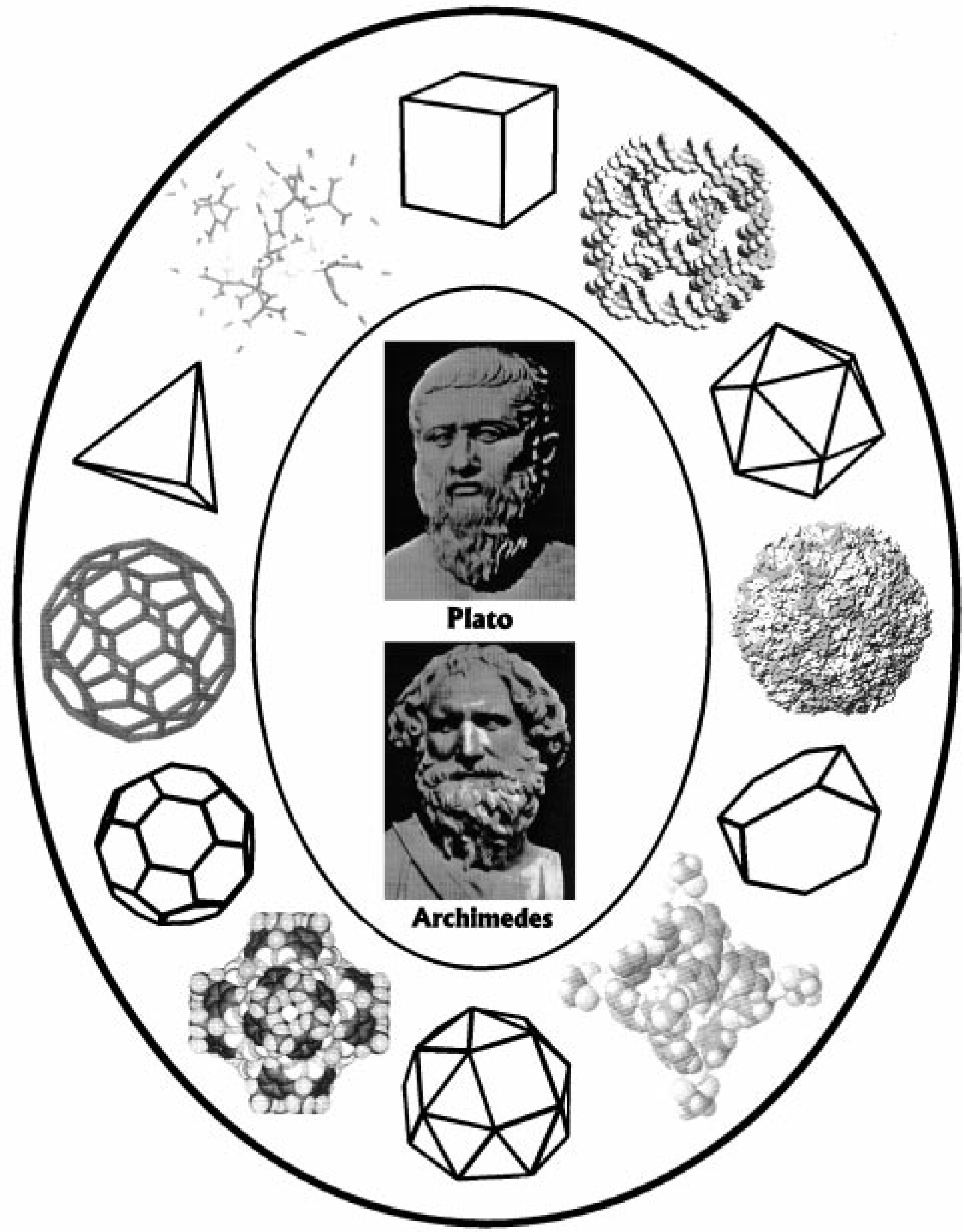
Platonic and Archimedean solids represent the limited number of ways in which more than three identical chemical subunits that correspond to regular polygons may be arranged along the surface of a sphere to approximate a spherical shell.



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The underlying geometrical principles can be used for the classification of organic, inorganic, and biological host frameworks (some of which are shown here) and to identify synthetic opportunities for new containers.

Structural Classification and General Principles for the Design of Spherical Molecular Hosts

Leonard R. MacGillivray and Jerry L. Atwood*

Complexes made by hosts that completely surround their guests provide a means to stabilize reactive and transient chemical intermediates, to transfer biologically active molecules to target cells, and to construct molecular scale devices. Whereas nature has utilized amino acids, in the form of polypeptide chains, to construct shell-like hosts of nanoscale dimensions (for example, viruses and ferritin) that exhibit certain functions (for example, packaging of DNA and Fe cores), chemists have a myriad of organic and inorganic building blocks at their disposal. These may be used to synthesize diverse families of shells as demonstrated by the emergence of container molecules, ions, and assemblies (for example, cryptands, carcerands, polyoxometallates, inorganic-organic cages, and molecular capsules). Synthetic containers of nanoscale dimensions remain rare, however, and with interests in chemical synthesis moving towards the fabrication of nanoscale molecular frameworks and the miniaturization of functional microstructures, it seems likely that the structures of biological shells will continue to inspire the design of synthetic analogues. It is clear that if chemists are to proceed with the endeavor of synthesizing shell-like hosts then a design strategy for the construction of such frameworks would be desirable, with a method that translates features related to the structures of biological shells to synthetic systems. Here, we demonstrate such an approach. In particular, we have structurally classified a variety of organic, inorganic, and biological host frameworks and show that their structures may be cataloged according to principles of solid geometry in which the five Platonic and 13 Archimedean solids may be used as models for spheroid design. In essence, the method relies on recognizing the relationship between the convex uniform polyhedra and container molecules where, in both cases, identical subunits and bonding arrangements make up each shell. This systematic approach has led us to identify containers that have yet to be synthesized or discovered and we propose such systems as targets for chemical synthesis.

Keywords: host-guest chemistry · macrocycles · nanostructures · noncovalent interactions · topochemistry

1. Introduction

Since the introduction of the cryptands,[1] chemists have strived to design discrete spherical molecular hosts similar to those found in nature (for example, spherical viruses, fullerenes). Such frameworks possess cavities capable of entrapping atomic and/or molecular sized guests and have applications in chemistry (for example, catalysis),[2] biology (drug delivery),[3] and materials science (molecular devices).[4] Self-assembly,[5, 6] the building of molecular architecture with identical chemical subunits, has been a central theme and, at the highest level of sophistication, has yielded monomolecular[7] and supramolecular dimeric capsules[2] capable of packaging molecular guests.

In such a context, a recent discovery in our laboratory of a self-assembling molecular spheroid[8] has prompted us to examine the topologies of these and related hosts with a view to understand their structures on the basis of symmetry. In addition to providing a grounds for classification, such an approach allows one to identify similarities at the structural level that may not seem obvious at the chemical level, and may be used to design future systems. Notably, this approach has led us to identify from principles of solid geometry limited designs that are possible for the construction of spherical shells, those being the five Platonic and 13 Archimedean solids.[9] Herein we now present a general design strategy for the construction of spherical molecular hosts.

2. Spheroid Design

Our strategy stems from ideas developed within host–guest[10] and supramolecular chemistry.[11] As is the case of spherical viruses[3] and fullerenes,[4] an appropriately sized,

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Figure 1. Hollow spherical shell S.

shaped, and functionalized guest is packaged within the interior of a host such that it is completely surrounded or enclosed. From a geometrical standpoint, this may be achieved by centralizing the guest within a hollow spherical shell S (Figure 1). We note, however, that it is impossible to mimic S from a chemical standpoint since atoms and molecules are discrete entities whereas the surface of S is uniform. Thus, an alternative procedure must be employed to design a spherical molecular host.

2.1. Self-Assembly

In a paper that described the structure of regular viruses,[12] Caspar and Klug have shown that viral capsids use self-assembly to construct spherical shells up to a hundred nanometers in diameter by utilizing identical copies of proteins as chemical subunits. Such a design strategy is desirable since it employs an economy of information,[6, 12] which gives rise to a host whose subunits exist in identical chemical environments, the exposed surface area is at a minimum, and strain energy is distributed evenly along its surface.[4] This process is also amenable for spherical shells at the angstrom level as realized with the discovery of buckminsterfullerene or C_{60}.[13] Notably, in the extreme case, an infinite number of identical subunits placed along the surface of a sphere will lead to a shell topologically equivalent to S. Thus, to construct a spherical molecular host one must ultimately consider the number of subunits n for spheroid design and their placement along the surface of the shell.

2.2. Subunits for Spheroid Design and Self-Assembly

To construct a spherical shell from a single subunit, $n=1$, the only structure obtainable is S. It is impossible to construct a spherical molecular host from a single chemical entity (as outlined above) and therefore S does not represent a self-assembled spherical framework.

For $n=2$, each subunit must cover one half of the surface of the sphere. This can only be achieved if the subunits exhibit curvature and they are placed such that their centroids lie at a maximum distance from each other. These criteria place two points along the surface of a sphere, separated by a distance equal to the diameter of the shell. We assign these positions the north and south poles. As a consequence of this arrangement, there exists two structure types for $n=2$. The first belongs to the point group D_{h} and consists of two identical subunits attached at the equator (Figure 2a). Since it is impossible to create a shell-like hemisphere that possesses ∞-fold rotation symmetry by using atoms and molecules, this structure is not obtainable from a chemical standpoint. The second belongs to the point group D_{nd} and its simplest

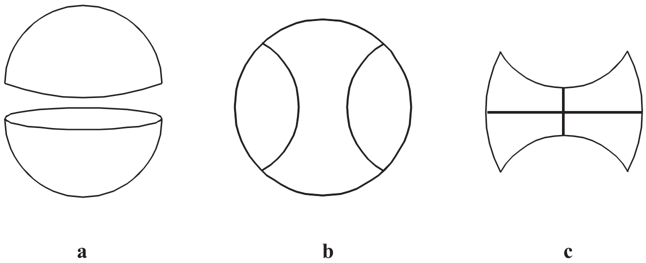

Figure 2. Shells with $n=2$: a) $D_{\infty\mathrm{h}}$ symmetry, b) $D_{2\mathrm{d}}$ symmetry (tennis ball), c) subunit of $D_{2\mathrm{d}}$ shell depicting the four asymmetric units.

