



KINETIC ANALYSIS OF SCHIFF'S BASE HETEROCYCLIC COMPOUNDS USING SPECTROSCOPIC TECHNIQUE

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ABSTRACT

Several physicochemical techniques were used for the kinetic analysis of Schiff base metal complexes in high oxidation state and their applications. Schiff-based heterocyclic component derived from the condensation reaction with Pyrazole aldehyde, thioglycolic acid, 2-mercapto malonic acid and thiolactic acid by cyclo-condensation reaction, monitoring the change in concentration using the spectroscopic technique. The aim is to carry out the kinetic measurements. In kinetic analysis, the sequencing diagram shows the CC, TMA, and TLA were created by reporting the mole function of AS (|||) complexed by each ligand. The reaction rate is called kinetics. Kinetics is a powerful tool for studying the reaction mechanism, which provides detailed insight into the reaction. Chemical kinetics deals with chemically interacting systems, as the interactions continue, with observable macroscopic change in the properties of the system. Establishing a quantitative connection between the concentration of the reactants, products, catalyst, temperature, hydrostatic pressure, and the reaction rate is the aim of kinetic studies. Under conditions that resembled those of biological fluids, it was stimulated to evaluate the sequestering ability of ligands at pH=7.5, l=0.15 mol L⁻¹, and T=305.14 K. Due to the 2B1g2A1g transition, the electronic spectrum of the copper (II) complex has a wideband, a central wavelength of 651 nm, a square planar geometry, and encapsulation efficiencies of 9.4%, 2.3%, 19.2%, and 5.9%, respectively

Keywords: Schiff base, kinetic analysis, Pyrazole aldehyde, thioglycolic acid, 2- mercapto malonic acid, thiolactic acid, spectroscopic technique.

I INTRODUCTION

Kinetic study is the formation of derivatives of 4-thiazolidinone from Schiff base and thiolactic acid, thioglycolic acid, 2-mercapto malonic acid by cyclocondensation reaction and its dependance on various factors such as thiolactic acid, thioglycolic acid, 2-mercapto malonic acid concentration, Schiff base concentration, p-TsOH concentration, dielectric constant, ionic strength and temperature stability of the medium have been carried out. The thermal stability and breakdown behaviour of complexes have been examined using the thermo gravity metric approach at a heating rate of 10°C min⁻¹ in a nitrogen atmosphere. Thermal and spectroscopic

characterization will be used to show this [1]. According to the electrochemical investigation, the pyrrole ring stabilises the metal ion, increases the positive charge of the complex, and facilitates reduction. The powder X-ray diffraction technique has been used to identify the complexes' cell characteristics [2]. Heterocyclic Schiff bases are used to create the potent antibacterial compounds oxazolines, pyrazolines, and azetidinones. With their transition metal ligands, Schiff bases, which can be bidentate, tridentate, polydentate, or tetradentate, can form very stable complexes. They can only be utilised as complexing ligands if a functional group, typically a hydroxyl group, is placed close enough to the condensation site to react with a metal ion and form a five- or six-membered ring.

