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A PROPOSED INVERSION MECHANISM FOR THE FORMATION OF LEVOGLUCOSAN FROM PHENYL β-D-GLUCOSIDE AND TRIMETHYLGLUCOSYLAMMONIUM COMPOUNDS

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The formation of 1,6-anhydrohexoses and heptoses by the action of hot alkali on phenyl β-D-glycosides has been recently suggested by Montgomery, Richtmyer, and Hudson (1, 2) as a method of distinguishing the β-glycosides from their α isomers. The α isomers form anhydrohexoses in only a few cases, and then much more slowly than do the corresponding β isomers. Alkyl glycosides were shown to be stable under the same conditions. The preparation of 1,6-anhydro sugars by the action of hot alkali on the phenyl β-D-glycosides bears a striking similarity to their preparation by the action of hot alkali on trimethyl glycosylammonium halides (3). That the two reactions probably proceed by similar mechanisms has been suggested (2).

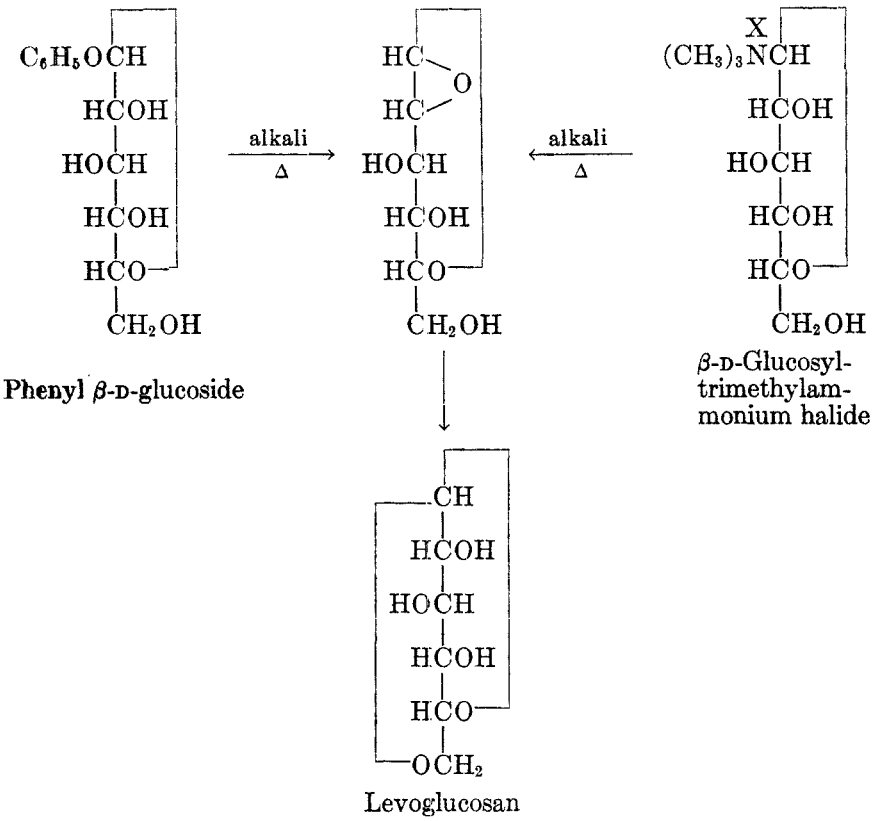
The mechanism of formation of levoglucosan from a trimethylglycosylammonium halide and hot alkali was suggested by Micheel and Micheel (4) as passing through an unstable intermediate before the formation of the stable glucosan. They suggested that from stereochemical consideration the intermediate in question probably possessed a 1,3-anhydro ring.

The formation of a β-1,6-anhydro ring from a phenyl β-glycoside or a trimethyl-β-glycosylammonium halide must involve either retention of configuration or an even number of "Walden" inversions. In the light of the recent work of Lucas, Winstein, and co-workers, no mechanism is now postulated which gives total retention in one step. It is true that the ionization mechanism can give up to 50% retention by producing racemization. Racemization, as meaning the production in equal quantities of α and β-1,6-anhydro sugars, is not possible in the reaction under consideration since only one 1,6-anhydro sugar is capable of formation. However, the carbon atom in question would be open to attack by hydroxide ions etc. on the reverse side from that attacked by the number six hydroxyl. It may be assumed that in any case there is competition between hydroxide ions and the number six hydroxyl on the β side. Considering the relatively high yields obtained in nearly all cases (1, 2) (*e.g.* 85% isolated of 1,6-anhydroglucose from phenyl β-D-glucoside), it seems highly improbable that any mechanism involving more than a trace of reaction on the α side is operative. Except for the high yields and other experimental data to be introduced later, one might consider the possibility of a single product arising from an ionization mechanism due to the asymmetric nature of the synthesis or to the possibly greater reactivity of the number six hydroxyl over other attacking groups. The use of rate studies as a means of mechanism analysis is of no avail in the present case due to the pseudo first order nature of intramolecular inversions.

