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Chemoselective reduction of aromatic nitro and azo compounds in ionic liquids using zinc and ammonium salts

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Abstract—Nitroarenes were chemoselectively reduced to the corresponding amines using zinc and aqueous ammonium salts in ionic liquids as a safe and recyclable reaction medium. Our results specify the effect of ammonium salts in the process; the combination of Zn/NH_4Cl in [bmim][PF_6] or Zn/HCO_2NH_4 in [bmim][BF_4] were the suitable conditions for the reduction of nitroarenes. Azobenzenes were also smoothly reduced to hydrazobenzenes with Zn/HCO_2NH_4 (aq.) in recyclable [bmim][BF_4] without any over reduction to the corresponding anilines.

The development of practical methodologies using convenient reaction media which are more environmentally benign, is one of the leading concerns of any chemical synthesis. In recent years, the use of ionic liquids as a recyclable reaction medium, to replace volatile organic solvents has received considerable attention.[1] Some of the important reactions which have been successfully executed in ionic liquids are transition metal-catalyzed olefin hydrogenation,[2] oxidation,[3] Diels–Alder[4] and Wittig[5] reactions, metal-mediated allylations,[6] etc. However, to date metal-mediated reductions in ionic liquids have received little attention.[7] We report herein a convenient and practically simple procedure for zinc-mediated chemoselective reduction of aromatic nitro compounds to amines using ammonium salts in imidazolium ionic liquids in 73–94% of yield. This, to our knowledge, is the first report of zinc-mediated reductions in ionic liquids.

The reduction of nitroarenes to the corresponding amines is an important transformation since many aromatic amines exhibit biological activities and find a multitude of industrial applications, being intermediates for the synthesis of dyes, pharmaceuticals, and agricultural chemicals. There are a variety of methods for the reduction of nitro compounds reported in the literature; the most popular being catalytic hydrogenation[8] and metal-mediated reduction.[9] Conventional reductions of nitroarenes using zinc metal require an organic solvent, corrosive reagents such as NH_3, conc. HCl, aq. NaOH, high temperatures, prolonged reaction times and moreover use substantial amounts of zinc metal. Although reduction in an aqueous medium employing 7.25 equiv. of Zn at 80°C was reported recently,[10] the advantage with ionic liquids is the high solubility of nitro substrates at ambient temperature, making it more general.

We probed the title reaction employing [bmim][PF_6] and [bmim][BF_4] as ionic liquids[11] and evaluated the suitability of various ammonium salts as additives. Our investigations revealed that for [bmim][PF_6], ammonium chloride is the additive of choice while [bmim][BF_4] gave good results in the presence of ammonium formate (Table 1). Use of 4 equiv. of Zn, 3 equiv. of ammonium salt in 10:1 ionic liquid and water gave a clean reaction to furnish aniline from nitrobenzene. Formation of side-products such as azoxy- and azo- (or hydrazobenzene, in some cases) resulted in changing ammonium salt, but were significantly suppressed in favor of aniline by increasing the amount of zinc to six equivalents (entries 3, 5, 7 and 8). Interestingly, the reaction did not proceed in the absence of either ammonium salt or water.

Mechanistically, reduction of a nitro group to amino is known[9b,c] to involve nitroso **6** and hydroxylamine **4** intermediates, which are considered to be responsible for the formation of azoxy- **2**, azo- **3** and hydrazobenzene **7** as depicted in Scheme 1. However, cleavage of the N–N bond of hydrazobenzene **7** to aniline **5**, reported to be a facile reaction,[9c,12] is ruled out under

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Keywords: ionic liquids; zinc; reduction; nitroarenes; anilines; azo compounds; hydrazobenzenes.

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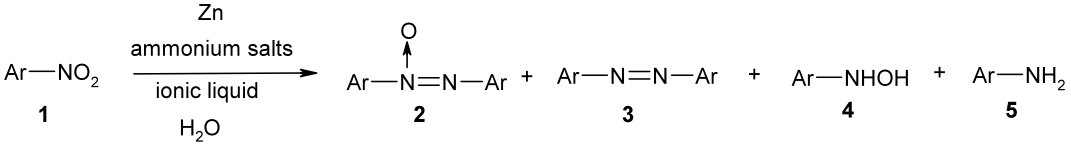
Table 1. Zinc mediated reduction of nitrobenzenes in ionic liquids using different ammonium salts[a]



