

# Greener Solvent-Free Reactions on ZnO

Mona Hosseini-Sarvari

*Department of Chemistry, Faculty of Science, Shiraz University, Shiraz,  
I. R. Iran*

## 1. Introduction

Due to the growing concern for the influence of the organic solvent on the environment as well as on human body, organic reactions without use of conventional organic solvents have attracted the attention of synthetic organic chemists. Although a number of modern solvents, such as fluorinated media, ionic liquids and water have been extensively studied recently, not using a solvent at all is definitely the best option. Development of solvent-free organic reactions is thus gaining prominence.

During the last decades, a central objective in synthetic organic chemistry has been to develop greener and more economically competitive processes for the efficient synthesis of biologically active compounds with potential application in the pharmaceutical or agrochemical industries. In this context, the solventless approach is simple with amazing versatility. It reduces the use of organic solvents and minimizes the formation of other waste. The reactions occur under mild conditions and usually require easier workup procedures and simpler equipment. Moreover, it may allow access to compounds that require harsh reaction conditions under traditional approaches or when the yields are too low to be of practical convenience. Because of economy and pollution, solvent-free reactions are of great interest in order to modernize classical procedures making them more clean, safe and easy to perform. Reactions on solid mineral supports, reactions without any solvent/support or catalyst, and solid-liquid phase transfer catalysis can be thus employed with noticeable increases in reactivity and selectivity. Therefore the following benefits could be mentioned for solvent-free conditions:

1. Avoid of large volumes of solvent reduces emission and needs for distillation.
2. Simple work-up, by extraction or distillation.
3. The absence of solvents facilitates scale-up.
4. Reactions are often cleaner, faster, and higher yielding.
5. Recyclable solid supports can be used instead of polluting mineral acids.
6. Safety is enhanced by reducing risks of overpressure and explosions.

Zinc oxide was known for a long time, since it was a by-product of copper smelting. ZnO has been intensively studied since 1935 (Bunn, 1935) and the theory of semiconductors got a firm start. The interest in ZnO is fueled and fanned by its direct wide band gap ( $E_g \sim 3.3$  eV at 300 K), (Kakiuchi et al., 2006). ZnO also has much simpler crystal-growth technology, resulting in a potentially lower cost for ZnO base devices. ZnO has wide applications in the field of optoelectronics, (Kong & Wang, 2004) spintronics, (Sharma et al., 2003) piezoelectric

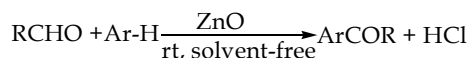
transducers, (Catti et al., 2003) and ultraviolet optoelectronics, (Wang et al., 2004). Consequently, ZnO is widely used as an additive into numerous materials and products including plastics, glass, rubber, ceramics, lubricants, paints, ointments, pigments, etc. In addition, with the development of industrialization, 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, use of non-toxic, environmentally friendly, and inexpensive solid catalysts to perform organic reactions has attracted considerable interest. Due to this, great efforts have been made by different research groups to achieve the goal of making the ZnO as catalyst in organic transformations. Interesting results have been achieved, such as the use of catalytic amounts of ZnO alone or mixed metals and metal oxides with ZnO as catalysts. In fact, ZnO as a heterogeneous catalysts can be easily separated from the reaction mixture and reused; it is generally not corrosive and do not produce problematic side products. Different classes of organic transformations have been studied and utilized using ZnO as heterogeneous catalysts, mainly exploited in the production of fine chemicals, is the subject of intensive studies in this area. Many catalytic ability of ZnO have been explored for various organic reactions facilitating synthesis of fine and specially chemicals. The application of ZnO catalyst not only is industrially important but also has academic merit. The present chapter review deal with the development in the use of ZnO as catalyst for a diverse range of organic transformations in solvent free conditions. Solvent-free organic reactions envisaged in the literature by utilizing ZnO catalyst are organized and are outline as below.

## 2. Solvent-free reactions catalyzed by ZnO

### 2.1 Friedel-Crafts acylation

Aromatic ketones are valuable intermediates in the production of various fine chemicals, which are synthesized mainly by Friedel-Crafts acylation of aromatics with acid chlorides or carboxylic anhydrides (Jackson & Hargreaves, 2009). Traditionally, these reactions have been carried out using stoichiometric amounts of liquid Bronsted acids or Lewis acids. Also aromatic ketones are the valuable intermediates or final compounds used in the production of pharmaceuticals, cosmetics, agrochemicals, dyes, and specialty chemicals. Nowadays, the restrictions imposed by the waste-minimization laws and economic considerations driven to the development of new catalytic technologies. Modern processes are in fact, based on solid catalysts.

Different researcher groups have been reported that ZnO exhibit one of the best performance in the Friedel-Crafts acylation of various benzene derivatives in solvent free-conditions, (Ashoka et al., 2010; Hosseini-Sarvari & Sharghi, 2004; Thakuria et al., 2007; Wang et al., 2008), (Scheme 1).



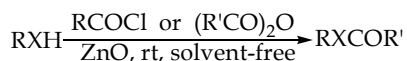
Scheme 1. Friedel-Crafts acylation on ZnO

### 2.2 Protection reactions

The use of protecting groups is very important in organic synthesis, often being the key for the success of many synthetic enterprises. The acylation of alcohols, phenols, amines, and

thiols are an important transformation in organic synthesis, (Greene & Wuts, 1999). Acylation of such functional groups is often necessary during the course of various transformations in a synthetic sequence, especially in the construction of poly functional molecules such as nucleosides, carbohydrates, steroids and natural products.

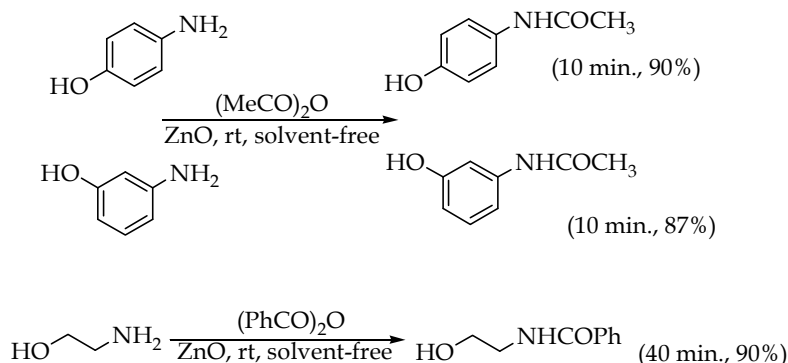
Hosseini-Sarvari and Sharghi, reported the acylation reaction of alcohols, phenols and amines under solvent-free conditions employing ZnO as catalyst (Scheme 2), (Hosseini-Sarvari & Sharghi, 2005).



