



Synthesis of Oximes from the Corresponding of Organic Carbonyl Compounds with $\text{NH}_2\text{OH}\cdot\text{HCl}$ and Oxalic Acid

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ABSTRACT

The oximation of a variety of aldehydes and ketones was carried out with $\text{NH}_2\text{OH}\cdot\text{HCl}$ in the presence of oxalic acid as catalyst under reflux conditions. The reactions were performed in CH_3CN with excellent yields (90-95%) of products in appropriate times (55-90 min).

Key words: Oximesaloximes, acetophenoneoximes, $\text{H}_2\text{NOH}\cdot\text{HCl}$, Oxalic acid.

INTRODUCTION

Oximes have been used for the protection and purification of carbonyl compounds in organic synthesis¹. Also, these compounds have antimicrobial²⁻³, antioxidant⁴, antitumor⁵, anti-depressive⁶, antiviral agents and anticonvulsant properties⁷. Recently, the oximation methods have been reviewed⁸ by us. The lack of information for the oximation of carbonyl compounds in the presence of oxalic acid and our ongoing attentions to the development of modified methods in organic synthesis⁸⁻¹⁵ encouraged us to investigate this transformation with $\text{NH}_2\text{OH}\cdot\text{HCl}$ in the presence of oxalic acid. So, herein, we describe a convenient method for the oximation of a variety of aldehydes and ketones to their corresponding alcohols with $\text{NH}_2\text{OH}\cdot\text{HCl}/\text{H}_2\text{C}_2\text{O}_4$ system.

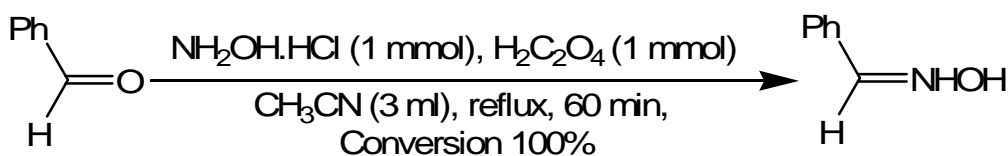
RESULTS AND DISCUSSIONS

In order to determine optimization reaction conditions for the oximation of aldehydes and ketones, benzaldehyde and acetophenone have been used as model compounds. The results showed that using $\text{NH}_2\text{OH}\cdot\text{HCl}$ (1 mmol) and $\text{H}_2\text{C}_2\text{O}_4$ (1 mmol) in CH_3CN (3 ml) was the best conditions for the oximation of benzaldehyde. The reaction was completed in 60 minutes with the excellent yield (95%) of the product as shown in scheme 1.

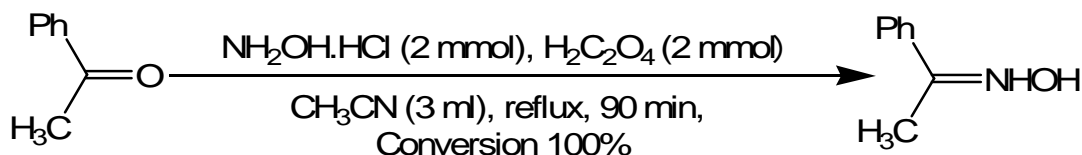
In order to evaluate the generality of the process, a variety of aldehydes were ground with hydroxylamine hydrochloride under optimized reaction conditions. In this approach, the corresponding aldoximes were obtained in quantitative yield (90-95%). The results have been reported in table 1 (entries 1-6).

The oximation of ketones was also carried out well by $\text{NH}_2\text{OH}\cdot\text{HCl}/\text{H}_2\text{C}_2\text{O}_4$ system, but due to the lower reactivity of ketones relative to aldehydes, the oximation requires higher molar amounts of $\text{NH}_2\text{OH}\cdot\text{HCl}$ (2 mmol) and $\text{H}_2\text{C}_2\text{O}_4$ (2mmol) vs. 1 mmol of the substrates (table 1, entries 7-12). The

results showed that using $\text{NH}_2\text{OH}\cdot\text{HCl}$ (2mmol) and $\text{H}_2\text{C}_2\text{O}_4$ (2mmol) in CH_3CN (3 ml) was the best conditions for the oximation of acetophenone. The reaction was completed in 90 minutes with the excellent yield (95%) as shown in scheme 2.



