A Kinetic Study of the Acid-Catalyzed Disproportionation of an Unsymmetrical Disulfide[1]

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The disproportionation of benzyl *p*-tolyl disulfide into an equilibrium mixture of *p*-tolyl and benzyl disulfides has been studied kinetically by an NMR method at 70° in acetic acid–1% H_2O containing 0.05–0.20 *M* sulfuric acid. The important experimental findings are as follows: (1) the reaction is subject to marked catalysis by added strong acid; (2) the kinetics show a second-order dependence on disulfide concentration; (3) the reaction can be effectively completely inhibited for significant periods of time by the addition of very small amounts of either *p*-toluenethiol or benzyl mercaptan, with the rate after the inhibition period being the same as in the absence of added mercaptan; (4) the reaction can be markedly accelerated by the addition of small amounts of *n*-butyl sulfide. The results seem to be best explained by a chain-type mechanism involving *ionic* intermediates. In the case of the ordinary acid-catalyzed disproportionation the chain-propagating steps involve nucleophilic attack by the disulfide on dithiosulfonium ions **2** and **3**. In the case of the *n*-butyl sulfide catalyzed reaction the propagating steps are thought to involve attack of the disulfide on di-*n*-butylthioalkylsulfonium ions (**4** and **5**).

Unsymmetrical disulfides undergo disproportionation (eq 1) under a variety of conditions. The mechanism for

$$2RSSR' \rightleftharpoons RSSR + R'SSR' \quad (1)$$

disproportionation in alkaline solution is believed[2,3] to involve a chain sequence of displacements on the disulfide by mercaptide ions (eq 2), which are themselves formed as one product of the alkaline hydrolysis of a small fraction of the disulfide.

$$RS^- + RSSR' \longrightarrow RSSR + R'S^- \quad (2a)$$

$$R'S^- + RSSR' \longrightarrow R'SSR' + RS^- \quad (2b)$$

The mechanism of the acid-catalyzed disproportionation is much less certain. Both Ryle and Sanger[3] and Benesch and Benesch[4] found that the disproportionation in HCl solutions was strongly inhibited by the addition of mercaptans. The rate also dropped off markedly with a decrease in HCl concentration. Neither group investigated whether catalysis by other mineral acids was more or less effective. Benesch and Benesch[4] observed that the disproportionation could be catalyzed by added alkyl or aryl sulfenyl chlorides and by hydrogen peroxide. In both investigations the data were presented as plots of percent disproportionation vs. time, and neither rate constants nor reaction order were determined. Both sets of authors proposed a chain-type mechanism (eq 3) for the acid-catalyzed disproportionation involving sulfenium ions as the key intermediate. This

$$RSSR' + H^+ \rightleftharpoons RS^+ + R'SH \quad (3a)$$

$$RS^+ + RSSR' \longrightarrow RSSR + R'S^+ \quad (3b)$$

$$R'S^+ + RSSR' \longrightarrow R'SSR' + RS^+ \quad (3c)$$

scheme seemed to fit well with the marked inhibition of the reaction by mercaptan, and also with the acceleration by added sulfenyl chlorides, since at that time sulfenyl chlorides were thought to form sulfenium ions fairly readily, something that we now know is not the case.[5]

Fava and Reichenbach[6] have investigated the acid-catalyzed exchange of radioactive thiophenol and phenyl disulfide (eq 4). They found that although HCl, HBr, or HI were

$$PhS^*H + PhSSPh \overset{H^+}{\rightleftharpoons} PhS^*SPh + PhSH \quad (4)$$

catalysts for the exchange, perchloric acid had no appreciable effect. Moreover, the relative catalytic effectiveness of the halogen acids was strongly dependent on the halogen in a manner that suggested that the anion of the acid played a key role as a nucleophile in the mechanism of the reaction.

These results and the formal kinetics of the reaction led to the proposal of the mechanism shown in eq 5 for the acid-catalyzed exchange. Cuiffarin and Fava[7] have pointed out

$$PhSSPh + HX \rightleftharpoons PhS\overset{+}{S}(H)Ph + X^- \quad (5a)$$

$$X^- + PhS\overset{+}{S}(H)Ph \xrightarrow[\text{determining}]{\text{rate}} PhSX + PhSH \quad (5b)$$

$$PhS^*H + PhSX \longrightarrow PhS^*SPh + H^+ + X^- \quad (5c)$$

that the mechanism observed for this exchange suggests that the HCl-catalyzed disproportionation of disulfides could well involve the mechanism shown in eq 6, rather

$$RSSR' + H^+ \rightleftharpoons RS\overset{+}{S}(H)R' \quad (6a)$$

$$Cl^- + RS\overset{+}{S}(H)R' \rightleftharpoons RSCl + R'SH \quad (6b)$$

$$RSCl + RSSR' \rightleftharpoons RS\overset{+}{S}(R)SR' + Cl^- \rightleftharpoons RSSR + R'SCl \quad (6c)$$

$$R'SCl + RSSR' \rightleftharpoons RS\overset{+}{S}(R')SR' + Cl^- \rightleftharpoons R'SSR' + RSCl \quad (6d)$$

than the one involving sulfenium ion intermediates favored by Ryle and Sanger[3] and Benesch and Benesch.[4]

