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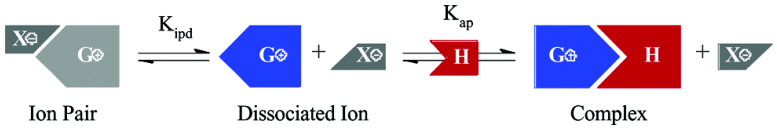

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Ion Pairing and Host−Guest Complexation in Low Dielectric Constant Solvents

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Abstract: We report an equilibrium treatment for complexation of ionic species in low dielectric constant media that explicitly includes ion pairing of one of the components. Experimental validation was achieved through study of pseudorotaxane formation between dibenzylammonium salts and dibenzo-24-crown-8. In particular, we show that concentration-dependent fluctuations in the apparent $K_{a,exp}$ values as usually reported are attributable to ion pairing, with dissociation constant K_{ipd}, and that the constant K_{ap} for complexation of the free cationic guest species, G^+, by the host crown ether is independent of counterion. More generally, using a simple extension of our model, we show the ability to diagnose the relative extent of ion pairing of the complex, which may be readily applied to other host−guest systems involving ionic species.

Ionic species have played a dominant role in supramolecular chemistry dating back to Pedersen's discovery of the alkalai metal templated formation of crown ethers.[1] Ionic components can act as hosts (H) or guests (G), but the latter role is more common.[2] To maximize attractive intermolecular interactions, many of these complexations have been carried out in low dielectric constant organic solvents such as dichloromethane, chloroform, acetone, or acetonitrile. Yet despite the known propensity of salts to ion pair in such solvents,[3] this factor has generally not been addressed.[4] We here report a treatment that explicitly includes the ion-pairing equilibrium for the ionic guest component and then adopt this treatment to a more general model suitable to a number of host−guest complexations involving one ionic component.

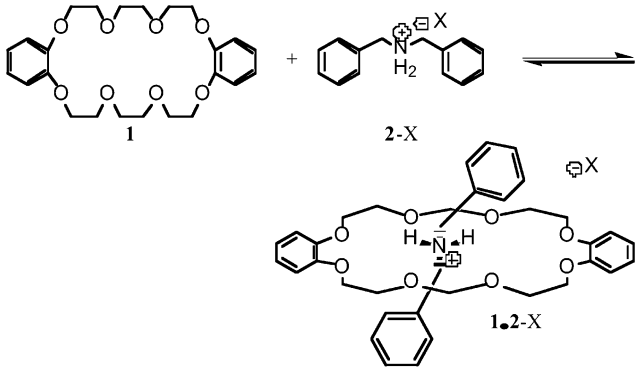
As frequently encountered in the literature, association constants for 1:1 complex formation are not explicitly defined. However, since the units are M^{-1}, it is assumed that they are of the form

$$H + G^+X^- \overset{K_{a,exp}}{\rightleftharpoons} H\cdot G^+X^- \qquad (1)$$

$$K_{a,exp} = \frac{[H\cdot G^+]}{[G^+X^-][H]}$$

An experimentally equivalent expression would apply if the salt and complex were both fully dissociated ionic species.

Piqued by our inability to reproduce association constants[5] reported for formation of pseudorotaxanes, we undertook studies using well-defined host and guest solutions made with volumetric flasks and to-deliver pipets. ^{1}H NMR spectra of solutions of dibenzo-24-crown-8 (**1**) and dibenzylammonium salts (**2**-X) reveal the system to undergo slow exchange: in addition to peaks associated with the starting compounds, new signals corresponding to complex formation (**1**•**2**-X) are readily discerned.[6] By integration, the complex stoichiometry (1:1), concentration, and $K_{a,exp}$ may then be determined.



