SYNTHESIS OF CHALCONES

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Abstract : Chalcones are the important constituent of many natural sources and possess a variety of biological activities. Four chalcone derivatives were synthesized by using two different methods. The compounds were synthesized by Aldol condensation of appropriate aromatic ketones or substituted aromatic ketones with benzaldehydes or substituted benzaldehydes. The compounds synthesized were purified by Column Chromatography and recrystallisation. The determination of the structure of synthesised compounds were done by its physical properties like Melting point and TLC followed by spectroscopic analysis.

Key words : Chalcone,Column Chromatography, Thin layer chromatography

I.Introduction

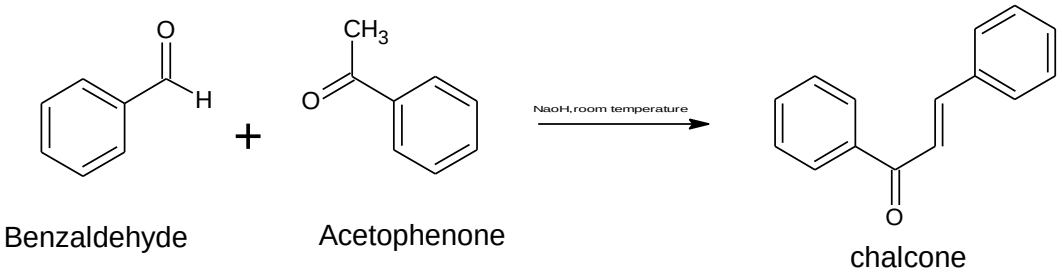
Chalcones and their derivatives form a large group of natural products. Chalcones are the natural pigments found in nature which form the central core for a variety of important biological compounds. They are the aromatic ketones and enones. They are important constituents of many natural sources. They are found abundant in plants and are also considered as a precursor of flavonoids and isoflavonoids. They possess a wide spectrum of biological activities such as antibacterial, antifungal, anticancer, anti-inflammatory, etc. Some Chalcones have been reported as the inhibitors of lipoxygenase, β-secretase, acyl- cholinesterase, butyrylcholinesterase, cyclooxygenase, andperoxisome. Chalcone shows biological activity mainly because of an enone pharmacophore in their structures. Cyclic ketones having α-hydrogen when treated with various aromatic aldehyde in alcohol in the presence of potassium hydroxide tends to form α, β-unsaturated compounds. Chalcones can be synthesized by using Claisen-Schmidt based catalyzed condensation of aromatic ketones or substituted aromatic ketones with benzaldehyde or substituted benzaldehyde.

They are also known as Benzylidene acetophenone and it was first isolated from Chinese licorice (Glycyrrhiza inflate). It has a 1,3-diaryl-1-one skeletal system which was recognized as the main pharmacophore for chalcones. From plants, stable chalcone moiety cannot be isolated due to the presence of enzyme chalcone synthetase which immediately converts chalcone toflavanones. Chalcone consists of two aromatic rings which are linked by an aliphatic three carbon chain. They are α, β-unsaturated ketones that consist of two aromatic rings having different substituents. These two aromatic rings are interconnected by electrophonic three carbon α, β- unsaturated carbonyl system that assumes a planar structure and contain the keto-ethylenic group (-CO-CH=CH-).

II.Research Methodology : Synthesis of 4 different chalcone derivatives was done by using two different methods like Solvent free Aldol condensation and Aldol condensation with solvent. Further the obtained products were purified with column chromatography and re-crystalised and then its structure was established on the basis of their physical properties viz. melting points and other spectroscopic techniques.

III.Materials and method:

A. C HALCONE



Benzaldehyde Acetophenone chalcone

Method I :

- Synthesis of Chalcones was carried out by using Aldol condensation. 20 ml Acetophenone and 20 ml Benzaldehyde were mixed in the presence of base NaOH as a catalyst.
- The reaction mixture was kept at 0-20^0 C temperature for 120 hours. The mixture was thenfilteredandwashedwithdistilledwatertoremoveaccesstorawmaterials.
- On completion of the reaction, it was monitored byTLC.
- Thin Layer Chromatography of reactants (Benzaldehyde and Acetophenone) and the obtained product Chalcone was carried out in hexane: ethyl acetate(12:2).
- It was sprayed with 5% H_2SO_4 where brown color Spot of the final product was observed.
- The reactant mixture was acidified with HCl in an ice bath and the solid was then filtered and crystallized byethanol.

