

Synthesis and Characterization of New Thio-Allyl-Triazole Ligand And Complexes with Selected transition Metals

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Abstract

The ligand, 3-(2-Propynyl) thio-4-allyl-5-phenyl-4H-1,2,4-triazole (L) was prepared and characterized by micro elemental analysis (CHN) and Infra-Red spectroscopy. Selected metals, which were Cu(II), Zn(II), Cd(II), Co(II), and Fe(III) were reacted with (L) to produce new complexes. These complexes were identified through micro elemental analysis, Infra-red and ultra-violet-visible spectroscopy and other techniques. Depending on the data obtained, chemical formulae and geometry of complexes were suggested.

Biological activity of the complexes against selected types of microorganisms was also examined.

Introduction

Metal complexes are suggested as a possible measure of drugs, since the action of many drugs is based on the ability of complex compound of metal ions to traverse biomembranes, whereas individual aqua-ions and ligands almost or completely lack this ability.

A case in point is antibiotics whose activity increases drastically in the presence of metal ions (1).

Metal chelates differ in their mode of action and activity in biological systems in accord with their structural considerations, e.g. inert, highly stable metal chelates have a considerable activity against microorganisms, fungi and viruses and are used in controlling the speed of neoplastic tissue.

An important and versatile class (2) of well established biologically active compounds are those with the -N-C-S moiety. This group is found in many basic structures of drugs either to be part of an open chain, e.g. thiocarbamates, isothiocyanates and thiosemicarbazides³, or involved in heterocyclic ring, e.g.

Mercepto derivatives of triazoles, oxadiazoles, and thiodiazoles (4).

The presence of the "soft" sulfur atom besides the "hard" nitrogen atom in this thioamide group, keeping aside the effects of the remainder of the molecule containing it, renders these molecules to be potent ligands with a wide diversity and versatility toward the transition elements. This property is the key for biological importance of these ligands in addition to other uses and applications.

A large number of 1,2,4-triazole derivatives have been synthesized in recent years. (5-8)

Many of these derivatives are reported to exhibit broad spectrum of biological effects (9-31).

Among the interesting ones are the tuberculotherapeutic (32), fungicidal (33), anti-inflammatory (34) and antibacterial (35) agents.

Biological significant triazole and its derivatives are well documented in the literature (1, 36). The bioactivities of these compounds together with similar heterocyclic have been correlated with their complexation ability with metal ions (37).

A great number of 1,2,4-triazole derivatives substituted with thiol, alkenylthio, aryl, substituted aryl, allyl, alkyl and 2-furyl, at one or more of the 3,4-and 5-positions of the 1,2,4-triazole ring were prepared and screened for their antibacterial activity (38).

In 1996, N.M.Hamodi and co-workers studied the interaction of amino-triazole with glutathione under physiological conditions and found that these derivatives were substrates for the enzyme.

In this work, we report the preparation of the ligand "3-(2-Propynyl) thio-4-allyl-5-phenyl-4H-1,2,4-triazole" (L), and some metal complexes. These compounds were prepared with the intention of finding new potentially biologically active compounds.

Experimental

Chemistry

Elemental microanalysis was carried out using (CHN) elemental analyzer model 5500 Carlo-erba instruments (Italy).

The metal content of the complexes was measured using atomic absorption technique by Pye Unicam of Philips Scientific Instrument which employed the Hollow Cathode Lamp of the Pye Unicam Ltd, Cambridge.

The IR spectra of the prepared compounds were recorded using Perkin-Elmer 1130 infra red

spectrophotometer as KBr disk in the range (4000-600) cm^{-1} .

The magnetic susceptibility values for the prepared complexes were obtained at room temperature using (Faraday Method, by placing the sample in a small Pyrex container suspended from a balance through a fine, Nylon thread to the center of electric magnet. For this purpose, Bruker Magnet 8.M.6 had been employed. The diamagnetic correction factor D was calculated using Pascal constants.

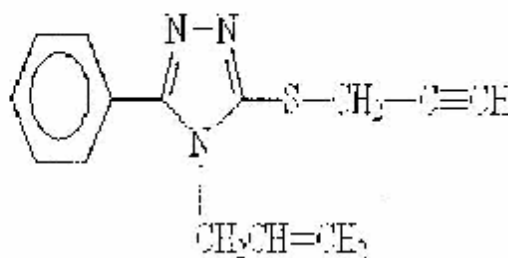
The electronic spectra of the complexes were obtained using Shimadzu-UV-Visible-160A, Ultraviolet spectrophotometer at room temperature using silica cells of 1.0cm length.

