IJST (2015) 39A4: 527-532
Iranian Journal of Science & Technology

http://ijsts.shirazu.ac.ir

Selective method for reduction of Oximes to amines in the presence of Cu nanoparticle

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Abstract

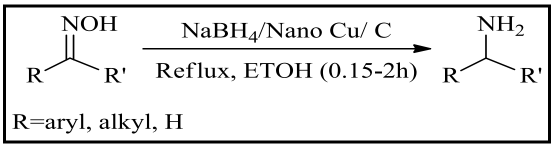
The selective reduction of oximes with sodium borohydride ($NaBH_4$) in the presence of nano Cu and charcoal was investigated. Cu nanoparticles are widely used as catalysts; efficacious catalyst: copper and copper alloy nanometer feature high efficacy and selectivity, and can be used as catalyst in some reactions. We have shown that $NaBH_4$ in the presence of charcoal is an efficient protocol for the reduction of oximes. Reduction reactions were carried out in EtOH (5 mL) as solvent under reflux condition at 70–80^{o}C. The product amines were obtained in high to excellent yields. The stereo-chemistry of the reduction by using nano Cu is distinctively different from the other methods.

***Keywords**:* Reduction; Oxime; $NaBH_4$; Nano-particle Cu; Charcoal

1. Introduction

Further development of the catalytic system will require advanced matrials that can selectively catalyze the specific chemical reactions with a high reactivity (Lim et al., 2010). Nanoparticles exhibit under high catalytic activity and chemical selectivity under mild conditions (Beller et al., 1996). A large number of reactions were catalyzed efficiently using nanoparticles (Roucoux et al., 2002). The extremely small sized particles maximized the surface area exposed to the reactant, allowing more reactions to occure at the same time, thus speeding up the process (Korta et al., 2009). Amines are important functional groups in a variety of biologically interesting materials, including biopolymers, drugs, and dyes (Miriyala et al., 2004).

Among the different procedures for their synthesis, reduction of oximes is particularly popular as it provides an efficient means to amine. $NaBH_4/CuSO_4$ (Rao et al., 2002), (Py) Zn $(BH_4)_2$ (Zeynizadeh et al., 2005), $NaBH_4/ZrCl_4/Al_2O_3$ (Zeynizadeh et al., 2011), $NaBH_3CN/MoCl_5/NaHSO.H_2O$ (Kouhkan et al., 2011) are combination systems which have been reported for reduction of oximes, though most of the reported methods are useful and efficient however, some of them suffer from disadvantages such as using strongly acidic or basic reaction conditions, offering low reduction capability and solvents prolong reaction the reduction of oximes produces hydroxylamine compounds, use of expensive volatile organic times, and finally perform the reaction at high temperature. In organic synthesis, increasing attention is being focused on green chemistry (Practor et al., 2010) using environmentally benign reagents and conditions (Zeynizadeh et al., 2013), which often lead to clean, ecofriendly, and highly efficient protocols through the simplified workups. Thus, the development and introduction of convenient methods which use green and mild reaction condition are still demanded. Herein, we report a rapid, efficient and practical method for green-solvent reduction of various aldoximes and ketoximes to corresponding amine by $NaBH_4$ in the presence of nano Cu supported on charcoal (Scheme 1).



Scheme1. Reduction variety oximes to amine

2. Experimental

All solvents and reagents were purchased from commercial sources with the best quality and they were used without further purification. Charcoal was used in activated form (Merck). Nano Cu and oximes are prepared in high purity according to the reported procedures in literature (Zeynizadeh et al.,

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Received: 17 August 2014 / Accepted: 14 December 2014

2013; Glavee et al., 1994). $^1H/^{13}C$ NMR, XRD and IR spectra were recorded on 300MHz Bruker Avance, Philips X'pert PW3040/60 and Thermo Nicolet Nexus 670 FT-IR spectrometer. All products are known and were characterized by their spectral data. Yields refer to isolated pure products. TLC was applied for monitoring of the reaction over silica gel 60 F_{254} aluminium sheet.

