[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

The Kinetics of the Oxidation of a Mercaptan to the Corresponding Disulfide by Aqueous Hydrogen Peroxide

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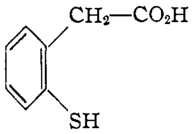
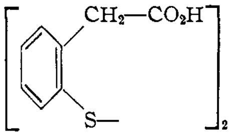
The kinetics of the oxidation of *o*-mercaptophenylacetic acid (I) to the corresponding disulfide (II) by hydrogen peroxide in aqueous solution have been studied spectrophotometrically. The rate in the *p*H range 2.44–7.17 in the presence of excess hydrogen peroxide was pseudo zero order and was expressed by the equation: $-\,d(RSH)/dt = k_0 = k_0'\,(H_2O_2)/(H^+)^{1/2} + k_0''/(H^+)^{1/2}$. Added ferrous ion increased the rate, the pseudo zero-order constant k_0 being proportional to the concentration of added ferrous ion; the rate was unaffected by added cupric ion, iodine, the disulfide II and sodium sulfate (ionic strength 0.05 and 0.1). Measurements at three temperatures gave an apparent activation energy of 17.8 kcal./mole. In the presence of ethylenediaminetetraacetic acid (EDTA), over the *p*H range 2.60–5.63 and with an excess of peroxide, the rate was given by the equation $-d(RSH)/dt = k_1\,(RSH) = k_1'\,(RSH)(H_2O_2)/(H^+)^{1/2}$. The pseudo first-order constant k_1 was independent of the EDTA concentration, of added ferrous ion, and showed no salt effect from added sodium sulfate. The temperature dependence of k_1 gave an apparent activation energy of 16.2 kcal./mole.

The oxidation of a mercaptan to its disulfide is a process of fundamental importance in organic chemistry and in biochemistry. Many studies have been made of the rate of oxygen uptake by solutions of cysteine, thioglycolic acid and glutathione, particularly as affected by trace amounts of heavy metal ions and by *p*H.[2] Kinetic studies on disulfide formation by oxidizing agents other than molecular oxygen are relatively few.[3]

The present paper reports a spectrophotometric study of the oxidation of *o*-mercaptophenylacetic acid (I) to the corresponding disulfide II by hydrogen peroxide in aqueous solution over the *p*H range 2–8; the effect of ferrous ion, of cupric ion, of sodium sulfate and of ethylenediaminetetraacetic acid was studied.


I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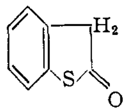
III

Compound I was chosen because it was desired to study the reaction in aqueous solution spectrophotometrically; thiophenol and its disulfide had unfavorable solubility properties, and *o*-mercaptobenzoic acid and its disulfide had unsuitable absorption characteristics. Hydrogen peroxide was selected as the oxidant because it was thought that oxidation by a metallic oxidizing agent might introduce complications by the formation of sulfur-metal complexes.

Ultraviolet Absorption Characteristics and Stability of I, II and III.—The mercapto compound I, its disulfide II and thioöxindole (III) were prepared as described in the Experimental section. Titration of the mercapto compound I with alkali in water gave a titration curve showing two inflections, corresponding to pK_1 4.28 and pK_2 7.67. These two values may be compared with those for phenylacetic acid[4] (pK 4.31) and thiophenol[5] (pK 8.20 in 60% aqueous ethanol). The ultraviolet absorption spectra for I, II and III are given in Fig. 1, and it is clear that mixtures of I and II can be analyzed for the disulfide by measuring the optical density at wave lengths above 305 mμ.

The disulfide was shown to follow Beer's law over the *p*H range 2.80–8.22 at 310 mμ; its solution (1.4×10^{-4} *M*) showed very little change in absorption at 310 mμ, and in *p*H, over a 6-day period. The mercapto compound showed changes in optical density after standing several hours or days. Part of this change was shown to be due to air oxidation to the disulfide; this became increasingly important at higher *p*H. However, the observed optical density changes accompanied by an increase of the *p*H in solutions of the mercapto compound could not be accounted for solely on this basis. The changes could be accounted for by assuming that compound I was cyclizing slowly to thioöxindole (III) on standing. It was shown that thioöxindole in aqueous solution appeared to be hydrolyzed to form the mercapto acid I, which was autoxidized slowly to the disulfide, as judged by *p*H and optical density changes; presumably the reverse change—the cyclization of I to III—is also possible, and this change explains the anomalies described above. The changes in the mercapto compound in solution were rather slow, and their interference with the kinetic measurements could be avoided by using freshly prepared solutions of the mercaptan. It was shown that the disulfide II was stable to excess hydrogen peroxide under the conditions of the runs and that it was the sole product of the oxidation, by an isolation experiment and by the agreement of the calculated and observed op-

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[1] Predoctoral Fellow of the United States Public Health Service, 1956.

