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Biomass derived ionic liquids: synthesis from natural organic acids, characterization, toxicity, biodegradation and use as solvents for catalytic hydrogenation processes

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ABSTRACT

Ionic liquids with natural organic derived anions (L-lactate, L-tartrate, malonate, succinate, L-malate, pyruvate, D-glucuronate, D-galacturonate) were easily prepared from tetrabutylammonium hydroxide and an excess of the corresponding acid with good yields. Their characterization was realized through classical NMR, IR, and elemental analysis techniques; their viscosity and TGA (thermogravimetric analysis) parameters were also determined. These ionic liquids showed good performance and recyclability in the selective catalytic hydrogenation of 1,5-cyclooctadiene (1,5-COD) into cyclooctene (COD) at room temperature under atmospheric H_2 pressure.
Antimicrobial toxicity assays toward a large panel of bacteria and fungi strains were also completed and biodegradation studies (Closed Bottle test, 28 days) were also performed.

1. Introduction

Ionic liquids (ILs) consist of an organic cation associated with an anion that may be either organic or inorganic.[1] They are liquids below 100 °C and many of them are liquids at room temperature (RTILs, Room Temperature Ionic Liquids). The rising interest attracted by ILs in the last two decades is due to their properties: low vapor pressure,[2] high thermal stability, and excellent solvation of a wide range of compounds.[3] Consequently, ILs have been considered as an alternative to volatile solvents in catalytic applications,[4–7] biocatalysis[8] synthetic chemistry,[9] electrochemistry,[10] analytical applications[11] or for separations and extractions.[12] A number of detailed reviews have expounded the advantages of using ionic liquids as new 'greener' solvent types.[9,13]

Concerning the catalysis domain and especially the hydrogenation field, numerous examples of the use of organometallic complexes in hydrogenation processes including the production of useful products and intermediates are already reported.[14] Catalytic reactions involving metal complexes in ionic liquids have been actively investigated, with many ionic liquids screened (nearly 300). The majority of these ionic liquids contain heterocyclic derivatives as cations, such as pyridinium, imidazolium, polyalkylammonium and recently synthesized guanidinium, piperidinium, pyrrolium, pyrrolidinium, morpholinium, cholinium, piperazinium, thiazolium, polycyclic examples, ionic liquids with bridged structures, binuclear or polynuclear, zwitterionic, hydrophobic (fluorinated), and chiral derivatives.[15] The unsaturated substrates in hydrogenation reactions in ionic liquids include:

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cyclohexene, cyclohexadiene, pent-1-ene, aromatic hydrocarbons (e.g., styrene and phenylacetylene), sorbic acid, copolymers of acrylonitrile, and butadiene as well as many other alkenes with more complex structures.[16] P.J. Dyson described in 2002 the use of classical ionic liquids for synthesis of organometallics and catalytic hydrogenations[17a] and extended its studies to kinetics and recycling in 2005.[17b] Next, Wasserscheid and co-workers showed in 2007 the capability of ionic liquids to assure superior catalytic systems for transition metal catalyzed hydrogenation.[4,18] In 2007, Keglevich and co-workers[19] reviewed data accumulated in recent years on the synthesis and use of phosphorous containing ionic liquids. Reactions studied included catalytic hydrogenations, transfer hydrogenations, oxidations, and hydroformylations. Recent papers in the field of catalysis, especially hydrogenation catalysis in ionic liquids, closely associated with principles of green chemistry[20] include using electroreduction, microwave, and sonochemical irradiation processes with organometallic complexes or nanoparticles.[14c, 21]

As the selective hydrogenation of fatty compounds can modify their physical properties for many application fields (e.g., cosmetics, agri-food, pharmacy), the selective hydrogenation of polyunsaturated compounds remains a constant challenge.[22] In 2000, Dupont and co-workers described the selective Pd-catalyzed hydrogenation of butadiene to but-1-ene or but-2-ene in BMIM·BF_4 or BMIM·PF_6 (BMIM: 1-butyl-3-methylimidazolium) and showed the possibility of recycling the catalytic system.[23] Other metal salts, such as $Co(acac)_2$, $Co(acac)_3$, $Fe(acac)_3$, and $Ni(acac)_2$ have also shown activities for this reaction. Since this study, more selective conditions involving Pd(0) nanoparticles induced from $Pd(acac)_2$ in [bmim][BF_4] have been found. A 72% yield of but-1-ene could be attained with a constant pressure of 0.4 MPa of hydrogen at 40 °C.[24] More recently, we studied the hydrogenation of phenyloctadiene in presence 0.03 equiv of $Pd(acac)_2$ in biodegradable ILs and these solvents allowed recyclability of the catalytic species and also a better selectivity in the formation of the phenyloct-2-ene.[25]

Concerning now the green aspect of these solvents, whereas ILs have very low toxicity in air because of their very low vapor pressure and low flammability,[17] many lipophilic ILs are toxic in aqueous media.[3,26]

This problem has become a real challenge for IL development and a great number of publications are dealing with their IL toxicity (inc. antibacterial and antifungal),[19,27] Furthermore, toxicity studies involving the nature of the cation and the anion have been already performed on a large number of ILs and showed that anions containing oxygenated chains and/or tetrabutylammonium cations are less toxic toward many strains.[3,28]

However data about IL biodegradation[29] and their bioaccumulation[30] are still lacking for many of the ionic liquids prepared, in particular ammonium salts. Specific imidazolium and pyridinium based ionic liquids have already been shown to be 'readily biodegradable' according to OECD (Organisation for Economic Co-operation and Development) rules.[31] Since 2002, Gathergood, Scammells and co-workers[29] developed some biodegradable ILs by modifying the structure of the imidazolium cation by adding ester or ether function groups. An alternative strategy is changing the nature of the anions as Davis and co-workers in 2002 or Keglevich and co-workers in 2011 with imidazolium or phosphonium cations (see examples in Fig. 1). It is reasonable to propose that an IL composed of a biodegradable anion and cation will be biodegradable as long as the IL compound is non-toxic under the test conditions. Where an IL contains a 'persistent' ion paired with a biodegradable counterion, it is possible to meet the requested threshold values established in the OECD biodegradation tests and for the salt to be classified as readily biodegradable. Under such circumstances the IL could not be called green nor sustainable.[32a,b,d]

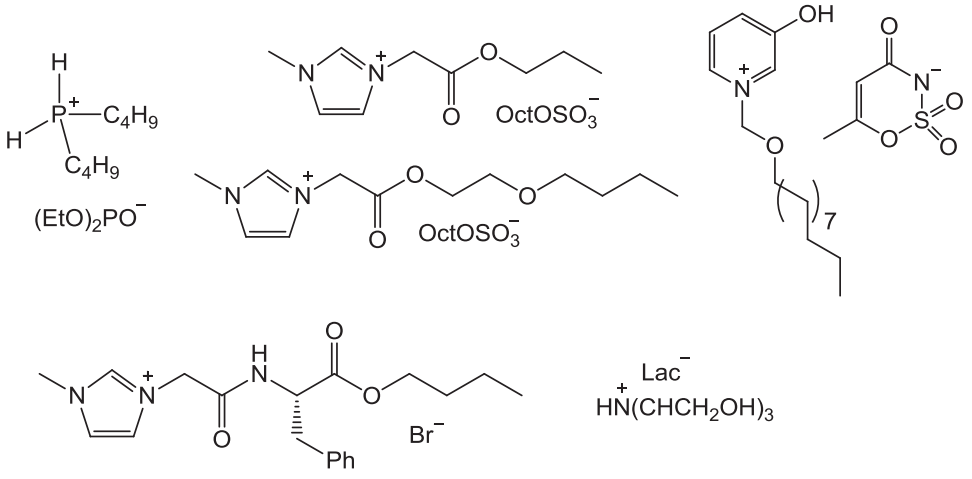


Fig. 1. Examples of biodegradable phosphonium, imidazolium and pyridinium ionic liquids.

Although limited, some data is available about biodegradability of ammonium based ionic liquids.[33] When mono, di and tri (2-hydroxyethyl)ammonium lactate ionic liquids were tested for biodegradability using BOD (Biochemical Oxygen Demand) method,[34] all were found to be readily biodegradable (60–95%)[35] (Fig. 2). Similarly, interesting results were obtained when NAILs (naphthenic acid ILs) were screened for biodegradation. Carboxylates of various cores were chosen as anions in ILs. Eight out of ten ILs were

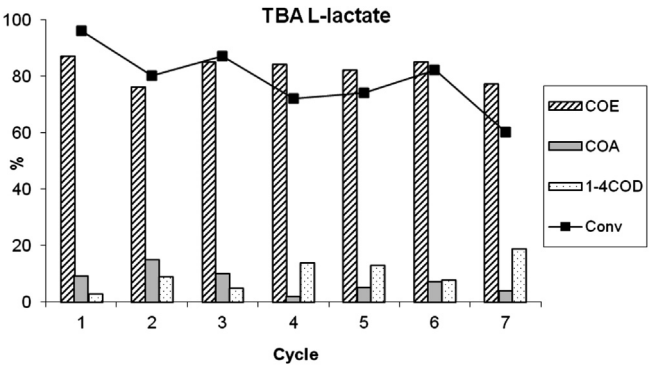


Fig. 2. Hydrogenation of 1-5-cyclooctadiene in water with TBA L-lactate **1**.

found to be 'readily biodegradable' (60–83%), when tested using Closed Bottle test.[36]

Pretti et al.[37] investigated the toxicity and biodegradation of cyclic ammonium based ILs. Both DABCO (1,4-diazabicyclo[2.2.2] octane) and morpholine based ILs containing bromide anion showed low biodegradability when measured by CO_2 headspace test. DABCO based ILs lied in the range of 5–30% whereas morpholinium ILs showed 22–40% biodegradation. Out of these results ethyl substituted ILs (for both DABCO and morpholinium) degraded better than decyl derivatives as expected. Above-mentioned results were corroborated by the work of Pernak and co-workers,[38] where benzylmorpholinium cation in ionic liquids did not biodegrade. Authors suggested that functionalised side chain instead of benzyl group would improve biodegradation. Wells and co-workers[39] studies have already shown that the long alkyl or glycol chain ILs show poor or no biodegradability. Recently a temperature study has been performed to enhance the biodegradability of a tetrabutylammonium IL, which was successful and biodegradation was enhanced from 23% at 30 °C to 64% at 45 °C From other compounds it is known that biodegradation is accelerated when temperature is increased.[40]

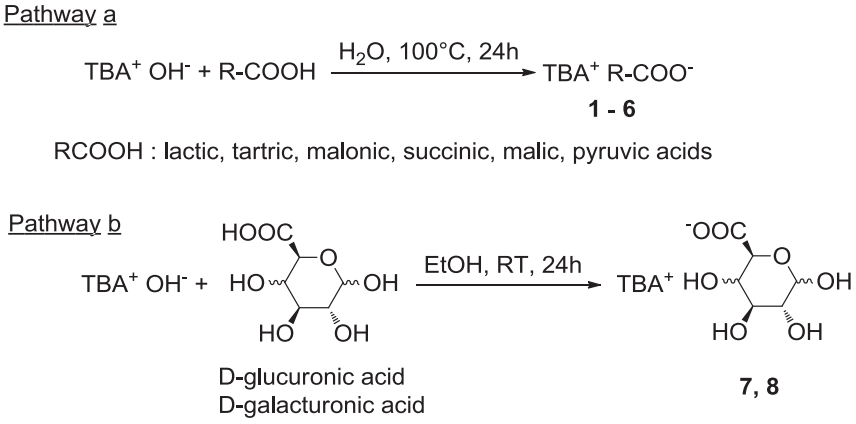
Of note, however the majority of biodegradation studies has focused on the effect of substitution of the cation of the ionic liquid.[29] While toxicity studies of a series of ionic liquids with the same cation and varying the anion are widely reported[27] almost all of these investigations do not include biodegradation data. That is an obvious lack of knowledge on biodegradability and greenness of IL.[32d]

As ILs are often used as solvent or co-solvent, their synthesis in a quick and efficient manner is required. In addition, making ILs from bio-resources, such as acids derived from biomass, could lead to easily obtained biodegradable and low toxicity ILs. Toxicity screening is thus included in this investigation so any undesirably high toxicity ionic liquids can be identified at an early stage. When combined with biodegradation and catalysis performance data, an assessment of an ionic liquid as 'fit for purpose' can be made.

