

## Chapter IV

# Ion Pairing in Fast-Exchange Host-Guest Systems: Concentration Dependence of Apparent Association Constants for Complexes of Neutral Hosts and Divalent Guest Salts with Monovalent Counterions

### 4.1. INTRODUCTION

Applications of ionic compounds in supramolecular chemistry can be dated back to Pederson's discovery of the alkalai metal templated syntheses of crown ethers.<sup>1</sup> They have been widely used as hosts and guests.<sup>2</sup> In our studies of host-guest complexes<sup>3</sup> we have frequently been unable to reproduce the association constants reported for complexes involving ionic species. The association constant, a basic parameter, is a measure of the binding strength between the host and the guest. It is well known that the value of the association constant depends on temperature and polarity of solvent. Recently our group demonstrated that the concentration dependence of a slow-exchange systems, dibenzo-24-crown-8/dibenzyl ammonium salts, in low dielectric constant solvents can be attributed to ion pairing of the salts and the dissociated nature of the complex.<sup>4</sup> Since many host-guest complexes are fast exchange systems,<sup>5</sup> it is important to study ion pairing in such systems. Here for the first time we report a study of concentration dependence of apparent experimental association constants of fast-exchange host-guest systems based on

dicationic paraquat derivatives with two monovalent counterions ( $G^{++}2X^-$ ) as guest species and neutral crown ethers as hosts. Over the course of these studies we show that such host-guest systems which exhibit variations in the apparent association constant,  $K_{a,exp} = [Complex]/[Guest][Host]$ , with concentration involve dissociated complexes, while those whose  $K_{a,exp}$  are invariant with concentration involve ion paired complexes.

## 4.2. RESULTS AND DISCUSSION

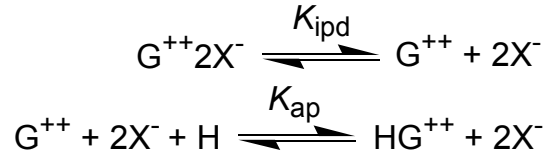
### A. Theory.

The association constants for 1:1 host-guest complex formation in the literature are generally not explicitly defined, but since the units are  $M^{-1}$ , it is assumed that they are of the form:

$$K_{a,exp} = [Complex]/[Host]_{uc}[Guest]_{uc}$$

where  $[Complex] = [Host]_c = [Guest]_c$ ,  $[Host]_{uc} = [Host]_0 - [Complex]$ , and  $[Guest]_{uc} = [Guest]_0 - [Complex]$ . Here the subscripts “c” and “uc” denote complexed and uncomplexed species, respectively.

The following treatment is based on the assumptions that a) the dicationic guest exists in solution as a monomer,  $G^{++}2X^-$ , b) after dissociation of the guest salt it is the free dication  $G^{++}$  that forms the complex, c) there are no other species present in the solutions. If the complex is not ion paired, we can derive



$$K_{ipd} = [G^{++}][X^{-}]^2/[G^{++}2X^{-}]$$

$$[G^{++}] = K_{ipd}[G^{++}2X^{-}]/[X^{-}]^2$$

$$K_{ap} = [HG^{++}]/[H][G^{++}]$$

$$[HG^{++}] = K_{ap}[H][G^{++}]$$

$$K_{ap} = [HG^{++}][X^{-}]^2/K_{ipd}[G^{++}2X^{-}][H]$$

$$K_{a,exp} = [HG^{++}]/[G^{++}2X^{-}][H] = K_{ap} K_{ipd}/[X^{-}]^2 \quad (\text{Eq. 1a})$$

$$\begin{aligned}
[X^{-}] &= 2([HG^{++}] + [G^{++}]) = 2\{K_{ap}[H][G^{++}] + K_{ipd}[G^{++}2X^{-}]/[X^{-}]^2\} \\
&= 2\{K_{ipd}K_{ap}[G^{++}2X^{-}][H]/[X^{-}]^2 + K_{ipd}[G^{++}2X^{-}]/[X^{-}]^2\} \\
&= \{2K_{ipd}[G^{++}2X^{-}](K_{ap}[H] + 1)\}^{1/3} \quad (\text{Eq. 1b})
\end{aligned}$$

The first term of Eq. 1b represents the fraction of free  $X^{-}$  resulting from the complexation and the second term represents that resulting from ion-pair dissociation.

$$K_{a,exp} = [HG^{++}]/[G^{++}2X^{-}][H] = K_{ap} K_{ipd}/\{2K_{ipd}[G^{++}2X^{-}](1 + K_{ap}[H])\}^{2/3} \quad (\text{Eq. 1c})$$

Note that  $K_{a,exp}$  is a function of both  $[G^{++}2X^{-}]$  and  $[H]$  and therefore is not a constant under these circumstances.

$$[\text{HG}^{++}]/[\text{G}^{++}2\text{X}^{-}]^{1/3} = K_{\text{ap}}K_{\text{ipd}}^{1/3}[\text{H}]/\{2(1 + K_{\text{ap}}[\text{H}])\}^{2/3} \quad (\text{Eq. 1d})$$

If  $K_{\text{ap}}[\text{H}] \gg 1$ ,

$$[\text{HG}^{++}]/[\text{G}^{++}2\text{X}^{-}]^{1/3} = K_{\text{ap}}^{1/3}K_{\text{ipd}}^{1/3}[\text{H}]^{1/3}/2^{2/3} \quad (\text{Eq. 1e})$$

Under this condition the free counterion is essentially all generated as a result of complexation.

On the other hand, if  $K_{\text{ap}}[\text{H}] \ll 1$ , essentially all of the free  $\text{X}^{-}$  is generated as a direct result of ion-pair dissociation and

$$[\text{HG}^{++}]/[\text{G}^{++}2\text{X}^{-}]^{1/3} = K_{\text{ap}}K_{\text{ipd}}^{1/3}[\text{H}]/2^{2/3} \quad (\text{Eq. 1f})$$

These two extreme cases depend on the value of  $K_{\text{ap}}$  and the concentration of the crown ether  $[\text{H}]$ . In the intermediate region,  $[\text{X}^{-}]$  will result from ion pair dissociation of the salt as well as the complexation.

A plot of  $\log([\text{HG}^{++}]/[\text{G}^{++}2\text{X}^{-}]^{1/3})$  vs.  $\log [\text{H}]$  (Eq. 1d) should yield limiting slopes of  $1/3$  at high values of  $\log [\text{H}]$  and  $1$  at low values, on the basis of limiting Eqs. 1e and 1f. This will enable estimation of  $K_{\text{ap}}$  and  $K_{\text{ipd}}$  from the two intercepts,  $\log\{K_{\text{ap}}^{1/3}K_{\text{ipd}}^{1/3}/2^{2/3}\}$  and  $\log\{K_{\text{ap}}K_{\text{ipd}}^{1/3}/2^{2/3}\}$ , respectively.

An alternative treatment is to apply the first two terms of the binomial expansion of the  $\{1 + K_{\text{ap}}[\text{H}]\}^{2/3}$  term of Eq. 1d, i.e.,  $(1 + (2/3)K_{\text{ap}}[\text{H}])$ , as an approximation. This leads to:

$$[G^{++}2X^{-}]^{1/3}/[HG^{++}] = (2^{2/3}/K_{ap}K_{ipd}^{1/3})(1/[H]) + (2^{2/3})(2/3)/K_{ipd}^{1/3} \quad (\text{Eq. 1i})$$

A plot of  $[G^{++}2X^{-}]^{1/3}/[HG^{++}]$  vs.  $1/[H]$  will enable estimation of  $K_{ap}$  and  $K_{ipd}$  from the slope and intercept.

If the ion paired complex can also form, we can derive



$$K_{ipc} = [HG^{++}2X^{-}]/([H][G^{++}2X^{-}])$$

The complex concentration measured under fast exchange will consist of both  $HG^{++}$  and  $HG^{++}2X^{-}$  and therefore

$$\begin{aligned} K_{a,exp} &= ([HG^{++}] + [HG^{++}2X^{-}])/[G^{++}2X^{-}][H] = [HG^{++}]/[G^{++}2X^{-}][H] + \\ & [HG^{++}2X^{-}]/[G^{++}2X^{-}][H] \\ &= K_{ap} K_{ipd}/\{2K_{ipd}[G^{++}2X^{-}](1 + K_{ap}[H])\}^{2/3} + K_{ipc} \end{aligned} \quad (\text{Eq.2a})$$

If complex formation involves only the free dissociated dication and essentially none of the complex is ion paired, then  $K_{ipc} = 0$ . In this case a plot of  $K_{a,exp}$  vs. either  $1/\{[G^{++}2X^{-}][H]\}^{2/3}$  or  $1/[G^{++}2X^{-}]^{2/3}$ , depending on the value of  $K_{ap}[H]$  ( $\gg 1$  or  $\ll 1$ ; see Eq. 1c), will be linear and have zero intercept.

