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Ternary cobalt complexes with amino acids: potentiometric study, modelization and solid-state investigation

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Abstract: A study in solution of new ternary complexes of cobalt (II) with the tetradentate ligand Schiff base (N,N'-bis (2-hydroxy acetophenone) ethylenediimine; H_2L) as primary ligand and the amino acid (histidine or tryptophan) as the secondary one has been realized by potentiometry. The stability constants of the complexes have been determined with the calculation program SIRKO. It has been found that the ternary complexes are more stable than the corresponding binary ones. The study has been completed by modelization of all the species found in solution by molecular mechanics with the program EMO (Energy of Molecule).

The complexes isolated in powdered form were characterized by elemental analysis, molar conductance, IR spectra, magnetic and electronic spectra. The spectral results support the binding of H_2L with two N and two O donor sites to cobalt ion and the binding of histidine or tryptophan by monodentate maner with O donor site, giving an octahedral geometry.

Magnetic and Electronic results show that the Cobalt (II) has been oxidized to Co(III) and has a low spin configuration.

Keyword : Cobalt, Amino acid, Potentiometric study, Molecular modeling, Synthesis.

Introduction

Because of their interesting physiological and pharmacological activities and their strong binding with metal ions, Schiff bases play a fundamental role in the formation of metal complexes that serve as models for biological systems[1, 2].

Cobalt complexes, besides existing in several stereochemical dispositions, interact with molecular oxygen ultimately oxidizing the complexes Co(II) to Co(III). The best known biological function of cobalt is its involvement in the coenzymes related to vitamin B_{12}[3, 4]. Also, certain cobalt (III) complexes react as anticancerous drugs[5]. In this way the chemistry of cobalt Schiff-base complexes has received great interest and it was shown that such ligands stabilize the Co(III) state[2]. It is noted that cobalt ion occurs in great variety of structural environments and in octahedral fields may give rise to either high- or low-spin complexes[3].

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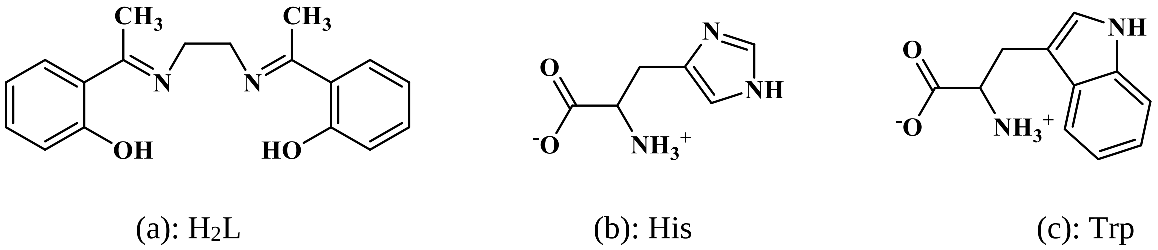
It is well established that ternary complexes play a decisive role in the activation of enzymes and also in the storage and transport of active substances through biological membranes. Ternary complexes containing an amino acid as a secondary ligand are of significance as they are potential models for enzyme-metal ion substrate complexes[6,7].

In the present paper we report the formation in solution of cobalt ternary complexes with H_2L: N,N'-bis (2-hydroxyacetophenone)ethylenediimine[2] as primary ligand and (His: histidine or Trp: tryptophan) as secondary one (Scheme. 1). In addition to the synthesis and characterizition of the same complexes.



Scheme 1. Structure of the ligands

Results and discussion

Solution state investigation and pH-metric titration curves

Representative titration curves obtained for the ternary system according to the sequence described in the experimental section are displayed in figures 1, 2. It is noted that the binary Co-H_2L curve shifts to lower pH compared to the H_2L curve. This is due to a release of protons on coordination.

The titration curve of Co-H_2L-His or Trp (Fig. 1, 2) shows that two species are formed, the first one begins to form at the pH range 3-6, and the second one around pH 7.

