Calcium Oxide Catalyzed Synthesis of Chalcone Under Microwave Condition

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Abstract: Calcium oxide was found efficient solid base catalyst for synthesis of chalcone under microwave condition. We employed this method for synthesis of various chalcone from various substituted ketone and aldehyde including *o*-hydroxy ketone and o-amino ketone. The merits of this methods are inexpensive and easily available solid base catalyst, shorter reaction time, high yield compared to other reported methods, avoid use of toxic regents and solvent free condition, applicable to base sensitive functional group.

Keywords: Calcium oxide, Chalcone, Microwave, Ketone, Aldehyde

Introduction

More than hundred years, diverse novel methods have been developed to speed up the chemical reactions. However, these developed suffer from demerits like use of toxic reagent and solvent, unwanted side reaction, drastic reaction condition, use of lot of solvent for isolation of product by extraction and purification using column chromatography due to these reasons causes lot of environmental problems. In recent years, environmental awareness was developed in scientists, therefore the development of technology is directed towards environmentally sound and ecofriendly methods. Now a days, to overcome these problems organic chemists developed ecofriendly methods like use of microwave, ultrasound, ball mill reaction, Grinding, solvent free reaction. The use of microwave energy is one of the ecofriendly methods to accelerate the organic reactions which may attract many researchers and have numerous rewards over conventional heating. Synthesis of organic molecules using microwave oven condition has merits over conventional heating such as short reaction time, easy workup procedure, no sideproduct, solvent free condition, high yield. Hence the use of microwave condition for the synthesis of organic molecule is considered as a part of green chemistry [1, 2].

Chalcones are class of natural product which includes a class of open chain flavonoids in which two aromatic rings are linked by a three carbon α, β-unsaturated carbonyl skeleton. The chalcones are main chemical intermediates for synthesis of flavonoids like flavanone, flavones and synthesis of bioactive heterocyclic [3, 4] as well as these compounds are main synthons for the preparation of five and six member ring systems [5] and intermediate for the synthesis of many pharmaceuticals [6].

Chalcones shows various biological activities due to presence of α, β-unsaturated carbonyl skeleton. The Chalcone exhibit biological activities like antimalarials[7], anti AIDS[8], anti viral[9], anti-inflammatory[10], anticancer[11], antibacterial[12], antituberculosis[13], antioxidants[14] and antileishmanials activity[15].

Due to its biological activity and key intermediates for synthesis of bioactive molecules, chalcones attracted many researchers for their synthesis. Many methods available for the synthesis of chalcones, the extensively used method is base catalyzed Claisen-Schmidt reaction in which the condensation of aromatic ketone with an aldehyde is carried out in the presence of bases like NaOH [16], KOH[17], $Ba(OH)_2$[18], $Ca(OH)_2$ [19], LiOH[20], magnesium t-butoxide[21], potassium carbonate[22], alumina[23], MgO[24], calcinated hydrotalcites[25], KF/natural phosphate[26]. Also this reaction is carried using acids like $AlCl_3$[27], dry HCl[28], $Zn(bpy)(OAC)_2$[29], $TiCl_4$[30],$Cp_2ZrH_2/NiCl_2$ [31], and $RuCl_3$ [32]. Apart from this method chalcones are synthesised from other methods like using BF_3. OEt_2[33], Suzuki coupling[34], Juliae Kocienski olefination[35]. However these methods are suffer from drawbacks like expensive catalyst, drastic reaction condition, use of toxic and hazardous solvent, longer reaction time, low yield, not applicable to acid and base sensitive functional group, addition of reactant and catalyst in cooling condition, isolation and purification of product requires lot of solvent. Hence there is scope to develop new methods in which these demerits are removed.

Calcium oxide is a white crystalline solid with a melting point of 2572°C. It is manufactured by heating limestone, coral, sea shells, or chalk, which are mainly $CaCO_3$, to drive off CO_2. Calcium oxide has wide application in industry like in making porcelain and glass; in purifying sugar, in preparing bleaching powder, in calcium carbide and calcium cyanamide, in water softeners, and in agriculture it is used for treating acidic soils. It is also uses to control pollution from power plants and remove phosphates from sewage [36]. Calcium oxide is found in soil and it does not show any toxic effect as well as its occurrence in nature not affect on environment, stable at high temperature and water stable, no flammable, explosive or oxidizing properties therefore it is considered as a green solid base catalyst. Here, we use calcium oxide for synthesis chalcone under microwave condition.

