Design, Formation and Properties of Tetrahedral M₄L₄ and M₄L₆
Supramolecular Clusters

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Received February 20, 2001

Abstract: The rigid tris- and bis(catecholamide) ligands H₄A, H₄B and H₄C form tetrahedral clusters of the type M₄L₄ and M₄L₆ through self-assembly reactions with tri- and tetravalent metal ions such as Ga₃, Fe₃, TiIV and SnIV. General design principles for the synthesis of such clusters are presented with an emphasis on geometric requirements and kinetic and thermodynamic considerations. The solution and solid-state characterization of these complexes is presented, and their dynamic solution behavior is described. The tris-catecholamide H₄A forms M₄L₄ tetrahedra with Ga₃, TiIV, and SnIV; (Et₃N)₄[Ti₃A₄] crystallizes in R₃c (No. 167), with a = 22.6143(5) Å, c = 106.038(2) Å. The cluster is a racemic mixture of homoconfigurational tetrahedra (all Λ or all Δ at the metal centers within a given cluster). Though the synthetic procedure for synthesis of the cluster is markedly metal-dependent, extensive electrospray mass spectrometry investigations show that the M₄A₄ (M = Ga₃, TiIV, and SnIV) clusters are remarkably stable once formed. Two approaches are presented for the formation of M₄L₆ tetrahedral clusters. Of the bis(catecholamide) ligands, H₄A forms an M₄L₆ tetrahedron (M = Ga₃) based on an “edge-on” design, while H₄C forms an M₄L₆ tetrahedron (M = Ga₃, Fe₃) based on a “face-on” strategy. K₄[Et₄N]₄[Fe₃C₆] crystallizes in I₄3d (No. 220) with a = 43.706(8) Å. This M₄L₆ tetrahedral cluster is also a racemic mixture of homocentric tetrahedra and has a cavity large enough to encapsulate a molecule of Et₄N+. This host–guest interaction is maintained in solution as revealed by NMR investigations of the Ga₃ complex.

Introduction

Nature provides stunning examples of noncovalently linked molecular clusters of high symmetry. Studied by electron microscopy and X-ray diffraction, the high symmetry of viruses has been recognized since the late 1950s. The protein coat of the human rhinovirus, among others, is composed of 60 copies of each of four protein subunits arranged in icosahedral symmetry. Viral protein coats are not the only high-symmetry molecular clusters of high symmetry. Studied by electron microscopy and X-ray diffraction, the high symmetry of viruses to illustrate mathematically the underlying geometric implications for a subunit capable of forming such closed-shell suprastructures. Thus, current trends toward the utilization of self-assembling identical subunits are not surprising. While the individual interactions holding protein subunits together (e.g., H-bonds, van der Waals interactions, and π–π interactions) have been recognized, it is less understood what algorithms direct the synergy of these interactions to form exclusively the observed clusters. An understanding of the natural algorithms utilized to induce a single stoichiometry and symmetry rather than a variety of oligomers and polymers should lead to the deduction of general design principles for synthetic self-assembled structures. Attempts have been made to illustrate mathematically the underlying geometric implications for a subunit capable of forming such closed-shell suprastructures. Viruses have been suggested as models for new supramolecular architectures without, however, providing explicit building instructions. We have suggested the utilization of a symmetry-based model for the synthesis of supramolecular structures have been cited in reference to the viral protein coats. As little as one gene is required to encode the protein that in turn contains all of the information necessary for multiple copies of the protein to self-assemble into the complete shell. This remarkable economy makes the synthesis of artificial shells by the self-assembly of a large number of small and simple subunits an attractive goal, particularly in view of the rather involved syntheses often required for the generation of even small molecular containers. Thus, current trends toward the utilization of self-assembling identical subunits are not surprising.

Received February 20, 2001
clusters by using metal–ligand interactions to generate the required symmetries. This building principle, “the coordination number incommensurate cluster formation model,” provides guidelines for the rational design of symmetric clusters, the larger of which have well-defined cavities. The great utility of such cavities has been shown by the chemistry made possible in the “inner phase” of calixarenes, carceplexes, and other host molecules. This is paralleled by the formation of polyoxometalates in the hollow interior of a virus purged of its RNA genetic material. Future growth of the field of nanotechnology depends on reliable and predictable container compounds.

The utilization of H-bonds for the construction of molecular clusters has resulted in spectacular supramolecular structures, but the use of the stronger, highly directional and well-studied metal–ligand interaction has also afforded discrete clusters of a variety of sizes, stoichiometries, and symmetries. Although early work has focused on the synthesis of helicates, the wide structural flexibility of coordination chemistry has made possible the realization of boxes, grids, rings, tetrahedra, cubes, rotaxanes, and catenanes.

While there are numerous accounts of the synthesis of M₄L₄-type (x = 4,6) tetrahedra, their syntheses have, at least initially, relied on fortuitous circumstance. Few early reports detailed underlying design principles, despite the fact that supramolecular chemistry has been described as a kind of molecular information science, which implies that the instructions “programmed” into each component of an assembly directly the formation of a distinct cluster topology. If this is indeed the case, then the compilation of the information required to instruct components to self-assemble into a predictable cluster should be the starting point of all synthetic efforts. In practicality, this means that the design of components in which the information for the formation of a cluster is inherent should begin the synthesis of a supramolecular cluster. Second, the required reaction conditions necessary for the successful assembly of the cluster should be evaluated. In a sense this sequence is standard procedure in organic synthesis when planning a target-oriented synthesis by means of retrosynthetic analysis.

It is the goal of this series of papers to develop a symmetry-based set of principles for the rational design and synthesis of supramolecular clusters. In this paper, examples for the synthesis and analysis of M₄L₄-type (x = 4,6) tetrahedra built using three different design approaches will be provided. In particular, the design, synthesis, and solution- and solid-state characterization of tetrahedral clusters based on ligands H₄A, H₄B, and H₄C (Figure 1) will be discussed. The design principles delineated here are conceived to be general and transferable to the design of metal–ligand clusters of varying symmetries, sizes, and compositions.

General Principles for the Formation of Metal–Ligand-Based Clusters. When planning the synthesis of clusters based on metal–ligand interactions, the general choice of ligand type, ligand backbone rigidity, metal type, and reaction conditions have to be considered. The particular geometric requirements for each cluster’s symmetry and stoichiometry have to be strictly fulfilled, since it is the metal-coordination geometry and the orientation of the interaction sites in any given ligand that provide the inherent information, or blueprint, for the self-assembly of a designed cluster. We will discuss each point of consideration separately, starting from more general requirements and followed by the design principles for the synthesis of particular cluster symmetries. Finally, the synthesis, structural characterization, and solution chemistry of tetrahedral M₄L₄ (x = 4,6) clusters will be detailed.

Choice of a Metal–Ligand Combination. The driving force for the formation of the cluster is derived from metal–ligand interactions. Thus, the choice of relatively strong metal-binding moieties, for example, chelating moieties, is preferred. Although a large number of clusters based on the interaction of monodentate amine- or pyridine-type donors with PtIV and PdII are known. The self-assembly product should be the thermodynamically favored cluster (for further thermodynamic considerations, see below); however, kinetic products such as nonstoichiometric oligomers and polymers will be formed at

Figure 1. Ligands H₄A, H₄B, and H₄C form tetrahedral clusters with tri- and tetravalent metal ions.
the onset of the reaction. Consequently, the metal–ligand bonds must be labile enough to allow the initially formed kinetic products to rearrange into the thermodynamic product. This requirement precludes, on one hand, the use of kinetically inert metals such as CrIII and Co III as building blocks, and, on the other hand, the use of kinetically disfavored metal chelators such as rigid tetradentate ligands such as the pyrrolic nitrogens in porphyrins. This requirement also suggests that the reaction conditions need to be chosen so as to facilitate the rearrangement of kinetic products to the thermodynamic product, that is, by lowering the pH of the solution or using higher reaction temperatures.

