Facile and Economical Reduction of Nitro Aromatic Compounds using Aluminium and Ultrasound Waves

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In the Name of Allah, The most Gracious, and The most Merciful

O my Lord! Increase me in knowledge." (Quran 20:114)

Dedicated to

My loving parents my papa Zahoor Ahmed, my amma Rashida Begum and my siblings

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Hadia Zahoor

Abstract

The reduction of nitro group to amine is one of the most important transformations in organic synthesis since the amino group is often used for further derivatization towards valuable products such as dye stuffs, textile auxiliaries, pharmaceuticals, agrochemicals, photographic materials, polymers, explosives, fibers, surfactants, cosmetics etc. Mono, di and tri nitro aromatic compounds were reduced using aluminium turnings and aluminium foil which are benign and cheap along with ultrasound waves in moderate yield under mild conditions. 2,4,6-triaminophenol was synthesized which was used as a standard in case of TLC analysis of picric acid. 1,3-dinitrobenzene was first synthesized using traditional nitrating mixture of acids. Picric acid was reduced for the first time using this milder approach. Picric acid was reduced with yield of 61%. Optimization of reaction conditions was done with nitro benzene, 1,3-dinitrobenzene and picric acid using methanol, acetone, their combination with water and pure water as reaction medium was also used. First of all optimization was done with nitrobenzene then with 1,3-dinitrobenzene and in the end with picric acid. For the solubility of organic substrates in pure water CTAB was used. Aluminium turnings were more efficient as compared to aluminium foil because of purity. Methanol showed shortest reaction time and greatest yield as compared to acetone and pure water. Aromatic amines were characterized by IR, NMR, HPLC and TLC. Presence of amino group in the products and absence of nitro groups was depicted by IR analysis. HPLC was done in order to check the purity of aromatic amine formed as a result of reduction. Single sharp peak confirmed the purity of product. NMR was used to confirm the structure of aromatic amines. TLC was used in order to monitor progress of reaction, completion and comparison with standards for product confirmation. Facile, mild, greener and economical procedure has been optimized for reduction of nitro aromatic compounds to obtain moderate yields. Shorter reaction times, milder reagents, easy availability of reagents and cost effectiveness associated with this method make this protocol industrially important.

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Abbreviations and Symbols

A	Acetone
Cmc	Critical Micelle Concentration
C-NMR	Carbon Nuclear Magnetic Resonance
DNA	Deoxyribonucliec acid
DNT	Dinitrotoluene
DMF	Dimethyl Formamide
GC	Gas Chromatography
H-NMR or PMR	Proton Nuclear Magnetic resonance
HPLC	High Pressure Liquid Chromatography
HTE	High Throughput Experimentation
IR	Infrared
LC MS	Liquid Chromatography Mass Spectroscopy
M	Methanol
Sm	Smarium
Sn	Tin
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TNT	Trinitrotoluene
W	Water
WGSR	Water gas shift reaction

Chapter 1

Introduction

1.1 Nitro aromatic compounds

Nitro aromatic compounds are the organic compounds in which at least one nitro group (-NO_2) is attached to an aromatic ring. Nitro group is an electron withdrawing group. The electron deficiency of nitro group is because of the two oxygen atoms that are bonded to partially positively charged nitrogen atom. Nitro group is capable of delocalizing pi electrons of benzene ring and imparts nitro aromatic compounds unique properties that make them important molecules in organic transformations [1]. Simplest of nitro arenes is nitro benzene in which one nitro group is attached to an aromatic ring.

1.1.1 Brief history

The earliest aromatic nitro compounds were obtained by Mitscerlch in 1834 by treatment of hydrocarbons with fuming nitric acid and hydrocarbons. Hydrocarbons were obtained from coal tar. By 1835 Laurent was working with naphthalene, he was nitrating naphthalene, it was the most pure aromatic hydrocarbon at that time. Dale told about mixed nitro compounds that were obtained from crude benzene at the annual meeting of the British Association for the Advancement of Science in 1838. Hoffman and Musprat reported mono-and di nitro benzenes by nitrating benzene through a mixture of nitric and sulfuric acid. The first time nitrobenzene was prepared on a small scale. It was carefully distilled to give a yellow liquid with a smell of bitter almonds. Nitrobenzene was sold to soap industries as ‘‘essence of mirbane.’’
The first nitro aromatic to be recognized was chloramphenicol. It was extracted from cultures of a soil mold and identified in 1949. Following the earlier (1943) discovery of the antibacterial activity of nitro furan derivatives researchers were motivated to find out the pharmacological activity of nitro group [2].

1.1.2 Naturally occurring nitro aromatic compounds

Nitro aromatic compounds are formed in atmosphere and in aqueous environment. These are produced as a result of natural combustion process of hydrocarbons. The

combustion of fossil fuels produces molecules that act as a substrate for nitration through nitrogen dioxide present in the atmosphere[3, 4]. In aqueous environments sunlight catalyzes halogenation and nitration results in the formation of nitro aromatics [5]. These are also formed as a result of various processes in microorganism such as bacteria, fungi and plants [6].

1.1.3 Synthetic nitro aromatic compounds

Nitro aromatics are synthesized by the process of nitration. Nitronium ions are generated as a result of acid reaction of sulphuric and nitric acid, these ions are added through electrophilic substitution into aromatic substrates. For example nitro benzene, nitro toluene and nitro phenol are synthesized using this approach [7]. Reaction conditions can be modified for direct ortho, meta and para substitution. Nitration is the dominant and oldest method for introducing the nitro group into aromatic systems [8]. Several other methods also exist:

1. Oxidation of amino compounds
2. Replacement of diazonium groups (nitro-Sandmeyer reaction)
3. Rearrangement of nitramines
4. Nucleophilic displacement reactions

Some of the synthetic nitro aromatic compounds are shown in figure 1.1.

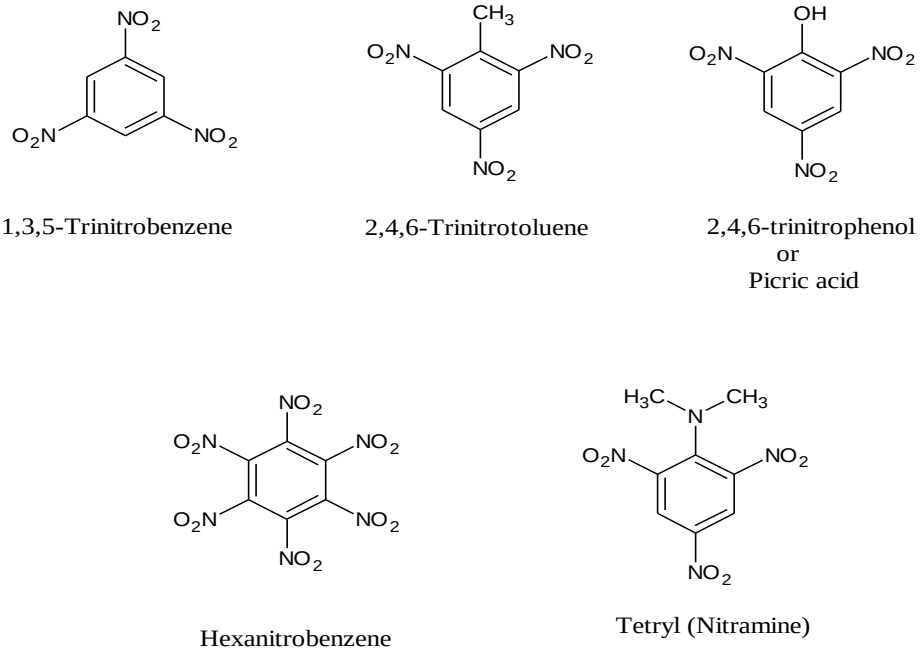


Figure 1.1. Examples of nitro aromatic explosives.

1.1.4 Uses of nitro aromatic compounds

Nitro aromatic compounds find diverse applications in almost every field [2, 9-11]. Some of the nitro aromatic compounds along with their uses are given bellow in table 1.1.

Table 1.1. Uses of nitro aromatic compounds.

Nitrobenzene	**1,3-dinitro benzene**	**1,3,5-trinitro benzene**	**4-chloronitro benzene**	**Pentachloro nitrobenzene**	**2-chloro nitrobenzene**
Used in the synthesis of polyurethane.	Used in explosives, formed as a byproduct in synthesis of TNT.	Used as an explosive.	Used for synthesis of chemicals such as nitrophenol, Nitroaniline etc.	Used as an organochlorine fungicide for control of various fungal diseases	Used for synthesis of para-anisidine, diaminophenol hydrochloride
Used in the synthesis of quinolone, azobenzene, Benzidene, isocyanates etc**.**	Used as an intermediate for the production of aramid fibres.	Used as a vulcanizing agent in the processing of natural rubber.	Used for synthesis of agricultural chemicals.	Used for soil and seed treatment against Rhizoctonia.	Used in corrosion inhibitors.
Synthesis of dyes such as nigrosine and magenta**.**	Used in the preparation of Amino cresols.	Used as an indicator in acid-base reactions in the pH range of 12.0–14.0.	Used for synthesis of antioxidants .	Used to inhibit slime formation in industrial water.	Used in the synthesis of agricultural chemicals.

1.1.5 Toxicity

Nitro aromatic compounds are used for synthesis of pesticides, dyes, polymers and pharmaceuticals, or as solvents (nitrobenzene) and explosives (2,4,6- trinitrotoluene). The same properties that allow nitro aromatic compounds to be useful in chemical applications also make them hazardous to the health of both humans and wildlife. Nitro aromatic compounds are abundantly present in industrial waste streams, surface waters and soils, representing an environmental threat. Several nitro aromatic compounds are on the U.S. Environmental Protection Agency's list of priority pollutants [12].

Nitro aromatic compounds are mutagenic. They interact with DNA and cause mutations and resulting mutagenicity have been reported in many papers for a variety of mono, poly and heterocyclic compounds [13].

An unfortunate result of the widespread use of nitro aromatic compounds is contamination of soil and groundwater. Improper handling and storage of agro chemicals (herbicides, pesticides etc) results in release of these chemicals into soil and ground water [14].

One of the major causes of contamination by nitro aromatic compound is the manufacture, storage, and handling of munitions. The army ammunition plants that produce explosives are the most highly contaminated locations [1]. The production and handling of waste waters produces three types of waste waters. One of them is "yellow water" that contains acids and it is not an issue. However other two contain energetic aromatic compounds that make them difficult to treat. "Red water is produced during the purification of TNT. Pink water is produced as a result of loading and assembly of munitions, it also contains TNT and other nitramines [15]. These waste waters cannot be degraded by normal treatment technologies.

1.1.6 Treatment methods

Following are the treatment processes that are used for treating contamination of nitro aromatics in soil and water.

1.1.6.1 Adsorption

It includes all those methods in which nitro aromatics are concentrated into another medium but are not converted into non-hazardous materials. Granular activated carbon is used for the treatment of both ground water and waste water of explosives [16].

1.1.6.2 Advanced oxidation process

This process involves the use of strong oxidizing agents such as hydrogen peroxide, ozone etc. Process can be carried out with or without catalyst [17]. They use Fenton's reagent (H_2O_2+Fe^{2+} alone or UV (254 nm) combination with Fenton's reagent was also used, for treatment of waste waters of explosives.

1.1.6.3 Bioremediation

Microorganisms have been used for ages to treat municipal and industrial wastes. [18]. The advantage of using microorganisms is low cost, easy operation etc. However this process is time consuming and sometimes substrates show resistance towards microorganism action

1.1.6.4 Phytoremediation

Phytoremediation is the process in which green plants are used to treat contaminated waste water. It is biotechnology which is not expensive and requires very less maintenance. The advantage of phytoremediation is that it tolerates high substrates concentration better than microorganism and able to degrade them as well [19].

1.2 Chemical reduction

One of the treatment methods that are used for the treatment of nitro aromatics contamination is chemical reduction. Different strategies are used for this process.

i. Hydrogenation
ii. Catalytic transfer hydrogenation
iii. Hydride transfer reductions
iv. Metal dissolving reduction
v. Metal free reduction methods

A variety of methods for the reduction of nitro groups have been reported. The most common method used is catalytic hydrogenation, using Raney Ni, Pd/C [20] or metal dissolving reduction, for example, Sn/HCl [21]. In addition, recently chemo selective reduction of nitro groups using metallic reducing reagents such as Sm [22], In [23], Sm/I_2 [24], Fe/THF [25] are also reported. Reduction in water Zn/H_2O [26], Fe/H_2O [27] also have been reported.

1.2.1 Advantages of chemical reduction

1) Chemical reduction works even in high contaminant concentration as compare to bioremediation.

2) Chemical reduction is quick even in some case reduction occurs in few minutes hence it is time saving.

3) Chemical reduction can be carried out with low cost reagents.

4) Chemical reduction can be done by simple set up without the need of specialized equipment.

I am using chemical reduction for nitro aromatic compounds.

1.3 Ultra sonication or sonochemistry

Ultra sonication is associated with the chemical effects that are produced when a chemical reaction is exposed to sound waves. The mechanism behind drastic increase in reactivity of chemical reaction is "Acoustic cavition [28] shown in figure 1.2.

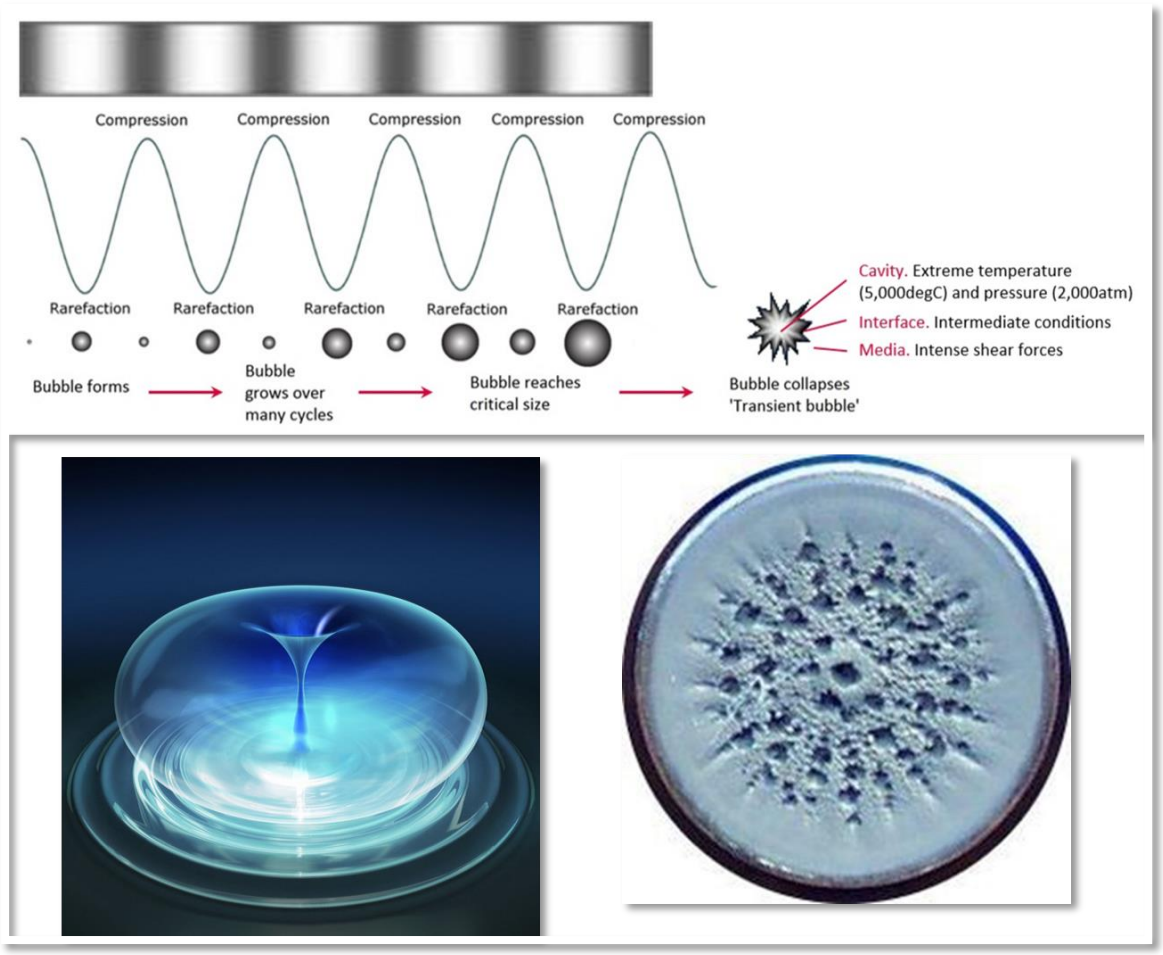


Figure 1.2. Illustration of Acoustic cavitation[28].