Result and Discussion:

In previous studies, we reported a highly efficient synthesis of flavanone under microwave condition [37] and in continuation of our interest in the development of green organic transformation [38]. We report here a simple and efficient synthesis of chalcones under microwave condition with high yield and no side product. First, we studied Claisen-Schmidt condensation reaction between benzaldehyde and acetophenone in the presence of calcium oxide as solid support. Benzaldehyde and acetophenone was dissolved in ethanol was added on calcium oxide to adsorbed after evaporating ethanol and we got free flowing powder. The resulting powder was exposed to microwave irradiation at 400W at power level 2 and progress of the reaction was monitored by TLC using (2:8) ethyl acetate and pet ether for an interval of 1minute and after 4 minute we observed that reaction proceed in the forward direction and formation of a new product. To indentify the structure of new product, after completion of reaction we workup the reaction mixture by adding 20mL ice cold water and neutralization with Conc. HCl, solid was precipitated. Solid was filtered on suction pump and wash with 20mL water, afforded crude product. The crude product purified by recrystallization from ethanol afforded pure product. The structure of the pure product was confirmed by spectroscopic method and spectral data match with chalcone. Next we decided to optimize reaction condition; we vary the amount of calcium oxide 10, 20, 40 mol% , 1:1 and 1:2 catalyst. It was found that 1:1 catalyst showed a maximum yield in short time interval. There was no reaction when condensation was carried out without calcium oxide which indicates that catalyst is necessary for the condensation reaction even under microwave conditions.

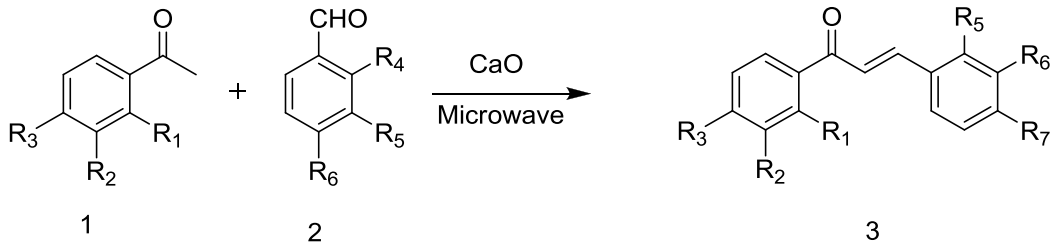
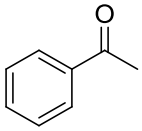
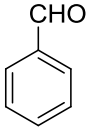
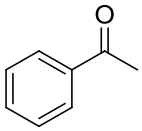
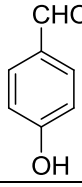
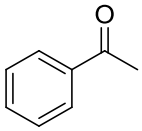
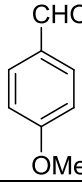
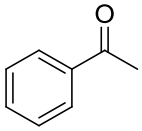
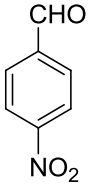
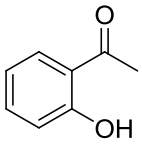
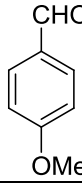
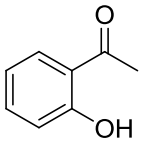
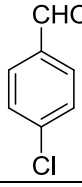
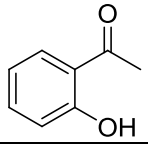
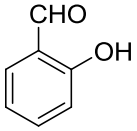
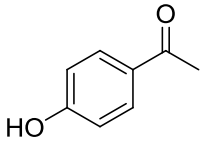
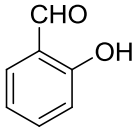
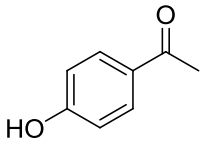
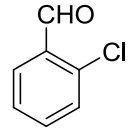


