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Efficient Combination of Recyclable Task Specific Ionic Liquid and Microwave Dielectric Heating for the Synthesis of Lipophilic Esters

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Abstract:

Mild and efficient esterification reactions of carboxylic acids with *neo*-pentanol were carried out using task-specific ionic liquids with hydrogen sulphate counteranion under microwave irradiation. The latent acidity of the ionic liquid was introduced by anion metathesis from hydrogen sulphate with the corresponding imidazolium or pyridinium halides. The catalyst [C_4-mim][HSO_4] modified with 5% of concentrated sulfuric acid was reused three times without considerable loss of activity in esterification using classical heating in oil bath.

Introduction

Ionic liquids (Ils) are ionic solvents that combine the advantages of both traditional molecular solvents and melt salts, are considered as promising new reaction media, and have found wide use in catalytic and noncatalytic reactions.[1] Not only can these useful materials dissolve many organic or inorganic substances, but they are also readily recycled. The interest in Ils is also a direct result of the diverse properties of these liquids and the way in which they may be systematically varied, e.g., the density, viscosity, and water miscibility. Since they also have effectively zero vapour pressure, this makes them ideal engineering solvents for reactive chemistry, allowing direct distillation of solutes from the solvent and simple solvent recycling without the production of volatile organic compounds[2] (VOCs).

In 1999, Davis, Jr. et al. introduced the term "task-specific ionic liquids" (TSILs) to describe IL which incorporate functional groups designed to confer particular properties or reactivities.[3] More recently, the same group described TSIL in which the cations were both intrinsically Brønsted acidic and nonvolatile.[4] This was done by covalently tethering an alkane sulfonic acid group to the IL cation.[5] The use of TSIL sulfonic acids to catalyze organic reactions is an area of ongoing activity, and these new catalysts were used as dual solvent−catalyst for Fisher esterification,[6] alcohol dehydrodimerization,[4] pinacol/benzopinacol rearrangements,[7] and electrophilic substitution of indoles with aldehydes.[8] With the TSIL sulfonic acids, it was observed in Fisher esterification reactions that the systematic introduction of a fixed quantity of water into the system resulted in higher ester yields.[6] Another approach for the acidic TSILs is to introduce the latent acidity in the counteranions. Our initial studies[9] involving the esterification of acetic acid with various alcohols by utilizing TSIL[10] with acidic counteranion revealed that the produced esters were not dissolved in these TSILs and were isolated in high yields with high purity. Using the same Brønsted acidic ILs, Jiang and Han have investigated their catalytic activity in Mannich reactions.[11] Central to our understanding of alternative viable protocols using IL technology was the role of the medium in organic processes. Accordingly, we report our continued studies using Brønsted acidic TSIL technology for several classical acid-promoted organic reactions under microwave dielectric heating.[12] The model reaction screened was Fisher esterification for the preparation of lipophilic esters.

Results and Discussion

Preparation of Acidic TSILs by Anion Metathesis. The general syntheses of ILs based on nitrogen-containing heterocycles involve a two-step process, whereby an organic halide salt is formed via alkylation using an haloalkane. The quaternization reaction is followed by a metathesis reaction using an alkali metal salt or by anion exchange using acid addition, e.g. concentrated sulphuric acid (97%). For this study, the following acidic TSILs were used: 1-butyl-3-methyl-imidazolium hydrogen sulphate ([C_4mim][HSO_4]), 1-hexyl-3-methyl-imidazolium hydrogen sulphate ([C_6mim][HSO_4], and *N*-butylpyridinium hydrogen sulphate ([C_4py][HSO_4]) (Scheme 1).

The preparation of the starting [C_4mim][Cl], [C_6mim][CI], and [C_4py][Cl] were realized via conventional heating methods[13] in refluxing solvents (or using solvent-free conditions) with the appropriate reaction temperature; the major

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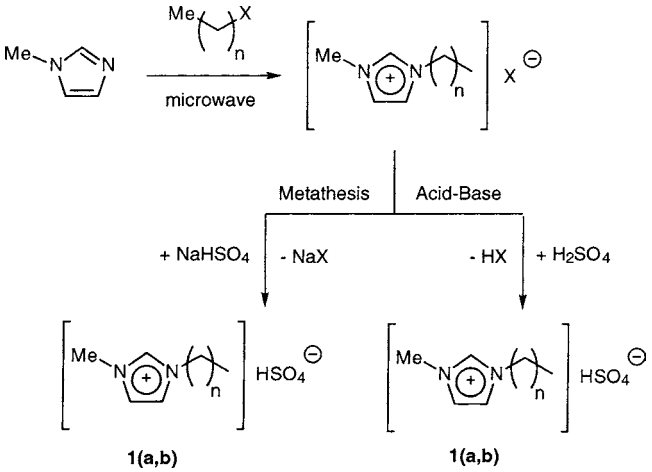
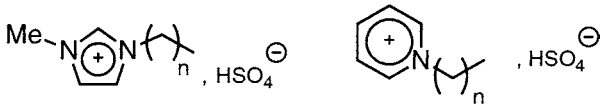
Scheme 1. **General preparation of acidic imidazolium based ionic liquids by metathesis or by acid−base**