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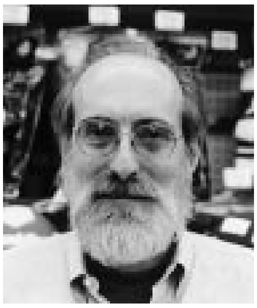

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member, $n = 2$, is topologically equivalent to a tennis ball (Figure 2b). Each subunit of this system is symmetrical and may be divided into four identical asymmetric units (Figure 2c), which implies that eight asymmetric units are required to design the shell. Thus, $n = 2$ represents the minimum number of subunits that may be used to construct a spherical molecular host by self-assembly.

For $n = 3$, each subunit must cover one third of the surface of the sphere. Following the design conditions described previously, placing three identical subunits along the surface of a sphere results in an arrangement in which their centroids constitute the vertices of an equilateral triangle (Figure 3a). As a result there is only one structure type for $n = 3$. The structure belongs to the point group D_{3h} and, as for the $n = 2$ system, the subunits must exhibit curvature (Figure 3b). Since each "arm" may be divided into four identical asymmetric units (Figure 3c), 12 asymmetric units are required to construct the shell.

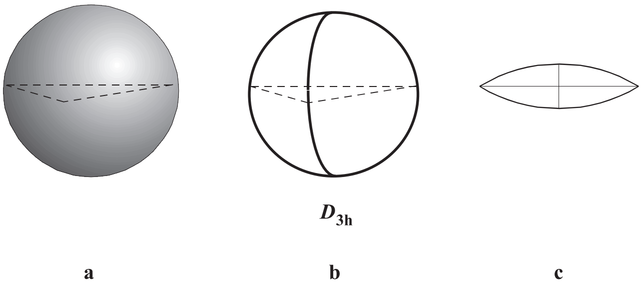

Figure 3. Shell with $n = 3$: a) equilateral triangle from S, b) D_{3h} symmetry, c) subunit of D_{3h} shell depicting the four asymmetric units.

For $n = 4$, positioning four points along the surface of a sphere such that they lie a maximum distance from each other places the points at the vertices of a tetrahedron (Figure 4a). This is the first case in which joining the points through line segments gives rise to a closed surface container. The container, a tetrahedron, is comprised of four identical subunits in the form of equilateral triangles, where surface curvature is supplied by edge sharing of regular polygons rather than the subunits themselves (Figure 4b). Each triangle may be divided into six asymmetric units as a result of its symmetry, (Figure 4c), which implies that 24 asymmetric units (4×6) are required to generate the shell. The tetrahedron belongs to the point group T_d and its polygons are related by combinations of twofold and threefold rotation axes.

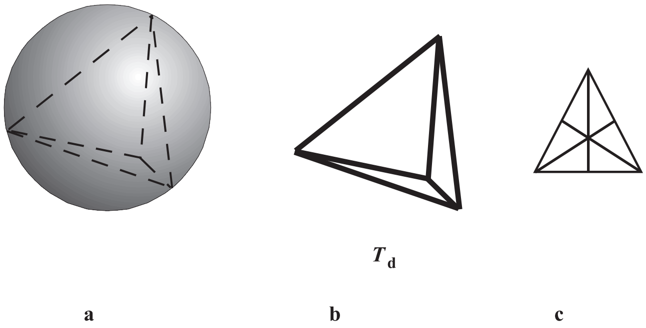

Figure 4. Shell with $n = 4$: a) equilateral triangles from S, b) T_d symmetry, c) subunit of T_d shell depicting the six asymmetric units.

2.3. Platonic Solids

The tetrahedron belongs to a family of five convex uniform polyhedra known as the Platonic solids (Figure 5, Table 1).[9] Each member of this family possesses cubic symmetry (that is, *32*, *432*, or *532* symmetry) and is made of the same regular polygons (for example, equilateral triangle, square) arranged in space such that its vertices and edges, and three coordinate directions, are equivalent. There is a finite number of such polyhedra as a consequence of the fact that there exists a limited number of ways in which identical regular polygons may be adjoined to construct a convex corner. Equilateral triangles may be adjoined in three ways while squares and pentagons may be adjoined in only a single manner. Moreover, it is impossible to create a convex corner from regular polygons with six or more sides since the sum of the angles around each vertex would be greater than or equal to 360°.[9] These principles give rise to five isometric polyhedra that are achiral and whose polygons are related by combinations of n-fold rotation axes. The Platonic solids include the tetrahedron, which belongs to the point group T_d, possesses *32* symmetry, and requires a minimum of 12 asymmetric units; the cube and octahedron, which belong to the point group O_h, possess *432* symmetry, and require a minimum of 24 asymmetric units; and the dodecahedron and icosahedron, which belong to the point group I_h, possess *532* symmetry, and require a minimum of 60 asymmetric units.[12] The number of asymmetric units required to generate each shell doubles if mirror planes are present in these structures.

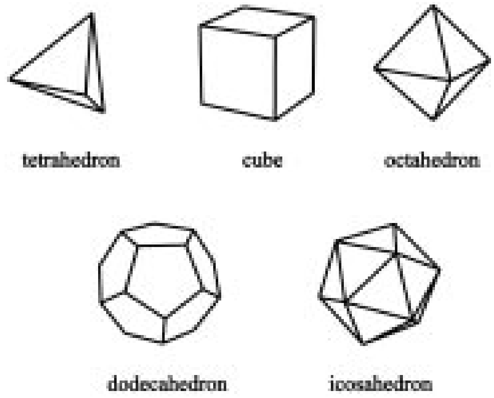

Figure 5. The five Platonic solids (see also Table 1).

Table 1. Platonic solids.

Solid	Vertices	Edges	Face type	Faces
tetrahedron	4	6	triangle	4
cube	8	12	square	6
octahedron	6	12	triangle	8
dodecahedron	20	30	pentagon	20
icosahedron	12	30	triangle	20

2.4. Archimedean Solids

In addition to the Platonic solids, there exists a family of 13 convex uniform polyhedra known as the Archimedean solids

(Figure 6, Table 2).[9] Each member of this family is made up of at least two different regular polygons and may be derived from at least one Platonic solid through either trunction or the twisting of faces. In the case of the latter, two chiral members, the snub cube and the snub dodecahedron, are realized. The remaining Archimedean solids are achiral. Like the Platonic solids, the Archimedean solids possess identical vertices, exhibit either *32*, *432*, or *532* symmetry, and require a minimum of either 12, 24, or 60 asymmetric units, respectively. The Archimedean solids possess a larger variety of polygons than the Platonic solids. These include the equilateral triangle, square, pentagon, hexagon, octagon, and decagon.

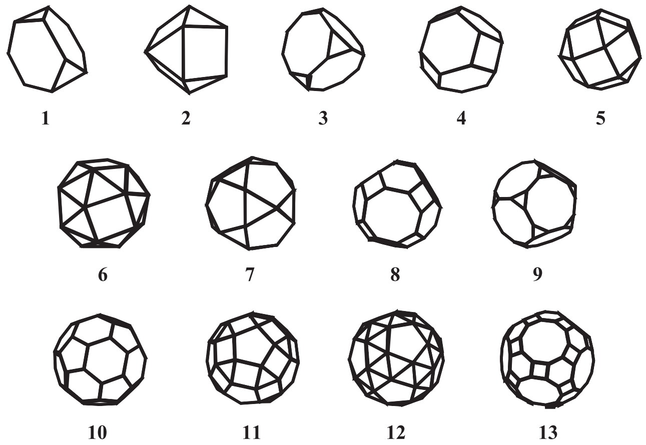

Figure 6. The 13 Archimedean solids, in order of increasing number of vertices. Truncated tetrahedron (1), cuboctahedron (2), truncated cube (3), truncated octahedron (4), rhombicuboctahedron (5), snub cube (6), icosidodecahedron (7), rhombitruncated cuboctahedron (8), truncated dodecahedron (9), truncated icosahedron (10), rhombicosidodecahedron (11), snub dodecahedron (12), rhombitruncated icosidodecahedron (13) (see also Table 2).

2.5. Models for Spheroid Design

It is our contention here that the Platonic and Archimedean solids represent the limited number of ways in which $n > 3$ identical chemical subunits that correspond to regular polygons may be arranged along the surface of a sphere to approximate *S*. As a result, these solids may be used as models for the construction of spherical molecular hosts. These polyhedra provide combinations of n-fold rotation axes and subunits in the form of regular polygons for self-assembly, which allow one to determine where along the surface of a sphere chemical subunits should be placed and the bonding arrangements they should adopt. In effect, the Platonic and Archimedean solids simplify the task of constructing spherical molecular hosts by facilitating a priori spheroid design, and serve as targets in chemical synthesis.

