SHORT PAPER

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Zinc/ammonium formate: a chemoselective and cost-effective protocol for the reduction of azides to amines

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A variety of alkyl and aryl azides were selectively reduced in high yields to the corresponding amines by reaction with ammonium formate in the presence of low cost commercial zinc dust at room temperature.

Keywords: azides, catalytic transfer hydrogenation, zinc, ammonium formate, amines

Reduction of the azide moiety to an amine constitutes a synthetically important process, and, since many azides can be prepared with regio- and stereocontrol, subsequent reduction permits a controlled introduction of the amine function. It has been used extensively in carbohydrate and nucleoside chemistry. Although quite a number of methods have been reported for this reductive process,[1–6] $LiAlH_4$ and Pd/C-H_2 are the most commonly used reagents systems. However, despite of their potential utility these methods often suffer from certain inconveniences such as, incompatibility with other functionalities and protecting groups, use of expensive and hazardous reagents, drastic reaction conditions, long reaction times and tedious product isolation procedure.

Ammonium formate is proved to be a versatile hydrogen donor for the catalytic hydrogen transfer reductions of wide variety of functionalities.[7-9] However, most of the ammonium formate reductions are achieved by the use of expensive catalysts like Pd/C, Ru/Ca, Pd/$CaCO_3$, Ru/C and Raney Ni. As part of our endeavour to develop low cost metals as catalyst for transfer reduction of important organic functional groups,[10–15] it was found that zinc can efficiently catalyse the reduction of several functionalities.[12–15] We now report a rapid, selective and cost-effective method for the reduction of azides to corresponding primary amines using catalytic transfer hydrogenation with ammonium formate as the hydrogen source, in the presence of commercial zinc dust.

$$\text{R-N}_3 \xrightarrow[\text{MeOH, r.t}]{\text{Zn/HCOONH}_4} \text{R-NH}_2$$

R= alkyl or aryl

Scheme 1

Azides were treated with zinc and ammonium formate in methanol to give corresponding amines in good to excellent yields (85–95%) at room temperature (Scheme 1). Under the present reaction conditions many other functionalities like halogens, acids, esters, methoxy *etc.* are tolerated. Several structurally varied azides are reduced to amines within 5 to 10 minutes, and the results are summarised in Table 1. The course of reaction was monitored by TLC and IR spectra and the products were characterised by comparison of their TLC, IR spectra, ^1H NMR spectra and melting points with authentic samples. A control experiment was carried out using azido compounds with ammonium formate, but without zinc, does not yield the desired product.

In earlier reports, catalytic transfer hydrogenation of azides to primary amines had been achieved with the systems Pd–C/ammonium formate[16] and Pd-C/hydrazine.[2] But these systems requires longer reaction time and expensive catalyst. Further, palladium lacks industrial potentiality due its pyrophoric nature. Thus, zinc/ammonium formate appears to be a mild and efficient reagent for the rapid reduction of azides to corresponding amines in high yields. Moreover, the easy availability of the reagent, operational simplicity, chemoselectivity and cost-effectiveness make this procedure extremely attractive.

Experimental

Reduction of azides. general procedure: A suspension of azide (10 mmol), ammonium formate (20 mmol) and zinc (2 equiv.) in methanol (10ml) was stirred at room temperature, under nitrogen until completion of the reaction. After the completion of the reaction (monitored by TLC), the reaction mixture was filtered through celite pad, washed with solvent and then the combined filtrate and washings were evaporated under vacuum. The residue was taken into chloroform or ether, washed twice with saturated brine solution and finally with water. The organic layer was dried over anhydrous sodium sulphate and evaporation of the organic layer followed by purification/separation either by preparative TLC or by column chromatography produced the corresponding amine.

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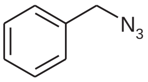
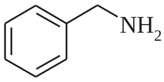
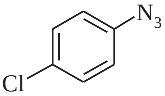
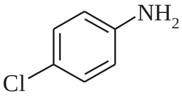
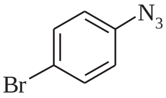
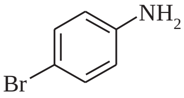
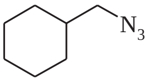
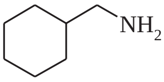
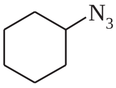
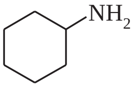
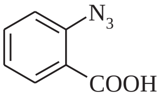
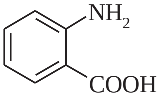
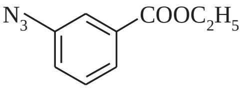
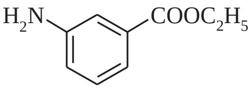
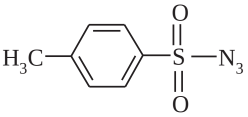
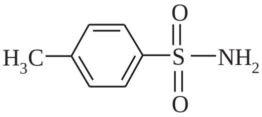
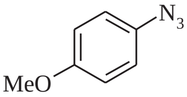
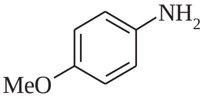
[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Zinc catalysed reduction of azides to amines with ammonium formate

Sample no	Azide	Time/min	Amine	Yield/%[a]	Melting point/°C	
					Found	Lit.
1		6		96	182–184[b]	184–185[17]
2		5		94	68–70	69–72[17]
3		6		96	64–65	62–64[17]
4		10		88	158–160[b]	161–163[18]
5		6		92	133–135[b]	134[18]
6		10		85	146	144–146[17]
7		6		93	170–172[b]	169–172[18]
8	CH_3-$(CH_2)_5$-N_3	8	CH_3-$(CH_2)_5$-NH_2	84	129–130[b]	131–132[17]
9		10		96	156–159	156–158[18]
10		5		94	58–60	57[18]

[a]Isolated yields are based on single experiment and the yields were not optimised. [b]Boiling point.

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