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Publisher *Taylor & Francis*

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Spectroscopy Letters

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597299>

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To cite this Article Asso, M. and Panossian, R.(1985) 'Copper and Nickel Interactions with Aspartate Containing Tetrapeptide', *Spectroscopy Letters*, 18: 10, 837 — 842

To link to this Article: DOI: 10.1080/00387018508062314

URL: <http://dx.doi.org/10.1080/00387018508062314>

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COPPER AND NICKEL INTERACTIONS WITH ASPARTATE CONTAINING
TETRAPEPTIDE .

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INTRODUCTION

Interactions between proteins or peptides and transition metal play an important role in biological systems (1-5) . An approach to the study of metal ion binding is the chemical synthesis of a metallo-model site and analogues thereof and the comparison of their metal ion binding characteristics (6,7) . Among the peptide models interacting with different metals we are engaged with the tetrapeptide segment Ac-Asp-Val-Asp-Ala-OH (Ac-DVDA-OH) which can be considered as a simplified model of calcium binding sites of several proteins (8,9) . Previous study in solution , argued to a high stability constant of metal-Ac-DVDA-OH complexes at neutral pH (10) . NMR results suggest the chelation of calcium or rare earth cations (Pr^{3+}) through the two carboxylate groups of aspartyl residues (11) . The main purpose of the present paper is to give a contribution to the study of interactions between copper and nickel and the tetrapeptide model by Infrared spectroscopy .

EXPERIMENTAL

Materials

The tetrapeptide has been synthesized after the solid phase method, purified through Sephadex G15 column and by HPLC procedure using Waters Associates model 204 instrumentation (7) . Copper and nickel complexes were obtained by dropwise and very slow addition of degased 5 M sodium hydroxyde solution into 1:1 molar ratio aqueous methanolic solution containing CuCl_2 or NiCl_2 and Ac-DVDA-OH yield a precipitate when the pH stabilizes at 6-7 . The solid phase is then isolated , thoroughly washed with water and methanol and dried (P_2O_5) over vacuum .

Analysis

IR spectra were recorded between 4000 and 200 cm^{-1} on a 225 Perkin Elmer spectrometer using KI pellets .

Copper and nickel analysis are made on a Instrumentation Laboratory 251 spectrophotometer . Quantitative amino acid analyses have been done on a Biotronik CC 7000 analyser .

Ac-DVDA-Cu(II) copper ; found : 0.125 , calculated : 0.1211
aspartic acid ; found : 0.440 , calculated : 0.4384
alanine ; found : 0.169 , calculated : 0.1673
valine ; found : 0.186 , calculated : 0.1904

Ac-DVDA-Ni(II) nickel ; found : 0.116 , calculated : 0.1143
aspartic acid ; found : 0.448 , calculated : 0.4418
alanine ; found : 0.170 , calculated : 0.1686
valine ; found : 0.190 , calculated : 0.1918

RESULTS AND DISCUSSION

The position and attribution of the main vibration bands of the ligand and its metal complexes are given in table 1 . With

regard to the ligand, the peptide groups are characterized by absorptions at 3219 cm^{-1} $\nu(\text{NH})$, 3087 cm^{-1} (harmonic), 1641 cm^{-1} (amide I), 1554 cm^{-1} (amide II), 1240 cm^{-1} (amide III) and 705 cm^{-1} $\gamma(\text{NH})$ (12-14). The characteristic absorptions of the carboxylic group are found at $2700\text{--}2400\text{ cm}^{-1}$ (harmonics, combinations), at 1708 cm^{-1} $\nu(\text{C=O})$, 1393 and 1228 cm^{-1} ($\nu(\text{CO}) + \delta(\text{OH})$) 908 cm^{-1} $\gamma(\text{OH})$. These various carboxylic absorptions are relatively weak indicating the presence of protonated carboxylic group. The carboxylate absorptions are found at 1535 cm^{-1} $\nu_{\text{as}}(\text{COO}^-)$ and 1402 cm^{-1} $\nu_{\text{s}}(\text{COO}^-)$. The other absorptions listed in table 1 are associated with the hydrocarbo-skeleton.

