# Symbolic Representation of the Molecular Conformation of Calixarenes

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**Abstract.** In calixarene chemistry there is a continuous search for new shaping units or substructures useful for molecular recognition or for the binding of ions. The problem of assigning their molecular conformations cannot be dealt with by the use of the dihedral angles as done until now, because this method contains intrinsic ambiguities. The new approach, proposed here, is based on the use of the set of $n$ pairs of torsion angles (conformational parameters) which involve the flexible part of the calixarene and it is free of ambiguities. Moreover, knowledge of the set of conformational parameters allows one to build straightforwardly three-dimensional molecular models. A symbolic representation of the molecular conformation of any calix[$n$]arene may be obtained by combining the Schöenflies symbol of the molecular symmetry together with the signs of the conformational parameters.

## 1. Introduction

In the calixarene research area there is a continuous search for new shaping units or substructures useful for molecular recognition and/or for the binding of ions. The inclusion ability towards neutral organic molecules and the complexing ability of functionalized calixarenes depend strongly on the conformation of the host macrocyclic molecules. Moreover, the selectivity in the binding of alkali metal cations by functionalized calixarenes is also strongly influenced by the stereospatial arrangement of the binding sites.

The conformational problem represents, therefore, one of the central problems in calixarene chemistry, and clear and unequivocal rules to define the conformations are necessary.

The molecular conformations of calix[$n$]arenes (**1**) which support various functional groups $R_1$ and various substituents at $R_2, R_3, R_4$ have been clearly established by X-ray diffraction studies [1, 2].

In these papers the molecular conformation of the macrocycle is, almost always, described by giving the dihedral angles formed by the least-squares planes through the phenolic units and a suitable 'reference plane' selected in the molecule.

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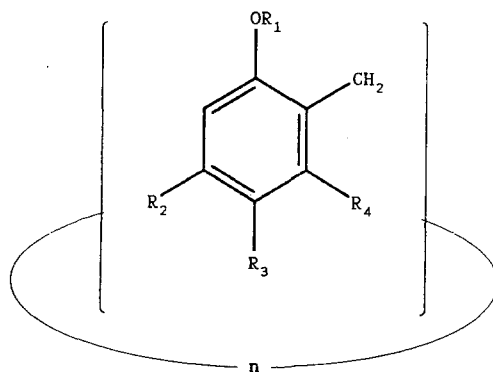
**1,**   $n = 4, 5, 6, 7, 8.$

For a long time this approach was considered satisfactory for calix[4]arenes because:

(a) there is a 'natural' choice for the reference plane in the macrocycle: it is the least-squares plane through the four $CH_2$ bridges;

(b) the use of the dihedral angles described above, together with the four names which characterize the conformers (cone, partial cone, 1,2 alternate cone, 1,3 alternate cone), allow complete descriptions of many calix[4]arenes.

However, such nomenclature has been shown to be incapable of covering all the possible conformations of calix[4]arenes. As a consequence, other names have been coined by authors and entered into current use to characterize unusual calix[4]arene conformations. But the lack of clear rules on when to apply such new names may create some confusion. This is the case, for example, of the p-tert-butylcalix[4]arene crown(6) Rb-picrate complex [3] described as being in a 'flattened partial cone' conformation; but it could equally well be described as being in a 'distorted cone' conformation, as the borderline between the two conformations has not been clearly established.

On the other hand, from a general point of view, the use of the dihedral angles in describing molecular conformations is, by itself, a source of ambiguities and misunderstanding. This is because any dihedral angle, between two non-oriented surfaces may be expressed by $\alpha°$ or $180 - \alpha°$. This is observed in the literature, where some papers report detailed descriptions of the molecular conformations of quite similarly shaped calixarene molecules, but the different choices made by the authors in the values of the corresponding dihedral angles lead to confusion and difficulties in comparing the structures.

As far as calix[4]arenes are concerned, the problem of understanding the true conformation from the reported values of the dihedral angles may be solved with the help of a perspective plot of the molecule. Even so some ambiguities still persist, as for example in all the cases of the so called 'distorted cone' conformations typical of the tetraester [4], tetraacetamide [5], and tetraketone [6] derivatives, where two phenolic rings are almost perpendicular to the 'reference plane'. In such cases it becomes very difficult to understand the correct values of the dihedral angles ($\alpha°$ or $180 - \alpha°$).

