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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION AND SCHIFF BASES N1, N3-DI (E)-BENZYLIDENE MONOHYDRIDE DERIVATIVES

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ABSTRACT

Schiff bases and their derivatives have attracted considerable attention in recent years due to their versatile applications in medicinal, pharmaceutical, and coordination chemistry. These compounds, typically formed through the condensation of primary amines with aldehydes or ketones, are known for their broad spectrum of biological activities, including antimicrobial, antifungal, anticancer, and anti-inflammatory properties. In the present study, the synthesis, structural characterization, and spectroscopic analysis of N1, N3-di(E)-benzylidene monohydrazide Schiff base derivatives were carried out to explore their potential utility in pharmaceutical chemistry. The synthesis was achieved via a condensation reaction between aromatic aldehydes and a dihydrazide precursor under mild reaction conditions, yielding the desired Schiff bases in good yields. The structures of the synthesized compounds were elucidated using a comprehensive suite of analytical techniques. Fourier-transform infrared spectroscopy (FTIR) confirmed the formation of the imine (C=N) functional group, a key characteristic of Schiff bases. Proton nuclear magnetic resonance (^1H NMR) and carbon-13 nuclear magnetic resonance (^13C NMR) spectroscopy provided detailed insights into the chemical environment of the hydrogen and carbon atoms, respectively, supporting the proposed molecular structures. Additionally, mass spectrometry was employed to verify the molecular weights and further corroborate the identity of the synthesized derivatives. The study contributes valuable structural information and confirms the successful synthesis of these novel Schiff base compounds. Given their established biological relevance and the structural diversity offered by the benzylidene and hydrazide moieties, the synthesized derivatives present promising candidates for further pharmacological evaluation. Future work will focus on investigating the biological activities of these compounds, with an emphasis on their antimicrobial and anticancer potential. Overall, this research underscores the significance of Schiff bases in drug discovery and their continued importance in medicinal chemistry.

Keywords: *Schiff bases, malonohydrazide, pharmacophore, aromatic compounds*

INTRODUCTION

Schiff initially described Schiff bases, which are the result of condensing primary amines with carbonyl compounds, in 1864. These compounds share the azomethine group, which has the generic formula RHC=N-R1, where R and R1 are heterocyclic, cycloalkyl, alkyl, or aryl groups that can be replaced in different ways. These substances are also referred to as azomethines, imines, or anils. The presence of a single pair of electrons in the nitrogen atom's sp2 hybridized orbital of the azomethine is a group of significant chemical and biological significance, according to several investigations. Due to the unique characteristic of the C=N group, synthetic flexibility, and relative ease of synthesis (1). Schiff bases of hydrazones are said to be biologically active due to the pharmacophore (-CO-NHN=C) (2). As a result, any chemical with this structural characteristic belongs to a significant class of pharmacological and medical medicines. In terms of several biological activities, including analgesic, anti-inflammatory, antidiabetic, antithrombotic, and antibacterial qualities, as well as anticancer, fungicidal, herbicidal, and tuberculostatic activity,

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carbohydrazides and their Schiff bases are highly significant biological molecules (2). Due to their favorable biological characteristics, they have been employed in numerous catalytic, anti-microbial, and anti-cancer research (3,4).

To achieve excellent yields without compromising the nucleophilicity of the amines, schiff bases—which are known for their biological significance and stability when connected to aryl groups—were synthesized by a condensation procedure aided by moderately acidic conditions. Thin-layer chromatography (TLC), infrared spectroscopy (IR), and melting point measurement were used to thoroughly evaluate the produced chemicals (5).

Because of their easy coordination to metal ions, structural divergence, and flexible entanglement, schiff bases stand out among other organic ligands. Because of azomethine (−C═N−) connections, which play a supportive role in stability, chelating capacity, and advantageous biological features, schiff base ligands have become increasingly important. By positively modifying the lipophilic/hydrophilic balance and the hard/soft property of coordinating metal ions, a well-designed Schiff base ligand scaffold can enhance the therapeutic profile of metal complexes (6).

The series that are synthesised in this study are condensation products of propanedihydrazide (commonly known as malonohydrazide) with derivatives of benzaldehyde.

MATERIALS AND METHODS

Materials Reagents:

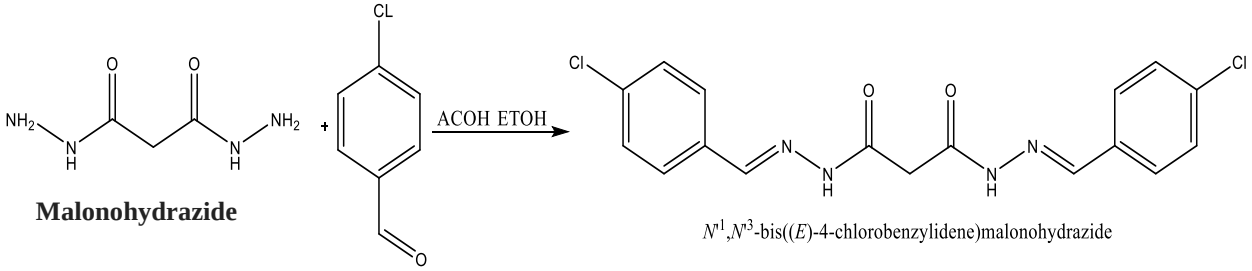
Analytical-grade chemicals were all utilized, and no additional purification was required.

Physical Measurements:

Gallen Kamp melting point apparatus was used to determine the melting points. IR spectra were recorded with Alpha, Bruker FT-IR instruments using potassium bromide pellets. NMR spectra were recorded for 1H NMR at 400 MHz and 13C NMR at 100 MHz on a Bruker AM 400 spectrometers with TMS as internal standard (δ = 0 ppm), and data are reported as follows: chemical shift, multiplicity (s = singlet, t = triplet, q = quartet, m = multiplet, and br = broad). For 13C NMR, spectra were obtained with complete proton decoupling. Finnigan MAT instrument was used to record the mass spectra (70 eV, EI-mode). Elemental analyses for C, H, N, and S were carried out using an Elmer 306.

