Reductive Dehalogenation of Arylhalides and Alkylhalides with Zinc in THF Saturated Aqueous Ammonium Chloride

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A low-cost and highly effective zinc/THF-saturated aqueous ammonium chloride has been developed for dehalogenation of arylhalides and alkylhalides in aqueous systems.

Keywords: Reductive dehalogenation; Zinc; Aqueous ammonium chloride.

In recent years, the halogens on aromatic rings have been used as potential protecting or blocking groups in synthetic organic chemistry.[1,2] Aryl chlorides are widely applied in the chemical industry. They intermix in industry waste water and daily waste water, and pollute water systems. Therefore, dechlorination of aryl chlorides is of great importance in preventing environmental pollution. Although in recent years, there have been many reports describing dechlorination of organic chlorides in the literature,[3,4] most of the dechlorinations were carried out in organic systems, few were carried out in aqueous systems.[5] Aromatic halides are readily reduced by metal-catalyzed transfer hydrogenolysis.[6] The process of reductive elimination of halogens from aromatic rings is relatively quite a difficult task. There are reports of the use of Pd(II) salts to give the corresponding dehalogenated compounds.[7]

Generally, debrominations have been carried out in hydrobromic acid in the presence of a suitable bromine scavenger such as aniline or phenol or sodium sulfite.[2,8] Dehalogenation by direct hydrogenolysis has been accompanied by the reduction of double bonds in the case of unsaturated halides and the formation of amines in the case of nitro halides. Dehalogenation of aromatic halides has been reported over palladium deposited on carbon[9] in the presence of a proton donor like limonene and pmenthene at 50-100 °C, but the nitrile group of *o/p* chlorobenzonitrile was also reduced. Cortese and Heck have achieved the dehalogenation of aromatic halides without affecting a nitrile group by employing triethylammonium formate/triarylphosphine catalyzed by palladium or palladium acetate at 50-100 °C. Nucleophilic reagents such as LiEt$_3$BH[10-11] and 2LiAlH(OCH$_3$)$_3$-CuI[12] have been used in dehalogenation reactions.

Other procedures for dehalogenation of aryl and alkyl halides involve: dehalogenation of chloroarenes by polymethylhydrosiloxane (PMHS) under palladium catalysis,[13] electrochemically reduced titanocene dichloride as a catalyst of reductive dehalogenation of organic halides,[14] reduction of alkyl halides with sodium cyanoborohydrate in hexamethylphosphoric triamide (HMPA),[15] ruthenium-catalyzed oxidative dehalogenation of organics (chloro, bromo-, iodo- and nitro-benzene, polychlorobenzenes, polychlorophenols),[16] hydrogenation and dehalogenation of aryl chlorides and fluorides by the sol-gel entrapped RhCl$_3$-aliquat 336 ion pair catalyst[17] and dehalogenation of organic halides using the NiCl$_2$·2H$_2$O-Li-DTBB (cat.) combination.[18]

In our studies, aqueous ammonium chloride has been found to be a good and versatile medium for hydrodehalogenation of alkyl and aryl halides by zinc under mild conditions.

The reaction of different arylhalides and alkylhalides materials, with zinc and saturated ammonium chloride in THF at room temperature, leads to the formation of the corresponding products resulting from a halogen/hydrogen exchange.

Iodo-benzene was readily reduced indicating that reaction occurred via the well-known radical mechanism. The present investigations revealed that alkyl and aryl halides were readily reduced by zinc in aqueous ammonium chloride; halo phenol and halo aniline are more easily dehalogenated than other aryl halides, and as we showed in our previous work, stirring of a mixture of aryl halides bearing aldehyde or ketone functional groups and zinc

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powder in THF-saturated aqueous ammonium chloride give the corresponding pinacols.[19]

