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Original Article

The Importance of Heterocyclic Compounds in the Production of Medicinal Compounds: Synthesis AND Characterization of New Derivatives 5-Amino-1,3,4-thiadiazole-2-thiol

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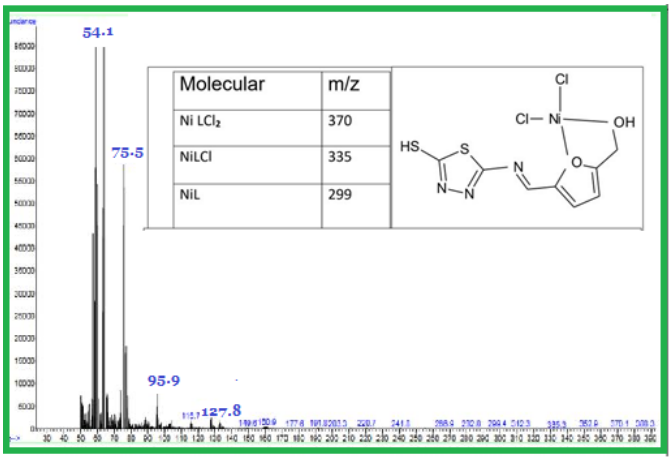
ABSTRACT

Heterocyclic compounds are of great importance in the production of medicinal compounds. In this study, a new compound (E)–(5-(((5-mercapto 1,3,4-thiadiazole-2-yl)imino)methyl)furan-2-yl-methanol) and its complexes with some transition metal ions Cr(III) and Ni(ll) were synthesized. The structure of the ligand and its complexes were characterized using the molar conductivity, FT-IR, ^{1}H-NMR, and mass spectral techniques. The HyperChem 7.51 program was utilized for theoretical study. The measurements data of Molar conductance reveal that the complexes are non-electrolytes. The ligand acts as a Bidentate in Ni complex coordinating through the oxygen atom of the furan ring and methoxy group and act as tridentate in Cr complex. This data is further supported by the manifestation of a band corresponding to the metal-oxygen and metal-nitrogen stretching vibration at 454–688 cm^{-1} and 314-466 cm^{-1} in the complexes, respectively. From the spectra data and theoretical study, we suggest a square planer for Ni^{+2} complex and octahedral geometry of the Cr^{+3} complexes.

GRAPHICAL ABSTRACT



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Introduction

Heterocyclic compounds are organic compounds containing at least one heteroatom in their composition. The most common ones containing nitrogen, oxygen, and sulfur may be triple, tetragon, pentagonal, or hexagonal [1-8]. The thiophene may contain two different atoms called (Azoles). These rings are derived from the above five rings, where the CH group is replaced by a nitrogen atom, such as Isothiazole, Isoxazole, IH, pyrazole, and Imidazole [9-11].

The thiadiazole ring, which contains nitrogen and sulfur in its composition, has received significant attention because it has a diverse coordination ability towards ions of mineral elements, especially in structures, biological applications, and bioactive compounds. From another point of view, the thiadiazole ring can have four distinguished isomersandit (Figure 1) [12–15].

