product on the basis of recovered starting material, together with some unidentified by-products. III-OH and V-OH were treated similarly, except that the product from III-OH was collected directly from the reaction flask in a cold trap. The results of the pmr analyses of the products are summarized in Table IV.

Pmr Studies. Both Varian Models A-60 and A-60A were used in the present study. The spectra of IV-ODNB, V-ODNB, and their nondeutrated analogs, were taken in chloroform-d_1 and all of the other spectra in carbon tetrachloride. The peak positions of the protons which were used in the analyses are collected in Table IX. The amount of scrambling in each of the reaction products was, in most cases, determined by integrations which were made several times in order to minimize the error. But, in those cases where the peak separations are not great enough, the spectra were taken with slower sweep time and the peak heights were used for analyses. An internal standard technique was also employed for the determination of the per cent scrambling in each of the olefinic products IV-Ol and V-Ol. For this purpose, desoxybenzoin was chosen and the methylene group absorption peak (δ 4.05) of the standard was compared with the vinyl proton peaks of the sample.

Oxidation of Thioethers to Sulfoxides by Iodine. II.[1] Catalytic Role of Some Carboxylic Acid Anions[2]

K.-H. Gensch, I. H. Pitman, and T. Higuchi

Contribution from the School of Pharmacy, University of Wisconsin, Madison, Wisconsin, and Department of Pharmaceutical Chemistry, University of Kansas, Lawrence, Kansas. *Received October 14, 1967*

Abstract: Mono- and dicarboxylate ions are shown to catalyze the oxidation by aqueous iodine of aliphatic and alicyclic thioethers to sulfoxides. For example, the rate of oxidation of tetrahydrothiophene to tetrahydrothiophene 1-oxide at pH 8 and 25° is 20 times faster in a 1×10^{-3} *M cis*-1,2-cyclohexanedicarboxylate buffer than in water (both solutions being 6×10^{-2} *M* in potassium iodide). Kinetic results suggest that acyloxysulfonium ions are intermediates in the oxidations and that these ions are converted to sulfoxides by nucleophilic displacements at the carbonyl carbon atom rather than by nucleophilic displacement at the positively charged sulfur atom.

The oxidation of thioethers to sulfoxides by aqueous iodine has been shown[1] to be strongly catalyzed by several inorganic nucleophiles, especially doubly charged anions such as HPO_4^{2-}, $HAsO_4^{2-}$, and CO_3^{2-}. To account for this catalysis, an oxidation mechanism was proposed[1] which involved (a) addition of iodine to the thioether followed by ionization of the complex to yield an iodosulfonium ion, (b) displacement of iodide from the iodosulfonium ion by the catalyst (*e.g.*, HPO_4^{2-}) to yield an acid sulfonium ion, and (c) hydrolysis of the acid sulfonium ion to yield the sulfoxide plus an acid derivative (*e.g.*, $H_2PO_4^-$).

The present report is concerned with details of the mechanism of catalysis of the same reaction by several polycarboxylate and monocarboxylate ions. Therefore, comparative kinetic data are presented for the iodine oxidation of tetrahydrothiophene to tetrahydrothiophene 1-oxide in aqueous phthalate, succinate, 2-phenylsuccinate, citrate, *cis*- and *trans*-1,2-cyclohexanedicarboxylate, acetate, propionate, and *n*-hexanoate buffers. Data for the oxidation of diethyl sulfide and benzyl methyl sulfide to diethyl sulfoxide and benzyl methyl sulfoxide, respectively, by iodine in *cis*-1,2-cyclohexanedicarboxylate buffers are also discussed.

We have shown in a preliminary communication[3] that phthalate ion catalyzed the iodine oxidation of tetrahydrothiophene to tetrahydrothiophene 1-oxide and that during the process phthalic anhydride was formed. We have also described[4] an asymmetric oxidation of benzyl methyl sulfide to optically active benzyl methyl sulfoxide by iodine in a *d*-2-methyl-2-phenylsuccinate buffer.

A likely intermediate in these oxidations is a positively charged acyloxysulfonium ion (*e.g.*, **3**). Conversion of this species to the sulfoxide could be initiated either by back-side attack of water or hydroxide ions on the sulfur atom or by nucleophilic attack (intramolecular or intermolecular) on the carbonyl carbon atom. The identification of phthalic anhydride during the iodine oxidation of tetrahydrothiophene in phthalate buffer[3] suggests that in this case, and possibly in other dicarboxylate systems, intramolecular reaction at the carbonyl carbon atom is the preferred route. However, the likely intermediate in monocarboxylate-catalyzed systems could not be converted to the sulfoxide by intramolecular nucleophilic attack. Reaction of monocarboxylate ions at the sulfur atom would only regenerate the same acyloxysulfonium ion and thus not affect the kinetics of the conversion to the sulfoxide. On the other hand, the monocarboxylate ion could participate in nucleophilic reactions at the carbonyl group either by acting as a nucleophile or as a general base (*cf.* the role of carboxylate ions in the hydrolysis of carboxylic acid anhydrides[5]). Thus, a kinetic dependence on the concentration of monocarboxylate ions of this step of the reaction would strongly suggest that the acyloxysulfonium ion was converted to the sulfoxide by reactions at the carbonyl carbon atom.

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[1] T. Higuchi and K.-H. Gensch, *J. Am. Chem. Soc.*, **88**, 5486 (1966).

[2] This research was supported in part by grants from the National Institutes of Health under GM-05830. Please address all correspondence to Professor T. Higuchi at Pharmaceutical Chemistry Laboratory, School of Pharmacy, University of Kansas, Lawrence, Kan. 66044.

[3] T. Higuchi and K.-H. Gensch, *J. Am. Chem. Soc.*, **88**, 3874 (1966).

[4] T. Higuchi, I. H. Pitman, and K.-H. Gensch, *ibid.*, **88**, 5676 (1966).

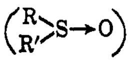
[5] A. R. Butler and V. Gold, *J. Chem. Soc.*, 2305 (1961); D. G. Oakenfull, T. Riley, and V. Gold, *Chem. Commun.*, 385 (1966).

Nucleophilic displacement at a site distant to the positively charged sulfur atom would make this system quite different to reactions such as the hydrolysis of alkoxysulfonium ions,[6] the hydrolysis of sulfinimines,[7] and the reactions of Grignard reagents with sulfinates,[8] which all proceed by back-side displacement on the sulfur atom.

