Halogen bonding drives the self-assembly of piperazine cyclophanes into tubular structures†‡

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Halogen bonding with 1,4-diiodotetrafluorobenzene leads to the self-assembly of piperazine cyclophanes into well-defined tubular structures with solvent inclusion.

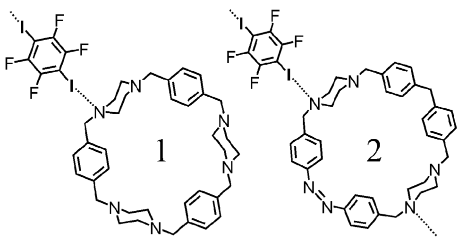
Recently, halogen bonding (XB) has increasingly facilitated the assembly of diverse supramolecular complexes and networks.[1] Among others, the construction of such systems is frequently based on the use of the strong and directional C–N···I–C supramolecular synthon, where I is an electron poor iodine atom and N is either an sp (typically cyano derivative), sp^2 (pyridine), or sp^3 (amine) nitrogen atom.[2] By the use of bisfunctional XB-donors and acceptors, *e.g.* 1,4-diiodotetrafluorobenzene (F_4DIB) and 4,4-bispyridine, 1D infinite chain structures have been routinely obtained.[3] More sophisticated 2D or 3D halogen-bonded architectures have often required the use of multi-functional donor and acceptor building blocks.[4]

Thanks to the strong electron withdrawing ability of fluorinated residues, iodoperfluorocarbons are particularly good XB-donors. This makes XB a first choice noncovalent interaction if self-assembly of hydrocarbons (HCs) with perfluorocarbons (PFCs) is pursued. The low affinity towards each other due to their distinct physical properties[5] is the driving force of PFC/HC segregation that is seen in countless halogen-bonded complexes (most of them reported by some of the current authors). Segregated PFC and HC domains in the form of columns or layers are usually observed.[6] With the possibility to exploit robust and directional XB along with PFC/HC segregation to direct the self-assembly of large molecular weight cyclophanes into hollow tubular or porous[2c,7] structures in mind, we challenged various piperazine cyclophanes with 1,4-diiodotetrafluorobenzene (F_4DIB).

Besides metal–organic frameworks, *viz.* polymeric structures of metal ions and bridging organic ligands,[7a] macrocycles are frequently used building blocks in the construction of organic tubular or porous materials.[7b] One of the most efficient systems is that of self-assembling peptide nanotubes, which are β-sheet-like structures of stacked flat cyclic peptides made up of alternating D- and L-amino acid units.[8] Other frequently used building blocks are phenyl acetyl macrocycles (PAMs)[9] or urea-functionalized macrocycles,[10] which are especially tailored to stack into columns producing porous materials. Goldberg has recently highlighted the crystal engineering aspects of nanoporous porphyrin materials.[11] From the toolbox of noncovalent interactions, hydrogen bonding (HB) is the most used for the formation of tubular structures and little effort has been devoted to the exploitation of other interactions.

In this communication we report the successful use of XB in the rational design of materials from the self-assembly of rigid macrocyclic building blocks. Piperazine cyclophanes[12] are structurally rigid rings, which delimit a nonpolar macrocyclic cavity large enough to accommodate small neutral guest molecules. In addition, the piperazine cyclophane ring bears multiple sp^3 N atoms as potential bonding sites for XB. Whilst piperazine cyclophanes **1**[13a] and **2**[13b] do not show the formation of channeled structures in the solid state, the single crystal X-ray structures of their 1 : 1 halogen-bonded complexes with 1,4-diiodotetrafluorobenzene (F_4DIB) show the stacking of cyclophane rings into tubular structures.

Cyclophane **1** (Scheme 1) was prepared§ from piperazine and 1,4-bis(bromomethyl)benzene using a modification of our previously published procedure,[12a] the azobenzene functionalized cyclophane **2** was prepared earlier.[13b] Colorless needle-like crystals of $\mathbf{1}_2\cdot F_4$DIB¶ were obtained by slow diffusion of diisopropyl ether vapor into a chloroform solution containing cyclophane **1** and F_4DIB. Based on the molecular structure of **1** it was assumed that **1** would provide a trigonal tecton[14] with three potential XB-donor sites. For this reason, molar ratios of 1 : 1, 1 : 2 and 1 : 3 (cyclophane : F_4DIB) were



Scheme 1 The molecular structures of **1**, **2**, and F_4DIB. The XB motif is shown with dotted lines.