Solutions of **1** and **2**-trifluoroacetate (TFA) were examined. Shown in Figure 1, $K_{a,exp}$[7a] varied 10-fold among the concentra-

(1) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017−7036.
(2) (a) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486−516. (b) 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. (c) Antonisse, M. M. G.; Reinhoudt, D. N. *Chem. Commun.* **1998**, 443−448. (d) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. L. *Chem. Rev.* **1995**, *95*, 2529−2586. (e) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S. *Chem. Rev.* **1991**, *91*, 1721−2085. (f) Merz, T.; Wirtz, H.; Vögtle, F. *Angew. Chem., Int. Ed.* **1986**, *25*, 567−568.
(3) Isaacs, N. *Physical Organic Chemistry*, 2nd ed.; Longmans: England, 1995; pp 56−62.
(4) A few exceptions include: (a) Bartoli, S.; Roelens, S. *J. Am. Chem. Soc.* **2002**, *124*, 8307−8315. (b) Kavallieratos, K.; Moyer, B. A. *Chem. Commun.* **2001**, *17*, 1620−1621. (c) Shukla, R.; Kida, T.; Smith, B. D. *Org. Lett.* **2000**, 2, 3099−3102. (d) Monk, P. M. S.; Hodgkinson, N. M.; Patridge, R. D. *Dyes Pigm.* **1999**, *43*, 241−251. (e) Hossain, M. A.; Schneider, H.-J. *Chem. Eur. J.* **1999**, *5*, 1284−1290. (f) Arnaud-Neu, F.; Asfari, Z.; Souley, B.; Vicens, J. *New J. Chem.* **1996**, *20*, 453−463. (g) Buschmann, H.-J.; Cleve, E.; Schollmeyer, E. *J. Solution Chem.* **1994**, *23*, 569−577. (h) Kolthoff, I. M. *Can. J. Chem.* **1981**, *59*, 1548−1551.
(5) For a discussion on measurements of association constants, see: Hirose, K. *J. Inclusion Phenom. Macrocyclic Chem.* **2001**, *39*, 193−209.
(6) (a) Gibson, H. W.; Yamaguchi, N.; Jones, J. W. *J. Am. Chem. Soc.* **2003**, *125*, 3522−3533. (b) Cantrill, S. J.; Youn, G. J.; Stoddart, J. F.; Williams, D. J. *J. Org. Chem.* **2001**, *66*, 6857−6872.
(7) (a) Calculated using [**1**] = [**1**]$_0$ − [**1**•**2**-TFA] and [**2**-TFA] = [**2**-TFA]$_0$ − [**1**•**2**-TFA]. (b) Since K_{ipd} is small, [**2**-TFA] may be calculated as in (a).

tions investigated and decreased with increasing [**1**] or [**2**-TFA]. Similarly, solutions of **1** and **2**-PF_6 yielded 14-fold variations in $K_{a,exp}$ and, significantly, decreased toward an asymptotic limit with increasing added [*n*-Bu_4NPF_6].[8] These studies show that $K_{a,exp}$ varies with (1) host concentration, (2) anion concentration, and (3) anion. Additionally, the chemical shifts associated with the complex are invariant with concentration and anion (PF_6^-, BF_4^-, TFA^-, Cl^-, OTs^-, MsO^-), indicating that the complex is not ion paired,[9] whereas the chemical shifts of the salts themselves are concentration dependent. As a whole, Figure 1 unambiguously demonstrates that use of eq 1 is not a valid treatment for these systems, a result of the implicit assumption that the ion-paired salt is the active component and that the complex is also ion paired (or, alternatively, that both the guest salt and complex are 100% dissociated).

To explain the observed concentration dependence and common ion effect, we consider ion pair dissociation as a preequilibrium step to produce free guest cation G^+, the active complex component

$$G^+X^- \overset{K_{ipd}}{\rightleftharpoons} G^+ + X^-$$

$$K_{ipd} = \frac{[G^+][X^-]}{[G^+X^-]}; \qquad [G^+] = \frac{K_{ipd}[G^+X^-]}{[X^-]}$$

$$H + G^+ + X^- \overset{K_{ap}}{\rightleftharpoons} H{\cdot}G^+ + X^-$$

$$K_{ap} = \frac{[H{\cdot}G^+]}{[G^+][H]}; \qquad [H{\cdot}G^+] = K_{ap}[G^+][H]$$

