

Synthesis, Characterization, and Biological Activity for a New Ligand 2,5-bis[(butan-2-ylidene)hydrazinyl]-1,3,4-thiadiazole with Some Transition Metal Complexes

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ABSTRACT

The new transitional metal (Fe(III), Co(III), Cr(III), Cu(II), and Ni(II)) complexes of ligand 2,5-bis[(butan-2-ylidene)hydrazinyl]-1,3,4-thiadiazole were prepared. All the prepared complexes were diagnosed by IR, elemental analyses, H-NMR, and mass spectral. The electronic behavior of their link data has been confirmed. It was concluded that ligand had coordination through nitrogen (N) and (NH). The ligand coordinated through the $[^{11}\text{NH}]$ and the nitrogen atom of shiff base (N^3). The appearance of a band more supports this view returned to the metal–nitrogen stretching vibration at $500\text{--}513\text{ cm}^{-1}$ in the complexes. From the results obtained, we suggested the tetrahedral geometry for Cu(II) and Ni(II) complexes, while Fe(III), Cr(III) and Co(III) [complexes were represented octahedral geometrics. All the synthesized complexes have been screened for anti-bacterial by using spread method and measurement inhibition zone with *Escherichia coli* and *Staphylococcus aureus* under dimethyl sulfoxide (DMSO).

Keywords: Biological Activity, Ligand, Synthesis, Transition metal complexes.

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INTRODUCTION

Over the past years, The resistance towards available drugs is rapidly becoming a major worldwide problem due to the conditioning of various viruses and bacteria to the current chemical used for treatments. The need to design new chemical compounds to overcome this problem has become one of the most important research areas nowadays. Thiadiazoles have been of great interest as compounds as anti-tumor.^{1,2} The studies show that thiadiazole derivatives have Different biological activities such as anti-fungal, anti-bacterial, anti-viral, anti-inflammatory activities.^{3,4}

Anti-microbial⁵ and anti tubercular^{6,7} activities, while its other compounds act as anti-convulsants^{8,9} or as an antidepressant, anxiolytic,¹⁰ anticancer, antioxidant, and radioprotective.¹¹⁻¹³ 1,3,4-Thiadiazole compounds are important in industry, agriculture and medicine.^{14,15} And it has application in pharmaceuticals, cyanine dyes, oxidation inhibitors, and metal complexation agents

The first one who described 1, 3, 4-Thiadiazole was Fisher in 1882, but the real nature of the ring system was described for the first time in 1890 by Freund and Kuh.¹⁶ The studies have shown that when a substitution occurs in locations (2,5) of

the Thiadiazole compound with two groups of thiol (SH), this will give the compound more power, leading to a wide range of uses.

In chemistry, thiadiazoles are a sub-family of azole compounds. Structurally they are five-membered heterocyclic compounds containing two nitrogen and sulfur atoms and two double bonds to give an aromatic ring, with the name thiadiazole originating from the Hantzsch-Widman nomenclature. Four possible structures exist depending on the relative positions of the heteroatoms; these forms do not inter-convert and hence are structural isomers and not tautomers (Figure 1). The compounds themselves are rarely synthesized and possess no particular application. However, compounds bearing them as a structural motif are fairly common in pharmacology.¹⁷⁻¹⁹

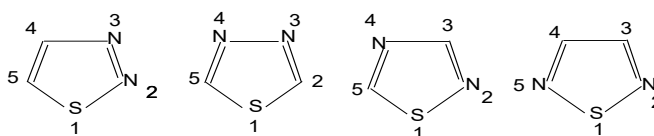


Figure 1: 1,2,3-Thiadiazole 1,3,4-Thiadiazole 1,2,4-Thiadiazole 1,2,5-Thiadiazole

EXPERIMENTAL

Materials

All the chemicals used were of reagent grade, Hydrazine hydrate (BDH), absolute ethanol (BDH), Hydrochloric acid (BDH), Sodium hydroxide, 2-Butanone, and carbon disulphide (BDH) was used. All the metal chlorides (NiCl₂.6H₂O, CuCl₂.6H₂O, CrCl₃.6H₂O, CoCl₃.6H₂O, FeCl₃.6H₂O) were purchased from (BDH) fine chemicals.

