

Synthesis, Characterization, and Evaluation of Antibacterial and Antifungal Activities of Novel Schiff Base Derivatives

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ABSTRACT

Background: Schiff bases and their derivatives are widely recognized for their diverse biological activities, including antimicrobial properties. The synthesis and structural characterization of these compounds contribute to the development of novel antimicrobial agents with potential clinical applications. **Objective:** This study aimed to synthesize and characterize a series of novel Schiff base derivatives and evaluate their antibacterial and antifungal activities using standard laboratory microbiological assays. **Methods:** A series of substituted thiazole derivatives were synthesized, starting from 3,5-dinitrobenzoic acid, which was converted into its acid chloride derivative. The acid chloride was then treated with p-hydroxybenzoic acid in pyridine as a solvent and a base, with a catalytic amount of DMF, to obtain 4-(3,5-dinitrobenzoate) benzoic acid [1]. Further reaction of compound [1] with thiosemicarbazide and phosphorus oxychloride (POCl₃) yielded 4-(5-amino-1,3,4-thiadiazol-2-yl) phenyl-3,5-dinitrobenzoate [2]. Schiff bases [3a-h] were synthesized by refluxing compound [2] with various substituted benzaldehydes in absolute ethanol with glacial acetic acid (GAA) as a catalyst. The newly synthesized compounds were structurally characterized using Fourier Transform Infrared Spectroscopy (FT-IR) and Proton Nuclear Magnetic Resonance Spectroscopy (¹H-NMR). Their purity was confirmed by melting point determination and Thin Layer Chromatography (TLC). The antibacterial and antifungal activities of the compounds were assessed using disk diffusion and minimum inhibitory concentration (MIC) methods against a panel of Gram-positive and Gram-negative bacterial strains, as well as fungal pathogens. **Results:** The synthesized Schiff base derivatives exhibited characteristic absorption bands in the FT-IR spectra, confirming the presence of azomethine (-C=N-) functional groups. The ¹H-NMR spectra provided further confirmation of structural integrity. Preliminary microbiological evaluation demonstrated that several Schiff base derivatives displayed promising antibacterial and antifungal activities, with notable inhibition zones against *Staphylococcus aureus*, *Escherichia coli*, *Candida albicans*, and *Aspergillus niger*. **Conclusion:** The synthesized Schiff base derivatives showed potential as antimicrobial agents, suggesting their possible application in pharmaceutical and clinical microbiology. Further studies, including in-depth cytotoxicity and mechanistic evaluations, are recommended to explore their full therapeutic potential.

Keywords: Synthesis, Antibacterial, Characterization, Schiff Bases

INTRODUCTION

Schiff bases are aldehyde or ketone analog in that the carbonyl group is converted to (C=N) group. It's resulted from the condensation of aldehyde or ketone with a primary amines[1, 2]. The majority of aromatic Schiff bases are water soluble, with the solubility of those containing carbohydrate increasing [3, 4]. Schiff's bases are

significant in medicine and pharmaceuticals that's due to its antibacterial and analgesic properties [5-10]. Thiadiazole is a five-membered heterocyclic compound containing two nitrogen atoms and one sulfur atom activating as hetero atoms [11-14]. They come in four different isomeric forms in nature:

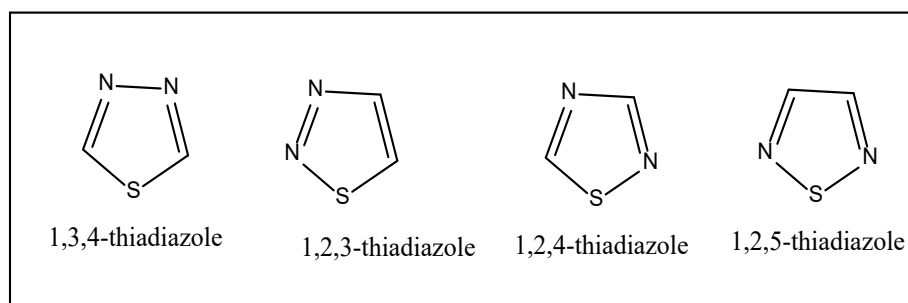


FIGURE 1: Isomeric System Types. 1,2,3- : 1,3,4- : 1,2,4- and 1,2,5- Thiadiazole.

EXPERIMENTAL SECTION

Preparation Of 3,5-Dinitro Benzoyl chloride

A mixture of 3,5-dinitrobenzoic acid (5g,0.031mole), (15mL) of (SOCl₂) and (3) drops dimethyl formamide was heated under reflux temperature about (2 hrs). then, the excess of thionyl chloride was removed. (Jabbar and Jassim,2019a).

Synthesis of 4-(3,5-Dinitrobenzoyl) oxy) Benzoic Acid

p-Hydroxy benzoic acid (0.057mole, 7g) in (dry pyridine or tri ethyl amine), after 3,5-dinitro benzoyl chloride (0.057mole, 15mL) gradually added, then refluxed about four hrs., with stirring, to check the reaction thin layer chromatography was applied the mixture then poured onto cooled acidified water. Finally collected the product by filtering, dried then re-crystallized from appropriate solvent.

