View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by UNT Digital Library

Diffusion of a Highly-Charged Supramolecular Assembly: Direct Observation of Ion-Association in Water[1]

Michael D. Pluth[ab], Bryan E. F. Tiedemann[ab], Herman van Halbeek[a], Rudi Nunlist[a], Kenneth N. Raymond[ab]

[a]*Department of Chemistry, University of California, Berkeley, California USA 94720-1460*

and

[b]*Chemical Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, CA 94720*

Understanding the solution behavior of supramolecular assemblies is essential for a full understanding of the formation and chemistry of synthetic host-guest systems.[2-6] While the interaction between host and guest molecules is generally the focus of mechanistic studies of host-guest complexes, the interaction of the host-guest complex with other species in solution remains largely unknown, although in principle accessible by diffusion studies. Several NMR techniques are available to monitor diffusion and have recently been reviewed.[7-9] Pulsed gradient spin-echo (PGSE) NMR methods have attracted increasing interest, since they allow diffusion coefficients to be measured with high accuracy; they have been successfully used with observation of ^{7}Li and ^{31}P nuclei as well as with ^{1}H NMR.[10,11] We report here the direct measurement of diffusion coefficients to observe ion-association interactions by counter cations with a highly-charged supramolecular assembly.

Raymond and coworkers have described the design and chemistry of a class of metal-ligand supramolecular assemblies over the past decade.[12-15] The $[Ga_4L_6]^{12-}$ (L = 1,5-bis(2,3-dihydroxybenzamido)naphthalene) (**1**) (Figure 1) assembly has garnered the most attention, with the exploration of the dynamics and mechanism of guest exchange as well as the ability of **1** to achieve either stoichiometric or catalytic reactions inside its interior cavity.[16-19] Recent studies have revealed the importance of counter cations in solution on the chemistry of **1**. During the mechanistic study of the C-H bond activation of aldehydes by $[Cp^{*}Ir(PMe_3)(olefin)^{+} \subset \mathbf{1}]^{11-}$ a stepwise guest dissociation mechanism with an ion-paired intermediate was proposed.[19] Similarly, in the mechanism for the hydrolysis of iminium cations generated from the 3-aza Cope rearrangement of enammonium cations in **1**, the presence of an exterior ion association was part of the kinetic model.[17] To further substantiate the indirect kinetic evidence for such ion-paired species, we sought to explore the solution behavior of **1** by studying the diffusion of **1** with varying alkali and tetraalkyl ammonium cations.

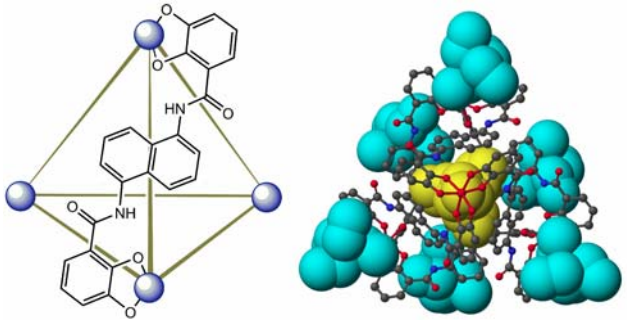

Figure 1. Left: Schematic of the $[Ga_4L_6]^{12-}$ assembly. Only one ligand is shown for clarity. Right: Model from the crystal structure $K_5(NEt_4)_6[NEt_4 \subset Fe_4L_6]$ showing encapsulated (yellow) and ion-associated (blue) NEt_4^{+} molecules. Hydrogens are omitted for clarity.

For large molecules in solution, such as synthetic supramolecular assemblies, the diffusion behavior of host and guest molecules can provide valuable information on host-guest interaction. One characteristic feature of a stable host-guest complex is that the host and guest molecules diffuse at the same rate in solution; this has been observed in a number of supramolecular systems.[20-26] In order to confirm that this system was suitable for study by diffusion NMR spectroscopy, a PGSE-DOSY spectrum was acquired of $[NEt_4 \subset \mathbf{1}]^{11-}$ (Figure 2), which shows that the host and guest molecules diffuse at the same rate. Quantitative analysis of the data, from monitoring the integral of host and guest resonances as a function of applied gradient strength, gave identical diffusion coefficients, confirming that the host and guest molecules diffuse together.

