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SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL EVALUATION OF SOME NOVEL PYRIMIDINE- BASED CHALCONE DERIVATIVES

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ABSTRACT

The synthesis and analysis of chalcone and its derivatives are vital in organic chemistry due to their wide-ranging biological activities. Chalcones, characterized as α, β-unsaturated carbonyl compounds, serve as essential intermediates in the formation of various heterocyclic compounds like flavonoids and isoflavonoids. This study involves synthesizing chalcone through the Claisen-Schmidt condensation reaction between acetophenone and m-chlorobenzaldehyde, and subsequently developing a pyrimidine derivative using urea and sodium ethoxide. The reaction progress was tracked with Thin Layer Chromatography (TLC), and the final compounds were characterized using UV, IR, NMR, and GC-MS techniques. The study's objective was to assess the biological properties of these chalcone derivatives, with a focus on their antibacterial activity. The results revealed that the synthesized pyrimidine derivative exhibited notable antibacterial effects against *Escherichia coli*, highlighting its potential for pharmaceutical applications.

KEYWORDS: Chalcone, pyrimidine derivative, claisen-Schmidt condensation, antibacterial activity, *escherichia coli.*

INTRODUCTION

The synthesis of chalcone and its derivatives is a significant focus in organic chemistry, largely due to the wide range of biological activities these compounds exhibit. Chalcones, characterized by their α, β-unsaturated carbonyl structure, are important intermediates in the production of various heterocyclic compounds such as flavonoids and isoflavonoids. The Claisen-Schmidt condensation is a well-known technique used for synthesizing chalcones, involving the reaction of an aldehyde with a ketone in the presence of a base to form the desired chalcone.

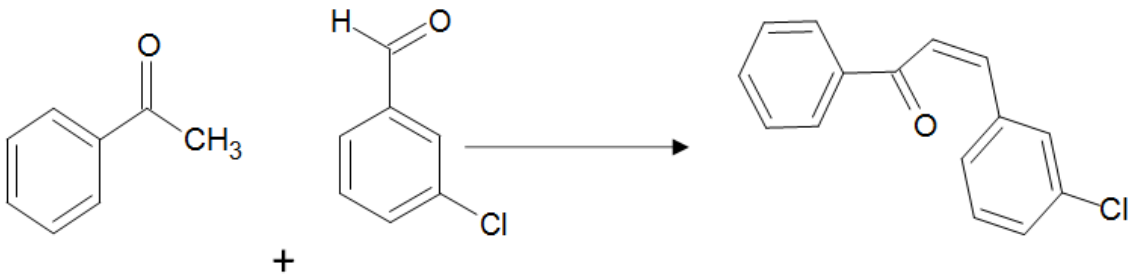
In this study, chalcone was synthesized by reacting acetophenone with m-chlorobenzaldehyde in ethanol, with sodium hydroxide serving as the base catalyst. The resulting chalcone was then reacted with urea and sodium ethoxide to create a pyrimidine derivative. Thin Layer Chromatography (TLC) was used to monitor the progress of the reactions, and the final products were characterized using various spectroscopic methods, including UV, IR, NMR, and GC-MS.

The objective of this research is to synthesize, characterize, and evaluate the biological properties of these chalcone derivatives, with a particular focus on their antibacterial activity. The findings from this study could pave the way for the development of new pharmaceutical agents derived from chalcone compounds.

EXPERIMENTAL

Synthesis of Chalcone

Equal amount of acetophenone and m-chlorobenzaldehyde were mixed with ethanol and add 40% NaOH solution till it become alkaline. This mixture is then incubated for 25^0c for 72 hrs. The precipitate was filtered and then washed with little amount of diethyl ether and recrystallized from ethanol. The completion of reaction was tested by thin layer chromatography using benzene and ethanol (4:1) as mobile phase.

