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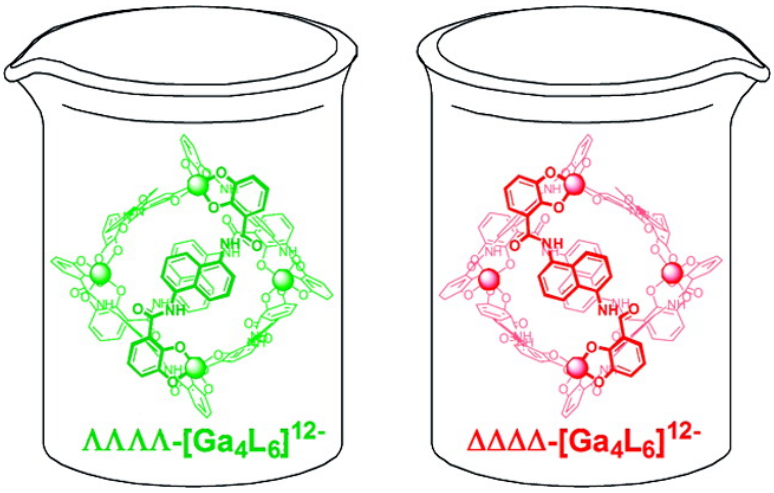

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Resolution of Chiral, Tetrahedral M_4L_6 Metal−Ligand Hosts[1]

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Abstract: The supramolecular metal−ligand assemblies of $M_4\mathbf{1}_6$ stoichiometry are chiral (M = Ga^{III}, Al^{III}, In^{III}, Fe^{III}, Ti^{IV}, or Ge^{IV}, $H_4\mathbf{1}$ = *N,N′*-bis(2,3-dihydroxybenzoyl)-1,5-diaminonaphthalene). The resolution process of ΔΔΔΔ- and ΛΛΛΛ-$[M_4\mathbf{1}_6]^{12-}$ by the chiral cation *S*-nicotinium (*S*-nic^+) is described for the Ga^{III}, Al^{III}, and Fe^{III} assemblies, and the resolution is shown to be proton dependent. From a methanol solution of $M(acac)_3$, $H_4\mathbf{1}$, *S*-nicI, and KOH, the ΔΔΔΔ-KH_3(*S*-nic)$_7$[(*S*-nic) ⊂ $M_4\mathbf{1}_6$] complexes precipitate, and the ΛΛΛΛ-K_6(*S*-nic)$_5$[(*S*-nic) ⊂ $M_4\mathbf{1}_6$] complexes subsequently can be isolated from the supernatant. Ion exchange enables the isolation of the $(NEt_4^+)_{12}$, $(NMe_4^+)_{12}$, and K^+_{12} salts of the resolved structures, which have been characterized by CD and NMR spectroscopies. Resolution can also be accomplished with 1 equiv of NEt_4^+ blocking the cavity interior, demonstrating that external binding sites are responsible for the difference in *S*-nic^+ enantiomer interactions. Circular dichroism data demonstrate that the $(NMe_4^+)_{12}$ and $(NEt_4^+)_{12}$ salts of the resolved $[Ga_4\mathbf{1}_6]^{12-}$ and $[Al_4\mathbf{1}_6]^{12-}$ structures retain their chirality over extended periods of time (>20 d) at room temperature; heating the $(NEt_4^+)_{12}[Ga_4\mathbf{1}_6]$ assembly to 75 °C also had no effect on its CD spectrum. Finally, experiments with the resolved $K_{12}[Ga_4\mathbf{1}_6]$ assemblies point to the role of a guest in stabilizing the resolved framework.

Introduction

The self-assembly of chiral supramolecular architectures has followed several strategies, with the resulting frameworks expressing stereospecific properties on a number of levels.[2−4] While the concept of an organic stereocenter is very familiar, a chemist's chiral tool box extends to stereogenic metal centers as well as to molecular level chirality, as seen in the right-handed DNA helix. Supramolecular syntheses can include components with predetermined stereocenters but can also generate new stereocenters or molecular level chirality through self-assembly itself.[2,5]

The introduction of carbon stereocenters into assembly components is a common approach to control supramolecular stereoconfiguration and achieve resolved structures. In metal−ligand assemblies, chiral moieties have been incorporated into ligand backbones[4,6,7] and appended to the ligand extremities or integrated into ancillary ligands,[4,7,8] and the use of a resolved inert metal precursor has also been reported.[9] In some cases chiral ligands influence the assembly process, determining metal center configuration and ultimately the handedness of the final architecture.

Yet one of the powerful aspects of self-assembly is that chiral structures and chiral centers (in the case of metal−ligand assembly) can be generated as a product of the assembly process; *chiral structures may be produced from achiral components*. We have previously reported the assembly of M_4L_6 structures in which mechanical coupling among the four stereogenic tris-bidentate metal centers produces only homochiral ΔΔΔΔ and ΛΛΛΛ configured products.[10−12] These M_4L_6 tetrahedral as-

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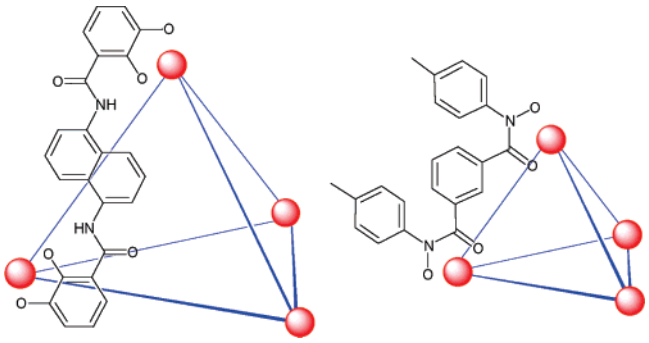

Figure 1. Schematic representations of the $M_4\mathbf{1}_6$ (left) and $M_4\mathbf{2}_6$ (right) tetrahedra.

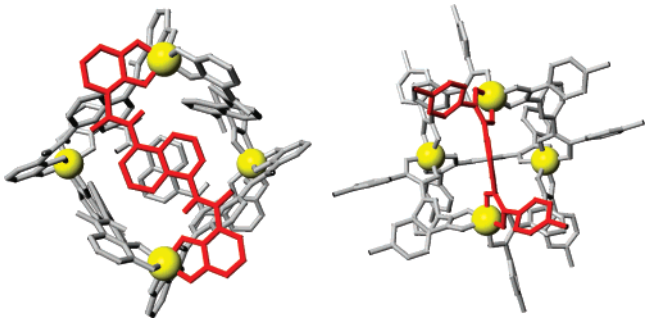

Figure 2. Crystal structures of $[Fe_4\mathbf{1}_6]^{12-}$ and $[Ga_4\mathbf{2}_6]$.[10,21] The C_2 axis is perpendicular to the ligand backbone of **1** but is in the plane of the ligand backbone of **2**.

semblies are composed of *achiral* components, yet form chiral supramolecular structures by virtue of the generation of chiral metal centers. Resolution of such assemblies, which are inherently chiral but contain no carbon stereocenters, can be difficult to achieve. The stereoconfiguration of the metal centers may be dynamic, thereby apparently precluding resolution. In several cases, structures have been resolved in the solid state by cocrystallization with a chiral counterion.[13,14] Spontaneous resolution upon crystallization[15] and chromatographic separation of enantiomers[16] have also been reported for a few assemblies.

Formation of the $[Ga_4\mathbf{1}_6]^{12-}$ tetrahedron relies on the lability of Ga^{III} ligand exchange, so that, out of the myriad of possible linkages, only the thermodynamically favored tetrahedral cluster forms. Yet, resolution of this cluster has been achieved with a chiral counterion, producing enantiomerically pure assemblies free of the resolving agent.[17,18] Given the extensive host−guest and encapsulated reaction chemistry known for this cavity-containing structure,[11,19,20] the potential to effect encapsulated asymmetric reactions is particularly intriguing and is the subject of ongoing investigation. Here we describe the resolution process, providing some evidence as to what factors control this remarkable phenomenon.

Homochiral M_4L_6 Tetrahedra. The chirality of the $[Ga_4\mathbf{1}_6]^{12-}$ tetrahedron (Figure 1, left) results from tris-bidentate coordination of the metal ions, which can each assume either Δ or Λ configuration. Thus, assembly of the $[Ga_4\mathbf{1}_6]^{12-}$ tetrahedron produces a racemic mixture of homochiral (ΛΛΛΛ and ΔΔΔΔ) structures; no other stereoisomers are formed.[10,11] This is in contrast to other M_4L_6 structures such as $[Ga_4\mathbf{2}_6]$ which crystallized as the S_4 symmetric ΔΔΛΛ isomer (Figure 1, right).[21] In solution all possible diastereomers, ΔΔΔΔ, ΔΔΔΛ, ΔΔΛΛ, and their respective enantiomers were observed in a nearly statistical ratio, and the isomers interconvert rapidly.[22]

These two M_4L_6 assemblies highlight the effect of mechanical coupling in supramolecular architectures. The C_2 axis of the bis-hydroxamate ligand **2** is coplanar with its phenyl backbone, and thus the ligand assumes an edge-on configuration with respect to the tetrahedron. In contrast, the C_2 axis of **1** is perpendicular to its naphthyl backbone, and therefore the ligand lies across the edge of $M_4\mathbf{1}_6$. The difference in ligand disposition in these structures can be seen in their crystal structures (Figure 2.)

