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Studies on the Mixed-Ligand Complexes. II.[1,2] Synthesis of the Mixed-Ligand Complexes between 8-Hydroxyquinoline-5-sulfonic Acid and L-Histidine with Metals

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Since some of oxine-like compounds showed antibacterial action in the presence of certain metal ions, this experiment was carried out to synthesize a model compound of mixed-ligand complexes of 8-hydroxyquinoline-5-sulfonic acid (abbr. as HQS below), being a water soluble oxine derivative, L-histidine (abbr. as His) and certain metal ions. The authors reported on the synthesis of the mixed-ligand complex of Co(III) containing oxine and glycine. In this paper His was used as a chelating amino acid, which is expected to form mixed-ligand complexes more easily than in the case of glycine in cooperating with HQS, since the stability constants[4] of His-metal complexes are much closer to those[5] of HQS-metal complexes.

Result and Discussion

Mixed-lignd complex of copper(II) was obtained as bluish green precipitates from a solution containing cupric ion, His·HCl, and HQS in the ratio of 1:1:1 at pH 6—7. Mixed-ligand complexes of nickel(II) and cobalt(III) were synthesized in the similar manner to that of copper(II), and the expected products were precipitated by an addition of EtOH. The results of elemental analyses of these complexes are shown in Table I, where the combining ratios of His:metal:HQS are 1:1:1 for copper and nickel and 2:1:1 for Co(III), the valence of which was deduced from the combining ratio of these complexes.

Table I. Results of Elemental Analyses of the Mixed-Ligand Complexes

	Analyses (%)					
	Calcd.			Found		
	C	H	N	C	H	N
$(C_9H_5NO_4SNa)Cu(II)(C_6H_8N_3O_2)\cdot 1/2H_2O$	38.05	11.84	2.96	38.09	11.59	3.39
$(C_9H_5NO_4SNa)Ni(II)(C_6H_8N_3O_2)\cdot 4H_2O$	33.89	10.54	3.95	33.44	10.76	3.95
$(C_9H_5NO_4SNa)Co(III)(C_6H_8N_3O_2)_2\cdot 4H_2O$	36.76	14.30	4.23	37.01	14.45	4.25

Moreover, in order to make sure of the purity of the products, thin-layer chromatography (TLC) was carried out with silicagel as a adsorbent. The *Rf* values obtained are shown in

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1) Part I: Y. Kidani, Y. Kato, and H. Koike, *Chem. Pharm. Bull.*, (Tokyo), **18**, 1921 (1970).

2) A part of this paper was presented at Kagaku-kankeigaku-kyokai Chubu-shibu Rengo Shuki-taikai, Oct. 1970, Nagoya.

3) Location: *Tanabe-dori, Mizuho-ku, Nagoya.*

4) D.D. Perrin and V.S. Sharma, *J. Chem. Soc.* (A), **1967**, 724.

5) L.G. Sillén and A.E. Martell, "Stability Constants of Metal Ion Complexes," Burlington House, London, 1964, p. 610.

Table II. *Rf* Values of the Mixed-Ligand Complexes and the Parent Complexes on Thin-Layer Chromatogram

Developer / Complexes	*n*-BuOH–Pyridine–H_2O (4:3:7)	Phenol–H_2O (7:3)	MeOH–H_2O (4:1)
HQS-Cu(II)-His	0.68	0.74	—
HQS-Ni(II)-His	—	0.72	0.50
HQS-Co(III)-His	—	0.24	—
$(His)_2Cu(II)$	0.48	0.75	—
$(His)_2Ni(II)$	—	0.72	0.44
$(His)_2Co(II)$	—	0.32	—
$(HQSNa)_2Cu(II)$	0.69	0.14	—
$(HQSNa)_2Ni(II)$	—	0.78	0.94
$(HQSNa)_2Co(II)$	—	0	—

Table III. *Rf* Values of the Complexes Decomposed in 1N HCl on Thin-Layer Chromatogram

Developer / Complexes	Phenol–H_2O (7:3)		
	Spot I	Spot II	Spot III
HQS-Cu(II)-His	0	0.36	0.46
HQS-Ni(II)-His	0	0.35	0.45
His	0	0.35	0.45
HQS	—	0.35	—
Cu(II)	0	—	—
Ni(II)	0	—	—
Co(II)	0	—	—

Table II, together with those of the parent complexes. In the case of copper, the *Rf* value of the mixed-ligand complex is completely different from that of $(HQS)_2Cu$, but similar to that of $(His)_2Cu$. However, the separation from $(His)_2Cu$ was achieved with a *n*-BuOH-pyridine-H_2O (4:3:7) mixture and the sample showed only one spot. Since the product regarded as a mixed-ligand complex of nickel was not separable from its parent complexes with a phenol-H_2O (7:3) solvent mixture, a MeOH-H_2O (4:1) mixture was employed to distinguish it from $(HQS)_2Ni$, but was not still separable from $(His)_2Ni$ as shown in Table II. For the both solvent mixtures the *Rf* values of the mixed-ligand complex of nickel are close to those of $(His)_2Ni$, but the fact that the former showed only one spot and contained HQS as shown in Table III, where the *Rf* values of the mixed-ligand complexes decomposed in 1N HCl solution are shown, differenciate itself from $(His)_2Ni$. Similarly, the mixed-ligand complex of Co (III) was separated from its parent complexes and regarded chromatographically to be pure.