Electric molar conductivity measurements were carried out at room temperature at the concentration (10^{-3}M) using digital conduct meter type T.P521 (WTW).

Gallenckamp M.F.B 600.01F melting point apparatus was used to measure the melting point of the prepared compounds.

All chemicals were of high purity are used as the manufacturers supplied them. Allyl isothiocyanate and Propargyl bromide were redistilled prior to use.

The ligand (L) was prepared according to the following procedure:



The Ligand (L)

The compound 3-mercapto-4-allyl-5-phenyl-4H-1,2,4-triazole was prepared^(15-18A) and used as a precursor for the ligand L.

To a stirred solution of 3-mercapto-4-allyl-5-phenyl-4H-1,2,4-triazole(0.1mol, 21.7g) in absolute ethanol (500ml), a solution of potassium hydroxide in ethanol(0.1mol,5.6g)was added followed by drop wise addition of (0.11mol,13.1g) of propargyl bromide, the mixture was refluxed for one hour. After cooling to room temperature, filtered and the filtrate was poured into cold

distilled water 1 liter. The precipitate was filtered and recrystallized from ethanol-water.

Metals complexes of (L) were prepared as follows: (A)Cu, Zn, Cd, Co and Fe complexes

Ethanolic solution of (1mmole) of the metal salts(chlorides of Cu(II), Zn(II), Cd(II), Co (II) and nitrate of Fe(II))was added to (2mmole) of L, dissolved in ethanol. The mixture was stirred at room temperature for 1hour.Fine precipitate was formed, washed with acetone and dried under vacuum at about 50°C.

Bacteriology

Biological activity of (L) and complexes were evaluated against representative gram-positive and gram-negative bacteria by agar plate method⁽¹⁹⁾. All the compounds were prepared freshly by dissolving them in dimethylformamid (DMF) to obtain a final concentration of 1000mg/ml and cultivated in nutrient agar. The results are found in table (4).

Discussion

The identification of the ligand (L) was carried out through elemental analysis:C,65.47%(calc.65.88%); H,5.13%(calc.5.10%);N, 16.52%(calc.16.47).

The olefinic group in the ligand responded positively to both Br_2/CCl_4 and KMnO_4 tests. The acetylenic group in the ligand responded positively to both K_2HgI_2 and Tollen's tests. The ligand has a white color and was found to be soluble in ethanol, carbon tetrachloride, diethyl ether, and DMF. It is found to be insoluble in the acetone and n-hexane.

Identification of the complexes was done using different available techniques. Among these techniques are the determinations of metal percentage by atomic absorption, Infra red spectroscopy, magnetic susceptibility and conductivity measurements.

Complex of (L) with	Color	Yield %	Melting Point, °C	M% Calc.	M% Found
Cu(II), C1	Green	76	(143-145)	11.95	12.85
Zn(II), C2	White	81	(133-136)d	11.11	14.50
Cd(II), C3	White	86	(146-148)	22.02	21.99
Co(II), C4	Blue	66	(168-170)d	12.90	12.75
Fe(III), C5	Brown	88	(130-102)c	11.86	11.75

Identification

The absorption bands for (L) and its complexes are shown in table (2), the absorption bands of the acetylenic group were of great help in the identification of complexes formed especially with respect to the type of bonding with metal. The (C=C) stretching vibration appears at (2111) cm^{-1} which does not involve absorption due to other groups of the studied ligand⁽¹⁹⁾. When the spectra of the complexes are compared with that of the ligand one of the following shift may take place, in the case of δ -bonding the $\nu(\text{C}=\text{C})$ shifts to a lower frequency by 90cm^{-1} and to still lower frequency by 570cm^{-1} in the case of strong π -bonding and by 225cm^{-1} for weak π -bonding, but when both δ and π are involved in bonding with the metal at the same time a red shift of $100\text{cm}^{-1(20)}$ is observed.

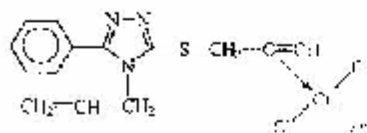
A-Copper (II) complex, C1

The IR spectrum of (C1) are shown in Table (2). The $\nu(\text{C}=\text{C})$ absorption band shift to a lower frequency by 570cm^{-1} and the band due to $\nu(\text{C}-\text{H})$ undergo a reduction in its intensity.