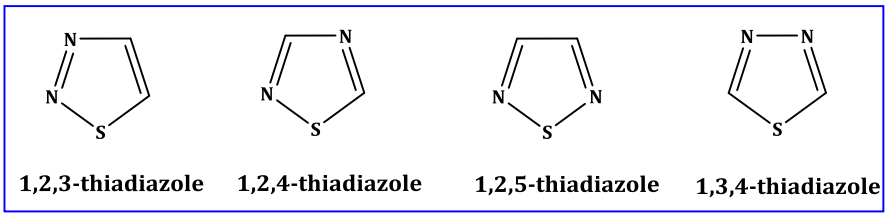

Figure 1: The tautomerism of the Thiadiazole ring

The isomer 1,3,4-thiadiazole is of great importance compared to the other three iso-fold. Where the interest in this aspect of modern chemistry began after the isolation and purification of active substances from plant and animal tissues, as well as those taken from microorganisms and their fermentation products, which became the focus of attention for researchers all over the world, as these compounds are considered biologically effective because they have a role in treating many urinary tract diseases and disinfectants, as well as anti-inflammatory agents, anti-fungal and anti-viral, and have recently been used in the equation of blood pressure [16–18]. As for the applied fields, it is involved in the composition of biological molecules, such as the nitrogenous bases that make up the nucleic acids (DNA, RNA) and the composition of pigments such as chlorophyll optical pigment and hemoglobin [19].

Heterocyclic compounds [20, 21] are also included in the synthesis of some types of vitamins such as vitamin B6 and vitamin C, where these rings contain nitrogen, which helps in their participation in the metabolism of amino acids. The thiadiazole derivative is of great importance in medical fields. It can be used as intermediate compound in The field of organic analysis, which is used to manufacture anticoagulant drugs, plant stimulants, and stimulants for acquired systemic immunity [22, 23]. The compound 5-amino-1,3,4 thiadiazole-2-thiol is of great importance through its anti-corrosion properties. It was absorbed on the surface of the metal and formed a layer that prevents metal corrosion [24–26].

Material and Methods

the FT-IR spectra in the range (4000-200) cm^{-1} were recorded as KBr discs for ligand and CsI discs for complexes using a Shimadzu FTIR spectrophotometer in Dhi-Qar university, college of science [27]. Molar conductance measurements were recorded in anhydrous DMSO at 25 °C using Inolabcond 720 [28]. The 1H-NMR spectrum at 400 MHz at room temperature in DMSO was recorded in d6 and mass spectrometry.

Synthesis of Ligand

In a circular flask, A mixture of potassium hydroxide (0.1 mol, 5.6 g) and thiosemicarbazone (4 g, 0.1 mol) dissolved in 100 mL of ethanol, to this solution (6 mL, 0.1 mol) of carbon disulfide was added. The mixture was heated under reflux for (24 h). The product was concentrated and carefully acidified with hydrochloric acid HCl (10%) to give a pale-yellow precipitate. Yield 74% melting point (237, 235 °C).

(E)–(5-(((5-Mercapto-1,3,4-thiadiazole-2-yl)imino)methyl)furan-2-yl-methanol)

In a 100 mL round flask, (0.04 mol, 5 g) of compound (A) was dissolved in 50 mL of absolute

ethanol and then (0.04 mol, 4.4 mL) was added from (vinyl furan-2-yl)methanol Heat the mixture with continuous stirring for a period of 3-4 h until the end of the reaction while observing the progress of the reaction through repeated examination by thin-layer chromatography (TLC). The solution is concentrated in half and left aside. We notice the formation of crystals Yellow. The precipitate formed is filtered, recrystallized with ethanol, and dried. The weight of the formed product is 3.2 g, the percentage of the product is (73%), and the melting point of the compound ranges from (-) as shown in the following Figures, and the resulting compound is symbolized by the letter B.