Assuming a mechanism of the reaction under study to involve the formation of Rad. as suggested previously,[20] it should proceed through three principal steps-dissolving of a compound to be reduced, electron capture from metal to give a Rad, and decay of the latter to yield eventually hydrodehalogenation products. The last step is believed to be a sequence of the irreversible fragmentation of Rad with the removal of halide ion to produce a radical,[21] its reduction and final protonation of anion (Scheme I). The addition of organic solvents to aqueous ammonium chloride considerably diminishes the role of the solubility factor, thus facilitating the reaction. The ammonium chloride concentration influence is most likely associated with the electron capture rate from the metal as depending both on the activation of the zinc surface and the solvation of the ensuing zinc cation, thus affecting the redox potential of the zinc.[20]
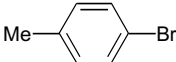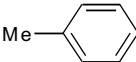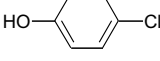
Scheme I

$$RX \xrightarrow{e^-} RX^{\cdot} \xrightarrow{-X^-} R^{\cdot} \xrightarrow{e^-} R^- \xrightarrow{H^+} RH$$
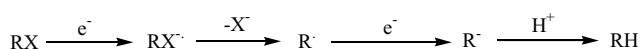
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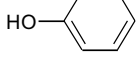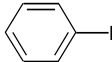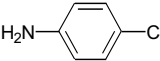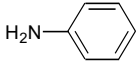
Melting points were measured by using the capillary tube method with an electro thermal 9100 apparatus. ^{1}H NMR spectra were recorded on a Bruker DRX-90 AVANCE by using TMS as an internal s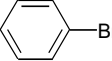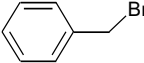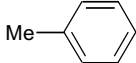tandard (CDCl$_3$ solution). IR spectra were recorded on KBr disks on the FT-IR Bruker Tensor 27. All the chemicals were purchased from Merck Company. All products were known compounds and identified by comparison of their spectra and physical data in the literature description.[22]

Reductive dehalogenation: General procedure

Compound **1-12** (1 mmol) was added to an excess amount of zinc powder (0.260 g, 4 mmol) in saturated aqueous ammonium chloride (4 mL) and THF (2 mL) and the mixture was stirred at room temperature; after 3-5 h the Zn powder had disappeared (Table 1). Unreacted zinc was separated and washed with water. Two phases of solution were extracted and then the solvent was evaporated and further purification was performed by flash chromatography to yield products.

For products such as benzene and hexane, after completion of the reaction, unreacted zinc was separated and two phases of solution were extracted. Pure products were obtained after the addition of water to the organic layer;

Table 1. Dehalogenation of alkyl and aryl halides

Entry	Substrates	Dehalogenation products	Time (h)	Yield (%)[a]
1	Me—C$_6$H$_4$—Br	Me—C$_6$H$_5$	4	94
2	HO—C$_6$H$_4$—Cl	HO—C$_6$H$_5$	3	96
3	C$_6$H$_5$—I	C$_6$H$_6$	3	98
4	H$_2$N—C$_6$H$_4$—Cl	H$_2$N—C$_6$H$_5$	3	97
5	C$_6$H$_5$—Br	C$_6$H$_6$	5	93
6	C$_6$H$_5$—CH$_2$Br	Me—C$_6$H$_5$	4	97
7	CH$_3$(CH$_2$)$_4$CH$_2$Br	CH$_3$(CH$_2$)$_4$CH$_3$	3	95
8	CH$_3$(CH$_2$)$_5$CH$_2$Br	CH$_3$(CH$_2$)$_5$CH$_3$	3	93
9	*p*-Br-C$_6$H$_4$-CHO	(*p*-Br-C$_6$H$_4$-CHOH)$_2$	1	80
10	*p*-Cl-C$_6$H$_4$-CHO	(*p*-Cl-C$_6$H$_4$-CHOH)$_2$	1	75
11	*o*-MeO-C$_6$H$_4$-CHO	(*o*-MeO-C$_6$H$_4$-CHOH)$_2$	1	60
12	*m*-MeO-C$_6$H$_4$-CHO	(*m*-MeO-C$_6$H$_4$-CHOH)$_2$	1	80

[a] Yields refer to isolated products.

water was added until, after shaking, two layers formed. The phases were separated; as THF is miscible with water; it was removed during separation of the aqueous layer and the combined organic layer was dried over MgSO₄, then further purification was performed by flash chromatography to yield products.

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