

## Facile and Efficient Selective Mono-nitration of Phenols under Solvent-free Conditions

S. Beheshti, E. Kianmehr,\* M. Yahyaee, and K. Tabatabai

School of Chemistry, University College of Science, University of Tehran, Tehran, Iran. \*E-mail: kianmehr@khayam.ut.ac.ir  
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Nitration of aromatic compounds is one of the most widely studied organic reactions.<sup>1</sup> Since the nitrated products are important intermediates for pharmaceuticals, perfumes, plastics and dyes; nitration of aromatic compounds is an industrially consequential reaction. Classical nitration method usually requires the use of an excess of nitric acid and the assistance of strong acids such as concentrated sulfuric acid. Usually nitration reactions are not selective and suffer from low regioselectivity<sup>2</sup> and over nitration<sup>2a,d</sup> and are the cause of environmental concerns regarding the disposal of the large excess of mixed acids and generating nitrogen oxide (NO<sub>x</sub>) fumes and leading to excess acid waste and added expense. The problems associated with mixed nitric and sulfuric acids have prompted the research for alternative methods. In literature a number of different methods including concentrated nitric acid, solid acids,<sup>3</sup> acid anhydrides or triflates,<sup>4</sup> peroxy nitrite,<sup>5</sup> metal nitrates,<sup>6,3c</sup> nitrogen oxides<sup>7,2a,b,d</sup> and organic nitrating agents<sup>8</sup> have been utilized by many investigators. Some of them are based on homogeneous procedure in solution while others depend upon reactions involving heterogeneous conditions. In some cases the reaction has been performed in expensive media such as ionic liquids.<sup>9</sup> Microwave assisted synthesis of unusual dinitro phytochemicals has also been studied recently.<sup>10</sup>

Nitration of phenols, among the aromatic compounds, also has been studied using various nitrating agents under different conditions.<sup>11</sup> However, there is a great need for new nitration methods that can overcome the problems such as low yield, low selectivity and over nitration.

Solvent free condition for organic synthesis has been of great interest in recent years.<sup>12</sup> Elimination of volatile organic solvents in organic synthesis is the most important goal in green chemistry. Solvent free organic reactions make synthesis simpler, save energy and prevent solvent wastes hazards and toxicity. A new nitration process of phenols in the solid state has been the focus of the present work.

Conversions of various phenolic compounds are shown in Table 1 and compared with previous results in solution. Different solid acids like, *p*-TsOH, mono and trichloro acetic acid and heteropolyacids were used that they either didn't work in the reaction condition or gave a very poor yield of nitrated products. We found that oxalic acid could be considered as the best solid acid for nitration of phenols in the solid state. In most of the abovementioned cases,

complete conversion of the starting phenols was achieved under the reaction condition. As it can be seen in Table 1, complete conversion to mononitrophenols occurred by microwave irradiation for a few minutes (entries 4, 6, 7, 9, 10). The reaction was studied at different molar ratio of reagents. Except entries 6 and 8, in which the use of equimolar reagents to phenols caused a decrease in the regioselectivity together with the formation of some byproducts, the reaction was completed by the use of 1.2 to 1.4 eq. of reagents. Phenol was nitrated to mononitrophenols, and the ratio of *ortho*-nitrophenol : *para*-nitrophenol was found to be 4 : 6, also a very small amount of *para*-benzoquinone was detected. *Para*-hydroquinone (entry 2) was oxidized to *para*-benzoquinone, exclusively. 2-Iodophenol and 3-Chlorophenol were nitrated to mononitrophenols with the 1 : 4 ratio of *ortho*-nitrated : *para*-nitrated product.

In conclusion, we have demonstrated that (CO<sub>2</sub>H)<sub>2</sub>/NaNO<sub>3</sub> is an extremely powerful and efficient nitrating agent for phenols under simple condition. Other development of this reagent in the solid state processes is in progress.

### Experimental Section

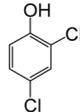
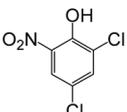
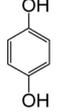
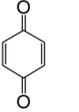
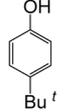
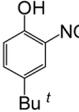
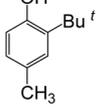
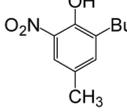
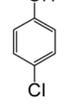
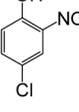
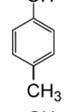
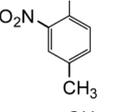
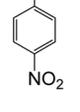
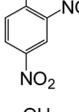
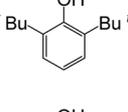
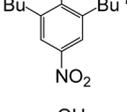
**General Procedure.** Nitrating agents are added to phenols in an agate mortar and are thoroughly ground for a few minutes at room temperature. The color of the reaction mixture changes to yellow or orange which is dependent on the used phenol. For cases that the reaction was not completed at the reaction condition at room temperature the reaction was followed by microwave radiation for a few minutes. Workup of the reaction is simply done by extracting with dichloromethane and evaporating the solvent under reduced pressure.

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**Table 1.** Nitration of phenols with (CO<sub>2</sub>H)<sub>2</sub>/NaNO<sub>3</sub> under solvent-free conditions at room temperature

| Entry | Phenol  | (CO <sub>2</sub> H) <sub>2</sub> /NaNO <sub>3</sub> | Time (Min.)     | Microwave (Min.) | Conversion (%) | Yield (%) | Product (s) <sup>a</sup>  | ref. <sup>c</sup>   |
|-------|---|---|-----------------|------------------|----------------|-----------|---|---|
| 1     |    | 1.2/1.2   | 5               | -                | 99             | 94        |    | 13 <sup>d</sup>   |
| 2     |    | 1.2/1.2   | 30              | -                | 98             | 94        |    |   |
| 3     |    | 1.2/1.2   | 10              | -                | 98             | 92        |    | 14, 15 <sup>e</sup>   |
| 4     |    | 1.4/1.4   | 5               | 1                | 87             | 81        |    |   |
| 5     |   | 1.4/1.4   | 1               | -                | 75             | 68        |   | 14, 15, 16 <sup>f</sup>   |
| 6     |  | 0.6/1.3   | 3               | 2                | 84             | 14, 59    |     |   |
| 7     |  | 1.2/1.2   | 30              | 2                | 92             | 17, 68    |     | 17 <sup>g</sup>   |
| 8     |  | 0.6/1.2   | 10              | -                | 71             | 63        |    |   |
| 9     |  | 1.4/1.4   | 10              | 3                | 91             | 86        |    | 14, 16 <sup>h</sup>   |
| 10    |  | 1.2/1.2   | 20              | 2                | 93             | 85        |    |   |
| 11    |  | 1.2/1.2   | 15 <sup>b</sup> | -                | 81             | 28, 42, 4 |    | 13 <sup>i</sup> , 14 <sup>j</sup> , 16 <sup>k</sup> , 18 <sup>l</sup> |

<sup>a</sup>All the nitro compounds are known compounds and characterized by physical and spectral analysis. <sup>b</sup>Reaction was done at 40 °C. <sup>c</sup>Some known results of nitration of phenol derivatives in solution. <sup>d</sup>5 min. and 94% yield. <sup>e</sup>92% and 2 hours. <sup>f</sup>78% and 1 hour. <sup>g</sup>91% and 6 hours. <sup>h</sup>78% and 3 hours. <sup>i</sup>35% (ortho) and 58% (para). <sup>j</sup>51% (ortho) and 47% (para). <sup>k</sup>32% (ortho) and 9% (para). <sup>l</sup>42% (ortho) and 46% (para)

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