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Ionic Liquids and its Application in Organic Synthesis

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ABSTRACT

Ionic liquids comprise ionic species but remain in a liquid state and have a melting point below 100°C. The significant characteristics of ionic liquid are its low vapour pressure and thermal stability. It can dissolve in both polar and non-polar substances, etc. The ionic liquids are salts in which one or both ions are large. The cation has a low degree of symmetry. These factors tend to reduce the lattice energy of the crystalline form, resulting in a low melting point. Ionic liquids are considered substitutes for volatile organic solvents due to its low vapour pressure; this characteristic appraise it as green solvents. Currently, the applications Ionic Liquids (ILs) are growing and are a highly vital topic in the fields of chemistry and organic synthesis.

Keywords: *Green Solvent; Ionic Liquid; Low Vapour Pressure; Organic Synthesis*

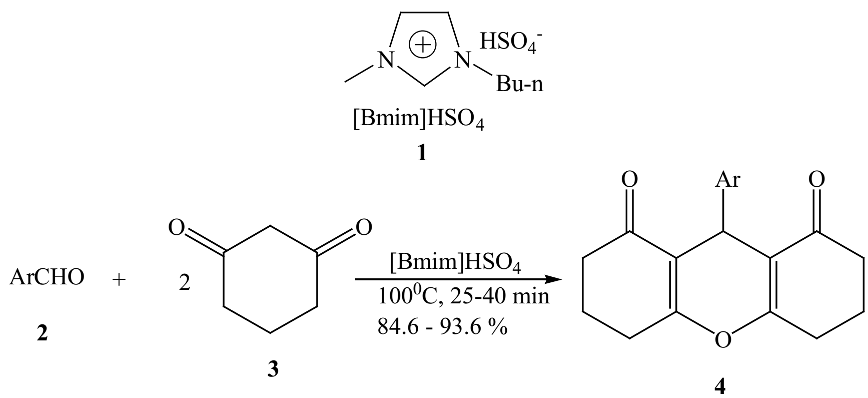
Introduction

Molecular solvents are generally used in most synthetic reactions. These organic solvents are inflammable, health hazards, expensive, high vapour pressure, extra care in handling and are difficult to recycle. Nowadays a novel class of solvent has been developed, which is ionic liquids characterised by low vapour pressure, liquid at room temperature and recyclable. In ionic liquids, the ionic species are composed of organic or inorganic cations and anions.

The thermodynamic and kinetic reactions carried out in ionic liquids are different from those carried out in conventional organic solvents. It is known as “green solvent” due to its eco-friendly nature and its unique characteristics. These many interesting properties make them of great interest to all chemists and scientists. In recent years, ionic liquid has been used by several chemists and scientists in chemical synthesis regarding environmental approaches. They have enormous and interesting attention in green synthesis, and in this short review, an attempt was made to capture a few of the works published. Several authors have reviewed ionic liquids including (Welton, 1999; Lei, 2017; Lei, 2024). The low melting point below 100°C of ionic liquids was first suggested in 1914 by Paul Walden. Ionic liquid from molecular level to industrial level has been demonstrated by Dong *et al*. (2017). Both or one ionic components of the ionic liquids are large, and the cations have a low degree of symmetry; this tends to minimise their lattice energy of the crystalline form, resulting in a low melting point

