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Reactivity of ionic liquids

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Abstract—Ionic liquids are becoming widely used in synthetic organic chemistry and yet relatively little attention has been paid to the intrinsic reactivity of these low temperature molten salts. Clues to the non-innocent nature of many ionic liquids are contained in the reports of altered reactivity of dissolved substrates, unexpected catalytic activity and unforeseen by-product formation. In this review, we focus on the reactivity *of* ionic liquids, as opposed to reactivity *in* ionic liquids (although discussion of the latter is often included where it aids understanding of the former).

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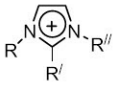
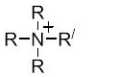
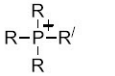
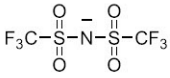
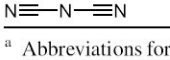
1. Introduction

Ionic liquids are defined as pure compounds, consisting only of cations and anions (i.e., salts), which melt at or below 100 °C.[1] Many are liquid at 25 °C (and are sometimes called room temperature ionic liquids or RTILS) but, as this is a somewhat arbitrary definition all ionic liquids are considered, along with the related higher melting salts, where these shed light on the mechanism of action or reaction of ionic liquids. While the range of ionic liquids reported in the literature is large and includes esoteric compounds such as those based on carborane anions[2] or ferrocenylmethyl cations,[3] a relatively small number of structural motifs appear commonly in ionic liquid cations and the range of anions, while larger, is also restricted. Structures and abbreviations for commonly occurring cations and anions are provided in Table 1.

It is noteworthy that while the term ionic liquid, used to describe a low temperature molten salt, has only moved into common usage relatively recently, reports of 'fused salts' as useful reaction media appeared more than 50 years ago and were reviewed by Gordon in 1969.[4] Later reports of 'molten salt solvents' include the development of tetra-alkylammonium tetraalkylborides.[5] In addition, the literature on chromatographic applications of fused salts or ionic liquids should not be ignored by the synthetic chemist as the stability data and intermolecular interactions (or even reactions) described are directly applicable to preparative synthetic organic chemistry in ionic liquids. A recent excellent review of the field, containing a comprehensive summary of ionic liquid properties, is published by Poole.[6]

Ionic liquids have been widely vaunted as greener solvents, suitable for a range of organic reactions and providing possibilities such as control of product distribution,[7] enhanced rate[8] and/or reactivity,[9] ease of product recovery,[10] catalyst immobilization,[11] and recycling.[12] At the same time, their use obviates much of the need for control of fugative emissions and/or combustion risks by replacement of volatile organic compounds (VOCs) widely used as solvents in organic reactions. Closer scrutiny reveals that ionic liquids are neither completely non-volatile nor non-flammable. The so-called protic ionic liquids[13] (where H^+ transfer possibilities exist) may be 'distilled' under reduced pressure by reversion to neutral acid and base and reconversion to the salt upon cooling and condensing.[14] True distillation (i.e., without decomposition and recombination of decomposition products) of some dialkylimidazolium, tetra-alkylphosphonium, and tetra-alkylammonium-based ionic liquids has recently been demonstrated, albeit that the distillation occurred at relatively slow rates, even at very low pressures.[15] Demonstrated lack of flammability of most bulk ionic liquids[16] is a direct consequence of the infinitesimal vapor pressure of the ionic liquid,[17] however, many ionic liquids are combustible![18]

Table 1. Structures and abbreviations for commonly occurring cations and anions

	Abbreviation	R	R′	R″
	[Hmim][a]	H	H	Me
	[mmim]	Me	H	Me
	[emim]	Et	H	Me
	[bmim]	*n*-Bu	H	Me
	[pmim]	*n*-Pent	H	Me
	[hmim]	*n*-Hex	H	Me
	[bpim]	*n*-Bu	H	*n*-Pent
	[bbim]	*n*-Bu	H	*n*-Bu
	[beim]	*n*-Bu	H	Et
	[bmmim]	*n*-Bu	Me	Me
	[hmmim]	*n*-Hex	Me	Me
	[mPhmim]	Me	Ph	Me
	[bPhmim]	*n*-Bu	Ph	Me
	[hPhmim]	*n*-Hex	Ph	Me
	[C_2Py][b]	ET		
	[C_4Py]	*n*-Bu		
	[C_5Py]	*n*-Pent		
	[C_6Py]	*n*-Hex		
	[$C_3(SO_3H)$Py]	*n*-Pr(SO_3H)		
	[bmpy][c]	*n*-Bu		
	[hmpy]	*n*-Hex		
	[$N_{2,2,2,6}$][d]	Et	*n*-Hex	
	[$N_{4,4,4,6}$]	*n*-Bu	*n*-Hex	
	[$N_{4,4,4,4}$]	*n*-Bu	*n*-Bu	
	[$N_{6,6,6,6}$]	*n*-Hex	*n*-Hex	
	[$N_{7,7,7,7}$]	*n*-Hep	*n*-Hep	
	[$N_{8,8,8,8}$]	*n*-Oct	*n*-Oct	
	[$P_{6,6,6,14}$][d]	*n*-Hex	*n*-Tetradecyl	
	[Tf_2N]			
CH_3COO^-	[AcO]			
	[dca]			

[a] Abbreviations for di(or tri)alkylimidazolium cations reflect the first letters of 1,3-substituents (and 2 substituents where these are included) followed by 'im'.

[b] Pyridinium cations are designated by C_x, where *x* is the number of carbon atoms of the alkyl substituent, followed by 'Py'.

[c] Pyrrolidinium cations are designated in similar manner to imidazolium, i.e., first letters of *N*-substituents followed by 'py'.

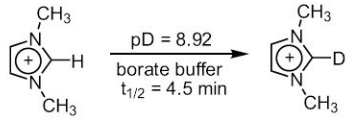
[d] Tetra-alkylammonium and tetra-alkylphosphonium as N or P, respectively, followed by subscripted numbers indicating the number of C-atoms of the alkyl chains. Anion abbreviations are standard symbols for the ions or as indicated.

In this review we focus on the reactivity of ionic liquids, both intentional (as in ionic liquid reactants or Brønsted acid ionic liquids) and coincidental (as in the fortuitous formation of active catalytic species or reactions of nucleophilic anions). For general reviews or treatment of specific topics, the reader is referred to a number of excellent books[19] and recent general reviews[20] as well as those covering specific topics such as catalysis (including biocatalysis) in ionic liquids,[21] synthesis of organometallic complexes in ionic liquids,[22] biphasic systems and supported ionic liquids,[23] solvent properties,[24] ionic liquids with fluorine containing anions,[25] analytical applications of ionic liquids,[26] chiral ionic liquids,[27] electrochemistry in ionic liquids,[28] and physical properties of ionic liquids.[29] In addition, a number of special issues[30,31] have appeared covering a range of topics including ionic liquids as green solvents,[32] physical and thermodynamic data,[33] and organometallic chemistry in ionic liquids.[34] The 'non-innocent' nature of some specific ionic liquids has been addressed by Dupont and Spencer.[35] Unsubstantiated or unexplained accounts of 'catalysis' by the ionic liquid itself have generally not been included in this review, unless another point is also demonstrated; in many cases, the catalytic activity is almost certainly due to the presence of minor impurities (such as residual acid), while in others a dearth of information makes it difficult to ascertain the likely genesis of the 'catalytic activity' noted. In addition, no attempt to deal with electrochemical reactivity has been made, both because this is a huge topic worthy of an entirely separate review and because electrochemistry is seldom (perhaps unfortunately) a method of choice for preparative synthetic work.

2. The incompatibility of imidazolium-based ionic liquids with bases

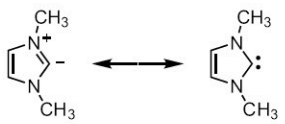
2.1. Formation of *N*-heterocyclic carbenes

It was recognized as early as 1964 that the C(2)-proton of the 1,3-dialkylimidazolium cation is acidic and can be exchanged under mild conditions (Scheme 1).[36]



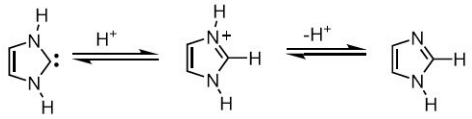
Scheme 1.

The deprotonation of the 1,3-dialkylimidazolium cation results in the formation of a stable carbene, which is strongly stabilized by the presence of the two adjacent nitrogen atoms (Scheme 2).



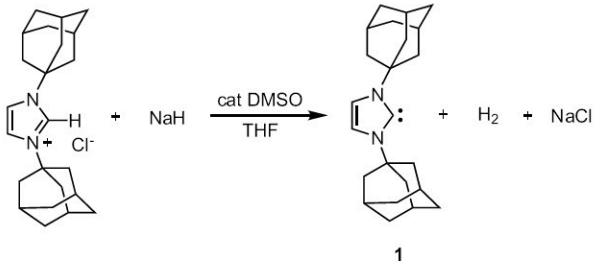
Scheme 2.

The pK_a of the simple imidazolium cation has been determined in both DMSO[37] and H_2O[38] and was found to be in the range of 21–24. Amyes et al. have calculated the equilibrium constant and ΔG^o for the conversion of the singlet carbene to neutral imidazole via a 1,2-hydrogen shift (Scheme 3) in water to be 5×10^{16} and −22.7 kcal/mol, respectively.[38] The concerted 1,2-shift is however symmetry forbidden and hence the reaction to give imidazole occurs in two steps as shown in Scheme 3.



Scheme 3.

Arduengo et al. achieved a breakthrough by isolating and fully characterizing a stable singlet *N*-heterocyclic carbene, 1,3-di-1-adamantylimidazol-2-ylidene, by deprotonation of an imidazolium salt (Scheme 4).[39,40]

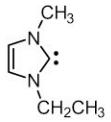


1

Scheme 4.

Crystal structure analysis of **1** confirmed the significantly reduced N–C–N bond angle of 102.2° (compared to the typical value of 108.5–109.7° for the corresponding angle in imidazolium salts). The length of the C–N bond was also significantly increased from the value found in imidazolium rings, suggesting a reduced π-delocalization in the carbene. The change in π-delocalization was also confirmed by ^{1}H NMR studies on the carbene in which the imidazole ring protons exhibited an upfield shift to δ 6.91 from δ 7.92 in **1**.

The gas phase proton affinity of the *N*-heterocyclic carbene, 1-ethyl-3-imidazol-2-ylidene **2**, has been determined to be 251.3±4 kcal/mol, confirming the strongly basic nature of these carbenes.[41]

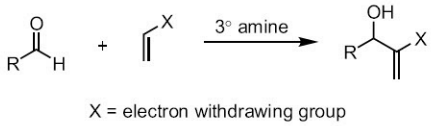


2

The acidity of the C(2) hydrogen in 1,3-dialkylimidazolium salts and the basicity of the resulting *N*-heterocyclic carbenes have significant implications in the chemistry of ionic liquids.[42] Noting these properties, it becomes immediately obvious that imidazolium-based ionic liquids are likely to be unstable under basic conditions and caution must be exercised in interpreting results obtained in reactions studied in such ionic liquids, under basic conditions. Several documented examples of the reactivity of ionic liquids under basic conditions are summarized below.

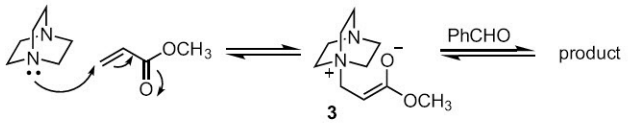
2.2. The Baylis–Hillman reaction in ionic liquids

The Baylis–Hillman reaction typically involves a tertiary amine catalyzed coupling between the α-position of an activated alkene and an aldehyde (Scheme 5).[43] Although several 3° amines have been used for this reaction, the base of choice now is diazabicyclo[2.2.2]octane (DABCO).



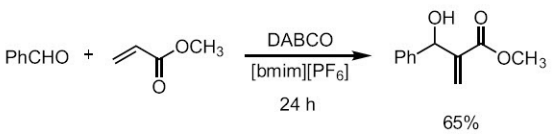
Scheme 5.

Although the Baylis–Hillman reaction is atom efficient and allows the generation of a highly functionalized molecule in a single step, it suffers from slow reaction rates (often requiring days for completion), even under solvent-free conditions and in the presence of a large amount of base. Several attempts have been made to accelerate the Baylis–Hillman reaction. These include the use of ultrasound,[44] microwave irradiation,[45] and the use of Lewis acids.[46] Mechanistic studies show that the Baylis–Hillman reaction most likely proceeds via an addition–elimination mechanism that is initiated by a Michael-type nucleophilic attack on the alkene by the 3° amine to produce a zwitterionic species such as **3**, which then attacks the aldehyde to give the product (Scheme 6).



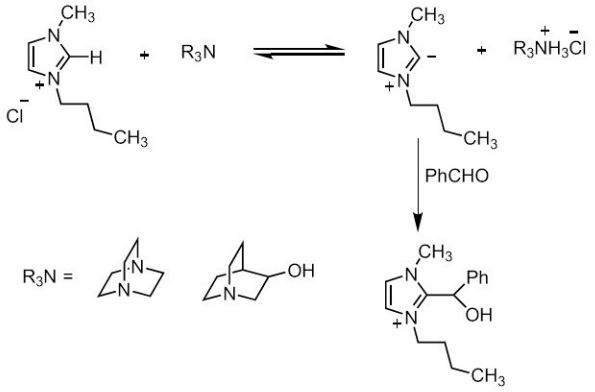
Scheme 6.

