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A Chiral Nanosheet Connected by Amide Hydrogen Bonds

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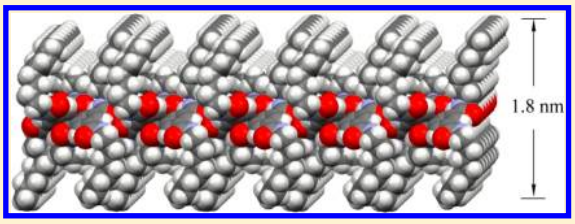
Supporting Information

ABSTRACT: A chiral organic nanosheet spontaneously assembled under mild conditions from *N*,*N*′,*N*″-tris(*n*-octyl)benzene-1,3,5-tricarboxamide, which is a C_3-symmetric supramolecular atropisomer. Similar to the β-pleated sheets of polypeptides, the hydrogen bonded backbone of the chiral sheet does not involve side chains. The sheetlike structure was directly observed by TEM and confirmed by powder and single crystal X-ray diffraction analysis. The generality of the chiral nanosheet was demonstrated by an inverted tricarboxamide with significant structural differences.



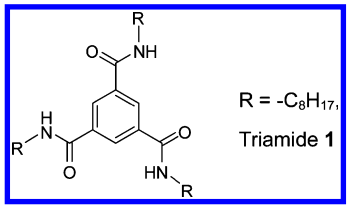
Organic sheets formed by spontaneous self-assembly are ubiquitous in nature. The cell membranes of almost all living organisms and many viruses are made of a lipid bilayer, which is a well-known example of such sheets. As a two-dimensional chiral structure, β-pleated sheets comprise 20–28% of all residues of globular proteins and play a key role in living systems.[1] They are formed by a spontaneous self-assembly process via amide hydrogen bonds. The higher-level association of β-sheets has been implicated in many human diseases including Alzheimer's and type II diabetes.[2,3] Given the importance of β-sheets in biological systems, structural mimicry of such organic chiral structures is of fundamental importance, as the chiral surface of the sheet can serve as a platform for enantioselective synthesis[4,5] or chemical/biological detection.[6] Other applications of chiral sheets include membrane-based chiral separation and molecular device construction. Recently, crystalline achiral nanosheets have been successfully self-assembled from peptoid polymers[7] and bis-acylurea,[8] respectively. However, the laboratory construction of chiral sheets from achiral molecules remains elusive. Herein, we report the first example of a chiral organic nanosheet spontaneously assembled from an achiral molecule by amide hydrogen bonds. The sheet self-assembled from *N*,*N*′,*N*″-tris(*n*-octyl)benzene-1,3,5-tricarboxamide (**1**), a C_3-symmetric triamide with three alkyl chains of eight carbon atoms (Scheme 1).

In the last several decades, C_3-symmetric compounds bearing amide groups have demonstrated a variety of practical and theoretical applications such as liquid crystals,[9] low molecular weight organogelators,[10] polyvalent inhibitors,[11] artificial receptors,[12] nucleating/clarifying agents for isotactic polypropylene,[13] dendrimers,[14] porous coordination polymers,[15] supramolecular polymers,[16] organic diodes,[17] and chiral amplification.[18] C_3-symmetric triamides have received such attention because they provide perhaps an optimum balance between enhanced properties, such as binding and ease of synthesis and analysis.[19] Our interest in C_3-symmetric triamides resides in their ability to form nanomaterials. The facile chiral nanosheets form under a variety of conditions. Parts a and b of Figure 1 show the transmission electron microscope (TEM) image of a sheet formed by injecting an acetone solution of triamide **1** into water with stirring and then evaporating under ambient conditions. The crystalline sheet thus formed has an irregular shape with rough edges. By slowly evaporating a dilute acetone/H_2O (1:3) solution, sheets with smooth edges were obtained (Figure 1c). We found it of interest to note that slowly evaporating triamide **1** in a neat solvent grade acetone, approximately half of the material formed irregularly shaped sheets (Figure 1d), while the other rolled to form rods (Figure 1e). By using the nonpolar solvent heptane, the majority of the sheets rolled to form long fibers, although some thin sheets could still be seen (Figure 1f).

Regardless of their appearance under TEM, powder X-ray diffraction (XRD) confirmed that they have the same or very similar crystalline isoforms (Figure 2). It is notable that the powder of compound **1** obtained directly from the synthesis without further processing also has the same powder XRD pattern. The highest peak at 4.4° corresponds to diffracting planes nearly 2 nm thick.