Synthetic Schemes:

Scheme 1



Malonohydrazide

p-chloro benzaldehyde

N^1,N^3-bis((*E*)-4-chlorobenzylidene)malonohydrazide

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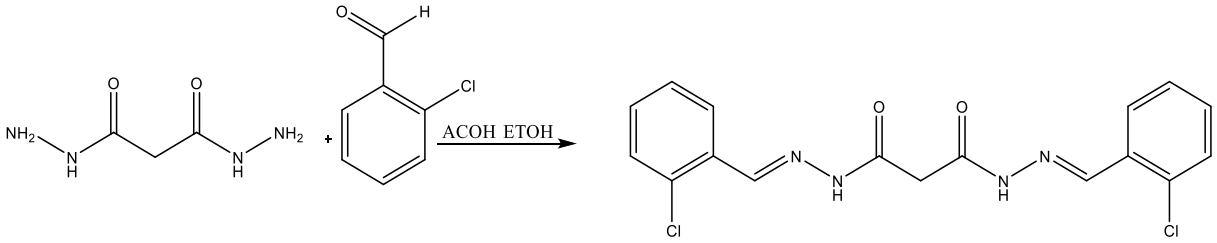
Take malonohydrazide (0.132 g) and p-chloro benzaldehyde (0.142 g) in two different beakers. Add 10 ml ethanol in each beaker. Stirring with 3 HR. Add two drops of acetic acid (CH_3COOH) followed by refluxing it. The product is thus obtained. The mixture was further cooled and the solids were filtered, washed with ethanol, and dried. The reaction was monitored continuously with the help of thin layer chromatography (TLC) and melting point.

Scheme 2



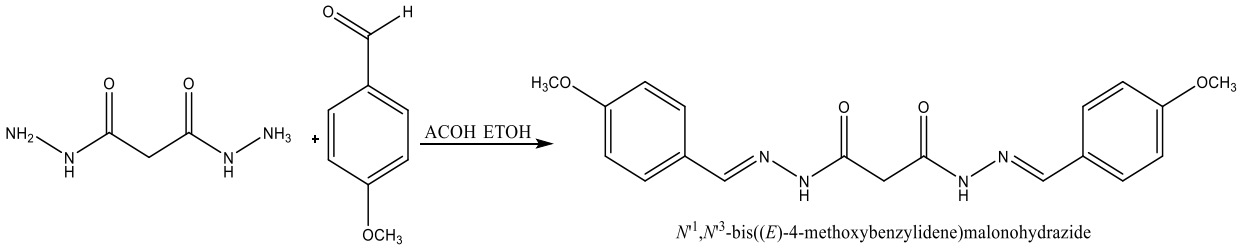
N^1,N^3-bis((*E*)-2-chlorobenzylidene)malonohydrazide

Malonohydrazide 2-chloro benzaldehyde

Take malonohydrazide (0.132 g) and o-chloro benzaldehyde (0.142 g) in two different beakers. Add 10 ml ethanol in each beaker. Stirring with 3 HR. Add two drops of acetic acid (CH_3COOH) followed by refluxing it. The product is thus obtained. The mixture was further cooled and the solids were filtered, washed with ethanol, and dried. The reaction was monitored continuously with the help of thin layer chromatography (TLC) and melting point.

Scheme 3

Malonohydrazide 4-Methoxy benzaldehyde



N^1,N^3-bis((*E*)-4-methoxybenzylidene)malonohydrazide

Malonohydrazide 4-Methoxy benzaldehyde

Take malonohydrazide (0.132 g) and 4-methoxy benzaldehyde (0.142 g) in two different beakers. Add 10 ml ethanol in each beaker. Stirring with 3 HR. Add two drops of acetic acid (CH_3COOH) followed by refluxing it. The product is thus obtained. The mixture was further cooled and the solids were filtered, washed with ethanol, and dried. The reaction was monitored continuously with the help of thin layer chromatography (TLC) and melting point.

RESULTS AND DISCUSSION

Compunds (1-3) were synthesized according to Schemes 1 – 3. All the Schiff bases of malonohydrazide were characterized using FTIR and NMR analysis.