2.1. The procedure for preparation of nano copper as literature (Glavee et al., 1994).

The 1000 mL round bottom designed for direct connection to vacuum line and adapted with a sidearm to allow for addition of solution in vacuo was charged with $NaBH_4$ (0.15g, 4mmol) in an inert atmosphere box. The reaction vessel was then connected to the vacuum line, evacuated to ~10^{-3} Torr and isolated from the diffusion pumps. A water solution of $CuCl_2 \cdot 2H_2O$ (0.01 M, 200 ml, 2mmol) was added in ~45s. The light green Cu^{2+} solution first yielded on contact with $NaBH_4$ a yellow-brown solution and then a brown-black gelatinous precipitate with gas evolution. The reaction was visually complete within 2 min. the precipitate was filtered and washed with three 20mL portions of prepurged water and then acetone (~20mL) and dried in vacuo yielding a filmy coppery material (0.10g, 79%). X-ray powder diffraction analysis of the powder indicated metallic copper with crystalline size ~30 nm.

2.2. A typical proceeding for reduction of Acetophenone oxime to α Phenylethylamine with $NaBH_4$/Nano Cu/Charcoal system.

A mixture of Nano Cu (0.189g, 3mmol) and charcoal (0.175g) was ground in a mortar. Acetophenone oxime (0.135g, 1mmol)was then added and grinding of the reaction mixture was continued for a moment. The contents was then transferred in a round-bottomed flask (15ml) equipped with a magnetic stirrer and condenser, and ETOH (2ml) was added to mixture. Reducing agent (0.148g, 4mmol) was added portion wise to the reaction mixture under reflux condition for 2.10h. TLC monitored the progress of the reaction (eluent; CCl_4/EtO). After completion of the reaction, CH_3CN(1mL) was added to the reaction mixture and stirred for an additional 10 min. The mixture was filtered and the charcoal separated and then add KOH (2mmol) was added to aqueous solution and stirred for 30min. The mixture was extracted with CH_2Cl (3×10ml) and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded the pure liquid α-phenylethylamine in 92% yield (Table 3).

3. Results and Discussion

Although the combined system of $NaBH_4$ and $CuSO_4$ has been reported for reduction of oximes (Rao et al., 2002), use of expensive volatile organic solvents, mixture of products, long reaction times and tedious workup procedures put some restrictions on the use of these protocols for practical applications. So, in continuation of our research program directed to the application of nanocatalyst (Zeynizadeh et al., 2013; Bagheri et al. 2013; Zeynizadeh et al., 2013), we found that $NaBH_4$ in the presence of nano copper supported on Charcoal reduces various aldoximes and ketoximes to the corresponding amines. In order to obtain the optimum reaction conditions, we performed reduction of benzaldoxime as a model compound with sodium borohydride under different conditions.

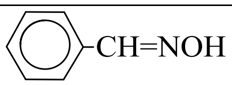
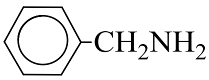
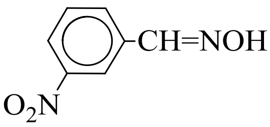
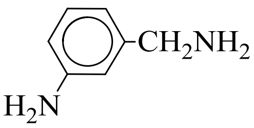
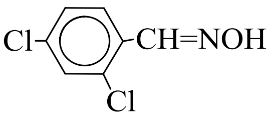
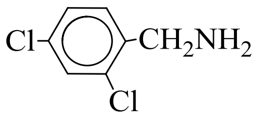
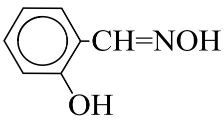
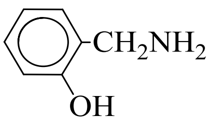
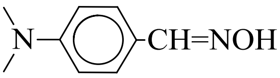
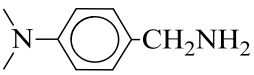
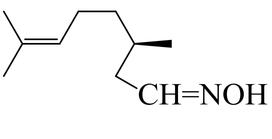
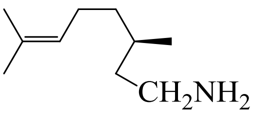
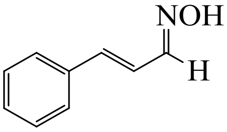
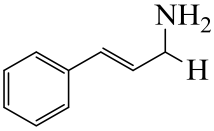
The effect of various molar ratio, solvent and use of charcoal was investigated in the typical experiment (Table 1). As seen, the combination system of $NaBH_4$ with Nano Cu supported on charcoal showed a perfect efficiency for reduction of benzaldoxime, we think that by the immobilization of nano Cu on charcoal, the interaction of oxime, $NaBH_4$ and nano Cu in both of the systems is increased. As it's seen, the solely $NaBH_4$ or nano copper or bulk Cu did not show any efficiency even at the prolonged reaction time (entries 5, 6 and 7). In addition, the results showed that the 4 mmol of $NaBH_4$ in the presence of nano Cu (2 mmol) supported on charcoal (175mg) perfectly reduces one mmol of benzaldoxime to benzylamine within 1.5 h. The reaction was carried out at reflux temperature (70-80 ^oC) with the simple reaction procedure and workup. The utility of $NaBH_4$/Nano Cu/Charcoal system was further examined on reduction of various aldoxime and ketoxime. Table 2, 3 show the general trend and versatitility of this synthetic protocol.

