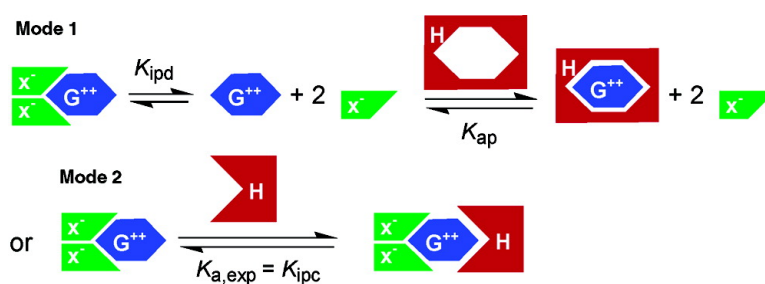


## Ion Pairing in Fast-Exchange Host–Guest Systems: Concentration Dependence of Apparent Association Constants for Complexes of Neutral Hosts and Divalent Guest Salts with Monovalent Counterions

Feihe Huang, Jason W. Jones, Carla Slebodnick, and Harry W. Gibson

*J. Am. Chem. Soc.*, **2003**, 125 (47), 14458-14464 • DOI: 10.1021/ja036606f • Publication Date (Web): 05 November 2003

Downloaded from <http://pubs.acs.org> on March 30, 2009



### More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 18 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

[View the Full Text HTML](#)

# 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

Feihe Huang, Jason W. Jones, Carla Slebodnick, and Harry W. Gibson\*

Contribution from the Department of Chemistry, Virginia Polytechnic Institute & State University, Blacksburg, Virginia 24061

Received June 10, 2003; E-mail: hwgibson@vt.edu

**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. This 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 paraquats or viologens ( $G^{2+}2X^{-}$ ) and crown ethers (H). The bis(hexafluorophosphate) salts of viologens are predominantly ion paired in acetone; the value of the dissociation constant of paraquat bis(hexafluorophosphate) was determined to be  $4.64 (\pm 1.86) \times 10^{-4} M^2$ . 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  $K_{a,exp}$ , ( $= [\text{complex}]/[H][G^{2+}2X^{-}]$ ) which is well fit by the treatment, according to mode (1), yielding  $K_{ap} = 106 (\pm 42) M^{-1}$ . 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 and therefore  $K_{a,exp}$  is not concentration dependent for these systems, mode (2). X-ray crystal structures support these solution-based assessments in that there is clearly ion pairing of the cationic guest with its  $PF_6^{-}$  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 of the hosts and dispositions of the guest species within them.

## Introduction

Applications of ionic compounds in supramolecular chemistry can be dated 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 the association constants of slow exchange (NMR) systems involving at least one ionic species in low dielectric constant solvents can be attributed to ion pairing of the salts and the dissociated nature of the complex.<sup>4</sup> Because many host–guest complexations are fast exchange (NMR) systems,<sup>5</sup> we have studied and report here for the first time the effects of ion pairing on complexations of dicationic paraquat derivatives with two monovalent counterions ( $G^{2+}X^{-}$ ) 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,  $K_{a,exp} = [\text{complex}]/[\text{host}][\text{guest}]$ , with concentration

- (1) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017–7036.  
(2) (a) Merz, T.; Wirtz, H.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **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*, 7301–7306.  
(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.; Fronczek, F. R.; Gibson, H. W. *J. Am. Chem. Soc.* **2003**, *125*, 9272–9273. (e) Huang, F.; Gibson, H. W.; Bryant, W. S.; Nagvekar, D. S.; Fronczek, F. R. *J. Am. Chem. Soc.* **2003**, *125*, 9367–9371. (f) Huang, F.; Zakharov, L. N.; Rheingold, A. L.; Jones, J. W.; Gibson, H. W. *Chem. Commun.* **2003**, 2122–2123.

- (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. *Catenanes, Rotaxanes and Knots*; Sauvage, J.-P., Dietrich-Buchecker, C. O., Eds; Wiley-VCH: Weinheim, 1999. 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.

involve dissociated complexes, whereas those whose  $K_{a,\text{exp}}$  are invariant with concentration involve ion paired complexes.

