

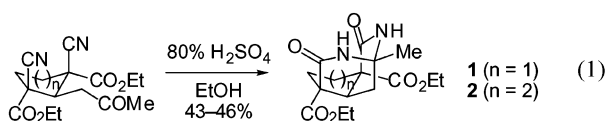
The Bicyclic *N,N'*-Diacylaminal: A New Motif for Molecular Self-AssemblyRobert B. Grossman,* Kazuyuki Hattori, Sean Parkin, Brian O. Patrick, and Melissa A. Varner
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The principles governing noncovalent self-assembly have been studied intensely recently because of their potential relevance to nanotechnology.^{1–3} There remains a need to develop new “supramolecular synthons” that can be used to create supramolecular structures with novel three-dimensional architectures. We now report a new molecular recognition motif, the bicyclic *N,N'*-diacylaminal (“amidal”). In the solid state, the amidals described here self-assemble into either “supramolecular chair cyclohexanes” occupied by two aromatic solvent molecules or infinite tapes. The amide dimers sustaining these supramolecular structures are not coplanar, making these structures uniquely three-dimensional.

We have recently reported tricyclic amidals **1** and **2** (eq 1).⁴



Amidal **1** crystallizes from toluene, chlorobenzene, and benzotrifluoride in the triclinic space group *P1* in the stoichiometry $(\mathbf{1})_3 \cdot (\text{solvent})$ (mps 197–199 °C). Only minor differences (mostly involving the CO₂Et groups) distinguish the three types of **1** within each crystal, and the three $(\mathbf{1})_3$ sets of the three crystals are nearly superimposable. In each crystal, six amidals (each independent molecule and its enantiomer) self-assemble into a squat cylindrical hexamer occupied by two aromatic guests (Figures 1 and 2). Each monomer makes two hydrogen bonds to each of its neighbors, and the vertical orientation of the amidals alternates around the hexamer, endowing the hexamer with approximate *D*_{3d} and exact *C*_i symmetry. The cavities of the hexamers are lined at the top and bottom by the CH₂CH₂ groups of **1** and in the middle by the CONH groups. The hexamers stack to form six-sided straws occupied by aromatic solvent. These straws are close-packed into roughly hexagonal arrays, like bundles of pencils. The approximate *D*_{3d} symmetry of the hexamers allows them to be regarded as supramolecular analogues of chair-shaped cyclohexane. The only previously reported “supramolecular chair” is sustained by C–H···π interactions and lacks an occupant.⁵ By contrast, our chairs are sustained by more robust amide dimers, and, in each chair, two arenes sit locked in intimate embrace.

The volumes of the interiors of the cylinders in the three crystals, computed by subtracting the atomic volumes of the atoms making up the cylinders from the volume of the unit cell,⁶ are approximately 340, 330, and 342 Å³, respectively, at room temperature. (Each contracts by 11 Å³ at 90 K.) Each pair of guests is calculated to occupy 282, 272, and 319 Å³, respectively, at room temperature. Only in $(\mathbf{1})_6 \cdot (\text{C}_6\text{H}_5\text{CF}_3)_2$ is the volume of the cylinder occupied fully

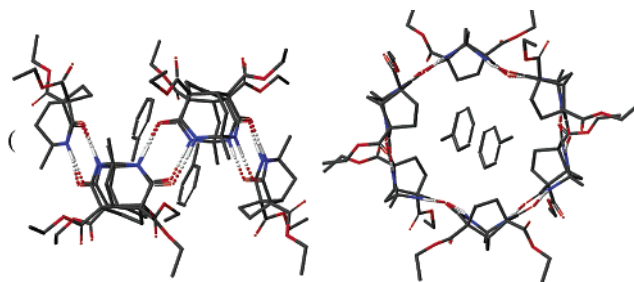


Figure 1. Views of $(\mathbf{1})_6 \cdot (\text{C}_7\text{H}_8)_2$ down a pseudo-*C*₂ axis (left) and the *S*₂ axis (right). Only NH hydrogens and major conformers of disordered CO₂Et groups are shown for clarity. O, red; C, gray; N, blue; H, white.

