MONOSACCHARIDES

COMMUNICATION 3. REACTION OF THE TRIPHENYL PHOSPHITE–METHYL IODIDE COMPLEX WITH SOME CARBOHYDRATE DERIVATIVES

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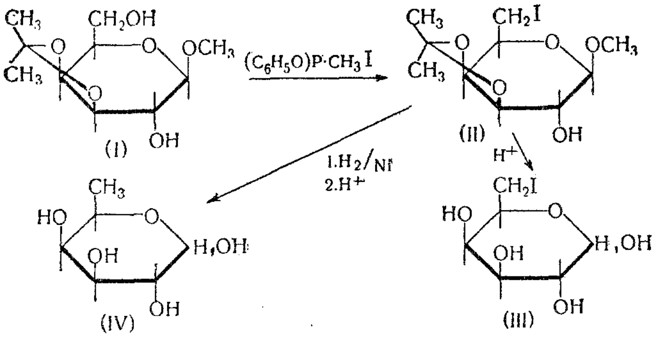
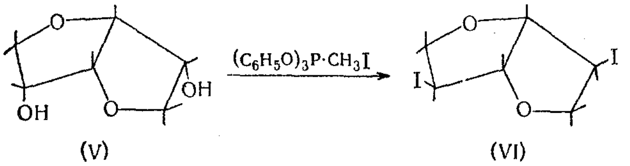
In a search for a reaction leading to the direct replacement of an isolated hydroxy group in sugar derivatives by halogen with the object of using the product for the synthesis of deoxy and amino sugars, we investigated the reaction of triphenyl phosphite–halogen complexes with diisopropylidene-D-glucose and diisopropylidene-D-galactose [1, 2]. This work showed that the result of this reaction depends on the character of the hydroxy groups to be replaced and, in particular, their spatial positions. As this reaction could have much preparative interest, we investigated it further for the case of some carbohydrate derivatives containing hydroxy groups of various types. As reagent we used crystalline triphenyl phosphite–methyl iodide complex [3], which is stable when kept under a layer of ether and is more convenient to use thenthe dibromide used previously [1, 2]. The reaction was caried out under standard conditions, namely in dry benzene solution at room or slightly elevated temperature (up to 50°) for several tens of hours, after which the reaction products were isolated by means of preparative adsorption chromatography on alumina. An invaluable aid in the investigation and isolation of the reaction products was provided by chromatography in an unfixed thin layer of alumina [4], which enabled us to make a rapid analysis of the compositions of complex mixtures, select conditions for preparative chromatographic separation, and follow its course.

The replacement of a hydroxy group by an iodine atom under the action of $(C_6H_5O)_3P \cdot CH_3I$ is a bimolecular nucleophilic-substitution reaction. As shown previously [2], a hydroxy group whose spatial position makes such reaction difficult remains inert to the action of the reagent, even under fairly severe conditions. In the present work this was confirmed by the fact that we succeeded in effecting the selective substitution of the primary hydroxygroup at C_6 in 3,4-O-isopropylidene-β-methyl-D-galactopyranoside (I):

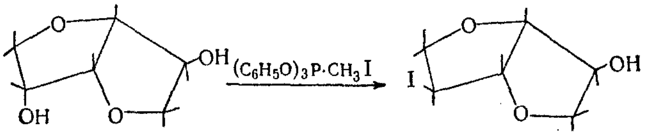


The reaction went in almost the same way, without touching the 2-hydroxyl, whether one or two molecular proportions of $(C_6H_5O)_3P \cdot CH_3I$ were used. This is probably associated with its exo-position in a bicyclic system of the cis-perhydroindan type, which creates steric hindrance to S_N2 reaction. The action of $(C_6H_5O)_3P \cdot CH_3I$ on 3,4-O-isopropylidene-β-methyl-D-galactoside is accompanied by the formation of some by-products, the nature of which has remained unelucidated; among them, however, we did not succeed in detecting the dihalogen dideoxy derivative.

