SYNTHESIS AND STRUCTURAL STUDIES OF
SOME CYCLIC ACETALS OF HEXITOLS

A Thesis submitted by
SUSAN ELIZABETH HARWOOD,
a candidate for the Degree of
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Royal Holloway College,
University of London,
Englefield Green,
Surrey.
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All the crystalline compounds have been characterized and systematic structural studies have been made upon them. The structures of the 2,4-isooxocetals have been established, and the structure of the crystalline di-2-butylidene-β-glucoitol has been indicated.
This thesis contains an account of the synthesis, and the structural studies, of some cyclic acetics of hexitols.

2,4-O-Furfurylidene-D-glucitol, two di-O-furfurylidene-D-glucitols, and three tri-O-furfurylidene-D-glucitols have been isolated, of which the 2,4-monoacetal and possibly one of the diacetals and one of the triacetals were previously known. The previously unknown butylidene acetals, 2,4-O-butylidene-D-glucitol, 3,4-O-butylidene-D-glucitol, and 1,3;2,4-di-O-butylidene-D-glucitol, have been isolated, together with syrupy di-O-butylidene- and tri-O-butylidene-D-glucitols of unknown composition. 2,4-O-Isobutylidene-D-glucitol and a syrupy tri-O-isobutylidene-D-glucitol have also been prepared by similar methods.

All the crystalline compounds have been characterised and systematic structural studies have been made upon them. The structures of the 2,4-monoacetals have been established, and the structure of the crystalline di-O-butylidene-D-glucitol has been indicated.
by partial hydrolysis, after it had been established that it was a 1,2,3,4-diacetal.

Kinetic studies have been made on the hydrolysis of various monoacetals of D-glucitol in hydrochloric acid of varying strength. It has been shown that the stabilities of the 2,4-, 3,4-, and 4,6-O-butylidene-D-glucitols do not differ significantly from one another. It has also been shown that these three monoacetals, and possibly further cyclic acetals, exist in equilibrium with each other in aqueous hydrochloric acid. The Arrhenius energies of activation and frequency factors have been determined for 2,4-O-butylidene-D-glucitol and 2,4-O-isobutylidene-D-glucitol, in N and 2N hydrochloric acid.

Various polymeric materials have been obtained from the reaction of acrolein with a number of different polyhydroxy compounds.
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A great deal of interest has been taken in the formation of cyclic acetals and ketals of polyhydric alcohols, since Warin's condensed ethylene glycol with acetaldehyde in 1861. Since both alkylidene and acylidene derivatives research in this field has followed several different routes, and several acetal and ketal derivatives have been used for the isolation of polyhydric alcohols, isolated from natural sources, and from mixtures of reaction products such as those resulting from the reduction of \( \psi \)-glucose, \( \psi \)-fructose, and malonate.

A considerable amount of research has been directed towards the determination of the exact structures of these cyclic acetals and ketals, with relation to the polyhydroxy compound. This work has led to a consideration of which ring structures should be the most stable, and it has become possible to predict the products likely to be formed by the condensation of a given carbonyl compound with a given polyhydric alcohol.

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A great deal of interest has been taken in the formation of cyclic acetals and ketals of polyhydric alcohols, since Wurtz\(^1\) condensed ethylene glycol with acetaldehyde in 1861. With both alkylidene and arylidene derivatives research in this field has followed several different routes, e.g. acetal and ketal derivatives have been used for the characterisation of polyhydric alcohols, isolated from natural sources\(^2,3\), and from mixtures of reaction products such as those resulting from the reduction of \(\text{D-glucose}\)^4, \(\text{D-sorbose}\)^5, and maltose\(^6\).

A considerable amount of research has been directed towards the determination of the exact structures of these cyclic acetals and ketals, with relation to the polyhydroxy compound. This work has led to a consideration of which ring structures should be the most stable, and it has become possible to predict the products likely to be formed by the condensation of a given carbonyl compound with a given polyhydric alcohol.

The formation of cyclic acetals and ketals as intermediates in the preparation of partially substituted polyhydric alcohols has been found useful. Alkylidene and
arylidene groupings have been used in this type of work, since they are specific for given pairs of hydroxy groups. They may be formed simultaneously or successively, and by varying the carbonyl compound used the specificity may be directed to the blocking of different pairs of hydroxyl groups. Also they may be formed or removed under fairly mild conditions, without causing inversion of configuration at asymmetric centres, and once in position they do not appear to migrate readily.

Very many different methods of synthesising cyclic acetals have been reported in the literature. The reaction between an aldehyde and a glycol is a two step reversible condensation reaction, in which the hemiacetal intermediate cyclises to form an acetal, with the elimination of a molecule of water.

\[
\begin{align*}
\text{RCHO} + \text{G-CH}_2\text{O} & \quad \rightleftharpoons \quad \text{RCHO} + \text{G-CH}_2\text{O} \\
\text{G-CHR} & \quad \rightleftharpoons \quad \text{G-OH} + \text{H}_2\text{O}
\end{align*}
\]

It was shown by Meunier, at the end of the nineteenth century, that acetal formation is catalysed by acidic substances. The catalysts most frequently employed are concentrated sulphuric acid, hydrochloric acid, both aqueous concentrated and gaseous, and concentrated hydrobromic acid; also the Lewis acids zinc chloride and
cupric sulphate have been used; others mentioned are phosphorus pentoxide, iodine, and anhydrous sodium sulphate. Weaker acids have also been used, such as oxalic acid, toluene-p-sulphonic acid and dilute sulphuric acid.

In many cases the products formed in the condensation of a given pair of reactants are independent of the catalyst used, although this is not always so. Hann, Haskins, and Hudson \(^\text{10}\) found that two isomeric dibenzylidene derivatives could be formed from 1,6-di-\(\pmb{\text{O}}\)-benzoyldulcitol by varying the reaction conditions; using hydrogen chloride as catalyst at room temperature leads to one derivative, but zinc chloride, also at room temperature, yields another. The latter 2,3,4,5-di-\(\pmb{\text{O}}\)-benzylidene-1,6-di-\(\pmb{\text{O}}\)-benzoyldulcitol may be converted to the former by treatment with benzaldehyde and zinc chloride at 60°C.

The acidity of the catalyst used may affect the degree to which acetalisation takes place, although this is not always true. A strongly acidic catalyst is likely to bring about the formation of a fully substituted product, whereas another catalyst may lead to the formation of a partially substituted polyhydric alcohol. For example, von Vargha \(^\text{11}\) found that in the reaction between acetone and 1,2-\(\pmb{\text{O}}\)-isopropylidene-\(\pmb{\text{D}}\)-mannitol 1,2:5,6-di-\(\pmb{\text{O}}\)-isopropylidene-\(\pmb{\text{D}}\)-mannitol was the product when the
catalyst was cupric sulphate, but 1,2:3,4:5,6-tri-ß-
isopropylidene-D-mannitol was formed in the presence of
concentrated sulphuric acid.

The reaction between a glycol and a carbonyl
compound, in the absence of an acidic catalyst, may
proceed only as far as the hemiacetal. However if
azeotropic distillation is employed to remove water from
the system then the equilibrium position will be altered,
and the cyclic acetal may be formed. Benzene, toluene,
and xylene have been found to be suitable water-
immiscible solvents.

Since D-glucitol has six hydroxyl groups it
is clear that there is the possibility of many different
cyclic acetals being formed, depending upon which pairs
of hydroxyl groups condense with the aldehyde. Thus it
would seem reasonable to obtain a variety of products
from a given reaction mixture; in fact it is generally
found that one product predominates.

Hann and Hudson suggested that in such a
condensation reaction there is a succession of reactions,
some of which may be in competition, and a state of
reversible equilibrium involving a number of acetals is
finally attained. However if one acetal were to
crystallise out during the reaction, as is often the case,
then the equilibrium would be altered, this may cause
this product to predominate. Exchange reactions have illustrated that the condensation is reversible, since ethylidene acetal...gl acid in the presence of concentrated sulphuric acid. The instability of furfuraldehyde in the presence of acids is well known. Williams and Dunlop showed that the decomposition of furfuraldehyde under acidic conditions is dependant upon its own concentration in the solution, the hydrogen ion concentration, and the temperature; an increase in any of these factors increases the rate of decomposition. The products of the decomposition of furfuraldehyde are formic acid and a resinous tar of unknown structure. This instability of furfuraldehyde in acidic media causes complications in the formation of furfurylidene cyclic acetals, as the reaction is acid catalysed.

Hoover prepared the furfurylidene derivatives of ethylene glycol and glycerol in the absence of acidic catalysts. In these cases he found that the removal of water from the reaction mixture, by azeotropic distillation, was sufficient to shift the equilibrium of the condensation reaction to the side of cyclic acetal formation.

Bredereck and Papademetriu prepared mono-
furfurylidene- and tri-O-furfurylidene- derivatives of \( \text{D-glucitol} \), from \( \text{D-glucitol} \) and a three fold excess of furfuraldehyde, using \( \text{2H nitric acid} \) as the condensing agent. The tri-O-furfurylidene-\( \text{D-glucitol} \) (m.p. 186-7°) was the main product in a 3.5% yield. Concentration of the alcoholic mother liquors from the crystallisation of the tri-O-furfurylidene-\( \text{D-glucitol} \) yielded the mono-O-furfurylidene-\( \text{D-glucitol} \) (m.p. 192-3°). They prepared a di-O-furfurylidene-\( \text{D-glucitol} \) (m.p. 202-3°) by partial hydrolysis of the tri-O-furfurylidene-\( \text{D-glucitol} \), with dilute acetic acid in absolute ethanol. They did not carry out any systematic structural studies on these compounds. However they did form di-O-triphenylmethyl-mono-O-furfurylidene-\( \text{D-glucitol} \) and mono-O-triphenylmethyl-di-O-furfurylidene-\( \text{D-glucitol} \), thus concluding that the parent compounds of these derivatives contained two, and one free primary hydroxy groups, respectively. Then by analogy with the O-benzylidene-\( \text{D-glucitols} \) they concluded that the structures would be 2,4-O-furfurylidene-\( \text{D-glucitol} \), 2,4:5,6-di-O-furfurylidene-\( \text{D-glucitol} \) and 1,3:2,4:5,6-tri-O-furfurylidene-\( \text{D-glucitol} \).

R.C. Hockett\(^{19,20}\) formed a mono-O-furfurylidene-\( \text{D-glucitol} \) (m.p. 192-3°) as an intermediate in the synthesis of \( \text{L-xylose} \); it was prepared from \( \text{D-glucitol} \)
and furfuraldehyde in a 1:1 mole ratio, in the presence of dilute sulphuric acid. Since \( \alpha \)-xylose was obtained in a good yield after treatment of this intermediate with lead tetraacetate, followed by acid hydrolysis, he assumed that it was in fact 2,4-\( \alpha \)-furfurylidene-\( \alpha \)-glucitol.

Holst prepared tri-\( \alpha \)-butylidene-\( \alpha \)-glucitols to be used as plasticisers in resin formation. He condensed \( \alpha \)-butyraldehyde with \( \alpha \)-glucitol, using dioxan as solvent for the reactants and concentrated sulphuric acid as the condensing agent. He reported that two tri-\( \alpha \)-butylidene-\( \alpha \)-glucitols were formed, both oils with boiling points 162-7° and 172-7° at 4 mm. Hg.

\( \alpha \)-glucitol may be represented by the Fischer projection formula (A), or by the more representative picture (B), showing the staggered conformation of the carbon chain and the relative positions of the hydroxyl groups and the hydrogen atoms.

\[
\begin{align*}
\text{CH}_2\text{OH} \quad \text{CH}_2\text{OH} \\
\text{H-C-OH} \quad \text{H-C-OH} \\
\text{HO-C-H} \quad \text{HO-C-H} \\
\text{H-C-OH} \quad \text{H-C-OH} \\
\text{H-C-OH} \quad \text{H-C-OH} \\
\text{CH}_2\text{OH} \quad \text{CH}_2\text{OH}
\end{align*}
\]
Where — represents bonds projecting above the plane of the paper
— represents bonds in the plane of the paper
— — — represents bonds projecting below the plane of the paper.

Thus it may be seen that there is the possibility of the existence of a number of structural isomers for the cyclic acetals of D-glucitol, depending upon which pairs of oxygen atoms form the acetal rings, and also that derivatives may contain one, two, or three acetal rings.

Cis and trans stereoisomers may be formed for each possible ring system, as was recognised by Fischer in 1894. Ness, Hann, and Hudson obtained two isomers of 1,3:5,7-di-O-benzylidene-D-perseitol, one with m.p. 153–5°, and the other with m.p. 280 ± 2°; the former acetal was converted to the latter by recrystallisation from a pyridine/alcohol mixture. They concluded that these were stereoisomers since they yielded identical tri-O-benzoyl and tri-O-methyl derivatives. More recently Brimacombe, Baggett, Foster, Stacey, and Whiffen have made a structural
study of the two 1,5-0-benzylidenglyceritols, m.p. 83-4° and m.p. 63-4°. From a consideration of the hydrogen bonding data of these two compounds (0.005M solutions in carbon tetrachloride) in the infrared region they have been able to prove conclusively that they are, respectively, the cis and trans isomers of the same structural form.

They noted that there was a considerable amount of intramolecular hydrogen bonding in the trans isomer, although it can only occur in conformation IIa which has the phenyl group in the sterically unfavourable axial position, whereas conformation IIb has both phenyl and hydroxyl groups in equatorial positions. They suggest that intramolecular hydrogen bonding may exert a significant stabilising effect.

By analogy it would appear likely that the cyclic acetals of D-glucitol should exist in similar isomeric forms. Preferentially the ring systems would take up the chair conformation, and also they would
be most stable if bulky substituents were in an equatorial position rather than in an axial position; however this equilibrium may be affected by the formation of hydrogen bonds, as shown in the structures of trans-1,3:0-
benzylideneglyceritol. With a fused ring system, as in 1,3:2,4:5,6-tri-0-methylene-D-glucitol, the stereochemistry may be considered as analogous to that of the deca
tines 26.

\[
\begin{align*}
\text{CH}_2-O & \text{-CH}_2 \\
\text{CH}_2-O & \text{-CH}_2 \\
\end{align*}
\]

The various ring systems that may exist in compounds containing cyclic acetals are the five-membered, or 1,3-dioxolan ring system; the six-membered, or 1,3-dioxan ring system; and the seven-membered, or 1,3-dioxepan ring system. Compounds containing larger ring systems have not been isolated. Derivatives of D-glucitol containing both five- and six-membered rings are known. So far no D-glucitol derivative containing a seven-membered ring has been reported, although such a
ring system is known, e.g. in 2,5-G-methylene-D-mannitol.

It has been found that when D-glucitol reacts with an aldehyde, derivatives containing certain ring systems are formed; other permutations of the available hydroxyl groups do not lead to the formation of cyclic acetals. Hann and Hudson\textsuperscript{13,23} considered all the data available on the cyclic acetals of D-glucitol, and other polyhydric alcohols, and drew up a table showing which rings are formed. This indicates which rings one would expect to be formed when condensing an aldehyde with D-glucitol, and other alcohols.

Barker and Bourne\textsuperscript{27} developed a nomenclature for cyclic acetals, indicating the relative positions of the cyclised hydroxyl groups. If the acetal ring is formed with hydroxyl groups on adjacent carbon atoms, then the ring is an \( \alpha \)-ring (a five-membered ring); if the ring is formed by condensation with hydroxyl groups on carbon atoms separated by another carbon atom then a \( \beta \)-ring has been formed (a six-membered ring); and so on. Further the relative spatial positions of the hydroxyl groups are shown, using the Fischer projection formula of the compound as reference: if the cyclised hydroxyl groups are on the same side of the molecule in the Fischer projection formula then the ring will be a cis-ring (C); if the ring forming hydroxyl groups are
on opposite sides then the ring is designated a trans-ring (T). Since the terminal carbon atom of a carbon chain has free rotation any cyclic acetal formed by condensation with a hydroxyl group on this carbon atom cannot be of cis or trans configuration. Thus acetal rings may be $\alpha, \beta, \gamma$... if the cyclisation involves a primary hydroxyl group, or $\alpha$, $\beta$, $\gamma$, $\delta$, $\epsilon$, etc., if both the hydroxyl groups involved are secondary.

Barker and Bourne\textsuperscript{27} also extended the Hann-Hudson rules to cover virtually all known cases of the formation of cyclic acetals of the polyhydric alcohols. The extended rules give the order of preference for the formation of cyclic acetal rings as firstly a $\beta$-ring, then a $\alpha$-ring, and then an $\alpha$, $\alpha$, $\beta$, $\beta$, or $\gamma$-ring. In certain cases these rules are not obeyed, such as when the polyhydric alcohol has already been partially substituted.

Barker, Bourne, and Whiffen\textsuperscript{28} sought a theoretical approach towards which rings were likely to be preferentially formed, by considering the preferred conformation of the polyhydric alcohol. The most stable conformation of a carbon chain is the planar zig-zag form, with the substituents on each carbon atom in a fully staggered position with relation to substituents on adjacent carbon atoms\textsuperscript{29}. This conformation of a hexitol,
such as D-glucitol, is such that the distances between all the groups are just greater than the sum of their van der Waals radii, and thus the non-bonded interactions are at a minimum. X-ray crystallography has confirmed that a carbon chain does in fact take up such a conformation.

The distances between the oxygen atoms in the 1,3-dioxolan and 1,3-dioxan rings can be calculated. To obtain the necessary distance between two oxygen atoms in a polyhydric alcohol, to enable such a ring to be formed, carbon-carbon bonds may be rotated or bond angles may be distorted slightly. However, any such alterations in the molecule would require energy, cause a certain degree of strain, and may also bring repulsive forces into play. Thus as the necessary degree of distortion increases the likelihood of the ring being formed decreases, and similarly the stability of a ring formed under such circumstances will be reduced.

Barker, Bourne, and Whiffen correlated the required distances between ring forming oxygen atoms with the actual distances between pairs of oxygen atoms in polyhydric alcohols. They found that a \( \beta \)-ring could be formed with very little strain; thus it would be formed preferentially. Then considering the degrees of strain that would be set up in forming subsequent rings they found that the \( \beta \)-ring would be formed next. In fact
their theoretical approach to the subject yielded results that were in agreement with those found experimentally for the order of formation of cyclic acetal rings.

Mills also considered the stereochemistry of cyclic acetal formation, but in terms of the stability of the rings when formed: an unstrained 1,3-dioxolan ring should be nearly planar, and an unstrained 1,3-dioxan should take up the chair conformation, with the most stable rings those having their substituents in an equatorial position. The relative stability of the rings when formed depends upon the degree of deviation from these requirements. This approach led to results which agreed with those found by Barker, Bourne, and Whiffen.

Applying these results to D-glucitol, the 2,4-ring should be the first ring to be formed, followed by the 1,3-ring, and finally the 5,6-ring should be formed. The stability of the rings should be in the same order, the 2,4-ring being the most stable.

The structures of cyclic acetals of polyhydric alcohols may be determined by similar techniques to those used in carbohydrate chemistry. For D-glucitol, a hexitol, mono-, di-, and tri-acetal derivatives may be formed, containing four, two, and no free hydroxyl groups, respectively. The number of free hydroxyl groups in a
molecule may be ascertained by quantitative determinations of the uptake of acetyl groups, in the acetylation of the compound. The presence of free primary hydroxyl groups will be shown by their characteristic reactions, such as the formation of the triphenylmethyl derivative. Periodate oxidation, in conjunction with subsequent determinations of liberated formaldehyde and formic acid, and the isolation of the fragmented cyclic acetal, will further indicate the structure of the compound, since the carbon chain will be split between each pair of vicinal hydroxyl groups. Such determinations assist in the elucidation of structures of partially substituted polyhydric alcohols. No direct structural determinations may be carried out on triacetal derivatives of a hexitol, such as D-glucitol, because the methods available, as described above, in fact only determine the positions of free hydroxyl groups in the molecule.

The positions of the rings in triacetal derivatives have been deduced by examining their preparation mixtures, isolating the partially substituted derivatives present, and determining their structures. These compounds are then treated as direct precursors of the triacetal main product. A second method of deducing such structures has been by partially hydrolysing the triacetal, followed by structural determinations on
mono- and diacetal products$^{31,32}$. Similar deductions are made in assessing the structure of a diacetal derivative, since structural determinations will have shown only which two hydroxyl groups are free.

These structural determinations are made on the assumption that ring migration does not occur in either the formation or the hydrolysis of an acetal ring, and that the rings are formed in a strict order of progression, and are hydrolysed in a strict reversal of that order. Whether this assumption is valid may be questioned, although generally it has been accepted. Reeves$^{33}$ found evidence of a ring migration. The action of glacial acetic acid on a mono-O-benzylidene-1,4-anhydro-$D$-mannitol converted it to 2,3-O-benzylidene-1,4-anhydro-$D$-mannitol, and oxidation of these two compounds with lead tetraacetate in glacial acetic acid showed that the benzylidene ring had migrated. Thus it may be concluded that only the structures of monoacetal derivatives of $D$-glucitol, and other hexitols, are proved rigorously.

Infrared spectroscopy has indicated that the 1,3-dioxolan ring is very slightly puckered$^{34}$, and that the 1,3-dioxan ring is in either the chair or the boat conformation$^{35}$. By analogy with 1,4-dioxan, which infrared spectroscopy has shown to exist in the chair conformation, and by considering the ring system in the
light of general conformational analysis it may be assumed that the 1,3-dioxan ring does exist in the chair conformation\textsuperscript{35}. It was thought that it might be possible to assign peaks in the infrared spectrum of a cyclic acetal compound to either the 1,3-dioxolane ring system or the 1,3-dioxan ring system, thus indicating whether it contained five- or six-membered rings, or both. Barker, Bourne, Pinkard, and Whiffen\textsuperscript{36} have made a study of the spectra of 1,3-dioxolane and its derivatives; however they did not find it possible to assign any peaks with certainty to the 1,3-dioxolane ring system. If it did become possible for infrared spectroscopy to indicate the presence of five- or six-membered rings in a molecule it would be an extremely useful aid to work on cyclic acetals, since it would be a direct method of structural determination.

The acid hydrolysis of cyclic acetals has been the subject of much work, and these studies have resulted in a knowledge of the mechanism of the reaction. Also the kinetics of the breakdown of various acetal rings have afforded a considerable understanding of the effects of size and substituents on the stability of the ring.

It has been found that if an optically active alcohol is used to form a cyclic acetal no racemisation of the alcohol occurs in its subsequent hydrolysis\textsuperscript{37}. 
This means that the acetal ring must break between the carbonyl carbon and the oxygen atoms, thus leaving the asymmetric carbon atoms of the alcohol intact.

Ceder has shown that the breakdown of the acetal ring is almost certainly unimolecular through the formation of a carbonium ion, after the protonation of the ring to give the oxonium ion. The carbonium ion then reacts with water to release the alcohol and the carbonyl compound.

Leutner in his work on the rates of hydrolysis of cyclic acetals and ketals has shown that the substituents on the alcohol carbon atoms, and the nature
of the carbonyl compound affect their stability. He found that the replacement of an hydrogen atom by a methyl group in the carbonyl compound increases the rate of hydrolysis, whereas a similar replacement in the alcohol lowers the rate; this presumably means that in the former case the stability of the compound is decreased, while in the latter it is increased. Laurent et al\textsuperscript{40} found by reaction kinetics that the stabilities of 1,3-dioxolan and 1,3-dioxan are very similar in aqueous acid media.

Hockett and co-workers\textsuperscript{41} have studied the rate of hydrolysis of 4,6-\(\text{\(\beta\)}\)-ethyldene-\(\text{\(D\)}\)-glucitol in aqueous sulphuric acid, by following the change in optical rotation with time. Since the final optical rotation was not significantly different from that of \(\text{\(D\)}\)-glucitol itself, they considered that the hydrolysis to \(\text{\(D\)}\)-glucitol and acetaldehyde took place without the formation of appreciable concentrations of rotationally significant intermediates. From the graph given they found, rather surprisingly, that this compound is more stable in 1.0N acid than in 0.5N.

Although much work has been done on the hydrolysis of acetals, and of 1,3-dioxolan and 1,3-dioxan, very little has been published on the kinetics of the hydrolysis of cyclic acetals of hexitols.
Acrolein has been condensed with alcohols to form acetals, and in many cases it was found that the condensation was accompanied by addition across the olefinic linkage. Fischer and Smith found that provided the concentration of the acid catalyst was kept low cyclic acetals were formed in 60% yields in the reaction between acrolein and 1,2- and 1,3-glycols, with very little addition across the double bond. However they found that the more complex polyol, D-glucitol gave a much smaller yield (33%) of the triacetal, and much polymer was formed. They suggested that the structure of this compound is 1,2:3,4:5,6-tri-O-allylidene-D-glucitol.

Since acrolein contains two highly reactive groups, the carbonyl group and the olefinic group, it forms polymers very readily. In dilute hydrochloric acid it dimerises to form 3-formyl-5,6-dihydro-\(\alpha\)-pyran. There are many references in the literature to its use in resin formation, and it yields a large variety of products.
This study of the synthesis and reactions of certain cyclic acetals of hexitol was undertaken, in part, as a result of financial support by the Sugar Research Foundation of America. The project was concerned with the condensation of \( \alpha, \beta \)-unsaturated carbonyl compounds with hexitol, with a view to applying the results obtained with similar acetals of sucrose. It was realized that this extension could involve a difficult problem, viz. that sucrose is hydrolyzed under even the mildest of acid conditions.

The hexitol used was \( \beta \)-glucitol, and the carbonyl compounds chosen to comply with these requirements were acetaldehyde and furfuraldehyde. Butyraldehyde was included since it was felt that a study of more stable alkylidene cyclic acetals would help in an understanding of cyclic acetals in general. The question of ring stability and the effect of the \( R \) substituent on the cyclic acetal group, \( \text{RCH} \equiv \text{O} \), has been considered in relation to the compounds synthesized.

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Thus the subjects which have been studied for
this thesis fall into three sections: synthetic and structural studies of the furfurylidene- and butylidene-D-glucitols, a study of the relative stabilities of monoacetal derivatives of D-glucitol, and the effect of acrolein on different polyhydric alcohols under different conditions. This latter section will be discussed separately since the products were polymers.
Three furfurylidene-\(\text{D}\)-glucitols were known when this work was started (see p. 11). However the yields of these compounds, reported by Bredereck and Papademetriu\(^{16}\), were relatively low. In contrast to this Hockett\(^{19},^{20}\) had reported preparing the same monoacetal in exceptionally good yields, in the presence of aqueous sulphuric acid.

Neither of these papers gave accounts of any systematic structural studies having been carried out on these compounds, although structures were suggested in each case. In the former paper the structures were suggested by analogy with structures previously assigned to benzylidene-\(\text{D}\)-glucitols. In the light of more recent papers\(^{13},^{27}\) it would seem that the 2,4:5,6- structure put forward for the diacetal (i.e. containing \(\beta\) and \(\alpha\)-rings) was unlikely. Hockett assumed that he had formed the 2,4-monoacetal, since he obtained \(\text{L}\)-xylose from the compound, although the glycol oxidation was carried out in glacial acetic acid, conditions under which Reeves\(^{33}\) had found ring migration to occur.

Thus an attempt has been made to find improved methods of synthesis for the di- and tri-\(\text{D}\)-furufurylidene-\(\text{D}\)-glucitols, and structural studies have been made on
the furfurylidene compounds obtained.

Throughout the work on the synthesis of the furfurylidene-β-d-glucitole compounds, some decomposition of furfuraldehyde. As soon as acid was added to freshly distilled furfuraldehyde (which has a pale yellow colour), even in catalytic quantities, darkening of the aldehyde could be observed; in the reaction mixture became heated the intensity of the colour could increase more rapidly. This colouration was noted earlier even in the formation of the acetone, and the overall acidity of the reaction mixture one month later, and under more vigorous conditions the reaction mixture could become a deep brown-black colour. Also, it is noted in the more vigorous reactions a thick black tar came from at the bottom of the flask.

Fullep and Williams have reported that in aqueous acidic furfuraldehyde undergoes decomposition to form formic acid (not in a mole to mole ratio) and a material tar. This tar may be separated into two fractions: the aqueous soluble fraction is medium brown in colour and has high tinctorial power, and the aqueous insoluble fraction is almost black in colour and insoluble in all common organic solvents; this latter fraction is thought to be an advanced transformation of the former. They
Throughout the work on the synthesis of the furfurylidene-D-glucitols complications were encountered, due to the decomposition of furfuraldehyde. As soon as acid was added to freshly distilled furfuraldehyde (which has a pale yellow colour), even in catalytic quantities, darkening of the aldehyde could be observed; if the reaction mixture were heated the intensity of the colour would increase more rapidly. This colouration was quite marked even in the formation of the monoacetal, when the overall acidity of the reaction mixture was about 0.6N, and under more vigorous conditions the reaction mixture would become a deep mauve-black colour. Also, frequently in the more vigorous reactions a thick black tar would form at the bottom of the flask.

Dunlop and Williams\textsuperscript{15} have reported that in acidic media furfuraldehyde undergoes decomposition to form formic acid (not in a mole to mole ratio), and a resinous tar. This tar may be separated into two fractions: the acetone soluble fraction is medium brown in colour and has high tinctorial powers, and the acetone insoluble fraction is almost black in colour and insoluble in all common organic solvents; this latter fraction is thought to be an advanced transformation of the former. They
found the rate of decomposition of furfuraldehyde to be given by

$$\frac{d(\text{furfuraldehyde})}{dt} = k[\text{furfuraldehyde}][H^+]/[H_2O]$$

and also they found that the rate increases quite rapidly with temperature.

There are many references in the literature to the polymerisation of furfuraldehyde, and to its stabilisation. Its decomposition is caused by atmospheric oxidation and hydroquinone appears to be the most favoured antioxidant although, even in quite high concentrations, hydroquinone does not stop the decomposition. Therefore in most cases a large excess of furfuraldehyde was used, to compensate in some measure for that lost in decomposition. There seems to be little doubt that the degree of decomposition was fairly high in the cases where insoluble tars were formed in the reaction mixture.

All the furfurylidene products which were crystalline were white when pure. However difficulties were encountered in extracting these compounds from the resinous tars, and after extraction in obtaining them without any trace of mauve or brown colouration. It was noted that the melting point was not affected when the compound was only slightly tinted. This was presumably due to the furfuraldehyde decomposition product having high
tinctorial powers, and thus a minimal trace of impurity being sufficient to cause marked decolouration of the compound. Activated animal charcoal was found to be satisfactory in removing traces of this impurity.

2,4-O-Furfurylidene-\(\ddot{\text{D}}\)-glucitol was prepared by the same method as Hockett\(^{19,20}\) (Expt. 1). The crude monoacetal was obtained in very good yields (ca. 90\%); purification of the product resulted in a substantial loss of material, the final yields being 40-45\%. In the first Patent (1952)\(^{19}\) Hockett does not mention a yield for the mono-\(\ddot{\text{D}}\)-furfurylidene-\(\ddot{\text{D}}\)-glucitol, but gives 80-90\% yields for the \(\text{L}\)-xylose, based on the \(\ddot{\text{D}}\)-glucitol taken; in the second Patent (1958)\(^{20}\), although Ruskin and Hockett quote a 70\% yield of 2,4-O-furfurylidene-\(\ddot{\text{D}}\)-glucitol, it would appear from the figures given that the yields should be 20\%. Thus it seems possible that the purification techniques described in Experiment 1b are superior to those of the 1958 Patent.

