Synthesis of Chalcone Derivatives and its Anti-Microbiological Activities

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Abstract

Chalcones are organic substances that are naturally found in plants, especially those in the Fabaceae family. fused aromatic rings connected by a 3-C unsaturated carbonyl system make up the chemical building blocks of their basic chemical composition. Chalcones are biologically active in a variety of ways, including as antioxidants, anticancer agents, anti- inflammatory agents, antibacterial agents, and antiviral agents. Scavenging free radicals,inducing cancer cell apoptosis, obstructing the proliferation and division of cancerous cells, and lowering inflammation by preventing the manufacturing of interleukins and enzymes are all abilities of these substances. Also, it has been discovered that chalcones contain antibacterialand antiviral properties that prevent the growth of a variety of bacteria, fungi, and viruses as well as their replication.

Key words:

Chalcone, Chalcone Synthesis, substituted chalcone derivatives, antimicrobial agents

1. INTRODUCTION

A group of chemical compounds known as chalcones is composed of two aromatic rings joinedby a system of α, β-unsaturated carbonyls. They occur naturally in a diverse range of plant species and a few fungi and bacteria and are widely dispersed. They have been the focus of substantial research because of the variety of biological activity they exhibit and the potential therapeutic uses they may have.

Chalcones' antibacterial effects are among their most well-known biological activity. They have been discovered to have activity against a variety of microbes, such as viruses, fungi, andbacteria. According to studies, chalcones can stop bacteria including Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa from growing and multiplying.

Other research has investigated manufacturing chalcone derivatives with particular functionalgroups to

determine their antimicrobial activity. Chalcone derivatives with nitro or chloro substituents, for example, were synthesized and tested for antimicrobial action against a varietyof bacterial strains. The findings revealed that a number of the derivatives had strong antimicrobial properties against the bacteria tested.

Chalcones have a variety of biological properties, including anti-inflammatory, cancer- fighting, antioxidant, anti-diabetic, and antibacterial activity. They have been shown to have effective antimicrobial properties, fungicidal, and antiviral activity against various pathogens. Aspergillus fumigatus, Candida albicans, and Trichophyton rubrum are only a few examples of human pathogenic fungi that chalcones have been discovered to have antifungal efficacy.

Chalcones have been shown to have a strong anti-inflammatory effect by suppressing the generation of pro-inflammatory cytokines and enzymes. They have also shown substantial anticancer efficacy by inducing apoptosis, reducing angiogenesis, and preventing cell cycle progression. Furthermore, chalcones have been shown to exhibit antioxidant action by neutralizing free radicals and defending cells against oxidative stress.

Another innovative technique for synthesizing chalcones is enzymatic synthesis, which utilizesenzymes such as aldolases and transketolases to catalyze the condensation reaction between aldehydes and ketones. This method has the advantage of being environmentally friendly, as itrequires mild reaction conditions and does not generate toxic waste products.

In recent years, there has been growing interest in the synthesis of chalcone derivatives, whichare compounds in which one or both of the aromatic rings are substituted with different functional groups. These derivatives have been synthesized to improve chalcones' biological activity or target specific diseases. Chalcone derivatives have been synthesized using a varietyof methods, including Claisen-Schmidt condensation, Michael addition, and Wittig reaction.

Chalcones have anti-diabetic properties by controlling blood sugar levels, increasing glucose uptake, and blocking glucosidase and aldose dehydrogenase enzymes. They have also demonstrated antimalarial effectiveness by preventing Plasmodium falciparum activity.

Finally, chalcones have a broad spectrum of biological functions and have shown medicinal potential. More research is required into the mechanisms of action of chalcones and their potential as lead compounds for the creation of novel medications. the synthesis of chalcone derivatives and their evaluation for anti-microbial activity is an important area of research thathas the potential to lead to the development of new anti-microbial agents. While many chalconederivatives have been synthesized and evaluated for their anti-microbial activity, further research is needed to fully understand their mechanisms of action and to optimize their anti- microbial properties.