Characterization

FTIR spectra

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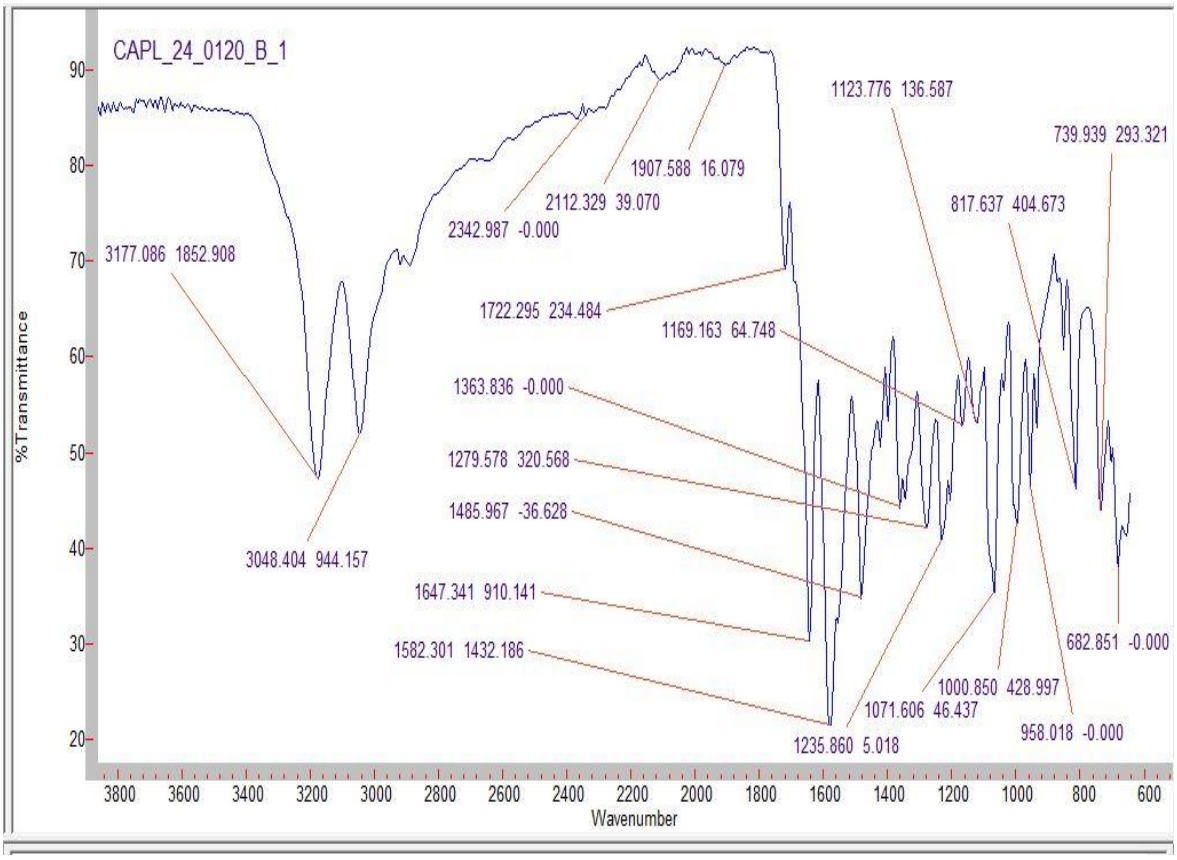

Figure 1 IR Spectrum of Compound 1

The synthesized Schiff base shows considerable absorption in its IR spectrum. At 1722 cm−1, the experimental value of νC=O is visible. At 1647 cm−1, the strong band of νC = N was found [29]. At 3048 cm−1, the νC–H stretching is detected. The observation of a strong peak at 817 cm−1 is indicative of out π(C–H) interactions. A significant absorption detected at 1582 cm−1 suggests the stretching vibration peak of the benzene ring's C=C backbone. A number of peaks that can be seen in the 3048–2342 cm−1 range are caused by aromatic C–H bonds. Strong bands were seen in the 1000–1071 cm–1 range where the C–O stretching was seen. The reason behind the steep peak found at 682 cm−1 is the C–H bending.

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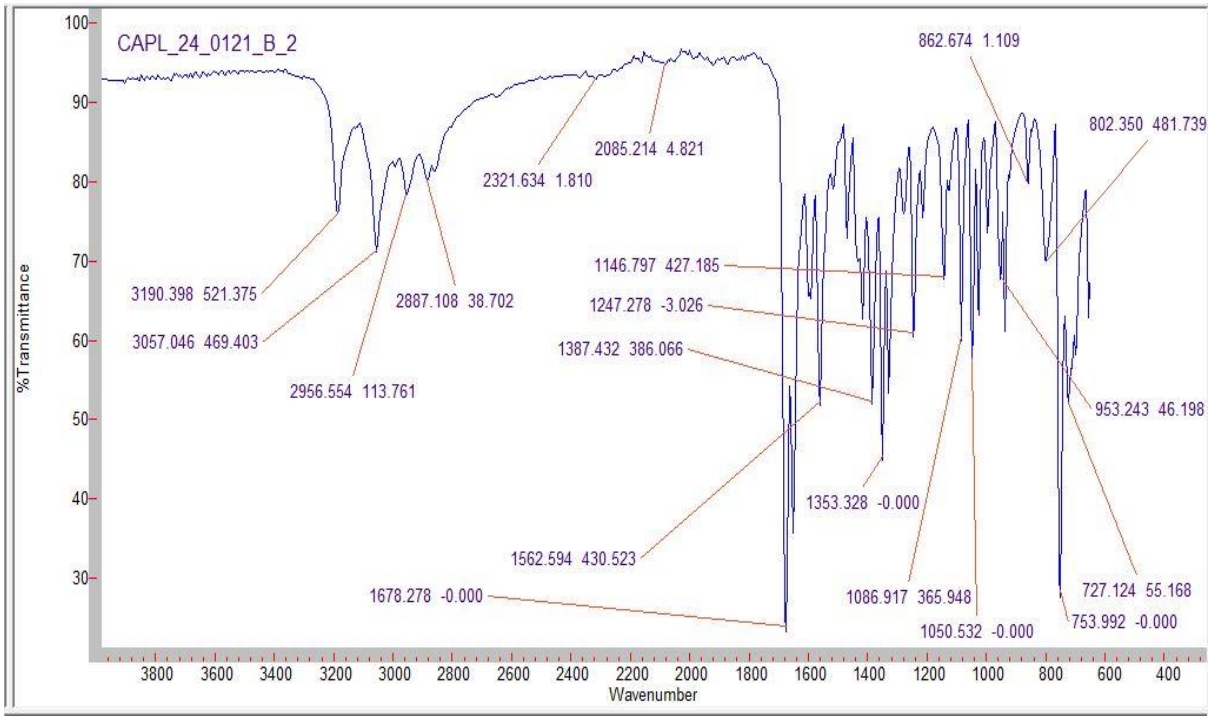

