Rapid, convenient and solvent-free green approach for the synthesis of aryloximes using ZnO nanoparticles as an efficient catalyst

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ABSTRACT

Freshly prepared ZnO nanoparticles were used as an effective heterogeneous Lewis acid catalyst for the synthesis of aryloximes. The conversion of arylaldehydes and arylketones into the corresponding oximes (up to quantitative yields) was achieved by simply mixing the liquid reactants and hydroxylamine hydrochloride with ZnO nanoparticles under solvent-free condition. The procedure was carried out under wet conditions for solid reactants. The advantages of this method include mild reaction conditions, one-pot procedure, operational simplicity and use of inexpensive and non-toxic catalyst.

Keywords: Aryloximes, Solvent-free, ZnO nanoparticles, One-pot procedure.

1. Introduction

Nowadays, organic chemists have been confronted with a new challenge of finding novel methods in organic synthesis that can reduce and finally eliminate the impact of volatile organic solvents and hazardous toxic chemicals on the environment. So, the use of non-toxic, environmentally friendly and inexpensive solid catalysts to perform organic reactions has attracted considerable interest. Due to this, different research groups reported the ZnO catalyzed organic transformations [1-5]. In fact, ZnO as a heterogeneous catalyst can be easily separated from the reaction mixture and reused; it is generally not corrosive and does not produce problematic side products. Solvent-free organic reactions using ZnO catalyst were reported in the literature [6-8]. Conversion of carbonyl functionalities into oximes is an important reaction in organic chemistry. Oximes are highly crystalline compounds that find applications not only for protection, but also for purification and characterization of carbonyl compounds [9]. Conversions into nitriles [10], nitro compounds [11], nitrones [12], amines [13], and synthesis of azaheterocycles [14] are some of the synthetic applications of oximes.

They are also extensively used as intermediates for the preparation of amides by the Beckmann rearrangement [15]. In inorganic chemistry, oximes act as a versatile ligand.

In continuation of our interest to use MgO, high surface area ZnO/MgO, ionic liquids (IL’s), water or solventless systems as green reaction media [16-23], in this report, we wish to highlight our results on using ZnO nanoparticles as an efficient catalyst for the synthesis of oximes (Scheme 1). This rapid and efficient solvent-free method is expected to be an attractive procedure for the conversion of aldehydes and ketones to oximes from the viewpoint of green chemistry.

2. Experimental

2.1. General

All reagents were purchased from Merck Company and used without further purification. Infrared spectra were

Scheme 1. ZnO nanoparticles catalyzed solvent-free synthesis of oximes from aldehydes and ketones.
recorded using KBr pellets on a Perkin Elmer FT-IR spectrometer. NMR spectra were recorded on a Bruker Avance AC-400 instrument using TMS as internal standard (1H at 400 MHz and 13C at 100 MHz). X-ray diffraction (XRD) was performed by using a Bruker AXF (D8 Advance) X-ray power diffractometer with a Cu Kα radiation source (λ=0.154056 nm) generated at 40 kV and 35 mA. Scanning electron microscopy (SEM) (VEGA/TESCAN) was used for morphology study of ZnO nanoparticles. Mass spectra, using electron ionization (EI)-mass spectrometry (MS), were recorded on a Shimadzu GCMS-QP-2000A mass spectrometer. Elemental analyses were conducted using the Perkin-Elmer 240C elemental analyzer and their results were found to be in good agreement with the calculated values.

2.2. Synthesis of aldoximes and ketoximes using ZnO nanoparticles, General procedure

Arylaldehydes or ketones (1 mmol) and hydroxyl amine hydrochloride (1 mmol) and ZnO nanoparticles (10 mol%) were mixed thoroughly and stirred at temperature as shown in Table 1. The completion of reaction was monitored by TLC using (EtOAc: petroleum ether 1:4) as mobile phase and the products were purified via recrystallization from EtOAc: petroleum ether.

Selected spectral data

2-Hydroxybenzaldehyde oxime (2a):
White solid. IR (KBr): ð = 3118.61 (OH), 1605.63 (C=N) cm⁻¹. ¹H NMR (400 MHz, TFAA): ð= 8.13 (s, 1H, OH), 7.69-7.73 (t, 1H), 7.60-7.62 (d, 1H, J = 8 Hz), 7.18-7.24 (m, 2H) ppm. ¹³C NMR (100 MHz, CDCl₃): ð= 157.71, 152.75, 132.02, 131.74, 121.13, 120.18, 117.58 ppm. MS: m/z = 137.10 (M⁺, 100). Anal. Calcd for C₆H₅NO₂: C, 61.33; H, 5.12; N, 10.09; O, 23.35%. Found: C, 61.33; H, 5.12; N, 10.09; O, 23.35%.