Choice of a Suitable Ligand—Backbone Combination. The geometry of a particular ligand and its known interaction with a metal ion (see below) should contain all of the information required for the successful self-assembly of the desired cluster. This mandates a predetermined conformation of the ligand. Thus, the orientation of multiple binding units within a ligand must be either rigidly fixed or at least somewhat conformationally restricted.

With respect to the above considerations, the catecholamide binding unit (Figure 2) is a good choice for use in cluster formations because of the high thermodynamic stability, yet kinetic lability, when coordinated to trivalent metal ions, such as CrIII, GaIII, and AlIII, in an octahedral coordination environment.20–23 The catecholamide functionality is a rigid binding unit as a result of a strong hydrogen bond between the amide hydrogen and the coordinating o-hydroxy oxygen (Figure 2a). This hydrogen bond imposes a coplanar arrangement of the amide with the catecholate unit, reducing the degrees of freedom in the ligand and making the conformation of the coordinated ligand calculable.

Due to the electronically preferred coplanarity of the amide functionality with aromatic systems, any combination of the catecholamide moiety with an aromatic backbone (e.g., a benzene or naphthalene backbone) produces a rigid oligobidentate ligand system that predisposes the coordinating groups in a highly predictable way. The crystal structure of the methyl-protected ligand MesoA illustrates these features. The methyl-protected catecholamides show the same H-bond pattern as the metalated catechol amides (Figure 2b). In contrast, the conformation of the catechol moiety of the unmetalated ligand is generally 180° rotated, the hydroxy functionality in the 2-position being shared between both hydroxy groups (Figure 2c). The compound MesoA crystallizes in the space group P21/a with approximate three-fold symmetry (Figure 3a). The H-bonds between the amide nitrogen and the catechol oxygen are clearly expressed. Also, as anticipated, the three catecholamide functionalities are, albeit to different degrees, predominantly coplanar to the central ring (Figure 3b).

Thermodynamic Implications of Ligand Rigidity. An example best illustrates the effect of ligand rigidity on the thermodynamics controlling complex formation. Consider the formation of an M2L3 helicate formed by a ligand (L) with two (bidentate) binding sites and a metal (M) with three acceptor sites (i.e., for three bidentate ligands forming a pseudooctahedral coordination sphere). The only M:L ratio that can satisfy the binding requirements of both the ligand and metal components of the cluster is 2M:3L. Now consider an equilibrium between two triple helicates of the stoichiometry M2L3 and its dimer, a tetrahedron of the stoichiometry M4L6:

\[
2\text{M}_2\text{L}_3 = \text{M}_4\text{L}_6
\]

\[
K_{eq} = \frac{[\text{M}_4\text{L}_6]}{[\text{M}_2\text{L}_3]^2} \approx 1
\]

Assuming a ligand system that has no unfavorable steric constraints and in which the M–L interactions are the sole driving forces for cluster formation, both geometries are equally possible, and the equilibrium constant should be approximately unity. If the initial concentration of the M2L3 triple helicate is 2 mM, then the concentration of the M4L6 tetrahedron will only be 4 μM! This example illustrates the widely recognized principle in supramolecular self-assembly: that entropy will favor the largest number of particles with the smallest possible stoichiometry. How, then, does one enforce the formation of assemblies with stoichiometries which are multiples of the empirical ratio of ligands to metals? Specifically, how does one expand selectively an M1L1 complex to an M4L4 cluster or, likewise, an M2L3 helicate to an M4L6 tetrahedron? The answer lies in the geometric constraints that must be incorporated into

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Figure 2. When coordinated to a metal (a), the catecholamide binding unit has a rigidly fixed geometry as a result of the hydrogen bond between the amide proton and the ortho-oxygen. This hydrogen bonding motif is preserved in the methyl-protected ligand (b), but reversed in the unmetalated, free ligand (c).

Figure 3. ORTEP diagram of Me6A illustrating (a) the molecular three-fold symmetry of the ligand and (b) its planar configuration.
the ligand design, prohibiting the formation of lower-order structures. This feat can be accomplished by making the ligand too rigid for more than one chelation site to simultaneously bind the same metal.

The ligand \( H_6 A \) when compared to the structurally similar enterobactin compound model \( H_6 X \) exemplifies this effect of rigidity (Figure 4). \( H_6 X \) differs from \( H_6 A \) only by the presence of the methylene groups between the phenyl backbone and the three ligand arms. This introduction of flexibility into the ligand allows all three catecholate moieties to chelate to one metal simultaneously. Even though the flexible ligand could easily adopt conformations to accommodate higher-order complexes of the stoichiometry \( M_4 X_n \), because the smallest combination is favored, only the \( M_1 X \) monomer can be detected. Removal of the methylene groups results in ligand \( H_6 A \). This ligand is unable to coordinate a single metal ion with more than one catechol group; as a result, attaining a coordinatively saturated \( M_1 L_1 \) stoichiometry is impossible. The alternative higher-order \( M_4 L_4 \) structure that this ligand is forced to form will be described below.

**Definition of Terms.** To describe our approach to the rational design of supramolecular clusters, it is useful to define terms that more accurately describe the relevant geometric relationships between the metal coordination spheres and the ligands. The vector that represents the interaction between a ligand and metal is the Coordinate Vector (Figure 5a). In the case of a monodentate ligand, this vector is simply the one directed from the coordinating atom (or electron pair) of the ligand toward the metal ion. In the case of a bidentate ligand, this vector bisects the coordinating atom (or electron pair) of the ligand toward the metal ion. In the case of a tridentate ligand, the coordinate vector of each catecholate unit must lie in the chelate plane (red face) at the metal vertex. The angle between the coordinate vectors of the three-fold symmetric ligands (represented by the large yellow faces) and the vertices are made up of (pseudo)octahedrally coordinated metal atoms (represented by the small red triangular faces) is depicted in Figure 7. The small red faces actually correspond to a trigonal prismatic geometry, having an approach angle near 23° (40° twist angle).

**Design of the Tetrahedral Clusters. Design Strategy for a Tetrahedral \( M_4 L_4 \) Cluster.** A tetrahedral cluster of the stoichiometry \( M_4 L_4 \) can be described as four metal ions in a tetrahedral array connected by four three-fold symmetric ligands: Each ligand acts as one face of a tetrahedron, while each metal ion acts as a vertex of the tetrahedron. Since a tetrahedron has three-fold symmetry through each vertex, the metal–ligand junction must also be able to achieve three-fold symmetry. One way this can be accomplished is by using a metal ion that prefers an (pseudo)octahedral geometry. Since each of the metal ions has six acceptor sites and the metal-to-ligand ratio is 1:1, then each ligand must have six donor sites. With these stoichiometric and geometric considerations in mind, the problem of designing a tetrahedral supramolecular assembly of the stoichiometry \( M_4 L_4 \) can be reduced to designing a rigid three-fold symmetric ligand that positions its three coordinate vectors correctly. This analysis can best be accomplished by determining the ideal approach angle for a cluster of this type.

A schematic representation of a tetrahedral \( M_4 L_4 \) cluster in which the faces of the tetrahedron are made up of strictly planar three-fold symmetric ligands (represented by the large yellow faces) and the vertices are made up of (pseudo)octahedrally coordinated metal atoms (represented by the small red triangular faces) is depicted in Figure 7. The small red faces actually represent the previously described chelate planes, which are perpendicular to the three-fold axis at each metal vertex. In this design, the coordinate vector of each catecholate unit must lie simultaneously in both the ligand plane (yellow face) and the chelate plane (red face) at the metal vertex. The angle between a three-fold axis and the associated faces in a tetrahedron is 19.4°. If the bound ligands are planar and coordinate as shown, this angle corresponds to the approach angle. The experimentally obtained approach angles for mononuclear tris(catecholates) are ~23°. This, in turn, implies that the planar ligand to be used in the formation of a tetrahedral cluster is required to distort only a few degrees from planarity to comply with the ideal approach angle at the metal centers.

