A New Description of Equilateral Five-membered Rings during Pseudorotation

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An equilateral, five-membered ring is described based on the assumption that during conformational changes the distances between atoms and the position of the centre of mass of the ring remain constant. In the course of pseudorotation the atoms move along three-dimensional curves whose projections on a mean plane of the ring are circles. Assuming a certain bond length of the initial regular pentagon, the model allows for high accuracy calculations of the geometry of any future conformations of the ring. Our model is compared with those of Kilpatrick and Adams.

Five-membered rings are very common in nature, especially furanose rings in nucleic acids or the D ring in steroids. The conformational flexibility of such rings plays an important role in the structure of entire molecules and consequently in their biological activity.

Models for pseudorotation of five-membered rings may be divided into three groups. The first is that of Kilpatrick *et al.*,[1] also used by other authors (Cremer and Pople [2]), the second is that formulated by Altona *et al.*,[3-6] and the third is that postulated by Adams *et al.*,[7] hereafter referred to as AGB. Each model has its disadvantages. In Kilpatrick's model, the endocyclic bond lengths do not remain constant during pseudorotation (Figure 1). Altona has contributed a description rather than a model of pseudorotation; it contains merely mathematical relationships between the valency or torsional angles and the pseudorotation parameters P and τ_m, which are adequate only for small values of the puckering amplitude q; no attention is given to the nature of the phenomenon. The AGB model, though lacking the disadvantages of Kilpatrick's model, is based on strict requirements limiting its application to small out-of-plane displacements of the atoms (see Discussion section) and does not fulfill Eckart's conditions.

Definition of the Model.—The approach to pseudorotation presented in this work is based on the following assumptions: (a) the z_j co-ordinate of atoms in the five-membered ring satisfies Kilpatrick's [1] relation (1) where q is the puckering amplitude

$$z_j = \sqrt{2/5}q\cos(\varphi + 4\pi j/5) \quad (1)$$

and φ the phase angle and (b) the x_j and y_j co-ordinates depend on the pseudorotation parameters of equations (2) and (3) and

$$x_j = F_j(q,\varphi) \quad (2)$$

$$y_j = G_j(q,\varphi) \quad (3)$$

functions F and G are periodic with respect to φ.

Thus we propose a parametric dependence on φ of the planar curve describing the motion of the projection of an atom on the plane of the unpuckered ring. In Kilpatrick's model this curve is a point; in the AGB model an interval, while in this paper it is postulated to be an ellipse. This ellipse is easily described by an equation in a local reference system of the atom concerned. The local reference system is determined by the two characteristic directions of the unpuckered five-membered ring, *i.e.* the direction defined by the geometrical centre of the planar ring and the atom in question, and the direction perpendicular to it. The first direction defines the p_j axis of the new system, the second the q_j axis (Figure 2). The planar ring is described by the points of intersection of the trajectories of the atoms with the mean plane. In our model the geometry of this planar ring is required for establishing these trajectories. The model is limited to an equilateral five-membered ring. Hence, we assume that the planar ring is a regular pentagon and is described unequivocally by its bond length R. The origin of the system of the jth atom is given by