Figure 2 IR Spectrum of Compound 2

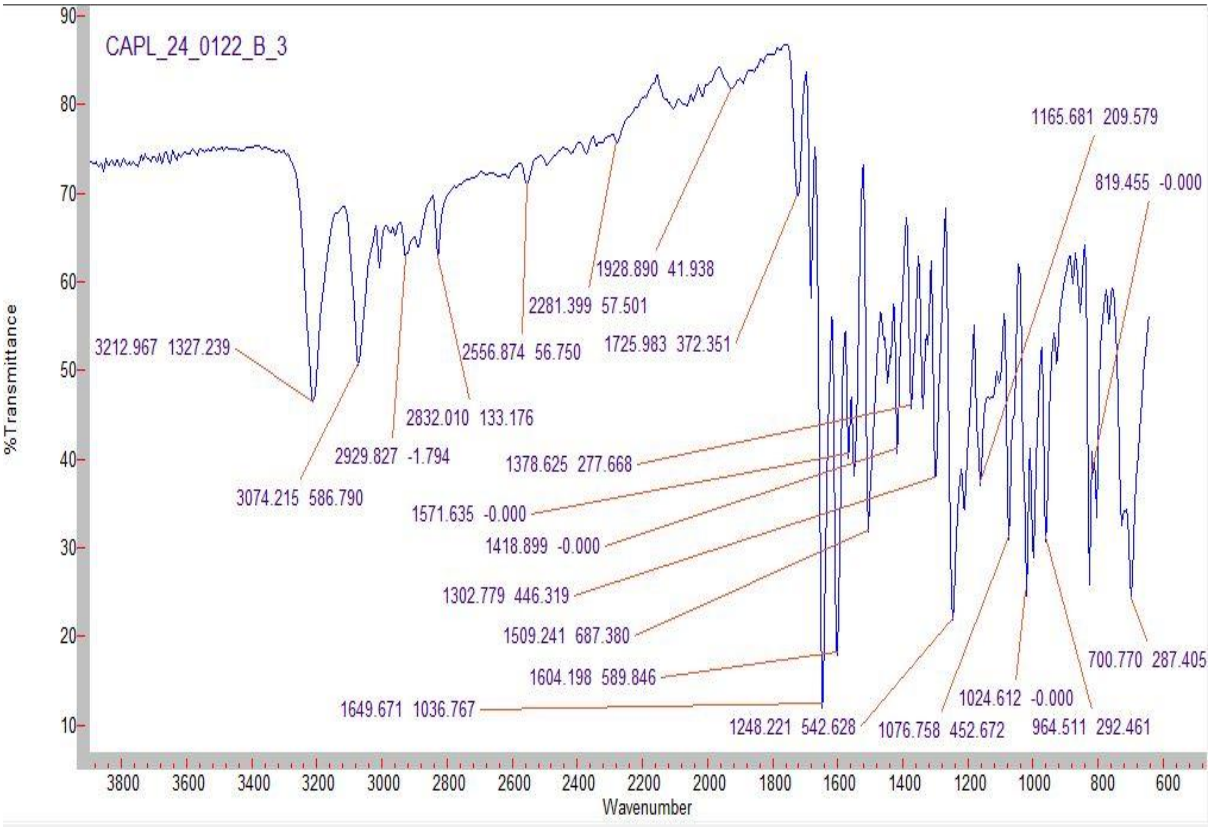

Figure 3 IR Spectrum of Compound 3

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[1]HNMR Spectra

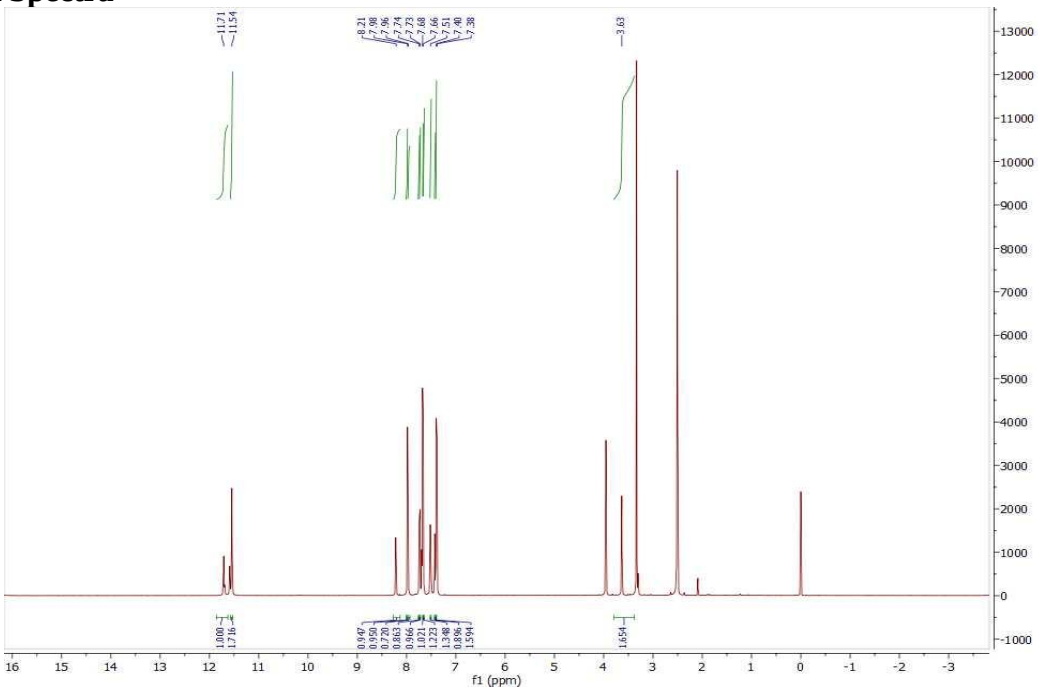

