Limitations of Cremer & Pople Parameters as Quantitative Descriptors of Ring Shapes in Comparative Stereochemistry

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Abstract

The interpretation of Cremer & Pople parameters presents more intricacies than is generally believed. The puckering Q depends on bond lengths as well as on φ and θ. Part of the interdependency is linked to one's conceptions of standard geometries, pseudorotation and inversion processes. A correct comparison of conformation from Cremer & Pople parameters can only be given per class of rings and requires the *a priori* definition of standard conformations.

Introduction

The various conformations of six-membered rings are nowadays often characterized with the help of polar coordinates Q, θ and φ (Cremer & Pople, 1975). Using this set of coordinates, all types of rings with a puckering Q can be mapped out on the surface of a sphere with radius Q (see *e.g.* Boeyens, 1978). The poles at $\theta = 0$ or $180°$ correspond to the rigid chair conformations, while the equator, at $\theta = 90°$, corresponds to the pseudorotational path of the flexible ·boat/twist-boat family. A specific form on the equator is further characterized by the pseudorotational angle φ. Other symmetrical forms, such as envelope (or sofa) and screw-boat (or 1,3-diplanar form), are located at specific points on the northern or southern hemisphere.

A logical nomenclature as well as a well defined atomic numbering scheme has been proposed by Boeyens (1978).

Since the Cremer & Pople parameters describe precisely those properties of a ring in which researchers in the field of conformational analysis are interested, it is tempting to use them in comparative geometrical studies. However, it has been pointed out (Zefirov & Palyulin, 1980) that a comparison of ring Q's con-

taining different bond lengths can lead to conclusions about their puckering which are inconsistent with other criteria accepted in stereochemistry.

Here we report some further limitations to the use of the Cremer & Pople parameters. In particular, we investigated whether the Cremer & Pople parameters can demonstrate generally, and quantitatively that a given ring is more puckered or that it is a more 'perfect' boat (or chair) than another ring.

The puckering amplitude

The Cremer & Pople total puckering amplitude Q for a six-membered ring is defined by:

$$Q^2 = \sum_{j=1}^{6} t_j^2,$$

where t_j are the perpendicular atomic displacements from a unique mean plane through the ring, as defined by equations (5)–(7) in Cremer & Pople (1975).

To study the behaviour of Q during conformational changes a 'standard' form must be chosen. In our calculations, a six-membered ring with equal valence angles, α, and unit bond lengths was considered. Petit (1983) has shown that, if only torsion angles ω change during pseudorotation, the puckering Q for a true-boat is given by:

$$Q(\mathrm{B}) = \left[\frac{4}{3}\left(\cos^2\frac{\alpha}{2} - \cos^2\alpha\right)\right]^{1/2}$$

and for a twist-boat by:

$$Q(\mathrm{TB}) = [\cos\alpha + \sqrt{3}\sin\alpha - 1]^{1/2}.$$

Thus, not only does Q vary linearly with the bond lengths, but it also decreases with increasing values of α. The formulae show that for all non-planar rings $Q(\mathrm{TB}) > Q(\mathrm{B})$ (see Table 1). Calculations, employing an algorithm devised by Dillen & Geise (1980), show that intermediate conformations have intermediate Q values.

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Table 1. *Q values as a function of α for true-boat and twist-boat forms with equal valence angles and unit bond lengths*

α	Q(B)	Q(TB)	α	Q(B)	Q(TB)
120	0·0000	0·0000	108	0·5774	0·5816
118	0·2446	0·2446	106	0·6177	0·6240
116	0·3438	0·3441	104	0·6537	0·6623
114	0·4182	0·4190	102	0·6859	0·6973
112	0·4794	0·4810	100	0·7146	0·7294
110	0·5319	0·5344	90	0·8165	0·8556
109·47	0·5443	0·5474			

Table 2. *Q values along the line $\varphi = 0$*

All forms have C_s symmetry: $|\omega_1| = |\omega_4|$, $|\omega_2| = |\omega_3|$, $|\omega_5| = |\omega_6| = 60°$. $\theta = 109·47°$ and bonds have unit length.

