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CONFORMATION OF ACYCLIC DERIVATIVES OF SUGARS

PART VI. CONFORMATIONS OF *aldehydo*-ALDOSE PERACETATES IN SOLUTION*†

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ABSTRACT

2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-ribose (**1**), its D-*arabino* (**2**), D-*xylo* (**3**), and D-*lyxo* (**4**) analogs, and 2,3,4,5-tetra-*O*-acetyl-6-deoxy-*aldehydo*-L-galactose (**5**) have been studied in chloroform-*d* solution by n.m.r. spectroscopy at 100 MHz. Signals of all protons were assigned, and verified by spin decoupling, and first-order coupling-constants were determined. The favored conformation of these compounds was shown to be the extended, planar, zigzag form[2], except when such a conformation would lead to an eclipsed, 1,3-interaction between pairs of substituents, in which case the favored conformation is a "sickle" form[3–5] in which the 1,3-interaction is alleviated, by rotation about a carbon–carbon bond of the chain, to give a different rotameric state. The diphenyl dithioacetals (**8** and **9**, respectively) of 2,3,4,5-tetra-*O*-acetyl-D-lyxose and 2,3,4,5-tetra-*O*-acetyl-6-deoxy-L-mannose were prepared, and their conformations studied; demercaptalation of these compounds by mercuric chloride proved to be more difficult than with the diethyl analogs.

INTRODUCTION

In the first paper in this series[2], it was noted that 2-(D-*arabino*-tetrahydroxybutyl)quinoxaline and its tetraacetate display vicinal, spin–spin coupling-constants consistent with a favored conformation having an extended, planar, zigzag arrangement of carbon atoms along the polyhydroxyalkyl chain. In a subsequent report[3], the coupling data for L-*xylo*-hexulose phenylosotriazole were interpreted in terms of a favored conformation generated from the planar, zigzag form by rotation through one-third of a revolution about the C-1–C-2 bond to remove the parallel, eclipsed 1,3-interaction between the hydroxyl groups at C-1 and C-3 of the tetrahydroxybutyl side-chain. In part III of the series[4], the fully acetylated dithioacetals were considered,

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[*] For part V in this series, see Ref. 1.

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and it was proposed therein that a conformation generated from the extended, planar, zigzag form by rotation through 120° about an internal carbon–carbon bond be designated by the term "sickle". Similar observations have been made with the fully acetylated diphenyl dithioacetals of D- and L-arabinose, D-xylose, and D-ribose[5], and with a number of fully acetylated phenylosotriazole derivatives[6]. The conformational stability of the pentose dialkyl dithioacetals has been correlated with their tendency to form 2,5-anhydrides when they are treated with one molar proportion of *p*-toluenesulfonyl chloride in pyridine[1].

The present report describes an n.m.r. spectral analysis of the four *aldehydo*-D-pentose tetraacetates and several related compounds in chloroform-*d* solution. The data permit assignment of favored conformations; these are found to be in excellent agreement with those predicted by application of the principles previously delineated[2–5].

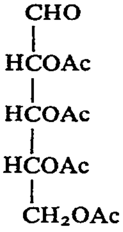
RESULTS AND DISCUSSION

Preparation of compounds. — 2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-ribose[7] (**1**), 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-arabinose[8] (**2**), 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-xylose[9] (**3**), and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-lyxose[10] (**4**) were prepared from the respective diethyl dithioacetals, as was 2,3,4,5-tetra-*O*-acetyl-6-deoxy-*aldehydo*-L-galactose[11] (**5**). The diphenyl dithioacetal (**6**) of D-lyxose was prepared crystalline, and converted into its syrupy tetraacetate (**8**). Diphenyl dithioacetals of the other D-aldopentoses had been prepared earlier in this laboratory[5]. It was found that demercaptalation of **8** to the *aldehydo*-aldose peracetate **4** by Wolfrom's general method[9,12] proceeds very sluggishly; elevated temperatures and longer times of reaction, relative to the conditions effective with the dialkyl dithioacetals, were required for conversion of **8** into **4**.

The crystalline diphenyl dithioacetal (**7**) of 6-deoxy-L-mannose (L-rhamnose) was also prepared, and converted into its syrupy tetraacetate (**9**). Attempts to convert **9** or its diethyl analog by demercaptalation into the corresponding acetylated *aldehydo* sugar were unsuccessful. The diphenyl dithioacetal **9** was recovered unchanged. The diethyl derivative was converted into a crystalline product that could be sublimed, but which behaved as an adduct of the anticipated *aldehydo* derivative and the starting material (see Experimental section).

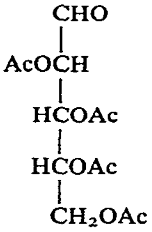
Spectral data. — The 100-MHz n.m.r. spectrum of each acetylated derivative (**1**–**5**, **8**, **9**) was measured at ~28° in chloroform-*d* containing 5% of tetramethylsilane as the internal standard and lock signal. Spectral analysis was effected, or verified, as necessary, by spin decoupling. The chemical shifts measured are given in Table I, and the first-order coupling-constants in Table II. The n.m.r. spectra of 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-arabinose (**2**) and 2,3,4,5-tetra-*O*-acetyl-6-deoxy-*aldehydo*-L-galactose (**5**) are presented in Figs. 1 and 2 as spectra representative of those of the pentose and 6-deoxyhexose derivatives, respectively.