These observations led to the conclusion that Copper (II) ion coordinate to the ligand through acetylenic group by π -bonding mode.

Conductivity measurements show the complex is non-ionic, table (3), therefore the following structure can be suggested:

B- Zinc (II), Cadmium (II) and Cobalt

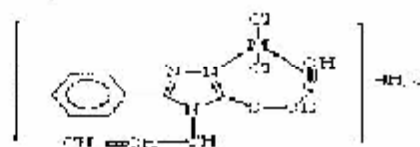


The IR spectra of three complexes shows similar behavior with no much difference compared to that of the ligand.

It gives shift of $\nu(\text{C}=\text{C})$ absorption band to a lower frequency and the band due to $\nu(\text{C}-\text{H})$ undergoes a reduction in its intensity.

Also the band at 1550cm^{-1} which correspond to $\nu(\text{C}-\text{N})$ shift to a lower frequency by 100cm^{-1} . These observations indicate the participation of both acetylenic group and nitrogen. A broad band which appeared at 3460cm^{-1} ⁽²¹⁾ indicates the presence of water molecule in the structure of the complex.

Tetrahedral geometry can be suggested for the three complexes:



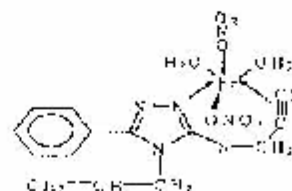
Where: M = Zn, Cd and Co

Conductivity measurements show the complexes are non-conductive, table (3).

C- Fe (III) complex, C5:

The IR spectrum of the complex was characterized by a broad band in the region (3000-3600) cm^{-1} which could be attributed to the $\nu(\text{O}-\text{H})$ of water molecule bonded to the Fe(III) ion. This is expected in Iron (III) complex due to its high affinity for water. The ligand can not displace all the water molecules found in the coordination sphere of the metal ion⁽²²⁾. The broadening of the band was also noticed in the region (1600-1700) cm^{-1} which is attributed to the bending vibration of water molecule. This broadening affects the shape of the spectrum and makes the interpretation more difficult. Also it show shift of $\nu(\text{C}=\text{C})$ absorption band to a lower frequency and the band due to $\nu(\text{C}-\text{H})$ undergo a reduction in its intensity.

Also the band at 1555cm^{-1} which correspond to $\nu(\text{C}-\text{N})$ shift to a lower frequency by 30cm^{-1} . These observations indicate the participation of both acetylenic group and nitrogen. Therefore the following structure is suggested for the (C5) complex:



The above complex is non-ionic due to the conductivity measurement, table (3).

Table (2) the absorption bands in infra-red spectra for (L) and its complexes, all data are in cm^{-1} .

Symbol	$\nu(\text{O-H})$	Thioamide band (II) $\nu(\text{C}=\text{N}+\text{C}=\text{S})$	Thioamide band (IV) $\nu(\text{C}-\text{S})$	$\nu(\text{C}=\text{N})$	$\nu(\text{C}=\text{C})$	$\nu(\text{C}-\text{H})$	$\delta(\text{C}-\text{H})$	$\delta(\text{O}-\text{H})$
L	-	1275(m)	770(m)	1550(m)	2100(w)	3035(m)	620(vw)	-
C1	-	1280(w)	770(m)	1550(m)	1530(w)	3030(w)	620(vw)	-
C2	3460	1260(m) 1290(w)	770(m) 730(m)	1540(m)	2020(w)	-	-	925(w)
C3	3480	1260(m) 1290(w)	770(m)	1540(w)	2030(w)	3030(m)	625(w)	920(w)
C4	3500	1260(m) 1290(w)	770(m)	1540(w)	2025(w)	3025(m)	620(w)	920(w)
C5	3360(b)	1240(vw) 1330(vw)	770(m)	1520(w)	2020(w)	-	-	920(vw)

Where: m=medium, w=weak, b= broad.

Electronic spectral analysis and magnetic measurements

The electronic spectra of Zn (II) and Cd (II) complexes in the visible region are of little help as because these ions have a d^0 configuration and their complexes do not exhibit any d-d transition. All the complexes of these metal ions were found to be diamagnetic.