But in dealing with the larger calix[$n$]arenes other difficulties arise:

(a) there is no 'natural' choice for the reference plane, and an alternative choice of a reference plane is not always straightforward;
(b) as the number of phenolic units increases, the number of the possible conformations also increases. Furthermore the folding of the phenolic units around the macrocycle is sometimes so complicated that it is difficult to recognize the choice made by the authors in assigning the dihedral angles between the phenolic units and the molecular reference plane.

An improvement in the understanding of the molecular geometry may not always be accomplished by reporting the dihedral angles between adjacent phenolic units; in this way only further ambiguities are introduced in the description of the molecular model.

These considerations lead us to conclude that it is necessary to find more general *conformational parameters* for calix[$n$]arenes.

## 2. Conformational Parameters

The aim of this paper is to identify parameters which permit one to readily understand the molecular conformation which will allow 3D molecular models (using C.P.K. or others) to be built easily. New conformational parameters may be found by thinking of the simplest rule which may be followed in building a molecular model of a calix[$n$]arene.

We can imagine starting from two adjacent phenolic units A and B, linked by a $CH_2$ group, with B lying in the same plane as A and on its right hand side. We may observe that any reciprocal orientation of the two phenolic rings may be obtained by adjusting by $\phi$ and $\chi$ degrees respectively the two torsion angles $C(1)—C(2)—C(3)—C(4)$ and $C(2)—C(3)—C(4)—C(5)$ (see Figure 1) which, therefore, may be termed *conformational parameters* $\phi$ and $\chi$. The whole molecule of the calix[$n$]arene may be built by repeating $n-1$ times such a process of linking together adjacent phenolic units.

Conversely, the molecular conformation of a known calix[$n$]arene may be described without ambiguities by reporting any $n-1$ pairs of conformational parameters $\phi$ and $\chi$ which account for the mutual orientations between adjacent phenolic rings, including the closure of the ring. But, in practice, the arbitrary choice of the 'first' phenolic unit (from which to start in the calculation of the torsion angles), suggests that the molecular conformation of a calix[$n$]arene is more completely described by giving the whole set of $n$ pairs of conformational parameters $\phi$ and $\chi$.
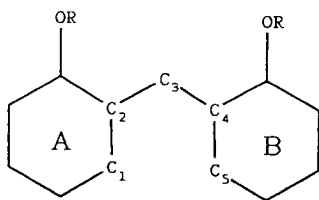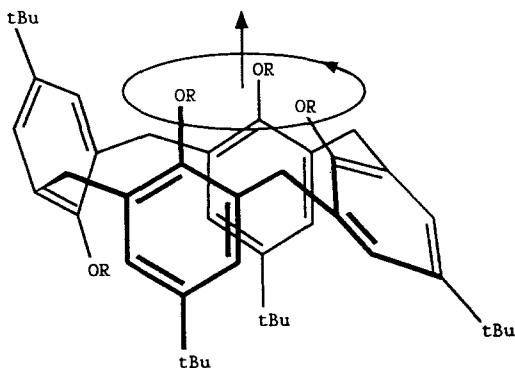


Fig. 1.

Fig. 2.

Moreover, the necessity of comparing different calix[$n$]arene conformations re-
quires the adoption of a general rule in selecting the sequence of calculations of the
$n$ pairs of torsion angles around the macrocycle. This implies, having to make a
choice, when possible, of the 'top side' of the molecule.

We suggest that the macroring which contains the maximum number of phenolic
oxygens to be taken as the 'top side'. Then the sequence of the torsion angles is
obtained by proceeding in the counterclockwise direction around the macroring as
shown in Figure 2 (right-hand rule).

For calix[$n$]arenes with an even number of phenolic units and with an equal
number of phenolic oxygens on each side, the right hand rule again holds if all the
$n$ $R_1$ groups are identical. For example this may be the case with calix[$n$]arenes in
the 1,3 or 1,2 alternate cone conformations. Once the 'top side' of the molecule has
been chosen it is only necessary to proceed in the counterclockwise direction around
the macroring. But if the $n$ $R_1$ groups are not identical, another criterion has to be
used to orient the calixarene molecule. We suggest that the 'top side' of the
molecule should be considered as the side which contains the maximum number of
non hydrogen atoms belonging to the $R_1$ groups. In any case, different criteria
chosen by authors have to be clearly reported to avoid misunderstandings.

