THE APPLICATION OF *ab initio* MOLECULAR ORBITAL THEORY TO THE ANOMERIC EFFECT.
A COMPARISON OF THEORETICAL PREDICTIONS AND EXPERIMENTAL DATA ON CONFORMATIONS AND BOND LENGTHS IN SOME PYRANOSES AND METHYL PYRANOSIDES

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ABSTRACT

Ab initio molecular orbital calculations on methanediol have been used to predict the favored orientations and interatomic distances of the C–O–C–O–R portion in pyranoses. The results found for methanediol suggest, for the sugars, favored conformations that are consistent with the observed anomeric and *exo*-anomeric effects. The calculations also show that shortenings of the C–O bond of the order of 0.01 to 0.04 Å, relative to methanol, are to be expected, and that the bond lengths have a strong conformational dependence. A comparison with the experimental data from the X-ray crystal-structure determinations, both for conformational angles and bond lengths, of eighteen pyranoses and methyl pyranosides shows agreement with the theory that is surprisingly good when consideration is taken of the experimental errors, the limitations of the theoretical model, and the expected differences in the structures of the crystal and the isolated molecule.

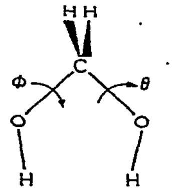
INTRODUCTION

In recent years, molecular orbital theory has developed to the point at which quantitative application to certain problems in stereochemistry is possible. The anomeric effect[1] in carbohydrate chemistry is one such example. The first study relevant thereto was made by Wolfe *et al.*[2], who examined the potential function for internal rotation about the C–O bond in fluoromethanol (FCH_2OH). They found a deep energy-minimum corresponding to a synclinal (*sc*) conformation for F–C–O–H, and the absence of an antiperiplanar (*ap*) minimum. Similar results on this and related molecules were obtained independently by Radom, Hehre, and Pople[3]. One of the molecules examined was methanediol, $CH_2(OH)_2$. The relative energies of possible structures of this molecule are particularly relevant to the favored conformations associated with the anomeric carbon atom in pyranoses and similar molecules containing the acetal-bond sequence –O–C–O–.

The present article has two main aims. Firstly, we now report further details of the theoretical potential-surface for the strongly coupled rotations about the C–O bonds in methanediol; in particular, we have included a study of the calculated changes in C–O bond-lengths associated with changes in conformation. Secondly, we have tested the extrapolation of these conformational and bond-length results for this simple, model compound against the experimental data from crystal-structure determinations on some of the simpler pyranoses and methyl pyranosides.

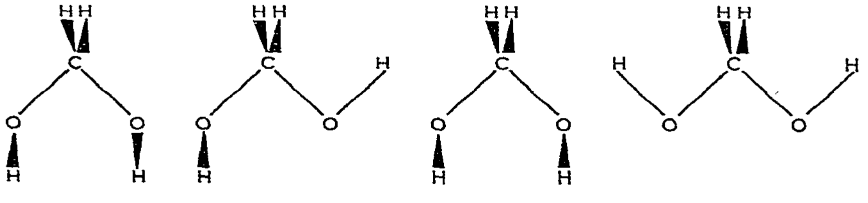
MOLECULAR ORBITAL CALCULATIONS ON METHANEDIOL

Potential surface for internal rotation. — Standard, closed-shell, self-consistent, molecular orbital theory[4] with the 4-31G basis set[5] was used in this study. In the first set of calculations, all bond lengths and angles were set at standard values[6] ($R_{CO} = 1.43$ Å, $R_{CH} = 1.09$ Å, $R_{OH} = 0.96$ Å, all bond-angles tetrahedral) and the energy was studied as a function of the two torsional angles ϕ and θ (I).



I

The energies for the four conformations II (+*sc*, +*sc*, $\phi = \theta = 60°$), III (+*sc*, *ap*, $\phi = 60°$, $\theta = 180°$), IV (+*sc*, −*sc*, $\phi = +60°$, $\theta = -60°$), and V (*ap*, *ap*, $\phi = \theta = 180°$) have been reported[3]. These are the four possible conformations consistent with a "staggered" arrangement of bonds about the C–O linkages. We have since reported energies for a wider range of points corresponding to a 60° grid on the (θ, ϕ) potential surface[7], and, with the aid of additional calculations, we have now constructed the energy contour-diagram shown in Fig. 1. Fig. 2 gives two sections of this surface, in which θ is varied while ϕ is fixed at values of 60° and 180°.