2. Results and discussion

2.1. Syntheses

2.1.1. Synthesis of ILs with tetrabutylammonium (TBA) as cation. Although anion metathesis is the most widely used method to form ionic liquids,[1] the Brönsted acid character of the reactants as well as the unavailability of certain mono-sodium (or mono-potassium) salts led us to prefer the acid-base pathway for the formation of ILs accordingly to the method developed by Ohno and co-workers.[41] Tetrabutylammonium hydroxide (TBAOH) could be prepared from tetrabutylammonium bromide (TBABr) by reaction of an excess of acid in the presence of an ion exchange resin,[38] but traces of bromide (classical measurement of bromide traces in the presence of silver salt) detected in the final ILs indicated that the exchange with the resin was not complete. As a consequence, the synthesis from cheap commercial TBAOH was therefore preferred (Scheme 1). Starting with sustainable acids obtained available from the biomass, corresponding ILs were prepared in refluxing water for 24 h with an excess of the corresponding acid required (Scheme 1, pathway a) and obtained with excellent yields (93–97%, Table 1). ILs from sugar acids were synthesized in absolute ethanol for 24 h at room temperature (Scheme 1, pathway b) with good yields (77–80%, Table 1).



Scheme 1. Formation of TBA ILs.

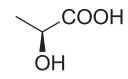
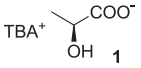
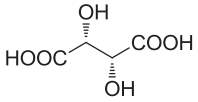
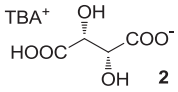
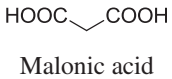
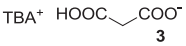
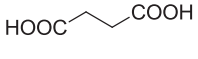
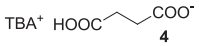
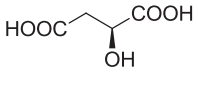
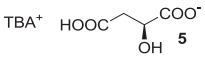
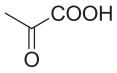
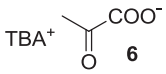
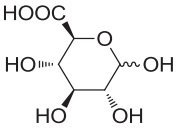
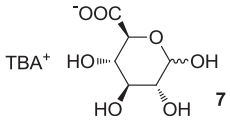
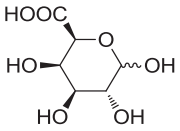
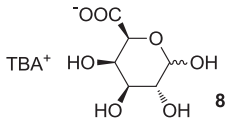
Synthesis of compounds (**1**, **2**, and **5**) has already been described,[41,42] however the characterization of the physicochemical properties of a majority have not been performed. So viscosity was determined at two different temperatures (25 °C and 80 °C) with a viscometer (Table 2). For ionic liquids **1** and **6**, the viscosity at 25 °C is quite different (respectively, 409.1 cP and 220 cP), whereas at 80 °C a value between 17 and 18 cP was found for both **1** and **6**. At 25 °C, TBA L-tartrate **2** was too viscous to permit the measurement and TBA L-malate **5** has also a high viscosity at room temperature, due to its gel aspect. The more hydroxyl groups the anion had, the more viscous the compound at 25 °C. For these compounds, the number of carbons also seemed to play a role on the viscosity at room temperature, because the less viscous ILs (**1** and **6**) had 3 carbons, and the more viscous ones (**2** and **5**) had 4 carbons. At 80 °C, compound **2** still remained very viscous with a viscosity measured at more than 3600 cP. However the viscosity of the ionic liquid **5** decreased to 266 cP on raising the temperature. Hydrogen bonds, governed by the nature of the anions, can influence the physicochemical properties including the viscosity of compounds **1**, **2**, **5**, and **6**.

For compounds **3**, **4**, **7**, and **8**, viscosity values unfortunately could not be determined at 80 °C, because of their waxy aspect (**3**, **4**) or their melting points situated between 80 °C and 100 °C (**7**, **8**).

The glass transition temperature (T_g) was determined by Differential Scanning Calorimetry (DSC). Respectively, for ILs **1** and **6**, and ILs **2**–**5**, T_g values were similar. T_g values for glycosidic acid derived ILs were higher and surprisingly above 0 °C for compound **8**.

Next, thermogravimetric analyses were performed to determine the decomposition temperature (T_{dec}) of the different compounds. With the exception of compound **3**, the decomposition

Table 1
Synthesis of TBA ILs

R–COOH	ILs	Pathway	Aspect	Yield (%)
 L-lactic acid	 **1**	a	Oil	97
 L -tartaric acid	 **2**	a	Oil	98
 Malonic acid	 **3**	a	Wax	99
 Succinic acid	 **4**	a	Wax	98
 L-malic acid	 **5**	a	Gelly	97
 Pyruvic acid	 **6**	a	Oil	93
 D-glucuronic acid	 **7**	b	Solid	80
 D-galacturonic acid	 **8**	b	Solid	77

temperatures of ILs derived from bioacids were above 200 °C and under 250 °C, which is low for ionic liquids. In fact, the thermal stability of ionic liquids is limited by the strength of heteroatom–heteroatom associations and carbon–hydrogen bonds[43] what could explain the low T_{dec} values for compounds **7** and **8** derived from osidic acids.

2.2. Catalytic hydrogenation

In the present study, the selective hydrogenation of the 1,5-cyclooctadiene (1,5-COD) was chosen as a model reaction to improve the ability of our ionic liquids to be 'selective' solvents and appropriate ones for the recycling process. Indeed, few examples dealing with selective hydrogenation of 1,5-COD describe selective hydrogenation processes conducted under harsh conditions (5–50 bar, 50–100 °C and 4–6 h) with different systems BMIM·PF_6/$Na_2[Ru_6C(CO)_{16}]$,[44] Ni catalyst coated with BMIM·$C_8H_{17}SO_4$[45] and BMIM·BF_4/Pd(acac)$_2$.[23]

In our study, the hydrogenation of 1,5-COD was realized by using $PdCl_2$ as without additional ligands in distilled water (5 mass equivalent compared to the IL) under 1 atm of hydrogen during 18 h at room temperature (Scheme 2). First attempts with cyclooctene (COE) and styrene showed that hydrogenation of carbon–carbon double bonds in these conditions was possible; COE and styrene were completely converted into cyclooctane (COA) and ethylbenzene, respectively, with water as solvent. The use of another solvent was required because of the high viscosity of the studied ILs. Among the available solvents, two were tested: propan-2-ol, a common co-solvent for hydrogenation with ionic liquids[46] and distillated water, a green solvent. But only hydrogenation of 1,5-COD performed in water gave a majority of COE.

In the absence of an ionic liquid, complete conversion of 1,5-COD into COA was obtained in water in the first run. Recycling the Pd catalyst led to the formation of COE until 87% was attained for the fourth and fifth runs (Table 3, entries 1a–e). In commercial TBABr or TBACl, the first runs led to mixtures of COE and COA, but also gave isomerization into 1,4-cyclooctadiene (1,4-COD). This isomerization had already been observed in presence of other metallic catalysts (CuO–Al_2O_3, CuO–SiO_2 or ZnO–Al_2O_3) via water gas shift reaction.[47] Furthermore, the first recycling in both ILs showed a large decrease in conversion as well as isomerization into 1,3-cyclooctadiene (1,3-COD) observed during the second cycle with TBACl (entry 3a).

With TBA L-lactate **1**, the conversion of 1,5-COD to COE proceeded with high selectivity until the sixth recycling where the conversion dropped. Isomerization product, 1,4-COD, was observed in all of the runs (Fig. 2).

Similar results were obtained with TBA L-tartrate **2**, TBA malonate **3**, and TBA L-malate **5** (See Figs. S5, S6, and S8 in ESD) but lower conversion and selectivity were observed by using the TBA pyruvate **6** (Fig. 3).

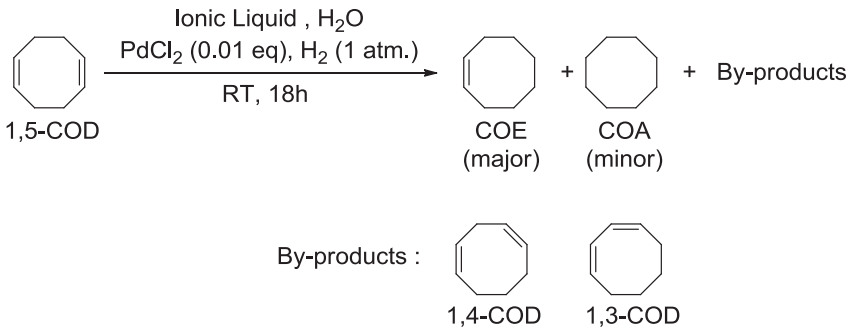
The highest conversions and selectivities were found with TBA succinate **4**, TBA D-glucuronate **7**, and TBA D-galacturonate **8** (Fig. 4). IL **8** gave excellent conversion of 1,5-COD into COE with low amounts of isomerized products, even after 10 cycles.

As BMIM ILs have previously been reported as appropriate solvents/additives in selective hydrogenation processes, under harsh conditions, using different metallic based catalysts (Pd, Fe, Ni, W, Ru etc.)[23,44,45] we compared the activity and selectivity between commercial BMIM ILs and the TBA ILs **1**–**8** under our hydrogenation conditions described herein. Conversion of 1,5-COD was very low in

Table 2
TBA ILs: viscocity, glass transition temperature, decomposition temperature

IL	Viscosity (cP)		T_g (°C)	T_{dec} (°C)[a]
	25 °C	80 °C		
1	409.1	17.9	−59.0	201.4
2	Nd	3689	−31.0	212.6
3	Nd	Nd	−34.8	170.1
4	Nd	106	−38.6	212.6
5	>40 000	266	−34.4	230
6	220	17.2	−59.3	Nd
7	Nd	Nd	−20.5	136
8	Nd	Nd	18.3	Nd

Nd: not determined.
[a] The values reported on Table 2 correspond to the onset temperature found by heating the compounds from 30 °C to 500 °C with a heating rate of 10 K min^{-1}.



Scheme 2. Selective hydrogenation of 1,5-cyclooctadiene in presence of ILs.

Table 3
Hydrogenation of cyclooctadiene in water and in mixtures water/commercial TBABr or TBACl

Entry	IL	Conv. (%)[a]	COE (%)[a]	COA (%)[a]	1,4-COD (%)[a]	1,3-COD (%)[a]
1a	—	100	—	100	—	—
1b[b]		100	65	35	—	—
1c[b]		99	82	17	1	—
1d[b]		100	87	13	—	—
1e[b]		93	87	6	7	—
2a	TBABr	100	55	45	—	—
2b[b]		17	63	6	31	
3a	TBACl	66	75	4	21	—
3b[b]		26	62	5	29	4

[a] Determined by GC.
[b] Recycling experiments.