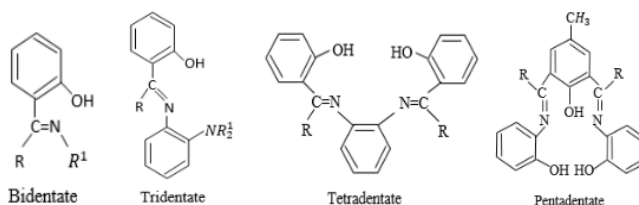


Figure 1: Some Schiff base ligand groups

In coordination chemistry, the Schiff bases of hydroxy, aldehydes and ketones were frequently utilized to create metal complexes [3]. A number of metalloenzymes are modelled after metal complexes comprising bi and tridentate Schiff bases that additionally contain nitrogen and oxygen donor atoms in order to efficiently catalyse the reduction of dinitrogen and dioxygen. Bhutani suggested creating a number of new benzothiazole-1,3,4-oxadiazole-4-thiazolidinone hybrid analogues (Tz1-Tz28) in an effort to find viable anti-diabetic medications. Schiff bases are essential in enzyme catalysis because they keep the carbonyl group oxidized. They also form a covalent bond with the substrate, which prevents it from diffusing away during the reaction. When an enzyme's amino group interacts with a carbonyl group in the substrate, a wide variety of enzymatic activities appear to use Schiff bases as crucial intermediates [5]. Water and five non-aqueous solvents are used to study the intramolecular base-catalyzed nitroaldol reaction between three freshly synthesised 2-(2-nitro alkyl) benzaldehydes (1a-c) that produces matching 2-nitro indan-1-ols (2a-c) [6]. Here is an illustration of the ligand.

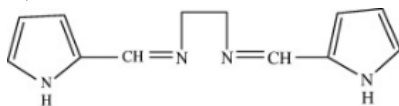


Figure 2: Ligand structure

coordination chemistry is a most outstanding and lively field of current research in chemistry. The metal complexes of coordination compounds are formed by the formation of bonds between metal ions and molecules with one or more unshared pairs of electrons called "ligands" [7]. When a metal ion binds with a negative ligand, there exists an ion pair interaction. Ion-dipole interaction occurs if the ligand is neutral [8]. The tendency is determined by the size of the macrocyclic cavity, the ligand's flexibility, and its proclivity for metal ion binding. The main contribution of the research are as follows

- Schiff's bases have been studied by reacting pyrazole aldehyde, thioglycolic acid, thiolactic acid, 2-mercapto malonic acid at reflux temperature.
- Kinetic study of the formation of derivatives 4-thiazolidinone from Schiff base and thiolactic acid/ thioglycolic acid/ 2-mercaptomalonic acid by cyclocondensation reaction and its dependence on various factors such as thiolactic acid/ thioglycolic acid/ 2-mercapto malonic acid concentration, Schiff base concentration, p-TsOH concentration, dielectric constant, ionic strength and temperature of the medium have been carried out.

II RELATED WORKS

The covalent bond, which prevents it from diffusing away during the reaction, and they function as electron sinks [9]. It has been discovered that a few polymeric Schiff bases have anti-tumor action. SAR and potential therapeutic usage of thiazole and its benzo fused derivatives, which block the processes underlying antibiotic resistance and are utilized to treat severe infections with drug resistance[10]. To examine the effect of N atoms on the effectiveness of the degradation, Yujie, et al. [11] proposed four typical NHCs for ozonation degradation in 2020: benzimidazole (BMZ), indazole (IDZ), indole (IDO), and benzotriazole (BTA). (TOF-MS) projected that the NHCs would deteriorate.

In 2020 Zou, et al., [12] had suggested that the *Lentinus edodes* stipe be optimized in terms of its pyrolytic behavior, decomposition mechanisms, kinetics, and product distributions (LES). In 2020 Hu, et al., [13] created a brand-new racemic 3-substituted-1-indanone-derived ricinolein substrate. Using the vinylogue dynamic kinetic resolution method, more asymmetric synthesis can be achieved. The stars serve to only show the origin and significance of the Schiff base technique as they are the fundamental units of matter [14]. The main research area in bio-inorganic chemistry at the moment is the study of metal-based anticancer drugs [15]. Large amount of synthetic work and an extensive theoretical treatment for understanding the structure and nature of bonding in coordination compounds [16]. Investigation of heterocyclic compounds of pyridine compounds with various metal complexes done in this paper [17]. Examining heterocyclic compounds with oxygen, sulphur, nitrogen, amino-nitrogen, azomethine nitrogen, and alcoholic or phenolic oxygen is a highly popular practise. Aromatic nitrogen heterocycles are a popular type of molecule in coordination chemistry [18].