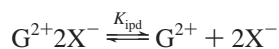
## Results and Discussion

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

$$K_{a,\text{exp}} = [\text{complex}]/[\text{host}]_{\text{uc}}[\text{guest}]_{\text{uc}}$$

where  $[\text{complex}] = [\text{host}]_{\text{c}} = [\text{guest}]_{\text{c}}$ ,  $[\text{host}]_{\text{uc}} = [\text{host}]_0 - [\text{complex}]$ , and  $[\text{guest}]_{\text{uc}} = [\text{guest}]_0 - [\text{complex}]$ . 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,  $G^{2+}2X^-$ , which is predominantly ion paired, (b) after dissociation of the guest salt it is the free dication  $G^{2+}$  that forms the complex, (c) there are no other species present in the solutions. If the complex is not ion paired, then we can derive



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

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

$$K_{\text{ap}} = [HG^{2+}]/[H][G^{2+}]$$

$$[HG^{2+}] = K_{\text{ap}}[H][G^{2+}]$$

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

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

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

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

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

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

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

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

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

Under this condition the free counterion is essentially all generated as a result of complexation and eq 1c becomes

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

In other words  $K_{a,\text{exp}}$  depends on both  $[G^{2+}2X^-]$  and  $[H]$  in this case.

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

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

and from eq 1c

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

That is, in this circumstance  $K_{a,\text{exp}}$  depends only on  $[G^{2+}2X^-]$  and not on  $[H]$ !

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

A plot of  $\log([HG^{2+}]/[G^{2+}2X^-]^{1/3})$  vs  $\log [H]$  (eq 1d) should yield limiting slopes of 1/3 at high values of  $\log [H]$  and 1 at low values, on the basis of limiting eqs 1e and 1g. This enables 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  $\{1 + K_{\text{ap}}[H]\}^{2/3}$  term of eq 1d, i.e.,  $(1 + (2/3)K_{\text{ap}}[H])$ , as an approximation. This leads to

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

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

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

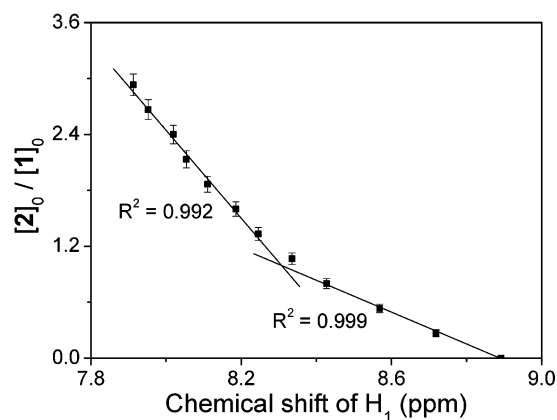


$$K_{\text{ipc}} = [HG^{2+}2X^-]/([H][G^{2+}2X^-])$$

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

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

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



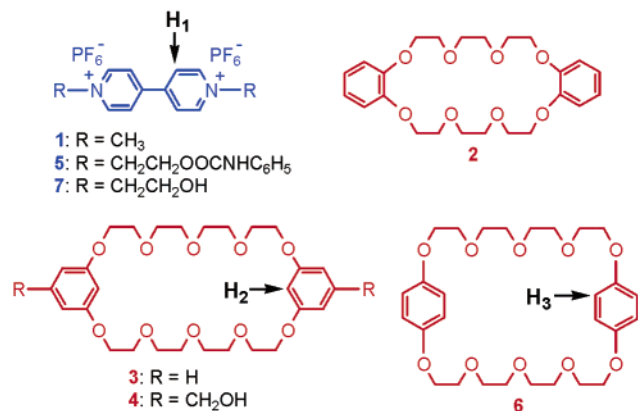
**Figure 1.** Mole ratio plot for **1** and **2**, 22 °C. The solvent is acetone-*d*<sub>6</sub>. [1]<sub>0</sub> and [2]<sub>0</sub> are initial concentrations of **1** and **2**. [1]<sub>0</sub> = 3.75 mM.

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

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

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

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

**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

[1] <sub>0</sub> (mM)	[2] <sub>0</sub> (mM)	$\Delta^a$ (ppm)	$\Delta/\Delta_0^b$	[1] <sub>uc</sub> or [2] <sub>uc</sub> <sup>c</sup> (mM)	[2] <sub>uc</sub> <sup>d</sup> (mM)	[1] <sub>uc</sub> (mM)	$K_{a,exp,2-1}$ (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.