Acoustic cavitation proceeds as follows. Sound waves like other energy waves consist of successive cycles of expansion and compression due to vibrations. In solution where weak points are present especially at trapped gases pockets. These are the points where small vapor filled bubbles are formed. The bubble expands with cycles of expansion and contract with compression cycle. Bubble grows in size as the time passes up to a critical size when pressure of bubble cannot tolerate external pressure resulting in catastrophic collapse.

Extreme environments having high temperature and pressures are produced .Effect of temperature is illustrated in figure 1.3. This whole phenomenon is known as acoustic cavitation. The bubbles have the diameter of 10 to 200 microns and the lifetime of 10 micro seconds. The temperature within the bubble 5000 degree Celsius and pressure of 2000atm [29]. Sonication bubbles act as micro reactors having high temperature and pressure

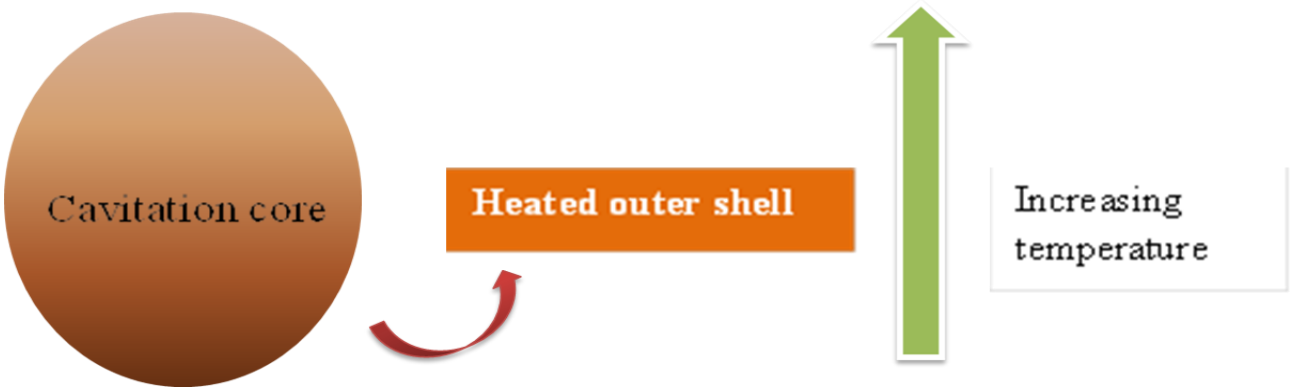


Figure 1.3. Effect of temperature [29].

1.3.1 Uses of sonochemistry

Applications of sonochemistry include dissolution and mixing in solutions, homogenization and cell disruption in biological samples, degreasing, emulsification [30] etc. It is also used in synthesis of new compounds [31].

1.3.2 Ultrasonic degradation

Ultrasonic degradation of various compounds has been reported in literature. For example dextran [32], glyceraldehyde [33], carbon tetrachloride [34] etc.

Sono chemical degradation of nitro aromatic compounds is of special interest. For example nitro phenol is degraded using sono chemical degradation [35]. 1,3-dinitro benzene is also degraded using this approach [15].
In my research work my purpose of using ultra-sonication was for the continuous removal of layer of alumina that is formed on the surface of aluminium. When aluminium is exposed to atmosphere thin, coherent, protective layer of alumina is formed on the surface of aluminium. This layer must be removed in order to expose fresh layer of aluminium for efficient reduction.

1.4 Micellar catalysis

Modern green trends are deeply changing the way chemical research evolves, in particular new evolution in the chemical synthesis and catalysis areas are nowadays strongly connected with green chemistry. This is essential to pass on these concepts to the new generation of scientists to make our environment greener and pollution free. The proper solvent selection to minimize toxicity, to fulfill energy demand, to reduce pollution is included in twelve principles of green chemistry. This is the reason scientists are promoting the use of greener solvents [36].
The term Environmental Factor, or E Factor was introduced by Sheldon, it is a measure of "greenness" associated with any reaction as shown in figure 1.4. By definition, it is related with the amount of waste created in a chemical reaction by weight, divided by the weight of isolated product.

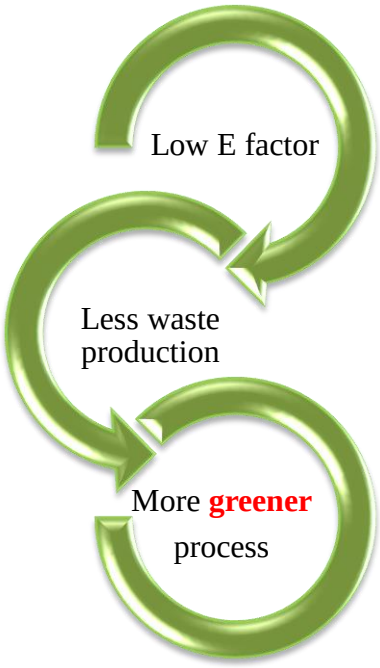


Figure 1.4. Relationship between E factor and environment [37].

Hence,

E factor = Kg of waste/Kg of desired product.

The major reason behind high E Factors is the use of organic solvent as reaction medium [37].

Water as solvent has been selected by Nature to carry out all kinds of chemical reactions. Water as a solvent has many advantages;

i. It is extremely economical solvent, non-toxic, non-flammable.
ii. It does not emit greenhouse gasses.
iii. It is naturally present in our environment.
iv. The energy necessary for purification of water is low and its E factor values zero, which means it is not considered a waste in chemical reaction.
v. Its acidity is tuneable.
vi. High values of heat capacity and heat of evaporation which allows easy control of exothermic reactions.
vii. Water is polar in nature and it contains hydrogen bond donor and acceptor at the same time which makes catalysis easier.

In one word water is the green solvent *of highest quality* [38].

Despite of useful properties of water it is not commonly used because non polar species are insoluble in water. In early 80's hydro formylation was performed using rhodium catalysts modified with sulfonate containing phosphine ligands [39]. Ever since, the researchers are coming out with different organic synthesis in water as a reaction medium [40].

The sequence of most chemical reactions involves workup in the usual way include dilution with water, followed by extraction with another additional organic solvent which is sometimes different from solvent used in the reaction. This whole process produces contaminated waste water containing different organics. From this point of view the green character of water in replacing organic solvents while using an organic solvent for extraction of products from water is questionable. But as far as water provides extra performance in terms of activity and selectivity, the use of limited amount of traditional solvents at the end of the reaction is alleviated.

Nature provides inspiration in the form of enzymes as highly active water soluble catalysts working in human body. Surfactants are the species that mimics enzymes and play a vital role in the selectivity of substrate as well as products and in the regulation of catalytic activity [41].

1.4.1 Surfactants and micelles

The word *amphiphile* was first introduced by Hartley [42]. Surfactants, surface active agents, or detergents are amphiphilic, organic, or organometallic compounds which form micelles in solution. Amphiphiles are the compounds consisting of two distinct regions. One region comprises of hydrophilic (water-attracting) portion and the other region comprises of hydrophobic (water repelling) portion as shown in figure 1.5. Hydrophilic region is known as head and hydrophobic region is known as tail.

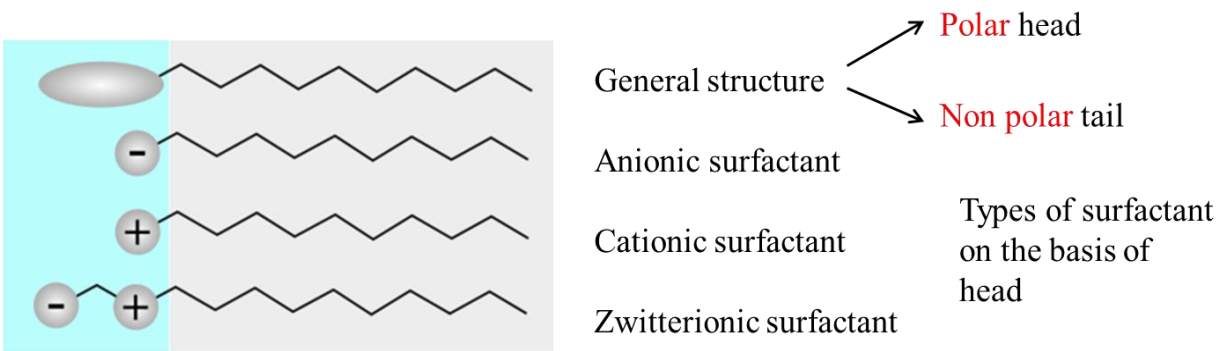


Figure1.5. Structure and types of surfactant.

Depending on the head surfactants are classified into following categories;

i. Cationic surfactants (if the head groups are cationic).
ii. Anionic surfactants (if the head groups are anionic).
iii. Zwitter ionic surfactants (if the head groups possess both cationic and anionic sites).
iv. Nonionic surfactants (if the head groups are nonionic).

Few examples of each category of surfactant is presented in table 1.2.

Table 1.2. Types and examples of surfactants.

Cationic Surfactants	**Anionic Surfactants**	**Zwitterionic Surfactants**	**Nonionic Surfactants**
Decyl ammonium bromide	Potassium dodecyl sulfate	N-Dodecyl/V.W-dimethylglycine	Polyoxyethylene Hexadecanol
Cetyltrimethyl ammonium bromide	Aluminum dodecylsulfate	Dodecylaminobenzyl phinic acid	Polyoxyethylene Dodecanol
1-Dodecyl Pyridinium iodide	Copper(II) dodecyl sulfate	Dodecyl-3-aminopropionic Acid	Polyoxyethylene Decanol

If water is present in excess the number of surfactant molecules increase on the air/water interface and on the walls of flask until saturation point. After which increase in concentration of micelle results in increase in free energy of system. In order to avoid that increase in free energy surfactants self-assemble themselves into aggregates known as micelles as shown in figure 1.6 and that concentration is known as critical micelle. cmc concentration is typically on the order of 10^{-3} to 10^{-4} M. The hydrophobic effect drives the formation of aggregates in solution. Micelle formation is spontaneous and reversible process. The typical lifetime of a surfactant micelle is of the order 10^{-3}-10^{-2}s [43, 44].

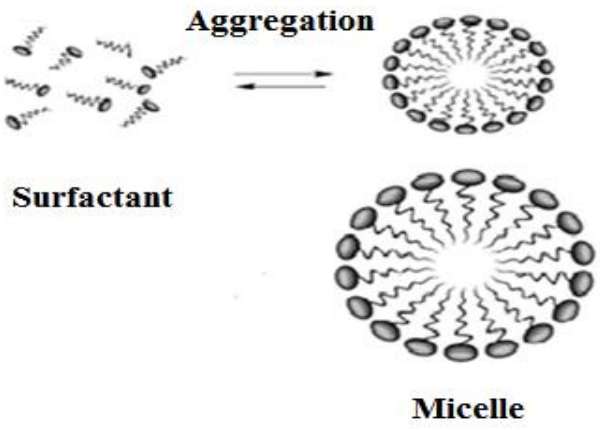
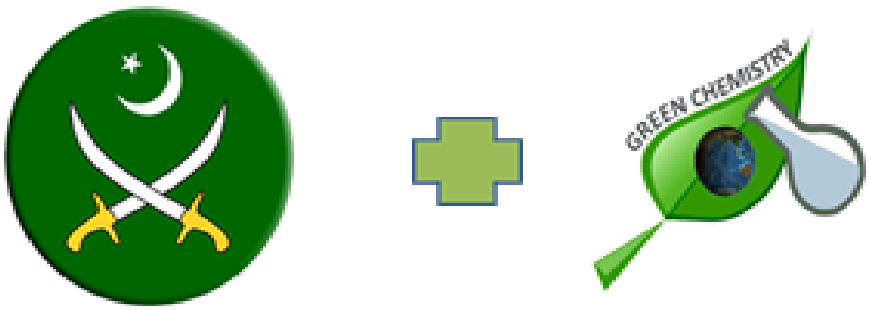


Figure 1.6. Micelle formation [43].

The use of surfactants under micellar conditions is the simplest method to achieve catalysis in water because it is very economical process. Micelles are not soapy solutions only instead they are much more than that. These are nano reactors with unique properties [45].

In my research work I have used CTAB (cetyltrimethyl ammonium bromide) in order to ensure better solubility of organic substrates in water

1.5 Motivation



My motivation behind this research work is the combination of two things. Firstly I wanted to do research that is defence related in order to serve my country. Tons and tons of expired TNT is dumped through explosion in our country. I wanted to reduce that expired TNT into material that can be used on industrial level for synthesis of useful materials. Secondly I wanted to do research and develop a method that is

nontoxic, mild, cheaper and nonhazardous for our environment so that I can make contribution towards greener and healthier environment.

1.6 Objectives

Main objectives of my research are as follows.

i. Chemoselective reduction of mono, di and tri nitro compounds using aluminium and ultrasound waves.
ii. Use of organic solvents, water and their combination for reduction.
iii. Use of pure water asa areaction medium for reduction for mono, di and trinitro aromatic compounds.
iv. Separation and isolation of products.
v. Optimization of reaction conditions.
vi. Analysis of reduced products using different analytical techniques.

1.7 Application

Picric acid which is an explosive material is reduced into useful aromatic amines. The reduction of nitro group to amine is one of the most important transformations in organic synthesis since the amino group is often used for further derivatization towards valuable products such as dye stuffs, textile auxiliaries, pharmaceuticals, agrochemicals, photographic materials, polymers, explosives, fibers, surfactants, cosmetics etc [46-50] as shown in figure 1.7. Aromatic amines are used as an intermediate for synthesis of azo dyes such as methyl orange, sunset yellow etc. p-nitro aniline is used mainly in the synthesis of dyes, antioxidants and medicines. Chloro anilines are used mostly in agriculture. 4,4-diamino-2,2-stilbenedisulfonic acid is used as raw material for optical brighteners. Aniline is used for the manufacture of isocyanates such as phenyl isocyanate which polymerizes to give polyurethane. Analgesics and sulfonamides are obtained from aromatic amines. Aromatic amines are converted into sulfanilic acid which is the parent compound of sulfa drugs [51].

