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Absolute pK_as of Sulfonamides in Ionic Liquids: Comparisons to Molecular Solvents

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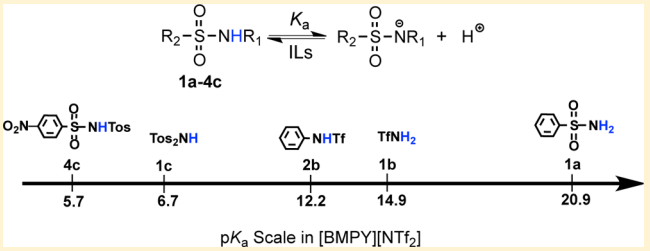
Supporting Information

ABSTRACT: Absolute pK_as of 25 sulfonamides in four ionic liquids (ILs) were measured spectroscopically with high precision and subsequently compared with those in conventional molecular solvents. It is found that the acidity order of these sulfonamides is as follows: in water > in DMSO > in ILs > in acetonitrile (ACN). The well-known solvent polarity index ε fails to explain the observed stronger bond-weakening effect of ILs in comparison to that of ACN, whose ε value is much greater. In addition, the regression analyses show that the pK_as of sulfonamides determined in ILs linearly correlate with these in molecular solvents of distinct properties, but with various slopes. A rationale and related discussion on the effect of solvation in ILs are presented.



INTRODUCTION

Solvents are ubiquitous and, in most circumstances, are indispensable in chemistry. In a sense, the selection of solvent based on the knowledge of solvation reflects a rational development of chemistry, which in return can significantly improve the image of organic reactions with regard to environmental issues.[1] In recent years, as it has become more and more crucial, many volatile organic solvents are listed as "unclean", and various room-temperature ionic liquids (RTILs) have come into play as their alternatives, in spite of a severe shortage of knowledge of their solvation behavior.

Ionic liquids are composed entirely of ions and exhibit unique properties that are significantly different from those of conventional molecular solvents.[2] As a rising mainstream medium category, ILs are labeled as green solvents[3] and have aroused enormous research interest in recent decades and have also been extensively used in industry.[4] In comparison to the tremendous attention paid to the development of their synthetic applications, fundamental aspects of the solvation phenomena of ILs are very scarce, however. As it is well-known that solvents have strong effects on the acidity of substrates by virtue of their differential strengths of solvation toward various species in solution, we believe that the study of pK_as in different media would provide a quantitative understanding in this regard.

Some acidity scales in various molecular solvents have been established in the past,[5] which allowed a good understanding of solvation behavior for conventional media. In contrast, there have been far fewer acidity studies in neat ILs, and the early works reported *relative* pK_as in most cases[6] that are not suitable for solvation studies. Although more recent works showed that the *absolute* acidity in ILs could be obtained electrochemically,[7] the narrow substrate scope and large uncertainty associated with irreversible electrode data make its use in solvation studies problematic. However, we have recently found that the overlapping indicator method, which has been dominantly used in molecular media for most of the authentic pK_a data known today,[8] can be well adopted to measure the acidities in ILs with high precision[9] and hence should be able to fulfill the current research need.

Sulfonamides are important compounds in the pharmaceutical and agricultural chemical industries. A large number of drugs, such as antimicrobials and diuretics, and several novel herbicides bear this sulfonamide moiety. This is mainly due to their unique structure that resembles the tetrahedral intermediate involved in many acyl substitutions and stabilized by proteases and esterases.[10] Sulfonamides are known to be more acidic than carboxamides. The knowledge of sulfonamide acidities is important to the pharmaceutical industry because it delivers valuable information on the mechanisms of drug actions and metabolisms. The acidities of sulfonamides have been investigated extensively in conventional molecular solvents.[11] However, until now almost no attention has been paid to the acidities of N–H bonds in ILs. On the other hand, a recent seminal study shows that the development of IL drugs and use of ILs as a drug delivery medium may bring a revolution to the pharmaceutical industry.[12] This, from another

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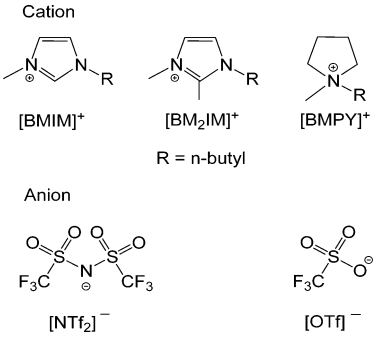
angle, points out the need for information on sulfonamide acidities in ILs, especially on their relation to the solvation strength of different types of media in a more quantitative manner.

