A General Geometrical Model for Pseudorotation Simulation in Five-membered Rings

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A geometrical model for simulation of pseudorotation in five-membered rings, based on the assumption that during pseudorotational changes the bond lengths and position of geometrical centre of the ring remain constant, is presented. The significance of the 'planar reference conformation' is discussed and the method of calculation of this conformation from the knowledge of the ring bond lengths is described. The 'planar reference conformations' of cyclopentane, tetrahydrofuran, and 1,3-dioxolane molecules calculated in this way are in a fair agreement with the corresponding *ab initio* results. The geometries of 183 β-D-furanoside fragments are reconstructed in the frame of our model and also those of Kilpatrick *et al.*, Adams *et al.*, and Altona and his co-workers. The results obtained within our model are the closest to the crystallographic ones. A special version of our model, parametrized for the furanose ring, is also presented.

The geometry of a puckered five-membered ring can be described by nine geometrical parameters, and if the condition of constant bond lengths is imposed, the number of variables is reduced to four. According to the concept of pseudorotation[1] these four parameters are additionally reduced to two pseudorotational co-ordinates q and φ. The aim of pseudorotational models is to establish the unequivocal relationships between two pseudorotational co-ordinates and the geometry of the ring described in terms of internal or cartesian co-ordinates. Having the pseudorotational model, energetical considerations can be carried out in order to find a pseudorotation path on the q,φ plane.

There are two ways of finding the relationships mentioned above. The first is geometrical,[1-9] and consists in constructing them from geometrical constraints basing on certain simplifications. The second is energetic,[10-13] and consists in calculating a four-parameter potential energy function $V(q,\varphi,\alpha_1,\alpha_2)$, and optimizing geometrical parameters α_1 and α_2 for each pair of q,φ values. This procedure leads to the relationships in question.[7] There is no doubt that energetic models of pseudorotation are physically more justifiable than geometrical ones; however, they are not devoid of certain disadvantages: (1) numerical calculations are much more complicated and laborious, especially when nucleoside or bigger molecules are taken into consideration; (2) the relationships found depend on the method of energy calculation; (3) the results obtained by energetic models are not transferable into rings of different bond lengths or different substituent atoms.

Taking into account disadvantages of energetic models the requirements for geometrical models can be formulated: (1) results obtained by such models ought to be consistent with experimental data; (2) relationships between pseudorotational co-ordinates and the geometry of the ring ought to be simple enough to permit rapid calculations; (3) the above relationships should give the possibility to apply them to different rings.

There are several geometrical models of pseudorotation proposed by Kilpatrick *et al.*,[1] Altona and his co-workers,[2-5] Adams *et al.*,[6] Diez and his co-workers,[7,8] Herzyk and Rabczenko:[9]

(1) The model for the equilateral five-membered ring introduced by Kilpatrick and his co-workers[1] and generalization of this model to cover any five-membered ring made by Diez *et al.*[7] (model A) do not describe the five-membered-ring geometry correctly because of physically unreasonable changes in bond lengths on the pseudorotation path in these models.

(2) The models presented by Adams *et al.*[6] and Diez *et al.*[7] (denoted in the original paper as B_1) though lacking the disadvantage mentioned above and describing the five-membered-ring geometry fairly correctly[7,14] do not permit rapid calculations because of the great complications of the proposed procedure. In the case of Adams' model a procedure for determining pseudorotational co-ordinates from cartesian co-ordinates has not been given. Furthermore such a procedure proposed by Cremer and Pople[10] cannot be applied in this case because of different definitions of puckering amplitudes in the Adams and Kilpatrick models.

(3) The model introduced by Altona and his co-workers[2-4] describes correctly only the equilateral five-membered-ring geometries and is adequate for small values of puckering amplitude.

(4) Diez *et al.*[7,8] proposed a generalization of the above model to cover any five-membered ring but it describes torsional and bond angles taken from Kilpatrick model in terms of Altona pseudorotational co-ordinates τ_m and P; thus it cannot be treated as an original model.

(5) The Altona model for the furanose ring[5] also does not give an excellent reconstruction of ring geometry (see 'Results and Discussion').

(6) The model presented by Herzyk and Rabczenko[9] permits rapid and accurate geometry calculations; however, its usefulness is limited only to equilateral five-membered rings.

In this paper we present a pseudorotation model which allows the calculation of the five-membered-ring geometry in a simple way, and does not imply a physically unreasonable variation in bond lengths. It may be applied to the rings of different bond lengths. The results obtained by this model with respect to the furanose system are in good agreement with crystallographic data.

