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Self-Assembly of Nanostructured Materials through Irreversible Covalent Bond Formation

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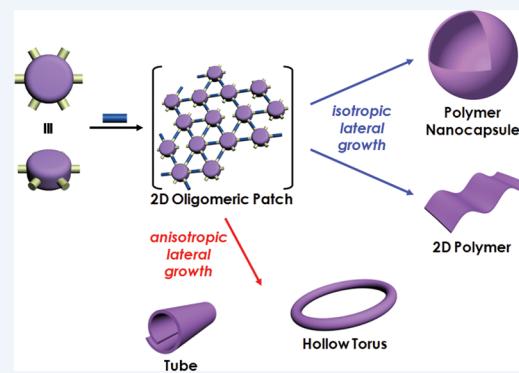
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CONSPECTUS: Over the past decades, numerous efforts have been devoted to synthesizing nanostructured materials with specific morphology because their size and shape play an important role in determining their functions. Self-assembly using weak and reversible interactions or bonds has provided synthetic routes toward various nanostructures because it allows a “self-checking” and “self-error-correcting” process under thermodynamic control. By contrast, the use of irreversible covalent bonds, despite the potential to generate more robust structures, has been disfavored in the synthesis of well-defined nanomaterials largely due to the lack of such self-error-correcting mechanisms. To date, the use of irreversible bonds is largely limited to covalent fixation of preorganized building blocks on a template, which, though capable of producing shape-persistent and robust nanostructured materials, often requires a laborious and time-consuming multistep processes. Constructing well-defined nanostructures by self-assembly using irreversible covalent bonds without help of templates or preorganization of components remains a challenge.

This Account describes our recent discoveries and progress in self-assembly of nanostructured materials through strong, practically irreversible covalent bond formation and their applications in various areas including drug delivery, anticancer therapy, and heterogeneous catalysis. The key to the success of this approach is the use of rationally designed building blocks possessing multiple in-plane reactive groups at the periphery. These blocks can then successfully grow into flat oligomeric patches through irreversible covalent bond formation without the aid of preorganization or templates. Further growth of the patches with or without curvature generation drives the system to the formation of polymer nanocapsules, two-dimensional (2D) polymer films, and toroidal nanotubular microrings. Remarkably, the final morphology can be specified by a few simple parameters: the reaction medium, bending rigidity of the system, and orientation of the reactive groups. Theoretical studies support the spontaneous formation of such nanostructured materials in terms of energetics and successfully predict or explain their size distributions. Although the lack of self-error-correcting mechanisms results in defect sites in these nanostructures, the high efficiency and relative simplicity of our novel approach demonstrates the potential power of using irreversible covalent bonds to generate a diverse range of shape-persistent and robust nanostructures that is likely to enrich the repertoire of self-assembled nanomaterials.



1. INTRODUCTION

One of the exciting developments in chemistry over the last several decades is construction of nanostructured objects or materials from small building blocks by self-assembly.^{1–5} Inspired by numerous examples in nature such as the DNA double helix and viral capsids, a wide variety of nanostructures with different levels of dimensions and complexity including nanospheres,^{6,7} nanocages,^{8,9} and nanotubes,^{10–12} as well as topologically nontrivial assemblies,¹³ have been generated. A common key to success for these structures has been the use of multiple, weak, noncovalent interactions between building blocks, which allow reversible and “self-error-correcting” processes that ultimately lead to the formation of the thermodynamically most stable species. Unfortunately, the weak and reversible nature of interactions utilized to hold the structure also result in nanostructures that are often not robust

enough to be useful for practical applications.¹⁴ Although more recently, dynamic covalent self-assembly in which reversible covalent bonds are formed under equilibrium control has been explored,^{14–16} the resulting nanostructures are still not sufficiently robust and can be disassembled under certain conditions such as hydrolytic environments. Alternatively, chemical fixation using irreversible covalent bonds after the self-assembly of nanostructures via reversible interactions or bonds has been studied; for instance, photochemical stitching of self-assembled nanotubes¹⁷ and reduction of imine bonds in molecular cages.¹⁸ However, this approach often requires a laborious multistep process, and sometimes the chemical fixation step causes loss of shape persistence.¹⁹