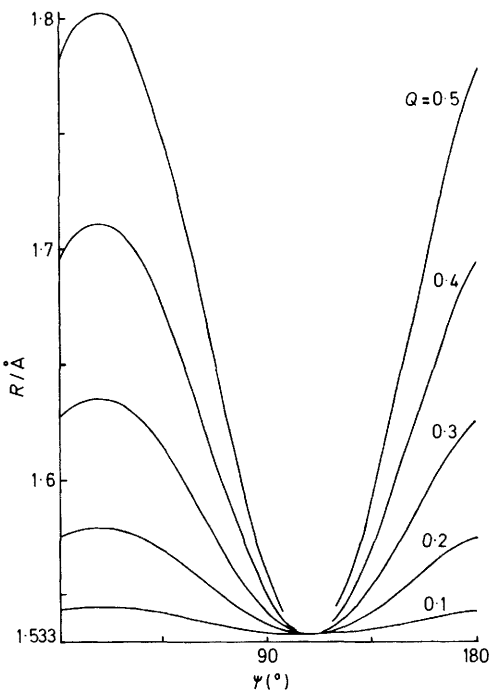

Figure 1. Distance between first and fifth atom of an equilateral ring of bond length 1.533 Å *versus* phase angle φ for several values of $Q = \sqrt{2/5}\,q$, calculated according to Kilpatrick *et al.*[1]

$$\overrightarrow{r_j} = \overrightarrow{r_j'} - \overrightarrow{a_j} \quad (4)$$

the vector in equation (4) where $\overrightarrow{r_j'}$ is the radius vector of the jth atom in the planar ring, and $\overrightarrow{a_j} = (\overrightarrow{r_j'}/r_j)a$, where a is the major axis of the ellipse. The ellipse described by the projection of the jth atom during its motion is given by equations (5)

$$p_j = a\cos[t(\varphi)] \quad (5)$$

$$q_j = b\cos[t(\varphi)] \quad (6)$$

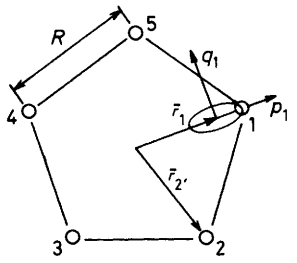

Figure 2. Elliptical trajectories of the atomic projections on the xy mean plane and local systems of co-ordinates (p_j, q_j). Small circles show the positions of the atoms in the planar ring. R is the bond length

and (6) where b is the minor axis of the ellipse. Constants a and b must be independent of φ and dependent on q. They also must be different for different starting geometries of the planar ring, defined by the bond length R.

The function $t(\varphi)$ was found on the basis of assumptions (7) and (8). It is given by equation (9). Hence substituting

$$\text{if } |z_j| = \max = \sqrt{2/5}q \text{ then } p_j = -a \quad (7)$$

$$\text{if } |z_j| = \min = 0 \quad \text{then } p_j = +a \quad (8)$$

$$t(\varphi) = 2(\varphi + 4\pi j/5) + \pi \quad (9)$$

equation (9) in equations (5) and (6), one can obtain a three-dimensional parametric curve described by the atom during pseudorotation in the local reference system (p_j,q_j,z_j) [equations (10)].

$$p_j = -a\cos2(\varphi + 4\pi j/5) \quad (10a)$$

$$q_j = -b\sin2(\varphi + 4\pi j/5) \quad (10b)$$

$$z_j = \sqrt{2/5}q\cos(\varphi + 4\pi j/5) \quad (10c)$$

Using the geometrical centre of the planar ring as the reference for the co-ordinate system, equations (10) became (11) where

$$x(j) = -a\cos(2\varphi_j)\cos\alpha_j + b\sin(2\varphi_j)\sin\alpha_j + r_j^x \quad (11a)$$

$$y(j) = -a\cos(2\varphi_j)\sin\alpha_j - b\sin(2\varphi_j)\cos\alpha_j + r_j^y \quad (11b)$$

$$z(j) = Q\cos\varphi_j \quad (11c)$$

$\varphi_j = \varphi + 4\pi j/5$, $Q = \sqrt{2/5}q$, and is the maximum possible deviation of atoms from the mean plane of the ring, α_j is the angle between vector $\vec{r_j}$ and the x-axis, and r_j^x and r_j^y are the x and y co-ordinates of the origin of the (p_j,q_j,z_j) system. The values of r_j^x and r_j^y are given by equations (12).

$$r_j^x = \left[\frac{R}{2\sin(\pi/5)} - a\right]\cos\alpha_j \quad (12a)$$

$$r_j^y = \left[\frac{R}{2\sin(\pi/5)} - a\right]\sin\alpha_j \quad (12b)$$

Curve (10) is shown in Figure 3 and its projections on the planes of the (p_j,q_j,z_j) reference system are shown in Figure 4.