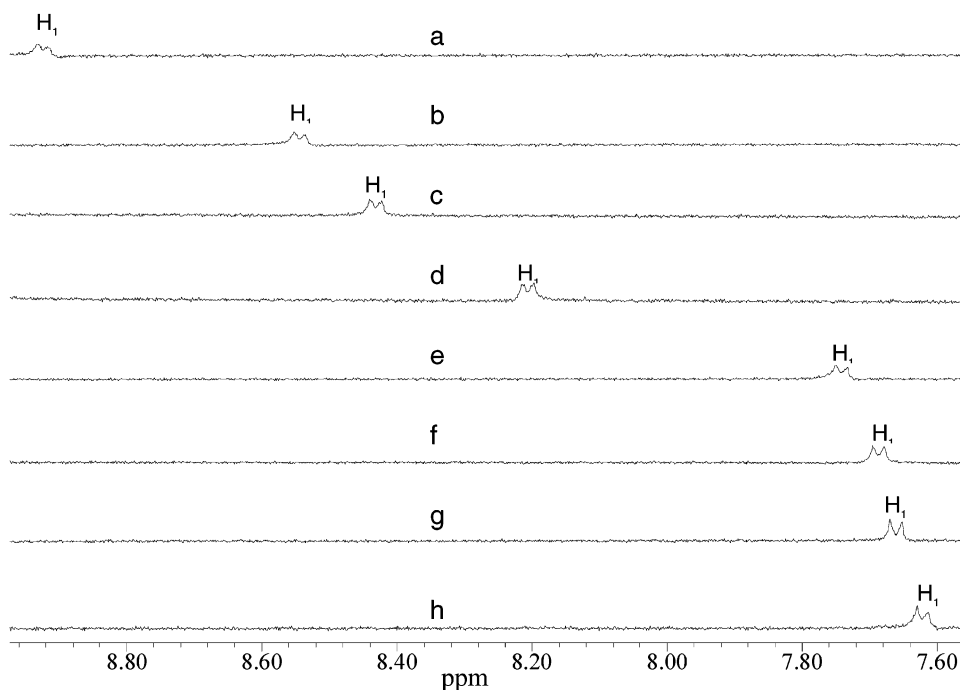
Figure 2). Spectra taken at  $-70$  °C were still in the fast exchange regime. On the basis of the NMR data,  $\Delta_0$ , the difference in  $\delta$  values for H<sub>1</sub> in **1** in the uncomplexed and fully complexed species, was determined by extrapolation of a plot of  $1/\Delta = 1/(\delta - \delta_u)$  vs.  $1/[2]_0$  (Figure 3) to be 1.32 ppm.  $K_{a,exp,2-1}$  values (Table 1) were then calculated on a point-by-point basis from  $K_{a,exp,2-1} = (\Delta/\Delta_0)/[1 - (\Delta/\Delta_0)]\{[2]_0 - (\Delta/\Delta_0)[1]_0\}$ .  $K_{a,exp,2-1}$  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,  $K_{ap,2-1}$  and  $K_{ipd,1}$  were calculated to be  $106 (\pm 42) \text{ M}^{-1}$  and  $4.64 (\pm 1.86) \times 10^{-4} \text{ M}^2$ .<sup>9</sup> It must be noted, however, that the limited solubility ( $\sim 30$  mM at 22 °C) of dibenzo-24-crown-8 (**2**) can contribute to the error in this treatment, because  $K_{ap}[H]$  is not significantly greater than one at high  $[H]$  values.

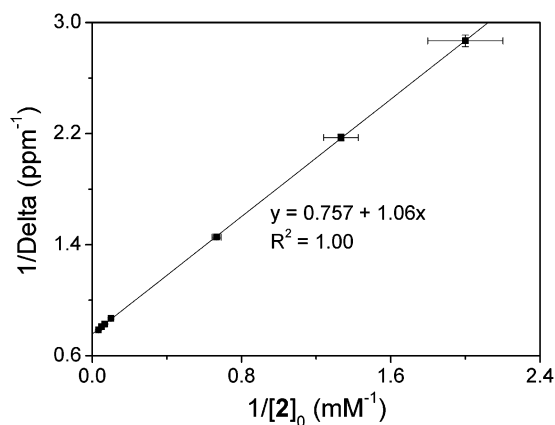
Furthermore, a plot of  $K_{a,exp}$  vs.  $1/[1]_{uc}^{2/3}$  (Figure 5) according to eq 2a for low  $[H]$  part was linear and had a zero intercept within experimental error ( $15.5 \pm 30.7$ ), meaning that  $K_{ipc}$  in eq 2a is approximately zero. Therefore, although the guest salt **1** is predominantly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

(9) According to eqs 1e and 1g, the intercepts of two best fit lines in Figure 4 give  $\log(K_{ap,2-1}^{1/3}K_{ipd,1}^{1/3}/2^{2/3}) = -0.631$  and  $\log(K_{ap,2-1}K_{ipd,1}^{1/3}/2^{2/3}) = 0.718$ . From these two equations, the values of  $K_{ap,2-1}$  and  $K_{ipd,1}$  were determined. Errors are based on errors of the intercepts.

