JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

Is Amine a Stronger Base in Ionic Liquid Than in Common Molecular Solvent? An Accurate Basicity Scale of Amines

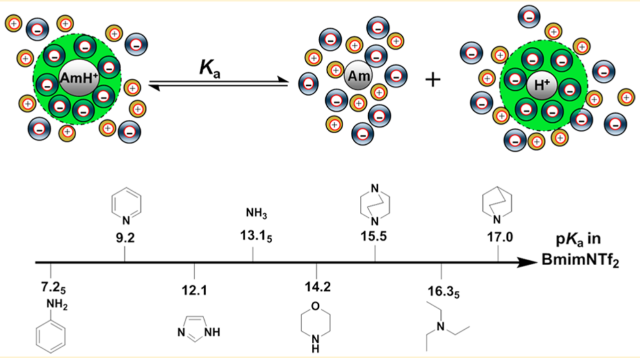
Chong Mao,[†] Zhen Wang,[†] Pengju Ji,*[,†] and Jin-Pei Cheng*[,†,‡]

[†]Center of Basic Molecular Science, Department of Chemistry, Tsinghua University, Beijing 100084, China

[‡]State Key Laboratory of Elemento-organic Chemistry, Collaborative Innovation Center of Chemical Science and Engineering, Nankai University, Tianjin 300071, China

S *Supporting Information*

ABSTRACT: The equilibrium basicities of 21 frequently used amines in two room-temperature ionic liquids (RTILs) were measured precisely. The standard deviation was much superior to that sparsely reported elsewhere. The data comparisons revealed that amines are stronger bases in ionic ligquids than in DMSO and water but weaker base than in acetonitrile (AN). Interestingly, regression analyses demonstrate that the basicity scales obtained in two RTILs correlate well with that in AN but not with those in water and DMSO.



The acidic dissociation constant (pK_a[1]) of organic compounds plays significant roles in the development of modern physical organic chemistry.[2] Accurate and reliable acidity scales[3] are indispensible tools for understanding organic reactions and are often key to elucidating reaction mechanism[4] and optimizing synthetic procedures and separation processes.[5] Additionally, pK_a's coupled with redox potentials provide a convenient way to evaluate homolytic bond dissociation energies (BDEs).[6] However, it is noted that related research in this regard in the past focused almost entirely on the phenomena in conventional molecular solvents or the gas phase but little in the rising mainstream medium system, the room-temperature ionic liquids (RTILs). The RTILs, which are solely composed of ions, have been applied as alternative solvents for a wide range of reactions in recent years.[7] Solvation by ionic liquids (ILs) surely cannot be expected to be the same as that by molecular solvents. Indeed, it was demonstrated in a number of studies that ILs exhibited specific solvation effects.[8]

Amines are frequently used as reactants or bases in organic synthesis[9] and have a history of applications in chemistry.[10] Because of their general importance, the basicity scales of amines have been intensively studied in common molecular solvents like water, acetonitrile (AN), DMSO, etc.[11] These scales reveal that the basicity of amine is very sensitive toward the media.[12] Recently, a few groups have also carried out studies on the basicity of amines in ILs, but they encountered much greater challenges compared with the studies in molecular solvents. For instance, Noto et al. reported the first investigation on the strength of some aliphatic amines in ILs using *p*-nitrophenol as the indicator.[13] Siani et al., on the other hand, measured the equilibrium constants of ion-pair formation for a few pyridines with trifluoroacetic acid in ILs.[14] In these works, the derived basicity was reported as a *relative* value because the pK_a of the indicator acid in ILs was unknown. As a consequence, the data cannot directly reflect the heterolytic bond dissociation energies in ILs and, therefore, cannot be used to compare the bond strength in IL with those in molecular media. Moreover, the span of the obtained scales was narrow (1−2 pK units or less) due to the use of a single indicator, so it would not be suitable for regression analysis either. It is also noted that the ion-pair effect was not deliberately avoided, and thus, the accuracy of the data could not be established. In addition, molecular solvents such as dichloromethane and dioxane were added to ILs. Though this was necessary in the respective measurements, the experiment conditions cannot be regarded as standard. More recently, Doherty[15] and then Pavez and co-workers[16] reported the first measurement of absolute pK_a values of several amines in neat ILs by an electrochemical method. This method provided a convenient approach to the acidity in ILs, which is obviously more useful and significant. However, the uncertainty was large (SD = ± 0.4−1.0 pK units), and whether the method can be used for substrates other than N−H compounds is in doubt.

In our previous work, we reported a general standard method for precise measurement of pK_a's (SD ≤ ± 0.05 pK unit) in neat RTILs. The acidity scales for series of C−H,[17] O−H,[18] and S−H acids[19] were consecutively established, which were proved to be intrinsic in nature and free from ion-pairing

Received: May 29, 2015
Published: July 28, 2015

DOI: 10.1021/acs.joc.5b01200
J. Org. Chem. 2015, 80, 8384−8389

complication. Broad pK coverage (up to 19 pK units) has been achieved by using the indicator overlapping strategy.[17−19]

Acidic dissociation of the conjugated acid of amine (Scheme 1a), the focus of the present work, is different from our earlier studies in that the substrates here are positively charged species instead of neutral ones (Scheme 1b). Investigations on such types of dissociation may broaden our understanding of the solvation behavior in ILs. In addition, the acidity scale of amines may serve as a good model to facilitate the rational design of other protic ILs which exhibited many important applications such as electrolyte in lithium ion batteries,[20] carbon dioxide capture,[21] etc. In this respect, the acidity data of high precision is critical.