The formation of a 1,3-anhydro ring as suggested by Micheel and Micheel

is not possible by an inversion mechanism in the case of glucose and galactose, in which the hydroxyl on carbon atom three and the reactive group on carbon one are *cis*. The formation of a 1,3-ring on the stable pyranose ring is unlikely, as it would involve enormous strain. It will also be shown later that substitution in the three position does not hinder the reaction.

It is suggested by the present authors that the phenoxyl or trimethylammonium groups are removed with the formation by inversion of an intermediate 1,2-anhydro sugar. This 1,2-anhydro sugar, in the case of glucose, then reacts by inversion with the nearest hydroxyl, that on carbon atom six, to form levoglucosan.



Phenyl β-D-glucoside

β-D-Glucosyltrimethylammonium halide

Levoglucosan

The formation of ethylene oxide rings from quaternary ammonium salts by the action of hot alkali has been known for some time. Rabe and Hallensleben (5) in 1910 and Read and Campbell in 1930 (6) used the method to prepare 1,2-diphenylethylene oxide. The latter authors prepared the optically active iso and normal 1,2-diphenyl-2-hydroxyethyltrimethylammonium hydroxides. On steam distillation, the iso compounds gave the inactive meso oxide, and the normal compounds the optically active oxides. They found that the *dextro* rotatory ammonium salt formed the *levo* rotatory oxide and *vice versa*. More recently Wilson and Lucas (7) have in a similar way prepared the *cis* and *trans*-epoxybutanes from the quaternary ammonium salts.

There is considerable evidence to show that inversion occurs during the opening of ethylene oxide rings. Earlier references are given by Wilson and Lucas (7), who also showed inversion to occur during the opening with water and a catalytic amount of perchloric acid. Subsequently, Winstein and Lucas (8) have shown that inversion occurred during the opening with glacial acetic acid. In 1928 Hickinbottom (9) split Brigl's anhydride (3,4,6-triacetyl-1,2-anhydroglucose) with a large number of alcohols. He found that all aliphatic alcohols tested, added to give the β-glucosides. Thus the work of Hickinbottom has shown that the acetate of the proposed intermediate in the formation of levoglucosan not only reacts with alcohols with inversion, but that it is predominantly the number one carbon atom which is inverted, a necessary assumption in the formation of levoglucosan.

That ethylene oxide rings are opened by reaction with alcohols under alkaline conditions has been shown by Ohle and Tessmar (10) with 5,6-anhydromonoacetoneglucose. They obtained predominantly substitution on carbon atom number six, giving another instance of preferential opening.

The action of hot alkali on various substituted glucosyltrimethylammonium halides and glucosides has given results that would be predicted on the basis of 1,2-anhydro formation. Micheel and Micheel (4) prepared 6-tritylglucosyltrimethylammonium chloride. On treatment of this compound with hot aqueous alkali no identifiable compound was isolated. By the use of methyl alcoholic alkali instead of aqueous alkali, they obtained methyl 6-trityl-β-D-glucoside. Thus again as in the preparation of levoglucosan, retention of configuration was involved requiring an even number of inversions. The hot aqueous alkali in the former case would be expected to open the oxide ring, giving a 6-tritylglucose which would probably form difficultly identifiable products with the hot alkali. The alcohol however, forms the glucoside, which is alkali-stable and easily identifiable. Substituion on carbon atom number six thus does prevent the formation of levoglucosan, but does not prevent the formation of the methyl β-glucoside with retention of configuration. This result is consistent with the assumption of a 1,2-anhydride as an intermediate.

Levoglucosans with various substituents in position four have been previously prepared from both the phenyl β-glycosides and glycosyltrimethylammonium halides of lactose, maltose, and cellobiose (2, 11, 12). Therefore substitution on position four has apparently little influence on the course of the reaction.