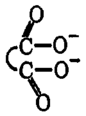
Postulated Mechanism for Oxidation in the Presence of Dicarboxylate Ions

The present results support the proposal[8] that the mechanism for the iodine oxidation of thioethers to sulfoxides in the presence of dicarboxylate ions is essentially the same as that postulated[1] for the similar oxidations in the presence of inorganic bases. Thus, the generalized reaction scheme for the oxidation of an aliphatic or alicyclic sulfide

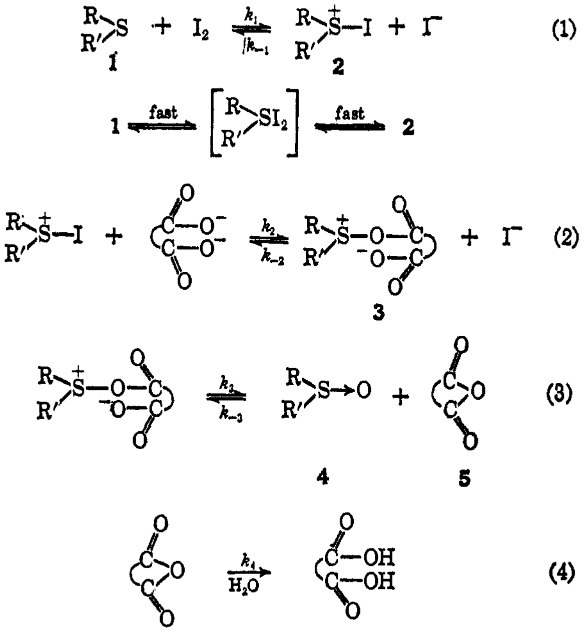
to the sulfoxide



catalyzed by a dicarboxylate ion



is believed to be



In aqueous solutions containing iodine and iodide ion, the concentration of free iodine $[I_2]$ relative to the total iodine concentration $[I_2]_T$ is given by

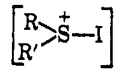
$$[I_2] = [I_2]_T/(1 + K_I[I^-]) \qquad (5)$$

where K_I (= 7.23 × 10^2 M^{-1} at 25°)[9] is the equilibrium constant for the reaction $I_2 + I^- \rightleftharpoons I_3^-$, and

$$[I_2]_T = [I_2] + [I_3^-] \qquad (6)$$

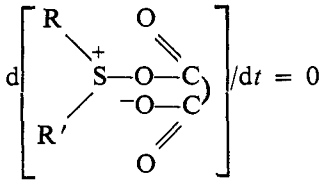
For the iodine oxidations (initial $[I_2]_T = 2.5 \times 10^{-5}$–$1 \times 10^{-4}$ M; [KI] = 1×10^{-2}–5×10^{-1} M) of aliphatic and alicyclic sulfides (5×10^{-4}–5×10^{-3} M) in aqueous solutions of dicarboxylate ions (1×10^{-2}–5×10^{-2} M) at constant pH, the rate of disappearance of $[I_2]_T$ (measured spectrophotometrically at 353 mμ) was pseudo first order with respect to $[I_2]_T$. Thus, in the absence of any evidence for an appreciable buildup in concentration of the iodosulfonium ion **2**, the acyloxysulfonium ion **3**, or the acid anhydride **5**, the following assumptions were made.

(a) Reaction 1 was a fast dynamic equilibrium reaction and, under the experimental conditions



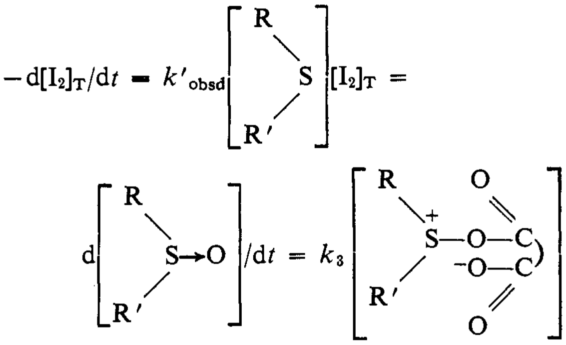
was always much less than

(b) The acyloxysulfonium ion was in low steady-state concentrations, *i.e.*



(c) Reaction 3 was essentially irreversible due to the rapid hydrolysis of the anhydride.

Hence, the rate law for the disappearance of $[I_2]_T$, in the presence of a considerable excess of sulfide, iodide ions, buffer ions, and at constant pH, would be expected to be



(7)

where the second-order rate constant, k'_{obsd}, was the one calculated from the observed pseudo-first-order rate constant, k_{obsd}, by dividing by

Applying a steady-state treatment to the concentration of acyloxysulfonium ion, we obtain

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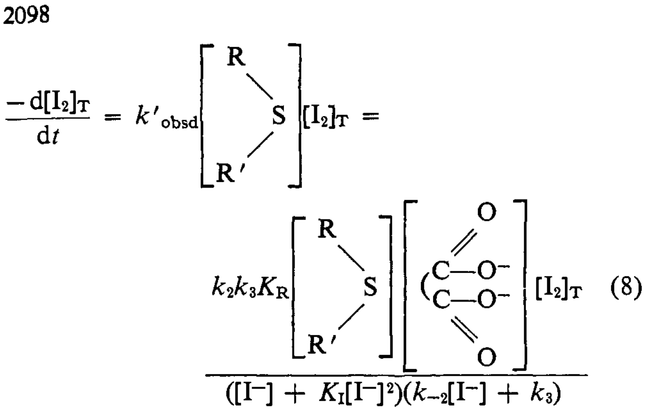
(6) C. R. Johnson and D. McCants, *J. Am. Chem. Soc.*, **87**, 5404 (1965).

(7) G. Kresze and B. Wustrow, *Ber.*, **95**, 2652 (1962); R. Appel and W. Buchner, *ibid.*, **95**, 849, 855 (1962); J. Day and D. J. Cram, *J. Am. Chem. Soc.*, **87**, 4398 (1965).

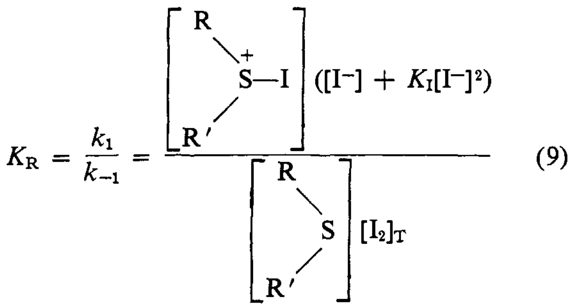
(8) K. K. Anderson, *Tetrahedron Letters*, 93 (1962).

(9) G. Daniele, *Gazz. Chim. Ital.*, **90**, 1068 (1960).



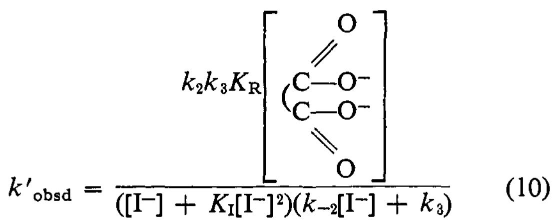
$$-\frac{d[I_2]_T}{dt} = k'_{obsd}\left[\begin{matrix}R\\ \diagdown\\ \quad S\\ \diagup\\ R'\end{matrix}\right][I_2]_T = \frac{k_2k_3K_R\left[\begin{matrix}R\\ \diagdown\\ \quad S\\ \diagup\\ R'\end{matrix}\right]\left[\begin{matrix}O\\ /\!\!/\\ \big(\begin{matrix}C{-}O^-\\ C{-}O^-\end{matrix}\\ \backslash\!\backslash\\ O\end{matrix}\right][I_2]_T}{([I^-] + K_I[I^-]^2)(k_{-2}[I^-] + k_3)} \quad (8)$$

where K_R, the equilibrium constant for reaction 1, is defined as



$$K_R = \frac{k_1}{k_{-1}} = \frac{\left[\begin{matrix}R\\ \diagdown^{+}\\ \quad S{-}I\\ \diagup\\ R'\end{matrix}\right]([I^-] + K_I[I^-]^2)}{\left[\begin{matrix}R\\ \diagdown\\ \quad S\\ \diagup\\ R'\end{matrix}\right][I_2]_T} \quad (9)$$

