

the carbonyl group were observed remarkably in the chelates of (VI), (IX), and (X) but not in the chelates of (I), (II), (III), and (IV). These observations also support the presumptions mentioned above on the chelating ability.

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Summary

Stabilities of copper, palladium, nickel, cobalt and iron chelates of various types of ligands involving mercapto and carbonyl groups was compared with each other qualitatively, and "Irving and Williams' stability series" was found to be applicable to these chelates. Apparent stability constants of these chelates were determined. From the results of these experiments, relationship between chelating abilities and chemical structures of the ligands were investigated.

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184. Hisashi Tanaka and Akira Yokoyama : Studies on the Sulfur-containing Chelating Agents. XII. Relationship between Chelating Ability and Chemical Structure of Ligand. (2).*

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In an attempt to make clear the relationship between chelating abilities and chemical structures of S-O-chelating ligands, shown in Chart 1 of Part 1,^{*1} qualitative investigations of their chelating abilities and apparent stability constants of the chelates were reported.^{*1} It was found that "Irving and Williams' stability series" was almost completely applicable to the chelates of the ligands (I~X). However, the order of the stabilities of both nickel and cobalt chelates could not be clarified, due to the difference of the ratio of ligand to metal at the time of accomplishment of chelate formation. The ratio was 2:1 and 3:1 in nickel and cobalt chelates, respectively. This paper deals with further investigations on the comparison of relative stabilities of the chelates and on the relationship between the chelating abilities and the chemical structures of the ligands obtained from the experimental results. In order to ascertain the comparison of the relative stabilities of the chelates, pH values were measured at the point of 50% extraction of the chelates in chloroform and also at the point of incipient chelate formations.

Relationship between Stabilities and pH at the Time of Extraction

Stability constants of the chelate are usually determined by the titrimetric, spectrophotometric and polarographic methods. However, in the case of neutral inner complex, as it is difficult to determine stability constant by the common methods, the pH at 50% extractability or at incipient precipitation have been used for the comparison

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of relative stability of the chelate. For example, this method has been applied for the investigation of the stabilities of the chelates with dithizone,¹⁾ oxine²⁾ and quinaldic acid.³⁾ As this method was considered to be most suitable to compare the stabilities of the chelates with the ligands (I~X), it was applied to compare the relative stabilities of the nickel and cobalt chelates, for the purpose of confirming the results of the qualitative investigation on the stabilities of these chelates.

As to the relationship between extractability and pH, according to Irving,⁴⁾ the chelates which is extracted at a lower pH is more stable when the pH values are compared at the point of same extractability, therefore the stabilities of the chelates could be compared from the following equation.

$$E = K \frac{Kc \cdot [HR]_0^n}{[H]_w^n} \quad (1)$$

Where E is extractability of metal, K is constant, Kc is stability constant of the chelate, $[H]_w$ is concentration of hydrogen ion in an aqueous phase, n is molar ratio of ligand to metal ion, and $[HR]_0$ is concentration of ligand in organic phase.

From this equation, it may be possible to compare the relative stabilities of the chelates, provided that pH is measured and compared each other at the same extractability, such as in 50%. In the relationship between extractability and pH, equation (2) could be derived.

$$\log E = n \log [HR]_0 + n \text{pH} + \text{const.} \quad (2)$$

When $[HR]_0$ is made excess and constant, linear relationship of a slope, n is observed between $\log E$ and pH, therefore n shows a ratio of ligand to metal.

For the comparison of the relative stabilities of various chelates by this method using equation (1), the value of n should be equal in each chelate. As previously reported,⁵⁾ the value of n in nickel and cobalt chelate with the ligands (I~X) was different from one another. Therefore, it may be necessary to give a consideration as described later in the part of the discussion.

pH at the Incipient Chelate Formation

As previously mentioned, it is impossible to compare the relative stabilities of the chelates directly by the above mentioned method, when a ratio of ligand to metal is different in each chelate. However, if the pH values are compared at the incipient chelate formation, the comparison of the relative stabilities should be available in the chelates with the ligands (I~X). Because, as previously reported,⁵⁾ in the cases of the cobalt and iron chelates, the ratio of the ligand to the metal was considered to be 2:1 at the incipient chelate formation and then the ratio changed to 3:1. In order to compare the relative stabilities of the palladium, nickel, cobalt, and iron chelates under the same condition, namely in the ratio of 2:1, pH values were measured at the incipient formation of each chelate. It could be presumed that if pH is lower, the chelate would be more stable, in the same manner as the comparison of pH at 50% extraction. Based upon the experimental results, it should be possible to compare the chelating abilities of the ligands (I~X).

- 1) H. Irving, R. J. P. Williams : Nature, **162**, 746(1948).
- 2) H. Goto : Nippon Kagaku Zasshi, **54**, 725 (1933).
- 3) J. F. Flagg : J. Am. Chem. Soc., **65**, 2346 (1943).
- 4) H. Irving, R. J. P. Williams : J. Chem. Soc., **1949**, 1841.
- 5) Part VIII : This Bulletin, **10**, 19 (1962).