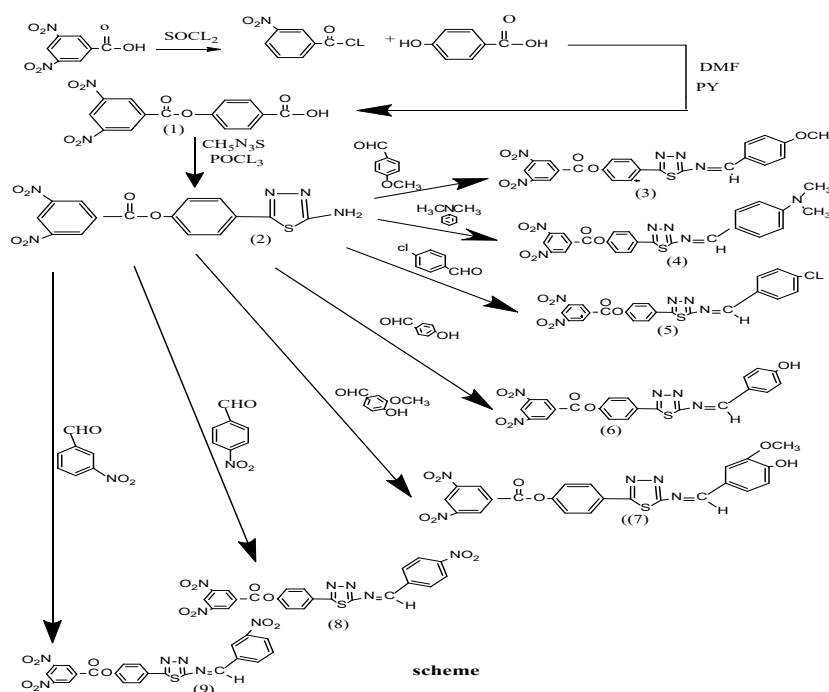
Preparing of Four-(5-Amino-1,3,4-Thiadiazol-2-yl) Phenyl 3,5-Dinitrobenzoate

For 5 hours, a combination of compound 1 (0.0370 mole, five gm), ($\text{NH}_2\text{NHCSNH}_2$) (0.0740 mole, 6.70 gm), in presence of POCl_3 (20 mL) mixed and refluxed.

After that gradually additions of cold water to that reaction (15 mL) and cooled the mixture, and then refluxed for two hours. The resultant was neutralized by (NaOH), producing a deep yellow precipitate which then filtered and finally dried.

Preparing of the New Schiff's Bases

The products of the reaction of [3], (0.7 gm., 0.0050 mole) with 4-chloro benzaldehyde (0.7gm.) or 4-nitro benzaldehyde (0.6gm) or 4-methoxy benzaldehyde (0.5gm) or 4-dimethylamino benzaldehyde (0.70gm) or 4-hydroxybenzaldehyde, (0.70gm) of vanilla, (0.7gm) of *m*-nitro benzaldehyde are heated under the reflux temperature for four hours in absolute (EtOH) (20 mL) with (three) drops of glacial acetic acid. The product was after that cooled, and the result finally recrystallized ethanol and collected by filtration. $\text{X} = 4\text{-Cl}$, 4-NO_2 , 4-OCH_3 , $m\text{-NO}_2$, $4\text{-N(CH}_3)_2$, 4-OH , 4-OH and 3-OCH_3



SCHEME 1

Results and Discussion

The prepared starting material containing carboxylic group which reacted after that with thiosemicarbazide and POCl_3 to get amino thiadiazole. Then the amino thiadiazole compound reacted with

substituted benzaldehyde to get Schiff bases by using glacial acetic acid and absolute (EtOH). The aldehydes involve nitro, bromo, methoxy, hydroxyl and N, N-dimethyl amino etc. Compound has confirmed by the appearance of the stretching bands at $(3500)\text{ cm}^{-1}$ belongs to (OH) of carboxylic acid besides the ester group at $(1750)\text{ cm}^{-1}$, figure 2.

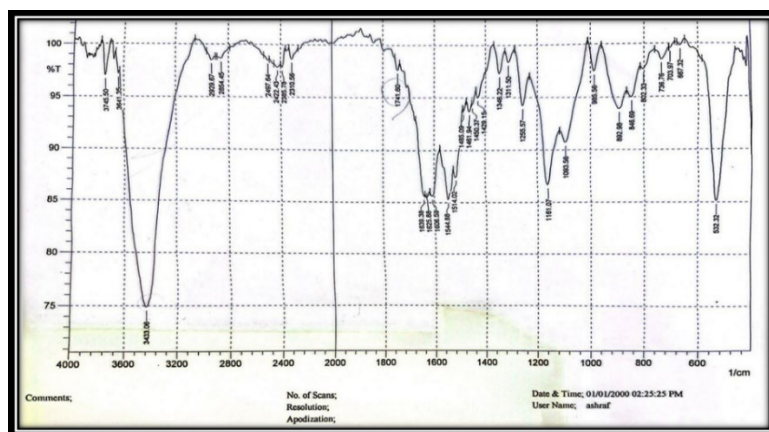
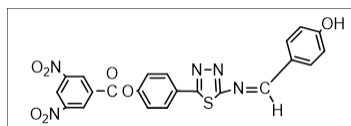


FIGURE 2: FTIR Spectrum.

Compound (2) was characterized through the appearance of the stretching bands at (3420 ,3330) cm^{-1} that attributed to terminal amino groups, figure 3. The spectrum of product appeared the two stretching bands at (3420) and (3330) cm^{-1} for amino (NH_2), and

showed the strong band at (1675) cm^{-1} assigned for endo ($\text{C}=\text{N}$) stretching band besides the strong band in the range (1295-1060) cm^{-1} assigned to ($\text{C}-\text{S}-\text{C}$) group. The prepared compounds may have antibacterial or antibacterial effect against different type of bacteria.

