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RECENT TRENDS ON APPLICATION OF IONIC LIQUIDS IN ORGANIC SYNTHESIS

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Ionic liquids have been identified as one of the new classes of solvents that offer opportunities to move away from traditional chemical processes to new, clean technologies in which waste streams are minimized. Ionic liquids are salts composed of organic cations and organic or inorganic anions. They are liquid at room temperature and by definition have low melting points (<150 °C). Compared to conventional organic solvents, the use of ionic liquids for synthesis, catalysis and extraction has a number of advantages determined by the unique combinations of their properties. These properties are significant when addressing the health and safety concerns associated with many solvent applications. This work reviews the latest trends on the application of ionic liquids in organic reactions.

Keywords: Ionic liquid, organic synthesis

Introduction

The green chemistry movement, which encompasses the application of environmentally sound chemicals and chemical processes, has widespread quickly in the last decades. One of its most important goals is to replace the hazardous volatile organic compounds required for mixing and dissolving with benign solvents. A wide range of solvent application have been investigated and in many cases the ionic liquid media, that are now studied because of their specific advantages in rate, specificity, and yield rather than simple VOC replacement, proved to satisfy the given requirements [1].

Generally, the term “ionic liquids” (IL) stands for liquids composed of ions. These are usually molten salts or molten oxides. Inorganic salts such as the sodium halogens are solid with melting point well above 500 °C. The novelty of ILs is the low melting temperature; they usually have a melting point arbitrarily fixed at or below 100 °C. If the melting point is below room temperature (~25 °C), the IL is called room-temperature ionic liquid (RTIL) [2].

It has been noted that the properties of molten salts as a solvent for chemical processes differ from those of aqueous and organic solvents. Some processes, for instance, the electrochemical reduction of aluminium from alumina, can be conducted only in molten salts and are impossible in aqueous solutions [3].

A book titled Ionic liquid for synthesis was published by Wasserschied and Welton [4] in 2007. It contains information about the physicochemical properties of ILs and the role of ILs in organic, inorganic and biocatalytic reactions.

The objective of our work is not to exceed a book concerning ILs but to draw attention to the recent trends of IL application focusing mainly on organic synthesis reactions, such as acylation, alkylation, condensation, esterification, hydrogenation, hydroformylation and oxidation.

Acylation

Friedel-Crafts acylation reactions are of great importance in the industrial manufacture of aryl ketones, and are used extensively in the production of pharmaceuticals such as the nonsteroidal anti-inflammatory drugs Ibuprofen and Naproxen. Conventionally, these reactions are catalysed by aluminium trichloride, using an acylating agent such as an acid chloride in a volatile organic solvent The Friedel-Crafts benzoylation of anisole with benzoic anhydride to yield 4-methoxybenzophenone has been carried out in a range of ILs using zeolite catalysts [5], as shown in *Fig. 1.* The rates of reaction were found to be significantly higher using ILs compared with organic solvents. Continuous-flow studies of successful IL systems indicate that the bulk of the catalysis is due to the formation of an acid via the ion exchange of the cation with the protons of the zeolite. The acid liberated was quantified using both titration experiments and ion-exchange experiments using sodium-exchanged zeolites.

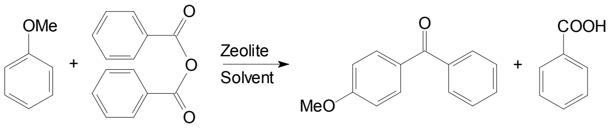

Figure 1: Scheme of the Friedel-Crafts benzoylation

Many acylation reactions have been demonstrated in acidic chloroaluminate(III) (Cl·$AlCl_3$) ILs. As with the conventional processes, difficulties remain from the reaction being noncatalytic in aluminium chloride ($AlCl_3$) which necessitates destroying the IL catalyst by quenching with water to extract the products. However, regioselectivity and reaction rates observed from acylation reactions in ILs were equal to the best published results. Friedel-Crafts acylation of benzene is promoted by Franklin acidic Cl·$AlCl_3$ ILs [6]: as is typical for acylation reactions, selectively monoacylated products are formed through deactivation of the aromatic ring by the first acyl substituent. The acylated products of these reactions show high selectivities to a single isomer: for example toluene, chlorobenzene and anisole are acylated in the 4-position with 98% specificity. Naphthalene is acylated in the 1-position which is the thermodynamically unfavoured product under conventional Friedel-Crafts acylation conditions compared to the derivatisation at the 2-position, the "normal" product [7].