Definition of the Model

General Description.—In the model presented here the cartesian co-ordinates of the ring atoms are determined by the Kilpatrick pseudorotational co-ordinates q and φ.[1] Our approach is based on the assumption that in the course of pseudorotation with puckering amplitude q = constant (rigid pseudorotation), the *j*th atom moves along a three-dimensional

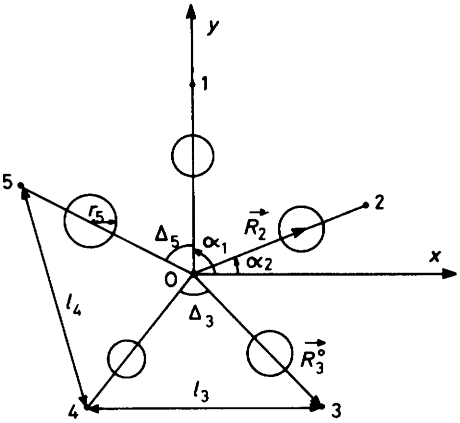

Figure. Projection of the ring-atom trajectories on the mean xy plane during rigid pseudorotation. Points 1—5 define ring-atom positions in the planar conformation (later called 'planar reference conformation')

curve whose position and dimension are dependent on q. The projection of such a curve on the mean plane of the ring defined by Cremer and Pople[10] is a circle with radius r_j, whose centre is determined[9] by the radius vector $\vec{R}_j$ (Figure). R_j values as well as r_j values are dependent on q and independent of φ. According to this we propose relationships (1) between the cartesian

$$x(j) = r_j[\sin 2(\varphi + 4\pi j/5)\sin\alpha_j - \cos 2(\varphi + 4\pi j/5)\cos\alpha_j] + R_j\cos\alpha_j \quad (1a)$$

$$y(j) = -r_j[\sin 2(\varphi + 4\pi j/5)\cos\alpha_j + \cos 2(\varphi + 4\pi j/5)\sin\alpha_j] + R_j\sin\alpha_j \quad (1b)$$

$$z(j) = (2/5)^{\frac{1}{2}} q \cos(\varphi + 4\pi j/5) \quad (1c)$$

co-ordinates of the jth atom and the pseudorotational co-ordinates q and φ where $j = 1$—5 and α_j is the angle between the vector $\vec{R}_j$ and the x-axis. The origin of the reference system is situated in the geometrical centre of the ring and the z-axis is perpendicular to the mean plane of the ring. Neither the direction of the x-axis nor the α_j angles are important in these considerations. However, the angles $\Delta_j = \alpha_{j+1} - \alpha_j$ are significant. In our model we assume that Δ_j values are independent of changes q and φ. The choice of these angles is discussed hereafter. Equations (1) correspond to equations (22) in ref. 9 concerning an equilateral ring; however, in that case R_j values as well as r_j values are independent of j. Radii r_j and radius vectors R_j are calculated assuming that the bond lengths l_j are constant on the pseudorotation path, *i.e.* by solving equations (2) with respect to R_j and r_j, provided that l_j are

$$[x(j + 1) - x(j)]^2 + [y(j + 1) - y(j)]^2 + [z(j + 1) - z(j)]^2 = l_j^2 \quad (2)$$

independent of q and φ. Co-ordinates $x(j)$, $y(j)$, and $z(j)$ are substituted from equations (1). The details of the solution of equations (2) are presented in Appendix 1. The R_j and r_j values obtained in this way ensure the constancy of the bond lengths on the pseudorotation path with an accuracy better than 0.5%, when q is less than 0.5 Å.

As may be seen from equations (1) φ as well as q are variables and thus not only rigid pseudorotation can be described by our model; however, in this case the meaning of parameters r_j and R_j is clearer.

In order to obtain pseudorotational co-ordinates q and φ from ring-atom cartesian co-ordinates [equations (1)], the procedure presented by Cremer and Pople[10] is applied with excellent results.

Calculation of R_j and r_j Values.—By solving equations (2) one can obtain (3) and (4) (see Appendix 1), which allow R_j and r_j values to be calculated directly from the bond lengths l_j and angles Δ_j. In equations (3) and (4) $\Delta_j = \alpha_{j+1} - \alpha_j$; $\delta = 4\pi/5$;

$$R_{j+1}^2 + R_j^2 - 2R_{j+1}R_j\cos\Delta_j = (\tfrac{1}{2})\{l_j^2 - Q^2[1 - \cos\delta] + l_j[l_j^2 - 2Q^2(1 - \cos\delta)]^{\frac{1}{2}}\} \quad (3)$$

$$r_{j+1}^2 + r_j^2 - 2r_{j+1}r_j\cos(2\delta + \Delta_j) = Q^4(1 - \cos\delta)^2/2\{l_j^2 - Q^2[1 - \cos\delta] + l_j[l_j^2 - 2Q^2(1 - \cos\delta)]^{\frac{1}{2}}\} \quad (4)$$

$Q = (2/5)^{\frac{1}{2}}q$; $j = 1$—5. From equations (3) and (4) it appears that R_j values decrease and r_j values increase with the increase of q. In other words, the circles which are the projections of the trajectory of the ring atoms on the mean plane approach the geometrical centre of the ring and become larger when the puckering amplitude increases.

