# Synthesis, *X*-Ray Crystal Structure, and Cation Transfer Properties of a Calix[4]arene Tetraketone, a New Versatile Molecular Receptor

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Treatment of *p*-t-butylcalix[4]arene with bromoacetone–potassium carbonate yields a crystalline tetraketone which shows exceptionally high phase-transfer activity towards alkali metal cations in aqueous solutions; *X*-ray and n.m.r. analyses show that the receptor possesses a cone conformation in which the carbonyl groups are pre-organised for ion binding.

The continuing search for new synthetic molecular receptors capable of host–guest relationships with organic and inorganic ions and neutral molecules has produced many novel macrocycles during the past decade.[1] Although structures based on the original crown ether–cryptand concepts still abound, there is growing interest in the use of cyclophanes as molecular receptors.[2] Metacyclophanes, in particular, present attractive possibilities owing to their rigid structures and their ability to pre-organise convergent electron-donating substituents into binding sites around the periphery of a central cavity.[3] The calixarenes[4] are a series of functionalised metacyclophanes with convergent phenolic groups ideally suited to functional group elaboration, a recent example of which was our introduction of ester groups as potential binding sites.[5] The spectacular ionophoric activity of the resulting alkyl calixaryl acetates towards aqueous $Na^+$, $K^+$, $Rb^+$, and $Cs^+$ prompted us to examine the ion-transport ability of other calixarene-supported ligands, and we now report the first derivative with pendant ketonic groups capable of exhibiting this type of receptor activity. We can thus compare directly the ion transport ability of the ester and ketonic groups.

Treatment of *p*-t-butylcalix[4]arene (**1**)[6] with bromoacetone–potassium carbonate in dry acetone under reflux furnished the crystalline tetraketone (**2**), m.p. 185—192 °C, whose n.m.r. spectrum (400 MHz) displayed singlets for the t-butyl, $-OCH_2CO-$, and -COMe groups ($\delta$ 1.07, 4.88, and 2.21, respectively), an AB system for the bridging methylene groups ($\delta$ 4.81 and 3.17; $J_{AB}$ 12.8 Hz), and a singlet for the aromatic protons ($\delta$ 6.80). These data are consistent with a cone conformation[4] in solution at room temperature, but do not provide information on the local environment of the carbonyl groups. *X*-Ray analysis of (**2**)† confirmed that the cone conformation (Figures 1 and 2) persists in the solid state and that the four pendant ketonic groups, though mutually *syn* with respect to the calixarene substructure, are asymmetrically disposed about the cavity.

The calixarene (**2**) lies about a crystallographic two-fold axis [the asymmetric unit contains half a molecule of (**2**), and an acetone of crystallisation (0.5 occupancy) disordered about an inversion centre]. The molecular conformation is defined by the interplanar angles which the aromatic rings A and B (Figure 1) make with the plane of the four $CH_2$ groups which

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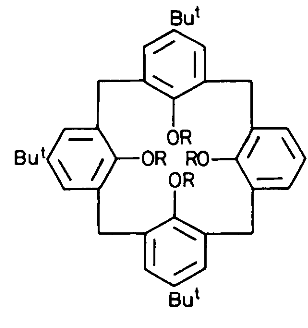
† *Crystal Data:* $C_{56}H_{72}O_8{\cdot}C_3H_6O$, $M_r$ = 931.3, orthorhombic, $a$ = 19.644(7), $b$ = 12.712(3), $c$ = 22.115(7) Å, $U$ = 5522 Å$^3$, $Z$ = 4, $D_c$ = 1.12 g cm$^{-3}$, $F(000)$ = 2016. $\lambda$(Mo-$K_\alpha$) = 0.71069 Å, $\mu$(Mo-$K_\alpha$) = 0.7 cm$^{-1}$. Space group *Pbcn* uniquely from systematic absences ($0kl$, $k = 2n + 1$; $h0l$, $l = 2n + 1$; $hk0$, $h + k = 2n + 1$). 2573 unique reflections ($2 < \theta < 20°$) collected with graphite monochromatized Mo radiation and a CAD4 diffractometer. 1442 observed reflections. The structure was solved with the aid of MULTAN 82[8] and refined (final $R$ = 0.094) by full matrix least-squares calculations using SDP-Plus[9] and our laboratory PDP 11/73 computer, with anisotropic thermal parameters for all non-hydrogen atoms of the calixarene. Co-ordinates were derived (from difference maps) for the disordered acetone of solvation and for the hydrogen atoms (C-H = 0.95 Å); the contributions of these atoms were included in the calculations, but they were not refined. The final round of calculations had 289 variables and 1442 'observed' reflections [having $I > 3\sigma(I)$], and converged with $R$ = 0.094, $R_w$ = 0.134. We attribute the relatively high $R$ factors to the effects of the disorder. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