The rate of the Baylis–Hillman reaction is enhanced in protic solvents such as methanol and also by use of bases such as 3-hydroxyquinuclidine, and this has been attributed to the involvement of hydrogen bonding.[47,48] As the acidic proton at C(2) is known to act as a donor to hydrogen bond acceptors,[49] it seemed reasonable to think that imidazolium-based ionic liquids would be a good choice of solvent for the Baylis–Hillman reaction. Following this line of argument, Afonso et al. reported the use of ionic liquids as solvents for this reaction.[8c] They reported that the Baylis–Hillman reaction between benzaldehyde and methyl acrylate in the ionic liquid, [bmim][PF_6], was 33 times faster than the reaction in CH_3CN, although only moderate yields of the desired product were obtained (Scheme 7). The relative reaction rates were measured by monitoring the disappearance of benzaldehyde by gas chromatography. The (incorrect) assumption that all of the benzaldehyde was being converted to the desired product led to the erroneous conclusion that the observed rate enhancement was ionic liquid induced.



Scheme 7.

Although Aggarwal et al. were unable to achieve good yields in the Baylis–Hillman reaction using ionic liquids, prompted by the above report, they revisited their own previous work. In an elegant study, they discovered that under the basic reaction conditions, the aldehyde was actually being consumed in a side reaction with the imidazolium cation, thus demonstrating convincingly that ionic liquids are not always inert solvents.[50] They showed that the acidic nature of the C(2) hydrogen of the imidazolium cation was responsible for this side reaction (Scheme 8).



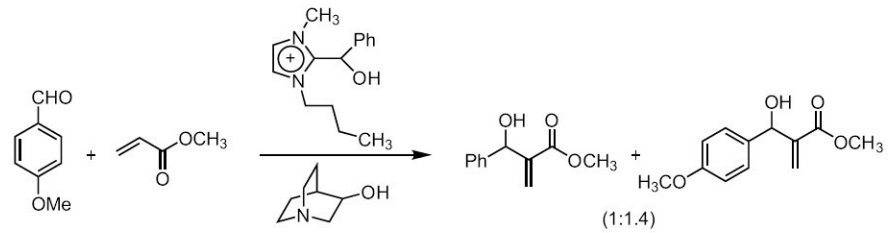
Scheme 8.

One frequently cited advantage of ionic liquids is that they can be easily recycled. However, in a further study, Aggarwal et al. also showed that caution must be exercised when using ionic liquids from one reaction for another. Since the formation of the adduct shown in Scheme 8 is reversible, if the ionic liquid from one run of a Baylis–Hillman is recycled and used in a different Baylis–Hillman reaction, a mixture of products is obtained as shown in Scheme 9.

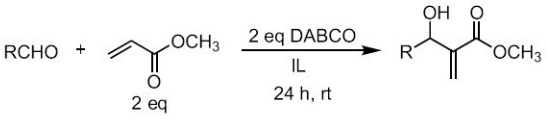
Since the problems associated with the use of imidazolium-based ionic liquids, in the Baylis–Hillman reaction, arise from the acidity of C(2) imidazolium cation, Hsu et al. synthesized an ionic liquid substituted at the 2-position and studied its utility in the Baylis–Hillman reaction.[51] They found that the Baylis–Hillman reaction between a variety of aldehydes and methyl acrylate proceeded smoothly in the ionic liquid, [bmmim][PF_6], in contrast to results obtained with [bmim][PF_6] (Scheme 10, Table 2).

Although substitution at the 2-position of the imidazolium cation prevents the side reaction seen in the Baylis–Hillman reaction, Handy and Okello have shown that even the 2-methyl substituted imidazolium cation is not completely inert.[52] They found that the 2-methyl group underwent slow proton exchange even in the presence of a weak base such as triethylamine (Scheme 11).

Further evidence for the acidic nature of this methyl group was obtained by analyzing the products obtained from attempted methylation of the imidazolium salt **4**. When **4** was treated with excess NaH and CH_3I, the expected product from methylation at C-2, **6** could not be detected. Instead product **5** was obtained (Scheme 12). None of the product **6** was detected.



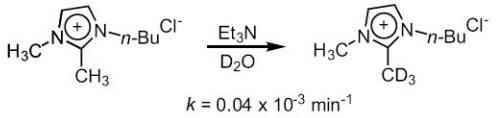
Scheme 9.



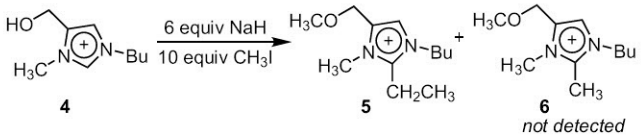
Scheme 10.

Table 2. Comparison of yields obtained from Baylis–Hillman reaction in [bmim][PF_6] and [bmmim][PF_6]

Aldehyde	Isolated yield (%)	
	[bmim][PF_6]	[bmmim][PF_6]
CH_3CH_2CHO	29	59
$CH_3CH_2CH_2CH_2CHO$	34	66
PhCHO	63	79
2-$CH_3OC_6H_4CHO$	50	61
4-$CH_3OC_6H_4CHO$	39	65
2-ClC_6H_4CHO	69	73
4-ClC_6H_4CHO	66	99
PhCH=CHCHO	23	57
CH_3CH=CHCHO	18	27



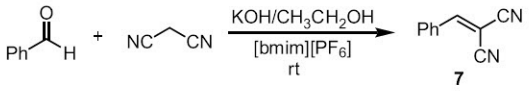
Scheme 11.



Scheme 12.

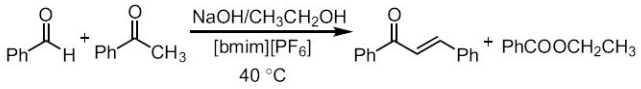
2.3. The Knoevenagel condensation and Claisen–Schmidt condensation in ionic liquids

The suitability of ionic liquids as solvents for the Knoevenagel condensation and Claisen–Schmidt condensation has been examined.[53] Formentín et al. found that although in the reaction of benzaldehyde with malononitrile in the presence of KOH dissolved in [bmim][PF_6], both starting materials were consumed, only low isolated yields of the styrene product **7** were obtained (Scheme 13). The yields improved as the substrate concentration was increased and also as the ionic liquid was reused. This indicated that the product was reasonably soluble in the ionic liquid and could be isolated in good yields only when the ionic liquid was saturated with the product. The ionic liquid could be reused up to five times without the need for additional base.



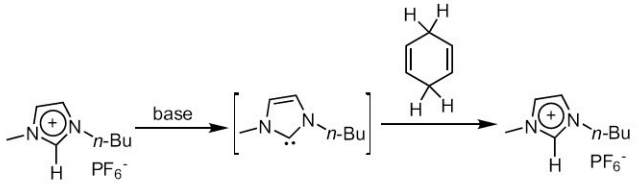
Scheme 13.

Low yields were also obtained in the Claisen–Schmidt condensation between acetophenone and benzaldehyde (Scheme 14). However, in this case ethyl benzoate was obtained as a by-product and the base was depleted after two cycles of reuse of the ionic liquid.



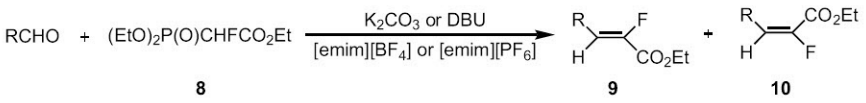
Scheme 14.

A control study in which the ionic liquid was reacted with the base in the absence of the aldehyde and ketone suggested that the base was being consumed by reaction with the imidazolium cation. This reaction is more pronounced at elevated temperatures and hence it was less of a problem in the catalytic Knoevenagel condensation, which was carried out at room temperature. Again, control studies showed that the source of the ethyl group was sodium ethoxide and not ethanol. A Cannizzaro-type reaction has been proposed to account for the formation of ethyl benzoate. However, this mechanism requires the transfer of hydride from the intermediate to a suitable acceptor. Since benzyl alcohol was not detected as a product, it is unlikely that the hydride acceptor was benzaldehyde. Thus the most likely hydride acceptor is the highly reactive carbene species generated from the imidazolium cation. The ability of the carbene to act as a hydride acceptor was confirmed by studying the reaction of [bmim][PF_6] in the presence of a base and added 1,4-cyclohexadiene, a well-known hydride donor (Scheme 15).



Scheme 15.

From these results it is clear that the widely used imidazolium ionic liquids are suitable, under basic conditions, only for a few select reactions and caution must be exercised when reactions are carried out using these ionic liquids in conjunction with bases, especially at elevated temperatures.

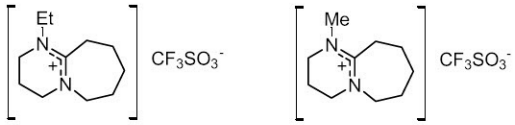


Scheme 16.

2.4. The Horner–Wadsworth–Emmons reaction in ionic liquids

Kitazume and Tanaka report that the Horner–Wadsworth–Emmons reaction between aldehydes and phosphonoacetates **8** in both [emim][BF_4] and [emim][PF_6] gave low yields of either product **9** or **10** (Scheme 16).[54] In light of the above discussions it appears that the low yields are likely due to the incompatibility of imidazolium-based ionic liquids with the strongly basic reaction conditions.

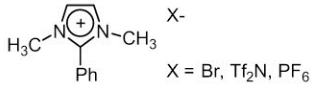
Good yields of the products were obtained when the reaction was carried out in the ionic liquids 8-ethyl-1,8-diazabicyclo[5,4,0]-7-undecene trifluoromethanesulfonate **11** and 8-methyl-1,8-diazabicyclo[5,4,0]-7-undecene trifluoromethanesulfonate **12**.



11 **12**

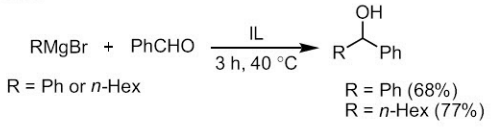
2.5. Ionic liquids suitable for use under strongly basic conditions

In light of the instability of several imidazolium-based ionic liquids under basic conditions, efforts have been directed toward development of ionic liquids suitable for use under such conditions. These are summarized here for the benefit of synthetic chemists. Jurćik et al. reported that imidazolinium-based ionic liquids containing a phenyl group at the C(2) position (cation=[mPhmim]) **13** are stable to a variety of strongly basic conditions.[55]



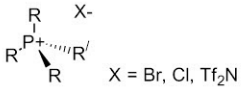
13

The Baylis–Hillman reaction between methyl acrylate and a variety of aromatic aldehydes using DABCO or quinuclidinol as the base was successfully carried out in these ionic liquids. Ionic liquid [mPhmim][Tf_2N] was also shown to be a suitable solvent for reactions involving Grignard reagents (Scheme 17). Control experiments showed that the ionic liquid did not undergo any deprotonation under the reaction conditions.



Scheme 17.

Ramnial et al. have developed phosphonium-based ionic liquids such as tetradecyl(trihexyl)phosphonium chloride **14** (CYPHOS® IL 101) for use under strongly basic conditions.[56]



14

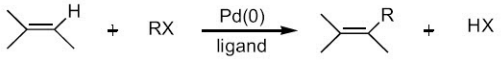
The ionic liquid [$P_{6,6,6,14}$][Tf_2N] could be dried with potassium metal, indicating its stability in the presence of such a strong base. Similarly, Grignard reagents, although air and moisture sensitive, dissolved in the [$P_{6,6,6,14}$][Tf_2N] and showed no signs of degradation after one month. Ionic liquids such as this offer an advantage over diethyl ether, the more conventional solvent for Grignard reactions: owing to the high heat capacity of ionic liquids, reaction solutions did not need to be cooled to the low temperatures often needed when ether is used as a solvent. In addition, the immiscibility of [$P_{6,6,6,14}$][Tf_2N] with both water and hexane allows for facile product separation. Although the formation of phosphorane **15** by abstraction of a hydrogen at one of the carbons adjacent to the phosphorous would be thermodynamically favorable, the authors suggest that the inertness of **14** toward reaction with bases is due primarily to the difficulty in accessing the acidic hydrogen.



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2.6. The Heck reaction in ionic liquids

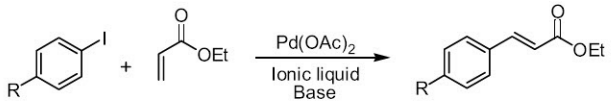
The palladium-catalyzed C–C coupling of an aryl or alkenyl halide with an olefin is known as the Heck reaction (Scheme 18) and has been the subject of numerous experimental and theoretical studies.[57–59] Interest in the Heck reaction is due to the versatility of this reaction and the relatively mild reaction conditions used. Typically, the Heck reaction with less reactive halides (bromides and chlorides) requires the use of phosphine ligands to stabilize the active palladium species. One drawback of the Heck reaction is that often the palladium catalyst cannot be recovered and reused.



Scheme 18.

In an effort to allow recycling of the catalyst, several groups have reported the use of ionic liquids as solvents for the Heck reaction. Carmichael et al. reported that ionic liquids provide a convenient medium for the Heck reaction, while allowing recycling of the catalyst.[60] However, during these investigations the non-innocent nature of some ionic liquids also began to emerge. Although, in this case, participation of the ionic liquid in the reaction proved advantageous rather than a nuisance.

In the Heck reaction of iodobenzene with ethyl acrylate, in both *N*-hexylpyridinium, [C_6Py], and *N*,*N*′-dialkylimidazolium-based ionic liquids (Scheme 19, Table 3), higher yields were obtained in the former ionic liquid than the corresponding reactions in the imidazolium salts. The addition of a phosphine ligand to the palladium species in the reaction in the pyridinium-based ionic liquid decreased the yield (entry 3) and higher temperatures were required to force the reaction to completion (entry 4). In contrast, a dramatic increase in reaction rate was seen upon addition of the ligand when the reaction was carried out in the imidazolium-based ionic liquid (Table 3, entry 5).

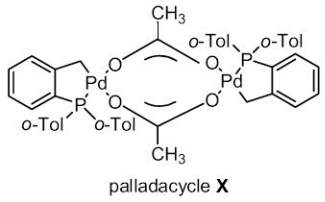


Scheme 19.

