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Description of ring puckering of furanose: An analytical approach

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Abstract. An analytical approach for the description of the ring puckerings from the endocyclic ring torsion angles of a five-membered saturated ring is given. This description is independent of any reference conformation. For the description, a revised notation for the endocyclic ring torsion angles has been suggested. The application of this method to the furanose ring is described in detail.

Keywords. Endocyclic ring torsion angles; twist puckering; envelope puckering; *endo* puckering; *exo* puckering.

1. Introduction

To arrive at the description of the puckered five-membered ring, crystallographers search for the best four-atom plane of the ring or refer the puckered atoms to a three-atom plane. Often to obtain the best plane, they try several possibilities and come up with unrealistic descriptions such as *endo-endo* or *exo-exo*. Altona and Sundaralingam (1972) used two parameters, the 'phase angle' of pseudorotation P and the degree of pucker, τ_m, to determine the puckering of a five-membered ring. Following Altona *et al* (1968), Altona and Sundaralingam (1972) expressed P in terms of endocyclic ring torsion angles (θs) of a saturated five-membered ring as follows:

$$\tan P = \frac{(\theta_2 + \theta_4) - (\theta_1 + \theta_3)}{2\,\theta_0\,(\sin 36 + \sin 72)}. \tag{1}$$

The second parameter τ_m or (θ_m) can be calculated from the following equation (Altona and Sundaralingam 1972)

$$\theta = \theta_0 \cos P. \tag{2}$$

In principle, the choice of $P = 0°$ can be anywhere in the pseudorotation plane as the value of P depends upon the maximum value of the torsion angle (refer equation (2)) and hence arbitrary. Altona and Sundaralingam (1972) selected the symmetrical C2′ *exo* — C3′ *endo* (T_2^3) as the standard conformation ($P = 0°$) for furanose ring. It may be noted that a few investigators (Sundaralingam 1969; Arnott and Hukins 1972; Pullman and Saran 1976) use the symbols τ_0, τ_1, τ_2, τ_3 and τ_4 for the endocyclic sugar ring torsion angles about the bonds O1′—C1′, C1′—C2′, C2′—C3′,

C3′—C4′ and C4′—O1′ respectively. To calculate P, τs should be converted to θs as follows:

$$\theta_0 = \tau_2,\ \theta_1 = \tau_3,\ \theta_2 = \tau_4,\ \theta_3 = \tau_0 \text{ and } \theta_4 = \tau_1.$$

Altona and Sundaralingam (1972) stated that the puckering of the sugar can be obtained from the sign and relative magnitude of the τ values of the furanose ring. In this paper, an analytical proof of describing the ring puckering from an inspection of the five endocyclic ring torsion angles and a few examples for the proof are given. For this purpose, the notations we follow in this paper for the endocyclic ring torsion angles (figure 1a) are σ_0, σ_1, σ_2, σ_3 and σ_4 corresponding to the rotation about the bond C2′—C3′, C3′—C4′, C4′—O1′, O1′—C1′ and C1′—C2′ respectively. As IUPAC-IUB Commission on Biochemical Nomenclature has suggested the symbol, τ, for bond angle, the use of this symbol (τ) for sugar ring torsion angles may be avoided. It may be noted that the subscripts for σs are the same as that of θs (Altona and Sundaralingam 1972). The reason in choosing the given subscript symbols for the sugar ring endocyclic torsion angles will be evident below.

2. Analytical approach

For this purpose, the ring vibration is described in terms of one twist and one bending mode. In figure 1b, bending angle X is defined as an angle made by NM and NO1′ and the twist angle Y is defined by the torsion angle C4′-C3′-C2′-C1′ using the two-fold symmetry as has been done in vibrational analysis of cyclopentane and related compounds (Ikeda and Lord 1972). As a twist angle is defined as a torsion angle, a twist axis can be replaced by a torsion axis. Thus, X and Y or, E^0 and σ_0, are sufficient to describe the ring puckering. In this paper following Sasisekharan (1973) and Pattabiraman *et al* (1980) E^0 refers to O1′ *endo* puckering and E_0 refers to O1′ *exo* puckering. Note that Altona and Sundaralingam (1972), used ${}^0E$ for O1′ *endo* and ${}_0E$ for O1′ *exo* puckerings. We will now show how from E^0 and σ_0 plot, the remaining four endocyclic torsion angles, can be obtained and at the same time qualitatively describe the ring puckering. Figure 2 shows the envelope and twist puckerings in the pseudorotational space for the furanose ring. In this figure, all the twist axes can be replaced by the corresponding torsion axes as shown. The positive envelope axis is denoted by *endo* and the negative envelope

