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Preparation sodium salts of phenylalanine, glycine and alanine complexes by using K2PtCl6, Cu(NO3)2.3H2O, HgCl2 and ZnCl2

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تحضير أملاح الصوديوم لمعقدات فينل ألانين والجليسين والألانين باستخدام كلوريد الزئبق الثنائي، كلوريد الزنك الثنائي، بوتاسيوم سداسي كلوروا البلاتينيوم ونترات النحاس المائية

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Abstract:
applications of complexes are very important in different sectors like the pharmaceutical industrial. So, this study aimed to preparation sodium salts of amino acids complexes by using K_2PtCl_6, Cu $(NO_3)_2.3H_2O$, $HgCl_2$ and $ZnCl_2$ as a ligand reaction with the sodium salts of the following amino acids: glycine (glyH), L-alanine (alaH), L-phenylalanine (pheH).
The following complexes were isolated: Na $[Pt(gly)Cl_4]$ $.0.5C_2H_5OH$, $[Cu(ala)_2].0.5C_2H_5OH$, $[Pt(ala)_3Cl].C_2H_5OH.4H_2O$, $[Pt(phe)_2Cl_2].0.5C_2H_5OH.1.5H_2O$, $[Hg(phe)_2].9H_2O$, $[Zn(phe)_2].C_2H_5OH$. The isolated complexes have been characterized by their elemental analysis's solubility, conductivity measurements, IR, electronic absorption and C^{13} NMR spectra.

Keywords: Metal complexes, Amino acids, Characterization.

الملخص:
تطبيقات المعقدات مهمة جدًا في مجالات مختلفة مثل الصناعات الدوائية، عليه استهدفت هذه الدراسة تحضير معقدات أملاح الصوديوم بواسطة معقدات K_2PtCl_6, Cu $(NO_3)_2.3H_2O$, $HgCl_2$ and $ZnCl_2$ كتفاعلات الليكاندات مع أملاح الصوديوم للأحماض الأمينية التالية: الجلايسيين (glyH)، L- ألانين (alaH)، L- فينيل ألانين (pheH). وتم الحصول على ست معقدات مختلفة:

Na $[Pt(gly)Cl_4]$ $.0.5C_2H_5OH$, $[Cu(ala)_2].0.5C_2H_5OH$, $[Pt(ala)_3Cl].C_2H_5OH.4H_2O$, $[Pt(phe)_2Cl_2].0.5C_2H_5OH.1.5H_2O$, $]Hg(phe)_2].9H_2O$, $[Zn(phe)_2].C_2H_5OH$
تم تشخيص هذه المركبات عن طريق تحليل العناصر المكونة لها وايجاد نسبتها بالإضافة إلى استعمال الطرق الفيزيائية الأتية: درجة الانصهار، الذائبية، التوصيل الكهربائي لمحاليلها، والأطياف تحت الحمراء والمرئية وفوق البنفسجية إلى الرنين المغناطيسي.

الكلمات المفتاحية: المعقدات، الأحماض الأمينية، التشخيص.

1. Introduction

proteins are built from Amino acid units [McMurry; 2004]. They are zwitterions that contain both basic amino and carboxylic acid groups. In addition, exists in aqueous solutions primarily in the form of a dipolar ion as shown in Figureure 1.

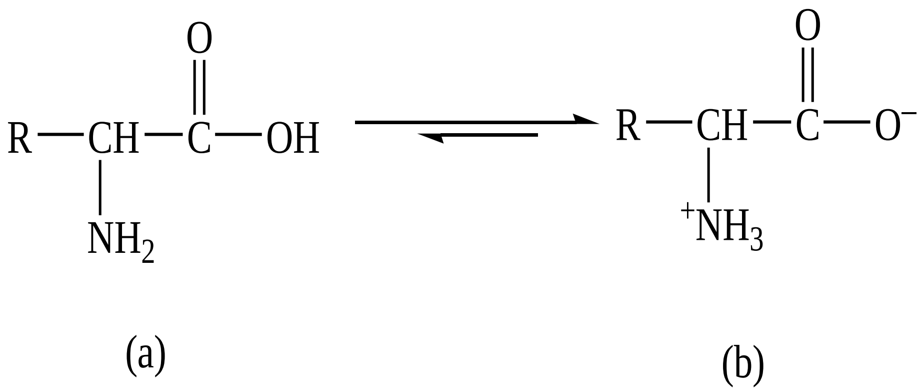

Figure 1 Amino acid: (a) uncharged form (b) zwitterionic form.