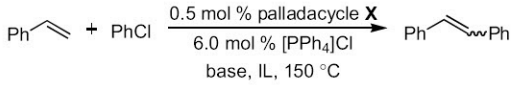
Table 3. Heck reaction of iodobenzene and ethyl acrylate to give *trans*-ethyl cinnamate with 2 mol % $Pd(OAc)_2$

Entry	Ionic liquid	Additive	Base	Temp (°C)	Time (h)	Yield (%)
1	[C_6Py][Cl]	None	Et_3N	40	24	99
2	[C_6Py][Cl]	None	$NaHCO_3$	40	24	98
3	[C_6Py][Cl]	Ph_3P (4 mol %)	$NaHCO_3$	40	24	82
4	[C_6Py][Cl]	Ph_3P (4 mol %)	$NaHCO_3$	100	24	82
5	[bmim][PF_6]	Ph_3P (4 mol %)	Et_3N	100	1	95–99
6	[pmim][Cl]	None	Et_3N	40	24	77

Herrmann and Böhm also found that the imidazolium-based ionic liquids gave less satisfactory results compared to tetraalkylammonium salts (Scheme 20, Table 4).[61,62]



palladacycle **X**



Scheme 20.

Table 4. Heck reaction of chlorobenzene and styrene in the presence of palladacycle **X**[a]

Ionic liquid	Base	Time (h)	Yield (%)[b]
[$N_{4,4,4,4}$][Br]	NaOAc	18	51
[$N_{4,4,4,4}$][Br]	*n*-Bu_4NOAc	15	52
[$N_{4,4,4,4}$][Br]	Et_3N	16	48
[$N_{4,4,4,4}$][Br]	Cs_2CO_3	15	45
[pmim][Br]	NaOAc	19	22
[bpim][Br]	NaOAc	16	11
[bbim][PF_6]	NaOAc	15	5

[a] Conditions: 1.0 equiv of chlorobenzene, 1.5 equiv styrene, 1.2 equiv base.
[b] GC yields.

These observations clearly suggested that either a catalytic species was involved or that the reaction proceeds through a different mechanism in the case of the imidazolium-based ionic liquids.

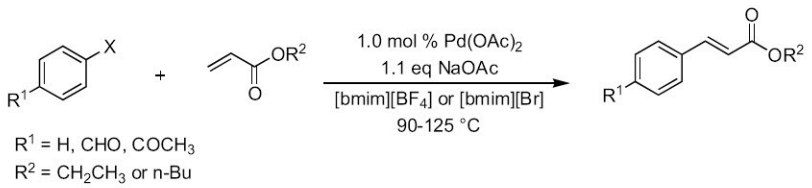
The Heck reaction could also proceed via formation of carbene species. Xu et al. obtained the first convincing evidence that carbene species are involved in the Heck reactions carried out in imidazolium-based ionic liquids.[63] The ionic liquid [bmim][Br] reacts with $Pd(OAc)_2$ to give *N*-heterocyclic carbene complexes of palladium. Interestingly, no carbene species was detected with $Pd(OAc)_2$ in [bmim][BF_4]. It is noteworthy that, with certain metals such as Ir, C(4) carbene complexes (as well as hydrogenated species) are also obtained in reaction with imidazolium salts.[64]

Xu et al. studied the Heck olefination reaction of aryl halides with acrylates (Scheme 21) as well as styrenes (Scheme 22) in the presence of $Pd(OAc)_2$ in the ionic liquids, [bmim][BF_4] and [bmim][Br].

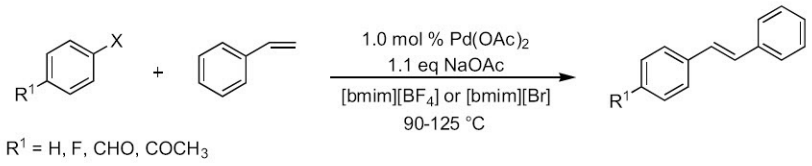
While in both ionic liquids a homogeneous yellow solution was obtained initially, in [bmim][BF_4] the slow precipitation of palladium black was observed. In addition, markedly better conversion and selectivity were noted in reactions carried out in [bmim][Br] relative to the reactions in [bmim][BF_4]. In order to determine the effect of the ionic liquid on these reactions a control study was done, in which $Pd(OAc)_2$ was heated in [bmim][Br] in the absence of the alkene and aryl halide, under conditions similar to those used in the Heck reaction. Rapid color changes from dark brown to red and then to yellow were observed and the products formed were extracted and analyzed by NMR and mass spectroscopy as well as elemental analysis. The characteristic chemical shifts of the olefin protons (δ∼7 in ^{1}H NMR spectrum) and the carbene carbons (δ 160–170 in ^{13}C NMR spectrum) suggested the formation of a mixture of palladium carbene complexes. In contrast to the results obtained in [bmim][Br], when $Pd(OAc)_2$ was heated in [bmim][BF_4], no such carbene species could be detected. The mixture of palladium carbene complexes was shown to contain the dimeric and monomeric carbene complexes, [$PdBr(\mu\text{-}Br)(bmiy)]_2$ (bmiy=1-butyl-3-methylimidazol-2-ylidene) **16** and [$PdBr_2(\mu\text{-}Br)(bmiy)_2$] **17** (Scheme 23).

The trans and cis isomers were separable by column chromatography and had distinct colors, the trans isomer being yellow, and the cis isomer, a white crystalline solid. Herrmann et al. had previously shown that the palladium complexes of carbene from 1,3-dimethylimidazolium cation were active catalysts in the Heck reaction.[65] In light of this observation, it should not come as a surprise that *trans*-**17** (the *syn*/*anti* mixture) in [bmim][Br] catalyzes the olefination of aryl halides.

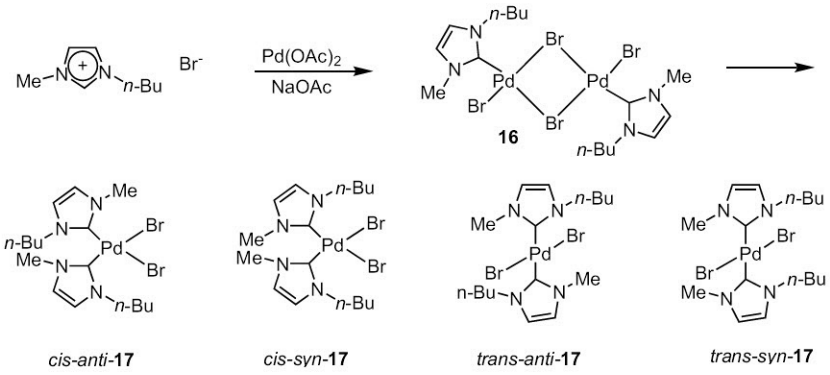
As can be seen from Table 5, [bmim][BF_4] proved to be a poor choice of an ionic liquid suggesting that the catalyst *trans*-**17** was being transformed into an inactive species in this ionic liquid. Indeed, when *trans*-**17** was heated in [bmim][BF_4] at 100 °C in the presence of NaOAc, a white solid resulted. Further experiments showed that this solid was inactive as a catalyst for the Heck reaction in



Scheme 21.



Scheme 22.

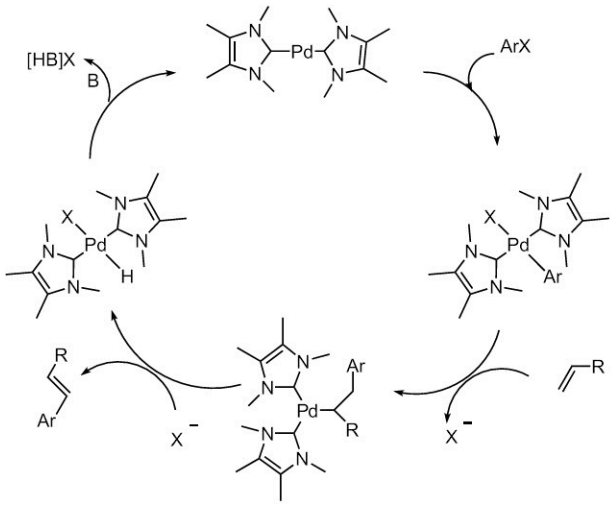


Scheme 23.

[bmim][BF_4]. Although, ^{1}H NMR studies suggested that this solid was a mixture of palladium carbene species, the mixture could not be separated into its components. The authors attribute the stability of *trans*-**17** in [bmim][Br] to the stabilization of the catalyst by bromide ions.

McGuiness et al. proposed (Scheme 24) that the oxidative addition of an aryl halide occurs to the active species, which is a 14-electron Pd(0) complex Pd(tmiy)$_2$, to give the Pd(II) aryl complex.[66] The dissociation of the halide ligand and concomitant olefin coordination, insertion, and β-hydride elimination lead to the product and give Pd(tmiy)$_2$HX. The active Pd(0) species is regenerated by the reductive elimination of HX in the presence of base.

In summary, it appears that *N*-heterocyclic carbenes can be generated from imidazolium cations to yield carbene complexes, which appear to be catalysts for the Heck reaction.



Scheme 24.

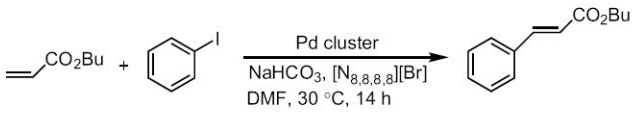
Table 5. Heck reaction catalyzed by *trans*-**17** in [bmim][Br] and [bmim][BF_4][a]

Substrate	Olefin	Ionic liquid	Temp (°C)	Conversion (%)	Selectivity (%)
Iodobenzene	Ethyl acrylate	[bmim][Br]	90	94	99
Iodobenzene	Ethyl acrylate	[bmim][BF_4]	90	35	56
Iodobenzene	Styrene	[bmim][Br]	100	93	98
Iodobenzene	Styrene	[bmim][BF_4]	100	11	93
4-Bromobenzaldehyde	*n*-Butyl acrylate	[bmim][Br]	100	71	90
4-Bromobenzaldehyde	*n*-Butyl acrylate	[bmim][BF_4]	100	3	

[a] Reaction conditions were same as shown in Scheme 19 except that 1.0 mol % of *trans*-**17** was used.

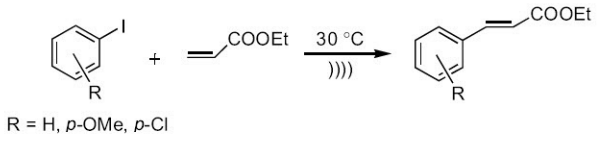
2.7. Generation of nanoparticles in ionic liquids

Following the elegant work of Xu et al.,[63] further studies suggested the possibility that the active catalyst in the Heck reaction is a palladium nanoparticle generated in situ from the palladium carbene species. In 1996, Reetz et al. showed that solutions of ammonium stabilized Pd clusters are useful catalysts for the Heck reaction.[67] For example, they successfully carried out the Heck reaction between iodobenzene and *n*-butyl acrylate in the presence of $[N_{8,8,8,8}][Br]$ stabilized 3 nm Pd clusters to afford *n*-butyl cinnamate (Scheme 25).



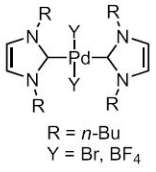
Scheme 25.

Prompted by these results, Srinivasan et al. subjected the reaction mixture from the Heck reaction of iodobenzene with ethyl acrylate in $[bbim][BF_4]$ carried out under ultrasound conditions to in situ transmission electron microscopy. These studies showed the presence of highly stabilized clusters of zero-valent Pd nanoparticles (Scheme 26).[68]



Scheme 26.

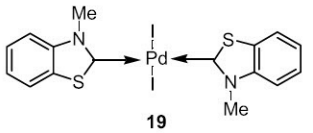
The authors demonstrated the formation of a Pd–carbene complex by subjecting a mixture of $Pd(OAc)_2$ or $PdCl_2$ and NaOAc in the ionic liquids, [bbim][Br] and [bbim]-$[BF_4]$, to ultrasonication for an hour. The formation of the carbene complex **18** was shown by ^1H NMR analysis.



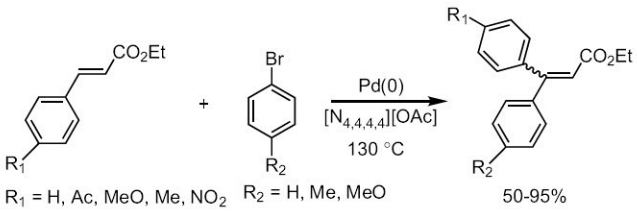
18

Hamill et al. studied the Heck reaction performed in an ionic liquid by in situ XAFS (X-ray absorption fine structure) and found the presence of palladium clusters of 0.8–1.6 nm diameter as the main species present during the reaction.[69] The size and stability of the Pd nanoparticles were found to depend upon the nature of the ionic liquid.

Calò et al. have also shown that palladium nanoparticles are formed when $Pd(OAc)_2$ or the catalyst **19** is dissolved in $[N_{4,4,4,4}][Br]$ and catalyze the stereospecific reaction of a variety of cinnamates with aryl halides (Scheme 27).[70,71] While poor stereoselectivity was observed in the absence of $[N_{4,4,4,4}][OAc]$, a significant increase in the rate of the reaction and stereoselectivity was observed in its presence. The formation of palladium nanoparticles (2–6 nm) in the presence of $[N_{4,4,4,4}][OAc]$ was confirmed by TEM analysis of the reaction.

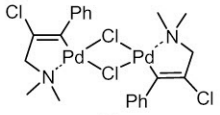


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Scheme 27.

Cassol et al. have carried out transmission electron microscopy (TEM) analysis of Pd nanoparticles dispersed in $[bmim][PF_6]$ before and after the arylation of *n*-butyl acrylate.[72] They also determined the extent of Pd leaching from the ionic liquid phase to the organic phase at different substrate concentrations. Stable and ligand-free Pd nanoparticles were prepared by reaction of the palladacycle **20** with a large excess of dimethylallene in CH_2Cl_2 at room temperature. TEM and ICP (inductively coupled plasma) analysis indicated that the Pd nanoparticles dispersed in the ionic liquid act as a reservoir of catalytically active Pd species.

