research and for awarding a Summer Faculty Fellow-ship to JRB. We are also grateful to Professor C. E. Strouse for supplying us with the TLS subroutines and to him and Dr E. Prince for several very helpful discussions.

References

ALLEN, F. H., TROTTER, J. & WILLISTON, C. S. (1970). *J. Chem. Soc. A*, pp. 907–911.

BAUDOUR, J. L., DÉLUGEARD, Y. & CAILLEAU, H. (1976). *Acta Cryst.* B32, 150–154.

BAUDOUR, J. L., DÉLUGEARD, Y. & RIVET, P. (1978). *Acta Cryst.* B34, 625–628.

BROCK, C. P. (1980). *Acta Cryst.* B36, 968–971.

BROCK, C. P. & DUNITZ, J. D. (1982). *Acta Cryst.* B38, 2218–2228.

BROCK, C. P. & HALLER, K. L. (1984). *J. Phys. Chem.* In the press.

BROCK, C. P., KUO, M.-S. & LEVY, H. A. (1978). *Acta Cryst.* B34, 981–985.

BROCK, C. P., NAAE, D. G., GOODHAND, N. & HAMOR, T. A. (1978). *Acta Cryst.* B34, 3691–3696.

BROCK, C. P. & WEBSTER, D.F. (1976). *Acta Cryst.* B32, 2089–2094.

CAILLEAU, H., BAUDOUR, J. L. & ZEYEN, C. M. E. (1979). *Acta Cryst.* B35, 426–432.

CHAPLOT, S. L., LEHNER, N. & PAWLEY, G. S. (1982). *Acta Cryst.* B38, 483–487.

CHOI, C. S. & PRINCE, E. (1976). *J. Chem. Phys.* 64, 4510–4516.

CROMER, D. T. & WABER, J. T. (1974). *International Tables for X-ray Crystallography*, Vol. IV, edited by J. A. IBERS & W. C. HAMILTON, Table 2.2A. Birmingham: Kynoch Press.

DUNITZ, J. D. & WHITE, D. N. J. (1973). *Acta Cryst.* A29, 93–94.

MAIN, P., LESSINGER, L., WOOLFSON, M. M., GERMAIN, G. & DECLERCQ, J. P. (1977). *MULTAN* 77. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

PRINCE, E. (1983). Personal communication.

PRINCE, E. & FINGER, L. W. (1973). *Acta Cryst.* B29, 179–183.

ROSENFIELD, R. E. JR, TRUEBLOOD, K. N. & DUNITZ, J. D. (1978). *Acta Cryst.* A34, 828–829.

SCHOMAKER, V. & TRUEBLOOD, K. N. (1968). *Acta Cryst.* B24, 63–76.

SHMUELI, U. & GOLDBERG, I. (1974). *Acta Cryst.* B30, 573–578.

SUTHERLAND, H. H. & MOTTRAM, M. J. (1972). *Acta Cryst.* B28, 2212–2217.

SUTHERLAND, H. H. & RAWAS, A. (1983). *Acta Cryst.* C39, 1568–1570.

TRUEBLOOD, K. N. (1978). *Acta Cryst.* A34, 950–954.

On the Correct Usage of the Cremer–Pople Puckering Parameters as Quantitative Descriptors of Ring Shapes – a Reply to Recent Criticism by Petit, Dillen and Geise

BY DIETER CREMER

Lehrstuhl für Theoretische Chemie, Universität Köln, Köln, D-5000, Federal Republic of Germany

Abstract

The Cremer–Pople puckering parameters define the conformation of a puckered ring in a quantitative, mathematically well defined manner. Recent results by Petit, Dillen & Geise [*Acta Cryst.* (1983), B39, 648–651] on six-membered-ring conformations are due to an erroneous definition of standard boat and twist-boat forms. This is shown by deriving the correct relationships between puckering parameters and internal ring angles for these forms.

