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Alkali cation 'conformational templation' in 1,5-bridged calix[8]arenes: a single crystal X-ray proof[†]

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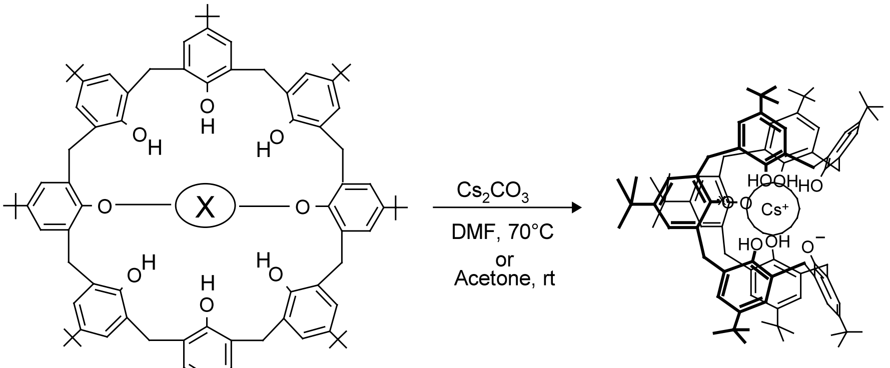
Abstract—X-Ray crystallography proves that alkali cations can act as conformational templates for 1,5-bridged calix[8]arenes **1**H_6–**3**H_6, folding their skeleton in a 'tub-shaped' conformation composed of four 3/4-cone clefts. This templation occurs even for neutral **1**H_6 to give a (**1**H_6Cs)$^+$·Cl^- complex, where Cs^+ was found perfectly fitting inside the eight calix[8]arene oxygens cavity. Conventional 'electrostatic' coordination with O atoms occurs whereas cation-π interactions can be excluded. © 2002 Elsevier Science Ltd. All rights reserved.

The ability of calixarene systems to interact with alkali metal ions has been long recognized and has led to several ionophores increasingly selective for a specific cation.[1] These interactions can generate a 'conformational templation' of the calixarene skeleton often invoked to explain the regiochemical or atropisomeric outcome in *O*-alkylation reactions.[2] This kind of templation can also alter the equilibrium distribution of conformationally mobile derivatives or it can reduce the rate of their interconversion.[3] Several examples of these phenomena are well documented in calix[4]arene series,[2,3] whereas they remain more limited for the homologue calix[6]arene family.[3b,4]

In these instances little information is often available concerning the exact mode of calixarene/cation interaction. Usually, a conventional 'electrostatic' coordination with donor atoms (oxygens) can be assumed, but the possibility of polyhapto aromatic or cation-π interaction[5] cannot be excluded a priori. In fact, Har-



1H_6 X = $CH_2CH_2CH_2CH_2$
2H_6 X = CH_2CH_2
3H_6 X = $CH_2CH_2OCH_2CH_2$

1H_5^-·Cs^+

Keywords: calixarenes; bridged calix[8]arenes; alkali cations; template effect; conformation; X-ray crystal structure.

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[†] Dedicated to the memory of Professor Guido Sodano (Università di Salerno).

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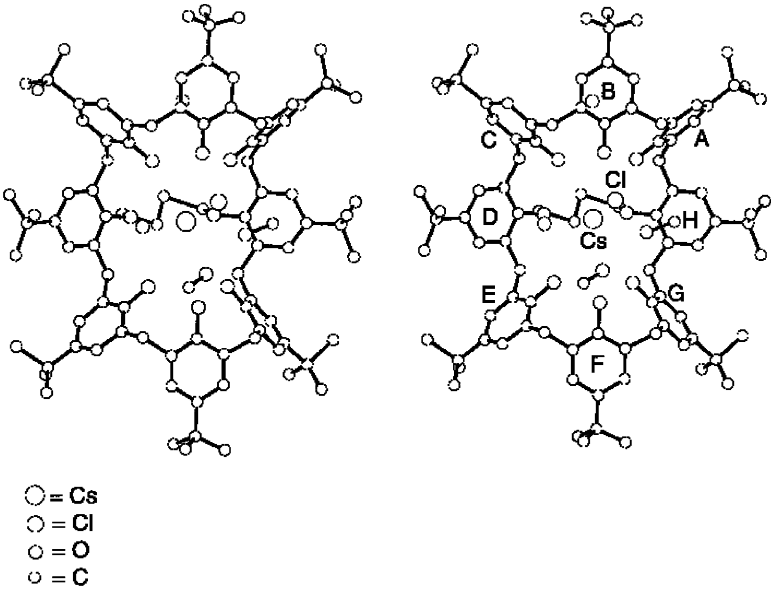

