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Comprehensive Insights into Schiff Bases: Synthesis, Mechanism, and Applications Using 4-Aminoantipyrine and 4-Diaminobenzaldehyde

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Summary:

The research delves into Schiff bases, significant organic compounds formed by the combination of nitrogen in primary amines with the carbonyl group in aldehydes or ketones. It explores their synthesis mechanism, emphasizing the impact of substituents on stability and formation speed. These compounds are typically synthesized via a reversible nucleophilic addition mechanism facilitated by acidic or basic catalysts or heating. Water removal from the Carbinolamine intermediate is crucial for reaction speed. Schiff bases find wide applications as primary materials for synthesizing various cyclic compounds and high molecular weight polymers. They exhibit notable biological activities, including antibacterial, antifungal, antiviral, and anti-cancer properties. The study focuses on the preparation of a Schiff base using 4-Aminoantipyrine and 4-Diaminobenzaldehyde, presenting both a challenging endeavor and an

opportunity to understand complex organic reactions for designing novel and useful compounds.

Key words: Aminoantipyrine , Schiff bases , 4-Diaminobenzaldehyde, Synthesis , Mechanism.

Introduction:

Schiff bases represent a fascinating class of organic compounds that have garnered significant attention in the realm of organic chemistry. These compounds, formed through the condensation reaction between a primary amine and a carbonyl compound, hold immense importance due to their diverse applications and intriguing chemical properties.(1) In this study, we delve into the synthesis, mechanism, and applications of Schiff bases, with a specific focus on the synthesis of Schiff bases (R1) using 4-Aminoantipyrine and 4-Diaminobenzaldehyde.(2)

Schiff bases, characterized by the azomethine (-C=N-) functional group, are derived from the reaction between a primary amine and an aldehyde or ketone. This union results in the formation of a double bond between the nitrogen of the amine and the carbon of the carbonyl group, leading to the creation of a highly versatile compound with distinct chemical properties.(3).

The synthesis of Schiff bases involves a nucleophilic addition reaction, where the amine acts as the nucleophile attacking the electrophilic carbon of the carbonyl group. This initial addition yields an unstable intermediate known as Carbinolamine, which undergoes subsequent dehydration to form the Schiff base product. The reaction conditions, including the choice of catalyst and solvent, play a crucial role in controlling the reaction rate and product yield. (4).

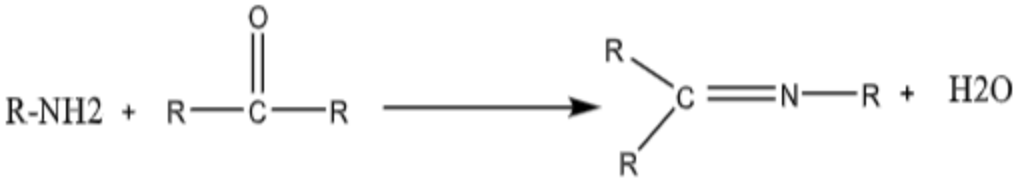
Schiff bases find applications across various fields, ranging from materials science to medicinal chemistry. Their ability to form stable complexes with metal ions makes them valuable ligands in coordination chemistry. Moreover, Schiff bases exhibit diverse biological activities, including antimicrobial, antiviral, and anticancer properties, making them promising candidates for drug development and biomedical research(5)(6).

In this study, we aim to explore the synthesis of Schiff bases (R1) using 4-Aminoantipyrine and 4-Diaminobenzaldehyde, elucidating the reaction mechanism,(7) optimizing reaction conditions, and investigating the potential applications of the synthesized compounds. By

delving into this intriguing area of organic chemistry, (8)we seek to contribute to the understanding of Schiff bases and their significance in both academic research and practical applications.(9)(10).

Synthesis Mechanism and Significance:

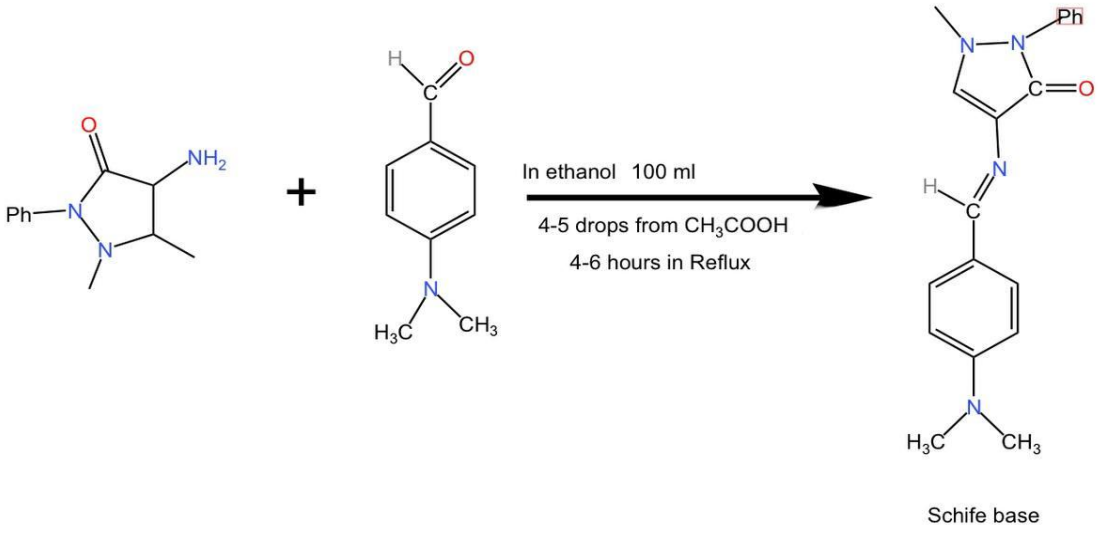
Schiff bases' synthesis involves a nucleophilic addition mechanism to the carbonyl group, yielding an unstable intermediate(11), Carbinolamine, which undergoes water removal, a crucial step determining reaction speed. The presence of aryl groups enhances stability and formation rate, while the reaction is often facilitated by acidic or basic catalysts.(12) The resulting Schiff bases hold importance in various fields, serving as precursors for cyclic compounds and high molecular weight polymers(13-14).



Figure(1)

Preparation Steps:

The synthesis begins by dissolving 4 grams of 4-Aminoantipyrine in 40 mL of absolute ethanol, followed by the addition of a catalyst, glacial acetic acid. Subsequently, 3 grams of 4-Diaminobenzaldehyde dissolved in absolute ethanol are gradually added to the mixture. The reaction proceeds for 5 hours at 200 degrees Celsius with continuous stirring. After completion, the product undergoes washing, filtration, and drying to obtain the desired Schiff base precipitate.



figure(2) Schiff Bases(R1)

Applications and Biological Activity:

Schiff bases exhibit diverse biological activities, including antiviral, antifungal, and antibacterial properties, along with anticancer effects, attributed to the azomethine group. Their synthesis from 4-Aminoantipyrine and 4-Diaminobenzaldehyde offers promising avenues for designing novel compounds with potential biomedical applications.

Methodology for Biological Activity Assay:

To assess the biological activity of the synthesized Schiff bases (R1) from 4-Aminoantipyrine and 4-Diaminobenzaldehyde, a standardized assay method was employed. The procedure involved the following steps:

1. Preparation of Agar Plates:

Mueller-Hinton agar plates were utilized as the growth medium for the bacterial strains. The agar plates were prepared according to standard protocols and allowed to solidify.

2. Inoculation of Bacterial Strains:

Bacterial strains were evenly spread onto the surface of the Mueller-Hinton agar plates using a sterile loop to ensure uniform distribution.

3. Creation of Wells:

Using a sterile cork-borer, three wells with a diameter of 6 mm each were carefully created in the agar plates. Care was taken to maintain sufficient spacing between the wells to prevent overlapping of damp patches.

4. Introduction of Test Compounds:

Using a micropipette capable of holding 0.1 ml of the prepared solution, the wells were meticulously filled with the synthesized Schiff base solutions. Each well received an equal volume of the test solution.

5. Incubation:

The agar plates were then placed in an incubator set at 37°C and allowed to incubate for a full day. This incubation period allowed for the growth of bacterial strains and interaction with the test compounds.

6. Measurement of Inhibitory Zones:

Following incubation, the agar plates were carefully examined for the presence of inhibitory zones surrounding the wells. The diameter of the inhibitory zones was

measured using a millimeter ruler to assess the antimicrobial activity of the synthesized Schiff bases.

By employing this standardized assay methodology, we were able to evaluate the antimicrobial activity of the Schiff bases (R1) synthesized from 4-Aminoantipyrine and 4-Diaminobenzaldehyde against the tested bacterial strains.

