A molecular turnstile in *para*-octanoyl calix[4]arene nanocapsules†

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The thermal treatment of different inclusion complexes of *para*-octanoyl calix[4]arene leads to the formation of a guest-free van der Waals nanocapsular structure possessing a remarkable stability caused by the high mobility of alkanoyl arms.

Most inclusion compounds of the clathrate type have metastable host frameworks that are stabilized by the presence of included guest species, classically referred to as the β form.[1] When guest molecules are removed, the host lattice is usually destroyed, transforming to a dense α form. Single crystals of organic materials, where the transformation between domains is driven by the gain or loss of some of the guest material, are not very common.[2–4] A typical example of a calixarene with extensively studied structure of inclusion complexes is *p-tert*-butylcalix[4]arene (tBC).[3,5–7] In comparison with tBC, amphiphilic calixarenes obtained by Friedel–Crafts acylation of the parent calix[4]arene[8,9] can provide a larger size cavity and therefore they are able to entrap significantly larger molecules. In a number of preceding papers,[4,10,11] we have described different types of inclusion complexes of *p*-hexanoyl calix[4]arene (C6OH). Here we report the transformations of inclusion complexes of *p*-octanoyl calix[4]arene (C8OH) (Fig. 1) and the formation of a stable guest-free capsular framework.‡

The complex of C8OH with acetone (**A**) crystallizes in triclinic $P\bar{1}$ space group.§ Despite the different symmetry, the complex looks similar (Fig. 2) to one with THF reported earlier,[12] *i.e.* one guest molecule is located deep in the calixarene cavity and stabilized by CH_3–π interaction with the calixarene benzene rings, and a second molecule makes a H-bond with the upper part of the calixarene.

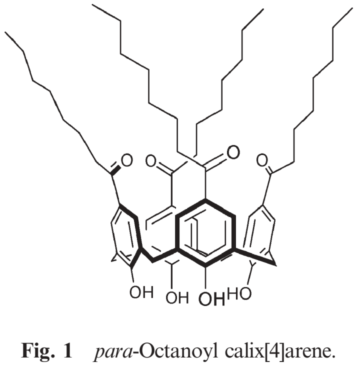

Fig. 1 *para*-Octanoyl calix[4]arene.

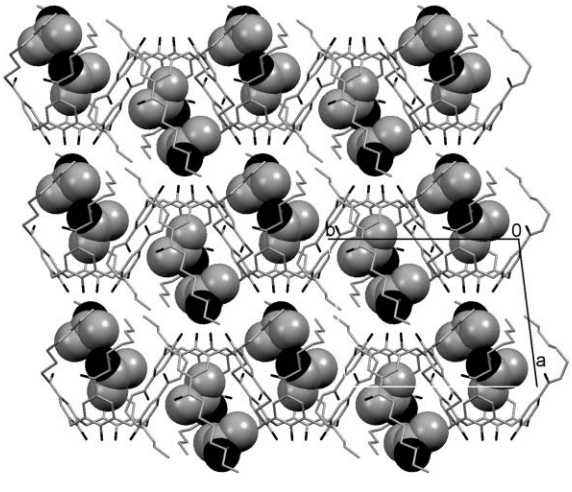

Fig. 2 Crystal packing from the crystal structure of complex **A**. Disorders and H-atoms are omitted for clarity.

A self-included structure of C8OH (**B**) was obtained upon crystallization from ethanol solution.§ The structure can be denoted as the dense α form and the calixarenes are present in an interdigitated bilayer structure which is very similar to that published elsewhere for a compound of the same composition.[9] However, these two structures certainly are different as our material ($P\bar{1}$ space group) cannot be refined in $P2_1/c$, the space group used for the previously reported structure.[9]