The main problem in calculating R_j and r_j is to determine Δ_j angles. It must be noted that in the case of the planar ring ($q = 0$) all r_j values are equal to zero and $\vec{R}_j$ vectors describe the positions of the ring atoms. Thus Δ_j angles may be obtained from a knowledge of the planar ring geometry.

Definition of the 'Planar Reference Conformation' and Choice of the Δ_j Angles.—The number of geometries of a planar ring with given bond lengths is infinite. Our task is to select the one geometry appropriate for our purpose, called according to Diez *et al.*[7] the 'planar reference conformation.' The planar five-membered rings seldom found in nature do not appear to be a good choice (see next section).

We propose a simple geometrical method for determination of the planar reference conformation from a knowledge of the bond lengths. It is based on the assumption that each Δ_j angle is proportional to the corresponding bond length l_j [equation (5)]. In the conformation obtained after substituting equation

$$\Delta_j = -2\pi l_j \Big/ \sum_{k=1}^{5} l_k \quad (5)$$

(5) into (3) (provided that $q = 0$) the geometrical centre of the ring is situated out of the origin of the reference system. This discrepancy is *ca.* 0.020 Å in the case of the furanose ring. In order to obtain appropriate Δ_j angles we shift the origin of the reference system into the geometrical centre of the ring and calculate the new Δ_j angles analytically. These new angles can be used to calculate R_j and r_j values as well as cartesian co-ordinates of the atoms of a given ring. Then in the course of pseudorotation the geometrical centre of the ring lies in the origin of the reference system and its position remains constant with an accuracy of 0.001 Å for furanose rings.

An algorithm for the calculation of the five-membered-ring geometry from bond lengths l_j and pseudorotational co-ordinates q and φ is presented in Appendix 2. The computer program in FORTRAN IV based on this algorithm can be obtained upon request from P. H.

It should be noted that the choice of the planar reference conformation is not rigorous and other planar reference conformations may be proposed. For example, in the case of energetic considerations such a conformation may be found by optimizing bond angles in the planar ring.

Table 1. Planar reference conformations of several molecules proposed by different authors

Molecule	∢X–C–C(°)	∢C–C–C(°)	∢C–X–C(°)	Reference
CP[a] X = CH_2	108.00	108.00	108.00	7, 11, 12, this work
THF[b] X = O	107.49	105.95	113.11	11
	108.2	105.7	112.2	12
	108.61	105.56	111.66	7[c]
	106.70	106.22	114.16	7[d]
	107.69	105.88	112.86	This work
THT[e] X = S	106.47	114.14	98.79	7[c]
	110.42	112.31	94.55	7[d]
	108.36	113.27	96.75	This work
THS[f] X = Se	105.84	116.62	95.08	7[c]
	110.67	114.22	90.21	7[d]
	108.37	115.37	92.53	This work
CPN[g] X = CO	106.66	108.11	110.47	11
	107.95	107.62	108.85	This work
	∢C–O–C(°)	∢C–C–O(°)	∢O–C–O(°)	
1,3-Dioxolane[h]	111.45	105.26	106.58	11
	110.1	105.8	108.3	12
	109.58	105.58	108.61	This work

[a] Cyclopentane, R(C–C) = 1.546 Å.[7] R(C–C) = 1.54 Å.[11,12] [b] Tetrahydrofuran (oxolane), R(C–C) = 1.54 Å, R(C–X) = 1.43 Å.[7,11,12] [c,d] First and second planar reference conformation, respectively;[7] in the original paper[7] there are only values of C–X–C angles; X–C–C angles, as well as C–C–C angles, are calculated by us from geometrical constraints. [e] Tetrahydrothiophene, R(C–C) = 1.536 Å, R(C–X) = 1.839 Å.[7] [f] Tetrahydroselenophene, R(C–C) = 1.537 Å, R(C–X) = 1.975 Å.[7] [g] Cyclopentanone, R(C–C) = 1.54 Å, R(C–X) = 1.52 Å.[11] [h] Bond lengths are the same as in tetrahydrofuran.