$|\omega_1|$	$|\omega_2|$	α	$\theta(°)^*$	Q	Remarks
0	60	109·47	90	0·5443	Boat form
1·72	55·15	112·0	88·4	0·5263	
4·28	48·74	115·0	86·0	0·5017	
7·63	41·24	118·0	82·8	0·4731	
12·28	31·82	121·0	78·1	0·4388	
16·80	23·31	123·0	73·2	0·4103	
20·02	17·47	124·0	69·4	0·3925	
25·39	8·01	125·0	62·6	0·3677	
30·0	0	125·264	56·1	0·3509	Envelope (=sofa) form
34·62	8·01	125·0	48·9	0·3388	
39·98	17·47	124·0	39·8	0·3315	
41·86	20·85	123·46	36·4	0·3310	Minimum-Q form
43·21	23·31	123·0	33·9	0·3313	
47·72	31·82	121·0	25·3	0·3372	
52·37	41·24	118·0	15·9	0·3526	
55·72	48·74	115·0	9·1	0·3713	
58·28	55·15	112·0	3·7	0·3912	
60	60	109·47	0	0·4082	Chair form

* Cremer & Pople θ parameter.

The φ dependency of the puckering, *i.e.* the variation of Q along the equator, is depicted in Fig. 1(a). The statement that pseudorotation can be described as a motion involving a change in φ at constant puckering amplitude can no longer be kept for standard forms with fixed valence angles. Disparities between $Q(B)$ and $Q(TB)$ run as high as 4·5% at α = 90° and increase even further when higher-membered rings are considered.

Next, we investigate the consequences of changing θ at constant φ, *i.e.* the change of a chair to a boat-like conformation along a meridian. Two paths are special. At $\varphi = 0°$ (+ $n60°$), the chair form changes *via* the envelope into a true-boat, whereas at $\varphi = 90°$ (+ $n60°$) the chair changes *via* the half-chair and the screw-boat forms into the twist-boat conformation. During these processes we keep bond lengths fixed at unit length, but allow the valence angles to vary in order to keep φ at the selected value and to retain symmetry. All forms on the $\varphi = 0°$ meridian have C_s symmetry, *i.e.* $|\omega_1| = |\omega_4|$, $|\omega_2| = |\omega_3|$ and $|\omega_5| = |\omega_6| = 60°$.

Conformations on the $\varphi = 90°$ meridian have C_2 symmetry, *i.e.* $|\omega_1| = |\omega_3|$ and $|\omega_4| = |\omega_6|$.

Numerical results are given in Tables 2 and 3. In Figs. 1(b) and 1(c) the puckering Q is plotted as a function of θ, resulting in curves which deviate strongly from a circle, the ideal Cremer & Pople curve.

It is noteworthy that the minimal value of Q is not found at one of the more symmetric forms.

The end points of the Q vectors as a function of φ and θ, presented in Fig. 2, map out a three-dimensional surface that is anything but a sphere.

It may seem that a logical way to improvement may be to change the definition of ring puckering into one based on the angular characteristics of the ring. Various approaches are possible using endocyclic torsion angles.
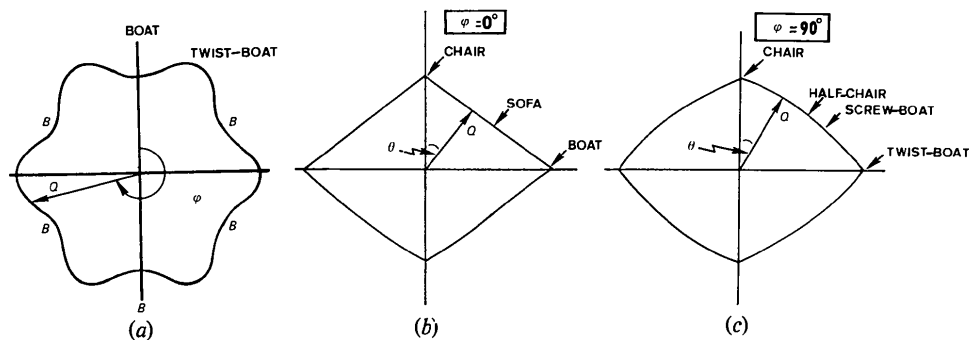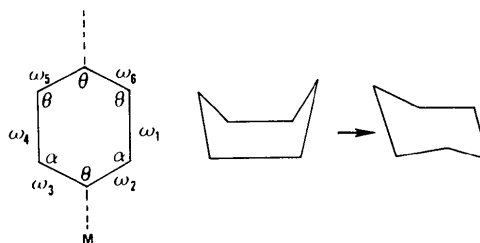

Fig. 1. Cross sections through the Cremer & Pople globe (*cf.* Fig. 2) for an idealized ring with unit bond lengths. See text for valence angles. (a) Section along the equator, $\theta = 90°$. Q is given as a function of φ for the change from true-boat forms to twist-boat forms (pseudorotation process). (b) Section along the meridian, $\varphi = 0°$. Q is given as a function of θ for the change from a chair form to a twist-boat (inversion process). (c) Section along the meridian, $\varphi = 90°$. Q is given as a function of θ for the change from a chair form to a true-boat (inversion process).