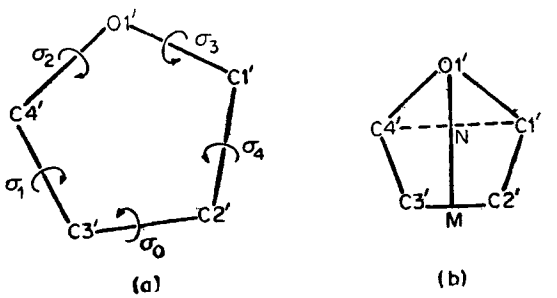

Figure 1. a. Notations for endocyclic torsion angles. b. One-bending and twist mode.

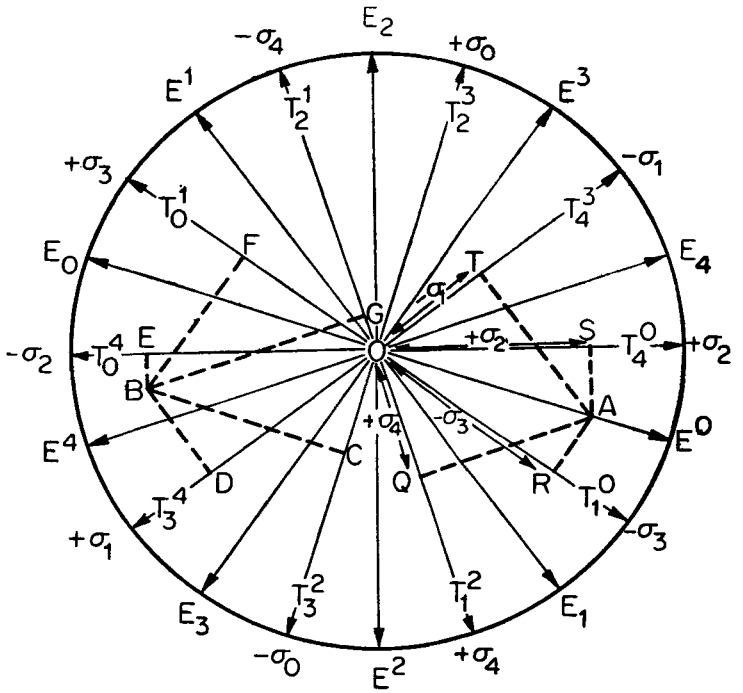

Figure 2. Pseudorotation wheel for sugar puckering. Note the twists (T) are replaced by the corresponding endocyclic ring torsion angles (σ).

axis by *exo*. The positive σ-axis is denoted by $+\sigma$ and the negative σ-axis as $-\sigma$. It may be noted that the envelope axes alternate between *endo* and *exo*; as also the σ-axes alternate between positive and negative axis.

Further, in the pseudorotational space, any point on an envelope axis corresponds to an envelope puckering of the atom denoted by the superscript; the torsion angle with this superscript is equal to zero degree. Thus, for example, any point on the E^0 axis or E_0 axis corresponds to O1′ envelope puckering and has a torsion angle (σ_0) about the bond (C2′-C3′) opposite to the atom O1′ equal to zero degree. Thus, the perpendicular torsion axis measures the torsion angle about the bond opposite to the atom of the envelope axis (see figure 2). In other words, a σ-axis with a subscript measures the torsion angle about the bond opposite to the atom indicated in the subscript.

The approach is divided into two sections, one for the envelope and the other for the twist puckerings.