[2] Some of the more significant papers on these topics are A. P. Mathews and S. Walker, *J. Biol. Chem.*, **6**, 21 (1909); O. Warburg, *Biochem. Z.*, **187**, 255 (1927); H. A. Krebs, *ibid.*, **204**, 322 (1929); C. Voegtlin, J. M. Johnson and S. M. Rosenthal, *J. Biol. Chem.*, **93**, 435 (1931); L. Michaelis, *ibid.*, **84**, 777 (1929); M. S. Kharasch, *et al.*, *ibid.*, **113**, 537 (1936); M. P. Schubert, THIS JOURNAL, **54**, 4077 (1932); J. S. Fruton and H. T. Clarke, *J. Biol. Chem.*, **106**, 667 (1934); E. S. G. Barron, *Advances in Enzymology*, **11**, 201 (1951); J. Xan, E. A. Wilson, L. D. Roberts and N. H. Horton, THIS JOURNAL, **63**, 1139 (1941); H. Lamfron and S. O. Nielsen, *ibid.*, **79**, 1966 (1957).

[3] (a) R. L. Eager and C. A. Winkler, *Can. J. Res.*, **26B**, 527 (1948); (b) R. E. Basford and F. M. Huennekens, THIS JOURNAL, **77**, 3873 (1955); (c) A. Schoeberl, *Ber.*, **64**, 546 (1931); (d) N. W. Pirie, *Biochem. J.*, **25**, 1565 (1931); (e) C. N. Satterfield, R. C. Reid and D. R. Briggs, THIS JOURNAL, **76**, 3922 (1954), among others.

[4] J. F. J. Dippy, *Chem. Revs.*, **25**, 179 (1939).

[5] G. Schwarzenbach, *Helv. Chim. Acta*, **15**, 1468 (1932).

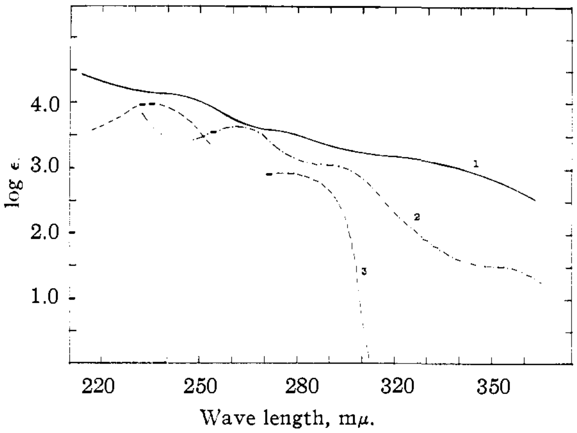

Fig. 1.—1, disulfide (II); 2, thioöxindole (III); 3, *o*-mercaptophenylacetic acid (I).

tical density values at 310 mμ at the end of the reaction.

It was shown that 10^{-2}–10^{-3} molar hydrogen peroxide solutions obeyed Beer's law over the 220–350 mμ range and that the absorption curve was the same at *p*H 2.60 as it was at neutrality.[6]

At *p*H above neutrality the hydrogen peroxide solutions decomposed to liberate oxygen and the absorption spectrum could not be measured. In following the formation of disulfide by measuring the optical density at 310 mμ, the observed value was corrected for the (small) absorption of hydrogen peroxide at this wave length.

Kinetic Runs: The Zero-order Reaction.—Preliminary runs using an excess of hydrogen peroxide gave results which were not pseudo first-order in (RSH) and which were not clearly zero-order. However, the use of painstaking precautions to ensure cleanliness of glassware and the use of a more carefully purified sample of the mercaptan gave results which were accurately described by the following zero-order equation, up to 60–90% completion of the reaction

$$-d(\mathrm{RSH})/dt = k_0 \qquad (1)$$

Figure 2 gives a plot of optical density *vs.* time for a typical run, the data for which are given in Table I. The constant k_0 is obtained from the slope of the plot of $\mathrm{O.D.}_t$ *vs.* t in accordance with the rate law

$$(\mathrm{RSSR}) = k_0t \text{ or}$$
$$k_0 = (\mathrm{O.D.}_t)/(\epsilon_{\mathrm{S-S}})/t \qquad (2)$$

where $\mathrm{O.D.}_t$ is the optical density corrected for the absorption of hydrogen peroxide at the time t and $\epsilon_{\mathrm{S-S}}$ is the molar extinction coefficient of the disulfide II at 310 mμ.

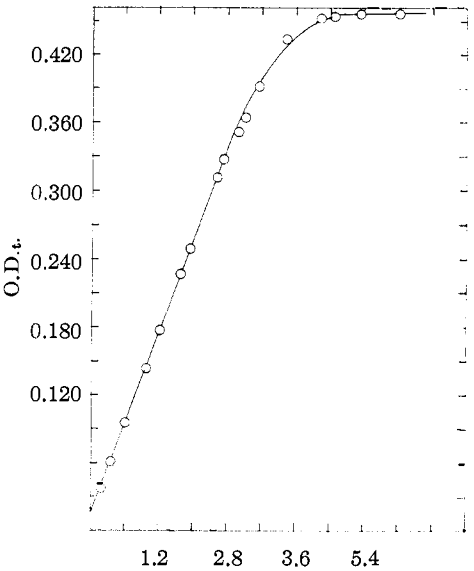

Fig. 2.