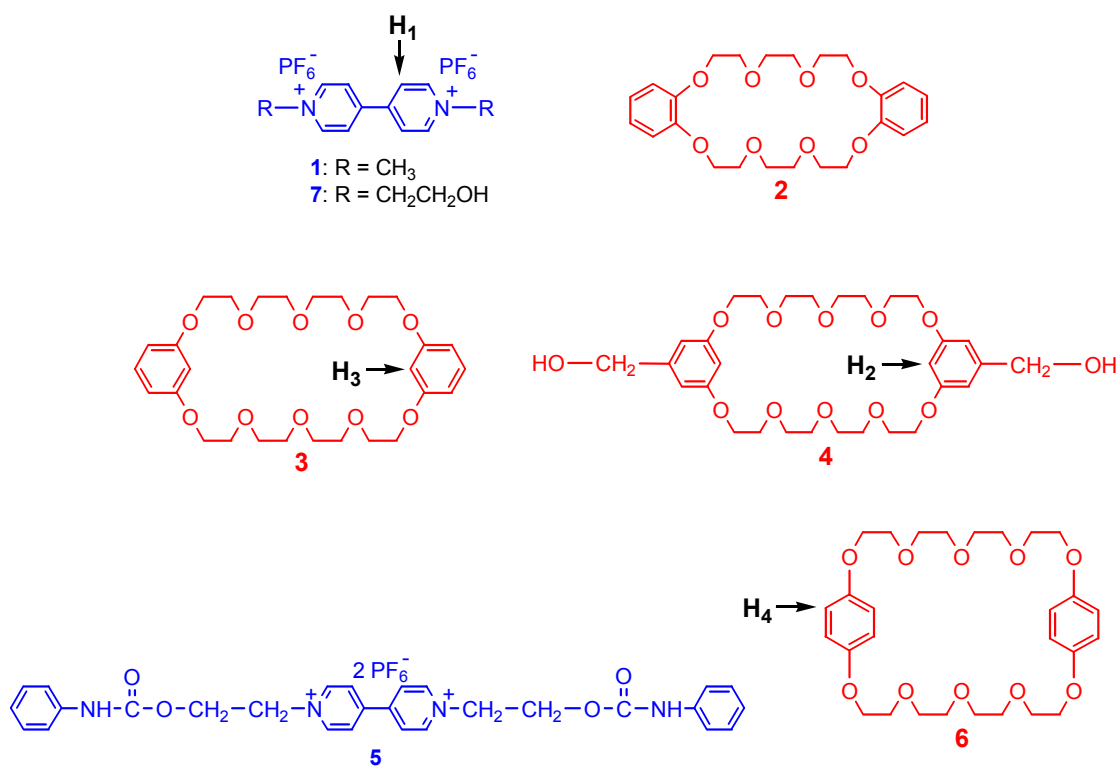
If complex formation takes place solely by way of the ion paired guest, then  $K_{ap} = 0$  and in this case,  $K_{a,exp}$  is a constant equal to  $K_{ipc}$  and independent of concentration. If

both processes occur,  $K_{a,exp}$  will exhibit concentration dependence and the contribution of both pathways can be quantitatively assessed. A plot of  $K_{a,exp}$  vs. either  $1/\{[G^{++}2X^-][H]\}^{2/3}$  or  $1/[G^{++}2X^-]^{2/3}$ , depending on the value of  $K_{ap}[H]$  ( $\gg 1$  or  $\ll 1$ ; see Eq. 1c), will have a y-intercept equal to  $K_{ipc}$ .

From Eq.2a when  $K_{ap} = 0$ , we can derive

$$[HG^{++}]/[G^{++}2X^-] = K_{a,exp} [H] \quad (\text{Eq.2b}),$$

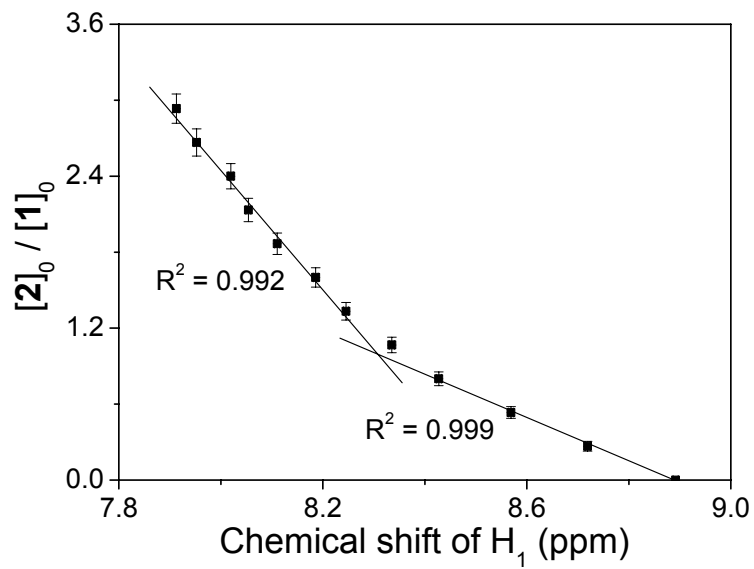
which is a form of the Scatchard equation.<sup>6</sup> A plot of  $[HG^{++}]/[G^{++}2X^-]$  vs.  $[H]$  (Eq. 2b) should yield a straight line with the slope of  $K_{a,exp}$  and an intercept of zero.



## B. Complexation between paraquat (1) and dibenzo-24-crown-8 (2).

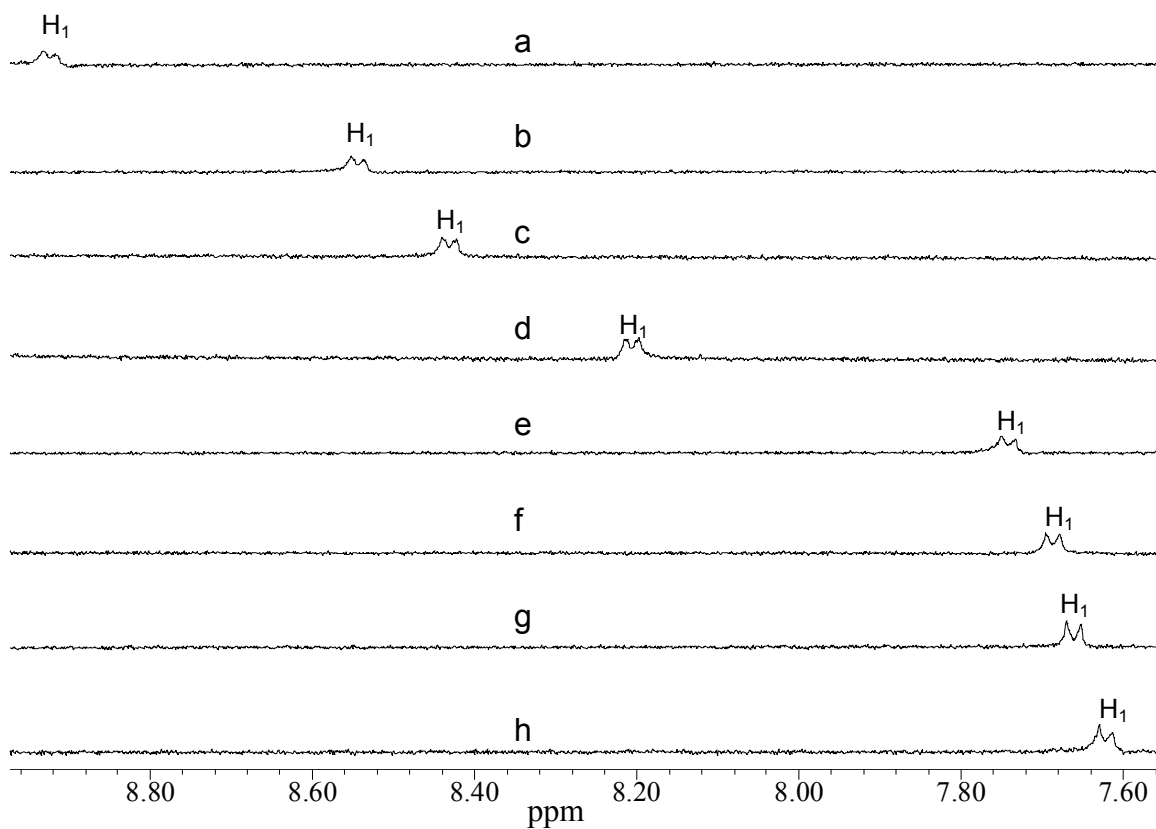
We recently found that **1** and **2** form a strong complex in acetone solution.<sup>7</sup> The stoichiometry of this complex was determined to be 1:1 by the mole ratio method<sup>8</sup> using proton NMR data of H<sub>1</sub> for **1** (Figure 1). Initial NMR studies were done with solutions which had a constant concentration of **1** (0.500 mM) and varying concentrations of **2** (0.500 to 30.0 Mm, Figure 2). Spectra taken at -70 °C were still in the fast exchange regime. Based on the NMR data,  $\Delta_0$ , the difference in  $\delta$  values for H<sub>1</sub> in **1** in the uncomplexed and fully complexed species, was determined by extrapolation of a plot of  $1/\Delta = 1/(\delta - \delta_u)$  vs.  $1/[\mathbf{2}]_0$  (Figure 3) to be 1.32 ppm.  $K_{a,exp,2\bullet 1}$  values (Table 1) were then calculated on a point-by-point basis from  $K_{a,exp,2\bullet 1} = (\Delta/\Delta_0)/[1-(\Delta/\Delta_0)]\{[\mathbf{2}]_0-(\Delta/\Delta_0)[\mathbf{1}]_0\}$ .  $K_{a,exp,2\bullet 1}$  varied up to 6-fold and decreased when initial concentrations of **1** or **2** increased, in accord with Eq. 1c or 2a. A log-log plot (Figure 4) was made for this complex according to Eq. 1d. The slope, 1.00, of the best fit line at low concentrations of **2** is equal to the ideal value, 1, for the case where the complex is 100% dissociated and  $K_{ap}[H] \ll 1$ .

The slope, 0.378, of the best fit line at high concentrations of **2** is close to the ideal value, 1/3, for the case where the complex is completely dissociated and  $K_{ap}[H] \gg 1$ . From the intercepts of these two lines,  $K_{ap,2\bullet 1}$  and  $K_{ipd,1}$  were calculated to be 106 ( $\pm$  42) M<sup>-1</sup> and  $4.64 (\pm 1.86) \times 10^{-4}$  M<sup>2</sup>.<sup>9</sup> It must be noted, however, that the limited solubility (~30 mM at 22°C) of dibenzo-24-crown-8 (**2**) can cause error in this treatment, since  $K_{ap}[H]$  is not significantly greater than one at high [H] values.