Published in Inorg. Chem. 2008, 47, 1411-1413

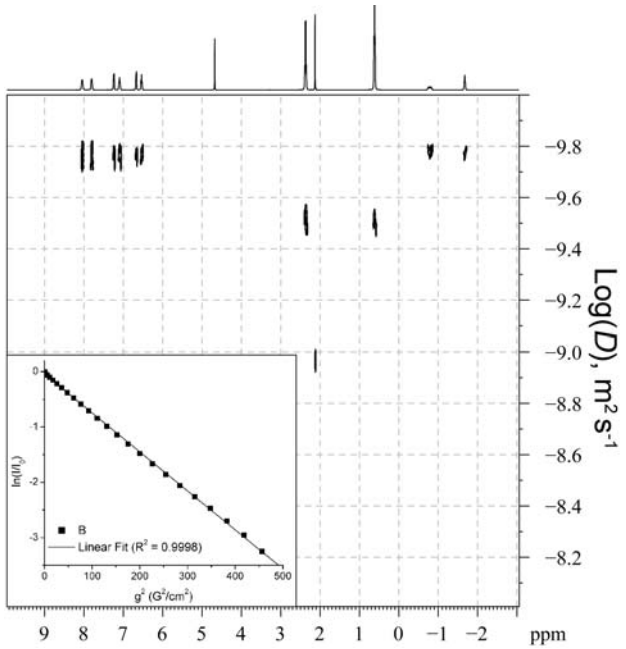

Figure 2. Two-dimensional diffusion spectrum of $[NEt_4 \subset 1]^{11-}$ in D_2O (400 MHz; 300K). Inset: Natural logarithm of normalized signal integrals of **1** as a function of the square of the applied gradient strength.

In order to investigate the effects of alkali cations on the solution behavior of **1**, five different alkali salts of the form $A_{11}[NEt_4 \subset Ga_4L_6]$ (A^+ = Li^+, Na^+, K^+, Rb^+, Cs^+) were prepared. Although the crystallographic radii of the alkali cations increase with atomic number, (r_{xrd}: $Li^+ < Na^+ < K^+ < Rb^+ < Cs^+$), the ionic mobilities observed in aqueous solutions decrease with increasing atomic number (r_{aq}: $Rb^+ \leq Cs^+ < K^+ < Na^+ < Li^+$), due to the size of the solvation shell for the cations.[27] The diffusion coefficient of $[NEt_4 \subset \mathbf{1}]^{11-}$ was measured for all five alkali salts in D_2O solutions, under two conditions: (a) with $A_{11}[NEt_4 \subset \mathbf{1}]$ in D_2O and (b) with $A_{11}[NEt_4 \subset \mathbf{1}]$ in D_2O with 100 mM ACl (Table 1).

	D_H, 10^{-6} cm^2 s^{-1}	
$A_{11}[NEt_4 \subset 1]$	**D_2O**	**D_2O w/ ACl**
$Li_{11}[NEt_4 \subset \mathbf{1}]$	2.19 ± 0.03	2.23 ± 0.02
$Na_{11}[NEt_4 \subset \mathbf{1}]$	2.37 ± 0.03	2.39 ± 0.02
$K_{11}[NEt_4 \subset \mathbf{1}]$	2.26 ± 0.03	2.40 ± 0.02
$Rb_{11}[NEt_4 \subset \mathbf{1}]$	2.42 ± 0.03	2.48 ± 0.03
$Cs_{11}[NEt_4 \subset \mathbf{1}]$	2.33 ± 0.04	2.36 ± 0.02

Table 1. Diffusion coefficient of $A_{11}[NEt_4 \subset \mathbf{1}]$ for alkali cations in D_2O and D_2O with 100 mM ACl at 300K.

