A Novel Iodination of Aromatic Rings Using Iodine/Metallic Nitrate

Mehman S. Yusubov**, Victor D. Filimonov**, Ho-Whan Jin, and Ki-Whan Chi*

Department of Chemistry, University of Ulsan, Ulsan 680-749, Korea

1Department of Organic Chemistry, Tomsk Polytechnical University, Tomsk 634004, Russia

1Department of Chemistry, Siberian Medical University, Tomsk 634050, Russia

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Aryl iodides have been used as pivotal precursors in organic synthesis and prepared by various reactions with iodine or other iodine compounds (KI, ICl, IF, N-iodoanilides). However, most of the reactions require the presence of Lewis acid, base or oxidizer to produce a reactive iodine species. Also, drastic conditions such as a strong acidic medium or a strong oxidizer in stoichiometric amounts have been used in many cases for the effective iodination of an aromatic ring.

In this paper, we would like to report a new and convenient synthetic method for the iodination of an aromatic ring using I₂ and nitrate. To a solution of anisole (3 mmol) and I₂ (1.7 mmol) in acetic acid (10 mL) was added sodium nitrate (0.3 mmol) at room temperature. The reaction mixture in a condenser-attached flask was heated at 85 °C for 6 hrs under a deoxygenated argon atmosphere. During the reaction, three additional portions of sodium nitrate (3 × 0.3 mmol) were added respectively at each first every hour. The resulting mixture was treated with 10% aqueous NaHSO₃ solution (20 mL) and extracted with ether (3 × 30 mL). The organic extracts were washed with brine (20 mL) and dried with Na₂SO₄. Evaporation of solvents in vacuo gave the crude iodination product. The crude product was purified by flash chromatography (hexane/benzene) with silica gel to afford 4-idoanisole in 92% yield.

By this new method, various aromatic rings with an electron-donating group can be successfully iodinated in good yield in the absence of strong acid (Table 1). It is quite peculiar that neither a strong acid nor acetic anhydride is necessary for the iodination. And the reaction needs only cheap and readily available chemicals. Moreover, the directional selectivity of iodination is excellent to produce para-idoaromatic ring except for toluene.

A change of the counter-cations of nitrate (NaNO₃, KNO₃, or Ca(NO₃)₂) makes little effect on the result of iodination. Thus, it is apparent that I₂ is activated by the action of NO₃⁻ not by any metallic cations.

The novel iodination with I₂/NO₃⁻ performed under a deoxygenated argon atmosphere reveals that 0.4 equivalent of nitrate is the least amount required for the quantitative iodination of anisole (Figure 1). On the other hand, 0.2 equivalent or less of nitrate is enough for the complete iodination if oxygen is bubbled through the reaction mixture. These results can be explained by the following equation which shows the formation of 3 equivalents of reactive I⁺ based on the quantity of nitrate used.

\[ \text{NO}_3^- + 4\text{H}^+ + 1.5\text{I}_2 \rightleftharpoons 3\text{I}^+ + \text{NO} + 2\text{H}_2\text{O} \]

In the presence of oxygen, however, a tentative intermediate NO might be further oxidized to NO⁺ followed by the oxidation of another I₂ to I⁺.

The fact that weakly-activated substrates (toluene, xylene) necessitate an elevated reaction temperature and more quantity of nitrate than 0.4 equivalent for a satisfactory iodination might be attributed to a relatively low reactivity of the substrates with I⁺ and partial loss of NO, oxidizing

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Table 1. Iodination of Aromatic Rings with I₂/NO₃⁻

