

## 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,  $\tau_m$ , 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 ( $\theta_s$ ) of a saturated five-membered ring as follows:

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

The second parameter  $\tau_m$  or ( $\theta_m$ ) can be calculated from the following equation (Altona and Sundaralingam 1972)

$$\theta = \theta_0 \cos P. \quad (2)$$

In principle, the choice of  $P = 0^\circ$  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 ( $P = 0^\circ$ ) for furanose ring. It may be noted that a few investigators (Sundaralingam 1969; Arnott and Hukins 1972; Pullman and Saran 1976) use the symbols  $\tau_0, \tau_1, \tau_2, \tau_3$  and  $\tau_4$  for the endocyclic sugar ring torsion angles about the bonds  $O1' - C1', C1' - C2', C2' - C3'$ ,

C3'—C4' and C4'—O1' respectively. To calculate  $P$ ,  $\tau$ s should be converted to  $\theta$ s 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  $\tau$  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  $\sigma_0, \sigma_1, \sigma_2, \sigma_3$  and  $\sigma_4$  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,  $\tau$ , for bond angle, the use of this symbol ( $\tau$ ) for sugar ring torsion angles may be avoided. It may be noted that the subscripts for  $\sigma$ s are the same as that of  $\theta$ s (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  $\sigma_0$ , 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  ${}^oE$  for O1' *endo* and  ${}_oE$  for O1' *exo* puckerings. We will now show how from  $E^0$  and  $\sigma_0$  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

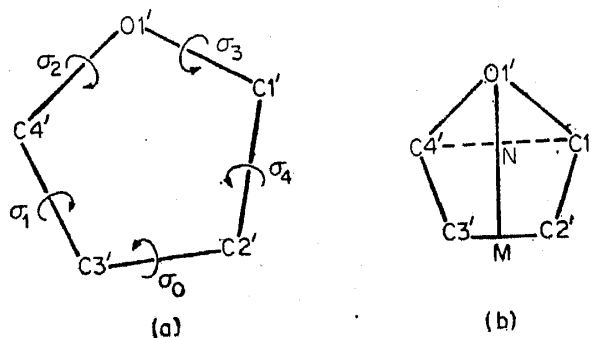


Figure 1. a. Notations for endocyclic torsion angles. b. One-bending and twist mode.

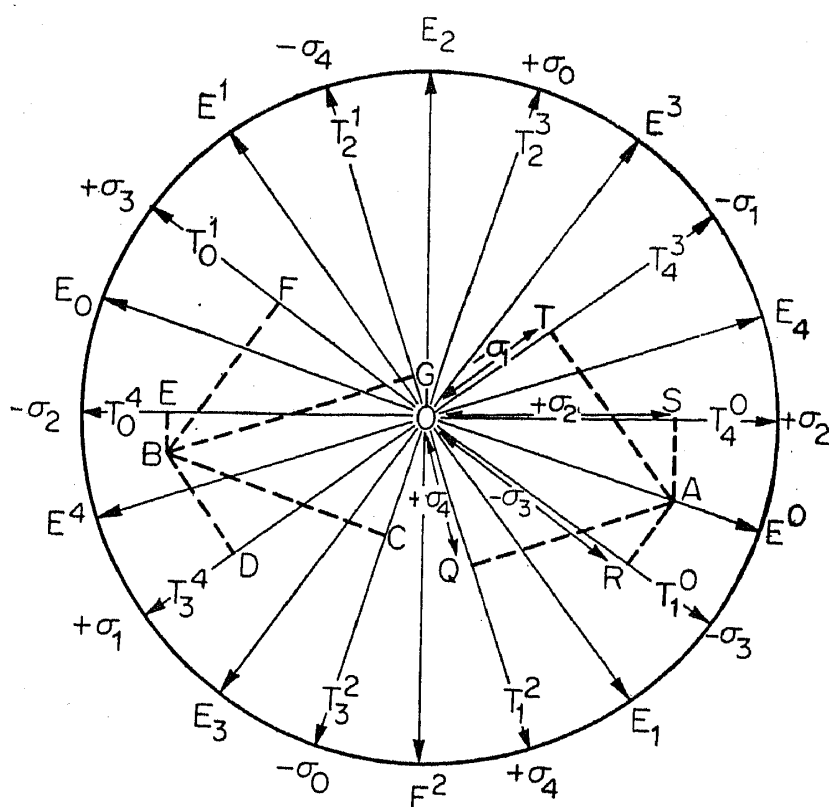


Figure 2. Pseudorotation wheel for sugar puckering. Note the twists ( $T$ ) are replaced by the corresponding endocyclic ring torsion angles ( $\sigma$ ).