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‡ CCDC 717658 and 717659. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b901473j

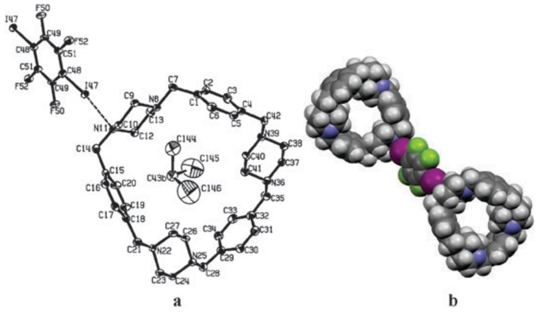

Fig. 1 Structure of $\mathbf{1}_2{\cdot}F_4DIB$. Hydrogen atoms (in a) and guest chloroform (in b) are omitted for clarity. XB distance and angle: [N11···I47] 2.851(5) Å and 170.8(2)°.

used in the experimental setup. Using 1 : 1 and 1 : 2 ratios, colorless needle-like crystals were obtained. In both cases the X-ray study revealed that the crystals were composed of cyclophane and F_4DIB in a 2 : 1 molar ratio (Fig. 1) showing a short N···I halogen bond. A packing diagram of $\mathbf{1}_2{\cdot}F_4DIB$ reveals segregated columns where the cavities of the cyclophanes are aligned on top of each other thus forming an infinite tubular structure (Fig. 2). Chloroform molecules (crystallization solvent) occupy the intramolecular cavities of **1**, which are aligned in between the adjacent $\mathbf{1}_2{\cdot}F_4DIB$ moieties (Fig. 2, right). The included chloroform was found to be severely disordered. Two orientations were found and refined with population parameters of 0.15 and 0.35 of which only one orientation is shown in Fig. 1 and Fig 2.

After removal of the solvent chloroform, subsequent VOID calculations[15] reveals that the roughly cylindrical voids represent 13% volume of the unit cell.

Orange plate-like crystals of $\mathbf{2}{\cdot}F_4DIB$,¶ suitable for X-ray structural analysis, were obtained by slow diffusion of diisoprophyl ether vapor into a chloroform solution of **2** and F_4DIB (1 : 1) (Fig. 3). Both piperazine subunits revealed energetically more preferred chair conformations, leaving electron lone-pairs of N atoms in axial positions, pointing inwards (N9, N43) and outwards (N12, N31) the macrocyclic cavity. As predicted, interaction sites (atoms N12 and N31) of the cyclophanes are connected with F_4DIB spacers resulting in "pearl necklace" like 1D chains, which are then assembled into well resolved columns, forming well-defined tubular structure as in $\mathbf{1}_2{\cdot}F_4DIB$. Besides the short N···I halogen bond, the structure is additionally stabilized by offset π···π stacking between F_4DIB molecules (Fig. 4, see legend). The voids between the piperazine macrocycles are filled with disordered chloroform (two orientations with the sum of populations of 0.5). The azobenzene moiety in **2** makes it more rigid[13b] and slightly larger providing an intramolecular cavity larger than in **1**. The perfect alignment of the macrocycles leads to slightly wider tubular packing. Omitting the solvent chloroform as in $\mathbf{1}_2{\cdot}F_4DIB$ reveals that the tubular voids make up to 16.4% of the unit cell volume.

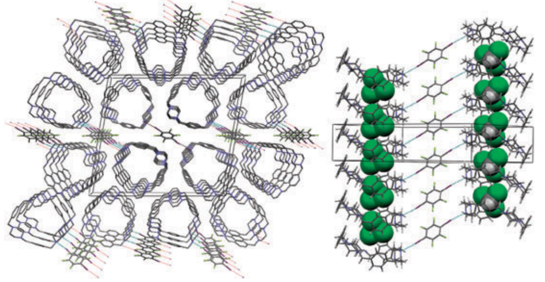

Fig. 2 The unit cell packing of $\mathbf{1}_2{\cdot}F_4DIB$. The XB-interaction is represented by dotted lines. The included chloroforms are omitted form the left plot.

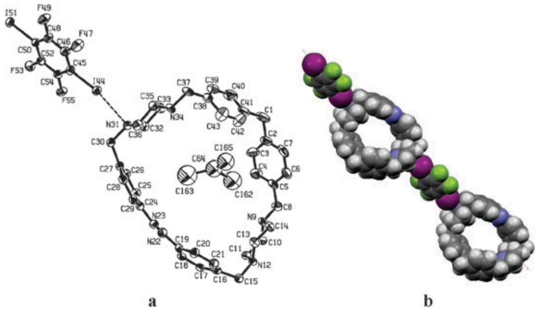

Fig. 3 Structure of $[\mathbf{2}{\cdot}F_4DIB]_n$. Hydrogen atoms (in a) and guest chloroform (in b) are omitted for clarity. XB distances and angles are: [N12···I51] 2.983(5) Å and 172.5(2)°, [N31···I44] 2.880(5) 168.9(2).

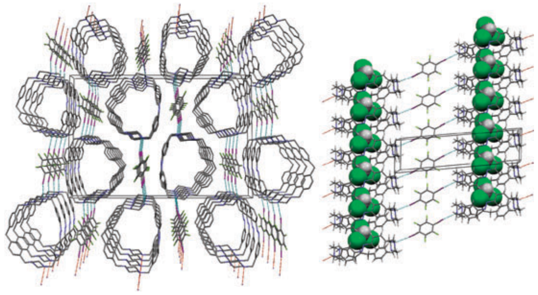

Fig. 4 The unit cell packing of $[\mathbf{2}{\cdot}F4DIB]_n$. The XB-interaction is represented by dotted lines. Offset π···π stacking with C46···F53 and C52···F47 distances of 3.169(6) and 3.187(6) Å, respectively. The included chloroforms are omitted form the left plot.