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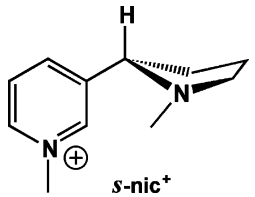

Figure 3. Chiral (*S*)-*N*-methyl-nicotinium (*S*-nic$^+$) cation used in $[M_4\mathbf{1}_6]^{12-}$ resolution.

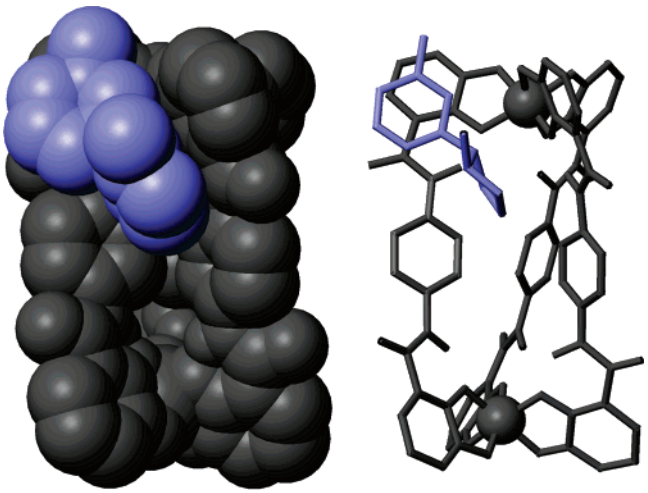

Figure 4. Space filling (left) and cylinder (right) representations of the crystal structure of ΛΛ-K(*S*-nic)$_5$[Ga$_2$**3**$_3$]. For simplicity, only one *S*-nic$^+$ counterion is included.[14]

Figure 2 shows that ligand **2** functions as a true edge of the M_4L_6 structure, whereas ligand **1** truncates the tetrahedral edge. The highlighted ligand of the $M_4\mathbf{2}_6$ structure connects two metal centers of the same chirality, but four of the other ligands of the ΔΔΛΛ structure span metal centers of opposite chirality, requiring that the two chelates of one ligand point to the same side of the ligand. The structure illustrates the ease with which the chelate groups of **2** can pivot on the ligand backbone, as both ligand configurations appear equally accessible. As a metal center of $M_4\mathbf{2}_6$ racemizes, the chelating hydroxamate moiety of **2** is able to twist back and forth without much disruption of the backbone position. In addition, the edge-on ligand orientation of **2** provides more freedom of movement for the ligand backbones within the structure.

In contrast, all six ligands of the $M_4\mathbf{1}_6$ structure adopt the same orientation with the two chelate groups of one ligand pointing in opposite directions. The truncated edge design of the structure inhibits a ligand orientation in which both chelate groups point in the same direction. In order for a metal center of $M_4\mathbf{1}_6$ to racemize, the naphthalene backbone must flip its orientation in the tetrahedral structure by 180°. Since the ligand backbones of $M_4\mathbf{1}_6$ are tightly packed in an edge-to-edge orientation, this motion appears to be impossible. The structural restrictions of the $M_4\mathbf{1}_6$ structure lead to a mechanical coupling (which does not exist in the edge-on $M_4\mathbf{2}_6$ tetrahedron) and enforce both the homochiral configuration of the structure and its inertness to stereoinversion.[23]

Resolution of $[M_4\mathbf{1}_6]^{12-}$ Tetrahedra. The resolution of the $[M_4\mathbf{1}_6]^{12-}$ tetrahedra relies on a specific interaction between the chiral (*S*)-*N*-methyl-nicotinium (*S*-nic$^+$) cation and tris-catecholate metal centers (Figure 3).[14,17,24] When the $[M_4\mathbf{1}_6]^{12-}$ assembly is prepared in methanol solution in the presence of *S*-nic$^+$, the ΔΔΔΔ enantiomer precipitates selectively from solution as the *S*-nic$^+$ salt. After isolation of the ΔΔΔΔ compound by filtration, the solution can be concentrated so that the ΛΛΛΛ compound precipitates with the addition of acetone.

It was determined that the ΔΔΔΔ-$[M_4\mathbf{1}_6]^{12-}$ precipitate can be redissolved in aqueous solution only with the addition of 3 to 4 equiv of strong base (KOH). This observation was verified for the Ga^{III}, Al^{III}, and Fe^{III} analogues and implies that the precipitated complex is multiply protonated. NMR characterization and elemental analysis support the formulation of these complexes as ΔΔΔΔ-KH_3(*S*-nic)$_7$[(*S*-nic) ⊂ $M_4\mathbf{1}_6$], in which K^+, $3H^+$, and 7 *S*-nic$^+$ ions are bound to the host exterior with one *S*-nic$^+$ ion encapsulated in the host cavity. The ΛΛΛΛ compounds have the general formula ΛΛΛΛ-K$_6$(*S*-nic)$_5$[(*S*-nic) ⊂ $M_4\mathbf{1}_6$]. These observations indicate that the stoichiometry of the resolution reaction is best represented as presented in Scheme 1 and suggests that control of the KOH stoichiometry is critical to the resolution process.

The most basic sites of the ΔΔΔΔ-(*S*-nic)$_7$[(*S*-nic) ⊂ $Ga_4\mathbf{1}_6]^{4-}$ complex are the pyrrolidine nitrogens of the *S*-nic$^+$ cations, since the highest pK_a of a Ga^{III} catecholamide complex is approximately 5.2.[25] The protonation constant of the *S*-nicotinium iodide salt, representing conversion of the monocation to the dication, was determined by potentiometric titration to be 6.09(1). Acid titration of a basic solution of the resolved ΔΔΔΔ-(*S*-nic)$_7$[(*S*-nic) ⊂ $Ga_4\mathbf{1}_6]^{4-}$ complex showed that the complex began to precipitate at pH 7.2. The resulting suspension buffered the solution between pH values of 7.1 and 7.2 throughout the addition of approximately 3 equiv of acid. The pK_a of an *S*-nic$^+$ cation ion paired to the assembly might be altered by its local environment, particularly if the protonated form of the pyrrolidine nitrogen points into the tetrahedral structure such that hydrogen bonding to a catecholate or carbonyl oxygen is possible.

The interaction of *S*-nic$^+$ with the $[M_4\mathbf{1}_6]^{12-}$ assemblies is not fully understood, as no crystal structure of the ΔΔΔΔ- KH_3-(*S*-nic)$_7$[(*S*-nic) ⊂ $M_4\mathbf{1}_6$] compounds has been obtained. However, the crystal structure of a smaller assembly, ΛΛ-K(*S*-nic)$_5$[Ga$_2$**3**$_3$] (Figure 4), provides some insight.[14] The π-acidic *S*-nic$^+$ pyridinium rings intercalate between two π-basic catecholate rings of the *fac*-configured tris-bidentate metal complex, while the pyrrolidine ring of *S*-nic$^+$ extends down into the helicate, pushing the ligands to twist in one direction as prescribed by the carbon stereocenter of the cation. The binding affinity of *S*-nic$^+$ for the ΛΛ helicate is approximately six times greater than its affinity for the ΔΔ helicate.[14]

Yet, resolution of the $[M_4\mathbf{1}_6]^{12-}$ structures occurs by way of precipitation of an *S*-nic$^+$ salt of the ΔΔΔΔ enantiomer,[17] suggesting that a different *S*-nic$^+$−assembly interaction is involved. That a number of the *S*-nic$^+$ counterions are protonated to the dication form in the resolved ΔΔΔΔ-(*S*-nic)$_7$[(*S*-nic) ⊂ $M_4\mathbf{1}_6]^{4-}$ salts may indicate that the protonated pyrrolidinium

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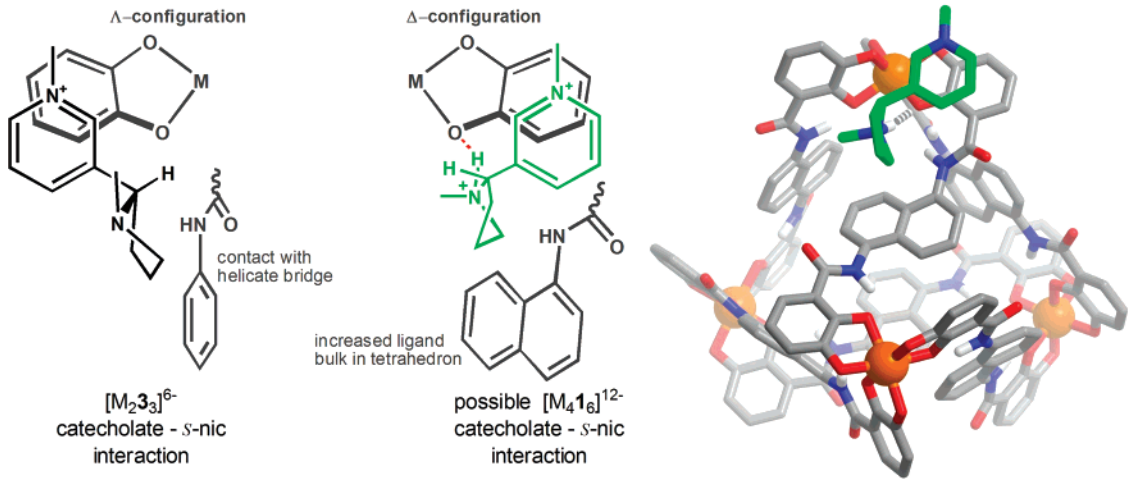

Figure 5. (Left) Simplified representation of the *S*-nic^{+}-$[M_2\mathbf{3}_3]^{6-}$ helicate interaction. (Middle) Proposed *S*-nic^{+} interaction with the $[M_4\mathbf{1}_6]^{12-}$ tetrahedron which might account for pyrrolidine protonation and the differences between the steric demands of the helicate and tetrahedron ligands. A pyrrolidinium−catecholate hydrogen bond is highlighted in red. (Right) Modeled *S*-nicH^{2+}−$[M_4\mathbf{1}_6]^{12-}$ interaction (CAChe, MM3),[27] carbons of the *S*-nicH^{2+} cation are shown in green for clarity.

