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Capsules, Cages and Three-dimensional Hosts: Self-assembly of Complementary Monomers

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Molecular capsules, cages and other three-dimensional hosts arising from the reversible assembly of complementary monomers are able to enclose space and encapsulate guest molecules. This article highlights work done in this area exemplifying the growing variety of non-covalent stabilising interactions being employed in host formation. These interactions include hydrogen bonding, ionic interactions, metal ion coordination as well as combinations thereof. Due to the protective environment offered by these hosts from the bulk phase solution, altered properties are often observed for encapsulated guests which is paving the way towards realising practical applications of such host systems.

Keywords: Molecular capsules; Metal ion coordination cages; Three-dimensional hosts; Guest encapsulation; Self-assembly

INTRODUCTION

Since its humble beginnings the field of host–guest or supramolecular chemistry has undergone tremendous growth and development. This can been seen in, amongst other things, the complexity of the molecular species used as host compounds. These hosts have developed from simple macrocyclic species to complex three-dimensional (3D) architectures and have been of interest for a variety of reasons: for example complexation, catalysis, sensors, detection, and sequestering. In recent times, host construction strategies have shifted from those based purely on the covalent bond to those involving both covalent bond formation and self-assembly principles based on intermolecular interactions. In particular, the enclosing of 3D space and guest encapsulation by molecular capsules [1–3].

Our focus in this article will be on the molecular components used for capsule construction and the intermolecular interactions used to hold these components together. We have chosen to report as many of the types of molecular frameworks used in capsule construction rather than focus on any particular structural motif. In addition, we have chosen selected pictorial examples only in each section so as to give the reader a flavour of the approaches used. References are however given to other work not represented pictorially. A brief discussion of our contribution to the field, with the incorporation of the porphyrin macrocycle into a capsular structure, is then presented.

COVALENT APPROACH TO THREE-DIMENSIONAL HOSTS

Cram's pioneering concept of molecules within molecules saw 'closed-surface, globe-shaped molecules with enforced hollow interiors large enough to incarcerate simple organic compounds, inorganic ions, or both' [4] constructed entirely using covalent chemistry. Typically two rim-functionalised resorcarene bowls were linked either directly or together with a difunctional spacer molecule, with appropriate guest templation to form a covalent container as shown schematically in Fig. 1(a). Reactants, solvents and impurities were imprisoned in the interior of these carcerands to form carceplexes with guest release only possible with breakage of the covalent bonds that form the wall linkages. Modifications to this initial container design produced hemicarcerands in which one of the linkages between the hemispheres was omitted or the size of the wall linkages was lengthened. The effect of this

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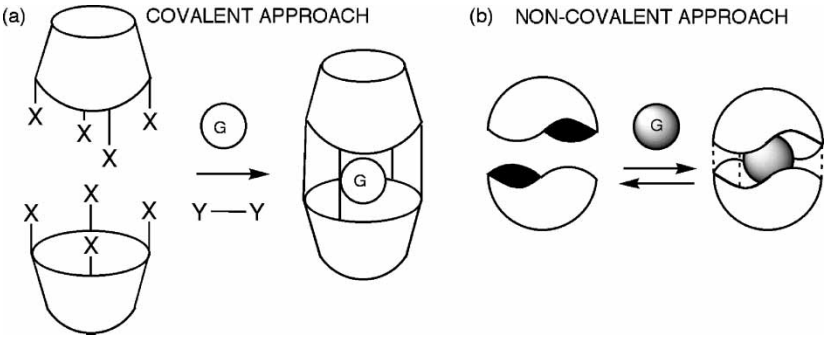


FIGURE 1 Schematic comparison of 3D hosts. (a) A covalent approach developed by Cram *et al.* where a container host was prepared under high dilution conditions from the linking of functionalised bowl shaped monomers (X and Y are reactive groups). In some cases the spacer Y–Y was not used. Solid lines represent the covalent bonds of the container host. (b) The reversible enclosing of space to form a molecular capsule using non-covalent interactions to hold the assembly together (represented by dashed lines). When a guest molecule (G) is bound within the resulting cavity space the capsule is referred to as an encapsulation complex.

was two-fold; 1) an increase in interior cavity size and 2) accessible guest exchange between the interior and exterior environments.

Although interesting properties have been demonstrated using carcerands or hemicarcerands [5–9], they are limited by their tedious synthesis. The irreversible nature of guest incarceration within cacerands is beyond the scope of this article, however excellent reviews have appeared in recent times [4,10–13].

The self-assembled counterparts of carcerands, formed using reversible bonds, are known as molecular capsules, see Fig. 1(b), and have been classified as encapsulation complexes when guests are included within the hollow interior [3]. The general synthetic simplicity of capsules compared to entirely covalent based approaches, along with the reversible nature of guest encapsulation, are particularly important for potential applications (e.g. reaction catalysis, drug delivery, sequestering agents). The following sections describe encapsulating capsule type hosts that are based on different structural motifs and are further divided by the types of stabilising interactions used in host formation.

SELF-ASSEMBLED CAPSULES USING PRE-FORMED BOWL COMPONENTS

When fully enclosing space using the aggregation of molecules, each of the components usually possesses a degree of curvature. This curvature is dependent on the number of components involved in the aggregation. Bowl shaped hosts (e.g. calixarenes, resorcarenes) are pre-organised for molecular recognition and possess curvature suitable for surrounding guest molecules in essentially a two-dimensional manner. As a result, a range of capsules that encapsulate molecules in a 3D manner have been constructed from the dimerisation of monomers with pre-formed concave geometries. For example, when fixed in the cone conformation, calixarene monomers functionalised with complementary fragments at either the narrow or wide rim readily self-assemble to form dimeric entities. The choice of rim substituents varies and is dependant on the intermolecular interaction that will be employed for capsule stabilisation. Each of the intermolecular interactions documented in capsules containing bowl shaped monomers will now be discussed in turn.

Assembly Using Hydrogen Bonding

Numerous calix[4]arene derivatised capsules have been reported in the literature *via* hydrogen bonding of two bowl shaped monomers [14–17]. The attractive architecture of the calixarenes, coupled with their straightforward synthesis, potential to be functionalised at the wide or narrow rim with combinations of complementary functionality suitable for non-covalent interactions has proven popular for capsule assembly. Therefore, only a few representative examples are discussed here (see Fig. 2) and illustrate the most common types of systems investigated. A number of comprehensive reviews provide more specific details regarding synthesis, characterisation and guest exchange studies [13–19].

Capsule 1 was assembled from a calix[4]arene monomer that was functionalised at the wider rim with carboxylic acid groups [20]. Since the interacting rims on each monomer contain identical functional groups the resulting capsule is classified as homodimeric. In this example, the monomer is *bis*-substituted resulting in a capsule assembled from four hydrogen bonds. Examples also exist where a tetra-functionalised monomer is used which resulted in the dimerisation being stabilised by a total of eight hydrogen bonds, one from each rim substituent [21].

The utilisation of different monomeric fragments to form a capsule has been termed heterodimerisation [22]. The self-assembly of calixarene based heterodimeric systems such as 2 (Fig. 2) is possible from the

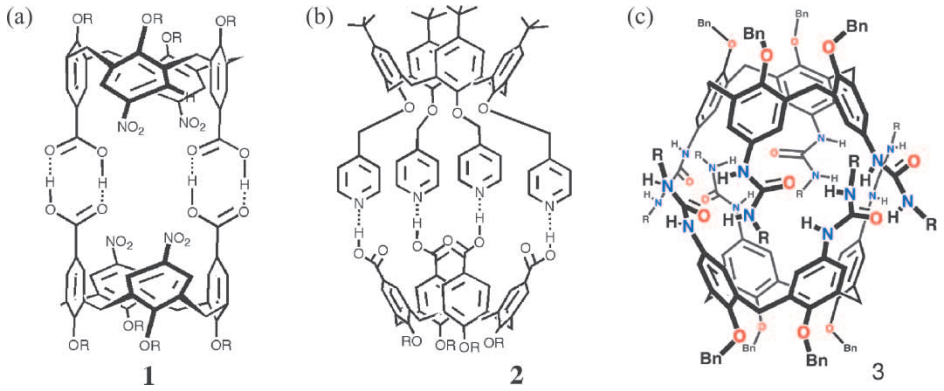


FIGURE 2 Selected examples of capsules formed from calixarene based monomers that have been assembled from the hydrogen-bonding of rim substituents. (a) Homodimeric capsule 1 formed from hydrogen bonding between opposing carboxylic acid rim substituents, R = propyl. Reproduced by permission of The Royal Society of Chemistry. (b) Heterodimeric capsule 2 that contain two different halves formed from hydrogen bonding between a pyridyl functionalised monomer with a complementary carboxylic acid functionalised monomer, R = octyl. Reprinted in part with permission from [24]. Copyright (1996) American Chemical Society. (c) Urea substituted monomers also hydrogen bond to form capsule dimers of type 3 and can also be homo- or heterodimeric depending whether the R and R′ substituents around the central binding region differ or are identical. Reprinted with permission from [18]. Copyright (1997) American Chemical Society.

complementary interaction between pyridyl and carboxylic acid functionalities on opposing calixarene rims. In such cases, either the wide or narrow rims have been functionalised and dimers formed from wide rim-to-wide rim interactions [23] as well as from narrow rim-to-wide rim interactions [24].

