Studies on the

1,2;5,6-Di-O-isopropylidene-D-hexofuranoses

by

Alan Stanley Tracey

A Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

in the Department

of

Chemistry

Simon Fraser University

1971

APPROVAL

Name: Alan Stanley Tracey

Degree: Doctor of Philosophy

Title of Thesis: Studies on the 1,2;5,6-Di-O-isopropylidene-
-D-hexofuranoses

Examining Committee:

_____ Dr. K. N. Slessor
Senior Supervisor

_____ Dr. W. A. Szarek
External Examiner
Queen's University

_____ Dr. E. J. Wells
Examining Committee:

_____ Dr. A. C. Oehlschlager
Examining Committee

_____ Dr. C. L. Kemp
Examining Committee
Biological Sciences

Date Approved: _____

For My Brother Howard.

Abstract

The family of compounds, the 1,2;5,6-di-$\underline{O}$-iso-propylidene-$\underline{D}$-hexofuranoses, have been investigated. The synthetic routes by which the $\underline{D}$-talo and $\underline{D}$-gulo compounds are obtained has been improved as well as a synthetic route for the $\underline{D}$-manno derivative, the only unknown member of this series. The synthesis of the four 1,2;5,6-di-$\underline{O}$-isopropylidene-$\underline{D}$-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--$\underline{O}$-isopropylidene-$\underline{D}$-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-$\underline{O}$-isopropylidene-$\underline{D}$-hexofuranoses were determined. Through a correspondence of coupling parameters, the $\underline{endo}$ and $\underline{exo}$ derivatives of these parent compounds are shown to have an essentially identical conformation to that of their parent. The $\underline{D}$-$\underline{ribo}$-hexofuranose family had the $^3T_4 \rightleftarrows V_4 \rightleftarrows {}^OT_4$ conformational

preference; the $\underline{D}$-lyxohexofuranose family had the $^4T_3 \rightleftharpoons {}^4V \rightleftharpoons {}^4T_O$ conformational preference; the xylo-hexofuranose family had the $V_O \rightleftharpoons {}^1T_O \rightleftharpoons {}^1V$ conformational preference; and the arabino family had the preference $^OT_1 \rightleftharpoons V_1 \rightleftharpoons {}^2T_1$. The ribo- and the lyxo-derivatives tend to be considerably more distorted from planarity then the xylo- and arabino-derivatives. The O_5-C_5-C_6-O_6 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-$\underline{O}$-isopropylidene--$\underline{D}$-hexofuranoses are influenced by their conformational preferences. This work attempts to identify and elucidate such effects in this family of compounds.

CONTENTS

LIST OF TABLES

LIST OF FIGURES

Acknowledgements

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 of 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

$$J_1 = k_1 \cos^2\varphi_1 - c \qquad k_1 = 8.5 \text{ Hz} \quad 0 \le \varphi_1 \le 90°$$

$$\text{(I)}$$

$$J_2 = k_2 \cos^2\varphi_2 - c \qquad k_1 = 9.5 \text{ Hz} \quad 90 \le \varphi_2 \le 180°$$

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

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 k_1 and k_2 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

$$J_{ea} = 5.5 \pm 1.0 \text{ Hz} \qquad J_{ae} = 2.9 \pm 0.4 \text{ Hz}$$
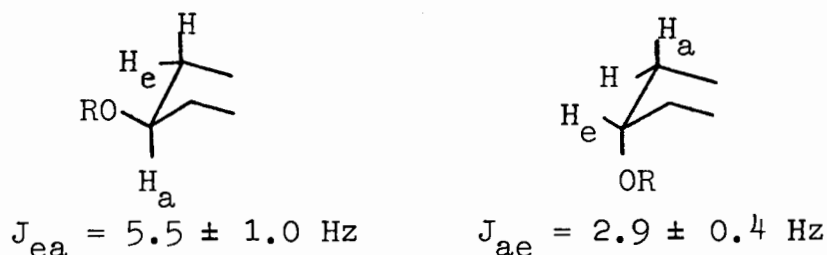
This appears to be a common effect and has been discussed in detail (20). It is evident that many factors influence

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-O-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-O--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-O-isopropylidene systems although the conformation
of 3-fluoro-3-deoxy-1,2;5,6-di-O-isopropylidene-α-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-O-iso-
propylidene-D-hexoses and their 3-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-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' (C_5, C_6 and substituents) is
presented and correlated with chemical properties of
these compounds.

Chapter II

Discussion

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-O 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-O-isopropylidene compounds (29). The 1,2-O-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-O-isopropylidene derivatives of D-talose (4), D-mannose (8), and D-gulose (7) could be readily prepared.

9   3   10   4

11   7   12   8
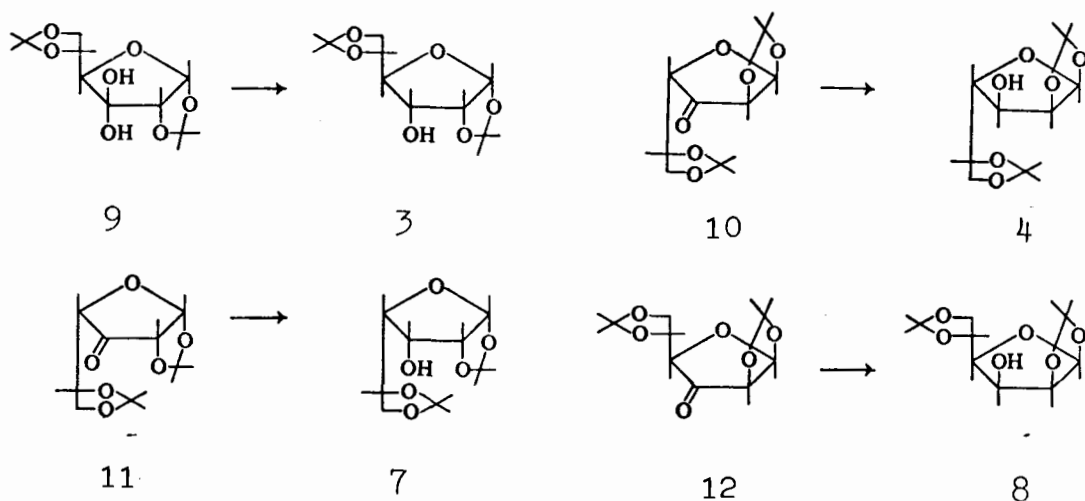
       1,2;5,6-Di-O-isopropylidene-β-D-talofuranose (4)
is known as a side product in the acetonation of D-talose (30).
The mannofuranose derivative has not previously been
prepared as acetonation of D-mannose gives only 2,3;5,6-
-di-O-isopropylidene-D-mannofuranose (31). 1,2;5,6-Di-
-O-isopropylidene-α-D-gulofuranose (7) has been synthesized
by Meyer zu Reckendorf (27) by conversion of the hydrated
1,2;5,6-di-O-isopropylidene-α-D-ribohexofuranos-3-ulose (9)
into the enol acetate (13). Reduction of this material
with sodium borohydride yielded the gulo derivative.
This reaction is complicated by loss of the 5,6-O-iso-
-propylidene acetal and the yield in the borohydride
reduction is often low due to this. Catalytic hydrogen-
ation of the enol acetate gave an excellent yield of the
3-O-acetate (27) and subsequent de-O-acetylation with
methoxide provided the gulose derivative (7) in very
high yield.
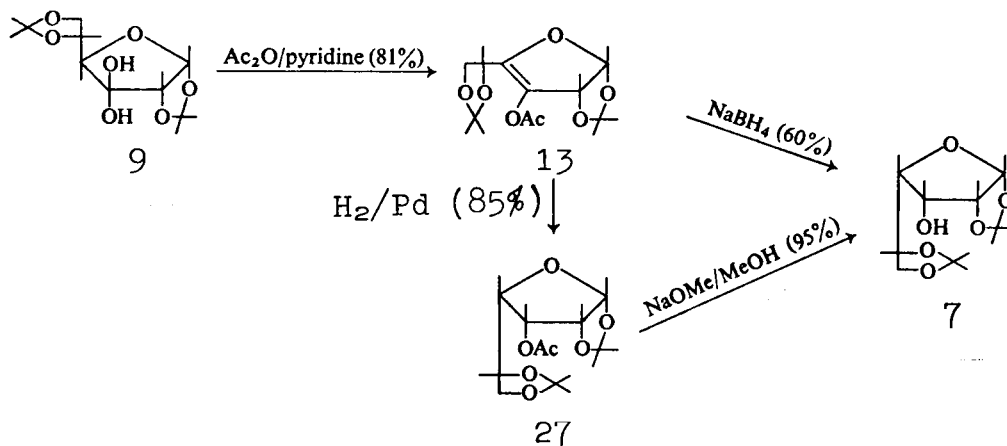
The 3-keto derivatives were prepared in good yield
using a slightly modified version of the ruthenium dioxide/
sodium periodate method of Parikh and Jones (32).
D-Altrose was prepared from methyl 4,6-O-benzylidene-α-
D-glucopyranoside as described by Richtmyer (33). The
preparation was modified by opening the epoxide ring
by acetolysis 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 acetolysis procedure required
about 1 hour for completion compared to 2 days for opening
with potassium hydroxide. De-O-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-O-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-O-isopropylidene-α-D-galacto-
-furanose (5) was readily prepared by hydroboration of
3-deoxy-1,2;5,6-di-O-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 postion 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 born out by the absence of a UV ketone
absorption at 325 mμ 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 phen-
omenon has already been reported for 1,2;5,6-di-O-iso-
-propylidene-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-α-D-ribohexofuranos-3-ulose (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*

Ketone	0.5 h	1.5 h	3.5 h	8 h	18 h
Acetonitrile containing 4.25 % water					
ribo† (9a)	2	7	14	26	45
arabino (12)	1	3	4	6	10
xylo (11)	5	14	17	17	17
lyxo (10)	2	4	9	17	29
Acetonitrile containing 10% water					
ribo† (9a)	34	69	82	83	84‡
arabino (12)	11	26	39	41	43
xylo (11)	25	34	38	39	39
lyxo (10)	23	46	60	61	61

*Measured on a Unicam SP?00 at 320 mμ at a sugar con-
centration 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 mμ after 5 min of being dissolved in water.
†The ribo ketone (9a) was prepared by vacuum distil-
lation 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-α-D-ribo
-hexofuranos-3-ulose in carbon tetrachloride (0.005 M).
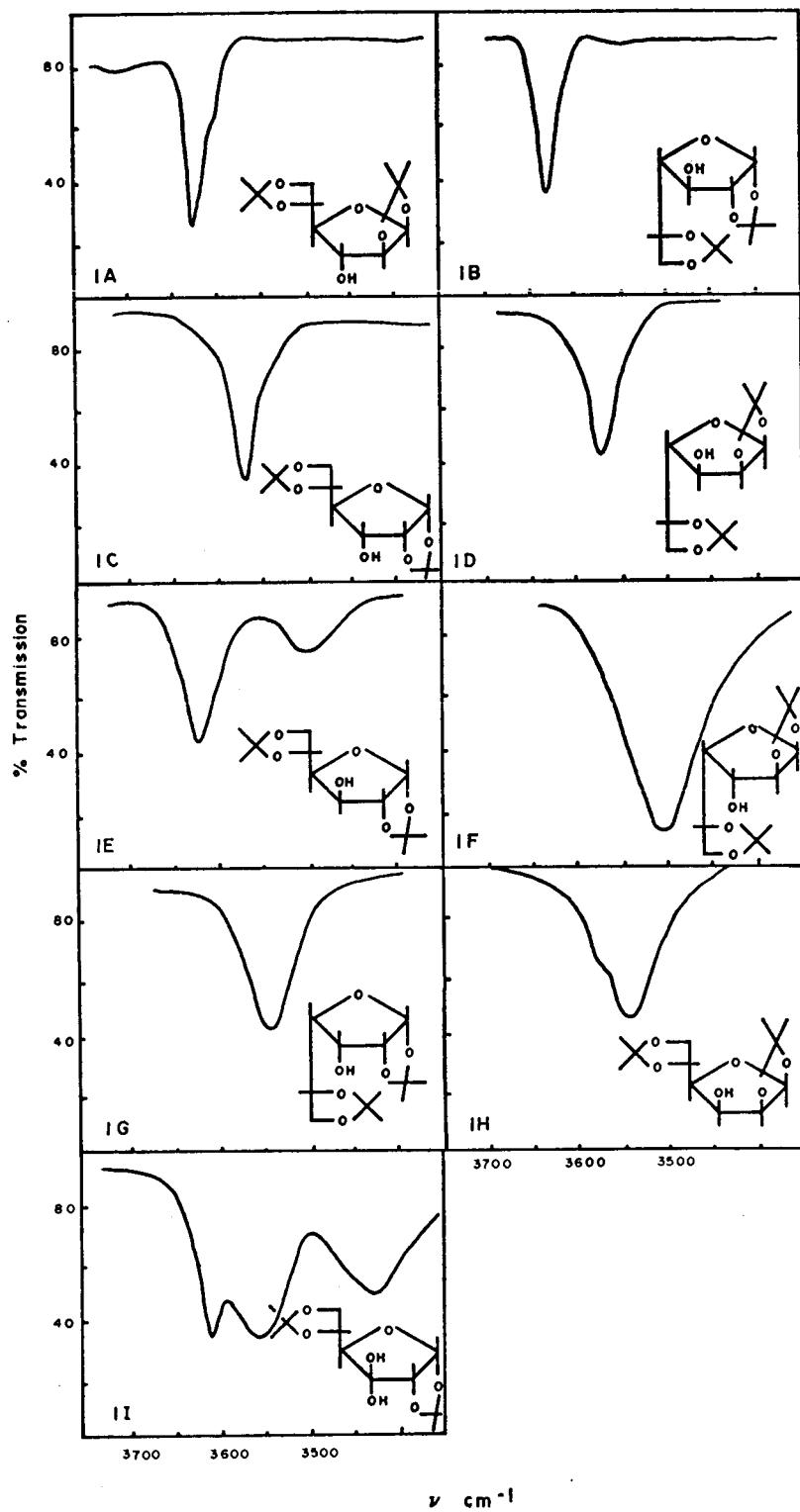
indicate a free hydroxyl on a secondary center ($\underline{42}$).
Figures 1C and 1D are compounds (allo (3) and talo (4))
in which the stereochemistry allows the hydroxyl to
hydrogen bond to the 2-oxygen in the 1,2-$\underline{O}$-isopropylidene
ring. This is in agreement with the position of the
bands in 1C and 1D at 3570 cm^{-1} indicating a 5 membered
hydrogen bond ring ($\underline{43}$)

$$C_2-O_2 \ldots H-O_3-C_3$$
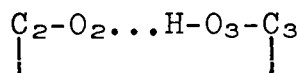
The stereochemistry of compounds 1E and 1F (gluco (1)
ido (2)) restricts any hydrogen bonding of the 3-OH to
the oxygen at C_5 involved in the 5,6-$\underline{O}$-isopropylidene
ring. Surprisingly, the spectra are quite different, the
glucose derivative having 2 peaks, one at 3622 cm^{-1} (free
OH) and 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 ($\underline{43}$).

$$C_3-O-H \ldots O_5-C_5-C_4$$
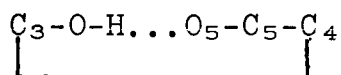
Hydrogen bonding of this type will prevent free rotation
of the 'tail' (C_5-C_6 and their substituents) about the
C_4-C_5 bond. At room temperature it is unlikely that
free rotation is completely hindered in the glucose der-
ivative. Thus the band at 3622 cm^{-1} can be attributed
to that fraction of the 3-OH in which the 'tail' is in
a rotamer that cannot be hydrogen bonded. The 1,2;5,6-
-di-$\underline{O}$-isopropylidene-β-$\underline{D}$-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 $\underline{D}$-C$_5$:$\underline{D}$-C$_3$ configuration ($\underline{D}$-gulo (7)
and $\underline{D}$-ido (2)), rotation about the C$_4$-C$_5$ bond is more
hindered than for the $\underline{D}$-C$_5$:$\underline{L}$-C$_3$ configuration ($\underline{D}$-gluco (1)
and $\underline{D}$-manno (8)).
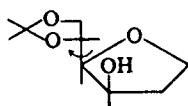
Rotation easier
D-C$_5$; L-C$_3$
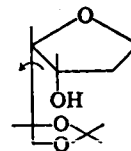
Rotation more difficult
D-C$_5$; D-C$_3$

It would seem that the formation of a 3-O-H...O$_5$ hydrogen
bond as well as the hindered rotation effectively maintains
the 'tail' of 1,2;5,6-di-$\underline{O}$-isopropylidene-β-$\underline{D}$-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 $\underline{D}$-C$_5$:$\underline{L}$-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-$\underline{O}$-isopropylidene unit thus
giving rise to the 3585 cm^{-1} shoulder. It is possible
that for the $\underline{D}$-C$_5$:$\underline{L}$-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 hy-
drogen 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 strenthen-
ing (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).
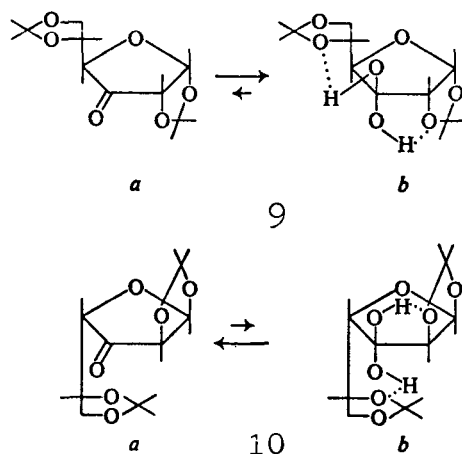
In its crystalline state, the latter exists in the
keto form. That this is not just a property of the crystal-
line material is obvious from the ease of extraction from

aqueous solution when compared to the hydrated keto glucose. That is, in spite of the ability of 1,2;5,6-
-di-O-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-O-acetyl-1,2;5,6-di-O-isopropylidene-α-D-erythrohex-
-3-enose (13) and 3-O-acetyl-1,2;5,6-di-O-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-O-isopropylidene-α-D-ribohexo-
-furanos-3-ulose (9), 1,2;5,6-di-O-isopropylidene-α-D-
-xylohexofuranos-3-ulose (11), 1,2;5,6-di-O-isopropylidene-

-β-D-lyxohexofuranos-3-ulose (10), and 1,2;5,6-di-O-
-isopropylidene-β-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 C_4-H bond leading to enolization (44).
That this process is difficult in these compounds has
been shown by attempts to introduce deuterium at the C_4
position by D_2O 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-O-isopropylidene-
-β-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 C_4 hydrogen.

In compounds 11 (1,2;5,6-di-O-isopropylidene-α-
-D-xylohexofuranos-3-ulose) and 12 (-β-D-arabinohexo-
-furanos-3-ulose) little steric hindrance to the approach
of the base to the C_4 hydrogen would be expected as
the 1,2-O-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 C_3-C_4 double bond might result in relief
of steric strain between the 1,2-O-isopropylidene group

Table II

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

Ketone	Time* (days)
9	3.8-4.3
11	1.5-1.8
10	22-24†
12	1.1-1.3

*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 dif-
ference between the rates of enol acetate formation from
11 and 12 would be expected. In 9 (1,2;5,6-di-O-iso-
propylidene-α-D-ribohexofuranos-3-ulose) and 10 (-β-D-
-lyxohexofuranos-3-ulose), the approach of the base to
the C_4-H will be hindered by the 1,2-O-isopropylidene
ring. That such an influence is of importance is sug-
gested by the stereospecific reduction of the C_4-C_5
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-O-isopropylidene
cis or trans to 'tail', the compounds with a D-C_5:D-C_4
configuration (ribo, arabino) react faster than their
analogues with an L-C_5:D-C_4 configuration (lyxo, xylo).

