

A Rapid and Convenient Method for the Synthesis of Aldoximes under Microwave Irradiation Using *in situ* Generated Ionic Liquids

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We have developed a chemoselective, simple and efficient method for the preparation of aldoximes using microwave irradiation in the presence of tribenzylamine or 1,4-diazabicyclo[2.2.2]octane or 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide as bases and useful precursors for *in situ* generation of ionic liquids.

Keywords: Oxime, Hydroxylamine hydrochloride, Ionic liquid, Microwave irradiation

INTRODUCTION

Oximes are highly crystalline materials and oximation is very efficient method for characterization and purification of carbonyl compounds. These compounds not only represent a useful series of derivatives of carbonyl compounds but also may be used as intermediates for the preparation of amides by the Beckmann rearrangement [1], nitrones [2], hydroximinoyl chlorides, nitrile oxide [3] and chiral α -sulfinyl oximes [4]. The usual method for preparation of oximes [5,6] involves treatment of carbonyl compounds with hydroxylamine hydrochlorides in a basic aqueous medium with adjusted pH. Application of microwave heating technique has been currently under intensive investigation [7] and has been recently reviewed [8]. The advantages of using microwave irradiation are: (a) decrease in the reaction time and (b) cleaner reaction with straightforward work-up. The coupling of microwave irradiation with ionic liquids enhance reaction rates due to the ionic character of ionic liquids which make them microwave active solvents with easier work-up and

simplified purification [9].

In recent years, ionic liquids have attracted intensive interest for their being a possible replacement of traditional solvents for organic reactions, particularly in the area of green chemistry, due to their advantageous properties, including negligible vapor pressure and high thermal and chemical stability. They have also been referred to as 'designer solvents' as their physical and chemical properties could be adjusted by a careful choice of cation and anion [10].

Microwave-assisted organic transformation coupled with ILs has attracted attention because of enhanced reaction rates, easier workup, and straightforward purification. The dipole characteristics of IL translate into rapid excitation by microwaves and consequently faster reactions [11].

In the past decade, there has been a great interest for development of new ionic liquids (ILs) [12]. Recently quaternary ammonium salts as ionic liquids were synthesized in good to excellent yields [13]. The dabco-based IL has shown wide electrochemical application as a highly stable electrolyte for lithium ion rechargeable batteries, fuel cells, capacitors, solar cells, actuators, and so on [14].

In continuation of our effort to develop new methods in

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organic transformations [15-20], we report here that tribenzylamine (TBA) or 1,4-diazabicyclo[2.2.2]octane (DABCO) or 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide (BDABCO) could serve as base and as precursors of ionic liquids for the preparation of aldoximes under microwave irradiation. This method is friendly to the environment.

EXPERIMENTAL

Products were characterized by comparison with authentic samples (^1H NMR, IR and GC spectrum, melting and boiling point, TLC) [5-6]. ^1H NMR spectra were recorded on a 250 MHz in CDCl_3 , IR spectra on a FT-IR-680 plus and GC spectra on a GC-14A shimadzu.

General Procedure for Preparation of Benzaldehyde Oxime

A mixture of 0.11 g (1 mmol) of benzaldehyde and 0.14 g (2 mmol) of hydroxylamine hydrochloride and 1 mmol of base ((tribenzyl amine (0.29 g) or 1,4-diazabicyclo [2.2.2] octane (0.11 g) or 1-benzyl-4-aza-1-azoniabicyclo [2.2.2] octane bromide (0.28 g)) was ground thoroughly in a mortar by a pestle. The mortar was covered with a watch glass and put inside a Samsung microwave (2450 MHz, 900 W). The completion of the reaction was monitored by TLC (EtOAc: cyclohexane (25:75)). After completion of the reaction, the mortar was removed from the oven and the mixture was cooled to room temperature and 10 ml of 5% aqueous HCl was added. The mixture was extracted with CH_2Cl_2 (2×5 ml).

The extracts were combined and dried (Na_2SO_4), evaporation of solvent under vacuum gave benzaldehyde oxime, in 98% yield, m.p.: 33-35 °C. The product could be further purified by recrystallization from normal-hexane.