.For the qualitative, quantitative, and volumetric determination of the central metal Ion, a variety of chelating agents are employed. Schiff bases are known to process a wide range of biological functions [19], and they have been reported as possible medicines. Larik et al. hypothesised [20] that the equivalent N-(4-phenyl-3-aryl-2(3H)-ylidene) substituted acetamides, both halogenated and non-halogenated, were produced by base-catalyzing the cyclization of the appropriate acetyl thioureas with phenacyl bromide. Guanghai, et al. [21] used trifluoromethanesulfonic acid (TfOH)/N, N'-dimethyl ethylenediamine (DMEDA) in dichloromethane (4a-4u) to synthesise a number of 2-thioimidazole-4-ones. Use of isothiocyanates and amino acetamides the rates at which this procedure creates functionalized 2-thioimidazole-4-ones. Dynamic kinetic asymmetric transformation (DyKAT) and catalytic kinetic resolution (KR) are two additional

and complementary methods for obtaining the chiral stereoisomers of both starting materials and reaction products, resulting in high efficiency [22].

In a previous study, [23] proposed that chiral phosphoric acid catalysis could be used to carry out asymmetric distant animations of anilines with azodicarboxylate to achieve kinetic resolution of tertiary propargylic amines, which results in the successful conversion of the chiral amination products and the recovered propargylic amines. According to Kaur, R., et al. [24], a variety of spectroscopic methods, including mass spectrometry, ^1H and ^{13}C NMR, and ^1H NMR, were supposedly utilised to create and characterise hydrazinyl linked sulfonate ester analogues of the 4-thiazolidinone nucleus in 2022. A promising method to inhibit carbonic anhydrase II called 3-ethyl-aniline hybrid aminothiazoles was put out by Ahmed, et al., [25] in 2022.

III PROPOSED METHOD

Heterocyclic compounds Heterocyclic structures are found in many natural products it characterised by one or more of the ring atoms of elements other than carbon. It can be labelled with the isotopes of hydrogen and subsequently employed to determine detailed biosynthetic and metabolic pathways. Acridine, dibenzothiophene, carbazole, and dibenzofuran are each heterocycles for the third family of chemicals. Based on their electrical structure, heterocyclic compounds can be effectively categorized. In terms of behavior, saturated heterocycles resemble acyclic derivatives. Tetrahydrofuran, thiolane, and pyrrolidine are saturated members of this family of heterocycles; their chemical reactivity is similar to that of acyclic ethers, sulphides, and 2°-amines, thus it won't be discussed here. Kinetics is a powerful tool for studying the reaction and hence provides detailed insight into the reaction mechanism. The kinetic study of heterocyclic compounds of derivatives 4-thiazolidinone from Schiff base such as thiolactic acid/ thioglycolic acid/ 2- mercaptobenzoic acid by cyclocondensation reaction and its dependence on various factors such as thiolactic acid/ thioglycolic acid/ 2-mercapto malonic acid concentration.

3.1 Kinetics study of 4-thiazolidinones by cyclocondensation reaction of Schiff bases and pyrazole aldehyde acid.

The rates of cyclocondensations were determined at various concentrations of aldehydes, by keeping the concentration of urea (0.1M) and ethyl acetoacetate. (0.1M) constant. The reaction was performed in acetic acid at 391K. The rate constants of the reaction have been calculated by using an equation of second order reaction at unequal concentration and graphically k, Values for the rate constants were calculated from the $\log(a-x)/(b-x)$ vs. time graphic. It was observed that the formation of 3, 4, dihydropyrimidinones followed the second order rate law and rate constants were fairly constants.

3.2 The cyclocondensation reaction between Schiff bases and thioglycolic acid is used to explore the kinetics of 4-thiazolidinones

It has been investigated how to create 4'-thiazolidinone by cyclocondensing Schiff bases with thioglycolic acid. The present communication examines the kinetics of the cyclocondensation of thioglycolic acid and Schiff bases to generate 4-thiazolidinone while using toluene-4-sulfonic acid as a catalyst.

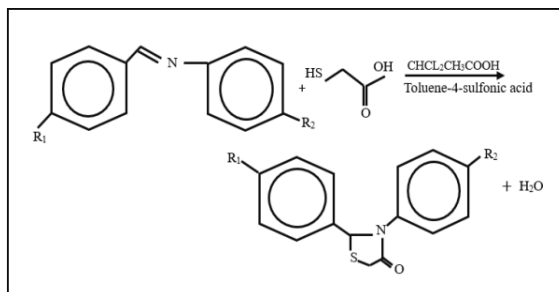


Figure 3: The second order kinetic derivation.