Alkylation

Amines and their derivatives have many functions in various natural products and unnatural synthetic targets. Because of their unique biological properties, substituted amines are widely used clinically as antihypertensive, antihistamine, and antiinflammatory drugs. The synthetic approaches to make secondary and tertiary amines include reductive alkylation the use of protecting groups, and direct N-alkylation. These traditional methods for the synthesis of amines typically require highly polar solvents such as dimethyl sulphoxide and dimethyl formamide at high temperatures with excess of alkyl halide or amine and harsh reaction conditions. The selective alkylation of amino groups within amine derivatives with a variety of alkyl halides was reported using ILs; 1-butyl-3-methylimidazolium iodide ([bmim]I) *(Fig. 2)* and 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF_6]) in the presence of triethylamine. The reaction was found to proceed under relatively mild conditions with excellent conversions and selectivities. The ILs, which could replace the high temperature use of highly polar organic solvents such as dimethyl formamide, 1,3-dimethyl-2 imidazolidinone, and dimethyl sulphoxide, were recycled and reused [8].

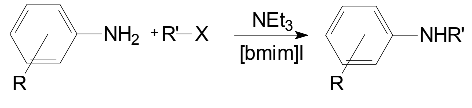

Figure 2: N-Alkylation of aniline derivatives in [bmim]I

SO_3H-functionalized ILs were synthesized and their catalytic performance for the tert-butylation of m-cresol with tert-butanol (TBA) were investigated. The reaction time, reaction temperature, molar ratio of m-cresol to TBA and the recycle number of the spent IL were examined. Under optimum reaction conditions, the conversion of m-cresol and the selectivity to 2-tert-butyl-5-methyl phenol (2-TBC) were 81% and 96%, respectively. No apparent loss of activity and selectivity of the IL were observed after four recycles. 2-TBC is a precursor for a number of commercially important antioxidants and a light protection agent for the bisphenos and thiobisphenols [9].

The optically active orthopalladated phenanthrylamine phase transfer catalyst has been produced and explored for asymmetric glycine alkylation by Mukherjee [10]. The catalyst (10 mol%) in toluene/chloroform with 50% aqueous KOH (25 °C) promoted benzylation of benzophenone imine tert-butyl glycine. The product was obtained in 85% yield and 15% enantiomeric excess (ee). Addition of the chiral IL N,N-dimethyl ephedrinium bis(trifluoromethansulfon)imidate enhanced reactivity and selectivity for PTC glycine alkylation. It appeared that the chiral IL had a cooperative effect to boost the ee content of an asymmetric reaction.

Alkylation of indole salts in different ILs was also reported. ILs increased the alkylation reaction rate of ambident indole anion and reduced the effects of counter ions and/or additives, the alkylation reaction rates being independent of the presence of small amounts of protic solvents or water [11].

Condensation

Condensation reactions are a useful way of making C–C bonds, with the elimination of a small molecule by-product [12]. A number of Lewis acid condensation reactions have been tried in Cl·$AlCl_3$ ILs. These are the Pechmann reaction [13], the Knoevenagel reaction [14], the Fischer Indole synthesis [15], and the Baeyer condensation [16]. While these have all given high conversions of starting materials under the best conditions, they suffer from having water as a principle by-product. Any water generated by the reaction reacts with the Cl·$AlCl_3$ species in the IL, so reducing its acidity and eventually destroying the IL. Other Lewis acid mediated reactions that have been conducted in Cl·$AlCl_3$ ILs include the cleavage of aromatic methyl ethers [17], acylative cleavage of ethers [18], esterifications [19], Diels-Alder cycloadditions [20], and the formation of 4-chloropyrans during an attempted Prins reaction [21] but, once again, the IL is consumed in the reaction or during product isolation. This problem, that the IL is consumed and cannot be considered to be a true catalyst for the reactions has arisen repeatedly with the use of Cl·$AlCl_3$ ILs.

The air stable 1-ethyl-3-methylimidazolium tetrafluoroborate ([emim][BF_4]), 1-ethyl-3-methylimidazolium hexafluorophosphate ([emim][PF_6]), 1-ethyl-3-methylimidazolium nonafluoro-1-butanesulfonate ([emim][NfO]) and 3-(5-carboxy-pentyl)-1-methylimidazolium tetrafluoroborate ([capemim][BF_4]) ILs were investigated [22] in the 1,3-dipolar cycloaddition of diethyl amionomalonate derived imidate and 2-ethoxybenzaldehyde. The first three ILs gave significant rate acceleration and good isolated cycloadduct yields when compared to solvent-free cycloaddition reaction conditions.