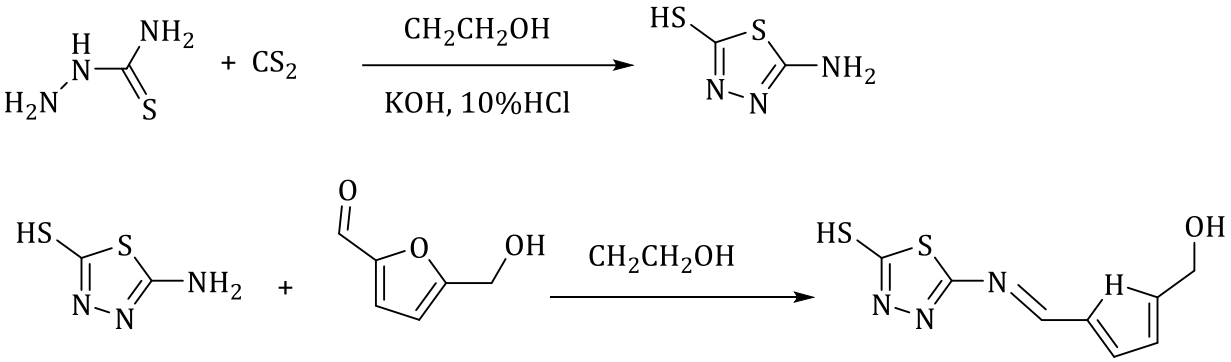

Figure 2: Ligand

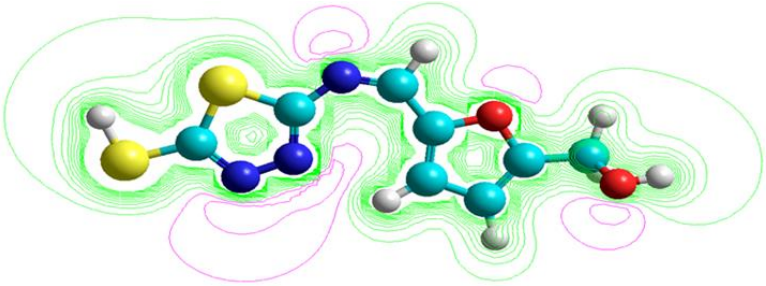

Figure 3: Electrostatic potential of ligand

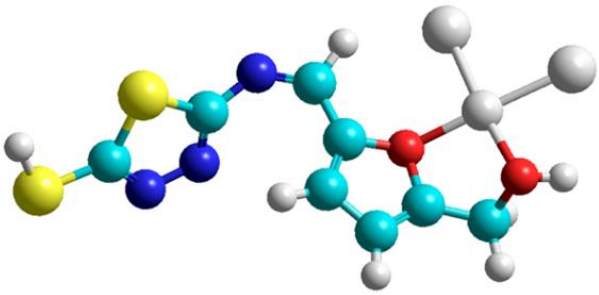

Figure 4: [Ni L CL_2] square plainer

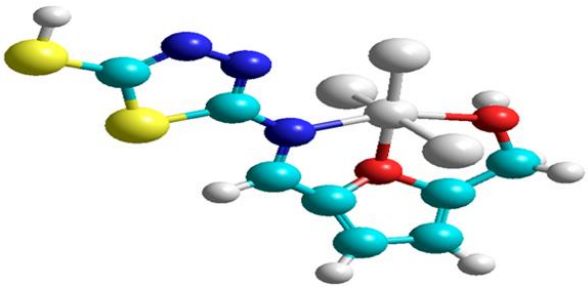

Figure 5: [$CrlCl_3$]

Synthesis of Metal Complexes

It should be noted that 0.002 mol of compound A (ligand) has been mixed in a 50 mL round flask with (0.002) mol of $FeCl_3.6HO$ and ($CrCl_3.6HO$) separately. The mixture was heated under reflux for 3-4 h. The reaction was monitored using the TLC technique [29]. The mixture was concentrated**,** the product was filtered and washed with water to get rid of residual salt. Then we recrystallized it with ethanol. To get the pure crystals, we dry them. The complexes with some physical properties can be listed in Table 1.

Table 1: Some physical properties

Symbol	Chemical formula	M.wt	Color	m.pc	Yield
L1	$C_7H_6N_4S_2$	241	Yellow	251-253	80%
L1C1	$NiLCl_2$	370	Brown	284-286	72%
L1C2	$CrLCL_3$	375	orange	293-297	71%

Results and Discussion

The prepared ligand and metal complexes were diagnosed with infrared spectra, NMR spectra, mass spectrometry, and molar conductivity (Figure 6).

