March 2009 Volume 4 Issue 1

Trade Science Inc.

Inorganic CHEMISTRY

An Indian Journal

Full Paper

ICAIJ, 4(1), 2009 [6-9]

Spectroscopic and thermal studies on copper(II) and cobalt(II)-losartan complexes

Ayman A.Gouda*, Soha Fahim

Chemistry Department, Faculty of Science, Zagazig University, Zagazig, (EGYPT)

Phone : +2 055 2423346

E-mail : aymanchimca@yahoo.com

Received: 28th January, 2009 ; Accepted: 2nd February, 2009

ABSTRACT

Losartan, the potassium salt of 2-*n*-butyl-4-chloro-5-hydroxymethyl-1-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methyl]imidazol, is an efficient antihypertensive drug. The complexes of Losartan ($C_{22}H_{22}ClN_6O$) with Cu(II) and Co(II) are studied. The complexes Cu[$(C_{22}H_{22}ClN_6O)_2.2H_2O$] $2H_2O$ and Co[$(C_{22}H_{22}ClN_6O)_2$].$2H_2O$ are prepared in aqueous solution at room temperature. The complexes are investigated and characterized by infrared spectra, elemental analysis and thermogravimetric analysis. A general mechanism describing the formation and the thermal decomposition of these complexes are suggested.

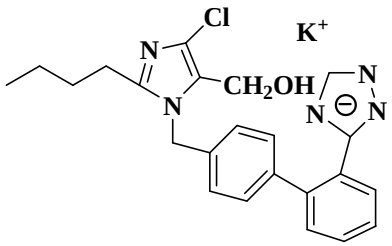
1.INTRODUCTION

Losartan potassium (LOS-K); 2-butyl-4-chloro-1-[p-(o-1H-tetrazol-5-ylphenyl)benzyl-imidazole-5-methanol potassium, (SCHEME 1) is a new non-peptide angiotensin II receptor antagonist with antihypertensive activity, due mainly to selective blockade on AT_1 receptors and the consequent reduced pressor effect of angiotensin II[1]. LOS-K is used in the management of hypertension with a lower incidence of side effects such as cough, which develops with typical angiotensin-converting enzyme inhibitors. It can be used alone or combined with the diuretic hydrochlorothiazide (HCTZ) in patients with moderate heart failure[2]. Structurally, Losartan is a biphenyltetrazol ring system attached to a substituted imidazol ring through a methylene spacer. Recently, single-crystal X-ray determinations of the structures of Losartan and its potassium salt were reported[3,4].

Copper and Cobalt are the essential transition elements that plays a fundamental role in the biochemistry of all aerobic organisms. On the other hand, losartan contains functional groups capable to bind the copper biometal in stable complexes. Therefore, the aim of the present study was directed to the development of the synthesis and characterization of a new copper or cobalt complexes of losartan K.

Synthesis of copper or cobalt-losartan complexes

The solid complexes are prepared at room temperature by mixing aqueous solutions of metal to ligand with a molar ration 1: 2. The copper complex (blue coulor) and cobalt complex (pink coulor) are formed at once the obtained precipitates were filtered, washed several times with bidistilled water and ethanol then dried over anhydrous $CaCl_2$. The solid complexes Cu [$(C_{22}H_{22}ClN_6O)_2.2H_2O$].$2H_2O$ and Co[$(C_{22}H_{22}ClN_6O)_2$].



SCHEME 1: Structure of Losartan potassium salt

TABLE 1: Elemental analysis of data of the solid complexes

Complex	C%	H%	N%	M%
[Cu $(C_{22}H_{22}ClN_6O)_2$. $2H_2O$] $.2H_2O$	52.92 (53.81)	3.78 (5.29)	17.09 (17.12)	Cu^{2+} (6.90)
[Co $(C_{22}H_{22}ClN_6O)_2$] $.2H_2O$	56.69 (56.13)	4.12 (5.10)	18.28 (17.86)	Co^{2+} (6.97)

