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A correlation-based predictor for Pair-Association in Ionic Liquids

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Abstract:

Pair association in Ionic Liquids is an important quantity that affects many of their physical and chemical properties. However, the association constant is a complex function of the component ions as well as of the solvent environment, and no single theory can compute or predict it with quantitative accuracy. In this work we analyze infinite-dilution association data from a number of recent conductance measurements, and develop a linear model correlating the association constant with two relevant interaction energies, *i.e.*, (1) the dielectrically screened coulomb attraction and hydrogen bonding between ion-pairs, and (2) the ion solvation energy, which in turn takes into account solvent-specific interactions like hydrogen-bond acidity/basicity and hydrophobic/hydrophilic interactions. The results reveal the unique nature of water as a solvent in that it affects ionic association in ways qualitatively different from other common solvents.

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1. Introduction and motivation

Unique chemical and physical properties and a wide range of potential application areas have propelled room-temperature Ionic Liquids (ILs)[1, 2] into one of the most intense research areas both in academia and in industry. In particular, almost zero vapor pressure at room temperature has provided a strong green chemistry driver for the study of ILs as novel solvents and liquid medium for many chemical processes of industrial interest.[3] The degree of ionic association within each IL is expected to have a major effect on many of its properties,[4-9] including liquid structure, viscosity, solubility, catalytic, chemical affinity, aggregate formation and so on. At the same time, the ionic association strength depends not only on the component cation and the anion of the IL, but can also be a strong function of the solvent medium (in which the IL is dissolved) as well as the detailed ionic density profile. One solvent in particular, i.e., water, plays an important role in IL applications. Most ILs are found to be strongly hygroscopic, and even a small amount of water can significantly affect their physical properties.[10] Detailed understanding of the ion-ion and ion-water interactions is, not surprisingly, a topic of great current interest,[11-14] and it is crucial to determine how and to what degree the ionic association strength is affected by the presence of water. An accurate predictive tool for the association constant should open up new opportunities not only for designer ILs but also in many other areas of chemical, biochemical, and pharmaceutical industries.

Determining the association constant of an ion-pair in a solvent has been a long-standing theoretical problem. Within the statistical mechanical framework the association constant K_A can be formally expressed in terms of an integral of the inter-ionic potential of mean force (PMF), or equivalently the ensemble-averaged anion-cation radial distribution function.[15] However, computing such quantity in any solvent is challenging even for the simplest ions like alkali halides.[16-18] This is because it involves accurate averaging over a very large number of solvent configurations for every relative position of the ion pair. Although clever sampling techniques have been developed to address such challenges, including umbrella sampling,[19] free energy perturbation,[20] thermodynamic integration,[21] and constrained molecular dynamics,[22] several roadblocks to the reliable prediction of the ionic association remain.[16] In addition, first-principles calculations are often prohibitive for such calculations, and one needs to develop accurate interaction potentials (or force fields) that can become an intensive effort in itself. The situation gets exacerbated with more complex ions like those involved in common ILs with their own configurational degrees of

freedom. It is thus of great importance to look for computationally tractable alternatives that can be used to predict ionic association in ILs with quantitative accuracy.

In this paper we attempt to develop an approach in which recent experimental results (see below) are correlated with independent variables (descriptors) that are computed using implicit solvation schemes. Such an approach avoids complex averaging over solvent configurations, and if effective, would alleviate the computational burden to the point such that first-principles quantum chemistry could be employed and no force field development would be necessary. Correlation-based methods have recently become popular in the field of ILs. Examples of correlated properties include physical and thermo-physical properties like molecular volume, heat capacity, and density,[23] melting point,[24] vaporization enthalpy,[25] and toxicity.[26, 27]

2. Infinite dilution

Given the complexity of the problem of ionic association, it is a common strategy to decouple the interaction of a given ion-pair with other pairs and focus on the association strength in the infinite dilution limit of the IL in a solvent. To this end, a handful of experiments have recently been performed[8, 9, 28-32] mostly on imidazolium-cation based ILs employing anions like chloride (Cl^-), bromide (Br^-), tetrafluroborate (BF_4^-), hexafluorophosphate (PF_6^-), bis(trifluoromethylsulfonyl)-imide (Tf_2N^-), etc. All these experiments involve ionic conductance measurements for very dilute solutions, and analyze the results by the Fuoss-Onsager conductance theory[33] or a more modern variant thereof, including the Lee-Wheaton equations[34, 35] and the low-concentration chemical model.[36]

In order to develop an appropriate correlation based on the above experiments we note that the ionic association is governed by the quantity $\Delta\mu = \mu^{0(+)} + \mu^{0(-)} - \mu^{0(\mathrm{IP})}$, where the three quantities to the right correspond to the standard-state chemical potential[37] of the cation, the anion, and the ion-pair respectively. The association constant K_A in the infinite dilution limit is related to $\Delta\mu$ through the equation (see Appendix A):

$$K_A = \frac{x}{c}\exp\left(\frac{\Delta\mu}{k_B T}\right) = \frac{M_S}{\rho_S}\exp\left(\frac{\Delta\mu}{k_B T}\right), \qquad (1)$$

where x and c are respectively the mole-fraction and the molarity of the ions in the solution ρ_S and M_S are respectively the mass density and the molecular weight of the solvent, k_B the Boltzmann constant, and T the absolute temperature. The usual unit conventions are: K_A (L/mol), ρ_S (kg/L), and M_S (kg/mol). From a computational point of view it would be Ideal to have the ability to directly compute the quantity $\Delta\mu$ (and thus the association constant K_A) from first-principles quantum chemistry. Unfortunately, as will become apparent later in this paper, the implicit-solvation-based density-functional-theory (DFT) based codes do not yet have the required accuracy, hence prompting our attempt to develop a correlation-based method. In the rest of the paper we adopt the following strategy: (1) analyze existing experimental data to uncover common trends in $\Delta\mu$ as a function of the cation, the anion, and the solvent; (2) decide on the appropriate physical quantities (i.e. descriptors) on which $\Delta\mu$ might potentially show the strongest dependence, and adopt sound approaches to compute them; and finally (3) develop a simple correlation model between $\Delta\mu$ and the descriptors.

3. Analysis of experimental results

Tables 1 and 2 organize the experimental data[28-32] on association constant as a function of varying cations and anions respectively, along with the corresponding values of $\Delta\mu$ obtained by using eq. (1). From such data we note the following points:

(1) For cations ion association decreases with increasing alkyl chain length, i.e., $C_4mim^+ > C_6mim^+ > C_8mim^+$ etc., *for all solvents other than water*, including dichloromethane (DCM), 1-pentanol, 1-propanol, acetone, methanol, and acetonitrile. Most of these studies involve the Br^- anion, and in some cases BF_4^-. This result is in agreement with the studies of ref. [32] and also follows the same trend as predicted by DFT calculations in the gas phase (see Table 3).

