Hydrogen-bonded dimers of a thiacalixarene substituted by carbamoylmethylphosphineoxide groups at the wide rim†

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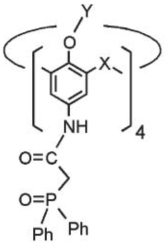
A thiacalix[4]arene derivative bearing four carbamoylmethylphosphineoxide groups at the wide rim forms hydrogen-bonded, dimeric capsules with S_8 symmetry in the crystalline state and in apolar solvents, where the inclusion of cationic guests could be proved by ^{1}H NMR and ESI mass spectra.

Calix[4]arene derivatives **1**, bearing four carbamoylmethylphosphineoxide (CMPO) functions at their wide rim, are excellent extractants for actinides and lanthanides.[1] They show not only high efficiency under acidic conditions, but also remarkable selectivities within the series of lanthanides and Americium over Europium.[2] The extraction is even better (the distribution coefficient *D* is higher by a factor of about 10) for analogous derivatives of a calix[4]arene rigidified by two short ether bridges at the narrow rim.[3] Although the extracted species are not exactly known, this result suggests that the extraction properties are strongly determined by the mutual arrangement of the four ligating CMPO functions.

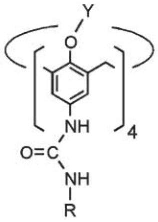
Thiacalix[4]arenes, in which the four methylene bridges of "usual" calix[4]arenes are replaced by sulfur,[4] have a slightly different size and shape.[5] Therefore analogous CMPO derivatives might have (eventually significantly) different complexation and extraction properties. With this intention, we tried to synthesize thiacalix[4]arene derivatives bearing four CMPO groups at the wide rim. Thus, we obtained compound **2**, which is not only the first tetra-CMPO derivative of a thiacalix[4]arene but also the first of a calix[4]arene with free hydroxyl groups (Y = H instead of alkyl).

The structure of **2** was initially confirmed by ^{1}H NMR and mass spectrometry ($[M + Na]^+$ = 1547.3, 100%).‡ In DMSO-d_6, singlets for OH (δ 12.45), NH (δ 9.98) and Ar–H (δ 7.59) (ratio 1 : 1 : 2), a doublet for CH_2 (δ 3.68, ^2J = 14.0 Hz, coupling with the phosphorous) and a set of signals typical for the phenyl residues are in agreement with the expected C_{4v} symmetry (Fig. 1a). However, the ^{1}H NMR spectra in aprotic, apolar solvents such as $CDCl_3$, CD_2Cl_2, tetrachloroethane-d_2, toluene-d_8 or *para*-xylene-d_{10} are different (see Fig. 1b). Two *meta*-coupled signals/doublets are found for the aromatic protons of the calixarene part (δ 7.44/8.38, ^2J = 2.7 Hz), and the two protons of the C(O)–CH_2–P(O) groups are now diastereotopic, appearing as two pairs of doublets. Such a pattern, which is in agreement with C_4 symmetry, is reminiscent of hydrogen-bonded dimers formed by tetraurea derivatives **3** of calix[4]arenes. However, it could also be explained by *intramolecular* hydrogen bonding between the NH and O=P groups of adjacent CMPO functions in the special case, where a connection Ar–NH–C(O)–CH_2–P=O···H–N–Ar (eight bonds including the hydrogen bond) between the *para*-positions of the phenolic units of the calixarene seems at least possible.

Single crystals of **2** were obtained by slow evaporation of a dioxane solution, and their structure could be solved by X-ray



1 X = CH_2
2 X = S, Y = H



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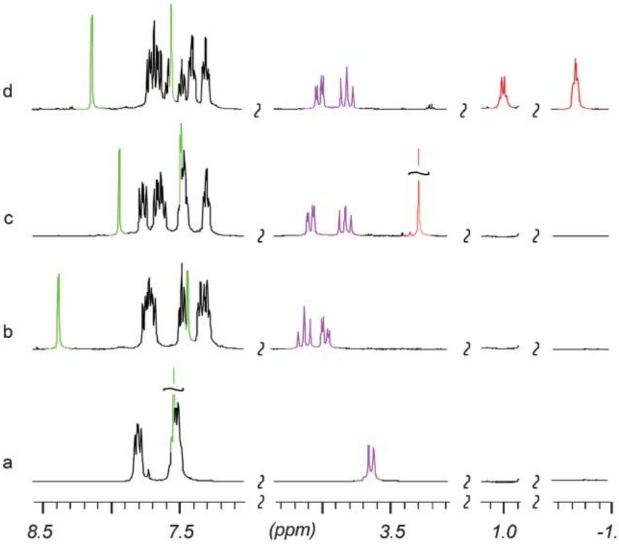

Fig. 1 Representative sections of the ^{1}H NMR spectra (400 MHz) of **2** (a) in DMSO-d_6, (b) in CD_2Cl_2, (c) in CD_2Cl_2 in the presence of cobaltocenium hexafluorophosphate and (d) in CD_2Cl_2 in the presence of tetraethylammonium hexafluorophosphate. Aromatic protons of the calixarene (green), protons of C(O)–CH_2–P(O) groups (purple) and of the included guest (red) are highlighted.