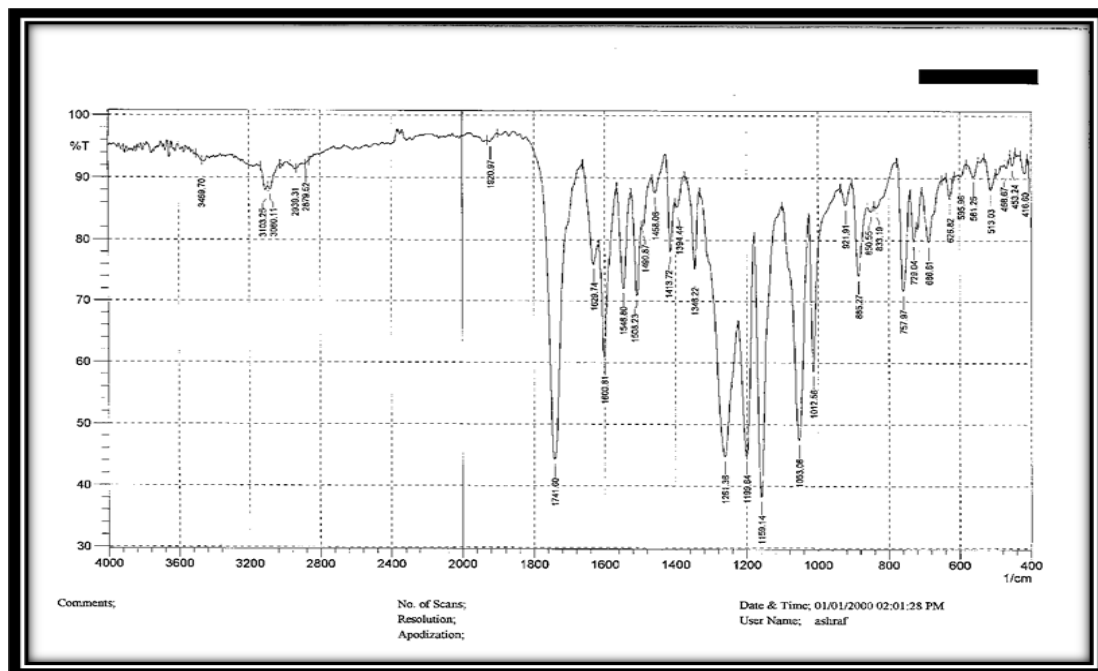
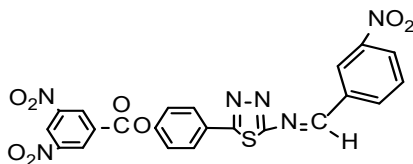


Figure 3: FTIR Spectrum of Compound 3.

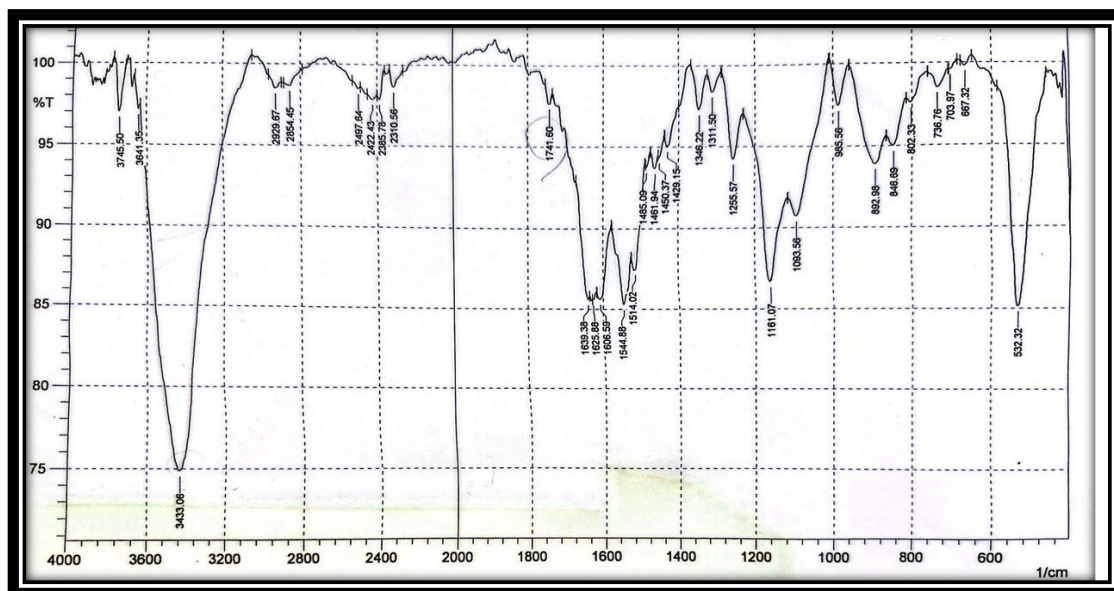
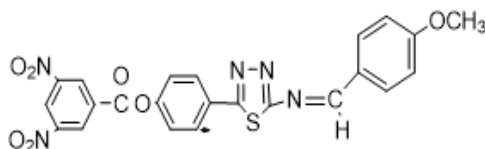


Figure 4: FT-IR Spectrum of Compound 3.