It was found that if the reaction mixture is stirred vigorously for a short time after the addition of the furfuraldehyde a homogenous solution is obtained (Expt. 1b); continued stirring beyond this point did not appear to alter the course of the reaction. Fairly rapidly thereafter the crystals of the product started to crystallise out. The addition of the methanol, when
it was considered that the reaction had gone to completion, assisted in two ways: firstly it enabled the mixture, which was by then a solid mass, to be worked until the product existed as separate crystals in a solution, thus enabling the neutralisation of the mixture to be effective; also the methanol had the effect of washing the crystals free of much of the mauve furfuraldehyde decomposition products. The crystals of the 2,4-o-furfurylidene-D-glucitol could then be filtered off and they were pale mauve in colour.

Considerable trouble was taken in attempting to raise the melting point of this product to 192-3°, as reported by both Bredereck\textsuperscript{16} and Hockett\textsuperscript{19,20}. Recrystallisation from 85\% ethanol readily raised the melting point to 186-7°, and from there after several recrystallisations to 190-1°. It was thought that the difficulty in raising the melting point above 186-7° might be due to traces of D-glucitol remaining, even after several recrystallisations. Ethanol was also used as a recrystallisation solvent, and it did raise the melting point much more readily to 190-1°. However rather large volumes of this solvent were required and this made the technique impracticable. Water is a satisfactory recrystallisation solvent for this material.

A further attempt to raise the melting point
to that given in the literature is described in Experiment 1a. The product (m.p. 185-7°) was extracted with ether in a Soxhlet apparatus since this would eliminate any possibility of traces of D-glucitol being in the product. The ether extract yielded the product in an amorphous form, which on recrystallisation from ethanol did give melting point of 193-5° when determined on a Kofler block with a microscope. The melting point was determined by this method so as to eliminate errors due to shrinkage of the compound.

The melting point of the 2,4-D-furfurylidene-D-glucitol could not be raised above 190-1° by normal methods of recrystallisation, and chromatographic development of the material (in B.E.W.) gave only one spot. When pure it recrystallised as white needles. It was noted that when this compound had been kept for about two months its melting point had dropped to 165-7°, and that the melting point then remained constant over further periods of up to a year. If the compound was then recrystallised its melting point was readily raised to 190-1°.

For the preparation of the di- and tri-D-furfurylidene-D-glucitols it was decided that new methods of synthesis should be considered, since the percentage yields quoted for these compounds by Bredereck and
Papademetriu were low (3.5% for the tri-\(\text{\text{-furfurylidene-D-glucitol, which on partial hydrolysis yielded the di-}\text{-furfurylidene-D-glucitol. There is no other reference in the literature to these compounds.}

Several variations on Hockett's method of preparation for the monoacetalt were tried, in the hope that it might be found possible to force this reaction further. The apparent advantages of this technique were that the furfuraldehyde does not decompose too rapidly under these conditions, and also that the \(D\)-glucitol is in solution in the sulphuric acid media. Chromatographic development of the crude reaction mixture in Experiment 1 showed no trace of the presence of di- and tri-substituted products. It was felt that the insolubility of the 2,4-\(\text{-furfurylidene-D-glucitol in the reaction mixture might account, to a considerable extent, for the fact that it does not undergo any further reaction, since it is well known that two phase reactions do not proceed so readily as those in a homogenous reaction mixture.

The variations on Hockett's method are described in Experiment 2a; they may be briefly summarised as increasing the temperature, increasing the acid strength, using trifluoroacetic acid instead of sulphuric acid, and using solvents for the reaction mixture - tetrahydrofuran and dimethylsulphoxide. In each case the
reaction mixture was examined chromatographically. This showed that in every variation the predominant product was still the monoacetal, although in some cases it showed that traces of di- and triacetals had also been formed. These reaction mixtures were not worked up as they did not appear to be profitable.

In the next set of experiments furfuraldehyde was condensed with D-glucitol in the presence of the weak Friedel-Crafts catalyst zinc chloride, with the aldehyde also acting as solvent for the reaction.

In the next set of experiments furfuraldehyde was condensed with D-glucitol in the presence of the weak Friedel-Crafts catalyst zinc chloride, with the aldehyde also acting as solvent for the reaction. This method proved satisfactory in producing both di- and tri-2-furfurylidene-D-glucitols, but only in small yields.

Zinc chloride has frequently been used as a condensing agent in acetal formation, since Fischer and Taube first reported its usefulness. A suggested course for the reaction is as follows:

\[
\begin{align*}
\text{H} - \text{C} - \text{O} - \text{H} + 2 \text{ZnCl}_2 & \rightarrow \text{H} - \text{C} - \text{O} - \text{ZnCl}_2 \\
\text{H} - \text{C} - \text{O} - \text{H} & \rightarrow \text{H} - \text{C} - \text{O} - \text{ZnCl}_2
\end{align*}
\]
Thus it would appear that the stability of the final complex enables the reaction to go to completion.

During this reaction considerable polymerisation of the furfuraldehyde took place, and the reaction was only once completed with entire success. Presumably this polymerisation is aided by the formation of the complex
C_{4}H_{3}O.CHO.ZnCl_{2}, in which the oxygen lone pair of electrons in the furan ring is localised by the zinc chloride, and thus the stability of the ring is reduced. This undesirable effect of the zinc chloride was minimised by keeping the temperature of the reaction below 50°, although some heat was required to enable the desired reaction to take place. If much polymerisation occurred the working up of the reaction mixture proved fruitless, and it was concluded that the products were occluded within the resin. This idea seemed feasible since the furfuraldehyde was a solvent for the reaction, as well as a reactant.

Two products were separated from this reaction mixture, and on purification these proved to be a di-O-furfurylidene-D-glucitol (II), m.p. 182-3°, and a tri-O-furfurylidene-D-glucitol (IIIa), m.p. 173-4°. These melting points do not agree with those quoted by Bredereck and Papademetriu\textsuperscript{16} (202-3° and 186-7°, respectively), and it may be questioned whether these compounds contain the same or different ring systems.

These two compounds with their characteristic melting points have been isolated only once, from this zinc chloride preparation. All subsequent efforts to obtain them, from either the same type of reaction mixture or from different reaction mixtures, have failed.
It must therefore be concluded that critical reaction conditions are required to form these compounds, as is the case for the formation of the two isomeric $2,3,4,5$-di-$\text{O}$-benzylidene-$1,6$-di-$\text{O}$-benzoyldulcitol $^{10}$ (see p. 8).

Since it was apparent that the techniques used so far left much to be desired it was decided that a reconsideration of the problem was necessary. The points considered were: a) the catalyst, b) the overall time of reaction, and c) improved methods of extraction.

In choosing a catalyst it was necessary to consider its effects on furfuraldehyde - obviously the situation would not be improved by using a condensing agent which at the same time decomposed one of the reactants. Thus various possible catalysts were examined for their effects on furfuraldehyde (Expt. 2c), and those which brought about rapid charring of the aldehyde were rejected immediately. After these tests it was decided that toluene-$p$-sulphonic acid and phosphoryl chloride were the most likely condensing agents for this reaction.

Toluene-$p$-sulphonic acid has frequently been used as a condensing agent. Phosphoryl chloride is a new catalyst for this type of work; so far it has been successful in condensing crotonaldehyde $^{46}$ and furfuraldehyde with $D$-glucitol. Since the reaction
conditions are not anhydrous (water is liberated in the reaction) it is clear that the phosphoryl chloride catalyst must undergo certain changes:

\[
\text{POCl}_3 + 3\text{H}_2\text{O} \rightarrow \text{H}_3\text{PO}_4 + 3\text{HCl}
\]

Therefore the reactive species of the phosphoryl chloride is unknown, however it may be assumed to be of an acidic nature since it is known that, in general terms, the reaction is acid catalysed. Phosphoryl chloride does cause some breakdown of the furfuraldehyde, but these effects are more than balanced by its efficiency in promoting condensation.

The reaction period using zinc chloride was six hours, and it seemed that this could be shortened appreciably thus reducing the time in which the furfuraldehyde could decompose. The simplest way of increasing the reaction rate of an equilibrium reaction is to remove one of the products, thus continually displacing the equilibrium in that direction. Since water is a product of this reaction its removal should increase the rate of acetal formation. This was effected by azeotropic distillation with benzene - a technique which has been used successfully in condensations of aldehydes with di- and triols\(^\text{12}\). The benzene provides an added advantage in limiting the temperature of the
reaction mixture to the boiling point of the benzene/water azeotrope.

This method appeared to shorten the time required for the reaction considerably (to about three hours). However it was found that the quantity of water collected in the Dean and Starke head was not an absolute guide to the extent of the reaction. If the heating were continued for sufficiently long the water collected was over 100% (based on the formation of a triacetal product). The additional water was assumed to be formed in the decomposition of the furfuraldehyde, and thus presumably a certain percentage of the water formed throughout the reaction originates from this source.

The major drawback to azeotropic distillation is the insolubility of D-glucitol in benzene, causing a two phase reaction mixture. On warming D-glucitol with a benzene/furfuraldehyde solution the hexitol gradually forms an oil at the bottom of the flask, thus reducing the possible reaction rate greatly. This problem will be discussed later.

The extraction methods described in Experiment 2d (using phosphoryl chloride as catalyst) follow similar classical techniques to those used for the zinc chloride preparation, based on extraction and
crystallisation using suitable solvents. However it was felt that these methods might well lead to the total loss of products which were yielded in small quantities, and thus in later work column separations were used. A typical example of this is described in Experiment 2e (when toluene-\(p\)-sulphonic acid was used as catalyst), the mother liquors from the extraction solutions were passed down an alumina column, with benzene as eluting solvent.

Using these two catalysts a tri-O-furfurylidene acetal with melting point 182-3°C was obtained (IIIb); when chromatographed in both \(n\)-butanol/ethanol/water and dimethyl sulphoxide/diisopropyl ether this triacetal ran in an identical manner to that of melting point 173-4°C (IIIa). When using toluene-\(p\)-sulphonic acid as catalyst a further tri-O-furfurylidene acetal with melting point 136-8°C (IIIc) was isolated; this compound behaved similarly to the former acetals in \(n\)-butanol/ethanol/water, but ran appreciably faster in dimethyl sulphoxide/diisopropyl ether. These acetals are further examples of the dependency of the products of acetal formation upon the catalyst.

As mentioned above, the \(D\)-glucitol was rather intractable under these reaction conditions and thus the question of the solubility of \(D\)-glucitol was
considered (Expt. 2f). It was found that D-glucitol could be brought into a homogenous solution with furfuraldehyde, with gentle warming. However the addition of even very small quantities of benzene immediately threw the D-glucitol out of solution in a gummy state, presumably due to the polarity of the hydroxyl groups. Dimethyl formamide is one of the more efficient solvents for D-glucitol and therefore a solution of D-glucitol in furfuraldehyde and dimethyl formamide was made. A small quantity of benzene was then added, again the D-glucitol was thrown out of solution immediately. From this it was concluded that it was unlikely that a homogenous reaction mixture could be obtained, if benzene was used for azeotropic distillation. The profitability of this has already been discussed.

2,4-O-Furfurylidene-D-glucitol contains two fewer hydroxyl groups than D-glucitol itself, and can readily be obtained in good yields, so this has also been used as a starting material. As would be expected a catalyst is required, and triacetal products have been isolated, IIIb and an oil which could not be crystallised, using phosphoryl chloride as condensing agent (Expts. 2g & 2h); the yields remained small.

From this work it is clear that completely satisfactory methods of synthesis of the di- and tri-
Q-furfurylidene-D-glucitol have not yet been found, although the monoacetal is very readily formed. As has been shown the instability of furfuraldehyde, under the conditions necessary for such a reaction, is the major problem involved: in decomposing it forms a product which occludes the desired products, making their extraction many times more difficult.

The acetals were shown to contain only furfuraldehyde and D-glucitol by their hydrolysis and the subsequent identification of the fragments. In each case the aldehyde was identified as its 2,4-dinitrophenylhydrazone derivative and since melting points of the crude products with authentic furfuraldehyde-2,4-dinitrophenylhydrazone were not depressed, in cases where there was sufficient of the acetal the D-glucitol was characterized as its benzoate. In other cases where the amounts of material available were limited (triacetals IIIb and IIIc) the hexitol was shown to be D-glucitol, and not mannitol, by paper isoelectric in sodium acetate-acetate buffer. This technique is well suited for such a problem since the acetals were hydrolysed using an anion resin, and thus the crude reaction mixture could be spotted directly onto the isoelectricogram.

This means that only very small amounts of the material
A. 2. **Structural studies of furfurylidene-D-glucitols**

Once the furfurylidene-D-glucitols isolated had been proved to be composed solely of furfuraldehyde condensed with D-glucitol, the structural studies were concerned with the number and configuration of the acetal rings. In most cases these were of a classical nature.

The acetals were shown to contain only furfuraldehyde and D-glucitol by their hydrolysis and the subsequent identification of the fragments. In each case the aldehyde was identified as its 2,4-dinitrophenylhydrazone derivative and mixed melting points of the crude products with authentic furfuraldehyde-2,4-dinitrophenylhydrazone were not depressed. In cases where there was sufficient of the acetal the D-glucitol was characterised as its hexaacetate. In other cases where the amounts of material available were limited (triacetals IIIb and IIIc) the hexitol was shown to be D-glucitol, and not mannitol, by paper ionophoresis in sodium metavanadate buffer. This technique is well suited for such a problem since the acetals were hydrolysed using an acid resin, and thus the crude reaction mixture could be spotted directly onto the ionophoretogram. This means that only very small amounts of the material
The number of furan ring systems present, in compounds I, II, and IIIa respectively, were determined spectrophotometrically by quantitatively measuring the optical density of the compounds in ethanolic solution. The measurements were made at 2,200\degree, the position of the strong furan absorption band, and the molar extinction coefficient was calculated (Expt. 4). It was found that the results compared very well (8,260 : 16,600 : 25,200), indicating that the compounds contain one, two, and three furan ring systems respectively, as was expected. It was noted that the molar extinction coefficient per furan ring system attached to a cyclic acetal was lower than that for furan itself (8,340 : 9,860). However these results are of the same order, and it is reasonable to expect some difference in the absorption in these two cases.

With the number of furan ring systems per molecule of compounds I, II, and IIIa now known it may be concluded that each compound contains a like number of acetal rings. To confirm this the number of free hydroxyl groups per molecule of these compounds, respectively, was next determined. For this the compound was acetylated with acetic anhydride in pyridine, and the excess anhydride was determined by titration with
sodium hydroxide (Expt. 5). These results showed that the expected numbers of free hydroxyl groups were present.

Compounds IIIb and IIIc were not similarly treated since they behave in a similar manner to IIIa under chromatographic development, and their elemental analyses are those of a triacetal; thus they may legitimately be assumed to be tri-O-furfurylidene-\(\beta\)-glucitols also.

These results together prove conclusively that compounds I and II are mono- and di-O-furfurylidene-\(\beta\)-glucitols respectively, and that compounds IIIa, IIIb, and IIIc are all tri-O-furfurylidene-\(\beta\)-glucitols. They have not yielded any information about the configuration of the compounds. Thus the following experiments were carried out to locate the positions of the free hydroxyl groups in compounds I and II.

Sodium metaperiodate oxidation was used to find if any pairs of vicinal hydroxyl groups were present. The spectrophotometric method of Aspinall and Ferrier\(^5\) was used to determine the periodate uptake (Expt 6). Since it was thought that sodium metaperiodate might attack the furan ring systems, the effect of this reagent on furfuraldehyde was studied. In fact it was found that the optical density of a sodium metaperiodate/
furfuraldehyde solution was the same as the sum of its separate components, after four hours. However it was noted that furfuraldehyde has a small absorption at the wave length used (2,230 Å), and therefore all measurements on I and II were made against an aqueous reference solution that was equimolar in the concentration of this compound. The results showed that both compounds contained one pair of vicinal hydroxyl groups (I - 1.05 molar uptake, II - 0.97 molar uptake).

If the vicinal pair of hydroxyl groups should contain a terminal carbon atom of the D-glucitol then formaldehyde would be liberated under these conditions. The molar production of formaldehyde was determined by a colorimetric method in which the violet coloured chromotropic acid complex is formed. These measurements are carried out in a concentrated sulphuric acid medium, which meant that the furfurylidene rings would be broken down, liberating furfuraldehyde. Furfuraldehyde forms a yellow coloured complex with chromotropic acid, and therefore it was necessary to take the readings against a reference solution containing the same quantity of furfuraldehyde as would be liberated from the compound under investigation. This work showed that both I and II contain free hydroxyl groups in either the 1 and 2, or the 5 and 6 positions of D-glucitol, since each
produced one mole equivalent of formaldehyde on periodate oxidation.

Formic acid determinations were not necessary as compound I does not contain the three adjacent hydroxyl groups which are required for it to be a product of periodate oxidation.

From these results it may be concluded that only two structures are possible for compound I:

\[ \text{2,4-\(\beta\)-furfurylidene-\(D\)-glucitol or 3,5-\(\beta\)-furfurylidene-\(D\)-glucitol.} \]

\[ \text{i.e.} \quad \text{or} \]

\[ \text{There can be hydroxyl groups on only one pair of adjacent carbon atoms (one being a terminal carbon atom); the other two hydroxyl groups must be situated with at least one acetal ring carbon atom between them, and between them and the vicinal pair of hydroxyl groups.} \]

For compound II the possible structures are

\[ \text{1,2,3,4-di-\(\beta\)-furfurylidene-\(D\)-glucitols and 3,4,5,6-di-\(\beta\)-furfurylidene-\(D\)-glucitols.} \]
i.e. \[ \text{H}_2\text{C}-0-q \]
\[ \text{H}-0-q \]
\[ q-0-0-H \]
\[ \text{H}-0-q \]
\[ \text{H}-0-\text{OH} \]
\[ \text{CH}_2\text{OH} \]

or

\[ \text{CH}_2\text{OH} \]
\[ \text{H}-0-\text{OH} \]
\[ q-0-0-H \]
\[ \text{H}-0-q \]
\[ \text{H}-0-\text{OH} \]
\[ \text{H}_2\text{O}-0-q \]

where \( q \) indicates the positions where acetal rings may be formed by cyclisation across any given pair with the furfurylidene group. Clearly both these arrangements give rise to three possible configurations for the acetal rings.

To establish which of the two possible positions for the vicinal pair of hydroxyl groups was correct, the sugar residues formed during periodate oxidation were identified in each case.

\[ \text{2,4-0-furfurylidene-D-glucitol} \]

\[ \text{2,4-0-furfurylidene-aldehydo-L-xylose} \]
and similarly for the di-O-furfurylidene-D-glucitol.

Thus the nature of the sugar liberated indicated that xylene had been formed
(Expt. 6). Thus compound II must be a 1,2,3,4-di-O-
furfurylidene-D-glucitol, and compound III must be a 1,2,3,4-di-O-
furfurylidene-D-glucitol.

It was found that the acidity produced by

the sodium periodate

in the aqueous solution of

the respective aldehydes was sufficient to cleave the furfurylidene

moiety, which could be detected with both silver nitrate and 2,4-dinitrophenylhydrazine, were present. They were assayed to be 3,5-difurfurylidene-

aldehyde-\(\text{D-xylose}\) and a 1,2,3,4-difurfurylidene-

aldehyde-\(\text{D-xylose}\), as could be expected.

\(\text{D-xylose}\) itself was isolated on compound I

by the method described in the 1952 report, where

the oxidation is brought about in glacial acetic acid (Expt. 9). The yield obtained
and similarly for the di-\(\text{O}\)-furfurylidene-\(\text{D}\)-glucitols. Thus the nature of the sugar liberated indicates the structure of the parent compound. In each case chromatography showed that xylose had been formed (Expt. 8). Thus compound I must be 2,4-\(\text{O}\)-furfurylidene-\(\text{D}\)-glucitol, and compound II must be a 1,2,3,4-di-\(\text{O}\)-furfurylidene-\(\text{D}\)-glucitol.

It was found that the acidity produced by the sodium metaperiodate\(^{54}\) in the aqueous solution of the compound was sufficient to cause a very slow breakdown of the furfurylidene rings (in the case of II it was three days before any free sugar was detected). This breakdown was so slow that it did not cause anomalous results when measuring the periodic uptake, as was the case with the but-2'-enylidene-\(\text{D}\)-glucitols\(^{46}\).

The chromatograms also showed that two new compounds, which could be detected with both silver nitrate and 2,4-dinitrophenylhydrazine sprays, were present. They were assumed to be 2,4-\(\text{O}\)-furfurylidene-aldehydo-\(\text{L}\)-xylose and a 1,2,3,4-di-\(\text{O}\)-furfurylidene-aldehydo-\(\text{L}\)-xylose, as would be expected.

\(\text{L}\)-xylose itself was isolated from compound I by the method described in the 1952 Patent\(^{19}\), where the oxidation is brought about by lead tetraacetate in glacial acetic acid (Expt. 9). The yield obtained
was only 17% compared with the 85–90% yields reported; this may be compared with the yields obtained for compound I (page 33).

The remaining work carried out on the furfurylidene-\(\alpha\)-glucitols was concerned with forming their derivatives, and the results obtained confirmed the structures already assigned. No derivatives of the tri-\(\alpha\)-furfurylidene-\(\alpha\)-glucitols could be formed because they do not contain any free hydroxyl groups.

Crystalline tetra-\(\alpha\)-acetyl and tetra-\(\alpha\)-toluene-\(\rho\)-sulphonyl derivatives could not be obtained from compound I, in both cases an intractable oil was formed. However the monoacetal did yield a di-\(\alpha\)-triphenylmethyl derivative, this confirmed the presence of two primary alcohol groups in compound I. This compound had been reported previously by Bredereck and Papademetriu\(^\text{16}\); it was found to be too soluble in ethyl acetate for this solvent to be used for recrystallisation, as is reported in that paper (Expt. 10).

The mono- and diacetal reacted with phenylboronic anhydride in ethanolic solution to yield their respective phenylboronates, as would be expected\(^\text{55}\). The phenylboronate groups are assumed to span the 1,3- and 5,6-positions in the monoacetal, and the 5,6-position in the diacetal, since acetal ring migration would not
be expected under the weakly acidic conditions provided by the phenylboronic anhydride. The anhydride was used in preference to phenylboronic acid since it reacts considerably faster with a diol due to the nucleophillic attack of the alcoholic oxygen on the ring boron\(^5\).

Compound II readily yielded a crystalline di-\(\beta\)-acetyl derivative, on treatment with acetic anhydride in dry pyridine. Since the di-\(\beta\)-acetyl-di-\(\beta\)-furfurylidene-\(\beta\)-glucitol obtained has a very similar melting point to compound II, and also the theoretical elemental analysis figures for the two compounds are almost identical, the formation of the derivative was confirmed by infrared analysis. This showed that the hydroxyl groups of compound II were no longer present in the derivative, whose spectrum also showed the presence of a \(C=O\) group (from the acetate grouping).

When this di-\(\beta\)-acetyl derivative was hydrolysed with sodium methyleate it again yielded a di-\(\beta\)-furfurylidene-\(\beta\)-glucitol, but the diacetal now melted at 198-200\(^\circ\) (compared with 182-3\(^\circ\) formerly). These two diacetals could not be interconverted by crystallisation, even with the aid of seeding. This phenomenon has been encountered previously in work on cyclic acetals: with 1,3:2,4-di-\(\beta\)-benzylidene-\(\beta\)-glucitol and 4,6-\(\beta\)-butylidene-
\(\beta\)-glucose\(^5\).
Chromatographically both the diacetals behaved identically, which indicates that they contain the same ring systems. Their infrared spectra are identical from 4,000-700 cm⁻¹ and this may be taken to indicate that they are polymorphs, as with the 1,3,5,7-di-Ω-benzylidene-Ω-perseitol®. However the perseitol acetals may be interchanged by recrystallisation from the lower to the higher melting form®

as is usual with polymorphic compounds, but this is not possible with the furfurylidene diacetals. Chromatography indicates that they contain the same rings with respect to the polyol, and thus any isomerism must arise from an acetal carbon atom. Therefore if the two furfurylidene diacetals are stereoisomers it would mean that the configuration of an asymmetric acetal carbon atom was altered during either the acetylation or the deacetylation; this seems unlikely since both reactions were carried out in basic media. Thus it seems more likely that the two diacetals are polymorphic compounds.

It seems most probable that the di-Ω-furfurylidene-Ω-glucitol of melting point 198-200° is the same diacetal as that reported by Bredereck and Papademetriu, with melting point 202-203°. It is now known that the diacetal which melts at 182-3° is a
1,2,3,4-di-O-furfurylidene-\(\beta\)-glucitol, and therefore the diacetal which melts at 198-200\(^\circ\) must also be a 1,2,3,4-di-O-furfurylidene-\(\beta\)-glucitol, providing these compounds are polymorphic as stated above. Thus it appears probable that Bredereck and Papademetriu assigned the wrong structure to their diacetal when they suggested that it was 2,4:5,6-di-O-furfurylidene-\(\beta\)-glucitol, a structure which seems rather unlikely, as was mentioned on page 29.
The only butylidene-$D$-glucitols previously known were those reported by Holst$^{21}$ (see p. 12). He condensed $D$-glucitol with $\mu$-butyraldehyde using concentrated sulphuric acid as the catalyst, and fractionally distilled the product to give two tri-$D$-butylidene-$D$-glucitols, which he did not characterise. Nothing was recorded that would indicate the structures of these triacetals. It seems probable that he was dealing with more than one isomer, but it is doubtful that either of his fractions were entirely homogenous$^{59}$.

Simultaneously Dr. D. Lewis (Royal Holloway College) was working on the but-2'-enyldene-$D$-glucitols, which he hydrogenated to form the corresponding butylidene-$D$-glucitols. Thus some of the results obtained were confirmed by comparison with these hydrogenated but-2'-enyldene-$D$-glucitols.

As with the furfurylidene-$D$-glucitols, methods of synthesis of these compounds have been found, and structural studies have been made.
B. 2. **Synthesis of butyldiene-\(D\)-glucitols**

Unlike the furfurylidene-\(D\)-glucitols, it was found that the mono- and tri-\(\beta\)-butyldiene acetals could be formed quite readily, by condensing \(n\)-butyraldehyde with \(D\)-glucitol under acidic conditions. The reactants were stable under the reaction conditions used and reasonable yields of the products were obtained throughout.

\(2,4-\beta\)-butyldiene-\(D\)-glucitol (compound IV) was obtained employing conditions very similar to those used to prepare its furfurylidene analogue (I) (Expt. 16). The \(n\)-butyraldehyde, in 1 : 1 mole ratio, was added to a solution of \(D\)-glucitol in aqueous sulphuric acid and the mixture was stirred until it was homogenous (ca. 10 min.), as before. However compound IV is considerably more soluble under these conditions than compound I, and it was found necessary to allow the reaction mixture to stand for four days after this, so that the maximum quantity of the product could crystallise out.

Chromatograms of this crude reaction mixture showed that a considerable quantity of the 3,4-acetal, as well as the 2,4-acetal, was present showing that a mixture of acetals is formed in this reaction. Presumably the 2,4-acetal becomes the chief product because it is
the least soluble under the given conditions. Once the 2,4-acetal has started to crystallise its concentration in the solution will be decreased, and the equilibrium will be shifted in the direction of producing more of it. Thus it is essential to leave the reaction mixture to crystallise for several days, if a good yield of compound IV is to be obtained. This situation was suspected by Hann and Hudson\textsuperscript{13}, although they offered no evidence to support it (see p. 9).

Tri-\(\text{D}\)-butyldiene-\(\text{D}\)-glucitols were obtained by two different methods: the one in a strong sulphuric acid medium, and the other with toluene-\(p\)-sulphonic acid as catalyst and the forward reaction being aided by azeotropic distillation. The main products obtained in both cases were oils and from their distillation under reduced pressure, and from the refractive index measurements made, it seemed that the same product could have been obtained in both cases. However the results obtained from their partial hydrolysae show that this cannot be so.

The preparation using concentrated sulphuric acid was a repetition of the method used by Holst\textsuperscript{21} (Expt. 17a). Dioxan is used as a solvent for the reaction. Concentrated sulphuric acid is added dropwise, with stirring, to a suspension of \(\text{D}\)-glucitol in \(n\)-butyraldehyde
and dioxan. As the acid was added the $D$-glucitol was gradually taken into solution, indicating that the reaction intermediates or products were formed rapidly. The reaction mixture was then heated at $100^\circ$ for one hour, and during this time it became a deep brown colour. Clearly some breakdown of organic material was being brought about by the strong sulphuric acid medium, but this was not thought to be too serious since good yields of the triacetal products were obtained (up to 75%), and no insoluble residue was discovered during the extraction procedures.

Holst obtained two isomeric triacetals from this reaction mixture, the one (40%) boiling at 162-167°/4 mm., $\alpha_D^{25} 1.4618$, $[\alpha_D^{25}] +10.0^\circ$ (g 10.0 in EtOH), and the other (22%) at 172-177°/4 mm. (not characterised further). This appeared to be the case in this work also until all the fractions were redistilled, then it was found that they all came over at similar temperatures at 0.1 mm. Since it was felt that it would be difficult to distinguish between two such similar boiling fractions (as reported by Holst) at this pressure the fractions were also distilled at 18-20 mm., but this still gave no indication that the product could be separated. The partial hydrolysis of this product (Va) did yield two diacetals however (see Expt. 18).
The second method of preparation proved to be an extremely efficient way of producing a tri-\(\text{O}-\)butylidene-\(\text{D}-\)glucitol. The reaction proceeded quite rapidly to 80-90\% completion, in the presence of toluene-\(\text{D}-\)sulphonic acid as catalyst. The azeotropic distillation with benzene removed the water as it was formed, and this was taken as a measure of the progress of the reaction. The reaction mixture remained a pale yellow colour throughout, showing that there was no decomposition (as there was when the furfurylidene-\(\text{D}-\)glucitols were being prepared by this method). The \(\text{D}-\)glucitol did not dissolve in the benzene solution as was to be expected. Nevertheless the reaction proceeded sufficiently readily under these conditions for the occurrence of the two phase reaction mixture not to be considered a drawback.

When the crude mixture cooled an oil separated out, which yielded crystals of compound IV. It is possible that this product is an intermediate in the preparation of the final product, and that therefore the triacetal obtained contains the 2,4-ring system. However, as will be shown later, there is considerable doubt as to whether this line of reasoning is valid.

The remainder of the reaction mixture yielded, after removal of the solvents, a syrupy triacetal, as mentioned above. This tri-\(\text{O}-\)butylidene-\(\text{D}-\)glucitol (\(\text{Vb}\))
could not be separated into different fractions by distillation either, although it yielded two mono- and two diacetals on partial hydrolysis.

