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N-Acetyl-DL-Tryptophanatometal(II) (Co(II), Ni(II) and Zn(II)) Complexes and their Amine Adducts

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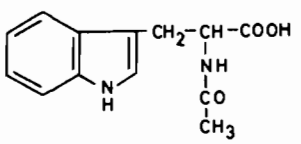
First row transition metal(II) complexes of N-acetyl-DL-tryptophan of the type $M(Actrp)_2 \cdot xH_2O$ (M = Co(II), Zn(II) and x = 2; M = Ni(II) and x = 3; Actrp = N-acetyl-DL-tryptophanato ion) and their amine adducts of the type $M(Actrp)_2B_2$ (B = py, 3-pic and 4-pic) were prepared and investigated by means of magnetic measurements, electronic and infrared spectroscopy. The diamagnetic zinc(II) complexes were also investigated in solution by means of ^1H n.m.r. spectroscopy. All the experimental results on solid complexes suggest that the carboxylate is coordinated to the metal atom. The effect of the amines in axial position results in a weakening of the strength of the amino acid in-plane coordination. ^1H n.m.r. spectra of the diamagnetic zinc(II) complexes indicate that the same type of amino acid coordination also exists in solution.

Introduction

Our studies on the interactions of potentially tetradentate N-protected amino acids, such as N-acetyl- and N-benzoyl-derivatives of glycine and alanine [1, 2] with transition metal ions have shown that the amino acid coordination invariably occurs toward the carboxylate group. As in a previous paper on the proton dissociation constants and the stability constants of Cu(II) complexes of tyrosine and tryptophan derivatives [3] it was suggested that the peptide-like nitrogen atom is involved in the metal coordination, as the copper(II) ion seems to promote the ionization of the peptide-like proton, in this work we investigate the interactions of the N-acetyl-DL-tryptophan (ActrpH) with metal ions which are found to favour peptide coordination like Co(II) and Ni(II), or not, like Zn(II) [4].



This work is also encouraged by the great interest in the biochemistry of cobalt(II) and zinc(II) [5] and, as has recently been suggested, by the fact that nickel(II) may also have a biological role in animals [6].

Experimental

Preparation of the Complexes

$M(Actrp)_2 \cdot xH_2O$ (M = Co(II), Zn(II) and x = 2; M = Ni(II) and x = 3) complexes were prepared by adding a methanolic solution containing metal(II) perchlorate hexahydrate (2 mmol) to a methanolic solution containing N-acetyl-DL-tryptophan (4 mmol), neutralized with a stoichiometric amount of potassium hydroxide in methanol, filtering of the potassium perchlorate precipitated, concentrating the solution and adding diethyl ether.

The $Co(Actrp)_2 \cdot 2H_2O$ was also obtained by reaction of freshly prepared stoichiometric amounts of cobalt(II) hydroxide and N-acetyl-DL-tryptophan in water and by concentrating the solution completely. All the adducts were prepared by adding an excess of amine to a $M(Actrp)_2 \cdot xH_2O$ solution in ethanol and cooling at 4–5 °C. In some cases diethyl ether was added to prompt the precipitation of the compounds.

Physical Measurements

The infrared spectra were recorded with a Perkin-Elmer 180 spectrophotometer in KBr pellets in the 4000–250 cm^{-1} spectral range. The electronic spectra of the solid compounds were recorded as mull transmission spectra with a Shimadzu MPS 50L spectrophotometer. The room-temperature magnetic moments were measured with the Gouy method, using $Ni(en)_3S_2O_3$ as calibrant and correcting for diamagnetism with the appropriate Pascal constants.

