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Nanoscale Objects: Perspectives Regarding Methodologies for Their Assembly, Covalent Stabilization, and Utilization

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Abstract In this review, we highlight some of the most recent advances in the design and utilization of organic nanoscale objects. Initially discussed is the preparation of well-defined nanoscale assemblies, typically the precursors of nanoscale objects, by programmed supramolecular interactions, and the subtle interplay between molecular structure and self-assembly is highlighted. The covalent stabilization of these supramolecular structures to produce robust nanoscale objects is then addressed from both intramolecular and intermolecular perspectives. Finally, the evolving field of the utilization of these nanoscale objects is described.

Keywords Nanostructured organic materials · Covalently-crosslinked supramolecular assemblies

1
Introduction

While the fashioning of organic molecules has only a short history, continuous developments in synthetic methodology have had a tremendous impact on the ability to prepare well-defined and complex molecular structures. The sophistication now available to the modern synthetic chemist permits amazingly complex architectures to be prepared, which can contain several levels of structural information. In this review, we will limit the discussions to organic systems, for which organic transformations [1, 2] with high degrees of regiochemical and stereochemical control have evolved to allow the syntheses of elaborate natural and synthetic products. This ability to mimic nature in the design of molecules is one of the driving forces behind the rapidly evolving field of nanotechnology, whereby synthetic organic chemistry is being extended to targets of increasing dimensions. As the size of the targets increases, new approaches to their design and new synthetic methodologies are being developed. Successful examples of these have most often involved a bottom-up supramolecular assembly of molecules or macromolecules that are compositionally and structurally programmed for assembly according to the rules of nature, involving a balance of intermolecular attractive and repulsive forces. Moreover, supramolecular assembly is applied in an iterative fashion, along with templating strategies and covalent stabilization to produce materials of high orders of complexity.

Equally important to both nanotechnology and the continued evolution of synthetic chemistry has been the development and further refinement of a range of analytical tools which, for the first time, has permitted a thorough investigation of the properties and characteristics of structures less than 50 nm in size. Using combinations of techniques, such as atomic force microscopy (AFM), transmission electron microscopy (TEM), and neutron-scattering, together with traditional spectroscopic tools, a direct correlation can now be obtained between minor structural changes at the atomic level and molecular organization on the 10–100 nm scale. This unprecedented ability has led to the concept of designer materials that have enormous potential in commercially important fields ranging from molecular/microelectronics to biocompatible surfaces. Arguably, one of the most exciting areas of designer materials to emerge as a result of these advances in molecular imaging is the concept of nanoscale objects – organic structures which are shape-persistent and have overall dimensions of between 5 and 100 nm.

In this review, we highlight some of the most recent advances in the design and utilization of nanoscale objects. Initially, the preparation of well-defined nanoscale assemblies, typically the precursors of nanoscale objects, by programmed supramolecular interactions is discussed and the subtle interplay between molecular structure and self-assembly highlighted. The covalent stabilization of these supramolecular structures to produce true nanoscale objects is then addressed from both intramolecular and intermolecular perspectives. Finally, the evolving field of the utilization of these nanoscale objects is described.

2
Nanoscale Assemblies by Supramolecular Interactions

Hierarchical assembly of supramolecular systems is ubiquitous in biological systems [3] and this level of sophistication is being approached by a number of recent studies where there is a direct correlation between molecular structure and self-assembly. Ghadiri et al. [4] have shown the power of hydrogen-bond-directed self-assembly of cyclic structures to give open-ended hollow tubular nanoscale assemblies in which the specific design of the macrocyclic ring leads to efficient stacking. The stacked assemblies are subsequently stabilized primarily by hydrogen-bonding. While the majority of the early work [5] in this area involves cyclic peptides, the range of possible structures has been extended recently to include heterocyclic triazole rings, **1**, prepared by Click Chemistry [6], and oligo(phenylethynyl) derivatives [7–9], which are primarily stabilized by π-π and hydrophobic interactions (Fig. 1). In each of these cases, assembly-active ends remain, which theoretically allow for the lengthwise growth to continue until a capping unit is encountered.

Nanoscale objects can also be constructed as limited growth, discrete entities, by the molecular recognition and self-assembly of small molecules that are designed for directional assembly into a closed structure. An elegant recent example of this is the construction of a molecular cage composed of three calix[4]arene end units, **2**, and six connecting barbiturate groups, **3**, reported by Crego-Calama, Reinhoudt et al. [10], where the structures and conformations of the small molecules direct and limit the assembly processes to the formation of enclosed cages. This provides a central cavity that is ca. 3 nm in diameter and 0.7 nm in height, which has demonstrated dynamic complexation and release of noncovalent guests (Fig. 2). Atwood and Szumna have utilized cationπ and hydrogen-bonding interactions geometrically placed within a molecular capsule to directionalize electrostatic interactions for the production of

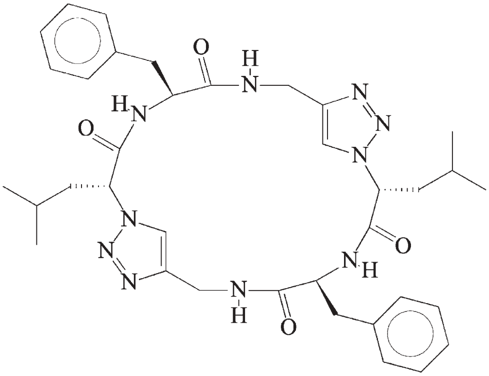

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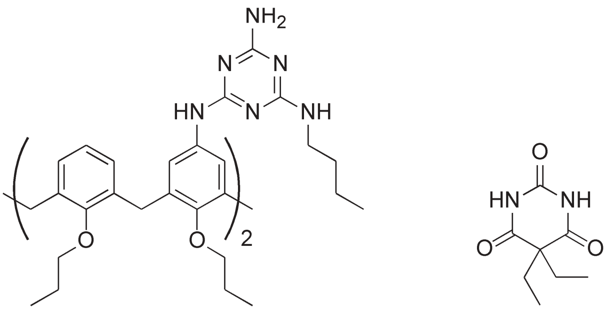
Fig. 1 Structure of self-assembling heterocyclic cyclic peptide, **1**