Two diacetals have been isolated. One has been characterised as a white crystalline solid, the other has remained an intractable oil. Neither of these compounds have been synthesised directly, they have been obtained only by partial hydrolysis of the triacetals. This was carried out by a variation of Appel’s method: the syrupy triacetals were heated at 85-88° with 60% acetic acid for about 1½ hours. Although some triacetal remained unchanged, these conditions were suitable since about 60% of the hydrolysed triacetal was obtained as a diacetal, and very little had been hydrolysed to free D-glucitol. The advantage of this method is that the acid can be pumped off rapidly, and this eliminates the necessity of neutralisation, which must inevitably be followed by deionisation. Thus the products can immediately be obtained in a reasonably pure state.

The mono-, di-, and triacetals present in the oil which remained after all the volatile matter had been removed by pumping were separated by treatment with different solvents. Addition of chloroform precipitated the monoacetals, and any free D-glucitol,
leaving the less polar di- and triacetals in solution. Removal of the chloroform from the remaining oil and the subsequent addition of petroleum ether (b.p. 60-80°) separated the soluble, unhydrolysed triacetals from the insoluble diacetals.

Hydrolysis of Va (prepared using concentrated sulphuric acid) yielded a crystalline diacetal, a syrupy diacetal, and compound IV. When benzene was added to the diacetal oil the crystalline diacetal, a 1,2,3,4-di-O-butyldiene-D-glucitol, compound VI, was precipitated in a relatively pure state as chunky white crystals. This compound can be purified by recrystallisation from water and has melting point 132-133°. It constituted about 15% of the hydrolysed triacetal. The remaining diacetal oil was the predominant product (ca. 55% of the hydrolysed Va) and it could not be obtained in a crystalline form. Thus two diacetals were obtained from a constant boiling triacetal oil. In contrast to this only one monoacetal, compound IV, was isolated. Hydrolysis of the different distillation fractions gave the same products in similar yields.

Hydrolysis of Vb (toluene-₃-sulphonic acid catalyst) gave different products. These were a syrupy diacetal containing only 2% of compound VI, and two monoacetals, compound IV and 3,4-O-butyldiene-D-glucitol
(VII). The importance of this triacetal therefore is that it yields compound VII, which has not been isolated from direct synthesis. Again about 55% of the hydrolysed triacetal was converted to the syrupy diacetal.

Compounds IV and VII were isolated from the crude monoacetal precipitation by fractional crystallisation from ethanol. IV, being the less soluble acetal, crystallised first and was followed by the considerably more soluble compound VII. From the percentage recovery of these two compounds from the crystallisation liquors it appeared that VII was present in twice the quantity of IV. About 50% of the crude material was recovered in a pure state, which should give a reasonable guide to the actual proportions of the two compounds present, bearing in mind that \(\alpha\)-glucitol was also present in the crude mixture.

It was found that compound VII exists in two distinct forms. The one is white needles, with melting point 112-113\(^\circ\)C, and the other a white flocculent mass, with melting point 109-110\(^\circ\)C. A mixed melting point of the two was not depressed, showing that they are the same compound, and yet it was found that the melting point of the flocculent form could not be raised to that of the crystalline form. The isolation of this compound is interesting since it contains the \(\alpha\)-ring
system, which is unexpected according to the Hann-Hudson and Barker-Bourne rules.

The results of the triacetal preparations and their subsequent hydrolyses may be summarised. From the physical measurements made both the triacetals, Va and Vb, appeared to be very similar, and they both boiled at a constant, although not characteristic, temperature under reduced pressure. However from their partial hydrolyses it is clear that they are different triacetals — different products are obtained. Also it seems probable that they are both a mixture of triacetals, since neither yields unique di- and mono-hydrolysis products, and both yield a syrupy diacetal and compound IV. At the same time the possibility of ring migration must not be excluded, especially as Vb yields almost exclusively one diacetal and two monoacetals, whereas Va yields two diacetals and only one monoacetal.

Thus, the work carried out on the synthesis of the butylidene-D-glucitols has shown that 2,4-O-butylidene-D-glucitol and various triacetals can readily be synthesised in good yields, and that satisfactory methods for the preparation of a crystalline 1,2,3,4-O-butylidene-D-glucitol and 3,4-O-butylidene-D-glucitol have been found.
B. 2. **Structural studies of butylidene-\(\beta\)-glucitols**

Much of the procedure used for assigning the basic structures to these acetals was identical to that used for the furfurylidene-\(\beta\)-glucitols, and thus only the variations will be discussed in detail. The structural studies carried out were concerned with the crystalline products obtained. As stated above the triacetals obtained are probably mixtures of triacetals, thus making structural studies pointless, but some possible structures for their constituents will be suggested from the inference of their partial hydrolyses.

3,4-\(\alpha\)-butylidene-\(\beta\)-glucitol (VII) was characterised by comparison with the compound obtained by hydrogenating 3,4-\(\alpha\)-but-2'-enyldene-\(\beta\)-glucitol (prepared by Dr. Lewis).

The nature of the constituent parts of 2,4-\(\alpha\)-butylidene-\(\beta\)-glucitol (IV) was determined by hydrolysing IV as before, and then characterising the fragments (Expt. 21). In this case the aldehyde was identified as its bisdimedone derivative, and it was shown that \(\alpha\)-butyraldehydebisdimedone was formed. This derivative was felt to be more satisfactory than the 2,4-dinitrophenylhydrazone derivative, due to the variability of the melting point of the latter. The hexitol fragment was characterised as its trisphenyl-
boronate derivative$^{55}$, and this showed that it was in fact $d$-glucitol. The yields of these derivatives were not quantitative, but they were such as to suggest that one mole of $n$-butyraldehyde had reacted with one mole of $d$-glucitol, as had been indicated by the elemental analysis of the compound, and also by its general behaviour.

The use of phenylboronate derivatives to characterise alcohols is relatively new, and it does seem to have much to recommend it. The derivative is precipitated as soon as phenylboronic anhydride in methanol is added to the polyhydric alcohol; also anhydrous conditions are not required for its formation whereas they are necessary if the acetate derivative is to be formed. Thus the preparation of this derivative is simpler and quicker.

The crystalline diacetal, VI, was not treated similarly since it yielded compound IV when partially hydrolysed (Expt. 20), which showed that it was formed from $d$-glucitol and $n$-butyraldehyde also. The triacetals Va and Vb were not so treated either, since similar deductions could be made.

The chromatographic behaviour of all these butylidene compounds, when compared with the furfurylidene-$d$-glucitols, indicated the number of free hydroxyl
groups that each contains, and in each case this was confirmed by its elemental analysis figures. Namely, that compounds IV and VII contain four free hydroxyl groups, compound VI contains two free hydroxyl groups, and Va and Vb contain none. This situation was confirmed for compound IV by its acetylation and determination of the acetylium uptake. The method was identical to that used previously (Expt. 22).

The next piece of work was concerned with the positions of the hydroxyl groups in compound IV. A quantitative periodate oxidation was carried out as before, and this showed the presence of one pair of vicinal hydroxyl groups (Expt. 23). Subsequently, a quantitative determination of the formaldehyde liberated during this treatment showed that the vicinal pair included a primary alcohol group. Since n-butyraldehyde does not form a coloured complex with chromotropic acid\textsuperscript{53} it was not necessary to add the calculated quantity of n-butyraldehyde to the reference solution in this case (Expt. 24).

To affirm the absolute configuration of compound IV the nature of the sugar which was formed when it was treated with sodium metaperiodate, and then hydrolysed, was determined. Ethylene glycol was added to the reaction mixture, to react with excess periodate,
before the acetal rings were removed by heating with an acid resin. Chromatograms of the resulting reaction mixture showed conclusively that xylose had been formed by these reactions (Expt. 25).

Thus compound IV must be 2,4-O-butylidene-D-glucitol.

\[
\begin{align*}
\text{CH}_2\text{OH} & \\
H-C-O & \\
\text{HO-C-H} & \text{CH}_2\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_3 & \text{CH}_2\text{OH} \\
H-C-O & \\
H-C-OH & \text{CH}_2\text{OH}
\end{align*}
\]

Compound VI was proved to contain a vicinal pair of hydroxyl groups in the 5 and 6 positions, since it could be converted to L-xylose by periodate oxidation followed by acid hydrolysis. This was carried out in two steps with the di-\(\beta\)-butylidene-aldehyde-L-xylose intermediate being isolated (Expts. 26 & 27). Since an aqueous solution of sodium metaperiodate is weakly acidic\(^{54}\), it was reacted with VI in the presence of sodium hydrogen carbonate. It was added dropwise to the suspension of VI in an aqueous solution of sodium hydrogen carbonate so that the overall pH of the mixture did not fall below 7, thus ensuring that no hydrolysis
of VI would occur during this reaction. This was essential since if there were any hydrolysis a mixture of various sugars and their mono- and dibutylidene derivatives would be obtained, which would make it very difficult to isolate the xylose diacetal intermediate.

By the time all the periodate had been added the solution had become homogenous, which suggests that the periodate oxidation had already taken place. The solution was then left to stand at room temperature for one hour, to ensure that the oxidation was complete. The mixture was then extracted with chloroform to isolate the required chloroform soluble aldehydo-compound. This di-\(\beta\)-butylidene-aldehydo-\(\text{L}\)-xylose was found to crystallise from petroleum ether as white needles and to have melting point \(108.5-109.5^\circ\). This compound was also characterised as its \(p\)-nitrophenylhydrazone derivative, which it formed when heated with an equimolar quantity of \(p\)-nitrophenylhydrazine in absolute ethanol. The crystals of di-\(\beta\)-butylidene-aldehydo-\(\text{L}\)-xylose-\(p\)-nitrophenylhydrazone were slow in crystallising out, but after three days in a refrigerator a 74\% yield was obtained.

The xylose diacetal was converted to \(\text{L}\)-xylose itself by hydrolysis with an acid resin in water. When the hydrolysis was complete the resin and the water
were removed and the resultant syrup was taken up in methanol. The \( \text{L-xylose} \) showed little inclination to crystallise out, and so the mixture was cooled to \(-15^\circ\) and then allowed to warm up slowly - this resulted in the crystals separating. The isolation and characterisation of this \( \text{L-xylose} \) proved that compound VI contains a vicinal pair of hydroxyl groups in the 5 and 6 positions.

Therefore compound VI is a 1,2,3,4-di-\( \text{O-} \)butylidene-\( \text{D-glucitol} \).

\[
\begin{align*}
\text{H}_2\text{C-O-q} \\
\text{H-C-O-q} \\
\text{q-O-C-H} \\
\text{H-C-O-q} \\
\text{H-C-OH} \\
\text{CH}_2\text{OH}
\end{align*}
\]

where \( q \) indicates the positions where acetal rings may be formed by cyclisation across any given pair with \( \text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_3 \).

Partial hydrolysis of this compound strongly suggests that it is in fact 1,3:2,4-di-\( \text{O-} \)butylidene-\( \text{D-glucitol} \), since compound IV is the only monoacetal which has been isolated from the hydrolysis reaction mixture (Expt. 20). If ring migration had taken place
during the acid hydrolysis, to yield the most stable monoacetal, it would be expected that some trace of the other monoacetal would have been found. Thus it may be assumed that the structure of this crystalline diacetal is 1,3:2,4-di-\(D\)-butylidene-\(D\)-glucitol. This is the structure which would be expected from theoretical considerations of the stabilities of the rings which could be formed.

No structural studies were carried out on the diacetal oil since distillation did not give a pure sample of it (Expt. 13). It was a high boiling liquid, as would be expected, and it analysed approximately as a diacetal. Infrared spectra of this syrup showed the presence of a carbonyl peak, which may well be due to there being a gradual breakdown of the compound because it contains unfavoured ring systems. This could account for the slightly low analysis figures.

No direct structural studies can be made on the triacetal syrups, since all the reactive centres of the \(D\)-glucitol are blocked. Partial hydrolysis does imply some knowledge of their structure, but the presence of the diacetal syrup (of unknown structure), in large yields, makes any deductions less certain. The structures of \(V_a\) and \(V_b\) may be deduced as follows, assuming no ring migration.
Partial hydrolysis of Va yields compound IV, containing the 2,4-ring, and compound VI containing the 1,3:2,4-ring systems. Thus Va should contain some 1,3:2,4:5,6-tri-\(\alpha\)-butyldene-\(D\)-glucitol, which would be expected from theoretical considerations of the most stable configuration of ring systems. Also since only the 2,4-monoacetal is obtained the syrupy diacetal should also contain the 2,4-ring system. Thus this diacetal could be the 2,4:5,6-diacetal formed from the 1,3:2,4:5,6-triacetal with the 1,3:2,4-diacetal, or it could arise from a different triacetal. The possible structures for such a triacetal are with rings linked in the 1,5:2,4:3,6-positions (i.e. with an eight and a seven membered ring) and in the 1,6:2,4:3,5-positions (i.e. with a nine membered ring).

Vb yields compounds IV and VII, thus it contains both the 2,4- and 3,4-ring systems and therefore it must be a mixture. Only a trace of the 1,3:2,4-diacetal (compound VI) was obtained, but a considerable amount of the syrupy diacetal was found; this must be taken to indicate that this syrup contains both the 2,4- and 3,4-ring systems, so it also must be a mixture. The absence of an appreciable quantity of compound VI means that Vb does not contain much of the theoretically most stable triacetal containing the 2,4-ring, unless
in this case it has yielded almost exclusively the 2,4;5,6-diacetal although the conditions were identical to those used for Va. Possible structures for a second 2,4-containing triacetal are the same as those described for the second triacetal of Va. For the triacetal containing the 3,4-ring system it seems most likely that the rings are linked at the 1,2;3,4;5,6-positions, since a 1,5;2,6;3,4- (i.e. two eight membered rings) or a 1,6;2,5;3,4- (i.e. a nine and a seven membered ring) triacetal seem much less probable.

From the hydrolysis of both Va and Vb a syrupy diacetal with the 2,4-ring system is required, and it must be different from the crystalline diacetal. Thus it can contain the 1,5;2,4-, the 1,6;2,4-, the 2,4;3,5-, the 2,4;3,6-, and the 2,4;5,6-rings. Correlating this with the possible triacetal structures given above the most likely structures for this diacetal are 2,4;3,5- and 2,4;3,6-substituted compounds, based on the assumption that the largest acetal ring present would be the least stable to acid hydrolysis, with the 2,4;5,6-diacetal which arises from the theoretically most stable triacetal. Considering this diacetal independently the 2,4;3,5- and 2,4;5,6-structures appear equally likely.

The case of the diacetal containing the 3,4-ring is simpler, since as explained above this
almost certainly arises from 1,2:3,4:5,6-tri-\(\text{\textbeta}\)-butylidene-\(\text{\textalpha}\)-glucitol. The 1,2- and 5,6-rings are both \(\text{\textalpha}\)-ring systems and it is therefore reasonable to expect these to be equally readily hydrolysed. This would give rise to a mixture of 1,2:3,4- and 3,4:5,6-diacetals, which would be very difficult to separate since they would behave very similarly. Such a mixture of diacetals could quite easily result in an intractable oil, as has been obtained in this case.

It can clearly be seen that this line of reasoning does lead to some surprising results. For V\(\text{\textbeta}\) it is necessary to postulate the presence of a triacetal either with an eight and a seven membered ring, or with a nine membered ring although there are no known examples of such large acetal ring systems. Such a postulation is not essential for V\(\text{\textalpha}\), but if it is to be excluded it is necessary to postulate that the 5,6 \(\text{\textalpha}\)-ring is approximately four times as stable as the 1,3 \(\beta\)-ring; this again seems unlikely. It seems much more reasonable that V\(\text{\textalpha}\) and V\(\text{\textbeta}\) are both a mixture of the 1,3:2,4:5,6- and 1,2:3,4:5,6-triacetals in different proportions, with V\(\text{\textalpha}\) containing a much higher percentage of the former acetal. The absence of the 3,4-monoacetal from V\(\text{\textalpha}\) may be explained as being due to a low proportion of the 3,4-containing triacetal, which would result in a
relatively small yield of compound VII, and also to the possibility that compound VII is converted by ring migration to the more stable 2,4-compound. Examples of ring migration are not unknown.

In the case of Vb the 3,4-monoacetals is found since it arises from a much larger proportion of the 3,4-containing triacetals. The presence of only a small quantity of compound VI after partial hydrolysis must be taken to indicate that only a small proportion of the 2,4-containing triacetals was present, since this diacetals should be the most stable to acid hydrolysis. The relatively higher proportion of compound IV obtained may be accounted for by ring migration, as above. The isolation of compound IV from the preparation mixture for Vb, indicating that it is a reaction intermediate, may be considered as analogous to the formation of a syrupy 1,2:3,4:5,6-tri-0-but-2'-enylidene-D-glucitol from 2,4-0-but-2'-enylidene-D-glucitol. In that work it was found that toluene-p-sulphonic acid preparations yielded a higher percentage (20%) of this syrupy triacetals than the crystalline 1,3:2,4:5,6-tri-0-but-2'-enylidene-D-glucitol (1-4%). The relative proportions indicated are comparable with those deduced in the present work (Vb preparation).

The presence of di- and triacetals as syrups
may be accounted for by a consideration of their conformations. Mills\textsuperscript{25} has shown that in both 2,4-mono- and 1,3:2,4-diacetals of \textsuperscript{2}D-glucitol the alkylidene residues at the acetal carbon atoms and the remainder of the polyol chains are in equatorial positions. Isomerism in these compounds is therefore unlikely. In this work these compounds have been found to be crystalline. In the 1,3:2,4:5,6-triacetal the 1,3:2,4-portion would again be expected to be free of isomerism, but the acetal carbon atom of the five membered 5,6-ring is likely to exhibit stereoisomerism. In support of this Mills quotes the difficulty encountered in preparing crystalline 1,3:2,4:5,6-tri-O-ethylidene-\textsuperscript{2}D-glucitol and the variable melting point given for 1,3:2,4:5,6-tri-O-benzylidene-\textsuperscript{2}D-glucitol. This interpretation may also account for the lack of a crystalline 1,3:2,4:5,6-tri-O-butylidene-\textsuperscript{2}D-glucitol.

The 1,2:3,4:5,6-triacetal has three asymmetric acetal carbon atoms and so eight isomers are possible; it is therefore quite reasonable to find that this substance is a syrup. Similarly four isomers of each of the proposed 1,2:3,4- and 3,4:5,6-diacetals are possible which, again, would make it extremely difficult to obtain crystalline samples of these compounds.

With the 3,4-monoacetal two stereoisomers
should be formed, due to the asymmetric acetal carbon atom, and this may account for the two distinct forms of this compound and for the two melting points. Probably the crystalline form melting from 112–113° is a pure stereoisomer, whereas the flocculent form (m.p. 109–110°) is a mixture of the two stereoisomers.

The derivatives which have been obtained from compound IV have confirmed its structure. It reacted with acetic anhydride in dry pyridine to yield a tetraacetate derivative; with phenylboronic anhydride in methanol to yield a bisphenylboronate derivative (the phenylboronate groups are assumed to span the 1,3- and 5,6-positions); and on treatment with triphenylmethylicloride in dry pyridine it yielded di-\(\text{O}\)-triphenylmethyl-2,4-\(\text{O}\)-butylidene-\(\text{D}\)-glucitol. The ditriphenylmethyl ether melted with effervescence and the actual temperature was variable. The highest melting point recorded was 94–95°, it was generally about 90°. Analysis of the compound showed that it is not solvated. The same phenomenon was observed for di-\(\text{O}\)-triphenylmethyl-2,4-\(\text{O}\)-but-2'-enylidene-\(\text{D}\)-glucitol. It is assumed that the triphenylmethyl groups are in the 1- and 6-positions. Together the formation of these derivatives indicates that compound IV contains four free hydroxyl groups, two of which are in the primary positions.
OTHER CYCLIC ACETALS OF HEXITOLS

Hockett's method of synthesising 2,4-monoacetals of D-glucitol has been found to be suitable for the preparation of furfurylidene-19,20, butylidene-, and but-2'-enylidene-46 cyclic acetals. Therefore the method was investigated to find if it were universally applicable.

It was found that 2,4-0-isobutylidene-D-glucitol (VIII) (47% yield), 2,4-0-propylidene-D-glucitol (19% yield), and 2,4-0-benzylidene-D-glucitol (33% yield) could be readily prepared by this method, taking the aldehyde and D-glucitol in approximately 1:1 mole proportions. In each case the acetal was obtained as crystals from the crude preparation mixture (Expts. 31, 32 & 34). Attempts to obtain crystals of 2,4-0-ethylidene-D-glucitol by the same method failed however (Expt. 35). This was assumed to be due to the greater solubility of this compound in the reaction mixture.

From the yields obtained it appears that the solubility of the monoacetal decreases as the size of the acetal chain increases, and that 2,4-0-propylidene-D-glucitol is the limiting case for this method of preparation. Thus it should be possible to form all 2,4-monoacetals of D-glucitol by this method, except
the methylene and ethylidene acetals.

When attempting to form a monoacetal of mannitol by Hockett's method it was found that it was impossible to form a solution of mannitol in 3N sulphuric acid. Therefore the suspension of mannitol in the sulphuric acid was shaken with furfuraldehyde for a long time, but no acetal formation could be detected by paper chromatography (Expt. 35). This was not surprising since in effect it was a three phase reaction mixture. It was concluded that this basic method is not readily applicable to the formation of monoacetals of mannitol.

A tri-{$\alpha$}-isobutylidene-{$\alpha$}-glucitol syrup was prepared from D-glucitol and iso-butylaldehyde using toluene-$p$-sulphonic acid as condensing agent and azeotropic distillation, under the same conditions as those used for the formation of the tri-{$\alpha$}-butylidene-$D$-glucitols and the tri-{$\alpha$}-furfurylidene-$D$-glucitols when using this catalyst. The triacetal syrup was obtained in good yield (75%), with a small amount of compound VIII (Expt. 36). This appears to be a satisfactory general method for the preparation of triacetals of D-glucitol, although it does yield a mixture of triacetal products. (A mixture of 1,3:2,4:5,6-tri-{$\alpha$}-but-2'-enyldene-$D$-glucitol and a syrupy tri-{$\alpha$}-but-2'-enyldene-$D$-glucitol was also prepared by this method.46)
Since compound VIII was used for reaction kinetics its structure was determined. The methods were the same as those used for compound IV, except that the aldehyde fragment formed during acid hydrolysis was characterised as its 2,4-dinitrophenylhydrazone derivative (Expts. 37-41). These results showed conclusively that the compound is 2,4-O-isobutylidene-β-glucitol. Also the di-O-triphenylmethyl and tetra-O-acetyl derivatives of compound VIII were formed by the methods used for the preparation of these derivatives of compound IV (Expts. 42 & 43). It was interesting to note that once more the di-O-triphenylmethyl derivative melted with effervescence.
When this work was embarked upon it was intended to be a straightforward study of the acid hydrolysis of cyclic acetals of D-glucitol, containing four carbon atoms in the acetal side chain. The butylidene compounds were chosen partly because their synthesis, structure, and hydrolysis had already been the subject of much work, and partly because their rate of hydrolysis in 1N and 2N hydrochloric acid was suitable for measurements to be made. As these compounds are optically active it seemed reasonable to study the reaction by following the change in optical rotation with time (all the compounds chosen had suitable optical rotations). This method of kinetic analysis however has revealed some interesting features of the reaction.

The compounds studied were 2,4-, 3,4-, and 4,6-0-butylidene-D-glucitol, that is all the known monobutylidene acetals of D-glucitol, and also 2,4-0-isobutylidene-D-glucitol and 2,4-0-but-2'-enyldene-D-glucitol, to compare the effect of branching and unsaturation in the acetal chain. From work previously carried out it was expected that the hydrolysis of any one of these compounds would liberate optically active D-glucitol, and the corresponding aldehyde. In his work
Hookett assumed this was so since the final rotation obtained in the hydrolysis of 4,6-O-ethylidene-D-glucitol was near to that of D-glucitol itself, but slightly on the side of the acetal compound.

The kinetics of the acetal hydrolysis in aqueous hydrochloric acid media appeared to be adequately represented by a first order equation. Thus throughout the first order rate constant, $k$, was evaluated from the well known first order equation:

$$\ln \frac{\alpha_0 - \alpha_\infty}{\alpha_t - \alpha_0} = kt$$

where $\alpha_0$, $\alpha_t$, and $\alpha_\infty$ are the observed optical rotations at times $t = 0$, $t = t$, and $t = \infty$, respectively. Graphs of $\log(\alpha_t - \alpha_0)$ against time were plotted, then

$$k = 2.303 \times \text{slope of graph}$$

As can be seen from Graphs 1, 7 and 8 good straight lines were obtained.

The fact that this reaction is first order with respect to the acetal was confirmed by determining the rate constant at various acetal concentrations. The results are shown in Graph 1, where it can clearly be seen that the rate constant is independent of the concentration of the acetal. 2,4-O-Butylidene-D-glucitol (IV) was used for these determinations, in 2N hydrochloric
acid at 38.6°. The figures obtained are shown in Table 1. These results may be taken as typical examples of those obtained.

The relationship between Hammett's acidity function, $H_0$, and the rate constant, $k$, has been employed to show that this cyclic acetal hydrolysis reaction does follow an $A-1$ mechanism (using Ingold's terminology). It was found for the hydrolysis of compound IV that log $k$ increases linearly with $-H_0$, and that the slope of the straight line is very close to unity (Graph 2). This means that the reaction is acid catalysed and is characterised by an essentially unimolecular rate step involving the conjugate acid of the acetal.

$$A + H^+ \rightleftharpoons AR^+ \quad \text{Equilibrium}$$

$$AR^+ \rightarrow X^+ \quad \text{Rate determining}$$

$$X^+ + H_2O \rightarrow \text{products} \quad \text{Fast}$$

where $A$ is the acetal and $X^+$ is a kinetic intermediate.

Thus the mechanism for the hydrolysis of IV is the same as that found by Ceder, for the hydrolysis of 2-substituted 1,3-dioxolans and 1,3-dioxans, with the rate determining step being the formation of the carbonium ion from the protonated acetal species (see p. 23). Since all the acetals under consideration are unsymmetrical two mechanisms are possible, depending upon which of the
carbon-oxygen bonds undergoes heterolysis in the rate determining step.

i.e. either

\[
\begin{align*}
 & \text{slow} \\
 & \text{fast} \\
 \end{align*}
\]

where R and \text{CHR} represent alkyl chains or heterocyclic rings, and are not essential.

Since the protonation of either oxygen is almost equally likely, hydrolysis occurs most probably by both these mechanisms simultaneously, since the
or

\[ \begin{align*}
\text{P}_1 & \quad \text{CHR} \\
\text{H}_2\text{O} - & \quad \text{CHR} \\
\text{H}_2\text{O} - & \quad \text{CHR} \\
\end{align*} \]

\[ \begin{align*}
\text{H}_2\text{O} & \quad \text{CHR} \\
\text{H}_2\text{O} & \quad \text{CHR} \\
\text{H}_2\text{O} & \quad \text{CHR} \\
\end{align*} \]

\[ \begin{align*}
\text{P}_1 & \quad \text{CHR} \\
\text{H}_2\text{O} & \quad \text{CHR} \\
\text{H}_2\text{O} & \quad \text{CHR} \\
\end{align*} \]

\[ \begin{align*}
\text{H}_2\text{O} & \quad \text{CHR} \\
\text{H}_2\text{O} & \quad \text{CHR} \\
\text{H}_2\text{O} & \quad \text{CHR} \\
\end{align*} \]

where \( \text{P}_1 \) and \( \text{P}_2 \) are polyol chains or hydrogen atoms, and are dissimilar.

Since the protonation of either oxygen is almost equally likely hydrolysis occurs most probably by both these mechanisms simultaneously, since the
difference between the stabilities of the two carbonium ions depends upon their structures, which are similar. Here the case of 4,6-O-butyldiene-D-glucitol may be different since a primary grouping is involved. It was not possible to distinguish between these pathways with the techniques available.

In comparing the rates of hydrolysis of the three different acetals containing the \(\beta\)-ring, namely 2,4-O-butyldiene-D-glucitol (IV), 2,4-O-isobutyldiene-D-glucitol (VIII), and 2,4-O-but-2'-enyldiene-D-glucitol (X) it was apparent that the but-2'-enyldiene radical resulted in a much less stable cyclic acetal than the other two radicals, as was expected. It was found that the hydrolysis of X in \(N\) hydrochloric acid was too fast to be followed with the apparatus available, so the rate of hydrolysis of this compound was compared with that of IV in 0.1\(N\) acid. The results showed that compound X hydrolyses nearly 10\(^3\) times faster than IV under these conditions (Table 3).

This may be readily accounted for by the unsaturation of the acetal carbon chain, which results in conjugative stabilisation of the carbonium ion. This makes the acetal carbon atom relatively more negative than would otherwise be the case, and supplements the effect due to the oxygen atom, assisting the carbonium
ion formation and promoting a considerably faster rate of reaction than when the acetal carbon atom is stabilised by resonance with the ether oxygen only.

\[
\begin{align*}
\text{CH}_2\text{CH}:\text{CH}_2\text{CH}_3 + \text{H}^+ &\rightarrow \text{CH}_2\text{CH}:\text{CH}_2\text{CH}_3^+ \\
\text{O} &\rightarrow \text{CH}_2\text{CH}:\text{CH}_2\text{CH}_3 \\
\text{O} &\rightarrow \text{CH}_2\text{CH}:\text{CH}_2\text{CH}_3 \\
\rightarrow &\text{OH} \\
\rightarrow &\text{OH} \\
\rightarrow &\text{H}_2\text{O} \\
\rightarrow &\text{CH}_3\text{CH}:\text{CH}_2\text{CHO} + \text{H}^+
\end{align*}
\]

As this electron releasing substituent does bring about a faster rate of hydrolysis these results may be taken as a confirmation that the reaction is unimolecular$^{64}$. Table 3 also shows that compound IV hydrolyses slightly faster than VIII (by a factor of 1.5). It had been thought that they would hydrolyse at almost identical rates since the isobutylidene grouping would be expected
to have very little difference in effect to that of the butylidene group. If there were any difference in rates then it was thought that the isobutylidene acetal would hydrolyse the faster, due to the inductive effect of the two methyl groups aiding the rupture of the carbon-oxygen bond.

\[
\begin{align*}
\text{CH}_3 \quad & \quad \text{OH} \quad \text{CH} \quad \text{O}^- \\
\text{CH}_3 \quad & \quad \text{OH} \quad \text{CH} \quad \text{O}^-. 
\end{align*}
\]

If in fact this did have any effect it would only be very slight since it is one carbon atom removed from the reactive centre. At present the difference in rates can only be accounted for by suggesting that the methyl groups of compound VIII inhibit the solvolysis of the protonated acetal form, thus making this species less stable and therefore less prevalent, which could then lead to a slower overall reaction rate.

When comparing the rates of hydrolysis of compounds IV and VIII at different temperatures it was found that a graph of the ratio of their rate constants, \( k_{\text{IV}} \) and \( k_{\text{VIII}} \) respectively, plotted against temperature is linear. This was found to be so at two acid strengths, 1.0N and 2.0N hydrochloric acid, but the slopes of the graphs are not the same: increasing the temperature
increases the rate constant \( k_{IV} \) more, with respect to that of compound VIII, in 1.0N acid than in 2.0N – see Graph 4. No adequate explanation of this can be put forward at the moment. It is felt that many more cyclic acetals must be analysed in this manner before worthwhile conclusions can be drawn from such results.