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This raised the question of whether strong, irreversible covalent bonds can be utilized directly for self-assembly of robust nanostructured materials. Initially, due to lack of “error-correcting” and “proof-reading” characteristics of reversible interactions or bonds, researchers often experienced the formation of random aggregates rather than well-defined nanostructures when irreversible covalent bonds were utilized without the aid of preorganization or templates. Serendipitously, however, we discovered that photopolymerization of rigid, disk-shaped building blocks possessing multiple in-plane reactive groups at their periphery and ditopic linear linkers without any aid of preorganization or templates resulted in robust hollow polymer nanocapsules with a narrow size distribution.²⁰ Further studies led us to confirm that our approach can be generalized; we were able to generate other robust nanostructures through irreversible covalent bonds by a careful choice of building blocks, linkers, and reaction media.²¹ Moreover, we discovered that by tuning these parameters, we can control the size, shape, properties, and functionality of these nanostructured materials. More recently, based on these studies, we have taken our repertoire of structures, which includes spheres,^{22–25} films,²⁶ toroids,²⁷ and tubular structures, and demonstrated some of their potential applications in various areas including therapeutics,^{23,24} catalysis,²⁵ and electronics. Our work challenges the conventional wisdom that construction of nanostructured materials with specific morphology via self-assembly requires reversible interactions. This Account is a documentation of our recent discoveries and progress in the self-assembly of well-defined and robust nanostructured materials through irreversible covalent bond formation and their applications.

2. POLYMER NANOCAPSULES

Polymer nanocapsules, which are defined as nanoscale shells made out of a polymer, have attracted a great deal of attention for a wide range of applications such as encapsulation, controlled release, imaging, and catalysis.^{28–30} A number of methods including template-assisted synthesis and micelle formation followed by covalent fixation have been implemented to construct hollow polymer nanocapsules.^{31–33} However, most of these methods require either templates or preorganized structures to form a core–shell structure first and subsequent removal of templates or cores to produce a hollow sphere. In this context, a direct, one-pot synthetic method would be a highly desirable alternative.

In 2007, we reported a serendipitous discovery that polymer nanocapsules with a highly stable structure and relatively narrow size distribution can form via photopolymerization without aid of any preorganization, templates, or emulsifiers.²⁰ UV irradiation of a mixture of perallyloxycurtobit[6]uril (**1a**), a disk-shaped macrocycle with 12 allyloxy groups laterally predisposed around the rigid core of curtobit[6]uril (CB[6]),^{34–38} and dithiol (**2a**) in methanol for 20 h followed by dialysis successfully produces polymer nanocapsule **3a** with an average diameter of 110 ± 30 nm and wall thickness of 2.1 ± 0.3 nm in high (>85%) yield (Figure 1). We also discovered that the size of the nanocapsule could be easily tuned by changing the reaction medium or the length of the dithiol linker. For example, the same reaction in chloroform instead of methanol produced polymer nanocapsules with an average size of 500 nm, while the photopolymerization of **1a** with a shorter dithiol linker, 1,2-ethanedithiol (**2b**), in methanol produced nanocapsule **3b** having an average size of 50 ± 10 nm. In

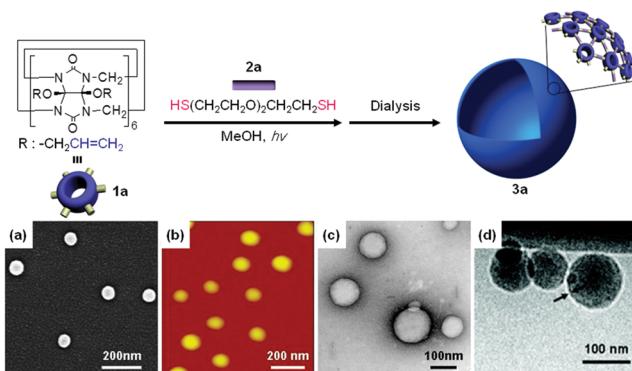


Figure 1. Synthesis of polymer nanocapsules **3a**: (a) SEM, (b) AFM, (c) TEM, and (d) cryo-TEM images of **3a**. The images in panels a–c are reproduced with permission from ref 20. Copyright 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim. The image in panel d is reproduced from ref 21. Copyright 2010 American Chemical Society.

general, better solvents or longer dithiol linkers led to the production of larger polymer nanocapsules.

Mechanistic studies using various techniques including dynamic light scattering (DLS) and scanning electron microscopy (SEM) suggested the following mechanism.^{20,21} At the very early stage of the reaction, the disk-shaped monomers form dimers and trimers as the multiple polymerizable groups at the periphery of the monomers become linked by thioether linkages. These dimers and trimers further react with each other laterally and grow into two-dimensional (2D) oligomeric patches. Once the patches grow to a certain size, they start bending to reduce their energy, and further reaction between the curved oligomeric patches generates a loosely cross-linked hollow sphere with minimum energy. Further cross-linking of the unreacted allyl groups of neighboring monomer units in the shell finally produces a mature, highly cross-linked robust polymer nanocapsule (Figure 2).

