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SYNTHESIS, CHARACTERIZATION AND THERMAL DECOMPOSITION OF *p*-IODO-PHENYLALANINE COMPLEXES OF COBALT OR NICKEL

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Abstract

New complexes of the non-natural amino acid (*p*-iodo-phenylalanine) with divalent cobalt and nickel ions have been synthesized. The composition of the complexes is $[M(IC_6H_4CH_2CHNH_2COO)_2]\cdot 2.5H_2O$ (*M*=Co, Ni) and the crystal structure belongs to orthorhombic system. Infrared spectra indicate the nature of bonding in the complex. The first stage in the thermal decomposition process of the complex shows the presence of crystal water. The thermal decomposition process of cobalt complex differs from that of nickel. The intermediate and final residues in the thermal decomposition process have been analyzed to check the pyrolysis reactions. Thermal analysis indicates that the iodine atom of the ligand may coordinate to the metal ion in the lattice.

Keywords: complex of amino acid with cobalt or nickel, crystal structure, infrared spectra, synthesis, thermal decomposition

Introduction

The complexes of many natural amino acids with various metal ions have been synthesized and very well studied. Now, the number of non-natural amino acids exceeds that of natural amino acids and various kinds of non-natural amino acids have widely been used in some fields, such as biology, biochemistry and medicine [1–4]. Therefore, to understand how various non-natural amino acids and metal ions can form complexes will be very interesting for applications of non-natural amino acids in biology and medicine.

The synthesis process for the complexes of some non-natural amino acids and metal ions differs from that for complex of natural amino acid due to special proper-

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ties of non-natural amino acids with different substitution group. For example, some non-natural amino acids are not soluble in aqueous media, hence, their complexes cannot be synthesized by a general method [5]. So, a few investigations on the complexes of non-natural acids and metal ions have been reported. Here, we will report the synthesis, crystal structure, infrared spectra and thermal decomposition of the complexes of *p*-iodo-phenylalanine with the Co^{2+} and Ni^{2+} ions. To check the pyrolysis reactions, the intermediates and final residue in the thermal decomposition process of the complex of cobalt have also been analyzed.

Experimental

All the chemicals used in synthesis are analytical grade. *p*-Iodo-phenylalanine is a dextrotatory stereoisomer from Shanghai ACI Biotech Co. Ltd. First, the aqueous solutions of cobalt and nickel nitrate were prepared and the concentrations were determined by EDTA titration. The concentration of the metal ions was about 0.17 M. *p*-Iodo-phenylalanine (1.00 mg) was dissolved in the sodium hydroxide solution (about $3.4\cdot10^{-2}$ M, 100 ml) and the concentration of the amino acid was about $3.4\cdot10^{-2}$ M. Then, the volume of the solution of cobalt or nickel nitrate required to give slightly more than the stoichiometric amount of the metal ion was added dropwise to the aqueous solution containing *p*-iodo-phenylalanine. The pH of the mixed solution was near 7. The mixed solution was heated at 50°C for 1.5 h, when a fine precipitate formed. The precipitate was separated by filtration and washed repeatedly with distilled water. Finally, the precipitate was dried in a vacuum desiccator over phosphorus pentoxide for a week. The fine crystalline product was pink (Co) or light green (Ni) colour and soluble in neither alcohol nor acetone.

Carbon, hydrogen and nitrogen in the products were determined by an Elementar Vario EL elemental analyzer and cobalt and nickel by EDTA titration. The results of the elemental analysis are listed in Table 1.

Table 1 The results of the elemental analyses for the products

Product		C	H	N	M
Co-compound	calculated/%	31.57	3.39	4.09	8.61
	found/%	30.95	3.43	3.93	8.70
Ni-compound	calculated/%	31.58	3.39	4.09	8.58
	found%	30.41	3.35	3.98	8.64

Characterization of X-ray diffraction for the resultants is carried out by a D/max-YB X-ray diffractometer, $CuK_{\alpha1}$ radiation, Ni filter; at room temperature. The lattice parameters are refined by a least squares refinement program. The calculated and experimental spacing d_{hkl} for the complex of nickel are listed in Table 2.

