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A Simple Reduction Method of Azo-Compounds to Amines Using Fe Powder in the Presence of NH_4Cl

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Summary. A series of azo-compounds were reduced to related aromatic amines in the presence of Fe powder and ammonium chloride. This one step protocol led to the formation of products in middle to high yields, especially when electron releasing substituted aromatic azo-compounds were reduced.

Keywords. Reduction; Azo-compounds; Amines; Ammonium chloride; Fe powder.

Introduction

It is well documented that most of primary amines are biologically active compounds or important building blocks for the synthesis of biologically active compounds [1–6]. Reduction of azo-compounds to amines is very important due to both industrial and synthetic applications. Sodium dithionite is usually employed as the reducing agent for reduction of aromatic nitro compounds, diazonium salts, pyridinium compounds, and other nitrogen-containing functional groups [7]. Reduction of aldehydes and ketones has also been reported with a hot solution of sodium dithionite. Oximes are also cleaved by the reagent to the parent carbonyl compounds [7]. However sodium dithionite is relatively unstable and tends to react with oxygen. This means that an excess amount of sodium dithionite is needed in processes where it is involved. Also sodium dithionite and its reaction products are environmentally important pollutants. Another disadvantage of this compound, as a reducing reagent, is its decomposition under heat. Catalytic reduction of azo-compounds is of interest because of the easy preparation of amines by regio- and stereo-controlled procedures [8–10].

Results and Discussion

The aim of this study is reduction of azo-compounds to corresponding aromatic amines under neutral, environmentally benign, and simpler conditions. The process is carried out by simply mixing of an azo-compound **1**, NH_4Cl, and Fe powder in water/ethanol as co-solvent (Fig. 1).

The major advantage associated with this protocol is formation of amines in middle to high yields, particularly when electron releasing substituted aromatic compounds such as **1d** are used. One more significance of this reduction method is that it can be carried out at room temperature and also under heating as compared to sodium dithionite which decomposes under heat. Aliphatic amines may be obtained similarly by coupling to an enol followed by reduction. This method also has the advantage of occurring under mild conditions. It is therefore of value in some cases as an alternative to the usual method for making aromatic amines, in which nitration is followed by reduction which involves vigorous and strongly oxidizing conditions. Moreover,

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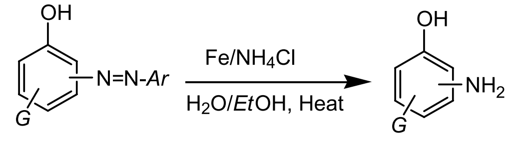


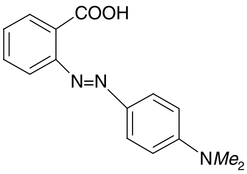
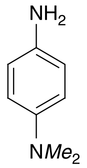
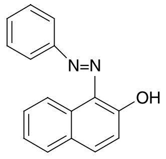
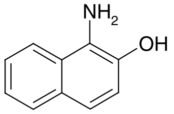
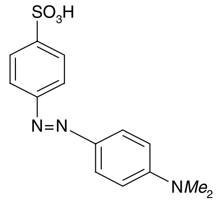
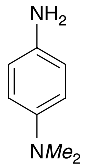
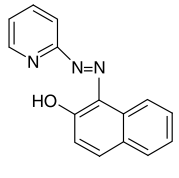
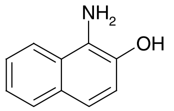
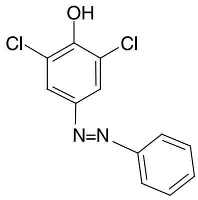
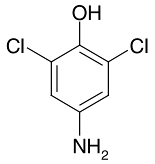
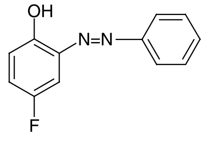
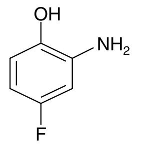
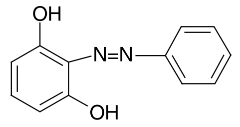
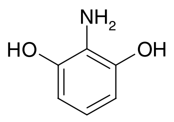
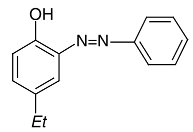
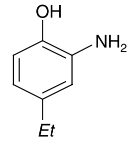
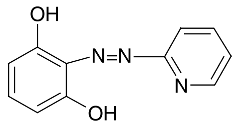
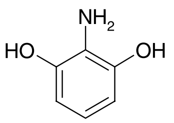
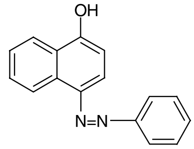
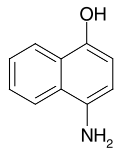
1 2

Fig. 1. General reduction of azo-compounds to amines

the procedure avoids problems associated with solvent use (cost, handling, safety, and pollution). Decreased reaction times are also realized because of the increased reactivity of the reactant in the liquid state.

