Crystal Engineering

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Spiraling Steroids: Organic Crystals with Asymmetric Nanometer-Scale Channels**

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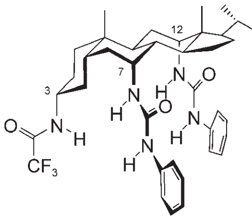
Crystalline microporous (or nanoporous) solids are widely sought and studied.[1] Such materials provide challenges for crystal engineering and find applications in catalysis, separation techniques, gas storage, sensors, lasers, and so forth. Robust structures with large voids are especially interesting, as they are able to accommodate the widest range of guests. Channels that measure ≥ 1 nm in diameter are fairly common in inorganic[1a–c] and, especially, metal–organic-framework (MOF)[1c–g] materials. However, purely organic structures with such dimensions are rare, especially if macrocyclic molecules are excluded.[2] We now report a new class of nanoporous organic crystals with chiral, unidirectional channels, tunable to diameters in excess of 14 Å.

This discovery arose from our program on steroid-based anion receptors.[3] The "cholapod" **1** belongs to a series of compounds derived from cholic acid **2**, in which hydrogen-bond donor units are deployed on the bile acid scaffold. The urea groups at C7 and C12 are constrained by the axial orientation of the C–N bond, such that the NH groups point towards each other. The amide moiety at C3 can also point inwards, thus cooperating in hydrogen-bond donation to anionic guests. Molecules from this family are powerful anion receptors,[4] and also act as anion carriers across bilayer membranes.[5]



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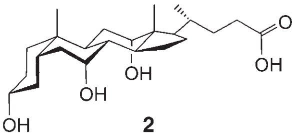

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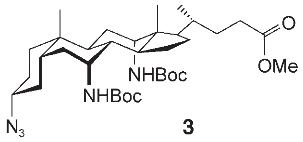
Cholapod **1** was prepared from **2** via intermediate **3**[6] (see the Supporting Information; Boc = *tert*-butoxycarbonyl).



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Crystallization from methyl acetate, which contained small amounts of water, gave needles up to 5 mm long and approximately 0.2 mm wide. The crystal structure was solved in the $P6_1$ space group.[7] The individual molecules were found to bind one molecule of water (see Figure 1 a). The trifluoroacetamide unit rotates such that the carbonyl group points inwards acting as an hydrogen-bond acceptor, whereas the urea groups act as hydrogen-bond donors to the oxygen atom from the water molecule. The hydrated steroids form columns parallel to the crystallographic *c* axis, reinforced by hydrogen-bonding interactions between the free O–H group of a water molecule contained in one complex and a carbonyl oxygen atom of a urea group in the next (Figure 1 b). The columns then pack in a hexagonal array to give channels centered on the *c* axis, defined by a right-handed spiral of steroids (Figure 1 c).[8] The internal surfaces possess an average diameter of 16.4 Å, with a minimum value of 14.3 Å (Figure 1 d).[7] The surfaces are formed mainly from hydrophobic CH and CF units, but also feature the carbonyl oxygen atoms from the ester groups. Around 30 % of the crystal volume is accessible to guests. The channels are filled with delocalized electron density, consistent with disordered solvent molecules. Face indexing of a single crystal showed

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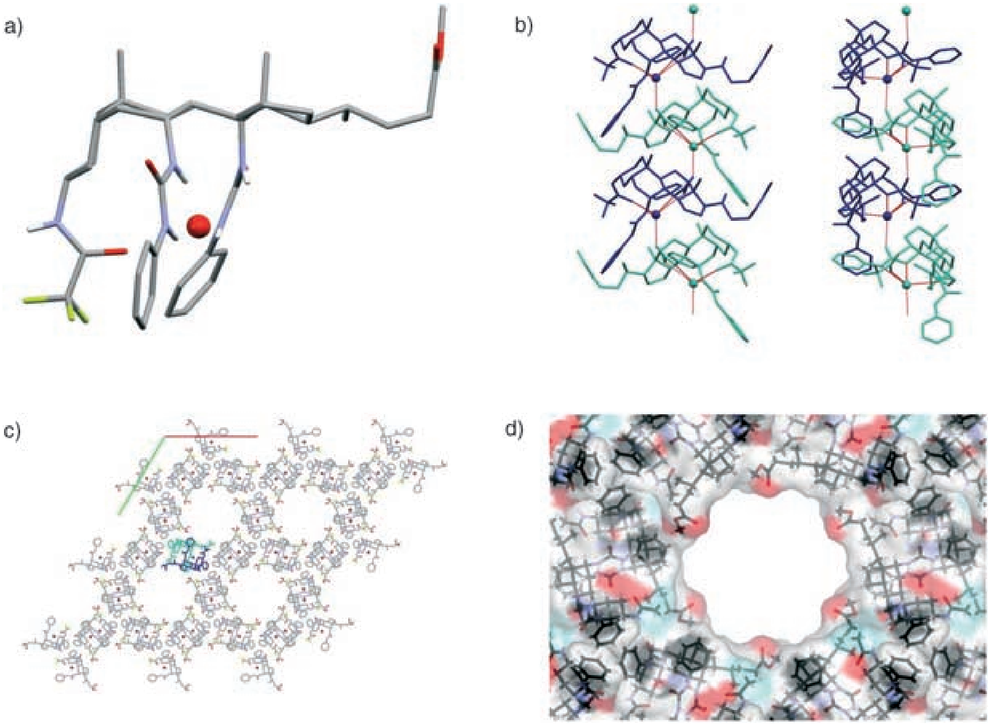