The analysis of the puckered forms of an N-membered ring is uniquely carried out by calculating the mean plane (MP) and the puckering parameters of the ring (Cremer & Pople, 1975*a*; Cremer, 1980). This approach is a generalization of the description of a puckered pentagon first given by Kilpatrick, Pitzer & Spitzer (1947). It can be used (*a*) to analyze a puckered ring in terms of its basis conformations (Cremer, 1980), (*b*) to make a quantitative comparison of puckered rings of different size and symmetry, (*c*) to generate all conformers along a pseudorotation cycle once the parameters of one conformer are known (Cremer, 1979, 1984), (*d*) to develop the conformational potential of a ring as a function of $N-3$ parameters q_m and φ_m (Cremer & Pople, 1975*b*; Cremer, 1979), (*e*) to define a ring substituent position in a unique manner (Cremer, 1980) and (*f*) to link the conformational analysis of ring compounds to that of alicyclic rotor molecules (Cremer, 1978).

The Cremer–Pople (CP) parameters have been designed in order to associate the shape of a puckered ring, its conformation and its interconversional motions with a mathematically well defined subset of internal coordinates. This is done by projecting from the $(3N-6)$-dimensional configuration space of an N-membered ring onto an $(N-3)$-dimensional conformation subspace (Cremer, 1980). Every point in this subspace corresponds to a nonplanar ring

conformer, which in turn corresponds *to an infinite number of different geometries* possessing the same $N-3$ puckering parameters but different combinations of bond lengths (N) and bond angles ($N-3$). This, however, is the essence of the definition of the term 'conformation'. For example, the conformation of an alicyclic molecule with an N-atom chain is described by $N-3$ dihedral angles. Again, every conformation possesses an infinite number of geometries, each being exactly defined by N bond lengths and $N-3$ bond angles. In order to reduce the number of possible geometries to just one reasonable standard geometry, $2N-3$ standard values for bond lengths and angles are selected. The same, of course, can be done in the case of ring conformations. In this way, rigid and semirigid pseudorotor models of N-membered rings are created (Cremer, 1979, 1984).

· More realistic conformational models, however, are obtained by minimizing the molecular energy in order to find the best set of $2N-3$ bond lengths and angles, which describe the equilibrium geometry of a given conformer with fixed puckering parameters. This is easily done with the aid of force-field, semi-empirical or *ab initio* methods (Cremer & Pople, 1975b; Cremer 1979, 1984).

In a recent paper, Petit, Dillen & Geise (1983) (PDG) have claimed that the interpretation of the CP puckering parameters cannot go beyond a semiquantitative description of ring conformations unless some precautions are made. PDG base their claim on an analysis of puckered six-membered-ring forms, in particular the D_{3d} symmetrical chair (C), the C_{2v} symmetrical boat (B) and the D_{2d} symmetrical twist-boat (TB) forms.

The number of independent internal coordinates of these forms can easily be obtained with the aid of group theory (Pople, Sataty & Halevi, 1980). For the C, the B, and the TB form two, four and four internal parameters are needed to fix their geometry exactly. If a standard bond length R is chosen, just one parameter remains to fix the D_{3d} symmetrical C form uniquely. This may be an angle α or, alternatively, a puckering amplitude $Q(C) = q_3$ (Cremer & Pople, 1975a). If α is chosen, Q is readily determined by:

$$Q(C) = R(\tfrac{1}{2} + \cos \alpha)^{1/2}. \tag{1}$$

Similarly, the angle α can be derived from a pre-chosen Q value:

$$\cos \alpha = \frac{Q^2}{R^2} - \frac{1}{2}. \tag{2}$$

In order to distinguish between B and TB forms, one of the four parameters may be the pseudorotation phase angle $\varphi \equiv \varphi_2$. It adopts values of $k(\pi/3)$ for the B and $k(\pi/3) + \pi/6$ ($k = 0, 1 \ldots$) for the TB forms. With φ and R being fixed, two additional angles α and β are needed to determine the puckering

amplitudes $Q(B) = q_2(B)$ and $Q(TB) = q_2(TB)$:

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

$$Q(TB) = R\left[2\cos\beta - \cos\alpha - 1 \right.$$
$$\left. + \cos\frac{\alpha}{2}\sqrt{2(3 + \cos\alpha - 4\cos\beta)}\right]^{1/2}. \tag{4}$$

Alternatively, R, φ, Q and α can be fixed and β evaluated from equations (5) and (6):

$$\cos\beta = -\left(\cos^2\frac{\alpha}{2} - \frac{3}{4}\frac{Q^2}{R^2}\right)^{1/2} \quad \text{(B forms)}; \tag{5}$$

$$\cos\beta = \frac{1}{2}\frac{Q^2}{R^2} - \cos\frac{\alpha}{2}\left(1 - \frac{Q^2}{R^2}\right)^{1/2} \quad \text{(TB forms)}. \tag{6}$$

According to group theory, however, *it is not possible to fix five parameters* (*e.g.* R, φ, Q, α and β) *of a puckered B or TB form at the same time*. This implies that with R, φ, α and β being set, automatically two conformers are generated, which belong to two different B–TB pseudorotation families characterized by two different Q values. This is exactly what PDG get when selecting R and φ and $\alpha = \beta$ as the four independent parameters. In this case equations (3) and (4) simplify to

$$Q(B) = R\left[\frac{4}{3}\left(\cos^2\frac{\alpha}{2} - \cos^2\alpha\right)\right]^{1/2} \tag{7}$$

$$Q(TB) = R[\cos\alpha - 1 + \sqrt{3}\sin\alpha]^{1/2}. \tag{8}$$

If one sets $Q(B) = Q(TB)$, a quartic equation in $\cos\alpha$ results, which possesses just one nontrivial solution, namely $\cos\alpha = -0.5$ and $\alpha = \beta = 120°$, *i.e.* the only conformer with $Q(B) = Q(TB)$ and $\alpha = \beta$ is the planar form. This result, however, rephrases only what is derived from group theory: Nonplanar B or TB forms with five independent parameters do not exist. In summary, the calculational results given by PDG in their Tables 1, 2, and 3 just confirm what is predicted by group theory: The C (as defined above and by PDG) possesses two, the B and TB four, the half-chair (HC) five and the envelope (E) (= sofa) six independent internal parameters. If R and the puckering parameters (Q for the C; Q and φ for B and TB; Q, φ and θ for HC and E) are set, no (C), one (B, TB, HC) and two (E) angles remain to be chosen independently.

In their paper, PDG consider the use of the six bond angles ω_j of a puckered six-membered ring in order to describe its shape *via* a puckering parameter $G = 10(1 - \sum \omega_j/720)$. Again, this is in conflict with group theory. The idea of conformational analysis is to associate the shape of a molecule with its large-amplitude vibrations, *e.g.* the shape of a nonplanar

ring with the out-of-plane vibrational modes of its planar form. According to group theory there exist just $N - 3$ modes and hence it is reasonable to project from $3N - 6$ to $N - 3$. On the other hand, no method exists which reduces from N bond (or dihedral) angles to $N - 3$ conformational parameters in an exact, mathematically well defined manner (Essén & Cremer, 1984). Thus any formula based on N rather than $N - 3$ parameters (bond and/or dihedral angles) cannot be used to describe a general (symmetrical or asymmetrical) puckered ring in $(N - 3)$-dimensional conformation space.

PDG claim that 'there is no straightforward relation between the conformation of a ring and the corresponding CP parameters'. They elucidate their point by re-examining results given by Takagi & Jeffrey (1979) on the puckering of the perhydropyran ring of α-L-xylopyranose. The experimentally determined geometry suggests an almost perfect $^1C_4$ chair conformation with $Q = 0\cdot575$ Å, $\theta = 0\cdot8°$ and $\varphi = 323\cdot2°$. Thus, it is reasonable to consider just the perhydropyran ring and to assume C_s symmetry for the chair form, which implies $\varphi = 0$ or $180°$. When experimental coordinates are averaged under this constraint, puckering parameters change to $Q = 0\cdot575$, $\theta = 0\cdot6$ and $\varphi = 0°$ in perfect agreement with the values given by Takagi & Jeffrey (1979).