Figures 3 to 14 show some examples of applications of the rule concerning
calix[$n$]arenes with $4 \leqslant n \leqslant 8$. (See note, p. 349.)

Apart from the values of the conformational parameters, their signs immediately
indicate the molecular shape of calix[$n$]arenes. In a general way, cone conforma-
tions are always characterized by the sequence $+-, +-, +-, +-$ (taken in
order: sign of $\phi$ sign of $\chi$, sign of $\phi$ sign of $\chi, \ldots$).

As shown in Figure 4, the partial cone conformation is characterized by the
sequence of signs $+-, +-, ++, --$. In fact, three subsequent phenolic units
are adjusted as in the cone conformation by setting at $+-, +-$ the two pairs of
torsion angles $\phi$ and $\chi$ which involve the two $CH_2$ bridges. The next $++$ pair
constrains the fourth phenolic unit to lie upside down with respect to the previous
ones. With the last pair of torsion angles set to $--$ values, a new inversion in the
orientation of the subsequent phenolic unit is imposed and then the closure of the
macroring is ensured. In this way, the interpretation of the sequence of signs
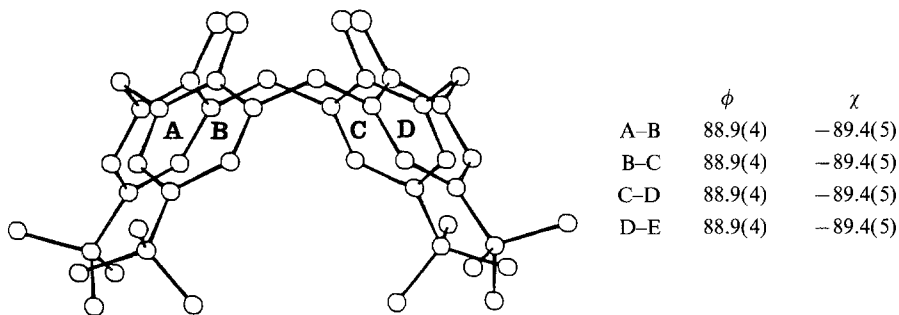
| | $\phi$ | $\chi$ |
|-----|--------|---------|
| A–B | 88.9(4) | −89.4(5) |
| B–C | 88.9(4) | −89.4(5) |
| C–D | 88.9(4) | −89.4(5) |
| D–E | 88.9(4) | −89.4(5) |

Fig. 3. The *p-tert*-butylcalix[4]arene 1:1 toluene complex: perspective view of the host molecule (the guest toluene molecule has been omitted).
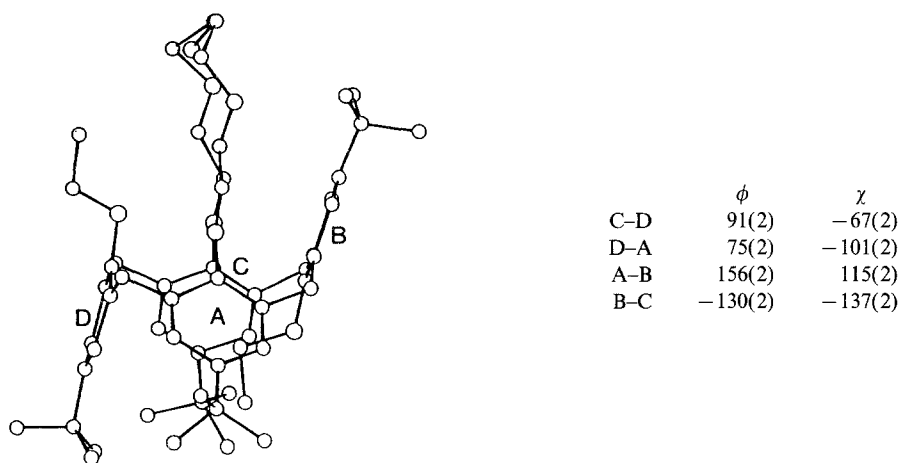


| | $\phi$ | $\chi$ |
|-----|--------|---------|
| C–D | 91(2) | −67(2) |
| D–A | 75(2) | −101(2) |
| A–B | 156(2) | 115(2) |
| B–C | −130(2) | −137(2) |