Analytical Methods and Physical Measurements

The FTIR spectra in the range 200–4000 cm⁻¹ were registered as CsI discs using a Shimadzu FTIR spectrophotometer, elemental C, H, and N (analysis conducted on a Thermofinigan flash analyzer. The ¹H-NMR spectra were recorded on a quicksilver-300BB NMR 300 spectrometer, return to the internal standard tetra methyl silane (TMS), d₆-DMSO used as a solvent. Mass spectra were registered in the range (0–800) m/e on a 5973 network mass selective detector. Melting points were identified in open capillary tubes by using an electrothermal melting point/ SMP3I apparatus.

Preparation of the Ligand

New ligand 2,5-bis[(butan-2-ylidene)hydrazinyl]-1,3,4-thiadiazole (Scheme 1) was prepared as follows:

A mixture of 0.32 mol of Hydrazine hydrate and (0.6 mol) of Sodium hydroxide was dissolved in (200 mL) absolute ethanol, to this solution 0.26 mol of carbon disulfide was added gradually. The resulting mixture was heated under reflux for 15 hours. The resultant mixture was concentrated and carefully acidified with hydrochloric acid HCl (10%) to give a yellow precipitate. The product was filtered and washed with cold water, recrystallized from ethanol to give the desired product 5-Amino-1,3,4-thiadiazole-2-thiol (A1) as yellow crystals,²⁰ yield (76%), m.p. 162–164°C.

A mixture (A1) (0.04 mol) and Hydrazine hydrate (0.1 mol) dissolved in ethanol (100 mL) was heated under reflux for 9 hours until the emission of hydrogen disulfide gas is over. The resultant mixture [B] was concentrated, and the white crystals were filtered and recrystallized from ethanol, Yield: (66 %), m. p. 173–175°C.

A mixture (B) (0.01 mol) and 2-Butanone (0.02 mol) dissolved in ethanol (25 mL) was heated under reflux for 3 hours. The resultant mixture [Ligand] was concentrated, and

the white crystals were separated, filtered, and recrystallized from ethanol (Scheme 1).

Preparation of Complexes

The Cr(III), Co(III), Fe(III), Ni(II) and Cu(II) complexes were synthesized by mix (0.01 mol) from ligand with (0.01 mol) from salts (CrCl₃.6H₂O), (CoCl₃.6H₂O), (FeCl₃.6H₂O), (NiCl₂.6H₂O), (CuCl₂.6H₂O) in 50 mL ethanol absolute and refluxed for 2 hours. then the precipitate was filtered and washed several times with ethanol, then the resultant solids, which separated, dried in air.

RESULTS AND DISCUSSION

TLC checked the ligand and its complexes, elemental analysis shown are (CHN) in Table 1, Physical properties, mmolar conductance and a melting point of all the compounds synthesize are tabulated in Table 2.