**Table 1.** % Extraction of alkali metal and ammonium picrates in $CH_2Cl_2$ at 20 °C.[a]

| Compound | $Li^+$ | $Na^+$ | $K^+$ | $Rb^+$ | $Cs^+$ | $NH_4^+$ |
|---|---|---|---|---|---|---|
| (**2**) | 31.4 | 99.2 | 84.1 | 53.7 | 83.8 | 23.0 |
| (**3**) | 15.0 | 94.6 | 49.1 | 23.6 | 48.9 | <5 |

[a] $2.5 \times 10^{-4}$ M receptor in $CH_2Cl_2$; $2.5 \times 10^{-4}$ M picric acid in 0.1 M aqueous MOH. Receptor solution (5 ml) was shaken (3 min) with picrate solution (5 ml) and % extraction was measured from absorbance of resulting $CH_2Cl_2$ solution at ca. 378 nm; values are ±2%. No picrate extraction in the absence of receptor.



(**1**) R = H
(**2**) R = $CH_2COMe$
(**3**) R = $CH_2CO_2Et$

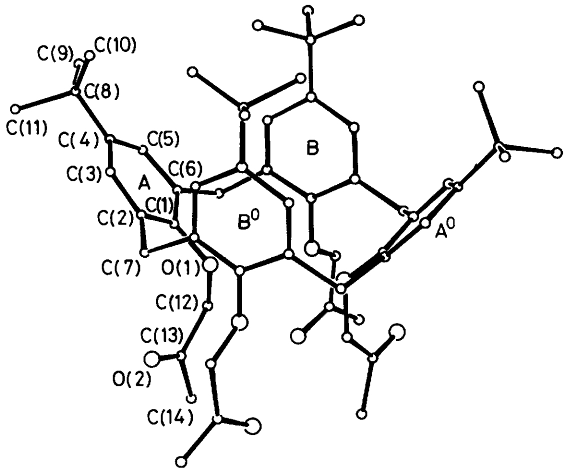


**Figure 1.** A view of molecule (**2**); carbon and oxygen atoms are shown as spheres of arbitrary radius.

link the rings (A 133, B 95°). Thus rings A and $A^0$ are almost normal to one another (interplanar angle 94.8°), and rings B and $B^0$ are almost parallel (interplanar angle 9.0°). An almost identical conformation was found for the closely related ethyl ester derivative (**3**), where the corresponding angles were 94.8 and 1.9°. The mutually *syn* $MeCOCH_2$– moieties form the base of the cavity, with phenolate O ··· O intramolecular contacts O(1A) ··· O(1A)$^0$ 3.55(1), O(1A) ··· O(1B) 3.26(1), O(1A) ··· O(1B)$^0$ 3.03(1), and O(1B) ··· O(1B)$^0$ 5.16(1) Å. The keto groups, while having a *cis*-conformation with respect to the phenolate oxygen atoms [torsion angles O(1)–C(12)–C(13)–O(2) 18 and 12° for A and B side chains respectively], are quite asymmetrically disposed about the cavity [torsion angles C(1)–O(1)–C(12)–C(13) −99 and 173° for A and B respectively], such that keto oxygen O(2A) is directed away from the cavity and O(2B) points towards it.