RESULTS AND DISCUSSION

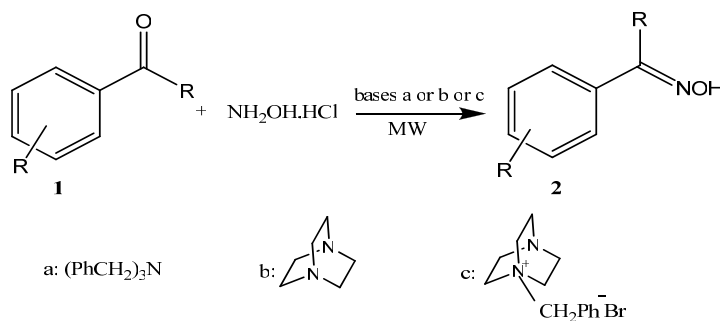
Hydroxylamine hydrochloride was reacted with several aliphatic and aromatic aldehydes and ketones using tribenzylamine (TBA) or 1,4-diazabicyclo[2.2.2]octane (DABCO) or 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide (BDABCO) as bases and microwave irradiation (Scheme 1) to give the corresponding oximes.

We believe that protonation of these organic bases during the reaction makes them ionic liquids and enhances the reaction rate under microwave irradiation. To evaluate the synergy between these bases and microwave irradiation, several experiments were performed. When benzaldehyde was treated with hydroxylamine hydrochloride without any bases under microwave irradiation, after 6 min of irradiation the yield of the benzaldehyde oxime was only 20%.

The reaction of benzaldehyde with hydroxylamine hydrochloride using these bases under solid state without microwave irradiation, attended after 15 min of grinding the mixture in a mortar by a pestle, the oxime yield was less than 30%. By using these bases under microwave irradiation, oximation proceeded in excellent yield and short reaction time (Table 1). Aromatic aldehydes were converted to the corresponding oximes in more than 75% yield in less than 4 min as a mixture of syn and anti isomers (E/Z). Based on TLC analysis in all cases the E-isomers were the major products (90:10 to 100:0). Oximation of ketones yielded 10-55% and required longer reaction times.

It is interesting to note that in these reactions, nitriles were not formed, and in the IR spectra the CN group was not observed around 2200 cm^{-1} . In IR spectra the OH and C=NOH group were observed around $3300\text{-}3500$ and $1640\text{-}1690\text{ cm}^{-1}$.

Another noteworthy aspect of this method is the exclusive reaction of aldehydes with hydroxylamine hydrochloride, in



Scheme 1

Table 1. Reaction of Carbonyl Compound **1** with Hydroxylamine Hydrochloride in the Presence of Bases

Entry	Substrate	DABCO		TBA		BDABCO		M.p. (°C) (lit. m.p.)
		Time (S)	Yield (%)	Time (S)	Yield (%)	Time (S)	Yield (%)	
a	PhCHO	70	98	90	98	100	98	33-35 (33-35) [5]
b	2-HOC ₆ H ₄ CHO	30	98	40	98	40	97	57-59 (57) ^b
c	2-MeOC ₆ H ₄ CHO	50	97	60	97	60	95	88-90 (87-89) [21]
d	3-MeOC ₆ H ₄ CHO	120	95	100	92	120	90	40-41 (40) [22]
e	4-MeOC ₆ H ₄ CHO	50	92	50	90	60	90	131-133 (132-134) [23]
f	2-ClC ₆ H ₄ CHO	140	90	160	92	180	90	72-74 (68-72) [21]
g	3-ClC ₆ H ₄ CHO	50	97	60	97	60	95	117-119 (118) ^b
h	4-ClC ₆ H ₄ CHO	200	87	210	88	240	85	145-147 (145-146) [23]
i	4-MeC ₆ H ₄ CHO	90	97	100	97	120	85	108-110 (107-109) [23]
j	3,4-(MeO) ₂ C ₆ H ₃ CHO	240	70	260	72	300	70	92-94 (92-94) [5]
k	PhCH=CHCHO	50	87	60	87	60	85	136-138 (136-138) [5]
l	4-NO ₂ C ₆ H ₄ CHO	240	70	250	70	300	70	128-130 (128-131) [5]
m	PhCOMe	210	55	230	55	240	55	56-58 (56-59) [21]
n	4-MeOC ₆ H ₄ COMe	180	60	200	60	180	55	86-88 (87) [22]
o	3,4-(MeO) ₂ C ₆ H ₄ COMe	240	38	240	35	240	20	139-141 (139-141) [5]
p	PhCOPh	300	12	300	10	300	5	138-140 (138-140) [5]
q	CH ₃ CHO	300	0	300	0	300	0	-
r	Cyclohexanone	300	0	300	0	300	0	-