drawbacks of these common methods are the long reaction time ([C_4mim][Cl] and [C_6mim][CI] = 4 days, [C_4py][Br] = 6 days) to afford good yields (96−97%) and also the use of excess irritant, volatile alkyl halides (1.5 equiv)/organic solvent as reaction medium. In view of our general interest in solventless organic synthesis mediated by microwave dielectric heating[14] ($\mu\omega$) the preparation of the 1,3-dialkyl imidazolium chloride and butyl pyridinium bromide have been realized according to a method previously developed in our laboratory[15] using a monomode microwave[16] reactor (Synthewave 402[17]). For the anion exchange using concentrated sulphuric acid[18] (97%), the main disadvantage of this procedure is the necessity either to minimize or, even better, to eliminate waste generation during the synthesis: (i) the large volume of HCl by-product formed during the anion exchange, (ii) the difficulties to eliminate completely the HCl impurities trapped in the ionic liquid product, (iii) and the long reflux time to remove the HCl by-product (from 48 to 72 h). For the anion exchange, the corresponding coordinating anion used was HSO_4 from the commercially available starting salt $NaHSO_4$. All the anion metathesis reactions were carried out in dry acetonitrile and stirring at room temperature under nitrogen for 3 days with conventional glassware. Then the insoluble salt (NaCl or NaBr) was filtered off and then dissolved in deionized water. The efficiency of the metathesis reaction was determined by measuring the chloride or bromide ion solution using the Mohr method.[19] After filtration of the crude reaction mixture on a pad of Celite to remove halide waste trapped in the TSIL, followed by evaporation of MeCN in vacuo, the acidic TSILs were isolated in high yields as mobile oils at room temperature. Then the acidic TSILs were dried under high vacuum at 80 °C for 6 h without decomposition.

Table 1. **Results for the preparation of acidic TSILs 1(a−c) by anion metathesis with $NaHSO_4$**



cmpd	*n*	TSIL	yield of **1** (%)[a]
1a	3	[C_4mim][HSO_4]	97
1b	5	[C_6mim][HSO_4]	94
1c	3	[C_4py][HSO_4]	96

[a] Yield of isolated product.

Ionic liquids containing halide contaminants are problematic since the halide content can seriously affect the usefulness of the TSIL as a catalyst for a given chemical reaction. In general, the presence of chloride or bromide ions increases the viscosity and decreases the density of ILs.[20] Usually, ILs can be easily washed to a point where no traces of halide ions are detectable in the washing water (by titration with $AgNO_3$ or by ion chromatography[21]). In our case, the halide-free preparation of [C_4mim][HSO_4], [C_6mim][HSO_4], and [C_4py][HSO_4] are significantly difficult because these acidic TSILs are completely miscible with water and cannot be extracted from aqueous solution with organic solvents, and removal of the halide ions by a washing procedure with water is not a suitable option. The halide impurities of acidic TSILs were evaluated by volumetric titration using Volhard's method (halide < 100 ppm). In this case, the acidic TSILs **1(a−e)** contain amounts of the alkali salts (80 < halide < 100 ppm), but we consider that this may not be a problem for catalytic applications in Fisher esterification. The efficiency of the anion metathesis was determined by measuring the HSO_4 ion content solution using volumetric titration with commercial NaOH solution and phenolphthalein as end-point indicator. Results of the synthesis of the free acidic TSILs using this procedure are outlined in Table 1 and were prepared on medium scale (up to 20 g) in good yields (94−96%).