The description of curve (11) is incomplete without knowledge of the values of constants a and b. These values were calculated assuming that the bond lengths in the ring are constant on the pseudorotation path, that is by solving

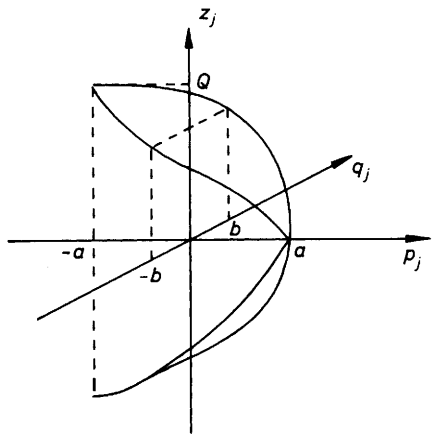

Figure 3. Trajectory of the jth atom given by equation (10) in the local reference system (p_j, q_j, z_j)

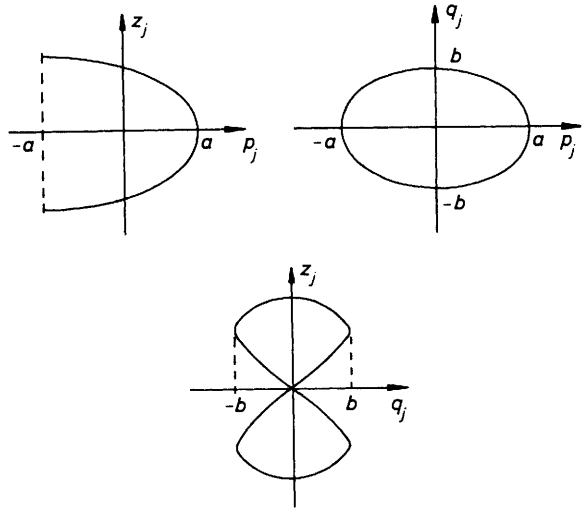

Figure 4. Projections of the trajectory of the jth atom on: (a) the p_j, z_j plane; (b) the p_j, q_j plane; (c) the q_j, z_j plane, in the (p_j, q_j, z_j) reference system

$$[x(j+1) - x(j)]^2 + [y(j+1) - y(j)]^2 + [z(j+1) - z(j)]^2 = R^2 \quad (13)$$

equation (13) with respect to a and b, provided that bond length R is independent of φ and q. $x(j)$,$y(j)$, and $z(j)$ were substituted from equations (11).

Calculated values of a and b for various Q and R values are given in Table 1; a and b are unequivocally defined for all values of Q and R. Thus there exists an unequivocal relationship between a and b. It was found to be very simple [equation (14)]. It was also found that equation (15) holds. The dependence of a on Q and R was found using the least-squares method and is in the form of a polynomial equation (16). The

$$b = 0.2361a \quad (14)$$

$$a/R = f(Q/R) \quad (15)$$

$$a = AR - BQ + CQ^2/R \quad (16)$$

Table 1. Constants a and b calculated from equation (13) for various values of R and Q

	Q/nm				
R/nm	0.01	0.02	0.03	0.04	0.05
0.140	10^{-5} a = 55	224	517	956	1 585
	10^{-5} b = 13	52	122	225	374
0.145	53	216	498	917	1 512
	13	51	117	216	357
0.150	52	209	480	882	1 446
	12	49	113	208	341
0.155	50	202	463	849	1 387
	12	48	109	200	327
0.160	48	195	448	819	1 333
	11	46	106	193	315

a and b in nm.

