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Short Communication

Zinc oxide as a regioselective and heterogeneous catalyst for the synthesis of chalcones at room temperature

Parmeshwar E. More [a,*], Babasaheb P. Bandgar [b], Vinod T. Kamble [c]

[a] Department of Chemistry, Shardabai Pawar Mahila Mahavidyalaya Shardanagar, Baramati, Dist. Pune 413115, India
[b] Organic Chemistry Research Laboratory, School of Chemical Sciences, Solapur University Solapur 413255, India
[c] Organic Chemistry Research Laboratory, School of Chemical Sciences, S.R.T.M. University Nanded 431606, India

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ABSTRACT

Zinc oxide catalyzed synthesis of chalcones has been carried out under solvent-free conditions at room temperature. Activated as well as unactivated aromatics smoothly underwent Friedel–Crafts acylation with α, β-unsaturated acid chlorides furnishing excellent yields of the corresponding chalcones. The zinc oxide can be recovered and reused at least three times without any appreciable loss in activity.

1. Introduction

Chalcones (1,3-diaryl-2-propene-1-ones) constitute an important group of natural products found in a number of plants or synthetically prepared. They display many biological activities such as anti-cancer [1], anti-inflammatory [2], antimitotic [3], anti-tubercular [4], cardiovascular [5], cell differentiation inducing [6], nitric oxide regulation modulatory [7] and anti-hyperglycemic agents [8].

The straightforward route leading to the synthesis of chalcones is Friedel–Crafts acylation of arenes with α,β-unsaturated aryl acid halides [9,10]. These methods have several limitations such as limited regioselectivity, need of stoichiometric amount of $AlCl_3$ and are not applicable to the synthesis of acid-sensitive chalcones. Recently, some solid material has been employed as a heterogeneous catalyst to synthesize chalcones, in particular NaNO3/natural phosphates [11] $LiNO_3$/natural phosphates [12], acidic clay [13] and ZnO supported metal oxides [14]. However, these methods are limited because special efforts are needed for the preparation of catalyst using harsh conditions or a high reaction time. The microwave irradiation in presence of solid catalysts has been also used for the synthesis of these compounds [15,16]; furthermore the recycling of catalyst is difficult due to structural modification by microwave. In order to overcome these limitations, synthetic chemists continue to develop new catalysts which carry out selective reactions under mild conditions.

Zinc oxide (ZnO) is an inexpensive and commercially available inorganic solid has been used as a catalyst in number of chemical transformations [17–22]. Herein, we report a new, simple, and regioselective synthesis of chalcones using ZnO as a catalyst under solvent-free conditions at room temperature (Scheme 1).

2. Experimental

2.1. General remarks

Zinc oxide was purchased from Sigma-Aldrich as bright blue-white color and odorless powder and used without any further purification. Melting points were determined in a capillary Electro-thermal melting point apparatus and are given uncorrected. ^{1}H NMR spectra were recorded using Varian Mercury YH-300 MHz spectrometer with TMS as an internal standard. Infrared spectra were taken with a Perkin Elmer 1310 spectrometer. Elemental analysis was recorded on ELEMENTAR (Vario EL, Germany).

2.2. General procedure

A mixture of α,β-unsaturated acid chloride (501 mg, 3 mmol), an aromatic compound (324 mg, 3 mmol) and zinc oxide (120 mg, 1.5 mmol) was stirred at room temperature (25–30 °C) for the specified time (Table 2). The progress of the reaction was monitored by TLC. After completion of the reaction, the product was extracted with dichloromethane (3 × 5 mL), and extract was washed with aq. $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4 and removal of the solvent under reduced pressure furnished analytically pure product with 92% yield (219 mg).

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* Corresponding author. Fax: +91 2112 254576.
E-mail address: morepe_2007@yahoo.co.in (P.E. More).

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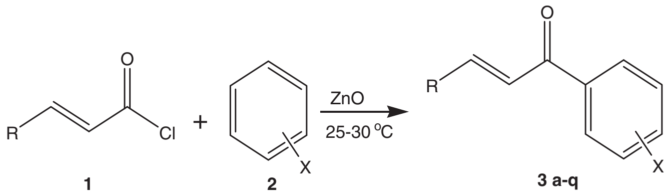


Scheme 1.

Table 1
Evaluation of catalytic activity of zinc oxide in the synthesis of 1-(4′-Methoxyphenyl)-3-phenylpropenone.