To extend the scope of the reducing reagent Fe/NH_4Cl for the reduction of azo-compounds, several azo-compounds **1a**–**1j** were prepared by reaction of corresponding diazonium salt with substituted aromatic compounds and tested for this transformation (Table 1). All azo-compounds were reduced completely with Fe/NH_4Cl under standard conditions to readily give the corresponding amines **2a**–**2j** in middle to good yields (65–95%) and high purity (95%, based on ^1H NMR spectra). In order to improve the yields, reactions were performed using different amounts of reagents. The best results were obtained using a 1:0.1:1 ratio of NH_4Cl:Fe:azo-compound. Using higher amounts of NH_4Cl did not improve the result. All amines were isolated as hydrochloride salts, which were transferred to free amines by neutralization with a NaOH solution. The major advantage of this method is toleration of some functional groups, such as C=C bonds and benzyl

Table 1. The reduction of azo-compounds to aromatic amines

Azo-compound	Aromatic amine	Yields/%	Azo-compound	Aromatic amine	Yields/%
 **1a**	 **2a**	85	 **1f**	 **2f**	90
 **1b**	 **2a**	80	 **1g**	 **2f**	90
 **1c**	 **2c**	74	 **1h**	 **2h**	65
 **1d**	 **2d**	95	 **1i**	 **2i**	72
 **1e**	 **2d**	82	 **1j**	 **2j**	88

groups, which are easily destroyed during catalytic hydrogenation. Ethanol as co-solvent of water and was necessary for the reaction due to solubility of reactants.

In conclusion, this study led to the development of a one-step synthetic strategy of amines involving reduction of azo-compounds in the presence of Fe powder and ammonium chloride.

Experimental Section

^{1}H NMR spectra were recorded on a Bruker (300 MHz) spectrometer. The IR spectra were recorded on a Galaxy FT-IR 300 spectrophotometer. Microanalyses were performed by the Elemental Analyzer (Elementar, Vario EL III); their results agreed favorably with calculated values. Reaction courses and product mixtures were monitored by thin layer chromatography. All starting materials were obtained from Fluka and Merck companies.

General Procedure

A mixture of 0.5 g ammonium chloride (0.01 mol), 100 cm^3 $H_2O/EtOH$, and 0.01 mol appropriate azo-compound was placed in a 250 cm^3 beaker. The mixture was stirred vigorously and 0.11 g Fe powder (2 mmol) were added. The temperature was slowly raised to the boiling point of the solvent. The stirring was continued for a further 15 min in an efficient fume cupboard. By that time the reduction is complete as indicated by the mixture becoming colorless again. The warm reaction mixture was then filtered to separate the product.

N,N-Dimethylbenzene-1,4-diamine hydrochloride (**2a**, $C_8H_{13}ClH_2$)
Colorless solid, mp > 200°C (dec); IR (KBr): $\bar{\nu} = 3357–3221$ (NH_2), 3123 ($CH_{aromatic}$), 2963 (CH_{aliph}), 1615 ($C{=}C_{aromatic}$), 1212 (C–N) cm^{-1}; ^{1}H NMR (300 MHz, *DMSO*-d$_6$): $\delta = 2.68$ (s, 2CH_3), 5.15 (bs, NH_2), 6.42 (d, 1$CH_{aromatic}$), 6.48 (d, 1$CH_{aromatic}$), 6.57 (d, 1$CH_{aromatic}$), 7.23 (d, 1$CH_{aromatic}$) ppm; ^{13}C NMR (300 MHz, *DMSO*-d$_6$: $\delta = 40.50$, 112.67, 115.56, 117.33, 127.11 ppm.

4-Amino-2,6-dichlorophenol hydrochloride (**2c**, $C_6H_6Cl_3NO$)
Colorless solid, mp > 200°C (dec); IR (KBr): $\bar{\nu} = 3233–3159$ (NH_2), 3104 ($CH_{aromatic}$), 1586 ($C{=}C_{aromatic}$) cm^{-1}; ^{1}H NMR (300 MHz, *DMSO*-d$_6$): $\delta = 5.00$ (bs, NH_2), 6.55 (m, 2$CH_{aromatic}$), 8.79 (s, OH) ppm; ^{13}C NMR (300 MHz, *DMSO*-d$_6$: $\delta = 114.06$, 123.94, 139.29, 143.40 ppm.