Entry	Ammonium salts	Ionic liquid	Time (h)	Ratio[b]	Yield[c] (%)
1	NH_4Cl	[bmim][PF_6]	7	**5**	93
2	NH_4Cl	[bmim][PF_6]	2.5	**1**:**4**:**5** 35:39:26	89
3	HCO_2NH_4	[bmim]PF_6]	2.5	**2**:**3**:**5** (9:3:88)[d]	80
4	NH_4Cl	[bmim][PF_6]	7.5	**5**	94
5	HCO_2NH_4	[bmim][PF_6]	10	**2**:**3**:**5** (5:2:93)[d]	83
6	HCO_2NH_4	[bmim][BF_4]	10	**5**	89
7	NH_4Cl	[bmim][BF_4]	16	**2**:**3**:**5** 7:6:87[d]	81
8	$(NH_4)_2SO_4$	[bmim][BF_4]	19	**2**:**3**:**5** (23:5:72)[d]	80

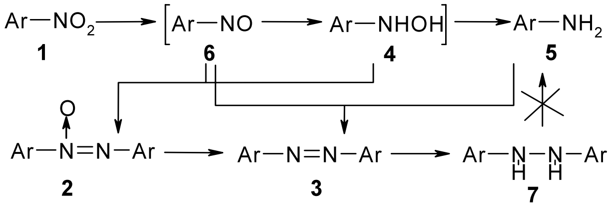
Entries 1–3, 6 (Ar=Ph), 4, 5, 7–8 (Ar=*p*-MePh).

[a] Zn (4 equiv.), 3 equiv. of NH_4Cl or HCO_2NH_4 or 1.5 equiv. of $(NH_4)_2SO_4$ by vigorously stirring in ionic liquids.

[b] The product distributions in all cases were determined by ^1H NMR integration at 400 MHz of the unpurified product mixtures obtained after ether extraction.

[c] Total yields of analytically pure products.

[d] 6 equiv. of Zn.



Scheme 1.

our reaction conditions as substantiated by selective reduction of azo- to hydrazobenzenes (vide infra). In accordance with the mechanistic proposal, we detected either hydroxylamine **4** or azoxy- **2**, azo- **3** and hydrazobenzene **7** by intercepting the reaction by giving insufficient time (entry 2) or by using incompatible additives (entries 3, 5, 7 and 8).

On the basis of the optimized conditions (Table 1), the reduction of nitroarenes were performed with Zn (4 equiv.)/NH_4Cl (3 equiv.) in 10:1 [bmim][PF_6]/water (Method A)[13] and Zn (4 equiv.)/HCO_2NH_4 (3 equiv.) in 10:1 [bmim][BF_4]/water (Method B)[14] under an inert atmosphere (Table 2). A number of aromatic nitro compounds were smoothly reduced to give excellent yields of the corresponding amines in either ionic solvent (Table 2). It was essential that the ionic liquid was thoroughly de-oxygenated under vacuum, to remove dissolved oxygen, before use and the reactions were found to be more sensitive in [bmim][BF_4] than [bmim][PF_6]. The reaction time as well as the yield of the reaction was perceptibly better in [bmim][PF_6]. In the course of the process, substituents such as chloro, iodo, fluoro, hydroxy or ketone were not affected.

The separation of products from ionic liquids is simple and involves, in most of the cases, direct extraction with ether. The crude product, so isolated, was of excellent purity for most purposes. The ionic liquids were easily recycled.[15] Thus, both [bmim][PF_6] and [bmim][BF_4] were reused to give the products without any decrease in yield or purity of the products (Table 3).

The ionic liquid [bmim][PF_6] was successfully reused for the successive reduction of three different nitrobenzenes to provide the corresponding amines in high yield (Table 4). No cross contamination of products was observed by 400 MHz ^1H NMR analysis.

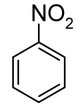
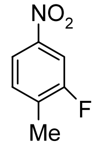
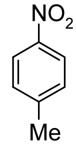
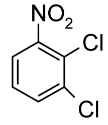
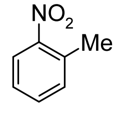
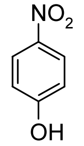
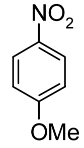
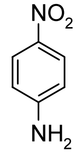
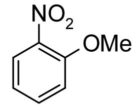
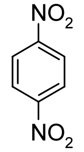
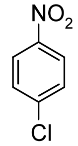
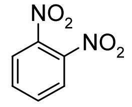
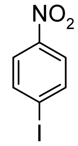
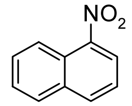
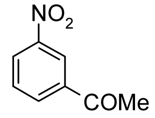
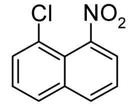
After achieving Zn-mediated efficient reduction of aromatic nitro compounds in ionic liquids, we employed the reaction system for the reduction of azobenzenes. The reduction of azobenzenes to hydrazobenzenes has been carried out using catalytic hydrogenation and a variety of other reduction methods.[16] However, most chemical methods require harsh reaction conditions, associated with poor yields, and lack of selectivity, since hydrazo derivatives undergo easy reductive cleavage to furnish amines. Furthermore, conventional Zn-mediated reduction requires carefully controlled conditions[17] to avoid benzidine rearrangement.