2 **3**

Fig. 2 Structure of calix[4]arene (**2**) and barbiturate (**3**) used in the 3:6 self-assembly of a molecular cage for dynamic guest complexation

anion-sealed single-molecule capsules [11]. This placement of the entire ion-pair within a molecular framework is a new approach to the preparation of anion receptors, based upon non-covalent packaging of the cationic tetramethylammonium salt within the cavity of the organic capsule molecule, **4**. In a recent report, a second-generation anion receptor (Fig. 3) was designed to optimize the electrostatic and hydrogen-bonding interactions, to contain the tetramethylammonium cation within the cavity, to attract a halide anion to seal the vessel, and also to provide for bulky groups along the upper rim to stabilize the directionally templated ion-pair. These systems represent extremely high levels of control over the self-assembly processes and illustrate the predictability that can be now achieved with the manners by which small molecules undergo well defined assembly to afford discrete structures. Progressing to large, polymeric self-assembling systems introduces a range of new difficulties as well as added opportunities.

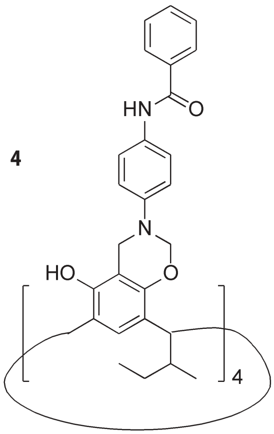


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Fig. 3 Atwood's second generation molecular capsule (**4**), which acts as a receptor for the directional non-covalent capture of ion-pairs

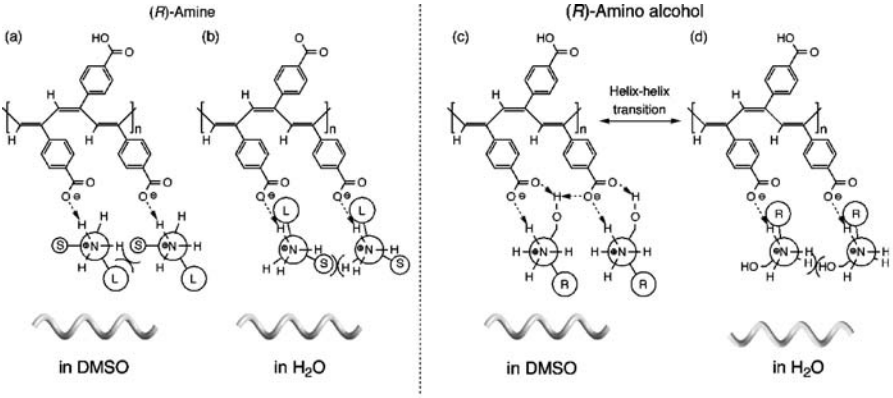

Fig. 4a–d Solvent induced helical transition in linear poly(*p*-carboxyphenyl)acetylenes

By extending the self-assembly process to polymeric systems, organizational control can also be induced by the addition of external agents and with reliance upon the increased conformational degrees of freedom of macromolecules, in effect mimicking biological systems such as chaperonins. One of the most dramatic illustrations of this ability to manipulate structural conformation is the solvent-induced switching of macromolecular helicity by the addition of optically active amino alcohols to linear poly(*p*-carboxyphenyl)acetylene chains [12]. The helical sense of the polymers exhibited opposite Cotton effect signs, as observed by circular dichroism, by simply changing the solvent from water to dimethylsulphoxide. As illustrated in Fig. 4, the model that has been proposed to explain this phenomenon involves a switching in the acid-base interactions under different solvent conditions. This example demonstrates the ability to alter molecular conformation and chirality by appropriate choice of the achiral or chiral external conditions (Fig. 4). The induction of chirality through a self-assembling event has also been observed during catenation and may lead to a new switching system where chirality appears on catenation but disappears on decatenation [13].

The intermolecular self-organization of polymeric or oligomeric units can also lead to a range of different nanoscale assemblies. A recent review by Discher and Eisenberg [14] clearly demonstrates the rich array of structures that can be obtained from the solution-mediated assembly of polymers, and further underscores the fact that the structural diversity possible with synthetic systems leads to a significantly greater array of chemical and physical possibilities when compared to biological systems, such as lipids. This diversity naturally leads to improved properties and functionality, critical criteria in many applications. Moreover, the ability to control the shapes of the assembling polymers, by control over their structure and topology [15], leads to further diversity in the supramolecular materials.

By a combination of coordination chemistry and electrostatic interactions, the fullerene-triggered unidirectional self-assembly of an acyclic zinc por-