2.6. Prisms and Antiprisms

In addition to the Platonic and Archimedean solids, and to complete the convex uniform polyhedra, there exist two infinite families of solids known as prisms and antiprisms (Figure 7, Table 3).[9] These polyhedra consist of two regular n-gons bisected by a perpendicular n-fold rotation axis and are

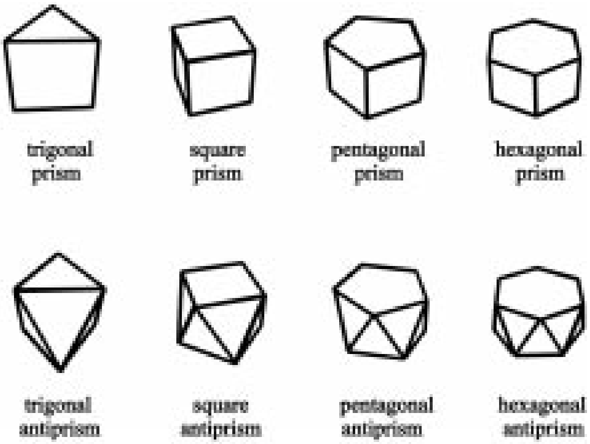

Figure 7. Prisms and antiprisms.

Table 3. Prisms and antiprisms.

Solid	Vertices	Edges	Faces
prism	$2n$[a]	$3n$	n squares (or n rectangles) + 2 n-gons
antiprism	$2n$	$6n$	$2n$ triangles + 2 n-gons

[a] n-fold rotation axis

Table 2. Archimedean solids.

Solid	Vertices	Edges	f(3)[a]	f(4)	f(5)	f(6)	f(8)	f(10)
(1) truncated tetrahedron	12	18	4	–	–	4	–	–
(2) cuboctahedron	12	24	8	6	–	–	–	–
(3) truncated cube	24	36	8	–	–	–	6	–
(4) truncated octahedron	24	36	–	6	–	8	–	–
(5) rhombicuboctahedron	24	48	8	18	–	–	–	–
(6) snub cube	24	60	32	6	–	–	–	–
(7) icosidodecahedron	30	60	20	–	12	–	–	–
(8) rhombitruncated cuboctahedron	48	72	–	12	–	8	6	–
(9) truncated dodecahedron	60	90	20	–	–	–	–	12
(10) truncated icosahedron	60	90	–	–	12	20	–	–
(11) rhombicosidodecahedron	60	120	20	30	12	–	–	–
(12) snub dodecahedron	60	150	80	–	12	–	–	–
(13) rhombitruncated icosidodecahedron	120	180	–	30	–	20	–	12

[a] f(n) where f denotes face and n indicates the number of sides of the face.

related by n twofold rotation axes. Prisms differ from antiprisms such that the n-gons of a prism are congruent whereas n-gons of an antiprism are related by a twist. As a result, joining the vertices of a prism through line segments gives rise to squares while the same procedure applied to an antiprism gives rise to alternating up and down triangles. Notably, the distance between the n-gons of prisms and antiprisms may be reduced or increased, which either flattens or elongates the solid, respectively. The minimalist members of both families are based upon the equilaterial triangle. As a result, prisms and antiprisms exhibit dihedral D symmetry. Prisms belong to the point group D_{nh}, while antiprisms belong to the point group D_{nd} ($n \geq 3$). With the exception of the cube (square prism) and octahedron (trigonal antiprism), the three coordinate directions of prisms and antiprisms are not equivalent. We therefore refer to these systems as pseudo-spherical.

2.7. Dihedral Symmetry: $n = 2$ and $n = 3$ Shells

Prisms and antiprisms may be used in a similar way to the Platonic and Archimedean solids for the construction of hosts based upon $n = 2$ and $n = 3$ subunits as a result of their dihedral symmetry. As stated, two identical subunits may be arranged to approximate S by using shells with D_{nd} symmetry. Likewise, three identical subunits may be arranged to approximate S by using a shell with D_{3h} symmetry. A common feature of these structures is dihedral symmetry where half of each shell is defined by a twofold rotation axis. Moreover, close inspection of these frameworks reveals that they are topologically equivalent to antiprisms and the trigonal prism, respectively. As a result, these polyhedra may be used as models for the construction of $n = 2$ and $n = 3$ structures. In fact, shells consisting of $n = 3$ subunits belong to the $n = 2$ family since their north and south poles are identical. Like the D_{nd} shells, there exists an infinite number of D_{nh} structures since there exists an infinite number of prisms. It must be stressed, however, that, unlike the Platonic and Archimedean solids, the subunits of these systems must exhibit curvature.

2.8. D_{2h} and D_{2d} Shells

Since the simplest members of prisms and antiprisms possess a threefold rotation axis of symmetry or greater, these polyhedra cannot be used as models for D_{2h} and D_{2d} shells. Moreover, it is impossible to construct a polyhedron without polygons. There exist, however, common objects that possess the symmetries of these frameworks, which may be considered for the construction of these shells. For example, a rugby ball with alternating gray and black patches possesses D_{2h} symmetry (Figure 8). On the other hand, a tennis ball, as pointed out previously, possesses D_{2d} symmetry (Figure 2b). As is the case for prisms and antiprisms, the three coordinate directions of D_{2h} and D_{2d} structures are not equivalent and their subunits must exhibit curvature. We therefore also refer to these systems as pseudo-spherical.

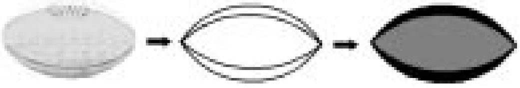

Figure 8. Rugby ball shell.

3. Examples from the Laboratory and from Nature

Our premise that pseudo-spherical and spherical molecular hosts may be classified into two categories, $n = 2$ and $n > 3$, according to principles of geometry, renders both organic and inorganic components viable for their design and permits the individual subunits to be held together by covalent and/or noncovalent bonds. Indeed, a common feature displayed by organic and inorganic chemists is that they must utilize space for assembling atoms into molecular frameworks. To demonstrate the utility of this approach, we now present selected examples of pseudo-spherical and spherical hosts from the laboratory and nature. We will begin with dihedral systems and work our way to cubic frameworks (Table 4).

Table 4. Summary of symmetries for shell-like hosts.

Solid or shell	Spherical or pseudo-spherical	Symmetry	Point group(s)	Asymmetric units
Platonic/Archimedean	spherical	icosahedral	I_h, I	120, 60
	spherical	octahedral	O_h, O	48, 24
	spherical	tetrahedral	T_h, T_d, T	24, 24, 12
prisms/antiprisms	pseudo-spherical	dihedral	D_{nh}, D_{nd}	$4n$, $4n$
rugby ball	pseudo-spherical	dihedral	D_{2h}	8
tennis ball	pseudo-spherical	dihedral	D_{2d}	8

3.1. "Tennis Ball" Shell (D_{2d})

Rebek et al. presented the first example of a supramolecular "tennis ball" (Figure 9a).[14] This system has been designated a molecular capsule and the subunits are based upon diphenyl glycoluril and durene, which self-assemble in chloroform by way of eight $N-H \cdots O$ hydrogen bonds. The methylene linkages between the glycoluril units and the aromatic moiety provide much of the curvature of this system. Since their introduction, Rebek et al. have constructed larger D_{2d} hosts[15] and revealed their molecular recognition properties.

In addition to organic components, inorganic components have been used for D_{2d} capsules. In particular, Müller et al. have demonstrated the ability of VO_5 square pyramids to assemble from aqueous media to form a D_{2d} polyoxovanadate shell $[HV_{22}O_{54}]^{5-}$, which encapsulates a perchlorate ion (Figure 9b).[16] Thorn et al. have also demonstrated the ability of such VO_5 units to form a D_{2d} shell by assembley with phosphonate ligands $[(V_2O_3)_2(O_3PPh)_4]^{2-}$, which entraps a fluoride ion (Figure 9c).[17]

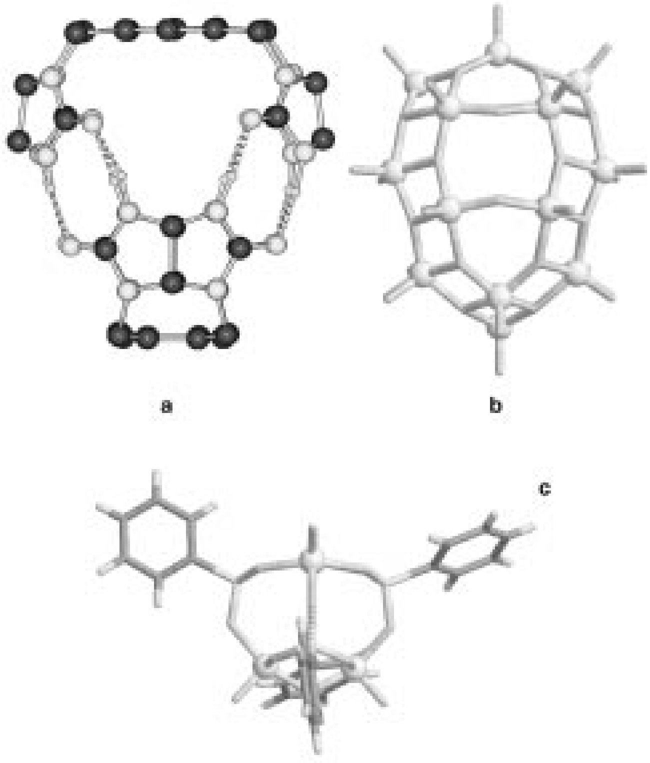

Figure 9. X-ray crystal structures of D_{2d} (tennis ball) hosts: a) a molecular capsule (Rebek et al.), b) the $[HV_{22}O_{54}]^{5-}$ ion, c) the $[(V_2O_3)_2(O_3PPh)_4]^{2-}$ ion (carbon atoms have been omitted for clarity) (atomic color scheme: gray = carbon, white = hydrogen, red = oxygen, blue = nitrogen, orange = vanadium, magenta = phosphorus).

