Studies on the

1,2;5,6-Di-O-isopropylidene-\textit{D}-hexofuranoses

by

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Title of Thesis: Studies on the 1,2,5,6-Di-O-isopropylidene-
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For My Brother Howard.
Abstract

The family of compounds, the $1,2;5,6$-di-$\alpha$-isopropylidene-$\alpha$-hexofuranoses, have been investigated. The synthetic routes by which the $\alpha$-talo and $\alpha$-gulo compounds are obtained has been improved as well as a synthetic route for the $\alpha$-manno derivative, the only unknown member of this series. The synthesis of the four $1,2;5,6$-di-$\alpha$-isopropylidene-$\alpha$-hexofuran-3-uloses is described and an investigation into the ease of hydration and enol-acetate formation from these ketones is discussed. Catalytic reductive and rearrangement reactions of these unsaturated derivatives are described.

The conformational preferences of the $1,2;5,6$-di-$\alpha$-isopropylidene-$\alpha$-hexofuranoses was determined by relating NMR parameters of these compounds to their parent 3-deoxy compounds. Conformational information for these compounds was established by a Dihedral Angle Estimation by Ratio Method (DAERM). The problems associated with assigning reasonable Karplus constants are accommodated in the modification by assigning a ratio to the two Karplus constants. Using this method, the conformational preferences of the four 3-deoxy-$1,2;5,6$-di-$\alpha$-isopropylidene-$\alpha$-hexofuranoses were determined. Through a correspondence of coupling parameters, the endo and exo derivatives of these parent compounds are shown to have an essentially identical conformation to that of their parent. The $\alpha$-ribo-hexofuranose family had the $^3T_4=V_4=^0T_4$ conformational
preference; the D-lyxohexofuranose family had the $^4T_o = ^4V = ^4T_o$ conformational preference; the xylo-hexofuranose family had the $V_0 = ^1T_o = ^1V$ conformational preference; and the arabino family had the preference $^0T_1 = V_1 = ^2T_1$. The ribo- and the lyxo-derivatives tend to be considerably more distorted from planarity then the xylo- and arabino-derivatives. The $\theta$ dihedral angle of all these compounds exhibited a twist of about 25°, a value in agreement with x-ray crystal structure determinations.

The reactions undergone by, and the physical states exhibited by, the 1,2;5,6-di-O-isopropylidene-D-hexofuranoses are influenced by their conformational preferences. This work attempts to identify and elucidate such effects in this family of compounds.
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Chapter 1

Introduction

Since the first observation of electron coupled interactions between nuclear spins,\((1, 2, 3)\), nuclear magnetic resonance has become one of the most powerful tools for the determination of the molecular structure of compounds in solution. A completely general theory of electron coupled nuclear spin-spin interactions was first developed by Ramsey \((4)\). Application of this theory to chemically useful problems was attempted by McConnell \((5)\) in his investigation of proton-proton and fluorine-fluorine couplings using a molecular orbital theory for ground state wave functions. A somewhat similar investigation was carried out by Karplus and Anderson \((6)\), who, using a valence bond approach investigated the geminal proton-proton couplings observed in methane. Extension \((7)\) of this theory to vicinal couplings resulted in the prediction that vicinal couplings were dependent on the dihedral angle in accordance with equation I. This result was in agreement with early studies by Lemieux \((8)\) and coworkers which had indicated that the proton-proton couplings in a series of acetylated pyranose sugars were dependent on the dihedral angle. The general shape of the curve throughout the range of angles was substantiated by the work of Anet \((9)\) and theoretically by the molecular orbital calculations of Conroy \((10)\), Fahey, Graham, and

\[
J_1 = k_1 \cos^2 \varphi_1 - c \quad k_1 = 8.5 \text{ Hz} \quad 0 \leq \varphi_1 \leq 90^\circ
\]

\[
J_2 = k_2 \cos^2 \varphi_2 - c \quad k_1 = 9.5 \text{ Hz} \quad 90^\circ \leq \varphi_2 \leq 180^\circ
\]
Piccioni (11), and Pople and his coworkers (12).

The dependency of coupling on electron withdrawing or donating substituents was indicated by the work of Bothner-By and Glick (13) from their study of a series of substituted ethanes. In a study of a series of hexachlorobicyclo[2,2,1] heptenes, K. L. Williamson (14) demonstrated that "very large (and unlikely) distortions of this bicyclic system would thus be necessary to account for the variations in J noted for these six compounds". By assuming minimal distortion of the molecules, a linear correlation between coupling constants and electronegativities was obtained.

In order to compensate for the effect of electronegativity and various other perturbations such as distortion from tetrahedral geometry and ring size (7, 15), empirical modifications of the values of k1 and k2 have been made (16, 17, 18). These modifications did not allow for the "configurational dependence" of coupling constants, an effect which had been extensively studied by Williams and Bhacca (19) in a series of steroidal alcohols and which resulted from a dependence of coupling on the orientation of the electronegative substituent, that is

\[
\begin{align*}
J_{ea} &= 5.5 \pm 1.0 \text{ Hz} \\
J_{ae} &= 2.9 \pm 0.4 \text{ Hz}
\end{align*}
\]

This appears to be a common effect and has been discussed in detail (20). It is evident that many factors influence
the magnitude of the Karplus constants but it has been demonstrated by Abraham and McLauchlin (17) that these constants, although different for different segments of a ring, are generally quite similar for corresponding fragments of closely related molecules.

The use of nuclear magnetic resonance as a structural probe in carbohydrate chemistry is well documented. Both pyranose and furanose forms of the carbohydrates have been studied. The furanose ring system is particularly interesting since it has several low energy conformations. Because of this, the conformational preferences exhibited by such compounds are particularly sensitive to the ring substitution pattern. Therefore, it is possible that subtle electrostatic and steric requirements for furanose derivatives could be revealed by studying the conformational preferences exhibited by these compounds. The nature of such interactions are of particular importance since RNA, DNA and many nucleotides and nucleosides contain the furanose ring system.

An important series of furanose carbohydrate derivatives is the 1,2:5,6-di-0-isopropylidene-hexofuranoses. These compounds are very useful as synthetic intermediates in carbohydrate chemistry while the presence of the furanose ring makes the stereochemical properties of these compounds of more general interest. In this respect the study by Abraham and coworkers (16) is important since it represents the only critical evaluation of the conformations of 1,2-0-isopropylidene-xylohexofuranoses. Although the work continues to have wide acceptance (21, 22, 23), its conclusions were obtained from the basically wrong assumption that the Karplus parameters were the same for different segments within the ring. Little work has been done on
other 1,2-\(\text{O}\)-isopropylidene systems although the conformation of 3-fluoro-3-deoxy-1,2;5,6-di-\(\text{O}\)-isopropylidene-\(\alpha\)-D-galactose has been investigated (21).

In order to re-evaluate the results of this early work, it was decided to prepare all the 1,2;5,6-di-\(\text{O}\)-isopropylidene-D-hexoses and their 3-\(\text{O}\)-acetyl, 3-deoxy, and 3-keto derivatives. The acetate derivatives provide NMR parameters which are independent of hydrogen bonding effects which might be present in the parent sugar. The ketones, useful as synthetic intermediates, also provide information concerning the stereospecificity of long range couplings. The deoxy sugars provide a means of access to interproton dihedral angles from NMR couplings without assigning Karplus constants.

Access to dihedral angles without assignment of Karplus constants is provided by a modified Karplus approach in which a ratio of Karplus constants is used. This procedure is first discussed for a number of compounds of known conformation, then applied to the deoxy furanose derivatives. An attempt is made to correlate conformations of the 1,2-5,6-di-\(\text{O}\)-isopropylidene-D-hexofuranoses with their 3-deoxy derivatives by obtaining a correspondence in NMR couplings between the various positions in the molecules. The conformations obtained from the NMR results are discussed in terms of x-ray diffraction structures of similar compounds. Evidence concerning rotameric preferences of the 'tail' (\(\text{C}_5\), \(\text{C}_6\) and substituents) is presented and correlated with chemical properties of these compounds.
A. Synthetic Procedures

The synthetic utility of the isopropylidene blocking group as an intermediate in the synthesis of specifically substituted carbohydrates has been recognized for many years (24, 25). Hydrolysis of the isopropylidene group occurs under mildly acidic conditions probably involving cleavage of the C-0 bond of the ketal (26). This is important when dealing with sugars which readily form 1,6-anhydro derivatives under acidic conditions as it allows hydrolysis of the acetal to the free sugar rather than to a mixture of anhydride and free sugar that one normally obtains upon acidic hydrolysis of a glycoside. An example is the quantitative yield of D-gulose from the 1,2;5,6-diketal (27) whereas under more strongly acidic conditions D-gulose yields 41% of the 1,6-anhydro-α-D-gulopyranose as well as the free sugar (28). Quite recently the application of oxidative methods to these derivatives has resulted in the facile synthesis of the rare hexoses, D-allose (29), and D-gulose (27).

Theander's synthesis of D-allose (3) from the keto compound (9) clearly indicated the stereospecific nature of the hydride reduction of 3-keto-1,2-0-isopropylidene compounds (29). The 1,2-0-isopropylidene group completely prevents reduction from the endo side of the furan ring and therefore a product with the hydroxyl group cis to the 1,2 ring is obtained. If the appropriate ketones were available, the 1,2;5,6-di-0-isopropylidene derivatives of D-talose (4), D-mannose (8), and D-gulose (7) could be readily prepared.
1,2;5,6-Di-Ø-isopropylidene-β-D-talofuranose (4) is known as a side product in the acetonation of D-talose (30). The mannofuranose derivative has not previously been prepared as acetonation of D-mannose gives only 2,3;5,6-di-Ø-isopropylidene-D-mannofuranose (31). 1,2;5,6-Di-Ø-isopropylidene-α-D-gulofuranose (7) has been synthesized by Meycr zu Reckendorf (27) by conversion of the hydrated 1,2;5,6-di-Ø-isopropylidene-α-D-ribohexofuranos-3-ulose (9) into the enol acetate (13). Reduction of this material with sodium borohydride yielded the gulose derivative. This reaction is complicated by loss of the 5,6-Ø-isopropylidene acetal and the yield in the borohydride reduction is often low due to this. Catalytic hydrogenation of the enol acetate gave an excellent yield of the 3-Ø-acetate (27) and subsequent de-Ø-acetylation with methoxide provided the gulose derivative (7) in very high yield.
The 3-keto derivatives were prepared in good yield using a slightly modified version of the ruthenium dioxide/sodium periodate method of Parikh and Jones (32). D-Altrose was prepared from methyl 4,6-O-benzylidene-α-D-glucopyranoside as described by Richtmyer (33). The preparation was modified by opening the epoxide ring by acetylation rather than with potassium hydroxide, directly providing a mixture of α- and β-D-altrose pentaacetates. This was an interesting result since acid catalysed opening of this epoxide provided only about 1% of methyl β-D-altropyranoside. The remaining products identified were methyl α-D-glucopyranoside (7%) and 3,6-anhydro-D-glucose (4%) (34). The acetylation procedure required about 1 hour for completion compared to 2 days for opening with potassium hydroxide. De-α-acetylation of the product provided D-altrose which was acetonated to give 1,2;5,6-di-O-isopropylidene-β-D-altrofuranose (6). Oxidation of this material yielded the desired keto sugar (12) as a sirup which crystallized after vacuum distillation. Borohydride reduction allowed isolation of the previously
unknown 1,2;5,6-di-0-isopropylidene-β-D-mannofuranose (8). D-Idose was prepared from its penta-acetate (35) and condensed with acetone to give the known 1,2;5,6-diacetonate (36). Oxidation yielded a crystalline ketone (10) which on borohydride reduction gave the known -β-D-talofuranose derivative (4) (37). 1,2;5,6-Di-0-isopropylidene-α-D-galacto-furanose (5) was readily prepared by hydroboration of 3-deoxy-1,2;5,6-di-0-isopropylidene-α-D-erythrohexofuran-3-enose as described by Paulsen and Behre (38).

The reduction of the four ketones with borodeuteride gave excellent yields of the 3-deutero-D-allose, -D-talose, -D-mannose, and -D-gulose, which were useful compounds for the spectroscopic studies described later. In an attempt to introduce deuterium at the 4-position, the ketones were treated with pyridine-D2O (2:1) (39) at temperatures ranging from 20 to 100° for periods of up to 1 hr. No introduction of deuterium was observed at either the 2 or 4 positions nor did any epimerization at the 4 position occur. Under the conditions used, the ketones decomposed at varying rates. Deuteration was checked by reisolation of the ketone, recrystallization and then NMR spectroscopy. The resistance to enolization is probably due to hydration of the ketone in aqueous solution. This is borne out by the absence of a UV ketone absorption at 325 μ in aqueous solutions of all the ketones. Optical rotatory dispersion studies (40) showed no anomalous dispersion in aqueous solution but strong Cotton effects when run in non-aqueous media. This phenomenon has already been reported for 1,2;5,6-di-0-isopropylidene-α-D-ribohexofuranos-3-ulose (9) (27). Attempts to epimerize the ketones in non-aqueous solution
(potassium-t-butoxide in DMSO) resulted in rapid decomposition of the starting material.

The observation that the ketones hydrated with varying ease (see Table I) was not too surprising. On isolation only one of the ketones was obtained as a hydrate, the others all existed in their keto modification as was indicated by the presence of a strong band at 1770-1780 cm\(^{-1}\) in the infrared, indicating ketone carbonyl, and the absence of a band at 3300-3600 cm\(^{-1}\) indicating the absence of hydroxyl. Crystalline 1,2,5,6-di-O-iso-propylidene-\(\alpha\)-D-ribohexofuranos-3-ulos (9) has been shown to be hydrated (27) and this was substantiated by the strong band at 3400 cm\(^{-1}\) and the complete absence of a ketone absorption.

In an attempt to explain the differential hydration of these substances, intramolecular hydrogen bonding studies were carried out by high resolution infrared spectroscopy on dilute carbon tetrachloride solutions. The applicability of this technique to conformational assignments in carbohydrate chemistry has been reviewed by Spedding (41). Infrared spectra were obtained at three concentrations (0.005M, 0.0025M, and 0.0012M) in carbon tetrachloride that had been dried over molecular sieve (Linde type 3A). In all nine compounds no observable peak change or shift occurred on changing concentration. The observed spectra are shown in Figure 1.

Figure 1A and 1B represent compounds (galacto (5) and altro (6)) in which intramolecular hydrogen bonding of the 3-hydroxyl would not be expected because of its distance from any suitable oxygen. The similarity of these spectra and the position of the band at 3630 cm\(^{-1}\)
Table I

Extent of hydration (%) of the 1,2;5,6-di-O-isopropylidene-D-hexofuranos-3-uloses*

<table>
<thead>
<tr>
<th>Ketone</th>
<th>0.5 h</th>
<th>1.5 h</th>
<th>3.5 h</th>
<th>8 h</th>
<th>18 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>ribo† (9a)</td>
<td>2</td>
<td>7</td>
<td>14</td>
<td>26</td>
<td>45</td>
</tr>
<tr>
<td>arabino (12)</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>xylo (11)</td>
<td>5</td>
<td>14</td>
<td>17</td>
<td>17</td>
<td>17</td>
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<tr>
<td>lyxo (10)</td>
<td>2</td>
<td>4</td>
<td>9</td>
<td>17</td>
<td>29</td>
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Acetonitrile containing 4.25 % water

<table>
<thead>
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<th>Ketone</th>
<th>0.5 h</th>
<th>1.5 h</th>
<th>3.5 h</th>
<th>8 h</th>
<th>18 h</th>
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<td>ribo† (9a)</td>
<td>34</td>
<td>69</td>
<td>82</td>
<td>83</td>
<td>84#</td>
</tr>
<tr>
<td>arabino (12)</td>
<td>11</td>
<td>26</td>
<td>39</td>
<td>41</td>
<td>43</td>
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<tr>
<td>xylo (11)</td>
<td>25</td>
<td>34</td>
<td>38</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>lyxo (10)</td>
<td>23</td>
<td>46</td>
<td>60</td>
<td>61</td>
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Acetonitrile containing 10% water

<table>
<thead>
<tr>
<th>Ketone</th>
<th>0.5 h</th>
<th>1.5 h</th>
<th>3.5 h</th>
<th>8 h</th>
<th>18 h</th>
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<tbody>
<tr>
<td>ribo† (9a)</td>
<td>34</td>
<td>69</td>
<td>82</td>
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<tr>
<td>arabino (12)</td>
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<tr>
<td>xylo (11)</td>
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<td>lyxo (10)</td>
<td>23</td>
<td>46</td>
<td>60</td>
<td>61</td>
<td>61</td>
</tr>
</tbody>
</table>

*Measured on a Unicam SP200 at 320 μΜ at a sugar concentration of 0.015-0.017M in 1 cm cells. Beer's law was obeyed for the ketones in acetonitrile over this concentration range giving ε values of (9a) 23, (12) 31, (11) 28, (10) 30. All the ketones showed no absorption at 320 μΜ after 5 min of being dissolved in water.

†The ribo ketone (9a) was prepared by vacuum distillation of the hydrated ketone (9b) (b.p. 112°/0.04 mm) to give a mobile syrup which crystallized, m.p. 38-39°.

‡After 18 h in acetonitrile containing 10% water the hydrated ribo ketone (9b) showed 85% hydration, confirming that equilibrium conditions had been reached.
Figure 1

Infrared spectra of the 1,2;5,6-di-O-isopropylidene-D-hexofuranoses and 1,2;5,6-di-O-isopropylidene-\(\alpha\)-D-ribo-hexofuranos-3-ulose in carbon tetrachloride (0.005 M).
indicate a free hydroxyl on a secondary center (42). Figures 1C and 1D are compounds (allo (3) and talo (4)) in which the stereochemistry allows the hydroxyl to hydrogen bond to the 2-oxygen in the 1,2-0-isopropylidene ring. This is in agreement with the position of the bands in 1C and 1D at 3570 cm\(^{-1}\) indicating a 5 membered hydrogen bond ring (43).

\[
\text{C}_2-\text{O}_2...\text{H}-\text{O}_3-\text{C}_3
\]

The stereochemistry of compounds 1E and 1F (gluco (1) ido (2)) restricts any hydrogen bonding of the 3-OH to the oxygen at C\(_5\) involved in the 5,6-0-isopropylidene ring. Surprisingly, the spectra are quite different, the glucose derivative having 2 peaks, one at 3622 cm\(^{-1}\) (free OH) and a less intense band at 3485 cm\(^{-1}\). This latter band indicates the larger \(\Delta \nu\) that could be expected from the formation of a 6 membered hydrogen bond ring (43).

\[
\text{C}_3-\text{O}-\text{H}...\text{O}_5-\text{C}_5-\text{C}_4
\]

Hydrogen bonding of this type will prevent free rotation of the 'tail' (C\(_5\)-C\(_6\) and their substituents) about the C\(_4\)-C\(_5\) bond. At room temperature it is unlikely that free rotation is completely hindered in the glucose derivative. Thus the band at 3622 cm\(^{-1}\) can be attributed to that fraction of the 3-OH in which the 'tail' is in a rotamer that cannot be hydrogen bonded. The 1,2;5,6-di-0-isopropylidene-\(\beta\)-D-idofuranose (2) spectrum (1F) shows only one band at 3502 cm\(^{-1}\) indicating complete hydrogen bonding to the 'tail'. Careful examination of
molecular models indicates that when the 'tail' and 3-OH are cis, that in the D-C$_5$:D-C$_3$ configuration (D-gulo (7) and D-ido (2)), rotation about the C$_4$-C$_5$ bond is more hindered than for the D-C$_5$:L-C$_3$ configuration (D-gluco (1) and D-manno (8)).

It would seem that the formation of a 3-OH...O$_5$ hydrogen bond as well as the hindered rotation effectively maintains the 'tail' of 1,2;5,6-di-O-isopropylidene-β-D-idofuranose (2) in one rotamer.

Figures 1G and 1H (gulo (7) and manno (8)) indicate the spectra in which the 3-OH is able to bond with either the 'tail' or the oxygen at the 2 position. The peaks at 3532 cm$^{-1}$ and 3538 cm$^{-1}$ respectively, indicate a preferential formation of the hydrogen bond to the 'tail'. The shoulder in the manno (1H) derivative at 3585 cm$^{-1}$ corroborates the evidence that the D-C$_5$:L-C$_3$ system (gluco and manno) has freer rotation about the C$_4$-C$_5$ bond. Such rotation would prevent complete hydrogen bonding to the 'tail' and allow the 3-OH to form a hydrogen bond to the 2 oxygen of the 1,2-O-isopropylidene unit thus giving rise to the 3585 cm$^{-1}$ shoulder. It is possible that for the D-C$_5$:L-C$_3$ system, intramolecular forces do not favor the rotamer required for hydrogen bonding and
force the tail into an alternate rotamer.

Figure 1 shows the spectrum of the hydrated 1,2;5,6-di-O-isopropylidene-α-D-ribohexofuranos-3-ulose (9). Both hydroxyl groups at the 3 position can hydrogen bond. The band at 3550 cm\(^{-1}\) is ascribed to the OH group hydrogen bonded to the C\(_2\) oxygen and the bands at 3608 and 3423 cm\(^{-1}\) to the other OH. The 3423 cm\(^{-1}\) band is attributed to the hydrogen bonded to the 'tail' and the 3608 cm\(^{-1}\) to free hydroxyl which is not able to form a bond because the 'tail' is in another rotamer. The apparent strengthening (lowering of the frequency) of these bonds is readily ascribed to the extra electronegative hydroxyl group at C\(_3\).

