetic sample in its optical rotation, infrared spectrum, and chromatographic mobility A confirmatory synthesis of 1,5-dideoxy-2,3-O-isopropylidene-4-O-benzoyl-L-arabitol was carried out as follows. 5-Deoxy-L-arabinose diethyl mercaptal (XX) was prepared in an analogous way to the D-isomer[14] and acetonated, and the acetonation product (XXI) was boiled with Raney nickel in alcohol and was converted into 1,5-dideoxy-2,3-O-isopropylidene-L-arabitol (XXII), which on benzoylation gave 1,5-dideoxy-2,3-O-isopropylidene-4-O-benzoyl-L-arabitol (XVII) and on hydrolysis – 1,5-dideoxy-L-arabitol (XIX).

The formation of 1,5-dideoxy-2,3-O-isopropylidene-4-O-benzoyl-L-arabitol in the course of the reaction investigated is evidence of the strict stereochemical orientation in replacement of hydroxyl by halogen under the action of $(C_6H_5O)_3P \cdot CH_3I$, for this product may be obtained only after a double inversion at C_4. This provides further confirmation of the S_N2 mechanism postulated from the reaction of $(C_6H_5O)_3P \cdot CH_3I$ with alcohols.

EXPERIMENTAL

Paper chromatography was carried out by the ascending method with the solvent system 4 : 1 · 1 butyl alcohol – acetic acid – water on chromatographic paper of Grade M from the Leningrad No. 2 mill. Thin-layer chromatography was carried out on plates carrying an unbound layer of alumina of Grade II activity by the method that we have described previously [15], mobile phases. a) benzene; b) chloroform; c) 1 : 1 benzene – petroleum ether. On paper the spots were detected with a potassium periodate-cuprate solution [16]; on the plates detection was carried out by spraying with concentrated sulfuric acid and then applying infrared heating. For preparative chromatography we again used alumina of Grade II activity, and the preparative separation was checked with the aid of thin-layer chromatography

Reaction of 1,3·4,6-Di-O-benzylidenedulcitol (I) with $(C_6H_5O)_3P \cdot CH_3I$. A suspension of 2,18 g of 1,3:4,6-di-O-benzylidenedulcitol [17] and 7.35 g of $(C_6H_5O)_3P \cdot CH_3I$ in 50 ml of dry benzene was stirred for 80 hours at room temperature. The main component of the resulting dark-red solution had R_f 0.87 (a),* and the solution also contained very small amounts of substances having R_f 0.20, 0.37, 0.50, 0.63, and 0.95 (a). The benzene solution was

* Here and below R_f values given with an indication of the solvent system in parentheses refer to thin-layer chromatograms, and those for which the solvent system is not indicated refer to paper chromatograms.

applied to a column containing 200 g of alumina, and elution was with benzene. Fractions containing the substance of Rf 0.87 (a) were evaporated, and the residue partially crystallized out. After recrystallization from alcohol we obtained 2.11 g (60%) of 1,6-diiodo-1,6-dideoxy-2,3:4,5-di-O-benzylideneduleitol (II); m.p. 127-128°; $[\alpha]_D^{26}$ 0° (c 8.75, $CHCl_3$). For "1,6-diiodo-1,6-dideoxy-2,3:4,5-di-O-benzylideneduleitol I" the literature [4] gives m.p. 127-128°

Found: C 41.49; 41.51; H 3.46; 3 47; I 43 82; 43.92%. $C_{20}H_{20}I_2O_4$. Calculated: C 41.55; H 3.49; I 43.89%

A solution of 1.74 g of the diiodo compound (II) in 20 ml of tetrahydrofuran and 1.68 ml of triethylamine was added to a suspension of 1.5 g of Raney nickel in 20 ml of alcohol, and the mixture was then stirred in an atmosphere of hydrogen. The theoretical amount of hydrogen was absorbed in the course of 30 minutes. Catalyst was filtered off and washed with hot alcohol. The solution was vacuum-evaporated, and the residue was extracted with benzene The extract contained a substance having Rf 0 (a). The benzene solution was filtered through a column of alumina. Evaporation of the filtrate gave 950 mg(97%) of 1,6-dideoxy-2,3:4,5-di-O-benzylideneduleitol (III); m p. 57-60°, $[\alpha]_D^{20}$ 0° (c 1.96; CH_3OH). Found: C 73.62; 73.70; H 6.89; 6.81%. $C_{20}H_{22}O_4$. Calculated: C 73.60, H 6.79%.