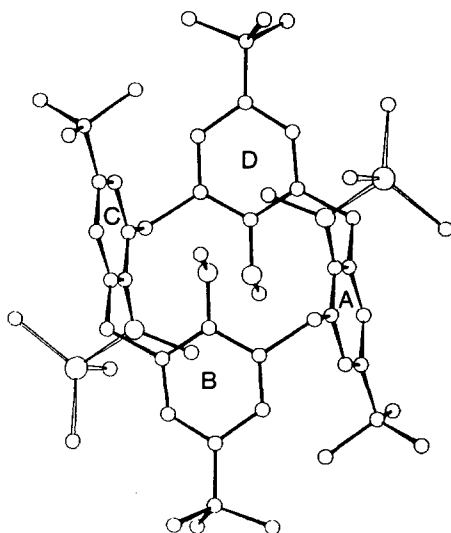Fig. 4. *p-tert*-Butylcalix[4]arene diethyl ether crown(5) in the partial cone conformation.

(+ +, − −, + +, − −) which characterizes the 1,3 alternate cone conformation shown in Figure 5, becomes quite simple. Starting from one phenolic unit and setting the signs of the two torsion angles, $\phi$ and $\chi$, around the CH$_2$ bridge to + +, a second phenolic unit is oriented upside down with respect to the first one, then with a − − pair of signs a third phenolic unit is connected oriented as the first one. With the third pair of signs set to + +, the fourth phenolic unit is oriented upside down with respect to the third one, namely it is oriented as the second one. The sequence − − is required to close the macroring.

Finally the 1,2 alternate cone conformation shown in Figure 6 is characterized by a sequence of signs + −, + +, − +, − −. The + − signs of the first pair of conformational parameters $\phi$ and $\chi$, orients the first two phenolic units in the cone conformation. The second pair of + + signs orients the third phenolic unit upside down with respect to the first two. Then the fourth phenolic unit is oriented as the third one, but upside down with respect to the first and the second ones by setting the third pair of $\phi$ and $\chi$ parameters at − + values. With the last pair of signs of
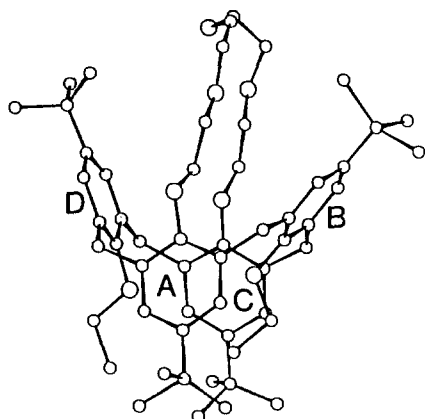
|     | $\phi$ | $\chi$ |
|-----|--------|--------|
| A–B | 161(1) | 110(1) |
| B–C | −131(1) | −126(1) |
| C–D | 131(1) | 128(1) |
| D–A | −130(1) | −149(1) |

Fig. 5. *p-tert*-Butylcalix[4]arene diethyl ether crown(5) in the 1,3 alternate cone conformation.



|     | $\phi$ | $\chi$ |
|-----|--------|--------|
| B–A | 81(2)  | −63(2) |
| A–D | 116(2) | 140(2) |
| D–C | −81(2) | 63(2)  |
| C–B | −116(2) | −140(2) |

Fig. 6. [*p-tert*-Butylcalix[4]arene methyl ether] [MeAlMe$_2$]$_2$ in the 1,2 alternate cone conformation.

$\phi$ and $\chi$ set at − − values (we again invert the orientation of the next phenolic unit with respect to the fourth one) we return to the first phenolic unit as required for the closure of the macroring.