The n.m.r. spectra of the dithioacetals[4] **8** and **9** are typical of fully acetylated



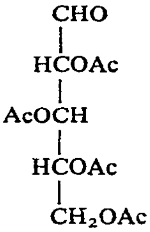
$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{HCOAc} \\ | \\ \mathrm{HCOAc} \\ | \\ \mathrm{HCOAc} \\ | \\ \mathrm{CH_2OAc} \end{array}$$

1



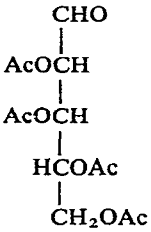
$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{AcOCH} \\ | \\ \mathrm{HCOAc} \\ | \\ \mathrm{HCOAc} \\ | \\ \mathrm{CH_2OAc} \end{array}$$

2



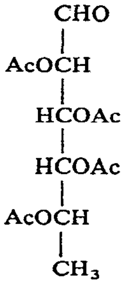
$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{HCOAc} \\ | \\ \mathrm{AcOCH} \\ | \\ \mathrm{HCOAc} \\ | \\ \mathrm{CH_2OAc} \end{array}$$

3



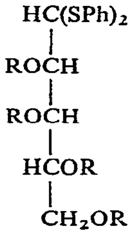
$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{AcOCH} \\ | \\ \mathrm{AcOCH} \\ | \\ \mathrm{HCOAc} \\ | \\ \mathrm{CH_2OAc} \end{array}$$

4



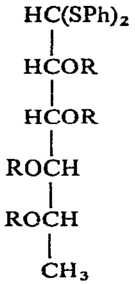
$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{AcOCH} \\ | \\ \mathrm{HCOAc} \\ | \\ \mathrm{HCOAc} \\ | \\ \mathrm{AcOCH} \\ | \\ \mathrm{CH_3} \end{array}$$

5



$$\begin{array}{c} \mathrm{HC(SPh)_2} \\ | \\ \mathrm{ROCH} \\ | \\ \mathrm{ROCH} \\ | \\ \mathrm{HCOR} \\ | \\ \mathrm{CH_2OR} \end{array}$$

6 R = H
8 R = Ac



$$\begin{array}{c} \mathrm{HC(SPh)_2} \\ | \\ \mathrm{HCOR} \\ | \\ \mathrm{HCOR} \\ | \\ \mathrm{ROCH} \\ | \\ \mathrm{ROCH} \\ | \\ \mathrm{CH_3} \end{array}$$

7
9

diphenyl dithioacetals[5]. A 10-proton multiplet for the aryl protons is observed at low field (τ ~2.5). The methine-proton signal at lowest field is that of H-3, near τ 4.2. The H-2 and H-4 signals are observed as partially overlapping multiplets near τ 4.6. A doublet near τ 5.6 is observed for H-1. In compound **8**, the H-5 and H-5′ signals appear as AB quartets at slightly higher field than H-1; the H-5 signal for compound **9** is a quartet of doublets at τ 5.14. The highest-field signals for compound **8** are the acetate-methyl resonances, whereas, for **9**, the chain-terminal methyl group resonates ~1 p.p.m. upfield from the acetate signals. All spin-couplings for compounds **8** and **9** can be determined directly from the spectra.

For the *aldehydo* derivatives **1–5**, the signal of H-1 (aldehyde proton) is the lowest-field signal, near τ 0.5, as observed with other *aldehydo*-sugar derivatives[13]. For the *lyxo* derivative **4**, the H-1 signal is a narrow doublet ($J_{1,2}$ = 0.8 Hz), whereas, in the four other examples, the H-1 signal is a singlet, indicating that $J_{1,2}$ is approximately zero. The H-3 signal appears at next lowest field (τ 4.1–4.5) as a quartet, followed at higher field by the resonances of H-2 and H-4, which occur at similar field (τ 4.5–4.8) for compounds **1–4** and overlap extensively for compound **5**. The H-2 resonance appears as a distinctive, sharp doublet for compounds **1–3** and **5** (and as a doublet of very narrow doublets for **4**). The results of spin-decoupling experiments verified that the remaining multiplet is the H-4 signal for the pentose derivatives, and that the four-line signal overlapping the H-2 signal for compound **5** is produced by H-4. For compounds **1–4**, the signals for H-5 and H-5′ form the AB portion of an ABX system and are observed as two separated, four-line patterns between τ 5.6 and 6.0. The

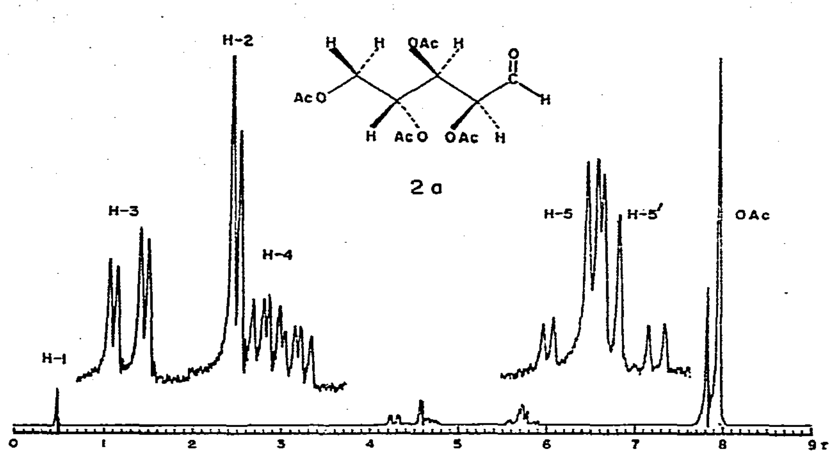


Fig. 1. The 100-MHz n.m.r. spectrum of 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-arabinose (2) in chloroform-*d*.