3.2. "Rugby Ball" Shell (D_{2h})

To our knowledge, the first D_{2h} host was synthesized by Vögtle et al.[18] The cage is based upon the cyclodimerization of tetrakis(proparglyic ether) units that are separated by covalently attached diyne spacers (Figure 10a). This host possesses two chemically distinct "windows" that allow access to its cavity.[18]

In a similar way to their D_{2d} system, Müller et al. have demonstrated the ability of VO_5 pyramids to form the D_{2h} shells $[H_2V_{18}O_{44}]^{4-}$ and $[V_{14}O_{22}(OH)_4(PhPO_3)_8]^{6-}$, each of which encapsulates either an azide ion, water molecules, or both (Figure 10b).[16, 19] Zubieta et al. have also reported the ability of such VO_5 pyramids to form the similar D_{2h} shell $[V_{12}O_{14}(OH)_4(PhAsO_3)_{10}]^{4-}$, which entraps two methanol molecules.[20]

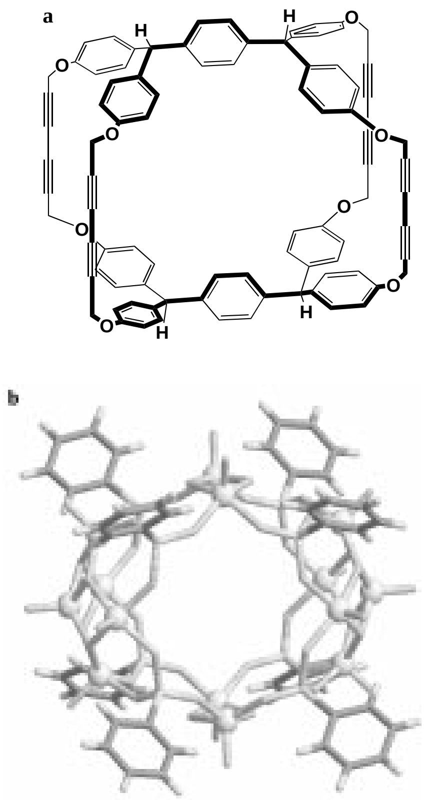

Figure 10. D_{2h} (rugby ball) hosts: a) a system based upon tetrakis(proparglyic ether) units (Vögtle et al.), b) the $[V_{14}O_{22}(OH)_4(PhPO_3)_8]^{6-}$ ion.

3.3. Prisms (D_{nh}, $n \geq 3$)

The [2.2.2]cryptand synthesized by Lehn et al. was the first $n = 2$ host (Figure 11a).[1] The subunits of this system possess idealized D_{3h} symmetry and are propagated at the north and south poles by sp^3 hybridized nitrogen atoms and may be divided into the six asymmetric units $[N(CH_2CH_2OCH_2)_3]/6$.

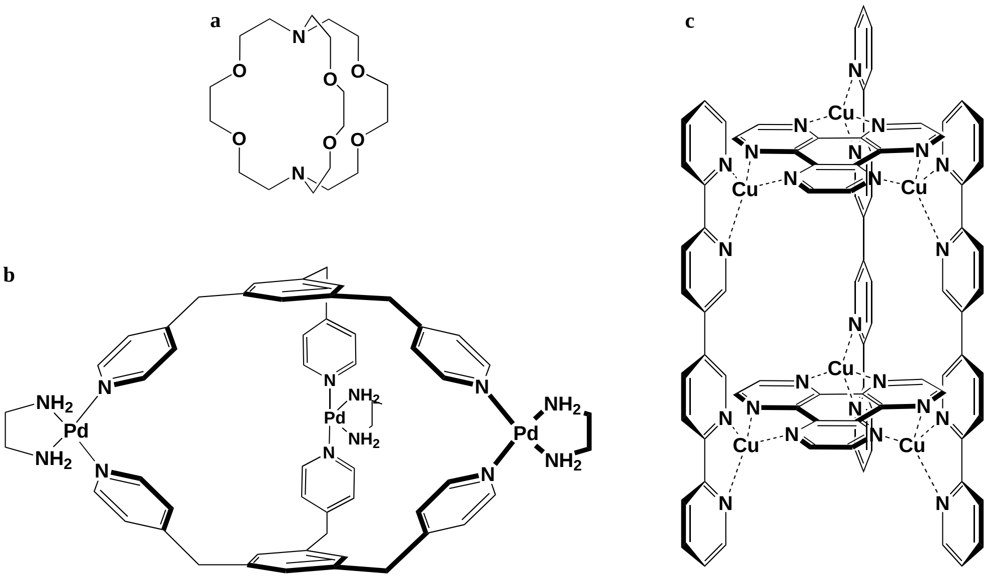

Figure 11. D_{3h} hosts: a) [2.2.2]cryptand, b) a metal–organic palladium host (Fujita et al.), and c) a metal–organic copper host (Lehn et al.).

Owing to the size of the subunits, the [2.2.2]cryptand is capable of complexing atomic cations.[1]

Following the introduction of the cryptands, a variety of D_{3h} hosts have emerged.[18, 21] To effect their binding properties, structural changes are often made at their poles and/or their side arms and, in some instances, metal ions are used. Examples include metal–organic cages (Figure 11 b, c).[22, 23] These systems are capable of binding molecular guests as a consequence of the larger sizes of their subunits.[18]

The carcerands, introduced by Cram et al., were the first D_{4h} hosts (Figure 12 a).[8] These molecules consist of cavitands covalently attached in a head-to-head fashion and are capable of incarcerating molecular guests such that they are unable to escape. Our lab has recently shown[24] that a similar host may be realized from calix[4]resorcinarenes through noncovalent bonds. Specifically, two *C*-phenethylcalix[4]resorcinarenes and eight isopropanol molecules were shown to assemble by way of 16 O–H ··· O hydrogen bonds to form a D_{4h} complex in the solid state. Beer et al. have also introduced a D_{4h} host based upon calix[4]arenes, aligned in a tail-to-tail fashion, which binds atomic sized cations (Figure 12 b).[25] Other D_{4h} systems include metal-based carcerands[26] and porphyrin dimers.[27]

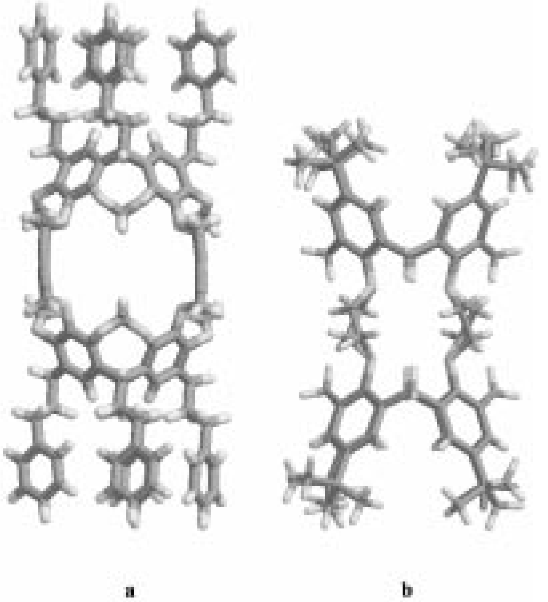

Figure 12. X-ray crystal structure of D_{4h} hosts: a) a carcerand (Cram et al.), b) a calix[4]tube (Beer et al.).

The C_{70} fullerene is an example of a D_{5h} shell (Figure 13 a). Each subunit of C_{70} is composed of 35 carbon atoms and is attached at the equator through five covalent bonds.[4] Pope et al. have described the formation of the shell-like polytungstate $[NaP_5W_{30}O_{110}]^{14-}$, which possesses approximate D_{5h} symmetry (Figure 13 b).[28] The anion, which is partly made up of five P_5W_6 units, was observed to entrap an exchangeable sodium ion in both solution and the solid state.[28]

Zimmerman et al. have recently presented an example of a dendrimeric assembly that exhibits D_{6h} symmetry (Figure 14 a).[29] The subunits are held together by six covalent bonds and contain 24 asymmetric units, each of which interacts at the north and south poles by way of hydrogen bonded carboxylic acid dimers. Kim et al. have also demonstrated the ability of a D_{6h} host based upon a "lidded" cucurbituril to function as a molecular capsule (Figure 14 b),[30] while Shinkai et al. have reported the design of a D_{6h} shell by linking two calix[6]arenes through bridging sulfur atoms (Figure 14 c).[31]

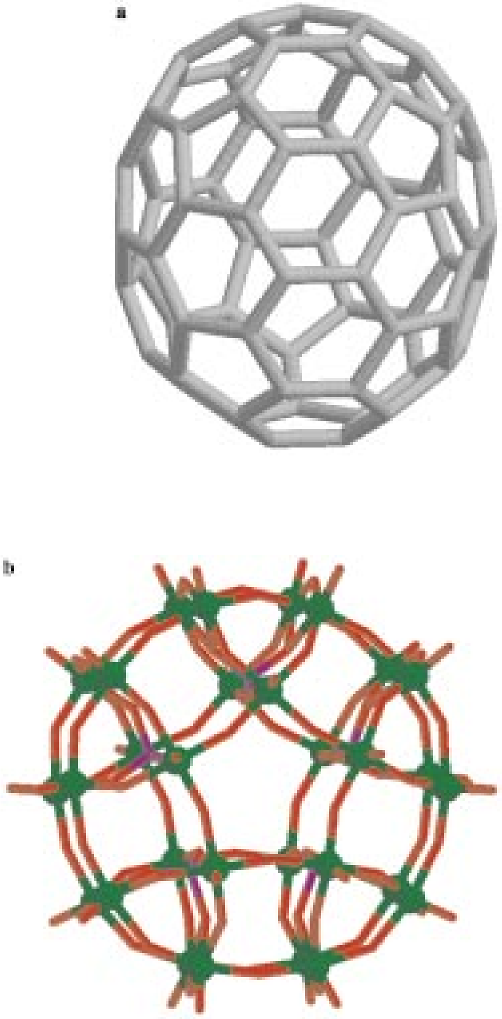

Figure 13. X-ray crystal structure of D_{5h} hosts: a) C_{70}, b) the $[NaP_5W_{30}O_{110}]^{14-}$ ion (atomic color scheme: green = tungsten)

