bromide was much smaller than the specific surface in the colloidal state but the decrease was not nearly as pronounced as upon flocculation with calcium bromide of the same concentration. Also, upon removal of the supernatant liquid and shaking with dilute potassium bromide no peptization was observed when flocculated with calcium bromide, but some peptization occurred when flocculated with cadmium bromide. The possibility of making the flocculation partly or entirely reversible by elimination of Schottky defects is being further studied.

Formation and Properties of Various Mercuric Mercapto Thioglycolates Formed in Reactions between Mercuric Mercury and Thioglycolic Acid

BY W. STRICKS, I. M. KOLTHOFF AND A. HEYNDRICKX

Reactions of thioglycolic acid (TSH) with mercuric mercury have been studied polarographically and compared with similar reactions of cysteine and glutathione reported previously. In the absence of chloride thioglycolic acid can form at least two compounds with mercury: $Hg(TS)_2$ and slightly soluble $Hg_2(TS)_2$ in which one mercury is bound firmly as mercaptide. In the presence of much chloride the formation of $Hg_2(TS)_2$ is suppressed by the complex $HgCl_4^-$. The apparent dissociation constants of three charge types of the mercuric mercapto thioglycolate were calculated from e.m.f. measurements. The charge of the carboxyl group was found to have little effect on the stability of the mercaptides. From the values of the dissociation constants at 12 and 25° the heats and entropies of formation were calculated. A comparison of the data obtained with thioglycolic acid, cysteine and glutathione indicates that the stability of the mercuric mercaptides of the three thiol compounds is determined almost entirely by the strength of the mercury–sulfur bonds; and that the uncharged amino group and the charged or uncharged carboxyl groups have little effect on the stability.

For an interpretation of some of the results obtained in a recent study[1] of the reactions between cysteine and reduced glutathione with mercuric mercury it appeared desirable to carry out a similar study with a compound containing only sulfhydryl and carboxyl as reactive groups. The present paper deals with a study of the thioglycolic acid (TSH)–mercuric system at varying pH and temperatures. Polarographically it is shown that mercury can form at least two reaction products with thioglycolic acid. Apparent dissociation constants, heats and entropies of formation of the mercapto mercuric thioglycolates have been calculated from e.m.f. measurements. The results are compared with those obtained with cysteine[1] and glutathione.[1]

Materials.—A "pure" product of thioglycolic acid from Eimer and Amend was purified and analyzed by methods described previously.[2] Stock solutions of the acid (0.01 and 0.2 M) were prepared with air-free water. Only freshly prepared solutions of the acid were used. All other stock solutions and chemicals were the same as used before.[1]

Experimental Methods.—The experimental details for the determination of current voltage curves, e.m.f. and pH measurements were identical with those given previously.[1] The characteristics of the capillary used in the present polarographic work were: $m = 2.17$ mg. sec.$^{-1}$; $t = 3.91$ sec. (open circuit); $m^{2/3} t^{1/6} = 2.104$ mg.$^{2/3}$ sec.$^{-1/2}$; $h = 60$ cm.

Dissociation constants of the mercuric mercaptides of thioglycolic acid were calculated from e.m.f. measurements of mercury metal in equilibrium with mercuric mercaptides in the presence of a large excess of uncomplexed acid. Under these conditions all the mercury in the solution is in the mercuric form. Mercurous thioglycolate is unstable and readily disproportionates into mercury metal and the mercuric compound.

Polarographic Measurements.—Air-free 10^{-3} M TSH solutions in the absence and presence of chloride ion were ti-

trated with 0.05 M mercuric solutions and complete polarograms were taken after each addition of mercury. The polarographic behavior of thioglycolic acid[2] and of its mercuric mercaptide is similar to that of cysteine[3] and glutathione.[4] For this reason polarograms are not presented in this paper. The diffusion currents (corrected for residual current and change in volume) of the various compounds present in the course of a titration were plotted against the volume of mercury solution added. An example of such a plot obtained with a solution at pH 5.57 in the absence of chloride is given in Fig. 1. Analogous to cysteine and glutathione the anodic diffusion current of TSH is found to disappear when TSH and mercury are present in a mole ratio 2:1. At this point only the reduction wave of mercury in the slightly dissociated mercaptide $Hg(TS)_2$ is observed

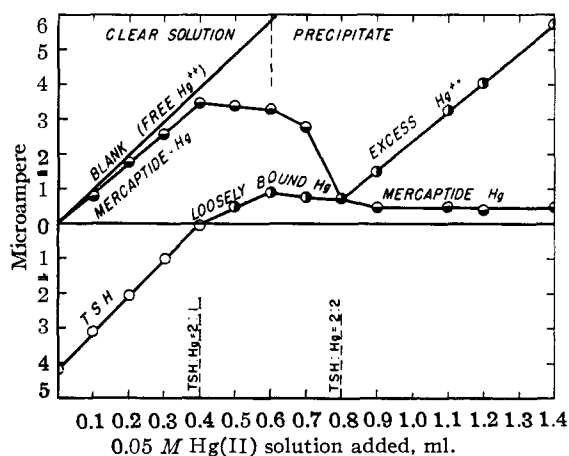0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2 1.3 1.4
0.05 M Hg(II) solution added, ml.

