

**SYNTHESIS AND CHARACTERIZATION OF 2,5-DIHYDROXY SUBSTITUTED CHALCONES USING SOCl<sub>2</sub>/EtOH****M.R.JAYAPAL<sup>\*1</sup>, K.SREENIVASA PRASAD<sup>2</sup> AND N.Y.SREEDHAR<sup>1</sup>**

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**ABSTRACT**

A novel method for the synthesis of 2,5-dihydroxy substituted chalcones via Aldol condensation is introduced. The HCl is generated in situ by the reaction of SOCl<sub>2</sub> with absolute ethanol. In the presence of SOCl<sub>2</sub> / EtOH as a catalyst, The structures of the synthesized compounds were confirmed by IR, mass spectroscopy and elemental analysis.

**KEYWORDS**

Chalcone, Aldol condensation, IR, Mass and Elemental spectral analysis.

**INTRODUCTION**

The Chemistry of chalcones has generated intensive scientific studies throughout the world. Especially interest has been focused on the synthesis and biodynamic activities of chalcones. The name "Chalcones" was given by Kostanecki and Tambor<sup>1</sup>. The most convenient methods are the Claisen-Schmidt condensation of equimolar quantities of an arylmethylketone with an aryl aldehyde in the presence of alcoholic alkali<sup>2</sup>. Chalcones are used to synthesize several derivatives like cyanopyridines, pyrazolines, isoxazoles, pyrimidines, having different heterocyclic ring systems<sup>3-6</sup>.

Chalcones or benzylideneacetophenone are the important constituents of natural sources. It was first isolated from Chinese liquorice (*Glycyrrhiza inflata*) Yerra et al., (2004). It has a 1,3-diaryl-1-one skeletal system, which was recognized as the main pharmacophore for chalcones. From plants, a stable chalcone moiety can't be isolated because of the presence of an enzyme chalcone

synthetase (CSH) which immediately converts chalcones into flavonone.

Chalcones and its derivatives are an important group of natural products and have been reported to possess varied biological and pharmacological activity. Yuh-Hee et al. (2002) synthesized different series of chalcone derivatives, which are having 90% inhibitory activity against *Mycobacterium tuberculosis*.

Several strategies for the synthesis of these systems, based on the formation of carbon-carbon bonds, have been reported. Among them the direct Aldol condensation and Claisen-Schmidt 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,<sup>7</sup> Ba(OH)<sub>2</sub><sup>8</sup> LiOH, microwave irradiation and ultrasound irradiation.<sup>9</sup> They are also obtained via Suzuki reaction,<sup>10</sup> Wittig reaction, 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-Schmidt condensation approach of using enol ether has emerged as an alternative pathway.

The aldol reaction is also performed under acidic medium,<sup>11</sup> using HCl, BF<sub>3</sub>, B<sub>2</sub>O<sub>3</sub>, p-toluenesulfonic acid etc. Recently various modified methods for the synthesis of chalcones has been reported, such as by using SOCl<sub>2</sub>,<sup>12</sup> natural phosphate, lithium nitrate,<sup>13</sup> amino grafted zeolites,<sup>14</sup> zinc oxide, water,<sup>15</sup> Na<sub>2</sub>CO<sub>3</sub>,<sup>16</sup> PEG<sub>400</sub>,<sup>17</sup> silicasulfuric acid,<sup>18-19</sup> ZrCl<sub>4</sub> and ionic liquid<sup>20</sup> etc. Jhala et al. synthesized chalcone using basic alumina under micro wave irradiation. 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 have been made to counter these problems. There is still a need for the development of selective and better strategies for the synthesis of  $\alpha$ ,  $\beta$ -unsaturated carbonyl compounds.