II III IV V

It is clear from these calculations that the (+*sc*, +*sc*) conformation is close to the minimum. There are two equivalent minima of this sort, the other being the

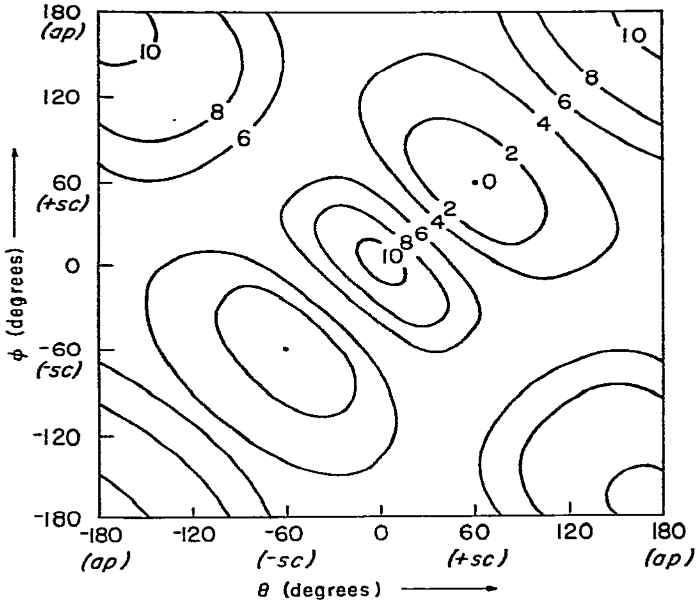


Fig. 1. Energy contours (kcal.mol^{-1}) on the potential surface for internal rotation in methanediol.

symmetry equivalent (*−sc, −sc*). There do not appear to be any other significant local minima, so that, for the isolated methanediol molecule, at least, *only this one type of rotamer is to be expected.* The structure of methanediol has not been deter-

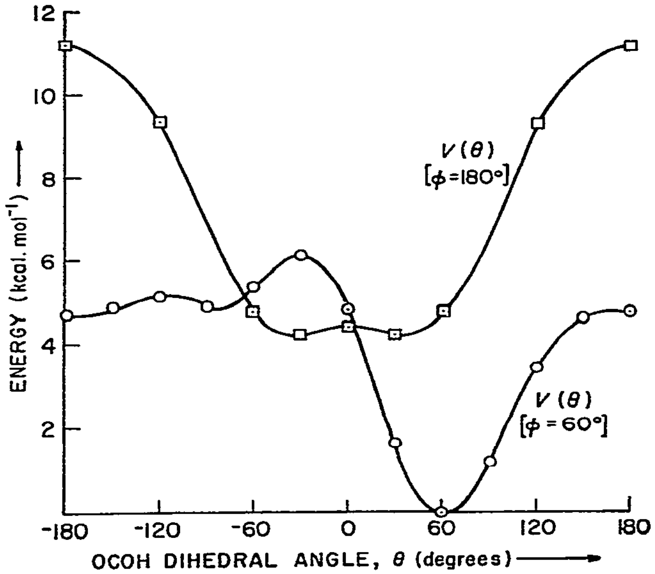


Fig. 2. Sections, $V(\theta)$, of the potential surface for internal rotation in methanediol for fixed values of ϕ.

mined experimentally, but the H–O–C–O–H bonds in chloral hydrate[8(a)] and the C–O–C–O–C skeleton in dimethoxymethane[8(b),(c)] have this same (+*sc*, +*sc*) arrangement.

When methanediol is used as a model for the anomeric center in pyranoses, one hydroxyl hydrogen atom is replaced by a ring-carbon atom of the sugar, and one of the torsion angles (for example, ϕ), is fixed by the configuration of the anomer and the conformation of the pyranose molecule. Sections of the full surface, such as those in Fig. 2, then represent potential curves for rotation about the exocylic, C–O anomeric bond. If ϕ is fixed at +60° (+*sc*), the energy clearly has a sharp minimum at $\theta \sim +60°$, corresponding to the (+*sc*, +*sc*) conformation. On the other hand, if ϕ is fixed at 180° (*ap*), there are two equivalent minima, at $\theta \sim +35°$ and $\theta \sim -35°$, corresponding to conformations (*ap*, +*sc*) and (*ap*, −*sc*), respectively. The conformation (*ap*, *ap*) lies at a maximum on the potential curve and is relatively unfavored.

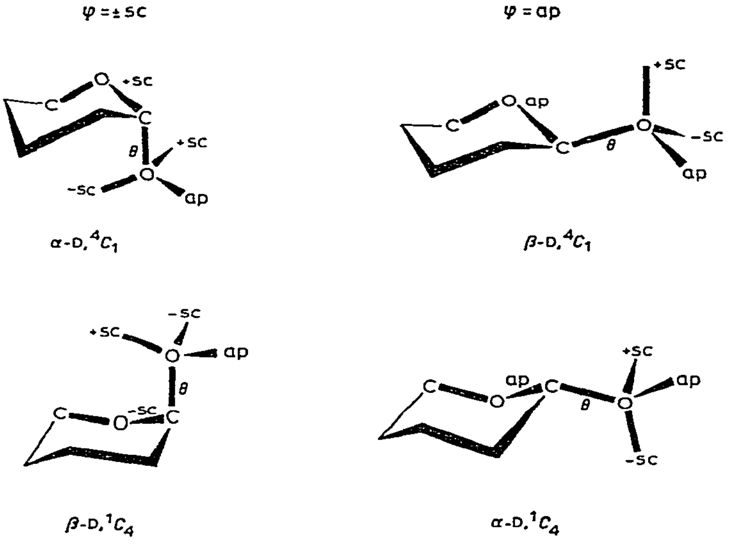


Fig. 3. Acetal orientations in pyranoses.

