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ARTICLE TYPE

Tailoring ionic liquid catalysts: structure, acidity and catalytic activity of protonic ionic liquids based on anionic clusters, $[(\text{HSO}_4)(\text{H}_2\text{SO}_4)_x]^-$ ($x = 0, 1, \text{ or } 2$)

Karolina Matuszek,^a Anna Chrobok,^{*a} Fergal Coleman,^b Kenneth R. Seddon^b and Malgorzata Swadzba-Kwasny^{*b}

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Aiming at inexpensive Brønsted-acidic ionic liquids, suitable for industrial-scale catalysis, a family of protonic ionic liquids based on nitrogen bases and sulfuric acid has been developed. Variation of the molar ratio of sulfuric acid, $\chi_{\text{H}_2\text{SO}_4}$, was used to tune acidity. The liquid structure was studied using ¹H NMR and IR spectroscopies, revealing the existence of hydrogen-bonded clusters, $[(\text{HSO}_4)(\text{H}_2\text{SO}_4)]^-$, for $\chi_{\text{H}_2\text{SO}_4} > 0.50$. Acidity, quantified by Gutmann Acceptor Number (AN), was found to be closely related to the liquid structure. The ionic liquids were employed as acid catalysts in a model reaction; Fischer esterification of acetic acid with 1-butanol. The reaction rate depended on two factors; for $\chi_{\text{H}_2\text{SO}_4} > 0.50$, the key parameter was acidity (expressed as AN value), while for $\chi_{\text{H}_2\text{SO}_4} < 0.50$ it was the mass transport (solubility of starting materials in the ionic liquid phase). Building on this insight, the ionic liquid catalyst and reaction conditions have been chosen. Conversion values of over 95% were achieved under exceptionally mild conditions, and using an inexpensive ionic liquid, which could be recycled up to eight times without diminution in conversion or selectivity. It has been demonstrated how structural studies can underpin rational design and development of an ionic liquid catalyst, and in turn lead to a both greener and economically viable process.

Introduction

Acid-catalysed processes are among the most important industrial transformations, including large-scale alkylation, isomerisation and esterification processes.¹ The use of conventional Brønsted acidic catalysts (HF, sulfuric or phosphoric acids, zeolites) bears various drawbacks, such as high volatility, toxicity, waste generation and limited solubility/phase contact with the starting materials.² Brønsted acidic ionic liquids may be promising greener alternatives to conventional Brønsted acids for catalysis, helping to overcome some of these drawbacks.

Structure and speciation of Brønsted acidic ionic liquids

Ionic liquids can be designed to carry a Brønsted acidic functionality in the cation, anion, or both; the possible locations of acidic protons within the structure of various ionic liquid ions are shown in Figure 1.

Here, we focus on ionic liquids^{3,4} prepared by proton transfer between sulfuric acid and a base, where the acid was used in various molar ratios, $\chi_{\text{H}_2\text{SO}_4} = 0.50, 0.67$ or 0.75 , see Eq. (1).

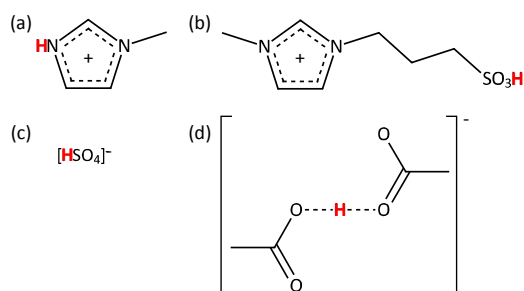


Figure 1. Locations of acidic protons (in red) on: (a) the 1-methylimidazolium cation, (b) the 1-methyl-3-(3-sulfonic acid)propylimidazolium cation, (c) the hydrogensulfate anion, and (d) the hydrogendi(acetate) anion.

For the $\chi_{\text{H}_2\text{SO}_4} = 0.50$ composition, the acidity may arise from the labile proton at the cation and also the hydrogensulfate anion, Figure 1(a) and 1(c). With an excess of sulfuric acid ($\chi_{\text{H}_2\text{SO}_4} = 0.67$ and 0.75), it is expected that the acidic protons incorporated in complex hydrogen-bonded anionic clusters, will be the main contributors to the acidity of the system. The existence of hydrogen-bonded anionic clusters, $[\text{A}(\text{HA})_x]^-$, has been demonstrated for halide-based ionic liquids, containing anions such as $[\text{Cl}(\text{HCl})]^-$,⁵ $[\text{Cl}(\text{HCl})_2]^-$,⁶ $[\text{Br}(\text{HBr})]^-$, $[\text{Br}(\text{HBr})_2]^-$, $[\text{Cl}(\text{HBr})]^-$,⁷ and $[\text{F}(\text{HF})_x]^-$,⁸ and analogous species are responsible for the Brønsted superacidity of Lewis acidic $[\text{C}_2\text{mim}]\text{Cl}-\text{AlCl}_3-$

HCl systems ($[\text{C}_2\text{mim}]^+ = 1\text{-ethyl-3-methylimidazolium}$).⁹ Complex anions have also been detected in liquids formed by carboxylic acid-base proton transfer, with the acid in excess, e.g. $[(\text{CF}_3\text{COO})(\text{CF}_3\text{COOH})]^-$,¹⁰ $[(\text{CH}_3\text{COO})(\text{CH}_3\text{COOH})_x]^-$,¹¹ and other hydrogen-bonded carboxylate anions.^{12,13} Finally, in mesylate and triflate ionic liquids, $[(\text{CH}_3\text{SO}_3)(\text{CH}_3\text{SO}_3\text{H})]^-$ and $[(\text{CF}_3\text{SO}_3)(\text{CF}_3\text{SO}_3\text{H})]^-$ clusters were shown to exist when combined with the corresponding acids;¹⁴ such systems were used to catalyse the dehydration of methanol to dimethyl ether.¹⁵ The structure of hydrogen-bonded anions, $[(\text{HSO}_4)(\text{H}_2\text{SO}_4)_x]^-$, has not been confirmed in ionic liquids, but their existence is well documented, for example in the Earth's stratosphere.¹⁶⁻¹⁸

Brønsted acidic ionic liquids by proton transfer in catalysis

Ionic liquids prepared by proton transfer are synthesised in a simple, inexpensive, solvent-free, one-step process. When such ionic liquids are based on sulfuric acid, they have negligible vapour pressure and are intrinsically halide-free. Consequently, they are truly sustainable solvents and catalysts, which have the potential for industrial applications. Ionic liquids based on monomeric hydrogensulfate anions, $[\text{HSO}_4]^-$, have been extensively used for catalysis.¹⁹ Moreover, in some cases, various amounts of sulfuric acid have been dissolved in these ionic liquids to enhance acidity,²⁰ but the structural aspect of these complex liquids has never been reported.

