Supporting Information

For

Guest and Subunit Exchange in Self-Assembled Ionophores

Mangmang Cai, Vladimir Sidorov, Yiu-fai Lam, Robert A. Flowers, II‡ and Jeffery T. Davis*

Department of Chemistry and Biochemistry, University of Maryland, College Park, MD 20742, ‡Department of Chemistry, University of Toledo, Toledo, Ohio

*Author to whom correspondence should be addressed.

E-mail: jd140@umail.umd.edu

Phone: 301-405-1845

Cesium-133 NMR Spectroscopy. Cesium-133 NMR spectra were obtained on a Bruker DRX-500 MHz spectrometer (65.6 MHz for ^{133}Cs). The ^{133}Cs chemical shifts were referenced to an external solution of 0.50 M CsI in D_2O at 298 K. Samples for ^{133}Cs NMR were prepared by addition of isoG **1** into solutions of $Cs^+BPh_4^-$ (of known concentration in either CD_3CN or 50%-50% CD_3CN-$CDCl_3$). H-1 NMR determined the stoichiometry, as illustrated in Figure 2 of the Supporting Information.

2D ^{1}H-^{1}H EXSY Measurements. Samples for the 2D EXSY NMR experiments were prepared by mixing the metal-free ligand isoG **1** with (isoG **1**)$_{10}$-$M^+BPh_4^-$ decamer complexes. The (isoG **1**)$_{10}$-$M^+BPh_4^-$ decamer complexes were prepared in $CDCl_3$ and characterized by ^{1}H NMR, then metal-free ligand isoG **1** was added to give a ratio of isoG **1**: (isoG **1**)$_{10}$-M^+ = 10:1. Similarly, samples were also prepared in the mixed solvent of 50%-50% CD_3CN-$CDCl_3$. These samples contained 40 mM of isoG **1** and 2.0 mM of Cs^+, giving a ratio of isoG **1**: (isoG **1**)$_{10}$-M^+ = 10:1.

Two-dimensional EXSY NMR spectra were recorded on a Bruker DRX-500 MHz spectrometer at various temperatures. The typical NOESY pulse sequence was used, with mixing times varying from 0.1 s to 1.3 s, and with relaxation time of 4.0. The sweep width in both dimensions was 7500 Hz (at 500 MHz). A total of 512 t_1 values were used, and 2048-point FIDs were acquired in the t_2 dimension. A line broadening of 2 Hz in F_2 dimension and 7 Hz in F_1 dimension was imposed prior to Fourier transformation. The total time that was required for each experiment was 18 h.

Sizable off-diagonal peaks were observed, indicating exchange between decamer and uncomplexed isoG **1**. The peak intensity, I_{ij} (i, j = monomer, complex) was measured using the WinNMR program (Bruker). The relationship between the 2D peak intensities (I_{ij}) at some specified mixing time (t_m) and the exchange rate constants is given by following equation:

$$I_{ij}(t_m) = (e^{-\mathbf{R}\,\tau m})_{ij}\, M_j^{o}$$

M_j^{o} is the equilibrium magnetization of the nuclei in site j and **R** has off-diagonal elements $\mathbf{R}_{ij} = -k_{ji}$, where k_{ji} is the first order rate constant for chemical exchange from site j to site i. The rate constants k_{ij} and k_{ji} were calculated using the matrix method (see Perrin, C. L.; Gipe, R. K. *J. Am. Chem. Soc.* **1984**, *106*, 4036-4038; and Perrin, C. L.; Dwyer, T. J. *Chem. Rev.* **1990**, *90*, 935-967):

$$R = -\tau_m^{-1} \ln A = -\tau_m^{-1} X(\ln \Lambda)X^{-1}$$

Where $R_{ij} = -k_{ji}$, $A_{ij} = I_{ij}(\tau_m / M_j^0$ and X is the square matrix of eigenvectors of A, such that $X^{-1}AX = \Lambda = \mathrm{diag}(\lambda_i)$ and $\ln \Lambda = \mathrm{diag}(\ln \lambda_i)$, with λ_i the *i*th eigenvalue of A. Calculations were done using MathCAD 7 software (MathSoft Inc.). The mean lifetime of exchange τ was calculated from the relationship to the measured first-order rate constants k_{ij} and k_{ji}, τ=1/k (k is the average exchange rate constant, $k = (k_{ij} + k_{ji})/2$).

