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Metal Complexes of Selenocysteamine

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In the reaction of selenocysteamine with nickel ion, formation of cationoid complex was confirmed by pH titration, elemental analysis, molar-ratio method and infrared spectra. On the basis of the formation of the cationoid complex, stability constants of cobalt, zinc, palladium and cadmium complexes of selenocysteamine were determined. In selenocysteamine, formations of the complexes were observed in more acid medium than in cysteamine.

Complexing agents containing selenohydryl group as a coordinating group have been scarcely studied,[2)] but it is of great interest in coordination chemistry to investigate their reactivities towards metal ions and to compare them with those of sulfur or oxygen containing analogues. As selenocysteamine is a selenium containing analogue of cysteamine which has been well known as a potential radiation protective agent, the radiation protective activity of selenocysteamine has attracted a great interest. As the complex formation of cysteamine may have connection to its radiation protective activity to some extent, as mentioned in the previous paper,[3)] the investigation of the complex formation of selenocysteamine was attempted in parallel with that of cysteamine. This paper deals with the complex formation of selenocysteamine with some of the bivalent metal ions such as nickel, zinc, lead, cobalt and cadmium.

Sum of the compositive macroscopic acid dissociation constants of selenocysteamine and cysteamine were determined as 16.00 and 18.80[3)] respectively. The proton affinity of selenocysteamine may therefore be considerably smaller than that of cysteamine. Hence the stability constants of selenocysteamine metal complexes are expected to be smaller than those of cysteamine metal complexes, if the stability constants of the metal complexes of these two ligands can be simply compared each other provided that these complexes have similar structures. While the structures of the metal complexes of both ligands are presumed to be different each other, because the considerable difference was observed between these two ligands in the degree of the contribution of zwitter-ionic form in the solution.[3)] The complex formation with nickel ion and the structure of the nickel complex have been studied in detail and the stability constants of other metal complexes were determined, and the results were discussed in comparison with those of cysteamine.

Experimental

Selenocysteamine Hydrochloride——Selenocysteamine hydrochloride was prepared according to the method described in the previous paper.[3)]

Selenocysteamine-Nickel Complex——Selenocysteamine hydrochloride and $NiSO_4$ or $NiCl_2$ were mixed in molar ratio of 2 to 1 in aqueous solution. To this solution, a little EtOH was added to separate a red-purple precipitate. This precipitate was separated and washed with H_2O and EtOH and dried over P_2O_5. *Anal.* Calcd. for $(H_3N^+CH_2CH_2Se)_2Ni\cdot 2Cl^-\cdot 2H_2O$: C; 12.00, H; 4.67. Found: C; 11.61, H; 4.39. *Anal.* Calcd. for $(H_3N^+CH_2CH_2Se)_2Ni\cdot SO_4^{2-}\cdot 2H_2O$: C; 10.37, H; 4.25. Found: C; 10.94, H; 4.14.

1) Location: *Shimoadachi-cho, Sakyo-ku, Kyoto.*
2) E. Sekido, Q. Fernando, and H. Freiser, *Anal. Chem.*, **37**, 1556 (1965).
3) H. Tanaka, H. Sakurai, and A. Yokoyama, *Chem. Pharm. Bull.* (Tokyo), **18**, 1013 (1870).

Cysteamine-Nickel Complex——Cysteamine–nickel complex was prepared by the method reported by Foye.[4]

Cysteamine-Nickel Chelate——Cysteamine–nickel chelate was prepared by the method reported by Jicha and Busch.[5]

pH Titration——Titrations were carried out in a same manner as in the previous paper.[3]

Measurements of Absorption Spectra——The absorption spectra of visible region were measured in the solution buffered with $Na_2B_4O_7$-HCl system by a Hitachi model EPS-2 recording spectrophotometer and Shimadzu model QV-50 spectrophotometer. The absorption spectra of infrared region were measured in KBr disks by a Koken DS-301 spectrometer.

Calculations of Stability Constants of Selenocysteamine Metal Complexes——The first and second stability constants were calculated from the titration curve of ligand–to–metal ratio of 2:1 by Bjerrum's method.[6] As it is considered from the acid dissociation of selenocysteamine reported before[3] that the amino group of selenocysteamine hydrochloride does not take part in the complex formation, only the first acid dissociation constant of selenocysteamine was used for the calculations.