The well known *p-tert*-butylcalix[4]arene derivatives (Figures 7, 8 and 9), which show two phenolic units almost perpendicular to the mean plane through the C atoms of the CH$_2$ bridges, described as 'distorted cone' conformations, are always characterized by sequences + −, + −, + −, + − and the deviations from the perfect cone conformation are accounted by comparison with the two values $\phi = 88.9(4)$ $\chi = -89.4(5)$ calculated for the *p-tert*-butylcalix[4]arene 1 : 1 toluene complex [9] shown in Figure 3.
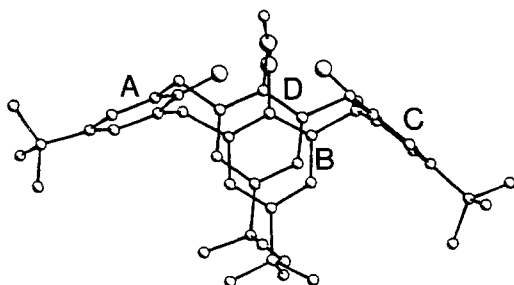
|     | $\phi$ | $\chi$ |
|-----|--------|--------|
| A–B | 74.0(4) | −124.0(3) |
| B–C | 102.0(4) | −63.0(4) |
| C–D | 64.0(4) | −107.8(4) |
| D–A | 116.2(4) | −58.1(4) |

Fig. 7. *p-tert*-Butylcalix[4]arene dimethoxy.
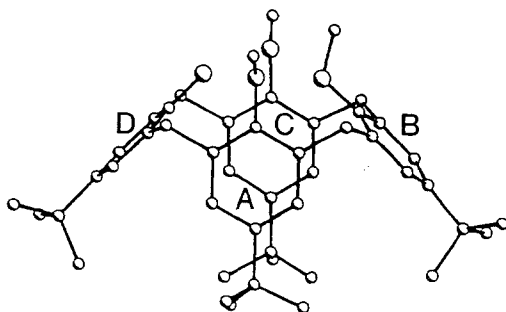


|     | $\phi$ | $\chi$ |
|-----|--------|--------|
| A–B | 100.4(7) | −68.3(7) |
| B–C | 66.2(7) | −97.1(7) |
| C–D | 98.9(7) | −62.6(8) |
| D–A | 60.5(8) | −99.0(7) |

Fig. 8. *p-tert*-Butylcalix[4]arene trimethoxy.
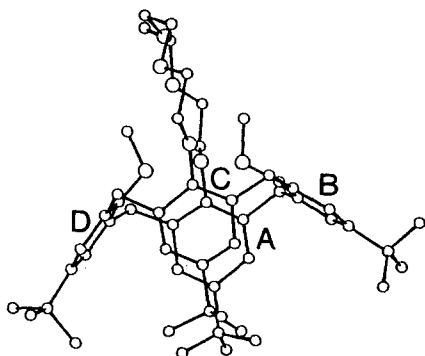


|     | $\phi$ | $\chi$ |
|-----|--------|--------|
| A–B | 103(2) | −63(2) |
| B–C | 62(2) | −106(2) |
| C–D | 97(2) | −62(2) |
| D–A | 60(2) | −92(2) |

Fig. 9. *p-tert*-Butylcalix[4]arene dimethyl ether crown(5).

The *p-tert*-butylcalix[4]arene crown(6) Rb-picrate complex [3] (see Figure 10), has already been cited as an example in which the current nomenclature seems inadequate. Using the above approach, it is conveniently described as in a 'cone' (although distorted) conformation rather than in a 'flattened partial cone' conformation, as the sequence of signs is always $+ -, + -, + -, + -$ and not $+ -, + -, + +, - -$.
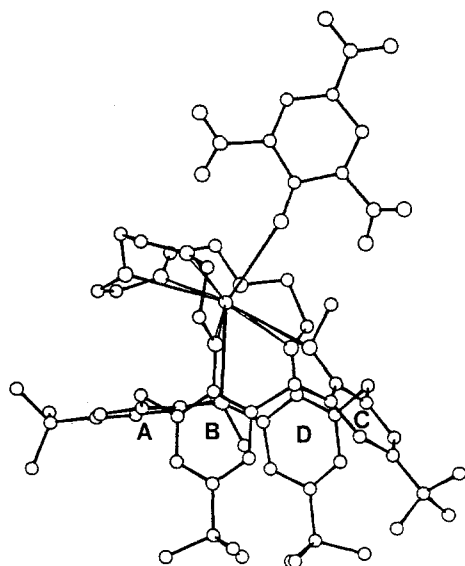
|     | $\phi$   | $\chi$   |
|-----|----------|----------|
| A–B | 143(1)   | −71(2)   |
| B–C | 64(2)    | −91(1)   |
| C–D | 89(1)    | −63(1)   |
| D–A | 73(1)    | −144(1)  |

