INTRAMOLECULAR GENERAL-BASE CATALYSIS OF o-CARBOXYL GROUP IN THE IODINE OXIDATION

OF o-METHYLTHIOBENZOIC ACID IN AQUEOUS MEDIA (1)

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Previously, we have shown that bromine in acetic acid-pyridine-water mixture is an excellent oxidation reagent which converts an organic sulfide selectively to the corresponding sulfoxide (2). In connection with this observation, the recent observation by Higuchi and his coworkers is quite interesting; they found that in the iodine oxidation of tetrahydrothiophene in aqueous media, dicarboxylate and phosphate dianions are efficient catalysts, while mono-carboxylate anion is a relatively poor catalyst as compared to these dianions (3).

We now wish to report that o-carboxylate group displays a remarkably large neighboring group effect in the iodine oxidation of o-methylthiobenzoic acid (I) in water.
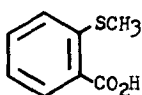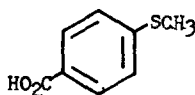
The kinetics were followed spectrophotometrically by observing the loss of triiodide ion ($355 \, m\mu$) in aqueous media buffered either by acetate or phosphate buffer and good pseudo-first order rate constants were obtained.

The rate of the oxidation of I was found to be dependent on the dissociation of o-carboxyl group (pKa 4.40) as shown in Fig. 1; the buffer concentration and the ionic strength of the solution did not affect the rate.

The oxidation of the p-isomer (II) was very sluggish; The rate was negligible in an acetate buffered media (pH 4-5, 35-100°C). In phosphate buffered solutions, the reaction did

take place but with a very slow rate (pH 7, 60°C) and the rate was apparently dependent on the buffer concentration (4).
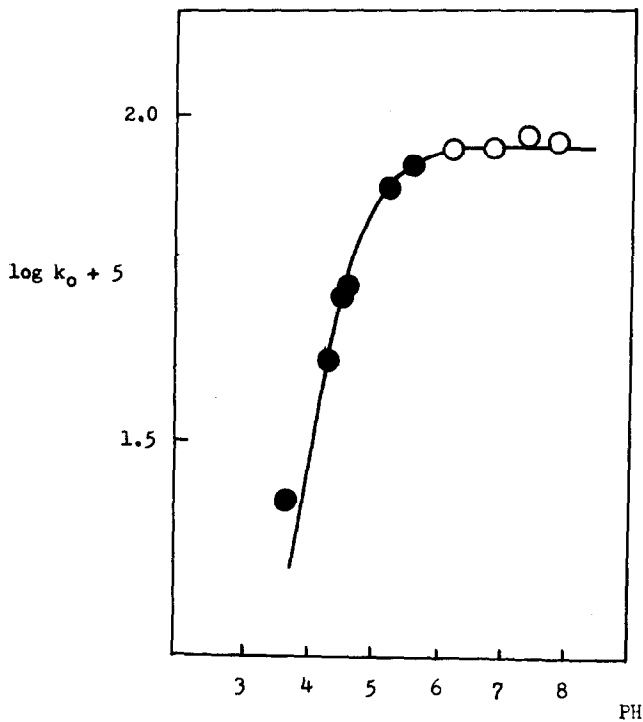

FIG. 1

Fig. 1   pH-rate profile for I in 20 % t-butanol-water (v/v),

35°C; $R_2S = 2 \times 10^{-4}M$; $I_2 = 4 \times 10^{-5}M$; $KI = 10^{-2}M$;

buffer = $10^{-2}M$; ● , acetate buffer; ○ , phosphate buffer;

———— , calculated curve using $k_{obs} = k_o' Ka/(Ka + [H^+])$, where

$k_o' = 9.01 \times 10^{-4}$ sec^{-1}, and pKa = 4.40 for I determined

spectrophotometrically in this solvent.