Table 1. Optimization experiments for reduction of benzaldehyde oxime with $NaBH_4$ under different conditions

Entry	Reaction components [a]	Molar ratio	Condition	Time(h)	Conversion (%)
1	Oxime/$NaBH_4$/Nano Cu	1:4:2	H_2O/reflux	2	80
2	Oxime/$NaBH_4$/Nano Cu/Charcoal	1:4:2	CH_3CN/reflux	2	80
3	Oxime/$NaBH_4$/Nano Cu/Charcoal	1:4:2	ETOH/reflux	1.5	100
4	Oxime/$NaBH_4$/Nano Cu/Charcoal	1:3:2	H_2O/reflux	2	100
5	Oxime/$NaBH_4$/bulk Cu/Charcoal	1:4:3	ETOH/reflux	3	10
6	Oxime/$NaBH_4$/bulk Cu	1:4:3	ETOH/reflux	3	0
7	Oxime/$NaBH_4$	1:4	ETOH/reflux	3	0

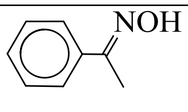
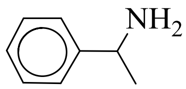
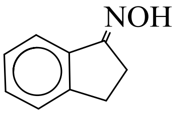
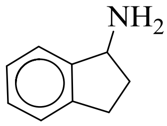
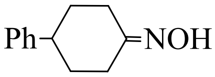
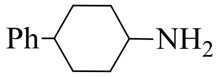
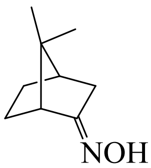
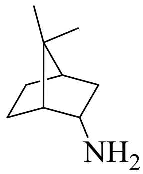
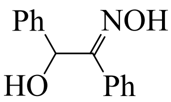
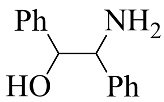
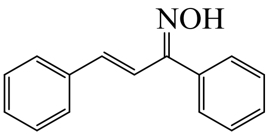
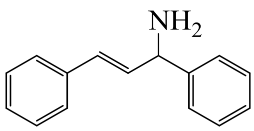
[a]Use 0.175 gr charcoal for every reaction

Table 2. Reduction of aldoximes to amines with $NaBH_4$/NanoCu/Charcoal[a]

Entry	Substrate	Product	Molar ratio Sub./$NaBH_4$/Nano Cu	Condition	Time (h)	Yeild (%)[b]
1			1:3:2	ETOH/reflux	1.5	92
2			1:5:2	ETOH/reflux	2	92
3			1:3:2	ETOH/reflux	1.5	90
4			1:3:2	ETOH/reflux	1.25	90
5			1:3:2	ETOH/reflux	2.20	96
6			1:3:2	ETOH/reflux	2.5	85
7			1:4:3	ETOH/reflux	2	92

