



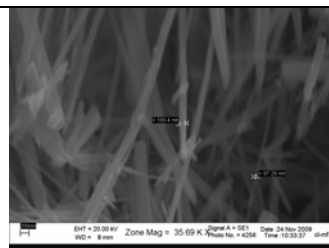
ZnO NANOTUBE AS REUSABLE CATALYST IN THE EFFICIENT AND SELECTIVE OXIMATION REACTION OF CARBONYL GROUPS UNDER SOLVENT FREE CONDITIONS

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A convenient and efficient procedure for the selective protection of carbonyl groups in the presence of ZnO nanotube, as reusable eco-friendly catalyst under solvent free conditions is described. The salient features of this methodology are cheaper process, easy availability of the catalyst, versatility, and the catalyst can be recovered after completion of the reaction and can be recycled without affecting the catalytic property.



INTRODUCTION

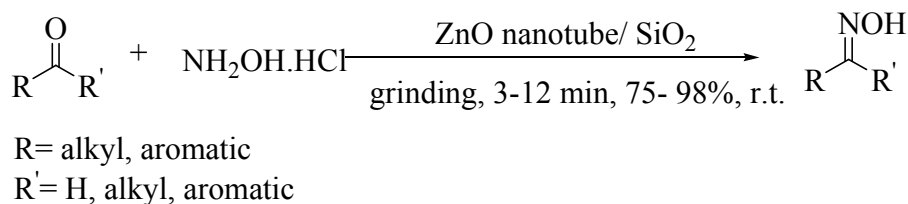
Since the first discovery of carbon nanotubes in 1991, considerable attention has been paid to study on one dimensional (1D) nanostructured materials including nanorods, nanowires and nanotubes, because of their remarkable physical properties and potential applications.¹ Among these 1D structures, tubular ZnO nanostructure have been investigated widely for their catalytic, electrical, optoelectronic, and photochemical properties.² It is also a versatile smart, biosafe and biocompatible material with excellent chemical and thermal stability, which can be directly used for biomedical applications without coating.³

Protection of carbonyl compounds as oximes is of great interest in synthetic organic chemistry, not only for protection, purification and characterization of carbonyl groups, but also for various functional group transformations such as into nitriles, nitro compounds, nitrones, amines and hetrocyclic compounds such as oxazoles and isoxazolines.⁴⁻⁹

Concerning pharmacology, several studies have shown that oximes present properties as antitumor, antimicrobial, antioxidant, anti-depressive, anti-convulsant, and antiviral agents, etc.^{10,11}

Therefore, synthetic organic chemists are interested in a facilitation of oxime synthesis. Although alternative methods exist, reaction of carbonyl compounds with hydroxylamine hydrochloride remains still the most important route. The classical method involves refluxing of an alcoholic solution of these reactants in the presence of sodium acetate or hydroxide.¹² The method has some drawbacks such as low yields, long reaction time and effluent pollution caused by used organic solvent. Recently, alumina, silica gel and TiO₂/SO₄²⁻ coupled with microwave irradiation without solvent has been proven to be an efficient method for the preparation of oximes. However, problems of generation of polluting HCl, high reaction temperature and occasionally low yields still present. Consequently, the development of new methods that are more efficient and lead to convenient and non-polluting procedures and better yields is desirable.¹³

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Scheme 1 – synthesis of oximes using ZnO nanotube as catalyst.

Owing to the widespread applications of the described compounds, and in continuation of our previous research on development of processes under solvent-free condition,¹⁴⁻¹⁶ Herein, we report on our findings, which resulted in a quick, simple and efficient method of oxime synthesis from carbonyl compounds without a solvent using ZnO nanotubes as catalyst.

