Stepped layers in the complexes of *para*-sulfonatocalix[6]arene with dimethylammonium and bis-6-aminohexylammonium cations†

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Solid-state structures of *para*-sulfonatocalix[6]arene with dimethylammonium and bis-6-aminohexylammonium cations are mainly based on hydrogen bond interactions. In the two complexes the calixarene molecule adopts a chair conformation with small varieties in geometry influenced by the number and types of intra- and intermolecular interactions developed by polar substituents. A stepped layer topology is induced by this chair conformation in the two complexes. Structural motifs present in the two systems generate channels, which in the first complex include dimethylformamide solvent molecules, while in the second case they include water molecules.

Introduction

Calixarenes are macrocyclic molecules[1] capable of complexing a large variety of molecules.[2] Among these macromolecules, the *para*-sulfonato derivatives present a particular interest due to their important aqueous solubility,[3] which has led to the development of these molecules in biological and biomedical applications.[4] *para*-Sulfonatocalix[*n*]arenes interact with a wide range of organic molecules, including ammonium cations[5] and neutral molecules.[6] We have previously observed solid-state inclusion of the arginine[7] and lysine[8] and the group of Raston has reported solid-state complexes with a number of other amino acids.[9,10] Geometry, size and charge of guest molecules prove, thus, to be extremely important in the recognition process. It has already been demonstrated that *para*-sulfonatocalix[*n*]arenes present anticoagulant properties showing behaviour similar to the glycosylaminoglycan chondroitin sulfate.[11] Strong complexation between the *para*-sulfonatocalix[*n*]arenes and Bovine Serum Albumin has been also demonstrated.[12] The title calix[6]arene derivative has an inhibitory effect on the lysyl-oxidase enzyme.[13] However it compound shows hepatotoxicity at doses above 13 mg kg^{-1} *in vivo*,[14] so some caution is required for the direct use by injection, however the major biomedical applications of the *para*-sulfonatocalix[*n*]arenes to date are in the *ex vivo* diagnostic of the prion protein, where such toxicity is not a factor.[4]

More than 75 solid state complexes of *para*-sulfonatocalix[4]-arene have been reported in the Cambridge Structural Database. The general topology observed in these systems is of: bilayers,[8] spheres and capsules.[15] As for the *para*-sulfonatocalix[6]arene, the solid state complexes determined until now are less numerous. The main part of these structures concerns complexation of *para*-sulfonatocalix[6]arene with transition metals (Ni, Co) or lanthanides (La, Eu). In these structures, *para*-sulfonatocalix[6]arene presents three different conformations: cone,[16] double cone[17] and chair.[18] The complexation of L-leucine by *para*-sulfonatocalix[6]arene was reported by Atwood and Raston.[19] The calixarene in the double cone conformation has multi-guest capability binding either L- or D-leucine in a single crystal in a bilayer type arrangement from a racemic mixture. The self assembly of this calixarene does not describe specific motifs, as is the case of *para*-sulfonatocalix[4]arene, which generally organizes in bilayers.[8] However, monolayers of *para*-sulfonatocalix[6]arene are observed in the complex with water,[17] bilayers in the complex with L-leucine[19] and "Ferris wheel" geometry is shown in the complex with 18-crown-6 and europium cations.[16]

In this paper, we present two solid state assemblies of *para*-sulfonatocalix[6]arene. The first assembly is formed by the complex with dimethylformamide and dimethylammonium cations, and the second involves the complex between one *para*-sulfonatocalix[6]arene and two bis-6-aminohexylammonium cations, solvated by five disordered molecules of water.

Experimental section

Synthesis and crystal growth

The crystallization of the complex **A** between *para*-sulfonatocalix-[6]arene, dimethylammonium cations and dimethylformamide (DMF), was achieved using the slow evaporation method. Thus a solution of 0.01 M of *para*-sulfonatocalix[6]arene was prepared in DMF.‡ This solution was allowed to evaporate at room temperature. Crystals were obtained several days later.

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‡ Two possibilities exist for the presence of dimethylammonium cations in the crystals: either trace amounts were present in the solvent or *para*-sulfonatocalix[6]arene degrades DMF to yield dimethylamine.