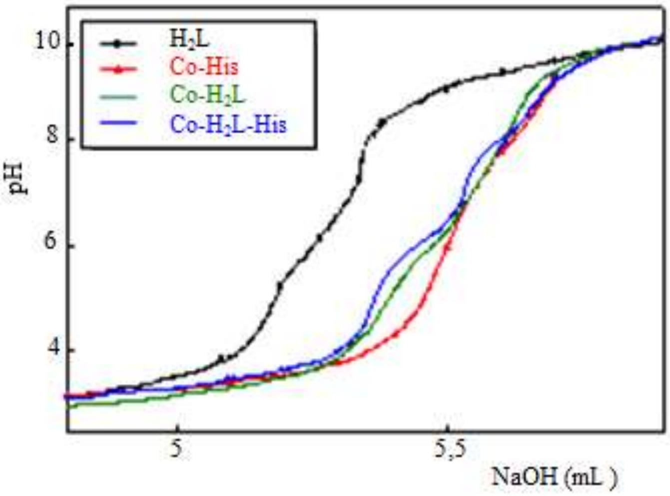


Figure 1. Titration curves of different species of Co-H_2L-His at 25.0 °C and ionic strength = 0.2 mol. L^{-1} (NaCl).

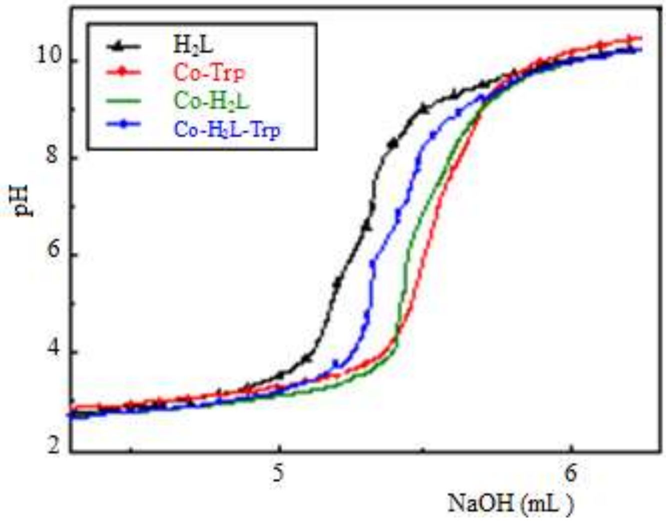


Figure 2. Titration curves of different species of Co-H_2L-Trp at 25.0 °C and ionic strength = 0.2 mol. L^{-1} (NaCl).

The comparison of the ternary Co-H_2L-His or Trp curve to the binary Co-H_2L and Co-His or Trp ones, shows a convergence with Co-H_2L curve and a divergence with Co-His or Trp curve, we can deduce that the two ligands do not coordinate simultaneously to the metal but there is a formation of Co-H_2L binary complex as primary stage then the coordination of histidine or tryptophan as secondary stage to form Co-H_2L-His or Trp ternary complex.

Formation constants

The stability constants β_{ha} of ternary complexes (Table 1) are defined by equation (1), where ML is Co-H_2L binary complex, H is proton and A is amino acid (His or Trp).

$$ML + h\,H^+ + a\,A^- \rightleftharpoons [ML\,(A)_a\,H_h]^{h-a} \qquad (1)$$

They show that the complex of Co-H_2L-Trp system is more stable than ones of Co-H_2L-His.

In order to compare the stability of the cobalt ternary complexes formed in relation to their corresponding binary, we have used the calculation method of the constant Δlog K[7] which corresponds to equation (2):

$$\text{Co-His/Trp} + \text{Co-}H_2L \rightleftharpoons \text{Co-}H_2L\text{-His/Trp} + \text{Co} \qquad (2)$$

This constant show the effect of the coordination of a second ligand different from the first on the stability of the complex formed.

The value of Δlog K of every ternary complex in relation to the binary MA (Table 1) shows that the ternary complexes formed are more stable than the corresponding binary and that they are favored[7-9]. The difference of stability may be due to the fact that the ternary complexes contain a bigger number of donor sites comparatively to the binary complexes, this give them a bigger stability. Since the complexes stability increases when the chelation increases.

Table 1. Formation constant values for the ternary complexes (water- ethanol 90 / 10 % vol./vol., T = 25.0 ± 0.1°C, µ = 0.2 mol. L^{-1} NaCl).