Results and Discussions

The titration curves of the solutions in which nickel ion and selenocysteamine or cysteamine are mixed in various molar ratios are shown in Fig. 1. In selenocysteamine, each titration curve showed clear pH jump at the point where a-value corresponds to the molar ratio, namely when the ratios of selenocysteamine to nickel are 1:1, 2:1 and 10:1 the pH jump were observed at a=1,2 and 8—10 respectively. On the contrary, in cysteamine, pH jump were always observed at a=4, regardless the ratio of cysteamine to nickel. In the case of cysteamine, the formation of a chelate[5] should be considered, whereas in the case of selenocysteamine the same type of the chelate as in cysteamine can not be considered and either the formation of a complex of cysteamine–to–nickel–ratio of 2:1 or the formation of a chelate of cysteamine–to–nickel–ratio of 1:1 should be considered (Table I). Judging from the result of the titration, in selenocysteamine the complex formation should be reasonable rather than the chelate formation which requires the liberation of 2 protons in the titration of 1:1 molar ratio. In this complex formation 1 mole from 2 mole of nickel ion added participates in the complex formation to form the cationic complex. The absorption spectrum of this complex is shown in Fig. 2. The color of the complex is pink at pH 8.0. The determination of the ratio of selenocysteamine to nickel by the molar ratio method at pH 8.0 indicated that the ratio is 2 to 1 as shown in Fig.

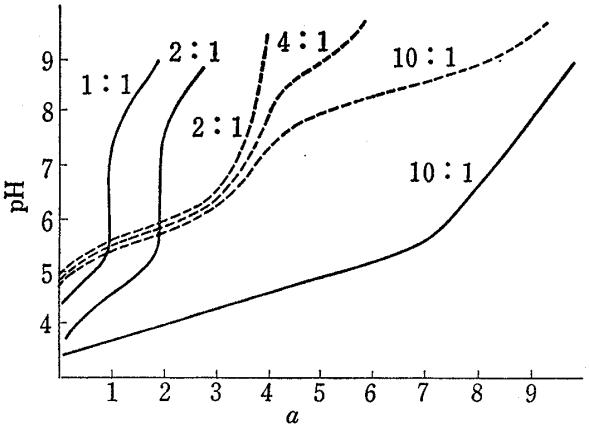

Fig. 1. Titration Curves

——: selenocysteamine-Ni^{2+}
------: cysteamine-Ni^{2+}
a: moles of KOH added per mole of metal ion

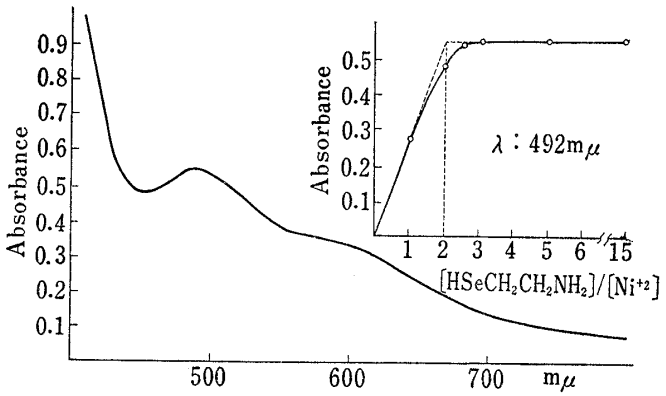

Fig. 2. Absorption Spectrum and Molar Ratio Method

pH 8.00
concentration of Ni^{2+}: 4×10^{-3}M

4) W.O. Foye and J. Mickles, *J. Pharm. Sci.*, **53**, 1030 (1964).
5) D.C. Jicha and D.H. Busch, *Inorg. Chem.*, **1**, 872 (1962).
6) A. Albert and E.P. Serjeant, "Ionization Constants of Acid and Bases," Methuen & Co. Ltd., London, 1962.

2, and supported the above-mentioned complex formation. In addition, the cationic complex isolated from the solution in which selenocysteamine and nickel ion are mixed in the ratio of 2 to 1, was proved to be the complex of selenocysteamine–to–metal–ratio of 2 to 1 by elemental