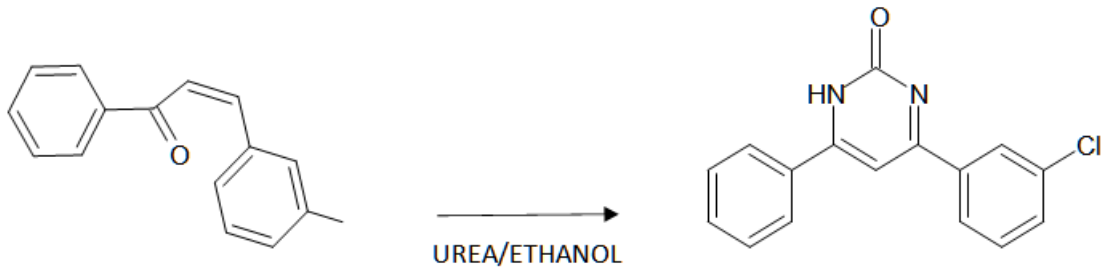


Acetophenone **m-chlorobenzaldehyde** **Chalcone**

Scheme-1: Synthesis of Chalcone.

Synthesis of Chalcone Derivative

Synthesised chalcone and urea were dissolved in absolute ethanol and sodium ethoxide is also dissolved in absolute ethanol and both the solution were mixed together and refluxed for 24 hours and then incubated at 25°C for 48 hours. The precipitate was filtered and completion of reaction was monitored by TLC. The final product is recrystallised by ethanol.



Chalcone **Pyrimidine derivative of chalcone**

Scheme -2: Synthesis of Chalcone Derivative.

RESULTS AND DISCUSSION

Physical Characterization

Compound	Molecular formula	Molecular weight (g/mol)	Colour	Rf value	Solubility
Chalcone	$C_{15}H_{11}ClO$	242.70	Light yellow	0.82	Soluble in chloroform, benzene. Slightly soluble in ethanol and water
Pyrimidine derivative of chalcone	$C_{16}H_{13}ClN_2O$	284.74	light yellow to yellow colour	0.76	Organic solvents such as chloroform, benzene, and ethanol. Slightly soluble in Water and some other polar solvents.

Thin Layer Chromatography

Measured quantity of calcium sulphate was mixed with distilled water, this mixture is then spread on a TLC plate and it is then dried and activated in an oven for 10 minutes at 110^0 c Hexane and ethanol in the ratio 4:1 was taken in beaker and kept for chamber saturation. Sample spotting Sample and chalcone as the reference were dissolved in benzene and spotted using a capillary tube on the TLC plate and allow it to dry. After that place the plate in the mobile phase and allow to reach a height of $3/4^{th}$ and measure the distance travelled by the solvent. Then place the plate in iodine chamber for visualization of spot.

Rf = Distance travelled by the solute / Distance travelled by the solvent

UV Spectroscopy

The absorption maxima of Pyrimidine derivative of chalcone were found to be 317nm.

IR Spectroscopy

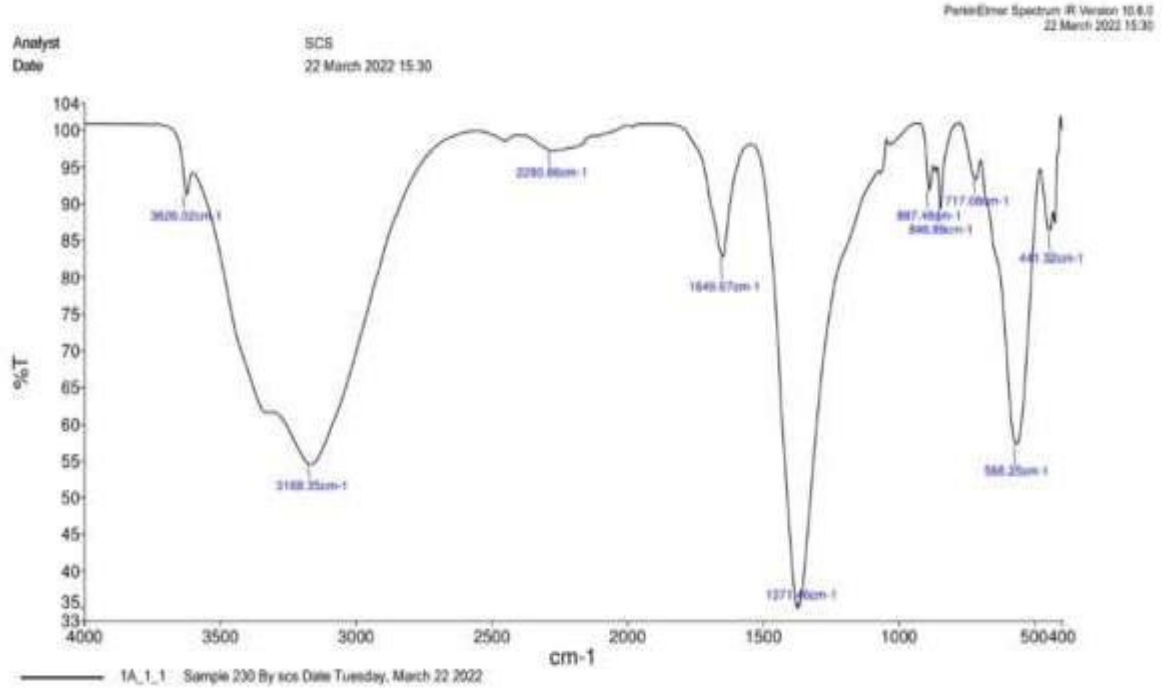
The Infra-Red spectrum of the prepared compound proved to be really helpful in arriving at several conclusions related to establishment of the structure. These conclusions were conducted related with other investigative findings, which were supportive of expected structure for the product.

