# Weakly Polar Aprotic Ionic Liquids Acting as Strong Dissociating Solvent: A Typical "Ionic Liquid Effect" Revealed by Accurate Measurement of Absolute pKa of Ylide Precursor Salts

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**Ⓢ** *Supporting Information*

**ABSTRACT:** Absolute $pK_a$s of selected salts with different counter-anions were measured with high precision in four aprotic ionic liquids (AILs), which enables a detailed examination of solvation effect of ILs on salts. Interestingly, the counter-anions of the ylide precursor salts, protic amine, and phenol salts of this study, though differing dramatically in size and electron dispersion, were found to have no effect on the respective $pK_a$s of the substrates. This indicates that the ionic species generated upon acidic dissociation of the salts in weakly polar AILs of low dielectric constant ($\varepsilon$: 10−15) are not ion-paired, or in other words, behave like "free ions" as if in strongly dissociating molecular solvents of high polarity (e.g., DMSO). This suggests that the widely assumed ion-pairing phenomenon, an issue of much debate, is not important in the AILs under our experimental conditions, presenting a typical "ionic-liquid effect" on the solvation of charged species in AILs.

As a rising mainstream solvent, ionic liquids (ILs), the so-called "designer's solvent", have sparked tremendous research interests during the past decade.[1] Compared with the rapid development of synthetic applications of ILs, the fundamental research on chemical transformations in ILs are severely lagged behind, however. This is in sharp contrast to the good understandings in molecular solution chemistry. As a consequence, some crucial information, such as detailed solvent properties, solvation behaviors of ILs, is not yet clear. Unlike molecular solvents, ILs are composed entirely of cations and anions, and thus, their solvation behaviors cannot be expected to be exactly the same as those found in molecular media. Indeed, ILs may show unique solvation effects under certain circumstances that are not likely to occur in molecular solvent. Though this so-called "ionic liquid effect" was observed in only a few cases until present,[2] it does provide a distinct chance to gain insight into the fundamental differences of solvation between these two conceptually diverse media under comparison. It is known that acid−base equilibria are closely associated with the polarity of solvent.[3] Thus, perturbation of solvent polarity may cause significant shift to the equilibrium, which can be directly "sensed" by measuring the equilibrium constant ($pK_a$). Therefore, acidity study has often bee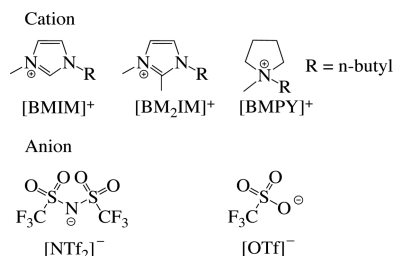n viewed as a very useful probe to reveal valuable information on the microscopic properties of solvent systems.[4] However, the research in this aspect had focused almost entirely on the conventional molecular solvent systems in the past, and hence, chances to disclose the governing factors in ILs with respect to their unique roles in solvation are actually much depressed. Although we have recently carried out a systematic study on the absolute $pK_a$s of several series of C−H acids,[5] O−H acids,[6] and S−H acids[2c] in RTILs (room temperature ILs), which indeed revealed important information regarding the solvation of the cation and anion of ILs, the previous works only covered neutral molecules, and the knowledge on the solvation effect of ILs on ionic substrates is yet very limited. Compared with the acidic dissociation processes of neutral substrates, ionic species are more complicated in that different degree of solvation of initial ionic substrates may result in various solvent solvated entities, such as free ions and ion pairs, depending on the polarity of the solvent.[3] The present work intends to find if there is anything different or interesting regarding the solvation in ILs.