Results and Discussion

Checking the Method of Finding the Planar Reference Conformation of the Ring.—We compared the planar reference conformations of several rings determined by means of our method with the corresponding ones found by other authors. In our considerations we examined the planar reference conformations of cyclopentane, tetrahydrofuran (oxolane), 1,3-dioxolane, and cyclopentanone molecules calculated by Cremer and Pople[11] and Cremer[12] by means of their energetical model (4-31G[11] and 6-31G*[12] *ab initio* studies). We also considered the planar reference conformations of cyclopentane, tetrahydrofuran, tetrahydrothiophene, and tetrahydroselenophene molecules proposed by Diez *et al.*[7] This comparison is presented in Table 1. It can be seen that our planar reference conformations of tetrahydrofuran and 1,3-dioxolane are in good agreement with the 4-31G and 6-31G* ones, respectively; however, in the case of tetrahydrofuran the first planar reference conformation of Diez is also in good agreement with the 6-31G* value. The bond angles of our planar reference conformations of tetrahydrofuran, tetrahydrothiophene, and tetrahydroselenophene are almost average values of the angles in the two planar reference conformations considered by Diez and his co-workers.[7]

Our model was applied to the description of the furanose ring. Three nearly planar conformations of the furanose ring* were found from *X*-ray crystallographic data.[15–17] A planar reference conformation based on these crystallographic results was also proposed by Altona and his co-workers.[5] Table 2 presents the comparison of our planar reference conformations of the corresponding furanose rings with the conformations mentioned above. From Table 2 it appears that there is a discrepancy between crystallographic and our planar reference conformations; however, in the case of the one proposed by Altona and his co-workers this discrepancy is small. In order to use the conformations mentioned above for our purpose, a correction of Δ_j° angles obtained from equation (5) should be performed. New Δ_j' angles, based on a planar crystallographic conformation, are as in equation (6) where Δ_j^{c} is Δ_j and $\Delta_j^{\circ c}$ is

$$\Delta_j' = \Delta_j^{\circ}\,\Delta_j^{c}/\Delta_j^{\circ c} \qquad (6)$$

Δ_j° [equation (5)] in the crystallographic conformation.

We performed calculations of the geometries of 183 β-D-furanoside fragments using Δ_j angles based on the average planar reference conformation of the three crystallographic conformations mentioned above and on that proposed by Altona and his co-workers, but the results were worse than those obtained using Δ_j angles calculated by our method (see Table 3). This may be explained by intramolecular forces resulting from additional cyclization of the ring which could cause the variation of the Δ_j angles, assumed to be constant in our model. This is why the planar crystallographic conformation cannot be treated as the planar reference conformations for our purpose.

Test of our Model and Comparison with Other Models.—In order to check our model and compare it with other models, we examined a set of 183 β-D-furanoside fragments obtained from the Cambridge Crystallographic Database. The quality of reconstruction of the geometry of the crystallographic ring from the pseudorotational co-ordinates describing this geometry was chosen as the criterion of the correctness of the model. For each of the 183 β-D-furanoside fragments we found the pseudorotational co-ordinates q, φ and τ_m, P by means of the methods of Cremer and Pople[10] and Altona,[3,4] respectively. Next, we reconstructed internal co-ordinates from pseudorotational co-ordinates using several models and we compared them with the crystallographic ones. The following models were examined in our analysis:

HR	—the model described in this paper
HR1	—the HR model simplified in such a way that r_j values are approximated by the corresponding values obtained for an equilateral ring,[9] that is $r_j = AL - BQ + CQ^2/L$ where $Q[= (2/5)^{\frac{1}{2}}q]$ is the maximum possible deviation of ring atoms from the mean plane, $L[= (l_j + l_{j-1})/2]$ is the average of the bond lengths juxtaposed to the jth atom, and A—C are the constants in Table 3 of ref. 9
KPS	—the Kilpatrick[1] model; x and y co-ordinates of atoms are determined by the planar reference conformation of a given ring by means of the method described in the previous part
AGB	—the Adams model;[6] the planar reference conformation is the same as in the KPS model
ALT1	—the Altona model[2–4]
ALT2	—the ALT1 model parametrized for furanose rings.[5]

In our considerations we compared the root-mean-square (r.m.s.) deviations for bond angles σ_θ, torsional angles σ_τ, and the sums of bond angles $\sigma_{\Sigma\theta}$ which means $\sigma_x = \{[(1/n_x)\text{-}\sum_i^{n_x}(x_i^{\text{cryst}} - x_i^{\text{calc}})]^2\}^{\frac{1}{2}}$ where n_x is the number of compared quantities and cryst and calc designate the crystallographic and calculated values, respectively.