2. EXPERIMENTAL SECTION

MaterialsChemicals

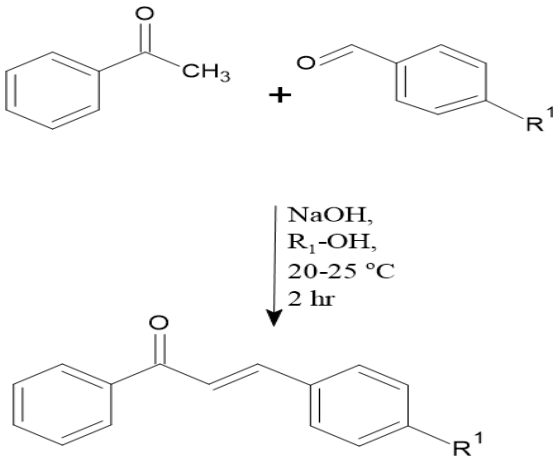
Solvent:
Ethyl aceta n-hexan

1. Acetophenone
2. Sodium hydroxide
3. Methanol
4. 3-nitro Benzaldehyde
5. 4-Hydroxy Benzaldehyde

2.2. Methods

The general procedure of chalcone:

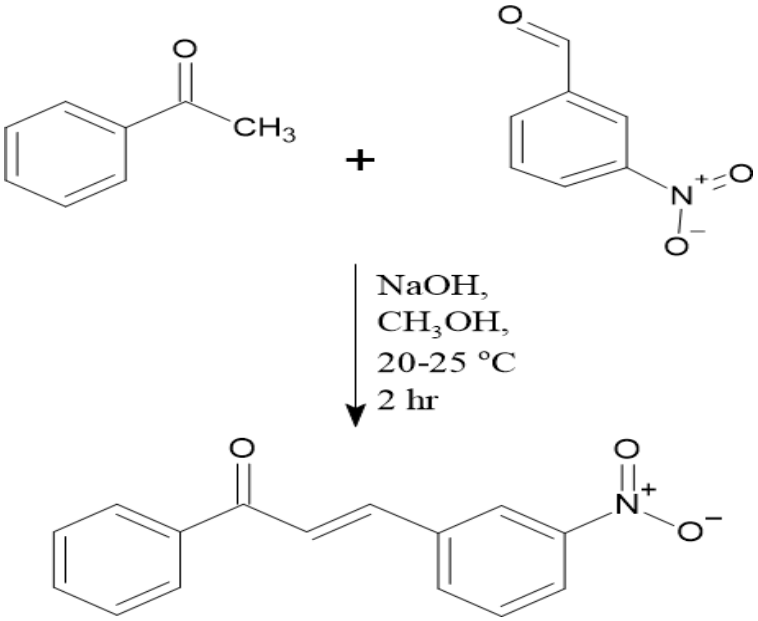
Chalcones were created using a well-documented base-catalyzed Claisen-Schmidt condensation reaction with the right acetophenones and substituted benzaldehydes [16]. In a
250 ml round-bottomed flask with a magnetic stirrer, a combination of benzaldehyde derivatives (1 ml) and acetophenone derivatives (12.7 ml) was dissolved in 10 ml rectified spirit. When the solution become murky after vigorous stirring for two hours, 5.5 gramme of NaOH in 50 ml of distilled water was then added dropwise to the reaction mixture. Using a cold water bath on the magnetic stirrer, the reactiontemperature was kept between 20 and 25 The reaction mixture was neutralised by 0.1–0.2N HCl, which caused the precipitation, aftervigorously stirring for two hours. The unrefined chalcones were filtered out, dried in the air, and recrystallized using rectified



Scheme 1 chalcone derivative

The procedure of chalcone using 3-nitro benzaldehyde

A mixture of acetophenone (6.35 ml), 3-nitrobenzaldehyde (7.15 gm), NaOH (2.5 gm), distilledwater (25 ml), and methanol (15.25 mL) was kept at ambient temperature for 2 h followed by dilution with ice-cold water, acidification with cold dilute hydrochloric acid, and extraction with ether. The purity of the compound was evaluated using thin-layer chromatography usingethyl acetate/ n-hexane as a solvent. And also evaluated by ^{1}H NMR, IR.