Dimers of type 3 have been formed from wide rim urea functionalised calix[4]arenes and represent the most studied type of calixarene based capsules. The eight urea groups interact at the equatorial region between the two calixarene monomers directing sixteen hydrogen bonds in a head-to-tail fashion around the centre of the capsule. Combination of different urea monomers resulted in the assembly of mixtures of homo- and heterodimers [22,25]. The use of larger R substituents on the urea functionality provided additional molecular entanglement between the capsule monomers. This sterically based interaction may be considered as stabilising the capsule since it effectively inhibits dimer dissociation [26].

The resulting cavity interiors produced from the dimerisation of calixarene bowls proved rather compact in size (~200 Å^3) [15] limiting guest encapsulation studies to small single molecules. Thus, an obvious extension was to increase the host size. This was achieved by either expanding the macrocycle size (e.g. calix[5]arene [27] and calix[6]-arene [28–31]) or placing spacing units (either covalently [32] or non-covalently [33–39]) between monomeric units. In some cases the use of polar hydrogen bonding solvents as bridging molecules between host components has also resulted in

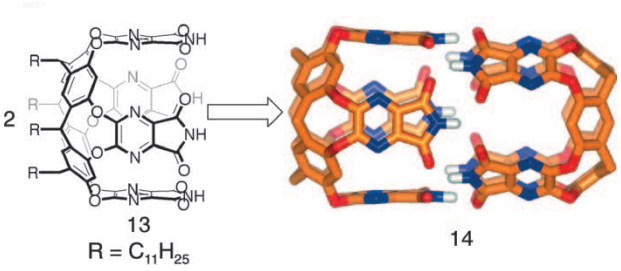


FIGURE 3 (a) A monomeric calixarene bowl functionalised with imide walls, R = undecyl. (b) Dimerisation *via* hydrogen bonding resulted in the formation of cylindrical capsule 5 with increased interior volume (460 Å^3) compared to normal calixarene based capsules. This interior has proven suitable for numerous guest exchange and reaction catalysis studies. Illustration used with permission. Copyright (2002) National Academy of Sciences, U.S.A.

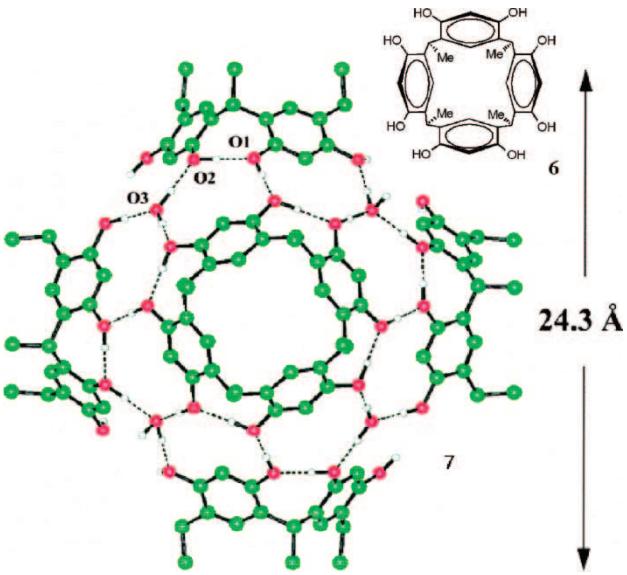


FIGURE 4 Formation of an extra large self-assembled capsule 7 from six monomeric units. Assembly of monomers 6 with eight water molecules formed a spherical hexamer stabilised by sixty hydrogen bonds. One monomeric unit has been removed from the central back position and minimal hydrogen bonds are shown to aid in visualisation. Illustration used with copyright permission of Nature (http://www.nature.com/).

solvent stabilised molecular capsules that previously only formed ill-defined aggregates [39,40].

One illustrative example of increased capsule size is provided by nanometer sized host 5 constructed by Rebek (Fig. 3). Covalent modification of the resorcinarene bowl monomers with imide wall moieties yielded an elongated cylinder, which when allowed to dimerise, was stabilised by eight rim-to-rim hydrogen bonds (Fig. 3) [32]. The internal cavity volume increased from $\sim 200\,\text{Å}^3$ to $460\,\text{Å}^3$, ample for pairwise encapsulation of guests, a necessity if capsules are to act as reaction chambers [41,42]. Capsule 5 has been extensively studied with a wide range and combination of guest molecules providing much insight into the properties of encapsulated guests as compared to those in the bulk solution [42–49]. The success of 5 in guest encapsulation is very evident as it continues to be actively investigated by the Rebek team [50–62]. An excellent review examining the size aspects of large molecular hosts is that by Rudkevich [63].

An alternative approach to creating larger capsules was first realised by Atwood and co-workers who used multiple bowl fragments to facilitate the assembly of giant capsules [64]. Similar systems have also been reported by Mattay *et al.*, [65] Rebek [66–68] and an electrochemically driven assembly by Kaifer [69]. The spherical host 7 (Fig. 4) resulted from the hexameric assembly of resorcarene units with eight water molecules *via* sixty hydrogen bonds and is structurally considered to closely mimic spherical viruses [70]. The internal volume was calculated at $1375\,\text{Å}^3$, spacious enough to encapsulate large guests (e.g. fullerenes, porphyrins), although the nature of the encapsulated species was not determined from the X-ray crystallographic investigations reported.

Even though the enclosed volume of capsule 7 was large, the disordered arrangement of guest species within the host made understanding the identity and position of guests difficult. Modification of the macrocyclic substituents to incorporate additional hydrogen bonding sites directed towards the interior enforced internal order between host and guest, whilst still maintaining the correct information for assembling the hexameric capsule [71].

Atwood has further developed the potential application of self-assembled capsules as delivery vehicles by patenting the preparation of the hexameric assembly [72]. Since "smart" drugs contain specific receptors to bind to target cells, the possible pharmaceutical benefits of encapsulating an active drug within a nano-sized capsule and delivering it to the required site are expected to be considerable. The direct delivery of drugs may also result in reduced dosages since the drug will be concentrated at the specific site of need, which may in turn minimise harmful treatment side effects [73].

Assembly Using a Combination of Non-covalent Interactions

The stability of a self-assembled capsule can be improved by combining various intermolecular forces in a cooperative manner. For example, hydrogen bonded assemblies and encapsulation complexes can exist in competitive polar solvents enhancing their applicability to biological systems [40,74–76].

The construction of a calix[4]arene based capsule using at least eight hydrogen bonds between wider rim substituents and $\pi-\pi$ interactions, and whose formation was solvent dependent, has been reported [75]. The carboxyl and amine moieties of opposing acrylamide rim substituents interact forming eight hydrogen bonds while π- 'face-to-face' interactions between nitrile groups on the amide residue of the host and the aromatic moiety of the calix[4]arene add further stabilisation from $\pi-\pi$ interactions. In contrast to this, previously reported urea functionalised calix[4]arene capsules of Rebek [16,77,78] or Bohmer [22] have monomers held together with sixteen equatorial hydrogen bonds. Thus, the extra stabilisation provided by the $\pi-\pi$ interactions allows capsule formation to be observed with only eight hydrogen bonds.

The combination of hydrogen bonding with favourable $\pi-\pi$ interactions to favour calix[4]arene encapsulation complexes has been independently reported by Rebek [40], Atwood [74], Kobayashi [76] and Bohmer [26] with the latter example being stabilised by an additional entanglement of bulky amide residues upon dimerisation. Each of these examples were shown to form in polar solvents, illustrating the benefit of using different non-covalent interactions cooperatively to prevent solvation of the hydrogen bonds.

Assembly Using Ionic Interactions

The first molecular capsule assembled by ionic interactions was reported by Hong in 1996 and was assembled by charged hydrogen bonds between oppositely charged bowl shaped cyclotriveratrylene derivatised monomers [79]. Concentration dependent non-covalent assembly was accomplished from complementary interactions between a trisacid and a trisamine monomer in polar DMSO. The interior volume of the capsule was calculated to be $150\,\text{Å}^3$ and it was found to be a suitable host for small neutral guests exchanging slowly on the NMR timescale between interior and exterior environments.

Reinhoudt recently reported capsule 10a (Fig. 5(a)) from the dimerisation of oppositely charged calix[4]-arene units (8 and 9a) in solvent systems containing up to 40% water [80]. Multiple ionic interactions

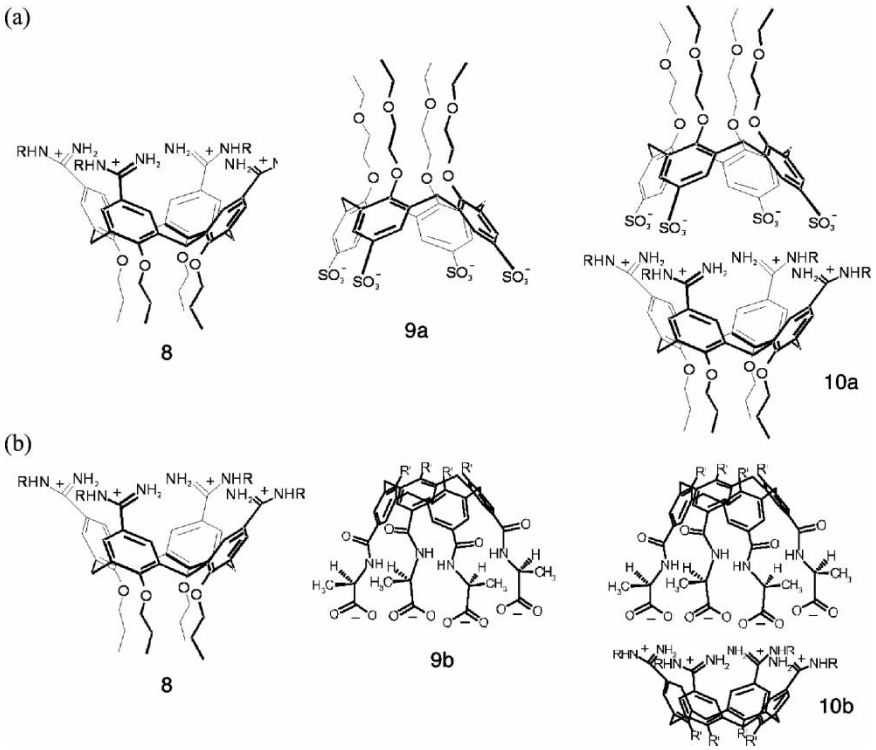


FIGURE 5 Dimerisation of oppositely charged calix[4]arene monomers to form molecular capsules. (a) Assembly of amidinium functionalised calix[4]arene 8 with oppositely charged monomer 9a occurred even in polar solvent and provided a suitable cavity for encapsulation of cationic guests, R = propyl. Reprinted in part with permission from [80]. Copyright (2002) American Chemical Society. (b) Modification of 9a to amino acid functionalised monomer 9b assembled with the amidinium monomer resulted in a water soluble molecular capsule also shown to include guest molecules. Reprinted with permission from [81]. Copyright (2003) American Chemical Society.