For the complex **B** between *para*-sulfonatocalix[6]arene and bis-6-aminohexylammonium cations, a solution of 0.01 M of *para*-sulfonatocalix[6]arene in methanol was layered slowly onto an aqueous solution of bis-6-aminohexylamine in water at equal molar concentrations, in order to obtain an interface between the two solutions. Crystals were obtained by liquid diffusion at room temperature after several days.

X-Ray crystallography

Crystal data were collected on a Nonius KappaCCD diffractometer. Data were corrected for Lorentz and polarisation effects but not for absorption. The two structures were solved using direct methods and Fourier techniques (SHELXS86[20]) and were refined by full matrix least squares on F^2 ($I > 2\sigma(I)$) using the program SHELXL97.[21]

H-Atoms were included in geometric positions and refined as 'riding' atoms with isotropic thermal parameters based upon the corresponding bonding carbon atom [$U_{iso} = 1.2U_{eq}$, $U_{iso} = 1.5U_{eq}$ for CH_3 and OH hydrogen atoms].

For complex **B** the refinement was unstable due to the high temperature factors of guest bis-6-aminohexylammonium molecules most probably caused by disorder and the presence of disordered water molecules. The above was, also a direct reflection of the number of observations as well as of the data resolution. Consequently, restraints on the bond lengths of the guest molecules were applied to keep a reasonable geometry for the bis-6-aminohexylammonium cations.

Table 1 X-Ray crystallographic and experimental data for the complex of *para*-sulfonatocalix[6]arene with dimethylammonium and bis-6-aminohexylammonium cations

Complex of **1** with	**A**	**B**
Chemical formula	$C_{42}H_{30}O_{24}S_6\cdot 6C_2H_8N\cdot 2C_3H_7NO$	$C_{42}H_{30}O_{24}S_6\cdot 2C_{12}H_{32}N_3\cdot 10H_2O$
Formula mass/g mol^{-1}	1533.78	1707.84
Space group	*P*1	*P*1
a/Å	12.2408(5)	11.8372(4)
b/Å	12.4420(5)	12.2645(4)
c/Å	12.8054(5)	15.1670(6)
α/°	87.975(2)	106.721(2)
β/°	70.696(2)	111.948(2)
γ/°	75.688(2)	91.773(2)
Z	1	1
V/Å^3	1781.2(1)	1932.7(1)
ρ_{calc}/g cm^{-3}	1.430	1. 467
Data collection		
Diffractometer detector	CCD	CCD
Type of radiation	MoKα	MoKα
Radiation λ/Å	0.71073	0.71073
T/K	100(2)	100(2)
θ range/°	3.04–21.26	2.99–21.97
Crystal colour	Colourless	Colourless
Crystal size/mm	0.40 × 0.25 × 0.05	0.30 × 0.20 × 0.05
No. different reflections	22 771	21 525
R_{int}	0.033	0.034
No. of independent reflections	3941	4656
No. of reflections with $F_o > 4\sigma(F_o)$	3439	3797
No of parameters (restraints)	466(0)	502(16)
R factor all	0.079	0.155
R factor gt.	0.065	0.135
Goodness of fit on F^2	1.15	1.85

Crystal and refinement data are summarized in Table 1.

Results and discussion

Solid state structure of the two complexes are described as follows; the chemical formula of *para*-sulfonatocalix[6]arene (**1**) is given in Fig. 1.

The first complex (**A**) formed between **1** and dimethylammonium cation with dimethylformamide (DMF) as solvent involves one anion of **1** associated with two molecules of DMF and six dimethylammonium cations. The second solid-state system (**B**) involves one anion of *para*-sulfonatocalix[6]arene with two bis-6-aminohexylammonium cations and ten water molecules. Four water molecules are disordered over eight sites and solvate the whole assembly providing a strong effect on the self-organization of the system as will be discussed later.