Two possible explanations for this effect seem
reasonable; a D-configuration at C_5 imparts some type of
steric instability to the sugar and as a result increases
the rate of enolization, or an L-configuration at C_5
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-α-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-α-D-gulofuranose (27) while reduction of 14 provided the corresponding 3-O--acetyl-1,2;5,6-di-O-isopropylidene-β-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-β-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-α-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 surgaces to give a high percentage of the alkyl cycloalkene; that is,

97.6% of 1-methylcyclopentene and 94.2% of 1-ethylcyclo-
pentene (46). An attempt was made to identify and iso-
late 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%
H_2SO_4 and heat) came up a different colour from the
starting material (13). NMR spectroscopy showed that
this compound (15) was substantially different in struc-
ture 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 τ and a
coupling of 4.1 Hz consistent with an assignment of H_1
for this proton (47). On the basis of this assignment
H_2 is found at 5.12 τ with an H_2 to H_3 coupling of
6.2 Hz which indicated that H_2 and H_3 were cis. This
required the acetate group (7.9 τ) 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 τ occurs as a tripleted doublet,
being coupled to the two C_6 hydrogens at 5.5 τ. The
four isopropylidene methyls are found at 8.6 τ. The
assignment of the ring protons was verified by the for-
mation 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 τ and the collapse of the signal at 5.50 τ to a single peak as well as the collapse of the quartet at 5.12 τ 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-O-acetyl-1,2;5,6--di-O-isopropylidene-α-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 prereduced catalyst resulted in 20% to 60% deuteration, dependent on the extent of prereduction 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-erythrohex-trans--4-enose) whose NMR spectrum had no peak in the acetate region, but had four isopropylidene methyl groups and a D_2O 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 C_5 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-acetyl-
ation afforded 1,2;5,6-di-O-isopropylidene-β-D-manno-
-furanose (8) identical to that obtained by borohydride
reduction of 1,2;5,6-di-O-isopropylidene-β-D-arabino-
-hexofuranos-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 appen-
dix.
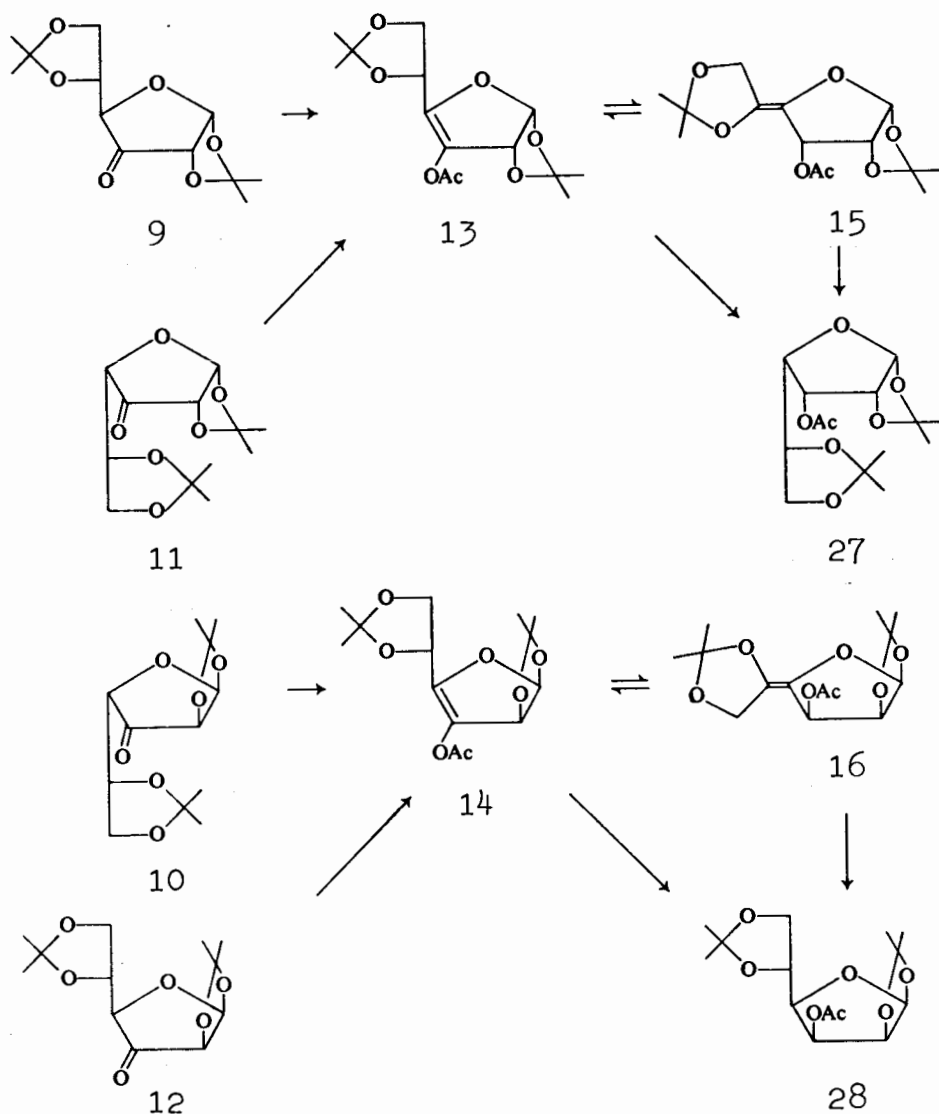
Reduction of 13 or 15 over platinum in anhydrous ether proceeded quite slowly compared with the reduction over palladium, requiring at least 24 hours compared with 7 hours for the palladium reduction. Thin layer chromatography indicated the formation of two major compounds, one having R_f corresponding to 3-O-acetyl--1,2;5,6-di-O-isopropylidene-α-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-O-isopropylidene-α-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-O-isopropylidene--α-D-erythrohex-3-enose (50). Reduction of this compound with deuterium gas provided the specifically 3,4--dideuterated 19, which was used in later spectroscopic analyses.

15

13

19
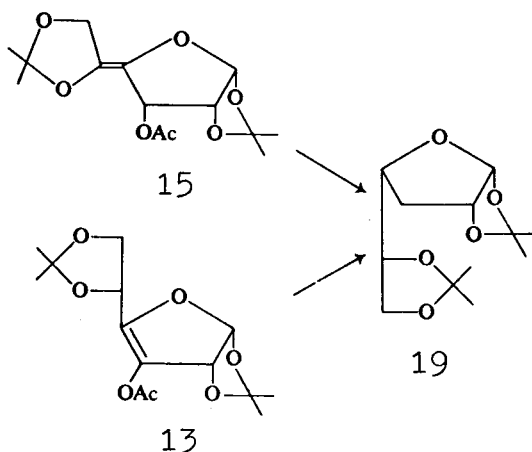
Hydrogenolysis of 14 occurs under conditions identical to that of the hydrogenolysis of 13 and in similar yield. The NMR spectrum was consistent with the expected product, 3-deoxy-1,2;5,6-di-O-isopropylidene-β-D-arabino-hexofuranose (20). The mass spectrum gave a large peak $(M-15)^+$ at m/e 229 and 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).

14   28
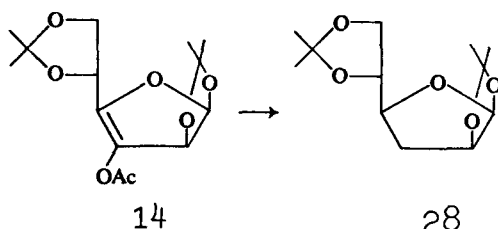
3-Deoxy-D-arabinohexose (51) was acetonated and the product was found identical by IR, NMR, mass spectoscopy, melting point, and optical rotation to the product of hydrogenolysis of 14. This work adds conclusive evidence, therefore, that the 3-deoxy-di-O-isopropylidene-D-hexose prepared by Rembarz (52) 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-ulose 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 rearrange-
ment by substituting platinum for palladium failed in
that a major pathway of this reaction was the hydrogen-
olytic 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-O-benzylidene-
-α-D-arabinohexopyranose. This compound was prepared
by lithium aluminum hydride oxirane opening of methyl
2,3-anhydro-4,6-O-benzylidene-α-D-mannopyranoside, a
synthetic route described by D. A. Prins (54). Oxida-
tion of this compound (55, 56), followed by sodium boro-
hydride reduction afforded methyl 4,6-O-benzylidene-3-
-deoxy-α-D-ribohexopyranoside (55). Acetolysis, followed
by de-O-acetylation provided 3-deoxy-D-ribohexose which
upon acetonation gave 3-deoxy-1,2;5,6-di-O-isopropyl-
-idene-α-D-ribohexofuranose (17). Subsequent to this
preparation, work in our lab established the utility of
triphenyl phosphine/carbon tetrachloride as a means of
introducing chlorine into the 3 position of 1,2;5,6-di-
-O-isopropylidene-α-D-allofuranose (3) and -β-D-talo-
-furanose (4) to yield the 3-chloro-3-deoxy-1,2;5,6-di-
-O-isopropylidene-α-D-glucofuranose and -β-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 stereo-
chemistry of the lithium aluminum hydride reduction of
these chlorodeoxy sugars, 3-deuterio-1,2;5,6-di-O-iso-
-propylidene-α-D-allofuranose was converted into
3-chloro-3-deoxy-3-deuterio-1,2;5,6-di-O-isopropylidene-
-α-D-glucofuranose. Reduction, followed by isolation
and distillation gave 3-deoxy-3-deuterio-1,2;5,6-di-O-
-isopropylidene-α-D-allofuranose. Table III presents
the $J_{2,3}$ couplings of this and some related compounds.
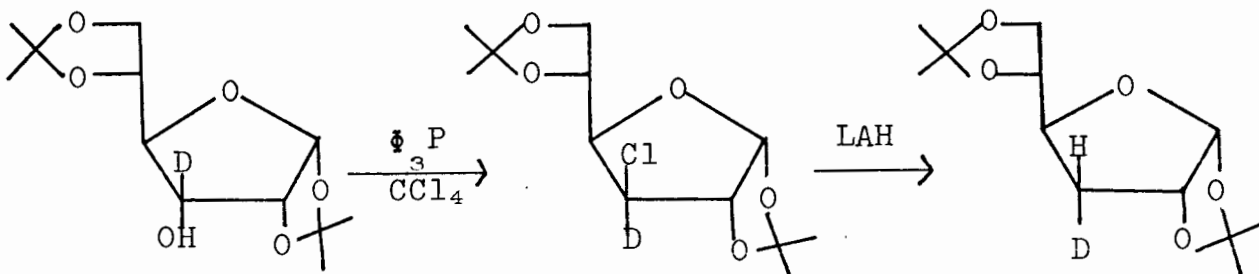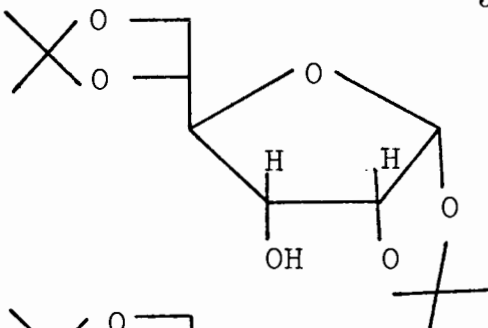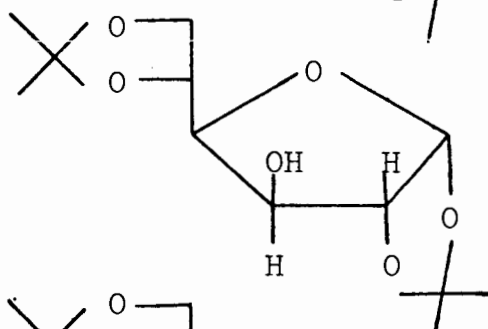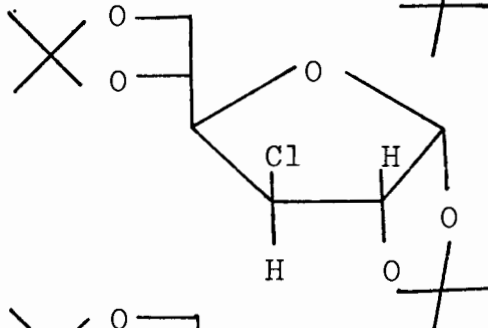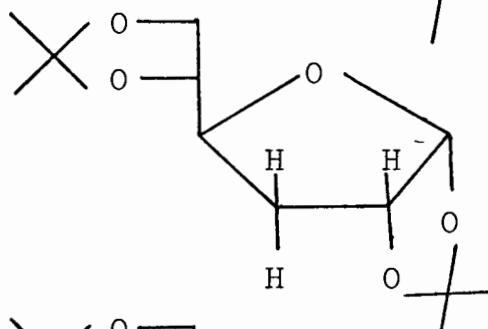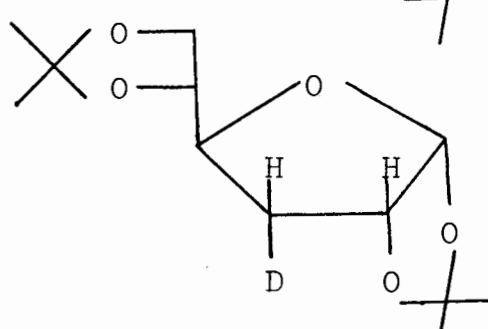
From Table III the $J_{2,3}$ coupling of the 3-deoxy-
-3-deuterioallofuranose can be seen to be close to 5 Hz
which is indicative of a cis arrangement of H_2 and H_3
as drawn. The reduction of the 3-chloro-D-glucose
derivative therefore must have taken place with retention
of configuration about C_3.

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*

	$J_{2,3}$ (cis)	$J_{2,3}$ (trans)
	5.0	---
	---	~0.5
	---	~0.5
	4.8	~0.5
	4.8	---

*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 ($\underline{7}$), has main-
tained its essential features after several years of
experimental and theoretical investigations. The lim-
itations of the equation have been stressed by a number
of workers ($\underline{59}$, $\underline{60}$, $\underline{61}$), including Karplus himself ($\underline{15}$).
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 ($\underline{60}$, $\underline{62}$) to changes in mag-
nitude 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 accom-
modated 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 ($\underline{7}$),
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 with-
out explicit consideration of the electronic pertur-
bations 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 ($\underline{63}$)
and found to work well for systems to which it is applic-
able ($\underline{64}$, $\underline{65}$). Requiring couplings between protons of
a dimethylene group,

$$- \underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}} - \underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}} -$$
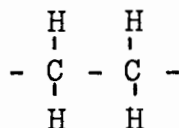
the 'R value' method is necessarily severely limited
in application although under some circumstances it may
be used with couplings into a methylene group (65).

$$
\begin{array}{cc}
H & R \\
| & | \\
- C - C - \\
| & | \\
H & H
\end{array}
$$
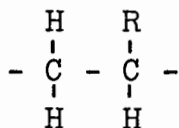
In DAERM the form (I) of the Karplus equation (7) is
used.   J is the vicinal coupling constant; k, the
Karplus constant; Φ, the dihedral angle subtended by
the coupled nuclei; and c, a constant.

a) $J_1 = k_1 \cos^2\Phi_1 - c$ $0 \leq \Phi_1 \leq 90°$

(I)

b) $J_2 = k_2 \cos^2\Phi_2 - c$ $90 \leq \Phi_2 \leq 180°$

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, cnd 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 Φ_1 and Φ_2 are
less than 90°, and therefore II is obtained, where ω
is the projection angle of the methylene protons.

$$
\frac{J_1 + c}{J_2 + c} = \frac{\cos^2\Phi_1}{\cos^2(\omega-\Phi_1)}
$$

(II)

Assuming a regular tetrahedral system ($\omega = 120°$),
and using the theoretical value of 0.28 for c (7), a
complete solution for the angles Φ_1 and Φ_2 is possible
from the coupling constants, J_1 and J_2, without know-
ledge of the Karplus constant, k_1, for that system.

Figure 2

Four arrangements of the $-\overset{|}{C}-\overset{|}{C}-H$ system
$H\ \ H$

Case A

$\Phi_1\ <\ 90°$
$\Phi_2\ <\ 90°$

$\omega\ =\ \Phi_1\ +\ \Phi_2$

Case B

$\Phi_1\ <\ 90°$
$\Phi_2\ >\ 90°$

$\omega\ =\ \Phi_1\ +\ \Phi_2$

Case C

$\Phi_1\ <\ 90°$
$\Phi_2\ >\ 90°$

$\omega\ =\ \Phi_2\ -\ \Phi_1$

Case D

$\Phi_1\ >\ 90°$
$\Phi_2\ >\ 90°$

$\omega\ =\ \Phi_2\ -\ \Phi_1$

Cases B and C can be resolved in a similar manner, as shown below.

$$\text{Case B} \qquad \frac{J_1 + c}{J_2 + c} = \frac{k_1 \cos^2\Phi_1}{k_2 \cos^2(\omega-\Phi_1)} \qquad \text{(III)}$$

$$\text{Case C} \qquad \frac{J_1 + c}{J_2 + c} = \frac{k_1 \cos^2\Phi_1}{k_2 \cos^2(\omega+\Phi_1)} \qquad \text{(IV)}$$

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 Φ_1 provides the expression:

$$\tan \Phi_1 = \frac{-\cos \omega \pm [(k_1/k_2)(J_2 + c)/(J_1 + c)]^{\frac{1}{2}}}{\sin \omega} \qquad \text{(V)}$$

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 Φ_1.

If the expression

$$J = a \cos^2\Phi_1 + b \cos\Phi_1 - c \qquad \text{(VI)}$$

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

$$\tan \Phi_1 = \frac{-1(2 \cos \omega + \frac{b/a}{\cos\Phi_1}) \pm [(\frac{b/a}{\cos\Phi_1})^2 + 4(\frac{J_2+c}{J_1+c})(1+\frac{b/a}{\cos\Phi_1})]^{\frac{1}{2}}}{2 \sin \omega}$$

$$\text{(VII)}$$

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 Φ_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 ang-
ular relationship between vicinally coupled nuclei, as
well as the elctronic 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 temp-
erature proton NMR parameters of octadeuterocyclohexane

obtained by Garbisch and Griffith (<u>66</u>). 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

Set	Observed Coupling Constants		Calculated Dihedral Angles		Calculated Karplus Constants	
	J_1	J_2	Φ_1	Φ_2	k_1	k_2
i	3.65	13.12	55	175	12.14	13.49
ii	3.65	13.12	70	50	32.78	36.43
iii	13.12	3.65	1	121	13.40	14.89
iv	13.12	3.65	50	70	32.78	36.43

‡ In all Tables and discussion, Φ_1 is the cis angle; Φ_2 is the trans angle; k_1 the calculated Karplus constant for less than 90°; k_2 for greater than 90°.

Table V

DAERM Calculations* on 2.96 and 3.65 Hz Couplings

Set	Observed Coupling Constants		Calculated Dihedral Angles		Calculated Karplus Constants	
	J_1	J_2	Φ_1	Φ_2	k_1	k_2
v	2.96	3.65	32	152	4.52	5.02
vi	2.96	3.65	62	58	14.32	15.91
vii	3.65	2.96	23	143	4.61	5.13
viii	3.65	2.96	58	62	14.32	15.91

*$k_1/k_2 = 0.9$, $\omega = 120°$
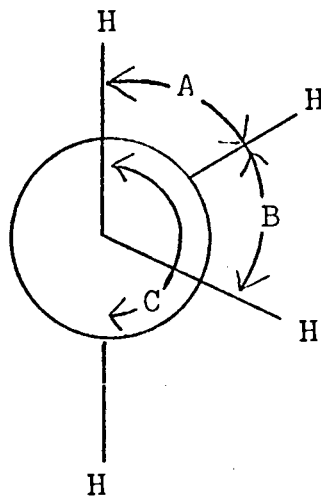
A, 55-58°, gives rise to J_{ae} coupling of 3.65 Hz;
B, 62-65°, gives rise to J_{ee} coupling of 2.96 Hz; and
C, 175-178°, gives rise to the J_{aa} coupling of 13.12 Hz.
It is important to note that the assignments were made
without prior knowledge of the proton identities and
without assigning numerical values to the Karplus con-
stants. DAERM predicts a flattened chair conformation
with proton assignments identical to those of Garbisch
and Griffith (66).