The sheet structure was further confirmed by X-ray crystallography. Single crystals were obtained by slow evaporation of an ethyl acetate solution of triamide **1**. The X-

Scheme 1. Structural Formula of *N*,*N*′,*N*″-Tris(*n*-octyl)benzene-1,3,5-tricarboxamide



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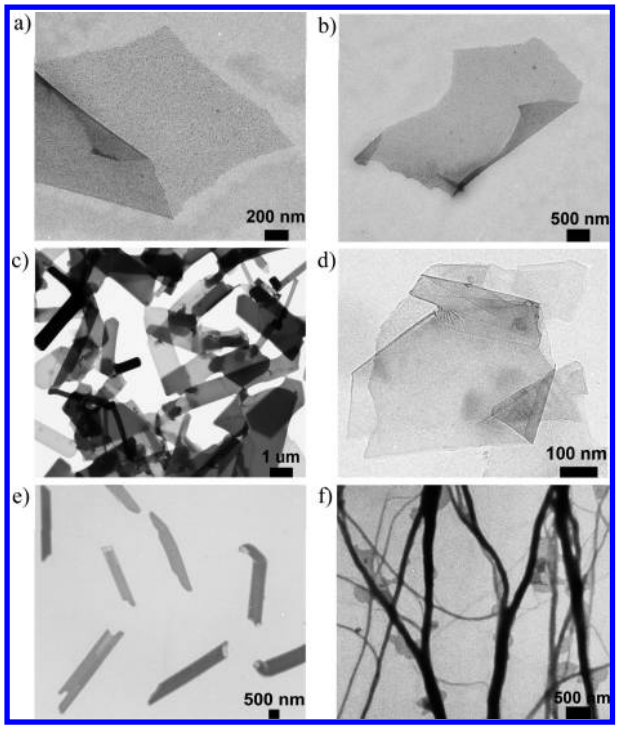

Figure 1. TEM images of tricarboxamides **1**: (a and b) the triamide sheet obtained by injecting 100 μL of 2×10^{-3} M acetone solution into 10 mL of H_2O with stirring and then evaporating the solvents; (c) sheets with smooth edges from a solution of 1.25×10^{-4} M acetone/H_2O (1:3); (d) sheets from slowly evaporating 10^{-3} M acetone solution; (e) rolled sheets from slowly evaporating 10^{-3} M acetone solution; (f) fibers formed with rolled thin sheets by evaporating 2×10^{-4} M triamide heptane solution.

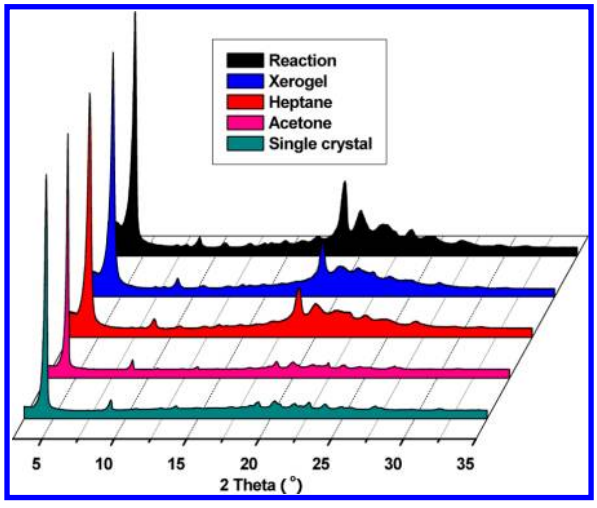

Figure 2. Powder XRD of compound **1** showing that the same or very similar crystalline isoform was obtained from a variety of conditions. (1) black: powder obtained directly from the synthesis without further processing; (2) blue: xerogel from 50 mg/mL cyclohexane solution; (3) red: powder obtained by the slow evaporation of 10^{-3} M heptane solution under ambient conditions; (4) pink: powder obtained by the slow evaporation of 10^{-3} M acetone solution under ambient conditions; (5) dark cyan: ground crystals obtained by the same conditions under which single crystals were grown.

ray structure of **1** displays hydrogen bonding sheets as shown in Figure 3.[20,21] Each molecule is connected to six neighbors through intermolecular hydrogen bonds between the N—H

