ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Synthesis and Characterization of 4-Hydroxy Chalcones Using PEG-400 as a Recyclable Solvent.

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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 recyclable PEG-400 as an alternative reaction solvent. The reaction is clean with excellent yield, shorter reaction time and reduces the use of volatile organic compounds (VOCs). The structures of the synthesized compounds were confirmed by IR, mass spectroscopy and elemental analysis.

Keywords: Chalcone, Claisen-Schmdit condensation, PEG-400, IR, Mass and Elemental spectral analysis.

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ISSN: 0975-8585

INTRODUCTION

Chalcones are a group of compounds with various substitution patterns on the two aromatic rings of 1, 3-diphenyl-2-propen-1-one. Chalcones 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 anti-bacterial, anti-fungal, anti-inflammatory, anti tumor, insect anti-feedant and anti-mutagenic [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 k/y 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.

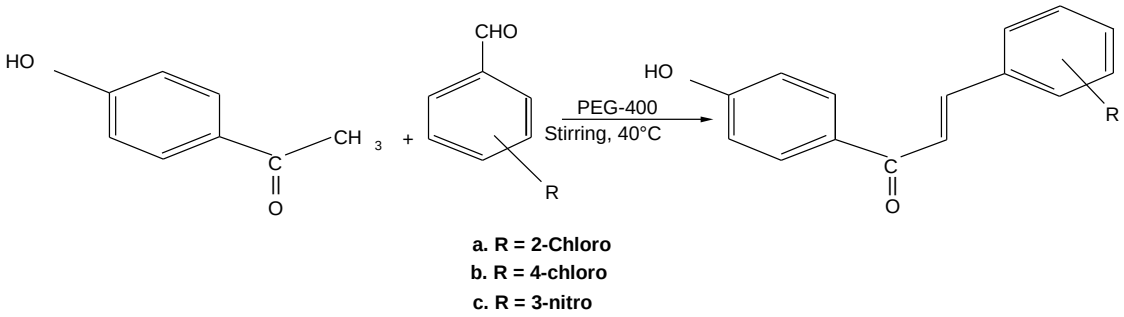
The oxygenated chalcone, licochalcone A, has been previously described as a moderately potent anti bacterial compound with activity against Gram-positive bacteria. Rapid development of resistance to clinically important Gram-positive bacteria is a serious public health threat. *Staphylococcus aureus* can produce a number of diseases affecting humans and animals. Therefore the search for novel bactericidal compounds is the object of continuous investigation [11-17]. Additionally, chalcones with basis amino functions have been reported to have enhanced selectively and potency in biological properties [18].

Herein for the first time we describe a simple and convenient method for the synthesis of chalcones using poly ethylene glycol (PEG) has been found to be an interesting solvent system. In continuation of own work on chalcones as precursors in the synthesis of various heterocycles [19], we have planned to synthesize a series of novel hetero chalcones by applying the principles of green chemistry, using PEG-400 as an alternative reaction medium [20]. PEG is an environmentally benign reaction solvent, is it non-toxic, inexpensive, potentially recyclable and water soluble, which facilitates its removal from the reaction product.

MATERIALS AND METHODS

All the products were synthesized and characterized by their spectral analysis. Chemicals, 4-hydroxy acetophenone, 2-chloro benzaldehydes, 4-chloro benzaldehydrs, 3-nitro benzaldehydes 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 SHIMADZU – LCMS 2010 Spectrometer. Elemental analysis was carried out on a FLASH EA 1112 SERIES CHN REPORT THERMO FINNIGAN. Chalcones were synthesized by clasien- Schmidt condensation [21] using PEG-400 as reaction solvent. The chemicals and solvents used were of laboratory grade and were purified completion of the reaction was monitored by thin layer chromatography on pre-coated sheets of silica gel-G (Merck, Germany) using iodine vapour for detection. The synthetic pathway is presented in Scheme 1 and physicochemical data and spectroscopic data for the synthesized compounds are given Table (1-3).

ISSN: 0975-8585

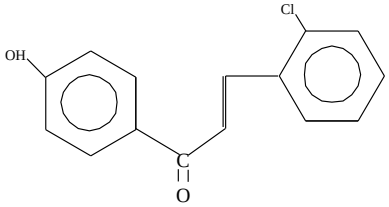


a. R = 2-Chloro
b. R = 4-chloro
c. R = 3-nitro

Scheme 1: Synthetic diagram of 4-hydroxy substituted chalcones

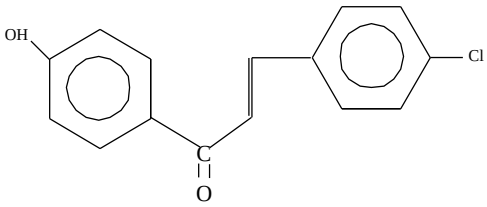
1) Synthesis of 3-(2-chlorophenyl)-1-(-4-hydroxyphenyl) prop-2-en-1-one

An equimolar mixture of 4-hydroxy acetophenone, 2-chlorobenzaldehyde and KOH (2mmol) was stirred in PEG-400 (15 ml) at 40°C for 1 hour. After the completion of the reaction (monitored by TLC), the crude mixture was worked up in ice-cold water (100 ml). The product which separated out was filtered. The filtrate was evaporated to remove water leaving PEG behind. The same PEG was utilized to synthesize further chalcone.



