

A Note on a Geometrical Method for Characterizing the Nature of Puckering in Pyrrolidine and Furanose Rings

BY N. ELANGO AND S. PARTHASARATHY

Department of Crystallography and Biophysics, University of Madras, Guindy Campus, Madras–600 025, India*

(Received 29 December 1982; accepted 19 September 1983)

Abstract

A geometrical method for determining the conformation of five-membered rings is described. A Fortran program has been written for this purpose. The application of this method to a few cases is described.

Introduction

Characterization of the puckering of pyrrolidine and furanose rings is important owing to the occurrence of these as part of proline and pentose sugar residues in proteins and nucleic acids, respectively. Altona & Sundaralingam (1972) (A–S) have proposed a method based on the use of two pseudorotation parameters τ_m and P calculated from the five torsion angles of the ring atoms. Cremer & Pople (1975) (C–P) proposed a method based on the use of two puckering parameters q and φ calculated from the atomic coordinates of the ring atoms. Taylor (1980) has derived theoretical expressions for standard deviations for the C–P parameters. Rao, Westhof & Sundaralingam (1981) have pointed out the minor shortcomings in A–S and C–P procedures and have also given an exact method for obtaining the A–S parameters τ_m and P . They have also derived theoretical expressions for the standard deviations of τ_m and P . They have further pointed out that the A–S and C–P methods are the same for all practical purposes and obtained the relationship between the A–S and C–P parameters.

Since a puckered ring is a geometrical object it is possible to approach the problem of finding the nature of puckering from a purely geometrical point of view. In this note we propose a geometrical solution to the problem of characterizing the puckering of five-membered rings. A Fortran program which determines the conformation of the ring from known atomic coordinates by the present method has been written.

Notation and nomenclature

We shall refer to the plane defined by any three consecutive atoms of the ring as a three-atom plane

(TAP hereafter). We shall denote the TAP formed by the atoms $i-1, i, i+1$ by π_i .† We can form five TAP's from the ring atoms, namely $\pi_i, i = 1$ to 5. With respect to any such plane we shall use the term the *other two atoms* (OTA hereafter) to refer to the two atoms of the five-membered ring other than the three atoms which define the given TAP. Let $D_{i,1}$ and $D_{i,2}$ be the deviations of the OTA from the TAP π_i such that $D_{i,1}$ corresponds to atom $i+2$ and $D_{i,2}$ to atom $i+3$. Let us denote $(|D_{i,1}| + |D_{i,2}|)/2$ by d_i and refer to it as the average deviation of OTA from plane π_i . From the actual examples studied, it is found that in the case of either a pyrrolidine or a furanose ring only one of the five TAP's has unique geometrical properties (for details see *Discussion*). Such a unique plane would be the proper TAP for characterizing the nature of puckering of the five-membered ring. We shall designate this unique plane as the proper TAP and denote it by π_P .

With respect to the plane π_P the atom of the OTA group for which the deviation is larger is said to have *major* puckering and the other atom is said to have *minor* puckering. We shall symbolically denote the atoms involved in major and minor puckering by M and m , respectively. We denote the reference atom‡ by R , the deviation of atoms M, m and R from π_P by Δ_M, Δ_m and Δ_R , respectively, and the standard deviations in Δ_m and Δ_M by σ_m and σ_M , respectively.

The ring can exist in either envelope (E , say) or twist (T , say) conformation. If $|\Delta_m| = |\Delta_M|$ (within experimental accuracy) then the conformation will be of the symmetric twist type. We follow the notation of Sundaralingam (1971) to represent the conformation.§

Description of the method

The present method consists of the following steps:
(i) From the atomic coordinates of the five atoms of

† While assigning values 1 to 5 to i if the value of any of $i-1, i+1, i+2, i+3$ becomes other than 1, 2, 3, 4 and 5, it must be reduced modulo 5 in order to bring it to the range 1 to 5. (e.g. plane π_5 is constituted by atoms 4, 5 and 1. Here $i+1 = 6$ which is equal to 1 reduced modulo 5).

