UDC 547.569-386 : 546.56

50. **Hisashi Tanaka and Akira Yokoyama :** Studies on the Sulfur-containing Chelating Agents. II. Syntheses of β-Mercaptoketones and their Copper Chelates. (2).

(*Faculty of Pharmacy, University of Kyoto*[1])

In the previous paper,[2] it was shown that β-mercapto-β-phenylpropiophenone and its derivatives are prepared by the addition of hydrogen sulfide to α-benzylideneacetophenones and that they formed a chelate compound with copper.

This paper describes the syntheses of several β-mercaptoketones, using the same method as that described in the previous paper, and their copper-chelate compounds. In an attempt to examine the effect of various substituents in β-mercapto-β-phenylpropiophenones on chelate formation, attempt was made to synthesize β-mercapto-β-phenylpropiophenones with substituents such as methyl, chloro, methoxyl, or nitro, and also β-mercapto-β-(1-naphthyl)propiophenone. The results are summarized in Table I and it was found that in some cases corresponding mono- and di-sulfides were also separated.

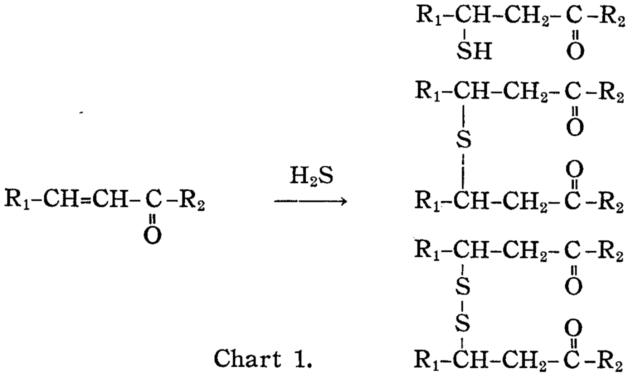

Chart 1.

Table I. Result of the Addition of Hydrogen Sulfide to α,β-Unsaturated Ketones

Starting material	Product
α-*m*-Methylbenzylideneacetophenone $R_1 = m\text{-}H_3C\text{-}C_6H_4\text{-}$, $R_2 = C_6H_5\text{-}$	β-Mercapto-β-(*m*-tolyl)propiophenone (I)
α-*p*-Chlorobenzylideneacetophenone $R_1 = p\text{-}Cl\text{-}C_6H_4\text{-}$, $R_2 = C_6H_5\text{-}$	β-Mercapto-β-(*p*-chlorophenyl)propiophenone (II) Bis(1-*p*-chlorophenyl-3-phenyl-3-oxopropyl) sulfide (III) Bis(1-*p*-chlorophenyl-3-phenyl-3-oxopropyl) disulfide (IV)
α-Benzylidene-*p*-chloroacetophenone $R_1 = C_6H_5\text{-}$, $R_2 = p\text{-}Cl\text{-}C_6H_4\text{-}$	β-Mercapto-β-phenyl-*p*-chloropropiophenone (V) Bis(1-phenyl-3-*p*-chlorophenyl-3-oxopropyl) sulfide (VI) Bis(1-phenyl-3-*p*-chlorophenyl-3-oxopropyl) disulfide (VII)
α-Benzylidene-*p*-methoxyacetophenone $R_1 = C_6H_5\text{-}$, $R_2 = p\text{-}CH_3O\text{-}C_6H_4\text{-}$	β-Mercapto-β-phenyl-*p*-methoxypropiophenone (VIII) Bis(1-phenyl-3-*p*-methoxyphenyl-3-oxopropyl) disulfide (IX)
α-*p*-Nitrobenzylideneacetophenone $R_1 = p\text{-}O_2N\text{-}C_6H_4\text{-}$, $R_2 = C_6H_5\text{-}$	Bis(1-*p*-nitrophenyl-3-phenyl-3-oxopropyl) sulfide (X)
α-1-Naphthylideneacetophenone $R_1 = 1\text{-}C_{10}H_7\text{-}$, $R_2 = C_6H_5\text{-}$	β-Mercapto-β-(1-naphthyl)propiophenone (XI)

As shown in Table I, mercaptoketones, monosulfides, and disulfides formed simultaneously and it was very difficult to separate them from each other and purify them. These mercaptoketones are very unstable towards alkali, as reported previously, so that alkali could not be used for their separation. Therefore, fractional recrystallization from

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[1] Yoshida, Sakyo-ku, Kyoto (田中 久, 横山 陽).