The results of the comparison of the models are presented in Table 3. It can be seen that the results attained by the HR and HR1 models are the best, especially with respect to the torsion

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* Note that all the planar furanose rings examined have additional rings.

Table 2. Comparison of bond angles in nearly planar crystallographic conformations of the furanose rings (A—C), and the planar reference conformation proposed by Altona and co-workers (D) with the corresponding ones obtained in this work, and mean difference of Δ_j angles between the compared pairs ($\sigma\Delta_j$)

	∢O(4′)–C(1′)–C(2′)(°)	∢C(1′)–C(2′)–C(3′)(°)	∢C(2′)–C(3′)–C(4′)(°)	∢C(3′)–C(4′)–O(4′)(°)	∢C(4′)–O(4′)–C(1′)(°)	$\sigma\Delta_j$	Reference
A[a]	108.9	104.1	107.0	107.3	112.7	0.08	15
	109.61	103.72	107.01	107.69	111.96		This work
B[b]	108.4	105.7	106.2	106.4	113.2	0.18	16
	108.80	104.68	107.61	105.22	113.70		This work
C[c]	110	103	105	104	118	0.25	17
	108.95	105.04	103.47	104.89	117.65		This work
D[d]	108.5	105.3	106.2	107.1	113.0		5
	108.36	105.71	106.60	106.91	112.42	0.03	5[e]
	108.52	105.56	106.68	106.92	112.31		This work

Bond lengths C(1′)–C(2′) to O(4′)–C(1′) are equal to:

[a] 1.550, 1.567, 1.510, 1.464, 1.404 Å, respectively;[15]

[b] 1.542, 1.509, 1.528, 1.455, 1.366 Å, respectively;[16]

[c] 1.54, 1.56, 1.61, 1.40, 1.33 Å, respectively;[17]

[d] 1.529, 1.527, 1.526, 1.449, 1.411 Å, respectively.[5]

[e] Previous conformation[5] modified by us in order to fulfil ring-closure condition.

Table 3. R.m.s. deviations for bond angles σ_θ, torsional angles σ_τ, and sums of bond angles $\sigma_{\Sigma\theta}$, obtained reconstructing the ring geometry of 183 β-D-furanoside fragments by different models

Models	σ_θ(°)	σ_τ(°)	$\sigma_{\Sigma\theta}$(°)
KPS	1.74	1.25	1.19
AGB	4.40	1.13	1.27
ALT1		0.63	
ALT2	1.71	1.00	2.43
HR	1.56	0.30	0.04
HR[a]	1.66	0.32	0.04
HR[b]	1.59	0.31	0.04
HR1	1.58	0.31	0.04

[a,b] Model HR with a planar reference conformation described in terms of Δ_j' angles [equation (6)] based on the conformation average of the three nearly planar crystallographic conformations,[15–17] and on the planar reference conformation proposed by Altona and his co-workers,[5] respectively.

angles. The rings reconstructed by those models are closest to the crystallographic ones in terms of the least-squares criterion. Moreover, the sum of bond angles in the ring created by the HR and HR1 models is extremely close to the crystallographic one. This is a significant result because there exists a direct relationship between the sum of bond angles in the equilateral five-membered ring and the puckering of the ring, as derived by Dunitz[18] and Abillon,[19] and confirmed experimentally for furanose rings.[5,20] The high accuracy of the reconstruction of the sum of bond angles allows us to use it as a measure of the puckering amplitude in the HR and HR1 models. It is noteworthy that the simplified HR1 model gives results almost as good as the HR model. Moreover we checked that the bond lengths change on the pseudorotation path by no more than 0.5% (the same value as for the HR model).

The poor results obtained by the AGB model may be explained by the fact that the puckering amplitude q is defined differently in the AGB than in the HR and KPS models. This problem was discussed elsewhere.[7–9] The difference of definitions implies the inability to apply the q value obtained by means of Cremer and Pople's procedure[10] in AGB model. It was shown[7] for the cyclopentane molecule that, if $q = 0.416$ Å in KPS model, the corresponding value in AGB model is 0.435 Å.

Considering the results attained by the KPS model, the variability of the ring bond lengths must be taken into account. The r.m.s. deviation for bond lengths in the KPS model is 0.039 Å, while in the HR model as well as in the HR1 model it is 0.001 Å. Furthermore, in the KPS model the variation of the bond lengths during rigid pseudorotation is *ca.* 6% for a furanose ring with q 0.47 Å, while in the HR model the corresponding value is <0.5%.

