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RESEARCH ARTICLE

Microwave Assisted Regeneration of Carbonyl Compounds from their Oximes using Copper Nitrate over TBAB.

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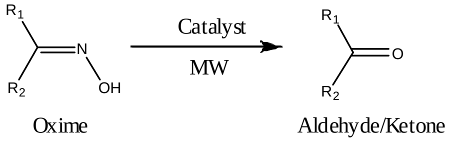
Abstract

New eco-friendly and efficient method has been developed for the deoximation of various aldoximes, ketoximes and oximes of some sterically hindered compounds under solvent free conditions using microwave irradiations and new catalytic system such as copper nitrate [$Cu(NO_3)_2.3H_2O$] over tetrabutylammonium bromide (TBAB). Moderate to high yields of the carbonyl compounds were obtained from the corresponding oximes when deoximated under these conditions. The products were identified on the basis of comparison of their melting points/boiling points and spectroscopic data: IR, ^{1}H-NMR and ^{13}C-NMR and with those of the authentic samples.



Key words : Carbonyl compounds, $Cu(NO_3)_2.3H_2O$, Deoximation, Dry-media, Microwave irradiations, TBAB.

Introduction

Aldehydes and Ketones are important organic compounds which incorporate a carbonyl functional group C=O. They undergo a variety of reactions that lead to many different products, which are important for pharmaceuticals, agricultural chemicals, material sciences and serve as important synthetic intermediates for countless organic reactions (Smith and March, 2007). Therefore, it becomes necessary to protect them during various organic reactions. One of the simplest potential routes for the protection of carbonyl group in aldehydes and ketones is to convert them into their oximes and after the completion of desired reaction convert them back into their corresponding carbonyl compound (Shriner *et al*, 1997; Greene and Wuts, 2007). A plethora of examples of procedures for the regeneration of carbonyl compounds from oximes have been reported. The classical method for cleavage of oximes to aldehydes and ketones include acid hydrolysis, which is not suitable for acid sensitive compounds (Friedman and Kosower, 1955). Many classical reagents are known for the oxidative (Tamami and Kiasat, 2000; Singh *et al*, 2003; Gupta *et al*, 2007; Zhang *et al*, 2011), reductive (Majireck *et al*, 2010) and hydrolytic (Quan *et al*, 2011) cleavage of oximes. However, in view of some limitations like use of harsh reaction conditions, limited yields of carbonyl compounds and production of environmentally harmful bi-products etc., there is still a need for developing new eco-friendly methods for this reaction.

In recent times, organic synthesis under solvent-free conditions using microwave (MW) irradiations has become increasingly popular (Dewan, 2006). Major advantages of the use of MW irradiations for conducting organic reactions include avoiding the use of organic solvents leading to clean, eco-friendly and efficient reactions (Dewan and Singh, 2003; Dewan *et al*, 2004; Dewan and Sharma, 2014). Because of our interest in carrying out organic reactions in dry media conditions by utilizing microwave energy, we report herein the rapid deoximation of aldoximes and ketoximes in the presence of $Cu(NO_3)_2.3H_2O$ over TBAB under solvent-free conditions.

Materials and Method

All reactions were performed under unmodified domestic microwave oven. TLC analyses were run on a glass plate (Silica gel G) and were visualized using iodine chamber, used for monitoring of progress of reaction. ^{1}H-NMR and ^{13}C-NMR were recorded on a 400MHz spectrometer in $CDCl_3$ using TMS as internal standard.

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Procedure for the deoximation of oximes

200 mg $Cu(NO_3)_2.3H_2O$ and 50 mg TBAB and the oxime of 4-nitrobenzaldehyde (166 mg, 1 mmol) were mixed thoroughly in a 10 mL pyrex beaker and irradiated at 450 W (52 °C) for 65 sec. The progress of the reaction was monitored by TLC (CCl_4 : ethyl acetate/39 : 1). After completion of the reaction, reaction mixture was extracted with diethyl ether, filtered and the filtrate was evaporated off to yield the product, 4-nitrobenzaldehyde in 92 % yield. Same procedure was followed for the regeneration of other carbonyl compounds from their oximes under the similar reaction conditions.

4- Nitrobenzaldehyde (1): M.P. 103 °C. Lit m.p. (Vogel, *et al*, 1996; Mendham *et al*, 2000).

2- Nitrobenzaldehyde (2): M.P. 41 °C. Lit m.p. (Vogel *et al*, 1996; Mendham *et al*, 2000).