[2] Part I : This Bulletin 8, 275(1960).

various solvents was repeated for separation and purification. However, in the case of β-mercapto-β-phenyl-*p*-chloropropiophenone (V), the separation was so difficult that only traces of (V) were obtained as purified crystals. The formation of (V) was confirmed from the results of Rheinboldt test[1] and copper-chelate formation. Addition of hydrogen sulfide to α-*p*-nitrobenzylideneacetophenone did not occur when dimethylformamide or ether was used as a solvent under various conditions, and corresponding monosulfide was obtained when toluene and triethylamine were used as a solvent and catalyst, respectively.

Generally, as described in the experimental part, the addition of hydrogen sulfide was greatly affected by the type of solvent used. From this fact, it is presumed that the dissociation of hydrogen sulfide and the catalyst, such as triethylamine and piperidine in various organic solvents, has some effect on the addition reaction.

As described above, β-mercaptoketone with a nitro group could not be obtained by the addition of hydrogen sulfide, so that a different method of preparation was attempted.

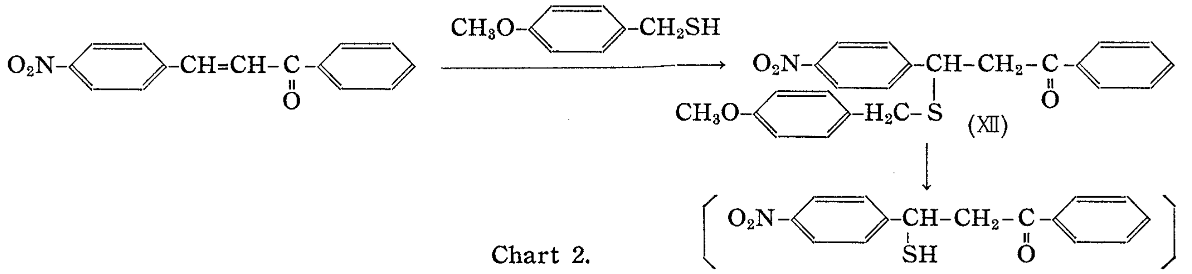

Chart 2.

In compound (XII), linkage between sulfur and carbon of *p*-methoxybenzyl group was expected to be cleaved rather easily by the influence of a methoxyl group and a corresponding thiol would be obtained if (XII) is decomposed by the acid in a proper way. This idea was derived from the fact reported by Gierer[2] that vanillyl phenyl sulfide and vanillyl ethyl sulfide were decomposed by treatment with hydrochloric or hydrobromic acid, and thiophenol and ethanethiol were respectively obtained.

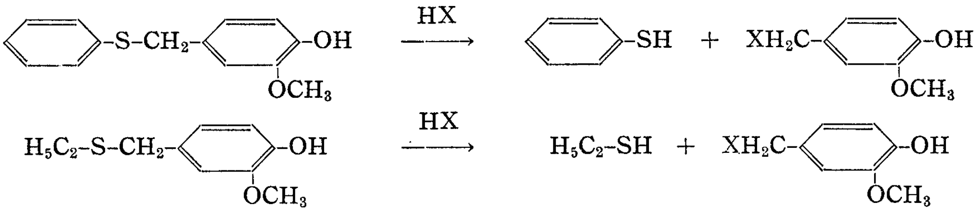

Chart 3.

p-Methoxyphenylmethanethiol was first prepared from *p*-methoxybenzyl chloride and thiourea, and added to α-*p*-nitrobenzylideneacetophenone to form β-(*p*-methoxybenzylthio)-β-(*p*-nitrophenyl)propiophenone (XII). (XII) was treated with hydrochloric or hydrobromic acid under various conditions in an attempt to obtain mercaptoketone, but no decomposition occurred and (XII) was recovered almost completely.

β-Mercaptoketones obtained showed a red or orange color with the Rheinboldt test[1] and formed chelate compounds with Cu^{2+}, irrespective of the substituents.