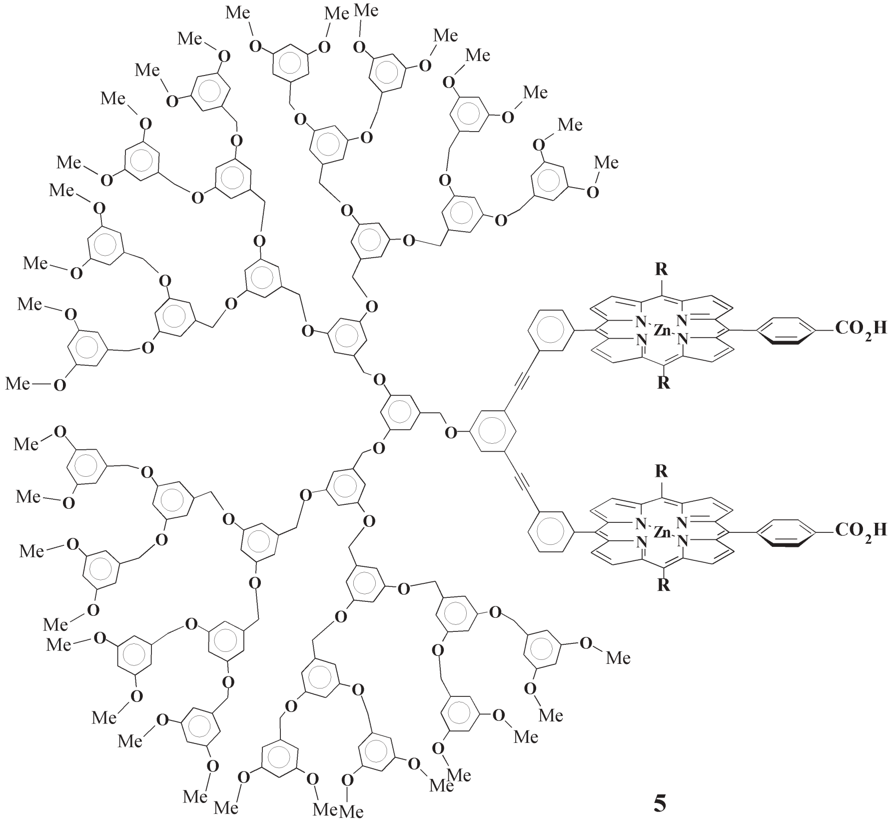

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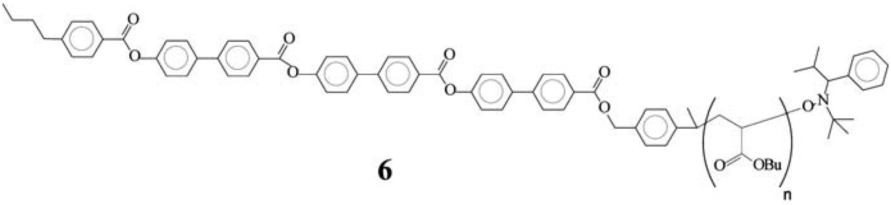
Fig. 5 Structure of dendritic bis(porphyrin), **5**, which undergoes specific self-assembly in the presence of C_{60} to give well-defined nanorods

phyrin dimer bearing a large fourth-generation poly(benzyl ether) dendritic wedge, **5**, has recently been reported by Aida et al. (Fig. 5) [16]. No discrete organization of the dendrimer was observed in either the absence of C_{60} or when the six acid groups (R=-Ph-CO_2H) were esterified. However, in the presence of the fullerene, the carboxylic acid derivative initially formed an inclusion-like complex with the fullerene coordinated between the two porphyrin rings. This complex then induced one-dimensional aggregation through the dimerization of the carboxylic acid side group to give untangled, discrete nanoscale objects, having very high aspect ratios and diameters of 12 nm, in agreement with that estimated from molecular modeling of two dendritic porphyrins.

These selective interactions, built into the structures on the Ångström level and drawing inspiration from biomolecular interactions, can also be employed to create other nanoscale assemblies. Illustrative examples have involved the use of quaternary hydrogen-bonding units [17], nucleobases [18], or biotin–streptavidin interactions [19]. An intriguing variation on this theme, only demonstrated on a microscopic scale as yet, involves the recent use of magnetic interactions in thin nanorods (diameter~0.4 µm and length 2.2 µm) composed of alternating sections of Au and Ni which gives rise to three-dimensional self-assembly into highly stable nanoobjects [20]. These nanoobjects are essentially "bundles" of individual rods in which the alternating layers of Au and Ni align and defects in the packing or alignment of the rods were rare (<1%). While not organic in nature, the process used for manufacture of the rods could easily be applied to polymeric materials and suggests that a combination of magnetic forces with specific surface chemistries for interaction may be powerful tools in future self-assembling strategies.

In concert with the potential use of external fields to induce supramolecular assembly, other relatively new approaches to controlling molecular organization have been developed. One of the most exciting involves architectural differences, for example the self-assembly of diblock or triblock copolymers in which one of the segments is a rigid rod with a great tendency to order and the others are flexible coils that have low tendencies toward ordering. In addition to this ordering difference, variations in molecular architecture have also been shown to have a powerful effect on the ability of these rod-coil block copoly-



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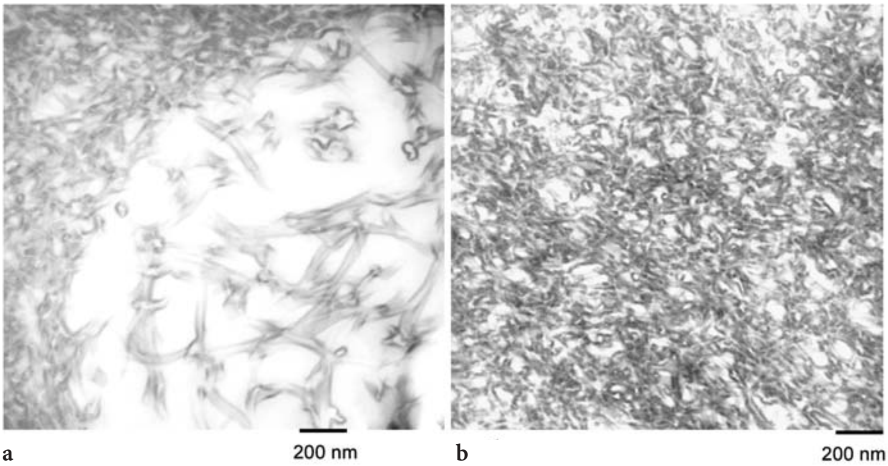