TABLE I. Analyses and Magnetic Moments of the Solid Complexes.[a]

	Color	C%		H%		N%		μ_{eff} B.M.
		calcd	found	calcd	found	calcd	found	
$Co(Actrp)_2 \cdot 2H_2O$	amethyst	53.32	53.31	5.17	5.19	9.58	9.42	4.65
$Co(Actrp)_2(py)_2$	pink	61.08	60.53	5.13	5.16	11.88	11.53	4.43
$Co(Actrp)_2(3\text{-pic})_2$	pink	62.02	61.98	5.48	5.62	11.43	11.61	4.65
$Co(Actrp)_2(4\text{-pic})_2$	pink	62.02	62.12	5.48	5.60	11.43	11.39	4.56
$Ni(Actrp)_2 \cdot 3H_2O$	pale green	51.74	51.82	5.35	5.39	9.29	8.93	3.24
$Ni(Actrp)_2(py)_2$	pale green	61.10	60.83	5.13	5.60	11.89	12.32	2.94
$Ni(Actrp)_2(3\text{-pic})_2$	pale green	62.03	61.18	5.49	6.00	11.43	11.11	3.19
$Ni(Actrp)_2(4\text{-pic})_2$	pale green	62.03	61.70	5.49	5.81	11.43	11.02	2.97
$Zn(Actrp)_2 \cdot 2H_2O$	white	52.73	52.79	5.11	5.13	9.47	9.21	dia.
$Zn(Actrp)_2(py)_2$	white	60.53	60.31	5.08	5.24	11.78	11.58	dia.
$Zn(Actrp)_2(3\text{-pic})_2$	white	61.48	60.60	5.44	5.39	11.33	10.59	dia.
$Zn(Actrp)_2(4\text{-pic})_2$	white	61.48	60.91	5.44	5.31	11.33	10.56	dia.

[a]Abbreviations: Actrp = N-acetyl-DL-tryptophanate ions; py = pyridine; 3-(or 4-)pic = 3-(or 4-)methylpyridine.

TABLE II. Room-temperature Electronic Spectra and Ligand Field Parameters (cm^{-1}) of the Solid Complexes.

		ν_1	ν_3		Dq	B	β^a	ν_2 calcd		
$Co(Actrp)_2 \cdot 2H_2O$	solid	8000	18180sh	21050	920	950	0.98	17170		
$Co(Actrp)_2(py)_2$	solid	8700	19800	21050sh	985	820	0.84	18550		
$Co(Actrp)_2(3\text{-pic})_2$	solid	8420	19610	20920sh	960	820	0.84	17980		
$Co(Actrp)_2(4\text{-pic})_2$	solid	8600	20080	21190	980	840	0.87	18360		
		ν_1	ν_2	ν_3	Dq	β	β^a	Dq^b	B^b	$\beta^{a,b}$
$Ni(Actrp)_2 \cdot 3H_2O$[c]	solid	8510	14810	25000	850	850	0.80	790	980	0.93
$Ni(Actrp)_2(py)_2$	solid	9300	15670	26670	930	960	0.91	960	910	0.86
$Ni(Actrp)_2(3\text{-pic})_2$	solid	9390	15800	25970sh	940	910	0.86	980	825	0.78
$Ni(Actrp)_2(4\text{-pic})_2$	solid	9550	15750	26320sh	955	890	0.84	970	870	0.82

[a]$\beta = B/B_o$; the values of the Racah parameter B_o for the free ions are 971(Co(II)) and 1056(Ni(II)) (21). [b]Calculated from ν_2 and ν_3. [c]A band appearing at 13250 cm^{-1} may be assigned to a forbidden singlet transition.

^1H n.m.r. spectra were obtained with a Jeolco model C-60HL spectrometer for solution in CD_3OD or $CDCl_3$ using TMS as internal standard.

Analyses

Nitrogen, carbon and hydrogen were analyzed by Mr. Giuseppe Pistoni using a Perkin-Elmer 240 Elemental Analyser.

Results and Discussion

The prepared compounds, their analyses and the abbreviated names of the amino acid and of the amines are reported in Table I. All the hydrate compounds are stable in air and soluble in methanol, while the amine adducts, which are strongly hygroscopic and rapidly lose the amines, are also soluble in apolar solvents, such as chloroform.