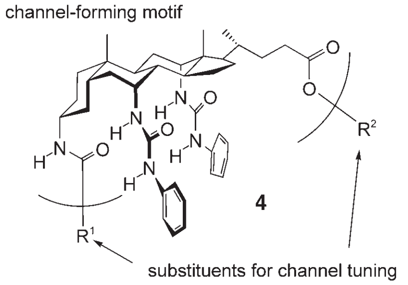
Figure 1. Representations of the crystal structure of **1**: a) A single molecule of **1** with the bound water molecule (red sphere; hydrogen atoms bound to carbon have been removed for clarity). b) Columns of **1**·H_2O parallel to the channel axis shown from two perspectives (the steroid molecules are shown in green and blue and the hydrogen-bonding interactions in red). c) The packing of columns to give channels, viewed along the channel axis (steroid molecules in one column are highlighted in green and blue). d) Interior surface of a channel, calculated by using a 1.4-Å probe; the surface is color coded according to the underlying atoms (red: oxygen, blue: nitrogen, green: fluorine).

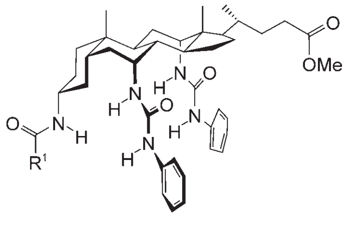
that, as expected, the channel axis coincided with the long axis of the needles.

The contents of the channels were investigated by ^1H NMR spectroscopic analysis. Crystals of **1** were removed from the solvent, air-dried,[9] and dissolved in deuterated acetone (99.96 atom % D) under anhydrous conditions.[7] Integration of the NMR spectrum implied a composition of **1**·0.75 MeOAc·3.5 H_2O.[10] Even allowing for the single H_2O molecule bound to each molecule of **1**, this result implies that water is concentrated in the channels and explains our observation that small amounts of water aid crystallization. The solvent was lost and the crystals became opaque on vacuum drying;[11] however, X-ray powder diffraction showed that the channel structure was maintained.[7] Solvent exchange was also demonstrated. Samples removed from MeOAc were washed with diethyl ether or toluene, air-dried,[9] and analyzed by ^1H NMR spectroscopy. In both cases, the MeOAc had disappeared and the replacement solvent was present (approximately 0.5 equiv). Vacuum-dried samples suspended in toluene also absorbed the solvent. When these toluene-solvated crystals were washed briefly (approximately 30 s) with CH_2Cl_2, the toluene was retained. Thus, solvent exchange is slow, which is consistent with absorption into the nanoporous framework.

The structure of **1** is notable in several respects. First, the channels are among the largest observed for purely organic systems. Second, they are persistent and accessible, as shown above. Inclusion complexes of bile acid derivatives are well known and well studied,[12] but the formation of such large, physically robust pores is unprecedented. The crystals are chiral and also lack any regular axis of symmetry, so the pores are aligned in one direction. Finally, the interactions which govern the packing do not seem to involve the terminal CF_3 and methyl ester groups, both of which point into the channels. This suggests a generalizable motif 4, with potential for tuning. These interactions suggest the generalized motif of **4**, which can be potentially used to tune channel width and properties by variation of the R^1 and R^2 groups.

Considering this last point, we examined other steroids of type **4** from our anion-receptor program. Compounds **5**[13] and **6**[7]





5: R^1 = NHPh
6: R^1 = O*t*Bu

crystallized as needles and were subjected to X-ray crystallographic studies. Both **5** and **6** formed nanoporous structures in which the disposition of the steroid nuclei was almost identical to that in **1**. However, the variation of the R^1

group induced significant changes. In the case of **5**, the bulky NHPh group protrudes into the channel and, more importantly, displaces the OMe unit from the channel wall. The ester group rotates to create a more irregular, narrower pore with an average diameter of 15.7 Å (minimum diameter = 11.6 Å; Figure 2).[7] In the case of **6**, the O*t*Bu group seems to create an intermediate situation, in which the ester groups are randomly distributed between the two orientations. If an alternating arrangement is assumed, the average and minimum diameters are 16.4 and 12.3 Å, respectively.[7] The crystal structures of **1**, **5**, and **6** are compared in Figure 3, which highlights the position of the terminal R^1 groups at the channel surfaces.

