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The self-assembly of six-petal microflowers by hydrogen-bonded shape-persistent triangular aromatic hydrazide derivatives

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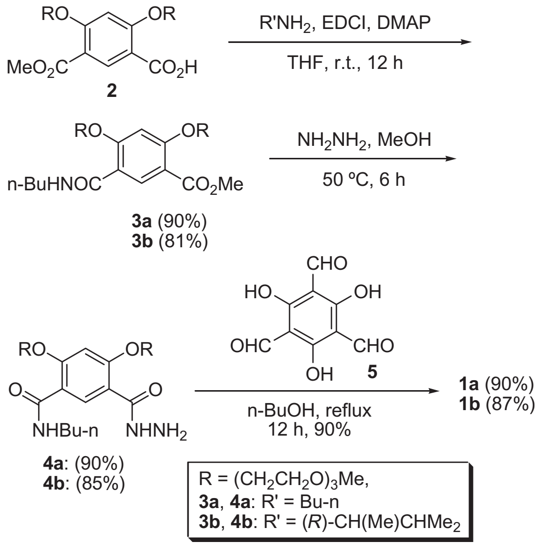
ABSTRACT

Six-petal microflowers have been self-assembled in methanol from C_3-symmetric shape-persistent triangular aromatic hydrazide derivatives. Nine intramolecular hydrogen bonds are used to enhance the planarity of the aromatic backbone, while six 2-(2-(2-methoxyethoxy)ethoxy)-ethoxyl groups are appended to the rigid aromatic backbone. Scanning electron microscopy (SEM) images show that the molecules form unique six-petal flower-like aggregates in methanol. A self-assembling mechanism that is similar to the formation of snowflakes has been proposed.

The self-assembly of aromatic molecules into well-defined supramolecular architectures has received considerable interest in the past decades due to their fundamental and practical importance. In this context, the aggregation of several C_3-symmetric aromatic systems has been extensively investigated, which lead to the formation of supramolecular liquid crystals,[1] vesicles,[2] and organogels,[3] or the generation of supramolecular chirality.[4] We have recently utilized the intramolecular hydrogen bonding to induce linear aromatic amide or hydrazide molecules to adopt folded or extended conformations.[5] The hydrazide-based shape-persistent oligomers that bear amphiphilic or hydrophobic side chains may stack to form vesicles or organogels.[6] Herein, we report that two hydrogen-bonded shape-persistent triangular aromatic hydrazide derivatives can self-assemble into unique six-petal flower-like architectures. To the best of our knowledge, this is the first example that organic aromatic molecules stack to produce snowflake-styled aggregates, although several examples of six-petal flower-shaped structures that are obtained from inorganic salts have been reported.[7]

Triangular compounds **1a**–**c** have been designed and prepared. Nine six-membered N–H···OR hydrogen bonds are introduced to enhance the planarity of the aromatic backbones,[8] whereas six 2-(2-(2-methoxyethoxy)ethoxy)-ethoxyl groups are appended to balance the amphiphilicity of the whole molecules. The synthesis of these molecules is straightforward. The synthetic routes for **1a** and **1b** are provided in Scheme 1.[9] Thus, acid **2**[6a] was first coupled with the related amines to give **3a** and **3b**, respectively, in high yields. The two ester intermediates were then treated with an excess of hydrazine monohydrate in hot methanol to yield compounds **4a** and **4b**, which were further reacted with trialdehyde **5**[10] to produce **1a** and **1b** in high yields. ^{1}H NMR spectra of the crude products in $CDCl_3$ showed that all the starting materials were consumed and one set of signals was exhibited. Considering the sensitivity of the ^{1}H NMR technique, we proposed that the triangular products should be formed in ⩾95% yield. Instead of using simple benzene-1,3,5-tricarbaldehyde, compound **5** was chosen for the reactions because it could form three stable six-membered O–H···N intramolecular hydrogen bonds,[11] which remarkably rigidified and stabilized the core of the aromatic systems. The synthesis of compound **1c** is shown in Scheme 2. The key precursor **7** was first prepared by tolylation of ol **6**[12] in chloroform. Then, compound **8** was coupled with *n*-butylamine to give **9**. The diol was



Scheme 1. The synthesis of triangular compounds **1a** and **1b**.