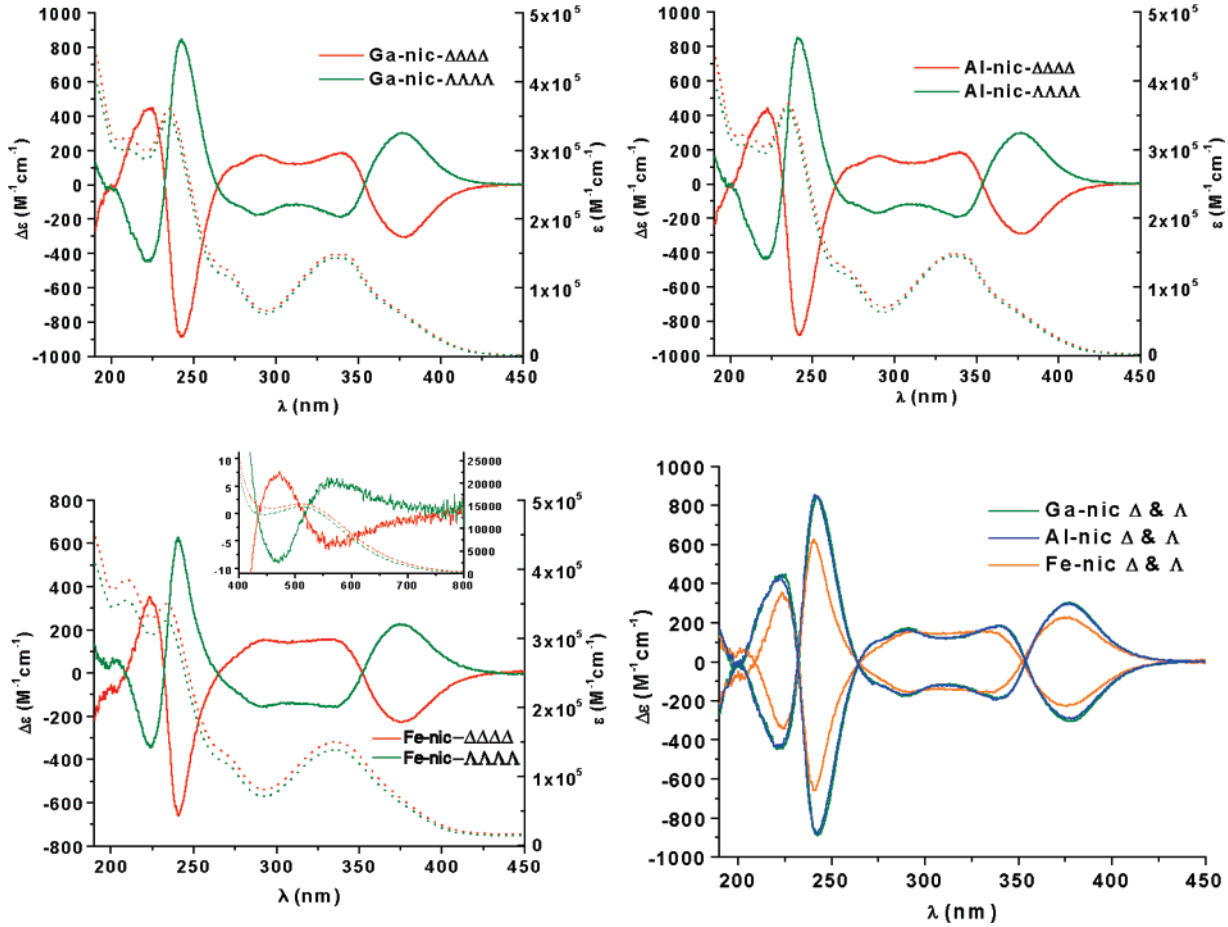

Figure 6. CD (solid lines) and UV−vis (dotted lines) spectra of the *S*-nic^{+} salts of the resolved $[Ga_4\mathbf{1}_6]^{12-}$, $[Al_4\mathbf{1}_6]^{12-}$, and $[Fe_4\mathbf{1}_6]^{12-}$ tetrahedral assemblies.

Scheme 1

$$\mathbf{12}\ H_4\mathbf{1} + \mathbf{8}\ Ga(acac)_3 + \mathbf{14}\ (S\text{-nic})I + \mathbf{21}\ KOH \xrightarrow[MeOH]{} \Lambda\Lambda\Lambda\Lambda\text{-}K_6(S\text{-nic})_6[Ga_4\mathbf{1}_6] + \Delta\Delta\Delta\Delta\text{-}KH_3(S\text{-nic})_8[Ga_4\mathbf{1}_6]_{(ppt)} + \mathbf{24}\ Hacac + \mathbf{21}\ H_2O + \mathbf{14}\ KI$$

nitrogen points into the anionic metal catecholate oxygens in order to hydrogen bond with them, thereby raising the effective pK_a of the pyrrolidinium, as described previously. Assuming that the π-acidic pyridinium ring anchors the cation between catecholate rings in the same manner observed in the helicate structure, interaction with a Δ chirality metal center causes the pyrrolidine nitrogen to point toward the catecholate oxygens, as shown in Figure 5,[26] such that a protonated pyrrolidine nitrogen can hydrogen bond to the catecholate oxygens. In turn, some reorientation of the pyrrolidine ring may be necessary to

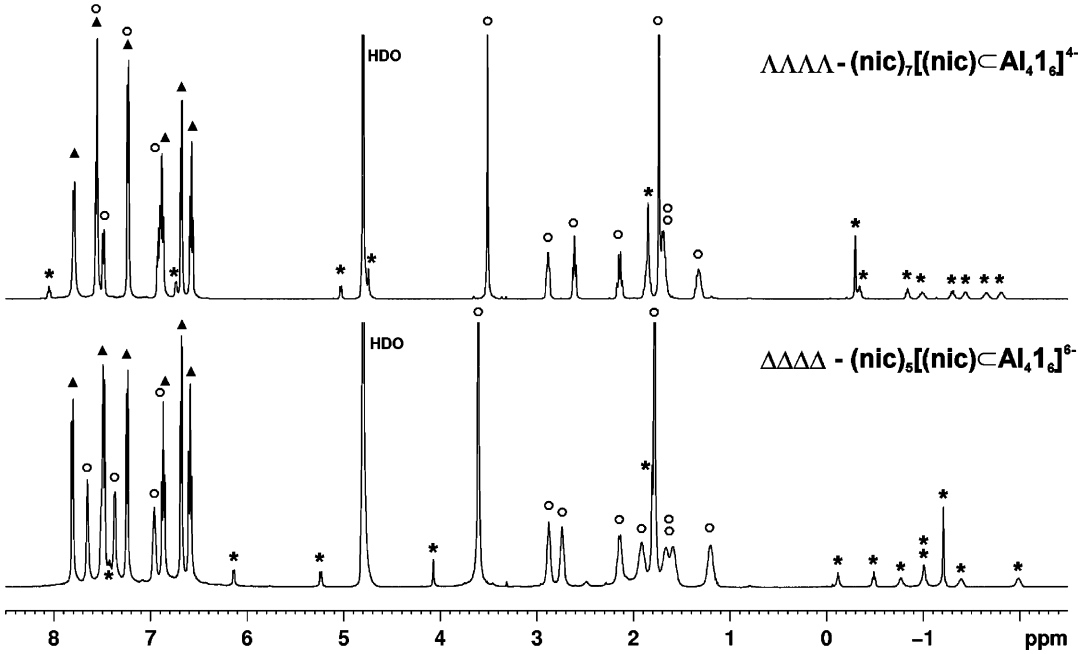

Figure 7. ^{1}H NMR (500 MHz, D_2O) spectra of the ΛΛΛΛ-(*S*-nic)$_7$[(*S*-nic) ⊂ $Al_4\mathbf{1}_6]^{4-}$ and ΔΔΔΔ-(*S*-nic)$_5$[(*S*-nic) ⊂ $Al_4\mathbf{1}_6]^{6-}$ complexes (▲ = host; ○ = exterior *S*-nic$^+$; * = encapsulated *S*-nic$^+$).