Fig. 6a, b Structure of rod-coil block copolymer, **6**, and transmission electron microscopy images of a RuO_4-stained film cast from THF and annealed at 125 °C for 48 h. **a** The edge of the film showing cylindrical aggregates lying parallel and perpendicular to the substrate. **b** The center of the film mers to assemble into well-defined nanostructures. The pioneers in this new direction have been Stupp et al. [21–23], who have developed a range of structures, each programmed to assemble into one-dimensional nanoribbons, two-dimensional sheets or three-dimensional mushroom-like structures by simply varying the chemical structure and architecture of the block copolymers. A recent example [24] building upon this work involved the synthesis of rod–coil polymers consisting of an aromatic ester rod and an amorphous vinyl polymer coil, **6**. In both the solid state and in solution, **6** revealed a range of unusual nanostructures, the formation of which was driven by the stacking of the aromatic polyester unit (Fig. 6). It is also interesting to speculate that the high degree of definition observed for the nanostructures is a result of the monodisperse nature of the rod units, in both this work and that of Stupp, which further promotes and enhances crystallization/stacking.

3

Covalent Stabilization of Supramolecular Assemblies Leading to Nanoscale Objects

One of the key attributes of supramolecular assemblies is the dynamic nature of the molecular organization, which leads to exchange of individual molecules between molecular clusters. This has been exploited by Meijer et al. [25] in the design of a novel family of telechelic polymers bearing hydrogen-bonding termini, which exhibit unique physical and mechanical properties when compared to their counterparts that lack the terminal molecular recognition elements. These materials illustrate the influence that can be exerted by single, intermolecularly attractive units. Owing to the ability of the small concentration of sophisticated chain end groups to alter the properties of commodity polymer chains, this approach and these materials are expected to dramatically impact a variety of commercially important applications, where external stimuli such as heat or dilution trigger the polymers to behave like a fluid that is easy to process by the manufacturer or consumer. However, in many other applications it is highly desirable to have a static structure that is not affected by reversibility. To this end, significant effort has been devoted in recent years to the covalent stabilization of supramolecular assemblies, which leads to discrete nanoscale objects that have fundamentally different properties and structural characteristics when compared to the individual constituents of the assembly.

Arguably, one of the first examples of covalent stabilization involves the core-crosslinking of polymer micelles to give a crosslinked nanoparticle surrounded by a corona of linear polymer chains [26–29]. This concept has been revolutionized in recent years by the concept of shell-crosslinked nanoparticles in which it is the coronal chains of the polymer micelle that are crosslinked, leaving the central core comprised of linear chains that are covalently linked to the inner surface of the crosslinked membrane capsule. The shell-crosslinked nanoparticle possesses a degree of structural organization, having a well-defined external shell the nature and crosslink density of which can be controlled, an interfacial layer and a central core composed of linear chains. Armes et al. [30] has effectively combined both concepts, shell-crosslinking and core-crosslinking, to afford an intermediate structure in which a central layer is crosslinked. Using a triblock copolymer, for which the central block contains reactive groups that can be used for crosslinking, a hybrid nanoobject is created in which a central core of linear chains is surrounded by a crosslinked shell/layer that is, itself, surrounded by a corona of linear polymer chains. The broad nature of these concepts allow a wide variety of polymeric blocks and copolymer architectures to be used and results in tremendous structural diversity for these nanoobjects [31], leading in turn to tremendous potential for applications.

Such a covalently stabilized nanostructure can be manipulated physically and/or chemically under varying conditions while still retaining its individuality and altering the discrete size, shape and structure, each of which is dictated originally by the supramolecular assembly of linear polymer chains. This is an exciting and emerging area of current interest – the regiocontrolled physical and chemical manipulation of well-defined nanostructures preformed by supramolecular assembly to produce, ultimately, nanomaterials through iterative processes that could not be obtained via supramolecular assembly alone. A recent example of the structural diversity that can be exercised for the subsequent thermal reshaping of the nanostructures involved the preparation of nanodroplets of polyisoprene fluid contained within a poly(acrylic acid-*co*-acrylamide) shell from polyacrylic acid-*b*-isoprene block copolymers (Fig. 7) [32, 33].

Comparative TEM and AFM analyses of the shell-crosslinked nanostructures revealed discrete particles, the size and shape of which were dictated by the glass transition temperatures (T_gs) of the inner core domains. The core T_g values for shell-crosslinked nanoparticles containing polyisoprene within their internal region were controlled by both the microstructure [32] and chemical nature [33] of the core polymer chains. Polyisoprene prepared by anionic polymerization in hexane or by living radical polymerization exhibited a low T_g

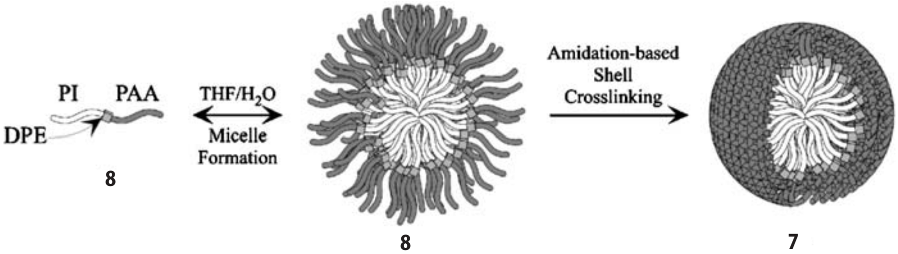

Fig. 7 Synthetic approach for the formation of shell-crosslinked nanoparticles, **7**, from poly(acrylic acid-*b*-isoprene) block copolymers, **8**. *DPE* Diphenylethylene, *PI* polyisoprene, *PAA* poly(acrylic acid)