In this study, protonic ionic liquids based on sulfuric acid are used in a model Fischer esterification, exploiting their ability to adopt the dual roles of solvent and catalyst.^{21,22} Fischer esterification is an equilibrium reaction, which achieves good rates in a homogenous process, but it reaches equilibrium at ca. 67% conversion. When Brønsted acidic ionic liquids are used instead, poor solubility of the ester products in the ionic liquid layer causes phase separation, driving the equilibrium towards the product.²³

Previously, Fischer esterification reactions have been carried out in ionic liquids containing protonic cations, Figure 1(a),^{21,22} and protonic anions, Figure 1(c),^{21,22,24,25} the ionic liquids adopting the dual roles of catalyst and solvent. The influence of a number of parameters (*viz.* reaction temperature, catalyst loading, reactant ratios and ionic liquid structure) on the reaction has been investigated. The best results were achieved with ionic liquids based on the $[\text{HSO}_4]^-$ anion, which was typically used in stoichiometric or higher than stoichiometric quantities relative to the starting materials.^{12,19,26} Moreover, it was attempted to correlate Brønsted acidity, expressed as Hammett acidity function (H_0), with the activities of ionic liquids as esterification catalysts. However, the correlation was rather poor, suggesting that the acidity was not the sole, or even dominant, factor affecting the process.^{19,23}

Aim of this study

Here, it is attempted to correlate the liquid structure of protonic ionic liquids with their physico-chemical properties (in particular acidity and miscibility with reactants) and, building on that, design an optimal ionic liquid to be used as a solvent and catalyst in a model esterification reaction. This is proposed as a generic approach to tailoring ionic liquids as a replacement of hazardous acids in industrially-relevant reactions, which is why the cynosure is to generate both environmentally and economically sustainable processes.

Experimental

Materials

1,8-Diazabicycloundec-7-ene (DBU), 1-methylpyrrolidine, 1,4-diazabicyclo[2.2.2]octane (DABCO), 1-methylimidazole, triethylamine, octane, triethylphosphine oxide, sulfuric acid (95%), and glacial acetic acid were purchased from Sigma-Aldrich and used as received. 1-Butanol was purchased from Avantor Performance Materials Poland S.A.

Synthesis

Protonic ionic liquids. In a typical procedure, a base (1 mol eq.) was placed in a round-bottomed flask equipped with a stirring bar. The flask was placed in an ice bath and stirred vigorously; then, the required amount of sulfuric acid (1, 2, or 3 mol eq.) was added dropwise, and the mixture was stirred for at least 1 h. Subsequently, the ionic liquid produced was dried under high vacuum (80 °C, 10^{-2} bar, overnight).

Esterification procedure. In a typical experiment, a mixture of 1-butanol (1 mol) and ionic liquid (1, 5, 10, 12 or 15 mol %) was placed in a round-bottomed flask (10 cm³) equipped with a magnetic stirring bar. The appropriate amount of acetic acid (1-2 mol) was added to the flask, which was immersed in an oil bath and fixed with a reflux condenser, and then the mixture was stirred vigorously (30, 50 or 90 °C, 1-8 h, 1000 rpm). The reaction was monitored by GC analysis, with octane as internal standard. The ester product phase-separated from the ionic liquid layer and was decanted after the reaction.

Recycling experiments. In a typical experiment where the ionic liquid was recycled, reactions were scaled up by a factor of ten. A mixture of 1-butanol (10.0 mol) and ionic liquid (12 mol %) was placed in a round-bottomed flask (100 cm³) equipped with a magnetic stirring bar. Acetic acid (15 mol) was added to the flask immersed in an oil bath and fixed with a reflux condenser, and the mixture was stirred vigorously (30 °C, 1 h, 1000 rpm). The ester product phase-separated from the ionic liquid layer and was decanted after the reaction. The ionic liquid was stirred under vacuum (70 °C, 10^{-2} bar, 6 h) to remove water, and subsequently used in the next cycle of esterification.

Analyses

¹H NMR spectroscopy. In a glovebox, dry, neat ionic liquids were loaded into NMR tubes (5 mm, borosilicate glass) containing sealed capillaries with *d*₆-dimethylsulfoxide (an external lock). ¹H NMR spectra were recorded at 80 °C using a Bruker AvanceIII 400 MHz spectrometer.

Acceptor Number Determination. For each ionic liquid, three samples (*ca.* 1 g each) were weighed out in a glovebox, and mixed with a ³¹P NMR probe molecule, triethylphosphine oxide (TEPO), at different TEPO concentrations (3-10 mol%). After dissolution of TEPO was ensured, the solutions were loaded into NMR tubes, containing sealed capillaries with *d*₆-dimethylsulfoxide (an external lock).