Toward this end, here we have measured 68 absolute acidity values of 25 sulfonamides in 4 ILs (Scheme 1) with high precision with a standard deviation (SD) of ≤±0.05 pK units. A variety of structurally different sulfonamides (Scheme 2), such as benzenesulfonamides (**1a**−**8a**), trifluoromethylsulfonamides (**1b**−**6b**) and several acidic sulfonamides (**9a**, **10a**, **7b**−**11b**, and **1c**−**4c**), were included in this work. The measured pK_a data (Table 1) are compared with the known acidities in molecular solvents by regression analysis, which revealed insightful and interesting information regarding the change in solvation strength by ILs and molecular media.

Scheme 1. Cations and Anions of the ILs Used in This Study[a]



[a]The ILs are [BMIM][OTf], [BMIM][NTf_2], [BMPY][NTf_2], and [BM_2IM][NTf_2].

RESULTS AND DISCUSSION

Table 1 shows that the acidity scale of these N−H acids spreads over 15 pK units, which covers by far the largest energetic span and substrate collection for one R−H acid family in ILs and provides rich information on the effect of structural change on the N−H acidity in ILs. For examples, an additional sulfonyl group causes a dramatic increase in the acidity of **1a** (20.9) by as much as 14 orders of magnitude in comparison to that of **9a** (6.3), while a carbonyl group makes the acidity of **7b** (6.7) 1.6 × 10^8 times stronger than that of **1b**, due to its strong inductive as well as resonance stabilization effect on the sulfonamide nitrogen anion. This is supported by the fact that the carbon acid $PhSO_2CH_2SO_2Ph$ (pK_a = 19.2 in [BMPY][NTf_2][9a]) is much less acidic than its analogue **9a** in ILs; apart from the fact that the electronegativity of N is greater than that of C, the large acidity difference (ΔpK_a ≈ 13) may also be a consequence of a significant p−d π resonance between the anion center and sulfonyl group of sulfonamides.[14]

The structure and composition of the ILs in this study have a pronounced effect on the N−H acidic dissociation equilibrium. Normally, the anion of IL plays a dominant role in the acidity, due to the relatively large proton solvation energy ($\Delta G_{Solv}^*(H^+)$) by the anion (−258 kcal mol^{-1} for [NTf_2]$^-$), in comparison with that by the cation on the deprotonated species of various substrates.[15] From Table 1, the acidity of individual sulfonamide decreases in the sequence [BMIM][OTf] > [BMIM][NTf_2] > [BMPY][NTf_2] > [BM_2IM][NTf_2], which is consistent with our previous observations for other series of acids.[9] It is not difficult to understand that these sulfonamides are more acidic in [BMIM][OTf] than in [BMIM][NTf_2]. This could be ascribed to a more localized negative charge and smaller size of [OTf]$^-$ in comparison to [NTf_2]$^-$, both leading to a stronger solvation of protons. The trend of pK_a change in the ILs with [NTf_2]$^-$ as the common counteranion could be