The preparation of levoglucosan from phenyl β-D-glucoside (1) takes about nine hours under reflux in 1.3 *N* potassium hydroxide solution. A sample of phenyl tetramethyl-β-D-glucoside was prepared (13), and after being heated with 1.3 *N* sodium hydroxide at 120° for two weeks, was recovered unchanged. This indicated that the presence of the *beta* phenoxyl group alone was not sufficient for a reaction to occur under these conditions. It also minimizes the chance that levoglucosan formation is an ionization reaction since substitution of the hydroxyls would be expected to have little influence in such a case. Reaction by the ionic mechanism is due to the formation of an ion caused by the instability of the molecule under the conditions of the reaction, and is not due to attack by other groups.

Phenyl 3-methyl-β-D-glucoside, which was synthesized earlier by Helferich and Lang (14), was prepared and found to react readily with hot alkali to give the theoretical amount of phenol (isolated as the tribromide) and a compound which will be reported later. The ready reaction of the 3-methylglucoside apparently eliminates the possibility of a 1,3-ring as the intermediate.

The preparation of phenyl 2,3-dimethyl-β-D-glucoside was accomplished. This on treatment with alkali for two days gave no detectable phenol, and the original compound was recovered unchanged. Since substitution on positions six, four, and three did not hinder reaction or stabilize the compounds, it was assumed that substitution on position two was responsible. Such hinderance would be expected only if the number two hydroxyl was involved, as in the formation of a 1,2-anhydro ring.

The preparation of phenyl 2,3-dimethyl-β-D-glucoside and finally of 2,3-dimethyl-D-glucose by the partial and complete hydrolysis, respectively, of phenyl 2,3-dimethyl-4,6-benzylidene-β-D-glucoside gave good results and is suggested as a practical way of obtaining the dimethylglucose, in view of the availability of phenyl β-D-glucoside (15). The conversion of phenyl β-D-glucoside to its 4,6-benzylidene derivative and the subsequent methylation and hydrolysis gave excellent yields and easily crystallizable compounds.

EXPERIMENTAL PART

Action of alkali on phenyl β-D-glucosides. Phenyl tetramethyl-β-D-glucoside (2 g.) was heated with 200 ml. of 1.3 *N* sodium hydroxide in a bomb at 120° for two weeks. All of the starting material was recovered unchanged.

Phenyl 3-methyl-β-D-glucoside (2 g.) was added to 100 ml. of 2.6 *N* potassium hydroxide and heated for twenty-four hours. The solution was neutralized to methyl orange and distilled under reduced pressure. Bromine water was added to the distillate and the resulting precipitate of tribromophenol filtered off. The yield of tribromophenol was 2.5 g. which was practically the theoretical amount. The residue from the distillation was extracted with methyl alcohol. The methyl alcohol was evaporated leaving a sirupy residue which has not as yet crystallized. This product is being investigated further and a report will be made later.

Phenyl 2,3-dimethyl-β-D-glucoside was heated with 100 ml. of 2.6 *N* potassium hydroxide for forty-eight hours. No precipitate was obtained on addition of bromine water to the distillate. The residue from the distillation was dissolved in a small amount of water and on cooling, phenyl 2,3-dimethyl-β-D-glucoside crystallized. The amount recovered also indicated that no reaction had occurred.

Phenyl 4,6-benzylidene-β-D-glucoside. A mixture of 100 g. of crude phenyl β-D-glucoside, 400 g. of benzaldehyde, and 105 g. of powdered anhydrous zinc chloride was shaken in a stoppered bottle for five hours. The mixture was poured into a large beaker and mixed well with about 250 ml. of water followed by 400 ml. of ligroin (b.p. 30–40°). The crystals which formed were filtered off and washed with ligroin and water. The product was recrystallized from about 1.7 liters of 95% alcohol. The yield of phenyl 4,6-benzylidene-β-D-glucoside varied from 105–112 g. (82–87%). The glucoside after two additional recrystallizations from alcohol melted at 194.5–195° (corr.)., $[\alpha]_D^{25}$ −56.5° (*c* = 2, acetone). Phenyl 4,6-benzylidene-β-D-glucoside is soluble in acetone, ethyl acetate, hot benzene, and hot chloroform; sparingly soluble in hot alcohol; slightly soluble in cold chloroform and insoluble in ligroin, cold benzene, and cold alcohol.