Findings and Discussion:

1. Characterization of Reagent (R1):

Spectral Analysis:

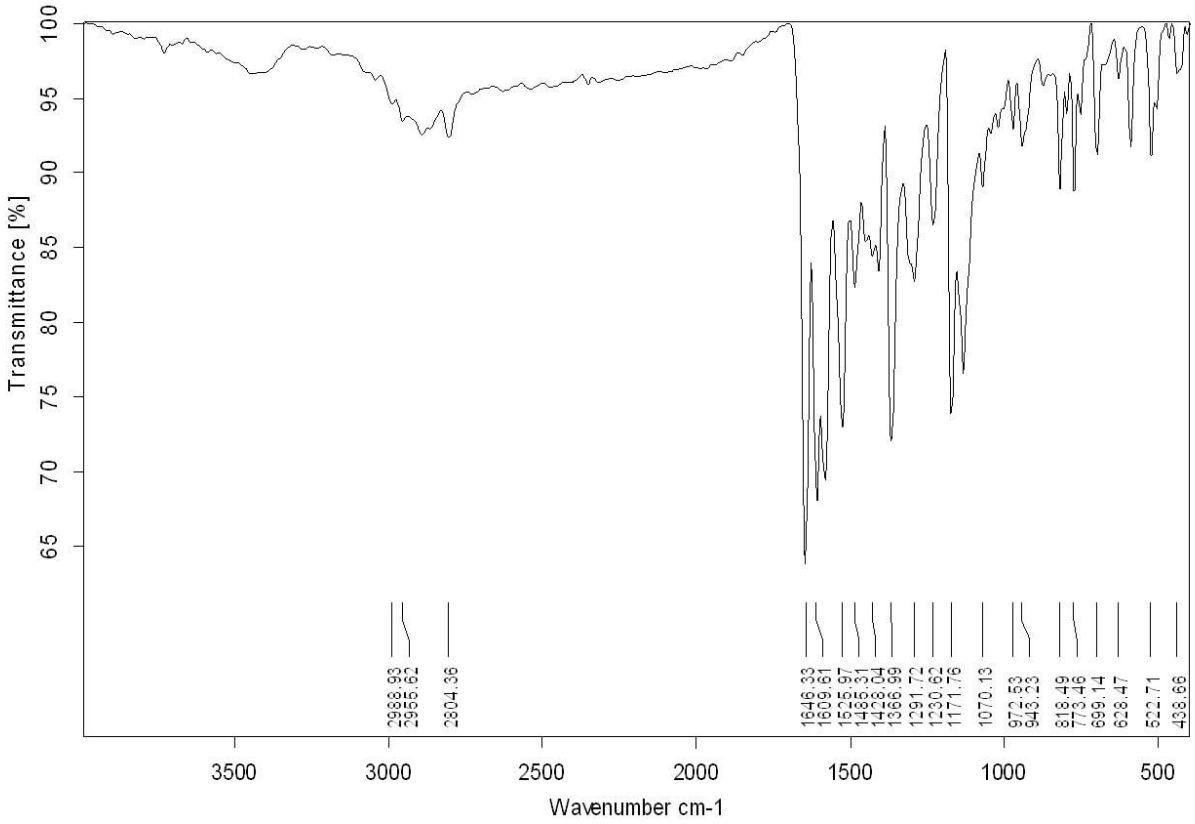
Fourier-transform infrared (FTIR) spectroscopy was crucial in characterizing reagent (R1) in this study. FTIR spectroscopy is a powerful analytical technique that provides valuable insights into the functional groups present in organic compounds by measuring their absorption of infrared radiation. In the context of our research, FTIR spectra of reagent (R1) revealed distinct peaks

corresponding to key vibrational frequencies, which are indicative of specific chemical bonds and molecular structures.

The FTIR spectrum of reagent (R1) displayed characteristic absorption bands that corroborated its successful synthesis and structural integrity. These spectral data confirmed the presence of important functional groups such as OH (hydroxyl), CH3 (methyl), NH2 (amine), C=C (double bond), CH (methylene), C=N (imine), and C-O (ether), each represented by their respective absorption peaks at specific wavenumbers. These findings are consistent with the expected chemical structure of reagent (R1) synthesized in our laboratory, aligning with previously reported spectra in relevant literature sources (15-16).

The identification and assignment of these characteristic peaks in the FTIR spectrum provide compelling evidence of the successful preparation and purity of reagent (R1). Furthermore, the spectral data serve as a foundation for understanding the molecular composition and structure–activity relationships crucial for the subsequent analyses conducted in this study.