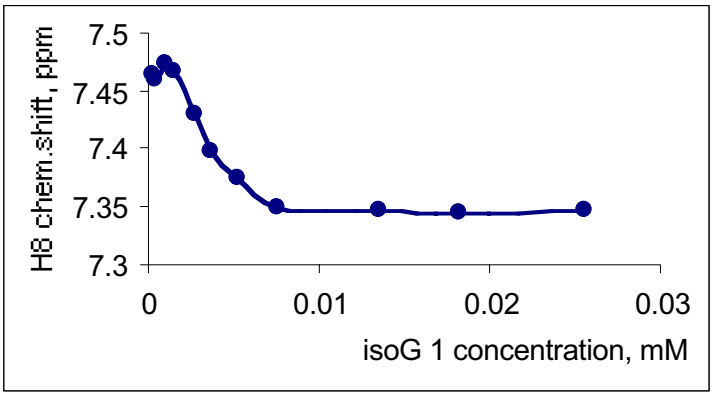

Fig. 1. The ^{1}H NMR spectrum of cation-free isoG **1** is concentration dependent**.** This plot illustrates the chemical shift of the aromatic H8 proton in a 1:1 $CDCl_3$-CD_3CN solution as a function of the concentration of isoG **1**. We conclude that the observed changes in the ^{1}H NMR spectrum are due to non-specific self-association of cation-free isoG **1**. These NMR results are consistent with isothermal titration calorimetry and VPO data described in the text of the paper

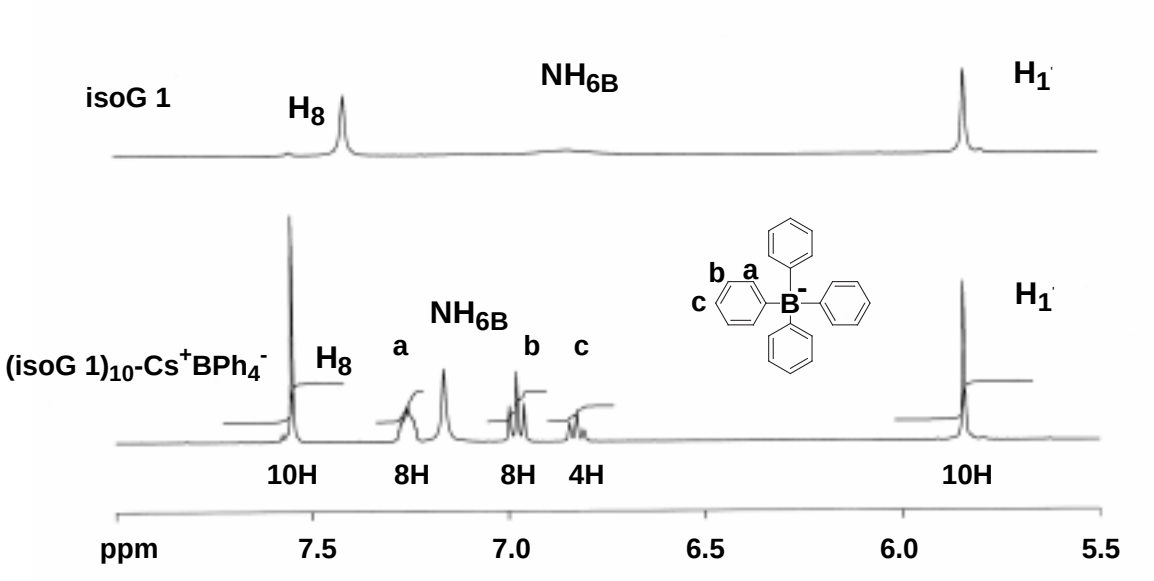

Fig. 2. Representative ^{1}H NMR spectra of metal-free isoG **1** (top) and (isoG **1**)$_{10}$-$Cs^+BPh_4^-$ decamer. The decamer sample was generated by titration of isoG **1** into a solution of $Cs^+Ph_4B^-$ in CD_3CN. The isoG **1** to Cs^+Ph_4B stoichiometry in complex was determined by comparing the integration of the BPh_4^- signals (the ortho-, meta-, and para-protons) with the integration of signals corresponding to the complexed isoG **1**.

