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Synthesis, Characterization & Biological Activity Assessment of a New Oxadiazole Derivative Based on Nicotinic Hydrazide and Using It for Extraction of Ni and Co from Aqueous Solutions

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ABSTRACT: In a recent study, a novel chemical generated from 1,3,4-oxadiazole was synthesized by mixing transition metals with nicotinic hydrazide using their water-dissolved chloride salts. To determine the chemical properties of the bonds and their chains, H1-NMR, FT-IR, and mass spectrometry (MS) methods were used. In addition, conduction sensitivity measurements were performed. The size of the inhibitory zone for Candida Kruse, Candida albicans, Pseudomonas aeruginosa, and Staphylococcus aureus, was assessed after generated complexe was tested against bacteria by means of the diffusion method. The Hyper Chem program was used to do theoretical calculations utilizing the MP3 approach in order to examine the stability energy of compounds and pinpoint the precise sites where they form complexes with metal elements.

Keywords: Nicotinic hydrazide, Oxadiazole, MS spectrometry, Extraction, H^1-NMR and FT-IR.

1. INTRODUCTION

A crucial and broad field of study inorganic chemistry, analytical chemistry, heterocyclic chemistry has synthetic, industrial, theoretical, and medical significance. One popular kind of medication that mimics naturally occurring molecules with physiological activity is called a heterocyclic compound. More than two-thirds of the almost 20 million chemical compounds identified at the end of the 20th century were aromatic, and roughly half were hetero-aromatic. Heterocyclic chemistry is still a productive source of novel compounds [1].

The series consists of the numbers 1, 3 and 4. Oxadiazole is an extremely flexible heterocyclic compound that has attracted a lot of research over the past 20 year [2]. The oxadiazole ring is created through substituting pyridine like nitrogen (-N=) atoms at sites three and four for two (-CH=) methane groups in furan [3]. This modification reduction the aromaticity of oxadiazole rings conjugated ($CnH2n-2$) diene and provides it new characteristics. Electrophilic replacements on the oxadiazole ring are challenging due to the low electron density of the carbon atoms. Therefore, attacks on the nitrogen atoms that are electrophilic are favored. The substitution of electron-releasing groups for the ring may result in nucleophilic assaults. Oxadiazole, on the other hand, frequently shows resilience to such attacks. The

nucleophilic substitution reactions that halogen-substituted oxadiazoles can carry out are similar to those that take place at the sp2 carbon atoms in aliphatic compounds [4]. The chemical formula for the has showing in Figure 1.

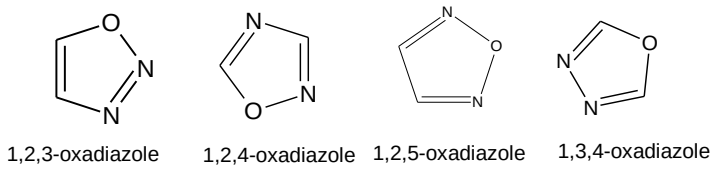

Fig. 1: Configurations of oxadiazole isomers [5,6]

Numerous biological activities are exhibited by oxadiazole compounds, including antibacterial [7], antifungal [8], and anti-inflammatory properties [9]. Derivatives of 2,5-disubstituted 1,3,4-oxadiazole, for example, has shown to have significant anti-tumor effects against leukemia, colon cancer, and breast cancer in addition to efficiently preventing HIV replication [10,11]. These substances are commonly used to treat arthritis and exhibit qualities as analgesics, insecticides, herbicides [12], and plant growth regulators. Tags encapsulate the user's text. Oxadiazole is one of the therapeutically important drugs, along with itraconazole, ravuconazole, posaconazole, and voriconazole. Among the numbers were medications with therapeutic value [13,14].

Organic compounds with ring topologies show significant nonlinear optical properties, according to empirical measurements. 1,3,4-Oxadiazole, a significant five-membered molecule in heterocyclic chemistry, has shown promise for application in materials in recent years [15]. Because of the wide range of uses for these ligands and their metal complexes, we tried to create a new series of these multiplexes.

2. MATERIALS AND METHODS

2.1. Prepare of $5-(\text{pyridine}-3-\text{yl})-1,3,4-\text{oxadiazole}-2-\text{thione}$ (A)

An ethanol reflux was caused with $nicotinic\ hydrazide$ $(7.75\ g, 0.05\ mol)$, KOH $(3.3\ g, 0.05\ mol)$, and CS_2 $(4\ ml, 0.05\ mol)$. $(150\ ml)$; the solvent was acidified using $hydrochloric\ acid$. (10%) to filter, precipitate, and recrystallize [16]. It yielded 93.3% and was pale yellow, MP 221°C. Additionally, TLC examined it.

2.2. Prepare of $3-(5-\text{hydrazine}-1,3,4-\text{oxadiazol}-2-\text{yl})$ pyridine(B)

Overnight, a combination of (A) and $N_2H_2.H_2O$ $(3.53\ g, 0.2\ mol)$ was refluxed in $(70\ ml)$ CH_3OH. whitish precipitate's presence in the circular flask [17]. 75% of the material was filtered and recrystallized at 225°C. The emission of hydrogen sulfide gas was measured using TLC and lead acetate detection.

2.3. Ligand4 $-[(1E)-1-\{2-[5-(\text{pyridin}-3-\text{yl})-1,3,4-\text{oxadiazol}-2-$ yl] hydrazinylidene}ethyl]phenol

By condensing (6 g 0.03 mol) of (B) and $(3\ ml)$of $1-(4-hydroxyphenyl)ethanone\ in$ $(80\ ml)$ DMF, the azomethine groups were created based on Schiff-Base reactions. The fluid was then refluxed for 12 hr. TLC chromatography was used to detect it [18]. Ice water is filled with the heated solution. A yellowish-white ligand molten

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at 230°C is obtained by forming crystals, filtering them, and repeatedly washing them with water, producing 73%. To ascertain the emission of hydrogen sulfide gas and TLC, it is investigated using lead acetate detection (figure 2).