The second order kinetics is supported by the linear plots of $\log [(a-x)/(b-x)]$ vs. time and $1/(a-x)$ vs. time. Any one of the reactants' concentrations can be used to determine how quickly a reaction will proceed.

3.3 Kinetics study of 4-thiazolidinones by cyclocondensation reaction of Schiff bases and thiolactic acid

There has been research done on heterocyclic compound kinetics. The production of 4-thiazolidinone is governed by second order kinetics in general. Thiazolidinone is synthesised using Schiff bases. The cyclization agent thiolactic acid is employed in the manufacture of 4-thiazolidinone. Numerous pharmacological effects are displayed by 4-thiazolidinone and its derivatives. The Grunwald-Winstein equation can also be used to analyze the solvent effect.

Table : 1 Variation of [TLA] at constant [SB], [p-TSA] and Temperature

Sl.no	SB	$K \times 10^3$ By calculation	$K \times 10^3$ By graphical
1	0.05	3.513	3.522
2	0.04	3.485	3.403
3	0.03	3.471	3.467
4	0.02	3.454	3.420
5	0.01	3.440	3.345

With an increase in the medium's dielectric constant, the rate of the cyclocondensation reaction increases. This might be caused by a shift in the reaction's transition state as well as an increase in the medium's ionizing power.

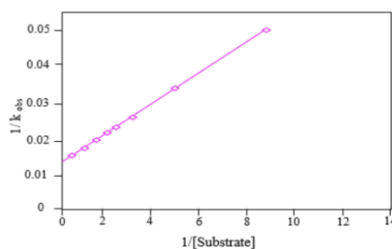


Figure 4: Dependence of the rate on the thiolactic acid concentration

Experiments are conducted at four different temperatures to determine how TA concentrations affect response speeds.

3.4 Kinetics study of 4-thiazolidinones by cyclocondensation reaction of Schiff bases and 2-mercapto malonic acid.

A number of 4-thiazolidinones and 2-azetidinones have been synthesised by combining various aromatic or heterocyclic aldehydes with 4,4'-diaminodiphenylsulfone to form the Schiff's bases. Schiff's bases were cyclocondensed using 2-mercapto propionic acid to provide 2-azetidinone derivatives and 4-thiazolidinone derivatives.

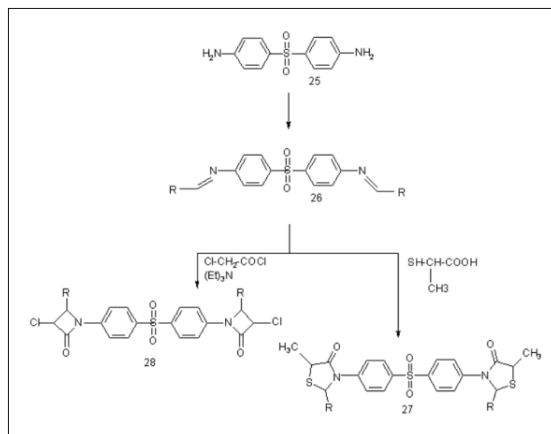


Figure 5: Schiff's base cyclocondensation with 2-mercapto propionic acid produced 4-thiazolidinone derivatives.

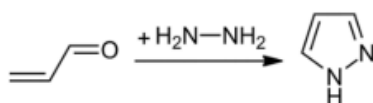
Schiff's bases were cyclo condensed with 2-mercapto propionic acid, and 2-azetidinone derivatives were produced when Schiff's bases were cyclo condensed with chloroacetyl chloride while triethylamine was present.

IV RESULTS AND KINETIC ANALYSIS OF SCHIFF BASE

Kinetics is a powerful tool for studying the reaction and hence provides detailed insight into the reaction mechanism. Chemical kinetics deals with chemically interacting systems, as the interactions continue, with observable macroscopic change in the properties of the system with time. From the kinetic runs, the rate of reaction can be determined with respect to each reactant.

