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Aromatic nitration with bismuth nitrate in ionic liquids and in molecular solvents: a comparative study of $Bi(NO_3)_3 \cdot 5H_2O/[bmim][PF_6]$ and $Bi(NO_3)_3 \cdot 5H_2O/1,2$ -DCE systems

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ABSTRACT

A suspension of bismuth nitrate pentahydrate (BN) in [bmim][PF₆] or [bmim][BF₄] imidazolium ionic liquid (IL) is an effective reagent for ring nitration of activated aromatics under mild conditions without the need for external promoters. Nitration can also be effected in 1,2-DCE, MeCN, or MeNO₂ without additives. Nitration of activated arenes (anisole, toluene, ethylbenzene, cumene, *p*-xylene, mesitylene, durene, and 1,3-dimethoxybenzene) is considerably faster (time to completion) in BN/[bmim][PF₆] relative to BN/ 1,2-DCE and there are also differences in isomer distributions (for anisole, toluene, and ethylbenzene). With introduction of strongly deactivating substituents (-CHO; -MeCO; $-NO_2$) the BN/IL system is no longer active but reactions still proceed with BN/1,2-DCE in reasonable yields. The ready availability and low cost of BN, simple operation, and absence of promoters, coupled to recycling and reuse of the IL, provide an attractive alternative to classical nitration methods for activated arenes. Switching from Bi(NO₃)₃:5H₂O/[bmim][PF₆] to Bi(NO₃)₃:5H₂O/1,2-DCE increases the scope of the substrates that can be nitrated.

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Bismuth nitrate pentahydrate BN is a widely used reagent in organic synthesis and is perhaps best known as a versatile oxidant.^{1,2} It has also been employed as a mild Lewis acid in various transformations and often under microwave irradiation.³ The utility of BN as reagent for *ipso* nitration of arylboronic acids was also recently reported.⁴ Despite wide synthetic application, the utility of BN as a nitrating agent for aromatics is relatively underexplored and possibly underappreciated. Earlier studies showed that BN is effective for nitration of phenolic compounds in conjunction with a solid acid, typically in organic solvents under microwave (MW) irradiation⁵ or by grinding.⁶ Earlier reports on nitration of representative arenes with BN indicated that it must be used in conjunction with other promoters. The following systems have been reported: silica/ sulfuric acid,⁷ silica/THF under MW,⁸ and montmorillonite/acetic anhydride.9 The BN/montmorillonite/THF system was used to nitrate pyrazoles.¹⁰

In previous studies from our laboratory BN was employed as a mild and efficient Lewis acid for generation of 'tamed' propargylic cations in ionic liquids ILs for propargylation of 1,3-carbonyl compounds and 4-hydroxycoumarin,^{11a} as well as indoles and carbazoles,^{11b} and for coupling with allylsilane.^{11c} In continuation of our earlier work on aromatic nitration in ILs,¹² we sought to explore the utility and scope of aromatic nitration with BN in ILs. BN can

be dissolved in imidazolium ILs and in ethylammonium nitrate (EAN) in catalytic amounts which allows its use as a Lewis acid under homogeneous/semi-homogeneous conditions,¹¹ but to employ it as a nitrating reagent requires that reactions are carried out under heterogeneous conditions. By using mesitylene as a representative substrate, control experiments were performed in ILs and in molecular solvents (Table 1). Quantitative nitration was

Table 1

Screening of $Bi(NO_3)_3 \cdot 5H_2O$ as nitrating agent in ILs and in molecular solvents

	-	Bi(NO ₃)₃ [·] 5H₂O 85 °C	NO ₂	-
Run	Equivalents of	IL and molecular	Time	Yield ^a
#	Bi(NO ₃) ₃ ·5H ₂ O	solvent	(h)	(%)
1	0.66	[bmim][PF ₆]	5.0	0
2	1.0	[bmim][PF ₆]	3.0	84
3	1.5	[bmim][PF ₆]	1.5	100
4	1.5	[bmim][BF ₄]	1.5	97
5	1.5	$[C_2H_5NH_3][NO_3]$	48	0
6	1.5	CH ₃ CN	24	75
7	1.5	1,2-DCE	24	96
8	1.5	CH ₃ NO ₂	24	94

^a Determined by GC–MS.