Table 2. Dependence of major axis of the ellipse on Q and R values found using the least-squares method, according to the equation $a = AR - QB + CQ^2/R$

Q/R range					
from	to	A	B	C	Accuracy of fit (nm)
0.0	0.1	0.0	0.0015	0.7937	10^{-5}
0.1	0.2	0.0010	0.0195	0.8708	10^{-5}
0.2	0.3	0.0115	0.1224	1.1239	10^{-5}
0.3	0.4	0.0820	0.5800	1.8693	2×10^{-5}
0.4	0.5	0.9086	4.5205	6.5832	2×10^{-4}

constants A—C are collected in Table 2. Substituting co-ordinates (11) and parameters a and b [equations (14), (16)] in equation (13), we found that on the pseudorotation path the bond lengths are constant with an accuracy of 10^{-5} nm.

The model described by equation (11) does not fulfill Eckart's conditions. During pseudorotation the centre of mass of the ring rotates in the xy plane about the z axis in the direction opposite to the direction of the motion of atomic projections on the xy plane. The motion discussed is an artifact resulting from the fact that the trajectory of an atom intersects the mean plane at the apex of the planar pentagon [equation (8)]. Hence, when the atom crosses the mean plane it ' pulls ' the whole ring towards the point of intersection. The motion of the centre of mass is eliminated by adding to equations (11a and b) the corrections x_c and y_c, respectively [equations (17) where

$$x_c = R_{cm}\sin 2\varphi \quad (17a)$$

$$y_c = R_{cm}\cos 2\varphi \quad (17b)$$

R_{cm} is the radius of rotation of the centre of mass]. The radius R_{cm} was found to depend on the constants a and b [equation 18)]. Hence, substituting equation (14) into (18) one obtains

$$R_{cm} = (a—b)/2 \quad (18)$$

$$R_{cm} = 0.3820a \quad (19)$$

(19). When correction (17) is taken into consideration, the trajectory of the jth atom is given by equations (20).

$$x(j) = -a\cos 2(\varphi + 4\pi j/5)\cos\alpha_j + b\sin 2(\varphi + 4\pi j/5)\sin\alpha_j + r_j^x + \left(\frac{a-b}{2}\right)\sin 2\varphi \quad (20a)$$

Table 3. Dependence of the radius of the circle r_c on Q and R values found using the least-squares method, according to the equation $r_c = AR - BQ + CQ^2/R$

Q/R range					
from	to	A	B	C	Accuracy of fit (nm)
0.0	0.1	0.0	0.0	0.485	10^{-5}
0.1	0.2	0.0008	0.0145	0.5479	10^{-5}
0.2	0.3	0.0082	0.0843	0.7116	10^{-5}
0.3	0.4	0.0534	0.3741	1.1773	2×10^{-5}

$$y(j) = -a\cos 2(\varphi + 4\pi j/5)\sin\alpha_j - b\sin 2(\varphi + 4\pi j/5)\cos\alpha_j + r_j^y + \left(\frac{a-b}{2}\right)\cos 2\varphi \quad (20b)$$

$$z(j) = \sqrt{2/5}q\cos(\varphi + 4\pi j/5) \quad (20c)$$

One can thus unequivocally obtain the co-ordinates of the jth atom in the ring for all given values of parameters φ, q, and R from equations (20) using equations (12), (14), and (16). Correction (17) introduces an additional rotation of the whole ring, and therefore does not affect the geometry of the ring, *i.e.* the interatomic distances and torsional and bond angles.