On the other hand, it might be expected that a cyclic secondary hydroxyl with a spatial position favorable to nucleophilic substitution would be readily replaced by iodine under the action of $(C_6H_5O)_3P \cdot CH_3I$. To verify this supposition we chose 1,4: 3,6-dianhydro-D-mannitol (V) and 1,4: 3,6-dianhydro-D-sorbitol (VII) as model compounds; each dianhydrohexitol contains two secondary hydroxyls in a bicyclic system of the cis-perhydropentalene type, and moreover in dianhydrosorbitol one hydroxyl, and in dianhydromannitol both hydroxyls, occupy endo positions that favor replacement



(V) (VI)

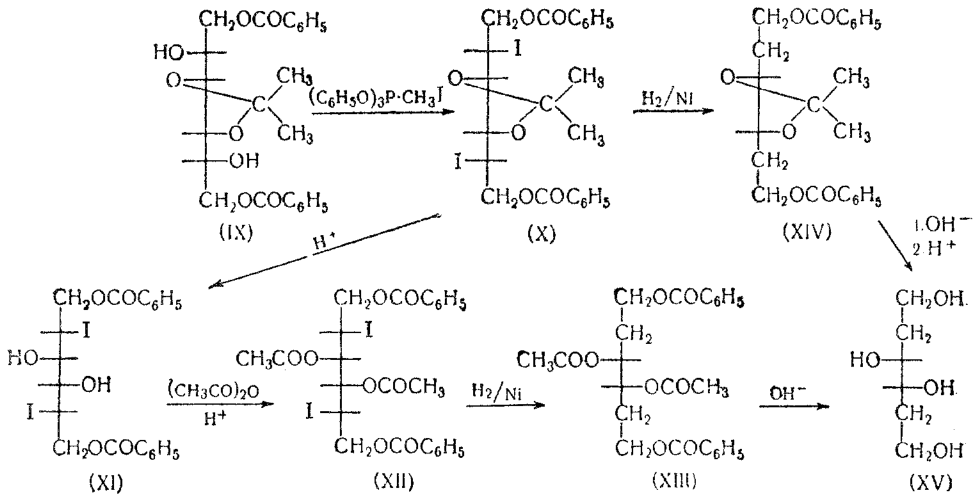


(VII) (VIII)

Actually, in 1,4: 3,6-dianhydro-D-mannitol both hydroxyls are readily replaced by iodine with formation of 2,5-diiodo-2,5-dideoxy-1,4: 3,6-dianhydro-L-iditol (VI) in quantitative yield. In the case of 1,4: 3,6-dianhydro-D-sorbitol (VII), reaction is accompanied by the formation of by-products, and we did not succeed in separating the resulting complex mixture completely. In spite of the fact that the main reaction product was not isolated in an analytically pure state, chromatographic data show it to be a monoiodo derivative, probably 2-iodo-2-deoxy-1,4: 3,6-dianhydro-L-iditol (VIII).

Hence, in bicyclic systems replacement under the action of (C$_6$H$_5$O)$_3$P·CH$_3$I is undergone only by those hydroxy groups whose spatial positions ensure attack of the carbon atom from the rear, as the mechanism of S$_N$2 reactions demands. In this connection it may be mentioned that data on the preparation of the 3-iodo-3-deoxy derivative from diisopropylidene-D-glucose and (C$_6$H$_5$O)$_3$P·CH$_3$I given in a short communication from Lee and El Sawi [5], which appeared simultaneously with our first paper [1] and was in conflict with its findings, appeared to be doubtful in that the spatial position of the hydroxy group in 1,2: 5,6-di-O-isopropylidene-D-glucofuranose is highly unfavorable to an S$_N$2 reaction. In fact, on repeating the reaction of diisopropylidene-D-glucose with (C$_6$H$_5$O)$_3$P·CH$_3$I we did not succeed in obtaining the 3-iodo-3-deoxy derivative (judging from the results of the hydrogenation of the reaction product); in all probability the compound obtained by Lee and El Sawi was actually 6-iodo-6-deoxy-1,2: 3,5-di-O-isopropylidene-D-glucose.

