Kingdom of Saudi Arabia
Imam Muhammad ibn Saud Islamic University
College of Science
Department of Chemistry

Synthesis and Characterization of 3-(4-chlorophenyl)-1-phenyl-2-propenone

A graduation Research Project

Submitted to the Department of Chemistry in partial fulfillment of the requirements for the completion of the degree of Bachelor of Science in Chemistry

BY

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Abstract

In this project, 3-(4-chlorophenyl)-1-phenyl-2-propenone was synthesised by Claisen-Schmidt condensation between a *p*-chlorobenzaldehyde and an acetophenone in sodium hydroxide, yielding approximately 59% product. The structure of 3-(4-chlorophenyl)-1-phenyl-2-propenone was confirmed by FT-IR spectroscopy.

الملخص:

في هذا المشروع، تم تحضير ٣-(٤-كلوروفينيل)-١-فينيل-٢-بروبينون بواسطة تكاثف كلايزن-شميدت بين بارا-كلوروبنزالدهيد وأسيتوفينون في وجود هيدروكسيد الصوديوم، بنسبة إنتاجية تبلغ حوالي ٥٩%. تم تأكيد بنية ٣-(٤-كلوروفينيل)-١-فينيل-٢-بروبينون بواسطة مطيافية الأشعة تحت الحمراء.

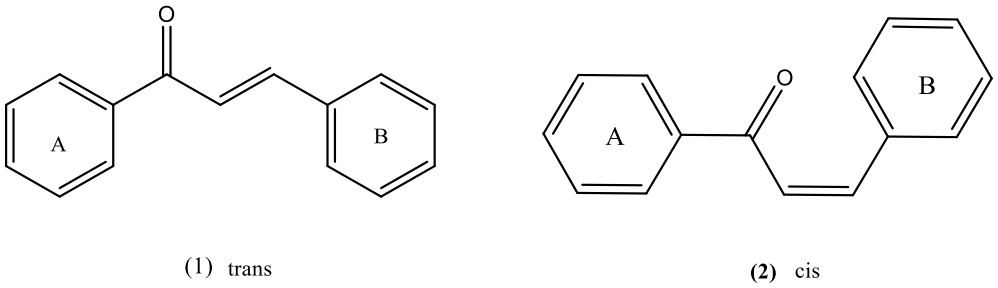
List of Abbreviations

Celsius	**°C**
Centimetre -1	**cm^{-1}**
1,8-Diazabyciclo[5.4.0]undec-7-ene	**DBU**
Fourier transform infrared spectroscopy	**FTIR**
Milliliter	**Ml**
Melting point	**M.P.**
Microwave	**MW**
Potassium Bromide	**KBr**
Hydroxide Potassium	**KOH**
Percent sign	**%**
Sodium hydroxide	**NaOH**
Tetrahydrofuran	**THF**

1. Introduction

Chalcone moieties are common building blocks of flavonoids found in many natural products such as vegetables, fruits, teas, etc. and they can also be synthesised in the lab. They are also known as 1,3-diphenyl-2-propen-1-ones and play an essential role in the biosynthesis of flavonoids and isoflavonoids. The term "chalcone" comes from the Greek word "chalcos" which means "bronze" and they are recognised for their polyphenolic structure and vibrant colours ranging from yellow to orange. [1–3]

Their core structure features an α,β-unsaturated carbonyl system that links two aromatic rings, typically existing in either the (E) or (Z) configuration. In nature, the trans (E) isomer is more common because it is more stable whereas the cis (Z) isomer is less stable due to steric hindrance between the carbonyl group and the A-ring (Figure 1). Chalcones are important not only as precursors in biosynthesis but also for their structural variety and associated biological activities [4].



(1) trans (2) cis

Figure 1: Structurer of chalcone

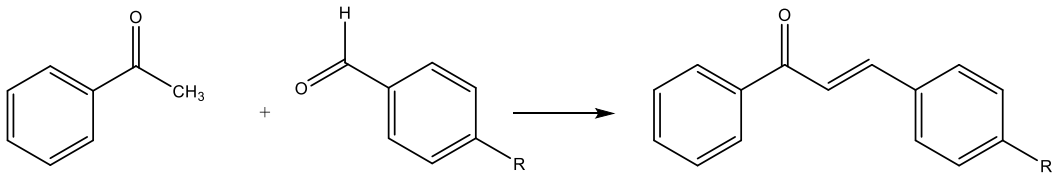
Chalcones contain both a ketone and an aldehyde, forming a structure known as an enone. Some other names of chalcones include aldol products, benzalacetophenone and phenyl styryl ketone [5]. Natural chalcones are crystalline solids that are stable and soluble in organic solvents and acidic and alkaline water producing a deep red or orange-red colour. A pink hue from concentrated sulphuric acid indicates a positive Wilson test, and when treated with alcoholic ferric chloride, chalcones can show a range of colours [6]. They also possess various biological properties including anti-inflammatory, antimicrobial, antifungal, antioxidant, and anti-tumor effects [7].