were afforded by incorporation of amidinium moieties onto the wider rim of one monomer while the wider rim of the opposing calix[4]arene was flanked with sulfonato groups. Characterisation of the dimer by NMR spectroscopy indicated that the calixarene monomers were most likely assembled with opposing charges facing each other. Unusually, a portion of one propyl chain from monomer 8 was found to be positioned within the capsule as evidenced by changes in proton chemical shift resonances (later confirmed by an X-ray crystal structure) [81]. This encapsulated propyl chain proved beneficial in guest encapsulation studies since guests of a better fit for the interior capsule space (acetylcholine, N-methylquinuclidinium and tetramethylammonium cations) were preferentially bound within 10a which could be indirectly monitored by the chemical shift changes of propyl chain proton resonances in an uncomplexed environment.

More recently Reinhoudt replaced monomer 9a with the amino acid functionalised monomer 9b and assembled a second molecular capsule 10b (Fig. 5(b)) using ionic interactions [81]. Capsule 10b was found to be water soluble (buffered at pH 9) as well as being capable of encapsulating guest species and this has initiated studies for its potential use as a drug delivery vehicle under physiological conditions.

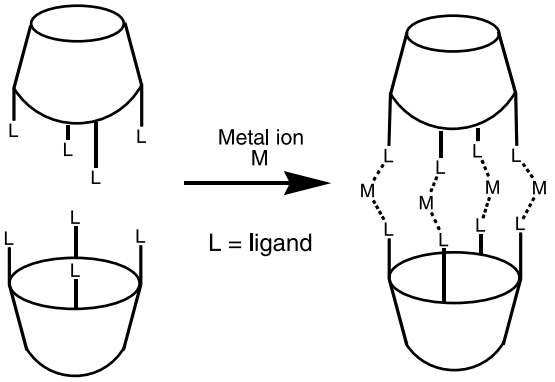
Similar calix[4]arene based capsules assembled in polar solvents *via* ionic interactions have also been reported independently by Schrader [82,83] and Shuker [84]. Schrader's report was an extension of earlier research on ball-shaped assemblies from highly charged tripod hosts which dimerised in water and other polar solvents [85–87]. The resulting interior cavity was found to be too small for guest inclusion.

Assembly Using Metal Ion Coordination

In a similar manner to the functionalisation of calixarene bowls with substituents capable of hydrogen bonding, metal ion mediated self-assembly of capsules has been achieved by ligand incorporation onto bowl rims and subsequent complexation with metal ions [88–91]. This is shown schematically below. A benefit of metal ion mediated assembly of calixarene derivatised monomers is the elongation in capsule length as a result of ligand attachment to the bowl rim [92]. To illustrate the scope of metal ion mediated capsule assembly (from hosts with pre-organised binding cavities) a selection of ligand and metal ions are listed in Table I.

The assembly of metal ion coordinated heterodimers is much less common [93] than hydrogen

TABLE I Metal mediated assembly of capsules from monomers with pre-formed bowl type geometries illustrating the seemingly endless opportunities for complexation between appropriate ligands.



Ligand Type	Metal ion	Reference
Nitrile	Pd(II) or Pt(II)	[89,158,159]
Pyrimidine	Pd(II)	[91,160,161]
Pyridyl	Pd(II)	[90,162–166]
Dithiocarbamate	Cu(III)	[167]
Iminodiacetate	Co(II) or Fe(II)	[168–170]

bonded dimers due to the difficulties associated with controlling metal ion coordination between different ligands [94]. However, very recently both homo- (12 and 13) and hetero-dimeric capsules (14) have been described where changing of the ligand between the pyridyl and nitrile flanked monomers, in the presence of palladium complexes, (see Fig. 6) provided selectivity in capsule formation.

Successful capsule assembly has not been limited to the use of bowl-shaped components. In particular, Rebek and co-workers have efficiently formed capsules from modular units by introducing curvature into complementary host structures by the incorporation of the glycouril unit. Capsules based on these units are discussed in the following section.

SELF-ASSEMBLED CAPSULES FROM MONOMERS CONTAINING GLYCOURIL UNITS

A article on molecular capsules would not be complete without summarising the valuable contributions to the field by Rebek and co-workers, even though this has been the subject of other recent papers and reviews [3,13,14,18,95–97]. Rebek and co-workers, have reported numerous capsular systems (Fig. 7) based on a building block approach utilising the glycouril unit. As shown in Fig. 7, the glycouril unit is an attractive building block due to its versatile derivatisation chemistry and ideal structural characteristics, possessing both curvature and multiple hydrogen bonding groups.

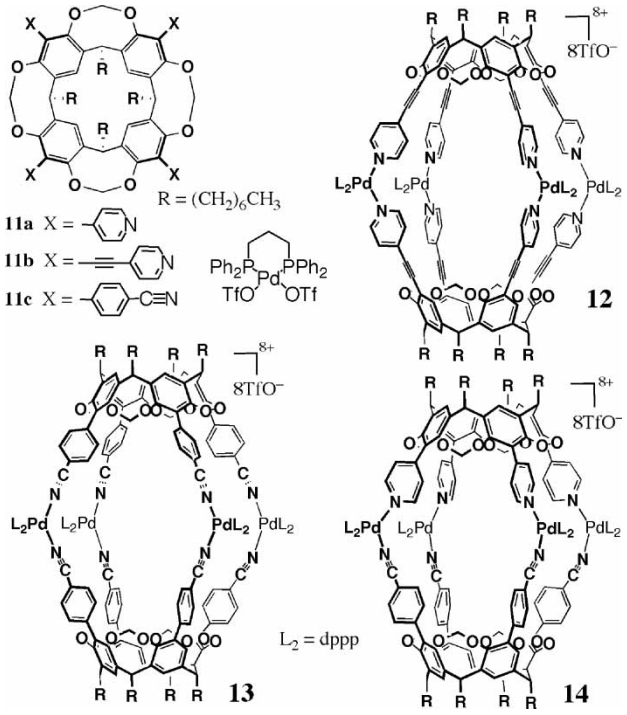


FIGURE 6 Formation of capsule structures using bowl shaped monomers appended with ligands such as pyridyl and nitrile. Addition of palladium initiated the formation of homodimeric (12 and 13) as well as heterodimeric 14 capsules. Reprinted with permission from [94]. Copyright (2004) American Chemical Society.

The first self-assembled capsule reported by Rebek was termed the *tennis ball* [98] (also referred to as the *baseball*) [95,99] so called because of their resemblance to the overall shape of such balls. The tennis ball host structure is comprised of two substituted glycourils attached to a central durene spacer as shown in Fig. 8. The inbuilt curvature of the capsule monomer results from a combination of the folding of the seven membered rings within the structure and the glycouril units on the sides, with the latter also providing eight hydrogen bond donor or acceptor sites. Two self-complementary monomers were shown to self-assemble in organic solvents that were non-competitive in hydrogen bonding to form a homodimer, as evidenced by changes in the proton NMR spectrum. No encapsulated solvent guest resonances were observed initially and it was thought that the capsule was either empty or occupied by dissolved atmospheric gases. Molecular modelling of the tennis ball capsule estimated an interior cavity volume between 50 and 55 $Å^3$ [98]. Methane [100] and xenon [101] were deemed suitably sized for inclusion and were readily incorporated within the capsule as directly observed by NMR spectroscopy. The presence of suitably sized guest molecules was shown to favour dimerisation to the extent that competitive hydrogen bonding solvents did not cause dimer dissociation due to solvation of the hydrogen bonds.