[a]All reaction were carried out in 0.175gr of Charcoal. [b]Yields refer to isolate pure products

Table 3. Reduction of ketoximes to amines with $NaBH_4$/Nano Cu/Charcoal[a]

Entry	Substrate	Product	Molar ratio Sub./$NaBH_4$/Nano Cu	Condition	Time (h)	Yeild (%)[b]
1			1:4:3	ETOH/reflux	2.10	92
2			1:4:3	ETOH/reflux	2.30	95
3			1:4:3	ETOH/reflux	1.40	90
4			1:4:3	ETOH/reflux	2.50	94
5			1:4:3	ETOH/reflux	3.20	91
6			1:5:3	ETOH/reflux	2	90

[a]All reaction were carried out in 0.175gr Charcoal.[b] Yields refer to isolate pure products

The case study in Table 2 shoes that aldoximes containing nitro group were reduced completely to the corresponding diamines under the experimental conditions. This means that the present protocol reduces nitro and oxime functional groups with the same reactivity (Table 2). Further investigation resulted in reduction of α, β-unsaturated aldoximes or ketoximes with $NaBH_4$/Nano Cu system (5:3) and 175mgr charcoal was carried out in a perfect regioselectivity. Therefore, conjugated oximes were reduced to the corresponding allylic amines in high yields (Table 2). Briefly, in this paper the excellent capability of $NaBH_4$/Nano Cu/Charcoal system for reduction of various aldoximes and ketoximes to the corresponding amines within 1-3.20h at reflux condition is shown. The method also exhibited high efficiency and regioselectivity in the reduction of conjugated aldoximes and ketoximes. Therefore, high yield, quick reaction times, simple reaction procedure and workups are the advantages which make this protocol a useful addition to the present methodologies.

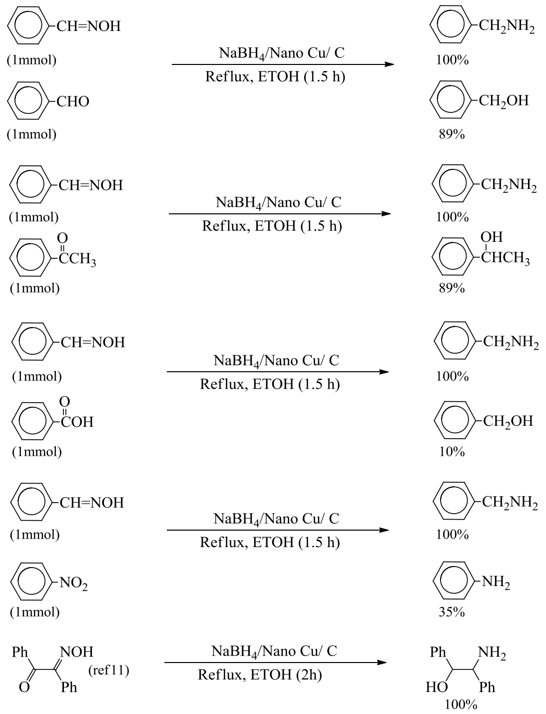
In order to show the efficiency of this method, we compared our results with those reported in the literature for $Mg/HCOONH_4$ $(Py)Zn(BH_4)_2$ (Abiraj et al., 2004), $(Py)Zn(BH_4)_2$ (Zeynizadeh et al., 2005), $NaBH_4/ZrCl_4/Al_2O_3$ (Zeynizadeh et al., 2011), $NaBH_3CN/MoCl_5/NaHSO.H_2O$ (Kouhkan et al., 2011) as shown in Table 4.

We researched effective of these protocols for reduction oximes in the presence of many functional groups such as carbonyl compounds, nitro, carboxylic acids and we found that $NaBH_4$ in the presence of nano copper supported on charcoal mainly reduces and the oximes compounds are completed to corresponding amines (Scheme 2).