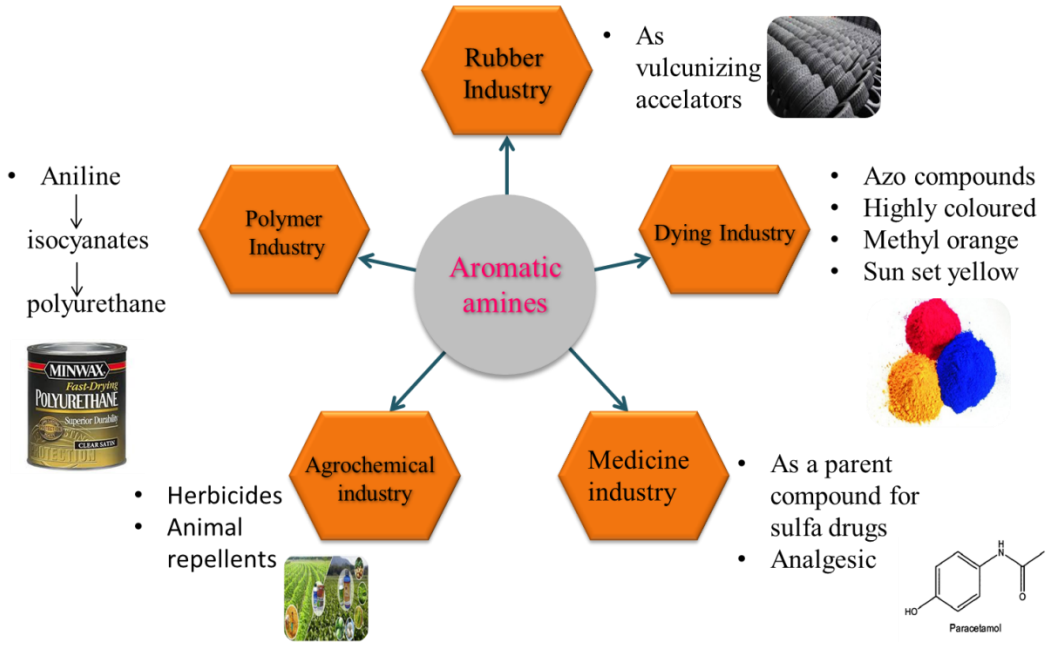


Figure 1.7. Applications of aromatic amines [47-49].

1.8 Scope

- Picric acid is reduced for the first time using aluminium and ultrasound waves.
- Combination of organic solvents is used for the first time in combination with aluminium and ultrasound waves.
- Water as a reaction medium is employed for the first time in combination with aluminium and ultrasound waves.

This greener protocol is a novel method for the reduction of nitro aromatics using aluminium, milder reagents, easy set up and easy work up of reaction which is time aving. Aluminium turnings and aluminium foil is used for the first time with water as a reaction medium. Reduction using this procedure is mild, facile and economical.

1.9 Characterization techniques

Following are the characterization techniques used for analysis of products.

1.9.1 Infrared spectroscopy

Infrared spectroscopy is widely used nondestructive technique for the detection of different functional groups. Each functional groups show peak in a specific region confirming the presence of that functional group in product.

Infrared radiations are used in Infrared spectroscopy. When these radiations interact with a molecule it induces excitation from ground energy state to a higher energy state. The wavelength absorbed is directly proportional to difference of energy between excited and ground state that specific wavelength is characteristic for different functional groups present in structure of the molecule As a result of excitation vibrations are produced in the molecule. There are two types of vibrations one is stretching on and the other one is the bending vibrations. Frequency of bending vibration is low as compare to stretching vibrations.

Sample analyzed in case of IR is easily recoverable; there is no destruction of sample. IR can analyze different type of samples.

1) Powder samples.
2) Solid KBr pallets.
3) Liquid samples.

Plot that is produced on screen contains wave number on x axis and %transmittance or absorbance along y axis.

1.9.2 Thin layer chromatography

TLC or thin layer chromatography is a form of plane chromatography which is performed on a glass or aluminium foil coated with stationary phase usually silica gel, aluminium oxide and cellulose. Sample is applied with the help of dropper, micropipette or a capillary tube at the bottom of the plate. Then plate is placed in a TLC tank containing solvent mixture which is mobile phase. Mobile phase ascends on the TLC through capillary action resulting in the separation of components of a mixture shown in figure 3.9. After that TLC is visualized under UV lamp or placed in iodine jar. This techniques comes very handy, requires less time and better resolution of spots than paper chromatography.

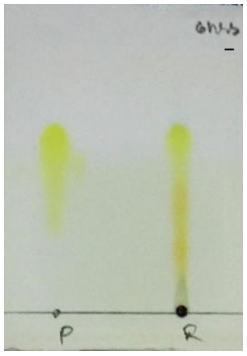


Figure 1.8. TLC plate showing separation of mixture denoted by R.

1.9.3 High performance liquid chromatography

It is an analytical technique that is used to separate a mixture and identify each component of mixture. It involves the passage of pressurized spectroscopic grade solvents through a column containing sample on solid adsorbent. Each component of mixture interacts with solid adsorbent in a different way leading to different flow rates. In this way different components are separated. Column is made up of usually silica and its length varies according to analysis. Pressurized solvents that are used in case of HPLC refer to the mobile phase and include water, methanol, acetonitrile etc. Solid adsorbent material present in the column refers to the stationary phase including silica, polymers etc. Schematic illustration of HPLC is shown if figure 3.10.

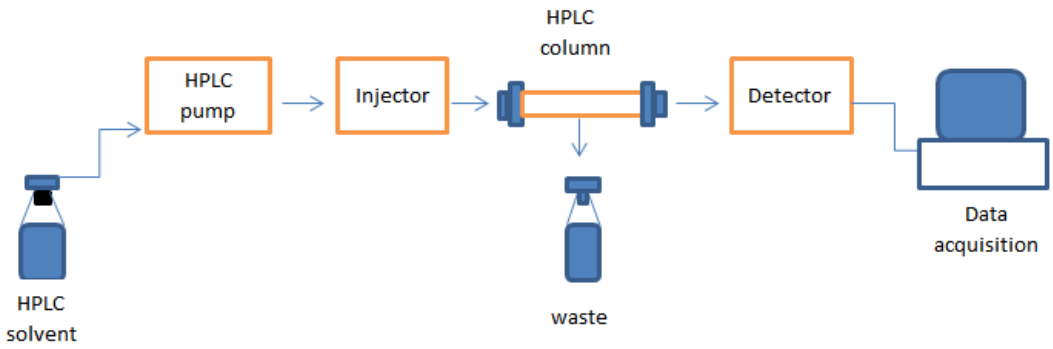


Figure 1.9. Schematic illustration of HPLC.

1.9.4 Nuclear magnetic resonance spectroscopy

NMR spectroscopy is a well-known technique for determination of structure in case of organic molecules. It is a nondestructive technique of analysis. For NMR sample is dissolved in an organic solvent including chloroform, benzene etc. It is associated with magnetic properties of atomic nuclei. Chemical shifts give the evidence of the nature of functional groups present. An NMR spectrum consists of a plot of frequencies of the absorption peaks versus peak intensities. Chemical shift values range in case of proton NMR spectra of the organic compounds are explained by the range from +14 to 0 ppm and by the spin-spin coupling between the protons.

There are two types of NMR spectroscopy.

1) Carbon nuclear magnetic resonance spectroscopy.

2) Proton nuclear magnetic resonance spectroscopy.

^{13}C NMR used in the identification of carbon atoms present in different organic compound, just as proton NMR recognizes hydrogen atoms in a sample. ^{13}C NMR is considered as an important tool for the chemical structure identification of a compound. It detects only the isotope ^{13}C as ^{12}C is not detectable because it is NMR inactive due to zero net spin.

Chapter 2

Literature review

The reduction of nitro aromatic group is powerful and widely used transformation for the introduction of amino group in the molecule. New synthetic strategies are required which are efficient, mild, easy to handle, chemo selective and greener in approach.

2.1 Hydrogenation

G. Neri et al. [52] reported catalytic hydrogenation of 2,4-dinitrotoluene (DNT) . The whole process was carried out in a batch slurry reactor and the catalyst used was 5% Pd/C. Reaction intermediates are identified by GC and HPLC analysis. They found that three intermediates were involved in the reduction of 2,4-dinitro toluene into 2,4-diamino toluene. These were 4 hydroxylamine-2-nitro toluene, 4-amino 2-nitrotoluene and 2-amino-4-nitrotoluene. The mechanism proposed intermediates are formed from DNT through three parallel reactions. Then these intermediates are hydrogenated to diaminotoluene (DAT) by a series of consecutive reactions.

2.1.1 Heterogenous catalytic system

Marcel Hoogenraad et al. [53] reported chemo-selective reduction of nitro compounds containing different functional groups. Hydrogenation was carried out on three important compounds in pharmacy that contain nitro groups using high throughput experimentation (HTE) methods. Different combinations were used in order to find out which combination work better for which substrate. Screening was also performed that showed best reaction condition and combination for each substrate. Analytical techniques used were HPLC chromatography, using an external standard. Side products were identified by LC MS and NMR was used to confirm the products formed.

A very active area of research in the last few decades was the preparation of different supported nanoparticles. Their main advantages were improved reactivity, easy recovery and selectivity of heterogenous catalyst. One of the first examples of selective nanoparticles for the nitro reduction, was reported by Corma and Serna [54]. Gold nanoparticles were supported on TiO_2 or Fe_2O_3. Gold nanoparticles catalyzed the chemo-selective hydrogenation of functionalized nitroarenes with H_2

under mild reaction conditions. There was no accumulation of intermediates especially hydroxylamine. This procedure was compatible with other moieties such as alkenes, aldehydes, nitriles and amides.

M. Lakshmi Kantam et al. [55] reported reduction of nitro aromatic compounds into anilines using palladium that was stabilized using magnesium oxide. Catalyst combination was efficient, chemo-selective and mild. Reduction was done through molecular hydrogen. Yields were good to excellent and the catalyst was reusable. Good activity up to ten cycles of reuse. Catalyst showed tolerance for wide range of functional groups using this methodology. Progress of the reactions was monitored using TLC and GC. Products were characterized using NMR and IR spectroscopic methods.

Hao Wu et al. [56] reported a novel catalyst for the hydrogenation of nitro benzene. They prepared recyclable heterogenous palladium nanoparticles which were stabilized using collagen fibers. To improve the stabilization and immobilization of nanoparticle s on the collagen fibers Epigallocatechin-3-gallate (EGCG) was used. Size of the palladium nanoparticles was about 3-4 nm. Hydrogenation was done under mild conditions. For all the benzenes that were para substituted the order of hydrogenation was as follows

$$p\text{-}OH > p\text{-}NH_2 > p\text{-}CH_3 > p\text{-}Cl$$

The synthesized catalysts were stable, recycled for five times and can be stored in air for two months, due to the strong interactions between EGCG-CF and Pd(0) nanoparticles.

Annie J. Kasparian et al. [57] reported chemo-selective reduction of nitro groups using active aryl halides. Sulfided platinum catalyst was used for the hydrogenation purpose. This hydrogenation approach was efficient. Catalyst was used in very small amount of about 0.10 mmol% and reaction temperature was also low and so the hydrogenation pressure. The high chemoselectivity was attributed to the poisoning effect of the sulphur, which occupies the active sites of platinum therefore enhancing the selectivity in reduction. Yields were also high.

2.1.2 Homogeneous catalytic systems

Homogenous catalytic systems involve the use of molecular hydrogen for the transformation of nitro group into an amino group. Raj. M. Deshpande et al.[58] did chemoselective hydrogenation of substituted nitro aromatics using water soluble complex of iron. The major purpose of their study was to use aqueous phase in order to eliminate the problems related to separation of products and catalyst recovery. They investigated iron ethylenediamine tetra aceticacid disodium salt (Fe^{II}/$EDTANa_2$) as a catalyst for the hydrogenation of nitro-aromatics in a biphasic system. During this method catalyst remained in the aqueous phase whereas solvent substrate and product forms an immiscible phase. Water controlled the exothermicity of reaction at the same time making this process a greener approach. This system was associated with high chemoslectivity and catalyst that can be recycled multiple times.GC was used for the analysis of products.

Amit A. Deshmukh et al. [59] reported the hydrogenation of nitro aryls using Ru(II) Phenanthroline complex using molecular hydrogen in aqueous media. The chemoselectivity of process was very high with complete conversion of substrate. The highest selectivity was achieved at 160 ℃ and pressure of about 2.75 MPa. Metal-to-ligand charge transfer occurs in case of interaction of Ru complex with water. Water was the best solvent with high selectivity however the order for hydrogenation for various solvents is given as follows

methanol < n-butanol < isopropanol < water

This method was cheaper and used ecofriendly solvent but due to leaching of metal in case of catalyst this catalyst cannot be used.

Xin Huang et al. [60] synthesized highly active and selective catalyst. They bayberry tannin (BT) to synthesize a homogeneous Pd(0) catalyst which was used for the hydrogenation of substrates in biphasic system. The main purpose of using BT was to constrain the Pd(0) nanoparticles in the aqueous phase. This was done through interaction between phenolic hydroxyls of BT and Pd. Other functions included control of the particle size and agglomeration prevention. Reactions were carried out at 20 bar and 50 °C. Homogeneous BT-stabilized Pd(0) nanoparticles can be used again and again without the loss in activity and can be stored upto three months without agglomeration.

Gerrit Wienhofer et al. [61] reported hydrogenation of nitro arenes using iron phosphine complexes. Formic acid was used as stoichiometric agent. The complex $[FeF(L_1)][BF_4]$ was synthesized by using $Fe(BF_4)_2.6H_2O$. and phosphine. Reaction conditions include temperature of 120 $^{\circ}$C, concentration of substrate was 0.5 mmol substrate and pressure of hydrogen was 20 bar. Different functional groups were tolerated such as ketones, halogens, terminal and internal double bonds, esters, and ethers. Iron complex was able to activate hydrogen and this method was used for hetero aromatic substrates with good chemoselectivity. Products were analyzed using GC.

2.1.3 Water/gas shift reaction

Kotohiro Nomura[62] reported selective reduction of nitro compounds using ruthenium carbonyl complexes. The reduction was proceeded by-producing hydrogen gas generated from the water-gas shift reaction (WGSR) shown below in equation 2.1.

$$CO+H_2O \longrightarrow CO+H_2$$

Scheme 2.1. Water gas shift reaction [62].

Nitro groups are reduced in high yields using this approach. Small amounts of amines such as dibutylamine, piperidine and triethylamine; were added in the reaction mixture. GC MS was used for the analysis of products. The reduction proceeded in the presence of $Ru_3(CO)_2$ complex under CO (20 atm) /H_20 conditions (150°C) with high yields. Addition of amines resulted in increased rate of reaction. Aromatic nitro compounds were reduced without the other unsaturated groups such as C=O, C=N and C=C being reduced making this approach chemoselective with high yields.

FabioRagaini. and SergioCenini [63] reported the reduction of nitrobenzene using rhodium carbonyl complex in water as a solvent shown in scheme 2.2.

$$PhNO_2 \xrightarrow[CO,\ H_2O]{[Rh(CO)_4]} PhNH_2$$

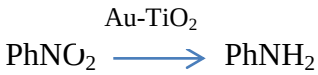
Scheme 2.2. Reduction of nitro group into amino group using Rh complex [63].