(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.; Slobodnick, C.; Golen, J. A.; Rheingold, A. L.; Gibson, H. W., unpublished results.  
 (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.



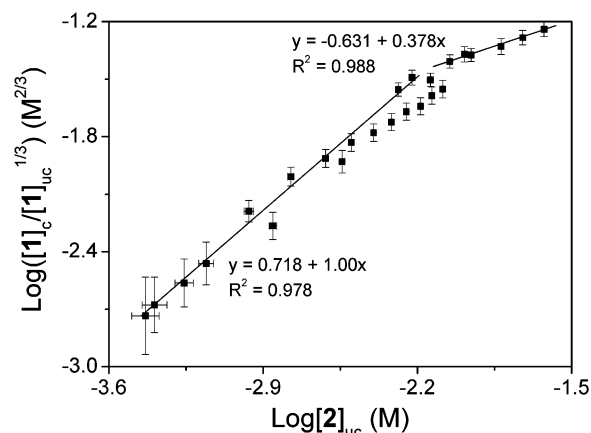
**Figure 2.** Partial  $^1\text{H}$  NMR spectra (400 MHz, acetone- $d_6$ , 22  $^\circ\text{C}$ ) of (a) 0.500 mM **1**, (b) 0.500 mM **1** and 0.500 mM **2**, (c) 0.500 mM **1** and 0.750 mM **2**, (d) 0.500 mM **1** and 1.50 mM **2**, (e) 0.500 mM **1** and 10.0 mM **2**, (f) 0.500 mM **1** and 15.0 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  $^\circ\text{C}$ .  $[1]_0$  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.

In application of eq 1d by the approximations of eq 1e and 1g, because of the limits of  $K_{\text{ap}}[\text{H}] \ll 1$  and  $K_{\text{ap}}[\text{H}] \gg 1$ , not all data are useful. To utilize all of the data and obtain alternative estimates of the equilibrium constants, we can use eq 1i. From a plot of  $[\text{G}^{2+}2\text{X}^-]^{1/3}/[\text{HG}^{2+}]$  vs  $1/[\text{H}]$  (Figure 6) for all data shown in Table 1, the values of  $K_{\text{ap}}$  and  $K_{\text{ipd}}$  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  $K_{\text{ap}}$  and overestimated  $K_{\text{ipd}}$ .<sup>4</sup> That appears to be the case here as well. Thus, we believe the values determined from Figure 4 are preferred.

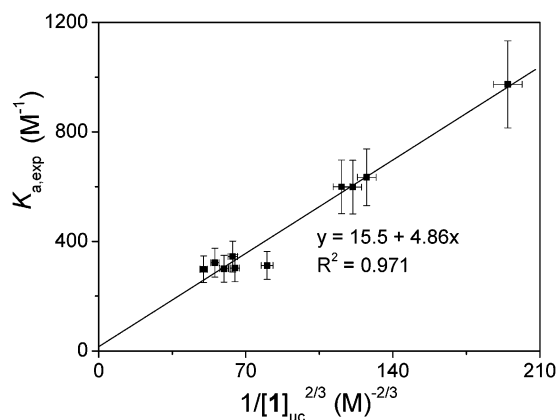
X-ray crystallography has long been used as a guide to low energy structures existing in solution, although such deductions can be misleading. The complex between **1** and **2** has a 1:2 stoichiometry in the solid state (Figure 7).<sup>7</sup> From this structure, we deduce that one possible reason for the lack of ion-pairing



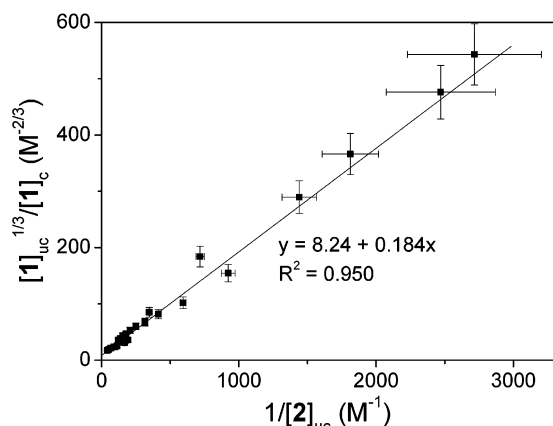
**Figure 4.** Log–log plot of eq 1d for the complexation between **1** and **2** in acetone- $d_6$ , 22  $^\circ\text{C}$ .

of **2**·**1** in solution is that it is difficult for a  $\text{PF}_6^-$  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, the more efficient packing of the 2:1 structure and, of course, its lower solubility. In fact, 2:1 (host to paraquat) complex single crystals were grown even from a solution with excess paraquat.