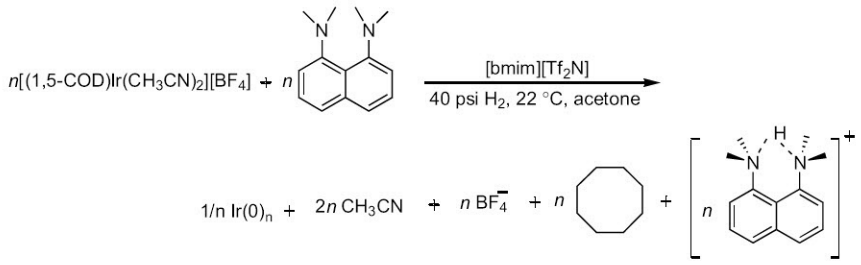


20

It is clear from these studies that palladium nanoparticles are formed during the course of the Heck reaction in $[bmim][PF_6]$.[73] However, it remains unclear whether the reaction is promoted by the nanoparticles themselves or whether they serve as a reservoir for Pd, allowing continual regeneration of the catalyst. It must be noted that some of the recent work by Cassol and others[73,74] points to the role of nanoparticles as reservoirs for Pd species.

Evidence for formation of *N*-heterocyclic carbenes from imidazolium-based ionic liquids and the subsequent ligation of a nanocluster by the carbene has also been obtained using ^2H NMR studies.[75] Ott et al. studied Ir(0) nanoclusters synthesized by reduction of $[(1,5\text{-COD})Ir(CH_3CN)_2]BF_4$ under H_2 in the presence of a strong base, proton sponge™, in acetone along with varying amounts of the ionic liquid $[bmim][Tf_2N]$ (Scheme 28).

When D_2 was used instead of H_2, deuterium incorporation was seen at the 2-H, 4-H, 5-H, and 8-H positions of the bmim cation. Control experiments in which the carbene precursor was omitted showed that no deuterium incorporation into the imidazolium cation occurs, thus eliminating the possibility that carbene formation was occurring by deprotonation of C(2) carbon of the imidazolium cation by proton sponge™. The observed results were explained via the formation of *N*-heterocyclic carbene by oxidative addition of the imidazolium cation, H/D scrambling on the nanocluster



Scheme 28.

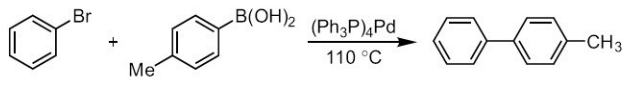
surface, and reductive elimination yielding a C–D bond. The observance of an induction period when studying the kinetics of deuterium incorporation, as a function of time, showed that the true catalysts were nanoclusters and not the nanocluster precursor.

The hydrogenation of olefins using palladium nanoparticles that are stabilized by ligands has been carried out in an ionic liquid.[76] Huang et al. showed that phenanthroline protected palladium nanoparticles (2–5 nm) are very active and reusable catalysts for hydrogenation of olefins. When the hydrogenation was attempted in the absence of phenanthroline, precipitation of Pd particles was seen and the system was inactive after three runs.

Stable iridium and rhodium nanoparticles have been formed in the ionic liquid [bmim][PF_6] and used as catalysts for hydrogenation of arenes.[77] Transmission electron microscopy (TEM) and X-ray diffraction studies show the formation of $[Ir(0)]_n$ and $[Rh(0)]_n$ nanoparticles with 2.0–2.5 nm in diameter. The ionic liquid had to be dry because the presence of water led to the formation of phosphates, HF, and transition metal fluorides.

2.8. The Suzuki coupling, Stille coupling, and Sonogashira reaction in ionic liquids

The palladium-catalyzed Suzuki coupling reaction between aryl halides or aryl triflates and arylboronic acids is a useful method to generate biaryls.[78,79] The Suzuki coupling has been well-studied in ionic liquids (Scheme 29, Table 6).[80–82]



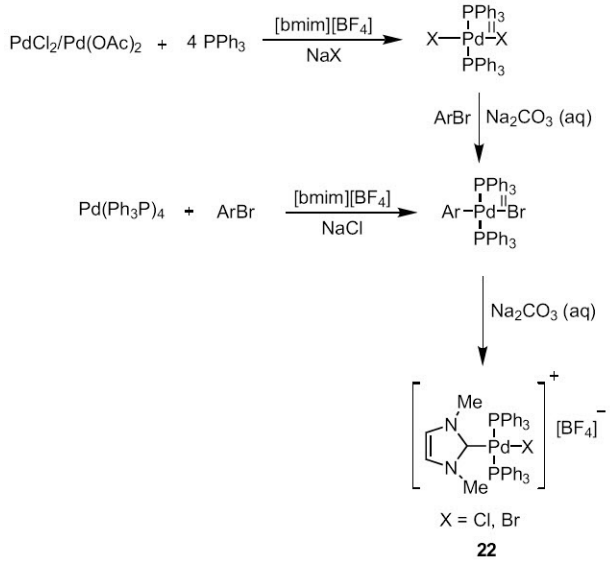
Scheme 29.

Table 6. Suzuki reaction of bromobenzene and *p*-tolylboronic acid

Entry	Solvent	Catalyst loading (mol %)	Time	Yield[a] (%)
1	[bmim][BF_4]	1.2	3 h	92[b]
2	[bmim][BF_4]	1.2	10 min	68[b]
3	[bmim][BF_4]	1.2	3 h	29[c]
4	Toluene	3.0	6 h	90[d]
5	Toluene	3.0	20 min	13[d]
6	Dioxane	3.0	6 h	88
7	Dioxane	3	20 min	29

[a] Isolated yield.
[b] The palladium/phosphine catalyst $(Ph_3P)_4Pd$ was initiated in the ionic liquid by heating with a halide source at 110 °C under an inert atmosphere.
[c] Uninitiated reaction.
[d] Halide source not used.

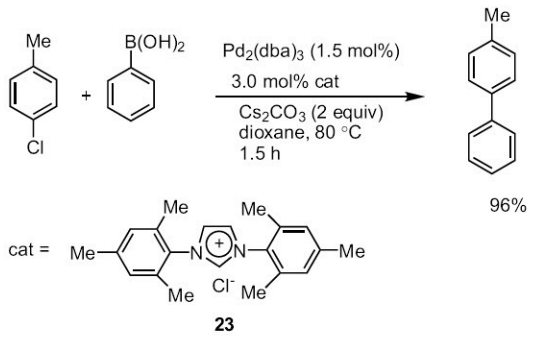
As indicated in Table 6, McLachlan et al.[82] found that it was necessary to perform an initiation of the palladium/phosphine catalyst in ionic liquid by adding a halide source and heating the mixture to 110 °C under an inert atmosphere. In the absence of such initiation, lower yields were obtained (Table 6, entry 3) and catalyst decomposition was observed. Mathews et al. had previously demonstrated (Scheme 30) the in situ formation of a mixed phosphine–imidazolylidene palladium complex **22** in the ionic liquid [bmim][BF_4].[81]



Scheme 30.

These results suggested the involvement of *N*-heterocyclic carbenes in the Suzuki coupling reaction, but did not definitely prove their participation. Zhang et al. showed that 1,3-bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene **23** catalyzed the coupling reaction between 4-chlorotoluene and phenylboronic acid in dioxane at 80 °C.[83] Since imidazol-2-ylidene carbenes are not very stable to air and moisture, the carbene ligand was generated in situ from the salt **23** using Cs_2CO_3 as the base (Scheme 31).

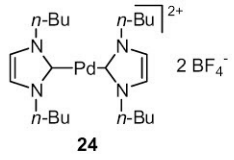
McLachlan et al. used ESIMS to detect the formation of [bPhmim] cations.[82] These cations could also be produced from independently synthesized $[(Ph_3P)_2Pd(bmim)X]^+$ (X=Br or Cl) complexes in [bmim][BF_4]. It is proposed that the 1-butyl-2-phenyl-3-methylimidazolium cation most likely arises via reductive elimination from a palladium complex containing both the imidazolylidene and a phenyl ligand, thus confirming the intermediacy of *N*-heterocyclic carbenes in the Suzuki coupling. Such reductive eliminations

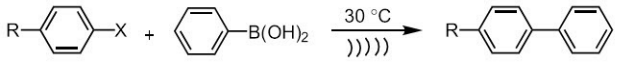


Scheme 31.

to give 2-arylimidazolium cations have been documented in the literature.[66,84]

The Suzuki coupling reaction of halobenzenes with phenylboronic acid has been carried out under mild conditions in an ionic liquid with methanol as a co-solvent using ultrasound (Scheme 32).[85] The authors reported that the co-solvent was necessary to solubilize the phenylboronic acid.





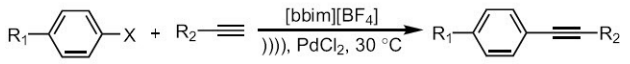
R = H, Cl, OCH_3, CH_3, NO_2
X = Br, Cl, I

Scheme 32.

This approach, which required inert conditions, always led to the formation of inactive Pd black, thus preventing recycling of the catalyst. A modified process was sought in which the Pd–biscarbene complex **24** was synthesized and used as the catalyst for the Suzuki coupling using only methanol under sonochemical conditions. These conditions allowed the reaction to be carried out in the presence of air and no Pd black was detected. However, in contrast to the ultrasound promoted Heck reaction in ionic liquids, no Pd nanoparticles could be detected under the conditions employed for Suzuki coupling.

Calò et al. have shown that Pd nanoparticles are efficient catalysts for Suzuki coupling and Stille coupling reactions of aryl halides in quaternary ammonium salts (Scheme 33).[86]

Gholap et al. have demonstrated that the copper- and ligand-free Sonogashira reaction catalyzed by Pd(0) nanoparticles proceeds under ultrasound irradiation in the ionic liquid [bbim][BF_4] (Scheme 34).[87]



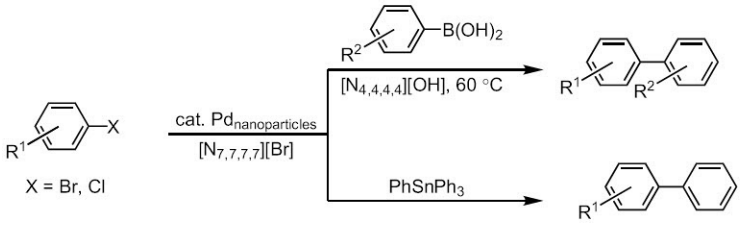
R_1 = H, CH_3, NO_2, CHO
R_2 = aryl, cyclohexyl
X = I, Br

Scheme 34.

The formation of Pd(0) nanoparticles was investigated in this reaction by subjecting the reaction mixture (after a successful Sonogashira reaction between iodobenzene and 1-ethynylbenzene in acetone and [bbim][BF_4] under sonochemical conditions) to in situ TEM analysis. In both cases Pd(0) nanoparticles were detected. Control experiments showed that both ultrasound and the ionic liquid were necessary for the formation of these Pd(0) nanoparticles.

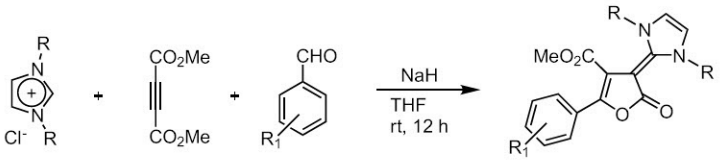
2.9. Carbenes as reagents

Nair et al. have taken advantage of the facile generation of carbenes from imidazolium-based ionic liquids and synthesized functionalized furanones (Scheme 35).[88]



$Pd_{nanoparticles}$ {2.5 mol % $Pd(OAc)_2$ + 12.5 mol % $[N_{4,4,4,4}][OAc]$}

Scheme 33.



R = 1-(2,4,6-trimethylphenyl)

R^1 = 3-Cl (65%), 3-H (57%), 3-NO_2 (79%), 4-CH_3 (45%), 1-furyl (42%), 1-benzo- (62%), 4-OMe (25%),

Scheme 35.

3. Reaction of the ionic liquid cation

Reaction of the imidazolium cation to provide a reactive carbene and/or *N*-heterocyclic complexes, as described above, is probably the most important (and underestimated) form of ionic liquid cation reactivity. However, as the popular imidazolium cation is aromatic in nature, one might expect competition between cation and substrate in, for example, electrophilic aromatic substitution reactions.

3.1. Nitration

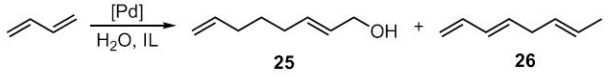
Laali and Gettwert described the use of ionic liquid solvents with a wide range of nitrating agents for the nitration of aromatics.[89] Initially, $[NO_2][BF_4]$ was combined with [emim] ionic liquids to provide the reactive system.[90] With chloroaluminate, BF_4^- or PF_6^- anions, nitration of the imidazolium ring at C(4) or C(5) was noted, although [emim][OTf] appeared inert to nitration. This latter result is somewhat unexpected as, in all cases, metathesis reactions were noted and $[NO_2][OTf]$ has been previously described as an effective nitrating agent.[91]

A further study by Lancaster and Liopis-Mestre highlights the importance of choosing an inert cation for this purpose.[92] For example, the lowest yields were obtained in the imidazolium-based ionic liquids. This was attributed to the nitration of the imidazolium ring under the reaction conditions. The best solvent was found to be $[bmpy][Tf_2N]$. Rajagopal and Srinivasan used a similarly inert ionic liquid, ethyl ammonium nitrate, to effect nitration of phenols with ultrasound activation.[93]

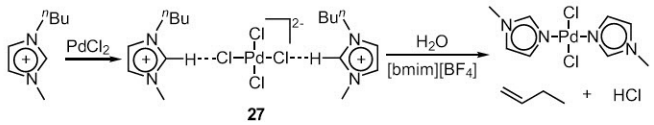
Remarkably, both the use of a fused salt in aromatic nitration reactions and the relative inertness of tetraalkylammonium cations in such reactions were described by Gordon more than 40 years ago.[94] This reaction is discussed in Section 4 as a reaction of the ionic liquid anion.