The azobenzene was treated with 4 equiv. of Zn, HCO_2NH_4 (3 equiv.) in 10:1 [bmim][BF_4] and water (entry 1, Table 5).[18] The reaction was completed within 25 minutes to furnish near quantitative yields of hydrazobenzenes. The reduction of azobenzene was found to be relatively slow in [bmim][PF_6], nevertheless hydrazobenzene was obtained in 96% yield (Table 5, entry 2). The reaction was generalized for other azobenzenes to give hydrazobenzenes in high yield (Table 5). The ionic liquid [bmim][BF_4] could be recycled effectively (Table 6).

In summary, we have demonstrated the zinc-mediated smooth reduction of nitroarenes to amines and azobenzenes to hydrazobenzenes in ionic liquids in the pres-

Table 2. Zinc-mediated reduction of aromatic nitro compounds to amines in ionic liquids

$$ArNO_2 \xrightarrow[\text{[B] Zn, } HCO_2NH_4\text{, [bmim][}BF_4\text{]:}H_2O\text{ (10:1)}]{\text{[A] Zn, } NH_4Cl\text{, [bmim][}PF_6\text{]:}H_2O\text{ (10:1)}} ArNH_2$$

Entry	Ar-NO₂	Method[a]	Time (h)	Yield (%)[b]	Entry	Ar-NO₂	Method[a]	Time (h)	Yield (%)[b]
1		A	7	93	9		A	7	93
		B	10	87			B	9	87
2		A	7.5	94	10		A	8	90
		B	9	92			B	10	89
3		A	16	85	11		A	8	77[c]
4		A	8	85	12		A	8	79[c]
		B	12	89			B	10	76[c]
5		A	9	83	13		A	10	78[c,d]
		B	11	81			B	11	81[c,d]
6		A	10	89	14		A	9	73[c,d]
							B	12	73[c,d]
7		A	7	81	15		A	8	82
		B	10	89			B	11	84
8		A	8	91	16		A	18	85
		B	12	90					

[a] Method A=Zn (4 equiv), NH_4Cl (3 equiv), [bmim][PF_6]:H_2O (10:1), rt; Method B=Zn (4 equiv.), HCO_2NH_4 (3 equiv) [bmim][BF_4]:H_2O (10:1), rt.

[b] Isolated yields of analytically pure amines.

[c] Extraction with diethyl ether was inefficient due to lower solubility of the product.

[d] 8 equiv of Zn, 6 equiv. of NH_4Cl or HCO_2NH_4 was used.

Table 3. Recycling of ionic liquids for the reduction of nitrobenzene to aniline

Cycle	1	2	3	4
Yield (%), using [bmim][PF_6] (Method A)	93	95	92	87
Yield (%), using [bmim][BF_4] (Method B)	87	93	86	

ence of suitable ammonium salts. The advantages include a safe reaction medium, high selectivity, easy product isolation and simple recovery of ionic liquids.

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Table 4. Recycling ionic liquids: crossed experiments

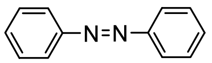
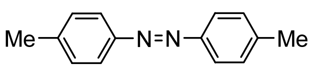
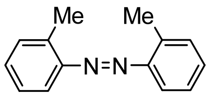
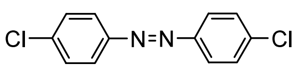
$$\text{Ar-NO}_2 \xrightarrow[\text{[bmim][PF}_6\text{]:H}_2\text{O (10:1)}]{\text{Zn, NH}_4\text{Cl}} \text{Ar-NH}_2$$

Substrate (Ar)	Cycle	Time (h)	Yield (%)[a]
Ph	1	7	91
(p-MeC_6H_4)	2	8	95
(p-ClC_6H_4)	3	7	89

[a] Isolated yields of pure amines. No contamination of products was observed for the experiments conducted.