From a comparison of the rate constants for both compounds IV and VIII at three different temperatures it was found that increasing the acid strength from 1.0N to 2.0N caused about a 3.3 fold increase in the rate constant. These results are shown in Table 5.

Jones in similar work on the hydrolysis of acetals found that increasing the acid strength 10 times, from 0.0001N to 0.001N, increased the rate constant about 10 fold. Interpreting these and the present results in terms of rate increase with \( \text{pH} \), they are of the same order (10 : 6.6). This is considered to be quite good agreement when allowance is made for the difference in the concentrations of acid used, and the fact that the \( \log k / H_0 \) relationship applies to this reaction.

Also, from a study of the figures obtained from the hydrolysis of compounds IV and VIII, it was found that increasing the temperature brought about a similar increase in rate constant to that found by Jones in his work. He reported a 2~4 fold increase in rate
constant for a 10° rise in temperature and from Table 6 it can be seen that a comparable increase has been found for compounds IV and VIII. Here it should be noted that the temperature intervals are 8.6° and 11.0°, from 30.0°-38.6° and from 38.6°-49.6°, which give rise to 2.4~3.7 fold increases in the rate constants.

The hydrolysis of 3,4-0-butylidene-_-glucitol (VII) and 4,6-0-butylidene-_-glucitol (IX) gave surprising results since neither hydrolysed significantly faster than compound IV. These results are shown in Graphs 7 and 8. The relative rate constants for IV : VII : IX in 2N hydrochloric acid are 1.00 : 1.27 : 1.05, and in 1N acid 1.00 : 1.30 : 1.27. (The reason for the variation in the ratios for compound IX is not known.) These relatively small increases in the rate constants were unexpected since it was thought that a βG-ring should be considerably more stable than either a β- or an αT-ring, and thus compounds VII and IX were expected to hydrolyse appreciably faster than compound IV. However if the rate of hydrolysis were governed by the stability of the carbonium ion formed in the rate determining step, and not by the size and position of the ring, these results would be reasonable since in each case very similar carbonium ions would be formed. Such a possibility is supported by the fact that
2,4-\(\theta\)-but-2'-enyldene-\(\beta\)-glucitol, which yields a carbonium ion which can be stabilised by resonance, does hydrolyse many times faster (see p. 89).

The higher rate constants for the opening of the 3,4-ring (IV : VII = 1.00 : 1.29) may be due to the carbonium ion formed being more stable due to the greater ease of \(p\)-orbital overlap, from the hemiacetal oxygen to the carbonium ion, in a planar five-membered ring compared with a six-membered ring which has the chair conformation. Leggeter et al.\textsuperscript{66} have drawn attention to this greater ease of opening of 1,3-dioxolan rings compared with 1,3-dioxan rings, in treatment with lithium aluminium hydride and aluminium chloride.

When the hydrolysis of 4,6-\(\theta\)-butylidene-\(\beta\)-glucitol was being studied the results were compared with those found by Hockett et al.\textsuperscript{41}, for the hydrolysis of 4,6-\(\theta\)-ethyldene-\(\beta\)-glucitol. In the present study it has been found that the former acetal (IX) was more readily hydrolysed as the acid strength was increased (ratio of rate constants for acid normalities 0.5 : 1.0 : 2.0 = 74.6 : 189 : 528). This is in direct contrast to the results shown graphically in the Hockett paper: they show the ethyldene acetal to hydrolyse more rapidly in 0.5N sulphuric acid than in 1.0N. However
there seems no reason to question the validity of the results reported in this thesis since they are in agreement with the generally accepted results obtained for acid catalysed reactions and they are comparable with the results found for the other compounds under investigation. Unfortunately Hookett only quotes the calculated rate constant for the hydrolysis in 1.0N acid and makes no comment on the relative rate constants for the two acid strengths.

It is interesting to compare the rate constants obtained for the hydrolysis of these 4,6-acetals. Hookett reports that the rate constant for the hydrolysis of 4,6-0-ethylidene-D-glucitol in 1.0N sulphuric acid \( (H_0 = +0.13) \) at 24\(^\circ\) as \( 5.4 \times 10^{-4} \text{ min}^{-1} \). The calculated rate constant for the hydrolysis of 4,6-0-butylidene-D-glucitol in hydrochloric acid of the same \( H_0 \) strength at 38.6\(^\circ\) is \( 6.5 \times 10^{-4} \text{ min}^{-1} \) (evaluated from a graph of \( \log k \) plotted against \( H_0 \)). It should be noted that these rate constants were determined in different mineral acids and thus a comparison of their values, even at the same \( H_0 \) value, is not absolute, as has been shown by Timell for the acid hydrolysis of glycosides\(^67\). Allowance must also be made for the difference in temperatures, as has been discussed on page 92 (i.e. there is a 2.5\( \sim \)3.5 fold increase in rate constant for
a 10° rise in temperature). It can then be seen that increasing the acetal chain length has resulted in only a very small increase in rate constant - between a 1.5 and a 4 fold increase. This was to be expected since lengthening the acetal chain would be unlikely to cause any radical change in the stability of the acetal ring.

As has been shown by the straight line first order plots of Graphs 1, 7, and 8, and by the $H_0$ agreement of Graph 2, these hydrolyses appeared to be simple first order reactions going to near completion, without any significant formation of side products. However on closer examination of the evidence it became clear that the situation was not quite so simple.

For all the acetals, except 4,6-0-butylidene-$D$-glucitol (IX), it was noted that if the initial specific rotation of the compound in the hydrolysis reaction mixture were calculated by extrapolating the graphs of $\log[100(\alpha_t - \alpha)]$ against time back to zero time it differed from the value obtained for the specific rotation of that compound in water. It was also found that the difference changed when the acid strength was varied, e.g. for compound IV $[\alpha]_5^{5461} -9.2^0$ (in water), $[\alpha]_5^{5461} -10.8^0$ (in N HCl), $[\alpha]_5^{5461} -11.3^0$ (in 2N HCl); see Table 9. For compounds IV and VIII it was also shown
that the difference in rotation values altered with temperature (Table 10), and it seems reasonable to assume that this would apply to the other compounds under investigation, excluding the 4,6-acetal.

It may be seen that the extrapolated value gives a more negative specific rotation in each case. This could indicate that the change is brought about by the presence of another compound of negative rotation; however it would seem that such an additional compound is not involved in the hydrolysis of the 4,6-acetal.

Another possible explanation is that in all the acetals, except the 4,6-acetal, the hydrogen bonding which most probably occurs between the hydrogen atom of the primary hydroxyl group of carbon 6 and the ring oxygen of carbon 4 is destroyed when protonation of the acetal ring occurs. This could alter the asymmetry of the molecule and so result in a different specific rotation, although since acetals are only very weak bases the proportion of protonated acetal present would be small. If this is the case presumably hydrogen bonding in the 4,6-acetal does not affect the asymmetry of the molecule. It was hoped that if this were the cause of the anomalous results for the 2,4- and 3,4-acetals that evidence of the hydrogen bonding might be found in the infrared spectra of the compounds, and
that a variation in their spectra would be seen when they were in acidic media. However no splitting of the hydroxyl peak was found, using a Unicam S.P. 100. Thus this possibility has not been confirmed; but neither can it be dismissed.

Dr. Lewis\textsuperscript{57} found similar anomalous results when he attempted to hydrolyse 2,4-\textsuperscript{O}-methylene-\textsuperscript{D}-glucitol with hydrochloric acid, although the change of rotation was so small in acids of comparable strength to those used above that no definite parallel could be established.

In an effort to clarify the situation the reaction mixtures were examined by paper chromatography. The solvent systems used were methyl ethyl ketone and the same solvent containing 4\% phenylboronic anhydride. These techniques did help to elucidate the matter since the former solvent will separate a 2,4-acetal of \textsuperscript{D}-glucitol from 3,4- and 4,6-acetals, and the latter will separate the 3,4-acetal from the other two. The limitation in this is that no solvent system has yet been found that will separate the 4,6-acetal from both the 2,4- and the 3,4-acetals.

The chromatography showed that in each case a mixture of cyclic acetals as well as \textsuperscript{D}-glucitol and \textsuperscript{n}-butyraldehyde were present in the equilibrium mixture. Hydrolysis of the 2,4-acetal (IV) under the acid
conditions used yielded some 3,4-acetal (VII), hydrolysis of the 3,4-acetal yielded some 2,4-acetal, and hydrolysis of the 4,6-acetal (IX) yielded both the 2,4- and 3,4-acetals. (As explained above the presence of the 4,6-acetal could not be detected.) From this it must be supposed that the equilibrium set up in each case contains a mixture of these three (and possibly more) cyclic acetals.

\[
\begin{align*}
2,4\text{-acetal} & \rightleftharpoons D\text{-glucitol} + n\text{-butyraldehyde} \\
3,4\text{-acetal} & \rightleftharpoons 4,6\text{-acetal}
\end{align*}
\]

This situation is not unrealistic since the 3,4-acetal has been detected in the reaction mixture for the synthesis of the 2,4-acetal (Expt. 16). It is realised at this stage that the equilibrium mixture may contain further cyclic acetals, which are as yet unknown and undetected, for example the 1,3-acetal.

A comparison of the optical rotations of the equilibrium mixtures obtained in the hydrolysis of compounds IV, VII, and IX shows that they approximate to the same value (see Table 11). This supports the theory that in each case an equilibrium between a mixture of cyclic acetals is reached, as shown above.

It now becomes obvious that the matter under discussion is rather more complicated than was originally
believed. It is no longer possible to postulate that
the hydrolyses are

\[
\text{acetal} \rightleftharpoons D\text{-glucitol} + n\text{-butyraldehyde}
\]

with the equilibrium favouring the right hand side
and with no rotationally significant intermediates,
although Hookett assumed otherwise, with good reason,
in his work (see p. 24). There is now definite evidence
of the presence of further optically active compounds.
Also the assumption that the reaction goes to near
completion is no longer valid since it was based on
the optical rotation of the equilibrium mixture being
due to the remaining acetal and \(D\text{-glucitol} \) only; it is
not possible to deduce the composition of the equilibrium
mixture from the optical rotation alone when it contains
more than two optically active compounds. From this it
becomes evident that these reactions cannot be
satisfactorily studied using a polarimeter only, since
in each case there are at least three different optically
active compounds present.

Further information about the composition of
the equilibrium mixture was gained by examining its
ultraviolet spectrum. From the optical density measurements
made on the \(n\text{-butyraldehyde} \) absorption band at 2,820\( \text{\AA} \) it
was estimated that the equilibrium mixture obtained in
the hydrolysis of compound IV in \(N\) hydrochloric acid
at 38.6° contained 35% free n-butyraldehyde. This value is not absolute since it was found that n-butyraldehyde itself is not stable under the conditions used, it forms a new compound with a strong absorption band at 2,370-2,380°. This is now thought to be due to the n-butyraldehyde slowly undergoing an aldol condensation reaction in the acid medium. However these results do show that the reaction does not proceed to near completion.

When interpreting the results obtained certain assumptions may be made. In the initial stages of the reaction the observed optical rotation may be assumed to be due to the acetal taken, since the percentages of the other acetals present must be small and hence the rotation due to them may be ignored. Thus in the early stages of the reaction the change in optical rotation must be proportional to the decrease in the concentration of the acetal taken. Then, providing the hydrolysis reactions are kinetically controlled, first order rate constants may be evaluated from the slopes of the graphs. Indeed this situation appears to occur for a sufficiently long time to give good first order plots.

The Arrhenius energies of activation and the frequency factors have been evaluated from the rate constants obtained for the hydrolysis of 2,4-0-butyldene-
$\beta$-glucitol and of $2,4-O$-isobutyldiene-$\beta$-glucitol at different temperatures. The Arrhenius energies of activation were calculated using the Arrhenius equation:

$$\ln k = -\frac{E_a}{RT} + \text{const.}$$

where $k$ is the rate constant determined at temperature $T$, $E_a$ is the Arrhenius energy of activation, and $R$ is the gas constant.

A graph of $\ln k$ against $1/T$ was plotted and $E_a$ was calculated from the slope of the graph, in each case. The frequency factors were then calculated using the appropriate value of $E_a$ found above and substituting into the other form of the Arrhenius equation:

$$k = Ae^{-E_a/RT}$$

where $A$ is the frequency factor.

The results obtained are shown in Graph 12 and Table 12. From the Table it can be seen that a higher activation energy is required for the hydrolysis of the butyldene acetal, and also a higher frequency factor, although this compound hydrolyses slightly faster. On page 90 it was suggested that the higher rate constant was due to solvolyis stabilising the protonated acetal form of compound IV and thus causing a higher proportion of that form to be present. This
suggestion is compatible with the present results since
the observed activation energy would include the solvation
energy of the solvated reactive species for the hydrolysis
of compound IV, whereas such a term would not be included
in the activation energy for the hydrolysis of
2,4-0-isobutylidene-D-glucitol, if solvolysis were
inhibited by the two methyl groups; thus the former
case would require a higher activation energy. Similarly
such a situation would lead to a higher frequency factor
for compound IV since this term is dependant upon the
change in entropy. A greater entropy change would be
expected between a solvated protonated acetal form and
the final products than between a non-solvated protonated
acetal form and the final products.

The changes in the optical rotation of the
reaction mixture for the formation of butylidene cyclic
acetals of D-glucitol were also recorded. For this
equimolar solutions of D-glucitol and n-butyraldehyde
in 2N acid were taken so as to give a 2% solution of
acetal, if acetal formation were complete. It was
found that there was a very rapid rise in negative
rotation initially, followed by a slower decrease in
rotation following a similar curve to that found in
the hydrolysis of compound IV (Graph 13). The specific
rotation of the equilibrium mixture was the same as
that obtained in the hydrolyses of the butylidene acetals. This reaction was studied in both hydrochloric and sulphuric acids to find whether the rotational peak was associated with the acid radical. In both cases identically shaped peaks were obtained and thus this possibility was excluded.

The rapid attainment of such a peak in this reaction, followed by the fall off to the equilibrium rotation, is characteristic of a kinetically controlled first stage followed by a thermodynamically controlled second and final stage. The first stage is one in which the free energy of activation is lower than at any subsequent stage and so a faster reaction takes place, but the product obtained is less stable than the ultimate product of the reaction.

The only known compound with a high negative rotation is the 4,6-acetal (IX), and thus of the known acetals this appears to be the only one which could account for the results, if it were formed initially. This then indicates that the 4,6-acetal is an intermediate product which rearranges to give compounds with less negative rotations which are thermodynamically more stable. If this is correct then presumably the 4,6-acetal is formed initially because a primary hydroxyl group is more reactive to acetal condensation than a secondary
hydroxyl group. This is in agreement with results found by Foster, which show that in acetal formation the protonated aldehyde attacks the primary hydroxyl groups first, and that the rings formed rearrange to form the thermodynamically most stable rings. These results strongly suggest that the 1,3-acetal must also be formed since the two primary hydroxyl groups should show similar reactivity.
From this work on cyclic acetals of D-glucitol it may be concluded that in each case the condensation of the aldehyde with the polyol results in the formation of a number of different cyclic acetals, with the predominant products at equilibrium being the thermodynamically most stable cyclic acetals. Since the kinetic studies have indicated that the 2,4- and 3,4-0-butylideneacetals have similar stabilities it must be assumed that the greater yield of the 2,4-acetal is due to its lower solubility in the reaction mixture, which would then shift the equilibrium of the mixture in the direction of its formation.

Thus there are two factors which govern which product (or products) will predominate: firstly the thermodynamic stabilities of the various cyclic acetals which may be formed, and secondly the solubilities of the various products in the reaction mixture. Clearly the latter consideration does not apply to homogenous reaction mixtures. For di- and triacetals the problem becomes much more complicated than for monoacetals since the stability of more than one ring must be considered, and also the structure of the final product
may be affected by that of the monoacetal made preferentially under the conditions used. From this work, and that of Dr. Lewis, it appears that the 1,2:3,4:5,6-triacetal (containing two \( \alpha \)-rings and an \( \alpha \)-ring) is a more favoured triacetal than had previously been thought.

Unfortunately it has not been possible to establish the relative proportions of the various acetals present in a reaction mixture at equilibrium. It had been hoped that certain deductions concerning the monoacetals could be made from the kinetic work. However any deductions made would be of little value since the 1,3-acetal, of unknown optical rotation, is almost certainly present.

Since this work has shown that ring migration does occur under the acid hydrolysis conditions often used in structural determination of cyclic acetals it must be concluded that results so obtained may only be taken to indicate structures, they do not prove the structures of the compounds rigorously.
E. CONDENSATIONS WITH ACROLEIN

The section of work concerned with the condensation products of acrolein and polyhydric alcohols is being discussed separately from the previous work since the majority of the products obtained were polymeric, and thus they cannot be compared with those previously described. This \( \alpha,\beta \)-unsaturated carbonyl compound was used to comply with the requirements of the Sugar Research Foundation of America's project. When it was found that the condensation reactions yielded much polymeric matter the work was directed towards their production because the Research Foundation was interested in such resinous materials. It soon became evident that this work required a more thorough understanding of cyclic acetals, and then attention was turned to those acetals previously discussed.

Fischer and Smith\textsuperscript{43} reported isolating a tri-O-allylidene-\( D \)-glucitol, in 33\% yield together with much polymer, from the condensation reaction between acrolein and \( D \)-glucitol, using toluene-\( p \)-sulphonic acid as catalyst and azeotropic distillation to remove the water as it was formed. This work was repeated, but the products obtained were in a much lower yield and became very viscous on keeping; they
were thought to be either polymeric or to polymerise on keeping.

In attempts to improve the yield of the triacetal nitrobenzene was added to the reaction mixture since this appeared to increase the solubility of the \(D\)-glucitol in the benzene solution. Also a few drops of thiophen were added as a free radical trap, to inhibit the polymerisation should this be brought about by a free radical chain reaction. This reaction yielded a compound which was thought to be a tri-\(\text{D}-\)allyliden-\(\text{D}-\)glucitol; the product was obtained in a 9\% yield and became extremely viscous quite rapidly, this was thought to be due to polymerisation (see Expt. 44b).

It was found that when acrolein alone is heated with toluene-\(p\)-sulphonic acid, in the same concentration as that used in the condensation reactions with \(D\)-glucitol, polymerisation occurs (Expt. 45a). The product so obtained behaves differently however, it forms a glass-like orange resin on standing for a short time at room temperature. Presumably this type of polymerisation accounts for some of the polymer formation in the condensation reactions between \(D\)-glucitol and acrolein.

Acrolein polymerises in a similar manner.
when treated with phosphoryl chloride at room temperature but in this case it is quite clear that the polymerisation is accompanied by contraction as fissures appear in the resin during the final stages of its formation, and at the same time it shrinks away from the walls of its container. After about three weeks no further changes in the resin were noted, even after storing for two years.

When phosphoryl chloride is added in catalytic quantities to a suspension of D-glucitol in acrolein, at room temperature, it causes the D-glucitol to be taken slowly into solution, and at the same time the solution becomes more viscous. After a few hours the reaction mixture is a very viscous pale yellow solution, and the viscosity increases on further standing (Expt. 46a). Since all the D-glucitol is taken into solution presumably a reaction between it and the carbonyl compound takes place, this is probably a condensation reaction since it is known that phosphoryl chloride does promote such reactions (e.g. in the formation of tri-O-furfurylidene-D-glucitols and tri-O-but-2'-enyldiene-D-glucitols46). The increasing viscosity of the product was assumed to be due to its polymerisation. Chromatographic development of this solution, in n-butanol/ethanol/water, gave a long streak which could be detected with silver
nitrate reagent, acidic 2,4-dinitrophenylhydrazine, and aqueous potassium permanganate. The streaking seemed to indicate that the material is polymeric, and the detection to indicate that the \( \text{D-glucitol} \) is not fully substituted and also that some unsaturation remains in the product.

To gain more knowledge of this reaction samples were removed from the reaction mixture at intervals and developed chromatographically in 2-butanol/ethanol/water (Expt. 46b). This confirmed that a reaction between \( \text{D-glucitol} \) and acrolein does take place since the chromatograms showed a strong \( \text{D-glucitol} \) spot initially which decreased in intensity with time, and the products formed could be detected with acidic 2,4-dinitrophenylhydrazine which showed that they contain acrolein. It was noted that after only half an hour there was a strong streak of the polymeric material noted above. These chromatograms also indicated the presence of a reaction intermediate which runs at the same rate as monoacetal derivatives of \( \text{D-glucitol} \). Thus it is suggested that the initial reaction between \( \text{D-glucitol} \) and acrolein is a condensation reaction to yield a mono-O-allylidene-\( \text{D-glucitol} \). Unfortunately the long streak assumed to be due to polymeric material passes through the expected positions of any di- and
triacetal derivatives and thus they could not be detected if they were present. After 7½ hours the chromatograms showed the polymeric material to be the predominant product, with only a trace of \(\beta\)-glucitol and the reaction intermediate remaining.

On standing this polymeric material becomes more and more viscous until it is a rubbery solid, and finally this sets into a pale yellow, perfectly transparent resin. This resin is superior to that produced from acrolein alone in that there is no contraction during the final stages of polymerisation. It was found that if the viscous solution is warmed gently the polymerisation is much more rapid and the glass-like resin is obtained after about an hour. This resin is unaffected by water, dilute alkali and acid, and the common organic solvents. When heated it is unaffected until ca. 150°, with further heating it swells but only slightly; its colour remains unaltered until ca. 250°, from then on it slowly becomes more orange. It was tested at temperatures up to 300° and no significant changes were observed. It was also found that the resin could be machined quite satisfactorily, although here it has the disadvantage of giving off unpleasant acrolein vapours. The resin can be kept for several years without any apparent deterioration.

The action of phosphoryl chloride upon acrolein
mixed with other polyhydroxy compounds and their derivatives was next examined (Expt. 47). It was found that the monoacetal derivatives of D-glucitol, 2,4-\(\text{O}-\)but-2'-enylidene-D-glucitol and 2,4-\(\text{O}-\)furfurylidene-D-glucitol, behave in a similar manner to D-glucitol itself. They are taken completely into solution and polymerisation occurs, however the resultant resin remains slightly rubbery. The resin formed with 2,4-\(\text{O}-\)but-2'-enylidene-D-glucitol is clear and pale yellow in colour, but that formed using the furfurylidene acetal is dark brown and slightly opaque, presumably due to the phosphoryl chloride causing some decomposition of the furfurylidene compound. Thus it seems likely that resins with slightly different properties could be obtained by varying the acetal derivative of D-glucitol.

None of the other compounds tested, except for sucrose octaacetate, were taken completely into solution, although in each case a small portion appeared to dissolve; sucrose octaacetate did dissolve and the solution became slightly viscous, but no resinification occurred. With the polyhydroxy compounds examined - mannitol, glucose, fructose, sucrose - an orangy resin formed above the undissolved solid, and in all respects they appeared very similar to the resin formed from acrolein alone. However in each case where a derivative
of a polyhydroxy compound was used - $1,3:4,6$-$\text{di-O-methylene-}\text{D-mannitol}$, mannitol hexaacetate, glucose pentaacetate, sucrose octaacetate - no resinification occurred. The reason for this difference in behaviour is not known.

Acrolein does not form a crystalline monomeric monoacetal with $\text{D-glucitol}$, in the presence of $3\text{N}$ sulphuric acid, although propionaldehyde and crotonaldehyde both form crystalline monoacetal derivatives of $\text{D-glucitol}$ under such conditions. When acrolein was added to a syrup of $\text{D-glucitol}$ in $3\text{N}$ sulphuric acid no crystallisation took place, and on standing the solution slowly became more viscous until finally it became a rubbery solid. When the reaction mixture was neutralised after standing for one day it was found that the oil, which remained after all the volatile matter had been removed, could not be distilled. Using a pressure of 0.1 mm. the oil turned brown with decomposition at about 120°.

Glucose, fructose, and sucrose were treated with acrolein in the same manner as the $\text{D-glucitol}$ above. In all three cases the sugar would not dissolve completely when warmed with the sulphuric acid; since the sucrose must have been hydrolysed under such conditions it was assumed that the undissolved solid in this case was a mixture of glucose and fructose. Thus in each case
the acrolein was added to a mixture containing some suspended solid, and therefore it was decided to shake the reaction mixture for 12 hours at room temperature before leaving it to stand. In each case an orange coloured, slightly rubbery resin formed. The undissolved glucose remained finely distributed through the resin making it appear opaque, but the solid particles in the other two sank to the bottom leaving a clear resin above.
Chroomatography

Descending chromatography was used. Chromatograms were run on Whatman No. 1 paper, and the following solvent systems were used.

B.E.R.

- The stationary phase was water, and the
  moving phase was propanol/ethanol/water (40:17:13 w/w).

This solvent was found suitable for separating mono-, di-, and tri-acetals of β-glucitol, and their

capivenes.

**EXPERIMENTAL SECTION**

B.E.S./B.I.P.E.

- The stationary phase was diethyl sulfoxide (B.E.S.), and the moving phase was diisopropyl
  ether (B.I.P.E.) saturated with diethyl sulfoxide
  (ca. 1%). To achieve this stationary phase the chromatography
  paper was dipped in a 20% solution of diethyl sulfoxide
  in benzene, and then blotted to remove the surplus
  solution. Anhydrous magnesium sulphate was put in the
  trough with the diisopropyl ether solution since the
  presence of much moisture adversely affected the running
  of the chromatogram. The compounds to be developed were
  applied to the paper in chloroform solution.

This solvent was very satisfactory for separating

compounds containing two or fewer free hydroxyl groups.
Chromatography

Descending chromatography was used. Chromatograms were run on Watman No. 1 Paper, and the following solvent systems were used.

B.E.W.\textsuperscript{72} - The stationary phase was water, and the moving phase was \textit{n}-butanol/ethanol/water (40:11:19 \textit{v/v}). This solvent was found suitable for separating mono-, di-, and triacetals of \textit{D}-glucitol, and their derivatives.

D.M.S./D.I.P.E.\textsuperscript{73} - The stationary phase was dimethyl sulphoxide (D.M.S.), and the moving phase was diisopropyl ether (D.I.P.E.) saturated with dimethyl sulphoxide (ca. 1\%). To achieve this stationary phase the chromatography paper was dipped in a 20\% solution of dimethyl sulphoxide in benzene, and then blotted to remove the surplus solution. Anhydrous magnesium sulphate was put in the trough with the diisopropyl ether solution since the presence of much moisture adversely affected the running of the chromatogram. The compounds to be developed were applied to the paper in chloroform solution.

This solvent was very satisfactory for separating compounds containing two or fewer free hydroxyl groups.
If more free hydroxyl groups were present the compound would remain on the base line.

M.E.K. - The stationary phase was water, and the moving phase was methyl ethyl ketone/water (11:1 v/v).

This solvent was used to separate configurational isomers of monoacetals: 2,4-monoacetals run slightly slower than 3,4- or 4,6- monoacetals in this solvent.

M.E.K./(PhBO)₃ - Again the stationary phase was water, but the moving phase was a 4% solution of phenylboronic anhydride in methyl ethyl ketone/water (11:1 v/v).

This solvent was also used to separate configurational isomers of monoacetals, however in this solvent 3,4-monoacetals run slower than 2,4- and 4,6- monoacetals.

The following spray reagents were used to locate the compounds, after the chromatograms had been dried.

AgNO₃ - The chromatogram was dipped in a silver nitrate solution [saturated aqueous solution of silver nitrate (2.5 ml.) in acetone (500 ml.), with 2% water added], allowed to dry at room temperature, then it was sprayed with ethanolic sodium hydroxide [sodium hydroxide (2 g.) dissolved in water (2 ml.) and made up to 100 ml. with ethanol]. The chromatograms were preserved by dipping in
a dilute aqueous ammonia solution, after all the spots had appeared.

This spray detected compounds containing a vicinal pair of hydroxyl groups, or aldehyde groups, and compounds which yielded such groupings under the alkaline conditions of the spray.

$\text{KIO}_4/\text{AgNO}_3$ - The paper was very lightly sprayed with a saturated aqueous solution of potassium periodate, allowed to dry at room temperature, and then treated with $\text{AgNO}_3$, as above.

This spray was used to assist in the development of chromatograms run in M.E.K. and in M.E.K./($\text{PhBO}_2$)$_3$, where $\text{AgNO}_3$ alone was not entirely satisfactory.

$\text{DNP.H. 75}$ - The paper was sprayed with a saturated solution of 2,4-dinitrophenylhydrazine in 2N hydrochloric acid.

This spray was used to locate acetals, which are detected by the distinctively coloured spots of the 2,4-dinitrophenylhydrazone derivative of the aldehyde which is liberated by the acid hydrolysis of their acetal rings.

$\text{KPr 76}$ - The paper was sprayed heavily with potassium periodatocuprate [$\text{copper sulphate pentahydrate (12.5 g.)}$ was dissolved in boiling water (400 ml.), then potassium
periodate (23 g.) and a concentrated aqueous solution of potassium hydroxide (56 g.) were added. Next potassium persulphate (20 g.) was added very slowly to the hot solution, after which the solution was boiled for 20 min. After cooling the solution was decanted off and diluted to 500 ml. with water, then 500 ml. 2N potassium hydroxide was added. The KPr was stored in a polythene bottle in a refrigerator. The spots appeared as livid white on a dark yellowy background, and were preserved by lightly spraying the spots only with roseaniline [roseaniline (0.3 g.) dissolved in acetic acid (100 ml.) and then diluted to 1 litre].

This reagent was used to detect sugars and polyhydroxy compounds.

$\text{KMnO}_4$ - The paper was lightly sprayed with a dilute aqueous solution of potassium permanganate.

This reagent detects easily oxidisable compounds as white spots on a pink background. The spots were marked immediately as the background soon fades.

$\text{p-Anisidine}^7$ - The paper was sprayed with $\text{p-anisidine reagent} \left[\text{p-anisidine hydrochloride (2 g.) dissolved in a minimum of methanol, and the solution then made up to 100 ml. with } \text{p-butanol}\right]$, and then the paper was dried at ca. 100°.

This spray locates sugars in their distinctive
Column Chromatography

The necessary details of this technique are given in the experiments in which it is used.

Paper ionophoresis

Electrophoretograms were run on Whatman No. 3 Paper, using a high voltage electrophoresis machine.

Sodium metavanadate buffer (1.5% aqueous solution of sodium metavanadate, pH 8.6) was used. The electrophoretograms were dried at ca. 100°C, until the location of the compounds could be seen clearly. To further locate the compounds the papers were dipped in a saturated solution of potassium permanganate in acetone; on drying at room temperature the spots appear as yellow on a brownish background, which soon fades.

This system was used to distinguish between D-glucitol and mannitol.

Elemental analyses

The analyses for carbon, hydrogen, and nitrogen were carried out by Alfred Bernhardt (Germany) or Weiler and Strauss (Oxford).

The analysis for boron present in phenylboronates was determined by hydrolysing the compound with 50% aqueous
ethanol, with gentle warming. When all the compound had
dissolved the solution was cooled to room temperature
and mannitol was added. The liberated phenylboronic acid
was then directly titrated against 0.1N sodium hydroxide,
using phenol phthalein as indicator. The titre was
adjusted using a blank containing the same amount of
mannitol, and then the percentage boron in the compound
taken was calculated.

**Infrared spectra**

The infrared spectra of the new compounds were
recorded using a Perkin Elmer Infracord spectrophotometer.