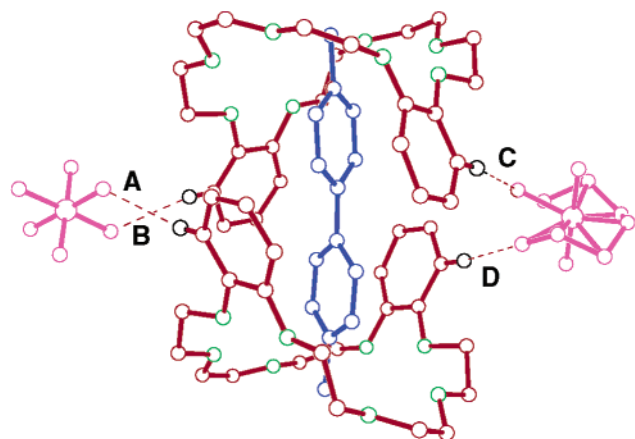
One may be tempted to attribute the concentration dependence of  $K_{\text{a,exp.2-1}}$ , a parameter based on 1:1 stoichiometry, to the presence of 2:1 stoichiometry in solution, because the 2:1 complex is observed in the solid state. However, this is not the case as the mole ratio plot in Figure 1 clearly proves that the complex between **2** and **1** has a 1:1 stoichiometry in solution.



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

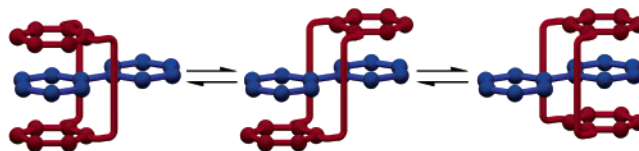


**Figure 6.** Relationship between  $[1]_{\text{uc}}^{1/3}/[1]_{\text{c}}$  and  $1/[2]_{\text{uc}}$  according to eq 1i.



**Figure 7.** X-ray crystal structure of the complex  $2_2 \cdot 1 \cdot 7 \cdot 2$  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···F distances (Å) **A** = 2.47, **B** = 2.47, **C** = 2.44, **D** = 2.44; C–H···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.

**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 diol derivative (**4**) forms a taco, or folded, complex with **1**<sup>11</sup> and extended this recognition motif to preparations of a pseudo-



**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.

**Table 2.**  $K_{a,\text{exp}}$  Values at Different Initial Concentrations for the Complexation between **1** and **4**

$[4]_0$ (mM)	$[1]_0$ (mM)	$\Delta^a$ (ppm)	$\Delta/\Delta_0^b$	$[4]_{\text{c}}$ or $[1]_{\text{c}}^c$ (mM)	$[1]_{\text{uc}}^d$ (mM)	$[4]_{\text{uc}}$ (mM)	$K_{a,\text{exp},4\cdot 1}$ ( $\text{M}^{-1}$ )
0.500	1.50	0.319	0.606	0.303	1.20	0.197	$1.28 \times 10^3$
0.500	2.50	0.377	0.716	0.358	2.14	0.142	$1.18 \times 10^3$
0.500	6.00	0.470	0.892	0.446	5.55	0.0540	$1.49 \times 10^3$
0.600	2.40	0.371	0.704	0.422	1.98	0.178	$1.20 \times 10^3$
0.750	2.25	0.359	0.682	0.511	1.74	0.239	$1.23 \times 10^3$
1.00	2.00	0.337	0.640	0.640	1.36	0.360	$1.31 \times 10^3$
1.50	1.50	0.269	0.511	0.767	0.733	0.733	$1.43 \times 10^3$

<sup>a</sup> For  $\text{H}_2$  of **4**. <sup>b</sup>  $\Delta_0 = 0.526$  ppm. <sup>c</sup> “c” means complexed. <sup>d</sup> “uc” means uncomplexed.

**Table 3.**  $K_{a,\text{exp}}$  Values at Different Initial Concentrations for the Complexation between **3** and **5**

$[3]_0$ (mM)	$[5]_0$ (mM)	$\Delta^a$ (ppm)	$\Delta/\Delta_0^b$	$[3]_{\text{c}}$ or $[5]_{\text{c}}^c$ (mM)	$[5]_{\text{uc}}^d$ (mM)	$[3]_{\text{uc}}$ (mM)	$K_{a,\text{exp},3\cdot 5}$ ( $\text{M}^{-1}$ )
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  $\text{H}_2$  of **3**. <sup>b</sup>  $\Delta_0 = 0.478$  ppm. <sup>c</sup> “c” means complexed. <sup>d</sup> “uc” means uncomplexed.