Table 4
Hydrogenation of 1,5-cyclooctadiene in BMIM ILs

Entry	IL	Conv. (%)[a]	COE (%)[a]	COA (%)[a]	1,4-COD (%)[a]	1,3-COD (%)[a]
1a	BMIMBr	26	53	4	45	—
1b[b]		17	61	3	32	4
2a	BMIMCl	96	90	5	5	—
2b[b]		18	71	24	5	—
3a	BMIM L-lactate	100	28	72	—	—
3b[b]		100	50	50	—	—
3c[b]		100	55	45	—	—
3d[b]		100	45	55	—	—
3e[b]		100	41	59	—	—

[a] Determined by GC.
[b] Recycling experiments.

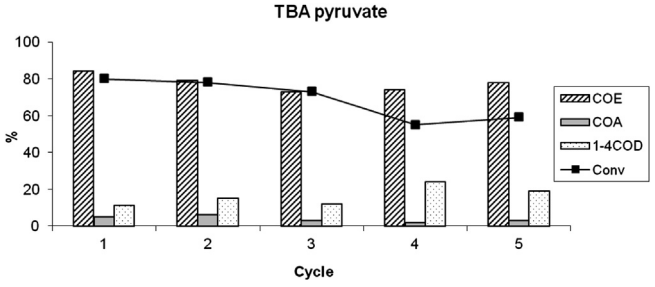


Fig. 3. Hydrogenation of 1,5-cyclooctadiene in water with TBA pyruvate **6**.

BMIMBr (Table 5, entries 1a and 1b) and the formation of isomerized products was significantly high. In BMIMCl, although a high conversion and selectivity for COE in the first run was demonstrated (entry 2a), the conversion of the substrate decreased drastically in the second run to 18%. With BMIM L-lactate, which was also commercially available, quantitative conversion of 1,5-COD was observed during the 5 runs but yielded a majority of COA.

Using our mild conditions, ionic liquids **1**–**8** derived from TBA were more suitable than BMIM ILs. Furthermore, the use of a Pd-based catalyst in TBA ILs is novel because in general hydrogenation of alkenes or dienes in ILs are largely performed with Ru or Rh catalysts in imidazolium IL derivatives.[48] In all cases herein, results with ILs (neat or as additive) were different to those obtained in only water. The presence of IL shade an effect on the hydrogenation of 1,5-COD and could inhibit the reaction (e.g., Table 4, entry 1a) as well as permit the selective formation of COE (Table 4, entries 8a–j), due to the hydrogenation of the second carbon–carbon double bond of COD requiring more energy.[49] It is well known that the solubility of gases in ILs is lower than in common organic solvents.[4] To our knowledge, there are few studies dealing with the solubility of gases in ILs/solvents mixtures [4], and no study for the solubility of hydrogen in our conditions, i.e., a mixture of TBA ILs and water (1:5). Considering the different results (Tables 3 and 4), the solubility of hydrogen in an aqueous medium containing ILs/H_2O seems to be lower than the solubility of hydrogen in water alone. These hypotheses could be reinforced by the fact that the starting solutions with or without ILs were generally orange-red due to the dispersion of $PdCl_2$ in them. After the introduction of the hydrogen atmosphere, the solution without ILs becomes black more quickly than experiments containing an IL. This could signify a more rapid reduction of the Pd(II) into Pd(0) and consequently a higher reactivity with hydrogen.

2.3. Antimicrobial toxicity screening study

For the antifungal studies, compounds were screened against the following yeast strains: *Candida albicans* ATCC 44859, *C. albicans* ATCC 90028, *Candida parapsilosis* ATCC 22019, *Candida krusei* ATCC 6258, *C. krusei* E28, *Candida tropicalis* 156, *Candida glabrata* 20/I, *Candida lusitaniae* 2446/I, *Trichosporan asahii* 1188 and filamentous fungi (*Aspergillus fumigatus* 231, *Absidia corymbifera* 272, *Trichophyton mentagrophytes* 445). MIC values for antifungal study were defined as 80% inhibition (IC_{80}) of the control growth for yeast and 50% inhibition (IC_{50}) of the control growth for filamentous fungi (Table S1, See ESD). The MIC values for most fungi were recorded after 24 h and 48 h except for the dermatophytic strain (*T. mentagrophytes* 445), which was determined after 72 h and 120 h.

The results show that all ionic liquids were non-toxic to all 12 fungi strains up to 1 mM concentration.

Next, bacteria were screened against four Gram positive organisms *Staphylococcus aureus* ATCC 6538, *S. aureus* MRSA HK5996/08, *Staphylococcus epidermidis* HK6966/08, *Enterococcus* sp. HK14365/08 and four Gram negative organisms *Escherichia coli* ATCC 8739, *Klebsiella pneumoniae* HK11750/08, *K. pneumoniae*-ESBL positive HK14368/08 and *Pseudomonas aeruginosa* ATCC 9027 (Table S2, see ESD). MIC values for the antibacterial study were defined as 95% inhibition (IC_{95}) of the control growth. These results

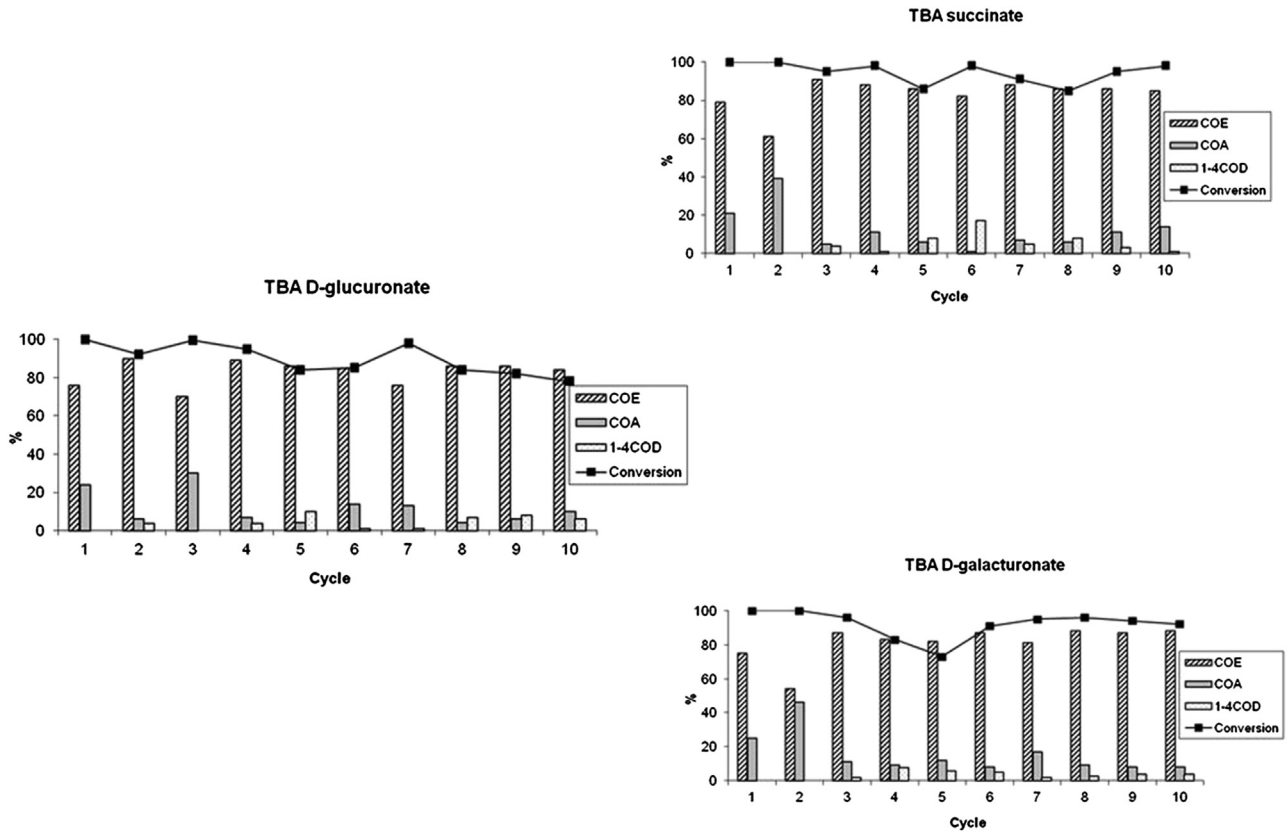


Fig. 4. Hydrogenation of 1,5-cyclooctadiene in water with TBA succinate **4**, TBA D-glucuronate **7**, and TBA D-galacturonate **8**.

Table 5
IC_{50} determination

Entry	Compound	IC_{50} value (mM)				
		E. coli	*B. subtilis*	*P. fluorescens*	*P. putida* (CP1)	*P. putida* (KT2440)
1	TBABr	03.13–06.25	25.00–50.00	06.25–12.50	25.00–50.00	12.50–25.00
2	TBAOH·30H_2O	06.25–12.50	12.50–25.00	12.50–25.00	12.50–25.00	12.50–25.0
3	**1**	12.50–25.00	06.25–12.50	12.50–25.00	06.25–12.50	12.50–25.00
4	**2**	06.25–12.50	03.13–06.25	03.13–06.25	03.13–06.25	12.50–25.00
5	**3**	12.50–25.00	06.25–12.50	06.25–12.50	06.25–12.50	12.50–25.00
6	**4**	12.50–25.00	03.13–06.25	12.50–25.00	06.25–12.50	12.50–25.00
7	**5**	06.25–12.50	03.13–06.25	03.13–06.25	03.13–06.25	03.13–06.25
8	**6**	12.50–25.00	06.25–12.50	06.25–12.50	06.25–12.50	12.50–25.00
9	**7**	06.25–12.50	25.00–50.00	25.00–50.00	25.00–50.00	25.00–50.00
10	**8**	12.50–25.00	25.00–50.00	25.00–50.00	25.00–50.00	25.00–50.00

show that all ionic liquids, TBABr, TBACl, and **1**–**8**, were non-toxic to all 8 bacteria strains up to 1 mM concentration. Table S1 and S2 (See ESD) combined demonstrate that the ionic liquids do not exhibit high antimicrobial toxicity to a wide range of bacteria and fungi.

Finally, IC_{50} values for the ionic liquids were also determined after 18 h against a screen of 5 bacteria (Table 5).

Table 5 shows the IC_{50} values for 5 bacteria. The effect of changing the anion can be observed by comparing TBA salts (Table 5, entries 2–10) to TBABr (Table 5, entry 1). The highest antibacterial toxicity was found for TBA salts containing carboxylic acid, carboxylate, and hydroxyl groups. TBA L-malate **5** has IC_{50} values for the 5 bacteria strains between 3.13 and 12.5 mM (Table 5, entry 7) and TBA L-tartrate **2** IC_{50} values in the range 3.12–25 mM (Table 5, entry 4). The lowest antibacterial toxicity ionic liquids were the sugar carboxylate derivatives TBA D-glucuronate **7** and TBA D-galacturonate **8**. Both ionic liquids have IC_{50} values between 25 and 50 mM for the 4 bacteria (*B. subtilis*, *Pseudomonas fluorescens*, *Pseudomonas putida* (CP1) and *P. putida* (KT2440)) while **8** is less toxic than **7** to *E. coli* (12.5–25 mM vs 6.25–12.5 mM, Table 5, entry 10 vs 9).