Two di-O-isopropylidene compounds are capable of double hydrogen bonding in their hydrated keto form. The first is the keto glucose (9) that we have just discussed, the second the keto idose derivative (10).

In its crystalline state, the latter exists in the keto form. That this is not just a property of the crystalline material is obvious from the ease of extraction from
aqueous solution when compared to the hydrated keto glucose. That is, in spite of the ability of 1,2;5,6-di-0-isopropylidene-β-D-idofuranose to form a strong hydrogen bond with its 'tail', its hydrated ketone is not stabilized by such formation. It appears that the reason for this is that in the very rigid conformation that must be adopted to simultaneously form two hydrogen bonds there is steric interaction of the 'tail' with the furan ring. From inspection of molecular models, this does not seem to be the situation in the hydrated keto D-glucose derivative (9b).

The hydrogen bonding results must be regarded with care as they pertain only to dilute, non-polar solutions and will not be applicable to aqueous systems. Nevertheless, the information one can derive from such results allow a much better appreciation of the forces acting within the molecule and thus a better understanding of the chemistry of these compounds. As will be shown later, these results are in complete agreement with evidence obtained from conformational studies by NMR spectroscopy.

Treatment of the four ketones with pyridine-acetic anhydride (7:3) led to the formation of the enol acetates; 3-0-acetyl-1,2;5,6-di-0-isopropylidene-α-D-erythrohex-3-enose (13) and 3-0-acetyl-1,2;5,6-di-0-isopropylidene-β-D-threohex-3-enose (14). During the formation of the two enol acetates from their parent ketones a marked difference in the rate of formation of the final products was observed. 1,2;5,6-Di-0-isopropylidene-α-D-ribohexofuranos-3-ulose (9), 1,2;5,6-di-0-isopropylidene-α-D-xylohexofuranos-3-ulose (11), 1,2;5,6-di-0-isopropylidene-
-\(\beta-D\)-lyxohexofuranos-3-ulose (10), and 1,2;5,6-di-\(\alpha\)-isopropylidene-\(\beta-D\)-arabinohexofuranos-3-ulose (12) as 1% solutions of the sugar in 30% acetic anhydride in pyridine at 36° yielded the unsaturated sugars. A qualitative comparison of reaction rates was provided by following the reactions by TLC until complete. The results are given in Table II.

It is seen that there is a wide disparity in the time required for the complete formation of the enol acetates. No ready explanation for this wide variance is obvious. The rate controlling step is, presumably, the breaking of the C4-H bond leading to enolization (\(^{44}\)). That this process is difficult in these compounds has been shown by attempts to introduce deuterium at the C4 position by D\(_2\)O exchange in pyridine. The replacement of pyridine with a stronger base, triethylamine, in the enol ester formation of 14 from 1,2;5,6-di-\(\alpha\)-isopropylidene-\(\beta-D\)-lyxohexofuranos-3-ulose (10) greatly increased the rate, the complete reaction requiring about 24 hours instead of 3 weeks, strengthening the presumption that the rate determining step is the base-catalyzed removal of the C4 hydrogen.

In compounds 11 (1,2;5,6-di-\(\alpha\)-isopropylidene-\(\alpha\)-\(D\)-xylohexofuranos-3-ulose) and 12 (\(\beta-D\)-arabinohexofuranos-3-ulose) little steric hindrance to the approach of the base to the C4 hydrogen would be expected as the 1,2-\(\alpha\)-isopropylidene is trans to this hydrogen. Any interference present would be provided by one or more of the rotamers of the 'tail'. At the same time, the formation of the C3-C4 double bond might result in relief of steric strain between the 1,2-\(\alpha\)-isopropylidene group
Table II

Times for the formation of enol acetates from 1,2;5,6-di-O-isopropylidene-\(\beta\)-hexofuranos-3-uloses in acetic anhydride-pyridine (3:7) at 36°

<table>
<thead>
<tr>
<th>Ketone</th>
<th>Time* (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>3.8-4.3</td>
</tr>
<tr>
<td>11</td>
<td>1.5-1.8</td>
</tr>
<tr>
<td>10</td>
<td>22-24†</td>
</tr>
<tr>
<td>12</td>
<td>1.1-1.3</td>
</tr>
</tbody>
</table>

*The times given are estimated from a series of TLC plates which were run on the reaction mixture.
†This time may be longer than given. After this length of time breakdown products begin appearing on the TLC plates.
and the 'tail'. From such considerations little difference between the rates of enol acetate formation from 11 and 12 would be expected. In 9 (1,2;5,6-di-0-isopropylidene-α-D-ribohexofuranos-3-ulose) and 10 (-β-D-lyxohexofuranos-3-ulose), the approach of the base to the C₄-H will be hindered by the 1,2-0-isopropylidene ring. That such an influence is of importance is suggested by the stereospecific reduction of the C₄-C₅ double bond in compounds 15 and 16. As the 'tail' and 1,2-isopropylidene group are trans, little relief from steric strain would be expected. The hindered base approach is a plausible reason for the decreased rates for the ribo and lyxo ketones but does not explain the factor of five in the rates of enol acetate formation from these materials.

A closer look at Table II indicates a similar effect: enol acetate formation from 9 is faster than from 10. A correlation between these results is obtained by simply noting that D and L-isomers are chemically indistinguishable so that, apart from ring fusion, i.e. 1,2-0-isopropylidene cis or trans to 'tail', the compounds with a D-C₅:D-C₄ configuration (ribo, arabino) react faster than their analogues with an L-C₅:D-C₄ configuration (lyxo, xylo).

Two possible explanations for this effect seem reasonable; a D-configuration at C₅ imparts some type of steric instability to the sugar and as a result increases the rate of enolization, or an L-configuration at C₅ in some way offers a greater interaction to approach of the base, reducing the rate of enolization and hence the rate of reaction.
An attempt to form 13 by treating the ketone (9) with isopropenyl acetate resulted in the formation of 1,2-O-isopropylidene-3,5-di-O-acetyl-\(\alpha\)-D-ribohexofuranos-3-ulose in good yield (45). Reduction of 13 in ethanol over palladium black provided an almost quantitative yield of 3-O-acetyl-1,2;5,6-di-O-isopropylidene-\(\alpha\)-D-gulofuranose (27) while reduction of 14 provided the corresponding 3-O-acetyl-1,2;5,6-di-O-isopropylidene-\(\beta\)-D-mannofuranose (28) in comparable yield. The identification of the compound was verified by de-O-acetylation of 1,2;5,6-di-O-isopropylidene-\(\beta\)-D-mannofuranose (8).

Reduction of 13 with deuterium gas over palladium black in ethanol (or ether) resulted in scrambling of deuterium and hydrogen throughout the 3, 4, and 5 positions as judged by NMR spectroscopy. This indicated that either some sort of exchange reaction was occurring on the catalytic surface, or that the double bond was migrating to the exo cyclic position as shown in compound 15. Stabilization of the exocyclic double bond by an ether oxygen could perhaps account for this. Unfortunately, this does not explain why a corresponding rearrangement does not occur when 3-deoxy-1,2;5,6-di-O-isopropylidene-\(\alpha\)-D-erythrohex-3-enose is reduced with deuterium gas under similar conditions. Here as for the previous case a stabilization of about 5 kcal/mole would be expected since the difference in the heats of hydrogenation of some related compounds are of this order (104). On the other hand, it has been found that methylene and ethylene cycloalkanes rearrange on catalytic surfaces to give a high percentage of the alkyl cycloalkene; that is,
97.6% of 1-methylcyclopentene and 94.2% of 1-ethylcyclopentene (46). An attempt was made to identify and isolate a rearranged product if it did in fact exist. To this end 13 was partially reduced in ethanol and the fully reduced 3-O-acetyl-1,2;5,6-di-O-isopropylidene-α-D-gulofuranose (27) was removed by crystallization. Thin layer chromatography of the mother liquor indicated a product corresponding to complete reduction, a minor second product and a material with an \( R_f \) corresponding to the starting material but which on development (10% \( \text{H}_2\text{SO}_4 \) and heat) came up a different colour from the starting material (13). NMR spectroscopy showed that this compound (15) was substantially different in structure from the starting material. Partial reduction of 13 in ether gave a much higher yield of 15, which finally, under optimal conditions was formed in an approximately 65% yield of crystalline product.

The NMR spectrum of 15 in chloroform showed a low field doublet with a chemical shift of 4.09 \( \tau \) and a coupling of 4.1 Hz consistent with an assignment of \( \text{H}_1 \) for this proton (47). On the basis of this assignment \( \text{H}_2 \) is found at 5.12 \( \tau \) with an \( \text{H}_2 \) to \( \text{H}_3 \) coupling of 6.2 Hz which indicated that \( \text{H}_2 \) and \( \text{H}_3 \) were cis. This required the acetate group (7.9 \( \tau \)) to be cis to the oxygen at C$_2$, the expected arrangement since catalytic reduction gave only the D-gulo compound (27). The C$_3$ hydrogen at 4.35 \( \tau \) occurs as a tripled doublet, being coupled to the two C$_6$ hydrogens at 5.5 \( \tau \). The four isopropylidene methyls are found at 8.6 \( \tau \). The assignment of the ring protons was verified by the formation of 15 containing deuterium in the C$_3$ position.
This was accomplished by rearranging 13 in ether solvent in the presence of deuterium rather than hydrogen. NMR showed the loss of the signal at 4.35 $\tau$ and the collapse of the signal at 5.50 $\tau$ to a single peak as well as the collapse of the quartet at 5.12 $\tau$ to a doublet. The mass spectrum of 15 gave a parent peak at m/e 300 corresponding to a compound isomeric with 13. No significant peak at m/e 101 was observed. This is an important peak as it has been shown by DeJongh and Biemann (48) to be the peak resulting from the loss of the 5,6 carbons complete with their isopropylidene group. The IR spectrum showed an absorbance at 1740 cm$^{-1}$ indicating the presence of an ester carbonyl. The presence of the double bond, although not clearly discernable in the IR, was confirmed by reduction over palladium to 3-$\alpha$-acetyl-1,2;5,6-di-$\alpha$-isopropylidene-$\alpha$-$D$-gulofuranose (27). Reduction of 15 with deuterium gave a scrambling pattern identical to that obtained from reduction of 13 with deuterium. Although a pure 4,5-dideuterated compound was not formed, at least this reduction established that the isomerization of 13 to 15 on the palladium surface is a reversible reaction. During the preparation of the deuterated analogue it was found that isotopic purity greater than about 80% was not attainable. Attempts to deuterate with a prerduced catalyst resulted in 20% to 60% deuteration, dependent on the extent of prerduction of the catalyst. This suggested exchange with the solvent. Reduction of the 3-deuterated analogue with deuterium or palladium gave a reasonably high degree of isotopic purity (approximately 70%) throughout the 3, 4, and 5 positions compatible with structure 15. It thus seems
that equilibrium between 13 and 15 is set up on the catalyst surface prior to reduction. Such allylic rearrangements have been observed on catalytic surfaces in several systems (46, 49).

Treatment of 15 with 0.01N NaOMe in methanol gave a product (1,2;5,6-di-O-isopropylidene-α-D-erythrose-5-enose) whose NMR spectrum had no peak in the acetate region, but had four isopropylidene methyl groups and a D₂O exchangeable hydrogen. The mass spectrum of this compound gave a parent m/e at 258, confirming the loss of acetate on treatment with base. The absence of a significant peak at m/e 101 indicated that no ordinary 5,6-O-isopropylidene group was present.

The configuration about C₅ in 15 is difficult to establish but can be inferred from the stereochemistry of the reduction product. Cis reduction of the double bond must occur trans to the 1,2-O-isopropylidene group as this results in the known D-gulo product (27). In the hope that NMR could be useful in resolving stereochemical problems of this nature through use of the observed long range coupling, it was decided to attempt the synthesis of the other geometric isomer, 16, which should be preparable from 1,2;5,6-di-O-isopropylidene-α-D-lyxohexofuranos-3-ulose (10), or β-D-arabinohexofuranos-3-ulose (12). That 14 was the product obtained on treating the lyxo or arabino hexose derivatives with acetic anhydride/pyridine was confirmed by nuclear magnetic resonance and mass spectroscopy. The mass spectrum of 14 was very similar to that of 13 with a parent m/e peak at 300 and a large peak at m/e 101. Reduction of this compound yielded 3-O-acetyl-1,2;5,6-di-O-isopropylidene-β-D-mannofuranose (28), which was
identified by NMR and mass spectroscopy. De-O-acetylation afforded 1,2;5,6-di-O-isopropylidene-β-D-mannofuranose (8) identical to that obtained by borohydride reduction of 1,2;5,6-di-O-isopropylidene-β-D-arabinofuranose-3-ulose (12).

Under catalytic rearrangement conditions, 14 was converted into the desired 16 in approximately 65% yield as judged by NMR spectroscopy. Compound 16 did not crystallize and attempts to purify it in other ways failed or resulted in decomposition. The NMR parameters determined for the impure product are given in the appendix.
Reduction of 13 or 15 over platinum in anhydrous ether proceeded quite slowly compared with the reduction over palladium, requiring at least 24 hours compared with 7 hours for the palladium reduction. Thin layer chromatography indicated the formation of two major compounds, one having \( R_f \) corresponding to 3-0-acetyl-1,2;5,6-di-0-isopropylidene-\( \alpha \)-D-gulofuranose (27). The NMR spectrum of the reaction mixture supported this assignment. The second spot had an \( R_f \) different from that of the starting material and NMR spectroscopy indicated that this compound was 3-deoxy-1,2;5,6-di-0-isopropylidene-\( \alpha \)-D-arabinohexofuranose (19). The product was purified and found identical by NMR, IR, mass spectoscopy, melting point, and optical rotation to 19, prepared by the reduction of 1,2;5,6-di-0-isopropylidene-\( \alpha \)-D-erythrohex-3-enose (50). Reduction of this compound with deuterium gas provided the specifically 3,4-di-dideuterated 19, which was used in later spectroscopic analyses.
Hydrogenolysis of 14 occurs under conditions identical to that of the hydrogenolysis of 13 and in similar yield. The NMR spectrum was consistent with the expected product, 3-deoxy-1,2;5,6-di-O-isopropylidene-β-D-arabinofuranose (20). The mass spectrum gave a large peak (M-15)+ at m/e 229 and a large peak at m/e 101. High resolution mass spectroscopy showed this to be 101.0620 which is in good agreement with the calculated value of 101.0602 and our observed value of 101.0610 for the 'tail' of 1,2;5,6-di-O-isopropylidene-α-D-glucofuranose (1).

3-Deoxy-D-arabinohexose (51) was acetonated and the product was found identical by IR, NMR, mass spectoscopy, melting point, and optical rotation to the product of hydrogenolysis of 14. This work adds conclusive evidence, therefore, that the 3-deoxy-di-O-isopropylidene-D-hexose prepared by Rembarz (52) from 3-deoxy-D-arabinohexose is in fact the 1,2;5,6 diketal as postulated by Prokop and Murray (53) and not the 1,2;4,6 diketal originally proposed.

This work has shown that enolization of the 1,2;5,6-di-O-isopropylidene-D-hexofuranos-3-ulos systems occurs between carbons three and four. No evidence of 2,3 double bond formation was encountered in agreement with Bredt's rule. The rearrangement of the enol acetate
to an exocyclic double bond system was surprising since the reaction was reversible, indicating the exo form to be more stable, the opposite to that of the 1-alkyl-cyclopentenes. An effort to eliminate this rearrangement by substituting platinum for palladium failed in that a major pathway of this reaction was the hydrogenolytic cleavage of the acetoxy group. Since both the enol acetate, 13, and the rearranged 15 gave the same products on platinum reduction, it seems likely that the double bond rearrangement occurs on the platinum surface as well.

The 3-deoxy-D-arabinohexose used in this study was prepared readily from methyl 3-deoxy-4,6-0-benzylidene-\(\alpha\)-D-arabinohexopyranose. This compound was prepared by lithium aluminum hydride oxirane opening of methyl 2,3-anhydro-4,6-0-benzylidene-\(\alpha\)-D-mannopyranoside, a synthetic route described by D. A. Prins (54). Oxidation of this compound (55, 56), followed by sodium borohydride reduction afforded methyl 4,6-0-benzylidene-3-deoxy-\(\alpha\)-D-ribohexopyranoside (55). Acetolysis, followed by de-0-acetylation provided 3-deoxy-D-ribohexose which upon acetonation gave 3-deoxy-1,2;5,6-di-0-isopropylidene-\(\alpha\)-D-ribohexofuranose (17). Subsequent to this preparation, work in our lab established the utility of triphenyl phosphate/carbon tetrachloride as a means of introducing chlorine into the 3 position of 1,2;5,6-di-0-isopropylidene-\(\alpha\)-D-allofuranose (3) and -\(\beta\)-D-talo-furanose (4) to yield the 3-chloro-3-deoxy-1,2;5,6-di-0-isopropylidene-\(\alpha\)-D-glucofuranose and -\(\beta\)-D-idofuranose respectively (57). X-ray crystal structure analysis (58) established unequivocally the product of chlorination of
the talo derivative. Reduction of the chlorides with lithium aluminum hydride provided the corresponding 3-deoxy derivatives.

In order to better understand the mode and stereochemistry of the lithium aluminum hydride reduction of these chlorodeoxy sugars, 3-deuterio-1,2;5,6-di-O-isopropylidene-\(\alpha-D\)-allofuranose was converted into 3-chloro-3-deoxy-3-deuterio-1,2;5,6-di-O-isopropylidene-\(\alpha-D\)-glucofuranose. Reduction, followed by isolation and distillation gave 3-deoxy-3-deuterio-1,2;5,6-di-O-isopropylidene-\(\alpha-D\)-allofuranose. Table III presents the \(J_{2,3}\) couplings of this and some related compounds.

From Table III the \(J_{2,3}\) coupling of the 3-deoxy-3-deuterioallofuranose can be seen to be close to 5 Hz which is indicative of a \textit{cis} arrangement of \(H_2\) and \(H_3\) as drawn. The reduction of the 3-chloro-\(D\)-glucose derivative therefore must have taken place with retention of configuration about \(C_3\).

Acetylation of the 1,2;5,6-di-O-isopropylidene-\(D\)-hexofuranoses proceeded readily in acetic anhydride/pyridine to yield the corresponding 3-O-acetyl derivatives.
Table III

$J_{2,3}$'s for Selected Diacetone Hexoses*

<table>
<thead>
<tr>
<th>$J_{2,3}$ (cis)</th>
<th>$J_{2,3}$ (trans)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.0</td>
<td>---</td>
</tr>
<tr>
<td>---</td>
<td>~0.5</td>
</tr>
<tr>
<td>---</td>
<td>~0.5</td>
</tr>
<tr>
<td>4.8</td>
<td>~0.5</td>
</tr>
<tr>
<td>4.8</td>
<td>---</td>
</tr>
</tbody>
</table>

*Couplings in Hz measured in CDCl$_3$. 
These were prepared since they provided spectroscopic information independent of possible hydrogen bonded species.
B. Conformational Analysis

B-1. DAERM

The equation relating dihedral angle and coupling constant, reported by Karplus in 1959 (7), has maintained its essential features after several years of experimental and theoretical investigations. The limitations of the equation have been stressed by a number of workers (59, 60, 61), including Karplus himself (15). The variation of the theoretically derived constants \( k_1 \) and \( k_2 \) with molecular and substituent properties, such as ring size and electronegativity have been noted and these have been attributed (60, 62) to changes in magnitude of the electron exchange term, which is the major contributor to the Karplus constants, \( k_1 \) and \( k_2 \).

This thesis presents conformational results based on calculation of dihedral angles from a modified Karplus equation. Variations of Karplus constants are accommodated in this method through the assumption that the ratio of the Karplus constants \( k_1/k_2 \) is a constant. From the theoretical parameters calculated by Karplus (7), the ratio \( k_1/k_2 \) is very nearly equal to 0.9. Using accurate coupling constants, dihedral angles can be calculated for a hydrogen vicinal to a methylene function without prior assignment of Karplus constants and without explicit consideration of the electronic perturbations affecting the system. This process is termed the 'Dihedral Angle Estimation by the Ratio Method' (DAERM). An attempt ('R value' method) to separate electronic from stereochemical effects has been reported (63) and found to work well for systems to which it is applicable (64, 65). Requiring couplings between protons of a dimethylene group,

\[
\begin{array}{c}
\text{H} \\
\downarrow \\
\text{C} \\
\downarrow \\
\text{H}
\end{array}
\quad
\begin{array}{c}
\text{H} \\
\downarrow \\
\text{C} \\
\downarrow \\
\text{H}
\end{array}
\]
the 'R value' method is necessarily severely limited in application although under some circumstances it may be used with couplings into a methylene group (65).

\[
\begin{array}{c}
\text{H} \\
\text{C} \\
\text{C} \\
\text{H}
\end{array}
\]

In DAERM the form (I) of the Karplus equation (7) is used. J is the vicinal coupling constant; k, the Karplus constant; \( \phi \), the dihedral angle subtended by the coupled nuclei; and c, a constant.

\[ a) \quad J_1 = k_1 \cos^2 \phi_1 - c \quad 0 \leq \phi_1 \leq 90^\circ \quad (I) \]

\[ b) \quad J_2 = k_2 \cos^2 \phi_2 - c \quad 90^\circ \leq \phi_2 \leq 180^\circ \]

The four possible arrangements of a hydrogen adjacent to a methylene group in a saturated system are shown in Figure 2. Only cases A, B, C, and C will be discussed as case D is seldom, if ever, found in ring systems. From case A, the two equations describing the system are Ia and Ib, where \( k_1 = k_1 \) since both \( \phi_1 \) and \( \phi_2 \) are less than \( 90^\circ \), and therefore II is obtained, where \( w \) is the projection angle of the methylene protons.

\[
\frac{J_1 + c}{J_2 + c} = \frac{\cos^2 \phi_1}{\cos^2 (w-\phi_1)}
\]

Assuming a regular tetrahedral system \( (w = 120^\circ) \), and using the theoretical value of 0.28 for c (7), a complete solution for the angles \( \phi_1 \) and \( \phi_2 \) is possible from the coupling constants, \( J_1 \) and \( J_2 \), without knowledge of the Karplus constant, \( k_1 \), for that system.
Figure 2

Four arrangements of the -C-C-H system

Case A
\[
\hat{\phi}_1 < 90^\circ \\
\hat{\phi}_2 < 90^\circ \\
w = \hat{\phi}_1 + \hat{\phi}_2
\]

Case B
\[
\hat{\phi}_1 < 90^\circ \\
\hat{\phi}_2 > 90^\circ \\
w = \hat{\phi}_1 + \hat{\phi}_2
\]

Case C
\[
\hat{\phi}_1 < 90^\circ \\
\hat{\phi}_2 > 90^\circ \\
w = \hat{\phi}_2 - \hat{\phi}_1
\]

Case D
\[
\hat{\phi}_1 > 90^\circ \\
\hat{\phi}_2 > 90^\circ \\
w = \hat{\phi}_2 - \hat{\phi}_1
\]
Cases B and C can be resolved in a similar manner, as shown below.