**Design Strategies for the Synthesis of \( M_4 L_4 \) Tetrahedral Clusters.** Similar to the aforementioned \( M_4 L_4 \) tetrahedral cluster,
a tetrahedral cluster of stoichiometry $M_4L_6$ has four metal ions at the four vertices of a tetrahedron. In contrast, however, these four metal ions are linked by six two-fold symmetric ligands, each ligand acting as one of the six edges of the tetrahedron. Again, the interaction between a metal ion and the three ligands converging at each corner of the tetrahedron generates a three-fold axis through the formation of an (pseudo)octahedral coordination sphere around the metal. The smallest assembly that could result from the simultaneous satisfaction of the two- and three-fold symmetry requirements is an $M_2L_3$ complex. To avoid the entropically favored smaller cluster, geometric constraints must be incorporated into the rigid ligand design. We have described two different approaches to the rational design of such clusters.$^{27,28}$ Both approaches employ an ideally planar $C_2$-symmetric bis(bidentate) ligand with a rigid backbone, but the orientation of the $C_2$ axis of the cluster with respect to the mean plane of the ligand differs.

In the first design strategy, which we call the “Edge On” approach, the two-fold axis of the tetrahedron is coplanar with the plane defined by the ligand (Figure 8).$^{27}$ Since the coordinate vectors must lie within the chelate planes at each of the four metal vertices, the angle between the coordinate vectors within a given ligand must be 70.6°. (This angle is the supplement of the dihedral angle between a metal ion and the three ligands acting as one of the six edges of the tetrahedron.) A 60° angle is formed between the chelate vectors for ligand $H_4B$; thus, the targeted tetrahedral structure can be achieved with only slight out-of-plane twisting by each of the chelating groups. The 60° angle between the coordinate vectors of ligand $H_4B$ is the geometric implement enforcing the formation of the $M_4L_6$ assembly, since an $M_2L_3$ helicate would require that the coordinate vectors be parallel.$^{29,30}$

An alternative design strategy for an $M_4L_6$ tetrahedron can be envisioned in which the two-fold axis of the tetrahedron is perpendicular to the plane of the ligand. This type of design strategy we will call the “Face On” approach (Figure 9).$^{31}$ If the ligand conformation is strictly planar, then the approach angle is 35.3°, identical to that of a perfect octahedral metal complex (equivalent to a twist angle of 60°). Mononuclear tris-(catecholamide) complexes of Ga$^{III}$ and Fe$^{III}$ are known to be slightly distorted toward a trigonal prismatic coordination geometry (ca. 40° twist angle or 23° approach angle). Thus, slight out-of-plane twists of the ligands would be required to ideally accommodate these metals. Slight rotation of the catechol amide moiety along the backbone—amide axis can be envisioned to accomplish the required deviation.

The selectivity in the ligand $H_4C$ for the formation of an $M_4L_6$ cluster versus a $M_2L_3$ helix is achieved using a naphthalene spacer, which causes the two catechol binding units to be offset from one another when the ligand is in the conformation 109.4°, the angle between the three-fold axes in a tetrahedron.)

Figure 6. When designing high-symmetry clusters it is often useful to consider the Approach Angle of a chelating ligand around a metal center, rather than the twist angle. The approach angle can more easily be compared to the angles generated by a given cluster.

Figure 7. In this $M_4L_6$ design, the ligand $H_4A$ will act as the face of the tetrahedron. The angle at which the extended three-fold plane crosses an adjacent three-fold axis is analogous to the approach angle of the ligand arm with the metal located at the tetrahedron vertex.

Figure 8. In this “Edge-On” $M_4L_6$ design, the ligand $H_4B$ will act as one of the edges of the tetrahedron with the two-fold axis of the cluster being coplanar with the ligand. In this design, the angle between the coordinate vectors of the two-fold ligand is the primary consideration.

Figure 9. In this “Face On” $M_4L_6$ design, the ligand $H_4C$ will act as one of the faces of the tetrahedron.
required for helicate formation, thus disfavoring the formation of a helicate (Figure 10).

Molecular Modeling. Prior to the actual ligand synthesis, the feasibility of the proposed metal–ligand systems is explored using molecular mechanics calculations. Although these calculations do not guarantee that the proposed structure will form, they help eliminate structures that are nonviable due to unfavorable inter- and intraligand steric interactions. When comparing results of the molecular modeling calculations with actual crystal structures, it becomes evident that while the gross structure can be predicted fairly accurately, effects of hosts inside the clusters (or the absence of guests) cannot be predicted. Nor can it be predicted that certain clusters require a guest to be formed. Nevertheless, we find molecular modeling to be an indispensable tool in the design of the clusters presented here.

Results and Discussion

Ligand Syntheses. All ligands used in this study belong to the same class of bis- and tris(catecholamides). They all were synthesized following established routes (Scheme 1). Polyamines 1, 2, or 3, either commercially available or synthesized by reduction of the corresponding commercially available nitro compounds, were reacted with the acid chloride of 2,3-dimethoxybenzoic acid (4) under standard amide bond-forming conditions (excess Et₃N in CH₂Cl₂). The resulting O-methyl-substituted ligands Me₆A, Me₄B, and Me₄C were deprotected by reaction with BBr₃ to produce, in generally excellent overall yields, the polycatecholamide ligands H₆A, H₄B, and H₄C, respectively.

Synthesis of M₄A₄ Clusters. Ligand H₆A reacts with stoichiometric amounts of Ga(acac)₃ under basic conditions (3 equiv of KOH) in MeOH to give a precipitate whose ¹H NMR (300 MHz, D₂O) indicates the formation of one defined and highly symmetric species. The mass spectrum (ESI, cation detection) of the GaIII complex, as its K⁺ salt, shows the expected molecular ion. The X-ray crystal structure of the GaIII complex, as its K⁺ salt, shows the expected structure.

Figure 9. In this “Face-On” M₃L₆ design, the two-fold axis of the cluster is perpendicular to the ligand plane. In this design, the approach angle is the primary consideration.

Figure 10. Ligand H₄C is deterred from forming an M₂L₃ cluster because of the offset of the chelating units created by the use of the naphthalene scaffold. Rotation around the arene–N bond puts the ligand in the conformation required to form an M₄L₆ tetrahedral cluster.

Scheme 1. Synthesis of Ligands H₆A, H₄B, and H₄C Used in This Study

(33) For instances in which the cluster formed only in the presence of a guest see: Xu, J. D.; Parac, T. N.; Raymond, K. N. Angew. Chem., Int. Ed. 1999, 38, 2878–2882.
two major peaks at m/z 1463.4 and 988.6. Under these low-resolution conditions, the first peak can be assigned to the species \([\text{Ga}_4\text{A}_4]^{12-14K^+}\) or \([\text{Ga}_4\text{A}_4]^{6-7K^+}\) and is, therefore, not unambiguously indicative of the formation of a tetrahedron. The peak at m/z 988, however, attributed to the trication \([\text{Ga}_4\text{A}_4]^{12-15K^+}\) provides an indication for the formation of the desired cluster since it cannot be rationalized by a metal:ligand stoichiometry lower than 4:4; thus, this evidence strongly suggests the formation of the tetrahedron.

Despite these encouraging results, we were unsuccessful at growing crystals suitable for analysis by X-ray diffraction. Presumably the –12 charge of these tetrahedra and their good solubility in MeOH, H_2O, DMSO, and DMF forestalled the formation of high-quality single crystals.

The overall charge of the cluster can be reduced by using higher-oxidation state metals; for instance, M^IV metal ions will reduce the charge from –12 to –8. Pseudooctahedral tris-(catecholate) complexes of V^IV, Sn^IV, and Ti^IV, for example, are known. While the formation of the V^IV tris(catecholate) species is most sensitive to the particular conditions chosen, the opposite can be said for the formation of the Sn^IV and Ti^IV species. For these reasons we chose to investigate the use of Sn^IV and Ti^IV in the construction of these self-assembled clusters.