(2) Replacing the hydrogen atom attached to the 2-carbon on the imidazolium ring by a methyl group can have a significant weakening of ion association, thereby lowering the association free energy by more than 1 kcal/mol (see ref. [32] and the discussion in the first paragraph of section 3 below). It is interesting to note that weak ion-association in the dilute limit does not necessarily translate into lower melting point or lower

viscosity of the IL. In fact 2-C substitution has recently been shown to lead to an increase in melting point and viscosity in some ILs,[38-40] an explanation of which requires considerations of the relative importance of electrostatic and hydrogen-bond interactions as well as the effects of configurational order and entropy in the solid and the liquid phases.

(3) The story in water is interesting. According to Refs. [28] and [31] the association strength increases with increasing alkyl chain length on the cation, i.e., *exactly the opposite of the behavior in all other solvents. However, ref. [29] disagrees* (see Table 1). More quantitative insight on this follows from DFT-based implicit solvent calculations, as discussed in section 4.

(4) Experimentally, the trend BF_4^- > PF_6^-> Tf_2N^- observed in DCM (ref. [32]) agrees with gas-phase DFT results (Table 3). The trend BF_4^- > PF_6^- is also observed for acetone and acetonitrile (ref. [28]). The trend is reversed (i.e., BF_4^- < PF_6^- < Tf_2N^-) in water (ref. [28] and [31]). This is similar to the trend for alkyl chain-length in cations (i.e., the trend in water is opposite of that in other, i.e., less polar, solvents).

(5) Within the halogen group it appears that Cl^- > Br^- for all solvents, as expected from gas-phase calculations (Table 3) as well as conductance experiments in water (ref. [29]).

(6) The relative association strengths of halogens as compared to BF_4^-, PF_6^-, etc., are more complex, and the differences are also much more profound. In low-polar solvents like DCM one expects the same trend as in the gas-phase, only scaled by the dielectric constant. However, in polar (protic or aprotic) solvents the degree of anion solvation becomes an important issue. To summarize, one sees the trend Cl^- > BF_4^- in DMSO, Cl^- < BF_4^- in methanol, Br^- ~ BF_4^- in acetone, and Br^- < BF_4^- in water and acetonitrile.

(7) The magnitude of association energy *differences* within each trend seem to be consistent between various experimental references. However the observed association energies in ref. [28] appear to be 1.5-2.0 kcal/mol higher than all other works. This might be due to various factors including different analysis method of the limiting conductance,[33-36] different levels of dilution employed, and so on.

4. DFT calculations in the implicit solvent environment – ground state structures and total energy

If one were to consider a solvent as a structure-less dielectric medium, the quantity $\Delta\mu$ to a first approximation would be expected to correlate with the gas-phase pair-binding energy $\Delta E = E^{(+)} + E^{(-)} - E^{(IP)}$ scaled down by the dielectric constant of the solvent [E is the internal energy, and the superscripts indicate the cation, anion, and ion-pair respectively]. A standard method to compute this quantity is to employ density-functional-theory (DFT) in conjunction with an implicit solvent model. In this work the DFT calculations were carried out using the code DMol[3],[41] while implicit solvation was represented within the Conductor-like screening model (COSMO) framework.[42, 43] The electronic wave functions in these calculations were expanded in a double-numeric-polarized (DNP) basis set on a *medium* integration grid, and a nonlocal gradient-corrected Hamiltonian was used with the gradient-corrected exchange-correlation functional due to Perdew, Burke, and Ernzerhof (PBE).[44]

As a first step, the isolated cation, the anion, and ion-pair structures were structurally optimized in vacuum (i.e., gas phase). Keeping the experimental results in mind, we focused on imidazolium-based cations with three different alkyl chain lengths: C_4mim^+, C_6mim^+, and C_8mim^+, and four different anions: Cl^-, Br^-, BF_4^-, and PF_6^-. For all the ILs considered, the most stable ion-pair structures involved the anion being in proximity of the H atom attached to the 2-C atom of the imidazolium ring. This is the main reason why ion association is strongly reduced upon substituting this hydrogen by a methyl group ($C_4m_2im^+$ in Table 1). For Cl^- the most stable structure involves the anion in the imidazolium plane (referred to below as the "*in-plane*" structure), while for Br^-, BF_4^-, and PF_6^- the structure with the anion above the plane (referred to below as the "*above-plane*" structure) is slightly more stable (by ~ 1-2 kcal/mol) than the in-plane structure. The gas-phase pair-binding energies ΔE of the most stable structures are summarized in Table 3. These ΔE values as well as results on the relative stability of *in-plane* and *above-plane* structures for different anions are in good agreement with earlier gas-phase *ab initio* calculations,[45, 46] thus validating the accuracy of the DFT parameters used in this work.

Next, to obtain ΔE in the solvent phase we employed the implicit solvent approximation using the COSMO[42, 43] approach in which the solvent is treated as a continuum with an appropriate dielectric constant (ε). For each solvent the molecular geometries of the individual ions, as well as the ion-pair structures were re-optimized in the COSMO environment. Upon doing so we observe the following results in all solvents (the smallest dielectric constant

considered was ε = 8.9, corresponding to DCM): (1) for Cl^- the *in-plane* geometry continues to remain the most stable structure, while for Br^- the stability switches from the *above-plane* structure in the gas phase (Fig. 1(a)) to the *in-plane* structure (Fig. 1(b)) in any solvent. Furthermore, the halogen anion (Cl^- or Br^-) aligns itself in nearly a straight line with respect to the 2C-H bond, which is a strong indication of the formation of a hydrogen-bond between the cationic hydrogen and the halogen (Fig. 1(b)); (2) for BF_4^- and PF_6^- only a slight perturbation of the gas-phase geometry is induced by COSMO, and the *above-plane* structure continues to be the most stable in all solvents (Figs. 1(c) and (d)).