2.1 *Envelope puckering*

Point A lies on E^0 axis as shown in figure 2. To obtain the five endocyclic ring torsion angles; OA is projected on all the five σ-axes as shown. Thus, OT, OS, OR and OQ which are the projections of OA on the various σ-axes give the torsion angles σ_1, σ_2, σ_3 and σ_4 in degrees. Since the projection of OA on σ_0-axis is zero, the torsion angle σ_0 is zero. It is readily seen from figure 2 that the projection of OA on σ_1-axis is negative; on σ_2-axis, it is positive; on σ_3-axis it is negative and on σ_4-axis it is positive. Thus, it is clear that the sign of any one of the ring torsion

angles in the case of an envelope puckering is opposite to that of the neighbouring torsion angle on both sides. Also, it will be noticed that for any conformation such as *A* on the *endo* axis E^0, the sign of σ_1 is negative. It is readily seen that if the point *A* is to lie on the *exo* axis E_0, the sign of σ_1 will be positive. Thus, for all the ten envelope puckerings, one of the corresponding torsion angles will be zero degree and the sign of the next torsion angle in the sequence σ_0, σ_1, σ_2, σ_3 and σ_4 will be negative for *endo* conformations and positive for *exo* conformations.

In practice none of the torsion angles of the ring is exactly zero degree. Therefore, all conformations with the minimum-most torsion angle less than $|5|^\circ$ have been characterised as envelope puckering. It may be noted that the limiting value for the minimum-most torsion angle need not be less than 5°. Depending upon the co-ordinates of the molecule reported, this value can be $(5+1)^\circ$. Table 1 lists the values of the five endocyclic torsion angles observed in crystal structures reported in literature. Two examples, one for *endo* and the other for *exo* puckerings, are given below from table 1.

Table 1. Endocyclic ring torsion angle and puckering of the sugar moiety in crystal structures of nucleoside derivatives.

Compound	Endocyclic torsion angles in degrees					Sugar puckering
	σ_0	σ_1	σ_2	σ_3	σ_4	
1	2	3	4	5	6	7
1. Xanthosine dihydrate (Koyama *et al* 1976)	−36·0	21·3	3·7	−27·4	39·7	E^2
2. Hydrogen bonded complex of adenosine and 5-bromo-uridine (5-bromouridine part) (Haschemeyer and Sobell 1965)	38·2	−41·1	26·2	−3·8	−21·3	E^3
3. Deoxyadenosine mono-hydrate (Watson *et al* 1965)	−34·4	33·7	−19·9	−2·4	23·9	E_3
4. 2′-Deoxycytidine. HCl (Subramanian and Hunt 1970)	36·9	−31·9	14·2	9·8	−29·5	${}^3T_2$
5. Deoxycytidine-5′-phosphate (Viswamitra *et al* 1971)	−25·8	31·1	−25·8	7·9	11·7	${}_3T^4$
6. Guanosine dihydrate and inosine dihydrate (Guanosine dihydrate Mol. B) (Thewalt *et al* 1970)	−31·9	10·9	16·9	−38·3	44·0	${}_1T^2$
7. 2′-0-Methyladenosine (Mol. B) (Prusiner and Sundaralingam 1976)	34·8	−25·7	5·2	17·5	−32·8	E_2
8. 5′-Methylammonium-5′-deoxy-adenosine iodide monohydrate (Saenger 1971)	−36·9	31·3	−12·6	−11·6	30·9	T^2
9. Arabinofuranosylthymine (Tougard 1973)	−9·2	−16·8	37·8	−42·9	32·0	${}^0T_1$

Examples

(i) Out of the five endocyclic torsion angles of the sugar in the compound, xanthosine dihydrate (No. 1 in table 1), σ_2 has the lowest value and $|\sigma_2|$ is less than 5°. Therefore, the atom C2′ is puckered in an envelope form. Since the sign of the next torsion angle σ_3 is negative, the puckering of the sugar in this compound is C2′ *endo* i.e. E^2.

(ii) Since σ_3 has the lowest value among the five endocyclic torsion angles of the sugar in the compound, deoxyadenosine monohydrate (No. 3 of table 1), and the sign of the next torsion angle, σ_4 is positive, the puckering of the sugar in this compound is C3′ *exo i.e.* E_3.