R = alkyl and aryl; R' = Ph, Me; X=O, NH

Scheme 2. Protection of alcohols, phenols, and amines by ZnO

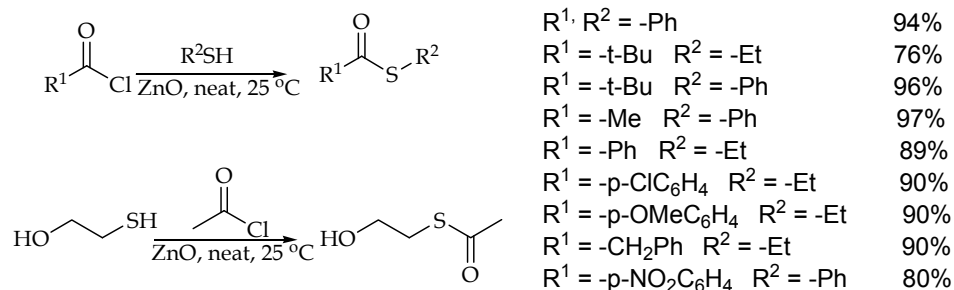
The catalyst was successfully applied for acylation of a diverse range of alcohols, phenols and amines. In the case of alcohols and phenols, an acid chloride was preferred over the corresponding acidic anhydride. The reaction with acid anhydride was too slow to have practical application. Both primary and secondary alcohols react very well and tertiary alcohol is also acylated smoothly without any side products observed. Also, the reactions of amines with  $\text{Ac}_2\text{O}$  were so fast in comparison to those of the aliphatic alcohols that the selective protection of an amine in the presence of aliphatic alcohols appeared to be a distinct possibility. Also, the amino group in aminophenol was selectively acylated (Scheme 3).



Scheme 3. Selectivity in the protection by ZnO

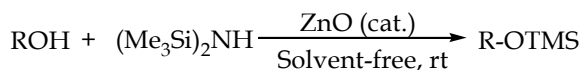
Similarly, in another studies, *O*-acylation of alcohols and phenols with acid chlorides were performed employing ZnO and nano ZnO, (Moghaddam & Saeidian 2007; Tammaddon et al., 2005; Tayebbe et al., 2010).

Recently, Bandgar and co-workers reported a convenient and efficient synthesis of thiol esters *via* the reaction of acyl chlorides with thiols using ZnO as catalyst under solvent-free conditions at room temperature. Major advantages associate with this protocol includes mild reaction conditions, short reaction time, excellent yields and recyclability of the catalyst, (Scheme 4) (Bandgar et al., 2009).



Scheme 4. Synthesis of thiol esters using zinc oxide

In addition, ZnO as economical and heterogeneous catalyst was reported for the silylation of alcohols, phenols and naphthols (Shaterian & Ghashang, 2007) (Scheme 5).



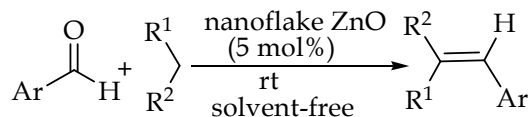
R = Aryl, primary, secondary, and tertiary aliphatic

Scheme 5. Silylation of alcohols, phenols, and naphthols using ZnO

### 2.3 Knoevenagel condensations

*Knoevenagel* (Knoevenagel, 1898) condensations which are one of the most important C-C bond forming reactions have been widely used in the synthesis of important intermediates or products for coumarin derivatives, cosmetics, perfumes, pharmaceuticals, calcium antagonists, and polymers.

Hosseini-Sarvari and co-workers (Hosseini-Sarvari et al., 2008) were reported that nano powder ZnO could be used as catalyst for *Knoevenagel* condensation. This condensation was performed using various aliphatic, aromatic, and heterocyclic aldehydes with malononitrile under solvent-free conditions in a one-step process. Most of the reactions investigated with nano ZnO catalysts were almost complete in 5 min to 3 h duration to produce the corresponding electrophilic alkenes in 90-98% yield (Scheme 6, and Table 1).



Scheme 6. Knoevenagel condensation using nano ZnO

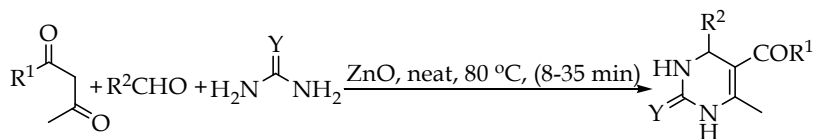
Entry	Ar	R <sup>1</sup>	R <sup>2</sup>	Time (min)	Isolated Yields (%)
1	Ph	CN	CN	210	90
2	4-MeC <sub>6</sub> H <sub>4</sub>	CN	CN	180	90
3	4-MeOC <sub>6</sub> H <sub>4</sub>	CN	CN	150	90
4	2-MeOC <sub>6</sub> H <sub>4</sub>	CN	CN	180	95
5	4-ClC <sub>6</sub> H <sub>4</sub>	CN	CN	10	98
6	4-HOC <sub>6</sub> H <sub>4</sub>	CN	CN	180	90
7	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	CN	CN	10	98
8	3-ClC <sub>6</sub> H <sub>4</sub>	CN	CN	180	90
9	2-ClC <sub>6</sub> H <sub>4</sub>	CN	CN	30	90
10	2-Thienyl	CN	CN	120	90
11	4-Pyridyl	CN	CN	5	98
12	2-Furyl	CN	CN	180	95
13	4-ClC <sub>6</sub> H <sub>4</sub>	CN	CO <sub>2</sub> Et	240	90
14	4-ClC <sub>6</sub> H <sub>4</sub>	CN	OMe	1440	0
15	4-ClC <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	Cl	60	90
16	4-ClC <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	CO <sub>2</sub> Et	300	90

Table 1. Knoevenagel condensation using nano flake ZnO (0.004 g) at 25 °C under solvent-free conditions

## 2.4 Biginelli reaction

The three-component condensation reaction between aldehyde,  $\beta$ -ketoester, and urea under strong acidic conditions to furnish 3,4-dihydropyrimidin-2(1H) was known as the Biginelli reaction.

Bahrami and co-workers reported a simple, efficient and practical procedure for the Biginelli reaction using ZnO as a novel and reusable catalyst under solvent-free conditions (Bahrami et al., 2009). The reaction proceeds efficiently under these conditions, and the dihydropyrimidiones were produced in high yields (Scheme 7).



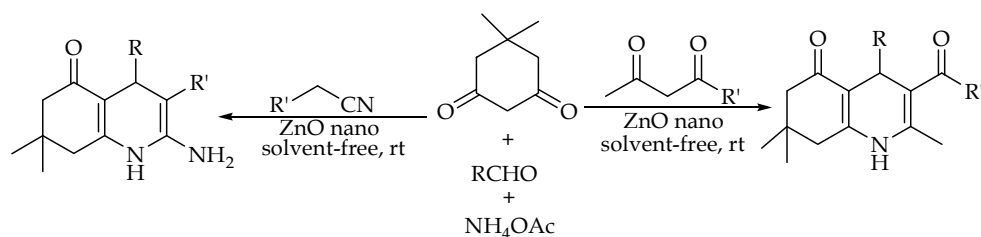
Scheme 7. Solvent-free synthesis of dihydro pyrimidinones catalyzed by ZnO

## 2.5 Hantzsch condensation

Described more than one century ago by Hantzsch, (Hantzsch, 1881) dialkyl 1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylates (1,4-DHP) have now been recognized as vital drugs. 1,4-DHP derivatives possess a variety of biological activities such as vasodilator, bronchodilator, anti-atherosclerotic, anti-tumor, geroprotective, hepatoprotective and anti-diabetic activity. In addition, recently preceding studies have suggested that 1,4-DHP

derivatives also provide an antioxidant protective effect that may contribute to their pharmacological activities. Oxidation of 1,4-DHP to pyridines has also been extensively studied. These examples clearly indicate the remarkable potential of novel 1,4-DHP and polyhydroquinoline derivatives as a source of valuable drug candidates and useful intermediates in organic chemistry. Many homogeneous and heterogeneous catalysts have been reported for the preparation of 1,4-DHP *via* the Hantzsch condensation, (Heravi et al., 2007; Kumar & Mauria, 2007).

