Crystalline inclusion complex of a calixarene with a nitroxide†

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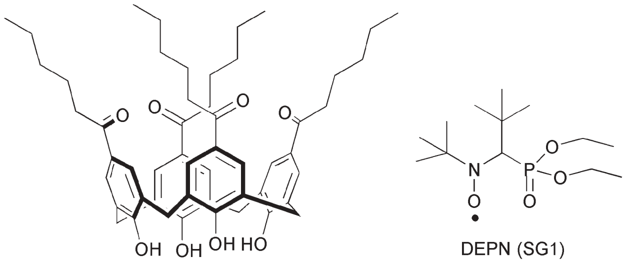
The first capsular crystalline inclusion complex of *para*-hexanoyl calix[4]arene with stable nitroxyl radical DEPN has been isolated and showed a low mobility of the radical in the capsule.

The isolation of stable radicals in an ordered rigid framework is of significant importance in organic magnetism[1] and may lead to new materials with controlled magnetic properties. Despite the fact that inclusion of stable free radicals into molecular nanocontainers in solutions is well known,[2] solid crystalline complexes of calixarenes with stable radicals[3] have not been described so far. In a recent communication[4] we have reported the crystal structure of a diamagnetic inclusion complex of *para*-hexanoyl calix[4]arene (Scheme 1) with 1-hydroxy-2,2,6,6-tetramethylpiperidine (TEMPO-H). This product was the result of our efforts to encapsulate the corresponding nitroxyl radical (TEMPO) in the calixarene. Now, having a critical mass of information about the inclusion abilities of the title calixarene[5–8] we have found a way to prepare the inclusion complexes with nitroxides. However, since the capsular complexes of acyl calixarenes are stabilized by host–guest and host–host van der Waals interactions,[7,8] the presence of *e.g.* alkyl groups in the potential guest is a crucial factor allowing the isolation of such complexes. In this sense, the stable nitroxyl radical with bulky substituents: *N*-(2-methylpropyl)-*N*-(1-diethylphosphono-2,2-dimethylpropyl)-aminoxyl called DEPN or SG1[9,10] (Scheme 1), has been chosen as an appropriate guest for complexation by *para*-hexanoyl calix[4]arene.



Scheme 1

The isolation of the inclusion complex was carried out by a combination of the usual methods of crystallisation. In order to overcome the significantly enhanced solubility of the calixarene in ethanol in the presence of the nitroxide[4] we have used ethanol–water mixtures with a controlled proportion of the latter.‡ This is an important factor because an excess of water may lead to the crystallisation of a partly self-included calixarene structure.[8] The capsular inclusion complex of the calixarene with nitroxide precipitates as yellow, large, square-like crystals resembling in shape the crystals of the capsular complexes described previously.[6,7] Single crystal X-ray analysis reveals the symmetry as tetragonal with a *P*4/*nnc* space group.§ DEPN is inserted into the calixarene pocket by one of the three methyl groups of the N–C(CH_3)$_3$ fragment providing the nessessary[7] CH–π interaction of the guest with the π-systems of four benzene rings of the calixarene (Fig. 1). The other tBu group as well as O–CH_2–CH_3 moieties serve to create additional van der Waals stabilisation of the capsule.

The complex is relatively stable at room temperature. The initial decay observed on the TGA trace (Fig. 2) can be attributed to a partial release of DEPN together with ethanol molecules. The presence of the latter cannot be confirmed by single crystal XRD but can be expected in analogy with previously described structures.[4,7,8] The total weight loss of *ca.* 16% corresponds fairly well to the theoretical amount (15.6%) of the nitroxide in the complex, *i.e.* 1 DEPN per capsule of 2 calixarene molecules. Of course, the presence of another form of calixarene inclusion, such as the partly self-included structure[8] cannot be ruled out completely. However, this is a very minor component because

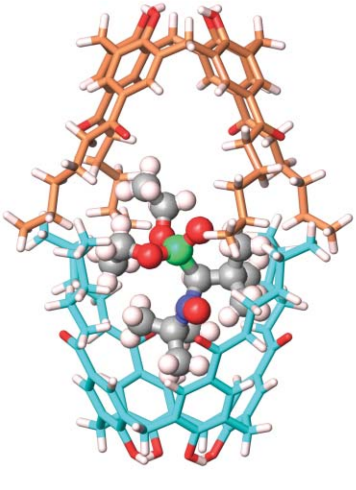


Fig. 1 Capsular complex of *para*-hexanoyl calix[4]arene with DEPN. Disorder has been removed for clarity.