3.2. Elimination reactions

Dullius et al. have effected catalytic hydrodimerization of 1,3-butadiene with Pd compounds dissolved in $[bmim][BF_4]$ to yield, primarily, telomere octa-2,7-dien-1-ol **25** and dimer 1,3,6-octatriene **26** (Scheme 36).[95] Ionic liquids $[bmim][BF_4]$ and $[bmim][PF_6]$ with a range of known Pd catalyst precursors were examined, but it was found that the use of the new catalyst precursor, $[bmim]_2PdCl_4$ **27** was the most effective. When water was added to **27** dissolved in $[bmim][BF_4]$, butene and HCl were evolved as the [bmim] ions underwent a β-elimination reaction (Scheme 37).



Scheme 36.



Scheme 37.

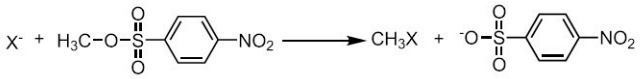
In quaternary ammonium salts, $R_4N^+OH^-$, elimination reactions may be induced by heating, resulting in elimination of an alkene via β-hydrogen abstraction: the well-known Hofmann elimination reaction.[96] The structure of the *N*-alkyl substituents determines the ease of elimination and thus the product distribution.[97] This will be discussed further (Section 7.1) as a significant route to volatile products during thermal degradation.

4. Reaction of the ionic liquid anion

Many reports of nucleophilic displacement reactions carried out in ionic liquid solvents have appeared. The use of ionic liquids obviates the need for phase transfer catalysts in reactions where the nucleophile is introduced in the form of an inorganic salt[98] and two-phase ionic liquid/aqueous systems are common.[99] Indeed many ionic liquids closely resemble phase transfer catalysts (PTCs)[100] and the work of Tundo et al. might well be considered as early reports of the advantages of carrying out nucleophilic substitution reactions in ionic liquids, as many of the PTCs used fulfill all the criteria required for ionic liquids.[101]

4.1. Nucleophilicity of halide ions

Remarkably, the first report of the nucleophilicity of halide ions in ionic liquids appeared in 1971,[102] but, as these solvents were referred to as 'molten quaternary ammonium salts', this work has been largely overlooked by later investigators. Many reports of enhanced nucleophilicity of anions dissolved in ionic liquids have appeared[103] and, in some cases, a change in the order of nucleophilicity of halide ions inferred.[103b] However, in a series of carefully executed kinetic and mechanistic studies using the nucleophilic attack of halide ions on methyl *p*-nitrobenzene sulfonate[‡] (Scheme 38), Welton and co-workers have demonstrated that the nucleophilicities of Cl^-, Br^-, and I^- ions are *lower* in ionic liquids than in non-hydrogen bond donor molecular solvents[104] and that changing orders of nucleophilicity in different ionic liquids,[105] reflected in reaction rates, are readily predicted by a classical Hughes–Ingold approach to solvent effects.[106]



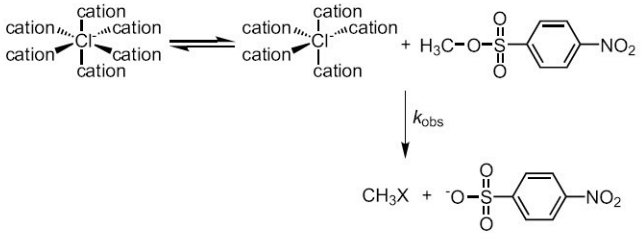
Scheme 38.

These comprehensive and methodically executed studies are summarized in a recent paper[107] and as the conclusions reached are germane to a large number of reported reactions *of* ionic liquids themselves (as opposed to reactions *in* ionic liquids), these are summarized here. It was found that there is no specific 'ionic liquid' effect and the classical Hughes–Ingold treatment of solvent effects on organic

[‡] Chosen as a probe reaction because both the starting material and ionic product are readily detected by UV–vis spectroscopy (a caution: 'spectroscopic grade' ionic liquids, which do not absorb above 240 nm are required for such studies).

reactions applies. Further, all halide nucleophilicities are decreased in ionic liquids (although increased rates of reaction due to improved mass transfer are possible, as the bulk ionic liquid behaves as a PTC) so that the rates of S_N2 reactions are lower in ionic liquids than in nonpolar molecular solvents.

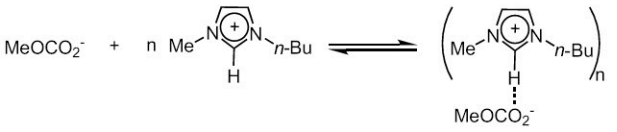
The ionic liquid is, however, not simply a passive spectator in all of the reactions and differences in apparent nucleophilicity are ascribed to the effect of hydrogen bonding between cations and anions (both added and intrinsic to the ionic liquid). For example, in imidazolium-based ionic liquids, C(2)–H forms strong hydrogen bonds to anions such as Cl^-[108] while the anion serves both to mediate solvent polarity and to compete for H-bonds.[105] In [mmim][Cl], the halide ion is coordinated by six cations within a radius of 6.5 Å[109] and it is reasonable to assume that similar interactions occur in all imidazolium ionic liquids lacking a C(2) substituent. Reaction of the nucleophile with the substrate is thus in competition with coordination of the cation to the nucleophile (Scheme 39). Thus, any factor leading to competition for cation to X^- (nucleophile) coordination, such as strong cation/anion interactions (e.g., as occurs in [bmim][BF_4]) will alter the nucleophilicity of X^-.[105] Changing the cation from [bmim] to the bulky [$N_{8,8,8,8}$] cation, which is a much poorer H-bond donor,[110] serves to decrease H-bond interactions with the anions, consequently increasing the nucleophilicity of added X^- and changing the order of reactivity to that predicted from gas phase reactivity.[111]



Scheme 39.

In S_N2 reactions in ionic liquids, the usual trend of increased solvent polarity leading to increased anion coordination, as occurs in polar molecular solvents, is not as clear cut, as ionic liquid 'polarity' appears to be influenced by the anion, while ionic liquid coordination (at least in imidazolium-type ionic liquids) is a function of the coordinating power of the cation.[112] If the energy of solvation of the anion is lower in ionic liquids, the formation of an encounter complex (preassociation mechanism) may become favorable.[112]

The effect of imidazolium cation H-bonding is not restricted to halides and Ross and Xiao have demonstrated deactivation of bases in [bmim][BF_4] due to hydrogen bonding between C(2)–H and oxygen containing anions, such as $MeOCO_2^-$ and AcO^- (Scheme 40).[113] Similarly, the Tsuji–Trost Pd(0) catalyzed allylic alkylation reaction (Scheme 41, Table 7) is inhibited by hydrogen bonding in the presence of [bmim][BF_4] such that addition of even a small quantity of ionic liquid to the reaction mixture in THF, resulted in reduction of the rate of reaction. NMR titration studies reveal the existence of a 2:1 complex: $[bmim_2 \cdot OAc]^+$ (Scheme 40). Thus the base (in alkylation reactions) is not available to effect deprotonation of the incipient nucleophile, HNu, vastly decreasing reaction rates.



Scheme 40.

Table 7. Effect of solvents on the neutral Tsuji–Trost reaction between phenylallyl carbonate and dimethyl malonate

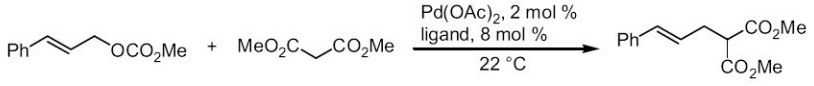
Solvent	Additive	Ligand	Time (h)	Conversion (%)
THF	—	PPh_3	0.33	100
[bmim][BF_4]	—	PPh_3	1.0	<1
[bmim][BF_4]	—	$P(4\text{-}MeOC_6H_4)_3$	1.0	<1
[bmim][BF_4]	—	$P(4\text{-}MeOC_6H_4)_3$	5.0	9
THF	—	$P(4\text{-}MeOC_6H_4)_3$	0.42	99
THF	[bmim][BF_4]	$P(4\text{-}MeOC_6H_4)_3$	0.90	63

The effect of hydrogen bonding is also invoked to account for differences in reactivity of ICl_2^- and Br_3^- in a range of ionic liquids.[114]

4.2. Nucleophilicity of water in ionic liquids

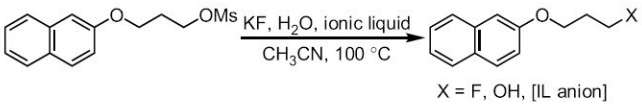
Hydrogen bonding is important in ionic liquids and directly affects the reactivity of added nucleophiles as well as that of the ionic liquid anion itself. This is demonstrated in the apparently reduced reactivity of H_2O in ionic liquids, allowing them to be used, without rigorous drying, in conjunction with water-sensitive compounds such as PCl_3 or $POCl_3$.[115] A similar water tolerance is noted in fluorination (with ^{18}F reactions carried out in ionic liquids,[116]) although the same authors also describe 'enhanced nucleophilicity of water in ionic liquids'.[117] While there seems to be ample evidence that water structure (at <20 M) is different in ionic liquids than in, for example, alcohol solvents, due to disruption of water–water hydrogen bonds[118] by C(2)–H···OH_2 hydrogen bonds, this seems to enhance reactivity in some reactions while decreasing it in others.

As noted, ionic liquid anions are themselves potential nucleophiles (though usually chosen for their poorly coordinating



Scheme 41.

nature,[119] charge diffuse character and thus, under normal circumstances, poor nucleophilicity) and hints of reactivity occur in a number of reports of investigations where the authors have taken the trouble to note (and identify) by-products. Thus, unexplained consumption of reagents,[105] preferential reaction of OAc^- or NO_3^- anions in nucleophilic fluorination reactions (Scheme 42, Table 8),[116] and formation of unexpected by-products[120] are due to reaction with the ionic liquid anion.



Scheme 42.

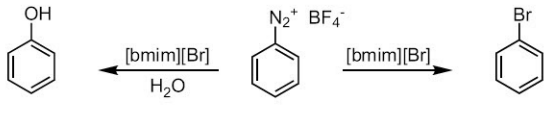
Table 8. The ionic liquid anion competes with F^- in nucleophilic displacement of OMs

Ionic liquid	Time (h)	Yield (%)		
		1[a]	**2**[a]	**3**[a]
[bmim][OTf]	4	79	15	—
[bmim][Tf_2N]	5	35	—	—
[bmim][OAc]	2	Trace	—	93
[bmim][NO_3]	2	Trace	—	90

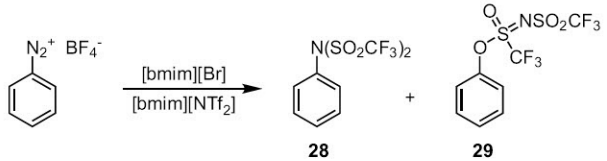
[a] Where these products are: **1**, X=F; **2**, X=OH; **3**, X=IL anion moiety.

4.3. Diazotization reactions

The non-innocent nature of ionic liquid anions is emphasized by remarkable competition between Br^- and the 'non-nucleophilic' anion Tf_2N^-. In a study of the effect of ionic liquids on the reactivity of arenediazonium salts in dediazotization processes, Chiappe et al. used either water or the ionic liquid anion nucleophilic quenching of the dissociated $PhN_2^+BF_4^-$ salt to yield phenol or bromobenzene, respectively (Scheme 43).[120] Remarkably, when the reaction was attempted in mixtures of [bmim][Br] and [bmim][Tf_2N] ionic liquids, the Tf_2N^- anion competed favorably with Br^- yielding, almost exclusively, products **28** and **29** resulting from nucleophilic trapping by the Tf_2N^- anion (Scheme 44), even in 3:1 mixtures favoring the Br^- containing ionic liquid!

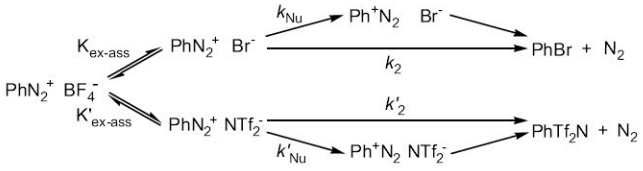


Scheme 43.



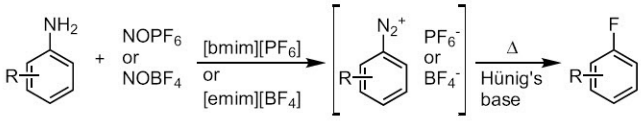
Scheme 44.

Reaction of $[PhN_2][BF_4]$ with 1:1 [bmim][Br]:[bmim]-[Tf_2N] in water yielded mainly the expected products, viz. bromobenzene and phenol products (9:1). That the effective competition of Tf_2N^- versus Br^- was restricted to reactions in ionic liquids implied that some particular characteristics of the ionic liquid were responsible for the apparently significantly enhanced nucleophilicity of Tf_2N^- (or suppressed nucleophilicity of Br^-). The 'ionic liquid effect' in this case is ascribed to the inhibitory effect of hydrogen bonding of the ionic liquid cation to Br^- anion on the metathesis reaction that must precede reaction of PhN_2^+.[120] The authors' proposal, summarized in Scheme 45, is that the relative magnitudes of equilibrium constants for exchange and association of Tf_2N^- for BF_4^- versus Br^- for BF_4^- are responsible for the vastly decreased efficacy of Br^- as a trapping nucleophile. Thus it is increased rate of exchange of non-hydrogen-bonded Tf_2N^- for BF_4^-, rather than a change in the intrinsic nucleophilicity of the anion, that yields the switch in reactivity. The authors stress that this phenomenon should only be of importance in reactions involving *short-lived reactive intermediates*.[120]



Scheme 45.