value (ca. –70 °C), which allowed for significant flattening of the nanoparticles upon deposition from water onto the substrate at room temperature. In contrast, the preparation of polyisoprene by anionic polymerization conducted in tetrahydrofuran (THF) or conversion to a hydrochlorinated polyisoprene afforded core materials that exhibited T_gs in excess of room temperature, and these materials remained spheres when deposited onto substrates and imaged at room temperature. Thermal treatment of the nanostructures containing the higher T_g core materials resulted in shaping of the structures, whereby their shapes conformed to that of the flat substrate. Moreover, complete chemical degradation and extraction of the core polymer chains, for example by ozonolysis of polyisoprene [34] or hydrolysis of poly(ε-caprolactone) [35], led to an even more flattened structure, essentially by removing the core and creating a "hollow" nanocage. It should be noted that these manipulations were not possible for the precursor polymer micelles due to complete loss of structure, which further demonstrates the validity and utility of the covalent stabilization approach.

Similar "hollowed-out" structures have recently been reported by Zimmerman et al. from either dendritic or star polymer precursors [36]. Instead of using a supramolecular assembly, covalent macromolecules are first prepared containing a cleavable core and crosslinkable groups at the chain ends; in these cases homoallyl groups were crosslinked by ring-closing metathesis reactions using Grubbs' Type 1 catalyst. Extremely efficient crosslinking of the chain ends was observed, possibly owing to proximity effects. Subsequently, the functionalized core could be removed to give a hollow, crosslinked macromolecule. The critical feature of structural retention has been demonstrated in these systems and, as in the shell-crosslinked nanoparticle case, degradation of the core for the non-crosslinked case results in disintegration of the macromolecule into smaller fragments. Furthermore, as a result of the chain termini connectivity for the crosslinked dendrimers, molecular imprinting with high to moderate degrees of selectivity can be achieved using guests that resemble the core fragment [37, 38].

The versatility inherent in this regioselective crosslinking approach has recently been utilized by a variety of groups to prepare well-defined and functional nanoobjects. Using small-molecule amphiphiles that contain a crosslinkable double bond, **9**, McQuade et al. [39] have been able to form reverse micelles at low water content and then covalently stabilize these dynamic structures to give crosslinked spheres, **10**, whose radii (ca. 3–5 nm) are similar to those of the pre-crosslinked reverse micelles (Fig. 8). Significantly, these nanoobjects were shown to be permeable and the carboxylate counterions on the interior could be exchanged with both fluorescent dyes and transition metal ions, **11**. In a similar vein to the dendritic catalysts developed by Fréchet et al. [40], these nanoobjects can act as catalysts in which reactants can enter the nanoparticle, undergo a chemical transformation in the interior and then exit.

A similar strategy has been used by Emrick et al. [41] and Nolte et al. [42] to stabilize interfacial assemblies of block copolymers leading to hollow spher-

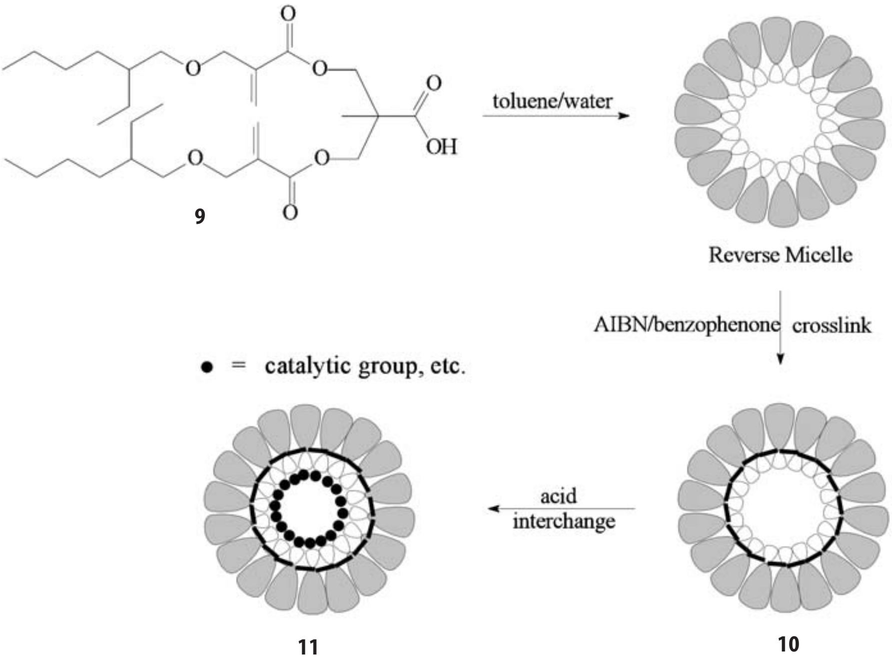

Fig. 8 Crosslinking reactions performed between polymerizable double bonds placed at the interface of amphiphilic small molecule assemblies provided for the preparation of stabilized reverse micelle nanostructures. *AIBN* Azobisisobutyronitrile

ical nanoobjects. By assembling graft copolymers of poly(octadiene)-*g*-poly(ethylene glycol) at the interface of toluene/water, discrete spherical assemblies can be obtained that have the poly(ethylene glycol) (PEG) chains directed into the bulk water phase and the poly(olefin) backbone located at the toluene/water interface [41]. These dynamic structures are then stabilized by crosslinking with a bis(cyclooctene)-functionalized PEG derivative to give toluene-filled nanocapsules that can be isolated and are now stable to a wide variety of solvent treatments. Other examples of semipermeable capsules prepared by self-assembly can also be found in a recent highlight article by Bergbreiter [43].