4.1 Preparation and analysis of pyrazole aldehyde

Unsaturated aldehydes are converted into pyrazoles by reacting them with hydrazine and then dehydrogenating them.

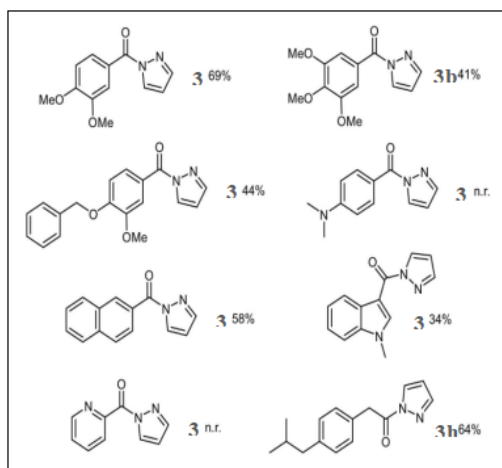


1,3-Diketones and Hydrazine are combined to create substituted pyrazoles. (Reactions of the Knorr kind). For instance, 3,5-dimethyl pyrazole is produced when acetylacetone and hydrazine combine.



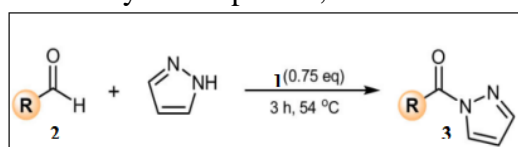
4.2 Preparation of acyl pyrazoles

The N-acyl pyrazole was isolated with low yield in the majority of instances. (3a–3c). There was one exception: when 4-(dimethylamino)benzaldehyde was used, no reaction was detected. (3d). We switched from using benzaldehydes to 4-isobutyl phenyl) acetaldehyde as a starting material to finish our screen, and this resulted in the production of the matching N-acyl pyrazole, 6h, with a 64% yield.



(a)

Using 2-naphthaldehyde as the aldehyde component, we then broadened the scope.

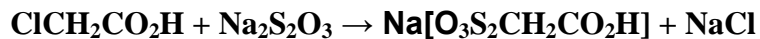


(b)

Figure 6: (a), (b) : Aldehydes are oxidatively amidated with pyrazole to produce acyl pyrazoles.

4.3 Preparation and analysis of thioglycolic acid

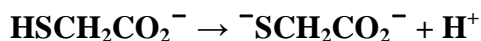
Alkali metal hydro sulphide and sodium or potassium chloroacetate are combined in an aqueous solution to produce thioglycolic acid.



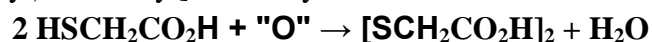
Thioglycolic acid has a pKa of 3.83, making it almost ten times more powerful than acetic acid.



The second ionization has a pKa of 9.3:



Thioglycolic acid is a reducing agent at high pH values. Dithiodiglycolic acid or 2-[(carboxymethyl) disulfanyl] disulfanyl disulfide is the resultant disulfide.



The sequencing diagram of CC, TMA, and TLA was created by reporting the mole function of AS (|||) complexed by each ligand. The graph is mentioned as follows

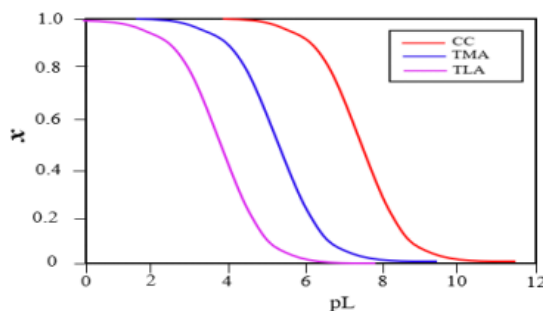


Figure 7: Sequestration diagram of CC, TMA and TLA

The sequencing graph was stimulated to assess the sequestering capacity of ligands under circumstances that mimicked those of biological fluids, at pH=7.5, $l=0.15 \text{ mol L}^{-1}$, and $T=305.14 \text{ K}$.