Scheme 1. Acidic Dissociation Equilibrium for (a) the Conjugated Acid (AmH^+) of Amine and (b) Previously Studied Neutral Substrate

$$\mathrm{AmH}^{\oplus} \xrightleftharpoons{K_{eq}} \mathrm{Am} + \mathrm{H}^{\oplus} \qquad \text{a)}$$

$$K_a = \frac{[\mathrm{Am}][\mathrm{H}^{\oplus}]}{[\mathrm{AmH}^{\oplus}]} \qquad K_b = \frac{[\mathrm{AmH}^{\oplus}]}{[\mathrm{Am}][\mathrm{H}^{\oplus}]}$$

Am = amine or ammonia

$$\mathrm{HA} \xrightleftharpoons{K_{eq}} \mathrm{A}^{\ominus} + \mathrm{H}^{\oplus} \qquad \text{b)}$$

HA = carbon acids, benzoic acids, benzenethiols

Here, we report the pK_a values of 21 amines in two standard RTILs, $BmimNTf_2$ and $BmpyNTf_2$ ($Bmim^+$ = 1-butyl-3-methylimidazolium; $Bmpy^+$ = *N*-butyl-*N*-methylpyrrolidinium).

The general procedure was introduced previously,[17−19] nine carbon acids with known pK_a values in two standard ILs, $BmimNTf_2$ and $BmpyNTf_2$[17] were rationally selected as indicators for the measurement (Table S1). To avoid possible complications, all of the substrates were prepared from triflimide acid ($HNTf_2$) and the corresponding amines or ammonia (Scheme 2). It is worth noting that most of these amine triflimide salts (AmH^+ NTf_2^-) are liquid at room temperature or solid with melting points below 100 °C and, hence, should be regarded as protic Brønsted ILs.

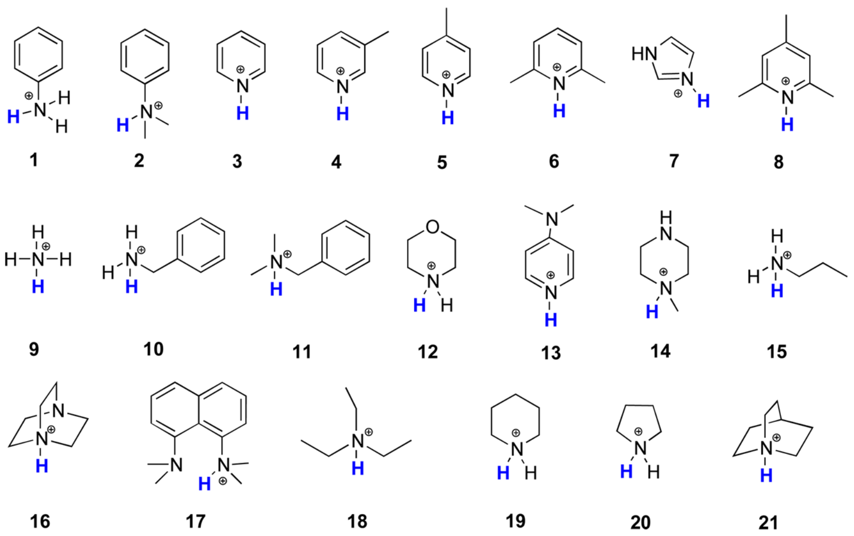
Table 1 lists the pK_a values of the protonated amines measured in this work in both ILs, along with previous literature data. As can be seen, this pK_a scale is more comprehensive and the data are more accurate than others in ILs (SI, Table S2, SD$\leq \pm 0.05$ vs 0.4−1.0[15,16]). Table 1 further revealed that the electrochemically derived data are obviously higher (by 0.4−2.6 pK units) than the present spectroscopically measured pK_as of the corresponding amines. This is not surprising since the electrochemical approach, while convenient, also sacrifices the accuracy of the measurement because the acid−base interaction in those systems (solvent and amine) was far from equilibrium and the amine concentration was too high to assume the activity coefficients to be unity.

The most interesting feature of the data in Table 1 is that it provides a direct comparison of the amine basicity among both ILs and the conventional molecular solvents. As a consequence, it enables us to partially answer the titled question. As immediately noted, the basicity order of amines is, in $H_2O \approx$ in DMSO < in ILs < in AN.

This order may not be anticipated from their respective polarity index (ε), which is H_2O (78.5) > DMSO (48.9) > AN (37.5) ≫ ILs (11.5 and ∼15, for $BmimNTf_2$ and $BmpyNTf_2$, respectively).[38,39] However, it is consistent with our earlier observations for similar comparisons of the C−H, O−H, and S−H acidities in molecular media with those in standard ILs which are imidazolium or pyrrolidinium based ILs with NTf_2^- or OTf^- as the anion.[17−19]

As also noted from Table 1, the pK_a values of the protonated amines in $BmimNTf_2$ are somewhat lower than those in $BmpyNTf_2$ in general, indicating the amine basicity in $BmimNTf_2$ is weaker than in $BmpyNTf_2$. This should be associated with a better stabilization of the amine by the C-2 proton of $Bmim^+$ through hydrogen bonding. A comparison of the acidity difference between these two ILs (∼0.30 pK units in average) in Table 1 with those in our earlier reports reveals that the pK_a difference found here for these amines (**1**−**21**) is smaller than those for benzoic acid[18] (ΔpK_a^{avg} = 1.12) and benzenethiols[19] (ΔpK_a^{avg} = 0.48). This can be understood on the basis of the C-2 hydrogen bonding stabilization by the