The reaction did not require any additives for faster reaction. Addition of bases produced negative effect on overall reaction. Complex of CO ligand with rhodium

provided an active catalyst for the reduction of nitro benzene to aniline. Reaction conditions included 0.07mmol of rhodium complex, water (5 ml), temperature was 200 degree Celsius and reaction time was about 1.5 h. Reaction was chemoselective for nitro group with 95 % yield.

Lequan Liu et al. [64] reported reduction of nitro aromatics using ferric hydroxide supported gold in the presence of carbon monoxide and water. Catalyst was prepared using co precipitation method. Selectivity higher than 98 % were obtained showing that catalyst is highly active and selective. Platinum and palladium catalyst were found to be less chemo-selective as compare to ferric oxide catalyst. Selective hydrogenation of aromatic nitro compounds were first efficiently achieved over Au/Fe(OH)x at 100–120 $^{\circ}$C for 1.5–6 h in the presence of WGSR.

Lin He et al. [65] reported chemo-selective reduction using gold catslyst and WSGR as hydrogen source at room temperature shown in scheme 2. Gold nanoparticles having diameter of 1.9 nm supported on titania showed the best catalytic activity. There was no formation of byproducts such as azo or azoxy compounds. Reaction conditions were optimized in order to get the best results. Pressure of 1 atm was used making this process cheap in terms of equipment as it was preceded in ordinary glass reactor.



Scheme 2.3. Reduction of nitroarene into amine using gold catalyst [65].

FA Westerhaus et al. [66] reported reduction of nitro aromatic compounds using cobalt oxide and nitrogen doped graphene catalyst. Catalyst that was synthesized was reused after each run .After each run catalyst was centrifuged then dried in oven Solvents used were water and THF and their ratios were 1:10 respectively. This approach showed broad range tolerance for different functional groups such as halogens esters and yielding amines with high selectivity. Reduction was preceded using nanostructured cobalt oxide yielding amines in high yields.

2.2 Catalytic transfer hydrogenation

Catalytic transfer hydrogenation methods eliminate the use of any specialized experimental apparatus for example reactors for high temperature and pressure. The

most commonly used reagents for this purpose include formic acid, ammonium formate, hydrazine etc.

T. V. Pratap and S. Baskaran [67] reported formation of formanilides using catalytic transfer hydrogenation. Anhydrous ammonium formate was used as a hydrogen source in the presence of Pd/C to produce formanilides that are very important in synthesis of biologically active compounds. Selectivity of method was tested using different substrates and method was selective in approach. Yields were good to high. Satisfactory spectroscopic data was obtained for each product.

Xia-Bing Lou et al. [68] reported transfer reduction of nitro arenes using gold nano particles. They used ammonium formate as hydrogen source. Gold particles were supported on titania and ammonium formate was used in ethanol. Ammonium formate act as a hydrogen source and also as formylating agent. Reaction conditions involved $PhNO_2$ (1 mmol), catalyst (metal:1 mol%), ethanol (10 ml), ammonium formate (5mmol). Chemo-selective reduction of nitro aromatic compounds occurred in high yields. Conversion and chemoselectivity were determined by GC (internal standard: n-decane) and GC-MS. Mild reaction conditions and low cost of ammonium formate made this process economical at industrial level.

Ivn Sorribes et al. [69] reported Mo_3S_4 cluster catalysts for the reduction of nitro aromatics They showed that that tri nuclear Mo_3S_4 hydrides functionalized with outer diphosphane ligands were highly active catalysts for the selective reduction of nitroarenes to amines. No trace of hydroxylamine was obsereved during the reaction. Reaction conditions involved nitroarene (0.1 mmol), reducing agent (3.5 equiv), catalyst (3 mol %), THF (2 ml). GC analysis was done using hexa decane. 89– 99 % yield was obtained. Use of pressurized sample infusion (PSI) ESI-MS technique, it was demonstrated that cluster catalysis was actually occurring without fragmentation of the catalytically active molybdenum hydride cluster.

Manoj B. Gawande et al. [70] for the first time applied core shell nanoparticles for reduction of nitro aromatic compounds. They used core shell Ag@Ni nanocatalyst. Oleyamine was used as reducing agent and triphenylphosphine as surfactant for preparation of core shell nanoparticles shown in figure 2.1.

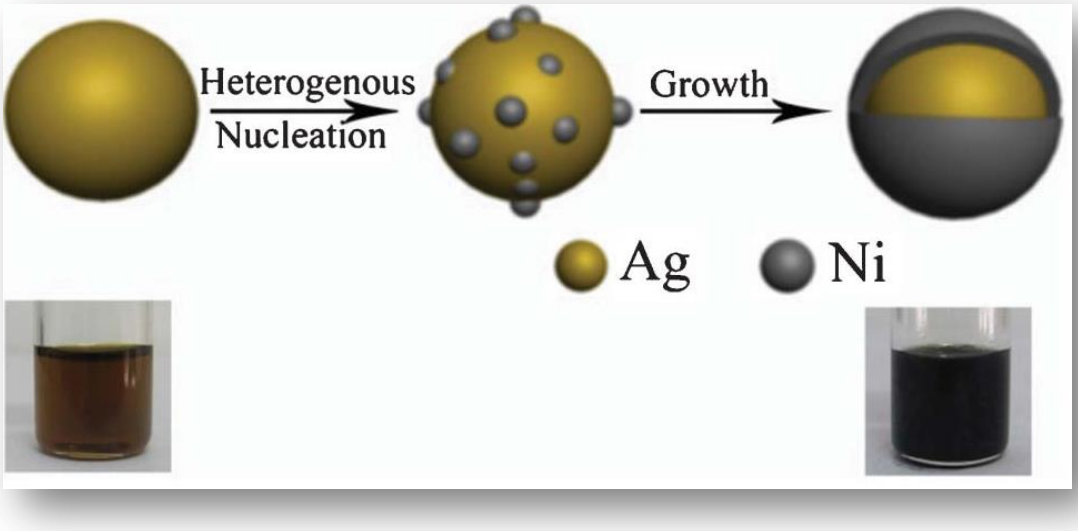


Figure 10. Synthesis of Ag@Ni core-shell magnetic nanocatalyst [70].

Isopropanol was used as a hydrogen source. One of the important features of Ag@Ni is that they were magnetically separable made them useful in applications on industrial scale. Reaction conditions involved nitroarene (1 mmol), KOH (1.5 mmol), 80° C, IPA (3 ml), 50 mg of catalyst. Reaction resulted in successful conversion of nitro compounds into amines with excellent yield (85-94 %).

Lei Yu et al. [71] reported mild and unique approach for reducing nitro arenes using formic acid as hydrogen source. Amines, formamides, benzimidazoles, and dimethlyated amines are prepared using gold based catalyst under mild conditions. GC analysis was done using n-decane as an internal standard. Various hydrogen sources were tested out of which formic acid showed best results and required no addition of extra base. 1 mmol of substrate, FA (3 mmol), catalyst (1 mol% metal), solvent (5 ml) was used.. There was no by product formation. Efficient catalytic system was developed to achieve reduction producing compounds of high synthetic utility in synthetic chemistry.

2.3 Hydride transfer reductions

Hydride transfer reductions involve the transfer of hydride from different sources such as catalyst, additives or from direct reaction. Among the most promising hydride reducing reagents include aluminium hydride [72], sodium borohydride [73], organo

silanes and siloxanes [74] due to their low cost and their ability to tolerate other functional groups.

Jonathan Lipowitz and Sheryl A. Bowman [74] reported polymethylhydrosiloxane as a reducing agent for nitroaromatic compounds. Hydrogenations using a Pd-on-charcoal catalyst provided an example of usefulness of PMHS under mild conditions. High yields were reported Hydrogenation in the presence of PMHS in ethanol at 40-60 degree Celsius yielded amines (95-98 %).

Omid Mazaheri and Roozbeh Javad Kalbasi [73] reported bifunctional catalyst for reduction of nitroarenes. Ni/mZSM-5 and Ni/H-mZSM-5 zeolites were synthesized using template method. Sodium borohydride was used as reducing agent. Catalysts synthesized were very stable and can be reused upto 7 times without the loss in activity. High yield, short reaction times and use of milder conditions made this process efficient and sustainable. Reaction conditions involved nitro arene (2 mmol), H_2O (3 ml), room temperature, catalyst (Ni/H-mZSM-5 or Ni/mZSM-5). TLC was used to monitor the progress of reaction and products were obtained after column chromatography.

Ronald J. Rahaim, Jr. and Robert E. Maleczka [75] reported pd catalyzed silicon hydride reduction of nitro groups in aliphatic and aromatic compounds. Nano particles from Palladium(II) acetate, aqueous potassium fluoride and polymethyl hydrosiloxane (PMHS) reduced nitro groups in high yields at room temperature in high yields.Reaction conditions involved 1 mmol of nitroarene, 5 mol % of $Pd(OAc)_2$, 4 equiv of PMHS, 2 equiv of KF, 2 ml of degassed H_2O, 5 ml of THF, room temperature. Products were isolated through flash chromatography. Replacement of PMHS/KF with Et_3SiH resulted in reduction of aliphatic nitro groups.

Behzad Zeynizadeh and Davood Setamdideh [76] reported reduction of nitro aromatic compounds using sodium borohydride and charcoal. The reaction conditions were optimized to get the best results. They showed that using 4 molar equiv of $NaBH_4$ per 1 molar equiv of substrate in the presence of charcoal (0.4 g), in a mixture of H_2O-THF (1:0.5 ml) at 50–60 degree Celsius is optimal for the complete conversion or reduction of substrate. $NaBH_4$ in the presence of charcoal gently liberates hydrogen gas, therefore hydride attack performs reductions. The hydrolysis of the produced amino-borate intermediate by the presence of water in the reaction mixture makes a

promotion in the reduction. TLC was used to monitor reactions and IR, H-NMR for analysis of product.

Sungho Park et al.[77] reported gold catalysts that were magnetically seperable for reduction of nitro aromatic compunds shown in figure 2.2. Reaction cinditions included nitroarene (0.30 mmol), gold catalyst (0.50 mol%), EtOH (3.0 ml) and hydrosilane (4.5 equiv. based on Si–H) were employed at room temperature under Ar. GC was done using p-cymene as an internal standard. Combination of gold catalyst and hydrosilane was employed for the first time reduced the nitro group in high yield.

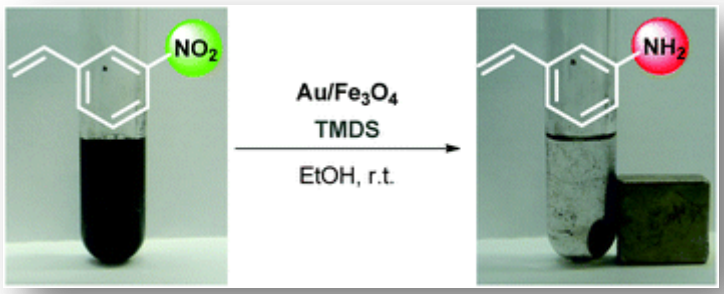


Figure 11. Illustration of reaction of magnetically separable gold catalyst [77].

2.4 Metal free reduction methods

Kwanghee Koh Park et al. [78] used sodium dithionite with dioctyl viologen for the reduction of nitro aromatics. Sodium dithionite was used as electron transfer catalyst in two phase system containing water and dichloromethane. Molar ratio that is used for viologen to the substrate was 1:20. Four electrons reduction resulted in the formation of hydroxylamine whereas 6 electrons resulted in complete reduction of nitro group into an amino group. Method is mild and chemo selective as it did not affect carbonyl, vinyl and cyano functional groups.

Maureen A. McLaughlin and David M. Barnes [79] reported elemental sulphur for the reduction of nitro aromatic compounds in the presence of a mild base. It was shown that 3 equiv each of S_8 and $NaHCO_3$ gave amines in moderate to high yields. This protocol was able to show functional group tolerance against cyano, ester, amide, and chloride. Temperature was kept 130 degree Celsius and DMF was used as a solvent.

This approach did not require the use of transition metals or hydrogen gas and threw light on the capacity of sulfur as an inexpensive 2-electron reductant.

Y Gao et al. [80] reported reduced grapheme oxide as a catalyst for reduction of nitro arene i.e. nitrobenzene. Reduced grapheme oxide promoted transfer of hydrogen from hydrazine and resulted in reduction of nitro benzene into aniline. Nitrobenzene was refluxed for 4 hours in neat hydrazine with 2 wt% graphene oxide resulted in product formation with high yield. This procedure was not further tested for substrates other than nitrobenzene.

Manoranjan Kumar et al. [81] reported glucose as a hydrogen source for reduction of nitro aromatic compounds using water as a solvent. D glucose was used in water and DMSO (1:1) Heating the reaction mixture only with glucose did not result in completion even after 24 hours. Four equivalents of base KOH resulted in selectivity of 99 %. All reactions were carried out using nitroarene (1 mmol), KOH (4 mmol), D-glucose (2 mmol), H_2O: DMSO (1 : 1, 4 ml) at 110 degree Celsius. A mild and practical method employing D-glucose as the hydrogen source with KOH was reported for the reduction of nitro arenes to their corresponding amine.

Sushila Sharma et al. [82] repoted vasicine an alkaloid for the reduction of nitro aromatic compounds in the presence of water as a solvent shown in figure 2.3.

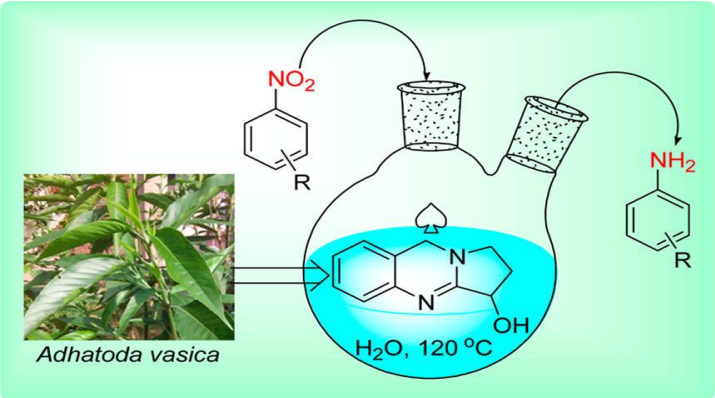


Figure 12. Vascine derived from adhota, used for reduction of nitro group [82].

Reaction conditions involved nitro substrate (0.5 mmol), reducing agent (0.75 mmol), H_2O (4 ml) at 120 °C. Method showed wide range of functional group tolerance against ketones, nitriles, esters, halogens, and heterocyclic rings. Reactions under base-free conditions and water as a solvent made this process advantageous.

1.5 Metal dissolving reductions

Metal dissolving reductions are one of the oldest methods to reduce nitro aromatic compounds [83], [84]. Metals with low oxidation state will act as an electron transfer reagent. Most commonly used metals include samarium [85], aluminium [86], iron [87], zinc [88], indium [89]. These electron transfer reagents act in combination with proton sources such as water, hydrochloric acid, ammonium chloride etc.

Bimal K. Banik et al. [85] reported reduction using samarium and iodine. Simple and convenient method resulted in reduction of nitro groups in the presence of methanol. Catalytic amounts of iodine was required otherwise there was no completion of reaction. Reaction conditions involved 50 mg of the nitro compound in 5 mL of dry methanol, 4 equivalents of samarium and 0.1 equivalent of iodine. Whole reaction was carried out in argon atmosphere. There was no dehalogenation and hydrogenolysis showing that procedure was chemo selective. Polycyclic amines which act as anti-cancer agents were synthesized using this approach.