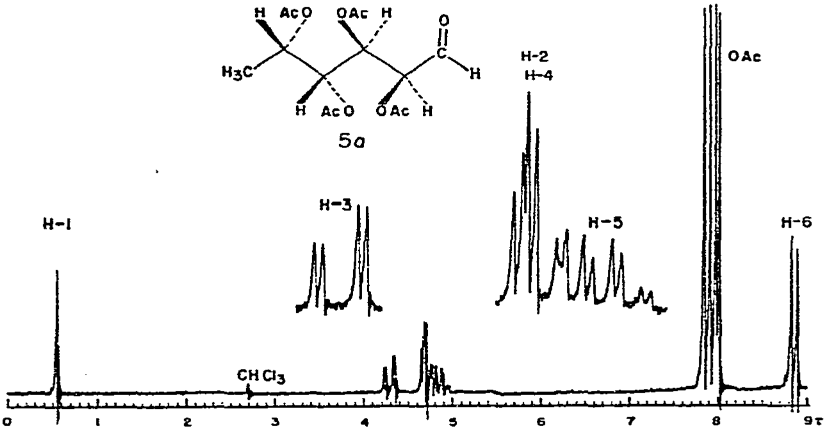


Fig. 2. The 100-MHz n.m.r. spectrum of 2,3,4,5-tetra-*O*-acetyl-6-deoxy-*aldehydo*-L-galactose (5) in chloroform-*d*.

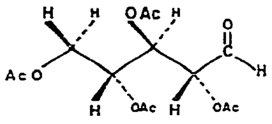
H-5 signal of the deoxyhexose derivative **5** appears at rather lower field (τ 4.81) as a well defined doublet of quartets, through coupling with H-4 and with the three equivalent protons of the methyl group containing C-6. The acetate signals of compounds **1–5** appear as a series of narrow singlets between τ 7.80 and 8.05, and the C-6 protons of compound **5** resonate at highest field (τ 8.85) as a doublet whose spacing gives $J_{5,6}$.

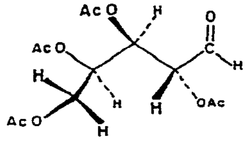
In all spectra listed, the difference in chemical shift between coupled pairs of protons is sufficient to justify the first-order analysis. The coupling $J_{2,3}$ is measured directly from the H-2 signal, and verified by observing the H-3 pattern, which, in turn, gives $J_{3,4}$. For compounds **1–4**, the remaining coupling-constants are available directly from the H-5 and H-5' signals, and the width of the H-4 multiplet ($J_{3,4}$ +

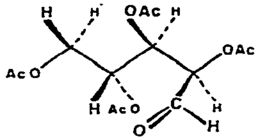
$J_{4,5} + J_{4,5'}$) is used for verifying the assignment of the last three coupling-constants. For compound **5**, the H-4 quartet gives the value of $J_{4,5}$ as well as of $J_{3,4}$, and the $J_{5,6}$ coupling is evident from the H-6 doublet. The definition in the H-5 octet is sufficient that the $J_{4,5}$ and $J_{5,6}$ values can also be measured directly from this octet.

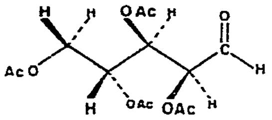
Conformational significance of the coupling data. — Based on the usual assumption[2–5] that torsional barriers to rotation about carbon–carbon single bonds are low, the molecules under consideration have sufficient energy at room temperature to permit equilibrium distribution of various possible conformers, according to their relative energies, into a statistical pattern as defined by thermodynamic relations. By further assuming that spin–spin coupling values[14] of 8–9 Hz between vicinal protons correspond to antiparallel disposition of these protons, and that vicinal couplings of 2–3 Hz correspond to a gauche arrangement with the protons at a dihedral angle of ~60°, it is possible to interpret the observed coupling data in terms of predicted, favored conformations.

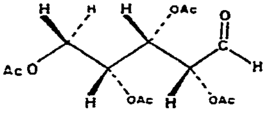
*2,3,4,5-Tetra-O-acetyl-*aldehydo-D-*arabinose* (**2**). The coupling data for compound **2** are entirely consistent with a favored conformation (**2a**) having a planar, zigzag backbone composed of carbon atoms 1–5 and the oxygen atom at C-5. The value of $J_{1,2}$ (~0 Hz) implies that H-1 and H-2 are approximately at right angles, and the same relationship between H-1 and H-2 evidently occurs in compounds **2**, **3**, and **5**, because