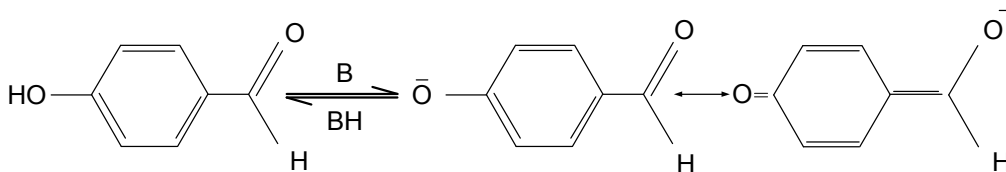
However, many of these methods suffered from harsh reaction condition, toxic reagents, strong acidic or basic conditions, prolonged reaction times, poor yields and low selectivity. Although, several modifications had been made to counter these problems. There is still a need for the development of selective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

According to the literature data the presence of hydroxy substituents in the aromatic aldehyde hinders the basis catalyze aldol reaction. The reason behind that is the

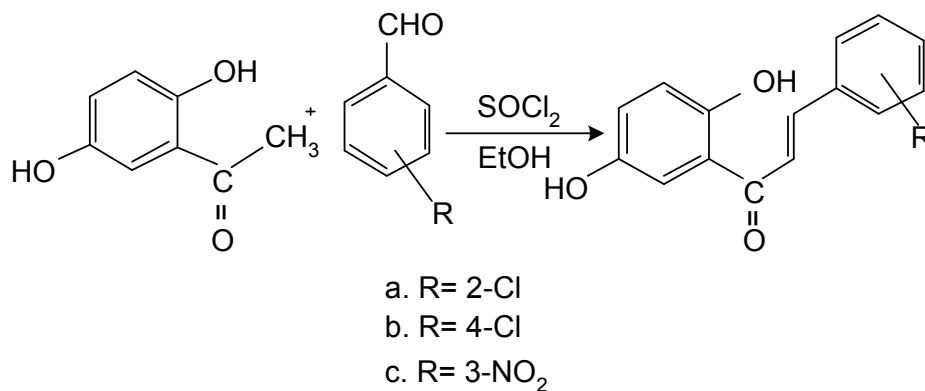
fact that the basis catalysts decrease the activity of the aldehyde component because of delocalization of the anion, which is illustrated below in Scheme 1. It is necessary to use protective group for the preparation of the hydroxy chalcones under basis conditions<sup>21</sup>. By using SOCl<sub>2</sub> as a convenient alternative to the gaseous HCl in the aldol condensation.

## MATERIALS AND METHODS

All the products were synthesized and characterized by their spectral analysis. Chemicals, 2,5-hydroxy acetophenone, 2-chlorobenzaldehydes, 4-chloro benzaldehydes, 3-nitrobenzaldehydes were purchased from S.D. fine Chemicals (India). Melting points were determined in an open capillary tube and or uncorrected. IR spectra were recorded in KBr on a JASCO FT/IR-5300 The mass spectra were recorded on LCMS – 2010 A DATA REPORT SHIMADZU Elemental analysis was carried out on a Flash EA 1112 SERIES CHN REPORT THERMO FINNIGAN. Chalcones were synthesized by aldol condensation<sup>23</sup> using SOCl<sub>2</sub>/ EtOH. The chemicals and solvents used were of laboratory grade and were purified completion of the reaction was monitored by thin layer chromatography on precoated sheets of silica gel-G (Merck, Germany) using iodine vapour for detection. The synthetic pathway is presented in Scheme 2 and physicochemical data and spectral data for the synthesized compounds are given Table(1-3).



**Scheme 1**  
**Anion delocalization of the aldehydic component**



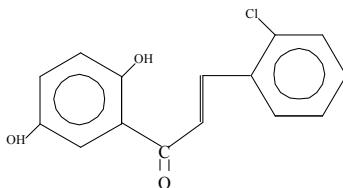
### Scheme 2

#### Synthetic diagram of 2,5 dihydroxy substituted chalcones

##### 1) Synthesis of 3-(2-chlorophenyl) -1- (2,5-dihydroxyphenyl) prop-2-en-1-one

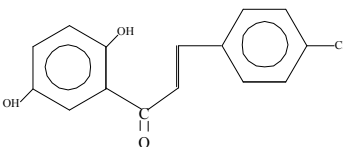
To a stirred mixed of 2,5-hydroxy acetophenone (0.01 mol) and 2-chloro benzaldehyde (0.01 mol) in absolute ethanol (5 ml) and thionyl chloride (0.05ml) dropwise and continue stirring for two hour at room

temperature. Allow to stand reaction mixture for 12 Hr. Precipitate the reaction mixture by addition of water. Filter the product, wash with cold ethanol and allowed to afford.



