Encapsulation and Stabilization of Reactive Aromatic Diazonium Ions and the Tropylium Ion Within a Supramolecular Host‡


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Supramolecular assemblies with internal cavities are being developed as nanoscale reaction vessels to protect or modify the reactivity of guest species through encapsulation. Diazonium cations and the tropylium cation were examined for their ability to encapsulate in the tetrahedral [Ga₄L₆]¹²⁻ supramolecular assembly. The 4-(diethylamino)benzenediazonium cation 1 readily formed a 1:1 host–guest complex with this assembly, and this encapsulation prevented 1 from reacting with 2,4-pentanedione in D₂O. The tropylium cation also formed a 1:1 host–guest complex with the [Ga₄L₆]¹²⁻ assembly, greatly slowing its decomposition in D₂O. Encapsulation in the protected environment of this host cavity alters the reactivity of these guest molecules, giving them greater stability.

Introduction

Chemists are beginning to develop cavity-containing supramolecular assemblies as nanoscale reaction vessels in which the reactivity of selectively encapsulated substrates can be directed by the properties of the host cavity.[1–12] Encapsulation can also stabilize reactive intermediates or protect solvent sensitive species.[8,13,14,15] The supramolecular [Ga₄L₆]¹²⁻ assembly (Figure 1) has been the focus of several studies involving guest encapsulation into the tetrahedral cavity of the assembly. High affinity guests include alkyl ammonium cations,[16] the chiral N-methylnicotinium cation,[17] crown ether complexes with alkali metal cations,[18] and cationic organometallic species that are catalysts.[19] From these examples, it is apparent that cationic charge, hydrophobicity, and compatible shape and size are necessary for strong encapsulation into the cavity of the [Ga₄L₆]¹²⁻ assembly. A remarkable feature of this cluster is its structural memory,[20] which makes it a stable, chiral nanoscale vessel.

Results and Discussion

To expand the application of this [Ga₄L₆]¹²⁻ assembly as a molecular reaction vessel, the reactive aromatic cations shown in Figure 2 were chosen as potential guests. The diazonium cations 1–3 were selected for their representative use in organic synthesis, and for their variation of geometry relative to the generally high-symmetry molecules known to be good guests. The tropylium cation 4 was selected for its small size and aromaticity, which would enable it to interact with the naphthyl groups on the inner faces of the cavity, and for its potential as a metal-binding ligand. Tropylium has been previously reported as a guest inside organic hosts assembled through hydrogen bonding.[21–23]

Figure 1. Schematic drawing of the [Ga₄L₆]¹²⁻ tetrahedron showing the structure of the ligand L; lines represent additional ligand molecules, one is shown, and spheres represent gallium ions

Figure 2. Structures of the test guest cations: 4-(diethylamino)benzenediazonium (1), 4-methoxybenzenediazonium (2), 5-chloro-2-methoxybenzenediazonium chloride (Diazo Red RC, 3), tropylium ion (4)
In order to test the ability of the assembly to encapsulate these diazonium cations, the respective tetrafluoroborate diazonium salts were dissolved in D2O and added to the [Ga4L6]12− assembly.[24] When I was added to a solution of the assembly in D2O, an upfield shift of the methyl triplet from δ = 1.20 to −1.10 ppm was observed in the 1H NMR spectrum (Figure 3), while the methylene resonances were seen as multiplets shifted from δ = 3.55 to δ = 0.37 ppm and 0.05 ppm. The large upfield shift seen for the alkyl resonances of I indicates its encapsulation into the tetrahedral assembly, as does the splitting of the diastereotopic methylene protons due to the chiral environment of the assembly cavity.[25] One aromatic signal of the encapsulated guest within the [I⊂Ga4L6]11− host–guest complex can be observed as a doublet at δ = 3.95 ppm shifted from δ = 6.85 ppm, but the other is most likely obscured by the large HDO resonance not shown. Similar spectra were observed with CD3OD as the solvent.

