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Synthesis and characterization of 2,4-dihydroxy substituted chalcones using aldol condensation by $SOCl_2$/ EtOH

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ABSTRACT

A novel method for the synthesis of 2,4-dihydroxy substituted chalcones via aldol condensessions is introduced. In the presence of $SOCl_2$/EtOH as a catalyst, Various substituted chalcones are synthesized by aldol condensation. The HCl is generated in situ by the reaction of $SOCl_2$ with absolute ethanol. The structures of the synthesized compounds were confirmed by IR, mass spectroscopy and elemental analysis.

Key words: Chalcone, aldol condensation, IR, Mass and Elemental spectral analysis.

INTRODUCTION

Chalcones are well known intermediates for synthesizing various heterocyclic compounds. The compounds with the backbone of chalcones have been reported to possess various antimicrobial[1], anti-inflammatory[2], analgesic[3], antiplatelet[4], antiulcerative[5], antimalarial[6], anticancer[7], antiviral[8], antileishmanial[9], antioxidant[10], antitubercular[11], antihyperglycemic[12], immunomodulatory[13], inhibition of chemcical mediators release[14], inhibition of leukotriene B_4[15], inhibition of tyrosinase[16] and inhibition of aldose reductase[17] activities. The presence of a reactive α,β - unsaturated ketone function in chalcones is found to be responsible for their antimicrobial activity.

Several strategies for the synthesis of these system, based on the formation of carbon-carbon bond 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[18],

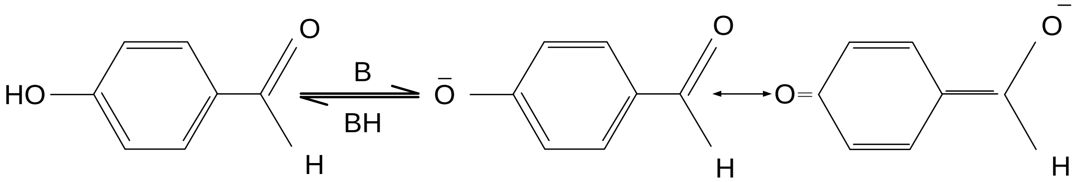
$Ba(OH)_2$[19] LiOH, microwave irradiation and ultrasound irradiation[20]. They are also obtained via Suzuki reaction[21], Witting reaction, Friedel-Crafts acylation with cinnamoyl chloride, or Photo-Fries rearrangement of phenyl cinnamates. In aldol condensation the preparation of chalcones requires 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[21], 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 by using $SOCl_2$[22], natural phosphate, lithium nitrate[23], amino grafted zeolites[24], zinc oxide, water[25], Na_2CO_3[26], PEG_{400},[27] silicasulfuric acid[28-29], $ZrCl_4$ and ionic liquid[30] 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 α, β-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 α,β-unsaturated carbonyl compounds.

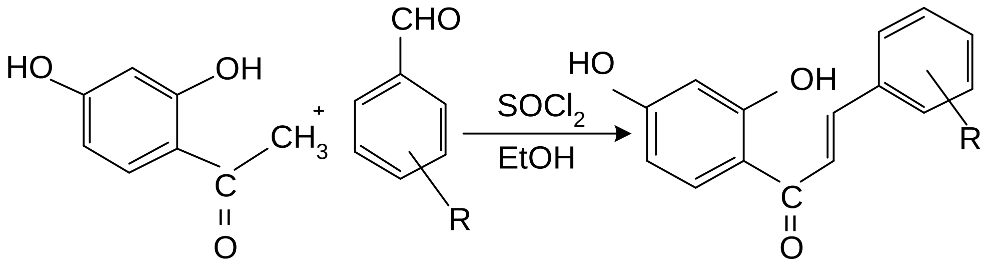
According to the literature data the presence of hydroxy substituents in the aromatic aldehyde hinders the basis catalyze aldol reaction. The reason behind that is the fact that the basis catalysts decrease the activity of the aldyhyde component because of delocalization of the anion, which is illustrated below in Scheme 1. It is necessary to use protective group for the preparation of the hydroxy chalcones under basis conditions[31]. By using $SOCl_2$ as a convenient alternative to the gaseous HCl in the aldol condensation.