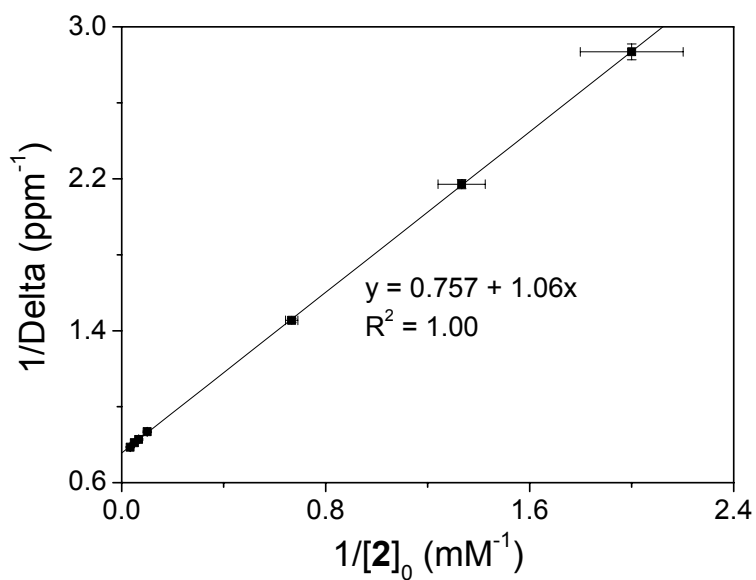


**Figure 1.** Mole ratio plot for **1** and **2**, 22°C. The solvent is acetone-*d*<sub>6</sub>.  $[1]_0$  and  $[2]_0$  are initial concentrations of **1** and **2**.  $[1]_0 = 3.75$  mM.





**Figure 2.** Partial  $^1\text{H}$  NMR spectra (400 MHz, acetone- $d_6$ , 22  $^\circ\text{C}$ ) of (a) 0.500 mM **1**, (b) 0.500 mM **1** and 0.500 mM **2**, (c) 0.500 mM **1** and 0.750 mM **2**, (d) 0.500 mM **1** and 1.50 mM **2**, (e) 0.500 mM **1** and 10.0 mM **2**, (f) 0.500 mM **1** and 15.0 mM **2**, (g) 0.500 mM **1** and 20.0 mM **2**, and (h) 0.500 mM **1** and 30.0 mM **2** showing the chemical shift of  $\text{H}_1$  at different concentrations of **2**. For any given solution  $\Delta = \delta - \delta_u$ ;  $\delta_u$  is defined in spectrum (a).

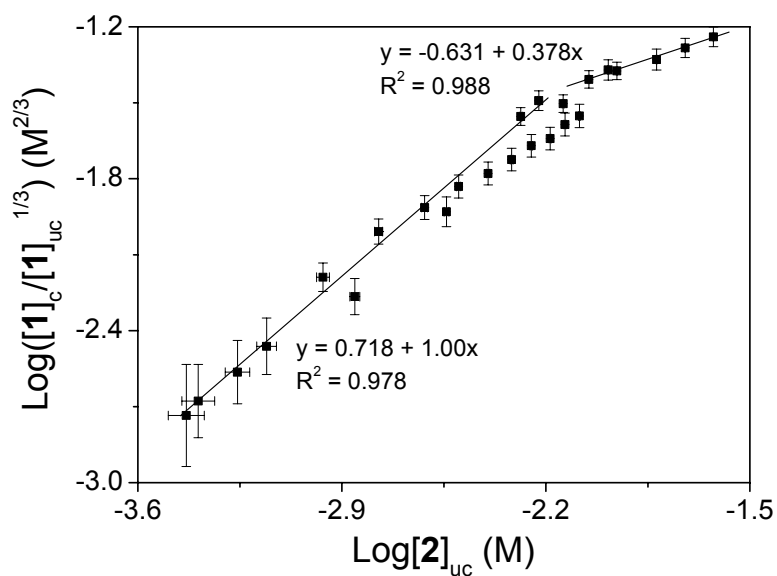


**Figure 3.** Relationship between  $1/\Delta$  and  $1/[2]_0$  for the complexation between **1** and **2** in acetone- $d_6$ , 22°C.  $[1]_0$  and  $[2]_0$  are initial concentrations of **1** and **2**.  $[1]_0$  is constant at 0.500 mM. This plot is based on NMR data shown in Figure 2.

**Table 1.**  $K_{a,exp}$  values at different initial concentrations for the complexation between **1** and **2**; only data for  $0.19 < \Delta/\Delta_0 < 0.83$  is shown.

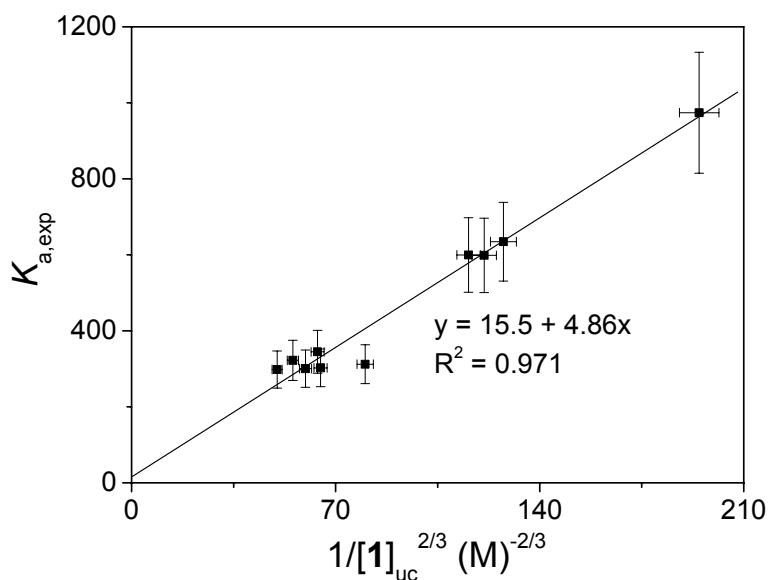
[ <b>1</b> ] <sub>0</sub> (mM)	[ <b>2</b> ] <sub>0</sub> (mM)	$\Delta^a$ (ppm)	$\Delta/\Delta_0^b$	[ <b>1</b> ] <sub>c</sub> or [ <b>2</b> ] <sub>c<sup>c</sup></sub> (mM)	[ <b>2</b> ] <sub>uc<sup>d</sup></sub> (mM)	[ <b>1</b> ] <sub>uc</sub> (mM)	$K_{a,exp,2\bullet 1}$ (M <sup>-1</sup> )
0.500	0.500	0.349	0.264	0.132	0.368	0.368	974
0.500	0.750	0.461	0.349	0.174	0.576	0.326	930
0.500	1.50	0.687	0.520	0.260	1.24	0.240	875
1.00	0.600	0.258	0.195	0.195	0.405	0.805	600
1.00	0.800	0.328	0.248	0.248	0.552	0.752	599
1.00	1.00	0.404	0.306	0.306	0.694	0.694	635
2.00	2.00	0.401	0.303	0.606	1.39	1.39	312
2.00	4.00	0.742	0.562	1.12	2.88	0.877	445
3.75	2.00	0.323	0.244	0.916	1.08	2.83	298
3.75	3.00	0.464	0.352	1.32	1.68	2.43	322
3.75	4.00	0.556	0.421	1.58	2.42	2.17	301
3.75	5.00	0.646	0.489	1.83	3.17	1.92	303
3.75	6.00	0.706	0.534	2.00	4.00	1.75	287
3.75	7.00	0.771	0.584	2.19	4.81	1.56	291
3.75	8.00	0.838	0.634	2.38	5.62	1.37	308
3.75	9.00	0.872	0.660	2.48	6.52	1.27	298
3.75	10.0	0.939	0.711	2.67	7.33	1.08	335
3.75	11.0	0.979	0.741	2.78	8.22	9.71	348
6.00	10.0	0.889	0.673	4.04	5.96	1.96	345
6.00	15.0	1.03	0.780	4.68	10.3	1.32	343
6.00	20.0	1.07	0.812	4.87	15.1	1.13	286
7.60	25.0	1.05	0.794	6.04	19.0	1.56	204
7.60	30.0	1.10	0.828	6.29	23.7	1.31	203
10.0	10.0	0.638	0.483	4.83	5.17	5.17	181
10.0	12.5	0.696	0.527	5.27	7.23	4.73	154
10.0	15.0	0.811	0.614	6.14	8.86	3.86	179
10.0	17.5	0.852	0.645	6.45	11.1	3.55	164

<sup>a</sup> For H<sub>1</sub> of **1**. <sup>b</sup>  $\Delta_0 = 1.32$  ppm. <sup>c</sup> “c” means complexed. <sup>d</sup> “uc” means uncomplexed.



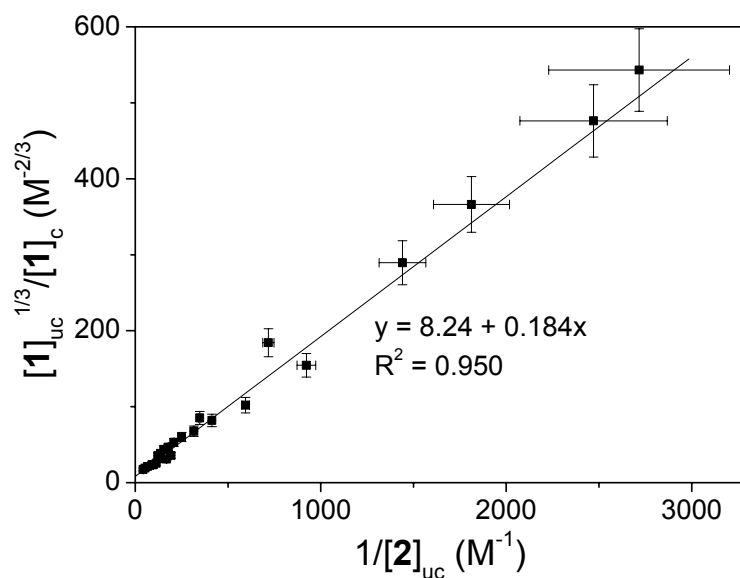
**Figure 4.** Log-log plot of Eq. 1d for the complexation between **1** and **2** in acetone- $d_6$ , 22°C.