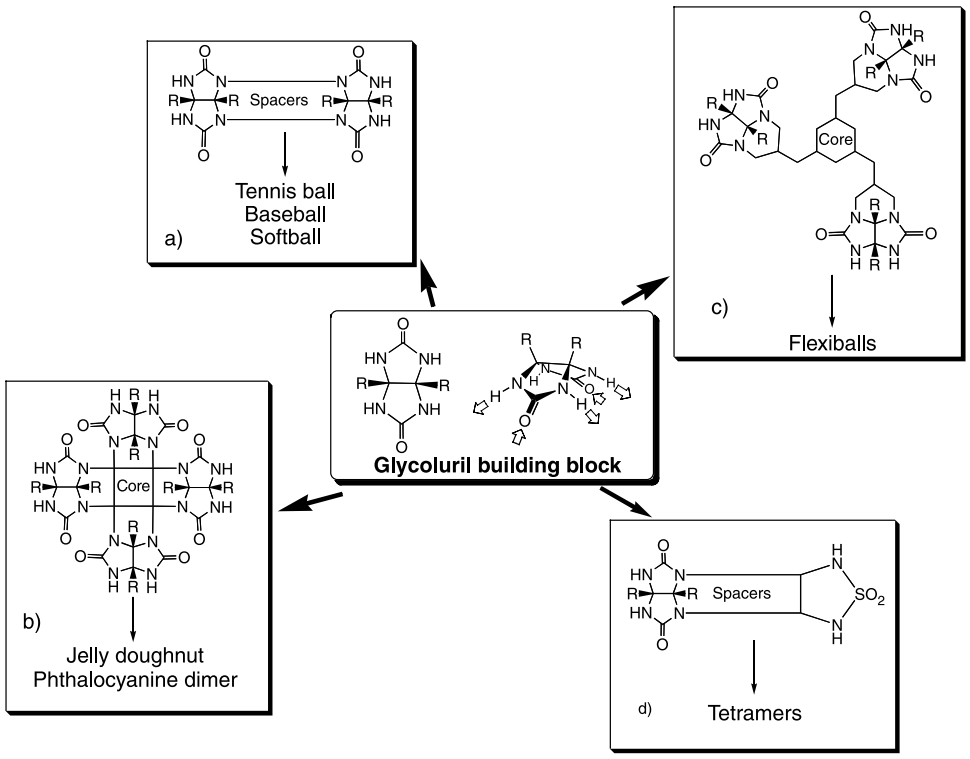


FIGURE 7 Chemical structure and molecular modelling representations of the glycouril building block (centre) R = substituents e.g. phenyl, ester. Arrows indicate the positions for hydrogen bonding to occur. The schematic representations of the various capsule monomers aim to summarise the variety of structures successfully used by Rebek *et al.* in capsule assemblies.

Although different properties of the self-assembled entities were examined, the tennis ball was limited by its small interior cavity size. Modifications to the tennis ball spacer (durene) has produced smaller [102], larger [103] and unsymmetrical [104] hosts whilst maintaining self-complementarity between the monomers for dimerisation. In addition, heterodimers have been formed from the combination of different monomers [104]. Variation of the glycouril substituents (from phenyl) was successful in producing dimers with increased solubility, which can be controlled from the exterior of the capsule rather than the encapsulated species (e.g. pH changes of peripheral amine groups or shielding of the hydrophilic hydrogen bonding seam by an ester functionality) [101]. Incorporating substituents on the durene spacer also allowed the interior environment to be altered for encapsulated guests that are either electron rich or electron deficient [105].

An extension of the monomer backbone to nine fused ring spacers between each glycouril end of the

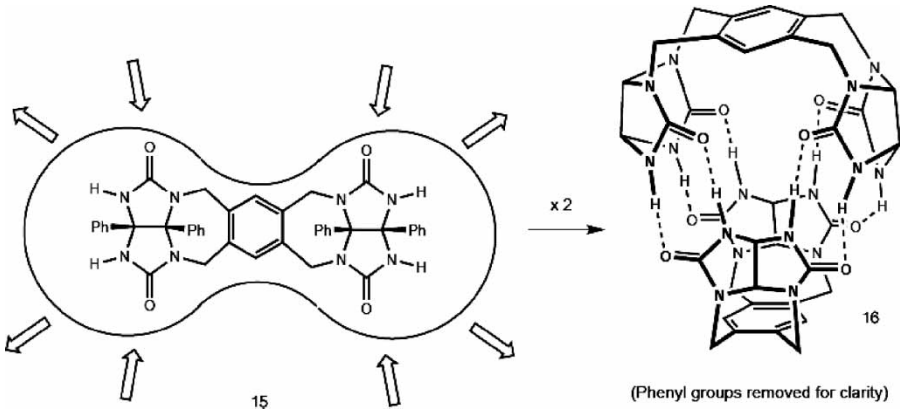


FIGURE 8 (a) Monomeric structure of Rebek's tennis ball. Arrows directed away and toward 15 respectively indicate hydrogen bond donor and acceptor sites. (b) Modelling representation of hydrogen bonded dimer 16 formed from two equivalents of 15 in the presence of suitable solvents and/or guests. Phenyl substituents have been removed from the glycouril moieties for clarity. Illustration from reference [14]. Used with permission from Wiley-VCH.

monomer produced, upon dimerisation, a larger capsule referred to as the *softball* reflecting its size and shape compared to the tennis ball capsule [106–109]. Molecular modelling indicated the softball capsule had a more spacious cavity size (240–320 Å^3), which allowed for greater variety of potential guests [3]. Guests as large as adamantane and ferrocene derivatives have shown to be complementary with respect to the interior size and shape, and hence were a good fit within the dimer [108].

The demonstration that two solvent molecules could be accommodated inside the softball capsule over timescales sufficient for chemical reaction, allowed the possibility of using these host systems as reaction catalysis chambers to be contemplated. Indeed, accelerated intermolecular chemical reactions have been documented [109–111]. One of the greatest advantages of using non-covalent interactions for capsule assembly is the reversibility of guest complexation. This potentially alleviates the problem of permanent guest entrapment and hence catalytic inhibition encountered with the covalently bonded carcerands.

The tennis- and soft-ball capsules possess interiors that are roughly spherical in shape implying that guests with an approximate spherical shape are preferentially encapsulated. To promote encapsulation of differently shaped guests a flattened spherical assembly was prepared by the linking of four glycouril moieties to a central core (Fig. 7b). This capsule, likened to a *jam or jelly doughnut* [112], has been shown to encapsulate disc-shaped guests preferentially [113]. More recently Rebek has reported the inclusion of a metallophthalocyanine core *tetra*-substituted with glycouril units providing sixteen hydrogen bonds sites to encourage dimerisation [114]. The overall box-shape was similar to the jelly doughnut capsule yet contained an increased internal volume of 275 Å^3, compared to 243 Å^3 for the jelly doughnut [113].

In the preceding examples the dual covalent attachment of glycouril units to backbone spacers provides a skeleton without rotational freedom between moieties. These materials were lengthy to synthesise and proved problematic with the formation of more than one stereoisomer being possible. However, the attachment of mono-functionalised glycouril units by a single covalent bond to the core structure (Fig. 7c) overcame this isomeric problem, due to free rotation of the glycouril moiety, and saw the development of *flexiballs* [115].

A final example of a glycouril based host is the assembly of four identical components to form a capsule (Fig. 7d) rather than the commonplace use of two monomers. In designing this system it was expected the most acidic proton of 17 (sulfamide) would pair with the most basic acceptor (the carbonyl oxygen of the glycouril) assembling four monomeric units in a head-to-tail arrangement to the pseudo-spherical shaped capsule 18 (see Fig. 9) [116]. Host curvature was introduced in a similar manner to the tennis-ball capsule monomer *via* a combination of the glycouril geometry and the folding of the adjacent seven membered ring.

Although the monomer appeared to have limited solubility in common organic solvents, except those that compete for the hydrogen bonds and hence disfavour assembly, NMR data acquired in the presence of an appropriately sized templating guest (e.g. adamantane derivatives) indicated the formation of 18 [116].

THREE-DIMENSIONAL METAL ION COORDINATION STRUCTURES

The popularity of metal ion coordination as an assembly motif in supramolecular chemistry is evident from the variety of different shaped structures that have been produced such as helices, cages, rings, knots, boxes, macrocycles, rods and grids, that have been the subject of numerous reviews [117–124]. The diversity in the types of organic ligands and metal ions used to construct capsules and cages in particular is illustrated in a selection of recent reports [125–129]. In each of these cases at least one guest molecule has been observed inside the cavity interior of the capsule or cage.

Utilising a molecular panelling approach, Fujita has been exceptionally successful at constructing 3D structures *via* metal ion coordination between multidentate ligands (the molecular panels) and *cis*-protected square planar platinum or palladium metal centres affording nanocages, cones, boxes, tubes, bowls, polyhedra and capsules [130,131]. Specifically, a highly symmetrical octahedral M_6L_4

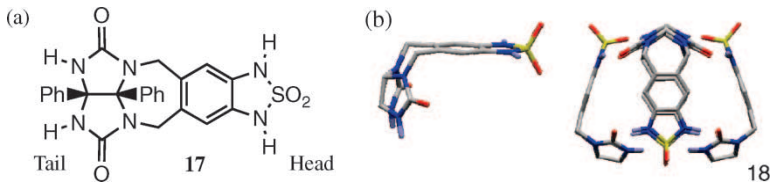


FIGURE 9 (a) Structure of monomeric host 17 indicating the complementary head and tail portions of the host. (b) Modelling representation of the tetrameric capsule assembled from four monomers held together through hydrogen bonding. Reprinted with permission from [116]. Copyright (1998) AAS (http://www.sciencemag.org).