Copper chelates were prepared by the method described in the previous paper and are listed in Table II. The ratio of ligand to copper was found to be 1:1 from the analytical data. In the case of the preparation of copper chelate from β-mercapto-β-phenyl-*p*-chloropropiophenone (V), an interesting fact was observed. It was found that copper chelate prepared from (V) did not contain chlorine and was found to be identical with the copper chelate obtained from β-mercapto-β-phenylpropiophenone. This was

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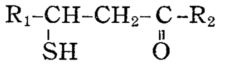
[1] H. Rheinboldt : Chem. Ber., **59**, 1311(1926).
[2] J. Gierer, B. Alfredsson : *Ibid.*, **90**, 1240(1957).

considered to be due to dechlorination by copper. As described above, the purification of (V) was so difficult that copper chelate was prepared directly from the reaction mixture without separation and purification of (V).

TABLE II. Copper Chelates of β-Mercaptoketones

Ligand

$R_1\text{-}\underset{\text{SH}}{\text{CH}}\text{-}CH_2\text{-}\underset{\text{O}}{\overset{}{\text{C}}}\text{-}R_2$

				Analysis (%)					
R_1	R_2	m.p. (°C)	Formula	Calcd.			Found		
				C	H	Cu	C	H	Cu
$m\text{-}H_3C\text{-}C_6H_4\text{-}$	$C_6H_5\text{-}$	90~91	$C_{16}H_{15}OSCu$	60.28	4.71	19.94	60.16	4.66	20.09
$p\text{-}Cl\text{-}C_6H_4\text{-}$	$C_6H_5\text{-}$	120	$C_{15}H_{12}OClSCu$	53.10	3.54	18.73	52.92	3.56	18.32
$C_6H_5\text{-}$ *	$p\text{-}Cl\text{-}C_6H_4\text{-}$	115	$C_{15}H_{13}OSCu$	59.11	4.24	20.85	59.53	4.37	20.71
$C_6H_5\text{-}$	$p\text{-}CH_3O\text{-}C_6H_4\text{-}$	128	$C_{16}H_{15}O_2SCu$	57.39	4.48	18.98	57.03	4.76	19.07
$1\text{-}C_{10}H_7\text{-}$	$C_6H_5\text{-}$	116~117	$C_{19}H_{15}OSCu$	64.32	4.23	17.91	64.28	4.33	17.97

* Dechlorination occurred

Experimental

α-*m*-Methylbenzylideneacetophenone—To a solution of *m*-tolualdehyde (5 g.) and acetophenone (5 g.) in EtOH (20 cc.), 10% NaOH (2 cc.) was added dropwise with stirring at room temperature and the mixture was allowed to stand for 2 days with occasional stirring. Crystals that separated out were collected and recrystallized from EtOH to pale yellow needles, m.p. 62~62.5°. Yield, 4 g. The m.p. did not agree with that reported by Giua.[3] *Anal.* Calcd. for $C_{16}H_{14}O$: C, 86.45; H, 6.35. Found: C, 86.31; H, 6.17.

β-Mercapto-β-(*m*-tolyl)propiophenone (I)—A solution of α-*m*-methylbenzylideneacetophenone (2 g.) and triethylamine (2 g.) in dehyd. Et_2O (100 cc.) was placed in a pressurized bottle, dry H_2S gas was introduced, and liquefied under dry ice-acetone chilling at −70° to −80°. After H_2S (12 cc.) was added, the mixture was allowed to stand over night at room temperature and heated at 40~50° for 7 hr. under pressure. Et_2O solution was washed with dil. HCl and H_2O, dried over Na_2SO_4, and evaporated to leave colorless crystals (2.5 g.) of (I). Recrystallization from EtOH gave colorless plates, m.p. 73°. Rheinboldt test, red. *Anal.* Calcd. for $C_{16}H_{16}OS$: C, 74.98; H, 6.29; S, 12.50. Found : C, 75.27; H, 6.31; S, 12.51.

β-Mercapto-β-(*p*-chlorophenyl)propiophenone (II), Bis(1-*p*-chlorophenyl-3-phenyl-3-oxopropyl) Sulfide (III), and Bis(1-*p*-chlorophenyl-3-phenyl-3-oxopropyl) Disulfide (IV)—i) To a solution of α-*p*-chlorobenzylideneacetophenone (3 g.) and triethylamine (1 g.) in dehyd. Et_2O (60 cc.), H_2S (15 cc.) was added as described above. After standing over night, the mixture was heated at 50° for 4 hr. under pressure. Crystals of (IV) (1 g.) that separated out were collected and recrystallized from $CHCl_3$ to colorless needles, m.p. 197°. *Anal.* Calcd. for $C_{30}H_{24}O_2Cl_2S_2$: C, 65.34; H, 4.36; O, 5.81. Found : C, 65.08; H, 4.64; O, 5.83.