The Fourier Transform Infrared Spectroscopy Spectral

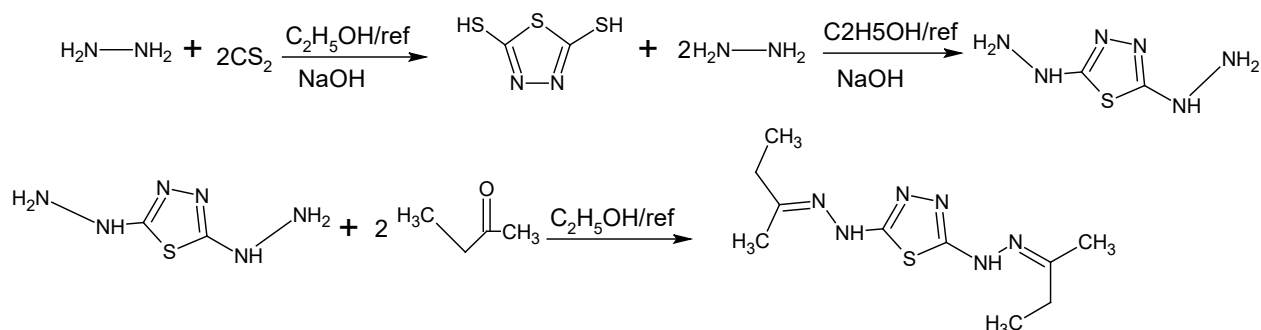
FT-IR spectrum for the free ligand showed five major bands at (3383) cm⁻¹, (2951) cm⁻¹, 1508 cm⁻¹, (1372, 1383) cm⁻¹ and (1033) cm⁻¹ returned to $\nu(\text{N-H})$, $\nu(\text{C-H})$,^{22,23} $(\text{C}=\text{N})$,^{24,25} (asymmetrical) C-S-C (symmetrical) C-S-C (and structure movement, respectively.^{21,26} New bands appeared at the (500–513) cm⁻¹ and (246–281) cm⁻¹ region refers to coordinate (M-N) and (M-Cl), respectively. This refers that the coordinate happened through atoms (Cl) and (N). The IR data for the ligand and its complexes are exhibited in Table 3 and Figure 2 as a model of all FTIR under study.

Nuclear Magnetic Resonance

The data of ¹H-NMR for the ligand showed good solubility in DMSO. The ¹H-NMR spectral data gave another confirmation for the suggested structure of the ligand. The spectra showed signals at 1.19 ppm and 1.6 ppm due to CH₃ and CH₂,²⁷ and another signal at 5.7 ppm and 2.5 ppm due to NH and CH₃, respectively.^{28,29} The ¹H-NMR of the ligand shown in Figure 3.

Table 1: Elemental analysis for the ligand

Experimental			Theoretical		
C%	H%	N%	C%	H%	N%
47.28	7.185	33.14	47.22	7.13	33.04



Scheme 1: Preparation of ligand

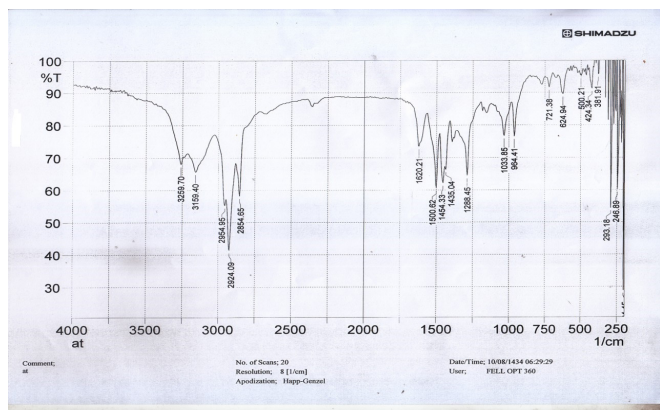
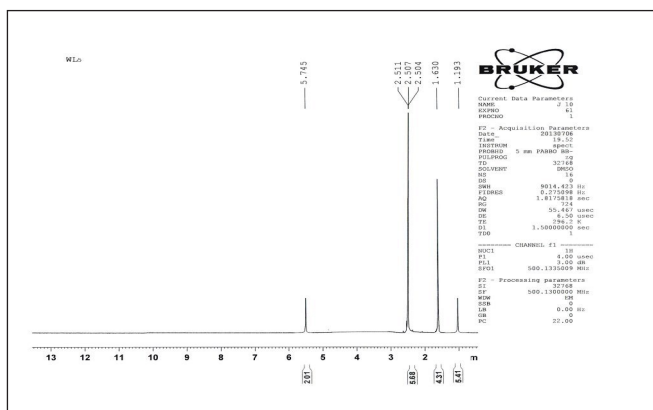
Table 2: Physical properties, conductance data of the ligand and its complexes