Prior to further application of DAERM, an invest-
igation of two main features of this method was carried
out. These were: 1) distortion of the system from
regular tetrahedral geometry ($\omega \neq 120°$), and 2) variation
of the parameter k_1/k_2. Using the octadeuterocyclo-
hexane 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 Φ_2 against values of ω.
The value of ω 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_{ae}, J_{ee} and J_{ae}, J_{aa} gives two curves intersecting at an ω value of 115°.

The Φ_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 ω 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 ω 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 ω 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 ω 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 ω with Φ

from ae /ee

from aa /ae

Φ_2 (degrees)

$\omega = \Phi_1 + \Phi_2$ (degrees)

Figure 4

Plot of ratio (k_1/k_2) versus ω
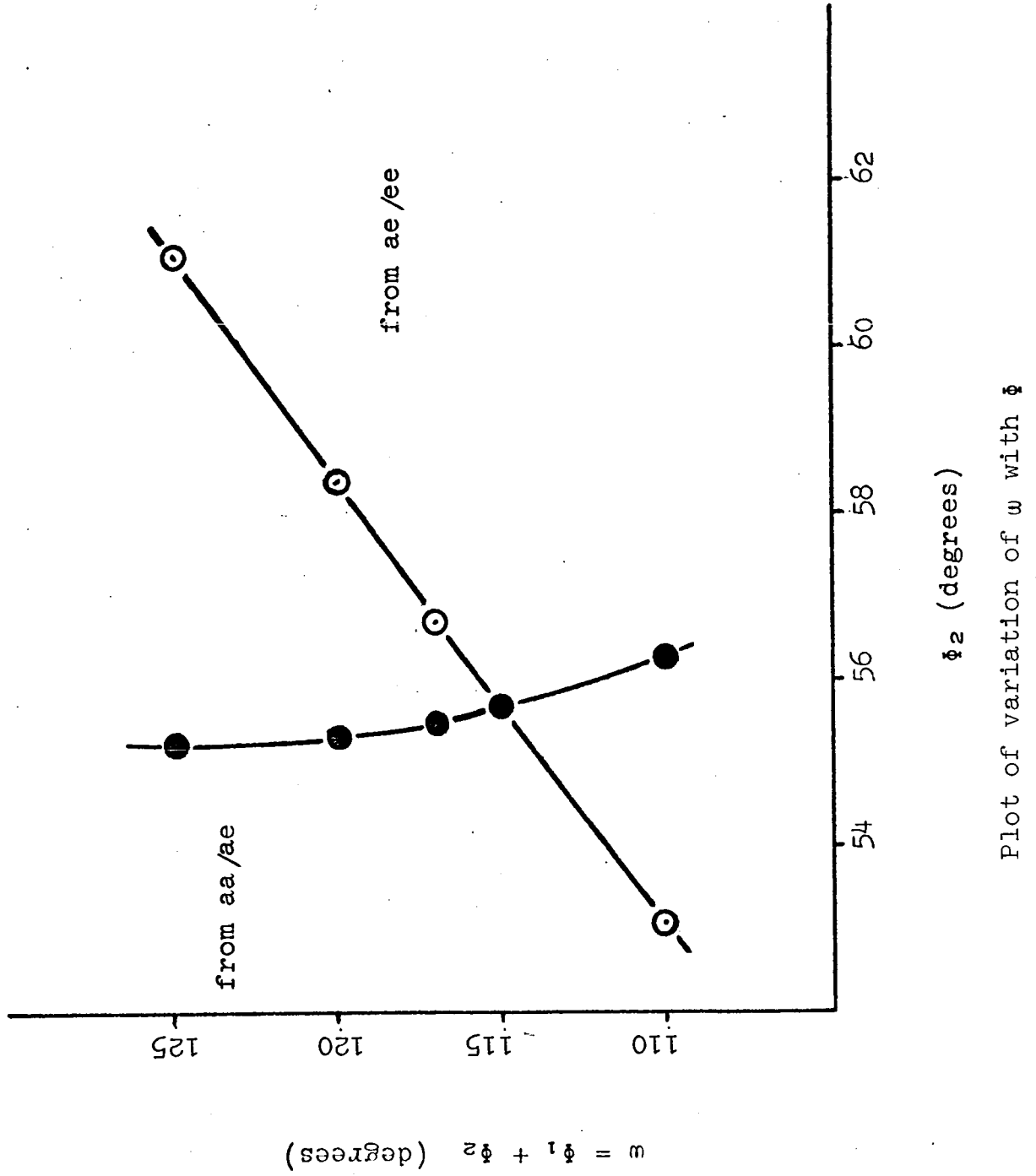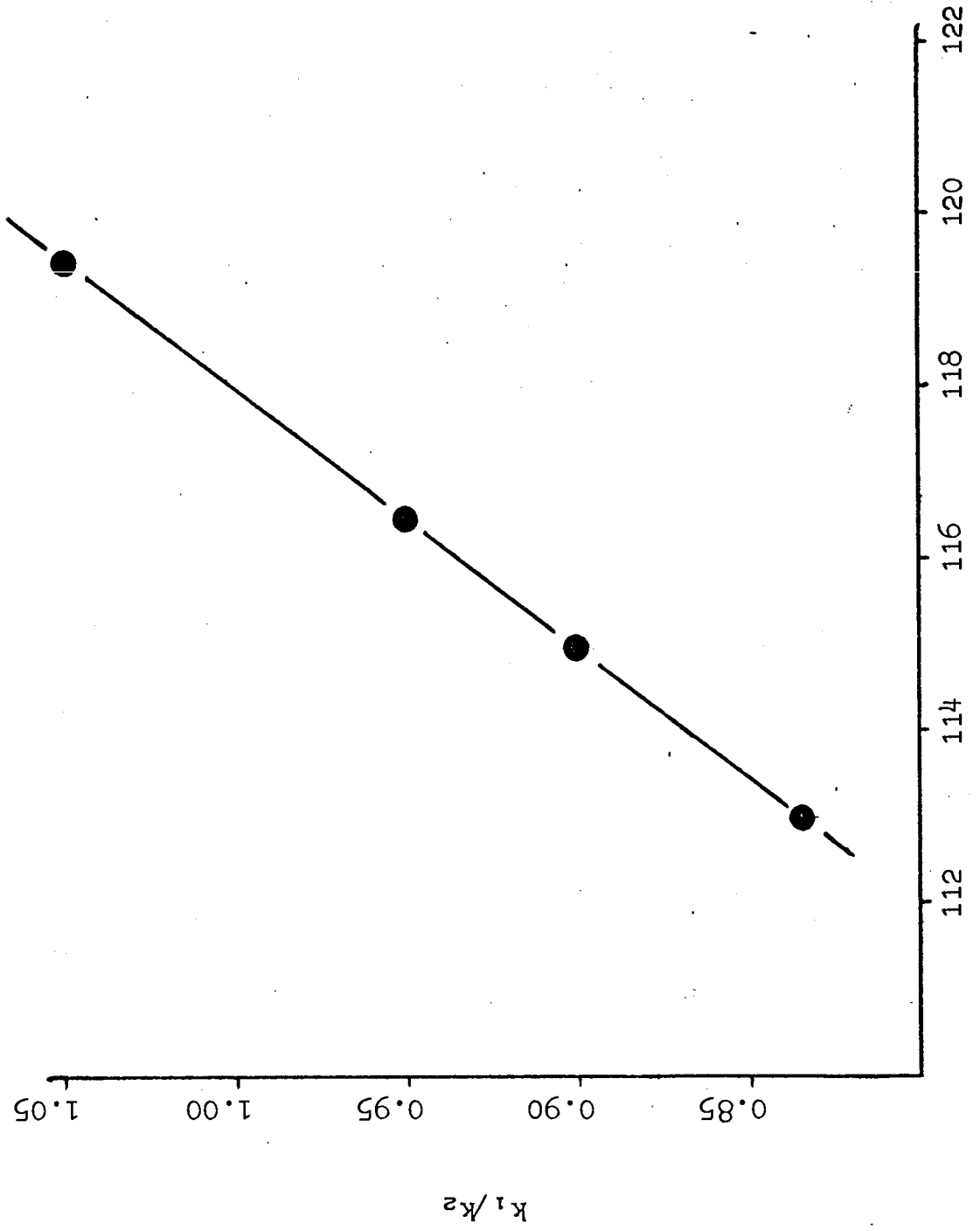
to cyclic molecules.

An essential prerequisite of DAERM is the avail-
ability 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 ω value of 115° are assigned from
which not only Φ_1 and Φ_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 Φ_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. ω = 120°, 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 conform-
ational 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]
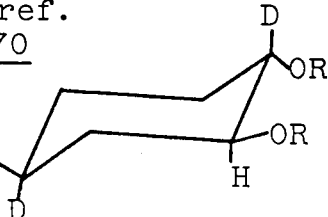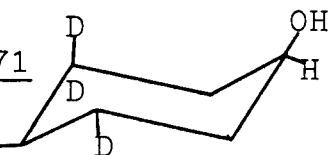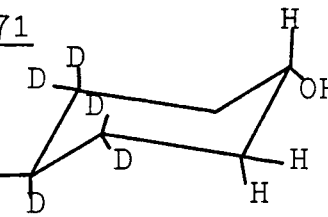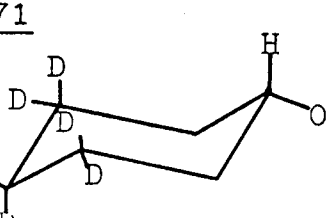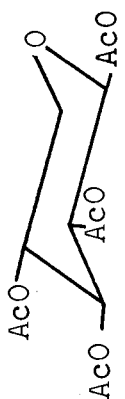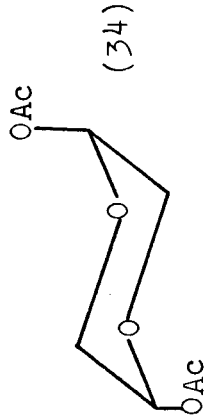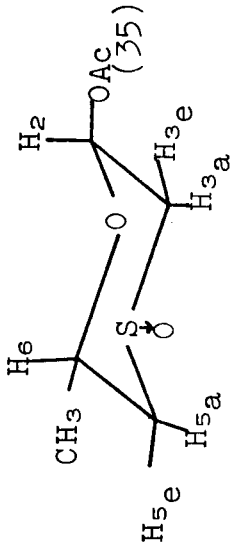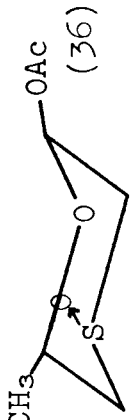
Compound		R	Solvent	Observed Coupling Constants			Calculated Angles		Calculated Karplus Constants	
				J_{aa}	J_{ea}	J_{ee}	Φ_1	Φ_2	k_1	k_2
ref. 70	29a	Ac	CCl_4	11.0	3.5	–	53	168	10.6	11.8
	29b	H	$CHCl_3$	11.0	4.5	–	50	165	11.0	12.2
	29b	D	D_2O	10.5	4.1	–	49	164	10.4	11.6
	29c	ditosyl	$CHCl_3$	7.9	3.6	–	46	161	8.2	9.1
	29d	isopropylidene	CCl_4	11.0	3.5	–	53	168	10.6	11.8
71	30		CCl_4	–	3.0	2.7	57	58	10.9	12.1
71	31		CCl_4	11.1	4.3	–	52	167	12.0	13.4
71	32a	H	CCl_4	9.8	3.9	–	49	164	9.8	10.9
	32a	D	D_2O	10.2	4.1	–	49	164	10.2	11.3
	32b	Ac	$CS_2(r.t.)$	9.3	3.9	–	48	163	9.4	10.4
	32b	Ac	$CS_2(-110°)$	11.4	4.2	–	51	166	11.2	12.5

Table VII

NMR & DAERM Data For Heterocycles[1]

ref.	Compound	Solvent	Coupling Constants		Calculated Angles		Calculated Karplus Constants	
			J_{cis}	J_{trans}	Φ_1	Φ_2	k_1	k_2
72	(33)	CHCl$_3$	4.2	8.1	43	163	8.1	9.0
73	(34)		1.5	1.0	57	63	5.9	6.6
74	(35)	CDCl$_3$	$J_{2,3e}$ 1.6 $J_{5e,6}$ 1.8	$J_{2,3a}$ 10.1 $J_{5a,6}$ 11.5	63 64	183 184	9.4 10.7	10.4 11.8
74	(36)	CDCl$_3$	$J_{2,3e}$ 1.9 $J_{5e,6}$ 1.9	$J_{2,3a}$ 9.8 $J_{5a,6}$ 10.8	61 62	181 182	9.1 10.0	10.1 11.1

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.
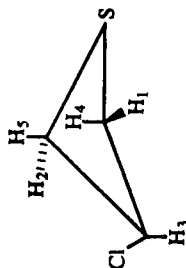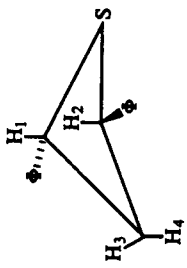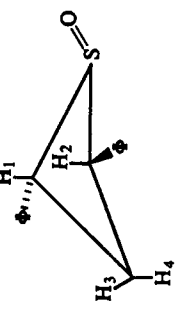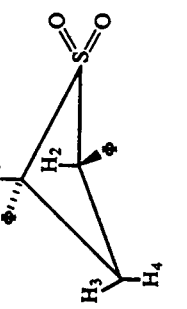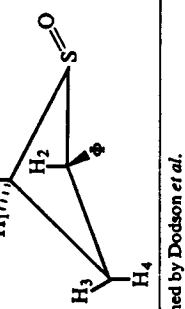
spectra of several thietanes. The results are presented
in Table VIII using the proton assignments of the original
workers (76, 77).

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 confor-
mation 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 electro-
negativity of the substituent. This inverse relation-
ship 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

Reference	Compound	No.	Reported coupling (Hz)		Reported angle	DAERM* angle	Calculated Karplus constants
78		37	$J_{1,3}$ 7.670	$J_{3,4}$ 9.343	27.6 / 152.9	29 / 156	10.3, 11.5
77		38	$J_{1,3}$ 7.35	$J_{1,4}$ 9.95	30.0 / —	32 / 159	10.5, 11.7
77		39	$J_{1,3}$ 9.53	$J_{1,4}$ 12.62	31.6 / 159.1	31 / 159	13.4, 14.9
77		40	$J_{1,3}$ 9.17	$J_{1,4}$ 11.12	27.7 / —	29 / 156	12.3, 13.6
77		41	$J_{1,3}$ 3.16, $J_{1,4}$ 8.79, $J_{2,3}$ 10.24, $J_{2,4}$ 11.90		91.0 / 36.5 / 26.5 / 154.0	126 / 2 / 27 / 155	9.1, 10.1 / 13.3, 14.8

*ω = 127.6 as assigned by Dodson et al.

Norbornenes

42

43

a $R_1 = -\overset{\displaystyle O}{\overset{\|}{C}}-OCH_3; R_2 = H$

b $R_1 = -H; R_2 = -\overset{\displaystyle O}{\overset{\|}{C}}-OCH_3$
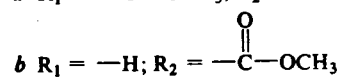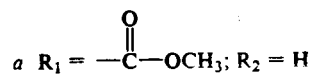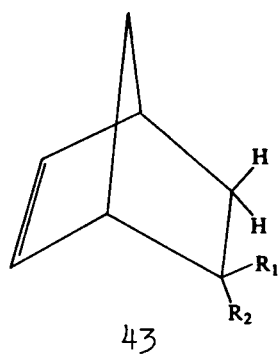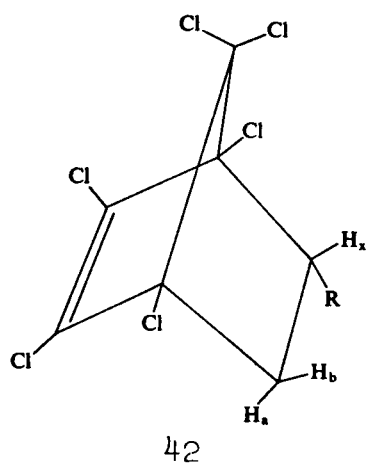
Table IX

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

Compound	R	J_{ax}	J_{bx}	Calculated Angles		Calculated Karplus Constants		Substituent Electronegativities from ref. 14
				Φ_{ax}	Φ_{bx}	k_1	k_2	
42a	-CN	4.6	9.3	12	132	10.0	11.1	2.49
42b	$\overset{O}{\overset{\|}{-C}}-OH$	4.4	8.5	13	133	9.2	10.2	2.60
42c	-Φ	4.2	8.9	11	131	9.5	10.6	2.75
42d	-Cl	3.2	8.0	8	128	8.4	9.4	3.25
42e	-OH	2.4	7.4	4	124	7.7	8.6	3.43
42f	-OAc	2.5	7.6	4	124	7.9	8.8	3.80

ω = 120°

group can be expected to be greater than the tetra-
hedral angle ($\underline{80}$). Assuming a distortion of a few
degrees ($\omega = 125°$), 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 ($\underline{81}$).

