



Research Article

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Multicomponent Synthesis of α -Acetamidoketones by using mix metal oxide CuO-SnO₂ as Versatile Catalyst

¹Deepak. M. Nagrik*, ²Shrikant S. Patil, ²Rameshwar S. Dhamak

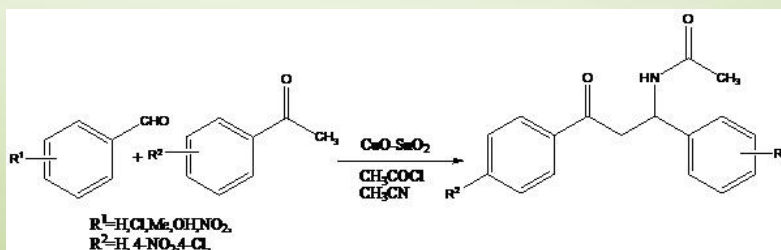
¹Department of Chemistry, G.S. College, Khamgaon, M.S., India-444303

²Department of Chemical Technology SGB Amravati University, Amravati, M.S., India-444602

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Abstract

Multicomponent reactions (MCRs) are emerged as one of the most imperative synthesis route in organic synthesis due to their wide application range in pharmaceutical chemistry. A variety of α -acetamido ketones were readily prepared in good to excellent yield (90.-95%) via four component reaction of aromatic aldehydes, enolizable ketones, acetonitrile, acetyl chloride in presence of mix metal oxide CuO-SnO₂ as versatile catalyst. The corresponding compounds were obtained in good to excellent yield, under mild conditions and ambient temperature.



Keywords: α -acetamidoketones, Multicomponent synthesis, Enolizable ketones, CuO-SnO₂

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*Corresponding author

Deepak. M. Nagrik

G.S. Science, Arts and Commerce College,
Khamgaon, Buldana, M.S., India-444303

E-mail: dmnagrik@gmail.com

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1. Introduction

Multicomponent reactions (MCRs) provide useful products in a single step without isolation of any intermediates; they are preferred over the other reactions. The MCRs constitutes to single step procedures and non isolation of intermediate moiety which leads to the synthetic route representing saving of both energy and raw materials.[1] These reaction (MCRs) have emerged as one of the most useful tool for synthetic transformation in organic synthesis due to their wide application in pharmaceutical chemistry for production of structural scaffolds and combinatorial libraries for drug discovery. One of the important reason for up growing vitality of MCRs is their key role in organic chemistry in generation of high complex structure by simple one pot process[2]. MCRs owed to the requirements of an environmentally friendly process by reducing the number of synthetic steps, energy consumption and waste production. The transformation of this useful technology into a most efficient and economic tools for combinatorial and parallel synthesis is done by many researchers^[3,4]. The multicomponent synthesis have attracted considerable interest due to its automated nature and exceptional synthetic efficiency from the point of view of synthesis of new chemicals along with the term green chemistry^[5]. Actually when we move through the period of evolution then its seems that, this concept is not unknown for us.

Adenine is a major constituent in basic unit in all living things i.e. nucleic acids viz.DNA and RNA was formed prebiotically by condensation of molecules of HCN in prebiotic atmosphere, under the influence of catalytic nature of NH_3 ^[6]. Since from this event, many MCRs have been developed over the years includes Strecker synthesis, Biginelli reaction and Mannich reaction.^[9] These MCRs are valuable because they leads to conversion of simple starting molecules to complex species in single step. This allow for quick approach to variant set of compounds^[10]. More transformations being carried out in a single step results in less waste product and purification time^[11]. More economical protocol is resulted upon optimization of these factors^[12]. Many factors are responsible for successful journey of a multicomponent reactions; that mainly includes the appropriate starting material, temperature conditions, solvents, catalytic conditions etc^[13]. Out of these, catalyst plays important role throughout the chemical transformations of initial components^[14]. The use of mix metal oxide for the synthesis of industrially important and biologically active molecules seems to be an important tool for elevating the status of synthetic organic chemistry. One of the most important chemical species in the list of novel hetero compounds is -acetamido ketones. The novelty of this compounds reflects through their biological and pharmaceutical properties^[15,16].