Thus, under the above conditions, the second-order rate constant, k'_{obsd}, for the disappearance of $[I_2]_T$ would be expected to be



$$k'_{obsd} = \frac{k_2k_3K_R\left[\begin{matrix}O\\ /\!\!/\\ \big(\begin{matrix}C{-}O^-\\ C{-}O^-\end{matrix}\\ \backslash\!\backslash\\ O\end{matrix}\right]}{([I^-] + K_I[I^-]^2)(k_{-2}[I^-] + k_3)} \quad (10)$$

Evidence in Support of the Mechanism

Formation of Cyclic Acid Anhydrides. Strong support for the mechanism came from the detection[3] of phthalic anhydride during the iodine oxidation of tetrahydrothiophene in phthalate buffer.

Further evidence for the formation of acid anhydrides in these systems was obtained by carrying out the oxidations in the presence of aniline and observing changes in uv absorbance at 280 mμ. Aniline absorbs strongly at this wavelength, whereas anilides, which are formed by acylation of aniline, absorb less strongly. Aniline did not react appreciably with the sulfides, sulfoxides, dicarboxylic acids, or iodine in these systems, but it does react with acid anhydrides to form anilides. Thus, a decrease in absorbance at 280 mμ during oxidations carried out in the presence of aniline provides indirect evidence that acid anhydrides are formed at some stage. The results in Table I for the iodine oxidation of tetrahydrothiophene in a *cis*-1,2-cyclohexanedicarboxylate buffer (5×10^{-2} *M*) containing aniline (5×10^{-4} *M*) at pH 7.43 and 25° indicate that the decrease of absorbance at 280 mμ can be accounted for on the basis that stoichiometric amounts of cyclic anhydride are formed. In these experiments, 5 ml each of aqueous solutions of buffer, aniline, sulfide, and iodine were mixed, and the absorbance was measured at 280 mμ. The absorbance values were compared with those of a mixture of 5 ml each of aqueous buffer and aqueous aniline plus 10 ml of water and 0.18, 0.20, and 0.22 ml, respectively, of a solution of *cis*-1,2-cyclohexanedicarboxylic anhydride (2.5×10^{-2} *M* in dioxane).

Table I. Evidence for Formation of *cis*-1,2-Cyclohexanedicarboxylic Acid Anhydride during Iodine Oxidation of Tetrahydrothiophene in *cis*-1,2-Cyclohexanedicarboxylic Acid Buffers (5×10^{-2} *M*) Containing Aniline (5×10^{-4} *M*) at pH 7.43 and 25°

Initial[a] $[I_2]_T$, 10^{-4} *M*	[Anhydride] added, 10^{-4} *M*	Initial $[C_4H_8S]$, 10^{-3} *M*	Optical density[b]
...	...	...	0.699
2.75	...	1.30	0.580
...	2.75	...	0.578
2.50	...	1.30	0.591
2.50	...	2.60	0.591
...	2.50	...	0.591
2.25	...	1.30	0.602
...	2.25	...	0.602

[a] Each iodine solution contained twice as much potassium iodide.
[b] Optical densities were measured on a Zeiss PMQ II spectrophotometer.

Constancy of k'_{obsd} Values When the Initial Sulfide Concentration Was Varied. In all the systems studied, values of k'_{obsd} were constant over a fourfold variation in the initial sulfide concentration. This behavior is consistent with the proposed mechanism.

Variation of k'_{obsd} with Total Buffer Concentration, $[\text{Buffer}]_T$. Results in Figure 1 show plots of k'_{obsd} against $[\text{phthalate}]_T$ calculated from the oxidation of tetrahydrothiophene (1.36×10^{-3} *M*) by aqueous iodine (initial $[I_2]_T = 1 \times 10^{-4}$ *M*; [KI] $= 2.5 \times 10^{-2}$ *M*) at pH 4.02 and 25°. In these experiments the ionic strength, μ, was not kept constant.[10] The direct proportionality between k'_{obsd} values and $[\text{phthalate}]_T$ at constant pH is consistent with rate law 10 which can be restated as

$$k'_{obsd} = \frac{k_2k_3K_R[\text{buffer}]_T\left(\frac{K_{a1}K_{a2}}{[H^+]^2 + K_{a1}[H^+] + K_{a1}K_{a2}}\right)}{([I^-] + K_I[I^-]^2)(k_{-2}[I^-] + k_3)} \quad (11)$$

where K_{a1} and K_{a2} are the first and second dissociation constants of the dicarboxylic acid. A similar proportionality was found in all the systems studied.

Variation of k'_{obsd} Values with pH. pH-rate profiles for the oxidation of tetrahydrothiophene (5–80×10^{-4} *M*) by iodine (initial $[I_2]_T = 2.5 \times 10^{-5}$ *M*; [KI] $= 6 \times 10^{-2}$ *M*) in *cis*-1,2-cyclohexanedicarboxylate (1×10^{-2} *M*) and phthalate buffer (1×10^{-2} *M*) at 25° and $\mu = 0.21$ (adjusted with potassium chloride) are shown as typical examples in Figure 2. The solid lines were calculated on the basis that only the dianions of the buffer acids catalyzed the reactions and that the uncatalyzed reaction rate was very small and could be neglected (see ref 1). Thus, the apparently limiting value of k'_{obsd} at pH values 2 units above the second pK_a of the appropriate buffer acid (*i.e.*, where the buffer acid is almost completely ionized) was divided by the factor $([H^+]^2 + K_{a1}[H^+] + K_{a1}K_{a2})/K_{a1}K_{a2}$ to obtain calculated

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(10) No direct study was made of the effect changes in ionic strength had on the measured rate constants. However, comparison of data obtained from systems where μ varied from 0.03 to 0.15, with data from the same system at constant ionic strength ($\mu = 0.21$, adjusted with potassium chloride) suggested that changes of this magnitude do not affect k'_{obsd} values more than ±5%.