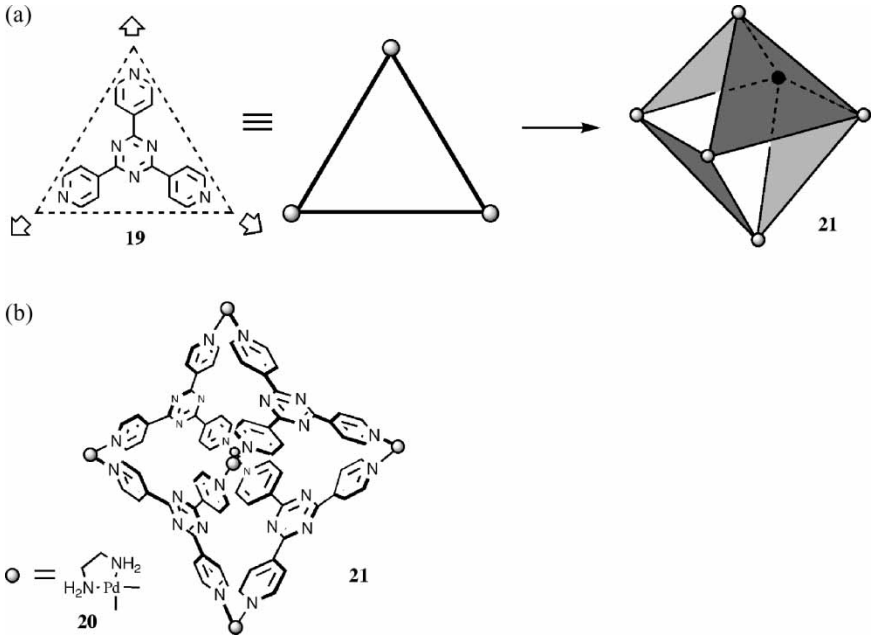


FIGURE 10 (a) A panelling approach used by Fujita to self-assemble supramolecular structures. The pyridyl ligands provide linkages at the corner of each triangle panel producing an octahedron where each alternating face is either a molecular panel (shaded) or portal (clear). (b) Palladium(II) mediated assembly of nanocage 21 from four triangular panels. The sizeable interior has been successfully shown to encapsulate a variety of guests with altered properties demonstrated. Reproduced by permission of The Royal Society of Chemistry.

type nanocage 21 (Fig. 10) self-assembled from four rigid tridentate ligands (or panels) 19 and six palladium metal ions 20 is of most relevance to this article [132]. Up to four neutral guest molecules have been included within the host as indicated by NMR spectroscopy and X-ray crystallography [133–135].

Fujita has described the microenvironments provided by hosts such as 21 as '*molecular safety boxes*' and '*molecular flasks*' since guest species can be stabilised, their properties regulated, functions altered and reactions made to occur within the confined nanospace [131,136]. In particular, the selective enclathration of two molecules of *cis*-4,4′-dimethylazobenzene that hydrophobically interacts to form a dimer analogous to a "ship-in-a-bottle" was demonstrated in 21 and sufficiently stabilised by the surrounding environment that *cis–trans* isomerisation was prevented [137]. The dimensions of the enclathrated dimer are significantly larger than the portals of 21 (by about 4 Å) suggesting that dimerisation is a post-enclathration process.

Other significant developments reported from enclathration of guest species within host 21 include:

- The room temperature $[4\pi + 2\pi]$ Diels-Alder reaction between 1,3-cyclohexadiene and naphthoquinone was accelerated 21-fold in the presence of 21 with the *endo*-adduct isolated by extraction [138].
- Styrene encapsulated in host 21 was converted to acetophenone *via* a Wacker oxidation through reverse phase-transfer catalysis in an aqueous media [139].
- The accelerated $[2\pi + 2\pi]$ homo- and cross-photodimerisation of large olefins included within 21 was achieved with high regio- and stereo-control yielding only *syn* and head-to-tail isomers [140,141].
- "Ship-in-bottle" synthesis of a trisilanol intermediate from sol-gel condensation since the smaller silane reagent is able to pass through the host portals but due to the increased size of the resulting trimer, cannot exchange to the bulk phase [142].
- Photochemical oxidation of adamantane was found to only occur when encapsulated within 21 [143].
- Demonstration of molecular logic (AND, OR gates) through bimolecular recognition between host 21 and guests such as *cis*-decalin and perylene [144].

Raymond and co-workers have adopted a similar coordinative approach towards creating high symmetry structures with a ligand preference favoured by multibranched bidentate ligands. Specifically, catecholamide and hydroxamate ligands have been frequently combined with labile metal ions to commonly produce complexes of types: M_2L_3; M_4L_4; and M_4L_6. A summary of these types has been reported [145,146] with types M_4L_4 and M_4L_6 of the most relevance to this research, since they enclose space and have been shown to include guest molecules. Coordination driven self-assembly was also utilised by Stang to target high-symmetry cages specifically resembling the Platonic and Archimedean solids. The fundamental principles are similar to the metal ion mediated

self-assembly utilised by Fujita and Raymond and have been comprehensively reviewed [119,122,147–149].

CAPSULES CONTAINING PHOTOACTIVE MOIETIES

The inclusion of porphyrin or phthalocyanine moieties into the structure of capsule type hosts permits the utilisation of the rich knowledge of photochemistry, electrochemistry or catalysis of these macrocycles. Recently Rebek has reported the inclusion of a phthalocyanine macrocycle into a glycouril based host that dimerises to form a solvent dependent molecular capsule [114]. The metallophthalocyanine core is *tetra*-substituted with glycouril units providing sites for sixteen hydrogen bonds that hold the capsule together. Molecular modelling of the dimer showed an overall box-shape similar to the jelly doughnut [112,113] previously synthesised by Rebek, but with an increased internal volume of 275 $Å^3$ (compared to 243 $Å^3$ for the jelly doughnut [113]).

The incorporation of porphyrins into capsular type structures was independently reported by Crossley [150], Warrener [151] and Hunter [152]. Each of these examples was assembled using metal ion coordination interactions between host metalloporphyrins and amino-functionalised guests that act as templates. However, these examples are not strictly capsule materials since the coordinating guest template fills the cavity, effectively precluding the encapsulation of additional guest molecules. Thus there was the need to remove the templating ligand from the centre of the structure so as to enable guest encapsulation.

The dimerisation of porphyrin containing host monomers to form a 3D structure without the aid of a guest template was first reported in 1995 [153]. In non-competitive solvents the αααα-atropisomer of two porphyrin units containing carboxylic acid functionalities self-assembled to a dimer through eight hydrogen bonds. Zinc(II) metallation of the porphyrin moieties, provided guest complexation opportunities and a variety of pyrazine derivatised guests were examined [154]. The carboxylic acid dimers that formed the pillars assembling the two porphyrin units created 'window-like' openings that facilitated the binding of pyrazine derivatives with bulky side chains and the chains were found to be protruding from these windows.

Shinkai also recently constructed a dimeric capsule with porphyrin walls terminated with pyridyl ligands suitable for coordination to palladium metal ions (Fig. 11) [155]. Although the dimer exists without a permanent guest template, the inclusion of a guest molecule within the dimer has only been shown for bipyridine derivative guest 23 which complexes to the metalloporphyrin walls.

In the previous examples, the use of the porphyrin macrocycle in molecular capsules generally served one of two purposes. Either the coordination properties of the metalloporphyrin were used to arrange components into 3D hosts around a templating guest or alternatively provided interior binding sites for guest complexation which increased guest residency time within the capsule.

Our own efforts towards a self-assembled porphyrin containing capsule differed from those outlined above because the coordination properties of the metalloporphyrins of our host acted as coordination sites for ligands suitably positioned on a complementary host. Essentially this removes the templating guest so that dimerisation of these self-complementary hosts creates a molecular capsule with a hollow interior which is available for further guest encapsulation [156]. The self-complementary *bis*-porphyrin cavities used possess curvature from the alicyclic backbone and were synthesised *via* a covalent building block approach (see Fig. 12). High pressure assisted coupling of block 25 and 4-pyridyl tetrazine 26 to construct *bis*-porphyrin cavity 27 which incorporates the porphyrin macrocycle into the host structure. Upon porphyrin metallation, the monomers become self-complementary and dimerisation results in the

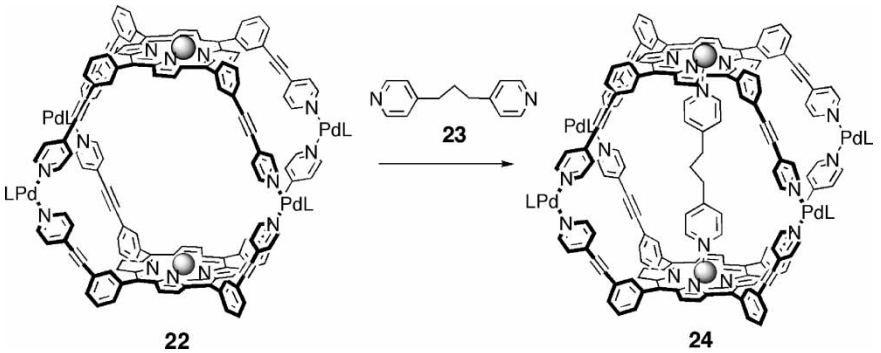


FIGURE 11 Porphyrin containing dimer 22 assembled from palladium(II) pyridyl interactions. When zinc is inserted into the porphyrins, two-point simultaneous binding was shown with a bipyridine guest to form encapsulation complex 24. Reprinted with permission from [155]. Copyright (2000) American Chemical Society.