Christopher J.Moody et al. [89] reported indium for the reduction of nitro aromatics. Wide range of nitro aromatic compounds was tested using indium powder in ethanolic ammonium chloride solution. Reaction conditions involved nitro compound (2.5 mmol) in ethanol (10 ml), saturated ammonium chloride solution (3 ml) and indium powder (2.0 g).Yields of the amines were high. This protocol showed functional group tolerance against halide, ester, amide and nitrile groups.

D. G. Desai et al. [88] reported the reduction of nitro arenes by zinc in DMF and water system. Iron was used along with ferric chloride. Reaction conditions included ferric chloride hexahydrate (15 mmol), Zinc dust (50 mmol) and nitrobenzene (5 mmol) and 100 degree Celsius. Dimethyl formamide and water were used in ratio of 1:1. Progress of reaction is monitored by TLC and products were characterized using IR and PMR.

Krishnamurthy Ramadas and Natarajan Srinivasan [87] reported convenient reduction by using iron and ammonium chloride. Reaction was carried out in a neutral medium and resulted in good yields of desired products. Reaction conditions were optimized and the ratio of substrate to that of iron and ammonium chloride was 1:3:5. TLC was

used to monitor the progress of reaction. Since the reaction was carried out in a neutral medium easy work up resulted in product isolation.

1.5.1 Aluminium and ultrasound mediated reductions

D.Nagaraja and M.A.Pasha [86] reported ultrasound mediated reduction using aluminium and ammonium chloride. Nitro aromatic compounds were refluxed using aluminium and ammonium chloride in methanol. Acoustic cavitation induced by ultrasound waves promoted reduction with greater rate. All the compounds were characterized by comparison with authentic sample. Reduction proceeds via single electron transfer mechanism.

M.A. Pasha et al. [90] reported reduction using aluminium and sodium hydroxide in methanol. Reaction conditions involved nitroarene (10mmol), aluminium foil (82mg, 30mgcut into small pieces) and methanol (10 ml) sodium hydroxide (8 g, 20 mmol). Contents were sonicated at 35KHz. Progress of reaction was monitored using TLC and GC MS. Functional group tolerance was shown against Substituents like –Cl, –NH_2,–CH_3, –OCH_3, –OH, –COOH groups.

MA Pasha and V.P. Jayashankara [91] did a comparative study by using different hydrogen sources to test which one gives the best result when used with aluminium in methanol. Anilines were formed as a result of reduction with aluminium. Reactions were performed in the presence and absence of ultrasound waves. Ultrasound mediated reactions gave better results. Out of different ammonium halides ammonium bromide showed best results with least reaction times and high yields.

Simplicity, cost effectiveness, easy availability of reagents, mild conditions, green methodology and practicality associated with use of aluminium and ultra sound mediated reactions fascinated me and forced me to use this approach in my research.

Chapter 3

Experimental work

This chapter will explain the experimental work plan to achieve the outlined objectives.

3.1 Synthesis of Meta dinitrobenzene or 1,3-Dinitrobenzene

3.1.1 Materials required

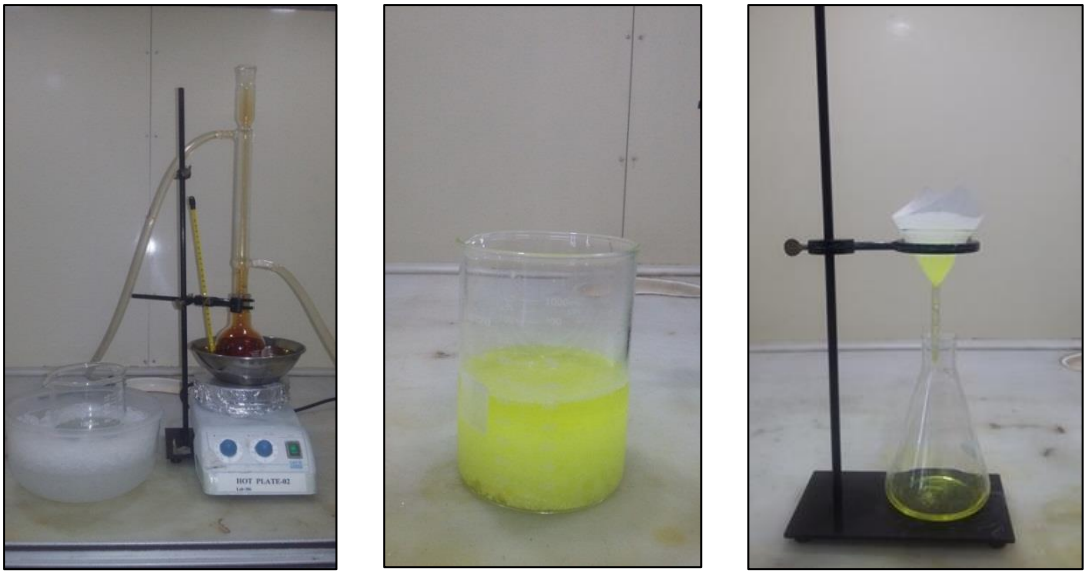
Concentrated sulphuric acid (100 %SigmaAldrich), Concentrated nitric acid, Nitrobenzene (Sharlau), Ethanol.

3.1.2 Procedure

Took 500 ml round bottom flask and placed 37.5 g or 21 ml of concentrated sulphuric acid and 22.5 g or 15 ml of nitric acid. Aromatic hydrocarbons are nitrated by the replacement of hydrogen with nitro group in the presence of mixture of nitric and sulphuric acid (mixed acid reagent).

Few pieces of unglazed porcelain were added in order to avoid bumping. Attached the reflux condenser and placed the whole assembly in fume hood. Slowly nitrobenzene was added in the form of portions of 3 ml. Total amount of nitrobenzene used was 12.5 ml. Each portion of nitrobenzene was added and shaking of the flask was done for thorough mixing. Then the mixture was heated for about 30 minutes at 100 degree Celsius shown in figure 3.1(a). Allowed the mixture to cool and then 500 ml of chilled water was added as shown in figure 3.1(b). The reaction mixture was filtered and then the residue was washed with water to ensure complete washing.

Transferred the crude product into 250 ml round bottom flask and then 120 to 130 ml of rectified spirit or ethanol was added. Using reflux condenser the mixture was heated until the solid dissolved. The solution was filtered using warm funnel shown in figure 3.1(c). Colorless crystals appeared on cooling shown in figure 3.2. Yield of reaction was 73 %, 15 g of meta-dinitrobenzene was formed [92].



(a) (b) (c)

Figure 3.1. (a) Reflux of nitrobenzene in acid mixture. (b) Addition of reaction mixture in chilled water. (c) Filtration of reaction mixture.

(c)

Figure 13. Needle shaped crystals of dinitrobenzene.

3.2 Synthesis of 2,4,6-triaminophenol

3.2.1 Materials required

Picric acid, Sodium borohydride, Charcoal, THF, Ethyl acetate, n-hexane, Carbon tetrachloride, Diethyl ether.

3.2.2 Procedure

15 ml round bottom flask equipped with condenser and magnetic stirrer was placed on hotplate. Solution of 229 mg of picric acid was made in water and THF(1:1.25ml).

Then 800 mg of charcoal was added and the solution was stirred for about 10 minutes at room temperature. Then transferred the whole assembly to a hotplate heated at 50-60 degree Celsius. To resulted mixture 444 mg of sodium borohydride was added in portions until the completion of reaction. Progress of reaction was monitored by TLC using ethyl acetate and n-hexane in ratio of 9:1 respectively. At the end of reaction the mixture was filtered and it was dried over anhydrous sodium sulphate. A short column chromatography of the resulting crude mixture was done using eluent carbon tetra chloride and diethyl ether in ratio of 5:3 respectively, resulted in pure product. Yield of the reaction was 97 % [76].

3.3 Reduction protocol using aluminium and ultrasound waves

3.3.1. Equipment used

Ultrasonic bath Elmasonic 60 H was used for all the reactions. Frequency of sonication bath was 37 kHz. Instrument is shown in figure 3.3.

Figure3.2. Elmasonic 60 H sonication bath.

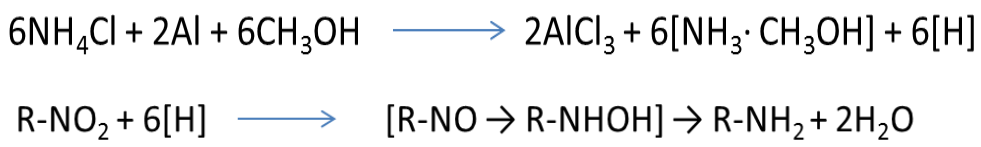
3.3.2 Optimization with nitrobenzene

3.3.2.1 Materials required

Nitrobenzene, Aluminium turnings, Ammonium chloride, Methanol, sodium hydroxide (Sigma Aldrich), Anhydrous sodium sulphate, Distilled water.

3.3.2.3 Experiment no 1

1 mmol of nitrobenzene, 3 mmol of aluminium turnings, 3 mmol of ammonium chloride were placed in 50 ml round bottom flask or conical flask. About 10 ml of methanol was added in reaction mixture, clear solution was formed shown in figure 3.4 (a) and then the reaction mixture was placed in sonication bath for 3 hours at 35 degree Celsius. Progress of reaction was monitored by TLC. Mobile phase used was n- hexane and ethyl acetate in the ratio of 7:3. On the completion of reaction solution turned yellowish orange as shown in figure 3.4(b) in appearance and there was no reactant left on the TLC plate shown in figure 3.4 (d). Reaction mixture was filtered. Solvent was evaporated using rotary evaporator. To the dried reaction mixture about 30 ml of distilled water was added. Resulting solution was acidic. It was neutralized by adding 4 M solution of sodium hydroxide until PH changes to 9. Then extraction was done by using 20 ml of ethyl acetate shown in figure 3.4(c). Organic layers containing product were combined, dried using anhydrous sodium sulphate and then solvent was evaporated to get solid product. Yield of aniline was 51 %. Scheme is shown in scheme 3.1.



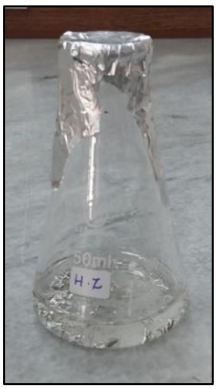
R = Aryl

Scheme 3.1. Reduction of nitrobenzene into aniline.

Given bellow table is depicting optimization done with nitrobenzene using different reaction conditions and using different amount of reagents.

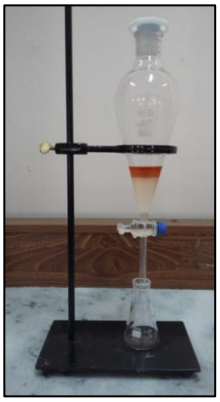
Table 3.1. Optimization of reaction conditions in case of nitro benzene.

Substrate	Ratio of RNO_2:Al:NH_4Cl	Time in hours	Temperature	Solvent	Colour **Yellow**
Nitrobenzene	2:3:3	3	40°C	Methanol	Yellow
Nitrobenzene	2:7:6	2	40°C	Methanol	Yellow
Nitrobenzene	2:3:3	2:30	40°C	Methanol+water=9:1	Dirty green
Nitrobenzene	2:3:3	1	40°C	Methanol+water=8:2	Dirty green



(a)

(b)



(c)

(d)

Figure 3.3. (a) Reaction mixture before sonication. (b) Reaction mixture after completion. (c) Solvent extraction with ethyl acetate. (d) TLC showing completion of reaction.

3.3.3 Optimization with 1,3-dinitrobenzene

3.3.3.1 Materials required

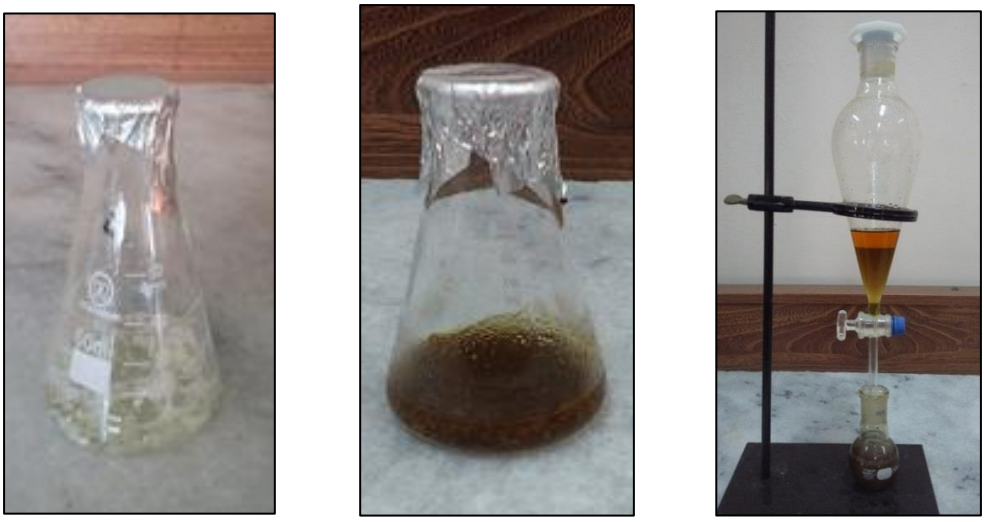
1,3-dinitro benzene, Aluminium turnings, Ammonium chloride, Methanol, Ethyl acetate, n-hexane, Anhydrous sodium sulphate and Sodium hydroxide.

3.3.3.2 Experiment no 2

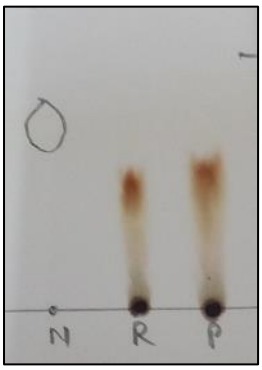
Took 50 ml round bottom flask and then 1 mmol of 1,3-dinitrobenzene, 6 mmol of aluminium turnings and 6 mmol of ammonium chloride were added. About 10 ml of methanol was added to mixture forming colorless solution shown in figure 3.5(a). The reaction mixture was placed in a sonication bath at 40 degree Celsius for 3 hours. Progress of reaction was monitored by TLC shown in figure 3.5(d). Mobile phase used was n-hexane and ethyl acetate in the ratio of 2:8. On the completion of reaction solution turned brown in appearance shown in figure 3.5(b) and there was no reactant left on the TLC plate. Reaction mixture was filtered. Solvent was evaporated using rotary evaporator. To the dried reaction mixture added about 30 ml of distilled water. Resulting solution was acidic. It was neutralized by adding 4 M solution of sodium hydroxide until PH changes to 9. Then solvent extraction was done by using 20 ml of ethyl acetate shown in figure 3.5(c). Organic layers containing product were combined dried using anhydrous sodium sulphate and then solvent was evaporated to get solid product. Yield of 1,3 diaminobenzene was 50 %.Given bellow table is depicting optimization done with 1,3-dinitrobenzene using different reaction conditions and using different amount of reagents.

Table 3.2. Optimization done in case of 1,3-dinitrobenzene.