2. Synthesis of chalcones derivatives

There are several methods for the synthesis of chalcones using conventional catalysts including:

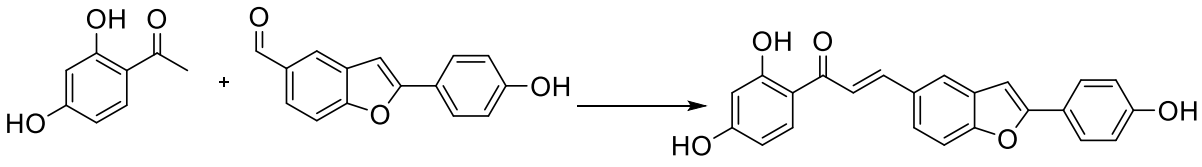
2.1.Claisen-Schmidt condensation

The Claisen-Schmidt condensation reacts acetophenone **(3)** with benzaldehyde **(4)** in the presence of acetic acid, potassium hydroxide, and ethanol for 24 hours to form chalcone derivatives **(5)** [8].



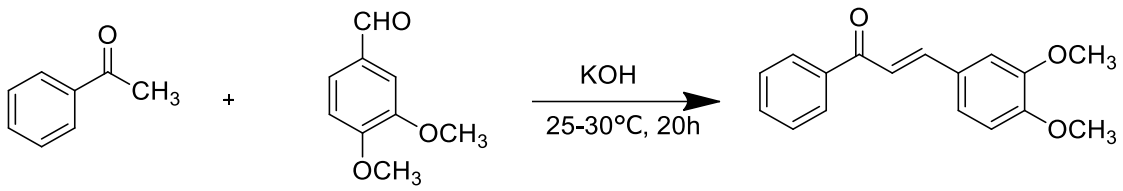
(3) **(4)** **(5)**

(E)-1-(2,4-dihydroxyphenyl)-3-(2-(4-hydroxyphenyl)benzofuran-5-yl)prop-2-en-1-one **(8)** is synthesised by reacting of 1-(2,4-dihydroxyphenylethenone)**(6)**, with 2-(4-hydroxyphenyl)benzofuran-5-carbaldehyde **(7)** in the presence of Et_3N [9].



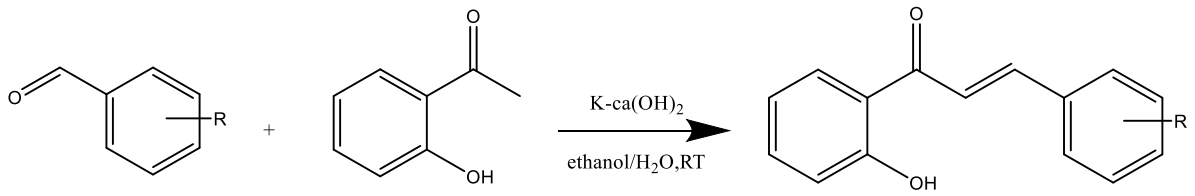
(6) **(7)** **(8)**

The chalcone derivative **(10)** was prepared by the condensation of acetophenone **(3)** with veratr aldehyde **(9)** in the presence of KOH [10].



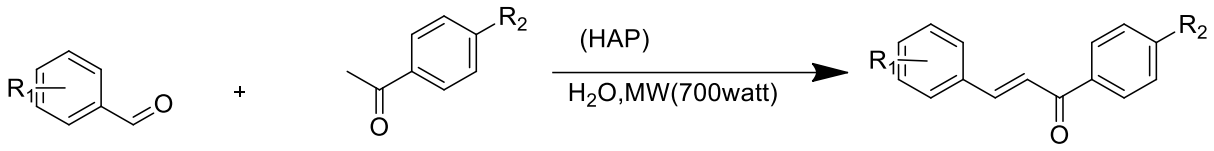
(3) **(9)** **(10)**

The chalcone derivatives **(13)** were prepared via Claisen-Schmidt condensation of benzaldehyde derivatives **(11)** with 2-hydroxy acetophenone **(12)** in the presence of K-$Ca(OH)_2$ isolated from eggshell waste [11].