The C3 carboxylate ILs TBA L-lactate **1** and TBA pyruvate **6** have similar toxicity. The IC_{50} values for *E. coli* (12.5–25 mM), *B. subtilis* (6.25–12.5 mM), *P. putida* (CP1) (6.25–12.5 mM), and *P. putida* (KT2440) (12.5–25 mM) are the same for both **1** and **6**, while TBA pyruvate **6** is more toxic than TBA L-lactate **1** to *P. fluorescens* (6.25–12.5 mM vs 12.5–25 mM, entry 8 vs 3). Ionic liquids with anions containing only a carboxylic acid and a carboxylate group (TBA malonate **3** and TBA succinate **4**) have the same IC_{50} values for *E. coli* (12.5–25 mM), *P. putida* (CP1) (6.25–12.5 mM) and *P. putida* (KT2440) (12.5–25 mM). However, while TBA succinate **4** is more toxic than malonate **3** to *B. subtilis* (3.12–6.25 mM vs 6.25–12.5 mM, Table 5, entry 6 vs 5), **3** is more toxic than **4** to *P. fluorescens* (6.25–12.5 mM vs 12.5–25 mM, Table 5, entry 5 vs 6). Comparing the IC_{50} values for the halide salt, TBABr with the biomass derived ILs the following trends are apparent. ILs **1**–**8** are less toxic to the Gram negative bacteria *E. coli*. Sugar derivatives TBA D-

glucuronate **7** and TBA D-galacturonate **8** are less toxic than TBABr to all 5 bacteria strains (Gram positive and negative) screened. Changing from a halide to L-lactate, L-tartrate, malonate, succinate, L-malate or pyruvate increased the toxicity of the ionic liquid to the Gram positive bacteria *B. subtilis* and Gram negative *P. putida* (CP1). For *P. fluorescens*, only TBA L-tartrate **2** and L-malate **5** were more toxic than TBABr. TBA L-malate **5** was also more toxic to *P. putida* (KT2440) than TBABr.

3. Biodegradation—Closed Bottle test

The biodegradability of the tetraalkylammonium salts was investigated in the Closed Bottle test. The test was valid according to the test guideline since sodium acetate was biodegraded up to 82% within 14 days (demand of at least 60%) and oxygen concentrations in all bottles did not fall below 0.5 mg L^{-1} at any time. Oxygen depletion in the inoculum blanks after 28 days was 0.82 mg L^{-1} and therefore less than 1.5 mg L^{-1}. The difference of extremes in replicate values of the removal of the test compound was less than 20% in all tests except for TBA succinate **4** where this validity criterion was not met.

The results of the biodegradation of the tetraalkylammonium salts are presented in Table 6. Of all the compounds tested, the sugar acid derivatives **7** and **8** had the highest biodegradabilities (18.6 and 22.6%, respectively), which were within the range of the variation of the results for the same compound in repeated tests that are due to differences in the composition of inoculum and number of bacteria present. None of the test compounds **1**–**8** passed the Closed Bottle test (pass level: 60%). Tetraethylammonium and tetramethylammonium bromide were also included in the study to investigate the effect of alkyl chain length on biodegradation. Both these bromide salts also failed the Closed Bottle test (OECD 301D) and are not classed readily biodegradable.

Table 6
Biodegradation studies (Closed Bottle test OECD 301D)

Entry	Compound	Biodegradation in % ThOD (theoretical oxygen demand)
1	TBABr	7.9
2	TBAOH·30H_2O	3.8
3	TEABr	0
4	TMABr	2.6
5	**1**	15.5
6	**2**	15.5
7	**3**	9.9
8	**4**	Nd
9	**5**	14.2
10	**6**	12.2
11	**7**	18.6
12	**8**	22.8

Nd—Not determined due to failing one of the validation requirements for the test.

There is no clear trend between the effect of the anion structure and biodegradability. Low biodegradation was observed for TBA bromide (7.9%), slightly higher for **1**, **2**, **3**, **5**, and **6** (9.9–15.5%).

According to the standard method, all tetraalkylammonium salts under investigation were not toxic since after 14 days the degradation was more than 25% in the toxicity control containing substance and sodium acetate each in a concentration of 5 mg O_2 L^{-1}. None of the examined compounds proved to be effective against the growth of the degrading bacteria present in the test vessels.

4. Conclusion

Ionic liquids with natural organic acid derived anions (L-lactate, L-tartrate, malonate, succinate, L-malate, pyruvate, D-glucuronate, D-galacturonate) were easily prepared from tetrabutylammonium hydroxide and an excess of the corresponding acid with good yields. Their characterization was realized through routine NMR, IR, elemental analysis, viscosity, and ATG techniques. These ionic liquids derived from TBA show good performance and recyclability in catalytic selective hydrogenation of 1,5-cyclooctadiene into cyclooctene at room temperature under atmospheric H_2 pressure. They are more suitable for selective hydrogenation of 1,5-COD into COE under milder conditions than commercial BMIM ILs.

Toxicity assays toward a large panel of bacterial and fungal strains were also performed. Ionic liquids containing D-glucuronate or D-galacturonate anions were the least toxic to the strains screened, and TBA L-tartrate and TBA L-malate the most toxic biomass derived examples prepared (antibacterial activity). All ionic liquids (**1**–**8**) were less toxic to *E. coli* than TBABr, however this trend did not apply to all ionic liquids for other Gram negative bacteria in the study (e.g., *P. putida*). None of the tetrabutylammonium salts, containing biomass derived anions (**1**–**8**) passes the Closed Bottle test nor tetrabutylammonium, tetraethylammonium or tetramethylammonium bromide. Thus these ions are classified as not readily biodegradable components of ILs according to this test. While none of the ionic liquids can be prioritized for further catalysis study based on passing Closed Bottle test (all failed), positively the series of ILs (**1**–**8**) all did not exhibit high antimicrobial toxicity. On-going investigations tackle the problem of low biodegradability, while maintaining good performance in the catalytic hydrogenation studies.

5. Experimental

5.1. General

All reagents were commercially available and used as received (L-lactic acid 90% from ACROS, TBAOH·30H_2O and D-galacturonic acid 98% from Aldrich, L-tartaric acid from Prolabo, malonic acid 99% from Jansen, succinic acid 99%, L-malic acid 99%, pyruvic acid 98%, and D-glucuronic acid 98% from Alfa Aesar). ^1H and ^{13}C NMR spectra were recorded on an AC 250 Bruker in $CDCl_3$, CD_3OD or acetone-d_6 with TMS as reference for ^1H spectra and $CDCl_3$ (δ 77.0), MeOD (δ 49.9) or acetone-d_6 (δ 30.6) for ^{13}C spectra. The infrared spectra were recorded with Spectrafile IR™ Plus MIDAC. C, H, and N analyses were performed on a Perkin Elmer 2400 CHN equipment. GC was recorded on a Hewlett–Packard HP-6890 gas chromatograph, fitted with DB-1 capillary column (25 m, 0.32 mm), a flame ionization detector and HP-3395 integrator;

Thermogravimetric analyses coupled with a mass spectrometer were performed between 30 °C and 500 °C under a constant flow of dry argon (50 mL/min) using a Simultaneous Thermal Analyzer STA 449C Jupiter from Netzsch, and a heating rate of 10 K/min. The isothermal drift and sensitivity values are 0.6 μg/h and 0.1 μg, respectively. Alumina crucibles were loaded with 10–20 mg of sample powder.

The mass spectrometer is a quadrupole QMS 403 Aëolos® with a stainless steel capillary and a SEV detector (Channeltron). The counting time for mass spectrometer is of 20 ms per m/z values (scanning width: m/z=10–150 amu) with a resting time of 1 s.

The DSC experiments were carried out on a Netzsch DSC 204F1 heat flux differential calorimeter at a heating/cooling rate of 10 K/min under a constant argon flow with 200 mL/min. The crucibles were loaded with 10–20 mg of sample powder/liquid. Samples were weighed in aluminum sample pans covered with a pierced lid. An empty aluminum sample pan with a pierced lid was used as a reference.

The viscosities measurements in cP (or mPa s) were performed with a Brookfield LV-DVII+ PRO viscometer using a CP51 cone spindle. The instrument was connected to a HUBER-ministat circulation-type thermo-regulated water bath, and measures were

realized between 298.15 and 353.15 K. The repeatability of the viscometer was of 0.20% with an uncertainty in the viscosity measurements of 1.00% of the full scale range, declared by the manufacturer.

5.2. Antifungal activity

In vitro antifungal activities of the compounds were evaluated on a panel of four ATCC strains (*C. albicans* ATCC 44859, *C. albicans* ATCC 90028, *C. parapsilosis* ATCC 22019, *C. krusei* ATCC 6258) and eight clinical yeast isolates (*C. krusei* E28, *C. tropicalis* 156, *C. glabrata* 20/I, *C. lusitaniae* 2446/I, *T. asahii* 1188) and filamentous fungi (*A. fumigatus* 231, *A. corymbifera* 272, *T. mentagrophytes* 445) from the collection of fungal strains deposited at the Department of Biological and Medical Sciences, Faculty of Pharmacy, Charles University, Hradec Králové, Czech Republic. Three ATCC strains were used as the quality control strains. All of the isolates were maintained on Sabouraud dextrose agar prior to being tested.

Minimum inhibitory concentrations (MICs) were determined by modified CLSI standard of microdilution format of the M27-A3 and M38-A2 documents.[50,51] Dimethyl sulfoxide (100%) served as a diluent for all compounds; the final concentration did not exceed 2%. RPMI 1640 (Sevapharma, Prague) medium supplemented with L-glutamine and buffered with 0.165 M morpholinepropanesulfonic acid (Serva) to pH 7.0 by 10 M NaOH was used as the test medium. The wells of the microdilution tray contained 200 μL of the RPMI 1640 medium with 2-fold serial dilutions of the compounds (1000–0.244 μmol/L for the new compounds) and 10 μL of inoculum suspension. Fungal inoculum in RPMI 1640 was prepared to give a final concentration of $5\times10^3 \pm 0.2$ cfu mL^{-1}. The trays were incubated at 35 °C and MICs were read visually after 24 h and 48 h. The MIC values for the dermatophytic strain (*T. mentagrophytes*) were determined after 72 h and 120 h. The MICs were defined as 80% inhibition (IC_{80}) of the control growth for yeasts and as 50% inhibition (IC_{50}) of the control growth for filamentous fungi. MICs were determined twice and in duplicate. The deviations from the usually obtained values were no higher than the nearest concentration value up and down the dilution scale.

5.3. Antibacterial activity

In vitro antibacterial activities[52] of the compounds were evaluated on a panel of three ATCC strains (*S. aureus* ATCC 6538, *E. coli* ATCC 8739, *P. aeruginosa* ATCC 9027) and five clinical isolates (*S. aureus* MRSA HK5996/08, *S. epidermidis* HK6966/08, *Enterococcus* sp. HK14365/08, *K. pneumoniae* HK11750/08, *K. pneumoniae*-ESBL HK14368/08) from the collection of fungal strains deposited at the Department of Biological and Medical Sciences, Faculty of Pharmacy, Charles University, Hradec Králové, Czech Republic. The above-mentioned ATCC strains also served as the quality control strains. All the isolates were maintained on Mueller-Hinton agar prior to being tested.

Dimethyl sulfoxide (100%) served as a diluent for all compounds; the final concentration did not exceed 2%. Mueller-Hinton agar (MH, HiMedia, Čadersky-Envitek, Czech Republic) buffered to pH 7.4 (±0.2) was used as the test medium. The wells of the microdilution tray contained 200 L of the Mueller-Hinton medium with 2-fold serial dilutions of the compounds (1000–0.244 μmol/L) and 10 L of inoculum suspension. Inoculum in MH medium was prepared to give a final concentration of 0.5 McFarland scale (1.5×10^8 cfu mL^{-1}). The trays were incubated at 37 °C and MICs were read visually after 24 h and 48 h. The MICs were defined as 95% inhibition of the control growth. MICs were determined twice and in duplicate. The deviations from the usually obtained values were no higher than the nearest concentration value up and down the dilution scale.