The calculated values are shown in parenthesis

TABLE 2: Infrared frequencies (cm^{-1}) and assignments for free losartan potassium, copper(II) and cobalt(II)-losartan complexes

Frequency*, cm^{-1}			Band assignments
Free ligand	Cu- complex	Co-complex	
3477 (s, sh)	3421 (sh, br)	3360 (s, br)	ν(H_2O)coordinated +
3420 (s)	3195 (s, br)	3203 (sh, s)	ν (H_2O) uncoordinated +
3390 (sh)	3124 (sh)	-	ν (N-H)
3219 (sh)	-	-	
3061 vw	3062 sh	3039 sh	
3039 sh	3036 vw	3036vw	ν (C-H) aliphatic and aromatic
2956s	2956s	2956 s	
2927 vs	2930 s	2929s	
2864 s	2867 s	2867 m	
1699m	1698 vw	1698 vw	
1678w	1677vw	1971 sh	ν (C-C) aromatic
1650s	1650 m	1648m	
-	1617 sh	1624m	δ (O-H), in plane
1609 sh	1576 s	1572 m	δ (N-H), in plane N=N C=C C=N + ν (ring)
1559 s	1540 vw	1540 vw	
1540 s	1503 s	1506 m	
1509 s	1460 vvs	1460 vvs	
1460vvs	1423vs	1424 s	
1423s		1423 s	
1358 m	1356 vs	1356 s	
1313 vw	1304 vvs	1307 vw	ν (C-C) + ν (C-N) + ν (C-H), in plane
1255s	1259 vvs	1255 vvs	
1202 vw	1190 vw	1189 w	
1159vw	1133vvw	1157 w	
1102 vw	1109m	1102 w	
1070 vw	1072 m	1072 w	ν (C-C-O) , out of plane + ν (C-N)
1010 s	999 vvs	1009 vs	
937vvw	933 w	933 w	
824m	841 m	824 m	δ (C-C-O), in plane
759 vs	790 m	759 vvs	
670 w	763vvs	668 w	
617 vvw	671 w	561 w	δ(C-H), out of plane + δ (O-H), out of plane+ δ (ring)+ ν (C-Cl)
561w	635 vvw	454 w	
522 vvw	565 m	419 w	
457 w	538m	-	
420 m	496vvw	-	
-	447w	-	

***s, strong; sh, sholder; br, broad; v, very; w, weak; m, medium**

$2H_2O$ were characterized by elemental analysis, TABLE 1, Infrared spectra and thermal properties TG (thermogravimetric analysis). The infrared spectra of the compounds obtained Cu[$(C_{22}H_{22}ClN_6O)_2$ $.2H_2O$].$2H_2O$ and Co[$(C_{22}H_{22}ClN_6O)_2$].$2H_2O$ and of

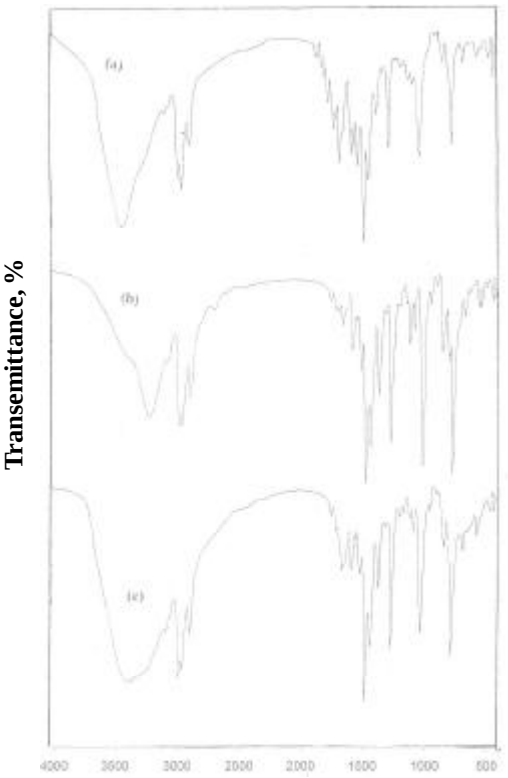


Figure 1: Infrared spectra of: (a) free losartan potassium, (b) copper(II)-losartan and (c) cobalt(II)-losartan complexes.

the TG decomposition products were recorded from KBr discs using a Genesis II FTIR spectrophotometer, Thermogravimetric (TG) of the compounds were carried out using a Shimadzu DT-50H computerized thermal system. Thermogravimetric analysis (TG) was carried out for the two solid complexes under a N_2 flow. Gravimetric analyses are made to determine the percentage of metal ions in the solid complexes.