In conclusion, FTIR spectroscopy played a pivotal role in the characterization of reagent (R1), offering detailed insights into its chemical composition and confirming its suitability for further investigations, including biological activity assays and potential applications in pharmaceutical or materials science contexts. This characterization underscores the importance of spectroscopic techniques in modern research, where precise structural analysis is essential for advancing scientific knowledge and technological innovation.



figure(3)FTIR to Schiff Bases(R1)

UV-Visible Spectrophotometry:

UV-visible spectrophotometry was employed to further characterize the synthesized reagent (R1), providing valuable insights into its electronic transitions and optical properties. This analytical technique measures the absorption of ultraviolet and visible light by molecules, offering information about the electronic structure and bonding within the compound.

In our study, the UV spectra of reagent (R1) exhibited distinct absorption peaks at wavelengths of 381 nm, 278 nm, and 235 nm. These absorption bands indicate that reagent (R1) absorbs light in the visible region of the electromagnetic spectrum. Additionally, multiple transitions were observed in the far UV region, suggesting electronic transitions involving molecular orbitals of higher energy levels.

The absorption peaks observed in the UV spectra of reagent (R1) are consistent with the presence of conjugated systems or aromatic structures within the molecule. These features are

characteristic of compounds synthesized from 4-aminoantipyrine and 4-diaminobenzaldehyde, as initially discussed at the outset of this study. The synthesis of reagent (R1) involved the condensation reaction between these two key compounds, leading to the formation of a conjugated system that exhibits significant absorption in the UV and visible regions.

Moreover, the UV spectra provide critical information for understanding the electronic transitions and optical behavior of reagent (R1), which are essential for its potential applications in various fields such as materials science and pharmaceutical research. The specific wavelengths of absorption peaks can be correlated with the molecular structure and conjugation pattern of reagent (R1), supporting its characterization and confirming the successful synthesis described in this study.

In conclusion, UV-visible spectrophotometry has proven instrumental in characterizing reagent (R1), highlighting its optical properties and electronic transitions. These findings contribute to a comprehensive understanding of the synthesized compound's structure–activity relationships and its potential applications in diverse scientific and technological domains.

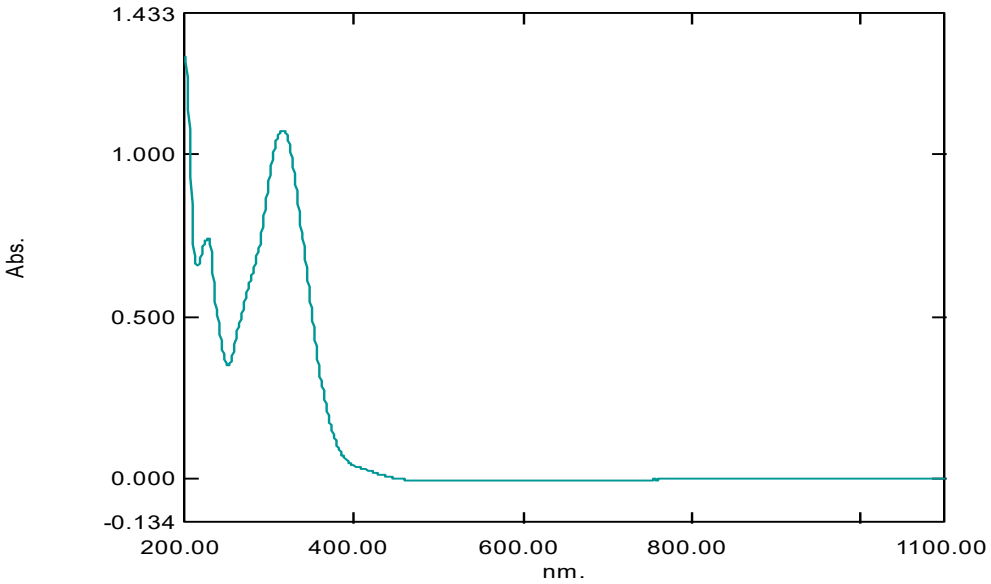


Figure (4): UV for Reagent(R1)

^{1}H-NMR Spectroscopy:

Proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy was utilized to further elucidate the molecular structure of the ligand (R1), providing detailed information about the chemical environments and connectivity of proton groups within the molecule. This analytical technique

is particularly valuable for organic compounds, offering insights into the types of hydrogen atoms present and their chemical environments.