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

Table X

Variation in ω for C-2 and C-3 of Bicyclo[2.2.1]hept-5-enes

Reference	Compound	R	ω	cis angle	trans angle k_1	k_1	k_2
14	42b	$-\overset{\displaystyle O}{\overset{\|}{C}}-OH$	120	13	133	9.2	10.2
			125	8	133	9.0	10.2
14	42e	$-OH$	120	4	124	7.7	8.6
		$-OH$	125	1	124	7.7	8.6
103	43a	$-\overset{\displaystyle O}{\overset{\|}{C}}-OCH_3$	120	10	130	10.0	11.1
			125	5	130	9.8	10.8
103	43b	$-\overset{\displaystyle O}{\overset{\|}{C}}-OCH_3$	120	11	131	9.6	10.7
			125	7	132	9.4	10.5

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-$\underline{O}$-isopropylidene ring and the 'tail', it seems probable that the 1,2;5,6-di-$\underline{O}$-isopropylidene-$\underline{D}$-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, C_2-C_3-C_4, of the furan ring (a) is the focal point of the conformational discussion. For DAERM, ω is the projection angle of the methylene protons along the C_2-C_3 or C_4-C_3 bond (b). Internal angles between carbon atoms involved

a

b
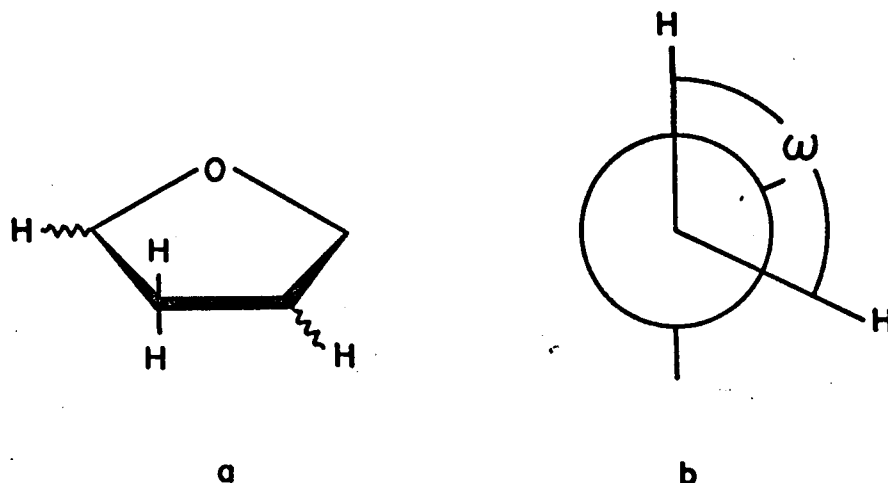
in a furan ring are known (69) to be smaller than the regular tetradedral value of 109.5°. Assuming constant p-character in the carbon bonding, the angle subtended by the hydrogens on a methylene function of a furan ring will necessarily be greater than the tetrahedral angle (81). Recognizing this effect, an ω 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 ω from the assigned values have minimal effect on any conformational arguments. With these values assigned, DAERM can now be applied to these 3-deoxy-$\underline{D}$-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--$\underline{O}$-isopropylidene-β-$\underline{D}$-arabinohexofuranose (20). Only 3-deoxy-1,2;5,6-di-$\underline{O}$-isopropylidene-α-$\underline{D}$-ribohexofuranose (17) was not completely analyzed since the 4,5; 5,6$_1$; and 5,6$_2$ 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
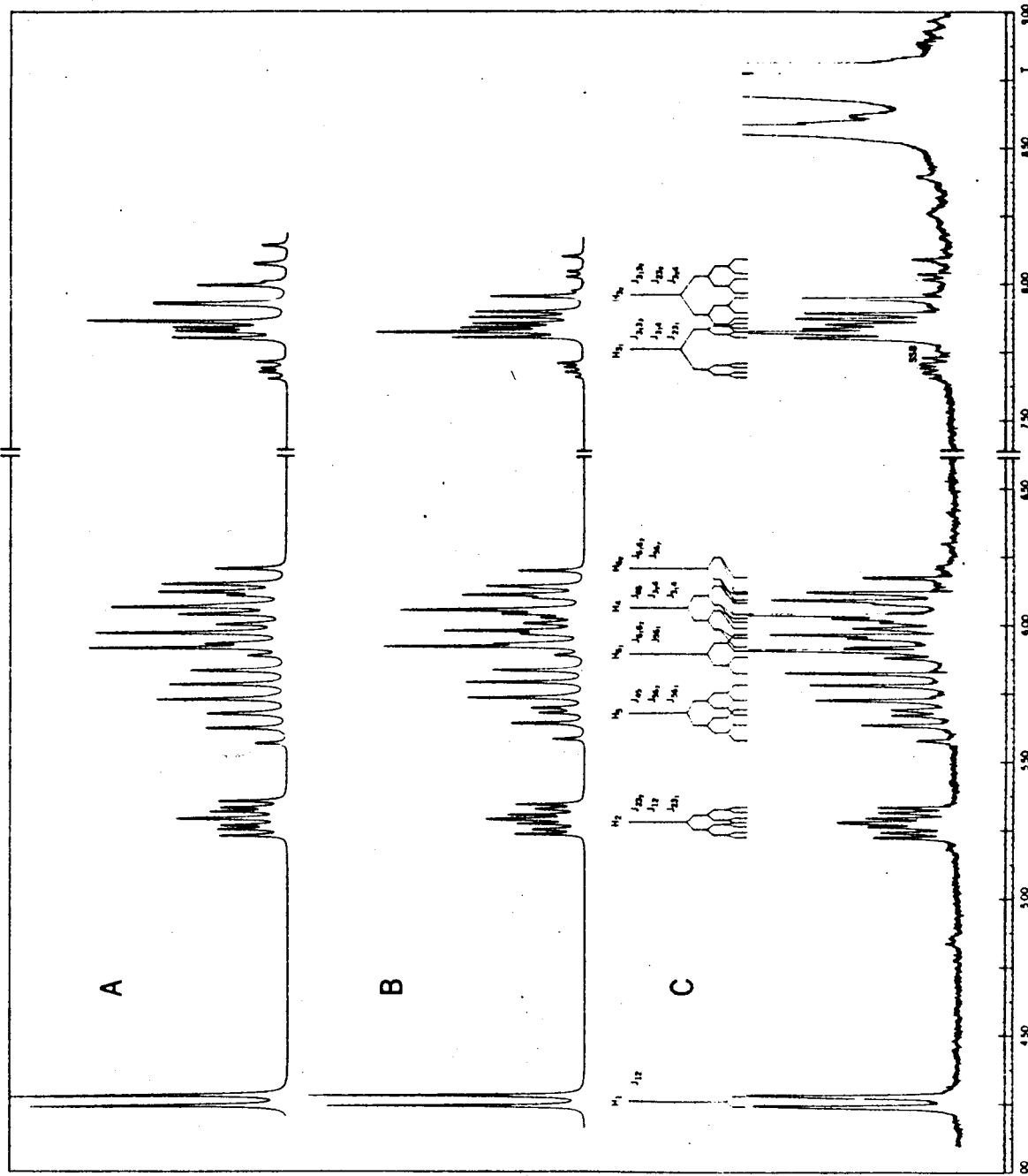
their NMR spectra and their molecular architecture, the four 3-deoxy-1,2;5,6-di-$\underline{O}$-isopropylidene-$\underline{D}$-hexofuranoses can be dealt with as two pairs, 3-deoxy-$\underline{D}$-ribohexofuranose (17) and 3-deoxy-$\underline{D}$-lyxohexofuranose (18); 3-deoxy-$\underline{D}$-xylohexofuranose (19) and 3-deoxy-$\underline{D}$-arabinohexofuranose (20). The NMR coupling parameters for these compounds are listed in Table XI.

Considering first 3-deoxy,1,2;5,6-di-$\underline{O}$-isopropylidene-α-$\underline{D}$-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 Φ_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-$\underline{O}$-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
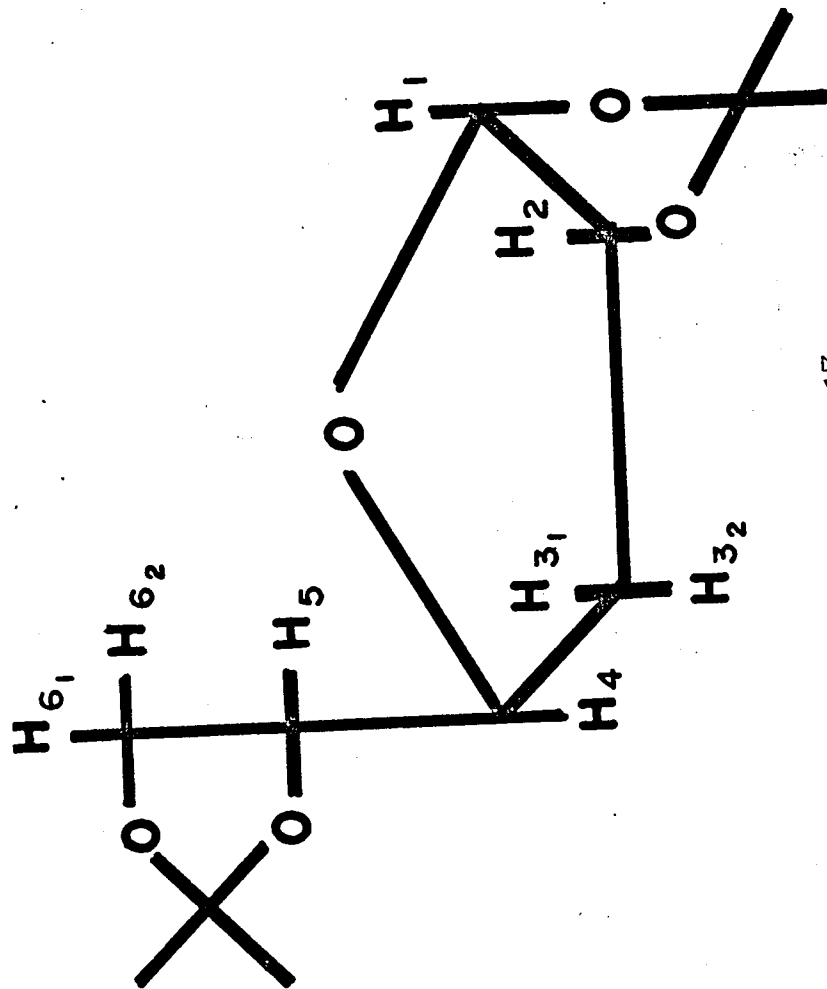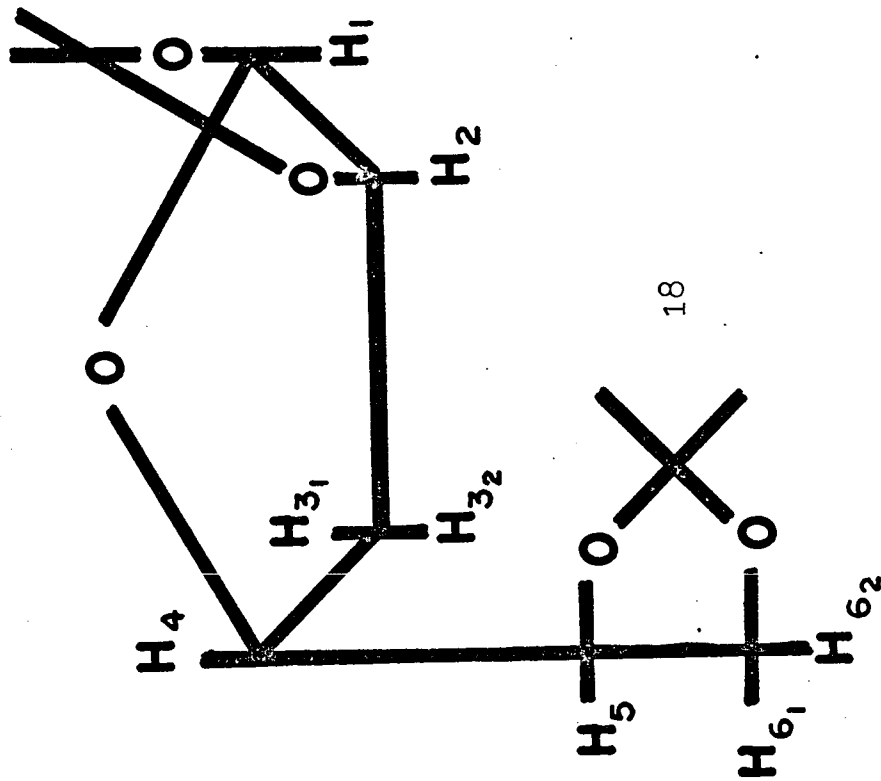
a α-ribo (17)   b β-lyxo (18)

Figure 6-2

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

a α-xylo (19)   b β-arabino (2C)

20

19
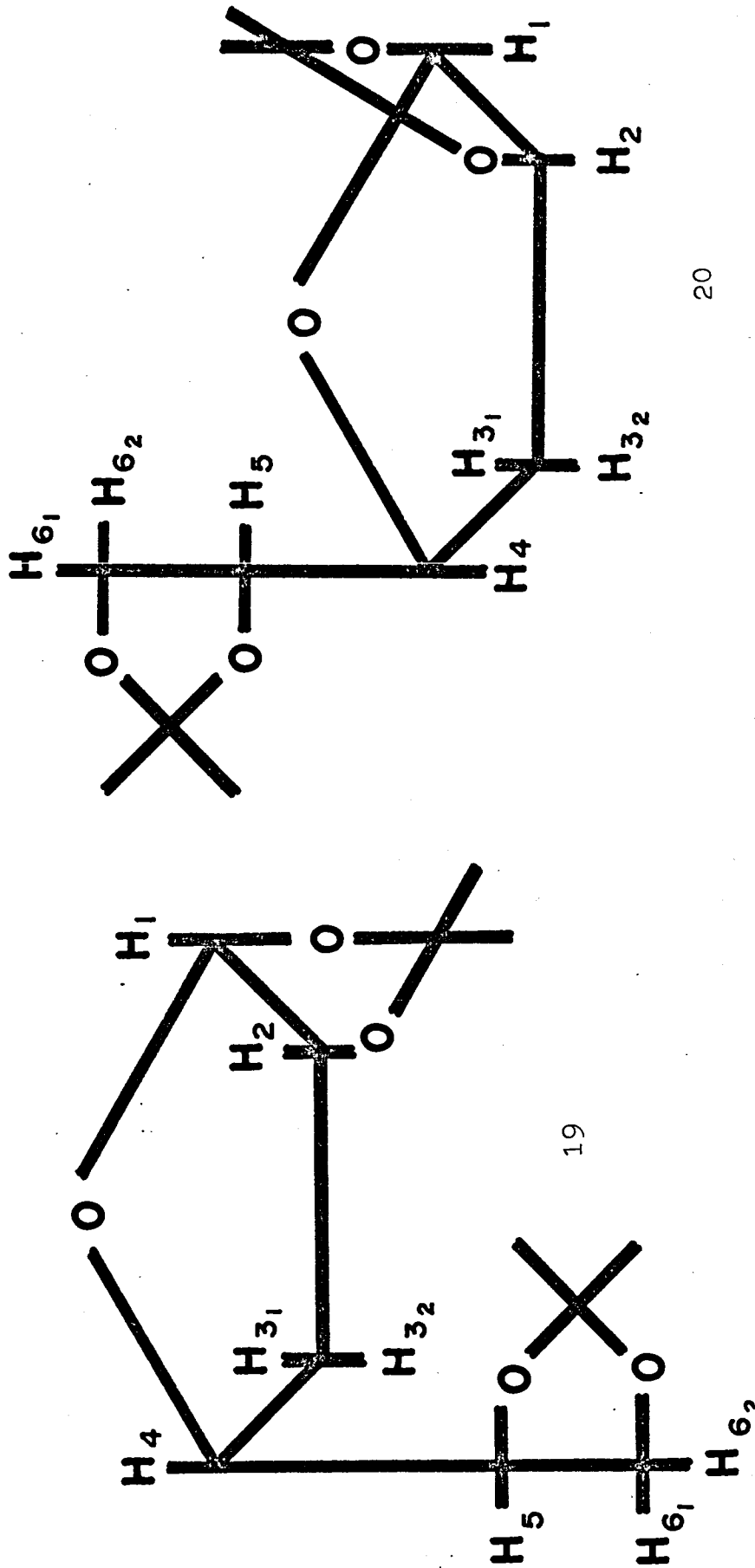
Table XI

Proton Couplings in the 3-Deoxy-1,2;5,6-di-O-isopropylidene-$\underline{D}$-hexoses*

Compound	$J_{1,2}$	$J_{2,3_1}$	$J_{2,3_2}$	$J_{3_1,3_2}$	$J_{3_1,4}$	$J_{3_2,4}$	$J_{4,5}$	$J_{5,6_1}$	$J_{5,6_2}$	$J_{6_1,6_2}$
17	3.68	4.79	0.41	-13.41	9.98	3.94	-	-	-	-
18†	3.52	0.55	4.76	-13.11	4.52	10.62	5.51	6.56	6.81	-8.28
19	3.78	6.30	1.35	-14.20	8.45	4.13	8.14	6.71	6.91	-8.27
20†	3.76	0.82	6.24	-14.74	2.63	8.45	9.65	6.13	5.61	-9.08

* All spectra run in CDCl₃ at 100 MHz; J's in Hz; iterative computer analyzed couplings.

† Measurements obtained from 220 MHz spectrum.

Table XII

DAERM Analysis* of Couplings in 19

Protons Coupled	Case	Observed J-1	Observed J-2	Calc θ-1	Calc θ-2	Calc k_1	Calc k_2
H-2,H-3$_1$,H-3$_2$	i	1.35	6.30	58	182	5.93	6.59
	ii	1.35	6.30	72	52	17.27	19.19
	iii	6.30	1.35	6	118	6.65	7.39
	iv	6.30	1.35	52	72	17.27	19.19
H-3$_1$,H-3$_2$,H-4	v	4.13	8.45	43	167	8.27	9.19
	vi	4.13	8.45	67	57	29.21	32.46
	vii	8.45	4.13	8	132	8.90	9.89
	viii	8.45	4.13	57	67	29.21	32.46

* $\omega = 124°$, $k_1/k_2 = 0.9$

Table XIII

Variation of ω and k_1/k_2 in Dihedral Angle Estimation*

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

ω	k_1/k_2	$J_{3_1,4}$	$J_{3_2,4}$	$\varphi_{3_1,4}$	$\varphi_{3_2,4}$	k_1	k_2
130°	0.9	8.45	4.13	2	132	8.7	9.7
124°	0.7	8.45	4.13	2	126	8.7	12.5
124°	0.8	8.45	4.13	5	129	8.8	11.0
124°	0.9	8.45	4.13	8	132	8.9	9.9
124°	1.0	8.45	4.13	10	134	9.0	9.0
120°	0.9	8.45	4.13	11	131	9.1	10.1
110°	0.9	8.45	4.13	19	129	9.8	10.9

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

Figure 7

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

iii/vii

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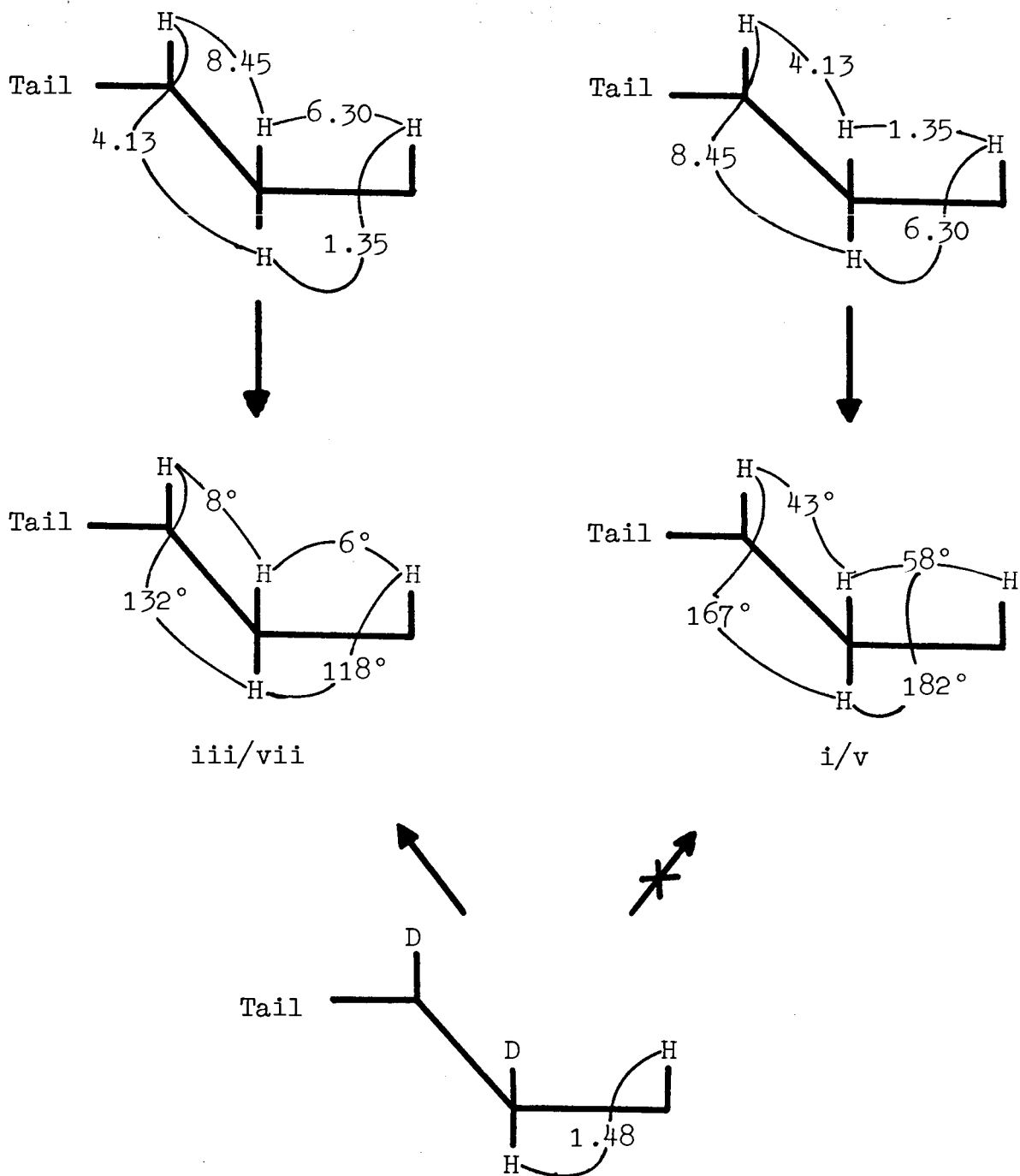
indicates a conformation in which the 'tail' involves less steric interactions than in (iii/vii) but requires a rather severe distortion towards the envelope ^2V form. The latter solution (iii/vii) appears less distorted although there are eclipsing interactions between the furan ring substituents.