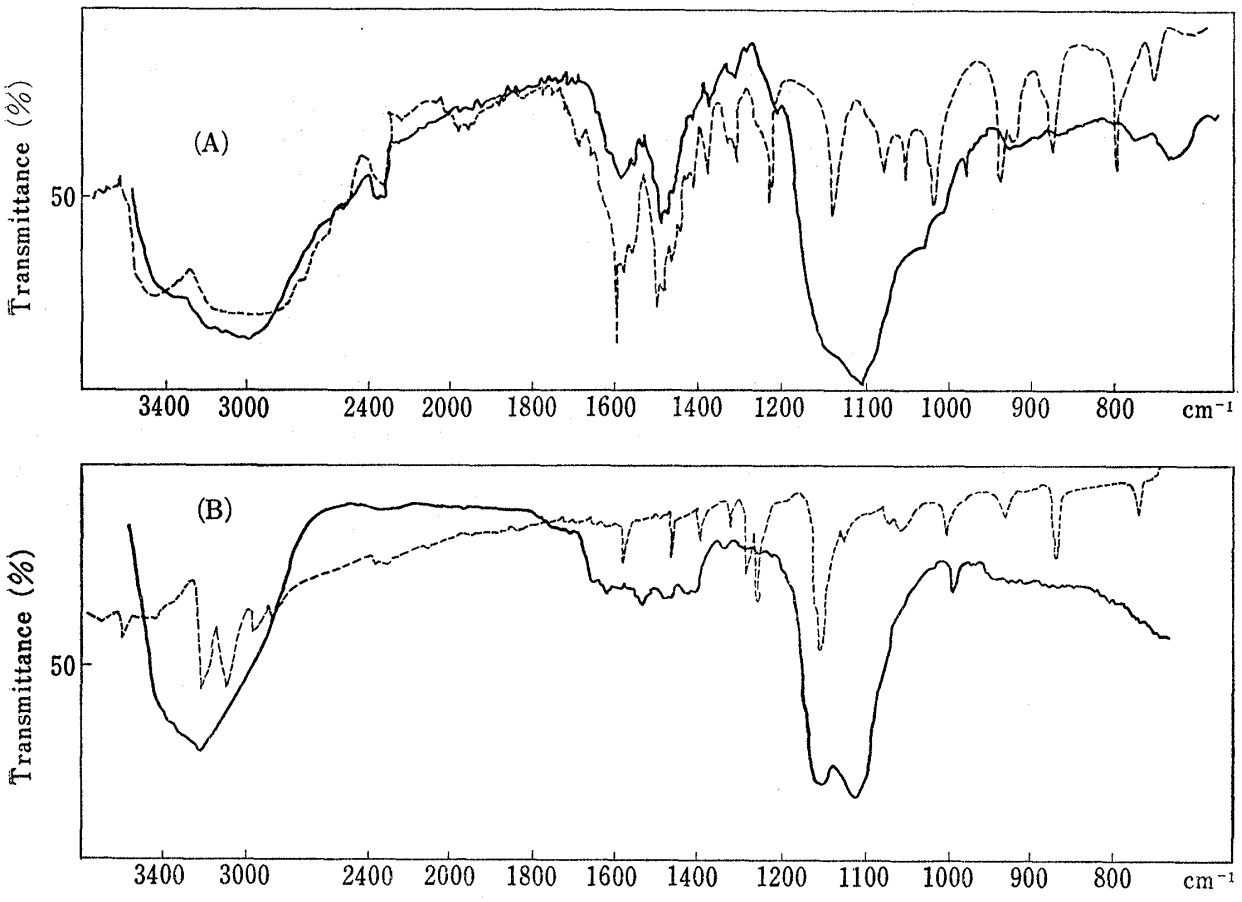

Fig. 3. Infrared Spectra (KBr disk)

(A) ——: selenocysteamine–nickel complex ------: selenocysteamine hydrochloride
(B) ——: cysteamine–nickel complex ------: cysteamine–nickel chelate

TABLE I. Possible Reactions of Selenocysteamine with Nickel Ion

Selenocysteamine: Ni^{2+}	Form: Complex	Form: Chelate
1:1	$\frac{1}{2}$ [Se–Ni–Se; CH_2–CH_2; CH_2–CH_2; NH_3^+ NH_3^+] $+\frac{1}{2}Ni^{2+}+H^+$	CH_2–Se, CH_2–NH_2 $>Ni^+ + 2H^+$
2:1	[Se–Ni–Se; CH_2–CH_2; CH_2–CH_2; NH_3^+ NH_3^+] $+2H^+$	CH_2–Se, CH_2–NH_2 $>Ni^+ + Se^- + 3H^+$; CH_2–CH_2–NH_3^+

analysis regardless the kind of anion as described in experimental part. The infrared spectra of selenocysteamine–nickel complex, cysteamine–nickel complex and cysteamine–nickel chelate were measured and compared them each other. As shown in Fig. 3, selenocysteamine–nickel complex showed almost similar spectrum to that in cysteamine–nickel complex over the range from 650 cm^{-1} to 4000 cm^{-1}. The absorption bands based on the ammonium and sulfate ion could be clearly observed in the spectrum. In conclusion, above observations supported the structure shown in Table I for selenocysteamine–nickel complex. The preference of the cationic complex in selenocysteamine may be reasonably explained from the fact that selenocysteamine is mainly present as zwitter-ionic form in solution in the wide range of pH.[3]