Dependence on *p*H and Peroxide Concentration.—The pseudo zero-order rate constant k_0 of eq. 1 was found to be proportional to the hydrogen peroxide concentration over the range of peroxide concentrations studied, 0.114 to 2.32×10^{-2} *M*, and was found to be inversely proportional to the square root of the hydrogen ion concentration in the *p*H range studied, 2.44–7.17. (The reaction was too rapid at high *p*H values, and, as mentioned above, autoxidation became troublesome at these higher *p*H's.) Hence

$$k_0 = k_0'(\mathrm{H_2O_2})/(\mathrm{H^+})^{1/2} \qquad (3)$$

The data on which this equation is based are summarized in Tables II and III. A plot of k_0 $(\mathrm{H^+})^{1/2}$ *vs.* $(\mathrm{H_2O_2})$ was linear and had an intercept (k_0'') of 0.12×10^{-9}; the existence of a positive intercept suggested that the oxidation of the mercaptan by dissolved oxygen made a contribution to the total observed rate. Furthermore, as required by eq. 3, a plot of log $k_0/(\mathrm{H_2O_2})$ *vs.* *p*H was a straight line.

Table I

Pseudo Zero-order Reaction (Run 46)

$(\mathrm{RSH}) = 5.92 \times 10^{-4}$ *M*; $(\mathrm{H_2O_2}) = 0.912 \times 10^{-2}$ *M*; *p*H = 3.90; 29.0°

t, sec.	$\mathrm{O.D.}_t$	$k_0 \times 10^7$,[a] mole. l.$^{-1}$ sec.$^{-1}$	Reaction, %
180	0.037	..	8.2
360	.061	1.82	13.5
600	.095	1.89	21.0
960	.143	1.86	31.6
1200	.177	1.87	39.1
1560	.227	1.89	50.1
1740	.249	1.86	55.0
2220	.312	1.84	68.9
2340	.327	1.83	72.2
2580	.352	1.79	77.7
2700	.364	1.78	80.4
2940	.392	1.76	86.5
∞	.453	..	100.0

[a] Average value $1.84 \pm 0.04 \times 10^{-7}$.

Effect of Ferrous Ion.—The addition of ferrous ion as ferrous sulfate was found to catalyze the oxidation reaction, the value of k_0 being proportional to the ferrous ion concentration in the range studied (0.247 to 5.40×10^{-6} *M*). All of the rates were of zero order, and the completion of the mercaptan oxidation was followed by a slower reaction characterized by a further increase in optical density in the 250–350 mμ range and the appearance of a brown color. A plot of k_0 $(\mathrm{H^+})^{1/2}/(\mathrm{H_2O_2})$ *vs.*

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[6] The measured extinction coefficients are in good agreement with those of A. J. Allmand and D. W. G. Style, *J. Chem. Soc.*, 598 (1930).

TABLE II

DEPENDENCE OF k_0 UPON (H_2O_2) AT 29° AND pH 3.84–3.90

(RSH)[a] × 10^4	(H_2O_2)[a] × 10^2	k_0 × 10^7, mole l.$^{-1}$ sec.$^{-1}$	k_0 × 10^6,[b] $(H^+)^{1/2}/(H_2O_2)$
4.04	0.238	0.541	0.253[b]
5.60	.251	0.541	.249
5.60	.627	1.23	.209
5.70	.114	0.281	.267
5.70	.569	1.14	.223
5.70	1.14	2.09	.205
7.73	0.232	0.585	.297
7.73	1.39	2.54	.219
7.73	2.32	4.14	.214

[a] In mole l.$^{-1}$. [b] Average value 0.237 ± 0.025 × 10^{-6}.

TABLE III

DEPENDENCE OF k_0 ON pH AT 29.0°

(RSH) × 10^4	(H_2O_2) × 10^2	pH	k_0 × 10^7, mole l.$^{-1}$ sec.$^{-1}$	$k_0/(H_2O_2)$ × 10^4, sec.$^{-1}$
5.03	2.04	2.44	0.358	0.0176
5.03	2.04	2.60	.575	.0283
5.48	0.601	3.58	.962	.160
5.92	.912	3.90	1.86	.204
5.92	.912	4.19	2.43	.266
5.92	.912	4.55	3.24	.355
5.67	.142	4.78	0.764	.540
5.67	.142	5.18	0.930	.657
5.67	.142	5.75	1.65	1.17
5.10	.0698	6.47	2.61	3.74
5.10	.0698	6.76	3.55	5.10
5.10	.0698	7.17	5.44	7.80

(Fe^{++}) gave a reasonably good straight line; the data on the ferrous ion catalysis are given in Table IV. Cupric ion in the range 1–4 × 10^{-6} M did not affect the rate of the reaction and neither did the addition of the disulfide II. Stirring and bubbling oxygen through the solution caused a slight increase in the rate; nitrogen gas was without effect. Iodine (1.25 to 6.25 × 10^{-6} M) increased the rate of oxidation moderately.