Fisher Esterification Reaction with Acidic TSILs 1(a−c). For the beginning of this study, the acid and the alcohol employed were propanoic acid, **2a**, and *neo*-pentanol, **3**. The reactions were carried out in a magnetically stirred glass reactor (capacity: 25 cm^3) fitted with a reflux condenser and a thermometer. The outlet of the reflux condenser was connected to a constant pressure of dry nitrogen gas, and the reactor was kept in a thermostated oil bath at 80 °C. Alcohol **3** and acid **2a** were successively added to the IL catalyst (**1a**, [C_4mim][HSO_4], or **1c**, [C_4py][HSO_4]) previously placed in the glass reactor, and the reaction progress was conveniently monitored by ^{1}H NMR spectroscopy. For comparison, some esterification reactions were also realized in [C_4mim][HSO_4] in the presence of H_2SO_4. The former

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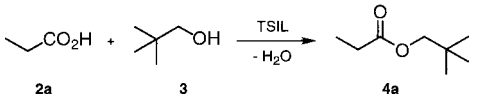
Table 2. **Results of esterification reactions of propanoic acid 2a[a] with *neo*-pentanol 3 at different reaction times in [C_4mim][HSO_4] or [C_4py][HSO_4] at 80 °C**



2a 3 4a

	3 conversion[b] (%) in	
reaction time (hour)	[C_4mim][HSO_4]	[C_4py] [HSO_4]
0.5	13	43
1	16	47
2	25	51
3	33	56
3.5	37	61
4	42	64
17	49	68
24	57	70

[a] Molar ratio of acid **2a**/alcohol **3**/TSI1 = 1/1/3. [b] Conversion of **3** into ester **4a** estimated by ^{1}H NMR (200 MHz in $CDCl_3$, TMS as internal reference).

reaction was carried out using the TSIL as catalyst in which H_2SO_4 was artificially added. The acidic content (HSO_4 with or without H_2SO_4) was measured by titration with sodium hydroxyde. Results of esterification reactions of **2a** with **3** in [C_4mim][HSO_4] or [C_4py][HSO_4] are outlined in Table 2.

As seen from the results of Table 2, the reaction rate in ionic liquid is dependent upon the ionic liquid chosen, and in this case, [C_4mim][HSO_4] gave a lower rate enhancement than [C_4py][HSO_4]. This suggests that the performance of the acidic ionic liquid catalyst is not dependent upon the butyl side chain of the cation, indicating the major impact of the cation on the catalytic performance. It is also possible that the better immiscibility of the resulting ester product **4a** with [C_4py][HSO_4] should facilitate the shift of the reaction equilibrium to the product side. The plausible mechanism for esterification is the following. The hydrogen sulphate counteranion of the acidic TSIL initiates the esterification by donating a proton to the carboxylic acid **2a** in step 1 (Scheme 2). After receiving the proton, the carboxylic acid **2a** becomes susceptible for a nucleophilic attack by the hydroxyl group of **3** (step 2), after which the reaction continues with water abstraction (step 3). The proton-donating step 1 is usually assumed to be rapid, while the nucleophilic substitution is slow. In the last step (step 4), the hydrogen sulphate counteranion is regenerated.

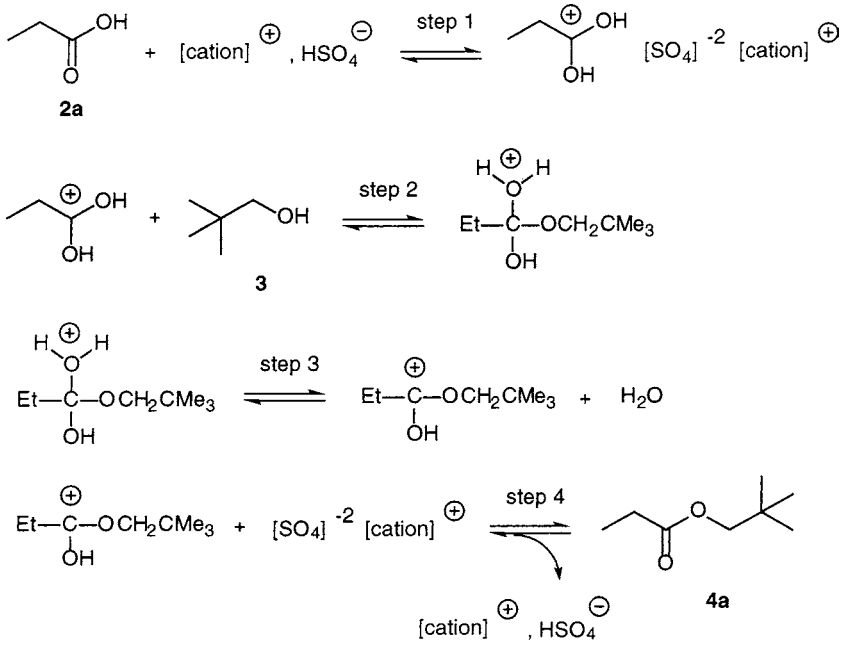
In the same manner, the properties of IL (polarity and electrostatic field of the cation) affect the esterification reaction considerably. It's noteworthy that at the end of the esterification reaction, the resulted ester **4a** is not soluble in the acidic TSIL catalyst. The upper layer contains the expected ester **4a** and could be separated from the TSIL catalyst in the bottom simply by decantation.