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 Φ_1 as the cis coupling and dihedral angle, respectively.

By analogy with the 3-deoxy-xylohexofuranose (19) derivative, the resonances in 3-deoxy-1,2;5,6-di-O-isopropylidene-β-D-arabinohexofuranose (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-α-D-xylohexofuranose (19) prefers a conformation $V_0 \rightleftarrows {}^1T_0 \rightleftarrows {}^1V$, where the conformational symbols are those defined by Hall and coworkers (83). The β-D-arabino derivative, 20, appears to have the ${}^OT_1 \rightleftarrows V_1 \rightleftarrows {}^2T_1$ 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
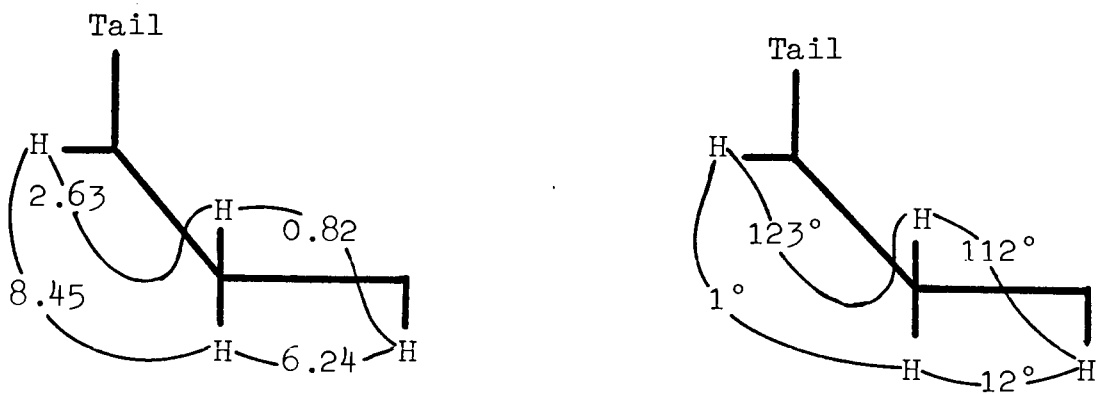
Calculated Karplus Constants

$$C\text{-}2 - C\text{-}3 \quad k_1 = 6.79, \ k_2 = 7.55$$
$$C\text{-}3 - C\text{-}4 \quad k_1 = 8.73, \ k_2 = 9.70$$

these molecules and inspection of molecular models indicates that the H_1-H_2 dihedral angle is probably not more than 10° and may well be considerably less.

Since the value of ω = 124° has been estimated, the effect of varying ω over a twenty degree range was investigated. Evidence is presented in Table XIII which indicates that conformational assignments are not appreciably changed by varying ω through reasonable limits. Similarly, variation of the value k_1/k_2, 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 H_2 to H_3 proton must have a corresponding cis coupling from that H_3 proton to H_4. 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

Figure 9

DAERM Analysis of 3-Deoxy-1,2;5,6-di-_O_-iso-

propylidene-β-_D_-lyxohexose

iii/v   iv/v
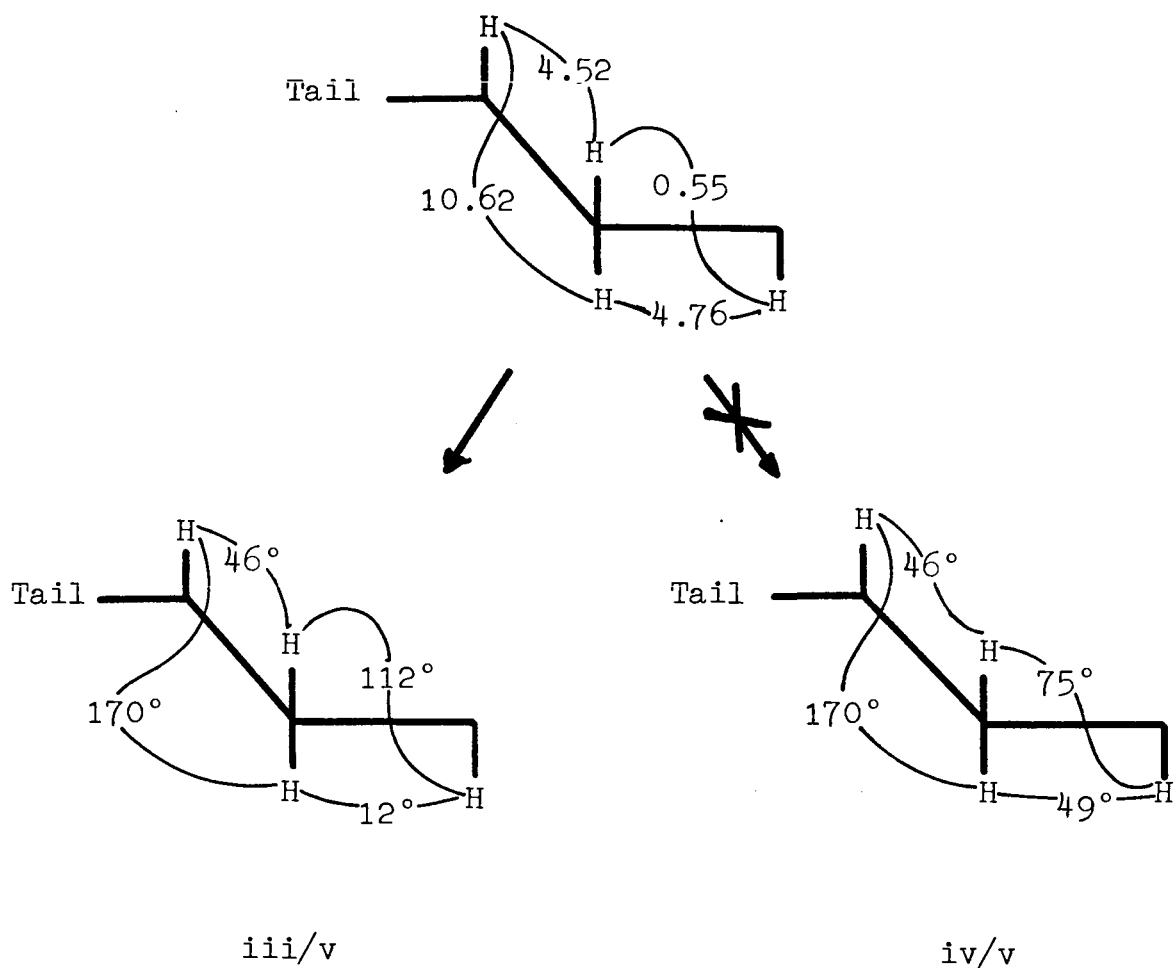
Table XIV

DAERM Analysis* of Couplings in

3-Deoxy-1,2;5,6-di-O-isopropylidene-β-D-lyxohexofuranose (18)*

Protons Coupled	Case	Observed $J-1$	Observed $J-2$	Calc $\theta-1$	Calc $\theta-2$	Calc k_1	Calc k_2
$H-2, H-3_1, H-3_2$	i	0.55	4.76	65	189	4.65	5.17
	ii	0.55	4.76	75	49	11.87	13.19
	iii	4.76	0.55	12	112	5.26	5.85
	iv	4.76	0.55	49	75	11.87	13.19
$H-3_1, H-3_2, H-4$	v	4.52	10.62	46	170	10.09	11.21
	vi	4.52	10.62	68	56	34.61	38.46
	vii	10.62	4.52	5	129	10.98	12.20
	viii	10.62	4.62	56	68	34.61	38.46

* $\omega = 124°$, $k_1/k_2 = 0.9$

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 $^4T_3 \rightleftarrows ^4V \rightleftarrows ^4T_0$.

DAERM calculations and similar reasoning yield the conformation of the remaining compound, 3-deoxy--1,2;5,6-di-$\underline{O}$-isopropylidene-α-$\underline{D}$-$\underline{ribo}$hexofuranose (17). The conformation of this derivative is very similar to the $\underline{lyxo}$ 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 $^3T_4 \rightleftarrows V_4 \rightleftarrows ^0T_4$ (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.; C_2/C_3, k_1 = 6.; and C_3/C_4, k_1 = 9. Hz.

Two main points emerge from these conformational studies of the 3-deoxy-1,2;5,6-di-$\underline{O}$-isopropylidene-$\underline{D}$--hexofuranoses. Firstly, the conformations of the furan ring in the four compounds fall into two classes. The

Figure 10

Conformation of

3-Deoxy-1,2;5,6-di-O-isopropylidene-α-D-ribohexo-
furanose
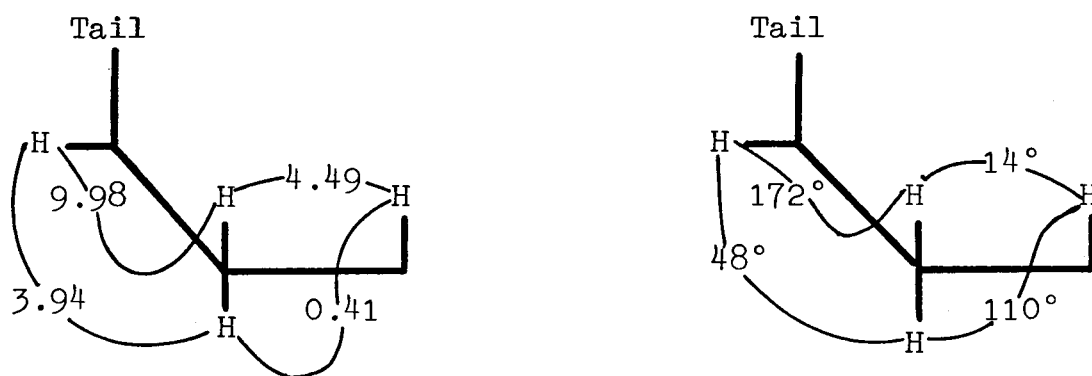
Calculated Karplus Constants

C-2 - C-3 $k_1 = 5.39$, $k_2 = 5.99$
C-3 - C-4 $k_1 = 9.42$, $k_2 = 10.46$

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 des-
cribed as $V_0 \rightleftarrows {}^1T_0 \rightleftarrows {}^1V$ and ${}^0T_1 \rightleftarrows V_1 \rightleftarrows {}^2T_1$ 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 ${}^3T_4 \rightleftarrows V_4 \rightleftarrows {}^0T_4$ and ${}^4T_3 \rightleftarrows {}^4V \rightleftarrows {}^4T_0$ 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 crystal-
lographic analysis (58) of 3-chloro-3-deoxy-1,2;5,6-
-di-O-isopropylidene-β-D-idofuranose clearly shows C_4
to be out of the plane. The furan ring in the chloro-
idose derivative closely approximates the ${}^4V$ conformation
on the crystalline state. A computer drawn represen-
tation 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 des-
cribing 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 con-
formations 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-iso-
propylidene-β-D-idose in the Crystalline State.
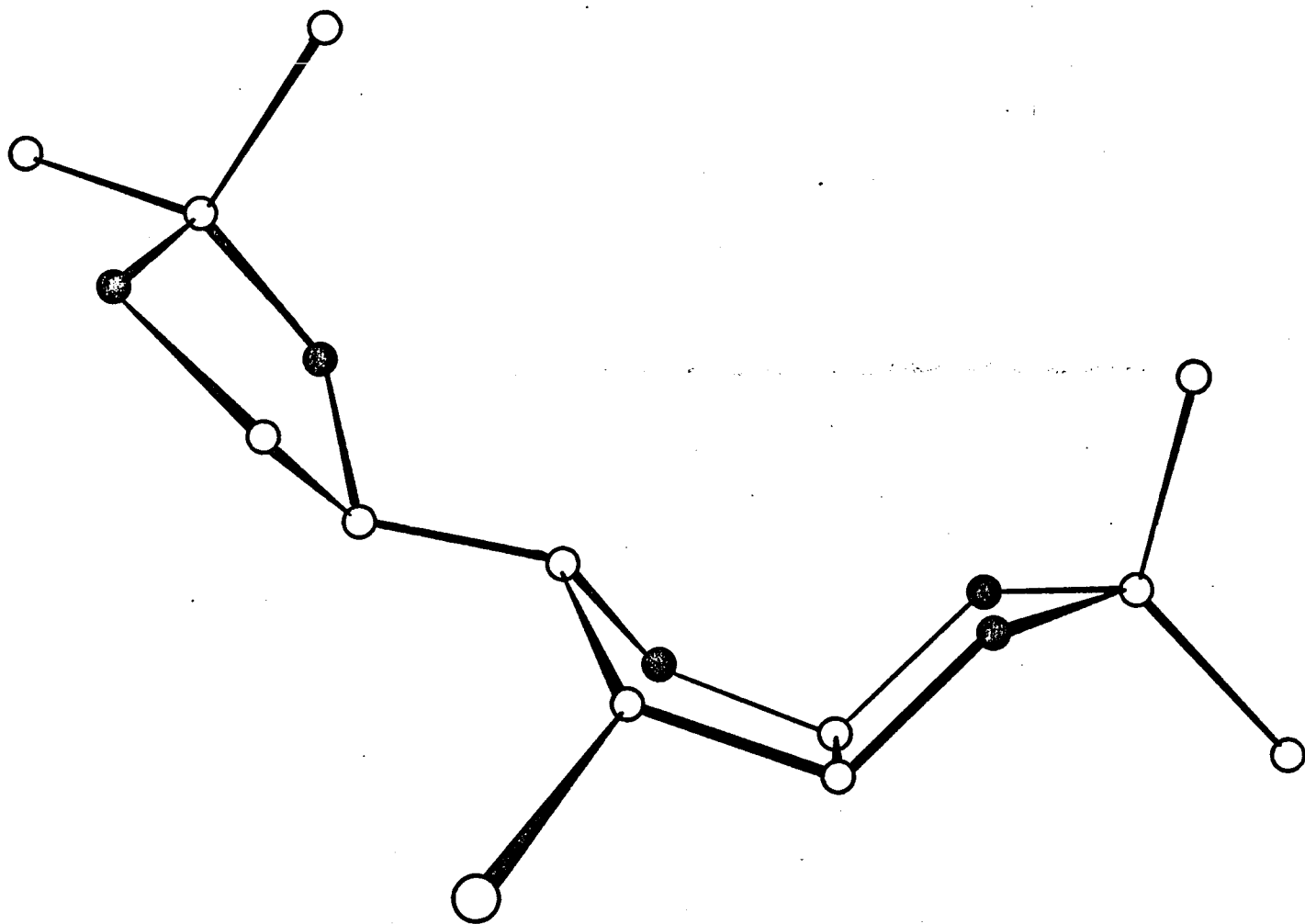
O Carbon   ● Oxygen   O Chlorine

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° 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-β-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-O-isopropylidene-D-hexoses

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

* $k_1/k_2 = 0.9$.

† $b/a = -0.053$.

Figure 12

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

Figure 12-1
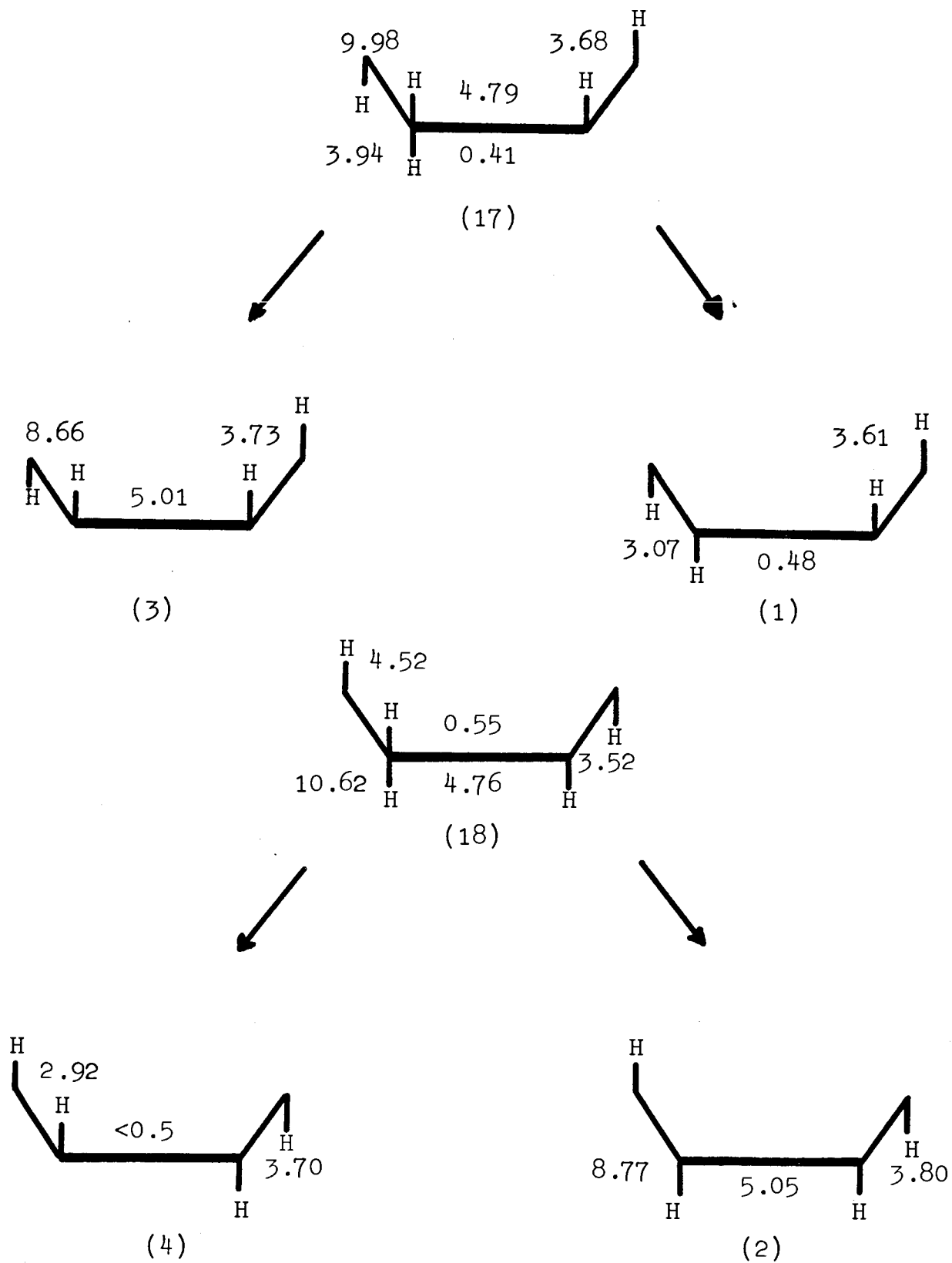
Figure 12-2
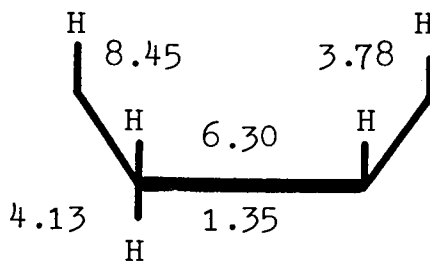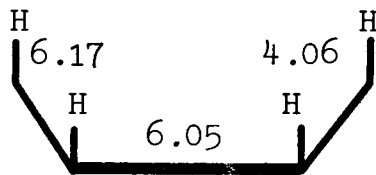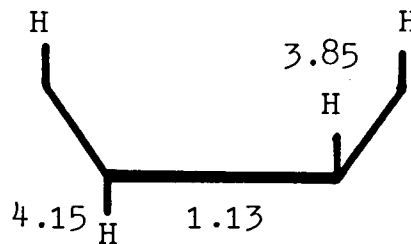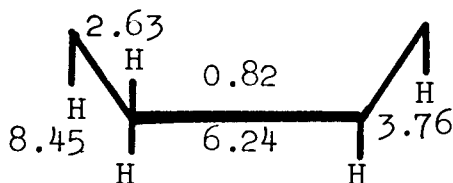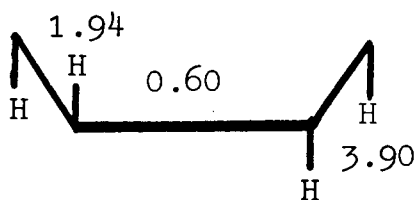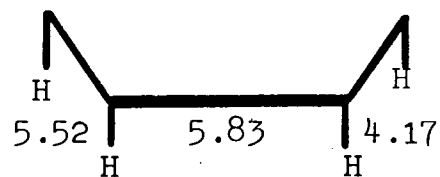
B-3. Diacetone Hexoses.