EXPERIMENTAL SECTION

All the products were synthesized and characterized by their spectral analysis chemicals, 2 4-dihydroxy acetophenon, 2-chloro benzaldehydes, 4-chloro benzaldehydrs, 3-nitro benzaldehydes were purchased from S.D. fine Chemicals (India). Melting points were uncorrected and determined in an open capillary tube. IR spectra were recorded in KBr on al JASCO FT /IR-5300. The mass spectra were recorded on LCMS-2010 DATA REPORT SHIMADZU. Elemental analysis was carried out on a FLASH EA 1112 SERIES CHN REPORT THERMO FINNIGAN. Chalcones were synthesized by aldol condensation using $SOCl_2$/ 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 spectroscopic data for the synthesized compounds are given Table (1-3).



Scheme 1: Anion delocalization of the aldehydic component

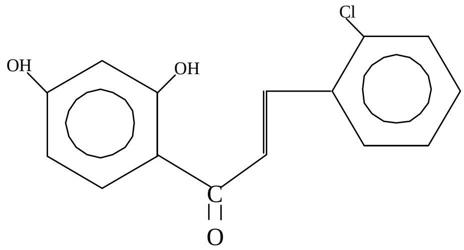


a. R= 2-Cl
b. R= 4-OH
c. R= 3-OH
d. R= 4 NO_2

Scheme 2: Synthetic diagram of 2,4 dihydroxy substituted chalcones

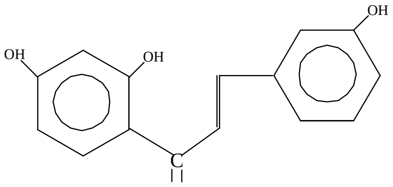
1) Synthesis of 3-(2-chlorophenyl)-1-(2,4-dihydroxyphenyl) prop-2-en-1-one

To a stirred mixed of 2,4-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.



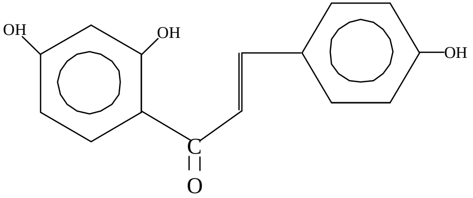
2) Synthesis of 1-(2,4-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one

Reaction with 2,4-dihydroxy acetophenone (1.2gm) and 4-hydroxy benzal- dehyde (1.1 gm), (2,4-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one was obtained by the above procedure.



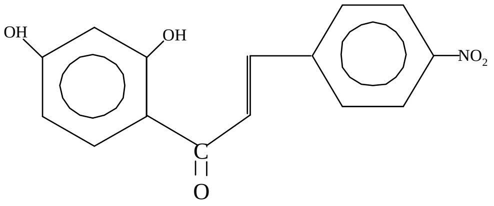
3) Synthesis of 1-(2, 4-dihydroxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one

A mixture of 2,4-dihydroxy acetophenone (1.1 gm) in ethanol (5ml) add thionyl chloride (0.05 ml) and 3-hydroxy benzaldehyde (1.1 gm); 1-(2-4-dihydroxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one was obtained by the above procedure.



4) Synthesis of 1-(2,4-dihydroxyphenyl)-3-(4-nitrophenyl)prop-2en-1-one

1-(2,4-dihydroxyphenyl)-3-(4-nitrophenyl)prop-2en-1-one was obtained by the above procedure except that starting material used was 2,4-dihydroxy acetophenone (1.4gm) in ethanol add thionyl chloride and 4 nitrobenzaldehyde. (1.2 gm)



RESULTS AND DISCUSSION

This paper reports a simple and effective method for the synthesis of chalocnes by an acid catalyzed aldol reaction were used SOCl as a convenient alternative to the gaseous HCl in the eldol condensation. The HCl is generated in situ by the reaction of $SOCl_2$ 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 $SOCl_2$/ Et OH as a catalyst. Synthesis of chalcone is a single step method. The synthesized chalcone derivatives were undergone physicochemical characterization and the obtained results are given in Table.2. 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 3) and mass spectroscopy helps to find the molecular weight of the synthesized compounds (Table 4). 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.