Fig. 10. The *p-tert*-buthylcalix[4]arene crown(6) Rb picrate complex.
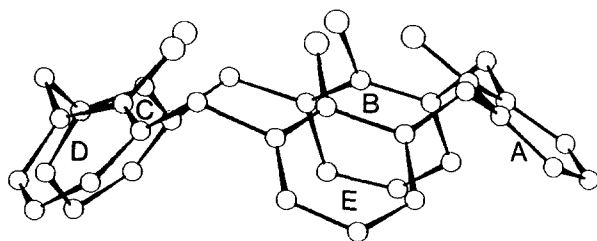
|     | $\phi$  | $\chi$  |
|-----|---------|---------|
| A–B | 96(1)   | −81(1)  |
| B–C | 76(1)   | −96(1)  |
| C–D | 77(1)   | −88(1)  |
| D–E | 98(2)   | −82(2)  |
| E–A | 85(2)   | −88(2)  |

Fig. 11. Calix[5]arene.

The conformational parameters for calix[5]arene (see Figure 11) show that it exists in the cone conformation without strong deviations of the two values $\phi$ and $\chi$ observed in the fourfold symmetric *p-tert*-butylcalix[4]arene 1 : 1 toluene complex.

As illustrated in Figure 12, the sequence of the signs in *p-tert*-butycalix[6]arene [11] is always of the type + − with two inversions (− +) which occur at the bridges between the B–C and E–F phenolic units. This reveals that the macrocycle is formed by two trimeric subunits (F–A–B) and (C–D–E), each of them organized in the cone conformation and linked together around the B–C and E–F methylene bridges which point their H atoms towards the interior of the macroring. The hydrogen atoms of the other CH$_2$ bridges (signs always + −) point towards the exterior of the macroring.

As an example of a calix[7]arene [12], the conformational parameters of the *p-tert*-butylcalix[7]arene 1 : 3 pyridine complex/clathrate is reported. The presence of a trimeric (G–A–B) and of a tetrameric (C–D–E–F) subunit is revealed by the

| | $\phi$ | $\chi$ |
|---|---|---|
| A–B | 91(2) | −100(2) |
| B–C | −95(2) | 9·(2) |
| C–D | 104(2) | −84(2) |
| D–E | 86(2) | −93(2) |
| E–F | −95(2) | 96(2) |
| F–A | 94(2) | −94(2) |
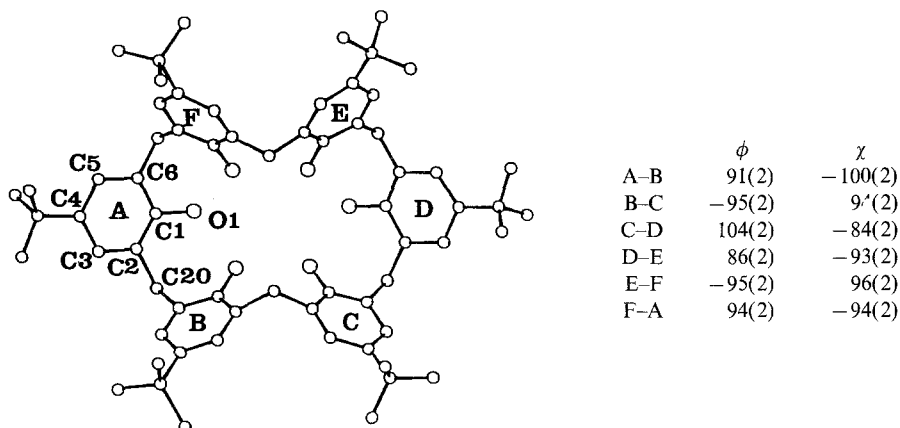
Fig. 12. *p-tert*-Butylcalix[6]arene.

