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Some Metal Complexes of 2-Mercaptopropionylglycine[1]

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Stability constants of complexes formed by zinc, cadmium, lead (II) and iron (II) with 2-mercaptopropionylglycine ($MPGH_2$) have been calculated from pH titration data at 25° and $\mu=0.15$ ($NaClO_4$). In case of mercury (II), titrations were performed with mercury (II)–iodide–$MPGH_2$ mixtures at $\mu=0.5$ (KNO_3). Mercury (II) complexes of $MPGH_2$ and other related compounds have been isolated and their structures were studied with infrared spectra.

Sulfhydryl compounds are widely distributed in animals, plants and microorganisms, participating in various enzymatic reactions, peptide-hormone activities and other important biological phenomena. They also function as antidotes against heavy metal ions by forming stable coordination compounds.[3] 2-Mercaptopropionylglycine is one of these compounds and has been reported to enhance the excretion of mercury,[4] copper[5] and iron[6] compounds.

Many investigations have been reported on the stability constants and structures of various metal complexes of sulfhydryl compounds. Among them sulfur-containing amino acids such as cysteine,[7–12] glutathione,[7,12] penicillamine,[8,10,13] cysteine esters[7,9,11,14] and methionine[15] have been studied in detail as chelating ligands. Most of these compounds are potentially terdentate ligands containing –SH, $-NH_2$ and –COOH groups as binding sites. 2-Mercaptopropionylglycine is a ligand of novel type bearing –SH, –CONH– and –COOH groups. Coordination of the –CONH– group has been studied in the Cu(II)-glycylglycine system,[16] but chelate formation by sulfhydryl and amide groups has not yet been reported, and it seems very interesting to compare stabilities of metal complexes of 2-mercaptopropionylglycine with those of cysteine and other related compounds.

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3) *e.g.* H.V. Aposhian, *Science*, **128**, 93 (1958).
4) I. Mita, *et al.*, The 23rd Meeting of Pharmaceutical Society of Japan, 1966; E. Sebe, *et al.*, *J. Kumamoto Med. Soc.*, **35**, 1261 (1961); T. Tsubaki and K. Shirakawa, *J. New Remedies and Clinics*, **15**, 1471 (1966); M. Ogata, *et al.*, *Med. Assoc. Okayama*, **80**, 297 (1968).
5) H. Miki, *J. Clin. Pediat.*, **12**, 111 (1964).
6) Y. Ohta, *Med. Assoc. Okayama*, **78**, 1297 (1966).
7) N.C. Li and R.A. Manning, *J. Am. Chem. Soc.*, **77**, 5225 (1955).
8) G.R. Lenz and A.E. Martell, *Biochemistry*, **3**, 745 (1964).
9) H. Shindo and T.L. Brown, *J. Am. Chem. Soc.* **87**, 1904 (1965).
10) D.D. Perrin and I.G. Sayce, *J. Chem. Soc.* (*A*), **1968**, 53.
11) V.M. Kothari and D.H. Busch, *Inorg. Chem.*, **8**, 2276 (1969).
12) T.J. Huang and G.P. Haight, Jr., *Chem. Commun.*, **1969**, 985.
13) *a*) Y. Sugiura, A. Yokoyama, and H. Tanaka, *Chem. Pharm. Bull.* (Tokyo), **18**, 693 (1970); *b*) Y. Sugiura and H. Tanaka, *ibid.*, **18**, 368 (1970); *c*) Y. Sugiura and H. Tanaka, *ibid.*, **18**, 746 (1970).
14) L.J. Porter, D.D. Perrin, and R.W. Hay, *J. Chem. Soc.*, (A), **1969**, 118.
15) C.A. McAuliffe, J.V. Quagliano and L.M. Vallarino, *Inorg. Chem.*, **5**, 1996 (1966); S.E. Livingstone and J.D. Nolan, *ibid.*, **7**, 1447 (1968); M.V. Verdis and G.J. Palenik, *Chem. Commun.*, **1969**, 1277; M.R. Marrison and F.J.G. Rossotti, *ibid.*, **1970**, 175.
16) M.K.Kim and A.E. Martell, *Biochemistry*, **3**, 1169 (1964).

In this paper are reported rather preliminary values of stability constants of 2-mercaptopropionylglycine complexes with Cd, Zn, Pb(II), Hg(II) and Fe(II) ions determined by the pH titration method on the "MLn only" approximation. Of these metal ions mercury(II) was found to form an extremely stable 1:2 complex with the present ligand in accordance with its high affinity for the sulfur atom. With aim of clarifying the other bonding site of the ligand, mercury(II) complexes of 2-mercaptopropionylglycine and other related compounds have been isolated and their structures were studied mainly with infrared (IR) spectra.