It was also found that co-ordinates $x(j)$ and $y(j)$ satisfy equation (21). It can be seen that the planar curve, describing

$$[x(j) - r_j^x]^2 + [y(j) - r_j^y]^2 = \left(\frac{a+b}{2}\right)^2 \quad (21)$$

the motion of the projection of the jth atom on the mean plane, proves to be a circle rather than an ellipse. The circle and the ellipse have a common centre and the length of the radius of the circle is the average of the lengths of the major and minor axes of the ellipse. Equations (20) can thus be simplified to (22)

$$x(j) = r_c[\sin 2(\varphi + 4\pi j/5)\sin\alpha_j - \cos 2(\varphi + 4\pi j/5)\cos\alpha_j] + r_j^x \quad (22a)$$

$$y(j) = -r_c[\sin 2(\varphi + 4\pi j/5)\cos\alpha_j + \cos 2(\varphi + 4\pi j/5)\sin\alpha_j] + r_j^y \quad (22b)$$

$$z(j) = \sqrt{2/5}q\cos(\varphi + 4\pi j/5) \quad (22c)$$

where r_c is the radius of the circle described by the projection of the jth atom on the mean plane. The dependence of the radius r_c on Q and R is similar to the dependence of a on Q and R [equation (23)]. The constants A—C are collected in Table 3.

$$r_c = AR - BQ + CQ^2/R \quad (23)$$

An algorithm for cyclopentane geometry calculation with respect to bond length R and pseudorotation parameters q and φ is presented in the Appendix.

The point of intersection of the trajectory of the jth atom with the mean plane is described by the radius vector, equation

$$\overrightarrow{r_j^{int}} = \overrightarrow{r_j'} - \left(\frac{a-b}{2}\right)\overrightarrow{(r_j'/r_j')} \quad (24)$$

(24), and lies closer to the geometrical centre of the ring than the jth apex of the planar pentagon by R_{cm}. The foregoing eliminates the arbitrary assumption discussed beforehand.

Table 4. Comparison of torsion angle values and sums of valency angles in cyclopentane obtained with AGB and HR models for envelope and twist conformations (R 0.1546 nm, q 4.35 × 10^{-2} nm)

	φ 0° (envelope)		φ 18° (twist)	
	AGB	HR	AGB	HR
∢C(2)–[C(3)–C(4)]–C(5) (°)	25.01	26.04	13.16	13.71
∢C(3)–[C(4)–C(5)]–C(1)	40.27	41.99	34.34	35.77
∢C(4)–[C(5)–C(1)]–C(2)	40.27	41.99	42.29	44.13
∢C(5)–[C(1)–C(2)]–C(3)	25.01	26.04	34.34	35.77
∢C(1)–[C(2)–C(3)]–C(4)	0.0	0.0	13.16	13.71
$\Sigma\theta_i$	522.30	520.33	522.30	520.33

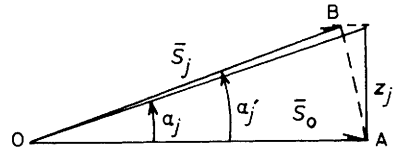

Figure 5. Description of the position of the jth atom according to Adams *et al.*[7] (AGB). Points O and A are in the xy plane. The xy plane is perpendicular to the plane of the diagram. O is the centre of the planar ring; A is the position of the jth atom in the planar ring; B is the momentary position of the jth atom in the puckered ring.

Discussion

Any geometrical features of the pentagon, such as atomic distances, valence angles, and torsional angles may be analytically established for all values of the pseudorotation parameters φ, Q, and R. Table 4 presents a comparison of some angle values obtained with the AGB model [7] and the model described in the present paper, referred to as HR. They were calculated using R 0.1546 and Q 2.75 × 10^{-2} nm (q 4.35 × 10^{-2} nm) which correspond to the values used by Adams *et al.*[7] Table 4 shows that the absolute values of torsional angles are larger in the HR model, while the sum of valence angles is smaller.This result may be interpreted as a tendency of the HR model to increase the amplitude of puckering q or a tendency of the AGB model to diminish it. A more detailed analysis confirms the latter hypothesis.

The basic quantity describing the displacement of the jth atom from the xy plane in the AGB model is the angular displacement of the vector $\overrightarrow{S_j}$ from this plane (Figure 5). This displacement is given by equation (25).[7] This approximation is

$$\alpha_j = \text{arctg}(z_j/S_0) \qquad (25)$$

valid only for small values of the angle α_j. The angle α_j described by equation (25) is smaller than the actual angle α_j' (see Figure 5); the amplitude of puckering q is thus diminished.