Infrared spectra of *p*-iodo-phenylalanine and the resultants in the range of 2000–4000 cm^{-1} was recorded by a FTIR spectrometer and the KBr-disc method. The infrared spectra are shown in Fig. 1.

Table 2 The experimental data and the calculated results for X-ray diffraction of $[Ni(IC_6H_4CH_2CHNH_2COO)_2]\cdot 2.5H_2O$ (orthorhombic; *a*=0.9887 nm, *b*=1.4739 nm, *c*=2.1585 nm)

h, k, l	d_{exp}/nm	d_{cal}/nm	h, k, l	d_{exp}/nm	d_{cal}/nm
1 0 0	0.9883	0.9886	0 2 6	0.3227	0.3223
1 1 2	0.6563	0.6554	3 1 2	0.3081	0.3082
1 0 3	0.5835	0.5827	1 3 5	0.3072	0.3081
0 1 4	0.5069	0.5067	0 1 7	0.3027	0.3018
1 1 4	0.4525	0.4519	0 5 0	0.2951	0.2948
1 3 0	0.4397	0.4399	3 1 3	0.2927	0.2936
2 2 1	0.4043	0.4033	1 1 7	0.2881	0.2887
1 0 5	0.3959	0.3956	3 0 4	0.2819	0.2812
1 1 5	0.3798	0.3811	3 1 4	0.2758	0.2763
0 2 5	0.3723	0.3725	1 4 6	0.2483	0.2491
0 0 6	0.3587	0.3597	3 1 6	0.2394	0.2389
1 4 0	0.3453	0.3453	2 2 8	0.2250	0.2255
1 4 1	0.3419	0.3409	2 6 1	0.2192	0.2188
1 1 6	0.3285	0.3295	0 7 6	0.1814	0.1817
2 0 5	0.3250	0.3252	–	–	–

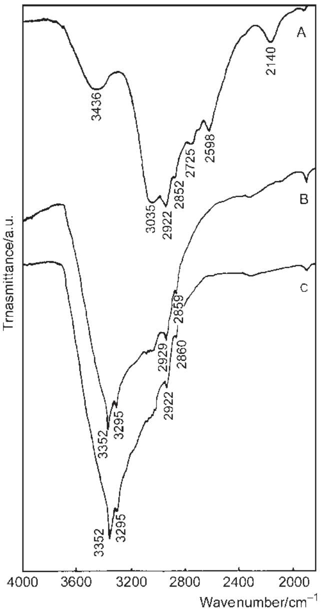

Fig. 1 Infrared spectra of *p*-iodo-phenylalanine and complexes of *p*-iodo-phenylalanine and divalent cobalt and nickel; A – *p*-iodo-phenylalanine; B – complex of *p*-iodo-phenylalanine and cobalt; C – complex of *p*-iodo-phenylalanine and nickel

Thermal analysis studies were performed by a LCT-1 differential thermal balance in air, with a heating rate of 10°C min^{-1}. The sample mass was 13.5 mg for the complex of cobalt and 9.0 mg for that of the complex of nickel. The reference is α-Al_2O_3. The thermogravimetric and differential thermal analysis curves are shown in Fig. 2. The possible pyrolysis reactions, experimental and calculated results for the complexes are summarized in Table 3.