Substitution for $[G^+]$ yields

$$K_{ap} = \frac{[X^-][H{\cdot}G^+]}{K_{ipd}[G^+X^-][H]}$$

$$K_{a,exp} = \frac{[H{\cdot}G^+]}{[G^+X^-][H]} = \frac{K_{ipd}K_{ap}}{[X^-]} \tag{2a}$$

$$[X^-] = [G^+] + [H{\cdot}G^+] = \frac{K_{ipd}[G^+X^-]}{[X^-]} + K_{ap}[G^+][H]$$

$$= \frac{K_{ipd}[G^+X^-]}{[X^-]} + \frac{K_{ipd}K_{ap}[G^+X^-][H]}{[X^-]}$$

$$= (K_{ipd}[G^+X^-] + K_{ipd}K_{ap}[G^+X^-][H])^{1/2} \tag{2b}$$

Substitution into eq 2a gives

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

$$\frac{[H{\cdot}G^+]}{[G^+X^-]^{1/2}} = \frac{K_{ipd}{}^{1/2}K_{ap}[H]}{(1 + K_{ap}[H])^{1/2}} \tag{2d}$$

This treatment[10] assumes that (a) the electrolyte and host exist in solution as monomers, (b) it is the free ammonium ion that forms the complex, the latter being fully dissociated, and (c) there are no other species present. Note from eq 2c that $K_{a,exp}$ is an inverse function of both $[G^+X^-]$ and [H], as observed in Figure 1.

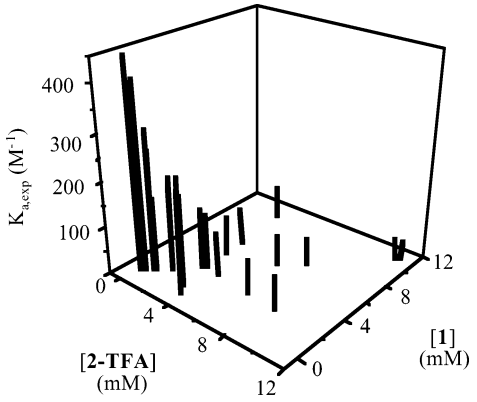


Figure 1. $K_{a,exp}$ vs [**1**], [**2**-TFA] in $CDCl_3/CD_3CN$ (3/2), 22 °C.

The first term of eq 2b represents the fraction of free X^- generated by ion-pair dissociation in an amount equal to free G^+ and the second term that formed via the complexation process in an amount equivalent to complex $H{\cdot}G^+$. In the absence of another added electrolyte containing X^-, if $K_{ap}[H] \gg 1$

$$[X^-] \approx (K_{ipd}K_{ap}[G^+X^-][H])^{1/2}$$

and from eq 2d

$$\frac{[H{\cdot}G^+]}{[G^+X^-]^{1/2}} = (K_{ipd}K_{ap}[H])^{1/2} \tag{2e}$$

Under this condition, the free counterion essentially results from complex formation. On the other hand, if $K_{ap}[H] \ll 1$

$$[X^-] \approx (K_{ipd}[G^+X^-])^{1/2}$$

In the absence of an added electrolyte containing X^-, virtually all free X^- is generated from ion pair dissociation and

$$\frac{[H{\cdot}G^+]}{[G^+X^-]^{1/2}} = K_{ipd}{}^{1/2}K_{ap}[H] \tag{2f}$$

X^- will be liberated by both pathways in the intermediate region.[11]

These two extreme cases depend on the relative values of K_{ipd} and K_{ap} and the initial concentrations of the host and guest species. Equation 2a is consistent with the decreased value of $K_{a,exp}$ for **1**·**2**-PF_6 observed when *n*-Bu_4PF_6 is added to the solutions, since this will increase $[PF_6^-]$.

A log−log plot of eq 2d for **1**/**2**-TFA (Figure 2)[7] has limiting slopes of 1/2 at high values of $[H{\cdot}G^+]/[G^+X^-]^{1/2}$ and 1 at low

(8) Investigations of DB24C8 and *n*-Bu_4NPF_6 solutions revealed no change in the ^1H NMR spectra under experimental conditions, indicating no interaction between macrocycle and salt.