³¹P NMR spectra were recorded at 80 °C, at 161.98 MHz, using a Bruker AvanceIII 400 MHz spectrometer. Phosphoric(V) acid, 85% solution in water, was used as an external reference. Three solutions of TEPO in hexane (*ca.* 5, 10 and 15 mol %) were prepared, and then measured at 27 °C. For each TEPO-ionic liquid system, the ³¹P NMR chemical shift for the infinite dilution of TEPO, δ_{inf} , was determined by extrapolation from the ³¹P NMR chemical shifts measured at different TEPO concentrations. The chemical shift of TEPO in hexane,

extrapolated to infinite dilution, $\delta_{\text{inf hex}}$, was used as a reference ($\delta_{\text{inf hex}} = 0$ ppm).

The AN values for all samples were calculated from the following formula: $\text{AN} = 2.348 \times \delta_{\text{inf}}$.^{27,28}

FT-IR spectroscopy. Infrared spectra of neat samples were recorded on a Perkin Elmer Spectrum 100 Series FT-IR spectrometer with a universal ATR accessory. Eight scans were acquired for each sample.

Gas chromatography. GC analysis was performed using a Perkin Elmer Clarus 500 chromatograph equipped with an SPBTM-5 column (30 m×0.2 mm×0.2 μm).

Results and Discussion

Synthesis and physical properties

Protonic ionic liquids were prepared by the reaction between sulfuric acid and tertiary/aromatic amines, following Eq. (1). The amines were selected such that the formed cations represented a variety of structures (aromatic, alicyclic, aliphatic) with a wide range of pK_a values (6.0–13.6), as shown in Figure 2. The anionic species were of the general formula $[(\text{HSO}_4)(\text{H}_2\text{SO}_4)_x]^-$ ($x = 0, 1, \text{ or } 2$), where x varied with the molar ratio of sulfuric acid, $\chi_{\text{H}_2\text{SO}_4}$, Eq. (1).

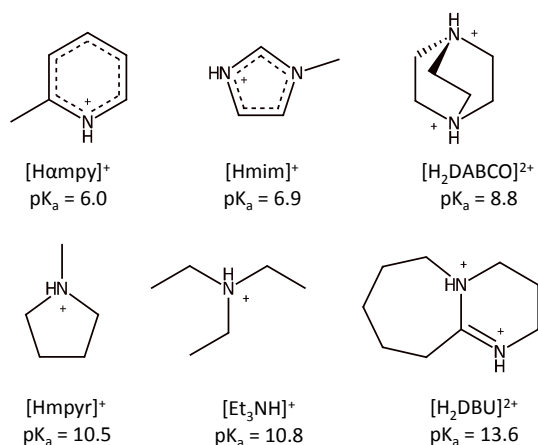


Figure 2. The structure of protonic cations used in this work.

Ionic liquids based on $[\text{Hampy}]^+$, $[\text{Hmim}]^+$, $[\text{Hmpyr}]^+$ or $[\text{Et}_3\text{NH}]^+$ and prepared by reaction of a base with an equimolar amount of sulfuric acid ($\chi_{\text{H}_2\text{SO}_4} = 0.50$) had melting points between 0–100 °C (see Supplementary Information), fulfilling the arbitrarily-assigned definition of an ionic liquid.²⁹ Systems based on the same cations, but containing an excess of sulfuric acid ($\chi_{\text{H}_2\text{SO}_4} > 0.50$), were all room-temperature ionic liquids, with glass transitions $T_g < 0$ °C.

In contrast, all systems based on $[\text{H}_2\text{DABCO}]^{2+}$ or $[\text{H}_2\text{DBU}]^{2+}$ were high-melting solids (doubly-charged cations increase the lattice energy, promoting crystallisation), hence these systems were not included in further studies.

Scanning (10 °C min⁻¹) thermogravimetric analysis (TGA) confirmed that the ionic liquids based on all four selected cations had good thermal stability ($T_d > 200$ °C), which makes them suitable not only for this particular study, but for most catalytic applications in organic chemistry. TGA curves are illustrated in the Supplementary Information.

Structural analysis

There were two foci of the structural studies: to confirm the existence of hydrogen-bonded anionic clusters, and to study the acidity of the labile protons. Since sulfuric acid is a strong acid, and the produced liquids have good thermal stability (with T_d well above boiling points of the corresponding bases), full protonation of the bases could be assumed for higher temperatures as well as ambient. The structure of hydrogen-bonded clusters of hydrogensulfate and sulfuric acid, $[(\text{HSO}_4)(\text{H}_2\text{SO}_4)_x]^-$ ($x = 0, 1, \text{ or } 2$), was anticipated to be very similar to the structure of hydrogensulfate-sulfuric acid clusters detected commonly in the upper layers of the Earth's atmosphere.^{16–18} As shown in Figure 3, the dinuclear and trinuclear clusters are believed bound with three and five strong hydrogen bonds, respectively.

To probe these assumptions, neat ionic liquids were studied using ¹H NMR and FT-IR spectroscopies.

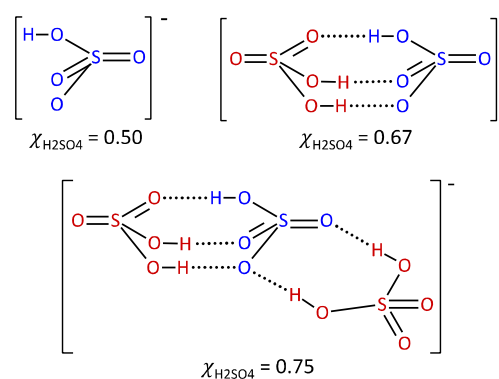


Figure 3. The structure of anionic species expected to exist in protonic ionic liquids based on sulfuric acid, depending on the mole fraction of the acid, $\chi_{\text{H}_2\text{SO}_4}$. For ease of comparison, atoms of the hydrogensulfate anion are represented in blue, and those of sulfuric acid are in red.

FT-IR spectroscopy. The structure of anionic species was studied using FT-IR spectroscopy. As a representative example, spectra of the $[\text{Hmpyr}][(\text{HSO}_4)(\text{H}_2\text{SO}_4)_x]$ system ($\chi_{\text{H}_2\text{SO}_4} = 0.50, 0.67$ and 0.75) are shown in Figure 4. Singly bound S-O stretches appear from 800 to 950 cm⁻¹ (black dashed line), double bonded S=O stretches fall in the 950–1300 cm⁻¹ range (red dashed line) and the SOH bend falls between 1350 and 1400 cm⁻¹.¹⁸ Key vibrational frequencies with assignments are listed in Table 1.