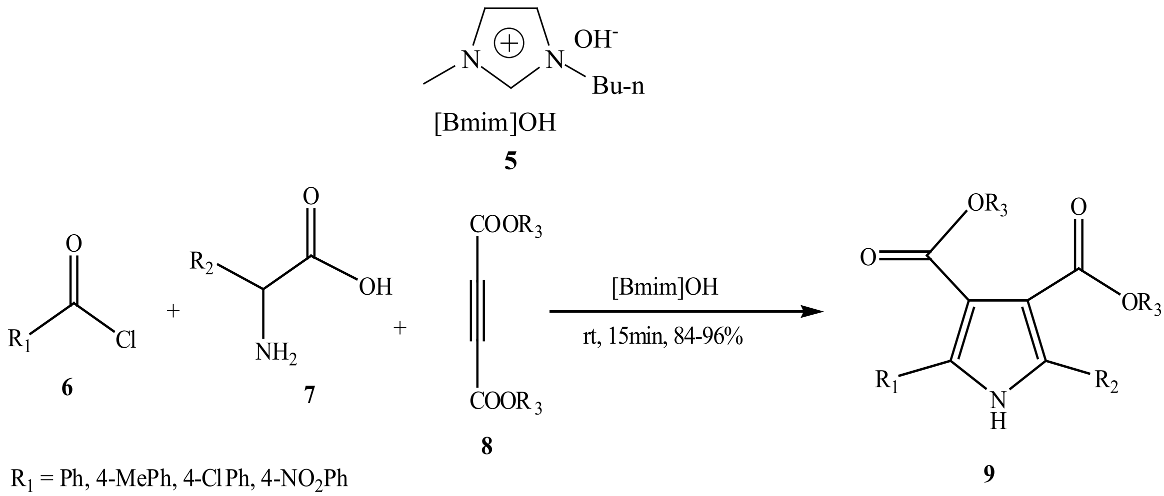
(Jaeger & Trucker, 1989). Ionic liquids, classified into simple salts and binary ionic liquids. The first one consists of a single anion and cation, while the second one is salts that involve equilibrium. $[EtNH_3][NO_3]$ is an example of simple salt, while mixtures of aluminum(III) chloride and 1,3-dialkylimidazolium chlorides are examples of binary ionic liquids. Sowbhagyam (2014) discussed the characteristics and applications of several ionic liquids, that served as a productive media for catalysis as well as synthesis reactions. Their tenable properties and design of ILs characterise their specific catalytic capabilities, enhancing reaction rates and selectivity. It is utilised in both homogeneous and heterogeneous catalysis reactions. The study concluded that Ionic liquids are recognised as innovative chemical agents for synthesis and are increasingly acknowledged as a more environmentally friendly alternative to commonly used solvents due to their design flexibility, recyclability, and non-volatility. Previously, Chaturvedi *et al*., (2014) had published a review explaining the recent developments in the area of task specific ionic liquids, particularly on their application in organic synthesis, nanoparticle synthesis and catalytic reactions. Here few of their applications are mentioned in organic synthesis.

Ma *et al*. (2007) have reported the green and productive synthesis of 9-aryl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione 4 by using different types of aromatic aldehydes 2 with cyclohexane-1,3-dione 3 (Scheme 1) by using $[Bmim]HSO_4$1. $[Bmim]HSO_4$ is a task specific acidic ionic liquid.



Scheme 1

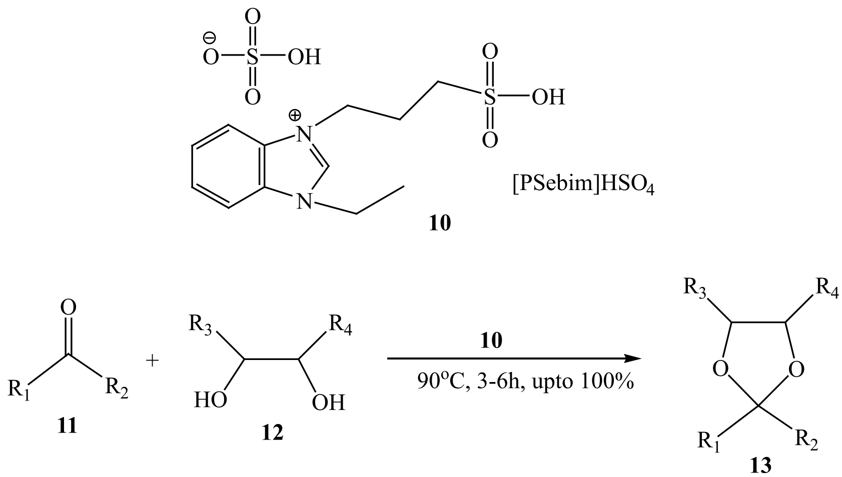
The other ionic liquid, 1-butyl-3-methylimidazolium hydroxide, [Bmim]OH 5, catalysed the three-component reaction of acid chlorides 6, dialkyl acetylenedicarboxylates 8 and amino acids 7 in water. This reaction produced a series of different pyrrole derivatives 9 with better yields (Yavari & Kowsari, 2008). They studied this reaction with other different kinds of ionic liquids, but it was found that [Bmim]OH was the most effective catalyst at 80ºC. This catalyst is basic functionalised. Benzoyl chloride, having an electron withdrawing group, gives a faster reaction (Scheme 2).



