

# Reductive coupling of nitroarenes to hydrazoarenes with aluminium and potassium hydroxide in methanol

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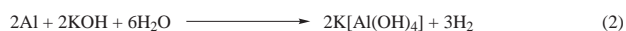
A simple and inexpensive procedure for the reductive coupling of nitroarenes to hydrazoarenes with aluminium and potassium hydroxide in methanol at ambient temperature is reported. The coupling is proposed to proceed by single electron transfer from aluminium.

The importance of nitroarenes in organic synthesis is based on the possibility of their modification and removal by a variety of reagents. Reduction of nitro compounds can be carried out by heterogeneous as well as homogeneous catalysts. Aromatic nitro compounds are reduced to amines by a variety of reagents.<sup>1</sup> The controlled reduction of nitroarenes to give coupled products namely, azoxyarenes, azoarenes and hydrazoarenes has been an interesting area of research synthetically and mechanistically. A variety of reagents have been used for the synthesis of azoxyarenes<sup>2</sup> and azoarenes.<sup>3</sup> Hydrazoarenes, on the other hand, have received little attention due to their tendency to undergo aerial oxidation. The reduction of nitroarenes to hydrazoarenes is usually achieved with Zn–NaOH,<sup>4a</sup> LAH–metal salts,<sup>4b</sup> Raney Ni–hydrazine hydrate,<sup>4c</sup> or electrochemical reduction.<sup>4d</sup> Recently samarium<sup>2f</sup> has been reported for the reduction of two nitroarenes to the corresponding hydrazoarenes.

Aluminium, though among the least expensive metals, has found limited applications in organic synthesis. Aluminium amalgam has been used to reduce aliphatic nitro compounds to the corresponding hydroxylamines<sup>5</sup> and amines.<sup>6</sup> Al–(NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> has been used for the conversion of nitroarenes to anilines<sup>7</sup> and Al–ZnO has been used for the reduction of nitrobenzene to hydrazobenzene in alkaline medium<sup>8</sup> though the procedure is quite tedious. Recently, we have reported the rapid pinacolization and reduction of aromatic carbonyls with aluminium and KOH in methanol at ambient temperature.<sup>9</sup> Encouraged by its synthetic utility, we decided to investigate the reactions of nitro compounds with aluminium and KOH in methanol.

## Results and discussion

In this paper, we report the reductive coupling of nitroarenes with aluminium and KOH in methanol at ambient temperature to give the corresponding hydrazoarenes. The hydrazoarenes are obtained in good yields by this convenient and inexpensive reagent in a fast reaction (15–55 min), compared to other commonly used procedures. In most cases, minor amounts of anilines were also obtained which could be removed easily by mild acidic wash. These reactions can be generalized as shown in eqn. (1). Our results are tabulated in Table 1.



Nitrobenzene did not react with aluminium in methanol in the absence of KOH or when KOH was replaced by NH<sub>4</sub>Cl, indicating the significance of an alkaline pH for the reaction.

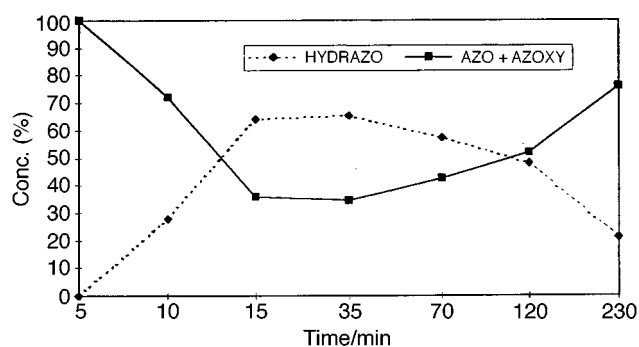


Fig. 1 Concentration of reductively coupled products vs. time.