The laws found for the replacement of cyclic secondary hydroxy groups should not hold when the hydroxy groups are in an open chain. It is, for example, known that in noncyclic structures the replacement of primary and secondary tosyloxy and mesyloxy groups occur at approximately the same ease [6]. In this connection we studied the reaction of 1,6-di-O-benzoyl-3,4-O-isopropylidene-D-mannitol (IX) with (C$_6$H$_5$O)$_3$P·CH$_3$I. It was found that the reaction product—the sirupy 1,6-di-O-benzoyl-2,5-diiodo-2,5-dideoxy-3,4-isopropylidene-L-iditol (X)* is formed in about 90% yield, which completely confirms the view just expressed



To prove the structure of the diiodie (X) formed it was hydrogenated over Raney nickel; after the hydrolytic removal of the isopropylidene and benzoyl groups we obtained the corresponding dideoxyhexitol (XV). On the other hand, on treatment with acids the diiodide underwent elimination of the isopropylidene group with formation of crystalline 1,6-di-O-benzoyl-2,5-dideoxy-2,5-diiodo-L-iditol (XI), which gave the crystalline diacetate (XII) on acetylation with acetic anhydride in presence of sulfuric acid; hydrogenation of the latter over Raney nickel led to 1,6-di-O-benzoyl-3,4-di-O-acetyl-2,5-dideoxy-D-sorbitol (XIII), which passed on hydrolysis into 2,5-dideoxy-D-sorbitol (XV). The structure of 2,5-dideoxy-D-sorbitol was confirmed by the fact that in periodate oxidation it absorbed one molecular proportion of HIO_4 with formation of neither formaldehyde nor acetaldehyde.

Hence, the replacement of a secondary hydroxy group in an open chain by halogen under the action of $(C_6H_5O)_3P\cdot CH_3I$ proceeds without complications and in high yield. From the point of view of the use of this reaction in synthesis, for the preparation of deoxy sugars the most promising direction appears to be its extension to derivatives of the aldo forms of monosaccharides. As our first example of this variant of the reaction, which was investigated mainly to elucidate the behavior of the mercaptal grouping, we report the reaction of $(C_6H_5O)_3P\cdot CH_3I$ with the diethyl and dibenzyl mercaptals of 2,3: 4,5-di-O-isopropylidene-D-galactose[*]. It was found that under the conditions of the reaction the mercaptal groups was not affected and the yield of the corresponding iodide was about 95%. The diethyl mercaptal of 6-iodo-6-deoxy-2,3: 4,5-di-O-isopropylidene-D-galactose (XVIII) gave the previously described diethyl mercaptal of 6-iodo-6-deoxy-D-galactose (XX) on acid hydrolysis; boiling of the iodides obtained from both mercapatals with Raney nickel in alcohol led to 2,3: 4,5-di-O-isopropylidene-1,6-dideoxydulcitol (XXI), which was converted into 1,6-dideoxydulcitol (XXII) on hydrolysis. Other cases of the reaction of $(C_6H_5O)_3P\cdot CH_3I$ with carbohydrate mercaptals which might present interesting possibilites of synthesis will be the subject of a further communication.

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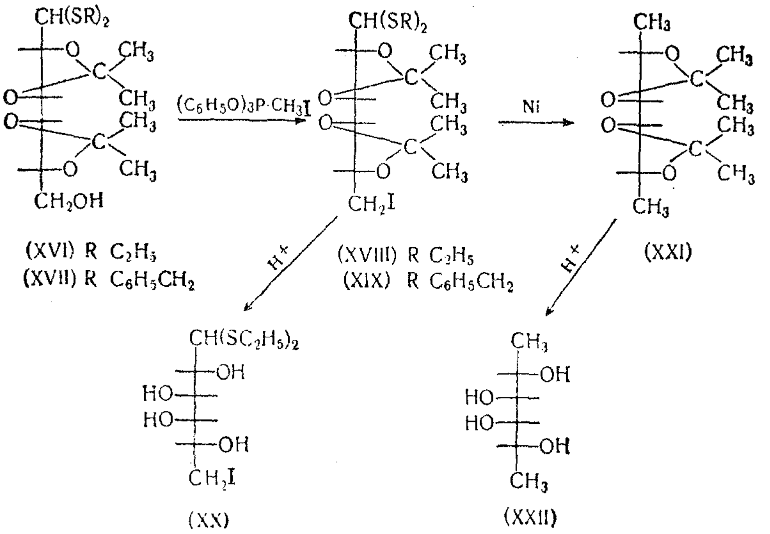
[*] The diethyl mercaptal of 2,3: 4,5-di-O-isopropylidene-D-galactose (XVI) was prepared following the analogy of the preparation of the dibenzyl mercaptal of 2,3: 4,5-di-O-isopropylidene-D-galactose [7]; on investigation by thin-layer chromatography on alumina [4] it was found that both these compounds contained impurities of greater chromatographic mobility, which were probably mercaptals of 2,3: 5,6-di-O-isopropylidene-D-galactose. Reaction with $(C_6H_5O)_3P\cdot CH_3I$ led to the disappearance of both of the original substances and the formation of a single reaction product, which can be explained by the displacement of the isopropylidene residue in the course of the reaction.