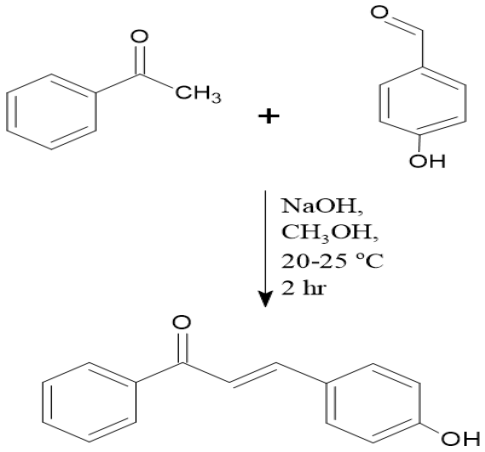


Scheme 2 3-nitro benzaldehyde

Figure 1 3-nitro benzaldehyde solution

The procedure of chalcone using 4-Hydroxy benzaldehyde

A mixture of acetophenone (6.35 ml), 4-hydroxy benzaldehyde (6.765 gm), NaOH (2.5 gm), distilled water (25 ml), and methanol (15.25 mL) was kept at ambient temperature for 2 h followed by dilution with ice-cold water, acidification with cold dilute hydrochloric acid, and extraction with ether. The purity of the compound was evaluated using thin-layer chromatography using ethyl acetate/ n-hexane as a solvent. And also evaluated by ^{1}H NMR, IR.



Scheme 3 p- hydroxy benzaldehyde

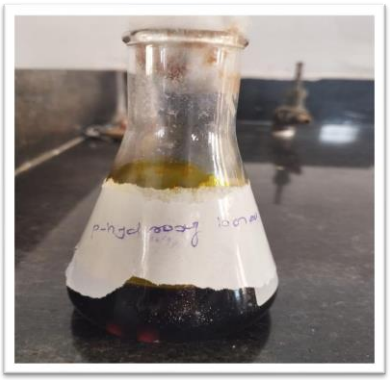


Figure 2 p-hydroxy benzaldehyde solution

Analysis data

No.	Code No.	R	Molecular Formula	Molecular Weight (g/m)	Yield (%)	M.P. °C	C %	H %	N %
1	1a	3- NO2,CHO	C7H5NO3	151.12	72	58.5	55.6%	3.4%	9.3%
2	1b	4-OH	$C_7H_6O_2$	122.12	80	117	68.8%	4.9%	

Antimicrobial activity

As chemists, pharmacists, and doctors first refined the active ingredients from plant and animaltissues, then subsequently from microorganisms and their fermentation by-products, the chemistry of therapeutically relevant compounds was born. Several of these compounds have been linked to therapeutic benefits for frequently poorly understood medical conditions. []. Several of these compounds have been linked to therapeutic benefits for frequently poorly understood medical conditions.

- **Principal:**

A standard inoculum of the test microorganism is used to inoculate agar plates. On the agar surface, paper discs with a diameter of about 6 mm and a desired concentration of the test substance are positioned. The Petri dishes are incubated in the proper environments. The test microorganism's germination and growth are typically inhibited by antimicrobial drugs that diffuse into the agar, and the diameters of the inhibitory growth zones are then determined. If the chemical prevents bacterial growth, a clean zone or ring forms around a disc following incubation.

- **Requirements**

1. Gram Positive OrganismBacillus Subtilis Staphylococcus aureus
2. Gram Negative Organsim

E. coli

Pseudomonas aeruginosa

3. Test Compound
4. Alcohol
5. Sterile Nutrient Agar
6. Glass Spreader
7. Sterile Petri Plates
8. Paper discs
9. Sterile Forceps

➢ **Inoculum preparation**

An appropriate broth was used to emulsify 4-5 colonies of the indicator organism fromthe slope of a stock culture to create the inoculum. The inoculation broth was incubated at 37°C until it reached the McFarland standard of 0.5 turbidity. This occurs in 2 to 8 hours.