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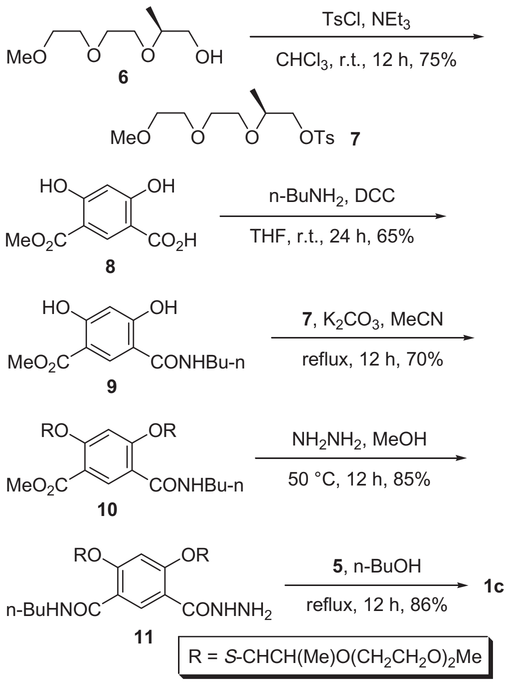
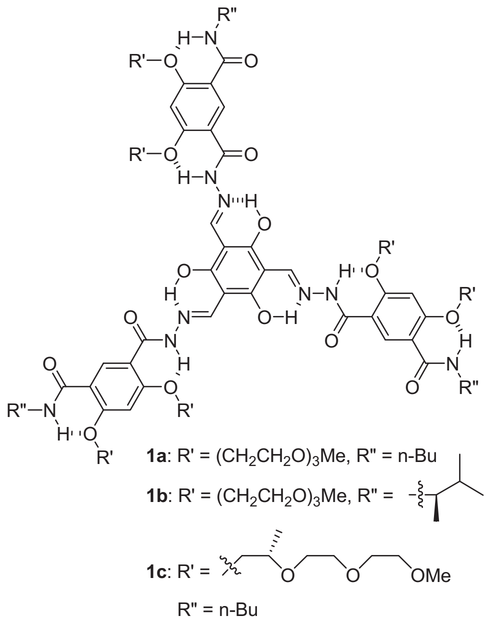


Scheme 2. The synthesis of triangular compound **1c**.

further reacted with tosylate **7** to produce ester **10**, which was treated with an excess of hydrazine to afford benzohydrazide **11**. Finally, this precursor was reacted with **5** to produce **1c** in 85% yield.



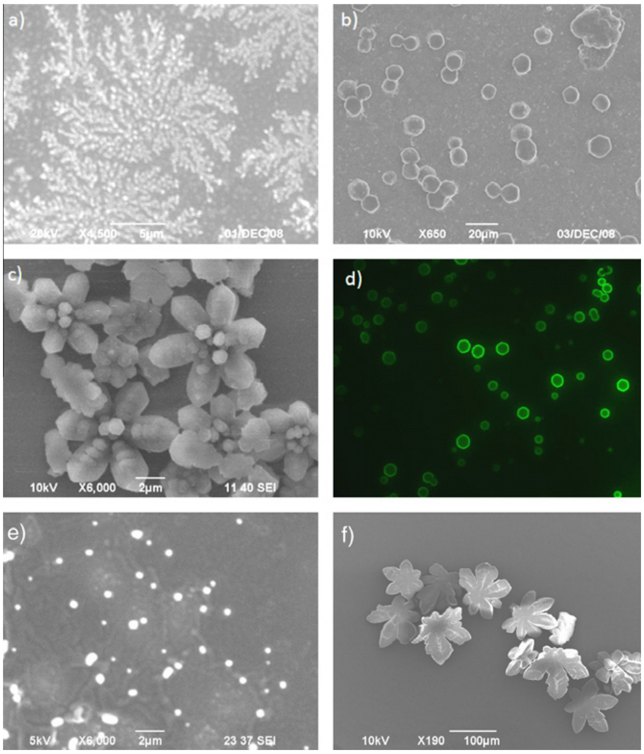


Figure 1. SEM images on mica surface: the samples of **1a** after its MeOH solution (1 mM) was evaporated in (a) 1 min, (b) 5 min, and (c) 30 min. (d) Fluorescence micrograph of the sample for obtaining the second image. The samples of (e) **1b** and (f) **1c**, after their MeOH solution (1 mM) was evaporated in 30 min.