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† Electronic supplementary information (ESI) available: Selected NMR and mass spectra of **2** and its dimers. See DOI: 10.1039/b601016d

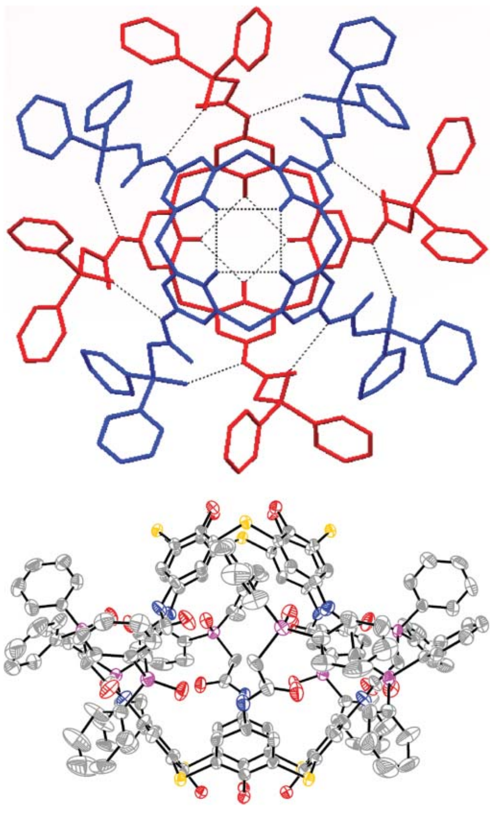

Fig. 2 Dimeric capsule **2·2**, seen along the four-fold axis (hydrogen bonds are indicated by dashed lines) and perpendicular to it (thermal ellipsoids at 30% probability).

diffraction.§ As shown in Fig. 2, two molecules of slightly different shape which lie about a common four-fold axis are arranged as a dimer. They are connected *via* their wide rims by *intermolecular* –N–H···O=P– hydrogen bonds (N···O distance 2.72/2.79 Å).[6] The packing of these dimers is illustrated in Fig. 3.

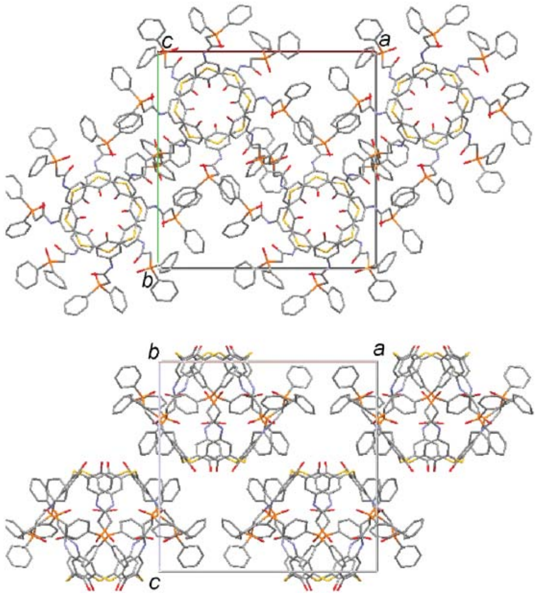

Fig. 3 Packing of the hydrogen-bonded dimers seen along the (top) c-axis and (bottom) b-axis.

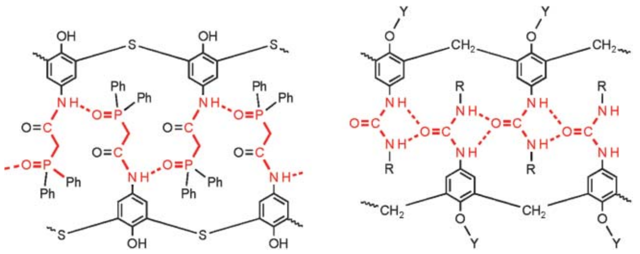

Fig. 4 Comparison of the hydrogen-bonded belts connecting dimeric capsules of tetra-CMPOs **2** and tetraureas **3**.

The arrangement found in the crystalline state strongly resembles the hydrogen-bonded dimeric capsules formed by tetraurea calix[4]arenes.[7] Fig. 4 gives a schematic comparison of the pattern of the hydrogen bonds.

