

SYNTHESIS, CHARACTERIZATION AND BACTERIAL ACTIVITY OF SOME METAL COMPLEXES OF N-PHENYL- Ń-(3-CARBOXYPHENOL) THIOUREA

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ABSTRACT

A thiourea ligand; N-phenyl- \dot{N} -(3carboxyphenol) thiourea (PCTH) is synthesized from the reaction of phenyl isothiocyanate with 3-aminobenzoic acid. Treatment of the ligand (PCTH) with metal salts MCl₂, where M = Cu(II), Zn(II), Pb(II) and Co(II) gave metallic complexes of the types: 1- [M(PCTH)₂Cl₂] where M=Cu(II) and Co(II) and 2- [M(PCT)₂] where M=Zn(II) and Pb(II). The ligand (PCTH) behaves as a bidentate and coordinated to the metal ion centers either through sulfur atom of its thioamide group and through nitrogen atom of the amine group or through oxygen atom of the carboxylic group. All the synthesized ligand metal complexes are characterized by micro-elemental analysis, IR spectroscopy and UV-Vis. spectroscopy, ¹H.NMR, ¹³C.NMR, conductivity and magnetic susceptibility measurements. Finally, bacterial activity of the ligand (PTCH) and its metal complexes are tested against Klebsiella pneumonia and Escherichia coli and gram-positive bacteria Staphylococcus aurous. Using well-diffusion method and the results are discussed.

Keywords: Thiourea derivative, Transition metal complexes, Bacterial activity.



$-\tilde{N}$ - فنيل – N تحضير ، تشخيص وقياس الفعالية البكتيرية لبعض معقدات

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الملخص

ان الليكاند مشتق الثايويوريا (PCTH) N-phenyl (3carboxyphenol) thiourea (PCTH) المحضر من تفاعل فنيل ايزونثايوسيانايد و -3 امينو حامض البنزويك . و تم تفاعل هذا الليكاند (PCTH) مع الاملاح المعدنية من نوع القنيل ايزونثايوسيانايد و -3 امينو حامض البنزويك . و تم تفاعل هذا الليكاند (PCTH) مع الاملاح المعدنية من نوع الاراي (M= 2Cl₂Cl₂Cl₂Cl₂Cl) حيث ,(II) مع الاملاح المعدنية من نوع Pb(II) M= Cu(II), Zn(II) حيث ,(II) حيث ,(II) مع الاملاح المعدنية من نوع (PCTH) حيث ,(II) مع الاملاح المعدنية من نوع (M= Pb(II) M= Cu(II), Zn(II) حيث ,(II) مع الاراي (Cu(II) and Co(II) وارتبط بالذرة المركزية اما عن طريق ذرة الكبريت او عن طريق ذرة النيتروجين لمجموعة الامين او عن طريق ذرة وارتبط بالذرة المركزية اما عن طريق ذرة الكبريت او عن طريق ذرة النيتروجين لمجموعة الامين او عن طريق ذرة الكمريانية و اطياف الاشعة تحت الحمراء و اطياف الاشعة فوق البنفسجية – المرئية ، PCTH ، المحسرة بواسطة التحليل الدقيق للعناصر، و قياس التوصيلية الكهريانية و اطياف الاشعة تحت الحمراء و اطياف الاشعة فوق البنفسجية – المرئية ، PCTH ، المحسرة بواسطة التحليل الدقيق للعناصر، و قياس التوصيلية الكهريانية و اطياف الاشعة تحت الحمراء و اطياف الاشعة فوق البنفسجية – المرئية ، PCTP ، المحفرات مقابل الكهريانية المعنوات المحضرة بواسطة التحليل الدقيق للعناصر، و قياس التوصيلية وكذلك قياس الحساسية المغناطيسية. واخيرا تم قياس الفعالية البايولوجبة لليكاند (PCTH) ، ومعقداتها اختبرت مقابل وكذلك قياس الحساسية المغناطيسية. واخيرا تم قياس الفعالية البايولوجبة لليكاند (PCTP) و معقداتها اختبرت مقابل وكذلك قياس الحساسية المغناطيسية . واخيرا تم قياس الفعالية البايولوجبة لليكاند (PCTH) و معقداتها اختبرت مقابل وكذلك قياس الحساسية المغناطيسية . واخيرات مقياس الفعالية البايولوجبة لليكاند (المائية ، PCTP) و .(PCTH) ، و .(Could بكني .