EXPERIMENTAL

1. General procedure for synthesis of ZnO nanotubes

Firstly, an aqueous solution of $\text{Zn}(\text{NO}_3)_2$ was prepared at room temperature in a glass bottle without seal under magnetic stirring by adding $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ (2.0 g) with 99.9% purity into 250 ml distilled water. Then, 0.15 g PEG (2000) with high purity and 1mol/L $\text{NH}_3 \cdot \text{H}_2\text{O}$ were dispersed in the above-prepared $\text{Zn}(\text{NO}_3)_2$ solution. Finally, the obtained mixture (pH = 10) was heated to 70 °C and continued with this constant temperature until the reaction was complete (24 h). Vigorous stirring was maintained throughout the entire process. The precipitate was filtered out, washed several times with alcohol and water, and then dried at 60 °C under air atmosphere.

2. General procedure for preparation of oximes from aldehydes and ketones in the presence of ZnO nanotubes under solvent free condition

Hydroxylamine hydrochloride (0.138 g, 2 mmol), ZnO nanotubes (0.071 g, 0.8 mmol), silica gel (0.43 g) and aldehyde (ketone) (1 mmol) were ground together in a mortar with a pestle at room temperature for a period of time as indicated in Tables 1 and 2. The progress of the reaction was monitored by TLC. After complete disappearance of the starting materials, the reaction mixture was poured with diethylether (2×10 mL) and filtered to remove silica gel and ZnO nanotubes. The filtrate mixed with water and extracted. The solvent was removed in vacuo to give the product which was recrystallized from suitable solvent and afforded the TLC and 1H-NMR pure products in 75-98 % isolated yields.

RESULT AND DISCUSSION

1. Investigation around the approach of ZnO nanotube preparation and its structural and morphological analysis

ZnO nanotubes was synthesized by reacting $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ with NH_3 in the presence of PEG

according to Liu *et al.*¹ The mechanism of the formation of zinc oxide crystals was usually accepted as shown in Scheme 2.

PEG not only promote the formation of crystalline ZnO nuclei but also it solutes wrap around the ZnO nuclei when ZnO crystals grow up along PEG chains. Thus, PEG can play a template role in the formation of ZnO nanotubes.

The X-ray diffraction (Fig. 1) and SEM (Fig. 2) measurements were utilized to characterize the structure of ZnO nanotubes. The powder X-ray patterns were carried out using a PW-1840 Philips diffractometer at room temperature utilizing $\text{Cu K}\alpha$ radiation wavelength of $\lambda = 1.5418\text{\AA}$. The peak position and intensities were obtained between 10 and 80° with a velocity of 0.02° per second. X-ray diffraction (XRD) can provide useful structural information for crystalline materials. Fig. 1 shows the X-ray diffraction pattern of ZnO nanotubes. The peak positions and their relative intensities are consistent with those of the standard powder diffraction patterns of ZnO (JCPDS File 36-1451), which proves that uniform polycrystalline structure of the ZnO nanotubes.

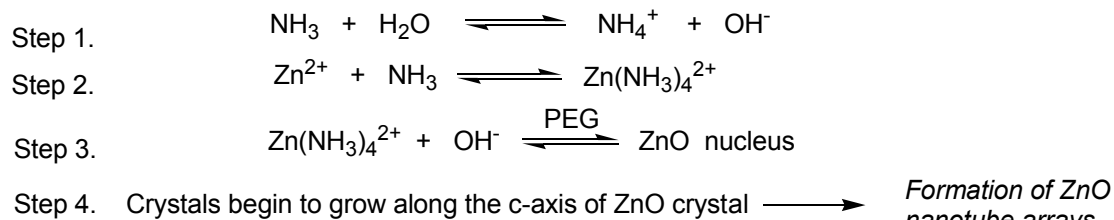
The structural and morphological characterization of ZnO nanostructure was performed by measuring SEM using a Philips XL30 scanning electron microscope. The surface morphologies of the ZnO nanotubes were shown in Fig. 2.