-acetamido ketones serves as an important starting material in the preparation of antibiotic drug such as nikkomycin or neopolyoxines^[17,18]. The ideal route for the synthesis of this class of compounds is Dakin-West reaction,^[19] in which the condensation of -amino acid with acetic anhydride in presence of base provides the -acetamido ketones via an azalactone intermediate is explained^[20]. other synthetic methods have been used for synthesis of -acetamido ketones through the multicomponent reaction of aldehyde, enolizable ketone, acetyl chloride, and acetonitrile in the presence of Cobalt Sulfate Heptahydrate Under Ultrasound Irradiation^[21], Silica Supported Tungstosilicic Acid, Zinc Hydrogen sulfate, AlCl_3 , FeCl_3 , Cellulose Sulfuric Acid, $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$, $\text{K}_5\text{CoW}_{12}\text{O}_{40} \cdot 3\text{H}_2\text{O}$, Amberlyst-15, Nafion-H[30], $\text{Mn}(\text{bpdo})_2\text{Cl}_2/\text{MCM-41}$, Heteropolyacid, PCl_3 , ZnO , I_2 and $\text{La}(\text{OTf})_3$, L-Proline as catalysts. From the review of literature it reveals that the synthetic evaluation of -acetamido ketones under green condition, especially by using different catalyst is still lacking. Recently, we have used heterogeneous basic catalyst CuO-SnO_2 [40] for the Dakin-West condensation reaction. Therefore, it was thought of interest for our research group to carry out an efficient multicomponent synthesis of -acetamido ketones by using mix metal oxide CuO-SnO_2 as versatile catalyst.

2. Experimental

2.1 General

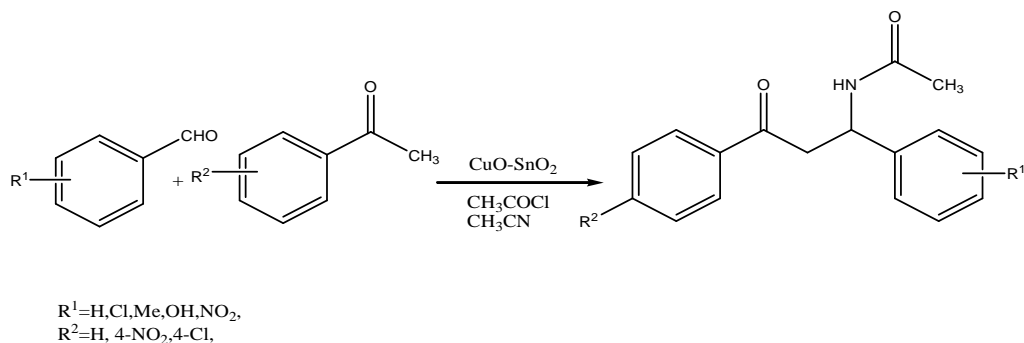
All commercially available chemicals and reagents were purchased from Aldrich and used without further purification. The melting points of all the synthesized compounds were recorded in precision digital melting point apparatus, Model MP-D and are uncorrected. The IR spectra of the synthesized compounds were recorded on Nicolet Instruments Corporation, USA make MAGNA 550 spectrometer. The PMR spectra were recorded on Varian, USA make Mercury plus-300 MHz NMR spectrometer. The GC-MS analysis of synthesized compounds was performed on Hewlett Packard make GCD-1800A EI source analyzer at Sophisticated Analytical Instrument Facility (SAIF), IIT Bombay, Powai, Mumbai, India.

2.2 General procedure for the synthesis of catalyst

$\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ (0.05 mol) and $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ (0.05 mol) were initially dissolved in 250 ml of water and then urea (0.2 mol) was added to the homogeneous mixture and transferred to an autoclave. The solution was allowed to reach to 180 °C within an hour (ramp time). The reaction was kept at this temperature for 2 hours (soak time) with an in-situ pressure of 12 atmospheres. After 2 hours, it was cooled to room temperature. The product was filtered, washed with water and acetone and dried at 110°C in a hot air oven. The initial pH of the experimental solution was acidic (pH ~ 4) and the final pH was alkaline (pH ~8). The final product was pale green in color.

2.3 Typical Experimental Procedure For The Preparation of α -acetamido ketones

In typical synthesis of α -acetamido ketones, mixture of aromatic aldehyde (10 mmol), enolizable ketone (10 mmol), acetyl chloride (10 mmol) and acetonitrile (10 mmol) was magnetically stirred (**Scheme : 1**) in presence of CuO-SnO₂ for the appropriate time at room temperature. The progress of reaction was monitored by TLC. After completion of the reaction, the reaction mixture was poured into ice water. The solid product was filtered, washed with ice water, and recrystallized from ethyl acetate to give the pure product. The reusability of the catalyst was checked by the reaction of benzaldehyde, acetophenone, acetyl chloride in the presence of acetonitrile using CuO-SnO₂ under reflux condition. The results indicate that the catalyst can be used five times without any loss of its activity. (**Table 2**)



Scheme 1: Synthesis of α -acetamido ketones

3. Results and Discussion

In order to explore our interest for the application of mix metal oxide CuO-SnO₂ in organic synthesis, we herein present a simple and efficient one-pot synthesis of α -acetamidoketones from enolizable ketones, aromatic aldehydes, acetonitrile and acetyl chloride in presence of mix metal oxide CuO-SnO₂ (**Scheme.1**). The present protocol provide a variety of α -acetamidoketones which are obtained in good to excellent yields.(90-95%). According to this procedure, the reaction proceeded smoothly at room temperature to afford the corresponding α -acetamidoketones in good yields.(**Table No.1**)