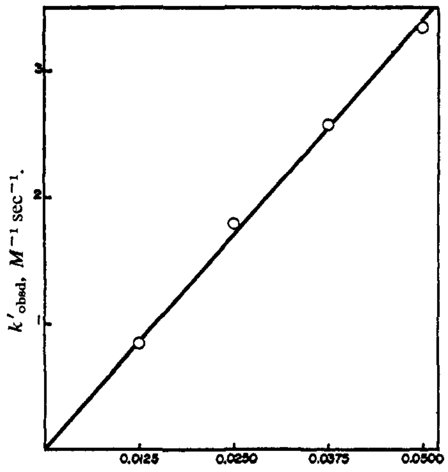


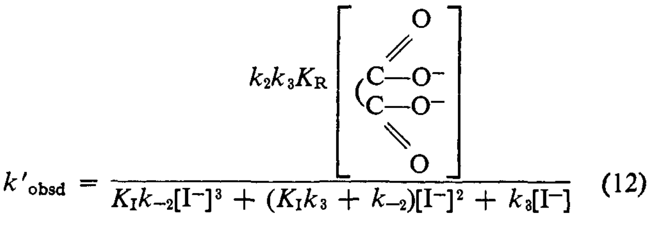
Figure 1. Variation of k'_{obsd} with total phthalate concentration when tetrahydrothiophene (1.36×10^{-3} M) was oxidized by aqueous iodine (initial $[I_2]_T = 1 \times 10^{-4}$ M; [KI] = 2.5×10^{-2} M) in phthalate buffers at pH 4.02 and 25°. Ionic strength was not kept constant.

values of k'_{obsd} at lower pH values. (In the phthalic acid system the factor $([H^+] + K_{a2})/K_{a2}$ was used because the first and second pK_a values are separated by more than 2 units). The pK_a values of the buffer acids, measured potentiometrically[11] at $\mu = 0.21$ (adjusted with potassium chloride) and 25°, were for *cis*-1,2-cyclohexanedicarboxylic acid pK_{a1} = 4.23 ± 0.03, pK_{a2} = 6.41 ± 0.02, and for phthalic acid pK_{a2} = 4.90 ± 0.03.

The results in Figure 2 are consistent with the proposed reaction scheme and indicate that the doubly charged anions are the main catalytic species. The slight divergence between measured and calculated values of k'_{obsd} at low pH values in the *cis*-1,2-cyclohexanedicarboxylate system is probably due to weak catalysis by the monoanions.

The acyloxysulfonium ions **3** which are postulated as intermediates in the above oxidations are likely to be very weak bases because they contain a positively charged sulfur atom, and the possibility of their being protonated to a significant extent in the pH regions studied is not expected.

Dependence of k'_{obsd} Values on [I$^-$]. The rate law 10 shows k'_{obsd} to be a complex function of [I$^-$]. As seen from an expanded form of this law



$$k'_{obsd} = \frac{k_2k_3K_R\left[\begin{array}{c}\mathrm{O}\\ /\!\!/ \\ \left(\begin{array}{l}\mathrm{C{-}O^-}\\ \mathrm{C{-}O^-}\end{array}\right. \\ \backslash\!\!\backslash \\ \mathrm{O}\end{array}\right]}{K_Ik_{-2}[I^-]^3 + (K_Ik_3 + k_{-2})[I^-]^2 + k_3[I^-]} \qquad (12)$$

k'_{obsd} would be expected to be nearly proportional to $1/[I^-]^3$ at sufficiently high [I$^-$] whereas at lower concentrations the manner in which k'_{obsd} varied with [I$^-$] would be determined by the [I$^-$] and the values of the rate constants k_{-2} and k_3. It is assumed that the initial [I$^-$] is considerably in excess of the concentration of iodine added. If this is not the case, relationships 8 and 10 are no longer valid as $d[I^-]/dt \neq 0$. In the present study only a very narrow range of [I$^-$] values could be employed because of the great sensitivity of k'_{obsd} values to changes in [I$^-$]. Over the narrow range of [I$^-$] used, plots of log k'_{obsd} against log [I$^-$] did give apparently straight lines. The slopes of such lines varied between −2 and −3 for each of the oxidations studied. In a system where the plot of log k'_{obsd} against log [I$^-$] gave a straight line with slope −3, it could readily be deduced that the rate constant, k_3, for cyclization of the acyloxysulfonium ion was smaller than the rate constant, k_{-2}, for displacement of the acyloxy group by iodide ion. Thus, for the plot to be a straight line with slope −3, $K_Ik_{-2}[I^-]^3$ must be greater than $(K_Ik_3 + k_{-2})[I^-]^2$ or k_{-2} must be greater than $\{K_I/(K_I[I^-] - 1)\}k_3$. Within the range $1/K_I < [I^-] < (K_I + 1)/K_I$ (which includes the range of [I$^-$] studied), the term $K_I/(K_I[I^-] - 1)$ will be greater than or equal to 1 and thus k_{-2} must be greater than k_3. The converse is not necessarily true and a slope of the above lines which approaches −2 indicates only that k_3 is greater than $\{(K_I[I^-] - 1)/K_I\}k_{-2}$, or, within the limits defined above, a slope approaching −2 indicates only that k_3 is greater than some fraction of k_{-2}.

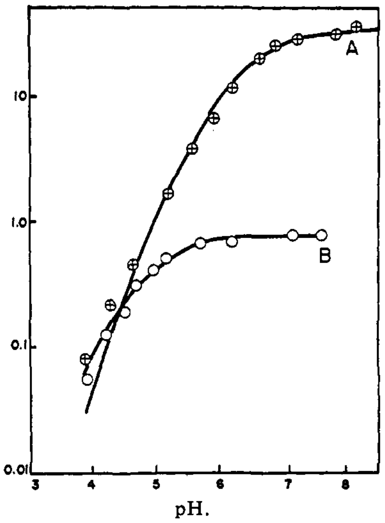
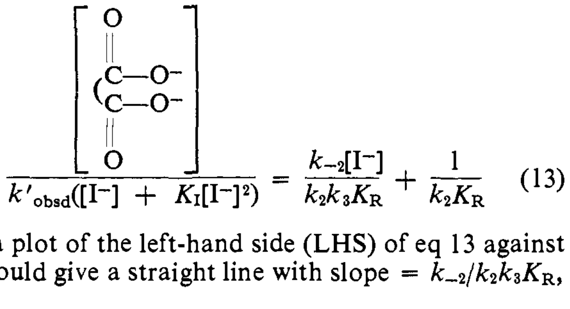


Figure 2. Plots of log k'_{obsd} against pH for the oxidation of tetrahydrothiophene ($5-80 \times 10^{-4}$ M) by iodine (initial $[I_2]_T = 2.5 \times 10^{-5}$ M; [KI] = 6×10^{-2} M) in (A) *cis*-1,2-cyclohexanedicarboxylate buffer (1×10^{-2} M) and (B) phthalate buffer (1×10^{-2} M) at 25° and μ = 0.21. The solid lines were calculated as described in the text.

More detailed information about the mechanism and the relative values of the constants k_2, k_{-2}, k_3, and K_R is obtained by rearranging relationship 10 to



$$\frac{\left[\begin{array}{c}\mathrm{O}\\ \| \\ \left(\begin{array}{l}\mathrm{C{-}O^-}\\ \mathrm{C{-}O^-}\end{array}\right. \\ \| \\ \mathrm{O}\end{array}\right]}{k'_{obsd}([I^-] + K_I[I^-]^2)} = \frac{k_{-2}[I^-]}{k_2k_3K_R} + \frac{1}{k_2K_R} \qquad (13)$$

Then a plot of the left-hand side (LHS) of eq 13 against [I$^-$] should give a straight line with slope = $k_{-2}/k_2k_3K_R$,

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[11] (a) A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," John Wiley and Sons, Inc., New York, N. Y., 1962; (b) K.-H. Gensch has unpublished rate and equilibrium constants for some of the systems treated in this paper. These results, which were obtained from independent experiments, are substantially the same as those reported here.