Table 3 Thermal decomposition data of $[Co(IC_6H_4CH_2CHNH_2COO)_2]\cdot 2.5H_2O$ and $[Ni(IC_6H_4CH_2CHNH_2COO)_2]\cdot 2.5H_2O$

Reaction	*T*/°C[a]	Total mass loss/%	
		found	calc.
$[Co(IC_6H_4CH_2CHNH_2COO)_2]\cdot 2.5H_2O$ ↓ $-H_2O$	100(endo)	6.7	6.6
$Co(IC_6H_4CH_2CHNH_2COO)_2$ ↓ $-CO$, $-NH_2$	250(exo)	12.6	12.8
$Co(IC_6H_4CH_2CHO)_2$ ↓ $-C_6H_4$	325(exo)	20.7	22.2
$Co(ICH_2CHO)_2$ ↓ $-I$, $-CH_2$, $-CH$, $-0.5O_2$	390(exo) 455(exo) 475(exo)	46.7	46.2
Co_2O_3		13.2[b]	12.1[b]
$[Ni(IC_6H_4CH_2CHNH_2COO)_2]\cdot 2.5H_2O$ ↓ $-H_2O$	120(endo)	6.7	6.6
$Ni(IC_6H_4CH_2CHNH_2COO)_2$ ↓$-(-C_6H_4-, -NH-)$	288(exo)	27.8	26.6
$Ni(ICH_2COO)_2$ ↓ $-ICH_2CH_2CO$, $-0.5O_2$	425(exo)	26.5	27.9
$ICH_2CH_2COONiO_{1/2}$ ↓ $-ICH_2CH_2CO$, $-0.5O_2$	450(exo)	27.4	27.9
NiO		11.6[b]	11.0[b]

[a] the temperature of the peak in DTA curve
[b] the percentage content of the metal oxide in the complex.

To confirm the reactions in the thermal decomposition process, the intermediates and resultant residue in the pyrolysis process of the complex of cobalt were also analyzed. First, a certain amount (185.9 mg) of the complex of cobalt was placed in an alumina crucible and heated in a muffle furnace at 255°C for 30 min. The percentage mass loss of the sample was measured and carbon, hydrogen and nitrogen in the pyrolysis product were determined by elemental analyzer. The residual product in alumina crucible was heated at 350°C for 30 min again, and the relative mass loss determined. Finally, the pyrolysis product in the alumina crucible was heated at 500°C for 30 min and the cobalt content of the resultant product was determined by colorimetric analysis. The results of the analyses are listed in Table 4.

Results and discussion

The results of elemental analyses indicate that the resultant compound is a complex of *p*-iodo-phenylalanine and cobalt or nickel with crystal water and the formula is $[M(IC_6H_4CH_2CHNH_2COO)_2]\cdot 2.5H_2O$ (M=Co, Ni).

All the peaks in X-ray diffraction patterns of each compound can readily be indexed by a set of lattice parameters according to orthorhombic symmetry. The results in Table 2 show that the calculated spacing d_{hkl} are consistent with the experimental ones. This indicates that the product is single phase and the crystal structure belongs to the orthorhombic system. The lattice parameters are a=0.9777 nm, b=1.4903 nm, c=2.1493 nm and V=3.1317 nm^3 for the complex of cobalt; a=0.9887 nm, b=1.4739 nm, c=2.1585 nm and V=3.1455 nm^3 for the complex of nickel. The effective ionic radius or Ni^{2+} ion (0.069 nm) is slightly larger than that of Co^{2+} ion in a low spin state (0.064 nm), but smaller than that of Co^{2+} ion in a high spin state (0.0745 nm) [6]. The fact that the cell volume of the complex of cobalt is slightly smaller than that of nickel might imply that the Co^{2+} ion in the complex is in a low spin state.

Table 4 The determination for the compositions of the pyrolysis products of $[Co(IC_6H_4CH_2CHNH_2COO)_2]\cdot 2.5H_2O$ at different temperature

Reaction and product		T/°C	Mass loss/ %[a]	Elemental content/%[b]			
				C	H	N	Co
$[Co(IC_6H_4CH_2CHNH_2COO)_2]\cdot 2.5H_2O$		255					
↓	calc./%		19.4	34.8	2.5	0.0	
$Co(IC_6H_4CH_2CHO)_2$	found/%		18.2	33.9	2.9	–	
$Co(IC_6H_4CH_2CHO)_2$		350					
↓	calc./%[c]		40.3				
I_2OCo	found/%		44.2				
I_2OCo		500					
↓	calc./%[d]		74.8				71.1
Co_2O_3	found/%		68.8				72.4

[a] the relative mass loss of the sample or intermediate before and after this step.