2. Application of ZnO nanotube as catalyst in oximation reaction

In this simple and efficient method, the starting carbonyl compounds were protected to the corresponding oximes in a mortar with grinding by a pestle in the presence of ZnO nanotube. The feasibility of the present oximation reaction was first examined using *p*-methoxy benzaldehyde as a model substrate. Thus, *p*-methoxy benzaldehyde (1 mmol) was thoroughly mixed with NH_2OHHCl (2 mmol) in the presence of a catalytic amount of ZnO nanotube (0.07) in a mortar with a pestle at room temperature and corresponding oxime was obtained in 91% yield within 6 min. It can be

emphasized that the reaction is clean, the work-up is straightforward and, from economical and environmental points of view, absence of solvent is favorable. Although the ZnO nanotube can be

efficiently catalyzed oximation reaction under solvent-free conditions and without using silica gel, the presence of silica gel (0.43 g) for facile grinding of reaction media is necessary.



Scheme 2 – mechanism of the formation of zinc oxide crystals.

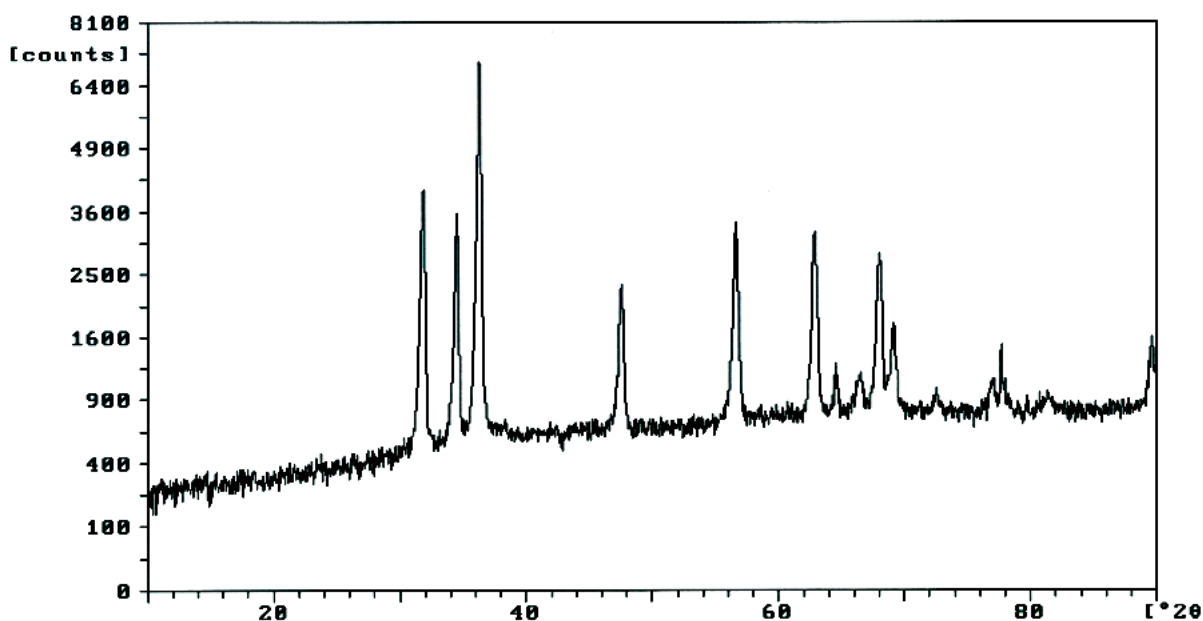


Fig. 1 – XRD pattern of the ZnO nanotubes.