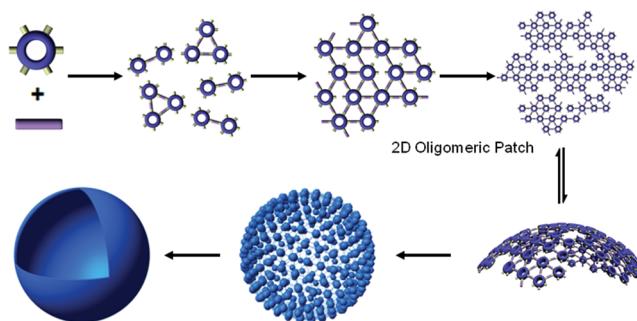


Figure 2. Formation mechanism of the polymer nanocapsule. Adapted from ref 21. Copyright 2010 American Chemical Society.

To better understand the spontaneous formation of nanocapsules from 2D patches, we also performed a theoretical analysis. The total energy, E , of the system can be described as below:

$$\begin{aligned} E = & -3e\left[\frac{8R^2}{d^2}(1 - \cos\theta) - \frac{2\pi R}{d}\sin\theta\right] \\ & + 4\pi\kappa(1 - \cos\theta) \\ = & 3ef(R, \theta) \end{aligned} \quad (1)$$

where R is the radius of curvature, d is the distance between two adjacent monomer units, θ is the angle of curvature, κ is the bending modulus, and ϵ is the bond energy. For a 2D oligomeric patch with a small radius (R is small), the total energy goes up as θ increases, which means that sphere formation is unfavorable at the early stage of the reaction. However, when R becomes larger than a critical value, R_c , the total energy abruptly goes down as θ increases and attains the minimum at $\theta = \pi$, which corresponds to a hollow sphere, indicating that the formation of a hollow nanosphere from the 2D patches is an energetically favorable process (Figure 3). In

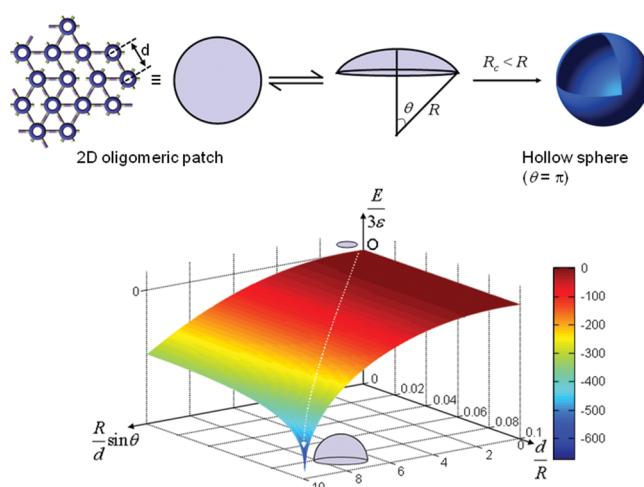


Figure 3. Theoretical studies on the formation of polymer nanocapsules. Adapted from ref 21. Copyright 2010 American Chemical Society.

addition, while energy dictates fewer larger spheres to form, entropy favors more smaller spheres; the size distribution of the sphere is thus determined by the free energy minimum of the system. The average size and size distribution of the hollow sphere predicted by the theory is qualitatively in good agreement with the experimental results.

Our studies led us to conclude that the facile, template-free approach to polymer nanocapsules is not limited to the specific monomer **1a** and appears to be applicable to any building block with a flat core and multiple in-plane reactive groups at the

periphery. Various building blocks including CB[5], triphenylene, and phthalocyanine derivatives were polymerized with ditopic or tritopic linkers through thiol–ene “click” reaction, acetal formation, amide formation, and N-alkylation reaction or without linkers through olefin metathesis (Table 1). All these cases successfully resulted in polymer nanocapsules. For instance, thiol–ene photopolymerization of 1,2,7,8,13,14-hexakisallyloxy triphenylene (**TP**, **4**) and 1,8-octanedithiol (**2c**) in acetonitrile produced polymer nanocapsules with an average diameter of 900 ± 120 nm.²⁰ Also, when a phthalocyanine derivative having eight terminal pentene moieties (**Pc**, **5**) was polymerized through a thiol–ene “click” reaction with **2b** initiated by a radical initiator or was polymerized through olefin metathesis, it produced polymer nanocapsules with average diameters of 210 ± 70 nm or 230 ± 70 nm, respectively.²⁴