To the best of our knowledge, there are no examples of hosts that possess D_{nh} ($n \geq 7$) symmetry. We note, however, that Klüfers et al. have demonstrated the ability of two γ-cyclodextrin molecules to assemble with 16 lead(II) ions to form a shell-like complex that possesses approximate D_8 symmetry as a result of the *anti* arrangement of the macrocycles.[32]

3.4. Antiprisms (D_{nd}, $n \geq 3$)

Rebek et al. recently introduced a D_{3d} molecular capsule (Figure 15).[33] Like its D_{2d} predecessor, the subunits of this capsule, each of which possesses six asymmetric units, are based upon glycoluril and their curvature primarily arises

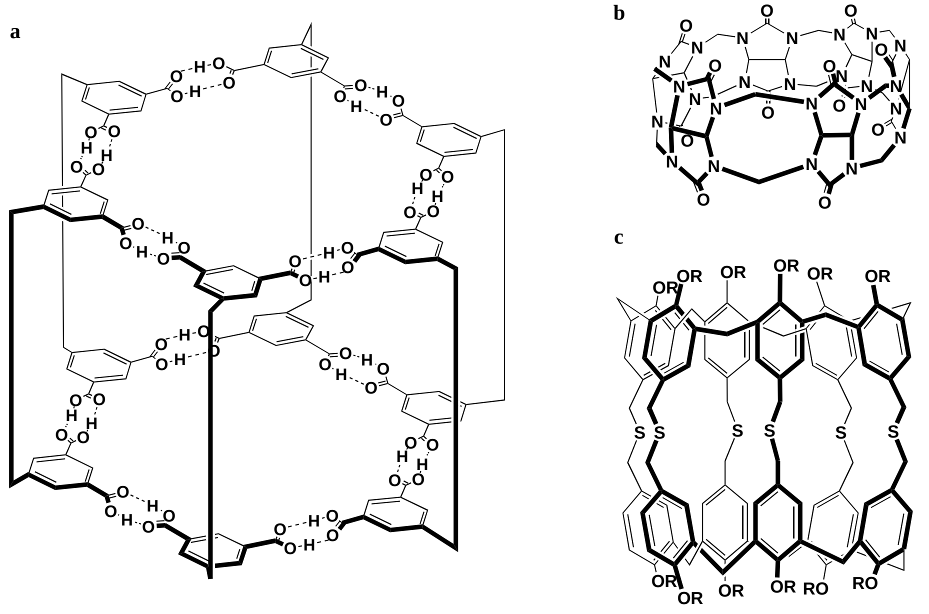

Figure 14. D_{6h} hosts: a) a dendrimeric assembly (Zimmerman et al.), b) cucurbituril (Kim et al.), c) a calix[6]arene shell (Shinkai et al.).

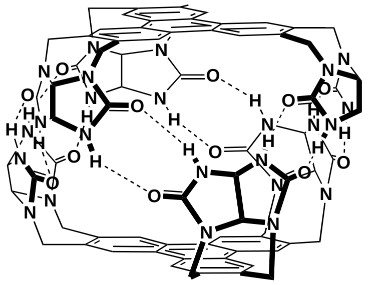

Figure 15. D_{3d} host: the flattened capsule from Rebek et al.

from methylene linkages to an aromatic core. The assembly is held together by 12 N–H ··· O hydrogen bonds.[33]

Prior to the D_{3d} capsule, Rebek et al. also introduced a D_{4d} host (Figure 16a).[34] The host is based upon a head-to-head alignment of two calix[4]arenes, with the subunits of this system being held together by a circular configuration of eight urea moieties that interact by way of 16 N–H ··· O hydrogen bonds. Notably, the D_{4d} symmetry of this host is only realized in the absence of the hydrogen bonds. According to molecular modeling studies this capsule is roomy enough to encapsulate two benzene molecules.[34]

Müller et al. have also shown that VO_5 pyramids assemble under selected conditions to give rise to the D_{4d} capsule $[H_4V_{18}O_{42}]^{8-}$ (Figure 16b).[35] The cavity of this ionic host accommodates a halide ion.[35] To our knowledge, there are no examples of hosts that possess D_{nd} ($n \geq 5$) symmetry.

3.5. Platonic Solids

The Platonic solids constitute a family of five convex uniform polyhedra made up of the same regular polygons and possess either *32*, *432*, or *532* symmetry. As a result the three coordinate directions within each solid are equivalent, which makes these polyhedra models for spheroid design.

3.5.1. Tetrahedral Systems (T$_d$, T$_h$, T)

The macrotricyclic spherand designed by Lehn et al. was the first tetrahedral host (Figure 17a).[36] The bridgehead nitrogen atoms, located at the corners of the tetrahedron, and the ethyleneoxy units, the edges, supply the threefold and twofold rotation axes, respectively. As a result, the spherand is composed of 24 asymmetric units, $[(N/3)\text{-}(CH_2CH_2)\text{-}(O/2)]/2$. Notably, this molecule and its tetraprotonated form has been shown to bind an ammonium and chloride ion, respectively. Schmidtchen et al. have introduced similar tetrahedral cages with edges comprised entirely of methylene bridges[37] while Vögtle et al. have demonstrated the synthesis of a hollow hydrocarbon called spheriphane (Figure 17b).[18]

Saalfrank et al. were the first to introduce metal-based tetrahedral cages by using metal ions as corner units and bridging malonate ligands as edges (Figure 17c).[38] Interestingly, these M_4L_6 cages are adamantane-like as a result of a bend in each ligand.[38] In terms of host–guest behavior, an Fe-based system has been shown to complex a single ammonium ion.[39]

Similar tetrahedral cages have emerged following the introduction of these metal-based systems. Raymond et al.[40]

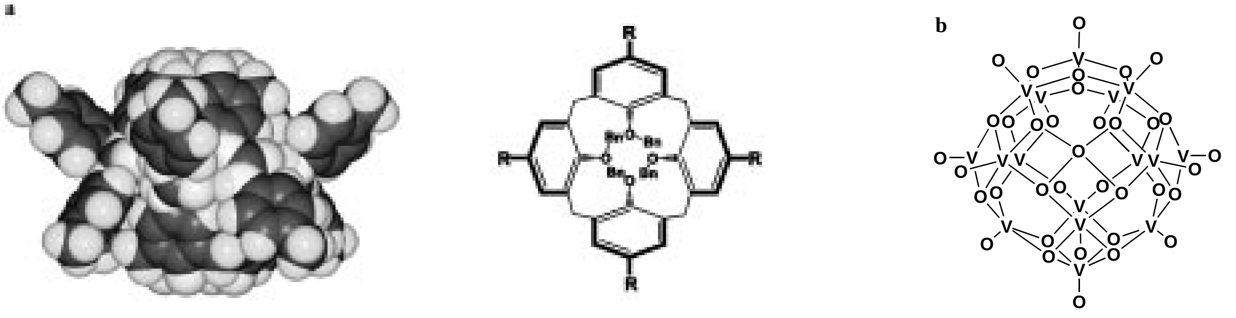

Figure 16. D_{4d} hosts: a) X-ray crystal structure of a calix[4]arene dimer (Rebek et al.), Bn groups are omitted for clarity (inset: iconic representation of the calix[4]arene, R = NH(CO)NH(C_6H_5), Bn = benzyl), b) the $[H_4V_{18}O_{42}]^{8-}$ ion.

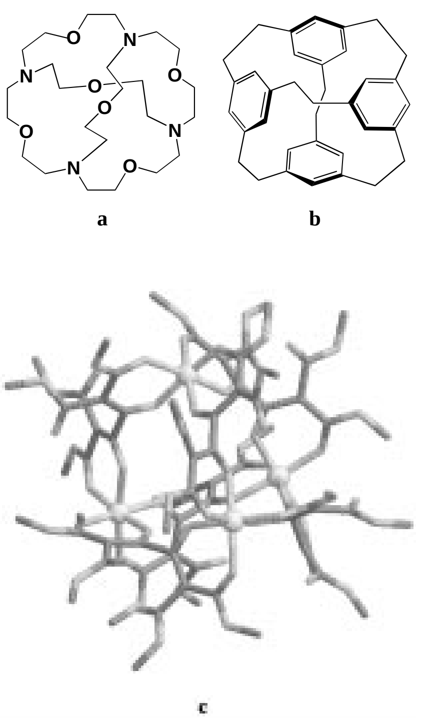

Figure 17. Tetrahedral hosts with T_d symmetry: a) a spherand (Lehn et âl.), b) spheraphane (Vögtle et al.), c) a metal-based cage (Saalfrank et al.) (atomic color sheme: orange = iron).

and Huttner et al.,[41] for example, have revealed that linear, rather than bent, bridging ligands may be used to form such cages. In the case of the former, bidentate ligands were used to completely fill the coordination sites around each metal center while, in the latter, monodentate ligands along with "stopper" units were employed. These hosts were shown to form complexes with four dimethylformamide molecules and a tetrafluoroborate ion, respectively.[40, 41]

Huan et al.,[42] Birker et al.,[43] and Bürgi et al.[44] have described the formation of the tetrahedral shell-like hosts $[H_{12}(VO_2)_{12}(C_6H_5PO_3)_8]^{4-}$, $[M^I_8M^{II}_6\{SC(Me)_2CH(NH_2)CO_2\}_{12}Cl]^{5-}$ (where $M^I_8M^{II}_6$ = $Cu^I_8Ni^{II}_6$, $Ag^I_8Ni^{II}_6$, $Ag^I_8Pd^{II}_6$), and $[ICd_8(SCH_2CH_2OH)_{12}]^{3+}$, which possess vanadium and sulfur atoms at the vertices of a icosahedron (Figure 18). These structures also possess phosphorus and metal ions at the centroids of triangular faces that correspond to the corners of a cube. As a result, these shells belong to the point group T_h, the point group of a volleyball (Figure 19).