The replacement of KOH by NaOH, however, led to only a very minor reaction with the recovery of most of the nitrobenzene. The role of solvent was also examined. Treatment of nitrobenzene with aluminium–KOH in water gave a very vigorous reaction, but only 10% (HPLC) of aniline was found in the reaction mixture besides the starting material. When the reaction was carried out in dry THF, only traces of the reduced products—azoxybenzene, azobenzene and aniline—were obtained with recovery of most of the nitrobenzene. Reactions in 1,4-dioxane–water (1:1, v/v) and ethanol (95%) produced a mixture of the various reduction products even after addition of several portions of Al–KOH. The reaction in dry methanol gave results identical to those obtained in commercial methanol. In summary, methanol is the solvent of choice for reductive coupling of nitroarenes to hydrazoarenes. Use of methanol was minimized to 10 mL g<sup>-1</sup> of Al, as dilution was observed to slow down the reaction. Reducing the KOH ratio (with respect to Al) also retarded the reductions.

Although most of the nitroarenes reacted completely within 5–10 min with 1:2:6 or higher molar ratio of substrate to aluminium to KOH, a mixture of the reduced products (*i.e.*, azo, azoxy and hydrazo derivatives) was obtained. The reaction of nitrobenzene and Al–KOH (molar ratio 1:2:6) was monitored by HPLC and the variation in hydrazobenzene concentration vs. time was plotted (Table 2, Fig. 1). The maximum reduction occurred in the first 15 min and aerial oxidation to azobenzene had set in after 35 min. Also the conversion to hydrazobenzene was only 65% using the above molar ratio. Therefore, higher molar ratios of aluminium and KOH added portionwise were employed to obtain high yield of hydrazoarenes.

In the reactions of 4-halonitrobenzenes, the chloro and bromo substituents were unaffected by this reagent whereas complete deiodination was observed in the reaction of 4-iodonitrobenzene (run 7, Table 1). In the reaction of 4-nitroanisole, a colourless reaction mixture was obtained which gave mainly the corresponding azoarene after work up, probably due to the

**Table 1** Reduction of nitroarenes with Al–KOH in methanol at ambient temperature

Run	Substrate	Molar ratio <sup>a</sup> substrate:Al	Time/ min	Yield (%) <sup>b</sup>			Mp (ArNHNHAr)/°C	
				ArNHNHAr	ArN=NAr	ArNH <sub>2</sub>	Obs. <sup>c</sup>	lit. <sup>13</sup>
1	Nitrobenzene	1:4	15	95	—	—	123–124	126–127
2	2-Nitrotoluene	1:6	25	83	—	2	153–155	158
3	4-Nitrotoluene	1:6	25	86	—	3	128–130	129.5–131
4	3-Nitrotoluene	1:4	15	95	—	2	36	37.5–38
5	4-Chloronitrobenzene	1:6	25	89	—	9	121–122	123–124
6	4-Bromonitrobenzene	1:10	45	86	—	—	126–128	130
7	4-Iodonitrobenzene	1:6	25	80 <sup>d</sup>	—	14 <sup>d</sup>	122–123	126–127
8	4-Nitrobiphenyl	1:10	55 <sup>e</sup>	65	—	31	163–165	167–169
9	4-Nitroanisole	1:6	25	—	56	25	162–163 <sup>f</sup>	165 <sup>f</sup>
10	1,4-Dinitrobenzene	1:6	25	—	46 <sup>g</sup>	37 <sup>g</sup>	163	165
11	1,4-Dinitrobenzene	1:0 <sup>h</sup>	10	<i>i</i>	—	—	—	—
12	Azoxybenzene	1:5 <sup>j</sup>	45	81	—	—	123–124	126–127
13	4-Nitroso- <i>N,N</i> -diethylaniline	1:4	15	32 <sup>k</sup>	—	67	—	—

<sup>a</sup> Aluminium powder was added in lots of 1:2 at 10 min intervals. Three molar equivalents of KOH per mole of Al and 10 mL of methanol per g of Al were also added accordingly in lots. <sup>b</sup> Isolated yield. <sup>c</sup> Melting point of crude isolated solid. <sup>d</sup> The deiodinated coupled products hydrazobenzene and aniline were obtained. <sup>e</sup> Dichloromethane was added to the reaction mixture after 45 min and the reaction mixture stirred for another 10 min to obtain complete conversion of the azoarene to hydrazoarene, which otherwise does not react due to low solubility in methanol. <sup>f</sup> The melting point and lit. mp are of the corresponding azo compound. <sup>g</sup> The products obtained are 4,4'-dimethoxyazobenzene and 4-anisidine. <sup>h</sup> 1,4-Dinitrobenzene was treated with 6 molar equivalents of KOH in methanol in the absence of any Al. <sup>i</sup> 1,4-Dinitrobenzene (56%) and 4-nitroanisole (42%) were obtained as analysed by HPLC. <sup>j</sup> 1:2 was added initially followed by 0:3 after 30 min. <sup>k</sup> HPLC relative ratios.