Figure 4 [1]HNMR of Compound 1

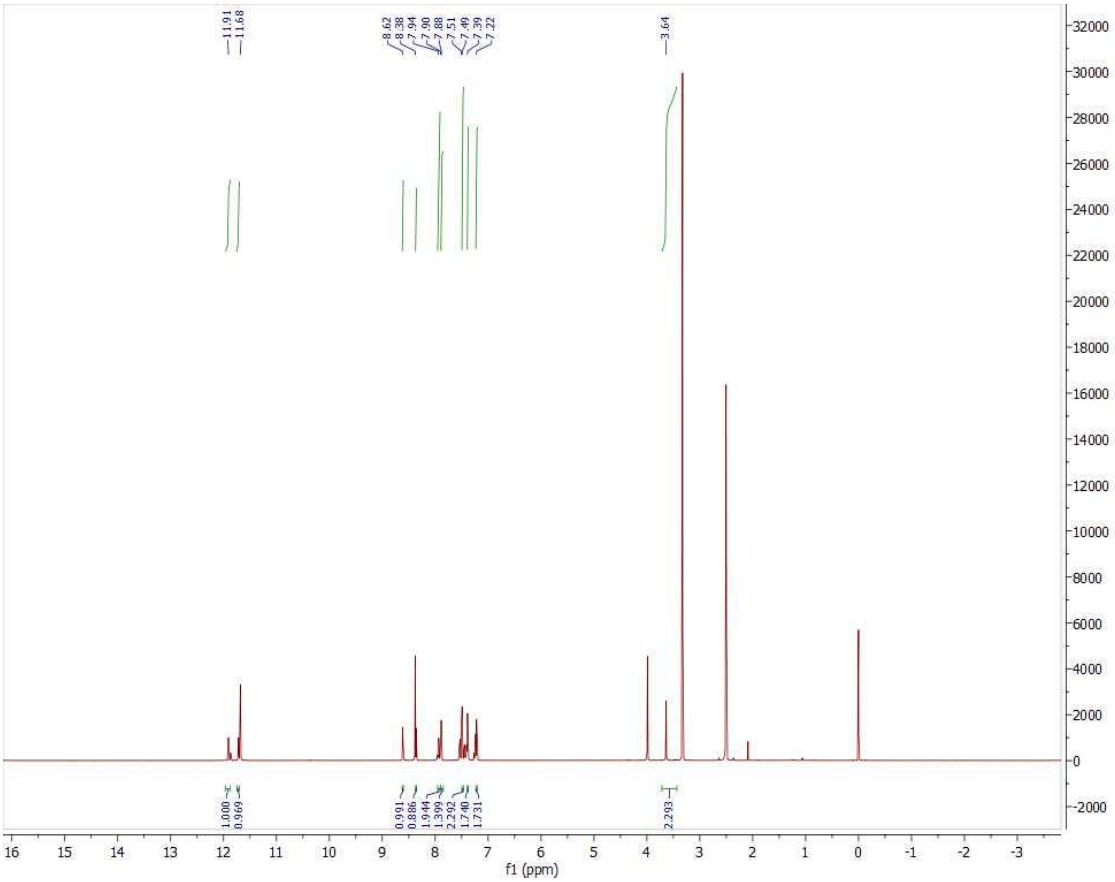

Figure 5 [1]HNMR of Compound 2

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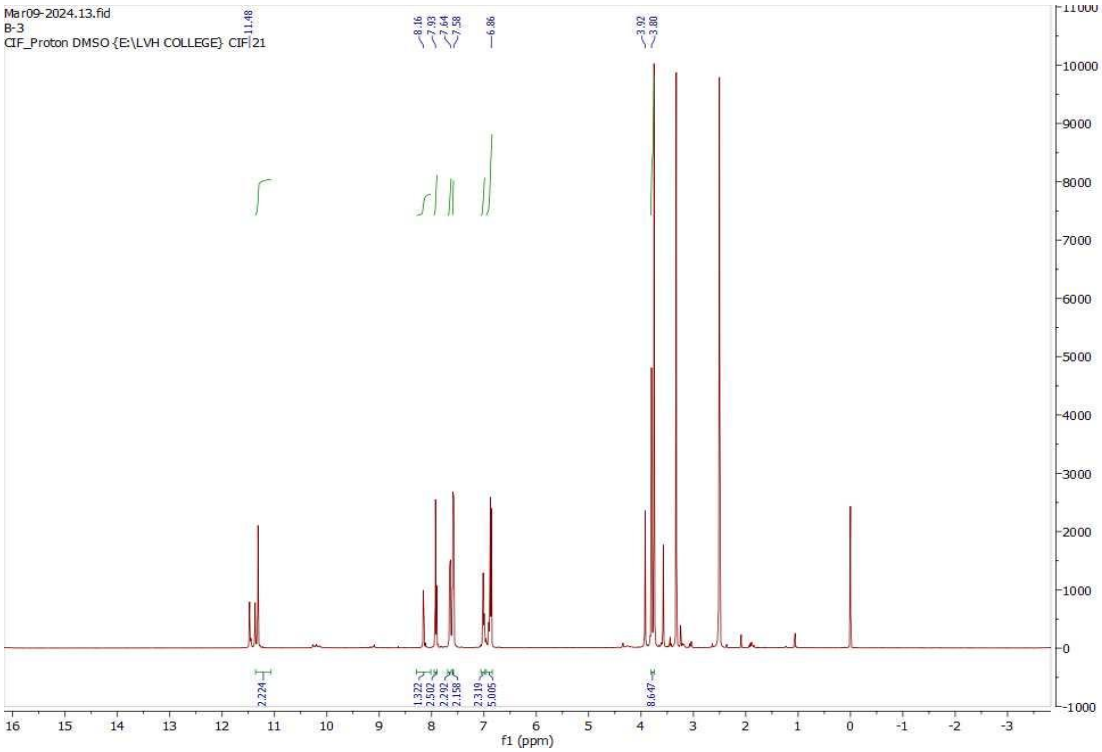

