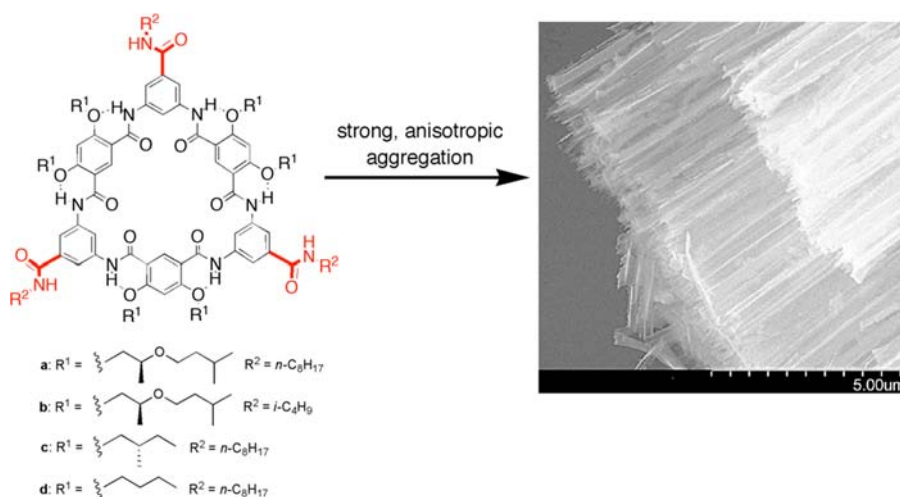


Aromatic Oligoamide Macrocycles
with a Backbone of Reduced ConstraintMark Kline,[†] Xiaoxi Wei,[†] and Bing Gong^{*,†,‡}*Department of Chemistry, The State University of New York at Buffalo, Buffalo,
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ABSTRACT



Oligoamide macrocycles with a backbone partially constrained by hydrogen bonds have been prepared. These macrocycles, carrying multiple H-bonding side chains, underwent strong aggregation in solution and form long fibers in the solid state. In contrast to the strong and specific complexation of the guanidinium ion by analogous macrocycles with fully H-bond-constrained backbones, these macrocycles failed to recognize the same cation, indicating that reducing backbone constraint has led to a drastic change in their cavity.

Rigid macrocycles¹ with a variety of backbones^{2–9} have attracted much attention. These macrocycles offer advantages including shapes unaffected by synthetic modifications, nondeformable lumens, and the presentation of functional groups at defined locations. Major progress has been made in recent years in the synthesis of rigid macrocycles.^{3–9} For example, we reported the efficient

preparation of macrocycles **1**,⁵ their larger analogs,¹⁰ and those with different backbones⁷ based on either one-pot^{5,10} or segment condensation.^{10,11} The formation of **1** and other macrocycles sharing similar backbones is characterized by

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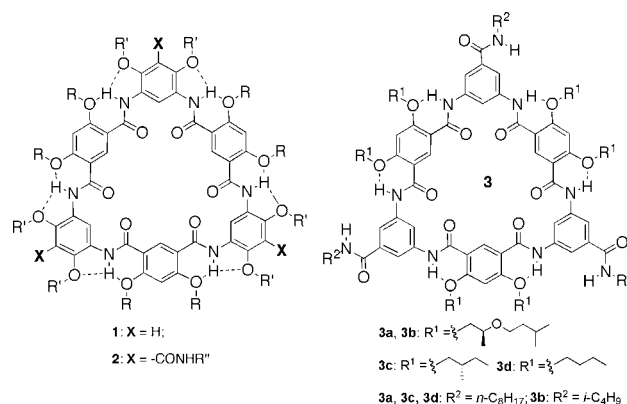
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very high efficiency that is attributed to the fully rigidified backbones of the corresponding oligomeric precursors.¹⁰ These macrocycles exhibited novel properties.¹² For example, macrocycles **1**, with their noncollapsible cavity having numerous hydrogen bond acceptors, showed very high selectivity toward the guanidinium ion.¹³ Macrocycles **1** formed transmembrane single ion channels with high conductance, presumably due to their columnar stacking.¹⁴ The strong columnar aggregation of **1** was confirmed by our recent structural studies.¹⁵

Besides their efficient formation, macrocycles **1** and their larger analogs offer multiple sites, including side chains and peripheral aromatic hydrogens, that are amenable to various structural modifications. In an attempt to better control the assembly of these cyclic compounds, we designed and prepared macrocycles **2** in which a secondary amide group was placed in between the two alkoxy groups of each of the three diaminobenzene residues.¹⁶ The introduced secondary amide groups, being sandwiched in between the alkoxy side chains and thus perpendicular to the plane of the benzene rings to which they are attached, should engage in intermolecular H-bonding interactions that force **2** to stack into H-bonded columns. In contrast to such an expectation, the ¹H NMR signals of **2** remain well

dispersed in a wide concentration range in CDCl₃, suggesting that these molecules, with secondary amide side chains being attached to their peripheries, abolished the otherwise strong aggregation observed for **1**.



Despite their drastically different propensity for aggregation, macrocycles **1** and **2** have very similar backbones that are rigidified by intramolecular three-center H-bonds and the same, nondeformable inner cavity. Indeed, with a cavity that is rich in amide O-atoms, macrocycles **2**, like **1**, also complex the guanidinium ion with very high selectivity,¹⁶ suggesting that additional amide side chains did not alter the property of the inner cavities of these macrocycles.

