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A dramatic effect of the ionic liquid structure in esterification reactions in protic ionic media

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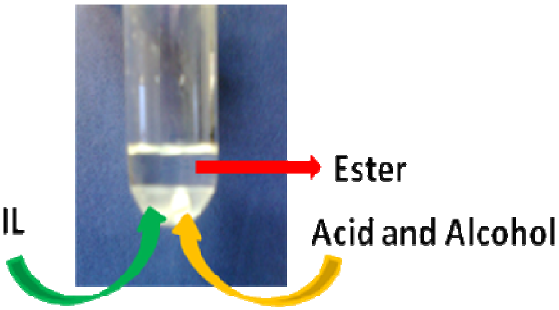

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A dramatic effect of the ionic liquid structure in esterification reactions in protic ionic media

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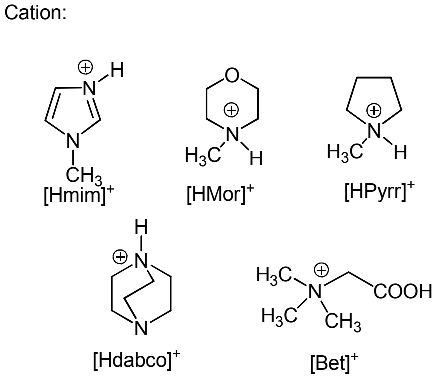
Brønsted acidic ionic liquids (ILs) have been synthesized and investigated as catalysts in esterification and transesterification reactions: simple and non-corrosive salts characterized by aliphatic cations associated with an "acidic" anion (in particular, $[HSO_4]^-$) gave the higher yields. A quite good correlation between IL acidity (H_0) and catalytic ability was found although also the hydrophilic nature of the ionic medium probably affects the process efficiency.

Introduction

The possibility to use Brønsted acidic ionic liquids (ILs) as catalysts and solvents in various reactions, instead of the corrosive acids, represents an attractive research area.[1] In this contest, the Fischer esterification of carboxylic acids with alcohols has been object of extensive investigation.[1,2] This equilibrium reaction, of industrial importance,[3] generally requires an acid catalyst and an excess of one of the reagents or a continuous removing of the formed water to shift the equilibrium towards the ester; water scavengers and/or the use of an additional solvent have been largely employed in the past to carry over the water in the form of azeotrope. However, such operations require large energy input to recycle the solvents and/remove the excess of reactants. Furthermore, the loss of volatile organic solvents to the atmosphere results into increase in the cost of production and also damage to the environment.[4]

Starting from 2002, Brønsted acidic ionic liquids have been proposed as catalysts and/or media to improve the Fischer esterification of organic substrates. Initially, Lewis acidic ILs (1-butylpyridinium chloride + aluminium(III) chloride) have been tested[5] but rapidly the interest has moved towards more the manageable Brønsted acidic salts and both ILs bearing a protonated acidic group on the cation alkyl chain (such as $-SO_3H$ and $-CO_2H$) or a proton on the quaternary nitrogen atom of cation, as well as ILs having an available proton on anion (HSO_4^-, $H_2PO_4^-$) have been screened.[6] Despite the variety of cations and anions which can give Brønsted acidic ionic liquids, the majority of the ILs (not necessarily Brønsted acidic ILs) nowadays reported for esterification are imidazole and pyridine derivatives[7] although simple triethylammonium salts ($[(C_2H_5)_3NH][HSO_4]$, $[(C_2H_5)_3NH][H_2PO_4]$ and $[(C_2H_5)_3NH][BF_4]$) have used with success in esterification of some carboxylic acids with primary alcohols.[8]

With the aim to develop new classes of "greener" ILs (*i.e.* salts prepared through more simple procedures and having a lower environmental impact[9]), we have prepared some Brønsted acidic salts simply by addition of an equimolar amount of a strong inorganic acid (HCl, H_2SO_4, HNO_3, CF_3COOH and H_3PO_4) to a commercial *N*-base, like morpholine, pyrrolidine, piperidine, betaine and imidazole.



Anion = Cl^-; HSO_4^-; NO_3^-; $H_2PO_4^-$; SO_4^{2-}; $CF_3CO_2^-$; BF_4^-

Scheme 1. Protic cations used in combination with the reported anions to obtained Brønsted acidic ILs.

Here, we report on the application of these salts (some of them have melting points higher than 100 °C and, consequently, cannot be defined ILs) in esterification and transesterification reactions proving a simple, sustainable and effective method to prepare and isolate esters. In particular, they have been tested in esterification of acetic acid with butanol, octanol and methyl-*β*-D-glucopyranoside. In all the investigated reactions, $[HPyrr][HSO_4]$ (followed $[HPip][HSO_4]$ and $[Hmim][HSO_4]$) was found to be the best catalytic environment suggesting that cation structure and counteranion acidity have an important role in the process. A quite good correlation between IL acidity (H_0) and catalytic ability has been found although the capability of these media to bind water and give a biphasic system with the formed ester surely favour the shift of the esterification reaction towards products, contemporaneously favouring ester recover. Finally, the same acidic salts were also tested in the transesterification of ethyl *trans*-cinnamate with methanol and octanol. Also in this case, the non-corrosive [HPyrr][HSO$_4$] gave the best results among all.