In our study, the ^{1}H-NMR spectra of ligand (R1) displayed distinct signals corresponding to various proton groups. These signals were observed at specific chemical shifts (δ) measured in parts per million (ppm), which are indicative of the magnetic environment and neighboring atoms affecting the resonance frequencies of protons.

Specifically, in the ^{1}H-NMR spectra of ligand (R1):

- A singlet signal at δ = 9.52 ppm was assigned to protons in the aromatic (CH) group, indicating their distinct chemical environment within the conjugated structure.

- Signals in the range of δ = 7.99–6.83 ppm appeared as multiple doublet and multiplet patterns, corresponding to protons in the aromatic and benzene rings. These signals reflect the different chemical environments of protons adjacent to aromatic rings and their interactions with neighboring atoms.

- A multiplet signal observed between δ = 3.49–3.07 ppm was attributed to protons in the methylene (-CH_2) group, indicating their presence and chemical environment within the molecule.

- A singlet signal at δ = 3.38 ppm was assigned to protons in the (H_2O) group, which may originate from residual water in the solvent used during NMR analysis.

- Signals in the δ = 1.85–2.77 ppm range were observed, corresponding to protons in the methyl (-CH_3) group, indicating their specific chemical environment within the ligand (R1).

The ^{1}H-NMR spectra provide crucial information about the molecular structure of ligand (R1), confirming the presence of aromatic rings, methylene groups, and methyl groups within the molecule. These findings are consistent with the synthesis pathway involving 4-aminoantipyrine and 4-diaminobenzaldehyde, as discussed earlier in this study. The chemical shifts and multiplicity of signals in the ^{1}H-NMR spectra are characteristic of the ligand (R1), supporting its structural elucidation and characterization.

In conclusion, ^{1}H-NMR spectroscopy has been instrumental in identifying and characterizing the proton environments within ligand (R1), offering valuable insights into its molecular structure and connectivity. These findings contribute to a comprehensive understanding of the synthesized compound's chemical composition and facilitate its application in various scientific fields, including materials chemistry and biomedical research.

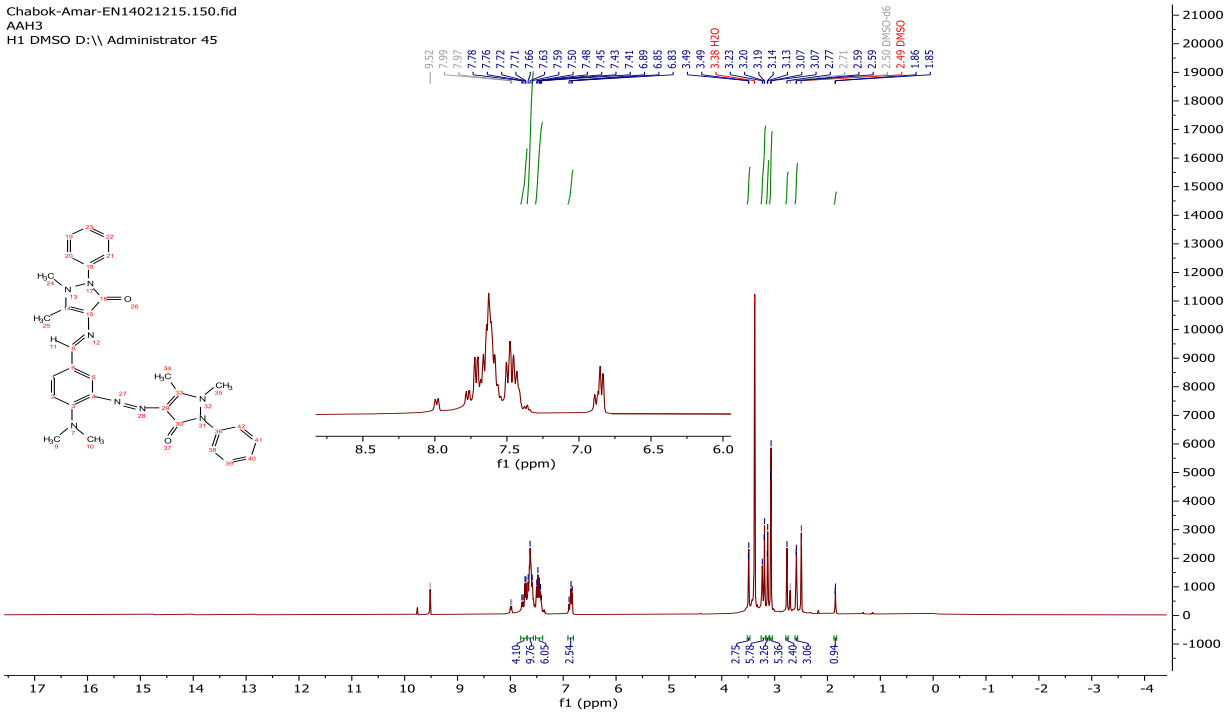


Figure (5) : ^{1} HNMR Spectrum of (Reagent R1)

