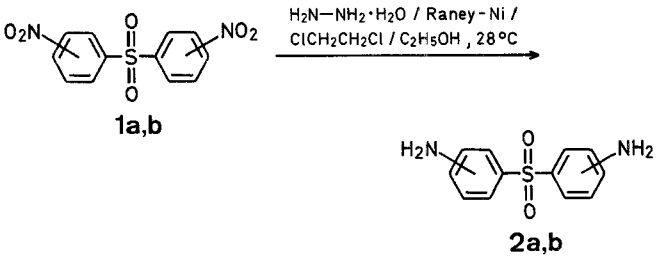

1a: 3,3′-dinitro→**2a:** 3,3′-diamino
1b: 4,4′-dinitro→**2b:** 4,4′-diamino

Catalytic Reduction of Nitroarenes with Hydrazine Hydrate in Suitable Solvents*

N. R. AYYANGAR**, A. G. LUGADE, P. V. NIKRAD, V. K. SHARMA

National Chemical Laboratory, Pune 411008, India

Since the introduction of the hydrogenation catalysts such as nickel, palladium, ruthenium, and platinum, the catalytic reduction with hydrazine has been widely studied. The method afforded an elegant route to the preparation of aromatic amines[1,2,3]. However, the reduction of nitro compounds having limited solubility in solvents commonly used for reductions with hydrazine has not been systematically investigated. Recently, the use of hydrazine in presence of ruthenium on carbon for selective reduction of 2,4-dinitroaniline to *p*-nitro-*o*-phenylenediamine was reported[2].

With an object of studying the effect of various catalysts in the presence of different solvents, we selected 3,3′-dinitrodiphenylsulphone **(1a)** and 4,4′-dinitrodiphenylsulphone **(1b)**; because of their comparatively poor solubility in ethanol, ethyleneglycol, dichloroethane, and methanol. In the present study, Raney nickel, 5% palladium on calcium carbonate, 8% palladium on carbon, Raney nickel with traces of platinum and iron(III) oxide hydroxide were used as catalysts with the above solvents. Reductions were carried out under different conditions to explore the effect of solvents and catalysts on the reactivity of hydrazine hydrate. The results are summarized in Table 1.

The reduction of **1a** to 3,3′-diaminodiphenylsulphone **(2a)** in the presence of Raney nickel in boiling ethanol gave a 90% yield and required 16 mol of hydrazine hydrate and 16 h of refluxing at 78 °C (Table 1). At 25–30 °C, there was no reduction of **1a** in ethanol or methanol even after 50 h. Changing the solvent to ethyleneglycol increased the yield of the reduction product to 98% at 30 °C, but lowered the reaction rate (50 h). In dichloroethane, 84% reduction was achieved at 30 °C in 20 h. Use of solvent combinations such as 1 : 1 v/v ethanol/ethyleneglycol or 1 : 1 v/v ethanol/dichloroethane dramatically enhanced the rate of reduction: 98–99% reduction was achieved in 10 h and 8 h, respectively, at 28 °C. Only 8 mol of hydrazine hydrate per mol of **1a** were required when the latter system was used as solvent; for the former system, the requirement was 16 mol for 98% reduction. Attempts to carry out the reduction in ethyleneglycol, dichloroethane, or the above mixtures at 78 °C resulted in sticky products which adhered to the flask. A similar pattern of solvent influence on the reduction of **1b** to 4,4′-diaminodiphenylsulphone **(2b)** was observed. Almost quantitative (98–99%) reduction of **1b** was achieved in 9 h with ethanol/dichloroethane as solvent at 28 °C using only 8 mol of hydrazine hydrate. Excellent reduction was thus achieved by adding hydrazine hydrate to the nitro compounds in the solvent combination ethanol/dichloroethane. In general, **1b** has poorer solubility in the solvents as compared to **1a** and hence its reduction was more sluggish.

