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4. **Hisashi Tanaka and Akira Yokoyama**: Studies on Sulfur-containing Chelating Agents. VIII.[*1] Syntheses of α,β-Unsaturated β-Mercapto-acid Esters and their Metal Chelates.

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In the previous papers, the syntheses of β-mercaptoketones[1] (A), β-mercapto-acid esters[2] (B), and their metal chelates were reported. This paper deals with the syntheses of α,β-unsaturated β-mercaptoketones (C) and acid esters (D), and their ability for chelate-formation with metals. In general, in the case of the chelate of a six-membered ring, presence of a conjugated double bond in the chelate ring makes the chelate more stable than that without a conjugated double bond. Accordingly, the chelates derived from (C) and (D) should be more stable than those from (A) and (B), and hence (C) and (D) would have stronger chelating ability than (A) and (B).

(A) $\text{R-}\underset{\text{SH}}{\text{C}}\text{-CH}_2\text{-}\underset{\text{O}}{\underset{\Vert}{\text{C}}}\text{-R}$ (B) $\text{R-}\underset{\text{SH}}{\text{CH}}\text{-CH}_2\text{-}\underset{\text{O}}{\underset{\Vert}{\text{C}}}\text{-OR}$

(C) $\text{R-}\underset{\text{SH}}{\text{C}}\text{=CH-}\underset{\text{O}}{\underset{\Vert}{\text{C}}}\text{-R}$ (D) $\text{R-}\underset{\text{SH}}{\text{C}}\text{=CH-}\underset{\text{O}}{\underset{\Vert}{\text{C}}}\text{-OR}$

Chart 1.

As α,β-unsaturated β-mercaptoketone (C), preparation of 1,3-diphenyl-1-mercaptopropen-3-one (Ia) was planned by the method reported by Tornetta.[3] As shown in Chart 2, thioxo form (Ib) could also be considered in this compound. However, there was indication whether the substance obtained was (Ia) or (Ib). Judging from the fact that the compound prepared did not react with metal ions and absorption band based on the mercapto group was not observed in its infrared spectrum, the compound obtained must be present in the thioxo form which does not have a chelating ability with metal ions.

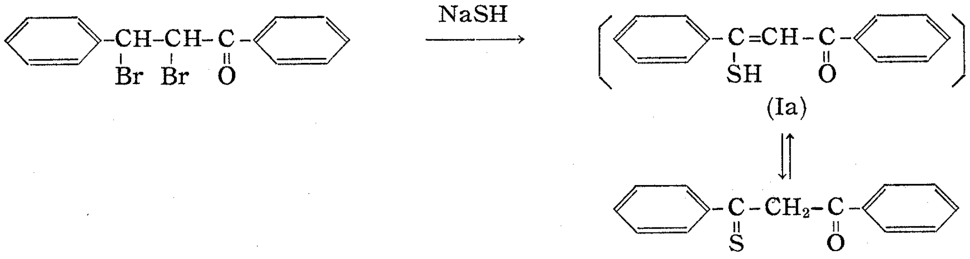

Chart 2.

Ethyl β-mercaptocinnamate (II), ethyl β-mercapto-*p*-nitrocinnamate (III), ethyl β-mercapto-*p*-chlorocinnamate (IV), and ethyl β-mercapto-*p*-methoxycinnamate (V) were prepared as the α,β-unsaturated β-mercapto-acid esters (D). The preparation of these compounds was carried out according to the method reported by Reyes,[4] as shown in Chart 3. (V) could not be obtained in a pure state, but the reaction product showed similar color reaction with metals as other α,β-unsaturated β-mercapto-acid esters and hence the formation of (V) was presumed. (II) was also obtained by other method as

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[*1] Part VII: H. Tanaka, A. Yokoyama: This Bulletin, **10**, 13 (1962).

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1) Part I. H. Tanaka, A. Yokoyama: This Bulletin, **8**, 275 (1960).

2) Part V. *Idem*: *Ibid.*, **9**, 66 (1961).