biomolecules such as amino acids are well known to serve as ligands for transition metals. For example, in many metalloproteins such as hemoglobin and vitamin B_{12}, the metal ions are bound to side chains of amino acid residues [Cotton; 1999]. Therefore, extensive work has been carried out in order to understand the structure of these biological systems. [Sabolovic and Rasmussen1995] did some calculations on Cu (II) complexes with some amino acid anions like L- alaninato and L-leucinato in addition to their N-alkylated derivatives such as N, N-diethyl-alaninato, N, N-dimethyl-valinato and N, N-dimethyl-isoleucinato and other, it was found that the bis-chelated Cu (II) compounds have distorted structures to avoid and suppress the intramolecular strain. More theoretical calculations were presented to explain why Cu(II) amino acid complexes are not planar in their crystal structures [Sabolović and Liedl; 1999].

Bukietyńska, *et al*; 2003 used potentiometric and spectroscopic techniques such as UV-visible and circular dichrois to study the complexation processes equilibrium of vanadium (III) with L-alanine and L-aspartic acid in aqueous solutions at various pH values. they were found that complexes of mononuclear amino acids with V(III) were coordinated by carboxylic groups formed in solution up to pH 4 for all L:M ratios of both systems. At pH 4.5-8, the predominant species present for the alanine system was ML_2 where alanine acted as a bidentated ligand (via N and O atoms) while at pH above 8.5, ML_2H^{2-} species were formed. However, the complexation of aspartic acid was more complicated due to the formation of dinuclear species with carboxylic and /or µ-oxo bridges.

Raman et al., 2013, explain that the synthesis, structural characterization, DNA interaction and in vitro antimicrobial and cytotoxic screening of copper (II) and zinc (II) Schiff-base complexes derived from a mino acid based pyrazolone derivatives were investigated. The coordinated Schiff-base complexes exhibited higher biological activity than the free ligand. Furthermore, the Schiff-base pyrral-L-histidine and its Co (II), Ni (II), Cu (II) and Zn (II) complexes were synthesized and characterized using various techniques. These data showed that the ligand is tridentate and the binding sites are azomethine nitrogen, imidazole nitrogen and oxygen of the carboxylate group. Moreover, the biological properties of the complexes were found to be higher than the free Schiff-base [Arish & Nair, 2012]

2. Experimental

2.1 Materials

The solvents used were analytical reagent grade.

Potassium bromide (KBr), glycine ($C_2H_5O_2N$), L-alanine ($C_3H_7O_2N$), copper (II) nitrate trihydrate [$Cu(NO_3)_2.3H_2O$] and potassium hexachloroplatinate (IV) [K_2PtCl_6] were purchased from BDH, Poole, United Kingdom.

L-phenylalanine ($C_9H_{11}O_2N$) were purchased from Park, United Kingdom.

Zinc (II) chloride ($ZnCl_2$) and sodium hydrogen carbonate ($NaHCO_3$) were purchased from S.D. Fine-Chem LTd, Mumbai.

Mercury (II) chloride ($HgCl_2$) was purchased from GCC, U.K.

2.2 Reactions of Metal Salts with Amino Acids:

The metal salts of Cu (II), Zn (II), Hg (II) and Pt (IV) were reacted with the sodium salts of amino acids: glycine (glyH), L-alanine (alaH), L-phenylalanine (pheH), All of the isolated complexes were dried at 40°C. They were obtained by the following procedures. A concentrated aqueous solution of the sodium salt of the glycine [glyH 0.030g, o.41mmol], L-alanine [alaH 0.17g, 1.9mmol], L-phenylalanine [pheH 0.067g, o.41mmol] and $NaHCO_3$ (o.34g, o.41mmol) in deionized water (10ml). The reaction mixture was refluxed at $70C^0$ for 5 hours and then filtered. The filtrate was evaporated to dryness under reduced pressure. The precipitate formed was washed well with ethanol, acetone and diethyl ether by centrifuge

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2.3 Physical Measurements

Melting points were determined on an electrothermal melting point apparatus and were uncorrected. The infrared absorption spectra were recorded on an FT-IR Tensor 27 spectrometer, Bruker spectrum 2000 over the range 4000-300 cm–1.