Fig. 1.—Titration of 40 ml. of 10^{-3} M thioglycolic acid (acetate buffer, 0.1 M KNO$_3$, 2.5 × 10^{-3}% gelatin, pH 5.57) with 0.05 M mercuric acetate. Plot of diffusion current *versus* ml. Hg(II) solution added: ☉,◑, i_d, measured at −0.1 v.; ◖, i_d, measured at −065. v.

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(1) W. Stricks and I. M. Kolthoff, THIS JOURNAL, **75**, 5673 (1953).

(2) D. L. Leussing and I. M. Kolthoff, *J. Electrochem. Soc.*, **100**, 334 (1953).

(3) I. M. Kolthoff and C. Barnum, THIS JOURNAL, **62**, 306 (1940).

(4) W. Stricks and I. M. Kolthoff, *ibid.*, **74**, 4646 (1952).

(starts at −0.3 v.). On further addition of mercury the height of the mercaptide wave decreases very slightly and another cathodic wave appears at a potential of about +0.25 v. The height of this wave increases along a line (denoted by "loosely bound Hg" in Fig. 1) of considerably smaller slope than that of the blank line, obtained by adding mercuric acetate to an acetate buffer in the absence of TSH. At a mole ratio TSH:Hg of about 1:1.5 a white precipitate is formed. Upon further addition of reagent a marked reduction in the height of the mercaptide wave occurs. At a mole ratio TSH:Hg = 1:1 (second end-point) the two cathodic waves are of the same height. These observations indicate that most of the mercury added after the first end-point is not present as free mercuric ion but is bound to the mercaptide. Apparently a slightly soluble compound Hg₂(TS)₂ is formed in which one mercury is bound firmly as mercaptide and one much more loosely, by way of the carboxyl groups. When more mercury is added after the second end-point the cathodic wave at the more positive potential increases in height again. The slope of this excess Hg⁺⁺ line (Fig. 1) is the same as that of the blank (free Hg⁺⁺) while the mercaptide wave remains constant in height.

Figure 2 presents results in a titration of a 10^{-3} M TSH solution in an acetate buffer (pH 5.6) which was 1 M in potassium chloride. In the presence of chloride ion no precipitate is formed and only one end-point corresponding to the formation of the mercaptide Hg(TS)₂ is detected. After this end-point the mercury line is parallel to the blank line and corresponds to the excess mercury complex HgCl₄⁼.
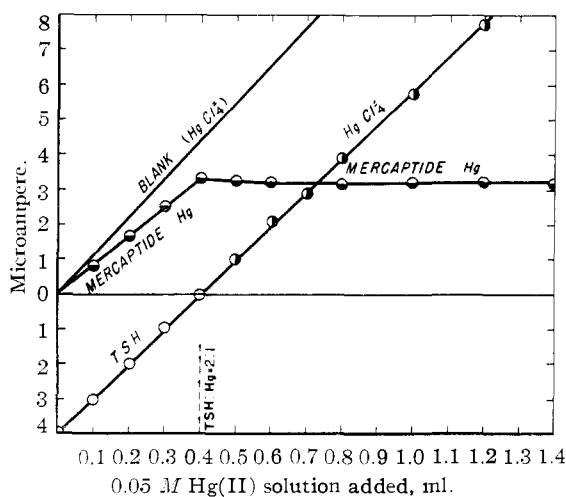

Fig. 2.—Titration of 40 ml. of 10^{-3} M thioglycolic acid (acetate buffer, M KCl, 2.5 × 10^{-3}% gelatin, pH 5.54) with 0.05 M mercuric acetate. Plot of diffusion currents versus ml. Hg(II) solution added: ☉,◑, i_d, measured at −0.15 v.; ●, i_d, measured at −0.70 v.

Comparing these results with those obtained with cysteine (RSH) and glutathione (GSH) it appears that TSH in the absence of chloride can form at least two (Hg(TS)₂ and Hg₂(TS)₂) while RSH and GSH can form at least three mercury compounds (Hg(RS)₂, Hg₂(RS)₂ and Hg₃(RS)₂) in which one mercury is bound firmly as a mercaptide. In the presence of chloride the three thio compounds behave identically, giving rise to formation of one mercaptide (Hg(TS)₂) only.

