# Synthesis and Characterization of Fe(II) Co(II) and Ni(II) Complexes with Captopril

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# Abstract

Complexes of Fe(II), Co(II) and Ni(II) with captopril (CapH<sub>2</sub>) in neutral and basic media have been synthesized. The structure of the complexes has been elucidated by metal, chloride analysis, molar conductances, infrared and electronic spectra. The ligand (CapH<sub>2</sub>) exhibited in neutral medium as a tridentate coordination, with the presence of two chloride ions and one water molecule in the complexes , and the presence of three water molecules after the deprotonation of both hydrogen atoms from the ligand in a basic medium to form the most probable octahedral geometry around each metal ion.

Keywords: Captopril complexes, Fe(II) complexes, Co(II) complexes, Ni(II) complexes.

#### Introduction

Captopril is 1- (3-mercapto-2-methyl propionyl)-proline and well known as a drug for the treatment of high blood pressure<sup>(1)</sup>. As well, it is considered as a versatile ligand with four potential donor atoms (S thiol, O amide and two O of the acid) which might be involved in coordination with metal ions. Complexes of captopril with Zn (II) were studied by several authors<sup>(2-4)</sup> in different pH ranges. Polymeric [Zn (Cap)] , were precipitated at pH < 6 while at pH range 6.0-8.2 Na<sub>2</sub> [Zn  $(Cap)_2$ ] were isolated<sup>(2)</sup>. Two molecules of Cap were bounded via sulfur and carbonyl oxygen to Zn(II) forming a four coordinated complexes. In  $[Zn(Cap)]_n$ complexes, cap is coordinated to zinc ion through the thiolate, carbonyl oxygen of one ligand and the bidentate carboxylate group of another. Atzei et al.<sup>(5)</sup> prepared metal complexes of the general formula Na<sub>2</sub>M (Cap)<sub>2</sub>  $.xH_2O$  (where M = Cd(II) or Ni(II), x= 7 and 4 respectively, Cap is a deprotonated captopril). These complexes were studied by mean of X-ray photoelectron spectroscopy indicating that Cap is bonded to the metal ions via the sulfur atom and carboxylic oxygen. Recently, [Co (Cap)<sub>2</sub> (OH)]<sub>2</sub> was synthesized and characterized by different spectral techniques<sup>(6)</sup>. The Co(III) ion is bonded with pseudo-octahedral geometry. Captopril molecules are coordinated via mercapto and amidic C=O groups to Co(III). Two S atoms are bridging two Co(III) ions. The OH ion completes the octahedral geometry. In the first study of organometallic compounds of captopril<sup>(6)</sup>, four  $R_2Sn(IV)$  (R = Me, Et, n-Bu and t-Bu) complexes of captopril were characterized by means of i.r, Raman and <sup>119</sup>Sn-NMR spectroscopy and electrospray mass spectroscopy. Additionally, the structure of Me<sub>2</sub>Sn(Cap) was determined by single crystal X-ray diffraction method. All compounds showed similar structures with slight different in the degree of distortion of bond angles. Each complex adopts a linear polymeric structure with trigonal bipyramid geometry around tin ion. The metal ions are linked by chelate type coordination of the thiolate group and the C=O of one ligand in the equatorial-axial position and axial coordination of carboxylate group of another<sup>(6)</sup>.

The aim of the present work is to prepare and characterize Fe (II), Co (II) and Ni (II) complexes with captopril.

# Experimental

# **Elemental analysis**

The metal and the chloride content of the prepared complexes were measured using standard procedure<sup>(7)</sup>. The analytical data were given in Table (1).

### **Physical measurements**

Molar conductance of the prepared complexes in dimethyl formamide (DMF) were measured using an electrolytic conductivity instrument model LF42 and the values are listed in Table (1).Infrared spectra were recorded as KBr discs using Perkin-Elmer 557 Spectrophotometer within the 400-4000 cm<sup>-1</sup> range. The electronic spectra were recorded on Shimadzu UV-160 Spectrophotometer for  $10^{-3}$  M solution of the complexes in DMF at 25 °C using 1 cm quartz cell.

#### Material

The captopril ligand was supplied from the General Organization of Drug and Medical Appliance, Ninevah, Iraq and used with no further purification. The metal (II) chlorides hexahydrated were of Analar BDH and used without further purification.

