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Template-Controlled Face-to-Face Stacking of Olefinic and Aromatic Carboxylic Acids in the Solid State

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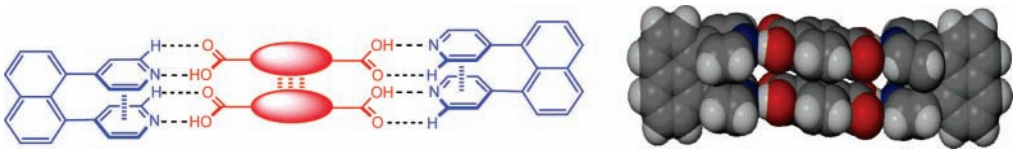
ABSTRACT



A rigid 1,8-dipyridylnaphthalene template for supramolecular organization of unsaturated dicarboxylic acids in the solid state has been developed. Self-assembly of the template and aromatic dicarboxylic acids generates nondistorted paracyclophane and pyridinophane architectures with perfectly superimposed π-systems. The dipyridyl template can be used to promote stereoselective solid-state dimerization of olefinic dicarboxylic acids.

Supramolecular self-assembly has become a widely recognized tool for the formation of well-defined noncovalent arrangements of organic building blocks and multicomponent solid materials with intriguing second-order optical nonlinear effects and semiconducting properties.[1] The principles of molecular recognition and association of complementary building blocks have also been exploited for template-assisted solid-state synthesis.[2] The high regularity, order, and control of intermolecular orientation of organic molecules in crystalline assemblies provide excellent opportunities for the development of reactions with distinguished stereo- and regiochemical selectivity in a solvent-free environment.[3] Topochemical polymerization of unsaturated carboxylic acids has been accomplished in the solid state through photochemical and γ-radiation-induced reactions of ammonium carboxylates.[4] Similarly, stereocontrolled solid-state photodimerization of ammonium salts of *trans*-cinnamic acid and *trans*-cinnamamide carboxylates affords truxinic acids and truxinamides with high stereoselectivity.[5] The efficacy of supramolecular chemistry has inspired the development of powerful templates suited to crystal engineering and solid-state synthesis. In particular, controlled π-stacking of aromatic and other unsaturated systems in the presence of

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multifunctional templates that serve as hydrogen bond donors, Lewis bases that undergo charge-transfer interactions with aryl and alkynyl halides, and transition metal coordination complexes have received increasing attention.[6]

We wish to describe a simple approach to both preorganization of small unsaturated organic molecules for stereoselective solid-state synthesis and cofacial assembly of aromatic π-systems mimicking paracyclophane topology with enforced face-to-face stacking. The use of 1,8-diheteroarylnaphthalenes for stereoselective recognition of carboxylic acids, amino acids, and other hydrogen bond donors has previously been reported from our laboratories.[7] To promote parallel packing of unsaturated dicarboxylic acids in the solid state, we decided to introduce a rigid bifunctional template bearing cofacial pyridyl rings that can serve as Brønsted base and hydrogen bond acceptor. We anticipated that cocrystallization of 1,8-bis(4′-pyridyl)naphthalene, **1**, with unsaturated dicarboxylic acids **2**−**5** would provide a four-component assembly in which two dipyridylnaphthalene templates preorganize two dicarboxylic acid molecules through OH···N and CH···O hydrogen bonding, Figure 1.

A single cocrystal suitable for X-ray diffraction analysis was obtained by slow evaporation of an equimolar solution of 1,8-dipyridylnaphthalene and fumaric acid in ethanol, Figure 2. Dipyridylnaphthalene **1** and fumaric acid **2** form a neutral tetrameric assembly stabilized by eight hydrogen bonds and face-to-face interactions between stacked pyridyl and olefinic π-systems.[8] The OH···N hydrogen-bonding lengths are 1.794 and 1.819 Å and the CH···O bonds are 2.516 and 2.576 Å. The separation of the nitrogen atoms is 3.929 Å, which is a consequence of slight splaying of the pyridyl rings. The rigid structure of **1** arranges the bridging fumaric acid molecules in close proximity to each other and the separation of the superimposed olefinic carbons ranges from 3.732 to 3.976 Å.

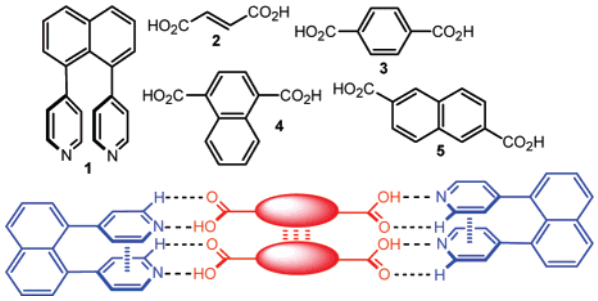

Figure 1. Structures of template **1**, dicarboxylic acids **2**−**5**, and enforced π-stacking.