الكلمات الدالة: مشتق الثايويوريا، املاح الفلزات ، الفعالية البكتيرية.



1. INTRODUCTION

Thiourea and its derivatives are important ligands for transition metals [1], which able to coordinate to a range of metal centers as ligands either from oxygen, nitrogen and sulfur donor atoms of thiourea derivatives [2]. Thiourea ligands and their metal complexes exhibit a wide range of biological activity including anticancer, fungicides, antimicrobial and show a broad spectrum of biological activities as anti-HIV[3].

In this study, we report herein the synthesis, characterization and antibacterial studies of thiourea derivative, namely N-phenyl- \tilde{N} -(3- carboxyphenol) thiourea (PCTH) as show in scheme (1), and its metal complexes of Cu(II), Zn(II), Pb(II) and Co(II) are synthesized, characterized, and their biological activities are measured.



Scheme (1): preparation the N-phenyl Ń-(3carboxyphenol) thiourea (PCTH).

2. Experimental

2.1. Reagents and starting materials

Phenylisothiocyanate, 3-aminobenzoic acid and cesium iodide were purchased from Fluka AG., ZnCl₂ and acetone are Merk products. CuCl₂.2H₂O, CoCl₂.6H₂O, PbCl₂.4H₂O, and methanol are from supplied by BDH. DMSO was purchased from Riedel.

2.2. Syntheses of the ligand

Phenylisothiocyanate (2.70 gr 0.02 mmol) was added to a solution of 3- amino benzoic acid (2.74 gr 0.02 mmol) in ethanol (25 cm³). The solution mixture was refluxed for 10 hours to give a white precipitate. Then the solution left to cool in ice-bath to give a white precipitate, which was filtered washed with ethanol and diethyl ether, dried and recrystallized from hot ethanol [4].



2.3. General procedure for preparation of metal complexes

The warm ethanolic solution of the ligand and metal salts solution were mix in the stoichiometric proportions (1:2), (metal: ligand) ratio for all divalent metal ions the resultant mixture was stirred and refluxed for (2 - 6) hours. The precipitate was formed, and then the solution mixture was cooled in ice - bath for complete precipitation. The product was filtered off, washed with ethanol and diethyl ether, and dried under vacuum.

2.4. Bacterial activity:

The bacterial activity of the ligand (PCTH) and its metal complexes was measured using well-diffusion method [5]⁻

2.5. Physical measurements:

Melting points were measured using Stuart Digital Melting point apparatus. Electronic spectra of the ligand and the complexes were carried out for $(1 * 10^{-3} \text{ M})$ solution in DMSO using a T60 UV/Vis spectrophotometer. The Infrared spectra of the ligands and complexes were recorded on a (Shimadzu) infrared spectrophotometer in the (250-4000) cm⁻¹ range using CsI disk. Elemental analysis was carried out on Perkin Elmer-2400 CHNS analyzer. The conductivities of the complexes were carried out for (1 * 10⁻³ M) solution in DMSO using Conductometer type (Cond. 720) conductivity meter. Magnetic measurements were recorded on an auto Magnetic Susceptibility balance Guoy method.

3. Results and Discussion

3.1 Elemental analysis

Elemental analysis data for the synthesized ligand and its metal complexes are shown in Table (1). They are consistent with the suggested stoichiometries. The color and melting points of the synthesized ligand and its metal complexes are also shown in Table (1).

3.2 Molar conductivities

Molar conductivities of all synthesized complexes are listed in Table (1). These measured values are compared with known molar conductivities [6], which indicates that they are non-electrolyte and consistent with the proposed formula for them.