Table 3. Q values along the line $\varphi = 90°$

All forms have C_2 symmetry: $|\omega_1| = |\omega_3|$, $|\omega_4| = |\omega_6|$. $\theta = 109\cdot47°$ and bonds have unit length.
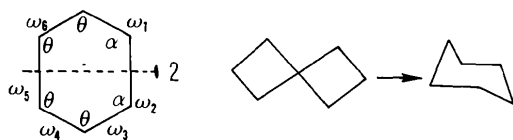
$|\omega_1|$	$|\omega_2|$	$|\omega_4|$	$|\omega_5|$	α	$\theta(°)$*	Q	Remarks
33·16	70·64	33·16	70·64	109·47	90	0·5474	Twist-boat
27·82	63·88	36·12	72·54	112·0	86·8	0·5237	
20·28	53·91	39·85	74·48	115·0	82·1	0·4916	
10·22	40·03	44·16	75·98	118·0	75·1	0·4525	
0	25·48	47·90	76·44	119·94	67·02	0·4184	Screw-boat
10·40	10·40	51·17	76·00	120·834	57·7	0·3907	
17·54	0	53·16	75·19	120·835	50·7	0·3766	Half-chair
27·45	14·43	55·59	73·38	120·0	39·9	0·3647	
33·69	23·43	56·91	71·81	118·957	32·6	0·3625	Minimum-Q
37·96	29·55	57·71	70·51	118·0	27·5	0·3636	
47·77	43·35	59·19	66·73	115·0	15·4	0·3749	
54·99	53·26	59·85	60·07	112·0	6·3	0·3919	
60	60	60	60	109·47	0	0·4082	Chair

* Cremer & Pople θ parameter.

About 15 years ago Buys & Geise (1968) noted that along the equator the ω_j can be approximated by:

$$\omega_j = \omega_{max} \cos\left[\varphi + \frac{2\pi j}{3}\right] \quad \text{with } j = 1, 2, \ldots, 6,$$

where ω_{max} presents itself as the definition of puckering. However, its range of applicability is very limited. Diez, Esteban, Guilleme & Bermejo (1981) proved that only for equilateral polygons is there one maximum torsion angle ω_{max} and one phase angle φ. For non-equilateral six-membered rings there are in principle six maximum torsion angles and six phases. Another definition of puckering, proposed by Zefirov & Palyulin (1980) is:

$$S^2 = \sum_{j=1}^{6} \sin^2\left(\frac{\omega_j}{2}\right).$$

Using the results from Tables 2 and 3, it is easily verified that for an idealized ring ($\alpha = 109\cdot47°$ and unit
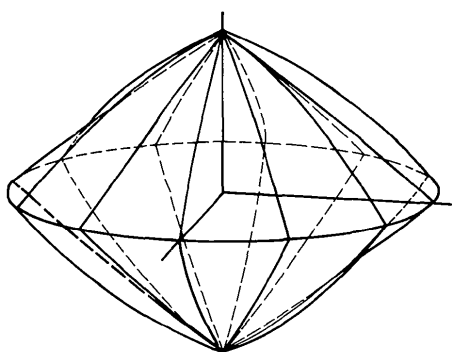

Fig. 2. The Cremer & Pople globe, presented as the end points of Q vectors as a function of φ and θ for an idealized ring system (unit bond lengths, see text for further details).

lengths) it holds that S(chair) = $1\cdot500$, S(boat) = $1\cdot000$ and S(twist-boat) = $0\cdot994$. Thus, S is, just as Q, a function of φ and θ, but independent of bond lengths.

Finally, a definition of puckering can be based on endocyclic valence angles, e.g. via

$$G = 10\left[1 - \frac{\sum \alpha_j}{720}\right].$$

G is independent of bond lengths and for idealized systems independent of φ, but not of θ.

The parameters φ and θ as determinants of ring shape

From the above it will be clear that there is no straightforward relation between the conformation of a ring and the corresponding Cremer & Pople parameters. Even for idealized systems the conformational map deviates strongly from a sphere. Of course, other models of the chair to boat-like conversion process can be constructed. The conformers met along the meridians will be different from those given above by having more or less symmetry. Each of such models will yield a globe (Q surface) slightly different from that of Fig. 2.

This lack of a one-to-one relation between the conformations of a ring and their representation by the Cremer & Pople coordinates may lead to ambiguities in interpretation, as in the examples below.