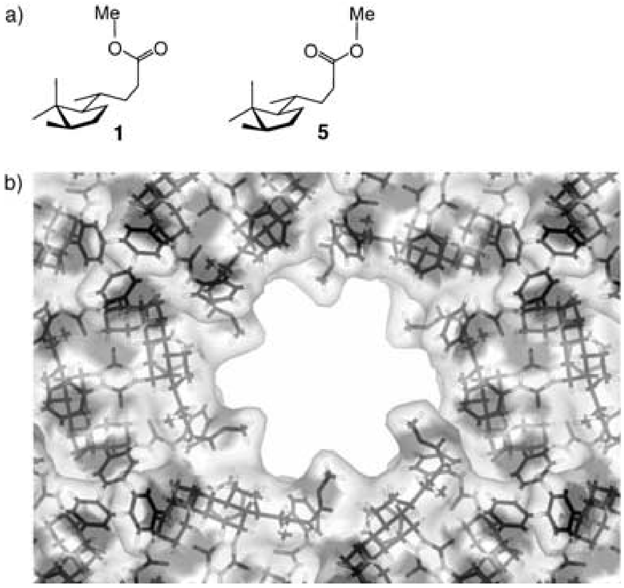


Figure 2. a) Orientation of the methyl ester groups in **1** and **5**. b) Interior surface of **5**. In contrast to **1** (see Figure 1 d) the OMe groups are directed inwards, thus creating protrusions in the channel wall.

To conclude, we have found a new steroid-based motif which generates robust, asymmetric, and nanoporous structures of unusual dimensions. The channels are codirected[14] and large enough to accommodate a wide variety of organic molecules, including, for example, dyes or substrates for catalysis. We will investigate such possibilities in future investigations, with a view to the development of novel functional organic materials.

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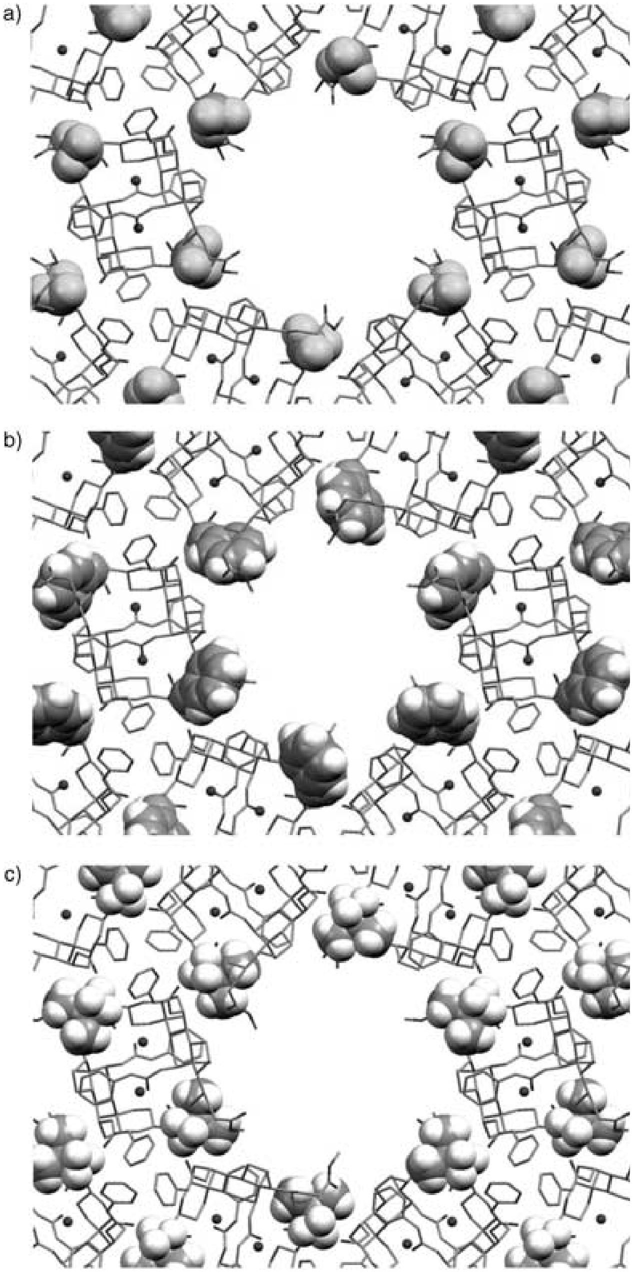

Figure 3. Structures of **1**, **5**, and **6** viewed down the channel axis, with terminal R^1 groups (see **4**) represented in the space-filling mode. a) Trifluoroacetamide **1** ($R^1 = CF_3$), b) trisurea **5** (R^1 = NHPh), c) carbamate **6** (R^1 = O*t*Bu).

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[9] Air was allowed to pass, for 10 minutes, through the crystals with a Hirsch or Buchner funnel.

[10] This formula implies that approximately half of the volume in the NMR sample that was accessible to the guest species was occupied by solvent molecules; the remainder was presumably replaced by air during the drying process.

[11] The crystals were evacuated by using an oil pump for 24 hours.

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[14] This term is used to imply that the channels are both directional (namely, asymmetric with respect to direction of view along the *c* axis) and aligned (pointing in the same direction).