Et_2O solution was washed with dil. HCl and H_2O, dried over Na_2SO_4, and evaporated. The residue was extracted with hot EtOH and colorless plates, m.p. 68°, of (II) (0.2 g.) were obtained. *Anal.* Calcd. for $C_{15}H_{13}OClS$: C, 65.10; H, 4.70; O, 5.79. Found : C, 65.29; H, 5.00; O, 5.67.

ii) To a solution of α-*p*-chlorobenzylideneacetophenone (5 g.) and triethylamine (1 g.) in a mixture of dehyd. $CHCl_3$ (40 cc.) and dehyd. Et_2O (60 cc.), H_2S (10 cc.) was added as described above. After the mixture was heated at 40° for 4 hr. under pressure, solvent was removed and the residue was dissolved in Et_2O leaving a mixture of (IV) and (III). A small amount of (III) separated from the mixture by extraction with hot EtOH and recrystallized from EtOH to colorless needles, m.p. 98~99°. *Anal.* Calcd. for $C_{30}H_{24}O_2Cl_2S$: C, 69.37; H, 4.66, Found : C, 69.26; H, 4.94.

(IV) (3 g.) was obtained from the residue, m.p. 197°.

β-Mercapto-β-phenyl-*p*-chloropropiophenone (V), Bis(1-phenyl-3-*p*-chlorophenyl-3-oxopropyl) Sulfide (VI), and Bis(1-phenyl-3-*p*-chlorophenyl-3-oxopropyl) Disulfide (VII)—i) To a solution of α-benzylidene-*p*-chloroacetophenone (4 g.) and triethylamine (1 g.) in dehyd. Et_2O (50 cc.), H_2S (14 cc.) was added as described above. After heating at 40° for 4 hr. under pressure, the mixture was allowed to stand for 4 days at room temperature, washed with dil. HCl and H_2O, and then evaporated. The residue was extracted with Et_2O. Insoluble crystals (VII) were collected and recrystallized from $CHCl_3$ to colorless needles, m.p. 160°. *Anal.* Calcd. for $C_{30}H_{24}O_2Cl_2S_2$: C, 65.34; H, 4.36; O, 5.81. Found: C, 65.16; H, 4.58; O, 5.67.

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3) M. Giua : Gazz. chim. ital., **46**, I, 293(1916).

Et_2O solution was evaporated, the residue was extracted with EtOH, and a small amount of colorless crystals (V), m.p. 81°, were obtained. Rheinboldt test, red.
ii) To a solution of α-benzylidene-*p*-chloroacetophenone (2 g.) and triethylamine (1 g.) in $CHCl_3$ (60 cc.), H_2S (10 cc.) was added as described above. After heating at 40° for 8 hr. under pressure, the mixture was washed with dil. HCl and H_2O, dried over Na_2SO_4, and the solvent was removed. The oily residue was extracted with Et_2O and crystals (VII) (0.5 g.) were obtained. Et_2O solution was evaporated and the residue was distilled under reduced pressure, affording a yellow-orange oil (VI) (0.5 g.) of b.p$_4$ 191°. The distillate crystallized after standing for a prolonged period. m.p. 30°. *Anal.* Calcd. for $C_{30}H_{24}O_2Cl_2S$: C, 69.37; H, 4.66. Found : C, 69.19; H, 4.83.

β-Mercapto-β-phenyl-*p*-methoxypropiophenone (VIII) and Bis(1-phenyl-3-*p*-methoxyphenyl-3-oxopropyl) Disulfide (IX)—i) To a solution of α-benzylidene-*p*-methoxyacetophenone (3 g.) and triethylamine (1 g.) in dehyd. EtOH (50 cc.), H_2S (14 cc.) was added as described above. After standing over night, the mixture was heated at 70~80° for 4 hr. under pressure. Colorless crystals (IX) that separated out were collected and recrystallized from $CHCl_3$ to colorless needles, m.p. 167~168°. Yield, 3 g. *Anal.* Calcd. for $C_{32}H_{30}O_4S_2$: C, 70.83; H, 5.57. Found : C, 70.55; H, 5.66.
ii) To a solution of α-benzylidene-*p*-methoxyacetophenone (5 g.) and triethylamine (1 g.) in $CHCl_3$ (50 cc.), H_2S (15 cc.) was added as described above. After heating at 30~40° for 3 hr. under pressure, the solvent was removed. The oily residue was extracted with Et_2O and insoluble crystals (IX) (4 g.) were obtained. Et_2O solution was washed with dil. HCl and H_2O, dried over Na_2SO_4, and evaporated. The oily residue was extracted with hot EtOH and colorless plates (VIII) (0.1 g.), m.p. 87°, were obtained when cooled. Rheinboldt test, red. *Anal.* Calcd. for $C_{16}H_{16}O_2S$: C, 70.57; H, 5.92. Found: C, 70.87; H, 6.18.