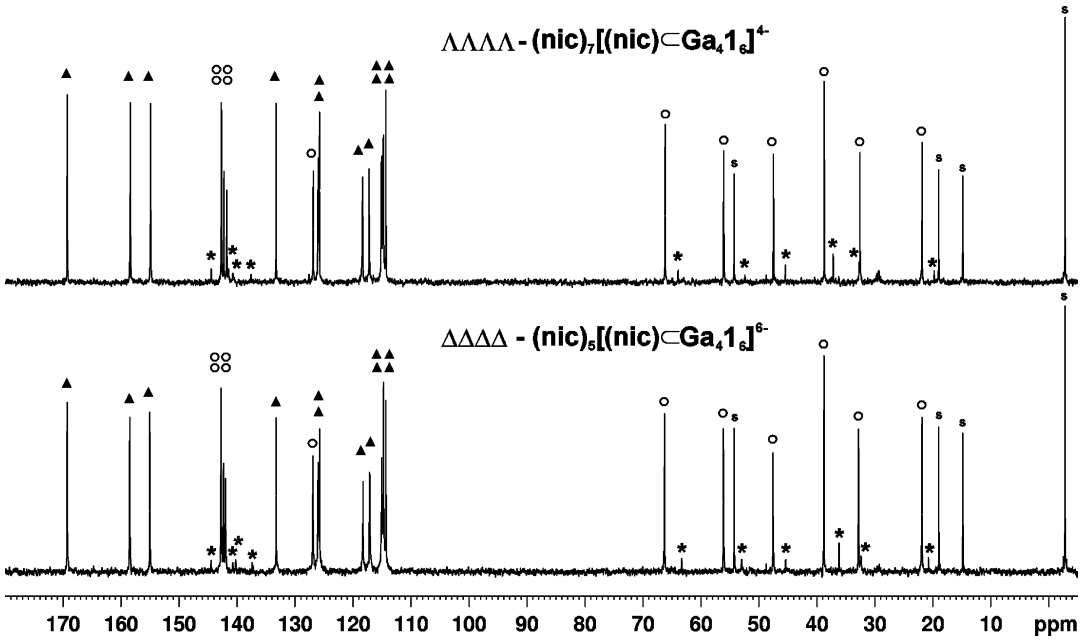

Figure 8. ^{13}C NMR (100 MHz, D_2O) spectra of ΛΛΛΛ-(*S*-nic$^+$)$_7$[(*S*-nic$^+$) ⊂ $Ga_4\mathbf{1}_6]^{4-}$ and ΔΔΔΔ-(*S*-nic)$_5$[(*S*-nic) ⊂ $Ga_4\mathbf{1}_6]^{6-}$ (▲ = host; ○ = exterior *S*-nic$^+$; * = encapsulated *S*-nic$^+$, s = internal standard).

accommodate the increased steric demand of the splayed naphthalene bridges of the $M_4\mathbf{1}_6$ tetrahedron. These factors, combined with solubility differences between the $[M_4\mathbf{1}_6]^{12-}$ tetrahedron and the $[M_2\mathbf{3}_3]^{6-}$ helicate, seem enough to account for the observed resolution phenomenon. Other factors that might influence the *S*-nic$^+$−$M_4\mathbf{1}_6$ interaction include inversion of the pyrrolidine nitrogen or an alternate anchoring of the pyridinium ring with the catecholate aromatic ring.

Nicotinium Salts of Resolved ΔΔΔΔ- and ΛΛΛΛ-$M_4\mathbf{1}_6$ Assemblies. The resolved *S*-nic$^+$ salts of the Ga^{III}, Al^{III}, and Fe^{III} $[M_4\mathbf{1}_6]^{12-}$ tetrahedra were investigated by CD and NMR spectroscopies. Figure 6 contains the CD and UV−vis spectra of each of the resolved species. The UV $\pi-\pi^*$ transitions of the catechol moiety produce a strong exciton couplet from which the absolute configuration of each complex could be determined.[17,28] The CD spectra of the ΔΔΔΔ- and ΛΛΛΛ-(*S*-nic)$_n$-[(*S*-nic) ⊂ $M_4\mathbf{1}_6$] diastereomers are nearly perfect mirror images

(26) An alternative model could involve *S*-nic$^+$ dimers connected by hydrogen bonding (this might better explain the observed stoichiometry of the $M_4\mathbf{1}_6$ resolution): *S*-nic$^+$ dimers might intercalate between $M_4\mathbf{1}_6$ ligands or might link one tetrahedron to another; as was found in *S*-nic$^+$−helicate interactions, the 2D NMR study confirms intercalation of the pyridinium ring into the metal catecholate cap of the structures vertices and orientation of the pyrolidine ring toward the naphthalene backbones. However, no more specific information could be deduced. In addition, base must be added to the solution in order to dissolve the precipitated ΔΔΔΔ complex.

(27) *CAChe Workstation Pro*, 5.04; Fujitsu Limited: 2002.
(28) Ziegler, M.; von Zelewsky, A. *Coord. Chem. Rev.* **1998**, *177*, 257−300.

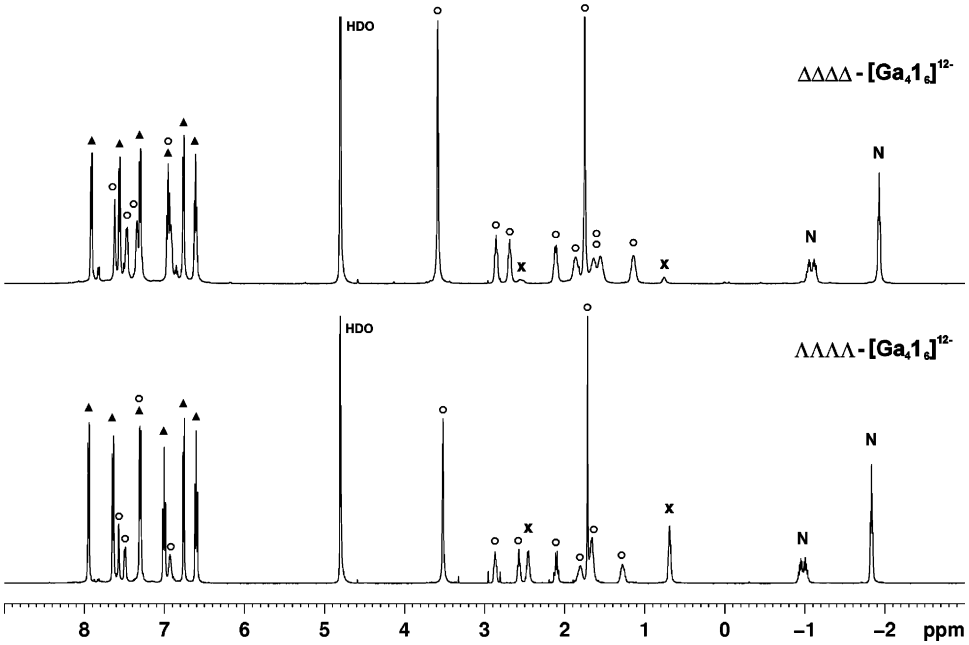

Figure 9. ^{1}H NMR (500 MHz, D_2O) of the *S*-nic$^+$ salts of the resolved [(NEt_4) ⊂ $Ga_4\mathbf{1}_6$]$^{11-}$ enantiomers (▲ = host; ○ = exterior *S*-nic$^+$; N = encapsulated NEt_4^+, x = external NEt_4^+).

of one another, demonstrating their complete separation.[29] In the Fe^{III} spectra, weak CD signals are observed between 440 and 700 nm, corresponding to ligand-to-metal charge-transfer transitions. The decreased intensity of the Fe^{III} bands as compared to those of Ga^{III} and Al^{III} is precedented[30] and is due to the smaller twist angle and thus decreased rotary strength of Fe^{III} tris-catecholate complexes as compared to the tris-catecholate complexes of Ga^{III} and Al^{III}.[31]

The [$M_4\mathbf{1}_6$]$^{12-}$ assemblies contain cavities capable of encapsulating small molecules.[10,11,19] Both ΔΔΔΔ and ΛΛΛΛ assemblies are found to encapsulate 1 equiv of the *S*-nic$^+$ resolving agent. The ΔΔΔΔ-[(*S*-nic) ⊂ $M_4\mathbf{1}_6$]$^{11-}$ and ΛΛΛΛ-[(*S*-nic) ⊂ $M_4\mathbf{1}_6$]$^{11-}$ host−guest complexes are diastereomers, and the *S*-nic$^+$ cation serves as a probe for host stereochemistry by NMR. Chemical shift differences between the two host−guest diastereomers are seen in both the ^{1}H and ^{13}C NMR spectra (Figures 7 and 8). The ^{1}H and ^{13}C data for the Ga^{III} and Al^{III} complexes are compiled in the Supporting Information.