In contrast, Nolte, Rowan et al. [42] have employed a rod–coil block copolymer derived from a polystyrene block and a thiophene-functionalized polyisocyanate block and examined its aggregation behavior in water/THF (5:1). Following equilibration, vesicles were obtained with diameters of 100–200 nm and a shell thickness of 10–20 nm. To stabilize the structure, the thiophene groups in the "skin" of the aggregate could be electrochemically polymerized and the resulting hollow nanocapsules were capable of including enzymes into their interior, thus affording an alternative route to stable, nanoscale reactors. Additionally, the use of a crosslinked thiophene stabilization strategy permits the construction of conducting vesicles with potentially tunable properties.

A common feature of the above examples is the use of a fluid/solvent-filled core to template the nanoscopic object. However it is also possible to use a solid, nanoscopic object as a support, thereby leading to a more uniform hollow capsule of predictable and tunable size after removal of the core. The major challenge in this strategy is designing the chemistry of the organic shell to be compatible with the conditions necessary for removal of the template. As a result, silica nanoparticles have been widely used since treatment with HF results in facile removal under conditions that are typically unreactive towards the organic shell. An initial report [44] on the use of surface-initiated, living, free-radical polymerization from silica nanospheres, coupled with benzocyclobutene crosslinking chemistry, has shown the importance of covalent stabilization in this strategy. As shown in Fig. 9, the growth of polystyrene from the surface of silica nanoparticles, followed by the removal of the silica template produces hollow nanostructures (Fig. 9a). However treatment of these particles with a good solvent such as THF leads to complete dissolution and a continuous thin film is obtained with no individual structures still recognizable (Fig. 9b). In direct contrast, if the styrene is copolymerized with 4-vinylbenzocyclobutene and then the polymer-coated silica nanoparticles crosslinked by heating at 250 °C before dissolution of the silica core with HF, a significantly more robust structure is obtained. Treatment with THF does not lead to dissolution of the individual polymer capsules; instead, individual particles are still obtained that have simply undergone collapse due to plasticization of the crosslinked polystyrene shell (Fig. 9c). This collapse process is reversible and the capsules can be "reinflated" under the appropriate conditions.

The versatility of this covalent stabilization of nanostructures is not restricted to spherical objects: a variety of other three-dimensional structures can also be produced using this methodology. By changing the hydrophilic/hydrophobic balance of di- or triblock copolymers, rod-like structures can initially be formed during the solution-mediated assembly process and, as described above, the structures may be stabilized by crosslinking of functional groups placed in either the shell [45, 46] or the core [47]. The resulting struc-

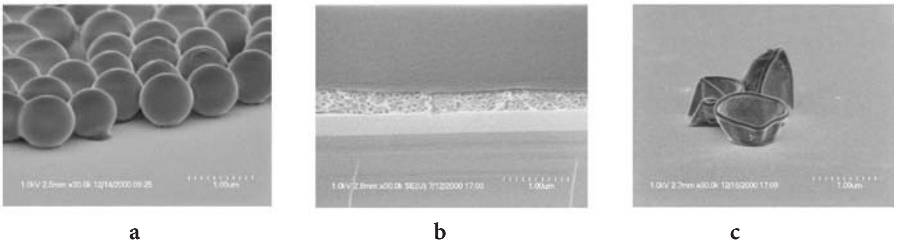

Fig. 9a–c Scanning electron microscopy images of **a** hollowed polystyrene capsules templated upon silica, **b** destruction of the polystyrene capsules by treatment with organic solvent, and **c** polystyrene capsules crosslinked via benzocyclobutene units and collapsed following treatment with organic solvent

tures have a diameter similar to that of the corresponding micelles (ca. 20–50 nm); however, they can be up to hundreds of micrometers in length, with persistent lengths from 500 nm to tens of micrometers.

The idea of stabilizing monolayers and bilayer vesicles of small molecule amphiphiles was introduced more than 20 years ago and has generated a significant amount of literature for both lamellar and nonlamellar phases [48, 49]. The success of these initial small-molecule studies has recently been translated to synthetic polymers or peptides, and the increased stability of the polymeric structures, combined with the greater statistical probability of efficient crosslinking owing to the large number of reactive groups, opens up a broader range of possible applications [50]. Recent examples include poly(ethylene glycol)-*b*-poly(butadiene) crosslinked assemblies and blending of these structures with non-crosslinkable poly(ethylene glycol)-*b*-poly(lactide) can be used to control their stability, porosity and mechanical properties [51]. Proceeding from simple diblock copolymers to more sophisticated structures such as triblock rod–coil block copolymers leads to a concomitant increase in the complexity of the macromolecular object obtained after crosslinking. Stupp et al. [21] has employed thermal crosslinking of butadiene units in low molecular weight triblock systems to create well-defined nanoscopic objects with a narrow size distribution by first controlling the self-assembly process. Of particular interest is the highly anisotropic nature of the objects obtained, 2×8 nm, which have a characteristic shape that resembles a mushroom and are able to self-assemble themselves to form materials that exhibit a liquid crystalline (LC) state. Proceeding even further from classical block copolymer substrates is the work of Emrick, Russell et al. [52] who prepared CdSe nanoparticles stabilized by ligands containing reactive vinylbenzene moieties. The crosslinkable nanoparticles can then be dispersed in toluene and an aqueous solution of a free radical initiator added. The nanoparticles are then able to assemble at the toluene/water interface, and heating of the mixture to 60 °C resulted in covalent linkage of the CdSe nanoparticles giving a robust two-dimensional sheet of up to several centimeters square, which can be manipulated and transferred to different solvents without physical destruction of the film.

In a slightly different application, the concept of covalent stabilization of a supramolecular assembly can also be used to trap linear polymer chains in a collapsed state [53]. In effect, this involves the controlled intramolecular collapse and crosslinking of a variety of different linear polymer structures (i.e., random, **12**, block, graft, star copolymers) to give the corresponding nanoparticles, **13** [54]. By the use of free radical or benzocyclobutene crosslinking chemistry, no change in molecular weight occurs, however gel permeation chromatography (GPC) and light-scattering analysis of the collapsed structure shows a substantial decrease in molecular volume which is fully consistent with the transition of a random coil chain to a collapsed three-dimensional nanoparticle (Fig. 10).