Furthermore, a plot of  $K_{a,\text{exp}}$  vs.  $1/[\mathbf{1}]_{uc}^{2/3}$  (Figure 5) according to Eq. 2a for low [H] part was linear and had a zero intercept within experimental error ( $15.5 \pm 30.7$ ), meaning that  $K_{\text{ipc}}$  in Eq. 2a is approximately zero. Therefore, although the guest salt **1** is predominantly ion paired in solution, the complex **2•1** is not and this results in concentration dependent  $K_{a,\text{exp}}$ .



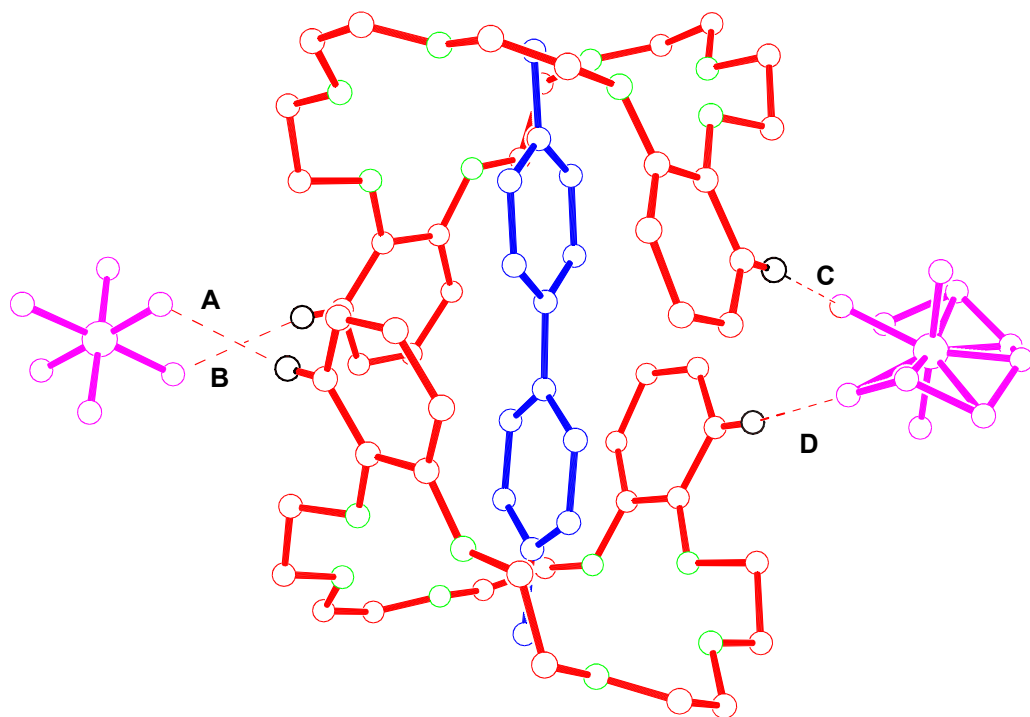
**Figure 5.** Relationship between  $K_{a,exp}$  and  $1/[1]_{uc}^{2/3}$  according to Eq. 1h for  $[2]_{uc} < 3.5$  mM for the complexation between **1** and **2** in acetone- $d_6$ , 22°C.

In application of Eq. 1d by the approximations of Eq. 1e and 1g, because of the limits of  $K_{ap}[H] \ll 1$  and  $K_{ap}[H] \gg 1$ , not all data are useful. In order to utilize all of the data and obtain alternative estimates of the equilibrium constants, we can use Eq. 1i. From a plot of  $[G^{++}2X^-]^{1/3}/[HG^{++}]$  vs.  $1/[H]$  (Figure 6) for all data shown in Table 1, the values of  $K_{ap}$  and  $K_{ipd}$  were estimated to be  $67.2 (\pm 11.1) \text{ M}^{-1}$  and  $2.12 (\pm 1.33) \times 10^{-3} \text{ M}^2$  from the slope and intercept. With the host-guest systems previously studied use of the approximation based on the binomial expansion underestimated  $K_{ap}$  and overestimated  $K_{ipd}$ .<sup>4</sup> That appears to be the case here as well. Thus, we believe the values determined from Figure 4 are preferred.

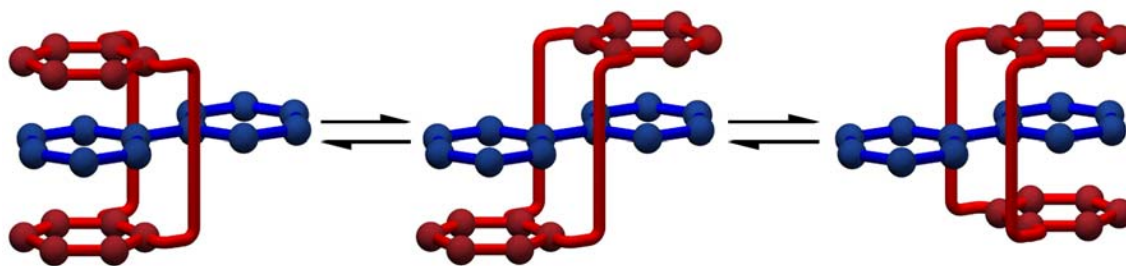


**Figure 6.** Relationship between  $[1]_{uc}^{1/3}/[1]_c$  and  $1/[2]_{uc}^{2/3}$  according to Eq. 1i.

X-ray crystallography has long been used as a guide to low energy structures existing in solution, although such deductions can be misleading. The complex between **1** and **2** has a 1:2 stoichiometry in the solid state (Figure 7).<sup>7</sup> However, from this structure, we deduce that one possible reason for the lack of ion-pairing of **2•1** in solution is that it is difficult for a  $PF_6^-$  counterion to ion pair with the paraquat dication which is confined to the small cavity of the host. In solution the flexibility of the crown ether is expected to allow rapid folding such that the benzo rings interact with both pyridinium rings of the guest as shown in Figure 8. Presumably the formation of the 2:1 complex in the crystal results from freezing the conformational equilibria shown in Figure 8 and the more efficient packing of the 2:1 structure. In fact, a 2:1 (the host to paraquat) complex resulted even from a solution with excess paraquat.<sup>3d</sup>



**Figure 7.** X-ray crystal structure of the complex  $2_2 \bullet 1$ .<sup>7</sup> **2** molecules are red, **1** molecule is blue,  $\text{PF}_6^-$  counterions are magenta, oxygens are green, and hydrogens are black. Selected hydrogen-bond parameters: C-F distances (Å) **A** = 3.31, **B** = 3.31, **C** = 3.38, **D** = 3.38; H $\cdots$ F distances (Å) **A** = 2.47, **B** = 2.47, **C** = 2.44, **D** = 2.44; C-H $\cdots$ F angles (deg) **A** = 148, **B** = 148, **C** = 174, **D** = 174. The  $\text{PF}_6^-$  counterion shown on the right is disordered over 2 positions, with each position constrained to 50% occupancy by symmetry.



**Figure 8.** Cartoon representations of possible co-conformations of the 1:1 complex between **1** (blue) and **2** (red) in solution, showing the interactions between both benzo rings of **2** with both pyridinium rings of **1**, thus preventing ion pairing of the complex.

### C. Complexation between bis(*m*-phenylene)-32-crown-10 (BMP32C10) derivatives and paraquat derivatives.

Stoddart et al. first reported the complexation between BMP32C10 (**3**) and **1**.<sup>10</sup> Later, we demonstrated that a BMP32C10 derivative (**4**) forms a taco, or folded, complex with **1**<sup>11</sup> and extended this recognition motif to preparations of a pseudorotaxane<sup>12</sup> of **1** based on a supramolecular cryptand involving chelation of the hydroxyl groups of **4** as well as a supramolecular poly(taco complex) based on **3** and **5**.<sup>13</sup> In the present work NMR characterizations were done using solutions with constant concentration of **4** (0.500 mM) and varying concentrations of **1** (0.500~30.0 mM). Based on these NMR data,  $\Delta_0$ , the difference in  $\delta$  values for H<sub>2</sub> in **4** in the uncomplexed and fully complexed species, was calculated as outlined above to be 0.526 ppm.  $K_{a,exp,4\bullet 1}$  values (Table 2) were then calculated from  $K_{a,exp,4\bullet 1} = (\Delta/\Delta_0)[\mathbf{4}]_0 / \{ \{ [\mathbf{4}]_0 - (\Delta/\Delta_0)[\mathbf{4}]_0 \} \{ [\mathbf{1}]_0 - (\Delta/\Delta_0)[\mathbf{4}]_0 \} \}$ , where  $[\mathbf{4}]_0$  is



the initial concentration of **4** and  $\Delta$  is the chemical shift change of H<sub>2</sub>. The same experiments were performed on the complex **3•5**. Based on proton NMR data of H<sub>3</sub> in **3**, the values of  $K_{a,exp,3•5}$  of the complex **3•5** were similarly calculated (Table 3). As can be seen,  $K_{a,exp,4•1}$  and  $K_{a,exp,3•5}$  are not concentration dependent and therefore correspond to the case where the complex is essentially completely ion paired, i. e., Eq. 2a,  $K_{ap} = 0$ . Scatchard plots (Figures 9 and 10) were made for both of the complexes according to Eq. 2b. The intercepts of the two lines are identical to the ideal value, 0, within experimental error. The slopes,  $1.23 (\pm 0.06) \times 10^3 \text{ M}^{-1}$  for **4•1** and  $536 (\pm 27) \text{ M}^{-1}$  for **3•5** are values of  $K_{a,exp,4•1}$  and  $K_{a,exp,3•5}$ , respectively.