5.4. Toxicity studies

IC_{50} values for the compounds were determined at The School of Biotechnology, Dublin City University using a modification of the broth microdilution method described by Amsterdam.[53] Strains were grown in nutrient broth overnight, washed with 0.01 M sodium phosphate buffer and the cell number adjusted to give an optical density reading of 0.07 at 660 nm. The antimicrobial activity of the ILs were tested in 96 well microplates. 180 μL of Mueller-Hinton broth was pipetted into column 1 of the wells and 100 μL into the other wells. 20 μL of the chemical solution was transferred into column 1 giving a concentration of 200 mM. 100 μL of the solution from column 1 was then transferred to the next column and mixed. The procedure was repeated to give a series of twofold dilutions. Each well was inoculated with 5 μL of bacterial culture. Wells containing medium only were used as blanks and wells containing medium and culture only were used as positive controls. The microplates were incubated overnight at 37 °C for *E. coli* and 30 °C for all other bacteria. The presence or absence of growth was determined by measuring the optical density of the wells at a wavelength of 405 nm using a plate reader. The IC_{50} values were determined as the concentration or range of concentrations that caused a 50% reduction in growth.

5.5. Closed Bottle test (CBT)

The CBT is one of six test methods described in the OECD Test Guidelines[54] to determine the ready biodegradability of organic chemicals. With a low nutrient content and a low bacterial density the CBT simulates the conditions of environmental surface water. One can assume that substances classified as 'readily biodegradable' are biodegradable in sewage treatment plants and therefore are not expected to reach or accumulate in the aquatic environment.

The test was performed in the dark at a room temperature of 20±1 °C in the laboratories of the Institute of Sustainable and Environmental Chemistry at Leuphana University Lüneburg as described in details elsewhere.[55] It consisted of four different test series. All series were run as duplicates. The 'blank series' contained only mineral medium and inoculum. The 'quality control' was prepared additionally with readily biodegradable sodium acetate to monitor the activity of the microorganisms. The 'test series' included besides medium and inoculum the test compound as only organic compound while the 'toxicity control' series contained additionally sodium acetate. The amount of sodium acetate and of each test compound corresponded to a theoretical oxygen demand (ThOD) of 5 mg L^{-1}. All test vessels contained the same mineral salt solution and were inoculated with two drops of inoculum from the effluent of the municipal sewage treatment plant in Lüneburg (Abwasser, Grün und Lüneburger Service GmbH, Germany; 250.000 population equivalents).

According to the guidelines, at least 60% decomposition of the reference substance sodium acetate is required within 14 days. Toxicity was assessed by comparing oxygen consumption as measured in the toxicity control bottles with the predicted level computed from the oxygen consumption in the quality control and in the test vessel containing only the test compound, respectively. A compound is labeled toxic if the difference between the predicted amount of oxygen consumption and the measured one exceeds 25%.[54]

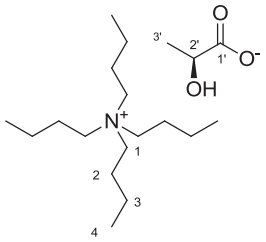
The process of aerobic biodegradation was monitored by measuring the biological oxygen demand of the microorganisms in accordance with international standard methods[56] at day 0, 0 (after

3 h), 1, 7, 14, 21 and 28 using sensor spots in the bottles and an oxygen electrode (Oxi 196 with EO 196-1.5 WTW Weilheim, Germany).

5.6. General procedure for ILs using acids obtained from biomass

The acid (0.74 mmol) was dissolved in distilled water (5 mL) (note: slight warming is necessary with succinic acid). Then, an aqueous solution of TBAOH·30H_2O (0.62 mmol in 10 mL of distilled water) was added dropwise. After addition, the mixture was stirred at 100 °C during 24 h. After cooling, the solvent was evaporated and the crude product washed with diethyl ether (3×25 mL) and dried in vacuo at 60 °C for 2 days.

5.6.1. Tetrabutylammonium L-lactate **1**.

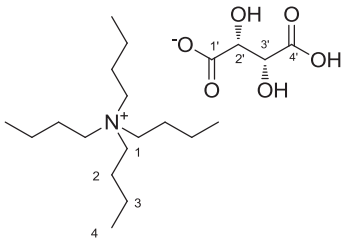


1

General procedure with L-lactic acid (61 μL, 0.74 mmol) and TBAOH·30H_2O (497 mg, 0.62 mmol). Tetrabutylammonium L-lactate **1** (200.1 mg, 0.60 mmol) was obtained as a colorless oil. Yield: 97%.

IR (film) cm^{-1}: 3600–3000 (ν_{OH}, ν_{N+}), 2963 (ν_{CH}), 2952 (ν_{CH}), 2876 (ν_{CH}), 1606 (ν_{COO-}), 1489, 1464, 1381, 1345, 1117 (ν_{CO} or ν_{CN}), 1093 (ν_{CO} or ν_{CN}), 1033 (ν_{CO} or ν_{CN}); ^{1}H NMR (250 MHz, CD_3–CO–CD_3): δ=4.00 (q, 1H, H-2′, $J_{2'-3'}$=6.8 Hz), 3.37 (m, 8H, H-1), 1.75 (quint, 8H, H-2, J_{1-2}=8.3 Hz, J_{2-3}=7.3 Hz), 1.40 (sext, 8H, H-3, J_{2-3}=J_{3-4}=7.3 Hz), 1.27 (d, 3H, H-3′, $J_{2'-3'}$=6.8 Hz), 0.95 (t, 12H, H-4, J_{3-4}=7.3 Hz); ^{13}C NMR (63 MHz, CD_3–CO–CD_3): δ=179.8 (C=O), 68.6 (C-2′), 60.1 (C-1), 25.2 (C-2), 22.1 (C-3′), 21.1 (C-3), 14.8 (C-4); $C_{19}H_{20}NO_3$,2H_2O Calcd C: 62.09%, H: 12.34%; N: 3.81%, Found C: 62.36%; H: 12.15%; N: 3.42%. MS (ESI+) 242.1 MS (ESI−) 89.

5.6.2. Tetrabutylammonium L-tartrate **2**.

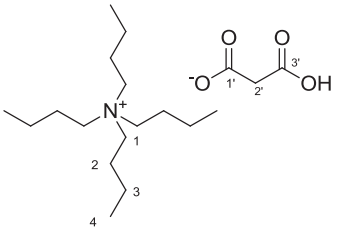


2

General procedure with L-tartaric acid (112.3 mg, 0.74 mmol) and TBAOH·30H_2O (498.4 mg, 0.62 mmol). Tetrabutylammonium L-tartrate (238.5 mg, 0.609 mmol) was obtained as a very viscous light yellow oil. Yield: 98%.

IR (film): 3600–3000 (ν_{OH}, ν_{N+}), 2973 (ν_{CH}), 2874 (ν_{CH}), 1734 (ν_{COOH}), 1652 (ν_{COO-}), 1468, 1379, 1120 (ν_{CO} or ν_{CN}), 1082 (ν_{CO} or ν_{CN}), 1069 (ν_{CO} or ν_{CN}); ^{1}H NMR (250 MHz, CD_3–CO–CD_3): δ=4.60 (large s, 2H, H-2′, H-3′), 3.44 (m, 8H, H-1), 1.79 (quint, 8H, H-2, J_{1-2}=7.7 Hz, J_{2-3}=7.4 Hz), 1.47 (hex, 8H, H-3, J_{2-3}=J_{3-4}=7.4 Hz), 1.07 (t, 12H, H-4, J_{3-4}=7.4 Hz); ^{13}C NMR (63 MHz, CD_3–CO–CD_3): δ=173.3 (C=O), 72.9 (C-2′, C-3′), 59.2 (C-1), 24.4 (C-2), 20.5 (C-3), 13.8 (C-4); Calcd $C_{20}H_{41}NO_6$, 0.7H_2O C: 59.44%, H: 10.57%; N: 3.47%, Found C: 59.33%, H: 9.95%; N: 3.45% MS (ESI+) 242.2 MS (ESI−) 148.8.

5.6.3. Tetrabutylammonium malonate **3**.

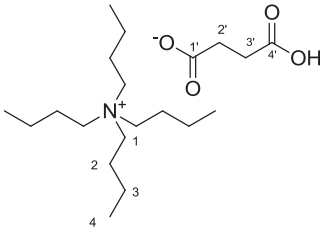


3

General procedure with malonic acid (73 mg, 0.76 mmol) and TBAOH·30H_2O (502.1 mg, 0.63 mmol). Tetrabutylammonium malonate (217.0 mg, 0.627 mmol) was obtained as a white wax. Yield: 99%.

IR (film): 3600–3100 (ν_{OH}, ν_{N+}), 2966 (ν_{CH}), 2939 (ν_{CH}), 2877 (ν_{CH}), 1738 (ν_{COOH}), 1645 (ν_{COO-}), 1485, 1471, 1376, 1352, 1192 (ν_{CO} or ν_{CN}), 1054 (ν_{CO} or ν_{CN}), 1062; ^{1}H NMR (250 MHz, CD_3–CO–CD_3): δ=3.39 (m, 8H, H-1), 2.77 (s, 2H, H-2′), 1.75 (quint, 8H, H-2, J_{1-2}=8.2 Hz, J_{2-3}=7.3 Hz), 1.38 (sext, 8H, H-3, J_{2-3}=7.3 Hz, J_{3-4}=7.2 Hz), 0.95 (t, 12H, H-4, J_{3-4}=7.2 Hz); ^{13}C NMR (63 MHz, CD_3–CO–CD_3): δ=173.7 (C=O), 60.0 (C-1), 40.2 (C-2′), 25.2 (C-2), 21.1 (C-3), 14.8 (C-4); $C_{19}H_{39}NO_4$·0.8H_2O Calcd C: 63.40%, H: 11.37%; N: 3.89%, Found C: 63.65%; H: 11.03%; N: 3.80%. MS (ESI+) 242.2 MS (ESI−) 103.0.

5.6.4. Tetrabutylammonium succinate **4**.

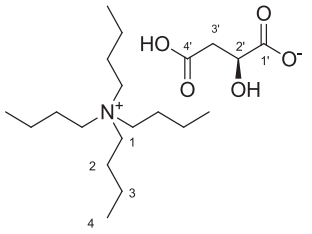


4

General procedure with succinic acid (88.9 mg, 0.75 mmol) and TBAOH·30H_2O (498.2 mg, 0.62 mmol). Tetrabutylammonium succinate (218.6 mg, 0.61 mmol) was obtained as a white wax. Yield: 98%.