These results suggest the following picture: (1) in the gas phase, the Coulomb interaction between the cation and the anion is stronger for the *above-plane* geometry, while H-bond interaction is stronger in the *in-plane* geometry. For strong H-bond donors (e.g., Cl^- or a naked F^-) the gain in H-bond interaction outweighs the loss in Coulomb interaction, resulting in higher stability of the *in-plane* geometry even in the gas phase. In fact, F^- is so reactive, that it can snatch away the cationic H (thereby forming HF) unless stabilized by a hydrogen-bond donor like water.[45, 47] For weaker hydrogen-bond donors (Br^-, BF_4^-, PF_6^-), on the other hand, the Coulomb interaction dominates over hydrogen-bonding and the *above-plane* geometry is more stable in the gas-phase; (2) in the solvent phase (for not too small dielectric constant, e.g., $\varepsilon \sim 10$ or larger), the Coulomb interaction gets screened by COSMO, while the hydrogen-bond interaction is not. For Br^-, whose hydrogen-bond basicity is weaker relative to Cl^- and yet stronger compared to BF_4^- and PF_6^-, the unscreened hydrogen-bond becomes the determining factor in stabilizing the *in-plane* geometry in a solvent. However, for very weak hydrogen-bond bases like BF_4^- and PF_6^- it is the coulomb interaction that dominates, and the *above-plane* structure continues to be the most stable geometry in all solvents.

In order to establish a correlation between the computed ΔE and the experimental $\Delta\mu$ we plot in Fig. 2(a) these values for a given ion pair, i.e., C_4mim^+ Br^- for a few different solvents. For consistency of analysis, we limit the discussion below to experimental values from the same group, i.e., ref. [28] only. A wider set of literature data can be used once K_A is appropriately standardized between different experiments, see the last paragraph, i.e., point (7) in section 2. For non-polar solvents ($1/\varepsilon > 0.04$ or so) there is a strong linear correlation between ΔE and $\Delta\mu$. However, while the ΔE values fall on a perfect straight line as a function of $1/\varepsilon$, thus indicating a simple dielectric scaling in COSMO, the experimental values display significant scatter for polar solvents (low $1/\varepsilon$ end). The lack of correlation

for such solvents becomes clear when one plots the ΔE vs. $\Delta\mu$ values for various solvents (Fig, (2(b)). The strong deviation from linearity, especially for water, indicates the importance of effects other than just dielectric scaling, a point elaborated in the discussions below.

Fig. 3 plots the ion-pair binding energy (ΔE) for ILs with the same cation C_4mim^+ and four different anions, i.e., Cl^-, Br^-, BF_4^-, and PF_6^-. Important observations from the COSMO calculations include:

(1) For all four anions ΔE decreases with increasing dielectric constant almost linearly as $1/\varepsilon$. At the same time, there is a finite ΔE value in the large ε limit (i.e., finite y-intercept). This is consistent with the discussion in the preceding paragraph that COSMO screens only the Coulomb interaction (by a $1/\varepsilon$ factor), while the H-bond interaction goes largely unscreened, and can be estimated from the large ε (i.e. $1/\varepsilon \rightarrow 0$) limit of ΔE.

(2) For all solvents, the binding energy ΔE follows the trend $Cl^- > Br^- > BF_4^- > PF_6^-$. The differences in ΔE between the anions shows only a weak variation as a function of the solvents (i.e., ε), which implies that *this trend is governed primarily by the hydrogen-bond basicity of the anions*, and not by the differences in Coulomb interactions due to varying anion sizes (which should be the determining factor in gas phase, see Table 3). However, this trend is in disagreement with the experimental results of ref. [28] and [32] in water where exactly the opposite trend is observed (see point (3) in section 3), and likely arises because COSMO does not incorporate hydrogen bond interactions of the solvent that can significantly affect ionic association.

(3) As a function of changing alkyl length in the cation (for the same anion Br^-), gas-phase calculations indicate that ΔE decreases with increasing chain length, i.e., $C_4mim^+ > C_6mim^+ > C_8mim^+$, which is in agreement with previous calculations.[45] However the differences in ΔE are only a few tenths of kcal/mol, which is two orders of magnitude smaller than between the different anions (see Table 3). Such small differences are primarily due to subtle changes in the charge distribution on the imidazolium ring for different alkyl chain lengths. The COSMO-computed ΔE is even smaller (see Fig. 3), only a few hundredths of kcal/mol or smaller.

(4) When one plots the ΔE vs. $\Delta\mu$ values for all ion pairs in all the solvents considered, as in Fig. 4, it becomes clear that there is a large amount of scatter with little predictive value. Not only are there quantitative disagreements, but even the trends as a function of cations and anions are in several cases opposite to what is seen experimentally.

5. Ion solvation energies using COSMO-RS

In order to improve the correlation between the computed binding energy and the experimental $\Delta\mu$, one needs to account for *solvent-specific* interactions like hydrogen bonds. To model such effects, one needs to go beyond the dielectric continuum approximation of COSMO. Several theoretical strategies have been devised to this end, as summarized and compared in a recent review.[48] Keeping in line with the COSMO method, we chose to employ its extension for real solvents, i.e., COSMO-RS,[49, 50] which represents both the solute and solvent molecules by a histogram of their surface screening charges called the σ-profile. All interactions, including coulombic, van der Waals, and hydrogen bond interactions are then defined in terms of these σ-profiles. One can use this formalism to compute the partition function, the Gibbs free energy, and many other thermodynamic quantities, although the computation of standard-state chemical potential (and therefore the quantity $\Delta\mu$) may not be straightforward.[51] Nevertheless, our motivation was to look for easily computable quantities that would correlate strongly with $\Delta\mu$. With this in mind we computed for each ion (cation and anion) a quantity (we loosely refer to below as the "solvation energy") defined by $\Delta G_{A,S} = G_{A,S} - E_{A,gas}$, where $G_{A,S}$ is the COSMO-RS computed Gibbs free energy of ion A in the solvent environment S, and $E_{A,gas}$ is the gas-phase energy. According to this definition, the more negative the $\Delta G_{A,S}$, the more stable the ion species A is in the solvent. Table 4 displays the computed results for the ions of interest in seven different solvents. The main results from Table 4 are summarized below:

(1) As a function of cations, we find that in *all solvents other than water* the solvation energy $\Delta G_{A,S}$ increases with the alkyl chain length, i.e., $C_4mim^+ > C_6mim^+ > C_8mim^+$. The trend is exactly reversed in water. The solvation energy in water is significantly smaller than in all other solvents, which indicates the presence of

strong hydrophobic interactions of the alkyl chains in water. Also, the differences in solvation energies between C_4mim^+, C_6mim^+, and C_8mim^+ (for any given solvent) is of the order of 1 kcal/mol. The observed differences in ion association (with varying cations) appear to be an order-of-magnitude smaller than the differences in solvation energy, which is reasonable given that association energy itself is the difference in free energy between the same ions in two different states (i.e., dissociated versus un-dissociated).