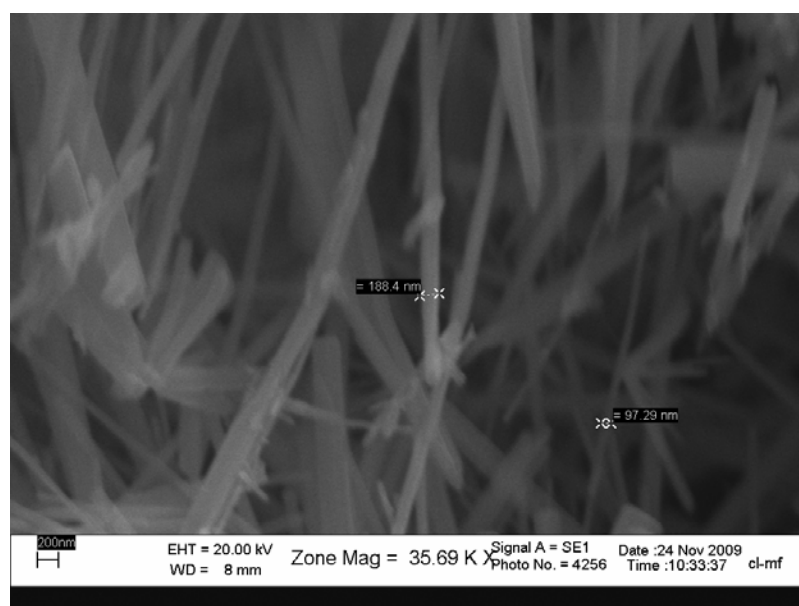
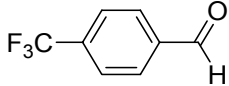
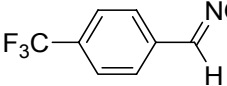
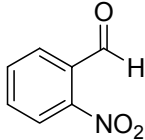
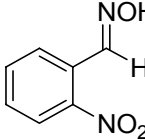
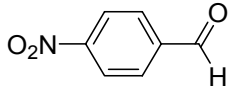
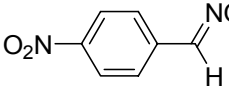
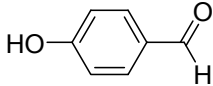
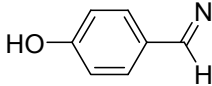
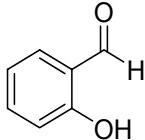
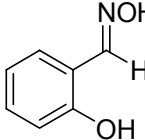
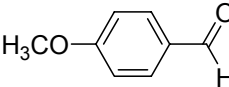
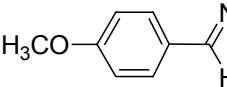
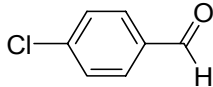
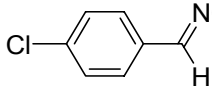
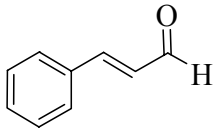
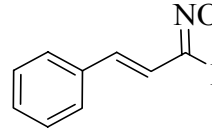
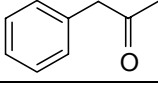
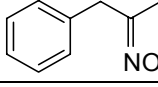
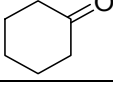
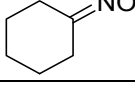
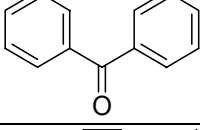
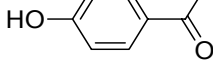
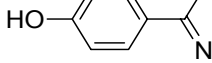


Fig. 2 – SEM image of ZnO nanotubes.

Table 1

Conversion of carbonyl compounds (1 mmol) into oximes using ZnO nanotubes (0.07 g), NH₂OH.HCl (2 mmol) and silica gel (0.43 g) under solvent free condition

Entry	Substrate	Product	Time (min)	Yield (%)	M.p. (°C) (lit. m.p.)
1			4	94	100-101 (101)
2			7	75	101-103 (103)
3			10	85	125-127 (128-130)
4			6	96	93-94 (92)
5			4	95	56-58 (57-59)
6			6	91	131-133 (131-133)
7			12	98	145-147 (146)
8			7	98	135-137 (136-138)
9			3	80	69-71 (70)
10			4	90	90-92 (91)
11		-	20	No reaction	-
12			20	Not completed	-

With the first successful result in hand, various types of aromatic aldehydes, with electron-donating (Table 1, entries 4 and 6) and withdrawing (Table 1, entries 1 and 3) groups, were rapidly condensed with hydroxylamine hydrochloride and afforded the corresponding oximes in excellent yields.