4-Chlorobenzaldehyde oxime (2b):
Pale yellow solid. ¹H NMR (400 MHz, CDCl₃): ð= 8.13 (s, 1H), 8.11 (s, 1H), 7.50-7.55 (m, 2H), 7.30-7.40 (m, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃): ð= 149.5, 129.2, 128.4 ppm. MS: m/z = 155.05 (M⁺, 100). Anal. Calcd for C₆H₅ClNO: C, 54.04; H, 3.89; Cl, 22.79; N, 9.00; O, 10.28%. Found: C, 54.14; H, 3.86; Cl, 22.58; N, 9.02; O, 10.27%.

4-Nitrobenzaldehyde oxime (2c):
Pale orange solid. ¹H NMR (400 MHz, CDCl₃): ð= 12.27 (s, 1H, OH), 8.29-8.32 (m, 2H), 8.21-8.24 (m, 2H), 7.67 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): ð= 147.02, 143.06, 136.23, 131.35, 123.60 ppm. MS: m/z = 155.05 (M⁺, 100). Anal. Calcd for C₆H₅NO₂: C, 50.61; H, 3.64; N, 16.86; O, 28.89%. Found: C, 50.60; H, 3.65; N, 16.80; O, 28.91%.

4-(Trifluoromethyl)benzaldehyde oxime (2d):
White solid. IR (KBr): ð = 3289.99 (OH), 1618.36 (C=N) cm⁻¹. ¹H NMR (400 MHz, CHCl₃): ð= 8.17 (s, 1H, OH), 7.63-7.70 (m, 5H) ppm. ¹³C NMR (100 MHz, CDCl₃): ð= 149.24, 127.37, 125.95, 125.90, 125.85, 125.80 ppm. MS: m/z = 189.00 (M⁺, 100). Anal. Calcd for C₆H₅F₃NO: C, 50.80; H, 3.20; F, 30.13; N, 7.41; O, 8.46%. Found: C, 50.85; H, 3.20; F, 30.13; N, 7.47; O, 8.40%.

4-Methoxybenzaldehyde oxime (2e):
White solid. IR (KBr): ð = 3448.11 (OH), 1600.90 (C=O) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): ð= 8.48 (s, 1H), 8.26 (broad s, 1H, OH), 7.26 (s, 1H), 6.86-6.93 (m, 2H), 3.83 (s, 3H, OCH₃), 3.82 (s, 3H, OCH₃) ppm. ¹³C NMR (100 MHz, CDCl₃): ð= 150.07, 133.13, 128.63, 124.72, 114.36, 55.47 ppm. MS: m/z = 151.15 (M⁺, 100). Anal. Calcd for C₆H₇NO₂: C, 63.56; H, 6.00; N, 9.27; O, 21.17%. Found: C, 63.50; H, 6.06; N, 9.28; O, 21.07%.

2,5-Dimethoxybenzaldehyde oxime (2f):
White solid. IR (KBr): ð = 3041.25 (OH), 1653.55 (C=O) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): ð= 8.75 (s, 1H, OH), 8.17 (s, 1H), 7.56-7.59 (m, 2H), 7.31-7.40 (m, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃): ð= 150.5, 130.2, 128.9, 127.2 ppm. MS: m/z = 121.12 (M⁺, 100). Anal. Calcd for C₆H₇NO₂: C, 69.41; H, 5.82; N, 11.56; O, 13.21%. Found: C, 69.38; H, 5.83; N, 11.58; O, 13.19%.

3-Nitrobenzaldehyde oxime (2i):
¹H NMR (400 MHz, CDCl₃): ð= 8.45 (s, 1H, OH), 8.21-8.24 (m, 2H), 7.89-7.92 (m, 1H), 7.56-7.60 (m, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): ð= 149.11, 147.96, 133.80, 132.10, 128.13, 123.72, 121.00 ppm. MS: m/z = 166.10 (M⁺, 100). Anal. Calcd for C₆H₅NO₂: C, 50.61; H, 3.64; N, 16.86; O, 28.89%. Found: C, 50.65; H, 3.59; N, 16.85; O, 28.89%.