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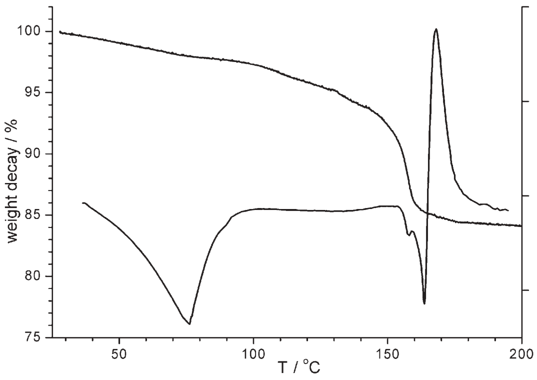

Fig. 2 TGA and DSC traces of the complex of *para*-hexanoyl calix[4]arene with DEPN.

powder X-ray diffraction patterns of the bulk material correspond well to those calculated from single crystal data (Fig. 3) taking into account the differences in temperatures (*ca.* 295 K for powder XRD and 125 K for single crystal XRD), as well as a non-random distribution of crystal orientations in the powder XRD sample holder. The slow release of ethanol causes a broad endothermic peak observed in the DSC trace of the freshly prepared complex (Fig. 2). Further heating leads to another phase transition followed immediately by melting of the material (endothermic peaks at *ca.* 175 °C) and by a reaction which proceeds in the liquid material (exothermic peak at *ca.* 180 °C).

Fig. 4 shows ESR spectra of the polycrystalline complex at elevated temperature in comparison with those taken from 0.5 mM solution of DEPN in ethanol. The spectrum in ethanol at 300 K shows six lines due to the hyperfine interaction (HFI) of the unpaired electron with the ^{14}N (a_N = 1.40 mT) and ^{31}P (a_P = 4.60 mT) nuclei, and the *g*-factor was found to be 2.0067, and these are close to the reported[10] values in dichloromethane: g = 2.0061, a_N = 1.43 mT, a_P = 4.53 mT. It is obvious that the line shapes in the ESR spectra taken from the crystalline sample will depend mainly on two factors: mobility of free radicals in the capsules and dipole–dipole interactions of unpaired electrons in neighbouring radicals. Since each capsule contains only one nitroxide molecule, the dipole–dipole interaction may be significant only between nearest neighbour radicals. From the tetragonal symmetry of the crystal lattice one can determine that each capsule is surrounded by 10 others. DEPN can have 8 equivalent positions in each capsule and the minimum distance between N–O groups of neighbouring nitroxides can be estimated from X-ray data as 9.5 Å, which is enough to contribute additional broadening to the ESR line width (*ca.* 0.4–0.9 mT). Such an estimate can be easily confirmed by comparison of ESR spectra taken at elevated temperatures. The changes in line width (Fig. 4) upon increase in temperature from 300 to 373 K are not really significant and the line widths are much broader than those in the ESR spectrum taken from 0.5 mM solution of DEPN in ethanol. Fig. 4 demonstrates that at low temperatures the spectrum is similar to that of DEPN in frozen ethanol, *i.e.* is determined by the anisotropies of g and HFI.[11] At higher temperatures (above *ca.* 300 K) the behaviour of the nitroxide begins to resemble motion in a viscous solvent.[11] The measured *g*-factor of DEPN in the capsule is 2.0064, *i.e.* smaller than in ethanol. This reflects a less polar environment for the nitroxide in the capsule. However, more precise ESR parameters, as well as quantitative conclusions about the mobility of nitroxide in the capsules, cannot be derived at the present stage due to the strong contribution of dipole–dipole interactions.

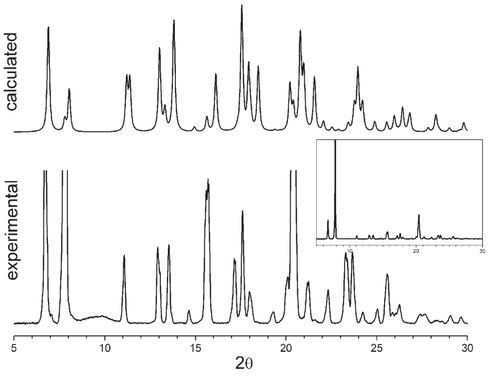

Fig. 3 Experimental (bottom) and calculated (top) powder X-ray diffraction patterns of the complex of *para*-hexanoyl calix[4]arene with DEPN. Inset (full diagram) clearly shows preferred orientation of crystals in the sample holder of the instrument.

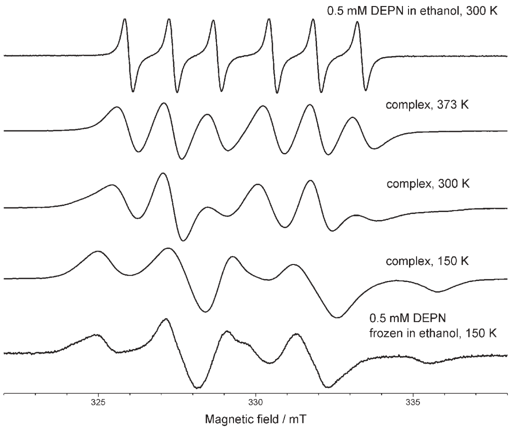

Fig. 4 ESR spectra (X-band) of the complex taken at elevated temperatures in comparison with the spectra of DEPN in ethanol solution.