Hantzsch condensation was thoroughly investigated employing ZnO catalyst, (Katkar et al., 2010, 2011; Moghaddam et al., 2009). Kassae and co-workers employed ZnO nano particles as an efficient and heterogeneous catalyst for synthesis of polyhydroquinoline derivatives under solvent free conditions at room temperature (Kassae et al., 2010). They were shown that in comparison with the same reaction catalyzed by commercially bulk ZnO (Moghaddam et al., 2009), use of ZnO nano particles reduced the reaction time with higher yields (Scheme 8).



Scheme 8. Hantzsch condensation catalyzed by nano ZnO

The catalytic activity and the ability to recycle and reuse ZnO nano particles were studied in this system (Table 2). The catalyst was separated by centrifuging the aqueous layer at 3,000 rpm at 20 °C for 3 min, and was reused as such for subsequent experiments under similar reaction conditions.

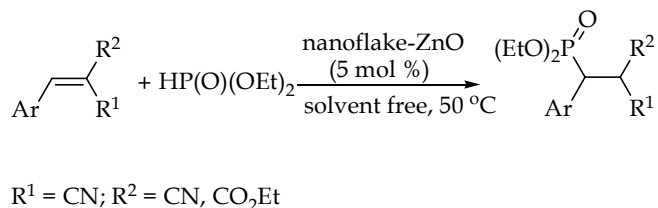
Run	Yields (%)	Recovery of nano ZnO (%)
1	98	99
2	97	99
3	97	98
4	93	96

Table 2. Reusability of the ZnO nano particles catalyst

## 2.6 Phospha-Michael addition

Similar to the Michaelis-Arbuzov and the Michaelis-Becker reaction the phospha-Michael addition, *i.e.* the addition of a phosphorus nucleophile to an acceptor-substituted alkene or alkyne, certainly represents one of the most versatile and powerful tools for the formation of P-C bonds since many different electrophiles and P nucleophiles can be combined with each other. This offers the possibility to access many diversely functionalized products. This reaction was investigated employing nano ZnO catalyst. Hosseini-Sarvari et al. reported that

nano flake ZnO exhibits the best performance in the phospho-Michael addition of phosphorus nucleophile to  $\alpha,\beta$ -unsaturated malonates under solvent-free conditions at 50 °C (Scheme 9) (Hosseini-Sarvari & Etemad, 2008).



Scheme 9. Phospha-Michael addition over nano ZnO

The authors were shown that, two kinds of ZnO (commercial ZnO and nano flake prepared ZnO, (20-30 nm)) were screened in the reaction between diethylphosphite and 2-((4-chlorophenyl)methylene)malononitrile (Table 3). As shown in Table 3, nano flake ZnO was found to be more effective than commercially ZnO in mediating the phospho Michael addition under solvent-free conditions. In order to examine the solvent effect and in quest for the deployment of a benign reaction medium, the reaction was explored in  $\text{CH}_2\text{Cl}_2$ ,  $\text{CH}_3\text{CN}$ , THF and water. The reaction in solvents required relatively longer reaction times and afforded moderate yields of the product.

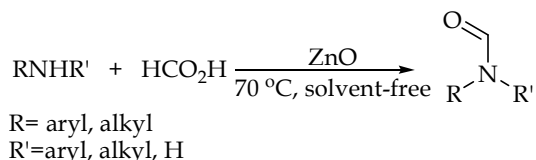
Entry	Catalyst	Solvent	Time (min)	Isolated Yield (%)
1	Commercially ZnO	Non	120	80
2	Nano flake ZnO	Non	30	98
3	Nano flake ZnO	$\text{CH}_2\text{Cl}_2$	180	43
4	Nano flake ZnO	$\text{CH}_3\text{CN}$	180	40
5	Nano flake ZnO	THF	180	40
6	Nano flake ZnO	$\text{H}_2\text{O}$	180	0

Table 3. Reaction between 2-((4-chlorophenyl)methylene)malononitrile with diethyl phosphite catalyzed by different crystallite of ZnO at 50 °C

## 2.7 N-Formylation of amines

Formamides are a class of important intermediates in organic synthesis. They have been widely used in the synthesis of pharmaceutically important compounds. A numerous methods have been reported for the formation of formamides (Green & Wuts, 1999). However, there are several factors such as low yield, difficulties in workup procedure and use of expensive reagents limiting their applications. This transformation was thoroughly investigated employing ZnO catalyst.

Recently, ZnO under solvent-free conditions have proved to be useful and reusable catalyst for N-formylation of amines using aqueous formic acid (85%) as formylating agent. This reaction was performed using various aliphatic, aromatic, heterocyclic primary and secondary amines under solvent-free conditions (Scheme 10) (Hosseini-Sarvari & Sharghi, 2006).

Scheme 10. *N*-Formylation of amines over ZnO

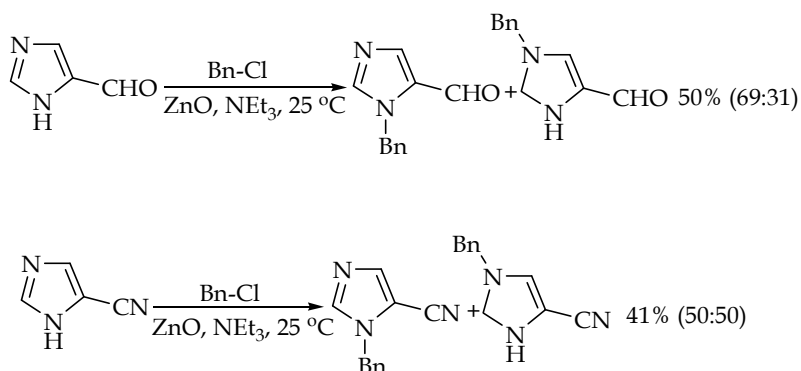
Also, prepared macroporous ZnO in presence of agar gel as template, later heated to 600 °C to produce the ZnO, has been used for the *N*-formylation of aniline (1 mmol) with formic acid (2.5 mmol) in solvent free conditions as indicated in Table 4 (Thakuria et al., 2007).

Entry	Catalyst	Catalyst (mmol)	Time (min)	Isolated Yield (%)
1	Commercial ZnO	0.50	10	99
2	ZnO (macroporous)	0.50	08	99
3	ZnO (macroporous)	0.25	120	55

Table 4. Comparison of *N*-formylation of aniline (1 mmol) with formic acid (2.5 mmol) by using ZnO as catalyst

## 2.8 *N*-Alkylation of imidazoles

Imidazole-4-carboxaldehyde and 4-cyanoimidazole were *N*-benzylated and *N*-methylated using benzyl chloride and methyl iodide on ZnO under basic conditions without solvent (Oresmaa et al., 2007). Oresmaa et al. reported that Et<sub>3</sub>N or K<sub>2</sub>CO<sub>3</sub> was added as base in the reaction on ZnO. They also investigated the effect of bases and catalyst on the product distribution of 1,4- and 1,5- substituted compounds (Scheme 11).