These polymer nanocapsules exhibited general features of polymeric materials such as solvent responsive swelling and deswelling²² as well as unique and intriguing properties dependent on the choice of building blocks and linkers. For example, thanks to the hollow interior, the polymer nanocapsules can be loaded with cargo molecules such as drugs either during the nanocapsule formation or by solvent dependent swelling and deswelling processes.^{20–23} Furthermore, the cavity of CB[6] is known to bind polyamines such as spermine or spermidine with an exceptionally high binding constant ($>10^9$ M⁻¹);³⁷ this aspect makes polymer nanocapsules made of CB[6] potentially useful in targeted drug delivery and imaging by allowing facile, modular, non-destructive postsynthetic surface modification of the polymer nanocapsules through host–guest chemistry.^{20,21} Introduction of a reducible disulfide linkage into a ditopic linker further enabled a reduction-triggered release of cargo molecules from polymer nanocapsule **6** into the cytoplasm of HepG2 hepatocellular carcinoma cells (Figure 4).²³ Additional functional moieties such as imaging probes and antifouling groups can also be introduced onto the surface in a modular manner, which suggests that these nanocapsules can be utilized as versatile platforms for developing future theranostic tools.

The postsynthetic modification of the CB[6]-based polymer nanocapsules is not limited to strong host–guest interactions of CB[6]. Their surface can also be decorated with metal nanoparticles ($M = Pd$, Au , and Pt) stabilized by the carbonyl

Table 1. Various Disk-Shaped Building Blocks and Polymerization Methods To Produce Polymer Nanocapsules

Building blocks	cucurbit[6]uril	cucurbit[5]uril	phthalocyanine	triphenylene
Linkers	ditopic			tritopic
Polymerization methods	<ul style="list-style-type: none"> • thiol–ene “click” reaction • olefin metathesis reaction 	<ul style="list-style-type: none"> • acetal formation reaction • amide formation reaction 	<ul style="list-style-type: none"> • N-alkylation reaction 	

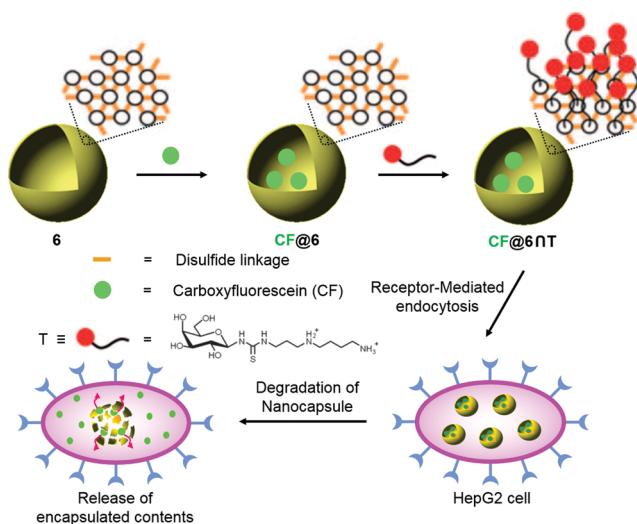


Figure 4. Schematic representation of the stimuli-responsive drug delivery of the polymer nanocapsules by introduction of reducible disulfide linkages and postsynthetic modification through strong host-guest chemistry. Adapted with permission from ref 23. Copyright 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

portals of the CB[6] as well as the sulfur residues on the surface of the nanocapsules.²⁵ The Pd-nanoparticle decorated polymer nanocapsules, in particular, demonstrated high stability and dispersibility in water as well as excellent catalytic activity and recyclability in carbon–carbon and carbon–nitrogen bond formation reactions in aqueous media, illustrating their great potential as a green catalyst (Figure 5).

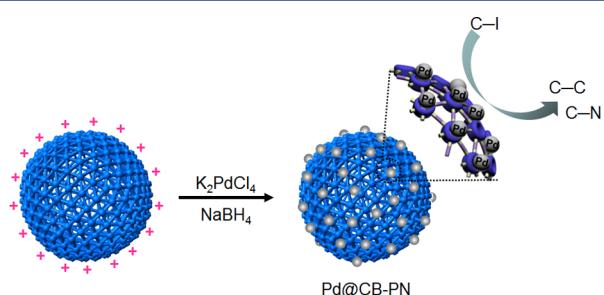


Figure 5. Synthesis of M@CB-PNs and their catalytic activity toward carbon–carbon and carbon–nitrogen bond formation. Adapted with permission from ref 25. Copyright 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