Phosphonium ylides, derived from $\alpha$-substituted triphenylphosphonium cations by removal of the $\alpha$-proton,[7] are important reactive intermediates for C=C bond formation (Wittig reaction[8]). Due to their synthetic importance, the $pK_a$ scales of ylide precursor salts have been established in DMSO[9] and in a number of molecular solvent mixtures.[10] Similarly, the $\alpha$-proton of N-substituted pyridinium cations can be removed by relatively strong bases to form nitrogenium ylides.[11] In addition, ILs were also found to be attractive solvent systems for Wittig reactions, owing to easier separation of products and efficient reuse of ILs.[12] Notably, the compositions of the ylide precursor salts are similar to these of ILs formed from anions and cations, and in this regard, the acidity study on these "salts dissolved in liquid salts" may offer an ideal opportunity to understand how and to what extent the cations and anions of ILs interact with the ionic solutes.[13] In this work, we wish to, first, report the absolute $pK_a$ values of some frequently used ylide precursor salts in four common AILs, [BMIM][NTf₂], [BMPY][NTf₂], [BM₂IM][NTf₂], and [BMIM][OTf] (Scheme 1) and, second, address the interesting chemistry disclosed for IL solvation based on detailed analysis of the $pK_a$ data.
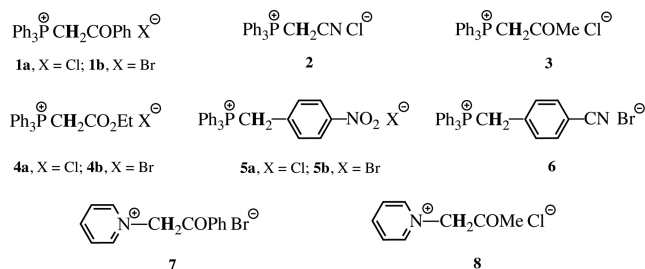
**Scheme 1. Cations and Anions of the ILs Used in This Study**





Figure 1. Correlation between pKₐs of triphenylphosphonium salts in [BMPY][NTf₂] with these in DMSO.

**Scheme 2. P-Substituted Triphenylphosphonium and N-Substituted Pyridinium Salts Used in This Work; the Acidic Hydrogens Are Indicated by Boldface Type**
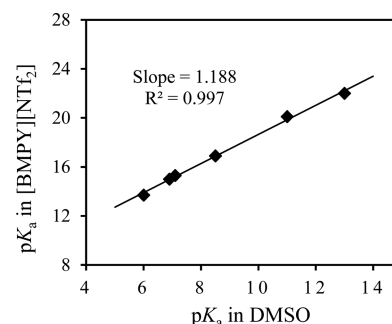


**Table 1. pKₐ Values of P-Substituted Triphenylphosphonium and N-Substituted Pyridinium Salts (Scheme 2) in ILs and a Molecular Solvent**

| salts | [BMPY] [NTf₂] | [BMIM] [NTf₂] | [BM₂IM] [NTf₂] | [BMIM] [OTf] | DMSO |
|---|---|---|---|---|---|
| 1a | 13.7 | 13.3 | 14.2 | 11.2 | 6.0 |
| 1b | 13.7 | 13.3 | | | |
| 2 | 15.0 | 14.8 | 15.4 | 12.5₅ | 6.9 |
| 3 | 15.3 | 15.0 | 15.8 | 12.7 | 7.1 |
| 4a | 16.9 | 16.9 | 17.5 | 14.2 | 8.5 |
| 4b | 16.9 | 16.9 | | | |
| 5a | 20.1 | 20.1 | 20.7 | 17.4 | 11.0 |
| 5b | 20.1 | 20.1 | | | |
| 6 | 22.0 | 21.9 | 22.6 | 19.3 | 13.0 |
| 7 | 18.1 | 17.7 | 18.6 | 15.5 | 10.7 |
| 8 | 19.7 (19.6₅ᶜ) | 19.4 | 20.2₅ | 17.2 | 11.8 |

ᵃIn pK units; standard deviation (SD): ≤±0.05 pK unit. ᵇReferences 9 and 11. ᶜValue in parentheses is for PyN⁺ CH₂COMe Br⁻.

The absolute pKₐ values of the ylide precursor salts in Scheme 2 (1a−8) were measured by UV−vis spectroscopic indicator overlapping method (SI).[5,6] The conjugated bases (ylides) of P-substituted triphenylphosphonium and N-substituted pyridinium salts were stable under the measurement conditions. Table 1 summarizes the measured pKₐ values of 1a−8 in ILs. It is worth mentioning that the AILs used in this work were scrupulously purified with water content less than 10 ppm (SI), and these pKₐ values were measured in high precision with standard deviation (SD) of ≤±0.05 pK units, superior to these obtained from electrochemical approaches.[14]

As can be seen from Table 1, the acidifying effect of triphenylphosphonium group is about $3.2 \times 10^4$ times (4.5 pK units) stronger than that of pyridinium group (1a and 7; 3 and 8) in all four ILs, probably due to a (p−d) π interaction between triphenylphosphonium group and the neighboring carbanion.[15] Although the salts are more acidic in DMSO than in ILs (Table

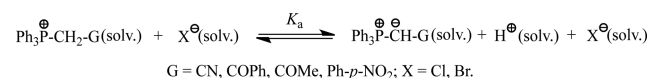1), the correlation between the pKₐs of salts (1a−6) in DMSO and ILs shows an excellent linearity with $R^2$ of 0.997 (Figure 1). This indicates that the absolute pKₐs measured in the ILs, like the acidities of carbon acids in DMSO that correlate well with these in the gas phase,[16] reflect the intrinsic order of C−H bond ionization.