**Case B**

\[
\frac{J_1 + c}{J_2 + c} = \frac{k_1 \cos^2 \phi_1}{k_2 \cos^2 (\omega - \phi_1)} 
\]  

(III)

**Case C**

\[
\frac{J_1 + c}{J_2 + c} = \frac{k_1 \cos^2 \phi_1}{k_2 \cos^2 (\omega + \phi_1)} 
\]  

(IV)

Having assumed a value of 0.9 for \(k_1/k_2\), complete solutions for cases B and C are possible. For example, solutions of B for \(\phi_1\) provides the expression:

\[
\tan \phi_1 = \frac{-\cos \omega \pm [(k_1/k_2)(J_2 + c)/(J_1 + c)]^{\frac{1}{2}}}{\sin \omega} 
\]  

(V)

If the condition for A holds, \(k_2 = k'_1\) and \(k_1/k_2 = 1\), whereas if condition C holds, \(-\cos \omega\) in the above expression is replaced by \(+\cos \omega\). The above expression is readily solved to obtain \(\phi_1\).

If the expression

\[
J = a \cos^2 \phi_1 + b \cos \phi_1 - c 
\]  

(VI)

is used to represent the angular relationship with the coupling (15), then cases A and B can be combined and

\[
\tan \phi_1 = \frac{-1(2 \cos \omega + \frac{b/a}{\cos \phi_1}) \pm [(\frac{b/a}{\cos \phi_1})^2 + 4(\frac{J_2+c}{J_1+c})(1+\frac{b/a}{\cos \phi_1})]^{\frac{1}{2}}}{2 \sin \omega} 
\]  

(VII)
Replacement of -1 by +1 provides the solutions for condition C. This equation can be solved by making the initial assumption that $b/a = 0$ then solving for $\phi_1$ and using this value as a first approximation in an iterative process. Convergence is rapid, generally requiring only 2 or 3 cycles of iteration. Even so, the method is not suitable for hand calculation and affords little improvement over the original expression (V).

In equation VII, the ratio $b/a = -0.053$ corresponds to a $k_1/k_2$ of 0.9. When this equation is used for comparison purposes it is referred to as DAERM II.

If electronegativity and other substituent effects are reflected in the magnitude of the Karplus constants, DAERM should result in a sensitive probe into the angular relationship between vicinally coupled nuclei, as well as the electronic situation prevailing in the system being investigated. Testing of DAERM was undertaken through application the method to ring systems having four to six atoms for which NMR parameters were available.

In order to easily evaluate the utility of DAERM, a short Fortran program was written for the IBM 360/50 computer. This program calculated the possible angle sets for a given set of coupling constants from equations II, III, and IV. DAERM provides two solutions for each set of coupling constants, one with both dihedral angles less than 90° (i.e. case A), the other with one angle less than, the other greater than 90° (i.e. either case B or C).

An example of the application of DAERM is provided by consideration of the computer analyzed, low temperature proton NMR parameters of octadeuterocyclohexane
obtained by Garbisch and Griffith (66). One signal indicated two couplings of 3.65 and 13.12 Hz and, without prior assignment of their origin, DAERM allows for the four possible solutions as seen in Table IV.

Solutions ii and iv are equivalent and can be rejected as the required Karplus constants are much too large. Unacceptable large calculated Karplus constants can often be used to rule out possible angular solutions and thus simplify the analysis. The second signal from octadeuterocyclohexane was analyzed as two couplings, 2.96 and 3.65 Hz. Again, without prior assignment, four solutions are possible, as seen in table V.

It is obvious that vi and viii are equivalent and viii can be discarded. From Table IV, the coupling of 3.65 Hz is associated with two possible angles (i and iii).

From Table V, the three solutions for the coupling of 3.65 Hz are v, 152°; vi (viii), 58°; and vii, 23°. The only compatible solutions are i and vi.
Table IV†

DAERM Calculations* on 3.65 and 13.12 Hz Couplings

<table>
<thead>
<tr>
<th>Set</th>
<th>J₁</th>
<th>J₂</th>
<th>Φ₁</th>
<th>Φ₂</th>
<th>k₁</th>
<th>k₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>i</td>
<td>3.65</td>
<td>13.12</td>
<td>55</td>
<td>175</td>
<td>12.14</td>
<td>13.49</td>
</tr>
<tr>
<td>ii</td>
<td>3.65</td>
<td>13.12</td>
<td>70</td>
<td>50</td>
<td>32.78</td>
<td>36.43</td>
</tr>
<tr>
<td>iii</td>
<td>13.12</td>
<td>3.65</td>
<td>1</td>
<td>121</td>
<td>13.40</td>
<td>14.89</td>
</tr>
<tr>
<td>iv</td>
<td>13.12</td>
<td>3.65</td>
<td>50</td>
<td>70</td>
<td>32.78</td>
<td>36.43</td>
</tr>
</tbody>
</table>

†In all Tables and discussion, Φ₁ is the cis angle; Φ₂ is the trans angle; k₁ the calculated Karplus constant for less than 90°; k₂ for greater than 90°.

Table V

DAERM Calculations* on 2.96 and 3.65 Hz Couplings

<table>
<thead>
<tr>
<th>Set</th>
<th>J₁</th>
<th>J₂</th>
<th>Φ₁</th>
<th>Φ₂</th>
<th>k₁</th>
<th>k₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>v</td>
<td>2.96</td>
<td>3.65</td>
<td>32</td>
<td>152</td>
<td>4.52</td>
<td>5.02</td>
</tr>
<tr>
<td>vi</td>
<td>2.96</td>
<td>3.65</td>
<td>62</td>
<td>58</td>
<td>14.32</td>
<td>15.91</td>
</tr>
<tr>
<td>vii</td>
<td>3.65</td>
<td>2.96</td>
<td>23</td>
<td>143</td>
<td>4.61</td>
<td>5.13</td>
</tr>
<tr>
<td>viii</td>
<td>3.65</td>
<td>2.96</td>
<td>58</td>
<td>62</td>
<td>14.32</td>
<td>15.91</td>
</tr>
</tbody>
</table>

* k₁/k₂ = 0.9, w = 120°
A, 55-58°, gives rise to $J_{ae}$ coupling of 3.65 Hz; B, 62-65°, gives rise to $J_{ee}$ coupling of 2.96 Hz; and C, 175-178°, gives rise to the $J_{aa}$ coupling of 13.12 Hz. It is important to note that the assignments were made without prior knowledge of the proton identities and without assigning numerical values to the Karplus constants. DAERM predicts a flattened chair conformation with proton assignments identical to those of Garbisch and Griffith (66).

Prior to further application of DAERM, an investigation of two main features of this method was carried out. These were: 1) distortion of the system from regular tetrahedral geometry ($\omega \neq 120^\circ$), and 2) variation of the parameter $k_1/k_2$. Using the octadeuterocyclohexane data with a $k_1/k_2$ constant of 0.9, the effect of distortion from tetrahedral geometry can be evaluated by plotting the calculated angle $\Phi_2$ against values of $\omega$. The value of $\omega$ was varied over the range 110-130°, which
is beyond the range of distortions expected for normal tetrahedral systems. Figure 3 shows the results in which the angles obtained from the two sets of couplings $J_{ee}$, $J_{ee}$ and $J_{aa}$ give two curves intersecting at an $\omega$ value of 115°.

The $\phi_2$ solutions should be the same from either set of couplings and as this value is influenced by the ratio $k_1/k_2$, the variation of $k_1/k_2$ with $\omega$ was investigated and the results presented in Figure 4.

Molecular orbital calculations (10, 11, 12), as well as valence bond calculations (7, 15, 62), provide results which indicate that a ratio greater than unity is not acceptable. If this is true, then Figure 4 indicates that $\omega$ for cyclohexane is less than 120°. This in turn suggests that if constant $p$-character is assumed for the bonding about carbon, the angle subtended by H-C-H at each methylene grouping in cyclohexane is smaller than the expected tetrahedral angle. Eliel et al (67) has calculated an H-C-H angle of 107.3° from the cyclohexane electron diffraction data of Hassel and Davis (68). This value corresponds to an $\omega$ value of approximately 116° (69) and is in keeping with a ratio of very nearly 0.9. Figures 3 and 4 emphasize the inter-relationship between $\omega$ and the $k_1/k_2$ ratio, and also provide an appreciation of the range permitted in the magnitude of the values.

From computer analyzed NMR parameters, the conformation of cyclohexane has been determined to a degree where ring flattening and distortion from tetrahedral geometry are apparent. This method is considered to be of significance in assigning conformational properties
Figure 3

Plot of variation of $\theta$ with $\psi$

$\theta = \psi_1 + \psi_2$ (degrees)

$\psi_2$ (degrees)

from $aa/ae$

from $ae/ee$
to cyclic molecules.

An essential prerequisite of DAERM is the availability of NMR coupling parameters of hydrogen nuclei vicinal to a methylene function. Four cyclohexyl systems for which such data were available are now considered. A ratio of 0.9 and $\omega$ value of $115^\circ$ are assigned from which not only $\psi_1$ and $\psi_2$ but the Karplus constants, $k_1$ and $k_2$, which correspond to these acceptable solutions, are calculated.

Table VI illustrates an essential point of DAERM. Although large variations exist in the reported coupling constants, all the $\psi_1$ are reasonably constant in the range 46-57° and the Karplus constants are rather variable. Possibly more striking is the series of 6-membered heterocycles shown in Table VII. Angles and constants were calculated using a ratio of 0.9 and tetrahedral geometry, i.e. $\omega = 120^\circ$, for the carbon atoms involved in the coupling. Rather large changes in the calculated Karplus constants are evident for these heterocyclic derivatives, but these seem to bear little relation to the conformation of the molecules. The conformational trends exhibited by these molecules is of interest as the oxygen heterocycles show the expected flattening and the sulfoxides the expected puckering due to the bonding angles of the hetero atoms (75). The conformational mobility of these compounds at room temperature results in time averaged dihedral angles and a general lowering of the calculated Karplus constants as can be seen in 32b, Table VI.

DAERM calculations on four-membered rings were made possible by the recent report of computer analyzed
Table VI
NMR & DAERM Data For Cyclohexane Derivatives\(^1\)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Observed Coupling Constants</th>
<th>Calculated Angles</th>
<th>Calculated Karplus Constants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(J_{aa})</td>
<td>(J_{ea})</td>
<td>(J_{ee})</td>
</tr>
<tr>
<td>ref. 70</td>
<td>CCl(_4)</td>
<td>CHCl(_3)</td>
<td>D(_2)O</td>
</tr>
<tr>
<td>29a Ac</td>
<td>11.0</td>
<td>3.5</td>
<td>-</td>
</tr>
<tr>
<td>29b H</td>
<td>11.0</td>
<td>4.5</td>
<td>-</td>
</tr>
<tr>
<td>29b D</td>
<td>10.5</td>
<td>4.1</td>
<td>-</td>
</tr>
<tr>
<td>29c ditosyl</td>
<td>7.9</td>
<td>3.6</td>
<td>-</td>
</tr>
<tr>
<td>29d isopropylidene</td>
<td>11.0</td>
<td>3.5</td>
<td>-</td>
</tr>
<tr>
<td>71 D</td>
<td>11.1</td>
<td>4.3</td>
<td>-</td>
</tr>
<tr>
<td>32a H</td>
<td>9.8</td>
<td>3.9</td>
<td>-</td>
</tr>
<tr>
<td>32b Ac</td>
<td>CS(_2)(r.t.)</td>
<td>9.3</td>
<td>3.9</td>
</tr>
<tr>
<td>32b Ac</td>
<td>CS(_2)(-110°)</td>
<td>11.4</td>
<td>4.2</td>
</tr>
<tr>
<td>ref.</td>
<td>Compound</td>
<td>Solvent</td>
<td>Coupling Constants</td>
</tr>
<tr>
<td>------</td>
<td>----------</td>
<td>---------</td>
<td>--------------------</td>
</tr>
<tr>
<td>72</td>
<td><img src="image" alt="Molecule 1" /></td>
<td>CHCl₃</td>
<td>$J_{\text{cis}}$: 4.2, $J_{\text{trans}}$: 8.1</td>
</tr>
<tr>
<td>73</td>
<td><img src="image" alt="Molecule 2" /></td>
<td></td>
<td>$J_{\text{cis}}$: 1.5, $J_{\text{trans}}$: 1.0</td>
</tr>
<tr>
<td>74</td>
<td><img src="image" alt="Molecule 3" /></td>
<td>CDCl₃</td>
<td>$J_{2,3_e}$: 1.6, $J_{2,3_a}$: 10.1, $J_{5_e,e}$: 1.8, $J_{5_a,e}$: 11.5</td>
</tr>
<tr>
<td></td>
<td><img src="image" alt="Molecule 4" /></td>
<td>CDCl₃</td>
<td>$J_{2,3_e}$: 1.9, $J_{2,3_a}$: 9.8, $J_{5_e,e}$: 1.9, $J_{5_a,e}$: 10.8</td>
</tr>
</tbody>
</table>
The calculated angles presented in Tables VI and VII must be treated with caution, since these are derived from first order couplings which may vary considerably from the actual values. In addition, some of these examples may exhibit errors due to the configurational dependence of electronegative substituents. These errors, combined with possible conformation mobility in these systems, limit the use of the calculated parameters to qualitative comparisons.
spectra of several thietanes. The results are presented in Table VIII using the proton assignments of the original workers (76, 77).

Four of the five compounds (37-40), gave DAERM angles in very good agreement with the reported angles, but the fifth, trans-2,4-diphenylthietane-1-oxide, 41, gave quite different solutions. In contrast to the conformation originally proposed, (77), DAERM indicates a molecule flattened slightly in a manner which allows the phenyl groups to approach pseudo-equatorial positions. The possibility of incorrect proton assignments was excluded since DAERM predicted an impossibly distorted molecule for the alternate assignment.

Five-membered rings have posed a complex problem in conformational analysis because of their very low barrier to pseudorotation. The bicyclo[2.2.1]heptane system is free from such complexities as the bridge locks the molecule in a single conformer. Table IX represents the first-order coupling constants obtained by Williamson (14) from a series of hexachlorobicyclo[2.2.1]heptenes with the DAERM angles and Karplus constants. Not unexpectedly, the magnitude of the Karplus constants appears to be inversely proportional to the electronegativity of the substituent. This inverse relationship has been predicted on a theoretical basis (15) and a number of examples of the inverse dependence of $J$ with electronegativity have been reported (see for example Williamson (14), Cohen and Schaefer (78)).

As the $C_1-C_2-C_3$ bond angle in these systems is found to be significantly smaller than the tetrahedral angle (79), the angle between hydrogens on the methylene
Table VIII

Conformational Analysis of some Thietanes

<table>
<thead>
<tr>
<th>Reference</th>
<th>Compound</th>
<th>No.</th>
<th>Reported coupling (Hz)</th>
<th>Reported angle</th>
<th>DAERM* angle</th>
<th>Calculated Karplus constants</th>
</tr>
</thead>
<tbody>
<tr>
<td>76</td>
<td><img src="image1.png" alt="Image" /></td>
<td>37</td>
<td>$J_{1,3}$ 7.670</td>
<td>27.6</td>
<td>29</td>
<td>10.3, 11.5</td>
</tr>
<tr>
<td>76</td>
<td><img src="image2.png" alt="Image" /></td>
<td>38</td>
<td>$J_{1,3}$ 7.35</td>
<td>30.0</td>
<td>32</td>
<td>10.5, 11.7</td>
</tr>
<tr>
<td>77</td>
<td><img src="image3.png" alt="Image" /></td>
<td>39</td>
<td>$J_{1,3}$ 9.53</td>
<td>31.6</td>
<td>31</td>
<td>13.4, 14.9</td>
</tr>
<tr>
<td>77</td>
<td><img src="image4.png" alt="Image" /></td>
<td>40</td>
<td>$J_{1,3}$ 9.17</td>
<td>27.7</td>
<td>29</td>
<td>12.3, 13.6</td>
</tr>
<tr>
<td>77</td>
<td><img src="image5.png" alt="Image" /></td>
<td>41</td>
<td>$J_{1,3}$ 3.16</td>
<td>91.0</td>
<td>126</td>
<td>9.1, 10.1</td>
</tr>
</tbody>
</table>

* $\omega = 127.6$ as assigned by Dodson et al.
Norbornenes

42

43

\[ a \ R_1 = \text{--C--OCH}_3; \ R_2 = \text{H} \]

\[ b \ R_1 = \text{--H}; \ R_2 = \text{--C--OCH}_3 \]
### Table IX

NMR & DAERM Data For Hexachlorobicyclo[2.2.1]hept-5-ene Derivatives

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>$J_{ax}$</th>
<th>$J_{bx}$</th>
<th>$\theta_{ax}$</th>
<th>$\theta_{bx}$</th>
<th>$k_1$</th>
<th>$k_2$</th>
<th>Substituent Electronegativities from ref. 14</th>
</tr>
</thead>
<tbody>
<tr>
<td>42a</td>
<td>-CN</td>
<td>4.6</td>
<td>9.3</td>
<td>12</td>
<td>132</td>
<td>10.0</td>
<td>11.1</td>
<td>2.49</td>
</tr>
<tr>
<td>42b</td>
<td>-C-OH</td>
<td>4.4</td>
<td>8.5</td>
<td>13</td>
<td>133</td>
<td>9.2</td>
<td>10.2</td>
<td>2.60</td>
</tr>
<tr>
<td>42c</td>
<td>-O</td>
<td>4.2</td>
<td>8.9</td>
<td>11</td>
<td>131</td>
<td>9.5</td>
<td>10.6</td>
<td>2.75</td>
</tr>
<tr>
<td>42d</td>
<td>-Cl</td>
<td>3.2</td>
<td>8.0</td>
<td>8</td>
<td>128</td>
<td>8.4</td>
<td>9.4</td>
<td>3.25</td>
</tr>
<tr>
<td>42e</td>
<td>-OH</td>
<td>2.4</td>
<td>7.4</td>
<td>4</td>
<td>124</td>
<td>7.7</td>
<td>8.6</td>
<td>3.43</td>
</tr>
<tr>
<td>42f</td>
<td>-OAc</td>
<td>2.5</td>
<td>7.6</td>
<td>4</td>
<td>124</td>
<td>7.9</td>
<td>8.8</td>
<td>3.80</td>
</tr>
</tbody>
</table>

$\omega = 120^\circ$
group can be expected to be greater than the tetra-
hedral angle \((80)\). Assuming a distortion of a few
degrees \((\omega = 125^\circ)\), both the amount of twist about
the \(C_2-C_3\) bond and the Karplus constants decrease by
a small amount (Table X). These latter results are in
better agreement with the magnitude of twists found by
X-ray studies \((81)\).

It should be noted that the ratio \(k_1/k_2 = 0.9\)
has been verified only for cyclohexane. The work of
Popie and coworkers \((12)\) indicates that this ratio
may decrease with electronegative substituents.
Table X

Variation in \( \omega \) for C-2 and C-3 of Bicyclo[2.2.1]hept-5-enes

<table>
<thead>
<tr>
<th>Reference</th>
<th>Compound</th>
<th>R</th>
<th>( \omega )</th>
<th>cis angle</th>
<th>trans angle ( k_1 )</th>
<th>( k_1 )</th>
<th>( k_2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>42b</td>
<td>-C-OH</td>
<td>120</td>
<td>13</td>
<td>133</td>
<td>9.2</td>
<td>10.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>125</td>
<td>8</td>
<td>9.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>133</td>
<td>9.0</td>
<td>10.2</td>
</tr>
<tr>
<td>14</td>
<td>42e</td>
<td>-OH</td>
<td>120</td>
<td>4</td>
<td>124</td>
<td>7.7</td>
<td>8.6</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>125</td>
<td>1</td>
<td>7.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>124</td>
<td>7.7</td>
<td>8.6</td>
</tr>
<tr>
<td>103</td>
<td>43a</td>
<td>-C-OC(_3)H(_3)</td>
<td>120</td>
<td>10</td>
<td>130</td>
<td>10.0</td>
<td>11.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>125</td>
<td>5</td>
<td>9.8</td>
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<td></td>
<td></td>
<td></td>
<td>130</td>
<td>9.8</td>
<td>10.8</td>
</tr>
<tr>
<td>103</td>
<td>43b</td>
<td>-C-OC(_3)H(_3)</td>
<td>120</td>
<td>11</td>
<td>131</td>
<td>9.6</td>
<td>10.7</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>125</td>
<td>7</td>
<td>9.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>132</td>
<td>9.4</td>
<td>10.5</td>
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</tbody>
</table>
B-2. Deoxy diacetone hexoses.