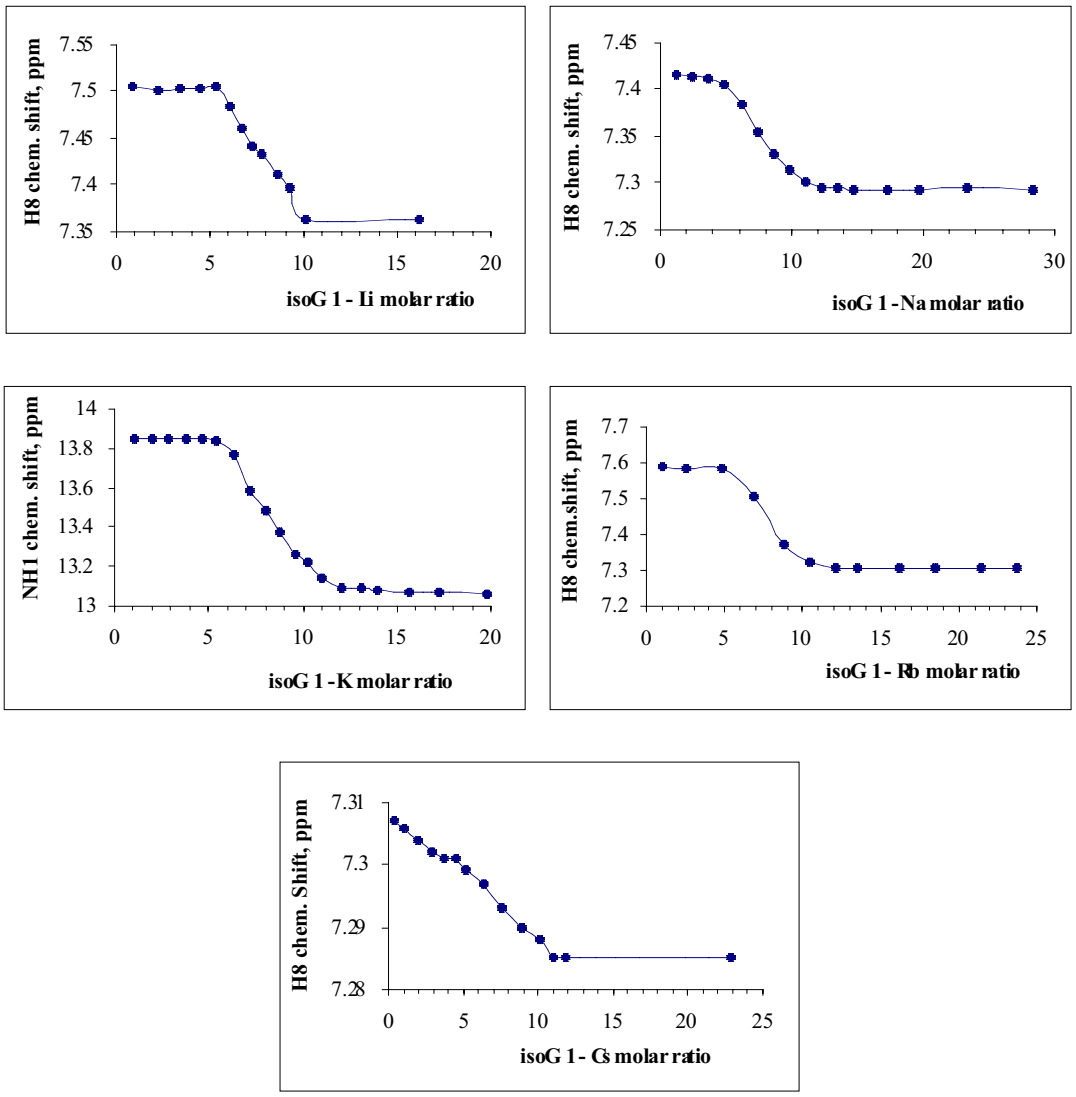

Fig. 3. Molar ratio ^{1}H NMR experiments for alkali cation complexation by isoG **1**. Experiments were done in a mixed 1:1 $CDCl_3/CD_3CN$ solvent using alkali tetraphenylborate salts. Relative stoichiometries were determined by integration of the tetraphenylborate and isoG NMR peaks, as described in Supplemental Figure #2. The salt concentrations ranged between 2.5 mM and 11.3 mM. All alkali metal cations, except Cs^+, show two inflection points corresponding to a 5:1 pentamer and 10:1 decamer complex. We observed only one inflection point in the isoG-Cs^+ experiment, corresponding to 10:1 decamer stoichiometry