Experimental

Materials——2-Mercaptopropionylglycine was synthesized by the Schotten–Baumann reaction between α-bromopropionyl chloride and glycine followd by condensation with thiobenzoic acid and hy drolysisin a basic medium.[17] White crystals (mp 95—97°) were obtained by recrystallization from ethyl acetate. Since the aqueous solution of this compound tends to be oxidized by atmospheric oxygen, a freshly prepared solution was used in each titration, and the ligand concentration was determined by an iodometric method. Perchlorates of cadmium, zinc and lead (II) were purchased from Shimakyu Chemical Co., Ltd. and used without further purification. Stock solutions of the metal salts were standardized by titration with ethylenediaminetetraacetic acid solutions supplied by Dojindo Co., Ltd. Iron (II) sulfate solutions were prepared employing Mohr's salt and determined by titration with cerium (IV) sulfate sloutions. Red mercury (II) iodide supplied by Wako Pure Chemical Industries, Ltd. was dissolved in water in the coexistence of excess potassium iodide. Purity of the HgI_2 specimen was determined by the JIS method.[18] Sodium perchlorate was purchased from Kanto Chemical Co., Ltd., and used without further purification. Carbonate-free sodium hydroxide solutions were prepared according to Ohtaki's direction[19] employing solid sodium hydroxide from Wako. Water was deionized through ion exchange columns and then distilled.

pH Titrations——All titrations were carried out at $25.0 \pm 0.1°$ employing a 200 ml five-necked flask equipped with a 5 ml micro-burette, a stirrer, electrodes of a pH meter, and nitrogen inlet and outlet tubes. A Beckman Expandmatic pH meter was used to determine hydrogen-ion concentrations. Aqueous solutions (100 ml in each case) were prepared from oxygen-free water and made up to an ionic strength of 0.15 with sodium perchlorate. In case of Hg (II), solutions were made up to an ionic strength of 0.5 with potassium nitrate and titrated with potassium hydroxide solutions in order to utilize stability data of Hg (II) iodide complexes reported by Sillén[20] and Marcus.[21]

Preparations of Mercury (II) Complexes of 2-Mercaptopropionylglycine and Related Compounds——Mercury (II) complexes of the following ligands were prepared.

$CH_3CH(SH)CONHCH_2COOH$	2-mercaptopropionylglycine ($MPGH_2$)
$CH_3CH(SH)CONHCH_2COOC_2H_5$	ethyl 2-mercaptopropionylglycinate (MPGEH)
$CH_3CH(SH)COOH$	2-mercaptopropionic acid (MPH_2)
$CH_3CH(SH)COOC_2H_5$	ethyl 2-mercaptopropionate (MPEH)
$CH_3CH(SH)CONH_2$	2-mercaptopropionamide (MPAH)

To a methanol suspension of red mercury (II) oxide was added a methanol solution of twice moles of $MPGH_2$ under stirring. Red powder of mercury (II) oxide disappeared resulting in a colorless solution. Methanol was evaporated on a steam bath. White crystals were obtained after recrystallization from water.

One gram of the above complex $Hg(MPGH)_2$ was dissolved in 50 ml of ethanol together with 1 g of *p*-toluenesulfonic acid. Esterification of the ligand proceeded on standing overnight and white precipitate of $Hg(MPGE)_2$ appeared and was recrystallized from benzene.

An aqueous solution of mercury (II) chloride was added to an aqueous solution of 2-mercaptopropionic acid (MPH_2) under agitation. A white precipitate of $Hg(MPH)_2$ was recrystallized from water. Reverse mixing of reactants is not satisfactory.

To a methanol suspension of red mercury (II) oxide was added twice moles of ethyl 2-mercaptopropionate (MPEH). After red powder of mercury (II) oxide disappeared, methanol was evaporated. Residual liquid complex Hg $(MPE)_2$ was purified by distillation *in vacuo*.

17) I. Mita, N. Toshioka and S. Yamamoto, Japan Patent 11616 (1964).
18) JIS K-8916, "JIS Handbook," 1968, p. 728.
19) H. Ohtaki, "Muki-yoeki-kagaku (Inorganic Solution Chemistry)," ed. by K. Yamasaki, J. Matsuura, N. Tanaka, and R. Tamamushi, Nankodo, Tokyo, 1968, p. 146.
20) L.G. Sillén, *Acta Chem. Scand.*, 3, 539 (1949).
21) Y. Marcus, *Acta Chem. Scand.*, 11, 599 (1957).

The mercury (II) complex of 2-mercaptopropionamide, $Hg(MPA)_2$, was prepared by the same method as for $Hg(MPGH)_2$, and recrystallized from methanol.