Anal. Calc'd for $C_{19}H_{20}O_6$: C, 66.26; H, 5.85.
Found: C, 63.37; H, 6.08.

Phenyl 2,3-dimethyl-4,6-benzylidene-β-D-glucoside. A solution of 100 g. of once-recrystallized phenyl 4,6-benzylidene-β-D-glucoside in 500 ml. of acetone was placed in a three-

necked flask equipped with a mechanical stirrer and seal, two burettes, and a distillation tube connected to a condenser. The flask was heated in a water-bath maintained at 50°. To the vigorously stirred solution was added dropwise from the burettes 220 ml. of methyl sulfate and 244 ml. of 50% sodium hydroxide, keeping the solution on the alkaline side at all times. The reagents were added at such a rate that the acetone distilled over slowly. After all reagents had been added the mixture was stirred for one hour, then diluted with 2 l. of water to dissolve the salts and the crystalline product filtered off. The yield crude was 106 g. (98%). Recrystallization was accomplished from a mixture of diethycellosolve and ethyl alcohol. After two additional recrystallizations the melting point was 179.2–179.7° (corr.), $[\alpha]_D^{25}$ −55.8° (c = 2, U.S.P. chloroform). Phenyl 2,3-dimethyl-4,6-benzylidene-β-D-glucoside is soluble in benzene and chloroform; moderately soluble in ethyl acetate and acetone; slightly soluble in hot alcohol and ligroin and insoluble in cold ligroin.

Anal. Calc'd for $C_{21}H_{24}O_6$: C, 67.72; H, 6.50.
Found: C, 67.65; H, 6.41.

2,3-Dimethyl-D-glucose. A mixture of 30 g. of once-recrystallized phenyl 2,3-dimethyl-4,6-benzylidene-β-D-glucoside and a solution of 48 g. of sulfuric acid in 500 ml. of water was steam distilled for three hours, maintaining the volume constant. The solution was cooled, neutralized with barium carbonate, and filtered. The filtrate was concentrated to dryness under reduced pressure, the residue dissolved in 250 ml. of ethyl acetate, and the solution filtered. The filtrate was concentrated to dryness under reduced pressure and the sirup dried in a vacuum oven. To the residue was added enough ethyl acetate to make a thin sirup. On scratching the flask the product crystallized and the crystals were filtered off. After recrystallization from ethyl acetate 9.2 g. was obtained. By reworking the residues an additional 4.5 g. was obtained, making an 82% yield in all; $[\alpha]_D^{25}$ 64.3° (c = 2, water) (equilibrium rotation); m.p. 110–111° (corr.).

Phenyl 2,3-dimethyl-β-D-glucoside. To a solution of 25 g. of phenyl 2,3-dimethyl-4,6-benzylidene-β-D-glucoside in 500 ml. of hot acetone was added 50 ml. of water containing 0.8 ml. of concentrated hydrochloric acid. The solution was refluxed for four hours, neutralized with an excess of potassium bicarbonate and concentrated to dryness under reduced pressure. To the residue was added 500 ml. of toluene, which was distilled off under 85 mm. pressure until the volume was reduced to 150 ml., and the mixture then filtered. As the filtrate cooled, crystals of phenyl 2,3-dimethyl-β-D-glucoside formed. The crystals were filtered off and the filtrate concentrated to obtain a second crop of crystals. The total yield was 17.5 g. (92%). For analysis the compound was recrystallized several times from water. The melting point was 97–98° (corr.), $[\alpha]_D^{25}$ −72.8° (c = 2, U.S.P. chloroform). Phenyl 2,3-dimethyl-β-D-glucoside is very soluble in acetone, alcohol, chloroform, and ethyl acetate, moderately soluble in benzene, sparingly soluble in toluene and cold water, but soluble in hot water and slightly soluble in hot ligroin (60°).

Anal. Calc'd for $C_{14}H_{18}O_6$: C, 59.57; H, 6.43.
Found: C, 58.90; H, 7.10.