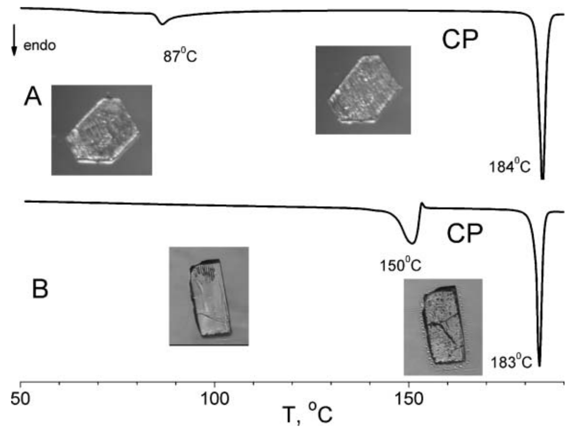

Fig. 3 DSC traces and single-crystal to single-crystal transformations of **A** (top) and **B** (bottom) into the **CP**. Sharp peaks at 184 and 183 °C correspond to the melting point of the material.

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The heating of **A** and **B** to *ca.* 130–150 °C (mp 183 °C) leads to the appearance of new phases and this process can be monitored by DSC (Fig. 3). The single crystal of **A** remains intact (Fig. 3 (top)) after such heating. In contrast, crystals of **B** do not survive heating (Fig. 3 (bottom)) and transform to polycrystalline material though keeping the shape of the original monocrystal. We also checked the behaviour of the $P2_1/n$ complex of C8OH with tetrahydrofuran described previously.[12] The single crystal of this complex also remains intact.

An X-ray diffraction study§ of a crystal of the new species obtained after thermal treatment of complex **A** reveals that the symmetry became tetragonal *P*4/*nnc*, almost identical to those of C6OH capsular complexes.[4,11] Fig. 4(a) shows the asymmetric unit of the structure (the molecule has crystallographic fourfold symmetry) and the resulting nanocapsule (**CP**) is shown in Fig. 4(b). It is worth noting that the nanocapsule does not contain any separate guest molecules. Here, the role of guests is played by those alkanoyl arms of the host calixarenes that are bent into the cavity. In addition, the transformation **A** → **CP** is irreversible. These features distinguish C8OH nanocapsules from those of C6OH,[4,11] where the presence of a separate guest is necessary, or from those of tBC and related compounds[13] where possible steric interactions of *tert*-butyl groups stabilizes the capsular structure, and where the transformations between forms generally are reversible.[3,15]

The single-crystal to single-crystal transformation in C8OH inclusion compounds can be ascribed to the fact that there are relatively flexible bowl-shaped molecules packed together in a layered motif (Fig. 2 and 4(c)), held together by hydrogen bonds between guest and host and, particularly, by weak non-directional van der Waals interactions. The rearrangement can be represented as a shifting of layers[3] accompanied by a twisting of the calixarene bowls, though this is a much simplified description of the mechanism.

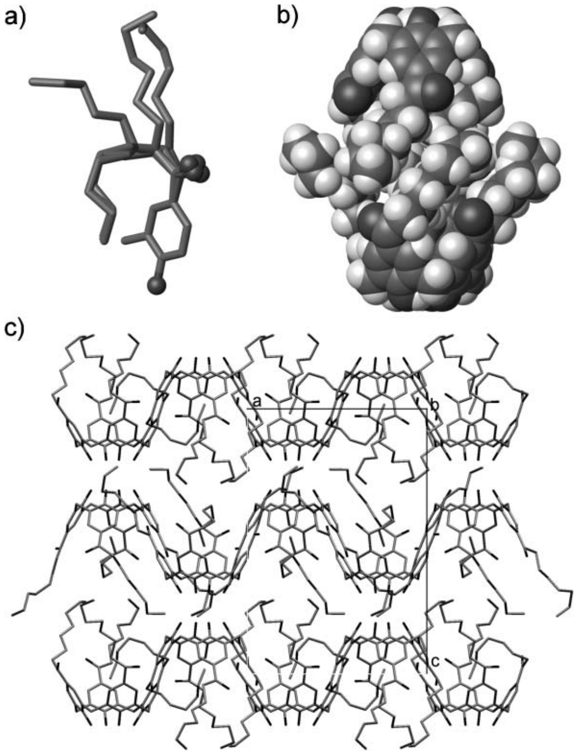


Fig. 4 Asymmetric unit (a), capsular structure (b), and crystal packing (c) of **CP**. H atoms are omitted in parts (a) and (c) for clarity.