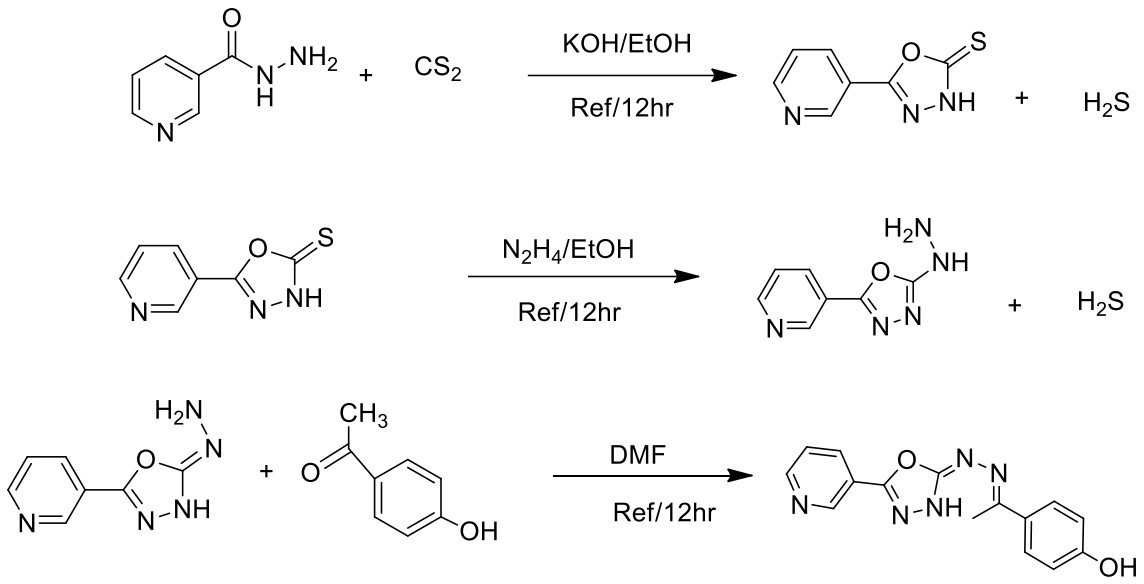

Fig. 2: **Preparation of ligand**.

2. 4. Preparation of the complexes

6-hydrate metal chloride salts (Cr^{3+}, CO^{2+}, and Ni^{2+}) were combined with 0.002 mol of the ligand in 150 ml of pure ethanol, and the mixture was heated to reflux for three hours to create the complexes. To get rid of any last salts and ligand residues, the mixtures were meticulously filtered and washed numerous times with cold ethanol and cold water after the reaction. After drying, the resultant complexes were subjected to TLC analysis [19].

3. RESULTS AND DISCUSSION

Analysis and physical measurements

Table 1: **Examination and quantification of physical properties**.

NO	***Formula***	***Color***	***M.Wt***	***M.P ^0C***	***Λ Scm^2/mol^{-1}***	***Yield***
1	$C_{15}H_{13}N_5O_2$	*Light yellow*	295	210 – 212	– – – – –	73 %
2	$[Cr(L)_2Cl_2]Cl$	*Pale yellow*	784	243 – 236	39.11	71 %
3	$[Ni(L)Cl_2]$	*yellow*	460	231 – 233	17.2	84 %
4	$[CO(L)Cl_2]$	*grey*	443	225 – 227	9.14	79 %

3. 1. FT – IR spectra

The produced complexes were subjected to FT-IR utilizing KBr disk to the ligand and CsI for complexes. The next table (Table 2) shows that the unbound ligand (L) showed six distinct bands, which were caused by (υOH) (3389) cm^{-1} due to (υOH), (3230) cm^{-1} due to (υNH), (1563) $cm^{-1}(\upsilon C = N)$, $(1286cm - 1)$ $(1362Cm^{-1})$ due to $(\upsilon C - O - C)$ sym, and $(\upsilon\ C - O - C)$ asy, respectively [20]. Coordinated $(M - N)$ and $(M - Cl)$ bonding caused additional bands to appear in the areas. $(273 - 289)$ cm^{-1} and $(524 - 528)$ $cm\ {-}^{1}$, in that order. When forming complexes, a new binding took place between nitrogen and metal atoms (524-528) cm^{-1} on the one hand and chlorine and metal (273-289) cm^{-1} on the other, which resulted in new packages appearing at 500-an indication of the formation of a new binding and a complex formation. As seen in Figures 3-6, Table 2

Table 2 : Fourier − transform infrared (FT − IR) spectra of ligands and their complexes.

Compound	*OH*	*NH*	*CH − Aromatic*	*CH − aliphatic*	*C = C Aromati*	*C = N Hetero*	*C − O − C Asy*	*C − O − C sy*	*M − N*	*M − Cl*
Ligand	3389	3230	3059	2845	1608	1563	1362	1286	---	---
$[Cr(L)_2Cl_2]Cl$	3417	3251	3059	2840	1608	1566	1360	1269	524	285
$[CO(L)Cl_2]$	3375	3250	3062	2839	1612	1523	1330	1288	528	289
$[Ni(L)Cl_2]$	3394	3260	3059	2845	1612	1523	1327	1288	524	273

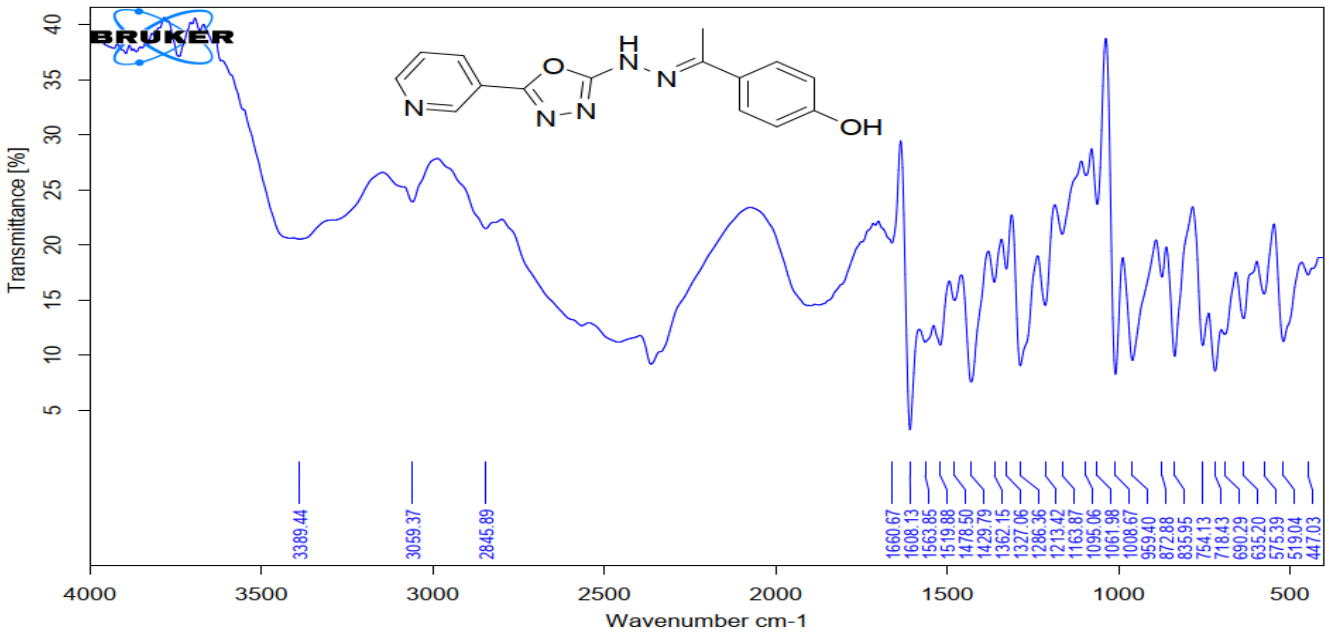

Fig. 3: FT − IR of ligand.