Phenyl tetramethyl-β-D-glucoside. Phenyl tetraacetyl-β-D-glucoside was simultaneously deacetylated and methylated in acetone solution. The procedure was similar to that used in the methylation of phenyl 4,6-benzylidene-β-D-glucoside. Five to six times the theoretical amount of methyl sulfate was used. The methylated glucoside was extracted from the reaction mixture with chloroform and the chloroform then removed by distillation in a steam-bath. Air was bubbled through the residue from the chloroform extract until crystallization occurred. The crystals were dissolved in glacial acetic acid and on dilution of the solution with water, long white needles of phenyl tetramethyl-β-D-glucoside formed. Recrystallization by the same procedure gave a product of m.p. 78.6–79° (corr.), $[\alpha]_D^{25}$ −47.9° (c = 2, U.S.P. chloroform). Voss and Wachs (13) recorded for this compound the melting point 78–78.5°. Phenyl tetramethyl-β-D-glucoside is very soluble in most organic solvents, sparingly soluble in cold ligroin, and slightly soluble in hot water.

Phenyl 3-methyltribenzoyl-β-D-glucoside. A mixture of 108 g. of 3-methyltetrabenzoyl-D-glucose (23), 200 ml. of a solution of anhydrous hydrogen bromide in glacial acetic acid (saturated at 0°), 550 ml. of benzene, and 150 ml. of dry ether was allowed to stand overnight.

The solution was then poured into ice, washed with two portions of ice-water, with a saturated potassium bicarbonate solution, and then dried over powdered calcium chloride. The solution was filtered from the calcium chloride and placed in a flask containing 400 g. of dry phenol and 200 g. of powdered Drierite. The solution was stirred for a short time, 75 g. of powdered silver carbonate was added and the mixture stirred for twenty-four hours. During this operation the flask was protected from moisture by a seal and a calcium chloride drying tube. At the end of this time the salts were filtered off and the filtrate washed first with sufficient alkali to remove the phenol and then with water. This solution was concentrated to a sirup, mixed with five volumes of hot alcohol, and set aside to crystallize. The product was recrystallized from glacial acetic acid. The yield was 60 g. (59%). After several recrystallizations from glacial acetic acid the constants were: m.p. 165.5–166° (corr.), $[\alpha]_D^{25}$ 2.5° (c = 2, U.S.P. chloroform). This material was of sufficient purity for the next step.

Phenyl 3-methyl-β-D-glucoside. Phenyl 3-methyltribenzoyl-β-D-glucoside was partially debenzoylated with potassium methoxide in a dioxane-methyl alcohol solution. Several volumes of water were added and the dioxane, methyl alcohol, and methyl benzoate distilled off under reduced pressure. When all methyl benzoate had distilled, sufficient potassium hydroxide was added to the aqueous solution to remove the remaining benzoyl group (14), and the solution allowed to stand overnight. The solution was then acidified with sulfuric acid, the precipitated benzoic acid filtered off and the last traces removed by extraction with ether. The solution was neutralized with a little potassium hydroxide and evaporated to dryness. The product was extracted from the salts with alcohol, the solvent removed by distillation, and the residue taken up in hot diethylcellosolve. On cooling, there were formed short needles of phenyl 3-methyl-β-D-glucoside, m.p. 150–150.2° (corr.), $[\alpha]_D^{25}$ −65.6° (c = 2, water). Previous authors (14) record m.p. 148.5–150° (corr.), $[\alpha]_D^{25}$ −59.0°.

DISCUSSION

The formation with inversion of a 1,2-anhydro ring as an intermediate in the preparation of levoglucosan by the action of hot alkali on phenyl β-D-glucoside or a trimethyl-β-D-glucosylammonium halide is an assumption which seems to explain most experimental facts fairly satisfactorily. It is difficult to see how the stability conferred on phenyl β-D-glucoside by methylation of the number two hydroxyl, and the complete retention of configuration in the formation of levoglucosan and methyl 6-trityl-β-D-glucoside could be explained otherwise by a modern mechanism. Any influence on the number one carbon atom due to the methylation would have to be transferred through two intermediate atoms or through the space between the methyl and the number one carbon atom. Over this distance any potential influence should be greatly diminished as the I effect is known generally to decrease rapidly with distance. Consideration of the ionic mechanism would thus necessarily involve an explanation of why such a minor change completely prevents the reaction with either the hydroxide ions or the number six hydroxyl, while blocking the six position only prevents reaction there, permitting a ready reaction with hydroxide and alkoxide ions, the latter with retention of configuration.

