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# Solvent-free NaOH-$Al_2O_3$ supported synthesis of 1,3-diaryl-2-propene-1-ones

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**Abstract :** A novel method for the synthesis of 1,3-diaryl-2-propene-1-ones via Claisen-Schmidt is introduced using NaOH-$Al_2O_3$ under solvent free conditions. The protocol offers several advantages such as simple procedure, fast reaction rate, mild reaction conditions and excellent yields.

**Keywords:** Aromatic aldehyde, Acetophenone and 1,3-diaryl-2-propene-1-ones.

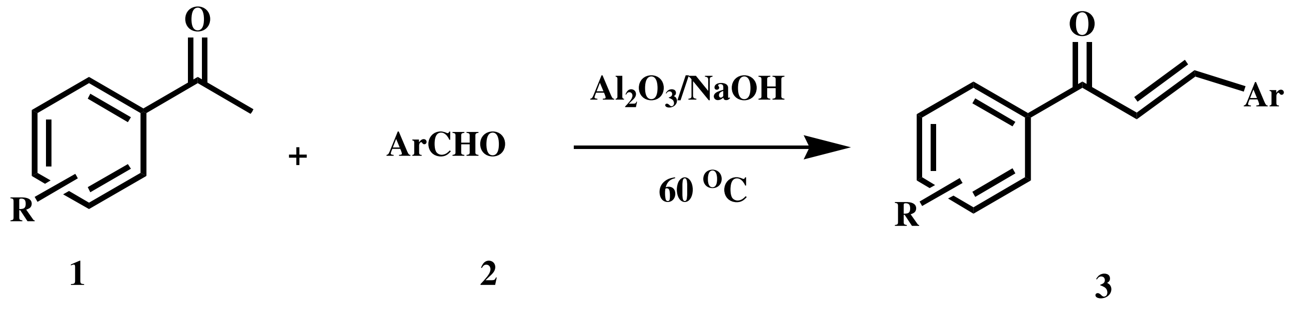
## Introduction

Chalcones (1,3-diaryl-2-propene-1-ones) are natural substances found in a number of plants or synthetically prepared. They display many biological activities[1] *viz.*, antiviral, anti-inflammatory, antimicrobial, antimitotic, antitumor, cytotoxicity, analgesic, and antipyretic properties. They also act as potential anti-ulcer, antifungal, anti-cancer[2] and antimalerial agents[3]. In addition these compounds are of a high interest due to their use as starting materials in the synthesis of a series of heterocyclic compounds[4] like, isoxazoles, quinolinones, thiadiazines, benzofuranones, benzodiazepine, tetrahydro-2-chromens[5], flavones etc. Moreover, these are important intermediates in many addition reactions of nucleophiles due to inductive polarization of carbonyl group at the β-position. These findings explain the significant interest of scientist in this particular group of compounds.

Several strategies for the synthesis of these systems based on the formation of carbon-carbon bond have been reported. Among them the direct aldol condensation and Claisen-Schimdt condensation still occupy prominent positions. The main method for the synthesis of chalcones is the classical Claisen-Schmidt condensation in the presence of aqueous alkaline bases[6], $Ba(OH)_2$[7], LiOH, microwave irradiation, ultrasound irradiation[8]. They are also obtained via the Suzuki reaction[9], Wittig reaction, by the Friedel-Crafts acylation with cinnamoyl chloride, or Photo-Fries rearrangement of phenyl cinnamates. In aldol condensation the preparation of chalcones requires at least two-steps aldol formation and dehydration. Since aldol addition is reversible, Mukaiyama or Claisen-Schimdt condensation approach of using enol ether has emerged as an alternative pathway. The aldol reaction is also performed under acidic medium[10], using HCl, $BF_3$, $B_2O_3$, p-toluenesulfonic acid, etc. Recently various modified methods for the synthesis of chalcones has been reported, such as using $SOCl_2$[11], natural phosphate, lithium nitrate[12], amino grafted zeolites[13], zinc oxide, water[14], $Na_2CO_3$ [15],PEG-400 [16], silica-sulfuric acid[17], $ZrCl_4$ and ionic liquid[18] etc. Jhala et al. synthesize chalcone using basic alumina under microwave irradiation[19].

However, many of these methods suffered from harsh reaction condition, toxic reagents, strong acidic or basic conditions, prolonged reaction times, poor yields and low selectivity. Although, several modifications had been made to counter these problems. There is still a need for the development of selective and better strategies for the synthesis of α-β-unsaturated carbonyl compounds.

Herein for the first time we describe a simple and convenient method for the synthesis of chalcones using NaOH-$Al_2O_3$ under solvent free condition, in excellent yields with short reaction time.



**Scheme-1**

## Experimental Section

### Materials and methods

Melting points were measured in open glass capillaries on a Perfit Electrothermal melting-point apparatus and are uncorrected. $^1$H NMR spectra were recorded at room temperature on a 300 MHz. Varian Inova Spectrometer in $CDCl_3$ using TMS as internal standard. A Samsung domestic microwave oven was used at 400W power level for all the experiments. The reactions were monitored by TLC using pre-coated plates (Merck). Column chromatography was performed using Acme silica gel (100–200 mesh). All reagents were obtained from commercial sources and used without further purification. Solvents for chromatography were distilled before use. The products were also characterized by comparison of their melting point with literature values.