3) B. Tornetta, S. Angello: Ann. Chim. (Rome), **48**, 581 (1958) (C. A., **53**, 6159 (1959)).

4) Z. Reyes, R.M. Silverstein: J. Am. Chem. Soc., **80**, 6367 (1958).

shown in Chart 3. Fischer reported that β-mercaptocinnamic acid (VI) was obtained by the addition of thiourea to phenylpropiolic acid.[5] (VI) was esterified to obtain (II), but the yield was very poor. Addition of thiourea to ethyl phenylpropionate was also carried out, but in this case, 2-amino-6-phenyl-4(H)-1,3-thiazine (VII) was obtained in a considerably good yield. Formation of (VII) was confirmed from its infrared spectrum with amide band at 1640 cm^{-1} and from microanalytical data. For further confirmation, infrared spectrum of 2-amino-6-phenyl-5,6-dihydro-4(H)-1,3-thiazine (VIII), prepared from β-bromohydrocinnamic acid and thiourea,[6] was also measured and compared with that of (VII). In the case of (VIII), amide band was observed at 1670 cm^{-1} and other part of absorption curve was almost similar to that of (VII). Accordingly, (VII) should have the structure shown in Chart 3.

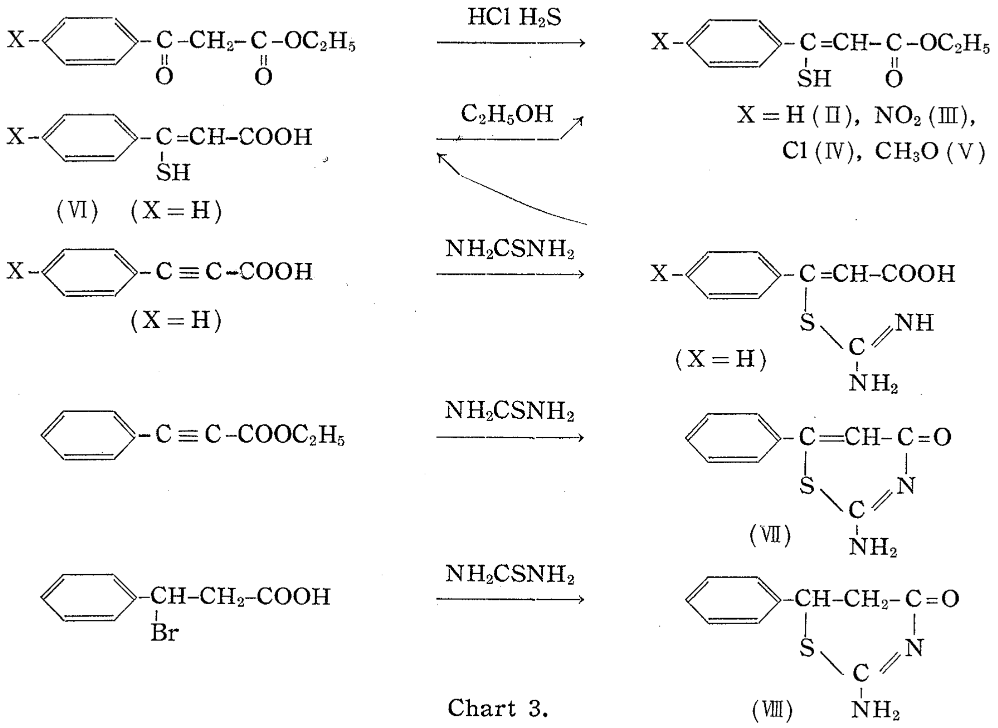

Chart 3.

