

# Regio-Selective Nitration of Phenols Using Phosphorus Based Ionic Liquids

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## ABSTRACT

Highly regio-selective mono nitration of phenols is accomplished using hydrated ferric nitrate as nitrating agent in phosphorous based ionic liquids in particular phosphonium ionic liquids viz, trihexyl (tetradecyl) phosphonium tetrafluoroborate (PIL-1) and trihexyl (tetradecyl) phosphonium chloride (PIL-2) as the solvents. Trihexyl (tetradecyl) phosphonium tetrafluoroborate (PIL-1) is found to be more suitable even though the nitration rate was low. The higher rate of nitration in case of trihexyl (tetradecyl) phosphonium chloride PIL-2 may be due to high acidity. In particular, excellent para selectivities were observed for the unsubstituted, ortho and meta substituted phenols. The quantitative conversion was observed during all reactions making this methodology attractive for synthetic and commercial utility.

**Keywords :** Phosphonium Ionic Liquids, Nitration, Phenols: Regio-Selective

## I. INTRODUCTION

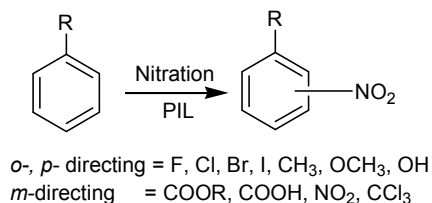
Nitration is a unit process<sup>1</sup> of great industrial importance generating commercially valuable intermediates and there is a great need for regio-selective pollution free processes. Usually, nitration reactions are not selective and are the cause of environmental concerns regarding the disposal of large excesses of mixed acids employed in these processes. Thus, the utility of the existing processes<sup>2,3</sup> are generally low. A variety of nitrating agents, including concentrated nitric acid, Yb(OTf)<sub>3</sub>, and Hf(OTf)<sub>4</sub> in conjunction with HNO<sub>3</sub>,<sup>4</sup> mixture of nitric acid with sulfuric acid, acetic anhydride, acetic acid, phosphoric acid, peroxy nitrite (ONOO-),<sup>5</sup> nitrogen oxides,<sup>6</sup> and several metal nitrates<sup>7</sup> have been employed.

Nitration of phenols lacks position selectivity for para isomer.<sup>8</sup> Various metal nitrates and supported metal nitrates are reported to effect para selectivity. The nitrating effect of various metal nitrates in the nitration of phenols was also studied for position selectivity of nitration.<sup>9</sup> Ferric nitrate in chloroform and chromium nitrate gave higher para selectivity. Ionic liquids like ([emim]OTf and [emim][CF<sub>3</sub>COO]-) were found to be

promising solvents in nitration of aromatics.<sup>10</sup> Good yields were observed for both activating and deactivating substrates. The use of 1,3-di-n-butylimidazolium tetrafluoroborate, [bbim]BF<sub>4</sub>, as a new room temperature ionic liquid in nitration of phenols with ferric nitrate at ambient conditions has been reported.<sup>11</sup> Nitration of various aromatic compounds using [bmim]BF<sub>4</sub>, [bm<sub>2</sub>im][N(Tf)<sub>2</sub>] and [bmpy][N(Tf)<sub>2</sub>] at 25°C were also studied using acyl nitrate generated in situ.<sup>12</sup> They observed that in activated system there was little difference between the ionic liquid and the molecular solvent. Dinitration of various aromatic compounds was reported using dilute nitric acid as nitrating agent in presence of 1-decyl-3-methylimidazolium trifluoromethanesulfonate and 1-butyl-3-methyl imidazolium trifluoromethane sulfonate.<sup>13</sup>

Recently, a new class of ionic liquids, known as phosphonium ionic liquids (PILs), where phosphorus acts as a cation, and differ from the imidazolium ionic liquids, has been introduced in organic reactions.<sup>14</sup> Phosphorous based ionic liquids are also found to be suitable solvents for electrophilic reactions such as sulfonation and nitration.<sup>15</sup>

This communication describes for the first time the regioselective mono nitration of phenols with hydrated ferric nitrate using trihexyl (tetradecyl) phosphoniumtetrafluoroborate (PIL-1) and trihexyl (tetradecyl) phosphonium chloride (PIL-2) as the room temperature ionic liquid as shown in the **Scheme 1**.



**Scheme 1.** Nitration of phenols with ferric nitrate in PILs

## II. Results and discussion

The results are summarized in Table 1 and 2. The reaction mixtures were homogeneous during nitration in both the ionic liquids and the reactions were monitored by TLC. All the reactions went to complete conversion at 30 °C for all substituted phenols in both PIL-1 and PIL-2 except for nitro and acetyl substituted phenols in PIL-1 where conversion was carried out at 60 °C. Addition of ferric nitrate in ionic liquids was mild exothermic process hence addition of ferric nitrate was done maintaining temperature at 30 °C. PIL-2 could be recovered by filtering the crude reaction product through silica gel.<sup>16</sup> It could be used at least 2 times for nitration of phenol. During nitration of *o*-carbomethoxyphenol and *p*-carbomethoxyphenol in PIL-2 the carbomethoxy group partially hydrolyzed to yield corresponding carboxylic acids in 5- 6% yield. This may be due to the presence of HCl in PIL-2. The nitration of phenols in PIL-2 required less hours than it required for reactions in PIL-1. However, it was more than that of [bbim][BF<sub>4</sub>].<sup>8a</sup>

