

Double-Line Hammett Relationship Revealed through Precise Acidity Measurement of Benzenethiols in Neat Ionic Media: A Typical “Ionic Liquid Effect”?

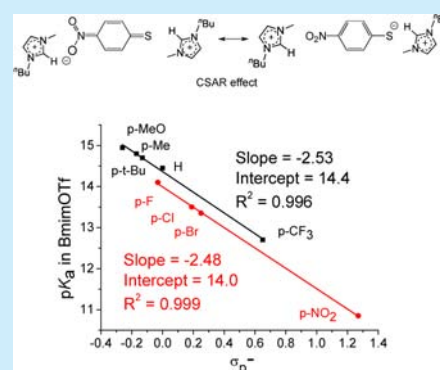
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S Supporting Information

ABSTRACT: Equilibrium acidities (pK_a) of 14 aromatic thiols in four pure room temperature ionic liquids (RTILs) were precisely determined and the corresponding acidity scales were established for the first time. Regression analyses show a distinct double-line Hammett relationship with similar slopes and excellent linearity (R^2 of 0.996–0.999) in all four ILs. This could be rationalized by a resonance enhanced effect of the IL cation to solvate the para substituent of feasible electronic structure (CSAR effect), revealing a typical and rarely seen “ionic liquid effect”.



Studies on pK_a have played important roles in the development of chemical science.^{2–5} The solvent is the key factor and often found to induce remarkable changes to the acid–base equilibria.^{1a,2b} In this regard, a great number of pK_a scales in various conventional molecular solvents have been established.^{6–9} Surprisingly, very few works have focused on the equilibrium acidity in ionic liquid,¹⁰ despite the fundamental differences between the ionic and molecular media and the definite need of these bond energetic quantities to understand the very complicated phenomena observed in the tremendous applications of this rising mainstream solvent system in chemistry, biology, and industry.¹¹

Indeed, a few fine groups have already carried out some investigations of the acid–base behaviors in ILs and reported the corresponding acidity data.^{12,13} However, as realized therewith, the studies were more difficult to conduct in ILs, which often suffered from one or several problems, such as, unavoidable molecular impurities in IL, narrow range of pK_a window, complications brought in by using concentrated solutions, and so on. Also, most acidity data reported are relative values against the pK_a of a particular indicator measured in a *different* solvent such as water¹² and hence cannot be used to assess the real energetic change between bond heterolysis in RTILs and in other media.

With our previous experiences on investigating various bond energies in molecular solvents,¹⁴ we have recently developed a methodology to study the absolute pK_a s for several series of carbon acids¹⁵ and oxygen acids¹⁶ in pure ILs under standard conditions. The method was verified to be free from ion-pairing perturbation and to be generally suitable for a broad range of

equilibrium acidity measurement with high precision. The standard bond parameters like pK_a provide the necessary quantitative tool for analyzing the interesting and seemingly mysterious behaviors of chemical transformations performed in ILs and for understanding the distinct influence of IL on the strength of chemical bonds as compared to other media. Obviously, research efforts on building such fundamental platform, which can also act as quantitative reference baseline for theoretical studies in ILs,¹⁷ need to be largely expanded.

To further understand the effect of the distinct solvation exerted by ionic media, in the present work, we extended our endeavor to the absolute acidities of benzenethiols that are believed to likely provide the information on how the direct linkage of functional group at the benzene ring would exert its resonance effect on the substrate acidity¹⁸ under a total ionic ambient. Thiols are among the most important compounds in both chemical and biological research and have been widely used for synthetic purpose in ILs as well.¹⁹ The acidity study of the S–H type acids in ILs was not reported before, and it is expected that the relevant knowledge may add a better understanding of the so-called “ionic liquid effect”.²⁰

The general method was outlined previously.^{15,16} Four standard ILs, i.e., BmimNTf₂, BmpyNTf₂, Bm₂imNTf₂, and BmimOTf (Bmim⁺ = 1-butyl-3-methylimidazolium; Bmpy⁺ = *N*-butyl-*N*-methylpyrrolidinium; Bm₂im⁺ = 1-butyl-2,3-dimethylimidazolium), were used as the media, and the indicators with

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known pK_a values were chosen for this work (Supporting Information, SI). The suspected protonation of indicator anions by IL, for example, by the imidazolium-based BmimOTf, can be excluded since the acidity difference between them is more than 11 orders of magnitude in DMSO.¹⁴

It is worth noting that the acidities measured in the present work were free from the perturbation of homoconjugation effect of the substrates found elsewhere.¹⁶ Similar to the case in DMSO,^{18c} there was no obvious variation of the benzenethiol pK_a value during the course of titration with the indicator base in ILs (SI). The obtained pK_a s of substituted benzenethiols are presented in Table 1.

