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A facile and efficient nucleophilic displacement reaction at room temperature in ionic liquids

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Abstract—We have investigated the use of room temperature ionic liquids as catalytic and environmentally benign solvents for the facile homogenous synthesis of benzyl salicylate by the nucleophilic displacement reaction between sodium salicylate and benzyl chloride. The reaction was found to proceed under relatively mild conditions with excellent conversion (up to 96%) without the use of PTCs. The ionic liquids were recycled and reused. The effect of temperature was also investigated. No by–products were observed after ^{1}H NMR and GC analysis. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

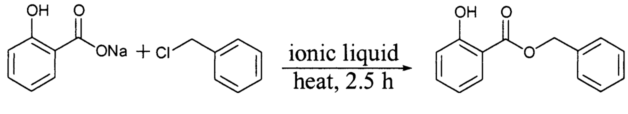
Benzyl salicylate, like other esters of aromatic acids, is used in the perfumery and flavor industries. Its main synthetic routes involve the use of phase transfer catalysts (PTCs) in the heterogeneous reaction between benzyl chloride and either sodium salicylate[1] or salicylic acid.[2] Other methods involve the reaction of benzyl alcohol with salicylic acid in the presence of a catalyst (e.g. organotin,[3] nonquaternizable tertiary amines[4]) or by transesterification[5] of benzyl alcohol with methyl salicylate using sodium methyl salicylate as catalyst. The reaction between salicylic acid and benzyl bromide proceeded slowly in 24 hours with 80% yield in the presence of tetraalkylammonium fluoride catalyst.[6] The main drawbacks of these methods are the generation of a number of undesired by-products (for example, benzyl alcohol, benzyl benzoate, salicylic acid, dibenzyl ether) as a result of hydrolysis and side reactions and a longer reaction time (8–24 hours) coupled with low yields.[6] The conventional PTC reactions involve the use of environmentally unfavourable halogenated solvents and catalyst separation is another major problem. We envisaged that the use of ionic liquids as catalyst and solvent will be advantageous in such a reaction where a homogenous mixture is formed and thus omitting the use of PTC. Moreover, the ionic liquids thus employed can be recycled and reused.

Room-temperature ionic liquids[7] are finding growing applications in separations[8] and organic transformations.[9–15] Recent examples of such transformations include hydrogenations,[9] Friedel–Crafts reactions,[10] Diels–Alder reactions,[11] Heck reactions,[12] Bischler–Napieralski reactions,[13] olefin hydrodimerizations[14] and olefin dimerizations.[15] Ionic liquids are emerging as novel replacements for volatile organic compounds (VOCs). The desirable advantages of ionic liquids such as lack of vapor pressure and thermal stability have made them excellent reaction media and environmentally benign solvents.

We report here an efficient, homogenous and environmentally friendly nucleophilic displacement reaction using ionic liquids as a substitute for heterogeneous and phase transfer catalysis methods. The reaction is investigated through the preparation of benzyl salicylate (Scheme 1).

2. Results and discussion

Nucleophilic displacement reactions using ionic liquids as solvents are rare in the literature.[16] We are not aware of such reactions involving salts of organic compounds



Scheme 1. Esterification of sodium salicylate with benzyl chloride.

Keywords: nucleophilic displacement; ionic liquids; sodium salicylate; benzyl salicylate.

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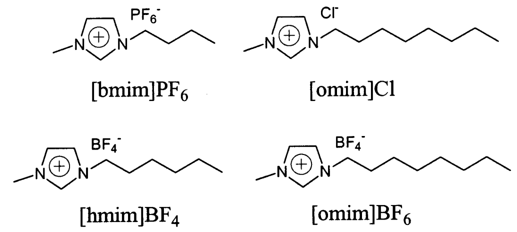

Figure 1. Structures of the ionic liquids.