The assumption of the formation by inversion of a 1,2-anhydro ring necessarily involves a *trans* configuration for the reactive group on carbon one and the hydroxyl group on the adjacent carbon atom. Phenyl α-D-glucoside which does not possess a *trans* hydroxyl on carbon two would be expected to be alkali-stable and has been found to be so (1). The mechanism involving an intermediate 1,2-anhydro ring has been suggested as the principal one operating

in the formation of levoglucosan. It is only to the glucose derivatives that the experimental data previously cited applies. It was of interest, however, to see how deductions made from the proposed mechanism would apply to other monoses. It was kept in mind that changes in the configuration sometimes cause large changes in chemical properties. A good example of such a change (16) is the formation by altrose of an equilibrium mixture with its 1,6-anhydride in a dilute acid solution, compared to the total lack of detectable anhydride formation with glucose or galactose under similar conditions.

It is to be expected that the stability of the phenyl glycosides would be dependent on the configuration of the hydroxyl on carbon two and relatively independent of other substituents or configuration in the molecule. When the hydroxyl on carbon two and the phenoxyl group are *trans*, reaction to form the intermediate oxide ring should occur irrespective of whether the phenoxyl is *alpha* or *beta*.

The formation of 1,6-anhydrides from phenyl β-glycosides which was suggested by Montgomery, Richtmyer, and Hudson (1) as a means of determining configuration, is readily explained by this mechanism. In the *beta* isomer the number six carbon atom presumably has a *cis* configuration with respect to the phenoxyl group on carbon one. The primary hydroxyl therefore can rotate only into position to invert carbon atom one of an intermediate anhydro ring formed by inversion of the *beta* isomer.

In Table I several phenyl glycosides are listed. They are divided into two groups depending on whether the hydroxyl on carbon two is *cis* or *trans* to the phenoxyl radical. This division is made in order to emphasize the relation of reactivity to configuration. It should be noted that on treatment of these compounds with hot alkali no original glycoside having the *trans* configuration was recovered unchanged and that the time of reaction was relatively short. In the case of the *cis* glycosides some were recovered unchanged and others which were converted to the glycosans underwent reaction very slowly. It is to be noted particularly that phenyl β-D-xyloside, in which there is no number six hydroxyl, reacts readily but forms a tar. Phenyl α-D-mannoside, in which the primary hydroxyl would be *cis* to the 1,2-anhydro ring of the proposed intermediate and thus could not react with it by inversion, also forms a tar. In this case, as with the xyloside, reaction can occur only with the hydroxide ions of the solution to form the sugar. Phenyl α-D-xyloside and phenyl α-D-glucoside, which are *cis* compounds and have similar rings, are stable as would be expected. Phenyl α-D-galactoside unexpectedly gives a high yield of 1,6-galactosan. It is to be noted that two thousand six hundred and eighty-eight hours was required, which is a very long time as compared to the nine hours required for the anomeric isomer. Since inversion of configuration occurs in this reaction it is possible that the primary hydroxyl slowly attacks the number one carbon atom with the removal of the phenoxyl radical. There is no evidence available for the possibility of a very slow racemization of the *alpha* phenoxyl with rapid reaction of the *beta* as it is formed. The reaction of phenyl β-D-mannoside (17) seems to be completely anomalous. The 57% yield indicates

a partial retention of configuration, yet the hydroxyl on carbon two is not in position to invert the number one carbon atom on removal of the phenoxyl. It is thus assumed that the reaction probably proceeds by another mechanism than that suggested for glucose derivatives.

The decomposition of quaternary ammonium hydroxides to give olefins and its use in the Hoffman exhaustive methylation is well known. That instead of olefin formation an ethylene oxide ring results if a hydroxyl is present on the adjacent carbon, has already been pointed out. If no hydrogens or hydroxyls are present on the adjacent carbon an alcohol is the principal product. In other cases a mixture of alcohol and olefin results, the ratio depending on the substituents on the *alpha* and *beta* carbon atoms (18, 19). The principal difference between the phenoxyl and trimethylammonium groups so far as this type

TABLE I

STABILITY OF PHENYL GLYCOSIDES TO HOT ALKALI[a]