EXPERIMENTAL

Paper chromatography was carried out by the ascending method with the solvent system butyl alcohol–acetic acid–water 4:1:1 and "M" chromatographic paper from the Leningrad No. 2 Factory. Thin-layer chromatography [4] was carried out on plates with an unfixed layer (1 mm) of alumina of grade II activity with the solvents: Benzene (A) and benzene–methanol 9:1 (B). For the detection of the spots of substances on the paper we used a potassium periodate solution containing copper sulfate [8]; for reducing sugars, p-anisidine-H_3PO_4; the detection of substances on plates was carried out by spraying with concentrated sulfuric acid with subsequent heating under an infrared lamp. For preparative chromatography we again used alumina of grade II activity; control over preparative separation was effected by thin-layer chromatography.

Reaction of $(C_6H_5O)_3P \cdot CH_3I$ with 3,4-O-Isopropylidene-β-methyl-D-galactopyranoside (I). To a suspension of 770 mg (0.00167 mole) of $(C_6H_5O)_3P \cdot CH_3I$ in 25 ml of dry benzene we added 390 mg (0.00167 mole) of 3,4-O-isopropylidene-β-methyl-D-glactopyranoside [9] and stirred for two days at room temperature. The reaction mixture contained the main reaction products with R_f 0.40 (B) and also small amounts of substances with R_f 0.12 (starting compound), 0.33, 0.48, and 0.95 (B). One ml of the benzene solution was heated for three hours with 1 ml of 50% aqueous methanol containing 1% of H_2SO_4, and the hydrolysis products were investigated by paper chromatography. The main product, 6-iodo-6-deoxy-D-galactose (III) with R_f 0.57, contained galactose (R_f 0.18) as impurity and traces of unidentified substances with R_f 0.05, 0.37, and 0.74. The reaction mixture was applied to a column containing 120 g of alumina, through which was passed a mixture of benzene and methanol with an increasing concentration of the latter (from 0 to 5%). The substance isolated in this way, R_f 0.40 (B), contained a very small admixture of reaction products with close values of R_f; yield 350 mg (about 60%); $[\alpha]_D^{20}$+ 120.5° (c 2.5; CH_3OH). After long standing the substance partially crystallized out; the crystals were separated and recrystallized from petroleum ether (b.p. 45-60°). We obtained 6-iodo-6-deoxy-3,4-O-isoproplidene-β-methyl-D-galactopyranoside, m.p. 82-84°. Found: C 35.49; 35.64; H 5.44; 5.42; I 35.69; 36.10%. $C_{10}H_{17}IO_5$. Caclulated: C 34.90; H 4.98; I 36.88%.

Twenty mg of sirupy 6-iodo-6-deoxy-3,4-O-isoproylidene-β-D-galactopyranoside (II) was heated for three hours at 100° with 1 ml of 1% sulfuric acid in 50% aqueous methanol, neutralized with $BaCO_3$, and chromatographed on paper. The hydrolysis product was a reducing sugar with R_f 0.57 (III) containing galactose (R_f 0.18) in traces as impurtiy.