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Table 2				
Nitration	of arenes	promoted	by	Bi(NO ₃) ₃ ·5H ₂ O

Entry	Arene	Solvent	Nitro products ^a (%)			Time (h)	Yield ^a (%)
1	OMe		OMe NO ₂	OMe NO ₂	O ₂ N OMe		
		[bmim]PF ₆ 1,2-DCE	21 38	-	79 61	1.5 10	100 100
2			NO2	NO ₂	O ₂ N		
		[bmim]PF ₆ 1,2-DCE	59 48	2 2	39 50	1.5 23	100 100
3	Et		Et NO ₂	Et	O ₂ N		
		[bmim]PF ₆ 1,2-DCE	48 37	3 trace	48 62 ^b	1.5 45	99 100
4			NO ₂		O ₂ N		
		[bmim]PF ₆ 1,2-DCE	16	-	69 85 ^b	1.5 24	85 85
^a Determin ^b By NMR.	ned by GC-MS.						

Table 3Nitration of arenes promoted by $Bi(NO_3)_3 \cdot 5H_2O$

Entry	Arene	Solvent	Nitro products ^a (%)		Time (h)	Yield ^a (%)
1		[bmim]PF ₆ 1,2-DCE	NO ₂		1.5 23	100 100
2		[bmim]PF ₆ 1,2-DCE	O ₂ N 100 96	O_2N NO ₂ $\overline{4}$	1.5 24	100 100
3	XX	[bmim]PF ₆ 1,2-DCE	NO ₂ 87 79		3 16	87 79
4	OMe	[bmim]PF ₆ 1,2-DCE	OMe NO ₂ OMe	O ₂ N OMe OMe 68 98	1.5 15 1.5 15	80 98 80 98

^a Determined by GC-MS.

Table 4

Nitration of arenes promoted by $Bi(NO_3)_3{\cdot}5H_2O$

Entry	Arene	Solvent	Nitro products ^a (%)		Time (h)	Yield ^a (%)
1	CI	[bmim]PF ₆ 1,2-DCE	CI NO ₂ 48 39	$ \begin{array}{c} $	15 40	100 98
2	Br	[bmim]PF ₆ 1,2-DCE	Br NO ₂ 28 42	$ \begin{array}{c} & & & \\ & &$	15 70	100 100
3	Br	[bmim]PF ₆	Br NO ₂	Br OMe NO ₂	1.5 23	100 100
4	NC	[bmim]PF ₆ 1,2-DCE	NC NO ₂	O ₂ N - 4	70 70	0 95
5	O ₂ N	[bmim]PF ₆ 1,2-DCE	O ₂ N NO ₂ 		48 48	0 94
6	OHC	[bmim]PF ₆ 1,2-DCE	OHC NO ₂	O ₂ N - 30	40 40	0 85
7	OMe O	[bmim]PF ₆ 1,2-DCE	OMe NO ₂ 42	O ₂ N OMe	70 70	0 47

^a Determined by GC-MS.

^b By NMR.

Table 5

Recovery and reuse of (bmim) PF₆



^a Determined by GC–MS.

achieved in [bmim][PF₆] or [bmim][BF₄] by using 1.5 equiv of BN at 85 °C, whereas no reaction occurred in EAN. For comparison, the same reaction was performed in MeCN, 1,2-DCE, and MeNO₂ (all heterogeneous). With the observation of near quantitative nitration in 1,2-DCE and MeNO₂, the former was chosen for comparative study with the ILs.

In the next phase of the study nitration of anisole, toluene, ethylbenzene, and cumene was investigated in [bmim][PF₆] and in 1,2-DCE under the same set of conditions.^{13,14} As shown in Table 2 reactions proceeded much faster in the IL as compared to 1,2-DCE and were typically complete within 1.5 h, whereas considerably longer reaction times were needed to reach the same conversions in 1,2-DCE. Isomer distribution in both systems is strongly *ortho/ para* (with little or no *meta* isomer being observed), but there are some variations in regioselectivity, with higher *ortho/para* ratios in IL relative to 1,2-DCE (except in anisole).

A similar reactivity trend was observed in the nitration of *p*-xylene, mesitylene, tetramethylbenzene, and 1,3-dimethoxybenzene (Table 3), with reactions in IL proceeding faster relative to 1,2-DCE under the same set of conditions and with some variation in product distribution. For instance, formation of the 2-nitro isomer in nitration of 1,3-dimethoxybenzene was only observed in the IL and dinitro-mesitylene was only detected in 1,2-DCE.