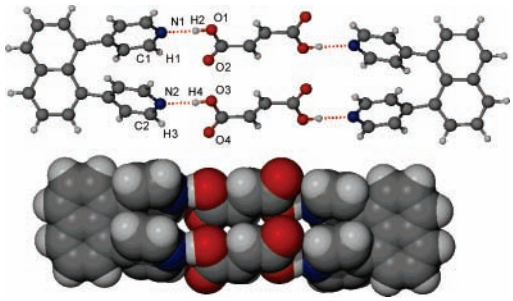

Figure 2. Ortep drawing (top) and space-filling view (bottom) of the crystal structure of cocrystal **1**·**2**. Selected crystallographic separations [Å] and angles [deg]: N1−N2 3.929, N1···H2 1.794, H1···O2 2.576, N2···H4 1.819, H3···O4 2.516, N1···H2−O1 174.85, N2···H4−O3 176.51, C1−H1···O2 127.89, and C2−H3···O4 129.48.

The aligned organization of two molecules of fumaric acid in **1**·**2** underscores the ability of the template to impose the congested arrangement of the cofacial pyridyl moieties on the bridging substrate. Since π-stacking of aromatic compounds is a common motif in biomolecules[9] and plays an important role in molecular recognition,[10] electronic properties of paracyclophanes and pyridinophanes,[11] and chemical

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engineering of new materials,[12] we decided to extend our approach to aromatic dicarboxylic acids. Cocrystals of **1** and acids **3**−**5** were formed upon slow evaporation of ethanol solutions. Crystallographic analysis revealed that the same supramolecular forces as encountered in **1·2** establish tetrameric π-stacked architectures in which two template molecules are bridged by two cofacial substrates, thus confirming the validity of our approach, Figure 3.

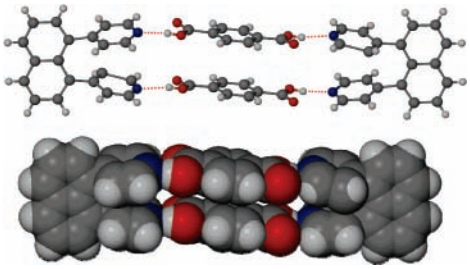


Figure 3. Ortep drawing (top) and space-filling view (bottom) of **1·3**. See the Supporting Information for crystallographic separations and bond angles.

The supramolecular structure of **1·3** resembles the architecture of paracyclophanes and pyridinophanes. The bridging terephthalic acids are perfectly aligned with $\pi\cdots\pi$ distances ranging from 3.676 to 3.683 Å. Similar to [2.2]paracyclophanes, the benzene moieties of **3** undergo enforced π-stacking and rotation about the C_2-axis is sterically hindered. However, the severe distortion of aromatic units inherent to [2.2]paracyclophanes is not observed in the supramolecular analogue **1·3**, which shows optimized π-overlap. Supramolecular paracyclophane synthesis was also successful with naphthalenedicarboxylic acids **4** and **5**, Figure 4. The corresponding assemblies have $\pi\cdots\pi$ distances ranging from 3.727 to 3.918 Å and 3.605 to 3.663 Å, respectively. The cocrystal structures demonstrate that our 1,8-dipyridylnaphthalene template provides a means for precise overlaying of complementary building blocks avoiding an offset arrangement of the olefinic and aromatic π-systems of **2**−**5**. Face-to-face stacking of superimposed aromatic units is particularly desirable for maximizing π-overlap and charge-transfer characteristics in organic semiconductors.[13] The ability of **1** to enforce π-stacking of perfectly planar cofacial arenes yields a nondistorted paracyclophane-like topology and underscores the usefulness of supramolecular synthesis.

Olefin photodimerization in solution is hampered by the coexistence of different substrate orientations and rapid cis/trans-isomerization upon irradiation prior to carbon−carbon bond formation. Both factors afford stereoisomeric adducts and byproducts, thus compromising stereoselectivity and yield. A parallel alignment and a centroid−centroid separation of 3.5−4.2 Å is a generally accepted prerequisite for dimerization of unsaturated compounds.[14] The use of a supramolecular template that preorganizes olefinic substrates within this range in the solid state offers a viable synthetic alternative with superior stereocontrol over reactions carried out in solution. A closer look at **1·2** shows that the rigid spatial arrangement of the cofacial pyridyl rings in the template forces two dicarboxylic acids into close proximity with an intermolecular distance between perfectly superimposed olefinic bonds of less than 4.0 Å. We therefore expected that the parallel orientation of **2** would favor highly stereoselective [2+2]cycloaddition to *cis*,*trans*,*cis*-cyclobutanetetracarboxylic acid, Scheme 1.