As shown in Fig. 3, the two values of $\phi = 60°$ and 180° correspond to the distinction between the α and β anomers of pyranoses and pyranosides, depending upon the conformation of the molecule. The energetically most stable conformations are, therefore, (+*sc*, +*sc*) for α-D-$^4C_1$ or (−*sc*, −*sc*) for β-D-$^1C_4$, and (*ap*, +*sc*) for both β-D-$^4C_1$ and α-D-$^1C_4$.

As has previously been shown[9], the interpretation of rotational potential functions in terms of electronic interactions can often be facilitated by "decomposition" of the total function into Fourier components. We illustrate such an approach here with the decomposition of the potential function $V(\theta)$ for internal rotation about one of the C–O bonds in methanediol when the disposition about the other

C–O bond is fixed ($\phi = 180°$). The function $V(\theta)$ may be separated into components, $V_n(\theta) = \frac{1}{2} V_n(1 - \cos n\theta)$, according to equation *1*.

$$V(\theta) = \tfrac{1}{2}V_1(1-\cos\theta) + \tfrac{1}{2}V_2(1-\cos 2\theta) + \tfrac{1}{2}V_3(1-\cos 3\theta) \qquad (1)$$

The values of $V(\theta)$ for $\theta = 0°$, 60°, 120°, and 180° lead to $V_1 = 7.65$, $V_2 = -0.97$, and $V_3 = -0.88$ kcal.mol^{-1}. The decomposed potential curves are shown in Fig. 4.

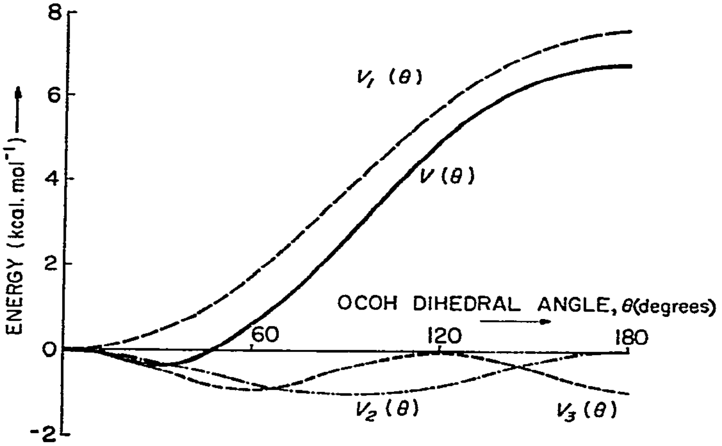
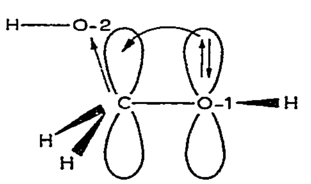


Fig. 4. Decomposition into Fourier components of the potential function $V(\theta)$ when $\phi = 180°$.

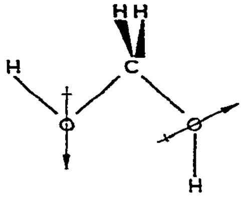
The threefold component $V_3(\theta)$ of the potential function shows the familiar tendency toward staggered conformations ($\theta = 60°$, 180°) over eclipsed conformations ($\theta = 0°$, 120°). The value of V_3 is, in fact, not greatly different from the theoretical value of V_3 for methanol[9] (1.12 kcal.mol^{-1}).

The negative V_2 term shows that the orthogonal ($\theta = 90°$) conformation VI is favored over the *syn*- or *anti*-periplanar conformations. This result can be rationalized in terms of stabilization due to charge delocalization in VI. Electron withdrawal in the C–O-2 bond in this conformation partially empties the 2*p* orbital on C, and thus facilitates the delocalization of the 2*p*-type lone pair on O-1. Such a stabilizing interaction is at a maximum in VI, but is not possible in the periplanar conformations. The importance of such interactions in the anomeric effect was recognized by Romers and Altona[1(b)].