Bis(1-*p*-nitrophenyl-3-phenyl-3-oxopropyl) Sulfide (X)—To a solution of α-*p*-nitrobenzylideneacetophenone (4 g.) and triethylamine (0.1 cc.) in toluene (100 cc.), H_2S (12 cc.) was added as described above. After heating at 80° for 5 hr. under pressure, the mixture was allowed to stand for 2 days. Colorless crystals (X) (1 g.) that separated out were collected and recrystallized from $CHCl_3$-EtOH to colorless needles, m.p. 158°. *Anal.* Calcd. for $C_{30}H_{24}O_6N_2S$: C, 66.66; H, 4.48; N, 5.18. Found : C, 66.44; H, 4.59; N, 5.16.

α-1-Naphthylideneacetophenone—To a solution of 1-naphthaldehyde (5 g.) and acetophenone (4 g.) in EtOH (50 cc.), 10% NaOH (4 cc.) was added with stirring at room temperature. Yellow needles that separated out were collected (9 g.) and recrystallized from EtOH, m.p. 69~70°. *Anal.* Calcd. for $C_{19}H_{14}O$: C, 88.34; H, 5.46. Found : C, 88.47; H, 5.67.

β-Mercapto-β-(1-naphthyl)propiophenone (XI)—To a solution of α-1-naphthylideneacetophenone (3 g.) in dehyd. Et_2O (100 cc.), a few drops of piperidine and H_2S (13 cc.) were added as described above. After heating at 40~50° for 2 hr., the mixture was washed with dil. HCl and H_2O, dried over Na_2SO_4, and evaporated. The oily residue was extracted with EtOH and colorless crystals (XI) (0.1 g.), m.p. 92~93°, were obtained after cooling. Rheinboldt test, orange-red. *Anal.* Calcd. for $C_{19}H_{16}OS$: C, 78.06; H, 5.52. Found : C, 78.15; H, 5.75.

***p*-Methoxyphenylmethanethiol**—A solution of *p*-methoxybenzyl chloride (17 g.) and thiourea (8.3 g.) in EtOH (40 cc.) was refluxed for 5 hr., 10% NaOH (60 cc.) was added, and heating was continued for 2 hr. After cool, the reaction mixture was acidified with dil. H_2SO_4, extracted with Et_2O, washed with H_2O, dried over Na_2SO_4 and evaporated. The oily residue was distilled under reduced pressure and a colorless oil, b.p$_{23}$ 126~128°, was obtained. Yield, 12 g. *Anal.* Calcd. for $C_8H_{10}OS$: C, 62.32; H, 6.54. Found : C, 62.53; H, 6.73.

β-(*p*-Nitrophenyl)-β-(*p*-methoxybenzylthio)propiophenone (XII)—α-*p*-Nitrobenzylideneacetophenone (2 g.) and *p*-methoxyphenylmethanethiol (1 cc.) were dissolved in toluene and 2 drops of piperidine were added. The mixture was heated on a water bath and allowed to stand for 4 days. Crystals that separated out were collected and recrystallized from EtOH to colorless needles, m.p. 101°. Yield, 2 g. *Anal.* Calcd. for $C_{23}H_{21}O_4NS$: C, 67.80; H, 5.20. Found : C, 67.51; H, 5.37.

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Summary

β-Mercaptoketones, β-mercapto-β-(*m*-tolyl)- and β-mercapto-β-(*p*-chlorophenyl)-propiophenone, β-mercapto-β-phenyl-*p*-chloropropiophenone, β-mercapto-β-phenyl-*p*-methoxypropiophenone, and β-mercapto-β-(1-naphthyl)propiophenone, were prepared by the addition of hydrogen sulfide to the corresponding α-benzylideneacetophenones and α-1-naphthylideneacetophenone. These mercaptoketones formed chelate compounds with copper and the ratio of ligand to copper was found to be 1:1.

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