TABLE IV

EFFECT OF FERROUS SULFATE ON k_0 AT 29.0°

(RSH) × 10^4	(H_2O_2) × 10^2	pH	($FeSO_4$) × 10^6	k_0 × 10^7, mole l.$^{-1}$ sec.$^{-1}$	$k_0(H^+)/(H_2O_2)$ × 10^6, mole$^{1/2}$l.$^{-1/2}$ sec.$^{-1}$
5.10	0.0698	6.47	0.00	2.61	0.215
5.45	1.17	3.90	0.247	2.58	0.247
5.03	0.0701	3.84	1.35	2.66	4.58
5.03	.0701	3.84	2.70	3.89	6.69
5.03	.0701	3.84	5.40	7.62	13.08

Effect of Ionic Strength.—The addition of sodium sulfate to the reaction mixture at an ionic strength of 0.1 and 0.05 increased the rate of the oxidation slightly; the effect, however, was accounted for entirely by the accompanying decrease in the pH caused by the salt, and there was no evidence of a salt effect.

Temperature Coefficient.—Rate measurements were carried out at three temperatures, 20.88, 29.00 and 39.85°. The Arrhenius plot of the data was linear, and yielded an activation energy value of 17.8 kcal. mole^{-1} for the zero-order reaction.

Effect of Ethylenediaminetetraacetic Acid (EDTA) on the Kinetics.—The catalytic effect of added ferrous ion on the rate of the oxidation and the persistence of pseudo zero-order kinetics under these conditions suggested that the reaction in absence of added ferrous ion was in fact being catalyzed by traces of heavy metal ions. The reaction was therefore studied in the presence of ethylenediaminetetraacetic acid (EDTA) which should decrease the effectiveness of any trace metal ions by complexing them.

The kinetics of the reaction were strikingly different in the presence of EDTA; the observed rates were pseudo first-order in mercaptan, in the presence of excess hydrogen peroxide.

$$-\,d(RSH)/dt = k_1(RSH) \qquad (4)$$

The results for a typical run are shown in Table V; the first-order plot of t $vs.$ 2.303 log [O.D.$_t$/(O.D.$_\infty$ O.D.$_t$)], where O.D.$_t$ is the optical density corrected for the absorption of hydrogen peroxide of the time t, and O.D.$_\infty$ is the corrected optical density at infinite time, gave a satisfactory straight line.

TABLE V

PSEUDO FIRST-ORDER REACTION IN PRESENCE OF EDTA
(RSH) = 7.09 × 10^{-4}; (H_2O_2) = 2.66 × 10^{-2}; (EDTA) = 0.858 × 10^{-4}; pH = 3.95; 29.0°

t, sec.	O.D.$_t$	2.3 log[O.D.$_t$/(O.D. − O.D.$_t$)]	k_1 × 10^3,[a] sec.$^{-1}$
600	0.142	0.350	0.583
900	.195	.520	.578
1200	.242	.700	.583
1560	.286	.903	.579
1800	.314	1.064	.591
2400	.362	1.400	.583
2940	.398	1.757	.598
3600	.427	2.187	.608
4020	.439	2.438	.606
4380	.447	2.650	.605
	.481	...	...

[a] Average value 0.591 ± 0.010 × 10^{-3}.

It was found that the first-order constants obeyed the equation

$$k_1 = k_1'(H_2O_2)/(H^+)^{1/2} \qquad (5)$$

The supporting data are given in Tables VI and VII; as required by eq. 5, a plot of $k_1(H^+)^{1/2}$ $vs.$ (H_2O_2) was linear and passed through the origin; hence, there was no contribution to the reaction due to air oxidation. Furthermore, a plot of log ($k_1/(H_2O_2)$) $vs.$ pH was linear. The observed pseudo first-order constants were unchanged by a tenfold increase in EDTA concentration (0.858 to 8.58 × 10^{-4} M) and remained unaffected by added ferrous ion (1.44 to 5.64 × 10^{-6} M) in the presence of 0.858 × 10^{-4} M EDTA. The rate constant was also unaffected by bubbling oxygen through the solution.

At pH 7.09, in the presence of 0.858 × 10^{-4} M EDTA, the kinetics reverted to zero-order; at pH 6.30, the initial zero-order kinetics became first-order during the latter part of the reaction. The observed zero-order rates of these two runs were in agreement with the quantitative relationships established earlier for the zero-order reaction. The first-order rate constant k_1 (2.58 × 10^{-3}) derived from the terminal rate of the run at pH 6.30 was one order of magnitude greater than that required

TABLE VI

DEPENDENCE OF k_1 UPON (H_2O_2) IN THE PRESENCE OF EDTA AT 29.0°

(RSH) × 10^4	(H_2O_2) × 10^2	(EDTA) × 10^4	pH	$k_1 \times 10^3$, sec.$^{-1}$	$k \times 10^{3,b}$ $(H^+)^{1/2}/(H_2O_2)$
4.71	1.39	0.858	4.04	0.373	0.256
7.09	0.665	.858	3.95	.134	.214
7.09	2.66	.858	3.95	.591	.236
7.09	5.32	.858	3.95	1.18	.235
5.53	2.61	.858	4.25	1.30[a]	.251
5.43	0.0656	8.58	5.29	0.0614	.212

[a] Ionic strength = 0.1. [b] Average value 0.234 ± 0.014 × 10^{-3}.