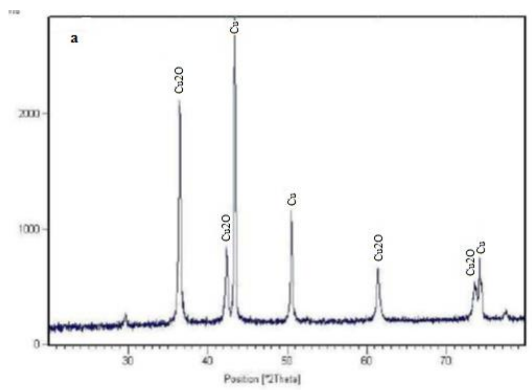
Table 4. Comparison of reduction of oximes to amines with with $NaBH_4$/Nano Cu/Charcoal system and other reported reaction systems

Entry	System	Condition	Time (min) /Yield (%)[a]			
			benzaldoxime	cinnamaldehyde oxime	Acetophenone oxime	Camphor oxime
1	Mg/$HCOONH_4$ (Abiraj et al., 2004)	MeOH/r.t	38/91	-	40/89	-
2	(Py)Zn$(BH_4)_2$ (Zeynizadeh et al., 2005)	THF/ reflux	180/94	-	-	90/92
3	$MoCl_5$/$NaHSO_4 \cdot H_2O$ (Kouhkan et al., 2011)	EtOH or DMF/ reflux	20/95 90/96	120/93 150/94	60/93 90/92	-
4	$ZrCl_4$/Al_2O_3 (Zeynizadeh et al., 2011)	solvent-free/ r.t	2/94	2/96	2/95	-
5	Nano Cu/Charcoal	ETOH/ reflux	90/92	120/92	130/92	150/94

[a]Yields refer to the isolated pure products



Scheme 2. Competitive reduction of oximes in the presence of nano copper supported on charcoal



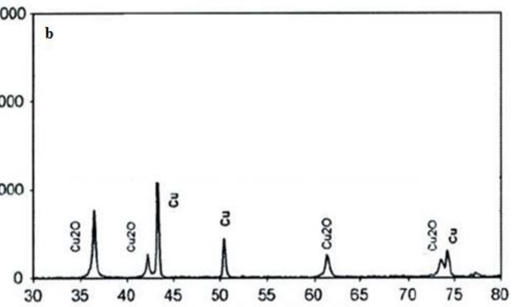
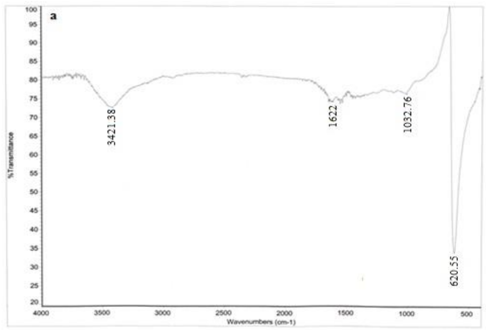


Fig. 1. XRD pattern of obtained sample (a) and (b) (Khanna et al., 2008)



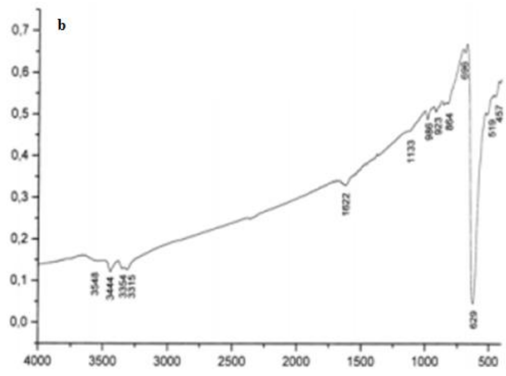


Fig. 2. Infrared spectra of the samples (a) and (b) (Usman et al., 2012)

4. Conclusion

In this paper, we have shown Cu Nanoparticle promoted reduction of various oximes by $NaBH_4$ in EtOH under reflux condition. This method offers some advantages in terms of clean reaction conditions, easy work-up procedure, short reaction time, and suppression of any side product. So we think that Cu Nanoparticle/Charcoal/ $NaBH_4$ system could be considered a new and useful addition to the present methodologies in this area.

Acknowledgments

The authors gratefully acknowledge the financial support of this work by the research council of Urmia University and Nano Research Center of Iran.

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