Results of the elemental analysis of these complexes are summarized in Table I. The mercury content of $Hg(MPGH)_2$ was determined by an electrolytic method, but this method was not satisfactory for other similar complexes and the gravimetric analysis as mercury (II) sulfide was employed. The ligand content of each compound was measured by an iodometric method after dissolution of the complex in hydrochloric acid.

TABLE I. Analytical Data of Mercury (II) Complexes with 2-Mercaptopropionylglycine and Related Compounds

Complex	% Found (% calcd)				
	C	H	N	Hg	Ligand
$Hg(MPGH)_2$	22.95	3.78	5.42	37.54	61.5
$=C_{10}H_{16}O_6N_2S_2Hg$	(22.88)	(3.07)	(5.34)	(38.21)	(61.9)
$Hg(MPGE)_2$	28.92	4.44	4.74	34.49	64.8
$=C_{14}H_{24}O_6N_2S_2Hg$	(28.94)	(4.16)	(4.82)	(34.53)	(65.5)
$Hg(MPH)_2$	17.74	2.54		47.15	50.9
$=C_6H_{10}O_4S_2Hg$	(17.54)	(2.45)		(48.82)	(51.2)
$Hg(MPE)_2$	26.38	4.07		40.42	56.2
$=C_{10}H_{18}O_4S_2Hg$	(25.72)	(4.32)		(42.95)	(57.1)
$Hg(MPA)_2$	17.47	3.15	7.03	46.89	50.6
$=C_6H_{12}O_2N_2S_2Hg$	(17.62)	(3.45)	(6.85)	(49.06)	(50.9)

Reaction of $Hg(MPA)_2$ with Copper(II) Perchlorate——Finely powdered $Hg(MPA)_2$ (200 mg) was added to an acetone solution of $Cu(ClO_4)_2 \cdot 6H_2O$ (200 mg) and stirred vigorously. After the mixture became transparent blue precipitate was separated out. The precipitate was filtered, washed with acetone (slightly soluble) and dried *in vacuo*. Yield 300 mg. The blue compound is very hygroscopic and changed to green mass, but the latter is no more hygroscopic and submitted to the elemental analysis. The weight increase was 10.8%. The perchlorate content of the unstable blue compound was determined gravimetrically as the nitron salt.

Found for the blue compound: ClO_4 22.7%. Calcd for $[Hg(MPA)_2]_3[Cu(ClO_4)_2]_2$: ClO_4 22.7%.

Found for the green compound: C, 11.1; H, 2.85%. Calcd for $[Hg(MPA)_2]_3[Cu(ClO_4)_2]_2 \cdot 10H_2O$: C, 11.2; H, 2.92%. The formula-weight ratio $[Hg(MPA)_2]_3[Cu(ClO_4)_2]_2 \cdot 10H_2O/[Hg(MPA)_2]_3[Cu(ClO_4)_2]_2$ is 1.103 coinciding with the observed weight increase of 10.8%.

Calculation, Result and Discussion

Acid Dissociation Constants

The pH titration curves of the dibasic acid, 2-mercaptopropionylglycine, are shown in Fig. 1 and 4. Since two steps of neutralization are well separated, acid dissociation constants were calculated independently from Eq. (1) and (2),

$$Q_1^H = \frac{[H^+](C_{OH}+[H^+]-[OH^-])}{C_{H_2L}-C_{OH}-[H^+]+[OH^-]} \quad (1)$$

$$Q_2^H = \frac{[H^+](C_{OH}+[H^+]-[OH^-]-C_{H_2L})}{2C_{H_2L}-C_{OH}-[H^+]+[OH^-]} \quad (2)$$

where C_{H_2L} represents the total concentration of the ligand in solution and C_{OH} that of base added in the particular buffer region under consideration. For computing hydrogen ion concentrations the activity coefficient was calculated to be 0.805 from theDebye- Hückel equation (3) employing Kielland's value of 9 Å for the ion-size parameter *a*.[22]

22) *a*) Chemical Society of Japan, "Kagaku-binran (Handbook of Chemical Data)," Pure Chemistry Part, Maruzen, Tokyo, 1966, p. 1049; *b*) J. Kielland, *J. Am. Chem. Soc.*, 59, 1675 (1937).

$$\log \gamma_i = -\frac{0.358 Z_i^2 \Gamma^{1/2}}{1+10^8 a \times 0.2325 \Gamma^{1/2}} \quad (3)$$

Here Γ is twice the ionic strength. The hydroxide-ion concentration was computed from the value[23] of $K_W = 1.008 \times 10^{-14}$ at 25°. As the molarity acid dissociation constants $pQ_1^H = 3.38$ and $pQ_2^H = 8.43$ were obtained. Thermodynamic acid dissociation constants were calculated to be $pK_1^H = 3.59$ and $pK_2^H = 8.87$ using $\gamma_{HL^-} = 0.768$ and $\gamma_{L^{2-}} = 0.347$ which were obtained from Eq. (3) assuming $a = 6$ Å for both the ligand anions L^- and L^{2-}.

