An Efficient Method for the Nitration of Phenols with NaNO₂ in the Presence of 3-Methyl-1-Sulfonic Acid Imidazolium Chloride

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Abstract. Nitrophenols can be obtained in high yields via nitrosation-oxidation of phenols by 3-methyl-1-sulfonic acid imidazolium chloride ([Msi][Cl]) as a new Bronsted acidic ionic liquid and NaNO₂ at room temperature. In situ generation of HNO₂ and a radical-chain mechanism via the nitrous acid catalyzed pathway appear to be applicable to phenol nitration using this reagent system.

Keywords: 3-Methyl-1-sulfonic acid imidazolium chloride ([Msi][Cl]); Bronsted acidic ionic liquid; Nitrosation-oxidation; Nitration; Nitrophenols; Sodium nitrite (NaNO₂).

INTRODUCTION

Ambient temperature ionic liquids, especially those based on 1,3-dialkylimidazolium cations, have gained considerable interest as promising alternative green solvents in organic synthesis [1]. These ionic liquids have several interesting properties, such as excellent chemical and thermal stability, non-volatility, non-coordinating natures, safety, good solvating capability, a wide liquid range, and ease of recycling [1]. Furthermore, their hydrophobic/hydrophilicity can be tuned by appropriate modification of the cations or anions [1]. Therefore, wide applications in catalytic and non-catalytic reactions have been found for room temperature ionic liquids [2-6]. In addition, the synthesis of task-specific ionic liquids which have a functional group in their framework may expand the applications of ionic liquids in organic chemistry [7,8]. Among ionic liquids, acidic ones have been successfully used in many organic transformations [7-10]. In continuation of our previous studies on the applications of acidic reagents and catalysts in organic synthesis [11,12], more recently, we have synthesized ionic liquid 3-methyl-1-

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methods for the nitration of phenols are known, newer methods continue to attract attention for their experimental simplicity and effectiveness. In this work, we wish to use [Msim]Cl/NaNO₂ as a new and efficient reagent for the nitration of phenolic compounds to give the corresponding nitrated phenols at high yields and short reaction times.

RESULTS AND DISCUSSION

During the course of our studies on the utilization of NO⁺ in functional group transformations [28], we thought that phenol (1) could be converted to p-nitrosophenol (2), selectively, by a 3-methyl-1-sulfonic acid imidazolium chloride (3 eq)/NaNO₂ (1 eq) system (1 equivalent of [Msim]Cl is needed for the oxidation step). Moreover, phenol nitrosation is rapid and yields almost entirely the p-nitro isomer which can be readily converted to p-nitrophenol via a mild oxidation with HNO₃ [29] etc. (Figure 2, path a). Therefore, we decided to produce p-nitrophenol via the nitrosation-oxidation strategy in a one-pot reaction under mild conditions [30]. We selected [Msim]Cl as the acid source (a proton source for the in situ generation of HNO₃ and NO⁺ under mild conditions)/NaNO₂ system for the nitration of phenols (Figure 2, path b). In most reported methods for the nitration of phenols, NaNO₂ (1 eq) was needed for the second step; in situ generation of HNO₃ for the oxidation of p-nitrosophenol (Figure 2, path a). In contrast to the reported procedures in aqueous media [31], we observed that nitrosation and oxidation were occurred simultaneously using the [Msim]Cl/NaNO₂ system. Thus, in this reaction, mono-nitration was occurred, and p-nitrophenol (3) as well as α-nitrophenol (4) were obtained at 39% and 50%, respectively, after 25 min (Figure 2, path b).

A good range of 4-substituted phenols (5) was also subjected to the nitration reaction in the presence of 3-methyl-1-sulfonic acid imidazolium chloride and NaNO₂ at room temperature (Figure 3). The nitration reactions proceeded under mild conditions at room temperature and afforded the products at high yields and short reaction times (Figure 3 and Table 1). The presented nitration reactions were readily carried out by grinding the nitrating agents and phenols (1 or 5) in a mortar. The mono-nitrophenols were obtained by a simple workup.

A competitive reaction was also performed between phenols and anisole. It was observed that exclusive phenol nitration proceeded; anisole remaining intact in the reaction mixtures after 24 hours (Figure 4). Selective mono-nitration of 4,4'-dihydroxydiphenyl (5 k) was also achieved by controlling the stoichiometric of the reagents (Table 1, entry 12).

The 3-Methyl-1-sulfonic acid imidazolium chloride/sodium nitrite system is similar to N₂O₄ (N₂O₄ ↔ NO⁺NO⁻) in the case of generation of HNO₃ (eq 1) and NO⁺ that work as a nitrosating agent (Figure 5, eq 2). Thus, on the basis of our observations, the previously reported results concerning the applications of N₂O₄ [32] and metal nitrate dinitrogen tetroxide complexes [M(NO₃)₃-nN₂O₄] [27], and the reported mechanism for the nitration of phenols [33], the following reported nitrous acid catalyzed mechanism may be approved (Figure 5) [19, 34].