Table 5. Reduction of azobenzene to hydrazobenzene[a]

$$\text{Ar—N=N—Ar} \xrightarrow[\text{bmimBF}_4\text{:H}_2\text{O (10:1), rt}]{\text{Zn, HCO}_2\text{NH}_4} \text{Ar—NH-NH-Ar}$$

Entry	Ar-N=N-Ar	Time	Yield[b] (%)
1		25 min	98
2		3 h[c]	96
3		35 min	94
4		30 min	83
5		1 h	89

[a] All reactions were performed using Zn (4 equiv), 3 equiv of HCO_2NH_4 by vigorously stirring in ionic liquids.

[b] Isolated yields of pure hydrazobenzenes.

[c] $[bmim][PF_6]:H_2O$ (10:1).

Table 6. Recycling of $[bmim][BF_4]$ for the reduction of azobenzene

Cycle	1	2	3	4
Yield (%)	98	94	100	96

Research (CSIR), New Delhi for financial assistance. J.D., R.K.G. and C.S. thank CSIR, U.G.C. for fellowships.

References

1. For recent reviews, see: (a) Welton, T. *Chem. Rev.* **1999**, *99*, 2071–2083; (b) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772–3789; (c) Sheldon, R. A. *Chem. Commun.* **2001**, 2399–2407; (d) Dupont, J.; de-Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667–3692.
2. (a) Steines, S.; Drieben-Holscher, B.; Wasserscheid, P. *J. Prakt. Chem.* **2000**, *342*, 348–354; (b) Dyson, P. J.; Ellis, D. J.; Parker, D. G.; Welton, T. *Chem. Commun.* **1999**, 25–26.
3. (a) Ansari, I. A.; Grée, R. *Org. Lett.* **2002**, *4*, 1507–1509; (b) Farmer, V.; Welton, T. *Green Chem.* **2002**, *4*, 97–102; (c) Ley, S. V.; Ramarao, C.; Smith, M. D. *Chem. Commun.* **2001**, 2278–2279.
4. (a) Earle, M. J.; McCormac, P. B.; Seddon, K. R. *Green Chem.* **1999**, 23–25; (b) Fischer, T.; Sethi, A.; Welton, T.; Woolf, J. *Tetahedron Lett.* **1999**, *40*, 793–796.
5. Boulaire, V. L.; Grée, R. *Chem. Commun.* **2000**, 2195–2196.
6. (a) Gordon, C. M.; Ritchie, C. *Green Chem.* **2002**, *4*, 124–128; (b) Law, M. C.; Wong, K. Y.; Chan, T. H. *Green Chem.* **2002**, *4*, 161–164.
7. For a singe report on Sm promoted reduction of aromatic nitro compounds in ionic liquid, see: Zheng, X. L.; Zhang, Y. M. *Chinese J. Chem.* **2002**, *20*, 925–928.
8. Tafesh, A. M.; Weiguny, J. *Chem. Rev.* **1996**, *96*, 2035–2052.
9. (a) Martin, E. L. *Org. Synth.* **1943**, *Coll. Vol. II*, 501–503; (b) Yu, C.; Liu, B.; Hu, L. *J. Org. Chem.* **2001**, *66*, 919–924; (c) Brady, E. D.; Clark, D. L.; Keogh, D. W.; Scott, B. L.; Watkin, J. G. *J. Am. Chem. Soc.* **2002**, *124*, 7007–7015; (d) Moody, C. J.; Pitts, M. R. *Synlett* **1998**, 1028.
10. Tsukinoki, T.; Tsuzuki, H. *Green Chem.* **2001**, *3*, 37–38.
11. 1-Butyl-3-methylimidazolium hexafluorophosphate, $[bmim][PF_6]$, and 1-butyl-3-methylimidazolium tetrafluoroborate, $[bmim][BF_4]$, were prepared following: (a) Guernik, S.; Wolfson, A.; Herskowitz, M.; Greenspoon, N.; Geresh, S. *Chem. Commun.* **2001**, 2314–2315, (b) Suarez, P. A. Z.; Dullius, J. E. L.; Einloft, S.; de-Souza, R. F., Dupont, J. *Polyhedron* **1996**, *15*, 1217–1219.
12. Gowda, S.; Abiraj, K.; Gowda, D. C. *Tetrahedron Lett.* **2002**, *43*, 1329–1331.
13. **General procedure for reduction of nitroarenes in $[bmim][PF_6]$ (Method A)**: Nitroarene (0.5 mmol), zinc metal (2 mmol), NH_4Cl (1.5 mmol) and water (0.1 ml) were added to $[bmim]PF_6$ (1 ml) and vigorously stirred at room temperature for the specified time under an argon atmosphere (Table 2). After consumption of the starting material, as monitored by TLC, Et_2O (3×5 ml) was added to the reaction mixture (a white suspension) with vigorous stirring for 5 min. The mixture was allowed to stand for 4 min and the clear supernatant liquid was decanted (through a filter paper). The combined ether extracts were concentrated to dryness and the crude product was found to be sufficiently pure (400 MHz ^1H NMR, 100 MHz ^{13}C NMR) in most of the cases. Where necessary, the crude product was purified by SiO_2 column chromatography. In cases (Table 2, entries 11–14), where the products were not fully extracted with diethyl ether, the reaction mixture was dissolved in CH_2Cl_2 (EtOAc can also be used in place of CH_2Cl_2), filtered, concentrated and then passed through a small silica gel column to afford the pure amines first, in the specified yields (Table 2), followed by the recovery of the ionic liquid (400 MHz ^1H NMR).

