December 2009 Volume 5 Issue 4

Organic CHEMISTRY

An Indian Journal

Trade Science Inc.

Full Paper

OCAIJ, 5(4), 2009 [412-415]

The efficient reduction of oximes to amines with Zn and acetic acid under ultrasonic irradiation

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Received: 8th September, 2009 ; Accepted: 18th September, 2009

ABSTRACT

Zn and Acetic acid, as a kind of reducing system can easily reduce a variety of aromatic aldoximes or ketoximes to their corresponding amines in high to excellent yields under ultrasonic irradiation at room temperature. As against the conventional methods, the reaction times were shorted by 1h-4h.

KEYWORDS

Ultrasonic Irradiation;
Zn;
Acetic acid;
Reduction;
Oxime;
Amine.

INTRODUCTION

Amines are very important organic compounds widely used as intermediates for the synthesis of a diversity of pharmaceutical[1] and polymeric products[2]. Therefore, synthetic methodologies for amines have evolved through the years from diverse precursors[3]. The transformation of oximes into amines is a synthetically important process and its value has been well established. A variety of oximes can easily be prepared from the corresponding aldehydes or ketones in excellent yields[4,5], which provides a feasible approach for preparing amines. Numerous new reagents have been developed for the reduction of oximes to amines, such as Lithium aluminum hydride[6], Sodium- Liquid Ammonia or Sodium- ethanol[7], Sodium amalgam[8], Catalytic hydrogenation[9]. However, these methods suffer from drawbacks, such as requiring anhydrous condition and the reaction conditions greatly depend on the structures of oximes. For example, the reduction of benzaldoxime to benzylamine goes in the presence of catalyst Raney nickel under the harsh reaction condition of 10.1MPa,100°C. Thus, development of a simple and efficient method for synthesizing amines is very desirable.

High-power ultrasound can generate cavitation within a liquid and through cavitation provide a source of energy which can be used to enhance a wide range of chemical processes[10]. The use of high-intensity ultrasound to enhance the reactivity of metals has become an important synthetic technique for many heterogeneous organic reactions, especially those involving reactive metals, such as magnesium, lithium and zinc[11-14]. The mechanism of the rate enhancements in reactions of metals has been unveiled by monitoring the effect of ultrasonic irradiation on the kinetics of the chemical reactivity of the solids, examining the effects of irradiation on surface structure and size distributions of powders and solids[15]. Ultrasonic irradiation of liquid, nickel, zinc, and copper powders leads to dramatic changes in structure, ultrasonic irradiation effectively removed the inactive surface oxide coating. The removal of such passivating coatings dramatically improves reaction rates. Based on this, we now report the application of ultrasonic technology to the reduction of oximes to Amines. The results showed that the reaction times were shorted by 1h-4h with yields of 93%-98% (Scheme 1). The simplified condition of the reaction is adaptable to the industrialized production.

$$R(R')C{=}NOH \xrightarrow[\text{Ultrasound}]{\text{Zn, AcOH}} R(R')CHNH_2$$

R: Alkyl, Aryl
R': H, Alkyl

Scheme 1

RESULTS AND DISCUSSION

A variety of aldoximes and ketoximes were reduced to their primary and secondary amines, respectively, in the presence of Zn and acetic acid under ultrasonic Irradiation with excellent yields. The reaction times and isolated yields of the products were summarized in TABLE 1. Compared with the classic methods reported in the relevant literatures, it not only shorten the reaction times, but also led to higher yields. By comparison, Benzylamine was obtained from Benzaldehyde oxime in the presence of Zn under reflux in acetic acid for 4hr, with 90% yield was provided. The reaction was completed in 60min under ultrasonic irradiation at room tempreture and gave yield of 94%. It is easy to see that ultrasonic irradiation can significantly promote the reaction.

