CHEMICAL ENGINEERING TRANSACTIONS

VOL. 43, 2015

Chief Editors: Sauro Pierucci, Jiří J. Klemeš
Copyright © 2015, AIDIC Servizi S.r.l.,
ISBN 978-88-95608-34-1; **ISSN** 2283-9216

A publication of AIDIC
The Italian Association
of Chemical Engineering
Online at www.aidic.it/cet

DOI: 10.3303/CET1543380

Sustainability Improvement of Chemical Processes using Amino Ionic Liquids as Catalysts in Water

Patrizia Primerano*[a], Maria Francesca Milazzo[a], Francesco Risitano[b]

[a]Dipartimento di Ingegneria Elettronica, Chimica e Ingegneria Industriale, Università di Messina, Viale Ferdinando Stagno d'Alcontres 31, 98166, Messina, Italy
[b]Dipartimento di Scienze Chimiche, Università di Messina, Viale Ferdinando Stagno d'Alcontres 31, 98166, Messina, Italy
Patrizia.Primerano@unime.it

Within the development of chemical processes, according to *Green Chemistry* and *Engineering* guidelines, the use of solvents, given their toxicity, must be greatly reduced or eliminated. Reactions, realized in the absence of solvent or using water, would be desirable. Unfortunately, these two alternatives are not always viable due to two main reasons: (1) the use of a solvent is mainly necessary to facilitate the mass and heat transfer; (2) water is an impractical solvent for organic transformations because most organic compounds are insoluble or have a low solubility in water. As a consequence, many efforts are being made to find less harmful reaction medium. Recently, a new generation of Ionic Liquids with a functional group incorporated in the side chain to meet the needs of specific reactions (TSILs) is gaining increasing interest, as they enclose both solvent and catalytic properties. In this context, a new basic type of Ionic Liquids (BILs), incorporating a β-amino group in the side chain was introduced (Primerano et al., 2013). In this paper the synthesis and use of a new IL of the above class, containing the acetate as anion, together with an estimate of related E-factors is presented. Some comments about the increasing environmental sustainability for the processes due the use of the previous and novel BILs in water are given.

1. Introduction

Ionic Liquids (ILs) continue to attract considerable attention in the context of green organic syntheses, due to their unique physical and chemical properties (low volatility and flammability, thermal stability, controlled miscibility and their ability to be easily recovered and recycled many times over). In this frame, popular imidazolium-based ILs (Safaei-Ghomi et al., 2010; Sarkar et al. 2011a, Sarkar et al. 2011b) play an important role within the class of Room-Temperature Ionic Liquids (RTILs), because of their wide use in many different areas, such as solvents in organic syntheses, polymerizations, nanoparticles' syntheses, in analytical chemistry, in extraction processes, as catalysts to improve the reaction time, the yield and the chemoselectivity of organic reactions (Yu et al. 2010), as enzyme-friendly co-solvents and as lubricant; they are also used in batteries, in hydrocarbon petroleum industries as green solvents (Dharaskar Swapnil, 2012), etc. Despite these successes, some drawbacks begin to emerge, which in some regard can limit their "greenness", such as their toxicity and/or thermal instability. Unfortunately, almost all the current ILs have no available supporting toxicological data, furthermore decomposition/degradation processes have not been sufficiently investigated. Moreover, most of the current synthetic protocols occur by using multi-step synthesis with hazardous reagents (as alkyl halides) in organic solvents and complex purification processes. Nowadays, as new protocols of synthesis that use less hazardous reagents in DMC (dimethyl carbonate) begin to appear (Holbrey et al., 2002; Wasserscheidet al., 2003), the replacement of hazardous and toxic organic solvents with less harmful ones has not yet found satisfactory solutions. For these reasons, the development of new approaches for the preparation and purification of ILs through simpler and more environmentally sustainable procedures that are also cost/time and atom efficient would be desirable. This trend also follows the concept of *Inherently Safer Design* (ISD) of chemical processes, which aim at achieving a higher level of safety by giving emphasis on eliminating or avoiding the hazards from manufacturing processed rather than relying on

Please cite this article as: Primerano P., Milazzo M.F., Risitano F., 2015, Sustainability improvement of chemical processes using amino ionic liquids as catalysts in water, Chemical Engineering Transactions, 43, 2275-2280 DOI: 10.3303/CET1543380

controlling the hazards (Fabiano et al., 2012); this was pointed as a strategic research lines by De Rademaeker et al. (2014).