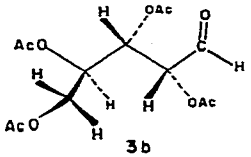

1a

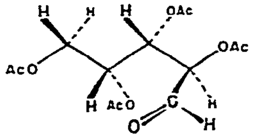

1b

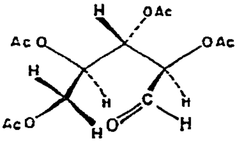

1c

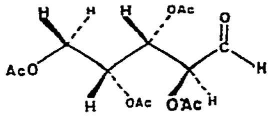

2a

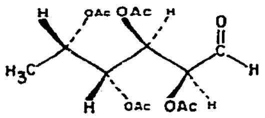

3a

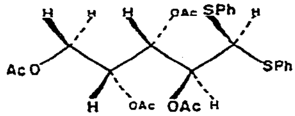

3b

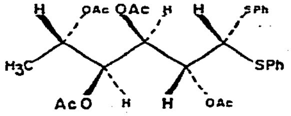

3c


3d


4a


5a

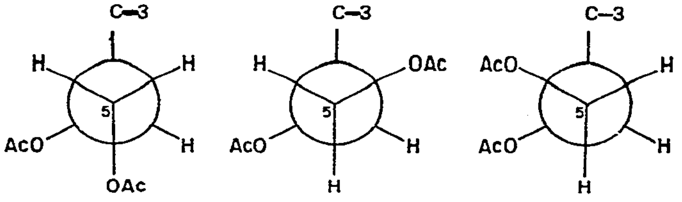

8a


9a

all of these compounds have $J_{1,2}$ ~0 Hz. Of the two possible C-1–C-2 rotamer states that would allow this angular relationship, the one having the C-1 carbonyl group almost eclipsed with C-3 is considered the more probable. Such an eclipsed orientation is well established for acetaldehyde and various other simple carbonyl compounds[15]. The other C-1–C-2 rotamer would lead to a parallel arrangement of C-1–O-1' and C-2–O-2 dipoles that is, presumably, unfavorable.

The values of $J_{2,3}$ and $J_{3,4}$ (2.2 and 8.6 Hz, respectively) are extreme, and indicate that there is overwhelming predisposition for a favored rotamer state having H-2 and H-3 gauche-disposed and H-3 and H-4 antiparallel; other conformations contributing to the conformational equilibrium[16] probably contribute less than ~5% of the total conformational population. It may be seen that any deviation from the conformation **2a** would lead to increased vicinal, eclipsing interactions, and all of the other staggered rotamers about C-2–C-3 or C-3–C-4 would be inconsistent with the observed coupling data (except for the other H-2–H-3 gauche rotamer, and this one would have a parallel interaction between O-2 and O-4).

The low value of the larger of the couplings ($J_{4,5'}$ 4.4 Hz) of H-4 with a proton on C-5 suggests that an equilibrium exists among the three C-4–C-5 rotamer states (see Fig. 3). Although the rotamer shown in **2a** (see also Fig. 3, A), having C-3 and O-5 antiparallel (H-4 antiparallel to one C-5 proton), probably preponderates, it is not exclusive. The conformer having O-5 antiparallel to O-4 (see Fig. 3, B) probably does not contribute substantially to the rotamer population, because it has a parallel, 1,3-interaction between O-5 and O-3; and, in any case, it would have H-4 antiparallel to one C-5 proton and lead to a large value for one of the two $J_{4,5}$ couplings. The third rotamer (see Fig. 3, C) would have O-5 staggered between C-3 and O-4, and would give rise to small values for both $J_{4,5}$ and $J_{4,5'}$. The values actually observed for these couplings suggest that rotamer A makes the major contribution, but that rotamer C also contributes substantially. An alternative explanation for the low value of $J_{4,5'}$, based on a favored C-4–C-5 conformation that is rotated somewhat from the fully staggered situation, cannot be excluded on the basis of the data at present available.



A most favored

B least favored

C intermediate

Fig. 3. Possible C-4–C-5 rotamer states for 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-ribose (**1**) and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-arabinose (**2**).

Conformation **2a** corresponds to maximum relief of steric interactions between small–medium–large sets of groups along each carbon–carbon bond, and is free from eclipsed, 1,3-interactions of substituents.

*2,3,4,5-Tetra-*O*-acetyl-6-deoxy-*aldehydo-L-*galactose* (**5**). This molecule, which is homomorphous with compound **2** at C-2–C-4, also gives n.m.r. spectral data entirely consistent with a conformation (**5a**) having an extended, planar, zigzag chain consisting of carbon atoms and O-5. The values of $J_{2,3}$ and $J_{3,4}$ (1.5 and 9.8 Hz, respectively) indicate that the rotamer state having H-2 and H-3 gauche, and H-3 and H-4 antiparallel, is strongly favored. The small value (2.1 Hz) of $J_{4,5}$ indicates that H-4 and H-5 are gauche in the way depicted in **5a**; the other possible gauche interaction would give rise to a parallel, 1,3-interaction between O-2 and O-4.

*2,3,4,5-Tetra-*O*-acetyl-6-deoxy-*L*-mannose diphenyl dithioacetal* (**9**). The coupling data for this compound accord very clearly with the planar, zigzag arrangement (**9a**). The couplings for antiparallel protons ($J_{2,3}$ 8.6 Hz, $J_{4,5}$ 8.5 Hz) and gauche ones ($J_{1,2}$ 3.0 Hz, $J_{3,4}$ 2.0 Hz) are probably extreme values, consistent with conformer **9a** as the only significant rotamer state.