Conductivity measurements were carried out at 25°C using 1×10–3 M solutions in deionized water on a BC 3020 digital conductivity meter.

Electronic absorption spectra were recorded on a double beam spectrophotometer "Shimadzu Corporation" UV-2401 (PC), using 1×10–5 M solutions in dimetyl sulfoxide at 25°C.

The ^{1}H- and ^{13}C-NMR spectra were recorded on a 400 and 100 MHz, respectively, Bruker Avanced III spectrphotoometer. Deuterated dimethyl sulfoxide (DMSO-d6) was used as a solvent with tetramethylsilane (Me4Si) as an internal standard.

3. Results and discussion:

The mixing ratios 1:1 molar of the amino acids and $NaHCO_3$ in water was used to prepare the sodium salts of amino acids. The complexes were synthesized by using metal: ligand molar ratios of 1:1 or 1:2 with slight excess of the ligand in some cases. The reaction mixtures were either stirred at room temperature for about 3 hours until precipitates appeared, as in the case of the reactions of Hg (II), Zn (II), Cu (II) salts with phenylalaninate, Hg (II) with serinate and Pt (IV) with cysteinate, or the mixtures were refluxed at about 70ºC for about 5-7 hours. In the case of the reaction of Cu (II) with alaninate, a blue solid was formed upon reflux while its reaction with serinate gave a clear blue solution which was allowed to cool then treated with excess acetone to give a blue solid. In the remaining reactions, the filtrates were evaporated to dryness under reduced pressure. The products formed in all cases were washed well with ethanol, acetone and diethyl ether by centrifuge and dried at 40°C.

The isolated complexes are all stable. The Pt (IV) complexes are yellow, the Cu (II) complexes are blue while both the Zn (II) and Hg (II) complexes are white solids. They have high decomposition points (186-279°C) and were obtained in almost good yields as shown in (Table 1).

Table 1: Some physical properties of the isolated complexes.

Complex	Yield (%)	Color	Decomp. point (°C)
$Na\,[Pt(gly)Cl_4].0.5C_2H_5OH$	56	yellow	186
$[Cu(ala)_2].0.5C_2H_5OH$	83	blue	257
$[Pt(ala)_3Cl].C_2H_5OH.4H_2O$	52	yellow	215
$[Pt(phe)_2Cl_2].0.5C_2H_5OH.1.5H_2O$	50	yellow	239
$[Hg(phe)_2]$. H2O	91	white	204
$[Zn(phe)_2].C_2H_5OH$	60	white	279

They are insoluble in common organic solvents (Table 2) such as ethanol and acetone except $[Pt(phe)_2Cl_2].0.5C_2H_5OH.1.5H_2O$ which is soluble in acetone. Moreover, they are all insoluble in DMSO and DMF except the Pt (IV) complexes with glycinate, phenylalaninate which are soluble in DMSO. The Pt (IV) complexes with alaninate and phenylalaninate are soluble in DMF. Some complexes are soluble in water as shown in Table 2.

Table 2: Solubility of the complexes.

Compound	EtOH	H_2O	Acetone	DMSO	DMF
$Na\,[Pt(gly)Cl_4].0.5C_2H_5OH$	-	+	-	+	-
$[Cu(ala)_2].0.5C_2H_5OH$	-	+	-	-	-
$[Pt(ala)_3Cl].C_2H_5OH.4H_2O$	-	+	-	-	+

$[Pt(phe)_2Cl_2].0.5C_2H_5OH.1.5H_2O$	-	-	+	+	+
$[Hg(phe)_2]$. H2O	-	-	-	-	-
$[Zn(phe)_2].C_2H_5OH$	-	-	-	-	-

(+) Soluble, (±) Slightly soluble, (-) Insoluble

They were characterized by elemental analyses (Table 3).

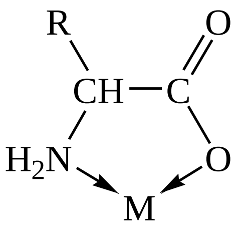
Table 3: Elemental analysis of the complexes.