The reaction of these α,β-unsaturated β-mercapto-acid esters with metals was tested by spot tests and the result is shown in Table I. In ammonium hydroxide alkaline solution, the ligands themselves became yellow, so that the reaction with metals could not be clearly observed. The chelates with magnesium, iron, cobalt, nickel, copper, zinc, palladium, gold, bismuth, and uranyl were extractable into organic solvents such as ethyl acetate and chloroform, but the precipitate produced from silver, mercury, cadmium, and lead was not extractable. The chelates of zinc and magnesium were so unstable that they were decomposed by dilute acetic acid. The recognizable limits of iron, cobalt, nickel, copper, palladium, platinum, and bismuth were measured. As shown in Table II, these ligands were considerably sensitive to iron, nickel, copper, and palladium.

The chelates of copper, nickel, cobalt, and iron were stable and were separated as a crystalline powder, and mechanism of formation and structures of these chelates were investigated.

The copper chelates were separated as an orange-red crystalline powder. As shown in Table III, the ratio of ligand to metal for chelates from the ligand (II) and (IV) was found to be 1:1 from microanalytical data, and the formation mechanism of copper

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5) E. Fischer, W. Brieger: Chem. Ber., **47**, 2469 (1914).
6) B.F. Coodrich: Brit. Pat. 629,486 (C.A., **46**, 7593 (1952)).

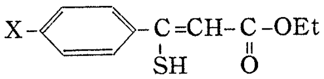
Table I. Spot Tests (in neutral solution)

Metal	Reaction	Metal	Reaction
Mg^{2+}	Pale yellow ppt.	Ag^{+}	Yellow ppt. *
Ca^{2+}	〃	Cd^{2+}	〃 *
Fe^{3+}	Green ppt.	Pt^{4+}	Pale yellow ppt.
Co^{2+}	Brown ppt.	Au^{3+}	Orange ppt.
Ni^{2+}	Orange-red ppt.	Hg^{2+}	Yellow ppt. *
Cu^{2+}	Orange ppt.	Pb^{2+}	〃 *
Zn^{2+}	Pale yellow ppt.	Bi^{3+}	〃
Pd^{2+}	Orange-red ppt.	UO_2^{2+}	Orange ppt.

* Insoluble in organic solvent.

Reagent : 1% EtOH solution of α,β-unsaturated β-mercapto-acid esters.

Table II. Recognizable Limit of Metals by α,β-Unsaturated β-Mercapto-acid Esters (in neutral solution)



Metal	Recognizable Limit (γ/0.05 cc.)		
	X = H	X = Cl	X = NO_2
Fe^{3+}	0.3	0.3	0.2
Co^{2+}	10.0	10.0	10.0
Ni^{2+}	0.5	0.5	0.3
Cu^{2+}	0.5	0.5	0.5
Pd^{2+}	0.1	0.1	0.1
Pt^{4+}	30.0	25.0	25.0
Bi^{3+}	1.0	1.0	0.5

Reagent : 5% EtOH solution of α,β-unsaturated β-mercapto-acid esters.

chelates was considered to be similar to that of β-mercaptoketones reported in Part IV.[7] On the contrary, in the case of the copper chelate of (III), ratio of the ligand to copper was found to be 2:1 from microanalytical data and extractable into organic solvents, so that this chelate is considered to be the copper(II) chelate. However, this chelate was unstable and readily changed into black-brown substance, which did not have a sharp melting point and was not extractable into organic solvents. From its microanalytical data, this substance consits of one mole of the ligand and one atom of copper. Therefore, the copper(II) chelate of (III) was considered to have changed into copper(I) mercaptide.

Nickel chelates were separated and purified as orange-red needles and consisted of two moles of the ligand to one atom of nickel.

Cobalt chelates were separated and purified as green needles and consisted of three moles of the ligand to one atom of cobalt. When the aqueous solution of cobalt(II) acetate and ethanolic solution of the ligand were mixed, brown chelate formed which was extractable into ether. However, green needles separated gradually from the ether solution. These needles were extractable into chloroform. Even when the chelate formation was carried out in a stream of hydrogen or in the presence of a reducing agent, brown chelate, which formed in the first step of chelate formation and was considered to be the cobalt (II) chelate, could not be separated. When the chelate formation was carried out in the presence of hydrogen peroxide, green needles precipitated out immediately and the formation of brown chelate was not observed. As in general, cobalt chelate has a strong tendency to take octahedral configuration with d^2sp^3 orbitals, and cobalt(II) chelates, in this case, are considered to change into stable cobalt(III) chelates of octahedral configuration.