‡ R stands for C' in the case of a proline residue and C(5') in the case of a sugar residue.

§ Recently, Chacko, Swaminathan & Veena (1983) have adopted this notation for proline residues (see also Swaminathan, 1980).

* Contribution No. 620.

Table 1. Results of application of the present method in a few actual cases

Name	Space group	<i>i</i>	$D_{i,1}$	$D_{i,2}$	d_i	Δ_R	Conformation*	
1. Formycin monohydrate	$P2_12_12_1$	1	0.8196	0.3783	0.5999		2T_1	
		2	-0.8886	-0.8188	0.8537			
		3	0.6994	0.9513	0.8254			
		4	-0.2392	-0.7606	0.4999			
		5	-0.4061 (6)	0.2207 (6)	0.3134	-1.2068	2T_1	
2. Potassium dihydrouridine 3-monophosphate hemihydrate	C2	1	0.8895	0.5293	0.7094			
		2	-0.8621	-0.8903	0.8762			
		3	0.5865	0.9265	0.7565			
		4	-0.0515	-0.6381	0.3448			
		5	-0.5626 (10)	0.0467 (7)	0.3047	-1.1787		
3. 7,2'-Anhydro- β -D-arabinosylorotidine (cyclo Ara-O)	P1	1	0.6907	0.1441	0.4174		1T_2	
		2	-0.9041	-0.7054	0.8047			
		3	0.8686	0.9751	0.9218			
		4	-0.5284	-0.9264	0.7274			
		5	-0.1511 (9)	0.4718 (13)	0.3115	-1.1821		
4. Cyclo (L-Ala-L-Pro-D-Phe) ₂	$P2_12_12_1$	1	0.9068	-0.6826	0.7947			
		2	0.7115	0.8710	0.7912			
		3	-0.3326	-0.7533	0.5430			
		4	-0.2140 (30)	0.3694 (31)	0.2917	-1.0903		
		5	0.6880	0.1910	0.4395			
5. Tosyl-L-prolyl-L-hydroproline monohydrate (i) Prolyl residue	P2 ₁	1	0.8085	0.5078	0.6582		${}^{\gamma}E$	
		2	-0.7367	-0.7809	0.7588			
		3	0.4651	0.7558	0.6104			
		4	-0.0079	-0.5118	0.2598			
		5	-0.4999 (36)	0.0071 (27)	0.2535	-1.2748		
		(ii) Hydroprolyl residue	1	-0.9064	-0.7479	0.8272		${}^{\beta}T^{\gamma}$
			2	0.7229	0.9284	0.8257		
			3	-0.2876	-0.7806	0.5341		
			4	-0.3275 (39)	0.2964 (31)	0.3119	-1.0924	
			5	0.7843	0.3012	0.5428		
6. Benzyloxycarbonyl- α -aminoisobutyryl- L-Pro-methylamide	$P2_12_12_1$	1	-0.6834	-0.4354	0.5594		${}^{\gamma}E$	
		2	0.6686	0.6929	0.6805			
		3	-0.3859	-0.6379	0.5119			
		4	-0.0126 (84)	0.4049 (105)	0.2088	-1.1738		
		5	0.4240	0.0121	0.2181			

Notes:

(1) For details of the structures see Prusiner, Brennan & Sundaralingam (1973); Emerson & Sundaralingam (1980); Smith, Chwang & Sundaralingam (1980); Brown & Teller (1976); Sabesan & Venkatesan (1971); Venkatramprasad, Shamala, Nagaraj, Chandrasekaran & Balaram (1979), respectively.

(2) $D_{i,1}$, $D_{i,2}$, d_i and Δ_R are in Å.

(3) The five-membered ring exists in an envelope conformation in structures [5(i)] and (6) while it exists in a twist conformation in all other structures.