Ion pairing of **4•1** and **3•5** in the solid state was confirmed by their X-ray crystal structures (Figure 11),<sup>11,13</sup> in which PF<sub>6</sub> counterions are close to the paraquat guests and directly connected to them by hydrogen bonds. In the case of **4•1** this is possible because the “front” side of the taco is accessible to the PF<sub>6</sub> anion for hydrogen bonding to the methyl groups and the “rear” cavity is sufficiently large to also permit the anion to hydrogen bond with the  $\beta$ -protons of **1**. In **3•5** both PF<sub>6</sub> anions have ready access to the  $\alpha$ - and NH-protons of the guest on the “open” or “front” side of the taco complex. Presumably this situation also exists in solution.

**Table 2.**  $K_{a,exp}$  values at different initial concentrations for the complexation between **1** and **4**.

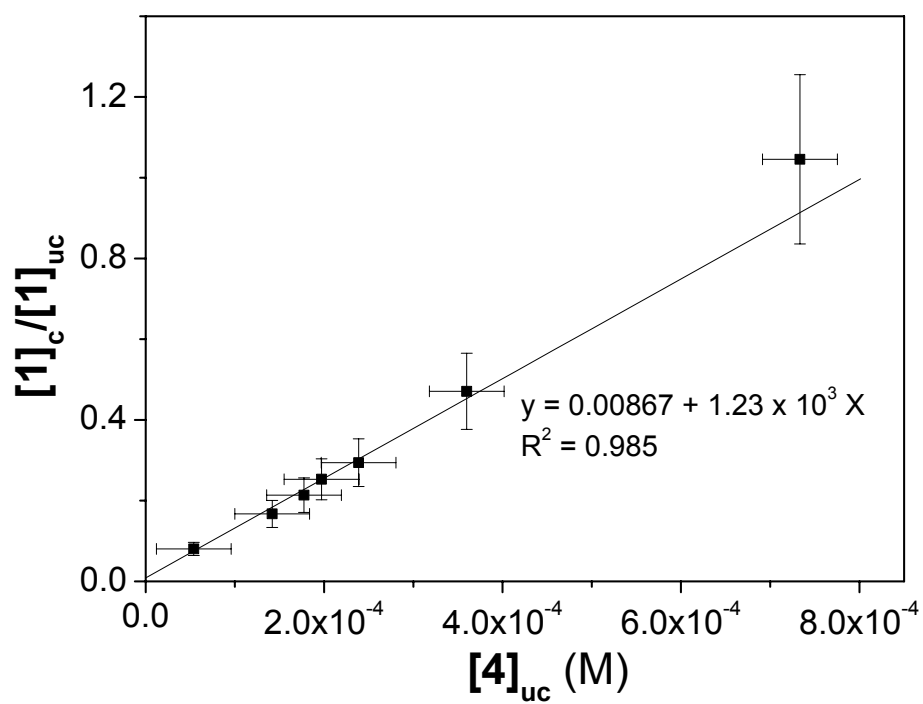
[4] <sub>0</sub> (mM)	[1] <sub>0</sub> (mM)	$\Delta^a$ (ppm)	$\Delta/\Delta_0^b$	[4] <sub>c</sub> or [1] <sub>c</sub> <sup>c</sup> (mM)	[1] <sub>uc</sub> <sup>d</sup> (mM)	[4] <sub>uc</sub> (mM)	$K_{a,exp,4\bullet 1}$ (M <sup>-1</sup> )
0.500	1.50	0.319	0.606	0.303	1.20	0.197	1.28E3
0.500	2.50	0.377	0.716	0.358	2.14	0.142	1.18E3
0.500	6.00	0.470	0.892	0.446	5.55	0.0540	1.49E3
0.600	2.40	0.371	0.704	0.422	1.98	0.178	1.20E3
0.750	2.25	0.359	0.682	0.511	1.74	0.239	1.23E3
1.00	2.00	0.337	0.640	0.640	1.36	0.360	1.31E3
1.50	1.50	0.269	0.511	0.767	0.733	0.733	1.43E3

<sup>a</sup> for H<sub>2</sub> of **4**. <sup>b</sup>  $\Delta_0 = 0.526$  ppm. <sup>c</sup> “c” means complexed. <sup>d</sup> “uc” means uncomplexed.

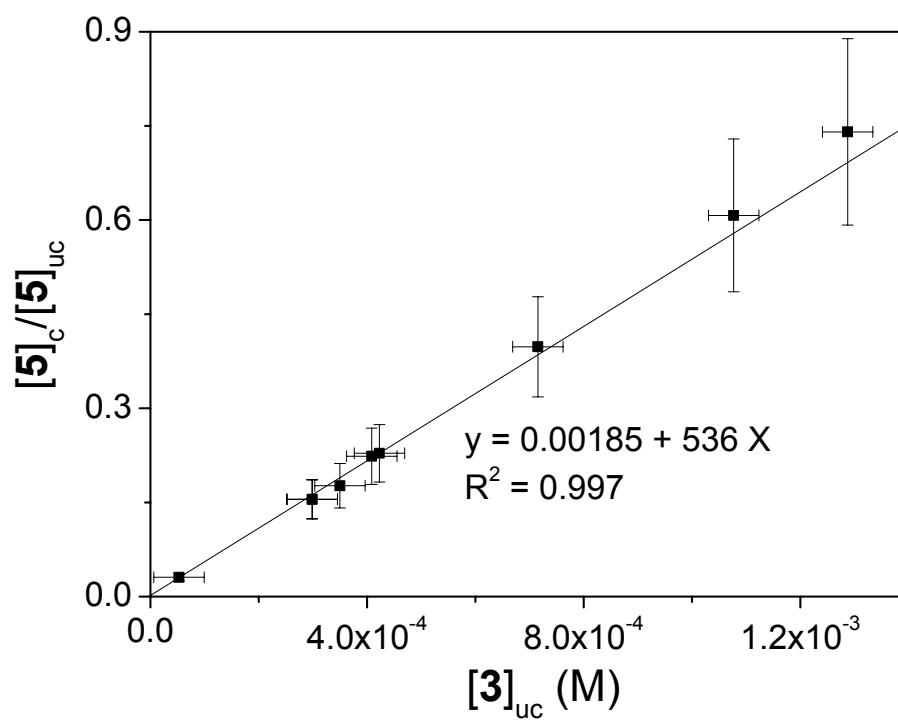
**Table 3.**  $K_{a,exp}$  values at different initial concentrations for the complexation between **3** and **5**.

[3] <sub>0</sub> (mM)	[5] <sub>0</sub> (mM)	$\Delta^a$ (ppm)	$\Delta/\Delta_0^b$	[3] <sub>c</sub> or [5] <sub>c</sub> <sup>c</sup> (mM)	[5] <sub>uc</sub> <sup>d</sup> (mM)	[3] <sub>uc</sub> (mM)	$K_{a,exp}$ (M <sup>-1</sup> )
0.500	0.500	0.0874	0.183	0.0914	0.409	0.409	547
0.500	1.00	0.143	0.300	0.150	0.850	0.350	505
0.500	1.50	0.192	0.403	0.201	1.30	0.299	519
0.500	15.0	0.428	0.895	0.447	14.6	0.0527	583
0.670	1.33	0.176	0.369	0.247	1.08	0.423	540
1.00	1.00	0.136	0.285	0.285	0.715	0.715	556
1.33	0.670	0.0910	0.190	0.253	0.417	1.08	564
1.50	0.500	0.0678	0.142	0.213	0.287	1.29	575