Table 1: Physicochemical characterization data for synthesized compounds

Compound Number	**Molecular formula**	**Molecular weight**	**Yield (%)**	**M.P°C**	**Elemental analysis**		
					C	H	N
1	$C_{15}H_{11}ClO_3$	274	93	180	66.56(65.75)	4.06(4.04)	-
2	$C_{15}\ H_{12}O_4$	256	94	182	70.41(70.37)	4.65(4.72)	-
3	$C_{15}H_{12}O_4$	256	91	178	70.48(70.37)	4.78(4.72)	-
4	$C_{15}H_{11}NO_5$	285	81	179	63.26(63.21)	3.85(3.69)	4.98(4.91)

Table 2: IR spectral data of synthesized compounds

Compound number	**Compound**	**IR. Spectral data**
1	3-(2-chlorophenyl)-1-(2,4-di-hydroxyphenyl)prop-2-en-1-one	IR (KBr) ν cm^{-1}, (-OH) 3232 cm^{-1}, (C=0) 1691 cm^{-1}, (C=C) 1595 cm^{-1}
2	1-(2,4-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one	IR (KBr) ν cm^{-1}, (-OH) 3177 cm^{-1}, (C=0) 1672 cm^{-1}, (C=C) 1633 cm^{-1}
3	1-(2, 4-dihydroxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one	IR (KBr) ν cm^{-1}, (-OH) 3194 cm^{-1}, (C=0) 1668 cm^{-1}, (C=C)1581 cm^{-1}
4	1-(2,4-dihydroxyphenyl)-3-(4-nitrophenyl)prop-2en-1-one	IR (KBr) ν cm^{-1}, (-OH) 3113 cm^{-1} , (C=0) 1693 cm^{-1}, (C=C)1601 cm^{-1}

Table 3: Mass spectral data of synthesized compounds

Compound number	Compound	Molecular weight	Mass spectral data
1	3-(2-chlorophenyl)-1-(2,4-dihydroxyphenyl) prop-2-en-1-one	274	274 M^{+2}
2	1-(2,4-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one	256	256 $M^{+}H$
3	1-(2, 4-dihydroxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one	256	256 $M^{-}H$
4	1-(2,4-dihydroxyphenyl)-3-(4-nitrophenyl)prop-2en-1-one	285	285 M^{+}

- 3-(2-chlorophenyl)-1-(2,4-dihydroxyphenyl) prop-2-en-1-one of $C_{15}H_{11}ClO_3$ with 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 peak at 1691 cm^{-1} suggesting the presence of (C=O) group. The IR peak at 1595 cm^{-1} indicates that the presence of (C=C) group. IR peak at 3,232 cm^{-1} indicates presence of (-OH). Melting point of the compound is 180°C which is uncorrected.
- 1-(2,4-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one have mole-cular formula $C_{15}H_{12}O_4$ and the molecular weight of the compound is equivalent to the molecular ion peak at (256 $M^{+}H$) of the compound. Hence m/z value confirms the molecular weight of compound. The IR peak at 1672 cm^{-1} suggesting the presence of (C=O) group. The IR peak at 1633 cm^{-1} indicates that the presence of (C=C) group. The IR peak at 3177 cm^{-1} indicates presence of (-OH) group. Melting point of the compound is 182 °C which is uncorrected.
- The molecular formula of 1-(2, 4-dihydroxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one is $C_{15}H_{12}O_4$ molecular ion peak at (256 $M^{-}H$) that m/z is equivalent to molecular weight of proposed compound Hence m/z value confirms the molecular weight of compound. The IR peak at 1668 cm^{-1} suggesting the presence of C=O group. The IR peak at 1581 cm^{-1} indicates that the presence of C=C group. IR peak at 3194 cm^{-1} indicates presence of (-OH) group. Melting point of the compound is 178 °C which is uncorrected.
- The obtained molecular ion peak of 1-(2,4-dihydroxyphenyl) -3-(4-nitrophenyl) prop-2-en-1-one (molecular formula, ($C_{15}H_{11}NO_5$) at 285 (M^{+}) that m/z is equivalent to molecular weight of proposed compound. Hence m/z value confirms the molecular weight of compound. The IR peak at 1693 cm^{-1} suggesting the presence of (C=O) group. The IR peak at 1601 cm^{-1} indicates that the presence of (C=C) group. IR peak at 3113 cm^{-1} indicates presence of (-OH) group. Melting point of the compound is 179°C which is uncorrected.

CONCLUSION

In conclusion, we found that chalcones can be synthesized in good yields from 2,4 dihydroxyacetophenones and aromatic banzaldehydes using the catalytic system $SOCl_2$ / EtOH. The synthesized compounds were characterized by TLC, melting point, IR spectroscopy, elemental analysis and mass spectroscopy. The results obtained form this study confirmed that the product has formed. Henceforth viewing these characteristic properties more compounds can be synthesized and subjected to pharmacological evaluation. These Chalcone derivatives may have variety synthesis and characterization of some new chalcone derivatives.

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