A similar phenomenon was noted in the formation of by-products in a 'one pot diazotization/fluorodediazotization' reaction reported by Laali and Gettwert (Scheme 46).[121] While ionic liquids containing BF_4^- and PF_6^- anions proved suitable for the reaction, competition for anions occurred in ionic liquids with CF_3COO^-, TsO^- or TfO^- anions (Scheme 47).

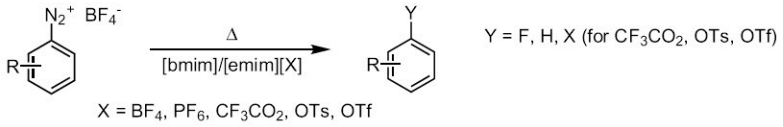


Scheme 46.

Reaction of the ionic liquid anion is starkly highlighted where the products are unexpected, as in the competition between Br^- and Tf_2N^- above, but there are numerous reports of the positive effect of reactivity of the anion.

4.4. Ionic liquid halide anions as catalysts

Tetrabutylammonium bromide, $[N_{4,4,4,4}][Br]$, is shown to be an effective catalyst for the formation of carbonates from alkenes (using *tert*-butyl hydroperoxide (TBHP) and carbon dioxide) as a direct consequence of intervention of the Br^- on in the reaction (Scheme 48).[122] The Br^- ion is oxidized to hypobromite, which participates in bromination of the olefin, yielding, along with H_2O, the bromohydrin and, in turn, the epoxide. Ring opening of the epoxide, via nucleophilic attack of the Br^- (from the ionic liquid solvent)



Scheme 47.

produces an oxyanion **30**, which reacts with CO_2 yielding the cyclic carbonate.

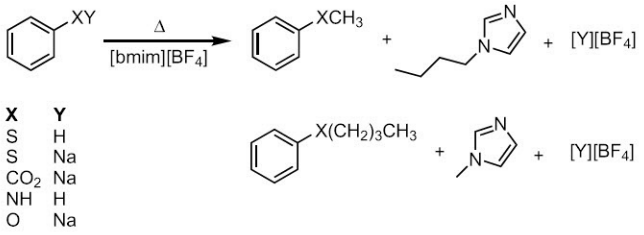
4.5. Degradation of ionic liquids in the presence of added nucleophiles

The reaction of imidazolium cations with added nucleophiles at elevated temperatures, via S_N2 attack of the nucleophile on electrophilic *N*-substituents yields neutral imidazoles and the conjugate acid of the anion as well as the (now alkylated) nucleophile (Scheme 49, Table 9).[123] These deleterious reactions were found to be facilitated under microwave heating and provide information about decomposition mechanisms (see Section 7.1).

4.6. Nitrations

Intentional reactivity of the ionic liquid anion falls perhaps into the realm of 'task-specific ionic liquids', however, as the work in question was an exploratory study by Gordon carried out in the true sense of 'discovery' we have chosen to include nitrations by $[R_4N][NO_3]$ ionic liquids (or, as described by the author, fused salts) as unintended reactions of the anion.[94] Molten quaternary ammonium nitrates were used as solvent and reactants converting, for example, dinitrohalobenzenes to dinitrohalophenols or picric acid depending on reaction conditions (Scheme 50).[94b]

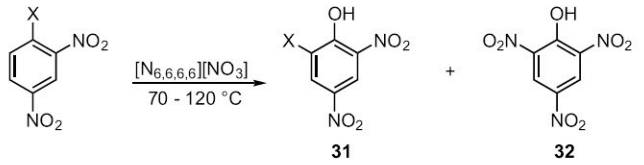
An extensive kinetic study and consideration of by-products led the author to conclude that the reaction proceeded by displacement of the halide by the oxyanion (NO_2^-) with concomitant formation of $[R_4N][X]$; oxidation of halide (by NO_3^-) and halogenation of the dinitrophenol nucleus to yield **31**. (The source of NO_2^- is described as a minor impurity in the quaternary ammonium salt, but could also be provided as a reagent.) Further reaction with $[R_4N][NO_2]$ results in formation of **32** by analogous processes.



Scheme 49.

Table 9. Reaction of added nucleophiles with $[bmim][BF_4]$, T=225 °C and MW power=20 W

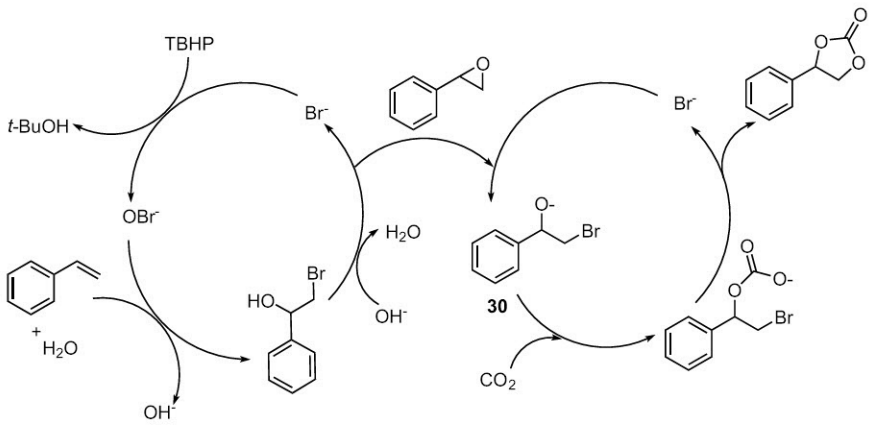
Nuc	Nuc-Me (%)	Nuc-Bu (%)	Substituted imidazoles (%)
PhSH	5	1	6
NaSPh	39	7	46
$NaPhCO_2$	27	13	40
$PhNH_2$	4	1	6 (includes dimethylaniline)
NaOPh	2	Trace	2



Scheme 50.

5. Acidic and basic ionic liquids

Although the unexpected reactivity of an ionic liquid can be a nuisance, an increasing number of ionic liquids are being designed with a specific reactivity in mind. These task-specific ionic liquids (TSILs) often serve the dual role of catalyst and reaction medium. In this review, attention is given to those manuscripts in which active participation by

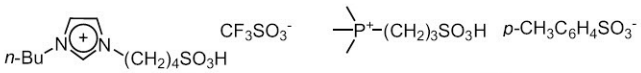


Scheme 48.

the ionic liquids is clearly demonstrated. Reports of enhanced reactivity in an ionic liquid, without any clear evidence for participation of the ionic liquid in the reaction, are generally not discussed. Lewis acidic ionic liquids, such as [cation][$Cl^-/AlCl_3$], are not included as the reactivity of such ionic liquids has been widely detailed in many comprehensive reviews[20,23b,124] and the historical development of these materials has been eloquently described by Wilkes.[20c]

5.1. Brønsted-acidic ionic liquids

Although referred to as a fused salt at the time, ethyl ammonium nitrate represents one of the very early examples of a Brønsted-acidic ionic liquid.[125] However, it is only in the last decade that Brønsted-acidic liquids have been specifically designed as catalysts, reagents and/or solvents in organic synthesis. Cole et al. designed acidic ionic liquids containing an alkane sulfonic acid group covalently attached to the ionic liquid cation.[126]

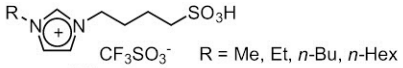


33 **34**

Ionic liquid **33** is a viscous liquid at room temperature while **34** is a glass-like material that liquefies at ca. 80 °C. In contrast to mixtures of strong acids dissolved in ionic liquids, which tend to emit noxious vapors, these task-specific Brønsted acids exhibited behavior more typical of ionic liquids. Neither compound fumed or exhibited any observable vapor pressure. Even when the ionic liquid **33** was heated at 150 °C under vacuum, loss of triflic acid was not observed. With ionic liquid **34**, washing with ether or toluene did not result in the extraction of any *p*-toluenesulfonic acid. These observations provide confirmation of the fact that these ionic liquids are not mere mixtures of a strong acid with dissolved zwitterions. Ionic liquid **34** was used to effect a variety of transformations such as esterifications, ether formation, and the pinacol–pinacolone rearrangement (Scheme 51).

In contrast to the results using **34**, although the conversion of 1-octanol to dioctyl ether with *p*-TsOH gave a better yield of the product, more by-products were also formed. A very poor yield (3%) of dioctyl ether was obtained when Nafion-117 was used as a catalyst. The pinacol–pinacolone rearrangement is typically carried out using H_2SO_4 or H_3PO_4 as a catalyst. Attempts have been made to replace these difficult to handle, corrosive acids with various solid acid catalysts. However, even the reactions in the presence of solid acids require the use of a volatile organic solvent, leading to difficulties in product isolation. The advantage of using **34** as a catalyst for the pinacol rearrangement was that the product pinacolone could be directly distilled from the reaction mixture.

Gu et al. have carried out the esterification of a variety of aliphatic acids with olefins using the ionic liquid **35**.[127]

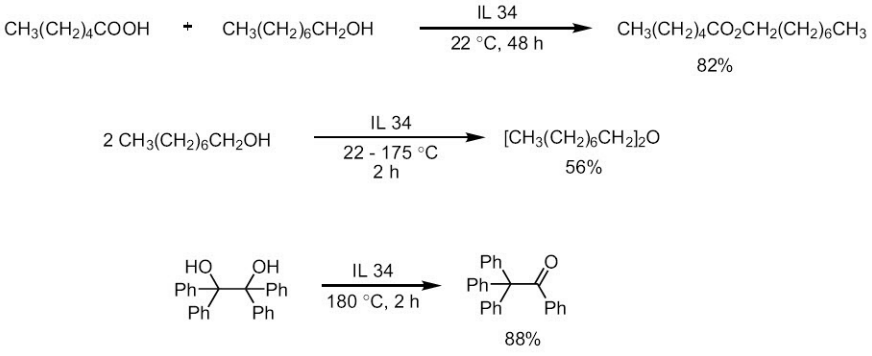


35

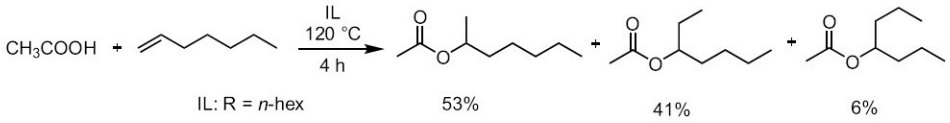
The best results were obtained with 3 equiv of the olefin in the ionic liquid (R=*n*-Hex), (Scheme 52).

The ester product is insoluble in the ionic liquid and hence it was separated from the ionic liquid by decantation. The excess olefin was extracted from the ionic liquid using toluene and the ionic liquid was reused after drying under vacuum at 80 °C. Since the authors do not report isolated yields of the ester product, it is hard to determine the practical utility of this method for esterifications.

Fei et al. have synthesized a series of Brønsted-acidic ionic liquids and determined their solid-state structure as well as pK_a values (Table 10).[128] The knowledge of pK_a is especially

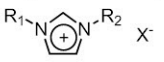


Scheme 51.



Scheme 52.

Table 10. pK_a values of carboxylic acids in H_2O at 25 °C

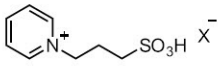


Entry	R^1	R^2	X	pK_a
1	CH_3	CH_2COOH	Cl	1.90
2	CH_3	CH_2COOH	BF_4	2.00
3	CH_3	CH_2COOH	CF_3SO_3	2.03
4	CH_3	$(CH_2)_3COOH$	Cl	3.83
5	CH_2COOH	CH_2COOH	Cl	1.33
6	$(CH_2)_3COOH$	$(CH_2)_3COOH$	Cl	3.46
7	CH_2COOH	CH_2COO^-	—	2.92

useful when selecting a Brønsted-acidic liquid as a solvent and catalyst for an application.

As with aliphatic dicarboxylic acids, the dicarboxylic acid with the shortest chain length (entry 5) was the most acidic in the series. The pK_a of the acid with R_2=CH_2COOH (entry 1) is much lower than that of chloroacetic acid, suggesting that the positively charged imidazolium group is a stronger electron withdrawing group than a chloro group. As with aliphatic carboxylic acids, the inductive effect of the imidazolium ring drops dramatically with increasing chain length (entry 6).

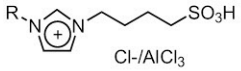
Xing et al. synthesized several water-stable Brønsted-acidic ionic liquids with an alkane sulfonic acid group and a pyridinium cation.[129]



[PSPy][BF_4], X = BF_4
[PSPy][H_2PO_4], X = H_2PO_4
[PSPy][HSO_4], X = HSO_4
[PSPy][pTSA], X = *p*-$CH_3C_6H_4SO_3$

Although the freshly synthesized ionic liquids [$C_3(SO_3H)$Py][BF_4], [$C_3(SO_3H)$Py][*p*-TSA], and [$C_3(SO_3H)$Py][HSO_4] are viscous colorless liquids at room temperature, with prolonged storage (several weeks) they solidify. These ionic liquids are readily soluble in water, methanol, and ethylene glycol monomethyl ether but are only partially miscible with esters, alkanes, and aromatic hydrocarbons. These ionic liquids were shown to be good catalysts for the esterification of benzoic acid with methanol, ethanol, and butanol. It was found that increasing the Brønsted acidity of the anion improved the catalytic activity of the ionic liquid. The best catalytic activity was found with the ionic liquid containing [HSO_4^-] as the anion. It is also likely that the varying catalytic activity is due to the fact that the product esters have varying solubility in the ionic liquids—the separation of the ester from the ionic liquid being a driving force for the reaction.