The Knoevenagel reaction is well known for its immense potential in the synthesis of electrophilic olefins from active methylene and carbonyl compounds. More than a century old now, a wide array of catalysts have been employed to accomplish this reaction, each affording variable yields of olefins. The Knoevenagel condensations of benzaldehyde and substituted benzaldehydes with diethyl malonate in Lewis acidic 1-butyl-3-methylimidazolium chloroaluminate, ([bmim]Cl·$AlCl_3$) and 1-butylpyridinium chloro-aluminate, ([bpy]Cl·$AlCl_3$) ILs *(Fig. 3)* was reported.

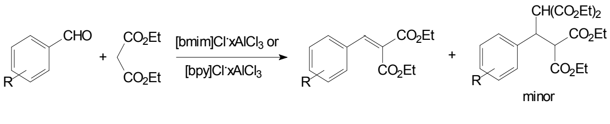

Figure 3: Reaction of benzaldehyde and substituted benzaldehydes with diethyl malonate in the Lewis acidic [bmim] Cl·$AlCl_3$ and [bpy]Cl·$AlCl_3$ ILs

The two ILs [bmim]Cl·$AlCl_3$ and [bpy]Cl·$AlCl_3$, served as an alternative media that catalysed Knoevenagel reactions. The synthesis of coumarins via Knoevenagel route was also demonstrated in these liquids. Considerable control over various products in these reactions can be exercised by variation of the parameters associated with the IL. The experimental procedure is simple and timesaving, avoiding cumbersome water removal steps [14].

A task-specific IL, $[H_3N^+–CH_2–CH_2–OH][CH_3COO^-]$ was synthesized and used as catalyst in the Knoevenagel condensation reaction of various kinds of aromatic aldehydes with ethyl cyanoacetate or malononitrile by Yue [23]. α,β-unsaturated carbonyl compounds were obtained in reasonable yields when the $[H_3N^+–CH_2–CH_2–OH][CH_3COO^-]$ catalyzed Knoevenagel reaction was carried out at room temperature for 60 min under solvent-free conditions. Only E-isomers were detected. After the removal of water the task-specific IL could be recycled and reused for five times without noticeably decreasing the catalytic activity.

Singer et al. conducted acylative cleavage of cyclic ethers in Lewis acidic 1-ethyl-3-methylimidazolium halogenoaluminate ([emim][X·AlX_3]) ILs and reported that these cleavages were sensitive to the 'bulk' Lewis acidity of the ionic solvent system [18]. The results support a mechanism in which there is initial formation of a polarized complex between Lewis acidic halogenoaluminate or $AlCl_3$ species present in solution and benzoyl chloride or the formation of benzoyl cation upon addition of benzoyl chloride to the system. O-Acylation of the ether then occurs to give an oxonium ion species that cleaves to give the most stable carbonium ion or which undergoes nucleophilic attack by iodine present in these systems. The lack of chlorine in any of the products isolated in this study indicates the latter of these two mechanistic possibilities is more likely. The differential results observed using ionic solvents of variable Lewis acidity suggest that this mechanism may be hindered by occupation of the etherial oxygen by some Lewis acidic species (i.e. $Al_2X_7^-$) other than acylinium ion when the strictly acidic solvent system is used.

High molecular weight aliphatic polyesters were synthesized in [$C_n$mim][PF_6] and [$C_n$mim][NTf_2] (where NTf_2: bis(trifluoromethylsulfonyl)imide) ILs (n = 4, 6, 8, 10, 12) via two-step polycondensation [24]. An oligoester with diol/diacid ratio higher than unity was essential for achieving high molecular weight product. Moreover, the molecular weight of the resulting polyesters was found to depend on the activity of the catalyst in the ILs and the miscibility of aliphatic polyester/IL. The former factor was dominated by the anion of the ILs. The latter factor could readily be tuned by varying the anion and/or the cation of the ILs. A clear correlation was found between the miscibility of aliphatic polyester/IL and the extent to which their solubility parameters matched. When the temperature dropped below the polyesters' melting points they formed crystals and were separated from the ILs. This crystallization-induced phase separation simplified the purification process. By simply removing the IL using methanol, then washing for 4 times, high-purity (>99%) polyester was obtained at yield up to 96.3%.