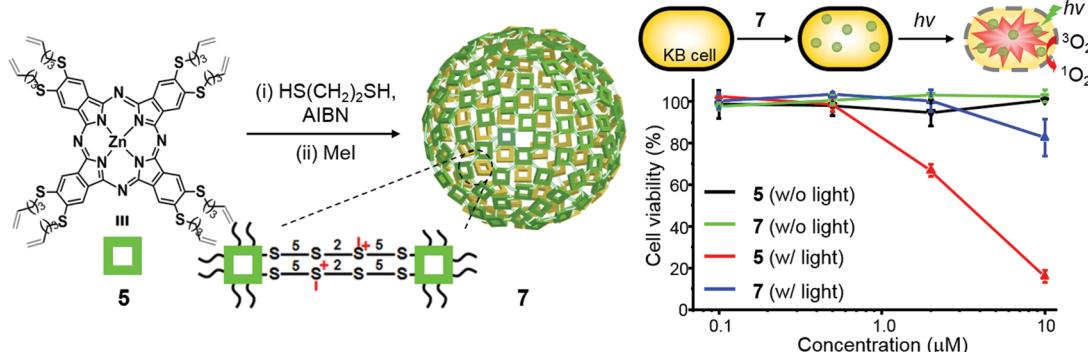


Figure 6. Synthesis of phthalocyanine-based nanocapsule 7 via thiol–ene “click” reaction. *In vitro* dark toxicity and phototoxicity of ZnPc monomer 5 and nanocapsule 7 toward KB cells. Adapted with permission from ref 24. Copyright 2013 Royal Society of Chemistry.

In addition, the phthalocyanine-based nanocapsules 7 with a very thin shell and hollow interior exhibited enhanced photodynamic efficacy toward cancer cells by overcoming aggregation problems commonly associated with photosensitizers (PS) as well as the low PS-loading efficiency of traditional nanocarriers (Figure 6).²⁴ The dispersibility of the nanocapsules in aqueous media can be improved by a subtle change in the peripheral reactive groups that allows spontaneous introduction of positive charges in the cross-linking chains during polymerization, which could make the nanocapsules more effective *in vitro* and even *in vivo*. The phthalocyanine nanocapsules also potentially allow postsynthetic modifications such as the introduction of targeting ligands that help deliver the nanocapsules to specific target sites and could even be useful for dual chemo- and photodynamic therapy via encapsulation of therapeutic agents. Preliminary studies suggest that subphthalocyanine nanospheres, similar to phthalocyanine nanocapsules, show great promise in photodynamic inactivation of antibiotic resistant bacteria.

3. TWO-DIMENSIONAL POLYMER FILMS

Two-dimensional polymers, which can be defined as free-standing, single-monomer-thick films with a covalently linked 2D network structure,²⁶ have attracted considerable attention not only because of their fundamental properties but also because of their potential applications in selective transport, molecular electronics, sensors, surface catalysis, and drug delivery, among others.³⁹ Even though theoretical studies predicted unusual mechanical and folding behavior of such materials,^{40,41} the lack of robust methods to produce 2D polymers as bulk material with macroscopic dimensions has, in general, hindered the investigation of their fundamental properties as well as their practical applications. Synthesis of atomically precise organic 2D polymers was, very recently, achieved by Schläter and King via solid-state topochemical photo-cross-linking of monomers preorganized as 2D layers in a crystal. Subsequently individual layers were isolated in solution from the swollen crystals.^{42–44} However, the synthesis of 2D polymers in solution without the aid of a template, interface or surface, or crystal packing remains a challenge.

As described in previous sections, reaction medium plays a key role in the formation of polymer nanocapsules and can modulate their size.²¹ Interestingly, in some solvents, we observed other morphologies besides hollow spheres. For instance, the photopolymerization reaction in DMF produced certain rolled or folded objects, which later turned out to be

multilayered polymer films. Encouraged by this result, we decided to develop a facile and general template-free method to synthesize free-standing, covalently bonded, 2D organic polymers. We used (1) rigid and disk-shaped building blocks having laterally predisposed reactive groups at the periphery, (2) short linkers for high bending rigidity, and (3) carefully chosen appropriate solvents, which would lead to rigid intermediates and allow them to remain flat and to grow into 2D polymers with macroscopic lateral dimensions and molecular-scale thickness. Indeed, when perallyloxyCB[6] **1a** was polymerized with 1,2-ethanedithiol **2b** in *N,N'*-dimethylacetamide (DMA), 2D polymer film **8a** with a size of several tens of micrometers was obtained as major product (Figure 7). Other monomers with a triphenylene or phthalocyanine core also produced 2D polymer films under similar conditions.