2.2 *Twist puckering*

Point *B* lies between E^4 and E_0 axes as shown in figure 2. The sugar puckering in this case is ${}^4T_0$. As before perpendiculars *BC*, *BD*, *BE*, *BF* and *BG* are drawn to σ_0, σ_1, σ_2, σ_3 and σ_4-axis respectively. The projections of *OB* on the axes give all the torsion angles. In this case, it is evident that none of the σ-angles is zero. The sign of σ_0 is the same as σ_4 (both negative) and the sign of σ_1 is the same as σ_3 (both positive). Also in this case $OG\ (-\sigma_4)$ and $OC\ (-\sigma_0)$ are smaller than the other projections. Hence, for the ${}^4T_0$ (C4′ *endo*-O1′ *exo*) puckering the σ_4 and σ_0 are both small and negative. Again, it will be noticed that the lowest torsion angle is σ_4 ($|\sigma_4| < |\sigma_0|$) and the sign of the adjacent torsion angle, σ_0, is negative. Further, the other lower value is σ_0 and the sign of the adjacent torsion angle, σ_1, is positive. Thus, for a twist puckering, adjacent two out of five torsion angles will be small and have the same sign. The sign of the torsion angle adjacent to each of the two small torsion angles in the sequence is negative for *endo* and positive for *exo* for the two puckered atoms.

For an ideal twist puckering, adjacent two out of the five torsion angles are small, equal and of the same sign. Two adjacent atoms of the ring are said to be equally puckered but in opposite direction. However, in practice, the two torsion angles are not exactly equal *i.e.*, the atoms are not equally puckered. The smaller of the two corresponds to the most puckered atom. Two examples for twist puckering, one for *endo-exo* and the other for *exo-endo* puckerings, are illustrated below from table 1.

Examples

(i) Out of the five ring torsion angles in arabinofuranosylthymine (No. 9 in table 1), σ_0 and σ_1 have the same sign (negative). Since $|\sigma_0| < |\sigma_1|$, atom O1′ is puckered most. Since the sign of σ_1 is *negative*, O1′ atom is *endo* puckered. As the sign of σ_2, adjacent to σ_1, is *positive*, C1′ atom is *exo* puckered. Hence, the sugar puckering in this case is O1′ *endo*-C1′ *exo* i.e., ${}^0T_1$.

(ii) The two torsion angles σ_3 and σ_4 in deoxycytidine-5′-phosphate (No. 5 in table 1) have the same sign (positive). Since $\sigma_3 < \sigma_4$, C3′ atom is most puckered. Since the sign of the next torsion angle to σ_3 in the sequence, σ_4 is *positive*, the atom C3′ is *exo* puckered. Following the rules, the atom C4′ is *endo* puckered. Hence, for this compound, the puckering of the sugar is C3′ *exo*-C4′ *endo* i.e., ${}_3T^4$.

The above proof is valid for *D*-configuration, of the ring and thus for *L*-configuration such as *L*-ribose, the sign convention should be reversed, that is to say, the sign of the next torsion angle in the sequence will be positive for *endo* and negative for *exo* conformations. This method is applicable to any five-membered ring including pyrrolidine ring, *L*-proline or *D*-proline as the case may be.

3. Conclusions

Ring puckering can be obtained by inspection of the torsion angles without recourse to a reference conformation. Thus, for an envelope puckering, the subscript of the minimum-most torsion angle of the five endocyclic torsion angles of the ring will be the most puckered atom. The conformation is *endo*, if the sign of the next torsion angle in the sequence σ_0, σ_1, σ_2, σ_3 and σ_4 is negative, and the conformation is *exo* if the sign of the next torsion angle is positive. For a twist puckering, the subscripts of the two torsion angles which are small relative to the remaining three torsion angles indicate the two atoms which are puckered. Following the above sign convention, the sign of the next torsion angle adjacent to the smallest of the two determines the nature of the puckering *endo* or *exo* of the most puckered atom. The other atom will be puckered opposite, giving rising to the two atom puckered conformations, *endo-exo* or *exo-endo* as the case may be.

Further, quantitatively the displacement of the puckered atom from the plane is given by (say) $d_{C2'} = l_{C1'-C2'}(\sin C1')(\sin \sigma_3)$. In the case of an envelope form, the displacement of the puckered atom can be obtained in two ways and the average of the two leads to the mean displacement of the puckered atom for the best plane passing through the remaining four atoms. The modified notation for the endocyclic ring torsion angles is of use for both crystallographers and the workers in the field of conformation of nucleic acids.

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