The diffusion coefficients measured in 100 mM ACl for the Na^+, K^+ and Cs^+ systems are all equal within experimental error. The smaller diffusion coefficient observed with Li^+ counterions is consistent with its much lower ionic mobility. To maintain charge neutrality, counterions must co-diffuse with the solvated host-guest anion; the observed diffusion coefficient of $[Et_4N \subset Ga_4L_6]^{11-}$ will thus depend on the mobility of the counter cation. Since Rb^+ has the highest ionic mobility in aqueous solution, the $[NEt_4 \subset \mathbf{1}]^{11-}$ anion diffuses fastest with Rb^+ cations. The diffusion coefficients in the presence of 100 mM ACl show that ACl has very little effect on the diffusion coefficient for Li^+, Na^+, and Cs^+, suggesting that the eleven counterions associated with the assembly are more than enough to saturate the ion-association sites of **1**.

Having observed a dependence on the diffusion rate of **1** with different alkali cations, we sought to investigate the ion-association of lipophilic cations, such as tetraalkyl ammonium salts. In order to probe these interactions, a solution of $K_{12}[\mathbf{1}]$ was titrated with NR_4^+ (R = Et, Pr) while monitoring the diffusion coefficients of the host (D_H). Addition of tetraalkyl ammonium cations decreased the diffusion coefficient of **1** (Figure 3). This indicates that after the first equivalent is encapsulated the excess NR_4^+ binds to the exterior of the host, increasing its overall size and decreasing its diffusion coefficient. Saturation occurs because the host has a limited number of available exterior binding sites – as many as six sites are suggested from the crystal structure of $K_5(NEt_4)_6[NEt_4 \subset Fe_4L_6]$ (Figure 1), with each ligand providing one π-basic naphthalene ring surface and two π-basic catechol ring surfaces for binding lipophilic cations.[13,15] Addition of NPr_4^+ has a more profound effect on the diffusion coefficient of **1** than the addition of NEt_4^+, suggesting that NPr_4^+ preferentially ion-associates to **1** when compared to NEt_4^+.

Published in Inorg. Chem. 2008, 47, 1411-1413

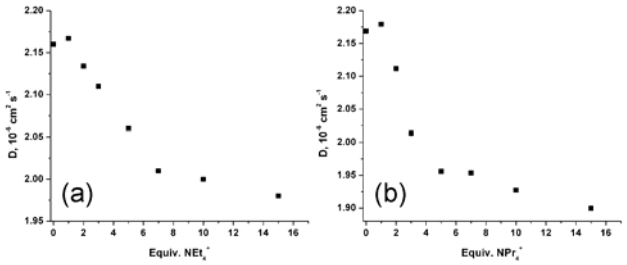

Figure 3. Ion pairing interactions cause the diffusion coefficient of **1** in D_2O to decrease with addition of a) Et_4NCl and b) Pr_4NBr.

The weak exterior binding interactions occur in parallel with the much stronger guest encapsulation equilibrium, causing most ion-association interactions to involve **1** with an encapsulated guest. The diffusion coefficient of **1** measured in the absence of guest is identical to that measured with one equivalent of NR_4^+ present. This suggests that $[Ga_4L_6]^{12-}$ and $[NR_4 \subset Ga_4L_6]^{11-}$ have similar hydrodynamic radii, and similar solvation shell sizes. To see if protonated solvent affects the diffusion behavior of **1**, the diffusion coefficient of $[NEt_4 \subset \mathbf{1}]^{11-}$ was monitored as a function of pH. Changing the pD from 8.0 to 13.0 showed no effect on the diffusion behavior of **1**, suggesting that protonated solvent species are not involved in ion-association with **1** (see supporting information). Although recent work has shown that neutral guests can enter **1** and be protonated and encapsulated, with a shift in the effective basicity of the guest of ~ 4 pK_a units,[28] this is not sufficient to generate guest H_3O^+ in the cavity. We conclude that the differences between solvation shells for z = -11 and z = -12 ions are small due to the large size of the clusters themselves.