Infrared Spectra

The spectra for L show a characteristic stretching absorption band at 3300 cm^{-1} belonging to the alcoholic OH group; this band looks wide because of the hydrogen bonding. The spectrum also showed a strong band in the 1620 cm^{-1} region Attributed to the (C=N) group. It is also observed in the spectrum stretching absorption band at 3062 cm^{-1}, 2931 cm^{-1} back to (CH aromatic, CH aliphatic) respectively. The spectrum also showed other bands at wave number 1527 cm^{-1}, 1504 cm^{-1} due to vibration stretching of the (C=C) and C=N cyclic respectively, A group of bands related to the thiadiazole ring is observed in 1396 cm^{-1}, 1273 cm^{-1}, 1064 cm^{-1} belong to the vibration for the (asy C-S-C, sy C-S-C, str.movment) group. In the spectrum of complexes, it has been observed that there is a change in the location and shape of the absorption band that belongs to the (C=N) group of azomethine and (C=N) located within the ring, which indicates the association of the metal with these groups. In the spectrum of complexes (Figures 7 and 8), new bands are observed at 628 cm^{-1}, 597 cm^{-1} belongs to the (M-N) group, as well as absorption bands at wave number 252 cm^{-1}, 281 cm^{-1} belong to the (M-Cl) group (Table 2).

Table 2: FT-IR spectral data

	FT-IR spectral data, cm^{-1}		
	C8H7N3O2S2 **L**	$[NiLCl_2]$**C1**	$[CrLCl_3]$**C2**
OH	3300	3282	3278
C=N	1620	1608	1635
CH Aromatic	3101	3167	3167
CH Aliphatic	2931	3930	2935
C=C	1527	1508	1508
C=N cyclic	1504	1508	1458
asyC-S-C	1396	1396	1396
syC-S-C	1226asy	1230sy	1219
Skeletal movement	1064	1022	1022
N-N	1192	1230	1218
M-N	___	605	594
M-Cl	___	304	304