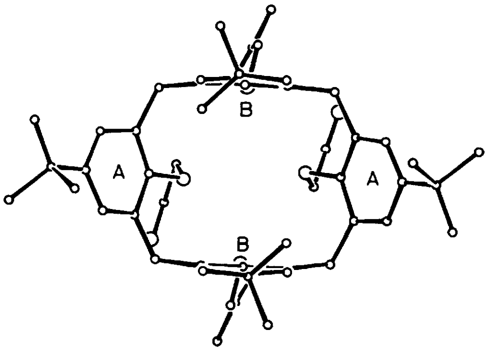


**Figure 2.** A view of molecule (**2**) almost normal to the plane of the four macrocyclic $CH_2$ carbon atoms.

The alkali metal picrate transfer technique was used to assess the ion transport ability of (**2**). The results (Table 1) reveal the broadest range of ionophoric activity so far exhibited by a calixarene receptor. Not only are there remarkably high levels of transport for $Na^+$, $K^+$, $Rb^+$, and $Cs^+$, with peak selectivity for $Na^+$ (99%), but the values for $K^+$, $Rb^+$, and $Cs^+$ are all significantly higher than those for the calix[4]arene ester (**3**); as a consequence the peak selectivity for $Na^+$ is not so pronounced. Furthermore, (**2**) is the first calixarene derivative to show appreciable activity towards $Li^+$ and $NH_4^+$. Thus in the tetramer calixarene series at least the ketonic carbonyl group is superior to the ester group in promoting ion transport. An important factor in the high selectivity and efficiency of tetraketone (**2**) is undoubtedly the pre-organisation of the binding groups in the rigid calixarene cone conformation (Figure 1 and 2). Chemical modification of (**2**) at the carbonyl group and/or the α-positions may lead to further new series of selective ionophores and receptors based on the calixarene substructure.

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## References

1 For recent overviews see B. Dietrich, *J. Chem. Ed.*, 1985, **62**, 954; H. Colquhoun, J. F. Stoddart, and D. J. Williams, *New Scientist*, 1986, **110**, 44.

2 E. Weber and F. Vögtle, *Top. Curr. Chem.*, 1981, **98**, 1; D. J. Cram and K. N. Trueblood, *ibid.*, p. 43; F. Vögtle, H. Sieger, and W. M. Müller, *ibid.*, p. 107.

3 D. J. Cram, S. P. Ho, C. B. Knobler, E. Maverick, and K. N. Trueblood, *J. Am. Chem. Soc.*, 1986, **108**, 2989, and references therein.

4 C. D. Gutsche, *Top. Curr. Chem.*, 1984, **123**, 1.

5 M. A. McKervey, E. M. Seward, G. Ferguson, B. Ruhl, and S. J. Harris, *J. Chem. Soc., Chem. Commun.*, 1985, 388. Similar studies have also been reported by S. K. Chang and I. Cho, *Chem. Lett.*, 1984, 477; *J. Chem. Soc., Perkin Trans. 1*, 1986, 211; A. Arduini, A. Pochini, S. Reverberi, R. Ungaro, G. D. Andreetti, and F. Ugozzoli, *Tetrahedron*, 1986, **42**, 2089.

6 C. D. Gutsche, B. Dhawan, K. H. No, and R. Muthukrishnan, *J. Am. Chem. Soc.*, 1981, **103**, 3782.

7 C. J. Petersen, *Fed. Proc. Am. Soc. Exp. Biol.*, 1968, **27**, 1305; K. E. Koenig, R. C. Helgesen, and D. J. Cram, *J. Am. Chem. Soc.*, 1976, **98**, 457.

8 P. Main, S. J. Fisk, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson (1980), MULTAN-80, Universities of York and Louvain.

9 G. M. Sheldrick, 1976, SHELX, a program for crystal structure analysis, University of Cambridge.