Carbohydrate Research, 74 (1979) 1–5

APPLICATION OF MOLECULAR MECHANICS TO THE STRUCTURE OF 1,6-ANHYDROPYRANOSES

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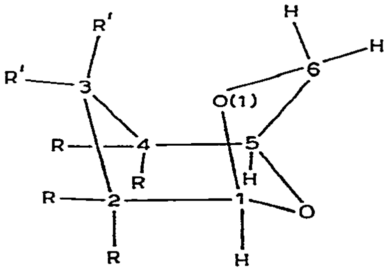
(Received November 6th, 1978; accepted for publication, December 25th, 1978)

ABSTRACT

Empirical force-field calculations have been applied to eight 1,6-anhydropyranoses, the crystal structures of which have been studied by single crystal X-ray, or neutron, diffraction analysis. The theoretical calculations reproduce closely the variations in conformation, between $^1C_4$ and E_0, which are observed for the pyranoid rings. The smaller conformational differences in the five-membered anhydro ring are not so well predicted. The calculated C–C bond lengths agree with those observed within 1.2 pm, with one exception. The C–O bond lengths show a larger deviation, 2.7 pm. The non-hydrogen atom valence angles agree within 1.9°.

INTRODUCTION

Empirical force-field methods or "molecular mechanics" have been shown to predict the dimensions of alkanes and non-conjugated alkenes to within the experimental limits of error of gas-phase and crystal X-ray diffraction methods[1,2]. The application of these methods to carbohydrates is more uncertain because of difficulties associated with the anisotropy of the electronic distribution about ring and glycosidic oxygen atoms and hydroxyl groups. However, a force-field calculation on α- and β-glucopyranose did give a value for the energy difference between the two that was consistent with experiment[3]. In that work, the empirical parameters were adjusted to give a good fit with the structure of α-D-glucopyranose, as observed by



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neutron diffraction[4], and good agreement was obtained for the bond lengths and valence angles.

In this study, we are testing the predictability for carbohydrates of a general purpose, molecular-mechanics program[5] against the molecular structural data provided by eight crystal-structure determinations of molecules of the type I, where R is H, OH, or OAc, and R′ is H, OH, NH_2, or NH_3^+. These also include a molecule having a 2,3-oxirane ring and a 3,4-dioxolane ring.

MOLECULAR-MECHANICS CALCULATIONS

The program used was Allinger's MMI[6,7], adapted for use on a DEC 1099 computer. The starting atomic parameters for the energy minimization were those from the crystal-structure determination*. Because of the problem of "false minima", there is no certainty that the structure corresponding to the energy minimization is that of lowest possible energy, nor can we say that a minimization starting from any other set of atomic coordinates would converge on the same structure.

RESULTS

The experimental data-set is given in the key to Fig. 1, which shows the overall comparison in calculated and observed conformations of the pyranoid rings. The agreement is excellent. The average differences in the Q, θ, and φ pyranose-ring puckering parameters[8] are 1.1 pm, 3.73°, and 6.17°, respectively. Particularly noteworthy are the two experimental points for molecule **8**, which correspond to two symmetry-independent molecules in the crystal structure. The difference between theory and experiment is clearly of the same order of magnitude as the conformational differences between the two molecules resulting from crystal-field forces.

In contrast, the conformational differences of the five-membered anhydro rings in these eight molecules show little correlation between theory and experiment, as shown in Table I. This could be the consequence of two approximations. One is that no distinction was made in the empirical force-field parameters between the C–O bonds, although they are known from X-ray structural data and ab-initio calculations[9,10] to have different bond lengths, valence angles, and torsion-angle potentials. The second is that the potential for conformational changes in the anhydro ring is pseudo-rotational in character, and very susceptible to the crystal-field forces, which were omitted from consideration.

The agreement between the experimental and theoretical bond-lengths and valence angles is summarized in Table II. Omitted from this summary is the C-2–C-3 bond in **8**. The shortening to 145.7 pm, 146.3 pm (146.7, 147.3 pm corrected for thermal motion) because of the oxirane ring was not reproduced by the theoretical calcula-

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*The starting atomic coordinates are given in the original crystal-structure papers. The lone-pairs were placed in equi-angular positions 50 pm from the appropriate atomic position.