Esterification Reactions in Modified [C_4mim][HSO_4] with Concentrated H_2SO_4 and Recycling. Esterification reactions of propanoic acid **2a** and *neo*-pentanol **3** in modified [C_4mim][HSO_4] with various ratios of H_2SO_4/[C_4-mim][HSO_4] are shown in Table 3.

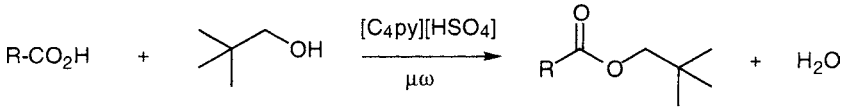
The experimental results indicate that the percentage of H_2SO_4 in [C_4mim][HSO_4] has an impact on the catalytic performance. For example, 50% of conversion was obtained after 30 min at 80 °C (entry 1) with 5% of concentrated H_2SO_4 in [C_4mim][HSO_4], and at the end of the reaction the produced ester **4a** is not dissolved in the modified [C_4mim]-[HSO_4] media. The catalytic performance of [C_4mim][HSO_4] for esterification was further increased with 15% of H_2SO_4 in acidic TSIL (entry 4) at same time, but at the end of esterification, the ester **4a** is partially soluble in the IL media, and traces of the *neo*-pentyl ether were detected after analysis of the bottom layer by ^{1}H NMR.

For economic reasons and comparison with traditional solvents used in esterification, easy recycling is an attractive

Scheme 2. **Mechanism of the esterification reaction between acid 2a, *neo-pentanol* 3 in acidic TSIL ([cation][HSO_4]) as catalyst**



Scheme 3. **Preparation of esters 4(a−d) from *neo*-pentanol 3 and acids 2(a−d) in [C_4py][HSO_4] as catalyst under microwave irradiation ($\mu\omega$)**



2(a-d) **3** **4(a-d)**

Table 3. **Esterification of propanoic acid 2a[a] with *neo*-pentanol 3 in [C_4mim][HSO_4] modified with concentrated H_2SO_4 after 30 min at 80 °C**

entry	% of H_2SO_4	**3** conversion (%)[b]
1	0	13
2	5	50
3	10	57
4	15	62

[a] Molar ratio of acid **2**/alcohol **3**/catalyst = 1/1/3. [b] Conversion of **3** into ester **4a** estimated by ^{1}H NMR (200 MHz in $CDCl_3$, TMS as internal reference).

Table 4. **Reuse of [C_4mim][HSO_4] modified with 5% of concentrated H_2SO_4 for esterification of propanoic acid 2a with *neo-pentanol* 3 into 4a[a]**

	conversion of alcohol **3a** in cycle:		
reaction time(h)	1	2	3
0.5	50	16	16
1	50	33	22
1.5	50	37	25
3	56	50	42
24	98	98	98

	yield of ester **4a** (%), after:				
cycle	1	2	3	4	5
decantation[b]	74	72	70	69	68
extraction[c]	21	19	20	21	21
global yield	95	91	90	90	89

[a] Conversion of **3** into ester **4a** estimated by ^{1}H NMR (200 MHz in $CDCl_3$, TMS as internal reference). [b] Yield of **4a** in the upper layer at the end of reaction after decantation at 25 °C (45 min.). [c] Yield of **4a** after elimination of the upper layer and washing of [C_4mim][HSO_4] with Et_2O.

property of the acidic TSILs. Consequently, we investigated the catalytic activity of recycled [C_4mim][HSO_4] modified with 5% of H_2SO_4 for esterification of propanoic acid **2a** with *neo*-pentanol **3**. As shown in Table 4, the catalyst (5% of concentrated H_2SO_4 in [C_4mim][HSO_4]) could be reused at least three times without loss of activity after 24 h for the conversion of alcohol **3** (cycle 1: 98%, cycles 2 and 3: 98%). Examination of the results in the bottom of Table 4 showed that the yield of isolated ester **4a** by decantation is 68−74% for the five cycles; one can conclude that reuse of the acidic TSIL catalyst (extraction of the soluble ester **4a** from the [C_4mim][HSO_4] layer by washing with diethyl ether followed by vacuum drying) plays an important role in terms of the catalytic activity of the acidic TSIL. After the fifth cycle, an 89% global yield for **4a** was observed.