Complex	m	l	h	a	Species	log $ß_{h\,a}$	Δlog K
Co-H_2L-His	1	1	0	1	$[CoL(His)]^-$	8.11 (0.10)	
	1	1	0	2	$[CoL(His)_2]^{2-}$	14.29 (0.16)	2.02
Co-H_2L-Trp	1	1	0	1	$[CoL\ (Trp)]^-$	9.71 (0.11)	
	1	1	0	2	$[CoL(Trp)_2]^{2-}$	17.28 (0.20)	5.06

m, l, h and a are respectively the metal, ligand, proton and amino acid stoichiometry

Species distribution curves

The species distribution curves of Co-H_2L-A systems (Fig. 3, 4) showed that the $[CoL(A)]^-$ species begins to form in the range of pH 2.7-3.5. Its curve shows a maximum formation of 75% for a pH value of 7.5.

The $[Co\ L(A)_2]^{2-}$ species begins to form at around pH=6 and its maximum formation occurs at pH=10.

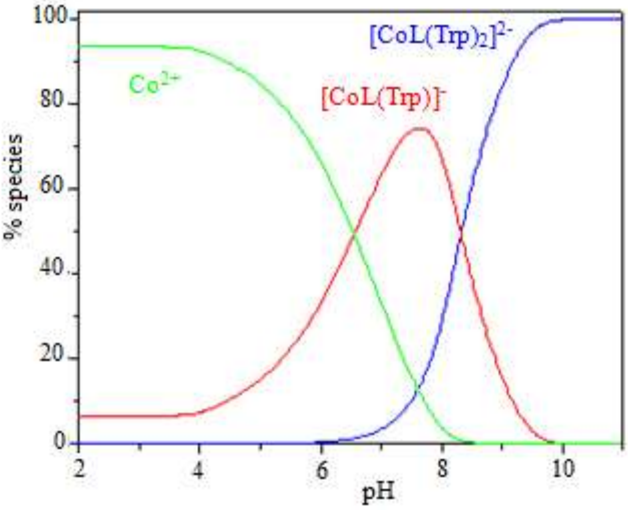


Figure 3. Species distribution curves of Co-H_2L-Trp as a function of pH, $[Co^{2+}] = 10^{-3}$ M

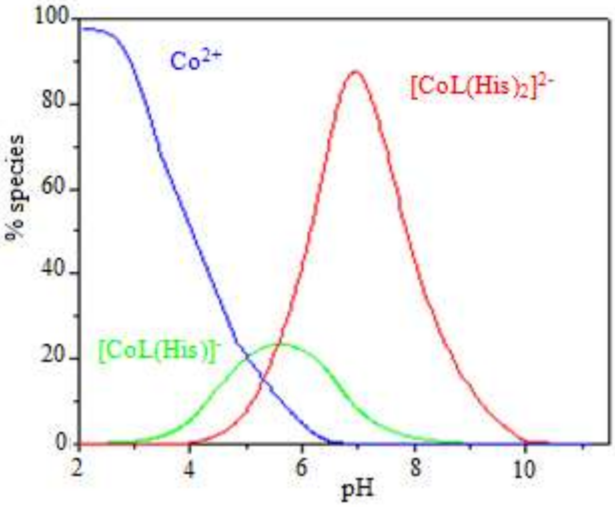


Figure 4. Species distribution curves of Co-H_2L-His as a function of pH, $[Co^{2+}] = 10^{-3}$ M

Molecular modelling

Binary complexes

Histidine and tryptophan bind the cobalt ion giving several coordination mode (monodentate or bidentate), in addition to a tridentate coordination probable with histidine[10-12].

Only coordination 4 and 6 around the central atom has been considered. The values of calculated minimized steric energy of the binary complexes show that the stability order of Co-His and Co-Trp complexes is classified in the following order: coordination 6 > coordination 4 (Table 2).

For coordination 4, the stability of Co-His (1:1) is in the following order: tridentate (NNO) > bidentate (NO) > monodentate (O) > monodentate (N) and the sequence for Co-Trp (1:1) complex is: bidentate (NO) > monodentate (O) > monodentate (N). Whereas, for coordination 6, the stability of Co-His (1:2) is as follows: tridentate (NNO) > bidentate (NO).

The more stable complexes are formed when histidine binds the metal in the tridentate maner and tryptophan in bidentate one.