In HR, HR1, KPS, and AGB models the knowledge of the planar reference conformation is of great importance. This feature does not concern the Altona models, ALT1 and ALT2, in which different pseudorotational co-ordinates τ_m and P are used instead of q and φ. In other words, Altona models cannot distinguish between rings with different bond lengths and/or different Δ_j angles. The ALT1 model gives good results only for equilateral rings. The applications of this model to non-equilateral rings was criticized by Diez and his co-workers.[7] The model ALT2, however, is parametrized for the furanose ring with bond lengths from C(1′) – C(2′) to O(4′) – C(1′) 1.529, 1.527, 1.526, 1.449, and 1.411 Å, respectively. Thus the application of the ALT1 model is equivalent to approximating a given ring by an equilateral ring. The application of the ALT2 model, however, is equivalent to approximating a given ring by a ring with the bond lengths mentioned above.

Parametrization of the HR Model for the Furanose Ring.—It was found for the equilateral ring[9] that all distances and angular quantities independent of φ can be expressed as a function of q/l, where l is the bond length. In the case of a non-equilateral ring, however, these quantities depend on the planar reference conformation in a more complicated way than in the equilateral ring. If the model is applied to a group of similar rings, the effect of the planar reference conformation on the quantities independent of φ is negligible. Quantities such as r_j, R_j radii, the sum of bond angles $\sum_{i=1}^{5} \theta_i$, and mean non-bonded atom–atom distance R_{NB}, can be expressed as functions of q. We propose equations (7)—(10) where A_j, B_j, R_j°, C, D, and

$$r_j = A_j q^2 \qquad (7)$$

$$R_j = R_j^\circ - B_j q^2 \qquad (8)$$

$$\sum_{i=1}^{5} \theta_i(°) = 540.00 - Cq^2 \qquad (9)$$

Table 4. Dependence of r_j, R_j radii, the sum of bond angles $\sum_{j=1}^{5} \theta_j$, and the mean non-bonded atom–atom distance in the 'mean furanose ring,' on q values according to equations (7)—(10), respectively, found using the least-squares method

$A_1 = 0.132$	$B_1 = 0.211$	$R_1^\circ = 1.255$
$A_2 = 0.123$	$B_2 = 0.194$	$R_2^\circ = 1.293$
$A_3 = 0.133$	$B_3 = 0.217$	$R_3^\circ = 1.287$
$A_4 = 0.122$	$B_4 = 0.190$	$R_1^\circ = 1.269$
$A_5 = 0.149$	$B_5 = 0.255$	$R_5^\circ = 1.224$
$C = 103.28$	$D = 0.337$	$R_{NB}^\circ = 2.407$

$$R_{NB} = R_{NB}^\circ - Dq^2 \qquad (10)$$

R_{NB}° parameters are dependent on the planar reference conformation. These parameters were calculated for a ring with bond lengths proposed by Altona and his co-workers,[5] which were very closed to the mean values of our set of 183 β-D-furanoside fragments. We called this ring the 'mean furanose ring.' The bond lengths in this ring were given in the previous section. The planar reference conformation of this ring may be described in terms of Δ_j angles. Δ_1—Δ_5 are: 73.73, 72.58, 73.29, 71.03, and 69.36°, respectively, and the numbering of atoms is C(1′) – 1, C(2′) – 2, C(3′) – 3, C(4′) – 4, and O(4′) – 5. The bond angles in this conformation are presented in Table 2 (final row). The parameters A_j, B_j, R_j°, C, D, and R_{NB}° were found by means of the least-squares method, fitting equations (7)—(10) to the corresponding quantities calculated for several q values from 0.0 to 0.45 Å. The results of this fitting are presented in Table 4. The accuracy of fitting of R_j, r_j, R_{NB} is better than 0.001 Å, while the accuracy of fitting $\sum_{i=1}^{5} \theta_i$ is better than 0.03°.

We reduced our set of 183 β-D-furanoside fragments to a set of 31 rings in which bond lengths differ from the bond lengths in the 'mean furanose ring' by no more than 0.010 Å. The mean error of the sum of bond angles calculated with equation (9) is 0.32° for the new reduced set of furanoside fragments and to 0.44° for the whole set.

Equation (9) can be used to calculate the puckering amplitude from the sum of bond angles in the ring. The mean error of q value calculated in such a way is equal to 0.002 Å for the new reduced set of furanoside fragments and to 0.006 Å for the whole set.