**Ultraviolet absorptions**

Optical densities in the ultraviolet region
were determined using a Unicam S.P. 500 or a Perkin Elmer
Ultracord spectrophotometer.

**Refractive indeces**

The refractive indeces of liquids were determined
using a thermostated Abbé refractometer and a sodium D line
lamp.

**Optical rotations**

Two instruments were used to determine optical
rotations. A Bellingham and Stanley polarimeter was used
for measurements using the sodium D line. For measurements
using the mercury 5461 line an Hilger Watts photoelectric polarimeter was used; this polarimeter was used for all the kinetic work, with a jacketed, thermostated cell.

The furfuraldehyde was obtained from C.I.L. Ltd. It was purified by distillation under reduced pressure (ca. 20 mm.), as it tends to polymerise when heated strongly. Freshly distilled furfuraldehyde darkens slowly in colour on standing.

The usual commercial grade of D-glucitol was used. Examination of this D-glucitol by paper chromatography in sodium metaperiodate at 3,500 volts for 11 hr. showed that some amintol was also present in this grade.

Experiment 1 Preparation of 2,4-D-furfurylidene-D-glucitol,

a) D-glucitol (19.7 g., 1 mol.) and 10 sulphuric acid (5.2 ml.) were gently warmed together until they gave a clear syrup. This syrup was then cooled to room temperature and the flask fitted with a stirrer. Furfuraldehyde (8.3 ml., 1 mol.) was added and the whole stirred vigorously during 1 hr., at room temperature. By this time the mixture had become solid with crystals, and was smooth in colour. Concentrated ammonia solution (3.7 ml.) was added and the whole mixed, to affect neutralisation of the sulphuric acid present. The crystals were washed with 95% ethanol, the liquor being deep pink in colour, and dried using a
A. **FURFURYLIDENE-D-GLUCITOLS**

**Materials**

The furfuraldehyde was obtained from B.D.H. Ltd., Poole; it was purified by distillation under reduced pressure (ca. 20 mm.), as it tends to polymerise when heated strongly\(^{15}\). Freshly distilled furfuraldehyde darkens slowly in colour on standing.

The usual commercial grade of $D$-glucitol was used. Examination of this $D$-glucitol by paper ionophoresis in sodium metavanadate at 3,500 volts for 1½ hr. showed that some mannitol was also present in this grade.

**Experiment 1** Preparation of 2,4-0-furfurylidene-$D$-glucitol, (I)$^{19,20}$.

a). $D$-glucitol (19.1 g., 1 mol.) and 3N sulphuric acid (5.2 ml.) were gently warmed together until they gave a clear syrup. This syrup was then cooled to room temperature and the flask fitted with a stirrer. Furfuraldehyde (8.3 ml., 1 mol.) was added and the whole stirred vigorously during 1 hr., at room temperature. By this time the mixture had become solid with crystals, and was mauve in colour.

Concentrated ammonia solution (1.1 ml.) was added and the whole mixed, to affect neutralisation of the sulphuric acid present. The crystals were washed with 95% ethanol, the liquors being deep pink in colour, and dried using a
Buchner funnel. They were then recrystallised from ethanol, m.p. ca. 170°. Yield 18.5 g. (68% theoretical). Further recrystallisation from the same solvent raised the m.p. to 185-187°. The product was then placed in a Soxhlet apparatus, using ether as solvent, and was extracted. On evaporation to dryness the ether solution yielded a solid which on crystallisation from ethanol gave white crystals of 2,4-O-furfurylidene-D-glucitol (I), m.p. 195-195°, determined using a Kofler block and microscope. (Found: C, 50.9; H, 6.0. Calc. for C11H16O7: C, 50.8; H, 6.20%). \( [\alpha]_D^{25} +1.90^\circ \) (c 2.2 in HZO).

\( R_f \) (B.E.W.) 0.58-0.60.

b). D-glucitol (50 g., 1 mol.) and 3N sulphuric acid (13.5 ml.) were warmed to a syrup and then cooled to room temperature. Furfuraldehyde (25 ml., 1.1 mol.) was added, and the whole stirred vigorously until a homogenous solution was obtained (ca. 10 min.). The mixture was then left to stand at room temperature. Crystals of the product started to crystallise out after about 5 min.; it was left to stand for about 1 hr. in all, by which time it was solid with crystals. Methanol (25 ml.) was added and the whole was worked to a paste, then concentrated ammonia solution (2.8 ml.) was added to neutralise the sulphuric acid present. The crystals were filtered off using a water pump, and were washed with ethanol (30 ml.). Yield 65.5 g.
(90% theoretical). The product was recrystallised from ethanol (10 parts) containing activated animal charcoal (10 g.). Further recrystallisations from the same solvent raised the m.p. to 190-191°. Yield 32 g. (45% theoretical).
This product was identical to I.

Experiment 2 Preparation of di-\(\alpha\)-furufurylidene-\(D\)-glucitol (II) and tri-\(\alpha\)-furufurylidene-\(D\)-glucitol (III).

2a) Variations on the experimental conditions of Expt. 1.

i) With tetrahydrofuran as solvent.

\(\alpha\)-glucitol (10 g., 1 mol.) and 3\(N\) sulphuric acid (2.7 ml.) were warmed to a syrup, then furfuraldehyde (23 ml., 5 mol.) and tetrahydrofuran (20 ml.) were added. The mixture was stirred for 2 hr. at room temperature.

ii) Heating the reaction mixture.

\(\alpha\)-glucitol (5 g., 1 mol.) and 3\(N\) sulphuric acid (1.4 ml.) were warmed to a syrup, then furfuraldehyde (11.5 ml., 5 mol.) was added and the whole heated gently for 4 hr. with stirring.

iii) With tetrahydrofuran as solvent, and heating the reaction mixture.

\(\alpha\)-glucitol (5 g., 1 mol.) and 3\(N\) sulphuric acid (1.4 ml.) were warmed to a syrup. Then furfuraldehyde (11.5 ml., 5 mol.) and tetrahydrofuran (20 ml.) were added and the whole was warmed gently for 4 hr., with stirring.
iv) With dimethyl sulphoxide as solvent.

\( \text{D-glucitol (1 g., 1 mol.)} \) was shaken with dimethyl sulphoxide (2 ml.) until a homogenous solution was obtained. Furfuraldehyde was added (2 ml., 4.4 mol.) and the mixture was stirred at room temperature for 4 hr.

v) Using trifluoroacetic acid as catalyst and dimethyl sulphoxide as solvent.

\( \text{D-glucitol (5 g., 1 mol.), furfuraldehyde (10 ml., 4.4 mol.), dimethyl sulphoxide (10 ml.), and trifluoroacetic acid (0.2 ml.)} \) were stirred together for 4 hr. at room temperature.

vi) Using 6N sulphuric acid.

\( \text{D-glucitol (5 g., 1 mol.) and 6N sulphuric acid (1.4 ml.)} \) were warmed to a syrup, then furfuraldehyde (10 ml., 4.4 mol.) was added and the whole was stirred at room temperature for 4 hr.

These reaction mixtures were examined by paper chromatography, using B.E.W. solvent and \( \text{AgNO}_3 \), \( \text{D.N.P.H.} \), and \( \text{KMnO}_4 \) sprays. In each case the formation of a mono-\( \text{O-} \)-furfurylidene-D-glucitol was indicated; in reaction mixtures ii, iii, v, and vi there was evidence that a trace of a further compound had been formed, with \( R_f \) ca. 0.85.
2b) Using zinc chloride as condensing agent.

i) Preparation of powdered, fused zinc chloride.

Zinc chloride sticks (50 g.) were placed in a porcelain dish and heated in a muffle furnace at 400° for 35 min. Then the molten zinc chloride was transferred to a vacuum desiccator, which was rapidly evacuated. When the zinc chloride had ceased foaming it was removed from the desiccator and powdered as quickly as possible. It was used immediately.

ii) Preparation of the furfurylidene derivatives of D-glucitol.

Powdered D-glucitol (25 g., 1 mol.) was mixed thoroughly with the freshly prepared zinc chloride, then furfuraldehyde (250 ml., 22 mol.) was added. The reaction mixture was warmed on a water bath at ca. 45° for 1 hr., with shaking. During this time the furfuraldehyde became darker in colour, finally becoming dark brown. The reaction mixture was then left to stand at room temperature for a further 5 hr., with occasional shaking. Water (50 ml.), chloroform (70 ml.), and petroleum ether (b.p. 60-80°) (20 ml.) were added, the whole shaken thoroughly, and the water layer then removed.

The chloroform/petroleum ether extract was washed with 10% sodium carbonate solution, and the solid which was precipitated was removed by filtration. The filtrate was repeatedly washed with sodium carbonate solution until it
was zinc chloride free, and then finally it was washed with water. Next all the volatile material was evaporated from the extract by using a rotary evaporator connected to an oil pump, and warming to 45-50°.

The residue was extracted with boiling diisopropyl ether. On standing the extract yielded crystals, and a further crop was obtained by concentrating the extract. They were recrystallised from ethanol, m.p. 167-169°. Further recrystallisations from the same solvent gave pure tri-O-furfurylidene-D-glucitol (IIIa), m.p. 173-174°, yield 0.3 g. (Found: C, 60.5; H, 4.85. C_{21}H_{20}O_{9} requires: C, 60.6; H, 4.84%. R_{f} (B.E.W.) 0.89; R_{f} (D.M.S./D.I.P.E.) 0.07-0.12.

The residue from the diisopropyl ether extraction was powdered and extracted with chloroform, to remove any remaining traces of triacetal derivatives. The remaining solid was taken up in a chloroform/ethanol mixture, which on cooling yielded crystals. These on recrystallisation from tetrahydrofuran gave pure di-O-furfurylidene-D-glucitol (II), m.p. 182-183°, yield 2.0 g. (Found: C, 56.4; H, 5.63. C_{16}H_{18}O_{8} requires: C, 56.8; H, 5.53%. R_{f} (B.E.W.) 0.79.

2c) Tests on possible catalysts.

Freshly distilled furfuraldehyde (10 ml.) was treated as follows at room temperature:

i) Thionyl chloride (1 drop) ... immediate charring
ii) Oxalic acid (1 crystal) ... no charring apparent

iii) Acetic acid (1 drop) ... no charring apparent, furfuraldehyde darkened

iv) Trifluoroacetic acid (1 drop) no charring apparent, more darkening than in iii

v) Toluene-n-sulphonic acid (1 crystal) very slow charring

vi) Phosphorous acid (1 drop) ... furfuraldehyde darkened

vii) p-Phosphoric acid (1 drop) ... furfuraldehyde darkened

viii) Methanolic hydrogen chloride ca. 4N (1 drop) charring

ix) Iodine (1 crystal) ... slow charring

x) Phosphoryl chloride (1 drop) very slow charring

2d) Using phosphoryl chloride as condensing agent.

D-glucitol (18.2 g., 1 mol.), furfuraldehyde (34 ml., 4.1 mol.), and benzene (75 ml.) were mixed together, then phosphoryl chloride (3 drops) was added. The reaction mixture was heated for 5 hr., with a Dean and Starke head to effect azeotropic distillation; 4 ml. water was collected (74% theoretical, based on conversion to triacetal product). The reaction mixture darkened in colour fairly rapidly, finally turning black. After cooling the solution was poured off, a black tar-like substance being left in the flask.

Activated animal charcoal was added to the solution and the whole was boiled for a few minutes, then hot filtered, twice. The solution was then an orange-pink colour, and yielded crystals on standing, m.p. 176-177°.
The remaining solution was evaporated until a viscous oil was obtained. This oil was extracted with diisopropyl ether and the extract rejected. The residue was taken up in ethanol and crystals separated out on standing, m.p. 153-155°. These were combined with the first crop of crystals, and repeated recrystallisation of this product from ethanol finally yielded a pure tri-O-furfurylidene-D-glucitol (IIIb), m.p. 181-182°, yield 0.4 g. (Found: C, 60.3; H, 4.87. \(\text{C}_{21}\text{H}_{20}\text{O}_9\) requires: C, 60.6; H, 4.84%). 

\[ R_f (B.E.W.) 0.89; R_f (D.M.S./D.I.P.E.) 0.47. \]

2e) Using toluene-\(\beta\)-sulphonic acid as condensing agent.

D-glucitol (10 g., 1 mol.), furfuraldehyde (15 ml., 5.5 mol.), and benzene (50 ml.) were mixed together. Toluene-\(\beta\)-sulphonic acid (ca. 0.1 g.) was added, and the reaction mixture was heated in an isomantle. A Dean and Starke head was provided to effect azeotropic distillation. The reaction mixture darkened after ca. 30 min. The source of heat was removed after 3 hr., 1.7 ml. water having been collected (57% theoretical, based on conversion to triacetal product).

The reaction mixture was allowed to stand overnight and was then filtered. The black gummy residue was washed twice with warm benzene, and these washings were added to the original filtrate. A small volume of pyridine was added to neutralise the acid present. The mixture was
then evaporated to dryness, using an oil pump. The residue was then taken up in methanol and again evaporated, then taken up in benzene and evaporated to dryness once more.

The resulting solid was crystallised from benzene (25 ml.), m.p. 148-150° (1.2 g.). This solid was extracted with boiling benzene and the residue rejected. The filtrate yielded crystals, m.p. 161-180°. Further recrystallisations from ethanol, and treatment with activated animal charcoal, raised the m.p. to 182-183°. This product was identical to the tri-\(\alpha\)-furfurylidene-\(D\)-glucitol, IIIb, obtained above. Yield 0.11 g.

The benzene mother liquors, from the first crystallisation of the above solid, were concentrated and passed down an alumina column, benzene being the eluting solvent. Earlier fractions yielded a solid which was crystallised from dioxan (10 ml.) + petroleum ether (b.p. 60-80°) (8 ml.), m.p. 79-88°. Further recrystallisations from ethanol, and treatment with activated animal charcoal, raised the m.p. to 136-138°, a pure tri-\(\alpha\)-furfurylidene-\(D\)-glucitol (IIIC). Yield 0.6 g. (Found: C, 60.3; H, 4.87. \(C_21H_{20}O_9\) requires: C, 60.6; H, 4.84%). \(R_f\) (B.E.W.) 0.89; \(R_f\) (D.M.S./D.I.P.E.) 0.58.

Later fractions yielded a solid which on crystallisation from ethanol proved to be identical with IIIb; yield 0.13 g.
2f) Tests on solutions of D-glucitol.

i) Initially warming D-glucitol with furfuraldehyde.

D-glucitol (9 g., 1 mol.) and furfuraldehyde (17 ml., 4 mol.) were warmed together gently, and a homogenous solution was obtained. On addition of a little benzene the D-glucitol was thrown out of solution in a gummy state.

ii) Using dimethyl formamide as solvent.

D-glucitol (9 g., 1 mol.), furfuraldehyde (17 ml., 4 mol.), and dimethyl formamide were warmed together gently until a homogenous solution was obtained. A little benzene was added and again the D-glucitol was thrown out of solution.

2g) Using 2,4-â-furfurylidene-D-glucitol as starting material, in the absence of a catalyst.

2,4-â-Furfurylidene-D-glucitol (6 g., 1 mol.), furfuraldehyde (20 ml., 7.2 mol.), and benzene (40 ml.) were mixed together thoroughly. The reaction mixture was then heated on a steam bath, with a Dean and Starke head. No water was evolved, and the reaction mixture was not treated further since no reaction had taken place.

2h) Using 2,4-â-furfurylidene-D-glucitol as starting material and phosphoryl chloride as condensing agent.

2,4-â-Furfurylidene-D-glucitol (6 g., 1 mol.), furfuraldehyde (20 ml., 7.2 mol.), benzene (40 ml.), and
phosphoryl chloride (2 drops) were mixed together. Then the reaction mixture was heated on an isomantle, with a Dean and Starke head, until no further water was evolved (7 ml. collected, 83% theoretical based on conversion to triacetal product). After the reaction mixture had cooled to room temperature sodium hydrogen carbonate (ca. 4 ml. saturated solution) was added to neutralise the acid, and then the mixture was filtered.

The filtrate was evaporated down to a thick oil which was taken up in chloroform and the solution left to stand. No crystals separated out. All volatile matter was then removed from the mixture using a rotary evaporator. The residue was taken up in a little benzene, and then passed down an alumina column, using benzene as eluting solvent. Earlier fractions yielded an oil that could not be obtained in a crystalline form. Chromatograms, run in B.E.W. and D.M.S./D.I.P.E., indicated that this oil was a tri-\(\text{O-furfurylidene-}^{\text{D}}\text{-glucitol. Later fractions yielded compound IIIb in an impure state, yield 0.6 g.}

**Experiment 3** Determination of the constituents of compounds I, II, and III respectively, by hydrolysis followed by identification of the products.

3a) Compound I.

I (0.4 g.), water (10 ml.), and Zeo-Karb 225 resin (Permutit Co. Ltd.) in the hydrogen form (2 ml.) were heated
together on a boiling water bath for 2 hr. The resin was filtered off, and washed well with water, these washings were added to the filtrate. Chromatograms of this solution, run in B.E.W. and sprayed with AgNO₃ and D.N.P.H., indicated the presence of only a hexitol (furfuraldehyde is too volatile to remain on the paper).

The solution was distilled to separate the volatile aldehyde. The distillate was collected in a flask containing a saturated solution of 2,4-dinitrophenylhydrazine in 2N hydrochloric acid, the 2,4-dinitrophenylhydrazone derivative of the aldehyde being precipitated immediately. This precipitate was filtered off and crystallised from ethanol, m.p. 202-203°; furfuraldehyde-2,4-dinitrophenylhydrazone has m.p. 202-203°. A mixed m.p. with authentic furfuraldehyde-2,4-dinitrophenylhydrazone was not depressed. The yield was 0.04 g. (12% theoretical).

The residue, remaining in the flask after the distillation, was taken up in pyridine and dried with anhydrous magnesium sulphate. The solution was filtered, the magnesium sulphate washed with a little more pyridine and the washings added to the filtrate. Acetic anhydride (1.5 ml.) was added and the mixture left to stand for 2 days at room temperature. The solution was then poured into iced water (ca. 20 ml.) and cooled. The solid which separated out was crystallised from ethanol, m.p. 97-98°.
The mixed m.p. with authentic $\beta$-glucitol hexaacetate was not depressed. Yield 0.26 g (39% theoretical).

3b) Compound II, treated similarly to I above.

II (0.05 g.) was hydrolysed for 3 hr. Chromatograms showed the presence of a hexitol and a trace of unreacted II. The 2,4-dinitrophenylhydrazone derivative had m.p. 201°, and the mixed m.p. with authentic furfuraldehyde-2,4-dinitrophenylhydrazone was not depressed. The hexaacetate derivative had m.p. 97-99°, and a mixed m.p. with authentic $\beta$-glucitol hexaacetate was not depressed.

3c) Compound IIIa, treated as compound I above.

IIIa (0.05 g.) was hydrolysed for 12 hr. Chromatograms showed that only a hexitol had been formed in the reaction. The furfuraldehyde-2,4-dinitrophenylhydrazone and $\beta$-glucitol hexaacetate derivatives were formed, and mixed m.p. with their respective authentic compounds were not depressed.

3d) Compound IIIb.

IIIb (ca. 0.005 g.), 50% ethanol(2 ml.), and Zeo-Karb 225 resin in the hydrogen form (0.1 ml.) were heated together on a boiling water bath for 4 hr., with occasional shaking. The reaction mixture was then examined by paper ionophoresis in metavanadate at 3,500 volts for 1½ hr., and the presence of $\beta$-glucitol was indicated.
An excess of a saturated solution of 2,4-dinitrophenylhydrazine in 2N hydrochloric acid was added to the remaining reaction mixture. A mixed m.p. of the precipitated 2,4-dinitrophenylhydrazone with authentic furfuraldehyde-2,4-dinitrophenylhydrazone was not depressed.

3e) Compound IIIc, treated as IIIb above.

The paper ionophoresis showed that D-glucitol had been liberated in the hydrolysis; and a mixed m.p. of the 2,4-dinitrophenylhydrazone derivative with authentic furfuraldehyde-2,4-dinitrophenylhydrazone was not depressed.

**Experiment 4** Spectrophotometric determination of the number of furan ring systems per molecule of compounds I, II, and IIIa respectively.

The ultraviolet absorption of the compounds, in ethanolic solution, was measured at 2,200 Å. The molar extinction coefficient was calculated from

\[ \log \frac{I_o}{I} = \varepsilon \cdot c \cdot d \]

where \( \log \frac{I_o}{I} \) is the optical density,
\( \varepsilon \) is the molar extinction coefficient,
\( c \) is the concentration in moles per litre,
and \( d \) is the path length of the cell (1 cm.).

Furan was used as the reference compound. Commercial furan was obtained from Hopkin and Williams and was redistilled, b.p. range 31.5-32.5°. A middle fraction
was taken.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Moles per litre</th>
<th>log $\frac{I_o}{I}$</th>
<th>$\varepsilon$</th>
</tr>
</thead>
<tbody>
<tr>
<td>furan</td>
<td>$7.198 \times 10^{-5}$</td>
<td>0.710</td>
<td>9,860</td>
</tr>
<tr>
<td>I</td>
<td>$7.399 \times 10^{-5}$</td>
<td>0.611</td>
<td>8,260</td>
</tr>
<tr>
<td>II</td>
<td>$2.504 \times 10^{-5}$</td>
<td>0.425</td>
<td>16,600</td>
</tr>
<tr>
<td>IIIa</td>
<td>$1.843 \times 10^{-5}$</td>
<td>0.465</td>
<td>25,200</td>
</tr>
</tbody>
</table>

Thus the ratio of the molar extinction coefficients of the compounds is

$I : II : IIIa = 8,260 : 16,600 : 25,200 = 1 : 2 : 3$

which corresponds, approximately, to the presence of one, two, and three furan rings per molecule, respectively.

**Experiment 5** Determination of the number of free hydroxyl groups per molecule of compounds I, II, and IIIa respectively, by acetylation.

An approximately 0.1N sodium hydroxide solution was standardised against potassium hydrogen phthalate, using phenol phthalein as indicator. (Found: 0.0988N). A solution of acetic anhydride (ca. 1 g.) in pyridine (20 ml.) was prepared - Ac.

5a) Control.

Ac. (2 ml.) was boiled for 5 min. then poured into water (ca. 40 ml.). This solution was then titrated against the sodium hydroxide. Found: 2 ml. Ac. $\equiv 21.08$ ml. NaOH.

5b) Compound I.

I (0.0567 g.) and Ac. (2 ml.) were boiled together
for 1½ hr. and the solution was then poured into water (40 ml.). This solution was then titrated against the sodium hydroxide. Titre = 12.09 ml. NaOH.

- Moles CH₃CO₂H consumed per mole of I = 3.71

5c) Compound II.

II (0.0457 g.) and Ac. (2 ml.) were boiled for 1½ hr., and then poured into water (40 ml.). A solid was precipitated, and filtered off, it was washed well with water and the washings were added to the filtrate. The filtrate was then titrated against the sodium hydroxide. Titre = 18.16 ml. NaOH.

- Moles CH₃CO₂H consumed per mole of II = 2.14

5d) Compound IIIa.

IIIa (0.0460 g.) and Ac. (2 ml.) were boiled together for 1½ hr., then poured into water (40 ml.). The solid which was precipitated was filtered off and washed with water; the washings were added to the filtrate. The filtrate was titrated against the sodium hydroxide. Titre = 21.07 ml. NaOH.

- No acetylation had taken place.

A mixed m.p. of the precipitated solid with pure IIIa was not depressed, thus unchanged IIIa had been recovered.

Thus compounds I, II, and IIIa contain four, two, and no free hydroxyl groups respectively.
Experiment 6 Determination of the number of pairs of vicinal hydroxyl groups per molecule of compounds I, II, respectively, by periodate oxidation.

The periodate uptake was determined spectrophotometrically, the absorption being measured at 2,230 μ.

A calibration curve relating optical density to the percentage conversion of the periodate to iodate was made. An approximately 0.015M sodium metaperiodate solution was standardised using arsenious oxide and iodine (found: 0.01563), and an equimolar potassium iodate solution was prepared (0.8553 g. in 250 ml.). Portions of these two solutions were then mixed in the required proportions, a 250 fold dilution was made, and then the optical densities of the composite solutions were determined.

<table>
<thead>
<tr>
<th>% IO₄⁻</th>
<th>% IO₃⁻</th>
<th>log Iₒ/I</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>0.137</td>
</tr>
<tr>
<td>25</td>
<td>75</td>
<td>0.269</td>
</tr>
<tr>
<td>50</td>
<td>50</td>
<td>0.401</td>
</tr>
<tr>
<td>75</td>
<td>25</td>
<td>0.537</td>
</tr>
<tr>
<td>100</td>
<td>0</td>
<td>0.652</td>
</tr>
</tbody>
</table>

The calibration curve was plotted from these results - Graph A.

The action of periodate on furfuraldehyde was studied by using a solution of furfuraldehyde (0.4 ml.) in water (250 ml.) from which the following solutions were prepared:
Graph A - Calibration Curve to convert optical density measurements to percentage uptake of periodate.
i) 1 ml. furfuraldehyde solution + 9 ml. sodium metaperiodate
ii) 1 ml. furfuraldehyde solution + 9 ml. water
iii) 1 ml. water + 9 ml. sodium metaperiodate.

These solutions were left to stand at room temperature for 4 hr. Then 1 ml. of each solution was diluted to 250 ml., and the optical density measured, against a reference solution of water.

<table>
<thead>
<tr>
<th>Solution</th>
<th>( \log \frac{I_0}{I} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>i.</td>
<td>0.618</td>
</tr>
<tr>
<td>ii.</td>
<td>0.014</td>
</tr>
<tr>
<td>iii.</td>
<td>0.601</td>
</tr>
</tbody>
</table>

Thus furfuraldehyde is unattacked by periodate under these conditions.

A solution of the compound in the sodium metaperiodate (10 ml., \( 15.63 \times 10^{-5} \) mole) was prepared, and then left to stand at room temperature. After suitable time intervals 1 ml. aliquots were removed and diluted to 250 ml. The optical densities of these solutions were determined using an equimolar solution of the compound in water as reference. 2,5-\( \alpha \)-Methylene-\( \alpha \)-mannitol (mmm.) was used as a standard for the method.
Thus compounds I and II both contain one pair of vicinal hydroxyl groups.

**Experiment 7** To determine whether the vicinal hydroxyl groups are in the 1,2- or 5,6-positions in compounds I and II respectively, by estimation of the formaldehyde liberated by periodate oxidation.

The formaldehyde was estimated colorimetrically with chromotropic acid\(^{52}\), using a green filter (Ilford 604). A calibration curve relating colorimetric absorption to moles per litre formaldehyde was plotted, using 2,5-O-methylene-D-mannitol as the standard compound.

The following solutions were prepared:

1. Chromotropic acid (0.5 g.) dissolved in water (50 ml.), then 66% sulphuric acid (200 ml.) added.
2. 20% aqueous sodium bisulphite.
3. 0.4% aqueous thiourea.
4. 0.015M sodium metaperiodate (used in Expt. 6).
A solution of 2,5-O-methylene-β-mannitol (0.0811 g.) in solution (4) (10 ml.) was made up, and left to stand for ca. 3 hr. at room temperature. The following dilutions of this solution were then made: (i) 1 ml. → 50 ml.; (ii) 1 ml. → 20 ml.; (iii) 1 ml. → 10 ml. Then 1 ml. of each (i), (ii), and (iii), and 1 ml. water (iv), were treated as follows: solution (2) (0.1 ml.) and solution (1) (8.4 ml.) were added and the composite solutions heated in a boiling water bath for 20 min.; finally solution (3) (0.5 ml.) was added. The colorimetric determinations were made, using 66.6% sulphuric acid as the reference solution; (iv) provided a subsidiary blank.

<table>
<thead>
<tr>
<th>Solution</th>
<th>Absorption</th>
<th>HCHO absorption</th>
<th>Mole/l. HCHO</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i)</td>
<td>0.148</td>
<td>0.106</td>
<td>8.35 × 10⁻⁵</td>
</tr>
<tr>
<td>(ii)</td>
<td>0.306</td>
<td>0.264</td>
<td>20.88 × 10⁻⁵</td>
</tr>
<tr>
<td>(iii)</td>
<td>0.554</td>
<td>0.512</td>
<td>41.76 × 10⁻⁵</td>
</tr>
<tr>
<td>(iv)</td>
<td>0.042</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The calibration curve was plotted from these results - Graph B.

A solution of the compound in solution (4) (10 ml.) was prepared. After standing at room temperature for ca. 3 hr. 1 ml. of this solution was diluted to 10 ml., then 1 ml. of the diluted solution was treated in the same manner as the 2,5-O-methylene-β-mannitol above. The subsidiary blank was prepared from an aqueous furfuraldehyde solution, such that the final solution was equimolar in furfuraldehyde to the solution containing the compound, after the acid hydrolysis.
Graph B - Calibration Curve to convert colorimetric absorption into moles per litre of formaldehyde.

Colorimetric Absorption

Moles per litre HCHO x 10^-5
Thus the vicinal hydroxyl groups in both compounds, I and II, are in the 1,2- or 5,6-positions.

Experiment 8 Identification of the sugar liberated by oxidation followed by acid hydrolysis, of compounds I and II respectively, by paper chromatography.

8a) Compound I, using lead tetraacetate.

I (1 g., 1 mol.) was warmed into solution in water (26.8 ml.), and then added to a hot solution of lead tetraacetate (1.7 g., 1.2 mol.) in glacial acetic acid (10.9 ml.). The mixture was shaken well for 10 min., then N sulphuric acid (9 ml.) was added and the whole heated on a water bath for 7 hr. A slight excess of barium chloride was added to precipitate the excess sulphate ions, and the precipitated sulphate was removed by filtration. The filtrate was concentrated to a small volume.

Chromatograms of the concentrate, run in B.E.W. for 3 days, with L-arabinose and L-xylose, and D-glucitol as standards, and sprayed with KPr and AgNO₃ showed clearly that xylose had been liberated in the reaction.
8b) Compound I, using sodium metaperiodate.

I (1 g., 1 mol.), sodium metaperiodate (1 g., 1.2 mol.), and water (10 ml.) were shaken to obtain a homogenous solution, and then left to stand for 4 hr., at room temperature.

Chromatograms run in B.E.W. and sprayed with AgNO₃ showed that xylose had been formed, and also a new compound, which could also be detected with D.N.P.H., R_f 0.77 (2,4-Ω-furfurylidene-aldehyde-L-xylose).

8c) Compound II, using sodium metaperiodate.

II (0.05 g., 1 mol.), sodium metaperiodate (0.035 g., 1.1 mol.), and water (10 ml.) were left to stand for 1 day at room temperature. Chromatograms showed no evidence of a sugar having been liberated. The solution was left to stand for a further 2 days.

Chromatograms run in B.E.W. for 1 day showed that a sugar had been liberated, and also a new compound with R_f 0.89 which could be detected with D.N.P.H. (di-Ω-furfurylidene-aldehyde-L-xylose). Chromatograms run in B.E.W. for 3 days, with L-arabinose and L-xylose as standards, and sprayed with β-anisidine and AgNO₃ showed that the sugar formed in the reaction was xylose.
Experiment 9 Preparation of L-xylose from compound I.  