Table 2. Steric energy of Co-His and Co-Trp complexes (kJ/mol)

Species	Coordination mode	Coordination 4	Coordination 6
Co-His (1:1)	tridentate (NNO)	6.24	-8.98
	bidentate (NO)	12.36	8.92
	monodentate (O)	71.06	36.67
	monodentate (N)	223.06	127.05
Co-His (1:2)	tridentate (NNO)	-	-25.16
	bidentate (NO)	7.57	5.09
Co-Trp (1:1)	bidentate (NO)	12.67	-2.71
	monodentate (O)	16.88	1.88
	monodentate (N)	32.25	17.03
Co-Trp (1:2)	bidentate (NO)	523.47	80.64

Histidine complexes give the lowest steric energy which is in agreement with the potentiometric results (Co-His: log ß$_{1\,1}$=6.09 and E(kJ/mol)= -8.98; Co-Trp: log ß$_{1\,1}$=4.65 and E(kJ/mol)= -2.71).

Based on molecular modeling, the optimised geometry found for all complexes is octahedral. The optimised geometry of the Co-H_2L complex (Fig. 5) is distorted octahedral where the two water molecules are of trans-configuration.

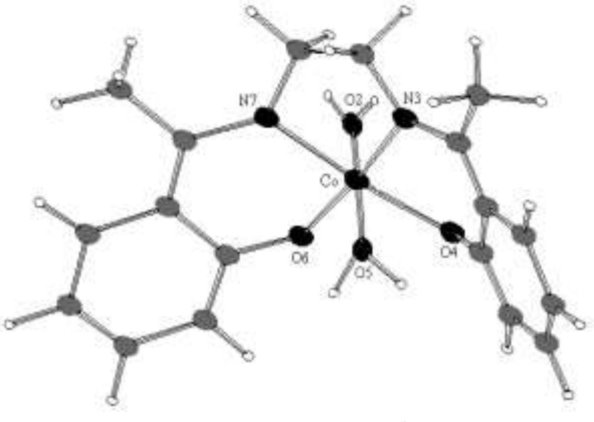


Figure 5. Optimized geometry of the Co-H_2L complex

Ternary complexes

The values of steric energy for the ternary complexes (Table 3) obtained when coordination 6 around the central atom is considered, the ligand H_2L coordinates the metal through N and O atoms in the tetradentate form and histidine and tryptophan coordinate with it in monodentate manner and show that the tryptophan complexes are more stable than those of histidine. This is in accordance with the values of their stability constants obtained by potentiometry (Co-H_2L-His: log $ß_{0\,1}$=8.11 and E(kJ/mol)= 578.96; Co- H_2L-Trp: log $ß_{0\,1}$=9.71 and E(kJ/mol)= 437.62).

The tryptophan complexes are more stable than those of histidine because the electron-donor effect of the indole group in tryptophan is more important than that of imidazole group of histidine (the indole group reinforces the negative charge of oxygen which gives a more stable complex).

Table 3. Steric energies in kJ/mol of the Co-H_2L-(His or Trp) ternary complexes

Complex	Steric Energy
Co-H_2L-His	
1 1 1(monodentate)	578.96
1 1 2(monodentate)	621.91
Co-H_2L-Trp	
1 1 1(monodentate)	437.62
1 1 2(monodentate)	607

The optimized geometry of the ternary complexes (Fig. 6) is a distorted octahedral; where H_2L surrounds the cobalt atom and the two other axial sites are occupied by an amino acid and a water molecule in (111) molar ratio and by two amino acids in (112) molar ratio.