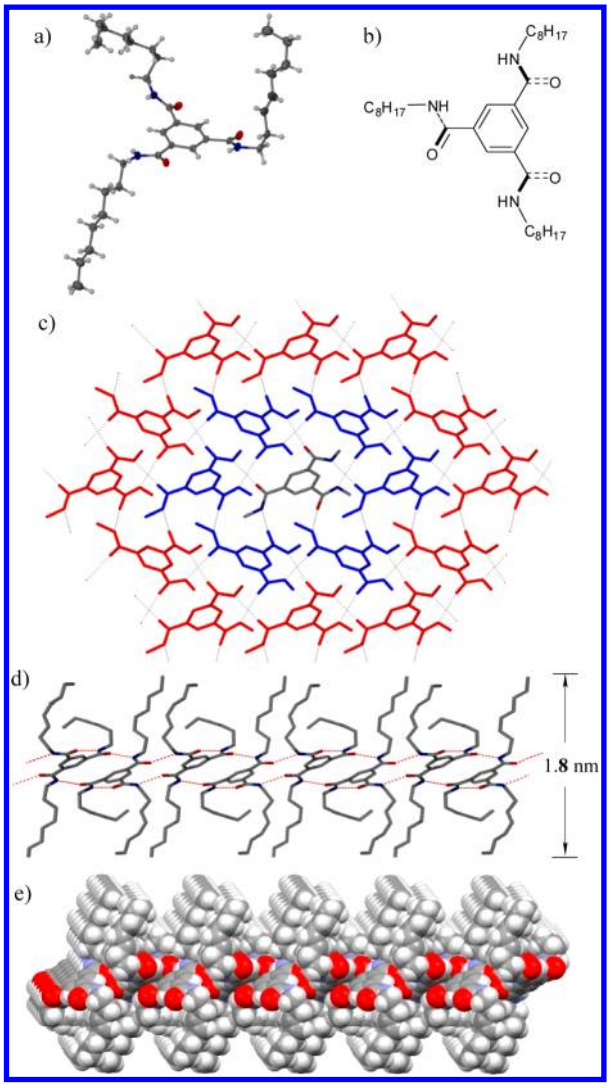

Figure 3. Crystal structure of tricarboxamide **1**: (a) Oak Ridge thermal ellipsoid plot (ORTEP) representation at 50% electron density; (b) chiral conformation of the triamide; (c) top view of a capped stick model demonstrating a chiral amide hydrogen bonded network (The hydrogen atoms are omitted and the side chains are replaced with carbon atoms for simplicity. Molecules are different colors to show each molecule is connected to six neighbors through intermolecular hydrogen bonds.); (d) side view of a capped stick model showing one layer of the sheet; (e) space-filling perspective of the sheet showing the chiral surfaces and edges. Only 60 (10 × 6) molecules are shown for clarity.

and C═O groups of the three carboxamides (Figure 3c, each side chain is replaced with a carbon atom for simplicity). The crystal structures consist of a supramolecular sheet extended in the crystallographic *ab* plane through the hydrogen bonded network. The six hydrogen bonds are 2.80, 2.87, 2.80, 2.81, 2.81, and 2.87 Å, respectively. The average hydrogen bond length in the supramolecular sheet is 2.83 Å, which is 0.14 Å shorter than those found in a triple helical crystal structure of *N*,*N*′,*N*″-tris(2-methoxyethyl)benzene-1,3,5-tricarboxamide (R = $-CH_2CH_2OCH_3$, Scheme 1),[22] which shows that the sheet backbone hydrogen bonds are slightly stronger.

The different forms of the nanosheet observed by TEM are presumably due to the stability of the hydrogen bonds on the edges of the sheets in different solvents. The presence of H_2O offered both hydrogen acceptors and donors stabilizing the

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hydrogen bonds on the edges of the sheet. Thus, crystals and sheets with smooth edges were obtained from a mixture of acetone and H_2O. The sheet edges were less stabilized in pure acetone, so sheets with rough and rolled edges were obtained. In the nonpolar solvent heptane, the solvent molecules stabilize the two hydrophobic faces of the sheet, which disturbs stacking of the sheets. Meanwhile, the hydrophilic edges of the sheets are unstable in a nonpolar environment, so the sheets roll onto themselves into fibers to minimize the surface area of the edges.

In the amphipathic structures, two nearest neighboring molecules formed complementary conformations with three alkyl arms. One molecule portrays an "up−up−down" conformation and the other a "down−down−up" conformation with respect to the hydrogen bonded sheet planes (Figure 3d). Therefore, the polar amide cores are sandwiched by two layers of nonpolar alkyl chains. This sheet structure with nonpolar and polar segments separate from each other is similar to the lipid bilayer of a cell membrane. Each layer is close to 2 nm thick, and the supramolecular sheets are mainly stabilized by two forces: hydrogen bonding between amides and the hydrophobic effect between peripheral nonpolar *n*-octyl chains. No $\pi-\pi$ stacking within or between the supramolecular sheets was observed: only van der Waals forces of the alkyl chains standing or lying on the surface of each sheet. The transparent plane-shaped crystals of **1** could be carefully peeled into a delicate thin film using adhesive tape or a sharp knife. When rubbed, the crystals and powder form of triamide **1** felt like wax. These physical properties of the crystals of **1** can also be understood by its sheet structure.