Since the single crystal of **B** did not remain intact during the thermal treatment, it was not possible to confirm the structure of the new phase by single-crystal X-ray diffraction. However, the comparison of powder X-ray diffraction patterns (ESI†) unambiguously confirms that the new phase appearing above 150 °C from structure **B** is more than likely the capsular structure **CP**. The rearrangement **B** → **CP** is irreversible, so the capsular form is thermodynamically preferable to other structures, including dense phase **B**.

Aiming to discover the driving force responsible for the rearrangement, we performed ^{13}C CP-MAS NMR investigation of **CP** (Fig. 5). One can see that only one sharp CH_3 signal (12.5 ppm) is present in the spectrum, in agreement with the high symmetry of the crystal lattice. This also indicates that fast exchange between disordered positions of alkanoyl arms occurs. The high mobility of the arms was confirmed by the dipole dephased ^{13}C CP-MAS spectrum[14] of **CP**. Fig. 5 shows that it was not possible to significantly suppress the alkanoyl $^{13}CH_2$ signals of the calixarene with the standard 40 μs[14] dephasing delay.

Therefore, we postulate that the greater stability of **CP** has its origin in the freedom of movement of the alkanoyl arms also allowing self-inclusion, and, hence, by an entropic component to the free energy of the structure.

The slow guest release accompanied by transformation of complex **A** (or the complex with THF) into **B** (or similar structure[9]) is a process typically occurring during storage of the former complexes at ambient temperature. Single crystals do not survive such storage but the powder X-ray diffraction indicates the

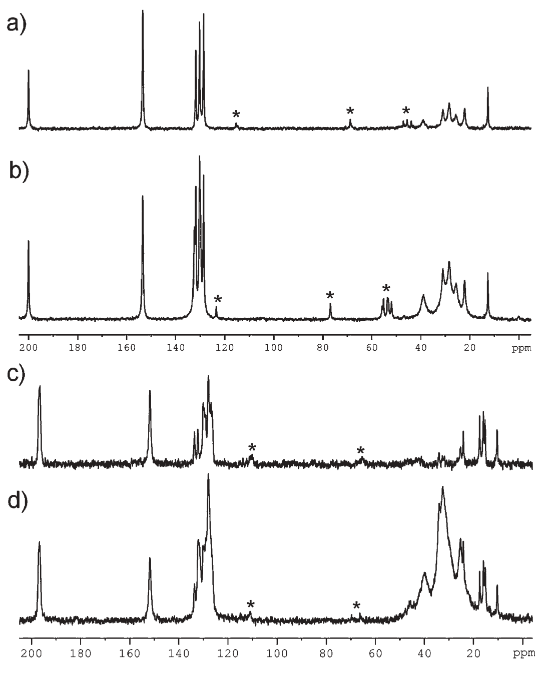
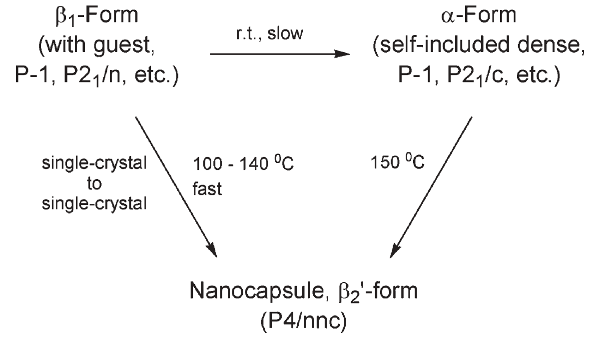


Fig. 5 ^{13}C CP-MAS (b, d) and dipole dephased CP-MAS (a, c) spectra of compounds **CP** (a, b) and **B** (c, d). Spinning side bands are marked with *.