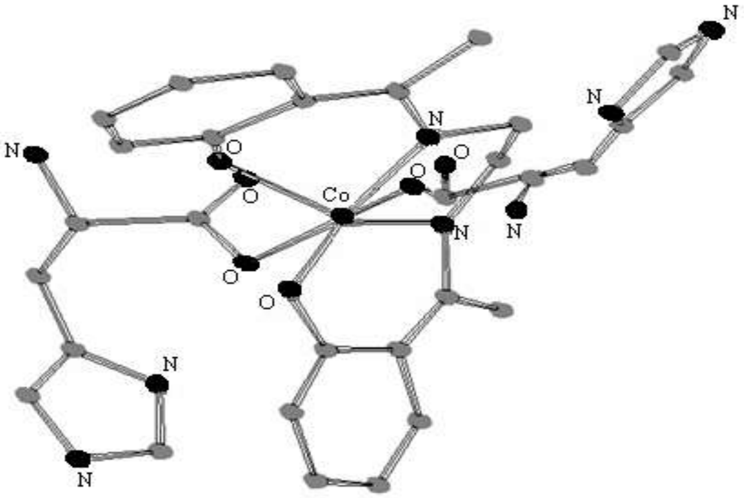


Figure 6. Optimized geometry of the Co-H_2L-His (112) complex

Characterization of solid ternary complexes

The analysis of complexes are consistent with the stoechiometry proposed and are summarized in Table 4. The conductivity data of the complexes (10^{-3} M) in DMF indicate that they are non-electrolytes [13].

Table 4. Physical properties and analytical data of the cobalt ternary complexes

Complex Formula	Formula Weight	Colour	Decomp. Temp.(°C)	Found (Calculated) %				Λ (DMF) ($\Omega^{-1}.cm^{2}.mol^{-1}$)
				C	H	N	Co	
[CoL(His)(H_2O)]	524.93	Light	235	54.80	5.73	12.98	11.60	70
Co C_{24} H_{28} N_5 O_5		Brown		(54.86)	(5.33)	(13.33)	(11.23)	
[CoL(Trp)(H_2O)]	573.93	Light	238	60.21	5.80	9.76	10.68	63
Co C_{29} H_{31} N_4 O_5		Green		(60.63)	(5.40)	(9.75)	(10.27)	

Infrared Spectra

The IR spectra of the ternary complexes show bands around 3300 and 3100 cm^{-1} which may be assigned to the simultaneous presence of coordinated water and NH_3^+ of amino acids. The OH vibrational band, appearing at about 3050 cm^{-1} for H_2L ligand, disappears completely in the complexes. This proves that this ligand is bonded after deprotonation to the metal by the oxygen of the phenolic group.

In the complexes, the vibration bands of C=N and C-N in H_2L appear at a lower frequency compared to those observed in the ligand.

The vibration band of C-NH_3^+ which is around 1300 cm^{-1} on the IR spectra of histidine and tryptophane does not show any shift on the complexes spectra. This proves that the group NH_3^+ is not implicated in the complexation. The spacing between the bands $(COO^-)_{sym}$ and $(COO^-)_{asym}$ on the complexes spectra confirms that the amino acids are coordinated to the metal via their COO^- group[14].

Metal-ligand band is further supported by new frequencies occurring in the 600-400 cm^{-1} range and which have been tentatively assigned to the vibration of Co-O and Co-N bonds, respectively[15]. The FT-IR results of ligands and their complexes are reported in Table 5.

Table 5. Main absorbance bands in FT-IR spectra and their assignments for the ligands and their complexes

Compounds	N $(OH)_{H2O}$ Coord.	ν (OH)	ν (C=N)	ν (C-N)	ν (C-O)	ν $(NH_3)^+$	ν (COO^-) asym	ν (COO^-) sym	ν Co-N	ν Co-O
H_2L	-	3054	1611	1292	1065	-	-	-	-	-
His	-	-	-	-	-	3127	1568	1416	-	-
Trp	-	-	-	-	-	3078	1666	1414	-	-
Co-H_2L- His	3356	-	1542	1235	1092	3103	1639	1389	611	520
Co-H_2L-Trp	3405	-	1585	1233	1098	3070	1550	1438	575	415

^{1}H NMR Spectra

The presence of H_2L ligand in the ternary complexes is confirmed by the appearance of hydrogen aromatic ring peaks in the range 6.3-7.3 ppm in their ^{1}H-NMR DMSO-d^6 solution spectra. The resonance line due to the H_2L phenolic proton is absent for the complexes. This shows that this ligand is bonded in the deprotonated form. This is consistent with the conclusion drawn from the infrared spectra.

The protons signals of –C=CH- and N=CH- cyclic groups for histidine are observed at 7.5 and 8.5 ppm respectively[12] (Fig. 7).

The proton signals of C_6H_4 and -C=CH- groups for tryptophan are present around 7.2 ppm and at 8 ppm respectively (the spectrum is not shown here).