Ⓢ A 3D rotatable image in MOL format is available.

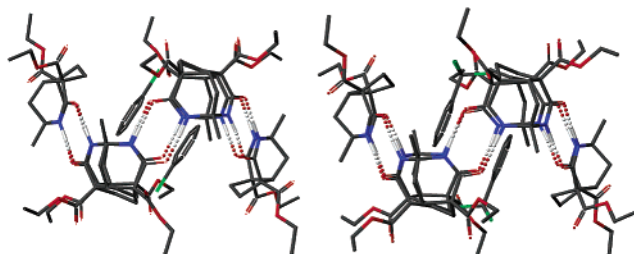


Figure 2. View of $(\mathbf{1})_6 \cdot (\text{C}_6\text{H}_5\text{Cl})_2$ (left) and $(\mathbf{1})_6 \cdot (\text{C}_6\text{H}_5\text{CF}_3)_2$ (right) down pseudo-*C*₂ axes. Only NH hydrogens and major conformers of disordered CO₂Et groups are shown for clarity. Halogens are green.

Ⓢ 3D rotatable images of $(\mathbf{1})_6 \cdot (\text{C}_6\text{H}_5\text{Cl})_2$ and $(\mathbf{1})_6 \cdot (\text{C}_6\text{H}_5\text{CF}_3)_2$ in MOL format are available.

by the guests; in the others, the excess space is evident from the increased thermal motion of the guests.

In $(\mathbf{1})_6 \cdot (\text{C}_7\text{H}_8)_2$, the two guests are arranged in a face-to-face and CH₃-to-center orientation, whereas in $(\mathbf{1})_6 \cdot (\text{C}_6\text{H}_5\text{Cl})_2$ and $(\mathbf{1})_6 \cdot (\text{C}_6\text{H}_5\text{CF}_3)_2$, they are arranged in a face-to-face and edge-to-edge orientation. These observations can be explained by the attractive nature of the CH₃–arene interaction and the repulsive nature of the Cl– and CF₃–arene interactions. Still, the spaces occupied by the solvent molecules in the two crystals coincide fairly closely, as one would expect.

To our knowledge, the solid-state structures of **1** are the first examples of *nonplanar* cyclic hexamers held together by *R*₂²(8)-type⁷ hydrogen bonds (carboxylic acid dimers, amide dimers, and the like).⁸ In related work, spherical calixarene hexamers held together only by hydrogen-bonded OH groups and H₂O molecules have been reported,⁹ and a hexamer held together by pyridine-alcohol hydrogen bonds and consisting of two different units has been shown to encapsulate two molecules of nitrobenzene.¹⁰ Glycoluril groups, which resemble the bicyclic amidal present in **1** (Figure 3), are assembled into a cylindrical hexameric structure

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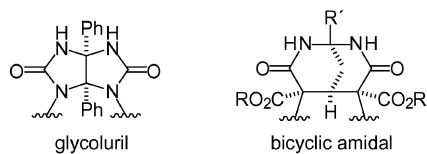


Figure 3. Comparison of the supramolecular synthons, glycoluril and bicyclic amidal.

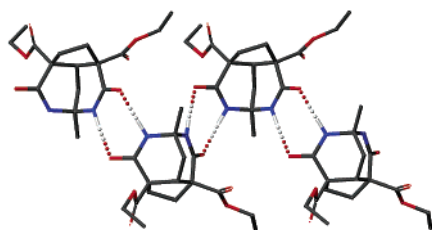


Figure 4. Four-monomer segment of $(1)_n$ grown from nitrobenzene. Only NH hydrogens are shown for clarity. The four-monomer segments grown from benzene and heptane- CH_2Cl_2 are similar.

via $R_2^2(8)$ -type hydrogen bonds in Rebek's dimeric "jelly doughnut",¹¹ but in this compound alternate glycolurils are *covalently* held in the orientations necessary for formation of the cylinder. The same is true for de Mendoza's dimeric triureidocalix[6]arenes, which are held together by $R_1^2(6)$ -type hydrogen bonds.¹² By contrast, the self-assembly of the cyclic hexamers of **1** requires the organization of six separate molecules per hexamer.¹³