R_1 = Ph, 4-MePh, 4-ClPh, 4-NO_2Ph
R_2 = Ph, Bn, *i*-Bu
R_3 = Me, Et

Scheme 2

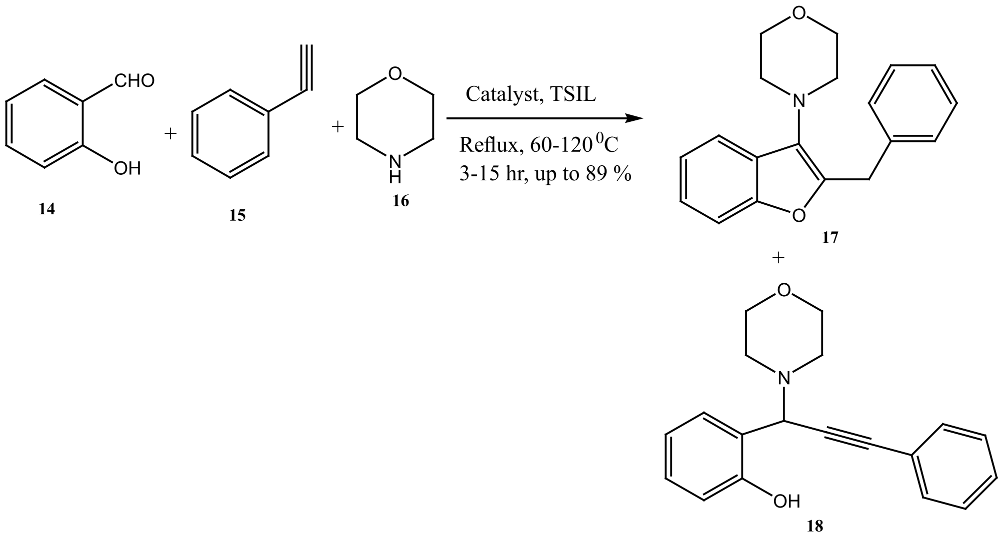
Wang, Jiang and Dai (2008) proposed many ionic liquids, which were based on Brønsted acidic benzimidazolium, and used it for catalytic reactions in the acetalisation of many different ketones 11 with substituted 1,2-ethanediols 12. This reaction produced acetals 13 in good yields (Scheme 3). However, they used different other types of catalysts, while it was found that the 1-ethyl-3-(3-sulfopropyl)benzimidazolium hydrogen sulfate, [PSebim]HSO_4 10, an ionic liquid, was most efficient and high yielding acetalisation reaction for this reaction.