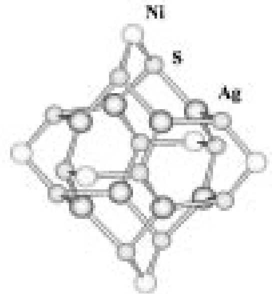

Figure 18. Tetrahedral host with T_h symmetry, X-ray crystal structure of the $[Ag^I_8Ni^{II}_6\{SC(Me)_2CH(NH_2)CO_2\}_{12}Cl]^{5-}$ ion showing the positions of the Ag, Ni, and S atoms.

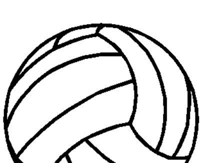

Figure 19. A volleyball, an object that possesses T_h symmetry.

3.5.2. Octahedral Systems (O_h, O)

We now describe four octahedral hosts related to the Platonic solids. Three are based upon the cube while one possesses features of both a cube and octahedron.

The first is a cyclophane-based system reported by Murakami et al. (Figure 20a).[45] The sides of the host consist of tetraaza[3.3.3.3]paracyclophane units and its octaprotonated cation has been shown to bind anionic guests.[45] The molecule possesses 48 asymmetric units of $\{(N/3)\text{-}(CH_2)\text{-}((C_6H_4)/2)\}/2$.

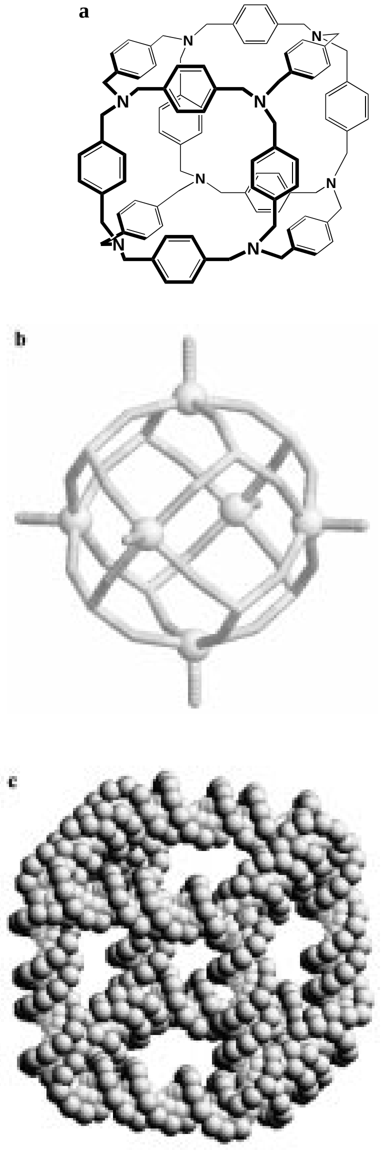

Figure 20. Octahedral hosts: a) a cyclophane-based cube (Murakami et al.), b) X-ray crystal structure of the $[(VO_6)(RPO_3)_8]^+$ (R = tBu, $OSiMe_3$) ion, c) DNA-based cube (Chen and Seeman; printed with permission by Professor Nadrian Seeman, for further details see http:\\seemanlab4.chem. nyu.edu).

The second is a polyoxovanadate, $[(VO_6)(RPO_3)_8]^+$ (R = tBu, $OSiMe_3$), reported by Zubieta et al.[46] and Thorn et al.,[17] which consists of VO_5 pyramids and phosphonate ligands (Figure 20b). The vanadium atoms of the shell are located at the vertices of an octahedron while the phosphorus atoms are located at the corners of a cube, thus displaying the dual relationship of these polyhedra. In both cases, the host has been shown to complex a chloride ion.[46, 17]

The third is a gold selenide cube $[NaAu_{12}Se_8]^{3-}$ reported by Huang and Kanatzidis.[47] The anion is made up of eight selenium atoms and 12 gold atoms. A sodium cation occupies the center of the complex.[47]

The fourth is a cube synthesized by Chen and Seeman, the components of which are based upon deoxyribonucleic acid (DNA) (Figure 20c).[48a] The directionality and ability of the double helix to form branched junctions[48b] are exploited for the edges and vertices, respectively. Interestingly, each face of this molecule forms a cyclic strand that is catenated with strands of adjacent faces. Molecular modeling experiments indicate the length of each edge to be approximately 68 Å.[48a]

3.5.3. *Icosahedral Systems (I_h, I)*

Spherical viruses are icosahedral molecular hosts related to the Platonic solids (Figure 21a).[3] These hosts consist of identical copies of proteins that assemble by way of non-covalent forces and range from 15 to 90 nm in diameter, and encapsulate strands of ribonucleic acid (RNA). Although spherical viruses require a minimum of 60 subunits, most are made up of 60*n* (*n* = 2, 3, 4..) subunits because of a reduction in the symmetry of their polygons (Figure 21b). This process, known as triangulation, gives rise to quasi-equivalent positions along the surface of the shell that enable the virus particle to cover the RNA with the largest number of subunits. Since only certain triangulations are permitted by symmetry, it is possible to classify virus structures into a coherent system.[12]

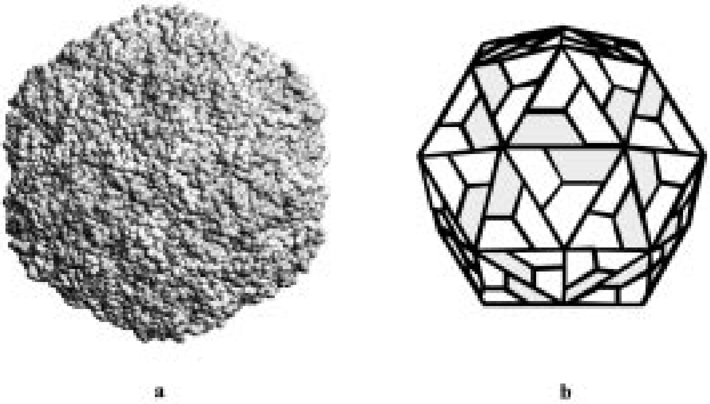

Figure 21. An icosahedral host, a) X-ray crystal struture of the rhinovirus, a spherical virus linked to the common cold, b) a schematic representation of the rhinovirus displaying triangulation (color scheme: red, green, blue spheres = amino acids).

Kretschmer et al. have recently described the ability of 12 $CpSmCl_2$ units (Cp = cyclopentadienyl) to form the neutral samarium-based shell $[Cp_{12}Sm_{12}(\mu_3\text{-}Cl)_{24}]$, in which 12 samarium atoms are located at the vertices of a icosahedron and 20 chloride ions are at the vertices of a dodecahedron.[49] The remaining chloride ions form a tetrahedron at the center of the shell.

3.6. Archimedean Solids

The Archimedean solids constitute a family of 13 convex uniform polyhedra made up of two or more regular polygons and, like the Platonic solids, possess either *32*, *432*, or *532* symmetry. As a result, the three coordinate directions within each solid are equivalent, which makes these polyhedra, in addition to the Platonic solids, models for spheroid design.

3.6.1. *Truncated Tetrahedron (1)*

Fujita et al.,[50] Stang et al.,[51] and Hartshorn and Steel[52] have recently described the synthesis of M_6L_4 cages that are topologically analogous to a truncated tetrahedron (Figure 22). These systems, which may be regarded as inverted M_4L_6 frameworks, consist of metal ions and aromatic-based bridging ligands that constitute the twofold and threefold rotation axes, respectively. Notably, owing to the presence a chiral stopper unit, the system reported by Stang et al. possesses *T* symmetry and is therefore chiral.[51] In terms of host–guest behavior, X-ray crystallographic studies have revealed the assembly reported by Fujita et al. to form a complex with four adamantyl carboxylate ions while that of Hartshorn and Steel to encapsulate a molecule of dimethylsulfoxide.[50, 52] According to mass spectrometric data, the cage reported by Stang et al. associates with four triflate ions.[51]

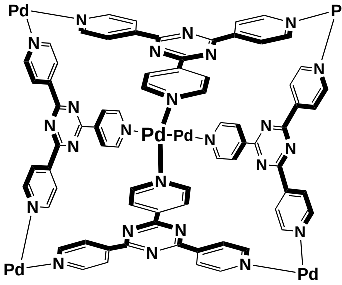

Figure 22. A metal-based cage (Fujita et al.): a host based upon the truncated tetrahedron.