Scheme 11. *N*-Alkylation of imidazoles over ZnO

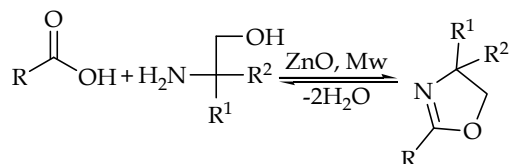
## 2.9 Synthesis of oxazolines

Oxazolines have been of great interest due to their versatility as protecting groups, as chiral auxiliaries in asymmetric synthesis, and as ligands for asymmetric catalysis. ZnO was a



useful catalyst for the preparation of 2-oxazolines from carboxylic acids (Dotani, 1997; Ishikawa, 1999; Morimoto & Ishikawa, 1997).

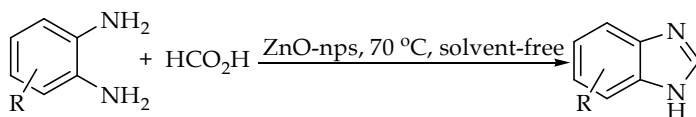
Recently, Garcia-tellado and co-workers (Garcia-tellado et al., 2003) investigated the synthesis of 4, 4-disubstituted-2-oxazoline using ZnO in solvent-free microwave-assisted conditions. They were shown that zinc oxide was found to be the most efficient. It acts both as a solid support and as a soft Lewis acid catalyst. Other acidic solid supports (montmorillonites KSF and K10, calcinated  $\text{Al}_2\text{O}_3$ ,  $\text{SiO}_2$ ) were unsuccessful. They also described that the zinc oxide seems to play a double role: it creates a polar environment for the microwave catalysis (polar solid support) and activates the carbonyl group for the condensation (Lewis acid catalyst) (Scheme 12).



Scheme 12. Synthesis of 4, 4-disubstituted-2-oxazoline using ZnO

## 2.10 Synthesis of benzimidazole derivatives

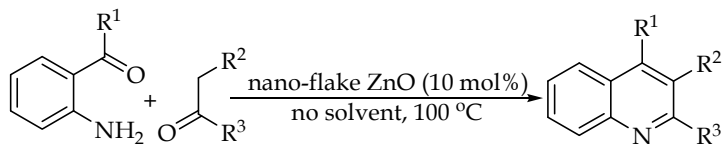
Recently, a synthesized nano particle ZnO catalyzes the synthesis of benzimidazoles with formic acid in excellent yields (Scheme 13) (Alinezhad et al., 2012). Benzimidazoles are important natural and synthetic heterocyclic compounds. Some of their derivatives are marketed as antifungal, antihelmintic, and antipsychotic drugs and other derivatives have been found to possess some interesting bioactivities. The method which was reported by Alinezhad and co-workers avoids the use of expensive reagents and the reaction is performed under solvent-free condition, making it efficient and environmentally benign. The advantages of this method include the ease of preparation of nano particle ZnO; reusable, nontoxic, and inexpensive heterogeneous nano catalyst; mild reaction conditions; easy and clean workup; and convenient procedure.



Scheme 13. Synthesis of benzimidazoles by nano particle ZnO

## 2.11 Synthesis of quinolines

Quinolines are well known for a wide range of medicinal properties being used as antimalarial, antiasthmatic, antihypertensive, antibacterial and tyrosine kinase inhibiting agent. Recently, the author reported syntheses wide range of quinolines have investigated by using nano ZnO as a heterogeneous solid catalyst under solvent-free condition (Scheme 14) (Hosseini-Sarvari, 2011).



Scheme 14. Synthesis of quinolines catalyzed by nano ZnO

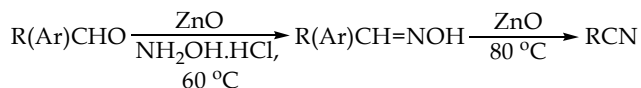
From Table 5, the author examined some other metal oxides in the synthesis of ethyl 2,4-dimethylquinoline-3-carboxylate. Also, in order to examine the solvent effect, the reaction was explored in toluene, THF, CH<sub>3</sub>CN, and water. The reaction in organic solvents required relatively longer reaction times and afforded trace yields of the product.

Entry	Catalyst (mol %)	Solvent	Time (h)	Isolated Yield (%)
1	Nano-flake ZnO (10)	None	4	98
2	Nano-flake ZnO (10)	Toluene	24	trace
3	Nano-flake ZnO (10)	THF	24	trace
4	Nano-flake ZnO (10)	CH <sub>3</sub> CN	24	trace
5	Nano-flake ZnO (10)	H <sub>2</sub> O	24	0
6	Nano-flake ZnO (5)	None	12	85
7	Nano-flake ZnO (2)	None	24	67
8	Nano-flake ZnO (20)	None	4	95
9	Nano-particle ZnO (10)	None	12	80
10	Commercially ZnO (10)	None	11	90
11	Commercially MgO (10)	None	24	40
12	Commercially TiO <sub>2</sub> (10)	None	8	75
13	Commercially CaO (10)	None	24	73

Table 5. Synthesis of ethyl 2,4-dimethylquinoline-3-carboxylate at 100 °C

## 2.12 Synthesis of nitriles

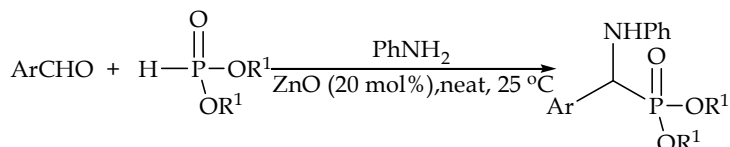
The cyano moiety is a highly important not only due to its synthetic value as precursor to other functionalities but also due to its presence in a variety of natural products, pharmaceuticals and novel materials. Although a plethora of methods are known for access to the cyano functionality, dehydration of aldoximes remains a convenient route. ZnO has been used for the synthesis of Nitriles from the dehydration of aldehydes under solvent-free conditions (Hosseini-Sarvari, 2005; Reddy & Pasha, 2010). The author reported the combination of ZnO and acetyl chloride accelerated the catalytic dehydration of aldoximes into nitriles dramatically (Scheme 15).



Scheme 15. Synthesis of nitriles using ZnO

### 2.13 Synthesis of $\alpha$ -aminophosphonates

Due to the biological activities of  $\alpha$ -aminophosphonates, the search for new catalysts leading to an efficient and practical methodology for the synthesis of these compounds is highly desired. Kassaei et al. reported that zinc oxide nanoparticles were used as an effective catalyst in the solvent-free, three-component couplings of aldehydes, aromatic amines and dialkyl phosphites at room temperature to produce various  $\alpha$ -amino phosphonates. Major advantages with this protocol include short reaction times, mild reaction conditions, easy workup and generality (Scheme 16) (Kassaei et al., 2009).