RESULTS AND DISCUSSION

Characterization of copper and cobalt losartan complexes. The infrared spectra of the two solid complexes (Figure 1), show shift and splitting of several bands than that of the free ligand (losartan K), which indicated that these complexes are formed. The bidentate ligand (losartan K) was protonated through the nitrogen atom of imino group in the tetrazol ring (-N-H) and the ionized oxygen atom attached with imidazol ring (-CH_2-O^-).the protonation of nitrogen atom is indicated by the shift and change strength of N-H bands in infrared spectra of the two complexes. The (N-H) bands in the free ligand appear at 3437 (s, sh),

Full Paper

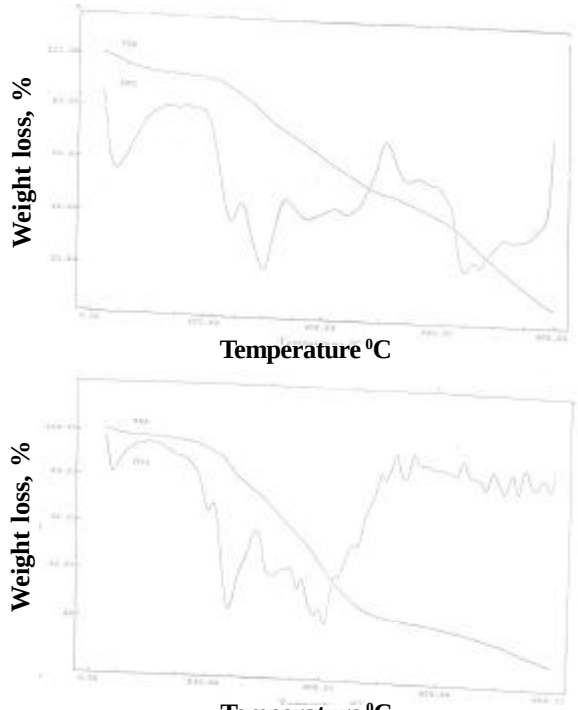


Figure 2: Thermograms of (a) copper(II)-losartan and (b) cobalt(II)-losartan complexes

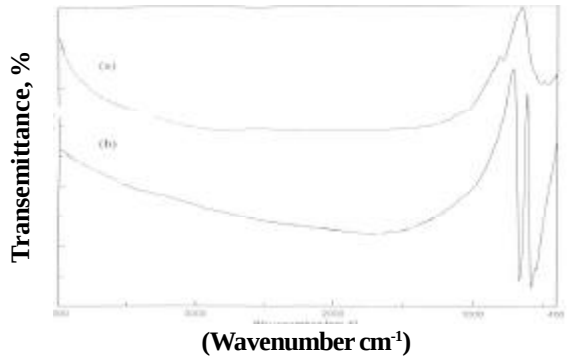


Figure 3: Infrared spectra of the final thermal decomposition products: (a) copper(II) oxide and (b) cobalt(II) oxide

3420 (s), 3390 (sh) and 3219 (sh) cm^{-1}, TABLE 2. In copper complex, $Cu[(C_{22}H_{22}ClN_6O)_2.2H_2O].2H_2O$, the υ (N-H) bands appear at 3421 (sh, br), 3195 (s, br) and 3124 (sh). The broad band at 3421 (sh,br) was associated with ν (O-H) of coordinated water and that at 3195 (s,br) was accompanied by ν (O-H) of uncoordinated water[5].