I (2.8 g., 1 mol.) and water (75 ml.) were heated together and then added to a hot solution of lead tetraacetate (4.8 g., 1.2 mol.) in glacial acetic acid (30 ml.), with stirring. After ca. 5 min. stirring N sulphuric acid (25 ml.) was added and the whole was warmed on a boiling water bath for 7 hr. A slight excess of barium chloride was added to precipitate the excess sulphate ions, and the precipitated sulphate was filtered off. On standing over the weekend inorganic crystals were precipitated, and removed, then the solution was treated with Biodeminrolit. The solution was then evaporated down to a small volume, no crystals separated out. Chromatograms run in B.E.W. and sprayed with p-anisidine indicated the presence of xylose in this solution. It was then evaporated down to dryness and the oily residue taken up in methanol. After 2 weeks crystals separated out and were triturated with ethanol, m.p. 143-144°, yield 0.28 g. (17% theoretical). A mixed m.p. with authentic L-xylose was not depressed. An attempt to recrystallise part of the product from ethanol proved unsuccessful.

Experiment 10 Preparation of di-O-triphenylmethyl-2,4-D-furfurylidene-D-glucitol, from compound I.  

I (0.2 g., 1 mol.), triphenylmethyl chloride (0.4 g., 2.1 mol.), and dry pyridine (5 ml.) were heated
together on a boiling water bath for 2 hr., and then poured into iced water (20 ml.). An oil separated out and was scratched to a solid mass. An attempted crystallisation from ethyl acetate was unsuccessful, an oil was recovered. The ethyl acetate was removed and then the oil was taken up in petroleum ether (b.p. 100-120°), and the solution left to stand at room temperature. After some days white crystals were deposited on the walls of the flask, m.p. 214°. These crystals could not be recrystallised from ethyl acetate (too soluble), petroleum ether (b.p. 60-80°) (insoluble), or from ethyl acetate/petroleum ether. Finally the crystals were boiled with ethanol, and then the ethanol was decanted off, m.p. 223-224°. (Found: C, 78.4; H, 5.82. Calc. for C₄₉H₄₄O₇: C, 78.9; H, 5.95%).

Experiment 11 Preparation of tetra-O-acetyl-2,4-O-furfurylidene-D-glucitol, from compound I.

11a) Anhydrous sodium acetate (0.2 g.) was warmed into solution with acetic anhydride (3 ml., 40 mol.), then I (0.2 g., 1 mol.) was added and the whole heated on a boiling water bath for 1 hr. The solution was then poured into iced water (ca. 20 ml.). Neither crystals, or an oil separated out.

11b) I (0.2 g., 1 mol.), acetic anhydride (0.5 ml., 7 mol.), and dry pyridine (5 ml.) were boiled together for
1½ hr. Then the solution was poured into iced water (20 ml.). The oil which separated out could not be obtained in a crystalline form.

Experiment 12 Preparation of tetra-\(\text{O}\)-toluene-\(\text{p}\)-sulphonyl-2,4-\(\text{O}\)-furfurylidene-\(\text{D}\)-glucitol, from compound I.

12a) I (0.5 g., 1 mol.), toluene-\(\text{p}\)-sulphonyl chloride (1.8 g., 4.9 mol.), and dry pyridine (3 ml.) were mixed together, and then left to stand for 1 day at room temperature, crystals of pyridine hydrochloride separated out. The mixture was poured into iced water (20 ml.), a pink coloured oil separated out. The oil was taken up in hot ethanol, and in hot methanol, in both cases it was deposited on cooling in a semi-solid state. The oil could not be obtained in a crystalline form.

12b) I (0.2 g., 1 mol.) was dissolved in 10% sodium hydroxide (2 ml.), then a solution of toluene-\(\text{p}\)-sulphonyl chloride (0.6 g., 4 mol.) in acetone (5 ml.) was added and the mixture shaken for 20 min. It was then poured into iced water (20 ml.). The semi-solid which separated out could not be obtained in a crystalline form.

Experiment 13 Preparation of 2,4-\(\text{O}\)-furfurylidene-\(\text{D}\)-glucitol-bis-phenylboronate, from compound I.

I (0.2 g., 1 mol.), phenylboronic anhydride (1 g., 4.2 mol.), and ethanol (25 ml.) were warmed together
until a clear solution was obtained. This was then left to stand at room temperature for 2 hr., by which time all the product had precipitated, m.p. ca. 170°, yield 0.32 g. (96% theoretical). Crystallisation of the product from ethanol/petroleum ether (b.p. 60-80°) gave pure 2,4-O-furfurylidene-D-glucitol-bis-phenylboronate, m.p. 177-178°. (Found: C, 64.5; H, 5.05; B, 4.97. C_{25}H_{22}B_{2}O_{7} requires: C, 65.9; H, 5.13; B, 5.01%). \[\alpha\]D^24 + 40.5 (c 0.9 in CHCl₃).

**Experiment 14**

a) Preparation of di-O-acetyl-di-O-furfurylidene-D-glucitol, from compound II.

II (0.1 g., 1 mol.) was added to acetic anhydride (0.3 ml., 10 mol.) in dry pyridine (0.7 ml.), and then left to stand at room temperature for 1 hr. Water (2.5 ml.) was added and the crystalline diacetate which separated out was filtered off, m.p. 183-4°, yield 0.11 g. (88% theoretical). The product was recrystallised from ethanol (2 ml.) to give pure di-O-acetyl-di-O-furfurylidene-D-glucitol, m.p. 184-186°; a mixed m.p. with compound II was 20° lower. (Found: C, 56.6; H, 5.52. C_{22}H_{20}O_{10} requires: C, 56.9; H, 5.26%).


The compound (0.08 g.) was dissolved in chloroform (1 ml.) and was then added to sodium methyleate (0.1 ml.). On stirring a gel was obtained, which on standing formed crystals, m.p. 194-196°. Recrystallisation from ethanol
(6 ml.) gave a constant m.p. 198-200° for di-O-furfurylidene-D-glucitol, yield 0.04 g., (62% theoretical).

Compound II, m.p. 182-183°, could not be converted to this second form, m.p. 198-200°, by crystallisation even with seeding; nor could the 198-200° form be converted to the 182-183° form by crystallisation.

**Experiment 15 Preparation of di-O-furfurylidene-D-glucitol-phenylboronate, from compound II.**

II (0.05 g., 1 mol.), phenylboronic anhydride (0.1 g., 2 mol.), and ethanol (2 ml.) were warmed together on a water bath for 1 hr., and then left to stand at room temperature overnight. Crystals separated out, m.p. 197-199°, yield 0.05 g. (80% theoretical). Recrystallisation from petroleum ether (b.p. 60-80°) gave di-O-furfurylidene-D-glucitol-phenylboronate, m.p. 204-205°. (Found: C, 62.3; H, 4.68; B, 2.27. C₂₂H₂₁B₂O₈ requires: C, 62.3; H, 4.99; B, 2.55%).
2, \( \alpha \)-Furfurylidene-\( \alpha \)-glucitol, (I), M.P. 191-2\( ^\circ \), in Nutol.
\[ \text{DI-O-FURFURYLIDENE-} \text{D-GLUCITOL, M.P. 182-3°, IN Nujol.} \]
\[ \text{DI-O-FURFURYLIDENE-} \text{D-GLUCITOL, M.P. 198-200°, IN Nujol,} \]
\[ \text{DI-O-ACETYL-DI-O-FURFURYLIDENE-} \text{D-GLUCITOL, M.P. 184-6°, IN Nujol,} \]
B. **BUTYLIDENE-D-GLUCITOLS**

**Materials**

The 2-butyraldehyde was obtained from B.D.H. Ltd., Poole, and was purified by drying over anhydrous magnesium sulphate, followed by distillation at atmospheric pressure.

The commercial grade of D-glucitol was used.

**Experiment 16**  Preparation of 2,4-O-butyridene-D-glucitol (IV).

D-glucitol (18 g., 1 mol.) and 3N sulphuric acid (5 ml.) were warmed to a syrup, and then cooled to room temperature. 2-Butyraldehyde (9 ml., 1 mol.) was added and the mixture stirred until it was homogenous (ca. 10 min.). The reaction mixture was then left to stand at room temperature for 4 days, the product slowly crystallising out. Then concentrated ammonia solution (ca. 1.1 ml.) was added to neutralise the acid present, and methanol (40 ml.) to make the mixture more mobile. After stirring well the crystalline product was filtered off, m.p. 144-146°C, yield 9.0 g. (39% theoretical). Recrystallisation from ethanol gave white needles of 2,4-O-butyridene-D-glucitol, IV, m.p. 157-158°C (4.76 g., 20%). (Found: C, 50.9; H, 8.4.

C₁₀H₂₀O₆ requires: C, 50.8; H, 8.52%). [α]₂⁴ D -9.6 (c 1.9 in H₂O); [α]₂⁵ D -4.8 (c 1.9 in 4% w/v 60% aqueous methanolic (PhBO)₃). Rf (B.E.W.) 0.60.

Chromatograms of the initial filtration liquors in
and in M.E.K./(PhBO)$_3$ indicated the presence of 3,4-0-butyldene-D-glucitol.

**Experiment 17** Preparation of tri-0-butyldene-D-glucitol (V).

17a) Using concentrated sulphuric acid as condensing agent[^21].

D-glucitol (91 g., 1 mol.), n-butyraldehyde (147 ml., 3.3 mol.), and dioxan (500 ml.) were mixed together thoroughly, then concentrated sulphuric acid (25 ml.) was added dropwise with stirring. During the addition of the acid the D-glucitol was slowly taken into solution. The mixture was then heated on a steam bath for 1 hr., during this period the solution darkened, finally being a dark brown colour. The mixture was then cooled to 40°, then poured into water (1½ l.), containing sodium hydroxide (40 g.) to neutralise the acid. This solution was then extracted with petroleum ether (b.p. 60-80°) (1 l.). The petroleum ether extract was dried with anhydrous magnesium sulphate and then filtered. The filtrate was evaporated down to a small volume.

The residue was distilled at 0.2 mm., the following fractions being collected:
- Forerun: 38-60°, 4.5 g.; and 60-136°, 4.0 g.;
- Fraction A: 136-139°, 36.5 g.; Fraction B: 141-144°, 19.4 g.;
- Fraction C: 150-160°, 20.4 g.; Fraction D: 161-162°, 12.2 g.

Total weight of main fractions 88.5 g. (51% theoretical).
Each fraction was redistilled:

Fraction A: 142–145°/0.1 mm., n_D^{25} 1.4605, [α]_D^{20} +6.3° (ε 1.8 in EtOH); also 222–225°/18–20 mm., n_D^{25} 1.4602; pale yellow.

Fraction B: 140–143°/0.1 mm., n_D^{25} 1.4611, [α]_D^{20} +3.0° (ε 1.7 in EtOH), pale yellow.

Fraction C: 142–145°/0.1 mm., n_D^{25} 1.4612, [α]_D^{15} +6.7° (ε 1.7 in EtOH), pale yellow.

Fraction D: 141–143°/0.1 mm., n_D^{25} 1.4611; 144–146°/0.1 mm., n_D^{25} 1.4618; 146–148°/0.1 mm., n_D^{25} 1.4635. [α]_D^{16} +2.7° (ε 1.7 in EtOH), taken on the middle cut. The colour increased with each cut, from yellow to deep orange.

The fractions were tri-O-butylidene-D-glucitol, Va. (Found: C, 62.8; H, 9.37. C_{18}H_{32}O_{6} requires: C, 62.8; H, 9.37%).

Another preparation gave a 75% yield of the tri-O-butylidene-D-glucitol, Va.

17b) Using toluene-p-sulphonic acid as condensing agent.

D-glucitol (18 g., 1 mol.), n-butyraldehyde (40 ml., 4.3 mol.), benzene (50 ml.), and toluene-p-sulphonic acid (0.1 g.) were heated together, with a Dean and Starke head to effect azeotropic distillation; 4.5 ml. water was collected (83% theoretical, based on conversion to triacetal product). On cooling an oil separated out at the bottom of the flask, which on standing crystallised. The supernatant liquid was decanted off, and the crystals were recrystallised.
from ethanol, m.p. 157-158°; a mixed m.p. with IV showed that this product was also 2,4-\textsuperscript{buc}but-ylidene-D-glucitol, yield 0.73 g. (3% theoretical).

The supernatant liquid was poured through Biodeminrolit and then the benzene and excess n-butyaldehyde were distilled off. The remaining oil was distilled at 0.1 mm. and the following fractions were collected:

Forerun: 70-160°, 8 g., \(n_D^{25}\) 1.4518;
Fraction A: 160-162°, 22.7 g. (67% yield), \(n_D^{25}\) 1.4600;
Fraction B: 164-166°, 2 g., \(n_D^{25}\) 1.4618.

Fraction A redistilled: 136-138°/0.1 mm., \(n_D^{25}\) 1.4596, \([\alpha]_D^{23}\) +7.2° (c 10.5 in EtOH), Vb.

Another preparation gave an 86% yield of the tri-O-butylidene-D-glucitol, Vb.

Experiment 18 Partial hydrolysis of Va.

18a) Fraction A.

Fraction A (27 g.) and 60% acetic acid (120 ml.) were heated together on a water bath at 85-88° for 1 hr. 20min. Then the acetic acid, water, and liberated n-butyaldehyde were distilled off under reduced pressure as quickly as possible. The remaining oil was taken up in chloroform (100 ml.) and left to stand overnight. The crystalline monoacetal which had separated out was filtered off (2.14 g., 14% based on hydrolysed triacetal). Recrystallisation from ethanol gave 2,4-\textsuperscript{buc}butylidene-D-glucitol, m.p. 156-157°
All the chloroform was evaporated off the chloroform soluble di- and triacetals, and the residual oil was then shaken well with petroleum ether (b.p. 60-80°). The petroleum ether soluble triacetal was removed from the insoluble diacetals; recovery of unchanged triacetal was 5.1 g. (19%). The diacetal oil was then taken up in benzene, and the solution left to stand overnight, during which time a crystalline diacetal separated out (2.45 g., 14% based on hydrolysed triacetal). This crystalline di-O-butylidene-D-glucitol (VI) was recrystallised from water to m.p. 132-133°. (Found: C, 57.6; H, 9.0. C_{14}H_{26}O_{6} requires: C, 57.9; H, 9.34%). \[\alpha\]_{D}^{22} +1.6° (c 1.6 in EtOH).

A syrupy diacetal was recovered from the benzene (11 g., 60% of hydrolysed triacetal). This was distilled.:

- Forerun: 140-166°/0.1 mm., 1.3 g.
- Fraction A: 166-169°/0.1 mm., 2.7 g., n_{D}^{25} 1.470 (Found: C, 57.1; H, 8.65. C_{14}H_{26}O_{6} requires: C, 57.9; H, 9.34%).
- Fraction B: 169-189°/0.1 mm., 5.2 g.

18b) Fraction B.

Fraction B (16.5 g.) was treated as in 18a above. Crude monoacetal (2.66 g., 25%) was obtained, which on recrystallisation yielded pure IV (42% recovery). The crystalline diacetal (2.16 g., 17%), and the syrupy diacetal (6.04 g., 46%) were both isolated; and also some unchanged triacetal (1.22 g., 7%).
Experiment 19 Partial hydrolysis of Vb.

Vb (70 g.) and 60% acetic acid (310 ml.) were heated on a water bath at 86-87° for 1½ hr., then all the volatile matter was evaporated off as quickly as possible, under reduced pressure. The oil was then taken up in chloroform and on standing the monoacetals were precipitated (13.8 g., 43% based on hydrolysed triacetal). The monoacetals were taken up in ethanol (100 ml.), the first crop of crystals yielded were pure 2,4-0-butylidene-D-glucitol, (IV), (2.54 g., 18% recovery). The mother liquors were then evaporated down to about 30 ml. The crystals which separated out had m.p. 112-113°, subsequent crops were flocculent, m.p. 109-110° (the melting point of this form could not be raised to that of the crystalline product, however a mixed m.p. of the two forms was not depressed). Total yield of this 3,4-0-butylidene-D-glucitol (VII) was 4.14 g. (30% recovery from crude monoacetal). The compound was characterised by a mixed m.p. with a known sample of this compound, prepared by Dr. Lewis from 3,4-0-but-2'-enylidene-D-glucitol. \([\alpha]_D^{21} +37.2^\circ\) (e 1.7 in H\(_2\)O).

The chloroform was evaporated off the chloroform soluble oils, which were then taken up in petroleum ether (b.p. 60-80°). The unchanged triacetal was removed in the petroleum ether layer (23.3 g., i.e. 33% unreacted), and the remaining diacetal (21.6 g., 55% of hydrolysed triacetal)
was shaken with benzene. A few crystals of the crystalline diacetal (VI) separated out (0.89 g., 2.3% of hydrolysed triacetal); the bulk of the diacetal remained as the oil.

**Experiment 20  Partial hydrolysis of compound VI.**

VI (2.0 g.) and 60% acetic acid (20 ml.) were heated on a water bath at 89-90° for 3 hr., and then all the volatile matter was evaporated off as quickly as possible under reduced pressure. The remaining oil was taken up in chloroform, and on standing monoacetal was precipitated (0.3 g.). On recrystallisation from ethanol this yielded pure 2,4-\(\beta\)-butyldiene-\(\beta\)-glucitol (IV) (0.16 g., 10%). The chloroform soluble material remained an oil.

**Experiment 21  Determination of the constituents of compound IV.**

IV (0.5 g., 1 mol.), water (20 ml.), and Zeo-Karb 225 resin in the hydrogen form (0.3 ml.) were heated on a boiling water bath for 1 hr. Then the volatile matter was distilled off into a liquid nitrogen trap, at 20 mm. pressure. Water (20 ml.) was added to the flask and the process repeated, twice. The distillate was added to dimedone (0.6 g., 1.01 mol.) in water (40 ml.). After 2 days yield of \(\pi\)-butyraldehyde-bisdimedone was 0.40 g. (0.57 mol.). M.p. and mixed m.p. with authentic specimen 127-128°. The residue in the flask was extracted with warm methanol (10 ml.)
and added to phenylboronic anhydride (0.66 g., 1 mol.) in methanol (2 ml.). Yield of D-glucitol-tris-phenylboronate 0.58 g. (0.62 mol.), m.p. and mixed m.p. with authentic specimen 183-184°.

**Experiment 22** To determine the number of free hydroxyl groups per molecule of compound IV.

The method was identical to that used in Expt. 5.

Found: Moles CH₃CO₂H consumed per mole IV = 3.95

Thus compound IV contains four free hydroxyl groups per molecule.

**Experiment 23** To determine the number of pairs of vicinal hydroxyl groups per molecule of compound IV.

The method used is described in Expt. 6.

Found: Moles periodate consumed per mole IV = 1.08 (at 3 hr.) and 0.97 (at 8½ hr. and 21 hr.)

Thus compound IV contains one pair of vicinal hydroxyl groups.

**Experiment 24** To determine whether the vicinal hydroxyl groups are in the 1,2- or 5,6-positions in compound IV.

The method used is described in Expt. 7. Since n-butyraldehyde shows no reaction with chromotropic acid none was included in the subsidiary blank.

Found: Moles HCHO liberated per mole IV = 0.97

Thus compound IV contains a pair of vicinal
hydroxyl groups in either the 1,2- or 5,6-positions.

Experiment 25 Identification of the sugar liberated from compound IV, by oxidation followed by acid hydrolysis, using paper chromatography.

A little IV was dissolved in some water, then an excess of sodium metaperiodate was added, and the mixture was left to stand at room temperature for ½ hr. Then some ethylene glycol was added to react with the excess periodate, after which the solution was hydrolysed by warming gently for ½ hr. with Zeo-Karb 225 resin in the hydrogen form. The solution was then decanted from the resin, and was developed chromatographically for 3 days in B.E.W., with D-arabinose and L-xylose as standards.

The chromatograms showed that the liberated sugar was xylose. Thus the vicinal hydroxyl groups of compound IV are in the 5,6-positions.


VI (2.0 g., 1 mol.) was added to water (20 ml.) containing sodium hydrogen carbonate (0.2 g.), a suspension was obtained with pH ca. 7.5. Then a solution of sodium metaperiodate (1.8 g., 1.2 mol.) in water (15 ml.) was added dropwise, so that the pH of the acetal solution never fell
below 7. This took ca. ½ hr., by which time all the 
diacetal was in solution. This solution was left to stand 
at room temperature for 1 hr., and was then extracted with 
chloroform. The extract was evaporated to dryness and the 
crude product was obtained in 80% yield (1.54 g.). This 
material was recrystallised from petroleum ether (b.p. 60-80°) 
and yielded di-\(\beta\)-butylidene-aldehydo-\(\beta\)-xylose, m.p. 108.5-
109.5°, yield 0.8 g. (45% theoretical). (Found: C, 60.6; 
H, 8.5; \(\text{C}_{15}\text{H}_{22}\text{O}_5\) requires: C, 60.4; H, 8.6%)

Di-\(\beta\)-butylidene-aldehydo-\(\beta\)-xylose (0.20 g., 1 mol.), 
and \(\text{p}\)-nitrophenylhydrazine (0.115 g., 1 mol.) in absolute 
ethanol (3 ml.) were heated at 75-85° for 1½ hr. The mixture 
was then filtered, and the filtrate left in a refrigerator 
for 3 days. The crude product, m.p. 178-179°, yield 0.22 g. 
(74% theoretical) which had separated out was recrystallised 
from petroleum ether (b.p. 60-80°)/ethanol (2:1, v/v), to 
give pure di-\(\beta\)-butylidene-aldehydo-\(\beta\)-xylose-\(\text{p}\)-nitrophenyl-
hydrazone, m.p. 181-182°. (Found: C, 57.8; H, 6.96; N, 10.8. 
\(\text{C}_{19}\text{H}_{27}\text{N}_3\text{O}_6\) requires: C, 58.0; H, 6.90; N, 10.8%).

\(\alpha\)\(\text{D}\) \(-147.2°\) (c 1.5 in EtOH).

**Experiment 27** Preparation of \(\beta\)-xylose from compound VI.

VI was converted to di-\(\beta\)-butylidene-aldehydo-
\(\beta\)-xylose as described in Expt. 25 above. Then the diacetal-
xylose (0.25 g.), water (5 ml.) and Zeo-Karb 225 resin in 
the hydrogen form (0.5 ml.) were heated together at 100° for
4 hr. The resin was filtered off, and washed well with water, and the combined filtrate and washings were evaporated down to a syrup. This syrup was taken up in methanol and cooled to -15°. On warming very slowly crystalline L-xylose separated out, m.p. and mixed m.p. with authentic L-xylose 142-143°, yield 0.09 g. (62% theoretical).

Thus compound VI must contain a pair of vicinal hydroxyl groups at positions 5 and 6.

**Experiment 28 Preparation of di-O-triphenylmethyl-2,4-O-butylidene-D-glucitol, from compound IV.**

IV (1.5 g., 1 mol.), triphenylmethyl chloride (3.54 g., 2 mol.), and dry pyridine (25 ml.) were heated together on a boiling water bath for 3 hr., after which the solution was poured into cold water (50 ml.). The mixture was then extracted with chloroform (3×20 ml.); the chloroform extract was washed well with water, and then all the chloroform was evaporated off. The residual mixture was taken up in a methanol/ethanol mixture, and was scratched until crystals separated out, yield 3.33 g. (75% theoretical). The product was crystallised from ethanol, after hot filtration, m.p. 68-70° (indistinct). It was then recrystallised from petroleum ether (b.p. 60-80°) and gave m.p. 94-95° (with effervescence). (Found: C, 80.3; H, 6.87. C_{48}H_{48}O_{6} requires: C, 80.0; H, 6.71%). [α]_{D}^{21} +9.5 (c 1.7 in CHCl₃).
Experiment 29  Preparation of tetra-O-acetyl-2,4-O- 
butylidene-D-glucitol, from compound IV.

IV (0.2 g., 1 mol.) was added to acetic anhydride
(0.8 ml., 20 mol.) in dry pyridine (2 ml.) and the solution
was heated under reflux for 1½ hr. The solution was then
poured into iced water (10 ml.) and the mixture was stirred
well. Crystals of the product separated out, m.p. 61-62°,
yield 0.25 g. (76% theoretical). The tetra-O-acetyl-2,4-O-
butylidene-D-glucitol was recrystallised from 40% aqueous
methanol to m.p. 67-68°. (Found: C, 53.6; H, 7.0. \(\text{C}_{18}\text{H}_{28}\text{O}_{10}\)
requires: C, 53.5; H, 7.0%). \([\alpha]_D^{22}-7.9°\) (c 2.2 in \(\text{CHCl}_3\)).

Experiment 30  Preparation of 2,4-O-butylidene-D-glucitol-
bis-phenylboronate, from compound IV.

IV (0.2 g., 1 mol.) in water (1.6 ml.) was added
to phenylboronic anhydride (0.18 g., 2 mol.) in methanol
(1 ml.), when both solutions were warm. The solid mass which
separated out was filtered off, and then taken up in ethanol,
a little water was added and the solution was left to stand.
After several days crystals of the product separated out,
m.p. 66-67°, yield 0.17 g. (50% theoretical). Recrystallisation
from petroleum ether (b.p. 60-80°) yielded pure 2,4-O-
butylidene-D-glucitol-bis-phenylboronate, m.p. 82-84°,
(0.14 g., 41%). (Found: C, 64.5; H, 6.5; B, 5.1. \(\text{C}_{22}\text{H}_{26}\text{B}_2\text{O}_6\)
requires: C, 64.7; H, 6.4; B, 5.3%). \([\alpha]_D^{20}-6.1°\) (c 1.4 in
\(\text{CHCl}_3\)).
2,4-O-BUTYLIDENE-D-GLUCITOL, M.P. 157-80, IN NUJOL,

3,4-O-BUTYLIDENE-D-GLUCITOL, M.P. 112-30, IN NUJOL,
Di-O-butyldiene-D-glucitol, M.P. 132-3°, in Nujol, —
Di-O-butyldiene-D-glucitol, B.P. 166-9°/0.1 m.m. , smear, —
C. OTHER CYCLIC ACETALS OF HEXITOLS

Experiment 31 Preparation of 2,4-D-iso-butylidene-D-glucitol, VIII.

D-glucitol (18 g., 1 mol.) and 3N sulphuric acid (5 ml.) were warmed to a syrup, and then cooled to room temperature. Iso-butyraldehyde (9 ml., 1.0 mol.) was added and the mixture was stirred until a homogenous solution was obtained (ca. 10 min.). The mixture was left to stand for 3 days at room temperature, during which time the product crystallised out. Then concentrated ammonia solution (ca. 1.1 ml.) and ethanol (ca. 40 ml.) was added and the whole was stirred, to neutralise the acid present and to make the mixture more mobile. The crystalline product was filtered off, m.p. 146-153°, yield 11 g. (47% theoretical). Recrystallisation from ethanol gave white needles of 2,4-D-iso-butylidene-D-glucitol, VIII, m.p. 163-164°. (Found: C, 50.5; H, 8.30%. C₁₀H₂₀O₆ requires: C, 50.8; H, 8.52%). \([\alpha]^{30}_{D} = -3.6^0 (c 2.0 \text{ in } H₂O), R_f (B.E.W.) 0.60.\)

Experiment 32 Preparation of 2,4-D-propylidene-D-glucitol.

D-glucitol (50 g., 1 mol.) and 3N sulphuric acid (14 ml.) were warmed to a syrup, and after cooling to room temperature propionaldehyde (23 ml., 1.2 mol.) was added. The mixture was then stirred until it was homogenous, after which it was left to stand at room temperature for 4 days.
During this time the product slowly crystallised out. The acidity was neutralised with concentrated ammonia solution (3 ml.), and ethanol (20 ml.) was added. The crystals were then filtered off and recrystallisation from ethanol gave white needles of 2,4-α-propylidene-β-glucitol, m.p. 151-152°, yield 11.7 g. (19% theoretical). (Found: C, 48.6; H, 8.15. \( \text{C}_9\text{H}_{18}\text{O}_6 \) requires: C, 48.6; H, 8.15%). \([\alpha]_{D}^{26} \approx -10.9 \) (c 1.5 in \( \text{H}_2\text{O} \)). \( R_f \) (B.E.W.) 0.60.

**Experiment 33** Preparation of 2,4-α-ethylidene-β-glucitol.

β-glucitol (18.2 g., 1 mol.) and 3N sulphuric acid (5.2 ml.) were warmed to a syrup and then allowed to cool to room temperature. Acetaldehyde (9 ml., 1.6 mol.) was added, and after stirring until a homogenous solution was obtained, it was left to stand at room temperature. No crystals of the product separated out on standing.

**Experiment 34** Preparation of 2,4-α-benzylidene-β-glucitol.

β-glucitol (18.2 g., 1 mol.) and 3N sulphuric acid (5.2 ml.) were warmed to a syrup, allowed to cool to room temperature, and then benzaldehyde (14 ml., 1.4 mol.) was added, and the whole was stirred until a homogenous solution was obtained. This was left to stand overnight, during which time the product crystallised out, forming a solid mass. The product was recrystallised from water containing sufficient sodium carbonate to neutralise the sulphuric acid. Further
recrystallisation from water gave pure 2,4-O-benzylidene-\(\text{D-glucitol}\), m.p. and mixed m.p. with authentic sample 176-177°, yield 9.0 g. (33% theoretical).

**Experiment 35** Preparation of a mono-O-furfurylidenemannitol.

Mannitol (18 g., 1 mol.) was added slowly to 3N sulphuric acid (5 ml.) with warming. The mannitol would not dissolve completely to form a clear syrup, on cooling the mannitol recrystallised. Furfuraldehyde (8 ml., 1 mol.) was added and the whole was shaken at room temperature for 2 days. Chromatographic development of the crude reaction mixture, in B.E.W., indicated the presence of mannitol only, no cyclic acetals had been formed.

**Experiment 36** Preparation of tri-O-isobutyldene-\(\text{D-glucitol}\), using toluene-\(\text{p-sulphonic acid}\) as catalyst.

\(\text{D-glucitol}\) (18 g., 1 mol.), iso-butyraldehyde (40 ml., 4.3 mol.), benzene (50 ml.), and toluene-\(\text{p-sulphonic acid}\) (0.1 g.) were heated together, with a Dean and Starke head to effect azeotropic distillation, until no more water was being formed (5.1 ml. water collected, 94% theoretical based on conversion to triacetal product). On cooling an oil separated out at the bottom of the flask, and it crystallised on standing. The supernatant liquid was decanted off and the crystals were recrystallised from ethanol, m.p. and mixed m.p. with compound VIII 162-163°, showing this product to be 2,4-O-isobutyldene-\(\text{D-glucitol}\).
The supernatant liquid was poured through Biodeminrolit to remove the catalyst, and then the benzene and excess iso-butyraldehyde were distilled off. The remaining colourless oil gave a fraction with constant b.p. 132-134°/0.1 mm., tri-O-isobutylidene-D-glucitol, yield 25.6 g. (75% theoretical). (Found: C, 62.1; H, 9.10. \( \text{C}_{18}\text{H}_{32}\text{O}_{6} \) requires: C, 62.8; H, 9.37%). \( \mu_{D}^{25} = 1.4551; \) \( \alpha_{D}^{25} = 7.9° \) (c 10.2 in EtOH).