Apparent Dissociation Constants, Heats and Entropies of Formation of the Mercapto Mercuric Thioglycolates.—In order to obtain values of the dissociation constants of the mercapto thioglycolates which are strictly comparable to those of the corresponding cysteinates and glutathionates, all measurements and calculations were carried out in the same way as reported in the previous study.[1]

Thus the dissociation constants of the thioglycolates were calculated from the mercury ion activity determined in a given mixture of mercury(II) and an excess of TSH at an ionic strength of 1 ± 0.1 and concentrations instead of activities of the ionized forms of TSH and its mercaptides were used in the calculations.

The mercuric ion activity was calculated from e.m.f. measurements $vs.$ S.C.E., using the equation

$$\text{e.m.f.} = E_0 + \frac{RT}{2F} \ln (a_{Hg^{++}}) - 0.2420 + 0.00076 (t - 25)$$

(1)

where $E_0 = 0.854$ volt[5] is the standard potential ($vs.$ N.H.E.) of the mercury–mercuric system and t indicates temperature in °C.

The variation of the concentration of the charge forms of thioglycolic acid and of its mercaptides with pH have been considered in the calculation of the dissociation constants of these mercaptides.

The charge types of thioglycolic acid can be denoted by the symbols

a	b	c	d
TSH	TSH	TS⁻	TS⁻
|	|	|	|
COOH	COO⁻	COO⁻	COOH

where the letters above the symbols express concentrations of the various species.

The two over-all constants $K_1 = [(H^+)(b + d)]/a = 2.5 × 10^{-4.6}$ and $K_2 = (H^+)c/(b + d) = 2.8 × 10^{-11.6}$ of the acid differ to such a large extent that the concentrations of the various charge species can be related without appreciable error by the equations

$$K_1 = \frac{b(H^+)}{a} = \frac{c(H^+)}{d}$$

(2)

$$K_2 = \frac{c(H^+)}{b} = \frac{d(H^+)}{a}$$

(3)

Total thioglycolic acid $= a + b + c + d =$

$$c\left\{\frac{(H^+)^2}{K_1K_2} + \frac{(H^+)}{K_2} + 1 + \frac{(H^+)}{K_1}\right\}$$

(4)

The correctness of equation 2 and consequently also of equations 3 and 4 is substantiated by the fact that the dissociation constant of ethyl-S-thioglycolic acid ($K = 1.83 × 10^{-4}$)[7] is practically equal to K_1 of thioglycolic acid. Since it is generally assumed that the carboxyl group in the S-ester (in this case the ethyl ester) behaves in the same way as that in TSH, the dissociation constant of the

TSH
\|
COOH

carboxyl group in TSH can be considered to be

\|
COOH

equal to K_1.

Equation 4 was used to calculate the concentration of each of the species of thioglycolic acid at a given pH. The dissociation constants of the various species of the mercaptide (Hg(TS)₂) can now be expressed as

(5) W. M. Latimer, "The Oxidation States of the Elements and their Potentials in Aqueous Solutions," Prentice-Hall, Inc., New York, N. Y., 1952, p. 179.

(6) D. L. Leussing and I. M. Kolthoff, This Journal, 75, 3904 (1953).

(7) L. Ramberg, Ber., 40, 2588 (1907).

(8) L. R. Ryklan and C. L. A. Schmidt, Arch. Biochem., 5, 89 (1944).

$$Hg(STCOOH)_2 \overset{e}{\underset{d}{\rightleftharpoons}} Hg^{++} + 2\underset{COOH}{|}\overset{TS^-}{|} \quad ; K_I = \frac{[Hg^{++}]d^2}{e} \quad (5)$$

$$HOOCTSHgSTCOO^- \overset{g}{\underset{d}{\rightleftharpoons}} Hg^{++} + \underset{COOH}{|}\overset{TS^-}{|} + \underset{COO^-}{|}\overset{TS^-}{|} \; ;$$

$$K_{II} = \frac{[Hg^{++}]dc}{g} \quad (6)$$

$$Hg(STCOO^-)_2 \overset{f}{\underset{c}{\rightleftharpoons}} Hg^{++} + 2\underset{COO^-}{|}\overset{TS^-}{|} \; ; K_{III} = \frac{[Hg^{++}]c^2}{f} \quad (7)$$

$$Hg(STCOOH)_2 \overset{e}{\underset{g}{\rightleftharpoons}} HOOCTSHgSTCOO^- + H^+;$$