Room-temperature Electronic Spectra and Magnetic Moments of the Solid Compounds

The electronic spectral data and ligand field parameters of the complexes are listed in Table II. The coordination geometry of the cobalt(II) and nickel(II) complexes are interpreted on the basis of their electronic and magnetic properties. In fact the room-temperature electronic spectra of all the complexes are typical of hexacoordinated cobalt(II) and nickel(II). The observed spin-allowed transitions in the complexes have energies which agree with the secular equation for octahedral metal(II) ions. The energies

TABLE III. More Relevant I.r. Bands (cm^{-1}) of the Solid Complexes.

	$\nu(NH)_i$	$\nu(NH)_p$	$\nu(OCO)$	$\nu(OCO)_{sym}$	$\Delta\nu$
ActrpH	3387 vs 3335m	2970mb	1710vs	1235vs	475
d-ActrpD	2525vs 2475m	2230ms	1700vs	1233s	467
ActrpNa	3400vs	3280sb	1588vs	1398vs	190
d-ActrpNa	2530vs 2435sb	2400s 2360ms	1585vs	1400vs	185
$Co(Actrp)_2 \cdot 2H_2O$	3400ms	3298m	1614vsb	1415vs	199
$Co(Actrp)_2(py)_2$	3400m	3275ms	1630vs	1403vs	227
$Co(Actrp)_2(3\text{-pic})_2$	3400m	3280ms	1635vs	1402vs	233
$Co(Actrp)_2(4\text{-pic})_2$	3400m	3285ms	1613vs	1405vs	208
$Ni(Actrp)_2 \cdot 3H_2O$	3402s	3300sh	1612vsb	1412vs	200
$Ni(Actrp)_2(py)_2$	3400ms	3285m	1638vs	1408vs	230
$Ni(Actrp)_2(3\text{-pic})_2$	3405m	3278ms	1632vs	1401vs	231
$Ni(Actrp)_2(4\text{-pic})_2$	3405m	3285ms	1615vs	1404vs	211
$Zn(Actrp)_2 \cdot 2H_2O$	3400ms	3295mb	1600vsb	1415vs	185
$Zn(Actrp)_2(py)_2$	3402m	3288ms	1615vs	1391vs	224
$Zn(Actrp)_2(3\text{-pic})_2$	3390sh	3275ms	1610vs	1388vs	222
$Zn(Actrp)_2(4\text{-pic})_2$	3400sh	3280ms	1610vsb	1430, 1385vs	

represent the next electronic transitions from the $^4T_{1g}(F)$ ground state to the next higher excited state, $^4T_{2g}(F)(\nu_1)$, $^4A_{2g}(F)(\nu_2)$ and $^4T_{1g}(P)(\nu_3)$ for the cobalt(II) and from the $^3A_{2g}(F)$ ground state to $^3T_{2g}(F)(\nu_1)$, $^3T_{1g}(F)(\nu_2)$ and $^3T_{1g}(P)(\nu_3)$ higher excited states for the nickel(II).

The presence of amines in the adducts suggests that their symmetry is not pure O_h, but that tetragonal distortion leads to a symmetry closer to D_{4h}. This causes some modifications of the electronic spectra from that expected for O_h symmetry.

The effect of the tetragonal distortion in our complexes is evidentiated by the broadness of their low energy band and by the splitting of the band at 18000–21000 cm^{-1} in the cobalt(II) complexes. In particular the B values, calculated with ν_1(=10 Dq), ν_2 and ν_3 bands greater than those calculated with only the sharp ν_2 and ν_3 transitions in the nickel(II) complexes, confirm that some distortion from O_h symmetry is present [7].