##### 2) Synthesis of 3-(4-chlorophenyl) -1-(2,5-dihydroxyphenyl) prop -2-en-1-one

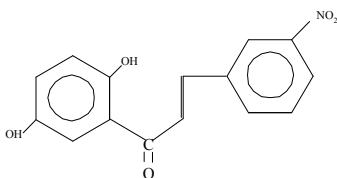
Reaction with 2,5-dihydroxy acetophenone (1.2 gms) and (4-chlorobenzal dehyde (1.1 gms), 3-(4-chlorophenyl) -1 (2,5- dihydroxyphenyl) prop -2-en-1-one obtained by the above procedure.



##### 3) Synthesis of 1-(2,5-dihydroxyphenyl)-3-(3-nitrophenyl)prop-2-en-1-one

1-(2,5-dihydroxyphenyl)-3-(3-nitrophenyl) prop-2-en-1-one was obtained by the above procedure expect that the starting material

used was 2,5-dihydroxy acetophenone (2 gms) in ethanol add thionylchloride (0.05) and 3-nitrobenzaldehyde (1.3 gm)



## RESULTS AND DISCUSSIONS

This paper reports a simple and effective method for the synthesis of chalcones by an acid catalyzed aldol reaction we used  $\text{SOCl}_2$  as a convenient alternative to the gaseous HCl in the aldol condensation. The HCl is generated in situ by the reaction of  $\text{SOCl}_2$  with absolute ethanol. Chalcones are obtained in good to good to excellent yields. Our purpose was to synthesize a series of chalcones, starting from benzaldehyde and acetophenone or their substituted derivatives using  $\text{SOCl}_2$ / EtOH as a catalyst. Synthesis of chalcone is a single step method. The synthesized chalcone derivatives were undergone physicochemical characterization and spectro chemical data the obtained results are given in Table.1-3.

The yields of the synthesized compounds were found to be significant. The structure of the synthesized compounds was confirmed by IR, Mass and elemental analysis. Elemental analysis showed that the percentage of the nitrogen, hydrogen and carbon was found experimentally is equivalent to the calculated values in all compounds. All the compounds give the characteristic IR peak that proved that the presence of particular functional group (Table 2) and mass spectroscopy helps to find the molecular weight of the synthesized compounds (Table 2). The Chalcone derivatives showed that the molecular ion peak that equivalent to the molecular weight of proposed compound. Hence m/z value confirms the molecular weight of the respective synthesized compound.

**Table1**  
*Physicochemical characterization data for synthesized compounds*

Compound number	Molecular formula	Molecular Weight	Yield (%)	MP (°C)	Elemental analysis		
					C	H	N
1	$\text{C}_{15} \text{H}_{11} \text{ClO}_3$	274	85	180	65.48 (65.75)	3.96 (4.04)	-
2	$\text{C}_{15} \text{H}_{11} \text{ClO}_3$	274	89	182	65.71 (65.75)	4.10 (4.04)	-
3	$\text{C}_{15} \text{H}_{11} \text{NO}_5$	285	81	190	63.18 (63.21)	3.89 (3.89)	4.98 (4.91)