Figure 1. Stereoview of the X-ray crystal structure of the cesium conformational template $(\mathbf{1}H_6Cs)^+ \cdot Cl^-$. The labeling of aromatic rings is indicated, while H atoms are omitted.

rowfield and co-workers have unambiguously demonstrated by X-ray crystallography that cesium cation can be included within the π-basic cavity of a calix[4]-arene.[6a,b] Similar *endo*-calix inclusion has also been observed by Floriani and co-workers for Li^+, Na^+, and K^+ using calix[4]arene/transition metal complexes.[6c] Therefore, a detailed characterization of the complexation mode of alkali cations by a calixarene is often deemed necessary.[6b]

Regarding the larger calix[8]arenes, we only very recently described the first example of solution state preorganization of poorly functionalized calix[8]arenes $\mathbf{1}H_6$–$\mathbf{3}H_6$ induced by alkali cation templation.[7] Here we wish to report the single crystal X-ray structure of a cesium complex of $\mathbf{1}H_6$, which not only confirms the presence of this templation, but also provides a detailed description of the calix[8]arene–alkali cation interaction mode.

As previously described, 1,5-tetramethylene-bridged calix[8]arene $\mathbf{1}H_6$, prepared in 90% yield by alkylation of *p*-*tert*-butylcalix[8]arene with $I(CH_2)_4I$ in the presence of Cs_2CO_3 in DMF, is conformationally mobile.[7] However, upon treatment with alkali metal carbonates, it is easily converted to salts, exemplified by $\mathbf{1}H_5^- \cdot Cs^+$, in which a strong reduction of conformational mobility is observed due to cation templation.[7] A sample of this material, quickly washed with diluted HCl, afforded single crystals suitable for X-ray analysis by slow evaporation from a CH_2Cl_2/MeOH solution.

The crystal structure[8] (Fig. 1) shows that the calix[8]arene skeleton is folded in a geometry composed by four well-defined 3/4-cone clefts (rings ABC, CDE, EFG, and GHA) whose cavities are alternately oriented above and below the mean molecular plane. In each triad the 'cone' pitch appears to be smoother than a typical calix[4]arene C_{4v}-cone[1] as indicated by the canting angle of each ring [A 36(1), B 59(1), C 37(1); C 50(1), D 104(1), E 42(1); E 45(1), F 60(1), G 43(1); G 44(1), H 106(1), A 51(1)°]. The opposite bridged rings D and H form an angle of 44(1)°, while the conformationally more free opposite rings B and F are almost coplanar forming an angle of 8(1)°. The calix[8]arene conformation can be symbolically represented, according to Ugozzoli and Andreetti,[10] by the regular sequence of − +, − +, + −, + −, − +, − +, + −, + − for the ϕ and χ dihedral angles. It is very similar to the D_{2d} structure of 1,5:3,7-doubly bridged calix[8]arenes[11] and to that of the alkali cation template model[7] and we propose the name 'tub-shaped' for this folded calix[8]arene geometry.[12]

The cesium cation is situated at the center of the structure (Fig. 2) approximately in the plane of the four