The Dq and B values of the hydrate bis(N-acetyl-DL-tryptophanato) metal(II) complexes closely resemble those found for the MO_6 chromophore [8, 9] indicating a ligand field strength of the N-acetyl-DL-tryptophan similar to that of water, while those of the adducts, intermediate between the values found for MO_6 and MN_6 chromophores [8, 9], suggest the probable presence of MO_4N_2 chromophore, the amines being coordinated. This and the fact that the shape and positions of the d–d bands of the complexes are practically identical to those found for the corresponding Co(II) and Ni(II) complexes of the N-acetyl-L-, α-N-benzoyl-DL- and benzoyl-β-alanine [10–12], N-acetyl-DL-valine [1] and N-acetyl-DL-leucine [13], for which it was suggested that the carboxylate group only is coordinated to the metal atoms, strongly indicate that in the N-acetyl-DL-tryptophanate complexes the carboxylate is coordinated to the metal atom.

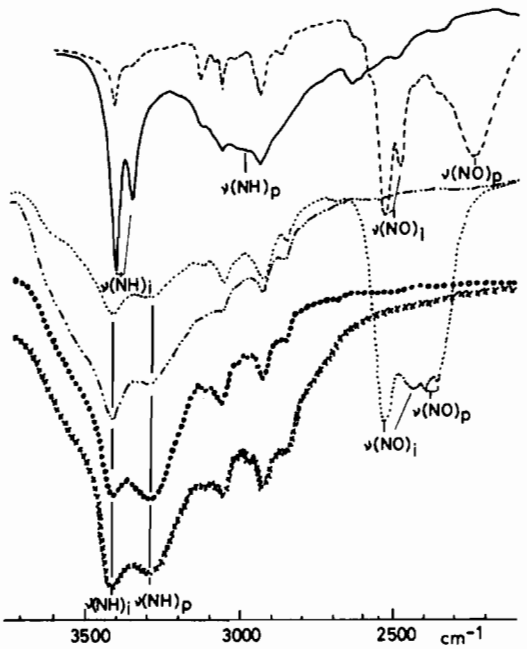


Fig. 1. Infrared spectra of the N-acetyl-DL-tryptophan (———) and its deuteriated analogue (-------), the sodium salt (—·—·—) and its deuteriated analogue (.....), the aquo complexes (oooooo) and the amine adducts (XXXX).

The ligand field strength order of the adducts further agrees with the basicity order of the amines

TABLE IV. ^{1}H N.m.r. Results for the Ligands and the Zinc(II) Complexes.

		δ/p.p.m.						c.p.s.
		CH_3CO	CH_3py	CH_2	CHCOO	NH_p	NH_i	$J^{HH}_{HN_pH}$
ActrpH	CD_3OD	1.90		3.25	4.75			
ActrpNa	CD_3OD	1.89		3.33	4.68			
$Zn(Actrp)_2 \cdot 2H_2O$	CD_3OD	1.86		3.34	4.78			
$Zn(Actrp)_2(py)_2$	$CDCl_3$	1.85		3.33	5.00	6.21	9.59	8.25
$Zn(Actrp)_2(3\text{-pic})_2$	$CDCl_3$	1.90	2.35	3.36	4.91	6.33	9.39	8.25
$Zn(Actrp)_2(4\text{-pic})_2$	$CDCl_3$	1.83	2.36	3.33	4.91	6.40	9.19	8.15

[14] for the nickel(II) complexes, while it reverses it for the cobalt(II) complexes.

The room-temperature magnetic moments (Table I) also support the proposed stereochemistries corresponding to possible tetragonal symmetries [15].

Infrared Spectra

One of the most important features of the i.r. spectra (Table III) is found in the 3700–2200 cm^{-1} region (Fig. 1). In fact in this region there appear the N–H stretching vibrations of the indole (3387vs, 3335m cm^{-1} $\nu(NH)_i$) and of the peptide (2970mb cm^{-1} $\nu(NH)_p$) groups of the amino acid, which are shifted in the deuterated amino acid at 2525vs, 2475m and at 2230ms cm^{-1}, respectively. The assignment of these bands is confirmed by the fact that, although the ligand does not appear in the zwitterionic form, the NH of the peptide group is involved in intermolecular hydrogen bonding, while the NH of the indole group is not involved with hydrogen bonds, as is shown in the crystal structure of the N-acetyl-L-tryptophan [16].