**Table 2** Product composition from the reaction of nitrobenzene with Al–KOH in methanol<sup>a</sup>

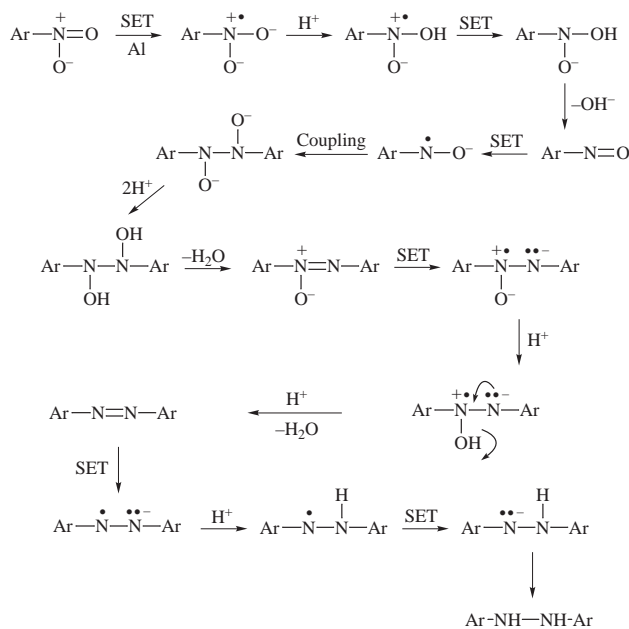
Time/ min	Hydrazobenzene (HPLC %)	Azobenzene + Azoxybenzene (HPLC %)
5	0	100
10	28	72
15	64	36
35	65.4	34.6
70	57.5	42.5
120	48	52
230	21	76

<sup>a</sup> Molar ratio PhNO<sub>2</sub>:Al:KOH 1:2:6; methanol 10 mL g<sup>-1</sup> of Al.

rapid aerial oxidation of hydrazoarene (run 9). The reduction of 1,4-dinitrobenzene with Al–KOH produced unexpected products namely, 4,4'-dimethoxyazobenzene and 4-anisidine (run 10). The reaction of 1,4-dinitrobenzene with KOH and methanol in the absence of any aluminium gave 4-nitroanisole (run 11). This suggests that 1,4-dinitrobenzene is first converted into 4-nitroanisole, which then undergoes reductive coupling with Al–KOH. The isolation of 4,4'-dimethoxyazobenzene in an independent reaction of 4-nitroanisole using a lower ratio of 1:2:6 points to the intermediacy of azoxyarenes which was further substantiated by the reduction of azoxybenzene to hydrazobenzene with aluminium and KOH in methanol (run 12). 4-Nitroso-*N,N*-diethylaniline on treatment with aluminium and KOH under identical reaction conditions gave the corresponding hydrazoarene and aniline (run 13). This experiment supports the intervention of nitrosoarene as yet another intermediate in the reductive coupling of nitroarenes. When run 1 was repeated in the presence of equimolar aniline, aniline was recovered unchanged besides hydrazobenzene (92%) after work up. Since aniline is not consumed in the reaction, the possibility of nitrosoarenes condensing with anilines followed by SET reduction is ruled out.