Amidal **1** also crystallizes from $\text{C}_6\text{H}_5\text{NO}_2$ and C_6H_6 , but in the stoichiometry $1 \cdot (\text{solvent})$; it also crystallizes from heptane- CH_2Cl_2 containing 1:1 $\text{C}_6\text{H}_5\text{Cl}:\mathbf{1}$ in the stoichiometry $1 \cdot (\text{CH}_2\text{Cl}_2)_2$ (mps 197–199 °C; orthorhombic, monoclinic, and orthorhombic space groups $Pbca$, $P2_1/n$, and $Pna2_1$, respectively). In these crystals, **1** again self-assembles via $R_2^2(8)$ -type hydrogen bonds, but to form infinite tapes instead of hexamers (Figure 4). Infinite tapes sustained by $R_2^2(8)$ -type hydrogen bonds are common, but those in which the hydrogen-bonded units are not coplanar are rare.^{1,2,14} The manner in which the tapes and the solvent pack differs dramatically among the three crystals (see the Supporting Information).

What causes **1** to crystallize as infinite tapes from some solvents and as hexamers from others? $\text{C}_6\text{H}_5\text{NO}_2$ and $\text{C}_6\text{H}_5\text{CF}_3$ are about the same size, so self-assembly may require a fairly nonpolar guest. Benzene is probably simply too small to fill $(1)_6$ to Nature's satisfaction. In any case, it is clear that the balance between hexamer and infinite tape is subtle. The incorporation of CH_2Cl_2 into the crystal even when $\text{C}_6\text{H}_5\text{Cl}$ is present also demonstrates the weak nature of the interaction between $(1)_6$ and its guests. The behavior of **1** is reminiscent of that of 1,3-cyclohexanedione, which crystallizes from C_6H_6 as a planar cyclic hexamer surrounding a C_6H_6 molecule and from THF as an infinite tape.¹⁵

Amidal **2**, which has one more CH_2 group than **1**, crystallizes from CH_3CN in the monoclinic space group $P2_1/n$. Crystallization from other solvents has failed to give crystals suitable for X-ray analysis. Only one independent molecule of **2** and no solvent is present in the asymmetric unit. In the crystal, **2** self-assembles into an infinite tape remarkably similar to those formed by **1** (Figure 5).

Two explanations can be offered for the inability of **2** to self-assemble into a hexamer. First, the extra CH_2 group in the bridge in **2**, which necessarily juts into the cavity, may simply be too large. Second, the 106° dihedral angle between the planes of the two amide groups of **2** (as compared to 114° in **1**) may be too small to allow its assembly into a hexamer.

The nonplanarity of the hexamers of **1** has implications for the synthesis of topologically complex, three-dimensional supramo-

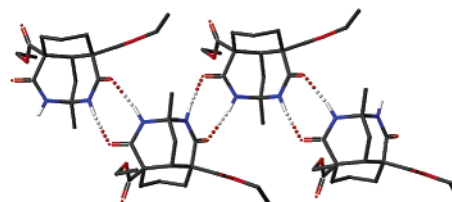


Figure 5. A four-monomer segment of $(2)_n$. Only NH hydrogens are shown for clarity.

lecular architectures.^{2,16} Conceivably, amidals with varying dihedral angles and substitution patterns would self-assemble in other interesting ways. The ability to control the solid-state structure of **1** with the crystallization solvent also creates interesting possibilities for supramolecular synthesis. The easy syntheses of **1** and **2** bode well for the preparation of other self-assembling monomers based on the bicyclic amidal motif. Future work will explore just how general is this assembly motif, whether two guests can be induced to undergo unusual reactions, and the design of molecular recognition devices based on the bicyclic amidal.

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Supporting Information Available: Details of the X-ray studies of **1** and **2** (PDF). An X-ray crystallographic file is available in CIF format. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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