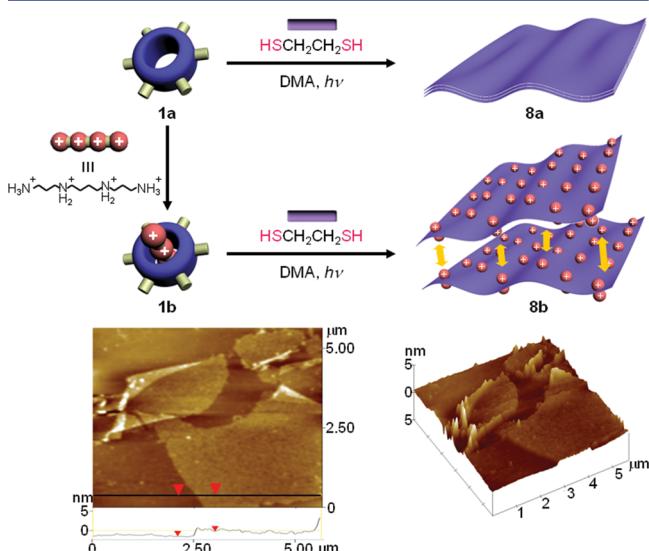


Figure 7. Schematic representation of synthesis of 2D polymer films and AFM images of single-monomer-thick 2D polymer film **8b**. Adapted from ref 26. Copyright 2013 American Chemical Society.

Taken together, these results suggest a unifying view for the covalent self-assembly of polymer nanocapsules and 2D polymer films. At the early stage of the reaction, a 2D oligomeric patch is produced. If the 2D oligomeric patch has low bending rigidity or is produced in a poor solvent, it starts to generate a curvature and eventually forms a hollow sphere. On the other hand, when the 2D patch has high bending rigidity or is generated in a good solvent, it continues to grow in the lateral directions to produce a 2D polymer.

For better understanding of the formation mechanism of 2D network structures in solution, we performed Monte Carlo simulations, using a sphere with several reactive patches attached on its surface as a building block.²⁶ While a sphere with two reactive patches on opposite positions produced a linear polymer as expected, a sphere with four or six patches evenly distributed at the equator resulted in a 2D network structure. By contrast, a 3D random network structure was obtained with spheres having six reactive patches disposed in octahedral symmetry. This result was experimentally validated by the fact that the 2D polymer formation reaction using a 1:1 host–guest complex of **1a** and a spermine-based guest having two terminal olefin groups, instead of **1a**, produced a random polymer aggregate. These results suggest that the geometric aspect of a building block, that is, disposition of multiple (≥ 4)

sticky groups in the same plane of a rigid core, is one of the most important factors governing the formation of 2D network structures.

The 2D polymers synthesized via covalent self-assembly were significantly thicker than single-monomer-thickness, presumably due to multilayer stacking of the initially produced single-layer films. To synthesize single-monomer-thick 2D polymer films, we utilized host–guest chemistry to create electrostatic charges on the surface of the 2D films preventing their stacking via electrostatic repulsion. We finally achieved the single-layered 2D polymer film **8b** by polymerization of spermine@allyloxyCB[6] complex (**1b**), having four positive charges, with **2b** in DMA (Figure 7). The AFM height profile of the resulting 2D film showed a thickness of 2.0 nm, which is comparable to the height of **1b**, indicating successful synthesis of a free-standing, single-monomer-thick 2D polymer.

We tried to elucidate the internal structure of the 2D polymer by TEM but failed to get good images because it is extremely sensitive to the electron-beam. We thus decided to decorate each repeating unit of the 2D polymer with a small gold nanoparticle to visualize it by TEM. The high-angle annular dark field-scanning TEM (HAADF-STEM) images of the gold-nanoparticle-decorated 2D polymer clearly showed that despite many defect sites, gold nanoparticles appear uniformly distributed and each is surrounded by approximately six neighbors with an average distance of 3 nm. This distance is fairly consistent with that calculated for two neighboring CB[6] units based on an ideal hexagonal arrangement of the repeating unit in the 2D polymer.

Two-dimensional polymers with a laterally extended network and nanometer-size pores are expected to be useful as permselective membranes.⁴⁵ The 2D polymers synthesized from **1a** and dithiol linkers possess a quasi-hexagonal network structure with two different pores; one is the molecular cavity of CB[6], and the other is the interstitial space between adjacent CB[6] units. The latter serves as molecular separation channels, while the former provides a site for facile postsynthetic modification that can control the separation selectivity by host–guest chemistry. The membranes were prepared by a simple filtration of a dispersion solution of 2D polymers through a supporting membrane. A preliminary result suggests that the porosity and hydrophilic nature of the filter can easily be modified by introducing various charged guests utilizing the host–guest chemistry of CB, leading to selective separation of variety of small dyes, drugs, and other important organic molecules.

Moreover, the 2D polymer films made of aromatic building blocks such as triphenylene and phthalocyanine derivatives have great potential for development of π -conjugated 2D polymers exhibiting conducting or semiconducting behavior because charge carriers may travel easily along the 2D π -network. Although their carrier mobility is expected to be lower than that of graphene, a great variety of possible structures by utilization of different π -conjugated building blocks can possibly allow the tuning of electronic properties and may be advantageous for processing as well.