2, 4- Dimethoxybenzaldehyde (3): M.P. 68 °C. Lit m.p. (Vogel *et al*, 1996; Mendham *et al*, 2000).

4- Chlorobenzaldehyde (4): M.P. 46 °C. Lit m.p. (Vogel *et al*, 1996; Mendham *et al*, 2000).

4- Bromobenzaldehyde (5): M.P. 57 °C. Lit m.p. (Vogel *et al*, 1996; Mendham *et al*, 2000).

Benzophenone (6): M.P. 49 °C. Lit m.p. (Vogel *et al*, 1996; Mendham *et al*, 2000).

Acetophenone (7): B.P. 197 °C. Lit b.p. (Nobuta *et al*, 2011; Vogel, *et al*, 1996; Mendham *et al*, 2000).

Cyclohexanone (8): B.P. 157 °C. Lit b.p. (Vogel *et al*, 1996; Mendham *et al*, 2000).

4- Nitroacetophenone (9): M.P. 75 °C. Lit m.p. (Vogel *et al*, 1996; Mendham *et al*, 2000).

4-Methoxyacetophenone (10): M.P. 39 °C. Lit m.p. (Vogel *et al*, 1996; Mendham *et al*, 2000).

Testosterone propionate (11): M.P. 154 °C. Lit m.p. (Martin *et al*,1982).

Trans - androsterone (12): M.P. 181 °C. Lit m.p. (Beatrice *et al*, 2005; *Juan et al*, 2011; Sauri *et al*, 2013).

á - *Tetralone* (13): B.P. 114 °C. Lit b.p. (Yang *et al*, 2008; *Juan et al*, 2011; Sauri *et al*, 2013).

Results and Discussion

Since, previous methods for the deoximation reactions used harsh acid catalysts or reflux conditions, so they suffer from usual limitations. Therefore, we aimed at investigating rapid deoximation of aldoximes and ketoximes, under solvent-free conditions in the presence of new catalytic system such as $Cu(NO_3)_2.3H_2O$ over TBAB. $Cu(NO_3)_2.3H_2O$ helps in deoximation reaction by hydrolytic cleavage of the C=N bond. TBAB acts as phase transfer catalyst and is added to the reaction mixture to make the mixture homogeneous. Initially, $Cu(NO_3)_2.3H_2O$ alone was used to explore the formation of the desired product, 4-nitrobenzaldehyde from oxime of 4-nitrobenzaldehyde under microwave irradiations (Fig.1).

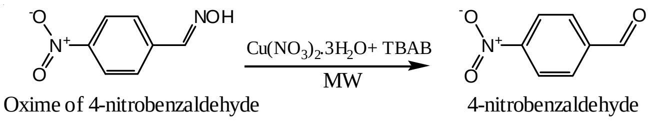


Fig.1. Rapid deoximation of oxime into carbonyl compound using new catalytic system

It was found that low temperature ranges did not support product formation. Very high temperature range also did not support product formation, as the reaction mixture started decomposing and the mixture turned black. So, the optimum temperature was found to be 52°C.

Accordingly, when the oxime was treated under microwave irradiations in an open vessel, the desired aldehyde product was formed, but it was obtained in low yield of 55%. However, when the reaction was carried out in presence of a mixture of $Cu(NO_3)_2.3H_2O$ and catalytic amount of a phase transfer catalyst, tetrabutylammonium bromide (TBAB), the product was obtained in about 92% yield in 65 seconds under the same reaction conditions. To examine the scope of newly developed protocol, structurally diverse arylaldoximes were then selected. The deoximation of their oximes was conducted in the presence of above mentioned catalytic system and corresponding aldehydes were obtained in good yield (Table 1).

With the satisfactory results from the deoximation of aldoximes, we turned our attention towards deoximation of ketoximes using the same approach. The above mentioned catalytic system worked well for the transformation of ketoximes with differently substituted electron withdrawing groups such as $-NO_2$ and electron releasing groups such as -OMe on the aromatic ring, into the corresponding ketones under the same reaction conditions (Table 2).

Another peculiar feature of the above mentioned compounds is that the oximes of steroidal compounds having ketonic group like testosterone propionate and trans-androsterone also underwent deoximation under the same reaction conditions and formed product in 70-71% yield, without any affect on the rings of compound. Deoximation of oxime of 1-tetralone, a sterically hindered compound with one phenyl ring, has also been done with the same procedure and the expected product was obtained in good yield (Table 3).

Table-1. Rapid deoximation of variously substituted aldoximes in presence of $Cu(NO_3)_2.3H_2O$ and TBAB.