Esterification Reactions in Acidic Ionic Liquid under Microwave Irradiations. The use of microwave ovens as tools for synthetic chemistry is a fast-growing area of research.[22] Since the first report of microwave-assisted organic synthesis (MAOS) by the groups of Gedye[23] and Giguere-Majestich[24] in 1986, the technique has been accepted as a method for reducing reaction times and for increasing isolated yields of products compared to times and yields with conventional methods. It is clear that the application of microwave technology to rapid synthesis would be of great value for the chemical community. At present, the application prospects of acidic TSIL coupled with microwave dielectric heating is evidenced by the growing number of paper detailing transformations using such a methodology.[25] For this esterification study under microwave, the acids employed were propanoic acid, **2a**, cyclohexane carboxylic acid, **2b**, 10-undecenoic acid, **2c**, phenyl acetic acid, **2d**, and the alcohol is *neo*-pentanol, **3** (Scheme 3).

The microwave instrument (Synthewave 402 reactor[26]) comprises a mono-mode (sometimes also called single-mode) microwave cavity that operates at a frequency of 2.45 GHz with continuous microwave irradiation power from 0 to 300 W. Inside the microwave cavity, the quartz reactor was exposed to microwave irradiations, and the reaction temperature was measured with the aid of an IR captor[27] (infrared thermometry) and software that enables on-line temperature/maximum temperature control by regulation of microwave power output.

The values presented in Table 5 were the optimized reaction conditions. Several experiments were performed at various powers and various reaction temperatures using solvent-free technique with a ratio of 1/1/3 acid **2**/*neo*-pentanol **3**/IL catalyst **1**, to find the most adequate reaction conditions under microwave dielectric heating (80 °C with [C_4py][HSO_4], Figure 1 for ester **4a**). As shown in Table 5 (entries 1−3), the [C_4py][HSO_4] catalyzes the esterification reactions efficiently with yields ranging from 89 to 95% and short reaction times (<3.5 h). Moderate reaction occurred when phenyl acetic acid **2d** was used (entry 4), indicating that the solubility of the starting material is also an important factor to determine the reactivity of acid using solvent-free methodology.

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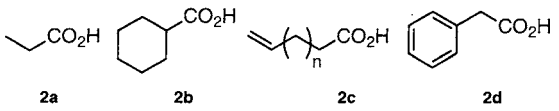
(27) Temperature measured by an IR captor: Prolabo, French Patent 622410, 14669 Fr, 1991.

Table 5. **Results for esterification of acids 2(a−d) with *neo*-pentanol 3 in [C_4py][HSO_4] under microwave dielectric heating at 80 °C**



2a 2b 2c 2d

entry	acid **2**[a]	yield of ester **4**[b] (%)	solubility[c]	reaction time[d] (h)
1	**2a**	95	Y/N	1.5
2	**2b**	90	Y/N	2.5
3	**2c**	89	Y/N	3.5
4	**2d**	40	N/N	4.5

[a] Molar ratio of acid **1a**/alcohol **2a**/catalyst = 1/1/3. [b] Yield of ester **3** at the end of reaction after decantation (45 min) at 25 °C. [c] Solubility of acid **1** and alcohol **2a** at the beginning of the reaction and solubility of the ester **3** at the end of the reaction in the acidic TSIL at 80 °C (Y = soluble and N = insoluble). [d] Reactions were run in the Synthewave 402 reactor (Prolabo) at 80 °C (Power = 75 W).

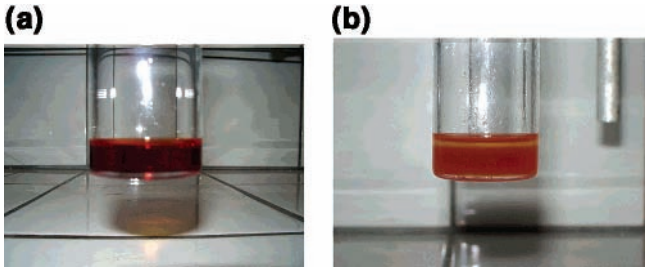


Figure 1. **Preparation of ester 4a from propanoic acid 2a (1 equiv) and *neo*-pentanol 3 (1 equiv) with [C_4py][HSO_4] (3 equiv) as catalyst in the Synthewave 402 reactor (Prolabo): (a) before microwave irradiation, 2a and 3 were soluble in the catalyst; (b) after microwave irradiation at 80 °C (1.5 h), the upper layer contained the expected ester 4a (95% yield) after decantation at 25 °C.**

In summary, the results obtained show that TSILs with acid counteranion coupled with microwave irradiation are suitable tools for esterification reactions using solvent-free experimental conditions. The major advantages of this methodology is that the expected esters were insoluble in the acidic TSIL (catalyst/solvent), and therefore they could be isolated simply by decantation with high yields. Furthermore, it is remarkable that the [C_4mim][HSO_4] modified with 5% of concentrated H_2SO_4 as catalytic system can be reused at least three times without significant loss of activity. The use of an easily accessible and recyclable acidic TSIL by anion metathesis in medium scale makes this procedure quite simple, more convenient, and environmentally benign. Further studies are directed now in our laboratory to the evaluation and the scope of acidic TSILs in pharmaceutical chemistry mediated by microwave technology.