Experiment 37 Determination of the constituents of compound VIII.

VIII (1.0 g., 1 mol.), water (4 ml.), and Zeo-Karb 225 resin in the hydrogen form (0.5 ml.) were boiled together under reflux for 1 hr. The resin was then filtered off and washed with water, the washings and filtrate were combined. This solution was then distilled, the distillate being collected in a flask containing a saturated solution of 2,4-dinitrophenylhydrazine in 2N hydrochloric acid, the 2,4-dinitrophenylhydrazone derivative of the aldehyde being precipitated immediately. It was filtered off and crystallised from ethanol, m.p. and mixed m.p. with authentic iso-butyraldehyde-2,4-dinitrophenylhydrazone 179-180°.

The residue in the flask was taken up in water (1.5 ml.) and then phenylboronic anhydride (1.3 g., 3 mol.) in hot methanol (1.5 ml.) was added. A solid was precipitated
immediately, it was filtered off and then washed with cold water and then with hot methanol. It was recrystallised from ethanol/petroleum ether (b.p. 60-80°) and had m.p. and mixed m.p. with authentic D-glucitol-tris-phenylboronate 182-183° (0.44 g., 0.25 mol.).

Experiment 38 To determine the number of free hydroxyl groups per molecule of compound VIII.

The method was identical to that used in Expt. 5.

Found: Moles CH₃CO₂H consumed per mole VIII = 3.81
Thus compound VIII contains four free hydroxyl groups.

Experiment 39 To determine the number of vicinal hydroxyl groups per molecule of compound VIII.

The method used is described in Expt. 6.

Found: Moles periodate consumed per mole VIII = 1.04 (after 4 hr.) and 1.00 (after 22 hr.).
Thus compound VIII contains one pair of vicinal hydroxyl groups.

Experiment 40 To determine whether the vicinal hydroxyl groups are in the 1,2- or 5,6-positions in compound VIII.

The method used is described in Expt. 8. Since iso-butyraldehyde gives no colouration with chromotropic acid none was included in the subsidiary blank.

Found: Moles HCHO liberated per mole VIII = 1.02
Thus compound VIII contains a pair of vicinal hydroxyl groups
in either the 1,2- or 5,6-positions.

Experiment 41  To identify the sugar liberated from compound VIII by periodate oxidation followed by acid hydrolysis, using paper chromatography.

The method used was as described in Expt. 26. The chromatograms showed that the sugar liberated was xylose. Thus the vicinal hydroxyl groups of compound VIII are in the 5,6-positions.

Experiment 42  Preparation of di-O-triphenylmethyl-2,4-O-isobutylidene-D-glucitol, from compound VIII.

VIII (0.2 g., 1 mol.), triphenylmethyl chloride (0.45 g., 2.0 mol.), and dry pyridine (5 ml.) were heated together on a boiling water bath for 3 hr. The solution was then poured into cold water (15 ml.) and stirred, and the mixture extracted with chloroform. The chloroform extract was washed with water and then the chloroform was evaporated off, leaving an oil. This oil was taken up in an ethanol/water mixture and left to stand; crystals of the product separated out after a few days. Recrystallisation from an ethanol/methanol mixture gave di-O-triphenylmethyl-2,4-O-isobutylidene-D-glucitol, m.p. 79° (with effervescence), yield 0.36 g. (75% theoretical). (Found: C, 79.3; H, 6.73. C_{48}H_{48}O_{6} requires: C, 80.0; H, 6.71%).
Experiment 43 Preparation of tetra-0-acetyl-2,4-0-isobutylidene-D-glucitol, from compound VIII.

VIII (0.2 g.) was taken and treated exactly as IV in Expt. 29. The tetra-0-acetyl-2,4-0-isobutylidene-D-glucitol product had m.p. 65-66°, yield 0.2 g. (62% theoretical). (Found: C, 53.7; H, 7.09. C_{18}H_{28}O_{10} requires: C, 53.5; H, 6.98%).
TRI-O-ISOBUTYLIDENE-δ-GLUCITOL, SMear.
D. KINÉTIC STUDIES

Materials

2,4-0-butyldiene-\( \text{D} \)-glucitol (IV) was prepared as in Expt. 16, 3,4-0-butyldiene-\( \text{D} \)-glucitol (VII) was prepared as described in Expts. 17b and 19, and 2,4-0-isobutyldiene-\( \text{D} \)-glucitol (VIII) as described in Expt. 31. Pure samples of 4,6-0-butyldiene-\( \text{D} \)-glucitol (IX) and 2,4-0-but-2'-enyldiene-\( \text{D} \)-glucitol (X) were very kindly supplied by Dr. Lewis.

Pure \( \text{n} \)-butyraldehyde was obtained as described on p. 155. \( \text{D} \)-glucitol was purified by converting it to its pyridine complex, by treatment with hot, dry pyridine. The complex was then filtered off, leaving the mannitol in solution, and was washed with more pyridine. The complex was then converted back to \( \text{D} \)-glucitol by repeated treatment with hot methanol followed by removal of all volatile material by evaporation under reduced pressure, until the \( \text{D} \)-glucitol was free of pyridine. The \( \text{D} \)-glucitol was then crystallised from acetone. Ionophoresis of the purified \( \text{D} \)-glucitol, in sodium metavanadate, showed it to be free of mannitol.

The hydrolyses were mainly carried out in 1N and 2N hydrochloric acid, which was prepared from volumetric standard 5N hydrochloric acid, supplied by B.D.H. Ltd., Poole. The required quantity of the 5N acid was pipetted into
a 20 ml. volumetric flask, which was then made up to the mark at the required temperature. Weaker acid strengths were prepared from a similar 1N hydrochloric acid solution; the required sulphuric acid was obtained similarly.

**Apparatus**

The hydrolyses were carried out in a water jacketed polarimeter tube, the temperature of which was thermostatically controlled to ±0.05° by an electrically operated water thermostat.

The optical rotations of the reaction mixtures were followed using a Hilger Watts Polarimeter which was accurate to ±0.003°.

The ultraviolet spectra of the reaction equilibrium mixtures were recorded using a Perkin Elmer Ultracord.

**Velocity measurements**

20 ml. of the required strength of hydrochloric acid was transferred to a round bottomed quickfit flask, and was allowed to reach thermal equilibrium at the required temperature. Then the acetal sample, of known weight, was introduced into the acidic medium by means of a hollow stopper, and the whole was shaken for ca. 10 sec., during which time the acetal dissolved completely. The shaking was not carried out vigorously since this resulted in considerable occlusion of air within the solution. The
solution was then transferred to the polarimeter tube which was already at the required temperature. The start of the reaction was taken as the instant at which the acetal sample came in contact with the acid medium, when they were shaken together. It was found that the first reading could be taken from about 1 min. after the start of the reaction.

No abnormal readings were found at the beginning of the run. Thus it seemed that the adverse effect of the slight cooling of the acid medium between its removal from the thermostat for the addition of the acetal, and its being placed in the polarimeter tube was suitably counteracted by the heat of solution.

Each hydrolysis was examined in duplicate and the differences between the values of the rate constants were never greater than 3% for any of the compounds, under any of the conditions.
Results

**Table 1**

Hydrolysis of 2,4-O-butyridene-D-glucitol (IV) in 2N HCl at 38.6°.

a) 5% solution.

<table>
<thead>
<tr>
<th>Time</th>
<th>(x)</th>
<th>(x_t-x_0)</th>
<th>(\log[100(x_t-x_0)])</th>
</tr>
</thead>
<tbody>
<tr>
<td>2½ min.</td>
<td>0.985°</td>
<td>0.614</td>
<td>1.788</td>
</tr>
<tr>
<td>4</td>
<td>0.925</td>
<td>0.554</td>
<td>1.746</td>
</tr>
<tr>
<td>6</td>
<td>0.872</td>
<td>0.501</td>
<td>1.700</td>
</tr>
<tr>
<td>10</td>
<td>0.782</td>
<td>0.411</td>
<td>1.614</td>
</tr>
<tr>
<td>14</td>
<td>0.722</td>
<td>0.351</td>
<td>1.545</td>
</tr>
<tr>
<td>22</td>
<td>0.611</td>
<td>0.240</td>
<td>1.380</td>
</tr>
<tr>
<td>27</td>
<td>0.555</td>
<td>0.184</td>
<td>1.265</td>
</tr>
<tr>
<td>32</td>
<td>0.511</td>
<td>0.140</td>
<td>1.146</td>
</tr>
<tr>
<td>38</td>
<td>0.474</td>
<td>0.103</td>
<td>1.013</td>
</tr>
<tr>
<td>43</td>
<td>0.452</td>
<td>0.081</td>
<td>0.909</td>
</tr>
<tr>
<td>∞</td>
<td>0.371</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

From Graph 1, \(k = 495 \times 10^{-4}\) min⁻¹.

b) 2% solution.

<table>
<thead>
<tr>
<th>Time</th>
<th>(x)</th>
<th>(x_t-x_0)</th>
<th>(\log[100(x_t-x_0)])</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 min.</td>
<td>0.430°</td>
<td>0.283</td>
<td>1.452</td>
</tr>
<tr>
<td>4</td>
<td>0.388</td>
<td>0.241</td>
<td>1.382</td>
</tr>
<tr>
<td>6</td>
<td>0.367</td>
<td>0.220</td>
<td>1.342</td>
</tr>
<tr>
<td>10</td>
<td>0.330</td>
<td>0.183</td>
<td>1.263</td>
</tr>
<tr>
<td>14</td>
<td>0.298</td>
<td>0.151</td>
<td>1.179</td>
</tr>
<tr>
<td>20</td>
<td>0.258</td>
<td>0.111</td>
<td>1.045</td>
</tr>
<tr>
<td>25</td>
<td>0.234</td>
<td>0.087</td>
<td>0.940</td>
</tr>
<tr>
<td>30</td>
<td>0.210</td>
<td>0.063</td>
<td>0.799</td>
</tr>
<tr>
<td>35</td>
<td>0.198</td>
<td>0.051</td>
<td>0.708</td>
</tr>
<tr>
<td>55</td>
<td>0.166</td>
<td>0.019</td>
<td>0.279</td>
</tr>
<tr>
<td>∞</td>
<td>0.147</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1b) From Graph 1, \( k = 504 \times 10^{-4} \text{ min}^{-1} \).

c) 0.5% solution.

<table>
<thead>
<tr>
<th>Time</th>
<th>( \alpha )</th>
<th>( \alpha_t - \alpha )</th>
<th>( \log [100(\alpha_t - \alpha)] )</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 min.</td>
<td>0.105(^0)</td>
<td>0.073</td>
<td>0.863</td>
</tr>
<tr>
<td>7</td>
<td>0.101</td>
<td>0.069</td>
<td>0.839</td>
</tr>
<tr>
<td>13</td>
<td>0.088</td>
<td>0.056</td>
<td>0.748</td>
</tr>
<tr>
<td>19</td>
<td>0.073</td>
<td>0.041</td>
<td>0.613</td>
</tr>
<tr>
<td>24</td>
<td>0.062</td>
<td>0.030</td>
<td>0.477</td>
</tr>
<tr>
<td>31</td>
<td>0.053</td>
<td>0.021</td>
<td>0.322</td>
</tr>
<tr>
<td>( \infty )</td>
<td></td>
<td>0.032</td>
<td></td>
</tr>
</tbody>
</table>

From Graph 1, \( k = 508 \times 10^{-4} \text{ min}^{-1} \).

**Table 2**

Hydrolysis of 2,4-\( \alpha \)-butylidene-D-glucitol (IV) in HCl at 38.6\(^0\).

<table>
<thead>
<tr>
<th>Acid molarity</th>
<th>( 10^4k )</th>
<th>( \log 10^4k )</th>
<th>( -H_\circ )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1M</td>
<td>5.90 min(^{-1})</td>
<td>0.771</td>
<td>-0.98</td>
</tr>
<tr>
<td>1.0</td>
<td>149</td>
<td>2.172</td>
<td>+0.20</td>
</tr>
<tr>
<td>2.0</td>
<td>507</td>
<td>2.705</td>
<td>+0.69</td>
</tr>
<tr>
<td>3.0</td>
<td>957</td>
<td>2.981</td>
<td>+1.05</td>
</tr>
<tr>
<td>4.0</td>
<td>2730</td>
<td>3.436</td>
<td>+1.40</td>
</tr>
<tr>
<td>5.0</td>
<td>5790</td>
<td>3.762</td>
<td>+1.76</td>
</tr>
</tbody>
</table>

From Graph 2, slope (of \( \log 10^4k \) v. \( -H_\circ \) ) = 1.0.
Table 3
Comparison of rate constants, $k_{IV}$, $k_{VIII}$, and $k_X$, for the hydrolysis of 2,4-0-butylidene-$D$-glucitol (IV), 2,4-O-isobutylidene-$D$-glucitol (VIII), and 2,4-O-but-2'-enylidene-$D$-glucitol (X), respectively, in HCl at $38.6^\circ$.

<table>
<thead>
<tr>
<th>Normality of acid</th>
<th>$10^4k_{IV}$</th>
<th>$10^4k_{VIII}$</th>
<th>$10^4k_X$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.05N</td>
<td>3280 min$^{-1}$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.10</td>
<td>5.90 min$^{-1}$</td>
<td></td>
<td>5320</td>
</tr>
<tr>
<td>1.0</td>
<td>149</td>
<td>96.6 min$^{-1}$</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>507</td>
<td></td>
<td>327</td>
</tr>
</tbody>
</table>

Table 4
Comparison of the rate constants, $k_{IV}$ and $k_{VIII}$, for the hydrolysis of 2,4-O-butylidene-$D$-glucitol (IV) and 2,4-O-isobutylidene-$D$-glucitol (VIII), respectively, in HCl, at different normalities and temperatures.

<table>
<thead>
<tr>
<th>Normality of acid</th>
<th>Temp.</th>
<th>$10^4k_{IV}$</th>
<th>$10^4k_{VIII}$</th>
<th>$k_{IV}/k_{VIII}$</th>
<th>Slope of Graph 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0N</td>
<td>30.0$^\circ$</td>
<td>48.5 min$^{-1}$</td>
<td>38.7 min$^{-1}$</td>
<td>1.253</td>
<td>0.0345</td>
</tr>
<tr>
<td></td>
<td>38.6</td>
<td>149</td>
<td>96.6</td>
<td>1.542</td>
<td></td>
</tr>
<tr>
<td></td>
<td>49.6</td>
<td>550</td>
<td>293</td>
<td>1.877</td>
<td></td>
</tr>
<tr>
<td>2.0N</td>
<td>30.0</td>
<td>184</td>
<td>135</td>
<td>1.363</td>
<td>0.0224</td>
</tr>
<tr>
<td></td>
<td>38.6</td>
<td>502</td>
<td>327</td>
<td>1.535</td>
<td></td>
</tr>
<tr>
<td></td>
<td>49.6</td>
<td>1660</td>
<td>938</td>
<td>1.770</td>
<td></td>
</tr>
</tbody>
</table>
Table 5
Comparison of rate constants, $k_{2.0\text{N}}$ and $k_{1.0\text{N}}$, for the hydrolysis of 2,4-O-butylidene-D-glucitol (IV) and 2,4-O-isobutylidene-D-glucitol (VIII) in 2.0N and 1.0N HCl, respectively, at different temperatures.

<table>
<thead>
<tr>
<th>Temp.</th>
<th>$k_{1.0\text{N}}$</th>
<th>$k_{2.0\text{N}}$</th>
<th>$k_{2.0\text{N}}/k_{1.0\text{N}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30.0°</td>
<td>48.5 min$^{-1}$</td>
<td>184 min$^{-1}$</td>
<td>3.3</td>
</tr>
<tr>
<td>38.6</td>
<td>149</td>
<td>502</td>
<td>3.4</td>
</tr>
<tr>
<td>49.6</td>
<td>550</td>
<td>1660</td>
<td>3.0</td>
</tr>
<tr>
<td>VIII</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30.0</td>
<td>38.7</td>
<td>135</td>
<td>3.5</td>
</tr>
<tr>
<td>38.6</td>
<td>96.6</td>
<td>327</td>
<td>3.4</td>
</tr>
<tr>
<td>49.6</td>
<td>293</td>
<td>938</td>
<td>3.2</td>
</tr>
</tbody>
</table>
Table 6

Comparison of rate constants, \( k_{30.0} \), \( k_{38.6} \), and \( k_{49.6} \), at temperatures 30.0°, 38.6°, and 49.6°, respectively, for the hydrolysis of 2,4-\( \alpha \)-butylidene-D-glucitol (IV) and 2,4-\( \alpha \)-isobutylidene-D-glucitol (VIII) in HCl at different normalities.

<table>
<thead>
<tr>
<th>Normality of acid</th>
<th>Temp.</th>
<th>( 10^4k )</th>
<th>Ratios</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.0N</td>
<td>30.0°</td>
<td>48.5 min(^{-1})</td>
<td>( k_{38.6}/k_{30.0} = 3.1 )</td>
</tr>
<tr>
<td></td>
<td>38.6</td>
<td>149</td>
<td>( k_{49.6}/k_{38.6} = 3.7 )</td>
</tr>
<tr>
<td></td>
<td>49.6</td>
<td>550</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>30.0</td>
<td>184</td>
<td>( k_{38.6}/k_{30.0} = 2.7 )</td>
</tr>
<tr>
<td></td>
<td>38.6</td>
<td>502</td>
<td>( k_{49.6}/k_{38.6} = 3.5 )</td>
</tr>
<tr>
<td></td>
<td>49.6</td>
<td>1660</td>
<td></td>
</tr>
<tr>
<td>VIII</td>
<td>1.0</td>
<td>38.7</td>
<td>( k_{38.6}/k_{30.0} = 2.5 )</td>
</tr>
<tr>
<td></td>
<td>38.6</td>
<td>96.6</td>
<td>( k_{49.6}/k_{38.6} = 3.0 )</td>
</tr>
<tr>
<td></td>
<td>49.6</td>
<td>293</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>30.0</td>
<td>135</td>
<td>( k_{38.6}/k_{30.0} = 2.4 )</td>
</tr>
<tr>
<td></td>
<td>38.6</td>
<td>327</td>
<td>( k_{49.6}/k_{38.6} = 2.9 )</td>
</tr>
<tr>
<td></td>
<td>49.6</td>
<td>938</td>
<td></td>
</tr>
</tbody>
</table>
### Table 7

Hydrolyses in 2N HCl at 38.6°.

<table>
<thead>
<tr>
<th>Time</th>
<th>( \alpha )</th>
<th>( \alpha_t - \alpha_0 )</th>
<th>log ( [100(\alpha_t - \alpha_0)] )</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 min.</td>
<td>0.204°</td>
<td>0.226</td>
<td>1.354</td>
</tr>
<tr>
<td>4</td>
<td>0.188</td>
<td>0.210</td>
<td>1.322</td>
</tr>
<tr>
<td>9</td>
<td>0.122</td>
<td>0.144</td>
<td>1.158</td>
</tr>
<tr>
<td>15</td>
<td>0.080</td>
<td>0.102</td>
<td>1.009</td>
</tr>
<tr>
<td>20</td>
<td>0.047</td>
<td>0.069</td>
<td>0.839</td>
</tr>
<tr>
<td>30</td>
<td>0.016</td>
<td>0.038</td>
<td>0.580</td>
</tr>
<tr>
<td>39</td>
<td>-0.001</td>
<td>0.021</td>
<td>0.322</td>
</tr>
<tr>
<td>46</td>
<td>-0.009</td>
<td>0.013</td>
<td>0.114</td>
</tr>
<tr>
<td>( \infty )</td>
<td>-0.022</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

From Graph 7, \( k = 638 \times 10^{-4} \) min\(^{-1} \).

c) 0.375% solution of 4,6-O-butylidene-D-glucoitol (IX).

<table>
<thead>
<tr>
<th>Time</th>
<th>( \alpha )</th>
<th>( \alpha_t - \alpha_0 )</th>
<th>log ( [100(\alpha_t - \alpha_0)] )</th>
</tr>
</thead>
<tbody>
<tr>
<td>2½ min.</td>
<td>0.217°</td>
<td>0.199</td>
<td>1.299</td>
</tr>
<tr>
<td>4</td>
<td>0.193</td>
<td>0.175</td>
<td>1.243</td>
</tr>
<tr>
<td>6½</td>
<td>0.172</td>
<td>0.154</td>
<td>1.188</td>
</tr>
<tr>
<td>10</td>
<td>0.150</td>
<td>0.132</td>
<td>1.121</td>
</tr>
<tr>
<td>13</td>
<td>0.129</td>
<td>0.111</td>
<td>1.045</td>
</tr>
<tr>
<td>17</td>
<td>0.109</td>
<td>0.091</td>
<td>0.959</td>
</tr>
<tr>
<td>21</td>
<td>0.089</td>
<td>0.071</td>
<td>0.851</td>
</tr>
<tr>
<td>30</td>
<td>0.064</td>
<td>0.046</td>
<td>0.663</td>
</tr>
<tr>
<td>55</td>
<td>0.025</td>
<td>0.007</td>
<td>0.085</td>
</tr>
<tr>
<td>( \infty )</td>
<td>0.018</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

From Graph 7, \( k = 528 \times 10^{-4} \) min\(^{-1} \).
Hydrolyses in N HCl at 38.6°.

a) 2% solution of 2,4-D-butyldiene-D-glucitol (IV).

<table>
<thead>
<tr>
<th>Time</th>
<th>$\alpha$</th>
<th>$\Delta \alpha$</th>
<th>$\log \left[100(\alpha - \alpha_0)\right]$</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 min.</td>
<td>0.429°</td>
<td>0.285</td>
<td>1.455</td>
</tr>
<tr>
<td>5</td>
<td>0.407</td>
<td>0.263</td>
<td>1.420</td>
</tr>
<tr>
<td>7</td>
<td>0.398</td>
<td>0.254</td>
<td>1.405</td>
</tr>
<tr>
<td>11</td>
<td>0.384</td>
<td>0.240</td>
<td>1.380</td>
</tr>
<tr>
<td>15</td>
<td>0.370</td>
<td>0.226</td>
<td>1.354</td>
</tr>
<tr>
<td>21</td>
<td>0.352</td>
<td>0.208</td>
<td>1.318</td>
</tr>
<tr>
<td>32</td>
<td>0.320</td>
<td>0.176</td>
<td>1.246</td>
</tr>
<tr>
<td>48</td>
<td>0.285</td>
<td>0.141</td>
<td>1.149</td>
</tr>
<tr>
<td>70</td>
<td>0.243</td>
<td>0.099</td>
<td>0.998</td>
</tr>
</tbody>
</table>

From Graph 8, $k = 149 \times 10^{-4}$ min$^{-1}$.

b) 0.375% solution of 3,4-D-butyldiene-D-glucitol (VII).

<table>
<thead>
<tr>
<th>Time</th>
<th>$\alpha$</th>
<th>$\Delta \alpha$</th>
<th>$\log \left[100(\alpha - \alpha_0)\right]$</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 min.</td>
<td>0.240°</td>
<td>0.261</td>
<td>1.417</td>
</tr>
<tr>
<td>5</td>
<td>0.232</td>
<td>0.253</td>
<td>1.403</td>
</tr>
<tr>
<td>10½</td>
<td>0.210</td>
<td>0.231</td>
<td>1.364</td>
</tr>
<tr>
<td>16</td>
<td>0.186</td>
<td>0.207</td>
<td>1.316</td>
</tr>
<tr>
<td>23</td>
<td>0.161</td>
<td>0.182</td>
<td>1.260</td>
</tr>
<tr>
<td>31</td>
<td>0.134</td>
<td>0.155</td>
<td>1.190</td>
</tr>
<tr>
<td>41</td>
<td>0.108</td>
<td>0.129</td>
<td>1.111</td>
</tr>
<tr>
<td>68</td>
<td>0.054</td>
<td>0.075</td>
<td>0.875</td>
</tr>
</tbody>
</table>

From Graph 8, $k = 194 \times 10^{-4}$ min$^{-1}$.
Table 8 (cont.)

c) 0.5% solution of 4,6-O-butyldiene-\(\beta\)-glucitol (IX).

<table>
<thead>
<tr>
<th>Time</th>
<th>(\lambda)</th>
<th>(\lambda - \lambda_0)</th>
<th>(\log[100(\lambda - \lambda_0)])</th>
</tr>
</thead>
<tbody>
<tr>
<td>2½ min.</td>
<td>0.297°</td>
<td>0.268</td>
<td>1.428</td>
</tr>
<tr>
<td>5</td>
<td>0.288</td>
<td>0.259</td>
<td>1.413</td>
</tr>
<tr>
<td>8</td>
<td>0.271</td>
<td>0.242</td>
<td>1.384</td>
</tr>
<tr>
<td>14</td>
<td>0.244</td>
<td>0.215</td>
<td>1.332</td>
</tr>
<tr>
<td>23</td>
<td>0.208</td>
<td>0.179</td>
<td>1.253</td>
</tr>
<tr>
<td>32</td>
<td>0.182</td>
<td>0.153</td>
<td>1.185</td>
</tr>
<tr>
<td>41</td>
<td>0.158</td>
<td>0.129</td>
<td>1.111</td>
</tr>
<tr>
<td>53</td>
<td>0.132</td>
<td>0.103</td>
<td>1.013</td>
</tr>
<tr>
<td>65</td>
<td>0.110</td>
<td>0.081</td>
<td>0.909</td>
</tr>
</tbody>
</table>

From Graph 8, \(k = 189 \times 10^{-4}\) min\(^{-1}\).
Table 9

Specific rotations of 2,4-0-butylidene-D-glucitol (IV), 3,4-0-butylidene-D-glucitol (VII), 2,4-0-isobutylidene-D-glucitol (VIII), and 4,6-0-butylidene-D-glucitol (IX) in various media at 38.6°.

<table>
<thead>
<tr>
<th></th>
<th>IV</th>
<th>VII</th>
<th>VIII</th>
<th>IX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>-9.2°</td>
<td>+36.4°</td>
<td>-7.6°</td>
<td>-31.0°</td>
</tr>
<tr>
<td>0.1N HCl</td>
<td>-10.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5N HCl</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.0N HCl</td>
<td>-10.8</td>
<td>+34.8</td>
<td>-8.3</td>
<td>-31.9</td>
</tr>
<tr>
<td>2.0N HCl</td>
<td>-11.3</td>
<td>+31.8</td>
<td>-9.0</td>
<td>-31.3</td>
</tr>
<tr>
<td>3.0N HCl</td>
<td>-11.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.0N HCl</td>
<td>-12.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.0N HCl</td>
<td>-13.3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2,4-0-but-2'-enylidene-D-glucitol (X) has been excluded since it has a very small specific rotation (+0.3°), which meant that all calculated values could be within experimental error.

Table 10

Specific rotations of 2,4-0-butylidene-D-glucitol (IV) and 2,4-0-isobutylidene-D-glucitol (VIII) at different temperatures in various media.

<table>
<thead>
<tr>
<th></th>
<th>IV</th>
<th></th>
<th>VIII</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature</td>
<td>30.0°</td>
<td>38.6°</td>
<td>49.6°</td>
<td>30.0°</td>
</tr>
<tr>
<td>Water</td>
<td>-11.0°</td>
<td>-9.2°</td>
<td>-8.7°</td>
<td>-8.6°</td>
</tr>
<tr>
<td>1.0N HCl</td>
<td>-11.3</td>
<td>-10.8</td>
<td>-9.6</td>
<td>-8.7</td>
</tr>
<tr>
<td>2.0N HCl</td>
<td>-12.3</td>
<td>-11.3</td>
<td>-10.5</td>
<td>-9.3</td>
</tr>
</tbody>
</table>
Table 11

Observed equilibrium rotations in the hydrolyses of 2,4- (IV), 3,4- (VII), and 4,6-0-butylidene-D-glucitol (IX) at 38.6°, all values being adjusted to a 0.375% initial acetal concentration.

<table>
<thead>
<tr>
<th></th>
<th>IV</th>
<th>VII</th>
<th>IX</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-0.027</td>
<td>-0.022</td>
<td>-0.021</td>
</tr>
<tr>
<td></td>
<td>-0.027</td>
<td>-0.021</td>
<td>-0.022</td>
</tr>
</tbody>
</table>

in 2.0N HCl

Table 12

Arrhenius activation energies, $E_a$, and frequency factors, $A$, for the hydrolyses of 2,4-0-butylidene-D-glucitol (IV) and 2,4-0-isobutylidene-D-glucitol (VIII).

<table>
<thead>
<tr>
<th></th>
<th>$E_a$</th>
<th>$A$</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>21.9 cal. mole$^{-1}$</td>
<td>$10^{13}$</td>
</tr>
<tr>
<td></td>
<td>24.2</td>
<td>$10^{13}$</td>
</tr>
<tr>
<td>VIII</td>
<td>19.2</td>
<td>$10^{10}$</td>
</tr>
<tr>
<td></td>
<td>20.2</td>
<td>$10^{10}$</td>
</tr>
</tbody>
</table>

in 2.0N HCl

- from Graph 12.
Table 13

The formation of 2,4-D-0-butylidene-D-glucitol (IV) from D-glucitol and n-butyraldehyde at 30.0°.

a) In 2N HCl

<table>
<thead>
<tr>
<th>Time</th>
<th>( \alpha )</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 min</td>
<td>-0.320°</td>
</tr>
<tr>
<td>9</td>
<td>-0.364</td>
</tr>
<tr>
<td>13</td>
<td>-0.392</td>
</tr>
<tr>
<td>15</td>
<td>-0.395</td>
</tr>
<tr>
<td>20</td>
<td>-0.388</td>
</tr>
<tr>
<td>28</td>
<td>-0.368</td>
</tr>
<tr>
<td>35</td>
<td>-0.342</td>
</tr>
<tr>
<td>50</td>
<td>-0.310</td>
</tr>
<tr>
<td>60</td>
<td>-0.287</td>
</tr>
<tr>
<td>80</td>
<td>-0.260</td>
</tr>
<tr>
<td>100</td>
<td>-0.232</td>
</tr>
<tr>
<td>140</td>
<td>-0.200</td>
</tr>
</tbody>
</table>

b) In 2N H\(_2\)SO\(_4\)

<table>
<thead>
<tr>
<th>Time</th>
<th>( \alpha )</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 min</td>
<td>-0.207°</td>
</tr>
<tr>
<td>7</td>
<td>-0.259</td>
</tr>
<tr>
<td>10</td>
<td>-0.304</td>
</tr>
<tr>
<td>15</td>
<td>-0.346</td>
</tr>
<tr>
<td>20</td>
<td>-0.366</td>
</tr>
<tr>
<td>25</td>
<td>-0.370</td>
</tr>
<tr>
<td>30</td>
<td>-0.360</td>
</tr>
<tr>
<td>40</td>
<td>-0.340</td>
</tr>
<tr>
<td>50</td>
<td>-0.317</td>
</tr>
<tr>
<td>60</td>
<td>-0.296</td>
</tr>
<tr>
<td>90</td>
<td>-0.246</td>
</tr>
<tr>
<td>120</td>
<td>-0.217</td>
</tr>
</tbody>
</table>

- for Graph 13.
Graph I. Plot of $\log\left[100(x_t - x_0)\right]$ against time for the hydrolysis of 2,4-O-butylenediene-D-glucitol in 2N HCl at 38.6°.