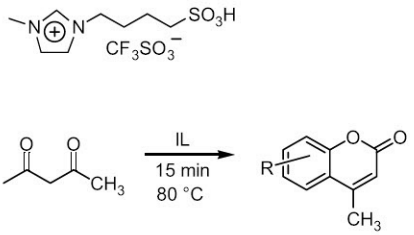
Wang et al. have synthesized and characterized dual acidic ionic liquids in which the cation contains Brønsted acidity and the anion contains Lewis acidity.[130] The acidities of these ionic liquids were determined by IR spectroscopy using pyridine as a probe.



Cl-/$AlCl_3$

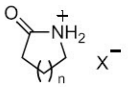
The coordination of pyridine to the Lewis acidic sites as well the formation of a pyridinium ion by protonation by the Brønsted acid could be easily determined by characteristic bands in the IR spectrum.[130]

Gu et al. have carried out the synthesis of coumarins via the Pechmann condensation using a Brønsted-acidic ionic liquid as both catalyst and solvent (Scheme 53, Table 11).[131]



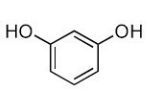
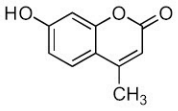
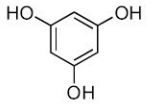
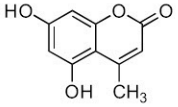
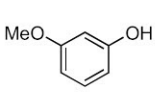
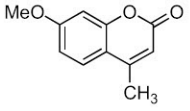
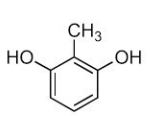
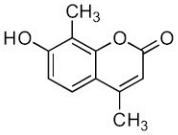
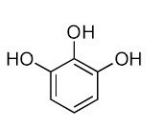
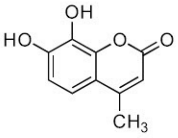
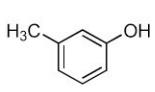
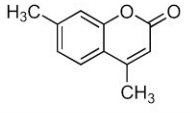
Scheme 53.

Du et al. have synthesized a series of lactam-based ionic liquids and measured their properties such as density, viscosity, electrochemical stability, and thermal stability.[132]



n = 1 or 3, X = BF_4, CF_3CO_2, PhCOO, $ClCH_2CO_2$, NO_3, H_2PO_4

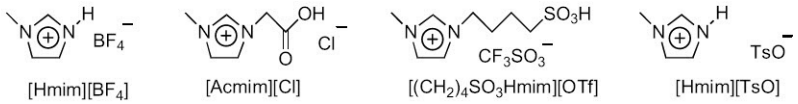
Table 11. Pechmann condensation between phenols and methylacetoacetate in [MBSIm][CF_3SO_3]

Entry	Phenol	Product	Time (h)	Yield (%)
1			1	95
2			1	90
3			1	92
4			1.5	92
5			0.5	94
6			4	76

They have also carried out the Beckmann rearrangement of cyclohexanone oxime to caprolactam in such an ionic liquid that served the dual role of catalyst and reaction medium (Scheme 54).[133] On an industrial scale, the Beckmann rearrangement is carried out with corrosive oleum, which is then neutralized using ammonium hydroxide. As a consequence, a large amount of ammonium sulfate is also produced as a by-product. One difficulty in using acidic ionic liquids has been that the caprolactam product, owing to its basic nature will combine with the ionic liquid making product separation practically impossible. The use of a caprolactam-based ionic liquid coupled with a dynamic exchange between the caprolactam product and the ionic liquid allowed for facile product isolation.

However, even with the present method, extraction of the desired caprolactam with ether only affords the product in a 42% yield indicating that there is still an interaction present between the ionic liquid and the caprolactam product. Better yields (80%) were obtained when the product was isolated by chromatography.

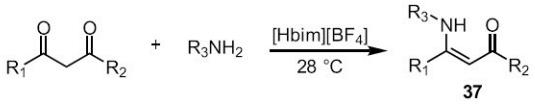
Gholap et al. have shown that 3,4-dihydropyrimidine-2-(1*H*)-ones **36** can be synthesized in good yields by the reaction of aromatic or aliphatic aldehydes with ethyl acetoacetate and urea at room temperature in the Brønsted-acidic ionic liquid [Hbim][BF_4] under sonochemical conditions (Scheme 55).[134]



A downfield shift in the δ value of the carbonyl group in ^{13}C NMR spectra of both *p*-tolualdehyde and ethyl acetoacetate in one equivalent of the ionic liquid suggested that the NH proton of [Hbim][BF_4] was hydrogen bonded with the carbonyl oxygen of the aldehyde as well as that of the β-keto ester of ethyl acetoacetate. Similar evidence was obtained from IR spectra wherein a shift to a lower wavenumber for the C=O stretch was observed.

Based on these observations, a mechanism for the reaction was proposed in which the carbonyl groups of both the aldehyde and ethyl acetoacetate are activated by bonding with the Brønsted-acidic ionic liquid.

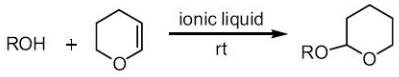
Gholap et al. have also carried out the synthesis of β-enaminones **37** in the Brønsted-acidic ionic liquid [Hbim][BF_4] (Scheme 56).[135]



Scheme **56**.

As in the previous example, evidence for the activation of the carbonyl group of the 1,3-diketone by the acidic ionic liquid was obtained using ^{13}C NMR and IR spectroscopy.

The tetrahydropyranylation of a variety of alcohols has been carried out in a series of Brønsted-acidic ionic liquids (Scheme 57).[136]



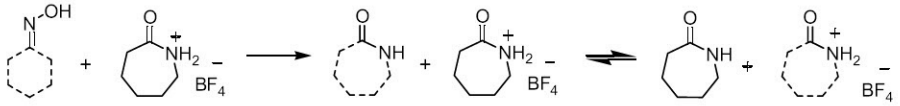
Scheme **57**.

The best results were obtained with [Hmim][BF_4] and [Hmim][TSO] while [Acmim][Cl] and [$(CH_2)_4SO_3$Hmim][OTf] proved ineffective.

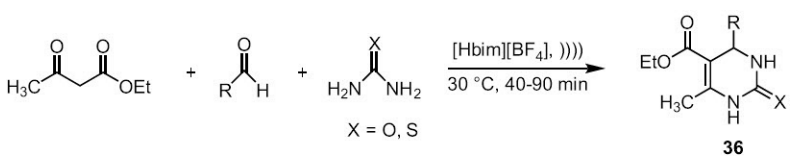
5.2. Brønsted-basic ionic liquids

Ranu and Banerjee demonstrated the use of a tailor-made, task specific, and stable ionic liquid [bmim][OH] as a catalyst and reaction medium for Michael addition. This ionic liquid provides an efficient and convenient procedure for Michael addition of active methylene compounds to conjugated alkenes in one step without requiring any other catalyst or an organic solvent (Scheme 58).[137]

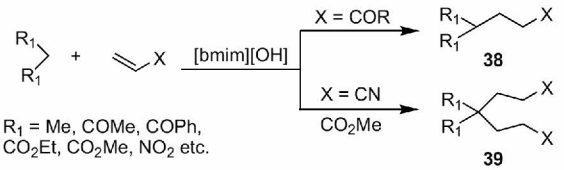
A variety of structurally diverse active methylene compounds underwent Michael additions with several α,β-unsaturated ketones, carboxylic esters, and nitriles by this



Scheme **54**.



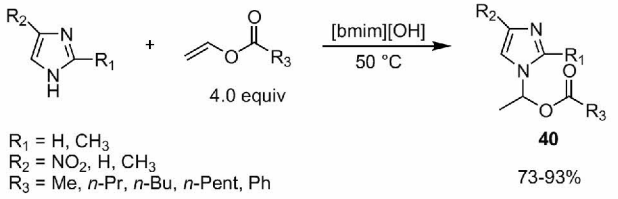
Scheme **55**.



Scheme 58.

procedure to provide the corresponding adducts **38** or **39** in high yields.

The same ionic liquid was employed by Xu et al. as both catalyst and reaction medium for the Markovnikov addition of *N*-heterocycles to vinyl esters, yielding **40**, under mild conditions (Scheme 59).[138] Mechanistic studies demonstrate active participation of the ionic liquid in the reaction. The C(2) hydrogen serves as hydrogen bond with the carbonyl group of the ester while the hydroxide anion serves as a catalytic base to deprotonate the N–H in the imidazole.



Scheme 59.

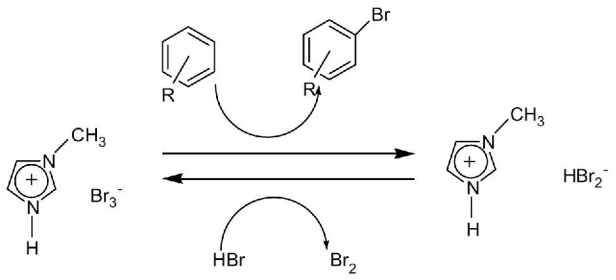
6. Ionic liquids as reagents or catalysts

In addition to acting as catalysts, several ionic liquids have been designed to serve the dual purpose of reagent and solvent. The concept of task-specific ionic liquids (TSILs), i.e., ionic liquids with specific functionality designed to act as reagents, catalysts, separation or sequestering agents (amongst other possibilities), has been highlighted[139] and reviewed[140] recently. Here the focus is on ionic liquids that provide synthetic advantages, such as safer delivery of reactive species, greater selectivity or improved yields.

6.1. Halogenating reagents

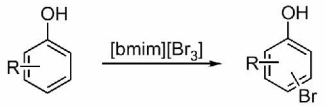
Chiappe et al. have demonstrated the use of ionic liquid solvents and elemental bromine in the bromination of alkenes.[141] The observed product distributions noted were considered to imply reaction with either added Br_2 or Br_3^-, depending on the ionic liquid used. Bromochlorides were obtained when Cl_2 was added to stilbene or styrene in [bmim][Br], presumably by the action of the $BrCl_2^-$ ions.[141]

This leads logically to the formulation of X_3^- containing ionic liquids as halogenating agents and, indeed, [bmim][Br_3] and [Hmim][Br_3] have been effectively used as aromatic brominating agents (Scheme 60).[142] Conversion was found to be higher when the protic ionic liquid, crystalline [Hmim][Br_3] (mp 70 °C) was employed (compared to [bmim][Br_3]), but product distributions in both ionic liquids were similar. The design of these and many other ionic liquids



Scheme 60.

synthesized as halogenating agents, including [bmim][Br_3] (Scheme 61, Table 12),[143] [hmim][ICl_2], [bmim][IBr_2],[144] and pentylpyridinium tribromide [C_5Py][Br_3][145] follow conceptually from Djerassi and Scholz's use of crystalline pyridine hydrobromide perbromide (mp 132–134 °C) as an easily handled brominating agent.[146] Since this early report in 1948, a number of similar reagents have been described, though not all constitute ionic liquids.



Scheme 61.

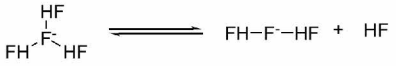
Table 12. Monobromination of activated aromatics with [bmim][Br_3]

Substrate	Time (min)	Temp (°C)	Product	Yield (%)
Phenol	2	0	4-Bromophenol	96
4-Chlorophenol	60	25	2-Bromo-4-chlorophenol	92
2-Chlorophenol	60	25	4-Bromo-2-chlorophenol	90
3-Chlorophenol	60	25	4-Bromo-3-chlorophenol	90
4-Methylphenol	2	-5	2-Bromo-4-methylphenol	95
2-Methoxyphenol	2	0	4-Bromo-2-methoxyphenol	94
Anisole	10	0	4-Bromoanisole	95
1-Methoxynaphthalene	60	25	4-Bromo-1-methoxy naphthalene	92
2-Methoxy naphthalene	60	25	1-Bromo-2-methoxy naphthalene	94
2-Naphthol	60	25	1-Bromo-2-naphthol	92

6.2. HF Source

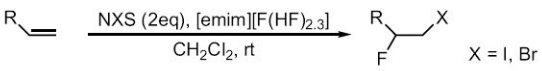
Yoshino et al. have demonstrated halofluorination of alkenes using a combination of *N*-halosuccinimide and 3-ethyl-1-methyl-imidazolium oligo hydrogen fluoride [emim]-[$F(HF)_{2.3}$] ionic liquid as an HF source.[147] Prepared by the direct reaction of [emim][Cl] and anhydrous HF, the apparently non-stoichiometric value of 2.3 arises from rapid exchange between the $F(HF)_2$ and $F(HF)_3$ anions (Scheme 62). Remarkably, this reagent is stable in air and to moisture.[148]

The iodofluorination and iodobromination products (with *N*-iodosuccinimide and *N*-bromosuccinimide, respectively



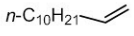
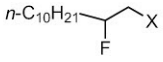
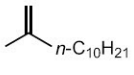
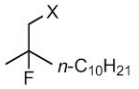
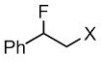
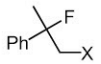
Scheme 62.

(Scheme 63)) of various aliphatic, cyclic, and aryl alkenes were obtained in good yields and with high regioselectivity (Table 13). Chlorofluorination was less successful.[147]



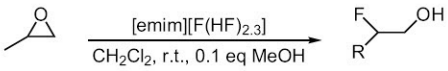
Scheme 63.

Table 13. Iodofluorination and iodoalkylation of alkenes using NBS and NIS[a]

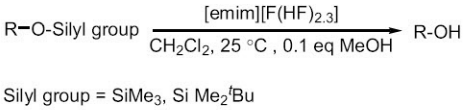
Alkene	Time (h)	Product	Yield (%) X=I	Yield (%) X=Br
	3		80	86
	1		91	90
	1		95	90
	1		70	81
	1		88	87

[a] NBS (*N*-bromosuccinimide), NIS (*N*-iodosuccinimide).

The same ionic liquid HF source was employed, with methanol, in ring opening reactions of epoxides (Scheme 64),[149] and deprotection of silyl ethers (Scheme 65), which occurred in almost quantitative yield.[149] The method is mild enough to leave alkynyl silanes untouched, while effectively cleaving the TBDMS ether.