Two hundred mg of sirupy 6-iodo-6-deoxy-3,4-O-isopropylidene-β-methyl-D-galactopyranoside (II) was hydrogenated as a solution in 25 ml of alcohol over about 0.5 g of Raney nickel in presence of three drops of diethylamine until the absorption of hydrogen stopped. Catalyst was filtered off, and the solution was diluted with water and extracted with chloroform. The extract was washed with water, dried with Na_2SO_4, and vacuum-evaporated; the residue was hydrolyzed as described above. By paper chromatography of the hydrolysis products we found fucose (IV) with R_f 0.32 with a trace of galactose impurity, R_f 0.18. The structure of fucose was confirmed by reactions specific for 6-deoxy sugars [10].

Reaction of 1,4: 3,6-dianhydro-D-mannitol (V) with $(C_6H_5O)_3P \cdot CH_3I$. To a suspension of 2.45 g (0.0053 mole) of $(C_6H_5O)_3P \cdot CH_3I$ in 25 ml of dry benzene we added 365 mg (0.0025 mole) of 1,4: 3,6-dianhydro-D-mannitol (II); the reaction mixture was stirred for 24 hours at room temperature. Already after 18 hours the original substance could not be detected chromatographically; the only reaction product had R_f 0.92 (A). The dark-red homogeneous solution was filtered through a column containing 100 g of alumina; elution was with benzene. The filtrate was vacuum-evaporated, and the residue crystallized out. The yield of 2,5-dideoxy-2,5-diiodo-1,4: 3,6-dianhydro-L-iditol (VI) was 915 mg (100%). The substance was crystallized from methanol; m.p. 84-85°; $[\alpha]_D^{26}$ + 136.5° (c 3.1; $CHCl_3$). The literature gives: m.p. 61-62° (from CH_3OH) [11]; m.p. 69-70° and $[\alpha]_D$ 101.4° [12]; m.p. 61-63° (from alcohol) and $[\alpha]_D^{19}$ + 107.9° (c 1.97; $CHCl_3$); [13]; m.p. 65-66° (from CH_3OH); $[\alpha]_D^{22}$ + 110° (c 0.645; $CHCl_3$). Found: C 20.13; 20.00; H 2.44; 2.44; I 68.76; 69.08%. $C_6H_8I_2O_2$. Calculated: C 19.69; H 2.20; I 69.30%.

Reaction of 1,4: 3,6-Dianhydro-D-sorbitol (VII) with $(C_6H_5O)_3P \cdot CH_3I$. To a suspension of 2.8 g (0.00605 mole) of $(C_6H_5O)_3P \cdot CH_3I$ in 25 ml of dry benzene we added 0.890 g (0.0061 mole) of 1,4: 3,6-dianhydro-D-sorbitol [15]. The reaction mixture was stirred for three days at room temperature, in the course of which there was some resinification and darkening of the solution. In chromatography of the reaction mixture on plates of alumina we found the main product, R_f 0.54 (B), and a whole series of less intense spots: R_f 0.05, 0.23, 0.39, 0.56, 0.71, and 0.97 (B). On the basis of the value of R_f the main product must be regarded as 2-iodo-2-deoxy-1,4: 3,6-dianhydro-L-iditol (VIII). In separation of the reaction mixture in a column of alumina we could not isolate the substance with R_f = 0.54 (B) in an analytically pure state.

Reaction of 1,2: 5,6-Di-O-isopropylidene-D-glucofuranose with $(C_6H_5O)_3P \cdot CH_3I$. A solution of 1.17 g (0.0045 mole) of 1,2: 5,6-di-O-isopropylidene-D-glucofuranose in 50 ml of dry benzene was refluxed with 4.15 g (0.009 mole) of $(C_6H_5O)_3P \cdot CH_3I$ for 20 hours; the benzene solution was washed several times with sodium carbonate solution, dried with Na_2SO_4, and vacuum-evaporated. The residue was dissolved in 50 ml of methanol, about 0.5 g of Raney nickel was added, and hydrogenation was carried out at room temperature with dropwise addition of a solution of 0.5 g of KOH in methanol. Catalyst was filtered off, and the filtrate was diluted with water and extracted with ether; the ether extract was washed with water, dried with calcium chloride, and evaporated. The residue was boiled with 100 ml of 50% aqueous methanol containing 1% of sulfuric acid for two hours; the mixture was cooled and neutralized with barium hydroxide. The precipitate was separated, and the solution, after concentration, was investigated by paper chromatography, when we detected only quinovose, R_f 0.36, with a little glucose impurity, R_f 0.18. Compounds corresponding in chromatographic behavior to 3-deoxyglucose were not detected.