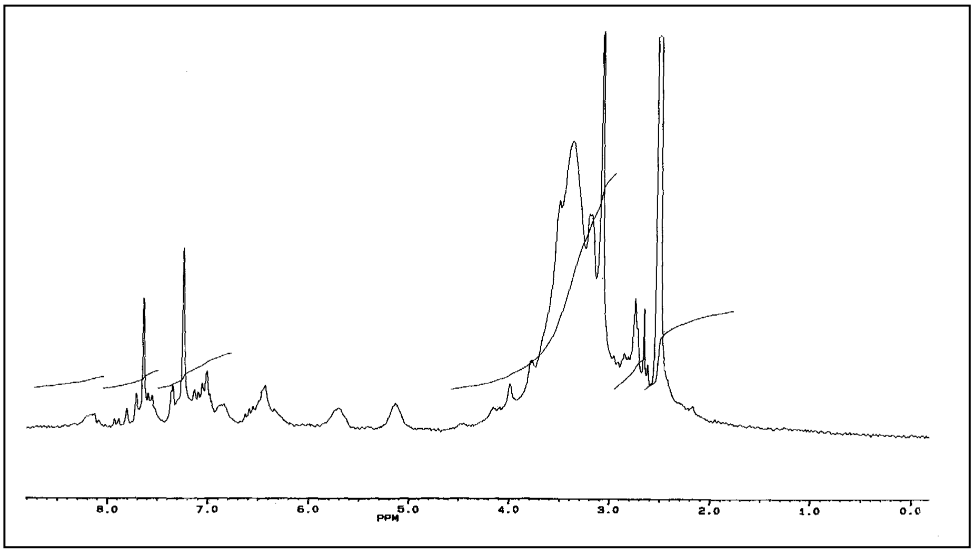


Figure 7. 1H-NMR Spectrum of Co-H2L-His complex in DMSO-d6.

Electronic Spectra

The values of magnetic susceptibility for the ternary cobalt complexes reveal that they are diamagnetic. Also, they indicate the oxidation of cobalt(II) to cobalt(III) complexes[16].

The electronic spectra of the cobalt(III) complexes recorded in DMF solution display three characteristic absorption of high intensity in the near-UV region at 26300-38000 cm^{-1}, which are due to the intra-ligand transitions (n → π* and π → π*).

The band observed in the region 17094-17636 cm^{-1} is assigned to the d-d transition ($^1A_{1g} \rightarrow {}^1T_{1g}$ (ν_1)) and the shoulder around 24000 cm^{-1} to the ($^1A_{1g} \rightarrow {}^1T_{2g}$ (ν_2)) transition. These results suggest an octahedral configuration for cobalt(III) chelates[17]. The ligand field parameters have also been calculated using equations suggested from the Tanabe-Sugano diagram[18]. The spectroscopic results are given in Table 6.

By examining the trend of the 10Dq values obtained, it may be seen that the energy of the octahedral field in the ternary cobalt(III) complexes with tryptophan is higher than the histidine one. The diminution of the β parameter from histidine to tryptophan is attributed to the increase of covalent character of the metal-ligand bonds[19].

Table 6. Electronic spectral and ligand field parameters data of the cobalt ternary complexes

Complex	Electronic Transitions ν (cm^{-1})^{a}	ε^{b}	Assignments	10Dq (cm^{1})	B (cm^{-1})	β
Co-H$_2$L-His	17094	23	$^1A_{1g} \rightarrow {}^1T_{1g}$	19130	480	0.45
	23809	120	$^1A_{1g} \rightarrow {}^1T_{2g}$			
	26385	200	$n \rightarrow \pi^*$			
	33333	400	$\pi \rightarrow \pi^*$			
	38759	1640	$\pi \rightarrow \pi^*$			
Co-H$_2$L-Trp	17636	48	$^1A_{1g} \rightarrow {}^1T_{1g}$	19853	474	0.44
	24390	130	$^1A_{1g} \rightarrow {}^1T_{2g}$			
	26315	3142	$n \rightarrow \pi^*$			
	34129	19200	$\pi \rightarrow \pi^*$			
	37735	27200	$\pi \rightarrow \pi^*$			

^{a}Wave number in cm^{-1}; ^{b}Absorption molar coefficient in $l.mol^{-1}.cm^{-1}$

On the basis of the above results, the following structure (Fig. 8) may be proposed for the ternary cobalt(III) complexes, where the environment of the metal ion is octahedral in which H_2L is bonded in tetradentate manner and, the other sites are being occupied by one amino acid and H_2O.