After confirming the high reduction ability of hydrazine hydrate in the presence of Raney nickel and the solvent mixture ethanol/dichloroethane, we decided to study the influence of this solvent system on the effectiveness of hydrazine hydrate as a reducing agent in presence of other catalysts. The reductions were carried out under identical conditions varying only the catalysts and the time required for optimum reductions. The results are summarized in Table 2.

In the presence of 5% palladium on calcium carbonate, 95% reduction of **1a** was achieved in 10 h at 60–70 °C; whereas 8% palladium on carbon provided 92% reduction in 9 h at the same temperature. No appreciable reduction was observed at 28–30 °C in presence of these catalysts. The rate of reduction was enhanced when traces of platinum were added to the Raney nickel (98% reduction in 5 h at 28 °C, requiring 8 mol of hydrazine hydrate). In contrast to the reduction of **1a**, surprisingly, the reduction of **1b** in the presence of palladium on calcium carbonate and palladium on carbon was not possible and only the starting nitro compound **1b** could be isolated even at 70 °C. However, Raney nickel in the presence of traces of platinum reduced **1b** in 6 h at 28 °C giving a 98% yield of **2b** and consuming only 8 mol of hydrazine hydrate. Thus, among the catalysts tested, Raney nickel mixed with traces of platinum appears to be the best catalyst for these reductions in ethanol/dichloroethane.

Hydrazine hydrate (100%) in the presence of finely divided iron(III) oxide hydroxide was reported to be an excellent reagent for the reduction of aromatic nitro compounds[3]. It was of interest, therefore, to explore the effect of solvents on the reduction of **1a** and **1b** in presence of hydrazine hydrate and iron(III) oxide hydroxide, using solvents ethanol, ethyleneglycol, dichloroethane, methanol, and suitable combinations thereof.

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Table 1. Effect of Solvent on the Reduction of **1a, b** to **2a, b**

Substrate	Product	Reaction conditions				Yield [%][a]
		Solvent (ml)	Ratio **1**: hydrazine hydrate	Temperature [°C]	Time [h]	
1a	**2a**	C_2H_5OH (150)	1:8	78°	8	62
		C_2H_5OH (150)	1:16	78°	16	90
		ethylene-glycol (150)	1:16	30°	50	98
		$ClCH_2CH_2Cl$ (100)	1:16	30°	20	84
		1:1 C_2H_5OH/ ethylene-glycol (100)	1:16	30°	10	98
		1:1 C_2H_5OH/ $ClCH_2CH_2Cl$ (100)	1:8	28°	8	98-99
1b	**2b**	C_2H_5OH (150)	1:16	78°	16	50
		C_2H_5OH (150)	1:16	78°	32	74
		ethylene-glycol (150)	1:16	28°	72	85
		ethylene-glycol (150)	1:24	28°	72	97
		$ClCH_2CH_2Cl$ (100)	1:16	30°	20	60-65
		1:1 C_2H_5OH/ ethylene-glycol (100)	1:16	30°	12	93-95
		1:1 C_2H_5OH/ $ClCH_2CH_2Cl$	1:8	28°	9	98-99

[a] Yield of isolated product.

Table 2. Effect of Catalyst on the Reduction of **1a, b** to **2a, b** in 1:1 Ethanol/Dichloroethane

Substrate	Product	Catalyst	Reaction conditions			Yield[a] [%]
			Ratio **1**: hydrazine hydrate	Temperature [°C]	Time [h]	
1a	**2a**	Raney nickel	1:8	28°	8	98
		5% Pd-$CaCO_3$	1:8	60-70°	10	95
		8% Pd—C	1:8	60-70°	9	92
		Raney nickel/Pt	1:8	28°	5	98
1b	**2b**	Raney nickel	1:8	30°	9	98-99
		5% Pd—$CaCO_3$	1:8	70°	10	0
		8% Pd—C	1:8	70°	10	0
		Raney nickel/Pt	1:8	28°	6	98

[a] Yield of isolated product.