Concentrated sulfuric acid contains molecular H_2SO_4 in equilibrium with $[\text{HSO}_4]^-$ and $[\text{H}_3\text{SO}_4]^+$ ions;³⁰ characteristic vibrations for both species of interest: H_2SO_4 and $[\text{HSO}_4]^-$ were detected (see Table 1), in agreement with the literature.^{31,32} The $\chi_{\text{H}_2\text{SO}_4} = 0.50$ system is expected to contain only $[\text{HSO}_4]^-$; indeed, the spectrum features one S-OH vibration at 844.2 cm⁻¹, symmetric S=O stretch at 1020.5 cm⁻¹ and a complex multiplet corresponding to various vibrations of the $\{\text{SO}_3\}$ unit, with the most intense band at 1150.8 cm⁻¹.³² Complex anions present in $\chi_{\text{H}_2\text{SO}_4} = 0.67$ and 0.75 have structures naturally similar to sulfuric acid, with both H_2SO_4 and $[\text{HSO}_4]^-$ present. Vibrational frequencies for $[\text{HSO}_4]^-$ are intermediate between those found in $\chi_{\text{H}_2\text{SO}_4} = 0.50$ and in pure acid. Bands originating from the S-OH bending vibrations are less prominent and blue-shifted compared to the pure acid, since this motion is restricted by very strong

hydrogen bonding in the clusters.

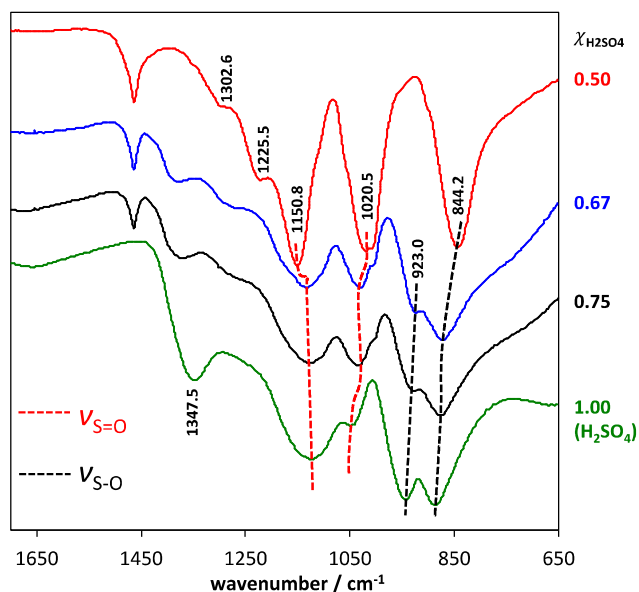


Figure 4. FT-IR spectra of neat [Hmpyr][(HSO₄)(H₂SO₄)_x] system, for $\chi_{\text{H}_2\text{SO}_4} = 0.50, 0.67$ and 0.75 , compared to the FT-IR spectrum of neat sulfuric acid.

Table 1. Assignments of selected vibrational frequencies in the FT-IR spectra of neat [Hmpyr][(HSO₄)(H₂SO₄)_x] system, for $\chi_{\text{H}_2\text{SO}_4} = 0.50, 0.67$ and 0.75 , and for sulfuric acid.

$\chi_{\text{H}_2\text{SO}_4}$	$\nu_{\text{S-O}}$		$\nu_{\text{S=O}}$		S-OH bend H ₂ SO ₄
	[HSO ₄] ⁻	H ₂ SO ₄	[HSO ₄] ⁻	H ₂ SO ₄	
0.50	844.2	-	1020.5	1150.8	-
0.67	871.6	923.1	1030.6	-	1131.4
0.75	874.7	928.1	1036.8	-	1126.4
1.00	885.6	942.7	1047.1	-	1125.5

¹H NMR spectroscopy. ¹H NMR spectra of the [Hmpyr][(HSO₄)(H₂SO₄)_x] system, for $\chi_{\text{H}_2\text{SO}_4} = 0.50, 0.67$ and 0.75 , are shown in Figure 5.

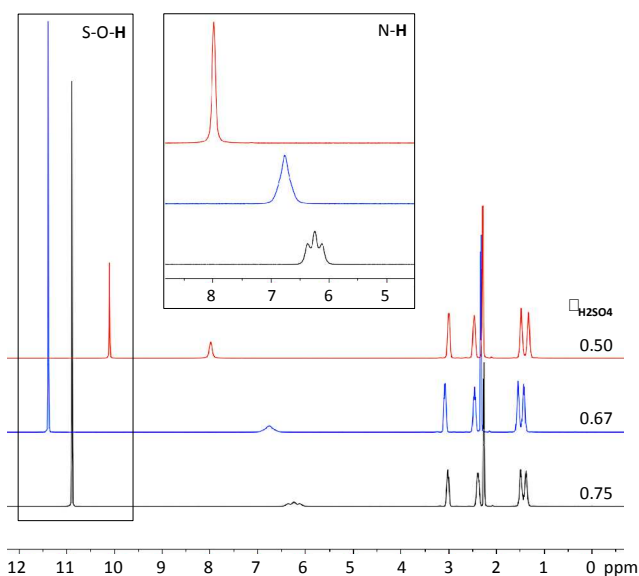


Figure 5. ¹H NMR spectra (400.112 MHz, 80 °C, neat) of the [Hmpyr][(HSO₄)(H₂SO₄)_x] system, for $\chi_{\text{H}_2\text{SO}_4} = 0.50, 0.67$ and 0.75 .