![Figure 3](image_url) 1H NMR resonances of the 4-(diethylamino)benzenediazonium cation (I) encapsulated inside the [Ga4L6]12− assembly.

In initial experiments with [Ga4L6]12− synthesized from Ga(acac)3 (acac = acetylacetonate), addition of one equivalent of I resulted in the formation of a 1:1 host–guest complex, while addition of subsequent equivalents reacted with residual 2,4-pentanedione present in the NMR sample. Thus, encapsulation of the diazonium cation I occurs faster than the spontaneous reaction of I with the dione, and the sequestration of I in the host cavity is sufficiently rapid and strong to prevent this reaction subsequently. However, this host–guest complex is not indefinitely stable; a 1H NMR spectrum of the solution taken after five days showed no indication of the encapsulated guest. No decomposition products of the diazonium cation were identified.

When 4-methoxybenzenediazonium (2) and 5-chloro-2-methoxybenzenediazonium (3) were added to solutions of the [Ga4L6]12− assembly in CD3OD, the 1H NMR spectra revealed no shift of the diazonium cation signals in the presence of the tetrahedral host. This observation was surprising, given the ready encapsulation of I and the generally similar size, geometry, and charge of these three diazonium cations. The encapsulation behavior of I is most likely due to its greater hydrophobicity arising from the two ethyl groups on the amino nitrogen as compared with the presence of only one methyl group on the methoxy oxygen of 2 and 3. The additional hydrophobic interactions between these four aliphatic carbon atoms and the naphthyl groups that comprise the “walls” of the tetrahedral cavity make encapsulation of diazonium cation I favorable relative to 2 and 3.

Encapsulation experiments with the tropylion cation 4 were conducted in the same manner as those for the diazonium cations. Addition of one equivalent of 4 to the [Ga4L6]12− assembly in D2O results in the shift of the tropylion singlet from δ = 6.45 to 2.95 ppm (Figure 4, a). Integration of this upfield-shifted tropylion signal indicates that this cation is encapsulated as a guest inside the tetrahedral assembly with a 1:1 ratio. Addition of a second equivalent of tropylion ion results in a second broad resonance at δ = 5.18 ppm (Figure 4, b). The upfield shift of this resonance, compared to the resonance of free tropylion in D2O, indicates that the second equivalent of aromatic tropylion cation interacts with the [Ga4L6]12− assembly by ion-pair association with the highly-charged assembly, as seen with other counter cations.

![Figure 4](image_url) 1H NMR spectra in D2O of (a) the [Ga4L6]12− assembly + 1 equiv. 4; (b) + 2 equiv. 4; (c) sample in spectrum b after 20 h

After 20 h in solution (Figure 4, c), the encapsulated tropylion signal is still sharp, while the signal for the tropylion associated with the assembly was noticeably broadened, and the signal for free tropylion at δ = 6.45 ppm is unobservable. Free tropylion completely decomposes in D2O after approximately 24 h, so it seems that encapsulation of this cation in the hydrophobic environment of the [Ga4L6]12− cavity has significantly increased its stability.[26] The small aromatic peaks at δ = 7.05 and 6.70 ppm in Figure 4 (a, b) are most likely from tropylion decomposition products as reported by Oda et al.[27] When the same experiments were repeated in CD3OD, the tropylion ion reacted with the solvent to give the methoxyl adduct before encapsulation could occur (data not shown).

Conclusion

In summary, four reactive aromatic cations, which differ in geometry and hydrophobicity, have been tested as potential guest molecules inside the [Ga4L6]12− assembly. Of the...
three diazonium cations examined, only the 4-(diethylamino)benzenediazonium cation 1 is encapsulated by the supramolecular host. The spectra indicate that the small, aromatic tropylium cation, in addition to being a good guest, is involved in ion-pair interactions with the [Ga₄L₆]¹²⁻ assembly. Decomposition of the diazonium cation 1 and the tropylium cation 4 by solvolysis is slowed by encapsulation. The observed encapsulation of the reactive tropylium and diazonium cations is another example of the possibilities of new chemistry within the [Ga₄L₆]¹²⁻ cluster, a “nanoscale flask,” which provides a protective environment for reactive cation guests.