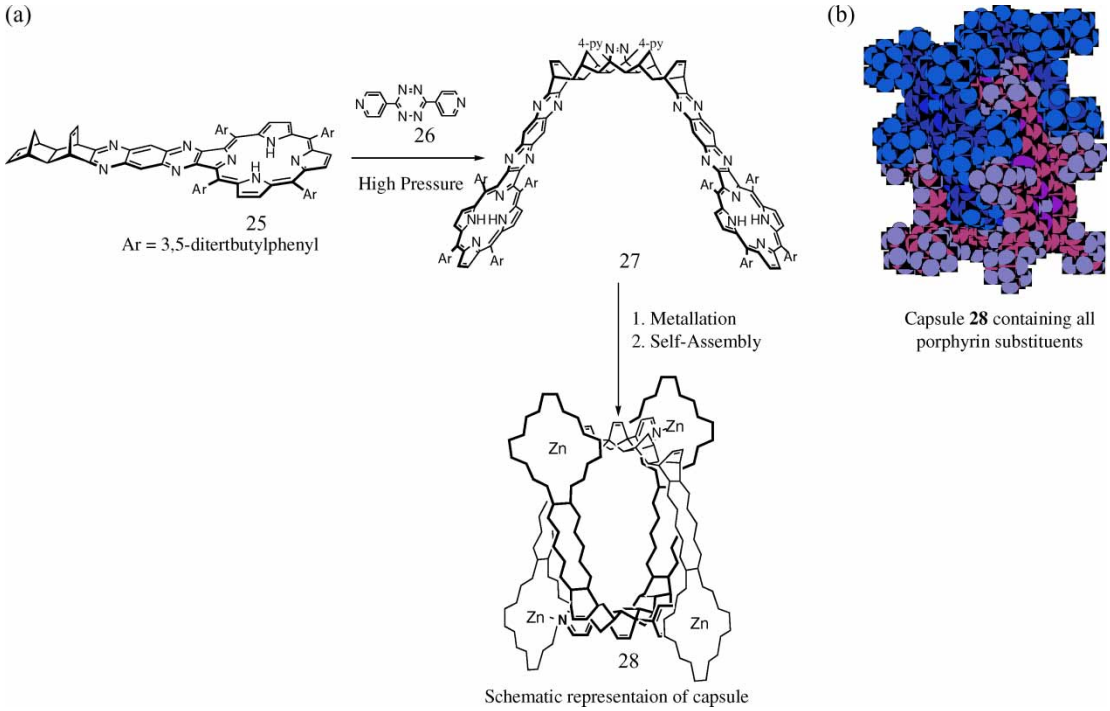


FIGURE 12 (a) High pressure coupling of porphyrin block 25 with coupling reagent 26 to produce the *bis*-porphyrin monomer 27. Upon porphyrin metallation cavity 27 becomes self-complementary and assembles to form molecular capsule 28. (b) Molecular modelling of the final capsule structure indicating the shielded nature of the capsule interior.

formation of a molecular capsule with a hollow interior as shown in Fig. 12(a). Molecular modelling (Fig. 12(b)) shows that the capsule interior is significantly shielded from the bulk solution by the substituents on the porphyrin periphery effectively prohibiting rapid guest escape.

Data has been obtained supporting the dimeric nature of capsule 28 which contains an interior cavity of sufficient size for multiple guest encapsulation (570 ± 40 Å^3) as estimated from molecular modelling [156,157]. However, to date, guest encapsulation has only been observed by mass spectroscopy, with extensive NMR investigations using a number of different guests and solvents systems failing to identify any encapsulated species. Work currently in progress is focused on understanding this capsular system particularly as regards guest encapsulation and exchange.

CONCLUSION

As indicated by the diversity of designs and methods used to arrange simple, complementary components into functional 3D hosts it is obvious capsule research is flourishing internationally. This is reflected in the variety of curved molecules used as structural motifs in capsule construction, all of which contain functionality suitable for intermolecular interaction. To this end, hydrogen bonding has certainly been the most exploited interaction with capsules forming with as few as four hydrogen bonds to as many as sixty. This is followed by metal ion coordination using predominantly divalent transition metals and predominately nitrogenous ligands. Thirdly, ion pairing using cationic amidinium functionality has been successfully used to construct calixarene based capsules. Future capsules will no doubt be constructed using a combination of intermolecular interactions due to the advantageous properties that result from such synergistic cooperation.

The introduction of specific moieties into capsular systems will expand investigations into their use. Specifically, the introduction of photoactive molecules such as porphyrins and phthalocyanines allows the utilisation of the photo- and electro-chemical properties of these macrocycles in combination with capsule characteristics. As modifications and improvements continue to be made to 3D systems the potential applications of such systems will be further probed with increasing practicality to modern society appearing possible in the near future.