Recently, Primerano et al. (2013) have proposed a synthesis of new ILs in aqueous solution characterized by having an amino-tertiary aliphatic portion in the side chain. These showed a successful activity as promoters of dibromination nucleophilic reactions of C = C bonds of electron-rich and poor-alkenes, as well as solvents. Due to their potential characteristics of base-catalysts, they can replace external bases, which could lead to unwanted products because of the acidic nature of the proton H-2 sandwiched between the two nitrogen atoms of imidazolium cation (Canal et al., 2006; Aggarwal et al., 2002); given the potentials of such ILs, we decided to broaden the range of this new class of composts by preparing an IL with the acetate as anionic portion instead of BF_4^- or PF_6^- or ClO_4^-, which are potential toxic. A preliminary estimate of the E-factor is also presented in order to quantify the improvement of the sustainability in preparing these ILs.

2. Materials and methods

2.1 Materials

All solvents and reagents were obtained from commercial sources and, where necessary, they were purified before use. Merck Kiesel gel 60F254 plates were used for TLC, and Merck Silica gel 60 (0.063–0.100 mm) was used for flash column chromatography. IR spectra were recorded in Nujol with a Nicolet Impact 410D spectrometer. ^1H and ^{13}C NMR spectra were obtained on a Varian 500 MHz spectrometer. The chemical shifts (δ) and coupling constants (J) are expressed in ppm and hertz respectively. Microanalyses were carried out on a Carlo Erba EA 1102.

2.2 General experimental procedures

2.2.1. Preparation of imidazolium acetate IL

N-Methylimidazole (1 mmol) was added to equivalent amounts of 2-(diethylamino) ethyl chloride hydrochloride and NaOH in 5 mL water (Figure 1). The resulting mixture (~ 100 °C) was stirred at refluxing for 12 h. After cooling at room temperature, an equivalent amount of sodium acetate (AcONa) was added and the stirring was continued for further 1 h. The evaporation of water under vacuum left a solid residue, from which the IL was extracted by warmed EtOH (yield = 93 %). As an alternative, the same IL was quantitatively prepared from pure isolated imidazolium chloride IL (Primerano et al., 2014).