(2) As a function of anions we find that in solvents like water (and to a lesser extent methanol) with strong hydrogen-bond acidity, the halogen ions Cl^- and Br^- show a much higher dissolution affinity as compared with BF_4^- or PF_6^-. This would explain why halogens have a smaller ionic association in such solvents as compared to BF_4^- or PF_6^-. In effect, water not only screens the coulomb attraction between the ion pairs, but also screens the hydrogen-bond. The hydrogen-bond screening is more effective for strong hydrogen-bond bases like the halogens, thus lowering their association with the imidazolium cation relative to the weaker hydrogen-bond bases like BF_4^- or PF_6^-.

6. Predictive correlation

The above discussion is mainly qualitative and shows the usefulness of solvation energies in addressing some of the shortcomings of the dielectric approximation. The question is whether we can quantitatively improve upon the scatter in Fig 4 by a simple additive inclusion of the $\Delta G_{A,S}$ numbers of Table 4. Below we describe a two-step procedure toward this goal.

As a first step, we seek to improve the correlation of Fig. 2(b) by focusing on the ion-pair C_4mim^+ Br^- in various solvents and defining a modified binding energy as:

$$\Delta E'_{0,S} = \Delta E_{0,S} - \alpha_0 (\Delta G_{0^+,S} + \Delta G_{0^-,S}) \,, \qquad (2)$$

where "0^+" and "0^-" denote our reference cation C_4mim^+ and reference anion Br^- respectively, "0" denotes the reference ion-pair C_4mim^+ Br^-, and α_0 is a constant that is optimized to obtain the highest linear correlation between $\Delta E'$ vs. $\Delta\mu$. A linear regression fit is then used to rescale the quantity $\Delta E'$, i.e., $\Delta E'' = b_0 + b_1 \Delta E'$, which is then used

for prediction purposes. The filled symbols in Fig. 5 represent the $\Delta E''$ vs. $\Delta\mu$ plot for the reference ion pair in various solvents for the optimized parameter value $\alpha_0 = 0.25$, and the regression constants $b_0 = -5.75$ and $b_1 = 0.285$. Clearly, the inclusion of solvation effects significantly improves the correlation as compared to Fig. 2(b).

Next, we define a modified binding energy for a general ion-pair by including deviations δ (ΔG) of ion solvation energy from that of the reference ion. Thus, for an ion pair C^+A^- we define:

$$\Delta E'_{CA,S} = \Delta E'_{0,S} + \alpha_+ \delta(\Delta G_{C^+,S}) + \alpha_- \delta(\Delta G_{A^-,S}) , \qquad (3)$$

where the deviations in cationic and anionic solvation energies are defined as:

$$\delta(\Delta G_{C^+,S}) = \Delta G_{C^+,S} - \Delta G_{0^+,S} \text{ and } \delta(\Delta G_{A^-,S}) = \Delta G_{A^-,S} - \Delta G_{0^-,S} , \qquad (4)$$

and α_+ and α_- are constants that are optimized to obtain the highest correlation between the computed $\Delta E'$ and the experimental $\Delta\mu$ data. We then define the rescaled quantity $\Delta E'' = b_0 + b_1\Delta E'$ for all general ion pairs using the same regression constants b_0 and b_1 as obtained above for the reference ion pair system. Fig. 5 plots this rescaled $\Delta E''$ vs. $\Delta\mu$ for the optimized parameter values $\alpha_+ = 0.30$ and $\alpha_- = 0.04$ respectively with the open symbols indicating all ion-pairs other than the reference pairs (which are indicated by the filled symbols). Clearly the correlation is much more improved as compared to the raw COSMO results (Fig. 4) with the exception of two points which correspond to $C_4mim^+BF_4^-$ and $C_4mim^+PF_6^-$ in acetonitrile (see Table 2). Upon exclusion of these two points the correlation coefficient between $\Delta\mu$ and $\Delta E''$ is $r = 0.987$, with a maximum deviation of only 3.9% of $\Delta\mu$ from its predicted value.

7. Summary

The present work is motivated by the need to develop a predictive formula for the pair-association constant of ionic liquids in various solvents. An analysis of recent conductance measurements in dilute IL solutions reveals complex dependence of this association constant on the cation, the anion, and the solvent. In particular, in non-polar solvents the association strength increases with decreasing alkyl chain length of the cation, and increasing hydrogen-

bond basicity of the anion. Both these trends get reversed in polar, hydrogen-bond active solvents like water. Given that determining such association constant from explicit solvent models is a significant computational challenge even for simple ions like alkali halides, we sought to develop a correlation-based predictive tool using the recent experimental results. Two relevant energies were chosen as descriptors, i.e., (1) the pair-binding energy (ΔE) in which the Coulombic part of the cation-anion interaction is dielectrically screened, and (2) the solvation energy (ΔG) of the individual ions that takes into account solvent-specific interactions like hydrogen-bond acidity/basicity and hydrophobic/hydrophilic interactions. The hope was that implicit-solvent calculations of both the above energies would be adequate in developing a good correlation with the experimentally observed association.

To compute ΔE we represented the solvent as a continuum dielectric within the COSMO framework. We find that such an approximation dielectrically screens only the Coulomb part of the cation-anion interaction, but not the hydrogen-bond interaction between the ion-pair. In non-polar solvents with low hydrogen bond activity this is a good approximation, while it can fail dramatically in H-bond active solvents. This is particularly true for solvents like water, where in addition to strong screening of the H-bond interaction between ion-pair, one also needs to take into account possible hydrophobic/hydrophilic interactions of functional groups of cations that can significantly affect ionic association.

To incorporate such effects into the association constant, it was necessary to include in our descriptor set the solvation energy (ΔG) of each component ion computed by a more realistic solvent model, *i.e.*, COSMO-RS. This immediately produces a number of experimentally observed trends not obtainable with just ΔE. For instance, the inclusion of ΔG (along with ΔE) leads to an increasing association strength with increase in alkyl chain length of a cation in water, and results in the lowering of the association of a halogen ion like Cl^- or Br^- relative to weak hydrogen bases like BF_4^- or PF_6^-. The first effect can be clearly attributed to an increasing degree of hydrophobicity, while the second effect arises from strong hydrogen-bonding of the halogen ions with water.

Finally, we show that such insights can be translated into a quantitatively accurate predictor of ion-association strength for a general ion pair in a general solvent. As we demonstrate in section 6 a linear combination of the COSMO-computed ion-pair binding energy (ΔE) and the COSMO-RS computed ion-solvation energy (ΔG) can

indeed be used to construct a predictor of association strength with a high level of accuracy. The work also clarifies water's unique role in ionic liquid chemistry.