Figure 6 [1]HNMR of Compound 3

^{13}C NMR

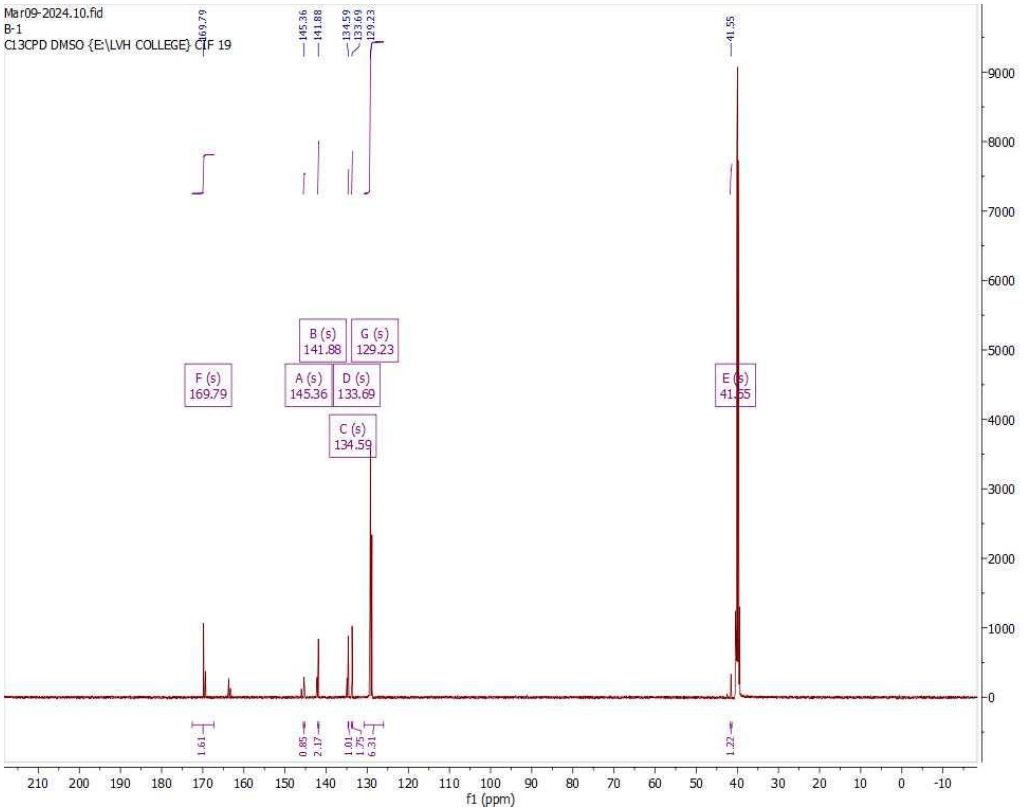

Figure 7 [13]CNMR of Compound 1

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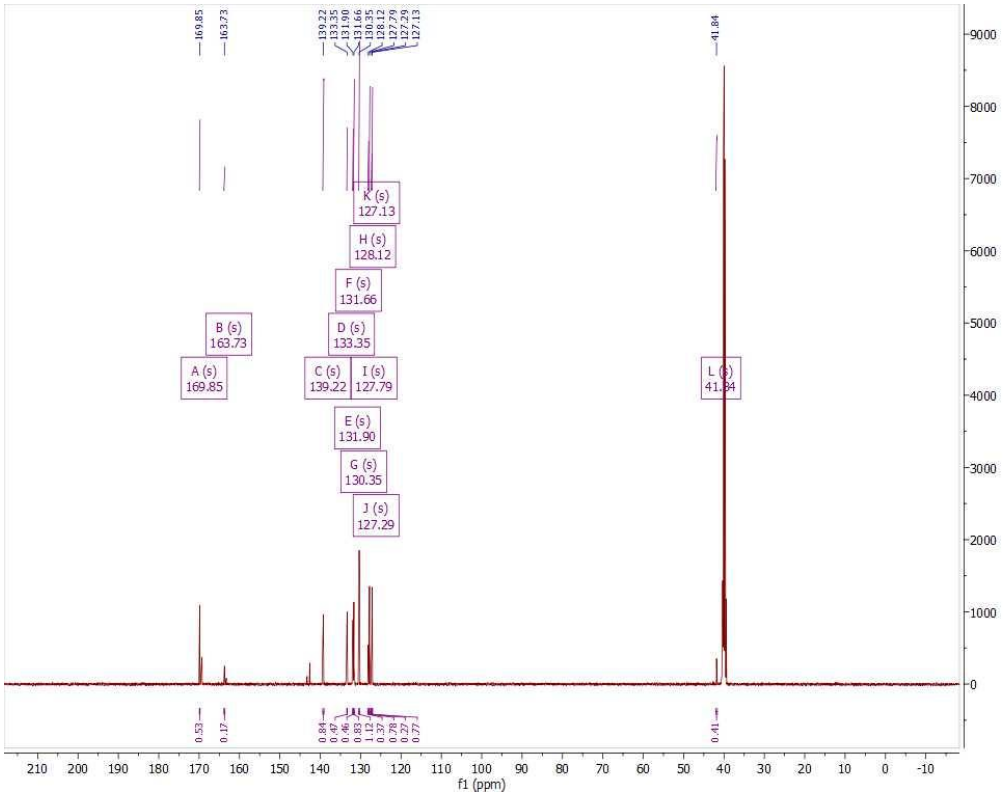