Methods and Results

1) Measurement of pH at 50% extraction : A solution of the ligand (20 mg.) in 5 cc. of CHCl_3 was mixed with 5 cc. of solution of Ni^{2+} or Co^{2+} (500 γ) in Sørensen's buffer solution, in the test tube with a glass stopper and shaken for 5 hr. at room temperature. After the complete extraction of the chelate, aqueous phase was separated. Ni^{2+} or Co^{2+} remaining in the aqueous phase was determined colorimetrically with dimethylglyoxime⁶⁾ in the case of Ni^{2+} and with ammonium thiocyanate⁷⁾ in the case of Co^{2+} . Extractabilities at various pH were calculated and extraction curves of the nickel and cobalt chelates were drawn and pH values at the extractability of 50% ($\log E=0$) were obtained. The ratio of ligand to metal at the time of extraction, namely the value of n , were calculated from the equation (2). The results are shown in Table I.

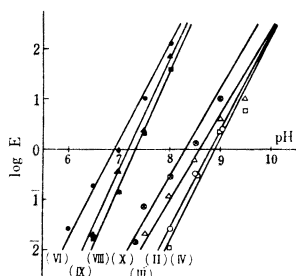


Fig. 1. Extraction Curve of Ni^{2+}

Ligand	Ligand	Ligand
(II) —○—	(VI) —●—	(X) —⊗—
(III) —△—	(VIII) —■—	
(IV) —□—	(IX) —▲—	

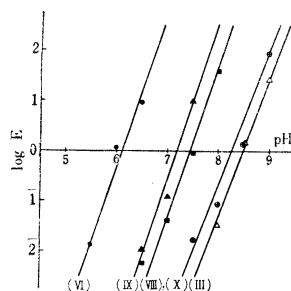


Fig. 2. Extraction Curve of Co^{2+}

Ligand	Ligand	Ligand
(III) —△—	(VIII) —■—	(X) —⊗—
(VI) —●—	(IX) —▲—	

In the case of VII, the ligand was so unstable⁸⁾ that this experiment was impossible.

TABLE I. pH at the Point of 50% Extractability and the Ratio of the Ligand to the Metal (n)

Ligand	pH (n)	
	Ni-chelate	Co-chelate
(II)	8.8 (1.7)	—
(III)	8.6 (1.6)	8.5 (3.1)
(IV)	8.9 (1.8)	—
(VI)	6.9 (2.0)	6.1 (3.3)
(VIII)	7.3 (2.2)	7.4 (2.8)
(IX)	7.2 (2.2)	7.2 (3.0)
(X)	8.3 (1.6)	8.2 (2.7)

Ligand ; (II) $\text{R}=\text{C}_6\text{H}_5^-$, $\text{R}'=\text{C}_2\text{H}_5^-$, (III) $\text{R}=\text{C}_6\text{H}_5^-$, $\text{R}'=\text{C}_2\text{H}_5^-$,
 (IV) $\text{R}=\text{C}_6\text{H}_5^-$, $\text{R}'=p\text{-CH}_3\text{OC}_6\text{H}_4^-$, (VI) $\text{R}=\text{C}_6\text{H}_5^-$, $\text{R}'=\text{C}_2\text{H}_5^-$,
 (VIII) $\text{R}=\text{C}_2\text{H}_5^-$, (IX) $\text{R}=\text{C}_2\text{H}_5^-$, (X) $\text{R}=\text{C}_6\text{H}_5^-$

General formulas of the ligands are shown in Chart 1 of Part 1⁸⁾.

6) E. B. Sandell : "Colorimetric Determination of Traces of Metals" 474 (1950). Interscience Publishers. Inc., New York.

7) *Idem* : *Ibid.*, 281.

8) Part IX : This Bulletin, 10, 25 (1962).

2) Measurement of pH at incipient chelate formation : Metal solutions ($10^{-2}M$) of various pH were prepared by using buffer solution (HCl-KCl, AcOH-AcONa, H_3BO_3 -borax). EtOH solutions ($10^{-2}M$) of the ligands were prepared. Color reactions were observed when 2 drops of metal solution and 1 drop of ligand solution were mixed in the test tube with shaking. The lowest pH values, when the color reaction could be recognized, are shown in Table II.

TABLE II. pH of the Incipient Chelate Formation

Ligand	pH of the incipient chelate formation				
	Pd	Cu ^(a)	Ni	Co	Fe
(I)	1>	1	—	—	—
(II)	1>	1	4.2~4.4	—	—
(III)	1>	1	3.8~4.0	6.0	—
(IV)	1>	1	5.8~6.0	—	—
(VI)	1>	1>	2.2~2.4	3.0	4.5
(VII)	1>	1>	3.6~3.8	—	—
(VIII)	1>	1>	4.0~4.2	4.2	—
(IX)	1>	1>	3.6	4.0~4.2	7.0~7.2
(X)	1>	1>	3.8~4.0	5.8~6.0	—

Ligand; (I) R, R' = C₆H₅, (II), (III) R = C₆H₅, R' = C₂H₅,
 (IV) R = C₆H₅, R' = *p*-CH₃OC₆H₄, (VI) R = C₆H₅, R' = C₂H₅,
 (VII) R = C₆H₅, (VIII), (IX) R = C₂H₅, (X) R = C₆H₅

a) These chelates are cuprous chelates, so that their stabilities may not be compared with those of other bivalent metal chelates. Though they are extremely stable.