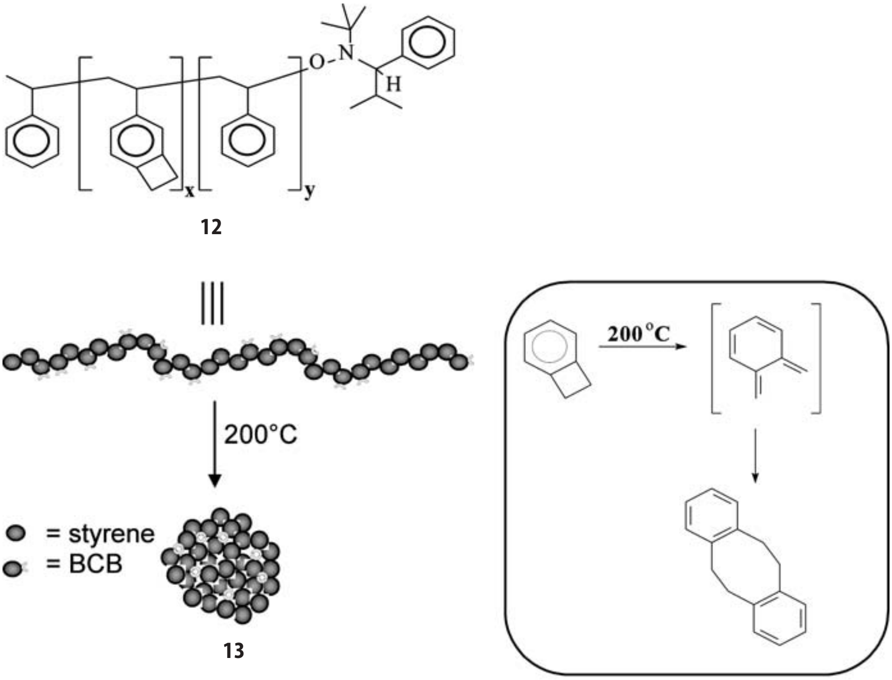

Fig. 10 Collapse of random copolymer, **12**, using benzocyclobutene chemistry (see *insert*) to give the nanoparticle, **13**. *BCB* benzocyclobutene

4
Utility of Supramolecular Assemblies and Nanoscale Objects

With the continued improvement in analytical techniques and instrumentation for examining physical properties on ever-diminishing size scales, it is now possible to investigate materials on the nanometer size scale. These dimensions are only slightly larger than the molecules themselves, and so bulk materials properties may no longer be observed. This leads to many physical and mechanical properties that are not only different to those observed for traditional systems, but in select cases are not even predicted by long-standing theories. This fascinating and exciting possibility is one of the fundamental reasons for developing strategies leading to well-defined nanoscale objects. To further promote the study of nanoscopic materials and to justify the increased funding levels and scientific interest, it is critical that the unique properties associated with these systems, which cannot be accessed with bulk materials or conventional structures, be exploited. Some of the most promising initial targets for nanoscale organic materials include studies of quantum-confined behavior, and use as templates for inorganic nanostructures, as novel delivery diagnostic systems for biomolecules, and as additives for enhancing the properties of traditional bulk materials.

An intriguing recent example of a diagnostic system based on supramolecular assembly is the temperature-sensitive zinc porphyrin complex of Tsuda, Aida et al. [55], which displays a stepwise color change from green to yellow to red on heating from 0 to 50 to 100 °C. Over this temperature range, the pyridyl-substituted zinc porphyrin complex adopts a cyclotetrameric structure in solution. This temperature-driven assembly process is affected by the substitution pattern of the porphyrin and shows the dramatic influence of molecular structure on physical properties induced by nanometer scale processes.

The influence of nanostructure on physical properties has also been recently demonstrated in the breakdown at nanometer size scales of a classical theory of Einstein from 1906 [56], in which he predicts that the addition of particles to a fluid should increase the fluid's viscosity. Experimentally, this has been demonstrated for an extremely diverse range of systems from normal liquids such as water to viscous polymer melts. However, available synthetic techniques only allowed relatively large particles (diameter >100 nm) to be prepared and studied as viscosity modifiers [57]. Recent work by Mackay, Hawker et al. [58] using nanoscopic objects prepared by the covalent collapse and stabilization of linear polystyrene chains has shown that the addition of nanoparticles with a size similar to that of the fluid molecules (linear polystyrene molecules) causes an unexpected decrease in viscosity, directly opposite to that predicted by the theory of Einstein. The exact mechanism for this anomalous behavior is not yet known, although it is clear that the "quantum-like" size of the nanoparticles causes severe distortion of the linear polystyrene chains of the surrounding fluid in contrast to larger particles, which do not cause any distortion. This change in conformation and free volume of the polymer results in the viscosity decrease. This leads to the important conclusion that Einstein's original theory is not wrong, but that it does not address the use of nanoparticles and, rather, at these small dimensions different physics come into play.

Similar nanoscopic confinement leading to enhanced properties has been observed by Kato [59] in the construction of highly efficient nanostructured ion-conducting films. By specifically designing a monomer containing a mesogen, a polymerizable methacrylate unit and an imidazolium ionic liquid moiety, LC smectic structures can be assembled in which the orientation induced by the mesogen causes a molecular, layered structure to be formed. The inherent thermal instability of such an LC system limits its usefulness; however, the presence of the polymerizable double bonds allows the nanostructure to be covalently stabilized. As shown in Fig. 11, this results in a two-dimensional sheet structure in which alignment and covalent stabilization of the imidazole groups in discrete planes gives rise to significantly enhanced ion conduction. In addition, the presence of ion-insulating layers leads to an increased conductance (ca. two to three orders of magnitude) in the direction parallel to the smectic layer compared to the perpendicular direction.

