

Note

A new reagent for selective reduction of nitro group

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The nitro group in aromatic nitro compounds containing reducible substituents such as methyl, carboxylic acids and phenols, and halogens are selectively and rapidly reduced at room temperature to the corresponding amines in good yield by employing hydrazine glyoxylate in the presence of zinc powder or magnesium powder. It has been observed that hydrazine glyoxylate is more effective than hydrazine, glyoxylic acid, hydrazinium monoformate or ammonium monoformate and reduction of the nitro group occurs without hydrogenolysis in the presence of low-cost magnesium compared to expensive metals like palladium, platinum, ruthenium, *etc.* The products have been characterized by comparison of their TLC, infrared spectra and melting points.

Keywords: Selective reduction, nitro compounds, amino compounds, hydrazine, glyoxylic acid

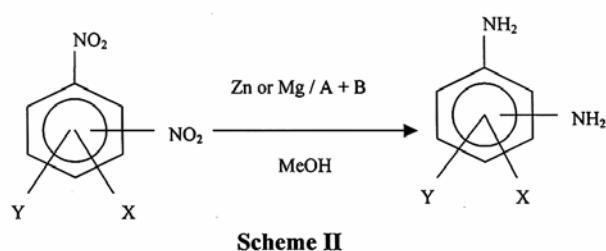
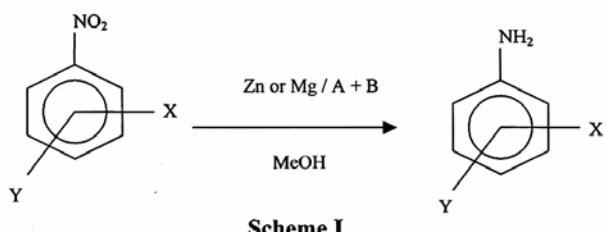
The nitro group in aromatic nitro compounds also containing reducible substituents such as ethane, nitriles, carboxylic acid, phenol, halogen, ester, *etc.*, cannot be reduced selectively with the reagents used commonly for the reduction of nitro group alone. This is due to the ease of reduction of other functional groups present along with the nitro group. Hence, special reagents are required for the above purpose. From the literature it is observed that when formic acid, ammonia or hydrazine hydrate was used with metal, though the reaction proceeds, the efficiency is very low. Further, ammonium formate has been used with metal which is also found to be inefficient in bringing about the required reduction.

However, metal and hydrazine formate system was found to be very effective for the selective reduction of nitro groups in the presence of other reducible functional groups. Further, these reactions in the absence of metal fail to yield the desired product. Rapid and selective reduction is of importance for the preparation of amino derivatives in the organic synthesis both practically and industrially, particularly

when a molecule has other reducible moieties¹⁻⁵. The synthesis and study of the biological activity of aromatic amines and their derivatives is an active area of research^{6,7}. Numerous new reagents have been widely used⁸, but they have many limitations. For example, catalytic hydrogenation⁹⁻¹¹ of nitro or azido compounds in the presence of palladium on carbon or platinum on carbon requires precautions, because of their flammable nature in air. Besides this, many methods require compressed hydrogen gas, which is highly diffusible and flammable. To overcome these difficulties, several new methods have been developed^{12,13}. In addition to the above said limitations, most of these methods lack the desired generality for true synthetic utility. Moreover, reflux for hours together under reducing conditions can cause a number of side reactions, such as rearrangements, cyclization in poly functional nitro compounds, *etc.* Even with hydrazine formate also, the reaction has been carried out under nitrogen atmosphere which involved complicated experimental procedures. Hence, in the present work, the nitro-amino conversion reactions with hydrazine glyoxylate-metal system was examined and it was found that this reagent is efficient for the above conversion and the reactions were carried out in presence of air, hence no special precautions are needed. The reactions were also carried out at RT or with gentle warming so that it was convenient to handle the procedure. In the present work, a rapid and simple reduction of aromatic nitro compounds to the corresponding amine derivatives by using either zinc powder and hydrazine glyoxylate or magnesium powder and hydrazine glyoxylate is demonstrated.

Results and Discussion

Aromatic nitro and substituted nitro compounds were reduced in good yield to the corresponding amino compounds under mild conditions in the presence of hydrazine glyoxylate and low cost metal powder such as magnesium or zinc¹⁴⁻¹⁷. The reaction yielded single product in all the cases with very high yield. The compounds obtained were identified by TLC and separated by column chromatography. The general scheme and conditions of the reactions are shown in **Schemes I and II**.



In the **Schemes I and II**

- A : Hydrazine hydrate (99%)
- B : Glyoxylic acid mono hydrate
- Zn : Zinc
- Mg : Magnesium
- MeOH : Methyl alcohol

The reduction of nitro compounds in the presence of zinc or magnesium powder and hydrazine glyoxylate was completed within 2 hr. The course of the reductions were monitored by thin layer chromatography and infrared spectra. The work-up and isolation of the products were easy and all the compounds reduced by this system were obtained in good yields. However, with magnesium powder the yields are comparatively low. The products were characterized by comparison of their TLC, infrared spectra and melting points with authentic samples. Control experiments were carried out using a few of the nitro compounds with hydrazine glyoxylate, but in absence of zinc or magnesium powder and did not yield the desired products. In order to test the selectivity of the procedure, reductions were attempted with benzoic acid and β -naphthol at

ambient temperature. However, these reactions failed to give any reduced product. The advantage of the present process is that all the reductions could be carried out in presence of air and not under nitrogen atmosphere which always simplifies the experimental conditions.