(11) **(12)** **(13)**

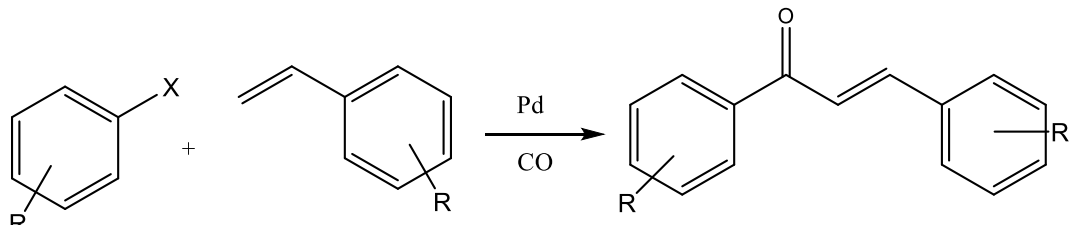
Solhy *et al*. reported the synthesis of several chalcone derivatives **(15)** through the condensation of benzaldehyde derivatives **(11)** with acetophenone derivatives **(14)** in the presence of hydroxyapatite (HAP) in water under microwave irradiation [12].



(11) **(14)** **(15)**

2.2. Heck's coupling reaction

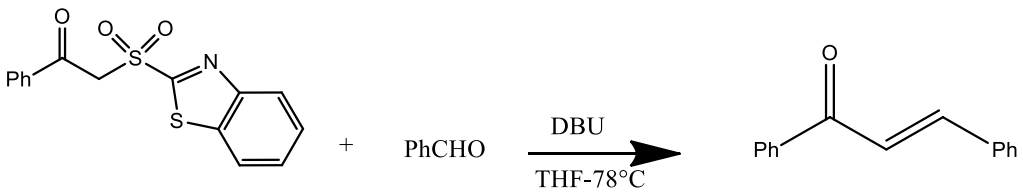
The treatment of aryl halide **(16)** and styrene derivatives **(17)** in the presence of monoxide and palladium as a catalyst produces chalcone derivatives **(18)** [13].



(16) **(17))** **(18)**

2.3. Julia coupling reaction

The reaction of Juliae-Kocienski olefination is described as a new application for the synthesis of chalcones derivatives **(21)** by reacting BT-sulfone1 **(19)** and benzaldehyde **(20)** in the presence of DBU as a base [14].