The ionization of 2-mercaptopropionylglycine may be represented by Eq. (4) and (5).

$$\underset{(H_2L)}{\underset{\displaystyle\overset{|}{SH}}{CH_3CHCONHCH_2COOH}} \overset{K_1^H}{\rightleftarrows} \underset{(HL^-)}{\underset{\displaystyle\overset{|}{SH}}{CH_3CHCONHCH_2COO^-}} \quad (4)$$

$$\underset{(HL^-)}{\underset{\displaystyle\overset{|}{SH}}{CH_3CHCONHCH_2COO^-}} \overset{K_2^H}{\rightleftarrows} \underset{(L^{2-})}{\underset{\displaystyle\overset{|}{S^-}}{CH_3CHCONHCH_2COO^-}} \quad (5)$$

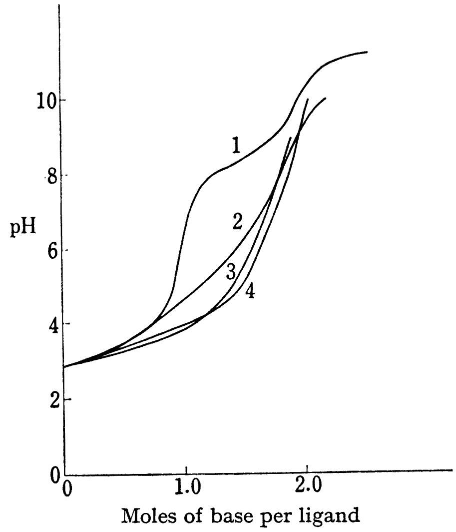


Fig. 1. Titration Curves for 2-Mercaptopropionylglycine in the Absence (Curve 1) and in thePresence of Zn^{2+}(2), Pb^{2+}(3) and Cd^{2+}(4) at 25.0° and $\mu = 0.15$ ($NaClO_4$)

$[MPGH_2] = 6.4 \times 10^{-3}$M, $[M^{2+}] = 2.2 \times 10^{-3}$M

Stability Constants

Fig. 2 shows titration curves for 1:1, 1:1.5, 1:2 and 1:3 molar ratios of Cd^{2+} to ligand. In each of the former three curves an inflection is observed when two moles of base is added per mole of ligand present, thus indicating the stepwise formation of 1:1 and 1:2 complexes. The curve for 1:3 molar ratio seems to involve neutralization of excess free ligand.

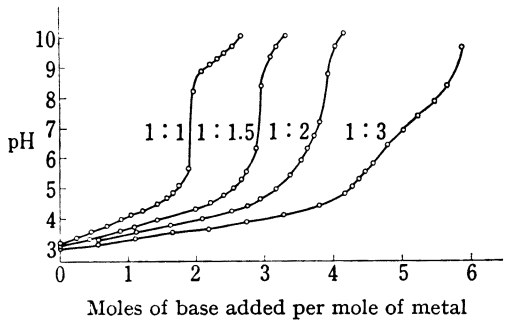


Fig. 2. Titration Curves for 1:1, 1:1.5, 1:2 and 1:3 Molar Ratios of Cd^{2+} to 2-Mercaptopropionylglycine at 25.0° and $\mu = 0.15$ ($NaClO_4$)

$[Cd^{2+}] = 1.988 \times 10^{-3}$M

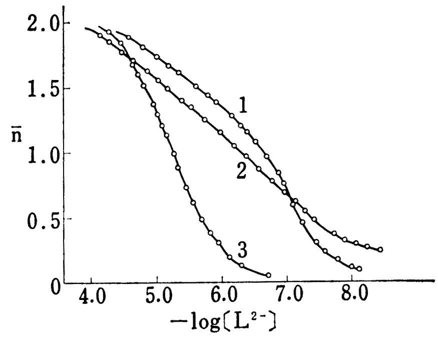


Fig. 3. Complex Formation Curves for pH Titrations of Cd^{2+} (Curve 1), Pb^{2+} (2), Zn^{2+}(3) and 2-Mercaptopropionylglycine at 25.0° and $\mu = 0.15$ ($NaClO_4$)

Concentrations were $[M^{2+}] = 1.988 \times 10^{-3}$M, $[MPGH_2] = 9.971 \times 10^{-3}$M.

Potentiometric titrations were repeated at various molar ratios of metal to ligand and formation curves as shown in Fig. 3 were obtained for Zn, Pb(II) and Cd complexes.

23) Ref. 22*a*) p. 1053.