Zubieta et al. have also demonstrated the formation of $[Mo_{16}(OH)_{12}O_{40}]^{8-}$, a cage topologically equivalent to a truncated tetrahedron.[53] This host is composed of four Mo^{VI} and twelve Mo^{V} centers and possesses a central $[Mo_{12}O_{40}]^{20-}$ core that encapsulates protons or a sodium ion.[53]

3.6.2. *Cuboctahedron (2)*

Gonzàlez-Duarte et al. have recently described the ability of eight cadium ions and 16 thiolate ligands to assemble from aqueous media to form the highly charged cage $[ClCd_8\{SCH(CH_2CH_2)_2N(H)Me\}_{16}]^{15+}$, the sulfur atoms of which sit at the vertices of a cuboctahedron.[54] The host contains a central chloride ion and an inner tetrahedral array of cadmium ions.[54] Interestingly, Ross et al. have considered through MM2 molecular model simulations the existence of a molecule containing eight benzene rings and either 12 oxygen or sulfur atoms, which they refer to as heterospherophane (Figure 23).[55] Although it is not mentioned in the original report, the shell exhibits a topology identical to a cuboctahedron.

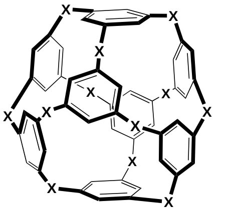

Figure 23. A theoretical organic shell based upon the cuboctahedron (X = O, S).

3.6.3. Truncated Octahedron (4)

Zhang and Seeman have constructed a DNA-based shell analogous to a truncated octahedron.[56] The edges of this molecule, each of which contains two turns of the double helix, contain 1440 nucleotides and the molecular weight of the structure, which is an overall [14]catenane, is 790 000 Daltons. Interestingly, the design strategy relies on a solid-support approach in which a net of squares is ligated to give the polyhedron. It is currently unclear what shape the molecule adopts in various media.[56]

Kretschmer et al. have described the formation of the lanthanide complex $[Cp_6Yb_6Cl_{13}]^-$, which conforms to a truncated octahedron.[49] The anion contains six ytterbium ions, located at the corners of an octahedron, and 12 bridging choride ions. A single chloride ion occupies the center of the shell.[49]

3.6.4. Rhombicuboctahedron (5)

Müller et al. have shown that 24 oxygen atoms of the polyoxometalate $[As_4Mo_6V_7O_{39}]^{2-}$ may be attributed to the structure of a rhombicuboctahedron.[57] Notably, a strong "tetrahedral distortion" of the ion is required for the host to correspond to the polyhedron. This shell has been shown to complex a sulfate ion in the solid state.[57]

3.6.5. Snub Cube (6)

We have recently demonstrated the ability of six calix[4]-resorcinarenes and eight water molecules to assemble in apolar media to form a spherical molecular assembly which conforms to a snub cube (Figure 24).[8] The shell consists of 24 asymmetric units, (each calix[4]arene lies on a fourfold axis and each H_2O molecule on a threefold axis), in which the vertices of the square faces of the polyhedron correspond to the corners of the calixarenes and the centroids of the eight triangles that adjoin three squares correspond to the water molecules. The assembly, which exhibits an external diameter of 24 Å, possesses an internal volume of about 1375 Å^3 and is held together by 60 O–H ⋯ O hydrogen bonds.

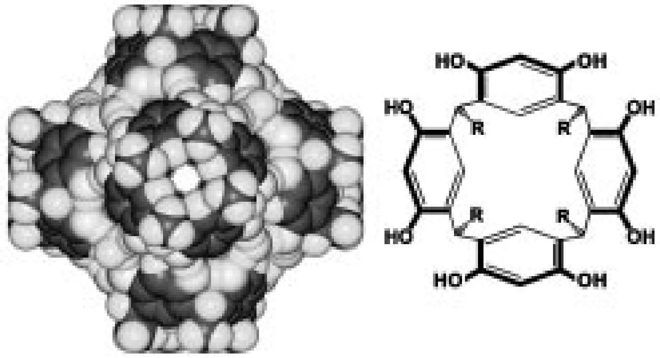

Figure 24. X-ray crystal structure of the calix[4]resorcinarene spheroid, a shell based upon the snub cube (inset: iconic representation of calix[4]resorcinarene, R = Me).

3.6.6. Truncated Icosahedron (10)

Buckminsterfullerene, an allotrope of carbon, is topologically equivalent to a truncated icosahedron, an Archimedean solid that possesses 12 pentagons and 20 hexagons (Figure 25).[4] Each carbon atom of this fullerene corresponds to a vertex of the polyhedron. As a result, C_{60} possesses 120 asymmetric units and is held together by 90 covalent bonds, the number of edges of the solid.[9]

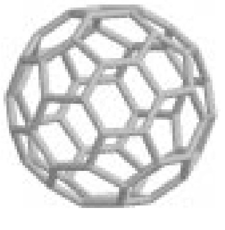

Figure 25. X-ray crystal structure of buckminsterfullerene, C_{60}, a shell based upon the truncated icosahedron.

3.7. Archimedean Duals

The polyhedra described thus far comprise two finite and two infinite families in which each solid consists of identical vertices, edges, and either a single or two or more regular polygons. It is of interest to note, however, that there exists a family of solids that are made up of irregular polygons and which may also be used as models for spheroid design. Known as Archimedean duals,[9] and sometimes referred to as the Catalan solids, these polyhedra are constructed by simply connecting the midpoints of the faces of an Archimedean solid together. Such a treatment gives rise to 13 polyhedra that possess two or more different vertices and identical irregular polygon faces (Figure 26). As a result, chemical subunits used to construct hosts that conform to these polyhedra cannot be based upon regular polygons.

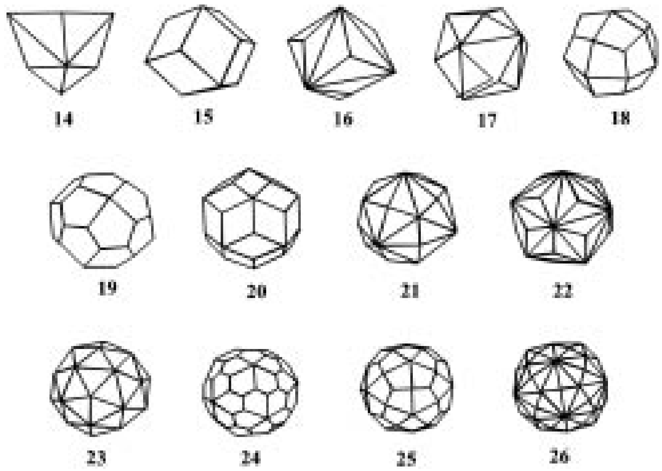

Figure 26. The 13 Archimedean duals derived from corresponding Archimedean solids (see Figure 6). Triakis tetrahedron (14), rhombic dodecahedron (15), triakis octahedron (16), tetrakis hexahedron (17), deltoidal icositetrahedron (18), pentagonal icositetrahedron (19), rhombic tricontahedron (20), disdyakis dodecahedron (21), triakis icosahedron (22), pentakis dodecahedron (23), deltoidal hexecontahedron (24), pentagonal hexecontahedron (25), disdyakis triacontahedron (26).

3.7.1. *Rhombic Dodecahedron (15)*

To the best of our knowledge, there is one host that conforms to the structure of an Archimedean dual. Harrison et al. have pointed out that the quaternary structure of ferritin, a major iron storage protein in animals, bacteria, and plants, corresponds to the structure of a rhombic dodecahedron.[58] This protein, which is approximately 125 in diameter, consists of 24 identical polypeptide subunits (Figure 27 a), and holds up to 4500 iron atoms in the form of hydrated ferric oxide with varying amounts of phosphate $[Fe_2O_3(H_2O/H_3PO_4)_n]$.[59] The subunits, which consist of four helix bundles, assemble by way of noncovalent forces and form dimers that correspond to the faces of the solid (Figure 27 b).

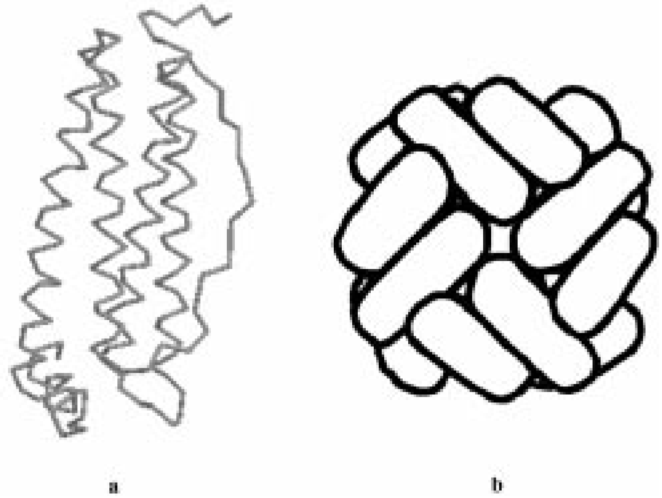

Figure 27. X-ray crystal structure of ferritin, a spherical host based upon the rhombic dodecahedron, a) carbon trace of the polypeptide subunit, b) the assembly displayed by the subunits. Blue ovals represent single subunits.

3.8. Irregular Polygons

It is also important to point out that if "partial" truncation is applied to the Platonic solids such that Archimedean solids are not realized, or if truncation is applied to the Archimedean solids, then the resulting polyhedra will not possess regular faces but, like the Archimedean duals, may be used as models for spheroid design as a consequence of their cubic symmetries. Indeed, it is striking to note that of the spherical molecular hosts designed to date, all have been constructed using chemical subunits that either correspond to regular polygons (for example, calix[4]arenes, VO_5 pyramids, tridentate bridging ligands) or form regular polygons (for example, carbon based hexagons and pentagons). Moreover, the realization that spherical shells may be constructed from polyhedra with irregular faces, as in the case of ferritin, implies that spherical shells based upon irregular polygons may be rationally designed.