Occasionally it happens that an experimental set of X-ray coordinates yields $\varphi = \theta = 0°$. From this result, the authors then characterize the ring in question as a *perfect* chair, although the bond lengths and angular characteristics show that the ring has no true symmetry (Fig. 3a). Also, the two-dimensional polar projection of the Cremer & Pople globe is sometimes used for classification purposes in sugar chemistry (Kothe, Luger & Paulsen, 1979). The poles are taken to represent the ideal, perfect chair forms, while ideal boat and twist-boat forms are depicted at equidistant points along the equator. In these examples, *the definitions of ideal, perfect forms* are based on φ and θ. Such a basis of definition is not without danger. The Cremer & Pople treatment of a six-membered ring is obviously a projection of 12 degrees of freedom onto three parameters. Thus many slightly different conformations may correspond to a certain set of Q, φ and θ. It is evident that if standard or ideal geometries are defined by bond lengths, valence and torsion angles the corresponding Cremer & Pople parameters may well be different from nice, round numbers. Moreover, these numbers are not transferable from system to system.

To elucidate our point we take the perhydropyran ring as an example. Fig. 3(a) gives the conformation of the ring as observed experimentally in α-L-xylo-pyranose (Takagi & Jeffrey, 1979). A definition of the 'ideal' form based on symmetry (e.g. averaging the
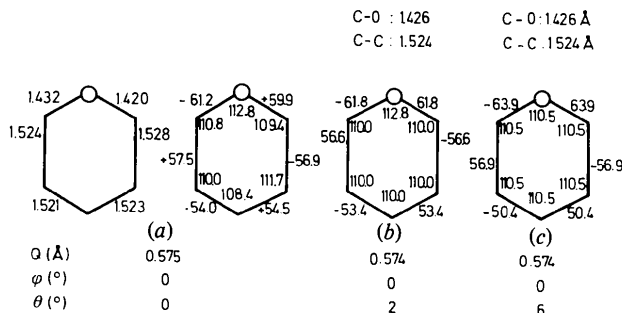
Fig. 3. Forms of the $^1C_4$ chair of perhydropyran: (a) observed by Takagi & Jeffrey (1979) in α-L-xylopyranose; (b) after partial symmetrization (see text); (c) after symmetrization of bonds and valence angles (see text).

bond lengths and five valence angles) corresponds to the φ and θ values of Fig. 3(b). Incorporation of all valence angles into the symmetrization (Fig. 3c) causes θ to deviate further from zero.

Note that the computational scheme (Dillen & Geise, 1980) to generate the specified forms ensures that the rings are closed. Which of the tetrahydropyran rings of Fig. 3 is the most perfect one is a matter of preference and remains the responsibility of the investigator.

Conclusion

Our analysis has shown that the interpretation of Cremer & Pople parameters is not as straightforward as is sometimes believed. With this coordinate system it is indeed possible to map out conformations with a given Q on the surface of a sphere. However, even for idealized molecules, each conformation has its own, particular value of Q. The conformational map for a real molecule will be similar, but not equal, to that of Fig. 2.

The inconsistency between conformational descriptors based on angular properties (ω_{max}, S, G) and the Cremer & Pople-based descriptors arises because only for infinitesimal displacements of a regular polygon from planarity is there a direct linear relationship between torsion angles and displacements. This condition, which was stated by Dunitz (1972) as well as by Cremer & Pople (1975), is seldom met in actual ring systems. Once this is appreciated, the Cremer & Pople

three-parameter description of a six-membered ring remains very attractive and convenient, despite its limitations. In fact, the Cremer & Pople method is to date the only systematic way of describing ring conformations regardless of ring size, and is the only scheme that, given θ, φ and Q, enables one to recalculate exactly the displacements t_j of the ring atoms from the Cremer & Pople mean plane. It is, however, obvious that one cannot in general reconstitute the complete conformational geometry from a given set of Q, φ and θ. The limitations in interpretative power for classification purposes are related to the fact that 12 degrees of freedom are compressed into three parameters. On the other hand a three-parameter system is convenient and pictorial. Other three-parameter systems may be designed, which may seem to have improvements on details, but their limitations will remain essentially the same.

A correct, quantitative comparison of conformations can only be given for one particular class of rings (e.g. tetrahydropyran derivatives) at a time, after a set of standard conformations is defined. The restriction, one class at a time, is to ensure the usefulness of Q by introducing as little variation as possible in bond lengths between the members of the class. The a priori definition of standard geometries is necessary to locate the appropriate points of reference in the two-dimensional projection of the Cremer & Pople globe.

In all other cases the interpretation of Cremer & Pople parameters cannot go beyond semi-quantitative statements.

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