Reduction of Nitroarenes to Aromatic Amines with Nanosized Activated Metallic Iron Powder in Water

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Abstract: A practical reduction of nitroarenes with nanosized activated metallic iron powder in water at 210 °C (near-critical water) has been developed. The reduction generates the corresponding aromatic amines in excellent yields.

Key words: nanosize, iron, nitroarenes, aromatic amines, reduction

Organic reactions carried out in water have received considerable attention in recent years.¹ Unfortunately most organic compounds are poorly soluble in water at ambient temperature. Nonetheless, the remarkable properties of water near its critical point ($T_c = 374$ °C, $P_c = 221$ bar) have promoted researchers to use it instead of organic solvents or ambient temperature water in organic synthesis. As temperature increases, water becomes more compatible as a medium for reaction of organics. For example, as temperature rises from 25 to 300 °C, the density of water decreases from 0.997 to 0.713 g/cm³, its dielectric constant (hydrogen bonding structure) decreases from 78.85 to 19.96, and its solubility parameter decreases from 23.4 to 14.5 (cal/cm³).^{1,2} Over the same temperature range, the dissociation constant of water, Kw increases by 3 orders of magnitude from ambient to near-critical conditions $(K_w = 10^{-11} \text{ at } 275 \text{ °C})$, providing hydronium and hydroxide ions that can act as modest acid or base in chemical reactions.² Although much of supercritical water research has been focused on the total oxidation of organic compounds and geochemical modeling,³ there are increasing numbers of papers which suggest that near-critical water is an excellent solvent for organic reactions because organic reactions in it offer many advantages over those in traditional organic solvents. For example, it is environmentally benign and separation of products from the reaction mixture is simplified.⁴

Aromatic amines, widely used as important intermediates in the synthesis of chemicals such as dyes, antioxidants, photographic, pharmaceutical and agricultural chemicals, can be obtained easily by the reduction of corresponding aromatic nitro compounds using catalytic hydrogenation⁵ and a variety of other reduction conditions. Many reductive agents have been recommended⁶ for this transformation and the most classic and practical reductants are zinc, tin, or iron in the presence of an acid.⁷ However, most of them lack the chemoselectivity over other functional groups and reduction of aromatic nitro compounds often yield a mixture of products.⁸ In addition, the reactions are performed in organic solvents or in the presence of acids, which pose waste-handling problems. Poliakoff reported a selective reduction of nitroarenes to anilines using metallic zinc in water at 250 °C (near-critical water) in high yields, but only 10% yield of aniline was observed from the reduction of nitrobenzene using iron powder under the reaction conditions.9 It is well known that the reactivity of metallic zinc ($E^0 Zn^{2+}/Zn = -0.763 V$) is superior to that of iron (E^0 Fe²⁺/Fe = -0.440 V), while metallic iron is cheap and commercially available. To perform the reduction of nitro compounds to amines with iron powder, the reaction should be carried out at higher temperature (>250 °C) owing to the low reactivity of iron metal.

Nanostructured materials have many magnetic, electronic, optical, biological, mechanical, and structural applications because of their unique properties.¹⁰ On account of their ultrahigh surface areas and controlled loose structure, nanosized palladium and nickel powders exhibit a very high catalytic activity in Heck reaction, Sonogashira reaction, Suzuki coupling, Stille coupling, Negishi reaction, Kumada reaction, hydrogenation of olefins, and amination reactions.¹¹ Most recently, copper, silver, gold, and palladium nanoparticles catalyzed reduction of aromatic nitro compounds to the corresponding amino derivatives have been also explored.^{11a,12} Here we wish to report the reduction of nitroarenes by using nanosized activated metallic iron powder in water at 210 °C (near-critical water) to the corresponding aromatic amines in good yields (Scheme 1).



Scheme 1

First of all, we investigated the reaction conditions for the reduction of nitroarenes with metallic iron powder in hot water. *p*-Nitrotoluene was chosen as a model compound for this study. The results are summarized in Table 1.