Diels–Alder reactions offer a powerful synthetic methodology to construct six-membered cycloadducts of biological importance with a fine control over their stereoselectivities. Sarma and Kumar [25] reported the combined effect of triflates (OTf) and ILs, such as 1-octyl-3-methylimidazolium tetrafluoroborate ([omim][BF_4]), 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide) ([emim][NTf_2]), 1-ethyl-3-methylimidazolium trifluoroacetate ([emim][TFA]), 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]), [bmim][PF_6], and [emim][BF_4], in the reactions of cyclopentadiene with methyl acrylate, methyl methacrylate and methyl trans crotonate. It was stated that Diels–Alder reactions carried out in ILs can be further accelerated by rare earth metal OTfs. It is possible to achieve good yields even after six recycles of ILs with OTfs.

The chiral bis(oxazoline)–copper complex catalyzed asymmetric Diels–Alder reaction of cyclopentadiene and 3-(acryloyl)oxazolidin-2-one was investigated in [bmim][BF_4], [bmim][PF_6], 1-butyl-3-methylimidazolium triflate ([bmim][OTf]) and 1-butyl-3-methylimidazolium antimonyfluoride ([bmim][SbF_6]) ILs [26]. For the study, Inda-BOX *(Fig. 4)* was chosen as a chiral ligand. A copper salt and slightly excess ligand were mixed in IL to form a ligand–metal complex. ILs were used for significant reactivity enhancement, stereoselectivity improvement and for the efficient recycling of the catalyst. With IL only, the reaction proceeded to some extent yielding a 91:9 endo/exo mixture of the racemic adduct in 15% yield and in the presence of 8 mol% $Cu(OTf)_2$, reaction was complete (90% yield) within 10 min, also providing racemic products in a similar diastereoselectivity (endo/exo = 91:9). It was concluded that the reaction could be catalyzed by the IL and the copper reagent itself and below a critical amount of the ligand–metal complex (0.85 mol% ligand and 0.6 mol% $Cu(OTf)_2$) the nonselective reaction would prevail.

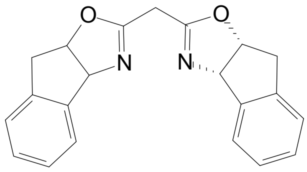

Figure 4: Structure of Inda-BOX

Esterification

Esterifications of alcohols with carboxylic acids in ILs as green reaction medium in catalytic quantities have been investigated. The application of ILs in esterification is advantageous because of three reasons; (1) ILs catalyse the esterification, (2) the resultant esters do not dissolved in the IL and therefore can be isolated easily, (3) the IL could be recovered and reused again with the evacuation of the reactor system containing IL [27]. Excellent conversion and selectivities were achieved, and the most of resultant esters could be easily recovered due to immiscibility with the ILs [19]. The esterification results of several alcohols with acetic or anchoic acids in the [bpy]Cl·$AlCl_3$ IL and in concentrated sulfuric acid were compared. For the esterification of iso-propyl, iso-pentyl, and benzyl alcohols with acetic acid the catalytic activities of IL were proved to be higher than that of the corresponding sulfuric acid, and there was not much difference in selectivities. For esterifications of benzyl alcohol, some by-products, i.e. benzyl chloride (~3%) in IL and phenymethylether (~4%) in sulfuric acid were found, respectively. It was indicated that the IL as esterification catalyst could be reused although the conversion is slightly decreased after the first esterification.

Hydrogenation

The new ‘air-stable’ ambient temperature ILs were used for the first time in 1995, liberating the worker from the constraints of working with solvents that were difficult to handle [28]. These experiments used Osborne’s catalyst, $[Rh(nbd)PPh_3][PF_6]$ (where nbd: norbornadiene) for the hydrogenation of pent-1-ene. In both $[SbF_6]$ and $[PF_6]$ ILs, the hydrogenation rates were significantly greater than in acetone. The separation of the product alkenes from the reaction mixture was simple and the catalyst containing IL solution could be recycled. At almost the same time a paper that is often overlooked came from DuPont and co-workers [29], using $RhCl(PPh_3)_3$ and $[Rh(cod)_2][BF_4]$ (where cod: cyclo-octadiene) for the hydrogenation of cyclohexene in $[bmim][BF_4]$. Here, the advantage claimed was effective recycling of the catalyst solution. The promise that ILs hold for providing systems for the reuse of expensive catalyst solutions and ligands is particularly appealing in this area and a number of reactions have been investigated.