4.4 Preparation of thiolactic acid

For the enzyme N-acetyl-muramyl-L-alanine amidase, the reagent trityl (triphenylmethyl) thiol can be used to stereoselectively introduce sulphur into peptide thioester substrates.

4.5 Preparation of 2- mercapto malonic acid

A 20 mL solution of 1 mole of malonic acid in DMF was made by two hours of refluxing, cooling, and then pouring onto ice. Acetic acid crystallized into a compound with a m.p. between 204 and 205°C, an 88% yield, and IR values of 3430, 3310 (OH), 1670, 1650 (C=O), and 1600 (C=N) cm^{-1} . The solid was recrystallized from ethanol with an 81% yield and a m.p. of 225-27°C. Its IR values were 3320-3100 cm^{-1} for NH₂, NH, 3010 cm^{-1} for CH aromatic, 2500 cm^{-1} for SH, 1700-1670 cm^{-1} for C=O, and 1300 cm^{-1} for C=S.

4.6 IR Spectra

The significant IR spectrum data are shown in Table 2. A noticeable band at 1619 cm^{-1} (L4) indicates that the ligand contains an azomethine group. A shift in $\nu(\text{C}=\text{N})$ to 1610–1594 cm^{-1} and the coordination of the nitrogen atom of the azomethine to the principal metal ion were both hypothesised. The 1:1 metal-to-ligand ratios and the absence of electrolysis of any of the complexes point to coordination of deprotonated naphthol oxygen with the metal ions. The phenolic tetradentate ligand's deprotonated oxygen and nitrogen atoms work along with the metal ions, according to IR data.

Table 2 Schiff bases' infrared spectrum data and their metal complexes

Compounds	$\nu(\text{C}=\text{N})$	$\nu(\text{C}=\text{C})$	$\nu(\text{M}-\text{N})$	$\nu(\text{M}-\text{O})$
(C ₂₃ H ₂₂ N ₂ O ₄)	1599	1519	-	-
[Cu(C ₂₃ H ₂₀ N ₂ O ₄)]	1594	1489	500	512
[Ni(C ₂₃ H ₂₀ N ₂ O ₄)]	1611	1493	452	518
[Zn(C ₂₃ H ₂₀ N ₂ O ₄)]	1620	1511	449	530

[Mn(C ₂₃ H ₂₀ N ₂ O ₄)]	1592	1520	443	520
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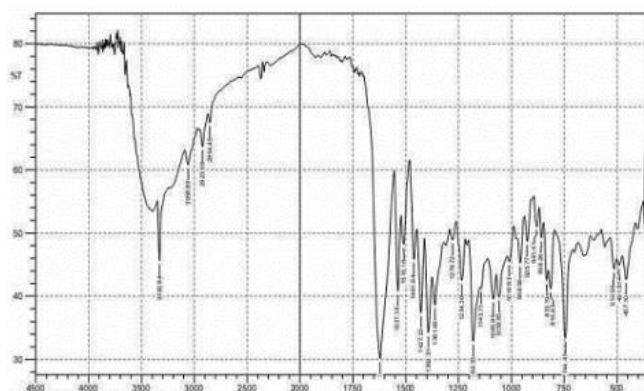


Figure 8: IR spectrum of Ligand L⁴

4.7 H NMR and C NMR spectra of ligands

The hydroxyl protons are responsible for the spectral 12.50 ppm signal for the Schiff base in the free ligand's H NMR spectrum. At 8.53 ppm, the two protons of CH=N go through the same chemical changes. Aromatic ring protons are allocated to the signal at 6.01 ppm and NCHN protons to the signal at 6.82–7.45 ppm.