1,2;5,6-Di-O-isopropylidene-α-D-ribohexofuranose derivatives

1,2;5,6-Di-O-isopropylidene-α-D-glucofuranose (1)
and -α-D-allofuranose (3) are the exo and endo hydroxylated
derivatives of 3-deoxy-1,2;5,6-di-O-isopropylidene-α-
-D-ribohexofuranose (17). The latter compound has been
assigned a conformational preference of $^3T_4 \rightleftarrows V_4 \rightleftarrows {}^OT_4$ on
the basis of DAERM calculations and the similarity of
the couplings outlined in Figure 12 leads us to believe
that the allose and glucose derivatives have essentially
the same conformational preference. The 7.3 Hz coupling
into the hydroxyl group of 1,2;5,6-di-O-isopropylidene-
-α-D-allofuranose (3) indicates an anti arrangement
of the H_3 and the hydroxyl proton since the magnitudes
of H-C-O-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-O-H
and the 2-O 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 tetra-
chloride solution. The NMR parameters are consistent
with the molecule, (1), being in the assigned confor-
mation and such a configuration readily allows formation
of the hydrogen bond to the 'tail'. In the allose
compound, (3), the coupling constant, $J_{4,5}$ of 4.55 Hz,
probably reflects the freedom of rotation of the 'tail'
whereas in glucose (1) the coupling constant, $J_{4,5}$
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 assign-
ment of $^3T_4 \rightleftharpoons V_4 \rightleftharpoons {}^0T_4$ for the conformational preference
of the glucose (1) and allose (3) derivatives.

1,2;5,6-Di-O-isopropylidene-β-D-lyxohexofuranose derivatives

    1,2;5,6-Di-O-isopropylidene-β-D-idofuranose (2)
and -β-D-talofuranose (4) are assigned the conformation
$^4T_3 \rightleftharpoons {}^4V \rightleftharpoons {}^4T_0$ of the parent 1,2;5,6-di-O-isopropylidene-
-β-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-O-isopropylidene-β-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-O-isopropylidene-β-D-lyxohexofuranose family
(18, 2, 4) are fully expected to share the $^4T_3 \rightleftharpoons {}^4V \rightleftharpoons {}^4T_0$
conformational preference. The ^4V conformation has
been found for 3-chloro-3-deoxy-1,2;5,6-di-O-isoprop-
ylidene-β-D-idofuranose from crystal structure analysis
(58) in agreement with the NMR results.

1,2;5,6-Di-O-isopropylidene-α-D-xylohexofuranose derivatives

    1,2;5,6-Di-O-isopropylidene-α-D-galactofuranose (5)
and -α-D-gulofuranose (7) are assigned a conformational
preference of $V_0 \rightleftharpoons {}^1T_0 \rightleftharpoons {}^1V$ on the basis of this assign-

ment for the 3-deoxy analogue (19), 1,2;5,6-di-$\underline{O}$-iso-
propylidene-α-$\underline{D}$-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 with-
in this family indicates a similar conformational pre-
ference. A coupling of about 8 Hz for the $J_{4,5}$ coup-
lings 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 galac-
tose (5) derivatives cannot form such a bond.

1,2;5,6-Di-$\underline{O}$-isopropylidene-β-$\underline{D}$-arabinohexofuranose family

The conformations of 1,2;5,6-di-$\underline{O}$-isopropylidene-
-β-$\underline{D}$-altrofuranose (6) and -β-$\underline{D}$-mannofuranose (8) are
assigned a conformational preference of ${}^{O}T_{1} \rightleftharpoons V_{1} \rightleftharpoons {}^{2}T_{1}$ by
analogy with the couplings of the 3-deoxy-arabinohexo-
furanose 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 $J_{4,5}$ 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 $O-C_6-C_5-O$ 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-O-isopropylidene Group
Analysis of $J_{5,6_1}$ $J_{5,6_2}$ Couplings

1,2;5,6-Di-O isopropylidene		Observed J-1	Observed J-2	Calculated Φ_1	Calculated Φ_2	Calculated k_1	Calculated k_2
-α-D-glucose	(1)	6.50	5.95	23	147	8.0	8.9
-β-D-idose	(2)	6.93	6.89	25	149	8.8	9.8
-α-D-allose	(3)	6.68	6.61	25	149	8.5	9.4
-β-D-talose	(4)	7.61	6.50	21	145	9.1	10.1
-α-D-galactose	(5)	7.15	6.70	23	147	8.8	9.8
-β-D-altrose	(6)	6.25	5.50	22	146	7.6	8.4
-α-D-gulose	(7)	7.20	6.50	23	147	8.8	9.7
-β-D-mannose	(8)	6.41	5.70	22	146	7.8	8.7
-3-deoxy-α-D-xylo-hexofuranose	(19)	6.91	6.72	24	148	8.7	9.6
-3-deoxy-β-D-arabino-hexofuranose	(20)	5.70	5.71	25	149	7.3	8.1

* $\omega = 124°$, $k_1 / k_2 = 0.9$.

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 D-C_4 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_6 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-α-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

1,2;5,6-Di-O-isopropylidene		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6_1}$	$J_{5,6_2}$	$J_{6_1,6_2}$
-α-D-ribohexofuranos-3-ulose	(9a)	4.4	N.C.†	N.C.	-	-	-	-
-α-D-ribohexofuranos-3-ulose. hydrate	(9b)	3.80	N.C.	N.C.	6.66	6.58	6.04	8.90
-β-D-lyxohexofuranos-3-ulose	(10)	4.40	N.C.	N.C.	1.85	7.62	6.95	8.41
-α-D-xylohexofuranos-3-ulose	(11)	4.4	N.C.	N.C.	6.08	6.39	6.91	8.50
-β-D-arabinohexofuranos-3-ulose	(12)	4.3	N.C.	N.C.	~6.	-	-	-
3-O-Acetyl-α-D-glucose	(21)	3.7	~0.5	~2.0	-	-	-	-
3-O-Acetyl-β-D-idose	(22)	3.8	0.6	2.3	-	-	-	-
3-O-Acetyl-α-D-allose	(23)	3.7	-	-	-	6.5	5.8	8.6
3-O-Acetyl-β-D-talose	(24)	3.8	-	-	-	-	-	-
3-O-Acetyl-α-D-galactose	(25)	3.8	~0.7	2.56	7.84	6.66	6.92	8.66
3-O-Acetyl-β-D-altrose	(26)	3.78	0.70	1.16	9.67	6.14	4.80	9.03
3-O-Acetyl-α-D-gulose	(27)	4.11	5.58	6.66	9.04	6.55	7.19	8.30
3-O-Acetyl-β-D-mannose	(28)	4.02	5.75	5.92	8.48	6.50	5.22	8.42

* CDCl$_3$ 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 $V_0 \rightleftharpoons {}^1T_0 \rightleftharpoons {}^1V$ of the parent to the ${}^1T_0 \rightleftharpoons {}^1V \rightleftharpoons {}^1T_2$ 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_2^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-O-isopropylidene-D-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-O-isopropylidene-α-D-galactofuranose. Sign determination was simplified by deuterium decoupling. The absolute values of some of the long range couplings are indicated in Table XVIII.

Table XVIII

Long Range Couplings*

1,2;5,6-Di-O-isopropylidene		$J_{1,3}$	$J_{2,4}$
-α-D-glucose	(1)	-	~0.
-β-D-altrose	(6)	-	~0.4
-β-D-lyxohexofuranos-3-ulose	(10)	N.C.	1.15
-α-D-xylohexofuranos-3-ulose	(11)	N.C.	0.8
-β-D-arabinohexofuranos-3-ulose	(12)	N.C.	0.9
3-deoxy-β-D-arabinohexofuranose	(20)	..5	-
3-O-Acetyl-β-D-idose	(22)	-	~0.
3-O-Acetyl-β-D-altrose	(26)	0.64	0.41

* 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-$\underline{O}$-isopropylidene-
-$\underline{D}$-hexoses. These studies demonstrate clearly that the
furan conformation is determined by the substitution
pattern of the 1,2-$\underline{O}$-isopropylidene unit and the 'tail'.
If the units are substituted on the furan ring in a
$\underline{cis}$ fashion, the ring tends to be flattened with one
or two of the atoms; C_1, C_2, and the ring oxygen, dis-
placed from the mean plane. If, however, the units are
substituted on the furan ring in a $\underline{trans}$ fashion, the
ring is considerably more distorted with one or two of
the atoms; C_3, C_4, and the ring oxygen, displaced in the
preferred conformers.

Two crystal structures exhibiting this $\underline{trans}$
arrangement ($\underline{58}$, $\underline{91}$) both show C_4 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 ($\underline{16}$). Again, x-ray structures confirm our
work, having O_1-C_1-C_2-O_2 torsional angles of 4.5° ($\underline{58}$),
9.0° ($\underline{91}$), and 4.6° ($\underline{92}$). Only gross distortion of the
tetrahedral nature of the position 1 and 2 carbons
would allow the H_1-C_1-C_2-H_2 torsional angle to be sig-
nificantly 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-C_5;D-C_4 configuration than for the D-C_5;L-C_4 configuration. This effect is most readily explained if it is assumed that the preferred rotamer of the 'tail' is one in which the C_5-oxygen is on the same side of the molecule as the C_1 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-C_5;D-C_4 case, the C_4 and C_5 protons are near eclipsed instead of near anti as suggested by other workers (103) for 1,2;5,6-di-O-isopropylidene-α-D-gluco-
furanose. On the other hand, the anti-configuration would be found in the D-C_5;L-C_4 case. This leaves the C_4 position more open to attack in the D-C_5;D-C_4 cases (ribo and arabino ketones) and provides more steric interaction in the D-C_5;L-C_4 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. H_4 and H_5 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 D_2O, indicating that the 'tail', now no longer forming a hydrogen bond to the C_3 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 H_5 to $H_6{}_1$, $H_6{}_2$ couplings (Table XVI). The $\underline{D}-C_5;\underline{D}-C_5$ configuration always affords a smaller calculated Karplus constant than the corresponding $\underline{D}-C_5;\underline{L}-C_4$ configuration. Similarly the $H_3{}_1$, $H_3{}_2$ to H_4 couplings exhibit a similar effect, the $\underline{D}-C_5;\underline{D}-C_4$ configuration providing smaller Karplus constants than for the alternate case.

DAERM calculations on the H_5 to $H_6{}_1$, $H_6{}_2$ 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.

Chapter 4

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 IR 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% H_2SO_4
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°, $[\alpha]_D$ -17.5° (c, 0.4, water). Lit. (93), 110-111°,
$[\alpha]_D$ -18.5° (c, 5, water).

1,2;5,6-Di-O-isopropylidene-α-D-ribohexofuranos-3-ulose (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°, $[\alpha]_D$ 37.5° (c, 0.4, water). Lit. (29), m.p. 108-110°,
$[\alpha]_D$ 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°, $[\alpha]_D$ 34°(c, 0.4,
water). Lit. (29), m.p. 76-77°, $[\alpha]_D$ 37.7° (c, 0.5, water).

* Periodate is added only if the blank RuO_2 is reformed
  after each addition of periodate.

1,2;5,6-Di-O-isopropylidene-β-D-idofuranose (2)

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-O-isopropylidene derivative
using zinc chloride (12 g), 85% phosphoric acid (0.5 ml)
in dry acetone (100 ml). The solution was stirred over-
night 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 chloro-
form (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-O-isopropylidene derivative, presumably the 1,2;5,6
furanose 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-O-isopropylidene-β-D-idofuranose (3.5 g),
m.p. 151-152°, [α]$_D$ 33.5° (c, 0.4, acetone). Lit. (36),
m.p. 151-152.5°, [α]$_D$ 36.0° (acetone).

1,2;5,6-Di-O-isopropylidene-β-D-lyxohexofuranose-3-ulose (10)

1,2;5,6-Di-O-isopropylidene-β-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° ($\underline{c}$, 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-$\underline{O}$-isopropylidene-β-$\underline{D}$-talofuranose (4)

1,2;5,6-Di-$\underline{O}$-isopropylidene-β-$\underline{D}$-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° ($\underline{c}$, 0.40, CHCl₃). Lit. ($\underline{30}$), m.p. 85-86°, $[\alpha]_D$ -25° ($\underline{c}$, 0.47, CHCl₃).

1,2;5,6-Di-$\underline{O}$-isopropylidene-α-$\underline{D}$-galactofuranose (5)

Prepared by hydroboration of 3-deoxy-1,2;5,6-di-
$\underline{O}$-isopropylidene-α-$\underline{D}$-erythrohexofuran-3-enose as described by Paulsen and Behre ($\underline{38}$), m.p. 94-95°, $[\alpha]_D$ -20.5° ($\underline{c}$, 0.4, CHCl₃). Lit., m.p. 97.5-98°, $[\alpha]_D$ -35.3 ($\underline{c}$, 0.8, methanol).

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

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
(45ml). 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 ob-
tained by extracting the aqueous solution once with chloro-
form (50 ml). Crystalline product (10 g of long needles)
was obtained melting at 58-59°. $[\alpha]_D^{22}$ -32° (c, 0.95, $CHCl_3$).
Lit. (27), m.p. 62-63°, $[\alpha]_D^{20}$ -33° (c, 1, $CHCl_3$).

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 $CHCl_3$ (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, CHCl₃).

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

Catalytic reduction of 3-O-acetyl-1,2;5,6-di-O-
-isopropylidene-α-D-erythrohexofuran-3-enose (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-α-D-gulofuranose
(2.7 g), m.p. 76-77°, recrystallized from petroleum ether
(65-110°). $[\alpha]_D$ 66.0° (c 0.36, CHCl₃). Calculated for
C₁₄H₂₂O₇: C, 55.62%, H, 7.33%. Found: C, 55.43%, H, 7.16%.

1,2;5,6-Di-O-isopropylidene-α-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, CHCl₃). Lit. (94). m.p. 105-106°,
$[\alpha]_D$ 7.5° (c, 1, CHCl₃).

1,2;5,6-Di-O-isopropylidene-α-D-xylohexofuranos-3-ulose (11)

1,2;5,6-Di-O-isopropylidene-α-D-gulofuranose (7)
(1.1 g) was oxidized by the RuO₂/IO₄⁻ 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 $C_{12}H_{18}O_6$: C, 55.8%; H, 6.96%. Found:
C, 55.63%; H, 6.89%.

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

Sirupy D-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-β-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-β-D-arabinohexofuranos-3-ulose (12)

1,2;5,6-Di-O-isopropylidene-β-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). Vaccuum distillation of the sirup (b.p.$_{0.01}$ 87°) gave
a colourless liquid which crystallized spontaneously. Re-
crystallization from petroleum ether (65-110°) gave
material (1.1 g) melting at 31-32°. $[\alpha]_D$ 21.7° (c, 0.45,
water). Calculated for $C_{12}H_{18}O_6$: C, 55.80%; H, 6.96%.
Found: C, 55.59%; H, 7.09%.

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

Borohydride reduction of 1,2;5,6-di-O-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). Recrystal-
lization of the product from petroleum ether (65-110°)
gave material (400 mg) melting at 52-53°. $[\alpha]_D$ 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-O-isopropylidene-β-D-threohex-3-enose (14)

Method A

1,2;5,6-Di-O-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 chloro-
form (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°, $[\alpha]_D^{20}$ 43.4° (c, 0.87, CHCl₃).
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-O-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-O-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-O-Acetyl-1,2;5,6-di-O-isopropylidene-α-D-erythrohex-trans--4-enose (15)

Method A

3-O-Acetyl-1,2;5,6-di-O-isopropylidene-α-D-erythro-hex-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°, $[\alpha]_D^{22}$ 67.8° (c, 0.814, CHCl$_3$). Anal. Calcd. for C$_{14}$H$_{20}$O$_7$: 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-erythro-
hex-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 CO_2 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°,$[\alpha]_D^{22}$ -19.0° (c, 0.918 CHCl₃). Anal. Calcd. for
$C_{12}H_{18}O_6$: 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-threohex-
-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 chroma-
tography have been unsuccessful.

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

3-O-Acetyl-1,2;5,6-di-O-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°, $[\alpha]_D^{22}$ -22.6° (c,
0.866, CHCl$_3$). Anal. Calcd. for C$_{14}$H$_{22}$O$_7$: C, 55.63%;
H, 7.28%. Found: C, 55.43%; H, 7.13%.

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

3-O-Acetyl-1,2;5,6-di-O-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 CO$_2$ 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-$\underline{O}$-isopropylidene-
-β-$\underline{D}$-mannofuranose prepared previously. M.p. and mixed
m.p. 52-53°, [α]$_D$ 12.3° ($\underline{c}$, 0.83, water).

3-$\underline{O}$-Acetyl-1,2;5,6-di-$\underline{O}$-isopropylidene-α-$\underline{D}$-glucofuranose (21)

1,2;5,6-Di-$\underline{O}$-isopropylidene-α-$\underline{D}$-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 acetyl-
ating 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]$_D^{22}$ -38.4 ($\underline{c}$, 1.07, CHCl$_3$). Lit. (98),
m.p. 62°, [α]$_D^{24}$ -38.5 ($\underline{c}$, 1.3, CHCl$_3$).

3-$\underline{O}$-Acetyl-1,2;5,6-di-$\underline{O}$-isopropylidene-β-$\underline{D}$- idofuranose (22)

Prepared from 2 in the same way as 21. M.p. 75.5-
76.5°, [α]$_D^{22}$ +16.6°, ($\underline{c}$, 0.67, CHCl$_3$). Lit. (100), for
the -$\underline{L}$-isomer, m.p. 77-78°, [α]$_D^{15}$ -12° ($\underline{c}$, 0.75, CHCl$_3$).