300 mg of 1,6-dideoxy-2,3·4,5-di-O-benzylideneduleitol (III) was boiled for two hours in 20 ml of 40% aqueous methanol containing 1% of sulfuric acid. The solution was cooled and neutralized with barium hydroxide. The precipitate was separated by centrifugation, and the solution was extracted with ether; the extract was vacuum-evaporated. Recrystallization of the residue from alcohol gave 1,6-dideoxyduleitol (IV), m p 180-182°, identical in melting point and chromatographic behavior on paper (Rf 0.51) to a known sample of 1,6-dideoxyduleitol [3]. For the melting point of 1,6-dideoxyduleitol the literature [5] gives 183-184° (from absolute alcohol). In the periodate oxidation of a sample of 1,6-dideoxyduleitol (IV) 3.15 molecular proportions of $NaIO_4$ were consumed already after 90 minutes and 2.2 molecular proportions of formic acid were liberated; a qualitative test for acetaldehyde was positive.

Reaction of 3,4:5,6-Di-O-isopropylidene-D-mannose Dibenzyl Mercaptal (V) with $(C_6H_5O)_3P \cdot CH_3I$. A solution of 2.7 g of 3,4 5,6-di-O-isopropylidene-D-mannose dibenzyl mercaptal (V) [18] in 25 ml of dry benzene was added to a suspension of 2.9 g of $(C_6H_5O)_3P \cdot CH_3I$ in 25 ml of dry benzene. The reaction mixture was heated for six hours at 100° and further for 36 hours at 50°. The solution obtained contained substances having Rf 0.92, 0.70, 0.50, and 0.25 and traces of the original compound, Rf 0.10 (a). By chromatography on a column containing 100 g of alumina with elution with benzene we isolated the substance having Rf 0.92 (a), which crystallized out when solvent was driven off; yield 1 g. After recrystallization from petroleum ether and methanol we obtained dibenzyl disulfide, m.p. 69-71° [the literature [19] gives m.p. 74° (from CH_3OH)].

3,4·5,6-Di-O-isopropylidene-D-mannose Diethyl Mercaptal (VI). This was prepared by a method analogous to that for 3,4:5,6-di-O-isopropylidene-D-mannose dibenzyl mercaptal [18]. The yield of sirupy product was nearly quantitative; $[\alpha]_D^{20}$ + 17.8° (c 2, $CHCl_3$).

Found· C 52 74; 53 00; H 8.60; 8.52; S 17.44; 17.70%. $C_{16}H_{30}O_5S_2$. Calculated: C 52.43, H 8.25, S 17.50%.

Reaction of 3,4:5,6-Di-O-isopropylidene-D-mannose Diethyl Mercaptal (VI) with $(C_6H_5O)_3P \cdot CH_3I$. A solution of 4.096 g of 3,4:5,6-di-O-isopropylidene-D-mannose diethyl mercaptal in 30 ml of dry benzene was added to a suspension of 5.68 g of $(C_6H_5O)_3P \cdot CH_3I$ in 20 ml of dry benzene, and the mixture was left for 4.5 days at room temperature. In the solution we then detected compounds having Rf 0.40, 0.60, 0 75, and 0 90 (a), as well as the original mercaptal (VI), Rf 0.15 (a). The benzene solution was evaporated, when considerable resinification was observed. The residue was extracted with carbon tetrachloride, and the extract was chromatographed on a column containing 100 g of alumina. Elution with carbon tetrachloride gave very small amounts of substances having Rf 0.90 (a) (identical in Rf with diethyl disulfide) and 0.75 (a) (halogen derivative), and also fractions containing a substance of Rf 0.60 (a), which were combined and evaporated; the residue partially crystallized out. After recrystallization from aqueous methanol we obtained ethyl 2,3:5,6-di-O-isopropylidene-1-thio-α-D-mannofuranoside (VII); yield 320 mg; m.p. 64-65°; $[\alpha]_D^{19}$ + 201.2° (c 3.58, absolute alcohol). Found: C 55.12, 55.31, H 8.15, 8.33; S 10.81, 10.73%. $C_{14}H_{24}O_5S$ Calculated: C 55.24; H 7.95; S 10.53%.