*2,3,4,5-Tetra-*O*-acetyl-*D*-lyxose diphenyl dithioacetal* (**8**). This compound is the enantiomorph of a lower homomorph of the mannose derivative **9**. It shows values for $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ (2.7, 8.8, and 2.0 Hz, respectively) that are almost identical with the corresponding couplings in **9**, and that indicate for **8** the planar, zigzag conformation **8a** as the only significant rotamer state along C-1–C-2–C-3–C-4. The relatively large values of $J_{4,5}$ and $J_{4,5'}$ (5.0 and 7.2 Hz, respectively) suggest that two of the C-4–C-5 rotamer states are substantially occupied (those having O-5 antiparallel either to C-3 or to O-4), whereas the third one (having O-5 eclipsed between O-5 and C-3) is not.

*2,3,4,5-Tetra-*O*-acetyl-*aldehydo-D-*lyxose* (**4**). The coupling data observed for the aldehyde **4** are qualitatively similar to those given by the *lyxo* dithioacetal analog **8** and the homomorph **9** having the same relative stereochemistry for C-1 to C-4. The general conformation **4a** is thus indicated for compound **4**. That this interpretation is somewhat of an oversimplification is evident from the fact that the "large" $J_{2,3}$ coupling is only 6.0 Hz, and the "small" $J_{3,4}$ coupling is as high as 4.0 Hz. A conformational equilibrium involving other rotamers about C-2–C-3 or C-3–C-4 is not an attractive hypothesis for explaining these observed couplings, because the other possible rotamers would give rise in each case to 1,3-interactions. It appears more probable that minor distortions of the chain, involving displacement of C-2 and C-3 somewhat from the approximate plane of the backbone of the molecule, cause sufficient changes in the dihedral angles between H-1, 2, 3, and 4 to give rise to the couplings observed, including the $J_{1,2}$ coupling (0.8 Hz) not observed with the other *aldehydo* derivatives. The values for $J_{4,5}$ and $J_{4,5'}$ resemble those for the dithioacetal analog (**8**), suggesting a similar arrangement, in **4** and **8**, along the C-4–C-5 bond. The favored conformation of **4** is thus considered to be a minor distortion of the conformation **4a**.

*2,3,4,5-Tetra-*O*-acetyl-*aldehydo-D-*ribose* (**1**). The spin-coupling data for compound **1** are inconsistent with an extended, planar, zigzag conformation (**1a**), because this shape would require large values for both $J_{2,3}$ and $J_{3,4}$, whereas the actual values are 2.8 and 8.9 Hz, respectively. The data require H-3 and H-4 to be antiparallel, but H-2 and H-3 must be gauche-disposed, a situation accommodated in the sickle conformation **1c**. The other possible C-2–C-3 rotamer in which H-2 and H-3 are gauche-disposed can be discounted, because it would have unfavorable vicinal (O-2 with O-3 and C-4) and 1,3 (C-1 with O-4) interactions. The values of $J_{4,5}$ (2.8 Hz) and $J_{4,5'}$ (4.3 Hz) resemble those of the D-arabinose analog (**2**) and, by the arguments used for **2**, suggest that the rotamer-state populations indicated in Fig. 3 apply also to compound **1**.

An alternative sickle conformation (**1b**) for **1**, derived by rotation of the planar, zigzag form **1a** about C-3–C-4, is not consistent with the observed data. A sickle conformation analogous to **1b** was found[4,5] to be the favored form of the dithioacetal analogs of compound **1**.

*2,3,4,5-Tetra-*O*-acetyl-*aldehydo-*D-xylose* (**3**). The relatively large values observed for $J_{2,3}$ and $J_{3,4}$ (4.5 and 5.1 Hz, respectively) are not consistent with the planar, zigzag conformation **3a**, which would be expected to give coupling values near 2 Hz for $J_{2,3}$ and $J_{3,4}$. The couplings observed suggest extensive population of rotamer states having H-2 and H-3 and/or H-3 and H-4 antiparallel, so that the 1,3-interaction between O-2 and O-4 present in conformation **3a** is relieved. Sickle conformations having H-3 and H-4 antiparallel (**3b**) or H-2 and H-3 antiparallel (**3c**) would allow about the same steric relief as compared to the extended form **3a**. An equilibrium between forms **3b** and **3c** appears a more probable conformational situation for **3** than the "U" conformation (**3d**) obtained by consecutive operation of both of the rotameric changes already described, because conformation **3d** would have a parallel, 1,3-interaction between C-1 and C-5. The values of $J_{4,5}$ and $J_{4,5'}$ (4.9 and 6.1 Hz, respectively) suggest that, as for compound **4**, the two C-4–C-5 rotamers having H-4 antiparallel to one proton at C-5 are populated, but the one having H-4 bisecting the dihedral angle of the methylene group is not appreciably populated.

Conclusions. — The data of the present investigation reinforce our previous arguments (from n.m.r. spectral studies in solution[2–5]) that the planar, zigzag conformation resulting from maximum staggering of small–medium–large sets of groups is the energetically favored state of acyclic carbohydrate derivatives, so long as parallel 1,3-interactions of substituent groups are absent; the data do not preclude the additional possibility of minor distortion of dihedral angles from the angle of maximum staggering.