3-$\underline{O}$-Acetyl-1,2;5,6-di-$\underline{O}$-isopropylidene-α-$\underline{D}$-allofuranose (23)

Prepared from 3 in the same way as 21. M.p. 74-75°,
[α]$_D^{22}$ 100.6° ($\underline{c}$, 0.73, CHCl$_3$). Lit. (99), m.p. 75.5-76.5°,
[α]$_D^{20}$ 107.6 ($\underline{c}$, 1.0, CHCl$_3$).

3-$\underline{O}$-Acetyl-1,2;5,6-di-$\underline{O}$-isopropylidene-β-$\underline{D}$-talofuranose (24)

Prepared from (4) in the same way as (21) except that (24) did not crystallize. $[\alpha]_D^{22}$ -7.4° ($\underline{c}$, 0.38, CHCl₃). Anal. Calcd. for $C_{14}H_{22}O_7$: C, 55.63%; H, 7.28%. Found: C, 55.84%; H, 7.32%.

3-$\underline{O}$-Acetyl-1,2;5,6-di-$\underline{O}$-isopropylidene-α-$\underline{D}$-galactofuranose (25)

Prepared from (5) in the same way as (21) except that (25) did not crystallize. $[\alpha]_D^{22}$ -7.5° ($\underline{c}$, 1.47, CHCl₃). Anal. Calcd. for $C_{14}H_{22}O_7$: C, 55.63%; H, 7.28%. Found: C, 55.50%; H, 7.15%.

3-$\underline{O}$-Acetyl-1,2;5,6-di-$\underline{O}$-isopropylidene-β-$\underline{D}$-altrofuranose (26)

Prepared from (6) in the same way as (21). M.p. 92-93°, $[\alpha]_D^{22}$ 14.4° ($\underline{c}$, 0.68, CHCl₃). Anal. Calcd. for $C_{14}H_{22}O_7$: C, 55.63%; H, 7.28%. Found: C, 55.48%; H, 7.37%.

3-Deoxy-1,2;5,6-di-$\underline{O}$-isopropylidene-α-$\underline{D}$-xylohexofuranose (19)

3-$\underline{O}$-Acetyl-1,2;5,6-di-$\underline{O}$-isopropylidene-α-$\underline{D}$-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 CO_2 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°, $[\alpha]_D^{22}$ -27.4°, (c, 0.972, $CHCl_3$). Lit. (50), m.p. 81°, $[\alpha]_D^{22}$ -38.1, (c, 4.11, ethanol).

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

Method A

3-O-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-iso--propylidene-β-D-mannofuranose (28). The deacetylated sirup was dissolved in water (15 ml) and extracted with petroleum ether (65-110°) (6x100 ml). The extracts were combined, dried over magnesium sulfate, filtered and evaporated. The product was distilled under high vaccuum

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, CHCl$_3$).

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, CHCl$_3$).
Lit. (52), sirup, [α]$_D^{20}$ 21.1°, (c, 1.5, CHCl$_3$). Anal.
Calcd. for C$_{12}$H$_{20}$O$_5$: C, 59.02%; H, 8.16%. Found:
C, 58.91%; H, 8.07%.

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

-galactofuranose

3-Deoxy-1,2;5,6-di-O-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-O-isopropylidene-α-D-allofuranose

3-Deuterio-1,2;5,6-di-O-isopropylidene-α-D-allo-
furanose (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,j
the solution was filtered, then evaporated to a sirup.
Vacuum distillation gave a mobile sirup which was redis-
tilled (b.p.$_{0.005}$ 78°) to provide 2.7 g of 3-chloro-3-
-deoxy-3-deuterio-1,2;5,6-di-O-isopropylidene-α-D-allo-
furanose. The chlorodeuterio sugar (500 mgm) was refluxed
with lithium aluminum hydride (500 mgm) in tetrahydro-
furan (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°, $[\alpha]_D^{18}$ -5.7 (c 4.2, ethanol) for the
non-deuterated compound.

Methyl 4,6-O-benzylidine-3-deoxy-α-D-erythrohexopyranosid-2-ulose

Methyl 4,6-O-benzylidine-3-deoxy-α-D-arabinohexo-
pyranoside (m.p. 109-110°, [α]$_D^{22}$ 96 (c 0.42, CHCl$_3$).
Lit. (52), [α]$_D^{22}$ 107.3 (c 0.94, CHCl$_3$), m.p. 111-112°)
(2 g) was dissolved in carbon tetrachloride (50 ml).
NaHCO$_3$ (80 mgm) in H$_2$O (20 ml) was added, followed by
RuO$_2$ (50 mgm). NaIO$_4$ (5% in H$_2$O) was added dropwise to
the continuously stirred solution. When the reaction mixture
went yellow (approximately 1/2 ml NaIO$_4$ 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]$_D^{22}$ 99°. Lit. (54), m.p. 114-115°, [α]$_D^{22}$ 109
(c 2, CHCl$_3$).

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

Methyl 4,6-O-benzylidene-3-deoxy-α-D-erythrohexo-
pyranosid-2-ulose was reduced with sodium borohydride
to provide the desired product (55). M.p. 185-186°,
[α]$_D^{22}$ 121° (c 0.39, CHCl$_3$). Lit. (54), m.p. 191-192°,
[α]$_D^{22}$ 115.8 (c 1.21, CHCl$_3$).

APPENDIX

Derivation of equation (V)

Solution for case B

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

Substitution of $\cos\omega\cos\phi_1 + \sin\omega\sin\phi_1$ for $\cos(\omega-\phi_1)$ then squaring gives

$$\frac{J_1 + c}{J_2 + c} = \frac{k_1}{k_2} \frac{\cos^2\phi_1}{\cos^2\omega\cos^2\phi_1+\sin^2\omega\sin^2\phi_1+2\sin\omega\cos\omega\sin\phi_1\cos\phi_1}$$

Dividing top and bottom of the right hand side of the equation by $\cos^2\phi_1$ gives

$$\frac{J_1 + c}{J_2 + c} = \frac{k_1}{k_2} \frac{1}{\cos^2\omega+\sin^2\omega\tan^2\phi_1+2\sin\omega\cos\omega\tan\phi_1}$$

Rearrangement of this equation provides

$$\sin^2\omega\tan^2\phi_1+2\sin\omega\cos\omega\tan\phi_1+\cos^2\omega - \frac{k_1}{k_2}\left(\frac{J_2 + c}{J_1 + c}\right) = 0$$

Solution of this quadratic for $\tan\phi_1$ gives the expression (V)

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

The following is the listing for the computer program DAERM which utilizes the equation V.

DAERM

```
C     DAERM
C     CALCULATION OF KARPLUS CONSTANTS AND ANGLES FOR METHYLENE FUNCTIONS.
C     UTILIZES THE EQUATION J=K*COS*COS-C
C
C     1.   CONTROL CARD. FORMAT(3F10.3)
C          RATIO,ANG,CON
C          RATIO  KARPLUS RATIO K1/K2
C               =0.9 FROM VALENCE BOND CALCULATIONS
C               IS PROBABLY LESS THAN THIS IF ELECTRONEGATIVE SUBSTITUENTS
C               ARE PRESENT.
C          ANG  ESTIMATED OMEGA VALUE
C               =120 FOR TETRAHEDRAL GEOMETRY.
C          CON  THIRD KARPLUS CONSTANT.
C               =0.23 FROM VALENCE BOND CALCULATIONS.
C
C     2.   TITLE  FORMAT(20A4)
C          TITLE  A TITLE OF UP TO 80 CHARACTERS.
C
C     3.   COUPLING CONSTANTS  FORMAT(2F10.4)
C          A1,A2
C          A1  THE FIRST COUPLING CONSTANT INTO THE METHYLENE GROUP.
C          A2  THE SECOND COUPLING INTO THE METHYLENE GROUP.
C               AN UNLIMITED NUMBER OF CARDS MAY BE USED HERE.
C               A NEGATIVE VALUE FOR A1 SENDS CONTROL BACK TO CARD 2 SO THAT
C               FURTHER HEADINGS MAY BE INSERTED IF REQUIRED.
C
C     4.   JOB IS TERMINATED BY A NEGATIVE VALUE FOR A2.
C
      DIMENSION EDIT(4),ANGL(4),THET(4)
      DIMENSION TITLE(20)
      READ(5,99)RATIO,ANG,CON
99    FORMAT(3F10.3)
      WRITE(6,101)RATIO,ANG,CON
101   FORMAT(1H1,16HKARPLUS RATIO IS,F8.3,41H  SUM OR DIFFERENCE OF DIHE
     1DRAL ANGLES IS,F8.1,28H  SECOND KARPLUS CONSTANT IS,F8.3)
200   READ(5,1,END=2)TITLE
1     FORMAT(20A4)
      WRITE(6,4)TITLE
4     FORMAT('0',20A4)
100   READ(5,15)A1,A2
15    FORMAT(2F10.4)
      IF(A1.LT.0) GO TO 200
      IF(A2.LT.0.0)GO TO 2
      SUM=(A2+CON)/(A1+CON)
      IF(SUM.LT.0.0)GO TO 10
      SUM=RATIO*(A2+CON)/(A1+CON)
      IF(SUM.LT.0.0)GO TO 10
      GO TO 11
10    WRITE(6,90)
90    FORMAT(' SUM UNDER SQRT IS NEGATIVE')
      GO TO 100
11    SUM=SQRT(SUM)
```

```
      SUM=SQRT(SUMB)
      ANGI=ANG*3.1416/180.
      ROOT(1)=(-COS(ANGI)+SUM)/SIN(ANGI)
      ROOT(2)=-(COS(ANGI)+SUM)/SIN(ANGI)
      ROOT(3)=(COS(ANGI)-SUMB)/SIN(ANGI)
      ROOT(4)=(COS(ANGI)+SUMB)/SIN(ANGI)
      I=0
   20 I=I+1
      IF(I.GT.4)GO TO 100
  502 ANGL(I)=ATAN(ROOT(I))
      IF(ANGL(I).LT.0.0)GO TO 20
C     CALCULATION OF KARPLUS CONSTANTS
      B1=(A1+COS0)/(COS(ANGL(I))*COS(ANGL(I)))
      B2=B1/RATIO
  70  THET(I)=ANGL(I)*180./3.1416
  13  IF (I.GT.2) GO TO 80
C     THETA PLUS PHI EQUALS THE SUM OF THE DIHEDRAL ANGLES
      PHI=ANG-THET(I)
  81  WRITE(6,62)ANG
  62  FORMAT( ' SUM OF DIHEDRAL ANGLES IS EQUAL TO',F8.1)
      WRITE(6,6)
      WRITE(6,61)A1,A2,THET(I),PHI,B1,B2
      GO TO 2
  80  PHI=ANG+THET(I)
  811 WRITE(6,63)ANG
  63  FORMAT( ' DIFFERENCE OF DIHEDRAL ANGLES IS',F8.1)
      WRITE(6,6)
   6  FORMAT(2X,'CIS COUPLING',5X,'TRANS COUPLING',5X,'CIS ANGLE',5X,'TR
     1ANS ANGLE',8X,'K1',10X,'K2')
      WRITE(6,61)A1,A2,THET(I),PHI,B1,B2
  61  FORMAT(F10.2,F13.2,F17.2,F15.2,F15.2,F11.2/)
      GO TO 2
  14  CONTINUE
   2  STOP
      END
```

Derivation of equation (VII)

$$\frac{J_1 + c}{J_2 + c} = \frac{a \cos^2\Phi_1 + b \cos\Phi_1}{a \cos^2(\omega-\Phi_1) + b \cos(\omega-\Phi_1)}$$

dividing top and bottom by 'a' provides

$$\frac{J_1 + c}{J_2 + c} = \frac{\cos^2\Phi_1 + b/a \cos\Phi_1}{\cos^2(\omega-\Phi_1) + b/a \cos(\omega-\Phi_1)}$$

$$= \frac{\cos^2\Phi_1 + b/a (\cos^2\Phi_1)/\cos\Phi_1}{\cos^2(\omega-\Phi_1) + b/a \cos(\omega-\Phi_1)}$$

Expansion of $\cos(\omega-\Phi_1)$ followed by division by $\cos^2\Phi_1$ gives the expression

$$\frac{J_1 + c}{J_2 + c} = \frac{1 + b/a (1/\cos\Phi_1)}{\cos^2\omega + \sin^2\omega \tan^2\Phi_1 + 2\sin\omega \cos\omega \tan\Phi_1 + b/a\cos\omega(1/\cos\Phi_1)}$$

$$+ b/a \sin\omega \tan\Phi_1 (1/\cos\Phi_1)$$

This can be rewritten as

$$\sin^2\omega \tan^2\Phi_1 + \tan\Phi_1 (2\sin\omega \cos\omega + b/a \sin\omega/\cos\Phi_1) + \cos^2\omega$$

$$+ b/a \cos\omega/\cos\Phi_1 - J_2+c/J_1+c (1 + b/a (1/\cos\Phi_1)) = 0$$

which on solution of the quadratic in $\tan\Phi_1$ provides the solution (VII) which can be solved by an iterative process as utilized in DAERM II.

DAERM II

Computer Program Utilizing Equation VII

```
C   DAERM II
C   CALCULATION OF KARPLUS CONSTANTS AND ANGLES FOR METHYLENE FUNCTIONS.
C   UTILIZES THE EQUATION J=A*COS*COS+B*COS-C
C   OBTAINS SOLUTIONS BY AN ITERATIVE TECHNIQUE
C
C   1.   CONTROL CARD. FORMAT(3F10.3)
C        RATIO,EOV,C
C        RATIO  KARPLUS RATIO B/A
C               =-0.053 FOR K1/K2=0.9
C               =-0.111 FOR K1/K2=0.8
C               =-0.177 FOR K1/K2=0.7
C        EOV  ESTIMATED OMEGA VALUE
C               =120 FOR TETRAHEDRAL GEOMETRY.
C        C   THIRD KARPLUS CONSTANT.
C               =0.28 FROM VALENCE BOND CALCULATIONS.
C
C   2.   TITLE   FORMAT(20A4)
C        TITLE   A TITLE OF UP TO 80 CHARACTERS.
C
C   3.   COUPLING CONSTANTS   FORMAT(2F10.4)
C        A1,A2
C        A1   THE FIRST COUPLING CONSTANT INTO THE METHYLENE GROUP.
C        A2   THE SECOND COUPLING INTO THE METHYLENE GROUP.
C             AN UNLIMITED NUMBER OF CARDS MAY BE USED HERE.
C             A NEGATIVE VALUE FOR A1 SENDS CONTROL BACK TO CARD 2 SO THAT
C             FURTHER HEADINGS MAY BE INSERTED IF REQUIRED.
C
C   4.   JOB IS TERMINATED BY A NEGATIVE VALUE FOR A2.
C
        DIMENSION TITLE(20)
        READ(5,99)RATIO,EOV,C
99      FORMAT(3F10.3)
        WRITE(6,101)RATIO,EOV,C
101     FORMAT(1H1,16H KARPLUS RATIO IS,F8.3,41H  SUM OR DIFFERENCE OF DIHE
       1DRAL ANGLES IS,F5.1,28H  SECOND KARPLUS CONSTANT IS,F8.3)
200     READ(5,1,END=22)TITLE
1       FORMAT(20A4)
        WRITE(6,4)TITLE
4       FORMAT('0',20A4)
100     READ(5,15)A1,A2
15      FORMAT (2F10.4)
        IF(A1.LT.0) GO TO 200
        IF(A2.LT.0.0)GO TO 22
        I=0
        ANGI=EOV*3.14159/180.
5       IF(I.GE.5)GO TO 100
        ANG=0.0
        RAT=0.0
        J=0
```

```
10      SUM=(RAT*RAT)/(COS(ANG)*COS(ANG))+4*((A2+C)/(A1+C))*(1+RAT/COS(ANG
       3))
        IF(SUM.GE.0.0) GO TO 6
        WRITE(6,80)
80      FORMAT( 'SUM UNDER SQRT IS NEGATIVE')
        GO TO 100
6       J=J+1
        SUM=SQRT(SUM)
50      IF(I-1)11,21,30
30      IF(I-3)31,41,100
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.0.001)GO TO 7
        IF(J.GE.10)GO TO 7
9       RAT=RATIO
        ANG=ANGL
        GO TO 10
7       I=I+1
        IF(ANGL.LT.0.0)GO TO 5
        A=(A1+C)/(COS(ANGL)*COS(ANGL)+COS(ANGL)*RAT)
        B=A*RAT
        THET=ANGL*180./3.14159
        IF((I-2).LE.0)GO TO 111
        GO TO 12
111     PHI=EQV-THET
        WRITE(6,90)SUM,J
90      FORMAT( ' THE SUM OF DIHEDRAL ANGLES IS EQUAL TO',F8.1,' THE NUMBE
       1R OF CYCLES IS',I3)
        WRITE(6,8)
8       FORMAT(2X,'CIS COUPLING',5X,'TRANS COUPLING',5X,'CIS ANGLE',5X,'TR
       1ANS ANGLE',6X,'A',11X,'B')
        WRITE(6,61)A1,A2,THET,PHI,A,B
61      FORMAT(F17.2,F15.2,F17.2,F15.2,F15.2,F11.2/)
        GO TO 5
12      PHI=EQV+THET
        WRITE(6,92)SUM,J
92      FORMAT( ' THE DIFFERENCE OF DIHEDRAL ANGLES IS EQUAL TO ',F8.1,' T
       2HE NUMBER OF CYCLES IS',I3)
        WRITE(6,8)
        WRITE(6,61)A1,A2,THET,PHI,A,B
        GO TO 5
14      CONTINUE
22      STOP
        END
```

Figure 13

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-O-isopropylidene-D-hexofuranoses

1,2;5,6-Di-O-isopropylidene		H_1	H_2	H_3	H_4	H_5	H_{6_1}	H_{6_2}
-α-D-glucose	(1)†	4.17	5.51	5.84	5.96	5.69	5.97	6.11
-β-D-idose	(2)	4.03	5.50	5.81	5.88	5.55	5.85	6.07
-α-D-allose	(3)	4.21	5.40	5.98	6.17	5.71	5.95	6.01
-β-D-talose	(4)	4.20	5.43	6.13	6.24	5.81	5.95	6.04
-α-D-galactose	(5)	4.13	5.45	5.90	6.13	5.64	5.93	6.16
-β-D-altrose	(6)	4.11	5.46	5.60	6.18	5.74	5.90	6.08
-α-D-gulose	(7)	4.23	5.35	5.73	6.09	5.49	6.32	6.37
-β-D-mannose	(8)	4.30	5.33	5.71	6.14	5.43	5.88	6.03

*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

1,2;5,6-Di-O-isopropylidene		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6_1}$	$J_{5,6_2}$	$J_{6_1,6_2}$	J_{H_3OH}**
-α-D-glucose	(1)†	3.61	0.48	3.07	7.27	6.46	5.95	8.60	4.3
-β-D-idose	(2)	3.70	<0.5	2.92	5.31	6.89	6.93	8.37	4.1
-α-D-allose	(3)	3.73	5.01	8.66	4.55	6.61	6.68	8.57	7.3
-β-D-talose	(4)	3.80	5.05	8.77	4.97	6.50	7.61	8.26	9.0
-α-D-galactose	(5)	3.85	1.13	4.15	7.48	6.70	7.15	8.67	4.0
-β-D-altrose	(6)	3.90	0.60	1.94	9.51	6.25	5.49	8.94	4.0
-α-D-gulose	(7)	4.06	6.05	6.17	8.80	6.64	7.30	8.66	6.3
-β-D-mannose	(8)	4.17	5.83	5.52	8.36	6.41	5.69	8.76	5.2

*CDCl$_3$ solutions at room temperature in Hz.