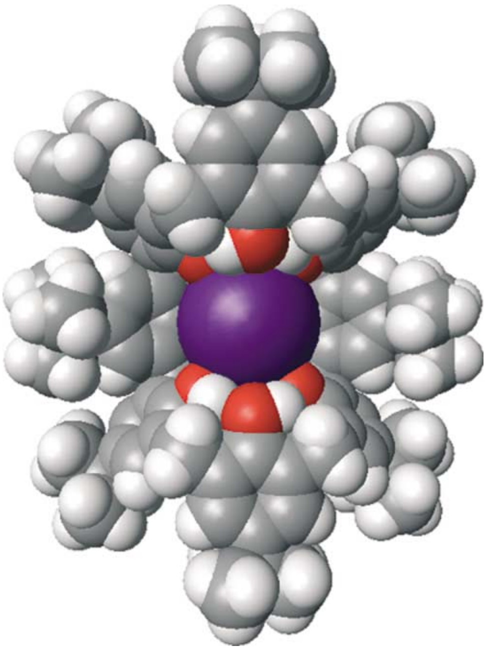

Figure 2. Space-filling model of $(\mathbf{1}H_6Cs)^+ \cdot Cl^-$ showing the perfect fitting of Cs^+ inside the eight calix[8]arene oxygens cavity (CH_3OH molecules and Cl^- anion are omitted).

oxygen atoms of hydroxyls of rings A, C, E, and G (Cs···O distances are 3.39, 3.32, 3.47, and 3.43 Å, respectively). From the bottom the cation is shielded by the $O(CH_2)_4O$ bridge attached to rings D and H (Cs···O distances are 3.08 and 3.13 Å, respectively), while the remaining O atoms of rings B and F (Cs···O distances 3.95 and 4.31 Å, respectively), are at the top. From this side the cation is further interacting with two CH_3OH molecules (Cs···O distances 3.17 and 4.76 Å), one water molecule (Cs···O distance 3.45 Å), and one Cl^- anion (Cs···Cl distance 4.50 Å). The Cl^- anion also interacts with the oxygen atom of hydroxyl of ring B (Cl^-···O distance 2.91 Å) and with the two CH_3OH molecules (Cl^-···O distances 3.26 and 3.11 Å). Since no other cations are present in the lattice the material has to be formulated as $(\mathbf{1}H_6Cs)^+\cdot Cl^-$. Therefore, in this particular case the Cs^+ cation is able to template the calix[8]arene conformation even in its neutral form[13] by means of electrostatic coordination typical of crown ether complexes (where Cs···O distances of 3.0–3.3 Å are found).[14] The Cs-aromatic centroid distances range between 4.66 and 6.87 Å and precisely 6.00, 6.58, 5.92, 4.66, 6.02, 6.87, 5.99, and 4.70 Å for A, B, C, D, E, F, G, and H ring, respectively. They are quite longer with respect to those of typical Cs-π interactions (3.57–3.61 Å) found in calix[4]arene systems.[6a,b] Therefore, the presence of true cation-π interactions in $(\mathbf{1}H_6Cs)^+\cdot Cl^-$ can be excluded. Rings D and H appear to be folded toward the Cs^+ cation, as indicated by their canting angles, to give only a very weak interaction, if any.

Two water molecules, not involved in H-bonds, are also found within the ABC and CDE 3/4-cone cavities at van der Waals contacting distances (the *O*-centroid distances are 4.29, 3.96, and 4.25 Å for ABC and 5.11, 4.11, and 5.33 Å for CDE, respectively). Interestingly, two networks of strong H-bonds OA···OB···OC and OE···OF···OG (O···O distances of 2.58, 2.57, 2.62, and 2.58 Å, respectively) are present, which probably contribute to stabilization of the folded *tub-shaped* conformation. No intermolecular H-bonds are present.

In conclusion, the present work unambiguously proves the ability of alkali cations to template the folding of calix[8]arene skeleton and suggests a probable template effect in the synthesis of 1,5:3,7-doubly-bridged derivatives. These results also indicate an intrinsic propensity of the macrocycle to fold, which can be exploited (and has to be taken into account) in the design of new calix[8]arene-based hosts.