Scheme 16. ZnO nanoparticle catalyzed the synthesis of  $\alpha$ -amino phosphonates

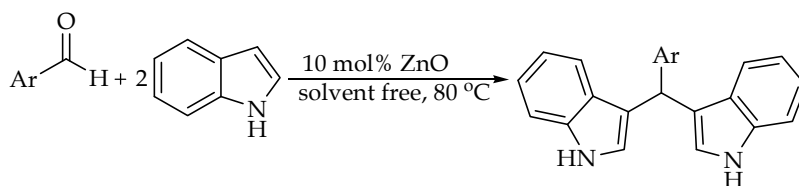
More recently, the author has utilized the nano ZnO catalyst for synthesis of  $\alpha$ -aminophosphonic esters bearing a ferrocenyl moiety revealed that only few papers have been published on the synthesis of these compounds (Hosseini-Sarvari, 2011). To expand the scope of this novel transformation, the author used nano ZnO as catalyst for the synthesis of a range of new ferrocenyl aminophosphonates. A mechanistic proposal for the role of nano ZnO as the catalyst was also investigated. The activities of several other nano and bulky metal oxides and catalysts reported recently have been compared with nano ZnO. This study shows that the yield of desired product in the presence of nano ZnO is comparably higher than other catalysts used (Table 6).

Entry	Catalyst	Time (h)	Conversion (%)	Yield (%)
1	Bulky ZnO	12	90	84
2	Bulky Fe <sub>2</sub> O <sub>3</sub>	24	0	0
3	Bulky basic-Al <sub>2</sub> O <sub>3</sub>	12	49	45
4	Bulky CuO	24	6	Trace
5	Bulky MgO	24	0	0
6	Bulky CaO	24	0	0
7	Bulky TiO <sub>2</sub>	12	56	50
8	Nano TiO <sub>2</sub>	12	58	50
9	Nano MgO	24	0	0
10	Mg(ClO <sub>4</sub> ) <sub>2</sub>	12	7	Trace
11	H <sub>3</sub> PW <sub>12</sub> O <sub>40</sub>	24	0	0
12	No catalyst	24	4	Trace
13	Nano ZnO	2	100	95

Table 6. Comparison of catalytic activity of nano ZnO catalyst with several other catalysts for the synthesis of diethyl anilino(ferrocenyl)methyl phosphonate

### 2.14 Synthesis of bis(indolyl)methanes

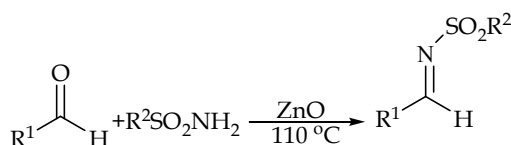
Bis(indolyl)methanes are the most active and highly recommended cruciferous substances for promoting beneficial estrogen metabolism and inducing apoptosis in human cancer cells. The electrophilic substitution reaction of indoles with aldehydes is one of the most simple and straightforward approaches for the synthesis of bis(indolyl)methanes. Hosseini-Sarvari successfully synthesized bis(indolyl) methanes by the reaction of indole with various aldehydes in the presence of ZnO catalyst in solvent-free conditions (Scheme 17). It was observed from this study that ZnO is an efficient catalyst for the synthesis of bis(indolyl)methanes in terms of product yields, reaction temperature, and reaction times ( Hosseini-Sarvari, 2008).



Scheme 17. Synthesis of bis(indolyl)methanes by ZnO

### 2.15 Synthesis of *N*-Sulfonylaldimines

*N*-sulfonylimines have been increasing importance because they are one of the few types of electron-deficient imines that are stable enough to be isolated but reactive enough to undergo addition reactions. ZnO was reported as a mediated for preparations of *N*-sulfonylimines under solvent-free conditions by conventional heating (Scheme 18). The advantages of this method are as follows: *i*) there is no need of toxic and waste producing Lewis acids; *ii*) work-up is simple; *iii*) the reaction procedure is not requiring specialized equipment; *iv*) zinc oxide powder can be re-used; and *v*) solvent-free condition (Hosseini-Sarvari & Sharghi, 2007).

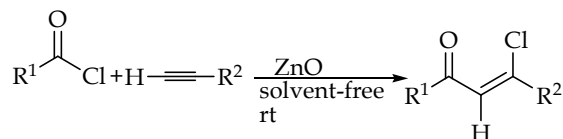


Scheme 18. Preparations of *N*-sulfonylaldimines under solvent-free conditions by ZnO

### 2.16 Synthesis of $\beta$ -Chloro- $\alpha,\beta$ -unsaturated Ketones

A useful reaction for the synthesis of  $\beta$ -Chloro- $\alpha,\beta$ -unsaturated ketones (as synthetic intermediates particularly for the synthesis of heterocyclic systems) involves the addition of acid chloride derivatives to terminal alkynes. However, the addition of acid chlorides to alkynes often proceeds with concomitant decarbonylation. Recently, ZnO was shown a useful catalyst for the addition of acid chlorides to terminal alkynes, afforded (*Z*)-adducts selectively without decarbonylation at room temperature under solvent-free conditions (Scheme 19). This protocol benefits from short reaction times, operational

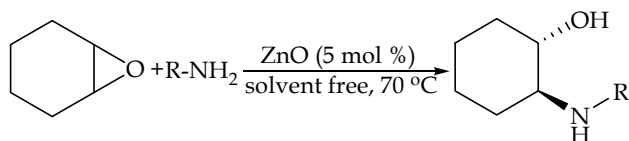
simplicity, neutral reaction conditions, reusability of the catalyst, avoidance of solvents, reduced environmental and economic impacts, and chemo selectivity. No toxic reagent or by product were involved and no laborious purifications were necessary (Hosseini-Sarvari & Mardaneh, 2011).



Scheme 19. Addition of acid chlorides to terminal alkynes, catalyzed by ZnO

### 2.17 Ring-opening of epoxides

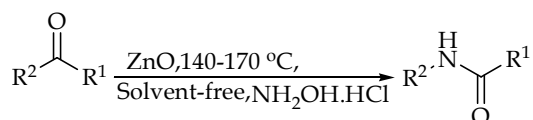
$\beta$ -Amino alcohols are synthesized by acid catalyzed ring-opening of epoxides. Hosseini-Sarvari carried out the ring-opening of cyclohexene oxide, phenoxy oxide, styrene oxide, and epichlorohydrine oxide with various aromatic amines toward the synthesis of  $\beta$ -amino alcohols catalyzed by ZnO, affording high yields of products under solvent-free conditions and the reaction is also regioselective (Scheme 20) (Hosseini-Sarvari, 2008).