A DMF solution of 1 equiv of H_6A combined with 1 equiv of SnCl_4 and an excess of Et_3N, heated under reflux for 12 h, produces a clear and colorless solution which, when evaporated to dryness under vacuum, results in the formation of a pale pink microcrystalline solid of the composition \([\text{Sn}_4\text{A}_4](\text{Et}_3\text{NH})_8\cdot x\text{Et}_2\text{NHCl}\) \((x = 3–4)\). Attempts to remove the excess triethylammonium chloride by recrystallization of the salt mixture from a variety of solvents failed to produce a triethylammonium-free product. The \(^1H\) NMR (300 MHz, DMSO-\(d_6\)) spectrum indicated the formation of only one defined species in which the ligand is located in a three-fold symmetric environment (Figure 11b). The proton signals for the hydroxy groups of the ligand (Figure 11a) disappeared, and all other signals shifted in a way consistent with complex formation. In particular, the NH proton shifted downfield as expected due to the H-bond produced upon complexation. Addition of an aliquot of excess ligand did not cause any shift or line-broadening of the peaks of the metal complex (Figure 11c), even at temperatures up to 100 °C.

Likewise, the addition of 1 equiv of excess SnCl_4 to the cluster dissolved in DMF does not affect the spectrum (Figure 11d). These experiments demonstrate that the single set of resonances observed in the \(^1H\) NMR spectrum are not a result of a rapidly exchanging polymeric system, but rather they are attributable to a discrete metal–ligand species. It seems reasonable to predict that pronounced cooperativity effects prevent fast ligand-exchange processes in these types of tethered clusters. The electrospray mass spectrum of the \([\text{Sn}_4\text{A}_4]^{3-}\) complex further provided data to prove the formation of the desired M_4L_4 tetrahedron (see below).

The analogous Ti^IV complex \([\text{Ti}_4\text{A}_4](\text{Et}_3\text{NH})_8\) was prepared by a modified procedure. A solution of Ti(On-Bu)_4 in MeOH was combined with H_6A in MeOH/excess Et_3N. The solution quickly turned orange and, after 12 h, a gelatinous orange precipitate formed. The \(^1H\) NMR spectrum of a DMSO-\(d_6\) extract of this precipitate taken at 25 °C shows the presence of a mixture of (polymeric) compounds. Heating of the sample to 120 °C results, over the course of several hours, in a partial simplification of the spectrum. This experiment provided the guide for the next step: dissolution of the centrifuged and washed precipitate in DMF under reflux for 12 h. This step facilitated the rearrangement of the kinetic product mixture into one thermodynamic product. \(^1H\) NMR spectra of samples taken from this solution showed the presence of one major product characterized by a single set of sharp resonances. Gas-phase diffusion of MeOH into this DMF solution produced orange crystals of \([\text{Ti}_4\text{A}_4](\text{Et}_3\text{NH})_8\). The \(^1H\) NMR spectrum of the crystals dissolved in DMSO-\(d_6\) was very similar in appearance to those observed for the Ga^III and Sn^IV species, giving an indication of successful cluster formation. This finding was also supported by the electrospray mass spectrum of the complex (see below).

While this procedure produced crystals of analytical and single-crystal X-ray diffraction quality (see below), it also highlights the disadvantage of using the much less kinetically labile ion Ti^IV, as compared to Ga^III or Fe^III. The kinetic product is not the desired cluster and is removed from the metal–ligand equilibrium by precipitation. A rearrangement step at elevated temperature and in a polar donor solvent is required to produce the designed thermodynamic product. The use of bases other than Et_3N (i.e., NaOH, KOH, CsOH, morpholine, pyridine) did not produce the clusters cleanly, while the use of MeOH produced the cluster with greatly reduced solubility in MeOH and DMSO. These observations provide some rationalization of the fact that in the solid (crystal structure) and gas phase (mass spectrum) this octaanionic cluster (and the clusters to be described below) shows a very strong association with its triethylammonium counterions. Evidently, these interactions provide additional driving force for the formation of the desired clusters in a crystalline state. The reaction of a variety of Ti^IV sources (TiCl_4 or freshly precipitated TiO_2) in hot or cold DMF did not produce the expected cluster in a clean fashion. Likewise, the clean formation of the Sn^IV-based cluster was not possible with the methodology detailed for the Ti^IV-based tetrahedron. We assume that the differences of the metals and metal sources with respect to Lewis acidity, rate of hydrolysis, etc. require individualized reaction conditions. It should be noted, however, that once formed the respective clusters could be detected by NMR and mass spectrometry under a wide range of reaction conditions, attesting to the high thermodynamic stability of the products; only their isolation and preparation by simple means required the individualized procedures.

**Crystal Structure of \([\text{Ti}_4\text{A}_4](\text{Et}_3\text{N})_8\).** Slow gas-phase diffusion of MeOH at room temperature into a DMF solution of...
the reason for the larger than expected (19.4°) approach angle of 28°. It should be noted that this is not the first tetrahedral cluster with stoichiometry \( \text{M}_4 \text{L}_4 \); a related cluster has appeared in the literature.\(^{39}\) Although the formation of this cluster was reported as serendipitous, its structure and formation highlight the building principles exemplified here. In particular, the fact that the ligand used in these studies was flexible and, depending on the size of the metal used, formed \( \text{M}_4 \text{L}_4 \) or \( \text{M}_6 \text{L}_3 \) complexes demonstrates the importance of incorporating rigidity into the ligand design. And as detailed above, our design does not allow the formation of an ML species. [A tetrahedral \( \text{Ti}_4 \text{L}_4 \) cluster in which a tetrahedral M–M bond containing tetrahedral arrangement of four Ti\(^{IV} \) ions is capped by four ligands is only related by stoichiometry and not connectivity.\(^{38}\)]

**Synthesis of \( \text{M}_4 \text{L}_6 \) Clusters.** The synthesis and characterization of an \( \text{M}_4 \text{L}_6 \) tetrahedral cluster based on the “Edge On” design (see Figure 8) has been previously reported using a bis(hydroxamate) ligand.\(^{29,40}\) A catecholate version based on ligand \( \text{H}_4 \text{B} \) is described here. Reaction of 6 equiv of \( \text{H}_4 \text{B} \), 4 equiv of \( \text{Ga(acac)}_3 \), and 12 equiv of KOH in methanol led to the precipitation of a white microcrystalline product after six to 8 h. The solubility of the cluster is much lower in methanol than that of the analogous helicates,\(^{29,31}\) but both are readily soluble in water. The \(^1\)H NMR spectrum of the complex in \( \text{D}_2 \text{O} \) shows only one set of peaks, indicating that the ligands in the complex are in symmetry-related environments and that the \( \text{C}_2 \) axis of the ligand is maintained. This type of spectrum could be interpreted as the averaged position of the peaks if the ligands are in rapid exchange. This possibility can be ruled out by examining the \(^1\)H NMR spectrum of the cluster prepared in the presence of excess ligand. Analogous to the previously described experiments with complexes of \( \text{H}_4 \text{A} \), the spectrum of the mixture shows two sets of peaks, one for the complex and one for the excess ligand. In this case, however, these results do not rule out the presence of an \( \text{M}_4 \text{L}_3 \) cluster. If lone pair donation of the amide nitrogens into the aromatic backbone of \( \text{H}_4 \text{B} \) is insufficient to disfavor large deviations from planarity, then the chelate groups could rotate around the N–arene bond to be perpendicular with the backbone. This conformation would allow for the correct arrangement of coordinate vectors and chelate planes for an \( \text{M}_4 \text{L}_3 \) cluster.