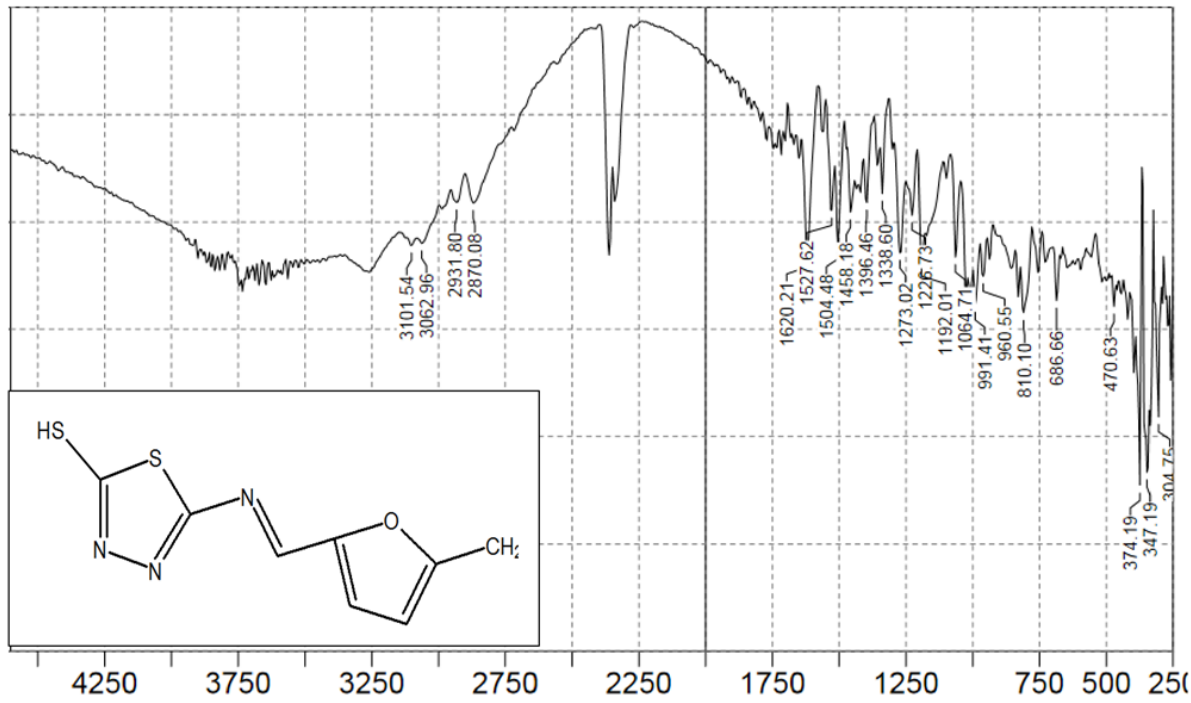

Figure 6: IR spectrum of the prepared ligand

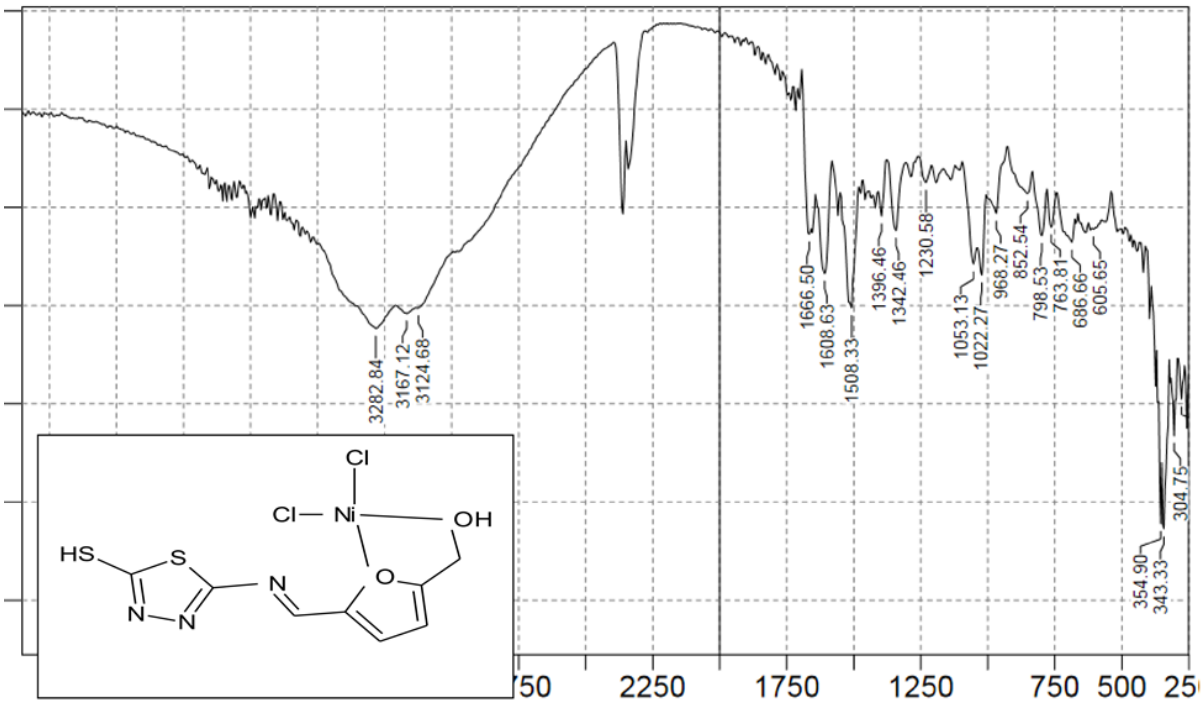

Figure 7: IR spectrum of the complex [$NiLCl_2$]