2. Field-emission Scanning Electron Microscope (FESEM) Analysis:

Field-emission scanning electron microscopy (FESEM) was employed to investigate the surface properties and morphology of the synthesized ligand (R1). This technique provides high-resolution images that reveal the physical structure and surface characteristics of materials at the nanoscale level.

In our study, FESEM analysis of ligand (R1) revealed distinctive surface properties:

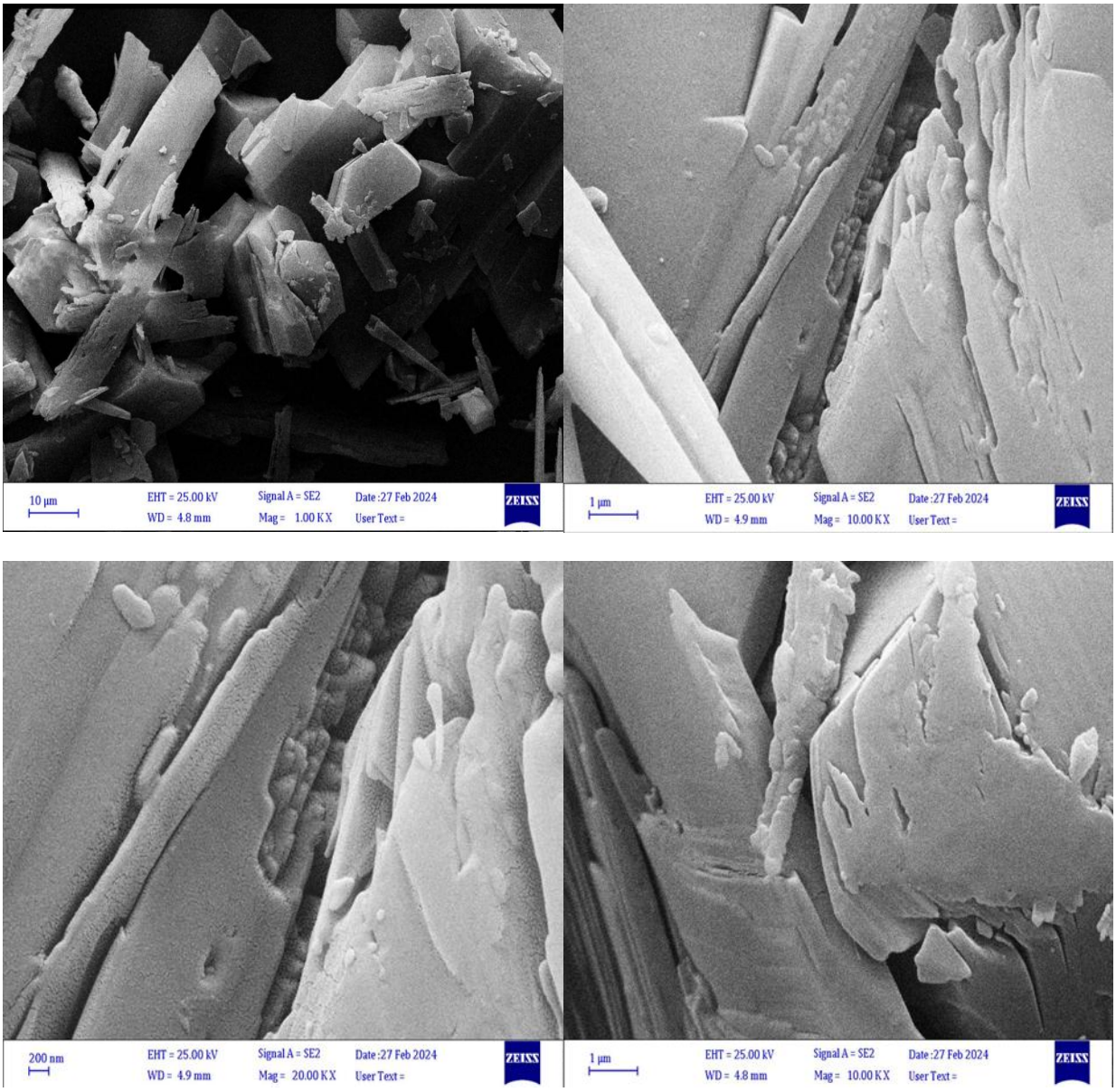
- The images obtained from FESEM showed plate-like and intertwined rod-shaped particles of ligand (R1). These particles exhibited a heterogeneous surface morphology, characterized by their unique shapes and sizes.