As shown in Table 1, although aliphatic ketones (Table 1, entries 9 and 10) could be transformed into oximes in short reaction times, aromatic ketones (Table 1, entries 11-12) did not undergo this reaction even after 20 minutes grinding. So in order to evaluate the efficiencies of method, the reaction of some aromatic ketones was carried out in an oil bath (80°C). As shown in Table 2, good

results have been obtained in the protection of aromatic ketones with hydroxylamine hydrochloride under solvent free condition in the presence of ZnO nanotubes in an oil bath.

It should be pointed out that the catalyst does not need activation and is recycled many times under the same conditions with fresh reactants to yield similar results without significant loss of activity.

Nanostructure effect of ZnO in this reaction was also investigated by the oximation reaction of *p*-methoxy benzaldehyde catalyzed by normal zinc oxide, as before, Scheme 3.

The reaction time increased twice relative to ZnO-nanotube, which obviously demonstrate the more effectiveness of ZnO nanotube structure. It can attributed to its more porous structure and large surface area.

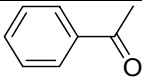
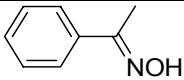
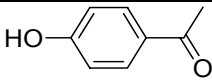
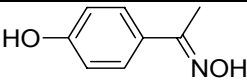
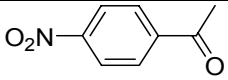
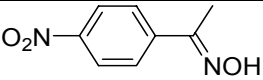
The effect of the solvent on the performance of promoted catalyst was also investigated (Table 3).

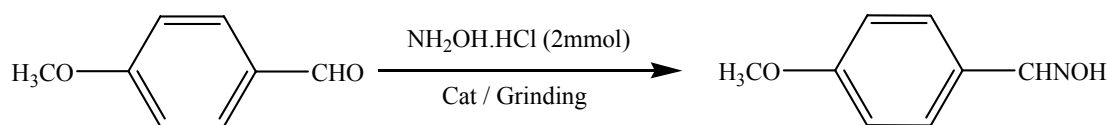
The results for oximation reaction of cinnamaldehyde under optimize reaction condition clearly revealed that, according to required time and the isolated yield, the best results were obtained under solvent-free conditions.

In order to show the chemoselectivity of the method, a competitive reaction was conducted as shown in Scheme 4. A 1: 1 mixture of *p*-nitrobenzaldehyde (1 mmol) and *p*-nitroacetophenone (1 mmol) was reacted with NH_2OHHCl (2 mmol) in the presence of ZnO nanotubes (0.07 g) and silica gel (0.43 g) under solvent free conditions, Monitoring of reaction was clearly shown after 10 min only *p*-nitrobenzaldehyde reacted and *p*-nitroacetophenone was intact. Thus the presented protocol is potentially applicable for the chemoselective protection of aldehydes in the presence of ketone function.

Table 2

Conversion of some aromatic ketones (1 mmol) into oximes in an oil bath (80°C) using ZnO nanotubes (0.07 g), $\text{NH}_2\text{OH.HCl}$ (2 mmol) and silica gel (0.43 g) under solvent free condition

Entry	Substrate	Product	Time (min)	Yield (%)	M.p. (°C) (lit. m.p.)
1			15	90	57-58 (56-58)
2			25	80	137-139 (139)
3			22	85	172-174 (174)



Cat: ZnO/SiO₂ 12 min/ 89%
ZnO-nanotube/SiO₂ 6 min/ 91%

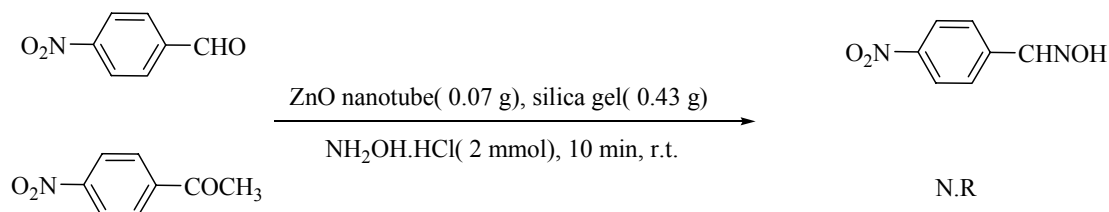
Scheme 3 – Oximation of *p*-methoxy benzaldehyde catalyzed by normal zinc oxide.