For $\chi_{\text{H}_2\text{SO}_4} = 0.50$, the most downfield-shifted signal ($\delta = 10.1$ ppm) corresponds to the proton of the [HSO₄]⁻ anion. Protonation of 1-methylpyrrolidine is evidenced by the weakly shielded proton ($\delta = 8.0$ ppm).

For $\chi_{\text{H}_2\text{SO}_4} = 0.67$, the most downfield signal ($\delta = 11.4$ ppm) integrates to three protons located on the dinuclear cluster, [(HSO₄)(H₂SO₄)₂]⁻. They are deshielded relative to the [HSO₄]⁻ proton, because they are partaking in strong hydrogen bonds, each shared between two oxygen atoms: S-O-H...O-S (see Figure 3); Hou *et al.*¹⁷ calculated (*ab initio*) the average hydrogen-bond distance to be as low as 1.656 Å. Strong internal hydrogen bonds in the dinuclear anion result in weaker external hydrogen-bonding interactions with the cation. As a consequence, the signal of the N-H proton is shifted upfield by *ca.* 0.5 ppm; noteworthy, the shape of the peak is non-Lorentzian.

For $\chi_{\text{H}_2\text{SO}_4} = 0.75$, the signal at 10.9 ppm integrates to five protons corresponding to the trinuclear complex, [(HSO₄)(H₂SO₄)₂]⁻. These protons are partaking in hydrogen bonds, which are strong, but on average weaker (1.704 Å)¹⁷ than those of the dinuclear system (1.656 Å) – hence the upfield shift of this signal compared to $\chi_{\text{H}_2\text{SO}_4} = 0.67$. The signal corresponding to the N-H proton is shifted even more upfield and split into a multiplet, indicating that it is strongly bound to nitrogen (weakly interacting with the anion, and not exchanging).

For all studied ionic liquids, there are two sets of protons in the 6-12 ppm region of the ¹H NMR spectrum; one originating from N-H protons in the cations, and the other from the S-O-H protons in the anions. Their chemical shifts are listed in Table 2 and ¹H NMR spectra are available in Supplementary Information.

Table 2. Signals corresponding to N-H and S-O-H protons in ¹H NMR spectra (400.112 MHz, 80 °C, neat) of protonic ionic liquids, based on four different bases and three mol ratios of H₂SO₄, compared to pK_a of the cations

cation	pK _a	$\chi_{\text{H}_2\text{SO}_4}$	$\delta_{\text{N-H}} / \text{ppm}$	$\delta_{\text{S-O-H}} / \text{ppm}$
[Hampyr] ⁺	6.0 ³³	0.50	13.35	10.45
		0.67	12.64	11.47
		0.75	12.04 (m)	10.96
[Hmim] ⁺	7.0 ³⁴	0.50	11.16 ^a	
		0.67	10.77	11.20
		0.75	10.57	10.97
[Hmpyr] ⁺	10.5 ³⁵	0.50	7.99	10.11
		0.67	6.76	11.39
		0.75	6.24 (m)	10.89
[Et ₃ NH] ⁺	10.7 ³⁵	0.50	solid at 80 °C	
		0.67	6.08	11.44
		0.75	5.58	11.03

^a Very broad signal, corresponding to both protons in equilibrium

The chemical shifts of labile anionic protons, $\delta_{\text{S-O-H}}$, depend markedly on the $\chi_{\text{H}_2\text{SO}_4}$ value, but not significantly on the cation: for all studied systems, irrespective of the cation structure, $\delta_{\text{S-O-H}}$ values are below 10.5 ppm for $\chi_{\text{H}_2\text{SO}_4} = 0.50$, increase to *ca.* 11.5 ppm for $\chi_{\text{H}_2\text{SO}_4} = 0.67$ and decrease to *ca.* 11.0 ppm for $\chi_{\text{H}_2\text{SO}_4} = 0.75$. The N-H protons are more shielded for higher $\chi_{\text{H}_2\text{SO}_4}$ values; dinuclear and trinuclear anions are less basic than [HSO₄]⁻, hence they have weaker interactions with the protonated bases. For aromatic cations, the $\delta_{\text{N-H}}$ signals are strongly shifted downfield, even >13 ppm. However, this arises from the

interaction with the aromatic ring, and despite strong deshielding, these protons are not very labile, as demonstrated by the presence of non-Lorentzian peaks, and the observation of multiplets in some spectra (Supplementary Information) indicates that they do not exchange rapidly on the NMR timescale.

The question arises, how do these measurements of chemical shifts relate to the bulk acidity of the studied ionic liquids? By extension, how does the catalytic activity of ionic liquids, *i.e.* their ability to protonate organic molecules, relate to the observed ^1H NMR chemical shifts?

Gutmann Acceptor Number measurements presented themselves as the perfect way to answer the above questions, because they probe the strength of protonation of a weak base, TEPO, by the acid of interest. AN values were measured for all ionic liquids but $[\text{Et}_3\text{NH}][\text{HSO}_4]$, which was solid at the temperature of the experiment (80 °C). In Table 3, AN values for ionic liquids with different cations and $\chi_{\text{H}_2\text{SO}_4}$ values are compared.

Table 3. AN values measured for protonic ionic liquids, based on four different bases and three mol ratios of H_2SO_4

cation	$\chi_{\text{H}_2\text{SO}_4}$	AN
[Hampy] ⁺	0.50	65.5
	0.67	116.7
	0.75	120.4
[Hmim] ⁺	0.50	73.3
	0.67	119
	0.75	120.7
[Hmpyr] ⁺	0.50	96.5
	0.67	117
	0.75	121.5
[Et ₃ NH] ⁺	0.50	-
	0.67	118
	0.75	121

For systems with $\chi_{\text{H}_2\text{SO}_4} > 0.50$, where hydrogen-bonded cluster anions are present, AN values appear to be independent of the cation, with AN = 118±1 for $\chi_{\text{H}_2\text{SO}_4} = 0.67$, and AN = 120.5±1 for $\chi_{\text{H}_2\text{SO}_4} = 0.75$. In contrast to the order of acidity that could be inferred from the ^1H NMR chemical shifts, AN values for $\chi_{\text{H}_2\text{SO}_4} = 0.75$ are consistently slightly higher than those for $\chi_{\text{H}_2\text{SO}_4} = 0.67$.