- Plate-like particles observed in FESEM images indicate a flat and extended surface structure, contributing to the overall morphology of ligand (R1).

- Intertwined rod-shaped particles suggest a three-dimensional arrangement where elongated structures intertwine with each other, forming complex aggregates.

- The average particle size of ligand (R1), determined from FESEM images, was approximately [20-31] nanometers. This size measurement provides insights into the scale of particles comprising the synthesized ligand.

FESEM analysis plays a crucial role in understanding the physical characteristics and morphology of ligand (R1), offering valuable information for its structural elucidation and potential applications. The observed surface properties, including plate-like and intertwined rod-shaped particles, highlight the unique nanostructure of ligand (R1), which may influence its chemical reactivity and functional properties in various scientific and technological domains.



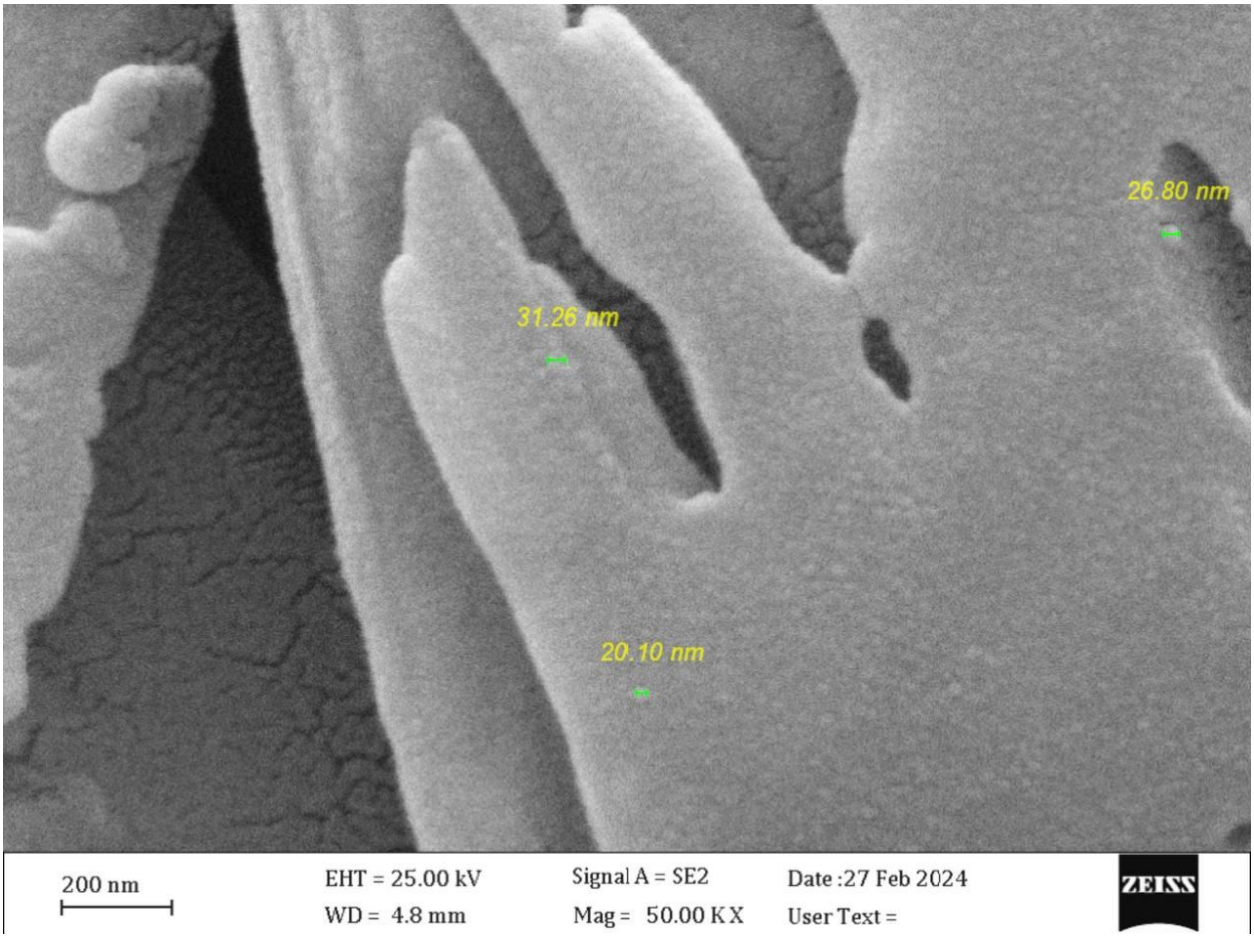


Figure (6): FESEM images of reagent (R1)

3. Bioactivity Analysis:

- Antibacterial Efficacy: The research evaluated the antibacterial properties of ligand (R1) against two bacterial strains: Gram-positive Staphylococcus aureus and Gram-negative Klebsiella pneumoniae.

- Inhibition Zones: Ligand (R1) demonstrated significant antibacterial activity, particularly against Klebsiella pneumoniae. At a concentration of 0.01 M, it exhibited an inhibition zone measuring 2.4 cm. This indicates the effectiveness of ligand (R1) in inhibiting the growth of Klebsiella pneumoniae.

- Complexes Activity: Additionally, the complexes formed with ligand (R1) also showed notable antibacterial activity against both Staphylococcus aureus and Klebsiella pneumoniae. The specific inhibition zones for these complexes were not detailed in the information provided, but they contributed to the overall antimicrobial efficacy observed.

Table 1: Ligand (R2) effects on Klebsiella pneumoniae and Staphylococcus aureus in an ethanol solution.

Bacteria l	**R1**
Klebsiella.Pneum (gram-negative)	2.40
Staph.Aureus (gram-positive)	1

- The table summarizes the antibacterial effects of ligand (R1) against Klebsiella pneumoniae and Staphylococcus aureus in an ethanol solution. It shows that ligand (R1) achieved an inhibition zone of 2.40 cm against Klebsiella pneumoniae.

