Anal. Calcd. for $C_4H_2O_3N_2Br_2$: N, 9.83. Found: N, 9.93.

Summary

1. Ethyl cyanomalonate, ethyl dicyanoacetate and methyl dicyanoacetate failed to condense with urea (or thiourea) in the presence of sodium ethylate to give the nitrile and 4-imidonitrile, respectively, of 2,4,6-triketohexahydropyrimidine-5-carboxylic acid.

2. 4-Imidobarbituric acid reacted with fused urea to give 2,6-diketo-4-ureidohexahydropyrimidine-5-carboxylamide, which could not be converted by hydrolysis to the corresponding 2,6-diketo-4-imidohexahydropyrimidine-5-carboxylamide. Interaction with bromine water led to the formation of 5,5-dibromobarbituric acid.

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[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

Rate Characteristics of the Oxidation of Disulfide-Acids by Hydrogen Peroxide

BY GEORGE G. STONER AND GREGG DOUGHERTY

As a means of studying the oxidation of disulfides, the action of hydrogen peroxide on four aliphatic disulfide-acids was followed by determinations of peroxide and acidity. The reactions were conducted at 30 and 40° for dithiodiacetic acid and β,β'-dithiodipropionic acid, and at 30° for α,α'-dithiodipropionic acid and γ,γ'-dithiodibutyric acid. Disulfide and hydrogen peroxide were allowed to react in proportions to satisfy the over-all equation to sulfonic acid, illustrated as follows with dithiodiacetic acid.

$$(\text{—}SCH_2CO_2H)_2 + 5H_2O_2 \longrightarrow 2HO_3SCH_2CO_2H + 4H_2O$$

The solutions were initially 0.1 *M* with respect to disulfide-acid and 0.5 *M* with respect to hydrogen peroxide, 0.005 mole of acid and 0.025 mole of peroxide having been diluted to 50 g. with water or dioxane–water as solvent. Table I is a list of experiments and conditions. The resulting curves are in Fig. 1.

TABLE I

EXPERIMENTAL CONDITIONS AND COMPOSITIONS OF SOLUTIONS

				Solvent[d]	
Expt.[a]	Disulfide[b]	Water added,[c] g.	Dioxane, g.	Dioxane, %	D_{30}[e]
1a, 1b	Blank	0	47.16	94	3.8
2a, 2b	Blank	47.16	0	0	76.7
3a, 3b	A	46.25	0	0	76.7
4[f]	A	45.74	0	0	76.7
5[g]	A	44.85	0	0	76.7
6a, 6b	A	6.98	39.27	80	10.4
7a, 7b	A	2.07	44.18	90	5.5
8a, 8b	A	0	46.25	94	3.8
9a, 9b	B	6.95	39.16	80	10.4
10a, 10b	B	2.05	44.06	90	5.5
11a, 11b	B	0	46.11	94	3.8
12	C	6.95	39.16	80	10.4
13	D	6.92	39.05	80	10.4

[a] Reaction temperature was 30° except for the "b" series of experiments, in which cases it was 40°. [b] Weights of disulfide-acids were as follows: A, dithiodiacetic acid, 0.91 g.; B, β,β'-dithiodipropionic acid, 1.05 g.; C, α,α'-dithiodipropionic acid, 1.05 g.; and D, γ,γ'-dithiodibutyric acid, 1.19 g. [c] This weight did not include water in the Superoxol. In each run 2.84 g. of Superoxol was used. [d] In calculating composition of solvent, hydrogen peroxide was regarded as water because of its large and similar dielectric constant. [e] Dielectric constants for 30°. The corresponding values for 40° are less by *ca.* 5%. Åkerlöf and Short, THIS JOURNAL, **58**, 1241 (1936). [f] Concd. sulfuric acid (0.51 g., 0.005 mole) was added as a catalyst. [g] Sulfoacetic acid (1.4 g., 0.01 mole) was added as a catalyst.

Experimental Part

Materials.—Disulfide-acids were prepared from corresponding Bunte salts as described previously.[1] Data for m. p. and equivalent weight, calculated and found, were, respectively, as follows: dithiodiacetic acid, 102–103°, 91.1, 91.1; β,β'-dithiodipropionic acid, 154°, 105.1, 106; α,α'-dithiodipropionic acid, 127–135°, 105.1, 106; and γ,γ'-dithiodibutyric acid, 103–105°, 119.2, 120. The Superoxol analyzed 29.2% hydrogen peroxide. Purified[2] *p*-dioxane was distilled from sodium as it was needed. The sulfoacetic acid[3] melted at 86–89°. Bath temperatures were constant to 0.05°, and were calibrated against a platinum resistance thermometer.

Procedure.—The weights of substances which were used in each experiment are in Table I. Distilled water was weighed into a tared flask, followed by Superoxol, dioxane, and disulfide-acid, the latter being dissolved immediately. After mixing, solutions were transferred at once to 10-inch test-tubes which were placed in a well-stirred water-bath, the temperature of which was either 30 or 40°. Tubes were kept stoppered except during the withdrawal of samples for titration. In sampling, a 2.00-cc. portion was pipetted into a freshly mixed solution of 50 cc. of 2% potassium iodide and 15 cc. of cold 1:1 sulfuric acid. After being stoppered for five minutes in the dark it was

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(1) Stoner and Dougherty, THIS JOURNAL, **63**, 987 (1941).