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[7] Part IV. H. Tanaka, A. Yokoyama : This Bulletin, 8, 1012 (1960).

Iron chelates were produced from iron(III) chloride and the ligands, in a ratio of 1:3, and soluble in most of the organic solvents. Even when iron(II) chloride was used, the ratio of the ligand to the metal was 3:1 and the chelates, either from ferric ion or ferrous ion, were found to be quite identical by the mixed melting point test and absorption spectra in the visible, ultraviolet, and infrared regions. From these facts, it is presumed that iron(II) chelate is unstable and readily changes into iron(III) chelate, analogously to the case of cobalt chelates. In general, ferric ion oxidizes thiols to disulfides, but in the present case, α,β-unsaturated β-mercapto-acid esters were not oxidized and iron(III) chelates were separated. This showed that these α,β-unsaturated β-mercapto-acid esters are stable against oxidation and stability of the resulting iron(III) chelates is high.

Infrared spectra of (II) and its copper, nickel, cobalt, and iron chelates in chloroform solution were measured. In the case of (II), the absorption bands of mercapto group and ester group were observed at 2480 cm^{-1} as intramolecularly hydrogen-bonded mercapto group[4] and at 1665 cm^{-1}, respectively. In the case of metal chelates, the absorption of mercapto group disappeared and considerable shift of the absorption maximum of the ester groups to a lower frequency was observed. Namely, the absorption maximum of the ester group was observed at 1640 cm^{-1} in copper chelates, at 1590 cm^{-1} in nickel chelate, at 1600 cm^{-1} in cobalt chelate, and at 1595 cm^{-1} in iron chelate. In the case of chelates produced from the esters of β-mercaptohydrocinnamic acid (B), shift of the absorption maximum of the ester group was hardly observed, as reported in Part V.[2] This difference in infrared spectra suggests that α,β-unsaturated β-mercapto-acid esters (D) have stronger chelating ability than the saturated esters (B). The absorption spectra of the chelates in ultraviolet and visible regions are shown in Figs. 1, 2, 3, and 4.

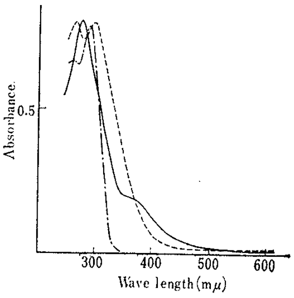


Fig. 1.

——— Cu chelate of (II)
--------- 〃 (IV)
(5×10^{-5} mole in $CHCl_3$)
– – – – Ligand (II)
(5×10^{-5} mole in $CHCl_3$)

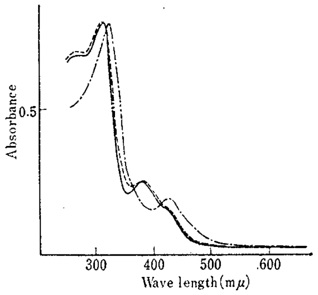


Fig. 2.

——— Ni chelate of (II)
– – – – 〃 (III)
--------- 〃 (IV)
(2.5×10^{-5} mole in $CHCl_3$)

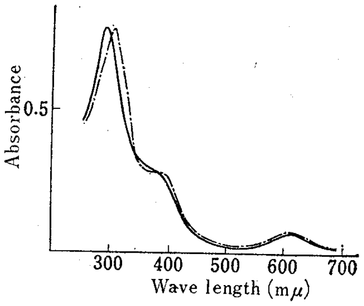


Fig. 3.