Scheme 2. Structures of Aminium and Ammonium Involved in This Work



DOI: 10.1021/acs.joc.5b01200
J. Org. Chem. 2015, 80, 8384−8389

Table 1. pK_a Values of Amine and Ammonia in RTILs and Molecular Solvents

amine	pK_a **BmimNTf$_2$**^{a}	pK_a BmpyNTf$_2$^{a}	pK_a (H_2O)	pK_a (DMSO)	pK_a (AN)	ref data BmimNTf$_2$	ref data BmpyNTf$_2$
1	7.2_5	7.6	4.6^b	3.6^i	10.6^o	8.1^x	
2	8.6	9.2	5.1^c	2.5^j	11.4^p	9.1^x	
3	9.2	10.0	5.2^b	3.4^i	12.3^o	10.5 ± 1^y	10.4 ± 1^y
4	10.1	10.5	5.6^b		13.7^q	11.2 ± 0.4^y	12.3^x
5	10.7	11.2	6.0^b	4.1^k	14.5^q		
6	11.7	12.3	6.7^b	4.5^l	14.1^p	13.2 ± 0.4^y	12.9 ± 1^y
7	12.1	12.6	7.0^d	6.4^m	13.8^r		
8	12.9	13.0	7.4^b		15.0^p	15.2 ± 0.4^y	15.2 ± 1^y
9	13.1_5	13.4	9.2^b	10.5^i	16.5^o		
10	13.5	13.8	9.5^e	10.2^m	16.8^o		
11	14.2	14.4	9.0^e	7.6^n	16.6^s		
12	14.2	14.4	8.1^b	9.2^m	16.6^o	16.6^x	16.9^x
13	15.5	15.4	9.9^f		17.7^t		
14	15.4	15.4	$9.8_5{}^e$		18.0^u		
15	15.5	15.6	$10.7_5{}^e$	11.1^i	18.0^v		
16	15.5	15.8	8.8^d	8.9^g			
17	16.0	16.0	12.0^g	7.5^g	18.6^p		
18	16.3_5	16.6	10.7^d	9.0^i	18.8^p	18.9^x	18.8^x
19	16.4	16.6	11.2^b	10.9^m	18.9^o	18.4^x	19.2^x
20	16.6	16.8	$11.3_5{}^e$	11.1^m	19.6^o		
21	17.0	17.1_5	11.4^h	9.8^g	19.5^w		

[a] SD ≤ ±0.05. [b] Reference 22. [c] Reference 11a. [d] Reference 23;. [e] Reference 24. [f] Reference 25. [g] Reference 26. [h] Reference 27. [i] Reference 11f. [j] Reference 11e. [k] Reference 28. [l] Reference 29. [m] Reference 30. [n] Reference 31. [o] Reference 11d. [p] Reference 11b. [q] Reference 32. [r] Reference 33. [s] Reference 34. [t] Reference 35. [u] Reference 11c. [v] Reference 36. [w] Reference 37. [x] Reference 16. [y] Reference 15.

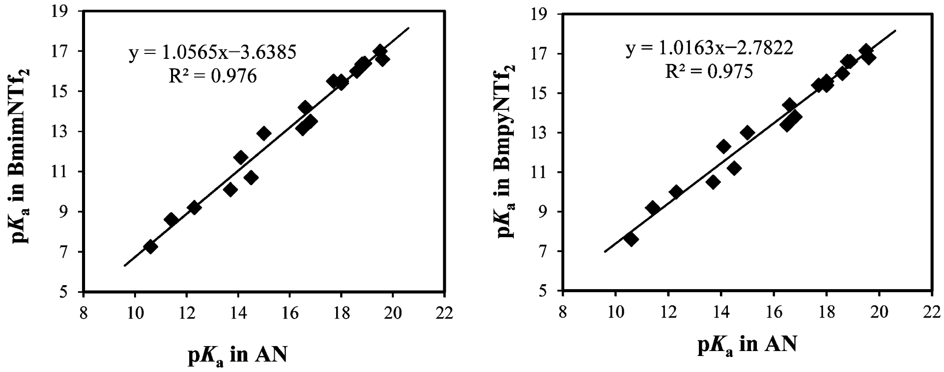


Figure 1. Correlations between measured amine pK_a's in ILs with those in AN.

Bmim$^+$ cation toward benzoate and thiolate anions, indicating that the cation of ILs can exert quite different influence on various types of acidic dissociation equilibrium in Scheme 1.

It is well-known that the counteranion of ILs can significantly affect the acidity of compound, largely due to the stronger solvation of proton, which plays a more pronounced role than the cation stabilization effect in promoting acidic dissociation.[13] Similar to the phenomenon observed previously, pyridine (**3**) is about 10 times more acidic in BmimOTf (exptl pK_a = 8.3) than in BmimNTf$_2$. It is not difficult to understand that the acidity difference should be ascribed to a more localized negative charge and smaller size of OTf$^-$ compared to NTf$_2$$^-$, both leading to a stronger salvation of proton.