$$K_x = \frac{[H^+]g}{e} \quad (8)$$

$$HOOCTSHgSTCOO^- \overset{g}{\underset{f}{\rightleftharpoons}} Hg(STCOO^-)_2 + H^+;$$

$$K_y = \frac{[H^+]f}{g} \quad (9)$$
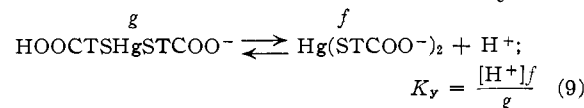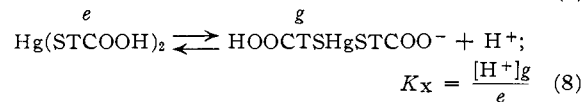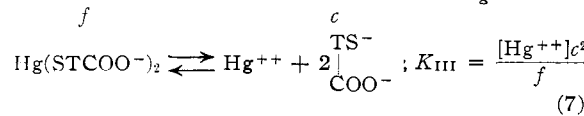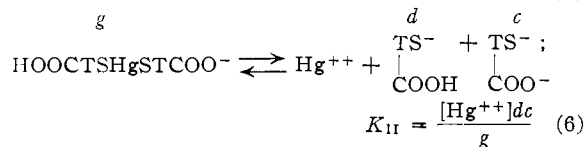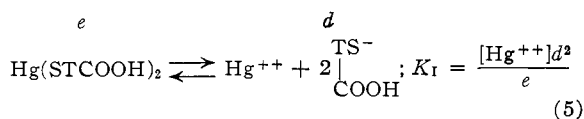
Combining equations 5 with 6 and 6 with 7 and substituting from equation 2 yields

$$K_x = \frac{K_I}{K_{II}} K_1 \quad (10)$$

and

$$K_y = \frac{K_{II}}{K_{III}} K_1 \quad (11)$$

From equations 10 and 11 it is seen that the dissociation constants of the carboxyl groups in the mercaptide can be calculated from the constants K_I, K_{II}, K_{III} and K_1. Specific examples of the calculation of the constants K_I, K_{II} and K_{III} have been given previously.[1] The values of the dissociation constants K_1 and K_2 of thioglycolic acid are assumed to be the same at 12 and 25°, since the heats of dissociation of the SH and carboxyl group are very small.[9] The concentration of the species with uncharged carboxyl groups can be neglected over a pH range from 13 to 6 at 25° and from 13 to 4.7 at 12° while the species with charged carboxyl groups can be neglected within the pH range 0 to 1.5 at 25° and from pH 0 to 2 at 12°. The constant K_{II} can be calculated from measurements in solutions in the intermediate pH range (2.4 to 5 at 25° and 2.5 to 4 at 12°).

Measurements were carried out over the entire pH range with mixtures of varying mercury and thioglycolic acid concentrations at 25 and 12°, respectively. The experimental data and the constants K_I, K_{II} and K_{III} are given in Tables I and II. The variation of the mercuric ion concentration with pH for mixtures of the same total concentration in mercury (10^{-3} M) and TSH (6×10^{-2} M) is illustrated graphically in Fig. 3. It is seen that at pH greater than 11 the pHg^{++} becomes practically independent of the hydrogen ion concentration. The curve is similar to those obtained with cysteine and glutathione and the following equation relating hydrogen ion and mercury ion concentration can be derived[1]

$$\left\{ \frac{[H^+]^2}{K_1K_2} + \frac{[H^+]}{K_2} + 1 + \frac{[H^+]}{K_1} \right\}^2 =$$

$$[Hg^{++}] \frac{(A-2B)^2}{B} \left\{ \frac{[H^+]^2}{K_1^2K_I} + \frac{1}{K_{III}} + \frac{[H^+]}{K_1K_{II}} \right\} \quad (12)$$

(9) E. J. Cohn, Ergeb. Physiol., **33**, 781 (1931).

in which A and B are the total concentrations of thioglycolic acid and of mercury, respectively. K_1 and K_2 are the dissociation constants of TSH.

TABLE I

APPARENT DISSOCIATION CONSTANTS AT 25° OF MERCURIC MERCAPTO THIOGLYCOLATE (Hg(TS)₂) IN CONVENTIONAL BUFFER SOLUTIONS ADJUSTED WITH KCl OR KNO₃ TO AN IONIC STRENGTH OF ONE