Reaction of 1,6-Di-O-benzoyl-3,4-O-isopropylidene-D-mannitol (IX) with $(C_6H_5O)_3P \cdot CH_3I$. To a suspension of 3.3 g (0.00715 mole) of $(C_6H_5O)_3P \cdot CH_3I$ in 50 ml of dry benzene we added 1.5 g of 1,6-di-O-benzoyl-3,4-O-isopropylidene-D-mannitol [16], and the reaction mixture was heated at 50°. Already after 24 hours the main component of the solution was a substance with R_f 0.79 (A); the original compound, R_f 0.17 (A), was present in smaller amount. After two days the solution was cooled, and we separated the substance with R_f 0.79 with the aid of preparative chromatography in a column of 120 g of alumina with elution with benzene. The fractions were vacuum-evaporated, and we obtained sirupy 1,6-di-O-benzoyl-2,5-diiodo-2,5-dideoxy-3,4-O-isopropylidene-L-iditol (X); yield 2.05 g (90%); $[\alpha]_D^{26}$ + 17.4° (c 2.2; $CHCl_3$).

Three hundred mg of sirupy 1,6-di-O-benzoyl-2,5-diiodo-2,5-dideoxy-3,4-O-isopropylidene-L-iditol (X) was dissolved in 5 ml of acetic acid containing 10% of concentrated HCl; after four hours the mixture was vacuum-evaporated in the cold, and the residue was crystallized from benzene. We obtained 1,6-di-O-benzoyl-2,5-diiodo-2,5-dideoxy-L-iditol (XI); yield 152 mg (54%). m.p. 163-165° (decomp); $[\alpha]_D^{20}$ -19° (c 5.7; dioxane). Found: C 39.43; 39.52; H 3.27; 3.41; I 41.35; 41.29%. $C_{20}H_{20}I_2O_6$. Calculated: C 39.37; H 3.30; I 41.59%.

To a suspension of 100 mg of 1,6-di-O-benzoyl-2,5-diiodo-2,5-dideoxy-L-iditol (XI) in 3 ml of acetic anhydride we added one drop of concentrated sulfuric acid and then shook the mixture. After a few minutes the precipitate dissolved completely. After 24 hours the solution was poured into 20 ml of 10% CH_3COONa; the precipitate that formed was extracted with chloroform, and the extract was washed with $NaHCO_3$ solution and with water, dried with Na_2SO_4, and evaporated the residue was crystallized from methanol. The yield of 1,6-di-O-benzoyl-3,4-di-O-acetyl-2,5-diiodo-2,5-dideoxy-L-iditol (XII) was 100 mg (88%); m.p. 111-111.5°; $[\alpha]_D^{20}$ -21° (c 2; $CHCl_3$); R_f 0.43 (A). Found: C 41.46; 41.42; H 3.61; 3.49; I 36.56; 36.76%. $C_{24}H_{24}I_2O_8$. Calculated: C 41.52; H 3.48; I 36.56%.

2.55 g (0.00405 mole) of sirupy 1,6-di-O-benzoyl-2,5-diiodo-2,5-dideoxy-3,4-O-isopropylidene-L-iditol (X) was dissolved in 50 ml of absolute alcohol, about 1.5 g of Raney nickel was added, and hydrogenation was carried out with slow addition of an alcoholic solution of 1.12 ml (0.0081 mole) of triethylamine. When the theoretical amount of hydrogen had been absorbed, the catalyst was filtered off and washed with hot alcohol; the solution was evaporated. The residue was a sirup (yield 1.25 g), which was a mixture of three substances, R_f 0.50 (main component), 0.62, and 0.77 (A). A solution of this sirup in petroleum ether was applied to a column of 100 g of alumina and eluted with a mixture of petroleum ether and benzene with an increasing concentration of the latter (from 0 to 50%). Fractions containing the substance having R_f 0.50 (A) were combined and evaporated. We obtained 1,6-di-O-benzoyl-3,4-O-isopropylidene-2,5-dideoxy-D-sorbitol (XIV); yield 580 mg (38%); $[\alpha]_D^{20}$ + 28.8° (c 3.6; $CHCl_3$). Found: C 70.18; 70.09; 6.84%. $C_{23}H_{26}O_6$. Calculated: C 69.33; H 6.58%.