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APPENDIX A: Derivation of eq. (1)

Let us consider a dilute IL solution with mole-fraction x of IL, a fraction α of which are dissociated ions, and the rest, i.e., (1-α) is in the form of ion-pairs (i.e. associated). One can then write the following expressions for chemical potential for the cations (+), anions (-), and the ion-pairs (IP):

$$\mu_+ = \mu_+^0 + k_B T \ln(\alpha\gamma_{+x}x), \quad \mu_- = \mu_-^0 + k_B T \ln(\alpha\gamma_{-x}x), \text{ and } \mu_{IP} = \mu_{IP}^0 + k_B T \ln((1-\alpha)\gamma_{IP}x),$$

where the quantities with superscript "0" are the corresponding standard-state chemical potentials, and γ the corresponding activity coefficients. Under equilibrium condition: $\mu_{IP} = \mu_+ + \mu_-$. Thus,

$$k_B T \ln\left[\frac{(1-\alpha)}{x\gamma_{+x}\gamma_{-x}\alpha^2}\right] = \mu_+^0 + \mu_-^0 - \mu_{IP}^0 = \Delta\mu . \qquad \text{(A1)}$$

For dilute solutions of interest here the mole-fraction activity coefficients are essentially the same as the molality-scale activity coefficients, i.e., $\gamma_{+x}\gamma_{-x} = \gamma_\pm^2$.[52] Thus, we have: $\ln\left[\frac{(1-\alpha)}{x\gamma_\pm^2\alpha^2}\right] = \frac{\Delta\mu}{k_B T}$. The ionic association constant is conventionally defined as:[53]

$$K_A = \frac{(1-\alpha)}{c\gamma_\pm^2\alpha^2} , \qquad \text{(A2)}$$

where c is the molar concentration (i.e. molarity) of the solute. From eqs. (A1) and (A2) one obtains:

$K_A = \frac{x}{c}\exp\left(\frac{\Delta\mu}{k_B T}\right)$, which is the first half of eq. (1). For a dilute solution, $\frac{x}{c} \approx \frac{M_S}{\rho_S}$, from which the second half of eq. (1) follows.

Table 1. Effect of cations on ionic association strength (T = 25 °C).

Solvent	Anion	Cation	K_A (L/mol)	$\Delta\mu$ (kcal/mol)	Reference
Water	Br^-	C_4mim^+	66	4.86	[28]
		C_6mim^+	71	4.90	
		C_8mim^+	79	4.97	
		$C_{10}mim^+$	84	5.00	
		$C_{12}mim^+$	96	5.08	
Water	Br^-	C_4mim^+	6.0	3.44	[29]
		C_5mim^+	5.7	3.41	
		C_6mim^+	5.4	3.38	
Water	BF_4^-	C_4mim^+	5.2	3.36	[31]
		C_6mim^+	6.0	3.44	
		C_8mim^+	6.2	3.46	
Acetonitrile	Br^-	C_4mim^+	152	4.72	[28]
		C_6mim^+	130	4.63	
		C_8mim^+	120	4.58	
Methanol	Br^-	C_4mim^+	193	5.02	[28]
		C_6mim^+	147	4.85	
		C_8mim^+	138	4.82	
Acetone	Br^-	C_4mim^+	668	5.40	[28]
		C_6mim^+	651	5.38	
		C_8mim^+	631	5.36	
1-Pentanol	Br^-	C_4mim^+	4622	6.31	[28]
		C_6mim^+	4393	6.28	
		C_8mim^+	4182	6.26	
DCM	BF_4^-	C_4mim^+	38.4	3.79	[32]
		C_6mim^+	35.1	3.74	
		C_8mim^+	32.3	3.69	
		$C_4m_2im^+$	6.3	2.72	

Table 2. Effect of anions on ionic association strength (T = 25 ^{o}C).

Solvent	Cation	Anion	K_A (L/mol)	$\Delta\mu$ (kcal/mol)	Reference
Water	C_4mim^+	Br^-	66	4.86	[28]
		BF_4^-	105	5.14	
		PF_6	113	5.18	
Water	C_4mim^+	Cl^-	7.9	3.60	[29]
		Br^-	6.0	3.44	
		I^-	5.8	3.42	
Water	C_4mim^+	BF_4^-	5.2	3.36	[31]
		PF_6^-	6.3	3.44	
		Tf_2N^-	8.0	3.46	
DMSO	C_4mim^+	Cl^-	13.4	3.10	[30]
		BF_4^-	4.6	2.47	
Acetonitrile	C_4mim^+	Br^-	152	4.72	[28]
		BF_4^-	712	5.63	
		PF_6^-	683	5.61	
Methanol	C_4mim^+	Cl^-	15.5	3.52	[30]
		BF_4^-	37.7	4.05	
Acetone	C_4mim^+	Br^-	668	5.40	[28]
		BF_4^-	747	5.46	
		PF_6^-	692	5.42	
DCM	C_4mim^+	BF_4^-	38.4	3.79	[32]
		PF_6^-	15.2	3.24	
		Tf_2N^-	11.6	3.08	

Table 3. Gas-Phase ion-pair binding energies (ΔE) from DFT calculations

Cation	Anion	ΔE (kcal/mol)
C_4mim^+	Cl^-	101.6
C_4mim^+	Br^-	97.6
C_6mim^+	Br^-	97.3
C_8mim^+	Br^-	97.2
C_4mim^+	BF_4^-	84.5
C_4mim^+	PF_6^-	77.4

Table 4. Solvation energies (see section 4 for definition) of various ions in different solvents (COSMO-RS)

Solvents →	Water	DMSO	Acetonitrile	Methanol	Acetone	1-pentanol	DCM
Cations							
C_4mim^+	-43.6	-52.1	-49.1	-50.7	-52.8	-51.3	-51.3
C_6mim^+	-43.0	-52.8	-49.5	-51.3	-53.7	-52.2	-52.1
C_8mim^+	-42.6	-53.8	-50.1	-52.2	-54.8	-53.3	-53.1
Anions							
Cl^-	-94.3	-74.0	-76.1	-82.3	-70.4	-79.6	-77.7
Br^-	-87.9	-71.7	-73.6	-75.6	-68.4	-72.7	-74.1
BF_4^-	-69.7	-62.6	-63.4	-60.1	-59.4	-57.5	-61.4
PF_6^-	-58.0	-58.4	-58.3	-54.0	-55.3	-52.0	-54.8