Table (1): Color, melting point, elemental analysis and conductivity data for the synthesized thiourea derivative (PCTH) complexes.

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No.	Compounds	Color		$(\Omega^{-1}.cm^2.$			
		(M.P).(°C)	С %	Н %	N %	S %	mol ⁻¹)
	Ligand (PCTH)	White	59.39	4.63	9.75	11.32	
		(195)	(61.75)	(4.44)	(10.29)	(11.77)	
1	[Cu(PCTH) ₂ Cl ₂]	Green	49.78	3.28	8.30	9.47	8.9
		(215)	(49.52)	(3.56)	(8.25)	(9.44)	
2	$[Zn(PCT)_2]$	White	45.92	3.60	8.55	10.33	11.9
		(170)	(45.55)	(3.82)	(8.85)	(10.13)	
3	$[Pb(PCT)_2]$	White	37.43	3.98	7.54	8.32	16.2
		(250)	(37.21)	(3.72)	(7.23)	(8.28)	
4	[Co(PCTH) ₂ Cl ₂]	Bright-	46.43	3.76	9.00	10.33	17.3
		Blue (98)	(46.02)	(3.86)	(8.94)	(10.24)	

3.3.¹H N.M.R.

The 1H- N.M.R. for free ligand were recorded at 300 MHZ by using a DMSO solvent Fig. (1)._The ¹H- N.M.R. spectra showed principal signals, the signals at δ (3.5 – 4.5) ppm for ligand (PCTH) may be due (NH) (1H), while the multiple peak at δ (6 -8)ppm which assigned to phenyl ring in free ligand. The single peak appear at (10 - 13.2) ppm assigned (OH) for carboxylic group at deshield [8].



Fig. (1): ¹H NMR of free ligand.

F2 SI

3.4 ^{13C} N.M.R.

The 13C spectrum of free ligand Fig.(2) shows signals at (123.6 - 131) ppm for ring carbon. The signal at (139.24 -139.65) for carbon attached (NH), while the signal at (166.98 -167.01) ppm for (C=O) it appear singlet, and the other peak appear singlet at (179.8 – 180.03) ppm which assigned to (C=S) [9], [10].



Fig.(2): ¹³C NMR of free ligand.

3.5 Electronic spectra

The UV spectral diagrams of the free ligand (PCTH) show band at about 37313 cm⁻¹ is assigned to $(n \rightarrow \pi^*)$ absorption for ligand [11].



The electronic spectrum of Cu(II) complex shows tow bands at 43478 and 22727 cm⁻¹, Table (2), which are denoted to Cu-ligand charge transfer transition [12], and $(_{2}B_{1}g \rightarrow _{2}B_{2}g)$ transition [13] respectively, suggesting a octahedral structure for the Cu(II) complexes. The electronic spectra of Zn(II), Pb(II) and Co(II) complexes show bands in range (43478 - 43470) cm⁻¹, which are assigned to charge transfer or internal ligand transitions [14], [15].

3.6 Magnetic susceptibility

The magnetic susceptibility of Cu(II) complex is 2.01 B.M. Table (2), which confirms a octahedral geometry around Cu(II). The magnetic susceptibility of Zn(II) and Pb(II) complex are zero which denote to that they are diamagnetic and have tetrahedral arrangements around metal centers [16]. While the magnetic susceptibility of Co(II) complex, is (4.95) B.M. this values of magnetic moment is higher than the spin-only value (3.87 B.M) for their unpaired electrons and may be ascribe to substantial orbital contribution to the moment which is applicable of which suggests an octahedral geometry around the metal [17].

No	Compounds	Band ab	sorption	Assignment	µeff (B.M)	
110.	Compounds	cm ⁻¹	nm	issignment	Geometry	
	Ligand (PCTH)	40000	250	$n \rightarrow \pi^*$		
1	[Cu(PCTH),Cl,]	40000	250	Intraligand	2.01 O.h.	
I		22727	440	$_2B_1g \rightarrow _2B_2g$		
2	[Zn(PCT) ₂]	43478	230	С.Т.	T.h.	
3	[Pb(PCT) ₂]	43470	232	С.Т.	T.h.	
4	[Co(PCTH) ₂ Cl ₂]	43478	230	С.Т.	4.950.h.	