The hydrogenation of benzene and other arenes by molecular catalysts is a fascinating and controversial area of research, in which many highly innovative catalysts have been evaluated. Arene hydrogenation is not just a topic of academic interest, but has industrial application such as the synthesis of cyclohexane (a precursor to adiptic acid used to produce nylon), removal of aromatic compounds from fuels, and as a way to prevent paper from yellowing without addition of bleaches, since the compounds responsible for the yellowing are aromatic macromolecules [30, 31]. All industrial arene hydrogenation catalysts are heterogeneous, including a system that converts benzene to cyclohexene, which is subsequently converted into cyclohexanol.

Ionic-liquid-like copolymer poly[(N-vinyl-2 pyrrolidone)-co-(1-vinyl-3-butylimidazolium chloride)] (NVP-co-VbimCl) stabilized rhodium nanoparticles were used to catalyze the hydrogenation of benzene and other arenes in ILs [32]. The nano particle catalysts can endure forcing conditions (75 °C, 40 bar H_2), resulting in high reaction rates and high conversions compared with other nano particles that operate in ILs. The hydrogenation of benzene attained record total turnovers of 20000, and the products were easily separated without being contaminated by the catalysts. Other substrates, including alkyl-substituted arenes, phenol, 4-n-propyl-phenol, 4-methoxylphenol, and phenyl-methanol, were studied and in most cases were found to afford partially hydrogenated products in addition to cyclohexanes. In-depth investigations on reaction optimization, including characterization of copolymers, transmission electron microscopy, and an infrared spectroscopic study of nanocatalysts were also undertaken.

A very effective and simple IL based system for arene hydrogenation based on K_2PtCl_4 and [N-octyl-3-picolinium]Cl·$AlCl_3$ was identified by Geldbach and Dyson. Benzene is partially miscible in the IL phase whereas the cyclohexane product is immiscible. This gives rise to the ideal situation of high reactions rates, not impeded by phase problems, with the ideal separation properties. It is likely that further optimization of this system will be possible, for example, by using mixtures of different salts which may lead to heteronuclear nanoparticles catalysts with greater activity [30].

The selective heterogeneous catalytic reduction of phenyl acetylene to styrene over palladium, supported on calcium carbonate, is reported in both an IL and a molecular solvent [33]. In the case of IL experiments, the 1-butyl-3-methyl imidazolium bis(trifluoromethyl-sulfonyl)imide ($[bmim][NTf_2]$) was recycled after reaction by solvent extraction with diethyl ether until no reagents or products could be observed by either ^1H-NMR or Raman spectroscopy. Good reproducibility was found with fresh IL and fresh catalyst compared with recycled IL and recycled catalyst. No palladium was detected in the IL reaction mixture and no reaction was observed in the absence of catalyst either in the fresh or recycled IL. Overall the comparison of the resistances in the IL and the heptane showed that the lower reaction rates when using IL was attributed to the mass transfer of hydrogen within the liquid.

Structured supported IL-phase (SSILP) catalysis, which is a new concept with the advantages of ILs used as solvents for homogeneous catalyst and the further benefits of structured heterogeneous catalysts, was studied [34]. It was achieved by confining the IL with the transition metal complex to the surface of a structured support consisting of sintered metal fibers (SMFs). In an attempt to improve the homogeneity of the IL film, the SMFs were coated by a layer of carbon nanofibers (CNFs). The IL thin film immobilized on CNF/SMF supports presented a high interface area, ensuring efficient use of the transition metal catalyst. The regular structure of the support with high porosity (>80%) allowed a low pressure drop and even gas-flow distribution in a fixed-bed reactor. The high thermoconductivity of the CNF/SMF support suppressed the formation of hot spots during exothermic hydrogenation reactions. The selective gas-phase hydrogenation of 1,3-cyclohexadiene to cyclohexene over a homogeneous Rh catalyst immobilized in IL supported on CNF/SMF was used as a test reaction to demonstrate the feasibility of the SSILP concept. The catalyst $[Rh(H)_2Cl(PPh_3)_3/IL/CNF/SMF]$ showed a turnover frequency of 150-250 h^{-1} and a selectivity of >96%. High-pressure ^{1}HNMR and $^1H\{^{31}P\}$ NMR spectroscopy was used to provide insights into the nature of the active catalytic species.

