Supramolecular Chemistry

DOI: 10.1002/anie.200801226

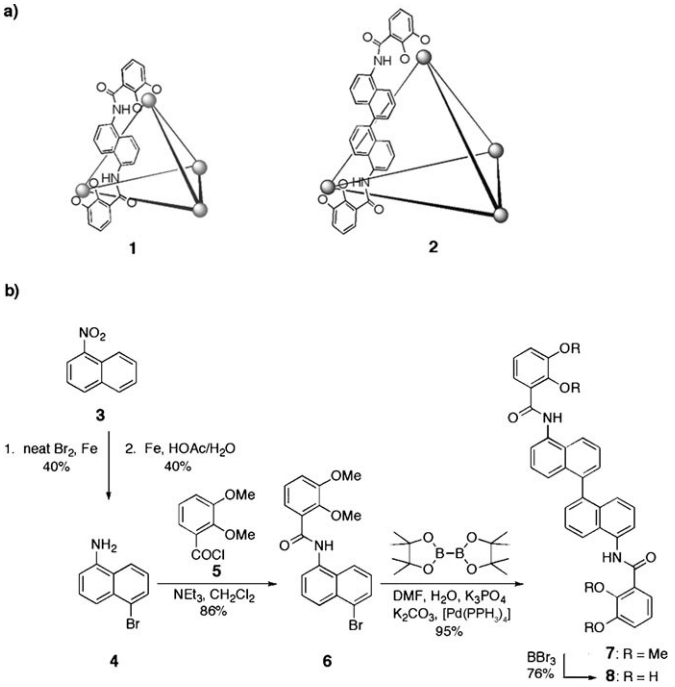
Design and Formation of a Large Tetrahedral Cluster Using 1,1′-Binaphthyl Ligands**

*Shannon M. Biros, Robert M. Yeh, and Kenneth N. Raymond**

Many chemists have been fascinated with the development of discrete supramolecular structures that encapsulate guest molecules. These structures can be assembled through covalent[1,2] or hydrogen bonds,[3] electrostatic[4] or metal–ligand interactions.[5,6] These host structures have provided valuable insight into the forces involved in small-molecule recognition. Our work has focused on the design and study of metal–ligand clusters of varying sizes.[7,8] The $[M_4L_6]^{12-}$ cluster **1** with a naphthalene derivative as the ligand[9] (Scheme 1 a) has demonstrated diastereoselective guest binding[10] and chiral-induction properties[11] as well as the ability to catalyze reactions carried out inside the cavity in an enzymelike manner.[12] However, the size of the cavity (ca. 300 to 500 Å^3) has often limited the scope of substrates for these transformations.[13]

In searching for new ligands for the construction of larger M_4L_6 tetrahedra, we explored the derivatization of the 1,1′-binaphthalene (binaph) core (Scheme 1 a). When substituted in the 5,5′ positions with catecholamides (**8**), the 1,1′-binaphthalene unit, in the pseudo-C_{2h} conformation, achieves optimal relative positioning of the chelating groups for formation of an M_4L_6 tetrahedron. This bis-catecholate ligand is approximately 6.7 Å longer than the original naphthalene ligand used to form cluster **1**, resulting in a calculated cavity size of at least 700 Å^3.[14]

The synthesis of bis-catecholate ligand **8** was accomplished in the modular manner shown in Scheme 1 b. Selective bromination of nitronaphthalene **3** followed by reduction with iron in acetic acid gives mono-amine **4**[17]. Acylation with the acid chloride of 2,3-dimethoxybenzoic acid (**5**) provides the aryl bromide **6** in good yield. This aryl bromide can be dimerized efficiently under modified Suzuki conditions and globally deprotected by using BBr_3 to give final product **8**.



Scheme 1. a) Schematic diagrams of $[M_4L_6]^{12-}$ clusters: **1** with a naphthalene derivative as ligand[9] and **2** with a larger binaphthyl derivative as ligand; b) synthesis of binaph ligand **8**.

In the case of the naphthalene-based cluster **1**, the assembly can be prepared at room temperature and in the absence of guest molecules due to the rigid nature of the host ligands. The cavity of this "empty" cluster is likely filled with solvent molecules. Not surprisingly, with binaph ligand **8**, cluster formation requires both heating (due to the additional six freely rotatable bonds) and the presence of a suitable guest to thermodynamically template the assembly. As guests for this system tetraalkylammonium salts were chosen due to a readily available range of sizes and their compatibility with supramolecular assemblies.[3,7,8] The thin outer layer of positive charge on these salts is highly complementary to the electron-rich interior surface of the cluster's aromatic walls. Dissolution of ligand **8** (6 equiv) in methanol with an excess of R_4NBr, base (KOH), and $[Ga(acac)_3]$ (4 equiv) followed by heating provides the desired Ga–binaph host–guest complexes. The ^{1}H NMR spectra of these complexes are shown in Figure 1.

