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SYNTHESIS OF CHALCONE ANALOGUES BY ULTRASONICATION

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ABSTRACT

In this work, an attempt was made to synthesize new chalcones by Claisen - Schmidt condensation of substituted benzaldehydes with 4-aminoacetanilide in the presence of base catalyst. In this study we attempt to change the technique for synthesis of Chalcone, we used utrasonigation method for the same. The synthesized chalcone derivatives were characterized by FT-IR. In a wide search program towards new and efficient antimicrobial agents, substituted chalcones have been synthesized by condensing benzaldehyde derivatives with acetophenone derivatives in dilute Ethanolic sodium hydroxide solution at room temperature according to Claisen – Schmidt condensation. The structures of these compounds have been investigated by infra red spectroscopy.[4]

KEYWORDS: Chalcone, Claisen - Schmidt condensation.

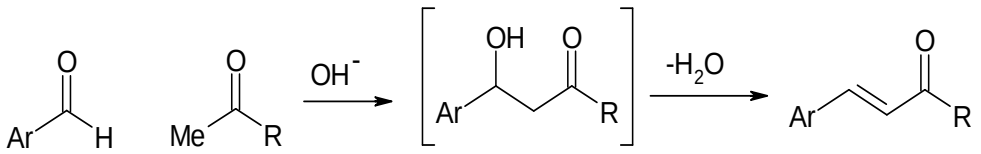
INTRODUCTION

Chalcones come under an aromatic Ketone that forms the central core for a variety of important biological compounds. Claisen–Schmidt condensation between acetophenone and benzaldehyde gives chalcone. This reaction is catalyzed by acids and bases under homogeneous or heterogeneous conditions.[1,2,3]

The framework 1,3-diphenylprop-2-en-1-one is the well know by the generic term “chalcone ,” a name coined by Kostanecki & Tambor.

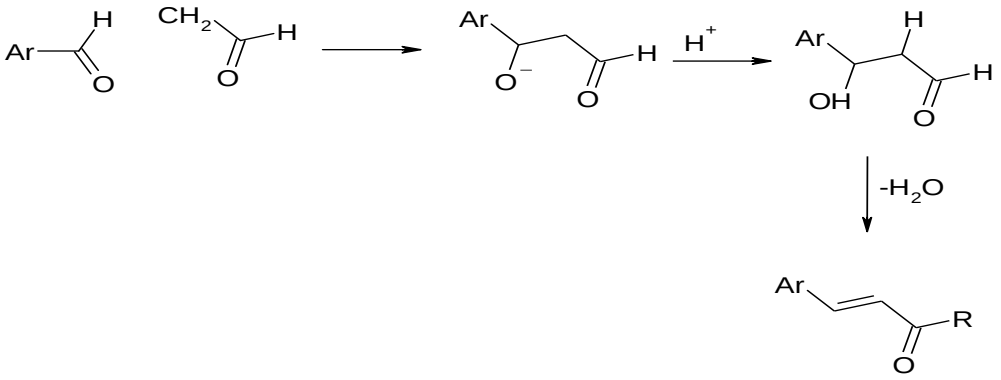
It is known as benzaldehyde & benzylidene acetophenone Chalcone is belonging to the flavonoids family. These open-chain flavonoids have two aromatic ring that are linked by an aliphatic three-carbon chain & occur mainly as polyphenolic compound whose colour change from yellow to orange.[1]

A retro synthetic analysis of α β-unsaturated Ketones leading to various methods of synthesis. These methods are equally application to aromatic aldehydes. Aromatic aldehydes condense with aliphatic or mixed alkyl Ketones in the presence of aqueous alkali to form α β unsaturated Ketones (the Claisen –Schmidt reaction).[1]



Reaction: Claisen –Schmidt reaction

The first step is a condensation of the aldol types involving the nucleophilic addition of the carbonyl – carbon of the aromatic aldehyde. Dehydration of the hydroxyketone to form the conjugated unsaturated carbonyl compound occurs spontaneously.[1]



Describes the preparation of a range of α β-unsaturated Ketones including benzylidene acetone, furfurylideneacetone and benzylidence-acetophenone. The conversion of this latter compound into β-phenylpropio-phenone is readily achieved by hydrogenation at atmosphere pressure over an active platinum catalyst.[1]

The formation of w-nitrostyrenes by reaction of nitroalkanes with aromatic aldehydes in the presences of aqueous alkali may be classified with reaction of the clasien-Schmidt type.