TABLE VII

DEPENDENCE OF k_1 UPON pH IN PRESENCE OF EDTA AT 29.0°

(RSH) × 10^4	(H_2O_2) × 10^2	(EDTA) × 10^4	pH	$k_1 \times 10^3$, sec.$^{-1}$	$k_1/(H_2O_2) \times 10^1$, mole^1, sec.$^{-1}$ l.
5.53	1.30	0.858	2.60	0.0614	0.0471
7.09	5.32	.858	3.95	1.18	.221
4.71	1.39	.858	4.04	0.373	.268
4.71	1.39	4.29	4.53	0.637	.458
4.71	1.39	8.58	5.63	2.18	1.57
5.43	0.131	0.858	6.30	2.58[a]	19.7
5.53	0.130	0.858	7.09	[b]	

[a] This value is from the terminal rate; $k_0 = 0.437 \times 10^{-6}$ mole l.$^{-1}$ sec.$^{-1}$ from initial rate. [b] $k_0 = 1.13 \times 10^{-6}$ mole l.$^{-1}$ sec.$^{-1}$.

at this pH by the results of previous runs under pseudo first-order conditions in the presence of EDTA.

The run at pH 5.29 (Table VI), in which mercaptan and peroxide concentration were nearly equal, did not follow the expected rate law

$$-d(RSH)/dt = k_2(RSH)(H_2O_2) \qquad (6)$$

but showed instead first-order dependence on mercaptan concentration (eq. 4) like the other runs in the presence of EDTA. This result indicated that the reaction between the mercaptan and peroxide was not stoichiometric, at least under these conditions, and that less than one mole of hydrogen peroxide was required to oxidize one mole of mercaptan.

Measurements on the pseudo first-order reaction in the presence of 0.858 × 10^{-4} M EDTA at 21.50, 29.00 and 41.70° yielded a linear Arrhenius plot, giving an activation energy of 16.2 kcal./mole.

Discussion

The experimental results reported above do not permit a dogmatic proposal for the reaction mechanism. The following points have to be considered in discussing the reaction: (1) the rate law

$$-d(RSH)/dt = k_0'(H_2O_2)/(H^+)^{1/2} \qquad (3)$$

(2) The catalytic effect of ferrous ion. (3) The effect of EDTA in changing the kinetics to follow the rate law

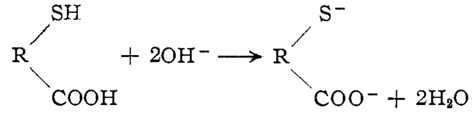
$$-d(RSH)/dt = k_1'(RSH)(H_2O_2)/(H^+)^{1/2}$$

(4) The persistence of the above rate law when (RSH) and (H_2O_2) are of comparable magnitude in presence of EDTA. (5) Lack of a salt effect with sodium sulfate.

Points (1), (2) and (3) suggest, as mentioned above, that the oxidation involves the interaction of a heavy metal ion with the peroxide as the slow step; an alternative possibility is that the metal ion is completely converted to a complex by the mercaptan and that the complex is then oxidized. Both these paths would explain the zero-order kinetics in the presence of excess peroxide.

The inverse square root hydrogen ion dependence which we observe also has been noted by Satterfield[3e] in the oxidation of hydrogen sulfide by peroxide over a pH range of 1.2–4.0. This type of pH dependence is *not* in agreement with a mechanism involving as the sole reactive species a singly or doubly charged anion such as would be produced by the processes

$$H_2O_2 + OH^- \longrightarrow HO_2^- + H_2O$$
$$RSH + OH^- \longrightarrow RS^- + H_2O$$



The pH dependence *is* compatible with a mechanism in which the reactive complex has the stoichiometric composition $(H_2O)(RSH)(OH^-)^{1/2}M$, where M is the heavy metal ion. It is also possible to imagine a chain process which would give the observed pH dependence. From recent work by Lamfron and Nielsen,[2] air oxidation of iron–thioglycolate complexes appears to involve free radicals.

The suggestion that the above complex is the reactive intermediate is reasonable in view of the demonstration by Schubert[2] that complexes of cobalt or iron with mercapto acids are important in autoxidation of the mercapto group.[7] Neville has shown that ferrous ion catalyzes the oxidation of cysteine by hydrogen peroxide through the intermediate formation of ferrous complexes.[8]

The appearance of hydroxyl ion in the reactive complex is in agreement with many earlier observations[2,3] that oxidation of mercaptans proceeds more rapidly at higher pH and hence probably involves the mercaptide ion, RS^-, as the reactive species.

There is no assurance that the mechanism of the oxidation in the presence of EDTA is the same as it is in its absence, and indeed it is difficult to present a single mechanism which agrees with all the facts. However, the pH and peroxide dependence and the activation energy are the same in the presence of EDTA as in its absence.

The absence of a salt effect might be taken to indicate that the reaction involved free radical intermediates instead of ions; however, the reaction of hydrogen peroxide with iodide ion has been shown to involve only a small salt effect.[9]

Various aspects of this problem are being investigated further.

(7) *Cf.* A. E. Martell and M. Calvin, "Chemistry of the Metal Chelate Compounds," Prentice-Hall, Inc., New York, N. Y., 1953, p. 382 ff. The structures of some of the cobalt complexes recently have been revised by R. G. Neville and G. Gorin, THIS JOURNAL, **78**, 4891, 4893 (1956).