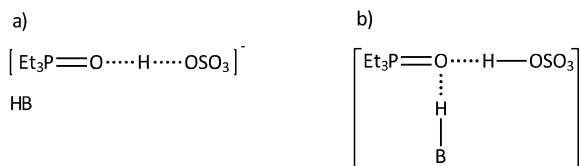


Figure 6. Proposed interaction of TEPO (a) with the $[\text{HSO}_4]^-$ anion in the presence of strong protonated base, which is effectively undissociated, and does not effectively interact with TEPO; and (b) in the presence of a weakly protonated base, which behaves like a very weak acid, causing a 'levelling effect' and weakening the overall acidity of the system.

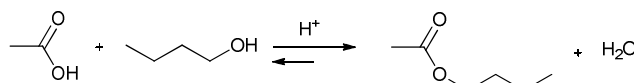
In systems where $\chi_{\text{H}_2\text{SO}_4} = 0.50$, TEPO is exposed to two weak acids: $[\text{HSO}_4]^-$ ($\text{p}K_a = 1.92$)³⁶ and a protonated amine (see Table 2). Protonated strong bases form – by definition – very weak acids ($\text{p}K_a > 10$); these adducts cannot compete effectively with $[\text{HSO}_4]^-$ for TEPO, as shown in Figure 6(a); consequently, the acceptor number for $[\text{Hmpyr}][\text{HSO}_4]$ is quite high, AN = 96.5. In

contrast, protons in $[\text{Hampy}]^+$ and $[\text{Hmim}]^+$ are more acidic; they may form strong hydrogen bonds with TEPO, competing with $[\text{HSO}_4]^-$, Figure 6(b).

The AN study demonstrates that the acidities of ionic liquids based on sulfuric acid and different bases can be tuned within a wide range, by changing the base and tuning $\chi_{\text{H}_2\text{SO}_4}$. For $\chi_{\text{H}_2\text{SO}_4} > 0.50$, high acidities can be achieved, with AN = *ca.* 120, which is comparable to values for other strong acids (AN_{CF₃COOH} = 105.5, AN_{CF₃SO₃H} = 129.1).²⁷ Systems based on the $[\text{HSO}_4]^-$ anion ($\chi_{\text{H}_2\text{SO}_4} = 0.50$) offer milder and tuneable acidities, lower than that of formic acid (AN = 83.6).²⁷

Esterification of 1-butanol catalysed by protonic ionic liquids

Esterification of acetic acid with 1-butanol (Scheme 1) is an equilibrium reaction: without catalyst, the maximum conversion is limited to 66.7%.^{19,37} In a reaction catalysed by sulfuric acid (homogenous liquid-phase system), it was been possible to shift the equilibrium further to the right, achieving 77.5% conversion. Brønsted acidic ionic liquids can adopt the dual roles of solvent and catalyst; the formed ester phase-separates from the reaction mixture, which allows for a further shift in equilibrium.^{19,37}



Scheme 1. Model esterification reaction of acetic acid with 1-butanol

All the ionic liquids studied here are inexpensive and easily prepared, presenting themselves as industrially viable catalysts. Furthermore, the AN studies indicate that their acidity can be easily tuned. Having gained a good understanding of their structure and quantified their acidity by AN, now we set out to understand how the ionic liquid properties relate to their catalytic activity, and demonstrate their applicability in practice, in an catalytic process.

Key parameters affecting the reaction

Screening esterification experiments were performed under very mild conditions (30 °C, 12 mol % of ionic liquid, 2 h reaction time). Yield of the ester produced using different ionic liquids (circles) and AN values measured for those ionic liquids (bar chart) are compared in Figure 7. In general, there is a good correlation between AN values and the yield of the ester; *i.e.* low yields were obtained for $\chi_{\text{H}_2\text{SO}_4} = 0.50$ and much higher for $\chi_{\text{H}_2\text{SO}_4} = 0.67$ or 0.75 ; indeed, higher yields of ester were obtained for $\chi_{\text{H}_2\text{SO}_4} = 0.75$ than for $\chi_{\text{H}_2\text{SO}_4} = 0.67$, in agreement with increasing AN. However, ionic liquids based on $[\text{Hmim}]^+$ do not appear to follow this trend.

To understand this discrepancy between AN values and reactivity in $[\text{Hmim}]^+$ -catalysed reactions, the phase behaviour of the reaction mixture components was investigated by simple visual observation (Table 4). It was observed that, at 30 °C, acetic acid was miscible with all studied ionic liquids, and the product (ester) always phase-separated from the mixture. The crucial difference was observed for 1-butanol, which was weakly miscible/immiscible with ionic liquids based on the $[\text{Hmim}]^+$ cation, but miscible with other systems (see Table 4). Reduced miscibility of 1-butanol had a detrimental impact on mass transport, and in consequence on the yield of butyl acetate, as clearly shown in Figure 7.