In order to demonstrate that the exterior *S*-nic$^+$ cations are responsible for the resolution of the [$M_4\mathbf{1}_6$]$^{12-}$ assemblies, the cavity of [$Ga_4\mathbf{1}_6$]$^{12-}$ was blocked with a stronger binding guest, NEt_4^+. The resolution reaction was carried out as described previously, except that slightly more than 1 equiv of NEt_4Cl was added to the reaction solution prior to the addition of (*S*-nic)I. The resulting *S*-nic$^+$ salts of the ΔΔΔΔ- and ΛΛΛΛ-[(NEt_4) ⊂ $Ga_4\mathbf{1}_6$]$^{12-}$ enantiomers were isolated and analyzed by CD spectroscopy and ^{1}H NMR . While the ^{1}H NMR spectra show the characteristic 1:1 binding of NEt_4^+ within the tetrahedral assemblies, the CD spectra confirm the separation of the ΔΔΔΔ and ΛΛΛΛ enantiomers (Figures 9 and 10), demonstrating that the interaction of the *S*-nic$^+$ cation with the assembly interior does not play a role in the assembly resolution.

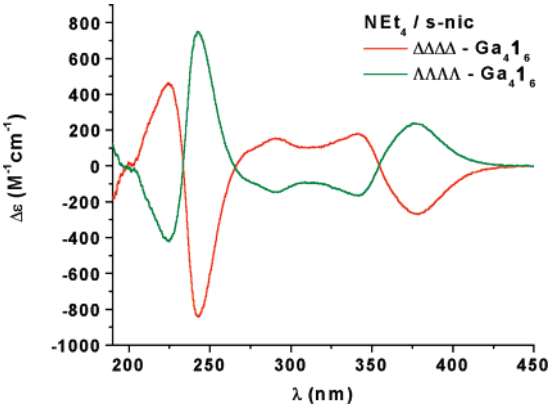

Figure 10. CD spectra of the *S*-nic$^+$ salts of the resolved [(NEt_4) ⊂ $Ga_4\mathbf{1}_6$]$^{11-}$ enantiomers.

Ammonium Salts of Resolved ΔΔΔΔ- and ΛΛΛΛ-$M_4\mathbf{1}_6$ Assemblies. Removal of the *S*-nic$^+$ resolving agent was accomplished by cation exchange chromatography under basic conditions (0.01 M KOH) in order to inhibit assembly racemization. Replacement of *S*-nic$^+$ by both NEt_4^+ and NMe_4^+ was achieved, and the resulting [$M_4\mathbf{1}_6$]$^{12-}$ complexes were found to contain between 11 and 12 equiv of NR_4^+ with a K^+ occasionally substituting for an alkyl ammonium cation. No residual *S*-nic$^+$ was detected by ^{1}H NMR for the Al^{III} or Ga^{III} assemblies, and the spectra for the NEt_4^+ salts of the resolved tetrahedral resemble that reported for the unresolved [(NEt_4) ⊂ $Ga_4\mathbf{1}_6$]$^{11-}$ host−guest complex. (Small chemical shift differences are observed due to differences in the number of exterior counterions.)

(29) *S*-nic$^+$ itself has negligible CD intensity in this wavelength region, and any specific effect it might have on the ΔΔΔΔ-host structure is disrupted by the addition of base necessary to solubilize the *S*-nic$^+$ ΔΔΔΔ-$M_4\mathbf{1}_6$ salt.

(30) Tor, Y.; Shanzer, A.; Scherz, A. *Inorg. Chem.* **1990**, *29*, 4096−4099.
(31) Borgias, B. A.; Barclay, S. J.; Raymond, K. N. *J. Coord. Chem.* **1986**, *15*, 109−123. Karpishin, T. B.; Stack, T. D. P.; Raymond, K. N., *J. Am. Chem. Soc.* **1993**, *115*, 182−192. Kepert, D. L. *Inorganic Sterochemistry*; Springer-Verlag: Berlin, 1982. The differences in CD intensity imply that the $M_4\mathbf{1}_6$ framework can accommodate some range of tris-catecholate twist. Structures of the previously reported [$Ge_4\mathbf{1}_6$]$^{8-}$, for example, would be expected to demonstrate greater tris-catecholate twist. Twist differences are likely accommodated by distortions in the ligand amide junctions.

Table 1. Summary of $[M_4\mathbf{1}_6]^{12-}$ CD Data[a]

complex	Ga^{III}	Al^{III}	Fe^{III}
ΔΔΔΔ-(*S*-nic)$_6$[$M_4\mathbf{1}_6$]$^{6-}$	225 (+448); 242 (−889); 291 (+173); 340 (+187), 379 (−306)	223 (+443); 242 (−883); 290 (+165); 339 (+187); 378 (−292)	223 (+356); 241 (−659); 292 (+155); 339 (+146); 376 (+228); 468 (+7); 565 (−6)
ΛΛΛΛ-(*S*-nic)$_8$[$M_4\mathbf{1}_6$]$^{4-}$	221 (−448); 243 (+848); 288 (−177); 339 (−190); 377 (+304)	221 (−437); 241 (+854); 288 (−170); 337 (−194); 377 (+298)	224 (−344); 241 (+627); 292 (−157); 337 (−159); 375 (+228); 468 (−8); 565 (+6)
ΔΔΔΔ-$(NEt_4)_{12}$[$M_4\mathbf{1}_6$]	225 (+664); 241 (−1102); 290 (+223); 340 (+230); 375 (−329)	225 (+701); 242 (−1173); 290 (+219); 339 (245); 375 (−339)	225 (+544); 241 (−869); 293 (+198); 337 (+191); 374 (−253); 465 (8); 560 (−7)
ΛΛΛΛ-$(NEt_4)_{12}$[$M_4\mathbf{1}_6$]	225 (−655); 242 (+1086); 290 (−216); 341 (−230); 375 (+330)	225 (−620); 242 (+1050); 289 (−197); 341(−225); 376 (+302)	225 (−583); 241 (+927); 292 (−212); 337 (−204); 371 (+267); 465 (−8); 560 (+7)
ΔΔΔΔ-$(NMe_4)_{12}$[$M_4\mathbf{1}_6$]	222 (+485); 241 (−870); 289 (+173); 338 (+194); 372 (−265)	n.d.	n.d.
ΛΛΛΛ-$(NMe_4)_{12}$[$M_4\mathbf{1}_6$]	223 (−473); 241 (+850); 288 (−179); 337 (−192); 373 (+267)	n.d.	n.d.

[a] Sample concentrations were 0.5 mM and were prepared in 5 mM KOH solution (n.d. = not determined).

CD spectra of the NEt_4^+ salts of the resolved $[M_4\mathbf{1}_6]^{12-}$ complexes demonstrate that they retain their enantiopurity throughout the ion exchange process (Table 1).[32] The basic (5 mM KOH) 0.5 mM solutions were stored under nitrogen for 45 days and then remeasured to reveal CD signals at least 80% as intense as those initially measured for the Ga^{III} and Al^{III} compounds, while the Fe^{III} complexes retained no CD activity after 45 days. Subsequent heating of the Ga^{III} samples to 75 °C for 24 h had no effect on the observed CD spectra (Figure 11).

Similar observations were made for the tetramethylammonium salts ΔΔΔΔ- and ΛΛΛΛ-$(NMe_4)_{11}$[$NMe_4 \subset Ga_4\mathbf{1}_6$]. These complexes were obtained in a fashion similar to that of the tetraethylammonium salts, through ion exchange chromatography. Again, no significant loss of optical activity was observed after the ion exchange process, and solutions of the complexes retained their chirality for extended periods of time (retention of >90% optical activity after 30 days at room temperature).

Resolved "Empty" ΔΔΔΔ- and ΛΛΛΛ-$M_4\mathbf{1}_6$ Assemblies. Even though encapsulated NMe_4^+ is usually easily replaced by other guest molecules, the use of the resolved $(NMe_4^+)_{12}$ $M_4\mathbf{1}_6$ assemblies has its limitations. Some guest molecules of interest (such as substrates for encapsulated reaction chemistry) have similarly low binding constants, and full replacement of NMe_4^+ is not possible in those cases. In light of this consideration, we sought to obtain the K^+_{12} salts of the resolved assemblies, starting from the ΔΔΔΔ-$(NMe_4)_{11}$[$NMe_4 \subset Ga_4\mathbf{1}_6$] and ΛΛΛΛ-$(NMe_4)_{11}$[$NMe_4 \subset Ga_4\mathbf{1}_6$] products, and replacing NMe_4^+ with K^+. Ion exchange chromatography turned out to be problematic, and the best protocol to replace NMe_4^+ with K^+ is in basic methanol solution with a very large excess of KI. As in the previous ion exchange reactions, the chirality of the supramolecular assemblies ΔΔΔΔ-K_{12}[$Ga_4\mathbf{1}_6$] and ΛΛΛΛ-K_{12}[$Ga_4\mathbf{1}_6$] is retained throughout the ion exchange process.