Table 1 also shows that the pKₐ values of an individual salt in various ILs follow an order of [BM₂IM][NTf₂] > [BMPY]-[NTf₂] ≈ [BMIM][NTf₂] > [BMIM][OTf], which is consistent with our previous observation for the neutral C−H acids in these ILs.[5] Similar to previously observed,[2c,5,6] the anion of ILs plays a dominant role on the acidity of the substrate, which can be rationalized by comparing the size and electron density of oxygen and nitrogen in [OTf]⁻ and [NTf₂]⁻, respectively. As a consequence, a stronger solvation toward proton by [OTf]⁻ than [NTf₂]⁻ should be responsible for the considerable acidity difference of ~2.4 pK units, which corresponds to a differential solvation energy of 3.3 kcal mol⁻¹ toward proton. However, the cation moiety of the ILs has only limited influence on the pKₐ values of the substrates.

Interestingly, Table 1 also shows that, albeit bromide and chloride anion are quite different in size and basicity and they are much smaller than the anions of ILs, the halogen anion has practically no effect on the acidities of P-substituted triphenylphosphonium salts (compare entries 1a/1b, 4a/4b, and 5a/5b) and N-substituted pyridinium salts (8) in ILs. We also measured the acidities of several triphenylphosphonium salts with nitrate (NO₃⁻) as the counteranion (such as 1 and 4, when X = NO₃⁻). The measured acidity of the salt with nitrate is the same as that with chloride or bromide ion as counteranion. This suggests that the counter-anions must not be in the immediate vicinity of the phosphonium/pyridinium cation to affect the positive charge of the latter in these ILs; in other words, there is no specific ion pair formation under our experimental conditions. This may be contradictory to one's intuitive thought. The far enough separation of the solute cation and anion should most likely be caused by strong Coulombic interactions between the solute and IL ions in terms of strong ionic solvation (eq 1). Logically, this also says that the pKₐ in this work represents "free-ion" acidity as usually seen in strongly polar solvents like water and DMSO, rather than "ion-pair" acidity as in non- or weakly polar molecular media, a crucial criterion for thermodynamic parameter to be used as a standard quantity.

Dissociation equilibrium for ylide precursor salts in the ILs:

$$Ph_3\overset{\oplus}{P}\text{-}CH_2\text{-}G(solv.) + X^{\ominus}(solv.) \underset{}{\overset{K_a}{\rightleftarrows}} Ph_3\overset{\oplus}{P}\text{-}\overset{\ominus}{C}H\text{-}G(solv.) + H^{\oplus}(solv.) + X^{\ominus}(solv.)$$

G = CN, COPh, COMe, Ph-p-NO₂; X = Cl, Br.

To further test the validity of the above deduction, we next synthesized and measured the acidities of several protic amine salts (**9−11**) and para-substituted phenol salts (**12**) (Scheme 3)

**Scheme 3. Structure of Protic Amine and Phenol Salts; the Acidic Hydrogens Are Indicated by Boldface type**



X = Cl, NTf_2 and OTf



**12**
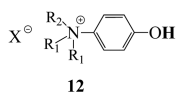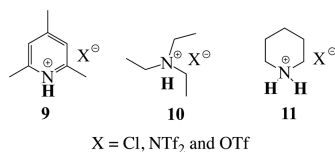
$R_1$= n-$C_8H_{17}$, $R_2$ = $CH_3$; X = I, $BAr^F_4$, where $Ar^F$ stands for 3,5-bis(trifluoromethyl)phenyl