Discussion

As seen in Figs. 1 and 2, extraction curve of nickel chelate crosses to that of cobalt chelate and therefore pH value of nickel chelate is lower than that of cobalt chelate at the incipient chelate formation. Judging from this fact, the ratio of the ligand to the metal in cobalt chelates are considered to be 2:1 at the incipient chelate formation and nickel chelates should be more stable than cobalt chelates in the state of the ratio of 2:1. As to the ratio of the ligand to the metal, as seen in Figs. 1 and 2 and Table I, slope of the extraction curve (*n*) is 2 in nickel chelates and that is 3 in cobalt chelates. This result agrees with the ratio obtained by the continuous variation method.

As seen in Table II, comparing the pH values at the incipient chelate formation, the order of the stabilities of various kinds of the chelates is palladium chelate, copper chelate, nickel chelate, cobalt chelate, and iron chelate. This result agrees with that obtained from the qualitative studies reported in the preceding paper.*¹ From all these results, "Irving and Williams' stability series" is confirmed to be applicable to the chelates of ligands (I~X).

Summarizing the above discussion and the results on the qualitative studies reported in the preceding paper,*¹ the relationship between chemical structures of the ligands and their chelating abilities would be concluded as follows. Among all ligands, aromatic mercapto compounds (VII, VIII, IX, X) and unsaturated mercapto compound (VI), in which conjugated double bond is present in their chelating ring have a stronger chelating ability. While aliphatic mercapto compounds (I, II, III, IV) are weaker chelating agents than the formers. Comparing the chelating abilities among the ligands which have conjugated double bond in their chelate ring, unsaturated mercapto compound (VI) is a stronger chelating agent than aromatic mercapto compounds (VII, VIII, IX, X). This relationship is considered to be similar between the chelating ability of 2,4-pentanedione

and that of salicylaldehyde. As to the type of carbonyl group, thiolic acid ester is the strongest and the chelating ability decreases in the order of thiolic acid ester, ester, amide, and ketone.

The authors extend their gratitude to Prof. T. Uno for his helpful advices.

Summary

Stabilities of copper, palladium, nickel, cobalt, and iron chelates of various types of ligands involving the mercapto and the carbonyl group were compared each other by measuring the pH at 50% extractability of the chelates into chloroform and at incipient chelate formation. From the results of these experiments, relationship between chelating abilities and chemical structures of the ligands was confirmed. The ligands which involve conjugated double bond in their chelate ring and those involve thiolic acid ester group were found to have stronger chelating ability.

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181. Shigeru Kobayashi and Chizuru Kuraishi : A Synthesis of 2'-Acetyl-5,5',6'-trimethoxy-2-biphenylcarboxylic Acid.

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In the course of the project to synthesize hydroxyapogalanthamine,¹⁾ the transformation product of galanthamine by hydroiodic acid, an attempt was made to prepare key intermediate 2'-carboxy-5,5',6'-trimethoxy-2'-biphenylacetic acid (X) via 2'-acetyl-5,5',6'-trimethoxy-2-biphenylcarboxylic acid (IX : R=H).

As a starting material for the synthesis of the latter compound, 2'-iodo-4'-methoxyacetophenone (II : R=Me) reported by Oki²⁾ was necessary. He claimed to obtain this as a sole product, m.p. 68~70°, by the Friedel-Crafts reaction of 3-iodoanisole (I) with acetyl chloride in the presence of aluminum chloride. On repetition of this reaction under the identical conditions as used by him, two major products, compound A, C₉H₉O₂I, m.p. 45~47° and compound C, C₈H₇O₂I, m.p. 52~54° and two minor ones, compound B, C₉H₉O₂I, m.p. 70~71° and compound D, C₈H₇O₂I, m.p. 131~132° were isolated. Among them the compounds A and B were non-phenolic while the compounds C and D were phenolic. Obviously Oki isolated only the compound B from the reaction mixture and assigned to it the structure 2'-iodo-4'-methoxyacetophenone (II : R=Me) without any convincing evidence. Since, oxidation of the compound B with potassium hypochlorite yielded 4-iodo-2-methoxybenzoic acid (VI), identical with an authentic sample obtained by the methylation of methyl 2-hydroxy-4-iodobenzoate (V)³⁾ followed by hydrolysis, this should be 2'-methoxy-4'-iodoacetophenone (III : R=Me). In accordance with this assignment, the compound B was shown to be identical with the pro-

*1 Showa-machi, Nagasaki (小林 茂, 倉石千鶴).

1) S. Uyeo : Hand book XVth. I.U.P.A.C. Congress, Paris, p.207 (1957).

2) M. Oki : Bull. Chem. Soc. Japan., **26**, 331 (1953).

3) P. Brenaus, C. Prost : Compt. rend., **178**, 1010 (1924) (C. A., **18**, 1657 (1924)).