These conclusions have been further confirmed in subsequent reports on other series of acyclic carbohydrate derivatives[17]. For molecules in the solid state, it is possible that lattice forces may profoundly affect the conformation, and it cannot necessarily be assumed that the favored conformation of a molecule in the crystal is the same as that adopted when the molecule is surrounded by a sheath of solvent molecules. Nevertheless, a high degree of correlation is evident between the results of X-ray crystallography on alditol derivatives and the conformations in solution described in the present series of papers. The planar, zigzag conformation is adopted in the solid state by DL-arabinitol[18], galactitol[19], D-mannitol[20], and the D-arabinonate

TABLE I

CHEMICAL-SHIFT DATA (100 MHz) FOR COMPOUNDS **1**, **2**, **3**, **4**, **5**, **8**, AND **9** IN CHLOROFORM-*d*

Compound	*Configuration*	*Chemical shifts* (τ) *in chloroform*-d								
		H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-5'*[a]	*H-6*	*Acetyl groups*[b]	*Phenyl*
1	*ribo*	0.48	4.56	4.42	4.74	5.67	5.90		7.86, 7.96, 7.99, 8.04	
2	*arabino*	0.47	4.60	4.30	4.73	5.66	5.84		7.82, 7.93, 7.94 (6)	
3	*xylo*	0.44	4.60	4.33	4.52	5.57	5.90		7.80, 7.88, 7.95 (6)	
4	*lyxo*	0.49	4.82	4.48	4.59	5.68	5.96		7.91, 7.97, 8.00, 8.04	
5	*galacto*	0.48	4.65	4.24	4.66	4.81		8.86	7.82, 7.90, 7.97, 8.00	
8	*lyxo*	5.60	4.57	4.23	4.65	5.73	6.13		8.00, 8.04 (9)	2.30–2.44, 2.52–2.73
9	*manno*	5.62	4.65	4.10	4.77	5.14		8.85	7.97, 8.02, 8.03, 8.05	2.32–2.44, 2.54–2.80

[a] When two protons are present at C-5, the one resonating at lower field is designated H-5, and the one resonating at higher field is designated H-5'.
[b] Three-proton singlets, unless otherwise indicated in parentheses.

ion[21], none of which have parallel 1,3-interactions in this conformation. In contrast, it was shown by Tanaka and coworkers[22] that the ribitol chain in crystalline riboflavine hydrobromide monohydrate is not the planar, zigzag arrangement (which would have a parallel 1,3-interaction) but a bent-chain conformation (having no 1,3-interaction). With the demonstration that similar bent (sickle) conformations are adopted in the solid state by ribitol[23], xylitol[24], and D-glucitol[25] (all of which would have a 1,3-interaction in the extended conformation), it has been proposed by Jeffrey and Kim[26] that the generalization[3–5], derived from solution studies, that these molecules adopt a sickle conformation to escape eclipsed 1,3-interactions can be extended to include the solid state. The behavior of the D-gluconate ion, which, in the solid state, has been reported[27] to adopt a planar, zigzag form even though it can be seen that a 1,3-interaction is present, remains, however, an exception to this rationalization.

Reliable predictions of the favored conformations of acyclic sugars and related molecules in solution may prove useful in interpreting the course of chemical and biochemical processes, especially ring-forming reactions[1].

TABLE II

FIRST-ORDER COUPLING-CONSTANTS FOR COMPOUNDS **1**, **2**, **3**, **4**, **5**, **8**, AND **9**, MEASURED AT 100 MHz IN CHLOROFORM-*d*

Compound	*Configuration*	*Coupling constants, Hz*						
		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{4,5'}{}^{a}$	$J_{5,5'}{}^{a}$	$J_{5,6}$
1	*ribo*	<0.2	2.8	8.9	2.8	4.3	12.5	
2	*arabino*	<0.2	2.2	8.6	3.0	4.4	12.6	
3	*xylo*	<0.2	4.5	5.1	4.9	6.1	12.2	
4	*lyxo*	0.8	6.0	4.0	4.7	6.3	12.1	
5	*galacto*	<0.2	1.5	9.8	2.1			6.6
8	*lyxo*	2.7	8.8	2.0	5.0	7.2	11.7	
9	*manno*	3.0	8.6	2.0	8.5			6.1

[a] See footnote *a* of Table I.

EXPERIMENTAL

General methods. — Melting points were measured with a Thomas–Hoover "Unimelt" oil-bath apparatus. Optical rotations were measured with a Perkin–Elmer Model 141 automatic polarimeter and a 1-dm tube. T.l.c. was performed with Silica Gel G, and column chromatography with Silica Gel 7734 (E. Merck, Darmstadt, Germany); plates were activated at 110°. Indication was effected with sulfuric acid. U.v. spectra were recorded with a Cary Model 14 spectrophotometer, and i.r. spectra with a Perkin–Elmer Model 137 i.r. spectrophotometer. N.m.r. spectra were measured at 100 MHz with a Varian HA-100 spectrometer in the frequency-sweep mode, with 5% of tetramethylsilane as the lock signal and internal standard, according to the general procedures reported earlier[4,5]. X-ray powder diffraction data give interplanar spacings, Å, for CuKα radiation. Relative intensities were estimated visually: m, moderate; s, strong; v, very; w, weak. The strongest lines are numbered (1, strongest); double numbers indicate approximately equal intensities. Elemental analyses were performed by W. N. Rond.