In the sodium salt, as the hydrogen bonding of the peptide group is removed, the $\nu(NH)_p$ is shifted at higher energies (3280sb cm^{-1}), while the $\nu(NH)_i$ is stationary (3400vs cm^{-1}) with respect to the ligand. These bands shift in the deuteriated analogue at 2530vs, 2435sb, 2400s, 2360s cm^{-1}. As on complex formation these bands do not significantly change in shape and position with respect to those of the sodium salt, we may exclude the coordination of these groups to the metal atom.

From the study of the ketonic band, which appears at 1620vs, 1635sh and 1630–50 (generally as a shoulder) cm^{-1} in the amino acid, its sodium salt and the complexes, respectively, we may exclude the coordination of this group to the metal atom. This is consistent with the fact that the oxygen (peptide) atom is only weakly basic [4].

Therefore the carboxylate group remains the only group of the ligand available for metal-binding, in fair agreement with the conclusion obtained from the electronic spectra. Trends in positions of and separation between antisymmetric and symmetric carboxylate stretching bands provide the most useful observation for assigning its coordination type [1, 17, 18]. The reported $\Delta\nu$ ($\nu(OCO)_{as} - \nu(OCO)_{sym}$) value for the sodium salt (190 cm^{-1}) may be assumed to typify N-acetyl-DL-tryptophanate ion. The $\Delta\nu$ values of the aquo complexes, being similar to that of the sodium salt, suggest 'symmetrical' bidentate coordination of the carboxylate group. In fact when the C–O bonds remain equivalent, no difference in the CO_2 stretching frequencies is expected in the complexes with respect to free carboxylate ion.

For the adducts the $\Delta\nu$ values (208–233 cm^{-1}), greater than those of the ionic ligand and of the aquo complexes, may be attributed to the presence of unequivalent C–O bonds. This supports an 'asymmetric' bidentate coordination of the carboxylate group, as a consequence of the *trans* effect of the additional pyridines in axial position, which lowers the metal–amino acid in-plane coordination strength.

The first data of the crystal structure of a $Cu(Actrp)_2(py)_2 \cdot 2H_2O$ complex, in which the amino acid appears to coordinate to the copper(II) atom toward the carboxylate group [19], confirm the conclusions obtained from the electronic and infrared spectra.

Our results are also in agreement with the crystal structure of another tryptophanato derivative complex, the glycyl-L-tryptophanatocopper(II)trihydrate [20], in which the indole group appears uncoordinated. But in contrast to what is found in our complexes, in the glycyl-L-tryptophanatocopper-(II) trihydrate [20] the peptide nitrogen is coordinated to the metal. This apparent difference of behavior between the N-acetyl-DL-tryptophan and the glycyl-L-tryptophan is justified, as in the complex formation the nitrogen (peptide) atom of the glycyl-L-tryptophan may be shared by two five-membered chelate rings. This fulfils one of the geometrical conditions recognized as governing the participation of a nitrogen (peptide) atom in multidentate chelation [4].

^1H N.m.r. Spectra

The ^1H n.m.r. spectra (Table IV) of the diamagnetic zinc(II) complexes support symmetrical structures of the complexes also in solution, as they are very simple and strictly similar to those of the amino acid and its sodium salt. They further suggest that the carboxylate group is coordinated to the metal atom also in solution, as the αCHCOO group is more affected by coordination than the other groups. The coupling between the NH_p and the αCH (the J of which is not reported, as the bands are not resolved) groups also indicate that the NH_p group is not involved either in the metal(II) coordination or in hydrogen bonding in deuterochloroform solution.

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