Scheme 2. Structures of Sulfonamide Derivatives Involved in This Work

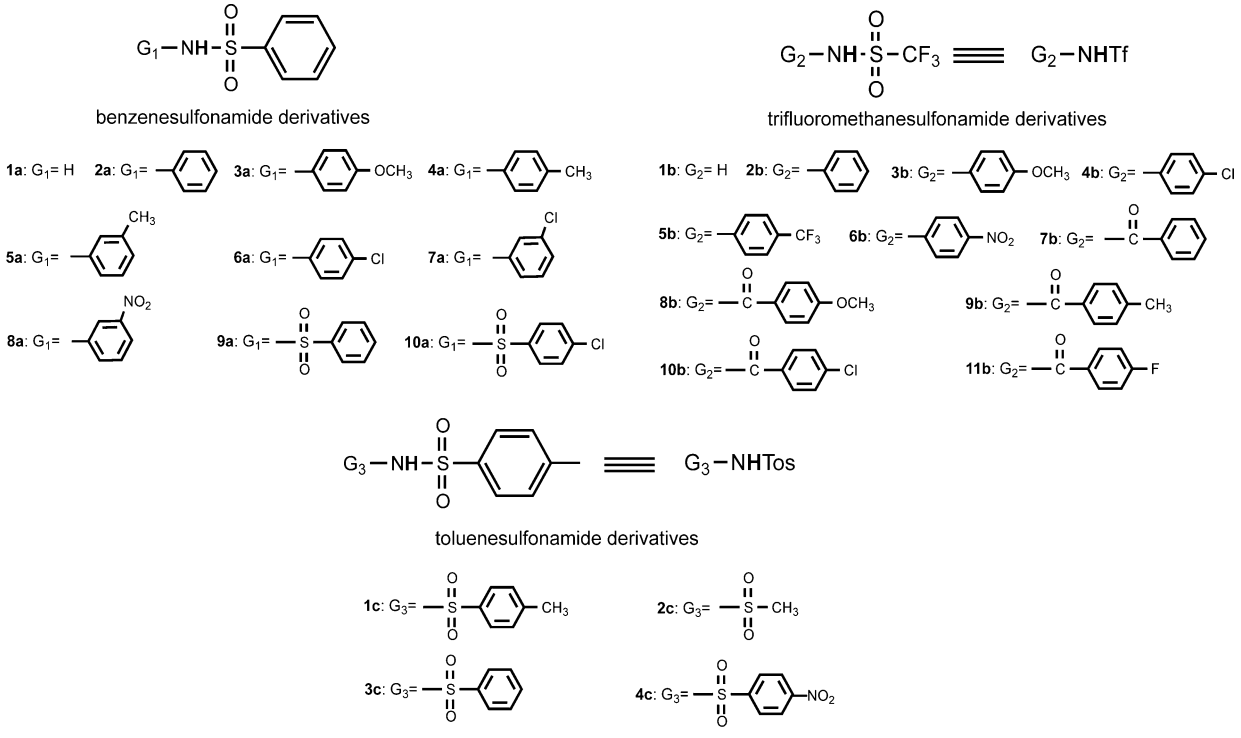


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Table 1. pK_a Values of Sulfonamides (Scheme 2) in ILs and Molecular Solvents