➢ **Procedure**

- Use 4 sterile Petri dishes and top them with nutrient agar (autoclaved).
- Using a glass spreader, apply 0.1 mL of your 24-48-hour-old bacterial culture on the surfaceof nutrient Agar dishes.
- Place the disc holding the substance on the agar plates using sterile forceps or a disc dispenser.

- Right away, lightly press it down with the tool to make sure the disc is completely in touch with the agar surface. After a disc has made contact with the agar surface, do not move it again because instantaneous drug diffusion happens.
- For 24 hours, incubate plates at 37°C or another temperature that promotes growth.
- After the incubation period, monitor the zone of inhibition and read and record

Bacterial Images:

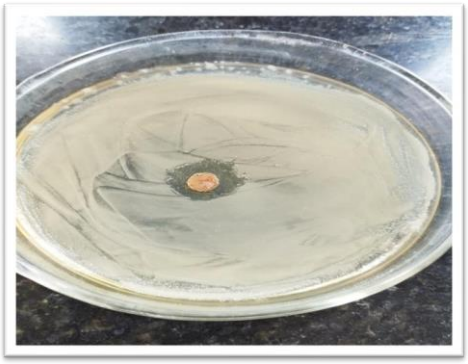


Figure 3 Antimicrobial of Ecoli (-)

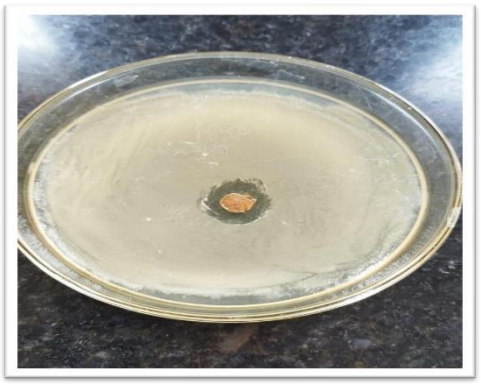


Figure 4 Antimicrobial of Bacillus (+)

Figure 5 Antimicrobial of Ecoil (-)

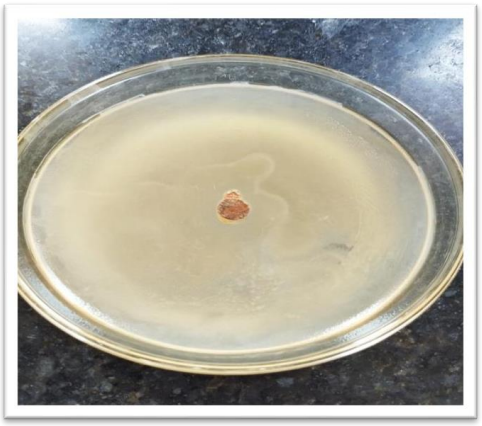


Figure 6 Antimicrobial of Bacillus (

4. RESULT AND DISUCSSION

The results of the current study demonstrated that the green chemistry employed was a powerful instrument that could be utilised to create and produce chalcones in pure water catalysed by sodium hydroxide and to produce,,-unsaturated ketones in high yields. This method isolates the products in nearly pure form without the use of any organic solvents by filtering the final aqueous reaction mixture after it had cooled to room temperature. The structures of the generated compounds were verified by IR, elemental microanalysis (CHN), and other physicochemical criteria. The synthetic chalcone derivatives displayed severaldistinct, crisp bands in the infrared spectrum, with the bands between 1635 and 1660 cm-1 showing the presence of the carbonyl C=O group of the generated ketone, which was conjugated to both aromatic and alkene systems. The fundamental microanalysis revealed thatthe results and the estimated percentages agreed well. The percentage differences between theestimated and observed values were found to fall within the realm of accurate estimation.ThermoCal10 melting point apparatus (Analab scientific Pvt. Ltd.) was used to determine the melting points, which are uncorrected. Aluminum sheets that had silica gel 60 F254 percolated through them underwent TLC.

None of the chemicals were purified before use; they were all of LR grade. The aldehydes, ethanol, sodium hydroxides, and phenyl urea utilised came from Merck in Bombay, India. Allthe solvents were used exactly as they were sent by Merck in Mumbai, India.