COMPOUND	PRODUCT	PER CENT	TIME, HRS.	CONC'N KOH, *N*
Trans				
β-Xyloside	Tar	—	3	1.3
β-Glucoside	Glucosan	88	9	1.3
β-Galactoside	Galactosan	91	9	1.3
α-Mannoside	Large rot. change	—	336	1.3
β-Lactoside	Subst. glucosan	81	8	2.6
β-Cellobioside	Subst. glucosan	—	24	2.6
β-α-Glucoheptoside	Heptosan	60 (as benzoate)	8	2.6
Cis				
α-Xyloside	Recovered		48	1.3
α-Glucoside	Recovered		336	1.3
α-Galactoside	Galactosan	85	2688	2.6
β-Mannoside	Mannosan	57	120	2.6

[a] Montgomery, Richtmyer, and Hudson (1, 2, 17).

of reaction is concerned lies in their relative ability to attract electrons. As evidenced by the lack of appreciable olefin or alcohol (sugar) formation in the case of phenyl α-D-glucoside, for example, the phenoxyl may be assumed to be a weaker electron attracting group than the trimethylammonium radical, since quaternary ammonium hydroxides under similar conditions, as noted previously, form either olefins or alcohols.

By the introduction on the phenyl nucleus of an electron attracting group of sufficient strength it should be possible to increase the total electron attraction of the phenoxyl radical to permit olefin formation as with the quaternary ammonium hydroxides.

In Table II are shown the relative stabilities of the glucosides of several substituted phenols. The important fact to be noted is the marked increase in reactivity of the *p*-acetyl and the *o*-nitro and *p*-nitro substituted phenoxyl groups

as compared with the unsubstitued phenoxyl group. Not only is the reaction very rapid with the substituted phenoxyls but with the nitro substituted, both the *cis* and the *trans* isomers react readily. The *cis* may react to form principally olefins or sugar followed by decomposition to give tars. The lower yield of levoglucosan from the *trans* nitrophenoxyl compound as compared with compounds in which the phenoxyl group is less negatively substituted suggests that other mechanisms may also be operative. Perhaps the ionic mechanism may be involved to some extent, since the trend is toward the ionic mechanism as the strength of the elctron attraction increases. The suggestion (20) that a nearly complete Walden inversion can occur by the ionic mechanism alone seems open to question. If the ionic mechanism is operative to any extent in the case of the *cis* nitro compounds, the formation of some glucosan would be a possibility.

Winstein and Henderson (21) have shown that the oxygen of a methoxyl can in certain cases invert an adjacent atom with the formation of a ring involving an oxonium ion. An attacking ion inverts the carbon atom, breaking

TABLE II

STABILITY OF GLUCOSIDES OF SUBSTITUTED PHENOLS TO HOT ALKALI[a]

COMPOUND	PRODUCT	PER CENT	TIME, HRS.	CONC'N KOH, *N*
Trans				
o-Cresyl β-D-glucoside	Glucosan	85	22	1.3
p-Xenyl β-D-glucoside	Glucosan	90	10	1.3
p-Acetylphenyl β-D-glucoside	Glucosan	85	3	1.3
o-Nitrophenyl β-D-glucoside	Glucosan	60	3 (very rapid)	1.3
p-Nitrophenyl β-D-glucoside	Glucosan	60	3	1.3
Cis				
o-Nitrophenyl α-D-glucoside	Tar	—	3	1.3
p-Nitrophenyl α-D-glucoside	Tar	—	3	1.3

[a] Montgomery, Richtmyer, and Hudson (1).

the ring and thus gives an over-all retention of configuration. The unsubstituted phenoxyl group in phenyl 2,3-dimethyl-β-D-glucoside apparently does not have sufficient electron attraction to permit such a reaction. However, with negatively substituted phenoxyl groups possessing stronger electron attraction this might be possible. In such a case a substitutent on the number two hydroxyl would not prevent the formation of levoglucosan.

The report of Micheel and Micheel (22) that trimethyl-(2-desoxy-2-amino-β-D-glucosyl)ammonium hydroxide on heating evolved trimethylamine suggests the possibility of the formation of an ethylenimine ring. No report of the formation of ethylenimine rings from such compounds has been found but it is certainly a possibility.

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SUMMARY

A double Walden inversion is proposed as the mechanism for the formation of levoglucosan by the action of hot alkali on phenyl β-D-glucoside and trimethyl-β-D-glucosylammonium halides. It is suggested that a 1,2-anhydro (ethylene oxide) ring is formed as the intermediate which then reacts by inversion with the proximate hydroxyl of carbon atom number six.

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