With regard to the molecular geometry, **1** adopts a chair conformation, in both complexes (Fig. 2). This conformation represents a particular case of the usual 1,2,3-alternate conformation. The specificity of this conformation is due to the arrangement of two opposite aromatic rings of **1** which describe planes parallel to *ac* and *ab*, respectively for the complexes **A** and **B**. Small differences are noted related to the geometry of calixarene molecules in this conformation; angles of 94.0 and 92.0° in complex **A**, and 94.6 and 100.9° in complex **B**, are measured between these planes and the adjacent rings (Fig. 2a and b). The conformational variation is closely related to the intermolecular interactions formed by the sulfonate moieties with the local environment that induce different orientations of the aromatic rings. This explains the specificity of the intramolecular interactions formed by **1** in the two complexes. As shown in Fig. 2c and d, intramolecular hydrogen bonds are formed between phenolic groups of the calixarene. Two pairs of hydrogen bonds are formed in the complex **A**, between the phenolic moieties of the two pairs of aromatic rings, which project along and above the crystallographic plan *ac* (2.641(5) Å). For complex **B**, besides the analogous hydrogen bonds (of 2.612(7) Å), the formation of two additional hydrogen bonds between the phenolic moieties of the two aromatic rings parallel to *ab* and the adjacent phenolic groups is observed presenting values of 2.762(8) (as illustrated in Fig. 2d). Formation of these additional hydrogen

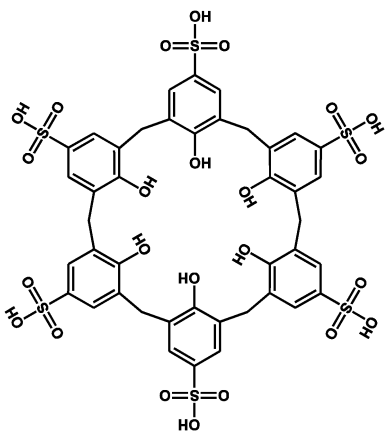

Fig. 1 Chemical formula for *para*-sulfonatocalix[6]arene (**1**).

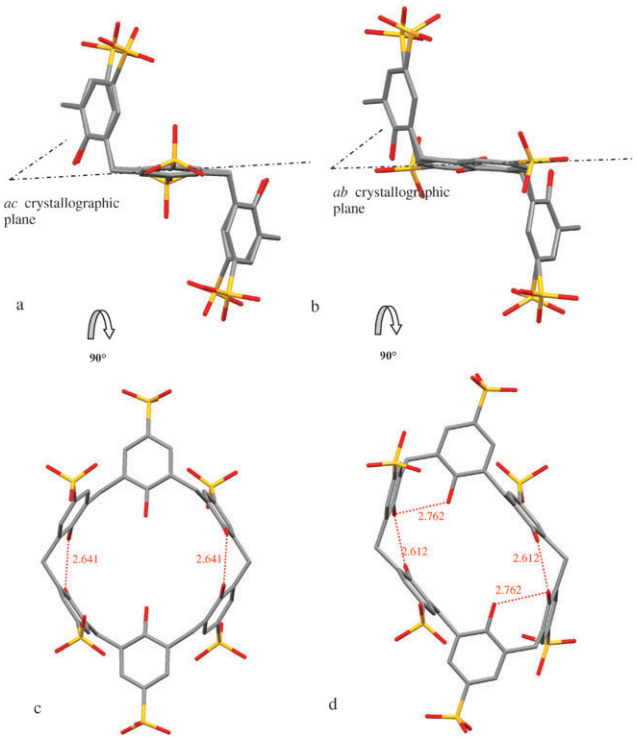

Fig. 2 a,b—View of the chair conformation adopted by the molecule of **1** in the complexes **A** and **B**, respectively; c,d—top view of the molecule of **1** with the representation of the intramolecular hydrogen bonds developed by the phenolic moieties.

bonds is due to the reorientation of the aromatic rings of **1** parallel to the crystallographic plane and thus is responsible for the variation of the geometry of the calixarene molecule in the two complexes.

The topology that characterizes the two solid state systems is represented by stepped layers of *para*-sulfonatocalix[6]arene (Fig. 3).

In complex **A** the centrosymmetric chair conformation of the **1** provides two identical binding sites for DMF guests leading to 1 : 2 host–guest inclusion stoichiometry. The sulfonate groups play an important role in the organisation of the structure. In complex **A**, these groups develop a large network of hydrogen bonds with the other elements of the system, except for the solvating molecules. Short contacts between neighbouring calixarenes exist *via* two homologous pairs of hydrogen bonds. One of the pairs of hydrogen bonds is formed between the phenolic group of one calixarene that is a hydrogen donor and the sulfonate group of the neighbouring calixarene. The phenolic group of this latter molecule is reciprocally the hydrogen bond donor to the sulfonate moiety of the first one (these hydrogen bonds are shown in red in Fig. 4). All other hydrogen bonds formed by the sulfonate moieties involve the dimethylammonium cations. Twelve dimethylammonium cations participate in hydrogen bond formation with the acidic functions of the molecule of **1** (shown in blue in Fig. 4).