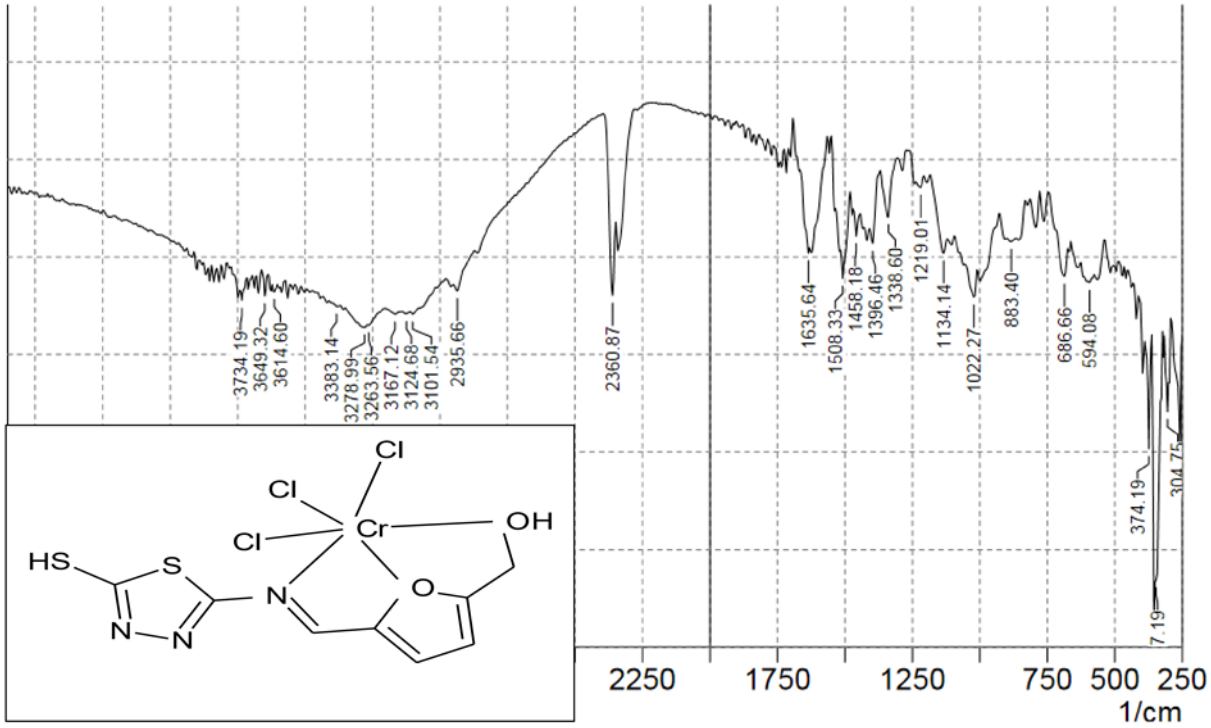

Figure 8: IR spectrum of the complex [$CrLCl_3$]

Nuclear Magnetic Resonance Spectra (^{1}H-NMR)

The ^{1}H-NMR spectral data for the ligand showed a multi-signal at 6.7, 7.4 ppm and with the integration of two protons belonging to the aromatic ring protons observed in the spectrum signal at 4.5 ppm, 2H) due to (CH_2-OH). The spectrum also showed a single at position (8.4 ppm, 1H) belonging to the azomethine proton (N=CH), and there is another single signal at the (5.6 ppm, 1H) that belongs to the (N-H) proton.

Two signals of the used solvent (DMSO-d_6) appear in the NMR spectrum of the prepared compounds (Table 3), the first at 2.5 ppm and the other at 3.3 ppm belonging to the presence of water in the solvent.