(9) For a brief discussion on ion pairing of complexes, see: Vögtle, F.; Weber, E. In *Chemistry of Ethers, Crown Ethers, Hydroxyl Groups and Their Sulphur Analogues*; Patai, S., Ed.; Wiley, Chichester, U.K., 1980; Vol. 1, pp 120−121.

(10) This equilibrium treatment of pseudorotaxane formation has not appeared in the literature to our knowledge, although ion pairing of **2**-Cl formed the basis of a reported pseudorotaxane fluorescence sensor. Montaldi, M.; Prodi, L. A. *Chem. Commun.* **1998**, 1461−1462. A similar derivation was reported for complexation of smaller crowns with alkalai metal salts, but only up to eq 2a and it was not used analytically to estimate the constants. D'Aprano, A.; Salomon, M.; Mauro, V. *J. Solution Chem.* **1995**, *24*, 685−702.

(11) If estimated values of K_{ap} and K_{ipd} are known a priori, binding study concentrations should ideally be varied such that results above and below the breakpoint, i.e., $K_{ap}[H] = 1$, are produced.

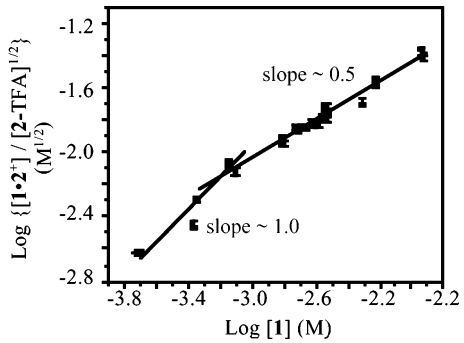


Figure 2. Plot of eq 2d for **1**/**2**-TFA in $CDCl_3/CD_3CN$ (3/2), 22 °C.

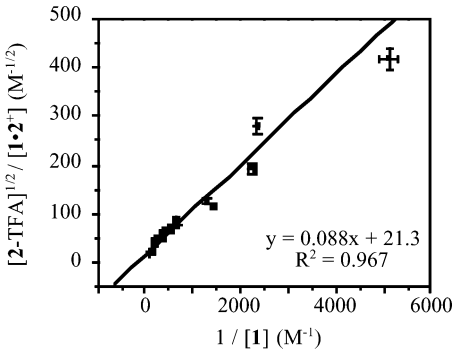


Figure 3. Plot of eq 2g for **1**/**2**-TFA in $CDCl_3/CD_3CN$ (3/2), 22 °C.

values, as expected on the basis of limiting eqs 2e and 2f, yielding $K_{ap} = (6.4 \pm 0.8) \times 10^2$ M^{-1} and $K_{ipd} = (2.2 \pm 0.4) \times 10^{-4}$ M.[12]

In cases where K_{ipd} is relatively large, as with **2**-PF_6, it becomes difficult to apply eq 2f in the limit of ion-pair dissociation dominance as the low component concentrations required test the bounds of ^{1}H NMR detection. An alternative treatment is to apply the first two terms of the binomial expansion of the $\{1 + K_{ap}[H]\}^{1/2}$ term of eq 2d as an approximation.[13] This leads to

$$\frac{[G^+X^-]^{1/2}}{[H{\cdot}G^+]} = \frac{1}{K_{ipd}{}^{1/2}K_{ap}}\left(\frac{1}{[H]}\right) + \frac{1}{2K_{ipd}{}^{1/2}} \qquad (2g)$$

A plot of the left-hand side of eq 2g vs 1/[H] for **1**/**2**-TFA is linear (Figure 3); the slope and intercept yield $K_{ap} = (4.9 \pm 2.3) \times 10^2$ M^{-1} and $K_{ipd} = (5.5 \pm 1.2) \times 10^{-4}$ M, in reasonable[14] agreement with the results from eq 2d and Figure 2. Analogous plots for a series of **2**-X salts under similar conditions yield Table 1.[15]