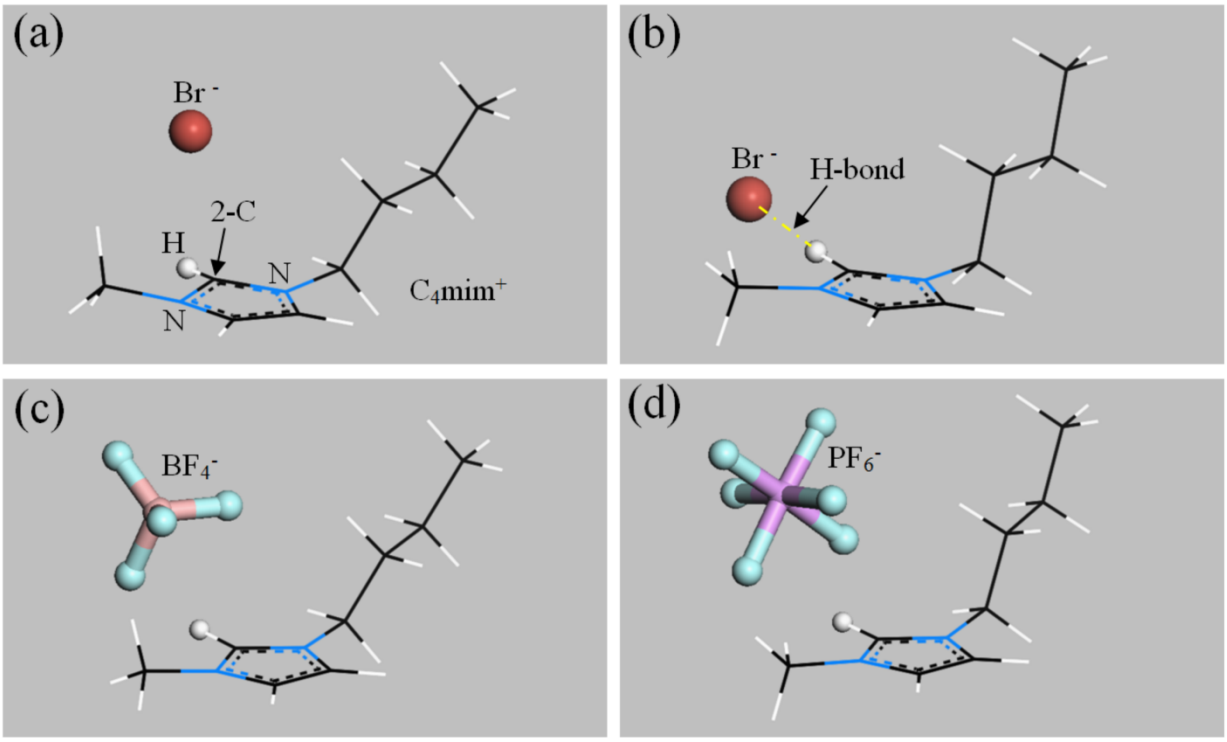
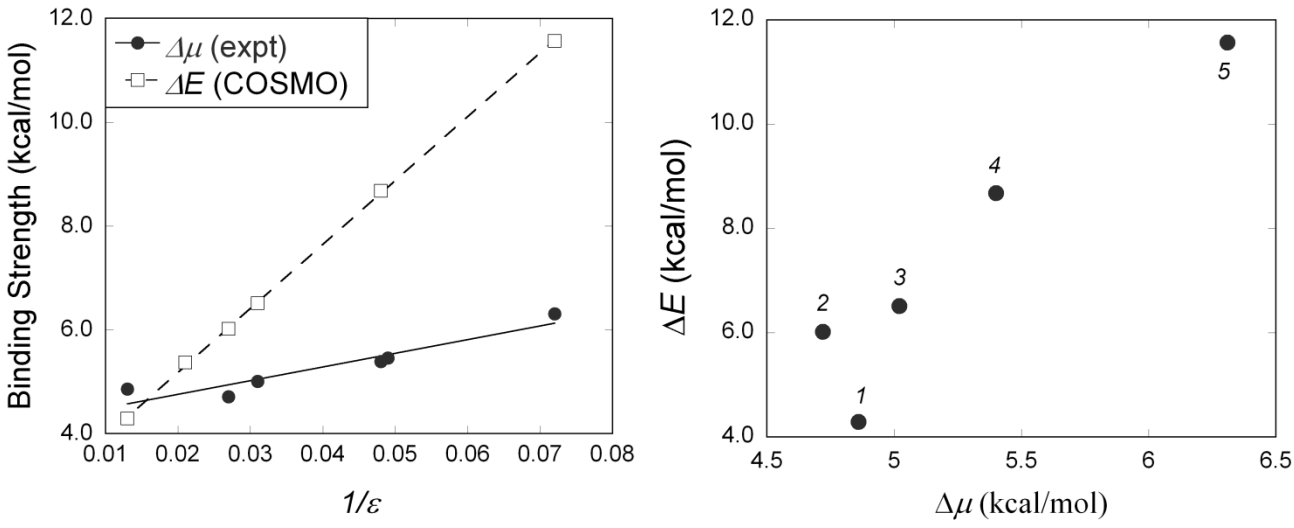


Fig. 1. DFT/COSMO-optimized most stable structure of various ion-pairs for the same cation C_4mim^+. The anion (solvent) is: (a) Br^- (gas phase); (b) Br^- (water); (c) BF_4^- (water); and (d) PF_6^- (water). The anion and the cationic hydrogen atom connected to the 2-C atom are displayed in ball & stick, while the rest are displayed in the stick representation. In Figs. (a), (c), and (d) the anions are *above* the plane of the imidazolium ring, while in Fig. (b) the anion is *in* the imidazolium plane being bonded to the 2-C-hydrogen through a hydrogen-bond (H-bond). The 2-C and the N-atoms on the imidazolium ring are indicated in Fig. (a). The ion-pair structure with Cl^- is similar to Fig. (b) both in the gas phase and in water, while those with BF_4^- and PF_6^- in the gas phase are similar to Figs. (c) and (d) respectively. Color scheme (online): H (white), C (black), N (blue), Br (red), B (light red), P (magenta), F (light blue).



(a) (b)

Fig. 2. (a) Experimentally observed $\Delta\mu$ in our reference system $C_4mim^+Br^-$(ref. [28]) compared with DFT-computed pair-binding energy (ΔE) in implicit solvent (COSMO) as a function of the inverse dielectric constant ($1/\varepsilon$). Solvents employed in increasing order of $1/\varepsilon$ are: water (0.013), DMSO (0.021), acetonitrile (0.027), methanol (0.031), acetone (0.048), 1-propanol (0.049), and 1-pentanol (0.072); (b) ΔE vs. $\Delta\mu$ plot showing strong deviation from linearity, especially for water; the solvents are 1: water, 2: acetonitrile, 3: methanol, 4: acetone, 5: 1-pentanol.