The catalyst was prepared according to the method described in the literature[4]. The particle size of 0.5 to 1.0 μ was obtained by milling the catalyst for 48 h in the above solvents in a glass tube containing steel rods. In presence of ethanol, 98% reduction of **1a** was achieved in 10 h at 78 °C requiring only 6.4 mol of hydrazine hydrate (Table 3). In presence of refluxing methanol, however, only 90% conversion was achieved in 10 h; it could be raised to 98% after 18 h. Surprisingly, the solvent combinations ethanol/ethyleneglycol and ethanol/dichloroethane showed no influence on the reduction of **1a** and **1b** and almost all the starting compounds were recovered. Only 75% reduction of **1b** was achieved in 10 h when ethanol was used as a solvent and 98% reduction needed 18 h in refluxing ethanol. In refluxing methanol using 8 mol of hydrazine hydrate per mol of **1b**, 63% reduction was attained in 10 h, which could be raised to an optimum 93% in 22 h. Reduction of **1a** and **1b** with only 6.4 mol of hydrazine hydrate in presence of iron(III) oxide hydroxide in boiling ethanol is feasible. Under ideal conditions, 2 mol of hydrogen should be available from 1 mol of hydrazine. However, in presence of Raney nickel, hydrazine decomposes to give ammonia[5,6] in addition to nitrogen and hydrogen as shown below.

$$3\ N_2H_4 \xrightarrow{\text{Raney-Ni}} 2\ NH_3 + 2\ N_2 + 3\ H_2$$

Table 3. Effect of Solvents on the Iron(III) Oxide Hydroxide-Catalysed[a] Reduction of **1a, b** to **2a, b**

Substrate	Product	Solvent	Reaction conditions			Yield[b] [%]
			Ratio **1**: hydrazine hydrate	Temperature [°C]	Time [h]	
1a	**2a**	C_2H_5OH	1:6.4	78°	10	98
		1:1 C_2H_5OH/ ethyleneglycol	1:6.4	78°	10	0
		1:1 C_2H_5OH/ $ClCH_2CH_2Cl$	1:6.4	78°	10	0
		CH_3OH	1:8	65°	10	90
		CH_3OH	1:8	65°	18	98
1b	**2b**	C_2H_5OH	1:6.4	78°	10	75
		C_2H_5OH	1:6.4	78°	18	98
		1:1 C_2H_5OH/ ethyleneglycol	1:6.4	78°	10	0
		1:1 C_2H_5OH/ $ClCH_2CH_2Cl$	1:6.4	78°	10	0
		CH_3OH	1:8	65°	10	63
		CH_3OH	1:8	65°	22	93

[a] 50 mmol of **1**, 0.5 g of iron(III) oxide hydroxide, and 200 ml of solvent used.
[b] Yield of isolated product.

Thus, 1 mol of hydrogen is available from 1 mol of hydrazine and for the reduction of 1 mol of the dinitrodiphenylsulphones, 6 mol of hydrazine are required.

In all the above reductions, the work-up of the diamines was extremely simple. The solution was filtered to remove the catalyst and evaporation of the solvent gave the diamines in better than required purity. The only impurity of starting dinitro compounds, if present, was removed by column chromatography. There was no evidence for the formation of partial reduction products (i.e. products with one amino and one nitro group). There was also no evidence of the reduction of the sulphone group to sulphoxide or sulphide. It was therefore concluded that the optimum yield of diaminodiphenylsulphones **2** was the result of judicious choice of solvent system and catalyst with optimum consumption of hydrazine hydrate. The diamines **2a** and **2b** are valuable as intermediates for polymers, drugs (dapsone), and dyes.