**Experimental Section**

¹H NMR spectra were obtained with a DRX-500 spectrometer at 500 MHz. Chemical shifts for ¹H NMR spectra are referenced to SiMe₄. Ga(NO₃)₃·xH₂O and tetrafluoroborate salts of the cations 4-(diethylamino)benzenediazonium (1) and 4-methoxybenzenediazonium (2), and tropylium tetrafluoroborate (4) were purchased from Aldrich and used as received. 4-Chloro-2-methoxybenzenediazonium chloride was purchased from Aldrich and further purified prior to use. Unless otherwise noted, the K₁₂Ga₄L₆ assembly was synthesized using Ga(NO₃)₃·xH₂O as the gallium source.

**Purification of 4-Chloro-2-methoxybenzenediazonium Chloride (Diazoo Red RC, 3):** The diazoon compound 3 as purchased from Aldrich contained ZnCl₂ as a stabilizing agent. Because this ZnCl₂ caused precipitation of the [Ga₄L₆]¹²⁻ assembly, it was necessary to purify this compound before use. To obtain pure 3, the diazoon chloride was dissolved in water, K₂CrO₄ was added, and the yellow ZnCrO₄ precipitate was filtered. To the remaining solution, NaBF₄ was added, and the fluoroborate salt of 3 was obtained as a white precipitate, filtered, and dried under vacuum.

**Synthesis of K₁₂Ga₄L₆ from Ga(NO₃)₃:** The tetrahedral assembly K₁₂Ga₄L₆ was synthesized as described previously,[25] using 1.5 equiv. Ga(NO₃)₃·xH₂O as the gallium source. The reaction mixture was stirred for 4 h in methanol, and the volume of the pale yellow solution was reduced to < 1 mL under N₂. Diethyl ether (≈ 30 mL) was added to precipitate the assembly, and the yellow-green precipitate was collected by centrifugation and dried under vacuum overnight. The assembly formed using this method is more sensitive to oxidation in solution than the assembly obtained from Ga(acac).

**Addition of Diazonium Cations to the [Ga₄L₆]¹²⁻ Assembly:** The tetrafluoroborate salts of the diazonium cations (1–3, 0.5 and 1 equiv.) in either D₂O or CD₃OD solutions were added to solutions of K₁₂Ga₄L₆ (0.5 mL, 5 mM) in D₂O or CD₃OD. Of these three diazonium cations, only the 4-(diethylamino)benzenediazonium cation was encapsulated as a guest molecule. NMR signals are reported for the encapsulated species only.

![Addition of Diazonium Cations to the [Ga₄L₆]¹²⁻ Assembly](image)

**Addition of the Tropylium Cation to the [Ga₄L₆]¹²⁻ Assembly:** ¹H NMR experiments were carried out in 5 mM solutions (0.5 mM) of ether-precipitated K₁₂Ga₄L₆ in D₂O. Equivalents of [C–H₃][BF₄] were added from a freshly-prepared solution in D₂O. Experiments in CD₃OD were not possible due to the reactivity of the tropylium cation. NMR signals are reported for the encapsulated species only. When more than one equivalent of tropylium cation was added the [Ga₄L₆]¹²⁻ assembly, a second broad signal at δ = 5.18 ppm in the ¹H NMR spectrum was observed. This signal is attributed to tropylium cation associated with the outside of the assembly, and causes the encapsulated tropylium signal to broaden and shift slightly upfield.

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**References**

Due to the reactivity of these diazonium cations with ketones, the $[\text{Ga}_4\text{L}_6]^{12-}$ assembly was synthesized using GaNO$_3$ instead of Ga(acac)$_3$ (acac = acetylacetonate) and precipitated with diethyl ether instead of acetone to eliminate the presence of ketones in solutions of the $[\text{Ga}_4\text{L}_6]^{12-}$ assembly.