†acetone-d$_6$ solution.

**J_{H_3OH} not computer analyzed.

Table XXI

Proton Chemical Shifts* for

3-O-Acetyl-1,2;5,6-di-O-isopropylidene-D-Hexofuranoses

1,2;5,6-Di-O-isopropylidene		H_1	H_2	H_3	H_4	H_5	H_{6_1}	H_{6_2}
-α-D-ribohexofuranos-3-ulose	(9a)	3.88	5.62	----	6.0	5.68	5.94	6.04
-α-D-ribohexofuranos-3-ulose.hydrate	(9b)	4.18	5.72	----	6.08	5.57	5.86	5.91
-β-D-lyxohexofuranos-3-ulose	(10)	3.88	5.61	----		5.56 to	6.03	
-α-D-xylohexofuranos-3-ulose	(11)	3.94	5.49	----	5.85	5.66	5.90	6.03
-β-D-arabinohexofuranos-3-ulose	(12)	3.99	5.53	----	5.82	5.65		6.0
3-O-Acetyl-α-D-glucose	(21)	4.16	5.54	4.77		5.75 to	6.05	
3-O-Acetyl-β-D-idose	(22)	4.04	5.50	4.82		5.70 to	6.35	
3-O-Acetyl-α-D-allose	(23)	4.22	5.16	5.16	----	5.75 to	5.96	6.14
3-O-Acetyl-β-D-talose	(24)	4.17	5.21	5.21	----	5.80 to	6.13	
3-O-Acetyl-α-D-galactose	(25)	4.11	5.42	5.10	6.15	5.55	5.97	6.17
3-O-Acetyl-β-D-altrose	(26)	4.13	5.44	4.68	6.02	5.68	5.91	6.05
3-O-Acetyl-α-D-gulose	(27)	4.20	5.19	4.92	5.93	5.39	5.91	6.45
3-O-Acetyl-β-D-mannose	(28)	4.29	5.24	4.83	5.98	5.50	5.92	6.03

*   CDCl₃ solution with TMS as internal standard (10.0τ).

Table XXII

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

1,2;5,6-Di-O-isopropylidene	H	H_1	H_2	H_{3_1}	H_{3_2}	H_4	H_5	H_{6_1}	H_{6_2}
3-Deoxy-α-D-ribohexofuranose	(17)	4.21	5.27	7.83	8.26	5.88	6.18	~5.9	~5.9
3-Deoxy-β-D-lyxohexofuranose	(18)	4.20	5.28	8.01	8.29	5.75	5.87	5.96	6.18
3-Deoxy-α-D-xylohexofuranose	(19)	4.22	5.27	7.78	8.16	5.90	5.58	5.97	.6.39
3-Deoxy-β-D-arabinohexofuranose	(20)	4.28	5.29	7.68	7.81	6.02	5.71	5.91	6.13

Table XXIII

Proton Chemical Shifts for

the Unsaturated Sugar Derivatives

1,2;5,6-Di-O-isopropylidene

		H_1	H_2	H_3	H_4	H_5	H_{6_1}	H_{6_2}
3-O-Acetyl-α-D-erythrohex-3-enose	(13)	3.94	4.66	----	----	5.26	5.95	6.06
3-O-Acetyl-β-D-threohex-3-enose	(14)	4.09	5.12	4.35	---	----	5.47	5.50
3-O-Acetyl-α-D-erythrohex-trans-4-enose	(15)	3.96	4.61	---	---	5.31	5.88	6.01
3-O-Acetyl-α-L-erythrohex-cis-4-enose	(16)*	4.03	5.10	4.58	---	----	5.48	5.48

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

Table **XXIV**

Proton Coupling Constants for
the Unsaturated Sugar Derivatives

1,2;5,6-Di-O-isopropylidene		$J_{1,2}$	$J_{2,3}$	$J_{2,5}$	$J_{3,6_1}$	$J_{3,6_2}$	$J_{5,6_1}$	$J_{5,6_2}$	$J_{6_1,6_2}$
3-O-Acetyl-α-D-erythro-hex-3-enose	(13)	5.42	----	|0.48|	----	----	6.84	6.32	-8.18
3-O-Acetyl-β-D-threo-hex-3-enose	(14)	5.40	----	----	----	----	6.81	6.93	-8.23
3-O-Acetyl-α-D-erythro-hex-trans-4-enose	(15)	4.07	4.18	----	2.06	2.07	----	----	-16.06

COMPOUND INDEX

Number	Compound Name	Structure	Pages in Thesis Synthesis	NMR	IR
1.	1,2;5,6-di-O-isopropylidene- -α-D-glucofuranose		89	76	12,79
2	1,2;5,6-di-O-isopropylidene- -β-D-idofuranose		8,90	76	12,79
3	1,2;5,6-di-O-isopropylidene- -α-D-allofuranose		89	76	12
4	1,2;5,6-di-O-isopropylidene- -β-D-talofuranose		8,91	77	12
5	1,2;5,6-di-O-isopropylidene- -α-D-galactofuranose		8,91	77	9
6	1,2;5,6-di-O-isopropylidene- -β-D-altrofuranose		7,94	78	9
7	1,2;5,6-di-O-isopropylidene- -α-D-gulofuranose		6,19,93	77	9

Nr.	Struktur				Verbindung
8		8,19	78	13,79	1,2;5,6-di-O-isopropylidene--β-D-mannofuranose
9		7,89	82	14	1,2;5,6-di-O-isopropylidene--α-D-ribohexofuranos-3-ulose
10		8,90	82	—	1,2;5,6-di-O-isopropylidene--β-D-lyxohexofuranos-3-ulose
11		7,93	82	—	1,2;5,6-di-O-isopropylidene--α-D-xylohexofuranos-3-ulose
12		7	82	—	1,2;5,6-di-O-isopropylidene--β-D-arabinohexofuranos-3-ulose
13		15,92	81	—	3-O-acetyl-1,2;5,6-di-O-iso-propylidene-α-D-erythrohex--3-enose

No.	Structure	Ref.			Name
14		15,22	—	—	3-O-acetyl-1,2;5,6-di-O-iso-propylidene-β-D-threohex-3-enose
15		19	20	21	3-O-acetyl-1,2;5,6-di-O-iso-propylidene-α-D-erythrohex-trans-4-enose
16		22	23	—	3-O-acetyl-1,2;5,6-di-O-iso-propylidene-α-L-erythrohex-cis-4-enose
17		26	66	—	3-deoxy-1,2;5,6-di-O-iso-propylidene-α-D-ribohexo-furanose
18		26	63	—	3-deoxy-1,2;5,6-di-O-iso-propylidene-β-D-lyxohexo-furanose

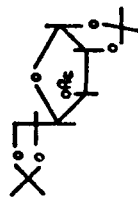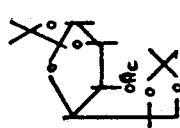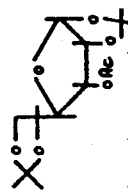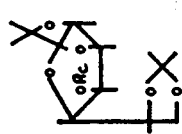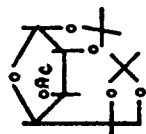| No.	Structure			
19	3-deoxy-1,2;5,6-di-O-iso-propylidene-α-D-xylohexo-furanose	24,100	54	—
20	3-deoxy-1,2;5,6-di-O-iso-propylidene-β-D-arabino-hexofuranose	25,101	61	—
21	3-O-acetyl-1,2;5,6-di-O-iso-propylidene-α-D-glucofuranose	99	81	—
22	3-O-acetyl-1,2;5,6-di-O-iso-propylidene-β-D-idofuranose	99	81	—
23	3-O-acetyl-1,2;5,6-di-O-iso-propylidene-α-D-allofuranose	99	81	—

№	Name		81		%
24	3-O-acetyl-1,2;5,6-di-O-iso-propylidene-β-D-talofuranose	—	81		100
25	3-O-acetyl-1,2;5,6-di-O-iso-propylidene-α-D-galactofuranose	—	81		100
26	3-O-acetyl-1,2;5,6-di-O-iso-propylidene-β-D-altrofuranose	—	81		100
27	3-O-acetyl-1,2;5,6-di-O-iso-propylidene-α-D-gulofuranose	—	81		19,93
28	3-O-acetyl-1,2;5,6-di-O-iso-propylidene-β-D-mannofuranose	—	81		22,98

References

1. W. G. Proctor and F. C. Yu, Phys. Rev. 81 20 (1951).

2. E. L. Hahn and D. E. Maxwell, Phys. Rev. 84 1246 (1951).

3. H. S. Gutowski and D. W. McCall, Phys. Rev. 82 748 (1951).

4. N. F. Ramsey, Phys. Rev. 91 303 (1953).

5. H. M. McConnell, J. Chem. Phys. 24 460 (1956).

6. M. Karplus and D. H. Anderson, J. Chem. Phys. 30 6 (1959).

7. M. Karplus, J. Chem. Phys. 30 11 (1959).

8. R. U. Lemieux, R. K. Kullnig, N. J. Bernstein, and
    W. G. Schneider, J. Amer. Chem. Soc. 80 6098 (1958).

9. F. A. L. Anet, Can. J. Chem. 39 789 (1961).

10. N. Conroy, Adv. Org. Chem. 2 265 (1960).

11. R. C. Fahey, G. C. Graham, and R. L. Piccioni, J. Amer.
    Chem. Soc. 88 193 (1966).

12. G. E. Maciel, J. W. McIver, Jr., N. S. Ostlund, and
    J. A. Pople, J. Amer. Chem. Soc. 92 4497 (1970).

13. A. A. Bothner-By and R. E. Glick, J. Chem. Phys. 25
    362 (1956).

14. K. L. Williamson, J. Amer. Chem. Soc. 85 516 (1963).

15. M. Karplus, J. Amer. Chem. Soc. 85 2870 (1963).

16. R. J. Abraham, L. D. Hall, L. Hough, and K. A. McLauchlin,
    J. Chem. Soc. 3699 (1962).

17. R. J. Abraham and K. A. McLauchlin, Molec. Phys. 5
    513 (1962).

18. R. U. Lemieux, J. D. Stevens, and R. R. Fraser, Can.
    J. Chem. 40 1955 (1962).

19. D. H. Williams, and N. S. Bhacca, J. Amer. Chem. Soc.
    86 2742 (1964).

20. L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry' (Pergamon Press 1969), p. 283.

21. J. S. Brimacombe, A. B. Foster, R. Hems, J. H. Westwood, and L. D. Hall, Can. J. Chem. 48 3946 (1970).

22. B. Coxon, Carbohyd. Res. 12 313 (1970).

23. L. Hough, A. C. Richardson, 'Rodd's Chemistry of Carbon Compounds, Vol. 1, Part F, Sec. Ed., S. Coffey, Editor (Elsevier Publishing Company 1967), p. 156.

24. A. N. DeBelder, Advan. Carbohyd. Chem. 20 220 (1965).

25. S. A. Barker and E. J. Bourne, Advan. Carbohyd. Chem. 7 137 (1952).

26. (a) E. H. Cordes, 'Progress in Physical Organic Chemistry' Vol. 4, A. Streitwieser and R. W. Taft, Eds., (Interscience Publishers, Inc., 1967), p.1
(b) P. M. Collins, Tetrahedron 21 1809 (1965).

27. W. Meyer zu Reckendorf, Angew. Chem. Int. Ed. 6 177 (1967).

28. E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, 'Conformational Analysis', (Interscience Publishers, Inc., 1965), p. 417.

29. O. Theander, Acta. Chem. Scand. 18 2209 (1964).

30. W. Bosshard, Helv. Chim. Acta. 18 482 (1935).

31. O. Th. Schmidt, Methods Carbohyd. Chem. 2 319 (1963).

32. (a) H. Nakata, Tetrahedron 19 1959 (1963).
(b) V. M. Parikh and J. K. N. Jones Can. J. Chem. 43 3452 (1965).

33. N. K. Richtmyer, Methods Carbohyd. Chem. 1 107 (1962).

34. J. G. Buchanan and J. Conn, J. Chem. Soc. 201 (1965).

35. H. Paulsen, W-P. Trautwein, F. G. Espinosa, and K. Heyns, Chem. Ber. 100 2822 (1967).

36. K. Iwadare, Bull. Chem. Soc. Jap. 19 27 (1944).

37. J. S. Brimacombe and P. A. Gent, Carbohyd. Res. 9 231 (1969).

38. H. Paulsen and H. Behre, Carbohyd. Res. 2 80 (1966).

39. G. M. Cree and A. S. Perlin, Can. J. Biochem. 46 765 (1968).

40. C. R. Haylock, Optical Rotary Dispersion of the 1,2;5,6-Di-0-isopropylidene-D-hexofuranoses. B.Sc. Thesis, Simon Fraser University, Burnaby, B.C. (1969).

41. H. Spedding, Advan. Carbohyd. Chem. 19 23 (1964).

42. K. Nakanishi, 'Infrared Absorption Spectroscopy', (Holden-Day, Inc. and Nankodo Company, Ltd, 1962), p. 30.

43. L. P. Kuhn, P. von R. Schleyer, W. F. Batinger, Jr., and L. Eberson, J. Amer. Chem. Soc. 86 650 (1964).

44. H. O. House, 'Modern Synthetic Reactions', (W. A. Benjamin, Inc. 1965), p. 166.

45. K. N. Slessor and A. S. Tracey, Can. J. Chem. 47 3989 (1969).

46. J. Herling, J. Shabtai, and E. Gil-Av, J. Amer. Chem. Soc. 87 4107 (1965).

47. R. J. Abraham, L. D. Hall, L. Hough, and K. A. McLauchlin, J. Chem. Soc. 3699 (1962).

48. D. C. DeJongh and K. Biemann, J. Amer. Chem. Soc. 86 67 (1964).

49. P. N. Rylander, 'Catalytic Hydrogenation Over Platinum Metals', (Academic Press, 1967), p. 96.

50. F. Weygand and H. Wolz, Chem. Ber. 85 315 (1952).

51. G. Rembarz, Chem. Ber. 93 622 (1960).

52. G. Rembarz, J. Prakt. Chem. 19 315 (1963).

53. J. Prokop and D. H. Murray, J. Pharm. Science 57 1697 (1968).

54. D. A. Prins, J. Amer. Chem. Soc. 70 3955 (1948).

55. K. Antonakis, Bull. Soc. Chim. Fr. 1 122 (1969).

56. A. Rosenthal and P. Catsoulacos, Can. J. Chem. 47 2747 (1969)

57. C. R. Haylock, L. D. Melton, K. N. Slessor, and
    A. S. Tracey, Carbohyd. Res. 16 395 (1971).

58. F. W. Einstein and K. N. Slessor, Unpublished work.

59. J. W. Emsley, J. Feeny, and L. H. Sutcliffe, 'High
    Resolution Nuclear Magnetic Resonance, Vol. 2 ,
    (Pergamon Press Ltd, 1966).

60. M. Barfield and D. M. Grant, 'Advances in Magnetic
    Resonance', Vol. 1, J. S. Waugh, Ed., (Academic Press,
    1965).

61. Ref. 20, p. 280.

62. M. Barfield and M. Karplus, J. Amer. Chem. Soc. 91 1 (1969).

63. J. B. Lambert and R. G. Keske, Tetrahedron Lett. 4755 (1967).

64. H. R. Buys, Rec. Trav. Chim. 88 1003 (1969).

65. J. B. Lambert, Accts. Chem. Res. 4 87 (1971).

66. E. W. Garbisch and M. G. Griffith, J. Amer. Chem. Soc.
    90 6543 (1968).

67. E. L. Eliel, N. L. Allinger, S. J. Angyal, and
    G. A. Morrison, 'Conformational Analysis', (Inter-
    science Publishers Inc., 1965), p. 455.

68. M. Davis and O. Hassel, Acta. Chem. Scand. 17 1181 (1963).

69. J. B. Hendrickson, J. Amer. Chem. Soc. 83 4537 (1961).

70. R. U. Lemieux and J. W. Lown, Tetrahedron Lett. 1229 (1963).

71. F. A. L. Anet, J. Amer. Chem. Soc. 84 1053 (1962).

72. R. U. Lemieux and J. Howard, Can. J. Chem. 41 308 (1963).

73. L. D. Hall, Carbohyd. Res. 4 429 (1967).

74. A. B. Foster, T. D. Inch, M. H. Qadir, and J. M. Webber, Chem. Commun. 1086 (1968).

75. Reference 67, p. 249.

76. W. D. Keller, T. R. Lusebrink, and C. H. Sederholm, J. Chem. Phys. 44 782 (1966).

77. R. M. Dodson, E. H. Jancis, and G. Close, J. Org. Chem. 35 2520 (1970).

78. A. D. Cohen and I. Schaefer, Molec. Phys. 10 209 (1966).

79. D. A. Brueckner, T. A. Hamor, J. M. Robertson, and G. A. Sim, J. Chem. Soc. 799 (1962).

80. Reference 67, p.448.

81. C. Altona and M. Sundaralingam, J. Amer. Chem. Soc. 92 1995 (1970).

82. A. A. Bothner-By and S. M. Castellano, 'Computer Programs for Chemistry', Vol. 1, Ed. D. F. DeTar, (W. A. Benjamin, Inc., 1968), p.10.

83. L. D. Hall, P. R. Steiner, and C. Pedersen, Can. J. Chem. 48 1155 (1970).

84. K. N. Slessor and A. S. Tracey, Can. J. Chem. 48 2900 (1970).

85. R. J. Ferrier, Advan. Carbohyd. Chem. 24 199 (1969).

86. M. Spencer, Acta Cryst. 12 59 (1959).

87. R. U. Lemieux and R. Nagarajan, Can. J. Chem. 42 1270 (1964).

88. R. R. Fraser, M. Kaufman, P. Morand, and G. Govil, Can. J. Chem. 47 403 (1969).

89. S. A. Black, L. D. Hall, K. N. Slessor, and A. S. Tracey, Submitted to Can. J. Chem.

90. L. P. Kuhn and R. A. Wires, J. Am. Chem. Soc. 86 2161 (1964).

91. J. S. Brimacombe, P. A. Gent, and T. A. Hamor,
    J. Chem. Soc. (B), 1566 (1968).

92. J. S. Brimacombe, J. G. H. Bryan, and T. A. Hamor,
    J. Chem. Soc. (B), 514 (1970).

93. O. Th. Schmidt, Methods Carbohyd. Chem. $\underline{2}$ 320 (1963).

94. O. Theander, Acta Chem. Scand. $\underline{17}$ 1751 (1963).

95. F. H. Newth and L. F. Wiggins, J. Chem. Soc. 1734 (1950).

96. K. Freudenberg and R. M. Hixon, Ber. Deut. Chem. Ges.
    $\underline{56}$ 2119 (1923).

97. K. Iwadare, Bull. Chem. Soc. Jap. $\underline{16}$ 144 (1941).

98. I. E. Muskat, J. Amer. Chem. Soc. $\underline{56}$ 2449 (1934).

99. M. Haga, M. Takano, and S. Tejima, Carbohyd. Res.
    $\underline{14}$ 237 (1970).

100. N. Baggett and R. W. Jeanloz, J. Org. Chem. $\underline{28}$ 1845 (1963).

101. E. J. Hedgley, W. G. Overend, and R. A. C. Rennie,
     J. Chem. Soc. 4701 (1963).

102. F. A. L. Anet, H. H. Lee, and J. L. Sudmeier,
     J. Amer. Chem. Soc. $\underline{89}$ 4431 (1967).

103. I. Armitage, and L. D. Hall, Can. J. Chem. $\underline{49}$ (2770) (1971).

104. M. A. Dolliver, T. L. Gresham, G. B. Kistiakowsky,
     E. A. Smith, and W. E. Vaughan, J. Amer. Chem. Soc.
     $\underline{60}$ 440 (1938).