Aromatic nitrations in ionic liquids: the importance of cation choice

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Aromatic substrates can be nitrated in high yields and with efficient use of the nitrating agent in ionic liquids, although a suitably inert ionic liquid cation must be used.

Ionic liquids continue to excite interest as alternative solvents for organic reactions.[1] One reaction of academic, synthetic and industrial interest is aromatic nitration.[2] Strategies for improving this notoriously "ungreen" reaction have included the use of clays[3,4] or zeolites[5–7] as solid supports, or perfluorocarbons[8] as solvents. Yet to date, ionic liquids have only been used in two studies of aromatic nitration. Laali and Gettwert used a range of nitrating agents in the nitration of mainly activated substrates[9] whilst Srinivasan and Rajagopal used iron nitrate in the nitration of phenols.[10] In this work we have achieved the nitration of a range of aromatic substrates including chlorobenzene and bromobenzene by using HNO_3–Ac_2O in an ionic liquid.

Ionic liquids have many useful physical properties, not least of which is their generally low miscibility with hydrocarbons. In this study, we deliberately used an excess of substrate to nitrating agent and then studied the extent of reaction under a range of conditions and the efficiency with which the nitrating agent is used. We used 4 different ionic liquids derived from 3 different cations, shown in Fig. 1 (where bmim = 1-butyl-3-methylimidazolium, bm_2im = 1-butyl-2,3-dimethylimidazolium and bmpy = 1-butyl-1-methylpyrrolidinium).†

The nitrating agents used are all (fairly) mild, being acyl nitrates formed *in situ* from the reaction of acetic (or trifluoroacetic) anhydride with the nitrate salt or nitric acid. The results of nitrations of toluene by these systems are shown in Table 1.

A range of nitrate salts were used in all of the ionic liquids to see whether the identity of the cation (even in the ionic liquid) might influence reaction times or selectivities, as often observed
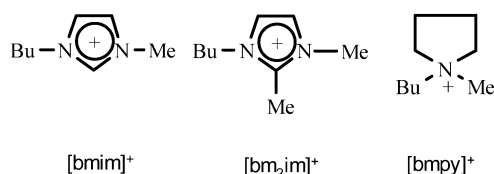

Fig. 1

Table 1 The nitration of toluene by acyl nitrates at 25 °C in ionic liquids and dichloromethane; yields after 1 h

Solvent	System	Yield (%)	Time/h	o-/p-
CH_2Cl_2	HNO_3–Ac_2O	35	1	1.4
[bmim][BF_4]	HNO_3–Ac_2O	35	1	1.5
[bmim][N(Tf)$_2$]	HNO_3–Ac_2O	42	24	1.5
[bm$_2$im][N(Tf)$_2$]	HNO_3–Ac_2O	63	1	1.4
[bmpy][N(Tf)$_2$]	HNO_3–Ac_2O	93	1	1.3
[bmpy][N(Tf)$_2$]	NH_4NO_3–TFAA	4	1	1.1
[bmpy][N(Tf)$_2$]	$Cu(NO_3)_2$–TFAA	18	1	1.3
[bmpy][N(Tf)$_2$]	$Fe(NO_3)_3$–TFAA	25	1	1.4
[bmpy][N(Tf)$_2$]	HNO_3–TFAA	32	1	1.0
[bmpy][N(Tf)$_2$]	HNO_3	<1	1	—

where the cation has been immobilised on clay or zeolite supports. Preliminary studies showed that when the salts were treated with acetic anhydride, no nitrotoluene was produced. When the system was modified by use of trifluoroacetic acid anhydride, nitrotolouenes were produced, but in low yield. These reactions were more effective in [bmpy][N(Tf)$_2$] than in any of ther other ionic liquids studied. However, the HNO_3–TFAA system gave very poor yield in the other ionic liquids and only a low yield in [bmpy][N(Tf)$_2$].

The reactions of the HNO_3–Ac_2O system with toluene in the ionic liquids generally gave low yields in the ionic liquids, and within 1 h the reaction had stopped. Further reaction did not occur if left, suggesting that the reagent had been entirely depleted. This is in contrast to the reaction in dichloromethane, in which the yield after 1 h was low, but which, if left, gave a near quantitative yield of nitrotoluenes. However, it is clear that the reaction in [bmpy][N(Tf)$_2$] does not fit that trend. Instead 93% of the nitric acid used has been converted into nitrotoluenes within 1 h.

In both acyl nitrate systems, the regioselectivity of nitration is fairly similar, although the reactions in [bmpy][N(Tf)$_2$] are apparently slightly more *p*- selective than the other systems.