4. POLYMER MICRORINGS

As described in previous sections, we developed a novel synthetic method for nanometer-sized polymer hollow spheres and 2D polymer films involving shape-directed covalent self-assembly by utilizing highly symmetric flat and rigid-core building blocks with multiple polymerizable groups isotropi-

cally predisposed in all directions and linear linkers. Based on these results along with the aid of theoretical analysis, we determined that the isotropic orientations of multiple functional groups in the building blocks are crucial in determining the morphology of the resulting polymers. We thus anticipated that anisotropic orientations of such functional groups in a tecton with reduced symmetry might result in higher-order nanostructures with different morphology.

As conjectured, when we subjected the rectangular-shaped monomer 2,3,6,7-tetrakis(allyloxy)anthraquinone (**9**), which has four allyl groups predisposed in anisotropic directions, to ultraviolet irradiation in the presence of dithiol **2a** in tetrahydrofuran, we discovered that the resulting polymer was neither a 2D polymer nor sphere but rather a micrometer-sized hollow ring, **10** (Figure 8).²⁷ SEM and AFM studies revealed

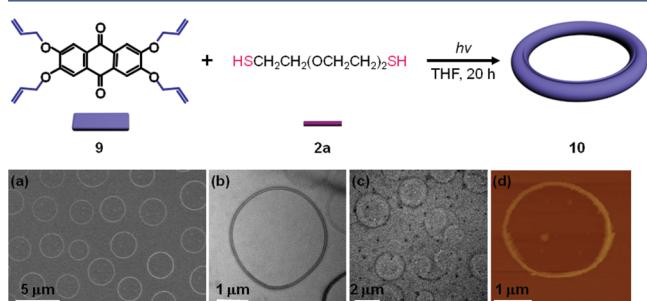


Figure 8. Synthesis of polymer microring **10** from monomer **9** and dithiol **2a**: (a) SEM, (b) HR-TEM, (c) cryo-TEM, and (d) AFM images of **10**. The images in panels a–d are adapted with permission from ref 27. Copyright 2014 Nature Publishing Group.

that the cross-linked polymer **10** consists of well-dispersed, toroidal microrings of a relatively uniform size with an average outer diameter of $2.7 \pm 0.7 \mu\text{m}$. HR-TEM indicated that the microrings were hollow toroids, and cryogenic TEM unequivocally confirmed that **10** is composed of shape-persistent toroidal microrings in solution.

We investigated the role of monomer concentration in controlling the size of the microrings. In a microring-forming concentration range, the outer diameter of the microrings became smaller while the cross-sectional diameter became larger as the initial monomer concentration increased. To understand the formation mechanism of microrings, we monitored the reaction by SEM. A series of SEM images taken during the reaction revealed that the formation of ellipsoidal 2D patches was followed by the rolling-up of the patches in a longitudinal direction. Afterward, the straight rolled tubes bent down to form arc-shaped tubes and grew further to become hollow nanotubular toroids. Based on these results, we hypothesize that the rectangular shape of the monomer directs the ellipsoidal patches to roll up as a nanotube, which then bends back on itself to form an energetically stable microring (Figure 9). The formation of hollow nanotubular toroids was also investigated by theoretical studies.²⁷ Based on energetic considerations, the toroid formation from a linear tube is spontaneous. Similar to the case of hollow spheres as discussed above, the energy dictates the formation of fewer larger rings, whereas the entropy favors the formation of more smaller rings. The distribution of ring size is determined by minimizing the free energy of the system.

The facile, one-pot synthesis of such a topologically interesting structures may provide a unique opportunity to

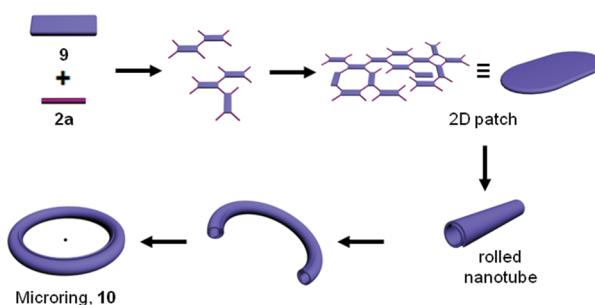


Figure 9. Proposed formation mechanism of microrings. Adapted with permission from ref 27. Copyright 2014 Nature Publishing Group.

investigate their fundamental physical properties and discover novel applications. For example, these microrings with a hollow nanotubular rim could be used as microring resonators, which have a wide range of applications including signal processing filters, sensors, and modulators.⁴⁶ Also, the encapsulation of electrochemically or magnetically active molecules such as fullerenes may allow the nanotubular microrings to be a versatile platform for oscillators and composites with novel electromagnetic properties.⁴⁷

5. CONCLUSION AND FUTURE PERSPECTIVES

While self-assembly under thermodynamic control leads to the formation of the most energetically stable species, kinetic control over self-assembly permits us to access many different states of a system. However, lack of detailed understanding of the kinetics of the self-assembly process has often hampered the design of kinetically controlled self-assembly systems. Thus, construction of well-defined nanostructures through irreversible stitching of building blocks has often been regarded as an impractical task.