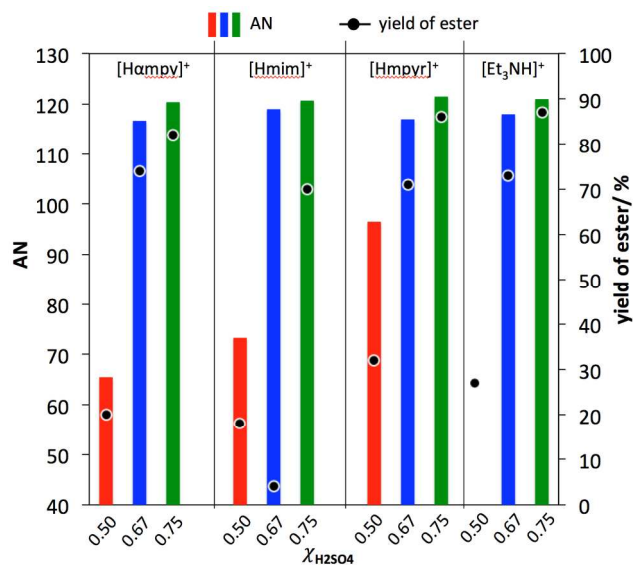


Figure 7. Yield of butyl acetate in reactions catalysed with ionic liquids based on sulfuric acid and four different bases, compared with AN values measured for these ionic liquids

Table 4. Miscibility of organic reactants and products (visual observation) with the ionic liquid layer, under the reaction conditions (30 °C)

cation	$\chi_{\text{H}_2\text{SO}_4}$	miscibility with the ionic liquid phase at 30 °C [‡]		
		BuOH	MeCOOH	MeCOOBu
[Hampy] ⁺	0.50	Y	Y	N
	0.67	Y	Y	N
	0.75	Y	Y	N
[Hmim] ⁺	0.50	N	Y	N
	0.67	N	Y	N
	0.75	N	Y	N
[Hmpyr] ⁺	0.50	Y	Y	N
	0.67	Y	Y	N
	0.75	Y	Y	N
[Et ₃ NH] ⁺	0.50	Y	Y	N
	0.67	Y	Y	N
	0.75	Y	Y	N

[‡] Y - miscible with ionic liquid; N - immiscible with ionic liquid

To confirm that difference in conversion derives from structural variations in the anion, and not merely from changing concentrations of sulfuric acid, an experiment was performed whereby the reactants:sulfuric acid ratio remained constant, but the amount of base (2-picoline) in the system was varied, to form $\chi_{\text{H}_2\text{SO}_4} = 0.50, 0.67$ and 0.75 compositions. After 2 h reaction at 30 °C, with molar ratio of alcohol to acid 1:1, the following yields of ester were obtained for the respective $\chi_{\text{H}_2\text{SO}_4}$ values: 20, 68 and 74%. This clearly demonstrates that differences in the ionic liquid structure affect the conversion, despite identical nominal acid concentration.

20 The influence of process parameters on the model reaction

Having understood that the reaction rate depends on the $\chi_{\text{H}_2\text{SO}_4}$ value of the ionic liquid and potential mass transport constraints (i.e. miscibility of an ionic liquid with 1-butanol), and taking into consideration that the reaction equilibrium can be shifted towards the product by using excess of one of the reactants and by phase-separation of the ester, reaction conditions could be studied.

The reaction was carried out at 30 °C, which was demonstrated

to be a viable temperature, much lower than literature reports on similar reactions in ionic liquids, where temperatures around 80-90 °C are used.^{19,23,26} The ionic liquid of choice was [Et₃NH][(HSO₄)(H₂SO₄)₂]; it dissolves both starting materials, has high acid content ($\chi_{\text{H}_2\text{SO}_4} = 0.75$), thus providing high reaction rate, and is based on a very inexpensive amine, which makes it industrially viable.

Reaction rate has been studied as a function of the ionic liquid content (1-15%, expressed as mol % per 1-butanol content) to find the optimum catalyst loading (Figure 8).

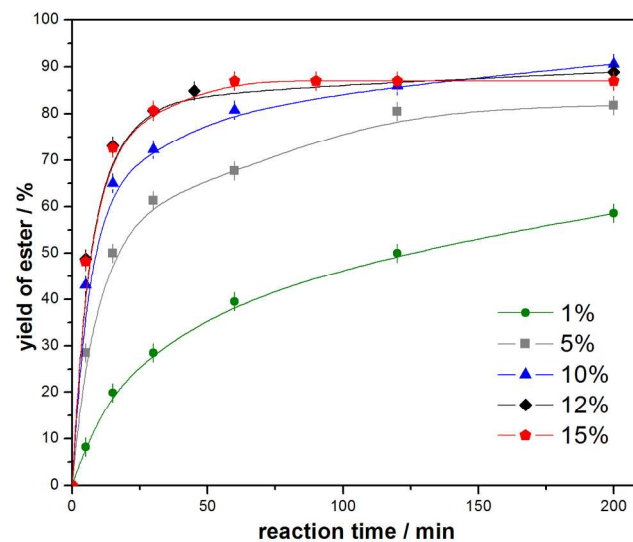


Figure 8. Yield of the ester product for the esterification of 1-butanol with acetic acid, at 30 °C, catalysed by [Et₃NH][(HSO₄)(H₂SO₄)₂], as a function of time; curves correspond to different ionic liquid loadings (expressed as mol % per 1-butanol), as shown on the graph.

As shown in Figure 8, for $\geq 12\%$ of ionic liquid, the reaction rate remains constant; moreover, even 5% of ionic liquid provides a very good reaction rate, with 80% yield of butyl acetate after 2 h. However, it is important to note that the final yield of the ester is highest for 10-12% loadings of ionic liquid. It appears that for lower ionic liquid content, the ester may not phase-separate completely, pushing the equilibrium to the left, and for higher loadings ($>12\%$), acidic hydrolysis of the ester starts counterbalancing the reaction upon its formation. In conclusion, 12% loading of ionic liquid has been selected as the optimum.

The influence of reactants ratio on reaction rate and on the final yield of butyl acetate has been studied at 30 °C, using two different loadings of [Et₃NH][(HSO₄)(H₂SO₄)₂]: 12% and, as a comparison, 5% (Figure 9). As expected, the use of 50 mol % excess of acetic acid resulted both in higher reaction rates and in increased conversions. Under chosen conditions (12% of ionic liquid, 50% excess of acetic acid), butyl acetate was synthesised in greater than 95% yield.