The values of K_{ipd} from Table 1 are in accord with reported values for tetraalkylammonium salts[16] and concur with the observation that PF_6 salts are generally the most dissociated.[17]

Table 1. Values of K_{ap} and K_{ipd} for Various **2**-X Salts When Mixed with **1** in $CDCl_3/CD_3CN$ (3/2), 22 °C, as Estimated from Eq 2g

X^-	K_{ap} (M^{-1})	K_{ipd} (M)
PF_6	$(5.6 \pm 0.6) \times 10^2$	$(2.6 \pm 0.7) \times 10^{-2}$
BF_4	$(5.8 \pm 1.2) \times 10^2$	$(2.5 \pm 1.6) \times 10^{-2}$
OTs	$(4.3 \pm 0.2) \times 10^2$	$(1.1 \pm 0.1) \times 10^{-3}$
TFA	$(4.9 \pm 2.3) \times 10^2$	$(5.5 \pm 1.2) \times 10^{-4}$
TFA[a]	$(6.4 \pm 0.8) \times 10^2$	$(2.2 \pm 0.4) \times 10^{-4}$

[a] Calculated according to eq 2d (Figure 2).

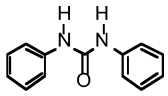
Table 2. $K_{a,exp}$ of **1**/**2**-Cl as a Function of Added Anion Host **3** [$CDCl_3/CD_3CN$ (3/2), 22 °C]

$[1]_0$ (mM)	$[2\text{-Cl}]_0$[a] (mM)	$[3]_0$[a] (mM)	% **1** complexed	$K_{a,exp}$ (M^{-1})
2.0	4.2	0.00	26	1.3×10^2
2.0	4.3	0.30	34	1.9×10^2
2.0	4.2	0.57	38	2.3×10^2

[a] Concentrations were determined by integration of each species relative to **1**.

Moreover, the values of K_{ap} for each salt are also in decent agreement, as mandated by this equilibrium treatment.

The predictive power of this model has been validated by several research groups, who report increased extents of complexation as a result of binding both the cation and anion via ditopic[4a−b,18] or molecularly separate hosts.[19] In light of this model, the use of tightly ion paired guests may afford better opportunity for efficient binding than their weakly paired counterparts, since well-solvated, charge-delocalized anions are much more difficult to bind than are small, charge-localized anions. The literature contains similar viewpoints with respect to other systems.[18,19] In the present case, we have adopted such a dual-binding strategy to the complexation of tightly paired **2**-Cl by **1**, implementing 1,3-bis(4-nitrophenyl)urea (**3**), a known anion host.[20] Despite the poor solubility of both **2**-Cl and **3** in our solvent system,[21] the results of Table 2 unambiguously demonstrate the advantage gained by diminishing the concentration of free X^- in such systems.



3

Acknowledging that direct complexation of an ion-paired ligand is also a real possibility in a number of host−guest systems,[22] we have extended our simple model by allowing for