After keeping the mother liquor obtained after separation of crystals of the complex for *ca.* 1 month a very small amount of new crystals was found in the vial. A full analysis of these species was not possible but single crystal X-ray diffraction studies revealed the structure of the new material as a partially self-included form of the calixarene with *tert*-butylamine incorporated between calixarene molecules and coordinated to the latter *via* N–H···O=C hydrogen bonds (Fig. 5): 3 C=O groups from 3 calixarenes are in close proximity to the amino group with N···O distances 2.69, 2.74, and 2.81 Å. It is not clear from crystallographic data whether *tert*-butylamine is present in the ammonium form or it has simply an NH_2 group with three different orientations toward carbonyls. It is also not possible to derive conclusions about the calixarene being either in anionic or neutral forms. In the final structure, a site occupancy of 0.5 was assigned to two of three hydrogens (shown in Fig. 5 as off-white balls).

The formation of *tert*-butylamine is quite remarkable because it indicates the instability of DEPN in this system with the most

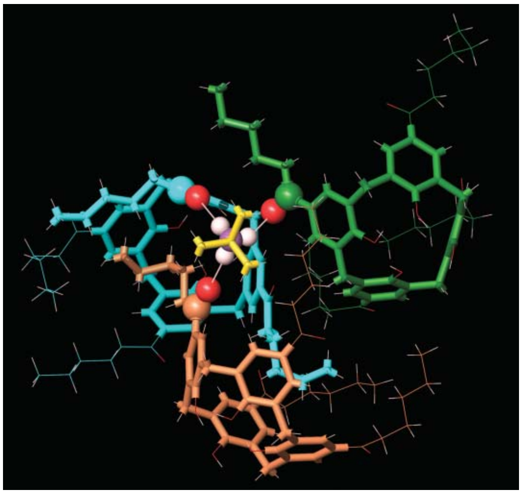

Fig. 5 Partly self-included form of *para*-hexanoyl calix[4]arene with *tert*-butylamine incorporated between 3 calixarene molecules. Functional groups participating in H-bonding are shown in ball–stick mode.

anticipated decay pathway *via* the formation of the corresponding hydroxylamine (in analogy with TEMPO[4]) and several further steps of decomposition. It is also worth noting that the calixarene in this case serves not only as a reagent for DEPN but also as a supramolecular trap for the reaction product. The instability of DEPN[12] and of similar nitroxides has been widely discussed[13] as one of the main reasons of its successful application in the nitroxide mediated polymerization of acrylates, although no studies of products of DEPN decomposition have been published so far to the best of our knowledge.

In summary, we have successfully isolated and characterized the first solid inclusion complex of a calixarene with nitroxide and opened the way for an ordered incorporation of stable free radicals into these organic zeolites. A detailed study of the behaviour and mobility of encapsulated nitroxides is under way and will be published in a subsequent paper.

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Notes and references

‡ In a typical procedure, 200 mg (0.625 mmol) of DEPN (purity *ca.* 90%) were dissolved in 3.0 ml of absolute ethanol. 103 mg (0.125 mmol) of *para*-hexanoyl calix[4]arene were added and the mixture was stirred in slightly boiling ethanol until a clear solution had been obtained. Immediately thereafter (long heating of the solution should be avoided due to instability of DEPN) 0.5 ml of water were slowly dropped into the hot solution. The mixture became opaque and a new portion of ethanol (1.5 ml, the amount may be slightly different) was *slowly* added by dropping into the mixture until the latter became homogeneous again. The stirring bar was removed by means of a magnet and the hot solution was immediately placed in a stove preheated at 80 °C. The cap in the vial with the solution was not tightly closed so the latter was allowed to evaporate slowly (*ca.* 0.5 ml of the solvent evaporated). The slow cooling of the solution (*ca.* 5 °C h^{-1}) with preventing of shaking afforded big (up to 2 × 2 mm) yellow crystals of the complex. Yield 54 mg (45%).

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

Capsular complex. The complex has crystallographically imposed 4_2 symmetry. $C_{117}H_{157}NO_{20}P$, $M = 1928.41$, tetragonal, $a = 15.534(1)$ Å, $c = 22.658(2)$ Å, $V = 5467.2(7)$ Å^3, $T = 125.0(1)$ K, space group $P4/nnc$, $Z = 2$, μ(Mo-Ka) = 0.074 mm^{-1}, 63264 reflections measured, 3808 unique ($R_{int} = 0.0295$) which were used in all calculations, $R(F^2) = 0.0891$ (all data).

Complex of the calixarene with *tert*-butylamine. The asymmetric unit has two calixarene molecules and one *tert*-butylamine, all on general positions. $C_{108}H_{139}NO_{16}$, $M = 1707.20$, monoclinic, $a = 13.612(1)$ Å, $b = 42.409(3)$ Å, $c = 16.274(1)$ Å, $\beta = 94.94(1)^\circ$, $V = 9360(1)$ Å^3, $T = 125.0(1)$ K, space group $P2_1/c$, $Z = 4$, μ(Mo-Ka) = 0.074 mm^{-1}, 123801 reflections measured, 13592 unique ($R_{int} = 0.0778$) which were used in all calculations, $R(F^2) = 0.1161$ (all data).

CCDC 661588 and 661589, respectively. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b714738d

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