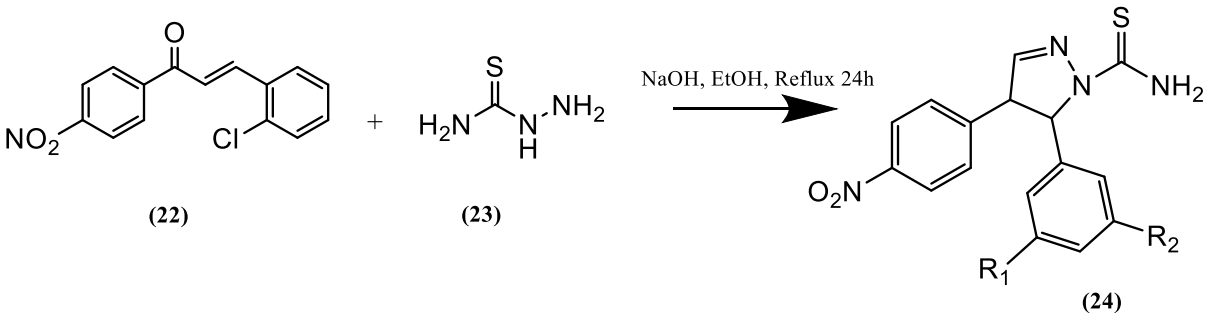


(19) **(20)** **(21)**

3. Reactions of chalcones derivatives

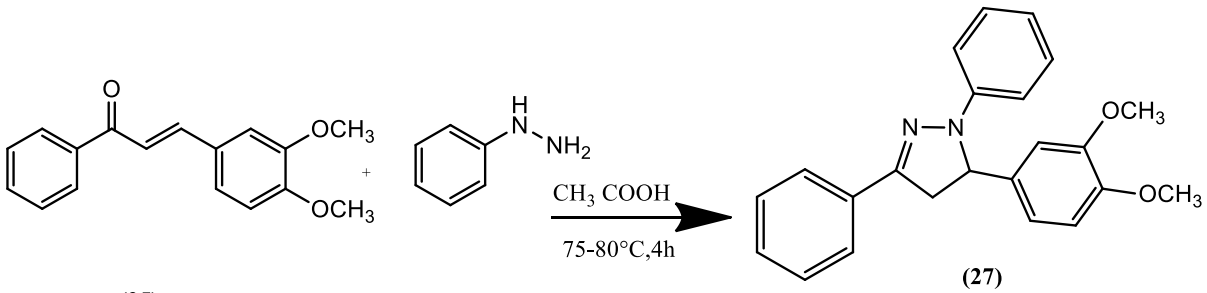
3.1. 3.1 Synthesis of pyrazoline derivative

Synthesis of pyrazoline derivative **(24)** *via* the one-pot reaction of chalcone **(22)** and thiosemicarbazide **(23)** in the presence of sodium hydroxide [15].



(22) **(23)** **(24)**

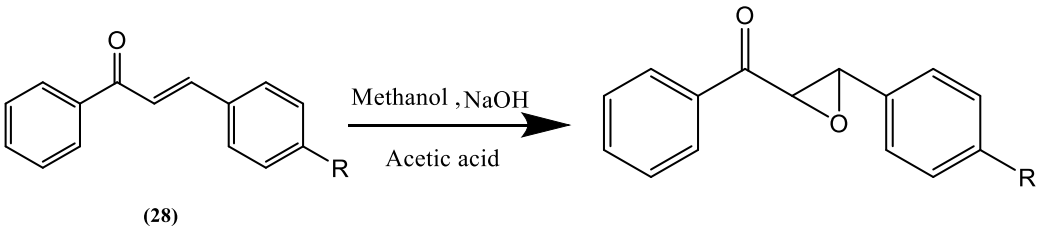
The condensation of chalcone **(25)** with phenylhydrazine **(26)** in the presence of acetic acid produces (3,4-dimethoxyphenyl)-1,3-diphenyl-4,5-dihydro-1H-pyrazole **(27)** [10].



(25) **(26)** **(27)**

3.2 Synthesis of epoxidation

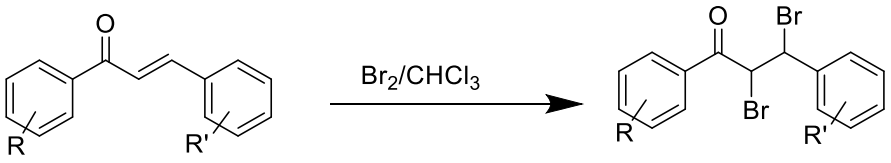
The condensation of chalcone derivatives **(28)** in the presence of methanol, sodium hydroxide and acetic acid produces chalcone-epoxide derivatives **(29)** [8].



(28) **(29)**

3.3 Synthesis of 2,3-dibromo chalcones

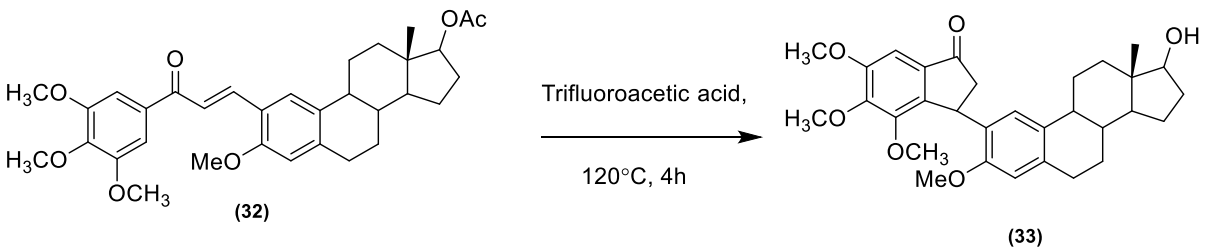
The synthesis of the 2,3-dibromo chalcones derivatives **(31)** was achieved by the reaction of chalcone derivatives **(30)** in the presence of bromine in chloroform [16].