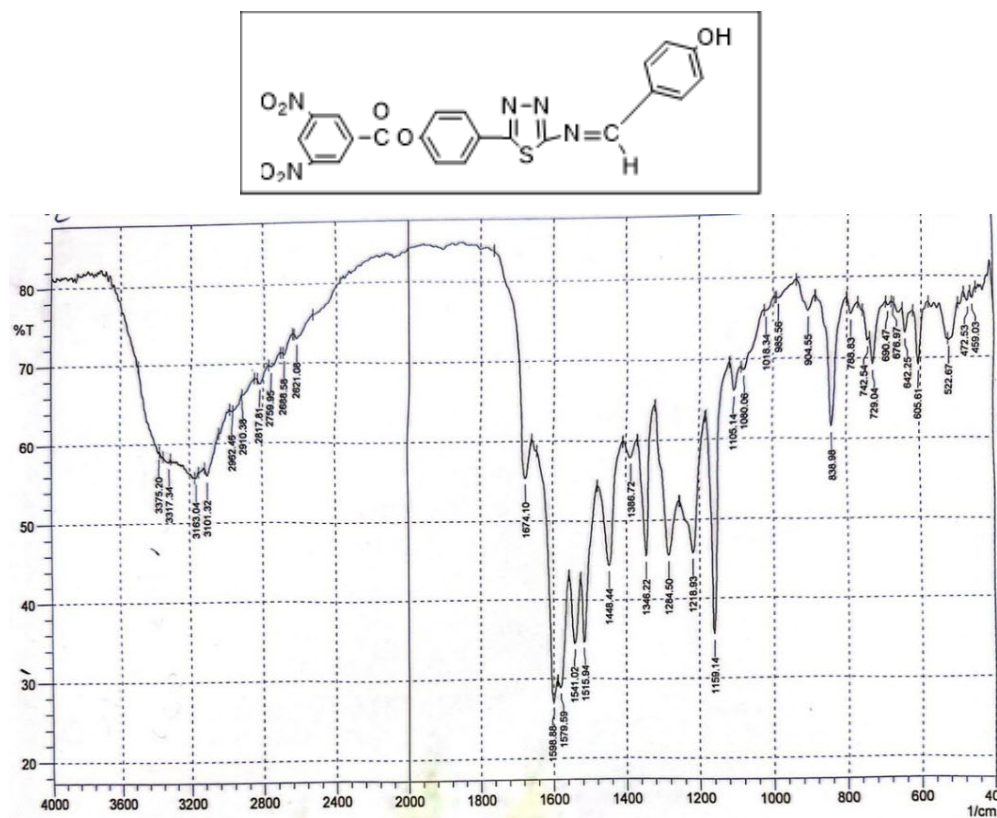
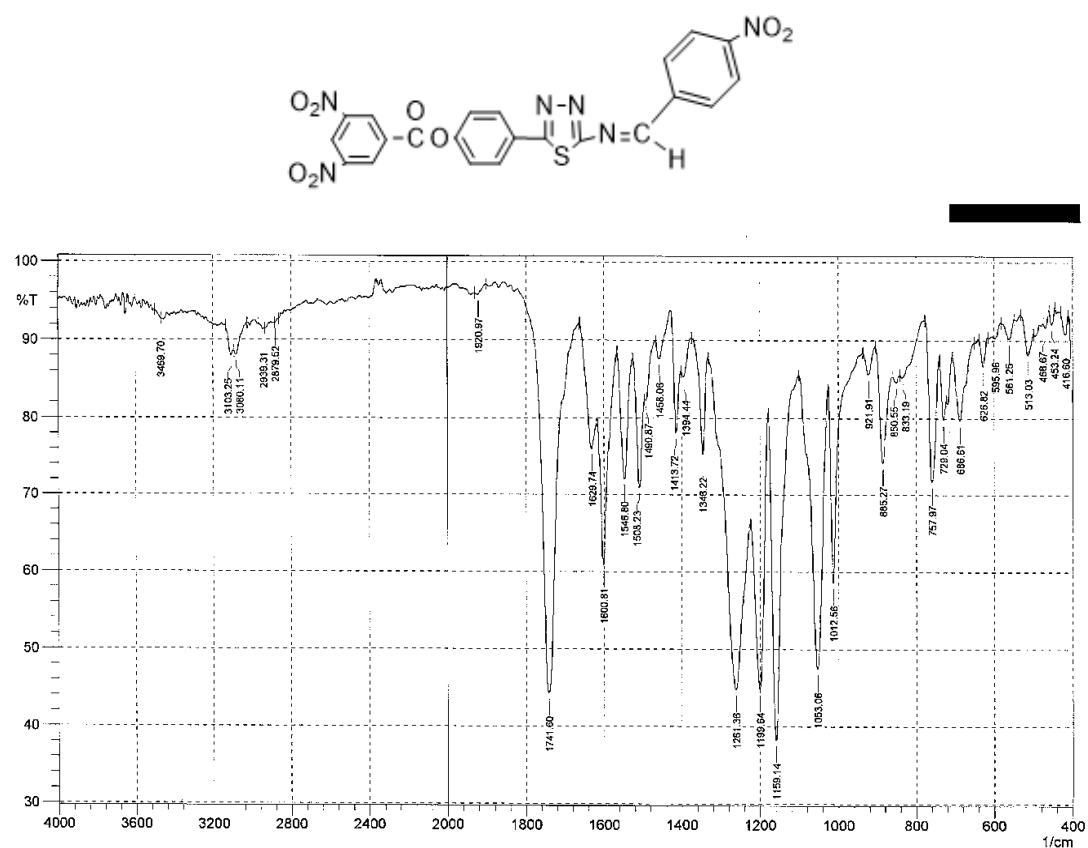