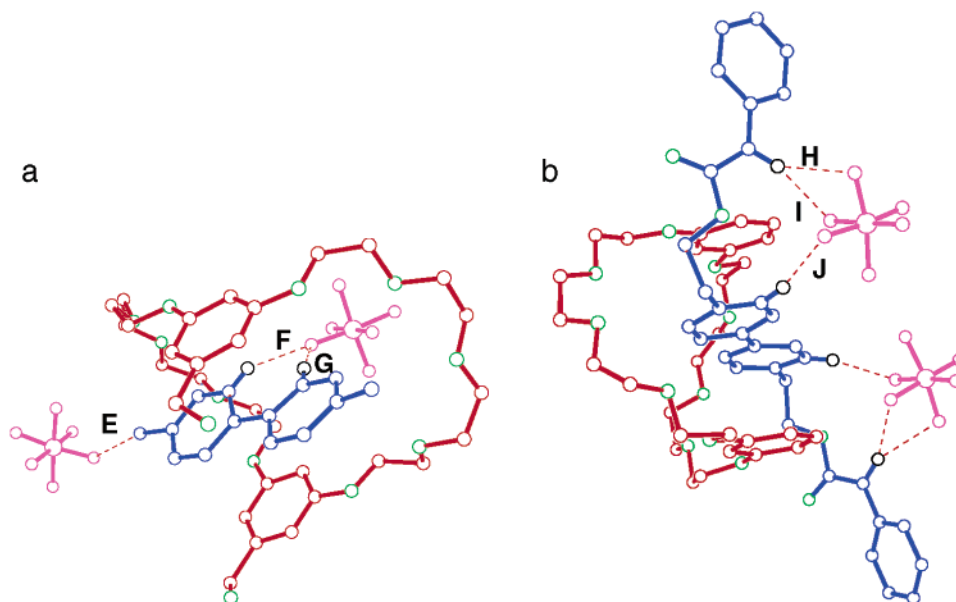
rotaxane<sup>12</sup> of **1** based on a supramolecular cryptand involving chelation of the hydroxyl groups of **4** as well as a supramolecular poly(taco complex) based on **3** and **5**.<sup>13</sup> In the present work, NMR characterizations were done using solutions with constant concentration of **4** (0.500 mM) and varying concentrations of **1** (0.500~30.0 mM). On the basis of these NMR data,  $\Delta_0$ , the difference in  $\delta$  values for  $\text{H}_2$  of **4** in the uncomplexed and fully complexed species, was determined as outlined above to be 0.526 ppm.  $K_{a,\text{exp},4\cdot 1}$  values (Table 2) were then calculated from  $K_{a,\text{exp},4\cdot 1} = (\Delta/\Delta_0)/[1 - (\Delta/\Delta_0)]\{[1]_0 - (\Delta/\Delta_0)[4]_0\}$ , where  $[4]_0$  is the initial concentration of **4** and  $\Delta$  is the chemical shift change of  $\text{H}_2$ . The same experiments were performed on the complex **3**·**5**. On the basis of proton NMR data of  $\text{H}_2$  of **3**, the values of  $K_{a,\text{exp},3\cdot 5}$  of the complex **3**·**5** were similarly calculated (Table 3). As can be seen,  $K_{a,\text{exp},4\cdot 1}$  and  $K_{a,\text{exp},3\cdot 5}$  are not concentration dependent and therefore correspond to the case where the complex is essentially completely ion paired, i.e., eq 2a,  $K_{\text{ap}} = 0$ . Scatchard plots were made for both of the complexes according to eq 2b.<sup>14</sup> The intercepts of the two lines

(10) Allwood, B. L.; Spencer, N.; Shahriari-Zavareh, H.; Stoddart, J. F.; Williams, D. J. *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*, 13 378–13 379.

(13) Huang, F.; Fronczek, F. R.; Gibson, H. W. *Chem. Commun.* **2003**, 1480–1481.



**Figure 9.** 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.

are identical to the ideal value, 0, within experimental error. The slopes,  $1.23 (\pm 0.07) \times 10^3 \text{ M}^{-1}$  for **4·1** and  $536 (\pm 11) \text{ M}^{-1}$  for **3·5** are values of  $K_{a,\text{exp},4\cdot1}$  and  $K_{a,\text{exp},3\cdot5}$ , respectively.