In a low-resolution positive ion electrospray mass spectrum, strong signals are seen for the \([\text{Ga}_4 \text{B}_6]^{2+}\) doubly charged, the \([\text{Ga}_4 \text{B}_6]^{15}\text{K}^{+}\) triply charged, and the \([\text{Ga}_4 \text{B}_6]^{16}\text{K}^{+}\) quadruply charged ions. Because the charge states of the peaks could not be verified, the doubly and quadruply charged ions might be assigned to the full and half mass peaks of a corresponding \([\text{Ga}_4 \text{B}_6]^{7}\text{K}^{+}\) cluster. The triply charged ion, however, cannot be rationalized by the smaller \( \text{M}_4 \text{L}_3 \) cluster and appears to be diagnostic in assigning the structure as a tetrahedron.

**Synthesis of \( \text{M}_4 \text{C}_6 \) Clusters.** Reaction of 6 equiv of \( \text{H}_4 \text{C} \), 4 equiv of \( \text{Ga(acac)}_3 \), 12 equiv of KOH, and 12 equiv of \( \text{Et}_4 \text{NCl} \) in methanol leads to a yellow precipitate which analyzes as \( \text{K}_4(\text{Et}_4 \text{N})[\text{Ga}_4 \text{C}_6]\cdot\text{H}_2 \text{O} \) that shows unusual features in the \(^1\)H NMR spectrum (Figure 14).\(^{27}\) A ratio of seven \( \text{Et}_4 \text{N}^{+} \) counterions to six ligands is observed, with the seven counterions being split into two sets in a ratio of 6:1. The larger set of \( \text{Et}_4 \text{N}^{+} \) peaks (\( \delta = 2.49, \text{q}; 0.72, \text{t} \)) is shifted slightly upfield from free \( \text{Et}_4 \text{NCl} \) (\( \delta = 3.26, \text{q}; 1.27, \text{t} \)), while the smaller set is shifted substantially upfield, showing up at negative ppm (\( \delta = -0.70, \text{m}; -1.59, \text{t} \)). The upfield shifts of the exterior \( \text{Et}_4 \text{N}^{+} \) resonances are attributed to a strong \( \pi^- \text{cation naphthalene and catechol rings of the ligands and the Et}_4 \text{N}^{+} \) counterions (vide infra). On

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clusters). It should be noted that computer modeling of the M-4 rotation group metal centers) giving rise to molecular symmetry of the pure molecule correctly predicted that it would have homoconfigurational (i.e., all S or C) symmetry isomers of the cluster were computationally unique. The [M-Fe-4 C-6] 12- anion lies on a crystallographic three-fold axis with T molecular symmetry; hence, the crystal is a racemic mixture of tetrahedra that have homoconfigurational (all S or all C) iron centers. As also observed in solution with the Ga-III complex, one of the Et-4 N counterions is located inside the cluster cavity (Figure 15a). The cluster is a tightly closed “box,” with no aperture through the surface, as demonstrated by a space-filling model (Figure 15b).

Crystal Structure of K-5(Et-4 N)-[Fe-4 C-6]. The Fe-III analogue was prepared in a manner similar to that for the Ga-III complex. NMR studies of the Fe-III analogue were precluded by the tetrahedral cluster. The Fe-Fe distances in the cluster are, on average, 12.8 Å, bringing the overall size of the cluster just into the nanometer regime. The naphthalene rings are twisted along the arene–N bond, so that they bend into the cavity. The hydrogen bonds between the amide proton and the coordinated catechol oxygen are still maintained, however. The angles between the least-squares planes calculated for the naphthalene backbone and the catechol rings are, respectively, 38.0° and 13.6° for one ligand and 20.7° and 65.3° for the other. We interpret this ligand distortion as a result of van der Waals interactions between the cluster and the encapsulated Et-4 N+. This van der Waals contact is clearly seen in Figure 16, which depicts a 2 Å thick slice through the center of the tetrahedral cluster. Solution studies (vide infra) suggest that this van der Waals contact is a result of more than just crystal-packing forces. There appears to be a strong π-cation interaction between the aromatic rings of the ligands and the Et-4 N+ counterions.

The crystal packing of the [Fe-4 C-6] 12- anion and the exterior Et-4 N+ cations is such that each dodecaanion is surrounded by eight molecules of water and three molecules of methanol in the cubic space group I-43d (No. 220). One-third of the compound is crystallographically unique. The [Fe-4 C-6] 12- anion lies on a crystallographic three-fold axis with T molecular symmetry; hence, the crystal is a racemic mixture of tetrahedra that have homoconfigurational (all S or all C) iron centers. As also observed in solution with the Ga-III complex, one of the Et-4 N counterions is located inside the cluster cavity (Figure 15a). The cluster is a tightly closed “box,” with no aperture through the surface, as demonstrated by a space-filling model (Figure 15b).

The Fe-Fe distances in the cluster are, on average, 12.8 Å, bringing the overall size of the cluster just into the nanometer regime. The naphthalene rings are twisted along the arene–N bond, so that they bend into the cavity. The hydrogen bonds between the amide proton and the coordinated catechol oxygen are still maintained, however. The angles between the least-squares planes calculated for the naphthalene backbone and the catechol rings are, respectively, 38.0° and 13.6° for one ligand and 20.7° and 65.3° for the other. We interpret this ligand distortion as a result of van der Waals interactions between the cluster and the encapsulated Et-N+. This van der Waals contact is clearly seen in Figure 16, which depicts a 2 Å thick slice through the center of the tetrahedral cluster. Solution studies (vide infra) suggest that this van der Waals contact is a result of more than just crystal-packing forces. There appears to be a strong π-cation interaction between the aromatic rings of the ligands and the Et-N+ counterions.

tetracapped and exterior Et$_4$N$^+$
cations, the titration of K$_5$(Et$_4$N)[Ga$_4$C$_6$] (D$_2$O, 300 MHz) with
Et$_4$NCl was followed by $^1$H NMR spectroscopy (Figure 19).
The catechol resonances show little change, although they are
shifted slightly upfield with increasing equivalents of Et$_4$N$^+$. The
naphthalene resonances are shifted downfield, and protons of the encapsulated Et$_4$N$^+$ cations are shifted upfield. Initially,
a linear change is observed, but a leveling off occurs after six to
eight equivalents of Et$_4$N$^+$ per equivalent of [Ga$_4$C$_6$]$^{12-}$ have
been added. Similar inspection of the two $^1$H resonances for
the exterior Et$_4$N$^+$ cations reveals sigmoidal-shaped curves with
infection points near eight equivalents$^{45}$ of Et$_4$N$^+$ per equivalent
of [Ga$_4$C$_6$]$^{12-}$ (corresponding to one Et$_4$N$^+$ on the interior and
six to seven Et$_3$N$^+$ on the exterior of the cluster). Thus, an
apparent equivalence point, corresponding to one Et$_4$N$^+$ inside
the cluster cavity and six to seven Et$_4$N$^+$ cations on the exterior
of the cluster, is consistently indicated by all of the observed
resonances.

These observations, along with the reproducible isolation of
the cluster as the K$_5$(Et$_4$N)[M$_4$C$_6$] salt (M = Ga$^{III}$, Fe$^{III}$) and
the packing of the exterior Et$_4$N$^+$ cations around the [Fe$_2$C$_6$]$^{12-}$
anion in the crystal structure, attest to a well-defined super-
structure of the Et$_4$N$^+$ cations and the [M$_4$C$_6$]$^{12-}$
tetrahedral dodecaanion. The exterior of the tetrahedral cluster is surrounded by six Et$_4$N$^+$ cations, one Et$_4$N$^+$ per ligand in the cluster. This
association might be explained in terms of a strong π–cation
interaction between the aromatic rings of the ligands and the
alkylammonium cations. It has been established that electrostatic
interactions play a prominent role in prototypical π–cation
interactions, and fundamental gas-phase studies have established
the π–cation interaction to be among the strongest of nonco-
valent binding forces.$^{43}$

An inspection of the CH$_2$ resonance of the encapsulated Et$_4$N$^+$
is also revealing (Figure 20). Initially, the CH$_2$ resonance of
the encapsulated Et$_4$N$^+$ is a simple quartet. This feature in the
$^1$H NMR spectrum of K$_5$(Et$_4$N)[Ga$_4$C$_6$] contrasts with that in the
spectrum of K$_5$(Et$_4$N)[Ga$_4$C$_6$], in which the methylene
resonance is a complex multiplet. Addition of Et$_4$NCl to the
solution of K$_5$(Et$_4$N)[Ga$_4$C$_6$] not only causes the proton
resonances to shift, but it also causes the quartet to gradually
split into a multiplet. Seemingly, in the absence of the adhering
exterior Et$_4$N$^+$ cations, the cavity is large enough that the
encapsulated Et$_4$N$^+$ does not “see” the chirality of the cluster
host. The walls of the cluster are compressed, however, as the
exterior Et$_4$N$^+$ cations adhere to the surface. The cavity then
becomes smaller, and the encapsulated Et$_4$N$^+$ begins to experi-
ence the chiral environment of the T symmetry cluster host.
These results imply that the cavity size is affected by the
presence of Et$_4$N$^+$ cations on the cluster exterior.