Beside this dense network of intermolecular hydrogen bonds generated by the sulfonate moieties, the phenolic groups of the two aromatic rings of **1** parallel to *ac* crystallographic plane

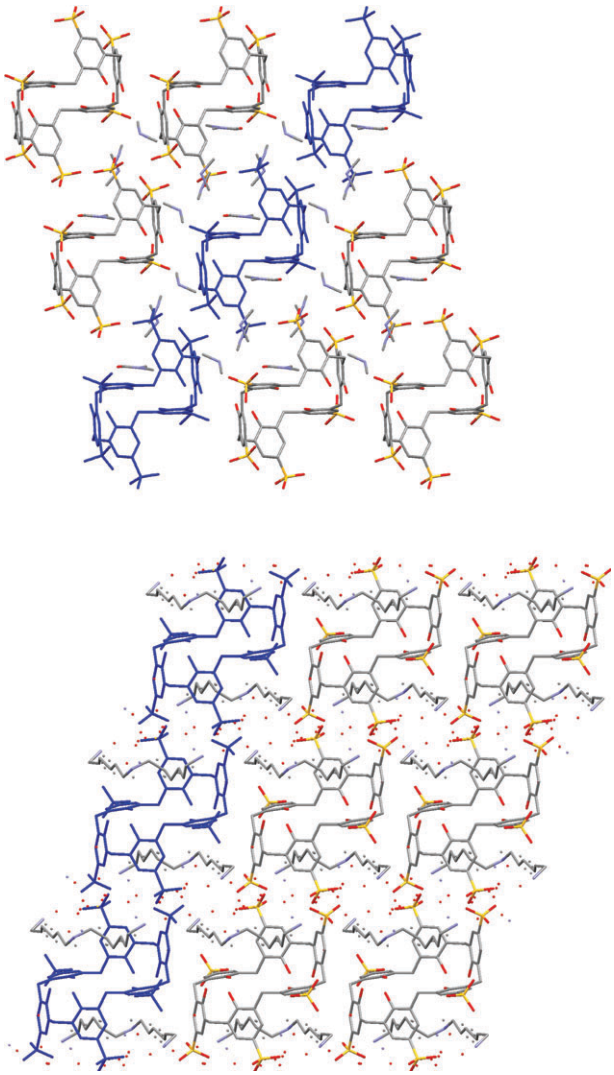

Fig. 3 Packing of the complex **A** (top) and **B** (bottom) along *c* and *a* crystallographic axis, respectively, with the representation, in blue of the stepped layers of calixarene molecules.

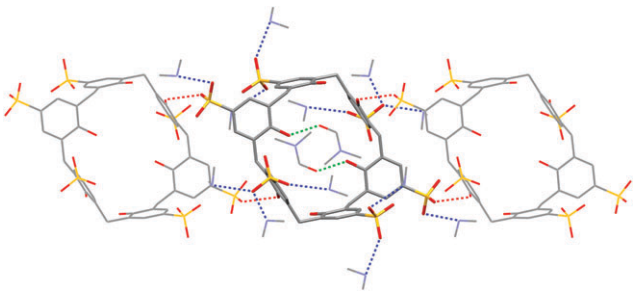

Fig. 4 Representation of hydrogen bonds formed by the polar groups of one calixarene with the environment in complex **A**; hydrogen bonds between two calixarenes are colored in red, hydrogen bonds formed by **1** with dimethylammonium in blue and with DMF in green.

are hydrogen bond donors to the oxygen atoms of two molecules of DMF (in green in Fig. 4).