*Preparation of 2,3,4,5-tetra-*O*-acetyl-*aldehydo-D-*ribose* (**1**), -D-*arabinose* (**2**), *and* -D-*xylose* (**3**), *and 2,3,4,5-tetra-*O*-acetyl-6-deoxy-*aldehydo-L-*galactose* (**5**). — These *aldehydo*-sugar derivatives were prepared by the method of Wolfrom and coworkers[9,12] from the corresponding tetra-*O*-acetyl-*aldehydo*-aldose diethyl dithioacetals[4], and had melting points and specific rotations in good agreement with the values recorded in the literature sources noted: **1** (Ref. 7), **2** (Ref. 8), **3** (Ref. 9), and **5** (Ref. 11).

D-*Lyxose diphenyl dithioacetal* (**6**). — D-Lyxose (Pfanstiehl Laboratories, Waukegan, Illinois) (10 g) was dissolved in 20 ml of conc. hydrochloric acid presaturated with hydrogen chloride gas at 0°. Benzenethiol (20 ml) was immediately added, and the mixture was shaken at ~25° until it had become homogeneous (about 20 min), whereupon it was poured into 500 ml of ice–water. The white solid that separated was filtered off after 1 h, washed with water, and then dissolved in ethanol (250 ml). The solution was decolorized with charcoal, diluted with water until slight turbidity remained at 50°, and then warmed slightly to give a clear solution. After refrigeration for 2 days, the solution gave crystalline **6** as white whiskers; yield 4.4 g. Addition of water to the mother liquors gave a further 3.2 g of crystalline **6**; total yield 7.6 g (30%), m.p. 63–64°, $[\alpha]_D^{21}$ $-79.0 \pm 0.6°$ (*c* 1.1, ethanol); λ_{max}^{KBr} 3.05 (OH), 3.55 (CH), 6.40, 6.80, 6.90, 7.85, 9.10, 9.65, 13.60, and 14.60 μm (ArH); λ_{max}^{EtOH} 256 (ε 9,500) and 216 (sh) nm (16,500); X-ray powder diffraction data: 9.82 s (3), 7.98 vw, 6.33 w, 5.48 vw, 5.28 vw, 4.96 m, 4.79 vs (1), 4.48 m, 3.70 m, 3.50 s (2), 3.15 w, and 2.83 vvw.

Anal. Calc. for $C_{17}H_{20}O_4S_2$: C, 57.95; H, 5.68; S, 18.18. Found: C, 58.15; H, 5.85; S, 18.28.

L-*Rhamnose diphenyl dithioacetal* (**7**). — To 40 ml of conc. hydrochloric acid presaturated at 0° with hydrogen chloride was added L-rhamnose monohydrate (25 g) and benzenethiol (45 ml), and the mixture was shaken for 24 h at ~25°. The resulting, red mixture was poured into 500 ml of ice–water, giving a precipitate of **7** that was filtered off and washed with water (300 ml) and ether (100 ml); yield 26.5 g (55%). Recrystallization from 3 liters of boiling water gave **7** as broad, filmy, colorless platelets that formed mats on filtration; yield 15.5 g (34%), m.p. 124–125.5°, $[\alpha]_D^{21}$ $+74.8 \pm 0.5°$ (*c* 1.1 ethanol); λ_{max}^{KBr} 3.05 (OH), 3.45 (CH), 6.35, 6.85, 7.05, 7.95, 8.40, 9.35, 11.10, 13.45, and 14.60 μm (ArH); λ_{max}^{EtOH} 257 (ε 10,000) and 216 (sh) nm (17,500); X-ray powder diffraction data: 7.13 m (3), 5.99 vw, 5.05 w, 4.72 vs (1), 3.62 s (2), 3.48 vw, 3.22 w, and 2.42 vvw.

Anal. Calc. for $C_{18}H_{22}O_4S_2$: C, 59.02; H, 6.01; S, 17.49. Found: C, 58.92; H, 6.12; S, 17.32.

In a subsequent preparation under the same conditions, but with a 7-day period of reaction, the isolable yield of **7** was only 8%.

*Tetra-*O*-acetyl-*D-*lyxose diphenyl dithioacetal* (**8**). — A solution of **6** (1.1 g) in anhydrous pyridine (10 ml) containing acetic anhydride (5 ml) was kept for 6 h at room temperature, and then poured into ice–water (250 ml). A clear syrup formed which was extracted into dichloromethane (100 ml). The extract was washed with water, dried (magnesium sulfate), and evaporated, to give **8** as a clear, colorless syrup, yield 1.6 g (98%), which was purified for analysis by distillation; b.p. 150° (bath) at 10 mtorr, $[\alpha]_D^{23}$ −30 ±0.5° (*c* 1.6, chloroform); R_F 0.65 (5:2 benzene–ethyl acetate); λ_{max}^{film} 3.40 (CH), 5.60 (OAc), 6.30, 6.70, 6.85, 7.25, 8.10, 9.40, 13.50, and 14.40 μm (ArH); λ_{max}^{EtOH} 252 (ε 7,500) and 217 (sh) nm (15,000); for the n.m.r. data, see Tables I and II.

Anal. Calc. for $C_{25}H_{28}O_8S_2$: C, 57.69; H, 5.38; S, 12.30. Found: C, 57.67; H, 5.31; S, 12.42.