Hg(II) added, M	TSH added, M	pH	p-(Hg^{++})	$K_I \times 10^{45}$	$K_{II} \times 10^{45}$	$K_{III} \times 10^{44}$
5×10^{-4}	4×10^{-2}	>13	44.20			1.9
5×10^{-4}	4×10^{-2}	>13	44.10			2.4
5×10^{-4}	8×10^{-2}	>13	45.14			0.92
10^{-3}	4×10^{-2}	>13	43.75			2.6
10^{-3}	4×10^{-2}	>13	43.73			2.8
10^{-3}	6×10^{-2}	>13	44.31			1.7
10^{-3}	6×10^{-2}	>13	44.31			1.7
10^{-3}	8×10^{-2}	>13	44.66			1.3
2×10^{-3}	10^{-1}	>13	44.81			0.72
2×10^{-3}	8.16×10^{-2}	12.55	44.36			1.3
5×10^{-4}	4×10^{-2}	12.51	44.12			2.3
10^{-3}	6×10^{-2}	11.13	44.22			1.4
5×10^{-4}	4×10^{-2}	10.85	43.92			1.6
5×10^{-4}	5×10^{-2}	10.66	44.20			1.0
10^{-3}	6×10^{-2}	10.34	43.74			0.9
10^{-3}	6×10^{-2}	9.18	41.70			1.1
5×10^{-4}	4×10^{-2}	9.07	41.58			0.82
10^{-3}	6×10^{-2}	8.81	40.98			1.1
5×10^{-4}	5×10^{-2}	7.80	39.11			1.2
10^{-3}	6×10^{-2}	7.40	38.01			1.6
2×10^{-3}	6×10^{-2}	6.98	36.95			1.3
10^{-3}	6×10^{-2}	6.97	37.09			1.9
10^{-2}	6×10^{-2}	5.97	35.27			1.3
5×10^{-4}	2×10^{-2}	4.72	32.19		1.6	
10^{-3}	6×10^{-2}	4.68	32.65		4.7	
10^{-3}	6×10^{-2}	3.84	31.16		3.8	
10^{-3}	6×10^{-2}	2.42	28.53		8.6	
5×10^{-4}	1.94×10^{-2}	1.46	25.95	5.3		
5×10^{-4}	4×10^{-2}	1.10	25.82	5.7		
10^{-3}	4×10^{-2}	1.05	25.63	3.4		
10^{-3}	2×10^{-2}	0.82	24.38	4.7		
10^{-3}	4×10^{-2}	0.85	25.01	5.5		
10^{-3}	6×10^{-2}	0.86	25.41	5.5		
10^{-3}	8×10^{-2}	0.84	25.76	3.9		
			Av. K	4.9	4.7	1.5

TABLE II

APPARENT DISSOCIATION CONSTANT AT 12° OF MERCURIC MERCAPTO THIOGLYCOLATE (Hg(TS)₂) IN CONVENTIONAL BUFFER SOLUTIONS ADJUSTED WITH KCl OR KNO₃ TO AN IONIC STRENGTH OF ONE

Hg(II) added, M	TSH added, M	pH	p(Hg^{++})	$K_I \times 10^{46}$	$K_{II} \times 10^{46}$	$K_{III} \times 10^{46}$
5×10^{-4}	8×10^{-2}	13.15	46.78			2.0
10^{-3}	6×10^{-2}	13.00	46.13			2.5
10^{-3}	8×10^{-2}	13.10	46.50			1.9
10^{-3}	6×10^{-2}	12.62	46.11			2.6
5×10^{-4}	4×10^{-2}	10.81	45.69			2.6
5×10^{-4}	5×10^{-2}	10.64	45.89			1.9
10^{-3}	6×10^{-2}	10.38	45.36			2.4
10^{-3}	6×10^{-2}	8.82	42.55			3.7
10^{-3}	6×10^{-2}	8.73	42.37			3.1
5×10^{-4}	5×10^{-2}	7.70	40.42			3.6
10^{-3}	6×10^{-2}	7.16	38.99			5.6
10^{-3}	6×10^{-2}	5.72	36.26			4.0
5×10^{-4}	2×10^{-2}	4.72	33.46			4.7
10^{-3}	6×10^{-2}	4.73	34.19			4.3
10^{-3}	6×10^{-2}	3.71	32.40		1.4	
10^{-3}	6×10^{-2}	2.30	29.76	1.7		
5×10^{-4}	4×10^{-2}	1.11	27.15	2.8		
10^{-3}	2×10^{-2}	0.90	25.63	2.7		
10^{-3}	6×10^{-2}	0.88	27.00	1.5		
			Av. K	2.2	1.4	3.0
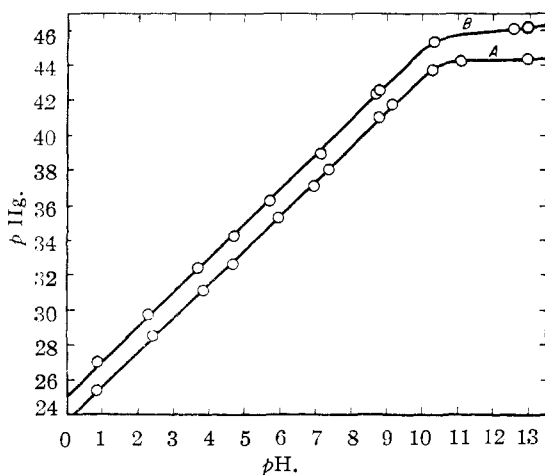
Fig. 3.—pHg $vs.$ pH of mixtures $10^{-3} M$ in Hg(II) and 6 × $10^{-2}M$ in thioglycolic acid: A, at 25°; B, at 12°.