In addition to the hydrogen bonds in which the calixarene molecule is involved, a hydrogen bond exists also between the

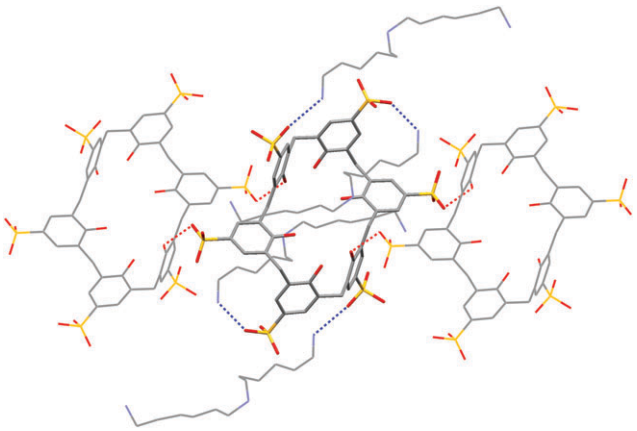

Fig. 5 Representation of hydrogen bonds formed by the polar groups of one calixarene with the environment in complex **B** (possible hydrogen bonds with water molecules omitted for clarity); hydrogen bonds between two calixarenes are colored in red, hydrogen bonds formed by **1** with bis-6-aminohexylammonium cations in blue.

Table 2 Hydrogen bonds for **A** (Å and °)[a]

D–H···A	*d*(D–H)	*d*(H···A)	*d*(D···A)	∠(DHA)
O(1B)–H(1B)···O(1C)	0.84	1.80	2.641(5)	176.1
O(1C)–H(1C)···O(4A)[b]	0.84	1.75	2.592(5)	174.8
N(1Y)–H(1Y4)···O(1S)[c]	0.92	2.13	2.961(7)	150.3
N(1Y)–H(1Y4)···O(2C)	0.92	2.34	2.806(6)	111.0
N(1Y)–H(1Y5)···O(3B)[d]	0.92	1.93	2.834(6)	167.6
N(1X)–H(1X1)···O(4B)	0.92	2.00	2.916(6)	172.6
N(1X)–H(1X1)···O(2B)	0.92	2.49	3.083(6)	122.6
N(1X)–H(1X2)···O(3C)[e]	0.92	2.00	2.773(7)	140.3
N(1Z)–H(1Z4)···O(3A)[f]	0.92	1.93	2.846(8)	174.3
N(1Z)–H(1Z5)···O(3C)	0.92	2.07	2.861(7)	143.4
N(1Z)–H(1Z5)···O(2C)	0.92	2.32	3.149(8)	150.3

[a] $-x, -y + 2, -z + 1$. [b] $x, y, z - 1$. [c] $-x, -y + 1, -z + 1$. [d] $-x + 1, -y + 1, -z + 1$. [e] $x, y, z + 1$. [f] $x, y - 1, z - 1$.

Table 3 Hydrogen bonds for **B** (Å and °)

D–H···A	*d*(D–H)	*d*(H···A)	*d*(D···A)	∠(DHA)
O(1C)–H(1C)···O(1A)[a]	0.84	1.90	2.612(7)	142.0
O(1B)–H(1B)···O(1C)	0.84	1.94	2.762(8)	167.8
O(1A)–H(1A)···O(2B)[b]	0.84	1.78	2.567(8)	155.2
N(1X)–H(1X1)···O(1W)[c]	0.91	2.09	2.84(2)	138.4
N(1X)–H(1X1)···O(2C)[d]	0.91	2.26	3.14(3)	161.8
N(1X)–H(1X2)···O(3A)[e]	0.91	2.02	2.88(2)	155.3
N(1X)–H(1X3)···O(5W)[f]	0.91	1.88	2.78(2)	168.6
N(2X)–H(2X3)···O(2B)[g]	0.92	2.27	3.14(2)	158.5
N(2X)–H(2X4)···O(3W)	0.92	1.78	2.69(3)	170.5
N(3X)–H(3X5)···O(3B)[h]	0.92	2.90	3.3 (1)	110.0
N(3X)–H(3X4)···O(4W1)	0.92	2.43	2.9(1)	108.6
N(3X)–H(3X3)···O(4C)[i]	0.92	2.19	3.0(1)	146.1
N(1)–H(1E)···O(3A1)[e]	0.91	1.76	2.65(3)	163.8
N(1)–H(1F)···O(1W)[c]	0.91	1.62	2.29(3)	127.4
N(1)–H(1F)···O(2C1)[d]	0.91	2.46	3.01(3)	118.9
N(2)–H(2F)···O(3W1)	0.92	1.79	2.71(5)	178.6
N(2)–H(2G)···O(4W)[h]	0.92	1.82	2.59(4)	139.9
N(3)–H(3C)···O(2W)[g]	0.94	2.17	2.95(6)	139.8
N(3)–H(3D)···O(3B)[i]	0.94	2.36	3.15(6)	141.6
N(3)–H(3E)···O(4W)	0.94	1.54	2.31(5)	136.6