[b] the contents of C, H, N or Co in the pyrolysis product.

[c] partial loss of iodine atoms in this step (350°C) is not considered, hence, the calculated relative mass loss is smaller than the experimental one.

[d] partial loss of iodine atoms in the last step (350°C) is not considered, hence, the calculated relative mass loss in this step is larger than the experimental one.

Figure 1 shows that infrared spectra of the complexes are considerably different from that of *p*-iodo-phenylalanine. The two absorption peaks at 3352 and 3295 cm^{-1} in the infrared spectra of the complexes can be assigned as the characteristic absorption peaks from antisymmetric and symmetric stretching vibrations of the N–H bonds in the complex of amino acid and metal ion [7]. This assignment can be confirmed by

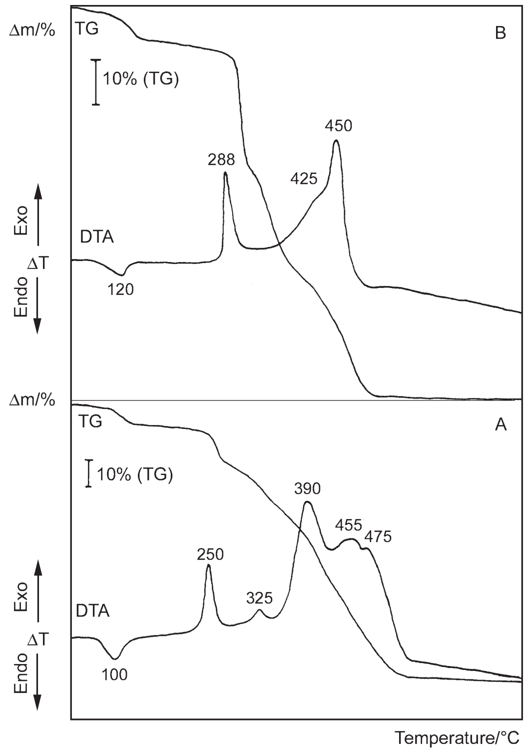

Fig. 2 Thermogravimetric and differential thermal analysis curves of complexes of *p*-iodo-phenylalanine and cobalt and nickel; A – complex of *p*-iodo-phenylalanine and cobalt; B – complex of *p*-iodo-phenylalanine and nickel

the relationship between the frequency of antisymmetric stretching vibration (ν_{as}) and that of symmetric stretching vibration (ν_s) of the N–H bond in the amino group: ν_s=345.5+0.876ν_{as} [8]. If we assume ν_{as}=3352 cm^{-1}, according to this formula, ν_s should be 3282 cm^{-1}, which is very close to the experimental ν_s (3295 cm^{-1}). The free amino acid always exists as an inner salt, hence, there are both the protonated amino group $-NH_3^+$ and deprotonated carboxyl group ($-COO^-$) in a free amino acid [9]. An amino group ($-NH_2$) can exist only in the complex of amino acid and metal ion. The absorption peak at about 2860 and 2922 cm^{-1} in the infrared spectra *p*-iodo-phenylalanine and complexes is from antisymmetric and symmetric stretching vibrations of the C–H bond in the methylene group ($-CH_2-$), respectively [10]. The peaks at 2725 and 2598 cm^{-1} in the infrared spectrum of *p*-iodo-phenylalanine are characteristic for the aliphatic carboxyl acid [10]. Disappearance of the two absorption peaks in the infrared spectra of the complexes also shows the formation of the metal salt. The absorption peak at 3436 cm^{-1} in the infrared spectrum of *p*-iodo-phenylalanine is from the vibration of the O–H band in the intramolecular hydrogen bond. Due to the presence of the crystal waters in the complexes, the absorption peak from the vibration of the O–H bond in the infrared spectra of the complexes will become very intense and overlap the absorption peak at 3352 cm^{-1}, so it leads to the appearance of a wide band in the left side of the most intense peak at 3352 cm^{-1} in the infrared spectra of the complexes.