130 mg of ethyl 2,3·5,6-di-O-isopropylidene-1-thio-α-D-mannofuranoside (VII) was dissolved in 10 ml of absolute alcohol, 1 g of Raney nickel was added to the solution, and the mixture was boiled for four hours. The precipitate was then separated and washed with hot alcohol; the filtrate was evaporated, and the residue formed a colorless sirup (120 mg). The sirup was dissolved in 1.5 ml of methanol and three drops of concentrated hydrochloric acid and three drops of water were added. The mixture was heated for one hour at 80°, cooled to room temperature, and

slowly evaporated in a vacuum without the application of heat. The crystals that separated were filtered off and recrystallized from methanol We obtained 60 mg (85%) of 1,4-anhydro-D-mannitol (IX); m p 144-145°, $[\alpha]_D^{18}$ -24.8° (c 7.2; water). The literature gives m.p. 146-147° (from alcohol), $[\alpha]_D^{20}$-23.7°(C 1.043, water)[7], m.p. 148°, $[\alpha]_D$-23.75° (c 8.0; water) [8].

Found: C 43.87, 43.90; H 7.37, 7.42%. $C_6H_{12}O_5$ Calculated· C 43.90, H 7.37%

2,3-O-Isopropylidene-5-O-benzoyl-L-arabinose Dibenzyl Mercaptal (X). A solution of 1.4 g of benzoyl chloride in 5 ml of pyridine was added dropwise over a period of 20 minutes to a stirred cooled (-20°) solution of 3 8 g of L-arabinose dibenzyl mercaptal [20] in 25 ml of anhydrous pyridine. Stirring was continued for eight hours at -10°, and then the reaction mixture was kept for 16 hours at 0° and 20 hours at 20°, after which it was poured into 200 ml of 10% acetic acid The oil which then precipitated rapidly solidified. The product was filtered off washed with water, vacuum-dried over NaOH and H_2SO_4, and recrystallized from benzene. The yield of unpurified 5-O-benzoyl-L-arabinose dibenzyl mercaptal, m p 102-107°, was 4 3 g

To a solution of 2 8 g of this substance in 50 ml of acetone we added 1.5 g of anhydrous copper sulfate and 0.2 ml of concentrated sulfuric acid, and the mixture was stirred for 24 hours at room temperature The precipitate was filtered off, the solution was neutralized with anhydrous sodium carbonate and again filtered, and the filtrate was vacuum-evaporated. The yellowish sirupy residue (yield 2.75 g) was a mixture of three substances, Rf 0.10 0.50, and 0.70 (a). The main component of this mixture, which had Rf 0.10 (a) and 0.45 (b), was isolated by chromatography on a column containing 120 g of alumina, elution was with a mixture of benzene and chloroform with continuous rise in the chloroform content The yield of 2,3-O-isopropylidene-5-O-benzoyl-L-arabinose dibenzyl mercaptal (X) was 2.15 g, $[\alpha]_D^{26}$-146° (c 3 9, $CHCl_3$)

2,3-O-Isopropylidene-5-O-benzoyl-L-arabinose Diethyl Mercaptal (XI). A mixture of 4.5 g of 5-O-benzoyl-L-arabinose diethyl mercaptal, prepared analogously to the D-isomer [21], 3 g of anhydrous copper sulfate, 0 4 ml of concentrated sulfuric acid, and 100 ml of acetone was stirred for 24 hours at room temperature. The precipitate was then separated, the solution was neutralized with anhydrous sodium carbonate and again filtered, and the filtrate was vacuum-evaporated. The residue (5 g) was dissolved in a little chloroform and chromatographed on a column containing 200 g of alumina, elution was with chloroform. The yield of 2,3-O-isopropylidene-5-O-benzoyl-L-arabinose diethyl mercaptal (XI) was 4.25 g (82.5%), Rf 0.25 (b); $[\alpha]_D^{20}$-73.5° (c 3.86; benzene)

Found· C 57.00, 57.07, H 7.16, 7.13, S 15 78,15.77%. $C_{19}H_{28}O_5S_2$ Calculated: C 56.96, H 7.07, S 16.00%.

Reaction of 2,3-O-Isopropylidene-5-O-benzoyl-L-arabinose Dibenzyl Mercaptal (X) with $(C_6H_5O)_3P \cdot CH_3I$. A solution of 145 mg of 2,3-O-isopropylidene-5-O-benzoyl-L-arabinose dibenzyl mercaptal (X) in 10 ml of dry benzene was added to a suspension of 350 mg of $(C_6H_5O)_3P \cdot CH_3I$ in 10 ml of dry benzene. The reaction mixture was heated for 40 hours at 50°, and in the course of this treatment the original compound of Rf 0.45 (b) was converted almost completely into a substance having Rf 0.81 (a). The benzene solution was applied to a column containing 50 g of alumina, and elution with benzene gave 170 mg of a sirupy substance containing halogen; Rf 0.81 (a), $[\alpha]_D^{20}$ - 91° (c 3.75, $CHCl_3$).