The spectrum when analyzed showed peaks for the following.

- A sharp absorption at 1649, indicating the C = O stretch, suggestive of carbonyl compound, that too an amide derivative in particular
- A strong absorption at 3168, invading the C – H stretch, suggestive of alkene compound.
- A medium absorption at 3626, was supposed to be

the indication of N – H stretch in amides.

- A sharp and strong absorption at 1371 were suggestive of C – N stretch in amides/ amines.
- Bending vibrations of C = C, in alkenes were identified by the absorptions at 887.
- The stretch of C – Cl, was understood by the absorption at 846.
- Aromatic C – H bending, identified by signal at 717.



Source Spectra Results	
Spectrum Name	Number Of Peaks
1A_1_1	10

List of Peak Area/Height		
Peak Number	X (cm-1)	Y (%T)
1	3626.02	91.30
2	3168.35	54.51
3	2280.86	97.24
4	1649.67	82.74
5	1371.46	34.90
6	887.48	91.89
7	846.89	89.28
8	717.08	93.35
9	566.25	57.34
10	441.32	86.54

Figure 1: IR spectrum of chalcone derivative.

NMR Spectroscopy

The spectrum when analyzed showed peaks for the following.

- singlet at 3.343 'H' of N-H
- peak at 2.3 to 2.6 ‘H' of CH in 'C=CH’ linkage
- peak at 7.1 to 7.4 ‘H' of aromatic ring