Experimental

Materials and Methods

Chemicals, including *N*-methylimidazole, *N*-methylmorpholine, *N*-methylpyrrolidine, *N*-methylpiperidine, DABCO and betaine were purchased from Sigma-Aldrich with purities > 98%. *N*-Methylimidazolium hydrogen sulfate [Hmim][HSO$_4$], *N*-methylimidazolium sulfate [Hmim]$_2$[SO$_4$], *N*-methylimidazolium dihydrogen phosphate [Hmim][H$_2$PO$_4$], *N*-methylimidazolium trifluoroacetate [Hmim][CF$_3$CO$_2$], *N*-methylimidazolium nitrate [Hmim][NO$_3$], *N*-methylimidazolium chloride [Hmim]Cl, *N*-methylmorpholinium hydrogen sulfate [HMor][HSO$_4$], *N*-methylmorpholinium sulfate [HMor]$_2$[SO$_4$], *N*-methylmorpholinium chloride [HMor]Cl, *N*-methylpiperidinium hydrogen sulfate [HPip][HSO$_4$], *N*-methylpiperidinium sulfate [HPip]$_2$[SO$_4$], *N*-methylpyrrolidinium hydrogen sulfate [HPyrr][HSO$_4$], *N*-methylpyrrolidinium chloride [HPyrr]Cl, betaine chloride ([Bet]Cl), betaine nitrate ([Bet][NO$_3$]), betaine hydrogensulfate ([Bet][HSO$_4$]) and betaine tetrafluoroborate ([Bet][BF$_4$]) were prepared by addition dropwise of an equimolar amount of the proper acid to the selected base or zwitterion. The mixtures were stirred for 4 to 5 h at 60°C to ensure that all of the bases are reacted. Then, water was removed at reduced pressure to obtain a colorless viscous liquid or a solid.

N-methylimidazolium hydrogen sulfate [Hmim][HSO$_4$] m.p. 39 °C: ^{1}H NMR (250 MHz, D$_2$O δ, ppm) 3.21 (s, 3H, CH_3N-); 6.77 (s, 2H, aromatic); 7.97 (s, 1H, aromatic). ^{13}C NMR (63 MHz, DMSO-d$_6$, δ ppm) 34.27, 118.18, 121.83, 134.18.

N-methylimidazolium sulfate [Hmim]$_2$[SO$_4$], hygroscopic white solid, m.p. 62 °C: ^{1}H NMR (250 MHz, DMSO-d$_6$, δ ppm) 3.77 (s, 3H, CH_3N); 7.22 (s, 1H, aromatic); 7.39 (s, 1H, aromatic); 8.33 (s, 1H, aromatic) 7.20 (br, 1H, N$^+$-H). ^{13}C NMR (63 MHz, DMSO-d$_6$, δ ppm) 34.02, 121.76, 123.67, 136.69.

N-methylimidazolium dihydrogen phosphate [Hmim][H$_2$PO$_4$] m.p. 137 °C: ^{1}H NMR (250 MHz, CDCl$_3$, δ ppm) 3.7 (s, 3H, NCH_3); 6.88 (s, 1H, aromatic), 7.35 (s, 1H, aromatic); 8.92 (s, 1H, aromatic; 9.87 (N$^+$-H).

N-methylimidazolium trifluoroacetate [Hmim][CF$_3$CO$_2$], hygroscopic white solid, mp 55 °C: ^{1}H NMR (250 MHz, CDCl$_3$, δ, ppm) 3.93 (s, 3H, NCH_3); 7.14 (s, 1H, aromatic), 7.35 (s, 1H, aromatic); 8.92 (s, 1H, aromatic); 9.87 (br N$^+$-H). ^{13}C NMR (63 MHz, CDCl$_3$, δ ppm): 35.8, 121.3, 122.1, 136.3; 162.1.

N-methylimidazolium nitrate [Hmim][NO$_3$], hygroscopic white solid, mp 67 °C: ^{1}H NMR (250 MHz, D$_2$O δ, ppm) 3.75 (s, 3H, NCH_3); 7.33 (s, 2H, aromatic), 8.46 (s, 1H, aromatic). ^{13}C NMR (63 MHz, coaxial tube at 70 °C, δ ppm): 35.2, 118.3, 122.1, 134.3.