Found· C 55.31, H 4.94, I 19 30, S 9.87%. $C_{20}H_{31}IO_4S_2$ Calculated· C 54.89; H 4.92; I 20.00, S 10.10%

This substance was dissolved in 15 ml of alcohol, 2 g of Raney nickel was added, and the mixture was boiled for 4 hours. The precipitate was then separated and washed with hot alcohol, the solution was evaporated, and the residue was boiled for 3 hours with 20 ml of 80% acetic acid and again vacuum-evaporated. To remove traces of acetic acid the operation of adding and evaporating toluene was repeated several times. The sirupy residue was dissolved in 15 ml of absolute methanol, a few drops of a 0.5 N solution of barium methoxide in methanol were added, and the mixture was boiled for three hours. The solution was cooled, and 5 ml of water and solid carbon dioxide were added. It was then evaporated, and the residue was extracted with acetone. According to paper chromatography the extract contained the two substances (XVIII) and (XIX) having close Rf values (0.57 and 0.60). In the periodate oxidation of the mixture of (XVIII) and (XIX) 1.25 moles of $NaIO_4$ was consumed per mole of the dideoxypentitol; hence, the mixture contained 1,4-dideoxy-D-xylitol (XVIII) and 1,5-dideoxy-L-arabitol (XIX) in the ratio of about 3 : 1.

Reaction of 2,3-O-Isopropylidene-5-O-benzoyl-L-arabinose Diethyl Mercaptal (XI) with $(C_6H_5O)_3P \cdot CH_3I$. A solution of 2.45 g of 2,3-O-isopropylidene-5-O-benzoyl-L-arabinose diethyl mercaptal (XI) in 20 ml of dry benzene was added to a suspension of 3 g of $(C_6H_5O)_3P \cdot CH_3I$ in 30 ml of dry benzene. The reaction mixture was heated for 24 hours at 50°, after which by chromatography on a column containing 150 g of alumina and elution with benzene

we isolated a sirupy substance of R_f 0.74 (a), which contained halogen; yield 2.2 g; $[\alpha]_D^{20}$-48.5° (c 3.85; benzene). In the system (c) this substance gave two distinct spots of (XIII) and (XIV), R_f 0.42 and 0.56, of which the spot with R_f 0.42 was much the more intense.

700 mg of this mixture was dissolved in 50 ml of absolute alcohol, 10 g of Raney nickel was added, and the mixture was boiled for 6 hours The alcoholic solution obtained after filtration and washing of the precipitate was vacuum-evaporated, the residue was extracted with benzene, and the extract was evaporated; the sirupy residue (230 mg) was a mixture of two substances (XVI) and (XVII), R_f 0.36 and 0.51 (c), 0.46 and 0.61 (a), with an appreciable predominance of the less mobile substance.

The mixture of (XVI) and (XVII) was chromatographed on a column containing 80 g of alumina; elution was with a mixture of petroleum ether and benzene with an increasing concentration of the latter. In this way we obtained 1,5-dideoxy-2,3-O-isopropylidene-4-O-benzoyl-L-arabitol (XVII) [R_f 0.61 (a); yield 26 mg; $[\alpha]_D^{20}$ + 17° (c 4.68; $CHCl_3$), and 1,4-dideoxy-2,3-O-isopropylidene-5-O-benzoyl-D-xylitol (XVI) [R_f 0 46 (a); yield 40 mg; $[\alpha]_D^{20}$-25.6° (c 4.95; $CHCl_3$)]. A fraction containing both substances (130 mg) was subjected to hydrolysis to remove the isopropylidene and benzoyl groups, as described above for the product of the reaction of 2,3-O-isopropylidene-5-O-benzoyl-L-arabinose dibenzyl mercaptal (X) with $(C_6H_5O)_3P \cdot CH_3I$. The solution obtained was investigated by paper chromatography, and the same two substances (XVIII) and (XIX), R_f 0 57 and 0 60, were found

