



Studies of Some Mixed ligand Ternary Metal Complexes of N Acetyl Cysteine with Zinc (II) and Nickel (II) Metal ions

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Abstract

Mixed metal complexes of N acetyl cysteine as a primary ligand and some amino acids such as alanine, methionine, tryptophan, aspartic acid and glutamic acid used as secondary ligands with metal ions zinc (II) and nickel (II) were synthesized. The prepared ternary complexes were characterized by elemental analysis, thermal analysis, molar conductivity measurement and IR, UV-Visible spectral studies. The spectral studies indicated octahedral geometry for nickel (II) complexes and a tetrahedral geometry was proposed for zinc (II) complexes.

Keywords: N acetyl cysteine, amino acids, mixed metal complexes.

Introduction

Studies on mixed ligand complexes of amino acids and their derivatives are of immense biological interest because such complexes show interesting properties like antibacterial, antifungal, anticancer etc¹⁻⁶. Mixed ligand complex formation occurs widely in systems where metal ions and two or more different ligands are present⁷. Way back in 1971 it was reported by Hallman et.al⁸ that at the physiological pH of 7.4 about 98% of copper (II) in the simulated plasma solution is present as a mixed complex of copper-histidine-cysteine, while as substantial percentage of zinc (II) was also found as a zinc-cysteine-histidine complex.

Mixed ligand complexes also play important role in the catalytic centers of metalloenzymes and metal activated enzymes, thus investigation and the interaction between various transition metals and amino acids and their ternary complexes can be used as metalloenzyme models⁹⁻¹⁰. Considering the importance of the mixed ligand complexes of amino acids this paper reports the synthesis and characterization of ternary complexes of zinc (II) and nickel (II) with N-acetyl cysteine (Nac) as a primary ligand and various secondary ligands viz, alanine (Ala), methionine (Met), tryptophan (Trp), aspartic acid (Asp) and glutamic acid (Glu)

Material and Methods

N-acetyl cysteine, alanine, methionine, tryptophan, aspartic acid and glutamic acid used were obtained from Merck India. Zinc and nickel nitrate was purchase from BDH. All other chemicals used were analytical grade (BDH) products. The optical absorption spectrum for different mixed-ligand ternary metal complexes over the range $(2-3) \times 10^{-4}$ mol dm⁻³ in DMSO was recorded on a Shimadzu UV-160 spectrophotometer. The

spectra's of these solutions in one cm quartz cells was recorded in the wave length region of 220-800nm. Thermogravimetric analysis of the prepared complexes was carried out using Perkin Elmer STA 6000 analyser. The infrared spectra in the solid state, and the C, H, and N contents of the isolated complexes were determined at IITR Roorkee (Uttarakhand).

Synthesis of Mixed-ligand complexes: The ternary metal complexes have been prepared by using the following general method. A solution of N-acetyl cysteine (5 mmol) in 10ml distilled water was added to a solution of 10ml of secondary ligand i.e methionine, alanine, tryptophan, aspartic acid and glutamic acid (5 mmol) in distilled water. To this ligand solution a 10ml (5 mmol) of aqueous solution of metal (Zn²⁺ and Ni²⁺) nitrate was then added slowly with continuous stirring. The pH of the reaction mixture was adjusted so that the precipitation of the complexes takes place by means of an aqueous solution of 0.01 M KOH. Constant stirring for about 4 to 5 hours at 50°C yielded solid precipitate of ternary metal complexes. The precipitate was filtered and washed with cold distilled water and dried out.

Results and Discussion

The color, conductivity data, elemental analysis data along with some other physical properties of the synthesized complexes are listed in table 1. From the elemental analysis data the tentative molar ratio of the mixed ligand complexes viz Metal: L₁: L₂ comes out to be 1:1: 1, where L₁= primary ligand and L₂= secondary ligand respectively. The conductivity of the complexes in DMSO (table 1) shows that they have non-electrolytic character¹¹. The solubility of the complexes has been found to be almost negligible in some well know solvents though they show partially solubility in DMF and DMSO.