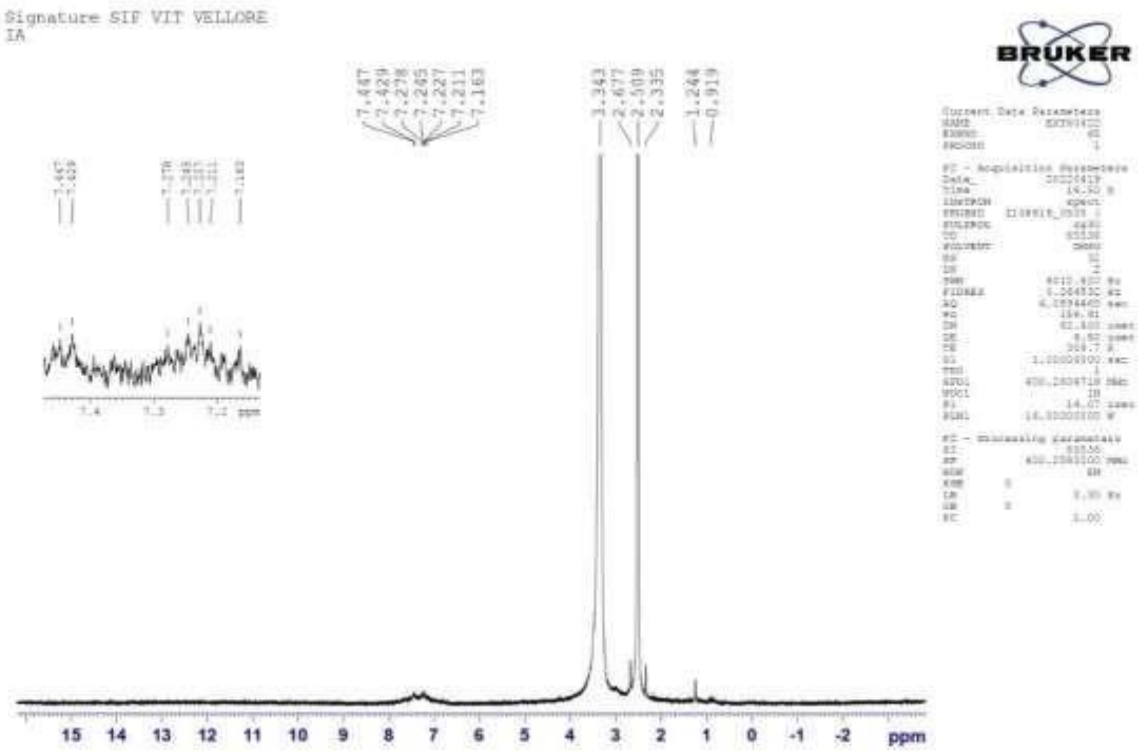


Figure 2: NMR spectrum of chalcone derivative.

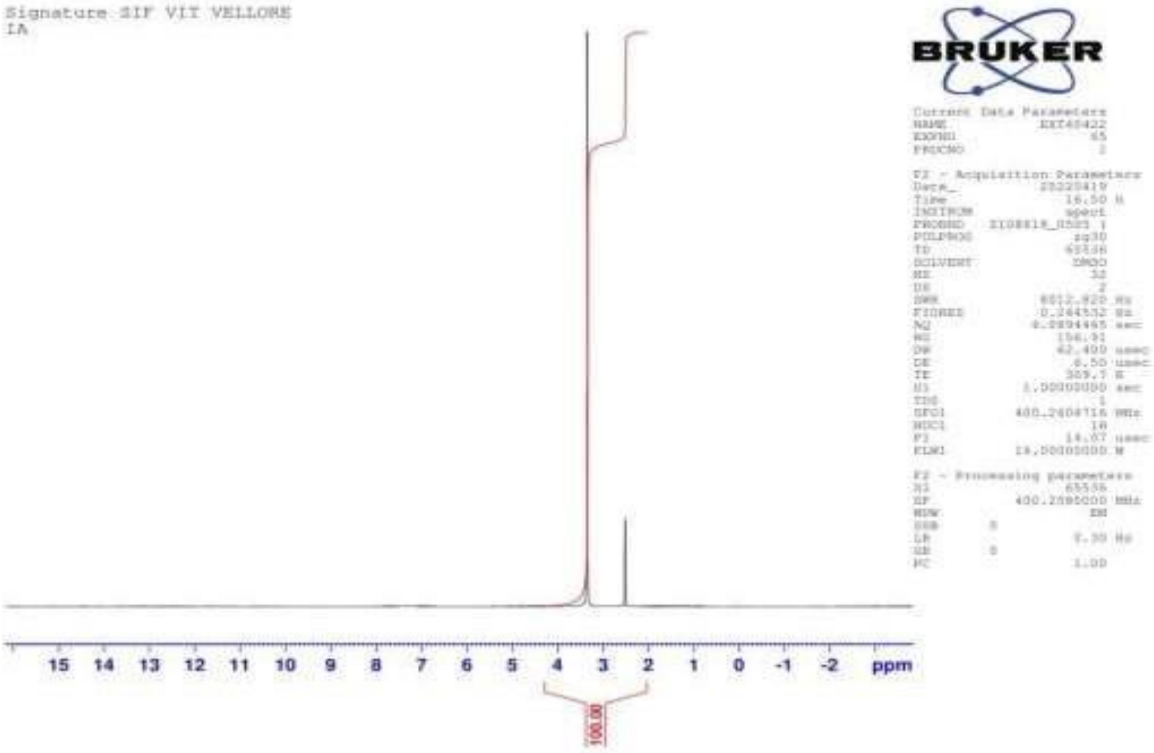
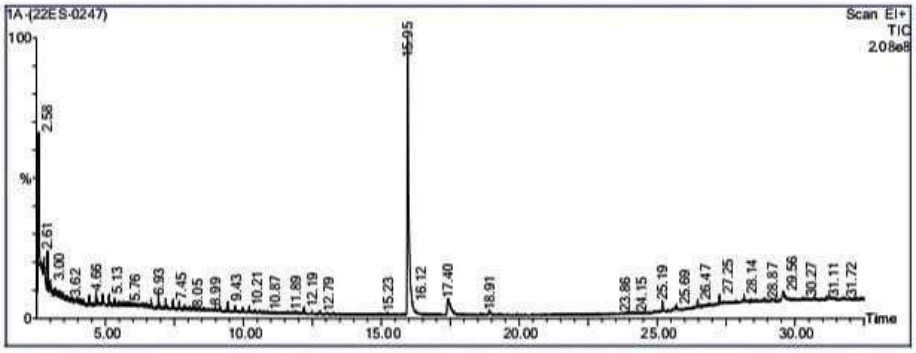