(32) The CD bands for the NEt_4^+ salts of the resolved tetrahedra are clearly more intense (~20%) than those of the *S*-nic$^+$ analogues. This was true for both enantiomers of each metal complex and cannot be attributed to experimental error. The NEt_4^+ cations interact strongly with the assembly and may affect its structure. In contrast, the CD spectra of the NMe_4^+ salts of the resolved assemblies are less intense than those of the *S*-nic$^+$ salts.

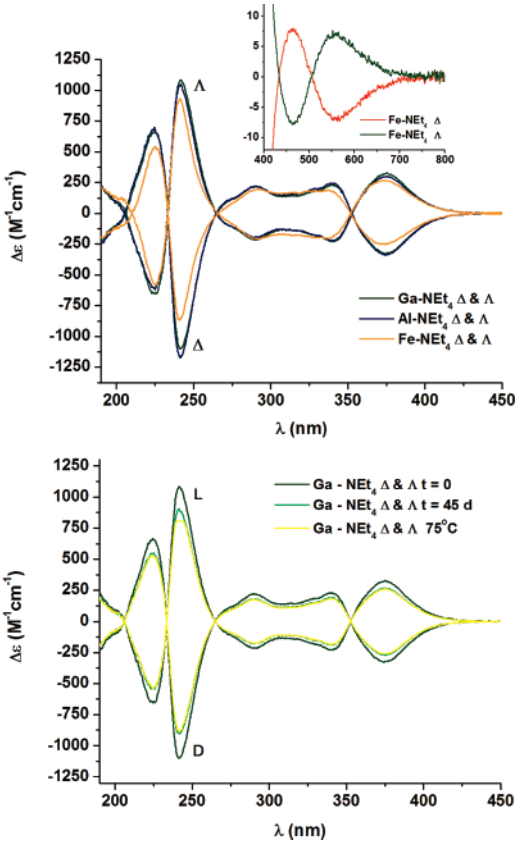

Figure 11. (Top) CD spectra of the NEt_4^+ salts of the ΔΔΔΔ- and ΛΛΛΛ-enantiomers of $[Ga_4\mathbf{1}_6]^{12-}$, $[Al_4\mathbf{1}_6]^{12-}$, and $[Fe_4\mathbf{1}_6]^{12-}$. (Bottom) CD spectra of the Ga^{III} compounds taken immediately after preparation of the 0.5 mM solution, after 45 days, and then after 24 h of heating to 75 °C.

Significantly, the resolved "empty" (or guest-free) structures are much less robust. Neutral solutions of ΛΛΛΛ-K_{12}[$Ga_4\mathbf{1}_6$] in water and methanol showed decay of CD activity over the course of an hour (Figure 12). Addition of base (5 mM KOH) to those solutions resulted in considerable stabilization of the chiral structure, presumably by preventing proton catalyzed dissociation of the catechol amide ligands.

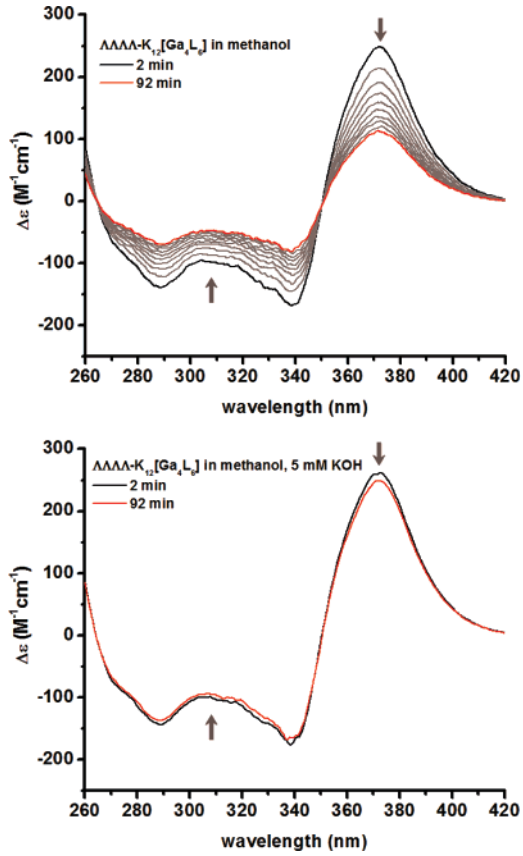

Figure 12. (Top) CD spectra of ΛΛΛΛ-$K_{12}[Ga_4\mathbf{1}_6]$, monitored in MeOH at 10 min intervals. (Bottom) CD spectra of ΛΛΛΛ-$K_{12}[Ga_4\mathbf{1}_6]$ in MeOH with 5 mM KOH. Spectra were recorded at 10 min intervals.

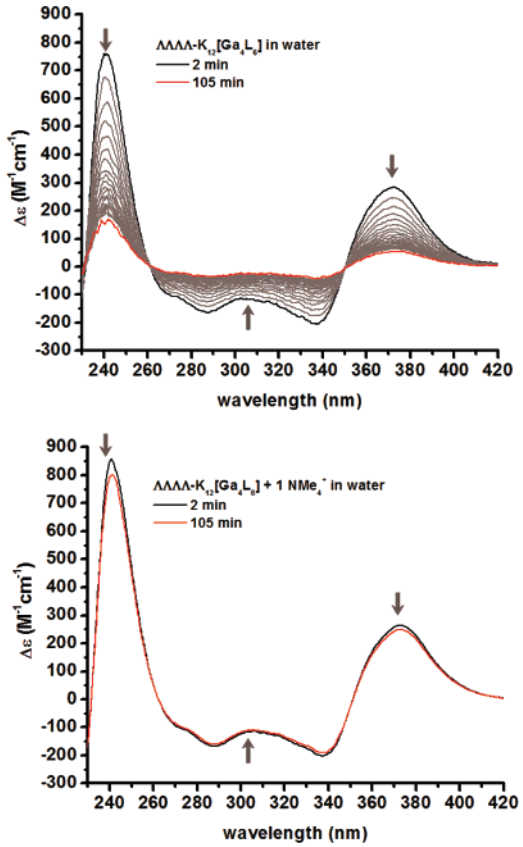

Figure 13. (Top) CD spectra of ΛΛΛΛ-$K_{12}[Ga_4\mathbf{1}_6]$, monitored at neutral pH in H_2O. Spectra were taken in 5 min intervals. (Bottom) CD spectra of ΛΛΛΛ-$K_{12}[Ga_4\mathbf{1}_6]$ in the presence of 1 equiv of NMe_4^+, monitored at neutral pH in H_2O.

Stabilization of the labile "empty" assemblies could also be achieved by the addition of a guest molecule. Remarkably, the addition of only 1 equiv of NMe_4^+ slows racemization (or decomposition) significantly (Figure 13).

Thus the ΔΔΔΔ-$K_{12}[Ga_4\mathbf{1}_6]$ and ΛΛΛΛ-$K_{12}[Ga_4\mathbf{1}_6]$ assemblies, when used in basic medium or in conjunction with 1 equiv of NMe_4^+, provide an important platform for applications in chiral catalysis and/or chiral resolutions, as they are thermodynamically accessible to guests of moderate binding strength (stronger than NMe_4^+).

Conclusion. Examination of the resolution of $M_4\mathbf{1}_6$ tetrahedral reveals that the process is proton dependent and relies on interactions of the chiral *S*-nic$^+$ counterion with the exterior of the anionic host. Unlike in the *S*-nic$^+$ interaction with smaller helicate structures in which association with the ΛΛ-M_2L_3 enantiomer is stronger, here the protonated ΔΔΔΔ-KH_3(*S*-nic)$_7$-[(*S*-nic) ⊂ $Ga_4\mathbf{1}_6$] salt precipitates, separating it from the soluble ΛΛΛΛ-K_6(*S*-nic)$_5$[(*S*-nic) ⊂ $Ga_4\mathbf{1}_6$]. This phenomenon highlights the complexity of supramolecule properties and the challenge in predicting or planning the solution behavior of such structures. The exchange of the resolving *S*-nic$^+$ agents for achiral guests and the subsequent stability of the chiral supramolecular framework powerfully demonstrate the robustness of the structure, while the ability to create resolved $M_4\mathbf{1}_6$ salts of weakly or non-binding guests is critical to the development of asymmetrically influenced encapsulated chemistries.

Experimental Section

General. ^{1}H NMR spectra were recorded on a Bruker DRX 500 MHz spectrometer, while ^{13}C NMR spectra were recorded on a Bruker 400 MHz spectrometer. Circular dichroism spectra were measured with a JASCO J-810 spectrapolarimeter. A Varian Cary 300 spectrophotometer was used to collect UV−vis spectra. Elemental analyses were performed at the UCB Analytical Facility. Potassium analyses were performed by Desert Analytics. Compounds $H_4\mathbf{1}$[10] and *N*-methylnicotinium iodide[33] were synthesized as previously reported.