The host–guest assemblies formed from the binaph ligands and the tetraalkylammonium salts Pr_4N^+, Bu_4N^+,

[*] S. M. Biros, R. M. Yeh, K. N. Raymond
Department of Chemistry
University of California
Berkeley, CA 94720-1460 (USA)
Fax: (+1) 510-486-5283
E-mail: raymond@socrates.berkeley.edu
Homepage: http://www.cchem.berkeley.edu/knrgrp/home.html

[**] We gratefully acknowledge financial support from the Director, Office of Science, Office of Basic Energy Sciences, and the Division of Chemical Sciences, Geosciences, and Biosciences of the US Department of Energy at LBNL under Contract No. DE-AC02-05CH11231. We thank Prof. R. G. Bergman, M. D. Pluth, C. J. Hastings, and B. E. Tiedemann for helpful discussions and Dr. Ulla Anderson for assistance with mass spectrometry experiments.

Supporting information for this article (detailed procedures for the preparation of compounds **4**, **6**, **7**, **8**, and all Ga_4L_6–guest complexes as well as the characterization data) is available on the WWW under http://dx.doi.org/10.1002/anie.200801226.

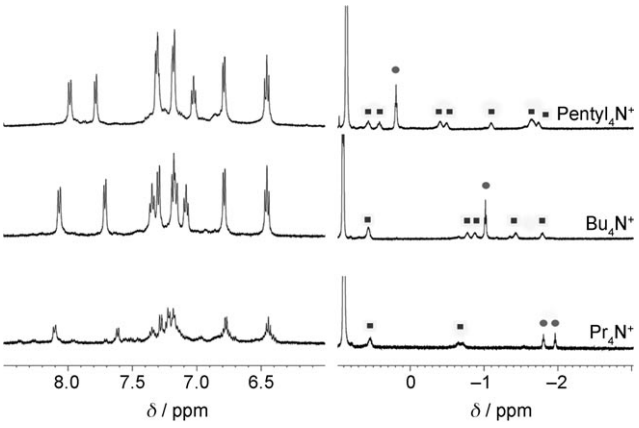


Figure 1. Upfield and host-ligand portions of the ^{1}H NMR spectra (500 MHz, CD_3OD) of Ga–binaph complexes with a series of tetraalkylammonium salts as guests: Pr_4N^+, Bu_4N^+,and $(n\text{-pentyl})_4N^+$; peaks marked with ● represent CH_3 groups and peaks marked with ■ represent the CH_2 groups of bound guest molecules.

and $(n\text{-pentyl})_4N^+$ are readily soluble in methanol and, to a lesser extent, water. As expected, the resonance signals corresponding to bound guest molecules are shifted upfield ($\Delta\delta \approx 3$ ppm) in response to the shielding effect of the aromatic host ligands. Integration of the ^{1}H NMR spectra indicates that the host–guest complexes have a stoichiometry of six binaph ligands to one interior (bound) R_4N^+ to six exterior (free) R_4N^+ cations. These exterior ions are likely involved in cation–π interactions with the aromatic faces of each ligand.[9] The presence of peaks for both free and bound guest molecules in the ^{1}H NMR spectra show that these complexes are kinetically stable on the NMR time scale. Cation–π[15] and CH–π interactions between host and guest as well as desolvation effects likely contribute favorably to host–guest complex formation.

$[Ga_4(binaph)_6]^{12-}$ complexes containing Bu_4N^+ or $(n\text{-pentyl})_4N^+$ show nine resonance signals in the aromatic region of the ^{1}H NMR spectrum corresponding to the host hydrogen atoms (Figure 2). This indicates that the complexes have overall *T* symmetry with each gallium center having the same configuration, much like their naphthalene predecessor. The complex with Pr_4N^+ as the guest molecule shows nine groups of aromatic resonance signals in this region, although in this case there is some degree of asymmetry between the ligands. This is likely a factor resulting from the ligands "puckering" in toward the cavity to maximize contact with the smaller guest molecules. This host also demonstrates size selectivity: Et_4N^+ is too small to efficiently template the Ga_4L_6 assembly, while $(n\text{-hexyl})_4N^+$ is too large.