Figure 3: NMR spectrum of chalcone derivative.

GC MASS Spectroscopy

The chromatogram of GC analysis showed the appearance of peak at a value of 15 Rt. There were no other peaks to be considered in the chromatogram suggesting any presence of unreacted components. There were peaks which were very negligible and too low in intensity to be counted as a by-product.



#	RT	Scan	Height	Area	Area %	Norm %
1	4.419	384	7,476,485	282,601.1	1.773	2.34
2	4.664	433	10,201,017	362,071.2	2.272	2.99
3	4.894	479	7,971,188	334,093.2	2.097	2.76
4	5.330	566	5,728,114	245,010.3	1.538	2.03
5	6.925	885	9,442,258	271,296.9	1.702	2.24
6	7.185	937	7,901,395	263,632.1	1.654	2.18
7	15.954	2690	203,934,416	12,090,967.0	75.875	100.00
8	17.405	2980	11,613,746	1,402,367.1	8.800	11.60
9	25.188	4536	8,180,081	320,027.0	2.008	2.65
10	29.560	5410	5,195,524	363,223.9	2.279	3.00

Figure 4: Gc Mass Spectrum of Chalcone Derivative.

BIOLOGICAL EVALUATION

ANTIBACTERIAL ACTIVITY

Antibacterial activity is defined as the ability of active principle [drug moiety] to inhibit the growth of bacteria, prevent the formation of microbial colonies or kill the microorganism.

Procedure

Step 1: - Preparation of inoculum

Measure 1.5 g of nutrient broth powder and transfer it to a sterile beaker containing 100ml of distilled water. Place the beaker over the flame and stir the mixture using a sterile glass rod and after boiling turn off the flame and allow it to cool. Then aseptically transfer *Escherichia coli* and incubate it at 24^{o} C for 24 hours.

Step 2: -Preparation of agar media

Measure 9g agar and transfer it to a sterile beaker containing 300ml of distilled water and then boil the solution and allow it to cool. after cooling the solution transfer it to a previously sterilized Petri dish and allow it to form a gel.

Step 3: -Addition of drug

For isolation of individual colonies, the agar plate surface is spread by a volume of microbial inoculum by streak method. After spreading the inoculum, a well is made at the center of petri dish and finally drug of concentration 2mg/ml, 5mg/ml, 0.2mg/ml and 0.5mg/ml was added in the well respectively and incubate it for 48 hours. Zone of inhibition was measured.

RESULT

The result proved that the derived compound had good antibacterial activity at 5 mg/ml concentration with zone of inhibition of 18.22mm diameter against E. coli.

Figure 5: Antibacterial Activity.

CONCLUSION

The synthesis of chalcone and its derivatives is an important area in organic chemistry, mainly because of the wide range of biological activities these compounds can exhibit. Chalcones, identified by their α, β-unsaturated carbonyl structure, play a vital role as intermediates in the production of various heterocyclic compounds. The Claisen-Schmidt condensation is a common method for creating chalcones, involving the reaction of an aldehyde with a ketone in the presence of a base. The purpose of this research was to investigate the synthesis, characterization, and biological activity of these chalcone derivatives, with a particular emphasis on their antibacterial properties. The findings indicated that the pyrimidine derivative synthesized in this study showed notable antibacterial activity, especially against **Escherichia coli**, indicating that these compounds

could be promising candidates for pharmaceutical development.

In summary, the successful synthesis and detailed characterization of chalcone and its pyrimidine derivative highlight their potential as biologically active compounds, suggesting that they could be valuable in future pharmaceutical applications.

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