(e.g. sodium salicylates). These reactions are normally carried out in a heterogeneous medium using a PTC to facilitate the reaction between the organic reactants and the salts. The use of a PTC is important to activate the anions and also to provide the contact between the reactants in order for the reaction to proceed. The effectiveness of the four ionic liquids, [omim]Cl, [hmim]BF_4, [omim]BF_4 and [bmim]PF_6 (Fig. 1), as catalysts and solvents in the nucleophilic displacement reactions was examined in the preparation of benzyl salicylate. Since the ionic liquids used for this study contain bulky, nitrogen-based, organic cations, it is thought that they may act like nitrogen-based PTCs. These ionic liquids could also activate the anions for the reaction and thus result in an enhanced reaction rate.[16] The solubility of sodium salicylate in these ionic liquids was investigated at 100°C since the solubility at room temperature was low. Therefore, sodium salicylate was added portionwise under vigorous stirring to four test tubes containing 2 mL each of the four ionic liquids preheated to 100°C. Addition was stopped when a slight cloudiness was observed. The solubility test results in the four ionic liquids are shown in Table 1. It is clear that sodium salicylate showed a more enhanced solubility in [hmim]BF_4 compared to its solubility in the other ionic liquids. A comparable solubility was observed in [omim]Cl and [omim]BF_4 while minimum solubility was obtained in [bmim]PF_6. It is interesting to note that further addition of sodium salicylate to [omim]Cl, [hmim]BF_4 and [omim]BF_4 ionic liquids resulted in a more cloudy and viscous but still homogenous solution while sodium salicylate precipitated out when more was added to [bmim]PF_6. The influence of the different cations and anions as well as the effect of polarity on the solvating ability of ionic liquids is still being investigated.[7]

Initial reaction investigations[17] were done using [hmim]BF_4 as a model ionic liquid reaction medium in view of its high solvating ability for sodium salicylate. The reaction procedure involved the addition of benzyl chloride to a preheated (100°C) and well-stirred solution of sodium salicylate in [hmim]BF_4. The amount of sodium salicylate was 1.5 times the stoichiometric amount of benzyl chloride. Initially, a clear homogenous reaction mixture was observed which then turned cloudy after 20 minutes due to sodium chloride formation indicating the onset of the reaction. As time passed more sodium chloride was formed and the reaction mixture turned cloudy due to poor solubility of sodium chloride in the ionic liquid. The reaction was found to proceed smoothly with high conversion (GC analysis, Fig. 2) and the identity of the product was confirmed by ^{1}H NMR[18] spectroscopic analysis where no decomposition or by-products were observed. The effect of temperature change on the conversion was also investigated using the [hmim]BF_4 ionic liquid. The above reaction was repeated essentially under the same conditions except that the reaction was done at 120°C instead of 100°C. It can be seen clearly from Fig. 3 that appreciable change is observed when the reaction temperature is increased from 100 to 120°C especially at the beginning of the reaction. The most dramatic change was observed in the first half hour where the

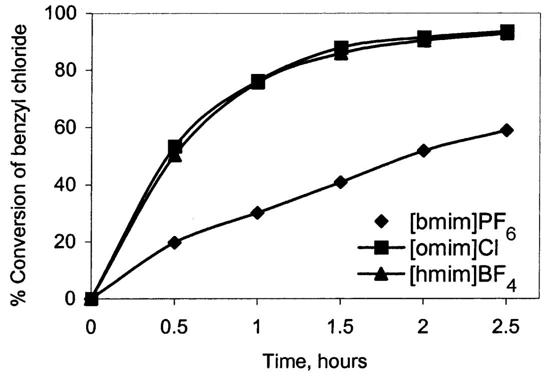

Figure 2. Conversion of benzyl chloride at 100°C.

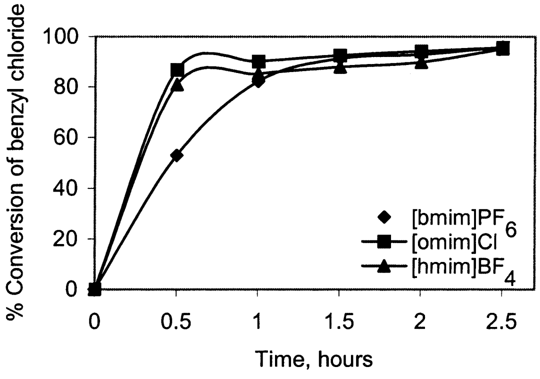

Figure 3. Conversion of benzyl chloride at 120°C.