Having established that NR_4^+ cations interact strongly with the exterior of **1**, the magnitude of this interaction was probed through competition with other counter cations. When additional KCl is added to a solution of $K_{11}(NR_4)[NR_4 \subset \mathbf{1}]$ the observed diffusion coefficient of the exterior alkylammonium cation rapidly increases. One NR_4^+ cation is encapsulated by the cluster and is slow to exchange, while the other NR_4^+ cation on the exterior forms an ion association and is in rapid exchange with the unassociated NR_4^+ cation on the NMR timescale. Thus the observed diffusion coefficient is the population average. In the absence of salt, the exterior NR_4^+ diffusion rate is only slightly faster than the host-guest complex, consistent with tight ion association. The added salt disrupts the ion-association of NR_4^+ to the exterior of **1**, causing the diffusion coefficient of the exterior NR_4^+ cation to increase (Figure 4). Displacement of the ion-associated NPr_4^+ requires a higher concentration of KCl when compared to the displacement of NEt_4^+, again showing stronger ion-association by the more lipophilic NPr_4^+.

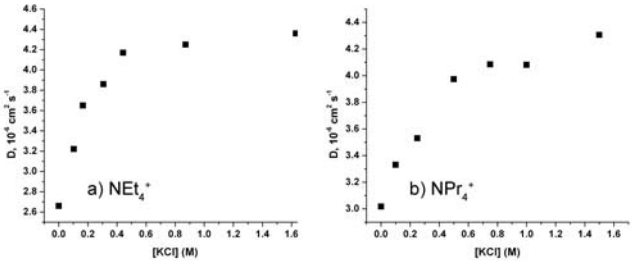

Figure 4. Diffusion coefficient of exterior NR_4^+ as a function of KCl concentration. Addition of KCl to **1** in D_2O with a) 2 equivalents of Et_4NCl and b) 2 equivalents of Pr_4NBr results in higher diffusion coefficients observed for the exterior alkylammonium cation, because the added salt disrupts ion pairing to the host exterior.

Much larger diffusion coefficients are observed for the free alkylammonium cations in the absence of **1**. For NEt_4^+ with 1 M KCl, interaction with $[NEt_4 \subset \mathbf{1}]^{11-}$ reduced the observed diffusion coefficient of the exterior cation to less than half the value observed in the absence of host, despite the 100-fold excess of KCl; similar effects were observed with NPr_4^+, although attenuated. Thus the favorable exterior interactions between NR_4^+ and **1** cannot be solely attributed to simple coulombic attractions, since K^+ will exhibit similar, if not higher, coulombic attractive forces to the anionic host. If NR_4^+ binding were caused by coulombic attraction alone, a large excess of KCl would eliminate any interactions with the anionic host, and the observed NR_4^+ diffusion rate would be equal to that observed in the absence of host. This is clearly not the case, and additional attractive forces must be involved, such as cation-π binding and/or van der Waals interactions.

In conclusion, we have shown that lipophilic cations ion-associate with **1** in solution. This suggests a stepwise guest encapsulation mechanism where the freely solvated cationic guest first ion-associates with **1**, followed by encapsulation. Calorimetric studies that quantitatively probe the magnitude of these competing equilibria agree with the model described here.[29] This stepwise guest exchange mechanism has broad implications in other supramolecular systems where the solvation environment of the host molecule and of the bulk solution is dissimilar.

Acknowledgment. We gratefully acknowledge financial support from the the Director, Office of Science, Office of Basic Energy Sciences, and the Division of Chemical Sciences, Geosciences, and Biosciences of the U.S. Department of Energy at

LBNL under Contract No. DE-AC02-05CH11231 and an NSF predoctoral fellowship to M.D.P. We thank Professor Giuseppe Arena and Carmelo Sgarlata (Universitá di Catania) for helpful discussions.

Supporting Information Available: Experimental procedures and analytical details. This information is available free of charge via the Internet at http://pubs.acs.org.