**Table 2. $pK_a$ Values for the Protic Amine and Phenol Salts (Scheme 3) with Various Counteranion ($X^-$) in [BMIM][NTf_2] (SD $\leq \pm0.05$)**

| amine salts | X = Cl | X = NTf_2 | X = OTf |
|---|---|---|---|
| **9** | 12.9 | 13.0 | 12.9 |
| **10** | 16.4 | 16.4 | 16.3 |
| **11** | 16.4 | 16.4 | 16.4 |
| phenol salts | X = I | | X = $BAr^F_4$ |
| **12** | 20.5 | | 20.4 |

in IL [BMIM][NTf_2] (Table 2). As can be seen very clearly, the acidity of these salts is also independent of the counteranion $X^-$, regardless of the dramatic change of counter-anions in their size (cf. $Cl^-$ vs $NTf_2^-$), charge delocalization and binding ability (cf. $I^-$ vs $BAr_4^{F-}$). For instance, when the $X^-$ anion of **12** is changed from the relatively small and localized iodide to a much bulky and extensively delocalized borate anion, its acidity in [BMIM][NTf_2] remains basically the same (cf. Table 2, entry 4). This is in sharp contrast to the recent finding that the acidity of the phenol salt **12** is much more acidic with $BAr_4^{F-}$ as counteranion than with $I^-$ in a non- (or weakly) polar molecular solvent $CCl_4$, where ion-pairing is presumably dominant.[17] In other words, the present observation added a strong support to the "free ion" issue, i.e., the cation and anion of the solute salt in our IL must be far apart from each other rather than being ion-paired. It is worth noting that a similar phenomenon (i.e., a "free ion" status) was also found in the $pK_a$ measurement in DMSO,[17,18] a typical dipolar aprotic molecular solvent of high polarity ($\varepsilon = 46.5$[19]). The above suggests that, despite the apparently low overall polarity of aprotic IL as indexed by $\varepsilon$ (10−15),[20] the ILs in this study behave, nonetheless, like a strongly dissociating solvent, presumably by virtue of the strong solvating ability of its cation and anion, respectively, with the solute anion and cation, and hence provides an excellent example for the rarely seen "ionic liquid effect".

To sum up, in the present work 50 absolute $pK_a$ values of the ylide precursor salts (**1−8**), protic amine salts (**9−11**), and *para*-ammonium phenol salts (**12**) in several neat aprotic ILs were measured with high precision. Detailed examinations of the data show that the acidities of these organic salts are all independent of their counteranions. This implies that the solvated cations and

anions of the substrate salts in the weakly polar aprotic ILs applied in this work behave like "free ions" as if in strongly dissociating polar molecular media of high dielectric constant like DMSO, demonstrating a typical "ionic liquid effect" on the solvation of charged species. The present observation is clearly not in line with the ion association assumption in neat ILs proposed for solute salts in some previous literature.[21]

## ASSOCIATED CONTENT

**ⓢ Supporting Information**

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b02607.

Detailed $pK_a$ measurement procedures, indicators used in this work and their corresponding $pK_a$s in the ILs; UV−vis spectra for the representative measurements; synthesis and characterization of salts (PDF)

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**Notes**
The authors declare no competing financial interest.

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## REFERENCES

(1) (a) Tang, S.; Baker, G. A.; Zhao, H. *Chem. Soc. Rev.* **2012**, *41*, 4030. (b) Hallett, J. P.; Welton, T. *Chem. Rev.* **2011**, *111*, 3508. (c) Bara, J. E.; Camper, D. E.; Gin, D. L.; Noble, R. D. *Acc. Chem. Res.* **2010**, *43*, 152. (d) Pinkert, A.; Marsh, K. N.; Pang, S.; Staiger, M. P. *Chem. Rev.* **2009**, *109*, 6712. (e) Armand, M.; Endres, F.; MacFarlane, D. R.; Ohno, H.; Scrosati, B. *Nat. Mater.* **2009**, *8*, 621.

(2) (a) Newington, I.; Perez-Arlandis, J. M.; Welton, T. *Org. Lett.* **2007**, *9*, 5247. (b) Hallett, J. P.; Liotta, C. L.; Ranieri, G.; Welton, T. *J. Org. Chem.* **2009**, *74*, 1864. (c) Wang, Z.; Ji, P.; Li, X.; Cheng, J.-P. *Org. Lett.* **2014**, *16*, 5744.

(3) Reichardt, C.; Welton, T. *Solvents and Solvent Effects in Organic Chemistry*, 4th ed.; Wiley-VCH: Weinheim, 2011.

(4) Isaacs, N. *Physical Organic Chemistry*, 2nd ed.; Prentice Hall: London, 1996.

(5) Deng, H.; Li, X.; Yuan, C.; He, J.-Q.; Cheng, J.-P. *J. Org. Chem.* **2012**, *77*, 7291.