One hundred mg of 1,6-di-O-benzoyl-3,4-O-isopropylidene-2,5-dideoxy-D-sorbitol (XIV) was dissolved in 10 ml of absolute methanol, 0.5 ml of about 0.5 N $Ba(OCH_3)_2$ in methanol was added, and the mixture was boiled for three hours; 5 ml of water was then added, H_2SO_4 was added to a pH of about 1, and the mixture was boiled further for two hours. The solution was cooled and neutralized with $Ba(OH)_2$, the precipitate was separated by centrifugation, and the solution was evaporated. The residue was an amorphous substance, and in paper chromatography it gave a single spot with R_f 0.36. After recrystallization from aqueous acetone we obtained 2,5-dideoxy-D-sorbitol (XV); yield 20 mg; $[\alpha]_D^{20}$ + 13.2° (c 3.8; water).

On periodate oxidation of 18 mg of 2,5-dideoxy-D-sorbitol 0.91 of a molecular proportion of $NaIO_4$ was consumed in only 90 minutes; after 16 hours the consumption of $NaIO_4$ was 1.01 of a molecular proportion. Qualitative reactions for formaldehyde and acetaldehyde were negative.

Twenty mg of 1,6-di-O-benzoyl-3,4-di-O-acetyl-2,5-diiodo-2,5-dideoxy-L-iditol (XII) was hydrogenated over Raney nickel in presence of triethylamine. The hydrogenation product was a substance with R_f 0.32 (A) with some admixture of compounds with R_f 0.16, 0.54, and 0.92 (A). The mixture was hydrolyzed by the action of $Ba(OCH_3)_2$ in methanol and chromatographed on paper; the main product was 2,5-dideoxy-D-sorbitol (XV), R_f 0.36, identical with the product described above.

Diethyl Mercaptal of 2,3:4,5-Di-O-isopropylidene-D-galactose (XVI). Ten g of D-galactose diethyl mercaptal was introduced into a cooled solution of 3 ml of concentrated H_2SO_4 in 100 ml of acetone, and complete dissolution occurred after a few minutes. The solution was left overnight at room temperature, neutralized with anhydrous sodium carbonate, filtered, and evaporated. The residue was dissolved in petroleum ether, filtered, and again evaporated. The resulting sirup was dried at 50-60° (0.1 mm); yield 11.5 g (90%); $[\alpha]_D^{22}$ -67.7° (c 3.9; $CHCl_3$). Found: C 53.07; 52.92; H 8.17; 8.45; S 17.33; 17.56%. $C_{16}H_{30}O_5S_2$. Calculated: C 52.43; H 8.25; S 17.50%.

On chromatography on plates of alumina it was found that the substance was heterogeneous and, apart from the main component with R_f 0.50 (B), it contained a little impurity of R_f 0.69 (B). This mixture was used in further work without separation.

Reaction of the Diethyl Mercaptal of 2,3:4,5-Di-O-isopropylidene-D-galactose (XVI) with $(C_6H_5O)_3P\cdot CH_3I$. To a suspension of 2.0 g (0.0043 mole) of $(C_6H_5O)_3P\cdot CH_3I$ in 20 ml of dry benzene we added a solution of 1.48 g (0.004 mole) of diethyl mercaptal of 2,3:4,5-di-O-isopropylidene-D-galactose (XVI) in 20 ml of dry benzene, and the mixture was stirred for five days at room temperature. The reaction mixture contained a reaction product with R_f 0.10 (original substance), 0.30, and 0.60 (A). The benzene solution was applied to a column of 100 g of alumina, and after elution with benzene we obtained 1.750 (92%) of the sirupy diethyl mercaptal of 6-deoxy-6-iodo-2,3: 4,5-di-O-isopropylidene-D-galactose (XVIII); $[\alpha]_D^{20}$ -37° (c 4; $CHCl_3$).

