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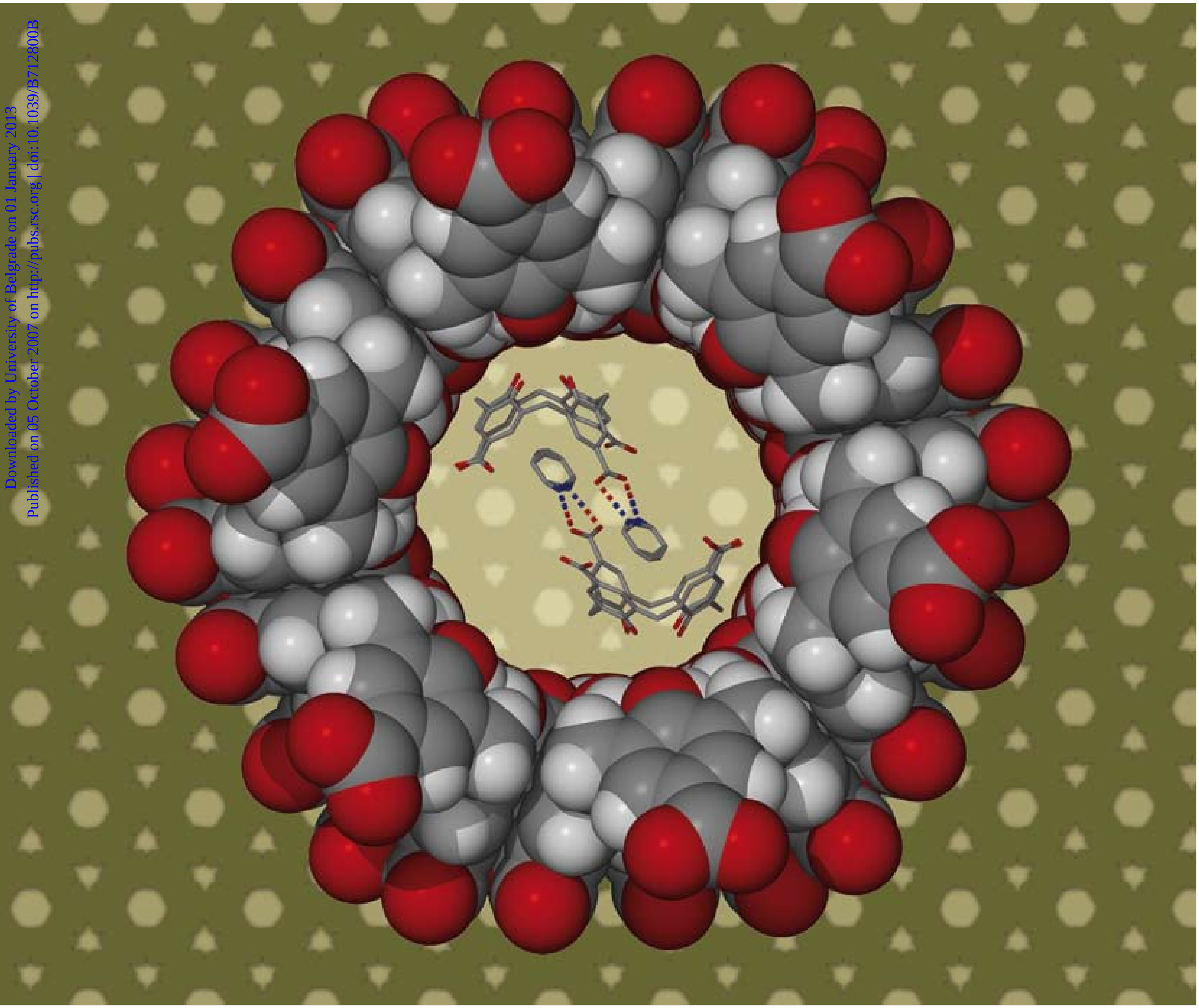

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LETTER

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Large diameter non-covalent nanotubes based on the self-assembly of *para*-carboxylatocalix[4]arene