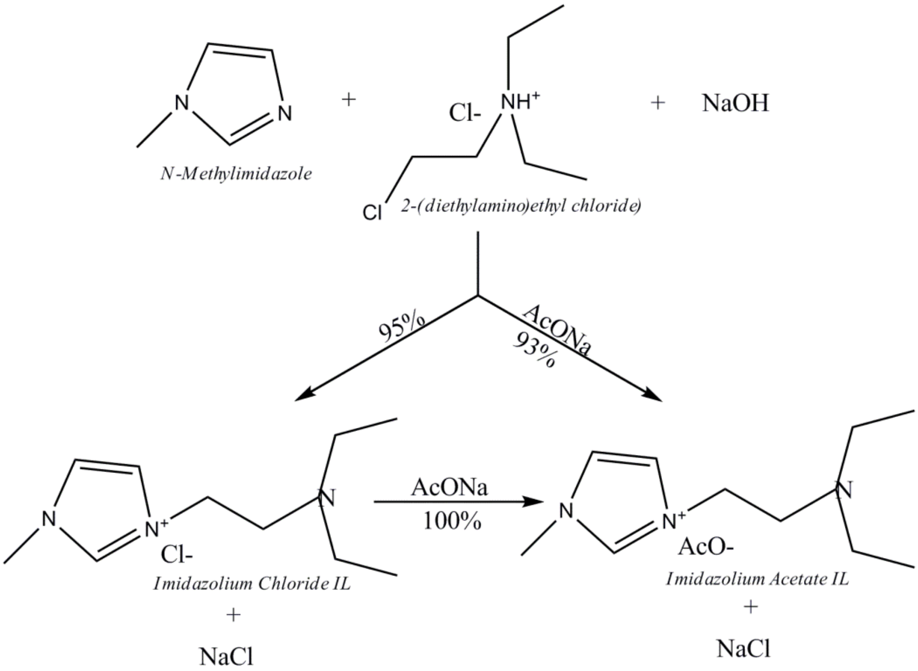

Figure 1: Preparation of the imidazolium acetate IL

Imidazolium acetate IL (93 %): [1H NMR, (300 MHz, $CDCl_3$): δ= 10.49 (s, 1H); 7.41 (d, J=1.69, 1H); 7.22 (d, J=1.69, 1H); 4.24 (t, J=5.65, 2H); 3.93 (s, 3H); 2.72 (t, J=5.65, 2H); 2.44 (q, J=7.11, 4H); 1.84 (s, 3H); 0.82 (t, J=7.11, 6H). 13C NMR, (75 MHz, $CDCl_3$): δ=177.52, 139.35, 122.54, 122.15, 52.77, 47.81, 46.77, 46.65, 36.08, 24.92, 11.55] $C_{12}H_{23}N_3O_2$ (%): calcd C 59.75; H 9.54; N 17.43; found C 59.92; H 9.59; N 17.51.

2.2.2. General procedure for dibromination of alkenes

In a 25 mL flask containing imidazolium acetate IL (30 %) and water (5 mL), pure 1-octene or cyclohexene or chalcone (3.0 mmol) was added. The flask was immersed in an ice-water bath to maintain the reaction mixture between 0 °C and 10 °C. Under a continuous stirring, Br_2 (3.0 mmol) was added dropwise by a syringe as rapidly as the colour was destroyed. After all the bromine was added, stirring was continued for additional 15 minutes at room temperature (Figure 2). 1-trans-dibromo-cyclohexane and 1,3-diphenyl-trans-2,3-dibromo-1-propanone (solids) were collected by filtration and purified by crystallization in the minimum amount of boiling methanol (yield, respectively, 84 % and ~ 100 %), while the remaining aqueous solution containing imidazolium acetate IL was ready for reuse. In the case of liquid 1,2-dibromooctane, the resulting mixture after Br_2 addition was extracted with ethyl acetate (3 times with 10 mL) and the extract was washed with water and dried over anhydrous sodium sulfate (Na_2SO_4), while the remaining aqueous solution containing imidazolium acetate IL was ready for reuse as above. The solvent evaporation left the crude product, which was purified by flash chromatography over silica gel (hexane-ether 9:1) to provide pure 1,2-dibromo-octane (90 %) as a colourless oil.