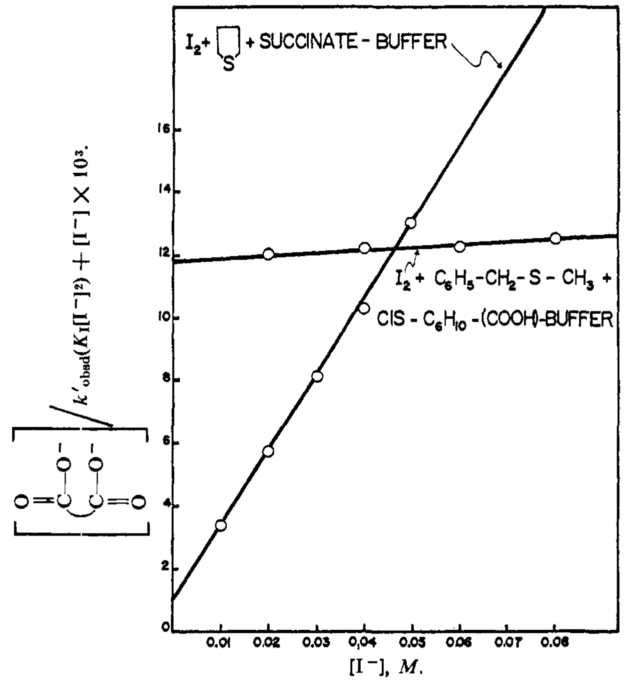
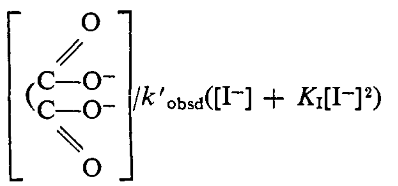


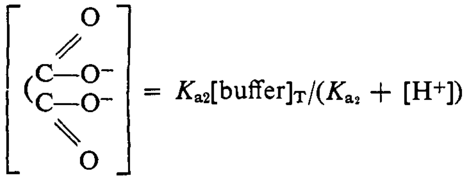
Figure 3. Plots of the left-hand side of relationship 13 against $[I^-]$ for (A) the iodine oxidation (initial $[I_2]_T = 1 \times 10^{-4}$ *M*) of tetrahydrothiophene (1.53×10^{-3} *M*) in succinate buffer (1×10^{-2} *M*) at pH 6.9, 25°, and varying ionic strength, and (B) the iodine oxidation (initial $[I_2]_T = 2.5 \times 10^{-5}$ *M*) of benzyl methyl sulfide (4.21×10^{-4} *M* in *cis*-1,2-cyclohexanedicarboxylate buffer (1×10^{-2} *M*) at pH = 6.40, $\mu = 0.21$, and temperature 25°.

intercept on the y axis = $1/k_2K_R$, and ratio slope/intercept = k_{-2}/k_3. In the oxidations reported here, straight lines were obtained from the above type of plot. For example, results in Figure 3 show plots against $[I^-]$ of



$$\left[\begin{matrix} \text{O}\\ \text{C—O}^-\\ \text{C—O}^-\\ \text{O}\end{matrix}\right] / k'_{\text{obsd}}([I^-] + K_I[I^-]^2)$$

for (A) the iodine oxidation (initial $[I_2]_T = 1 \times 10^{-4}$ *M*) of tetrahydrothiophene (1.53×10^{-3} *M*) in succinate buffer ($[\text{succinate}]_T = 1 \times 10^{-2}$ *M*; pH 6.90; μ not constant), and (B) the iodine oxidation (initial $[I_2]_T = 2.5 \times 10^{-5}$ *M*) of benzyl methyl sulfide (4.21×10^{-4} *M*) in *cis*-1,2-cyclohexanedicarboxylate buffer [*cis*-1,2-cyclohexanedicarboxylate]$_T$ = 1×10^{-2} *M*; pH 6.40; $\mu = 0.21$). The calculations for these plots were made from data obtained at pH values greater than the pK_{a2} value of the buffer acid. Thus, the concentration of dianion was obtained from the identity



$$\left[\begin{matrix} \text{O}\\ \text{C—O}^-\\ \text{C—O}^-\\ \text{O}\end{matrix}\right] = K_{a2}[\text{buffer}]_T/(K_{a_2} + [H^+])$$

Values of $1/k_2K_R$ and k_{-2}/k_3 obtained in this way are estimated to be within ±10% of the absolute values.[11b]

Comparison of the Catalytic Strength of a Series of Dicarboxylate Ions

Values of the second-order rate constant, k'_{obsd}, for the oxidation of tetrahydrothiophene, diethyl sulfide, and benzyl methyl sulfide in several dicarboxylate buffers (and citrate buffer) containing different concentrations of potassium iodide are given in Table II.

Because k'_{obsd} values are a function of the concentrations of iodide ion and dicarboxylate ion (see relationship 10) they must be normalized before meaningful comparisons can be made between values calculated from different sets of data. Normalized values of this constant, k'_N values, which are included in Table III, were calculated by multiplying k'_{obsd} values for oxidations in solutions containing 6×10^{-2} *M* potassium iodide by a factor to allow for the concentration of monoionic buffer acid (weakly catalytic) in equilibrium with the diionized form (strongly catalytic) in a 1×10^{-2} *M* solution of the buffer. The factor was

$$\frac{10^{-2}([H^+]^2 + K_{a1}[H^+] + K_{a1}K_{a2})}{[\text{buffer}]_T K_{a1}K_{a2}}$$

(see relationship 11). These k'_N values are thus the expected second-order rate constants for oxidations in a 1×10^{-2} *M* solution of the buffer which is at a pH where the buffer acid is completely ionized and which contains 6×10^{-2} *M* potassium iodide.

Calculated values of the constant, k_2K_R, and the rate-constant ratio, k_{-2}/k_3, which were calculated from the experimental results in Table II, are also collected in Table III together with the thermodynamic[12] and effective pK_a values of the buffer acids.

The value of the equilibrium constant, K_R, for the reversible formation of the iodosulfonium ion from the thioether and iodine is expected to be independent of the buffer in the system. Hence, for oxidations of tetrahydrothiophene in various buffers, differences in k_2K_R values presumably reflect differences in k_2 values and therefore differences in the nucleophilicities of the ions in the displacement reaction. Results in Table III show that the nucleophilicities of the ions in this reaction apparently increase in the order, citrate > *cis*-1,2-cyclohexanedicarboxylate > phthalate > succinate > *trans*-1,2-cyclohexanedicarboxylate > phenylsuccinate. This is not the order expected from the basicities of the ions except perhaps when comparisons are made between closely related pairs of ions. For example, *cis*-1,2-cyclohexanedicarboxylate (pK_{a2}^{eff} = 6.41) is a stronger nucleophile than *trans*-1,2-cyclohexanedicarboxylate (pK_{a2}^{eff} = 5.68). Deviations from the expected order of nucleophilicities are most likely due mainly to steric requirements of the displacement reaction.