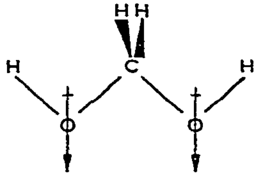


VI

The largest contribution to $V(\theta)$ comes from the V_1 term; this shows that the



VII



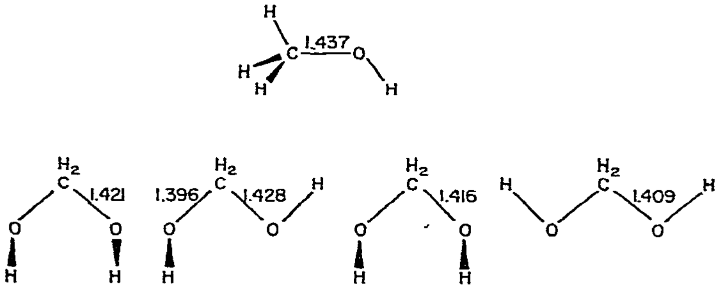
VIII

sp (VII, $\theta = 0°$) is strongly favored over the *ap* (VIII, $\theta = 180°$) conformation. This result is consistent with the dipole–dipole interactions, which are more favorable in VII than in VIII. Dipole–dipole interactions were invoked by Edward[10] to explain the experimental observation of the anomeric effect.

We stress that the total potential function $V(\theta)$ is the *sum* of the $V_1(\theta)$, $V_2(\theta)$, and $V_3(\theta)$ contributions. It is often assumed in conformational studies that staggered conformations are the stable structures. This is true when the V_3 term in the potential function is more important than the V_1 and V_2 terms, but is *not* the case for methanediol; here, the staggered (*ap*, *ap*) conformation is located at a potential maximum. The absence of the "expected" minimum at $\theta = 180°$ may be seen to be due largely to the unfavorable dipole interactions (V_1 term), and due partly to the unfavorable arrangement for lone-pair delocalization (V_2 term) in this conformation.

Although decomposition of the potential function $V(\theta)$ when $\phi = 60°$ is more complicated than the foregoing, because of the lower symmetry, the same qualitative arguments may be used to rationalize the favored conformations. Both dipole–dipole and delocalization effects are important. In particular, although the (+*sc*, +*sc*) and (+*sc*, −*sc*) conformations are equally favored in terms of electron delocalization and bond staggering, the latter conformation has considerably higher energy because of unfavorable dipole–dipole interactions.

Bond-length calculations. — In a second set of calculations, we restricted our attention to the four conformations (II–V) having staggered bonds. However, instead of using a completely standard geometrical model, the C–O bond-lengths were varied until the energy was minimized. All other lengths and angles were held at standard



(+*sc*, +*sc*) (+*sc*, *ap*) (+*sc*, −*sc*) (*ap*, *ap*)

Fig. 5. Calculated bond-lengths (Å) for methanol and methanediol.

values. A similar procedure was conducted for methanol in the staggered conformation. The C–O bond-lengths obtained in this way are given in Fig. 5, and the corresponding energies in Table I. As may be seen, the relative energies are very similar to those obtained with standard bond-lengths. However, the C–O bond-lengths show marked shortening in methanediol, relative to methanol. In addition, there is a strong *conformational dependence* of the calculated C–O bond-lengths in methanediol. Some of the variation in bond length may be rationalized on the basis of the delocalization effect already mentioned. In fact, it was the experimental observation of such bond-length changes in related systems that prompted Romers and Altona[1(b)] to postulate interactions of the type shown in VI. The effect of such interactions (VI) is to strengthen C–O-1 and weaken C–O-2. From Fig. 5, it may be seen that, in the (+*sc*, *ap*) conformation, the +*sc* C–O bond is, indeed, considerably shorter than the *ap* bond. On the other hand, the two C–O bonds in the (+*sc*, +*sc*), (+*sc*, −*sc*) conformations are equal in each case, and are shorter than the C–O bond in methanol. These results were to be expected, because lone-pair electron-donation by oxygen can occur equally in both directions in these structures. The shortening of the C–O bonds in the (*ap*, *ap*) conformation is not explained by the interactions shown in VI.

TABLE I

ENERGIES FOR METHANOL AND METHANEDIOL, WITH OPTIMIZED C–O BOND-LENGTHS

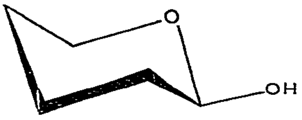
Molecule	*Total energy (hartrees)*	*Relative energy*[a] *(kcal.mol*$^{-1}$*)*
Methanol	−114.87023	
Methanediol (+*sc*, +*sc*)	−189.62529	0.0 (0)
(+*sc*, *ap*)	−189.61829	4.4 (4.7)
(+*sc*, −*sc*)	−189.61656	5.5 (5.4)
(*ap*, *ap*)	−189.60782	11.0 (11.2)

[a] Values in parentheses are relative energies calculated by using standard bond-lengths (from ref.3).