The obvious advantages of the current method over previously known methods are:

- (i) Selectivity of the reduction of nitro compound, in the presence of other reducible or hydrogenolysable groups,
- (ii) Easy to operate under simple experimental conditions,
- (iii) Rapid reduction,
- (iv) High yields of substituted amines,
- (v) Avoidance of strong acid medium,
- (vi) No requirement of pressure apparatus and
- (vii) Less expensive.

This method will therefore be of general application especially in cases where rapid, mild and selective reduction is required. The reaction conditions and analytical data are summarized in **Tables I and II**. The NMR and mass spectra of some representative compounds are recorded and the data is presented in **Table III**.

The proposed mechanism for the nitro to amino conversion is shown.

Mechanism

The electron withdrawing groups like $-COOH$ decrease the electron density over phenyl ring and hence the electrons supplied by the nitrogen of NO_2 group is pulled towards the ring which makes this nitrogen less susceptible for abstraction of proton.

Experimental Section

Commercially available chemicals (Analar or equivalent grade) were used as received and the solvents were purified by distillation according to

Mechanism

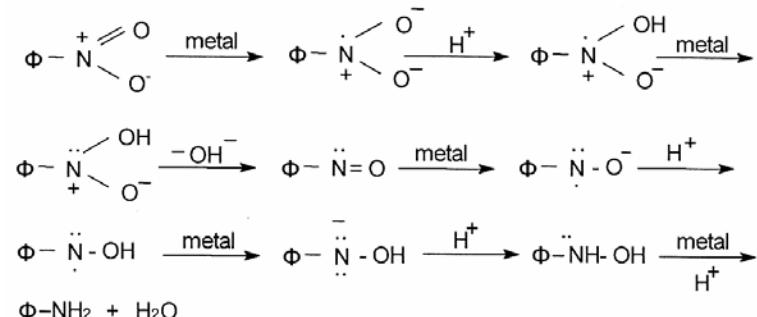


Table I — Zinc catalyzed reduction of nitro compounds using hydrazine glyoxylate

1318	Nitro Compd	Reaction time (min)	Product	Yield (%)m.p. (°C)	
				Found	Lit.
	<i>o</i> -Nitro phenol	2	<i>o</i> -Aminophenol	93	173-74
	<i>m</i> -Nitro phenol	INDIAN J ₂ CHEM., SECB, SEPTEMBER 2009	<i>m</i> -Aminophenol	94	121-23
	<i>o</i> -Nitro benzoic acid	30	Anthranilic acid	90	144-45
	<i>m</i> -Nitro benzoic acid	30	<i>m</i> -Amino benzoic acid	80	172-73
	<i>p</i> -Nitro benzoic acid	30	<i>p</i> - Amino benzoic acid	80	185-86
	<i>m</i> -Dinitro benzoic acid	120	<i>m</i> -Diamino benzoic acid	80	235-37
	<i>o</i> -Nitrochloro benzene	2	<i>o</i> -Chloroaniline	92	99-100
	<i>m</i> -Nitrochloro benzene	2.5	<i>m</i> -Chloroaniline	92	120-23
	<i>p</i> -Nitrochloro benzene	2	<i>p</i> -Chloroaniline	93	70-71
	<i>o</i> -Nitrobromo benzene	2.5	<i>o</i> -Bromoaniline	94	115-17
	<i>m</i> -Nitrobromo benzene	3	<i>m</i> -Bromoaniline	94	118-21
	<i>p</i> -Nitrobromo benzene	2.5	<i>p</i> -Bromoaniline	95	65-66
	<i>p</i> -Nitrocinnamic acid	3	<i>p</i> -Aminocinnamic acid	90	265-68
	<i>p</i> -Nitrobenzonitrile	2.5	<i>p</i> -Aminobenzonitrile	91	84-85
	2,4-Dinitrophenol	2	2,4-Diaminophenol	95	79-80
	<i>o</i> -Nitrotoluene	2.5	<i>o</i> -Toluidine	93	142-44
	<i>m</i> -Nitrotoluene	2.5	<i>m</i> -Toluidine	92	124-26
	<i>p</i> -Nitrotoluene	2	<i>p</i> -Toluidine	94	44-45
	<i>o</i> -Dinitrobenzene	3	<i>o</i> -Phenylenediamine	93	101-04
	<i>m</i> -Dinitrobenzene	2.5	<i>m</i> -Phenylenediamine	93	63-65

Table II — Magnesium catalyzed reduction of nitro compounds using hydrazine glyoxylate