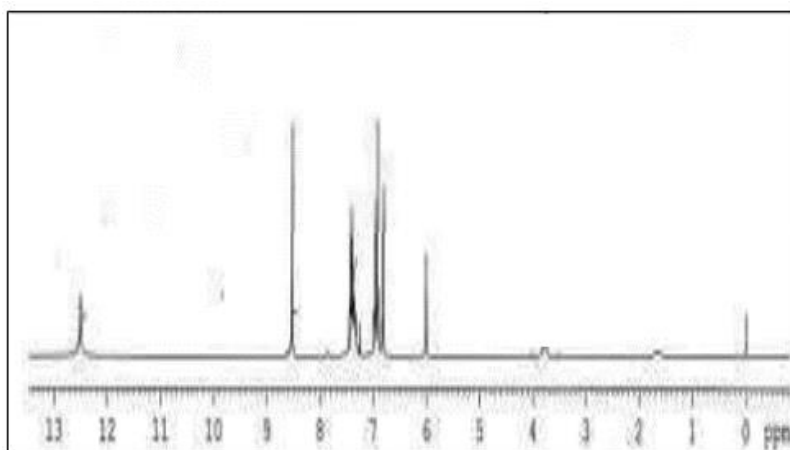


Figure 9: Spectrum of the ligand (L⁴) HNMR

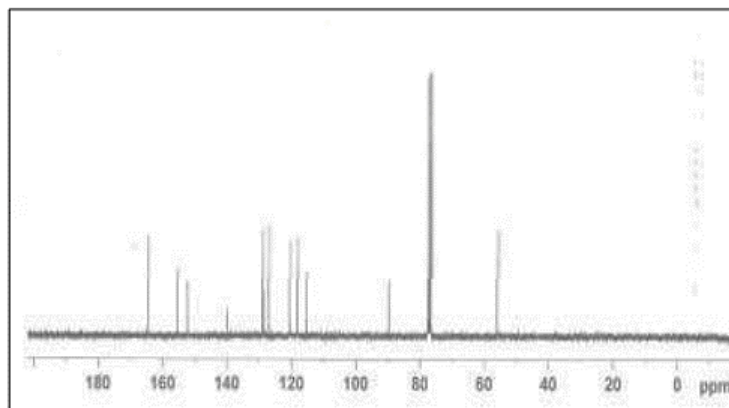


Figure 10: Spectrum of the ligand (L)

4.8 UV-Visible Spectra

A stable band at 273 nm, due to aromatic ring transitions, may be seen in the UV spectra of the ligands and their metal complexes in DMSO. The n- π^* and π - π^* type transitions are responsible for the moderately prominent band at 382 nm in the ligand spectra that serves as another representation of the azomethine group. Due to the $2B_{1g} \rightarrow 2A_{1g}$ transition, the copper (II) complex's electronic spectrum features a broad band with a 651 nm central wavelength and a square planar geometry.

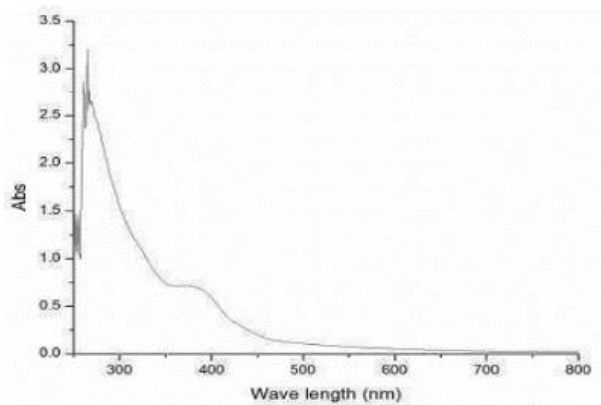


Figure 11: Electronic spectrum of Ligand L

Due to the absence of d-d transitions and charge transfer between the ligand and metal, the zinc complex produces only one intense band at 409 nm.

V CONCLUSION AND FUTURE WORK

Kinetics of a few Schiff bases In this article, heterocyclic compounds of pyrazole aldehyde, thioglycolic acid, thiolactic acid, and 2-mercapto malonic acid are prepared along with spectral (UV-visible, IR, H- NMR, and C-NMR) measurements. Values for the frequency factors are fewer than $10 \text{ dm}^3 \text{ mol}^{-1} \text{ sec}^{-1}$. It suggests that 4-thiazolidinone derivatives are formed by the formation of complexes. Indicating the presence of an ion-ion type reaction, the rate of the

cyclocondensation reaction is directly related to the medium's dielectric constant. The findings demonstrate that metal complexes are more energetically active than the comparable ligands. Increases in the antibacterial.

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