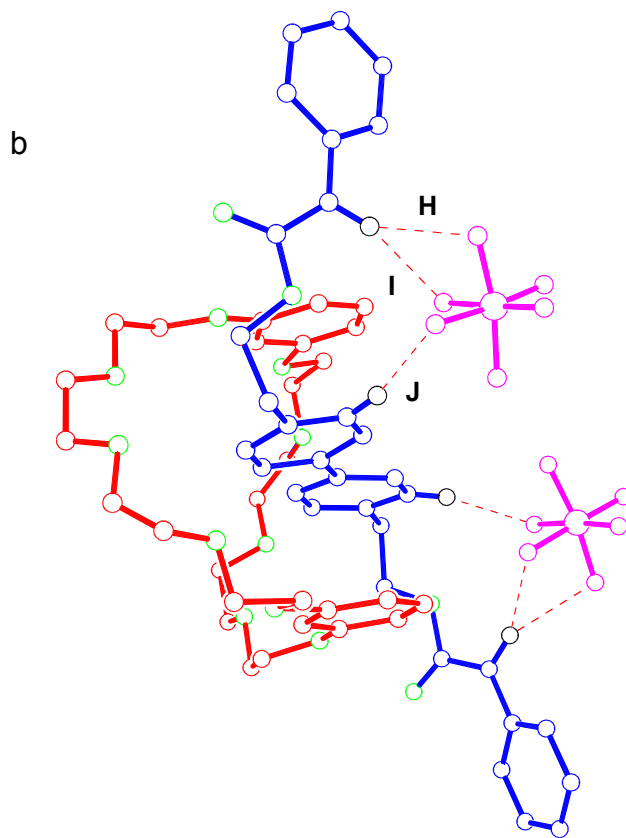
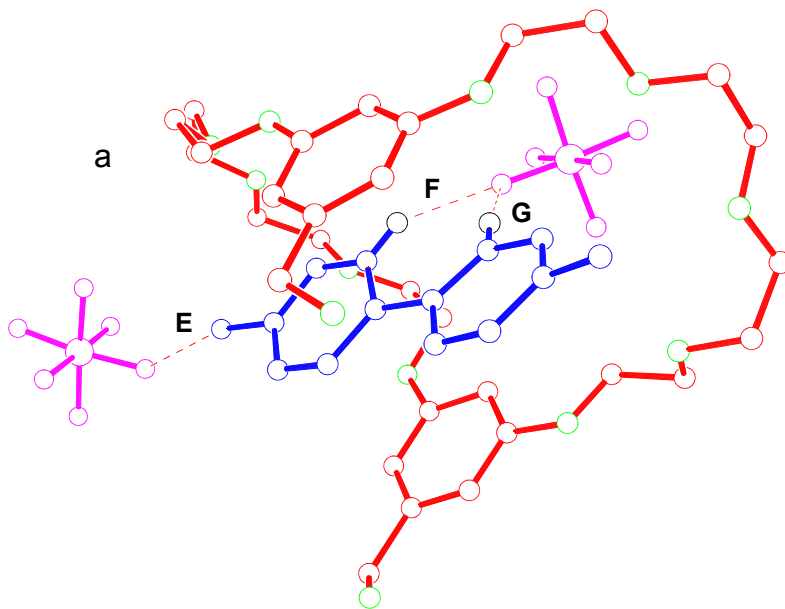
<sup>a</sup> for H<sub>3</sub> of **3**. <sup>b</sup>  $\Delta_0 = 0.478$  ppm. <sup>c</sup> “c” means complexed. <sup>d</sup> “uc” means uncomplexed.



**Figure 9.** Plot of Eq. 2b for the complexation between **1** and **4** in acetone- $d_6$ , 22°C.



**Figure 10.** Plot of Eq. 2b for the complexation between **3** and **5** in acetone- $d_6$ , 22°C.



**Figure 11.** X-ray crystal structures of **4•1**<sup>11</sup> (a) and **3•5**<sup>13</sup> (b). Host (**4** or **3**) is red, guest (**1** or **5**) is blue, PF<sub>6</sub><sup>-</sup> counterions are magenta, oxygens are green, and hydrogens are black. Selected hydrogen-bond parameters: C(N)-F distances (Å) **E** = 2.99, **F** = 3.27, **G** = 3.24, **H** = 3.28, **I** = 3.37, **J** = 3.34; H...F distances (Å) **F** = 2.34, **G** = 2.42, **H** = 2.37, **I** = 2.42, **J** = 2.38; C(N)-H...F angles (deg) **F** = 168, **G** = 144, **H** = 149, **I** = 157, **J** = 167. H...F distance and C-H...F angle of the hydrogen bond **E** are not available because hydrogens on the methyl groups in **4•1** were not determined.

#### **D. Complexation between bis(*p*-phenylene)-34-crown-10 (BPP34C10) and paraquat derivatives.**

Stoddart et al. first discussed the complexation between BPP34C10 (**6**) and **1**.<sup>14</sup> Later they reported the BPP34C10/paraquat diol complex, **6•7**.<sup>15</sup> BPP34C10 derivatives have become the most commonly used host for paraquat derivatives.<sup>5</sup> Based on proton NMR data of H<sub>4</sub>, the values (Tables 4 and 5) of  $K_{a,exp}$  of the complexes **6•1** and **6•7** were determined. As shown for **4•1** and **3•5**,  $K_{a,exp}$  values of **6•1** and **6•7** do not exhibit concentration dependence. Plots (Figures 12 and 13) were made for **6•1** and **6•7** according to Scatchard equation 2b. Again, the intercepts of two plots are zero within experimental error. From the slopes we determined  $K_{a,exp,6•1} = 728 (\pm 73) \text{ M}^{-1}$  and  $K_{a,exp,6•7} = 376 (\pm 38) \text{ M}^{-1}$ .

Ion pairing of complexes **6•1** and **6•7** in the solid state was confirmed by their X-ray crystal structures (Figure 14).<sup>14,15</sup> In both crystal structures, PF<sub>6</sub><sup>-</sup> counterions are adjacent to the viologens and directly connected to them by hydrogen bonds. In **6•1** the

protruding methyl groups of the pseudorotaxane-like complex are readily accessible for H-bonding to the PF<sub>6</sub> anion. In the pseudorotaxane **6•7** the diagonal positioning of guest **7** in the spacious cavity of the host allows its  $\beta$ -protons to H-bond with the PF<sub>6</sub> anions on opposite sides. Again the solid state interactions are consistent with ion pairing of the complexes in solution.

**Table 4.**  $K_{a,exp}$  values at different initial concentrations for the complexation between **6** and **1**.

[ <b>6</b> ] <sub>0</sub> (mM)	[ <b>1</b> ] <sub>0</sub> (mM)	$\Delta$ (ppm)	$\Delta/\Delta_0$	[ <b>1</b> ] <sub>c</sub> or [ <b>6</b> ] <sub>c</sub> <sup>c</sup> (mM)	[ <b>1</b> ] <sub>uc</sub> <sup>d</sup> (mM)	[ <b>6</b> ] <sub>uc</sub> (mM)	$K_{a,exp}$ (M <sup>-1</sup> )
1.00	10.0	0.403	0.862	0.862	9.14	0.138	683
0.500	2.50	0.275	0.589	0.295	2.21	0.205	650
0.600	2.40	0.269	0.576	0.345	2.05	0.255	660
0.750	2.25	0.258	0.552	0.414	1.84	0.336	670
1.00	2.00	0.235	0.504	0.504	1.50	0.496	678
1.50	1.50	0.189	0.404	0.605	0.895	0.895	756
2.00	1.00	0.123	0.263	0.526	0.474	1.47	751

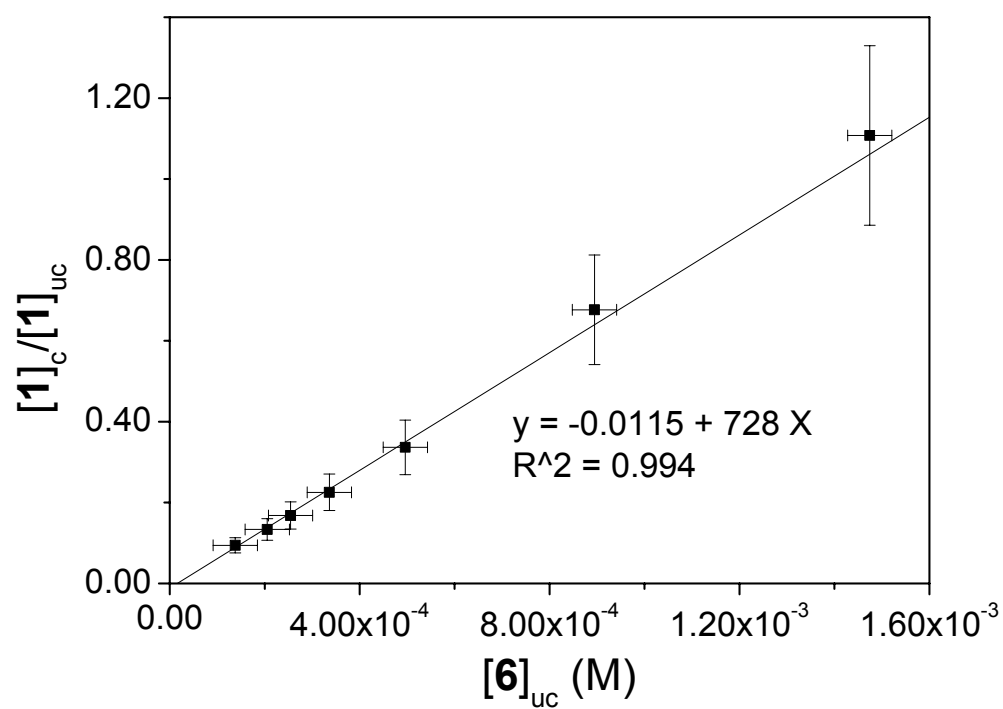
<sup>a</sup> for H<sub>4</sub> of **6**. <sup>b</sup>  $\Delta_0 = 0.467$  ppm. <sup>c</sup> “c” means complexed. <sup>d</sup> “uc” means uncomplexed.

**Table 5.**  $K_{a,\text{exp}}$  values at different initial concentrations for the complexation between **6** and **7**.