Scanning electron microscopy (SEM) images showed that compound **1a** formed dendrites that consisted of particles of nano scales (Fig. 1a), when its solution in methanol was evaporated quickly. With the evaporation rate being slowed down, hexagonal platelets and then six-petal flower-shaped crystals were generated selectively (Fig. 1b and c). The formation of the hexagonal platelets was also confirmed by the fluorescent microscopy image (Fig. 1d). The average diameter of the hexagonal platelets was estimated to be about 12 μm (calculated from 30 platelets), while the diameter of the six-petal flowers ranged from 4 μm to 11 μm. This difference implied that their formation followed different growth mechanisms. The SEM images of compound **1b** revealed that this triangular molecule did not generate any of the above ordered structures (Fig. 1e), probably due to the steric effect of the larger 3-methylbutan-2-yl groups, which were close to the aromatic core and presumably weakened the stacking of the aromatic backbone. Compound **1c** formed the similar six-petal flowers (Fig. 1f). This compound has six chiral side chains, but its assembled flowers did not display an observable chiral bias. The SEM images also showed that the samples obtained by evaporation of the mixture solution of **1a** and **1c** within the molar ratio of 9:1–1:9 in methanol all generated six-petal flower-shaped crystals, suggesting that their aggregation might follow the identical mechanism. The introduction of the chiral atom in **1b** and **1c** were originally used to test if a chiral differentiation was induced for the flower-shaped aggregates, which we did not observe from the SEM images.

The maximum absorbance wavelength of compound **1a** in the UV–vis spectra in methanol was shifted from 382 nm to 340 nm, when the concentration was increased from 0.5 μM to 7 μM. The large blue shifting indicated that it stacked in a H-aggregation (face-to-face) form even in very dilute solution.[13,14] Diluting the solution of **1a** in CD_3OD from 5 mM to 0.2 mM caused the signal of its H-5 proton of the peripheral benzene ring in the ^1H NMR spectra to shift downfield by 0.08 ppm. This result supported that the molecule further stacked at higher concentrations. The X-ray diffraction (XRD) of the dried samples of **1a** obtained by evaporating its solution (1 mM) in methanol or the mixture of methanol and water (1:1) revealed a broad peak at 0.40 nm and a strong, sharp peak at 1.6 nm, respectively. The former peak might be attributed to a less compact stacking of the aromatic backbone,[15] while the latter peak was close to the size of the backbone

(1.7 nm) and thus suggested a column-styled structure in the solid state.

To get more insight into the formation mechanism of the unique flower-shaped crystals, the effect of the media was also studied for compound **1a**. Adding benzene to the solution of methanol remarkably impeded the formation of the flowers. When the content of benzene was increased to 10% (v/v), no ordered structures were observed on the SEM image. This result further supported that stacking interaction played a key role for the formation of the assembled flowers. The existence of benzene not only decreased the polarity of the medium, but also, presumably more importantly, stacked with the aromatic systems of **1a** and thus weakened their own stacking.

The self-assembling behavior of compound **1a** in the mixture of methanol and water was also investigated by SEM. The results are presented in Figure 2. Before the content of water was increased to 50%, six-petal flowers were always observed on the SEM images (Fig. 2a–c). However, further increase of water resulted in the selective formation of new leaf-like crystals (Fig. 2d). When the content of water was increased to 90%, hexagonal rod-like crystals were generated exclusively (Fig. 2e and f), although their average size was considerably smaller that that formed by quickly evaporating the solution of **1a** in methanol (Fig. 1b). These results may be rationalized by considering that, with the increase of the medium polarity, the stacking of the aromatic systems was continually enhanced and consequently the crystals grew more quickly from the two ends of the small platelets. As a result, the growth from the side was suppressed.

It is reasonable to propose that the crystal growth of the new aromatic systems in the polar medium was a thermodynamically and dynamically balanced process. For the formation of the six-petal flowers, the first step should be the nucleation of the stacked aggregates into the hexagonal plates. These small crystals were always observed to co-exist together with the larger flower-shaped structures, as shown in Figs. 1c and 2a. For the formation of the hexagonal platelets, the triangular molecules might need to stack in a dislocated manner (Fig. 3). Once the hexagonal crystal cores were formed, they were grown more quickly from the corners than from the smooth facets, as established for the formation of snowflakes,[16] to produce the sectored flowers (Fig. 3). When the content of water was high enough, the stacking interaction was enhanced. Growth from the ends became overwhelming and the long prisms were eventually formed.