Experimental Section

General. Thin-layer chromatography (TLC) was accomplished on 0.2-mm precoated plates of silica gel 60 F-254 (Merck). Visualisation was made with ultraviolet light (254 and 365 nm) or with a fluorescence indicator. IR spectra were recorded on a IRFT BIORAD 175C spectrophotometer. ^{1}H NMR spectra were recorded on BRUKER AC 300 P (300 MHz) and BRUKER ARX 200 (200 MHz) spectrometers, ^{13}C NMR spectra on BRUKER AC 300 P (75 MHz) spectrometer. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Data are given in the following order: δ value, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), number of protons, coupling constants J are given in Hertz. The mass spectra (HRMS) were taken respectively on a MS/MS ZABSpec TOF Micromass (EBE TOF geometry) at an ionizing potential of 8 eV for the acidic TSILs **1(a−c)** and on a VARIAN MAT 311 at an ionizing potential of 70 eV for the other compounds in the Centre Régional de Mesures Physiques de l'Ouest (CRMPO, Rennes). Reactions under microwave irradiations were realized in the Synthewave 402 reactor (Merck Eurolab, Div. Prolabo, France). Acetonitrile was distilled over calcium chloride after standing overnight and stored over molecular sieves (3 Å). Solvents were evaporated with a BUCHI R200 rotary evaporator. All reagents were purchased from Acros, Aldrich Chimie, Fluka France and used without further purification. The starting 1-butyl-3-methylimidazolium chloride [C_4mim][Cl], 1-hexyl-3-methylimidazolium chloride [C_6-mim] [Cl] and *N*-butyl-pyridinium bromide [C_4py][Br] were synthesized in large scale according to our previous method[15] under microwave dielectric heating.

Standard Experimental Procedure for the Preparation of Acidic TSILs 1(a−c) by Anion Exchange. *I-Butyl-3-methylimidazolium Hydrogen Sulphate [C_4mim][HSO_4]* ***(la).*** A mixture of 1-butyl-3-methylimidazolium chloride [C_4mim]-[Cl] (20 g, 114.5 mmol) and sodium hydrogen sulphate (13.74 g, 114.5 mmol) in dry acetonitrile (400 mL) was stirred vigorously at 25 °C under nitrogen for 4 days. After elimination of the precipitated salt (NaCl) on a filter paper, the resulting filtrate was quickly refiltered through a pad of Celite to remove some residual salt and finally concentrated by rotary evaporation to give a mobile liquid in 97% yield (26.2 g). The acidic ionic liquid [C_4mim][HSO_4] **1a** was further dried under high vacuum (10^{-2} Torr) at 60 °C for 12 h. and was stored in the dark at 4 °C under nitrogen. The HSO_4 content of **1a** was evaluated by addition of 0.47 g of [C_4mim][HSO_4] in 25 mL of deionized water (Water Plus HPLC, Carlo Erba Reagenti ref 28070) under vigorous magnetic stirring. To this mixed acidic solution were added two drops of phenolphthalein solution indicator, and 15 mL of 0.2 N NaOH solution were poured in the resulting mixture. Titration from a standard solution of 0.1 N H_2SO_4 solution gave an end point volume of 10 mL with a permanent pink color (calcd: 10 mL). ^{1}H NMR (300 MHz, CD_3CN, TMS): δ 0.93 (t, 3H, J = 7.1 Hz); 1.25 (m, 2H); 1.75 (m, 2H); 3.85 (s, 3H); 4.16 (t, 2H, J = 7.3 Hz); 7.50 (m, 2H, H-4, H-5); 8.99 (br s, 1H, H-2); 11.02 (br s, 1H, HSO_4). ^{13}C NMR (75 MHz, CD_3CN, TMS): δ 13.76 (q, J = 127 Hz); 19.88; 32.61 (tm, J = 125 Hz); 36.72 (q, J = 144 Hz); 49.96 (tm, J = 144 Hz); 123.20; 124.59 (dm, J = 202 Hz, C-4, C-5); 137.75 (dm, J = 221 Hz, C-2). HRMS *m/z*: 375.1612 found (calcd for $C_{16}H_{31}N_4O_4S^+$ [$2C^+$, HSO_4^-]$^+$ requires 375.1612).

