Research Article

Melamine Nitrate: A Novel and Efficient Reagent for Regioselective Nitration of Phenols

Yong-qiang Chen and Hong Jiang

Department of Chemistry, College of Science, Huazhong Agricultural University, Wuhan, Hubei 430070, China

Correspondence should be addressed to Hong Jiang, jianghong0066@126.com

Received 2 April 2011; Accepted 5 May 2011

1. Introduction

Nitration of aromatic compounds is one of the most important and widely studied reactions and industrial processes. The typical nitration procedure requires use of mixed acids such as concentrated nitric acid and sulfuric acid. Nitrophenols are important intermediates for the manufacture of drugs and pharmaceuticals [1]. But phenols are highly reactive; therefore the nitration of phenols by mixed acids is always associated with the formation of dinitro compounds, oxidized products, and unspecified resinous materials. So a lot of mild nitration processes for phenols have been developed to overcome these shortcomings. Especially, in recent years, various nitrate salts for phenols have been reported [2–10]. However, some of the nitrating reagents are poorly regioselective and uneconomical. Considering these concerns, there is still a good scope for research towards finding economic, mild reagents for regioselective nitration of phenols.

Melamine is a widely used fire retarder in polymers. The amino groups of melamine are stable to oxidation condition such as H₂O₂, in which it can form stable adduct with H₂O₂ [11, 12]. This inspired us to think that melamine may be stable in oxidative acid such as nitric acid. So in this paper we prepared the melamine nitric acid complex (MN) (Figure 1) and used it as nitrating reagent.

Herein we report this efficient and facile nitration procedure for phenols using MN (Scheme 1). The preparation of melaminium nitrate is simple by the direct reaction of melamine with nitric acid at room temperature.

2. Results and Discussions

Table 1 summarized the results of nitration of phenol by MN in different solvents such as CCl₄, CH₂Cl₂, and CHCl₃; the highest yield of 2-nitrophenol was isolated in acetone (Table 1, entry 1). So in the following reactions, acetone was used as solvent. Different other catalytic acids like, acetic acid, benzoic acid, and sulfuric acid were also tested but they either gave trace product (in acetic acid or benzoic acid) or very complicated products (in sulfuric acid); so p-toluene sulfonic acid was chosen as catalytic acid.

The results of nitration reactions of other phenolic compounds by using MN as nitrating reagent were summarized in Table 2.

Ortho-orientation relative to hydroxyl group and mono-nitration of phenolic compounds was observed. For example, 4-Methoxy-2-nitrophenol was isolated in 96% yield by the nitration of 4-methoxyphenol in acetone solution (Table 2, entries 2). In the cases of 4-methylphenol and 4-phenylphenol, ortho-nitro relative to the OH group products...
### Table 1: Nitration of phenol with different solvents by MN.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Entry</th>
<th>Solvent</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acetone</td>
<td>90</td>
<td>3</td>
<td>CH&lt;sub&gt;2&lt;/sub&gt;Cl&lt;sub&gt;2&lt;/sub&gt;</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>CCl&lt;sub&gt;4&lt;/sub&gt;</td>
<td>82</td>
<td>4</td>
<td>CHCl&lt;sub&gt;3&lt;/sub&gt;</td>
<td>77</td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated yields for 2-nitrophenol after silica gel chromatography.

### Table 2: Nitration of phenolic compounds with MN.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Product&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Time (h)</th>
<th>Temp&lt;sup&gt;c&lt;/sup&gt; (°C)</th>
<th>Yield&lt;sup&gt;d&lt;/sup&gt; (%)</th>
<th>Mp (lit) &lt;sup&gt;e&lt;/sup&gt; (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OH</td>
<td>OH NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>0.5</td>
<td>rt</td>
<td>90</td>
<td>44–45 (44–45)</td>
</tr>
<tr>
<td>2</td>
<td>OH OCH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>OH NO&lt;sub&gt;2&lt;/sub&gt; OCH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>1.5</td>
<td>Rt</td>
<td>96</td>
<td>79–80 (79–80)</td>
</tr>
<tr>
<td>3</td>
<td>OH CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>OH NO&lt;sub&gt;2&lt;/sub&gt; CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>2</td>
<td>rt</td>
<td>97</td>
<td>32–33 (34–36)</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td>1.5</td>
<td>rt</td>
<td>95</td>
<td>66–67 (66)</td>
</tr>
<tr>
<td>5</td>
<td>HO OH</td>
<td>HO OH O&lt;sub&gt;2&lt;/sub&gt;N</td>
<td>3</td>
<td>rt</td>
<td>89</td>
<td>82–83 (84)</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>HO OH NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>24</td>
<td>rt</td>
<td>No</td>
<td>124–125 (125–127)</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>HO NO&lt;sub&gt;2&lt;/sub&gt; OH</td>
<td>2</td>
<td>rt</td>
<td>93</td>
<td>101–102 (104–106)</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>CHO CHO OCH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>24</td>
<td>rt</td>
<td>No</td>
<td>172–173 (171)</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td></td>
<td>0.05</td>
<td>ref</td>
<td>90</td>
<td>113–114 (116)</td>
</tr>
</tbody>
</table>

<sup>a</sup> For compounds resorcinol, phloroglucinol, 2-hydroxybenzaldehyde, 4-hydroxy benzaldehyde, methyl 2-hydroxybenzoate, 4-hydroxybenzoic acid, their results were not listed in this table because they could not be nitrated with MN.