The linear correlation of acidities of a series of compounds between various solvents may provide information on the universal or specific solvation pattern in different media. The correlations between the pK_a's of amines determined in ILs and these in molecular solvents were performed. Interestingly, the correlation between pK_as in BmimNTf$_2$ and BmpyNTf$_2$ with those in AN provides a quite good linear relationship with R^2 = 0.976 and 0.975, respectively (Figure 1), while the pK_as in the ILs are poorly correlated with those in DMSO (R^2 = 0.726) and water (R^2 = 0.903) (Supporting Information, Figure S9). In fact, the linear correlations among the pK_a between these molecular solvents are also poor (Supporting Information, Figure S10). Traditionally, both AN and DMSO are labeled as dipolar aprotic solvent, and have a similar dipole moment and Dimroth−Reichardt's E_T^{30} value.[12] However, compared with DMSO, the lone pair in the nitrogen atom of AN is sp hybridized; therefore, the ability of accepting hydrogen is weakened. Indeed, this can be reflected from the comparison of the Kamlet−Taft solvent parameter β value for DMSO (0.76) and AN (0.40),[12] and mainly due to this, more specifically, AN and DMSO are also considered as typical protophobic and protophilic aprotic solvents, respectively. Though correlations between the acidities of compounds with similar structure, such as benzoic acid derivatives, etc., may provide fairly linear relationship, normally poor correlations are observed for various types of compounds with different structures in AN and DMSO (Supporting Information).

Likewise, the β values of $BmimNTf_2$ and $BmpyNTf_2$ are 0.24 and 0.25, respectively,[39] which indicate that, like AN, they also have a limited hydrogen-bond-accepting ability. As mentioned previously, acidic dissociation of these protic amine salts is different from previously studied cases in that it produces a proton and a neutral amine with very different proton-accepting or -donating abilities based closely on individual amine structures (Scheme 1). Therefore, it can be expected that the sensitivity of ILs solvation toward the structure variation of amines during the acidic dissociation process should not be as strong as that for DMSO but similar to that of AN.

In summary, the equilibrium basicities/acidities of a broad range of commonly used amines were measured in two standard ILs with high precision. These thermodynamic values revealed that amines are stronger base in ILs than in DMSO and water but weaker base than in acetonitrile (AN). Regression analyses showed that the pK_a values of these amines in ILs are linearly correlated with those in AN but not with those in DMSO and water; therefore, the collective solvation effect on the dissociation equilibrium of these compounds in ILs is similar to that in AN. We envisage that this highly accurate acidity scale of amines may serve as a reference in the development of computational methodology in ILs and, more importantly, as a guideline for the rational design of nitrogen-containing functionalized ILs.

■ EXPERIMENTAL SECTION

Materials. All of the chemicals were purchased from commercially available sources and used directly except as otherwise noted. Solid compounds used for synthesis were carefully recrystallized, and the liquid ones were distilled before use. All ionic liquids (ILs) were synthesized and purified on the basis of literature procedures.[40] In addition, ILs were dried in vacuo at 70 °C for 5 h before use and were stored in desiccators under argon. The water contents of ILs are less than 10 ppm, which was determined by the Karl Fischer titration. The indicators used were synthesized and characterized by known methods.[41−43]

pK_a Measurement. The principle and measurement procedures were similar to those previously reported.[17] In brief, taking a typical run as an example, the pK_a measurement began by degassing and weighing the UV cell, and then 1.5 mL of IL and 40 mg of base were added into the cell. An indicator with known pK_a was added in a dropwise manner after the cell was weighed again, and a baseline was recorded on the UV instrument. Monitor was performed with a UV instrument, after the base was fully consumed by normally 6−8 drops of the indicator, and an excess amount of indicator solution was added. During the titration, the spectrum and weight for each addition was recorded. Next, the target acid of interest was added in several portions. The weight of the UV cell and the corresponding spectrum were also recorded upon each addition. The corresponding pK_a was obtained with the data derived from the change of absorbance and the amount of acid added.

Synthesis and Characterization of Amine Salts. General synthetic procedure: to a stirred solution of amine compound (5 mmol) in 25 mL of methanol was added dropwise an equivalent molar amount of $HNTf_2$ in 15 mL of methanol. The reaction mixture was refluxed for 5 h and then cooled to ambient temperature. The solvent was removed in vacuo, and the residue was purified by recrystallization (PE/DCM) or dried under vacuum. These salts were stored in the glovebox due to their very hygroscopic property. The NMR spectra of amine salts were recorded on a 400 MHz spectrometer. HRMS spectra were recorded on an Orbitrap analyzer.

*Aniline·HNTf₂ (**1**):* yield 89% (1.87 g); white solid; mp 74−75 °C; ^{1}H NMR (400 MHz, D_2O) δ 7.39−7.47 (m, 5H), 7.31 (d, 3H); ^{13}C NMR (100 MHz, D_2O) δ 130.1, 129.9, 129.1, 122.8, 119.2 (q, J_{C-F} = 321.0 Hz); HRMS (ESI$^+$) calcd for $[C_6H_8N]^+$ 94.0651, found 94.0656; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9180.

*N,N-Dimethylaniline·HNTf₂ (**2**):* yield 90% (1.81 g); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.33 (d, 6H), 7.55−7.59 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 131.23, 131.16, 120.1, 119.9 (q, J_{C-F} = 320.0 Hz), 48.2; HRMS (ESI$^+$) calcd for $[C_8H_{12}N]^+$ 122.0964, found 122.0964; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9179.

