OPINION

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"Inherent chirality" and curvature

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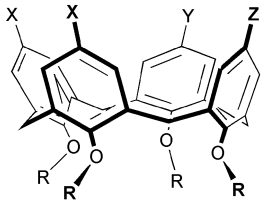
"Inherent chirality" in molecules like calix[4]arenes, fullerenes, and uranyl-salophen complexes can be related to the presence of curvature. This observation serves as a basis for the introduction of a new chirality descriptor.

The expression "inherently chiral" was first introduced by Böhmer[1] to indicate calix[4]arenes with a XXYZ (**1**) or WXYZ (**2**) substitution pattern at the upper rim. These molecules belong to the C_1 group of symmetry and are therefore chiral. Furthermore, fullerenes with a chiral molecular framework,[2–4] like C_{76}, C_{78}, and C_{84}, are referred to as "inherently chiral" even in the lack of any apparent analogy with Böhmer's calixarenes.[5]



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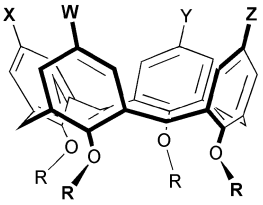

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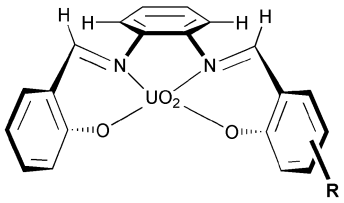

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In a recent paper, we described non-symmetrically substituted uranyl-salophen complexes (*e.g.*, **3**) as "inherently chiral".[6] In these species the metal ion is not a stereogenic centre in the strict sense, but because of its steric bulk dissymmetrises the entire structure, thereby forcing a curvature in an otherwise planar ligand. When presenting our results we sometimes experienced disagreement over the use of the expression "inherent chirality". Admittedly, such an expression might give the wrong impression that it is aimed at emphasising the notion that only in the given class of compounds is chirality a pervasive property of the entire molecule. This is clearly not the case. In fact, our definition of chirality in non-symmetrically substituted uranyl-salophen complexes as "inherent" was implicitly based on the idea that it can be related to inherent chirality in calix[4]arenes and fullerenes. In our opinion, in all such compounds chirality may be viewed as arising from the introduction of a curvature in an ideal planar structure that is devoid of symmetry axes in its bidimensional representation[7] (Fig. 1). Such a structure would be chiral in a two dimensional space,[8] but is indeed achiral in the three-dimensional world because the plane on which it lies is itself a symmetry plane. The curvature eliminates this symmetry plane and makes the structure chiral. According to this idea, in all the species referred to as "inherently chiral" racemisation occurs, or would occur at least in principle, through inversion of the curvature. Tetramethoxy and tetraethoxycalix[4]arenes, like their parent compounds, are conformationally mobile, but the presence at the lower rim of alkyl groups larger than ethyl blocks the ring-inversion process.[9] Similarly, the curvature inversion occurs very rapidly in structurally simple, sterically unhindered uranyl complexes such as **3**, but is strongly retarded upon introduction of bulky substituents in place of the hydrogens shown in **3**.[6] Inversion of the curvature of the robust fullerene skeleton is clearly unfeasible, and can only be envisaged with some imagination.[7]

The above relation between inherent chirality and curvature provides a basis for the definition of a simple and intuitive chirality descriptor. In the case of calix[4]arenes, once the carbons of the bridges are labelled as *a*, *b*, *c*, *d* according to the sequence rules,[10] an ideal observer standing on the concave side of the surface will see the three highest priority atoms *a*, *b*,