Substrate	Ratio of RNO_2:Al:NH_4Cl	Time (hours)	Temperature	Solvent	Colour
Dinitrobenzene	1:3:3	5	40°C	Methanol	Brown
Dinitrobenzene	1:6:6	3	40°C	Methanol	Brown
Dinitrobenzene	1:6:6	4	40°C	Methanol+water=9:1	Brown
Dinitrobenzene	1:6:6	5	40°C	Methnaol+Water=8:2	Brown



(a) (b) (c)



(d)

Figure 3.4. (a) Reaction mix before sonication. (b) Reaction mixture after completion. (c) Solvent extraction with ethyl acetate (d) TLC showing progress of reaction.

3.3.4 Optimization with picric acid

3.3.4.1 Materials required

Picric acid, Aluminium turnings, Ammonium chloride, Methanol, Ethyl acetate, n-Hexane, Anhydrous sodium sulphate and Sodium hydroxide.

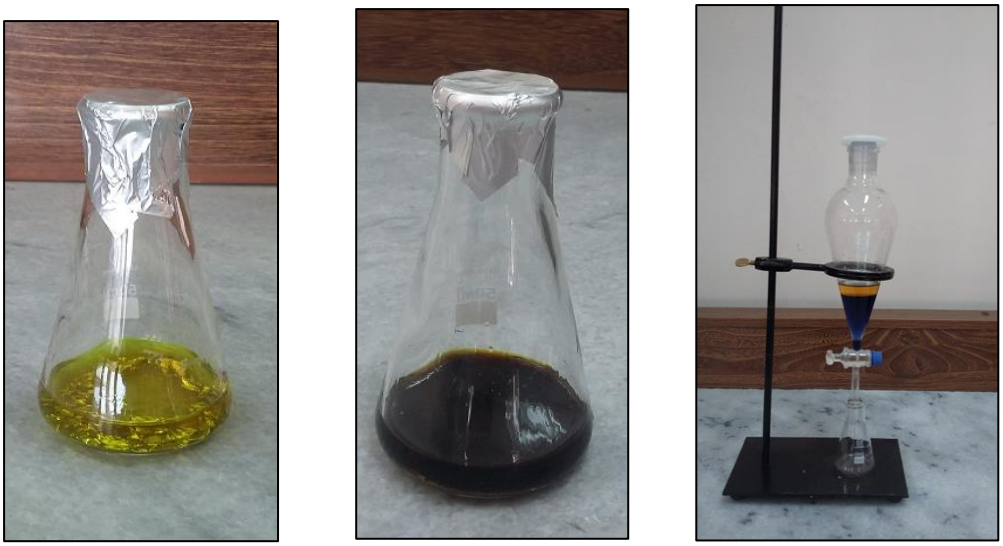
3.3.4.2 Experiment no 3

1 mmol of picric acid, 18 mmol of aluminium turnings and 27 mmol of ammonium chloride were added in 50 ml conical flask. About 10 ml of methanol was added to mixture forming yellow solution shown in figure 3.6 (a). The reaction mixture was

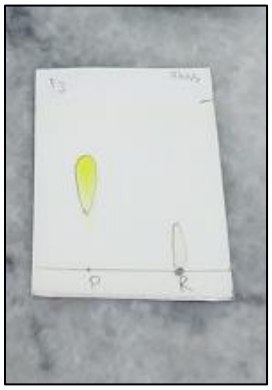
placed in a sonication bath at 40 degree Celsius for 9 hours. Progress of reaction was monitored by TLC. Mobile phase used was n hexane and ethyl acetate in the ratio of 1:9. On the completion of reaction solution turned viscous dark brown in appearance shown in figure 3.6(b) and there was no reactant left on the TLC plate shown in figure 3.6(d). Reaction mixture was filtered. Solvent was evaporated using rotary evaporator. To the dried reaction mixture added about 30 ml of distilled water. Resulting solution was acidic. It was neutralized by adding 4M solution of sodium hydroxide until PH changes to 9. Then solvent extraction was done by using 20 ml of ethyl acetate shown in figure 3.6(c). Organic layers containing product were combined dried using anhydrous sodium sulphate and then solvent was evaporated to get solid product. Yield of 2,4,6 triaminophenol was 61 %.Given bellow table is depicting optimization done with picric acid using different reaction conditions and using different amount of reagents.

Table 3.3. Optimization of reaction conditions in case of picric acid.

Substrate	Ratio of RNO_2:Al:NH_4Cl	Time (hours)	Temperature	Solvent	Colour
Picric acid	1:3:3	6hours: 40minutes	40°C	Methanol	Dark brown
Picric acid	1:9:18	9	40°C	Methanol	Dark brown
Picric acid	1:18:27	3	40°C	Methanol	Dark brown
Picric acid	1:27:27	12	40°C	M+W=9:1	Dark brown



(a) (b) (c)



(d)

Figure 3.5. (a)Reaction mixture before sonication (b)Reaction mixture after completion (c) Solvent extraction with ethyl acetate (d)TLC showing completion of reaction.

3.4 Water mediated reduction reactions using Aluminium and ultrasound waves

3.4.1 Optimization with nitrobenzene

3.4.1.1 Materials required

Nitrobenzene, Aluminium foil, Ammonium chloride, 2 wt% solution of CTAB (cetyl trimethylammonium bromide), Sodium bicarbonate, Dilute solution of hydrochloric acid Anhydrous sodium sulphate, Distilled water.

3.4.1.2 Experiment no 1

8 ml of 2 wt% solution of CTAB and 2 ml of dilute solution of hydrochloric acid were added in 50 ml conical flask. Then 1 mmol of nitrobenzene was added in the flask and sonication was done for about 15 minutes to form clear solution containing no insoluble material. Then 6 mmol of aluminium foil and 3 mmol of ammonium chloride were added to conical flask.. Then the reaction mixture was sonicated in sonication bath for about 3 hours at 40 degree Celsius, resulted in completion of reaction. Progress of reaction was monitored by TLC (n hexane : ethyl acetate = 7:3). After the completion of reaction the reaction mixture was filtered and 30ml of water was added. Concentrated solution of sodium bicarbonate was added effervescence appeared shown in figure 3.7. After about 15 minutes the solution was filtered and organic matter was then extracted into ethyl acetate (3 portions of 20 ml each). Combined organic layers were dried using anhydrous sodium sulphate and solvent was evaporated using rotary evaporator. Yield of reaction was 48 %.

Figure 3.6. Effervescence on addition of $NaCHO_3$.

3.4.2 Optimization with 1,3- dinitrobenzene

3.4.2.1 Materials required

1,3-dinitrobenzene, Aluminium foil, Ammonium chloride, 2 wt% solution of CTAB (cetyltrimethyl ammonium bromide), Sodium bicarbonate, Dilute solution of hydrochloric acid, Anhydrous sodium sulphate, Distilled water.

3.4.2.2 Experiment no 2

About 8 ml of 2 wt% solution of CTAB and 2 ml of dilute solution of hydrochloric acid were placed in 50 ml conical flask. Then 1 mmol of 1,3-dinitro benzene was added in the flask and sonication was done for about 15 minutes to form clear solution containing no insoluble material. Then 6 mmol of aluminium foil and 6 mmol of ammonium chloride were added to resulting mixture. The reaction mixture was placed in sonication bath for about 6 hours at 40 degree Celsius until the completion of reaction. Progress of reaction was monitored by TLC (n-hexane : ethyl acetate = 2:8). After the completion of reaction filtered the reaction mixture was filtered and rest of work up was same as mentioned in 3.4.1.Yield was 46 %.

3.4.3 Optimization with picric acid

3.4.3.1 Materials required

Picric acid, Aluminium foil, Ammonium chloride, 2 wt% solution of CTAB (cetyltrimethyl ammonium bromide), Sodium bicarbonate, Dilute solution of hydrochloric acid Anhydrous sodium sulphate, Distilled water.

3.4.3.2 Experiment no 3

8 ml of 2 wt% solution of CTAB and 2 ml of dilute solution of hydrochloric acid were placed in 50 ml conical flask. Then 1 mmol of picric acid was added in the flask and sonicated for about 15 minutes to form a yellow solution containing no insoluble material. Then 9 mmol of aluminium foil and 9 mmol of ammonium chloride were added to resulting mixture. Then sonication was done in sonication bath for about 14 hours at 40 degree Celsius resulted in completion of reaction. Progress of reaction was monitored by TLC (n hexane : ethyl acetate = 1:9). After the completion of reaction mixture was filtered and work up was same as mentioned in section 3.4.1.Yield of reaction was 47 %.

3.5 Water mediated reduction with aluminium on heating

3.5.1 Materials required

Materials are same as mentioned in section 3.4.1.1.

3.5.2 Experiment no 1

About I mmol of nitrobenzene was placed in 50 ml conical flask. Then12 mmol of aluminium, 2 mmol of ammonium chloride were added in 10 ml of methanol. The reaction mixture was heated on a hot plate maintained at 60 degree Celsius for about 8 hours with continuous stirring. Completion of reaction was depicted by TLC and the color of solution turned brown as shown in figure 3.8. Work up was same as explained in experiment no 1 of section 3.4.1.2.

Figure 3.7. Brown colour of reaction mixture on completion of reaction.

Chapter 4

Results and discussion

This chapter will throw light on the results obtained from experimental procedures and confirmation of product formation from various techniques.

4.1 Optimization results

Optimization was done using varying amounts of starting material, catalyst, solvent and salt. Optimization was done with all the substrates including nitrobenzene, 1,3-dinitrobenzene and picric acid. M indicates methanol, A stands for acetone, S for substrate and W for water in table 4.1. All optimization procedures are summarized in the form of table 4.1.

Table 4.1. Optimization done with nitrobenzene,1,3-dinitrobenzene and picric acid.

Starting material	**Solvent**	**Time (hour)**	**T ^{o} C**	**S:Al:NH_4Cl**	**Colour**
Nitrobenzene	Methanol	3hrs	35	2:03:03	Yellowish orange
Nitrobenzene	Methanol	3hrs	35	2:06:03	Greenish
Nitrobenzene	Methanol	2hrs	35	2:07:06	light yellow
Nitrobenzene	Methanol	5hrs	40	1:03:03	light yellow
Nitrobenzene	Methanol	1.5hrs	40	1:03:03	Conc,dark yellow
Nitrobenzene	M+W=9:1	4hrs	40	2:03:03	Dirty green
Nitrobenzene	M+W=9:1	2:30hrs	40	2:03:03	Dirty green
Nitrobenzene	M+W=7:3	5hrs	40	2:03:03	Viscous green
Nitrobenzene	M+W=8:2	1hr	40	2:03:03	Green
Nitrobenzene	M+W=8:2	5hrs (Incomplete)	40	2:03:12	Yellow
Nitrobenzene	A+W=8:2	3hrs (Incomplete)	40	2:03:03	Clear solution
Nitrobenzene	A+W=7:3	3hrs	40	2:03:03	Light yellow

Nitrobenzene	A+W=6:4	3hrs	40	2:03:03	Dark yellow
Nitrobenzene	W+A=5:5	No Reaction	40	2:03:03	Clear solution
Nitrobenzene	W+A=6:4	1hr	40	2:03:03	Viscous white
Nitrobenzene	W+A=6:4	2:30hrs (No reaction)	40	2:06:06	Clear solution
Nitrobenzene	Water	3.5hrs	40	1:06:03	Yellowish orange
1,3-dinitrobenzene	Methanol	3hrs	40	1:06:06	Brown
1,3-dinitrobenzene	M+W=8:2	5hrs	40	1:06:06	Brown
1,3-dinitrobenzene	A+W=6:4	6hrs	40	1:06:06	Brown
1,3-dinitrobenzene	Water	6hrs	40	1:06:06	Brown
Picric acid	Methanol	6:40hrs	40	1:03:03	Viscous dark brown
Picric acid	Methanol	14hrs (incomplete)	40	1:09:09	Viscous dark brown
Picric acid	Methanol	9hrs	40	1:09:18	Viscous dark brown
Picric acid	Methanol	4hrs	40	1:18:27	Dark brown
Picric acid	M+W=9:1	14hrs (incomplete)	40	1:18:27	Viscous dark brown
Picric acid	M+W=8:2	14hrs (incomplete)	40	1:18:27	Viscous dark brown
Picric acid	M+W=9;1	12hrs	40	1:36:54	Viscous dark brown
Picric acid	M+W=8:2	8hrs	40	1:36:54	Viscous dark brown
Picric acid	M+W=7:3	6hrs	40	1:36:54	Viscous dark brown

Picric acid	M+W=6:4	6hrs	40	1:36:54	Viscous dark brown
Picric acid	M+W=9:1	13:30hrs	40	1:18:09	Viscous dark brown
Picric acid	M+W=8:2	13:30hrs	40	1:18:09	Viscous dark brown
Picric acid	M+W=8:2	7hrs	40	1:27:09	Viscous dark brown
Picric acid	M+W=9:1	9hrs	40	1:27:09	Viscous dark brown
Picric acid	M+W=9:1	8hrs	40	1:27:09	Viscous dark brown
Picric acid	M+W=6:4	8hrs	40	1:27:09	Viscous dark brown
Picric acid	M+W=7:3	8hrs	40	1:27:09	Viscous dark brown
Picric acid	M+W=9:1	12hrs	40	1:27:27	Viscous dark brown
Picric acid	M+W=8:2	8hrs	40	1:27:27	Viscous dark brown
Picric acid	M+W=7:3	7hrs	40	1:27:27	Viscous dark brown
Picric acid	M+W=6:4	5hrs	40	1:27:27	Viscous dark brown
Picric acid	Water	9hrs	40	2:24:04	Dark brown

Out of all these optimization best results are selected with minimum reaction time and lesser amount of reagents after repeated experiments. Table 4.2 is tabular presentation of best results.

Table 4.2. Best Optimization results.

Starting material (S)	**Aluminium form**	**S:Al:NH_4Cl**	**Solvent**	**Time (hour)**	**Temperature** ^{o} C	**Yield %**	**Product**
Nitrobenzene	Turnings	1:3:3	Methanol	1.5	40	51	Aminobenzene
	Turnings	1:3:3	M+W=8:2	2	40	49	Aminobenzene
	Turnings	1:3:3	A+W=6:4	3	40	46	Aminobenzene
	Al foil	1:3:6	Water	3	40	48	Aminobenzene
1,3-dinitrobenzene	Turnings	1:6:6	Methanol	3	40	50	1,3-Diaminobenzene
	Turnings	1:6:6	M+W=8:2	5	40	47	1,3-Diaminobenzene
	Turnings	1:6:6	A+W=6:4	6	40	45	1,3-Diaminobenzene
	Al foil	1:6:6	Water	6	40	46	1,3-Diaminobenzene
Picric acid	Turnings	1:6:6	Methanol	7	40	61	2,4,6-Triaminophenol
	Turnings	1:18:27	Methanol	3	40	61	2,4,6-Triaminophenol
	Turnings	1:27:27	M+W=9:1	12	40	59	2,4,6-Triaminophenol
	Turnings	1:27:27	M+W=8:2	6	40	56	2,4,6-Triaminophenol
	Turnings	1:27:27	M+W=7:3	7	40	54	2,4,6-Triaminophenol
	Turnings	1:27:27	M+W=6:4	5		51	2,4,6-Triaminophenol
	Turnings	1:27:27	Water	9	40	47	2,4,6-Triaminophenol
	Al foil	1:9:9	Water	14	40	47	2,4,6-Triaminophenol

All the nitro aromatic compounds showed moderate yields on reduction with aluminium and ultrasound waves. On increasing reaction temperature reactions were completed in relatively shorter time. Different solvent combinations were used for reduction purpose. Methanol was used in the model reaction. Further optimization

was done using combination of methanol with water, acetone with water and in the last pure water was used as a reaction medium for reduction of poly nitro aromatics. In this way different solvents were tested for the reduction. Moreover two forms of aluminium were used for the reduction of poly aromatic compounds i.e turnings and foil. Reductions with aluminium foil took more time as compare to reactions with turnings and yielded mixture of products.