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Nitrate</th>
<th>mmol of Nitrate</th>
<th>Temp. (°C)</th>
<th>Time (hr)</th>
<th>Yield (%)</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>anisole</td>
<td>NaNO₃</td>
<td>1.2</td>
<td>85</td>
<td>6</td>
<td>92</td>
<td>4-idoanisole</td>
</tr>
<tr>
<td>anisole</td>
<td>NaNO₃</td>
<td>0.6</td>
<td>85</td>
<td>4</td>
<td>92⁺</td>
<td>4-idoanisole</td>
</tr>
<tr>
<td>anisole</td>
<td>KNO₃</td>
<td>1.2</td>
<td>85</td>
<td>6</td>
<td>90</td>
<td>4-idoanisole</td>
</tr>
<tr>
<td>anisole</td>
<td>Ca(NO₃)₂·4H₂O</td>
<td>0.6</td>
<td>85</td>
<td>6</td>
<td>92</td>
<td>4-idoanisole</td>
</tr>
<tr>
<td>diphenylether</td>
<td>NaNO₃</td>
<td>2.4</td>
<td>85</td>
<td>21</td>
<td>70⁺</td>
<td>4,4'-diido-diphenylether</td>
</tr>
<tr>
<td>9-methylcarbazole</td>
<td>NaNO₃</td>
<td>0.6</td>
<td>30</td>
<td>21</td>
<td>87⁺</td>
<td>3,6-diido-9-methylcarbazole</td>
</tr>
<tr>
<td>9-benzylcarbazole</td>
<td>NaNO₃</td>
<td>0.6</td>
<td>30</td>
<td>10</td>
<td>88⁺</td>
<td>9-benzyl-3,6-diidoarbazole</td>
</tr>
<tr>
<td>aniline</td>
<td>Ca(NO₃)₂·4H₂O</td>
<td>0.6</td>
<td>65</td>
<td>30</td>
<td>37</td>
<td>4-idoacetanilide</td>
</tr>
<tr>
<td>acetanilide</td>
<td>Ca(NO₃)₂·4H₂O</td>
<td>0.6</td>
<td>105</td>
<td>24</td>
<td>47⁺</td>
<td>4-idoacetanilide</td>
</tr>
<tr>
<td>durene</td>
<td>NaNO₃</td>
<td>1.2</td>
<td>116</td>
<td>6</td>
<td>65</td>
<td>1-ido-2,3,5,6-tetramethylbenzene</td>
</tr>
<tr>
<td>mesitylène</td>
<td>NaNO₃</td>
<td>1.2</td>
<td>116</td>
<td>4</td>
<td>81</td>
<td>1-ido-2,4,6-trimethylbenzene</td>
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<tr>
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<td>1.2</td>
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<td>2</td>
<td>90</td>
<td>1-ido-2,4-dimethylbenzene</td>
</tr>
<tr>
<td>toluene</td>
<td>Ca(NO₃)₂·4H₂O</td>
<td>3.0</td>
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<td>2.5</td>
<td>61⁺</td>
<td>iodotoluenes</td>
</tr>
<tr>
<td>chlorobenzene</td>
<td>Ca(NO₃)₂·4H₂O</td>
<td>3.0</td>
<td>116</td>
<td>13</td>
<td>0</td>
<td>1-chloro-4-iodobenzene</td>
</tr>
</tbody>
</table>

⁺ 3.0 mmol of substrate, 1.7 mmol of I₂, nitrate and 10 mL of acetic acid were used under an argon atmosphere unless otherwise specified.
⁻ yields of pure and isolated products. All the structures were identified by IR, NMR data and melting points. Oxygen was bubbled through the reaction mixture. GC yield. para : ortho = 61 : 39.
Figure 1. Effect of NO$_3^-$ on the iodonation of anisole at 85 °C.

Researchers for their generous support (96-03-033054).

References

4. mp 174-175 °C (heptane/benzene); IR (KBr) 554 cm$^{-1}$;
5. 1H NMR (100 MHz, CDCl$_3$/TMS) δ 5.36 (s, 2H), 7.00-7.22 (m, 7H), 7.62 (d, 2H), 8.28 (s, 2H); C 44.82%, H 2.57%, N 2.75% for C$_{10}$H$_{12}$N$_2$, found C 44.68%, H 2.63%, N 2.46%.

\[
\begin{align*}
2\text{H}^+ + \text{NO}_3^- & \rightarrow \text{NO}_2^- + \text{H}_2\text{O} \\
\text{NO}_2^- + \text{I}_2 & \rightarrow \text{I}^- + \text{INO}_2 \\
\text{INO}_2 & \rightarrow \text{I}^- + \text{NO}_3^- \\
\text{NO}_3^- + 2\text{H}^+ + 0.5\text{I}_2 & \rightarrow \text{I}^- + \text{NO} + \text{H}_2\text{O} \\
\text{NO}_3^- + 4\text{H}^+ + 1.5\text{I}_2 & \rightarrow 3\text{I}^- + \text{NO} + 2\text{H}_2\text{O (net)}
\end{align*}
\]

However, it is not easy to rationalize every step of the tentative mechanism since I$^-$ has been known to exist as a kinetically independant species only in a strongly acidic condition.


Polystyrene-Pendant Hydrazinium Salt as a Novel Grafting-Onto Cationic Initiator

Moon-Suk Kim, Kyu-Wan Lee, Sang-Bong Lee*, and Jin-San Yoon

Advanced Chemical Technology Division, Korea Research Institute of Chemical Technology, Taejon 305-600, Korea
*Polymer Engineering Division, Inha University, Inchon 402-751, Korea
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The interest in graft copolymers arises in part from the protection exerted by the grafts on the backbone. This specific feature has led to a number of applications such as emulsifiers, surface-modifying agents, coating materials, and compatibilizers in polymer blends. Lots of grafting methods involving cationic polymerization might be summarized as