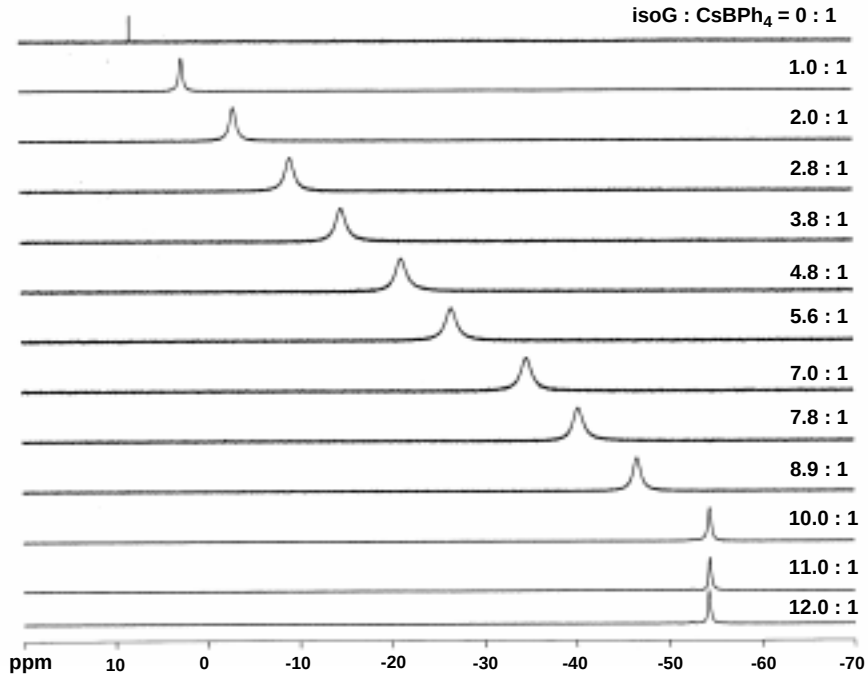

Fig. 4. Stack plot of ^{133}Cs NMR spectra. Titration of isoG **1** into a $CsBPh_4$ solution (10 mM) in CD_3CN demonstrated: (i) fast exchange of Cs^+ between the solvated and bound states; and (ii) the complex formed is a decamer, (isoG **1**)$_{10}$-$Cs^+BPh_4^-$.

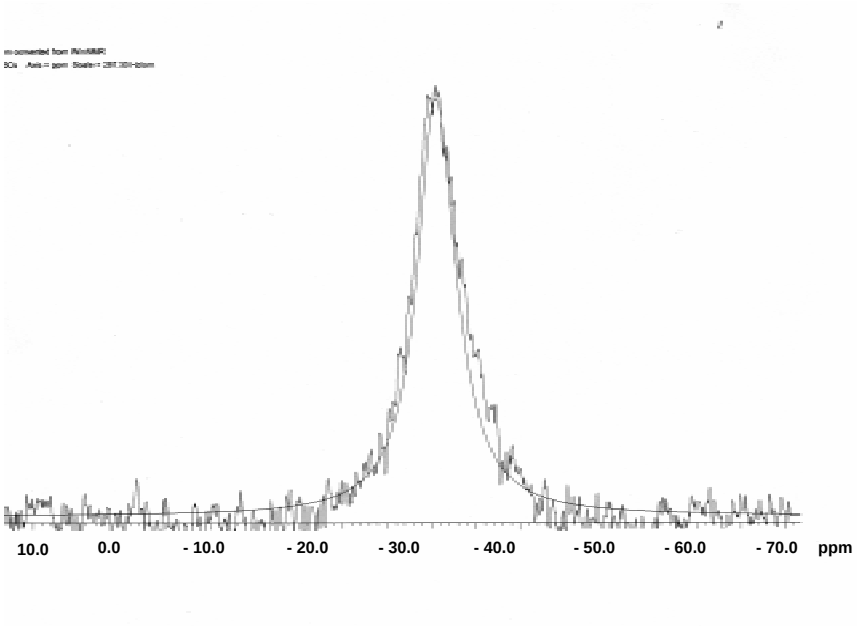

Fig. 5. Determination of the Cs^+ exchange rate. Experimental ^{133}Cs NMR spectra were imported into the g-NMR 4 program (Cherwell Scientific, Palo Alto, CA, 94303) for computer simulation of Cs^+ exchange and for calculation of the mean lifetime (τ) of Cs^+ in the decamer complex (isoG **1**)$_{10}$-$Cs^+BPh_4^-$. Simulated data were iteratively fit to the experimental data. The experimental and simulated data for a sample containing a solution of (isoG **1**)$_{10}$-Cs^+ Ph_4B^- (1 mM) and Cs^+ Ph_4B^- (1 mM) in 50% $CDCl_3$-50% CD_3CN at 25 °C is shown. Line-shape analysis provided a mean lifetime of τ=0.061 ms for bound Cs^+.