The unexpected lack of aggregation for **2** indicates that even a modest structural variation could result in a drastic change in properties, which prompted us to explore additional modifications on these macrocycles. For example, removing some of the alkoxy side chains from **1** (or **2**) would reduce the number of intramolecular H-bonds, leading to oligoamide backbones with increased rotational freedom and also allowing the attachment of various side chains onto the benzene residues. This may lead to macrocycles with novel behavior.

Based on these considerations, we designed macrocycles **3**, which can be regarded as being derived from **1** by removing the alkoxy groups, i.e., the corresponding intramolecular H-bonds, away from the diaminobenzene residues while attaching additional amide side chains. Macrocycles **3** may also be regarded as being derived from **2** by removing the alkoxy groups away from the diaminobenzene residues of the latter. The backbone amide H-atoms of **3** should still be involved in intramolecular H-bonds with the remaining alkoxy oxygens, while the side chain amide groups of **3** should be able to engage in intermolecular H-bonding.¹⁷

The preparation of **3** was first attempted by treating the corresponding monomeric diacid chloride and diamines based on the similar one-pot procedures we reported for preparing **1**.⁵ In contrast to the efficient formation of **1**, the attempted one-pot reaction failed to yield **3** in any meaningful yields. This result indicates that, without the kind of H-bond-constrained conformations¹⁸ that are characteristic

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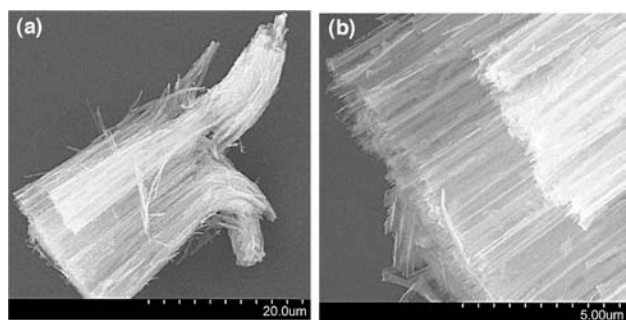


Figure 1. (a) The SEM image of a sample of **3d** reveals a fibrous bundle. (b) Enlarged (zoomed-in) SEM image of the same sample showing the edge of the fibrous bundle.

The involvement of the side chain amide groups of **3** in intermolecular H-bonding was probed with IR spectroscopy (see the SI). In comparison to that of a trimer sharing part of the backbone and the same side chain, the IR spectrum of **3d** (1 mM) in CHCl_3 indicates that the side chain amide carbonyls give a stretching band with a prominent shoulder from 1647 and 1641 cm^{-1} that noticeably shifts (22 cm^{-1}) to a lower frequency. In CHCl_3 containing 17% CH_3CN , this shoulder weakened noticeably (see the SI). These results are consistent with the involvement of the side chain amide groups of **3d** in an intermolecular H-bonding interaction. The high directionality of multiple H-bonding, along with backbone stacking interaction, may very likely lead to well aligned stacks consisting of these macrocycles.

That **3d** indeed engaged in directional aggregation was revealed by scanning electron microscopy (SEM). As shown in Figure 1, the SEM image of a solid sample of **3d** reveals long, largely straight fibers with lengths over tens of micrometers. The fibers consist of closely packed filaments with diameters around 0.4 μm . The SEM image provides clear evidence indicating the highly anisotropic nature of the self-assembly of this macrocycle.

As we reported, the internal cavity of **1** or **2** contains six well positioned, inward-pointing amide oxygen atoms and binds the guanidinium ion strongly and specifically.^{13,16}

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Surprisingly, examining samples of **3a** or **3d** mixed with guanidinium chloride or guanidinium tetraphenylborate under a variety of conditions (i.e., ratios of 1:1, 1:5, 1:10, and 1:1000, in different solvents, and standing for 3 or 16 h) using MALDI-FTICR failed to detect any interaction between **3** and the guanidinium ion. Given the rigidity of benzene rings and backbone amide groups, it is unlikely that the backbones and cavities of **3** would collapse. Instead, this observation suggests that the cavity of these macrocycles is different from that of **1** or **2**. Replacing the three-center H-bonds of **1** or **2** with the two-center H-bonds of **3** may have resulted in some (or all) of the backbone amide groups to twist away from being nearly coplanar with the benzene residues. The resultant cavity can no longer bind the guanidinium ion due to the absence of well-positioned, inward pointing amide O-atoms.

In summary, we have prepared a new series of aromatic oligoamide macrocycles with a backbone of reduced H-bond constraints, which allows the introduction of additional secondary amide side chains. The synthesis of macrocycles **3**, whose precursors do not have fully rigidified, crescent conformations, could only be achieved by coupling their oligomeric precursors. With amide side chains capable of multiple intermolecular H-bonding, macrocycles **3** exhibited strong aggregation. The directional assembly of **3** was indicated by SEM, which revealed very long fibers consisting of closely packed filaments. Unlike the nearly exclusive binding of the guanidinium ion observed for **1** and **2**, macrocycles **3** failed to show any binding of this ion. This surprising result is explained by the backbone of **3**, which is only partially constrained and thus encloses a cavity that does not have well-positioned amide oxygens necessary for effective binding. These findings indicate the structural-functional richness of aromatic oligoamide macrocycles. Further studies on these macrocycles should reveal additional novelties.

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Supporting Information Available. Synthesis, compound characterizations, and additional spectroscopic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

The authors declare no competing financial interest.