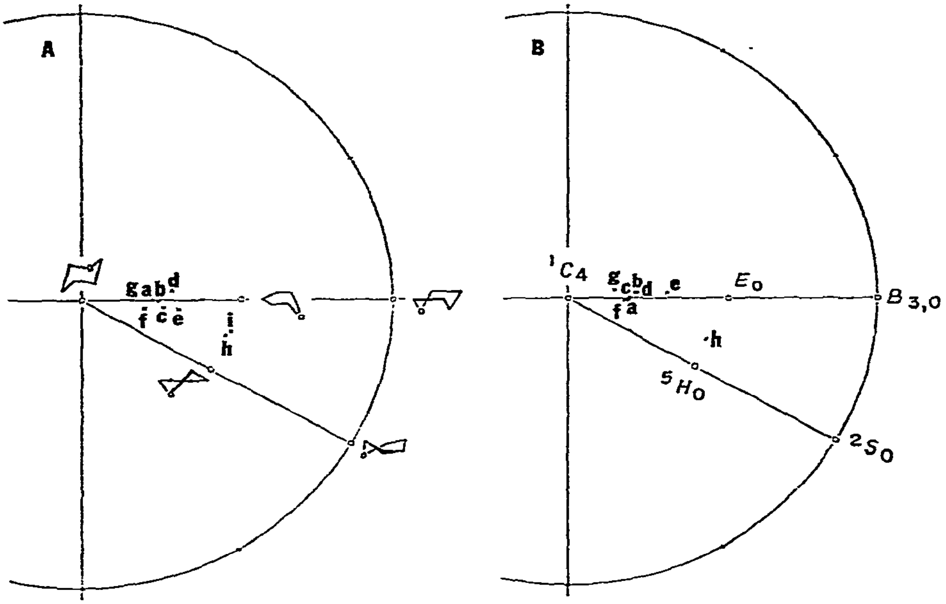

Fig. 1. Stereograms[11] of the θ and φ puckering parameters[8] for 1,6-anhydropyranose derivatives; (A) experimental values, (B) theoretical values. As all the φ values lie between 150 and 190°, only this portion of the total stereogram is reproduced.

Key:		Q_{exp} (pm)	Q_{theory} (pm)
a	1,6-Anhydro-β-D-glucopyranose[12,13] (1)	61.0	63.0
b	3-Amino-1,6-anhydro-3-deoxy-β-D-glucopyranose[14] (2)	61.5	62.6
c	1,6-Anhydro-2,3,4-tri-*O*-acetyl-glucose[15] (3)	61.7	62.7
d	3-Ammonio-1,6-anhydro-3-deoxy-β-D-glucopyranose chloride monohydrate[16] (4)	61.6	61.4
e	1,6-Anhydro-3,4-*O*-isopropylidene-β-D-talopyranose[17] (5)	63.0	61.5
f	2,3-Di-*O*-acetyl-1,6-anhydro-β-D-galactopyranose[18] (6)	62.4	63.3
g	2,7-Anhydro-D-altroheptulopyranose[19] (7)	64.4	63.5
h i	1,6:2,3-Dianhydro-β-D-gulopyranose[20] (8)	62.9 63.1	62.2

tions, which gave a normal value of 152.7 pm. Otherwise, the overall agreement for the C–C bond lengths was very good. That for the C–O bond lengths was less good, the theoretical values tending to be shorter than the experimental (the thermal-motion corrections increase these discrepancies, as they lengthen the observed values). The agreement in the valence angles is reasonably good, with no obvious distinction between those between C–C bonds and C–C and C–O bonds.

In general, the agreement between the calculations and the experimental data was remarkably good, taking into account the fact that the theoretical method used makes no distinction between ring and glycosidic oxygen atoms, hydroxyl oxygen atoms, and carbonyl oxygen atoms, and no corrections were made for the distortions resulting from crystal-field forces.

TABLE I

PUCKERING PARAMETERS[a] FOR THE ANHYDRO RINGS IN 1,6-ANHYDROPYRANOSES

Compound[b]	q		φ	
	Experimental	*Theoretical*	*Experimental*	*Theoretical*
1	41.9	43.6	41.39	39.97
2	42.3	44.4	49.99	49.35
3	35.5	44.0	36.60	43.73
4	41.3	45.2	55.67	47.32
5	41.2	43.4	40.04	51.88
6	42.1	44.2	43.89	42.62
7	41.2	43.9	41.54	47.66
8	40.0	44.3	25.06	17.55
	40.6		27.07	

[a]Ref. 8. q are in pm, φ in degrees. The anhydro ring is numbered in the program so that C-1 is atom 1, O-5 is atom 2, proceeding clockwise around the ring when viewed from C-3. [b]The key to the molecules is given in the caption to Fig. 1.

TABLE II

COMPARISON OF OBSERVED AND CALCULATED BOND-LENGTHS AND VALENCE-ANGLES IN 1,6-ANHYDROPYRANOSES

Bond	$\bar{\Delta}^a$	$\lvert\bar{\Delta}\rvert^b$
C–C	+0.3	1.2
C–O$_r$	−2.3	2.7
C–OH	−2.1	2.3
C–C–C	−0.3	1.9
C–C–OH	−0.4	1.7
C–O$_r$–C	−1.6	2.5
C–C–O$_r$	+0.9	1.7
O$_r$–C–O$_r$	+1.2	1.6

[a]$\bar{\Delta}$ is the mean deviation $\Sigma(b_{calc} - b_{obs})/n$, where n is the number of bonds or angles compared. Bond-length deviations are in picometers, bond angles in degrees. [b]$|\bar{\Delta}|$ is the mean-square-root deviation $[\Sigma(b_{calc} - b_{obs})^2/n]^{1/2}$, where n is the number of bonds or angles compared.

ACKNOWLEDGMENTS

This research was supported by the U. S. Public Health Service, National Institutes of Health Grant No. GM-24526. A Fellowship of the Ministry of Education, Government of Korea, is gratefully acknowledged (Y.J.P.).

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