**Table 1.** Nitration of phenols using trihexyl (tetradecyl) phosphoniumtetrafluoroborate (PIL1)

S. No.	Substrate	Time	Conversion	Yields %		
				Ortho	Para	Others
1	H	3.0 h	quantitative	18	75	7

2	<i>o</i> -Cl	2.5 h	quantitative	15	76	9
3	<i>o</i> -OCH <sub>3</sub>	4.0 h	quantitative	14	72	14
4	<i>o</i> -COCH <sub>3</sub>	3.0 h	>90%	---	82	18
5	<i>o</i> -NO <sub>2</sub>	6.0 h	>90%	---	83	17
6	<i>o</i> -COOCH <sub>3</sub>	5.0 h	quantitative	---	83	17
7	<i>m</i> -CH <sub>3</sub>	3.0 h	quantitative	11	73	16
8	<i>p</i> -Cl	3.0 h	quantitative	91	---	9
9	<i>p</i> -CH <sub>3</sub>	3.0 h	quantitative	86	---	14
10	<i>p</i> -COCH <sub>3</sub>	2.5 h	>90%	83	---	17
11	<i>p</i> -NO <sub>2</sub>	6.0 h	>90%	82	---	18
12	<i>p</i> -COOCH <sub>3</sub>	5.0 h	quantitative	82	---	18
13	<i>p</i> -OCH <sub>3</sub>	4.0 h	quantitative	79	---	19

As is evident from Table 1 and Table 2, though in both ionic liquids regioselectivity of ortho and para isomers were same, the ratios of *ortho*: *para* were different. In PIL-1, phenol, *ortho* and *meta* substituted phenols afforded the *p*-nitrophenols in very high selectivity and isolated yields were 72–83%. In PIL-2, in all reactions *ortho* and *meta* substituted phenols afforded 71-80% *p*-nitrophenols. In case of phenol, ortho selectivity was much more in PIL-2 as comparison with PIL-1. In both ionic liquids para substituted phenols afforded very high selectivity and isolated yields were 79–91% in PIL-1 and 82-97% in PIL-2. Regioselectivity of nitration of phenols was comparable with [bbim][BF<sub>4</sub>].<sup>8a</sup> All of the isolated nitrophenols are known compounds and were characterized by their spectral data.<sup>17</sup> Neither the *m*-isomer nor the dinitrated products could be detected. After recovering of the mono nitro products, the rest of the reaction mass could only be isolated as a mixture difficult to resolve and separate into individual components by chromatographic techniques for their identification. In all probability these constitute a complex mixture of polymeric/oxidized products designated as others in the **Tables 1** and **Table 2** to account for the mass balance.

**Table 2.** Nitration of phenols using trihexyl (tetradecyl) phosphonium chloride (PIL-2)

S. No	Substrate	Time	Conversion	Yields %		
				Ortho	Para	others
1	H	1.5 h	quantitative	42	58	---
2	<i>o</i> -Cl	2.5 h	quantitative	11.01	80	9
3	<i>o</i> -OCH <sub>3</sub>	5.0 h	quantitative	9	73	18
4	<i>o</i> -COCH <sub>3</sub>	6.0 h	quantitative	---	75	25
5	<i>o</i> -NO <sub>2</sub>	4.0 h	quantitative	---	78	22
6	<i>o</i> -COOCH <sub>3</sub>	4.0 h	quantitative	---	78	22
7	<i>m</i> -CH <sub>3</sub>	2.5 h	quantitative	14.3	71	14.7
8	<i>p</i> -Cl	2.5 h	quantitative	92	---	8
9	<i>p</i> -CH <sub>3</sub>	2.5 h	quantitative	97	---	3
10	<i>p</i> -COCH <sub>3</sub>	3.0 h	quantitative	87	---	13
11	<i>p</i> -NO <sub>2</sub>	4.0 h	quantitative	87	---	13
12	<i>p</i> -COOCH <sub>3</sub>	3.5 h	quantitative	82	---	18
13	<i>p</i> -OCH <sub>3</sub>	5.0 h	quantitative	82	---	18

#### Representative procedure for the preparation of nitrates:

To a solution of phenol (Entry 1) (1.92 g, 20 mmol) in trihexyl (tetradecyl) phosphoniumtetrafluoroborate (PIL-1) (5.0 g), Fe(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O (4.85 g, 12 mmol) was added in single lot and was stirred vigorously at 30 °C under nitrogen atmosphere. Reaction was monitored by TLC. After completion of reaction (absence of starting phenol), reaction mixture was extracted with n-hexane (3 X 20 ml). Organic layer was washed with brine (10 ml), dried over sodium sulphate and the solvent evaporated under reduced pressure. Crude product was chromatographed over silica gel to isolate first PIL in hexane and then *o*-nitrophenol (0.5 g, 18%) and *p*-nitrophenol (2.08 g, 74.8%). Melting points of all the nitrophenols are compared with melting points reported in literature.

### III. Conclusion

In conclusion, the mono nitration of phenols with ferric nitrate has been achieved with high regio-selectivities in excellent isolated yields using both PIL-1 and PIL-2 as solvent. Trihexyl (tetradecyl) phosphoniumtetrafluoroborate (PIL-1) was found to be more suitable even though the nitration rate was low. The higher rate of nitration in case of trihexyl (tetradecyl) phosphonium chloride (PIL-2) may be due to high acidity. In particular, excellent *para*-selectivities were observed for the unsubstituted, *o*- and *m*-substituted phenols. The quantitative conversion was observed during all reactions making this methodology attractive for synthetic and commercial utility.

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