Infra red Spectra: The i.r. frequencies of the mixed metal complexes are given in table 2. In the free form N acetyl cysteine which is the primary ligand shows prominent bands in the 1592-1655 cm^{-1} and 1370-1430 cm^{-1} regions which are attributable to the asymmetric and symmetric stretching vibration of the carboxylate group. These bands are shown, however in the 1560-1570 cm^{-1} and 1378-1382 cm^{-1} regions for complexes which indicate participation of this group in the coordinate bond formation with the metal ion. Furthermore free N acetyl cysteine displays a band in the 2548 cm^{-1} region due to SH stretching, this band disappears in the spectra of the complexes which indicates coordination of the thiolate S with the metal ion. The ir spectra of amino acids (secondary ligands) in the free form exhibit broad band's at 3040 and 2960 cm^{-1} due to asymmetric and symmetric vibrations of the amino group (NH_2), these bands however are shifted to higher regions in the range 3177-3140 cm^{-1} and 3050-3025 cm^{-1} , respectively, in the spectra of metal complexes, suggesting coordination of the amino group through nitrogen with the metal ion. Free amino acids also display bands in the 1585-1690 cm^{-1} region due to $\nu_{\text{asymmetric}}(\text{COO}^-)$ vibrations and in the 1390-1420 cm^{-1} region due to $\nu_{\text{symmetric}}(\text{COO}^-)$ vibrations. These bands are however shifted to lower regions in the 1565-1578 cm^{-1} range and 1375-1384 cm^{-1} range in the spectra of complexes indicating the coordination of the carboxylate group via oxygen with the metal ion¹². The presence of hydrated water molecule for the complexes (4, 5) is indicated by the presence of a broad band in the high frequency region of 3450-3550 cm^{-1} , while for the rest of complexes no such band is obtained¹².

Thermal Analysis: Investigations based on the thermal analysis conducted for the prepared complexes revealed further information about their structural features. For the complexes (4, 5) a two step TG curve is obtained, first a weight loss step in the 65-118 $^{\circ}\text{C}$ range is observed, this is consistent with the loss of one non coordinated water molecule. Then the second step at a higher temperature range of 260-280 $^{\circ}\text{C}$ is observed corresponding to the breakdown and decomposition of the complexes. The thermogravimetric analysis for the complexes (1-3) showed the absence of water of hydration as abrupt weight loss was observed at high temperatures in the 260-280 $^{\circ}\text{C}$ which corresponds to the decomposition of the ternary metal complexes.

Electronic spectra: The electronic spectral details of the prepared mixed metal complexes are given in table 3. For the complexes (1-3) a high coefficient band in the 270-300 nm region is observed, which is followed by another band at 410-475 nm, the first band is accredited as a charge-transfer band and is mainly due to ligand to metal charge transfer (L-M CT transitions)¹³, while as the second band can be ascribed to an intraligand transition of the amino acid moieties. However for the Ni^{2+} complexes (4, 5) in addition to the intraligand and L-M CT transitions additional distinct band in the 577-620 nm region and a weak shoulder band in 368-390 nm region are also observed. The bands were assigned to ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}(\text{F})$ and ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}(\text{P})$ transitions respectively, which correspond to an octahedral structure for Ni^{2+} complexes¹⁴.

Table-1
Analytical and physical data of the mixed metal complexes

Complex	Color	m.p $^{\circ}\text{C}$ (Decomp.)	Found (calcd.) (%)				$\lambda_{\text{M}} \text{ Ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$
			C	H	N	S	
[Zn(Nac)(Met)] 1	Dull white	260-270	31.78 (31.83)	5.28 (5.34)	7.44 (7.41)	16.61 (16.97)	11
[Zn(Nac)(Ala)] 2	Dull white	262-270	45.26 (45.37)	4.97 (5.08)	8.87 (8.82)	10.80 (10.09)	11
[Zn(Nac)(Trp)] 3	grayish white	265-268	44.77 (44.40)	4.41 (4.89)	9.45 (9.70)	7.45 (7.40)	12
[Ni(Nac)(Asp)].H ₂ O 4	Pale bluish green	260-265	29.13 (29.08)	4.31 (4.34)	7.63 (7.53)	8.93 (8.62)	12
[Ni(Nac)(Glu)].H ₂ O 5	Pale bluish green	265-260	40.67 (31.19)	4.25 (4.71)	7.65 (7.27)	8.11 (8.33)	12