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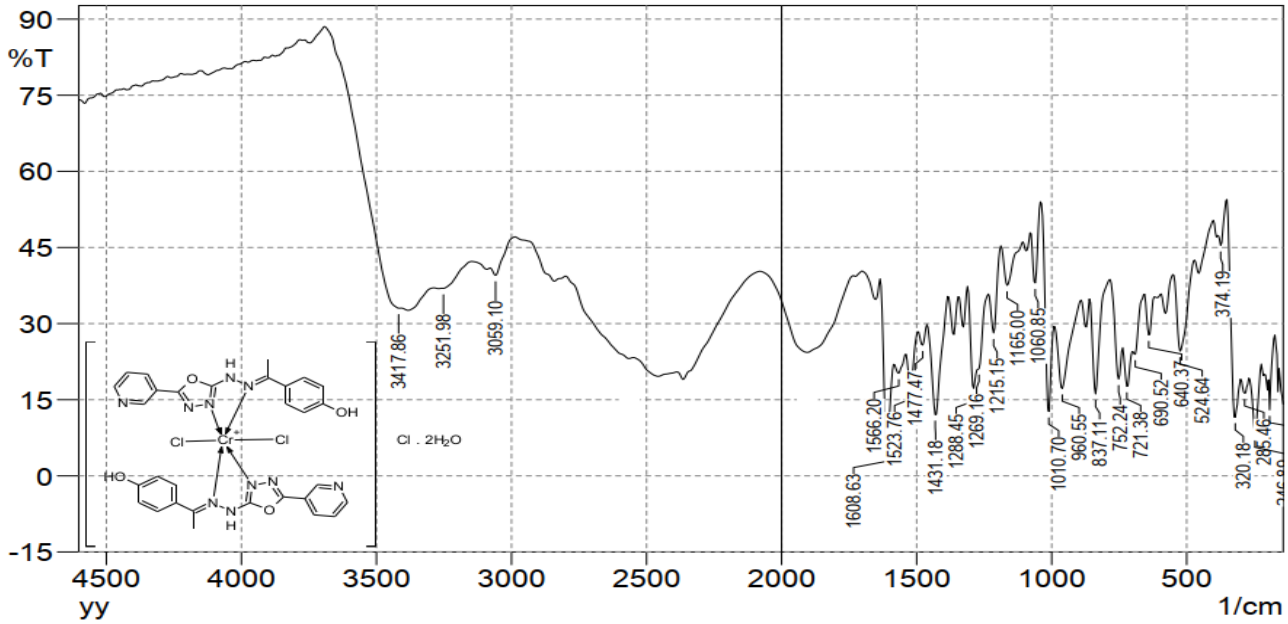


Fig. 4: $\mathbf{FT-IR\ of\ [Cr(L)2Cl_2]\ Cl.2H_2O.}$

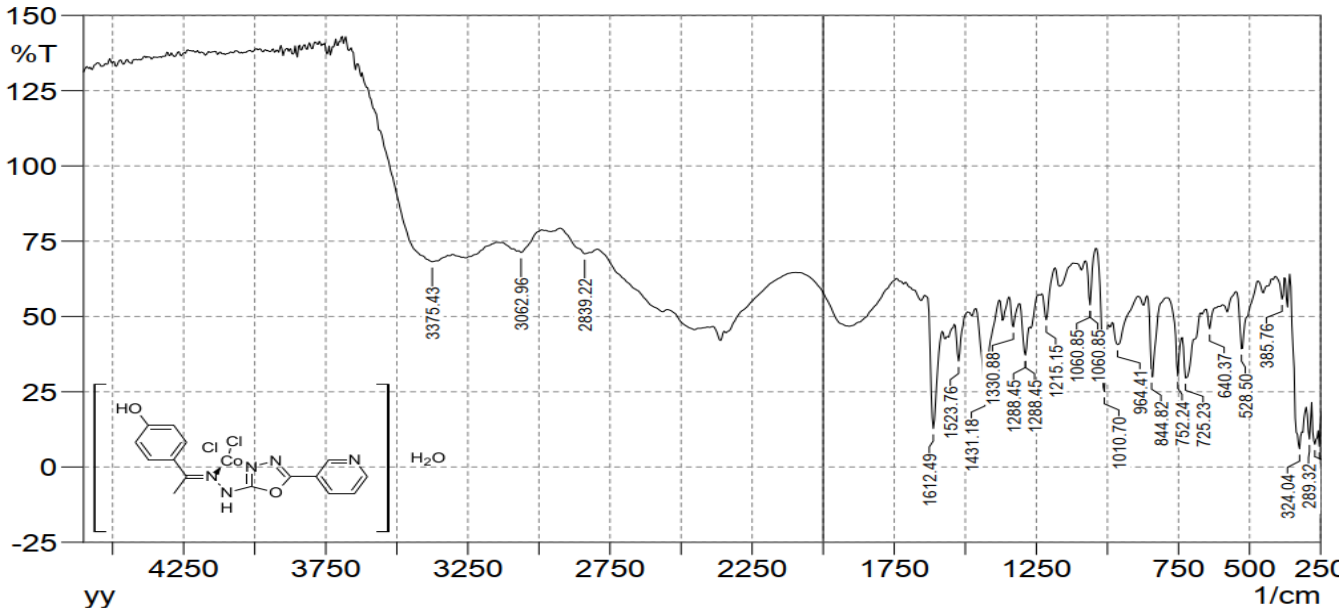
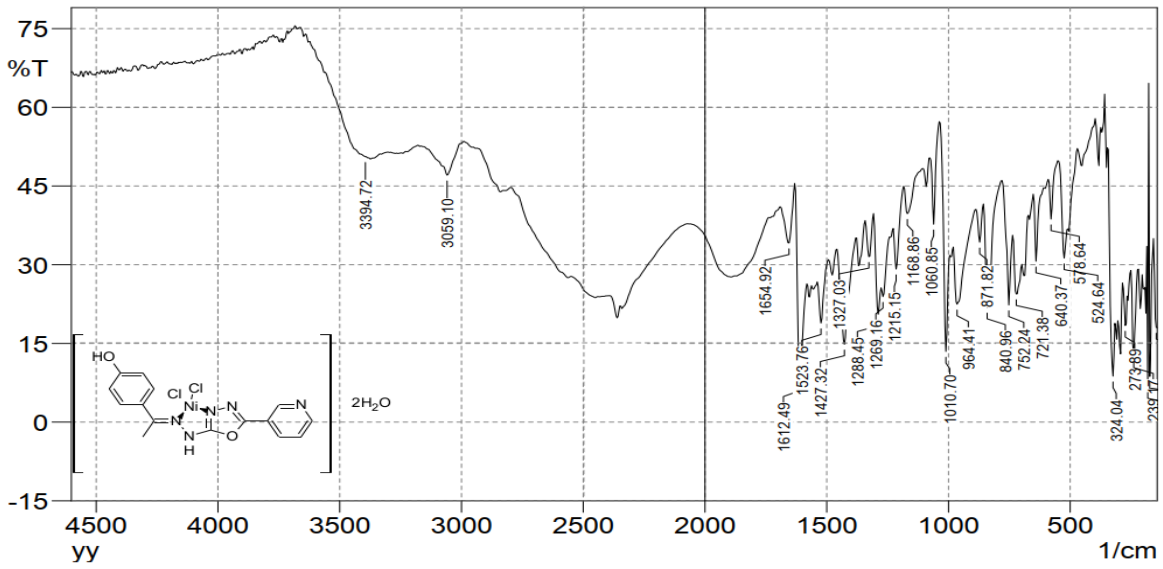


Fig. 5: : $\mathbf{FT-IR\ of\ [Co\ (L)Cl_2]H_2O.}$



ig. 6: FT − IR of $[Ni\ (L)Cl_2]2H_2O$.