Scheme 1:



Scheme 2:

EXPERIMENTAL

All substrates and reagents were purchased from commercial sources with the best quality. IR and ^1H NMR spectra were recorded on PekinElmer FT-IR RXI and 300 MHz Bruker spectrometers, respectively. The products were

characterized by their ^1H NMR or IR spectra and comparison with authentic samples (melting points). All yields referred to isolated pure products. The purity of products was determined by TLC and ^1H NMR. Also, reactions were monitored by TLCs utilizing plates cut from silica gel 60 F₂₅₄ aluminum sheets.

Table 1: Oximation of Carbonyl Compounds (1 mmol) by $\text{NH}_2\text{OH}\cdot\text{HCl}/\text{H}_2\text{C}_2\text{O}_4$ under Reflux Conditions in CH_3CN (3 mL)

Entry	Aldehydes	Products	Time/min.	Yield ^c /%
1 ^a	benzaldehyde	benzaldehydeoxime	60	95
2 ^a	4-bromobenzaldehyde	4-bromo benzaldehydeoxime	55	95
3 ^a	4-nitrobenzaldehyde	4-nitrobenzaldehydeoxime	60	90
4 ^a	4-methylbenzaldehyde	4-methyl benzaldehydeoxime	60	94
5 ^a	2-methoxybenzaldehyde	2-methoxy benzaldehydeoxime	60	91
6 ^a	4-methoxybenzaldehyde	4-methoxy benzaldehydeoxime	60	94
7 ^b	acetophenone	acetophenoneoxime	90	95
8 ^b	4-methylacetophenone	4-methylacetophenone oxime	90	93
9 ^b	benzalacetone	benzalacetoneoxime	90	94
10 ^b	Benzophenone	Benzophenoneoxime	80	90
11 ^b	9H-fluoren-9-one	9H-fluoren-9-one oxime	80	91
12 ^b	cyclohexanone	cyclohexanoneoxime	60	95

^a The reaction has been carried out by $\text{NH}_2\text{OH}\cdot\text{HCl}$ (1 mmol)/ $\text{H}_2\text{C}_2\text{O}_4$ (1mmol). ^bThe reaction has been carried out by $\text{NH}_2\text{OH}\cdot\text{HCl}$ (2mmol)/ $\text{H}_2\text{C}_2\text{O}_4$ (2mmol). ^c Yields refer to isolated pure products ($\pm 3\%$)

A typical procedure for the oximation of aldehydes with NH₂OH·HCl/H₂C₂O₄ system

In a round-bottomed flask (10 mL) equipped with a condenser, a mixture of benzaldehyde (0.106 g, 1mmol), NH₂OH·HCl (0.07 g, 1 mmol) and oxalic acid (0.09 g, 1 mmol) in CH₃CN (3 mL) was prepared. The mixture was stirred under reflux conditions for 60 min. The progress of the reaction was monitored by TLC. After completion of the reaction, H₂O (10 mL) was added and the reaction mixture was continued to stirring for 5 min. The product has been extracted with CH₂Cl₂ (30 mL). The mixture was dried over anhydrous Na₂SO₄. Evaporation of the solvent and a short column chromatography of the resulting crude material over silica gel (eluent; CCl₄/Et₂O: 5/2) afforded the pure benzaldehyde oxime (0.115 g, 95 % yield, table 1, entry 1).

A typical procedure for the oximation of ketones with NH₂OH·HCl/H₂C₂O₄ system

In a round-bottomed flask (10 mL) equipped with a condenser, a solution of acetophenone (0.120 g, 1 mmol) NH₂OH·HCl (0.14 g, 2mmol) and oxalic acid (0.18 g, 2mmol) in CH₃CN (3 mL) was prepared. The mixture was stirred under reflux conditions for 90 min. The progress of the

reaction was monitored by TLC. After completion of the reaction, H₂O (10 mL) was added and the reaction mixture was continued to stirring for 5 min. The product has been extracted with CH₂Cl₂ (30 mL). The mixture was dried over anhydrous Na₂SO₄. Evaporation of the solvent and a short column chromatography of the resulting crude material over silica gel (eluent; CCl₄/Et₂O: 5/2) afforded the pure acetophenone oxime (0.128 g, 95% yield, table 1, entry 7).

CONCLUSION

In this context, the oximation of a variety of aldehydes and ketones was carried out efficiently with NH₂OH·HCl/H₂C₂O₄ system. The reactions were performed in CH₃CN under reflux conditions. This new protocol for the oximation of carbonyl compounds could be a useful addition to the present methodologies.

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