#### **Preparation of complexes**

Two type of the complexes were prepared:

# 1. [MCl<sub>2</sub>(H<sub>2</sub>O)CapH<sub>2</sub>] ; where M = Fe(II), Co(II) and Ni(II); CapH<sub>2</sub> = Captopril (Type I)

To a stirred solution of  $MCl_2.6H_2O$  (1 mmol) in distillated water (25 ml), a solution of the captopril (1 mmol) in ethanol (25 ml) was added dropwise with refluxing for (2hr).The volume of the mixture was reduced to half its volume by the evaporation . The precipitate thus formed was filtered off, washed with ethanol then dried.

# 2. [M(Cap)(H<sub>2</sub>O)<sub>3</sub>] (Type II)

Equimolar quantities of MCl<sub>2</sub>.6H<sub>2</sub>O in H<sub>2</sub>O (25 ml) and CapH<sub>2</sub> in ethanol (25 ml) were mixed. Alkaline solution of 1 M KOH was added untill the pH was (8-9).The mixture was refluxed for (3hr). The volume of the mixture was reduced to half its volume by evaporation. The precipitate thus formed was filtered off, washed with with ethanol then dried.

#### **Results And Discussion**

Two types of complexes were synthesized in neutral and basic media.In the basic medium the reaction of the

metal chloride solution with the captopril was followed by the addition of two equivalent of KOH solution, the ligand underwent deprotonation in the first step followed by its inclusion in the metal ion coordination sphere. Hence both types of complexes were synthesized according the following reactions:

1. MCl<sub>2</sub>.6H<sub>2</sub>O + CapH<sub>2</sub> $\longrightarrow$  [M(CapH<sub>2</sub>)Cl<sub>2</sub>.H<sub>2</sub>O] + 5H<sub>2</sub>O type I



Type I

2. MCl<sub>2</sub>.6H<sub>2</sub>O + CapH<sub>2</sub> + 2KOH  $\longrightarrow$  [M(CapH<sub>2</sub>)(H<sub>2</sub>O)<sub>3</sub>] + 2KCl + 5H<sub>2</sub>O type II

They are stable in the solid state. The prepared complexes were insoluble in water, methanol and ethanol but soluble in dimethyl formamide and dimethyl sulfoxide at room temperature. Results of elemental analysis (Table1) are in a good agreement with the suggested formula of stoichiometric ratio 1:1 of M: ligand of both types as depicted below:



Type II

M = Fe(II), Co(II), Ni(II)

The molar conductivities values in DMF at  $10^{-3}$  M (Table 1) are lying within the range of 25-40  $\Omega^{-1}$ .mol<sup>-1</sup>.cm<sup>2</sup> indicating a non-electrolytic character of both types of complexes<sup>(8)</sup>.

The coordination sites of the ligand involved in bonding with metal ions for both types of complexes had been specified by careful comparison of the infrared spectra of the synthesized complexes with that of the parent ligand (Table II). The ligand basically composed of different groups of potent ability to coordinate with the metal ions. These groups are, carboxylic (COOH), carbonyl (C=O) and the mercapto (SH). There are three vibrations of interest in carboxylic group. These are v(OH), v(C-O) + v(C-O) $\delta$ (O-H) and v(C=O) stretching at 3472, 1443 and 1689 cm<sup>-1</sup> related to the above categories respectively<sup>(9)</sup>. In case of type I complexes, the v(C=O) of carboxylic group were shifted to lower values ( $\Delta v = 63-82 \text{ cm}^{-1}$ ) and the  $v(C-O) + \delta(O-H)$  of the same group were almost unaltered confirm that the (COOH) group is coordinately bonded to the metal ions via the oxygen lone pair of electrons of (C=O) not by that of  $(O-H)^{(10)}$ . Whilst, in type II complexes, the disappearance of the stretching frequencies related to (COOH) groups and appearance of new  $v_{asy}$  and  $v_{sym}$  models of (COO<sup>-</sup>) group at 1579-1585 cm<sup>-1</sup> and 1362-1384 cm<sup>-1</sup> respectively,( the  $\Delta v = 195-205$ cm<sup>-1</sup>) are consistent with the unidentate coordination of the carboxylate  $group^{(11)}$ .