No	Compound	Molecular formula	Color	Λ Scm ² mol ⁻¹	Melting Point
1	Ligand	S ₆ N ₁₈ H ₁₀ C	white	—	196-198
2	[Cr(L)2Cl ₂]Cl	Cr(C ₁₀ H ₁₈ N ₆ S) ₂ Cl ₃	Dark green	37.81	320 d*
3	[Fe(L)2Cl ₂]Cl	Fe(C ₁₀ H ₁₈ N ₆ S) ₂ Cl ₃	black	39.2	278-276
4	[Co(L)2Cl ₂]Cl	Co(C ₁₀ H ₁₈ N ₆ S) ₂ Cl ₃	green	39	256-258
5	[Ni(L)Cl ₂]	Ni(C ₁₀ H ₁₈ N ₆ S)Cl ₂	brown	5.75	221-223
6	[Cu(L) Cl ₂]	Cu(C ₁₀ H ₁₈ N ₆ S)Cl ₂	Light green	6.1	295-297

d*=decomposition

Table 3: The IR data of the ligand and its metal complexes

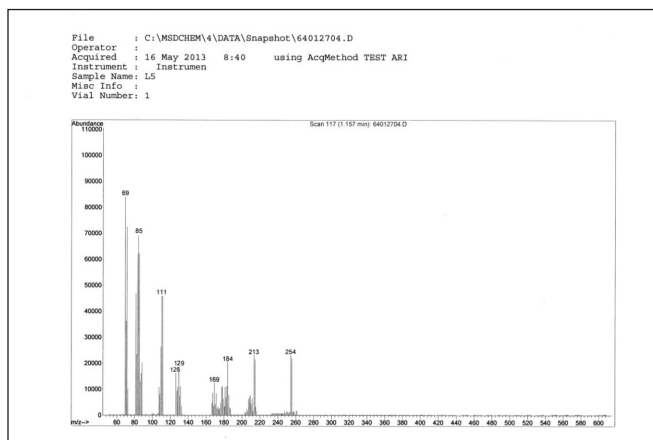
NO	Compound	ν N - H	ν C - H	ν C=N	ν C-S-C	Structure movement	M-Nv	M-Cl v
L	S ₆ N ₁₈ H ₁₀ C	3383	2951	1508	1383asy 1372sy	1033	—	—
3	[Co(L) ₂ Cl ₂]Cl	3236	2924	1516	1392 asy 1315 sy	1056	511	254
5	[Cu(L) Cl ₂]	3259	2924	1500	1454 asy 1435sy	1033	500	246
2	[Fe(L) ₂ Cl ₂]Cl	3360	2924	1516	a1385 sy 1376sy	1029	513	281


Figure 2: IRs Spectra of [Cu(L)Cl₂]

Figure 3: ¹H-NMR spectra of the ligand (C₁₀H₁₈N₆S)

The Mass Spectra

The mass spectra of the ligand shown molecular ion [M]⁺ peak at (254) m/z which matches the molecular formula (S₆N₁₈H₁₀C)k. The other peaks are due to the fragments like [C₄H₇N]⁺ at (69) m/z, [C₂N₂S]⁺=(85)m/z, [C₂NS₄]⁺=(111)m/z, [C₃H₂N₄S]⁺=(126) m/z, [C₂H₃N₅S]⁺=(129) m/z [C₄H₅N₆S]⁺=(169)m/z, [C₅H₈N₆S]⁺=(184)m/z and [C₇H₁₃N₆S]⁺=(213) m/z as shown in Figure 4.

The mass spectral of the complex [Cr(L)2Cl₂]Cl showed a molecular ion peak at 665 m/z, which is equivalent to the molecular mass of Cr(III) complex. This complex showed another fragmentation peaks at 629, 594, and 559 m/z due to [loss'one, two, and three] of chlorine atoms Sequentially. The complex spectrum is shown another fragment ion peak at 305 m/z due to [Cr(L)]⁺.