3. 2. Nuclear Magnetic Resonance(H^1 − NMR)

The proposed ligand configuration is further supported by the H^1–NMR spectrometry (500 MHz, DMSO-d_6 + D_2O). (CH_3), (OH), and (NH) were responsible for peaks in the spectra at chemical changes of 2.4 ppm, 10.03 ppm, and 12.9 ppm, respectively [20]. The protons of the pyridine and benzene rings, respectively, are responsible for several signals in the range (δ) (7.5-8.03 ppm) and (8.4-8.8 ppm) [21]. Figure 7 displays the H^1-NMR ligands. The appearance of clear band of (CH_3), (OH), and (NH) aggregates in the predicted locations is indicative of the obvious synthesis of ligand formation, as one shows in the fig. 7.

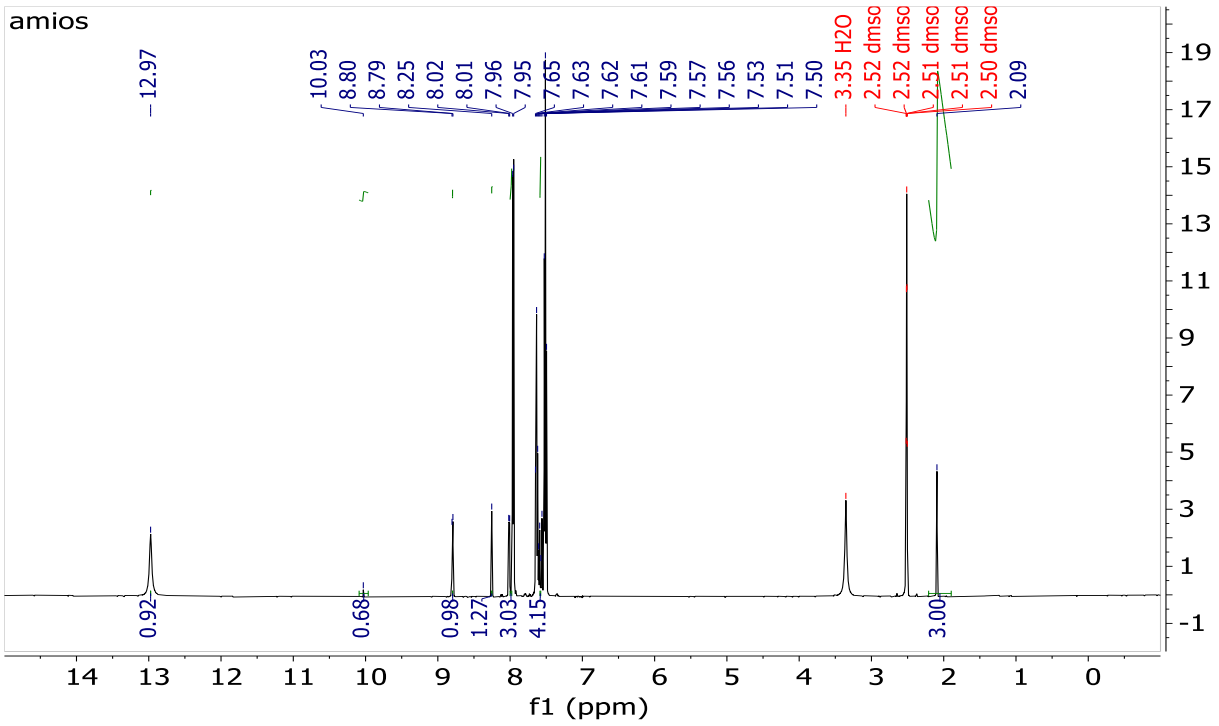


Fig. 7: H^1 − NMR of ligand.

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3.3. Mass Spectrum

The peak of the ligand's molecular ions at $[M]^+$ at (295) m/z $[C_{15}H_{13}N_5O_2]^+$ was seen in the mass spectrometer. The remaining peaks, such as $[C_{15}H_{12}N_5O]^+$ at (278) m/z, $[C_{14}H_9N_5O]^+$ at (263) m/z, $[C_{10}H_9N_4O_2]^+$ at (217) m/z, $[C_8H_5O]^+$ at(187) m/z, $[C_7H_7N_5O]^+$ at (177) m/z, $[C_7H_5N_4O]^+$ at (146) m/z, $[C_6H_4N_2]^+$ = (104) m/z, $[C_6H_9N_3O_2]^+$ at (191) m/z, $[C_6H_4N_2O]^+$ at (120) m/z, $[C_6H_5O]^+$ at (93) m/z, $[C_5H_4N]^+$ at (78) m/z, and $[C_2N_2O]^+$at (68) m/z.

Complex's MS photographs are being examined. A peak is seen in molecules of the chemical $[Cr(L)_2Cl_2]Cl$ with a (m/z) of 748.5(m/z). Because of the cost of 1, 2, & 3 Cl atom, the complex displayed the additional peaks at (713) m/z, (677.5) m/z, and (642). Due to [Cr (L)]$^+$. and [Cr], the complex spectrum displayed additional peak at (347 m/z) and (52) m/z.

Molecular ions peak at (425) m/z is visible in the complex's mass spectra $[Co(L)\ Cl_2]$. Due to the sequential loss of Cl atoms 1 and 2, the compound displayed additional peaks at (389.5) m/z and (354) m/z. Ion peaks are visible in the complex spectrum at (130) m/z because of $[Co\ Cl_2]^+$, (94.5) because of $[Co\ Cl]^+$, and (59) m/z because of [Co]. The compounds' mass spectrum is shown in (Fig. 9).

The peak of the molecular ion at (424) m/z is visible in the mass spectra of the complex $[Ni(L)\ Cl_2]$. As can be observed, the complexs displayed peak at (388.5) m/z & (354) m/z, respectively, as a result of the sequential loss of Cl atoms 1 and 2. The complex spectrum exhibits peaks at (129) m/z due to$[Ni\ Cl_2]^+$, (93.5) due to $[Ni\ Cl]^+$, and (58) due to [Ni]. The outcome of the aforementioned data analysis (mass spectroscopy, H^1-NMR, and FT-IR,) supported the suggested arrangement of the produced complexes As seen in Figure 8.