(30) **(31)**

3.4. Synthesis of indanone derivative

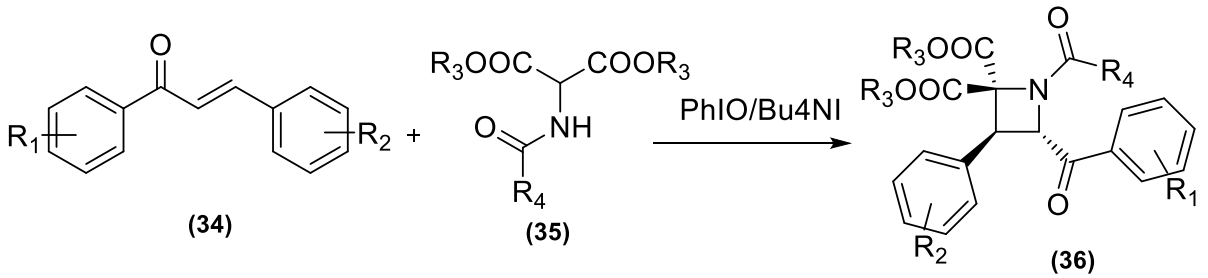
Zhu and coworkers reported the synthesis of a steroidal indanone derivative **(33)** by the reaction of steroidal chalcone **(32)** in the presence of trifluoroacetic acid [1]**.**



(32) **(33)**

3.5. Synthesis of azetidine derivatives

Ye *et.al.* synthesized azetidine derivatives **(36)** by condensation of 2-aminomalonates **(35)** with chalcone derivatives **(34)** in the presence of $PhIO/Bu_4NI$ under grinding [17].

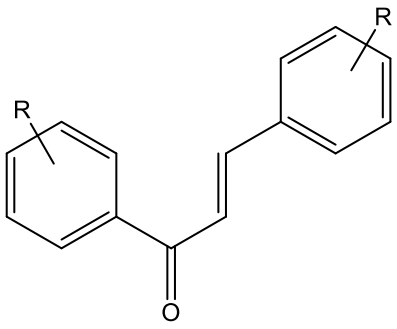


(34) **(35)** **(36)**

4. Medicinal applications of chalcones

4.1 Antiprotozoal activity

Souza *et al*. reported the synthesis of chalcone derivatives **(37)** by Claisen-Schmidt condensation between acetophenone and aromatic aldehydes using basic catalysts at room temperature. The three novel compounds **(37)** exhibited potential antiprotozoal activities [18].



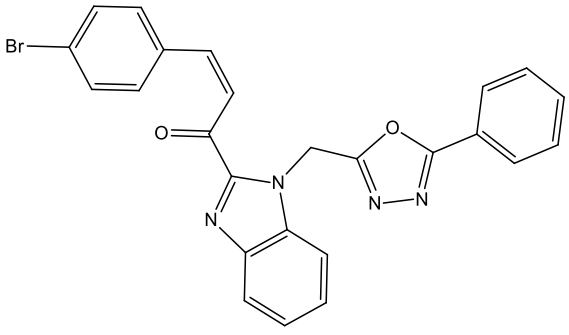
(37)

H	1-naphthyl
4'-OCH_3	1-naphthyl
4'-OCH_3	4-COH_3
3,4-methylendioxy	1-naphthyl

.

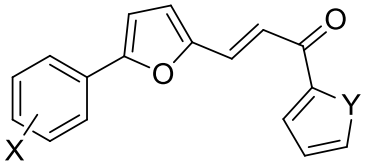
4.2 Antibacterial activity

The chalcone **(38)** possessed the most potent antibacterial activity [19].



(38)

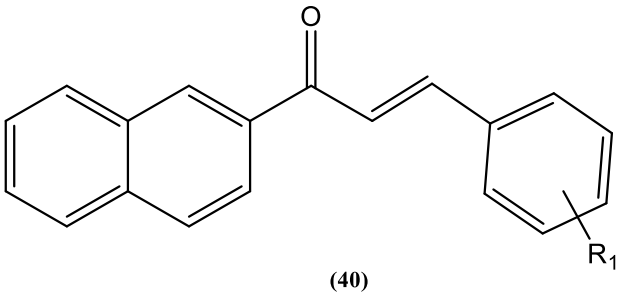
Abdula *et al* reported the synthesis and potent anti-antibacterial activity of (*E*)-chalcone derivatives **(39)** [20].