### General experimental procedure

A mixture of 4-hydroxy acetophenone **1a** (0.136 g, 1 mmol,), benzaldehyde **2a** (0.106 g, 1 mmol,), and sodium hydroxide (0.08 g, 2 mmol) were dissolve in dichloromethane (2 mL). The solution is adsorbed on neutral alumina (1.5 g) and air-dried. The mixture stirred at 60 $^{O}$C temperatures for appropriate time under solvent free condition. The progress of the reaction was monitored by TLC. After completion of reaction excess ethanol was added and filtered to remove insoluble inorganic material. The filtrate was poured on crushed ice and neutralized with dilute HCl. Solid products were separated by filtration and chromatographied for further purification.

The products were identified by comparison with physical and spectral data given in the literature.

### Results and Discussion

Environmental pressure to reduce waste has driven studies into ‘‘Green’’ chemistry. One of the biggest industrial concerns is replacement of volatile organic solvents. Recently solvent free chemical reactions in combination of solid supported reagents, such as $Al_2O_3$ was used to carry out a wide range of reaction in shorter times as compare to other conventional reaction methods[20]. In a model reaction, different aromatic aldehyde, acetophenone and sodium hydroxide were adsorbed on neutral alumina, and mixture stirred at 60 $^{O}$C temperatures for 1 to 2 hr. The progress of the reaction was monitored by TLC. After completion of reaction, the usual work-up afforded pure chalcones in an excellent yield (85-95%). The reaction proceeds cleanly at 60 $^{O}$C temperatures, however at room temperature using solvent it required longer reaction time (Table-2). The reaction proceeds very cleanly and no undesirable side products were observed. To evaluate the synthetic utility of the process, several substituted chalcones were also have been prepared by the established procedure[6]. IR spectra of chalcones showed characteristic band at near region 1625 cm$^{-1}$ due to >C=O stretching vibrations. All the chalcones showed absorption in the region 1575-1610 cm$^{-1}$ due to (-CH=CH-) ethylenic double bond. $^1$H NMR spectra showed characteristic doublet signal near $\delta$6.85 and $\delta$7.95 due to olefinic $\alpha,\beta$-protons. These findings are in agreement with confirmation of product.

The protocol offers several advantages such as simple procedure, solvent free, mild reaction conditions and excellent yields.

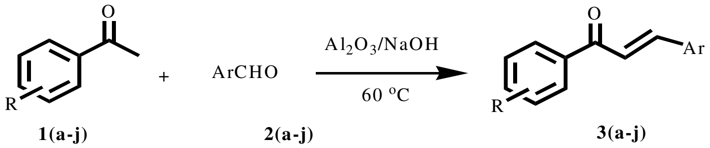
### Conclusion

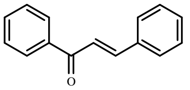
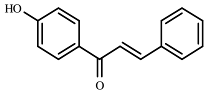
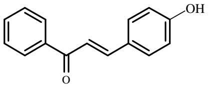
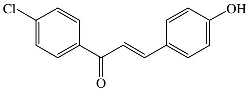
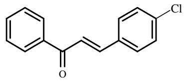
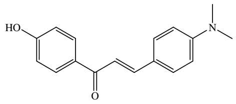
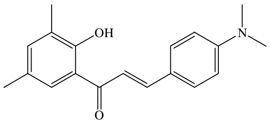
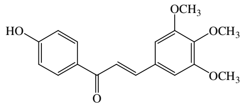
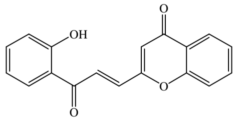
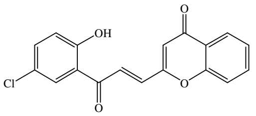
In summary, we have developed an efficient and mild protocol for the synthesis of chalcones via Claisen-Schmidt condensation using NaOH-$Al_2O_3$ under solvent free condition. The procedure is simple and ecofriendly can be used as an alternative to the existing procedure.

### Acknowledgement

The authors are thankful to the **Principal Dr. P. L. More,** Dnyanopasak College, Parbhani, and **Principal Dr. R. S. Agrawal,** J. E. S. College, Jalna, for encouragement during the process of carrying out this work.