*Pyridine·HNTf₂ (**3**):* yield 91% (1.64 g); white solid; mp 57−58 °C; ^{1}H NMR (400 MHz, D_2O) δ 8.83 (d, 2H), 8.65−8.69 (m, 1H), 8.10−8.14 (m, 2H); ^{13}C NMR (100 MHz, D_2O) δ 147.0, 141.2, 127.4, 119.2 (q, J_{C-F} = 321.0 Hz); HRMS (ESI$^+$) calcd for $[C_5H_6N]^+$ 80.0495, found 80.0500; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9178.

*3-Picoline·HNTf₂ (**4**):* yield 88% (1.64 g); white solid; mp 60−61 °C; ^{1}H NMR (400 MHz, D_2O) δ 8.64 (s, 1H), 8.62 (d, 1H), 8.49 (d, 1H), 7.97−8.00 (m, 1H), 2.58 (s, 3H); ^{13}C NMR (100 MHz, D_2O) δ 147.6, 140.6, 139.1, 138.1, 126.7, 119.2 (q, J_{C-F} = 320.4 Hz), 17.6; HRMS (ESI$^+$) calcd for $[C_6H_8N]^+$ 94.0651, found 94.0655; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9181.

*4-Picoline·HNTf₂ (**5**):* yield 88% (1.66 g); white solid; mp 76−77 °C; ^{1}H NMR (400 MHz, D_2O) δ 8.62 (d, 2H), 7.92 (d, 2H), 2.69 (s, 3H); ^{13}C NMR (100 MHz, D_2O) δ 161.7, 140.0, 127.7, 119.1 (q, J_{C-F} = 319.9 Hz), 21.5; HRMS (ESI$^+$) calcd for $[C_6H_8N]^+$ 94.0651, found 94.0655; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9179.

*2,6-Lutidine·HNTf₂ (**6**):* yield 85% (1.65 g); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.90 (s, 1H), 8.32 (t, 1H), 7.67 (d, 2H), 2.79 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4, 146.7, 125.2, 119.6 (q, J_{C-F} = 320.3 Hz), 19.3; HRMS (ESI$^+$) calcd for $[C_7H_{10}N]^+$ 108.0808, found 108.0809; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9179.

*Imidazole·HNTf₂ (**7**):* yield 85% (1.48 g); white solid; mp 73−74 °C; ^{1}H NMR (400 MHz, D_2O) δ 8.71 (s, 1H), 7.50 (s, 2H); ^{13}C NMR (100 MHz, D_2O) δ 133.4, 124.0, 119.3 (q, J_{C-F} = 319.2 Hz), 119.0; HRMS (ESI$^+$) calcd for $[C_3H_5N_2]^+$ 69.0447, found 69.045 3; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9180.

*2,4,6-Collidine·HNTf₂ (**8**):* yield 87% (1.75g); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 2H), 2.71 (s, 6H), 2.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 152.5, 125.8, 119.8 (q, J_{C-F} = 321.2 Hz), 22.1, 19.3; HRMS (ESI$^+$) calcd for $[C_8H_{12}N]^+$ 122.0964, found 122.0964; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9178.

*Ammonia·HNTf₂ (**9**):* yield 95% (1.42 g); white solid; mp 183−184 °C; ^{13}C NMR (100 MHz, D_2O) δ 119.3 (q, J_{C-F} = 319.4 Hz); HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9178.

*Benzylamine·HNTf₂ (**10**):* yield 90% (1.75 g); white solid; mp 98−99 °C; ^{1}H NMR (400 MHz, D_2O) δ 7.40−7.47 (m, 5H), 4.70 (s, 3H), 4.13 (s, 2H); ^{13}C NMR (100 MHz, D_2O) δ 132.6, 129.2, 128.8, 119.3 (q, J_{C-F} = 320.1 Hz), 43.2; HRMS (ESI$^+$) calcd for $[C_7H_{10}N]^+$ 108.0808, found 108.0810; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9179.

*N,N-Dimethylbenzylamine·HNTf₂ (**11**):* yield 89% (1.85 g); white solid; mp 51−52 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.42−7.52 (m, 5H), 4.24 (d, 2H), 2.87 (d, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.0, 130.9, 129.8, 127.9, 119.8 (q, J_{C-F} = 321.0 Hz), 62.4, 43.2; HRMS (ESI$^+$) calcd for $[C_9H_{14}N]^+$ 136.1121, found 136.1119; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9179.

*Morpholine·HNTf₂ (**12**):* yield 89% (1.63 g); white solid; mp 63−64 °C; ^{1}H NMR (400 MHz, D_2O) δ 4.70 (s, 2H), 3.90−3.92 (m, 4H), 3.24−3.27 (m, 4H); ^{13}C NMR (100 MHz, D_2O) δ 119.3 (q, J_{C-F} = 318.4 Hz), 63.7, 43.2; HRMS (ESI$^+$) calcd for $[C_4H_{10}NO]^+$88.0757, found 88.0760; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9182.

*DMAP·HNTf₂ (**13**):* yield 91% (1.73 g); white solid; mp 109−110 °C; ^{1}H NMR (400 MHz, CD_3CN) δ 7.96 (d, 2H), 6.84 (d, 2H), 3.18 (s, 6H); ^{13}C NMR (100 MHz, CD_3CN) δ 158.7, 139.5, 121.0 (q, 333.29 Hz), 108.0, 40.6; HRMS (ESI$^+$) calcd for $[C_5H_{13}N_2]^+$ 101.1073, found 101.1075; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9179.