Method II (Dry Procedure) :

- T

he procedure involves grinding Acetophenone with one equivalent of sodium hydroxide and Benzaldehyde derivative for ten minutes using a mortar and pestle. The Chalcone is then isolated by suction filtration after washing with water

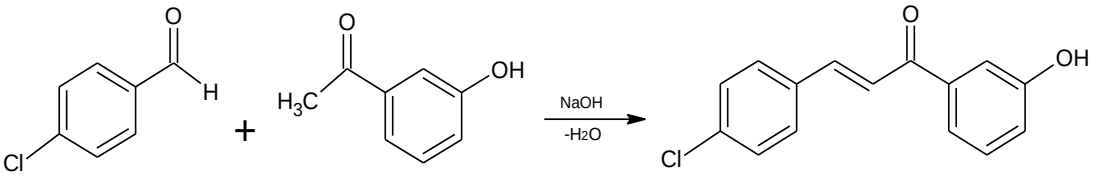
- A

lthough the crude Chalcone is often found to have sufficient purity for product characterization, recrystallization is performed with 95% ethanol to remove traces of impurities.

- A

fter purification & crystallization of the product, variety of techniques (melting point) determination, thin-layer chromatography (TLC), NMR and IR spectroscopy) are used in order to determine the structure of that chalcone.

B. 3 -HYDROXY-4-CHLOROCHALCONE



4-Chlorobenzydehyde m-hydroxyacetophenone 3-hydroxy -4chlorochalcone

Method I :

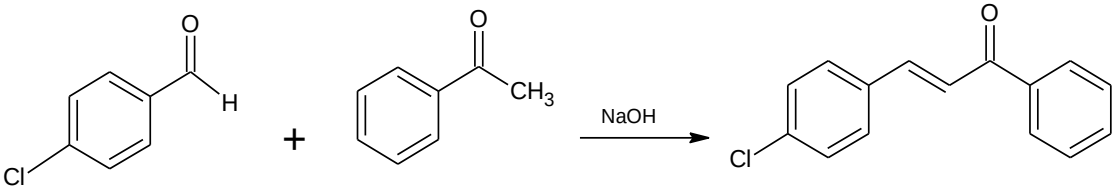
- Synthesis of Chalcones was carried out by using Aldol condensation. 20 ml m-hydroxy acetophenone and 20 ml 4-chlorobenzaldehyde were mixed in the presence of base NaOH as a catalyst.
- The reaction mixture was kept at 0-20^0 C temperature for 120 hours. The mixture was then filtered and washed with distilled water to remove access to raw materials.
- On completion of the reaction, it was monitored byTLC.
- Thin Layer Chromatography of reactants (4-chlorobenzaldehyde and m-hydroxy acetophenone) and the obtained product Chalcone was carried out in hexane: ethyl acetate(12:2).
- It was sprayed with 5% H_2SO_4 where brown color Spot of the final product was observed.
- The reactant mixture was acidified with HCl in an ice bath and the solid was then filtered and crystallized byethanol.

Method II (Dry Procedure) :

- The procedure involves grinding m-hydroxyacetophenone with one equivalent of sodium hydroxide and benzaldehyde derivative for ten minutes using a mortar and pestle. Each chalcone is then isolated by suction filtration after washing with water
- Although the crude chalcone is often found to have sufficient purity for product characterization, recrystallization is performed with 95% ethanol to remove trace impurities.
- Once isolate their product, they use a variety of techniques (melting point) determination, thin-layer chromatography (TLC), NMR and IR spectroscopy) in order to determine the identity of their chalcone.

C. 4

-CHLOROCHALCONE



4-Chlorobenzaldehyde Acetophenone 4-Chloro-Chalcone

Method I :

- Synthesis of Chalcones was carried out by using Aldol condensation. 20 ml Acetophenone and 20 ml 4-chlorobenzaldehyde were mixed in the presence of base NaOH as a catalyst.
- The reaction mixture was kept at 0-20^0 C temperature for 120 hours. The mixture was thenfilteredandwashedwithdistilledwatertoremoveaccesstorawmaterials.
- On completion of the reaction, it was monitored byTLC.
- Thin Layer Chromatography of reactants (4-Chlorobenzaldehyde and Acetophenone) and the obtained product Chalcone was carried out in hexane: ethyl acetate(12:2).
- It was sprayed with 5% H_2SO_4 where brown color Spot of the final product was observed.
- The reactant mixture was acidified with HCl in an ice bath and the solid was then filtered and crystallized byethanol.