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References

[1] Steed, J. W. Atwood, J.L. *Supramolecular Chemistry*; John Wiley & Sons: London, 2000.
[2] Atwood, J. L., Steed, J. W., Eds.; *Encyclopedia of Supramolecular Chemistry*; Marcel Dekker: New York, 2004.
[3] Hof, F.; Craig, S. L.; Nuckolls, C.; Rebek, J. J. *Angew. Chem., Int. Ed. Engl* **2002**, *41*, 1488.
[4] Cram, D. J.; Cram, J. M. *Container Molecules and Their Guests*; The Royal Society of Chemistry, 1994.
[5] Cram, D. J.; Tanner, M. E.; Thomas, R. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1024.
[6] Warmuth, R. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1347.
[7] Warmuth, R.; Marvel, M. A. *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 1117.
[8] Marquez, C.; Nau, W. M. *Angew. Chem. Int. Ed. Engl.* **2001**, *40*, 4387.
[9] Warmuth, R.; Maverick, E. F.; Knobler, C. B.; Cram, D. J. *J. Org. Chem.* **2003**, *68*, 2077.
[10] Jasat, A.; Sherman, J. C. *Chem. Rev.* **1999**, *99*, 931.
[11] Warmuth, R.; Yoon *J. Acc. Chem. Res.* **2001**, *34*, 95.
[12] Gibb, B. C. In *Encyclopedia of Supramolecular Chemistry*; Atwood, J. L., Steed, J. W., Eds.; Marcel Dekker: New York, 2004; p 189.
[13] Turner, D. R.; Pastor, A.; Alajarin, M.; Steed, J. W. *Struct. Bond* **2004**, *108*, 97.
[14] de Mendoza *J. Chem. Eur. J.* **1998**, *4*, 1373.
[15] Bohmer, V.; Shivanyuk, A. In *Calixarenes in Action*; Ungaro, R., Mandolini, L., Eds.; Imperial College Press: London, 2000; p 203.
[16] Rebek, J. J. *Chem. Commun.* **2000**, 637.
[17] Bohmer, V.; Vysotsky, M. O. *Aust. J. Chem.* **2001**, *54*, 641.
[18] Conn, M. M.; Rebek, J. J. *Chem. Rev.* **1997**, *97*, 1647.
[19] Rebek, J. J. *Acc. Chem. Res.* **1999**, *32*, 278.
[20] Struck, O.; Verboom, W.; Smeets, W. J. J.; Spek, A. L.; Reinhoudt, D. N. *J. Chem. Soc. Perkin Trans.* **1997**, *2*, 223.
[21] Shivanyuk, A.; Paulus, E. F.; Bohmer, V. *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 2906.
[22] Mogck, O.; Bohmer, V.; Vogt, W. *Tetrahedron* **1996**, *52*, 8489.
[23] Koh, K.; Araki, A.; Shinkai, S. *Tetrahedron Lett.* **1994**, *35*, 8255.
[24] Vreekamp, R. H.; Verboom, W.; Reinhoudt, D. N. *J. Org. Chem.* **1996**, *61*, 4282.
[25] Castellano, R. K.; Kim, B. H.; Rebek, J. J. *J. Am. Chem. Soc.* **1997**, *119*, 12671.
[26] Vysotsky, M. O.; Thondorf, I.; Bohmer, V. *Chem. Commun.* **2001**, 1890.
[27] Yanase, M.; Haino, T.; Fukazawa, Y. *Tetrahedron Lett.* **1999**, *40*, 2781.
[28] Arduini, A.; Domiano, L.; Ogliosi, L.; Pochini, A.; Secchi, A.; Ungaro, R. *J. Org. Chem.* **1997**, *62*, 7866.
[29] Rincon, A. M.; Prados, P.; de Mendoza, J. *J. Am. Chem. Soc.* **2001**, *123*, 3493.
[30] Rincon, A. M.; Prados, P.; de Mendoza, J. *Eur. J. Org. Chem.* **2002**, 640.
[31] Arduini, A.; Ferdani, R.; Pochini, A.; Secchi, A.; Ugozzoli, F.; Sheldrick, G. M.; Prados, P.; Gonzalez, J. J.; de Mendoza, J. *J. Supramol. Chem.* **2002**, *2*, 85.
[32] Heinz, T.; Rudkevich, D. M.; Rebek, J. J. *Nature (London)* **1998**, *394*, 764.
[33] Ma, S.; Rudkevich, D. M.; Rebek, J. J. *J. Am. Chem. Soc.* **1998**, *120*, 4977.
[34] Cho, Y. L.; Rudkevich, D. M.; Rebek, J. J. *J. Am. Chem. Soc.* **2000**, *122*, 9868.
[35] MacGillivray, L. R.; Diamente, P. R.; Reid, J. L.; Ripmeester, J. A. *Chem. Commun.* **2000**, 359.
[36] Murayama, K.; Aoki, K. *Chem. Commun.* **1998**, 607.
[37] Rose, K. N.; Barbour, L. J.; Orr, G. W.; Atwood, J. L. *Chem. Commun.* **1998**, 407.
[38] Shivanyuk, A.; Rissanen, K.; Kolehmainen, E. *Chem. Commun.* **2000**, 1107.
[39] Shivanyuk, A.; Friese, J. C.; Doring, S.; Rebek, J. J. *J. Org. Chem.* **2003**, *68*, 6489.
[40] Shivanyuk, A.; Rebek, J. J. *Chem. Commun.* **2001**, 2374.
[41] Chen, J.; Rebek, J. J. *Org. Lett.* **2002**, *4*, 327.
[42] Chen, J.; Korner, S. K.; Craig, S. L.; Lin, S.; Rudkevich, D. M.; Rebek, J. J. *Proc. Natl Acad. Sci. USA* **2002**, *99*, 2593.
[43] Heinz, T.; Rudkevich, D. M.; Rebek, J. J. *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 1136.
[44] Tucci, F. C.; Rudkevich, D. M.; Rebek, J. J. *Am. Chem. Soc.* **1999**, *121*, 4928.
[45] Korner, S. K.; Tucci, F. C.; Rudkevich, D. M.; Heinz, T.; Rebek, J. J. *Chem. Eur. J.* **2000**, *6*, 187.
[46] Hayashida, O.; Sebo, L.; Rebek, J. J. *J. Org. Chem.* **2002**, *67*, 8291.
[47] Craig, S. L.; Lin, S.; Chen, J.; Rebek, J. J. *J. Am. Chem. Soc.* **2002**, *124*, 8780.
[48] Shivanyuk, A.; Rebek, J. J. *J. Am. Chem. Soc.* **2002**, *124*, 12074.
[49] Hayashida, O.; Shivanyuk, A.; Rebek, J. J. *Angew. Chem. Int. Ed. Engl.* **2002**, *41*, 3423.
[50] Scarso, A.; Shivanyuk, A.; Hayashida, O.; Rebek, J. J. *J. Am. Chem. Soc.* **2003**, *125*, 6239.
[51] Shivanyuk, A.; Rebek, J. J. *Angew. Chem. Int. Ed. Engl.* **2003**, *42*, 684.
[52] Shivanyuk, A.; Scarso, A.; Rebek, J. J. *Chem. Commun.* **2003**, 1230.
[53] Zhao, Y.-L.; Houk, K. N.; Rechavi, D.; Scarso, A.; Rebek, J. J. *J. Am. Chem. Soc.* **2004**, *126*, 11428.
[54] Rechavi, D.; Scarso, A.; Rebek, J. J. *J. Am. Chem. Soc.* **2004**, *126*, 7738.
[55] Scarso, A.; Onagi, H.; Rebek, J. J. *J. Am. Chem. Soc.* **2004**, *126*, 12728.
[56] Scarso, A.; Rebek, J. J. *J. Am. Chem. Soc.* **2004**, *126*, 8956.
[57] Amaya, T.; Rebek, J. J. *J. Am. Chem. Soc.* **2004**, *126*, 6216.
[58] Scarso, A.; Trembleau, L.; Rebek, J. J. *J. Am. Chem. Soc.* **2004**, *126*, 13512.
[59] Yamanaka, M.; Shivanyuk, A.; Rebek, J. J. *Proc. Natl Acad. Sci. USA* **2004**, *101*, 2669.
[60] Yamanaka, M.; Rebek, J. J. *Chem. Commun.* **2004**, 1690.
[61] Amaya, T.; Rebek, J. J. *Chem. Commun.* **2004**, 1802.
[62] Amaya, T.; Rebek, J. J. *J. Am. Chem. Soc.* **2004**, *126*, 14149.
[63] Rudkevich, D. M. *Bull. Chem. Soc. Jpn* **2002**, *75*, 393.
[64] MacGillivray, L. R.; Atwood, J. L. *Nature (London)* **1997**, *389*, 469.
[65] Gerkensmeier, T.; Iwanek, W.; Agena, C.; Frohlich, R.; Kotila, S.; Nather, C.; Mattay, J. *Eur. J. Org. Chem.* **1999**, 2257.
[66] Shivanyuk, A.; Rebek, J. J. *Proc. Natl Acad. Sci. USA* **2001**, *98*, 7662.
[67] Shivanyuk, A.; Rebek, J. J. *Chem. Commun.* **2001**, 2424.
[68] Shivanyuk, A.; Rebek, J. J. *J. Am. Chem. Soc.* **2003**, *125*, 3432.
[69] Philp, I. E.; Kaifer, A. E. *J. Am. Chem. Soc.* **2002**, *124*, 12678.
[70] MacGillivray, L. R.; Atwood, J. L. *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 1018.
[71] Atwood, J. L.; Barbour, L. J.; Jerga, A. *Proc. Natl Acad. Sci. USA* **2002**, *99*, 4837.
[72] Atwood, J. L. *United States Patent and Trademark Office*;: United States, 2003; p 14.
[73] http://www.missouri.edu/~news/releases/junjul02/atwoodnano.html
[74] Atwood, J. L.; Barbour, L. J.; Jerga, A. *Chem. Commun.* **2001**, 2376.
[75] Kuhnert, N.; Le-Gresley, A. *Chem. Commun.* **2003**, 2426.
[76] Kobayashi, K.; Ishii, K.; Sakamoto, S.; Shirasaka, T.; Yamaguchi, K. *J. Am. Chem. Soc.* **2003**, *125*, 10615.
[77] Shimizu, K. D.; Rebek, J. J. *Proc. Natl Acad. Sci. USA* **1995**, *92*, 12403.
[78] Hamann, B. C.; Shimizu, K. D.; Rebek, J. J. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1326.
[79] Lee, S. B.; Hong, J. *Tetrahedron Lett.* **1996**, *37*, 8501.
[80] Corbellini, F.; Fiammengo, R.; Timmerman, P.; Crego-Calama, M.; Versluis, K.; Heck, A. J. R.; Luyten, I.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **2002**, *124*, 6569.
[81] Corbellini, F.; Di Costanzo, L.; Crego-Calama, M.; Geremia, S.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **2003**, *125*, 9946.
[82] Zadmard, R.; Schrader, T.; Grawe, T.; Kraft, A. *Org. Lett.* **2002**, *4*, 1687.
[83] Zadmard, R.; Junkers, M.; Schrader, T.; Grawe, T.; Kraft, A. *J. Org. Chem.* **2003**, *68*, 6511.
[84] Brewster, R. E.; Shuker, S. B. *J. Am. Chem. Soc.* **2002**, *124*, 7902.
[85] Grawe, T.; Schrader, T.; Gurrath, M.; Kraft, A.; Osterod, F. *Org. Lett.* **2000**, *2*, 29.
[86] Grawe, T.; Schrader, T.; Gurrath, M.; Kraft, A.; Osterod, F. *J. Phys. Org. Chem.* **2000**, *13*, 670.
[87] Grawe, T.; Schrader, T.; Zadmard, R.; Kraft, A. J. *Org. Chem.* **2002**, *67*, 3755.