The next diagnostic band in the free ligand is that for the carbonyl group (N-CO) which appeared at 1748 cm<sup>-1</sup>. This band is negatively shifted ( $\Delta v = 33-53$  cm<sup>-1</sup>) and ( $\Delta v = 57-90$  cm<sup>-1</sup>) for the type I and II respectively. This interpreted as due to the coordination of the carbonyl groups with the metal ions<sup>(12)</sup>. A medium intensity band at 2566 cm<sup>-1</sup> is assignable to the S-H group was in the spectrum of the ligand<sup>(9)</sup>. This band was shifted to lower

values ( $\Delta v = 25.56 \text{ cm}^{-1}$ ) as a consequence of the coordination of the sulfur atom with metal ion in type I complexes. Whilst in type II complexes, the absence of the v(SH) band<sup>(13)</sup> and the appearance of new bands at (320-345 cm<sup>-1</sup>)<sup>(14)</sup> indicate the deprotonation of SH group and formation of metal-sulfur coordination bonds<sup>(15)</sup>. New bands of a broad intensities were appeared in the region 3420-3443 cm<sup>-1</sup> were attributed to water molecules coordinated to the metal ions of both types of complexes and this was supported by appearance of new band at 440-460 cm<sup>-1</sup> assigned the M-O bonds<sup>(16)</sup>.

The electronic spectra data of the complexes are shown in Table (I). Fe(II) complexes in both types showed a broad absorption band at 13340 cm<sup>-1</sup> for type I and at 15125 cm<sup>-1</sup> for type (II) referring to  ${}^{5}T_{2}g(D) \rightarrow {}^{5}Eg(D)$ transition in an high spin octahedral environment<sup>(17)</sup>. The Co(II) complexes exhibited three bands at 12204-12326, 19379, 19607 cm<sup>-1</sup> and 25826, 25510 cm<sup>-1</sup> for type I and II respectively. These bands were attributed to the transition  ${}^{4}T_{1}g(F) \rightarrow {}^{4}T_{2}g(F)$ ,  ${}^{4}T_{1}g(F) \rightarrow {}^{4}A_{2}g(F)$ ,  ${}^{4}T_{1}g(F)$  $\rightarrow$  <sup>4</sup>T<sub>1</sub>g(P) for high spin octahedral geometry<sup>(18)</sup>. The electronic spectra of the Ni(II) complexes in both types showed d-d bands in the region 12879, 13432 cm<sup>-1</sup>; 19920, 19617 cm<sup>-1</sup> and 24752, 24630 cm<sup>-1</sup>. These are assigned to the spin-allowed transition  ${}^{3}A_{2}g(F) \rightarrow {}^{3}T_{1}g(P)$ ,  ${}^{3}A_{2}g(F) \rightarrow {}^{3}T_{1}g(F)$  and  ${}^{3}A_{2}g(F) \rightarrow {}^{3}A_{2}g(F)$ respectively, consistent with their well-defined high spin octahedral configuration<sup>(19)</sup>. The magnetic values are in a good agreement of the high spin metal ions(II) octahedral geometries(Table(I)). In conclusion, the ligand captopril coordinated with the divalent metal ions throught the carbonyl oxygen of the carboxylic group, the carbonyl oxygen of tertiary amide group and the mercapto sulfur in the type I complexes and with the same groups after deprotonation of both hydrogen atoms from the

carboxylic and the mercapto groups in the type II complexes to give with the presence of two chloride ions and one water molecules in type I and three water

molecules in type II the most probable octahedral geometry around each metal ion.

	No	Complex	m.p.	Analysis % found/(calc.)		٨	$\mu_{eff}$	<b>Band</b> $(am^{-1})$		Assignment	
	110.	(Color)	°C	М	Cl	AM DMF	B.M.	Balle (clif)		Assignment	
Type I	1	[Fe(CapH <sub>2</sub> )Cl <sub>2</sub> (H <sub>2</sub> O)] (Brown)	209-211	15.50 (15.38)	19.54 (19.31)	36	4.92	ν	13340	${}^{5}T_{2}g(D) \rightarrow {}^{5}Eg(D)$	
	2	[Co(CapH <sub>2</sub> )Cl <sub>2</sub> (H <sub>2</sub> O)] (Yellow)	228-230	16.22 (16.18)	19.27 (19.17)	31	3.45	$     \begin{array}{c}       \nu_1 \\       \nu_2 \\       \nu_3     \end{array} $	12204 19379 25826	${}^{4}T_{1}g(F) \rightarrow {}^{4}T_{2}g(F)$ $T_{1}g(F) \rightarrow {}^{4}A_{2}g(F)$ $T_{1}g(F) \rightarrow {}^{4}T_{1}g(P)$	
	3	[Ni(CapH <sub>2</sub> )Cl <sub>2</sub> (H <sub>2</sub> O)] (Green)	194-196	16.16 (16.10)	19.28 (19.20)	40	2.46	v1 v2 v3	12879 19920 24752	${}^{3}A_{2}g(F) \rightarrow {}^{3}T_{1}g(P)$ ${}^{3}A_{2}g(F) \rightarrow {}^{3}T_{1}g(F)$ ${}^{3}A_{2}g(F) \rightarrow {}^{3}T_{2}g(F)$	
Type II	4	[Fe(Cap)(H <sub>2</sub> O) <sub>3</sub> ] (Dark Brown)	250-252	17.22 (17.03)	-	25	4.87	ν1	15125	${}^{5}T_{2}g(D) \rightarrow {}^{5}Eg(D)$	
	5	[Co(Cap)(H <sub>2</sub> O) <sub>3</sub> ] (Deep Yellow)	244-246	18.00 (17.91)	-	38	3.41	$     \begin{array}{c}       \nu_1 \\       \nu_2 \\       \nu_3     \end{array} $	12326 19607 25510	${}^{4}T_{1}g(F) \rightarrow {}^{4}T_{2}g(F)$ ${}^{4}T_{1}g(F) \rightarrow {}^{4}A_{2}g(F)$ ${}^{4}T_{1}g(F) \rightarrow {}^{4}T_{1}g(P)$	
	6	[Ni(Cap)(H <sub>2</sub> O) <sub>3</sub> ] (Light Green)	234-236	17.94 (17.62)	-	25	2.49	$v_1$ $v_2$ $v_3$	13432 19617 24630	${}^{3}A_{2}g(F) \rightarrow {}^{3}T_{1}g(P)$ ${}^{3}A_{2}g(F) \rightarrow {}^{3}T_{1}g(F)$ ${}^{3}A_{2}g(F) \rightarrow {}^{3}T_{2}g(F)$	