N-methylimidazolium chloride [Hmim]Cl, hygroscopic white solid, mp 78 °C: ^{1}H NMR (250 MHz, CDCl$_3$, δ ppm) 3.5 (s, 3H, NCH_3); 6.82 (s, 1H, aromatic), 6.87 (s, 1H, aromatic); 8.54 (s, 1H, aromatic; 10.7 (N$^+$-H). ^{13}C NMR (63 MHz, coaxial tube, δ ppm): 35.2, 118.3, 122.1, 134.3.

N-methylmorpholinium hydrogen sulfate [HMor][HSO$_4$], hygroscopic white solid, mp 32 °C: ^{1}H NMR (250 MHz, D$_2$O, δ ppm) 2.85 (s, 3H, N$^+$CH$_3$); 3.20 (m, 2H, HCN$^+$); 3.46 (m, 2H, HCN$^+$); 3.80 (m, 2H, HCO); 4.09 (m, 2H, HCO).^{13}C NMR (63 MHz, D$_2$O, δ ppm) δ: 42.66; 52.60; 63.31.

N-methylmorpholinium sulfate [HMor]$_2$[SO$_4$], deliquescent white solid: ^{1}H NMR (250 MHz, D$_2$O, δ ppm) 2.90 (s, 3H, N$^+$CH$_3$); 3.20 (m, 2H, HCN$^+$); 3.53 (m, 2H, HCN$^+$); 3.80 (m, 2H, HCO); 4.09 (m, 2H, HCO).^{13}C NMR (63 MHz, D$_2$O, δ, ppm) δ: 42.60; 52.70; 63.42.

N-methylmorpholinium chloride [HMor]Cl, deliquescent crystals : ^{1}H NMR (250 MHz, D$_2$O, δ ppm) 2.93 (s, 3H, N$^+$CH$_3$); 3.20 (m, 2H, HCN$^+$); 3.50 (m, 2H, HCN$^+$); 3.80 (m, 2H, HCO); 4.09 (m, 2H, HCO).^{13}C NMR (63 MHz, D$_2$O, δ, ppm) δ: 42.66; 52.70; 63.38.

N-methylpiperidinium hydrogen sulfate [HPip][HSO$_4$], m.p. 32 °C: ^{1}H NMR (250 MHz, D$_2$O δ ppm): 1.2-1.7 (m, 6H); 2.74 (s, 3H, N$^+$CH$_3$); 2.85 (m, 2H); 3.38 (m, 2H).

N-methylpiperidinium sulfate [HPip]$_2$[SO$_4$], hygroscopic white solid: ^{1}H NMR (250 MHz, D$_2$O δ ppm): 1.2-1.7 (m, 6H); 2.74 (s, 3H, N$^+$CH$_3$); 2.85 (m, 2H); 3.38 (m, 2H).

N-methylpyrrolidinium hydrogen sulfate [HPyrr][HSO$_4$], m.p. 34 °C: ^{1}H NMR (250 MHz, D$_2$O, ppm): 3.36 (t, 2H, NCH_2), 2.76 (t, 2H, NCH_2), 2.62 (s, 3H, NCH_3), 1.85–1.73 (m, 4H, NCH$_2$$CH_2$).

N-methylpyrrolidinium chloride [HPyrr]Cl, m.p. 158-160 °C: ^{1}H NMR (250 MHz, D$_2$O, ppm): 3.30 (t, 2H, NCH_2), 2.75 (t, 2H, NCH_2), 2.60 (s, 3H, NCH_3), 1.85–1.73 (m, 4H, NCH$_2$$CH_2$).

Betaine hydrogen chloride ([Bet]Cl), m.p. 240 °C: ^{1}H NMR (250 MHz, D$_2$O, δ ppm): 3.28 (s, 9H, (CH_3)$_3$N$^+$); 4.26 (s, 1H, COOH); 4.85 (s, 2H CH$_2$). ^{13}C NMR (63 MHz, D$_2$O, δ ppm): 54.5, 64.0, 168.3.

Betaine nitrate ([Bet][NO$_3$]), highly hygroscopic white solid, m.p 128 °C: ^{1}H NMR (250 MHz, D$_2$O, δ ppm): 3.28 (s, 3H, (CH$_3$)$_3$N$^+$); 4.25 (s, 1H, COOH); 4.85 (s, 2H, CH$_2$). ^{13}C NMR (63 MHz, D$_2$O, δ ppm): 54.5, 64.2, 171.2.

Betaine hydrogen sulfate ([Bet][HSO$_4$]) m.p. 148 °C: ^{1}H NMR (250 MHz, D$_2$O, δ ppm): 3.28 (s, 3H, (CH$_3$)$_3$N$^+$); 4.25 (s, 1H, -COOH); 4.85 (s, 2H, CH$_2$). ^{13}C NMR (63 MHz, D$_2$O, δ ppm): 54.5, 64.0, 171.3.

Betaine tetrafluoroborate ([Bet][BF$_4$]), m.p. 200 °C: ^{1}H NMR (250 MHz, DMSO-d$_6$, δ ppm): 3.19 (s, 3H, (CH$_3$)$_3$N$^+$); 4.29 (s, 2H, CH$_2$). ^{13}C NMR (63 MHz, D$_2$O, δ ppm): 53.5, 63.0, 166.3.