2) Synthesis of 3-(4-chloro phenyl)-1-(4-hydroxyphenyl) prop-2-en-1-one

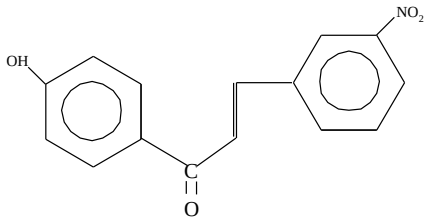
Reaction with 4-hydroxy acetophenone (1gm) and 4-chlorobenzaldehyde (1.1 gm); 3-(4-chlorophenyl)-1-(4-hydroxyphenyl)prop-2-en-1-one was obtained by the above described procedure.



3. Synthesis of 1-(4-hydroxyphenyl)-3-(3-nitro phenyl) prop-2-en-1-one

A mixture of 4-hydroxy acetophenone (1.0 gm) in PEG-400 (5ml) and 3-nitro benzaldehyde (1.1 gm), 1-(4-dihydroxyphenyl)-3-(3-nitro phenyl) prop-2-en-1-one was obtained by the above described procedure.

ISSN: 0975-8585



RESULTS AND DISCUSSIONS

The Claisen-Schmidt condensation is an important C-C bond formation for the synthesis of 1,3-diaryl-2-propen-1-ones (chalcones). It is generally carried out of the use of strong bases such as NaOH or KOH in polar solvents (MeOH or DMF). The aim of the present study was to develop an efficient protocol using PEG-400 as a recyclable reaction solvent to obtain 1,3-diaryl-2-propen-1-ones with good to excellent yields in a short span of time without formation of any side product.

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 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-(2-chlorophenyl)-1-(4-hydroxyphenyl) prop-2-en-1-one have the molecular formula of $C_{15}H_{11}ClO_2$. The molecular ion peak at 259 (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 1691 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 3261 cm^{-1} indicates presence of (-OH) group. Melting point of the compound is 180°C which is uncorrected.

The molecular formula of 3-(4-chlorophenyl)-1-(4-hydroxyphenyl) prop-2-en-1-one is $C_{15}H_{11}ClO_2$. The obtained molecular ion peak at 259 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 1591 cm^{-1} indicates that the presence of (C=C) group. IR band at 2982 cm^{-1} indicates presence of (-OH) group. Melting point of the compound is 190°C which is uncorrected.

ISSN: 0975-8585

The obtained molecular ion peak of 1-(4-hydroxyphenyl)-3-(3-nitro phenyl) prop-2-en-1-one (molecular formula $C_{15}H_{11}NO_4$) at 269 (M^{+2}) 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 1651cm^{-1} suggesting the presence of (C=O) group. The IR band at 1606 cm^{-1} indicates that the presence of (C=C) group. IR band at 3142 cm^{-1} indicates presence of (-OH) group. Melting point of the compound is 182 °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	$C_{15}H_{11}ClO_2$	259	80	180	69.58 (69.56)	4.23 (4.28)	-
2	$C_{15}H_{11}ClO_2$	259	82	190	69.71 (69.56)	4.35 (4.28)	-
3	$C_{15}H_{11}NO_4$	269	83	182	66.85 (66.97)	4.14 (4.28)	5.28 (5.20)

Table.2: IR spectral data of synthesized compounds

Compound Number	Compound	IR. Spectral data
1	3-(2-chlorophenyl)-1-(-4-hydroxyphenyl) prop-2-en-1-one	IR (KBr) *v* cm^{-1} 3261 cm^{-1}(-OH) 1691 cm^{-1} (C=0) 1591 cm^{-1} (C=C)
2	3-(4-chlorophenyl)-1-(4-hydroxyphenyl) prop-2-en-1-one	IR (KBr) *v* cm^{-1} 2982 cm^{-1}(-OH) 1682 cm^{-1} (C=0) 1591 cm^{-1} (C=C)
3	1-(4-hydroxyphenyl)-3-(3-nitro phenyl) prop-2-en-1-one	IR (KBr) *v* cm^{-1} 3142 cm^{-1}(-OH) 1651 cm^{-1} (C=0) 1606 cm^{-1} (C=C)

Table IV.3: Mass spectral data of synthesized compounds

Compound number	Compound	Molecular Weight	Mass spectral data
1	3-(2-chlorophenyl)-1-(4-hydroxyphenyl) prop-2-en-1-one	259	259 M^{+2}
2	3-(4-chlorophenyl)-1-(4-hydroxyphenyl) prop-2-en-1-one	259	259 M^{+2}
3	1-(4-hydroxyphenyl)-3-(3-nitro phenyl) prop-2-en-1-one	269	269 M^{+2}

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