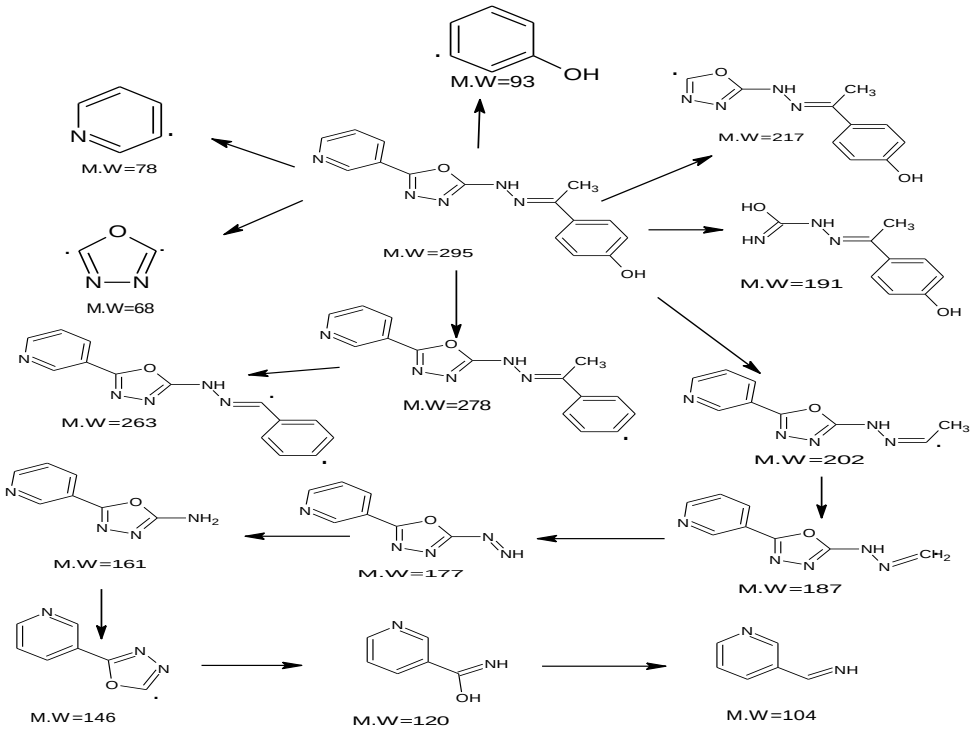

Fig. 8: Fragment of ligand.

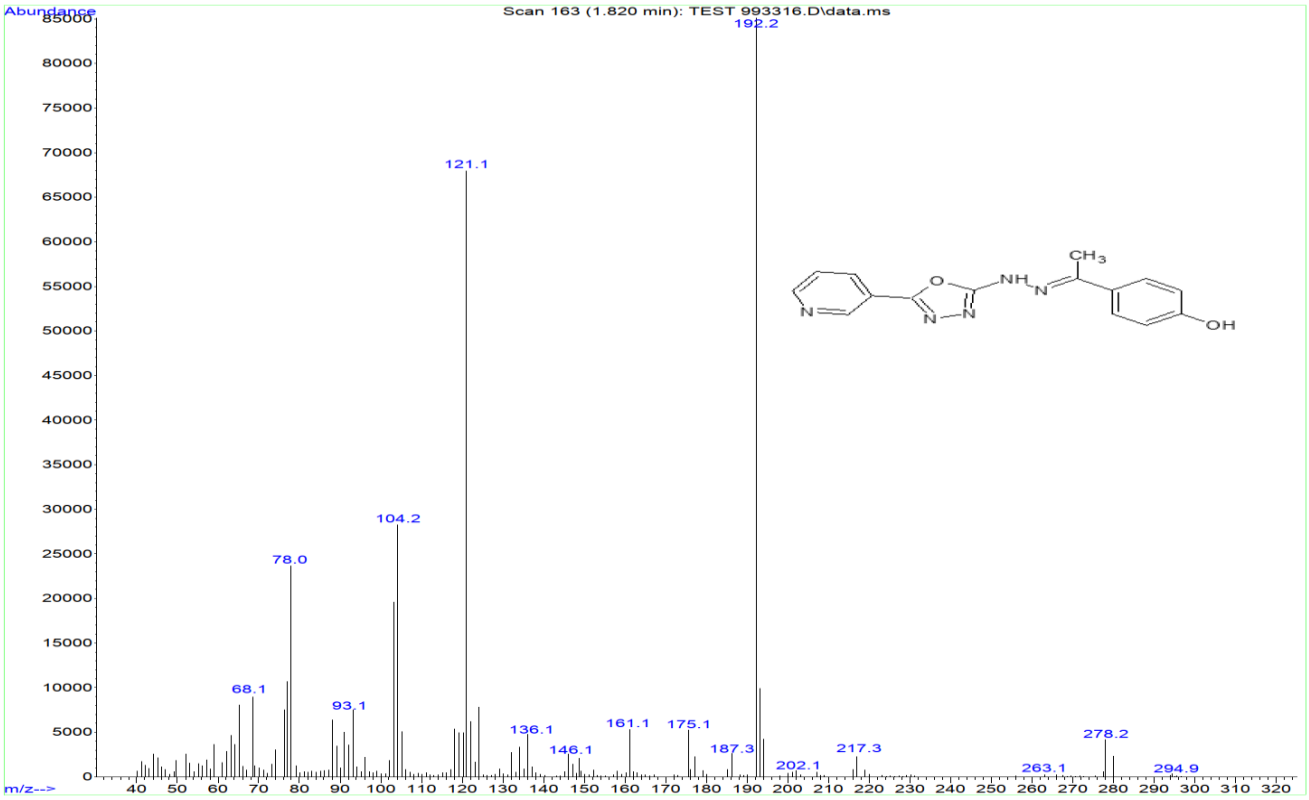

Fig. 9: Mass spectrum of ligand.