	pK_a						
sulfonamide[a]	[Bmpy][NTf_2][b]	[Bmim][NTf_2][b]	[Bm_2im][NTf_2][b]	[Bmim][OTf][b]	water	DMSO	ACN
$PhSO_2NH_2$ (**1a**)	20.9	20.2_5	21.9	18.1	9.4[c]	15.2[d]	24.6[d]
p-MeO-PhN**H**SO_2Ph (**3a**)	18.7	18.2	19.3	16.1	8.9[e]	14.2[e]	22.9[e]
p-Me-PhN**H**SO_2Ph (**4a**)	18.4	17.7_5	19.1	15.7	8.6[e]	13.9[e]	22.6[e]
m-Me-PhN**H**SO_2Ph (**5a**)	18.2	17.6	18.9	15.5	8.5[e]	13.7[e]	22.7[e]
PhN**H**SO_2Ph (**2a**)	18.0	17.4	18.7	15.4	8.2[e]	13.5[e]	22.6[e]
p-Cl-PhN**H**SO_2Ph (**6a**)	17.1_5	16.7	17.7_5	14.6	7.9[e]	12.7[e]	21.6[e]
m-Cl-PhN**H**SO_2Ph (**7a**)	16.7	16.3	17.4	14.3	7.7[f]	11.7[e]	
m-NO_2-PhN**H**SO_2Ph (**8a**)	15.7	15.3	16.2	13.3		11.2[e]	20.4[e]
TfNH_2 (**1b**)	14.9	14.4_5	15.5	12.8	6.3[g]	9.7[h]	
PhN**H**Tf (**2b**)	12.2	11.8	12.7	9.9_5	4.5[g]		
p-MeO-PhN**H**Tf (**3b**)	12.9	12.4	13.3_5	10.6	4.9[g]		
p-Cl-PhN**H**Tf (**4b**)	11.4	11.0	11.8	9.2	3.9[g]		
p-CF_3-PhN**H**Tf (**5b**)	10.6	10.2_5	11.0	8.5			
p-NO_2-PhN**H**Tf (**6b**)	9.4_5	9.0_5	9.8	7.6			
p-MeO-PhCON**H**Tf (**8b**)	7.2	6.7					11.6[i]
TosN**H**SO_2Me (**2c**)	7.2	6.6					
p-Me-PhCON**H**Tf (**9b**)	7.0	6.6					11.5[i]
Tos_2N**H** (**1c**)	6.7	6.2			1.7[k]		12.0[j,k]
PhCON**H**Tf (**7b**)	6.7	6.2_5					11.1[i]
$PhSO_2$N**H**Tos (**3c**)	6.5	6.0					
$PhSO_2$N**H**SO_2Ph (**9a**)	6.3	5.8 (9.7[l])			1.4_5[f]		11.3[j]
p-F-PhCON**H**Tf (**11b**)	6.3	5.9					10.7[i]
p-Cl-PhCON**H**Tf (**10b**)	6.3	5.8					10.4[i]
p-Cl-$PhSO_2$N**H**SO_2Ph (**10a**)	5.9	5.3					
p-NO_2-$PhSO_2$N**H**Tos (**4c**)	5.7	5.0					10.1[j]

[a]The acidic hydrogens are indicated by boldface type. [b]In pK_a units, SD: ≤ ± 0.05 pK unit. [c]Reference 11e. [d]Reference 11f. [e]Reference 11g. [f]Reference 11b. [g]Reference 11a. [h]Reference 13. [i]Reference 11m. [j]Reference 11j. [k]Reference 11i. [l]Reference 7c, in [EMIM][NTf_2], where [EMIM]$^+$ = 1-ethyl-3-methylimidazolium. The value is simulated on the basis of electrochemical measurement.

rationalized on the basis of the extent of charge delocalization and the accessibility of the cation moiety toward the sulfonamide anion. For example, the observed stronger acidity of sulfonamide in [BMIM][NTf_2] in comparison to that in the other two ILs with [NTf_2]$^-$ as a common anion should be due to the less hindered [BMIM]$^+$ moiety in comparison to the other two and its C_2−H that is capable of providing an H bond with the sulfonamide nitranion.

Table 1 also shows that the acidities of sulfonamides in various solvents follow the order in water > in DMSO > in [BMIM][OTf] > [BMIM][NTf_2] > [BMPY][NTf_2] > [BM_2IM][NTf_2] > in ACN, which actually reflects the order of solvability for these solvents.[7b] This sequence is beyond one's expectation, however, because AILs are known for their relatively low polarity (ε = 10−15[16]), which would otherwise suggest a weaker acidity in ILs than in ACN, whose dielectric constant is much greater (ε = 36.1[17]). Nonetheless, as we recently found, the cations and anions in AILs should exist essentially as "free ions" rather than as ion pairs[9e] (showing an "ionic liquid effect"[9c,e,18,19]), and so it may not be too great a surprise to see that some classical parameters suitable for describing properties in molecular media (such as ε) may not always be so for certain properties in ILs. Thus, the presently observed but yet unanticipated unusually strong N−H bond weakening ability of the low-polarity ILs could be understood by considering that the IL's anion and cation should be able to act separately in stabilizing the proton and the incipient sulfonamide nitranion upon deprotonation by virtue of their respective solvability (via Coulombic, resonance, π−π interactions, etc.) toward ions of opposite charges. This in situ situation occurring in a solvation process in IL is not exactly the same as the status of an IL in a dielectric constant measurement,[16] and thus, this should be the reason behind the unusually strong N−H bond weakening ability of these superficially weakly polar ILs.