1-Hexyl-3-methylimidazolium Hydrogen Sulphate [C_6mim]-[HSO_4] (1b). The acidic ionic liquid **1b** was prepared according to the method used for the synthesis of **1a** from

1-hexyl-3-methylimidazolium chloride [C_6mim][Cl] (20.37 g, 100 mmol) and sodium hydrogen sulphate (12 g, 100 mmol) that gave the desired [C_6mim][HSO_4] **1b** in 94% yield (24.84 g). ^{1}H NMR (300 MHz, CD_3CN, TMS): δ 0.87 (t, 3H, J = 7.1 Hz); 1.30 (m, 6H); 1.96 (m, 2H); 3.86 (s, 3H); 4.15 (t, 2H, J = 7.3 Hz); 7.54 (m, 2H, H-4, H-5); 8.20 (br s, 1H, HSO_4); 8.89 (s, 1H, H-2). ^{13}C NMR (75 MHz, CD_3-CN, TMS): δ 14.34 (q, J = 123 Hz); 23.01; 26.32; 30.61; 31.68 (tm, J = 122 Hz); 38.28 (q, J = 144 Hz); 50.63 (t, J = 123 Hz); 123.32; 124.73 (dm, J = 202 Hz, C-4, C-5); 137.22 (dm, J = 220 Hz, C-2). HRMS *m*/*z*: 431.2692 found (calcd for $C_{20}H_9N_4O_4S^+$ [$2C^+$, HSO_4^-]$^+$ requires 431.2692).

*1-Butyl-pyridinium Hydrogen Sulphate [C_4py][HSO_4] (**1c**).* The acidic ionic liquid **1c** was prepared according to the method used for the synthesis of **1a** from 1-butyl-pyridinium bromide [C_4py][Br] (20 g, 92.6 mmol) and sodium hydrogen sulphate (22.23 g, 185.2 mmol) that gave the desired [C_6mim][HSO_4] **1b** in 96% yield (20.7 g). ^{1}H NMR (300 MHz, CD_3CN, TMS): δ 0.92 (t, 3H J = 7,3 Hz); 1.36 (m, 2H); 1.96 (m, 2H); 4.67 (t, J = 7.5 Hz); 8.10 (t, J = 7 Hz, 2H, H-2, H-6); 8.36 (br s, 1H HSO_4); 8.56 (m, 1H, H-4); 9.00 (d, J = 5.6 Hz, 2H, H-3, H-5). ^{13}C NMR (75 MHz, CD_3CN, TMS): δ 12.31 (qm, J = 125 Hz); 18.42 (tm, J = 127 Hz); 32.44 (tm, J = 128 Hz); 60.89 (tm, J = 145 Hz); 127.88 (dm, J = 172 Hz, C-3, C-5); 144.21 (dm J = 192 Hz, C-4); 145.13 (dm, J = 172 Hz, C-2, C-6). HRMS *m*/*z*: 136.1127 found (calcd for $C_9H_{14}N^+$, C^+ requires 136.1126).

Standard Experimental Procedure for Esterification of Propanoic Acid 2a with *neo*-Pentanol 3 in an Oil Bath with 1a: [C_4mim][HSO_4], 1c: [C_4py][HSO_4], or with 1a Modified with Concentrated H_2SO_4. *Reuse of the Acidic Catalyst.* Into a glass reactor fitted with a reflux condenser and a thermometer were added 3 equiv of the acidic TSIL **(1a**: [C_4mim][HSO_4] or **1c**: [C_4py][HSO_4] or **1a** modified with 5% of concentrated H_2SO_4). Then *neo*-pentanol **3** (1 equiv) and propanoic acid **2a** (1 equiv) were successively placed in the catalyst media. The outlet of the reflux condenser was connected to a constant pressure of dry nitrogen, and the reactor was kept in a thermostated oil bath at 80 °C (variation ±10 °C). The esterification reaction was typically allowed to proceed for a reaction time ranging from 1.5 to 24 h (see Tables 2, 3, and 4). Reaction progress was conveniently monitored by ^{1}H NMR spectroscopy [in $(CD_3)_2SO$ or $(CD_3)_2$-CO with TMS as internal reference] on a BRUKER ARX 200 spectrometer and also by TLC on precoated plates of silica gel 60F 254 (Merck). At the end of the esterification, the upper layer which contains the desired ester **4** was separated carefully from the acidic catalyst by decantation. The bottom layer was reused in a further run after washing twice with Et_2O (10 mL/g of catalyst) under vigorous magnetic stirring at 25 °C for 30 min. The washing layer was separated by decantation and concentrated by rotary evaporation, and the resulting distillate was controlled by ^{1}H NMR spectroscopy. The catalyst in the reactor was dried under high vacuum (10^{-2} Torr) at 60 °C for 6 h and was controlled by mass balance and eventually by ^{1}H NMR spectroscopy. This control experiment was realized at each run.