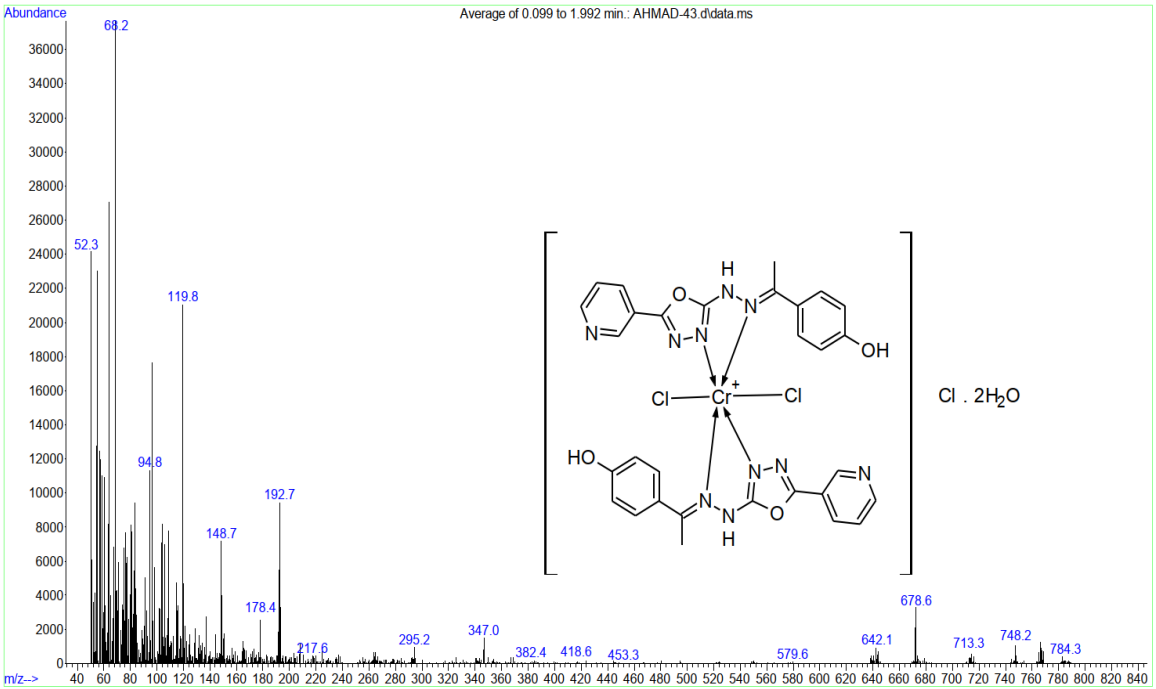

Fig. 10: : Mass spectrum of of $[Cr(L)2Cl_2]$ Cl.2H₂O.

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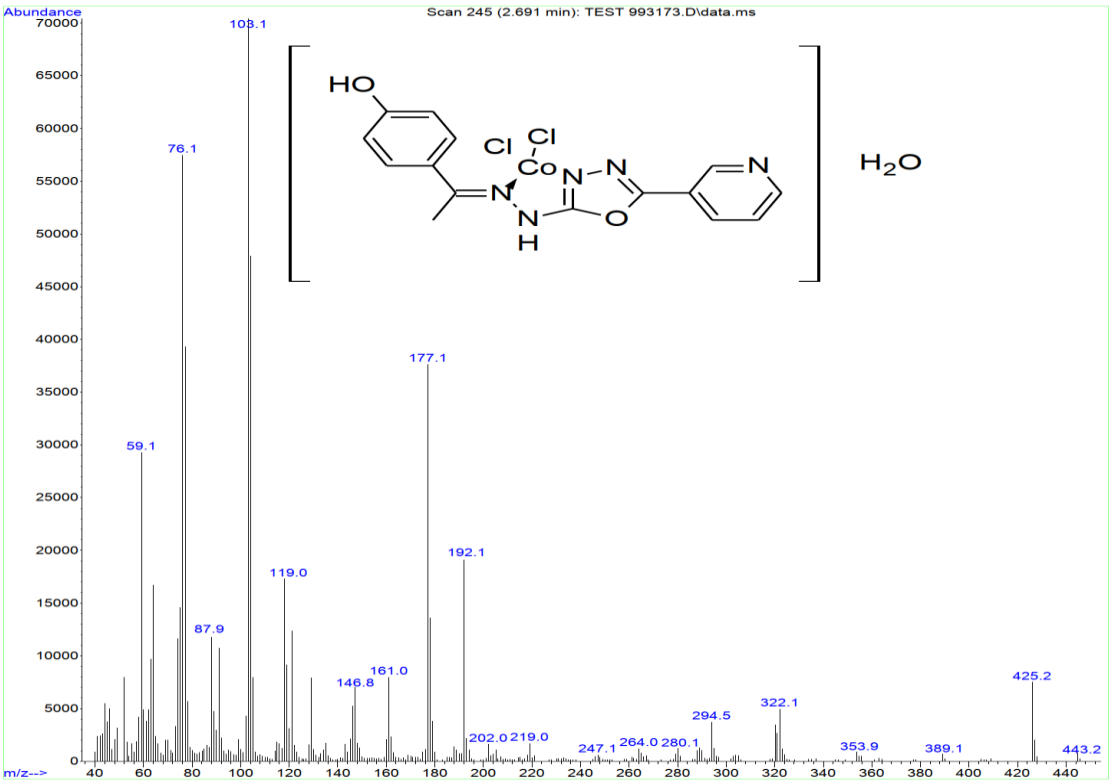

Fig. 11: Mass spectrum of $[Co\ (L)Cl_2]H_2O$.

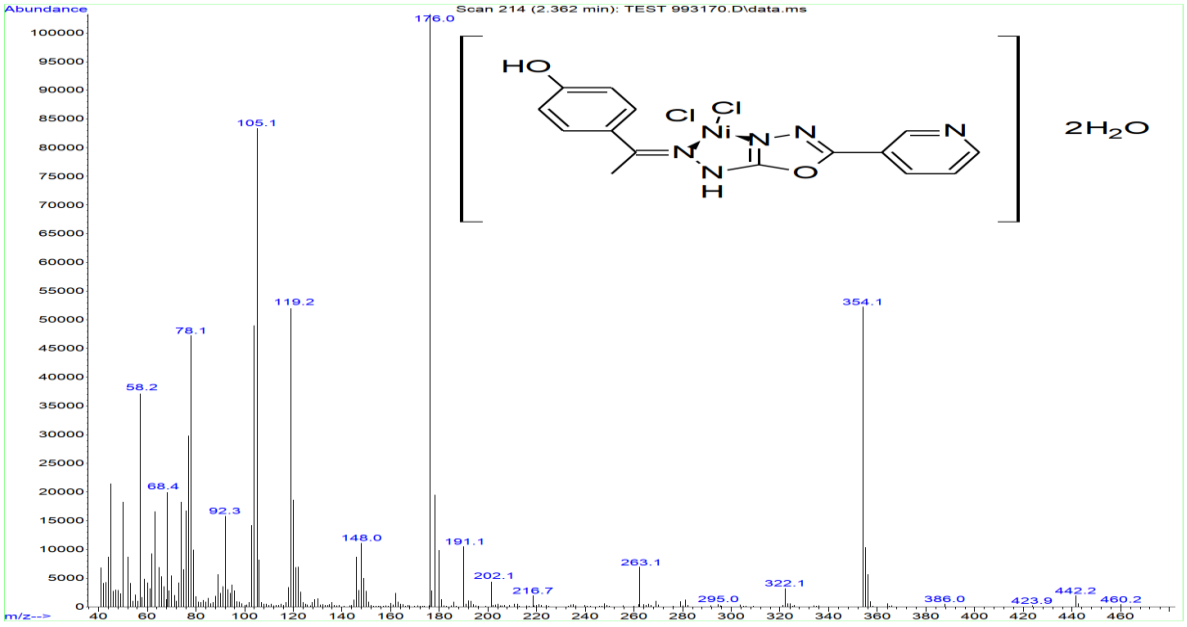

Fig. 12: Mass spectrum of $[Ni\ (L)\ Cl_2]\ 2H_2O$.

