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Ion Pairing in Ethanol/Water Solution Probed by Electrophoretic and Diffusion NMR

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Ion-specific effects are ubiquitous[1,2] and have been reported in a wide range of fields including protein solubility,[3] surface tension,[4] and bacterial growth.[5] Often, ions exhibit a specific order concerning the magnitudes of the effects they induce; that order is often quoted as the Hofmeister series.[6] Although the arrangement of cations and anions in their respective Hofmeister series is somewhat dependent on the phenomenon observed, the rough trends are persistent. Recently, there has been increasing interest in ion specific effects and in unraveling the mechanisms behind the observed phenomena.

Both direct cation−anion attraction and interactions between ions and nonpolar interfaces may contribute to ion-specific effects for macromolecules.[7,8] For the latter type of interactions at interfaces between water and less polar media, sizes and polarizabilities of ions have been pointed out as significant factors.[9] There are numerous studies[10] on cation−anion interactions, but not all of those relate to the Hofmeister series. One approach has been to study interactions between small ions and charged entities present in proteins and surfactants;[8,11,12] one model[13] stipulates that ion pairs are formed preferentially between oppositely charged ions with equal water affinities. Since most experiments on ion pairing rely on indirect observations, quantitative and more direct data are desirable. Here, we provide such data for ion pairing between eight anions along the Hofmeister series and the tetramethylammonium ion (TMA^+), used as a model for a cationic entity, in an ethanol−water mixture.

Probing ion pairing by pulsed field gradient spin echo NMR,[14] where information about the degree of association between molecular species is extracted from the obtained self-diffusion coefficients,[15] is well established. However, since diffusion coefficients are inversely proportional to the hydrodynamic radius, the sensitivity to association is limited, in particular for ions of similar size. As has been shown,[16] a combination of electrophoretic NMR (eNMR) and diffusion NMR experiments may give a direct and accurate estimate of the association of molecules and ions. This approach can be particularly useful when only one of the anion or cation resonances of an ion pair is available, since otherwise, in a diffusion-only approach, measurements over a wide concentration interval are required.

In the present study, ion pairing was probed by eNMR and diffusion NMR experiments measuring the electrophoretic mobility μ_{obs} and self-diffusion coefficient D_{obs}, respectively, of the TMA^+ ion. In pure aqueous solution, TMA^+ and common inorganic monovalent anions[17,18] are completely dissociated as was also confirmed in our preliminary experiments. Ion pairing increases upon adding ethanol;[17] for our experiments, the TMA salts were dissolved in deuterated 95% (v/v) ethanol/water solution. Results obtained at the 2 mM TMA^+ concentration are presented below (trends at 10 mM are similar, see Supporting Information). Electrophoretic mobilities were obtained from the eNMR signal phase modulation upon increasing electric field strength as previously described[19] (see experimental details in Supporting Information).

At the time scale of the NMR experiments, ions are in fast exchange between their dissociated and associated states and are therefore characterized by an average charge which is the population average of the charges of all possible states of association. Based on this assumption and at the explored low salt concentration, the extent of ion pairing was estimated from the average (nominal) charge of TMA^+ z, which was calculated from D_{obs} and μ_{obs} (see Supporting Information) through

$$z = \frac{\mu_{\mathrm{obs}} k_{\mathrm{B}} T}{e D_{\mathrm{obs}}} \tag{1}$$

As far as we know, no other experimental technique enables accurate and simultaneous measurements of both the diffusion coefficient and electrophoretic mobility. Note also that a measure of charge is obtained without a titration series.

We characterize ion pairing by the average fraction of associated anions per unit formal charge expressed as

$$p = (1 - z)/z_{\mathrm{anion}} \tag{2}$$

where z_{anion} is the formal charge of the anion; $p = 0$ corresponds to complete dissociation. As shown in Figure 1, there is a clear correlation between ion pairing and the anion ionic radii. The radius is not equivocally defined for polyatomic ions, but using data from different sources[20] makes no large difference.

Ion polarizability, partly dependent on ion size,[21] is an important factor for aqueous anions.[22] Here we find that the correlation

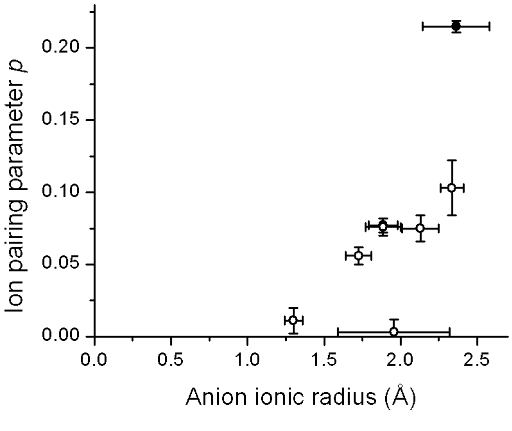

Figure 1. Ion pairing characterized by the fraction of associated anions per formal unit charge p correlated with the ionic radii[20] of monovalent (○) anions and the divalent sulfate (●) anion. Vertical error bars represent the standard deviation ($\pm\sigma$) estimated from experiments made in triplicate. Horizontal bars indicate the range of literature values for ionic radii.[20]

10.1021/ja904959y CCC: $40.75

between ion pairing and anion polarizability (Figure 2) is weaker than that between ion pairing and ionic radii. This may indicate that the difference between the anions is primarily due to direct anion−cation interactions. The Gibbs free energy of solvation of anions,[8,23] sometimes recognized as significant in Hofmeister-type phenomena, shows no correlation with ion pairing (see Supporting Information).