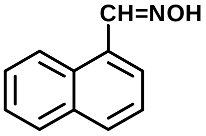
Substitution pattern on the aromatic ring has an influence on the reaction rate. The reduction of aryl aldoximes with electron donating substituents like dimethylamino group (entry 8) and methoxy group (entries 9,10) was slow and with electron withdrawing substituents, such as chloro group (entries 2,3 and 4) and nitro group (entry 5) were readily reduced. Aryl aldoxime with a substituted nitro group showed a selectivity and was readily reduced with 1.2 molar amounts of reducing agent without affecting the nitro group(entry 5), but with further molar amounts of reducing agent the simultaneous reduction of the nitro group took place (entry 6). 1-Naphthalene aldoxime (entry 13) shows further reactivity relative to others with consumption of lower molar of equivalents of the reducing reagent (1: 0.8).

In anticipating Fe and Acetic acid reduction, experiments were also performed by using Oximes with Fe and Acetic acid under ultrasonic irradiation for 1.5h. Even after a longer period the yields were only 10-15%, which clearly indicated that reducing Oximes to Amines with Fe and acetic acid under ultrasonic irradiation was not feasibility.

TABLE 1: Reduction of oximes to amines

Entry	Substrate	Molar Ratio Subs. /Reag.	Product	Time (h)	Yield (%)	Mp or Bp(?)	
						Find	Report[16,17]
1	$C_6H_5CH{=}NOH$	1:1.2	$C_6H_5CH_2NH_2$	1h	94%	183-184	184-185
2	$3\text{-}ClC_6H_4CH{=}NOH$	1:1.2	$3\text{-}ClC_6H_4CH_2NH_2$	0.8h	93%	110-112	110-112
3	$4\text{-}ClC_6H_4CH{=}NOH$	1:1.2	$4\text{-}ClC_6H_4CH_2NH_2$	0.9h	96%	215-216	215
4	$2,4\text{-}Cl_2C_6H_3CH{=}NOH$	1:1.2	$2,4\text{-}Cl_2C_6H_3CH_2NH_2$	0.7h	98%	257-259	258-260
5	$4\text{-}O_2NC_6H_4CH{=}NOH$	1:1.2	$4\text{-}O_2NC_6H_4CH_2NH_2$	0.6h	93%	266	265
6	$4\text{-}O_2NC_6H_4CH{=}NOH$	1:2	$4\text{-}H_2NC_6H_4CH_2NH_2$	1.3h	95%	101/0.05	101/0.05mmHg
7	$2\text{-}HOC_6H_4CH{=}NOH$	1:1.2	$2\text{-}HOC_6H_4CH_2NH_2$	0.5h	96%	129-130	129
8	$4\text{-}(CH_3)_2N\text{-}C_6H_4CH{=}NOH$	1:1.2	$4\text{-}(CH_3)_2N\text{-}C_6H_4CH_2NH_2$	1.7h	96%	149-150	150/1mmHg
9	$4\text{-}CH_3OC_6H_4CH{=}NOH$	1:1.2	$4\text{-}CH_3OC_6H_4CH_2NH_2$	1.5h	94%	235-236	236-237
10	$2\text{-}CH_3OC_6H_4CH{=}NOH$	1:1.2	$2\text{-}CH_3OC_6H_4CH_2NH_2$	2h	95%	226/724	227/724mmHg
11	$C_6H_5(CH_3)C{=}NOH$	1:1.2	$C_6H_5(CH_3)CHNH_2$	1.1h	95%	186-188	188
12	Furfuraldoxime	1:1.2	Furfurylamine	1.4h	94%	145-147	145-146
13[a]	$C_{10}H_7CH{=}NOH$	1:0.8	$C_{10}H_7CH_2NH_2$	0.3h	98%	290-292	290-293

[a] **The structure of the compound (entry 13) is**



In Conclusion, we have described an efficient and convenient method to reduce Oximes to Amines with Zn and acetic acid under ultrasonic Irradiation, which bring some practical values with mild reaction conditions, cleaner reactions, and simple experimental procedures.

EXPERIMENTAL

All reagents were commercially available. Oximes were prepared according to literature procedure[4,5]. TLC was used to monitor the reaction process. TLC was GF_{254} thin layer chromatography with Carbon tetrachloride / ether(5/2) used as eluent.

IR spectra were recorded on a IR Prestige-21/ FTIR-8400S spectrometer. ^{1}H-NMR spectra were obtained on a Brucker ADVANCE(400MHz) spectrometer using TMS as internal standard and DMSO as solvent. Melting point were determined with an electrothermal micromelting point apparatus and uncorrected. All the liquid reagents were fresh distilled. The products were also characterized by comparison of their melting points and boling points with literature values.