For the oxidations of several different sulfides in a common buffer the values of both K_R and k_2 are expected to vary, and in different directions. Thus, the more basic sulfide is likely to produce the larger value of K_R due to stabilization of the positive charge in the iodosulfonium ion. For similar reasons the k_2 value for this system is likely to be smaller than that arising during the displacement of iodide ion from the iodosulfonium ion of a less basic sulfide. For oxidations in

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[12] Taken from G. Kortum, W. Vogel, and K. Andrussow, "Dissociation Constants of Organic Acids in Aqueous Solution," Butterworth & Co. (Publishers) Ltd., London, 1961.

Table II. Iodide Dependence of k'_{obsd}[a] Values for the Oxidation of Thioethers by Iodine in Polycarboxylic Acid Buffers at 25°

Buffer ion	$[\mathrm{Buffer}]_T$, M	μ	pH	$[\mathrm{I}^-]$, M	k'_{obsd}, M^{-1} sec^{-1}	Slope of plot of log k'_{obsd} *vs.* log $[\mathrm{I}^-]$
Tetrahydrothiophene						
cis-1,2-Cyclohexane-dicarboxylate	0.01	0.21	6.39	0.02	148	−2.2
				0.04	32.2	
				0.06	15.0	
				0.08	6.92	
				0.10	4.28	
	0.01	0.21	7.22	0.02	265	−2.2
				0.04	68.0	
				0.06	27.0	
				0.08	14.5	
				0.10	7.6	
trans-1,2-Cyclohexane-dicarboxylate	0.01	0.21	5.10	0.06	0.144	−2.8
				0.08	0.0599	
				0.10	0.032	
				0.12	0.0197	
				0.14	0.0136	
	0.01	0.21	6.75	0.06	0.749	−2.7
				0.08	0.359	
				0.10	0.174	
				0.12	0.119	
Phthalate	0.01	0.21	6.72	0.03	6.31	−2.8
				0.04	2.75	
				0.05	1.46	
				0.06	0.86	
Succinate	0.01	...[b]	6.96	0.01	36.2	−2.8
				0.02	5.65	
				0.03	1.8	
				0.04	0.81	
				0.05	0.411	
				0.06	0.244	
dl-Phenylsuccinate	0.15	0.4	5.04	0.06	5.72	−2.4
				0.08	2.90	
				0.10	1.69	
Citrate	0.01	...[b]	7.23	0.04	9.8	−3.0
				0.06	3.07	
				0.08	0.128	
				0.10	0.067	
				0.12	0.0383	
Diethyl Sulfide						
cis-1,2-Cyclohexane-dicarboxylate	0.01	...[b]	7.11	0.04	10.5	−2.0
				0.05	6.61	
				0.062	4.30	
				0.07	3.40	
				0.08	2.58	
Benzyl Methyl Sulfide						
cis-1,2-Cyclohexane-dicarboxylate	0.01	0.21	6.40	0.02	1.32	−2.0
				0.04	0.335	
				0.06	0.150	
				0.08	0.083	

[a] Calculated from the measured pseudo-first-order rate constant, k_{obsd}, by dividing by [thioether]. [b] Not constant.

cis-1,2-cyclohexanedicarboxylate, values of $K_{\mathrm{R}}k_2$ decrease in the expected order of basicity of the sulfides (*i.e.*, tetrahydrothiophene > diethyl sulfide > benzyl methyl sulfide) suggesting that changes in K_{R} values are the predominant effects within this series. Similar effects were found for oxidations in phenylsuccinate buffer.

A small value of the ratio k_{-2}/k_3 indicates that there is a greater tendency for the acyloxysulfonium ion to be converted to the sulfoxide than for it to react with iodide ion leading to displacement of the acyloxy moiety. For oxidations of tetrahydrothiophene in dicarboxylate buffers (and citrate buffer) values of this ratio increase in the order *cis*-1,2-cyclohexanedicarboxylate < phenylsuccinate < *trans*-1,2-cyclohexanedicarboxylate < phthalate < succinate < citrate. This is the order expected if the k_{-2} values are similar throughout this series and the k_3 values are a measure of the rate of cyclization of dicarboxylate moiety to yield the cyclic anhydride plus the sulfoxide. For example, the carbonyl moieties in the *cis*-1,2-cyclohexanedicarboxylate derivative are likely to be more favorably orientated than those in the *trans* derivative for cyclization, thereby leading to a larger value of k_3. Similarly, because substitution of the carbon atoms in succinic acid derivatives usually[13] increases the rate at which they cyclize to the cyclic anhydride, the k_3 value for the phenylsuccinate derivative is expected to be greater than

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[13] T. C. Bruice and U. K. Pandit, *J. Am. Chem. Soc.*, **82**, 5858 (1960); T. Higuchi, L. Eberson, and J. McRae, *ibid.*, **89**, 3001 (1967).

Table III. Comparison of Calculated Rate Constants for the Oxidation of Thioethers by Iodine in Polycarboxylic Acid Buffers at 25°

Buffer ion	pK_a^T of buffer acid[a]	pK_a^{eff} of buffer acid[b]	k'_N,[c] M^{-1} sec^{-1}	K_Rk_2,[c] M^{-1} sec^{-1}	k_{-2}/k_3,[c] M^{-1}
		Tetrahydrothiophene			
cis-1,2-Cyclohexane-dicarboxylate	4.32	4.23 ± 0.03	30.9[d]	1.1×10^4 [d]	7[d]
	6.76	6.41 ± 0.02			
trans-1,2-Cyclohexane-dicarboxylate	4.18	4.17 ± 0.02	0.78[d]	5.9×10^2 [d]	33[d]
	5.93	5.68 ± 0.03			
Phthalate	2.95	...	0.86	3.1×10^3	210
	5.41	4.90 ± 0.02			
Succinate	4.21	...	0.244	1.0×10^3	264
	5.64	...			
dl-Phenylsuccinate	3.78	...	0.763	2.9×10^2	8.3
	5.55	5.04[e]			
Citrate	3.13	...	3.07[f]	2.5×10^4	500
	4.76	...			
	6.40	...			
		Diethyl Sulfide			
cis-1,2-Cyclohexane-dicarboxylate			5.11	1.54×10^3	0.7
		Benzyl Methyl Sulfide			
cis-1,2-Cyclohexane-dicarboxylate			0.31	8.3×10^1	0.7

[a] From ref 12. [b] Measured potentiometrically at 25° and μ = 0.21 unless otherwise stated. [c] Calculated from the data in Table II. [d] Mean values from two experiments at different pH values. [e] pH of a 75% neutralized solution of the buffer acid. [f] This is the value of k'_{obsd} at pH 7.23.

that for the succinate derivative. If a back-side attack of hydroxide ion on the sulfur atom of the acyloxysulfonium ion was the predominant route to the sulfoxide, then the same properties of the acyloxy moiety which facilitated hydroxide attack would also favor iodide attack. In this case, oxidation of a particular sulfide in a series of buffers would be expected to give fairly constant values of k_{-2}/k_3. The large differences in values of this ratio for the systems studied strongly suggest that the acyloxysulfonium ions formed by dicarboxylate ions are converted to sulfoxides by a reaction (cyclization) at the carbonyl carbon atom rather than one at the sulfur atom.