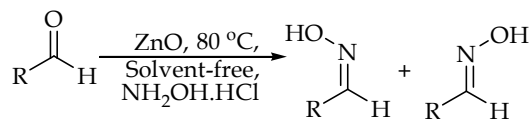
Scheme 20. Synthesis of  $\beta$ -amino alcohols catalyzed by ZnO

### 2.18 Beckmann rearrangement

The Beckmann rearrangement is a fundamental and useful reaction, long recognized as an extremely valuable and versatile method for the preparation of amides or lactams, and often employed even in industrial processes. The conventional Beckmann rearrangement usually requires the use of strong Bronsted or Lewis acids, *i.e.* concentrated sulfuric acid, phosphorus pentachloride in diethyl ether, hydrogen chloride in acetic anhydride, causing large amounts of byproducts and serious corrosion problems. The ZnO catalyzed Beckmann rearrangement of various aldehydes and ketones in solvent-free conditions (Scheme 21) in good-to-excellent yields (60-95 %) (Sharghi & Hosseini, 2002). It was found that various types of aldehydes in the presence of ZnO were condensed cleanly, rapidly and selectively with hydroxylamine hydrochloride at 80°C in 5-15 min to afford the corresponding *Z*-isomer of the oximes (OH *syn* to aryl) in excellent yields. Only a small amount of *E*-isomer, *i.e.* ca. 10-20% was obtained. (Scheme 22).



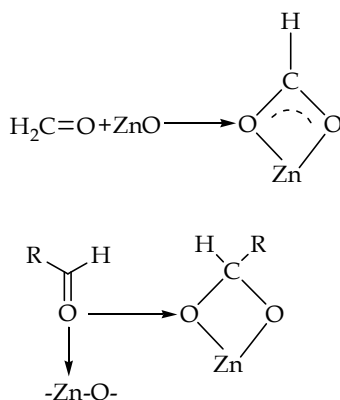
Scheme 21. Beckmann rearrangement catalyzed by ZnO



Scheme 22. Synthesis of oximes catalyzed by ZnO

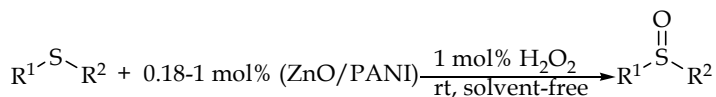
### 2.19 Oxidation reactions

Oxygen anions on metal oxide surfaces can act as Lewis as well as Brønsted bases. As such, they may oxidize adsorbed organics. The most common examples of such reactions in the metal oxide surface science literature are nucleophilic oxidations of carbonyl compounds. Aldehydes are oxidized to the corresponding carboxylates on a number of oxide surfaces such as ZnO. Higher alcohols and aldehydes also form carboxylate intermediates on ZnO (Vohs et al., 1986, 1988, 1989). Other related species such as esters exhibit similar chemistry; oxidation of methyl formate on the ZnO (001) surface (Scheme 23).



Scheme 23. Oxidation of methyl formate on the ZnO surface

Recently, a new synthetic method for the oxidation of sulfides on ZnO surface has been reported (Shiv et al., 2009) in the presence of  $\text{H}_2\text{O}_2$  under solvent-free conditions (Scheme 24). The results reveal that PANI/ZnO composite has high activity and selectivity compared to the raw ZnO.



$\text{R}^1$  = aryl, alkyl

$\text{R}^2$  = alkyl

Scheme 24. Selective oxidation of sulfide with ZnO

### 3. Conclusion

This chapter review describes various organic reactions on ZnO. During the past decades, numerous organic reactions have been developed using ZnO as a non-toxic metal oxide in response to the demand for more environmentally benign organic syntheses. This development promotes the use of ZnO because of its unique properties, as described in this review. ZnO appear to be attractive for conducting organic reactions in solvent-free condition, reusability of ZnO, especially nano ZnO. When a new reaction is discovered, a devoted chemist can no longer ignore the possibility of performing the reaction using the ZnO. Thus, ZnO is a new, useful, and powerful catalyst for organic reactions.

In addition, many efforts could be found in the literature to improve the activity and stability of the ZnO catalysts, including promotion of the catalyst with transition metals like Pt, Pd, Fe, Mn, and etc. and mixed metal oxides such as TiO<sub>2</sub>, ZrO<sub>2</sub>, CaO, CuO, etc. which was not mentioned here. ZnO and its promoted versions are much more promising for various organic reactions of practical significance and are expected to gain great interest in the coming years.

### 4. Acknowledgment

The author thank the Shiraz University Research Council for their financial support.

### 5. References

- Alinezhad, H., Salehian, F., & Biparva, P. (2012). Synthesis of benzimidazole derivatives using heterogeneous ZnO nanoparticles. *Synthetic Communication*, Vol. 42, No. 1, (September 2011), pp. 102-108, ISSN 0039-7911
- Ashoka, S., Chithaiah, P., Thipperudaiah, K. V., & Chandrappa, G. T. (2010). Nanostructural zinc oxide hollow spheres: A facile synthesis and catalytic properties. *Inorganica Chimica Acta*, Vol. 363, No. 13, (October 2010), pp. 3442-3447, ISSN 0020-1693
- Bahrami, K., Khodaei, M. M., & Farrokhi, A. (2009). Highly efficient solvent-free synthesis of dihydropyrimidinones catalyzed by zinc oxide. *Synthetic Communication*, Vol. 39, No. 10, (April 2009), pp. 1801-1808, ISSN 0039-7911
- Bandgar, B. P., More, P. E., Kamble, V. T., & Sawant, S. S. (2009). Convenient and efficient synthesis of thiol esters using zinc oxide as a heterogeneous and eco-friendly catalyst. *Australian Journal of Chemistry*, Vol. 61, No. 12, (April 2009), pp. 1006-1010, ISSN 0004-9425
- Bunn, C.W. (1935). The lattice-dimensions of zinc oxide. *Proceeding of the Physical Society*, Vol. 47, No. 5, (September 1935), pp. 835-842, ISSN 0370-1328
- Catti, M., Noel, Y., & Dovesi, R. (2003). Full piezoelectric tensors of wurtzite and zinc blende ZnO and ZnS by first-principles calculations. *Journal Physics and Chemistry Solids*, Vol. 64, No. 11, (April 2003), pp. 2183-2190, ISSN 0022-3697
- Dotani, M. (1997). Jpn. Kokai Tokkyo Koho, JP Patent 09048769 A 19970218
- García-Tellado, F., Loupy, A., Petit, A., & Leilani Marrero-Terrero, A. (2003). Solvent-free microwave-assisted efficient synthesis of 4,4-disubstituted 2-oxazolines. *European Journal of Organic Chemistry*, (November 2003), pp. 4387-4391, ISSN 2153-2249
- Green, T. W., & Wuts, P. G. M. (1999). *Protective Groups in Organic Synthesis*, 3rd ed., Wiley-Interscience, New York, ISBN 0-471-16019-9