Figure 8 ^{13}CNMR of Compound 2

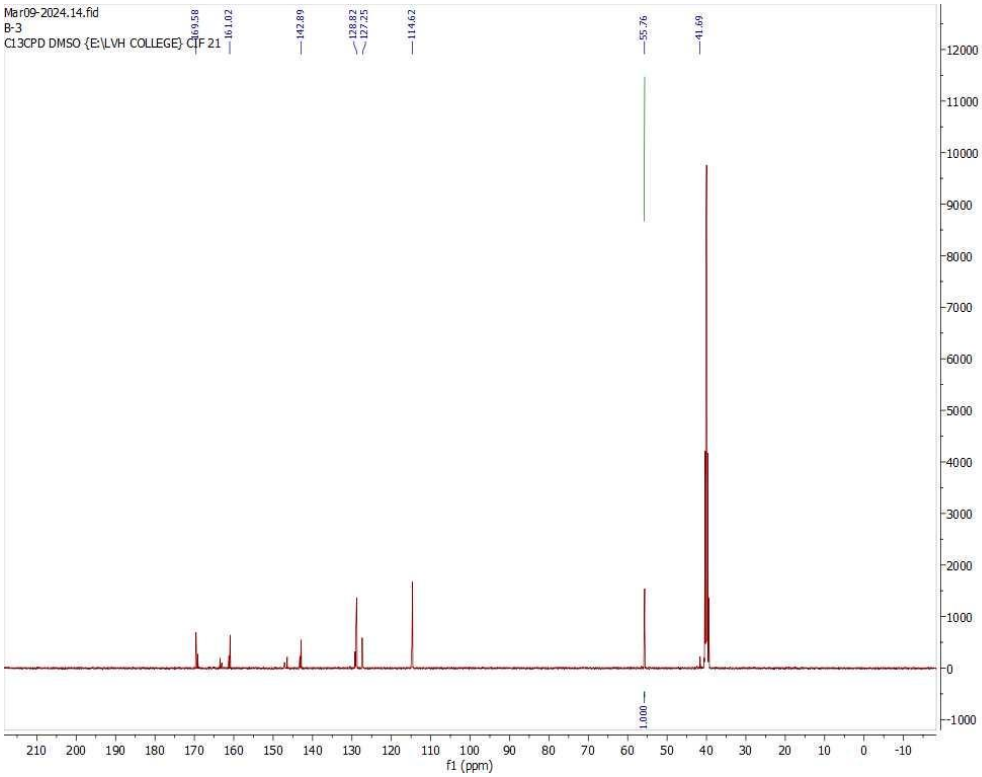

Figure 9 ^{13}CNMR of Compound 3

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The structural characterisation of the Schiff bases is further supported by the 13C NMR spectra. Table 1 lists the 13C NMR spectrum data of compounds (1–3). The quantity of signals detected is consistent with the presence of carbon atoms that are magnetically nonequivalent, as determined by comparing the results with published values. By comparing the experimental chemical shifts with those derived from the incremental technique, the aromatic carbon found in the Schiff bases' structures was identified. The suggested structures match the 13C-NMR spectral data of the Schiff bases.

Table 1 ^{1}HNMR and ^{13}CNMR data of compounds 1-3

Compound No.	Name	^{1}H NMR	^{13}C NMR
1	N^1,N^3-bis((E)-4-chlorobenzylidene)malonohydrazide	(500 MHz, DMSO-d_6) δ 11.71 (s, 1H), 11.54 (s, 1H), 8.21 (s, 1H), 7.98 (s, 1H), 7.96 (d, J=8Hz 1H), 7.74 (s d, J=8Hz 1H), 7.73 (d, J=8Hz 1H), 7.67 (d, *J* = 4.4 Hz, 1H), 7.66 (d, J=8.2Hz 1H), 7.51 (d, *J* = 8.02 Hz, 1H), 7.43 (d, *J* = 8.0 1Hz, 1H), 7.40 (d, *J* = 8.01Hz, 1H), 3.63 (s, 2H).	^{13}C NMR (126 MHz, DMSO-d_6) δ 169.79, 145.36, 141.88, 134.59, 133.69, 129.23, 41.55.
2	N^1,N^3-bis((E)-2-chlorobenzylidene)malonohydrazide	(500 MHz, DMSO-d_6) δ 11.91 (s, 1H), 11.72 (s, 1H), 8.62 (s, 1H), 8.36 (s, 1H), 7.94 (s, 2H), 7.88 (s, 1H), 7.49 (s, 2H), 7.39 (s, 2H), 7.22 (s, 2H), 3.64 (s, 2H).	(126 MHz, DMSO-d_6) δ 169.85, 163.73, 139.22, 133.35, 131.90, 131.66, 130.35, 128.12, 127.79, 127.29, 127.13, 41.84.
3	N^1,N^3-bis((E)-4-methoxybenzylidene)malonohydrazide	(500 MHz, DMSO-d_6) δ 11.48 (s, 2H), 8.16 (d,J=8Hz 2H), 7.93 (s, 2H d,J=8.1Hz 2H), 7.64 (d,J=8Hz 2H), 7.58 (s, 2H), 6.86 (d,J=8.1Hz 2H), 3.92 (s, 3H), 3.80 (s, 2H).	126 MHz, DMSO-d_6) δ 169.58, 161.02, 142.89, 128.82, 127.25, 114.62, 55.76.41.13

Mass Spectra

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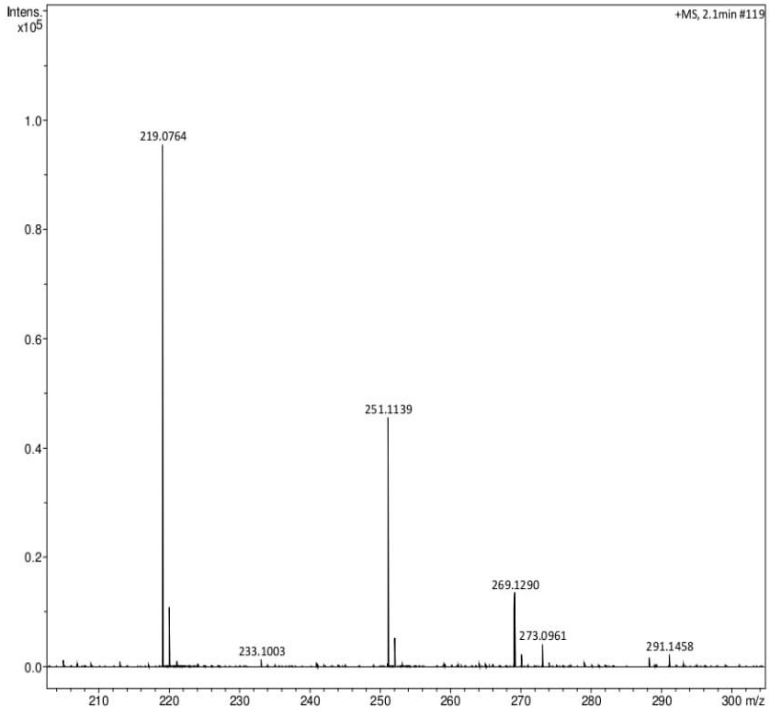