Although some difficulties remain, our work opens the possibility that various nanostructures with a narrow size distribution can be synthesized through the formation of irreversible covalent bonds without the aid of any preorganization or templates by rational design of the building blocks and careful choice of linkers and reaction media. Our approach has shattered the notion that well-defined nanostructures cross-linked by irreversible covalent bonds can form only through chemical fixation after self-assembly of monomers.

We have also begun to understand how the irreversible stitching of the flat and rigid building blocks having multiple in-plane reactive groups can produce the well-defined nanostructured materials. Although at the moment it is difficult to elucidate the detailed formation mechanism of the various nanostructures at the molecular level, our work to date strongly suggests that multiple in-plane reactive groups of the building blocks are responsible for the polymerization of the monomers predominantly in the lateral dimensions. This may prevent the formation of random aggregates usually expected during typical irreversible cross-linking of monomers and lead to the formation of intermediate 2D patches, a key step in a successful kinetically controlled self-assembly process.

Also, we have been able to establish some fundamental properties of irreversible covalent-bond mediated self-assembly. Most notably, the reaction medium and bending rigidity of the linkers play an important role in determining the final size and shape of nanostructures; in general, poor solvents and flexible linkers drive the system to polymer nanocapsule formation while good solvents and rigid linkers promote the formation of

2D films in the cases of isotropic systems. Furthermore, the geometry and symmetry of the reactive groups play a crucial role; anisotropic orientations of reactive groups result in anisotropic lateral growth and rolling of intermediate 2D patches, which eventually leads to the formation of toroidal microrings (Figure 10).

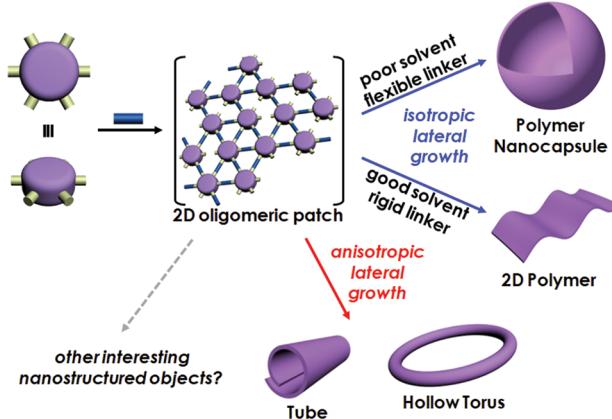


Figure 10. Self-assembly of nanostructured materials through irreversible covalent bond formation.

The work presented here provides only a starting point for the synthesis of various nanostructures through irreversible covalent bond formations. There may be many other interesting and hierarchical nanostructures accomplished by controlling other factors such as chirality, turbulence, gravitational field, electric or magnetic field, and mechanical force. Indeed, preliminary results suggest that well-controlled turbulence of the reaction media in microfluidic channels does affect the morphology significantly, resulting in helical ribbons with one-handedness. We also envision that more than two different building blocks with different shapes and properties and orthogonal reactive groups can be incorporated to build more complex nanostructures and expand the versatility of our approach.

A wealth of new building blocks and improvements in controlling methods are already helping us expand our approach to new research avenues for robust and shape-persistent nanomaterials. The use of irreversible covalent bonds does still possess some limitations, one of which is the generation of defects in the nanostructures due to the lack of self-repairing mechanisms. A possible solution for generating robust and defect-free nanostructures may be utilization of strong yet reversible covalent bonds such as strong carbon–carbon double bonds shuffled by olefin metathesis. Although they may be not sufficiently reversible to achieve defect-free nanostructures all the time, their incorporation may strengthen our approach. Robust nanostructured materials with dynamic and stimuli-responsive behavior are likely to be the key step in the development of artificial “smart” materials inspired by complex adaptive systems in nature that can work as well as or even better than their natural counterparts. We envisage that continuing progress will unveil the considerable untapped potential of self-assembly of nanostructured materials using irreversible covalent bonds.

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Notes

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