The scope of the method is not limited to the reduction of dinitrodiphenylsulphones described above. Simple nitroarenes and their substituted derivatives **3** can also be reduced advantagously in ethanol or ethanol/dichloroethane with hydrazine hydrate and Raney nickel. As expected, simple nitroarenes with good solubility in solvents could be reduced completely within short periods. Thus, nitrobenzene **(3a)** and 1-nitronaphthalene **(3b)** were reduced by hydrazine hydrate in presence of Raney nickel in ethanol/dichloroethane at 40-50 °C within 2 h giving aniline **(4a)** and 1-aminonaphthalene **(4b)**, respectively, in 99% yield (Table 4).

$$\underset{\mathbf{3}}{Ar{-}NO_2} \xrightarrow[ClCH_2CH_2Cl\ /\ C_2H_5OH\ ,\ 28\text{-}30\,^\circ C]{H_2N{-}NH_2\cdot H_2O\ /\ Raney\text{-}Ni\ /} \underset{\mathbf{4}}{Ar{-}NH_2}$$

Each mol of nitroarene **3** needed 3 mol of hydrazine hydrate in conformity with theoretical requirement. In ethanol, 4-nitrotoluene **(3c)** required 6 h at 78 °C to give 95% of 4-aminotoluene **(4c)**. The same reduction could be achieved in ethanol/dichloroethane at 55-60 °C within 2.5 h to give 99% of the product. When the reduction of 4-nitrochlorobenzene **(3d)** was carried out in ethanol at 78 °C for 6 h, 92% of 4-chloroaniline **(4d)** was isolated. In this case we could also isolate

Table 4. Reduction[a] of Nitroarenes **3** to Aminoarenes **4** with Hydrazine Hydrate/Raney Nickel

Substrate **3** No.	Ar	Product	Reaction conditions: Solvent	Temperature [°C]	Time [h]	Yield [%][b]	m.p. [°C] or b.p. [°C]/torr: found	Ref.[7]
3a	C_6H_5	**4a**	1:1 $C_2H_5OH/ClCH_2CH_2Cl$	40–50°	2	99 (100)	184°/760	184°/760
3b	1-naphthyl	**4b**	1:1 $C_2H_5OH/ClCH_2CH_2Cl$	40–50°	2.5	99 (100)	49°	48–50°
3c	4-H_3C—C_6H_4	**4c**	C_2H_5OH	78°	6	95	45°	45°
		4c	1:1 $C_2H_5OH/ClCH_2CH_2Cl$	55–60°	2.5	99 (100)		
3d	4-Cl—C_6H_4	**4d**	C_2H_5OH	78°	6	92	71°	71°
		4d	1:1 $C_2H_5OH/ClCH_2CH_2Cl$	50–60°	2.5	98		
3e	2-HO—C_6H_4	**4e**	C_2H_5OH	78°	6	95	173°	174°
		4e	1:1 $C_2H_5OH/ClCH_2CH_2Cl$	50–55°	2	99		
3f	4-H_2N—C_6H_4	**4f**	C_2H_5OH	78°	6	99	139°	140°
		4f	1:1 $C_2H_5OH/ClCH_2CH_2Cl$	55–60°	2.5	99		
3g	3-O_2N—C_6H_4	**5**	C_2H_5OH	78°	10[c]	85	113–114°	114°
		5	1:1 $C_2H_5OH/ClCH_2CH_2Cl$	50–60°	3	94		
		4g	1:1 $C_2H_5OH/ClCH_2CH_2Cl$	50–60°	6[c]	96	62°	63–64°
3h	4-(2,4-di-Cl—C_6H_3O)C_6H_4	**4h**	C_2H_5OH	78°	12	99	70–71°	—[d]
		4h	1:1 $C_2H_5OH/ClCH_2CH_2Cl$	50–60°	4	99		

[a] Nitroarene **3**: hydrazine hydrate ratio 1:3; 0.3 g of catalyst; 10 ml of solvent per g of **3**; 0.1 mol of **3** used.
[b] Yield of isolated product, yield by G.L.C. in brackets.
[c] Nitroarene **3**: hydrazine hydrate ratio 1:6.
[d] Ref.[8] gives m.p. 62°C, the product **4h** was characterised by spectral and microanalytical data:

$C_{12}H_9Cl_2NO$	calc.	C 56.7	H 3.5
(254.2)	found	56.9	3.3

M.S.: m/e=254 ($M^{\cdot+}$).
I.R. (Nujol): ν=3280, 3200, 1610, 1500, 1470, 1390, 1280, 1250, 1200, 1110, 1060, 850 cm^{-1}.
^{1}H-N.M.R. (CCl_4): δ=3.40 (s, 2H, exchangeable with D_2O); 7.4 ppm (m, 7H).

orange 4,4′-dichloroazobenzene (8%, m.p. 178°C, Lit.[9], m.p. 178°C) as a minor product. When the reduction was carried out in ethanol/dichloroethane at 50–60°C for 2.5 h, the yield of **4d** increased to 98% and that of 4,4′-dichloroazobenzene fell to 2%. Both 2-nitrophenol **(3e)** and 4-nitroaniline **(3f)** could be reduced with hydrazine hydrate/Raney nickel in ethanol at 78°C and 6 h to give pure 2-aminophenol **(3e)** and 1,4-diaminobenzene **(3f)** in 95% and 99% yields, respectively. When the reductions were carried out in ethanol/dichloroethane at 50–55°C for 2 h and 55–60°C for 2.5 h, respectively, 99% yields of 2-aminophenol **(4e)** and 1,4-diaminobenzene **(4f)** were obtained. In both these cases, the products were pure, colourless crystals. Commercial 2-aminophenol is usually contaminated by coloured phenoxazine type impurities[10]. The 2-aminophenol obtained by the present method was free from this impurity.

Reduction of 1,3-dinitrobenzene **(3g)** with hydrazine hydrate (6 mol per mol of **3g**) in ethanol at 78°C for 10 h gave only 3-nitroaniline **(5)** in 85% yield. However, when the reduction was carried out in ethanol/dichloroethane at 50–60°C for 6 h using the same ratio of hydrazine hydrate to **3g**, 1,3-diaminobenzene **(4g)** was obtained in 96% yield. By using only 3 mol of hydrazine hydrate per mol of **3g** in ethanol/dichloroethane at 50–60°C, only 3-nitroaniline **(5)** was isolated in 94% yield in 3 h. Reduction of 2,4-dichloro-4′-nitrodiphenyl ether **(3h)** with hydrazine hydrate/Raney nickel in ethanol at 78°C needed 12 h to give 99% of 2,4-dichloro-4′-aminodiphenyl ether **(4h)**. When the solvent system was changed to ethanol/dichloroethane at 50–60°C, the same result was obtained within 4 h; the ether linkage was unaffected.

Features of the present method are: (1) the stable, crystalline products can easily be isolated in high yield and purity, (2) the reaction conditions are sufficiently mild that sulphone and ether groups are not affected, (3) dinitro compounds can be reduced almost quantitatively by using the required amount of hydrazine hydrate, and (4) the work-up procedure is simple.

Reduction of Dinitrodiphenylsulphones 1a, b to Diaminodiphenylsulphones 2a, b:

80% Hydrazine hydrate solution (5 ml) is added to a stirred, 1:1 mixture of dichloroethane and ethanol (100 ml) and 3,3′-dinitrodiphenylsulphone[12] **(1a**; 3.04 g, 10 mmol). The mixture is kept at 28°C under stirring and Raney nickel (0.2 g) is added. Stirring is continued at 28°C until a clear colourless solution is obtained. (T.L.C. on silica gel, 1:9 v/v benzene/ethyl acetate). The reaction is complete in 8 h. The mixture is then filtered to remove the catalyst and evaporation of the solvent gives the product **2a**; yield: 2.44 g (98%); m.p. 168°C (Ref.[11], m.p. 168°C); m.m.p. not depressed.