Further analysis of the ^{1}H NMR spectra of these complexes reveals information about the conformation of bound guest molecules. As the alkyl chain length of the guest molecule increases from propyl to pentyl, the resonance signal corresponding to the methyl group progressively shifts downfield (see Figure 1). This indicates a coiling of the alkyl chains toward the center of the cavity as the size of the guest increases.[16] Diastereotopic splitting of the geminal methylene proton resonance signals of the bound guest molecule is also observed (see Figure 1), indicating that the host cavity is chiral in nature.

Further evidence for host–guest complex formation is provided by 2D NOESY experiments (Figure 2). For $\{Bu_4N^+\subset[Ga_4(binaph)_6]\}^{11-}$ (where ⊂ denotes encapsulation), strong NOE cross peaks are observed between the proton resonance signals of the guest molecule and those of the aromatic protons of the host ligands. This indicates close through-space contacts between host and guest, concurrent with a stable host–guest complex.

Quaternary phosphonium salts bearing aromatic substituents are also suitable guests for this host. Triphenylpropyl-, triphenylbutyl- and tetraphenylphosphonium efficiently template the assembly of $[Ga_4(binaph)_6]^{12-}$. The $\{Ph_4P^+\subset[Ga_4(binaph)_6]\}^{11-}$ complex retains overall *T* symmetry (Figure 3). However, the aromatic regions of the ^{1}H NMR spectra of $\{[Ph_3PrP^+\subset[Ga_4(binaph)_6]\}^{11-}$ and $[Ph_3BuP^+\subset[Ga_4(binaph)_6]\}^{11-}$ show 36 sets of resonance signals corresponding to the aromatic hydrogen atoms of the host ligands. This indicates a decrease in the overall symmetry of the host–guest complex, likely resulting from a hindered rotation of the C_3-symmetric guest inside the host's cavity. A second possible explanation for these complex ^{1}H NMR spectra is that a different host–guest assembly is formed in the presence of a non-ideal guest for the Ga_4L_6 structure. These theories are difficult to prove without X-ray structural data, however high-resolution mass spectra of these complexes (see below) support the formation of a complex with $[Ga_4L_6\text{-}(R_4P^+)]$ stoichiometry.

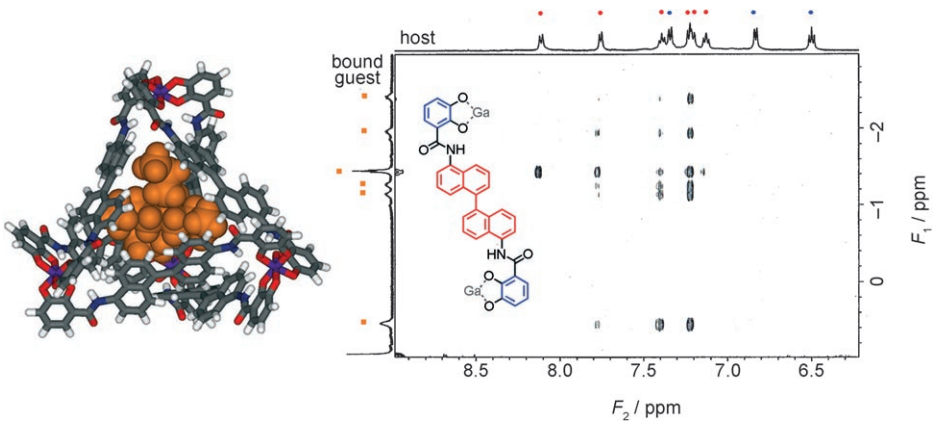


Figure 2. Left: Minimized structure (host: CPK colors, guest: orange CPK spheres; CAChe, version 6.1, MM3); right: 2D NOESY spectrum (500 MHz, CD_3OD) of $\{Bu_4N^+\subset[Ga_4(binaph)_6]\}^{11-}$.

The host–guest complexes were further analyzed using high-resolution ESI-QTOF mass spectrometry. The identity of the complexes can be readily confirmed by their complex isotopic pattern at various charge states. For instance, the predicted