2,3-O-Isopropylidene-5-deoxy-L-arabinose Diethyl Mercaptal (XXI). 1 g of 5-deoxy-L-arabinose diethyl mercaptal (XX) of m.p. 105-106°, prepared analogously to the D-isomer [14], was dissolved in 30 ml of cooled acetone containing 0.3 ml of concentrated sulfuric acid. The solution was kept for 24 hours at room temperature and then neutralized with anhydrous sodium carbonate, filtered, and evaporated. The residual sirup, amounting to 1 g, was dissolved in benzene and chromatographed on a column containing 75 g of alumina; elution was with benzene and chloroform. The resulting sirup (900 mg) consisted of 2,3-O-isopropylidene-5-deoxy-L-arabinose diethyl mercaptal (XXI); R_f 0.42 (b), $[\alpha]_D^{20}$ -65° (C 2.04; $CHCl_3$).

Found. C 51.28, 51.48, H 8.56; 8.77; S 22.68, 22.45%. $C_{12}H_{24}O_3S_2$ Calculated: C 51.39, H 8.62; S 22.87%.

1,5-Dideoxy-2,3-O-isopropylidene-4-O-benzoyl-L-arabitol (XII). 650 mg of 2,3-O-isopropylidene-5-deoxy-L-arabinose diethyl mercaptal (XXI) was dissolved in 50 ml of absolute alcohol, 7 g of Raney nickel was added, and the mixture was boiled for 4 hours. After filtration and the washing of the precipitate with hot alcohol the solution was vacuum-evaporated. We obtained sirupy 1,5-dideoxy-2,3-O-isopropylidene-L-arabitol (XXII); R_f 0.23 (b); yield 250 mg (67%).

To a solution of this sirup in 10 ml of pyridine at 0°, 0.4 ml of benzoyl chloride was added. The mixture was kept for 15 hours at 0° and 24 hours at 20°; it was then poured into 100 ml of ice water, and the precipitated oil was extracted with chloroform. The extract was washed with dilute hydrochloric acid, saturated sodium bicarbonate solution, and water; it was dried with sodium sulfate and vacuum-evaporated. The sirup obtained (400 mg) was chromatographed on a column containing 50 g of alumina; elution was with petroleum ether and benzene. We obtained 1,5-dideoxy-2,3-O-isopropylidene-4-O-benzoyl-L-arabitol (XVII); yield 350 mg (85%); R_f 0.61 (a), $[\alpha]_D^{20}$ + 19.3° (c 4.67; $CHCl_3$); almost identical in optical rotation and in chromatographic behavior to the substance of R_f 0 61 (a) prepared from 2,3-O-isopropylidene- 5-O-benzoyl-L-arabinose (XI) and completely identical to it in infrared spectrum. It should be noted that the infrared spectra of (XVII) and (XVI) are appreciably different in the region 700-1100 cm^{-1}.

1,5-Dideoxy-L-arabitol (XIX). 100 mg of 5-deoxy-L-arabitol diethyl mercaptal (XX) was dissolved in 10 ml of alcohol, 1 g of Raney nickel was added, and the mixture was boiled for 4 hours. The precipitate was separated and washed with hot alcohol; the solution was concentrated in a vacuum and investigated by paper chromatography. The only substance present in the solution [(XIX), R_f 0.60] was identical in chromatographic behavior to the more mobile substance of the mixture of dideoxypentitols obtained in the experiments with 2,3-O-isopropylidene-5-O-benzoyl-L-arabinose mercaptals. This identity was verified in the solvent systems: 2 : 1 : 2 ethyl acetate - pyridine - water [R_f 0.79 and 0.91 for the mixture, 0.91 for (XIX)], 4 : 1 : 5 isopentyl alcohol – formic acid – water [R_f 0.45 and 0.51 for the mixture, 0.51 for (XIX), and 84 : 16 butyl alcohol – water [R_f 0.48 and 0.55 for the mixture, 0 55 for (XIX)]

SUMMARY

1. In the reaction of isopropylidene and benzylidene derivatives of monosaccharides with $(C_6H_5O)_3P \cdot CH_3I$ the replacement of a hydroxy group by an iodine atom may be accompanied by the displacement of acetal groupings.

2. The reaction of isopropylidene derivatives of carbohydrate mercaptals with $(C_6H_5O)_3P \cdot CH_3I$ may proceed with displacement of the acetal protecting grouping and cleavage of the mercaptal grouping.

3. The replacement of hydroxyl by halogen in partially acylated monosaccharide derivatives may be accompanied by partial interchange of the acyl group and the halogen atom

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