Ion pairing of **4·1** and **3·5** in the solid state was confirmed by their X-ray crystal structures (Figure 9),<sup>11,13</sup> in which PF<sub>6</sub><sup>−</sup> counterions are connected to the paraquat guest through 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><sup>−</sup> 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 β-protons of **1**. In **3·5**, both PF<sub>6</sub><sup>−</sup> anions have ready access to the α- and NH-protons of the guest on the “open” or “front” side of the taco complex. Presumably, this situation also exists in solution and folding of the crown ether in the opposite directions results in decomplexation. This is in contrast to the picture for **2·1** shown in Figure 8, in which folding does not cause decomplexation.

**D. Complexation between bis(*p*-Phenylene)-34-crown-10 (6, BPP34C10) and Paraquat Derivatives.** Stoddart et al. first discussed the complexation between BPP34C10 (**6**) and **1**.<sup>15</sup> Later, they reported the BPP34C10/paraquat diol complex, **6·7**.<sup>16</sup> BPP34C10 derivatives have become the most commonly used host for paraquat derivatives.<sup>5</sup> On the basis of proton NMR data for H<sub>3</sub>, the values (Tables 4 and 5) of  $K_{a,\text{exp}}$  of the complexes **6·1** and **6·7** were determined.  $K_{a,\text{exp}}$  values of **6·1** and **6·7** do not exhibit concentration dependence. Plots were made for **6·1**

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

[6] <sub>0</sub> (mM)	[1] <sub>0</sub> (mM)	Δ <sup>a</sup> (ppm)	Δ/Δ <sub>0</sub> <sup>b</sup>	[1] <sub>c</sub> or [6] <sub>c</sub> <sup>c</sup> (mM)	[1] <sub>uc</sub> <sup>d</sup> (mM)	[6] <sub>uc</sub> (mM)	$K_{a,\text{exp},6\cdot1}$ (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>3</sub> of **6**. <sup>b</sup> Δ<sub>0</sub> = 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**

[6] <sub>0</sub> (mM)	[7] <sub>0</sub> (mM)	Δ <sup>a</sup> (ppm)	Δ/Δ <sub>0</sub> <sup>b</sup>	[6] <sub>c</sub> or [7] <sub>c</sub> <sup>c</sup> (mM)	[7] <sub>uc</sub> <sup>d</sup> (mM)	[6] <sub>uc</sub> (mM)	$K_{a,\text{exp},6\cdot7}$ (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>3</sub> of **6**. <sup>b</sup> Δ<sub>0</sub> = 0.493 ppm. <sup>c</sup> “c” means complexed. <sup>d</sup> “uc” means uncomplexed.

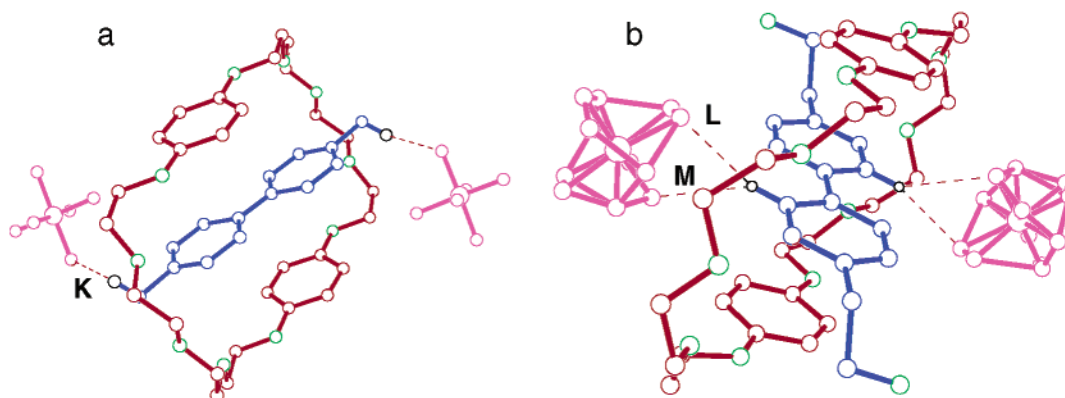
and **6·7** according to Scatchard eq 2b.<sup>14</sup> Again, the intercepts of the two plots are zero within experimental error. From the slopes, we determined  $K_{a,\text{exp},6\cdot1} = 728 (\pm 25) \text{ M}^{-1}$  and  $K_{a,\text{exp},6\cdot7} = 376 (\pm 38) \text{ M}^{-1}$ .

Ion pairing of complexes **6·1** and **6·7** in the solid state was confirmed by their X-ray crystal structures (Figure 10).<sup>15,16</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-

(14) See Supporting Information.