A future example of the above reaction types is provided by the condensation between an aromatic aldehydes and an ester (the Claisen reaction, eg. the synthesis of ethyl cinnamate), which requires a more powerfully basic catalyst eg. Sodium ethoxide to effect conversion of the ester into the corresponding anion.[1]

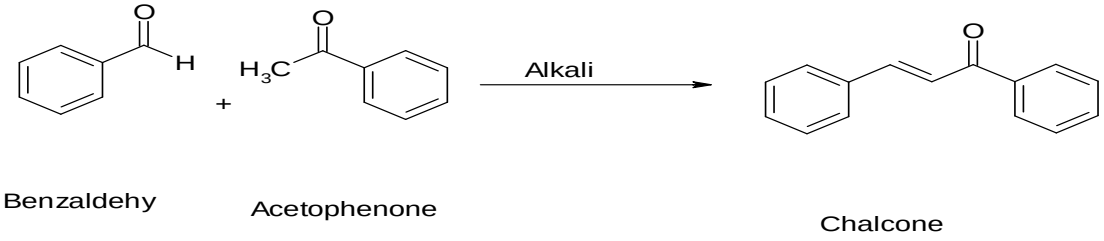
chalcones derivatives have received a great deal of attention due to their relatively simple structures and wide variety of pharmacological activities reported for these compounds include Antibacterial, anti-malarial antitumor activities anti-inflammatory, antifungal etc. For these reasons, the synthesis of chalcones and their functionalized derivatives is a primary objective. Herein we report the activity of chalcone derivatives by synthesizing a series of molecules and evaluating their antibacterial activity against eight microorganism strains of Gram positive and negative antifungal profile against *Staphylococcus aureus* and *Penicllium* sps. In this study, only the feature associated with "B" ring of the chalcone moiety was changed by keeping the basic skeleton intact. Three compounds found most active *in-vitro* against *Staphylococcus aureus* and *Penicllium* sps. Compared to standard drug.[2]

Uses

Now days, several chalcone are use for treatment of

1. Stomach cancer
2. Pain
3. Parasitic infection
4. Viral disorders
5. Gastritis
6. Food additive
7. Cardiovascular diseases

Experimental Work (Mechanism)[1,6]

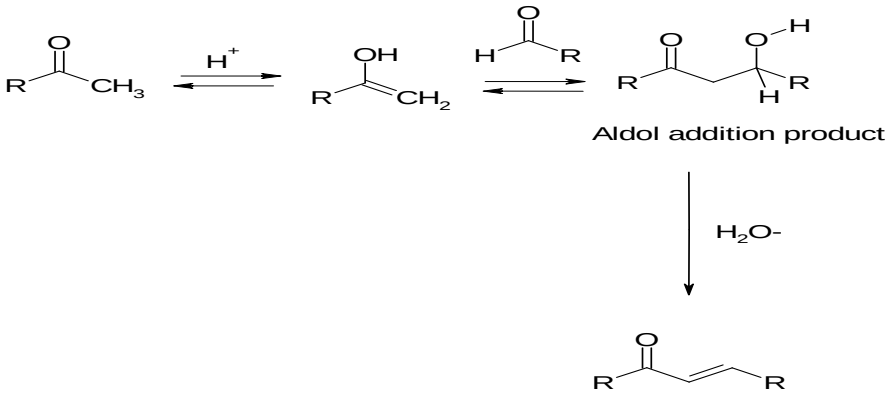


Benzaldehy Acetophenone Chalcone

General Scheme

- The first part of this reaction is an aldol reaction, the second part dehydration– an elimination reaction.
- Dehydration may be a companied by decarboxyllation when an activate decarboxyl group is present.
- The aldol addition product can be dehydrated via two mechanism; A strong base like potassium t-butoxide or sodium hydroxide in an enolate mechanism Or in an acid catalyzed end mechanism.
- Depending on the nature of the desired product, the aldol condensation may be carried out under two broad types of conditions.
- Kinetic control or thermodynamic control.
- The name aldol condensation in also commonly used especially in the bio-chemistry to refer to just the first in (addition) stage of the process the aldolases reaction itself as catalyzed aldolases.