(8) R. G. Neville, *ibid.*, **79**, 2456 (1957).

(9) F. Bell, R. Gill, D. Holden and W. F. K. Wynne-Jones, *J. Phys. Chem.*, **55**, 874 (1951).

Preparation of Materials.—*o*-Nitrophenylpyruvic acid was prepared by condensation of ethyl oxalate with *o*-nitrotoluene with potassium ethoxide,[10] at room temperature, and was oxidized with hydrogen peroxide in alkaline solution to *o*-nitrophenylacetic acid. The product was obtained in 62–69% over-all yield and melted at 140–141°, in agreement with the reported value, after one recrystallization from chloroform–hexane.

o-Aminophenylacetic acid was prepared by reduction of *o*-nitrophenylacetic acid in ethanol with hydrogen and palladium[11]; the uptake of hydrogen was essentially quantitative, and, since the product rapidly cyclizes to oxindole, it usually was used without further purification. A sample recrystallized from cold benzene–methanol melted at 114–116°; the reported value[11] is 119–120°.

o-**Mercaptophenylacetic Acid.**—The procedure of Marschalk[12] was modified, after considerable experimentation, as follows:

o-Aminophenylacetic acid (12.08 g., 0.080 mole) was dissolved in 32 ml. (0.080 mole) of 10% sodium hydroxide, 40 ml. of water was added and the resulting solution was mixed with 80 ml. of 1 *N* aqueous sodium nitrite. After cooling to 0°, this solution was added slowly to a stirred mixture of 85 ml. of 2 *N* hydrochloric acid and 80 g. of ice. Stirring was continued for 0.5 hr., after which time part of the diazonium salt precipitated out. The resulting slurry was added in small portions to an aqueous solution containing 14.8 g. of potassium ethyl xanthate, 60 ml. of 2 *N* sodium carbonate and 24 ml. of water. The solution of the xanthate was kept at 45° throughout the addition and for 0.5 hr. longer. The alkaline solution of the xanthate ester (III) was brought to room temperature, acidified to *p*H 4 with concentrated hydrochloric acid and extracted with ether. The ethereal solution was dried, evaporated, and the resulting red-brown oily residue was subjected to hydrolysis in boiling 1:1 ethanol–water mixture containing 18 g. of potassium hydroxide. The hydrolysis was continued for 48–72 hr., the mixture being kept under nitrogen throughout this time. After cooling to room temperature ice was added, and the hydrolysis mixture was acidified to *p*H 4. The resulting precipitate was collected, dried and extracted with light petroleum ether. Removal of the petroleum ether gave a light yellow residue (6.35 g., 44%) of *o*-mercaptophenylacetic acid (IV), m.p. 95–96°. Colorless, or nearly colorless plates, m.p. 98–99°, resulted from a chromatographic purification of the petroleum ether extract which was carried out as follows: *o*-mercaptophenylacetic acid, dissolved in a minimum amount of benzene and diluted with a threefold volume of petroleum ether, was chromatographed on a 20-fold amount by weight of activated silica gel. Elution of the column was made with 1:3 petroleum ether–benzene. Collected fractions (250–500 ml.) were removed under vacuum and the solid residues recrystallized from benzene–hexane; m.p. 98–99°. The reported melting point was 96°.

The mercaptophenylacetic acid also was obtained by alkaline hydrolysis of thioöxindole (Marschalk); the thiooxindole was prepared by steam distillation of crude mercaptophenylacetic acid in dilute hydrochloric acid solution.

Diphenyl Disulfide *o,o'*-**Diacetic Acid.**—*o*-Mercaptophenylacetic acid was dissolved in 5% bicarbonate and heated on the steam-bath for 1 hr., which caused air oxidation. The solution was set aside overnight, was then treated with charcoal, filtered and was then acidified with mineral acid. The disulfide was recrystallized from aqueous ethanol or aqueous acetic acid and melted at 146–147°.

Anal. Calcd. for $C_{16}H_{14}O_4S_2$: C, 57.46; H, 4.22. Found: C, 57.56; H, 4.33.

Kinetic Runs and Spectrophotometric Determinations.—All water used for the preparation of reagent solutions was ordinary distilled water purified by passing through an ion-exchange column. Gases dissolved in the purified water were removed by boiling, and the distilled water was allowed to cool under a stream of nitrogen from which oxygen and carbon dioxide were removed by bubbling the gas through absorption vessels containing aqueous vanadyl sulfate, aqueous barium hydroxide and distilled water.

All apparatus used for the preparation of stock solutions and for kinetic runs was treated with cleaning solution, rinsed several times with tap water, ten times with ordinary distilled water and ten times with distilled water purified by the ion-exchange method.

Stock solutions of the thiol and of the disulfide were prepared immediately before use by stirring a weighed amount of the solid with purified distilled water in a volumetric flask with the aid of a magnetic stirrer until complete solution was achieved. Hydrogen peroxide solutions were prepared immediately before use by dilution of the required volume of 30% reagent grade (Baker analyzed) unstabilized hydrogen peroxide. The exact hydrogen peroxide content was determined by spectrophotometric analysis in the wave length region 250–320 mμ. Molar extinction coefficients of hydrogen peroxide in this wave length range were determined from the O.D. values of solutions analyzed permanganimetrically.