The stability constants of nickel, zinc, lead, cobalt and cadmium complex of selenocysteamine were determined from the titration curves shown in Fig. 4, and the formation curves shown in Fig. 5. The calculations were carried out by the use of first acid dissociation constant of selenocysteamine, on the assumption that these complexes may be the cationic complex. The results are shown in Table II. The stability constants (log β) decreases in the order, cadmium, lead, nickel, zinc and cobalt. In comparison of the complex formation of selenocysteamine with that of cysteamine, it is a remarkable characteristic of selenocysteamine that the complex formation takes place even in very acid medium. A similar observation was reported in selenoxine and thioxine.[2] In selenocysteamine, the complex is hydrolyzed in neutral solution before the beginning of the dissociation of the protonated amino groups and the com-

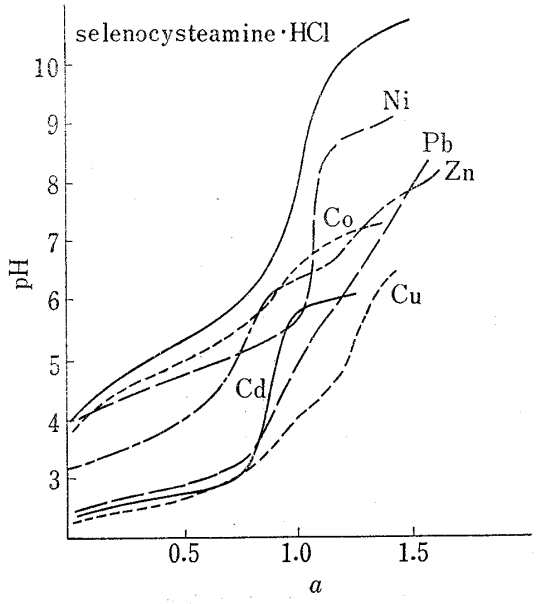

Fig. 4. Titration Curves

a: moles of KOH added per mole of selenocysteamine·HCl

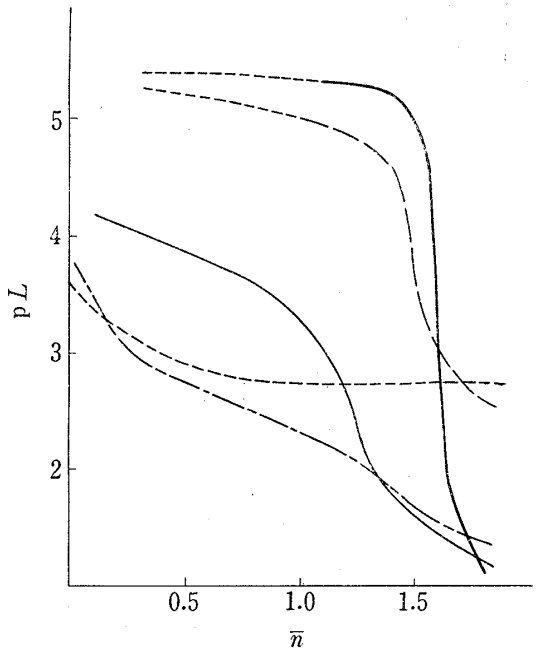

Fig. 5. Formation Curves of Selenocysteamine Metal Complexes

——: Cd ------: Pb ——: Co
--------: Ni ——: Zn

Table II. Stability Constants of Metal Complexes of Selenocysteamine

	Ni	Co	Zn	Pb	Cd
log K_1	2.93	2.76	3.85	>5.2	>5.4
log K_2	2.77	1.65	1.68	3.50	4.86
log β_2	5.70	4.41	5.53	>8.7	>10.2

22°, μ=0.1

plex is extremely unstable in alkaline medium. This character of the metal complexes of selenocysteamine may be due to the character of selenium as a ligand atom rather than the structure of the complex.

The above-mentioned difference in the character of the complexes between selenocysteamine and cysteamine may give a suggestion of the considerable difference in bond character between selenium–metal and sulfur–metal. The complex formations of selenocysteamine and cysteamine with copper will be discussed in the succeeding paper.