The spectra of the copper and nickel complexes are very similar their comparison with the spectra of the free ligand leads to the following observations :

- the absorptions of the peptide group are not affected by coordination, suggesting that these groups do not play a significant part in the complexation ;
- the carboxylic infrared bands of Ac-DVDA-OH disappear upon complexation, while new bands characteristic of coordinated carboxylate group appear. A band, observed at 1582 cm^{-1} for the copper complex and at 1592 cm^{-1} for the nickel complex is attributed to $\nu_{\text{as}}(\text{COO}^-)$ vibration. A strong band at 1405 cm^{-1} for Ac-DVDA-Cu(II) and at 1415 cm^{-1} for Ac-DVDA-Ni(II) attributable to coordinated $\nu_{\text{s}}(\text{COO}^-)$ vibration replaced the medium absorption $\nu_{\text{s}}(\text{COOH})$ in the spectra ligand ;
- the peaks associated with the hydrocarbon skeleton are unchanged upon complexation,
- no significant spectral perturbation of the vibrations associated with peptidic -NH was observed.

This result, combined with those deduced from nmr line width is consistent with the Ac-DVDA-OH being coordinated to the copper or nickel cation through carboxylate group of the two aspartyl side chains. It ensues, that contrary to C terminal

TABLE I
Waves numbers and attributions of IR vibrations of Ac-DVDA-OH and its copper and nickel complexes .

Ac-DVDA-OH		Complexes		Attributions			
		Cu		Ni			
cm ⁻¹	I	cm ⁻¹	I	cm ⁻¹	I	mode	group
3279	s	3280	s			$\nu(\text{NH})$	(amide)
3087	w	3080	w	3080		harmonic	(amide)
2966	w	2955	w	2955	w	$\nu(\text{CH}), (\text{CH}_2), (\text{CH}_3)$	(sq. H, C)
2938	w	2940	w	2940	sh		
2877	w	2880	w	2880	sh		
2700-2400 w, b						harmonic combinations	(COOH)
1720	sh					$\nu(\text{C=O})$	(COOH)
1708	s						
1660	sh						
1641	vs	1624	vs	1650	vs	$\nu(\text{C=O})$	(amide)
		1582	s	1592	s	$\nu_{\text{as}}(\text{COO}^-)$	(COO ⁻) coord.
1554	s	1554	s	1542	s	$\delta(\text{NH}) + \nu(\text{CN})$	(amide)
1535	sh					$\nu_{\text{as}}(\text{COO}^-)$	(COOK)
1450	w	1454	w	1450	sh	$\delta_{\text{a}} + \delta_{\text{s}}(\text{CH}_3)$	(sq. H, C)
1402	m	1405	s	1415	s	$\nu_{\text{s}}(\text{COO}^-)$	(COOK) and (COO ⁻) coord.
1393	m					$\delta_{\text{OH}} + \nu_{\text{CO}}$	(COOH)
1370	m	1370	m	1370	m	$\delta_{\text{s}}(\text{CH}_3)$	(sq. H, C)
1310	w	1325	w	1320	m		(sq. H, C)
1290	w	1280	w	1285	w		
1240	m	1235	m	1232	m	$\nu(\text{CN}) + \delta(\text{NH})$	(amide)
1228	m					$\nu(\text{CO}) + \delta(\text{OH})$	(COOH)
1195	w	1194	w	1190	w		(sq. H, C)
1185	w	1180	sh				
1150	w	1155	w	1152	w		
1118	w	1115	w	1110	w		
1050	w	1050	w	1055	w		
965	w						(COOH)
958	w	955	w	960	w		
930	w	930	w	930	w		
908	w, b					$\gamma(\text{OH})$	
852	w	850	w	855	w		(sq. H, C)
768	w	770	w	765	w		
705	m, b	700	m, b			$\gamma(\text{NH})$	(amide)

b: broad , vs: very strong , s: strong , m: medium , w: weak , sh: shoulder

short peptides complexed by these transition elements (15-17) , when at least two aspartyl residus in an Asp-X-Asp type sequence are present , peptidic nitrogen seem to be not implicated in the metal coordination .

Infrared spectra of the 1:1 Ni(II) and Cu(II) solid state complexes of Ac-DVDA-OH havethe same specificity of coordination A preferential structure where Cu(II) or Ni(II) is bound simultaneously with carboxylate groun of the two aspartyl residues was proposed by a chelating mode .

ACKNOWLEDGMENTS

The authors express their gratitude to the Centre National de la Recherche Scientifique for the necessary research facilities and Dr. M Guiliano for helpful discussion .

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Received: 07/15/85

Accepted: 08/20/85