According to Xu significant improvements could be achieved in the hydrogenation of halonitrobenzenes to the corresponding haloanilines over easily available catalysts in $[bmim][BF_4]$ and $[emim][BF_4]$ ILs with excellent selectivity of lower dehalogenation. The selective hydrogenation of halonitroaromatics could be applicable to monohalo- and polychloro-substituted nitrobenzenes as well [35].

Hydroformylation

Even though there is already a highly efficient aqueous or organic biphasic industrial process for the hydroformylation of olefins, hydroformylation in ILs is extensively studied. This process can only be used with short-chain (≤ 5 C) olefins because heavier olefins are insufficiently soluble in water for an effective reaction to occur. ILs with higher solubilities for these higher olefins can offer the possibility of replacing the water layer and extending the usefulness of the biphasic technique [2].

Olivier-Bourbigou and co-workers [36] investigated the hydroformylation of 1 hexene in a variety of ILs with imidazolium and pyrrrolidinium cations and a range of different anions. Initially they introduced the rhodium as $[Rh(CO)_2(acac)]$ (where acac: acetylacetonate) with four equivalents of the charged triphenylphosphine monosulfonate (TPPMS) and measured the turnover frequency (TOF) of the catalyst in the different ILs. For the $[BF_4]$, $[PF_6]$, [OTf], and trifluoroacetate ($[CF_3CO_2]$) ILs they found that the TOF of the reaction was dependent upon the solubility of the 1-hexene in the IL, possibly suggesting a mass transfer limited process. However, when they used three different trifluoromethanesulfonimid ($[(CF_3SO_2)_2N]$) based ILs the TOF did follow the solubility of the 1-hexene in these ILs, but the TOF's of the whole set were lower than expected when compared to the other ILs. It is not at all clear why this discrepancy exists. Given that the $[(CF_3SO_2)_2N]$ ion is one of the least basic of the anions used [37], and that $[(CF_3SO_2)_2N]$ ILs are generally at the low end of IL viscosities [38], one might have expected any deviation to be in the other direction. When this puzzle is solved it may be possible to design ILs that will give greater reactivities.

The ILs $[bmim][BF_4]$, $[bmim][PF_6]$ and 1,2-dimethyl-3-butyl-imidazolium hexafluorophosphate ($[bdmim][PF_6]$) were investigated as potential media for hydroformylation catalysis in a liquid–liquid biphase reaction environment [39]. The study used the rhodium/tppti* (tppti* = tri(m-sulfonyl) triphenyl phosphine [bdmim] salt) system as the catalyst and hexene-1 as the substrate, which enabled the produced heptanal to be conveniently isolated from the IL by phase separation. All catalyst evaluations were carried out in high-purity ILs to avoid any decomposition of the catalyst, substrate and/or IL. The activity of the biphasic IL system containing the Rh/tppti* catalyst was approximately one order of magnitude lower than that observed for the conventional Rh/PPh_3 catalyst in toluene. The Rh/tppti* catalyst system showed a decrease of activity in the semicontinuous hydroformylation of hexene-1 due to catalyst deactivation and/or metal loss. The loss of rhodium metal from the IL phases appears to be correlated to the solubility characteristics of the IL and the concentration of the aldehyde in the organic phase. In support of this theory, the IL $[bmim][PF_6]$ gave the best results due to its very low miscibility with polar substances. A high-pressure NMR (HP-NMR) study revealed that the solution structure of $HRh(^{13}CO)(tppts)_3$ (tppts = tri(msulfonyl) triphenyl phosphine sodium salt) in $[bmim][BF_4]$ was similar to that of $HRh(^{13}CO)(PPh_3)_3$ in toluene-d^8. The HP-NMR investigation at elevated syngas pressures showed that $HRh(^{13}CO)(tppts)_3$ lies in equilibrium with $HRh(^{13}CO)_2(tppts)_2$.

In 2006 Yan and Zhang [40] developed new hybrid phosphine–phosphoramidite ligands for the Rh-catalyzed aymmetric hydroformylations of styrene and vinyl acetate, where excellent enantio-selectivity as high as 99% was achieved. Nevertheless, chiral ligands are usually expensive, mainly due to the tedious synthesis pathways. The investigation of asymmetric catalytic reaction associated with the biphasic system is of significant importance from both the fundamental and industrial points of view.