In Table 1, we compare typical geometric parameters with those of the first X-ray structure of a tetraurea dimer **3** (Y = $CH_2C(O)OC_2H_5$, R = *p*-$C_6H_4CH_3$).[8] The distance between the reference planes defined by the sulfur atoms and the methylene carbon atoms, respectively, is larger for **2**, and also the diagonal distance between the nitrogen atoms (attached to the calixarene in **3**) and the P=O and C=O oxygen atoms. Consequently, the estimated volume of the internal cavity is about 370 Å^3, which is nearly twice the internal volume of **3·3** (~200 Å^3). Although such a volume surely cannot be empty, no definite indication of guest inclusion was found in the crystalline state.

Such dimers may not necessarily exist in solution. However, if tetraethylammonium cations (in the form of their hexafluorophosphate salt) are added to a solution of **2** in CD_2Cl_2, $CDCl_3$ or tetrachloroethane-d_2, a triplet at δ −1.22 (CD_2Cl_2, rt) appears in the ^1H NMR spectrum (Fig. 1d).‡ Integration reveals a ratio of $[Et_4N]^+$: **2** = 1 : 2, and this is clear evidence for the inclusion of the cation in a dimeric capsule.[9] As for the dimers of **3**, the inclusion of cobaltocenium cations[10] could be shown analogously (Fig. 1c). Surprisingly, even triethylammonium cations are included, although $[Et_3NH]^+$, as a Brønsted acid, could compete with the dimerisation by protonation of the P=O groups. In CD_2Cl_2 or $CDCl_3$, a second set of signals for **2** and a triplet at δ −1.36 upon addition of $[Et_3NH]^+Cl^-$ can be explained by the additional formation of capsules with $[Et_3NH]^+$ as guest, which is further confirmed by ESI-MS ($[2M + Et_3NH]^+$ = 3153.8). No spectral change is observed in tetrachloroethane-d_2, toluene-d_8 and *para*-xylene-d_{10}. $[Et_3NH]^+$ probably cannot compete with the excess of these solvents, which are better guests than $CDCl_3$ or CD_2Cl_2.

It is therefore very likely that **2** forms hydrogen-bonded dimers in all the aprotic, apolar solvents mentioned above. Most probably, such dimers, with overall S_8 symmetry (composed of two C_4-symmetric molecules of opposite chirality), will contain at least one solvent molecule as a guest.

While the formation of dimeric capsules and the inclusion of cationic guests is well established by these experiments, it remains an open question whether this unexpected dimerisation is due to the special geometric properties of thiacalix[4]arenes compared to calix[4]arenes or to the presence of free hydroxyl groups in **2**, which might stabilize the favorable cone conformation. Further studies will also be devoted to characterizing the kinetic and thermodynamic stability of these capsules, and to explore the range of their potential guests.

Table 1 Comparison of cavity shape and size of dimers **2·2** and **3·3** in the crystalline state

	2·2	**3·3**
Distance of main planes defined by bridges X	11.26 Å	9.78 Å
Inclination of aromatic units towards the main plane	123.3/129.1°	115.9/117.6°
Rotation around the common four-fold axis	44.5°	42.9°
Distance between adjacent X[a]	5.53/5.53 Å	5.10/5.11 Å
Diagonal distance between X[a]	7.82/7.82 Å	7.21/7.22 Å
Diagonal O–O distance P=O/C=O[a]	13.69/12.16 Å 11.70/12.46Å	— 11.64/11.21 Å
Diagonal N–N-distance[a]	10.09/10.81 Å	9.30/9.48 Å

[a] Due to the four-fold axis, all of these atoms are situated at the corners of regular squares.

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Notes and references

‡ *Synthesis of* **2**: Triethylamine (6.6 ml) was added to a suspension of tetraaminothiacalix[4]arene[11] (1.00 g, 1.43 mmol) and *para*-nitrophenyl(diphenylphosporyl)acetate[1,3] (2.17 g, 5.70 mmol) in dry chloroform (30 ml) under a nitrogen atmosphere and the reaction mixture was stirred for 26 h at rt. Methanol (100 ml) was added and the crystalline residue was filtered and washed with methanol (3 × 5 ml). The residue was then dissolved in toluene (200 ml), the ammonium salt removed by filtration and the solvent evaporated. The residue thus obtained was dried for 1 h under vacuum (10 mmHg) at 100 °C to yield compound **2** (0.65 g, 59%) as a colorless powder. Mp > 250 °C decomp. ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 3.68$ (d, 8 H, $J = 14.0$ Hz, CH_2–P), 7.53 (m, 24 H, Ar–H), 7.59 (s, 8 H, Ar–H), 7.82 (m, 16 H, Ar–H), 9.98 (s, 4 H, NH) and 12.45 (s, 4 H, OH); ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 39.32$ (d, $J = 63.4$ Hz, CH_2–P), 120.95 (s), 127.64 (s), 128.44 (d, $J = 12.1$ Hz), 130.12 (s), 130.59 (d, $J = 9.6$ Hz), 131.75 (s), 133.46 (d, $J = 101.2$ Hz), 155.85 (s) and 162.91 (s); ^{31}P NMR (162 MHz, DMSO-d_6): $\delta = 27.06$. MS (ESI): *m*/*z* (%) = 1547.3 (100), $[M + Na]^+$.