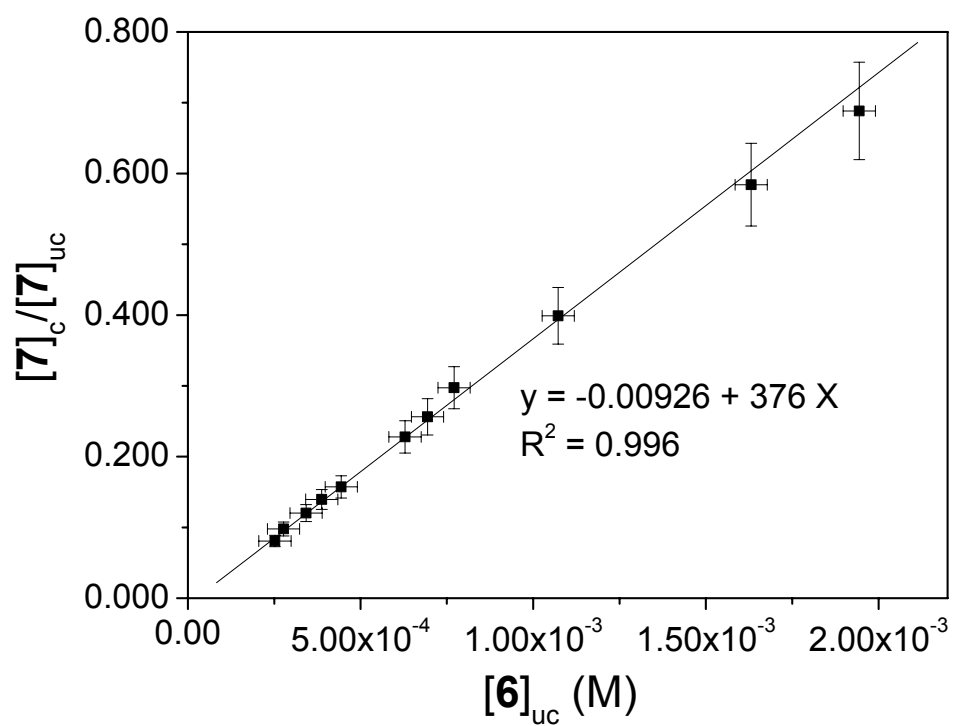
[ <b>6</b> ] <sub>0</sub> (mM)	[ <b>7</b> ] <sub>0</sub> (mM)	$\Delta$ (ppm)	$\Delta/\Delta_0$	[ <b>6</b> ] <sub>c</sub> or [ <b>7</b> ] <sub>c</sub> (mM)	[ <b>7</b> ] <sub>uc</sub> <sup>d</sup> (mM)	[ <b>6</b> ] <sub>uc</sub> (mM)	$K_{a,\text{exp}}$ (M <sup>-1</sup> )
1.00	1.00	0.113	0.229	0.229	0.771	0.771	386
1.00	1.50	0.151	0.306	0.306	1.19	0.694	369
1.00	5.00	0.302	0.612	0.612	4.39	0.388	360
1.00	10.0	0.369	0.748	0.748	9.25	0.252	321
0.500	2.50	0.220	0.446	0.223	2.28	0.277	353
0.600	2.40	0.212	0.430	0.258	2.14	0.342	352
0.750	2.25	0.201	0.408	0.306	1.94	0.444	354
1.00	2.00	0.183	0.371	0.371	1.63	0.629	362
1.50	1.50	0.141	0.285	0.428	1.07	1.07	372
2.00	1.00	0.0909	0.184	0.369	0.631	1.63	358
2.25	0.750	0.0670	0.136	0.306	0.444	1.94	354

<sup>a</sup> for H<sub>4</sub> of **6**. <sup>b</sup>  $\Delta_0 = 0.493$  ppm. <sup>c</sup> “c” means complexed. <sup>d</sup> “uc” means uncomplexed.

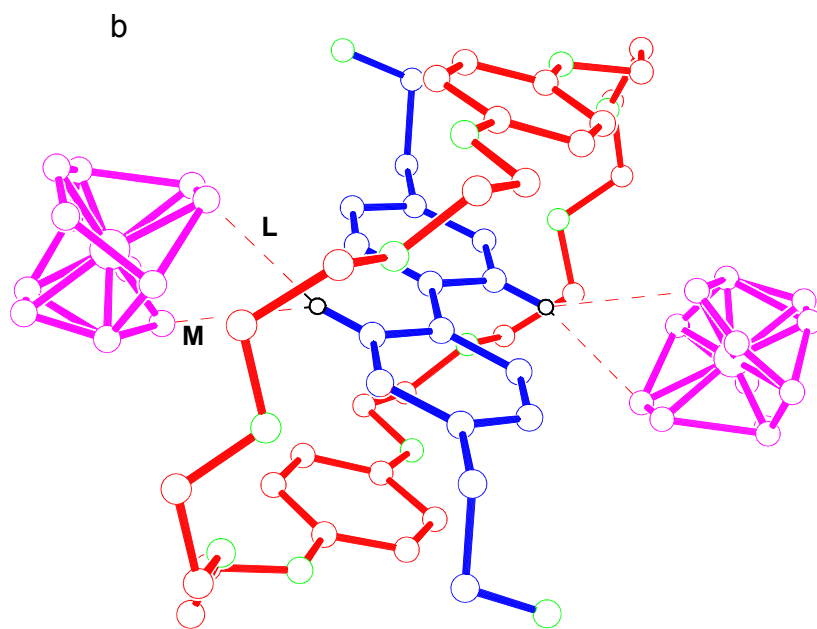
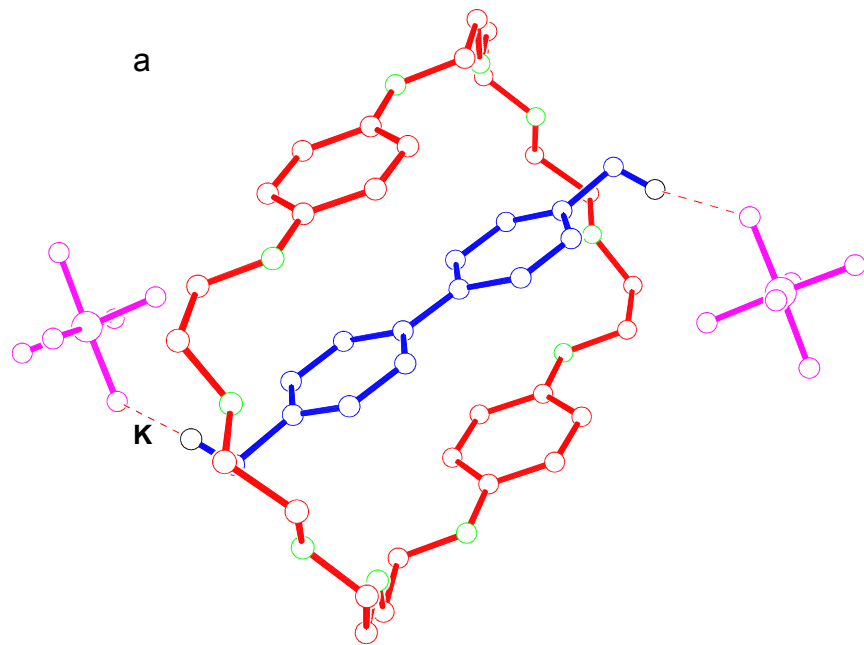




**Figure 12.** Plot of Eq. 2b for the complexation between **6** and **1** in acetone- $d_6$ , 22°C.



**Figure 13.** Plot of Eq. 2b for the complexation between **6** and **7** in acetone- $d_6$ , 22°C.



**Figure 14.** X-ray crystal structures of **6•1**<sup>14</sup> (a) and **6•7**<sup>15</sup> (b). Host (**6**) is red, guest (**1** or **7**) is blue, PF<sub>6</sub><sup>-</sup> counterions are magenta, oxygens are green, and hydrogens are black. Selected hydrogen-bond parameters: F-C distances (Å) **K** = 3.36, **L** = 3.21, **M** = 3.30; H···F distances (Å) **K** = 2.53, **L** = 2.36, **M** = 2.46; C-H···F angles (deg) **K** = 145, **L** = 147, **M** = 147. The PF<sub>6</sub> counterions in **6•7** are disordered.

### 4.3. CONCLUSIONS

The concentration dependence of apparent association constants,  $K_{a,exp}$ , of fast exchange host-guest systems was studied using complexes based on viologens and crown ethers. While the bis(hexafluorophosphate) salts of paraquat derivatives are predominantly ion paired in acetone (and other low dielectric constant solvents presumably) the complex based on dibenzo-24-crown-8 and paraquat is not ion paired in solution, resulting in concentration dependence of  $K_{a,exp}$ . The value of the ion pair dissociation constant [ $K_{ipd} = 7.72 (\pm 0.77) \times 10^{-4} \text{ M}^2$ ] of paraquat bis(hexafluorophosphate) in acetone-d<sub>6</sub> was determined from study of its complexation with dibenzo-24-crown-8. However, four complexes of two different bis(*m*-phenylene)-32-crown-10 derivatives and bis(*p*-phenylene)-34-crown-10 with viologens are ion paired in solution, as shown by the fact that  $K_{a,exp}$  is not concentration dependent for these systems involving hosts with freer access to bound guests. X-ray crystal structures support these solution-based assessments in that there is clearly ion pairing of the cationic guest and its PF<sub>6</sub><sup>-</sup> counterions in the solid states of the latter four examples whereas the former does not.

The equilibrium treatment presented here is applicable to any complexation process involving a dicationic guest having monovalent counterions and a neutral host in low dielectric media in which the salt is predominantly ion paired. Conversely, the treatment can be readily adapted to the situation in which a neutral guest interacts with a dicationic host having two univalent counterions. Moreover, the protocols can readily be applied to systems in which a dianion having univalent counterions is the guest species for a neutral host. Application of this treatment enables one to determine whether the complex is ion paired in solution: if so, there will be no concentration dependence of  $K_{a,exp}$ ; if not,  $K_{a,exp}$  will exhibit concentration dependence. Moreover, if both free guest ion and the ion pair undergo complexation the contribution of both modes can be measured.

#### 4.4. ACKNOWLEDGEMENTS

Acknowledgement is made to the National Science Foundation via grant DMR-0097126. We also thank Edgar Rodriguez for the rendering of Figure 6.

#### 4.5. EXPERIMENTAL

**2** was purchased and used as received. All other compounds were prepared by literature procedures.

The 400 MHz  $^1\text{H}$  NMR spectra were recorded on a Varian Inova Instrument. All complexes discussed in this paper have 1:1 stoichiometry in solution and are fast exchange systems by 400 MHz  $^1\text{H}$  NMR.