Procedure for esterification of acetic acid with alcool (butanol or octanol)

Generally, to 1 g of the selected Brønsted acidic IL, 2 ml of the selected alcool (butanol or octanol) and 1 equivalent mole of acetic acid (Carlo Erba, 99.9%) were added. In the case of octanol, the reaction mixtures were heated for 4 h at 110°C. Then, products were separated just by decanting, when two layers were formed, or by extraction with ethyl ether. The crude reaction mixtures were analyzed by NMR and GC-MS. With some selected ILs, reactions were carried out also modifying temperature and time. Results are shown in Table 1 and 3.

Procedure for esterification of acetic acid with *β*-methyl-D-glucopyranoside

To 1.5 g of the selected Brønsted acidic ILs ([Hmim]Cl or [Hmim][NO$_3$] or [Hmim][HSO$_4$] or [Hmim][H$_2$PO$_4$]) 0.5 g (0.00258 moles) of *β*-methyl-D-glucopyranoside and 1.1

equivalent mole of acetic acid (Carlo Erba, 99.9%) were added. The reaction mixtures were heated for 4 h at 60°C. Then, products were extracted with ethyl ether and, after solvent evaporation at reduced pressure, the crude reaction mixtures were analyzed by NMR. Results are reported in Table 4.

Procedure for transesterification of ethyl *trans*-cinnamate.

Transesterification using methanol

To 1 g (0.00567 moles) of ethyl *trans*-cinnamate 3 equivalents of methanol and an equimolar amount of the selected Brønsted acidic IL ([HPyrr][HSO_4], [Hmim][HSO_4], [Bet][H_2SO_4], [HMor]Cl and [HPip][HSO_4]) were added and the reaction mixtures were heated at 90°C for 30 h into a reactor fitted with a reflux condenser. After stopping, the products were extracted with ethyl ether and, after solvent evaporation at reduced pressure, the crude reaction mixtures were analyzed by NMR. Results are reported in Table 5.

Transesterification using octanol

To 1 g (0.00567 moles) of ethyl *trans*-cinnamate equimolar amounts of octanol as well as equimolar amounts of the selected Brønsted acidic ILs ([Hmim][HSO_4](1:1) and [Hmim][HSO_4](1:1.1)) were added. After stopping the reaction, products were extracted with ethyl ether and, after solvent evaporation at reduced pressure, the crude reaction mixtures were analyzed by NMR. Results are reported in Table 6.

Determination of IL Brønsted acidity

The Brønsted acidity of some selected ILs was evaluated from the determination of the Hammett functions (H_0) by UV-visible spectroscopy. Standard solutions of ILs (200 mmol/L) and 4-nitroaniline (0.2 mmol/L) in water were prepared and the UV-vis spectra were recorded at 25 °C both in the absence (1.5 ml of dye solution mixed with 1.5 ml water) and in the presence of IL (1.5 ml of dye solution mixed with 1.5 ml of IL solution). The values of H_o have been calculated based on the intrinsic pK_a of the indicator (4-nitroaniline) in water and the molar ratio of protonated and unprotonated dye [I]/[IH^+] using the following equation:

$$H_o = pK(I)_a + \log([I]/[IH^+])$$

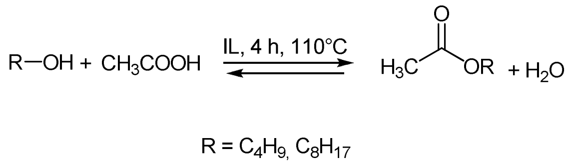
According to Lambert–Beer's Law, the value of [I] and [HI^+] were calculated from the UV–vis spectra, on the basis of the absorbance values at 380 nm (absorption maximum).

Corrosion test

A stainless steel plate with 46 mm length, 12 mm width and 0.5 mm thickness (previously polished, cleaned and dried to constant weight) was completely immersed in the IL (*ca.* 15 g) contained in a suitable tube and maintained at 85 °C for 24 h. At the end of the process, the stainless steel sheets were took out of the IL, washed in water, dried and weighted. The corrosiveness of stainless steel plates by the ILs was calculated from the mass loss and the exposing surface area. The results of corrosion tests are summarized in Table 2.

Results and Discussion

Several imidazolium, morpholinium, pyrrolidinium, piperidinium dabco and betaine based Brønsted acidic ILs were used as solvents and catalysts in esterification and transesterification reactions (Scheme 1, not all of them were used in each reaction).



Scheme 2. Fischer esterification of acetic acid.