Returning to the yields of nitrotoluenes obtained in the various ionic liquids, there is an interesting pattern. The lowest yield (i.e., the least efficient use of the nitrating agent) is obtained in the [bmim]$^+$ ionic liquids, with [bm$_2$im]$^+$ being somewhat better and [bmpy]$^+$ giving very high yields. This observation can be turned around, so that instead we consider the stability of the ionic liquid towards the nitrating agents. Within the literature, the nitration of bases is well known and Ridd has demonstrated the nitration of imidazolium salts.[11]

In order to study this, we put ionic liquid, nitric acid and acetic anhdride together in the same proportions as before, but without the substrate. The reaction was quenched and the product was analysed by FAB+ MS. Where the ionic liquid cation was [bmim]$^+$, peaks due to the addition of 45 or 90 mass units (1 or 2 nitro groups) were observed. The same observation was made where the cation was [bm$_2$im]$^+$. Thus the low efficiency of use of the nitrating agent is explained.

Having established that the best cation was [bmpy]$^+$, we started to study the range of substrates (activated and deactivated) that could be nitrated using the nitric acid–Ac_2O system. These reactions became homogeneous except where mesitylene was substrate. The results of these reactions are shown in Table 2. For comparison, the same reactions were performed in dichloromethane, which is an excellent solvent for aromatic nitrations.

In the nitration of activated substrates there was little difference between the ionic liquid and the molecular solvent. For example, in the nitration of mesitylene, high yields of nitroaromatic product were achieved in each system. In the nitration of anisole, the yields were similar, although the reaction was significantly more *p*- selective in [bmpy][N(Tf)$_2$] than in dichloromethane. The nitration of toluene showed near identical regioselectivity in the two solvents, but the yield was significantly higher in the ionic liquid.

The nitration of deactivated substrates shows greater impact of using the ionic liquid. As is shown by the table, under the

Table 2 Nitration of aromatic substrates at 25 °C; yields after 1 h

Substrate	[bmpy][N(Tf)$_2$]		Dichloromethane	
	Yield (%)	o-/p-	Yield (%)	o-/p-
Mesitylene	63	—	85	—
Toluene	91[a]	1.5	33[b]	1.4
Anisole	89	2.0	96	2.7
Bromobenzene	63	0.28	0	—
Chlorobenzene	50	0.28	0	—
Nitrobenzene	< 1[c]	—	< 1[c]	—

[a] Includes *ca.* 3% 3-nitrotoluene. [b] Includes *ca.* 1% 3-nitrotoluene. [c] 24 h, *m*-dinitrobenzene only.

reaction conditions employed in dichloromethane, the yield of bromonitrobenzenes is very low. Under the same conditions in [bmpy][N(Tf)$_2$], the yield is 63%. The result of chlorobenzene nitration is similar, with again a low yield in the molecular solvent and a yield of 50% in the ionic liquid.

The limit of the system appears to be reached in the nitration of nitrobenzene. The reaction was sluggish even in the ionic liquid, and a yield of less than 1 % was achieved, even after 24 h.

We must now address the solvent properties of the ionic liquid. There appear to be two possible explanations for the difference between the reaction in dichloromethane and in [bmpy][N(Tf)$_2$].

The first is that the reagent and the substrate are both charge neutral but reacting to form a charged intermediate. The fact that the outcomes of nucleophilic substitutions (using charged reagents) can be predicted using the Hughes–Ingold rules for ionic liquids has been discussed elsewhere.[12] The same rules show (in the case of neutrally charged nucleophiles), that the rate of reaction would be increased by using an ionic liquid. We could be observing a related effect in this work.

The HNO$_3$–Ac$_2$O system is generally thought to be a molecular nitrating agent, although it is proposed that this compound may be a nitronium ion carrier, dissociating before reaction to give the free nitronium ion as shown (eqn. 1) below.

$$AcONO_2 = AcO^- + NO_2^+ \qquad (1)$$

This allows a second possible explanation. In the ionic liquid, it would not be unreasonable to expect the complete dissociation of acetyl nitrate to nitronium acetate. This would be expected to be a more potent nitrating agent and thus give the higher yields or shorter reaction times that are generally observed.

There is an additional consideration, based on the properties of the ionic liquid cations and anions, and on the reagents and intermediates of the nitration. If we consider aromatic nitration by the nitronium ion, the rate determining step is the formation of the Wheland intermediate which, once formed, undergoes rapid deprotonation to give the nitroaromatic product. To enhance the rate of the reaction, the rate of formation of the Wheland intermediate must be increased. This is illustrated in Fig. 2. If the Wheland intermediate can interact more strongly with the ionic liquid than with the molecular solvent then we would expect an increase in yield after unit time.
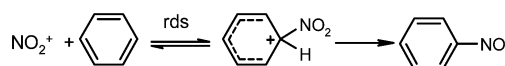
Fig. 2

Clearly, these proposals will need to be tested further, and this will best be achieved by a thorough kinetic and mechanistic study. This work is ongoing. This work has shown that, by using an ionic liquid, it is possible to achieve high yields of nitroaromatic products using HNO$_3$–Ac$_2$O, and even to nitrate compounds that might otherwise not react with this reagent. We have shown that the regioselectivity is no lower than in a molecular solvent, and that in fact we can achieve higher *p*-selectivity in some cases. We have also shown that it is necessary to chose a suitable ionic liquid, *i.e.*, one which is stable to nitration itself.

Notes and references

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