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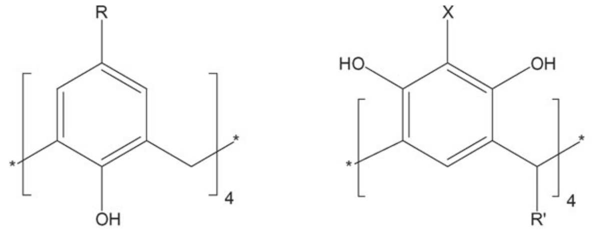
Non-covalent nanotubular assemblies with large core diameters are rare. Here we show that simple crystallisation of *para*-carboxylatocalix[4]arene from pyridine results in the formation of one such assembly, facilitated by back-to-back packing of calixarenes and the well known pyridine–carboxylic acid interaction.

The self-assembly of topologically-directional molecules has attracted much interest in recent times.[1] Controlling self-assembly is a significant challenge, and in order to generate large superstructures, such as molecular nanocapsules and nanotubes, one must often vary the ratios of the co-crystallising species or other parameters in a multi-component system; an approach that can be costly in both time and materials. These structures are often characterised by single crystal X-ray crystallography, and in some cases, this method offers the only avenue of valuable insight into the self-assembly of numerous components.

Within the large family of calix[*n*]arenes, the cyclic tetramers (when bearing lower rim OH functionality) typically assume a bowl-shaped conformation that resembles a truncated cone (for example, see *para*-^{t}Bucalix[4]arene (**1**), Scheme 1).[2] This, coupled with the fact that the molecular framework can be easily altered to afford a chosen functionality, provides the chemist with a useful starting point for experimentation in such controllable self-assembly. There are many documented calix[4]arene derivatives, but to date, only a limited number have been used to form large non-covalent nanocapsule assemblies. These include *para*-sulfonatocalix[4]arene (SO$_3$[4]),[3] the *C*-alkylresorcin[4]arenes[4] and the *C*-alkylpyrogallol[4]arenes (**2**, **3** and **4**, respectively, Scheme 1).[5] In nanocapsule assemblies of SO$_3$[4], the molecule must deviate from bilayer packing, and twelve monomers associate in a back-to-back fashion, imparting curvature on the resulting structures.[3] Although deviation from bilayers is also a prerequisite for nanocapsules based on resorcin[4]arenes and pyrogallol[4]arenes,[4–6] six molecules of each form head-to-head structures based on an octahedron, the former also incorporating structural water molecules.[4]

Covalent oligomers of peptides, ureas and carbohydrates have all been assembled into nanotubular assemblies.[7] Although this is the case, a number of recent studies point towards the fact that calixarenes are particularly well suited conformationally toward nanotube formation.[3a,8–11] With respect to calix[4]arenes, *para*-sulfonatocalix[4]arene (**2**),[3a] *C*-methylresorcin[4]arene (**5**),[8] calix[4]hydroquinone (**6**),[9] calix[4]arene dimethoxycarboxylic acid (**7**, and its *O*-methyl ester derivative **8**)[10] and *C*-hexylpyrogallol[4]arene (**9**) have all been engineered into non-covalent nanotubular assemblies containing channels within the resulting structures.[11] All of these assemblies have been characterised by X-ray diffraction. For **2**,[3a] **5** and **9**,[8,11] these bowl-shaped molecules must be combined with various different co-crystallising species in order to effect the formation of nanotubular assemblies, while **6**, **7** and **8** all form non-covalent nanotubes by simple crystallisation from water (**6**),[9] water–methanol (**7**)[10a] or chloroform–methanol mixtures (**8**).[10b] The diameter of the helical nanotube based on **2** is amongst the widest reported to date for a self-assembled multi-component system, and accommodates disordered hydrated lanthanum and sodium ions.[3a] The extended packing of **6** results in the formation of rectangular-shaped voids that have a 1 nm^2 cross-section and that run throughout the structure.[9] Notably, these voids have been used to form ultrathin silver nanowires in a controlled manner.