According to the Bjerrum's method apparent stability constants were obtained as follows:

	Cd^{2+}	Pb^{2+}	Zn^{2+}
$\log K_1' = -\log[L^{2-}]$ at $\bar{n} = 0.5$	7.21	7.37	5.70
$\log K_2' = -\log[L^{2-}]$ at $\bar{n} = 1.5$	5.65	5.15	4.83

Here $\bar{n}$ is the average number of ligands bound per metal ion. To correct for the overlapping of K_1 and K_2 steps Takamoto's Eq. (6) and (7) were employed.[24]

$$\log K_1 = -\log[L^{2-}]_{0.5} + \log\left(1-\frac{3[L^{2-}]_{0.5}}{[L^{2-}]_{1.5}}\right) \qquad (6)$$

$$\log K_2 = -\log[L^{2-}]_{1.5} - \log\left(1-\frac{3[L^{2-}]_{0.5}}{[L^{2-}]_{1.5}}\right) \qquad (7)$$

Here $[L^{2-}]_{0.5}$ and $[L^{2-}]_{1.5}$ denote concentrations of free ligand at $\bar{n}=0.5$ and 1.5 respectively. Corrected values of thermodynamic stability constants are listed in Table II.

A titration curve for 1:2 molar ratio of Fe^{2+} to ligand is given in Fig. 4 together with that for the pure ligand. Formation constants of iron(II) complexes seem to be lower than those of other metals examined and the pH region of chelate formation is higher. The second buffer region extends through pH 9 and the second inflection point can not be observed. This may suggest liberation of another proton from the Fe(II) complex. Two sources of proton can be considered. One is a water molecule coordinated to Fe(II) and the other is the amide group of the ligand. Kim and Martell[16] investigated infrared spectra of Cu(II)-glycylglycine 1:1 complexes is D_2O solutions and found that at pD$\gtrsim$5.5 the amide proton was liberated prior to dissociation of the aguo proton.

Similar behavior might be observed in the present case, too. If the following equilibrium is assumed for the Fe^{2+}-$MPGH_2$ system, the apparent stability constant of the deprotonated complex is calculated as log Q_1=4.98.

$$Fe^{2+} + L^{2-} \rightleftarrows Fe(L\text{-}H)^- + H^+, \qquad Q_1 = \frac{[Fe(L\text{-}H)^-][H^+]}{[Fe^{2+}][L^{2-}]} \qquad (8)$$

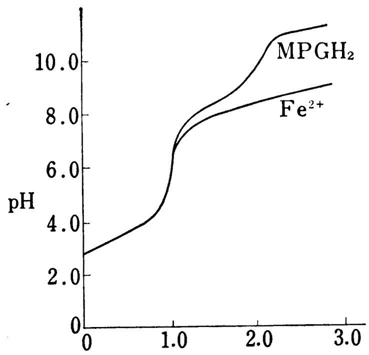


Fig. 4. Titration Curves for 2-Mercaptopropionylglycine and for a Mixture of Fe^{2+} and the Ligand at 25.0° and μ=0.15 ($NaClO_4$)

$[MPGH_2]=6.340\times10^{-3}$M, $[Fe^{2+}]=3.200\times10^{-3}$M

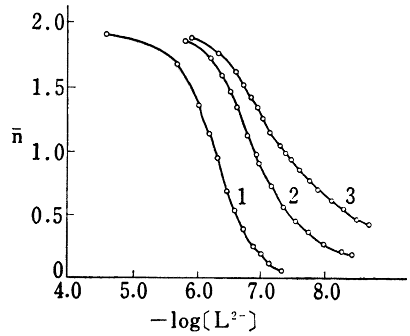


Fig. 5. Complex Formation Curves for pH Titrations of Hg^{2+} and 2-Mercaptopropionylglycine in the Presence of Potassium Iodide at 25.0° and μ=0.5 (KNO_3)

$[MPGH_2]=6.400\times10^{-3}$M, $[Hg^{2+}]=2.185\times10^{-3}$M, $[I^-]$=0.2M (Curve 1), 0.1M (2) and 0.05M (3)

24) S. Takamoto, Ref. 19) p. 199.

In case of mercury stability constants are so large that accurate values could not been obtained by the usual titration method. According to the method which Droll, Block and Fernelius[25] employed in determination of stability constants of palladium acetylacetonate complexes, potentiometric titrations were performed with mercury(II)–iodide–$MPGH_2$ mixtures. Complex formation reactions involved in this system are as follows:

$$Hg^{2+} + I^- \rightleftarrows HgI^+ \qquad Q_1^I = [HgI^+]/[Hg^{2+}][I^-] \tag{9}$$
$$HgI^+ + I^- \rightleftarrows HgI_2 \qquad Q_2^I = [HgI_2]/[HgI^+][I^-] \tag{10}$$
$$HgI_2 + I^- \rightleftarrows HgI_3^- \qquad Q_3^I = [HgI_3^-]/[HgI_2][I^-] \tag{11}$$
$$HgI_3^- + I^- \rightleftarrows HgI_4^{2-} \qquad Q_4^I = [HgI_4^{2-}]/[HgI_3^-][I^-] \tag{12}$$
$$Hg^{2+} + L^{2-} \rightleftarrows HgL \qquad Q_1 = [HgL]/[Hg^{2+}][L^{2-}] \tag{13}$$
$$HgL + L^{2-} \rightleftarrows HgL_2^{2-} \qquad Q_2 = [HgL_2^{2-}]/[HgL][L^{2-}] \tag{14}$$
$$Hg^{2+} + L^{2-} + I^- \rightleftarrows HgLI^- \qquad \beta_{1,1} = [HgLI^-]/[Hg^{2+}][L^{2-}][I^-] \tag{15}$$
$$Hg^{2+} + L^{2-} + 2I^- \rightleftarrows HgLI_2^{2-} \qquad \beta_{2,1} = [HgLI_2^{2-}]/[Hg^{2+}][L^{2-}][I^-]^2 \tag{16}$$

Then the average number of MPG ions ligated to a mercury ion is expressed by Eq. (17).

$$\bar{n} = \frac{[HgL]+[HgLI^-]+[HgLI_2^{2-}]+2[HgL_2]}{\sum_{n=0}^{2}\sum_{m=0}^{4}[HgL_nI_m{}^{(2-2n-m)+}]} = \frac{[L^{2-}](Q_1+\beta_{1,1}[I^-]+\beta_{2,1}[I^-]^2)+2[L^{2-}]^2Q_1Q_2}{1+[L^{2-}](Q_1+\beta_{1,1}[I^-]+\beta_{2,1}[I^-]^2)+[L^{2-}]^2Q_1Q_2+\sum_{m=1}^{4}[I^-]^mQ_1{}^I\cdots Q_m{}^I} \tag{17}$$

Here the coordination number of mercury(II) is presumed as four. If we put

$$Q' = Q_1 + \beta_{1,1}[I^-] + \beta_{2,1}[I^-]^2 \tag{18}$$

Eq. (17) is simplified to (19).

$$\bar{n} = \frac{Q'[L^{2-}]+2Q_1Q_2[L^{2-}]^2}{1+Q'[L^{2-}]+Q_1Q_2[L^{2-}]^2+\sum_{m=1}^{4}Q_1{}^I\cdots Q_m{}^I[I^-]^m} \tag{19}$$

The last term of denominator may be calculated by use of data by Sillén[20] and Marcus[21] at 25.0° and μ=0.5 (KNO_3): log Q_1=12.87, log Q_1Q_2=23.82, log $Q_1Q_2Q_3$=27.49, log $Q_1Q_2Q_3Q_4$ =29.86.

Solutions containing mercury (II) iodide (2.185×10^{-3} M), $MPGH_2$ (6.400×10^{-3} M) and potassium iodide in several concentrations were titrated at μ=0.5 (KNO_3) with a potassium hydroxide solution, and complex formation curves as shown in Fig. 5 were obtained.

Apparent acid dissociation constants of $MPGH_2$ were also determined to be pQ_1^H=3.27 and pQ_2^H=8.23 at μ=0.5 (KNO_3). The following Q' and Q_1Q_2 values were obtained from the data in Fig. 5.

$[I^-]$, M	Q'		Q_1Q_2
0.05	1.1×10^{33}		6.7×10^{39}
0.10	1.4×10^{33}		5.9×10^{39}
0.20	2.0×10^{33}		4.2×10^{39}
		av.	5.6×10^{39}

A plot of Q' vs $[I^-]$ gave a nearly straight line as shown in Fig. 6. As the intercept of this straight line Q_1 was obtained as 7.7×10^{32} (log Q_1=32.9), and hence Q_2 7.3×10^6 (log Q_2=6.86).

As shown in Table II stability constants (K_1) of 2-mercaptopropionylglycine with divalent metal ions are in the order: Hg≫Pb≳Cd>Zn>Fe. The same trend is also noticed for cysteine and glutathione complexes. The extraordinarily large value of Q_1 for Hg(II) is ascribable to the large affinity of the metal for the sulfhydryl group, but drop of the Q_2 value from Q_1

25) H.A. Droll, B.P. Block and W.C. Fernelius, *J. Phys. Chem.*, **61**, 1000 (1957).