R_1, R_2 = Ph, 4-MePh, 4-MeOPh, 4-NO_2Ph, Cyclohexanone, Me/Et
R_3, R_4 = Me

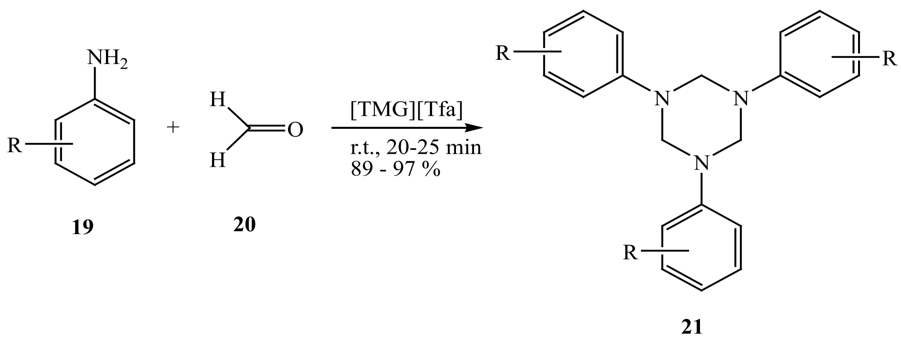
Scheme 3

Zhang *et al*. (2011) reported a most efficient and practical synthesis of benzo[b]furan 17 and propargylamine 18. The reaction of 2-hydroxybenzaldehyde 14, phenylacetylene 15 and morpholine 16 yield product 17 and 18. This reaction was carried out in the presence of different types of ionic liquids, such as [Bmim]OAc, [Bmim]BF_4 and Bmim]PF_6 (Scheme 4). While it was found that the use of [Bmim]BF_4, the compound propargylamine 18 produced more affordably, with the use of other ionic liquids [Bmim]PF_6 and [Bmim]OAc, the compound of benzo[b]furan 17 produced affordably with good yield because of the hydrophobic nature of ionic liquid.



Scheme 4

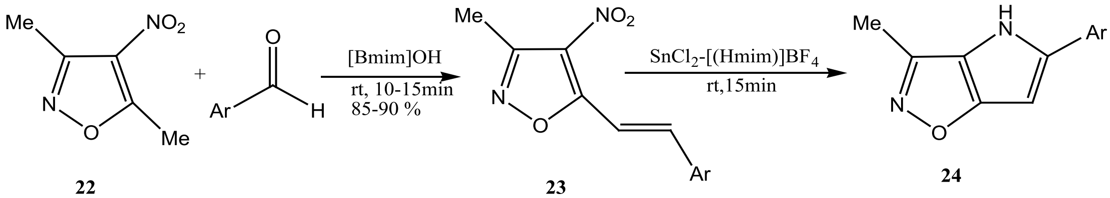
Dandia, Jain and Sharma (2014) reported the condensation reaction, in which the different substituted aniline 19 reacts with formaldehyde 20 to produce a derivative of 1,3,5-triazine 21 in the presence of ionic liquid 1,1,3,3-tetramethylguanidine trifluoroacetate [TMG][Tfa] (Scheme 5). This reaction was one of the green synthesis methods for the preparation of triazine derivatives. This compound showed great activity against *Mycobacterium tuberculosis*.



R= 2/3/4-F; 2/3/4-CF_3; 2-Cl,5-CF_3; 2-CF_3, 4-NO_2; 2-Br, 4-F; H; 4-Me;4-OMe; 4-Cl; 4-Br

Scheme 5

An effective method has been developed by Rajanarendar *et al*. (2010) for the synthesis of pyrrolo[2,3-d]isoxazoles 24 from the reaction between 3,5-dimethyl-4-nitroisoxazole 22 and several aldehydes. This reaction is carried out by using different types of ionic liquids: 1-Hexyl-3-methylimidazolium tetrafluoroborate [Hmim]BF_4 and 1-methyl-3-butylimidazolium hydroxide [Bmim]OH. The compound 22 undergoes Knoevenagel condensation with different types of aldehyde 1 to produce nitrostyrylisoxazoles 23 through condensation with ionic liquid [Bmim]OH, which is further converted into compound 24 with [Hmim]BF_4 and $SnCl_2$ (Scheme 6). The ionic liquid [Hmim]BF_4 gives excellent yield (85-92%) of compound 24 at room temperature.



Ar = Ph, 4-MeC_6H_4, 4-MeOC_6H_4, 4-ClC_6H_4, 2-ClC_6H_4, 2,4-$Cl_2C_6H_3$, 3,4-(O-CH_2-O)C_6H_3, 2-MeC_6H_4, 4-N$(Me)_2C_6H_4$, 2,6-$Cl_2C_6H_3$, 2-OHC_6H_4, 3-MeO, 4-OHC_6H_3

Scheme 6

Conclusion

Ionic liquids are essentially molten salts, meaning they are composed entirely of ions, specifically organic or inorganic cations and anions. Ionic liquids are considered a green solvent due to their low vapour pressure and recycling nature. Ionic liquids give a wide range of organic synthetic reactions. Ionic liquid has been used by several chemists and scientists in chemical synthesis regarding environmental approaches. They have enormous and interesting attention in green synthesis. Regarding advantages of green chemistry, hopefully, the industry will alter conventional methods of synthesis of compounds with greener ones.

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