Preliminary experiments were carried out at 110°C, working with a 1:1 molar ratio of octanol and acetic acid (Scheme 1) and using *ca.* 1 g of the selected IL, the solvent-catalyst loading being around 60% w/w (based on the mass of octanol) corresponding to the IL/octanol molar ratios % reported in Table 1. To assess the catalytic ability of the selected ILs conversions were evaluated by NMR. Data are reported in Table 1. Experiments carried out at shorter reaction times showed that 4 hours assured equilibrium conditions, at least in the case of the more efficient media.

Table 1. Esterification of acetic acid with octanol, conversions and yields after 4 h at 110°C

Entry	IL	IL/alcool (%)	Ester : alcohol[a]	Recovered material (%)
1	[Hmim][HSO_4][b]	46	76:24	83
2	[Hmim][HSO_4]	46	82:18	85
3	[Hmim][HSO_4]	25	80:20	82
4	[HMor][HSO_4]	42	80:20	85
5	[HPyrr][HSO_4]	45	92: 8	95
6	[HPip][HSO_4]	42	88:12	87
7	$[HPip]_2[SO_4]$	30	55:45	63
8	$[HMor]_2[SO_4]$	28	41:59	68
9	$[Hmim]_2[SO_4]$	32	20:80	63
10	[Hmim][H_2PO_4]	46	21:79	83
11	[Hmim][NO_3]	48	62:38	65
12	[HPyrr]Cl	60	24:76	81
13	[Hdabco]Cl	55	20:80	75
14	[HMor]Cl	60	34:66	55
15	[Hmim][CF_3CO_2]	42	43:57	85
16	[HBet]Cl	54	85:15	85

[a] Determined by NMR. [b]Reaction carried out at 75 °C.

No by-product arising from side reactions has been detected in all the examined reactions. In the case of [Hmim][HSO_4], experiments were also carried out at 75 °C and varying IL loading from 60% w/w to 30% w/w (Table 1, entries 1-3). A moderate effect of the temperature and an extremely low effect of IL loading was observed. Similar results were also obtained in the case of [HPyrr][HSO_4] and [HPip][HSO_4] showing that, at least with these highly active systems, lower amounts of IL can be sufficient.

It is noteworthy that for all ILs having HSO_4^-, SO_4^{2-}, NO_3^- and $H_2PO_4^-$ as counteranion, after the stopping of the reactions, when the temperature was brought to room conditions, two phases were formed (Figure 1); the lower phase was constituted by the IL and water and the upper layer by the formed ester and unreacted alcohol. This latter could be easily separated from the IL by simply decanting into another flask. A product recover (ester and eventually unreacted alcohol) higher than 80% characterized ILs having as counteranion HSO_4^- and $H_2PO_4^-$. Since this procedure gave lower recovers in the case of SO_4^{2-} and NO_3^- based ILs (ranging from 50-60%) for these latter catalytic systems product extraction with ethyl ether was also applied, a moderate increase in product recover was observed. In all examined cases, the IL (lower layer) could be dried under reduced pressure to remove the water formed during the esterification process and eventually recycled.

In the case of [Hdabco]Cl and [HPyrr]Cl, since at room temperature the reaction mixture was practically an unique solid phase enclosing the reaction product, ethyl ether was used to recover the product. On the other hand, another situation characterized the same process in [HMor]Cl; at room temperature the IL solidified and formed the lower layer whereas the ester constituted the upper liquid layer. Hence, the solvent-free separation could be applied also in this case.

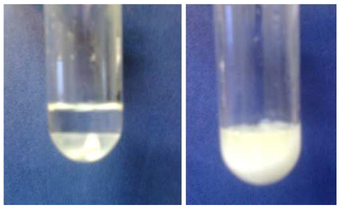


Figure 1. Situation at the end of reaction. Left: Two different layers are formed. Top layer (ester + unreacted alcohol) lower layer (IL + water formed during the reaction). Right (reaction in [Hdabco]Cl: just one solid layer was formed.

On the basis of the data reported in Table 1 it is possible to establish that the catalytic activity of the investigated Brønsted acidic ILs follows the order: [HPyrr][HSO_4] > [HPip][HSO_4] > [HBet]Cl > [Hmim][HSO_4] > [HMor][HSO_4] > [Hmim][NO_3] > $[HPip]_2[SO_4]$ > [Hmim][CF_3COO] > $[HMor]_2[SO_4]$ > [HMor]Cl > [HPyrr]Cl > [Hmim][H_2PO_4] >$[Hmim]_2[SO_4]$ = [Hdabco]Cl. The Brønsted acidic ILs having hydrogen sulfate as the counteranion give the best results: [HPyrr][HSO_4] is able to assure up to 92% of conversion in four hours at 110 °C with a product recover higher than 95%. On the other hand, Brønsted acidic ILs having the unprotonated sulfate as anion give significantly lower conversions. This behavior suggests that the presence of a sufficiently acidic proton on the anionic component of the IL plays an important role in the activation of the reaction. About this, it is noteworthy that when [Hmim][H_2PO_4] was used as catalyst and solvent only very low conversions were obtained (21%) suggesting a lower acidity of the $[H_2PO_4]^-$ protons with respect the acidic proton of $[HSO_4]^-$ also in the non aqueous environment charactering neat ILs.