3.4. Biological Activity

$Gram-positive\ \ Staphylococcus\ aureus$ & $Gram-negative\ bacteria$ were the two bacterial species against which the ligands & its complex was evaluated for biotic activity. A typical treatment for Pseudomonas aeruginosa is ampicillin, which is regarded as the gold standard for this illness. Additionally, fluconazole and itraconazole, two common medications, were used to screen for two different species of fungi (Candida Krusei and Candida albicans). Millimeters were used to measure the inhibition of bacteria and fungi. Nutrient agar was used as a culture standard. The solvent used was DMSO. A disk sensitivity test revealed that the concentration of all the compounds in this diluent was 10-3. The plates were kept at 37°C for a full day of incubation. It can be inferred from Table 3's results that every chemical possesses antifungal qualities & strong antibacterial as illustrated in Fig. 13.

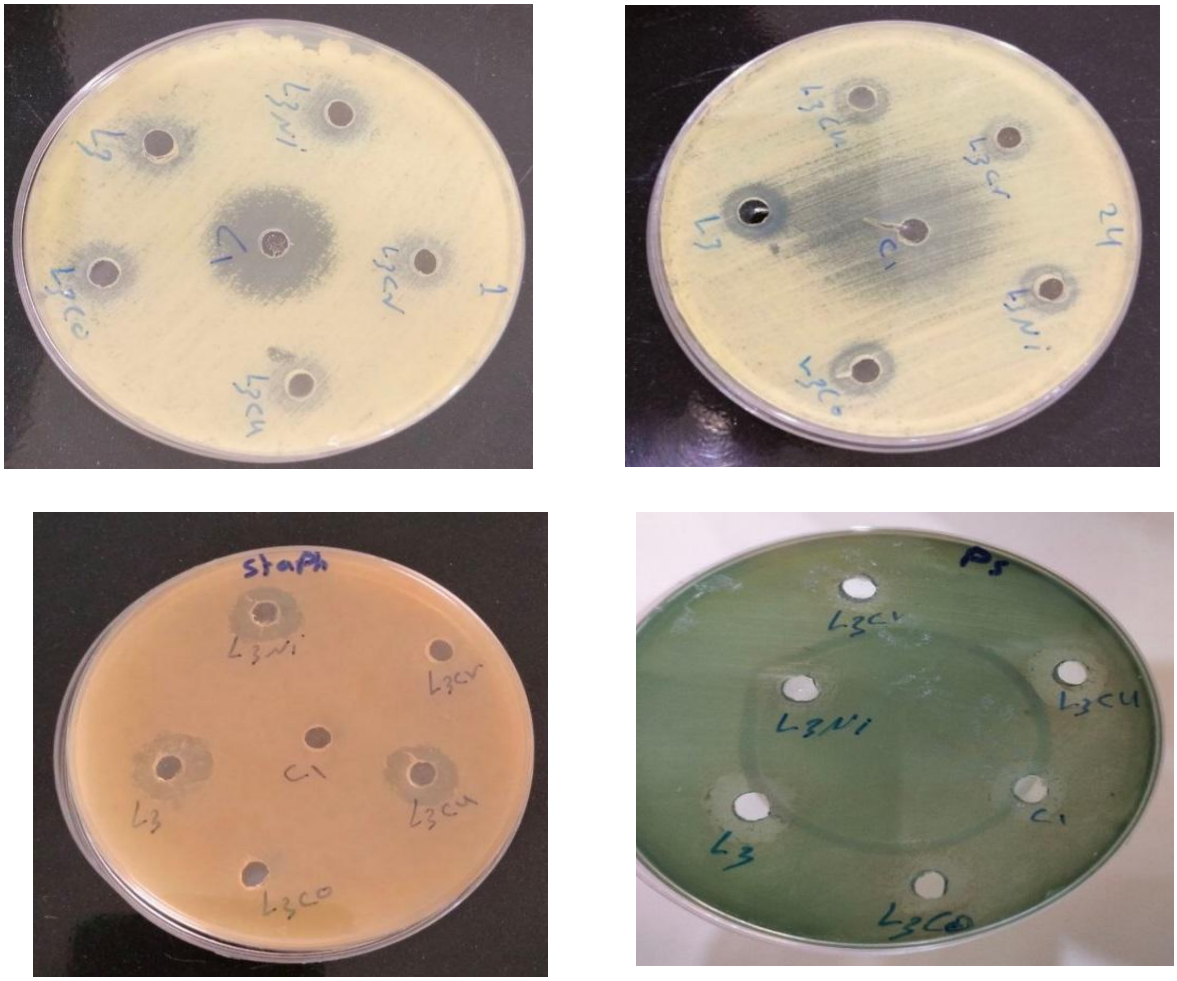

***Fig*. 13**: ***Antibacterial and anti − fungi activity* (*inhibition zone*)**

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Table 3: The zone growth inhibition (mm).

NO.	*Compounds*	*Candida kruse*	*Candida albians*	*Staph +Ve*	*Psedo −Ve*
1	$C_{15}H1_3N_5O_2$ (L)	15	10	18	18
2	$[Cr(L)_2Cl_2]Cl$	10	11	8	0
3	$[Ni(L)Cl_2]$	12	11	14	0
4	$[C_O(L)Cl_2]$	12	11	0	16

3.5. Solvent Extraction Procedure

The oxadiazole derivative typically coordinates with the metal ion through the nitrogen and/or oxygen atoms in the heterocyclic ring, creating a chelated structure.

- The general reaction for this process can be represented as:

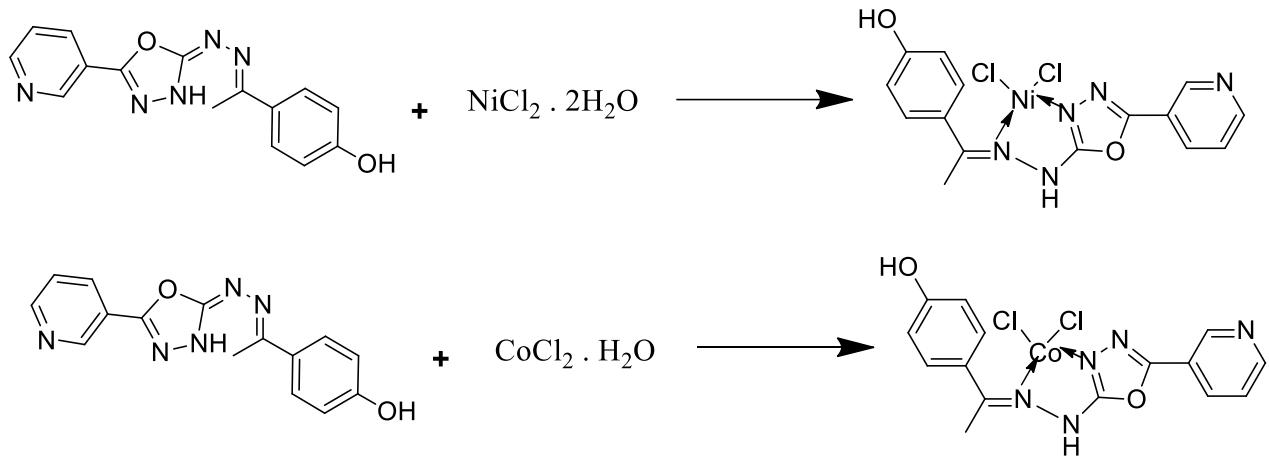

Fig. 14: Preparation of complex $[Ni(L)Cl_2]$ and $[Co(L)Cl_2]$.