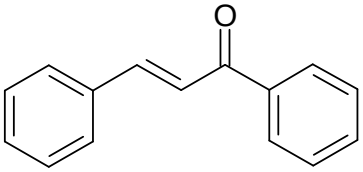
- However, the aldol reaction is not formally a condensation reaction. Because it does not involve the loss of small molecule.
- The reaction between an aldehyde and ketone having an alpha-hydrogen with an aromatic carbonyl compound lacking an alpha-hydrogen is called the clainsen – schmidt condensation.
- This reaction is named after two of this pioneering investigators Rainer Ludwig claisen an J. G Schmidt, who independentally Publised on this topic in 1880 and 1881.
- An example is the synthesis of dibenzalideneacetone. Quantitative yields in claisen– schmidt reaction have been reported in the absence of solvent using sodium hydroxide as a base and plus benzaldehydes. Because the enolizeble nucleophilic carbonyle compound and the electrophilic carbonyl compound are the two different chemical, the claisen schmidt reaction is an example of crossed aldol process.



- Aldol condensation is important in the organic synthesis, because they provide a good way to form carbon – carbon bond.
- For example – The Robinson Annulation reaction sequence features on aldol condensation,
- The Wieland – Miescher ketone product in an important starting material for many organic synthesis
- Aldol condensation are also commonly discussed in university level Organic Chemistry classes as a good bond forming reaction that demonstrates important reaction mechanism.
- In its usual form, it involves nucleophilic addition of a ketone enolate to an aldehyde to form a Beta – hydroxy ketone Or "Aldol" (Aldehyde + Alcohol), a structural unit found in many naturally occurring molecules & pharmaceuticals.

Chalcone profile

- **Chemical structure**



- **Chemical Name:** Chaalcone, Trans- Chalcone
- **I.U.P.A.C. Name :** 1,3-Diphenylprop 2-en-1-one
- **Melting Point:** 55 to 57 ℃
- **Molecular Weight :** 208.26 g/cm

Procedure[1]

- Take a solution of 2.2g of sodium hydroxide in 20.0 ml of water & 10.0g of rectified spirit in 100ml volumetric flask.
- The flask in a bath of crushed ice pours in 5.2g of freshly distilled ACETOPHENONE. (Desity1.03)
- Add 4.6g pure benzaldehyde (temp-25) (limit-15-30°C), Density (1.04g/cm3).
- The mix is so thick that is stirrer no longer effective (1-2hour)
- Leave the reaction mix in an ice chest or Refrigerator or overnight.
- In Buchner funnel or sintered glass fennel (wash with cold water)
- Washing are neutral to litmus then 20ml of ice cold rectified spirit.
- Crude chalcone (wt-88g& melts at 50-54°C)
- Recrystallized from rectified spirit warmed to 50°C (YEILD)
- Pure benzylideneacelophenol (pale yellow solid).

RESULT AND DISCUSSION

- Benzaldehyde + Acetophenone $\xrightarrow{NaOH}$ Chalcone

Table 2: Physical Data of Chalcone Derivatives.

Sample code	Molecular formula	Molecular weight	Theoretical yield	Practical yield	% Practical yield	R_f	m.p. °C
Ch01 (Acetophenone + Benzaldehyde)	$C_{15}H_{12}O$	208 gm	22.50 gm	18.30 gm	81.33 %	0.61	56-58
Ch02 (Acetophenone + p-anisaldehyde)	$C_{16}H_{14}O_2$	238gm	17.93gm	15.14gm	84.43%	0.64	76-78
Ch03 (Acetophenone + m-nitrobenzaldehyde)	$C_{14}H_{11}NO_3$	241gm	18.33gm	17.25gm	94.10%	0.48	120-125

IR Spectroscopy

The IR spectrum of the sample was recorded and the functional groups were interpreted as per the structure and where found to be appropriate or matching the structure of the drug. Fig 1 & Fig 2 gives the IR spectra of the pure drug.