A remarkable feature of the sheet is the supramolecular chirality.[23] Each triamide molecule contains three stereogenic axes. The six atoms within each amide are nearly planar, and each amide group is partially tilted with respect to the core aryl ring to fulfill requirements of the hydrogen bonds' orientations and close packing of the molecules. Two of the three amides are pointing toward the same direction (Figure 3b). The torsion angles are 15, 16, and 34°, respectively. The distances of three C−C single bonds connecting the amide groups and benzene ring are approximately 1.51 Å, which is close to the typical bond length of a C−C single bond, showing that there is only weak conjugation between them. However, due to the hydrogen bonds, the amide groups are not free to rotate around the C−C single bond axes in this supramolecular atropisomer,[24,25] resulting in a three-dimensional chiral conformation fixed in the hydrogen bonded network as show in Figure 3b and c. All the triamide molecules in a sheet adopt the same conformation. Consequently, the hydrogen bonded sheet is chiral. The triamide **1** formed chiral crystals with a $P2_1$ space group, and each sheet in a crystal has the identical chirality. It is interesting to notice that one of three *n*-octyl arms in compound **1** is significantly curved to fill up the space. As a result, the neighboring sheets are packed like meshing gears to achieve close packing. Remarkably, the grooves on the surface of the sheet are also chiral as a consequence of the chiral hydrogen bonded network (Figure 3e).

The sheet represents a fundamental and prevalent structure not limited to triamides with long alkyl side chains. The crystal structures of *N*,*N*′,*N*″-tris(methyl)benzene-1,3,5-tricarboxamide (R = $-CH_3$, Scheme 1) and *N*,*N*′,*N*″-tris(ethyl)-benzene-1,3,5-tricarboxamide (R = $-CH_2CH_3$, Scheme 1) showed the same sheet structure as well.[26,27] Just like the β-sheets of polypeptides, the hydrogen bonded backbone of the chiral sheet does not involve side chains. Thus, different functional groups with suitable sizes can be introduced onto the chiral structure to tune the properties of the sheet and achieve the desired functionality.

The generality of the chiral sheet structure is further demonstrated by forming a similar sheet using *N*,*N*′,*N*″-(benzene-1,3,5-triyl)tris(3-cyclopentylpropanamide) **2** as shown in Figure 4a. The C_3-symmetric inverted triamide **2**

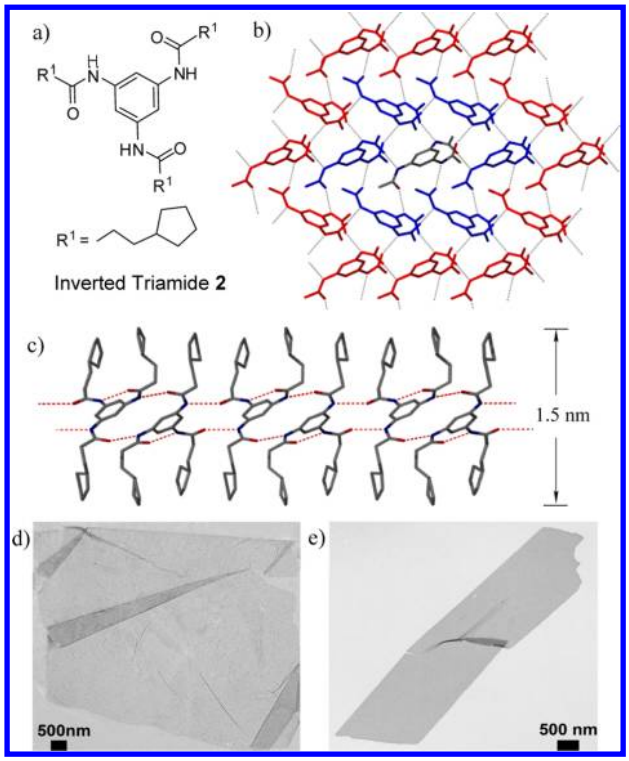

Figure 4. Inverted tricarboxamides **2**: (a) chemical structure; (b) top view of a capped stick model showing the chiral amide hydrogen bonded network of **2** (simplified by the same method of Figure 3c); (c) a side view of a capped sticks model showing one layer of the sheet; (d) TEM image of the nanosheets from 100 μL of 2×10^{-3} M ethyl acetate solution injected into 10 mL of H_2O under stirring and then evaporating the mixed solvent; (e) TEM image of the inverted triamide obtained by injecting 100 μL of 2×10^{-3} M ethanol solution into 10 mL of H_2O with stirring and then evaporating the mixed solvent.

has two significant structural differences from triamide **1**: (1) the amide group is connected onto the aryl core by an N atom of amide instead of a C═O group; (2) the side chain contains a 5-membered ring rather than a linear alkyl group.