Table 1. List of α -acetamido ketones compounds synthesized by four component reaction using mix metal oxide CuO-SnO₂

S. No	Compounds	Name of compounds	Yield (%)	Time (hr)	M.P (°C)
1	a	-Acetamido- α -(phenyl) propiophenone	90	5	100-102
2	b	-Acetamido- α -(4-methylphenyl) propiophenone	92	8	110-112
3	c	-Acetamido- α -(3-nitrophenyl) propiophenone	95	8	114-116
4	d	-Acetamido- α -(4-nitrophenyl) propiophenone	90	6	145-147
5	e	-Acetamido- α -(4-chlorophenyl) propiophenone	92	8	142-144
6	f	-Acetamido- α -(phenyl) - 4-chloropropiophenone	93	10	110-112
7	g	-Acetamido- α -(4-chlorophenyl)-4-chloropropiophenone	94	10	138-140
8	h	-acetamido- α -(2-methoxy)-4-nitro propiophenone	95	8	145-146

Reaction conditions: Aromatic aldehyde=10mmol, Enolizable ketone=10mmol, Acetyl chloride =10mmol and Acetonitrile=10mmol, CuO-SnO₂ Catalyst, All compounds are well characterized by spectroscopic techniques such as IR, NMR, GC-MS.

Table 2. Reusability of the catalyst in the reaction of aromatic aldehydes, enolizable ketone, acetyl chloride and acetonitrile in presence of CuO-SnO₂ catalyst under reflux condition

Run No.	% Yield
1	90
2	89
3	88
4	87
5	87

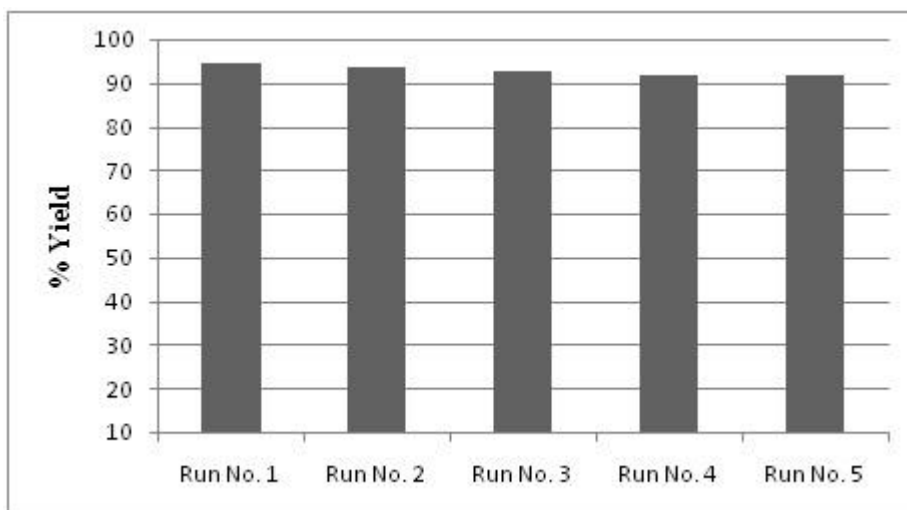


Figure 1. Graphical representation of Reusability of the catalyst in the reaction of aromatic aldehydes, enolizable ketone, acetyl chloride and acetonitrile in presence of CuO-SnO₂ catalyst under reflux condition

The representative data of compounds:

-acetamido- -(2-methoxy)-4-nitro propiophenone (Table-1, Entry h):

¹HNMR(CDCl₃, 300MHz): 2 (s, 3H), 3.55 (dd, *J*=6.9 and 17.5 Hz, 1H), 3.6 (dd, *J* = 6.5 and 17.5 Hz, 1H), 3.9(s, 3H), 5.7 (dd, *J* = 6.9 and 16 Hz, 1H), 6.7 (d, *J* = 6.9 Hz, 1H), 6.9 (m, 2H), 8.1 (m, 3H), 8.3 (m, 3H); IR (KBr, cm⁻¹)3255, 1664, 1647, 1545, 1515, 1328, 1230, 832, 748; MS(*m/z*,%) 344 (M+2+, 1.87), 342 (M+, 10.65), 299 (100), 150(85), 107 (25), 77 (17.8), 43 (27.6, CH₃-CO⁺).

4. Conclusion

In conclusion, we have reported an efficient procedure for the synthesis of -acetamido ketones using mix metal oxide CuO-SnO₂ catalyst. The major advantage of this method is that the ease of work-up. This method also offers some other merits such as clean synthesis, high yields of products, shorter reaction times and use of various substrates, which make it useful and attractive strategy for the synthesis of -acetamido ketones.

5. Acknowledgement

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