4.2 Characterization results

4.2.1 TLC results

Thin layer chromatography is a handy analysis technique used in the organic chemistry for checking progress of reaction and also completion of reaction by comparing with standard. TLC was done using glass supported silica plates.

Nitrobenzene

Nitrobenzene was the first substrate containing single nitro group for the reduction. TLC was used to check progress of reaction. 3 spots were applied first was of the reactant that is nitrobenzene, second spot was of the reaction mixture and the third spot was of the standard which was aniline or aminobenzene. Aniline was the expected product of reduction of nitro benzene with aluminium and ultrasound waves. Mobile phase used was combination of two solvents i.e n-hexane and ethyl acetate. The relative ratio of n-hexane to ethyl acetate was 7:3 respectively. After the completion of reaction spot of reaction mixture travelled at distance equal to the distance covered by aniline as shown in figure 4.1. This confirmed the formation of expected product.

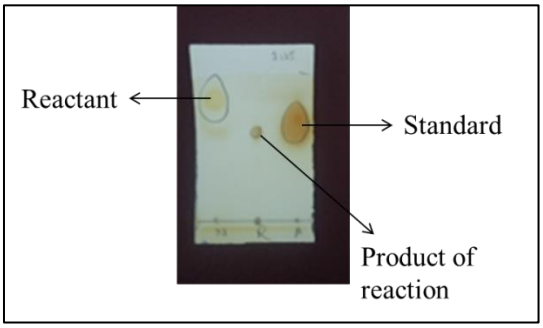


Figure 4.1. TLC showing completion of reaction and formation of aniline.

1,3-diaminobenzene

1,3-dinitroitrobenzene was the second substrate containing two nitro groups at 1 and 3 position for the reduction. TLC was used to check progress of reaction . 3 spots were applied first was of the reactant that is 1,3-dinitrobenzene, second spot was of the reaction mixture and the third spot was of the standard which was 1,3-diaminobenzene. 1,3-diaminobenzene was the expected product of reduction of dinitrobenzene with aluminium and ultrasound waves. The relative ratio of n-hexane to ethyl acetate was 2:8 respectively. After the completion of reaction spot of reaction mixture travelled at distance equal to the distance covered by standard shown in figure 4.2. This confirmed the formation of expected product.

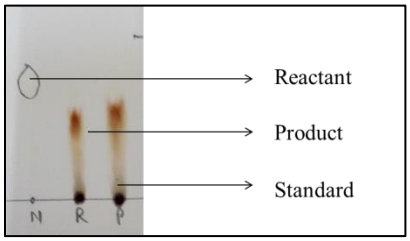
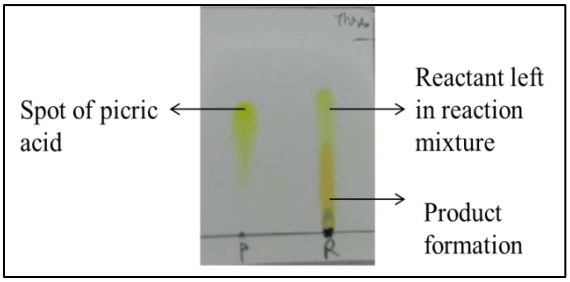


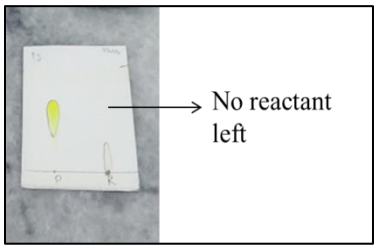
Figure 4.2. TLC showing completion of reaction and formation of 1,3-diaminobenzene.

.**Picric acid**

Picric acid was the third substrate containing three nitro groups at 2,4and 6 position for the reduction. TLC was used to check progress of reaction. 2 spots were applied first was of the reactant that is picric acid, second spot was of the reaction mixture. In case of picric acid there was no standard available so completion of reaction was equal to the time when there was no reactant left. Figure 4.3 (a) shows the TLC in which the reaction was not complete and reactant was still there whereas (b) shows the TLC where reaction was complete and there was no reactant left. In this way completion of reaction of reaction was determined. The relative ratio of n-hexane to ethyl acetate was 1:9 respectively.



(a)



(b)

Figure 4.3. (a) TLC showing incomplete reaction. (b) TLC showing completion of reaction.

2,4,6-triaminophenol was the expected product formed from reduction of picric acid. It was confirmed by comparison with standard which was also synthesized in the laboratory. Standard and product of aluminium reduction travelled at same distance confirming the synthesis of 2,4,6-triaminophenol shown in figure 4.4.

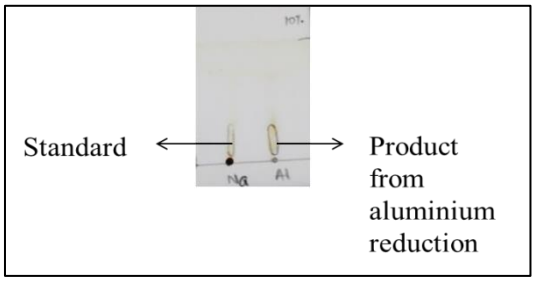


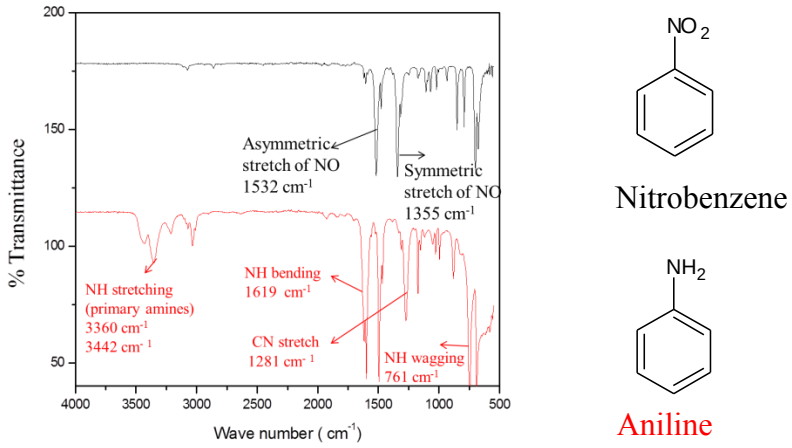
Figure 4.4. TLC showing comparison of product with standard.

4.2.2 IR analysis

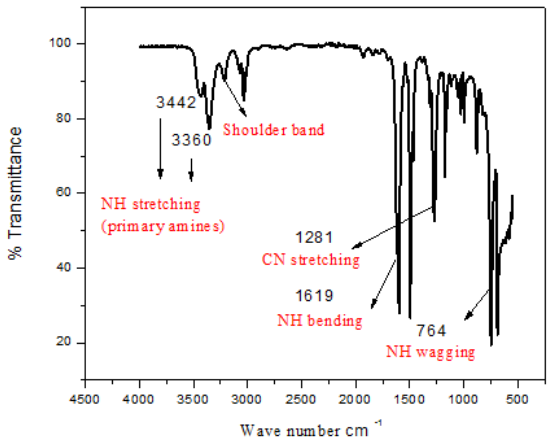
Infrared analysis is an analytical tool that confirms various functional groups present in our product. This technique is used for the qualitative analysis of products.

Amino benzene

Amino benzene is the reduction product of nitrobenzene. Figure 4.5 (a) shows the comparison of reactant i.e. nitro benzene with product amino benzene. The nitro group shows strong signal at 1400 to 1600 cm^{-1} which are completely disappeared in aminobenzene. IR analysis of amino benzene showed various peaks that tell about the functional groups present in the structure of amino benzene. Amino benzene consists of phenyl ring attached to an amino group. Figure 4.5 shows IR spectra of amino benzene.



(a)



(b)

Figure 4.5. (a) Comparison of IR spectrum of nitrobenzene and amino benzene. (b) IR spectrum of aminobenzene.

The characteristic IR absorption of symmetric and asymmetric stretching vibrations of NH_2 are shown in the region of 3300-3500 cm $^{-1}$. NH_2 bending vibrations are depicted by peak at 1619 cm $^{-1}$. NH_2 wagging vibrations are also observed at 764 cm $^{-1}$. Ring carbon and nitrogen stretching vibrations are shown at 1281 cm $^{-1}$.

1,3-diaminobenzene

1,3-diaminobenzene is the product of reduction of 1,3-dinitrobenzene. Figure 4.6 shows the comparison of reactant i.e. 1,3-dinitrobenzene with product 1,3-diamino benzene. The nitro group group shows strong signal at 1400 to 1600 cm^{-1} which are completely disappeared in 1,3-diaminobenzene. This compound also showed various peaks in the IR spectra confirming different functional group vibrations. 1,3-diaminobenzene consists of two amino groups at 1 and 3 positions. IR spectra of 1,3-diaminobenzene is shown in figure 4.6.

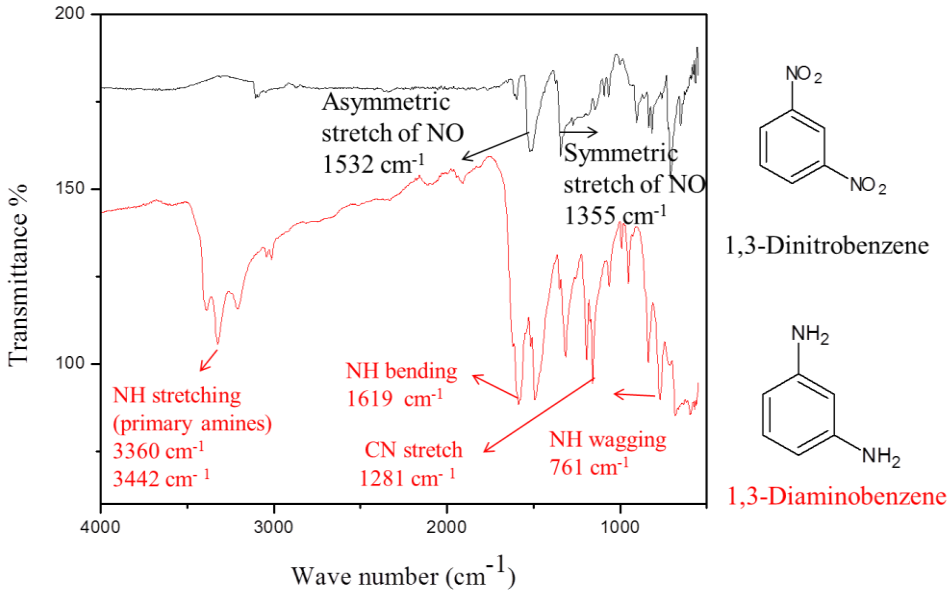
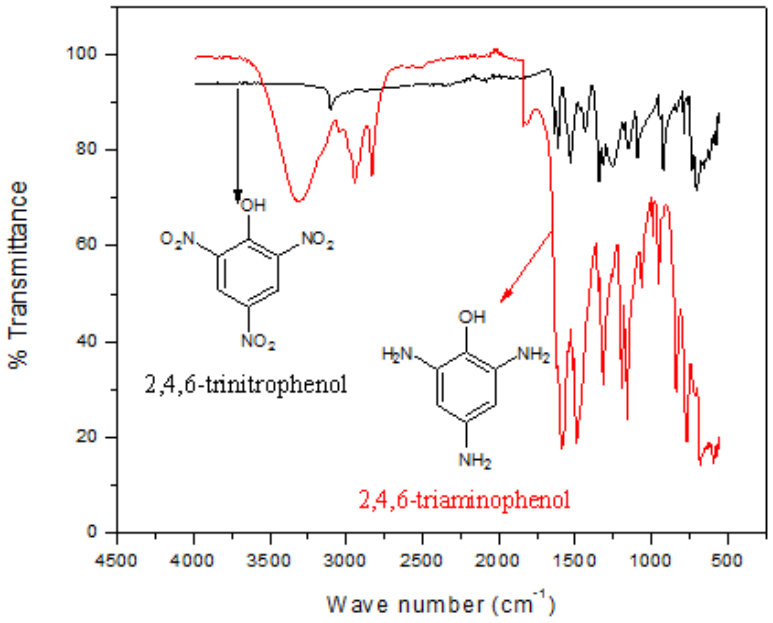


Figure 4.6. Comparison of IR spectrum of 1,3-dinitrobenzene and 1.3-diaminobenzene..

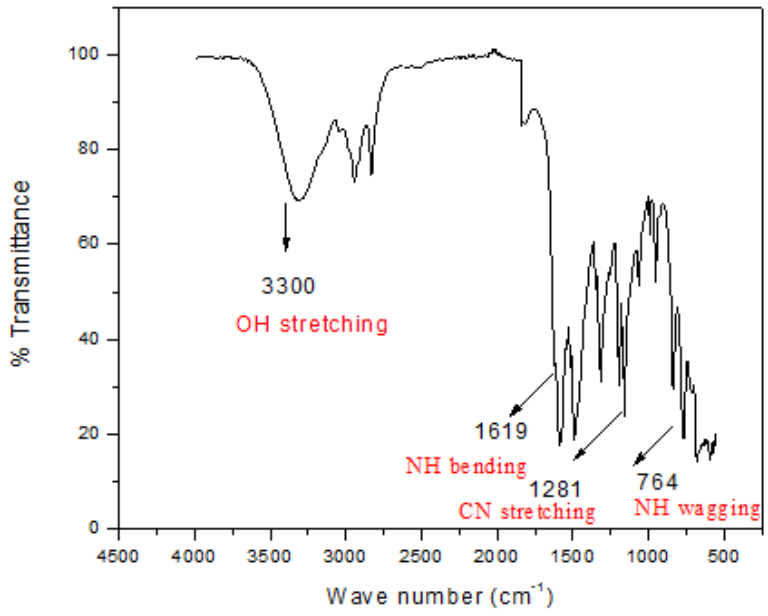
Like amino benzene 1,3-diaminobenzene also showed characteristic IR absorption in the region 3000 to 3500 cm $^{-1}$. NH_2 stretching vibrations are clearly visible. Bending vibrations are also shown at 1619 cm $^{-1}$.CN stretching and NH wagging are shown at 1281 cm $^{-1}$ and 764 cm $^{-1}$ respectively.

2,4,6-Triaminophenol

2,4,6-triaminophenol is the reduction product of picric acid. It consists of 3 amino groups at 2,4 and 6 postions and one hydroxyl group at 1 position. Figure 4.6 (a) shows the comparison of reactant i.e. 2,4,6-trinitrophenol with product 2,4,6-triaminophenol. The nitro group shows strong signal at 1400 to 1600 cm^{-1} which are completely disappeared in 2,4,6-triaminophenol. IR spectra of 2,4,6-triaminophenol is shown in the figure 4.7.



(a)



(b)

Figure 4.7. (a) Comparison of IR spectrum of 1,3-dinitrobenzene and 1.3-diaminobenzene. (b) IR spectrum of 1,3-diaminobenzene.

Broad phenolic OH stretching is observed in the region 3200 to 3550 cm $^{-1}$. NH_2 bending vibrations are depicted by peak at 1619 cm $^{-1}$. NH_2 wagging vibrations are also observed at 764 cm $^{-1}$. Ring carbon and nitrogen stretching vibrations are shown at 1281 cm $^{-1}$.