Table 3

Oximation of Cinnamaldehyde in various solvent

Solvent	C ₂ H ₅ OH	CH ₃ CN	CH ₂ Cl ₂	CHCl ₃	Et ₂ O	Solvent free
Reaction conditions	[rt/45/75]	[rt/10/70]	[rt/120/99]	[rt/300/Nc]	[rt/80/65] --	[rt/7/98]
[tem/ time (min)/ Yield (%)]	[ref/5/70]	[ref/5/72]	[ref/45/80]	[ref/165/Nc]	-----	

Nc: refer to not completed reaction
rt: refer to room temperature
ref: refer to reflux



Scheme 4 – Competitive reactions of aldehyde and ketone.

To evaluate the efficiency of this method for the scaling up experiment, protection of *p*-methoxy benzaldehyde was also performed on 5 mmol scale. Result show that inspite of little increasing time of reaction, corresponding oxime obtained without appreciable decrease in the yield.

In conclusion, we have developed a easy way to operate, safe and cost-effective method for the protection of carbonyl groups under solvent-free conditions by use of catalytic amount of ZnO nanotubes. The salient features of the present protocol are mild reaction conditions, greater selectivity, cleaner reaction profile, environmentally friendly, excellent yields with experimental simplicity, which makes it potentially useful for the industrial applications.

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REFERENCES

- J. Liu and X. Huang, *J. Solid State Chem.*, **2006**, *179*, 843-848.
- B. Gen, X. Liu, X. Wei and S. Wang, *Mater. Res. Bull.*, **2006**, *41*, 1979-1983.
- J. A. Rodriguez, T. Jirsak, J. Dvorak, S. Sambasivan and D. Fischer, *J. Phys. Chem. B*, **2000**, *104*, 319-328.
- A. R. Hajipour, F. Rafiee, A. E. Ruoho, *J. Iran. Chem. Soc.*, **2010**, *7*, 114-118.
- H. Sharghi and M. Hosseini, *Synthesis*, **2002**, *8*, 1057-1060.
- G. L. Kad, M. Bhandari, K. Jasamrit, R. Raman and S. Jasvinder, *Green Chem.*, **2001**, *3*, 275-277.
- L.V. B. Hoelz, B. T. Gonçalves, J. C. Barros and J. F. Mendes da Silva, *Molecules*, **2010**, *15*, 94-99.
- A. R. Kiasat, F. Kazemi and K. Nourbakhsh, *Phosphorus, Sulfur and Silicon*, **2004**, *179*, 1193-1196.
- R. Fazaeli, S. Tangestaninejad and H. Aliyan, *Catal. Commun.*, **2007**, *8*, 205-210.
- H. J. Park, K. Lee, S. J. Park, B. Ahn, J. C. Lee, H. Cho and K. I. Lee, *Bioorg. Med. Chem. Lett.*, **2005**, *15*, 3307-3312.
- H. A. Dondas and N. Yaktubay, *Farmaco*, **2003**, *58*, 1011-1015.
- I. Damjanovic, M. Vukicevic and R. D. Vukicevic, *Monatsh. Chem.*, **2006**, *137*, 301-305.
- J. T. Li, X. L. Li and T. S. Li, *Ultrason. Sonochem.*, **2006**, *13*, 200-202.
- A. R. Kiasat, A. Mouradzadegan, S. Elahi and M. Fallah-Mehrjardi, *Chin. Chem. Lett.*, **2010**, *21*, 146-150.
- A. R. Kiasat and M. Fallah-Mehrjardi, *Synth. Commun.*, **2010**, *40*, 1551-1558.
- A. R. Kiasat, B. Mokhtari, A. Savari and F. Kazemi, *Phosphorus, Sulfur and Silicon*, **2008**, *183*, 178-182.