All distances in the five-membered ring independent of φ, such as a and b or the mean non-bonded atom–atom distance, calculated in the frame of the HR model, satisfy relationship

$$X/R = \text{F}(Q/R) \qquad (26)$$

(26) where X is any distance independent of φ. All the angular quantities independent of φ, such as the sum of the valence angles or the sum of the squares of the torsional angles, satisfy the following relationship: $X = \text{f}(Q/R)$. The relationships permit an easy approximation of the quantities X by means of the least-squares fit. They also show that puckering of the ring is better described by the ratio Q/R than by the puckering amplitude q. Hence, the ratio Q/R may be called the degree of puckering of the ring.

Table 5. Dependence of sum of valence angles on Q and R, according to the equation $\Sigma\theta_i$ (°) = $A + BQ/R - CQ^2/R^2$

Q/R range					
from	to	A	B	C	Accuracy of fit (°)
0.0	0.1	540.00	0.08	610.11	10^{-2}
0.1	0.2	539.75	2.94	−620.91	10^{-1}
0.2	0.3	579.48	−314.67	0.00	1
0.3	0.4	503.27	242.52	1 019.55	1

Table 6. Dependence of mean non-bonded atom–atom distance on Q and R values according to the equation $R_{NB} = AR + BQ - CQ^2/R$

Q/R range					
from	to	A	B	C	Accuracy of fit (nm)
0.0	0.1	1.6180	0.0020	1.2782	10^{-5}
0.1	0.2	1.6161	0.0337	1.4178	10^{-5}
0.2	0.3	1.5964	0.2152	1.8601	10^{-4}
0.3	0.4	1.4911	0.9268	3.0389	2 × 10^{-4}

Our approximations for the sum of valence angles in the ring and the mean non-bonded atom–atom distance are presented in Tables 5 and 6. Our approximation for the sum of valence angles is more accurate than the formula proposed by Dunitz.[8]

Conclusions

The model proposed in this work describes most accurately pseudorotation in an equilateral five-membered ring. It ensures the constancy of the bond length for all values of the pseudorotation parameters φ and q. Unlike the Adams model,[7] ours fulfills Eckart's condition of immobility of the centre of mass. Furthermore, its application is not limited to small values of the puckering amplitude q. Our model permits a rapid calculation of the co-ordinates of the atoms in the ring for all given values of parameters φ, q, and R.

The model is being adapted to irregular five-membered rings.

Appendix

An algorithm for cyclopentane geometry calculation with respect to bond length R and pseudorotational parameters q and φ is as follows:

j = atom number
φ = phase angle (°)
q = amplitude of puckering (nm)
R = bond length (nm)
$\varphi_j = \pi\varphi/180 + 4\pi j/5$
$\alpha_j = \pi/10 + (6 - j)4\pi/5$
$Q = \sqrt{2/5}q$
$r_c = R[A - BQ/R + C(Q/R)^2]$ (A—C are listed in Table 3)
$r_j^x = \{R/[2\sin(\pi/5)] - 1.6179r_c\}\cos\alpha_j$
$r_j^y = \{R/[2\sin(\pi/5)] - 1.6179r_c\}\sin\alpha_j$
$x(j) = +r_c[\sin(2\varphi_j)\sin\alpha_j - \cos(2\varphi_j)\cos\alpha_j] + r_j^x$
$y(j) = -r_c[\cos(2\varphi_j)\sin\alpha_j + \sin(2\varphi_j)\cos\alpha_j] + r_j^y$
$z(j) = Q\cos(2\varphi_j)$

$x(j)$, $y(j)$, and $z(j)$ are cartesian co-ordinates of the jth atom (nm).

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