Compound		**Analysis:**	**calculated (found) %**		
		C	**H**	**N**	**S**
Na $[Pt(gly)Cl_4].0.5C_2H_5OH$		7.884 (7.340)	1.544 (1.383)	3.065 (3.936)	
$[Cu(ala)_2].0.5C_2H_5OH$		31.996 (31.553)	5.750 (5.296)	10.663 (10.781)	
$[Pt(ala)_3Cl].C_2H_5OH.4H_2O$		21.554 (21.149)	5.263 (4.986)	6.857 (6.650)	
$[Pt(phe)_2Cl_2].0.5C_2H_5OH.1.5H_2O$		39.788 (40.028)	4.570 (4.474)	4.885 (5.574)	
$[Hg(phe)_2]$. H2O		39.523 (37.714)	4.055 (3.811)	5.122 (5.985)	
$[Zn(phe)_2].C_2H_5OH$		54.621 (54.564)	5.959 (6.123)	6.371 (6.132)	

The complexes $[Hg(phe)_2]$. H2O, $[Zn(phe)_2].C_2H_5OH$ and $[Cu(phe)_2].2.5H_2O$ are insoluble in common available solvents. Therefore, no conductivity measurements could be done for them. However, their insolubility might support their non-ionic nature. The complexes $[Cu(ala)_2].0.5C_2H_5OH$, $[Pt(phe)_2Cl_2].0.5C_2H_5OH.1.5H_2O$, $[Hg(ser)_2].9H_2O$ and $[Cu(ser)_2]$ behave as neutral non-electrolytes in water. The slight conductance observed may be due to some dissociation, decomposition or hydrolysis of these complexes. The complex Na $[Pt(cys)_2Cl_3].0.5C_2H_5OH.3H_2O$ showed a molar conductance of 91 ohm^{-1} cm^2 mol^{-1} which suggests that the complex is a 1:1 electrolyte. The complex $[Pt(ala)_3Cl].C_2H_5OH.4H_2O$ gave a high value of 368 ohm^{-1} cm^2 mol^{-1} which indicates that there are three to four ions and thus suggesting that it undergoes complete hydrolysis in solution. However, when its conductivity was carried out in DMF a value of 28.8 ohm^{-1} cm^2 mol^{-1} was obtained. This value supports the non-ionic neutral formula proposed for this complex since 1:1 electrolytes show a value of 65-90 ohm^{-1} cm^2 mol^{-1} DMF [Girolami, *et al;* 1999]

IR Spctra

The reported IR spectra of free amino acids which exist in the zwitterionic from, H_3N^+ CH(R) COO^-, exhibit a wide, broad band at about 3400 cm^{-1} in the region of the N–H stretching vibrations, ν(NH). In addition to another band at about 1600 cm^{-1}, assigned to the COO^- asymmetric stretching vibrations, ν(COO^-), containing a contribution of the δ($^+NH_3$) bending mode. However, the IR spectra of the reported coordinated amino acid anions in the complexes show the ν(NH) mode in the area 3100-3200 cm^{-1} and the ν(COO^-) in the region 1620-1690 cm^{-1}. These shifts in both stretching vibrations were reported to confirm the bidentate coordination of the amino acid anion to the metal through $–NH_2$ and $–COO^-$ groups forming a 5-membered chelate ring, as shown in below:



Similarly, the IR spectra of our complexes were studied along with their corresponding and related free amino acids. In the IR spectrum of $Na[Pt(gly)Cl_4].0.5C_2H_5OH$, confirms the bidentate coordination of the glycinate anion through the $–NH_2$ and $–COO^–$ groups to Pt(IV). The strong broadband at 3440 $cm^{–1}$ may be assigned to ν(O–H) of ethanol. The low frequency region shows three bands 506, 458 and 419 $cm^{–1}$ which may be assigned to ν(Pt–N) and ν(Pt–O). The IR spectrum of $[Cu(ala)_2].0.5C_2H_5OH$ shows a series of bands in the region of the O–H and N–H stretching vibrations at 3313(s), 3281(s), 3241(vs) and 3139(m) $cm^{–1}$. The first band may be assigned to the ν(O–H) of ethanol while the other three to ν(N–H) of bonded $–NH_2$ groups. Moreover, the IR spectrum of $[Pt(ala)_3Cl].C_2H_5OH.4H_2O$ is characterized by the presence of a very strong, very broad band centered at 3424 with peaks at 3225 and 3108 $cm^{–1}$. The first band may be assigned to ν(O–H) of ethanol and water of hydration and ν(N–H) of free $–NH_2$ groups. Free alanine shows a very strong band at 3446 $cm^{–1}$ with peaks at 3086 and 3016 $cm^{–1}$. the IR spectrum of $[Pt(phe)_2Cl_2].0.5C_2H_5OH.1.5H_2O$ exhibits a strong very broad band at 3450 $cm^{–1}$, which may be assigned to ν(O–H) of ethanol and water of hydration. The medium broad band at 3221 and the weak bands at 3097 and 3049 $cm^{–1}$, may be assigned to ν(N–H) of bonded $–NH_2$ groups. Moreover, the complex shows ν($COO^–$) at 1656 $cm^{–1}$, while the corresponding band of free phenylalanine is at 1626 $cm^{–1}$. The IR spectra of the bis-chelated complexes of phenyalaninate with Hg (II), Zn (II) and Cu (II) show some similarities. They have a medium to broad band in the range 3433-3460 $cm^{–1}$ which may be assigned to ν(O–H) of water of hydration or ethanol. They also show several medium to strong sharp bands in the range 3333-3020 $cm^{–1}$ which may be assigned to ν(N–H). Moreover, these complexes show strong to very strong broad band in the range 1613-1661 $cm^{–1}$, which may be assigned to ν($COO^–$) These results confirm the coordination of phenyalaninate through the $–NH_2$ and $–COO^–$ groups. It is to be mentioned that ν($COO^–$) of amino acid complexes are affected by coordination as well as intermolecular interactions [Nakamoto *et al.*, 2003].

Table 4: Electronic spectra of the complexes*

Complex	λ max (nm)	ε x$10^{–3}$ (1$mol^{–1}$ $cm^{–1}$)	Assignment
Na $[Pt(gly)Cl_4].0.5C_2H_5OH$ a	259br	6.58	LMCT
$[Cu(ala)_2].0.5C_2H_5OH$ b	284	2.43	LMCT
$[Pt(ala)_3Cl_2].C_2H_5OH.4H_2O$ c	254 265 272br	33.21 2.88 3.61	LMCT LMCT LMCT
$[Pt(phe)_2Cl_2].0.5C_2H_5OH.1.5H_2O$ a	339 341br	2.16 1.18	LMCT LMCT

The spectra of Pt (IV) complexes with glycinate, alaninate and cysteinate are characterized by the presence of an LMCT band, possibly from the chloride ions to eg*, in the range 254-259 nm while the alaninate complex shows other CT bands at 265 and 272 nm. However, the complexes with phenylalaninate and threoninate show similar broad LMCT bands at 339 and 341 nm which might indicate that both are from the same ligand which is possibly the bonded chloride to eg* level.

NMR Spectra

H^1-NMR spectra were very difficult analyze due to the presence of many – NH_2 groups from ligand and amino acid anion in addition to other functional groups such as hydroxyl, carboxylate, amide…. etc.

The C^{13}-NMR spectra of all complexes were carried out in deuterated water while the coordinated one is the anion of the amino acid. Furthermore, it has been reported that the coordination of amino acids to metal ions, like Pd (II) and Pt (II), also produces downfield shifts for the ligand carbon signals especially those of the carboxylate group ($COO^–$) and α–carbons. The extent of downfield shifts for $COO^–$ and α-C are 5-12 and 3-6 ppm,

respectively. Such values can be used to confirm the bonding mode of amino acids through the $–NH_2$ and $–COO^–$ groups.

4. Conclusion

In the present study, we managed to prepare some complexes of amino acids with Pt (IV),
Cu (II), Hg (II) and Zn (II). The reactions of metal salts of these ions namely, K_2PtCl_6, Cu $(NO_3)_2.3H_2O$, $HgCl_2$ and $ZnCl_2$ with amino acid anions resulted in the formation of the following types of complexes:

i. Mono-chelated complexes namely: Na $[Pt(gly)Cl_4].0.5C_2H_5OH$.

ii. Bis-chelated complexes namely: $[Cu(ala)_2].0.5C_2H_5OH$, $[Pt(phe)_2Cl_2].0.5C_2H_5OH.1.5H_2O$, $[Hg(phe)_2]. H2O$, $[Zn(phe)_2]. C_2H_5OH$, $[Cu(phe)_2].2.5H_2O$. The amino acid anions are found to coordinate as bidentate ligands through both $–NH_2$ and $–COO^-$ groups.

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