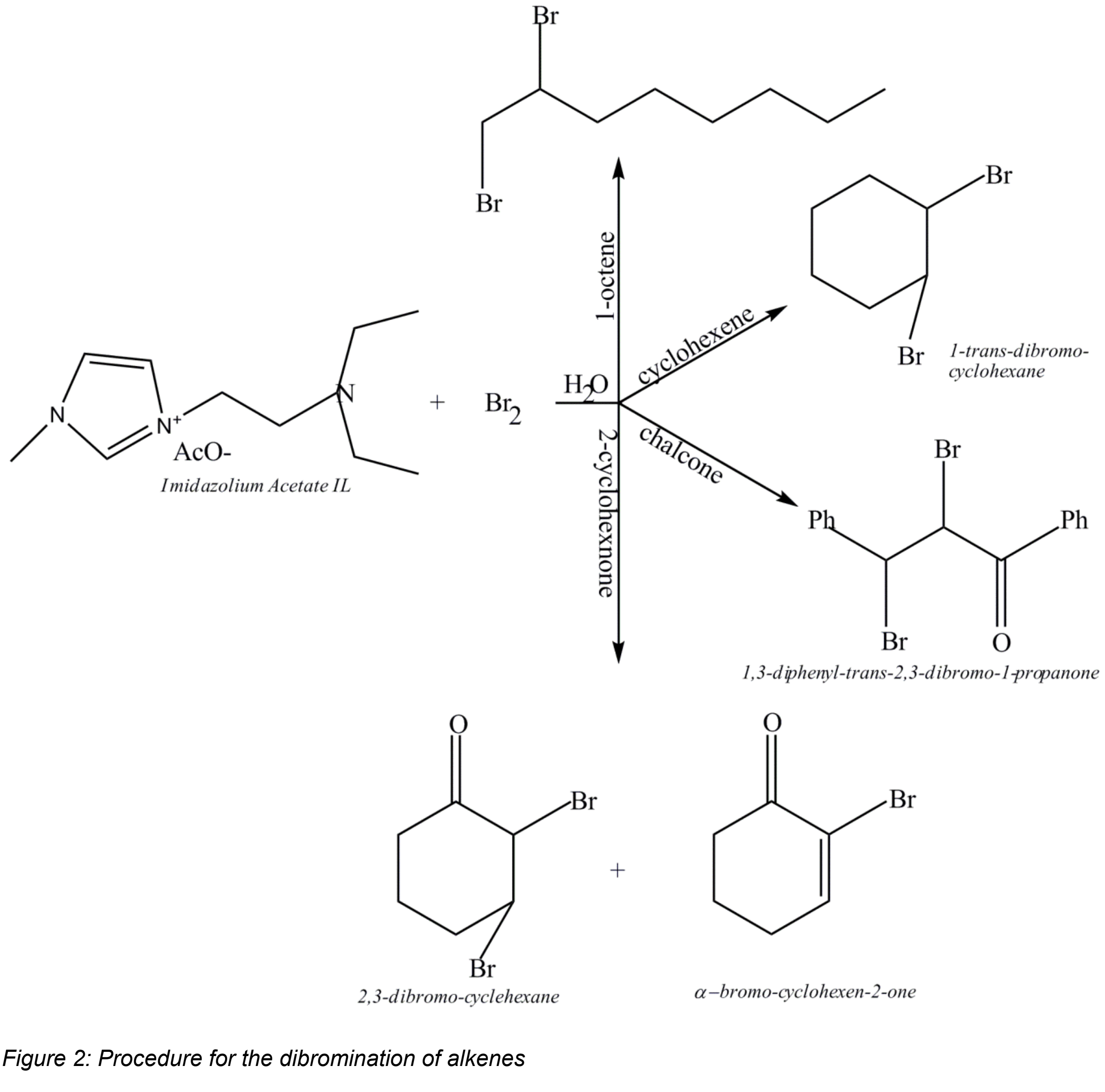

Figure 2: Procedure for the dibromination of alkenes

2.2.3. Synthesis of α-bromocyclohexen-2-one

Molecular Br_2 (1 mmol) was added dropwise using a syringe to a mixture of 2-cyclohexenone (1 mmol) and imidazolium acetate IL (1.2 mmol) in water (5 mL). The resulting mixture was stirred at room temperature until the reaction was completed (monitored by TLC), usually within 20 min and, then, extracted with ethyl acetate (10 mL). The organic phase was washed with water[1] (10 mL) and dried over anhydrous sodium sulfate. The solvent evaporation under vacuum left a crude product which was purified by flash chromatography over silica gel (hexane-ethyl acetate 10:1) to provide in excellent yield (80 %) pure α-bromocyclohexen-2-one (Figure 3). Its spectroscopic data (IR, 1H and 13C NMR) overlapped with those of an authentic sample (Bose et al., 2001; Jyothi and HariPrasad, 2009; Ponaras and Zaim, 1986; Ye and Shreeve, 2004). The acidic aqueous phase, instead, was treated with 10% NaOH until neutralization and, then, extracted with methylene chloride to recover BIL that was reused for subsequent conversions.