Table 1. pK_a Values of Benzenethiols in ILs

substituents	pK_a in ILs ^a			
	BmimOTf	BmimNTf ₂	BmpyNTf ₂	Bm ₂ imNTf ₂
<i>p</i> -MeO	14.9 ₅	17.7	18.4	19.1 ₅
<i>p</i> -Me	14.8	17.5	18.2 ₅	18.9 ₅
<i>p</i> -C(CH ₃) ₃	14.7	17.4	18.0	18.8 ₅
H	14.4 ₅	17.1 ₅	17.8	18.5
<i>p</i> -F	14.1	16.8 ₅	17.3 ₅	18.1
<i>p</i> -Cl	13.5	16.2 ₅	16.7	17.3 ₅
<i>p</i> -Br	13.3 ₅	16.1 ₅	16.5 ₅	17.2
<i>p</i> -CF ₃	12.7	15.3 ₅	15.8	16.4
<i>p</i> -NO ₂	10.8 ₅	13.5 ₅	13.7 ₅	14.2 ₅
<i>m</i> -Me	14.6 ₅	17.3 ₅	18.0	18.7
<i>m</i> -MeO	14.3	17.1	17.6	18.4
<i>m</i> -F	13.5	16.4	16.7	17.4
<i>m</i> -Br	13.1	16.1	16.2	16.9
<i>m</i> -CF ₃	12.8 ₅	15.6	16.1	16.7

^aIn pK units; SD $\leq \pm 0.05$.

Table 1 shows that the pK_a values of the selected benzenethiols cover a range of 10.85–14.95, 13.55–17.7, 13.75–18.4, and 14.25–19.15 in BmimOTf, BmimNTf₂, BmpyNTf₂, and Bm₂imNTf₂, respectively. Interestingly, the pK_a s of the parent benzenethiol in four ILs (14.45–18.5) are higher than in water (6.6^{6a}) and DMSO (10.3^{7b}). This may be counterintuitive by considering the charged nature of the ionic media, hence indicating the need of studying the distinct solvation effect of RTILs.

As seen in Table 1 the pK_a value of these S–H acids varies in different IL following an order of Bm₂imNTf₂ > BmpyNTf₂ > BmimNTf₂ > BmimOTf, which is similar to but greater than the trend of C–H acids¹⁵ found in our previous work, indicating that the acidifying effect of IL on S–H acidity is closely associated with the structure and composition of IL. The obviously stronger acidity of benzenethiol in BmimOTf than in the other three ILs with NTf₂⁻ as a common anion could be understood on the ground of charge density and the size of individual anion part of ILs. Being smaller in size and with more negative charge localized on the oxygen atom, OTf⁻ exhibits a stronger solvation effect on proton than NTf₂⁻. For example, the pK_a difference (ΔpK_a) for benzenethiol in BmimOTf (14.45) and BmimNTf₂ (17.15) is 2.7; as a good approximation, this ΔpK_a value can be considered to arise solely from the solvation energy difference of proton by the counteranion of two ILs under the comparison, which corresponds to a $\Delta\Delta G_s^*(H^+)$ of 3.7 kcal mol⁻¹. Similarly, the trend of pK_a change in the ILs with NTf₂⁻ as the common anion could be rationalized on the basis of the extent of charge delocalization and the ability of accessing the thiolate anion by

the cation part of the ILs. The lowest pK_a values found in BmimNTf₂, compared with those in the ILs with Bmpy⁺ and Bm₂im⁺ as the counteranion, is largely due to that Bmim⁺ is the least bulky cation in size among the three, which suggests that it would be subjected to less repulsion, therefore leading to a closer and thus stronger interaction with thiolate anion. In addition, the potential H-bond donating protons on the imidazolium ring, especially the most acidic one at 2-position ($pK_a = 22.0$ in DMSO^{14d}), may further strengthen the solvation of thiolate through H-bonding(s). A greater delocalization of the positive charge in Bm₂im⁺ than in Bmpy⁺ may be responsible for the higher pK_a values found in Bm₂imNTf₂. Clearly, the anion part of IL shows a stronger acidifying effect on the substrate than that of the cation. Nonetheless, the structure of the cation of IL, though has minor contribution to acidity, may play a significant role in tuning the acidity through nonbonding forces, such as hydrogen bonding and cation– π and π – π interactions.²¹ Generally, the acid and base equilibrium studies in ILs are more complicated than those in molecular solvents due to the fact that both cation and anion moieties of ILs interact with the dissociated and undissociated species. Thus, one should realize that normally a single set of parameter for the solvent polarity, such as E_T^{30} , ϵ , or π^* , could not give satisfactory interpretation for the solvation effect on solutes in ILs.¹²

To examine the remote substituent effect on the acidity of benzenethiols in ionic media, regression analyses were performed. As shown in Figure 1, excellent linearity ($R^2 =$