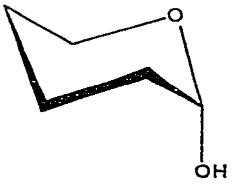
METHANEDIOL AS A MODEL FOR CARBOHYDRATE CONFORMATIONS

Before proceeding to survey the relevant experimental data on carbohydrate structures, we shall point out some of the limitations in using methanediol (or any other molecule, short of the complete carbohydrate) as a model system. Our calculations on methanediol suggest that certain electronic effects are operative, and that these effects lead to distinct conformational tendencies. *Other things being equal*, these same conformational tendencies will still be present in similar, but larger, systems. However, in reality, the differences between the system under investigation and the model must be taken into account when predictions are made. These additional effects will be superimposed upon the fundamental electronic effects operative in the small system; they may either re-inforce or oppose the conformational predictions, based on electronic considerations, made from the model system alone. If the effects are in opposition, the relative importance of the competing effects determines the favored conformation.

There are a number of differences between methanediol and pyranoses. (*i*) At least one of the hydroxyl hydrogen atoms of methanediol is replaced by a tetrahedral carbon atom in the sugars. One of the consequences of this replacement may be predicted by noting that the calculated[9] threefold (V_3) barrier (2.98 kcal.mol^{-1}) to rotation about the C–O bond in dimethyl ether, H_3C–O–CH_3, is considerably larger than for methanol[9], H_3C–OH (1.12 kcal.mol^{-1}). Thus, there is a greater tendency for staggered conformations. Reference to Fig. 4 shows that, if the V_3 term is increased, the potential minimum for $V(\theta)$ will move to values of θ that are closer to 60°. (*ii*) If structures having equatorially and axially attached hydroxyl groups are compared, it must be borne in mind that the conformations of cyclohexanol in which the hydroxyl group is equatorially and axially attached have unequal energies. This type of effect will thus also contribute to the conformational tendencies for the substituted tetrahydropyrans IX and X and for the pyranoses (although the magnitude of the effect may be different). In many of the conformations of the pyranoid sugars, still larger steric interactions occur, and these are also important in determining the conformation assumed by the molecule. (*iii*) Finally, it should be noted that the calculations made for methanediol refer to the isolated molecule at rest in the gas phase, and, consequently, the conclusions reached may actually be modified by molecular vibrations, by solvent effects in solution, or by crystal-field forces in the solid state. In addition, the results are subject to the inherent limitations of the theoretical method used, which involves single-determinant molecular orbital theory, a limited basis set, and standard bond-lengths and bond-angles.



IX



X

COMPARISON WITH CRYSTAL-STRUCTURE DATA

The torsion angles. — As illustrated in Fig. 3, the (+*sc*, +*sc*) or (−*sc*, −*sc*) conformations, predicted from the methanediol results to be the most stable, can only be obtained for the pyranoses having the α configuration and the $^4C_1$ conformation or the β configuration and the $^1C_4$ conformation. When the glycosidic oxygen atom is replaced by an even more electronegative atom, as in the glycosyl halides, this constitutes a statement of the anomeric effect[1].

As we are here concerned with the comparison with crystal-structure results, configurational equilibria cannot be considered; the predictions from theory have been matched against the conformational and structural data for the particular configuration found in the crystal. In all of the simple pyranoses and methyl pyranosides for which data are available, the conformation is $^4C_1$, and this corresponds to the least number of axially attached substituents on the pyranoid ring. In the results under discussion, the disposition about the angle ϕ is fixed close to 60° or 180° by the anomeric configuration and the conformation of the particular compound. Our conformational comparison is, therefore, limited to that about the anomeric (exocyclic) bond, θ, shown in Fig. 3. The orientational tendency about this bond, analogous to that influencing α,β configurational equilibria, has been referred to as the *exo*-anomeric effect[11,12].

The ϕ and θ conformational angles observed in the known crystal structures of the simpler pyranoses and methyl pyranosides are given in Table II. The small variations of ϕ from 60° or 180° constitute departures from the ideal, *trans*, cyclohexane ring geometry. For the α-pyranoses ($\phi = 60°$), the values of θ agree with the predictions made from the results with methanediol, except for α-L-rhamnose and for α-D-glucose in its urea complex, where the θ torsion angles lie in the adjacent, anticlinal sextant, *i.e.*, 90° to 150°. As O-1–H-1 is involved in intermolecular hydrogen-bonding in all of these structures, these deviations from 60° can be accounted for by the directional character of the intermolecular forces in the crystalline state. It is, indeed, surprising that these crystal-field forces are not so predominant in the solid state as completely to obscure the conformational tendencies predicted for the isolated molecules. In the methyl pyranosides, where the methyl group is not subject to directional, intermolecular hydrogen-bonding, the uniformity of the torsion angles is most striking. For the α anomers, the θ angles are very close to $+60°$, as predicted. In the β series, the θ values are close to $-70°$ for the methyl pyranosides, compared to the wider range of $-70°$ to $-116°$ for the free sugars. This result suggests that the replacement of one or both hydroxyl hydrogen atoms in methanediol by carbon atoms does, indeed, increase the V_3 (θ) term, as suggested in the previous Section. This effect would further deepen the minimum at 60° for the pyranosides, and would result in a more-pronounced minimum in the region of $\theta \sim \pm 60°$ for the β anomers. The absence of any conformations having $\theta \sim 180°$ supports our conclusion as to the importance of the $V_1(\theta)$ term.