| | $\phi$ | $\chi$ |
|---|---|---|
| A–B | 98.5(9) | −89.0(9) |
| B–C | −90.8(9) | 92.6(9) |
| C–D | 98.9(9) | −78.5(9) |
| D–E | 72(1) | −70(1) |
| E–F | 77.5(9) | 94.2(9) |
| F–G | −94.4(9) | 91.1(9) |
| G–A | 89.2(9) | −98.5(9) |
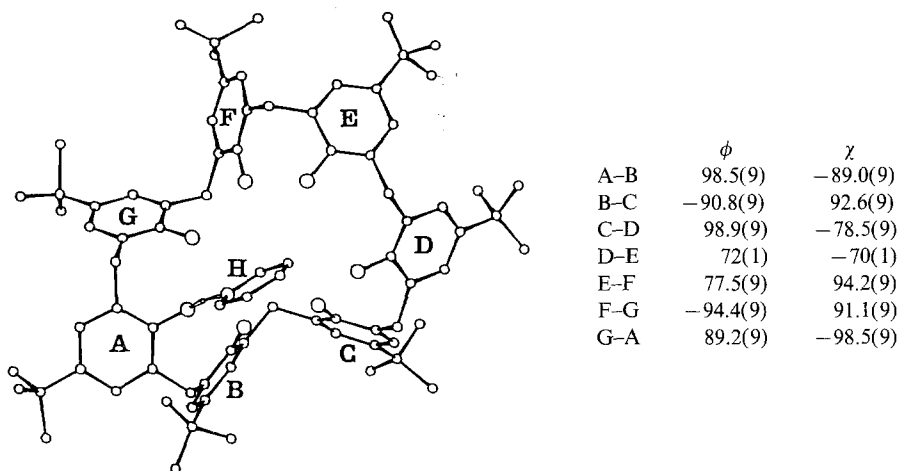
Fig. 13. The *p-tert*-butylcalix[7]arene 1:3 pyridine complex/clathrate (H is one pyridine molecule).

sequence of signs of the conformational parameters being always $+\,-$, but interrupted by two pairs $-\,+$ at the links B–C and F–G.

The interruption in the cyclic array of hydrogen bonds $O(D) \cdots O(E) 3.500(8)$ Å is also revealed by the two low values of the conformational parameters $\phi = 72(1)$ $\chi = -70(1)°$.

As an example of a calix[8]arene [13], the *up* and *down* in the 'undulated loop' conformation of *p-tert*-butylcalix[8]arene is detected by the continuous inversion of the signs of $\phi$ and $\chi$ as shown in Figure 14.

This immediately reveals that the H atoms of the $CH_2$ bridges point alternatively towards the exterior of the macroring in correspondence to a $+\,-$ pair, or towards the interior of the macroring in correspondence to a $-\,+$ pair.

It must be emphasized that the *p-tert*-butylcalix[8]arene, is a typical example in which an unequivocal choice of a 'top side' of the molecule is prevented because of

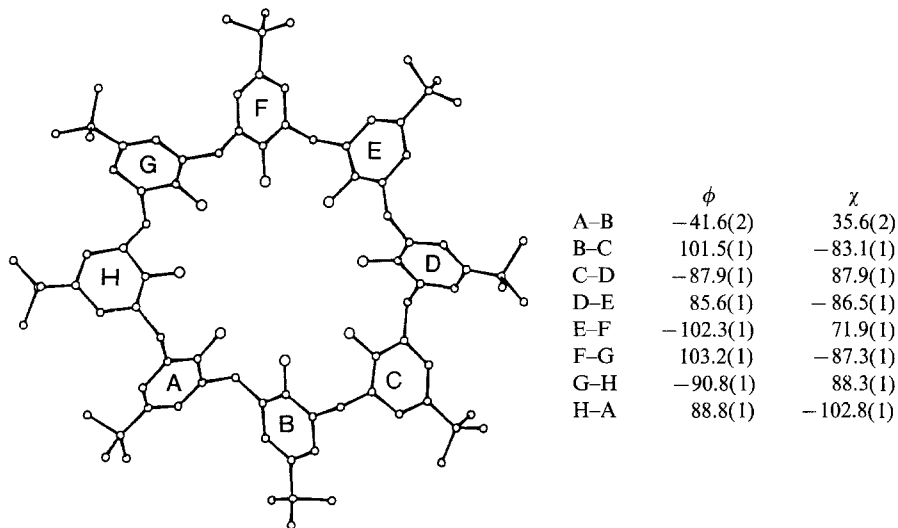| | $\phi$ | $\chi$ |
|---|---|---|
| A–B | $-41.6(2)$ | $35.6(2)$ |
| B–C | $101.5(1)$ | $-83.1(1)$ |
| C–D | $-87.9(1)$ | $87.9(1)$ |
| D–E | $85.6(1)$ | $-86.5(1)$ |
| E–F | $-102.3(1)$ | $71.9(1)$ |
| F–G | $103.2(1)$ | $-87.3(1)$ |
| G–H | $-90.8(1)$ | $88.3(1)$ |
| H–A | $88.8(1)$ | $-102.8(1)$ |