Scheme 1 Relationship among the phases of *p*-octanoyl calix[4]arene.

similarity of **B** and the structure obtained after two weeks storage of **A** at room temperature (see ESI†).

Scheme 1 summarizes the transformations that occur for the complexes of *p*-octanoyl calix[4]arene upon heating or during ambient temperature storage. The forms **B** and **CP** are the only stable structures of C8OH and they are separated by a significant potential barrier. However, **CP** is preferred because of an entropic component to the free energy of stabilization. The transformations depicted on Scheme 1 resemble those described for tBC.[15] In the case of C8OH, the nanocapsule **CP** combines features, which are specific to three different types of complexes of tBC:[3,6,7,15] a capsular *P*4/*nnc* structure like the β_2 form, and guest-free, low density β_0' and β_0 forms. However, the β_2 form of tBC seems to be most like the **CP**, so we can label the latter also as a β_2'-form (Scheme 1).

The general ability of amphiphilic calixarenes to form inclusion complexes of different types becomes very important for the purposes of encapsulation, reactions in controlled environments, and separation processes. C8OH capsules are in fact not empty because they always are self-included by the fragments of the host's alkanoyl arms. However, self-inclusion is not necessarily permanent because of the constant movement of the alkanoyl arms and relatively small molecules should be able to penetrate the capsules for sorption and storage. This feature may well provide additional advantages in the possible exploitation of such amphiphilic calixarenes and solid lipid nanoparticles[16] obtained from them, and such studies are in progress.

Notes and references

‡ *para-n*-Octanoyl calix[4]arene was synthesized as described in ref. 8. Crystals were grown by quick cooling followed by slow evaporation of acetone (complex **A**, 0 °C) or slow cooling (species **B**, ethanol) methods. After removal of excess of solvent by filter paper, the crystals were placed in a furnace preheated to 135 °C (for **A**) or 155 °C (for **B**) for 1 h. DSC measurements were performed on a TA instrument at scanning rate of 3 °C min^{-1}. ^{13}C CP-MAS NMR spectra were measured on a Bruker AMX 300 spectrometer.

§ The single-crystal structure studies were performed on a Bruker SMART diffractometer with Mo-Kα radiation. Structure were solved by direct methods and refined by full matrix least-squares method (SHELXL-97). All non-hydrogen atoms were refined anisotropically. Calculated positions were used for hydrogen atoms.

Complex **A**. $C_{66}H_{92}O_{10}$, M = 1045.40, triclinic, space group $P\bar{1}$, a = 12.632(2), b = 15.621(2), c = 15.658(2) Å, α = 90.081(2), β = 104.117(2), γ = 96.904(2)°, U = 2973.1(6) Å^3, T = 125(2) K, Z = 2, μ(Mo-Kα) = 0.077 mm^{-1}, 36 602 reflections measured, 16 295 unique ($R_{\rm int}$ = 0.0374) which were used in all calculations, $R(F^2)$ = 0.1726 (all data)

Complex **B**. $C_{60}H_{80}O_8$, M =929.24, triclinic, space group $P\bar{1}$, a = 11.609(3), b = 15.012(3), c = 15.233(4) Å, α = 77.218(7), β = 89.814(7), γ = 83.368(7)°, U = 2571(10) Å^3, T = 125(2) K, Z = 2, μ(Mo-Kα) = 0.078 mm^{-1}, 13 777 reflections measured, which were used in all calculations, $R(F^2)$ = 0.1346 (all data)

Complex **CP**. $C_{60}H_{80}O_8$, M = 929.24, tetragonal, space group *P*4/*nnc*, a = 15.402(1), c = 22.825(4) Å, U = 5415(1) Å^3, T = 125(2) K, Z = 4, μ(Mo-Kα) = 0.074 mm^{-1}, 31 912 reflections measured, 1712 unique ($R_{\rm int}$ = 0.074) which were used in all calculations, $R(F^2)$ = 0.1447 (all data)

CCDC 622041 (**A**), 622042 (**B**), 622040 (**CP**). For crystallographic data in CIF or other electronic format see DOI: 10.1039/b613972h.

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