(15) Allwood, B. L.; Spencer, N.; Shahriari-Zavareh, H.; Stoddart, J. F.; Williams, D. J. *Chem. Commun.* **1987**, 1064–1066.  $K_{a,\text{exp}}$  reported for **6·1** in this paper is  $730 \text{ M}^{-1}$  in acetone at room temperature by employing the titration methodology and following the charge-transfer band (435 nm) of the complex by absorption spectroscopy.

(16) Ashton, P. R.; Philp, D.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *Chem. Commun.* **1991**, 1680–1683. Ashton, P. R.; Ballardini, R.; Balzani, V.; Belohradsky, M.; Gandolfi, M. T.; Philp, D.; Prodi, L.; Raymo, F. M.; Reddington, M. V. *J. Am. Chem. Soc.* **1996**, *118*, 4931–4951.  $K_{a,\text{exp}}$  reported for **6·7** in the second paper is  $700 \text{ M}^{-1}$  in acetone at room temperature by employing the titration methodology and following the charge-transfer band (437 nm) of the complex by absorption spectroscopy.



**Figure 10.** X-ray crystal structures of **6·1**<sup>15</sup> (a) and **6·7**<sup>16</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><sup>−</sup> counterions in **6·7** are disordered.

like complex are readily accessible for H-bonding to the PF<sub>6</sub><sup>−</sup> anions. In the pseudorotaxane **6·7**, the diagonal positioning of guest **7** in the spacious cavity of the host allows its β-protons to H-bond with the PF<sub>6</sub><sup>−</sup> anions on opposite sides. Again, the solid-state interactions are consistent with ion pairing of the complexes in solution.

## 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. Although 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 [ $K_{ipd} = 4.64 (\pm 1.86) \times 10^{-4} \text{ M}^2$ ] of paraquat bis(hexafluorophosphate) in acetone-*d*<sub>6</sub> was determined from study of its complexation with dibenzo-24-crown-8, for which  $K_{ap} = 106 (\pm 42) \text{ M}^{-1}$ . However, four complexes from bis(*m*-phenylene)-32-crown-10 derivatives and bis(*p*-phenylene)-34-crown-10 with viologens are essentially 100% ion paired in solution, as shown by the fact that  $K_{a,exp}$  is not concentration dependent for these systems involving hosts with free access to bound guests by the counterions. 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 in the former there is 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 guest 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 any number of host–guest complexations involving electrolyte components in low dielectric constant media. 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.

## Experimental Section

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

The 400 MHz <sup>1</sup>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 at 22 °C by 400 MHz <sup>1</sup>H NMR.

All solutions were prepared as follows. Precisely weighed amounts of dried hosts and guests were added into separate screw cap vials. Acetone-*d*<sub>6</sub> was added with to-deliver volumetric pipets. Then specific volumes of each fresh solution were mixed to yield the desired concentrations. For example, to make three solutions, 10.0 mM **1**/10.0 mM **2**, 10.0 mM **1**/15.0 mM **2**, and 10.0 mM **1**/17.5 mM **2**, a 10.0 mM solution of **1** was made first by adding 5.00 mL acetone-*d*<sub>6</sub> with a 5.00 mL to-deliver pipet 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 that contained 2.69, 4.04, and 4.71 mg of **2** separately. <sup>1</sup>H NMR data were collected on a temperature controlled spectrometer. Acetone-*d*<sub>6</sub> was chosen as the solvent because all compounds used here have relatively good solubilities in it. Error bars were calculated based on a 0.05 mg deviation in weight, a 0.005 ppm deviation in chemical shift on proton NMR spectra, and a ±5% deviation in fractional complexation ( $\Delta/\Delta_0$ ) observed over the range 0.1 to 0.9. Standard errors in both the intercept and slope coefficients based on regression were used to determine errors in association constants.

**Acknowledgment.** Acknowledgment is made to the National Science Foundation (NSF) via grant DMR-0097126. J.W.J. acknowledges support from the Environmental Science Program, Office of Science, U.S. Department of Energy via the Higher Education Research Experience at Oak Ridge National Laboratories. We thank the NSF (Grant No. CHE-0131128) for funding of the purchase of the Oxford Diffraction Xcalibur2 single crystal diffractometer. The authors also thank Edgar Rodriguez for the rendering of Figure 8.

**Note Added after ASAP:** This manuscript was originally published on the Web 11/05/2003 with a word missing in the last paragraph of section C of the Results and Discussion and a word missing in the first paragraph of the Conclusions. The correct version was posted 11/06/2003.

**Supporting Information Available:** Plots of eq 2b for **4·1**, **3·5**, **6·1**, and **6·7**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JA036606F