* Conformation at 3σ level.

the ring calculate the deviations $D_{i,j}$, $i = 1$ to 5, $j = 1$ and 2, by standard procedures. (ii) Calculate the average deviations d_i , $i = 1$ to 5. (iii) Determine the proper TAP as the one for which d_i is the least (see Discussion). (iv) Calculate σ_M and σ_m and use these to determine the nature of the puckering of the ring as E or T . (v) Calculate the deviation Δ_R . (vi) The conformation of the ring will be

$$M\text{-exo-}m\text{-endo} \quad \text{or} \quad M\text{-endo-}m\text{-exo}$$

according as

$$\Delta_M \Delta_R < 0 \quad \text{or} \quad \Delta_M \Delta_R > 0,$$

respectively.

It may be noted that if one is interested in determining only the nature of ring puckering, steps (v) and (vi) need not be carried out since these steps are needed only when the conformation of the residue is needed relative to the reference atom (*i.e.* *exo-endo*).

Discussion

A Fortran program* for carrying out the above procedure has been written. The results obtained for a few typical cases using this program are given in Table 1.

The following points may be noted regarding Table 1.

(i) Here $i = 1$ to 5 stands for C^α , C^β , C^γ , C^δ and N, respectively, in the case of the pyrrolidine ring and for $C(4')$, $C(3')$, $C(2')$, $C(1')$ and O, respectively, in the case of the furanose ring (see Fig. 1).

(ii) The numbers within parentheses are the standard deviations in Δ_m and Δ_M as the case may be.

* A listing of the program and an Appendix to the paper have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38861 (21 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

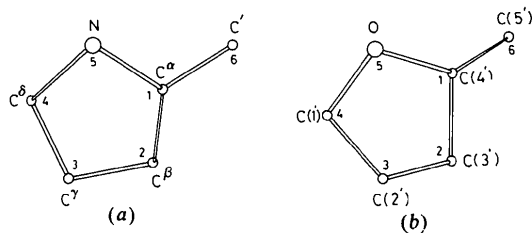


Fig. 1. Numbering of atoms in (a) proline and (b) furanose residues adopted in the present study.

(iii) The column headed by i gives the serial number of the central atom of the TAP.

It is found (see Table 1 for illustration) that in the case of every pyrrolidine or furanose ring studied the TAP for which the average deviation of the OTA is the *least* is the *only* plane for which the OTA lie on *opposite* sides of the corresponding TAP. Owing to this *geometrical uniqueness* of one of the five possible TAP's, such a plane would be the proper choice for describing the geometrical features of the ring. We shall therefore call such a TAP a proper TAP.

The nature of the ring puckering (E or T) in a given structure can be determined by making use of the values of the standard deviations of Δ_m and Δ_M as follows: In a given situation if $|\Delta_m| < k\sigma_m$ ($k = 1, 2$ or 3 as one may wish to choose) then the ring can be said to exist in the E conformation at the $k\sigma$ level. If $|\Delta_m + \Delta_M| < k(\sigma_m^2 + \sigma_M^2)^{1/2}$, the ring may be said to exist in the symmetric twist conformation at the $k\sigma$ level.† Otherwise, the ring may be said to exist in the twist conformation (T , say).

* Note that the standard deviation of the algebraic sum of Δ_m and Δ_M may be approximated by $(\sigma_m^2 + \sigma_M^2)^{1/2}$.

† The theoretical expressions for the calculation of σ_m and σ_M are derived in an Appendix. See deposition footnote.

The following point may be noted. Although the present geometrical procedure does not seem to be related to the pseudorotation method, the steps dealing with the determination of the proper TAP involve some sort of cycling in five discrete jumps around the ring (e.g. calculations involving planes 1, 2, 3; 2, 3, 4; 3, 4, 5; 4, 5, 1 and 5, 1, 2). The actual relationship, if any, between the geometrical and pseudorotation methods is not yet clear.

The authors are grateful to the referees for very useful comments and to Dr K. K. Chacko for useful discussion. One of the authors (NE) thanks the University Grants Commission, India, for financial assistance.

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