

A Novel Iodination of Aromatic Rings Using Iodine/Metallic Nitrate

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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-iodoamides).¹ However, most of the reactions require the presence of Lewis acid, base or oxidizer to produce a reactive iodine species.² 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.³

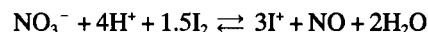
In this paper, we would like to report a new and convenient synthetic method for the iodination of an aromatic ring using I₂ and nitrate. To a solution of anisole (3 mmol) and I₂ (1.7 mmol) in acetic acid (10 mL) was added sodium nitrate (0.3 mmol) at room temperature. The reaction mixture in a condenser-attached 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 the 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-iodoanisole 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 pec-

uliar 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-iodoaromatic 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 equation⁵ which shows the formation of 3 equivalents of reactive I⁺ based on the quantity of nitrate used.



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⁺.^{3a}

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 loss⁵ of NO_x oxidizing

Table 1. Iodination of Aromatic Rings with I₂/NO₃^{-a}

Substrate	Nitrate	mmol of Nitrate	Temp. (°C)	Time (hr)	Yield ^b (%)	Product ^c
anisole	NaNO ₃	1.2	85	6	92	4-iodoanisole
anisole	NaNO ₃	0.6	85	4	92 ^d	4-iodoanisole
anisole	KNO ₃	1.2	85	6	90	4-iodoanisole
anisole	Ca(NO ₃) ₂ ·4H ₂ O	0.6	85	6	92	4-iodoanisole
anisole	—	0	85	6	0	4-iodoanisole
diphenylether	NaNO ₃	2.4	85	21	70 ^e	4,4'-diiodo-diphenylether
9-methylcarbazole	NaNO ₃	0.6	30	21	87 ^e	3,6-diiodo-9-methylcarbazole
9-benzylcarbazole	NaNO ₃	0.6	30	10	88 _c	9-benzyl-3,6-diiodocarbazole ⁴
aniline	Ca(NO ₃) ₂ ·4H ₂ O	0.6	65	30	37	4-iodoacetanilide
acetanilide	Ca(NO ₃) ₂ ·4H ₂ O	0.6	105	24	47 ^f	4-iodoacetanilide
durene	NaNO ₃	1.2	116	6	65	1-iodo-2,3,5,6-tetramethylbenzene
mesitylene	NaNO ₃	1.2	116	4	81	1-iodo-2,4,6-trimethylbenzene
m-xylene	Ca(NO ₃) ₂ ·4H ₂ O	1.2	116	2	90	1-iodo-2,4-dimethylbenzene
toluene	Ca(NO ₃) ₂ ·4H ₂ O	3.0	116	2.5	61 ^g	iodotoluenes
chlorobenzene	Ca(NO ₃) ₂ ·4H ₂ O	3.0	116	13	0	1-chloro-4-iodobenzene

^a 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.

^b yields of pure and isolated products. ^c All the structures were identified by IR, NMR data and melting points. ^d Oxygen was bubbled through the reaction mixture. ^e 3.3 mmol of I₂ were used. ^f GC yield. ^g para : ortho = 61 : 39.

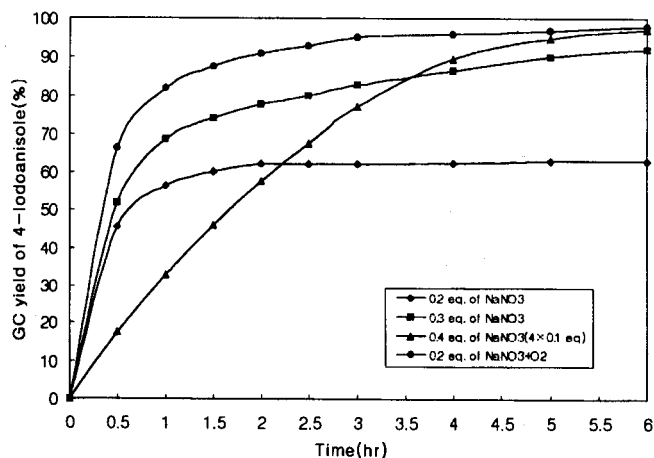


Figure 1. Effect of NO_3^- quantity on the iodination of anisole at 85 °C.

species at high temperature. In contrast, N-substituted carbazoles, strongly activated aromatic compounds, seem to undergo different reaction pathway since the iodination requires only 0.1 equivalent of nitrate in the absence of oxygen.

It is also interesting to note that the treatment of I_2/NO_3^- on phenylacetylene produces 1-iodo-2-nitro-1-phenylethene as a major product and no iodinated aromatic ring.⁶ This result sheds an important clue for the understanding of iodination mechanism⁷ and demonstrates the existence of INO_2 species⁸ during a reaction with I_2/NO_3^- .

In summary, an easy and novel synthetic method using I_2/NO_3^- is developed for the effective iodination of aromatic ring with an electron-donating group. This method does not require any strong acid or oxygen. In addition, under an oxygen atmosphere only 0.2 equivalent of nitrate is enough for the successful iodination.

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- mp 174-175 °C (heptane/benzene); IR (KBr) 554 cm^{-1} ; ^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 $\text{C}_{19}\text{H}_{13}\text{NI}_2$, found C 44.68%, H 2.63%, N 2.46%.
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$2\text{H}^+ + \text{NO}_3^-$	\rightleftharpoons	$\text{NO}_2^+ + \text{H}_2\text{O}$
$\text{NO}_2^+ + \text{I}_2$	\rightleftharpoons	$\text{I}^+ + \text{INO}_2$
INO_2	\rightleftharpoons	$\text{I}^+ + \text{NO}_2^-$
$\text{NO}_2^- + 2\text{H}^+ + 0.5\text{I}_2$	\rightleftharpoons	$\text{I}^+ + \text{NO} + \text{H}_2\text{O}$
$\text{NO}_3^- + 4\text{H}^+ + 1.5\text{I}_2$	\rightleftharpoons	$3\text{I}^+ + \text{NO} + 2\text{H}_2\text{O}$ (net)
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Polystyrene-Pendant Hydrazinium Salt as a Novel Grafting-Onto Cationic Initiator

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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 blend.¹ Lots of grafting methods involving cationic polymerization might be summarized as