FIGURE 5



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FIGURE 6

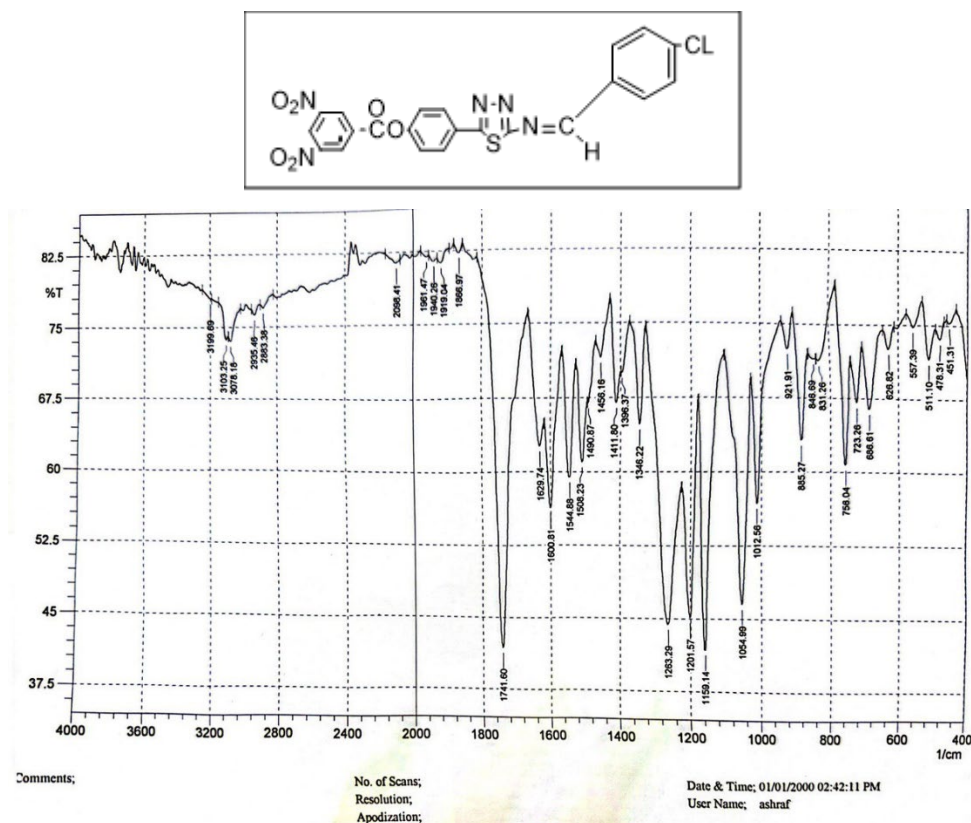


FIGURE 7

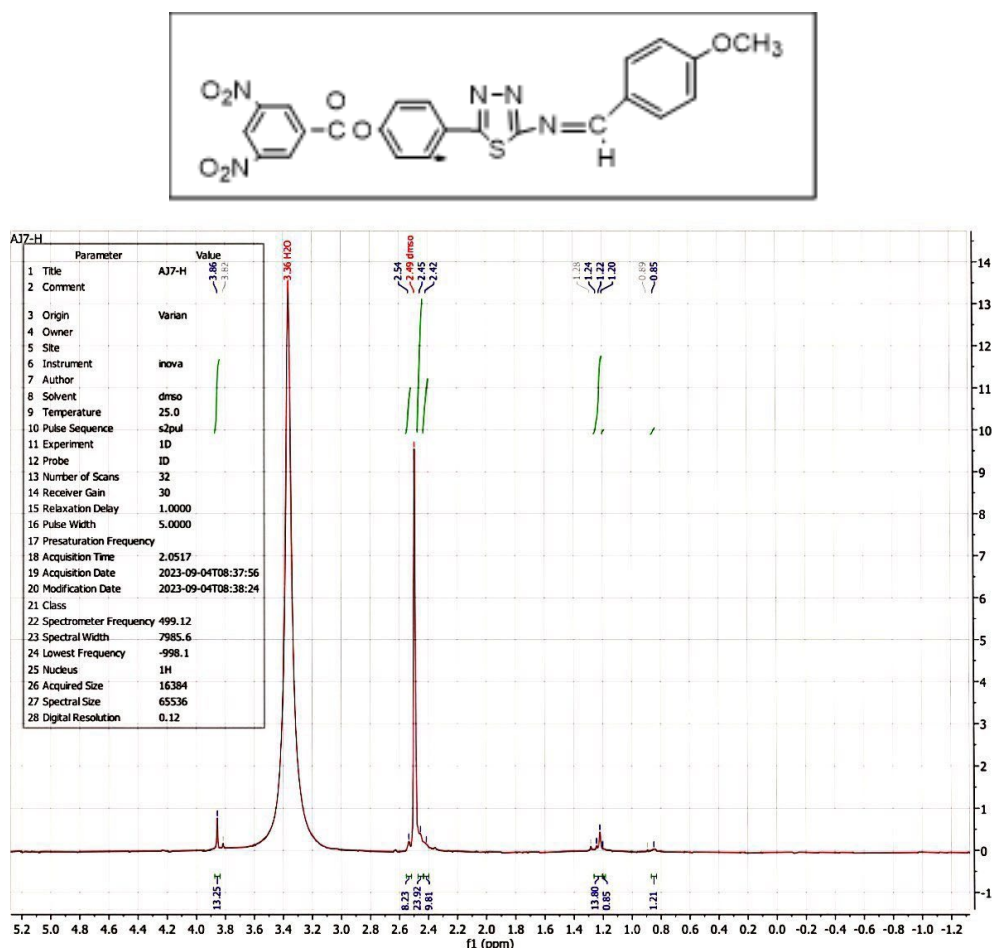