**Table.2**  
*IR spectral data of synthesized compounds*

Compound number	Compound	IR. Spectral data
1	3-(2-chloro phenyl) -1- (2,5-dihydroxy phenyl) prop-2-en-1-one	IR (KBr) $\nu \text{ cm}^{-1}$ , (-OH) $3310 \text{ cm}^{-1}$ , (C=O) $1591 \text{ cm}^{-1}$ , (C=C) $1481 \text{ cm}^{-1}$
2	3-(4-chloro phenyl) -1-(2,5- dihydroxyphenyl) prop -2-en-1-one	IR (KBr) $\nu \text{ cm}^{-1}$ , (-OH) $2982 \text{ cm}^{-1}$ , (C=O) $1682 \text{ cm}^{-1}$ , (C=C) $1626 \text{ cm}^{-1}$
3	1-(2,5-dihydroxyphenyl)-3- (3 nitro phenyl) prop-2-en-1-one	IR (KBr) $\nu \text{ cm}^{-1}$ , (-OH) $2986 \text{ cm}^{-1}$ , (C=O) $1692 \text{ cm}^{-1}$ , (C=C) $1632 \text{ cm}^{-1}$

**Table.3**  
*Mass spectral data of synthesized compounds*

Compound number	Compound	Molecular weight	Mass spectral data
1	3-(2-chloro phenyl) -1(2,5-dihydroxy phenyl) prop-2-en-1-one	274	$274 \text{ M}^{+2}$
2	3-(4-chloro phenyl) -1 (2,5- dihydroxy phenyl) prop -2-en-1-one	274	$274 \text{ M}^{+2}$
3	1-(2,5-dihydroxyphenyl) -3 – (3 nitro phenyl) prop-2-en-1-one	285	$285 \text{ M}^+$

→ 3-(2-chlorophenyl)-1-(2,5-dihydroxyphenyl)prop-2-en-1-one have molecular formula  $C_{15}H_{11}ClO_3$ . The molecular ion peak at 274 ( $M^{+2}$ ) showed that m/z is equivalent to molecular weight of proposed compound. Hence m/z value confirms the molecular weight of the compound. The IR band at  $1591\text{cm}^{-1}$  suggesting the presence of (C=O) group. The IR band at  $1481\text{cm}^{-1}$  indicates that the presence of (C=C) group. IR band at  $3310\text{cm}^{-1}$  indicates presence of (-OH) group. Melting point of the compound is  $180^\circ\text{C}$  which is uncorrected.

→ The molecular formula of 3-(4-chloro phenyl) - 1(2,5- dihydroxyphenyl) prop -2-en-1-one is  $C_{15}H_{11}ClO_3$ . The obtained molecular ion peak at 274 ( $M^{+2}$ ) showed that m/z is equivalent to molecular weight of proposed compound. Hence m/z value confirms the molecular weight of the compound. The IR band at  $1682\text{cm}^{-1}$  suggesting the presence of (C=O) group. The IR band at  $1626\text{cm}^{-1}$  indicates that the presence of (C=C) group. IR band at  $2982\text{cm}^{-1}$  indicates presence of (-OH) group. Melting point of the compound is  $182^\circ\text{C}$  which is uncorrected.

→ The obtained ion peak of 1-(2, 5-hydroxyphenyl)-3-(3 nitrophenyl) prop-2-en-1-one (molecular formula,  $C_{15}H_{11}NO_5$ ) at 285 ( $M^+$ ) showed that m/z is equivalent to molecular weight of proposed compound. Hence m/z value confirms the molecular weight

of compound. The IR band at  $1692\text{cm}^{-1}$  suggesting the presence of (C=O) group. The IR band at  $1632\text{cm}^{-1}$  indicates that the presence of (C=C) group. IR band at  $2986\text{cm}^{-1}$  indicates presence of (-OH) group. Melting point of the compound is  $190^\circ\text{C}$  which is uncorrected.

## CONCLUSIONS

In conclusion we found that 2,5 dihydroxy chalcones can be synthesized using the catalytic system  $\text{SOCl}_2 / \text{EtOH}$ . The synthesized compounds were characterized by TLC, melting point, IR spectroscopy, elemental analysis and mass spectroscopy. The results obtained from this study confirmed that the product has formed. Henceforth viewing these characteristic properties more compounds can be synthesized and subjected to pharmacological evaluation.

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