Next, we carried out a regression study on the sulfonamide acidities measured in the four ILs. All of the correlations between the pK_as in any two ILs show excellent linearity with R^2 = 0.999 (see Figure S3 in the Supporting Information; one example is shown in Figure 1). Furthermore, regression analyses between the pK_as in one representative IL ([BMPY][NTf_2]) and those in molecular solvents were performed. Remarkably, in spite of the tremendous differences in the solvent properties of water, DMSO, and ACN in comparison to ILs, good to excellent linearity is observed in all of the correlations (Figure 1). It is noteworthy that the slopes of the correlation between the pK_as in [BMPY][NTf_2] and in water are significantly greater than unity (slope 1.68), indicating a much lower sensitivity of sulfonamide acidity toward structure variation in water in comparison to that in AILs. This is understandable, because the negative charge of the sulfonamide anion can be better dispersed in water than in IL due to the greater solvability of water caused mainly by its strong hydrogen bonds. This reduces the charge density on nitrogen and weakens the influence of a structural change more significantly in comparison to the situation in ILs. On the other hand, the slopes of the correlations between the acidities in ILs (taking [BMPY][NTf_2] as an example) vs DMSO and vs ACN are all observed to be around unity (Figure 1, slope 1.00 and 1.02, respectively). Though this seeming coincidence in the

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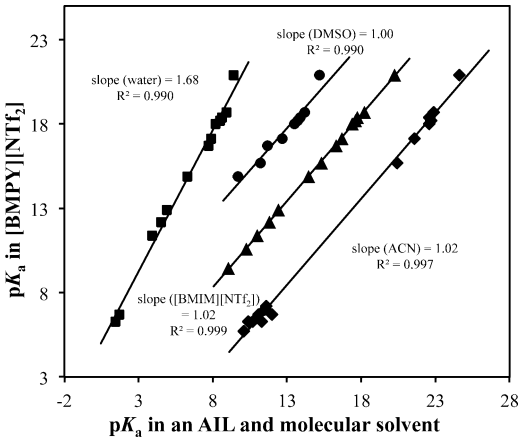

Figure 1. pK_as of sulfonamides in [BMPY][NTf_2] against those in [BMIM][NTf_2] and molecular solvent: solid squares, circles, triangles, and diamonds represent the pK_as in water, DMSO, [BMIM][NTf_2], and ACN, respectively.

slope values cannot be fully understood on the basis of our present knowledge of solvation, these correlation equations (1)−(3) (Scheme 3) together with those in the ILs mentioned above can provide a practical, very useful way for estimating unknown pK_as in these molecular and ionic solvents for relevant compounds.

Scheme 3. Acidity Correlation Equations between pK_as in ILs and Molecular Media

$$pK_a\,([BMPY][NTf_2]) = 1.68\,pK_a\,(water) + 4.24 \quad (1)$$

$$pK_a\,([BMPY][NTf_2]) = pK_a\,(DMSO) + 4.76 \quad (2)$$

$$pK_a\,(ACN) \approx pK_a\,([BMPY][NTf_2]) + 4.81 \quad (3)$$

In summary, the absolute acidities of 25 N−H acids (altogether 68 pK_a values) were accurately measured in 4 ILs. The wide energetic range (>15 pK units) of the obtained data enabled regression analyses among the pK_a scales in both ILs and molecular media, which exhibit excellent linear correlations of the acidity scales both in ILs and between the ILs and molecular solvents (water, DMSO, and ACN). Such relationships allow reasonable estimates for the unknown acidities of sulfonamides in these solvents. A detailed comparison among the acidity scales in these ionic and molecular media finds an interesting trend that the ILs of low ε value can show an unusually strong ability (vs ACN, ε = 36.1) in facilitating deprotonation. The absolute acidities and the solvation insights disclosed in this work may serve either as benchmark values or as reliable references for the development of appropriate theoretical solvation models and for mechanistic analyses in ILs.