A requirement of the postulated mechanism for these oxidations is that the best catalysts will be the ones producing the largest values of the rate constant, k_2, and the smallest values of the ratio k_{-2}/k_3. The results in Table III satisfy this requirement. It can be seen that while phenylsuccinate is a weaker nucleophile than succinate ion in its reaction with iodotetrahydrothiophinium ion (for phenylsuccinate $K_2K_R = 2.9 \times 10^2 M^{-1}$ sec^{-1}; for succinate $k_2K_R = 1 \times 10^3$ M^{-1} sec^{-1}) it is a better catalyst for the oxidation of tetrahydrothiophene ($k'_N = 0.76$ M^{-1} sec^{-1}) than succinate ion ($k'_N = 0.24$ M^{-1} sec^{-1}). The greater catalytic effect is apparently a result of the lower value of the ratio k_{-2}/k_3 for phenylsuccinate ($k_{-2}/k_3 = 8.32$ M^{-1} compared to $k_{-2}/k_3 = 264$ M^{-1} for succinate). A more striking example comes from a comparison of the catalytic effect produced by *cis*-1,2-cyclohexanedicarboxylate ion ($k'_N = 30.9$ M^{-1} sec^{-1}) compared to the trionized citrate ion ($k'_N = 3.07$ M^{-1} sec^{-1}) on the oxidation of tetrahydrothiophene. The former ion is the weaker nucleophile but it gives rise to a much smaller value of the ratio k_{-2}/k_3 (for *cis*-1,2-cyclohexanedicarboxylate $k_{-2}/k_3 = 6.6$ M^{-1}; for citrate $k_{-2}/k_3 = 500$ M^{-1}).

Oxidation of Tetrahydrothiophene in Monocarboxylate Buffers

In dilute aqueous solution monocarboxylate ions are weaker catalysts than dicarboxylate ions for the iodine oxidation of tetrahydrothiophene to tetrahydrothiophene 1-oxide. For example, $k'_{obsd} = 8 \times 10^{-2}$ M^{-1} sec^{-1} for the oxidation in acetate buffer ([acetate ion] = 2×10^{-2} M; [KI] = 3×10^{-2} M at 25°) compared to $k'_{obsd} = 1.80$ M^{-1} sec^{-1} for the oxidation in a more dilute succinate buffer ([succinate ion] = 1×10^{-2} M; [KI] = 3×10^{-2} M). The kinetics of the monocarboxylate ion catalyzed reactions are complicated by the fact that k'_{obsd} is not directly proportional to [anion] but approaches a direct proportionality to [anion]^2.

The kinetic results obtained from the oxidations in monocarboxylate buffers are in good agreement with an oxidation mechanism similar to that proposed for the dicarboxylate ion catalyzed reactions but in which the reaction leading to the formation of the sulfoxide (reaction 3) can proceed spontaneously in water but is also catalyzed by carboxylate ions. The main difference between the monocarboxylate ion and the dicarboxylate ion catalyzed reactions arises because intramolecular facilitation of this reaction is not possible in the former case, whereas it is believed to be the major route in the latter case.

Incorporation of this postulate into the rate relationship 10 leads to

$$k'_{obsd} = \frac{K_Rk_2(k_3 + k'_3[R''CO_2^-])[R''CO_2^-]}{(K_I[I^-]^2 + [I^-])\{k_{-2}[I^-] + (k_3 + k_3'[R''CO_2^-])\}} \quad (14)$$

where $R''CO_2^-$ is a monocarboxylate ion, k_3 is the first-

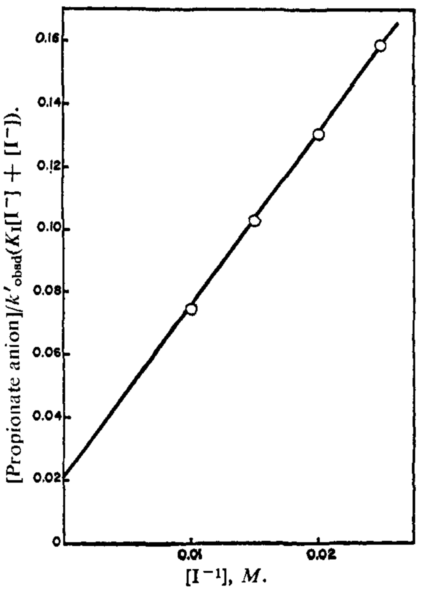
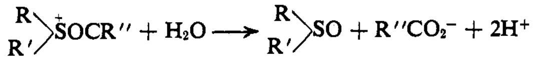


Figure 4. Plot of the left-hand side of relationship 15 against $[I^-]$ for the oxidation of tetrahydrothiophene (1.3×10^{-3} M) by iodine (initial $[I_2]_T = 1 \times 10^{-4}$ M) in propionate buffers (5×10^{-2} M) at pH 4.80 and 25° (μ not constant).

order rate constant for the reaction



$$\begin{matrix} R \\ R' \end{matrix}\!\!>\overset{+}{S}OCR'' + H_2O \longrightarrow \begin{matrix} R \\ R' \end{matrix}\!\!>SO + R''CO_2^- + 2H^+$$

and k'_3 is the second-order catalytic constant for the monocarboxylate ion, $R''CO_2^-$, in this reaction. By rearranging this relationship, we obtain

$$\frac{[R''CO_2^-]}{k'_{obsd}(K_I[I^-]^2 + [I^-])} = \frac{k_{-2}[I^-]}{K_Rk_2(k_3 + k'_3[R''CO_2^-])} + \frac{1}{K_Rk_2} \quad (15)$$

Hence, at constant buffer concentration and pH, plots of the LHS of this relationship against $[I^-]$ (from experiments carried out in the presence of different concentrations of potassium iodide) should give a straight line. The intercept of this line with the y axis would be $1/K_Rk_2$ and the ratio slope/intercept would be $k_{-2}/(k_3 + k'_3[R''CO_2^-])$. This type of straight-line relationship was obtained in all the systems studied. Results in Figure 4 show a typical plot for the oxidation of tetrahydrothiophene (1.3×10^{-3} M) by iodine (initial $[I_2]_T = 1 \times 10^{-4}$ M) in propionate buffers (5×10^{-2} M) at pH 4.80 and 25°. In these experiments the ionic strength was not kept constant.