On the other hand, only a moderate conversion was observed in [Hmim][NO_3] and [Hmim][CF_3CO_2], 62% and 43% respectively, whereas the Brønsted acidic ILs having Cl^- as counteranion gave lower conversions; the ester percentages ranged from 20 to 34%. The stronger interactions between cations and anions in ILs bearing highly coordinating anions (such as chloride and trifluoroacetate)[10] probably reduce the ability of IL cation to act as a catalyst although the role of other factors (such as water binding ability) cannot be excluded.

An evaluation of the role of the IL acidity in this reaction was performed determining the Hammett acidity functions (H_o) of seven ILs which give significantly different conversions under comparable conditions.

Table 2. Acidity (H_o) and corrosiveness of stainless steel by Brønsted acidic ILs

ILs	H_o	Corrosiveness[a] (mg/cm^2)
[Hmim][HSO_4]	1.93	0.08
[HPip][HSO_4]	1.58	0.05
$[Hmim]_2[SO_4]$	2.87	0.07[b]
[Hmim][H_2PO_4]	2.55	0.03
[Hmim][NO_3]	2.22	0.06
[Hmim][CF_3CO_2]	~3[b]	0.01
[Bet]Cl	1.47	ND

[a] The stainless steel sheets were polished, cleaned and dried to constant weight, then fully immersed in the same amount of IL (15g). After 24 h at 85 °C, the stainless steel sheets were took out of the IL, washed in water, dried and weighted. Being this IL a solid, having a high melting point, the experiment was carried out in the presence of 5% of water. [b] The absorbance change was too small to obtain a significant value.

The H_o values, reported in Table 2, were measured spectrophotometrically determining the protonation of an uncharged indicator (4-nitroaniline) in water in terms of the measurable ratio of $[I]/[IH^+]$. From the data reported in Table 2 the acidity decreases in the following order, [HBet]Cl > [HPip][HSO_4] > [Hmim][HSO_4] > [Hmim][NO_3] > [Hmim][CF_3CO_2] > $[Hmim]_2[SO_4]$ > [Hmim][H_2PO_4]. The strongest acids ([HBet]Cl, [HPip][HSO_4], [Hmim][HSO_4]) gave the highest yields, whereas considerably lower conversionswere achieved using ($[Hmim]_2[SO_4]$ and [Hmim][H_2PO_4]), which are the lowest acids.

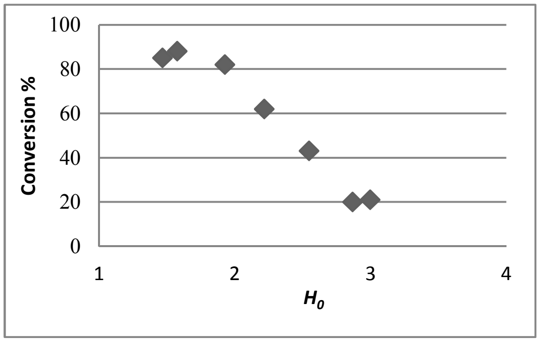


Figure 2. Relation between IL acidity (H_o) and conversion of acetic acid esterification with octanol

As previously observed,[11] the acidity of Brønsted acidic ILs in water, as well as in other polar solvents, depends on anion and

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cation nature: a fairly good correlation between the strength of the acid and the conversion (%) can be evidenced (Figure 2).

However, the deviations from a linear behavior characterizing the plot of Figure 2 suggest that the acidity of these media is not the sole factor affecting the efficiency of the process. Probably, as previously suggested[6h] in a recent paper, when the IL is used as in this study in a relevant amount its ability to bind the formed water and contemporaneously to give a biphasic system with the formed ester can shift the equilibrium towards products, increasing the process efficiency.

Finally, it is to note that when a task-specific ammonium-based salt, [HBet]Cl, bearing a carboxy group on the alkyl chain has been used, despite the presence of chloride as counteranion, a conversion comparable to that found in $[HSO_4]^-$ based ILs was obtained; the presence of the acidic group (–COOH) on cation is able to assure the catalytic effect. Although in principle the carboxylic group on IL could be esterified, probably the presence of the adjacent positive charge reduce this ability: no transformation on IL has been detected by NMR analysis. It is also to note that, since this IL is a high melting point solid and the product is not soluble in this medium it has been possible to recover the formed ester through a simple decanting procedure. [HBet]Cl may therefore represent a valid alternative to the other protic Brønsted acidic ILs.

On the other hand, since the best results were obtained using $[HPyrr][HSO_4]$, this IL has been selected for recycling experiments. After three recycles, conversion decreased from 92% to 85%, although the recovery of the product by simple decantation of the upper phase becomes less efficient (from 85% to 70%).