DOI: 10.1021/acs.joc.5b01200
J. Org. Chem. 2015, 80, 8384−8389

N-Methylpiperazine·HNTf$_2$ ***(14)***: yield 87% (1.66 g); white solid; mp 80−81 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 3.18−3.21 (m, 4H), 2.68 (s, 4H), 2.39 (s, 4H); ^{13}C NMR (100 MHz, CD_3OD) δ 121.2 (q, J_{C-F} = 322.9 Hz), 52.8, 45.8, 44.8; HRMS (ESI$^+$) calcd for $[C_5H_{13}N_2]^+$ 101.1073, found 101.1074; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9179.

Butylamine·HNTf$_2$ ***(15)***: yield 92% (1.63 g); colorless liquid; ^{1}H NMR (400 MHz, CD_3CN) δ 5.77 (s, 3H), 2.88−2.92 (m, 2H), 1.54−1.61 (m, 2H), 1.31−1.41 (m, 2H), 0.95 (t, 3H); ^{13}C NMR (100 MHz, CD_3CN) δ 120.9 (q, J_{C-F} = 316.8 Hz), 41.1, 30.1, 20.2, 13.7; HRMS (ESI$^+$) calcd for $[C_4H_{12}N]^+$ 74.0964, found 74.0969; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9177.

DABCO·HNTf$_2$ ***(16)***: yield 89% (1.75 g); white solid; mp 148−149 °C; ^{1}H NMR (400 MHz, CD_3CN) δ 3.11 (s, 12H); ^{13}C NMR (100 MHz, CD_3CN) δ 120.9 (q, J_{C-F} = 321.3 Hz), 45.6; HRMS (ESI$^+$) calcd for $[C_6H_{13}N_2]^+$ 113.1073, found 113.1074; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9178.

Proton Sponge·HNTf$_2$ ***(17)***: yield 83% (2.05 g); white solid; mp 131−132 °C; ^{1}H NMR (400 MHz, CD_3CN) δ 8.06 (d, 2H), 7.90 (d, 2H), 7.73 (t, 2H), 3.11 (d, 12 H); ^{13}C NMR (100 MHz, CD_3CN) δ 144.3, 135.7, 129.8, 127.3, 121.4, 120.1 (q, J_{C-F} = 321.0 Hz), 118.5, 46.7; HRMS (ESI$^+$) calcd for $[C_{14}H_{19}N_2]^+$ 215.1543, found 215.1538; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9180.

Triethylamine·HNTf$_2$ ***(18)***: yield 95% (1.81 g); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (s, 1H), 3.18−3.24 (m, 6H), 1.36 (t, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 119.8 (q, J_{C-F} = 321.0 Hz), 47.4, 8.7; HRMS (ESI$^+$) calcd for $[C_6H_{16}N]^+$ 102.1277, found 102.1280; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9180.

Piperidine·HNTf$_2$ ***(19)***: yield 94% (1.72 g); colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.63 (s, 2H), 3.22 (t, 4H), 1.81−1.87 (m, 4H), 1.69−1.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 119.6 (q, J_{C-F} = 320.9 Hz), 46.0, 22.3, 21.8; HRMS (ESI$^+$) calcd for $[C_5H_{12}N]^+$ 86.0964, found 86.0972; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9178.

Pyrrolidine·HNTf$_2$ ***(20)***: yield 95% (1.67 g); colorless liquid; ^{1}H NMR (400 MHz, D_2O) δ 3.35 (t, 4H), 2.02−2.09 (m, 4H); ^{13}C NMR (100 MHz, D_2O) δ 119.3 (q, J_{C-F} = 322.6 Hz), 45.6, 23.6; HRMS (ESI$^+$) calcd for $[C_4H_{10}N]^+$ 72.0808, found 72.0814; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9179.

Quinuclidine·HNTf$_2$ ***(21)***: yield 90% (1.76 g); white solid; mp 146−147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 3.32 (t, 6H), 2.17−2.22 (m, 1H), 1.91−1.96 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 119.8 (q, J_{C-F} = 318.7 Hz), 47.6, 22.9, 19.1; HRMS (ESI$^+$) calcd for $[C_7H_{14}N]^+$ 112.1121, found 112.1122; HRMS (ESI$^-$) calcd for $[C_2F_6NO_4S_2]^-$ 279.9178, found 279.9178.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01200.

> pK_a values of the indicators used in this work, UV−vis and NMR spectra, and diagrams of additional regression analyses (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: jipengju@mail.tsinghua.edu.cn.
*E-mail: jinpei_cheng@mail.tsinghua.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for financial grants from the National Natural Science Foundation of China (No. 21390401) and the Ministry of Education (No. 20131080083). We also acknowledge funding support from Tsinghua University. P.J. thanks the China Postdoctoral Science Foundation for Postdoctoral funding (No. 2014M550705).

■ REFERENCES

(1) (a) King, E. J. *Acid−Base Equilibria*; Pergamon Press: New York, 1965. (b) Bell, R. P. *The Proton in Chemistry*, 2nd ed.; Cornell University Press: Ithaca, NY, 1973.

(2) (a) Hammett, L. P. *Chem. Rev.* **1935**, *17*, 125−136. (b) Brønsted, J. N. *Chem. Rev.* **1928**, *5*, 231−338. (c) Taft, R. W. *Steric Effects in Organic Chemistry*; Newman, M. S., Ed.; Wiley: New York, 1956. (d) Hammett, L. P. *Physical Organic Chemistry*, 2nd ed.; McGraw-Hill: New York, 1970.