Residual aluminium (grey precipitate) could be observed in the otherwise colourless reaction mixture in all the reactions. The residual aluminium was recovered from the reaction mixture after complete conversion of nitrobenzene to hydrazobenzene as in run 1 and weighed. It was observed that only ~1.7 molar equivalents of Al (with respect to nitrobenzene) had been consumed for the reduction. An attempt to achieve the same

reduction with two lots of 1:1:3 and 0:1:3 (*i.e.*, total molar ratio 1:2:6) was, however, not successful. Based on the above observations, it is tentatively proposed that the reductive coupling of nitroarenes proceeds by single electron transfer (SET) from Al metal to nitroarenes with methanol acting as the source of protons as shown in Scheme 1. It is evident that



for the complete reduction of one molecule of nitroarene to hydrazoarene, a total of five SETs are required, *i.e.*, 1.67 molar equivalents of aluminium (Al→Al<sup>3+</sup>) for every mole of nitroarene. This is in agreement with our results. The high reduction potential of Al (Al<sup>3+</sup>/Al) in alkaline medium (−2.3 v) explains the necessity of KOH for the reductions. The drastically lower reactivity of Al–NaOH–methanol system may be due to the lower solubility of NaOH in methanol (which is limited to 1 g per 4.2 mL of methanol) compared to KOH. The sluggish reactions in aqueous solvents may be explained by the fact that the Al reacts vigorously with KOH in water to form aluminate (eqn. (2)) and this reaction competes with reduction

via SET. The quantitative recovery of Al from a control reaction of Al and KOH in methanol ruled out the reduction *via* evolved H<sub>2</sub>.

## Experimental

Proton NMR spectra were recorded on a Hitachi FT-NMR 60 MHz spectrophotometer using TMS as the internal standard. The IR spectra were recorded on a Shimadzu model-435. HPLC analyses were performed using an ODS-18 (Zorbax 150 × 4.6 mm) column with methanol as the eluent on a Shimadzu model LC-4A. Aluminium powder (SRL, 325 mesh), potassium hydroxide pellets (E. Merck) and methanol (Speck-pure) were used in all the reactions. 4-Nitroso-*N,N*-diethylaniline,<sup>10</sup> azoxybenzene<sup>11</sup> and 4-nitroanisole<sup>12</sup> were prepared by known procedures. All other nitroarenes were obtained from commercial sources and recrystallized/distilled before use.

## General procedure

Nitroarene (10 mmol), aluminium powder (0.54 g, 20 mmol) and methanol (5.4 mL) were placed in a 50 mL round bottomed flask mounted over a magnetic stirrer. A reflux condenser and mercury seal were attached to the flask and KOH (3.367 g, 60 mmol) was added. The contents were stirred at ambient temperature. A vigorous exothermic reaction ensued with rapid development of a yellow–orange colouration attributed to the formation of azoxy and azo compounds. The progress of the reaction was monitored by TLC (eluent: benzene–petroleum ether). Subsequently, aliquots of Al–KOH–methanol (equal to the first amount above) were added at 10 min intervals till the colouration disappeared and TLC showed only hydrazoarene and amine in the reaction mixture. The reaction was quenched by adding diethyl ether (30 mL) to the reaction flask. The contents of the flask were stirred and the diethyl ether solution decanted. The process was repeated twice with diethyl ether (2 × 15 mL) to extract the product from the methanol layer which retains the residual inorganic matter. The combined ether extract (~60 mL) was washed with 0.1 M HCl (3 × 10 mL), dried (anhyd. MgSO<sub>4</sub>) and the solvent distilled off on a rotavapour. The compound obtained was dried in a vacuum desiccator and identified to be the hydrazoarene by its mp, IR and NMR spectra. The acidic washings were combined, neutralized with NaHCO<sub>3</sub> and then extracted with diethyl ether (3 × 10 mL). The extract was dried over anhyd. K<sub>2</sub>CO<sub>3</sub> and the solvent distilled out on a rotavapour. The product after drying under vacuum was identified to be the corresponding amine by mp, mixed mp and NMR spectra.

## Recovery of residual aluminium after reduction of nitrobenzene to hydrazobenzene

The reaction of nitrobenzene (1.23 g, 10 mmol) was performed as above using two lots of Al–KOH–methanol. When the reaction mixture became colourless (after 5 min of the second additions), it was diluted with methanol (50 mL) and filtered at the pump. The contents of the flask were transferred completely into the filtration funnel and the residue was washed with methanol (5 × 10 mL) till the washings were no longer alkaline. Grey aluminium powder (0.620 g, 23 mmol) was obtained as the residue after filtration and drying under vacuum.

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