EXPERIMENTAL SECTION

General Considerations. ILs (Scheme 1),[20] carbon indicator acids (fluorene derivatives, Table S1 in the Supporting Information), and the base used in this work were synthesized and purified as described in previous work.[9] In addition, ILs were dried under vacuum 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 Karl Fischer titrations. Sulfonamides, except as otherwise noted, were commercially available and were carefully recrystallized and dried before used as substrates. The sulfonamides and indicator acids were kept in a glovebox. The principle of acidity measurement by the indicator overlapping method[11c,13] is introduced as eq 4:

$$HA + In^- \overset{K_{eq}}{\rightleftharpoons} HIn + A^-$$

$$pK_a = pK_{HIn} - \log K_{eq} = pK_{HIn} - \log \frac{[HIn][A^-]}{[HA][In^-]} \quad (4)$$

where HIn and HA denotes the indicator and substrate acids, respectively. It is worth noting that all the acidities of indicator acids were referenced to an anchor compound whose acidity was measured by self-dissociation (Supporting Information); therefore, the pK_as of these indicator acids are absolute values in essence. All manipulations were carried out under dry argon using standard Schlenk techniques. The pK_a measurement started by placing 1.5 mL of an IL solution of base (~5 × 10^{-4} M) into an empty UV cell with a three-way valve (Figure S1 in the Supporting Information), and then the spectrum for baseline was recorded on a UV instrument. Next an IL solution of an appropriate indicator acid (HIn) with known pK_a was added in a dropwise fashion until the UV absorbance did not increase with the addition. Then the IL solution (10^{-5}−10^{-4} M) of the substrate acid of interest (HA) was added in several portions. The weight of the UV cell and the corresponding spectrum were also recorded upon each addition. The pK_a of HA was then calculated from the change of absorbance and the amount of acid added.

Synthesis of Picric Derivatives as Indicators.[21] *a. 3-Chloropicric Acid (Scheme S1, **C**).* In a 100 mL three-neck round-bottom flask charged with 2.5 g (19.5 mmol) of 3-chlorophenol, in an acetone/dry ice bath, was added 10 mL of concentrated sulfuric acid (98% w/w, 0.183 mol) slowly, and then the temperature of reaction mixture was raised cautiously to 90 °C and kept at this temperature for 40 min before the temperature was reduced to 0 °C by a water and ice bath (NaCl/icewater). Again in the acetone/dry ice bath, 10 mL of fuming nitric acid (90% w/w, 0.214 mol) was added with caution in a dropwise fashion, and then the reaction temperature was raised to 80 °C and was held at this temperature for 50 min. After the system was cooled to ambient temperature, the reaction mixture was then poured into ice/water and the yellowish brown precipitates were collected and recrystallized once from water and twice from CCl_4 to give 2.3 g of a yellowish solid. Yield: 45%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.77 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 127.9.

*b. 3,5-Dichloropicric Acid (Scheme S1, **D**).* The starting material was 3,5-dichlorophenol, and the synthetic procedures were similar to these for 3-chloropicric acid (**C**) described above, which gave a yellow solid in a yield of 38%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.58 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 155.6, 143.1, 127.7, 121.0.

Synthesis of Sulfonamides. The commercially available (**1a**,**b**) and prepared sulfonamides (**2a**−**8a**, **2b**−**11b**, **3c**, and **4c**) were carefully recrystallized at least three times and stored in a glovebox before use in pK_a measurements. The synthetic procedures for the sulfonamides used in this work can be found elsewhere.[22]