IR (film): 3500–3200 (ν_{OH}, ν_{N+}), 2956 (ν_{CH}), 2932 (ν_{CH}), 2871 (ν_{CH}), 1727 (ν_{COOH}), 1553, 1400, 1335, 1304, 1127, 1069; ^{1}H NMR (250 MHz, CD_3–CO–CD_3): δ=3.42 (m, 8H, H-1), 2.44 (large s, 4H, H-2′, H-3′) 1.77 (quint, 8H, H-2, J_{1-2}=7.6 Hz, J_{2-3}=7.3 Hz), 1.40 (sext, 8H, H-3, J_{2-3}=7.3 Hz, J_{3-4}=7.2 Hz), 0.96 (t, 12H, H-4, J_{3-4}=7.2 Hz); ^{13}C NMR (63 MHz, CD_3–CO–CD_3): δ=177.1 (C=O), 60.1 (C-1), 33.3 (C-2′, C-3′), 25.1 (C-2), 21.2 (C-3), 14.8 (C-4). Calcd $C_{20}H_{41}NO_4$ C: 66.81%, H: 11.49%; N: 3.90%, Found C: 65.85%; H: 10.98%; N: 4.02%; MS (ESI+) 242.2 MS (ESI−) 117.1.

*5.6.5. Tetrabutylammonium L-malate **5**.*

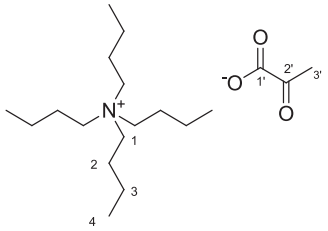


5

General procedure with L-malic acid (101.9 mg, 0.75 mmol) and TBAOH·30H_2O (501 mg, 0.63 mmol). Tetrabutylammonium L-malate (229.6 mg, 0.61 mmol) was obtained as a colorless gel. Yield: 97%.

IR (film): 3500–3200 (ν_{OH}, ν_{N+}), 2963 (ν_{CH}), 2935 (ν_{CH}), 2874 (ν_{CH}), 1721 (ν_{COOH}), 1594, 1489, 1461, 1379, 1263, 1168, 1069; ^{1}H NMR (250 MHz, CD_3–CO–CD_3): δ=4.28 (t, 1H, H-2′, $J_{2'-3'}$=6.4 Hz), 3.30 (m, 8H, H-1), 2.57 (m, 2H, H-3′, $J_{2'-3'}$=6.4 Hz, $J_{3'a-3'b}$=16 Hz), 1.66 (quint, 8H, H-2, J_{1-2}=8.2 Hz, J_{2-3}=7.4 Hz), 1.29 (hex, 8H, H-3, J_{2-3}=7.4 Hz, J_{3-4}=7.3 Hz), 0.84 (t, 12H, H-4, J_{3-4}=7.3 Hz); ^{13}C NMR (63 MHz, CD_3–CO–CD_3): δ=176.9 (C-1′), 173.6 (C-4′), 68.7 (C-2′), 60.2 (C-1), 41.4 (C-3′), 25.4 (C-2), 21.3 (C-3), 14.8 (C-4); $C_{20}H_{41}NO_5$, 0.5H_2O Calcd C: 62.47%, H: 11.01%; N: 3.64%, Found C: 62.00%; H: 10.57%; N: 3.40%. MS (ESI+) 242.2 MS (ESI−) 133.0.

*5.6.6. Tetrabutylammonium pyruvate **6**.*

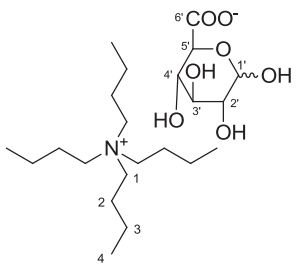


6

General procedure with pyruvic acid (52 μL, 0.73 mmol) and TBAOH·30H_2O (500.9 mg, 0.63 mmol). Tetrabutylammonium pyruvate (191.0 mg, 0.58 mmol) was obtained as a yellow oil. Yield: 93%.

IR (film): 3500–3100 (ν_{OH}, ν_{N+}), 2959 (ν_{CH}), 2935 (ν_{CH}), 2871 (ν_{CH}), 1721 (ν_{COOH}), 1461, 1375, 1338 (ν_{CO} or ν_{CN}), 1059; ^{1}H NMR (250 MHz, CD_3–CO–CD_3): δ=3.40 (m, 8H, H-1), 2.25 (s, 3H, H-3′), 1.77 (quint, 8H, H-2, J_{1-2}=8.2 Hz, J_{2-3}=7.3 Hz), 1.63 (sext, 8H, H-3, J_{2-3}=J_{3-4}=7.3 Hz), 1.22 (t, 12H, H-4, J_{3-4}=7.3 Hz); ^{13}C NMR (63 MHz, CD_3–CO–CD_3): δ=200.5 (C-1′), 168.7 (C-2′), 60.1 (C-1), 25.3 (C-2), 21.1 (C-3), 14.8 (C-4); MS (ESI+) 242.2$C_{19}H_{39}NO_3$, 1H_2O Calcd C: 65.66%, H: 11.89%; N: 4.03%, Found C: 65.80%; H: 11.46%; N: 3.98% MS (ESI+) 242.2 MS (ESI−) 87.1.

*5.6.7. Tetrabutylammonium D-glucuronate **7**.*

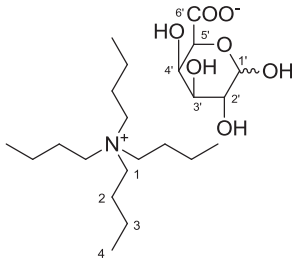


7

D-Glucuronic acid (1.193 g, 6.0 mmol) was dispersed in absolute ethanol (150 mL). A solution of TBAOH·30H_2O (4.02 g, 5.0 mmol) in absolute ethanol (100 mL) was added dropwise at room temperature and the resulting dispersion was stirred at room temperature during 24 h (solution became clear). After evaporation of the solvent under reduced pressure, 150 mL of acetone was added. A white solid formed almost immediately and was separated from the remaining liquid by filtration. The filtrate was evaporated and acetone added one more time to form a white solid. The two solids were combined and gave 1.749 g of tetrabutylammonium D-glucuronate (3.98 mmol) as a white solid. Yield 80%.

T_f: 95 °C. IR (KBr) cm^{-1}: 3500–3000 (ν_{OH}, ν_{N+}), 2963 (ν_{CH}), 2871 (ν_{CH}), 2731, 1611 (ν_{COO-}), 1475, 1431, 1349, 1318, 1291, 1158, 1117, 1065, 1024 (ν_{CO} or ν_{CN}), 949, 885 ^{1}H NMR (250 MHz, CD_3OD): δ=5.03 (d, 1H, H-1′α, $J_{1'\alpha-2'\alpha}$=3.4 Hz), 4.37 (d, 1H, H-1′β, $J_{1'\beta-2'\beta}$=7.7 Hz), 3.96 (d, H-5′α, $J_{4'\alpha-5'\alpha}$=10 Hz), 3.57 (t, 1H, H-3′α, $J_{3'\alpha-4'\alpha}$=8.6, $J_{2'\alpha-1'\alpha}$=9.1 Hz), 3.36 (d, 1H, H-5′β, $J_{4'\beta-5'\alpha}$=8.7 Hz), 3.26 (m, 3H, H-2′α, H-2′β, H-3′β), 3.14 (m, 9H, H-1; H-4′α), 3.07 (t, 1H, H-4′β, $J_{3'\beta-4'\beta}$=$J_{4'\beta-5'\beta}$=8.6 Hz), 1.55 (quint, 8H, H-2, J_{1-2}=8.0 Hz, J_{2-3}=7.3 Hz), 1.32 (sext, 8H, H-3, J_{2-3}=7.3 Hz, J_{3-4}=7.2 Hz), 0.91 (t, 12H, H-4, J_{3-4}=7.2 Hz); ^{13}C NMR (63 MHz, CD_3OD): δ=177.5 (C-6′α), 176.2 (C′-6β), 98.4 (C-1′β), 93.9 (C-1′α), 77.8 (C-3′β), 76.2 (C-4′β), 76.1 (C-5′β), 74.6 (C-3′α), 74.1 (C-4′α), 73.7 (C-2′β), 73.6 (C-5′α), 71.3 6 (C-2′α), 59.4 (C-1), 24.8 (C-2), 20.7 (C-3), 14.1 (C-4); $C_{23}H_{47}NO_6$ Calcd C: 60.66%, H: 10.41%; N: 3.22%, Found C: 59.68%; H: 10.11%; N: 3.30%. MS (ESI+) 242.2, MS (ESI−) 193.0.

*5.6.8. Tetrabutylammonium D-galacturonate **8**.*



8

D-Galacturonic acid mono hydrate (1.312 g, 6 mmol) was dispersed in absolute ethanol (150 mL). A solution of TBAOH·30H_2O (4.0027 g, 5 mmol) in absolute ethanol (150 mL) was added dropwise at room temperature and the resulting dispersion was stirred at room temperature during 24 h. After evaporation of the solvent under reduced pressure, acetone was added and the solution was kept at 4 °C for 2 days to precipitate the remaining D-galacturonic acid. The solid was then eliminated by precipitation and the filtrate kept at 4 °C for 2 days. After elimination of the solid, the filtrate was evaporated under reduced pressure. Tetrabutylammonium D-galacturonate (1.6793 g, 3.86 mmol) was obtained as a white solid. Yield: 77%.

T_f: 98 °C. IR (KBr) cm^{-1}: 3500–3000 (ν_{OH}, ν_{N+}), 2959 (ν_{CH}), 2874 (ν_{CH}), 2737, 1605 (ν_{COO-}), 1468, 1417, 1379, 1335, 1267, 1158, 1140, 1106, 1024 (ν_{CO} or ν_{CN}), 977, 881. ^{1}H NMR (250 MHz, CD_3OD) δ=5.15 (d, 1H, H-1′α, $J_{1'\alpha-2\alpha}$=3.3 Hz), 5.05 (d, 1H, H-1′β, $J_{1'\beta-2'\beta}$=6.4 Hz), 4.37 (m, 1H, H-4′α), 4.24 (dd, 1H, H-4′β, $J_{3'\beta-4'\beta}$=5.9 Hz, $J_{4'\beta-5'\beta}$=2.8 Hz), 4.17 (m, 1H, H-3′α), 4.03 (t, 1H, H-3′β, $J_{2'\beta-3'\beta}$=$J_{3'\beta-4'\beta}$=5.9 Hz), 3.92 (d, 1H, H-5′β, $J_{4'\beta-5'\beta}$=2.8 Hz), 3.74 (dd, 1H, H-2′α, $J_{1'\alpha-2'\alpha}$=3.3 Hz, $J_{2'\alpha-3'\alpha}$=6.9 Hz), 3.44 (d, 1H, H-5′α, $J_{4'\alpha-5'\alpha}$=4 Hz), 3.17 (m, 8H, H-1), 1.62 (quint, 8H, H-2 J_{1-2}=8.2 Hz, J_{2-3}=7.4 Hz), 1.37 (sext, 8H, H-3, J_{2-3}=7.4 Hz, J_{3-4}=7.3 Hz), 0.99 (t, 12H, H-4, J_{3-4}=7.3 Hz); ^{13}C NMR (63 MHz, CD_3OD): δ=176.8 (C-6′α), 176.6 (C′-6β), 104.4 (C-1′β), 97.7 (C-1′α), 86.3 (C-4′β), 84.7 (C-4′α), 83.1 (C-3′β), 79.4 (C-2′β), 79.3 (C-2′α), 77.7 (C-3′α), 74.3 (C-5′α), 73.6 (C-3′β), 59.6 (C-1), 24.9 (C-2), 20.8 (C-3), 14.6 (C-4); $C_{23}H_{47}NO_6 \cdot H_2O$ Calcd C: 58.25%, H: 10.44%; N: 3.09%, Found C: 57.99%; H: 10.18%; N: 3.13%. MS (ESI+) 242.2, MS (ESI−) 193.0.