- Hantzsch, A. (1881). Condensationprodukte aus aldehydammoniak und ketonartigen verbindungen. *Chemische Berichte*, Vol. 14, No. 2, (July 1881), pp. 1637-1638, ISSN 0009-2940.
- Heravi, M. M., Bakhtiari, K., Javadi, M. N., Bamoharram, F. F., Saeedi, M., & Oskooie, A. H. (2007). K<sub>7</sub>[PW<sub>11</sub>CoO<sub>40</sub>]-catalyzed one-pot synthesis of polyhydroquinoline derivatives via the Hantzsch three component condensation. *Journal of the Molecular Catalysis A: Chemical*, Vol. 264, No. 1-2, (March 2007), pp. 50-52, ISSN 1381-1169
- Hosseini-Sarvari, M., & Sharghi, H. (2004). Reactions on a solid surface. A simple, economical and efficient Friedel-Crafts acylation reaction over zinc oxide (ZnO) as a new catalyst. *Journal of Organic Chemistry*, Vol. 69, No. 20, (April 2004), pp. 6953-6956, ISSN 0022-3263
- Hosseini-Sarvari, M., & Sharghi, H. (2005). Zinc oxide (ZnO) as a new, highly efficient, and reusable catalyst for acylation of alcohols, phenols and amines under solvent free conditions. *Tetrahedron*, Vol. 61, No. 46, (September 2005), pp. 10903-10907, ISSN 0040-4020
- Hosseini-Sarvari, M. (2005). ZnO/CH<sub>3</sub>COCl: A new and highly efficient catalyst for dehydration of aldoximes into nitriles under solvent-free condition. *Synthesis*, No. 5, (November 2004), pp. 787-790, ISSN 0039-7881
- Hosseini-Sarvari, M., & Sharghi, H. (2006). ZnO as a new catalyst for N-formylation of amines under solvent-free conditions. *Journal of Organic Chemistry*, Vol. 71, No. 17, (April 2006), pp. 6652-6654, ISSN 0022-3263
- Hosseini-Sarvari, M., & Sharghi, H. (2007). A novel method for the synthesis of N-sulfonylaldimines by ZnO as a recyclable neutral catalyst under solvent-free conditions. *Phosphorus, Sulfur, Silicon, and Related Elements*, Vol. 182, No. 9, (September 2007), pp. 2125-2130, ISSN 1042-6507
- Hosseini-Sarvari, M. (2008). Synthesis of bis(indolyl)methanes using a catalytic amount of ZnO under solvent-free conditions. *Synthetic Communication*, Vol. 38, No. 6, (January 2008), pp. 832-840, ISSN 0039-7911
- Hosseini-Sarvari, M., & Etmad, S. (2008). Nanosized zinc oxide as a catalyst for the rapid and green synthesis of b-phosphono Malonates. *Tetrahedron*, Vol. 64, No. 23, (March 2008), pp. 5519-5523, ISSN 0040-4020
- Hosseini-Sarvari, M., Sharghi, H. & Etmad, S. (2008). Nanocrystalline ZnO for Knoevenagel condensation and reduction of the carbon, carbon double bond in conjugated alkenes. *Helvetica Chimica Acta*, Vol. 91, No. 4, (April 2008), pp. 715-724, ISSN 0018-019X
- Hosseini-Sarvari, M. (2008). Synthesis of β-aminoalcohols catalyzed by ZnO. *Acta Chimica Slovenica*, Vol. 55, No.2, (June 2008), pp. 440-447, ISSN 1318-0207
- Hosseini-Sarvari, M. (2011). Synthesis of quinolines using nano-flake ZnO as a new catalyst under solvent-free conditions. *Journal of Iranian Chemical Society*, Vol. 8, No. (July 2010), pp. 119-128, ISSN 1735-207X
- Hosseini-Sarvari, M. (2011). An efficient and eco-friendly nanocrystalline zinc oxide catalyst for one-pot, three component synthesis of new ferrocenyl aminophosphonic esters under solvent-free condition. *Catalysis Letters*, Vol. 141, (November 2010), pp. 347-355, ISSN 1011-372X
- Hosseini-Sarvari, M., & Mardaneh, Z. Selective and CO-retentive addition reactions of acid chlorides to terminal alkynes in synthesis of β-chloro-α,β-unsaturated ketones using ZnO. (2011). *Bulletin of the Chemical Society Japan*, Vol. 84, No. 7, (February 2011), pp. 778-782, ISSN 0009-2673
- Ishikawa, R. (1999). Jpn. Kokai Tokkyo Koho, JP Patent 11217376 A 19990810



- Jackson, S. D., & Hargreaves, J. S. J. (2009). *Metal Oxide Catalysis*, 692-694, ISBN 978-3-527-31815-5
- Kakiuchi, K., Hosono, E., & Fujihara, S. (2006). Enhanced photoelectrochemical performance of ZnO electrodes sensitized with N-719. *Journal of Photochemistry and Photobiology, A*, Vol. 179, Vo.1-2, (April 2006), pp.81-86, ISSN 1751-1097
- Kassae, M. Z., Movahedi, F., & Masrouri, H. (2009). ZnO nanoparticles as an efficient catalyst for the one-pot synthesis of  $\alpha$ -amino phosphonates. *Synlett*, Vol. 8, (December 2008), pp.1326-1330, ISSN1437-2096
- Kassae, M. Z., Masrouri, H., & Movahedi, F. (2010). ZnO-nanoparticle-promoted synthesis of polyhydroquinoline derivatives via multicomponent Hantzsch reaction. *Monatshefte fur Chemie*, Vol. 141, No. 3, (January 2010), pp. 317-322, ISSN 1434-4475
- Katkar, S. S., Mohite, P. H., Gadekar, L. S., Arbad, B. R., & Lande, M. K. (2010). ZnO-beta zeolite: as an effective and reusable heterogeneous catalyst for the one-pot synthesis of polyhydroquinolines. *Green Chemistry Letters and Review*, Vol. 3, No. 4, (December 2010), pp. 287-292, ISSN 1751-8253
- Katkar, S. S., Arbad, B. R., & Lande, M. K. (2011). ZnO-beta zeolite catalyzed solvent-free synthesis of polyhydroquinoline derivatives under microwave irradiation. *Arab Journal of Science and Engineering*, Vol. 36, No. 1, (January 2011), pp. 39-46, ISSN 1319-8025
- Knoevenagel, L. F. (1898). Condensation von malonsäure mit Aromatischen aldehyden durch ammoniak und amine. *Berichte der deutschen chemischen Gesellschaft*, Vol. 31, No. 3, (October 1898), pp. 2596-2619, ISSN 0365-9631
- Kong, X. Y., & Wang, Z. L. (2004). Polar-surface dominated ZnO nanobelts and the electrostatic energy induced nanohelices, nanosprings, and nanospirals. *Applied Physics Letters*, Vol. 84, No. 6, (December 2003), pp. 975-977, ISSN: 0003-6951.
- Kumar, A., & Maurya, A. R. (2007). Bakers' yeast catalyzed synthesis of polyhydroquinoline derivatives via an unsymmetrical Hantzsch reaction. *Tetrahedron Letters*, Vol. 48, No. 22, (March 2007), pp. 3887-3890, ISSN 0040-4039
- Moghaddam, F. M., & Saeidian, H. (2007). Controlled microwave-assisted synthesis of ZnO nanopowder and its catalytic activity for O-acylation of alcohol and phenol. *Material Science and Engineering: B*, Vol. 139, No. 2-3, (March 2007), pp. 265-269, ISSN 0921-5107
- Moghaddam, F. M., Saeidian, H. Mirjafary, Z., & Sadeghi, A. (2009). Rapid and efficient one-pot synthesis of 1,4-dihydropyridine and polyhydroquinoline derivatives through the Hantzsch four component condensation by zinc oxide. *J. Iran. Chem. Soc.*, Vol. 6, No. 2, (June 2009), pp. 317-324, ISSN 1735-207X
- Morimoto, M., & Ishikawa, R. (1997). Jpn. Kokai Tokkyo Koho, JP Patent 09301960 A 19971125
- Oresmaa, L., Taberman, H., Haukka, M., Vainiotalo, P., & Aulaskari, P. (2007). Regiochemistry of N-substitution of some 4(5)-substituted imidazoles under solvent-free conditions. *Journal of Heterocyclic Chemistry*, Vol. 44, No. 6, (November 2007), pp. 1445-1451, ISSN 0022-152X
- Reddy, M. B. M., & Pasha, M. A. (2010). Environment friendly protocol for the synthesis of nitriles from aldehydes. *Chinese Chemical Letters*, Vol. 21, No. 9, (December 2010), pp. 1025-1028, ISSN 1001-8417
- Sharma, P., Gupta, A. K., Rao, V., Owens, F. J., Sharma, R., Ahuja, R., Osorio, J. M., Johansson, B., & Gehring, G. A. (2003). Ferromagnetism above room temperature in bulk and transparent thin films of Mn-doped ZnO. *Nature Material*, Vol. 2, No. 10, (September 2003), pp. 673-677, ISSN 1476-1122