It is seen that at low pH the three last terms on the left side of equation 12 can be neglected as compared to the first term while on the right side the last two terms in the bracket are negligibly small as compared to the first term. Thus at low pH equation 12 can be written in the simplified form

$$[\text{H}^+]^2 = [\text{Hg}^{++}] \frac{(A - 2B)^2}{B} \frac{K_2^2}{K_I} \qquad (13)$$

or

$$2p\text{H} = p\text{Hg} - \log\left\{\frac{(A - 2B)^2}{B} \frac{K_2^2}{K_I}\right\} \qquad (14)$$

At low pH the equation is represented by a straight line of slope 2 as actually observed in Fig. 3, both at 25 and 12°.

The values of the three constants K_I, K_{II} and K_{III} are not affected by the composition of the buffers used. At 12° the three constants are practically equal. At 25° K_I and K_{II} are equal but K_{III} is slightly larger. Electrostatic repulsion between the two charged carboxyl groups might account for the larger K_{III} although the over-all effect of the carboxyl groups on the stability of the mercaptides is very small. This was found to be still more pronounced for the stability of the mercaptides of cysteine and glutathione which are not affected by the charge of the carboxyl groups at both 12 and 25°.[1]

From the values of K_I, K_{II} and K_{III} the constants K_X and K_Y can be calculated from equations 10 and 11. K_X is found to be 2.6 × 10^{-4} and 3.9 × 10^{-4} and K_Y is 7.8 × 10^{-5} and 1.2 × 10^{-4} at 25 and 12°, respectively.

The heat of formation of the various species of the mercaptides was calculated from the corresponding apparent dissociation constants at 12 and 25° and the entropies of formation were found from the relation $\Delta S = (\Delta H - \Delta F)/T$. The pK values of the three constants, the free energies $(RT \ln K)$, heats and entropies of formation of the various species of the mercaptides of thioglycolic acid are listed in Table III which, for comparison, also gives the data for the mercaptides of cysteine and glutathione. It is seen that the constants K_{III} of the thioglycolate and of the cysteinate are of the same order of magnitude, while the difference in the K_I values is rather large.

TABLE III

APPARENT DISSOCIATION CONSTANTS (pK-VALUES), FREE ENERGY, HEAT AND ENTROPY OF FORMATION OF MERCURIC MERCAPTO THIOGLYCOLATE Hg(TS)₂, CYSTEINATE Hg(RS)₂ AND GLUTATHIONATE Hg(GS)₂

	Hg(TS)₂ 12°	Hg(TS)₂ 25°	Hg(RS)₂ 12°	Hg(RS)₂ 25°	Hg(GS)₂ 12°	Hg(GS)₂ 25°
pK_I	45.66	44.31	41.82	40.25	42.29	40.96
pK_{II}	45.85	44.33	45.27	43.60	43.54	41.92
pK_{III}	45.52	43.82	45.10	43.57	43.47	41.58
ΔF_1, kcal.	−59.5	−60.4	−54.5	−54.8	−55.2	−55.9
ΔF_{II}, kcal.	−59.7	−60.4	−59.1	−59.5	−56.8	−57.1
ΔF_{III}, kcal.	−59.3	−59.7	−59.1	−69.3	−56.6	−56.6
ΔH_1, kcal.	−40.2		−46.9		−39.7	
ΔH_{II}, kcal.	−45.5		−49.9		−48.2	
ΔH_{III}, kcal.	−50.6		−54.5		−56.1	
ΔS_1, cal./deg.	+68		+27		+54	
ΔS_{II}, cal./deg.	+50		+32		+30	
ΔS_{III}, cal./deg.	+30		+16		+ 2	

The equality of the K_{III} values suggests that the uncharged amino groups in the mercury cysteinate (in alkaline medium) have little effect on the stability of the mercaptide while the larger K_I values of mercury cysteinate might be accounted for by electrostatic repulsion caused by the charged NH_3^+ groups which tends to decrease the stability of the mercury cysteinate. A similar effect of the charged amino group is indicated by the ratios of the dissociation constants K_I and K_{III} of the mercaptides to the hydrogen ion dissociation constants of the sulfhydryl group, K_2 of TSH and $K'_A(\frac{RSH}{NH_3^+} \rightleftarrows \frac{RS^-}{NH_3^+} + H^+)$ and $K'_D(\frac{RSH}{NH_2} \rightleftarrows \frac{RS^-}{NH_2} + H^+)$ of the corresponding species of RSH and GSH as given in Table IV.