CHARACTERISATION

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INFRARED SPECTROSCOPY

Although it does not provide comprehensive details on the molecular structure of organic compounds, the infrared spectroscopy approach is a valuable tool for determining the precisefunctional group for the identification of inter and intra-group interaction in compounds. Theidentification of compounds is how

it is employed, though.

The infrared spectroscopy method provides details on the atom's dipole, or more precisely, how it goes from the lower ground level to the upper exited level molecule. Because of this property, it is extremely helpful to organic chemists.

1) Synthesis of chalcone by using 2- hydroxy benzaldehyde

Examination of IR spectra reveals that all the compounds of chalcone showed a strong absorption near at 1644-1618 cm^{-1} and at 1685-1666 cm^{-I} demonstrating the existence of - CH=CH- and C—O group. The FT-IR Spectra of anisaldehyde revealed at the broadband at 1651 cm^{-1} were observed for the OH group, and the stretching vibration shows the existence ofthe OH group. Also, the shifting of the band confirms the OH group presence in the chalcone for the chalcone derivative.

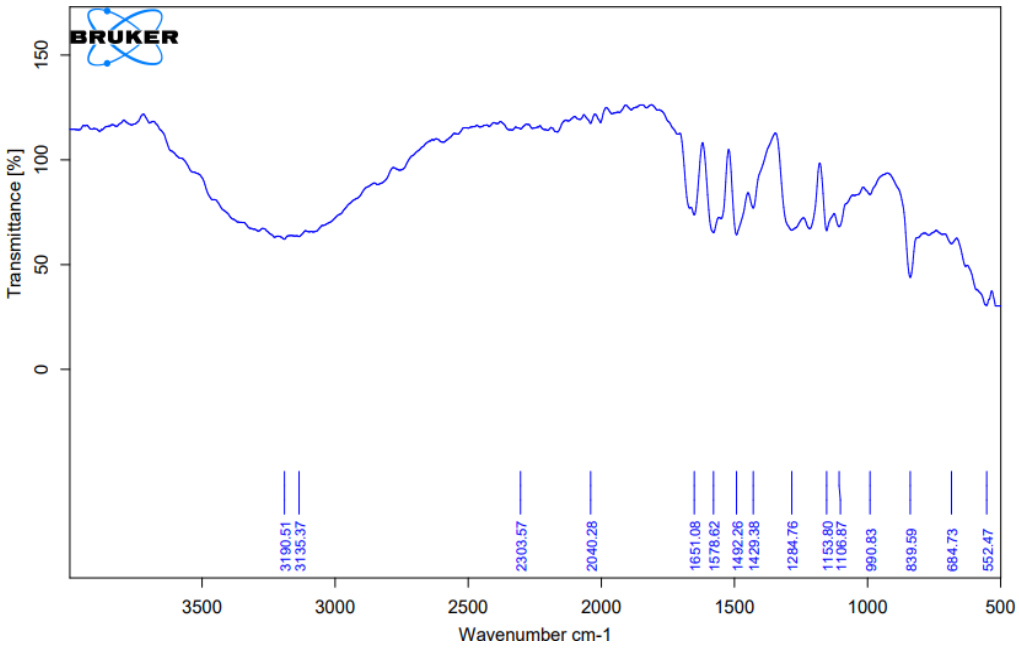
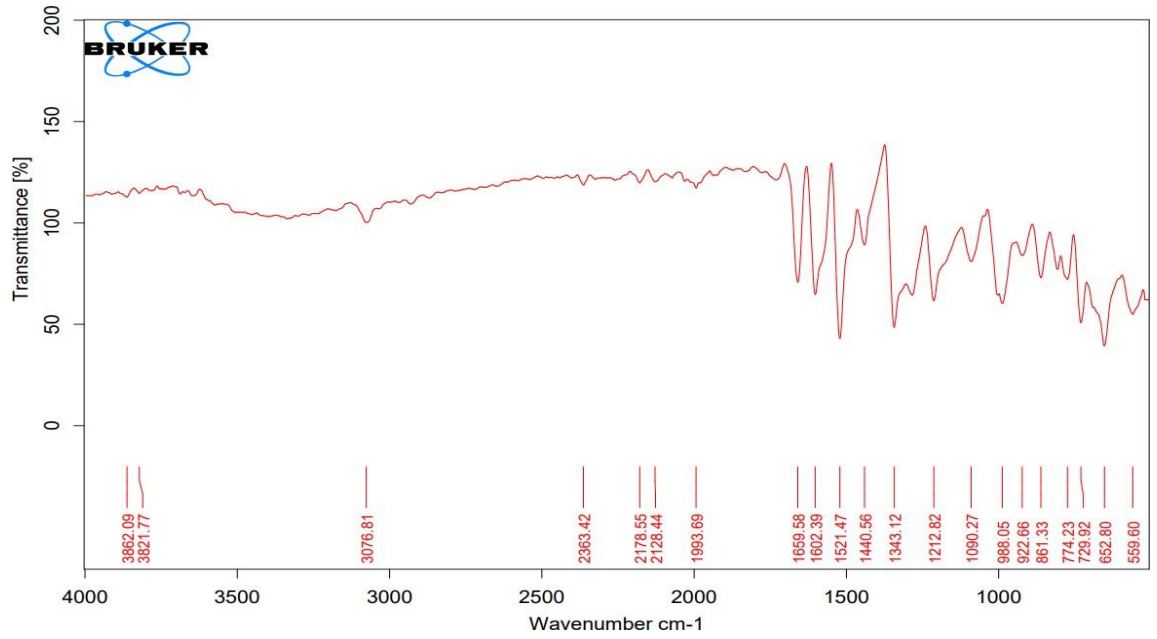