(39)

4.3 Antifungal activity

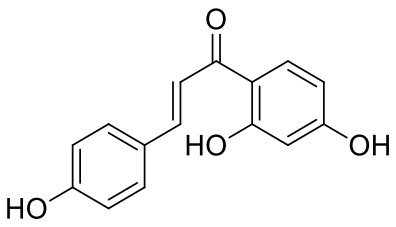
Nadia *et al*. synthesised chalcone derivatives **(40)** by treating 2-acetyl naphthalene with benzaldehyde in methanol and potassium hydroxide which exhibited antifungal activities [21].



(40)

4.4 Cardio-cerebrovascular diseases

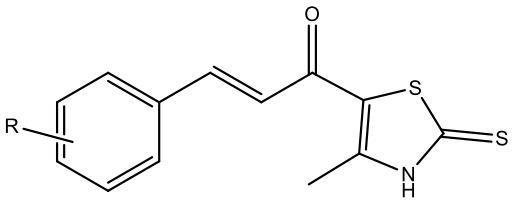
Zhan *et al.* reported that isoliquiritigenin **(41)** could be used to treat cardio-cerebrovascular diseases [22].



(41)

4.5 Anticancer activity

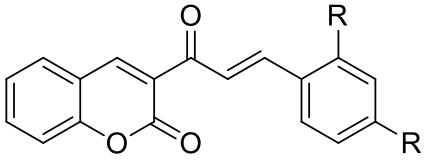
Hashem *et al.* reported the synthesis and anticancer activity of a series of thiazole chalcones **(42)** [23].



(42)

4.6 Antioxidant activity

Osipova *et al.* synthesised a chalcone derivative **(43)** by condensation between 3-acetyl-chromen-2-one with 2,4-dihydroxy- and 4-hydroxybenzaldehydes in the presence of piperidine which exerted anti-oxidant activities [24].



(43)

5. Experimental

5.1. Materials

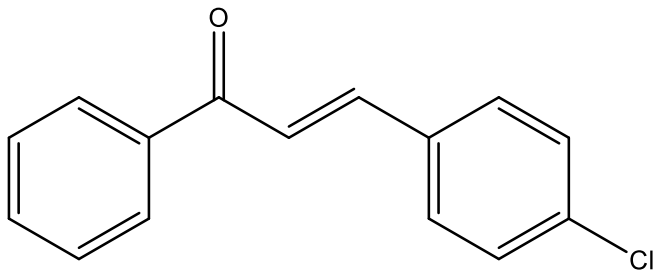
Acetophenone, ethanol and p-chlorobenzaldehyde were obtained from Sigma Aldrich.

5.2. Physical measurements

Melting ranges has been determined via Stuart apparatus SMP 30 melting point. The FT-IR spectra were collected on the use of KBr pellet on IR Prestige-21 SHIMADZE .

5.3. Synthesis of 3-(4-chlorophenyl)-1-phenyl-2-propenone (III)

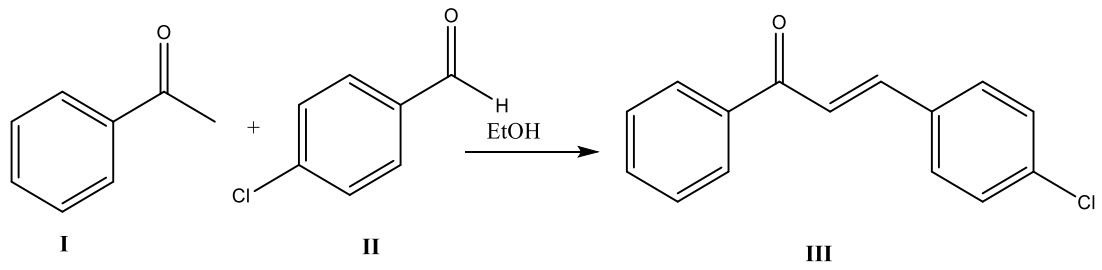
A mixture of acetophenone **I** (0.41 ml) and p-chlorobenzaldehyde **II** (0.5 g, 0.0035 mol) in ethanol (9 ml) and 20% NaOH solution (1 ml) were stirred for 30 minutes and left overnight. The obtained precipitate was filtered and recrystallization from ethanol to yield 0.5 g (59%) of compound **III (**M.P. 170°C). FT-IR (KBr, υ/cm^{-1}) : 3075 (C-H Ar.str.) , 2924 (C-H). 1648(C=O), 1627 (C=C), 1565, 1490 (C=C Ar).