[88] Fox, O. D.; Dalley, K.; Harrison, R. G. *Inorg. Chem.* **2000**, *39*, 620.
[89] Cuminetti, N.; Ebbing, M. H. K.; Prados, P.; de Mendoza, J.; Dalcanale, E. *Tetrahedron Lett.* **2001**, *42*, 527.
[90] Zhong, Z.; Ikeda, A.; Ayabe, M.; Shinkai, S.; Sakamoto, S.; Yamaguchi, K. *J. Org. Chem.* **2001**, *66*, 1002.
[91] Park, S. J.; Shin, D. M.; Sakamoto, S.; Yamaguchi, K.; Chung, Y. K.; Lah, M. S.; Hong, J. *Chem. Commun.* **2003**, 998.
[92] Pinalli, R.; Cristini, V.; Sottili, V.; Geremia, S.; Campagnolo, M.; Caneschi, A.; Dalcanale, E. *J. Am. Chem. Soc.* **2004**, *126*, 6516.
[93] Menozzi, E.; Pinalli, R.; Speets, E. A.; Ravoo, B. J.; Dalcanale, E.; Reinhoudt, D. N. *Chem. Eur. J.* **2004**, *10*, 2199.
[94] Kobayashi, K.; Yamada, Y.; Yamanaka, M.; Sei, Y.; Yamaguchi, K. *J. Am. Chem. Soc.* **2004**, *126*, 13896.
[95] Rebek, J. J. *Chem. Soc. Rev.* **1996**, 255.
[96] Rudkevich, D. M. In *Encyclopedia of Supramolecular Chemistry*; Atwood, J. L., Steed, J. W., Eds.; Marcel Dekker: New York, 2004; p 1231.
[97] Palmer, L. C.; Rebek, J. J. *Org. Biomol. Chem.* **2004**, *2*, 3051.
[98] Wyler, R.; de Mendoza, J.; Rebek, J. J. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1699.
[99] Rebek, J. J. *Pure Appl. Chem.* **1996**, *68*, 1261.
[100] Branda, N.; Wyler, R.; Rebek, J. J. *Science (Washington, D.C., 1883)* **1994**, *263*, 1267.
[101] Branda, N.; Grotzfeld, R. M.; Valdes, C.; Rebek, J. J. *J. Am. Chem. Soc.* **1995**, *117*, 85.
[102] Valdes, C.; Toledo, L. M.; Spitz, U.; Rebek, J. J. *Chem. Eur. J.* **1996**, *2*, 989.
[103] Valdes, C.; Spitz, U.; Kubik, S. W.; Rebek, J. J. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1885.
[104] Valdes, C.; Spitz, U. P.; Toledo, L. M.; Kubik, S. W.; Rebek, J. J. *J. Am. Chem. Soc.* **1995**, *117*, 12733.
[105] Garcias, X.; Rebek, J. J. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1225.
[106] Meissner, R.; Rebek, J. J. *Science (Washington, D.C., 1883)* **1995**, *270*, 1485.
[107] Meissner, R.; Garcias, X.; Mecozzi, S.; Rebek, J. J. *J. Am. Chem. Soc.* **1997**, *119*, 77.
[108] Kang, J.; Rebek, J. J. *Nature (London)* **1996**, *382*, 239.
[109] Kang, J.; Santamaria, J.; Hilmersson, G.; Rebek, J. J. *J. Am. Chem. Soc.* **1998**, *120*, 7389.
[110] Kang, J.; Rebek, J. J. *Science (Washington, D.C., 1883-)* **1997**, *385*, 50.
[111] Kang, J.; Hilmersson, G.; Santamaria, J.; Rebek, J. J. *J. Am. Chem. Soc.* **1998**, *120*, 3650.
[112] Grotzfeld, R. M.; Branda, N.; Rebek, J. J. *Science (Washington, D.C., 1883-)* **1996**, *271*, 487.
[113] O'Leary, B. M.; Grotzfeld, R. M.; Rebek, J. J. *J. Am. Chem. Soc.* **1997**, *119*, 11701.
[114] Lutzen, A.; Starnes, S. D.; Rudkevich, D. M.; Rebek, J. J. *Tetrahedron Lett.* **2000**, *41*, 3777.
[115] O'Leary, B. M.; Szabo, T.; Svenstrup, N.; Schalley, C. A.; Lutzen, A.; Schafer, M.; Rebek, J. J. *J. Am. Chem. Soc.* **2001**, *123*, 11519.
[116] Martin, T.; Obst, U.; Rebek, J. J. *Science (Washington, D.C., 1883-)* **1998**, *281*, 1842.
[117] Fujita, M. In *Comprehensive Supramolecular Chemistry*; Sauvage, J.-P., Hosseini, M. W., Eds.; Pergamon: New York, 1996; p 253.
[118] Linton, B.; Hamilton, A. D. *Chem. Rev.* **1997**, *97*, 1669.
[119] Stang, P. J. *Chem. Eur. J.* **1998**, *4*, 19.
[120] Jones, C. J. *Chem. Soc. Rev.* **1998**, *27*, 289.
[121] Fujita, M. *Chem. Soc. Rev.* **1998**, *27*, 417.
[122] Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853.
[123] Holliday, B. J.; Mirkin, C. A. *Angew. Chem. Int. Ed. Engl.* **2001**, *40*, 2022.
[124] Swiegers, G. F.; Malefetse, T. J. *Chem. Eur. J.* **2001**, *7*, 3636.
[125] Hartshorn, C. M.; Steel, P. J. *Chem. Commun.* **1997**, 541.
[126] Muller, I. M.; Robson, R.; Separovic, F. *Angew. Chem. Int. Ed. Engl.* **2001**, *40*, 4385.
[127] Aoki, S.; Shiro, M.; Kimura, E. *Chem. Eur. J.* **2002**, *8*, 929.
[128] Bell, Z. R.; Jeffery, J. C.; McCleverty, J. A.; Ward, M. D. *Angew. Chem. Int. Ed. Engl.* **2002**, *41*, 2515.
[129] Alam, M. A.; Nethaji, M.; Ray, M. *Angew. Chem. Int. Ed. Engl.* **2003**, *42*, 1940.
[130] Fujita, M.; Umemoto, K.; Yoshizawa, M.; Fujita, N.; Kusukawa, T.; Biradha, K. *Chem. Commun.* **2001**, 509.
[131] Sun, W.; Yoshizawa, M.; Kusukawa, T.; Fujita, M. *Curr. Opin. Chem. Biol.* **2002**, *6*, 757.
[132] Fujita, M.; Oguro, D.; Miyazawa, M.; Oka, H.; Yamaguchi, K.; Ogura, K. *Nature (London)* **1995**, *378*, 469.
[133] Kusukawa, T.; Fujita, M. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 3142.
[134] Kusukawa, T.; Yoshizawa, M.; Fujita, M. *Angew. Chem. Int. Ed. Engl.* **2001**, *40*, 1879.
[135] Sun, W.; Kusukawa, T.; Fujita, M. J. *Am. Chem. Soc.* **2002**, *124*, 11570.
[136] Bourgeois, J.-P.; Fujita, M. *Aust. J. Chem.* **2002**, *55*, 619.
[137] Kusukawa, T.; Fujita, M. J. *Am. Chem. Soc.* **1999**, *121*, 1397.
[138] Kusukawa, T.; Nakai, T.; Okano, T.; Fujita, M. *Chem. Lett.* **2003**, *32*, 284.
[139] Ito, H.; Kusukawa, T.; Fujita, M. *Chem. Lett.* **2000**, 598.
[140] Yoshizawa, M.; Takeyama, Y.; Kusukawa, T.; Fujita, M. *Angew. Chem. Int. Ed. Engl.* **2002**, *41*, 1347.
[141] Yoshizawa, M.; Takeyama, Y.; Okano, T.; Fujita, M. J. *Am. Chem. Soc.* **2003**, *125*, 3243.
[142] Yoshizawa, M.; Kusukawa, T.; Fujita, M.; Yamaguchi, K. J. *Am. Chem. Soc.* **2000**, *122*, 6311.
[143] Yoshizawa, M.; Miyagi, S.; Kawano, M.; Ishiguro, K.; Fujita, M. J. *Am. Chem. Soc.* **2004**, *126*, 9172.
[144] Yoshizawa, M.; Tamura, M.; Fujita, M. J. *Am. Chem. Soc.* **2004**, *126*, 6846.
[145] Caulder, D. L.; Raymond, K. N. *Acc. Chem. Res.* **1999**, *32*, 975.
[146] Caulder, D. L.; Raymond, K. N. *J. Chem. Soc. Perkin Trans.* **1999**, *1*, 1185.
[147] Stang, P. J.; Olenyuk, B. *Acc. Chem. Res.* **1997**, *30*, 502.
[148] Olenyuk, B.; Fechtenkotter, A.; Stang, P. J. *J. Chem. Soc. Dalton Trans.* **1998**, 1707.
[149] Seidel, S. R.; Stang, P. J. *Acc. Chem. Res.* **2002**, *35*, 972.
[150] Reek, J. N. H.; Schenning, A. P. H. J.; Bosman, A. W.; Meijer, E. W.; Crossley, M. J. *Chem. Commun.* **1998**, 11.
[151] Johnston, M. R.; Gunter, M. J.; Warrener, R. N. *Chem. Commun.* **1998**, 2739.
[152] Felluga, F.; Tecilla, P.; Hillier, L.; Hunter, C. A.; Licini, G.; Scrimin, P. *Chem. Commun.* **2000**, 1087.
[153] Kuroda, Y.; Kawashima, A.; Urai, T.; Ogoshi, H. *Tetrahedron Lett.* **1995**, *36*, 8449.
[154] Kuroda, Y.; Kawashima, A.; Hayashi, Y.; Ogoshi, H. J. *Am. Chem. Soc.* **1997**, *119*, 4929.
[155] Ikeda, A.; Ayabe, M.; Shinkai, S.; Sakamoto, S.; Yamaguchi, K. *Org. Lett.* **2000**, *2*, 3707.
[156] Johnston, M. R.; Latter, M. J.; Warrener, R. N. *Org. Lett.* **2002**, *4*, 2165.
[157] Johnston, M. R.; Latter, M. J. J. *Porph. Phthal.* **2002**, *6*, 757.
[158] Fochi, F.; Jacopozzi, P.; Wegelius, E.; Rissanen, K.; Cozzini, P.; Marastoni, E.; Fisicaro, E.; Manini, P.; Fokkens, R.; Dalcanale, E. J. *Am. Chem. Soc.* **2001**, *123*, 7539.
[159] Jacopozzi, P.; Dalcanale, E. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 613.
[160] Park, S. J.; Hong *J. Chem. Commun.* **2001**, 1554.
[161] Park, S. J.; Lee, J. W.; Sakamoto, S.; Yamaguchi, K.; Hong *J. Chem. Eur. J.* **2003**, *9*, 1768.
[162] Ikeda, A.; Yoshimura, M.; Udzu, H.; Fukuhara, C.; Shinkai, S. J. *Am. Chem. Soc.* **1999**, *121*, 4296.
[163] Zhong, Z.; Ikeda, A.; Shinkai, S. J. *Am. Chem. Soc.* **1999**, *121*, 11906.
[164] Ikeda, A.; Udzu, H.; Yoshimura, M.; Shinkai, S. *Tetrahedron* **2000**, *56*, 1825.
[165] Ikeda, A.; Sonoda, K.; Shinkai, S. *Chem. Lett.* **2000**, 1220.
[166] Ikeda, A.; Udzu, H.; Zhong, Z.; Shinkai, S.; Sakamoto, S.; Yamaguchi, K. J. *Am. Chem. Soc.* **2001**, *123*, 3872.
[167] Fox, O. D.; Brew, M. G. B.; Beer, P. D. *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 136.
[168] Fox, O. D.; Dalley, K.; Harrison, R. G. J. *Am. Chem. Soc.* **1998**, *120*, 7111.
[169] Fox, O. D.; Dalley, K.; Harrison, R. G. *Inorg. Chem.* **1999**, *38*, 5860.
[170] Fox, O. D.; Leung, J. F.; Hunter, J. M.; Dalley, K.; Harrison, R. G. *Inorg. Chem.* **2000**, *39*, 783.