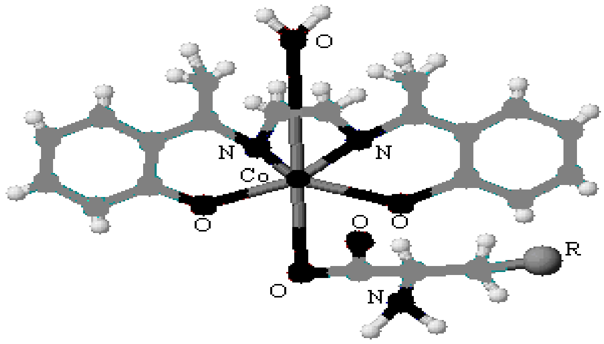
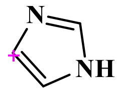


Figure 8. Structural scheme for the isolated ternary complexes

R:



For Histidine

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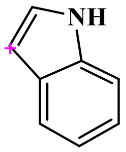

For Tryptophan

Conclusion

In solution; the Co-H$_2$L-His or Trp ternary complexes are formed by the coordination of histidine or tryptophan to the Co-H$_2$L binary complex, the ternary complexes formed are more stable than the corresponding binary, the complex of Co-H$_2$L-Trp system is more stable than the complex of Co-H$_2$L-His system and the optimised geometry found for the complexes is octahedral.

At solid state; the ternary complexes isolated are monomeric, non- electrolytes and H_2L is bonded to the metal center in tetradentate manner and the other sites are being occupied by one amino acid and H_2O.

Experimental section

All chemical reagents and solvent used were Fluka products and were used without purification.

Physical measurements

Potentiometric titrations were performed in the pH (concentration) mode, using a Tacussel PHN 81 pH meter equipped with a glass combined electrode and calibrated with standard buffer solutions. The conductivity values were determined in DMSO (10^{-3} mol/L) at 25°C using a Tacussel CD 810 conductivitymeter previously calibrated with a solution of KCl (10^{-2} and 10^{-1} mol/L) at the same temperature. Elemental analyses were carried out at the central service of analysis, CNRS, Vernaison (France). Decomposition points were measured using a Buchi 512 digital melting point apparatus. FTIR spectra were recorded from 4000-400 cm^{-1} on a FTS-7 Biorad Fourier transform spectrometer and KBr pellets were employed throughout. The electronic spectra of the complexes were registered from 1000-200 nm range on a 1601-SHIMADZU UV-visible spectrophometer connected to a computer. The ^{1}H-NMR spectra were obtained with a Brucker AM 300 spectrophotometer in 0-10 ppm range, (Université Claude Bernard, Lyon, France) using TMS as internal reference.

pH-metric titrations

pH-metric titrations of different Co-H_2L or His or Trp and Co-H_2L-His or Trp mixtures in 1:1 and 1:1:1 molar ratios respectively (10^{-3} mol/L for each) were performed at 25.0 ± 0.1°C and 0.2 mol/L (NaCl) ionic strength. Standardized carbonate-free NaOH solutions (0.1 mol/L) were used. In all cases the total volume was kept constant at 50 mL. The complexes solutions titrated are: Co-H_2L, Co-His, Co-Trp, Co-H_2L-His and Co-H_2L-Trp.

Determination of the formation constants

The protonation constants of the ligands were determined under the same experimental conditions as for the determination of the stability constants of the binary and ternary complexes. The calculations were performed using the computer program SIRKO[20-22]. The model selected was that which gave the best statistical fit and proved chemically consistent with the titration data[23].

Determination of the steric energy

The minimized steric energy of binary and ternary complexes was obtained using the computer program EMO[24] (Energy of Molecule).

Preparation of complexes

An aqueous solution (10 mL) containing 10 mmol of the metal salt $CoCl_2.6H_2O$ (2.37 g) was added to 50 mL of an ethanolic solution containing 10 mmol (2.96 g) of the ligand H_2L. To this mixture was added slowly with stirring an aqueous solution (50 mL) containing 20 mmol (3.10 g) of histidine or 20 mmol (4.08 g) tryptophan. Since the solubility of the free acid H_2L and the amino acid histidine or tryptophan is very low, a few drops of 0.1 mol/L NaOH solutions were added until the pH of the amino acid solutions attained the value 9. After stirring the mixture for twenty four hours, the precipitates formed were filtered, washed several times with acetonitrile and dried in vacuum over P_4O_{10}.