(III)

5.4. Results and Discussion

The reaction of acetophenone **I** with p-chlorobenzaldehyde **II** in ethanol as a solvent under stirring at room temperature for 30 minutes yielded 3-(4-chlorophenyl)-1-phenyl-2-propenone **III** as shown in scheme 1. The structure of product **III** was confirmed by FT-IR spectrometry.



I **II** **III**

Scheme 1: Synthesis of 3-(4-chlorophenyl)-1-phenyl-2-propenone **III**

The FT-IR spectrum of compound **III** showed absorption of weak bands at 3075 cm^{-1} attributed to the stretching of aromatic C-H and 2924 cm^{-1} for the stretching of olefin C-H. The medium intensity bands at 1648 and 1627 cm^{-1} were due to stretching a carbonyl group (C=O) and alkene (C=C), respectively. The bands at 1565 and1490 cm^{-1} for stretching of aromatic C=C.

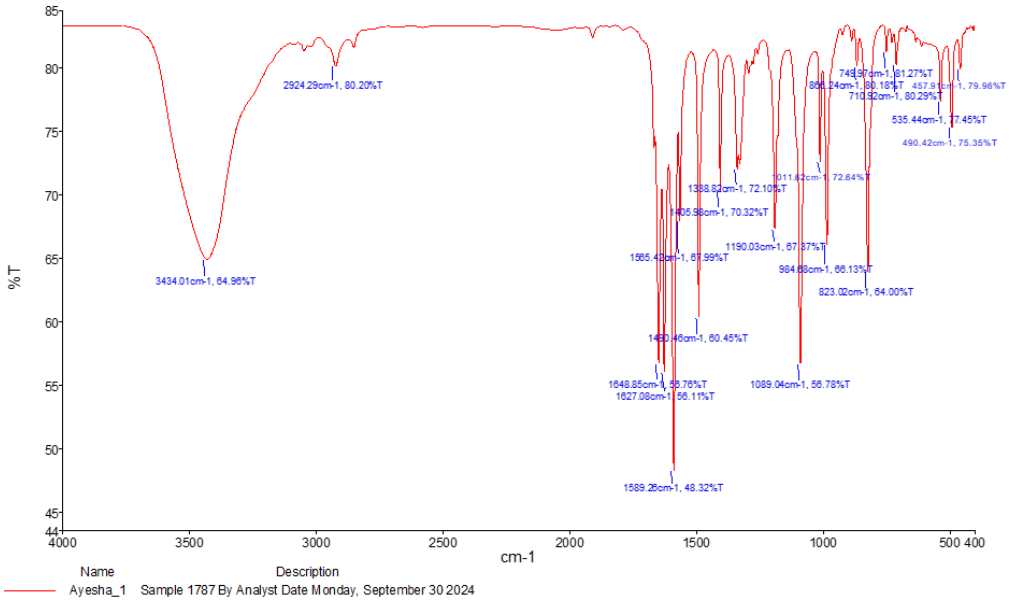
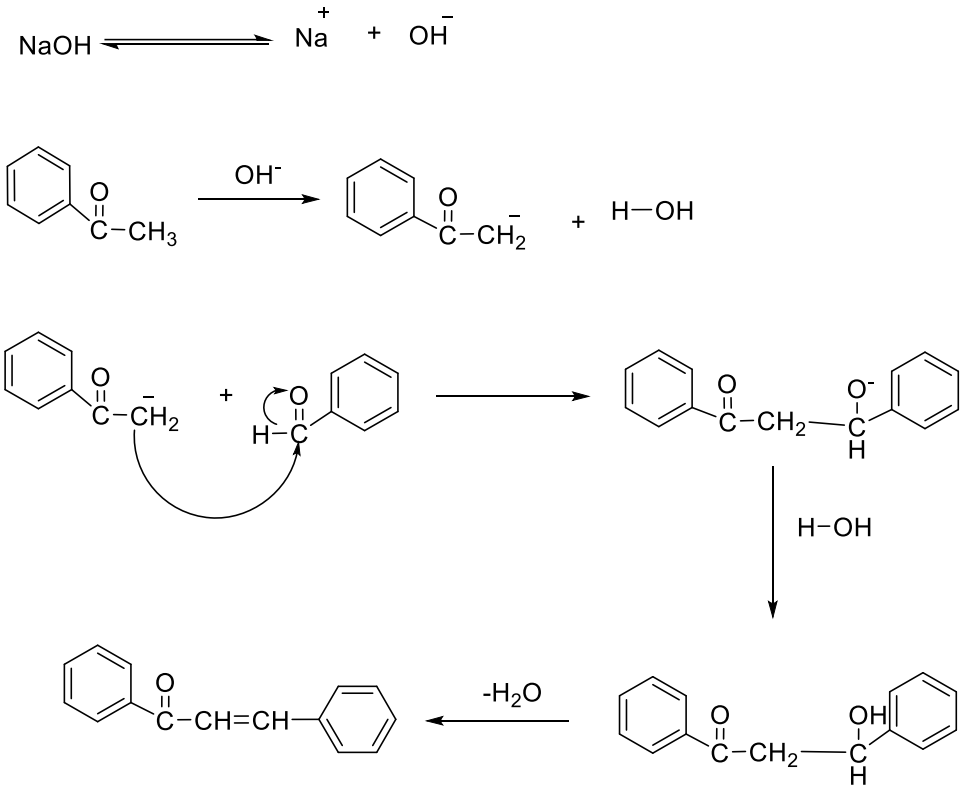