A variable-temperature $^1$H NMR spectroscopy experiment
showed that the encapsulated Et$_4$N$^+$ and the exterior Et$_4$N$^+$
cations of K$_5$(Et$_4$N)[Ga$_4$C$_6$] do not coalesce up to 100 °C in
D$_2$O. In fact, the peaks hardly shift. Inspection of the methylene
resonance of the encapsulated Et$_4$N$^+$ reveals that heating does
affect the interconversion of the diastereotropic protons, but even
at 100 °C the protons are not equivalent (Figure 21).

Additional evidence for the solution structure of K$_5$(Et$_4$N)[Ga$_4$C$_6$]
was obtained from 2D nuclear Overhauser effect spectroscopy (2D-NOESY).$^{45}$ Strong cross-peaks observed

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(44) Second derivative plots of the shifts of the proton resonances for
the exterior Et$_4$N$^+$ cations are both equal to zero at 8 equiv of Et$_4$N$^+$ per
equivalent of [Ga$_4$C$_6$]$^{12-}$. Note that the conditions for the experiments for
Figures 21 and 22 differ slightly, hence the slight mismatch of overlap.

(45) Frieboes, H. Basic One- and Two-Dimensional NMR Spectroscopy,
between the encapsulated Et₄N⁺ and only the naphthalene resonances of the cluster are consistent with the encapsulation of one molecule of Et₄N⁺ (Figure 22). Interestingly, cross-peaks are also observed between the six Et₄N⁺ cations located on the exterior of the cluster and the naphthalene and catechol protons on the ligands of the tetrahedral cluster. This evidence indicating that the exterior Et₄N⁺ cations also interact strongly with the aromatic sections of the cluster backbone is consistent with our findings from titration studies and the X-ray crystallographic results (vide supra).

The NOE changes the intensities of the observed signals as a result of dipole–dipole, or in effect through-space, relaxation of the nuclear spin. In small molecules with short rotational correlation times, tc, one type of relaxation mechanism dominates, which has the effect of amplifying the NOE signal. In large molecules with long rotational correlation times, a second type of relaxation mechanism dominates that has the effect of decreasing the NOE signal. Due to the large size of the cluster the majority of NOE peaks were found to be negative, indicating that the cluster is in the slow-tumbling regime. The encapsulated Et₄N⁺ is the only positive NOE peak observed, implying that it is tumbling inside the cluster cavity in the fast-tumbling regime independent of the slower-tumbling host cluster.

Cross-peaks were also observed between the encapsulated and exterior Et₄N⁺ cations. This observation suggested that the inner and outer Et₄N⁺ molecules are exchanging on the NMR time scale. While typical line-shape analysis of 1D NMR spectra is applicable to the study of processes occurring with rate constants between 1 and 10⁴ s⁻¹, the saturation transfer technique (NOESY and EXSY) is applicable to slower processes with rate
1.5 s, the intensity of the cross-peaks increased approximately than gas-phase behavior. We can confirm this because the results obtained by ESI-MS have been proven most useful in the analyses of self-assembled M complexes, in which stepwise replacement of Me4 N molecules can exit and enter. The ability of the guest molecule -

- constants on the order of 10^{-1} to 10^{2} s^{-1}. To confirm that these cross-peaks were indeed indicative of an exchange process, 2D exchange spectroscopy (EXSY) was employed. In the 2D-EXSY experiment, which is similar to the 2D-NOESY experiment, the cross-peaks provide a clear picture of the exchange process. 2D-EXSY spectra were recorded at different mixing times, \( \tau_m \). When the mixing time was increased from 0.75 to 1.5 s, the intensity of the cross-peaks increased approximately two-fold.

Since the crystal structure of K[Et4N][Ga4C6] has shown that the cluster is a tightly closed box lacking holes on the surface, the guest molecule can presumably only exit the cavity through openings created by structural fluctuations of the host cluster. The kinetic lability of Ga^{III} catecholate complexes enables ligands to partially dissociate from the metal ions and creates openings in the host cluster through which the guest molecules can exit and enter. The ability of the guest molecule to exit the cluster cavity is supported by competition experiments, in which stepwise replacement of Me2N⁺ for Pr₄N⁺, and Et₃N⁺ for Pr₄N⁺, is observed by ¹H NMR spectroscopy.

**Mass Spectrometry of the Tetrahedral Clusters.** In recent years, electrospray ionization mass spectrometry (ESI-MS) has been known most useful in the analyses of self-assembled MₙLₙ type clusters and the results obtained by ESI-MS have been regarded as indicative of the solution behavior of a species rather than gas-phase behavior. We can confirm this because the results obtained by ESI-MS correlate very well with all concurrent observations made by NMR and X-ray diffractometry. Nonetheless, ESI studies of such clusters remain nontrivial. The optimization of the spectra for the [Ti₃A₄],⁷⁺ cluster has been discussed in detail. The spectrum (MeOH-CH₂CN-H₂O, 4:4:1, v/v/v, cation detection mode) obtained for the [Ti₃A₄]⁺⁺ cluster, as its octakis-triethylammonium salt is shown in Figure 23. Clearly observable are two main clusters of peaks corresponding to mono- and dicaticonic clusters, respectively. The cluster of peaks is generated by exchange of protons for (ubiquitously present) Na⁺ ions. In addition, single peaks corresponding to species associated to triethylammonium ions can be identified. No peak which can be assigned to a MₓLₓ species with \( x, y \neq 4 \) can be identified, attesting to the unique stability of the tetrahedral supramolecular assembly.

When recording the ESI spectrum of the [Ti₃A₄]⁺⁺ cluster in the negative detection mode, we were pleased to find a dramatically improved spectrum (Figure 24). The extraordinarily simple spectrum shows four main peaks, which can be assigned to the hepta- ([(Ti₃A₄)⁶⁺-7H⁺]⁺ at m/z 2300.1), hexa- ([(Ti₃A₄)⁶⁺-6H⁺]⁻ at m/z 1149.6), penta- ([(Ti₃A₄)⁶⁺-5H⁺]³⁺ at m/z 766.1), and tetraprotonated ([(Ti₃A₄)⁶⁺-4H⁺]⁴⁺ at m/z 574.3) anion. This assignment was corroborated by the zoom scans over the narrow mass range of interest (inserts in Figure 24). The peak separation within the multiply charged clusters are, as indicated by the charge state of the ion generating the pattern, separated by \( \frac{1}{2}, \frac{1}{3}, \text{ and } \frac{1}{4} \text{ Da} \), respectively. The presence of up to a heptaprotonated metal–ligand complex without the observation of any fragmentation may seem unusual. However, the diprotonated mononuclear Ti^{IV} tris(catecholate) species is stable reflecting the high stability of the Ti^{IV} tris(catecholate) Ti–O bonds and the basicity of the resulting anionic complex. The strong association of the counterions through H-bonds to the anionic cluster was already described within the context of the description of the X-ray structure of this cluster, and we assume that, in addition to the electrostatic interactions, identical H-bonds are responsible for the adherence of the protons to the cluster, namely to the catecholate and the carbonyl oxygens. We surmise that the origin of the protons were the Et₃NH⁺ counterions. Under the drying conditions following the spraying of the analyte solution into the mass spectrometer, Et₃N evaporated, leaving the protons with the anion. Consistent with the absence of solid state and NMR evidence for the presence of a host–guest complex, no ions in the mass spectrum were observed that could have indicated an encapsulated species. Again, fragmentation of the cluster under the condition of the ESI-MS was not observed.