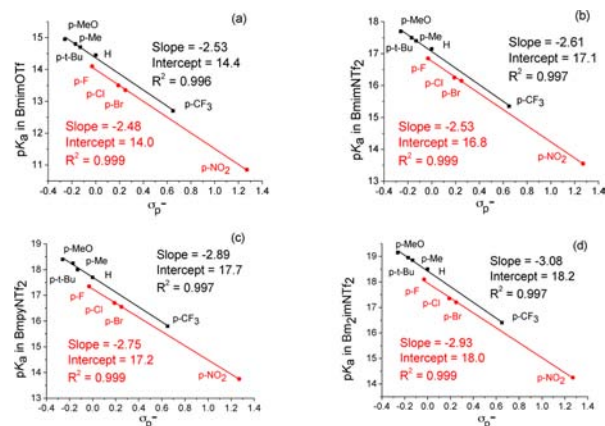


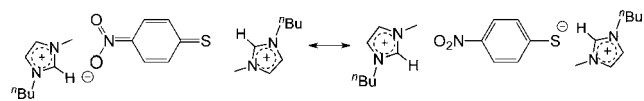
Figure 1. Hammett plot for the pK_a values of benzenethiols in (a) BmimOTf, (b) BmimNTf₂, (c) BmpyNTf₂, and (d) Bm₂imNTf₂.

0.997, black line) is observed for the Hammett plots with *p*-MeO, *p*-Me, *p*-C(CH₃)₃, *p*-H, and *p*-CF₃ as substituent in all four ILs. Interestingly, the data points for *p*-F, *p*-Br, *p*-Cl, and *p*-NO₂ as substituent present a separate line, which also shows excellent linearity ($R^2 = 0.999$, red line) in all ILs, basically parallel to the respective line mentioned above with similar slopes. Such a phenomenon here observed, an unusual double-line Hammett relationship, was not found elsewhere in any molecular solvent. Notably, Bordwell and Taft et al. investigated the acidity of substituted phenols in DMSO and correlated the DMSO data with the gas phase acidities.²² Their results showed that the resonance-induced acid-strengthening effect of the *p*-EWGs is significantly enhanced in DMSO, causing the corresponding points to deviate from the correlation line. This phenomenon was phrased as the substituent-solvation-assisted resonance (SSAR) effect,²² which appeared to be determined by a

solvent-enhanced stabilization of the negative charge toward the perimeter of the *p*-EWG through resonance delocalization.

Although the so-called SSAR effect is originally specified to interpret deviations observed in solution from that in the gas phase and it has never been applied in a single solvent, we believe that a similar mechanism could be deduced therefrom to understand the parallel double-line Hammett relationship observed herein. As depicted in Scheme 1, the *p*-EWGs like *p*-

Scheme 1. Cation-Solvation-Assisted Resonance (CSAR) Delocalization of the *p*-EWG Substituted Benzenethiolate



halogen, *p*-CN, *p*-NO₂, etc., are all capable of pulling the negative charge from the sulfur atom of thiolate anion toward themselves through resonance delocalization, which could be enhanced with the assistance of the cation in IL through a Coulombic-type solvation to exhibit an SSAR-like cation-solvation-assisted resonance (CSAR) effect (Scheme 1). However, no such mechanism is possible for all *p*-electron-donating groups as well as for *p*-CF₃ despite the latter is also an EWG.^{18c}

It should be pointed out that though some *p*-EWGs are capable of delocalizing a negative charge through resonance (e.g., nitro, cyano, carbonyl, etc.), the SSAR effect, even the CSAR effect, may not be easily detected in a single solvent unless (a) the physicochemical parameters (such as *pK_a*) used in linear regression are precisely measured to allow a scrupulous analysis and (b) the specific solvation of the π - or *p*-electron type *p*-EWGs by solvent molecule or by IL cation is feasible and is strong enough. Hence, it is understandable that the few known cases of SSAR effect in molecular solvent are often associated with *p*-nitro as substituent, of which solvation with suitable solvent molecule like DMSO may be strong enough, but never with weak EWGs like halogen.^{18,22} As for the CSAR effect presently observed for benzenethiols *pK_a*s in RTILs (Figure 1), it implies that both the mentioned criteria are met in the present cases and suggests that the IL cation can exert considerably stronger solvation toward the favorable π /*p*-type *p*-EWGs than molecular solvents. Such phenomenon found here specifically in ILs may provide an excellent example of the so-called “ionic liquid effect”, which is observed only in ILs.

In summary, the first S–H type acidity scales including 14 benzenethiols in RTILs were established. Hammett plots of the *pK_a* values of para-substituted benzenethiols in all four ILs show two distinct lines with similar slopes, which could be rationalized with the differential solvation effect of the IL cation on the *p*-EWGs, which allow an extended delocalization of the negative charge toward them (i.e., the CSAR effect), providing a sign of the so-called “ionic liquid effect”. These acidity data of thiols would be useful in synthetic as well as computational applications and also in understanding of the relevant reaction mechanisms in RTILs.

■ ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures; *pK_a* measured from each independent titration for benzenethiol; indicators used in this work and the corresponding *pK_a*s in ILs; UV–vis spectra for the representative measurements. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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