Figure 7. FT-IR Spectra of 2-hydroxybenzaldehyde

2) synthesis of chalcone by using 3-nitro benzaldehyde

IR spectra reveal that all the derivatives of chalcone were displayed. A strong absorption near1644-1618 cm^{-1} and at 1685-1666 cm^{-I} indicates being present -CH=CH- and C-O group. Fromfigure 8. The IR bands at 1669 cm-1 indicate that the 3-nitro group is present in the chalcone-derived substance and it's due to the shifting of bands at the region of the chalcone derivative.

Figure 8 .FT_IR spectra of 3-nitro benzaldehyde



NMR

A complementary method to IR spectrum analysis for eliciting specific information about the structure of organic compounds is nuclear resonance (NMR) spectrum analysis. The techniqueis known as PMR (Proton Magnetic Resonance) spectrum analysis since the nucleon is the most often investigated nucleus.

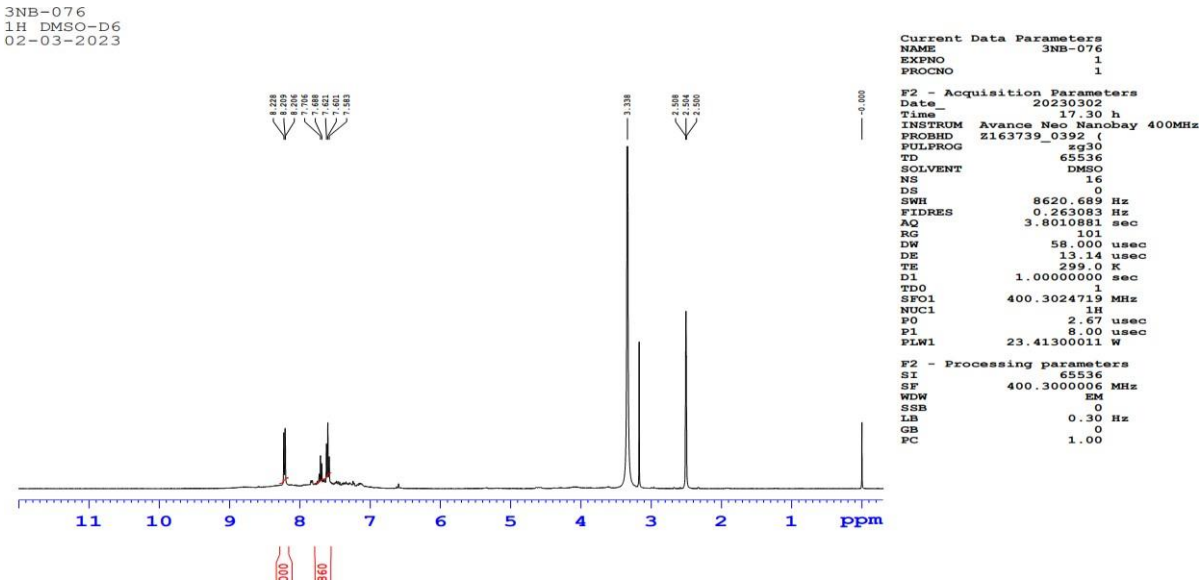
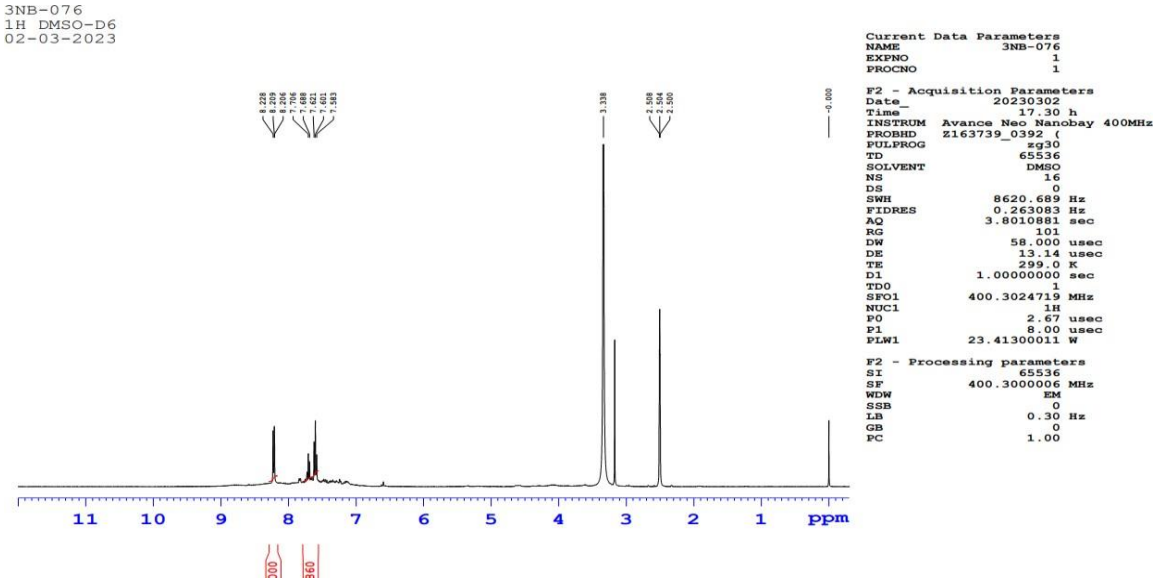


Figure 9. 3-nitro benzaldehyde

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5. CONCLUSION

The acquired results demonstrated that the synthesised chalcones analogues exhibit mild antibacterial activities, including those against Staphylococcus aureus. The outcomes have highlighted the significance of the locations of the electron-releasing groups (such as the methoxy and hydroxy groups or

When compared with the reference standard amoxicillin at both 0.5 ml (500 g) and 1 ml (1000 g) concentration levels, compounds 2 and 4 in the B ring showed superior antibacterial efficacythan other compounds. As compared to the reference standard fluconazole at concentrations of
0.1 ml (100 g), 0.5 ml (500 g), and 1 ml (1,000 g), findings from fungicidal screening showedthat chalcones with a pharmacophore such a nitro group have demonstrated stronger antifungalactivity than other chalcones. Concentration values of 1 ml (1000 g).

These findings imply that the heterocyclic derivatives can serve as a good design and development template for antibacterial products that are intended for commercial use. To clarify their mode of action, more research is required.

action. While reviewing the antimicrobial findings, it was found that there was an interesting structure-activity link, with electron-donating groups tending to diminish the antifungal activity and electron-withdrawing groups tending to boost the potency.

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