All these torsion-angle data are, therefore, consistent with the theory for methanediol, or show deviations that can be accounted for either by the crystal field-forces or by the anticipated approximations of this model compound. On the other hand, they do not provide conclusive evidence that the conformational energy-differences extrapolated from the theory are a necessary explanation of the observations. In all of the aldopyranoses and methyl aldopyranosides studied, the same conformations are favored on steric grounds* and can be derived by using the simple

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*These steric factors are not present in methanediol, but would, of course, be implicit in quantum-mechanical calculations performed at this same level on the complete carbohydrate molecule. Calculations on the larger molecules are, however, computationally very expensive; the time needed for computation increases, approximately, as the third *power* of the number of electrons.

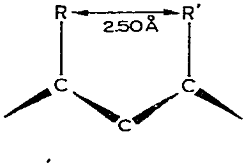
TABLE II

CONFORMATIONS AND BOND LENGTHS FOR THE HEMI-ACETAL OR ACETAL GROUPS IN PYRANOSES AND METHYL PYRANOSIDES

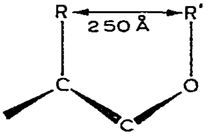
Compound	*Torsion angles*		*Relative bond-lengths*[a]				*References*
	ϕ	θ		ϕ	θ		
	(*degrees*)	(*degrees*)	C-5 — O-5	O-5 — C-1	C-1 — O-1-H		
α-D-Glucose	+61	+75	−01	−03	−40		13
α-D-Glucose–urea	+62	+97	+15	−15	−45		14
α-DL-Mannose	+57	+81	+15	+19	−34		15
α-L-Rhamnose·H_2O	−65	−97	+16	−07	−28		16
	−65	−94	+19	−05	−33		
β-DL-Arabinose	+61	+75	+21	+06	−34		17
α-Lactose·H_2O	+59	+45	−03	+15	−42		18
β-D-Glucose	−179	−96	+09	+05	−45		19
β-D-Lyxose	−175	−72	−06	+07	−64		20
Cellobiose	−176	−116	+08	−02	−48		19
				ϕ	θ		
			C-6 — O-6	O-6 — C-2	C-2 — O-2-H		
α-L-Sorbose	−60	−47	+12	−08	−13		21
α-D-Tagatose	+62	+45	+04	−01	−22		22
			C-5 — O-5	O-5 — C-1	C-1 — O-1	O-1 — CH_3	
Methyl α-D-glucopyranoside	+59	+63	+05	−15	−17	+01	23
Methyl α-D-galactopyranoside·H_2O	+62	+63	+11	−10	−23	+08	24
Methyl α-D-mannopyranoside	+60	+61	+21	−08	−22	+15	25
Methyl α-D-altropyranoside	+64	+64	+12	−11	−23	+01	26
Methyl β-D-xylopyranoside	+174	−72	−03	−06	−38	−01	27
Methyl β-maltopyranoside	+177	−70	+02	−11	−49	−06	28
Methyl β-cellobiopyranoside·MeOH	+180	−76	+04	+07	−49	+06	29

[a] The numbers under the bonds are bond-length differences (expressed in units of 10^{-3} Å) from the experimental value (1.428 Å) for methanol.

concept of non-overlapping, Van der Waals radii. With the $^4C_1$ conformation, these factors are the repulsive, nonbonding interactions that occur between H-1, or the methyl group, with the atoms attached axially on C-3 and C-5 and equatorially on C-2 for the α anomers, and axially or equatorially on C-2 for the β anomers. They are the three interactions shown in XI, XII, and XIII, where the separations are calculated for normal bond-distances and tetrahedral angles. By using the (Pauling) Van der Waals radii* of 2.0, 1.4, and 1.2 Å for CH_3, O, and H, these distances correspond to repulsive interactions, except for XI and XII when R = R′ = H. In consequence, the conformations favored by the theory for methanediol, that is, (+*sc*, +*sc*) or (−*sc*, −*sc*) in the α series and (*ap*, ±*sc*) in the β series, would also be predicted from nonoverlapping Van der Waals radii, except in two cases. These are (see Fig. 3): (+*sc*, *ap*) having an equatorially attached hydrogen atom on C-2 for an α-D-aldopyranose, and (*ap*, *ap*) having an equatorially attached hydrogen atom on C-2 for a β-D-aldopyranose, both in the $^4C_1$ conformation. In some configurations, these repulsive interactions are likely to be quite small; for example, they are probably less than 1 kcal.mol^{-1} for the 2.5-Å separations of hydrogen to oxygen, or hydrogen to methyl with a staggered orientation of the methyl group. Nevertheless, if the nonoverlapping of Van der Waals radii is strictly applied, it provides an unambiguous prediction of the conformations observed, except for α-D-mannopyranose and α-L-rhamnopyranose, where it fails to distinguish between (+*sc*, +*sc*) and (+*sc*, *ap*). The α-D-mannopyranose structure clearly favors the +*sc* torsion angle, and the angle for α-L-rhamnopyranose lies nearer to 60° than to 180°; these results are both consistent with those obtained for methanediol.