Figure 4: Mass spectra of A Ligand

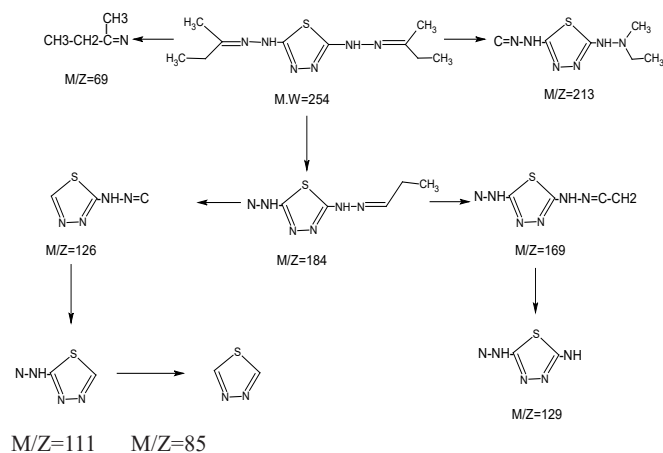

Scheme 2: Frigment of ligand

Table 4: Anti-bacterial screening data of the ligand and its metal complexes

Compound n	<i>Escherichia coli</i> Inhibition zone(mm)	<i>Staphylococcus Aurensk</i> Inhibition zone(mm)n
L= C ₁₀ H ₁₈ N ₆ S	11	22
Cr(L) ₂ Cl ₂]Cl]=A	21	26
[Co(L)2Cl ₂]Cl =B	28	15
[Cu(L)CL ₂] = C	32	27
Ciprofloxacin	30	25

The mass spectral of the complex [Fe(L)2Cl₂]Cl showed a molecular ion peak at 669 m/z, which is equivalent to the molecular mass of (III)Fe complex. This complex showed another fragment ion peaks at (634)m/z, (598) m/z, and (563) m/z due to loss of one, two and three of chlorine atoms sequentially. The complex spectrum has shown another fragmentation peak at (309)m/z due to [Fe(L)]⁺.

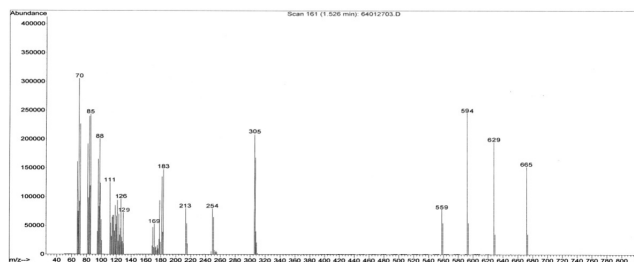
The mass spectral of the complex [Ni]L(Cl₂) showed a molecular ion peak at 383 m/z, equivalent to the molecular mass of Ni(II) complex. This complex has shown another fragmentation 2 peaks at 348 m/z and 311 m/z due to losing one and two chlorine atoms, respectively. The complex spectrum 9 shown another fragment ion 1 peaks at 129 m/z due to [Ni Cl₂]⁺. and 93 due to [Ni Cl]⁺ the mass 9 spectra of the 1 complexes shown 2 in Figure 5 (as a model of HNMR under study).

Biological Activity

The anti-bacterial activity for ligand and its complexes were assessed by using the agar well diffusion method. Two types of bacteria have been used, gram-negative bacteria as *Escherichia Colio* and Gram-positive bacteria as *Staphylococcus*. These types of bacteria were chosen because of their importance in the medical field as they cause many different diseases, using Ciprofloxacin as a standard drug. The inhibition zone was measured in millimeters. The dimethyl sulfoxide (DMSO) is used as a solvent. Nutrient agar was used as a culture medium, using a disk susceptibility test. These techniques include the exposure of an inhibition zone to the spread of bacteria on an

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Figure 5: Mass spectra of A Ligand [Cr(L)2Cl2]Cl

agar plate. The agar dishes were put in the incubator at 37°C for 24 hours.^{30,31}

The anti-bacterial data of the ligand and its metal complexes are tabulated in Table 4.

CONCLUSION

The ligand 2,5-bis[(butan-2-ylidene) hydrazinyl]-1,3,4-thiadiazole was successfully synthesized. The elemental analysis, ¹H NMR, IR, and mass spectral observations suggest the tetrahedral geometry was proposed for Ni(II), Cu(II), and octahedral geometry for the Cr(III), Co(III), Fe(III).

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