$[HPyrr][HSO_4]$ was also used as test solvent and catalyst for the esterification of acetic acid with butanol. Considering the lower boiling point of butanol, the reaction was initially carried out at four different temperatures ranging from 85 - 100 °C by working with a 1:1 molar ratio of butanol - acetic acid and an IL loading of 60% w/w (based on the mass of butanol). To evaluate the catalytic ability of the different ILs, reactions were stopped after 2-4 h and the conversions were evaluated by NMR. On the basis of these data, we decided that a temperature between 80-90°C and 2 h of reflux might represent the best conditions to evaluate the efficiency of acidic ILs in this reaction having practically reached the equilibrium.

Table 3. Esterification of acetic acid with butanol, conversions and yields after 2 h at 85°C [a]

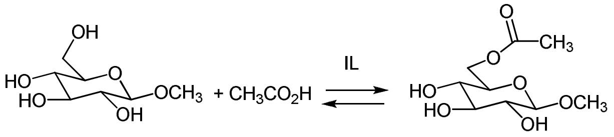
Entry	IL	IL/alcool (%)	Ester : alcohol[b]
1	$[HPyrr][HSO_4]$	24	90:10
2	$[HPip][HSO_4]$	23	75:25
3	$[Hmim][HSO_4]$	25	88:12
4	[HBet]Cl	29	85:15
5	$[HBet][HSO_4]$	21	79:21
6	$[HBet][NO_3]$	25	67:33
7	$[HBet][BF_4]$	22	65:35

[a] Yields of the recovered product (ester + unreacted alcohol) by decantation ranged around 85-90%. [b] Determined by NMR.

Therefore, the same conditions were applied to test the Brønsted acidic ILs reported in Table 3, which have been found to give the higher conversions in octyl acetate synthesis. In these media, at the end of the reaction also in the case of butyl acetate synthesis two phases were obtained and product was recovered simply by upper phase separation.

Once again, $[HPyrr][HSO_4]$ assured the higher conversion although comparable values were also obtained in $[Hmim][HSO_4]$ and [HBet]Cl. Nevertheless, recycling experiments confirmed the possibility to carry out at least three consecutive processes in these ILs without significant reduction in conversion.

The selectivity of the esterification reaction was checked using a more complex alcohol, methyl-*β*-D-glucopyranoside, a gluco-derivative characterized by a primary hydroxyl group and three secondary equatorial hydroxyl groups. As a consequence of the low solubility of the substrate in most of the synthesized acidic ILs the reactions were conducted at a lower reagent concentration (around 1.5 M) only in the ILs reported in Table 4. The behavior of the reaction was checked stopping the esterification at prefixed times (1, 2 and 4 h and eventually longer). The reaction mixtures were extracted with ethyl ether (extraction yield higher than 75%) and product distribution was analyzed by NMR.



Scheme 3. Esterification between methyl-*β*-D-glucopyranoside with acetic acid

In all investigated ILs, the reaction occurred with a high regioselectivity: only the acetyl derivative arising from esterification of primary hydroxyl group on C(6) was detected besides the unreacted product, conversions at different reaction times are reported in Table 4.

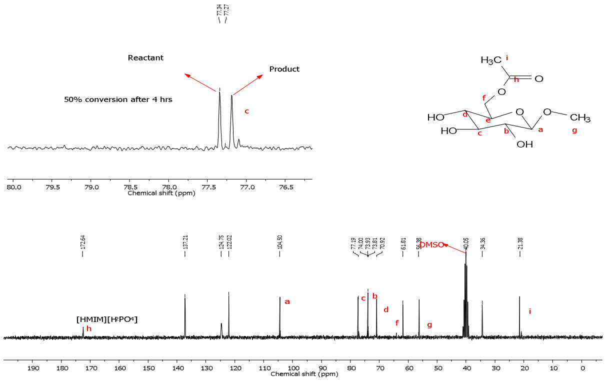


Figure 3. ^{13}C NMR of the crude reaction mixture arising from acetylation of methyl-β-D-glucopyranoside.

Table 4. Esterification of acetic acid with methyl-*β*-D-glucopyranoside[a]

ILs	1 h	2 h	4 h
[Hmim]Cl	NR	NR	NR
$[Hmim][NO_3]$	36%	50%	30%
$[Hmim][HSO_4]$	-----	60%	70%
$[Hmim][H_2PO_4]$	------	40%	50%

[a] Conversions were determined by NMR.

