Chiral Calixarene

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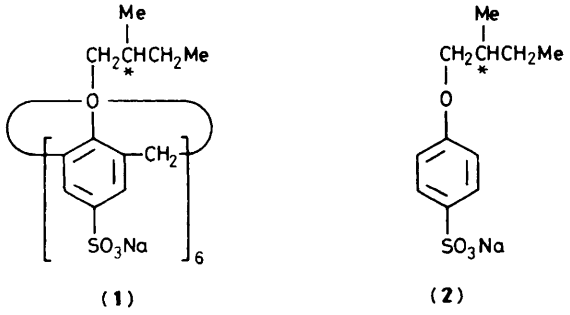
The chiral calixarene 5,11,17,23,29,35-hexasulphonato-37,38,39,40,41,42-hexakis[(*S*)-2-methylbutoxy]calix[6]arene (**1**) has been synthesised; its c.d. spectra are sensitive to conformational change and molecular complexation.

The chemistry of cyclodextrins has been a focus of interest in host–guest chemistry for the last two decades and many functionalised host molecules which can partly mimic the *in vivo* action of enzymes have been exploited.[1—3] Of particular interest is the ability of cyclodextrins to catalyse certain reactions asymmetrically,[1—3] owing to the presence of the chiral cavity made up of glucose units. Recently, we have been interested in the functionalisation of calixarenes (cyclic oligomers composed of benzene units as cyclodextrins are composed of glucose units).[4—7] It is known that calixarenes are capable of including small molecules in their cavities to form typical host–guest-type complexes in solution.[4,5] It thus occurred to us that introduction of chiral substituents into calixarenes would be of great value for development of a new class of chiral host molecules. We report here the first example of synthesis and characterisation of a chiral calixarene, 5,11,17,23,29,35-hexasulphonato-37,38,39,40,41,42-hexakis-[(*S*)-2-methylbutoxy]calix[6]arene, (**1**). We have found that the c.d. spectra of (**1**) give unusually large θ values in an aqueous system and are sensitive to inclusion of small guest molecules.

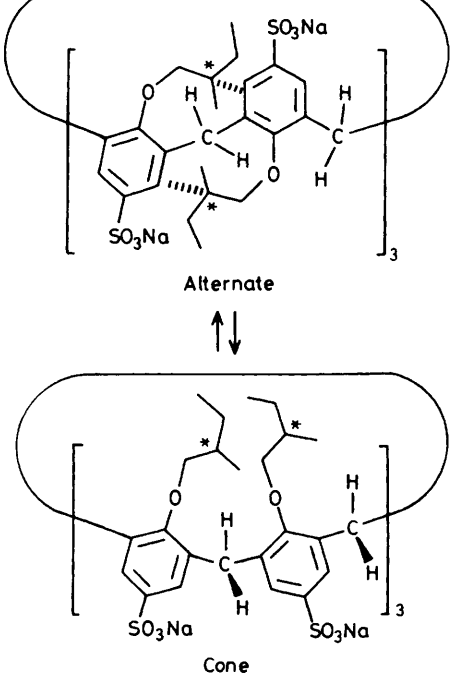
The chiral calixarene (**1**) was synthesised from (*S*)-1-bromo-2-methylbutane and calix[6]arene-*p*-hexasulphonate in a manner similar to that previously described.[4] The product was identified by i.r. and 400 MHz n.m.r. (JEOL GX-400) spectroscopy, and elemental analysis.†

In an aqueous system (20 °C, pH 6.9 with 0.067 M phosphate buffer) *p*-(*S*)-2-methylbutoxybenzenesulphonate (**2**),† a noncyclic analogue, did not give a perceptible c.d. spectrum at 220—300 nm {[(**2**)] = 0.12—2.0 mM}. Probably, the asymmetric carbon in the (*S*)-2-methylbutyl group is too far from the chromophoric benzene ring to affect it intramolecularly. In contrast, (**1**) gave a clear c.d. spectrum in this wavelength region [$\lambda_{max.}$ 236 (θ −14 100) and 269 nm (θ 3 300) at 20 °C in water–Me_2NCHO (98.6 : 1.4 v/v); see Figure 1]. These findings suggest that the c.d. band of the benzene chromophore is induced by the (*S*)-2-methylbutyl groups in the neighbouring benzene units but not by that in the same benzene unit. This situation is consistent with an 'alternate' conformation in which the (*S*)-2-methylbutyl group and the benzene ring are arranged alternately on the same side of the calixarene ring (see Scheme 1). In the past, discrimination between the calixarene conformers has been based only on ^1H n.m.r. spectroscopy;[7—10] the $ArCH_2Ar$ methylene protons of 'alternate' calixarenes resonate as a sharp singlet while those of 'cone' calixarenes give a pair of doublets because of their magnetic inequivalence. Aqueous solutions (**1**) gave a sharp singlet at δ 4.08 above room temperature, further support for the 'alternate' conformation.