- O 5% solution
- X 2% solution
- △ 0.5% solution
**GRAPH 2.** Plot of log $10^4k$ against $-H_0$

For the hydrolysis of

$2,4$-o-butylidene-3-GLUCITOL

in hydrochloric acid at $38.6^\circ$

**Slope = 1.0**
Graph 4: Plot of $K_{IV}/K_{VIII}$ against temperature.

- $\circ$ for 1N HCl
- $\triangle$ for 2N HCl

Slope = 0.0345

Slope = 0.0224
Graph 7. Plot of \[
\log \left[100 (x_0 - x) \right]
\] against time for the hydrolyses of mono-o-butyridene-2-glucitols in 2N HCl at 38.6°C.

- 2,4-acetal: \( K = 502 \times 10^{-4} \text{ min}^{-1} \)
- 3,4-acetal: \( K = 638 \times 10^{-4} \text{ min}^{-1} \)
- 4,6-acetal: \( K = 528 \times 10^{-4} \text{ min}^{-1} \)
Graph 8. Plot of \( \log_{100}(x_0 - x) \) against time for the hydrolyses of mono-\( \beta \)-butyridene-\( \beta \)-glucitols in N HCl at 38.6°C.

\( \bullet \) 2,\( \beta \)-Acetal from Graph, \( k = 1.49 \times 10^{-14} \text{ min}^{-1} \)
\( \times \) 3,\( \beta \)-Acetal \( k = 19.6 \times 10^{-4} \text{ min}^{-1} \)
\( \Delta \) 4,6-Acetal \( k = 189 \times 10^{-4} \text{ min}^{-1} \)
Graph 12. For activation energy, Eq

\[ \log K \text{ plotted against } \frac{1}{T} \times 10^3 \]

2,4-O-Butyridene-\( \alpha \)-glucitol, in NHCl
2N HCl
2,4-O-Isobutyridene-\( \alpha \)-glucitol, in NHCl
in 2N HCl

\[ \frac{1}{T} \times 10^3 \text{ (T in } ^\circ \text{C}) \]
GRAPH 13. OPTICAL ROTATION PLOTTED AGAINST TIME FOR FORMATION OF 2,4-O-BUTYLDENE-D-GLUCITOL

O in 2N HCl
x in 2N H₂SO₄ AT 30.0°
A - 2,4-0-BUTYLDENE-0-GLUCITOL IN WATER (10% SOLUTION)
B - 2,4-0-BUTYLDENE-0-GLUCITOL IN N HCl (20% SOLUTION) AT EQUILIBRIUM, AT 38.6°C.
C - O-BUTYRALDEHYDE IN WATER (0.306% SOLUTION).
E. CONDENSATIONS WITH ACROLEIN

Experiment 44 Preparation of tri-O-allylidene-\(\text{D-}\)glucitol.

a) Using method described by Fischer and Smith\(^{43}\).

\(\text{D-}\)glucitol (27.3 g., 1 mol.), acrolein (23.7 g., 3 mol.), benzene (70 ml.), and toluene-\(p\)-sulphonic acid (0.1 g.) were mixed together thoroughly, and then heated strongly with a Dean and Starke head for 10 hr.; 2.5 ml. water were collected (30% theoretical based on conversion to triacetal product). Unchanged \(\text{D-}\)glucitol remained at the bottom of the flask in a gelatinous state. The excess acrolein and benzene were removed under reduced pressure, and then an excess of calcium oxide in benzene was added to neutralise the acid catalyst. The benzene was then removed under reduced pressure and the residue was extracted with chloroform. The chloroform soluble extract was assumed to contain the required product; the chloroform was removed from this, and a very viscous yellow oil was obtained. 

\[ [\alpha]_D^{22} +2.27 \text{ (c 1.8 in CHCl}_3 \] . This product became more viscous and appeared to be mainly polymeric.

44b) Using the method of Fischer and Smith, with nitrobenzene added as solvent for \(\text{D-}\)glucitol, and thiophen as free radical trap.

\(\text{D-}\)glucitol (10 g., 1 mol.) and nitrobenzene (25 ml.) were heated together until they formed a solution. Then
acrolein (20 g., 7 mol.), benzene (80 ml.), toluene-$p$-sulphonic acid (0.1 g.), and thiophen (a few drops) were added and the whole was heated at ca. 110°, with a Dean and Starke head, for 20 hr.; 0.8 ml. water was collected (27% theoretical, based on conversion to triacetal product). The supernatant liquid was then decanted from the unchanged D-glucitol and was distilled under reduced pressure, to remove excess acrolein and benzene. Then calcium oxide was added with more benzene to neutralise the acidic catalyst, after shaking well the solution was filtered. The filtrate was then distilled to remove the benzene and nitrobenzene. The oily residue was then fractionally distilled to yield two fractions: Fraction A: b.p. 144-148°/0.4 mm., 1.3 g., $n_D^{25}$ 1.4963. Fraction B: 166-180°/0.4 mm., 0.6 g., $n_D^{25}$ 1.5008. Total yield 1.9 g., 12% theoretical. (Lit. values for tri-Å-allylidene-D-glucitol: b.p. 149-151°/0.9 mm., $n_D^{20}$ 1.4865. 43). On keeping this liquid became extremely viscous.

**Experiment 45 Effects of condensing agents on acrolein.**

45a) With toluene-$p$-sulphonic acid.

Acrolein (25 ml.) and toluene-$p$-sulphonic acid (0.1 g.) were boiled together for 4 hr., and then left to cool. After standing for a short time the mixture set to an orange-coloured, rock-hard solid.
b) With phosphoryl chloride.

Acrolein (8 ml.) and phosphoryl chloride (1 drop) were mixed together and then left to stand at room temperature. After 1 week the solution had become very viscous, and after 10 days it had become a rubbery solid. This then hardened with contraction, which caused fissures in the resultant orange coloured resin.

Experiment 46 Action of phosphoryl chloride on a mixture of D-glucitol and acrolein.

46a) D-glucitol (18 g., 1 mol.) and acrolein (25 ml., 4 mol.) were shaken together and then left to stand at room temperature; the D-glucitol remained as a suspension in the acrolein. Then phosphoryl chloride (3 drops) was added, the whole shaken together thoroughly, and then left to stand at room temperature. The D-glucitol was taken into solution very slowly, and after standing overnight a clear, very viscous, pale yellow solution was obtained (A). Chromatograms developed in B.E.W. gave a long streak which could be detected with AgNO₃, D.N.P.H., and KMnO₄. No D-glucitol was detected.

When part of (A) was warmed gently it gave a hard transparent solid after ca. 1 hr. When this solid was examined using a Kofler block and microscope it was noted that no changes occurred until ca. 150°; from then on it appeared to swell slightly; above 250° the substance became
more orange in colour; there was no sign of melting up to 300°. The swelling over the whole temperature range, although visible, was very slight.

It was also found that A became a glass-like solid after standing for ca. 3 weeks at room temperature.

46b) \( \text{D-glucitol (18 g., 1 mol.), acrolein (25 ml., 4 mol.),} \)
and phosphoryl chloride (3 drops) were shaken together and then left to stand at room temperature. Samples of the reaction mixture were removed at intervals, after \( \frac{1}{2} \) hr., 1½ hr., 2½ hr., 5 hr., and 7½ hr., and they were developed chromatographically in E.E.W. The positions of the compounds were detected with \( \text{AgNO}_3 \) and D.N.P.H. The chromatograms showed that after \( \frac{1}{2} \) hr. the reaction mixture contained much unchanged \( \text{D-glucitol} \), a compound in the position of a monoacetal of \( \text{D-glucitol} \) which could be detected with both reagents, and a streak of a faster running compound which could also be detected by both reagents. Chromatograms showed a continuous decrease with time of the quantity of \( \text{D-glucitol} \) present, at 7½ hr. only a trace could be detected. At the same time the streak increased in intensity until at 7½ hr. it appeared as the predominant product, with only a trace of the intermediate product remaining.
**Experiment 47** The action of phosphoryl chloride on acrolein mixed with various polyhydroxy compounds, and their derivatives.

The reactants were mixed in the proportions: acrolein - 8 ml., phosphoryl chloride - 1 drop, polyhydroxy compound - 6 g., and the mixture was left to stand at room temperature.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Acrolein polymerised with contraction, causing fissures in the resin.</td>
</tr>
<tr>
<td>D-glucitol</td>
<td>Obtained clear, pale yellow resin, no contraction. Rubbery solid after 1 week, glass-hard after 3 weeks.</td>
</tr>
<tr>
<td>2,4-O-but-2'-enylidene-D-glucitol</td>
<td>Obtained clear, yellow resin as with D-glucitol; slower setting and slightly more rubbery.</td>
</tr>
<tr>
<td>2,4-O-furfurylidene-D-glucitol</td>
<td>Dark brown resin formed, with decomposition of the furfurylidene compound.</td>
</tr>
<tr>
<td>Mannitol</td>
<td>Almost completely insoluble in acrolein mixture, acrolein polymerised.</td>
</tr>
<tr>
<td>1,3:4,6-di-O-methylene-D-mannitol</td>
<td>Insoluble in acrolein mixture, no resinification.</td>
</tr>
<tr>
<td>Mannitol hexaacetate</td>
<td>Insoluble in acrolein mixture, no resinification.</td>
</tr>
<tr>
<td>Glucose</td>
<td>Slightly soluble in acrolein mixture; yellow resin formed above unchanged glucose.</td>
</tr>
<tr>
<td>Compound</td>
<td>Result</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Glucose pentaacetate</td>
<td>Insoluble in acrolein mixture, no resinification.</td>
</tr>
<tr>
<td>Fructose</td>
<td>Obtained a very viscous solution above unchanged fructose.</td>
</tr>
<tr>
<td>Sucrose</td>
<td>A little sucrose appeared to be taken into solution. An orange resin set above unchanged sucrose, with contraction. It appears very similar to that obtained from acrolein alone.</td>
</tr>
<tr>
<td>Sucrose octaacetate</td>
<td>Obtained homogenous solution with slight increase in viscosity, no resinification.</td>
</tr>
</tbody>
</table>

Acrolein alone and D-glucitol are included for comparison purposes.

Experiment 48 Reaction of D-glucitol and acrolein in 3N sulphuric acid.

48a) D-glucitol (18 g., 1 mol.) and 3N sulphuric acid (5.2 ml.) were warmed to a syrup, and then cooled to room temperature. Acrolein (7 ml., 1 mol.) was added and the whole was shaken together, the solution was then left to stand at room temperature. The solution became more viscous with time and finally set into a rubbery solid.

48b) The reaction mixture was prepared as in Expt. 48a. After standing for 1 day methanol (15 ml.) and concentrated ammonia solution (1.1 ml.), to neutralise the acid, were added. Ammonium sulphate crystals were precipitated and
filtered off. All volatile matter was removed from the filtrate and then the remaining oil was heated for distillation at 0.1 mm. The oil would not distil, it darkened in colour, with decomposition, at ca. 120°.

**Experiment 49 Other reactions in 3N sulphuric acid.**

The reactants were mixed in the proportions:—compound (9 g.) and 3N sulphuric acid (2.6 ml.) and warmed to obtain, as far as possible, a homogenous solution. Then acrolein (3.5 ml.) added to the whole, the mixture shaken for 12 hr. and then left to stand, at room temperature.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>Obtained opaque rubbery resin, containing some unchanged glucose.</td>
</tr>
<tr>
<td>Fructose</td>
<td>Very small amount unchanged fructose remained below orange coloured rubbery resin.</td>
</tr>
<tr>
<td>Sucrose</td>
<td>Very small amount undissolved solid remains below an orange coloured rubbery resin, which hardens considerably on standing.</td>
</tr>
</tbody>
</table>
REFERENCES
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By T. G. Bonner, E. J. Bourne, Miss S. E. Harwood, and D. Lewis.

Condensation of D-glucitol with n-butyraldehyde in the presence of various catalysts has been studied, and the cyclic 2,4- and 3,4-mono-, 1,3:2,4-di-, and 1,3,2,4,5,6-tri-O-butylidene derivatives have been characterised. The structures assigned to the last two compounds are based on the assumption that there is no significant migration of acetal groups during partial hydrolysis. Independent correlation of structure for the acetics was possible using the known but-2'-enylidene glucitols.

D-Glucitol condenses with n-butyraldehyde in the presence of aqueous sulphuric acid to yield 2,4-O-butyldiene-D-glucitol (I) (21%) (cf. preparation of 2,4-O-furfurylidene glucitol). This material on acid hydrolysis was proved to be a glucitol derivative (isolation of glucitol as its trisphenylboronate) and an n-butyraldehyde derivative (isolation of n-butyraldehyde as its bisdimedone). The structure of the monoacetal (I) followed from the facts that it consumed 1 mol. of periodate and liberated 1 mol. of formaldehyde. The 2,4-O-butyldiene-L-xylose resulting from the oxidation was characterised as its crystalline p-nitrophenylhydrazone. Hydrolysis of the xylose acetal gave crystalline L-xylose (7%), which was characterised further as its tetra-acetate. The monoacetal (I) yielded a crystalline tetraacetate (identical with the product from reduction of tetra-O-acetyl-2,4-O-but-2'-enylidene-glucitol), a bisphenylboronate, and a ditriphenylmethyl ether, thus supporting the presence of four hydroxyl groups, two of which were probably primary. Confirmation of the structure followed when the monoacetal (I) was obtained by reduction of 2,4-O-but-2'-enylidene-D-glucitol.

Holst condensed glucitol and n-butyraldehyde using concentrated sulphuric acid as the catalyst, and fractionally distilled the product to give two syrupy tributylidene glucitols which he did not characterise. We could not repeat this fractionation, but partial acid hydrolysis of the syrupy distillate gave crystalline 1,3:2,4-di-O-butylidene-D-glucitol (II) (15%), 2,4-monoacetal (10%), and an intractable syrup. This result suggests that the triacetal product was indeed a mixture of isomers, one of which was 1,3,2,4,5,6-tri-O-butylidene-D-glucitol (III). The same diacetal (II) was obtained by reduction of 1,3:2,4-di-O-but-2'-enylidene glucitol, but its structure was proved independently by periodate oxidation in which 1 mol. of oxidant was consumed and 1 mol. of formaldehyde was liberated. The resulting crystalline 2,4:3,5-di-O-butylidene-aldehyde-L-xylose (42—67%) was characterised through its crystalline p-nitrophenylhydrazone. The dibutylidene xylose, as expected, mutarotated in chloroform, and on crystallisation from ethanol gave an unstable alcoholate. On acid hydrolysis it yielded xylose. The diacetal (II) gave a crystalline diacetate (identical
with the product from reduction of 5,6-di-O-acetyl-1,3:2,4-di-O-but-2'-enyldieneglucitol, a dibenzoate, and a monotriphenylmethyl ether monoacetate, thus substantiating the presence of two hydroxyl groups, of which one is probably primary. Partial acid hydrolysis of the diacetal gave the 2,4-monoacetal (10%), thus indicating that the diacetal was a 1,3:2,4-substituted compound.

Pure, crystalline tributylideneglucitol (III) was obtained by hydrogenation of crystalline 1,3:2,4:5,6-tri-O-but-2'-enyldieneglucitol. On partial hydrolysis it yielded the crystalline 1,3:2,4-diacetal (II) (41%)—thus proving its structure—and the 2,4-monoacetal (I) (15%). The identity of the diacetal was confirmed further by isolation of its dibenzoate, which was identical with the aforementioned sample.

When glucitol and the aldehyde were condensed using a trace of toluene-^-sulphonic acid as catalyst and removing the water of acetalisation by azotropic distillation with benzene, a different syrupy mixture of triacetals seemed to be formed, since acid hydrolysis, under the same conditions as for the hydrolysis of the triacetal product obtained using concentrated sulphuric acid, now yielded 3,4-O-butylidene-D-glucitol (IV) (13%) in addition to the 2,4-monoacetal (8%), but only a trace of the crystalline diacetal (II). The 3,4-monoacetal reduced 2 mol. of periodate and liberated 2 mol. of formaldehyde but no formic acid. The same monoacetal was obtained also by reduction of 3,4-O-but-2'-enyldiene-D-glucitol, thus confirming its structure. The isolation of a 3,4-monoacetal suggests that, barring ring re-arrangements, the original triacetal contained some 1,2:3,4:5,6-tri-O-butylidene-D-glucitol.

It is clear therefore that n-butyraldehyde and crotonaldehyde resemble other aldehydes in forming from glucitol a 2,4-monoacetal and a 1,3:2,4:5,6-triacetal, from which the 1,3:2,4-diacetal can be obtained by hydrolysis. However, it seems that the triacetal fraction is a mixture, containing also the 1,2,3,4:5,6-compound.

**Experimental**

Quantitative periodate oxidations 5 and formaldehyde determinations 6,7 used standard procedures. n-Butyraldehyde, present in the formaldehyde determination, does not interfere.8 Light petroleum refers to the fraction b. p. 60—80°.

_**Reduction of But-2'-enyldieneglucitols to Butylidene Derivatives.**—The compound dissolved in ethanol (5—10% w/v), except where stated, was reduced with hydrogen at room temperature and atmospheric pressure in the presence of a palladium catalyst (0-01—0-02 g./g. of compound).

_**Reduction of 2,4-O-But-2'-enyldiene-D-glucitol.**—The monoacetal (1-00 g.) in 80% aqueous ethanol, absorbed 1-01 mol. of hydrogen. The 2,4-O-butylidene-D-glucitol (Found: C, 50-85; H, 8-4. C19H20O6 requires C, 50-8; H, 8-6%) was crystallised from ethanol (10 ml.) as needles (0-86 g., 85%), m. p. 158—159°, [α]D -10° (c 1-9 in H2O), [α]D +9° (c 1-9 in 1% aqueous boric acid).

_**Condensation of n-Glucitol and n-Butyraldehyde in the Presence of Aqueous Sulphuric Acid.**—Equimolar amounts of polyol (18 g.) and n-butyraldehyde were used, as described for crotonaldehyde; 2,4-O-butylidene-D-glucitol was obtained (21%, from ethanol), m. p. and mixed m. p. with the aforementioned 2,4-monoacetal, 157—158°, [α]D +9° (c 1-9 in H2O), [α]D -9° (c 1-9 in 4% w/v 60% aqueous methanolic (PhBO)3).

_**Identification of the Products of Acid Hydrolysis of 2,4-O-Butylidene-D-glucitol.**—The compound (0-50 g.), water (20 ml.) and Zeo-Karb 225 ion exchange resin (Permutit Co. Ltd.) in the hydrogen form (0-3 ml.) were heated at 100° for 1 hr.; volatile matter was distilled off at 20 mm. into a trap cooled in liquid nitrogen. Water (20 ml.) was added to the residue, and the procedure was repeated twice. The distillate was added to dimedone (0-6 g.) in water (40 ml.). After 2 days the yield of n-butyraldehyde bisdimedone was 0-40 g., m. p. and mixed with authentic specimen, 127—128°. Recrystallised from ethanol, the material had m. p. 130°. The non-volatile residue was extracted with warm methanol (10 ml.) and the extract was added to phenylboronic anhydride (0-66 g., 1-0 mol.) in methanol (2 ml.). The yield of D-glucitol trisphenylboronate 9 was 0-59 g. (0-62 mol.). Recrystallised from ethanol—light petroleum it had m. p. 193—194°, not depressed in admixture with an authentic specimen.

_**Periodate Oxidation of 2,4-O-Butylidene-D-glucitol.**—(a) Quantitatively. The compound
triphenylmethyl groups are assumed to be at the methanol, the product (needles; 0-81 g., 53%), +9-5° within the range 70—80° (effervescence). After some hours at room temperature, the material had m. p. 6 8 — 6 9 ° , —7-9° (c 2-2 in water (20 ml.) containing sodium hydrogen carbonate (0-1 g.).

The reaction mixture was evaporated, and the residue was extracted with boiling ethanol. The ethanolic extract yielded crude L-xylose (0-05 g.) on cooling. Recrystallisation gave α-L-xylose (0-03 g., 7%), m. p. and mixed m. p. 144°. This material on acetylation gave tetra-O-acetyl-β-L-xylose (47%), m. p. and mixed m. p. 124°, from ethanol.

**Derivatives of 2,4-Octylidene-D-glucitol.**—(a) The monoacetal (0-385 g.), treated with acetic anhydride in pyridine, yielded 1,3,5,6-tetra-O-acetylated, 2,4-octylidene-D-glucitol, 0-40 g. (61%), m. p. 68—69°, [α] D 19 +7-9° (c 2-2 in CHCl 3 ) (Found: C, 53-6; H, 7-0%; n-alkali uptake, 9-72 ml./g., as needles from 10 parts 50% aqueous ethanol. Reduction of 1,3,5,6-tetra-O-acetyl-2,4-octylidene-D-glucitol also yielded the 4-octylidene acetal tetra-acetate, m. p. and mixed m. p. with the above specimen, 187—188-5°. 

Part (0-2 g.) in ethanol (2 ml.) was refluxed with p-nitrophenylhydrazine (0-16 g., 1 mol.) for 30 min. to yield 2,4-Octylidene-D-glucitol-p-nitrophenylhydrazone (0-04—0-11 g., 12—33%), m. p. 188—190° (Found: C, 53-3; H, 6-4; N, 12-2. C 15 H 23 N 2 O 4 requires C, 53-1; H, 6-2; N, 12-4%).

Part (0-6 g.) of the remaining butylidenexylose in water (50 ml.) was boiled with Zeo-Karb 255 ion exchange resin in the hydrogen form (a few grains) in an open flask for 15 min. The reaction mixture was evaporated, and the residue was extracted with boiling ethanol. The ethanolic extract yielded crude α-xylose (0-05 g.) on cooling. Recrystallisation gave α-L-xylose (0-03 g., 7%), m. p. and mixed m. p. 144°. This material on acetylation gave tetra-O-acetyl-β-L-xylose (47%), m. p. and mixed m. p. 124°, from ethanol.

(b) Holst's method, i.e., by using concentrated sulphuric acid. By condensing D-glucitol and the aldehyde, Holst 2 obtained two isomeric tributylidene derivatives—one (40%), b. p. 162—167°/4 mm., n D 20 1-462, [α] D 20 +10-0° (c 10-0 in EtOH), and the other (22%), b. p. 172—177°/4 mm. (not characterised further). In our hands, the method gave products which distilled from 136 to 162°/0-2 mm., with a small forerun at ca. 60°. The distillates (yield 50—80%) were redistilled (Found: C, 62-8; H, 9-2. C 15 H 23 O 4 requires C, 62-8; H, 9-4%), n D 20 1-461—1-463, [α] D 20 +2-3° to +7-0° (c 1-7 in EtOH), but did not afford a fraction of characteristic b. p.

(c) By using toluene-p-sulphonic acid. D-Glucitol (50 g.), n-butyrinaldehyde (100 ml., 4-14 mol.), benzene (100 ml.), and tolune-p-sulphonic acid (0-1 g.) were refluxed under a Dean and Stark head on a water-bath for 2 hr. More catalyst (0-1 g.) was then added and after a further 4 hr., 13-8 ml. (93%) of water had been collected. The solution was passed through Biodeminolit (Permutit Co. Ltd.) to remove the catalyst, and was then evaporated. The residue was distilled at 0-1 mm. A forerun, b. p. 48—60° was discarded;
the main fraction (81 g., 86%), had b. p. 143—148°, [α]D^20 +7-0° (c 10-0 in EtOH), ν^25 1-480.

Partial Acid Hydrolysis of the Triacetals obtained by Hohl's Method.— The triacetal fraction (130 g.), suspended in 60% aqueous acetic acid (576 ml.), was kept at 88—90° for 1 hr. The homogeneous solution was evaporated (both ca. 45°) and the cold residue was extracted with light petroleum using first a 200 ml., then a 50 ml. portion. The combined extracts contained unchanged starting material (25—32 g.). The light petroleum-insoluble material was dissolved in hot chloroform—benzene (130 ml. each), and allowed to cool, the 2,4-monoacetal (10—13 g.) crystallising. Recrystallisation from ethanol afforded the pure compound (46—78% recovery), m. p. and mixed m. p. 157—158°. The chloroform—benzene crystallisation liquors were evaporated and the residue (71 g.) was crystallised from a mixture of benzene (71 ml.) and light petroleum (100 ml.) to yield crude 1,3,2,4-diacetal. Crystallisation of this from benzene gave material (10—16 g.), m. p. 128—131°. Recrystallisation from benzene would not improve this value, but crystallisation from water gave material (50% recovery) of m. p. and mixed m. p. with the diacetal prepared below, 132°. The benzene—light petroleum liquors contained an intractable syrup.

Reduction of 1,3,2,4-Di-O-but-2'-enyldiene-D-glucitol.— The diacetal absorbed 2-01 mol. of hydrogen. The 1,3,2,4-di-O-butylidened-glucitol was crystallised from benzene to yield chunky crystals (69—80%), m. p. 130—132°, [α]D^20 +1-6° (c 1-6 in EtOH) (Found: C, 57-6; H, 9-0. C_{14}H_{28}O_{5} requires C, 57-9; H, 9-0%).

Periodate Oxidation of 1,3,2,4-Di-O-butyldiene-D-glucitol.—(a) Quantitatively. The compound consumed 0-98, 1-02, and 1-00 mol. of periodate (3-8 mol. initially present) after 1-75, 7-25, and 22 hr. respectively, and liberated 0-98 mol. of formaldehyde (theory, 1-0 mol.). (b) Qualitatively. Sodium periodate (0-9 g., 1-2 mol.) in water (15 ml.) was added during 12 min. to a fine suspension of the diacetal (1-0 g.) in water (25 ml.) containing sodium hydrogen carbonate (0-1 g.) at such a rate that the pH was ≈6-9. After a further 1 hr. at 20°, the solution was worked up as described for the 2,4-monoacetal. The distillate yielded formaldehyde bisdimedone (0-82 g., 0-81 mol.), m. p. and mixed m. p. 187—188°. The material in the chloroform extract was thric crystallised from 15 parts of light petroleum to yield needles of L-xylose, (66%), m. p. 94°, [α]D^20 +2-8° (c 1-6 in CHCl₃). A molecular weight analysis, by a standard cryoscopic procedure 18 with dry benzene as solvent, indicated that the compound was monomeric (Found: M, 256 ± 2. Calc.: M, 258-3) over the concentration range studied, i.e., up to 0-2M. The compound had a strong carbonyl absorption at 5-75 µ. Crystallisation of this material from ethanol gave a compound, presumably the hemiacetal, which showed a new strong carbonyl absorption band at 2-93 µm and virtually no absorption at 5-75 µm. This material was unstable — the m. p., at about 80—90°, was not reproducible, and different preparations gave different elemental combustion analysis values. Improved yields (67%) of the dibutylidene acetel were obtained by directly extracting it from the reaction mixture with chloroform.

2,4,3,5-Di-O-butyldenedaldehyde-1-xyllose (0-20 g.), p-nitrophenyldrazine (0-115 g.), and ethanol (3 ml.) were heated at 75—85° for 3 hr. The mixture was filtered, and the filtrate placed in a refrigerator for 3 days. The crude product, 0-22 g. (72%), m. p. 175—176° when recrystallised from ethanol gave the pure p-nitrophenyldrazone, needles (Found: C, 57-8; H, 7-0; N, 10-8). C_{18}H_{17}N_{2}O_{6} requires C, 58-0; H, 6-9; N, 10-7%). m. p. 182—184°, [α]D^20 —147-2° (c 1-5 in EtOH).

The xylose diacetal (0-25 g.), water (5 ml.), and Zeo-Karb 225 resin in the hydrogen form were kept at 100° for 4 hr. The resin was filtered off and washed, and the combined filtrate and washings were evaporated. The residual syrup crystallised from methanol gave l-xyllose, 0-09 g. (62%), m. p. and mixed m. p. 142—143°.

Derivatives of 1,3,2,4-Di-O-butyldiene-D-glucitol.—(a) 5,6-Di-O-acetyl-1,3,2,4-di-O-but-2'-enyldiene-D-glucitol * (60-60 g.) absorbed 2-14 mol. of hydrogen, and the 5,6-di-O-acetyl-1,3,2,4-di-O-butyldiene-D-glucitol formed was crystallised from 10 parts of 50% aqueous ethanol as needles (Found: C, 57-8; H, 8-2; N-alkali uptake, 5-27 ml./g. C_{18}H_{28}O_{5} requires C, 57-7; H, 8-1%; uptake, 5-34 ml./g.) (66%, m. p. 94°, [α]D^20 +2-8° (c 1-8 in EtOH). (b) 1,3,2,4-Di-O-butyldiene-D-glucitol, treated with acetic anhydride in pyridine, also yielded the diacetate (66%), m. p. and mixed m. p. with the above compound, 93—94°. (b) The diacetal (0-20 g.) in pyridine (1-4 ml.) was treated with benzoyl chloride (0-18 ml., 2-2 mol.) for 2 hr. The 5,6-dibenzozate crystallised from light petroleum as needles (0-14 g., 41%), m. p. 110°, [α]D^20 —30-0° (c 1-6 in CHCl₃) (Found: C, 67-8; H, 7-05; N-alkali uptake, 3-96 ml./g. C_{23}H_{32}O_{5} requires C, 67-45;...
H, 6-0%); uptake, 4-01 ml./g.). (e) The diacetal (1-0 g.) in pyridine (6-5 ml.) was treated with triphenylmethyl chloride (1 g., 1 mol.) for 27 hr. at room temperature. After being worked up in the usual way, the product was crystallised from light petroleum (30 ml.) to yield unchanged diacetal (0-2 g.; m. p. and mixed m. p. 131-5°). The crystallisation liquors were evaporated and the syrupy residue was dissolved in pyridine, and treated with acetic anhydride. The product was crystallised twice from light petroleum and then once from 75% aqueous ethanol to yield 0-89 g. of crude 1,3:2,4-diacetal, m. p. 21-6 g. [which yielded only a trace (0-89 g.) of crude 1,3:2,4-diacetal on crystallisation], acetal fraction (70-3 g.) was treated as described for the hydrolysis of the triacetals obtained mixed m. p. 157—158° (0-32 g., 15% based on the triacetal not recovered).

The semi-solid was hydrolysed as described for the hydrolysis of the mixed triacetals obtained mixed m. p. 155—158°. The chloroform-soluble material was a syrup.

The monoacetal (0-16 g., 10%), m. p. and that of monoacetal, 13-8 g. This material was crystallised from ethanol (100 ml.) to yield unchanged monoacetal (0-2 g.; m. p. and mixed m. p. 167—168°). The syrupy residue was dissolved in pyridine, and treated with acetic anhydride. The product was crystallised from light petroleum (30 ml.) absorbed 1-14 mol. of hydrogen. Crystallisation of the product from ethanol yielded 3,4-0-butylidene-D-glucitol (4-14 g., 13% based on material of m. p. 112—113°.

Reduction of 3,4-0-But-2'-enylidene-D-glucitol.—The compound consumed 1-97, 1-99, and 2-01 mol. of periodate (4-4 mol. initially present) after 1-5, 7, and 20-5 hr., respectively, and liberated 1-98 mol. of formaldehyde (theory, 2-0); no formic acid was found by volumetric analysis (theory, 0-0).

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Royal Holloway College, University of London, Englefield Green, Surrey. [Received, April 10th, 1964.]