References

1. (a) Böhmer, V. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 713; (b) Gutsche, C. D. *Calixarenes Revisited*; Royal Society of Chemistry: Cambridge, 1998; (c) *Calixarenes 2001*; Asfari, Z.; Böhmer, V.; Harrowfield, J.; Vicens J., Eds.; Kluwer: Dordrecht, 2001.
2. (a) Shinkai, S. *Tetrahedron* **1993**, *49*, 8933; (b) Yamamoto, H.; Sakaki, T.; Shinkai, S. *Chem. Lett.* **1994**, 469.
3. (a) Iwamoto, K.; Ikeda, A.; Araki, K.; Harada, T.; Shinkai, S. *Tetrahedron* **1993**, *49*, 609; (b) Ikeda, A.; Shinkai, S. *Chem. Rev.* **1997**, *97*, 1713.
4. (a) Otsuka, H.; Araki, K.; Shinkai, S. *Tetrahedron* **1995**, *51*, 8757; (b) Wang, Y.; Alvarez, J.; Kaifer, A. E. *Chem. Commun.* **1998**, 1457.
5. (a) Weiss, E. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1501; (b) Dougherty, D. A. *Science* **1996**, *271*, 163.
6. (a) Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; White, A. H. *J. Chem. Soc., Chem. Commun.* **1991**, 1159; (b) Assmus, R.; Böhmer, V.; Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1993**, 2427; (c) Zanotti-Gerosa, A.; Solari, E.; Giannini, L.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *Chem. Commun.* **1997**, 183.
7. Consoli, G. M. L.; Cunsolo, F.; Geraci, C.; Neri, P. *Org. Lett.* **2001**, *3*, 1605.
8. *Crystal data* for $(\mathbf{1}H_6Cs)^+\cdot Cl^-$: $C_{92}H_{102}O_8CsCl\cdot 2CH_3OH\cdot 2H_2O$, $M=1602.3$, triclinic, space group $P\overline{1}$ (no. 2), $a=14.758(5)$, $b=30.186(9)$, $c=12.236(4)$ Å, $\alpha=98.07(3)$, $\beta=105.68(3)$, $\gamma=83.56(3)°$, $U=5180(2)$ Å^3, $Z=2$, $D_c=1.03$ g cm^{-3}, $\mu(\mathrm{Cu}\ K\alpha)=3.43$ cm^{-1}, $F(000)=1688$. Prismatic crystals were grown by slow evaporation from a dichloromethane/methanol solution. A crystal (0.40×0.35×0.25 mm) was sealed with its mother liquid in a Lindemann capillary and used for data collection on a Rigaku AFC5R diffractometer at room temperature. Data were collected till $2\theta_{max}=124°$, LP and absorption corrected, 10816 considered unique. The structure was solved and refined with the SIR97 program.[9] The final isotropic refinement was based on 2814 reflections with $F_o>8.0\sigma(F_o)$ and 495 variable parameters (ratio 5.7): $R=0.113$, $R_w=0.133$, $\Delta\rho_{max}=1.15$ and $\Delta\rho_{min}=-0.45$ e Å^{-3}. Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-173842. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].
9. Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G. L.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *J. Appl. Cryst.* **1999**, *32*, 115.
10. Ugozzoli, F.; Andreetti, G. D. *J. Incl. Phenom.* **1992**, *13*, 337.
11. (a) Ikeda, A.; Akao, K.; Harada, T.; Shinkai, S. *Tetrahedron Lett.* **1996**, *37*, 1621; (b) Ikeda, A.; Suzuki, Y.; Akao, K.; Shinkai, S. *Chem. Lett.* **1996**, 963; (c) Geraci, C.; Chessari, G.; Piattelli, M.; Neri, P. *Chem. Commun.* **1997**, 921; (d) Geraci, C.; Bottino, A.; Piattelli, M.; Gavuzzo, E.; Neri, P. *J. Chem. Soc., Perkin Trans. 2* **2000**, 185.
12. In this conformation the eight $ArCH_2Ar$ carbons describe a geometry similar to that of the eight CH carbons of cyclooctatetraene commonly defined as 'tub-shaped'.
13. Obviously, Cl^- was introduced by neutralization of $\mathbf{1}H_5^-\cdot Cs^+$ salt during the quick washing with diluted HCl. At this regard, separate experiments showed that neutralization of $\mathbf{1}H_5^-\cdot Cs^+$ with 1 equiv. of HCl gave a conformationally less blocked inclusion compound (as indicated by broadened ^1H NMR resonances).
14. Fenton, D. E. In *Comprehensive Coordination Chemistry*; McCleverty, J. A.; Gillard, R. D.; Wilkinson, G., Eds.; Oxford: Pergamon Press, 1987; Vol. 3, p. 1.