——— Co chelate of (II)
– – – – 〃 (III)
(1.2×10^{-5} mole in $CHCl_3$)

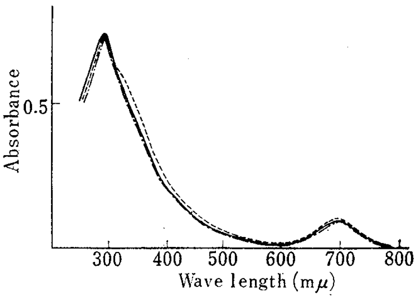


Fig. 4.

——— Fe chelate of (II)
– – – – 〃 (III)
--------- 〃 (IV)
(1.2×10^{-5} mole in $CHCl_3$)

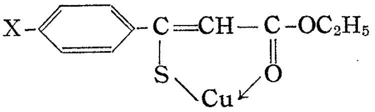
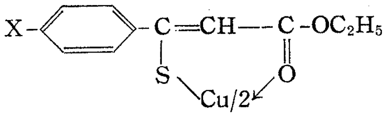
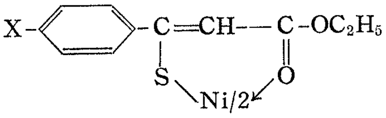
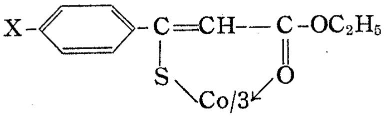
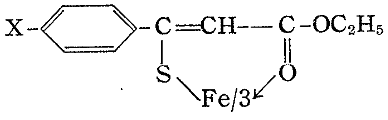
Experimental

Ethyl β-Mercapto-p-chlorocinnamate (IV)——Dehyd. EtOH (80 cc.) was saturated with dry HCl at 0° to 5°, H_2S was passed for 15 min., and a solution of ethyl *p*-chlorobenzoylacetate (5 g.) in dehyd. Et_2O (10 cc.) was dropped in slowly. A stream of H_2S was maintained during this addition and for 6 hr. thereafter. After standing overnight at room temperature, the solvent was evaporated in a diminished pressure. The residual oil was extracted with Et_2O, which was washed with H_2O and dried over Na_2SO_4. The solvent was evaporated and the risidue was distilled in a diminished pressure. The reddish oil (b.p$_5$ 130~134°) of (IV) was collected, dissolved in EtOH (20 cc.), and treated with $(AcO)_2Pb$ in H_2O. Pb-mercaptide was collected and washed with EtOH. (IV) was regenerated by passing H_2S through a suspension of the mercaptide in Et_2O. The solvent was evaporated and (IV) was obtained in a pure state. Yield, 2 g. *Anal.* Calcd. for $C_{11}H_{11}O_2ClS$: C, 54.43; H, 4.54. Found : C, 54.32; H, 4.88.

Esterification of (VI)——To a solution of (VI)[5] (3 g.) in dehyd. EtOH (50 cc.), dry HCl gas was introduced under ice cooling. After HCl was saturated, the mixture was allowed to stand overnight at room temperature and the solvent was evaporated. Residual oil was extracted with Et_2O, which was washed with H_2O, dried over Na_2SO_4, and evaporated. The residual reddish oil of (II) was distilled in a diminished pressure. Yield, 1.5 g. b.p$_4$ 130~135°.

Addition of Thiourea to Ethyl Phenylpropionate——A mixture of thiourea (2.1 g.) and ethyl phenylpropionate (4 g.) in Me_2CO (15 cc.) was refluxed for 25 hr. and the solvent was evaporated. Residual yellowish crystals (VII) were recrystallized from EtOH to colorless needles, m.p. 215°. Yield,

Table III. Metal Chelates

X	m.p. (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. Metal	Found C	Found H	Found Metal
Cu Chelate								
H	188~190	$C_{11}H_{11}O_2CuS$	48.80	4.07	23.48	48.84	4.03	23.61
Cl	218~220	$C_{11}H_{10}O_2ClCuS$	43.20	3.30		43.26	3.48	*
NO_2		$C_{11}H_{10}O_4NCuS$	41.84	3.19	20.12	41.26	3.59	21.70
* Unreasonable value was obtained.								
								