Figure 10 Mass spectrum of Compound 1

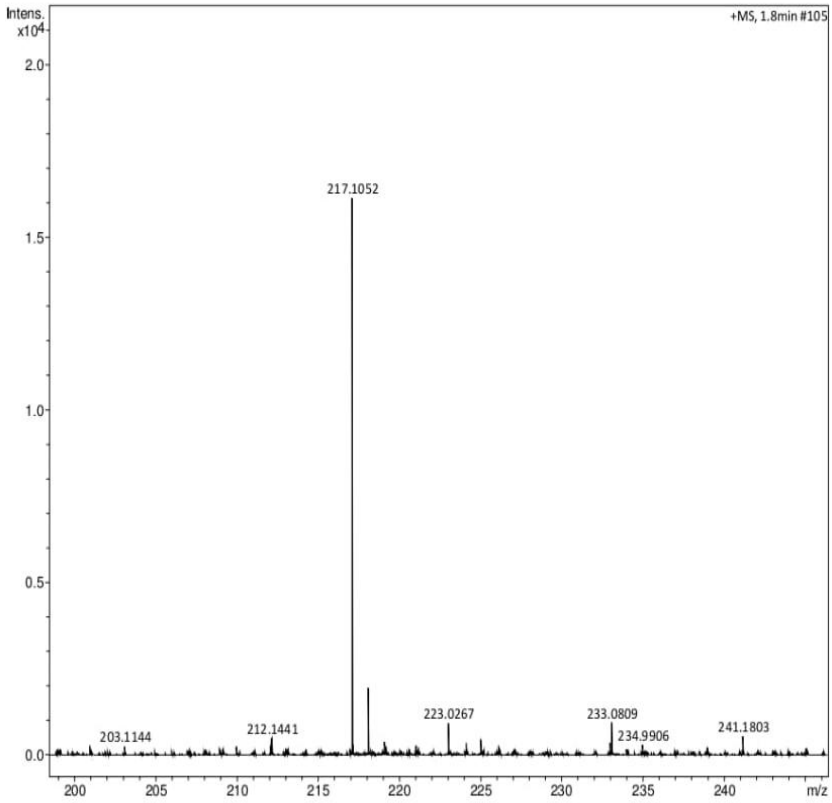

Figure 11 Mass spectra of Compound 2

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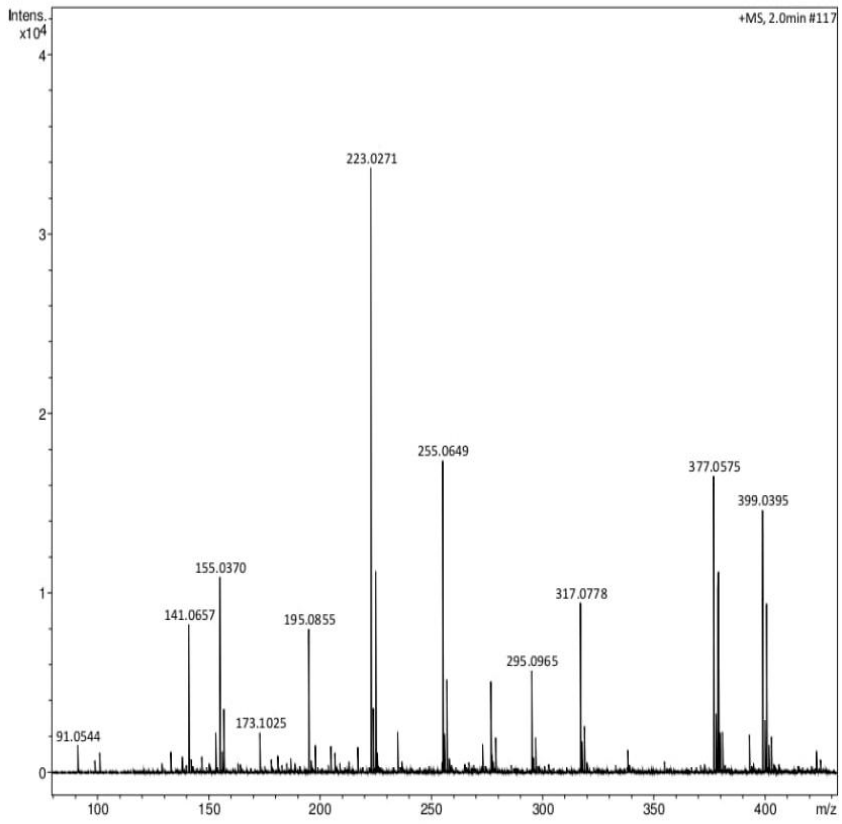

Figure 12 Mass spectra of Compound 3

The characterization of the compounds proves that the synthesis was successfully completed. The yield of the compounds ranged from 60-80%.

CONCLUSION

To synthesize, purify, characterize, and assess the antibacterial activity of novel Schiff's bases was the aim of the current investigation. The characterisation of various synthesized compounds was carried out using TLC and melting point analysis, revealing yields ranging from 60 to 80%. Multiple functioning vibrational modes are visible in characteristic infrared bands, indicating that the reaction has completed.

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