The averaging procedure carried out by PDG is erroneous since it tries to fix nine or ten parameters (three bond lengths, Q, φ, θ, and three or four internal angles) where only eight independent internal coordinates ($e.g.$ three bond lengths, Q, φ, θ, and two internal angles) are group-theoretically allowed.

In summary, the calculational results in Tables 1, 2, 3 and Figs. 1, 2, 3 of PDG reflect the hazards of using 'standard' ring forms without defining what is meant by conformation and conformational phenomena like puckering and pseudorotation. By selecting $2N$ bond lengths and bond angles for their 'standard' ring forms, PDG violate the hierarchy of parameters inherent to the CP approach: (1) $N - 3$ puckering parameters, (2) $2N - 3$ bond lengths and angles. Therefore, the PDG results do not allow any judgement on the use of the CP parameters as quantitative descriptors of ring shape; in particular, they do not reveal any limitations of the CP parameters.

References

Cremer, D. (1978). *J. Chem. Phys.* **69**, 4456–4471.
Cremer, D. (1979). *J. Chem. Phys.* **70**, 1898–1910, 1911–1927, 1928–1938.
Cremer, D. (1980). *Isr. J. Chem.* **20**, 12–19.
Cremer, D. (1984). *Isr. J. Chem.* **23**, 72–84.
Cremer, D. & Pople, J. A. (1975a). *J. Am. Chem. Soc.* **97**, 1354–1358.
Cremer, D. & Pople, J. A. (1975b). *J. Am. Chem. Soc.* **97**, 1358–1367.
Essén, H. & Cremer, D. (1984). *Acta Cryst.* B40, 418–420.
Kilpatrick, J. E., Pitzer, K. S. & Spitzer, R. (1947). *J. Am. Chem. Soc.* **64**, 2483–2488.
Petit, G. H., Dillen, J. & Geise, H. J. (1983). *Acta Cryst.* B39, 648–651.
Pople, J. A., Sataty, Y. A. & Halevi, E. A. (1980). *Isr. J. Chem.* **19**, 290–291.
Takagi, S. & Jeffrey, G. A. (1979). *Acta Cryst.* B35, 1482–1486.

The Conformations of Five Tetra- and Pentamethoxylated Phenyl Derivatives: Weberine Analogs and Polymethoprims

By Isabella L. Karle, Judith L. Flippen-Anderson, Joseph F. Chiang* and Alfred H. Lowrey

Laboratory for the Structure of Matter, Naval Research Laboratory, Washington, DC 20375, USA

Abstract

Crystal and molecular structure analyses by X-ray diffraction have established the conformations of methoxy groups on phenyl rings when there are four or more adjacent methoxy groups. In three of the compounds studied, the methyl C atoms are placed alternately above and below the plane of the aryl group in a regular fashion, while in two very similar compounds there are unexpected irregularities in the rotations about the C_{Ph}–O bonds and consequent crowding of adjacent OCH_3 groups. Relative potential-energy profiles calculated by the $MM2$ program for the rotation about C_{Ph}–O bonds in the free molecules do not provide any clues for the irregularities. The unexpected methoxy conformations appear to result from packing interactions. The structures determined were those of 5,6,7,8-tetramethoxy-1,2-dimethyl-1,2,3,4-tetrahydroisoquinoline hydrochloride (1-methylweberine.HCl) (compound 2) $[C_{15}H_{24}NO_4^+.Cl^-$, $M_r = 317\cdot81$, *Pbca*, $a = 10\cdot262$ (4), $b = 17\cdot865$ (4), $c = 18\cdot127$ (4) Å, $V = 3323\cdot23$ Å^3, $Z = 8$, $D_x = 1\cdot270$ g cm^{-3}, $F(000) = 1360$,

* Permanent address: Department of Chemistry, State University of New York, College at Oneonta, Oneonta, NY 13820, USA.