NO_2	173~175	$C_{22}H_{20}O_8N_2CuS_2$	46.52	3.52	11.19	46.58	3.71	11.89
Ni Chelate								
H	198~200	$C_{22}H_{22}O_4NiS_2$	55.85	4.65	12.42	55.56	4.84	12.72
Cl	214~215	$C_{22}H_{20}O_4Cl_2NiS_2$	48.74	3.72	10.83	49.00	4.01	11.07
NO_2	245	$C_{22}H_{20}O_8N_2NiS_2$	46.92	3.55	10.43	46.84	3.68	11.06
Co Chelate								
H	184~186	$O_{33}H_{33}O_6CoS_3$	58.24	4.85	8.66	57.36	4.99	8.67
NO_2	187	$C_{33}H_{30}O_{12}N_3CoS_3$	48.59	3.68	7.23	48.34	3.63	7.54
Fe Chelate								
H	139~140	$C_{33}H_{33}O_6FeS_3$	58.50	4.88	8.26	58.24	4.90	8.28
Cl	114~115	$C_{33}H_{30}O_6Cl_3FeS_3$	50.75	3.85	7.15	51.83	3.93	7.45
NO_2	158~160	$C_{33}H_{30}O_{12}N_3FeS_3$	48.78	3.66	6.87	48.77	3.92	6.38

3 g. *Anal.* Calcd. for $C_{10}H_8ON_2S$: C, 58.82; H, 3.95; N, 13.72; S, 15.67. Found: C, 58.59; H, 4.16; N, 14.00; S, 15.60.

Preparation of Copper Chelate——EtOH solution of the ligand and aqueous solution of excess $(AcO)_2Cu\cdot H_2O$ were mixed and warmed on a water bath with shaking for a few minutes. Orange-colored viscous oil that separated out was extracted with Et_2O, which was washed with H_2O and the solvent was evaporated. To the residual oil, petr. ether was added and orange crystals of Cu chelate were purified by reprecipitation from $CHCl_3$-EtOH. Microanalytical data and melting points of Cu chelates are shown in Table III.

Preparation of Nickel Chelate——EtOH solution of the ligand and aqueous solution of excess $(AcO)_2Ni\cdot 4H_2O$ were mixed and shaken for a few minutes. Orange-red Ni chelate that precipitated was collected and washed with H_2O and EtOH. Microanalytical data and melting points are shown in Table III.

Preparation of Cobalt Chelate——EtOH solution of the ligand and aqueous solution of excess $(AcO)_2Co\cdot 4H_2O$ were mixed and shaken for a few minutes. Brown oil that separated out was extracted with Et_2O, which was washed with H_2O and the solvent was evaporated in a diminished pressure at room temperature. Green crystals of Co chelate that separated gradually were collected and washed with H_2O and a small portion of Et_2O. Microanalytical data and melting points are shown in Table III.

Preparation of Iron Chelate——EtOH solution of the ligand and aqueous solution of excess $FeCl_3$ were mixed and shaken for a few minutes. Green oil that separated out was extracted with Et_2O, which was washed with H_2O and the solvent was evaporated in a diminished pressure at room temperature. To the residual oil, petr. ether was added and the green crystals of Fe chelate were collected and washed with H_2O and petr. ether. Microanalytical data and melting points are shown in Table III.

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Summary

α,β-Unsaturated β-mercapto-acid esters were prepared and their chelating ability with metals was investigated. α,β-Unsaturated β-mercapto-acid esters formed stable chelates with copper, nickel, cobalt, and iron. These chelates involve conjugated double bond in the chelate ring, so that they were more stable than the chelates without a conjugated double bond. The ratio of the ligand to the metal was found to be 1:1 or 2:1 in copper chelates, 2:1 in nickel chelates, 3:1 in cobalt chelates, and 3:1 in iron chelates. The preparation of α,β-unsaturated β-mercaptoketones was planned but the substance obtained was present in a thioxo form and did not have a chelating ability.

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