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 Table 1
 Reaction Conditions for the Reduction of p-Nitrotoluene with Iron Metal in Water^a

Entry	Iron Powder	Fe/p-Nitrotoluene	Temp (°C)	Time (h)	Yield (%) ^b
1	commercially available iron metal powder (ca. 325 mesh)	3:1	250	2	12
2	commercially available iron metal powder (ca. 325 mesh)	3:1	275	2	38
3	commercially available iron metal powder (ca. 325 mesh)	3:1	300	2	68
4	activated iron metal powder (ca. 325 mesh)	3:1	250	2	41
5	activated iron metal powder (ca. 325 mesh)	3:1	275	2	74
6	activated iron metal powder (ca. 325 mesh)	3:1	300	2	76
7	activated micron iron metal powder	3:1	250	2	70
8	activated micron iron metal powder	3:1	275	2	81
9	nanosized activated iron metal powder	3:1	275	2	84
10	nanosized activated iron metal powder	3:1	250	2	90
11	nanosized activated iron metal powder	3:1	230	2	93
12	nanosized activated iron metal powder	3:1	210	2	95
13	nanosized activated iron metal powder	3:1	190	2	89
14	nanosized activated iron metal powder	3:1	170	2	64
15	nanosized activated iron metal powder	1:1	210	2	51
16	nanosized activated iron metal powder	2:1	210	2	73
17	nanosized activated iron metal powder	4:1	210	2	96
18	nanosized activated iron metal powder	3:1	210	1	78
19	nanosized activated iron metal powder	3:1	210	3	95
20	nanosized activated iron metal powder	3:1	210	2	95°

^a Reaction conditions: *p*-nitrotoluene (1 mmol), tap water (10 mL) in a high T/p batch reactor system.

^b Isolated yields.

^c Distilled water (10 mL) instead of tap water (10 mL) was used.

As seen from Table 1, the particle size of metallic iron powder has a strong effect on the reduction of *p*-nitrotoluene in hot water. When the commercially available iron metal powder (ca. 325 mesh, 45 µm) was used for the reduction of *p*-nitrotoluene in water at 250 °C, only 12% yield of p-toluidine was obtained (entry 1, Table 1). However, activated micron iron metal powder was used, a good yield of *p*-toluidine was obtained (entry 7, Table 1) at 250 °C. As nanosized activated iron metal powder was used for this transformation, it is surprising that an excellent yield of *p*-toluidine was formed (entries 11-13, Table 1) even at lower reaction temperature (190–230 °C). The reaction temperature drops significantly as the particle size of iron powder used in the reduction is reduced to nanometer size. It may be due to the larger specific surface areas and higher activity of ultrafine iron particles. The reaction temperature also plays an important role in the reaction. It is evident that *p*-nitrotoluene could not be completely reduced to *p*-toluidine with commercially available iron metal powder (ca. 325 mesh, 45 μ m) in water at less than 275 °C (entry 2, Table 1), and only a moderate yield of *p*-toluidine was achieved at 300 °C because of the side reaction (entry 3, Table 1). The reactant could not be completely reduced to the corresponding amine with activated micron iron metal powder in water at less than 250 °C. Excellent yields of product were observed by using nanosized activated iron metal powder at temperature range of 190-250 °C, but the reaction was not complete at a lower temperature of 170 °C (entry 14, Table 1). The ratio of nanosized iron metal to p-nitrotoluene was also examined. The results showed that when the ratio of iron metal to p-nitrotoluene is less than 2:1, the reduction was not complete (entries 15 and 16, Table 1) and when the ratio equals or is more than 3:1, satisfactory results were obtained (entries 12 and 17, Table 1). The experiments also indicated that oxidized iron powder surface blocked the reduction (entry 1 vs entry 4, Table 1). We also investigated the effect of reaction time on the reduction of *p*-nitrotoluene and the results indicated that the reaction was not over when the reaction time is less than 2 hours (entry 18, Table 1). However, no increase of yield was observed when the reaction time was prolonged (entry 19, Table 1). It is noteworthy that tap water does not affect the effectiveness of the nanosized iron metal-mediated reduction of nitroarenes (entry 20 vs entry 12, Table 1). The optimized reaction conditions for the reduction of *p*-nitrotoluene with nanosized iron metal in water were found to be iron (3 equiv), *p*-nitrotoluene (1 equiv), H_2O (10 mL) at 210 °C for 2 hours.