Table 1. Solubility results of sodium salicylate at 100°C

	Solvent			
	[bmim]PF_6	[omim]Cl	[hmim]BF_4	[omim]BF_4
Solubility (g/2 mL)	0.1015	0.2170	0.6937	0.2798

conversion increased by ca. 30% when the reaction temperature was increased from 100 to 120°C (Figs. 2 and 3). After the reactions reached a certain conversion level (ca. 86–88%) the effect of temperature diminished and the reactions proceeded almost at a similar rate (Figs. 2 and 3) regardless of the reaction temperature. At this stage the bulk of the reactants had been consumed.

We then focused our attention on investigating the remaining ionic liquids employing the same reaction conditions used for the [hmim]BF_4 ionic liquid at 100°C (Fig. 2) and also at 120°C (Fig. 3). It was found that [bmim]PF_6 ionic liquid behaved in a similar fashion to that of [hmim]BF_4 at both reaction temperatures (100 and 120°C). The rate of formation of benzyl salicylate in [hmim]BF_4 at 120°C seemed to be slightly higher than that observed with [bmim]PF_6. It is important to note that benzyl salicylate was the sole product obtained in these reactions after analysis of the products by ^{1}H NMR and GC. Sampling of the product from the reaction using [omim]BF_4 ionic liquid was difficult due to the high viscosity of this ionic liquid. Only the conversion after 2.5 hours could be calculated and was found to be 92–95% at 120°C. These results show that the reaction rate is temperature dependant and most of the reaction actually takes place in the first half an hour.

The ionic liquids used in these reactions can be recycled and reused for subsequent reactions. The recycling process involved addition of H_2O (to water insoluble ionic liquids) to the used ionic liquid followed be separation of the layers. The water layer was decanted and the ionic liquid layer was concentrated under reduced pressure to remove traces of water and the resulting liquid was dried in vacuo. The reaction in the recycled [omim]Cl and [hmim]BF_4 ionic liquids at 120°C was investigated. The rate of the reaction as well as conversions were basically similar to those observed using fresh non-recycled samples of [omim]Cl and [hmim]BF_4 ionic liquids (Fig. 4). The products may also be removed from the ionic liquids by distillation or by using supercritical CO_2.[19]

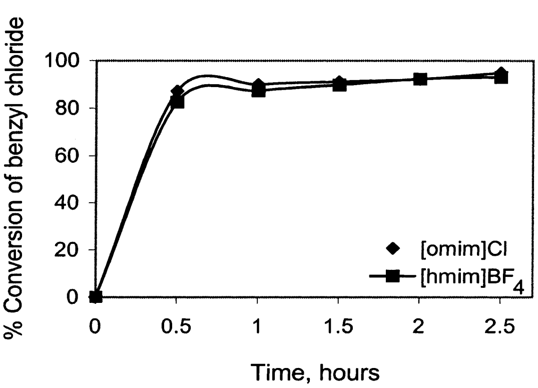

Figure 4. Conversion of benzyl chloride at 120°C in recycled [omim]Cl and [hmim]BF_4.

In conclusion, we have demonstrated that ionic liquids can be successfully used for nucleophilic displacement reactions involving organic substrates where one of the reactants is in the form of a salt. The reaction was found to proceed with high conversion (up to 96%) under relatively shorter reaction times and lower temperatures to give the desired benzyl salicylate as the sole product. The process is also significant from the viewpoint of pollution control where VOCs and PTC can be avoided while the ionic liquids can be recycled.

Acknowledgements

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17. *General procedure*: Benzyl chloride (0.11 g, 0.84 mmol) was added using a syringe to a preheated (100 or 120°C) and well-stirred solution of sodium salicylate (0.20 g, 1.25 mmol) in the ionic liquid (3 mL). Small samples (0.4 mL) of the reaction mixture were withdrawn using a syringe every 30 minutes. Each sample was diluted with light petroleum (5 mL) and the mixture stirred for 10 min. The light petroleum layer was analyzed by GC to determine the conversion of benzyl chloride.

18. ^{1}H NMR for benzyl salicylate: ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.40 (2H, s, Ar–CH_2), 6.85 (1H, t, $J=7.2$ Hz, Ar–H), 6.90 (1H, d, $J=8.3$ Hz, Ar–H), 7.35–7.89 (6H, 5×Ar–H and 1×Ar–H), 7.91 (1H, d, $J=1.4$ Hz, Ar–H), 10.77 (1H, s, OH).

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