$C_{12}H_{12}N_2O_2S$	calc.	C 58.04	H 4.88	N 11.30
(248.3)	found	58.23	5.03	11.64

M.S.: m/e=248 (M^+), 184, 168, 167, 140, 109, 108, 93, 92.
I.R. (Nujol): ν=3030, 3025, 1600, 1485, 1460, 1380, 1320, 1296 cm^{-1}.
^{1}H-N.M.R. (CH_3CN): δ=4.5 (br m, 4H, exchangeable with D_2O); 7.2 ppm (m, 8H).

Unreacted **1a** is separated by chromatography on silica gel (eluent, ethyl acetate); 0.45 g; m.p. 200°C (Ref.[12], m.p. 200–201°C); m.m.p. not depressed.

Similar reduction of 4,4′-dinitrodiphenylsulphone **(1b)** gives **2b**; yield: 2.43 g (98%); m.p. 178°C (Ref.[13,14], m.p. 178°C).

$C_{12}H_{12}N_2O_2S$	calc.	C 58.04	H 4.88	N 11.30
(248.3)	found	58.16	5.08	11.63

M.S.: m/e=248 (M^+), 232, 216, 184, 168, 167, 140, 109, 108, 93, 92.
I.R. (Nujol): ν=3025, 1595, 1520, 1495, 1455, 1375, 1275, 1150 cm^{-1}.
^{1}H-N.M.R. (CH_3CN): δ=4.7 (br m, 4H, exchangeable with D_2O); 7.10 ppm (q, 8H, J=10 Hz).

Unreacted **1b** is separated by chromatography on silica gel (eluent, ethyl acetate); 0.057 g; m.p. 256°C (Ref.[15,16], m.p. 256°C).

The products **2a, b** are analysed by the standard perchloric acid method[17] and by H.P.L.C. (column: μ porasil, 30 cm × 4 mm ϕ; degassed ethyl acetate as solvent; flow rate 2 ml/min, chart speed 3.75 cm/min; retention times: 1.1 min, 1.7 min for **1a** and **2a**, respectively; 1.1 min, 1.65 min for **1b** and **2b**, respectively).

In the case of reductions using different solvents ethanol, dichloroethane, or methanol and the catalysts, the work-up is identical (reaction conditions are mentioned in Tables 1, 2, and 3). When ethyleneglycol and ethanol/ethyleneglycol are used as solvents, the filtrate obtained after the removal of catalyst is diluted with water (1500 ml) and the precipitated product, obtained after 12 h of standing, is collected by filtration.

Reduction of Nitroarenes 3; General Procedure:

A mixture of nitroarene **3** (0.1 mol), 1 : 1 v/v ethanol/dichloroethane (10 ml per g of **3**), and hydrazine hydrate (0.3 mol) is stirred for 10 min at 28–30 °C. Then Raney nickel (0.3 g) is added with stirring in three portions over a period of 10 min. The reaction is vigorous and the temperature increases to 50–60 °C. (Temperature is not allowed to rise above 60 °C.) After 30 min, when the reaction has subsided, stirring is continued for 2 to 6 h at 50–60 °C. Complete conversion of the nitroarene can be confirmed by T.L.C. analysis on silica gel using benzene/ethanol (19 : 1) as eluent and colour development with iodine vapours. The catalyst is removed by filtration. The solvent is evaporated and the residue is recrystallized from methanol or ethanol. When ethanol alone is used, the reaction is carried out at 78 °C. The aminoarenes **4** are characterised by m.p., m.m.p., and microanalyses.

The orange coloured by-product *4,4'-dichloroazobenzene* is isolated from the reduction of 4-nitrochlorobenzene (**3d**); m.p. 178 °C (Ref.[18], m.p. 186–187 °C).

$C_{12}H_8Cl_2N_2$	calc.	C 57.4	H 3.2	N 11.1
(251.2)	found	57.5	3.4	10.6

M.S.: $m/e = 251$ (M^+).

I.R. (Nujol): $\nu = 1570$, 1555, 1480, 1400, 1155, 1090, 1015, 860, 725 cm^{-1}.

^1H-N.M.R. (CCl_4): $\delta = 7.5$ ppm (m, 8H).

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** Address for correspondence.

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