FIGURE 8

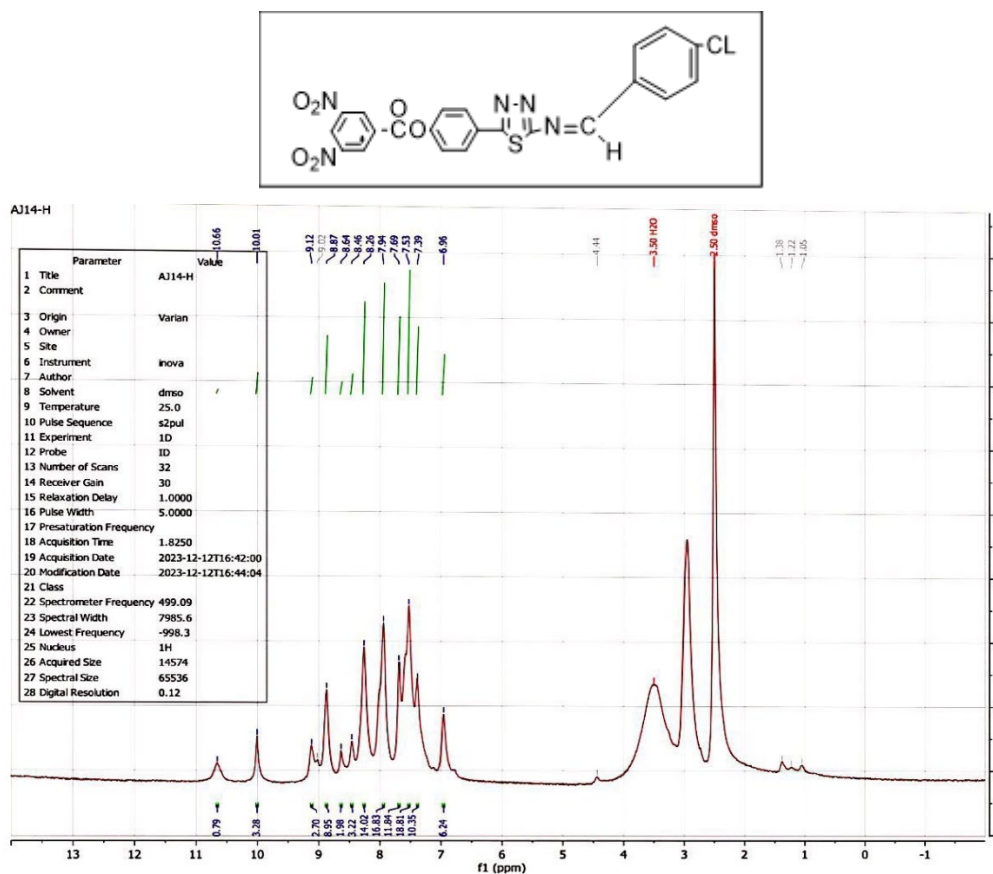


Figure 9

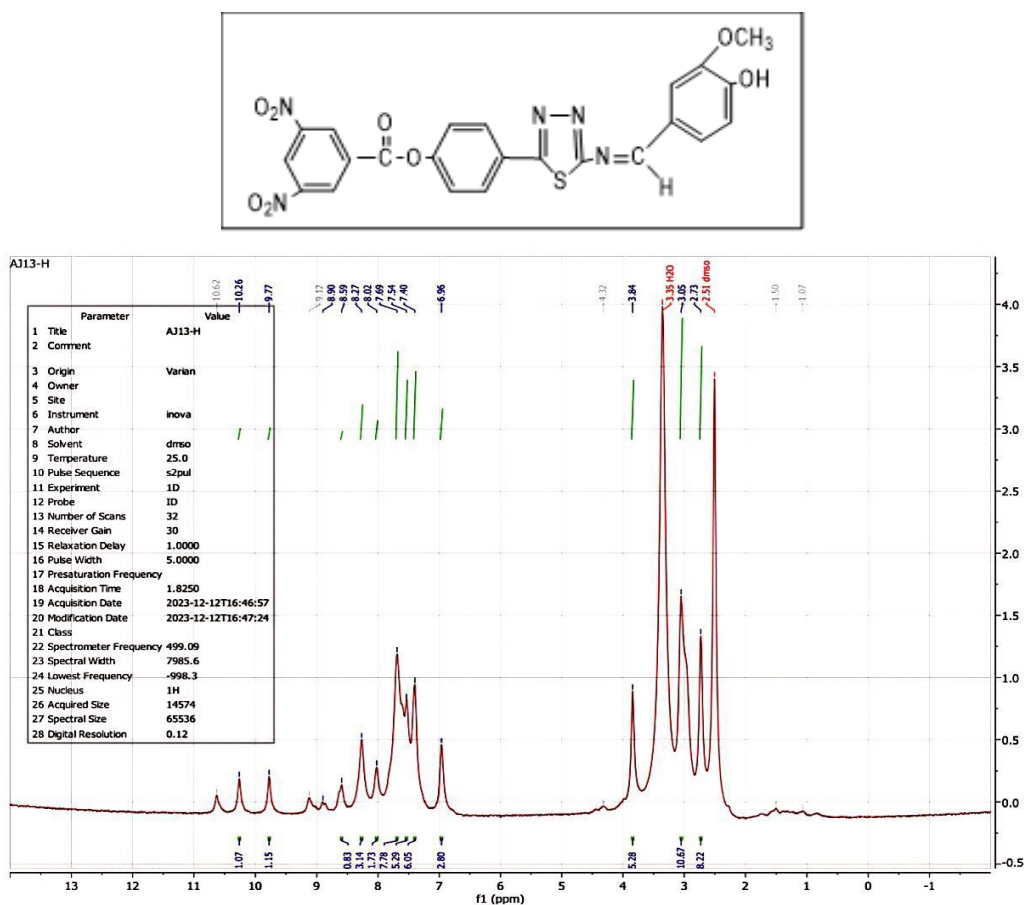


Figure 10

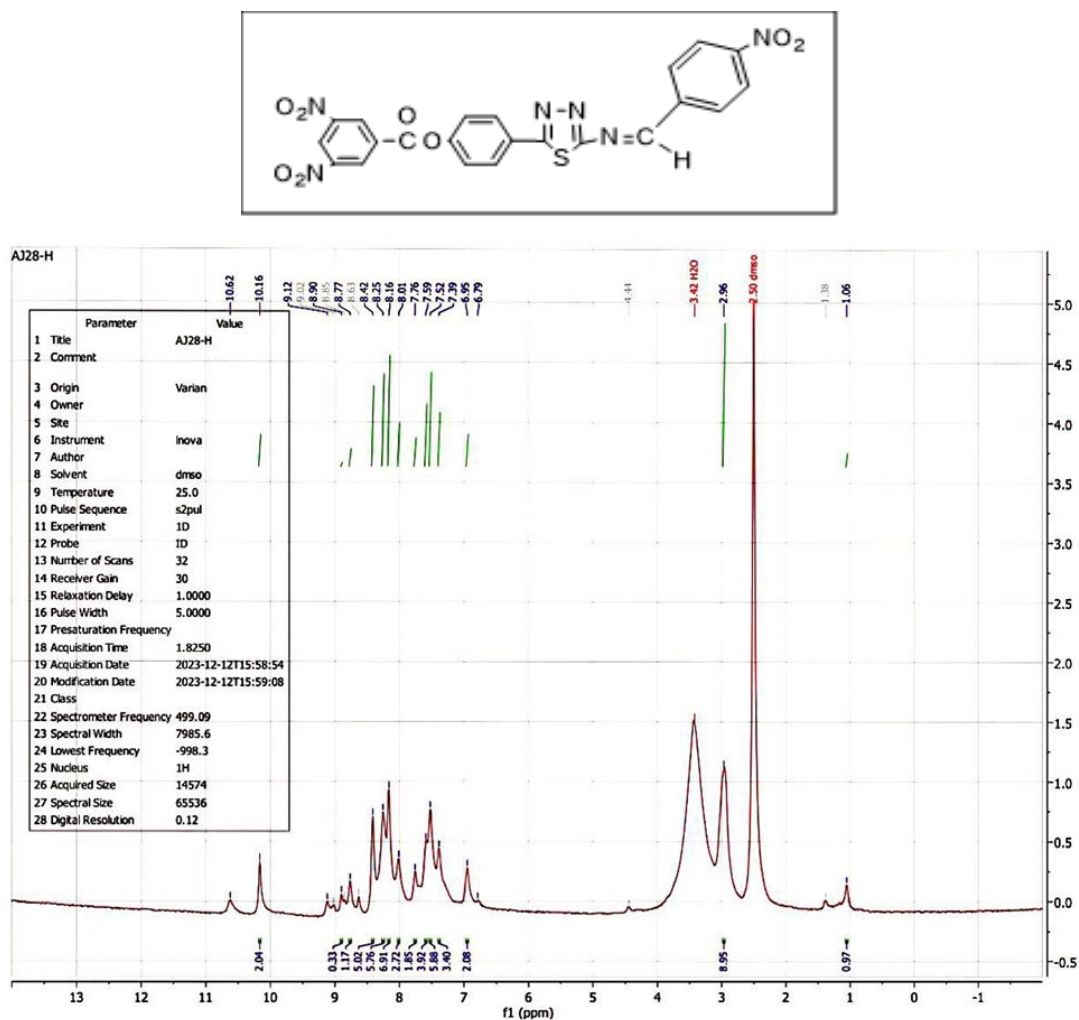