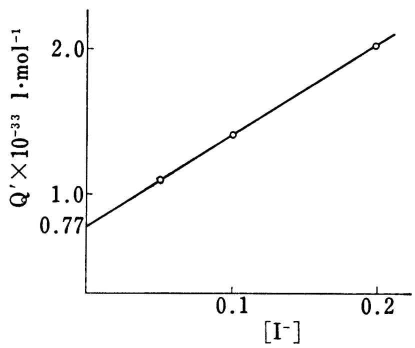


Fig. 6. A Plot of Q′ (Eq. 18) *vs.* [I⁻]

is quite remarkable. Stability constants of MPG-H_2 complexes are smaller than those of cysteine and glutathione complexes reflecting pQH values (at μ=0.15) of SH groups in these ligands[7]: glutathione > cysteine > $MPGH_2$. Cysteine and glutathione coordinate to a metal atom with SH and NH_2 groups.[7] By analogy $MPGH_2$ is assumed to coordinate to a metal atom with SH and CONH groups. The fact that $Hg(MPGH)_2$ can be transformed to $Hg(MPGE)_2$ by esterification with ethanol as described in the Experimental section indicates nonbonding of the carboxylic acid group to Hg(II).

Lower stabilities of $MPGH_2$ complexes in comparison with corresponding cysteine and glutathione complexes may be due to the smaller tendency of coordination of the amide group than that of the amine group. The carbonyl absorption of the amide group lies at an appreciably lower frequency than that of normal ketones indicating the resonance effect with the ionic form such as

$$-\underset{\large |}{\underset{O^-}{C}}=NH^+- \quad \text{or} \quad -\underset{\large \|}{\underset{OH^+}{C}}-N^-- $$

Such a resonance (electron delocalization) stabilization must contribute towards reduction of stabilities of metal complexes.

Table II. Stability Constants of Several Metal Complexes of 2-Mercaptopropionylglycine and Related Compounds[a]

		2-Mercapto-propionylglycine	Cysteine	Glutathione[b]
Cd^{2+}	log K_1	6.81	—	10.5
	log K_2	5.69	—	—
Pb^{2+}	log K_1	7.00	12.20,[b] 11.39[c]	10.6
	log K_2	5.16	—	—
Zn^{2+}	log K_1	5.16	9.86,[b] 9.04[c]	8.30
	log K_2	5.01	9.84,[b] 8.50[c]	—
Fe^{2+}	log Q_1	4.98	—	—
Hg^{2+}	log Q_1[d]	32.9		
	log Q_2[d]	6.9	43.6[e]	41.6[e]

a) Values were measured at 25.0±0.1° and μ=0.15 ($NaClO_4$) and corrected for activity coefficients except the iron(II) system, for which Q_1 defined by Eq. (8) is given.
b) data from ref. 7)
c) data from ref. 8)
d) concentration quotients at 25.0±0.1° and μ=0.5 ($KMNO_3$)
e) Values obtained polarographically by W. Stricks and I.M. Kolthoff, *J. Am. Chem. Soc.*, **75**, 5673 (1953).

Crystalline Mercury(II) Complexes of 2-Mercaptopropionylglycine and Related Compounds

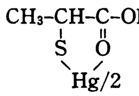
In the stability measurements mercury(II) ions were found to form quite stable 1:1 and 1:2 complexes with $MPGH_2$. Soft mercury(II) ions are well known to show a strong affinity for sulfhydryl groups, and may be unequivocally presumed to be linked with the ligand through the sulfur atom. However the other bonding site is not certain. To clarify this interesting problem crystalline complexes of mercury(II) with $MPGH_2$ and related compounds were synthesized, and their infrared spectra have been investigated. As listed in Table I crystalline complexes prepared are all charge-neutral bis complexes. Their characteristic infrared absorption bands are given in Table III.

TABLE III. Characteristic Infrared Absorption Bands of 2-Mercaptopropionylgycine and Related Compounds, and Their Mercury(II) Complexes

Compound[a]	ν_{NH}	ν_{CO} (carboxyl)	Amide I	Amide II
MPH_2[b]		1709		
$Hg(MPH)_2$[c]		1696, 1681		
MPEH[b]		1728		
$Hg(MPE)_2$[b]		1720, 1710		
MPAH[c]	3350, 3170		1670	1640
$Hg(MPA)_2$[c]	3430, 3350, 3200		1680, 1650, 1615, 1570(sh)	
$MPGH_2$[c]	3280, 3090(*W*)	1746	1637(sh), 1621, 1557	
$Hg(MPGH)_2$[c]	3280, 3100(*W*)	1728	1655(sh), 1640, 1550	
MPGEH[d]	3400	1735	1655	1510
$Hg(MPGE)_2$[d]	3360	1737	1655	1515

a) MPH_2: 2-mercaptopropionic acid, MPEH: ethyl 2-mercaptopropionate, MPAH: 2-mercaptopropionamide, $MPGH_2$: 2-mercaptopropionylglycine, MPGEH: 2-mercaptopropionylglycine ethyl ester
b) liquid *c*) in Nujol mull *d*) in chloroform