All solutions were prepared as follows. Precisely weighed amounts of dried chemicals were added into screw cap vials. Acetone- $d_6$  was added with to-deliver volumetric pipets. Then specific volumes of each fresh solution were mixed to yield the desired concentrations. For example, in order to make three solutions, 10.0 mM **1** and 10.0 mM **2**, 10.0 mM **1** and 15.0 mM **2**, and 10.0 mM **1** and 17.5 mM **2**, a 10.0 mM solution of **1** was made first by adding 5.00 mL acetone- $d_6$  with a 5.00 mL to-deliver pipette into a screw cap vial containing 23.81 mg (0.0500 mmol) of **1**. Then 0.600 mL of this solution was added with a 0.300 mL to-deliver pipet two times to three vials which contained 2.69, 4.04, and 4.71 mg of **2** separately.  $^1\text{H}$  NMR data were collected on a temperature controlled spectrometer. Acetone- $d_6$  was chosen as the solvent because all compounds used here have good solubilities in it. Error bars were calculated by assuming a  $\pm 5\%$  deviation in percent complexation ( $\Delta/\Delta_0$ ). Linear regressions were performed using the entire error range (abscissa and ordinate) at each data point; standard errors in both the intercept and slope coefficients based on regression were used to determine errors in association constants.

**Keywords:** ion pairs, association constant, concentration, complex, crown ethers

## REFERENCES

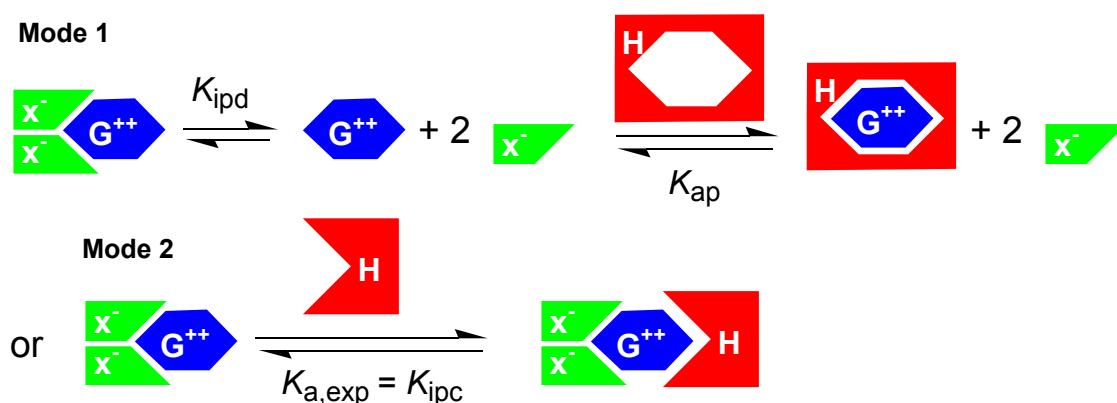
1. Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017-7036.
2. (a) Merz, T.; Wirtz, H.; Vögtle, F. *Angew. Chem., Int. Ed. Eng.* **1986**, *25*, 567-568. (b) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S. *Chem. Rev.* **1991**, *91*, 1721-2085. (c) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. L. *Chem. Rev.* **1995**, *95*, 2529-2586. (d) Antonisse, M. M. G.; Reinhoudt, D. N. *Chem. Commun.* **1998**, 443-448. (e) Andrews, P. C.; Kennedy, A. R.; Mulvey, R. E.; Raston, C. L.; Roberts, B. A.; Rowlings, R. B. *Angew. Chem., Int. Ed.* **2000**, *39*, 1960-1962. (f) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486-516. (g) Haj-Zaroubi, M.; Mitzel, N. W.; Schmidtchen, F. P. *Angew. Chem., Int. Ed.* **2002**, *41*, 104-107. (h) Schmidtchen, F. P. *Org. Lett.* **2002**, *4*, 431-434. (i) Lee, C.-H.; Na, H.-K.; Yoon, D.-W.; Won, D.-H.; Cho, W.-S.; Lynch, V. M.; Shevchuk, S. V.; Sessler, J. L. *J. Am. Chem. Soc.* **2003**, *125*, ASAP, May 21.
3. (a) Gibson, H. W.; Yamaguchi, N.; Hamilton, L.; Jones, J. W. *J. Am. Chem. Soc.* **2002**, *124*, 4653-4665. (b) Gibson, H. W.; Yamaguchi, N.; Jones, J. W. *J. Am. Chem. Soc.* **2003**, *125*, 3522-3533. (c) Jones, J. W.; Bryant, W. S.; Bosman, A. W.; Janssen, R. A. J.; Meijer, E. W.; Gibson, H. W. *J. Org. Chem.* **2003**, *68*, 2385-2389. (d) Huang, F.; Gibson, H. W.; Bryant, W. S.; Nagvekar, D. S.; Fronczek, F. *J. Am. Chem. Soc.* in press.
4. Jones, J. W.; Gibson, H. W. *J. Am. Chem. Soc.* **2003**, *125*, 7001-7004.

5. Reviews: Gibson, H. W. In *Large Ring Molecules*; Semlyen, J. A. Ed.; John Wiley & Sons: New York, **1996**; Ch. 6, pp 191-262. Harada, A. *Acta Polym.* **1998**, *49*, 3-17. Raymo, F. M.; Stoddart, J. F. *Chem. Rev.* **1999**, *99*, 1643-1664. Mahan, E.; Gibson, H. W. In *Cyclic Polymers*, 2nd ed.; Semlyen, A. J. Ed.; Kluwer Publishers: Dordrecht, **2000**; pp 415-560. Hubin, T. J.; Busch, D. H. *Coord. Chem. Rev.* **2000**, *200-202*, 5-52. Panova, I. G.; Topchieva, I. N. *Russ. Chem. Rev.* **2001**, *70*, 23-44.
6. Marshall, A. G. *Biophysical Chemistry*; J. Wiley and Sons: New York, **1978**; pp 70-77. Freifelder, D. M. *Physical Biochemistry*; W. H. Freeman and Co.: New York, **1982**; pp 659-660. Connors, K. A. *Binding Constants*; J. Wiley and Sons: New York, **1987**; pp 78-86.
7. Huang, F.; Slebodnick, C.; Golen, J. A.; Rheingold, A. L.; Gibson, H. W. Submitted to *Chem. Commun.*
8. Tsukube, H.; Furuta, H.; Odani, A.; Takeda, Y.; Kudo, Y.; Inoue, Y.; Liu, Y.; Sakamoto, H.; Kimura, K. In *Comprehensive Supramolecular Chemistry*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Vogtle, F., Lehn, J.-M., Eds.; Elsevier: New York, **1996**; Vol. 8, p 425.
9. According to Eqs. 1e and 1g, the intercepts of two best fit lines in Figure 4 give  $\log(K_{ap,2\bullet 1}^{1/3} K_{ipd,1}^{1/3} / 2^{2/3}) = -0.631$  and  $\log(K_{ap,2\bullet 1} K_{ipd,1}^{1/3} / 2^{2/3}) = 0.718$ . From these two equations, the values of  $K_{ap,2\bullet 1}$  and  $K_{ipd,1}$  were determined. Errors are based on errors of the intercepts.
10. Allwood, B. L.; Spencer, N.; Shahriari-Zavareh, H.; Stoddart, J. F.; Williams, D. J.



- J. Chem. Soc., Chem. Commun.* **1987**, 1058-1061.
11. Bryant, W. S.; Jones, J. W.; Mason, P. E.; Guzei, I. A.; Rheingold, A. L.; Nagvekar, D. S.; Gibson, H. W. *Org. Lett.* **1999**, *1*, 1001-1004.
  12. Jones, J. W.; Zakharov, L. N.; Rheingold, A. L.; Gibson, H. W. *J. Am. Chem. Soc.* **2002**, *124*, 13378-13379.
  13. Huang, F.; Fronczek, F. R. Gibson, H. W. *Chem. Commun.* **2003**, 1480-1481.
  14. Allwood, B. L.; Spencer, N.; Shahriari-Zavareh, H.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc. Chem. Commun.* **1987**, 1064-1066.
  15. Ashton, P. R.; Philp, D.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 1680-1683.

---

**TOC Graphic:**

**Abstract:** An equilibrium treatment of complexation of neutral hosts with dicationic guests having univalent counterions includes two possible modes: (1) dissociation of the ion pair prior to interaction of the free dication with the host to produce a complex that is not ion paired and (2) direct complexation of the ion pair to produce an ion paired complex. The treatment is easily modified for complexation of neutral guests by dianionic hosts, or divalent hosts by neutral guests. The treatment was tested by a study of fast exchange host-guest systems based on viologens ( $G^{2+}2X^{-}$ ) and crown ethers (H). The bis(hexafluorophosphate) salts of viologens are predominantly ion paired in acetone; the value of the dissociating constant of paraquat bis(hexafluorophosphate) was determined to be  $7.72 (\pm 0.77) \times 10^{-4} M^2$ . The complex based on dibenzo-24-crown-8 and paraquat bis(hexafluorophosphate) is

not ion paired in solution, resulting in concentration dependence of the apparent association constant  $K_{a,exp}$ , ( $= [\text{Complex}]/[\text{H}][\text{G}^{++}2\text{X}^-]$ ) which is well fit by the treatment, according to mode (1). However, the four complexes of two different bis(*m*-phenylene)-32-crown-10 derivatives and bis(*p*-phenylene)-34-crown-10 with paraquat derivatives are all ion paired in solution;  $K_{a,exp}$  is not concentration dependent for these systems, mode (2). X-ray crystal structures support these assessments in that there is clearly ion pairing of the cationic guest and its  $\text{PF}_6^-$  counterions in the solid states of the latter four examples in which access of the counterions to the guests is granted by the relatively large cavities and dispositions of the guest species within them.

---