3.9. Lower Symmetries

We have demonstrated that there exists three classes of convex uniform polyhedra, the Platonic solids, Archimedean solids, and prisms and antiprisms, along with two shells—the rugby ball and tennis ball shell—and the Archimedean duals, the frameworks of which may be used as models for the design of spherical and pseudo-spherical molecular hosts. Each host described here has been shown to conform to one of these figures, the lowest symmetry system belonging to the point group D_{2d}. It is, however, possible to construct shells that possess symmetry lower than D_{2d}. In some instances, such hosts can exhibit unique forms of stereoisomerism, which we will address.

3.9.1. *Shells with* D_n*,* S_{2n}*, or* C_{nh} *Symmetry*

Of the remaining eight point groups there are three that possess a principal C_n axis and either a C_2 axis or a mirror plane perpendicular to the C_n axis: D_n, S_{2n}, and C_{nh}.[60] If a shell belongs to one of these point groups, it can be demonstrated that the shell is based upon either a convex uniform polyhedron, the rugby ball or tennis ball shell, or an Archimedean dual. Such a host would not possess all the symmetry elements of one of these figures but would possess points along its surface that correspond to points along the surface of the solid or shell.

Three examples from the literature demonstrate these principles. The first involves the D_{4d} calix[4]arene dimer of Shimizu and Rebek (Figure 16 a).[34] As pointed out previously, this capsule possesses D_{4d} symmetry only if the hydrogen bonds that hold the shell together are ignored. Close inspection of this host with the hydrogen bonds intact, however, reveals that the shell possesses S_8 symmetry as a result of the unidirectionality of the urea hydrogen bond network.[34] Since the north and south poles of this assembly are identical, this host is based upon a square antiprism. The second involves Collet's cryptophanes.[61] It is well known that the synthesis of cryptophanes yields two geometrical isomers, *anti* and *syn*, which describe the relationship of the R substituents with respect to the bridges (Figure 28).[61] Although the *anti* and *syn* forms belong to different point

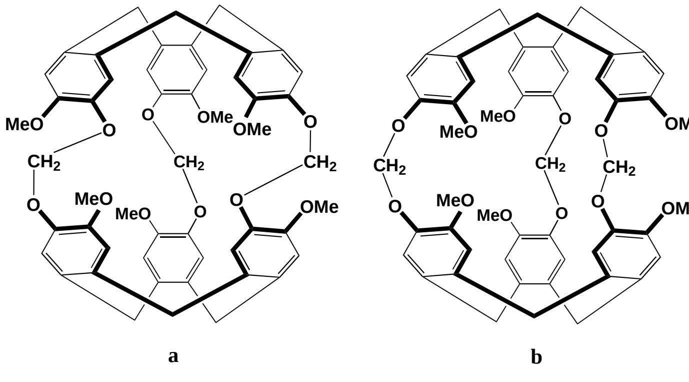

Figure 28. Collet's cryptophanes, shells based upon the trigonal prism, a) *anti* isomer (D_3 symmetry), b) *syn* isomer (C_{3h} symmetry).

groups, D_3 and C_{3h}, respectively, both isomers are based upon a trigonal prism. The third involves the calix[4]resorcinarene spheroid.[8] Symmetry considerations reveal that the highest symmetry representation of the assembly, with its hydrogen bonds intact, is D_2.[8] Nevertheless, the positions of the calixarenes and water molecules of this conformer correspond to points along the surface of a snub cube.

3.9.2. Shells with C_n*,* C_{nv}*,* C_s*,* C_i*, or* C_1 *Symmetry*

The five point groups that remain, C_n, C_{nv}, C_s, C_i, and C_1, cannot provide combinations of symmetry operations to produce a prism or antiprism.[60] As a result, shell-like hosts that belong to these point groups are neither spherical nor pseudo-spherical but can exhibit unique forms of stereoisomerism as a consequence of their non-uniform interiors and exteriors.

An example involves a carcerand designed by Reinhoudt et al. (Figure 29).[62] This molecule, which is constructed from two different calix[4]arenes, belongs to the point group C_{4v} and, as a result, forms carceplexes in which the guest can adopt two different orientations within its cavity and hence correspond to two different isomeric states.[62] Rebek et al. have also described the synthesis of a chiral molecular capsule with C_2 symmetry.[63] Specifically, the host was designed such that the ends of its subunits are different and, as Rebek et al. have shown,[63] form hitherto unknown diasteromeric host–guest complexes with chiral guests. A number of higher fullerenes also belong to such point groups (for example, C_{2v}-C_{78}).[4] As expected, in contrast to C_{60}, these cages possess increasing numbers of nonequivalent carbon atoms, as demonstrated by their ^{13}C NMR spectra.[4]

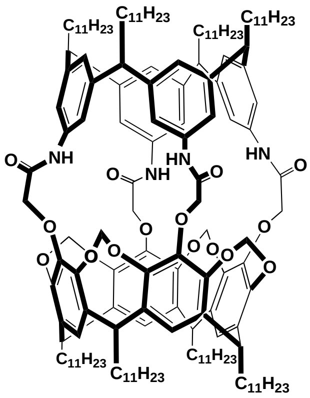

Figure 29. A C_{4v} carcerand (Reinhoudt et al.)

4. Synthesis

A symmetry based approach for constructing molecular architecture does not concern itself with the nature of the atoms that comprise the framework since it is the symmetry of the structure that ultimately dictates its design (see above). Selecting appropriate chemical subunits and devising synthetic schemes, however, remains a job of the chemist.

In such a context, further analysis of the data reveals that the syntheses of spherical and pseudo-spherical hosts may be divided into two categories: 1) spontaneous formation and 2) multistep design (Table 5). In the case of the former, hosts are constructed in a "single step" by simply adding the subunits together in an appropriate medium and allowing the assembly process to occur. Examples include polyoxometalates, molecular capsules, metal–organic cages, fullerenes, the calix[4]resorcinarene spheroid, ferritin, and spherical viruses. In each case, identical amounts of information are present in identical components and the final structure possesses properties not found in the individual subunits.[34] In the case of the second approach, a multistep procedure is employed in which many synthetic steps involve dissimilar components. Examples include cryptands, cryptophanes, carcerands, spherands, and DNA-based polyhedra. The subunits of these systems are typically held together by covalent bonds.

Table 5. Shell-like hosts—synthetic pathways and symmetries.

Spontaneous Formation—host (point group)	Multi-step design
buckminsterfullerene (I_h), spherical viruses (I)	DNA-based polyhedra (O)
ferritin (O), calix[4]resorcinarene spheroid (O)	spherands (T_d)
polyoxometallates (O_h, T_d, D)	cryptands, carcerands, cryptophanes (D_{nh})
metal-organic cages (T_d, T, D)	
molecular capsules (D)	

5. Self-Assembly

From the onset of our discussion we presented a notion that self-assembly is the building of molecular architecture with identical subunits. If this is the case, then each host described here has been designed by way of self-assembly as a consequence of symmetry requirements imposed by space. Cryptands and carcerands would be examples of self-assembly since identical subunits are used to design their frameworks. It seems to us, however, that the term self-assembly requires the resulting molecular framework to form in a single step.[11] Indeed, such a view would only encompass those shell-like hosts that form spontaneously rather than by way of multistep design. As a result, we believe that self-assembly, in relation to shell-like hosts, may be described as the single-step construction of molecular architecture from identical chemical subunits such that the final structure is ordered, and conforms to principles of geometry. Notably, such a description, in principle, also includes infinite frameworks, such as the assembly of atoms and molecules into crystals, and, as a result of structural organization, requires directional forces (for example, covalent, noncovalent, coordinate covalent bonds) to effect the assembly process.

6. Why the Platonic and Archimedean Solids?

With current interests in chemical synthesis moving towards the fabrication of nanometre scale molecular frameworks[64–67] and the miniaturization of functional microstructures,[68] it becomes apparent why the Platonic and Archimedean solids are appropriate models for shell design.

First, for a given chemical subunit, these solids inherently give rise to larger structures.[69] This may be illustrated by comparing four molecules that adopt the structures of three Platonic solids and an Archimedean solid: tetrahedrane,[70] cubane,[71] dodecahedrane,[72] and C_{60}.[4] In each molecule a carbon atom is located at the vertex of a polyhedron. Upon traversing the series, however, one observes a gradual increase in the size of these molecules. In fact, the increase is such that C_{60} is capable of entrapping a guest.[4]

Second, we note that these solids incorporate economy of design. This may be illustrated upon considering a sphere (guest) inscribed within either a tetrahedron (T_d), cube (O_h), or icosahedron (I_h) (host). One realizes upon comparing these hosts that the icosahedron facilitates encapsulation of the guest with the largest number of subunits (Table 4). Moreover, from a chemical perspective, the icosahedron allows the host to complex the guest with the smallest chemical subunits. Indeed, this feature could eliminate errors in subunit design and shell formation and, in principle, reduce certain "costs" of a given framework.

Thus, the Platonic and Archimedean solids not only provide a means for host design, but a way in which to maximize chemical information, and allows the chemist to, in effect, engineer host–guest systems.

7. Summary and Outlook

We have presented general principles for the design of spherical molecular hosts. The principles rely on the use of convex polyhedra as models for spheroid design. To demonstrate the utility of this approach, we have structurally classified a variety of organic, inorganic, and biological hosts as frameworks that can be rationally compared on the basis of symmetry, which reveals an interplay between symmetry, structure, and function.[73] Indeed, we anticipate these models to be amenable to the construction of hosts that conform to those solids not yet realized and to additional members of each family, where self-assembly will play a major role in their design, and usher in an era of spherical host–guest chemistry.[8, 74]

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