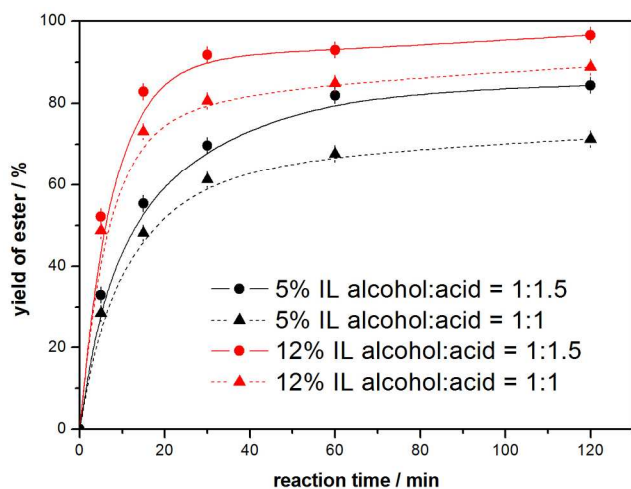


Figure 9. Yield of the ester product from the esterification of 1-butanol with acetic acid, at 30 °C, catalysed with $[\text{Et}_3\text{NH}][(\text{HSO}_4)(\text{H}_2\text{SO}_4)_2]$, as a function of time; curves correspond to different reactants ratios and different ionic liquid loading (expressed as mol % per 1-butanol), as shown on the graph.

Recycling study

Recycling of the ionic liquid was studied under the reaction conditions (30 °C, 12% of $[\text{Et}_3\text{NH}][(\text{HSO}_4)(\text{H}_2\text{SO}_4)_2]$, 50 mol % excess of acetic acid, 2 h). After each catalytic run, the product was decanted from above the ionic liquid layer, and unreacted starting materials were removed from the ionic liquid solution by vacuum distillation. In eight consecutive runs, no mass loss of the ionic liquid was observed. Yield of butyl acetate, although appearing to decline slightly, remained within the error bars of the measurement for all eight runs (mean yield = 98%, Figure 10).

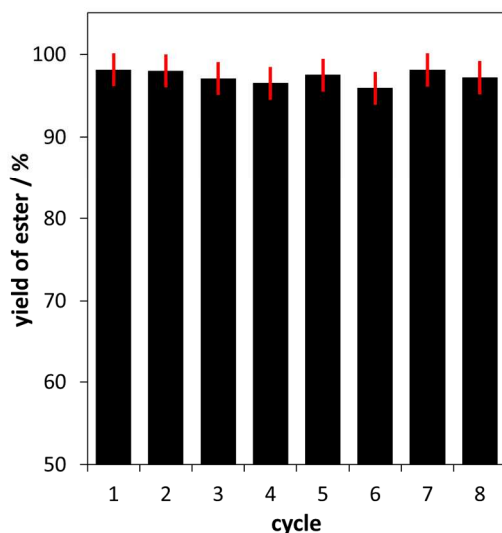


Figure 10. Yield of butyl acetate from the esterification of 1-butanol with acetic acid (30 °C, 12% of $[\text{Et}_3\text{NH}][(\text{HSO}_4)(\text{H}_2\text{SO}_4)_2]$, 50 mol % excess of acetic acid, 2 h) in consecutive recycling cycles.

Conclusions

The results discussed above expand and develop a family of inexpensive, easily prepared protonic ionic liquids based on sulfuric acid and various bases. The key development was to use

variable amounts of sulfuric acid ($\chi_{\text{H}_2\text{SO}_4} = 0.67$ and 0.75), which led to the formation of hydrogen-bonded anionic clusters, $[(\text{HSO}_4)(\text{H}_2\text{SO}_4)_x]^-$ ($x = 1$ or 2). The structure of the liquids was studied and confirmed by ^1H NMR and IR spectroscopies.

The acidity of these ionic liquids was quantified using Gutmann acceptor numbers. It was found that, for $\chi_{\text{H}_2\text{SO}_4} = 0.50$, AN values may vary in a wide range depending on the base used; they were higher in systems based on stronger bases, where the N-H proton was strongly bound to the base and did not compete for the probe with acidic anion, $[\text{HSO}_4]^-$. For $\chi_{\text{H}_2\text{SO}_4} = 0.67$ and 0.75 , acidity was independent of the cation, but depended only on the $\chi_{\text{H}_2\text{SO}_4}$ value. These ionic liquids were highly acidic (AN ≈ 120).

The two key parameters which determine the reaction rate of a model esterification reaction are: acidity of the ionic liquid (well correlated with AN values) and solubility of starting materials in the ionic liquid phase. For $\chi_{\text{H}_2\text{SO}_4} = 0.50$, where acidity (AN) is lower, it plays the crucial role. For $\chi_{\text{H}_2\text{SO}_4} = 0.60$ and 0.75 , where acidity is consistently very high, it ceases to be the main distinguishing parameter, and it is the miscibility of ionic liquid with alcohol that becomes the limiting factor. This miscibility is governed by the cation of the ionic liquid, as shown in Table 4. Importantly, AN values gave more insight into, and correlated better with, the observed catalytic activity than did the ^1H NMR chemical shifts of the labile protons.

Building on these fundamental structural results, esterification of acetic acid with 1-butanol was studied. The ionic liquid of choice, $[\text{Et}_3\text{NH}][(\text{HSO}_4)(\text{H}_2\text{SO}_4)_2]$, dissolved both starting materials well, and was highly acidic, thereby ensuring good reaction kinetics. Prepared from triethylamine and sulfuric acid, it was of very low cost; moreover, it was easily recycled multiple times without significant loss of activity. Using 50% excess of acetic acid, it was possible to consistently achieve conversions above 95% under exceptionally mild conditions.

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Notes and references

- ^a Department of Chemical Organic Technology and Petrochemistry, Silesian University of Technology, Krzywoustego 4, 44-100 Gliwice, Poland, E-mail: Anna.Chrobok@polsl.pl
^b QUILL, The Queen's University of Belfast, Belfast, BT9 5AG, United Kingdom, E-mail: m.swadzba.kwasny@qub.ac.uk
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