References

* To whom correspondence should be addressed. E-mail: raymond@socrates.berkeley.edu. Fax: +1 (510) 486-5283

1. Paper number 40 in the series Coordination Number Incommensurate Cluster Formation. For the previous paper in the series, see: Pluth, M. D.; Bergman, R. G.; Raymond, K. N. *submitted for publication*.
2. Oshovsky, G. V.; Reinhoudt, D. N.; Verboom, W., *Angew. Chem. Int. Ed.* **2007,** *46*, 2366.
3. Pluth, M. D.; Raymond, K. N., *Chem. Soc. Rev* **2007,** *36*, 161.
4. Biros, S. M.; Rebek, J., Jr., *Chem. Soc. Rev* **2007,** *36*, 93.
5. Schmuck, C., *Angew. Chem. Int. Ed.* **2007,** *46*, 5830.
6. Yoshizawa, M.; Fujita, M., *Pure Appl. Chem.* **2005,** *77*, 1107.
7. Cohen, Y.; Avram, L.; Evan-Salem; Tamar; Frish, L., *Analytical Methods in Supramolecular Chemistry*. Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, p 163.
8. Cohen, Y.; Avram, L.; Frish, L., *Angew. Chem. Int. Ed.* **2005,** *44*, 520.
9. Johnson, C. S., Jr., *Prog. NMR. Spectrosc.* **1999,** *34*, 203.
10. Fernández, I.; Martínez-Viviente, E.; Breher, F.; Pregosin, P. S., *Chem. Eur. J.* **2005,** 11, 1495.
11. Pregosin, P. S.; Martínez-Viviente, E.; Anil Kumar, P. G., *Dalton Trans.* **2003**, *21*, 4007.
12. Davis, A. V.; Fiedler, D.; Seeber, G.; Zahl, A.; van Eldik, R.; Raymond, K. N., *J. Am. Chem. Soc.* **2006,** *128*, 1324.
13. Davis, A. V.; Raymond, K. N., *J. Am. Chem. Soc.* **2005,** *127*, 7912.
14. Caulder, D. L.; Raymond, K. N., *J. Chem. Soc, Dalton Trans. Inorg. Chem.* **1999,** *8*, 1185.
15. Caulder, D. L.; Powers, R. E.; Parac, T. N.; Raymond, K. N., *Angew. Chem. Int. Ed.* **1998,** *37*, 1840.
16. Pluth, M. D.; Bergman, R. G.; Raymond, K. N., *Science* **2007,** *316*, 85.
17. Leung, D. H.; Bergman, R. G.; Raymond, K. N., *J. Am. Chem. Soc.* **2007,** *129*, 2746.
18. Fiedler, D.; van Halbeek, H.; Bergman, R. G.; Raymond, K. N., *J. Am. Chem. Soc.* **2006,** *128*, 10240.
19. Leung, D. H.; Bergman, R. G.; Raymond, K. N., *J. Am. Chem. Soc.* **2006,** *128*, 9781.
20. Allouche, L.; Marquis, A.; Lehn, J.-M., *Chem. Eur. J.* **2006,** *12*, 7520.
21. Chas, M.; Pia, E.; Toba, R.; Peinador, C.; Quintela, J. M., *Inorg. Chem.* **2006,** *45*, 6117.
22. Megyes, T.; Jude, H.; Grosz, T.; Bako, I.; Radnai, T.; Tarkanyi, G.; Palinkas, G.; Stang, P. J., *J. Am. Chem. Soc.* **2005,** *127*, 10731.
23. Avram, L.; Cohen, Y., *J. Am. Chem. Soc.* **2005,** *127*, 5714.
24. Biros, S. M.; Ullrich, E. C.; Hof, F.; Trembleau, L.; Rebek, J., Jr., *J. Am. Chem. Soc.* **2004,** *126*, 2870.
25. Burini, A.; Fackler, J. P., Jr.; Galassi, R.; Macchioni, A.; Omary, M. A.; Rawashdeh-Omary, M. A.; Pietroni, B. R.; Sabatini, S.; Zuccaccia, C., *J. Am. Chem. Soc.* **2002,** *124*, 4570.
26. Drain, C. M.; Russell, K. C.; Lehn, J.-M., *Chem. Commun.* **1996,** *3*, 337.
27. Stern, K. H.; Amis, E. S., *Chem. Rev.* **1959,** *59*, 1.
28. Pluth, M. D.; Bergman, R. G.; Raymond, K. N., *J. Am. Chem. Soc.* **2007,** *129*, 11459.
29. Sgarlata, C.; Tiedemann, B. E. F.; Arena, G.; Raymond, K. N. to be submitted for publication.