In the special situation where the term $k'_3[R''CO_2^-]$ is much larger than k_3, relationship 15 reduces to

$$\frac{[R''CO_2^-]}{k'_{obsd}(K_I[I^-]^2 + [I^-])} = \frac{k_{-2}[I^-]}{K_Rk_2k'_3[R''CO_2^-]} + \frac{1}{K_Rk_2} \quad (16)$$

Thus, if $k'_3[R''CO_2^-]$ is much greater than k_3 under the experimental conditions, then at constant iodide concentration a plot of the LHS of relationship 16 against $1/[R''CO_2^-]$ for various buffer concentrations should give a straight line with intercept on the y axis of $1/K_Rk_2$ and a value of slope/intercept = $k_{-2}[I^-]/k'_3$. Straight-line relationships such as this were found for all the systems studied. Results in Figure 5 show a typical plot of the LHS of relationship 16 against 1/[propionate ion] for the oxidation of tetrahydrothiophene (1.3×10^{-3} M) by iodine (initial $[I_2]_T = 1 \times 10^{-4}$ M; [KI] = 1×10^{-2} M) in various propionate buffers at pH 4.80 and 25°. In these experiments the ionic strength was not kept constant. This treatment yielded values for the constants of $1/K_Rk_2 = 2.6 \times 10^{-2}$ M sec, and $k_{-2}/k'_3 = 4.2$. These values compare reasonably well with the values, $1/K_Rk_2 = 2.3 \times 10^{-2}$ M sec, and $k_{-2}/k'_3 = 6.0$, which were calculated from plots of the LHS of relationship 16 against $[I^-]$ for the same oxidation in a propionate buffer (2.5×10^{-2} M) at pH 4.80 in the presence of different concentrations of potassium iodide.

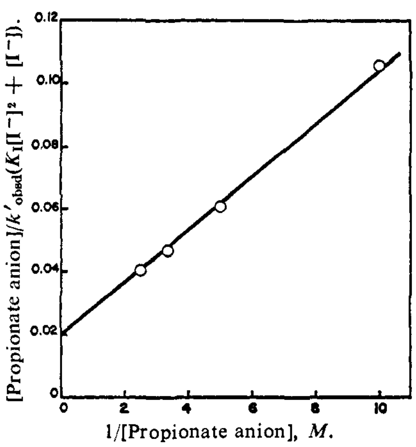


Figure 5. Plot of the left-hand side of relationship 16 against 1/[propionate anion] for the oxidation of tetrahydrothiophene (1.3×10^{-3} M) by iodine (initial $[I_2]_T = 1 \times 10^{-4}$ M; [KI] = 1×10^{-2} M) in various propionate buffers at pH 4.80 and 25°.

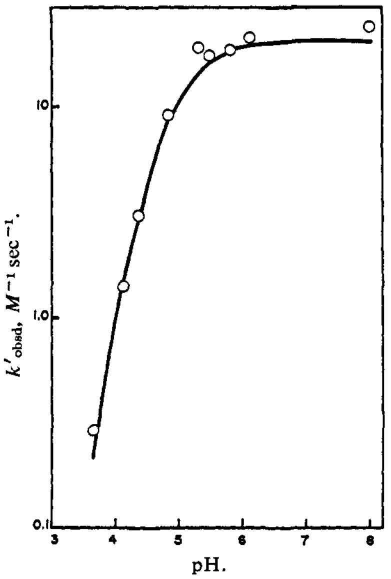


Figure 6. Plot of log k'_{obsd} against pH for the oxidation of tetrahydrothiophene (6×10^{-4}–1.5×10^{-3} M) by iodine (initial $[I_2]_T = 1 \times 10^{-4}$ M; [KI] = 1.5×10^{-2} M) in acetate buffers ($[acetate]_T = 1.5 \times 10^{-1}$ M; $\mu = 0.165$). The solid line was calculated as described in the text using values of $1/K_Rk_2 = 1.4 \times 10^{-2}$ M sec and $k_{-2}/k'_3 = 19.2$.

Further support for the proposed mechanism comes from comparison of calculated and experimental values of k'_{obsd} over a range of pH values at constant buffer and iodide concentration. For example, Figure 6 shows a

Table IV. Rate Constants for the Oxidation of Tetrahydrothiophene by Iodine in Monocarboxylic Acid Buffers at 25°

Buffer ion	$[\text{Buffer}]_T$, M	μ	pH	$[I^-]$, M	k'_{obsd}, M^{-1} sec^{-1}	K_Rk_2, M^{-1} sec^{-1}	k_{-2}/k'_3
Acetate[a]	0.15	0.195	4.58	0.015	4.95	71	19
				0.0225	1.78		
				0.030	0.79		
				0.0375	0.38		
				0.045	0.239		
Propionate	0.05	...[d]	4.80[b]	0.01	4.04	47.6	7
				0.015	1.36		
				0.02	0.615		
				0.025	0.33		
	0.20	0.87	4.80[b]	0.07	0.275	50	6
	0.40				0.91		
	0.60				1.77		
	0.80				2.75		
Propionate	0.0125	...[d]	4.80[b]	0.01	0.375	39	4
	0.025				1.32		
	0.0375				2.54		
	0.05				4.35		
Hexanoate[c]	0.05	...[d]	7.2	0.01	22.2	80	6
				0.02	3.75		
				0.03	1.3		
				0.04	0.55		

[a] pH of buffer 4.62 at half-neutralization. [b] pH of buffer at half-neutralization. [c] pH of buffer at half-neutralization. [d] Ionic strength not constant.

plot of k'_{obsd} against pH for the oxidation of tetrahydrothiophene (6×10^{-4}–1.5×10^{-3} M) by iodine (initial $[I_2]_T = 0.25$–1×10^{-4} M; $[\text{KI}] = 1.5 \times 10^{-2}$ M) in acetate buffers (1.5×10^{-1} M; $\mu = 0.165$). The solid line was calculated using relationship 14 together with values of the constant $1/K_Rk_2$, and the ratio k_{-2}/k'_3, which were obtained from different experiments in which the buffer concentration and pH were kept constant and the concentration of iodide ion was varied (see Table IV). In using relationship 14 it was assumed that k'_3[acetate ion] was always greater than k_3.

Thus, the experimental results were consistent with the mechanism proposed for these systems. The apparent carboxylate ion catalysis of the conversion of the acyloxysulfonium ion to the sulfoxide strongly suggests that this reaction is brought about by a displacement at the carbonyl carbon atom.

The mechanism of this catalysis is not immediately apparent. It seems unlikely that the monocarboxylate ions attack the carbonyl group in a nucleophilic reaction because no acid anhydrides could be detected either by direct observation or by the addition of aniline. It is possible that the monocarboxylate ions act solely as general bases in this reaction.

Experimental Section

Reagents. A reference sample of tetrahydrothiophene (0.05 ± 0.05 mol % impurities) was obtained[14] from the U. S. Bureau of Mines, Laramie, Wyo. Commercial tetrahydrothiophene was purified by passage over aluminum oxide (activity I, Woelm) followed by distillation in a spinning-band column. Small amounts of impurities (less than 1%) which reacted with iodine were removed by adding an equivalent amount of iodine to the aqueous stock solution of the sulfide. Diethyl sulfide was fractionated by distillation. Benzyl methyl sulfide was only treated by preoxidation with iodine as mentioned above. All other chemicals were reagent grade. Glass-distilled water was used throughout.

Rate Studies. Usual spectrophotometric procedures commonly employed for rate measurements were followed. For slower runs, reactants were mixed separately and then poured into the spectrophotometric cell. For faster reactions the solutions were mixed directly by injection into the cell.

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(14) The authors wish to thank the U. S. Department of Interior, Bureau of Mines, Laramie, Wyo., for generously providing this sample.