Figure 2 shows DTA and TG curves of the complexes of cobalt and nickel. The identical mass loss of two complexes in the dehydration reaction at a temperature (>50°C) means that the complexes contain the same number of water molecules. As the sample has been dried in a vacuum desiccator over phosphorus pentoxide for a week, the water molecule in the complex must be the lattice water, not the absorbed water. After dehydration, the thermal decomposition processes of two complexes are different. First, the complex of cobalt loses the $–NH_2$ and –CO group of the organic ligand, similarly to Hofmann degradation [11]. Then, the phenyl group of ligand is eliminated at about 280°C. There are four detectable exothermic peaks in DTA curve from 320 to 510°C. This indicates the successive occurrence of four decomposition reactions corresponding to the loss of the $–CH_2–$ and –CH group, I and partial oxygen atom from the ligand. At last, the resultant residue is Co_2O_3. After dehydration, the first mass loss for the complex of nickel is due to elimination of phenyl group at about 280°C. Then, the two pyrolysis reactions with similar mass loss occur from 400 to 460°C. In each pyrolysis reaction, a residual organic ligand is lost. Last, NiO is formed. All the data of DTA and the percentage mass losses and possible pyrolysis reactions have been summarized in Table 3.

The results of a thermal decomposition study of the cobalt complex using a larger sample to gain more information about reaction intermediates are presented in Table 4. At 255°C the mass loss was 18.2%, compared with a total loss 19.3% for the first two decomposition steps in the prior thermogravimetric analysis. The C, H, N analyses gave results close to those expected. The composition of the final residue as Co_2O_3 is confirmed by the analysis for Co in Table 4.

We have noted that the elimination of the iodine atom from the organic ligand always happens after the elimination of all the organic groups in the thermal decomposition process. In the complex, the organic ligand bonds to the metal ion through the oxygen atoms of carboxyl group. The dissociation energy (about 85 kcal mol^{-1}) of the C–C bond is much larger than that (about 53 kcal mol^{-1}) of the I–C bond [11]. Why the elimination of the iodine atom at the terminal of the ligand is more difficult than that of the $–CH_2$ or phenyl group in the main chain of the ligand? Perhaps, it is because the iodine atoms are coordinated to the metal ion. In the lattice, the terminal iodine atom of the ligand in a complex can bond to the metal ion in another complex by means of the lone pair elections. The formation of the bond between the iodine atom and metal ion must weaken the bonding of the iodine atom with carbon atom of the phenyl group, hence, make the pyrolysis elimination of the phenyl group in the main chain of the ligand easier than that of iodine atom at the terminal of the ligand.

Conclusions

New complexes of *p*-iodo-phenylalanine with cobalt and nickel have been synthesized and characterized. The complexes are crystalline powders with orthorhombic structure. The lattice parameters are: a=0.9777 nm, b=1.4903 nm and c=2.1493 nm for the complex of cobalt; a=0.9887 nm, b=1.4739 nm and c=2.1585 nm for the complex of nickel. The existence of two characteristic absorption bands from the antisymmetric and symmetric stretching vibration of the N–H bonds in the amino group ($–NH_2$) of the complex confirms the coordination of the amino acid to the cobalt or nickel ion. The thermal decomposition process of the complex of cobalt differs from that of nickel. Some of the pyrolysis reactions of the cobalt complex have been elucidated by analysis of the intermediate and resultant product. The fact that the elimination of the iodine atom at the terminal of the ligand is more difficult than that of other groups in the main chain of the ligand may indicate that the iodine atom is coordinated to the metal ion in the lattice.

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