(2) Eigenberger, *J. prakt. Chem.*, **130**, 75 (1931).

(3) Stillich, *ibid.*, **73**, 541 (1906), reported a m. p. of 84–86°.

titrated against standard sodium thiosulfate. In the meantime another 2.00-cc. portion was pipetted into 20 cc. of cold water and titrated against standard sodium hydroxide, phenolphthalein being the indicator. Blanks (experiments 1 and 2) indicated that less than 0.3% of the hydrogen peroxide decomposed within two hundred hours in dioxane at 30 or 40°. Corresponding extents of decomposition in water were 2.2 and 5.1%, respectively.

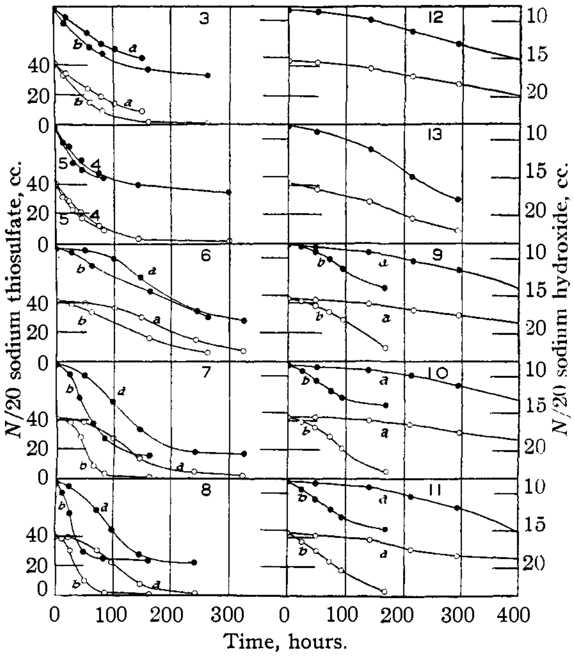

Fig. 1.—Oxidation rate curves for solutions of disulfide-acids (0.1 *M* initially) in dioxane–water by hydrogen peroxide (0.5 *M* initially). Experiments 3–13. ○, Titration against 0.05 *N* sodium thiosulfate (scale on left ordinate); ●, titration against 0.05 *N* sodium hydroxide (scale on right ordinate). Curves which are marked "b" are for 40°, others are for 30°. Curves for experiments 4 and 5 are corrected for extra alkali which was required to neutralize acidic catalysts (see Table I).

Results

In 80% dioxane at 30°, dithiodiacetic acid and γ,γ'-dithiodibutyric acid were oxidized at approximately the same rate, which was more than twice that for either α,α'- or β,β'-dithiodipropionic acid, the latter being attacked slightly more slowly. However, at 40° the rates were similar for dithiodiacetic acid and β,β'-dithiodipropionic acid.

The solvent was varied for dithiodiacetic acid and β,β'-dithiodipropionic acid. In these cases, reactions were slowest in 80% dioxane and next slowest in 90% dioxane, but a difference was barely evident in the case of β,β'-dithiodipropionic acid. For dithiodiacetic acid, reaction began most rapidly in water, but it was completed sooner in dioxane, and it was slower at all stages in solvents of intermediate compositions and dielectric constants. The decided acceleration in solvents which contained the smallest percentage of water would parallel a possibly greater catalytic effect of protons which were not solvated with water, as compared with that of unsubstituted oxonium ions. In the case of dithiodiacetic acid in water, the catalytic effect of 0.2 *N* sulfuric acid corresponded to a 10° increase in temperature, and that of 0.2 *M* sulfoacetic acid was even greater. The temperature coefficient was decidedly greater in solvents which had larger ratios of dioxane to water.

The characteristic of the curves (except those for reaction in water alone) of being initially concave with respect to the origin was related partly to the autocatalytic nature of the process but mainly to the several consecutive reactions which were involved. Usually curves which represented concentration of acid had initial slopes which were equivalent to those of curves for concentration of peroxide. That is, there was no pronounced increase in acidity as compared with amount of oxidation. Therefore acids were not produced until rather late in the series of consecutive reactions. This is consistent with an observation on the oxidation of disulfides by chlorine and water: fission of S–S linkages does not occur at least until after the so-called "disulfoxide" stage has been reached.[4] Furthermore, sulfinic acids were unlikely intermediates, inasmuch as sulfinoacetic acid has been found to decompose above −20° with evolution of sulfur dioxide,[5] and no gas was observed as a reaction product in our experiments.

Summary

A comparative rate study of the oxidation of four aliphatic disulfide-acids by hydrogen peroxide has been made with reference to some of the effects of structure, solvent and temperature.

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[4] Lee and Dougherty, *J. Org. Chem.*, **5**, 82 (1940).

[5] Reuterskiöld, *J. prakt. Chem.*, **127**, 269 (1930).