(3) (a) Serjeant, E. P.; Dempsey, B. *Ionisation Constants of Organic Acids in Aqueous Solution*; Pergamon Press: New York, 1979. (b) Streitwieser, A. *J. Org. Chem.* **2009**, *74*, 4433−4446 and references cited therein. (c) Bordwell, F. G.; Zhang, X.-M. *Acc. Chem. Res.* **1993**, *26*, 510−517. (d) Kutt, A.; Leito, I.; Kaljurand, I.; Soovali, L.; Vlasov, V. M.; Yagupolskii, L. M.; Koppel, I. A. *J. Org. Chem.* **2006**, *71*, 2829−2838.

(4) (a) Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw-Hill: New York, 1969. (b) Williams, A. *Free Energy Relationships in Organic and Bio-Organic Chemistry*; RSC Publishing: Cambridge, UK, 2003.

(5) Atherton, J. H.; Carpenter, K. J. *Process Development: Physicochemical Concepts*; Oxford University Press: Oxford, 2009.

(6) (a) Bordwell, F. G.; Cheng, J.-P.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 1229−1231. (b) Bordwell, F. G.; Cheng, J.-P.; Seyedrezai, S. E.; Wilson, C. A. *J. Am. Chem. Soc.* **1988**, *110*, 8178−8183. (c) Bordwell, F. G.; Cheng, J.-P. *J. Am. Chem. Soc.* **1991**, *113*, 1736−1743. (d) Bordwell, F. G.; Cheng, J.-P.; Ji, G.; Satish, A. V.; Zhang, X.-M. *J. Am. Chem. Soc.* **1991**, *113*, 9790−9795. (e) Bordwell, F. G.; Zhang, X.-M.; Cheng, J.-P. *J. Org. Chem.* **1991**, *56*, 3216−3219.

(7) (a) Sheldon, R. *Chem. Commun.* **2001**, 2399−2407. (b) Rogers, R. D.; Seddon, K. R. *Science* **2003**, *302*, 792−793. (c) van Rantwijk, F.; Sheldon, R. A. *Chem. Rev.* **2007**, *107*, 2757−2785. (d) Wasserscheid, P. In *Ionic Liquids in Synthesis*; Welton, T., Ed.; Wiley-VCH: Weinheim, 2008. (e) Armand, M.; Endres, F.; MacFarlane, D. R.; Ohno, H.; Scrosati, B. *Nat. Mater.* **2009**, *8*, 621−629. (f) Le Bideau, J.; Viau, L.; Vioux, A. *Chem. Soc. Rev.* **2011**, *40*, 907−925.

(8) (a) Dell'Anna, M. M.; Gallo, V.; Mastrorilli, P.; Nobile, C. F.; Romanazzi, G.; Suranna, G. P. *Chem. Commun.* **2002**, 434−435. (b) McLachlan, F.; Mathews, J. C.; Smith, P. J.; Welton, T. *Organometallics* **2003**, *22*, 5350−5357. (c) Newington, I.; Perez-Arlandis, J. M.; Welton, T. *Org. Lett.* **2007**, *9*, 5247−5250.

(9) (a) Notz, W.; Sakthivel, K.; Bui, T.; Zhong, G. F.; Barbas, C. F., III *Tetrahedron Lett.* **2001**, *42*, 199−201. (b) Chen, Y. K.; Yoshida, M.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2006**, *128*, 9328−9329.

(10) (a) Lawrence, S. A. *Amines: Synthesis, Properties and Applications*; Cambridge University Press: Cambridge, 2004. (b) Murugan, R.; Scriven, E. F. V. In *Pyridines: From Lab to Production*; Scriven, E. F. V., Ed.; Academic Press: New York, 2013.

(11) For the acidity scale of amines in H_2O, see: (a) Kaljurand, I.; Lilleorg, R.; Murumaa, A.; Mishima, M.; Burk, P.; Koppel, I.; Koppel, I. A.; Leito, I. *J. Phys. Org. Chem.* **2013**, *26*, 171−181. In AN, see: (b) Kaljurand, I.; Kütt, A.; Sooväli, L.; Rodima, T.; Mäemets, V.; Leito, I.; Koppel, I. A. *J. Org. Chem.* **2005**, *70*, 1019−1028. (c) Rõõm, E.-I.; Kütt, A.; Kaljurand, I.; Koppel, I.; Leito, I.; Koppel, I. A.; Mishima, M.; Goto, K.; Miyahara, Y. *Chem. - Eur. J.* **2007**, *13*, 7631−7643. (d) Coetzee, J. F.; Padmanabhan, G. R. *J. Am. Chem. Soc.* **1965**, *87*, 5005−5010. In DMSO, see: (e) Benoit, R. L.; Mackinnon, M. J.; Bergeron, L. *Can. J. Chem.* **1981**, *59*, 1501−1504. (f) Kolthoff, I. M.; Chantooni, M. K., Jr.; Bhowmik, S. *J. Am. Chem. Soc.* **1968**, *90*, 23−28.

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

(13) D'Anna, F.; Vitale, P.; Noto, R. *J. Org. Chem.* **2009**, *74*, 6224−6230.

(14) Angelini, G.; De Maria, P.; Chiappe, C.; Fontana, A.; Pierini, M.; Siani, G. *J. Org. Chem.* **2010**, *75*, 3912−3915.

(15) Barhdadi, R.; Troupel, M.; Comminges, C.; Laurent, M.; Doherty, A. *J. Phys. Chem. B* **2012**, *116*, 277−282.

