Sodium borohydride – Copper (II) acetyl acetonate: a ‘Greener’ approach to reduction of Aromatic Nitro substrates

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Abstract: The formation of amines through the reduction of the nitro functional group represents a fundamental transformation which is versatile in its being the synthesis of choice for a wide variety of organic molecules in diverse fields. New synthetic strategies for complex polyfunctional molecules have always presented a challenge in having to fulfill diverse criteria such as being highly efficient and selective concurrently, besides being ‘green’ and ‘environment friendly’. Hence although a plethora of methodologies are available in literature effecting this transformation, the quest for a method which is superior to the existing ones, will always post a challenge to the chemist. The present research work studies the use of sodium borohydride, a relatively mild and selective reducing agent, for bringing about this transformation in the presence of an inorganic complex. The method explores the viability of the reagent with aromatic substrates, both with electron donating as well as electron withdrawing substituents. The explored technique is also ‘green’ in being carried out in benign solvents such as water or aqueous ethanol.

Index Terms: Sodium borohydride, copper (II) acetyl acetonate, nitro, amine, reduction

I. INTRODUCTION

Aromatic amines are an important class of organic compounds used in the synthesis of a wide variety of pharmaceuticals, agrochemicals, dye intermediates, and pigments as well as in the manufacture of fine and speciality chemicals. The introduction of an amino group helps to act as a synthon and create further bond-formations thereby leading to the synthesis of complex molecules from simple building blocks. The first such attempt to explore the versatility of the amine functional group was made by Griess in 1858, wherein aromatic amines were transformed to the corresponding diazonium salts which in turn present a useful starting point for various stoichiometric and/or catalytic carbon-halogen, carbon-oxygen, carbon-sulphur, carbon-carbon or carbon-boron bond-forming reactions [1]. Nitro compounds have always served as an important precursor to amines. Traditionally, amines have been obtained by the reduction of nitro compounds through high pressure hydrogenation [2]. The simplest aromatic amine, aniline, was first produced on an industrial scale by treatment of nitrobenzene with iron in the presence of a small amount of hydrochloric acid popularly known as the Bechamp reduction. A wide variety of highly functionalized and chiral nitro derivatives which act as immediate precursors for the corresponding chiral amines are synthesized by conjugate addition reactions followed by the reduction of the nitro group. Keeping in mind the immense potential and significance of the aromatic amino group, the need for newer synthetic strategies for this functional group will always be present. Although the discovery of novel, chemo selective nitro reduction methods will always be desirable to a chemist; the significance of innovative catalytic reduction protocols cannot be denied keeping in view their properties.

Most of the methods hitherto discovered suffer from one or the other drawback while others give extremely poor yields. Traditional methods like Bechamp reduction involve the use of a large excess of the metal in a strong acid. The need for an alternative green methodology therefore arose. Some of the green techniques used for the reduction of nitroarenes are use of molecular hydrogen, hydrides, hydrazine hydrate, transfer hydrogenation, metal/organic reductants, light mediated electron transfer and biotic conditions as benign, clean, non-hazardous and non-polluting. Most of these methods however, either generate a lot of metallic waste during work-up or lack selective reduction in the presence of other functional groups.

The application of sodium borohydride as a mild reducing agent has brought about fundamental changes in the reduction of functional groups in modern organic synthesis. It is known that solely sodium borohydride does not reduce the nitro group under ordinary conditions [3]. However, the reducing power of this reagent or its polymeric analogue i.e. borohydride exchange resin (BER) undergoes a drastic change toward reduction of nitro groups by combination with transition metal halides or salts such as $NaBH_4/CoCl_2$ [4], $NaBH_4/FeCl_2$ [5], $NaBH_4/CuSO_4$ [6], $NaBH_4$/Co(pyridyl) [7], Borohydride exchange resin (BER); BER/$Ni(OAc)_2.4H_2O$; $CoCl_2$, $PdCl_2$, $Cu(OAc)_2$ are effective in the reduction of aliphatic or aromatic nitro compounds[8]. However, in all such cases, the reduction process either involved very high temperatures, use of solvents such as dry THF, dry ether, CH_3CN etc., stringent reaction conditions such as a nitrogen atmosphere, a high molar ratio of reducing agent and catalyst, low yields or a complicated work-up procedure involving the use of column chromatography for the separation of the several by-products formed. These prevented the use of these methods on a large scale in the industrial sector.

The present study therefore aims at carrying out the reduction process with the use of a novel inorganic coordination complex catalyst, copper acetyl acetonate. The primary aim of this work has been to observe the effect of electron withdrawing/electron donating groups on the ease of reduction process; to conduct a comparative study of reaction conditions/yields while using different substrates; and to investigate the role of copper acetylacetonate in the reduction process.

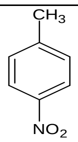
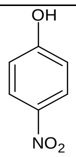
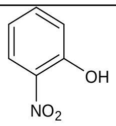
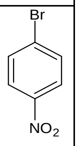
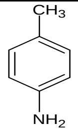
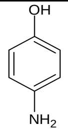
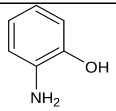
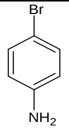
II. MATERIALS

All chemicals used were from MOLYCHEM Chemicals Ltd. Boiling point of the petroleum ether used was in the range of 60-80^{0}C. TLC refers to Thin Layer Chromatography and the silica gel used was from MOLYCHEMChemicals Ltd. All melting point recorded were measured in open capillary tubes on an electrothermal apparatus and are uncorrected. IR spectra were recorded on Agilent technologies FT-IR spectrometer (ν_{max} in cm^{-1}).