Table (I): Metal and chloride analysis, molar conductivities  $(\Omega^{-1}.mol^{-1}.cm^2)$  and the electronic spectra of the complexes

# Table (II): Selected I.R. absorption bands of the captopril (ligand) and its complexes

Group	Assignment	Ligand	Complexes						
Group	Assignment		1	2	3	4	5	6	
	v(C=O)	1689vs	1624m	1603s	1607m	-	-	-	
	$\nu$ (C-O)+ $\delta$ (OH)	1443m	1440m	1447m	1445m	-	-	-	
COOH	v(OH)	3472b	3474b	3471b	3475b	-	-	-	
	v(COO <sup>-</sup> )asy	-	-	-	-	1580s	1584m	1579s	
	v(COO <sup>-</sup> )sy	-	-	-	-	1370m	1362s	1384m	
N-C=O	v(C=O)	1748vs	1715s	1710s	1695m	1691m	1664s	1685s	
мен	v(SH)	2566m	2541m	2531m	2534m	-	-	-	
M-511	$\nu$ (M-S)	-	345m	322m	334w	320w	335m	328m	
МОЦ	v(OH)	3422b	3420b	3418b	3419b	3430w	3441s	3443b	
WI-OH <sub>2</sub>	v(M-O)	-	445m	442w	460m	451m	453w	440m	

 $vs{=}\;very\;sharp$  ,  $s{=}\;sharp$  ,  $m{=}\;medium$  ,  $b{=}\;broad$  ,  $w{=}\;weak$ 

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# تحضير وتشخيص معقدات الحديد (II)، الكوبلت (II)والنيكل (II)مع الكابتوبريل خلف ابراهيم خلو و عبير سالم محمد و احلام محمد احمد الدباغ

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ً المديرية العامة لتربية نينوي ، الموصل ، العراق

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#### الملخص

يتضمن البحث تحضير معقدات للحديد (II) والكوبلت (II) والنيكل (II) مع الكابتوبريل (CapH<sub>2</sub>) ذوات الصيغ العامة [M(Cap)Cl<sub>2</sub>H<sub>2</sub>O] و [M(Cap)(H<sub>2</sub>O)<sub>3</sub>] في كل من الوسط المتعادل والقاعدي على التوالي. تم تشخيص تراكيب هذه المعقدات من خلال تحليل محتوى العناصر والكلوريد والموصلية المولارية واطياف الاشعة تحت الحمراء وكذلك الاطياف الالكترونية. وقد ظهر بان الليكاند (CapH<sub>2</sub>) يتناسق بشكل ثلاثي السن حيث ترتبط تلاثة مواقع منه مع وجود ايوني كلوريد وجزيئة ماء واحدة في المعقدات المحضرة في الوسط المتعادل ووجود ثلاث جزيئات ماء بعد فقدان ذرتي الهيدروجين من الليكاند في المعقدات المحضرة في المحيطي الترتيب ثماني السطوح الاكثر احتمالا حول كل ايون فلزي.