Method II (Dry Procedure) :

- T

his method comprises of solvent-free Aldol condensation technique.

- T

he procedure involves grinding acetophenone with one equivalent of sodium hydroxide and benzaldehyde derivative for ten minutes using a mortar and pestle. Each Chalcone is then isolated by suction filtration after washing with water.

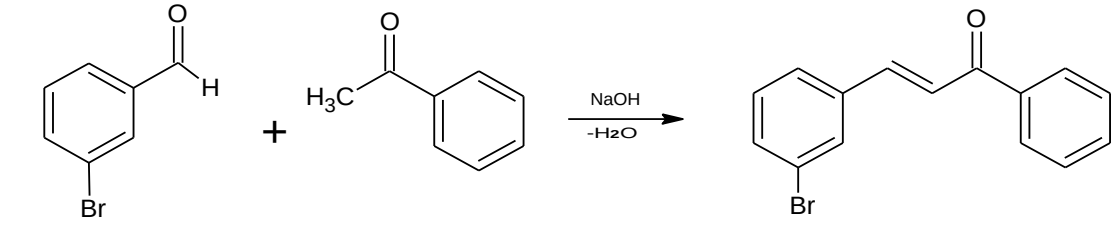
- A

lthough the crude chalcone is often found to have sufficient purity for product characterization, recrystallization is performed with 95% ethanol to remove trace impurities.

- O

nce the product was isolated , a variety of techniques for determination of the chalcone product like melting point (MP), thin-layer chromatography (TLC), IR and NMR spectroscopy were conducted.

D. 3 -BROMO-CHALCONE



3-Bromobenzaldehyde Acetophenone 3-Bromo-Chalcone

Method I:

- Synthesis of Chalcones was carried out by using Aldol condensation. 20 ml Acetophenone and 20 ml 3-

bromobenzaldehyde were mixed in the presence of base NaOH as a catalyst.

- The reaction mixture was kept at 0-20^0 C temperature for 120 hours. The mixture was thenfilteredandwashedwithdistilledwatertoremoveaccesstorawmaterials.
- On completion of the reaction, it was monitored byTLC.
- Thin Layer Chromatography of reactants (3-Bromobenzaldehyde and Acetophenone) and the obtained product Chalcone was carried out in hexane: ethyl acetate(12:2).
- It was sprayed with 5% H_2SO_4 where brown color Spot of the final product was observed.
- The reactant mixture was acidified with HCl in an ice bath and the solid was then filtered and crystallized byethanol.

Method II (Dry Procedure) :

- This method comprises of solvent-free aldol condensation technique.
- The procedure involves grinding acetophenone with one equivalent of sodium hydroxide and benzaldehyde derivative for ten minutes using a mortar and pestle. Each chalcone is then isolated by suction filtration after washing with water.
- Although the crude chalcone is often found to have sufficient purity for product characterization, recrystallization is performed with 95% ethanol to remove trace impurities.
- Once the product was isolated , a variety of techniques for determination of the chalcone product like melting point (MP), thin-layer chromatography (TLC), NMR and IR spectroscopy were conducted.

Column chromatography (CC): Column chromatography is a technique used to isolate chemical compounds from a mixture. It is a method used to separate substances based on differential adsorption of compounds to the adsorbent; compounds move through the column at different rates which allows them to get separated into fractions. This technique is widely applicable because it can be used with a wide range of solvents according to their polarities.

A column consists of :

Stationary phase:

The stationary phase or adsorbent in column chromatography is solid in nature. The most common stationary phase for column chromatography is silica gel.

Mobile phase:

The mobile phase or the eluent is a solvent used to move the compounds through the column. It is chosen according to its polarity so that effective separation of the compounds can be done. The order of polarity of solvent added is as follows:

Petroleum ether <Benzene <Ethyl acetate <Acetone <Methanol<Water.

Thin layer chromatograph (TLC):

A TLC can show how a mixture of compounds will behave when purified. The separation is first optimized using TLC before and after performing column chromatography.