axis by *exo*. The positive  $\sigma$ -axis is denoted by  $+\sigma$  and the negative  $\sigma$ -axis as  $-\sigma$ . It may be noted that the envelope axes alternate between *endo* and *exo*; as also the  $\sigma$ -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 ( $\sigma_0$ ) 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  $\sigma$ -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  $\sigma$ -axes as shown. Thus,  $OT$ ,  $OS$ ,  $OR$  and  $OQ$  which are the projections of  $OA$  on the various  $\sigma$ -axes give the torsion angles  $\sigma_1$ ,  $\sigma_2$ ,  $\sigma_3$  and  $\sigma_4$  in degrees. Since the projection of  $OA$  on  $\sigma_0$ -axis is zero, the torsion angle  $\sigma_0$  is zero. It is readily seen from figure 2 that the projection of  $OA$  on  $\sigma_1$ -axis is negative; on  $\sigma_2$ -axis, it is positive; on  $\sigma_3$ -axis it is negative and on  $\sigma_4$ -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  $\sigma_1$  is negative. It is readily seen that if the point *A* is to lie on the *exo* axis  $E_0$ , the sign of  $\sigma_1$  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  $\sigma_0, \sigma_1, \sigma_2, \sigma_3$  and  $\sigma_4$  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  $5^\circ$ . Depending upon the coordinates 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
	$\sigma_0$	$\sigma_1$	$\sigma_2$	$\sigma_3$	$\sigma_4$	
1	2	3	4	5	6	7
1. Xanthosine dihydrate (Koyama <i>et al</i> 1976)	-36.0	21.3	<u>3.7</u>	-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	<u>-3.8</u>	-21.3	$E^3$
3. Deoxyadenosine mono- hydrate (Watson <i>et al</i> 1965)	-34.4	33.7	-19.9	<u>-2.4</u>	23.9	$E_3$
4. 2'-Deoxycytidine. HCl (Subramanian and Hunt 1970)	36.9	-31.9	<u>14.2</u>	<u>9.8</u>	-29.5	$^3T_2$
5. Deoxycytidine-5'-phosphate (Viswamitra <i>et al</i> 1971)	-25.8	31.1	-25.8	<u>7.9</u>	<u>11.7</u>	$^3T^4$
6. Guanosine dihydrate and inosine dihydrate (Gua- nosine dihydrate Mol. B) (Thewalt <i>et al</i> 1970)	-31.9	<u>10.9</u>	<u>16.9</u>	-38.3	44.0	$^1T^2$
7. 2'-O-Methyladenosine (Mol. B) (Prusiner and Sundara- lingam 1976)	34.8	-25.7	<u>5.2</u>	17.5	-32.8	$E_2$
8. 5'-Methylammonium-5'- deoxy-adenosine iodide monohydrate (Saenger 1971)	-36.9	31.3	<u>-12.6</u>	<u>-11.6</u>	30.9	$T^2$
9. Arabinofuranosylthymine (Tougaard 1973)	<u>-9.2</u>	<u>-16.8</u>	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),  $\sigma_2$  has the lowest value and  $|\sigma_2|$  is less than  $5^\circ$ . Therefore, the atom C2' is puckered in an envelope form. Since the sign of the next torsion angle  $\sigma_3$  is negative, the puckering of the sugar in this compound is C2' *endo* i.e.  $E^2$ .

(ii) Since  $\sigma_3$  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,  $\sigma_4$  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  $\sigma_0$ ,  $\sigma_1$ ,  $\sigma_2$ ,  $\sigma_3$  and  $\sigma_4$ -axis respectively. The projections of  $OB$  on the axes give all the torsion angles. In this case, it is evident that none of the  $\sigma$ -angles is zero. The sign of  $\sigma_0$  is the same as  $\sigma_4$  (both negative) and the sign of  $\sigma_1$  is the same as  $\sigma_3$  (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  $\sigma_4$  and  $\sigma_0$  are both small and negative. Again, it will be noticed that the lowest torsion angle is  $\sigma_4$  ( $|\sigma_4| < |\sigma_0|$ ) and the sign of the adjacent torsion angle,  $\sigma_0$ , is negative. Further, the other lower value is  $\sigma_0$  and the sign of the adjacent torsion angle,  $\sigma_1$ , 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),  $\sigma_0$  and  $\sigma_1$  have the same sign (negative). Since  $|\sigma_0| < |\sigma_1|$ , atom O1' is puckered most. Since the sign of  $\sigma_1$  is *negative*, O1' atom is *endo* puckered. As the sign of  $\sigma_2$ , adjacent to  $\sigma_1$ , 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  $\sigma_3$  and  $\sigma_4$  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  $\sigma_3$  in the sequence,  $\sigma_4$  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  $\sigma_0, \sigma_1, \sigma_2, \sigma_3$  and  $\sigma_4$  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 rise 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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