General Procedure for [(*S*-nic) ⊂ $M_4\mathbf{1}_6$]$^{11-}$ Resolution. Ligand $H_4\mathbf{1}$ (6 equiv) was suspended in methanol and degassed. To this solution were added 11 equiv of KOH as a 0.50 M solution in methanol followed by 4 equiv of the metal as the tris-acetylacetonate complex. *S*-nic$^+$ iodide (12 equiv) was dissolved in a few milliliters of methanol and then added to the reaction solution. The solution was degassed again and left to stir at room temperature under a nitrogen atmosphere over night. The gallium and aluminum reaction solutions turned from yellow to orange with the addition of nicotinium. No color change was perceptible in the already dark red iron reaction. A precipitate usually formed during the first 30 min of the reaction; this was the ΔΔΔΔ-KH_3(*S*-nic)$_7$[(*S*-nic) ⊂ $M_4\mathbf{1}_6$] compound and was isolated by filtration, washed with methanol, and dried at 60 °C under vacuum. The remaining methanol solution was concentrated to a volume of a few milliliters, and the ΛΛΛΛ-K_6(*S*-nic)$_5$[(*S*-nic) ⊂ $M_4\mathbf{1}_6$] compound could be isolated by precipitation with acetone and filtration. These compounds were also dried at 60 °C under vacuum. NMR data for all nicotinium-resolved compounds are presented in Tables 1 and 2. Yields are based on the total M(acac)$_3$ used and are calculated separately for each stereo-

(33) Seemann, J. I.; Whidby, J. F. *J. Org. Chem.* **1976**, *41*, 3824−3826.

isomer. ^{1}H and ^{13}C NMR data for the Ga^{III} and Al^{III} *S*-nic$^+$ salts of ΔΔΔΔ- and ΛΛΛΛ-M_4**1**$_6$ assemblies are compiled in the Supporting Information.

ΔΔΔΔ-KH$_3$(*S*-nic)$_7$[(*S*-nic) ⊂ Ga$_4$1$_6$]. The gallium complexes were prepared from H_4**1** (303 mg, 0.704 mmol), $Ga(acac)_3$ (172 mg, 0.469 mmol), (*S*-nic)I (426.6 mg, 1.407 mmol), and 0.50 M KOH (2.58 mL, 1.29 mmol). Yield: 223 mg (42%). Anal. Calcd (Found) for $KGa_4C_{232}H_{223}N_{28}O_{36}\cdot 3H_2O$: C, 64.04 (64.00); H, 5.30 (4.95); N, 9.01 (8.63); K, 0.86 (1.26).

ΛΛΛΛ-K$_6$(*S*-nic)$_6$[(*S*-nic) ⊂ Ga$_4$1$_6$]. Yield: 220 mg (43%). Anal. Calcd (Found) for $K_6Ga_4C_{210}H_{186}N_{24}O_{36}\cdot 2H_2O$: C, 60.47 (60.52); H, 4.59 (4.53); N, 8.06 (7.75); K, 5.37 (5.01).

ΔΔΔΔ-KH$_3$(*S*-nic)$_7$[(*S*-nic) ⊂ Al$_4$1$_6$]. The aluminum complexes were prepared from H_4**1** (152 mg, 0.353 mmol), $Al(acac)_3$ (74.2 mg, 0.229 mmol), (*S*-nic)**I** (208.1 mg, 0.686 mmol), and 0.50 M KOH (1.29 mL, 0.648 mmol). Yield: 115.4 mg (45.7%). Anal. Calcd (Found) for $KAl_4C_{232}H_{223}N_{28}O_{36}\cdot 4H_2O$: C, 66.37 (66.55); H, 5.55 (5.13); N, 9.34 (8.64).

ΛΛΛΛ-K$_6$(*S*-nic)$_6$[(*S*-nic) ⊂ Al$_4$1$_6$]. Yield: 108 mg (47%). Anal. Calcd (Found) for $K_6Al_4C_{210}H_{186}N_{24}O_{36}$: C, 63.62 (63.56); H, 4.73 (4.74); N, 8.48 (8.19).

ΔΔΔΔ-H$_4$(*S*-nic)$_7$[(*S*-nic) ⊂ Fe$_4$1$_6$]. The iron complexes were prepared from H_4**1** (152 mg, 0.352 mmol), $Fe(acac)_3$ (81.0 mg, 0.229 mmol), (*S*-nic)I (209 mg, 0.689 mmol), and 0.50 M KOH (1.29 mL, 0.645 mmol). Yield: 106 mg (41%). Anal. Calcd (Found) for $KFe_4C_{232}H_{223}N_{28}O_{36}\cdot 5H_2O$: C, 64.32 (64.39); H, 5.42 (4.96); N, 9.05 (8.44); K, 0.90 (1.29).

ΛΛΛΛ-K$_6$(*S*-nic)$_6$[(*S*-nic) ⊂ Fe$_4$1$_6$]. Yield: 99.1 mg (40%). Anal. Calcd (Found) for $K_6Ga_4C_{210}H_{186}N_{24}O_{36}\cdot H_2O$: C, 61.82 (61.52); H, 4.60 (4.45); N, 8.24 (8.25); K, 5.39 (5.67).

General Procedure for NEt$_4^+$ Ion Exchange. The exchange of NEt_4^+ for *S*-nic$^+$ was accomplished by cation exchange chromatography, using DOWEX 50WX2-200 ion exchange resin. The resin was soaked overnight in methanol and rinsed thoroughly with methanol and water before the column was packed with approximately 200 mL of the wet resin. The column was then washed with alternating 1 L aliquots of 1 M HCl and KOH, before loading it with 0.4 M NEt_4Cl in an aqueous solution of 0.01 M KOH. Approximately 60 mg of each compound (0.011 to 0.014 mmol) were loaded on the column and eluted with 0.1 M KOH. Slow elution was critical to complete ion exchange. The aqueous fractions collected were dried by rotary evaporation and redissolved in approximately 2 mL of methanol. The NEt_4^+ product compounds were then precipitated with acetone, filtered, and dried at 60 °C under vacuum. The NEt_4^+ compounds were isolated in yields of 85−98%.

ΔΔΔΔ-(NEt$_4$)$_{11}$[(NEt$_4$) ⊂ Ga$_4$1$_6$]. ^{1}H NMR (500 mHz, D_2O): δ 13.68 (s, 12H, N*H*), 8.11 (d, J = 7.8 Hz, 12H, Ar$_n$*H*), 7.87 (d, J = 8.4 Hz, 12H, Ar$_n$*H*), 7.29 (d, J = 8.3 Hz, 12H, Ar$_c$*H*), 7.16 (t, J = 7.9 Hz, 12H, Ar$_n$*H*), 6.72 (d, J = 6.1 Hz, 12H, Ar$_c$*H*), 6.58 (d, J = 7.8 Hz, 12H, Ar$_c$*H*), 2.69 (q, J = 7.1 Hz, 88H, CH_2), 0.86 (t, J = 6.2 Hz, 132H, CH_3), −0.75 (m, 8H, CH_2), −1.63 (t, J = 7.1 Hz, 12H, CH_3). Anal. Calcd (Found) for $Ga_4C_{240}H_{324}N_{24}O_{36}\cdot 16H_2O$: C, 61.48 (61.53); H, 7.65 (7.44); N, 7.19 (7.02).

ΛΛΛΛ-K(NEt$_4$)$_{10}$[(NEt$_4$) ⊂ Ga$_4$1$_6$]. ^{1}H NMR (500 mHz, D_2O): δ 13.66 (s, 12H, N*H*), 8.11 (d, J = 7.6 Hz, 12H, Ar$_n$*H*), 7.87 (d, J = 7.7 Hz, 12H, Ar$_n$*H*), 7.29 (d, J = 8.0 Hz, 12H, Ar$_c$*H*), 7.16 (t, J = 7.6 Hz, 12H, Ar$_n$*H*), 6.72 (d, J = 7.0 Hz, 12H, Ar$_c$*H*), 6.59 (d, J = 7.8 Hz, 12H, Ar$_c$*H*), 2.65 (q, J = 7.2 Hz, 80H, CH_2), 0.83 (t, J = 6.8 Hz, 120H, CH_3), −0.75 (m, 8H, CH_2), −1.63 (t, J = 6.9 Hz, 12H, CH_3). Anal. Calcd (Found) for $KGa_4C_{232}H_{304}N_{23}O_{36}\cdot 14H_2O$: C, 61.09 (60.83); H, 7.31 (7.24); N, 7.09 (6.97).

ΔΔΔΔ-(NEt$_4$)$_{11}$[(NEt$_4$) ⊂ Al$_4$1$_6$]. ^{1}H NMR (500 mHz, D_2O): δ 13.51 (s, 12H, N*H*), 8.11 (d, J = 7.3 Hz, 12H, Ar$_n$*H*), 7.86 (d, J = 8.1 Hz, 12H, Ar$_n$*H*), 7.25 (d, J = 8.1 Hz, 12H, Ar$_c$*H*), 7.18 (t, J = 7.8 Hz, 12H, Ar$_n$*H*), 6.64 (d, J = 6.6 Hz, 12H, Ar$_c$*H*), 6.57 (d, J = 7.7 Hz, 12H, Ar$_c$*H*), 2.65 (br q, 88H, CH_2), 0.83 (br t, 132H, CH_3), −0.82 (m, 8H, CH_2), −1.66 (t, J = 7.0 Hz, 12H, CH_3). Anal. Calcd. (Found) for $Al_4C_{240}H_{324}N_{24}O_{36}\cdot 20H_2O$: C, 62.81 (62.85); H, 7.99 (7.62); N, 7.32 (7.09).