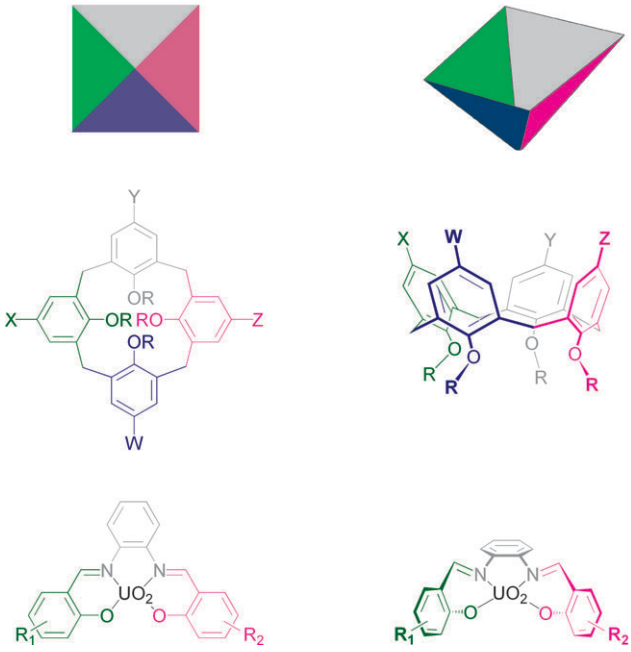

Fig. 1 Schematic representation of how non-symmetrical bidimensional structures (left) are turned into chiral species (right) by introduction of a curvature.

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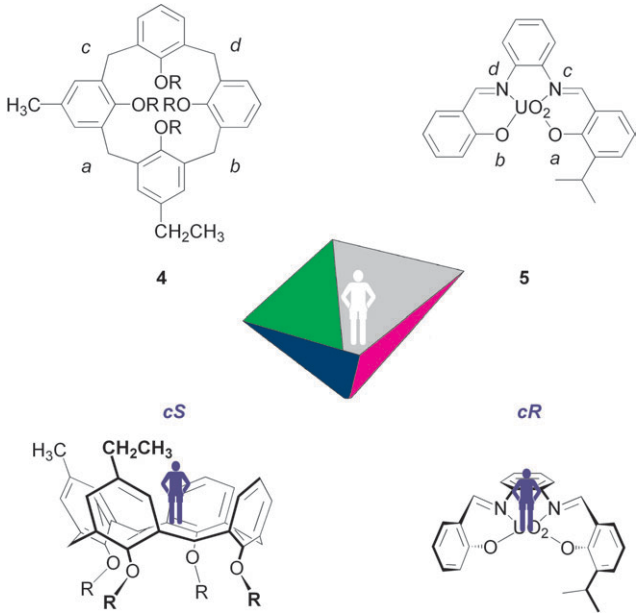

Fig. 2 Proposal of a chirality descriptor for inherent chirality.

and *c* describing a clockwise or a counterclockwise array. The calixarene will then be designated as *cR* or *cS*, respectively, where *c* stands for curvature. In the case of uranyl-salophen complexes, a similar procedure can be applied by considering the donor atoms of the ligand. Fig. 2, showing an observer standing in upward bowls, provides a graphical illustration of how this procedure is applied to compounds **4** and **5**. Obviously, this descriptor does not apply to inherently chiral fullerenes, because they contain only skeletal carbon atoms.

As a final statement, we believe that the word "inherent" should be considered just as a label that is not meaningful in itself, and can obviously be replaced by other terms, but simply serves to stress a common feature of chirality in certain classes of compounds, namely, its origin from molecular curvature.

References

1 V. Böhmer, D. Kraft and M. Tabatabai, *J. Inclusion Phenom. Mol. Recognit. Chem.*, 1994, **19**, 17.
2 D. E. Manolopoulos, *J. Chem. Soc., Faraday Trans.*, 1991, **87**, 2861.
3 J. M. Hawkins and A. Meyer, *Science*, 1993, **260**, 1918.
4 V. I. Sokolov, *Russ. J. Org. Chem.*, 1999, **35**, 12573.
5 W. H. Powell, F. Cozzi, G. P. Moss, C. Thilgen, R. J.-R. Hwu and A. Yerin, *Pure Appl. Chem.*, 2002, **74**, 629.
6 A. Dalla Cort, L. Mandolini, G. Palmieri, C. Pasquini and L. Schiaffino, *Chem. Commun.*, 2003, 2178.
7 Bidimensional representations of fullerenes are provided by the so-called Schlegel diagrams.[5] The transformation of a fullerene into a planar structure corresponding to a Schlegel diagram would require huge deformations of a large number of bonds. The ideal process of the turning inside out of a fullerene can be thought of as occurring *via* the planar structure.
8 E. L. Eliel and S. H. Wilen, *Stereochemistry of Organic Compounds*, Wiley, New York, 1994, pp. 486—487.
9 R. Ungaro, in *Calixarenes in Action*, eds. L. Mandolini and R. Ungaro, Imperial College Press, London, 2000, p. 1–10.
10 IUPAC 1968 Tentative Rules, Section E, Fundamental Stereochemistry, in *J. Org. Chem.*, 1970, **35**, 2849.