General Procedure for Preparation of Benzylamine (entry 1)

Benzaldehyde oxime (1.21g, 0.01mol), acetic acid (5ml), zinc powder (0.78g, 0.012mol) were respectively added in a dry 50ml conical flask and treated under Ultrasonic Irradiation at room tempreture. The progress of the reaction was monitored by TLC.After completion of the reaction, the mixture was extracted with dichloromethane (3 × 10ml), the extract was dried with anhydrous sodium sulfate. Then it was evaporated under reduced pressure afforded the crude product. The product was purified by recrystallization. Selected spectral data of some of the products are given below:

$C_6H_5CH_2NH_2$(entry 1) ^{1}HNMR($CDCl_3$): δ: 7.33(s, 5H), 3.90 (s, 2H), 1.41 (s, 2H); IR (ν, neat): 3367, 3278, 3039, 2940, 2857, 1600, 1492, 1450, 1388, 1052, 1025, 854, 780, 775, 730, 695cm^{-1}.

4-$ClC_6H_4CH_2NH_2$ (entry 3) ^{1}HNMR($CDCl_3$): δ: 7.26(s, 4H), 3.81 (s, 2H), 1.37 (s, 2H);IR (ν, neat): 3380, 3290, 3180, 3040, 2925, 2860, 1587, 1900, 1600, 1495, 1408, 1380,1095, 1020, 860, 815, 720, 650cm^{-1}.

2,4-$Cl_2C_6H_3CH_2NH_2$(entry 4) ^{1}HNMR ($CDCl_3$): δ: 7.45-7.11 (m, 3H), 3.90 (s, 2H), 1.52 (s, 2H);IR (ν, neat):3390, 3300, 3090, 3070, 2940, 2880, 1590, 1562, 1470, 1392,1260, 1200, 1098, 1100, 1050, 865, 820, 732, 740, 715, 700,650cm^{-1}.

4-$O_2NC_6H_4CH_2NH_2$(entry 5) ^{1}HNMR(DMSO-d_6): δ: 8.90 (bs, 3H), 8.37 (d, 2H), 7.81(d, 2H), 4.36(s, 2H).

4-$H_2NC_6H_4CH_2NH_2$(entry 6) ^{1}HNMR($CDCl_3$): δ: 7.16(d, 2H), 6.63(d, 2H), 3.82-3.53 (b, 2H), 3.74 (s, 2H), 1.51-1.37(b, 2H);IR (ν, neat): 3420, 3360, 3205, 3010, 2930, 2850, 1615, 1520, 1440, 1290, 1180, 1130, 1085, 1030, 880, 825cm^{-1}.

2-$HOC_6H_4CH_2NH_2$(entry 7) ^{1}HNMR($CDCl_3$): δ:7.25-6.81(m, 4H), 3.72 (s, 2H), 1.80 (s, 2H).

2-$CH_3OC_6H_4CH_2NH_2$ (entry 10) ^{1}HNMR ($CDCl_3$): δ: 7.34-6.61(m, 4H), 3.75 (s, 2H), 3.78 (s, 3H), 1.61 (s, 2H); IR (ν, neat): 3385,3300, 3200, 3000, 2940, 2830, 1600,1580, 1500, 1460, 1440, 1390, 1320, 1295, 1250, 1180, 1110, 1050, 1040, 900, 820, 760, 730cm^{-1}.

Furfurylamine(entry 12) IR (ν,neat): 3376, 3291, 3201, 3145, 3115, 2916, 2855, 1603, 1506, 1339, 1214, 1148, 1070, 1008, 920, 881, 807, 737, 600cm^{-1}.

$C_{10}H_7CH_2NH_2$(entry 13) ^{1}HNMR($CDCl_3$): δ: 7.93-7.21(m, 7H), 4.02(s, 2H), 1.34(s, 2H); IR(ν,neat): 3380, 3295, 3190, 3050, 2900, 2880, 2850, 1607, 1510, 1460, 1395, 1270, 1162, 966, 833, 790, 772, 735, 699cm^{-1}.

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