<sup>b</sup> All the products were characterized by <sup>1</sup>H NMR, MS and IR (see supplementary material available on line at doi: 10.1155/2011/753142).

<sup>c</sup> ref means reflux.

<sup>d</sup> Isolated yields after silica gel chromatography.

<sup>e</sup> Dictionary of Organic Compounds.
in excellent yields was also produced. Although the corresponding 3-nitro-1, 2-benzenediol was obtained in 89% yield by the nitration of catechol (Table 2, entry 5), under the same reaction conditions, the reactions of 1, 4-benzenediol, resorcinol, and phloroglucinol could not be carried out at room temperature. When 1, 4-benzenediol (Table 2, entry 9) was treated with MN under reflux for 24 h, it was oxidized to para-benzoquinone. When resorcinol or phloroglucinol was refluxed with MN, complicated tarry products were produced (not shown in Table 2). The unsuccessful nitration for resorcinol and phloroglucinol may be ascribed to the sterically crowded factor between 1,3-disubstituted hydroxy groups which is hardly to be attacked by nitronium ion. For entry 6, the conversion of 1-naphthol to 2-nitro-1-naphthol occurred within 0.5 h under reflux, whereas it did not work at room temperature. In contrast with 1-naphthol, 2-naphthol could react with MN much easier resulting in 1-nitro-2-naphthol at room temperature.

Though phenolic compounds bearing electron donating groups well behaved to afford the o-nitrophenoic compounds selectively, those with even moderately deactivating groups, such as 2-hydroxybenzaldehyde, 4-hydroxybenzaldehyde, methyl 2-hydroxybenzoate, and 4-hydroxybenzoic acid (all of them were not shown in Table 2) have no reaction at room temperature or under reflux by TLC monitor. However, the nitration of 3-methoxy-4-hydroxybenzaldehyde (entry 8, Table 2) was successful, which may be ascribed to the two activating groups, hydroxyl and...
methoxyl, attached to the benzene ring. One more advantage of this procedure is that no dinitrophenol product was formed by increasing the amount of MN.

A mechanism for the pronounced ortho-orientation nitration of phenols is postulated as Scheme 2. A hydrogen bond can be formed between phenolic compounds and MN. The hydrogen cation provided by p-toluenesulfonic acid attacked the hydroxyl group of nitric acid leading to the formation of nitronium cation. The nitronium cation will attack the ortho-position of hydroxyl group of phenol much easier from steric factor, resulting in the formation of the corresponding ortho-nitrophenols.

3. Conclusion

MN can serve as a high ortho-orientation nitrating agent for phenolic compounds bearing electron donating groups with p-toluenesulfonic acid as catalyst. The reagent in this reaction is a comparatively clean, safe, and facile to operate.

4. Experimental

All the chemicals were obtained from China Chemical Reagent Company. All products are known compounds and were characterized by m.p., IR, 1H NMR, and GC/MS. Melting points were determined on an RY-2 melting apparatus and are uncorrected. 1H NMR data were acquired on a Bruker AV 400 MHz CDCl3, or DMSO-d6 was used as solvent using TMS as an internal standard. IR spectra were recorded on an Avatar 330 infrared spectrophotometer (KBr pellet); only the most significant absorption bands are reported (ν max, cm−1). MS is performed on a Saturn 2000 mass spectrometer. Thin-layer chromatography (TLC) was performed on silica gel F254 plates using a 254 nm UV lamp (model UVG-54) or/and iodine vapor to monitor the progress of reactions.

4.1. Preparation of MN. In a round-bottomed flask (250 mL) equipped with a mechanic stirrer, a suspension of melamine (3.1 g, 25 mmol) and 10 mL HNO3 (20%, 32 mmol) was stirred at 20°C for 2 h. Then the reaction mixture was transferred to a crystallizing dish for slow evaporation of water under a mild air flow. After 3 days, MN as a white solid was obtained.

4.2. General Procedure for the Nitrination of Phenols. In a typical nitrination procedure, to a stirring mixture of acetone (15 mL) and phenol (0.56 g, 6 mmol) at room temperature, MN (1.3 g, 7 mmol) and the catalytic amount of p-toluenesulfonic acid (0.06 g, 0.4 mmol) were added. The mixture was stirred at room temperature for appropriate time. The progress of the reaction was monitored by TLC. At the end of the reaction, the mixture was filtered. Then, acetone was removed by evaporation to afford the crude product, which was chromatographed over silica gel to give the pure compound in high yield using hexane:ethyl acetate as eluents.

Similarly other phenolic compounds were nitrated under the similar conditions and their reaction times and yields are presented in Table 2. The compounds were confirmed by 1H NMR, MS, and IR spectrum.

Acknowledgment

The authors thank the National Natural Science Foundation of China (Grant no. 20702016).

References