Nine hundred-forty mg of the sirupy reaction product was dissolved in 70% alcohol, and a few drops of concentrated hydrochloric acid were added; the mixture was heated for 30 minutes at 70-80°. The precipitate that came down on cooling was separated and recrystallized from aqueous alcohol. We obtained the diethyl mercaptal of 6-iodo-6-deoxy-D-galactose (XX); yield 300 mg; m.p. 119-119.5° (decomp.). The literature [17] gives m.p. 123° (decomp.).

1.0 g of the sirupy diethyl mercaptal of 6-iodo-6-deoxy-2,3: 4,5-di-O-isopropylidene-D-galactose (XVIII) was dissolved in 50 ml of absolute alcohol, about 10 g of Raney nickel was added, and the mixture was boiled for four hours. The hot reaction mixture was filtered, and the precipitate was washed with hot alcohol. The alcoholic solution was diluted with an equal volume of water and 1 ml of concentrated HCl was added. The mixture was heated in a boiling water bath for two hours, cooled, and neutralized with lead carbonate. The precipitate was separated, and the solution was evaporated. The crystalline residue was recrystallized from absolute alcohol. The yield of

1,6-dideoxydulcitol (XXII) was 400 mg (77.5%); m.p. 179-181°; $[\alpha]_D^{20}$ 0° (c 2.5; water); R_f 0.51. The literature [18] gives m.p. 183-184°. Found: C 48.08; H 9.36%. $C_6H_{14}O_4$. Calculated: C 47.99; H 9.40%.

1.0 g of the diethyl mercaptal of 6-iodo-6-deoxy-2,3:4,5-di-O-isopropylidene-D-galactose (XVIII) was heated with Raney nickel as described above. The alcoholic solution of the reduction product was diluted with five volumes of water and extracted with ether. The ether solution was dried with sodium sulfate and evaporated in the cold; the residue was sublimed at 60° (12 mm). We obtained 2,3:4,5-di-O-isopropylidene-1,6-dideoxydulcitol (XXI); yield 350 mg (72.5%); m.p. 58-59.5°. The literature [18] gives m.p. 63-64°.

Reaction of the Dibenzyl Mercaptal of 2,3:4,5-Di-O-isopropylidene-D-galactose (XVII) with $(C_6H_5O)_3P \cdot CH_3I$. To a suspension of 2.31 g (0.005 mole) of $(C_6H_5O)_3P \cdot CH_3I$ in 30 ml of dry benzene we added a solution of 2 g (0.004 mole) of the dibenzyl mercaptal of 2,3:4,5-di-O-isopropylidene-D-galactose [7] ($[\alpha]_D^{20}$ -157° (c 3.9; $CHCl_3$)) in 35 ml of benzene. The reaction mixture was heated for 30 hours at 50°. The benzene solution was applied to a column containing 120 g of alumina; by elution with benzene we isolated a reaction product, R_f 0.85 (A), which, after removal of solvent in a vacuum, crystallized spontaneously; yield 2.4 g (98%). After recrystallization from petroleum ether (b.p. 45-60°), the dibenzyl mercaptal of 6-iodo-6-deoxy, 2,3:4,5-di-O-isopropylidene-D-galactose (XIX) had m.p. 86.5-87°; $[\alpha]_D^{19}$ -99.9° (c 2.1; benzene).

On reduction of the bibenzyl mercaptal of 6-iodo-6-deoxy-2,3:4,5-di-O-isopropylidene-D-galactose (XIX) under the conditions described above for the diethyl mercaptal (XVIII), we obtained 2,3:4,5-di-O-isopropylidene-1,6-dideoxydulcitol (XXI), which on hydrolysis gave 1,6-dideoxydulcitol (XXII), R_f 0.51.

SUMMARY

1. Sterically hindered hydroxy groups in bicyclic systems of the type of cis-perhydroindan and cis-perhydropentalene are not replaced by iodine under the action of $(C_6H_5O)_3P \cdot CH_3I$.

2. The conditions for the replacement of secondary hydroxy groups in an open chain by iodine are comparable with the conditions for the replacement of primary hydroxy groups under the action of $(C_6H_5O)_3P \cdot CH_3I$.

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