Standard Procedure Using a Focused Microwave Oven for Esterification of Acids 2(a−d) and *neo*-Pentanol 3. A mixture of [C_4py][HSO_4] **1c** (3 equiv), acid **2** (1 equiv), and *neo*-pentanol **3** (3 equiv) was placed in a cylindrical quartz reactor (∅ = 4 cm). The reactor was then introduced into a Synthewave 402 Prolabo microwave reactor [fitted with a stirring device and an IR temperature detector]. The stirred homogeneous liquid mixture was irradiated at 25% power level (75 W) for a reaction time ranging from 1.5 to 4.5 h. at 80 °C (see Table 5). Then the mixture was allowed to cool during 45 min. The upper ester layer was separated carefully from the acidic catalyst [C_4py][HSO4] **1c** by decantation. The bottom layer that contained the catalyst **1c** was washed with Et_2O according to the procedure described for "standard procedure for esterification reaction in oil bath".

*neo-Pentyl propanoate (**4a**):* yield = 95%. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 0.94 (s, 9H); 1.16 (t, 3H, J = 7.6 Hz); 2.34 (q, 2H, J = 7.6 Hz); 3.77 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 9.25 (qt, J = 128, 5.6 Hz); 26.46 (qm, J = 128 Hz); 27.69 (tq, J = 128, 4.5 Hz); 31.34 (m); 73.63 (tm, J = 148 Hz); 174.60 (m, C−l, C═O). IR (KBr): 1734 cm^{-1}. HRMS *m*/*z*: 144.1156 found (calcd for $C_8H_{16}O_2$ requires 144.1150), M^+.

*neo-Pentyl cyclohexylcarboxylate (**4b**):* yield = 90%. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 0.93 (s, 9H); 1.24−1.94 (m, 10H); 2.32 (m, 1H); 3.76 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 25.4 (m, C-3, C-5); 25.76 (m, C-4); 26.48 (m, C-1); 29.11 (m, C-2, C-6) 31.44 (m); 43.4 (dm, J = 127 Hz); 73.37 (tm, J = 146 Hz); 176.1 (m, C-1, C═O). IR (KBr): 1732 cm^{-1}. HRMS *m*/*z*: 198.1621 found (calcd for $C_{12}H_{22}O_2$ requires 198.1620), M^+.

*neo-Pentyl 10-undecenoate (**4c**):* yield = 89%. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 0.93 (s, 9H); 1.30−1.37 (m, 10 H); 1.61−1.63 (m, 2H); 2.02−2.05 (m, 2H); 2.30−2.35 (m, 2H); 3.77 (s, 2H); 4.90−5.02 (m, 1H, ═CH); 5.73−5.87 (m, 2H, $=CH_2$). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 25.06 (m); 26.46 (m); 28.91 (m); 29.07 (m); 29.19 (m); 29.29 (m); 31.29 (m); 33.80 (m); 34.43 (m, C-2); 73.57 (tm, J = 146 Hz); 114.17 (tm, J = 155 Hz); 139.10 (dm, J = 151 Hz); 174.02 (m, C-1, C═O). IR (KBr): 1737 cm^{-1}. HRMS *m*/*z*: 239.2014 found (calcd for $C_{15}H_{27}O_2$ requires 239.2011), $[M\text{-}CH_3]^+$.

*neo-Pentyl phenylacetate (**4d**):* yield = 40%. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 0.87 (s, 9H; 3.62 (s, 2H); 3.77-(s, 2H); 7.28 (m, 5H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 26.32 (qm, J = 123 Hz); 31.34 (m); 41.57 (tm, J = 129 Hz); 74.05 (tm, J = 146 Hz); 126.99 (dm, J = 170 Hz, C-4′); 128.52 (dm, J = 161 Hz, C-2′, C-6′); 129.3 (dm, J = 166 Hz, C-3′, C-5′); 134.22 (m, C-1′); 174.60 (m, C-1, C═O). IR (KBr): 1732 cm^{-1}. HRMS *m*/*z*: 206.1313 found (calcd for $C_{13}H_{18}O_2$ requires 206.1307), M^+.

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