**Table-1: Synthesis of chalcones using NaOH-$Al_2O_3$ under solvent free condition:**



| Entry | Chalcones (3a-i) | ReactionTime (min.) | M. P.$^{O}$C (Litt. M.P.)$^{A}$ | Yield$^{a}$ (%)$^{B}$ |
|---|---|---|---|---|
| **a** |  | 60 | 58-60<br>(54-56)[11] | 85 |
| **b** |  | 70 | 174-175<br>(172-174)[11] | 92 |
| **c** |  | 75 | 185-187<br>(180-181)[11] | 80 |
| **d** |  | 90 | 178-179<br>(173-174)[11] | 85 |
| **e** |  | 65 | 108-110<br>(113-114)[18] | 90 |
| **f** |  | 70 | 122-124<br>(120-122)[6] | 92 |
| **g** |  | 80 | 138-140* | 85 |
| **h** |  | 80 | 163-164* | 88 |
| **i** |  | 90 | 148-150* | 90 |
| **j** |  | 90 | 67-70* | 80 |

$^{A}$ Literature melting point $^{B}$Isolated and unoptimized yield. * New compound

**Table 2: Synthesis of 1-(4-hydroxyphenyl)-3-phenylprop-2-en-1-one under different reaction condition:**

| Entry | Catalyst | Solvent | Reaction cond | Reaction Time | Yield $^{b}$ (%) |
|---|---|---|---|---|---|
| **1** | NaOH | $C_2H_5OH$ | RT | 24 hr. | 70 |
| **2** | $Ba(OH)_2$ | DMSO | Reflux | 8 hr. | 68 |
| **3** | NaOH | Solvent free | MW | 6 min. | 70 |
| **4** | NaOH-$Al_2O_3$ | Solvent free | MW | 4 min. | 75 |
| **5** | NaOH | Solvent free | 60 $^{O}$C | 4 hr. | 75 |
| **6** | **NaOH-$Al_2O_3$** | **Solvent free** | **60 $^{O}$C** | **70 min.** | **92** |

$^{b}$Isolated and unoptimized yield.

## Spectral data of selected compounds:

3a) 1,3-Diphenyl prop-2-en-1-one:

$^1$HNMR (300 MHz, $CDCl_{3,}$ δppm): δ7.82(1H,d, β-H), 7.06 (1H,d, α-H), 8.02(dd, 2H), 7.45-7.72(m, 8H, Ar-H).

3b) 1-(4-hydroxyphenyl)-3-phenylprop-2-en-1-one:

$^1$HNMR (300 MHz, $CDCl_{3,}$ δppm): δ7.88( 1H,d, β-H), 6.86 (1H,d, α-H),6.95-7.72(9H,m, Ar-H), 10.75(1H,s, Ar-OH).

3d) 3-(4-chlorophenyl)-1-(4-hydroxyphenyl) prop-2-en-1-one:

$^1$H NMR (300 MHz,$CDCl_{3,}$ δppm): 7.88(1H,d, β-H), 6.86 (1H,d, α-H), 7.28-7.64(8H,m, Ar-H), 10.05 (1H,s, Ar-OH).

3e) 3-(4-chlorophenyl)-1-phenylprop-2-en-1-one:

$^1$H NMR (300 MHz, $CDCl_{3,}$ δppm): 7.80(1H,d, β-H), 7.236 (1H,d, α-H), 7.05-7.78 (9H,m, Ar-H), 10.05 (1H,s, Ar-OH).

3f) 3-(4-(dimethylamino)phenyl)-1-(4-hydroxyphenyl)prop-2-en-1-one

$^1$H NMR (300 MHz, $CDCl_{3,}$ δppm): 7.90 (1H,d, β-H), 6.85(1H,d, α-H), 9.25(1H,s, Ar-OH), 3.05(6H,s, $-N(CH_3)_2$), 7.05-7.80(8H,m, Ar-H).

3g) 3-(4-(dimethylamino)phenyl)-1-(2-hydroxy-3,5-dimethylphenyl)prop-2-en-1-one:

$^1$H NMR (300 MHz, $CDCl_{3,}$ δppm): 7.85(1H,d, β-H), 7.05(1H,d, α-H), 13.03(1H,s,Ar-OH), 3.08(6H,s, $-N(CH_3)_2$), 2.35 (6H, s,$Ar-CH_3$), 6.85-7.80(6H,m, Ar-H).

3h) 1-(4-hydroxyphenyl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one

$^1$H NMR (300 MHz, $CDCl_{3,}$ δppm): 8.20(2H,d, Ar-H), 7.40(2H,d,Ar-H),7.05(2H,s, Ar-H), 6.92(1H,d, β-H), 6.75 (1H,d, α-H), 3.80-3.90(9H,s, 3x $OCH_3$), 11.05(1H,s, Ar-OH).

3i) 3-(2-hydroxyphenyl)-3-oxoprop-1-enyl)-4H-chromen-4-one:

$^1$H NMR (300 MHz, $CDCl_{3,}$ δppm): 7.65(1H,d, β-H), 7.15(1H,d, α-H), 12.45(1H,s,Ar-OH), 8.65(s,1H,), 7.10-8.05(8H,m, Ar-H).

3j) 3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-4H-chromen-4-one:

$^1$H NMR ($CDCl_{3,}$ δppm): 7.85(1H,d,β-H), 7.15(1H,d,α-H), 12.75(1H, Ar-OH), 8.55(s,1H), 6.85-7.95(7H,m, Ar-H).

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