Nitro Compd	Reaction time (min)	Product	Yield (%)	m.p (°C)	
				Found	Lit.
<i>o</i> -Nitro phenol	2	<i>o</i> -Aminophenol	65	173-74	174
<i>m</i> -Nitro phenol	2	<i>m</i> - Aminophenol	60	122-23	123
<i>p</i> -Nitro toluene	30	<i>p</i> -Toluidine	75	43-44	45
<i>o</i> -Nitro benzoic acid	30	Anthranilic acid	75	143-44	145
<i>m</i> -Nitro benzoic acid	30	<i>m</i> -Amino benzoic acid	70	171-73	174
<i>p</i> -Nitro benzoic acid	30	<i>p</i> - Amino benzoic acid	60	184-86	186
<i>m</i> -Dinitro benzoic acid	120	<i>m</i> -Diamino benzoic acid	60	235-36	237
<i>o</i> -Nitrotoluene	3	<i>o</i> -Toluidine	92	142-44	144
<i>m</i> -Nitrotoluene	2	<i>m</i> -Toluidine	93	124-25	125
<i>o</i> -Nitrochlorobenzene	0.5	<i>o</i> -Chloroaniline	93	99-100	99
<i>m</i> -Nitrochlorobenzene	0.5	<i>m</i> -Chloroaniline	91	120-23	122
<i>p</i> -Nitrochlorobenzene	0.5	<i>p</i> -Chloroaniline	93	70-71	70
<i>o</i> -Nitrobromobenzene	1	<i>o</i> -Bromoaniline	94	115-17	116
<i>m</i> -Nitrobromobenzene	1	<i>m</i> -Bromoaniline	94	118-21	120
<i>p</i> -Nitrobromobenzene	1	<i>p</i> -Bromoaniline	93	65-66	66
<i>p</i> -Nitrocinnamic acid	3	<i>p</i> -Aminocinnamic acid	90	265-68	265-70
<i>p</i> -Nitrobenzonitrile	2.5	<i>p</i> -Aminobenzonitrile	92	84-85	83-85

Table III — Spectral data of some representative compounds

Compd	¹ H NMR (δ , ppm)	MS (M^+)
<i>o</i> -Aminophenol	8.9 (s,1H,OH),4.4 (s,2H,NH ₂), 6.649,6.587,6.543,6.4 (m,4H,aromatic).	109
<i>m</i> - Aminophenol	8.83 (s,1H,OH),4.85 (s,2H,NH ₂), 6.78,6.018,6.01,5.942 (m,4H,aromatic).	109
<i>o</i> -Toluidine	3.48 (s,2H,NH ₂),2.09 (s, 3H, CH ₃), 7.01,7.00,6.676,6.586 (m,4H,aromatic).	107
<i>o</i> -Amino benzoic acid (Anthrаниlic acid)	8.4(s,1H,COOH), 3.6 (s,2H,NH ₂), 7.72, 7.23, 6.761, 6.524 (m, 4H, aromatic).	137
<i>o</i> -Phenylenediamine	4.36 (s,4H,NH ₂), 6.504,6.382 (m,4H,aromatic),	108

standard methods. The melting points were determined on a Veego melting point apparatus and are uncorrected. The FTIR spectra in KBr disc were recorded on Nicolet Impact-400 spectrometer. ¹H NMR spectra in DMSO-*d*₆ as solvent and TMS as an internal standard were recorded on a Varian 300 MHz FT-NMR spectrometer. Mass spectra were recorded by employing electro spray ionization (QT, YA-105, Micro Mass, Waters).

Typical Procedure

Hydrazine glyoxylate was prepared by neutralizing slowly, equal moles of hydrazine hydrate (0.5 mL, 0.01 mole) and glyoxylic acid (0.92 g, 0.01 mole) with constant stirring. The obtained hydrazine glyoxylate solution was used as such for the reductions. A suspension of an appropriate nitro compound (0.01 mole) and zinc powder or magnesium powder was stirred with hydrazine glyoxylate at RT. After the completion of the reaction (monitored by TLC), the catalyst was filtered off. The residue was extracted with 15 mL of chloroform or diethyl ether. The extract was washed twice with 15 mL saturated sodium chloride solution and then with 10 mL water. The organic layer was dried over sodium sulphate and then concentrated to obtain the desired amino derivative.

In summary, zinc/hydrazine glyoxylate or magnesium/hydrazine glyoxylate provides a convenient system for the selective reduction of aromatic nitro compounds. The source of hydrogen for this catalytic transfer hydrogenation method is hydrazine glyoxylate, a novel hydrogen donor, which is in-expensive and more efficient than either hydrazine or glyoxylic acid. Most of the reactions were completed within 2 hr as indicated by the disappearance of the starting materials and formation of the product (TLC). This system however is not

helpful in obtaining directly an amino carbonyl compound, due to the formation of hydrazone derivatives with the donor.

Further, other than formic acid, it is hoped the glyoxylic acid is the only alternative compound which consists of both aldehydic and carboxylic acid groups, which can be used for the nitro to amino conversion. Thus, the reduction of nitro compounds can be accomplished with zinc or magnesium powder instead of expensive platinum or palladium, etc., without affecting the other reducible or hydrogenolysable substituents. The yields are virtually quantitative and analytically pure products are obtained.

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