In our ongoing structural studies into large supramolecular assemblies with calix[*n*]arenes, we have recently begun investigating the assembly of *para*-carboxylatocalix[4]arene (**10**, Scheme 1). Although this molecule has been ignored for the



R = ^{t}Bu, *p*-tBucalix[4]arene, **1**
R = $\mathrm{SO_3^-}$, *p*-sulfonatocalix[4]arene, **2**

R = OH, calix[4]hydroquinone, **6**
R = CO$_2$H, *p*-carboxylatocalix[4]arene, **10**

X = H, R' = alkyl, *C*-alkylresorcin[4]arenes, **3**
X = OH, R' = alkyl, *C*-alkylpyrogallol[4]arenes, **4**

X = H, R' = CH$_3$, *C*-methylresorcin[4]arene, **5**
X = OH, R' = C$_6$H$_{13}$, *C*-hexylpyrogallol[4]arens, **9**

Scheme 1 The structures of various calix[4]arenes that typically assume bowl-shaped conformations, some of which have also been shown to form non-covalent nanotube assemblies.

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most part, we anticipated **10** to be useful for the formation of metal–organic assemblies and perhaps non-covalent nanocapsules, amongst other things. Compound **10** was synthesised according to literature procedures,[12] is only sparingly soluble in water, and was found to be highly soluble in basic media. As this was the case, we employed pyridine as a solvent for crystallisation. Upon slow evaporation with standing over a number of days, colourless needle-shaped crystals formed. Analysis using conventional laboratory X-ray diffraction techniques found the crystals to be very weakly diffracting. Herein we show, using synchrotron radiation, that, when crystallised from pyridine, **10** forms non-covalent organic nanotubes through a previously unobserved back-to-back packing motif, as well as the frequently observed pyridine/carboxylic acid tecton.[13] The new kind of back-to-back motif affords a large internal nanotube core diameter of ~1.3 nm, which is amongst the widest reported to date.

Crystals of the pyridine solvate of **10** were of trigonal symmetry, and the structural solution was performed in space group *P*6/*mmc*.[‡] The asymmetric unit was found to contain half a molecule of **10**, that, upon symmetry expansion, showed the molecule to adopt the expected cone conformation. In addition, one-third of a disordered pyridine molecule in the asymmetric unit resides in the cavity of **10**. Further to this, diffuse electron density was present that was not associated with either the calixarene or the pyridine molecules. As **10** was crystallised from GPR grade pyridine by slow evaporation in air, this is assumed to be due to disordered pyridine and water molecules (although it was not possible to model these satisfactorily).

Symmetry expansion around the disordered pyridine molecule occupying the cavity of **10** shows that a carboxylato group from a neighbouring calixarene is in close proximity (Fig. 1). As the distance between the oxygen atoms of the carboxylato group and the nearest atom of disordered pyridine is ~2.75 Å, we presume this to be a carboxylic acid/pyridine interaction that is often observed between these functional groups in solid state studies.[13] Given the limited quality of the data, we are unable to say whether some carboxylic acid groups in **10** are deprotonated by the pyridine guest (and other disordered pyridines), but this could indeed be the case. Other atoms in the disordered pyridine guest are ~3.4 Å from the centroids of two aromatic rings of the calixarene, suggesting the presence of CH···π interactions, which would not be unexpected based on the inclusion of aromatic species in other calix[4]arenes. Furthermore, the centre of the disordered pyridine molecule is situated ~3.7 Å from the centre of one of the calixarene aromatic rings, suggesting a π-stacking interaction between host and guest.

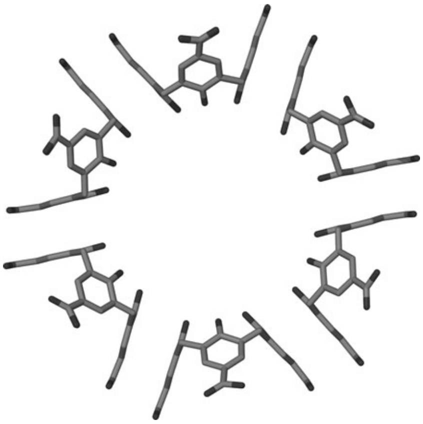

Fig. 2 Stick representation of one ring in the nanotubular assembly of **10 · pyridine** showing the previously unobserved hexameric back-to-back calix[4]arene self-assembly mode.