(6) Wang, Z.; Deng, H.; Li, X.; Ji, P.; Cheng, J.-P. *J. Org. Chem.* **2013**, *78*, 12487.

(7) (a) Lawrence, N. J. In *Preparation of Alkene: A Practical Approach*; Williams, J. M. J., Eds.; Oxford University Press: New York, 1996; Chapter 2, p 19. (b) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863. (c) Murphy, P. J.; Brennan. *Chem. Soc. Rev.* **1988**, *17*, 1. (d) Bestmann, H. J.; Vostrowsky, O. *Top. Curr. Chem.* **1983**, *109*, 85. (e) Boutagy, J.; Thomas, R. *Chem. Rev.* **1974**, *74*, 87.

(8) (a) Wittig, G.; Schöllkopf, U. *Chem. Ber.* **1954**, *87*, 1318. (b) Wittig, G.; Schöllkopf, U. *Chem. Ber.* **1955**, *88*, 1654.

(9) (a) Zhang, X.-M.; Bordwell, F. G. *J. Am. Chem. Soc.* **1994**, *116*, 968. (b) Zhang, X.-M.; Bordwell, F. G.; Bares, J. E.; Cheng, J.-P.; Petrie, B. C. *J. Org. Chem.* **1993**, *58*, 3051. (c) Zhang, X.-M.; Fry, A. J. *J. Org. Chem.* **1996**, *61*, 4101.

(10) For water−ethanol mixtures, see: (a) Fliszar, S.; Hudson, R. F.; Salvadori, G. *Helv. Chim. Acta* **1963**, *46*, 1580. (b) Aksnes, G.; Songstad, J. *Acta Chem. Scand.* **1964**, *18*, 655. (c) Johnson, A. W.; Amel, R. T. *Can. J. Chem.* **1968**, *46*, 461. For water−DMSO mixtures, see: (d) Moutiers, G.; Peng, Y. X.; Peignieux, A.; Pouet, M. J.; Terrier, F. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1287. (e) Bernasconi, C. F.; Fairchild, D. E.; Montanez, R. L.; Aleshi, P.; Zheng, H.; Lorance, E. *J. Org. Chem.* **2005**, *70*, 7721. For $CH_2Cl_2$−EtOAc mixture, see: (f) Issleib, K.; Lindner, R. *Justus Leibigs Ann. Chem.* **1967**, *707*, 120.

(11) Zhang, X.-M.; Bordwell, F. G.; Van Der Puy, M.; Fried, H. E. *J. Org. Chem.* **1993**, *58*, 3060.

(12) LeBoulaire, V.; Gree, R. *Chem. Commun.* **2000**, 2195.

(13) Lui, M. Y.; Crowhurst, L.; Hallett, J. P.; Hunt, P. A.; Niedermeyer, H.; Welton, T. *Chem. Sci.* **2011**, *2*, 1491.

(14) (a) Barhdadi, R.; Troupel, M.; Comminges, C.; Laurent, M.; Doherty, A. *J. Phys. Chem. B* **2012**, *116*, 277. (b) Millán, D.; Rojas, M.; Santos, J. G.; Morales, J.; Isaacs, M.; Diaz, C.; Pavez, P. *J. Phys. Chem. B* **2014**, *118*, 4412.

(15) Stephens, F. S. *J. Chem. Soc.* **1965**, 5640. (b) Stephens, F. S. *J. Chem. Soc.* **1965**, 5658.

(16) Taft, R. W.; Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 463.

(17) Samet, M.; Buhle, J.; Zhou, Y.; Kass, S. R. *J. Am. Chem. Soc.* **2015**, *137*, 4678.

(18) Bordwell, F. G.; Branca, J. C.; Hughes, D. L.; Olmstead, W. N. *J. Org. Chem.* **1980**, *45*, 3305.

(19) Casteel, J. F.; Sears, P. G. *J. Chem. Eng. Data* **1974**, *19*, 196.

(20) (a) Wakai, C.; Oleinikova, A.; Ott, M.; Weingärtner, H. *J. Phys. Chem. B* **2005**, *109*, 17028. (b) Huang, M.; Jiang, Y.; Sasisanker, P.; Driver, G. W.; Weingärtner, H. *J. Chem. Eng. Data* **2011**, *56*, 1494.

(21) For the ion pair issues in neat ILs, see a recent review: Kirchner, B.; Malberg, F.; Firaha, D. S.; Hollóczki, O. *J. Phys.: Condens. Matter* **2015**, *27*, 463002 and the references cited therein.