XI



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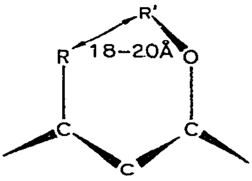

XIII

The α-(D or L)-ketoses provide, at present, the strongest evidence in support of the existence of local electronic effects that influence the conformation adopted. The conformation predicted by avoiding Van der Waals overlap for α-(D or L)-tagatose has a −*sc* torsion angle for O-6–C-2–C-1–O-1, as shown in Fig. 6, with an *ap* torsion angle for O-6–C-2–O-2–H(O-2). However, both observed angles are −*sc*, as predicted by the methanediol theory. The result is that H(O-2) lies between the line of centers $\text{O-2}\overset{2.86\ \text{Å}}{\cdots\cdots\cdots}\text{O-5}'$ of an adjacent molecule and $\text{O-2}\overset{2.68\ \text{Å}}{\cdots\cdots\cdots}\text{O-1}$ of the same molecule.

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*Recent crystal-structure studies indicate that 1.5 and 1.1 Å are more appropriate values for oxygen and hydrogen, respectively, when used for intramolecular separations, but this difference does not affect the arguments presented here.

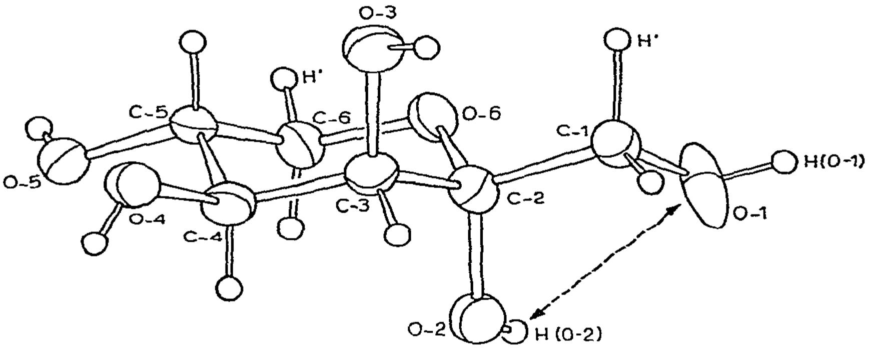

Fig. 6. α-D-Tagatopyranose in its crystal structure. The thermal ellipsoids are drawn at the 50%-probability level.

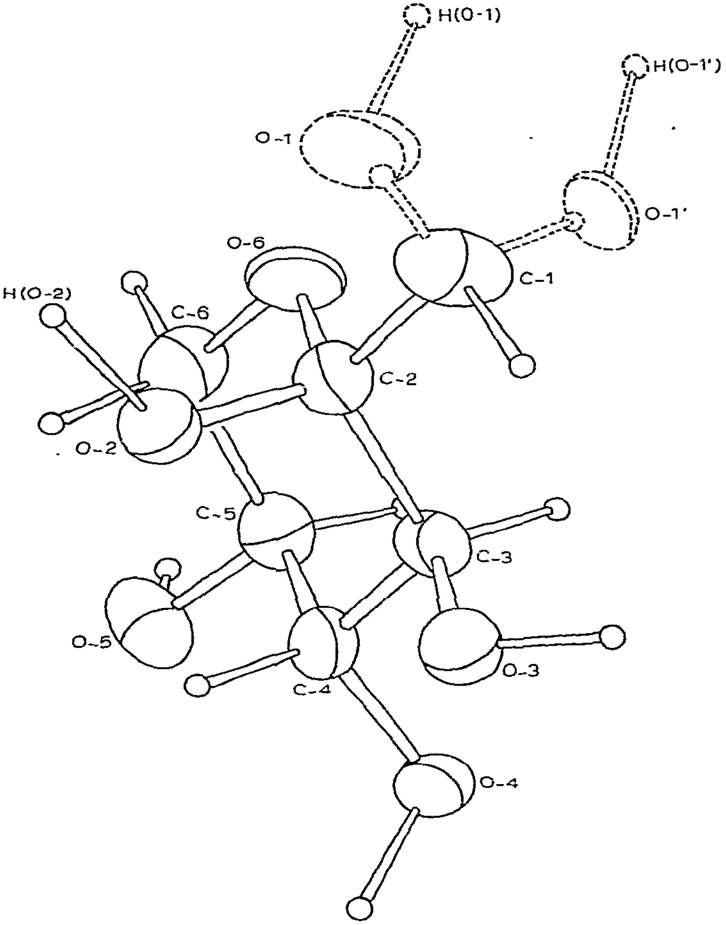

Fig. 7. α-L-Sorbopyranose in its crystal structure. The thermal ellipsoids are drawn at the 50%-probability level. The dotted lines represent the disorder of the primary alcoholic oxygen O-1, O-1′.