The oxidation of I was conducted in ^{18}O-enriched water, and the resulting sulfoxide (III) was reduced to o-methylthiobenzyl alcohol (IV). The results indicated that one atom of ^{18}O was incorporated exclusively in the sulfoxide oxygen. The solvent isotope effect for I was determined: $k_{H_2O}/k_{D_2O} = 2.3$ (36°C, pH 6.82, pD 7.08, phosphate buffer in water) (5).
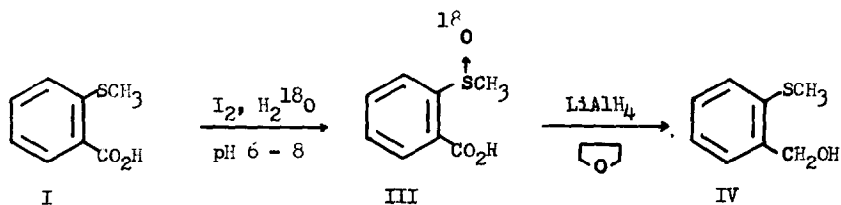
Atom % of ^{18}O: Water, 1.60; III, 0.67; IV, 0.20

The pH-rate profile and a large rate difference between the o- and p-isomer clearly demonstrate the intramolecular neighboring group participation of the dissociated o-carboxyl group of I in the reaction. As for the neighboring group participation, the following three mechanisms are conceivable: (a) nucleophilic attack of the carboxylate anion on the sulfur atom involving five membered cyclic intermediate (VI) which rapidly decomposes to give III, (b) general base catalyzed nucleophilic attack of water on the sulfur atom of VI and (c) general base catalyzed nucleophilic attack of water on the sulfur atom of V. In all these mechanistic schemes the preequilibrium formation of the iodosulfonium salt (V) is assumed (2, 6).

The ^{18}O experiment favors the path (c), although it does not necessarily rule out the possibility that $H_2^{18}O$ attacks exclusively on sulfonium sulfur of VI. On the other hand, the sizable isotope effect suggests that the proton transfer is involved in the rate-limiting step, and hence the mechanism (a) is ruled out. The path (b) needs buffer anion as the general base catalyst for the attack of water, and is not in accord with the experimental results.
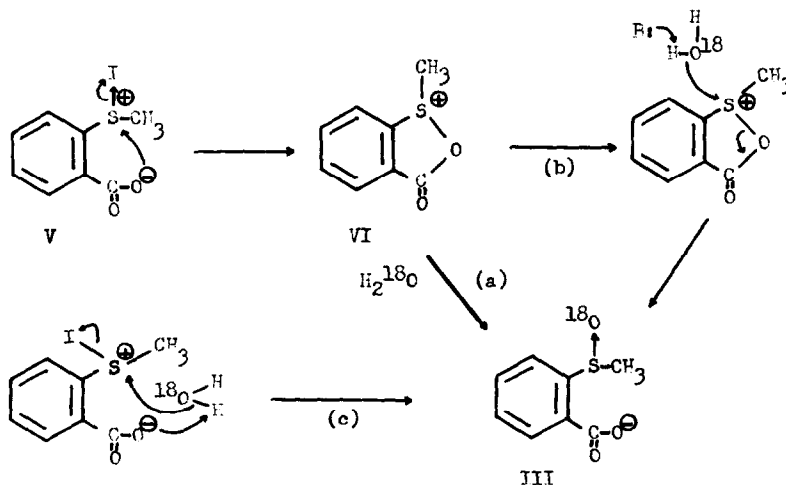
Thus, only the mechanistic scheme (c) satisfies all the experimental observations. This conclusion is rather unexpected in view of the facts that nucleophilic substitution is known to take place readily on the sulfonium sulfur and actually observed in the oxidation of tetrahydrothiophene catalyzed by phthalic acid dianion (3), while the five-membered cyclic intermediate is known to be involved in other ester hydrolysis (7).

Further works on the mechanism of this reaction are in progress in this laboratory.

<div align="center">REFERENCES</div>

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(4) The kinetics seemed to be complicating, presumably due to the reaction of phosphate with iodine.

(5) For a rigorous comparison, the entire pH-rate profile is necessary. However, pD 7.08 seems to be higher enough for the full dissociation of I. (See G. Dahlgren, Jr., and F. A. Long, J. Am. Chem. Soc., 82, 1303, (1960)).

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