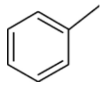
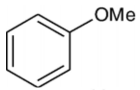
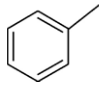
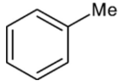
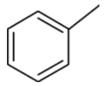
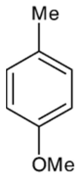
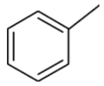
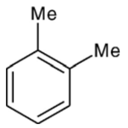
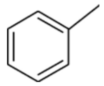
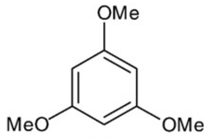
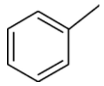
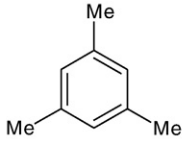
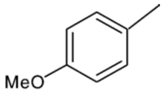
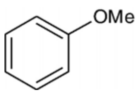
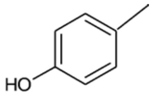
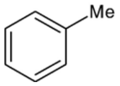
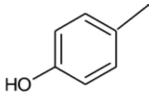
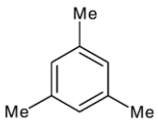
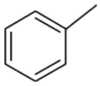
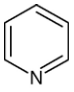
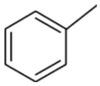
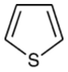
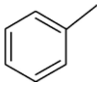
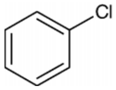
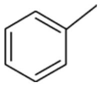
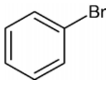
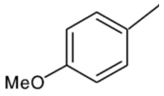
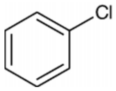
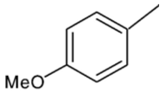
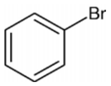
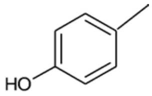
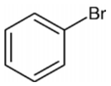
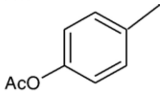
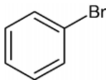
Entry	Amount of zinc oxide (mg)	Time (min)	Yield[a] (%)
1	0	45	ND
2	10	45	45
3	20	30	65
4	30	25	80
5	40	10	92
6	50	10	90
7	40	05	55

Reaction conditions: cinnamoyl chloride (167 mg, 1 mmol), 4-methoxy benzene (108 mg, 1 mmol) and zinc oxide.

3. Result and discussion

In search of the best experimental conditions, the reaction of cinnamoyl chloride (167 mg, 1 mmol) and methoxy benzene (108 mg, 1 mmol) in the presence of zinc oxide under solvent-free conditions was considered as a standard and model reaction. When the reaction was carried out in the absence of any catalyst the product was not detected (Table 1, entry 1). In the presence of zinc oxide the reaction was possible, and in order to determine the appropriate quantity of catalyst used, we investigated the model reaction at different concentrations of zinc oxide such as 10, 20, 30, 40, and 50 mg. The product yield was 45, 65, 80, 92 and 90%, respectively. This indicates that 40 mg of zinc oxide is sufficient to carry out the reaction smoothly. When the model reaction was run with 40 mg of zinc oxide and stopped at half time, 55% yield of product was obtained.

Table 2
ZnO catalyzed synthesis of chalcones.

Entry	– R	Substrate	Product	Time (min.)	Yield[a] (%)
a			3a	10	92
b			3b	15	89
c			3c	10	85
d			3d	10	83
e			3e	05	97
f			3f	07	96
g			3 g	10	90
h			3 h	10	87
i			3i	10	89
j			3j	09	92
k			3 k	10	89
l			3 l	130	86
m			3 m	120	86
n			3n	130	83
o			3o	60	92
p			3p	60	89
q			3q	45	89

[a] Yield of pure isolated products.

Various activated as well as unactivated aromatic compounds with α,β-unsaturated aromatic acid chlorides underwent smooth Friedel–Crafts acylation furnishing excellent yields of the chalcones with a short reaction time. Results are presented in Table 2. All activated aromatic compounds reacted very rapidly to furnish corresponding chalcones (Table 2, entries a–i) and no chromatographic separation is required to get pure products except in a few cases (Table 2, entries h, i and p). The regioselectivity is impressive as acylation occurred exclusively at the position para to OMe, Me, Cl and Br. Obviously time required for Friedel–Crafts reaction of unactivated/deactivated aromatic compounds is more as compared to that of activated aromatics. However, in the cases where the para positions are blocked the acylation proceeded in the ortho position (Table 2, entry c). This protocol is very well applicable to heterocyclic

Table 3
Reuse of recovered catalyst (ZnO).

No. of uses	Yield (%)	Recovery of ZnO (%)
1	97	95
2	93	92
3	90	90

compounds such as pyridine and thiophene (Table 2, entries j–k) producing the corresponding 3-acylated and 2-acylated chalcones respectively in excellent yields, which are otherwise problematic with $AlCl_3$ [9,23,24]. It is interesting to note that the reaction conditions are mild enough not to induce dealkylation of an ether residue ortho to the introduced acyl group (Table 2, entries c and e) as observed in the acylation reaction with carboxylic acid catalyzed by BF_3 [25]. And the yield of O-acylated chalcone in a short time (Table 2, entry q) is higher than the reaction catalyzed by BF_3-etherate [26].

In order to study, catalytic activity of recovered catalyst (ZnO), it was reused for the reaction of trimethoxybenzene with cinnamoyl chloride (Table 2, entry e). The results summarized in Table 3 indicated that recovered catalyst (ZnO) can be used at least three times without any appreciable loss in activity. The recovery of the catalyst (ZnO) was more than 90% by simple filtration and washing with dichloromethane. Furthermore, the selectivity of the catalyst (ZnO) was examined.

The utility of this protocol to synthesize important intermediates for drug molecules like flavopiridol and rohitukine is in progress in our laboratory.

4. Conclusion

In conclusion, we have developed a simple, clean and efficient procedure for the synthesis of chalcones using commerciality available inexpensive and non-toxic zinc oxide powder as a new catalyst. Without any activation, ZnO is directly used as a catalyst and not a supporting metal oxide. The effectiveness of this protocol is manifested in its regioselectivity and recyclability of the catalyst.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.catcom.2012.06.012.

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