The distances and angles are, respectively, H(O-2)··O-5′, O-2-H(O-2)··O-5′, 2.06 Å, 159°; H(O-2)··O-1, O-2-H(O-2)··O-1, 2.0 Å, 140°. This could be a bifurcated hydrogen-bond situation, but the observed anisotropy of the thermal ellipsoid for O-1 indicates an orientational disorder between two positions such as to increase the H(O-2)··O-1 distance, suggesting that, at the 2.0-Å separation, the H(O-2)···O-1 interaction is repulsive, not attractive.

A similar, but more distinct, orientational disorder was found in the structure of α-L-sorbopyranose. For this structure, there are four conformations having the same minimum Van der Waals overlap of two H···O, 2.5-Å separations. These are the (−*sc*, −*sc*) and (−*sc*, *ap*) conformations for C-6–O-6–C-2–O-2–H combined with the O-1 and O-1′ orientations for the primary alcohol group, as shown in Fig. 7. Here, the theoretically predicted (−*sc*, −*sc*) orientation about the C–O–C–O–H linkages is observed for both conformations about C-2–C-1, as shown by the disorder of the primary alcoholic oxygen atom in the crystal structure.

In summary, both (*a*) quantum-mechanical calculations of local electronic effects (as determined from a study of a simple model compound, namely, methanediol), and (*b*) a steric model based on the avoidance of overlapping Van der Waals radii, have been used to predict the orientation about the anomeric bonds in pyranoses and methyl pyranosides. A test of these predictions (*vide supra*) against data from eighteen recent crystal-structure determinations yielded the following results. (*i*) In fourteen compounds, the conformations favored by local electronic effects are also favored on the basis of avoiding Van der Waals overlap. The same conformations are observed in the crystal structures. (*ii*) In three instances, a number of conformations are equally favored on the basis of steric considerations. For each compound, the conformation observed is the one predicted on the basis of the local electronic effects. (*iii*) For α-D-tagatose, the conformation most favored by local electronic effects is sterically less favored. The conformation observed agrees with that predicted from the electronic considerations, and so these must therefore be more important than the steric interactions for this molecule.

The C–O bond-distances. — A shortening of the anomeric C-1–O-1 bond was observed in the earliest crystal-structure determinations of pyranoses[30], but it was not until 1967 that sufficient reliable data was accumulated to establish this observation as a general structural property for this group of compounds[31]. The theoretical C–O bond-distances for methanol and the methanediol conformations are given in Fig. 5. They predict a shortening, relative to methanol, of 0.016 Å for both bonds in the α pyranoses and of 0.041 and 0.009 Å for the *exo*-cyclic and ring C-1–O bonds, respectively, for the β configuration. Table II shows the observed values obtained from the crystallographic data. The theory cannot account for the observed distinction between the C–O bonds in the α anomers, because the two oxygen atoms are equivalent in the (+*sc*, +*sc*) or (−*sc*, −*sc*) conformations of methanediol. There is good agreement as to the order of magnitude of the bond-shortening in both the α and β anomers. The distinction between the exocyclic and ring-bond shortening predicted for the β anomers is observed; the agreement for methyl β-maltoside, for example, is within experimental error. The prediction that there will be a greater shortening for C-1–O-1 for the *β* anomers than for the *α* anomers is clearly observed for the methyl pyranosides. This comparison for the free sugars is ambiguous, because the structure determination of *β*-D-lyxopyranose was significantly less accurate than the determination for some of the other sugars. For the ketoses, the exocyclic bond-shortening appears to be present, but to be less in magnitude, as the anomeric carbon atom (C-2) has no hydrogen atom attached to it; but these molecules are still farther removed from the model compound studied, namely, methanediol.

CONCLUSIONS

The quantum-mechanical calculations for methanediol provide a link between the experimentally observed, conformational tendency known as the *anomeric effect* and the anomeric, bond-length shortening observed from crystal-structure determinations on pyranoses. The agreement between predicted and observed torsion-angles and bond-shortenings is as close as, or perhaps closer than, would be anticipated if there are taken into account the approximation of methanediol to the pyranoid, hemi-acetal bond system, the limits in accuracy of the X-ray diffraction structural data, and the fact that these molecules were observed in the solid state.

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