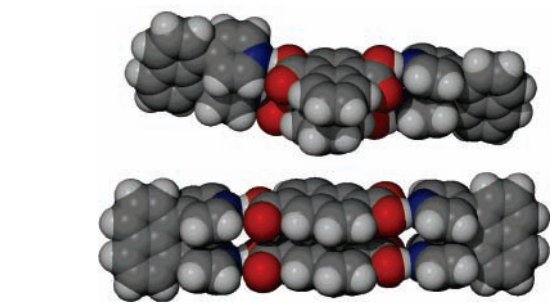
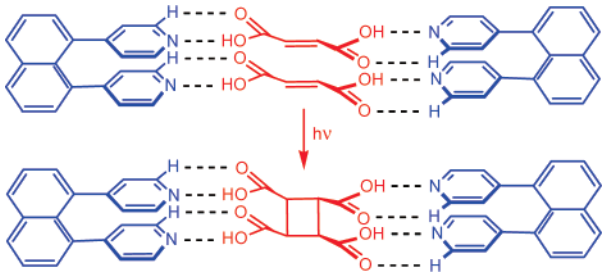


Figure 4. Structures of **1·4** (top) and of **1·5** (bottom). See the Supporting Information for crystallographic separations and bond angles.

Scheme 1. Photocyclization of Preorganized Fumaric Acid Molecules



A photoreaction of a powdered crystalline sample of **1·2** placed in a quartz tube under nitrogen atmosphere was performed with use of a medium-pressure wide band mercury lamp and monitored by ^{1}H NMR spectroscopy in D_2O. The reaction process is characterized by a decrease in the intensity

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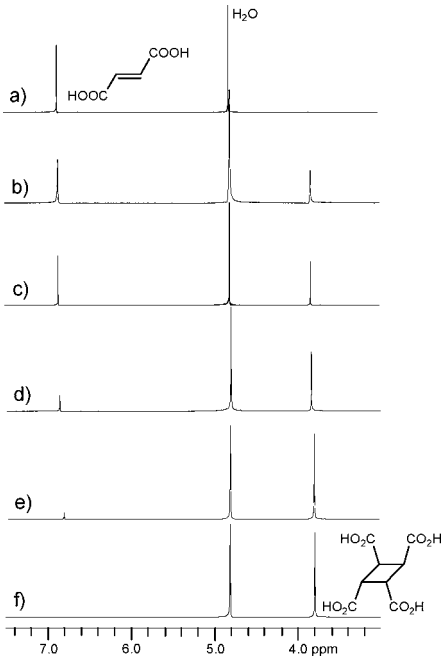

Figure 5. Monitoring of the template-assisted solid-state photodimerization of fumaric acid by ^{1}H NMR spectroscopy. Small aliquots of the irradiated cocrystals were separated between deuterated water and methylene chloride to recover **1** and to determine the conversion of **2** to cycloadduct **6**. Samples were analyzed at 0 (a), 5 (b), 10 (c), 24 (d), 48 (e), and 72 h (f).

of the olefinic fumaric acid proton signal at δ 6.86 ppm and the appearance of the aliphatic cyclobutanecarboxylic acid signal at δ 3.79 ppm. Photoirradiation resulted in quantitative and 100% stereoselective conversion of fumaric acid to *cis*,*trans*,*cis*-cyclobutanetetracarboxylic acid, **6**, and the template was fully recovered by extraction with methylene chloride, Figure 5.

We were able to grow a single crystal of **6** through slow evaporation of a solution of the photoreaction product in water to confirm the cis,trans,cis-configuration by crystallographic analysis, Figure 6.

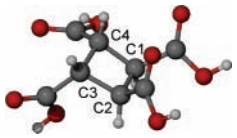

Figure 6. Crystal structure of *cis*,*trans*,*cis*-cyclobutanetetracarboxylic acid, **6**. Selected crystallographic separations [Å] and angles [deg]: C1−C2 1.565, C2−C3 1.570, C3−C4 1.561, C4−C1 1.533, C4−C1−C2 89.98, C1−C2−C3 89.07, C2−C3−C4 88.82, and C3−C4−C1 90.57.

In summary, we have identified the use of a highly congested 1,8-diheteroarylnaphthalene template bearing two cofacial pyridyl rings for supramolecular organization of unsaturated dicarboxylic acids in the solid state. The rigid structure of **1** enforces π-stacking of perfectly superimposed aromatic moieties in a tetrameric assembly that is stabilized by several hydrogen bonding and $\pi-\pi$ interactions. This approach yields nondistorted paracyclophane and pyridinophane architectures and may prove invaluable in the search for superior semiconductors and other organic materials. The dipyridyl template can also be used to promote solid-state dimerization of olefinic dicarboxylic acids. Cocrystallization with fumaric acid aligns two bridging substrate molecules in close proximity and provides an entry to stereoselective formation of *cis*,*trans*,*cis*-cyclobutanetetracarboxylic acid. The well-defined structure of the tetrameric assembly controls the stereochemical outcome of the photocyclization, which does not proceed with concomitant cis/trans-isomerization.

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Supporting Information Available: Synthetic procedures and X-ray diffraction data. This material is available free of charge via the Internet at http://pubs.acs.org.

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