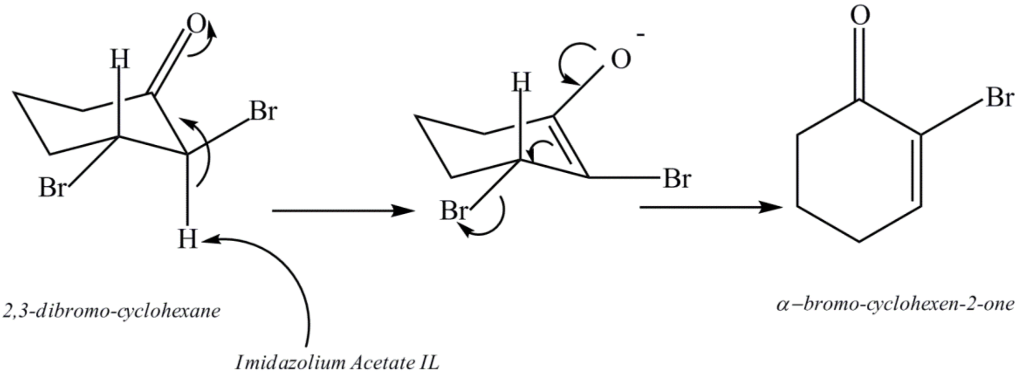

Figure 3: Synthesis of α-bromocyclohexen-2-one

2.3 E factor analysis

The E-factor (EF) is a parameter to measure the (potential) environmental acceptability of chemical processes. It can be estimated as the mass ratio of waste ($mass_{waste}$) to desired product ($mass_{product}$) or as the total mass of raw materials ($mass_{input}$) minus the mass of product divided by the mass of product (Sheldon, 2010) (Eq. 1):

$$EF = \frac{mass_{waste}}{mass_{product}} = \frac{mass_{input} - mass_{product}}{mass_{product}} \tag{1}$$

The amount of waste includes reagents, solvent losses (water is excluded), by-products, process aids and fuel; thus the EF is calculated by using the yield of the reaction.

The EFs was estimated for the following reactions for the alternative syntheses of ILs compared to those synthesised by Primerano et al. (2013) and Primerano et al. (2014).

3. Results and discussion

The preparation of imidazolium acetate IL is a "one-pot" consecutive multicomponent transformation (Figure 1), which occurs in water and proceeds via the initial formation of the imidazolium choride IL and the subsequent anion metathesis by addition of an acetate salt to the same reaction mixture.

Alternatively, the imidazolium chloride IL can be isolated and converted quantitatively in the imidazolium acetate IL, according to the method of Primerano et al. (2014). By means of both methods, however, the pure imidazolium acetate IL must be separated from NaCl by evaporation under vacuum of the aqueous medium and subsequent extraction with warm EtOH. From environmental point of view, this preparation and the previous one are less harmful than those conducted in organic solvents because a step of the whole traditional synthesis is eliminated and also because the EtOH is easily recoverable and reusable.

The imidazolium acetate IL is liquid at room temperature, thus, it could be used as a solvent. It is miscible with water and, at the same time, is able to solubilise organic compounds. It can be also considered in conducting organic reactions in aqueous phase. With this background, given the nature of the anion, it was initially tested for dibromination reactions in water of both selected electron-rich and -poor olefins (Figure 2). Results were

---

[1] A preliminary washing with NaOH (10%) was needed to remove any traces of phenolic by-products (Belmont and Paquette, 1985).

compared with those of the analogous ILs containing the anions PF_6^- or BF_4^-. Also these reactions efficiently proceeded in water to give vicinal dibromides at room temperature without the need of other catalysts or working in the dark, they also were completed in a short time, confirming once again the crucial role of the amine side chain and not of the anionic portion in the dibromination reaction. The reaction with 2-cyclohexenone is an exception: because its base-catalyst action under usual conditions (i.e. with the imidazolium acetate IL, catalytic amount equal to 30 %), the expected product 2,3-dibromo-cyclohexane (Nishiyama et al., 2000) was simultaneously obtained with another compound that was identified as α-bromocyclohexen-2-one, on the basis of its spectroscopic data and analytical. Using, however, an equimolar amount of 4, only α-bromocyclohexen-2-one was produced with acceptable yields (80 %), probably through the scheme described in Figure 3.

