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A NOVEL, CHEMOSELECTIVE AND EFFICIENT PRODUCTION OF AMINES FROM AZIDES USING $ZrCl_4/NaBH_4$

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Abstract: *A practical & cheaper reagent system $ZrCl_4/NaBH_4$ is used for the production of amines from azides is described.*

Reduction of the azide moiety to an amine constitutes a synthetically important process, and since many azides can be prepared with regio and stereo control, subsequent reduction permits a controlled introduction of the amine function[1]. The reaction is of wide applicability and has been effected with a variety of reagents some of them include $LiAlH_4$[2], zinc borohydride[3], samarium iodide[4], (BER)-nickel acetate[5], benzyl triethylammonium tetrathiomolybdate[6], Zn-$NiCl_2$ $6H_2O$-THF[7], $Zn(BH_4)_2$(dabco)[8], $MePh_3P^+BH_4^-$[8], and In/NH_4Cl[9] etc. Most of the available reagents reported have some disadvantages in relation to their general applicability, selectivity and longer reaction time.

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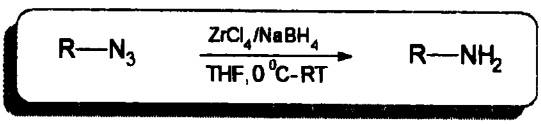
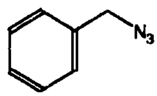
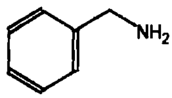
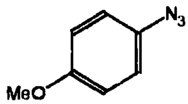
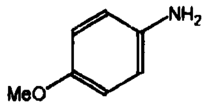
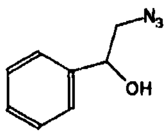
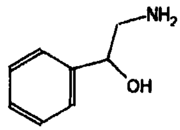
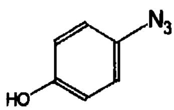
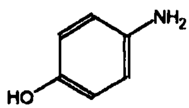
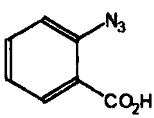
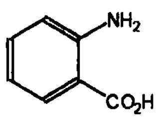
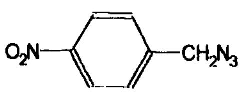
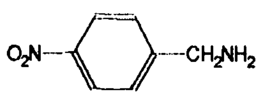
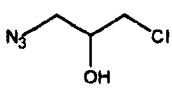
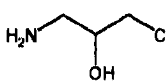
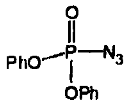
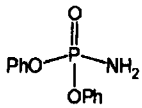
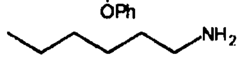
In the course of our program to explore the novel utilities of $ZrCl_4/NaBH_4$ reagent system,[10] it is observed that this reagent affects the production of primary amines from respective azides at room temperature. This reagent system is found to be much superior to In/NH_4Cl,[9] that we disclosed recently for the azide to amine transformation. In/NH_4Cl reagent system requires reflux reaction conditions in ethanol solvent for affecting the transformation. In this communication we disclose the reduction of aliphatic, aromatic azides to primary amines using the novel reagent $ZrCl_4/NaBH_4$. Treatment of one equivalent of azide with half equivalent of $ZrCl_4/NaBH_4$ reagent in dry THF solvent under nitrogen atmosphere at 0 °C to room temperature provided quantitative formation of the amines in less than 15 minutes. (**Scheme 1**).



Scheme 1

In a typical procedure, into a two-necked round bottom flask equipped with magnetic bead and nitrogen balloon adapter was placed $ZrCl_4$ (0.5eq), dry THF (5 ml) was syringed into the flask. Immediate formation of red brown solution was observed. The contents were cooled to 0 °C, $NaBH_4$ (2eq) was added in portion to the above solution. Red brown solution slowly turned to pale pink solution. To this reagent system at 0° C was added azide (1eq) in dry THF (5 ml). Contents were stirred magnetically. After complete addition of azide, ice cooling was removed and contents were brought to room temperature (35 °C). The progress of the reaction was monitored by TLC, clearly indicated the

Table

Entry	Substrate	Product	Yield (%)
1			95
2			94
3			90
4			87
5			90
6			92
7			87[b]
8			80[b]
9			80[b]

[a] All reaction were completed with in 15-20 minutes [b] Reaction completed in 2 hrs.

disappearance of the azide in 15 minutes. Contents were cooled and treated with 5% aq. HCl solution gave the separation of organic layer. THF was evaporated under vacuum, extracted into ethyl acetate (10 ml) successively washed with water, aq. $NaHCO_3$ and water, dried over anhydrous Na_2SO_4. Filtration followed by evaporation of the organic portion provided crude amine, this was further purified by silicagel column chromatography furnished pure amine (isolated yield was in the range of 80-95%). All the isolated amines were known, and gave satisfactory H^1 NMR, IR, and Mass spectral data.

Our results on the reduction of a number of aliphatic, aromatic azides, is summarized in the **Table**. Chloro (**entry** 7), nitro (**entry 6**), methoxy (**entry 2**) and carboxylic acid (**entry 5**) groups were not effected with the reagent system. In case of entry **5**, chemoselective reduction of azide was found in comparison with carboxylic acid. But, prolonged reaction time gave a mixture of reduced products. Aliphatic azides (entry **7, 8** & **9**) gave amines in longer reaction time (2 hrs.).

In conclusion, the present results demonstrate an efficient, chemoselective and rapid production of aliphatic & aromatic amines from azides in excellent yields under mild reaction conditions using $ZrCl_4/NaBH_4$.

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