[a] $-x - 1, -y + 1, -z + 1$. [b] $-x, -y + 1, -z + 1$. [c] $x, y - 1, z$. [d] $x, y - 1, z - 1$. [e] $x + 1, y - 1, z$. [f] $-x + 1, -y, -z$. [g] $-x, -y, -z$. [h] $-x - 1, -y, -z$. [i] $x - 1, y, z - 1$.

oxygen atom of the DMF and the protonated nitrogen of one of the dimethylammonium cations.

In complex **B** each partial cone of C6S acts as a host for bis-6-aminohexylammonium cation leading to 1 : 2 host–guest inclusion stoichiometry. The ammonium groups of the guest are situated near the anionic sulfonate groups of the C6S. Similarly, neighbouring *para*-sulfonatocalix[6]arenes are linked to each other *via* an alternating hydrogen bond formed between a phenolic moiety and a sulfonate group (colored in red in Fig. 5). The four remaining sulfonate groups form short contacts with bis-6-aminohexylammonium cations (values of 2.88 and 3.05 Å, shown in blue in Fig. 5) and also participate in possible hydrogen bonds with disordered water molecules.

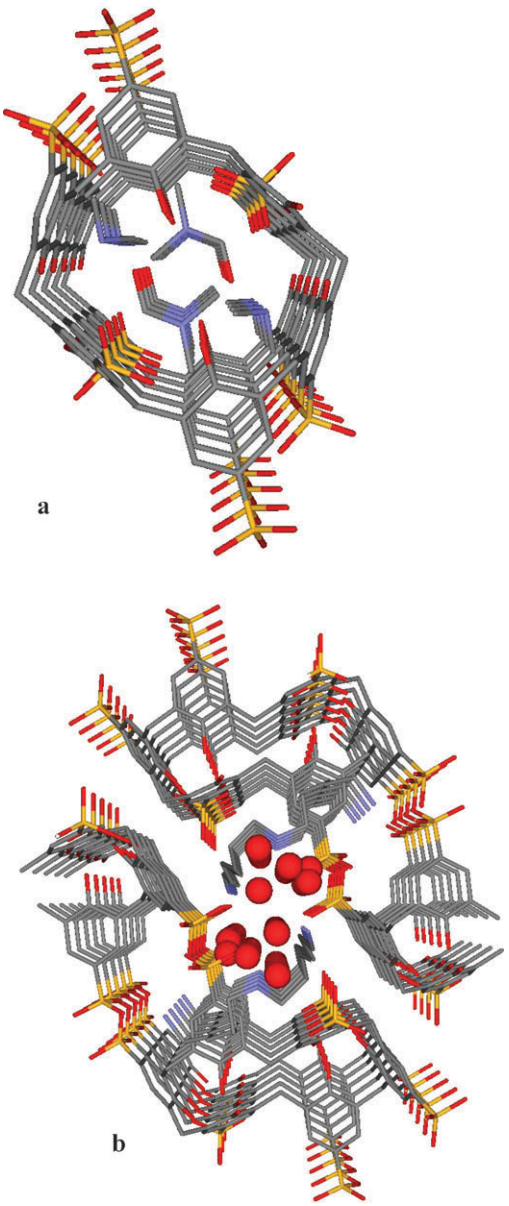

Fig. 6 Channels formed in the two complexes; a—solvated nanotube in the complex **A**, containing two molecules of DMF and two molecules of dimethylamonium; b—hydrated nanochannel in the complex **B**, containing disordered water molecules; here, for reasons of clarity, two molecules of calixarenes are not represented entirely.

All protonated nitrogen atoms also forms hydrogen bonds with water molecules.

Detailed geometry of hydrogen bonds in complexes **A** and **B** described above is given in Tables 2 and 3.