The infrared absorption spectra of these complexes are shown in Fig. 1. According to Koegel[6] the peak of His·HCl and His·Na salt at 2071 cm^{-1} is related to the ampholyte ion and is assigned as the N-H stretching vibrations which disappears to form chelate with metal ions. The corresponding peaks for 1635 and 1460 cm^{-1} of His·Na, assigned as asymmetric and symmetric stretching vibrations of the carboxyl group, respectively, are found around 1600 cm^{-1} as a broad band and at 1440—1460 cm^{-1} in the mixed-ligand complexes, indicating the bond formation between the carboxyl group and the metal ions. The peaks found at 1036 and 1160 cm^{-1} of HQS·Na salt was assigned as the symmetric and asymmetric stretching vibrations of the sulfo group,[7] which are subject to the hydrogen bond formation between

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7) T. Nortia, *Suomen Kemistilehti* (B), **1959**, 83.

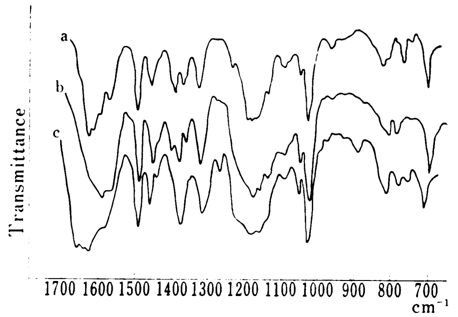

Fig. 1. Infrared Spectra of the Mixed-Ligand Complexes

a. His-Cu(II)-HQS b. His-Ni(II)-HQS
c. His-Co(III)-HQS

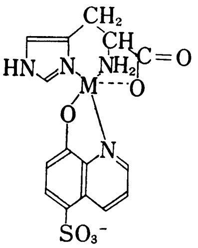

Fig. 2. Proposed Structure for His-Metal(II)-HQS Complex

H_2O and the sulfo group. The peaks of the symmetric stretching vibrations of the sulfo group in the mixed-ligand complexes are found at 1030—1038 cm^{-1} as a sharp and strong band, while the asymmetric stretching vibrations are observed as a broad band around 1160—1200 cm^{-1}. These infrared spectral data also support that the mixed-ligand complexes consist of HQS, His, and the metal ions. Considering from the works of Carlson[8] and Ogiso,[9] the following structure will be proposed for the bivalent metal complexes.

Experimental

Materials——All the reagents were of analytical grade and used without further purification. Thin-layer chromatography was carried out with Wakogel B-10.

Apparatus——Infrared absorption spectra were measured by KBr disc mthod with a Nihon Bunko JASCO, IR-S spectrophotometer.

Synthesis——HQS-Cu(II)-His Complex: 0.7 g of $CuCl_2 \cdot 2H_2O$ and 0.9 g of His·HCl·H_2Owere dissolved in 30 ml of H_2O and to this 0.56 g of HQS in 20 ml of 4×10^{-3} M NaOH green precipitates were formed, which were filtered off and washed with H_2O and EtOH. Yield 70%. mp >300°.

HQS-Ni(II)-His Complex: 0.7 g of $NiSO_4 \cdot 7H_2O$ and 0.53 g of His·HCl·H_2O were dissolved in 15 ml of H_2O and to this 0.56 g of HQS in 20 ml of 4×10^{-3} M NaOH aqueous solution was added. The pH of the solution was made up to 6—7 with 1 N NaOH and stirred for 3 hr in the presence of 0.5 g of charcoal at a room temperature. After filtration pale green precipitates were obtained with an addition of EtOH to the filtrate and purified with H_2O-EtOH. It is very soluble in H_2O and fairly soluble in MeOH. Yield 5%. mp >300°.

HQS-Co(III)-His Complex: 0.7 g of $CoSO_4 \cdot 7H_2O$ and 1.1 g of His·HCl·H_2O were dissolved in 15 ml of H_2O and to this 0.56 g of HQS in 10 ml of 4×10^{-3} M NaOH aqueous solution was added. The pH of the solution was made up to 6—7 with 1N NaOH. The resultant solution was heated on a water-bath for 1 hr in the presence of 0.5 g of charcoal. After filtration, the filtrate was evaporated to dryness and to this 10 ml of H_2O was added. The insoluble resdiue was separated by filtration and to the filtrate EtOH was added to yield oily products, which was separated by decantation from the supernatant. The oily procut was treated wtih EtOH to be solidified and reprecipitated with $H_2O \cdot$EtOH. Yield 10%. mp >300°.

Thin-Layer Chromatography——TLC was carried out on 0.20 mm thick plates (Wakogel B-10), which were activated at 110° for 1 hr. The solvent mixtures used were 1) *n*-BuOH-pyridine-H_2O (4:3:7), 2) phenol-H_2O (7:3), and 3) MeOH: H_2O (4:1).

Detection of the Spots——As to the detection of the components in the decomposition products of the complexes, the samples were dissolved in 1N HCl and developed with phenol-H_2O solvent mixture, then glycine was detected with ninhydrin and the metal ions were with dithizone. HQS was detected with its fluorescence. The detection of the mixed-ligand complexes were made with ninhydrin and dithizone.

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[9] T. Ogiso, *Yakugaku Zasshi*, **87**, 617 (1967).