(12) See Supporting Information for a description of the error analysis.
(13) Bittinger, M. L.; Ellenbogen, D. J.; Johnson, B. *Elementary and Intermediate Algebra*; Addison-Wesley Publishing Co.: Reading, MA, 1996; p 749.
(14) As this is an approximation, we are currently pursuing the use of curve fitting to better fit our data to eq 2d across the entire range.
(15) See Supporting Information for respective eq 2g plots.
(16) For R_4NX (R = Me, *n*-Pr, *n*-Bu, *i*-Am; X = PF_6, $B(C_6H_5)_4$, ClO_4, Cl, SCN) in CH_3CN $K_{ipd} = (2-4) \times 10^{-2}$ M (Barthel, J.; Iberl, L.; Rossmaier, J. Gores, H. J.; Kaukal, B. *J. Solution Chem.* **1990**, *19*, 321−337), in acetone $K_{ipd} = (1-3) \times 10^{-3}$ M (Savedoff, L. G. *J. Am. Chem. Soc.* **1966**, *88*, 664−667), and in CH_2Cl_2 $K_{ipd} = 1 \times 10^{-4}$ to 5×10^{-5} M (ref 8a and Romeo, R.; Arena, G.; Scolaro, L. M.; Plutino, M. R. *Inorg. Chim. Acta* **1995**, *240*, 81−92).
(17) (a) Nelson, S. F.; Ismagilov, R. F. *J. Phys. Chem. A* **1999**, *103*, 5373−5378. (b) Schmid, R.; Kirchner, K.; Dickert, F. L. *Inorg. Chem.* **1988**, *27*, 1530−1536.
(18) For example, see: (a) Levitskaia, T. G.; Bonnesen, P. V.; Chambliss, C. K.; Moyer, B. A. *Anal. Chem* **2003**, *75*, 405−412. (b) Arduini, A.; Brindani, E.; Giorgi, G.; Pochini, A.; Secchi, A. *J. Org. Chem.* **2002**, *67*, 6188−6194. (c) Casnati, A.; Massera, C.; Pelizzi, N.; Stibor, I.; Pinkassik, E.; Ugozzoli, F.; Ungaro, R. *Tetrahedron Lett.* **2002**, *43*, 7311−7314. (d) Berry, N. G.; Sambrook, M. R. *J. Am. Chem. Soc.* **2002**, *124*, 12469−12476. (e) Tongraung, P.; Chantarasiri, N.; Tuntulani, T. *Tetrahedron Lett.* **2002**, *44*, 29−32. (f) Mahoney, J. M.; Beatty, A. M.; Smith, B. D. *J. Am. Chem. Soc.* **2001**, *123*, 5847−5848. (f) Wisner, J. A.; Beer, P. D.; Drew, M. G. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 3606−3609.
(19) A few examples include: (a) Cafeo, G.; Gattuso, G.; Kohnke, F. H.; Notti, A.; Occhipinti, S.; Pappalardo, S.; Parisi, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 2122−2126. (b) Arduini, A.; Giorgi, G.; Pochini, A.; Secchi, A.; Ugozzoli, F. *J. Org. Chem.* **2001**, *66*, 8302−8308.
(20) (a) Pratt, M. D.; Beer, P. D. *Polyhedron* **2003**, *22*, 649−653. (b) Al-Sayah, M. H.; Branda, N. R. *Org. Lett.* **2002**, *4*, 881−884. (c) Werner, F.; Schneider, H.-J. *Helv. Chim. Acta* **2000**, *83*, 465−478. (d) Nishizawa, S.; Shigemori, K.; Teramae, N. *Chem. Lett.* **1999**, *11*, 1185−1186.
(21) The poor solubility of **2**-Cl renders us unable to observe complexation over a broad enough range of concentrations to implement the reported equilibrium treatment.
(22) (a) Böhmer, V.; Dalla Cort, A.; Mandolini, L. *J. Org. Chem.* **2001**, *66*, 1900−1902. (b) Kikucki, Y.; Sakamoto, Y. *Anal. Chim. Acta* **2000**, *403*, 325−332. (c) Okada, T. *J. Phys. Chem. B* **1998**, *102*, 3053−3059.

an additional equilibrium. For slowly exchanging systems, K_{ipc}

$$H + G^+X^- \overset{K_{ipc}}{\rightleftharpoons} H{\cdot}G^+X^-$$

$$K_{ipc} = \frac{[H{\cdot}G^+X^-]}{[G^+X^-][H]}; \qquad [H{\cdot}G^+X^-] = K_{ipc}[G^+X^-][H]$$

may be determined by direct integration of signals for both $H{\cdot}G^+X^-$ and $H{\cdot}G^+$. For fast exchange between $H{\cdot}G^+X^-$ and $H{\cdot}G^+$, the observed time-averaged complex signal will represent both species

$$[H{\cdot}G^+] + [H{\cdot}G^+X^-] = \frac{K_{ipd}K_{ap}[G^+X^-][H]}{[X^-]} + K_{ipc}[G^+X^-][H]$$

and

$$K_{a,exp} = \frac{[H{\cdot}G^+] + [H{\cdot}G^+X^-]}{[G^+X^-][H]} = \frac{K_{ipd}K_{ap}}{[X^-]} + K_{ipc} \quad (3a)$$

which differs from eq 2a only in the inclusion of a second equilibrium constant term. Thus

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

In the absence of another added electrolyte containing X^-, if $K_{ap}[H] \gg 1$

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

Under this condition, the first term represents the fraction of complex that exists as the free ion and the second term, that of the fraction which is ion paired. On the other hand, if $K_{ap}[H] \ll 1$, in the absence of an added electrolyte containing X^-

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

Again, the first term represents the fraction of complex that exists as the free ion and the second term the fraction which is ion paired.