Equations (1) together with (7) and (8) may be considered as a special version of our model parametrized for furanose rings with bond lengths close to the bond lengths in the 'mean furanose ring.' We called this new version HRF. Application of HRF as well as HR, ALT1, and ALT2 to the reconstruction of the geometries of 31 β-D-furanoside fragments mentioned above leads to the results presented in Table 5. It can be seen that in the new reduced set of furanoside fragments the HRF model gives results which are close to the corresponding ones obtained with the HR model. The ALT2 model gives better results with respect to bond angles; however, the reconstruction of torsion angles and especially of the sum of bond angles are rather poor. It can also be seen that the results obtained by the HRF model with our planar reference conformation are better than those obtained using the planar reference conformation of Altona and his co-workers;[5] however, the difference is negligible.

Conclusions

The purely geometrical model for pseudorotation simulation in the five-membered ring presented in this paper permits rapid determination of the atomic cartesian co-ordinates of the five-membered ring with given bond lengths, for all q and φ values. It ensures the constancy of bond lengths and the stability of the position of the geometrical centre of the ring during pseudorotational changes, with an accuracy better than 0.005 and 0.001 Å, respectively, for furanose rings. In this model as in all models based on the Kilpatrick pseudorotational co-ordinates q and φ, the knowledge of the planar reference conformation of the ring is of great importance. It is, however, the first time that the method of calculation of the planar reference conformation from the bond lengths is presented.

Table 5. R.m.s. deviations for bond angles σ_θ, torsional angles σ_τ, and sums of bond angles $\sigma_{\Sigma\theta}$ obtained reconstructing the ring geometry of 31 β-D-furanoside fragments with bond lengths close to the 'mean furanose ring,' by HRF, HR, ALT1, and ALT2 models

Models	σ_θ(°)	σ_τ(°)	$\sigma_{\Sigma\theta}$(°)
HRF	1.04	0.22	0.07
HRF[a]	1.10	0.23	0.07
HR	0.98	0.19	0.02
ALT1		0.57	
ALT2	0.70	0.96	2.24

[a] Model HRF with a planar reference conformation described in terms of Δ_j' angles [equation (6)] based on the conformation proposed by Altona and his co-workers[5] (see Table 2, penultimate row).

As checked for the furanose system, this model reconstructs most accurately the geometry of the five-membered ring. Its application is not limited to small values of puckering amplitude q.

The only structural variables in our model are the ring bond lengths. This implies that substituent–substituent interactions do not affect the geometry of the ring but merely the shape and height of the pseudoration barrier. Of course this simplification cannot always be physically justified but as our results show for furanoside fragments of nucleosides it is the case in many instances.

Given the co-ordinates of one conformer, the co-ordinates of any other conformer along the rigid pseudorotation path (q = constant) can be generated in a simple way. In general, however, this cannot be performed because the information about the character of pseudorotation (rigid or not) must be gained from energetic considerations. Such considerations concerning the real pseudorotation path in ribose and deoxyribose derivatives are now being investigated using the model presented.

Appendix 1

Equation (2) can be solved as follows. Substitution of $x(j)$, $y(j)$, and $z(j)$ from equations (1) into (2) gives (A1) where

$$A\cos^2(2\varphi_j) + B\cos(2\varphi_j)\sin(2\varphi_j) + C\sin^2(2\varphi_j) + D\cos(2\varphi_j) + E\sin(2\varphi_j) + F = l_j^2 \qquad (A1)$$

$\varphi_j = \varphi + 4\pi j/5$; A—F are parameters dependent on R_j, r_j, q and independent of φ. Equation (A1) must be valid for all φ and q values. It leads to one of the following conditions:

$$1\ A = B = C = D = E = 0;\ F = l_j^2$$
$$2\ A = C;\ B = D = E = 0;\ A + F = l_j^2$$

Condition 1 implies $q = 0$, so must be omitted. Condition 2 leads to equations (A2)—(A4) where the relations (A5)—(A8)

$$2v_{j.x}U_{j.x} + 2v_{j.y}U_{j.y} = Q^2\cos\delta(1 - \cos\delta) \qquad \text{(A2)}$$

$$-2v_{j.x}U_{j.y} + 2v_{j.y}U_{j.x} = -Q^2\sin\delta(1 - \cos\delta) \qquad \text{(A3)}$$

$$U^2{}_{j.x} + U^2{}_{j.y} + v^2{}_{j.x} + v^2{}_{j.y} + Q^2(1 - \cos\delta) = l_j{}^2 \qquad \text{(A4)}$$