TABLE IV

RATIOS K_{III}/K'_D AND K_I/K'_A FOR THIOGLYCOLIC ACID, CYSTEINE AND GLUTATHIONE

	K_{III}/K'_D 12°	K_{III}/K'_D 25°	K_I/K'_A 12°	K_I/K'_A 25°
TSH[a]	1.1 × 10^{-35}	0.54 × 10^{-33}	7.9 × 10^{-33}	1.7 × 10^{-34}
RSH	1.3 × 10^{-36}	0.9 × 10^{-33}	6.8 × 10^{-34}	2.5 × 10^{-32}
GSH	2.2 × 10^{-34}	1.7 × 10^{-33}	4.6 × 10^{-34}	10^{-32}

[a] For thioglycolic acid the ratios are K_{III}/K_2 and K_I/K_2, respectively.

The ratios K_{III}/K_2 and K_{III}/K'_D are of the same order of magnitude while the ratio K_I/K'_A for cysteine and the peptide is markedly larger than K_I/K_2 for thioglycolic acid. The difference in the values of these ratios for TSH and RSH can be accounted for almost entirely by the difference in the K_I values.

In this connection it is of interest to also compare the acid dissociation constants of the sulfhydryl group in amino acids, peptides, thioglycolic acid and aliphatic mercaptans. The values of pK'_A (for the species with the charged amino group) of cysteine, homocysteine and glutathione are 8.66,[1] 9.14[8] and 8.96[1] while the values of pK'_D (for the species with the uncharged amino group) are 10.51,[1] 10.52[8] and 8.82,[1] respectively. A comparison of pK'_A with pK'_D for cysteine and homocysteine shows that the charged amino group increases the acidity constant of the sulfhydryl group, an effect which diminishes with the distance of the two groups and is therefore not observed with glutathione.

The pK'_D values of the amino acids are in close agreement with the sulfhydryl dissociation constant of thioglycolic acid ($pK_2 = 10.45$) and of aliphatic mercaptans ($pK = 10.7$, extrapolated

value).[10] The lower pK'_D value of glutathione may be caused by the close vicinity of the sulfhydryl group to the peptide linkage. Analogous to observations on the carboxyl group in peptides,[11] this tends to ease the splitting off of the proton. Apparently the peptide linkage has a similar effect on the dissociation of the mercury in the mercaptide of glutathione as it has on the dissociation of hydrogen from the sulfhydryl group. This may largely account for the fact that pK_{III} of glutathione is markedly smaller than pK_{III} of cysteine (see Table III).

(10) E. J. Cohn and J. T. Edsall, "Proteins, Amino Acids and Peptides," Reinhold Publ. Corp., New York, N. Y., 1943.

(11) M. Zief and J. T. Edsall, THIS JOURNAL, **59**, 2245 (1937).

Heats and entropies of formation of the mercaptides of TSH, RSH and GSH are about of the same order of magnitude. The ΔH values increase in magnitude from the I to the III species while the ΔS values decrease in the same direction.

Comparison of the three thiol compounds indicates that the stability of the mercuric mercaptides is determined mainly by the strength of the mercury–sulfur bonds while uncharged amino and carboxyl groups, either charged or uncharged, have but little effect on the stability of these mercaptides.

MINNEAPOLIS, MINNESOTA

Rhenium Sulfides as Liquid-Phase Hydrogenation Catalysts. A Comparison with Molybdenum Sulfide and Cobalt Polysulfide

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Rhenium heptasulfide and rhenium disulfide hydrogenation catalysts have been prepared and examined for catalytic activity toward a variety of substrates in comparison with the well-known molybdenum sulfide and cobalt polysulfide catalysts. In these experiments rhenium heptasulfide was most active, rhenium disulfide less so, and molybdenum and cobalt sulfides much less so. Some advantages enjoyed by the rhenium heptasulfide hydrogenation catalyst are as follows: Consistent and easy reproducibility, activity maintained indefinitely by simple storage in a closed bottle, stability to hydrogenative decomposition at high temperatures, extreme resistance to "poisoning," insolubility in strong, non-oxidizing acids, and ability to saturate multiple bond systems without accompanying hydrogenolysis of carbon–sulfur bonds. Its chief disadvantages are its relatively high cost, due in considerable part to the lack of established demand for rhenium compounds, and the fact that it is not as active toward most non-sulfur containing compounds as some nickel, platinum and palladium catalysts.