^aIsolated oxime after purification. ^bThe melting points were getting from www.acros.com.

the presence of ketones. By treatment of one equivalent of aldehydes in the presence of one equivalent of ketones with two equivalent of hydroxylamine hydrochloride, only the aldehydes were selectively converted to the corresponding oximes and the ketones did not react at all. We evaluated and compared the chemoselectivity of our work with some of the reported methods (Table 2).

Therefore this method could be used selectively for the preparation of aldoximes of the compounds that contain both aldehyde and ketone functional groups. In comparison to aldoximes the ketoximes were formed in longer reaction times and lower yields.

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Table 2. Chemoselective Reaction of Aldehydes with Hydroxylamine Hydrochloride, in the Presence of Ketones

1 (Present work)	<p> $\text{Ph}-\text{CHO} + \text{Ph}-\text{CO}-\text{Me} \xrightarrow[\text{Ionic Liquids a, b, c (1 eq.)}]{\text{NH}_2\text{OH}\cdot\text{HCl (2 eq.)}}$ MW (70 S) </p> <p>0% (acetophenone oxime), 100% (benzaldehyde oxime)</p> <p> $\text{Ph}-\text{CH}(\text{Me})-\text{CHO} + \text{Ph}-\text{CO}-\text{Me} \xrightarrow[\text{Ionic Liquids a, b, c (1 eq.)}]{\text{NH}_2\text{OH}\cdot\text{HCl (2 eq.)}}$ MW (70 S) </p> <p>0% (acetophenone oxime), 100% (2-phenylpropanal oxime)</p> <p> $\text{Cyclohexanone} + \text{Ph}-\text{CHO} \xrightarrow[\text{Ionic Liquids a, b, c (1 eq.)}]{\text{NH}_2\text{OH}\cdot\text{HCl (2 eq.)}}$ MW (70 S) </p> <p>5% (cyclohexanone oxime), 95% (benzaldehyde oxime)</p> <p> $\text{2-MeO-C}_6\text{H}_4-\text{CHO} + \text{Ph}-\text{CO}-\text{Me} \xrightarrow[\text{Ionic Liquids a, b, c (1 eq.)}]{\text{NH}_2\text{OH}\cdot\text{HCl (2 eq.)}}$ MW (70 S) </p> <p>100% (2-methoxybenzaldehyde oxime), 0% (acetophenone oxime)</p>
2 [24]	<p> $\text{O}_2\text{N}-\text{C}_6\text{H}_4-\text{CHO} \xrightarrow[\text{NH}_2\text{OH}\cdot\text{HCl, 28 min, r.t.}]{0.4 \text{ g PMP-HTP}}$ </p> <p>87%</p> <p> $\text{O}_2\text{N}-\text{C}_6\text{H}_4-\text{COCH}_3 \xrightarrow[\text{NH}_2\text{OH}\cdot\text{HCl, 28 min, r.t.}]{0.4 \text{ g PMP-HTP}}$ </p> <p>100%</p>
3 [5]	<p> $\text{Ph}-\text{CH}(\text{Me})-\text{CHO} + \text{Ph}-\text{CO}-\text{Me} \xrightarrow[\text{NH}_2\text{OH}\cdot\text{HCl (2eq), r.t.}]{\text{Silica gel}}$ </p> <p>0% (acetophenone oxime), 100% (2-phenylpropanal oxime)</p>
4 [4]	<p> $\text{2-Cl-3-F-C}_6\text{H}_3-\text{CHO} \xrightarrow[\text{MW (3 min)}]{\text{Silica gel, NH}_2\text{OH}\cdot\text{HCl (2eq)}}$ </p> <p>100%</p> <p> $\text{3,4-MeO}_2\text{-C}_6\text{H}_3-\text{COCH}_3 \xrightarrow[\text{MW (3 min)}]{\text{Silica gel, NH}_2\text{OH}\cdot\text{HCl (2eq)}}$ </p> <p>100%</p>

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