Thus, if the sole active ligand is the fully dissociated ion, G^+, $K_{ipc} = 0$ and a plot of $K_{a,exp}$ vs $1/\{[G^+X^-][H]\}^{1/2}$ or, depending on the binding regime, $K_{a,exp}$ vs $1/[G^+X^-]^{1/2}$, will yield a straight line that passes through the origin. On the other hand, if the lone active ligand is the fully ion paired species, G^+X^-, then $K_{a,exp}$ will be independent of both $[G^+X^-]$ and [H] because $K_{ap} = 0$. In the intermediate region where the host is capable of binding both ion-paired and ion-dissociated ligands, the same plot will yield a straight line whose intercept will yield K_{ipc}. In this regard, our model is a diagnostic treatment to test for the relative extent of complexation of an ion-paired ligand versus a fully dissociated ionic ligand.

Turning again to **1**/**2**-TFA and utilizing the data under the limit of free ion generation via complex formation, $K_{ap}[H] \gg 1$, according to eq 3d, we predict the data to pass through the origin and to have a slope of $\sim 0.375\ \{(K_{ap}K_{ipd})^{1/2}\}$. Figure 4

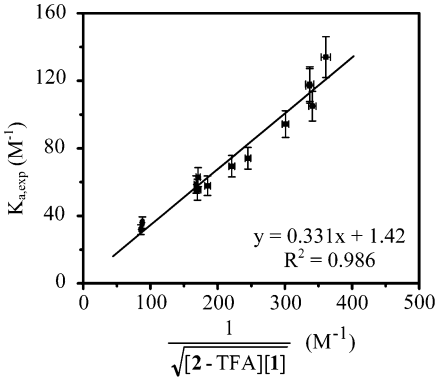


Figure 4. Plot of eq 3c for **1**/**2**-TFA in $CDCl_3/CD_3CN$ (3/2), 22 °C.

confirms our prediction, yielding an intercept of 1.42 ± 1.54 M^{-1} and a slope of 0.331 ± 0.010.

It should be noted that this equilibrium treatment is not limited to analysis of slowly exchanging ^1H NMR spectra, used here only as a first example which will be expanded upon in future reports; it is also applicable to fast exchange systems on a point by point basis once Δ_0 is known via Benesi−Hildebrand analysis[23] utilizing NMR or other spectroscopic measurements. In addition, it is worth mentioning that current models used to describe binding of polytopic species[24] such as the Scatchard[25] and Hill[26] treatments have been derived using equilibria which do not consider ion pairing. For complexation of salts in low dielectric media, these treatments are therefore inherently flawed. We are currently exploring the ramifications of ion pairing on multisite binding and will report these results at a later date. Finally, it is clear that a direct measurement of K_{ipd} in complexation studies involving ionic species in low dielectric constant media would greatly simplify the determination of binding constants. Toward this end, we are actively pursing independent methods of determining K_{ipd} and will also report such results at a future date.

In conclusion, determination of appropriate and meaningful constants for formation of complexes from ionic species in low dielectric constant media requires multiple experiments across a range of absolute and relative concentrations. This general treatment lends itself to a variety of complexation equilibria involving ionic species. Importantly, it also emphasizes the advantage gained upon complexation of both the cation and anion, either by ditopic or molecularly separate receptors.

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Supporting Information Available: experimental details and plots of eq 2g for **1**/**2**-PF_6, **1**/**2**-BF_4, **1**/**2**-OTs, and **1**/**2**-TFA. This material is available free of charge via the Internet at http://pubs.acs.org.

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