In another study, the [Msim]Cl/NaNO₂ system was examined for di-nitration of phenols. For this purpose, 6.2 eq of [Msim]Cl and 2 eq of NaNO₂ were reacted with 1 eq of p-methoxyphenol. In this reaction,
Table 1. Mono-nitration of phenols using [Msim]Cl/NaNO₂ system at room temperature.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)</th>
<th>M.p. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Found</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>3</td>
<td>25</td>
<td>39</td>
<td>111-114</td>
</tr>
<tr>
<td>2</td>
<td>5a</td>
<td>6a</td>
<td>15</td>
<td>94</td>
<td>72-73</td>
</tr>
<tr>
<td>3</td>
<td>5b</td>
<td>6b</td>
<td>15</td>
<td>96</td>
<td>89-90</td>
</tr>
<tr>
<td>4</td>
<td>5c</td>
<td>6c</td>
<td>15</td>
<td>95</td>
<td>87-89</td>
</tr>
<tr>
<td>5</td>
<td>5d</td>
<td>6d</td>
<td>20</td>
<td>93</td>
<td>139-142</td>
</tr>
<tr>
<td>6</td>
<td>5e</td>
<td>6e</td>
<td>25</td>
<td>87</td>
<td>61-64</td>
</tr>
<tr>
<td>7</td>
<td>5f</td>
<td>6f</td>
<td>25</td>
<td>91</td>
<td>139-141</td>
</tr>
<tr>
<td>8</td>
<td>5g</td>
<td>6g</td>
<td>20</td>
<td>93</td>
<td>52-54</td>
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<tr>
<td>9</td>
<td>5h</td>
<td>6h</td>
<td>35</td>
<td>90</td>
<td>121-123</td>
</tr>
<tr>
<td>10</td>
<td>5i</td>
<td>6i</td>
<td>25</td>
<td>91</td>
<td>60-62</td>
</tr>
<tr>
<td>11</td>
<td>5j</td>
<td>6j</td>
<td>30</td>
<td>89</td>
<td>177-180</td>
</tr>
<tr>
<td>12</td>
<td>5k</td>
<td>6k</td>
<td>40</td>
<td>78</td>
<td>181-183</td>
</tr>
<tr>
<td>13</td>
<td>1</td>
<td>3,4</td>
<td>24 h</td>
<td></td>
<td>–b</td>
</tr>
</tbody>
</table>

a: Isolated yields.

b: The reaction was not carried out in the absence of [Msim]Cl.

H⁺ + NO₂⁻ → HNO₂ (1)
HNO₂ + 2H⁺ → NO⁺ + H₂O (2)
2HNO₂ → N₂O₃ + H₂O (3)
N₂O₃ → NO + NO₂ (4)
2NO₂ → N₂O₄ (5)
2NO → N₂O₂ (6)
N₂O₂ + O₂ → N₂O₄ (7)

Figure 5. The proposed mechanism for the nitration of phenols.

mono- and di-nitrated products were obtained at 8% and 74% yields, respectively, within 50 min (Figure 6).

We also tried to use the [Msim]Cl/NaNO₂ system for the nitration of aniline; however, our attempt was not successful.

To compare the efficiency of the [Msim]Cl/NaNO₂ system for the nitration of phenols with other systems, we have tabulated the results of the mononitration of p-bromophenol under different reaction conditions in Table 2. As shown in Table 2, [Msim]Cl/NaNO₂ is superior to the previously reported reagent system.

**CONCLUSION**

In summary, we have introduced 3-methyl-1-sulfonic acid imidazolium chloride/NaNO₂ as an efficient and novel reagent for the efficient nitration of phenols. The promising points of this method are the simple experimental procedure, mild reaction conditions, safety, high yields, short reaction times and the minimization of chemical waste, as compared to their liquid phase counterparts.

**EXPERIMENTAL**

All Chemicals were purchased from the Merck or Fluka Chemical Company. The nitration products were characterized by comparison of their ¹H NMR, TLC and melting points with those in the authentic samples.
Melting points were recorded on a Stuart Scientific Apparatus SMP3 (UK) in open capillary tubes.

**Procedure for the Preparation of Ionic Liquid [Msim]Cl**
A round-bottomed flask (100 mL) was charged with 1-methylimidazole (0.410 g, 5 mmol) in dry CH₂Cl₂ (50 mL) and then chlorosulphonic acid (0.605 g, 5.2 mmol) was added dropwise over a period of 5 min at room temperature. After the addition was completed, the reaction mixture was stirred for 20 min, stood for 5 min, and the CH₂Cl₂ was decanted. The residue was washed with dry CH₂Cl₂ (3 × 50 mL) and dried under vacuum to give [Msim]Cl as a viscous colorless oil at 92% yield, 0.912 g [13].

**Typical Procedure for the Mono-Nitration of Phenol (1) Using [Msim]Cl/NaNO₂ System**
A mixture of compounds consisting of phenol (0.004 g, 1 mmol), [Msim]Cl (0.616 g, 3.1 mmol) and NaN₂O₂ (0.009 g, 1 mmol) was ground vigorously in a mortar at room temperature. After completion of the reaction, as monitored by TLC, the reaction mixture was extracted with EtOAc (2 × 15 mL) and the organic extracts were combined. Anhydrous NaN₂O₄ (0.5 g) was added to the extracts. After 3 min, the resulting mixture was filtered, and the solvent was evaporated to give the pure product. Notice: The reactions displayed in Figure 4, as well as entry 13 of Table 1, were performed in a 10 mL round-bottomed flask with magnetic stirring.

**Spectral Data of Ionic Liquid [Msim]Cl**
Viscous colorless oil: ¹H NMR (DMSO-d₆, 300 MHz): δ (ppm) 3.77 (s, 3H, CH₃), 7.46 (s, 1H), 7.51 (s, 1H), 8.54 (s, 1H), 13.96 (s, 1H); ¹³C NMR (DMSO-d₆, 75 MHz): δ (ppm) 36.5, 120.6, 124.2, 138.6; MS (m/z): 199 (M⁺+1), 198 (M⁺), 183 (M⁺-CH₃), 163 (M⁺-Cl), 82 (M⁺-CISO₂H), 67 (M⁺-CH₂CISO₂H); Anal. Calc. for C₆H₇ClN₂O₅S: C, 24.19; H, 3.55; N, 14.10. Found: C, 24.41; H, 3.69; N, 13.92.

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**REFERENCES**


**BIOGRAPHIES**

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