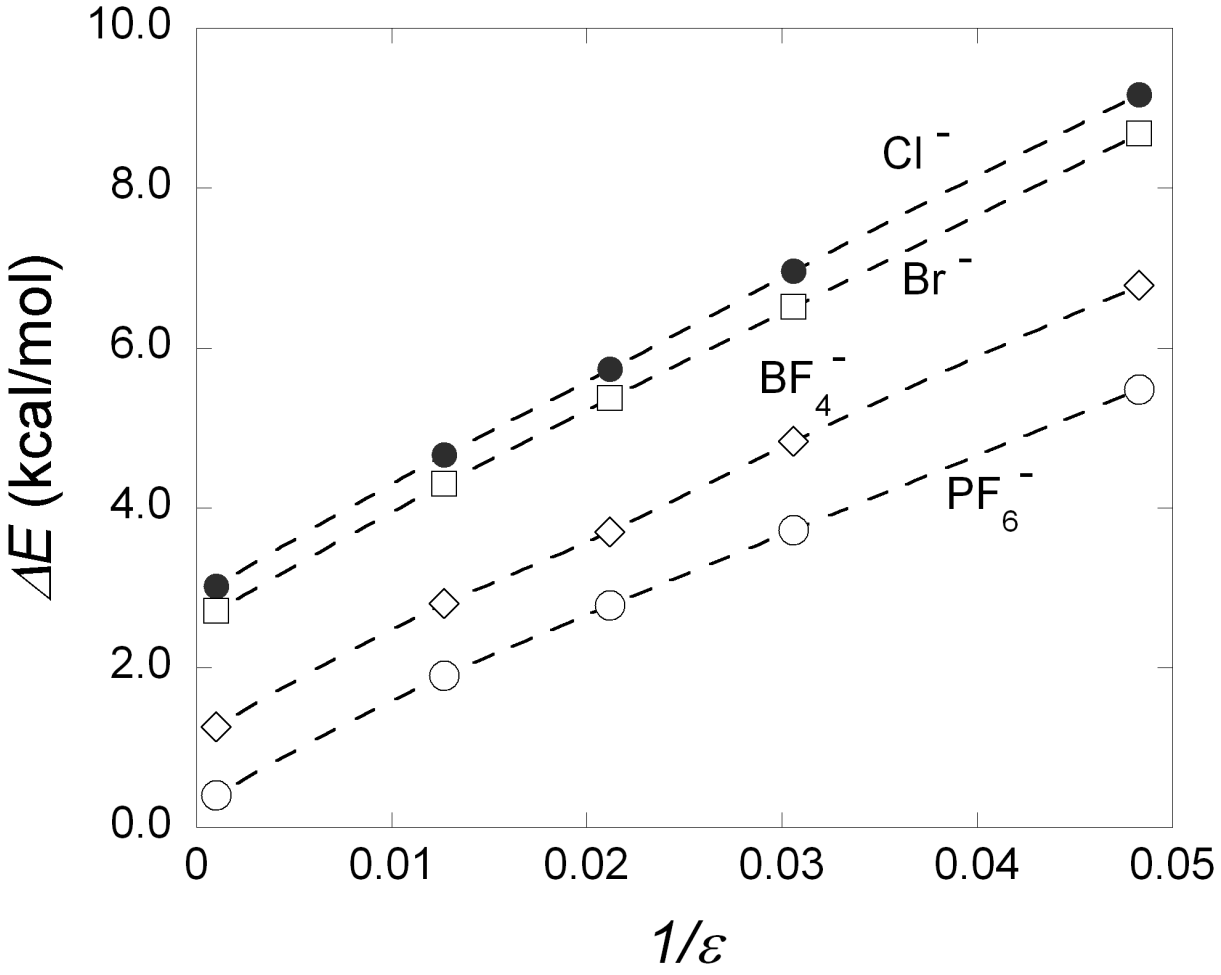


Fig. 3. DFT-computed pair-binding energy (ΔE) for ILs with the C_4mim^+ cation and four different anions in implicit solvent (COSMO) as a function of the inverse dielectric constant ($1/\varepsilon$). Solvents employed in increasing order of $1/\varepsilon$ are: water (0.013), DMSO (0.021), methanol (0.031), and acetone (0.048). Also included are results for a conductor environment with a large dielectric constant (ε = 999, i.e., $1/\varepsilon$ = 0.001). The non-vanishing y-intercept indicates residual unscreened binding, resulting primarily from hydrogen-bond interactions.

