$Co_2(CO)_8$ as Novel and Water-tolerant Reagent for the Conversion of Azides to Amines in Aqueous Media

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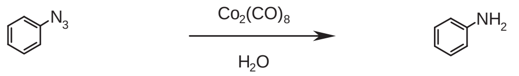
Azides are readily converted into their corresponding amines using a catalytic amount of $Co_2(CO)_8$ under mild conditions. The method is highly chemoselective and compatible with a variety of functionalities such as halides, esters, acids, ethers, nitro, cyano and olefinic double bonds present in the molecule.

The conversion of aromatic azides to aryl amines is an important transformation in organic synthesis, used to construct a variety of biologically active molecules, especially in heterocyclic and medicinal chemistry.[1] A number of reagents such as borohydrides, diborane, catalytic transfer hydrogenation, triphenylphosphine, hydrogen sulfide, tri-*n*-butyltin hydride, zinc-hydrochloric acid, etc. have been reported to bring about this conversion under various reaction conditions.[2] Among them $LiAlH_4$ and $Pd/C–H_2$ are the most commonly used reagents for this purpose. But these reagents have one or more limitations regarding to their general applicability, selectivity, commercial availability, operational convenience and toxicity. For example, $LiAlH_4$ is not tolerable to many functionalities such as $–CO_2R$, $–NO_2$, –COOH, etc., and on the other hand, diborane and catalytic hydrogenation are not suitable to compounds having carbon–carbon multiple bonds.[2] Indeed, $NaBH_4$ alone does not reduce azides to amines except for arylsulfonyl azides.[3] Subsequently, zinc borohydride, samarium iodide, benzyl triethylammonium tetrathiomolybdate, trimethylsilyl iodide, indium/ammonium chloride, ferrous sulfate/ammonia and ferric chloride/sodium iodide reagents, etc. have been employed for this conversion.[4–7] In spite of a large number of methods reported for this conversion there is always considerable interest in exploring more milder and selective reagents.

Recently, a great deal of attention has been focussed on the use of water as green solvent in organic synthesis. In addition to its abundance and for economical and safety reasons, water has naturally become as a substitute and an alternative environmentally benign solvent in organic synthesis.[8] The use of aqueous medium as solvent also reduces the harmful effects of organic solvents on the environment. However, there are no precedents on the use of metal carbonyls as catalysts for this transformation.

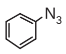
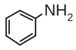
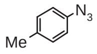
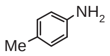
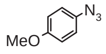
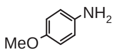
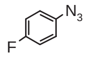
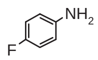
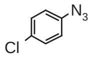
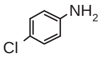
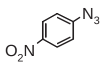
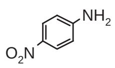
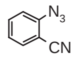
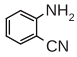
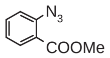
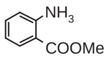
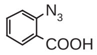
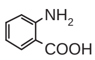
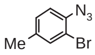
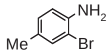
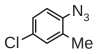
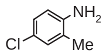
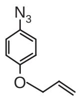
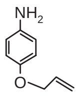
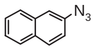
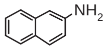
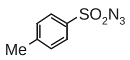
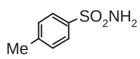
In this article, we describe a novel and efficient procedure for the conversion of azides to amines using $Co_2(CO)_8/H_2O$ reagent system under neutral conditions. Thus treatment of phenyl azide with 0.15 equiv. of cobalt octacarbonyl $[Co_2(CO)_8]$ in water at room temperature gave the aniline in 90% yield (Scheme 1).



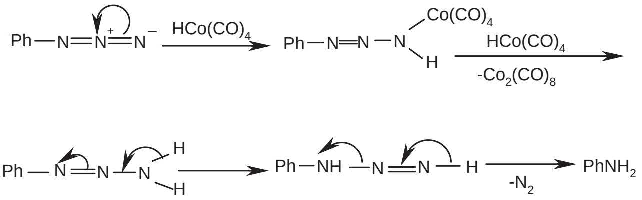
1 2a

Scheme 1.

Table 1. Conversion of azides to amines using $Co_2(CO)_8/H_2O$ reagent system

Entry	Azides	Product[a]	Time/h	Yield/%
a			3.0	90
b			2.5	88
c			4.5	85
d			2.0	87
e			5.0	83
f			4.0	90
g			5.0	87
h			5.5	85
i			5.0	75
j			4.0	89
k			4.0	90
l			2.0	85
m			3.5	90
n			3.0	75

[a] All products were characterized by ^1H NMR, IR and mass spectroscopy.
[b] Isolated and unoptimized yields.



Scheme 2.

Encouraged by the results obtained with phenyl azide, we turned our attention to various substituted azides. Interestingly, a variety of aryl azides underwent reduction under similar conditions to give the corresponding aryl amines. This method was equally effective for the reducion of both electron rich as well as electron-deficient azides. Aryl azides bearing nitro, cyano and ester functionalities on the aromatic ring are remained intact under the reaction conditions. In cases, the reactions proceeded smoothly at room temperature and the products were obtained in excellent yields. In the absence of catalyst, the reactions did not take place even after long reaction times (8–12 h). Among various solvents such as water, 1,2-dimethoxy ethane, tetrahydrofuran, acetonitrile, and methanol tested for conversion, water was found to give the best results. Further, we have carried out the experiments using various metal carbonyls such as $Co_2(CO)_8$, $Cr(CO)_6$, and $Fe(CO)_5$. Among them, cobalt octacarbonyl gave higher yields than others. The scope and generality of this process was illustrated with respect to various aryl azides and the results were presented in the Table 1.[9]

The possible mechanism is expected to be the initial attack of hydro carbonyl $[(HCo(CO)_4]$[10] on the azide nitrogen atom followd by formation of amine and release of nitrogen. (Scheme 2)

In summary, we have described a mild and efficient approach for the conversion of azides to amines using $Co_2(CO)_8/H_2O$ as the novel reagent system. The use of water as solvent makes this method simple and convenient. This method is very useful especially for the chemoselective reduction of azides to amines in the presence of other reducible functionalities such as nitro, cyano, esters, and halides.

References and Notes

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9 Experimental procedure: A mixture of aryl azide (1 mmol) and $Co_2(CO)_8$ (0.15 mmol) in water (10 mL) was stirred at room temperature. After complete conversion, as indicated by TLC, the reaction mixture was extracted with ethyl acetate (2 × 10 mL). The organic layers were dried over anhydrous Na_2SO_4 and purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate–hexane, 2:8) to afford pure aryl amine. All the products were fully characterized by ^{1}H NMR, IR and mass spectroscopy and also by the comparison with known products. The spectral data of all the products were identical with data reported in the literature.[3–7]

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