NMR spectra of dimeric capsules: ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = 3.97$ (dd, 8 H, $^2J_{P\text{–}H} = 5.2$ Hz, $^2J_{H\text{–}H} = 17.6$ Hz, HCH–P), 4.13 (dd, 8 H, $^2J_{P\text{–}H} = 17.6$ Hz, $^2J_{H\text{–}H} = 17.6$ Hz, HCH–P), 7.32 (m, 32 H, Ar–H), 7.44 (d, 8 H, $J = 2.7$ Hz, Ar–H), 7.48 (m, 16 H, Ar–H), 7.72 (m, 32 H, Ar–H), 8.38 (d, 8 H, $J = 2.7$ Hz, Ar–H), 9.39 (s, 8 H, OH) and 11.15 (s, 8 H, NH). ^{31}P NMR (162 MHz, CD_2Cl_2): $\delta = 30.2$.

Complex with $[Et_4N]^+[PF_6]^-$: ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = -1.22$ (t, 12 H, $J = 6.9$ Hz, N–CH_2–CH_3), 1.01 (q, 8 H, $J = 6.9$ Hz, N–CH_2–CH_3), 3.83 (dd, 8 H, $^2J_{P\text{–}H} = 17.0$ Hz, $^2J_{H\text{–}H} = 17.0$ Hz, CH_2–P), 4.03 (dd, 8 H, $^2J_{P\text{–}H} = 4.7$ Hz, $^2J_{H\text{–}H} = 17.0$ Hz, CH_2–P), 7.32 (m, 16 H, Ar–H), 7.42 (m, 16 H, Ar–H), 7.49 (m, 8 H, Ar–H), 7.58 (m, 16 H, Ar–H), 7.70 (m, 32 H, Ar–H), 8.15 (d, 8 H, $J = 2.4$ Hz, Ar–H), 9.29 (s, 8 H, OH) and 11.40 (s, 8 H, NH). ^{31}P NMR (162 MHz, CD_2Cl_2): δ 30.6. MS (ESI): *m*/*z* (%) = 3180.8 (100), $[2M + Et_4N]^+$.

Complex with $[Co(C_5H_5)_2]^+[PF_6]^-$: ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = 3.31$ (s, 10 H, included $[Co(C_5H_5)_2]^+$), 3.84 (dd, 8 H, $^2J_{P\text{–}H} = 18.5$ Hz, $^2J_{H\text{–}H} = 16.6$ Hz, CH_2–P), 4.09 (dd, 8 H, $^2J_{P\text{–}H} = 4.0$ Hz, $^2J_{H\text{–}H} = 16.6$ Hz, CH_2–P), 5.72 (s, free $[Co(C_5H_5)_2]^+[PF_6]^-$), 7.31 (m, 16 H, Ar–H), 7.49 (m, 32 H, Ar–H), 7.66 (m, 24 H, Ar–H), 7.78 (m, 16 H, Ar–H), 7.95 (d, 8 H, $J = 2.4$ Hz, Ar–H), 9.42 (s, 8 H, OH) and 11.40 (s, 8 H, NH). MS (ESI): *m*/*z* (%) = 3239.7 (100), $[2M + Co(C_5H_5)_2]^+$.

§ Crystal data for **2**: $C_{80}H_{64}N_4O_{12}P_4S_4 \cdot 5C_4H_8O_2 \cdot H_2O$, $M = 1984.01$, tetragonal, space group *P*4/*n*, $a = 22.1760(13)$, $c = 21.437(2)$ Å, $V = 10542.2(13)$ Å^3, $T = 173$ K, $Z = 4$, $D_c = 1.250$ g cm^{-3}, λ(Mo-K$_\alpha$) = 0.71073 Å, 68686 reflections measured, 9150 unique ($R_{int} = 0.149$) which were used in all calculations. The structure was solved by direct methods (SHELXS-97) and refined by full-matrix least-squares methods on F^2 with 610 parameters. $R_1 = 0.0991$ ($I > 2\sigma(I)$) and $wR_2 = 0.2268$, GOF = 0.930; max/min residual density 0.852/−0.360 e Å^{-3}. Due to the four-fold axis, the asymmetric unit contains two one-quarter molecules. The H atoms of the water molecules could not be found in a difference map and were therefore not included in the refinement. For one of the dioxane molecules, similarity restraints were used to keep its geometric parameters within a reasonable range. CCDC 294263. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b601016d

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