*2,3,4,5-Tetra-*O*-acetyl-6-deoxy-*L*-mannose diphenyl dithioacetal* (**9**). — A solution of **7** (10 g) in anhydrous pyridine (50 ml) containing acetic anhydride (40 ml) was kept overnight at room temperature and then processed as in the preceding experiment, to give **9** as a faintly yellow syrup; yield 10.4 g (70%). An analytical sample purified by distillation had b.p. 175° (bath) at 2 mtorr, $[\alpha]_D^{21}$ +31 ±0.5° (*c* 1.1, chloroform); R_F 0.75 (5:2 benzene–ethyl acetate); λ_{max}^{film} 3.45 (CH), 5.60 (OAc), 6.30, 6.70, 6.95 7.30, 8.15, 9.35, 10.30, 11.60, 13.35, and 14.55 μm (ArH); λ_{max}^{EtOH} 257 (ε 9,500) and 217 (sh) nm (18,500); for the n.m.r. data, see Tables I and II.

Anal. Calc. for $C_{26}H_{30}O_8S_2$: C, 58.40; H, 5.65; S, 11.99. Found: C, 58.13; H, 5.62; S, 12.18.

*2,3,4,5-Tetra-*O*-acetyl-*aldehydo-*D*-lyxose* (**4**). — Freshly prepared, finely divided cadmium carbonate (5 g) was added, with vigorous mechanical stirring, to a solution of mercuric chloride (15 g) in acetone (35 ml) in a 500-ml flask. After 1 h of continuous agitation, a solution of the dithioacetal **8** (2.1 g) in acetone (30 ml) was added, and the mixture was stirred constantly for 28 h, the temperature of the reaction mixture being maintained at 30 ±5°. The suspension was filtered into a Büchner flask containing fresh cadmium carbonate (1 g), the resulting suspension was evaporated to dryness at ~25°, and the solid was extracted with three 30-ml portions of warm dichloromethane. The extracts were combined, successively washed with 50-ml portions of saturated, aqueous potassium iodide (containing enough thiosulfate to discharge the iodine coloration) until the red color was no longer in evidence, and then with 50-ml portions of water, dried (magnesium sulfate), and evaporated to give a cloudy syrup (1.1 g) that, by t.l.c. and n.m.r. spectroscopy, contained ~75% of the starting material (**8**) and ~25% of compound **4**.

The mixture was resolved on a column (1 × 20 cm) of silica gel, at a flow-rate of eluant of 30 ml per min. Dichloromethane (200 ml) was used to elute the starting material, and elution with ether then gave 0.11 g (9% overall yield, or 35% conversion) of **4**, obtained as a clear, colorless syrup by evaporation under high vacuum at room temperature. Compound **4** had $[\alpha]_D^{22}$ +15 ±1° (*c* 1.1, alcohol-free chloroform); R_F 0.15 (5:2 benzene–ethyl acetate); λ_{max}^{KBr} 3.45 (CH), 5.70 (OAc), 5.90 (CHO), 6.25, 7.30, 8.20, and 9.55 μm; for the n.m.r. data, see Tables I and II.

Anal. Calc. for $C_{13}H_{18}O_9$: C, 49.06; H, 5.66. Found: C, 48.77; H, 5.48.

Wolfrom and Moody[10] reported no constants for this compound (prepared from the diethyl dithioacetal), but converted it into the crystalline *aldehydo*-D-lyxose aldehydrol hexaacetate.

Attempted purification of **4** by elution from silica gel at a low flow-rate led to extensive changes in the product eluted. Attempted distillation of **4** led to discoloration and decomposition.

*Attempted demercaptalation of 2,3,4,5-tetra-*O*-acetyl-6-deoxy-*L*-mannose diphenyl dithioacetal* (**9**) *and its diethyl analog*. — Treatment of **9** under the conditions used for converting the *lyxo* diphenyl dithioacetal **8** into the aldehyde **4**, but with a reaction time of 24 h at 35°, gave a product that, by t.l.c., appeared to be almost entirely unchanged starting material **9**.

Demercaptalation of 2,3,4,5-tetra-*O*-acetyl-6-deoxy-L-mannose diethyl dithioacetal (10 g) under the conditions of Wolfrom *et al.*[9] gave fine, white needles; yield 6 g, m.p. 165–167°, unchanged by recrystallization from ether–petroleum ether or by sublimation at 140° (bath)/5 torr. The product gave a single spot in t.l.c., and its n.m.r. spectrum in chloroform-*d* included signals at τ 0.5 (singlet, aldehyde C*H*O), 6.6 (quartet), and 8.7–9.0 (multiplet, C-6 of chain and CH_3 of SEt); the intensities of the lowest- and highest-field signals indicated slightly less than 1.5 dithioacetal residues per aldehyde group. Found: C, 49.82; H, 6.96; S, 9.60. $(C_{18}H_{30}O_8S_2)_3 \cdot (C_{14}H_{20}O_9)_2$ requires C, 49.73; H, 6.61; S, 9.71.

Newlin[28] reported the isolation of an uncharacterized syrup from this reaction, and Wolfrom, Konigsberg, and Moody[29] succeeded in isolating a crystalline 1-*O*-acetyl-1-bromo derivative by treatment of this syrup with acetyl bromide.

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