1-(Biphenyl-4-yl)ethanone oxime (2l):
White solid. IR (KBr): ð = 3075.03 (OH), 1672.67 (C=N) cm⁻¹. ¹H NMR (400MHz, CHCl₃): ð= 8.28 (s, 1H, OH), 7.71-7.73 (d, 2H, J = 8), 7.60-7.65 (m, 4H), 7.43-7.47 (t, 2H), 7.35-7.38 (t, 1H), 2.33 (s, 3H, CH₃) ppm. ¹³C NMR (100 MHz, CDCl₃): ð= 156.04, 142.18, 140.38, 135.12, 126.89, 127.68, 127.23, 127.09, 126.57, 12.31 ppm. MS: m/z = 211.12 (M⁺, 100). Anal. Calcd for C₁₄H₁₃NO: C, 79.59; H, 6.20; N, 6.63; O, 7.57%. Found: C, 79.55; H, 6.23; N, 6.65; O, 7.56%.
3. Results and Discussion

ZnO nanoparticles were prepared according to the literature [24]. Fig. 1 shows the SEM image of the ZnO nanoparticles. The XRD pattern of the ZnO nanoparticles is shown in Fig. 2. All the peaks of the XRD pattern are identified precisely to those of the ZnO wurtzite structure (Joint Committee on Powder Diffraction Standards (JCPDS) card number 36-1451). Diffraction peaks related to impurities were not observed in the XRD pattern, confirming the high purity of the product synthesized. The average crystalline size \(D\) of the nano-sized ZnO particles was estimated to be about 31.4 nm according to the Debye-Scherrer formula [25]. In the present solvent-free method, the effectiveness of ZnO nanoparticles in oxime synthesis under mild conditions is demonstrated using a broad spectrum of aldehydes and ketones with hydroxylamine hydrochloride in the absence of a base or any other additives. To search for the best reaction condition for oximation, a set of reactions has been carried out using different molar ratios of 4-trifluoromethyl benzaldehyde and hydroxylamine hydrochloride as substrates under various reaction conditions at different ratios of catalyst, ZnO nanoparticles (10-50 mol% with respect to substrate) and also in the absence of catalyst at different temperatures (Table 1). The results clearly show that the ZnO nanoparticles under solvent-free conditions are the most effective. It was found that the best yield of the product was obtained using 1/1 molar ratios of 4-trifluoromethyl benzaldehyde and hydroxylamine hydrochloride in the presence of ZnO nanoparticles (10 mol%) at room temperature (entry 7, Table 1). For comparison, the oxidation reaction of 4-trifluoro methylbenzaldehyde and benzophenone were also examined in the presence of ZnCl\(_2\) as a catalyst, and the related oximes were isolated in very lower yields.

The scope of this methodology was further extended by reaction of various aromatic aldehydes, containing electron-withdrawing or donating groups. Aromatic aldehydes were converted to the corresponding oximes in almost quantitative yields in the presence of ZnO nanoparticles (10 mol%) within very short reaction times, 5-15 min (entries 1-9, Table 2). As expected the rate of reaction was high for the aldehydes possessing electron-withdrawing groups compared with the aldehydes bearing electron-donating groups. Excellent yields were obtained with aromatic aldehydes bearing an electron-withdrawing group at the para position (entries 2-4, Table 2) and high yields were afforded with ortho- and meta-substituted aromatic aldehydes (entry 9, Table 2). Aromatic aldehydes bearing electron-donating groups afforded high yields of the desired products but in longer reaction times (entries 1, 5, 6, 8, Table 2). For ketones (less reactive than aldehydes), however, reactions were comparatively difficult and took a little longer time (25-120 min) at high temperatures in the presence of 15 mol% ZnO nanoparticles (entries 10-16, Table 2).

![Fig. 1. The SEM image of the ZnO nanoparticles.](image1)

![Fig. 2. The XRD pattern of the ZnO nanoparticles.](image2)
Table 1. Optimization of reaction conditions for the synthesis of oxime 2d.