Fig. 14. *p-tert*-Butylcalix[8]arene.

the continuous *up* and *down* of the oxygens. As a consequence, another set of conformational parameters, obtained from those reported in Figure 14 by the exchange of $\phi$ and $\chi$, could represent equally well the molecular conformation of the macrocycle. This is not a limitation of the method presented here but reflects the absence of a physical criterion to orient the molecule.

## 3. Symbolic Representation of the Molecular Conformation

As previously explained, the values of the $n$ pairs of conformational parameters allow a complete and unambiguous description of the molecular conformation of a calix[$n$]arene. It is noteworthy that the most important information concerning the arrangement of the phenolic rings around the macrocycle are displayed by the signs of $\phi$ and $\chi$. In particular, in the calix[4]arenes, it has been shown how the $n$ pairs of signs are able to select between the four conformers. This suggests that, in a general way, the signs of the conformational parameters may be used for a *symbolic representation* of the molecular conformation of calixarenes.

Here we propose to use as a compact *symbolic representation* that formed by the Schöenflies symbol, which accounts for the point symmetry of the molecule, followed by the independent pairs of the signs of the conformational parameters as follows:

sign of $\phi$, sign of $\chi$, sign of $\phi$, sign of $\chi$, sign of $\phi$, sign of $\chi$, ...

However, due to the cyclic character of the sequence of signs of the conformational parameter, there are, in principle, $n$ different ways to write the sequence of signs which characterize a calix[$n$]arene, depending on the choice of the 'first' phenolic unit. For example, for the partial cone conformation we could equally well write: $+-, +-, ++, --$ or $+-, ++, --, +-$ or $++, --, +-, +-$ or

$--, +-, +-, ++$. As a *convention* for the representative sequence of signs we suggest, that the sequence (or one of the sequences) which leaves the maximum number of pairs of signs $+ -$ on the left side be chosen among the $n$ possible choices. In the previous example of the partial cone conformation, the correct sequence of signs is therefore $+-, +-, ++, --$.

For example, the *p-tert*-butylcalix[4]arene 1 : 1 toluene complex (Figure 3), which possesses fourfold symmetry, may be identified by the symbol $C_4 +-$, it being understood that the other 3 pairs are all $+ -$. The *p-tert*-butylcalix[4]arene diethyl ether crown(5) (Figure 4), which has no internal symmetry, is represented by $C_1 +-, +-, +-, --$. Calix[5]arene (Figure 11) is represented by $C_1 +-, +-, +-, +-$.

The *p-tert*-butylcalix[4]arene methyl ether $[MeAlMe_2]_2$ (1,2 alternate cone conformation) (Figure 6), which lies on a centre of symmetry, is represented by the symbol $C_i +-, ++$.

## 4. The Zero Problem

Although not yet encountered among the values of the conformational parameters calculated for the small calix[$n$]arenes ($n \leqslant 8$) studied until now, it cannot be ruled out that, for larger calix[$n$]arenes, one of the two values, $\phi$ or $\chi$, may equal zero. The case of $\phi = \chi = 0$ may be considered highly improbable because it corresponds to two adjacent phenolic units in the same plane and this is expected to obstruct the closure of the macroring.

This poses the problem of which sign has to be used in the list of sign pairs in such a case.

We suggest adopting as a *convention* the zero as a symbol in the *symbolic representation* of the molecular conformation.

## Acknowledgements

## Note

All the values reported here have been calculated from the crystallographic data reported in the literature or retrieved from the Cambridge Crystallographic Data File.

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