Symmetry expansion around the aromatic rings of the calixarene shows that six molecules of **10** form a back-to-back self-assembled ring through one crystallographically-unique π-stacking interaction (aromatic centroid···centroid distance of 3.49 Å, Fig. 2 and Fig. 3). Notably, this is the first observation of this type of hexameric back-to-back stacking for calix[4]arenes in nanotubular assemblies. In the chiral helical nanotubes reported for **2**, sodium-bound pyridine *N*-oxide molecules act as spacers between back-to-back sulfonatocalix[4]arenes, intercalating within the nanotubule walls.[3a] This is one of the largest nanotubular assemblies built from small molecular building blocks reported to date, and the hexameric back-to-back assembly in the present case

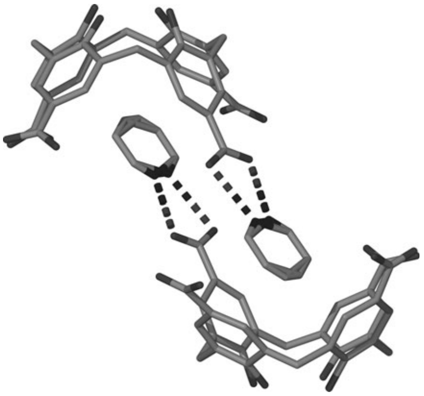

Fig. 1 Probable interactions between the carboxylato groups of **10** with disordered pyridine molecules that reside in the calixarene cavities.

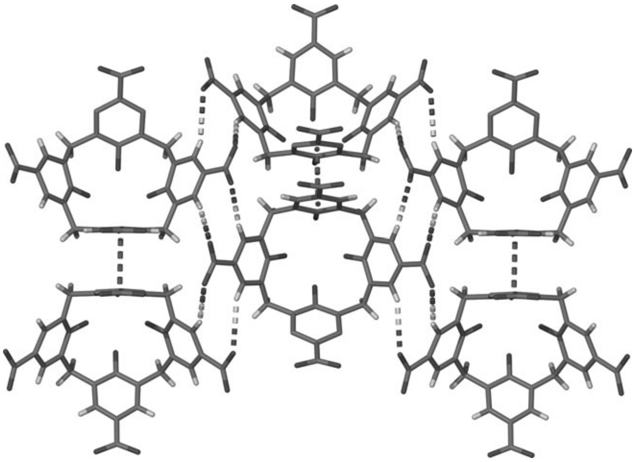

Fig. 3 The CH···O and π-stacking interactions found in the packing between neighbouring rings of *para*-carboxylatocalix[4]arene in the nanotubular assembly.

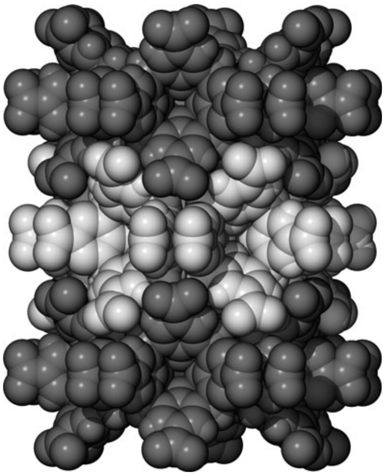

Fig. 4 Space-filling representation of three neighbouring rings in the nanotubular assembly of **10·pyridine**. The rings are shaded in an alternating fashion to show the interlocking between the carboxylato functionalities, which are orthogonal to the equator of each hexameric 'disc'.

represents an important extension to the known self-assembly of these type of architectures.

Examination of the way that neighbouring hexameric discs interact shows that these structural fragments interlock *via* the carboxylato groups that are orthogonal to the equator of each 'disc' (Fig. 3 and Fig. 4). This occurs by synergic CH$\cdots$O interactions between aryl hydrogen atoms of one 'disc' and oxygen atoms of the 'upper-rim' carboxylato groups of neighbouring 'discs' (by two crystallographically unique CH$\cdots$O distances of 2.822 and 2.998 Å). The extended structure shows that the organic nanotubes pack in a hexagonal fashion (Fig. 5), as was the case for the nanotubes based on **2**. The pyridine molecules form bridges at the closest contacts between neighbouring nanotubes through the dimerisation shown in Fig. 1.

