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Research Article

SYNTHESIS OF 2,6-DIHYDROXY SUBSTITUTED CHALCONES BY ALDOL CONDENSATION USING $SOCl_2$/ETOH

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ABSTRACT

A novel method for the synthesis of 2,6-dihydroxy substituted chalcones via aldol condensation. in the presence of $SOCl_2$ / EtOH as a catalyst. 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.

Keywords: Chalcone, Claisen-Schmdit condensation, IR, Mass and Elemental spectral analysis

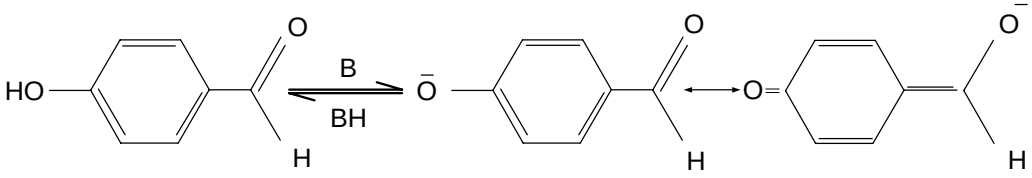
INTRODUCTION

Chalcones (1,3-diaryl-2-propen-1-ones) constitute an important class of natural products belonging to the flavonoid family, which have been reported to possess a wide spectrum of biological activities, including antibacterial, antifungal, anti-inflammatory, antitumor, insect antifeedant and antimutagenic [1-3]. Additionally, some of chalcone derivatives have been found to inhibit several important enzymes in cellular systems, such as xanthine oxidase [4] and protein tyrosine kinase [5,6]. Chalcones are also key precursors in the synthesis of many biologically important heterocycles such as benzothiazepine[7], pyrazolines [8], 1,4-diketones [9] and flavones [10]. Hence, the synthesis of chalcones has generated vast interest among organic as well as medicinal chemists.

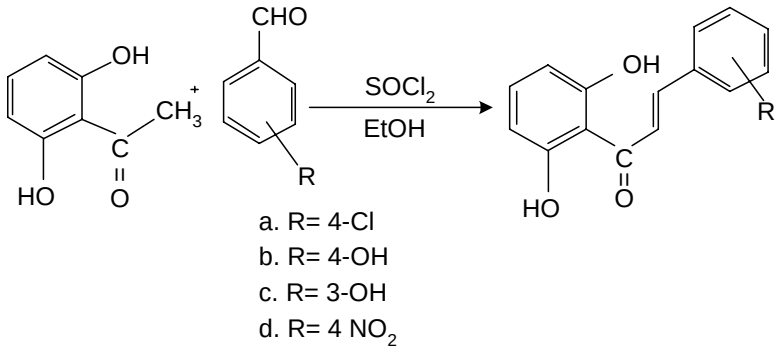
According to the literature data the presence of hydroxy substituents in the aromatic aldehyde hinders the basis catalyze aldol reaction[11]. The reaction behind that is the fact that the basic catalysts decrease the activity of the aldyhyde component because of delocalization of the anion, which is illustrated below in Scheme 1. It is necessary to use protective group for the preparation of the hydroxy chalcones under basis conditions[12]. By using $SOCl_2$ 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, 2,6-hydroxy acetophenone, 2-chlorobenzaldehyde, 4-chloro benzaldehyde, 3-nitrobenzaldehyde were purchased from S.D. fine Chemicals (India). All Melting points were uncorrected and determined in an open capillary tube. IR spectra were recorded in KBr on a JASCO FT/IR-5300 The mass spectra were recorded on LCMS-2010 DATA REPORT SHIMADZU Spectrometer 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 solvent 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).



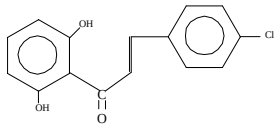
Scheme 1: Anion delocalization of the aldehydic component



Scheme 2: Synthetic diagram of 2,6, dihydroxy substituted chalcones

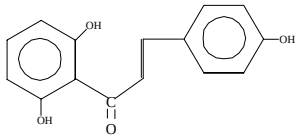
1) Synthesis of 3-(4-chlorophenyl)-1-(2,6-dihydroxyphenyl) prop-2-en-1-one

To a stirred mixed of 2,6-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 hours Precipitate the reaction mixture by addition of water. Filter the product, wash with cold ethanol and allowed to afford.



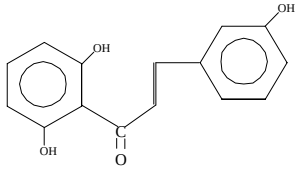
2) Synthesis of 1-(2,6-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one

Reaction with 2,6-dihydroxy acetophenone (2 gm) and 4-hydroxy benzal-dehyde (2.1gm);1-(2,6-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one was obtained by the above procedure.



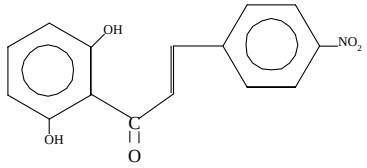
3) Synthesis of 1-(2, 6-dihydroxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one

A mixture of 2, 6-dihydroxy acetophenone (2.2 gm) in inethonol added thionyl chloride (0.05 ml) and 3-hydroxybenzaldehyde (2.1 gm); 1-(2,6-dihydroxy phenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one was obtained by the above procedure.