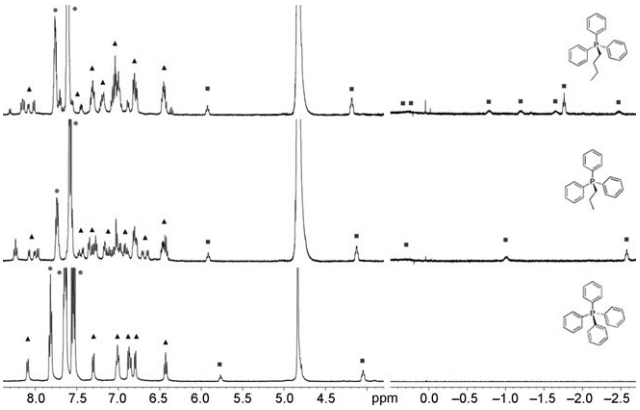


Figure 3. Aromatic and upfield regions of the ^{1}H NMR spectra (500 MHz, CD_3OD) of $[Ga_4(binaph)_6]^{12-}$ complexes with quaternary phosphonium guests: Ph_4P^+, Ph_3PrP^+, Ph_3BuP^+; ●: resonance signals of free guest molecules; ■: resonance signals of bound guest molecules (one signal for each complex is beneath the solvent peak at $\delta = 4.8$); ▲: resonance signals of the host $[Ga_4(binaph)_6]^{12-}$.

m/*z* peak for $[Bu_4N^+K_5\{Bu_4N^+\subset[Ga_4(binaph)_6]\}]^{5-}$ is 854.778, and the observed value is 854.779. The predicted isotopic splitting pattern of this peak is also in excellent agreement with the experimental data (see the Supporting Information).

We have described herein the use of a bis-catecholate-1,1′-binaphthalene ligand to form a novel self-assembled Ga_4L_6 cluster. This host binds larger guest molecules than previous assemblies we have reported. Future work will explore guest scope, the compatibility of host formation with varying metal centers, and the dynamics of guest exchange. In addition, the larger cavity will be exploited to facilitate reactivity.

Received: March 13, 2008
Published online: June 20, 2008

Keywords: chiral recognition · metal–ligand assembly · self-assembly · supramolecular chemistry

[1] F. Diederich, *Cyclophanes: Monographs in Supramolecular Chemistry*, Royal Society of Chemistry, Cambridge, **1991**.
[2] D. J. Cram, *Container Molecules and Their Guests*, *Vol. 4*, Royal Society of Chemistry, Cambridge, **1994**.
[3] F. Hof, S. L. Craig, C. Nuckolls, J. Rebek, Jr., *Angew. Chem.* **2002**, *114*, 1556; *Angew. Chem. Int. Ed.* **2002**, *41*, 1488.
[4] F. Corbellini, R. M. A. Knegtel, P. D. J. Grootenhuis, M. Crego-Calama, D. N. Reinhoudt, *Chem. Eur. J.* **2005**, *11*, 298.
[5] M. A. Pitt, D. W. Johnson, *Chem. Soc. Rev.* **2007**, *36*, 1441.
[6] M. Fujita, M. Tominaga, A. Hori, B. Therrien, *Acc. Chem. Res.* **2005**, *38*, 371.
[7] D. L. Caulder, K. N. Raymond, *Acc. Chem. Res.* **1999**, *32*, 975.
[8] D. W. Johnson, K. N. Raymond, *Inorg. Chem.* **2001**, *40*, 5157.
[9] D. L. Caulder, R. E. Powers, T. N. Parac, K. N. Raymond, *Angew. Chem.* **1998**, *110*, 1940; *Angew. Chem. Int. Ed.* **1998**, *37*, 1840.
[10] D. Fiedler, D. H. Leung, R. G. Bergman, K. N. Raymond, *J. Am. Chem. Soc.* **2004**, *126*, 3674.
[11] D. H. Leung, D. Fiedler, R. G. Bergman, K. N. Raymond, *Angew. Chem.* **2004**, *116*, 981; *Angew. Chem. Int. Ed.* **2004**, *43*, 963.
[12] M. D. Pluth, R. G. Bergman, K. N. Raymond, *Science* **2007**, *316*, 85.
[13] D. H. Leung, R. G. Bergman, K. N. Raymond, *J. Am. Chem. Soc.* **2007**, *129*, 2746.
[14] Cavity-volume calculations were carried out using Voidoo with a 1.4 Å diameter rolling ball on a minimized calculated structure (CAChe) of the $Ga_4(binaph)_6$ assembly: a) G. J. Kleywegt, J. Y. Zou, M. Kjeldgaard, T. A. Jones, *International Tables for Crystallography*, *Vol. F*, Springer, Heidelberg, **2001**; b) G. J. Kleywegt, T. A. Jones, *Acta Crystallogr. Sect. D* **1994**, *50*, 178–185.
[15] J. C. Ma, D. A. Dougherty, *Chem. Rev.* **1997**, *97*, 1303.
[16] L. C. Palmer, J. Rebek, Jr., *Org. Lett.* **2005**, *7*, 787.
[17] L. H. Klemm, J. W. Sprague, E. Y. K. Mak, *J. Org. Chem.* **1957**, *22*, 161.