The ESI spectrum (anion detection) exhibited by the corresponding Sn^{IV} cluster [Sn₃A₄]⁺⁺, as its triethylammonium salt, is similar to that of the Ti-analogue in that it shows a rich pattern of peaks attributable to cluster anions coordinated by x cations, resulting in various charge states (\( 8 - x \)), ranging from diionic to tetraanionic, with each group of peaks modulated by proton-to-triethylammonium exchange processes. It is interesting to note that not all possible peaks attributable to this exchange process are observed. For instance, the dicaticonic species, only 5 out of the 10 possibilities are observed, and only one tetraanionic species can be clearly identified.

The spectrum shown in Figure 25 was obtained from a cluster sample prepared with a slight excess of Sn^{IV}. The minor peaks at 1348.9 and 1406.4, and 2698.2 and 2813.6 m/z correspond numerically to the di- and monoanionic clusters with one and two Sn atoms as counterions, respectively, although the charge states were not confirmed in a zoom scan experiment.

**Figure 21.** Heating a solution of K[Et4N][Ga4C6] up to 100 °C does not cause the diasterotopic methylene protons to become equivalent.

Remarkably, even with an excess of metal, the cluster remains intact and non-M$_4^4$A$_4$ fragments are not observed. This is a particularly powerful demonstration of the cooperative effects holding the clusters together, resulting in extraordinary stability of the tetrahedral species, and mirrors the results obtained in solution and probed by NMR.

To conclude the mass spectral results, we believe that ESI-MS allows for an unambiguous characterization of the clusters, although we found that the optimization of the spectra required the empirical variation of the spray parameters, namely the solvents and ionization conditions used. Variation in the drying parameters (evaporation of the solvents) resulted in little or no changes within the parameters tested (capillary temperatures between 125 and 200 °C were probed). While it is nontrivial to infer a structure from a given composition, our data are consistent with the notion that the tetrahedral anionic structures for the complexes observed in the crystal structure are also preserved in solution under the conditions of electrospray mass spectrometry.

**Conclusions**

We have shown that carefully designed ligands requiring few synthetic steps can be combined with complementary metal ions to form tetrahedral tetranuclear clusters in a self-assembly process. The three design strategies outlined here are generally valid and will hopefully guide the design and synthesis of new clusters based on a variety of ligands and metals. Given the possibility of creating clusters with well-defined cavities, this seems a desirable goal in light of the rich chemistry anticipated in the inner-phase of these molecular hosts. We also anticipate that these rigid, kinetically and thermodynamically stable, metrically well-defined clusters will find a use as building blocks in nanotechnological applications.

**Experimental Section**

**General.** All NMR spectra were measured with Bruker 300, 400, or 500 MHz spectrometers. Chemical shifts are reported on the δ scale in ppm downfield from Na 3-(TMS)-propionate-2,2,3,3-d$_4$ in D$_2$O, from

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**Figure 22.** 2D-NOESY NMR spectrum (500 MHz, D$_2$O) of K$_5$[Et,N]$_7$[Ga$_4$C$_6$]. The horizontal axis shows the ligand resonances of the cluster, while the vertical axis shows signals corresponding to Et$_4$N$^+$.  

**Figure 23.** ESI(+)-MS of [Ti$_4$A$_4$][Et$_3$N]$_8$. Each of the peaks in the figure insert can be assigned to a cluster dication formed from the exchange of H$^+$ for K$^+$.  

**Figure 24.** ESI(−)-MS of [Ti$_4$A$_4$][Et$_3$N]$_8$. The inserts show that the charge states are confirmed for these ions using zoom scans.
TMS in DMSO-\textsubscript{d}\textsubscript{6}, and from the residual protonic solvent peak in MeOD and DMF. Melting points are uncorrected. Elemental analyses were performed at the UCB Analytical Facilities.

**Mass Spectrometry.** All electrospray experiments were carried out on a Finnigan LCQ quadrupole ion trap mass spectrometer (Finnigan MAT, San Jose, CA) equipped with a microspray ionization source. Transfer lines (deactivated fused silica tubing, 40 μm and 200 μm inner diameter, polyimide coated) between the syringe pump and ion source were purchased from Polymicro (Phoenix, AZ), and all the connection pieces (Peek or stainless steel with KEL-F fittings) were obtained from Upchurch Scientific (Oak Harbor, WA). Ionization was performed under microspray conditions at a flow rate of 0.4 μL·min\(^{-1}\) and a spray voltage of 2.8–3.5 kV. For anion detection the spray voltage was set with bovine insulin (in MeOH and 2% formic acid; \(c = 0.5 \text{ mg/mL}\)). The normal mass range (50–2000 Da) was performed and NaI (in MeOH:2-propanol 1:1 (v/v), or less during the acquisition (uncorrected ion gauge reading). The temperature of 175 °C, and all ion guide voltages were tuned to under vacuum at 70 °C, cooling the sample back to starting temperature, and recording the spectra, producing identical results. The accuracy of the temperature was ±0.1 K. For the 2D NOESY experiment, \(1 \times 10^{-6}\) mol of [K\(_4\)Et\(_4\)N][Ga\(_4\)TMS] was dissolved in 600 μL of D\(_2\)O. The spectrum was measured at 300 K on a 500 MHz Bruker DRX spectrometer using a NOESY sequence, with \(d1 = 2\) and \(d8 = 100\) ms.

**General Procedure for the Formation of the Ligands Me\(_A\), Me\(_B\), and Me\(_C\).** A four-fold stoichiometric excess per methoxy group of BBBr was added at −78 °C via syringe to a solution of the protected ligands Me\(_A\), Me\(_B\), and Me\(_C\) in dry CH\(_2\)Cl\(_2\) (~100 μL/5 mmol ligand). The reaction mixture was allowed to warm to room temperature and stirred overnight. Workup procedure A: Volatiles were removed under vacuum, and the remaining residue was suspended in water for 2 h at 100 °C. The white precipitates were collected by filtration and dried under vacuum at 70 °C. Workup procedure B: Unreacted BBBr was quenched by the careful addition of MeOH. The mixture was distilled while repeatedly adding portions of fresh MeOH until the distillate were boron-free (flame test: one drop of the distillate when lit on a cotton swap does not burn green). The products precipitated as crystalline material from the reduced hot methanolic solution were filtered off and dried.

1,3,5-Tris(2,3-dimethoxybenzamido)benzene (Me\(_A\)): prepared following the general procedure (workup method A) on a 25 mM scale at 86% yield: mp 208–209 °C. 1H NMR (300 MHz, CDCl\(_3\)) \(\delta 10.74\) (s, 2H), 8.56 (d, \(J = 7.5\), 2H), 7.88 (m, 4H), 7.00 (t, \(J = 8.1\) Hz, 2H), 7.26 (t, \(J = 8.1\) Hz, 2H), 7.15 (dd, \(J = 1.2\), 8.1 Hz, 4H), 4.09 (s, 6H), 3.90 (s, 6H). 1\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 165.6, 153.3, 146.6, 140.2, 132.2, 129.6, 124.9, 120.8, 115.9, 115.4, 61.8, 56.7. Anal. Calcd (Found) for C\(_{32}\)H\(_{28}\)N\(_8\): C 66.05 (65.75), H 5.54 (5.55). N 6.42 (6.29).