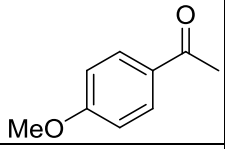
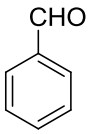
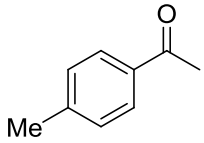
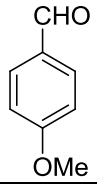
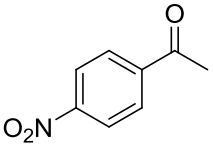
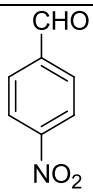
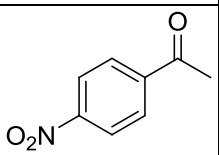
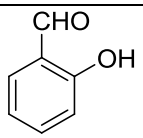
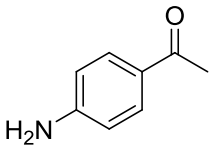
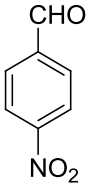
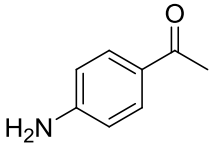
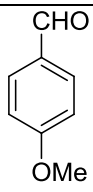
Figure 1 Synthesis of Chalcone under microwave condition using Calcium oxide as a catalyst

Next we explored the scope of reaction using different substituted benzaldehyde and substituted acetophenone with electron donating as well as withdrawing groups. The results are presented in Table 1. From table 1, it is clear that Claisen-Schmidt condensation reaction proceeds smoothly to furnish chalcone in good yield. As usual electron withdrawing groups

present on aldehyde and ketone proceeds very smoothly to afford chalcone in good yield; while substituent present on ortho-position gave a moderate yield due to steric effect.

Table 1: Synthesis of Substituted Chalcone under Microwave condition Using Calcium oxide as a catalyst[a]

Entry	Ketone(**1**)	Aldehyde(**2**)	Chalcone(**3**)	Time minutes	% Yield[b]
1			**3a**	5	88
2			**3b**	18	76
3			**3c**	24	79
4			**3d**	13	83
5			**3e**	32	78
6			**3f**	21	84
7			**3g**	41	73
8			**3h**	34	77
9			**3i**	38	68

10			**3j**	16	81
11			**3k**	13	83
12			**3l**	17	75
13			**3m**	24	64
14			**3n**	32	72
15			**3o**	45	57

a: Reaction condition: Substituted acetophenone(5mMol), Substituted benzaldehyde(5mmol) adsorbed on Calcium Oxide(5mMol) irradiated in Microwave for respective time b: isolated yield after purification

Conclusion:

Here, in this study we report facile, solvent free ecofriendly synthesis of chalcone under microwave condition. The merits of this method is avoid use of solvent, inexpensive and easily available catalyst, method is applicable to base sensitive functional group, easy work up and purification procedure, high yield short reaction time.

Experimental:

All reagents, chemicals and solvents were purchased from Loba, Merck, SRL and Sigma Aldrich. Microwave reactions were carried out using household microwave oven. TLC (pre-coated silica gel 60 F254) was used to monitor the progress of the reaction. Melting points were recorded by open capillary method and are uncorrected. IR spectra were recorded as KBr pellets using shizmude FTIR. The ^{1}H NMR spectra were obtained on a Bruker DRX-

300 Avance instrument using CDCl3 as solvent and TMS as internal standard at 300MHZ. All products are known compounds and their authenticity was ensured on the basis of spectroscopic data and on comparison with authentic samples.

General Procedure for Synthesis of Chalcone: Substituted acetophenone (5mmol) and Substituted benzaldehyde was dissolved in 5mL ethanol. This solution was poured on calcium oxide and well swirled. The solvent was removed under reduced pressure using a rotator evaporator. Resulting free flowing powder was taken in a 25mL beaker and irradiated in microwave oven at 400W for 15 minutes. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled, added to 20mL ice cold water and acidified with Conc. HCl, solid was precipitated, filter on suction pump, wash water and dried it. A pure sample was obtained by recrystallization from ethanol.

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