Formation of solvated channels is observed in both complexes. Thus in the complex **A**, one calixarene molecule constitutes the inner wall of a nanotube along the *b* axis, of approximate internal dimensions 5 × 5 Å, that contains two molecules of DMF and two dimethylamonium cations (Fig. 6a). The generated network of nanotubes is very dense and describes a rhombohedral-like packing. In the complex **B** the nanochannel formed along the *a* axis contains six disordered water molecules (Fig. 6b). This channel is formed by four calixarene molecules and two bis-6-aminohexylammonium cations, showing internal dimensions of approximately 5 × 6 Å. The presence of this water nanochannel explains the double position of the water molecules.

Conclusion

The two solid-state structures of *para*-sulfonatocalix[6]arene with dimethylammonium and bis-6-aminohexylammonium show certain similarities, including the chair conformation of the calixarene molecules, the self organization of the calixarenes in a stepped layer, the fact that the unity of the complexes is assured mainly by hydrogen bonds and the formation of channels including either DMF molecules or water molecules.

References

1 C. D. Gutsche, *Calixarenes Revisited*, Royal Society of Chemistry, Cambridge, 1998, p. 233.
2 L. Mutihac, H.-J. Buschmann, R.-C. Mutihac and E. Schollmeyer, *J. Inclusion Phenom. Macrocyclic Chem.*, 2005, **52**, 135.
3 M. Nishida, I. D. Masashi, I. Yoshida and S. Shinkai, *Bull. Chem. Soc. Jpn.*, 1997, **70**, 2131.
4 X. Florent Perret, Adian N. Lazar and Anthony W. Coleman, *Chem. Commun.*, 2006, 2425.
5 E. Da Silva, F. Nouar, M. Nierlich, B. Rather, M. J. Zaworotko, C. Barbey, A. Navaza and A. W. Coleman, *Cryst. Eng.*, 2003, **6**, 123.
6 G. Arena, A. Contino, F. G. Gulino, A. Magri, D. Sciotto and R. Ungaro, *Tetrahedron Lett.*, 2000, **41**, 9327.
7 A. N. Lazar, E. Da Silva, A. Navaza, C. Barbey and A. W. Coleman, *Chem. Commun.*, 2004, 2162.
8 M. Selkti, A. W. Coleman, I. Nicolis, N. Douteau-Guevel, F. Villain, A. Tomas and C. Rango, *Chem. Commun.*, 2000, 161.
9 J. L. Atwood, T. Ness, P. J. Nichols and C. L. Raston, *Cryst. Growth Des.*, 2002, **2**, 171.
10 P. J. Nichols and C. L. Raston, *Dalton Trans.*, 2003, **14**, 2923.
11 E. Da Silva, D. Ficheux and A. W. Coleman, *J. Inclusion Phenom. Macrocyclic Chem.*, 2005, **52**, 201.
12 L. Memmi, A. N. Lazar, A. Brioude, V. Ball and A. W. Coleman, *Chem. Commun.*, 2001, 2474.
13 D. Hulmes, A. W. Coleman and E. Aubert-Foucher, E99-FR1922 2000007585, 19990803, 2000.
14 M. Archimbaud, M. H. Henge-Napoli, D. Lilienbaum, M. Desloges and C. Montagne, *Radiat. Prot. Dosim.*, 1994, **53**, 327.
15 A. Drljaca, M. J. Hardie, C. L. Raston and L. Spiccia, *Chem.–Eur. J.*, 1999, **5**, 2295.
16 S. J. Dalgarno, M. J. Hardie, M. Makha and C. L. Raston, *Chem.–Eur. J.*, 2003, **9**, 2834.
17 J. L. Atwood, D. L. Clark, R. K. Juneja, G. W. Orr, K. D. Robinson and R. L. Vincent, *J. Am. Chem. Soc.*, 1992, **114**, 7558.
18 Z. Asfari, J. Harrowfield, P. Thuery and J. Vicens, *Supramol. Chem.*, 2003, **15**, 69.
19 J. L. Atwood, S. J. Dalgarno, M. J. Hardie and C. L. Raston, *Chem. Commun.*, 2005, 337.
20 G. M. Sheldrick, *SHELXS-86, Program for solution of crystal structures*, University of Goettingen, Germany, 1986.
21 G. M. Sheldrick, *SHELXl-97, Program for refinement of crystal structures*, University of Goettingen, Germany, 1997.