Introduction

A good hydrogenation catalyst should be active toward a variety of substrates at relatively low temperatures and should be resistant to "poisoning"; moreover, a useful degree of specificity of catalytic activity toward different reducible groups is highly desirable. The metal sulfide catalysts[2] as a group are outstanding in their resistance to "poisoning," but they show very little specificity of action, in large part due to the relatively high temperatures (250–500°) required for their use, which often results in considerable pyrolysis of the substrate(s).

In connection with a general investigation on the catalytic properties of rhenium and its compounds in organic reactions being carried out in these laboratories, preparations of rhenium disulfide and rhenium heptasulfide have been obtained which appear to be significantly superior in some reactions to sulfide catalysts heretofore reported. In the highly empirical science of contact catalysis comparisons are difficult because of differences in experimental conditions. In an effort to achieve valid comparisons two of the most widely employed sulfide catalysts, molybdenum sulfide,[3] and cobalt

polysulfide,[4] were prepared and studied along with the rhenium sulfides under closely similar conditions. It is recognized, of course, that cobalt polysulfide catalysts exhibit a rather specialized kind of activity but, since this activity is great, it seemed desirable to include it in the study.

The only specific references to the activity of rhenium sulfides as hydrogenation catalysts report that rhenium disulfide is a superior catalyst for the dehydrogenation of alcohols at 400–550°, but that the reverse reaction is little affected,[5] that rhenium heptasulfide hydrogenates cresol in part to gasoline at 450° and 1400 p.s.i.[6] and that coal, lignin, as-

(1) (a) Performed work on rhenium sulfides and cobalt polysulfide. (b) Performed work on the molybdenum sulfide.

(2) A valuable summary of the activity of various substances in catalytic hydrogenations and dehydrogenations covering the literature up to 1940 is provided by S. Berkman, J. C. Morrell and Gustav Egloff, "Catalysis," Reinhold Publ. Corp., New York, N. Y., 1940, pp. 809–906.

(3) The following few references are representative of the nearly one hundred references dealing with molybdenum sulfide catalysts: W. H. Jones, U. S. Patent 2,112,292 (Mar. 29, 1938); A. F. Nikolaeva

and P. V. Puchkov, J. Gen. Chem. (U.S.S.R.), **8**, 1153 (1938); **9**, 277 (1939); P. C. Condit, Ind. Eng. Chem., **41**, 1704 (1949); B. L. Moldavskii and S. Livshitz, J. Gen. Chem., (U.S.S.R), **4**, 948 (1934); V. F. Polozov, Khim. Tverdogo Topliva, **6**, 78 (1935) [C. A., **29**, 7294 (1935)]; Lee C. Cheney, British Patent 608,969 (Sept. 23, 1948); E. Krebs, W. Demann and H. Brochers, Tech. mitt. Krupp. Tech., **6**, 59 (1938) [C. A., **33**, 6257 (1939)]; Grant S. Stewart, U. S. Patent 2,490,488 (Dec. 6, 1949); E. I. Prokopetz, et al., J. Applied Chem. (U.S.S.R.), **11**, 1475 (1938); W. G. Appleby, et al., U. S. Patent 2,429,575 (Oct. 21, 1947); S. Andō, J. Chem. Ind., Japan, **41**, suppl. binding, 413 (1938); M. K. D'yakova and A. V. Losovoi, Compt. rend. acad. sci. U.R.S.S., **2**, 254 (1935) [C. A., **29**, 6396 (1935)].

(4) The following are representative of the literature on cobalt polysulfide catalysis: M. W. Farlow, et al., THIS JOURNAL, **70**, 1392 (1948); M. W. Farlow and F. K. Signaigo, U. S. Patent 2,402,613 and U. S. Patent 2,402,614 (June 25, 1946); W. A. Lazier, F. K. Signaigo and L. G. Wise, U. S. Patent 2,402,645 (June 25, 1946); W. A. Lazier and F. K. Signaigo, U. S. Patent 2,402,641 (June 25, 1946); and E. I. du Pont de Nemours, British Patent 577,279 (May 13, 1946).

(5) M. S. Platanov, J. Gen. Chem. (U.S.S.R.), **11**, 683 (1941) [C. A., **36**, 397 (1942)].

(6) N. v. de Bataafsche Petroleum Maatschappij, British Patent 358,180, July 29, 1930 [Gmelins Handbuch der anorganischen Chemie, 8th Ed., Verlag Chemie, Berlin, No. 70, p. 40].