PhNHSO$_2$Ph (**2a**), yield 72%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.37 (s, 1H), 7.80 (d, J = 7.2 Hz, 2H), 7.60−7.48 (m, 3H), 7.22 (t, J = 7.8 Hz, 2H), 7.14 (d, J = 7.7 Hz, 2H), 7.00 (t, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ140.0, 138.2, 133.3, 129.7, 129.6, 127.1, 124.5, 120.5.[22b]

p-MeO-PhNHSO$_2$Ph (**3a**), yield 58%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.94 (s, 1H), 7.69 (d, J = 7.1 Hz, 2H), 7.60−7.45 (m, 3H), 6.98 (d, J = 7.2 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 3.66 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 157.0, 139.9, 133.2, 130.5, 129.6, 127.1, 123.9, 114.7, 55.5.[22b]

p-Me-PhNHSO$_2$Ph (**4a**), yield 68%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.53 (s, 1H), 7.80 (d, J = 7.1 Hz, 2H), 7.60- 7.48 (m, 3H), 7.28 (d, J = 8.7 Hz, 2H), 7.15 (d, J = 8.7 Hz, 2H). 10.14 (s, 1H), 7.73 (d, J = 7.1 Hz, 2H), 7.58−7.49 (m, 3H), 7.04−6.95 (m, 4H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 139.9, 135.4, 133.9, 133.3, 130.0, 129.7, 127.1, 121.1, 20.8.[22b]

m-Me-PhNHSO$_2$Ph (**5a**), yield 69%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.29 (s, 1H), 7.80 (d, J = 7.2 Hz, 2H), 7.60−7.50 (m, 3H), 7.09 (t, J = 8.1 Hz, 1H), 7.16 (s, 1H), 6.98−6.88 (m, 2H), 6.82 (d, J = 7.9

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Hz, 1H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 140.0, 138.9, 138.1, 133.3, 129.7, 129.4, 127.1, 125.3, 121.0, 117.5, 21.5.[22b]

p-Cl-PhNHSO$_2$Ph (**6a**), yield 63%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.53 (s, 1H), 7.80 (d, J = 7.1 Hz, 2H), 7.60−7.48 (m, 3H), 7.28 (d, J = 8.7 Hz, 2H), 7.15 (d, J = 8.7 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 139.6, 137.1, 133.5, 129.7, 129.6, 128.7, 127.1, 122.0.[22b]

m-Cl-PhNHSO$_2$Ph (**7a**), yield 65%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.66 (s, 1H), 7.82 (d, J = 7.2 Hz, 2H), 7.63−7.50 (m, 3H), 7.24 (t, J = 8.1 Hz, 1H), 7.16 (s, 1H), 7.11 (d, J = 8.2 Hz, 1H), 7.05 (d, J = 7.9 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 139.8, 139.6, 133.9, 133.6, 131.3, 129.8, 127.1, 124.2, 119.5, 118.4.[22b]

m-NO$_2$-PhNHSO$_2$Ph (**8a**), yield 48%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.98 (s, 1H), 7.99 (s, 1H), 7.85 (d, J = 7.2 Hz, 2H), 7.81 (d, J = 7.9 Hz, 1H), 7.60−7.51 (m, 4H), 7.48 (t, J = 8.1 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 148.6, 139.6, 139.4, 133.7, 131.1, 129.9, 127.1, 125.7, 118.8, 113.9.[22b]

PhSO$_2$NHSO$_2$Ph (**9a**), yield 33%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.87 (s, 1H), 7.71 (d, J = 7.4 Hz, 4H), 7.51 (t, J = 7.2 Hz, 2H), 7.44 (t, J = 7.4 Hz, 4H). ^{13}C NMR (100 MHz, DMSO-d_6): δ144.3, 131.9, 128.9, 126.8.[22c]

p-Cl-PhSO$_2$NHSO$_2$Ph (**10a**), yield 31%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.65 (s, 1H), 7.74−7.68 (m, 4H), 7.50−7.45 (m, 3H), 7.41 (t, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 144.4, 143.5, 136.5, 131.8, 128.9, 128.8, 126.8.[22c]