Ferrous sulfate used was recrystallized analytical reagent (Merck reagent). Copper sulfate was used without further purification (C.P. Baker analyzed reagent). Iodine (Mallinckrodt U.S.P.) was purified by sublimation. Ethylenediaminetetraacetic acid was available in the form of a 34% aqueous solution of the tetrasodium salt (Versene, Bersworth Chemical Co., Framingham, Mass.).

Adjustments of *p*H were made with dilute solutions of perchloric acid and carbonate-free sodium hydroxide prepared from the corresponding reagent-grade chemicals.

All *p*H measurements were made with a Beckman *p*H meter model G equipped with micro-electrodes. Calibration of the *p*H meter was carried out with a 0.05 *M* potassium acid phthalate buffer of *p*H 4.01. The *p*H readings were reproducible within 0.02 *p*H unit.

All spectrophotometric measurements were carried out with a model DU Beckman spectrophotometer. The calibration of the instrument was checked repeatedly against the absorption spectrum of a solution containing 0.0400 g. of potassium chromate per liter in 0.05 *N* potassium hydroxide.[13] The calibration of the wave length scale appeared, as a result of these checks, to remain the same within 1 mμ. The O.D. readings in the majority of checks agreed with the reported values[12] within 3% at 300–350 mμ, within 3–5% at 250–300 mμ and 5–10% at 220–250 mμ. A hydrogen source was used for all measurements, except for several kinetic runs in which a tungsten source was used. The optical density readings at 310 mμ were taken at the maximum-sensitivity setting of the instrument with a slit-width of 1.05 ± 0.05 mm.

Fifty ml. of the stock solution of the thiol, or 55 ml. of a solution consisting of 50 ml. of thiol solution and 5 ml. of catalyst solution, and 100 ml. of hydrogen peroxide contained in separate flasks fitted with ground glass stoppers were brought to the required temperature in a water thermostat. The reaction was started by pipetting 5 or 10 ml. of the hydrogen peroxide solution into the flask containing the thiol solution to give a final volume of 60 ml. Measurement of time was started when one-half of the hydrogen peroxide solution had been transferred. After the reagents were thoroughly mixed by agitation, an aliquot was rapidly transferred into a clean and dry silica absorption cell placed in the cell compartment of a Beckman spectrophotometer, model DU. The temperature in the cell compartment was maintained at a given value by circulating water from the thermostat through four "thermospacers" arranged in pairs on each side of the cell compartment. Temperature fluctuations in the cell compartment did not exceed 0.05°. Optical density readings at 310 mμ were taken at suitable intervals. In several experiments, oxygen or nitrogen were bubbled through the reaction mixture with the aid of a capillary tube. In all cases ordinary tank oxygen and nitrogen were used without purification. The gas delivery tube was removed from the absorption cell prior to taking each reading.

Hydrogen peroxide solutions were analyzed after the completion of kinetic runs. It was shown by separate measurements that no detectable decomposition of the hydrogen peroxide stock solutions took place under the conditions of the kinetic runs in absence of the thiol. Likewise, the ultraviolet radiation necessary for the performance of O.D. readings did not give rise to a decomposition of hydrogen peroxide stock solutions or to an acceleration or retardation of the rates of oxidation.

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(11) G. Hahn and M. R. Tulus, *Ber.* **74**, 515 (1941).

(12) C. Marschalk, *J. prakt. Chem.*, [2] **88**, 237 (1913).

(13) G. W. Haupt, *J. Research Natl. Bur. Standards*, **48**, 414 (1952).

Isolation of the Disulfide from a Kinetic Run.—The thiol (20.6 mg.) was dissolved in 200 ml. of distilled water; 150 ml. of this solution was used for three kinetic runs. The reaction mixtures remaining after the completion of the runs were combined, and the unused thiol solution was added; the combined solutions corresponded to 175 ml. of the original thiol solution. The solution was allowed to stand 1 hr. to allow time for the oxidation of the newly added thiol. The solution was made 1 *M* in sulfuric acid, was extracted several times with chloroform, the chloroform was evaporated to dryness *in vacuo* and the residue was taken up in 2-3 ml. of chloroform. The solution was treated with charcoal, was filtered and petroleum ether was added until the solution was faintly cloudy. The solution after cooling yielded 8.6 mg. (48%) of the disulfide, m.p. 143-145°; the mixed m.p. with an authentic sample was 146-147°. This isolation of the disulfide, coupled with the spectral data on the oxidation solutions at the end of the reaction, indicates that the thiol is oxidized quantitatively to the disulfide and that the reaction stops at the disulfide stage.

ROCHESTER, N. Y.