The challenge of forming aligned nanoscale objects has also been addressed by University of Toronto researchers [46] who were able to form shell-crosslinked cylinders of poly(isoprene)-b-poly(ferrocenyldimethylsilane) by

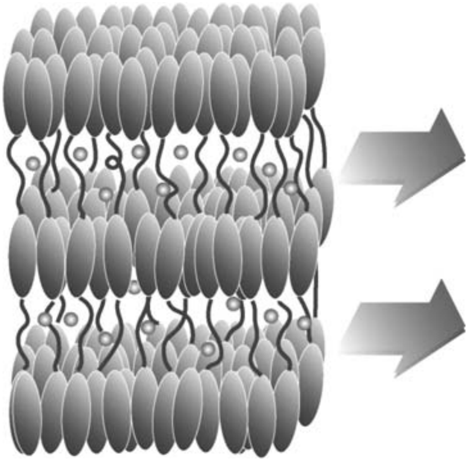

Fig. 11 Schematic representation of the 2-dimensional confinement of ion flow in a crosslinked smectic liquid crystal

Pt-catalyzed hydrosilylation of the pendent vinyl group of the coronal poly(isoprene) chains. Variation in the relative block lengths of the isoprene and ferrocenyldimethylsilane units allowed cylindrical self-assembled micelles to be obtained in contrast to spherical structures [45], with TEM analysis of the crosslinked structures giving a core diameter of 20 nm and lengths of 50–400 nm. While these resemble the values obtained for the dynamic self-assembled structure, the covalent stabilization is apparent in the stability of the nanostructures. The shell-crosslinked cylinders are stable in solvents common to both blocks, and from a technology viewpoint the ability to manipulate, align and pattern the covalently stabilized nanostructures is an enormous benefit. For example, complex micrometer-sized patterns of aligned nanocylinders can be prepared by capillary forces inside microchannels, and in a separate experiment, it was possible to convert the organic shell-crosslinked structures into ceramic materials by pyrolysis, possibly leading to magnetic properties.

The use of organic nanostructures as templates for the formation of inorganic materials with features' sizes in the nanometer size range is also of current technological interest in fields ranging from ultra-low dielectric constant thin films for advanced microelectronics [60] to artificial bone mimics. Stupp et al. [61] and, more recently, Sommerdijk et al. [62] have shown that the self-assembly of tailor-made amphiphiles allows the construction of a nanostructured fibrous scaffold which mimics the extracellular matrix. The high degree of sophistication in the design of the amphiphile, **14**, is evidenced by the five key structural components; a hydrophobic hexadecyl alkyl chain (region 1), a crosslinkable tetra(cysteine) fragment (region 2), a flexible tri(glycine) unit (region 3), a single phosphorylated serine residue that is designed to bind calcium ions and act as a nucleating site for the deposition of hydroxyapatite (region 4), and a RGD tripeptide cell adhesion ligand (region 5). Each subunit plays a spe-

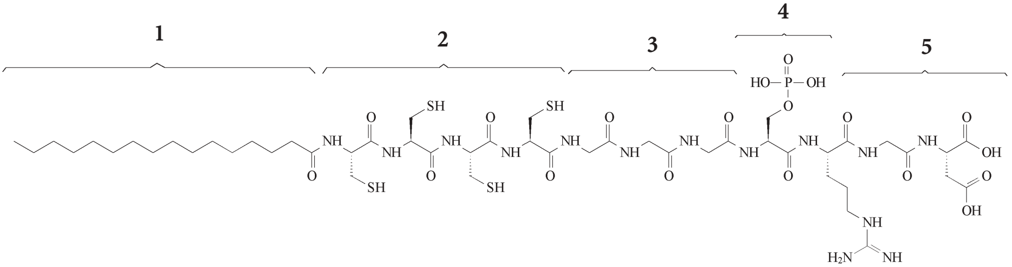

Fig. 12 Structure of the amphiphile, **14**, used in the production of material mimicking bone showing the five different structural regions, which are critical for performance

cific role in the biomineralization process and, as has been shown in the numerous examples above, the crosslinkable groups are essential to provide for covalent stabilization of the self-assembled complex (Fig. 12). Interestingly, the crosslinked fibers of **14** were able to direct the mineralization of hydroxyapatite, which gave rise to a similar alignment between the inorganic crystals/long axis of the fibers to that found for naturally occurring collagen fibers/hydroxyapatite.

5
Conclusions

The preparation of macromolecules having well defined topologies and presenting molecular recognition units in predetermined directions is maturing to the point that rational design strategies can lead to predictable supramolecular complexes that exhibit interesting structures and properties. This concept is not unique; rather, supramolecular chemistry is a rich and diverse field of study, yet there are many new advances that can be made with the preparation and study of molecules of increasing degrees of sophistication. Unique aspects arise when covalent stabilization is imparted within selective regions of the assemblies, especially following subsequent physical or chemical manipulation of the materials. Research directions often strive to mimic natural materials; however, highly novel and complex materials can be produced via the combination of biological design, synthetic materials, and creative design parameters, several examples of which have been highlighted here. This is a blossoming field of study, which will witness over the coming years many significant advances in fundamental knowledge, available materials and technological applications. These advances will be facilitated by the development of new synthetic methodologies and enhancements in analytical tools. This is certainly an exciting time for polymer chemists, with the opportunity to participate in the evolution of synthetic polymer chemistry for the preparation and characterization of elaborate and uniform nanostructured materials, in much the same way as organic chemistry has evolved over the past two centuries.

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