2-Amino-1,3-benzenediol hydrochloride (**2d**, $C_6H_8ClNO_2$)
Colorless solid, mp > 200°C (dec); IR (KBr): $\bar{\nu} = 3382$ (OH), 3321–3254 (NH_2), 3132 ($CH_{aromatic}$), 1613 ($C{=}C_{aromatic}$) cm^{-1}; ^{1}H NMR (300 MHz, *DMSO*-d$_6$): $\delta = 4.98$ (bs, NH_2), 6.47 (m, 3$CH_{aromatic}$), 6.96 (bs, 2OH) ppm; ^{13}C NMR (300 MHz, *DMSO*-d$_6$: $\delta = 114.30$, 116.06, 129.25, 149.26 ppm.

1-Aminonaphthalen-2-ol hydrochloride (**2f**, $C_{10}H_{10}ClNO$)
Colorless solid, mp > 200°C (dec); IR (KBr): $\bar{\nu} = 3325$ (OH), 3295–3212 (NH_2), 3085 ($CH_{aromatic}$), 1626, 1465 ($C{=}C_{aromatic}$) cm^{-1}; ^{1}H NMR (300 MHz, *DMSO*-d$_6$): $\delta = 4.92$ (bs, NH_2), 7.03 (m, 2$CH_{aromatic}$), 7.17 (m, 1$CH_{aromatic}$), 7.26 (m, 1$CH_{aromatic}$), 7.63 (m, 1$CH_{aromatic}$), 7.91 (m, 1$CH_{aromatic}$), 9.17 (bs, OH) ppm; ^{13}C NMR (300 MHz, *DMSO*-d$_6$: $\delta =$ 118.60, 119.31, 120.82, 123.62, 123.48, 125.65, 125.32, 128.35, 129.63, 136.75 ppm.

2-Amino-4-fluorophenol hydrochloride (**2h**, C_6H_7ClFNO)
Colorless solid, mp > 200°C (dec); IR (KBr): $\bar{\nu} = 3361$ (OH), 3217–3184 (NH_2), 3023 ($CH_{aromatic}$), 1626 ($C{=}C_{aromatic}$) cm^{-1}; ^{1}H NMR (300 MHz, *DMSO*-d$_6$): $\delta = 4.79$ (bs, NH_2), 6.08 (m, 1$CH_{aromatic}$), 6.33 (m, 1$CH_{aromatic}$), 6.52 (m, 1$CH_{aromatic}$), 8.91 (bs, OH) ppm; ^{13}C NMR (300 MHz, *DMSO*-d$_6$: $\delta = 100.90$, 114.56, 138.53, 140.55, 155.30, 158.37 ppm.

2-Amino-4-ethylphenol hydrochloride (**2i**, $C_8H_{12}ClNO$)
Colorless solid, mp > 200°C (dec); IR (KBr): $\bar{\nu} = 3261$, 3317 (NH_2), 3133 ($CH_{aromatic}$), 2965, 2895 ($CH_{aliphatic}$), 1626 ($C{=}C_{aromatic}$) cm^{-1}; ^{1}H NMR (300 MHz, *DMSO*-d$_6$): $\delta = 1.06$ (t, CH_3), 2.38 (q, CH_2), 4.40 (bs, NH_2), 6.21 (m, 1$CH_{aromatic}$), 6.43–6.50 (m, 2$CH_{aromatic}$), 8.67 (bs, OH) ppm; ^{13}C NMR (300 MHz, *DMSO*-d$_6$: $\delta = 16.55$, 28.13, 114.97, 118.23, 118.48, 120.23, 135.41, 139.62 ppm.

4-Aminonaphthalen-1-ol hydrochloride (**2j**, $C_{10}H_{10}ClNO$)
Colorless solid, mp > 200°C (dec); IR (KBr): $\bar{\nu} = 3317$ (OH), 3296–3261 (NH_2), 3142 ($CH_{aromatic}$), 1626, 1515 ($C{=}C_{aromatic}$) cm^{-1}; ^{1}H NMR (300 MHz, *DMSO*-d$_6$): $\delta = 4.99$ (bs, NH_2), 6.50 (d, 1$CH_{aromatic}$), 6.61 (d, 1$CH_{aromatic}$), 7.29 (m, 2$CH_{aromatic}$), 7.93 (m, 2$CH_{aromatic}$), 9.01 (s, OH) ppm; ^{13}C NMR (300 MHz, *DMSO*-d$_6$: $\delta = 108.62$, 109.31, 118.76, 122.56, 122.82, 124.60, 124.98, 125.58, 137.06, 144.46 ppm.

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