In cobalt complex, $Co[(C_{22}H_{22}ClN_6O)_2].2H_2O$ the ν (N-H) appears at 3360 (s,br) and at 3203(sh)cm^{-1}. The broad band at 3360 cm^{-1} was associated with ν(O-H) of uncoordinated water molecules.

The shift and change strength of bands in the range 1650-1550 cm^{-1} support the above results, where δ (H_2O) (in plane) appears at 1617 (sh) cm^{-1} in copper complex and at 1624 (sh) cm^{-1} in cobalt-complex. Also the δ (N-H) (in plane) shifted to 1576 (s) and 1572 (m) cm^{-1} in copper and cobalt complexes, respectively[5,6].

The coordination at ionized oxygen atom of the ligand was confirmed with the shift and change strength of ν(C-C-O). these band appears at 1010 (s) cm^{-1} in free ligand but appears at 999 (vvs) and 1009 (vs) cm^{-1} in copper and cobalt complexes, respectively[5].

The thermogravimetric analysis (TG) curves for the solid complexes were shown in (Figure 2). TABLE 3 gives the maximum temperature values for decomposition stages along with the corresponding weight loss values. These data support the proposed complex structures and also indicate that the decomposition of copper complex $Cu[(C_{22}H_{22}ClN_6O)_2.2H_2O].2H_2O$ occurs in four degradation steps. The first stage of decomposition occurs at a maximum temperature of 39.81^{0}C with no weight loss which may be due to break of hydrogen bonds or van der Waals bonds. The second step of degradation occurs at a maximum temperature of 153.6^{0}C with a weight loss of 3.268 %, this is associated with the loss of two uncoordinated water molecules. The third stage occurs at a maximum temperature of 205.7^{0}C which accompanied to a loss of two coordinated water molecules with a weight loss of 3.960%. The fourth step occurs at many maxima temperature in the range of 225-800^{0}C and associated with the degradation of organic molecules in the complex with a weight loss of 84.132% giving copper oxide CuO as a final residue equal 8.64% which agree quite with the calculated value 8.10%.

The infrared spectra of the final decomposition residue, (Figure 3), were supported these conclusions which show the absence of any bands associated with the losartan ligand but shows some bands characteristic of copper oxide, CuO.

Accordingly to these conclusions, the formation mechanism for this complex is as follows:

$$CuCl_2.2H_2O + 2(C_{22}H_{22}KClN_6O) + 2H_2O \rightarrow [Cu(C_{22}H_{22}ClN_6O)_2.2H_2O].2H_2O + 2KCl$$

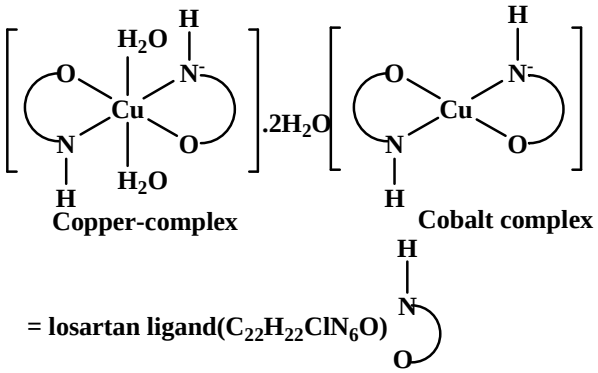
While the decomposition mechanism suggested as:

1. $[Cu(C_{22}H_{22}ClN_6O)_2.2H_2O].2H_2O \xrightarrow{153.6^0C} 2H_2O + [Cu(C_{22}H_{22}ClN_6O)_2.2H_2O]$

2. $[Cu(C_{22}H_{22}ClN_6O)_2.2H_2O] \xrightarrow{205.7^0C} 2H_2O + [Cu$

TABLE 3: The maximum temperature, T_{max}, ^0C, and weight loss values of the thermal degradation for copper(II) and cobalt(II)-losartan complexes