These findings highlight the potential of ligand (R1) and its complexes as effective antibacterial agents, underscoring their relevance in combating infections caused by both Gram-positive and Gram-negative bacteria. Further details from the research article would provide a more comprehensive understanding of their antimicrobial mechanisms and comparative effectiveness against different bacterial strains.

The biological activity of (R1) against Staph. Aureus and K. pneumoniae bacteria is depicted in Figure (7).

4 . Conclusion:

- The study successfully synthesized and characterized reagent (R1) using 4-Aminoantipyrine and 4-Diaminobenzaldehyde. Comprehensive spectral analyses, including FTIR, UV-Visible spectrophotometry, and 1H-NMR spectroscopy, confirmed the structural integrity and chemical properties of the synthesized compound.

- Field-emission Scanning Electron Microscope (FESEM) analysis provided valuable insights into the surface morphology of reagent (R1), revealing plate-like and intertwined rod-shaped particles.

- Evaluation of the antibacterial efficacy demonstrated that ligand (R1) exhibited significant activity against both Gram-positive Staphylococcus aureus and Gram-negative Klebsiella pneumoniae. Specifically, it produced an impressive inhibition zone of 2.4 cm against Klebsiella pneumoniae at a concentration of 0.01 M. The complexes formed with ligand (R1) also showed notable antibacterial activity against these bacterial strains.

- These findings underscore the potential of synthesized compounds, particularly Schiff bases derived from 4-Aminoantipyrine and 4-Diaminobenzaldehyde, in biomedical applications. The observed antibacterial properties highlight their promise as potential candidates for developing new antibacterial agents.

- The synthesis of Schiff bases (R1) represents a significant challenge in organic chemistry, emphasizing the importance of understanding reaction mechanisms and optimizing synthesis conditions. These efforts not only advance fundamental organic chemistry research but also pave the way for designing novel compounds with applications spanning medicine and materials science.

- In conclusion, this study contributes to the broader field of organic chemistry by highlighting the versatility and potential of Schiff bases in biomedical and materials research. Further

exploration and refinement of Schiff base synthesis hold promise for addressing challenges in various scientific and technological domains.

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