A- Cu (II) complex, C1

Cu (II) compounds are blue or green because of a single broad absorption band in the region (11,000-16,000) cm^{-1} (29). The d^9 ion is characterized by large distortion from octahedral symmetry and the band is unsymmetrical, being the result of a number of transitions, which are by no means easy to assign unambiguously. In the present work, the green (C1) complex shows a broad band at 15,774 cm^{-1} which can be assigned to the ${}^2B_{1g}$, ${}^2B_{2g}$ and ${}^2B_{1g} + {}^2E_g$ transitions. (24)

B- Cu (II) complex, C4

C4 complex spectrum in DMF shows three bands. The first two bands at 16,611 and 14,880 cm^{-1} were assigned to the transition

${}^4T_1g(F) \rightarrow {}^4T_1g(P)$ (ν_1), since this transition is known to be a triplet in the range (14,000-17,500) cm^{-1} in the divalent cobalt of tetrahedral geometry. This splitting is due to spin orbit coupling (32). Therefore ν_2 having been calculated as the average of these two bands.

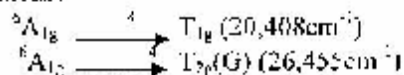
The third band which appears as a weak band at 9,345 cm^{-1} was assigned to the transition ν_2 ${}^4T_1g(F) \rightarrow {}^4A_2g$ while ν_3 could not be observed since it is expected to appear in a range out of the instrument scale so it was calculated using Tanabe-sugano diagram for d^7 system and found to be

6,266 cm^{-1} which belong to the transition ${}^4T_1g(F) \rightarrow {}^4T_2g(F)$ (23)

The different ligand field parameter has been calculated using the same diagram. Comparison of the results obtained in this work with the literature data suggests high spin tetrahedral geometry around Cobalt (II) ion. Magnetic measurements show that the complex is paramagnetic ($\mu_{eff} = 4.35$ B.M.) Table (3) which accordance with the high spin tetrahedral (26-29) the low ratio of u_2/v_1 (1.49) indicates the tetrahedral geometry (30). The molar conductivity measurement in DMF show that the complex was non-electrolyte.

C- Fe (III) complex, C5:

The electronic spectrum of C5 shows two bands; the first one at 20,408 cm^{-1} and the second at 26,455 cm^{-1} , they could be assigned to the transitions:



The value of the measured magnetic moment for C5 is (5.15 B.M.), which could be related to high-spin d^5 ferric ion so that an octahedral geometry is suggested to this complex (31).

From Tanabe-Sugano diagram for d^5 octahedral field, the value of $10Dq$ was found to equal to 20,695 cm^{-1} and the high value of nephelauxetic factor (β) (0.88) indicated the ionic character of the complex.

Table (3) Magnetic moment, conductivity, and suggested structure for complexes of (L)

Complex	Magnetic moment μ_{eff} (B.M.)	Conductivity M_{eq}	Suggested structure
C1	Diamagnetic	47	Square planar
C2	Diamagnetic	33	Tetrahedral
C3	Diamagnetic	37	Tetrahedral
C4	4.35	33	Tetrahedral
C5	5.15	22	Tetrahedral

Bactericidal activity

Preliminary screening experiments are intended to detect the *in vitro* activity of metal complexes. The complexation of (L) with all the metal ions use exhibited no activity except Zn (II) complex (C2) against both Staph.aureus and E-Coli, while Cd (II) and Fe (III) complexes (C3andC5) have an activity towards E-Coli and Staph. aureus respectively.

Table (4) Biological activity for ligand and complexes (at concentration of 1mg/mL).

Symbols	Staphylococcus aureus	Escherichia Coli
L	-	-
C1	-	-
C2	++	++
C3	-	++
C4	-	-
C5	++	-

Where: (-) no inhibition, (+) inhibition zone(6-8)mm, (++) inhibition zone(8-10)mm, (+++) inhibition zone(>10)mm

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الخلاصة

حصرت الليكاند [3-2- بروبيدين] (أبو-1 - ثلاثي - 5-هيدرو-2،4-هـ) (L)، شخصت عن طريق تحليل العناصر الذئق (CHN) والتحليل الطيفي تحت الحمراء. الفلزات المنتجة كانت [Fe(III), Co(II), Cd(II), Zn(II), Cu(II)] في عت مع الليكاند الجديدة. شخصت هذه المعقدات عن طريق تحليل العناصر الذئق (CHN) والتحليل الطيفي تحت الحمراء و الترمي فوق البنفسجية و تكتيات أخرى. أقرت الصيغ الكيميائية و الأشكال الهندسية للمعقدات على ضوء النتائج التي تم الحصول عليها. كذلك تم فحص الفعالية البيولوجية للمعقدات ضد أنواع مختلفة من المتعضيات البحرية.