5.7. General procedure for catalyses

5.7.1. Catalysis experiments. A Schlenk tube was charged with the ionic liquid (c.a. 400 mg) and the catalyst (3.5 mg, 0.02 mmol, 0.01 equiv/substrate) and left for 10 min under vacuum. Next, 1,5-cyclooctadiene (250 μL, 2 mmol, 1 equiv) and distilled water (2 mL, 5 equiv Mass compared to IL) were added under argon. The argon atmosphere was then replaced by hydrogen through a gas bag and the mixture was vigorously stirred for 18 h at room temperature. The aqueous phase was next extracted with Et_2O (3×5 mL) and the combined organic layers were dried over $MgSO_4$ and then filtered through cotton (1 μL was injected into GC to evaluate the conversion). The aqueous phase was kept in the Schlenk tube to be reused.

5.7.2. Recycling experiments. After a short vacuum/argon sequence (three times), the 1,5-cyclooctadiene (250 μL, 2 mmol, 1 equiv) was added, and the mixture was stirred vigorously for 18 h at room temperature under a hydrogen atmosphere (gas bag). Product isolation and characterization is the same as described above.

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Supplementary data

Results from catalysis studies (conversion, ratio of products, recycling) for hydrogenation of 1,5-cyclooctadiene in water Fig S1, and in water and IL (Figs. S2–S11) are provided in ESI. Antimicrobial screening data antifungal Table S1 and antibacterial Table S2 are also included. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.05.054.

References and notes

1. (a) *ACS Symp. Ser. 818*; Rogers, R. D., Seddon, K. R., Eds.; American Chemical Society: USA, 2002; (b) Welton, T. *Chem. Rev.* **1999**, *99*, 2071–2084.
2. Earle, M. J.; Esperança, J. M. S. S.; Gilea, M. A.; Lopes, J. N. C.; Rebelo, L. P. N.; Magee, J. W.; Seddon, K. R.; Widegren, J. A. *Nature* **2006**, *439*, 831–834.
3. Couling, D. J.; Bernot, R. J.; Docherty, K. M.; Dixon, J. K.; Maginn, E. J. *Green Chem.* **2006**, *8*, 82–90.
4. Wasserscheid, P.; Welton, T. *Ionic Liquids in Synthesis*; Wiley-VCH GmbH: Weinheim, Germany, 2002.
5. Olivier-Bourbigou, H.; Magna, L.; Morvan, D. *Appl. Catal., A* **2010**, *373*, 1–56.
6. Procuranti, B.; Myles, L.; Gathergood, N.; Connon, S. J. *Synthesis* **2009**, *23*, 4082–4086.
7. Myles, L.; Gore, R.; Spulak, M.; Gathergood, N.; Connon, S. J. *Green Chem.* **2010**, *12*, 1157–1162.
8. (a) Itoh, T. In *Biotransformation in Ionic Liquid in Future Directions in Biocatalysis*; Matsuda, T., Ed.; Elsevier Bioscience: The Netherlands, 2007; Chapter 1, pp 3–20; (b) Lozano, P. *Green Chem.* **2010**, *12*, 555–569; (c) van Rantwijk, F.; Sheldon, R. A. *Chem. Rev.* **2007**, *107*, 2757–2785; (d) Plaquevent, J.-C.; Levillain, J.; Guillen, F.; Malhiac, C.; Gaumont, A.-C. *Chem. Rev.* **2008**, *108*, 5035–5060.
9. Hallett, J. P.; Welton, T. *Chem. Rev.* **2011**, *111*, 3508–3576.
10. (a) Wei, D.; Ivaska, A. *Anal. Chim. Acta* **2008**, *607*, 126–135; (b) Buzzeo, M. C.; Evans, R. G.; Compton, R. G. *ChemPhysChem* **2004**, *5*, 1106–1120; (c) Galinski, M.; Lewandowski, A.; Stepniak, I. *Electrochim. Acta* **2006**, *51*, 5567–5580; (d) *Electrochemical Aspects of Ionic Liquids*, 2nd ed.; Ohno, H., Ed.; John Wiley & Sons: New Jersey, NJ, 2011.
11. (a) Liu, J.-F.; Jiang, G.-B.; Jönsson, J. A. *Trends Anal. Chem.* **2005**, *24*, 20–27; (b) Baker, G. A.; Baker, S. N.; Pandey, S.; Bright, F. V. *Analyst* **2005**, *130*, 800–808; (c) Pandey, S. *Anal. Chim. Acta* **2006**, *556*, 38–45; (d) Soukup-Hein, R. J.; Warnke, M. M.; Armstrong, D. W. *Ann. Rev. Anal. Chem.* **2009**, *2*, 145–168; (e) Sun, P.; Armstrong, D. W. *Anal. Chim. Acta* **2010**, *661*, 1–16.
12. (a) Baltus, R. E.; Counce, R. M.; Culbertson, B. H.; Luo, H. D.; DePaoli, W.; Dai, S.; Duckworth, D. C. *Sep. Sci. Technol.* **2005**, *40*, 525–541; (b) Han, X.; Armstrong, D. W. *Acc. Chem. Res.* **2007**, *40*, 1079–1086; (c) Arce, A.; Earle, M. J.; Katdare, S. P.; Rodriguez, H.; Seddon, K. R. *Phys. Chem. Chem. Phys.* **2008**, *10*, 2538–2542; (d) Luis, P.; Garea, A.; Irabien, A. *J. Membr. Sci.* **2009**, *330*, 80–89; (e) Gorri, D.; Ruiz, A.; Ortiz, A.; Ortiz, I. *Chem. Eng. J.* **2010**, *154*, 241–245; (f) Meindersma, G. W.; Hansmeier, A. R.; De Haan, A. B. *Ind. Eng. Chem. Res.* **2010**, *49*, 7530–7540.
13. (a) Pârvulescu, V. I.; Hardacre, C. *Chem. Rev.* **2007**, *107*, 2615–2665; (b) Plechkova, N. V.; Seddon, K. R. *Chem. Soc. Rev.* **2008**, *37*, 123–150; (c) Beadham, I.; Gurbisz, M.; Gathergood, N., Chapter 6 In *Handbook of Green Chemistry*, 1st ed.; Boethling, R., Voutchkova, A., Eds.; Designing Safer Chemicals; Wiley-VCH GmbH & KGaA: 2012; Vol. 9, pp 137–158.
14. (a) Sheldon, R. A.; Arends, I.; Hanefeld, U. *Green Chemistry and Catalysis*; Wiley-VCH: Weinheim, Germany, 2007; (b) Augustine, R. L. *Heterogeneous Catalysis for the Synthetic Chemist*; CRC: New York, NY, 1995; (c) Beletskaya, I. P.; Kustov, L. M. *Russ. Chem. Rev.* **2010**, *79*, 441–461.
15. Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772–3789.
16. (a) Kustov, L. M.; Vasina, T. V.; Ksenofontov, V. A. *Ross. Khim. Zh.* **2004**, *48*, 13–35; (b) Olivier-Bourbigou, H.; Magna, L. *J. Mol. Catal.* **2002**, *182–183*, 419–437; (c) Gordon, C. *Appl. Catal., A* **2001**, *222*, 101–110.
17. (a) Dyson, P. J. *Appl. Organomet. Chem.* **2002**, *16*, 495–500; (b) Dyson, P. J.; Dongbin, J. In *Multiphase Homogeneous Catalysis*; Cornils, B., Ed.; 2005; Vol. 2, pp 494–510.
18. Wasserscheid, P.; Schulz, P. In *Handbook of Homogeneous Hydrogenation*; De Vries, J. G., Elsevier, C. J., Eds.; 2007; Vol. 3, pp 1389–1420.
19. Keglevich, G.; Baan, Z.; Hermecz, I.; Novak, T.; Odinets, I. L. *Curr. Org. Chem.* **2007**, *11*, 107–126.
20. Anastas, P.; Warner, J. *Green Chemistry: Theory and Practice*; Oxford University: New York, NY, 1998.
21. Vollmer, C.; Janiak, C. *Coord. Chem. Rev.* **2011**, *255*, 2039–2057.
22. (a) Bhaduri, S.; Mukkesh, D. *Homogeneous Catalysis, Mechanisms and Industrial Applications*; Wiley: 2000; (b) Topsoe, H.; Clausen, B. S.; Massoth, F. E. *Hydrotreating Catalysis, Science and Technology*; Springer: 1996.
23. Dupont, J.; Suarez, P. A. Z.; Umpierre, A. P.; de Souza, R. F. *J. Braz. Chem. Soc.* **2000**, *11*, 293–297.
24. Umpierre, A. P.; Machado, G.; Fecher, G. H.; Morais, J.; Dupont, J. *Adv. Synth. Catal.* **2005**, *347*, 1404–1412.
25. Bouquillon, S.; Courant, T.; Dean, D.; Gathergood, N.; Morrissey, S.; Pegot, B.; Scammells, P. J.; Singer, R. D. *Aust. J. Chem.* **2007**, *60*, 843–847.
26. Anthony, J. L.; Maginn, E. J.; Brennecke, J. F. *J. Phys. Chem. B* **2001**, *105*, 10942–10949.
27. (a) Alvarez-Guerra, M.; Irabien, A. *Green Chem.* **2011**, *13*, 507–513; (b) Ranke, J.; Stolte, S.; Stormann, R.; Arning, J.; Jastorff, B. *Chem. Rev.* **2007**, *107*, 2183–2206; (c) Ranke, J.; Jastorff, B. *Environ. Sci. Pollut. Res.* **2000**, *7*, 105–114; (d) Pernak, J.; Sobaszkiewicz, K.; Mirska, I. *Green Chem.* **2003**, *5*, 52–56; (e) Pernak, J.; Goc, I.; Mirska, I. *Green Chem.* **2004**, *6*, 323–329; (f) Carson, L.; Chau, P. K. W.; Earle, M. J.; Gilea, M. A.; Gilmore, B. F.; Gorman, S. P.; McCann, M. T.; Seddon, K. R. *Green Chem.* **2009**, *11*, 492–497; (g) Arning, J.; Matzke, M. *Curr. Org. Chem.* **2011**, *15*, 1905–1917; (h) Pham, T. P.; Cho, C. W.; Yun, Y. S. *Water Res.* **2010**, *44*, 352–372; (i) Dou, R.-N.; Liu, S.-S.; Mo, L.-Y.; Liu, H.-L.; Deng, F.-C. *Environ. Sci. Pollut. Res.* **2011**, *18*, 734–742; (j) Nancharaiah, Y. V.; Francis, A. J. *Bioresour. Technol.* **2011**, *102*, 6573–6578; (k) Viboud, S.; Papaiconomou, N.; Cortesi, A.; Chatel, G.; Draye, M.; Fontvieille, D. *J. Hazard. Mater.* **2012**, *215*, 40–48; (l) Fatemi, M. H.; Izadiyan, P. *Chemosphere* **2011**, *84*, 553–563; (m) Hossain, M. I.; Samir, B. B.; El-Harbawi, M.; Masri, A. N.; Mutalib, M. I. A.; Hefter, G.; Yin, C.-Y. *Chemosphere* **2011**, *85*, 990–994; (n) Ventura, S. P. M.; Gardas, R. L.; Gonçalves, F.; Coutinho, J. A. P. *J. Chem. Technol. Biotechnol.* **2011**, *86*, 957–963; (o) Zhang, J.; Liu, S.-S.; Dou, R.-N.; Liu, H.-L.; Zhang, J. *Chemosphere* **2011**, *82*, 1024–1029; (p) Liwarska-Bizukojc, E. *Water, Air, Soil Pollut.* **2011**, *221*, 327–335; (q) Tong, Y.; Wang, Q.; Bi, Y.; Lei, M.; Lv, Y.; Liu, Y.; Liu, J.; Lu, L.; Ma, Y.; Wu, Y.; Zhu, S. *Open Biotechnol. J.* **2012**, *6*, 1–4; (r) Ventura, S. P. M.; Marques, C. S.; Rosatella, A. A.; Afonso, C. A. M.; Gonçalves, F.; Coutinho, J. A. P. *Ecotoxicol. Environ. Saf.* **2012**, *76*, 162–172.
28. (a) Stolte, S.; Arning, J.; Bottin-Weber, U.; Muller, A.; Pitner, W. R.; Welz-Biermann, U.; Jacstorff, B.; Ranke, J. *Green Chem.* **2007**, *9*, 760–767; (b) Arning, J.; Stolte, S.; Boschn, A.; Stock, F.; Pitner, W. R.; Welz-Biermann, U.; Jastroff, B.; Ranke, J. *Green Chem.* **2008**, *10*, 47–58; (c) Samori, C.; Malferrari, D.; Valbonesi, P.; Montecavalli, A.; Moretti, F.; Galletti, P.; Sartor, G.; Tagliavini, E.; Fabbri, E.; Pasteri, A. *Ecotoxicol. Environ. Saf.* **2010**, *73*, 1456–1464; (d) Larson, J. H.; Frost, P. C.; Lamberti, G. A. *Environ. Toxicol. Chem.* **2008**, *27*, 676–681; (e) Cho, C.-W.; Jeon, Y.-C.; Phuong Thuy Pham, T.; Vijayaraghavan, K.; Yun, Y.-S. *Ecotoxicol. Environ. Saf.* **2008**, *71*, 166–171.
29. (a) Coleman, D.; Gathergood, N. *Chem. Soc. Rev.* **2010**, *39*, 600–637; (b) Morrissey, S.; Pegot, B.; Coleman, D.; Garcia, M. T.; Ferguson, D.; Quilty, B.; Gathergood, N. *Green Chem.* **2009**, *11*, 475–483; (c) Gathergood, N.; Scammells, P. J. *Aust. J. Chem.* **2002**, *55*, 557–560; (d) Garcia, M. T.; Gathergood, N.; Scammells, P. J. *Green Chem.* **2004**, *6*, 466–474; (e) Garcia, M. T.; Gathergood, N.; Scammells, P. J. *Green Chem.* **2005**, *7*, 9–14; (f) Gathergood, N.; Scammells, P. J.; Garcia, M. T. *Green Chem.* **2006**, *8*, 156–160; (g) Stolte, S.; Steudte, S.; Igartua, A.; Stepnowski, P. *Curr. Org. Chem.* **2011**, *15*, 1946–1973; (h) Boethling, R. S.; Sommer, E.; DiFiore, D. *Chem. Rev.* **2007**, *107*, 2207–2227; (i) Markiewicz, M.; Stolte, S.; Lustig, Z.; Łuczak, J.; Skup, M.; Hupka, J.; Jungnickel, C. *J. Hazard. Mater.* **2011**, *195*, 378–382; (j) Deng, Y.; Besse-Hoggan, P.; Sancelme, M.; Delort, P.; Husson, A.-M.; Costa Gomes, M. F. *J. Hazard. Mater.* **2011**, *198*, 165–174; (k) Petkovic, M.; Seddon, K. R.; Rebelo, L. P. N.; Pereira, C. S. *Chem. Soc. Rev.* **2011**, *40*, 1383–1403; (l) Quijano, G.; Couvert, A.; Amrane, A.; Darracq, G.; Couriol, C.; Le Cloirec, P.; Paquin, L.; Carrie, D. *Chem. Eng. Sci.* **2011**, *66*, 2707–2712; (m) Quijano, G.; Couvert, A.; Amrane, A.; Darracq, G.; Couriol, C.; Le Cloirec, P.; Paquin, L.; Carrie,