We previously reported that water-soluble calixarenes solubilise various small molecules into aqueous solution by forming host–guest-type solution complexes.[4] It is interesting to investigate whether the conformation of the calixarenes changes upon inclusion of guest molecules. As shown in Figure 1, the c.d. band of (**1**) weakened with increasing octan-1-ol concentration. Similarly, the c.d. band intensity decreased on the addition of hexan-1-ol, heptan-1-ol, cyclohexanol, *etc.* These results suggest that the conformation changes from 'alternate' to 'cone' when these guest molecules are included in the cavity of (**1**). From plots of θ *vs.* guest concentration we estimated the association constants, (*K*):[11,12] $K = 1.4 \times 10^2$ for hexan-1-ol, 1.2×10^3 for heptan-1-ol, 7.8×10^3 for octan-1-ol, and *ca.* 80 $dm^3\ mol^{-1}$ for



† (**1**): i.r. (KBr) ν(CH) 2950, 2910, and 2860 cm^{-1}, ν(SO_3) 1180 and 1050 cm^{-1}; n.m.r.(D_2O) δ 0.66 (3H, CH_2Me), 0.70 (3H, CHMe), 0.95 and 1.29 (1H each, CH_2), 1.62 (1H, CH), 3.34 and 3.48 (1H each, OCH_2), 4.08 (2H, $ArCH_2Ar$), and 7.54 (2H, ArH). (**2**): i.r.(KBr) ν(CH) 3090, 3040, 2960, 2910, and 2860 cm^{-1}, ν(SO_3) 1180 and 1050 cm^{-1}; n.m.r.(D_2O) δ 0.91 (3H, CH_2Me), 0.99 (3H, CHMe), 1.22 and 1.52 (1H each, CH_2), 1.86 (1H, CH), 3.91 and 4.00 (1H each, OCH_2), 7.08 and 7.73 (2H each, ArH). Satisfactory elemental analyses were obtained for (**1**) and (**2**).



♦ **Scheme 1.** 'Alternate' and 'cone' conformations for calixarene (**1**).

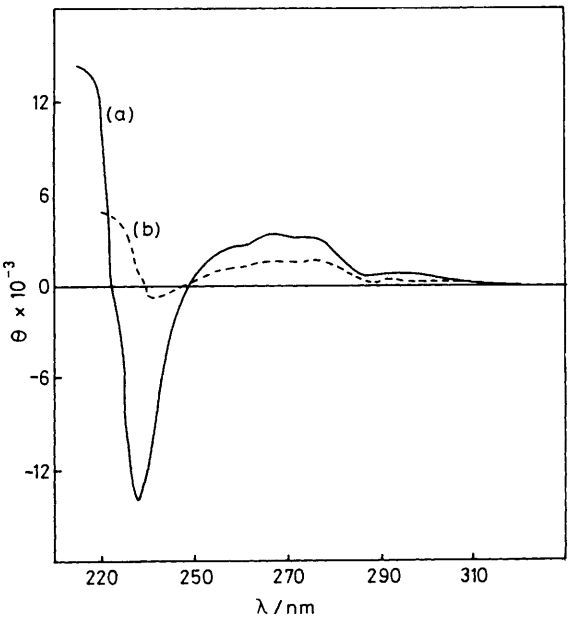


Figure 1. C.d. spectra of (**1**) in (a) the absence and (b) the presence of octan-1-ol. *Conditions:* 20 °C, pH 6.9 with 0.067 M phosphate buffer, water–Me_2NCHO (98.6 : 1.4 v/v), [(**1**)] = 3.30×10^{-4} M, [octan-1-ol] = 1.00×10^{-2} M.

cyclohexanol. In the ^1H n.m.r. spectrum [20 °C, D_2O–$(CD_3)_2NCDO$ (98.6 : 1.4 v/v)], the peak for the $ArCH_2Ar$ methylene protons was somewhat broadened by the addition of octan-1-ol {[(**1**)] = 3.30×10^{-4} M, [octan-1-ol] = 1.00×10^{-2} M}. At 0 °C it was broadened to such an extent that we could not use it as a conformational probe. Instead, the peak for the aromatic protons provided clear evidence for the expected conformational change.[4] In the presence of octan-1-ol the peak which was a singlet (δ 7.54) at 20 °C split into two peaks (δ = 7.46 and 7.54) at 0 °C, with a coalescence temperature of *ca.* 10 °C. Such a change in peak shape was not observed in the absence of octan-1-ol. This difference suggests that the (**1**)·octan-1-ol complex adopts the 'cone' conformation more readily than the vacant (**1**).

In conclusion, this study demonstrates that the conformational change in (**1**) is sensitively reflected by c.d. spectra. Thus, the chiral calixarene (**1**) provides a new approach for studies of the host–guest chemistry of calixarenes. Applications to separation of racemic compounds, asymmetric synthesis, *etc.* are being investigated.

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References

1 R. Breslow, *Acc. Chem. Res.*, 1980, **13**, 170.
2 I. Tabushi, *Acc. Chem. Res.*, 1982, **15**, 66.
3 M. L. Bender and M. Komiyama in 'Cyclodextrin Chemistry,' Springer-Verlag, New York, 1977.
4 S. Shinkai, S. Mori, H. Koreishi, T. Tsubaki, and O. Manabe, *J. Am. Chem. Soc.*, 1986, **108**, 2409.
5 S. Shinkai, H. Koreishi, K. Ueda, and O. Manabe, *J. Chem. Soc., Chem. Commun.*, 1986, 233.
6 S. Shinkai, K. Araki, H. Koreishi, T. Tsubaki, and O. Manabe, *Chem. Lett.*, 1986, 1351.
7 For a comprehensive review of calixarene chemistry see C. D. Gutsche, *Acc. Chem. Res.*, 1983, **16**, 161.
8 J. W. Cornforth, P. D'Arcy Hart, G. A. Nicolls, R. J. Rees, and J. A. Stock, *Br. J. Pharmacol.*, 1955, **10**, 73.
9 C. D. Gutsche and L. J. Bauer, *J. Am. Chem. Soc.*, 1985, **107**, 6052, 6059.
10 R. Ungaro, A. Pochini, G. D. Andretti, and P. Dominiano, *J. Inclusion Phenom.*, 1985, **3**, 35.
11 M. P. Mack, R. R. Hendrixson, R. A. Palmer, and R. G. Ghirardelli, *J. Am. Chem. Soc.*, 1976, **98**, 7830.
12 A. Ueno, H. Yoshimura, R. Saka, and T. Osa, *J. Am. Chem. Soc.*, 1979, **101**, 2779.