The furan ring like the cyclopentyl ring is flexible and has several low energy conformations. Because of this, any conformational data obtained at room temperature consists of a weighted time average from various low energy conformations. The arrangement of substituents around the furan ring may be instrumental in establishing a distinct conformational preference, particularly if intramolecular forces can occur only in specific conformers. Because of the constraining effects of the 1,2-0-isopropylidene ring and the 'tail', it seems probable that the 1,2;5,6-di-0-isopropylidene-D-hexoses retain a high degree of conformational purity at room temperature. If this is true, the NMR data obtained at room temperature will reflect this conformational preference.

In the following discourse, the section, C₂-C₃-C₄, of the furan ring (a) is the focal point of the conformational discussion. For DAERM, \( \omega \) is the projection angle of the methylene protons along the C₂-C₃ or C₄-C₃ bond (b). Internal angles between carbon atoms involved
in a furan ring are known (69) to be smaller than the regular tetrahedral value of 109.5°. Assuming constant p-character in the carbon bonding, the angle subtended by the hydrogens on a methylene function of a furan ring will necessarily be greater than the tetrahedral angle (81). Recognizing this effect, an \( \omega \) value of 124° has been selected for the DAERM calculations. A ratio of Karplus constants of 0.9 is assumed and evidence is presented to show that considerable deviations of either the ratio or \( \omega \) from the assigned values have minimal effect on any conformational arguments. With these values assigned, DAERM can now be applied to these 3-deoxy-\( \beta \)-hexose derivatives.

Spectral assignments were made on the basis of the easily recognized \( H_1 \) and \( H_2 \) resonances at low field and the complex methylene pattern of \( H_{31}, H_{32} \) at high field. The assignment of configuration to the methylene protons was made from the NMR results and, in one instance, a specifically deuterated analogue was prepared to confirm these assignments. All NMR spectra were computer simulated from first order data and an iterative fit to experimental data was performed using the LACOON III program of Bothner-By and Castellano (82). The necessity of computer analyzed data is indicated by a comparison of the first-order (Figure 5-A), fitted (5-B), and experimental (5-C) spectra for 3-deoxy-1,2;5,6-di-\( O \)-isopropylidene-\( \beta \)-\( D \)-arabinohexofuranose (20). Only 3-deoxy-1,2;5,6-di-\( O \)-isopropylidene-\( \alpha \)-\( D \)-ribohexofuranose (17) was not completely analyzed since the 4,5; 5,6; and 5,6\( \text{a} \) couplings were not obtainable.

From a consideration of the general appearance of
Figure 5

NMR Spectra for 3-Deoxy-1,2;5,6-di-O-isopropylidene-β-
D-arabinohexose (20)

A. Computer drawn spectrum on first order data

B. Computer drawn spectrum on computer fitted data

C. 100 MHz experimental spectrum
their NMR spectra and their molecular architecture, the four 3-deoxy-1,2,5,6-di-O-isopropylidene-α-D-hexofuranoses can be dealt with as two pairs, 3-deoxy-α-D-ribohexofuranose (17) and 3-deoxy-α-D-lyxohexofuranose (18); 3-deoxy-α-D-xylohexofuranose (19) and 3-deoxy-α-D-arabino- 

hexofuranose (20). The NMR coupling parameters for these compounds are listed in Table XI.

Considering first 3-deoxy,1,2,5,6-di-O-isopropylidene-α-D-xylohexofuranose (19), four solutions for the couplings from H_{2} to the H_{3}'s are obtained from DAERM. In Table XII and for all subsequent discussion, J_{1} is taken to be a cis coupling and \( \hat{\phi}_{1} \) the corresponding angle.

i and iii are both solutions for which few steric interactions within the molecule would be expected, but these have unexpectedly small Karplus constants. ii and iv do not seem to be reasonable solutions since they represent conformations in which there is a large torsional twist on the C_{2}-C_{3} bond and this places the 'tail' in a position where large steric interactions with the 1,2-0-isopropylidene group would be expected. The rather large values for the calculated Karplus constants also indicate that solutions ii and iv are not correct. DAERM analysis of the J_{31,4} to J_{32,4} couplings indicates that cases vi and viii can be eliminated since the Karplus constants are unacceptably large. As only very severe distortions of the furan ring could possibly make ii and iv compatible with any but cases vi and viii, cases ii and iv now must be eliminated and only i and iii; and v and vii remain as acceptable solutions.

The remaining problem is to decide which set of solutions is valid, i.e. i/v or iii/vii. The former (i/v)
Figure 6-1

3-Deoxy-1,2:5,6-di-O-isopropylidene-D-hexoses

a α-ribo (17)

b α-lyxo (18)
Figure 6-2

3-Deoxy-1,2;5,6-Di-O-isopropylidene-D-hexoses

a  α-xylo (19)  

b  β-arabino  (20)
Table XI

Proton Couplings in the 3-Deoxy-1,2;5,6-di-O-isopropylidene-D-hexoses*

<table>
<thead>
<tr>
<th>Compound</th>
<th>( J_{1,2} )</th>
<th>( J_{2,3_1} )</th>
<th>( J_{2,3_2} )</th>
<th>( J_{3_1,3_2} )</th>
<th>( J_{3_1,4} )</th>
<th>( J_{3_2,4} )</th>
<th>( J_{4,5} )</th>
<th>( J_{5,e_1} )</th>
<th>( J_{5,e_2} )</th>
<th>( J_{e_1,e_2} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>3.68</td>
<td>4.79</td>
<td>0.41</td>
<td>-13.41</td>
<td>9.98</td>
<td>3.94</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>18( ^\dagger )</td>
<td>3.52</td>
<td>0.55</td>
<td>4.76</td>
<td>-13.11</td>
<td>4.52</td>
<td>10.62</td>
<td>5.51</td>
<td>6.56</td>
<td>6.81</td>
<td>-8.28</td>
</tr>
<tr>
<td>19</td>
<td>3.78</td>
<td>6.30</td>
<td>1.35</td>
<td>-14.20</td>
<td>8.45</td>
<td>4.13</td>
<td>8.14</td>
<td>6.71</td>
<td>6.91</td>
<td>-8.27</td>
</tr>
<tr>
<td>20( ^\dagger )</td>
<td>3.76</td>
<td>0.82</td>
<td>6.24</td>
<td>-14.74</td>
<td>2.63</td>
<td>8.45</td>
<td>9.65</td>
<td>6.13</td>
<td>5.61</td>
<td>-9.08</td>
</tr>
</tbody>
</table>

* All spectra run in CDCl\(_3\) at 100 MHz; J's in Hz; iterative computer analyzed couplings.

\( ^\dagger \) Measurements obtained from 220 MHz spectrum.
Table XII

DAERM Analysis* of Couplings in 19

<table>
<thead>
<tr>
<th>Protons Coupled</th>
<th>Case</th>
<th>Observed J-1</th>
<th>Observed J-2</th>
<th>Calc θ-1</th>
<th>Calc θ-2</th>
<th>Calc k₁</th>
<th>Calc k₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-2,H-3₁,H-3₂</td>
<td>i</td>
<td>1.35</td>
<td>6.30</td>
<td>58</td>
<td>182</td>
<td>5.93</td>
<td>6.59</td>
</tr>
<tr>
<td></td>
<td>ii</td>
<td>1.35</td>
<td>6.30</td>
<td>72</td>
<td>52</td>
<td>17.27</td>
<td>19.19</td>
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<td></td>
<td>iii</td>
<td>6.30</td>
<td>1.35</td>
<td>6</td>
<td>118</td>
<td>6.65</td>
<td>7.39</td>
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<tr>
<td></td>
<td>iv</td>
<td>6.30</td>
<td>1.35</td>
<td>52</td>
<td>72</td>
<td>17.27</td>
<td>19.19</td>
</tr>
<tr>
<td>H-3₁,H-3₂,H-4</td>
<td>v</td>
<td>4.13</td>
<td>8.45</td>
<td>43</td>
<td>167</td>
<td>8.27</td>
<td>9.19</td>
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<tr>
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<td>vi</td>
<td>4.13</td>
<td>8.45</td>
<td>67</td>
<td>57</td>
<td>29.21</td>
<td>32.46</td>
</tr>
<tr>
<td></td>
<td>vii</td>
<td>8.45</td>
<td>4.13</td>
<td>8</td>
<td>132</td>
<td>8.90</td>
<td>9.89</td>
</tr>
<tr>
<td></td>
<td>viii</td>
<td>8.45</td>
<td>4.13</td>
<td>57</td>
<td>67</td>
<td>29.21</td>
<td>32.46</td>
</tr>
</tbody>
</table>

* w = 124°, k₁/k₂ = 0.9
Table XIII

Variation of $w$ and $k_1/k_2$ in Dihedral Angle Estimation*

<table>
<thead>
<tr>
<th>$w$</th>
<th>$k_1/k_2$</th>
<th>$J_{2,3_1}$</th>
<th>$J_{2,3_2}$</th>
<th>$\varphi_{2,3_1}$</th>
<th>$\varphi_{2,3_2}$</th>
<th>$k_1$</th>
<th>$k_2$</th>
</tr>
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<tbody>
<tr>
<td>130°</td>
<td>0.9</td>
<td>6.30</td>
<td>1.35</td>
<td>13</td>
<td>117</td>
<td>6.9</td>
<td>7.7</td>
</tr>
<tr>
<td>124°</td>
<td>0.7</td>
<td>6.30</td>
<td>1.35</td>
<td>10</td>
<td>114</td>
<td>6.8</td>
<td>9.7</td>
</tr>
<tr>
<td>124°</td>
<td>0.8</td>
<td>6.30</td>
<td>1.35</td>
<td>8</td>
<td>116</td>
<td>6.7</td>
<td>8.4</td>
</tr>
<tr>
<td>124°</td>
<td>0.9</td>
<td>6.30</td>
<td>1.35</td>
<td>6</td>
<td>118</td>
<td>6.6</td>
<td>7.4</td>
</tr>
<tr>
<td>124°</td>
<td>1.0</td>
<td>6.30</td>
<td>1.35</td>
<td>4</td>
<td>120</td>
<td>6.6</td>
<td>6.6</td>
</tr>
<tr>
<td>120°</td>
<td>0.9</td>
<td>6.30</td>
<td>1.35</td>
<td>2</td>
<td>118</td>
<td>6.6</td>
<td>7.3</td>
</tr>
<tr>
<td>110°</td>
<td>0.9</td>
<td>6.30</td>
<td>1.35</td>
<td>8</td>
<td>118</td>
<td>6.7</td>
<td>7.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>$w$</th>
<th>$k_1/k_2$</th>
<th>$J_{3_1,4}$</th>
<th>$J_{3_2,4}$</th>
<th>$\varphi_{3_1,4}$</th>
<th>$\varphi_{3_2,4}$</th>
<th>$k_1$</th>
<th>$k_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>130°</td>
<td>0.9</td>
<td>8.45</td>
<td>4.13</td>
<td>2</td>
<td>132</td>
<td>8.7</td>
<td>9.7</td>
</tr>
<tr>
<td>124°</td>
<td>0.7</td>
<td>8.45</td>
<td>4.13</td>
<td>2</td>
<td>126</td>
<td>8.7</td>
<td>12.5</td>
</tr>
<tr>
<td>124°</td>
<td>0.8</td>
<td>8.45</td>
<td>4.13</td>
<td>5</td>
<td>129</td>
<td>8.8</td>
<td>11.0</td>
</tr>
<tr>
<td>124°</td>
<td>0.9</td>
<td>8.45</td>
<td>4.13</td>
<td>8</td>
<td>132</td>
<td>8.9</td>
<td>9.9</td>
</tr>
<tr>
<td>124°</td>
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<td>8.45</td>
<td>4.13</td>
<td>10</td>
<td>134</td>
<td>9.0</td>
<td>9.0</td>
</tr>
<tr>
<td>120°</td>
<td>0.9</td>
<td>8.45</td>
<td>4.13</td>
<td>11</td>
<td>131</td>
<td>9.1</td>
<td>10.1</td>
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<tr>
<td>110°</td>
<td>0.9</td>
<td>8.45</td>
<td>4.13</td>
<td>19</td>
<td>129</td>
<td>9.8</td>
<td>10.9</td>
</tr>
</tbody>
</table>

* DAERM analysis of couplings into the methylene function of 3-deoxy-1,2;5,6-di-O-isopropylidene-\(\alpha\)-D-xylohexofuranose (19).
Figure 7

DAERM Analysis of
3-Deoxy-1,2;5,6-di-O-isopropylidene-α-D-xylohexofuranose

iii/vii

i/v
indicates a conformation in which the 'tail' involves less steric interactions than in (iii/vii) but requires a rather severe distortion towards the envelope \(^2V\) form. The latter solution (iii/vii) appears less distorted although there are eclipsing interactions between the furan ring substituents.

To establish unequivocally the proton assignment in 19, the NMR spectrum of specifically 3,4-dideuterated 19 was obtained. The disappearance of the large coupling (6.30 Hz) rather than the smaller (1.35 Hz) clearly indicates the conformation iii/vii is correct. This follows from the definition of \(J_1\) and \(\psi_1\) as the cis coupling and dihedral angle, respectively.

By analogy with the 3-deoxy-\(\text{xylo}\)hexofuranose (19) derivative, the resonances in 3-deoxy-1,2;5,6-di-O-isopropylidene-\(\beta\)-\(\text{D-arabin}\)ohexofuranose (20) were assigned and following similar reasoning, the resulting solutions were obtained as shown in Figure 8.

If the torsional twists of two adjacent bonds within a five-membered ring are defined, the geometry of the complete ring, within the limits of bond distortion, must be uniquely defined. Assignment of torsional angles between carbons 2, 3, and 4 thus indicates the position of carbon 1 and the ring oxygen. On this basis, the conformation of compounds 19 and 20 have been assigned. 3-Deoxy-1,2;5,6-di-O-isopropylidene-\(\alpha\)-\(\text{D-xylo}\)hexofuranose (19) prefers a conformation \(V_0=^1T_0=^1V\), where the conformational symbols are those defined by Hall and coworkers (83). The \(\beta\)-\(\text{D-arabin}\)o derivative, 20, appears to have the \(^0T_1=V_1=^2T_1\) system as its conformational preference. The degree of distortion from planarity is slight in both
Figure 8

Conformation of 3-Deoxy-1,2;5,6-di-O-isopropylidene-β-D-arabinohexopyranose

Calculated Karplus Constants

\[ \begin{align*}
  & C-2 - C-3 & k_1 = 6.79, k_2 = 7.55 \\
  & C-3 - C-4 & k_1 = 8.73, k_2 = 9.70
\end{align*} \]
these molecules and inspection of molecular models indicates that the H₁-H₂ dihedral angle is probably not more than 10° and may well be considerably less.

Since the value of $w = 124°$ has been estimated, the effect of varying $w$ over a twenty degree range was investigated. Evidence is presented in Table XIII which indicates that conformational assignments are not appreciably changed by varying $w$ through reasonable limits. Similarly, variation of the value $k₁/k₂$, as has been indicated previously, results only in small changes in dihedral angle. These changes are most conveniently compared by molecular models, from which it is readily seen that such variations result in little difference in the conformational assignment.

DAERM analysis of the 2,3 and 3,4 couplings of 3-deoxy-1,2;5,6-di-O-isopropylidene-β-D-lyxohexofuranose (18) is shown in Table XIV. Case ii can be rejected as a reasonable solution on the basis of the extreme distortion of the furan ring necessary to satisfy the angles. Cases vi and viii can be rejected because of their unacceptably large Karplus constants. Rejection of cases vi and viii leaves case i as an unacceptable solution as no reasonable conformation is compatible with iii or iv, as a trans coupling from H₂ to H₃ proton must have a corresponding cis coupling from that H₃ proton to H₄. There remain two solutions, iii/v, or iv/v (Figure 9). Conformation iii/v is taken as the correct conformation because iv/v requires a severe twisting in the furan ring. At the same time, the Karplus constants calculated for iii/v agree well with those obtained for the xylo (19) and arabino (20) derivatives.
DAERM Analysis of 3-Deoxy-1,2;5,6-di-O-iso-propylidene-β-D-lyxohexose

Figure 9

iii/v

iv/v
Table XIV

DAERM Analysis* of Couplings in
3-Deoxy-1,2;5,6-di-O-isopropylidene-β-D-lyxohexofuranose (18)*

<table>
<thead>
<tr>
<th>Protons Coupled</th>
<th>Case</th>
<th>Observed J-1</th>
<th>Observed J-2</th>
<th>Calc θ-1</th>
<th>Calc θ-2</th>
<th>Calc k_1</th>
<th>Calc k_2</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-2, H-3_1, H-3_2</td>
<td>i</td>
<td>0.55</td>
<td>4.76</td>
<td>65</td>
<td>189</td>
<td>4.65</td>
<td>5.17</td>
</tr>
<tr>
<td></td>
<td>ii</td>
<td>0.55</td>
<td>4.76</td>
<td>75</td>
<td>49</td>
<td>11.87</td>
<td>13.19</td>
</tr>
<tr>
<td></td>
<td>iii</td>
<td>4.76</td>
<td>0.55</td>
<td>12</td>
<td>112</td>
<td>5.26</td>
<td>5.85</td>
</tr>
<tr>
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<td>iv</td>
<td>4.76</td>
<td>0.55</td>
<td>49</td>
<td>75</td>
<td>11.87</td>
<td>13.19</td>
</tr>
<tr>
<td>H-3_1, H-3_2, H-4</td>
<td>v</td>
<td>4.52</td>
<td>10.62</td>
<td>46</td>
<td>170</td>
<td>10.09</td>
<td>11.21</td>
</tr>
<tr>
<td></td>
<td>vi</td>
<td>4.52</td>
<td>10.62</td>
<td>68</td>
<td>56</td>
<td>34.61</td>
<td>38.46</td>
</tr>
<tr>
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<td>vii</td>
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<td>4.52</td>
<td>5</td>
<td>129</td>
<td>10.98</td>
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<tr>
<td></td>
<td>viii</td>
<td>10.62</td>
<td>4.62</td>
<td>56</td>
<td>68</td>
<td>34.61</td>
<td>38.46</td>
</tr>
</tbody>
</table>

* w = 124°, k_1/k_2 = 0.9
at these positions. In view of the work of Abraham and McLauchlin (17), this last result should be expected. Having defined the torsional angles about carbon atoms 2, 3, and 4, the conformation of 18 is $^4T_3=^4W=^4T_0$.

DAERM calculations and similar reasoning yield the conformation of the remaining compound, 3-deoxy-1,2;5,6-di-0-isopropylidene-α-D-ribohexofuranose (17). The conformation of this derivative is very similar to the lyxo compound (18) in that the carbon atom at position 4 prefers to be displaced from the median plane of the furan ring. The conformational designation is thus suggested to be $^3T_4=^3V_4=^0T_4$ (Figure 10).

Inspection of molecular models indicate that the 1,2 dihedral angle for the compounds 17 and 18 is also small, probably less than 10°. This result is identical to that obtained for 19 and 20. This is not too surprising as the coupling constants for all four compounds are very similar (3.52-3.78 Hz). The average value, 3.68 Hz, indicates that the magnitude of the Karplus constant, $k_1$, is surprisingly small, approximately 4 Hz. This presumably reflects the strong electron-withdrawing character of the oxygens about carbon 1. In pyranose sugars the $H_1-H_2$ coupling constant is about one-half the predicted values because of electronegative substituents (85). It is significant that the size of the calculated Karplus constants increase from $C_1$ to $C_4$: $C_1/C_2$, $k_1 = 4.4$; $C_2/C_3$, $k_1 = 6.9$; and $C_3/C_4$, $k_1 = 9.1$ Hz.

Two main points emerge from these conformational studies of the 3-deoxy-1,2;5,6-di-0-isopropylidene-α-D-hexofuranoses. Firstly, the conformations of the furan ring in the four compounds fall into two classes. The
Figure 10

Conformation of

\[ 3\text{-Deoxy-1,2;5,6-di-0-isopropylidene-}\alpha\text{-D-ribohexo-}\]
\[ \text{furanose} \]

Calculated Karplus Constants

\[
\begin{align*}
  \text{C-2 - C-3} & \quad k_1 = 5.39, \ k_2 = 5.99 \\
  \text{C-3 - C-4} & \quad k_1 = 9.42, \ k_2 = 10.46
\end{align*}
\]
xylo (19) and arabino (20) derivatives have furan rings which seem to deviate only a small amount from planarity. Their conformational preferences are most readily described as $V_0^{-1}T_0^{-1}V$ and $0T_1^{-}=V_1^{-}=2T_1$ respectively. More pronounced is the preference of the ribo (17) and lyxo (18) derivatives for a conformation with $C_4$ displaced from the furan ring plane. The populated segment of the cycle of pseudorotation is $3T_4^{-}=V_4^{-}=0T_4$ and $4T_3^{-}=4V^{-}=4T_0$ for 17 and 18 respectively. Spencer (86) and Lemieux and Nagarajan (87) have suggested that puckering in five membered rings should involve either $C_2$ or $C_3$ as the atoms displaced. The proposed conformations of 17 and 18 with atom four out of the plane clearly are not in keeping with their suggestion. Recent x-ray crystallographic analysis (58) of 3-chloro-3-deoxy-1,2;5,6-di-O-isopropylidene-$\beta$-D-idofuranose clearly shows $C_4$ to be out of the plane. The furan ring in the chloroidose derivative closely approximates the $4V$ conformation on the crystalline state. A computer drawn representation of the final atomic positions found in the crystal structure is indicated in Figure 11.