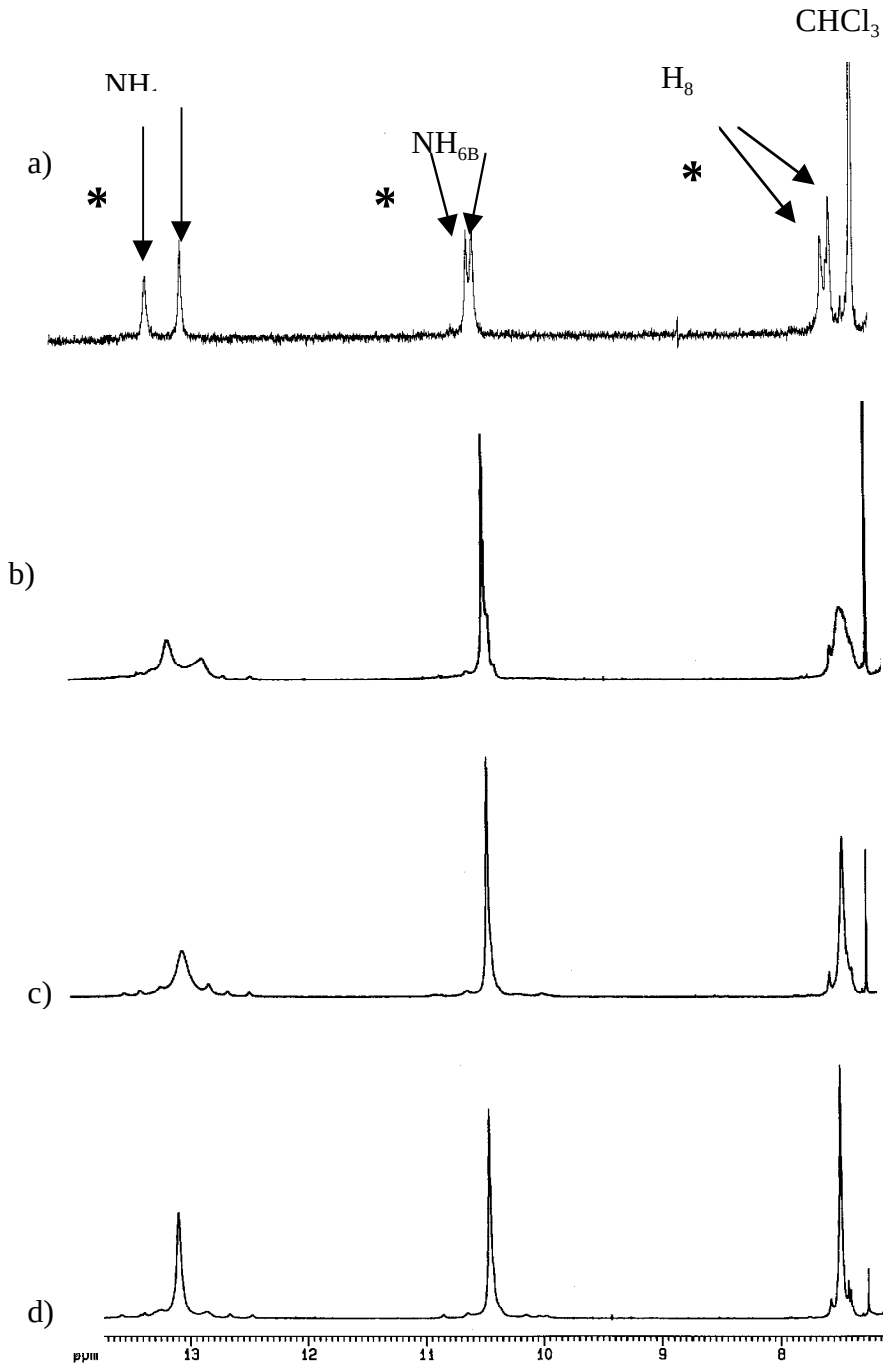

Fig. 6. NMR dilution experiments show exchange between the pentamer and decamer. In addition to being cation dependent, (see reference 12 in the paper), pentamer-decamer exchange was also concentration-dependant, indicating that exchange proceeds via a bimolecular mechanism. This Figure shows a region of the ^{1}H NMR spectra for a 1:2 mixture of (isoG **1**)$_{10}$-Li^{+} and (isoG **1**)$_{5}$-$Li^{+\cdot}$ in a 1:1 $CDCl_3$:CD_3CN solvent mix. Arrows marked with asterisk indicate the pentamer resonances. The total concentration of isoG **1** is a) 1.3 mM; b) 9.4 mM; c) 21.6 mM; d) 54.9 mM.