To determine the scope and limitation of arene nitration with BN a variety of other substrates were subsequently examined in both media and the results are summarized in Table 4. Whereas chlorobenzene, bromobenzene, and *p*-bromoanisole were quantitatively nitrated in both systems, longer reaction times were needed with 1,2-DCE to reach the same conversions. As in previous examples, variations in isomer distributions were also observed. Lowering arene reactivity further by introducing more deactivating substituents (runs 4–7) led to no reaction with BN/IL but reactions proceeded in 1,2-DCE to eventually give the nitro derivatives in respectable yields.

Additional insights were obtained via the reactions of *p*-methoxybenzaldehyde and *p*-methoxyacetophenone (runs 6 and 7) where products of nitro-deformylation and nitro-deacetylation were observed indicative of *ipso* substitution.

Relative reactivity of mesitylene and durene ($K_{\text{Mes}}/K_{\text{Dur}}$) is commonly used as a good indicator to distinguish between a classical polar mechanism ($S_{\text{E}}Ar$) and the single electron transfer (SET) mechanism.¹⁵ A $K_{\text{Mes}}/K_{\text{Dur}}$ <1 is typically indicative of SET mechanism.^{15b,c} Competitive nitration of mesitylene/durene (1:1) was examined in the present study via GC monitoring. Analysis of an aliquot withdrawn after 30 min showed only unreacted mesitylene and nitrodurene. In an effort to slow down the nitration sufficiently to determine $K_{\text{Mes}}/K_{\text{Dur}}$, the competitive reaction was performed in 1,2-DCE. But again due to a large difference in relative reactivity substrate selectivity could not be measured. These observations appear consistent with a SET process. The large difference in relative reactivity in IL versus 1,2-DCE, and observation of minor products arising from *ipso* substitution are also compatible with a SET mechanism for arene nitration with BN.¹⁶

Although BN is a readily available low cost reagent, the ability to recover and reuse the IL provides an added cost saving incentive. Table 5 summarizes the results of recovery and reuse of the IL for three runs showing a gradual decrease in the conversions from quantitative to 86%.

In summary the ready availability and the low cost of BN, simple operation under mild conditions, and the absence of promoters, coupled to recycling and reuse of the IL provide an attractive, environmentally more acceptable, alternative to classical nitration methods for activated arenes. Switching from $Bi(NO_3)_3$ ·5H₂O/[bmim][PF₆] to $Bi(NO_3)_3$ ·5H₂O/1,2-DCE increases the scope of the

substrates that can be nitrated. Although many mechanistic questions remain, relative reactivity trends suggest a SET mechanism for these heterogeneous nitration reactions.

Acknowledgment

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- 13. General procedure for the nitration of aromatic compounds in ionic liquid: The ionic liquid (3.5–4.0 mL) was charged into an oven-dried Schlenk tube under a nitrogen atmosphere and Bi(NO₃)₃:5H₂O (1.5 mmOl) was added. The respective aromatic compound (1 mmOl) was then introduced into the Schlenk tube under a nitrogen atmosphere. The reaction mixture was magnetically stirred, initially at rt for about 10 min followed by stirring in a pre-heated oil bath at 80–85 °C, until completion (as monitored by GC–MS). Once the reaction was over, the contents were cooled to rt and extracted with EtOAc–Hexane (2:3 vol/ vol), until the final extraction did not show a spot corresponding to the starting material or to the product. The combined organic extracts were washed with 10% NaHCO₃ solution, dried with MgSO₄, and concentrated to give the crude product. Isomer distributions were determined by GC–MS, and/or by ¹H NMR.
- 14. General procedure for the nitration of aromatic compounds in 1,2-dichloroethane: A mixture of aromatic compound (1 mmol) and Bi(NO₃)₃·5H₂O (1.5 mmol) in 1,2-DCE (4 mL) was stirred at 80–85 °C. On completion (as monitored by GC– MS), the contents were cooled to rt and dissolved in DCM (5 mL). The combined organic layers were washed with 10% NaHCO₃ solution, dried over MgSO₄, and concentrated under reduced pressure to give the crude product. Isomer distributions were determined by GC–MS, and/or by ¹H NMR.
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- 16. Observations made in mesitylene/durene competitive nitration (absence of nitromesitylene) appear unusual considering their independent reactions with BN (see Table 2 entries 2–3) and imply that the formation of durene radical cation is somehow suppressing a SET process for mesitylene!