As mentioned above, crystals of **10·pyridine** were very weakly diffracting, and it was only possible to obtain the presented solution by using long exposures to synchrotron radiation (4 sec). Several data collections of the same material were performed on these single crystals. The routine SQUEEZE was applied to the data set included within this article, and for the structure showing order, we arrived at a final *R*-factor of around 36% (set **A**‡).[14] It was possible to further model disorder within the calixarene framework and the pyridine guest molecule, resulting in a final *R*-factor of ~26% (set **B**‡), but the disordered solvent in the large channels could not be modelled effectively. In an effort to improve the atomic resolution, an exposure time of 10 seconds was employed, although no improvement was observed. The badly disordered calixarene and solvent molecules are the most likely reason for poor diffraction and the subsequent abnormally high *R*-factors associated with these crystals.

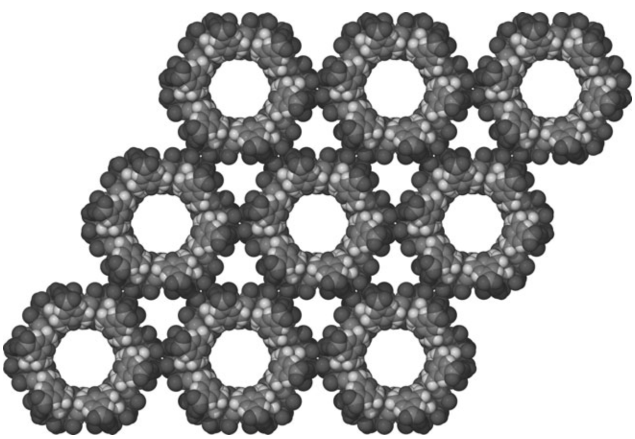

Fig. 5 View of hexagonally-packed nanotubes down the c-axis in the extended structure of **10·pyridine**. The visible channels are presumed to be occupied by disordered pyridine molecules.

To conclude, we have found that *para*-carboxylatocalix[4]arene forms non-covalent organic nanotubes, simply by crystallisation from pyridine. Spheres and tubes are intimately related. This is demonstrated at the molecular level not only by the relationship between C_{60} and SWNTs,[15,16] but also by the related nanocapsules and nanotubes formed from either *para*-sulfonatocalix[4]arene,[3a] *C*-methylresorcin[4]arene[4,8] or *C*-hexylpyrogallol[4]arene.[5,11] Given this, it is not unreasonable to expect that *para*-carboxylatocalix[4]arene will behave in a similar manner. Furthermore, the ease with which large cavity non-covalent nanotubes can be assembled is perhaps promising for the facile formation of related nanocapsular assemblies. This, along with the use of **10** in the formation of metal–organic assemblies/coordination polymers, is currently under way.

We would like to thank Professor Leonard J. Barbour for his assistance in the generation of selected graphics.

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‡ **Crystallographic data set A**: $C_{18.5}H_{14.5}N_{0.5}O_{12}$, M = 435.81, hexagonal, a = 28.9049(14), c = 21.444(2) Å, U = 15 516.3(19) Å, μ = 1.119 Mg m^{-3}, T = 150 (2) K, space group $P6/mcc$, Z = 24, synchrotron radiation (wavelength λ = 0.6710 Å), GOF = 8.168, agreement index R_1 = 0.3692, 82 857 reflections measured, 2123 unique (R_{int} = 0.0721) which were used in all calculations. The final $\omega R(F^2)$ was 0.750 (all data). CCDC CCDC 660905.
Crystallographic data set B: $C_{18.5}H_{14.5}N_{0.5}O_{12}$, M = 435.81, hexagonal, a = 28.9049(14), c = 21.444(2) Å, U = 15 516.3(19) Å, μ = 1.119 Mg m^{-3}, T = 150 (2) K, space group $P6/mcc$, Z = 24, synchrotron radiation (wavelength λ = 0.6710 Å), GOF = 5.893, agreement index R_1 = 0.2609, 82 857 reflections measured, 2123 unique (R_{int} = 0.0721) which were used in all calculations. The final $\omega R(F^2)$ was 0.6108 (all data). CCDC 660906.
For crystallographic data in CIF or other electronic format see DOI: 10.1039/b712800b

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