Experimental procedure:

The packing of column is done by wet method. The chalcone slurry was made with silica gel (60-120 mesh) and eluent petroleum ether and then kept in water bath for few minutes. The column was prepared by packing the column with cotton at the bottom. The stationary phase silica gel was used by making its slurry with petroleum ether. The silica gel slurry is added first and then the slurry of the extract was added and packed with cotton at the top.

Pure petroleum was used as the first solvent followed by mixture of 90% petroleum ether – 10% Benzene. Successive mixtures containing 20%, 30%, 40% followed till 100% Benzene.

The fractions were collected from the column and then distilled. The concentrated samples were collected in the test tube and then TLC for components were done.

The samples were again concentrated in the water bath and then crystallized with solvents. Melting point of the obtained pure compounds was determined in the laboratory.

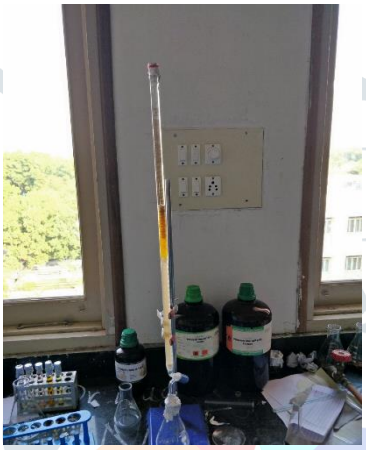


Fig.1: Column chromatography of Chalcone derivatives

IV.Results :

A. CHALCONE:

Molecular weight:
$C_{15}H_{12}O$

Molecular weight:
208.26g/mol

Melting point:
55^0 -57^0C

Fig.2: Chalcone product

Table 1: Yield ofChalcone

Chalcone product	Method	Weight	% Yield
Chalcone	Method I	1.7 g	58.41%
Chalcone	Method II (Dry)	1.9 g	65.29%

B. 3-HYDROXY-4-CHLOROCHALCONE:

Molecular formula:
$C_{15}H_{11}ClO_2$

Molecular weight :
258.7 g/mol

Melting Point :
83-85°C

Fig.3: 3-Hydroxy-4-chloroChalcone

Table 2: Yield of 3-Hydroxy-4-chloroChalcone

Chalcone product	Method	Weight	% Yield
4-hydroxy Chalcone	Method I	1.2 g	66.67%
4-hydroxy Chalcone	Method II (Dry)	0.9 g	50%

C. 4-CHLOROCHALCONE

Moleclular formula:
$C_{15}H_{11}ClO$

Moleclular weight :
242.7 g/mol

Melting Point :
113-117°C

Fig.4: 4-ChloroChalcone

Table 3: Yield of4-Chlorochalcone

Chalcone product	Method	Weight	% Yield
4-Chloro-Chalcone	Method I	1 g	58.1%
4-Chloro-Chalcone	Method II (Dry)	1.23 g	71.5%

D. **3-BROMO-CHALCONE**

Moleclular formula:
$C_{15}H_{11}BrO$

Moleclular weight :
287.15 g/mol

Melting Point :
83-85°C

Fig.5 : 3-Bromo-chalcone

Table 4: Yield of 3-Bromo-Chalcone

Chalcone Product	Method	Weight	% Yield
3-Bromo-Chalcone	Method I	1 g	64.5%
3-Bromo-Chalcone	Method II(Dry)	0.9 g	58%

V.Conclusion:

➢ Chalcone derivatives were synthesized by two methods, Aldol condensation and Solvent free Aldol condensation.

➢ The yield of the Chalcone product by Aldol condensation was 58.41% and by Solvent free Aldol condensation was 65.29%.

➢ The yield of the 3-Hydroxy-4-chloro Chalcone by Aldol condensation was 64.5% and by Solvent free Aldol condensation was 58%.

➢ The yield of the 4- Chloro Chalcone by Aldol condensation was 58.5% and by Solvent free Aldol condensation was 71.5%.

➢ The yield of the 3- Bromo Chalcone by Aldol condensation was 64.5% and by Solvent free Aldol condensation was 58%.

➢ The products were purified by Column Chromatography and then re-crystallized. The structure elucidation was done by comparing the MP of both the products with the MP available in literature followed by IR and NMR analysis of the product.

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