Figure 2: The Infrared spectrum of compound **III**

The proposed mechanism for the synthesis of 3-(4-chlorophenyl)-1-phenyl-2-propenone **III** is presented in the following scheme 2 [10].



Scheme 2: Proposed mechanism to the Synthesis of 3-(4-chlorophenyl)-1-phenyl-2-propenone **III .**

6. Conclusion

In conclusion, Chalcone derivatives are an important group of organic compounds that have gained significant attention because of their diverse biological activities and various chemical applications. In this project, we proposed, 3-(4-chlorophenyl)-1-phenyl-2-propenone was synthesized and characterized by Classes-Schmidt condensation between a 4-chlorobenzaldehyde and an acetophenone in the presence of Sodium hydroxide. The structure of chalcone **(III)** was confirmed by FT-IR spectroscopy.

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EDUCATION

IMAM MOHAMMAD BIN SAUD ISLAMIC UNIVERSTY
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SKILLS

- TEMWARK
- PROBLEM-SOLVING
- TEAM LEADRSHIP
- ORGANIZATION ANS TIME MANAGEMENT
- USE MICROSOFT PROGRAM

COURSES

- FUNDMENTALS OF MICROSOFT OFFICE PROGRAMS
- FIRST AID COURSE

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EDUCATION

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SKILLS

- PROBLEM-SOLVING
- TEAMLEADRSHIP
- ORGANIZATION ANS TIME MANAGEMENT

COURSES

- Water quality standards, techniques and laboratory measurements
- Requirements for the competence system of testing and calibration laboratories according to the international standard ISO 17025
- Occupational safety and health in chemical laboratories

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I'm seeking to work a job with an in environment which provides career advancement to Gain new experiences and skills, develop my good scientific knowledge, and be an effective member in the work environment.

EDUCATION

IMAM MOHAMMAD BIN SAUD ISLAMIC UNIVERSITY
Bachelor's degree in chemistry

SKILLS

- Leadership
- Teamwork
- Communication skills
- Work under pressure

COURSES

- Control of Substance Hazardous to Health
- Occupational safety and health according to OSHA standards
- Good manufacturing practice (GMP) certified by: TVTC 60 hours

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A dedicated chemistry student at Imam University, with a strong foundation in analytical and organic chemistry. Skilled in laboratory techniques, data analysis. Passionate about applying chemistry knowledge to solve real-world problems. Eager to contribute to academic and research excellence.

EDUCATION

IMAM MOHAMMAD BIN SAUD ISLAMIC UNVERSTY
BACHELOR SDEGREE IN CHEMISTRY

SKILLS

- **TEAMWORK**
- **CHEMICAL SAFETY AND HANDLING**
- **PROBLEM – SOLVING**
- **ANALYTICAL SKILLS**
- **USE MICROSOFT PROGRAM**

COURSES

General requirements for the competence of testing and calibration laboratories.

Fundmentals of Microsoft office programs

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