Yuan and co-workers [41] developed a biphasic catalytic system with water-soluble rhodium complexes of sulfonated (R)-2,2’-bis(diphenylphosphino)-1,1’-binaphthyl ((R)-BINAPS) in $[bmim][BF_4]$ IL for the asymmetric hydroformylation of vinyl acetate under mild conditions. The biphasic asymmetric hydroformylation of vinyl acetate *(Fig. 5)* provided 28.2% conversion and 55.2% enantiomeric excess when $[bmim][BF_4]$ toluene was used as the reaction medium at 333 K and 1 MPa for 24 h.

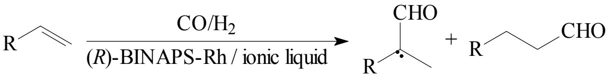

Figure 5: Asymmetric hydroformylation of vinyl acetate and styrene

The biphasic asymmetric hydrogenation of dimethyl itaconate in [bmim][BF_4] at 333 K and 2 MPa afforded 65% enantiomeric excess with an activity similar to the homogenous analogs. Both biphasic catalytic systems with (R)-BINAPS ligand could be reused several times without significantly decrease in the activity, enantio- and regio selectivities.

Oxidation

Although most ILs currently in use are stable to oxidation, and so they provide ideal solvents for oxidation processes, this chemistry has only developed in the last few years. Ni(acac)$_2$ has been used as the catalyst for a number of aerial oxidations of para-substituted benzaldehydes with moderate yields of the corresponding acids in [bmim][PF_6] [42]. In the absence of the catalyst very little oxidation was observed. The same combination of catalyst, IL and oxidant has also been used in the synthesis of ethylbenzene hydroperoxide from ethylbenzene [43]. However, in this case it is more accurate to describe the reaction system as a solution of the catalyst and IL in ethyl benzene. The two principle advantages of the IL are that it has a greater solubility in the ethylbenzene and the poorly coordinating anion competes less well for the metal centre than the previously used tetraalkylammonium halide salts. Jacobsen's catalyst has been used for asymmetric epoxidations with aqueous NaOCl in [bmim][PF_6]/CH_2Cl_2 (1:4) mixtures [44]. The mixed solvent system was used because the IL itself was solid at the reaction temperature. Yields and selectivities were similar to those in the absence of the IL, but the use of the IL gave faster reactions. The IL and the reaction products were found in the organic phase, which was separated from the aqueous phase. The CH_2Cl_2 was removed from the IL–catalyst–product mixture in vacuum, before the product was washed from the IL with hexane. The resultant solution of the catalyst in the IL could then be reused with a small drop in enantioselectivity.

Canoira and co-workers [43] carried out the air catalysed liquid-phase oxidation of ethylbenzene (EB) to ethylbenzene hydroperoxide (EBHP) by Ni^{2+} complexes. The use of a nickel soluble complex without acetyl-acetone ligands gave unsatisfactory results. Quaternary ammonium salts (R_4NBF_4) (R = n-Bu, Me) were used as co-catalysts, and the ammonium salt with the longer radical n-Bu gave better results. On the other hand, a catalytic system has been designed based on Ni(acac)$_2$ and [bmim][PF_6] and its reactivity has been explored in the oxidation with air of ethylbenzene at atmospheric pressure, showing that this catalytic system could be at the moment an alternative to the catalysts in use for this oxidation process.

The oxidation of aromatic aldehydes was reported [40] using the catalyst [Ni(acac)$_2$] and molecular oxygen at atmospheric pressure, as the oxidant, in the IL [bmim][PF_6], as shown in *Fig. 6.* The catalyst and IL could be recycled after extraction of the carboxylic acid product.