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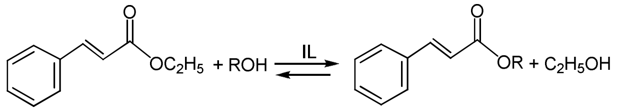
It is to note that in the case of [Hmim][NO_3] a decrease in conversion on increasing the reaction time from 2 to 4 h was observed. This peculiar behavior has to be attributed to the nature of [Hmim][NO_3] which, probably less than [Hmim][HSO_4], is able to "capture" the produced water. It is to note that in this case the product is soluble in the ionic liquid and the presence of increasing amounts of free-water after a given conversion (the water coordination ability of the nitrate anion is not infinite!), may favor the hydrolysis process and shift the equilibrium position towards reagents. It is noteworthy that also in this reaction the higher conversion was obtained in the IL having hydrogensulfate as counteranion, [Hmim][HSO_4]. Finally, attempts to increase the conversion prolonging the reaction beyond 4 h failed due to the formation of relevant amounts of polyacetylation products.

In this study also the possibility to use Brønsted acidic ILs in transesterification processes was checked investigating the reaction of ethyl *trans*-cinnamate with a small alkyl-chained alcohol (methanol) and with a longer alkyl-chained alcohol (octanol). Initially, the reaction with methanol was investigated in [HPip][HSO_4] and temperature and reaction time were varied to find the best conditions.



Scheme 4. Transesterification of ethyl *trans*-cinnamate

Practically, no reaction occurred, even after 24 h, until the temperature was raised to 90°C. Since, at this temperature we could not exclude that the moderate conversion (50%) was at least partially due to the volatility of methanol the reaction was carried out also using an excess (3 equivalents) of this reagent: conversion increased at 73%. The efficiency of other acidic ILs was also tested at 90 °C. Results are reported in Table 5.

Table 5. Transesterification of ethyl *trans*-cinnamate with methanol in various ILs[a]

Entry	IL	Conversion %	Recovered material %
1b	[HMor]Cl	NR	0
2c	[HMor]Cl	NR	0
3b	[HBet][HSO_4]	NR	0
4c	[HPyrr][HSO_4]	95	95
5b	[Hmim][HSO_4]	37	87
6b	[Hmim][HSO_4][b]	75	92
7b	[HPip][HSO_4]	73	90

[a] All the reactions were carried out at 90°C for 28 h. [b] In this experiment 1.1 equivalent of acid with respect to the nitrogen base was used to prepare [HPyrr][HSO_4].

Whereas no reaction was observed in chloride based ILs, also working with an excess of alcohol, conversions ranging from 40 to 95% characterized reactions performed in hydrogensulfate-based ILs. The best results were obtained, also for the transesterification process, in [HPyrr][HSO_4]. It is also noteworthy that, in particular in [Hmim][HSO_4] a significant increase in conversion was obtained working in the presence of a small excess of H_2SO_4, probably as a consequence of the superacidic behavior of species of the type, A---H-A^-, which should be present in the reaction mixture.

When the transesterification process of ethyl *trans*-cinnamate in [Hmim][HSO_4] was carried out using octanol, and an 1:1 molar ratio ester : alcohol, lower conversions were obtained under comparable conditions. However, the presence of a small excess of inorganic acid (H_2SO_4) significantly increased the conversion also in this case (Table 6).

Table 6. Transesterification of trans-ethyl cinnamate with octanol in various Brønsted acidic ILs[a]

Entry	Time (h)	Temp. (°C)	IL	Conversion %
1	5	80-90	[Hmim][HSO_4]	NR
2	38	75	[Hmim][HSO_4]	35
3	30	90	[Hmim][HSO_4]	25
4	30	90	[Hmim][HSO_4][b]	52

[a] The molar ratio of the ester and alcohol was 1:3. [b] In this case 1.1 eq of acid was used to prepare [HPyrr][HSO_4]. NR=no reaction

Finally, corrosive tests were carried out with six ILs using stainless steel plates and determining the weight loss after complete immersion in the selected ILs for 24 h at 85°C. The results (Table 2) showed that all the investigated ILs are practically noncorrosive media, in agreement with recent studies performed on analogous ILs.[6h,12]

Conclusions

In conclusion, these data show that the water scavenging nature of many Brønsted acidic ILs and the insolubility of many esters in these media strongly affect the catalytic efficiency of these salts in esterification and transesterification reactions. In both cases, protic ILs bearing Brønsted acidic onium (pyrrolidinium) or imidazolium cations, associated with the "acidic" [HSO_4]$^-$ anion, gave the highest yields. In the case of esterification of acetic acid with octanol and butanol a high conversion was also obtained using a task-specific ammonium-based IL, [HBet]Cl, bearing an acidic group (–COOH) on the alkyl chain. Nevertheless, acetylation of a relatively complex alcohol, such as methyl-β-D-glucopyranoside, in Brønsted acidic ILs occurs with high regioselectivity: only the acetyl derivative arising from esterification of the primary hydroxyl group on C(6) was detected, beside the unreacted product (30%), when the reaction was performed in [Hmim][HSO_4]. Finally, the improved catalytic ability of the 1:0.1 [Hmim][HSO_4]-H_2SO_4 mixture in the transesterification reaction, probably as a consequence of the superacidic behavior of species of the type, A---H-A^-, has been evidenced.

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Notes and references

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