3.7 Infra-Red Spectroscopy

The ligand N-phenyl- \tilde{N} -(3- carboxyphenol) thiourea (PCTH) was synthesized by reaction of equimolar amounts of Phenylisothiocyanate and 3- amino benzoic acid in ethanol. It is a white solid, soluble in methanol, ethanol, acetone and dichloromethane, but it is insoluble in water. The FT- IR spectrum for ligand (PCTH) shows a characteristic absorption bands at 3167, 3269, 1680 and 1309 cm⁻¹ assigned to v(N-H) stretching, v(O-H), v(C=O) and v(C=S) respectively [18], [19].

In complex (1) v(OH) is observed at 3306 cm⁻¹, indicating that the OH group has taken part in coordination, While in complexes (2 and 3) disappear assigned to coordinate with metals as deprotonated group [20]. v(N-H) in the complexes, it is found in the 3225- 3174 cm⁻¹ region suggesting the bonding through nitrogen atom in complex (2). v(C=O) observed at 1724 -1615 cm⁻¹ in indicating that the (C=O)group coordinate with metals in complex (1 and 4). v(C=S) observed at 1350 -1255cm⁻¹ in indicating that the (C=S)group coordinate with all metal complexes [21]. New bond formed between metal and N, O, Sand Cl [22] listed in Table (3).

No.	Compounds	υ(N-H)	υ(О-Н)	υ(C=O)	υ(C=S)	υ (M-N)	1) (M-O)	υ(M-S)	υ(M-Cl)
	Ligand (PCTH)	3176	3269	1680	1309				
1	[Cu(PCTH) ₂ Cl ₂]	3225	3306	1691	1255		387	320	270
2	$[Zn(PCT)_2]$	3320		1615	1310	420	374		
3	$[Pb(PCT)_2]$	3175		1724	1350		368	340	
4	[Co(PCTH) ₂ Cl ₂]	3174	3271	1689	1318		365	351	278

Table (3): Selected IR bands of the Thiourea and its metal complexes (cm⁻¹).

3.8 Bacterial activity of the ligand (PCTH) and its metal complexes

In vitro antibacterial screening was performed by the agar disc diffusion method. The bacterial species used in the screening were gram-negative bacteria *Klebsiella pneumonia* and *Escherichia coli* and gram-positive bacteria *Staphylococcus aurous*.

The measured biological activities of the ligand (PCTH) and its metal complexes are arranged in Table (4). The free ligand (PCTH) is sensitive against *Escherichia coli and* resistant against *Klebsiella pneumonia and Staphylococcus aurous*. The metal complexes (3 and 4) are resistant against *Klebsiella pneumonia*. The complexes (1 and 3) are sensitive against *Escherichia coli* bacterium while the other complexes are resistant.

The complexes (1 and 3) are sensitive against *Staphylococcus aurous* bacterium while the other complexes are resistant.



No.	Compound	Klebsiella pneumonia	Escherichia coli	Staphylocous aureus	
	Ligand (PCTH)	R	S	R	
1	[Cu(PCTH) ₂ Cl ₂]	S	S	S	
2	[Zn(PCT) ₂]	S	R	R	
3	[Pb(PCT) ₂]	R	S	S	
4	[Co(PCTH) ₂ Cl ₂]	R	R	R	
R: Resistant S: Sensitive					

 Table (4): Bacterial activity of ligand (PCTH) and its metal complexes

4. CONCLUSIONS

A novel ligand (PCTH) and its Cu(II), Zn(II), Pb(II) and Co(II) complexes were synthesized and fully characterized by various spectroscopic techniques and the bacterial activity was tested against different bacteria and the result show different activity of the free ligand and metal complexes.

According to elemental analysis, IR and uv-visible spectroscopy, conductivity and magnetic susceptibility data the following structures are proposed for the synthesized metal complexes as shown in Fig. (3).







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