4) Synthesis of 1-(2, 6-dihydroxyphenyl)-3-(4-nitrophenyl)prop-2en-1-one

1-(2,6-dihydroxyphenyl)-3-(4-nitrophenyl) prop-2 en-1-one was obtained by the above described procedure except that starting material used was 2,6-dihydroxy acetophenone (2.0) in ethanol (5ml) add $SOCl_2$ (0.05 ml) 4 nitro benzaldehyde. (2.1 gm).



RESULTS AND DISCUSSIONS

This paper reports a simple and effective method for the synthesis of chalcones by an acid-catalyzed aldol reactions we used $SoCl_2$ as a convenient alternative to the gaseous HCl in the Aldol condensation The HCl is generated in situ by the reaction of $SOCl_2$ with absolute ethanol. Chalcones are obtained in good to excellent yields.

Our purpose was to synthesize a series of chalcones. Starting from benzaldehyde and acetophenone or their substituted derivatives using $SOCl_2$/EtOH as a catalyst. 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 3). 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.

3-(4-chlorophenyl)-1-(2,6-dihydroxyphenyl) prop-2-en-1-one have the molecular formula of 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 1682 cm^{-1} suggesting the presence of (C=O) group. The IR band at 1591cm^{-1} indicates that the presence of (C=C) group. IR band at 3,212 cm^{-1} indicates presence of (-OH). Melting point of the compound is 198°C which is uncorrected.

The molecular formula of 1-(2,6-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one is $C_{15}H_{12}O_4$. The obtained molecular ion peak at 256 (M^+H) 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 1626 cm^{-1} suggesting the presence of (C=O) group. The IR band at 1527 cm^{-1} indicates that the presence of (C=C) group. IR band at 3234 cm^{-1} indicates presence of (-OH) group. Melting point of the compound is 140°C which is uncorrected.

The obtained molecular ion peak of 1-(2,6-dihydroxyphenyl)-3-(3-hydroxy phenyl) prop-2-en-1-one of (Molecular formula, C_{15} H_{12} O_4) 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 band at 1684 cm^{-1} suggesting the presence of (C=O) group. The IR band at 1599 cm^{-1} indicates that the presence of (C=C) group. IR band at 3369 cm^{-1} indicates presence of (-OH) group. Melting point of the compound is 190°C which is uncorrected.

1-(2,6-dihydroxyphenyl)-3-(4-nitrophenyl) prop-2 en-1-one have the mole-cular formula is $C_{15}H_{11}NO_5$. The molecular ion peak 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 1672 cm^{-1} suggesting the presence of (C=O) group. The IR band at 1591 cm^{-1} indicates that the presence of (C=C) group. IR band at 3200 cm^{-1} indicates presence of (-OH) group. Melting point of the compound is 192°C which is uncorrected.

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	71	198	66.54 (66.75)	4.06 (4.04)	-
2	C_{15} H_{12} O_4	256	75	140	70.41 (70.37)	4.68 (4.72)	-
3	C_{15} H_{12} O_4	256	81	190	70.18 (70.37)	4.58 (4.72)	-
4	C_{15} H_{11} NO_5	285	64	192	63.24 (63.21)	4.72 (3.89)	4.96 (4.91)

Table 2: Interpreted IR spectral data of synthesized compounds

Compound number	Compound	IR. Spectral data
1	3-(4-chlorophenyl)-1-(2,6-dihydroxyphenyl) prop-2-en-1-one	IR (KBr) *v* cm^{-1}, (-OH) 3212 cm^{-1}, (C=0) 1682 cm^{-1}, (C=C) 1591 cm^{-1}
2	1-(2,6-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one	IR (KBr) *v* cm^{-1}, (-OH) 3234 cm^{-1}, (C=0) 1626 cm^{-1}, (C=C) 1527 cm^{-1}
3	1-(2,6-dihydroxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one	IR (KBr) *v* cm^{-1}, (-OH) 3369 cm^{-1}, (C=0) 1684 cm^{-1}, (C=C)1599 cm^{-1}
4	1-(2,6-dihydroxyphenyl)-3-(4-nitrophenyl)prop-2-en-1-one	IR (KBr) *v* cm^{-1}, (-OH) 3200 cm^{-1} , (C=0) 1672 cm^{-1}, (C=C)1591 cm^{-1}

Table 3: Mass spectral data of synthesized compounds

Compound number	Compound	Molecular weight	Mass spectral data
1	3-(4-chlorophenyl)-1-(2,6-dihydroxyphenyl) prop-2-en-1-one	274	274 M^{+2}
2	1-(2,6-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one	256	256 $M^{+}H$
3	1-(2,6-dihydroxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one	256	256 $M^{-}H$
4	1-(2,6-dihydroxyphenyl)-3-(4-nitrophenyl) prop-2en-1-one	285	285 M^{+}

CONCLUSION

This method is a very efficient and selective method protocol for aldol condensation of 2,6-dihydroxy acetophenone and various aromatic aldehydes to produce high yields of 2,6,-dihydroxy substituted Chalcones in the presence of $SoCl_2$/EtOH catalytic system. 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. These Chalcone derivatives may have variety synthesis and characterization of some new chalcone derivatives.

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