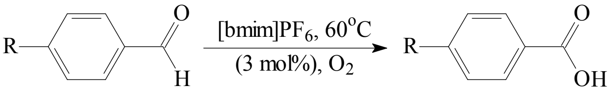

Figure 6: Oxidation of aldehydes

Metal-containing ZSM-5 (MZSM-5) molecular sieves catalysed cyclohexane oxidation with tert-butyl-hydroperoxide (TBHP) in [emim][BF_4] IL was carried out under mild conditions [45]. In [emim][BF_4] much higher activity was observed than in either the conventional molecular solvent or in the absence of a solvent. The as-received hydrogen-containing ZSM-5 (HZSM-5) was active, giving a conversion of 15.8% and selectivity of desired products (97.0%), which was higher than the best values reported for 4% conversion in the industrial oxidation process. In the oxidation two competing reactions occur, the decomposition of TBHP and the oxidation of substrate. The conversion and efficiency of TBHP had also been studied; the TBHP conversion was high for the catalysts used, while the efficiency of the oxidant was very low. The TBHP conversion was 74% and the TBHP efficiency was only 15.4%. Around 80% of the oxidant was unselectively decomposed after 12 h. It is important to note that the IL/MZSM-5 systems are very easily separated from the product mixture by simple decantation. Catalyst recycling experiments were carried out with repeated use of IL/MZSM-5 system. After each run, the separation step was operated carefully in order to ensure that there was no loss of the catalyst used in IL. The total amount of the recovered IL phase containing catalyst was measured accurately. Fresh IL, which was equivalent to the amount of IL being losed (about 2%), was added to the recovered IL/catalyst phase to make up to the initial concentration of IL, and then the next run was performed by adding 27.8 mmol cyclohexane and 55.6 mmol TBHP (85% in H_2O). It can be concluded that the desired product were obtained in the similar conversion, selectivity, and yield, indicating that both the IL and the catalyst were recoverable and reusable.

A number of ILs have been used as co-solvents for the 2-methyl-3,4 dihyroisoquinoliunium ([mdhqm]) catalyzed epoxidation of alkenes. Water miscible ILs gave systems with similar reactivities to the conventional acetonitrile based systems. Attempts to produce an aqueous/IL biphasic system that could be used to recycle the catalyst failed due to a lack of phase transfer between the aqueous and IL phases. Epoxidation of 1-phenyl-cyclohexene with [mdhqm][NTf_2] as catalyst in different co-solvent/water solvent systems applying the ILs [bmim][BF_4], [bmim][OTf], [bmim][SbF_6], [bmim][NTf_2] and 1-butyl-3-methyl pyridinium bis(trifluoromethyl-sulfonyl)imide ([bmpy][NTf_2]) was investigated [46]. Although both [bmim][BF_4] and [bmim][OTf] gave good conversions, only marginally lower than for the water/acetonitrile system, [bmim][OTf] gave the higher ones and was selected for subsequent investigations. It was found that the counter ion of the catalyst had no significant effect on the measured conversions in [bmim][OTf]. This is probably due to total fast exchange of the catalyst counter anion with the anion of the IL leading to the iminium cation being only associated with the [OTf] anion. This ion scrambling has been noted in polymerisation catalysis, and on the reactivity of anionic nucleophiles, where it was found that the counter cation of the nucleophile had no significant effect upon its reactivity and that cation of the IL determined its reactivity

Conclusion

ILs are salts composed of organic anions and organic or inorganic anions, which have low melting point. Their physical and chemical properties can be adjusted by the variation of the ions. The fine adjusting of properties is possible by the variation of the length and branching of the alkyl groups incorporated into the cation.

Ionic liquids have interesting advantages; they are non-flammable and have extremely low vapor pressure. These properties are significant when addressing the health and safety concerns associated with many solvent applications. Negligible vapor pressure solvent evaporation is eliminated, reducing the need for respiratory protection and exhaust systems.

They have liquid range more than 400 K. While many solvents will freeze or boil across such a large temperature range, ionic liquids maintain their volume and fluidity. This wide range of thermal stability allows for tremendous kinetic control of chemical processes. The wide temperature range is also helpful in temperature dependent separation processes.

Ionic liquids have higher density than water and miscible with substances having very wide range of polarities and can simultaneously dissolve organic and inorganic substances. These features of RTILs offer numerous opportunities for modifications of existing and for the development of new processes. In such cases, such processes would be impossible with conventional solvents because of their limited liquid range or miscibility.

As a replacement of classical organic solvents, the application of ILs offers a new and environmentally benign approach toward modern synthetic chemistry. IL technology has been successfully applied in several classical organic chemical reactions, such as hydrogenation, hydroformylation, condensation, oxidation, etc. Recently ionic liquids have been successfully employed as dual reagent (solvents + catalytic activity) for a variety of reactions, but their use as catalyst under solvent-free conditions still need to be given more attention.

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