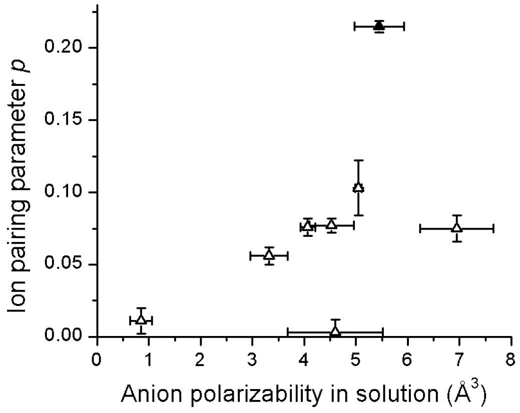

Figure 2. Ion pairing parameter *p* correlated with anion polarizability[20] in solution of monovalent (Δ) and divalent sulfate (▲) anions. Horizontal and vertical error bars are as defined in Figure 1.

As is tacitly indicated in Figures 1 and 2 and is explicitly shown in Figure 3, there is a Hofmeister relation in the ion pairing of the monovalent anions. A similar trend has been reported in aqueous solution for interactions between tetraalkylammonium ions and single-charged anions.[11,24] Although not straightforward, general trends (but not the magnitude of) in ion pairing along a series of salts seem to be alike in methanol, in ethanol/water solutions, and in water.[17,25]

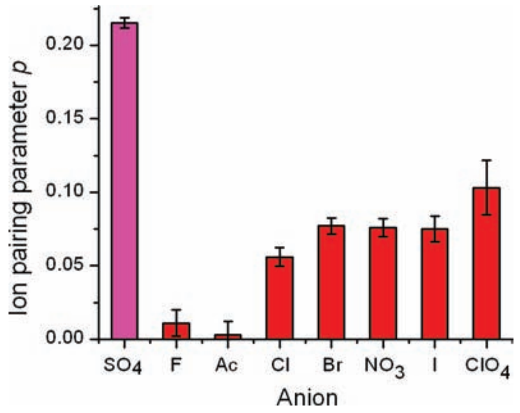

Figure 3. Ion pairing parameter *p* for ions in Hofmeister order.[2] Monovalent ions are in red, and the divalent sulfate is in magenta. Vertical error bars are same as those in Figure 1.

On the other hand, we observe that the extent of ion pairing per unit charge is much larger for the divalent sulfate ion than for the monovalent anions. Findings in the same direction are the experimental association constants that are larger for sulfate than for chloride in water[26] and are larger for alkali-earth ions than for alkali ions in acetonitrile.[27] In contrast, a computational study of the trimethylammonium group in aqueous solution[11] indicated a Hofmeister relation where sulfate had the weakest interaction with the cation and the perchlorate ion the strongest. In ion-pair chromatography experiments with tetrabutylammonium salts dissolved in a 30% methanol solution,[24] sulfate was less retained than the chaotropic iodide and perchlorate. The larger binding of sulfate in the present study might be caused by the different solvent compositions; the lower dielectric constant of the ethanol/water mixture makes electrostatic interactions dominant[25] which favors pairing to doubly charged ions. In a pure aqueous solution, electrostatic interactions between small ions become dominated by water−water interactions at distances >5 Å.[28]

In summary, we demonstrate that combining eNMR and diffusion NMR experiments can accurately measure the average charge carried by ions in solution. This average charge is used here as a quantitative indicator of ion pairing. Hence, we find that ion pairing of monovalent anions to TMA$^+$ ions in 95% (v/v) ethanol/water solution is ordered along the Hofmeister series. This finding is similar to what has been reported for that or comparable anions in aqueous solutions. We also find that, in our current solvent, the ion pairing of the double-charged sulfate is stronger than that shown by any of the investigated monovalent ions.

Acknowledgment. The Swedish Research Council (VR) and the Knut and Alice Wallenberg Foundation are thanked for financial support.

Supporting Information Available: Experimental details and illustrative electrophoretic NMR spectral series. Obtained diffusion coefficients and electrophoretic mobilities. Ion pairing vs the Gibbs free energy of solvation. This material is available free of charge via the Internet at http://pubs.acs.org.

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JA904959Y