Table-2
Most important infrared bands (cm^{-1}) of the various synthesized ternary metal complexes

Complex	$\nu(\text{OH})$	$\nu_{\text{asym}}(\text{NH}_2)$	$\nu_{\text{sym}}(\text{NH}_2)$	$\nu_{\text{asym}}(\text{COO})$	$\nu_{\text{sym}}(\text{COO})$	$\nu(\text{SH})$	$\nu(\text{M-S})$	$\nu(\text{M-N})$
[Zn(Nac)(Met)] 1	—	3174	3032	1565	1380	—	410	543
[Zn(Nac)(Ala)] 2	—	3177	3050	1569	1378	—	414	547
[Zn(Nac)(Trp)] 3	—	3159	3035	1566	1375	—	410	565
[Ni(Nac)(Asp)].H ₂ O 4	3500	3144	3025	1675	1382	—	404	532
[Ni(Nac)(Glu)].H ₂ O 5	3497	3140	3029	1578	1383	—	404	539

Table-3
Electronic spectral data of the mixed ligand complexes

Complex		$\lambda_{\max}(\text{nm})$	$\epsilon_{\max}(\text{mol}^{-1}\text{cm}^{-1}\text{L})$	Band assignment
[Zn(Nac)(Met)]	1	288 425	2565.61 78.93	ligand to metal charge transfer intraligand
[Zn(Nac)(Ala)]	2	297 448	2759.72 86.47	ligand to metal charge transfer intraligand
[Zn(Nac)(Trp)]	3	277 457	2658.74 79.99	ligand to metal charge transfer intraligand
[Ni(Nac)(Asp)].H ₂ O	4	276 598 379	2454.68 32.56 54.54	ligand to metal charge transfer ${}^3A_{2g} \rightarrow {}^3T_{1g}(F)$ ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$
[Ni(Nac)(Glu)].H ₂ O	5	290 605 380	2422.08 39.18 43.76	ligand to metal charge transfer ${}^3A_{2g} \rightarrow {}^3T_{1g}(F)$ ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$

Conclusion

It can be concluded on the basis of the above conducted studies that N acetyl cysteine acts as a bidentate ligand and coordinates with the metal ion via oxygen and sulfur atoms of carboxylate and thiol groups respectively, while as the amino acid moieties utilize the nitrogen atom of the amino group and oxygen atom of carboxylate group for coordinate bond formation. In view of the foregoing discussions we have suggested the following probable structure for the synthesized metal complexes.

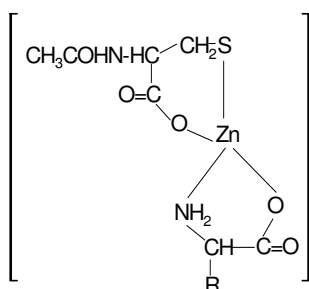


Figure-1

Suggested structure for [Zn (N-acetyl cysteine)(Aminoacid)] ternary complex

Where R= CH₃ for alanine, CH₂CH₂SCH₃ for methionine, for tryptophan.

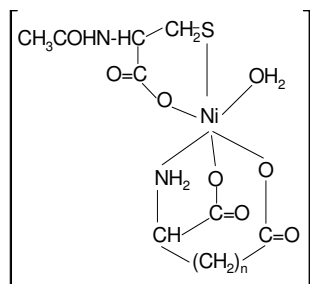
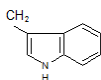


Figure-2

Suggested structure for [Ni (N-acetyl cysteine) ((aspartic or glutamic acid)).H₂O] ternary complex, such that n = 1 for aspartic acid and n = 2 for glutamic acid, respectively

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