In flexible molecules the observed NMR parameters represent a weighted average of the parameters describing all the individual conformers present. This allows two interpretations of a conformation assigned to a flexible molecule from NMR data. Either the molecule has a strong preference for the pseudorotational segment predicted or else, two or more widely differing conformations exist whose coupling parameters time-average to give the observed values. It is believed that the molecules 17 to 20 fit the first interpretation, that
Figure 11

Conformation of 3-Chloro-3-deoxy-1,2;5,6-di-O-isopropylidene-β-D-idose in the Crystalline State.

○ Carbon  ● Oxygen  ○ Chlorine
is, show a strong preference for the pseudorotational segment predicted. This expectation is based on the small trans $H_2$, $H_3$ coupling and the large trans $H_3$, $H_4$ couplings found in compounds 17 and 18. It is difficult to see how significant contributions from other conformers could leave this trans coupling ($H_2$ to $H_3$) small and at the same time retain the large trans ($H_3$ to $H_4$) coupling. Similarly, the large cis couplings found in compounds 19 and 20 indicate only one highly populated pseudorotational segment as any significant deviation from this segment can only lead to a reduction in the magnitude of these couplings and thus a strong preference for the pseudorotational segment predicted. To test this assumption, NMR spectra of two compounds were obtained at approximately $-40^\circ$ C. In no case were significant deviations from the corresponding couplings at room temperature found.

At this point it is interesting to speculate on the effect of the constant $c$ used in DAERM. Since the value of $c$ is small, it has a non-negligible effect on couplings only when they themselves are small. Although valence bond theory (7, 15) predicts a positive value for $c$, this is not true for molecular orbital theory (10, 11, 12). 3-Chloro-3-deoxy-1,2;5,6-di-O-isopropylidene-$\beta$-D-idofuranose displays a typical trans $H_2$ to $H_3$ coupling of approximately 0.5 Hz in solution. The x-ray data (58) indicates the angle corresponding to this coupling is about 95°. It is tempting to adjust $c$ to provide better agreement with this result. A $c$ of $+0.28$ gives an angle of about 100° to be compared with 112° from the valence bond value of $-0.28$. Since
all the small couplings (i.e. about 0.5 Hz couplings) are subject to considerable error and since the presence of other alternate conformations in solution is probable, it seems unwise to push this analogy any further. Use of this revised value of c has no effect on conformational assignments but does indicate that the puckering may be slightly more than that previously indicated. Table XV compares the results from the two values of c and also the results from DAERM II.

From a consideration of the molecular architecture of the isopropylidene hexoses, it is natural to divide the eight hexose derivatives into two distinct groups. The first group has the 1,2-O-isopropylidene unit and the 'tail' on the same side of the furan ring, the second has the 1,2 unit and the 'tail' on opposite sides of the ring. Figure 12 illustrates this point and relates the couplings found in the deoxy sugars to those assigned to their epimeric 3-hydroxy relatives.

Although Karplus constants and thus the vicinal coupling constants would be expected to be affected by replacement of H by OH, close similarity of the couplings indicates that there is little change in the conformation on going from the deoxy sugars to their hydroxylated derivatives. On this basis the endo and exo hydroxylated derivatives are assigned conformational preferences identical to those of their parent compounds.
Table XV
DAERM and DAERM II angular predictions for the
3-deoxy-1,2;5,6-di-0-isopropylidene-D-hexoses

<table>
<thead>
<tr>
<th>Compound</th>
<th>Position</th>
<th>DAERM* (c=0.28)</th>
<th>DAERM* (c=-0.28)</th>
<th>DAERM II+ (c=-0.28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>2 → 3 cis</td>
<td>14</td>
<td>25</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>trans</td>
<td>110</td>
<td>99</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>3 → 4 cis</td>
<td>48</td>
<td>50</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>trans</td>
<td>172</td>
<td>174</td>
<td>173</td>
</tr>
<tr>
<td>18</td>
<td>2 → 3 cis</td>
<td>12</td>
<td>21</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>trans</td>
<td>112</td>
<td>103</td>
<td>101</td>
</tr>
<tr>
<td></td>
<td>3 → 4 cis</td>
<td>46</td>
<td>48</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>trans</td>
<td>170</td>
<td>172</td>
<td>171</td>
</tr>
<tr>
<td>19</td>
<td>2 → 3 cis</td>
<td>6</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>trans</td>
<td>118</td>
<td>115</td>
<td>112</td>
</tr>
<tr>
<td></td>
<td>3 → 4 cis</td>
<td>8</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>trans</td>
<td>132</td>
<td>130</td>
<td>130</td>
</tr>
<tr>
<td>20</td>
<td>2 → 3 cis</td>
<td>12</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>trans</td>
<td>112</td>
<td>107</td>
<td>105</td>
</tr>
<tr>
<td></td>
<td>3 → 4 cis</td>
<td>1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>trans</td>
<td>123</td>
<td>122</td>
<td>120</td>
</tr>
</tbody>
</table>

* k₁/k₂ = 0.9.
† b/a = -0.053.
Figure 12

Observed couplings in Hz for the furanose ring hydrogens of the 3-deoxy and 1,2;5,6-di-0-isopropylidene-D-hexoses (read from right to left C-1, C-2, C-3, and C-4).
Figure 12-1

(17)

(3)

(1)

(18)

(4)

(2)
Figure 12-2

(19)

(7)

(5)

(20)

(6)

(8)
B.3. Diacetone Hexoses.

1,2;5,6-Di-\textsubscript{D}-isopropylidene-\textalpha;-\textD-ribohexofuranose derivatives

1,2;5,6-Di-\textsubscript{D}-isopropylidene-\textalpha;-\textD-glucofuranose (1) and \textalpha;-\textD-allofuranose (3) are the \textit{exo} and \textit{endo} hydroxylated derivatives of 3-deoxy-1,2;5,6-di-\textsubscript{D}-isopropylidene-\textalpha;-\textD-ribohexofuranose (17). The latter compound has been assigned a conformational preference of $^3T_4=V_4=^0T_4$ on the basis of DAERM calculations and the similarity of the couplings outlined in Figure 12 leads us to believe that the alloose and glucose derivatives have essentially the same conformational preference. The 7.3 Hz coupling into the hydroxyl group of 1,2;5,6-di-\textsubscript{D}-isopropylidene-\textalpha;-\textD-allofuranose (3) indicates an \textit{anti} arrangement of the H\textsubscript{3} and the hydroxyl proton since the magnitudes of H-C-0-H couplings are expected to be dependent on the dihedral angle subtended by the hydrogen nuclei (88, 62). This orientation of the hydroxyl group and the suggested conformation are completely consistent with the proposed hydrogen bond formation between the 3-0-H and the 2-0 of the 1,3-dioxolane ring. The IR studies also indicated that the glucose derivative (1) is able to hydrogen bond to the 'tail' in dilute carbon tetrachloride solution. The NMR parameters are consistent with the molecule, (1), being in the assigned conformation and such a configuration readily allows formation of the hydrogen bond to the 'tail'. In the alloose compound, (3), the coupling constant, $J_{4,s}$ of 4.55 Hz, probably reflects the freedom of rotation of the 'tail' whereas in glucose (1) the coupling constant, $J_{4,s}$ of 7.27 Hz, indicates a high proportion of a larger coupling and thus a more preferred rotamer. All
observations are in complete agreement with the assignment of $^3T_4=V_4=^0T_4$ for the conformational preference of the glucose (1) and allose (3) derivatives.

1,2;5,6-Di-0-isopropylidene-$\beta$-$D$-lyxohexofuranose derivatives

1,2;5,6-Di-0-isopropylidene-$\beta$-$D$-idofuranose (2) and -$\beta$-$D$-talofuranose (4) are assigned the conformation $^4T_3=^4V=^4T_0$ of the parent 1,2;5,6-di-0-isopropylidene-$\beta$-$D$-lyxohexofuranose (18). In the idose derivative (2), only hydrogen bonding of the 3-hydroxyl group to the 'tail' could be detected. The 4.1 Hz coupling into the hydroxyl group is consistent with formation of this bond, which has the effect of locking the conformation into that proposed. The 9.0 Hz coupling into the hydroxyl group of 1,2;5,6-di-0-isopropylidene-$\beta$-$D$-talofuranose (4) is consistent with hydrogen bond formation to the 2-oxygen of the 1,2-O-isopropylidene ring as in the allose derivative (3). Thus, all the members of the 1,2;5,6-di-0-isopropylidene-$\beta$-$D$-lyxohexofuranose family (18, 2, 4) are fully expected to share the $^4T_3=^4V=^4T_0$ conformational preference. The $^4V$ conformation has been found for 3-chloro-3-deoxy-1,2;5,6-di-0-isopropylidene-$\beta$-$D$-idofuranose from crystal structure analysis (58) in agreement with the NMR results.

1,2;5,6-Di-0-isopropylidene-$\alpha$-$D$-xylohexofuranose derivatives

1,2;5,6-Di-0-isopropylidene-$\alpha$-$D$-galactofuranose (5) and -$\alpha$-$D$-gulofuranose (7) are assigned a conformational preference of $V_0=^1T_0=^1V$ on the basis of this assign-
ment for the 3-deoxy analogue (19), 1,2;5,6-di-0-isopropylidene-α-D-xylohexofuranose. The $J_{4,5}$ couplings as well as the couplings into the hydroxyl function do not add any further information to the assignment but the general similarity of all the couplings within this family indicates a similar conformational preference. A coupling of about 8 Hz for the $J_{4,5}$ couplings of this family clearly indicates a conformational preference for the 'tail'. It is obvious that this preference is not regulated by hydrogen bond formation to the 'tail' since the deoxy xylohexose (19) and galactose (5) derivatives cannot form such a bond.

1,2;5,6-D-0-isopropylidene-β-D-arabinohexofuranose family

The conformations of 1,2;5,6-di-0-isopropylidene-β-D-altrofuranose (6) and -β-D-mannofuranose (8) are assigned a conformational preference of $\gamma T_1 = \nu_1 = 2 T_1$ by analogy with the couplings of the 3-deoxy-arabinohexofuranose derivative (20) shown in Figure 12. It is once more obvious that the 'tail' prefers an orientation independent of possible hydrogen bonding interactions. The forces responsible for such a high degree of rotamer preference might arise from attractive interactions between $C_5$ and the 1,2-isopropylidene ring oxygens or between $C_6$ and the furan ring oxygen. Conversely, repulsive electrostatic interactions might occur between the oxygens at one and five and the furan ring oxygen in certain rotamers.

In order to better evaluate the possible influence of hydrogen bonding on the orientation of the 'tail',
the temperature dependence of hydrogen bond formation was investigated (89). 1,2;5,6-Di-O-isopropylidene-β-D-mannose (8) and -β-D-idose (2) underwent no observable shift in equilibrium upon varying the temperature from -30 to +50°. 1,2;5,6-Di-O-isopropylidene-α-D-glucose (1) underwent a continuous change with temperature. A ΔH° of -3.1 ± 0.2 kcal was calculated, a value typical of O-H...O systems (90). The lack of free -OH in the idose (2) and mannose (8) derivatives is probably a result of other forces restraining the 'tail' to rotamers which may also hydrogen bond. That such influences are possible is evidenced by many J4,5 couplings, the magnitude of which cannot possibly represent freely rotating systems.

DAERM calculations were performed on the position 5 to 6 couplings in order to obtain the sense of puckering in the 'tail' and to give an estimate of the Karplus constants. The results are seen in Table XVI. DAERM indicates that the 'tail' is distorted from planarity and that this distortion is the same for all the compounds investigated. The x-ray crystal structure of 3-chloro-3-deoxy-1,2;5,6-di-O-isopropylidene-β-D-idofuranose (58) shows a twist of 25° in the O-C₆-C₅-O dihedral angle. Calculations on x-ray crystal structure data of 3-deoxy-3,4-C-(dichloromethylene)-1,2;5,6-di-O-isopropylidene-α-D-galactofuranose (91) show a twist of 24.9° for this tail in excellent agreement with the proton NMR results.

Inspection of Table XVI reveals a surprising variation in the Karplus constants, particularly since ring size and substitution patterns in the 'tail' are
### Table XVI

**DAERM* Calculations on the 5,6-Q-isopropylidene Group**

**Analysis of $J_{5,6}$ $J_{5,6}$ Couplings**

<table>
<thead>
<tr>
<th>1,2;5,6-Di-O-isopropylidene</th>
<th>Observed $J_{1}$</th>
<th>Observed $J_{2}$</th>
<th>Calculated $\phi_1$</th>
<th>Calculated $\phi_2$</th>
<th>Calculated $k_1$</th>
<th>Calculated $k_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>-(\alpha)-D-glucose</td>
<td>(1)</td>
<td>6.50</td>
<td>5.95</td>
<td>23</td>
<td>147</td>
<td>8.0</td>
</tr>
<tr>
<td>-(\beta)-D-idose</td>
<td>(2)</td>
<td>6.93</td>
<td>6.89</td>
<td>25</td>
<td>149</td>
<td>8.8</td>
</tr>
<tr>
<td>-(\alpha)-D-allose</td>
<td>(3)</td>
<td>6.68</td>
<td>6.61</td>
<td>25</td>
<td>149</td>
<td>8.5</td>
</tr>
<tr>
<td>-(\beta)-D-talose</td>
<td>(4)</td>
<td>7.61</td>
<td>6.50</td>
<td>21</td>
<td>145</td>
<td>9.1</td>
</tr>
<tr>
<td>-(\alpha)-D-galactose</td>
<td>(5)</td>
<td>7.15</td>
<td>6.70</td>
<td>23</td>
<td>147</td>
<td>8.8</td>
</tr>
<tr>
<td>-(\beta)-D-altrose</td>
<td>(6)</td>
<td>6.25</td>
<td>5.50</td>
<td>22</td>
<td>146</td>
<td>7.6</td>
</tr>
<tr>
<td>-(\alpha)-D-gulose</td>
<td>(7)</td>
<td>7.20</td>
<td>6.50</td>
<td>23</td>
<td>147</td>
<td>8.8</td>
</tr>
<tr>
<td>-(\beta)-D-mannose</td>
<td>(8)</td>
<td>6.41</td>
<td>5.70</td>
<td>22</td>
<td>146</td>
<td>7.8</td>
</tr>
<tr>
<td>-3-deoxy-(\alpha)-D-xylo-</td>
<td>(19)</td>
<td>6.91</td>
<td>6.72</td>
<td>24</td>
<td>148</td>
<td>8.7</td>
</tr>
<tr>
<td>hexofuranose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-3-deoxy-(\beta)-D-arabinio-</td>
<td>(20)</td>
<td>5.70</td>
<td>5.71</td>
<td>25</td>
<td>149</td>
<td>7.3</td>
</tr>
<tr>
<td>hexofuranose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* $\omega = 124^\circ$, $k_1/k_2 = 0.9$. 

*DAERM* denotes the **Double Angle of Reorientation Model**.
identical for all ten compounds. Recognizing that the NMR spectra of $D$- and $L$-isomers are identical, then these derivatives may be compared as five sets of $C_5$ isomers ($D$-$C_5$ vs. $L$-$C_5$ $D$-$C_4$). The sets are gluco/ido; allo/talo; altro/galacto; manno/gulo; and 3-deoxy-arabino/3-deoxy-xylo. It is observed that the first member of each set has the lower Karplus constants. It would appear likely that this variation is due to the proximity of $C_8$ to other furan ring substituents. The effect of solvent on the Karplus constants suggested previously may well be a more general example of such proximity effects.

1,2;5,6-Di-$O$-isopropylidene-$D$-hexofuranose derivatives

The 3-$O$-acetyl and 3-keto-derivatives of the 1,2;5,6-di-$O$-isopropylidene hexoses yielded much more complex spectra than those obtained from the parent compounds. Complete analysis was not achieved in several cases but the coupling constants that were obtained are given in Table XVII.

Comparisons of the coupling data in Table XVII and the values presented in Figure 12 appear to indicate that there is little change in conformation of the furan ring on acetylation of the 3-$OH$ group. It should be noted, although, that on acetylation of 1,2;5,6-di-$O$-isopropylidene-$D$-galactose (5), the position three to four coupling drops from $4.15$ Hz to $2.56$ Hz. At the same time the position two to three coupling goes from $1.13$ Hz to $0.7$ Hz. Comparison of these couplings with those obtained for the arabino-hexose family (6, 8, 20)
Table XVII

Proton Coupling Constants

<table>
<thead>
<tr>
<th></th>
<th>$J_{1,2}$</th>
<th>$J_{2,3}$</th>
<th>$J_{3,4}$</th>
<th>$J_{4,5}$</th>
<th>$J_{5,e_1}$</th>
<th>$J_{5,e_2}$</th>
<th>$J_{6,e_2}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2;5,6-Di-0-iso-propylidene</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-α-β-ribohexofuranos-3-ucose</td>
<td>(9a)</td>
<td>4.4</td>
<td>N.C.</td>
<td>N.C.</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>-α-β-ribohexofuranos-3-ucose.</td>
<td>(9b)</td>
<td>3.80</td>
<td>N.C.</td>
<td>N.C.</td>
<td>6.66</td>
<td>6.58</td>
<td>6.04</td>
</tr>
<tr>
<td>hydrate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-β-β-lyxohexofuranos-3-ucose</td>
<td>(10)</td>
<td>4.40</td>
<td>N.C.</td>
<td>N.C.</td>
<td>1.85</td>
<td>7.62</td>
<td>6.95</td>
</tr>
<tr>
<td>-α-β-xylohexofuranos-3-ucose</td>
<td>(11)</td>
<td>4.4</td>
<td>N.C.</td>
<td>N.C.</td>
<td>6.08</td>
<td>6.39</td>
<td>6.91</td>
</tr>
<tr>
<td>-β-β-arabinohexofuranos-3-ucose(12)</td>
<td>4.3</td>
<td>N.C.</td>
<td>N.C.</td>
<td></td>
<td>~6.</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3-0-Acetyl-α-β-glucose</td>
<td>(21)</td>
<td>3.7</td>
<td>~0.5</td>
<td>~2.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3-0-Acetyl-β-β-idose</td>
<td>(22)</td>
<td>3.8</td>
<td>0.6</td>
<td>2.3</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3-0-Acetyl-α-β-allose</td>
<td>(23)</td>
<td>3.7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>6.5</td>
<td>5.8</td>
</tr>
<tr>
<td>3-0-Acetyl-β-β-talose</td>
<td>(24)</td>
<td>3.8</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3-0-Acetyl-α-β-galactose</td>
<td>(25)</td>
<td>3.8</td>
<td>~0.7</td>
<td>2.56</td>
<td>7.84</td>
<td>6.66</td>
<td>6.92</td>
</tr>
<tr>
<td>3-0-Acetyl-β-β-altrose</td>
<td>(26)</td>
<td>3.78</td>
<td>0.70</td>
<td>1.16</td>
<td>9.67</td>
<td>6.14</td>
<td>4.80</td>
</tr>
<tr>
<td>3-0-Acetyl-α-β-gulose</td>
<td>(27)</td>
<td>4.11</td>
<td>5.58</td>
<td>6.66</td>
<td>9.04</td>
<td>6.55</td>
<td>7.19</td>
</tr>
<tr>
<td>3-0-Acetyl-β-β-mannose</td>
<td>(28)</td>
<td>4.02</td>
<td>5.75</td>
<td>5.92</td>
<td>8.48</td>
<td>6.50</td>
<td>5.22</td>
</tr>
</tbody>
</table>

* CDC13 solution measured in Hz, LAOCN III analyzed values given to 2nd decimal.

† N.C. no coupling present in molecule.
indicates that the molecule shifts its conformational preference after acetylation from the \( V_0=^T_0=^T_2 \) of the parent to the \( ^T_2=^V=^T_0 \) of the derivative. A similar result occurs if the compound is benzoylated but not if the hydroxyl group is replaced by fluorine (see NMR data ref. 21).

The magnitude of the coupling, \( J_{4,5} \) for the arabino- and xylohexose derivatives (25-28), indicates that the rotameric preference of the 'tail' is probably not significantly affected by the presence of the acetoxy group at \( C_3 \). Little information can be gained from the sparse results for the 3-keto compounds. A significant increase in the coupling \( J_{1,2} \) to about 4.4 Hz in these compounds can be attributed to the effect of carbonyl group electronegativity \( (J^V) \) as described by Cohen and Schaeffer (78).