The Co-H_2L-His and Co-H_2L-Trp complexes are fairly soluble in water, DMF and DMSO and practically in all organic solvents.

References

1- S. Djebbar-Sid, O. Benali-Baitich, J. P. Deloume, J. Mol. Struct., **2001**, *569*, 121-128.
2- L. Mishra, R. P. Krishna, K. Pandey, Spectrochim. Acta Part A: Mol. Biomol. Spectr., **2008**, *70*, 79-85.
3- F. A. Cotton, G. Wilkinson, C. A. Murillo, M. Bochman, Advanced Inorganic Chemistry, 6th Ed. Wiley: New York, **1992**, pp 829.
4- A. Adkhis, S. Djebbar, O. Benali-Baitich, A. Kadri, M. A. Khan, G. Bouet, Synth. React. Inorg. Met.-Oeg.Chem., **2003**, *33*, 35-50.
5- D. C. Ware, W. A. Denny, G. R. Clark, Acta. Cryst., **1997**, *53*, 1058-1059.
6- H. Hamrit, S. Djebbar-Sid, O. Benali-Baitich, M. A. Khan, G. Bouet, Synth. React. Inorg. Met-Org. Chem., **2000**, *30*, 1835-1848.
7- A. Rahman, L. Novel, Trans. Met. Chem, **2006**, *31*, 943-950.
8- F. B. Ansari, M. Farooqui, S. H. Quadri, Rzayan J. Chem., **2010**, *3*, 359-362.
9- S. Belaid, S. Djebbar, O. Benali-Baitich, M. Khan, G. Bouet, C. R. Chim., **2007**, *10*,568-572.
10- G. Ibrahim, G. Bouet, I. H. Hall, M. A. Khan, J. Inorg. Biochem., **2000**, *81*, 29-34.
11- B. Blaive, G. Legsai, R. Lai, J. Mol. Struct, **1995**, *354*, 245-250.
12- E. Farkas, E. A. Enyedy, G. Micera, E. Garribba, Polyhedron, **2000**, *19*, 1727-1736.
13- E. Farkas, H. Csoka, G. Micera, A. Dessi, J. Inorg. Biochem., **1997**, *65*, 281-286.
14- A. Adkhis, O. Benali-Baitich, M. A. Khan, G. Bouet, Synh. React. Inorg. Met.-Org. Chem., **2000**, *30*, 1849-1858.
15- R. J. Sundberg, R. B. Martin, Chem. Rev., **1974**, *74*, 471-490.
16- X. J. Victor, J. D. Ranford, Inorg. Chim. Acta, **2000**, *304*, 38-44.
17- W. J. Geary, Coord. Chem. Rev., **1971**, *7*, 81-122.
18- L. J. Bellamy, The Infrared Spectra of Complex Molecules, 3rd Ed., J. Wiley: New York, **1975**, pp 226.
19- N.V. Thakkar, J. R. Thakkar, Synh. React. Inorg. Met.-Org. Chem., **2000**, *30*, 1871-1887.
20- R. Pradhan, S. Mukhopadhyay, D. C. Bera, C. Simonnet, F. Sécheresse, R. Bhattacharyya, Inorg. Chem. Com., **1999**, *2*, 495-497.
21- R. L. De, K. Samanta, K. Maiti, E. Keller, Inorg. Chim. Acta, **2001**, *316*, 113-116.
22- A. B. P. Lever, Inorganic Electronic Spectroscopy, 2nd Ed., Elsevier: Amstedam, **1984**, pp 480, 508, 566.
23. A. Terbouche, S. Djebbar, O. Benali-baitich, M. Khan and G. Bouet, Revue Roumaine de Chimie, 2008, *53*, 101-106.
24- N. Tidjani-Rahmouni, S. Djebbar-Sid, H. Hamrit, O. Benali-Baitich, J. Soc. Alger. Chim., **2001**, *11*, 121-130.