**Figure 25.** ES(−)–MS of [Sn\(_4\)Me\(_6\)]\([\text{Et}_4\text{N}]_8\). The inserts show that the charge states are confirmed for these ions using zoom scans.
orange gelatinous precipitate was removed by centrifugation and suspended in DMF (20 mL). The suspension was heated under N₂ for 12 h. The resulting solution was filtered through Celite and either evaporated to dryness in vacuo, to produce 190 mg of a microcrystalline solid, or MeOH vapors were allowed to diffuse into this solution at room temperature over several weeks to produce 80 mg (yield 37%, first crop) of orange cuboid crystals.

Absorption isotherms of 

1H NMR (300 MHz, DMSO-d₆) δ 11.43 (s, 1.5H, NH), 8.2 (variably br s, 1H, NH), 7.12 (d, J = 6.5 Hz, 1.5H, ArH), 6.84 (s, 1.5H, ArH), 6.45 (t, 1H, J = 7.8 Hz, ArH), 6.21 (d, 1.5H, J = 7.8 Hz, ArH), 3.00 (q, 5H, J = 7.3 Hz, CH₂). 13C NMR (125 MHz, DMSO-d₆) δ 158.8 (C₀=O), 140.3, 138.7, 137.5, 118.5, 116.8, 115.4, 114.5, 112.9, 43.3, 8.3. ES(-)MS (100% CH₃CN) (Na⁺) 1219.8 [M + Na⁺] +, 1201.6 [M + Na⁺] -; 1193.5 [M + Na⁺] +, 1175.5 [M + Na⁺] -; 1185.6 [M + Na⁺] +, 1167.5 [M + Na⁺] -; 1177.5 [M + Na⁺] +, 1159.5 [M + Na⁺] -; 1189.5 [M + Na⁺] +, 1171.5 [M + Na⁺] -; 1199.5 [M + Na⁺] +, 1181.5 [M + Na⁺] -; 1209.5 [M + Na⁺] +, 1191.5 [M + Na⁺] -; 1219.5 [M + Na⁺] +, 1195.5 [M + Na⁺] -.

The mixture was heated at 90°C for 12 h and then was reduced to 5 mL. The powder was filtered and the solution changed from colorless to yellow. While the reaction mixture was stirred at room temperature overnight, the product precipitated as a yellow silky powder. This powder was isolated by ultracentrifugation and dried under vacuum (0.120 g, 0.029 mmol, 76%).

Absorption isotherms of 

1H NMR (300 MHz, D₂O) δ 13.60 (s, 12H, NH), 8.15 (d, J = 7.8 Hz, 12H, ArH), 7.91 (d, J = 8.6 Hz, 12H, ArH), 7.35 (dd, J = 1.5, 8.2 Hz, 12H, ArH), 7.20 (t, J = 8.2 Hz, 12H, ArH), 6.78 (dd, J = 1.5, 7.5 Hz, 12H, ArH), 6.63 (t, J = 7.9 Hz, 12H, ArH), 4.22 (q, J = 7.2 Hz, 6H, J₈/² = 5.7 Hz). 13C NMR (125 MHz, D₂O) δ (C) 172.4, 161.4, 157.7, 136.9, 124.9, 117.4, (CH₂) 129.1, 121.5, 120.3, 118.3, 117.8, 117.7, (CH₃) 54.5, 52.9, (CH₂) 9.1, 7.0. ES(-)MS (100% CH₃OH) (M⁺) 859.4 [M⁺ + 2K⁺ + 2H⁺]⁻, 868.9 [2 + 8H⁺]⁻, 891.8 [5 + 8H⁺]⁻, 914.8 [7 + 8H⁺]⁻, 946.9 [9 + 8H⁺]⁻, 1189.7 [11 + 8H⁺]⁻, 1202.3 [13 + 8H⁺]⁻, 1219.8 [15 + 8H⁺]⁻, 1232.7 [17 + 8H⁺]⁻, 1250.2 [19 + 8H⁺]⁻, 1263.0 [21 + 8H⁺]⁻, 1275.7 [23 + 8H⁺]⁻, 1293.5 [25 + 8H⁺]⁻, 1306.0 [27 + 8H⁺]⁻. Anal. (Found) for K₂Fe₃C₃H₆N₆O₆·3H₂O: C 58.57 (58.45), H 5.92 (5.65), N 6.51 (6.19).

Crystallography General. Crystal data for all structures investigated were collected using a Siemens SMART diffractometer equipped with a CCD area detector with graphite monochromated Mo Kα radiation (λ = 0.71073 Å). Frames corresponding to an arbitrary hemisphere of reciprocal space were collected by x-ray diffraction at room temperature using two detectors over two weeks by gas-phase diffusion of acetone into a methanol/water solution of the complex. Esprit-MS (100% CH₃OH) (M⁺) 613.8 [M⁺ + Na⁺] +, 641.7 [2 + 3Na⁺] +, 788.4 [2 + 3Na⁺] + + 2Na⁺] +, 1094.5 [3 + 4Na⁺] +, 1123.4 [3 + 3Na⁺] + + Na⁺] +, 1183.8 [3 + 5Na⁺] +, 1123.4 [3 + 3Na⁺] + + Na⁺] +, 1183.8 [3 + 5Na⁺] +, 1217.9 [3 + 6Na⁺] +, 1244.7 [3 + 6Na⁺] +, 1409.9 [3 + 7Na⁺] +. Anal. (Found) for K₂Fe₃C₃H₆N₆O₆·3H₂O·H₂O: C 60.65 (60.68), H 5.90 (5.83), N 6.72 (6.44).

Crystal data for all structures investigated were collected using a Siemens SMART diffractometer equipped with a CCD area detector with graphite monochromated Mo Kα radiation (λ = 0.71073 Å). Frames corresponding to an arbitrary hemisphere of data were collected using w scans of 0.3° counted for a total of 30 s (20 s for MeA) per frame at the temperatures noted. SAINT (50) and XPREP (50) were used for data reduction. Data were corrected for Lorentz and polarization effects. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as Supplementary Publication nos. CCDC-143379 (Me₆[Ti⁺₂]), and CCDC-1001077 (Et₄N⁺·[Ti⁺₂]).
Crystallography of Me6A. Clear blades of H3C6N3O6 having approximate dimensions of 0.15 × 0.10 × 0.05 mm were grown by vapor phase diffusion of Et2O into a CHCl3 solution of Me6A. T = −116 °C, monoclinic, P21/a (No. 14), a = 15.406(7) Å, b = 7.264(5) Å, c = 26.48(1) Å, β = 95.23(5)°, V = 2951(2) Å3, Z = 4, μ = 0.10 mm⁻¹, F(000) = 1296, ρcalcd = 1.38 Mg m⁻³. A red blocky crystal of dimensions 0.30 × 0.22 × 0.07 mm was grown by vapor diffusion of MeOH into a DMF solution of the complex; −103 ± 2 °C, trigonal, R3c (No. 167), with a = 22.6143(5) Å, c = 106.038(2) Å, V = 46963 Å³, Z = 12, μ = 0.279 mm⁻¹, F(000) = 19680, ρcalcd = 1.32 Mg m⁻³, 2θmax = 41.6°. Of the 49921 reflections collected 6019 were unique (Rint = 0.0978 for 4672 Friedel unique data, 542 parameters, 14 restraints, 3.75° < 2θ < 34.58°); for all 7336 data, wR2 = 0.3288, GOF = 1.205; max/min residual density +0.62/−0.32 e Å⁻³. Flack parameter = 0.03(5). 54

Acknowledgment. This work was supported by NSF grant CHE-9709621 and the exchange grants NSF INT-9603212 and NATO SRG951516. J.A.L. and S.K. gratefully acknowledge an unrestricted UCB gift fund. We are most appreciative to Dr. Frederick Hollander (CHEXRAY, UCB) for his assistance with the structure determinations.

Supporting Information Available: Details of the X-ray structure solutions for compounds Me6A, (Et₄N)₆[Ti₂A₄], and K₆(Et₄N)₅[Fe₄C₆] (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA0104507

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