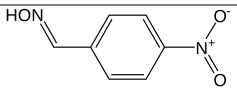
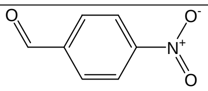
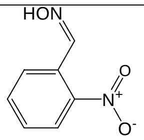
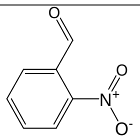
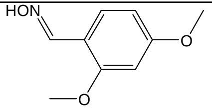
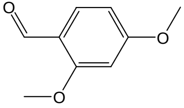
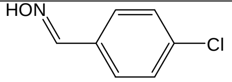
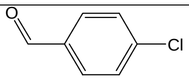
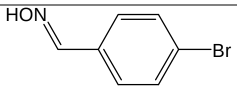
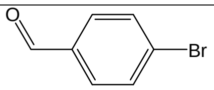
S. No.	Substrate	Product	Yield (%)	Time (Sec)
1	 Oxime of 4-nitrobenzaldehyde	 4-nitrobenzaldehyde	92	65
2	 Oxime of 2-nitrobenzaldehyde	 2-nitrobenzaldehyde	91	65
3	 Oxime of 2,4-dimethoxybenzaldehyde	 2,4-dimethoxybenzaldehyde	87	70
4	 Oxime of 4-chlorobenzaldehyde	 4-chlorobenzaldehyde	90	55
5	 Oxime of 4-bromobenzaldehyde	 4-bromobenzaldehyde	82	50

Table-2. Rapid deoximation of variously substituted ketoximes in the presence of $Cu(NO_3)_2.3H_2O$ and TBAB.

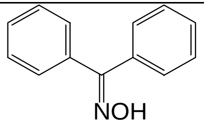
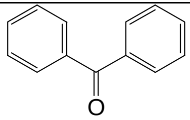
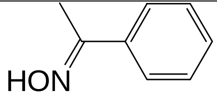
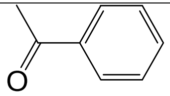
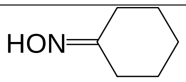
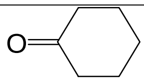
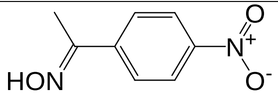
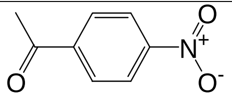
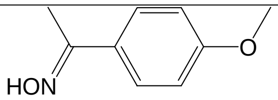
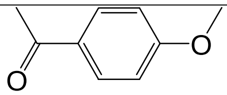
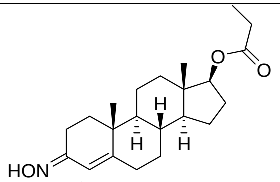
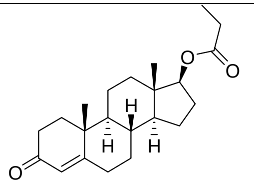
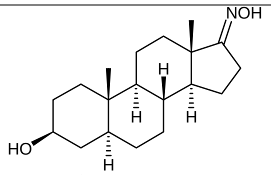
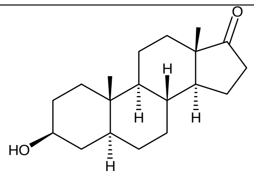
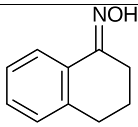
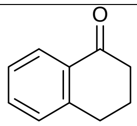
Sr. No.	Substrate	Product	Yield (%)	Time (sec)
1	 Oxime of benzophenone	 Benzophenone	91	50
2	 Oxime of Acetophenone	 Acetophenone	92	55
3	 Oxime of cyclohexanone	 Cyclohexanone	72	65
4	 Oxime of 4-nitroacetophenone	 4-nitroacetophenone	88	55
5	 Oxime of 4-methoxyacetophenone	 4-methoxyacetophenone	82	65

Table-3 Rapid deoximation of oximes of sterically hindered ketonic compounds in presence of $Cu(NO_3)_2.3H_2O$ and TBAB.

S. No.	Substrate	Product	Yield (%)	Time (sec)
1	 Oxime of testosterone propionate	 testosterone propionate	71	65
2	 Oxime of androsterone	 Androsterone	70	65
3	 Oxime of α-tetralone	 α-tetralone	70	70

Conclusion

The reaction protocols are rapid, manipulative, simple and selective in comparison to the conventional solution phase reactions which suffer from the use of organic pollutant solvents, long reaction times and low yields. The prominent advantage of the new catalytic system is that it affected only C=N bond of the oxime group while other functional groups remained intact.

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