Figure 11

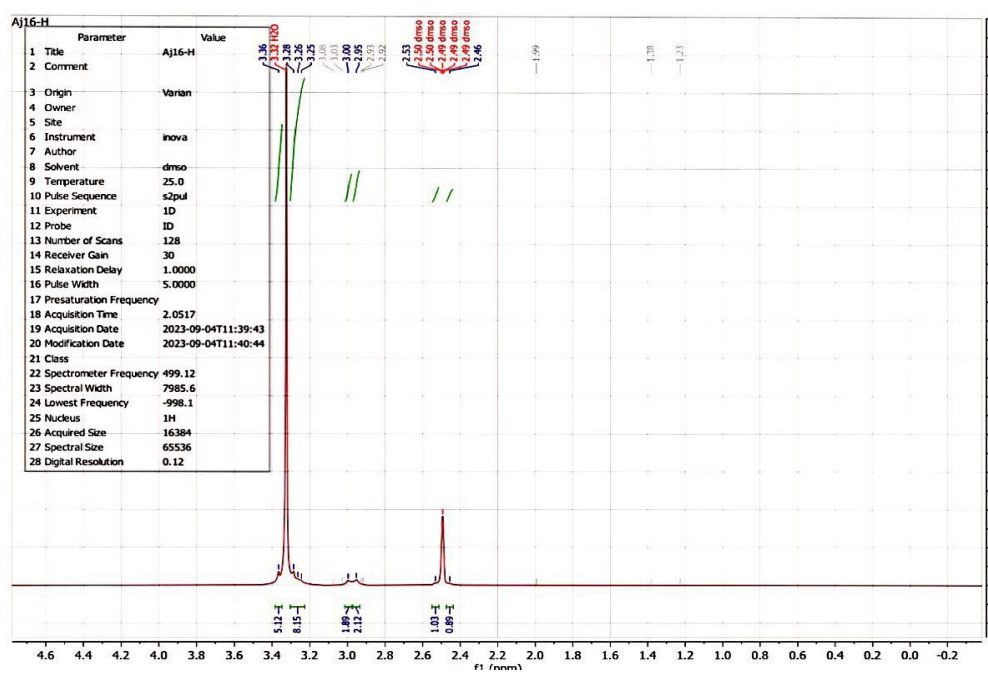


Figure 12

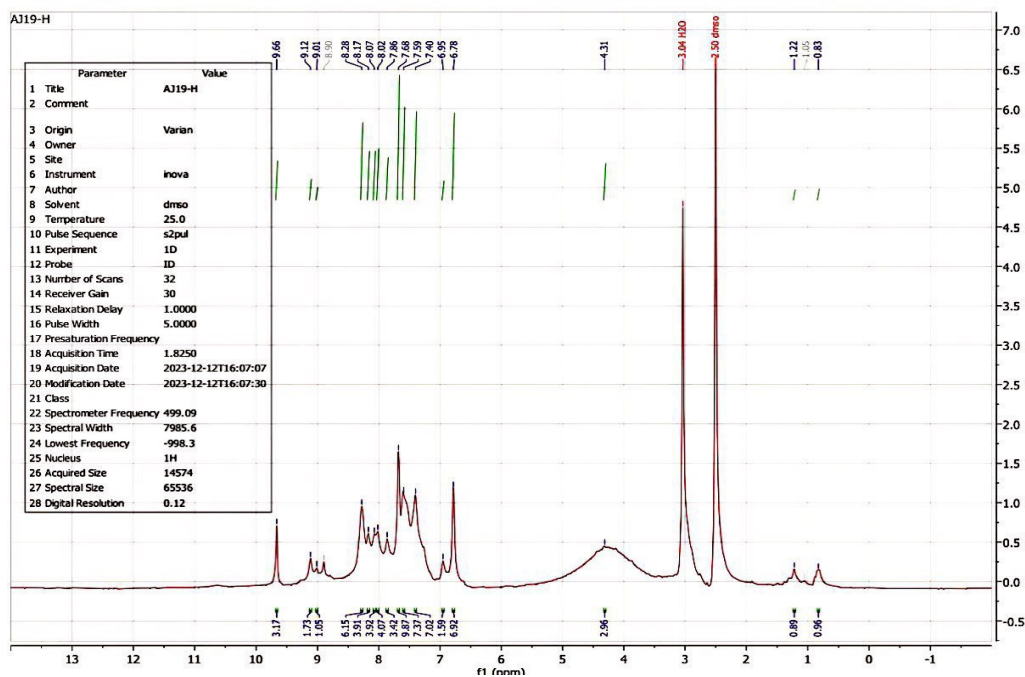
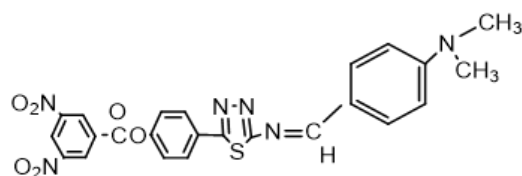