The ketones (9-12) exhibited rather large long range couplings from \( H_2 \) to \( H_4 \), across the carbonyl function. Long range couplings were found to be a general phenomenon in the 1,2;5,6-di-\( \alpha \)-isopropylidene-\( \alpha \)-hexofuranose system. Both long range 1,3 cis and 1,3 trans couplings were observed with the latter being generally larger. Trans \( H_2 \) to \( H_4 \) couplings were not observed although large \( H_2 \) to \( H_4 \) cis couplings were quite common. This is presumably a result of the difference in ring puckering found for the two ring systems. Double resonance was used to confirm some of the assignments and in one case the sign of the coupling was determined. \( J_{13} \) was found to be -0.55 Hz in 3-deoxy-3,4-dideuterio-1,2;5,6-di-\( \alpha \)-isopropylidene-\( \alpha \)-galactofuranose. Sign determination was simplified by deuterium decoupling. The absolute values of some of the long range couplings are indicated in Table XVIII.
<table>
<thead>
<tr>
<th>1,2;5,6-Di-O-isopropylidene</th>
<th>$J_{1,3}$</th>
<th>$J_{2,4}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$-D-glucose</td>
<td>(1)</td>
<td>$\sim 0$</td>
</tr>
<tr>
<td>$\beta$-D-altrose</td>
<td>(6)</td>
<td>$\sim 0.4$</td>
</tr>
<tr>
<td>$\beta$-D-lyxohexofuranos-3-uloose</td>
<td>(10)</td>
<td>N.C.</td>
</tr>
<tr>
<td>$\alpha$-D-xylolhexofuranos-3-uloose</td>
<td>(11)</td>
<td>N.C.</td>
</tr>
<tr>
<td>$\beta$-D-arabinohexofuranos-3-uloose</td>
<td>(12)</td>
<td>N.C.</td>
</tr>
<tr>
<td>3-deoxy-$\beta$-D-arabinohexofuranose</td>
<td>(20)</td>
<td>0.5</td>
</tr>
<tr>
<td>3-O-Acetyl-$\beta$-D-idose</td>
<td>(22)</td>
<td>$\sim 0$</td>
</tr>
<tr>
<td>3-O-Acetyl-$\beta$-D-altrose</td>
<td>(26)</td>
<td>0.64</td>
</tr>
</tbody>
</table>

* measured in CDCl$_3$, values in Hz.
N.C. no coupling observed.
(-) indicates a coupling not measured.
Chapter 3

Conclusions

The use of Dihedral Angle Estimation by the Ratio Method (DAERM) has clearly led to a new interpretation of the NMR spectra of the 1,2;5,6-di-O-isopropylidene-D-hexoses. These studies demonstrate clearly that the furan conformation is determined by the substitution pattern of the 1,2-0-isopropylidene unit and the 'tail'. If the units are substituted on the furan ring in a cis fashion, the ring tends to be flattened with one or two of the atoms; C1, C2, and the ring oxygen, displaced from the mean plane. If, however, the units are substituted on the furan ring in a trans fashion, the ring is considerably more distorted with one or two of the atoms; C3, C4, and the ring oxygen, displaced in the preferred conformers.

Two crystal structures exhibiting this trans arrangement (58, 91) both show C4 to be the displaced atom in a near envelope conformation. The conformations assigned in this work restrict the 1,2-dihedral angle to less than ten or twelve degrees, quite out of keeping with the 40-50° range reported by earlier workers from NMR studies (16). Again, x-ray structures confirm our work, having 01-C1-C2-02 torsional angles of 4.5° (58), 9.0° (91), and 4.6° (92). Only gross distortion of the tetrahedral nature of the position 1 and 2 carbons would allow the H1-C1-C2-H2 torsional angle to be significantly different from that defined by the oxygen atoms.

The present assignment of conformation is completely in keeping with the information obtained from studies of
hydrogen bonding in these molecules. It is difficult to ascertain whether the differences in ring conformation for the two systems (cis fused or trans fused) is important chemically since the over-riding effect is undoubtedly that of cis or trans ring substitution. On the contrary, though, it does appear that the 'tail' can have a significant effect on the chemistry of these compounds. This is indicated in Table II where the times required for enol acetate formation are faster for the D-C₅;D-C₄ configuration than for the D-C₅;L-C₄ configuration. This effect is most readily explained if it is assumed that the preferred rotamer of the 'tail' is one in which the C₅-oxygen is on the same side of the molecule as the C₁ and ring oxygens as found in the x-ray crystal structure of 1,2;5,6-di-O-isopropylidene-β-D-idofuranose. This means that in the D-C₅;D-C₄ case, the C₄ and C₅ protons are near eclipsed instead of near anti as suggested by other workers (103) for 1,2;5,6-di-O-isopropylidene-α-D-glucofuranose. On the other hand, the anti-configuration would be found in the D-C₅;L-C₄ case. This leaves the C₄ position more open to attack in the D-C₅;D-C₄ cases (ribo and arabino ketones) and provides more steric interaction in the D-C₅;L-C₄ case (lyxo and xylo ketones), and would therefore provide results such as those observed.

The infrared spectra displayed in Figure 1 are completely in accord with this. The gulose derivative at first sight seems anomolous with complete hydrogen bonding to the tail being indicated by the infrared spectrum. This of course is not possible if the
conformation is that indicate above (i.e. H₄ and H₅ anti in preferred conformers).

Optical rotatory dispersion studies of this molecule in various solvents indicate a major change in conformation on going from a solvent such as chloroform to water, the strongly positive curve of the former case being replaced by a strongly negative curve in the second case (40). Interestingly enough, the NMR spectrum changes very little in D₂O, indicating that the 'tail', now no longer forming a hydrogen bond to the C₃ oxygen, has simply rotated to the conformation preferred in the absence of such bonds (i.e. from eclipsed configuration to anti configuration).

It appears that this effect is also reflected in the magnitude of Karplus constants calculated for the H₅ to H₆, H₆ couplings (Table XVI). The D-C₅;D-C₅ configuration always affords a smaller calculated Karplus constant than the corresponding D-C₅;L-C₄ configuration. Similarly the H₃, H₃ to H₄ couplings exhibit a similar effect, the D-C₅;D-C₄ configuration providing smaller Karplus constants than for the alternate case.

DAERM calculations on the H₅ to H₆, H₆ couplings has also indicated that the 'tails' of all compounds are twisted in the same manner and to the same extent, the sense and extent of this twisting being confirmed by x-ray crystal structures. It is clear that previously unrecognized forces are maintaining relatively strong conformational preferences which keep the 'tail' in its twisted form and which provide the rotameric preference.
Experimental

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Evaporations were carried out under reduced pressure on Buchi rotatory evaporators at bath temperatures not exceeding 50°. Optical rotations were measured on a Perkin Elmer P22 Spectropolarimeter. Hydrogen bonding studies were performed in matched quartz cells of 1 cm path length on a Beckman IR 12. Normal TR spectra were obtained on the same instrument, the samples being prepared as KBr discs. The TLC was carried out on silica gel G, with 10% H₂SO₄ and heat being used for development. All NMR spectral parameters reported were obtained on a Varian HA-100 spectrometer, with TMS as internal reference. Spectral analysis was performed on an IBM 360/50 computer using the LAOCN III NMR program of Bothner-By and Castellano (82).
1,2;5,6-Di-O-isopropylidene-α-D-glucofuranose (1)

Prepared from D-glucose by the method of Schmidt (93), m.p. 110°, [α]D -17.5° (c, 0.4, water). Lit. (93), 110-111°, [α]D -18.5° (c, 5, water).

1,2;5,6-Di-O-isopropylidene-α-D-ribohexofuranos-3-ulse (9)

To 1,2;5,6-di-O-isopropylidene-α-D-glucofuranose (1) (5.0 g) in carbon tetrachloride (50 ml), sodium bicarbonate (0.4 g) in water (4 ml) was added. Ruthenium dioxide (40 mg) was added and 5% aqueous sodium metaperiodate was added dropwise* with stirring until the oxidation was complete as indicated by TLC. The mixture was separated and the aqueous phase extracted twelve times with an equal volume of chloroform. The organic phases were combined, dried over calcium chloride, filtered and evaporated to give a sirup which crystallized readily. Recrystallization from chloroform-petroleum ether (30-60°) (1:2) gave 9, m.p. 109-111°, [α]D 37.5° (c, 0.4, water). Lit. (29), m.p. 108-110°, [α]D 40.2° (c, 0.5, water).

1,2;5,6-Di-O-isopropylidene-α-D-allofuranose (3)

Prepared by the sodium borohydride reduction of (9) as described by Theander (29). M.p. 73-74°, [α]D 34°(c, 0.4, water). Lit. (29), m.p. 76-77°, [α]D 37.7° (c, 0.5, water).

* Periodate is added only if the blank RuO₂ is reformed after each addition of periodate.
Amorphous D-idose was prepared by the method of Paulsen et al. (35). The D-idose so produced (5 g) was converted into the known di-\(\beta\)-isopropylidene derivative using zinc chloride (12 g), 85\% phosphoric acid (0.5 ml) in dry acetone (100 ml). The solution was stirred overnight at room temperature and then neutralized by careful addition of 50\% aqueous sodium hydroxide. The mixture was then filtered, the precipitate washed thoroughly with acetone and the filtrate and washings combined and evaporated. The resultant thin sirup was dissolved in chloroform (75 ml) and washed with 1\% aqueous sodium bicarbonate (50 ml). The bicarbonate wash water was extracted once with chloroform (50 ml) and the extracts pooled, dried over calcium chloride, filtered and evaporated. A crystalline product was obtained by cooling a petroleum ether (65-110\°) solution of the material. The mother liquor contained an isomeric di-\(\alpha\)-isopropylidene derivative, presumably the 1,2;5,6 furano\(\beta\) derivative. This material could be retreated with the acetal forming reagents to produce further amounts of 2. Recrystallization from petroleum ether (65-110\°) gave 1,2;5,6-di-\(\alpha\)-isopropylidene-\(\beta\)-D-idofuranose (3.5 g), m.p. 151-152\°, \([\alpha]_D^0 33.5\° (c, 0.4, acetone). Lit. (36), m.p. 151-152.5\°, \([\alpha]_D^0 36.0\° (acetone).

1,2;5,6-Di-\(\alpha\)-isopropylidene-\(\beta\)-D-lyxohexofuranose-3-ulose (10)

1,2;5,6-Di-\(\alpha\)-isopropylidene-\(\beta\)-D-idofuranose (2) (1.3 g) was oxidized in the same manner as the glucofuranose derivative. The oxidation yielded a crystalline material (1.1 g), m.p.
87.5-88° from petroleum ether (65-110°), [\(\alpha\)]_D -21.0° (c, 0.4, water). Calculated for C_{12}H_{18}O_{6}: C, 55.8%; H, 6.96%. Found: C, 55.95%; H, 6.79%.

1,2;5,6-Di-\(\beta\)-isopropylidene-\(\beta\)-D-talofuranose (4)

1,2;5,6-Di-\(\beta\)-isopropylidene-\(\beta\)-D-lyxohexofuranos-3-ulose (10) (400 mg) was dissolved in ethanol:water (5:1) (50 ml) and sodium borohydride (50 mg) was added. The reduction was carried out at room temperature for thirty minutes after which time the solution was neutralized with carbon dioxide. Extraction of this solution with chloroform (4x50 ml) gave a solution which was dried with calcium chloride, filtered and evaporated to a sirup. The sirup was dissolved in chloroform (50 ml) and washed with 2% aqueous sodium bicarbonate (25 ml). The bicarbonate wash was extracted once with chloroform (50 ml), the chloroform layers combined, dried, filtered and evaporated to a sirup which crystallized. The reduced product (350 mg) was recrystallized from petroleum ether (65-110°), m.p. 83-84°, [\(\alpha\)]_D -25.0° (c, 0.40, CHCl₃). Lit. (30), m.p. 85-86°, [\(\alpha\)]_D -25° (c, 0.47, CHCl₃).

1,2;5,6-Di-\(\alpha\)-isopropylidene-\(\alpha\)-D-galactofuranose (5)

Prepared by hydroboration of 3-deoxy-1,2;5,6-di-\(\alpha\)-isopropylidene-\(\alpha\)-D-erythrohexofuran-3-enose as described by Paulsen and Behre (38), m.p. 94-95°, [\(\alpha\)]_D -20.5° (c, 0.4, CHCl₃). Lit., m.p. 97.5-98°, [\(\alpha\)]_D -35.3 (c, 0.8, methanol).
Method A
Prepared according to the method of Meyer zu Reckendorf (27) with the following minor changes. 1,2;5,6-Di-O-isopropylidene-α-D-ribohexofuranos-3-ulose (9) (hydrate) (10 g) was dissolved in 30% acetic anhydride in pyridine (45 ml). The solution was kept at 35° until the reaction was complete by TLC (4 days). Ice water (500 ml) was seeded with several crystals of the product and the reaction mixture was slowly added to the vigorously stirred solution. The solution was kept at zero degrees until crystallization was complete. The mixture was filtered, and the product washed thoroughly with water, then recrystallized from ethanol-water. A further small amount of product was obtained by extracting the aqueous solution once with chloroform (50 ml). Crystalline product (10 g of long needles) was obtained melting at 58-59°. [α]_{D}^{22} -32° (c, 0.95, CHCl₃). Lit. (27), m.p. 62-63°, [α]_{D}^{20} -33° (c, 1, CHCl₃).

Method B
1,2;5,6-Di-O-isopropylidene-α-D-xylohexofuranos-3-ulose (11) (150 mg) was dissolved in an acetic anhydride (1 ml)-pyridine (2 ml) mixture and the solution was kept at 35° for 30 hours. The solution was evaporated several times with toluene until no further pyridine was present. The resulting sirup was dissolved in CHCl₃ (25 ml) and washed with dilute (2%) aqueous sodium bicarbonate. The chloroform fraction was dried over magnesium sulphate, filtered and evaporated. The residue was crystallized from an ethanol-water solvent then recrystallized to give
material (95 mg) melting at 57.5-58.5°. The mixed melting point with material prepared from method A was 58-59°. \([\alpha]_D -31.4 (c, 0.94, \text{CHCl}_3)\).

3-\(O\)-Acetyl-1,2;5,6-di-\(O\)-isopropylidene-\(\alpha\)-\(D\)-gulofuranose (27)

Catalytic reduction of 3-\(O\)-acetyl-1,2;5,6-di-\(O\)-isopropylidene-\(\alpha\)-\(D\)-erythrohexofuran-3-ene (13) (3 g) in ether (60 ml) at room temperature and atmospheric pressure with palladium black for two hours gave upon filtration and evaporation of the solvent crystalline 3-\(O\)-acetyl-1,2;5,6-di-\(O\)-isopropylidene-\(\alpha\)-\(D\)-gulofuranose (2.7 g), m.p. 76-77°, recrystallized from petroleum ether (65-110°). \([\alpha]_D 66.0° (c 0.36, \text{CHCl}_3)\). Calculated for \(C_{14}H_{22}O_7\): C, 55.62%, H, 7.33%. Found: C, 55.43%, H, 7.16%.

1,2;5,6-Di-\(O\)-isopropylidene-\(\alpha\)-\(D\)-gulofuranose (7)

Deacetylation of the 3-\(O\)-acetate (27) (1.55 g) with 0.01N sodium methoxide (50 ml) for two hours followed by neutralization of the base with solid carbon dioxide gave the known gulose derivative (1.25 g), m.p. 103°, \([\alpha]_D 10.0° (c, 0.4, \text{CHCl}_3)\). Lit. (94). m.p. 105-106°, \([\alpha]_D 7.5° (c, 1, \text{CHCl}_3)\).

1,2;5,6-Di-\(O\)-isopropylidene-\(\alpha\)-\(D\)-xylolhexofuranos-3-ulose (11)

1,2;5,6-Di-\(O\)-isopropylidene-\(\alpha\)-\(D\)-gulofuranose (7) (1.1 g) was oxidized by the \(\text{RuO}_2/\text{IO}_4^-\) method described above. Only four extractions with chloroform were necessary to give the product (0.79 g) which crystallized
readily. Recrystallization from petroleum ether (65-110\°) gave the ketone, m.p. 76-77\°, \([\alpha]_D\) -58.5\° (c, 0.4, water). Calculated for \(\text{C}_{12}\text{H}_{18}\text{O}_6\): C, 55.8\%; H, 6.96\%. Found: C, 55.63\%; H, 6.89\%.

1,2;5,6-Di-O-isopropylidene-\(\beta\)-D-altrofuranose (6)

Sirupy \(\beta\)-altrose (33) (1.3 g) was dissolved in a mixture of dry acetone (100 ml) that contained zinc chloride (12 g) and 85\% phosphoric acid (0.5 ml). On working up the product as described above for 1,2;5,6-di-O-isopropylidene-\(\beta\)-D-idofuranose, the resultant sirup crystallized readily and could be recrystallized from petroleum ether (65-110\°) to yield the diacetone altrose (1.22 g), m.p. 87-88\°, \([\alpha]_D\) 28.5\° (c, 0.4, acetone). Lit. (94), m.p. 87-88\°, \([\alpha]_D\) 28.7\° (c, 1.04, acetone).

1,2;5,6-Di-O-isopropylidene-\(\beta\)-D-arabinovioschexofuranos-3-ulse (12)

1,2;5,6-Di-O-isopropylidene-\(\beta\)-D-altrofuranose (6) (1.65 g) was oxidized in the same manner as was the glucofuranose derivative. The oxidation yielded a non-crystalline material (1.28 g) after four extractions, which was free of impurities as judged by NMR and TLC (ethyl ether; toluene, 2:1). Vacuum distillation of the sirup (b.p. 0.01 87\°) gave a colourless liquid which crystallized spontaneously. Recrystallization from petroleum ether (65-110\°) gave material (1.1 g) melting at 31-32\°. \([\alpha]_D\) 21.7\° (c, 0.45, water). Calculated for \(\text{C}_{12}\text{H}_{18}\text{O}_6\): C, 55.80\%; H, 6.96\%. Found: C, 55.59\%; H, 7.09\%.
Borohydride reduction of 1,2;5,6-di-0-isopropylidene-β-D-arabinohexofuranos-3-ulose (12) (440 mg) was carried out in the same way as described for the conversion of the lyxo ketone (10) to the talofuranose (4). Recrystallization of the product from petroleum ether (65-110°) gave material (400 mg) melting at 52-53°. [α]$_D$ 12.5° (c, 0.4, water). Calculated for C$_{12}$H$_{20}$O$_6$: C, 55.37%; H, 7.75%. Found: C, 55.27%; H, 7.86%.

3-O-Acetyl-1,2;5,6-di-0-isopropylidene-β-D-threohex-3-enose (14)

**Method A**

1,2;5,6-Di-0-isopropylidene-β-D-arabinohexofuranos-3-ulose (12) (2.5 g) was dissolved in 30% acetic anhydride in pyridine (30 ml) and was kept at 35° until the reaction was judged complete by TLC (2 days). The solution was poured into ice water (300 ml) and extracted into chloroform (3x75 ml). The solution was evaporated and then distilled, b.p. 0.05 118°. The distillate crystallized and was recrystallized from ethanol-water to give crystals (1.5 g) melting at 57-58°, [α]$_D$ 43.4° (c, 0.87, CHCl$_3$). Anal. Calcd. for C$_{14}$H$_{20}$O$_7$: C, 56.0%; H, 6.67%. Found: C, 55.95%; H, 6.57%.

**Method B**

1,2;5,6-Di-0-isopropylidene-β-D-lyxohexofuranos-3-ulose (10) (2 g) was dissolved in 30% acetic anhydride in triethylamine (45 ml). The solution was kept at room temperature until the reaction was complete by TLC (1½-2 days).
The solution was evaporated down several times with toluene and then ethanol, care being taken to prevent the sirup from becoming too thick since de-0-acetylation appeared to occur quite readily. The product was taken up in ethanol, water was added, and the solution seeded. The short, chunky needles (1.5 g) of the recrystallized product were identical to the material produced in A above.

3-0-Acetyl-1,2;5,6-di-0-isopropylidene-α-D-erythrohex-3-enose (13)

**Method A**

3-0-Acetyl-1,2;5,6-di-0-isopropylidene-α-D-erythrohex-3-enose (13) (1 g) was dissolved in anhydrous ether (75 ml). This solution was added to a reduction vessel containing palladium black (300 mg) in anhydrous ether (30 ml) which had been prereduced for 1 hr at atmospheric pressure. The reaction vessel was flushed with hydrogen at atmospheric pressure, then stirred for 4 minutes. The solution was filtered and the catalyst washed with several small portions of ether. The ether solution was evaporated and the resulting product crystallized. Recrystallization from hot ethanol gave the product (650 mg) as cubes. M.p. 106-107°, [α] ^D 22 67.8° (c, 0.814, CHCl₃). Anal. Calcd. for C₁₄H₂₀O₇: C, 56.00%; H, 6.67%. Found: C, 55.80% H, 6.61%.

**Method B**

13 (0.5 g) was dissolved in anhydrous ether (50 ml) and added to a reduction flask containing palladium
black (75 mg). The system was flushed with deuterium gas several times and then reduced at atmospheric pressure for 22 minutes. The product was worked up as in Method A to yield a product (300 mg) identical to 15. Spectroscopy indicated that the 3-deuterio 15 had ~80% isotopic purity.

**1,2;5,6-Di-O-isopropylidene-α-D-erythrohex-trans-4-enose**

3-O-Acetyl-1,2;5,6-di-O-isopropylidene-α-D-erythrohex-trans-4-enose (15) (1 g) was dissolved in anhydrous methanol (100 ml) and 0.1N NaOMe in methanol (5 ml) was added. The reaction was followed by TLC until it was complete (approximately 4 hours). The solution was neutralized with solid CO₂ and evaporated. On evaporation the product crystallized and was recrystallized from petroleum ether (65-110°). Extremely fine needles of the recrystallized product (750 mg) were obtained. M.p. 89-90°, [α]D₂² -19.0° (c, 0.918 CHCl₃). Anal. Calcd. for C₁₂H₁₈O₆: C, 55.18%; H, 6.98%. Found: C, 55.93%; H, 6.91%.