III. PROCEDURE

In this communication, we discuss the reduction of aromatic nitro compounds to the corresponding amines by sodium borohydride in the presence of Copper (II) Acetylacetonate. Various aromatic nitro compounds bearing electron withdrawing or electron donating groups were reduced to corresponding amines on reaction with sodium borohydride and Copper (II) Acetylacetonate **(Fig.1)**.

Figure 1:
Aromatic Nitro substrates and their reduced products

Substrate	**A**	**B**	**C**	**D**
				
Product	**W**	**X**	**Y**	**Z**
				

IV.EXPERIMENTAL

General Procedure for the Reduction

To a suspension of Copper (II) Acetylacetonate (0.002 mol) in ethanol (20ml), a solution of sodium borohydride (0.01mol) in ethanol (10ml) was added with stirring and a guard tube was attached to it. The solution was then kept in ice-bath. To this solution was added the aromatic nitro substrate (0.01 mol) in ethanol (10ml) followed by the addition of sodium borohydride (0.02mol). The reaction mixture was stirred for 2 hours at room temperature. The conversion was monitored by TLC using Pet ether: Ethyl acetate as eluent. The solvent was removed under reduced pressure and the residual black solid was treated with concentrated HCl, till acidic (pH=3) and stirred for 15 minutes and filtered. The filtrate was basified with liquor ammonia till it slightly basic (pH=9-10). The product was extracted with ethyl acetate thrice and the organic layer was washed with water, brine solution and again water. The collective organic extracts were dried over anhydrous sodium sulphate. The solvent was removed to get the desired product.

V. RESULTS AND DISCUSSION

Reduction of p-Nitrotoluene(A) to p-Amino toluene (W)

Observations:

Weight of the product = 0.783 g; Theoretical yield = 1.070 g; Percentage yield = 73.18%;
Melting point = 44.2°C (lit: 44°C)
TLC: Solvent system = 10% ethyl acetate in Pet ether; R_f of reactant = 0.81; R_f of product = 0.37

Reduction of p-Nitrophenol (B) to p-Amino phenol (X)

Observations:

Weight of the product = 0.719 g; Theoretical yield = 1.090 g; Percentage yield = 65.96%; Melting point = 186.0°C (lit: 187.5°C)
TLC: Solvent system = 30% ethyl acetate in Pet ether; R_f of reactant = 0.81; R_f of product = 0.50

Reduction of o-Nitrophenol (C) to o-Amino phenol (Y)

Observations:

Weight of the product = 0.648 g; Theoretical yield = 1.090 g; Percentage yield = 59.44%; Melting point = 172.0°C (lit: 174°C)
TLC: Solvent system = 30% ethyl acetate in Pet ether; R_f of reactant = 0.82; R_f of product = 0.54

Reduction of p-Bromo nitrobenzene (D) to p-Bromo aniline (Z)

Observations:

Weight of the product = 0.597 g; Theoretical yield = 1.720 g; Percentage yield = 34.71%; Melting point = 63.8°C (lit: 64°C)
TLC: Solvent system = 10% ethyl acetate in Pet ether; R_f of reactant = 0.86; R_f of product = 0.57

It can be observed that all the reductions occurred smoothly and in good yield; however, with electron withdrawing substituent, the yield is lower than the corresponding substituent at a similar position of electron donating nature. It is also to be noted that amongst electron donating substituents, the ones at para position gave a better yield that their ortho counterparts. This may probably be accounted for by a steric hindrance occurring during the formation of the borohydride -copper acetyl acetonate – nitro group complex formed during the reduction process.

IR spectra of the substrates and the corresponding products clearly show the disappearance of the nitro peak and the appearance of the amino peak. There is a distinct peak which appears at the following regions in all the products:
3300 - 3000 cm^{-1} (NH stretch.), 1650-1550 cm^{-1}(NH bending), 1300-1250 cm^{-1} (C-N stretch.)

The N-H stretching between 3300-3000 cm^{-1}stretching is easily distinguishable from the OH stretching vibrations between 3500-3300 cm^{-1}.

VI. CONCLUSION

Aromatic nitro compounds bearing electron donating groups as well as electron withdrawing groups were reduced efficiently to their corresponding amines by the combination of NaBH4 with catalytic amounts of copper (II) acetylacetonate in ethanol. The reductions were completed within 100-120 minutes at room temperature. In terms of the reducing agent used, a practical ratio of 1:3 (substrate to sodium borohydride) produced the best results which is lower than most other reported methods. There is efficiency in terms of energy consumption, as the reaction proceeds with stirring at room temperature. The catalyst used is also 1/10th of the ratio of substrate: reducing agent, which makes it viable. Thus, the reported method shows good promise in terms of efficiency, shorter reduction times, ambient conditions of reaction, and easy work up procedure leading towards an environmentally benign reaction. It involves the use of ethanol/water as the solvent; reduction in the molar ratio of reducing agent and catalyst used and at the same time helps procure a comparatively higher yield which may be further investigated so as to be used for industrial processes involving the reduction of aromatic nitro to amino compounds.

The use of this inorganic complex, copper (II) acetylacetonate, as a more efficient catalyst for the probable boride-catalyzed reduction of aromatic nitro compounds, thus merits a synthetically useful addition to the present known methodologies.

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