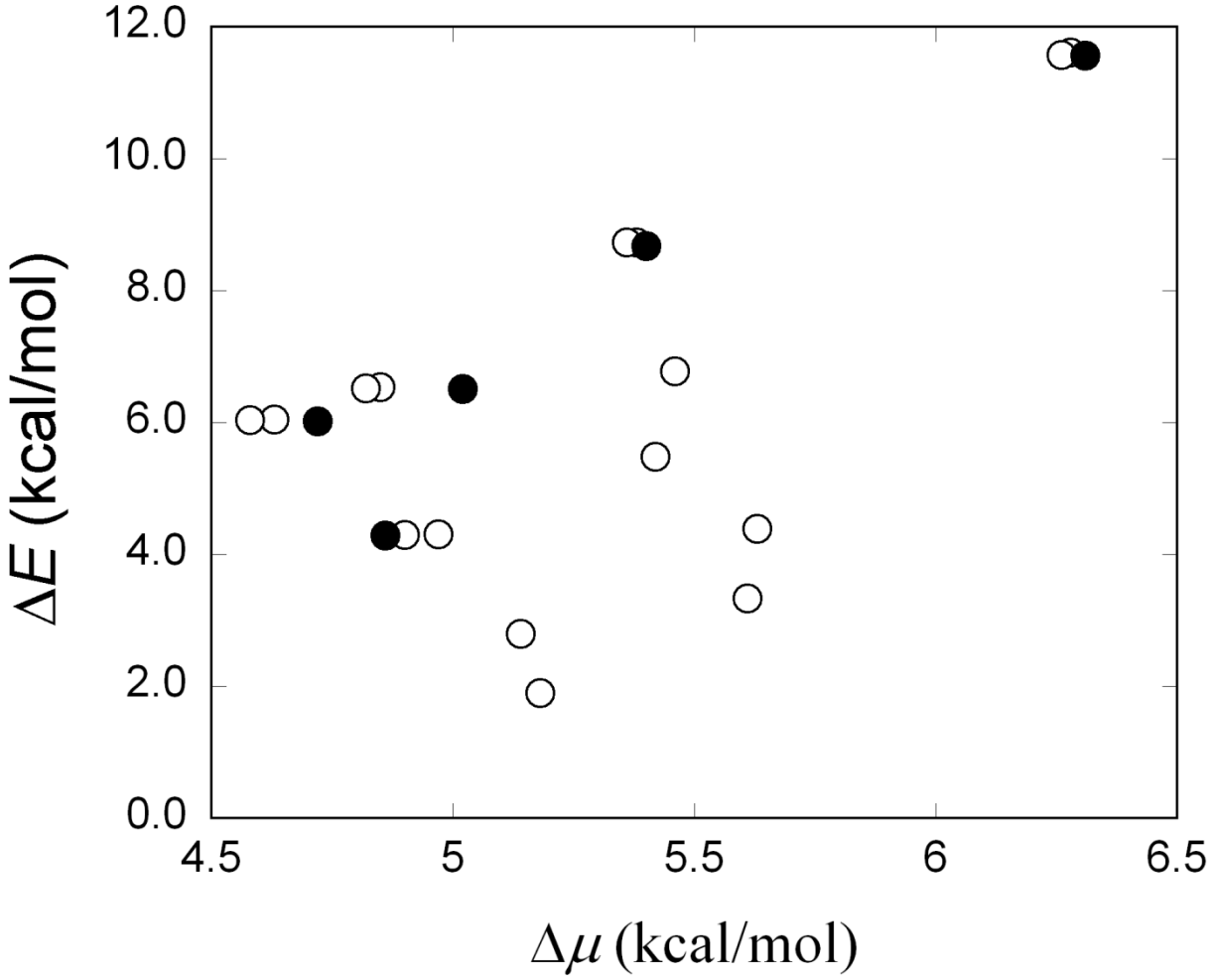


Fig. 4. COSMO-computed ΔE vs. experimental $\Delta\mu$ (only from ref. [28] for consistency) : data includes all ion-pairs in Tables 1 and 2 linked to ref. [28]. Filled symbols correspond to our reference pair $C_4mim^+Br^-$, i.e., corresponding to Fig. 2(b), while open symbols denote all other ion-pairs. The plot displays large scatter with little correlation.

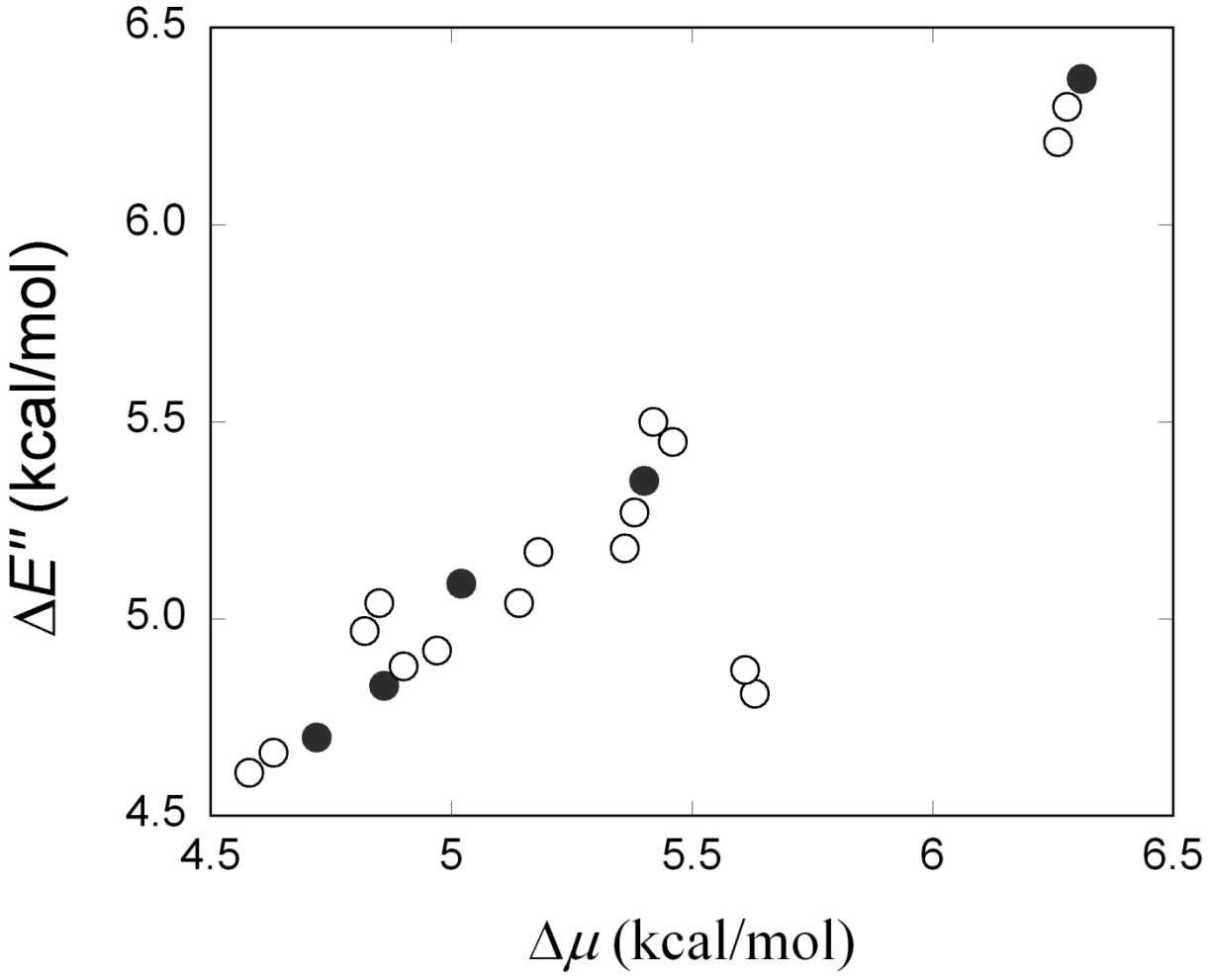


Fig. 5. Modified binding energy $\Delta E''$ vs. experimental $\Delta\mu$ (from ref. [28]) showing much more improved correlation as compared to Fig. 4. Filled symbols correspond to our reference pair $C_4mim^+Br^-$, while open symbols denote all other ion-pairs.