(16) Millán, D.; Rojas, M.; Santos, J. G.; Morales, J.; Isaacs, M.; Diaz, C.; Pavez, P. *J. Phys. Chem. B* **2014**, *118*, 4412−4418.

(17) Deng, H.; Li, X.; Chu, Y.; He, J.-Q.; Cheng, J.-P. *J. Org. Chem.* **2012**, *77*, 7291−7298.

(18) Wang, Z.; Deng, H.; Li, X.; Ji, P.; Cheng, J.-P. *J. Org. Chem.* **2013**, *78*, 12487−12493.

(19) Wang, Z.; Ji, P.; Li, X.; Cheng, J.-P. *Org. Lett.* **2014**, *16*, 5744−5747.

(20) (a) Menne, S.; Pires, J.; Anouti, M.; Balducci, A. *Electrochem. Commun.* **2013**, *31*, 39−41. (b) Chakrapani, V.; Rusli, F.; Filler, M. A.; Kohl, P. A. *J. Phys. Chem. C* **2011**, *115*, 22048−22053. (c) Egashira, M.; Todo, H.; Yoshimoto, N.; Morita, M.; Yamaki, J. *J. Power Sources* **2007**, *174*, 560−564. (d) Fang, S.; Zhang, Z.; Jin, Y.; Yang, L.; Hirano, S.; Tachibana, K.; Katayama, S. *J. Power Sources* **2011**, *196*, 5637−5644.

(21) (a) Wang, J.-Q.; Dong, K.; Cheng, W.-G.; Sun, J.; Zhang, S.-J. *Catal. Sci. Technol.* **2012**, *2*, 1480−1484. (b) Kawanami, H.; Sasaki, A.; Matsui, K.; Ikushima, Y. *Chem. Commun.* **2003**, 896−897. (c) Wong, W.-L.; Chan, P.-H.; Zhou, Z.-Y.; Lee, K.-H.; Cheung, K.-C.; Wong, K.-Y. *ChemSusChem* **2008**, *1*, 67−70.

(22) Rived, F.; Rosés, M.; Bosch, E. *Anal. Chim. Acta* **1998**, *374*, 309−324.

(23) Perrin, D. D. *Dissociation Constants of Organic Bases in Aqueous Solution*; Butterworths: London, 1972.

(24) Frenna, V.; Vivona, N.; Consiglio, G.; Spinelli, D. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1865−1868.

(25) Castro, E. A.; Cubillos, M.; Santos, J. G. *J. Org. Chem.* **2004**, *69*, 4802−4807.

(26) Benoit, R. L.; Lefebvre, D.; Frechette, M. *Can. J. Chem.* **1987**, *65*, 996−1001.

(27) Castro, E. A.; Muñoz, P.; Santos, J. G. *J. Org. Chem.* **1999**, *64*, 8298−8301.

(28) Halle, J.; Lelievre, J.; Terrier, F. *Can. J. Chem.* **1996**, *74*, 613−620 (extrapolated data).

(29) Benoit, R. L.; Frechette, M.; Lefebvre, D. *Can. J. Chem.* **1988**, *66*, 1159−1162.

(30) Crampton, M. R.; Robotham, I. A. *J. Chem. Res., Synop.* **1997**, 22−23.

(31) Ritchie, C. D.; Lu, S. Z. *J. Am. Chem. Soc.* **1990**, *112*, 7748−7756.

(32) Augustin-Nowacka, D.; Chmurzyñski, L. *Anal. Chim. Acta* **1999**, *381*, 215−220.

(33) Dadali, V. A.; Panchenko, B. V.; Litvinenko, L. M. *J. Org. Chem. USSR (Engl. Transl.)* **1980**, 1470−1477.

(34) Teitel'baum, A. B.; Kudryavtseva, L. A.; Bel'skii, V. E.; Ivanov, B. E. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1980**, *29*, 1571−1580.

(35) Kaljurand, I.; Rodima, T.; Leito, I.; Koppel, I. A.; Schwesinger, R. *J. Org. Chem.* **2000**, *65*, 6202−6208.

(36) Czaja, M.; Makowski, M.; Szociński, M.; Darowicki, K.; Chmurzyński, L. *J. Chem. Thermodyn.* **2006**, *38*, 606−610.

(37) Paolo, B.; Gioanna, G.; Aldo, L. *Gazz. Chim. Ital.* **1980**, *110*, 491−494.

(38) Cox, B. G. *Acids and Bases: Solvent Effects on Acid−Base Strength*; Oxford University Press: Oxford, 2013.

(39) Hallett, J. P.; Welton, T. *Chem. Rev.* **2011**, *111*, 3508−3576.

(40) Burrell, A. K.; Del Sesto, R. E.; Baker, S. N.; McCleskey, T. M.; Baker, G. A. *Green Chem.* **2007**, *9*, 449−454.

(41) Uno, M.; Seto, K.; Takahashi, S. *J. Chem. Soc., Chem. Commun.* **1984**, 932−933.

(42) Suzuki, H.; Koide, H.; Ogawa, T. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 501−504.

(43) Matthews, W. S.; Bares, J. E.; Bartmess, J. E.; Bordwell, F. G.; Cornforth, F. J.; Drucker, G. E.; Margolin, Z.; McCallum, R. J.; McCollum, G. J.; Vanier, N. R. *J. Am. Chem. Soc.* **1975**, *97*, 7006−7014.