14. **General procedure for reduction of nitroarenes in [bmim][BF$_4$] (Method B)**: To a solution of nitroarene (0.5 mmol) in [bmim]BF$_4$ (1 ml), zinc metal (2 mmol), HCO_2NH_4 (1.5 mmol) and water (0.1 ml) were added and vigorously stirred at room temperature for the specified time under an argon atmosphere (Table 2). After consumption of the starting material, as monitored by TLC, Et_2O (3×5 ml) was added to the reaction mixture (a white suspension) with vigorous stirring for 5 min. The mixture was allowed to stand for 4 min and the clear supernatant liquid was decanted (through a filter paper). The combined ether extracts were concentrated to dryness and the crude product was found to be analytically pure (400 MHz ^{1}H NMR, 100 MHz ^{13}C NMR) in most of the cases. Where necessary, the crude product was purified by SiO_2 column chromatography.
15. **Recycling experiments in [bmim][PF$_6$]**: The ionic liquids were recovered as follows after each cycle: The residue containing ionic liquid was dissolved in minimum amount of CH_2Cl_2 (or EtOAc), filtered through a filter paper, dried over Na_2SO_4 and the solvent was removed on a rotary evaporator. The ionic liquid was further dried at 70°C and 0.1 mmHg for 4 h. The recovered ionic liquid was analyzed by ^{1}H NMR and there was none of the amine product in it. This reaction was repeated for three more cycles using the ionic liquid recovered from the previous run under identical conditions as for cycle 1. The results are listed under Table 3. Similarly, the ionic liquid [bmim][BF$_4$] was recycled and used for three runs (Table 3).
16. (a) Alberti, A.; Bedogni, N.; Benaglia, M.; Leardini, R.; Nanni, D.; Pedulli, G. F.; Tundo, A.; Zanardi, G. *J. Org. Chem.* **1992**, *57*, 607–613; (b) Park, K. K.; Han, S. Y. *Tetrahedron Lett.* **1996**, *37*, 6721–6724; (c) Patil, M. L.; Jnaneshwara, G. K.; Sabde, D. P.; Dongare, M. K.; Sudalai, A.; Deshpande, V. H. *Tetrahedron Lett.* **1997**, *38*, 2137–2140 and references cited therein.
17. (a) Carlin, R. B.; Forshey, W. O., Jr. *J. Am. Chem. Soc.* **1950**, *72*, 793–801; (b) Shine, H. J.; Trisler, J. C. *J. Am. Chem. Soc.* **1960**, *82*, 4054–4058.
18. **Reduction of azobenzene**: Azobenzene (0.5 mmol), zinc metal (2 mmol, 131 mg), HCO_2NH_4 (93 mg, 3 mmol) and water (0.1 ml) were added to [bmim][BF$_4$] (1 ml) and the mixture was vigorously stirred at rt for the specified time (consumption of the starting material, as monitored by TLC, Table 5). Ether (3×5 ml) was added to the reaction mixture, stirred for a few minutes and decanted. The combined ether extracts were concentrated to dryness to give hydrazobenzenes in the specified yields (Table 5). The residue was dissolved in CH_2Cl_2 (or EtOAc), filtered, concentrated and dried under vacuum at 70°C and 0.1 mmHg for 1 h and reused for three more runs under identical conditions (Table 6).