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY, CAIRO UNIVERSITY AND AIN SHAMS UNIVERSITY]

Organic Sulfur Compounds. XXXIV. Synthesis of Ethylenes and Ethylene Sulfides by Action of Diazoalkanes on Thioketones

BY ALEXANDER SCHÖNBERG, ABD EL KADER FATEEN AND ABD EL MAGED AMINE SAMMOUR

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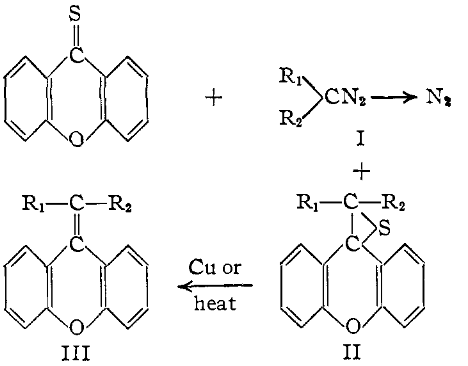
Various ethylene sulfides have been prepared by the interaction of diazoalkanes with xanthione and Michler thioketone. Some of these ethylene sulfides were allowed to react with copper bronze in boiling xylene, yielding the corresponding ethylene compounds. The ethylene derivatives IIIa, c and f show thermochromic properties, IIIc has piezochromic properties. Treatment of 2-(4′-methoxystyryl)-4-thio-α-naphthopyrone (VIIa) with diphenyldiazomethane in boiling benzene gave the ethylene derivative VIII. 2-Styryl-4-thio-α-naphthopyrone (VIIb) crystallizes from benzene as violet or yellow crystals. By crystallographic investigations, this phenomenon was elucidated.

Experiments with Xanthione and Michler Thioketone.—Schönberg and Nickel[1] found that xanthone with diphenyldiazomethane yielded the ethylene sulfide derivative II (R_1, R_2 = C_6H_5), which on treatment with copper bronze produced 9-(diphenylmethylene)-xanthene (III, R_1, R_2 = C_6H_5).

This reaction has now been extended with *p,p′*-dichlorodiphenyldiazomethane (Ia), *o*-chlorophenylphenyldiazomethane (Ib), *p*-nitrophenylphenyldiazomethane (Ic), *p*-xenylphenyldiazomethane (Id), methylphenyldiazomethane (Ie), di-*p*-tolyldiazomethane (If) and *p*-tolylphenyldiazomethane (Ig) (scheme A). The reactions led to the formation of ethylene sulfides, except with *p*-tolylphenyldiazomethane where the ethylene derivative IIIg was obtained, presumably by thermal decomposition of IIg. Similar pyrolytic decompositions have been observed by Schönberg and Vargha.[2] IId was not obtained analytically pure. The ethylene sulfides IIa, b, c and f as well as the impure IId were transformed to the corresponding ethylenes IIIa, b, c and f by refluxing in xylene with copper bronze.

SCHEME A



I, II and III

a, R_1, R_2 = $C_6H_4Cl(p)$

b, R_1 = $C_6H_4Cl(o)$, R_2 = C_6H_5

c, R_1 = $C_6H_4NO_2(p)$, R_2 = C_6H_5

d, R_1 = $C_6H_4{\cdot}C_6H_5(p)$, R_2 = C_6H_5

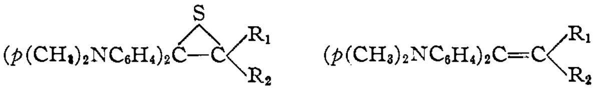
e, R_1 = CH_3, R_2 = C_6H_5

f, R_1, R_2 = $C_6H_4CH_3(p)$

g, R_1 = $C_6H_4CH_3(p)$, R_2 = C_6H_5

The action of various diazoalkanes on Michler thioketone led to the formation of the ethylene sulfides (IVa-d,h) or the ethylene derivatives (Ve-g) (Scheme B). The ethylene sulfide (IVa) was transformed to the corresponding ethylene (Va) on treatment with copper bronze in boiling xylene. When a benzene solution of Michler thioketone and diphenyldiazomethane was refluxed, Vg was obtained, while Staudinger[3] on working at room temperature obtained IVg. Vg previously has been prepared by a different method.[4]

SCHEME B



IV V

IV and V

a, R_1 = CH_3, R_2 = C_6H_5

b, R_1 = CH_3, R_2 = $C_6H_4CH_3(p)$

c, R_1, R_2 = $C_6H_4Cl(p)$

d, R_1 = $C_6H_3(CH_3)_2(2,5)$, R_2 = C_6H_5

e, R_1 = $C_6H_4Cl(o)$, R_2 = C_6H_5

f, R_1 = $C_6H_4{\cdot}C_6H_5(p)$, R_2 = C_6H_5

g, R_1, R_2 = C_6H_5

h, R_1, R_2 = $C_6H_4CH_3(p)$

The action of 9-diazofluorene on Michler thioketone led to the formation of bis-(*p*-dimethylaminophenyl)-dibenzofulvene (VI), which has previously been synthesized by a different method by Bergmann[5] and Hervey.

Attention is drawn to the very good yields obtained in the experiments given and to the fact

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[1] A. Schönberg and S. Nickel, *Ber.*, **64**, 2323 (1931).

[2] A. Schönberg and L. v. Vargha, *Ann.*, **483**, 176 (1930).

[3] H. Staudinger and J. Siegwart, *Helv. Chim. Acta*, **3**, 833 (1920).

[4] H. Staudinger, *ibid.*, **3**, 862 (1920).

[5] E. Bergmann and J. Hervey, *Ber.*, **62**, 893 (1929).