<table>
<thead>
<tr>
<th>Entry</th>
<th>1d (mmol)</th>
<th>3 (mmol)</th>
<th>Catalyst (%)</th>
<th>Temperature (°C)</th>
<th>Yield (%)^a</th>
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<td>2</td>
<td>1</td>
<td>10</td>
<td>25</td>
<td>85</td>
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<td>50</td>
<td>90</td>
<td>96</td>
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</table>

^aIsolated yield.

Table 2. Facile synthesis of aryloximes catalyzed by the ZnO nanoparticles.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product number</th>
<th>R¹</th>
<th>R²</th>
<th>Temperature (°C)</th>
<th>Time (min)</th>
<th>Yield (%)^a</th>
<th>m.p. (°C)</th>
<th>Ref.</th>
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<td>1</td>
<td>2a</td>
<td>H</td>
<td>2-OH</td>
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<td>10</td>
<td>90</td>
<td>118-120</td>
<td>110-116</td>
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<tr>
<td>2</td>
<td>2b</td>
<td>H</td>
<td>4-Cl</td>
<td>25</td>
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<td>95</td>
<td>105-106</td>
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<td>H</td>
<td>4-OMe</td>
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<td>H</td>
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<td>H</td>
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<td>60</td>
<td>100-101</td>
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^aIsolated yield after recrystallization.
Ketones with phenyl group are less reactive, but it was interesting to note that the less reactive benzophenone and 3,4-Diaminobenzophenone also, reacted with hydroxyl amine hydrochloride in 2 and 1.5 hours respectively at 90°C to give the corresponding oximes 2m and 2p in 60% yield (entries 13, 16, Table 2). 4-Chloroacetophenone and cyclohexylphenylketone afforded to related oximes 2n and 2o in 75% and 71% respectively at 90°C in the presence of 15 mol% of ZnO nanoparticles by wetting of the reaction mixture with ethanol (entries 14-15, Table 2).

4-Phenylacetophenone was reacted with hydroxyl amine hydrochloride and converted to related oxime 2l in 70% at room temperature (entry 12, Table 2). The unreacted materials were recovered from the reaction mixture. No observable difference in reactivity exerted by different substituents at phenyl groups in ketone or aldehyde and entities such as chloro, nitro and hydroxyl were found to be inert to the reaction condition. The reaction of cyclohexanecarboxaldehyde with hydroxylamine hydrochloride afforded to the related oxime, which can be converted to the much useful caprolactame via the Beckman rearrangement. The products were identified by their 1H NMR, 13C NMR, MS, IR spectral data and Elemental analysis. IR spectra supported this observation as no peak was observed around 1700 cm⁻¹ characteristic of the –C=O group. However, appearance of peaks around 3200-3450 and 1600-1680 cm⁻¹ are indicative of -OH and >C=N groups, respectively. In 1H NMR spectra, the -OH signal of oximes appeared within δ = 8.0-10.00 ppm as a broad singlet (characteristic signal).

As it can be seen from Table 2, good to high yields of the related oximes were prepared from the reaction of carbonyl compounds with hydroxylamine hydrochloride. Over the years, many reagents and catalysts have been developed for the synthesis of oximes such as NaOH [26, 28], Cu-SiO₂ [27], Bi₂O₃ [4]. Nano ZnO is a low cost, easily available, non-toxic, safe and stable material which has been used as an efficient catalyst in this work. For comparison, the reaction times and yields of some products of the present method and other reported methods were gathered in Table 3. These data clearly indicate that nano ZnO is superior in comparison with other catalysts.

Additionally, the recyclability of catalyst, which was readily recovered by extraction of the reaction mixture with ethyl acetate (12 ml×4), was investigated.

4-Chlorobenzaldehyde oxime and 4-methoxybenzaldehyde oxime with four times recycled catalyst were synthesized in comparable yields to the fresh catalyst (Table 4). It was observed that recovered catalyst could be satisfactorily used for the fifth run, whereas, sixth run of the recovered catalyst leads to poor yields and longer reaction times.
4. Conclusions
In summary, a variety of arylaldehydes and ketones were transformed to the related oximes using ZnO nanoparticles under mild conditions. It was found that nano ZnO is a highly effective, mild and convenient catalyst for the synthesis of aldoximes and ketoximes. Although the literature enumerates a number of procedures for conversion of aldehydes and ketones to related oximes, the simplicity, solvent-free conditions, and inexpensiveness of our procedure makes it a practical alternative.

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References