The simplest ligand 2-mercaptopropionic acid (MPH_2) shows an intense C=O stretching band at 1709 cm^{-1} and its mercury(II) complex $Hg(MPH)_2$ at 1696 and 1681 cm^{-1} as a doublet. Alexander and Busch[26] observed the C=O stretching band at 1640 cm^{-1} for the chelated glycine complex $[Co(NH_2CH_2COO)en_2]Cl_2$ and at 1600 cm^{-1} for the N-bonded unidentate glycine complex *cis*-$[CoCl(NH_2CH_2COO)en_2]Cl$, but at 1735 cm^{-1} for the acid complex *cis*-$[CoCl(NH_2CH_2COOH)en_2]Cl_2$. The observed infrared spectrum of $Hg(MPH)_2$ suggests that the carboxylic acid group coordinates to the metal atom with retention of a proton. The C=O band in the propionic ester complex $Hg(MPE)_2$ also appears as a doublet at 1710 and 1720 cm^{-1} showing a slight shift to the lower frequency side. Although in case of MPH_2 the SH stretching band is hidden by stronger absorption of the bonded OH group in the 2700—2500 cm^{-1} range, MPEH gives a weak but well-defined band at 2545 cm^{-1}. This SH stretching absorption disappears completely in $Hg(MPE)_2$, certifying ligation of the SH group. Thus the structures [1] are suggested for $Hg(MPH)_2$ and $Hg(MPE)_2$



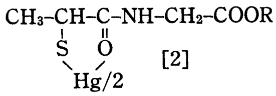
[1] R=H for $Hg(MPH)_2$
R=C_2H_5 for $Hg(MPE)_2$

2-Mercaptopropionamide(MPAH) shows two bonded NH stretching absorptions at 3350 and 3170 cm^{-1} and two bands at 1670 and 1640 cm^{-1} which may be assignable to the amide I and II, respectively.[27] On ligation to mercury(II) NH stretching absorption appears as three peaks at 3450, 3350, and 3200 cm^{-1}. Three peaks at 1680, 1650 and 1615 cm^{-1} and a shoulder at 1570 cm^{-1} are observed in the amide I and II region. It seems difficult to draw a conclusion from these IR data which of the oxygen and nitrogen atoms serves as a donor atom in $Hg(MPA)_2$.

26) M.D. Alexander and D.H. Busch, *Inorg. Chem.*, **5**, 1590 (1966).
27) L.J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed., Methuen, London, 1964, p. 203.

The amide complex further reacts with copper(II) perchlorate in acetone giving a blue compound of the composition $[Hg(MPA)_2]_3[Cu(ClO_4)_2]_2$. The NH stretching absorption in the 3400—3200 cm^{-1} range is splitted in a more complicated fashion and the amide I and II bands appear as four peaks at 1690, 1667, 1642 and 1575 cm^{-1}, the last being now a well-defined peak. The electronic spectrum of this compound was observed in Nujol mull to have an absorption maximum at 650 nm, which corresponds to 610 nm absorption of $Cu(NH_3)_4^{2+}$ ions in aqueous solutions,[28] suggesting the coordination of nitrogen atoms to the copper atom. Thus it seems probable to presume that the amide carbonyl group is linked to mercury in $Hg(MPA)_2$.

The carbonyl stretching absorption of the carboxyl group of free 2-mercaptopropionylglycine appears at 1746 cm^{-1} and that of $Hg(MPGH)_2$ at 1728 cm^{-1} indicating unequivocally non-participation of the carboxyl group in coordination. The NH stretching absorption is observed at 3280 and 3090 (weak) cm^{-1} and no band in the higher frequency region indicating that all the NH groups are capable of hydrogen bonding in the crystal state. The amide I band appears at 1637 (sh) and 1621 cm^{-1}, and the amide II at 1557 cm^{-1}. In $Hg(MPGH)_2$ these absorption bands appear at 3280, 3100 (*W*), 1655 (sh), 1640 and 1550 cm^{-1}, respectively, showing no significant shift. Thus any conclusive information concerning the second donor atom in $Hg(MPGH)_2$ can not be obtained from the IR data, although the oxygen coordination (formula 2) might be probable by analogy with $Hg(MPA)_2$. The IR spectrum of 2-mercaptopropionylglycine ethyl ester in chloroform shows the NH stretching absorption at 3400 indicating that the NH group is not hydrogen-bonded in this solution. On ligation to mercury this band shifts to 3360 cm^{-1}, but the amount of shift is small and not enough to evidence the nitrogen coordination. A similar structure [2] might be presumed for $Hg(MPGE)_2$.



[2]

R=H for $Hg(MPGH)_2$
R=C_2H_5 for $Hg(MPGE)_2$

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28) J. Bjerrum, C.J. Ballhausen and C.K. Joergensen, *Acta Chem. Scand.*, **8**, 1275 (1954).