Decomposition step	T_{max}, ^0C	Percentage of weight loss	
		Calculated	Found
1-[Cu $(C_{22}H_{22}ClN_6O)_2.2H_2O$] $.2H_2O$			
Step (1)	39.81	-	-
Step (2)	153.6	3.668	3.268
Step (3)	205.7	3.668	3.96
Step (4)	241.69, 357.22, 386.21, 511.34 and 700	86.14	84.132
Total loss		91.90	91.36
Residue		8.10	8.64
2-[Co $(C_{22}H_{22}ClN_6O)_2].2H_2O$			
Step (1)	42.66	-	-
Step (2)	150	3.83	3.41
Step (3)	242.17, 300.86, 359 and 648.38	87.24	87.09
Total loss		91.07	90.50
Residue		8.93	9.50



SCHEME 2 : The structure of copper(II) and cobalt(II)-losartan complexes

$(C_{22}H_{22}ClN_6O)_2$]

3. [Cu$(C_{22}H_{22}ClN_6O)_2$] $\xrightarrow{225-800^0C}$ CuO + Residual of losartan

The decomposition of cobalt losartan complex[Co$(C_{22}H_{22}ClN_6O)_2$].$2H_2O$ occurs in three degradation stages, (Figure 2), (TABLE 3). The first step occurs at a maximum temperature of 42.66^0C with no weight loss which may be due to cleavage of hydrogen bonds or van der Waals bonds. The second stage of degradation occurs at a maximum temperature of 150^0C and was accompanied by a weight loss of 3.41% corresponding to the loss of two uncoordinated water molecules, TABLE 2. The final step of degradation occurs at many maxima in the range of 200-800^0C with a weight loss of 87.09%, this was associated with the loss of organic molecules. This final stage was agreed quite with the theoretical value of weight loss of 87.24%. The total weight loss value 90.50% agrees with the calculated value 91.07%. The final residue 9.50% was agreed quite with the theoretical value 8.93% which corresponding to cobalt trioxide, Co_3O_4.

The infrared spectra of the final decomposition residue, (Figure 3), were supported these results which show the absence of all bands associated to the losartan ligand but show a group of bands characteristic of cobalt trioxide, Co_3O_4.

The formation mechanism of cobalt losartan complex was suggested as follows:

$CoCl_2.6H_2O + 2(C_{22}H_{22}KClN_6O) \rightarrow [Co(C_{22}H_{22}ClN_6O)_2].2H_2O + 4H_2O + 2KCl$

The thermal decomposition reaction of this complex can be summarized as follows:

1. [Co $(C_{22}H_{22}ClN_6O)_2$].$2H_2O$ $\xrightarrow{150^0C}$ $2H_2O$ + [Co$(C_{22}H_{22}ClN_6O)_2$]

2. [Co$(C_{22}H_{22}ClN_6O)_2$] $\xrightarrow{200-800^0C}$ Co_3O_4 + Residual of losartan

Finally, the suggested structures of the two complexes may be tetrahedral for copper (II) complex and square planar for cobalt (II) complex (SCHEME 2).

REFERENCES

[1] Martindale; 'The Complete Drug Reference', 33rd ed., Pharmaceutical Press, London, 921-922 **(2002)**.

[2] I.A.Reid, B.G.Katzung; 'Basic and Clinical Pharmacology', 8th ed., Librairie du Liban, Beirut, Lebanon, 292-298 **(2001)**.

[3] L.Tessler, I.Goldberg; Acta Crystallogr., Sect.E: Struct.Rep.Online, 60, o1830-o1832 **(2004)**.

[4] D.Fernandez, D.Vega, J.A.Ellena, G.Echeverria; Acta Crystallogr., Sect.C: Cryst.Struct.Commun., **58**, m418-m420 **(2002)**.

[5] J.A.Dean; 'Analytical Chemistry Handbook', Mc Graw-Hill, New York, Ch. 6 **(1995)**.

[6] K.Nakamoto; 'Infrared Spectra of Inorganic and Coordination Compounds', Wiley, New York, 3 **(1970)**.