Scheme 64.

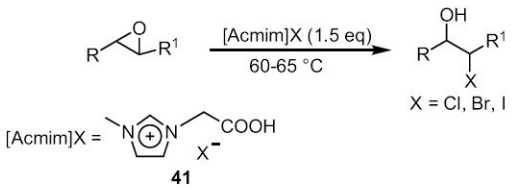


Scheme 65.

6.3. Conversion of epoxides to halohydrins

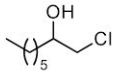
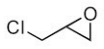
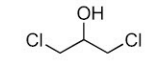
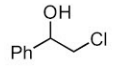
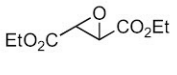
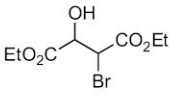
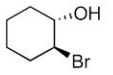
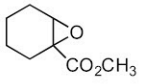
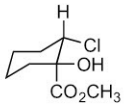
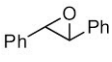
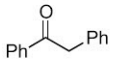
In an alternative to the method above, the generation of halohydrins from epoxides may be achieved with ionic liquids such as **41** (Scheme 66, Table 14).[150] Typically these transformations are carried out using HX or hypohalite–water, which often results in the formation of by-products.

The method is quite versatile and a wide variety of epoxides can be converted to the corresponding halohydrin in good



Scheme 66.

Table 14. Synthesis of β-halohydrins from 1,2-epoxides with [Acmim]X

Entry	Epoxide	Product	Time (h)	Yield (%)
1			1.5	95
2			1.4	80
3			1.5	87
4			1.5	76
5			1.5	86
6			1.5	85
7			1.5	85

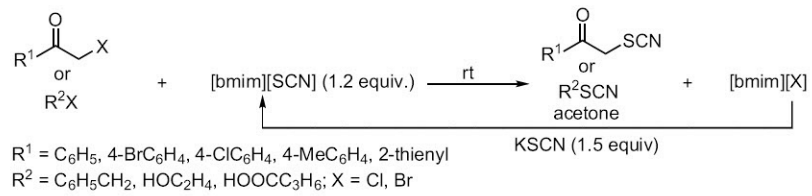
yields. However, *trans*-stilbene oxide (entry 7) did not yield the corresponding halohydrin. Instead, the epoxide underwent a rearrangement to give deoxybenzoin. This is also an interesting observation because the rearrangement of *trans*-stilbene oxide typically proceeds via a phenyl group migration to give diphenylacetaldehyde as the major product.[151]

6.4. Thiocyanation reagents

In an intentional nucleophilic reaction of the ionic liquid anion, [bmim][SCN] was used by Kamal and Chouhan for the conversion of alkyl halides to alkyl thiocyanates at room temperature.[152] The reaction proceeded in good yield with the ionic liquid acting as both solvent and reactant. The ionic liquid was regenerated by the reaction of [bmim][X] with KSCN (Scheme 67, Table 15).

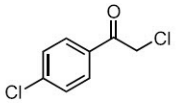
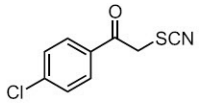
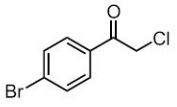
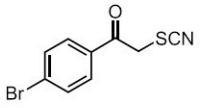
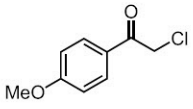
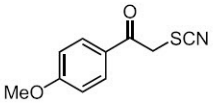
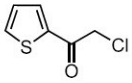
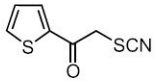
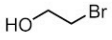
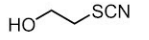
6.5. Oxidation catalysts

The 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) radical has been 'immobilized' by the addition of an ionic liquid as appendage and used, in the structurally related ionic liquid [bmim][PF_6], under biphasic conditions with water-soluble oxidants, as a catalyst for the metal-free, chemoselective oxidation of primary and secondary alcohols to aldehydes and ketones (Scheme 68).[153] Excellent conversions were

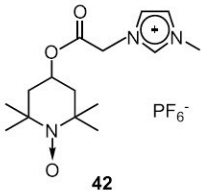


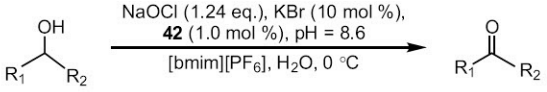
Scheme 67.

Table 15. Thiocyanation of alkyl halides using [bmim][SCN]

Halide	Product	Time (min)	Yield (%)
		9	93
		10	96
		15	90
		15	90
		24 h	80

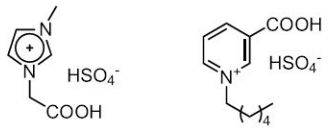
achieved (Table 16) and the catalyst remained immobilized in the ionic liquid phase and could be recycled.

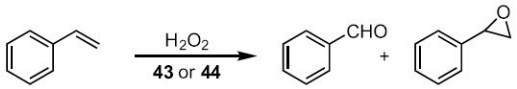




Scheme 68.

Ionic liquids based on imidazolium or pyridinium cations, with carboxylic acid functional groups appended to the *N*-substituents or the aromatic ring, have been described as precursors to peracids for olefin oxidation (Scheme 69, Table 17).[154]



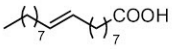
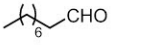
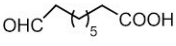
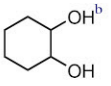
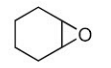
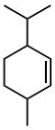
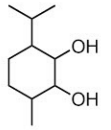


Scheme 69.

Table 16. Oxidation of alcohols by ionic liquid-supported nitroxyl catalysts

Alcohol	Product	Time (min)	Yield (%)
Benzyl alcohol	Benzaldehyde	5	94
4-Nitrobenzyl alcohol	4-Nitrobenzaldehyde	5	93
1-Phenylethanol	Acetophenone	10	96
Diphenylmethanol	Benzophenone	10	95
Cyclohexanol	Cyclohexanone	10	88
1-Octanol	Octanal	5	86

Table 17. Oxidation of olefins in TSIL system

Substrate	Product	Yield[a] (%)
		72
		6
		67
		70
		75
		73
		5
		82

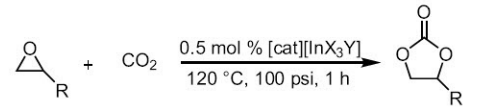
[a] Yield was based on the substrate converted and was determined by GC.
[b] *trans*-Diol was obtained.

6.6. Synthesis of cyclic carbonates using tetrahaloindate(III)-based ionic liquids

Varma and co-workers have reported the synthesis of a series of tetrahaloindate(III)-based ionic liquids for use in the coupling reaction of carbon dioxide and epoxides to generate cyclic carbonates.[155]

These thermally stable ionic liquids were synthesized by the microwave promoted reaction of indium chloride, InX_3, with

a variety of ionic liquids. Using FTIR and ^{13}C labeling NMR studies, the authors demonstrate the importance of hydrogen bonding between the halide ion and the ring protons of the imidazolium cation in determining catalytic activity of the ionic liquid (Scheme 70).



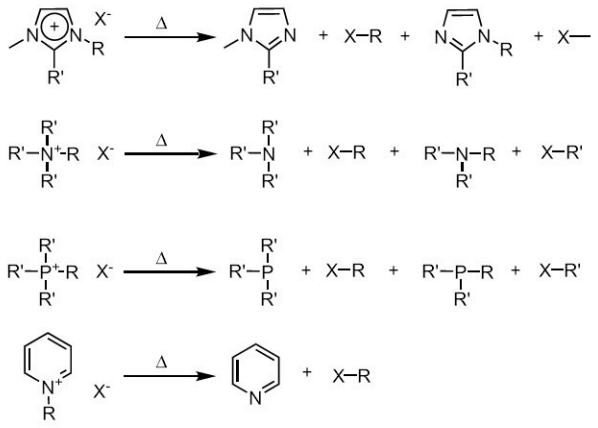
Scheme 70.

7. Decomposition reactions of ionic liquids

7.1. Thermal decomposition

Thermal decomposition of ionic liquids or degradation of ionic liquids by reaction with added reagents has been alluded to in the preceding sections and discussed in a previous review.[156] However, as one of the benefits of ionic liquids, when used as reaction solvents, is their wide liquid range and reportedly high thermal stability, which allows application at significantly elevated temperatures, this is briefly summarized here. Resistance to degradation (either by intramolecular reaction, reaction between cation and anion and/or reaction with the atmosphere) is sometimes overestimated, as 'thermal stability' is oft equated with the 'onset temperature of degradation' derived from step tangent analysis applied to data derived from fast scan (10 °C min^{-1}) thermogravimetric analysis (TGA), under a nitrogen atmosphere.[157] If long-term thermal stability of an ionic liquid is required, somewhat lower maximum operating temperatures are desirable.[158]

Most ionic liquids in use as reaction solvents are based on di(or tri)alkylimidazolium, pyridinium, tetra-alkylammonium or tetra-alkylphosphonium cations. In all cases, nucleophilic attack of the ionic liquid anion in a reverse Menschutkin-type reaction to yield neutral products (Scheme 71) is possible.[159,160] Clearly, within a series of ionic liquids with the same cation, degradation temperature and rate will depend largely on nucleophilicity of the anion[161,162] and ionic liquids containing a halide anion (or halide impurities) might be expected to be particularly prone to such reactions.[163]



Scheme 71.

Phosphonium halides are less prone to dealkylation via this mechanism[164] and a significant body of information on the relative stabilities of molten salts are contained in reports appearing in the chromatographic literature.[165] In all cases, potentially reactive alkylating agents and/or bases are generated and, while these might simply recombine to regenerate the ionic liquid,[166] other reactions may also be effected. Clearly, if the ionic liquid is degraded by reaction with nucleophilic anions, added nucleophiles in the form of reactants will have a similar effect. While this is dealt with extensively above it is important to note that such reactions are significantly enhanced at elevated temperatures.[123]

Decomposition of quaternary ammonium salts by a Hofmann elimination reaction is well known[159] and this route will provide potentially reactive terminal alkenes and amines, which may in turn accelerate the process. Both attack by nucleophilic anions and elimination has been reportedly enhanced in the presence of F^- ions.[167]

While phosphonium-based ionic liquids tend to be less prone to thermal decomposition, the presence of O_2 may lead to the formation of phosphine oxides[168] and transfer of O from oxygen containing anions, such as HSO_4^-, also leads to by-product formation.[169]

Although ultrasound has been used to promote the Heck reaction and Suzuki coupling in ionic liquids, as discussed in a previous section, Suslick et al. have investigated the stability of a variety of ionic liquids such as [bmim][Cl], [bmim][BF_4], [bmim][PF_6], urea ammonium nitrate (UAN), and decylmethylimidazolium tetraphenylborate under ultrasound conditions.[170] They report that during sonication, all of the imidazolium ionic liquids darkened from colorless to amber while UAN did not undergo a color change. ^1H NMR analysis of [bmim][Cl] and [bmim][BF_4] also indicated the appearance of new peaks in the imidazole region. Multibubble sonoluminescence (MSBL) spectra of [bmim][Cl] showed that products were arising from the decomposition of both the ionic liquid itself and its primary sonolysis products. The primary decomposition products from the imidazolium ionic liquids were identified to be *N*-alkylimidazoles and 1-alkyl halides. These results suggest that caution must be exercised when ionic liquids are used as solvents for ultrasound promoted reactions.

7.2. Hydrolysis and other degradation reactions

Even so-called air- and water-stable ionic liquids may be prone to hydrolysis. Ionic liquids containing PF_6^- ions are hydrolytically unstable, yielding PO_4^{3-} and HF[162] (it is worth considering how many 'uncatalyzed' reactions reported in [cation][PF_6] ionic liquids are, in fact, catalyzed by adventitious HF!). The rate of hydrolysis of PF_6^- anions is increased in the presence of nitric acid. Initially biphasic systems of aqueous HNO_3 and [xmim][PF_6] become monophasic as decomposition proceeds and the process is accelerated in the presence of SiO_2.[171] Ionic liquids with PO_4^{3-} anions have been prepared,[172] but a remarkable number of reactions

are still carried out in [cation][PF_6] ionic liquids with little regard for the possibilities arising from release of HF.

Similarly, ionic liquids derived from alkyl sulfate salts[173] such as $CH_3OSO_3^-$ and $CH_3CH_2OSO_3^-$ react with water at elevated temperatures yielding the corresponding alcohols and hydrogen sulfate, while the longer chain homologs are apparently more stable to hydrolysis.[174]

Relatively little attention has been paid to ion exchange reactions, either in aqueous solution or in two phase systems with aqueous solutions, although Rogers et al. have demonstrated significant leaching of [bmim] cations into acidic aqueous phases.[171] This may be overcome by the introduction of a sacrificial cationic species.[175] Such facile exchange has important implications for disposal of aqueous waste streams from reaction in, or with, ionic liquids. 'Scrambling' of alkyl substituents of tetraalkylammonium salts may occur in water in the presence of tertiary amines.[176]

As organic salts, ionic liquids are prone to oxidative degradation, particularly with vigorous oxidizing agents as has been demonstrated by Pernak et al. with $KMnO_4$[177] and O_3.[178] In another intentional degradation study, Stepnowski and Zaleska demonstrated that imidazolium and pyridinium ionic liquids are degraded by a combination of UV radiation and photocatalysis.[179]

8. Conclusions

It is evident from the increasing number of reports on use of ionic liquids as solvents, catalysts, and reagents in organic synthesis that they are not inert under many reaction conditions. While in some cases, their unexpected reactivity has proven fortuitous and in others, it is by design, it is imperative that when selecting an ionic liquid for a particular synthetic application, attention must be paid to its compatibility with the reaction conditions. Adequate care must be exercised especially when inferences are made regarding the role of ionic liquids in promoting a particular reaction pathway.

Acknowledgements

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