Table 3: Prepared compounds

Compound	Group	Sign type	Shift (ppm)	Integration
L	**CH_2-OH -**	Singlet	**4.5**	**3H**
	C-H -	Multiple	**(6.7, 7.4)**	**2H**
	N=CH--	Singlet	**5.6**	**1H**
	N-H =	Singlet	**8.4**	**1H**

Mass Spectra

In preparing and diagnosing ligands and their metal complexes, many researchers relied mainly on mass spectrometry to ascertain their structural formula [30–34]. Mass spectrometry confirms the structural formula by noting the fractionated aggregates of the prepared compound and determining their molecular weight through mass spectrometry.

Mass Spectra of the Ligand

The mass spectrum of the prepared ligand was characterized by the appearance of the molecular ion peak [MO] at m/z = 241, which is a strong peak with a high relative abundance due to the compound containing the successive pi system where resonance occurs between the double bonds or electronic doubles carried on the oxygen, nitrogen and sulfur atoms. As for the other peak, they are mentioned in Table 4.

Table 4: Molecular ion peaks

Molecular	m/z	Molecular	M/z
$C_8H_7N_3O_2S_2$	241	C_7H_6NO	36
$C_8H_6N_3OS_2$	224	C_4HN_2S	109
$C_7H_4N_3OS_2$	210	$C_5H_4O_2$	96
$C_8H_6NO_2S$	180	C_5H_4O	80
$C_6H_3N_3OS$	165	C_4H_2N	64
C_6H3N_3S	149	C_2HN_2	53

Mass Spectra of Complex [Ni LCl_2]

The mass spectrum showed the molecular ion package of the complex at 368 m/z, and the spectrum also showed another package at 333, 297 m/z, all indicating the loss of chlorine atoms from the compound, respectively, and this confirms the molecular formula of the complex (Figure 11).

Mass Spectra of Complex [$CrLCl_3$]

The mass spectrum showed the molecular ion package of the complex at 382 m/z, and the spectrum also showed another package at 364, 328m/z, all indicating the loss of chlorine atoms from the compound respectively, and this confirms the molecular formula of the complex (Figure 12).

Molar Conductivity

The molar conductivity of the prepared complexes depends on the number of ions outside the coordination sphere. It is considered one of the diagnostic methods for determining the identity of the complex [35, 36]. Through the values recorded while measuring the molar conductivity of the prepared complexes, it was found that they behave as neutral (non-electrolytic) compounds. This is due to the absence of ions outside the coordination ball. To verify this, a solution of $AgNO_3$ was added to the complex solution (dissolved in DMSO), where it was observed that the solution did not become turbid and did not form a white precipitate of silver chloride. These results are consistent with the structural formula of the complexes that were prepared (see Table 5).

Table 5: Structural formula of the complexes

No.	Complex	m (S.cm2.mole-1)	Electrolyte ratio
1	[$NiLCl_2$]	24.2	Non-Electrolyte
2	[$CrLCl_2$] Cl	35.3	Electrolyte 1:1

Conclusions

A novel chemical was created and its complexes with transition metal ions. Molar conductivity, FT-IR, ^{1}H-NMR, and mass spectral methods were used to analyze the ligand structure and its complexes. The HyperChem 7.51 application was used for a theoretical investigation using the PM3 approach to investigate the electrostatic potential of Ligands to locate the most active location. Molar conductance measurements demonstrate that the complexes are non-electrolytes. In Ni complex, the ligand operates as a Bidentate, coordinating between the oxygen atom of the furan ring and the methoxy group. In Cr complex, it acts as a tridentate. The band's appearance corresponding to the metal-oxygen and metal-nitrogen stretching vibrations at 454–688 cm^{-1} and 314-466 cm^{-1} in the complexes, respectively, supports these results. We propose a square planer for the Ni^{+2} complex and an octahedral geometry for the Cr^{+3} complexes based on the spectra data and theoretical analysis.

Authors' contributions

All authors have contributed significantly and met criteria for authorship. All the authors read and approved the final copy of the manuscript.

Conflict of Interest

We have no conflicts of interest to disclose.

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