Further, the addition of bromine is resulted completely stereoselective as previously reported: the cyclohexene producing trans-dibromo-cyclohexane isomer and trans-chalcone lead to erythro 1,2-diphenyl-trans-2,3-dibromo-1-propanone. By considering that the ILs containing PF_6^- or BF_4^- can be toxic as they can generate hazardous HF during recycling, they have high cost and limited disposability (Kamal et al., 2005) and the complete observed diastereoselectivity, the synthesis and reactivity of this imidazolium acetate IL appears interesting and overall environmentally benign compared with those of the previous synthesised ILs of the same class (Primerano et al., 2013; Primerano et al., 2014). This statement is evident from the calculation of the numbers of Sheldon given in Table1.

Table 1: Estimates of EF

Synthesis	Yield	EF	Reference
Traditional synthesis of IL incorporating BF_4^-	95	32.29	Primerano et al., 2013
Alternative synthesis of IL incorporating BF_4^-	95	6.55	Primerano et al., 2014
Synthesis of imidazolium chloride IL	95	0.48	Primerano et al., 2014
Synthesis of imidazolium acetate IL	93	0.63	Present work

4. Conclusions

An attempt was made to determine whether the imidazolium chloride IL can be used as solvent and catalyst. The use of imidazolium chloride IL, as starting material for ILs, having in common the imidazolium cation, was demonstrated (Primerano et al, 2014). For this purpose, the above reactions were repeated in the presence of imidazolium chloride IL; the results agreed with those of imidazolium acetate IL showing, therefore, that it remains unchanged and that the chloride anion does not enter into the side reactions to produce chlorinated by-products. Moreover, this evidence suggests that the quality, as base-catalysts, of these ILs derives from the side chain amino and not from the nature of the anion is suspected for the reactions with imidazolium acetate IL.

The potential of these ILs for organic synthesis and other uses are actually studied in our laboratories.

References

Aggarwal V.K., Emme I., Mereu A., 2002, Unexpected side reactions of imidazolium-based ionic liquids in the base-catalysed Baylis–Hillman reaction, Chem.Comm., 2002(15), 1612-1613.

Belmont S.T., Paquette L.A., 1985, Synthetic studies aimed at the dolastanes. An attempted A + C .fwdarw. ABC approach, J. Org. Chem., 50, 4102-4207.

Bose G., Barua P.M.B., Chaudhuri M.K., Kalita D., Khan A.T., 2001, A convenient and useful method of preparation of alpha-bromo enones from the corresponding enones using organic ammonium tribromide (OATB), Chem. Lett., 4, 290-291

Canal J.P., Ramnial T., Dickie D.A., Clyburne J.A. C., 2006, From the reactivity of N-heterocyclic carbenes to new chemistry in ionic liquids, Chem.Comm., 2006(17), 1809-1818.

De Rademaeker E., Suter G., Pasman H., Fabiano B., 2014, A review of the past, present and future of the European loss prevention and safety promotion in the process industries, Process Saf. Environ., 92(4), 280-291.

Dharaskar Swapnil A., 2012, Ionic Liquids (A Review): The Green Solvents for Petroleum and Hydrocarbon Industries, Res.J. Chem. Sci., 2(8), 80-85.

Fabiano B., Reverberi A.P., Del Borghi A., Dovì V.G., 2012, Biodiesel Production via Transesterification: Process Safety Insights from Kinetic Modeling, Theor. Found. Chem. Eng. 46(6), 676-680.