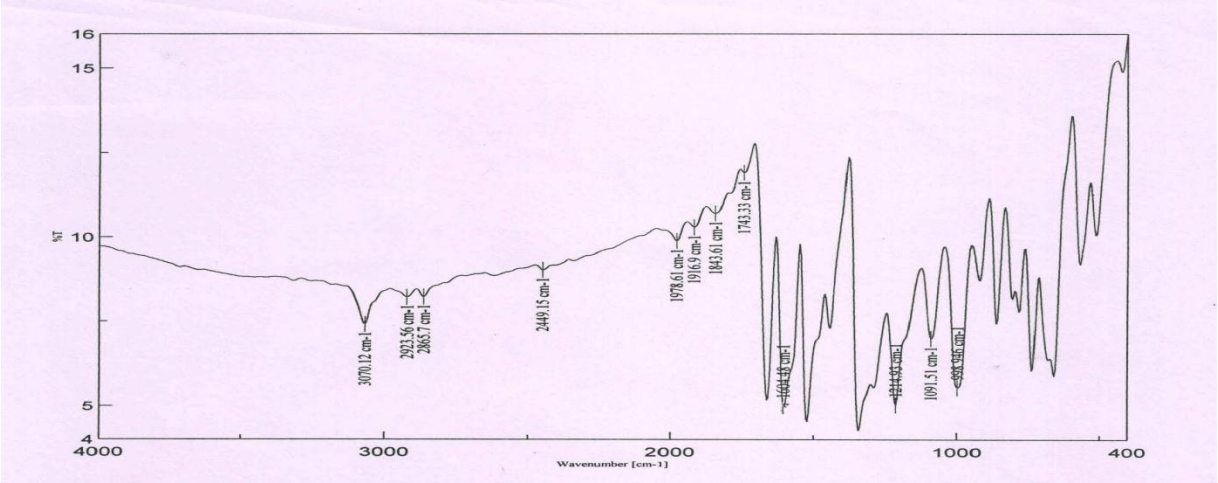


Fig. 01: Infrared spectra of Ch 02.

Interpretation: C-H Str (2950.55), C-H Str (3012.27), -CO- Str (1770.33),

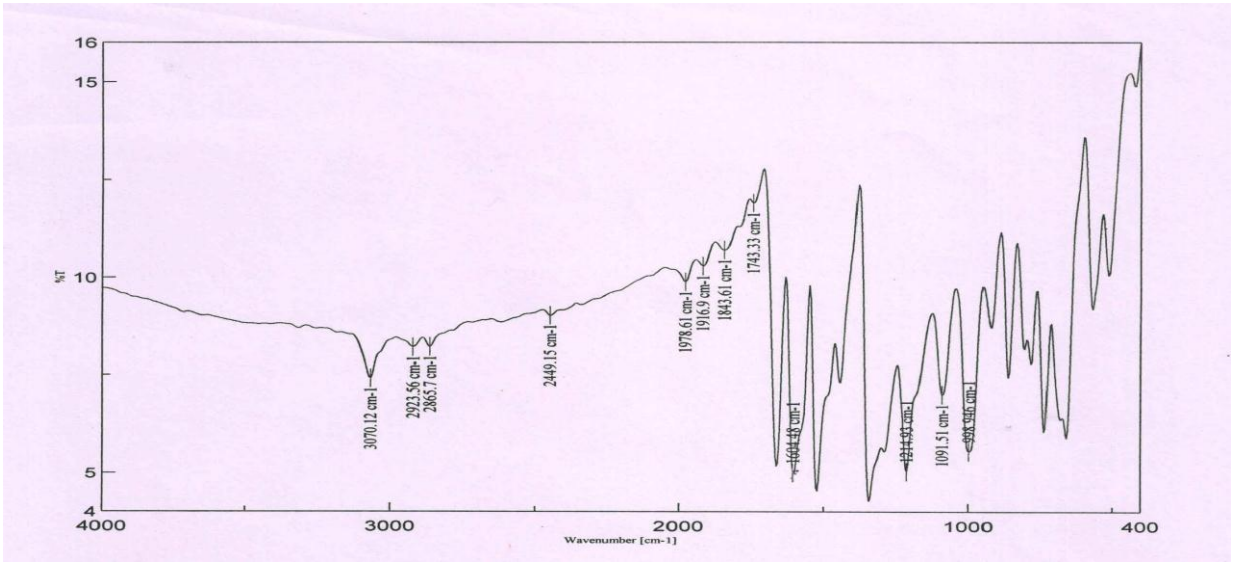


Fig. 01: Infrared spectra of Ch 03.

Interpretation: C-H Str (3070.12), -CO- Str (1743.33), -NO2 Str (1604.48).

Table 17: Antimicrobial activity.

Compound code	Gram negative Bacteria		Gram positive Bacteria	
	E. coli	*P. aureginosa*	*S. aureus*	*B. subtilis*
Ch01	**6.25**	**12.5**	**12.5**	**6.25**
Ch02	**6.25**	**6.25**	**12.5**	**12.5**
Gentamycin.	**3.12**	**3.12**	**3.12**	**3.12**

Antimicrobial activity

Compound shows good antimicrobial activity against gram –ve and gram +ve bacteria as compared with standard gentamycin. Compound **Ch01** shows good activity against gram –ve bacteria *Escherichia coli* and *Pseudomonas aeruginosa.* While compound **Ch02** shows good antimicrobial activity against gram +ve bacteria *Staphylococcus aureus* and *Bacillus substilis*.

Compounds **Ch01** and **Ch02** shows better antimicrobial activity as compare to standard.

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