4.2.3 HPLC results

HPLC stands for High Pressure Liquid chromatography. This analytical technique is used for qualititative, quantitative analysis and separation of mixtures. HPLC was done at School of Chemical and Materials Engineering. The model used was Perkin Elmer series 200 UV/Vis detector model.

Aminobenzene

Aminobenzene was the reduction product of nitrobenzene. HPLC was done in order to check the purity of compound. Amino benzene showed retention time of 3.25 minutes. Analysis conditions include 254nm wavelength, mixture of solvent containing methanol and water in ratio of 7:3, flow rate was 0.5 ml per min. Total elution time was ten minutes. C-18 column was used and its length was 10cm. Single peak confirms the purity of aminobenzene shown in figure 4.8. It also confirms that there was no other by product present and the product is pure. Moreover small retention time also shows that product was polar in nature as it interacted with nonpolar C-18 column for a very short time.

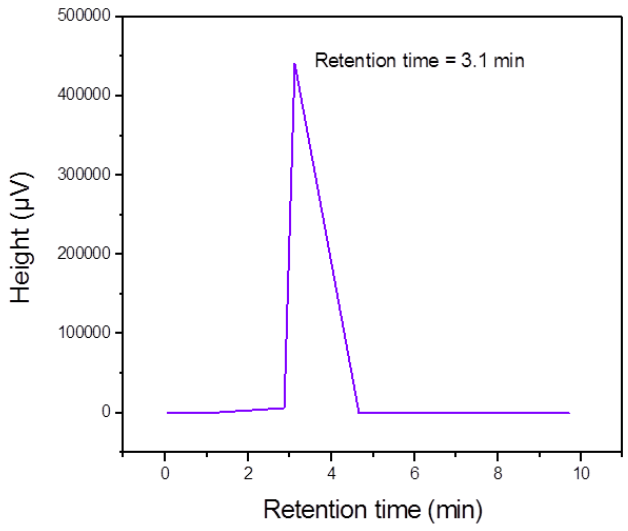


Figure 4.8. HPLC chromatogram of amino benzene.

1,3-Diaminobenzene

1,3-Diaminobenzene was the reduction product of 1,3-dinitrobenzene. HPLC was done in order to check the purity of compound. 1,3-diamino benzene showed retention time of 3.11 minutes. Analysis conditions include 254nm wavelength, mixture of solvent containing methanol and water in ratio of 7:3, flow rate was 0.5 ml per min. Total elution time was ten minutes. C-18 column was used and its length was 10cm. Single peak confirms the purity of 1,3-diaminobenzene shown in figure 4.9. It also confirms that there was no other by product present and the product is pure. Moreover small retention time also shows that product was polar in nature as it interacted with nonpolar C-18 column for a very short time.

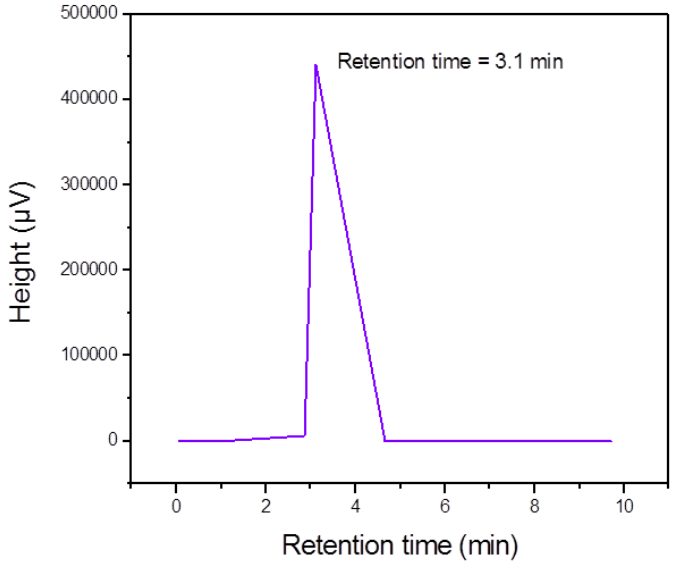


Figure 4.9. HPLC chromatogram of 1,3-Diamino benzene.

2,4,6-Triaminophenol

2,4,6-Triaminophenol was the reduction product of 2,4,6-trinitrobenzene. HPLC was done in order to check the purity of compound. 2,4,6-Triaminophenol showed retention time of 1.5 minutes. Analysis conditions include 254 nm wavelength, mixture of solvent containing methanol and water in ratio of 7:3, flow rate was 0.5 ml per min. Total elution time was ten minutes. C-18 column was used and its length was

10cm. Single peak confirms the purity of 1,3-diaminobenzene shown in figure 4.10. It also confirms that there was no other by product present and the product is pure. Moreover small retention time also shows that product was polar in nature as it interacted with nonpolar C-18 column for a very short time.

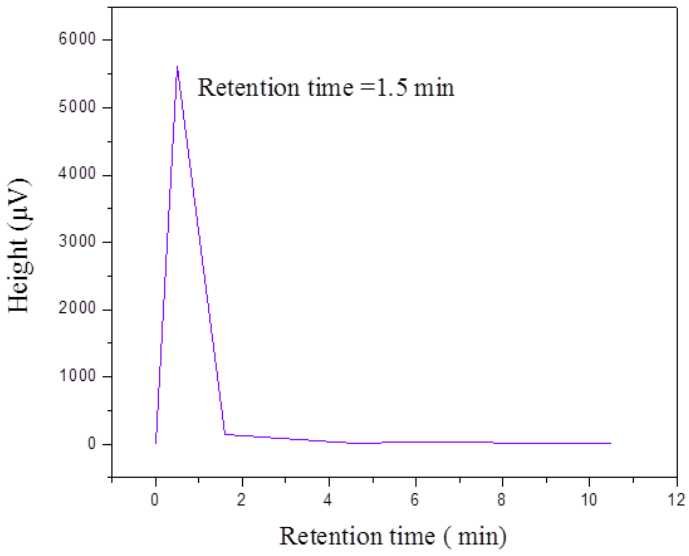


Figure 4.10. HPLC chromatogram of 2,4,6-Triaminophenol.

4.2.4 NMR results

H-NMR results

1,3-Diamonobenzene

4 signals were expected in case of 1,3-Diaminobenzene and 4 signals were observed in its proton NMR. Formation of 1,3-Diaminobenzene was confired by the proton NMR at 300 MHz using acetone as a solvent. The position of both amino groups was justified by splitting pattern in proton NMR. This compound exhibited two triplets at 5.944 and 6.91ppm, one doublet of doublet at 6.076 ppm and one singlet at 4.253 ppm shown in figure 4.11. The signal at 5.944 ppm of a proton as a triplet shows that there is meta coupling present, in its environment two protons are present at meta position to it. This signal at high up field value is due to shielding effect of two amino groups present in its vicinity. These amino groups donate electrons toward ortho positions. The peak for d and d' protons at 4.253 ppm is singlet and broad at the base which confirms the presence of amino groups. Also the integration demonstrated the

presence of four protons that's why the peak is of higher intensity. The peak at 6.076 ppm demonstrated doublet of doublet which is because of one ortho and meta coupling. These protons are chemically equivalent but they are not magnetically equivalent. The most deshielded signal of c proton appeared as triplet at 6.91ppm due to less availability of electrons at this position. Hence the splitting pattern clearly depicts that none of protons were present directly to C1 and C3. It revealed the presence of two amino groups.

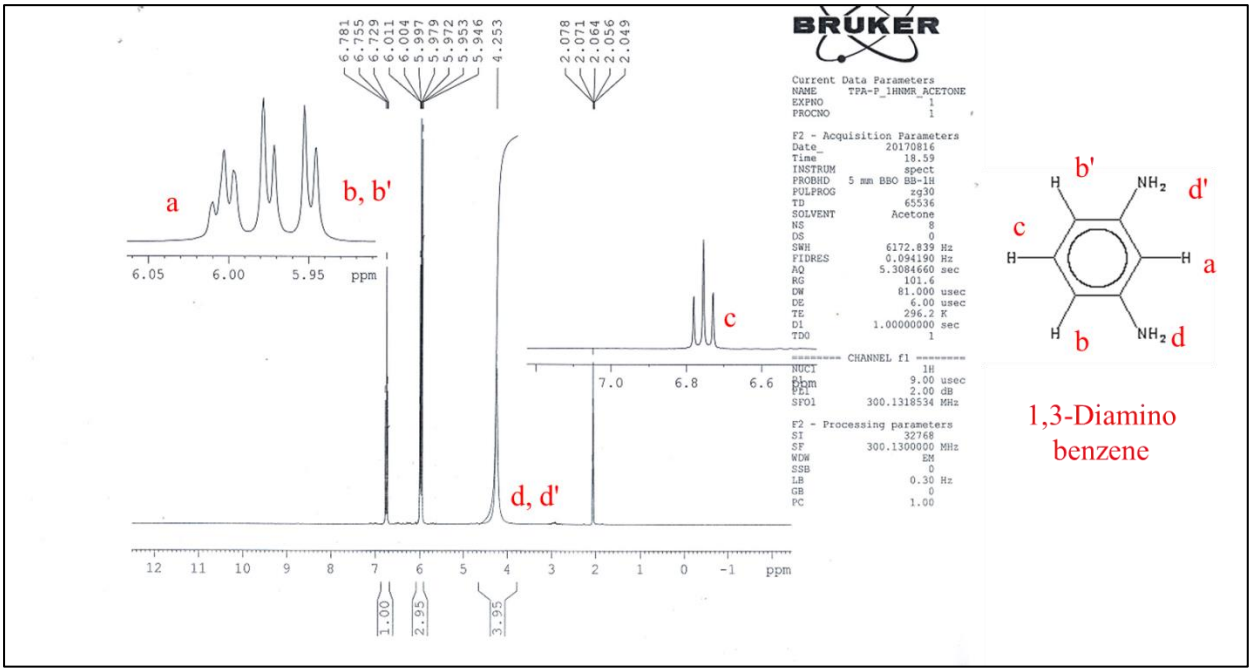


Figure 4.11. Proton NMR of 1,3-Diaminobenzene

^{13}C NMR results

1,3-Diaminobenzene

Formation of 1,3-Diaminobenzene was also confirmed through carbon NMR. Four signals were observed shown in figure 4.12. Signal for C1 and C3 is observed at 149.04 ppm. It is highly deshielded as carbon attached to is directly attached to an electronegative atom which is nitrogen. Signal for C2 is observed at 11.84 ppm It is most shielded one as it is ortho to both amino substituted carbon atoms. Signal for C4 and C6 is observed at 104.12 ppm. It is somewhat shielded as both carbons our ortho to carbon attached directly with an amino group. Amino group donates electrons to

ortho positions due to mesomeric effect. Signal for C5 carbon atom is observed at 29.38 ppm. It is deshielded as it is meta carbon with respect to carbons attached to amino group.

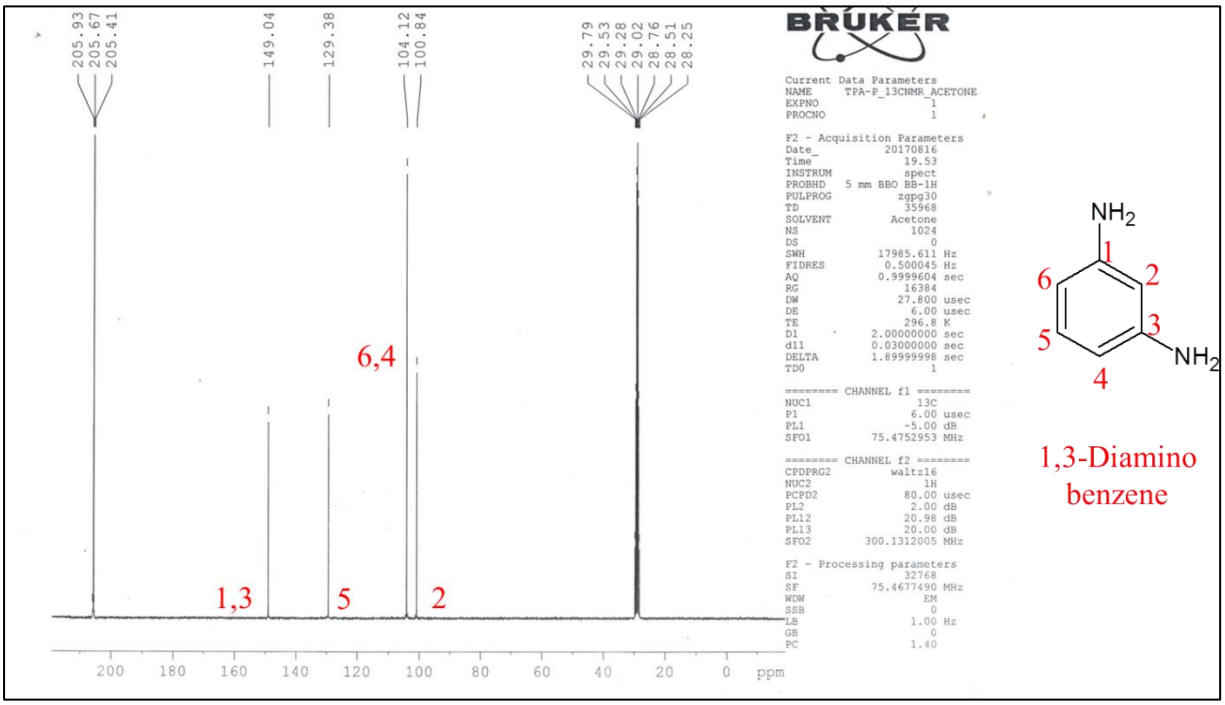


Figure 4.12. ^{13}C NMR of 1,3-Diaminobenzene.

Chapter 5

Conclusions and future prospects

Facile, mild, economical reduction of nitro aromatic compounds was achieved using aluminium and ultrasound waves. Ultrasound has been reported as an alternative energy source for the initiation of organic reactions, with the potential to accelerate chemical transformations, affect product distributions and improves yields. Mono, di and tri nitro aromatic compounds were reduced using aluminium and Ultrasound waves in good yields. Picric acid was reduced for the first time with up to 61 % yield. Two forms of aluminium were used including aluminium turnings and aluminium foil. Aluminium turnings showed best results with yields up to 61 %. Alumium foil was less efficient in reduction of nitro aromatic compounds because it was impure. Pure water and water in combination with organic solvent was used for reduction. Among organic solvent methanol was more efficient as compared to acetone as it is a protic solvent hence source of protons for reduction. Water showed less activity as compare to organic solvent because of the solubility issues of nitro aromatic compounds in water. TLC was used to monitor the progress, completion and confirmation of products through comparison with standards. IR analysis confirmed the conversion of aromatic nitro groups into aromatic amine, the building block of industrial importance. HPLC showed single peaks indicated purity of compounds. In short simple, mild, economical, chemo selective reduction of mono, di and tri substituted nitro aromatic compounds was done using aluminium in moderate yields with abundant, benign and cheap aluminium metal.

Picric acid being successfully reduced into amine product indicates that this protocol in future can be used for reduction of expired TNT (trinitro toluene), for its conversion into useful aromatic amine derivatives. Instead of dumping of expired TNT that material can be converted into useful starting material. Use of aluminium forms varying in particle size and morphology can be tested for reduction of nitro aromatic compounds.

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