$$U_{j.x} = -r_{j+l}\cos(2\delta + \alpha_{j+1}) + r_j\cos\alpha_j \qquad \text{(A5)}$$

$$U_{j.y} = -r_{j+1}\sin(2\delta + \alpha_{j+1}) + r_j\sin\alpha_j \qquad \text{(A6)}$$

$$v_{j.x} = R_{j+1}\cos\alpha_{j+1} - R_j\cos\alpha_j \qquad \text{(A7)}$$

$$v_{j.y} = R_{j+1}\sin\alpha_{j+1} - R_j\sin\alpha_j \qquad \text{(A8)}$$

apply and $Q = (2/5)^{\frac{1}{2}}q$:, $\delta = 4\pi/5$; j = 1—5. Solution of the system of equations (A2) and (A3) with respect to $U_{j.x}$ and $U_{j.y}$ gives (A9). Thus (A4) can be solved easily with respect to

$$U^2_{j.x} + U^2_{j.y} = Q^4(1 - \cos\delta)^2/4(v^2_{j.x} + v_{j.y}{}^2) \qquad \text{(A9)}$$

$h = v^2_{j.x} + v^2_{j.y}$. After substitution of $v_{j.x}$ by (A7) and $v_{j.y}$ by (A8) one can obtain (A10). Equations (A10) which are

$$h = R^2_{j+1} + \mathrm{R}_j{}^2 - 2R_{j+1}R_j\cos\Delta_j = (1/2)\{l_j{}^2 - Q^2(1 - \cos\delta) + l_j[l_j{}^2 - 2Q^2(1 - \cos\delta)]^{\frac{1}{2}}\} \qquad \text{(A10)}$$

equivalent to equations (3) may be solved numerically. r_j Values ought to be calculated from equations (A2) and (A3) but this system contains 10 equations and only five unknowns. In order to overcome this problem we calculate r_j values from equations (A9). Substitution of $U_{j.x}$ by (A5) and $U_{j.y}$ by (A6) gives (A11).

$$U^2_{j.x} + U^2_{j.y} = r^2_{j+1} + r_j{}^2 - 2r_{j+1}r_j\cos(2\delta + \Delta_j) = Q^4(1 - \cos\delta)^2/2\{l_j{}^2 - Q^2(1 - \cos\delta) + l_j[l_j{}^2 - 2Q^2(1 - \cos\delta)]^{\frac{1}{2}}\} \qquad \text{(A11)}$$

Equation (A11) which is equivalent to equation (4) may be solved numerically. However, r_j values obtained in such a way do not satisfy equations (A2) and (A3); thus r_j values are approximate. This approximation ensures that the ring bond lengths do not remain constant in the course of pseudorotation. Nevertheless the fluctuations of the bond lengths are negligible and in the case of furanose ring are 0.5%.

Appendix 2

The algorithm for five-membered ring geometry calculations from bond lengths l_j and pseudorotational co-ordinates q and φ is as follows:

(1) Reading of the bond lengths l_j

(2) Determination of the planar reference conformation
  (a) calculation of Δ_j angles from equation (5)
  (b) calculation of $R_j{}^{\circ}$ radii from equation (3), provided that $q = 0$
  (c) calculation of cartesian co-ordinates of the planar reference conformation $x_o(j) = R_j{}^{\circ}\cos\alpha_j$ and $y_o(j) = R_j{}^{\circ}\sin\alpha_j$ where α_1 may be of any value and $\alpha_{j+1} = \alpha_j + \Delta_j$

(3) Calculation of corrected Δ_j angles
  (a) calculation of cartesian co-ordinates of the geometrical centre of the planar reference conformation, x_c, y_c where $x_c = (1/5)\sum_{j=1}^{5} x_o(j)$ and $y_c = (1/5)\sum_{j=1}^{5} y_o(j)$
  (b) calculation of the cartesion co-ordinates of the planar reference conformation $x(j)$, $y(j)$ in the system of the geometrical centre of the ring so that $x(j) = x_o(j) - x_c$ and $y(j) = y_o(j) - y_c$
  (c) calculation of the new Δ_j angles by means of analytical geometry

$$\cos\Delta_j = \frac{x(j)x(j+1) + y(j)y(j+1)}{[x(j)^2 + y(j)^2]^{\frac{1}{2}}[x(j+1)^2 + y(j+1)^2]^{\frac{1}{2}}}$$

(4) Reading of the pseudorotational co-ordinates q and φ

(5) Calculation of R_j radii from equations (3)

(6) Calculation of r_j radii from equations (4)

(7) Calculation of the cartesian co-ordinates of the given ring from equations (1)

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