**3-O-Acetyl-1,2;5,6-di-O-isopropylidene-α-L-erythrohex-cis-4-enose**

3-O-Acetyl-1,2;5,6-di-O-isopropylidene-β-D-threo-hex-3-enose (14) (500 mg) was dissolved in anhydrous ether (50 ml) and reacted for 4 minutes with prereduced palladium catalyst as described for the formation of 3-O-acetyl-1,2;5,6-di-O-isopropylidene-α-D-erythrohex-3-enose (13, Method A). The mixture was filtered and the catalyst washed with several small portions of ether. The filtrate
and washings were combined and evaporated to a sirup which contained about 65% of the rearranged product as judged by NMR and TLC. All attempts to purify this compound by crystallization, distillation and chromatography have been unsuccessful.

3-О-Acetyl-1,2;5,6-di-О-isopropylidene-β-D-mannofuranose (28)

3-О-Acetyl-1,2;5,6-di-О-isopropylidene-β-D-threohex-3-enose (14) (300 mg) was dissolved in ethanol (50 ml) and reduced over palladium black (100 mg) for 8 hours at atmospheric pressure. TLC showed one major component with a trace of a minor component. The solution was filtered and evaporated to a sirup. The sirup was kept in the freezing compartment of a refrigerator (−20°) until crystallization started. The product was taken up in warm petroleum ether (65-110°), the solution cooled and seeded. The product crystallized out as flattened cubes (200 mg). M.p. 45-46°, [α]D22 -22.6° (c, 0.866, CHCl3). Anal. Calcd. for C14H22O7: C, 55.63%; H, 7.28%. Found: C, 55.43%; H, 7.13%.

1,2;5,6-Di-О-isopropylidene-β-D-mannofuranose (8)

3-О-Acetyl-1,2;5,6-di-О-isopropylidene-β-D-mannofuranose (180 mg) was dissolved in methanol (15 ml) and 0.01N NaOMe in methanol was added until the solution stayed slightly basic to pH paper. When deacetylation was complete as indicated by TLC, solid CO2 was added to neutralize the solution. Evaporation and recrystallization from petroleum ether (65-110°) gave material (130 mg)
identical in every way to the 1,2;5,6-di-O-isopropylidene-β-D-mannofuranose prepared previously. M.p. and mixed m.p. 52-53°, [α]D 12.3° (c, 0.83, water).

3-O-Acetyl-1,2;5,6-di-O-isopropylidene-α-D-glucofuranose (21)

1,2;5,6-Di-O-isopropylidene-α-D-glucose (1) (1 g) was dissolved in a mixture of pyridine (5 ml) and acetic anhydride (2 ml). The solution was kept overnight at room temperature. Repeated co-evaporation of the solution with toluene gave a slightly orange sirup free of acetylating reagents. The sirup was dissolved in chloroform (75 ml), treated with charcoal, filtered and evaporated. The residue crystallized readily and was recrystallized from petroleum ether (65-110°) to yield 950 mg of product melting at 59-60°, [α]D22 -38.4 (c, 1.07, CHCl3). Lit. (98), m.p. 62°, [α]D24 -38.5 (c, 1.3, CHCl3).

3-O-Acetyl-1,2;5,6-di-O-isopropylidene-β-D-idofuranose (22)

Prepared from 2 in the same way as 21. M.p. 75.5-76.5°, [α]D22 +16.6°, (c, 0.67, CHCl3). Lit. (100), for the -L-isomer, m.p. 77-78°, [α]D15 -12° (c, 0.75, CHCl3).

3-O-Acetyl-1,2;5,6-di-O-isopropylidene-α-D-allofuranose (23)

Prepared from 3 in the same way as 21. M.p. 74-75°, [α]D22 100.6° (c, 0.73, CHCl3). Lit. (99), m.p. 75.5-76.5°, [α]D20 107.6 (c, 1.0, CHCl3).
3-0-Acetyl-1,2;5,6-di-O-isopropylidene-β-D-talofuranose (24)

Prepared from (4) in the same way as (21) except that (24) did not crystallize. \([\alpha]^{22}_D -7.4^\circ (c, 0.38, \text{CHCl}_3)\).
Anal. Calcd. for \(\text{C}_{14}\text{H}_{22}\text{O}_7\): C, 55.63%; H, 7.28%. Found: C, 55.84%; H, 7.32%.

3-0-Acetyl-1,2;5,6-di-O-isopropylidene-α-D-galactofuranose (25)

Prepared from (5) in the same way as (21) except that (25) did not crystallize. \([\alpha]^{22}_D -7.5^\circ (c, 1.47, \text{CHCl}_3)\).
Anal. Calcd. for \(\text{C}_{14}\text{H}_{22}\text{O}_7\): C, 55.63%; H, 7.28%. Found: C, 55.50%; H, 7.15%.

3-0-Acetyl-1,2;5,6-di-O-isopropylidene-β-D-altrofuranose (26)

Prepared from (6) in the same way as (21). M.p. 92-93°, \([\alpha]^{22}_D 14.4^\circ (c, 0.68, \text{CHCl}_3)\). Anal. Calcd. for \(\text{C}_{14}\text{H}_{22}\text{O}_7\): C, 55.63%; H, 7.28%. Found: C, 55.48%; H, 7.37%.

3-Deoxy-1,2;5,6-di-O-isopropylidene-α-D-xylohexofuranose (19)

3-0-Acetyl-1,2;5,6-di-O-isopropylidene-α-D-erythro-hex-3-enose (13) (1.1 g) was dissolved in anhydrous ether (75 ml) and reduced over platinum (100 mg) for 24 hours. The mixture was filtered, evaporated to a thin sirup, taken up in chloroform (100 ml) and washed with dilute sodium bicarbonate solution. The chloroform fraction was dried over magnesium sulphate, filtered and evaporated. The resulting sirup was dissolved in methanol (25 ml) and
0.01N sodium methoxide in methanol was added until the solution stayed basic to pH paper. When de-O-acetylation of the 3-O-acetyl-1,2;5,6-di-O-isopropylidene-α-D-gulo-furanose (27) was complete as indicated by TLC, the base was neutralized with solid CO₂ and evaporated. Water (20 ml) was added and the product was extracted into petroleum ether (65-110°) (10x100 ml). The combined extracts were dried over magnesium sulfate, filtered and evaporated. The product was recrystallized from petroleum ether to give the crystalline product (0.6 g) as long needles. Melting point and mixed melting point with authentic material (50) 79-80°, [α] fool -27.4°, (c, 0.972, CHCl₃). Lit. (50), m.p. 81°, [α] fool -38.1, (c, 4.11, ethanol).

3-Deoxy-1,2;5,6-di-O-isopropylidene-β-D-arabinohexofuranose (20)

Method A

3-0-Acetyl-1,2;5,6-di-O-isopropylidene-β-D-threo-hex-3-enose (14) (250 mg) was dissolved in anhydrous ether (50 ml) and reduced with hydrogen over platinum for 24 hours at atmospheric pressure. The solution was filtered, the catalyst washed with ether, the filtrate and washings combined and evaporated to a sirup. The product was dissolved in anhydrous methanol (40 ml) and deacetylated as described in the preparation of (19) to remove the acetyl from the side product 3-O-acetyl-1,2;5,6-di-O-isopropylidene-β-D-mannofuranose (28). The deacetylated sirup was dissolved in water (15 ml) and extracted with petroleum ether (65-110°) (5x100 ml). The extracts were combined, dried over magnesium sulfate, filtered and evaporated. The product was distilled under high vacuum
b.p. 0.01 68°, to give a sirup (80 mg) which crystallized on standing in the refrigerator. M.p. 21-22°, [α]_D^{22} 24.1°, (c, 1.17, CHCl₃).

Method B

3-Deoxy-D-mannose (51) (2 g) was dissolved in acetone (60 ml) containing zinc chloride (4 g) and phosphoric acid (0.2 ml) and the solution stirred for 24 hours. The solution was then neutralized with 50% sodium hydroxide and the mixture filtered. The filtrate was evaporated to about 5 ml, dissolved in chlororform, and washed with dilute sodium bicarbonate solution. The chloroform solution was dried over magnesium sulfate, evaporated and distilled under high vacuum, b.p. 0.01 68°. The redistilled product (2.1 g) crystallized on standing in the refrigerator. Careful recrystallization from 30-60° petroleum ether gave material melting at 22-23°, [α]_D^{22} 27.5° (c, 0.40, CHCl₃). Lit. (52), sirup, [α]_D^{22} 21.1°. (c, 1.5, CHCl₃). Anal. Calcd. for C₁₂H₂₀O₅: C, 59.02%; H, 8.16%. Found: C, 58.91%; H, 8.07%.

3,4-Dideutero-3-deoxy-1,2;5,6-di-0-isopropylidene-α-D-galactofuranose

3-Deoxy-1,2;5,6-di-0-isopropylidene-α-D-erythro-hex-3-enose (2 g), prepared by the method of Weygand and Wolz (50) was dissolved in 95% ethanol (75 ml) and reduced over palladium black with deuterium at atmospheric pressure. After uptake of deuterium had ceased, TLC (ethyl ether:toluene--2:1) indicated the reaction complete.
The reaction mixture was filtered and evaporated to a sirup which crystallized spontaneously. Recrystallization from petroleum ether (65-110°) yielded long needles (1.8 g), m.p. 79-80°, \([\alpha]_D^{22} -27° (c, 0.82, CHCl_3)\). Lit. (84, 50), m.p. 81°, \([\alpha]_D -38.1° (c, 4.11, ethanol)\).

3-Deoxy-3-deuterio-1,2;5,6-di-0-isopropylidene-\(\alpha\)-D-allofuranose

3-Deoxy-3-deuterio-1,2;5,6-di-0-isopropylidene-\(\alpha\)-D-allofuranose (3.2 g) was dissolved in carbon tetrachloride (200 ml) and triphenylphosphine (9 g) was added. After 40 hr of reflux, the solution was cooled and petroleum ether (65-110°) (500 ml) was added. After one day at -20°C, the solution was filtered, then evaporated to a sirup. Vacuum distillation gave a mobile sirup which was redistilled (b.p. 0.005 78°) to provide 2.7 g of 3-chloro-3-deoxy-3-deuterio-1,2;5,6-di-0-isopropylidene-\(\alpha\)-D-allofuranose. The chlorodeuterio sugar (500 mgm) was refluxed with lithium aluminum hydride (500 mgm) in tetrahydrofuran (35 ml) for 40 hr. The excess hydride was destroyed with water and the mixture filtered through celite. The filtrate was concentrated and vacuum distilled to give 430 mgm of product which crystallized at low temperature; m.p. 10-11°, \([\alpha]_D^{22} -3.6° (c, 0.8, CHCl_3)\). Lit. (101), b.p. 0.3 74-78°, \([\alpha]_D -5.7 (c 4.2, ethanol)\) for the non-deuterated compound.
Methyl 4,6-O-benzylidene-3-deoxy-α-D-erythrohexopyranosid-2-ulose

Methyl 4,6-O-benzylidene-3-deoxy-α-D-arabinohexopyranoside (m.p. 109-110°, [α]D22 96 (c 0.42, CHCl3). Lit. (52), [α]D22 107.3 (c 0.94, CHCl3), m.p. 111-112°) (2 g) was dissolved in carbon tetrachloride (50 ml). NaHCO3 (80 mgm) in H2O (20 ml) was added, followed by RuO2 (50 mgm). NaIO4 (5% in H2O) was added dropwise to the continuously stirred solution. When the reaction mixture went yellow (approximately 1/2 ml NaIO4 solution), addition of periodate was stopped. Further periodate was added (~1/2 ml) after the mixture went black. This process was repeated until the oxidation was complete by TLC. The product was extracted into chloroform which was then dried with magnesium sulfate, and filtered. The solvent was removed on a rotary evaporator and the crystalline residue recrystallized from chloroform/petroleum ether (65-110°). The product (1.8 g) had a m.p. of 110-112° and [α]D22 99°. Lit. (54), m.p. 114-115°, [α]D22 109 (c 2, CHCl3).

Methyl 4,6-O-benzylidene-3-deoxy-α-D-ribohexopyranoside

Methyl 4,6-O-benzylidene-3-deoxy-α-D-erythrohexopyranosid-2-ulose was reduced with sodium borohydride to provide the desired product (55). M.p. 185-186°, [α]D22 121° (c 0.39, CHCl3). Lit. (54), m.p. 191-192°, [α]D22 115.8 (c 1.21, CHCl3).
Derivation of equation (V)

Solution for case B

\[
\frac{J_1 + c}{J_2 + c} = \frac{k_1 \cos^2 \xi_1}{k_2 \cos^2 (\omega - \xi_1)}
\]

Substitution of \(\cos \omega \cos \xi_1 + \sin \omega \sin \xi_1\) for \(\cos(\omega - \xi_1)\) then squaring gives

\[
\frac{J_1 + c}{J_2 + c} = \frac{k_1}{k_2} \frac{\cos^2 \xi_1}{\cos^2 \omega \cos^2 \xi_1 + \sin^2 \omega \sin^2 \xi_1 + 2 \sin \omega \cos \omega \sin \xi_1 \cos \xi_1}
\]

Dividing top and bottom of the right hand side of the equation by \(\cos^2 \xi_1\) gives

\[
\frac{J_1 + c}{J_2 + c} = \frac{k_1}{k_2} \frac{1}{\cos^2 \omega + \sin^2 \omega \tan^2 \xi_1 + 2 \sin \omega \cos \omega \tan \xi_1}
\]

Rearrangement of this equation provides

\[
\sin^2 \omega \tan^2 \xi_1 + 2 \sin \omega \cos \omega \tan \xi_1 + \cos^2 \omega - \frac{k_1}{k_2} \left( \frac{J_2 + c}{J_1 + c} \right) = 0
\]

Solution of this quadratic for \(\tan \xi_1\) gives the expression (V)

\[
\tan \xi_1 = \frac{-\cos \omega \pm \left[ (k_1/k_2)(J_2+c)/(J_1+c) \right]^{\frac{1}{2}}}{\sin \omega}
\]
The following is the listing for the computer program DAERM which utilizes the equation V.
DAERM

1. CONTROL CARD, FORMAT(3F10.3)
   RATIO, ANGLE, COS
   K1/K2 = 0.9 FROM VALENCE BOND CALCULATIONS
   IS PROBABLY LESS THAN THIS IF ELECTRONNEGATIVE SUBSTITUENTS
   ARE PRESENT.

2. ARI ETIMATEe OMEGA VALUE
   = 120 FOR TETRAHEDRAL GEOMETRY.

3. TOTHE KARPLUS CONSTANT.
   = 0.23 FROM VALENCE BOND CALCULATIONS.

4. TITLE FORMAT(20A4)
   TITLE A TITLE OF UP TO 80 CHARACTERS.

5. FORMAT CONSTANTS FORMAT(2F10.4)
   A1, A2
   A1 THE FIRST COUPLING CONSTANT INTO THE METHYLENE GROUP.
   A2 THE SECOND COUPLING INTO THE METHYLENE GROUP.
   AN UNLIMITED NUMBER OF CARDS MAY BE USED HERE.
   A NEGATIVE VALUE FOR A1 SENDS CONTROL BACK TO CARD 2 SO THAT
   FURTHER READINGS MAY BE INSERTED IF REQUIRED.

6. JNUM IS TERMINATED BY A NEGATIVE VALUE FOR A2.

DIMENSION INT(*), ANGL(4), TRET(4)
DIMENSION TITLE(20)
REAL (5, 4) RATIO, ANGL, COS

99 WRITE (6, 101) RATIO, ANGL, COS

101 FORMAT(14H16KARPLUS RATIO IS, F8.3, 4H SUM OR DIFFERENCE OF DIHE
      DRAL ANGLES IS, F8.1, 28H SECOND KARPLUS CONSTANT IS, F8.3)

200 REAR (5), 8 = 0 = 2 TITLE
   1 FOR AT (72A4)
   2 FOR AT (101, 20A4)
   15 FOR (1, 5) TITLE
   10 IF (1, L, 0) GO TO 20
   10 IF (2, L, 0) GO TO 2
   50 S1 = 0.2 + CUM /
   10 IF (S1 = 1.0, 0) GO TO 10
   50 S1 = A1 * (A2 + CUM) / (A1 + CUM)
   10 IF (S1 = 1.0, 0) GO TO 10
   60 S1 = 1.0
   10 WRITE (5, 99)

90 FOR ALL S1 UNDER SQRT IS NEGATIVE!)
   70 = 1.0
   11 SQ = SQRT (S1, 0).
SUM = SUM + SUMB
ANGI = ANG + 3.1416/180.
KNOT(1) = -COS(ANGI) + SUM / SIN(ANGI)
KNOT(2) = (COS(ANGI) + SUM) / SIN(ANGI)
KNOT(3) = (COS(ANGI) - SUM) / SIN(ANGI)
KNOT(4) = (COS(ANGI) + SUM) / SIN(ANGI)
100
20 I = I + 1
IF(I .GT. 4) GO TO 100
200 ANGL(I) = ATN(KNOT(I))
101 IF(AMGL(I) .LT. 0.01) GO TO 20
300 CALCULATION OF KARPLUS CONSTANTS
KL = (AL + C1 / (COS(AMGL(I)) * C1 * COS(AMGL(I))))
K2 = 1 / K1
700 THET(I) = AMGL(I) * 180. / 3.1416
110 IF(I .EQ. 2) GO TO 60
900 WRITE(6,2) ANGL
1000 PRINT *, 'SUM OF DIHEDRAL ANGLES IS EQUAL TO', F8.1
WRITE(6,4) ANGL
WRITE(6,5) AL, A2, THET(I), PHI, D1, B2
600 GO TO 2
800 PHI = ANG + KNOT(I)
810 WRITE(6,6) ANGL
900 PRINT *, 'DIFFERENCE OF DIHEDRAL ANGLES IS', F8.1
WRITE(6,7) ANGL
800 PRINT *, ' '5X,CIS COUPLING', '5X, 'TRANS COUPLING', '5X, 'CIS ANGLE', '5X, 'TRANS ANGLE', '5X, '10X, 'K2'
WRITE(6,8) AL, A2, THET(I), PHI, B1, B2
1000 GO TO 2
14 CONTINUE
2 STOP
Derivation of equation (VII)

\[
\frac{J_1 + c}{J_2 + c} = \frac{a \cos^2\xi_1 + b \cos\xi_1}{a \cos^2(w - \xi_1) + b \cos(w - \xi_1)}
\]

dividing top and bottom by 'a' provides

\[
\frac{J_1 + c}{J_2 + c} = \frac{\cos^2\xi_1 + b/a \cos\xi_1}{\cos^2(w - \xi_1) + b/a \cos(w - \xi_1)}
\]

\[
= \frac{\cos^2\xi_1 + b/a (\cos^2\xi_1)/\cos\xi_1}{\cos^2(w - \xi_1) + b/a \cos(w - \xi_1)}
\]

Expansion of \(\cos(w - \xi_1)\) followed by division by \(\cos^2\xi_1\) gives the expression

\[
\frac{J_1 + c}{J_2 + c} = \frac{1 + b/a (1/\cos\xi_1)}{\cos^2\omega + \sin^2\omega \tan^2\xi_1 + 2\sin\omega \cos\omega \tan\xi_1 + b/a \cos\omega (1/\cos\xi_1) + b/a \sin\omega \tan\xi_1 (1/\cos\xi_1)}
\]

This can be rewritten as

\[
\sin^2\omega \tan^2\xi_1 + \tan\xi_1 (2\sin\omega \cos\omega + b/a \sin\omega /\cos\xi_1) + \cos^2\omega + b/a \cos\omega /\cos\xi_1 - J_2 + c/J_1 + c (1 + b/a (1/\cos\xi_1)) = 0
\]

which on solution of the quadratic in \(\tan\xi_1\) provides the solution (VII) which can be solved by an iterative process as utilized in DAERM II.
DAERM II

Computer Program Utilizing Equation VII

DAERM II

CALCULATION OF KARPLUS CONSTANTS AND ANGLES FOR METHYLENE FUNCTIONS.

UTILIZES THE EQUATION J=A*COS*COS+B*COS-C

OBTAINS SOLUTIONS BY AN ITERATIVE TECHNIQUE

1. CONTROL CARD, FORMAT(3F10.3)
   RATIO, EDV, C
   RATIO KARPLUS RATIO B/A
   =-0.053 FOR K1/K2=0.9
   =-0.111 FOR K1/K2=0.8
   =-0.177 FOR K1/K2=0.7

   EDV ESTIMATED OMEGA VALUE
   =120 FOR TETRAHEDRAL GEOMETRY.

   THIRD KARPLUS CONSTANT.
   =0.26 FROM VALENCE BOND CALCULATIONS.

2. TITLE FORMAT(20A4)
   TITLE A TITLE OF UP TO 80 CHARACTERS.

3. COUPLING CONSTANTS FORMAT(2F10.4)
   A1, A2
   A1 THE FIRST COUPLING CONSTANT INTO THE METHYLENE GROUP.
   A2 THE SECOND COUPLING INTO THE METHYLENE GROUP.

   A NEGATIVE VALUE FOR A1 SENDS CONTROL BACK TO CARD 2 SO THAT
   FURTHER READINGS MAY BE INSERTED IF REQUIRED.