A variety of nitroarenes were reduced to the corresponding anilines with nanosized activated metallic iron powder in water at 210 °C. The reaction was carried out simply by stirring substrates in water with nanosized activated metallic iron powder under nitrogen without any other organics and additive for 2 hours. The results are summarized in Table 2. Substituent effects were also investigated. The results revealed that the electronic characteristics of general electron-donating groups (such as MeO, Me) or general electron-withdrawing groups (such as MeCO, Cl, Br, CO_2Et) on the aromatic ring were relatively insensitive to the reduction. However, an iodo group on the aromatic ring underwent reductive elimination of the iodine in a competitive process, but the chloro and bromo groups remained unchanged. The reactivity of halogen atoms in the aromatic ring is I > Br > Cl, which is consistent with the expected reactivity. Aliphatic nitro compounds inhibited the reduction, as well as *trans*- β -nitrostyrene, where the nitro group is attached to the carbon-carbon double bond.

Entry	Nitro compounds	Amines	Yield (%) ^b
1	PhNO ₂	PhNH ₂	95
2	<i>p</i> -MeC ₆ H ₄ NO ₂	<i>p</i> -MeC ₆ H ₄ NH ₂	96
3	<i>m</i> -MeOC ₆ H ₄ NO ₂	m-MeOC ₆ H ₄ NH ₂	91
4	<i>m</i> -MeC ₆ H ₄ NO ₂	m-MeC ₆ H ₄ NH ₂	94
5	<i>p</i> -MeCOC ₆ H ₄ NO ₂	<i>p</i> -MeCOC ₆ H ₄ NH ₂	92
6	p-EtO ₂ CC ₆ H ₄ NO ₂	p-EtO ₂ CC ₆ H ₄ NH ₂	94
7	p-FC ₆ H ₄ NO ₂	p-FC ₆ H ₄ NH ₂	95
8	p-ClC ₆ H ₄ NO ₂	<i>p</i> -ClC ₆ H ₄ NH ₂	95
9	p-BrC ₆ H ₄ NO ₂	<i>p</i> -BrC ₆ H ₄ NH ₂	90
10	<i>m</i> -ClC ₆ H ₄ NO ₂	m-ClC ₆ H ₄ NH ₂	91
11	o-ClC ₆ H ₄ NO ₂	o-ClC ₆ H ₄ NH ₂	89
12	$p-IC_6H_4NO_2$	p-IC ₆ H ₄ NH ₂ PhNH ₂	52° 37°
13	α -C ₁₀ H ₇ NO ₂	α -C ₁₀ H ₇ NH ₂	95

^a Reaction conditions: nitro compound (1 mmol), nanosized activated metallic iron powder (3 mmol), tap water (10 mL) in a high T/p batch reactor system at 210 $^{\circ}$ C for 2 h.

^b Isolated yields.

^c Determined by GC and NMR analysis of the reaction mixture.

It is well known that Fe reacts with H_2O at high temperature to form H_2 and Fe_3O_4 . During our investigation, we found that hydrogen gas was liberated and a brown precipitate of Fe_3O_4 was formed when nanosized activated iron powder in water at 210 °C. Although a study of the detailed reaction mechanism has not been undertaken, it is suggested that the reaction process that takes place is the hydrogenation of the nitro group by H_2 rather than direct reduction of the nitro group by iron.⁹ A more detailed study about the reaction mechanism is in progress in our laboratory.

In conclusion, a reliable and practical procedure for the preparation of aromatic amines has been developed, which involves the use of nanosized activated metallic iron powder as reductive agent for the corresponding nitro compounds in water at 210 °C. The advantages of the method are its simple operation, and it is environmentally benign. The present method is a new way of using nanosized iron powder directly in organic synthesis.

Iron metal powder (ca. 325 mesh), activated micron iron metal (<10 micron) powder, and nanosized activated iron metal powder were purchased from Aldrich Chemical Co. Other reagents were received from commercial supply without purification prior to use. Activation of iron metal powder (ca. 325 mesh) was according to the general method. Products were purified by flash column chromatography.

Reduction of Nitroarenes with Nanosized Activated Iron Powder in Water; General Procedure

Nitroarene (1 mmol) and nanosized activated metallic iron powder (168 mg, 3 mmol) were added to a high temperature and pressure stainless steel autoclave reactor charged with tap water (10 mL) under N₂ with stirring. The reactor was heated at 210 °C for 2 h. After cooling, Et₂O (2 × 10 mL) was added to extract the products. After the organic layer was dried (Na₂SO₄), the solvents were evaporated under reduced pressure. The product was purified by flash chromatography to yield the amine (Table 2).

All the products are commercially available and their analytical and spectral data were in agreement with the corresponding authentic samples.

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