Molecular modeling[16] of the cyclophane **2** shows that the intramolecular cavity is still slightly too small to allow the chloroform molecule (about 75 $Å^3$) to freely pass through the tubular channel. A conformational change of the host would be needed for it and thus in the current structure the guest is trapped in $\mathbf{2}{\cdot}F_4DIB$ between the adjacent cyclophanes.

Porous organic crystalline networks mediated through halogen bonding interactions are still very rare.[17] Different approaches have been pursued, like the dynamic self-assembly of nonporous materials around supramolecular templates,[17a] or the self-assembly of halophenoxycarbonyl benzenes.[17b] In this paper, robust and directional C–N···I–C interactions were used, supplemented by π···π stacking and van der Waals interactions between the adjacent molecules, in the co-crystal formation of $\mathbf{1}_2{\cdot}F_4DIB$ and $\mathbf{2}{\cdot}F_4DIB$ to direct the self-assembly of cyclophanes to tubular host frameworks. The preorganized rigid ring shape and XB acceptor sites of the cyclophane molecules offer an excellent way to organize molecules into desired tubular/porous architectures. The too small size of the intramolecular cavity lead to the inclusion of the solvent chloroform molecules thus preventing these materials from being truly porous in nature. Despite this, based on our results, it is expected that the use of XB with larger and similarly rigid macrocycles will lead to formation of truly porous organic materials and also to a better understanding of the potential role of halogen bonding as an important interaction in crystal engineering and materials chemistry.

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§ Molecule synthesis and characterisation details: 1,4-bis(bromomethyl)benzene (9.01 g, 34.1 mmol) and piperazine (2.94 g, 34.1 mmol) were dissolved in an acetonitrile : THF mixture (5 : 2, 800 mL). Solutions (43 mM) were added in a period of 8 h into a refluxing mixture of acetonitrile : THF (5 : 2, 450 mL) and potassium carbonate (15.2 g, 110 mmol). The cooled solution was filtered and evaporated to dryness. The crude product was purified by silica gel column chromatography (50 : 2 : 2, $CHCl_3$: THF : Et_3N). Yield (432 mg, 7 %). Decomposition above 573 K; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.15 (s, 12H), 3.53 (s, 12H), 2.32 ppm (s, 24H); ^{13}C NMR: δ = 136.77, 129.49, 62.64, 52.90 ppm; MS: m/z = 565.4 (M + H^+).

¶ *Crystal data for* $\mathbf{1}\cdot\frac{1}{2}(F_4DIB)$: $2(C_{36}H_{48}N_6)\cdot C_6F_4I_2\cdot CHCl_3$, M_w = 1650.84 g mol^{-1}, monoclinic, space group $P2_1/c$, a = 24.6450(7), b = 5.8927(2), c = 27.7544(6) Å, β = 99.404(2)°, V = 3976.5(2) Å^3, T = 123 K, Z = 2, D_{calc} = 1.379 g cm^{-3}, μ = 0.951 mm^{-1}, $F(000)$ = 1696, crystal size 0.50 × 0.10 × 0.05 mm, θ_{max} = 25°, 12 399 reflections collected, 6878 unique (R_{int} = 0.0524), 23 restrains, 478 parameters, GOF on F^2 = 1.066, final R indices for $I > 2\sigma(I)$ were R_1 = 0.0655, wR_2 = 0.1578. *Crystal data for* $\mathbf{2}\cdot\frac{1}{2}(F_4DIB)$: $2(C_{37}H_{42}N_6)\cdot 2(C_6F_4I_2)\cdot CHCl_3$, M_w = 2064.62 g mol^{-1}, monoclinic, space group $P2_1/n$, a = 5.9855(2), b = 33.665(1), c = 22.8345(8) Å, β = 95.906(2)°, V = 4576.8(3) Å^3, T = 173 K, Z = 2, D_{calc} = 1.498 g cm^{-3}, μ = 12.037 mm^{-1}, $F(000)$ = 2052, crystal size 0.40 × 0.20 × 0.10 mm, θ_{max} = 63.48°, 1 3440 reflections collected, 7310 unique (R_{int} = 0.0691), 14 restrains, 528 parameters, GOF on F^2 = 1.077, final R indices for $I > 2\sigma(I)$ were R_1 = 0.0594, wR_2 = 0.1613. Data were collected on a Bruker Kappa Apex II diffractometer with graphite-monochromatized Mo-Kα (λ = 0.71073 Å) radiation for $\mathbf{1}\cdot\frac{1}{2}(F_4DIB)$ and Cu-Kα (λ = 1.54184 Å) radiation for $\mathbf{2}\cdot\frac{1}{2}(F_4DIB)$. Collect software[18] was used for the data measurement and DENZO-SMN[19] for the processing. The structures were solved by direct methods with SIR97[20] and refined by full-matrix least-squares methods with WinGX-software,[21] which utilizes the SHELXL-97 module.[22] A few geometrical (DFIX, DANG and SADI) and thermal parameter (ISOR) restraints were used to fix severely disordered chloroform solvates to be chemically reasonable in both structures.

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