4. JOB IS TERMINATED BY A NEGATIVE VALUE FOR A2.

DIMENSION TITLE(20)
READ(5,99)RATIO, EDV, C
99 FORMAT(3F10.3)
WRITE(5,1)RATIO, EDV, C
1 FORMATT(10A1) RATIO IS, F8.3, 41H SUM OR DIFFERENCE OF DI
   KRAL ANGLES IS, F8.3, 28H SECOND KARPLUS CONSTANT IS, F8.3

200 READ(5,1,END=72) TITLE
1 FORMAT(20A4)
4 FORMAT(10A1) TITLE
100 READ(5,15) A1, A2
15 FORMAT(2F10.4)
IF(A1.LT.-5)GO TO 200
IF(A2.LT.-5)GO TO 22
I=0
ANG1=EDV*3.14159/180.
5 IF(1.LT.5)GO TO 100
A=0.0
RAT=0.0
J=0
SUM = (RAT*RAT)/(COS(ANG)*COS(ANG)) + 4*((A2+C)/(A1+C))*(1+RAT/COS(ANG))

IF (SUM.GE.0.0) GO TO 6
WRITE(6,1)

80 FORMAT ('SUM UNDER SQRT IS NEGATIVE')
GO TO 100

6 J = J + 1
SUM = SQRT (SUM)

50 IF (I-1) .LE. 11, 21, 70
30 IF (I-5) .LE. 11, 41, 100

11 ROOT = (-2*COS(ANGI)+RAT/COS(ANG))/SUM/(2*SIN(ANGI))
GO TO 20

21 ROOT = (-2*COS(ANGI)+RAT/COS(ANG)+SUM)/(2*SIN(ANGI))
GO TO 20

31 ROOT = (2*COS(ANGI)+RAT/COS(ANG)-SUM)/(2*SIN(ANGI))
GO TO 20

41 ROOT = (2*COS(ANGI)+RAT/COS(ANG)+SUM)/(2*SIN(ANGI))

20 ANGL = ATAN (ROOT)

IF (J.EQ.1) GO TO 9
IF (ABS (ANG-ANGL) .LE. 0.0001) GO TO 7
IF (J.GE.1) GO TO 7

9 RAT = RATE
ANGL = ANGL
GO TO 10

7 I = I + 1
IF (ANGL*L) .LE. 0.0) GO TO 5
A = (A1+C)/COS (ANGL)*COS (ANGL) + COS (ANGL)*RAT
B = A*RAT
TOE = ANGL .LE. 0.731, 14156
IF (.1-2) .LE. 0.14156) GO TO 111
GO TO 12

111 WRITE (6,10) J
WRITE (6,20) EM, J

90 FORMAT (4X, 'THE SUM OF DIOGENAL ANGLES IS EQUAL TO ', FB, 1, ' THE NUMBER OF CYCLES IS ', IC)
WRITE (6,30)

WRITE (6,50) A1, A2, THE1, PH1, A3

GO TO 5

12 RATE = RATE + 1
WRITE (6,90) J

92 FORMAT ('THE DIFFERENCE OF DIOGENAL ANGLES IS EQUAL TO ', FB, 1, ' THE NUMBER OF CYCLES IS ', IC)
WRITE (6,30)

14 CONTINUE

22 STOP
END
NMR spectrum of 3-deoxy-1,2;5,6-di-O-isopropylidene-α-D-xylohexofuranose; A, computed from data in tables XI and XXII; B, 100 MHz observed.
These tables give NMR parameters which have not been included in the main text.
Table XIX
Proton Chemical Shifts* for
1,2;5,6-Di-ɑ-Isopropylidene-D-hexofuranoses

<table>
<thead>
<tr>
<th>1,2;5,6-Di-ɑ-isopropylidene</th>
<th>H₁</th>
<th>H₂</th>
<th>H₃</th>
<th>H₄</th>
<th>H₅</th>
<th>Hₑ₁</th>
<th>Hₑ₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>-ɑ-D-glucose</td>
<td>(1)</td>
<td>4.17</td>
<td>5.51</td>
<td>5.84</td>
<td>5.96</td>
<td>5.69</td>
<td>5.97</td>
</tr>
<tr>
<td>-β-D-idose</td>
<td>(2)</td>
<td>4.03</td>
<td>5.50</td>
<td>5.81</td>
<td>5.88</td>
<td>5.55</td>
<td>5.85</td>
</tr>
<tr>
<td>-ɑ-D-allose</td>
<td>(3)</td>
<td>4.21</td>
<td>5.40</td>
<td>5.98</td>
<td>6.17</td>
<td>5.71</td>
<td>5.95</td>
</tr>
<tr>
<td>-β-D-talose</td>
<td>(4)</td>
<td>4.20</td>
<td>5.43</td>
<td>6.13</td>
<td>6.24</td>
<td>5.81</td>
<td>5.95</td>
</tr>
<tr>
<td>-ɑ-D-galactose</td>
<td>(5)</td>
<td>4.13</td>
<td>5.45</td>
<td>5.90</td>
<td>6.13</td>
<td>5.64</td>
<td>5.93</td>
</tr>
<tr>
<td>-β-D-altrose</td>
<td>(6)</td>
<td>4.11</td>
<td>5.46</td>
<td>5.60</td>
<td>6.18</td>
<td>5.74</td>
<td>5.90</td>
</tr>
<tr>
<td>-ɑ-D-gulose</td>
<td>(7)</td>
<td>4.23</td>
<td>5.35</td>
<td>5.73</td>
<td>6.09</td>
<td>5.49</td>
<td>6.32</td>
</tr>
<tr>
<td>-β-D-mannose</td>
<td>(8)</td>
<td>4.30</td>
<td>5.33</td>
<td>5.71</td>
<td>6.14</td>
<td>5.43</td>
<td>5.88</td>
</tr>
</tbody>
</table>

*CDCl₃ solutions at room temperature and internal TMS as standard (10.0τ).
†measured in acetone-d₆ solution.
Table XX

Proton Coupling Constants* for 1,2,5,6-Di-O-isopropylidene-D-hexofuranoses

<table>
<thead>
<tr>
<th>1,2,5,6-Di-O-isopropylidene</th>
<th>J_{1,2}</th>
<th>J_{2,3}</th>
<th>J_{3,4}</th>
<th>J_{4,5}</th>
<th>J_{5,e_1}</th>
<th>J_{5,e_2}</th>
<th>J_{e_1,e_2}</th>
<th>J_{H_2O}**</th>
</tr>
</thead>
<tbody>
<tr>
<td>-α-D-glucose</td>
<td>(1)†</td>
<td>3.61</td>
<td>0.48</td>
<td>3.07</td>
<td>7.27</td>
<td>6.46</td>
<td>5.95</td>
<td>8.60</td>
</tr>
<tr>
<td>-β-D-idose</td>
<td>(2)</td>
<td>3.70</td>
<td>&lt;0.5</td>
<td>2.92</td>
<td>5.31</td>
<td>6.89</td>
<td>6.93</td>
<td>8.37</td>
</tr>
<tr>
<td>-α-D-allose</td>
<td>(3)</td>
<td>3.73</td>
<td>5.01</td>
<td>8.66</td>
<td>4.55</td>
<td>6.61</td>
<td>6.68</td>
<td>8.57</td>
</tr>
<tr>
<td>-β-D-talose</td>
<td>(4)</td>
<td>3.80</td>
<td>5.05</td>
<td>8.77</td>
<td>4.97</td>
<td>6.50</td>
<td>7.61</td>
<td>8.26</td>
</tr>
<tr>
<td>-α-D-galactose</td>
<td>(5)</td>
<td>3.85</td>
<td>1.13</td>
<td>4.15</td>
<td>7.48</td>
<td>6.70</td>
<td>7.15</td>
<td>8.67</td>
</tr>
<tr>
<td>-β-D-altrose</td>
<td>(6)</td>
<td>3.90</td>
<td>0.60</td>
<td>1.94</td>
<td>9.51</td>
<td>6.25</td>
<td>5.49</td>
<td>8.94</td>
</tr>
<tr>
<td>-α-D-gulose</td>
<td>(7)</td>
<td>4.06</td>
<td>6.05</td>
<td>6.17</td>
<td>8.80</td>
<td>6.64</td>
<td>7.30</td>
<td>8.66</td>
</tr>
<tr>
<td>-β-D-mannose</td>
<td>(8)</td>
<td>4.17</td>
<td>5.83</td>
<td>5.52</td>
<td>8.36</td>
<td>6.41</td>
<td>5.69</td>
<td>8.76</td>
</tr>
</tbody>
</table>

*CDCl₃ solutions at room temperature in Hz.
†acetone-d₆ solution.
**J_{H_2O} not computer analyzed.
| Table XXI |
| Proton Chemical Shifts* for 3-0-Acetyl-1,2;5,6-di-0-isopropylidene- \( D \)-Hexofuranoses |

<table>
<thead>
<tr>
<th>1,2;5,6-Di-0-isopropylidene</th>
<th>H_1</th>
<th>H_2</th>
<th>H_3</th>
<th>H_4</th>
<th>H_5</th>
<th>H_6</th>
<th>H_7</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \alpha-\text{D-ribohexofuranos-3-ulse} ) (9a)</td>
<td>3.88</td>
<td>5.62</td>
<td>----</td>
<td>6.0</td>
<td>5.68</td>
<td>5.94</td>
<td>6.04</td>
</tr>
<tr>
<td>( \alpha-\text{D-ribohexofuranos-3-ulse} ) (9b)</td>
<td>4.18</td>
<td>5.72</td>
<td>----</td>
<td>6.08</td>
<td>5.57</td>
<td>5.86</td>
<td>5.91</td>
</tr>
<tr>
<td>( \beta-\text{D-lyxohexofuranos-3-ulse} ) (10)</td>
<td>3.88</td>
<td>5.61</td>
<td>----</td>
<td>5.56</td>
<td>to</td>
<td>6.03</td>
<td></td>
</tr>
<tr>
<td>( \beta-\text{D-arabinohexofuranos-3-ulse} ) (11)</td>
<td>3.94</td>
<td>5.49</td>
<td>----</td>
<td>5.85</td>
<td>5.66</td>
<td>5.90</td>
<td>6.03</td>
</tr>
<tr>
<td>( \beta-\text{D-arabinohexofuranos-3-ulse} ) (12)</td>
<td>3.99</td>
<td>5.53</td>
<td>----</td>
<td>5.82</td>
<td>5.65</td>
<td>6.0</td>
<td></td>
</tr>
<tr>
<td>3-0-Acetyl-( \alpha-\text{D-glucose} ) (21)</td>
<td>4.16</td>
<td>5.54</td>
<td>4.77</td>
<td>5.75</td>
<td>to</td>
<td>6.05</td>
<td></td>
</tr>
<tr>
<td>3-0-Acetyl-( \beta-\text{D-idose} ) (22)</td>
<td>4.04</td>
<td>5.50</td>
<td>4.82</td>
<td>5.70</td>
<td>to</td>
<td>6.35</td>
<td></td>
</tr>
<tr>
<td>3-0-Acetyl-( \alpha-\text{D-allose} ) (23)</td>
<td>4.22</td>
<td>5.16</td>
<td>5.16</td>
<td>----</td>
<td>5.75</td>
<td>5.96</td>
<td>6.14</td>
</tr>
<tr>
<td>3-0-Acetyl-( \beta-\text{D-talose} ) (24)</td>
<td>4.17</td>
<td>5.21</td>
<td>5.21</td>
<td>----</td>
<td>5.80</td>
<td>to</td>
<td>6.13</td>
</tr>
<tr>
<td>3-0-Acetyl-( \alpha-\text{D-galactose} ) (25)</td>
<td>4.11</td>
<td>5.42</td>
<td>5.10</td>
<td>6.15</td>
<td>5.55</td>
<td>5.97</td>
<td>6.17</td>
</tr>
<tr>
<td>3-0-Acetyl-( \beta-\text{D-altrose} ) (26)</td>
<td>4.13</td>
<td>5.44</td>
<td>4.68</td>
<td>6.02</td>
<td>5.68</td>
<td>5.91</td>
<td>6.05</td>
</tr>
<tr>
<td>3-0-Acetyl-( \alpha-\text{D-gulose} ) (27)</td>
<td>4.20</td>
<td>5.19</td>
<td>4.92</td>
<td>5.93</td>
<td>5.39</td>
<td>5.91</td>
<td>6.45</td>
</tr>
<tr>
<td>3-0-Acetyl-( \beta-\text{D-mannose} ) (28)</td>
<td>4.29</td>
<td>5.24</td>
<td>4.83</td>
<td>5.98</td>
<td>5.50</td>
<td>5.92</td>
<td>6.03</td>
</tr>
</tbody>
</table>

* CDCl_3 solution with TMS as internal standard (10.07).
Table XXII

Proton Chemical Shifts for the 3-Deoxy-
1,2;5,6-Di-O-isopropylidene-D-hexofuranoses

<table>
<thead>
<tr>
<th>1,2;5,6-Di-O-isopropylidene</th>
<th>H</th>
<th>H₁</th>
<th>H₂</th>
<th>H₃₁</th>
<th>H₃₂</th>
<th>H₄</th>
<th>H₅</th>
<th>H₆₁</th>
<th>H₆₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-Deoxy-α-D-ribohexofuranose</td>
<td>(17)</td>
<td>4.21</td>
<td>5.27</td>
<td>7.83</td>
<td>8.26</td>
<td>5.88</td>
<td>6.18</td>
<td>~5.9</td>
<td>~5.9</td>
</tr>
<tr>
<td>3-Deoxy-β-D-lyxohexofuranose</td>
<td>(18)</td>
<td>4.20</td>
<td>5.28</td>
<td>8.01</td>
<td>8.29</td>
<td>5.75</td>
<td>5.87</td>
<td>5.96</td>
<td>6.18</td>
</tr>
<tr>
<td>3-Deoxy-α-D-xylohexofuranose</td>
<td>(19)</td>
<td>4.22</td>
<td>5.27</td>
<td>7.78</td>
<td>8.16</td>
<td>5.90</td>
<td>5.58</td>
<td>5.97</td>
<td>~6.39</td>
</tr>
<tr>
<td>3-Deoxy-β-D-arabinohexofuranose</td>
<td>(20)</td>
<td>4.28</td>
<td>5.29</td>
<td>7.68</td>
<td>7.81</td>
<td>6.02</td>
<td>5.71</td>
<td>5.91</td>
<td>6.13</td>
</tr>
</tbody>
</table>
### Table XXIII

Proton Chemical Shifts for the Unsaturated Sugar Derivatives

<table>
<thead>
<tr>
<th>1,2;5,6-Di-0-isopropylidene</th>
<th>H₁</th>
<th>H₂</th>
<th>H₃</th>
<th>H₄</th>
<th>H₅</th>
<th>Hₑ₁</th>
<th>Hₑ₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-0-Acetyl-α-D-erythrohex-3-enose (13)</td>
<td>3.94</td>
<td>4.66</td>
<td>----</td>
<td>----</td>
<td>5.26</td>
<td>5.95</td>
<td>6.06</td>
</tr>
<tr>
<td>3-0-Acetyl-β-D-threohex-3-enose (14)</td>
<td>4.09</td>
<td>5.12</td>
<td>4.35</td>
<td>----</td>
<td>----</td>
<td>5.47</td>
<td>5.50</td>
</tr>
<tr>
<td>3-0-Acetyl-α-D-erythrohex-trans-4-enose (15)</td>
<td>3.96</td>
<td>4.61</td>
<td>----</td>
<td>----</td>
<td>5.31</td>
<td>5.88</td>
<td>6.01</td>
</tr>
<tr>
<td>3-0-Acetyl-α-L-erythrohex-cis-4-enose (16)*</td>
<td>4.03</td>
<td>5.10</td>
<td>4.58</td>
<td>----</td>
<td>----</td>
<td>5.48</td>
<td>5.48</td>
</tr>
</tbody>
</table>

* Results for this compound were obtained from an impure product.
Table XXIV

Proton Coupling Constants for the Unsaturated Sugar Derivatives

<table>
<thead>
<tr>
<th>Compound</th>
<th>$J_{1,2}$</th>
<th>$J_{2,3}$</th>
<th>$J_{2,5}$</th>
<th>$J_{3,e_1}$</th>
<th>$J_{3,e_2}$</th>
<th>$J_{5,e_1}$</th>
<th>$J_{5,e_2}$</th>
<th>$J_{6,1,e_2}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2;5,6-Di-O-isopropylidene</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-O-Acetyl-α-D-erythro-hex-3-enose</td>
<td>(13)</td>
<td>5.42</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-8.18</td>
</tr>
<tr>
<td>3-O-Acetyl-β-D-threo-hex-3-enose</td>
<td>(14)</td>
<td>5.40</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-8.23</td>
</tr>
<tr>
<td>3-O-Acetyl-α-D-erythro-hex-trans-4-enose</td>
<td>(15)</td>
<td>4.07</td>
<td>4.18</td>
<td>2.06</td>
<td>2.07</td>
<td></td>
<td></td>
<td>-16.06</td>
</tr>
<tr>
<td>Number</td>
<td>Compound Name</td>
<td>IR</td>
<td>NMR</td>
<td>Thesis</td>
<td>Synthesis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------</td>
<td>---------------</td>
<td>----</td>
<td>-----</td>
<td>--------</td>
<td>-----------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1,2;5,6-di-0-isopropylidene-α-D-glucofuranose</td>
<td>12,79</td>
<td>76</td>
<td>89</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1,2;5,6-di-0-isopropylidene-β-D-idofuranose</td>
<td>12,79</td>
<td>76</td>
<td>8,90</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1,2;5,6-di-0-isopropylidene-α-D-allofuranose</td>
<td>12</td>
<td>76</td>
<td>89</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1,2;5,6-di-0-isopropylidene-β-D-talofuranose</td>
<td>12</td>
<td>77</td>
<td>8,91</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1,2;5,6-di-0-isopropylidene-α-D-galactofuranose</td>
<td>9</td>
<td>77</td>
<td>8,91</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1,2;5,6-di-0-isopropylidene-β-D-altrofuranose</td>
<td>9</td>
<td>78</td>
<td>7,94</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1,2;5,6-di-0-isopropylidene-α-D-gulofuranose</td>
<td>9</td>
<td>77</td>
<td>6,19,93</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
8  1,2;5,6-di-0-isopropylidene-\(\beta\)-D-mannofuranose  13,79  78  8,19

9  1,2;5,6-di-0-isopropylidene-\(\alpha\)-D-ribohexofuranos-3- ulose  14  82  7,89

10  1,2;5,6-di-0-isopropylidene-\(\beta\)-D-lyxohexofuranos-3-ulose  -  82  8,90

11  1,2;5,6-di-0-isopropylidene-\(\alpha\)-D-xylohexofuranos-3-ulose  -  82  7,93

12  1,2;5,6-di-0-isopropylidene-\(\beta\)-D-arabinohexofuranos-3-ulose  -  82  7

13  3-O-acetyl-1,2;5,6-di-0-isopropylidene-\(\alpha\)-D-erythrohex-3-enose  -  81  15,92
14 3-O-acetyl-1,2;5,6-di-O-isopropylidene-β-D-threohex-3-enose

15 3-O-acetyl-1,2;5,6-di-O-isopropylidene-α-D-erythrohex-
    -trans-4-enose

16 3-O-acetyl-1,2;5,6-di-O-isopropylidene-α-L-erythrohex-
    -cis-4-enose

17 3-deoxy-1,2;5,6-di-O-isopropylidene-α-D-ribohexo-
    furanose

18 3-deoxy-1,2;5,6-di-O-isopropylidene-β-D-lyxohexo-
    furanose
<table>
<thead>
<tr>
<th>No.</th>
<th>Name</th>
<th>Rg</th>
<th>Mq</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>3-deoxy-1,2;5,6-di-(\beta)-isopropylidene-(\alpha)-D-xylohexofuranose</td>
<td>-</td>
<td>54</td>
</tr>
<tr>
<td>20</td>
<td>3-deoxy-1,2;5,6-di-(\beta)-isopropylidene-(\beta)-D-arabinohexofuranose</td>
<td>-</td>
<td>61</td>
</tr>
<tr>
<td>21</td>
<td>3-(\alpha)-acetyl-1,2;5,6-di-(\beta)-isopropylidene-(\alpha)-D-glucofuranose</td>
<td>-</td>
<td>81</td>
</tr>
<tr>
<td>22</td>
<td>3-(\alpha)-acetyl-1,2;5,6-di-(\beta)-isopropylidene-(\beta)-D-idofuranose</td>
<td>-</td>
<td>81</td>
</tr>
<tr>
<td>23</td>
<td>3-(\alpha)-acetyl-1,2;5,6-di-(\beta)-isopropylidene-(\alpha)-D-allofuranose</td>
<td>81</td>
<td>99</td>
</tr>
</tbody>
</table>
24  3-0-acetyl-1,2;5,6-di-0-isopropylidene-\(\beta\)-D-talofuranose

25  3-0-acetyl-1,2;5,6-di-0-isopropylidene-\(\alpha\)-D-galactofuranose

26  3-0-acetyl-1,2;5,6-di-0-isopropylidene-\(\beta\)-D-altrofuranose

27  3-0-acetyl-1,2;5,6-di-0-isopropylidene-\(\alpha\)-D-gulofuranose

28  3-0-acetyl-1,2;5,6-di-0-isopropylidene-\(\beta\)-D-mannofuranose
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73. L. D. Hall, Carbohydr. Res. 4 429 (1967).
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