FIGURE 13

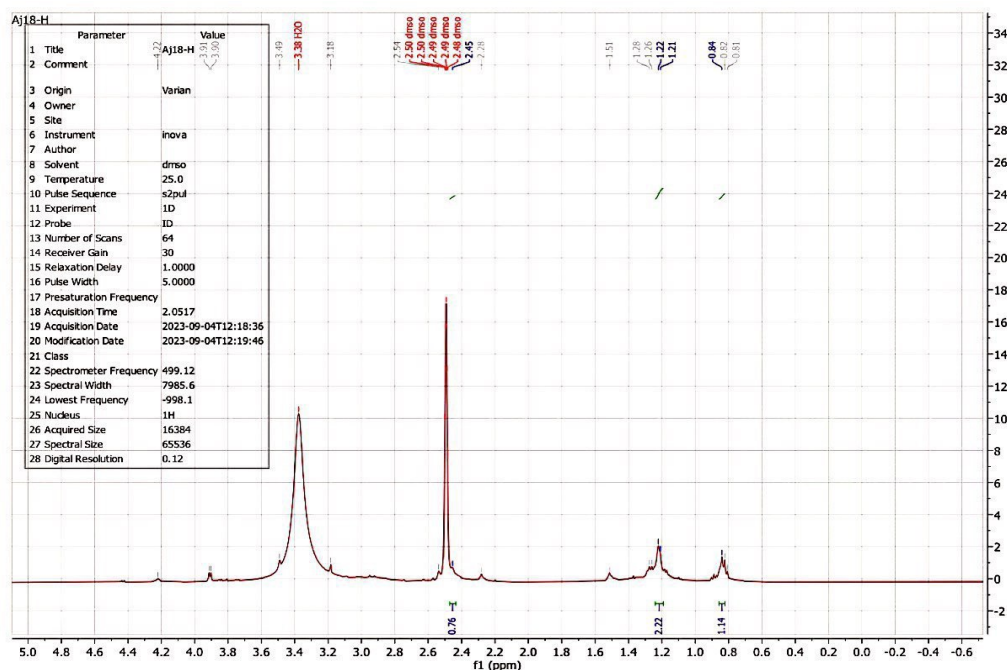
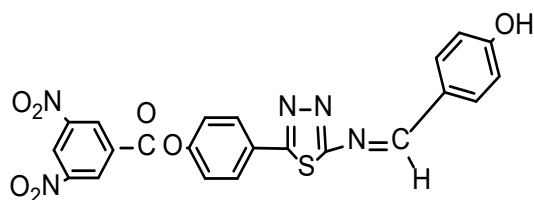


FIGURE 14

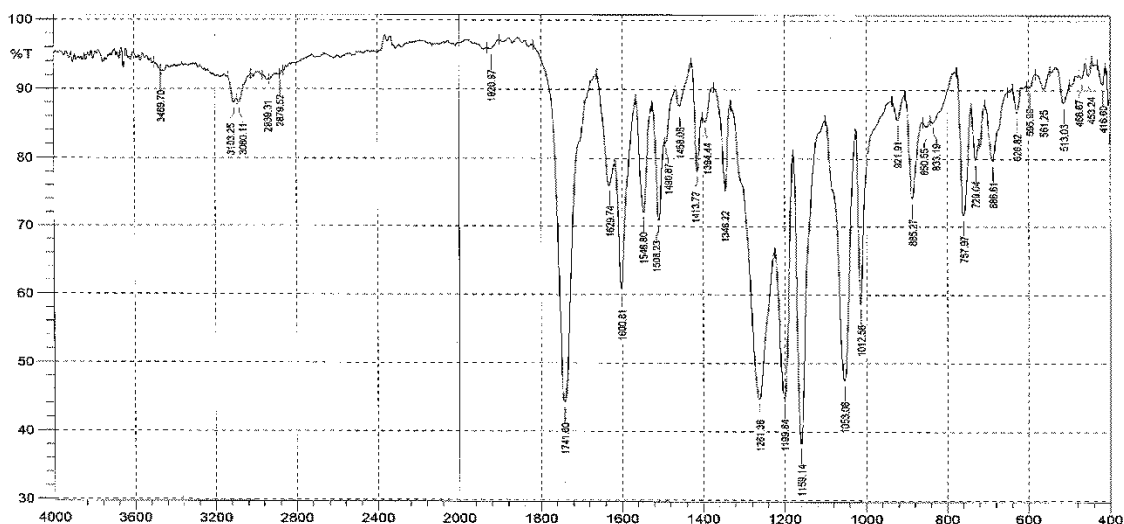


Figure 15

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