Holbrey, J.D., Reichert W.M., Swatloski R.P., Broker G.A., Pitner W.R., Seddon K.R., Rogers R.D., 2002, Efficient, halide-free synthesis of new, low cost ionic liquids: 1,3-dialkylimidozolium salts containing methyl- and ethylsulfate anions, Green Chem., 4, 407-413.

Jyothi D., HariPrasad S., 2009, A Remarkably Simple One-Step Procedure for the Preparation of α-Bromo-α,β-Unsaturated Carbonyl Compounds, Synlett., 2309-2311.

Kamal A., Rajasekhar Reddy D., Rajendar, 2005, A simple and green procedure for the conjugate addition of thiols to conjugated alkenes employing polyethylene glycol (PEG) as an efficient recyclable medium, Tetrahedron Lett., 46, 7951-7953.

Nishiyama T., Ono Y., Kurokawa S., Kimura S., 2000,Trifluoromethanesulfonic anhydride-promoted alpha-bromination of ketones with grignard reagent or magnesium bromide, Chem. Pharm. Bull., 48, 1999-2002.

Ponaras A.A., Zaim O., 1986, Synthetic elaboration of diosphenols. Replacement of hydroxyl by halogen, J. Org. Chem., 51, 4741-4743.

Primerano P., Cordaro M., Scala A., 2013, Direct sustainable bromination of alkenes in aqueous media and basic ionic liquids. Tetrahedron Lett., 54, 4061-4063.

Primerano P., Milazzo M.F, Risitano F., Matarazzo A., 2014, Sustainability Improvement of the TBECH Synthesis using Amino ILs as Catalysts in Water. A Facile and Environmentally-Friendly Procedure, forthcoming in J. Chem. Technol. Biot.

Safaei-Ghomi J., Emaeili M., 2010, Mild and Efficient Method for Oxidation of Alcohols in Ionic Liquid Media, Digest J. Nanomat. Biostr., 5(4), 865-871.

Sarkar A., Roy S.R., Parikh N., Chakraborti A.K., 2011a, Nonsolvent Application of Ionic Liquids: Organo-Catalysis by 1-Alkyl-3-methylimidazolium Cation Based Room-Temperature Ionic Liquids for Chemoselective N-tert-Butyloxycarbonylation of Amines and the Influence of the C-2 Hydrogen on Catalytic Efficiency, J. Org. Chem., 76(1), 7132–7140.

Sarkar D., Bhattarai R., Headley A.D., Ni B., 2011b, A Novel Recyclable Organocatalytic System for the Highly Asymmetric Michael Addition of Aldehydes to Nitroolefins in Water, Synthesis, 2011, 1993-1997.

Sheldon, R., 2010, Introduction to Green Chemistry, Organic Synthesis and Pharmaceuticals, in Green Chemistry in the Pharmaceutical Industry, Dunn P.J., Wells A.S., Williams M.T., Eds; Publisher: Wiley-VCH GmbH & Co. KGaA, Weinheim, 1-20.

Wasserscheid P., van Hal R., Bosmann A., Esser J., Jess A., 2003, New ionic liquids based on alkylsulfate and alkyl oligoether sulfate anions: synthesis and applications, vol. 856: Ionic Liquids and Green Solvents: Progress and Prospects, Eds. Rogers R.D., Seddon K.R.), ACS Symposium Series, American Chemical Society, Washington.

Ye C., Shreeve J.M., 2004, Structure-Dependent Oxidative Bromination of Unsaturated C-C Bonds Mediated by Selectfluor, J. Org. Chem., 69, 8561-8563.

Yu J.-I., Ju H.-Y., Kim K.-H., Park D.-W., 2010, Cycloaddition of carbon dioxide to butyl glycidyl ether using imidazolium salt ionic liquid as a catalyst, Korean J. Chem. Eng., 27(2), 446-451.