- Sharghi, H., & Hosseini, M. (2002). Solvent-free and one-step Beckmann rearrangement of ketones and aldehydes by zinc oxide. *Synthesis*, No. 8, (April 2002), pp. 1057-1060, ISSN 0039-7881
- Shaterian, H. R., & Ghashang, M. (2008). A highly efficient method for the silylation of alcohols, phenols, and naphthols using HMDS in the presence of zinc oxide (ZnO) as economical heterogeneous catalyst. *Phosphorus Sulfur Silicon Related Elements*, Vol. 183, No. 1, (February 2008), pp. 194-204, ISSN 1042-6507
- Shiv, P., Sharma, M. V. S., Suryanarayana, A. K., Nigam, A. S., Chauhan, A. S., & Tomar, L. N. S. (2009). [PANI/ZnO] composite: Catalyst for solvent-free selective oxidation of sulfides. *Catalysis Communication*, Vol. 10, No. 6, (February 2009), pp. 905-912, ISSN 1566-7367
- Tammaddon, F., Amrollahi, M. A., & Sharafat, L. (2005). A green protocol for chemoselective O-acylation in the presence of zinc oxide as a heterogeneous, reusable and eco-friendly catalyst. *Tetrahedron Letters*, Vol. 46, No. 45, (November 2005), pp. 7841-7844, ISSN 0040-4039
- Tayebee, R., Cheravi, F., Mirzaee, M., & Amini, M. M. (2010). Commercial zinc oxide (Zn<sup>2+</sup>) as an efficient and environmentally benign catalyst for homogeneous benzylation of hydroxyl functional groups. *Chinese Journal of Chemistry*, Vol. 28, No. 7, (July 2010), pp. 1247-1252, ISSN 1614-7065
- Thakuria, H., Borah, B. M., & Das, G. (2007). Macroporous metal oxides as an efficient heterogeneous catalyst for various organic transformations-A comparative study. *Journal of Molecular Catalysis A: Chemical*, Vol. 274, No. 1-2, (September 2007), pp. 1-10, ISSN 1381-1169
- Vohs, J. M., & Barteau, M. A. (1986). Conversion of methanol, formaldehyde and formic acid on the polar faces of zinc oxide. *Surface Science*, Vol. 176, No. 1-2, (October 1986), pp. 91-114, ISSN 00396028
- Vohs, J. M., & Barteau, M. A. (1988). Spectroscopic characterization of surface formates produced via reaction of HCOOH and HCOOCH<sub>3</sub> on the (0001) surface of zinc oxide. *Surface Science*, Vol. 197, No. 1-2, (January 1988), pp. 109-122, ISSN 00396028
- Vohs, J. M., & Barteau, M. A. (1988). Reaction pathways and intermediates in the decomposition of acetic and propionic acids on the polar surfaces of zinc oxide. *Surface Science*, Vol. 201, No. 3, (July 1988), pp. 481-502, ISSN 00396028
- Vohs, J. M., & Barteau, M. A. (1988). Alkyl elimination from aldehydes on zinc oxide: Relevance to allylic oxidation pathways. *Journal of Catalysis*, Vol. 113, No. 2, (October 1988), pp. 497-508, ISSN 0021-9517
- Vohs, J. M., & Barteau, M. A. (1989). Formation of stable alkyl and carboxylate intermediates in the reactions of aldehydes on the zinc oxide (0001) surface. *Langmuir*, Vol. 5, No. 4, (July 1989), pp. 965-972, ISSN 0743-7463
- Vohs, J. M., & Barteau, M. A. (1989). Activation of aromatics on the polar surfaces of zinc oxide. *Journal of Physical Chemistry: B*, Vol. 93, No. 26, (December 1989), pp. 8343-8354, ISSN 1520-6106
- Wang, X. Ding, Y. Summers, C. J., & Wang, Z. L. (2004). Large-Scale Synthesis of Six-Nanometer-Wide ZnO Nanobelts. *Journal of Physical Chemistry: B*, Vol. 108, No. 26, pp. 8773-8777, ISSN 1520-6106
- Wang, R., Hong, X., & Shan, Z. (2008). A novel, convenient access to acylferrocenes: acylation of ferrocene with acyl chlorides in the presence of zinc oxide. *Tetrahedron Letters*, Vol. 49, No. 4, (January 2008), pp. 636-641, ISSN 0040-4039



## **Green Chemistry - Environmentally Benign Approaches**

Edited by Dr. Mazaahir Kidwai

ISBN 978-953-51-0334-9

Hard cover, 156 pages

**Publisher** InTech

**Published online** 23, March, 2012

**Published in print edition** March, 2012

Green chemistry is chemistry for the environment. It is really a philosophy and way of thinking that can help chemistry in research and production to develop more eco-friendly solutions. Green chemistry is considered an essential piece of a comprehensive program to protect human health and the environment. In its essence, green chemistry is a science-based non-regulatory and economically driven approach to achieving the goals of environmental protection and sustainable development. Combining the technological progress with environmental safety is one of the key challenges of the millennium. In this context, this book describes the environmentally benign approaches for the industries as well as chemical laboratories. In order to provide an insight into step change technologies, this book was edited by green organic chemists.

### **How to reference**

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Mona Hosseini-Sarvari (2012). Greener Solvent-Free Reactions on ZnO, Green Chemistry - Environmentally Benign Approaches, Dr. Mazaahir Kidwai (Ed.), ISBN: 978-953-51-0334-9, InTech, Available from: <http://www.intechopen.com/books/green-chemistry-environmentally-benign-approaches/greener-solvent-free-reactions-on-zno->

**INTECH**  
open science | open minds

### **InTech Europe**

University Campus STeP Ri  
Slavka Krautzeka 83/A  
51000 Rijeka, Croatia  
Phone: +385 (51) 770 447  
Fax: +385 (51) 686 166  
[www.intechopen.com](http://www.intechopen.com)

### **InTech China**

Unit 405, Office Block, Hotel Equatorial Shanghai  
No.65, Yan An Road (West), Shanghai, 200040, China  
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元  
Phone: +86-21-62489820  
Fax: +86-21-62489821

© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.