ΛΛΛΛ-K(NEt$_4$)$_{10}$[(NEt$_4$) ⊂ Al$_4$1$_6$]. ^{1}H NMR (500 mHz, D_2O): δ 13.51 (s, 12H, N*H*), 8.11 (d, J = 7.3 Hz, 12H, Ar$_n$*H*), 7.86 (d, J = 7.3 Hz, 12H, Ar$_n$*H*), 7.25 (d, J = 7.3 Hz, 12H, Ar$_c$*H*), 7.18 (t, J = 7.9 Hz, 12H, Ar$_n$*H*), 6.64 (d, J = 6.4 Hz, 12H, Ar$_c$*H*), 6.57 (d, J = 7.8 Hz, 12H, Ar$_c$*H*), 2.65 (q, J = 7.2 Hz, 80H, CH_2), 0.83 (t, J = 7.0 Hz, 120H, CH_3), −0.81 (m, 8H, CH_2), −1.66 (t, J = 7.1 Hz, 12H, CH_3). Anal. Calcd (Found) for $KAl_4C_{232}H_{304}N_{23}O_{36}\cdot 12H_2O$: C, 64.00 (64.02); H, 7.59 (7.63); N, 7.40 (7.08).

ΔΔΔΔ-(NEt$_4$)$_{11}$[(NEt$_4$) ⊂ Fe$_4$1$_6$]. Anal. Calcd (Found) for $Fe_4C_{240}H_{324}N_{24}O_{36}\cdot 16H_2O$: C, 62.22 (62.36); H, 7.74 (7.66); N, 7.26 (7.01).

ΛΛΛΛ-K(NEt$_4$)$_{10}$[(NEt$_4$) ⊂ Fe$_4$1$_6$]. Anal. Calcd (Found) for $KFe_4C_{232}H_{304}N_{23}O_{36}\cdot 13H_2O$: C, 62.09 (62.02); H, 7.41 (7.17); N, 7.18 (6.96).

General Procedure for NMe$_4^+$ Ion Exchange. The exchange of NMe_4^+ for *S*-nic$^+$ was accomplished by cation exchange chromatography, using DOWEX 50WX2-200 ion exchange resin. The procedure is the same as that described for NEt_4^+ exchange, only that the column was loaded with 0.5 M NMe_4Cl in an aqueous solution of 0.01 M KOH. The NMe_4^+ compounds were isolated in yields of 84−95%.

ΔΔΔΔ-(NMe$_4$)$_{11}$[NMe$_4$ ⊂ Ga$_4$1$_6$]. ^{1}H NMR (500 MHz, D_2O): δ 13.47 (s, 12H, N*H*), 7.89 (m, ^3J = 7.7 Hz, 12H, napht-H), 7.87 (d, ^3J = 7.6 Hz, 12H, napht-H), 7.28 (d, ^3J = 8.3 Hz, 12H, cat-H), 7.14 (t, ^3J = 8.0 Hz, 12H, napht-H), 6.75 (d, ^3J = 7.2 Hz, 12H, cat-H), 6.60 (t, ^3J = 7.7 Hz, 12H, cat-H), 2.80 (s, br, 132 H, NMe_4, ext.), −0.62 (s, br, 12H, NMe_4, int.) ppm. Anal. Calcd (Found) for $Ga_4C_{192}H_{228}N_{24}O_{36}\cdot 18H_2O$: C, 56.92 (56.81); H, 6.57 (6.64); N, 8.30 (8.27).

ΛΛΛΛ-(NMe$_4$)$_{11}$[NMe$_4$ ⊂ Ga$_4$1$_6$]. ^{1}H NMR (500 MHz, D_2O): δ 13.47 (s, 12H, N*H*), 7.89 (m, ^3J = 7.7 Hz, 12H, napht-H), 7.87 (d, ^3J = 7.6 Hz, 12H, napht-H), 7.28 (d, ^3J = 8.1 Hz, 12H, cat-H), 7.14 (t, ^3J = 8.0 Hz, 12H, napht-H), 6.75 (d, ^3J = 7.2 Hz, 12H, cat-H), 6.60 (t, ^3J = 7.6 Hz, 12H, cat-H), 2.79 (s, br, 132 H, NMe_4, ext.), −0.62 (s, br, 12H, NMe_4, int.) ppm. Anal. Calcd (Found) for $Ga_4C_{192}H_{228}N_{24}O_{36}\cdot 18H_2O$: C, 56.92 (56.98); H, 6.57 (6.76); N, 8.30 (8.41).

General Procedure for K$^+$ Ion Exchange. The exchange of NMe_4^+ for K^+ was conducted in methanolic solution in the presence of a large excess of K^+. Between 95 and 103 mg of ΛΛΛΛ-(NMe$_4$)$_{11}$[NMe$_4$ ⊂ Ga$_4$**1**$_6$] or ΔΔΔΔ-(NMe$_4$)$_{11}$[NMe$_4$ ⊂ Ga$_4$**1**$_6$] (25.2−27.3 μM) were dissolved in 200 mL of methanol. To the yellow solution were added 5 mL of 0.5 M KOH in methanol and 10 g of KI. The solution was degassed and stirred at ambient temperature for 24 h. The volume of the solution was reduced by rotary evaporation to approximately 5 mL, which caused precipitation of a solid, presumably KI. The resulting suspension was filtered. The product was precipitated from the filtrate through addition of ∼200 mL of acetone. The light yellow precipitate was filtered off under a nitrogen stream and dried in vacuo overnight. The K^+ compounds were isolated in 36−41% yields.

ΔΔΔΔ-K$_{12}$[Ga$_4$1$_6$]. ^{1}H NMR (500 MHz, MeOH-d_4): δ 13.62 (s, 12H, N*H*), 8.06 (d, ^3J = 7.6 Hz, 12H, napht-H), 7.84 (d, ^3J = 8.5 Hz, 12H, napht-H), 7.26 (d, ^3J = 8.1 Hz, 12H, cat-H), 7.06 (t, ^3J = 7.9 Hz, 12H, napht-H), 6.67 (d, ^3J = 7.4 Hz, 12H, cat-H), 6.38 (d, ^3J = 7.9 Hz, 12H, cat-H) ppm. Anal. Calcd (Found) for $K_{12}Ga_4C_{144}H_{84}N_{12}O_{36}\cdot 16H_2O$: C, 48.12 (48.13); H, 3.25 (3.61); N, 4.68 (4.67).

ΛΛΛΛ-K$_{12}$[Ga$_4$1$_6$]. ^{1}H NMR (500 MHz, MeOH-d_4): δ 13.62 (s, 12H, N*H*), 8.07 (d, ^3J = 7.6 Hz, 12H, napht-H), 7.83 (d, ^3J = 8.5 Hz, 12H, napht-H), 7.25 (d, ^3J = 8.2 Hz, 12H, cat-H), 7.06 (t, ^3J = 7.9 Hz, 12H, napht-H), 6.67 (d, ^3J = 7.3 Hz, 12H, cat-H), 6.38 (d, ^3J = 7.9 Hz, 12H, cat-H) ppm. Anal. Calcd (Found) for $K_{12}Ga_4C_{144}H_{84}N_{12}O_{36}\cdot 16H_2O$: C, 48.12 (48.10); H, 3.25 (3.44); N, 4.68 (4.79).

Potentiometric Titration of *S*-nic$^+$ Iodide. The protonation constant for *S*-nic$^+$ iodide was determined in three potentiometric experiments.

A standard electrode calibration technique was used.[34] For each experiment 100.0 mL of electrolyte (0.1 M KCl) was combined with a weighed portion of *S*-nic$^+$ iodide (giving concentrations of 0.25, 0.37, and 0.37 mM). Each solution was titrated twice, first against 0.1 M KOH from pH 4 to 8 and then in reverse against 0.1 M HCl to return to pH 4. This gave six titrations with approximately 20 points collected for each. The results from each pair of titrations were combined for nonlinear least-squares refinement with the program HYPERQUAD,[35] giving the value and standard deviation for the protonation constant, 6.09(1).

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Supporting Information Available: CD spectra of ΔΔΔΔ- and ΛΛΛΛ-$(NMe_4)_{11}[NMe_4 \subset Ga_4\mathbf{1}_6]$ at $t = 0$ and 30 days; CD spectra of the NEt_4^+ salts of ΔΔΔΔ- and ΛΛΛΛ-$[Al_4\mathbf{1}_6]$ at 45 days. ^{1}H and ^{13}C NMR data for the Ga^{III} and Al^{III} *S*-nic$^+$ salts of ΔΔΔΔ- and ΛΛΛΛ-$M_4\mathbf{1}_6$ assemblies. HCl titration of ΔΔΔΔ-$(S\text{-nic})_7[(S\text{-nic}) \subset Ga_4\mathbf{1}_6]^{4-}$; potentiometric titration of *S*-nic$^+$ iodide. This material is available free of charge via the Internet at http://pubs.acs.org.

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