Here's a general procedure for the solvent extraction of nickel and cobalt using oxadiazole derivatives: Dissolve the oxadiazole derivative in a suitable organic solvent (dichloromethane). The concentration of the ligand in the organic phase typically ranges from 0.1 M to 1 M, depending on the amount of metal to be extracted. Prepare an aqueous solution of the metal ions (Ni^{2+} or Co^{2+}), typically from a metal salt (nickel chloride and cobalt chloride). The concentration of the metal ions should be known and controlled.

Mix the aqueous solution with the organic solution containing the oxadiazole ligand in a separatory funnel. The mixture is agitated to facilitate the complexation of the metal ions with the ligand and their transfer into the organic phase. After sufficient mixing, allow the phases to separate. The metal-oxadiazole complex will predominantly be in the organic phase, while the aqueous phase will contain any uncomplexed metal ions. The organic phase is then separated, and the metal can be quantified or stripped for further analysis [22- 30].

3.6. UV-Vis Spectroscopy of metal complexes

When a metal ion (such as Ni^{2+} or Co^{2+}) forms a complex with oxadiazole derivatives, the resulting complex typically exhibits absorption bands in the UV-Vis region (200–800 nm). The absorption spectrum of such a complex arises from various types of electronic transitions:

a. d-d Transitions (for d-block metals like Ni^{2+} and Co^{2+})

- Nickel(II) Complexes (Ni^{2+}): Nickel ions in the +2 oxidation state (Ni^{2+}) are d^8 systems. Nickel(II) complexes typically show absorption bands in the visible region due to d-d transitions, which are spin-allowed transitions between the energy levels of the d-orbitals in the metal.

- These bands typically appear in the range of 400–700 nm, depending on the geometry of the complex (octahedral, square planar, tetrahedral, etc.). For example, a typical Ni^{2+} complex might exhibit a strong absorption band around 450 nm (in a square planar geometry).

- Cobalt(II) Complexes (Co^{2+}): Cobalt in the +2 oxidation state (Co^{2+}) has a d^7 electron configuration, which also results in d-d transitions. Co^{2+} complexes typically exhibit absorption in the visible region (400–700 nm), with a prominent band around 420 nm for octahedral Co^{2+} complexes.

- The exact position of the absorption bands depends on the ligand field strength, which is influenced by the oxadiazole ligand.

b. Charge transfer transitions

- Ligand-to-Metal Charge Transfer (LMCT): When the oxadiazole ligand donates electron density to the metal center, a charge transfer transition may occur. This transition typically appears at shorter wavelengths, usually in the UV region (200–400 nm).

- Metal-to-Ligand Charge Transfer (MLCT): Conversely, if the metal ion can accept electron density from the ligand, an MLCT transition may also appear in the UV region, typically around 250–350 nm.

c. Ligand absorption

- The oxadiazole ligand itself may have absorption bands due to electronic transitions within its aromatic ring or heterocyclic structure. These bands are typically in the UV region (200–300 nm), and they are observed due to π-π^* transitions in the aromatic system of the oxadiazole ring [31- 32].

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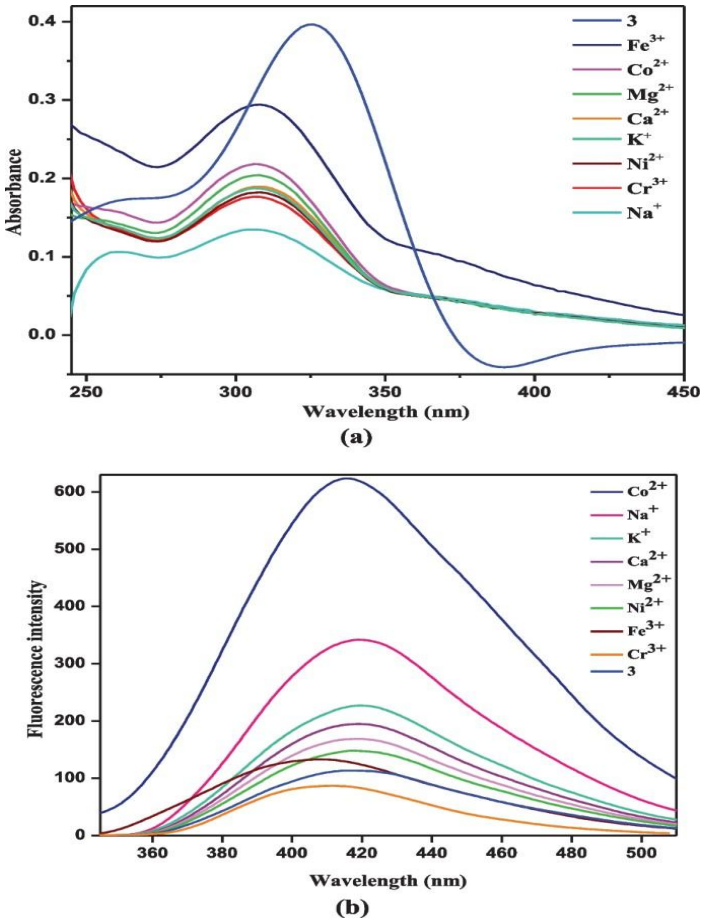

Fig. 15: UV–visible spectroscopy of Co, Ni forms a complex with oxadiazole derivatives. In addition to other elements that form complexes with the same ligand [33].

4. CONCLUSION

The prepared ligand is categorized as a bidentate. The MP3 approach in HyperChem can be used to theoretically analyze the electronic density distribution in order to identify the geometric forms & binding sites of the complex. Both and the N atom of the oxadiazole ring & the N atom of the azomethine group have a large distribution of electrical density. Additionally, the chromium complex's configuration was deduced. The nickel complex has a tetrahedral geometry, while the compound has an octahedral structure. The nickel complex also takes on a sp^3 configuration. In addition, the prepared ligands can be used as a material for extraction cobalt and nickel heavy metals from aqueous solutions; by forming precipitated solid complexes, it is possible to isolate them by filtration process.

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