Crystals of the inverted benzene triamide **2** were obtained from ethyl acetate, and the X-ray diffraction data was collected.[28,29] The six hydrogen bonds are 2.84, 2.90, 2.90, 2.90, 2.84, and 2.90 Å, respectively. The average hydrogen bond length in the supramolecular sheet based on the inverted triamide **2** is 2.88 Å, which is 0.05 Å longer than that of sheet based triamide **1**. The torsion angles between the carboxamide planes and the core aryl plane are 25, 28, and 48°, respectively. As expected, the angles are considerably higher than those of triamide sheet **1**, indicating less conjugation between the three amides and the benzene ring. The hydrogen donor (N−H) and the hydrogen acceptor (C═O) exchange their positions in the hydrogen bonded network (Figure 3c and 4b), demonstrating a key difference between the sheet of inverted triamide **2** and that of the triamide **1**. Nevertheless, the resulting chiral hydrogen

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bonded network of the inverted triamide **2** has the same pattern as triamide sheet **1**. Figure 4c shows one layer of the hydrogen bonding sheet of inverted triamide **2** with each layer about 1.5 nm thick. All the peripheral cyclopentyl groups are roughly perpendicular to the plane of the hydrogen bonded sheet. In contrast to triamide **1**, the inverted triamide **2** formed racemic crystals with a $P2_1/n$ space group, and the two neighboring sheets are a pair of supramolecular enantiomers.[23]

Injection of inverted benzene triamide 2-ethyl acetate solution into water with stirring followed by evaporating the mixed solvent produced sheets with rough edges (Figure 4d). The sheets were up to 100 mm^2. Following the same procedure using an ethanol solution of **2** gave rise to sheets with smooth edges (Figure 4e). The different shapes and sizes of the sheets obtained from ethyl acetate and ethanol solutions of **2** are consistent with our initial hypothesis that the polar solvent ethanol, which contains both hydrogen bond donors and acceptors, stabilizes the hydrogen bonds on the edges of the sheet better than ethyl acetate.

In summary, we discovered a thin and chiral sheet self-assembled from achiral small organic molecules. The morphology of the crystalline sheet can be varied depending on the solvents used. This finding provides an example for the construction of hydrogen bonded chiral nanosheets based on simple achiral compounds. The chiral surface of the sheet may have potential to be modified for applications used in different fields, such as chiral separation, analysis, catalysis, and synthesis.[30] The facile synthesis, generality, and adaptable nature[31] of the nanosheet structure demonstrate the possibility of these further studies. Moreover, this fundamental chiral sheet structure of C_3-symmetric triamides will offer a new way to understand and rationalize their known properties[9−19] and help to identify new applications in crystal engineering,[32] supramolecular chemistry,[33] and soft matter.[34]

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedure, full characterzation and spectra, and crystallographic data of compounds **1** and **2** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

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Notes

The authors declare no competing financial interest.

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(20) Crystal data for compound **1**: colorless, 0.60 × 0.30 × 0.10 mm^3, $C_{33}H_{57}N_3O_3$, M = 453.82, monoclinic, $P2(1)$, a = 11.9029(3) Å, b = 7.6500(2) Å, c =18.0677(5) Å, β = 97.230(2)°, V = 1632.11(7) $Å^3$; T = 150 (2) K, D_{calc} = 1.102 g cm^{-3}, Z = 2, reflections collected = 17918, independent reflections = 4875 (R_{int} = 0.0321), R values [$I > 2\sigma(I)$, 3656 reflections]: R_1 = 0.0561, $wR2$ = 0.1366; S = 1.091; CCDC 865143.
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(28) Crystal data for compound **2**: colorless, 0.40 × 0.30 × 0.10 mm^3, $C_{30}H_{45}N_3O_3$, M = 495.70, monoclinic, $P2(1)/n$, a = 12.2508(4) Å, b = 6.9026(2) Å, c = 33.6570(10) Å, β = 98.418(2)°, V = 2815.45(15) $Å^3$; T = 173 (2) K, D_{calc} = 1.169 g cm^{-3}, Z = 4, reflections collected = 27442, independent reflections = 5707 (R_{int} = 0.0287), R values [$I > 2\sigma(I)$, 3752 reflections]: R_1 = 0.0942, $wR2$ =0.2589; S = 1.033; CCDC 865142.
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