D. *Chem. Eng. J.* **2011**, *174*, 27–32; (n) Zhang, C.; Malhotra, S. V.; Francis, A. J. *Chemosphere* **2011**, *82*, 1690–1695; (o) Coleman, D.; Spulak, M.; Garcia, M. T.; Gathergood, N. *Green Chem.* **2012**, *14*, 1350–1356.
30. (a) Stolte, S.; Abdulkarim, S.; Arning, J.; Blomeyer-Nienstedt, A.; Bottin-Weber, U.; Matzke, M.; Ranke, J.; Jastorff, B.; Thoeming, J. *Green Chem.* **2008**, *10*, 214–224; (b) Pham, T. P.; Cho, C. W.; Jeon, C. O.; Chung, Y. J.; Lee, M. W.; Yun, Y. S. *Environ. Sci. Technol.* **2009**, *43*, 516–521.
31. Ford, L.; Harjani, J.; Atefi, F.; Garcia, M. T.; Singer, R.; Scammells, P. *Green Chem.* **2010**, *12*, 1783–1789.
32. (a) Cole, A. C.; Jensen, J. L.; Ntai, I.; Tran, K. L. T.; Weaver, K. J.; Forbes, D. C.; Davis, J. H. *J. Am. Chem. Soc.* **2002**, *124*, 5962–5963; (b) Keglevich, G.; Grun, A.; Hermecz, I.; Odinets, I. L. *Curr. Org. Chem.* **2011**, *15*, 3824–3848.
33. (a) Wenter, G. E.; McGrady, J.; Gosselink, E. P.; Cilley, W. A. *Eur. Pat. Appl.* **1981**, *36*; (b) Gledhill, W. E.; Saeger, V. W. *J. Ind. Microbiol.* **1987**, *2*, 97–100; (c) Waters, J.; Kleiser, H. H.; How, M. J.; Barratt, M. D.; Birch, R. R.; Fletcher, R. J.; Haugh, S. D.; Hales, S. G.; Marshall, S. J.; Pestell, T. C. *Tenside, Surfactants, Deterg.* **1991**, *28*, 460–468; (d) Durif-Varambon, B.; Bocard, C.; Gatellier, C.; Sillion, B. *Ger. Offen.* **1976**, DE 2558907 19760708. A distinction is made here between a surfactant and an ionic liquid. There is reported biodegradation data for higher MW_t ammonium salt surfactants.
34. ISO 5815. *Water Quality—determination of Bio-Chemical Oxygen Demand after 5 Day (BOD5)-dilution and Seeding Method*; 1989.
35. Pavlovica, S.; Zicmanis, A.; Gzibovska, E.; Klavins, M.; Mekss, P. *Green Sustainable Chem.* **2011**, *1*, 103–110.
36. Yu, Y.; Lu, X.; Zhou, Q.; Dong, K.; Yao, H.; Zhang, S. *Chem.—Eur. J.* **2008**, *14*, 11174–11182.
37. Pretti, C.; Renzi, M.; Focardi, S.; Giovani, A.; Monni, G.; Melai, B.; Rajamani, S.; Chiappe, C. *Ecotoxicol. Environ. Saf.* **2011**, *74*, 748–753.
38. Pernak, J.; Borucka, N.; Walkiewicz, F.; Markiewicz, B.; Fochtman, P.; Stolte, S.; Steudtec, S.; Stepnowski, P. *Green Chem.* **2011**, *13*, 2901–2910.
39. Wells, A. S.; Coombe, V. T. *Org. Process Res. Dev.* **2006**, *10*, 794–798.
40. (a) Abrusci, C.; Palomar, J.; Pablos, J. L.; Rodriguez, F.; Catalinac, F. *Green Chem.* **2011**, *13*, 709–717; (b) Bergheim, M.; Helland, T.; Kallenborn, R.; Kümmerer, K. *Chemosphere* **2010**, *81*, 1477–1485.
41. (a) Fukumoto, K.; Yoshizawa, M.; Ohno, H. *J. Am. Chem. Soc.* **2005**, *127*, 2398–2399; (b) Wu, L.; Wang, W.; Li, B. Shuomingshu CN 1749249 A 2006322, 2006; (c) Shan, Y.; Hou, Y.; Shi, S.; Lai, K.; Kong, A. Shuomingshu CN 1821228 A 20060823, 2006. (d) Kümmerer, K. *Green Chem.* **2007**, *9*, 899–907.
42. (a) Allen, C. R.; Richard, P. L.; Ward, A. J.; van de Water, L. G. A.; Masters, A. F.; Maschmeyer, T. *Tetrahedron Lett.* **2006**, *47*, 7367–7370; (b) Ingalsben, M. L.; St Denis, J. D.; McGahan, M. E.; Steiner, W. W.; Priefer, R. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 4984–4987; (c) Zhang, S.; Huang, Y.; Jing, H.; Yao, W.; Yan, P. *Green Chem.* **2009**, *11*, 935–938; (d) Quing, G.; Sun, T.; Chen, Z.; Yang, X.; Wu, X.; He, Y. *Chirality* **2009**, *21*, 363–373; (e) Quing, G.-G.; He, Y.-B.; Wang, F.; Quin, H.-J.; Hu, C.-G.; Yang, X. *Eur. J. Org. Chem.* **2007**, 1768–1778; (f) Vanderhoeven, S. J.; Lindon, J. C.; Troke, J.; Tranter, G. E.; Wilson, I. D.; Nicholson, J. K. *Xenobiotica* **2004**, *34*, 73–85.
43. Endres, F.; Zein El Abedin, S. *Phys. Chem. Chem. Phys.* **2006**, *8*, 2101–2116.
44. Zhao, D.; Dyson, P. J.; Laurenczy, G.; McIndoe, J. S. *J. Mol. Catal. A: Chem.* **2004**, *214*, 19–25.
45. Kernchen, U.; Etzold, B.; Korth, W.; Jess, A. *Chem. Eng. Technol.* **2007**, *30*, 985–994.
46. She, J.; Ye, L.; Zhu, J.; Yuan, Y. *Catal. Lett.* **2007**, *116*, 70–75.
47. Di Castro, V.; Furlani, C.; Fragale, C.; Gargano, M.; Rossi, M.; Ravasio, N. *Gazz. Chim. Ital.* **1987**, *117*, 43–50.
48. Dyson, P. J.; Geldbach, T. J. *Metal Catalysed Reactions in Ionic Liquids, Catalysis by Metal Complexes*; 2005; Vol. 2941–70.
49. Schmidt, A.; Schomäcker, R. *Ind. Eng. Chem. Res.* **2007**, *46*, 1677–1681.
50. Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Clinical Laboratory Standard Institute: Wayne, PA, 2008; Approved standard. Document M27-A3.
51. Reference Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi; Clinical Laboratory Standard Institute: Wayne, PA, 2008; Approved standard. Document M38-A2.
52. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically, 7th ed.; Clinical Laboratory Standard Institute: Wayne, PA, 2006; Approved Standard Document M07-A7.
53. Amsterdam, D. Susceptibility Testing of Antimicrobials in Liquid Media 72 In *Antibiotics in Laboratory Medicine*, 3rd ed.; Lorian, V., Ed.; Williams and Wilkins: Baltimore, MD, 1991.
54. OECD. *Guidelines for Testing of Chemicals: 301 D: Closed Bottle Test*; Organisation of Economic Cooperation and Development: Paris, France, 1992.
55. Haiß, A.; Kümmerer, K. *Chemosphere* **2006**, *62*, 294–302.
56. ISO 5414. Water Quality – Determination of dissolved oxygen In *German Standard Methods for the Examination of Water, Wastewater and Sludge*; VCH Verlagsgesellschaft: Wienheim, Basel, Cambridge, 1990.