PhNHTf (**2b**), yield 67%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.91 (s, 1H), 7.42 (t, J = 7.7 Hz, 2H), 7.29 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 135.3, 130.0, 127.1, 123.3, 120.2 ($^1J_{CF}$ = 322 Hz).[22b]

p-MeO-PhNHTf (**3b**), yield 59%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.60 (s, 1H), 7.21 (t, J = 8.3 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 3.75 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.6, 127.3, 126.5, 120.3 ($^1J_{CF}$ = 323 Hz), 55.7.[22b]

p-Cl-PhNHTf (**4b**), yield 72%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.02 (s, 1H), 7.49 (d, J = 8.8 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 134.4, 131.3, 130.0, 124.8, 120.1 ($^1J_{CF}$ = 321 Hz).[22b]

p-CF$_3$-PhNHTf (**5b**), yield 64%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.33 (s, 1H), 7.79 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.3 Hz, 2H).[22b]

p-NO$_2$-PhNHTf (**6b**), yield 68%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.12 (s, 1H), 8.26 (d, J = 9.0 Hz, 2H), 7.46 (d, J = 9.0 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 144.5, 143.1, 125.6, 121.4, 120.1 ($^1J_{CF}$ = 322 Hz).[22b]

PhCONHTf (**7b**), yield 59%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.16 (s, 1H), 7.93 (d, J = 7.3 Hz, 2H), 7.47 (d, J = 7.3 Hz, 1H), 7.40 (t, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.9, 131.6, 129.0, 128.3.[22d]

p-MeO-PhCONHTf (**8b**), yield 62%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.10 (s, 1H), 7.91 (d, J = 8.6 Hz, 2H), 6.98 (d, J = 8.7 Hz, 2H), 3.79 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.8, 163.1, 131.4, 127.0, 120.3 ($^1J_{CF}$ = 322 Hz), 113.9, 55.8.[22d]

p-Me-PhCONHTf (**9b**), yield 66%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.23 (s, 1H), 7.83 (d, J = 7.9 Hz, 2H), 7.23 (d, J = 7.9 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ168.9, 142.5, 133.0, 129.3, 129.1, 120.5 ($^1J_{CF}$ = 322 Hz), 21.5.[22d]

p-Cl-PhCONHTf (**10b**), yield 61%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.30 (s, 1H), 7.92 (d, J = 8.3 Hz, 2H), 7.43 (d, J = 8.3 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.9, 136.7, 135.8, 130.9, 128.5, 120.6 ($^1J_{CF}$ = 322 Hz).[22d]

p-F-PhCONHTf (**11b**), yield 49%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.43 (s, 1H), 7.98 (dd, J = 8.5 Hz, $^4J_{HF}$ = 5.9 Hz, 2H), 7.19 (t, J = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.8, 164.6 ($^1J_{CF}$ = 248 Hz), 133.5, 131.7 ($^3J_{CF}$ = 9 Hz), 120.6 ($^1J_{CF}$ = 323 Hz), 115.3 ($^2J_{CF}$ = 21 Hz).[22d]

MeSO$_2$NHTos (**2c**), yield 48%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.09 (s, 1H), 7.75 (d, J = 8.2 Hz, 2H), 7.39 (d, J = 8.1 Hz, 2H), 3.15 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 143.6, 138.5, 129.8, 127.3, 43.8, 21.5.[22c]

PhSO$_2$NHTos (**3c**), yield 28%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.80 (s, 1H), 7.75 (d, J = 7.4 Hz, 2H), 7.63 (d, J = 8.2 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.48 (t, J = 7.5 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 143.1, 142.8, 139.9, 132.7, 129.6, 129.2, 127.1, 127.0, 21.4.[22c]

p-NO$_2$-PhSO$_2$NHTos (**4c**), yield 25%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.76 (s, 1H), 8.21 (d, J = 8.7 Hz, 2H), 7.88 (d, J = 8.6 Hz, 2H), 7.54 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 7.9 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 151.6, 148.7, 142.6, 141.1, 129.0, 128.3, 126.8, 124.0, 21.3.[22c]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02182.

Picture of the UV cell, expansion of the indicator acidity scale, indicators used in this work and their corresponding pK_as in ILs, UV−vis spectra for representative measurements, regression analysis, and NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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