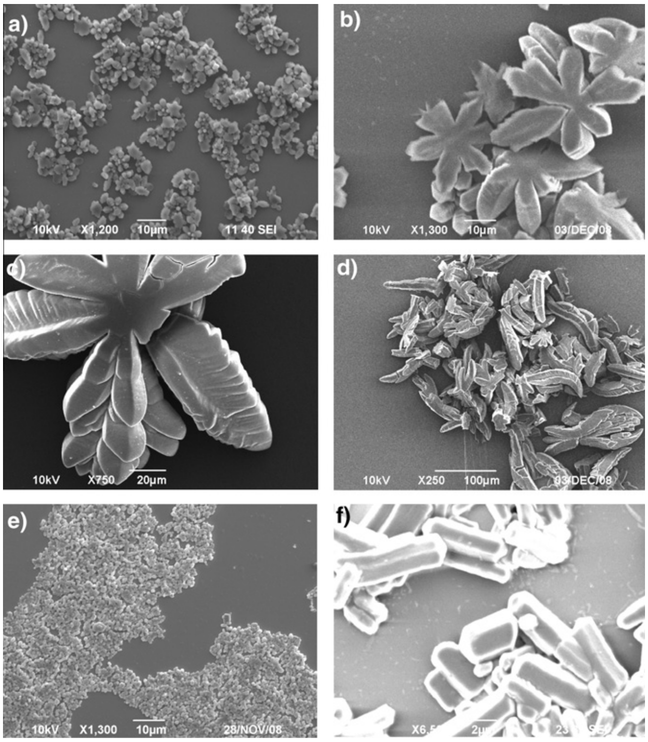


Figure 2. SEM images on mica surface of the samples of **1a**, after its solution in the mixture of MeOH and water (1 mM) was evaporated in 30 min. The content (v/v) of water is (a) 0%, (b) 30%, (c) 50%, (d) 70%, (e) and (f) 90%.

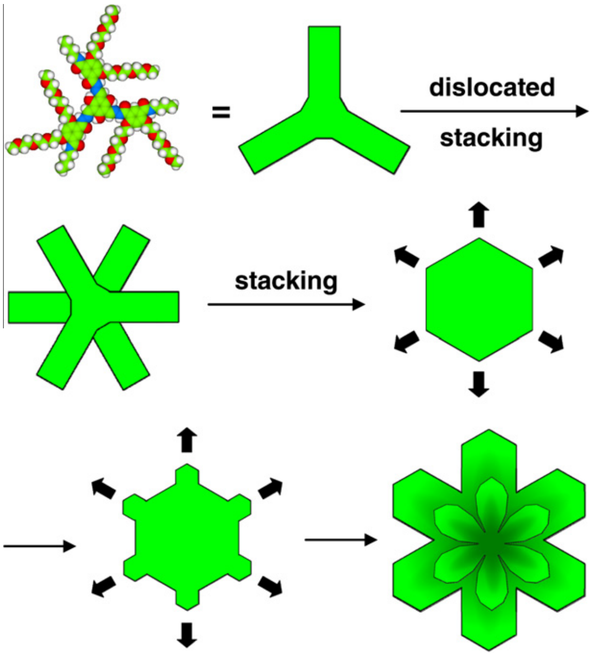


Figure 3. Possible mechanism for the formation of the six-petal flower-like aggregates of compounds **1a** and **1c**. After the hexagonal plates are formed, they grow more quickly from the corners than from the facets, like the process for the formation of snow-flakes.

In conclusion, we have demonstrated that hydrogen-bonded shape-persistent triangular aromatic hydrazides can self-assemble into six-petal flower-shaped crystals. The growth mechanism for this kind of unique supramolecular architectures has been proposed to resemble that for the formation of the snowflakes. The result illustrates that rationally designed rigid aromatic systems may exhibit new self-assembling property that is usually displayed by hard inorganic materials. In the future, we will investigate the structural factors that affect the formation of the flower-shaped crystals by designing new conjugated triangular molecules. The formation of the micro-scaled hexagonal rods also bodes well for future development of photo- and electro-active assembled structures. To realize this, large conjugated systems have to be designed.

Acknowledgments

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9. *Compound* **1a**: A solution of compounds **4a** (0.17 g, 0.30 mmol) and **5** (21 mg, 0.10 mmol) in butanol was heated under reflux for 12 h and then concentrated with a rotavapor. The resulting slurry was recrystallized from ether to give **1a** as a pale yellow solid (0.16 g, 90%). ^{1}H NMR (300 MHz, CDCl$_3$) δ: 13.36 (s, 3H), 11.06 (s, 3H), 8.67 (s, 3H), 8.43 (s, 3H), 7.62 (t, 3H), 5.97 (s, 3H), 4.44–3.28 (m, 96H), 1.60 (m, 6H), 1.41 (m, 6H), 0.98 (m, 9H). ^{13}C NMR (75 MHz, CDCl$_3$) δ: 164.37, 161.62, 159.96, 159.90, 159.33, 144.29, 136.45, 114.00, 112.09, 99.21, 96.08, 75.34, 39.70, 31.72, 28.36, 28.33, 20.38, 19.71, 19.39, 13.78. MS (MALDI-TOF): *m*/*z* 1857.4 [M+Na]$^{+}$. HRMS (ESI): calcd for $C_{87}H_{135}N_9O_{33}Na$: 1856.9067. Found: 1856.9055.
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