We felt that a further kinetic study of the acid-catalyzed disproportionation of an unsymmetric disulfide under appropriate conditions might be able to cast further light on the question of the mechanism of the reaction. Benzyl *p*-tolyl disulfide (**1**), p-$CH_3C_6H_4SSCH_2Ph$, seemed a particularly good substrate to use, since the singlet for the methylene protons in this disulfide occurs at somewhat different field, δ 3.83 ppm, than the singlet for the methylene protons of its disproportionation product, benzyl disulfide, 3.48 ppm.[8] Because of this one can follow the course of this particular disproportionation continuously by monitoring the relative intensity of the two different methylene peaks in a sample of the reaction solution contained in a thermostated nmr probe. In studying the acid-catalyzed disproportionation we also felt it desirable, in view of the experience of Fava and Reichenbach,[6] to use as a catalyzing acid

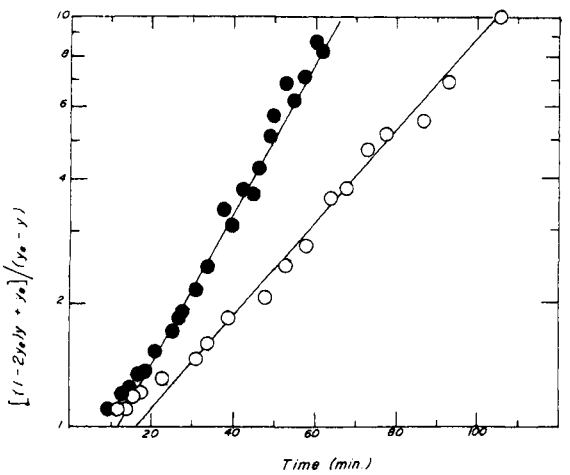


Figure 1. Kinetic data for the disproportionation of 1 in acetic acid–0.56 *M* H_2O containing 0.10 *M* H_2SO_4 plotted according to eq 9. ●, initial concentration of 1, 0.30 *M*; ○, initial concentration of 1, 0.20 *M*.

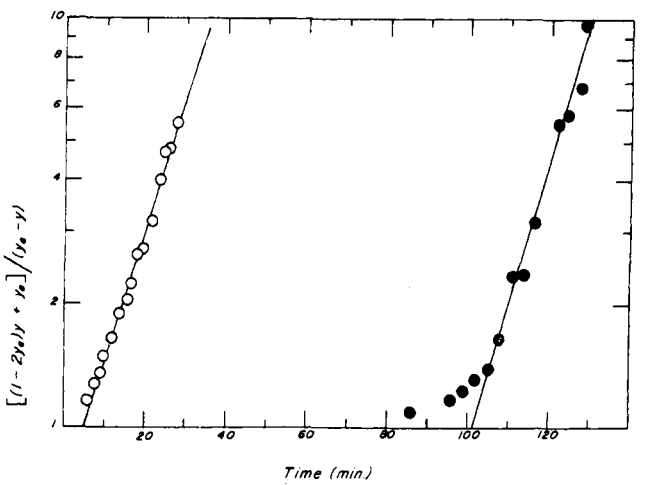


Figure 2. Effect of added thiol on the kinetics of the disproportionation of 1. Data plotted according to eq 9. Both runs in acetic acid–0.56 *M* H_2O as solvent with 0.15 *M* H_2SO_4 and an initial concentration of 1 of 0.30 *M*. ●, 3.6 × 10^{-4} *M* *p*-toluenethiol added; ○, no added thiol.

one whose conjugate base was not significantly nucleophilic.

For these reasons the specific system chosen for study was the disproportionation of benzyl *p*-tolyl disulfide (eq 1, R = $PhCH_2$, R′ = *p*-$CH_3C_6H_4$) in acetic acid–0.56 *M* water containing 0.05–0.20 *M* H_2SO_4 as acid catalyst. Despite the fact that the reaction can be followed continuously by NMR, the quality of the kinetic data was not as high as we had originally hoped. However, the kinetic data are of sufficient precision, and, in particular, the effects of certain additives are sufficiently striking that certain characteristics of the reaction are clearly apparent. These do provide some definite and useful insights into the mechanism of the acid-catalyzed disproportionation.

Results

The disproportionation of 1 was followed by observing the change in the relative intensity of the separate nmr signals for the methylene hydrogens of *p*-$CH_3C_6H_4SSCH_2Ph$ (1) and $PhCH_2SSCH_2Ph$ in solutions initially 0.20 or 0.30 *M* in 1. Acetic acid–0.56 *M* water containing 0.05–0.20 *M* H_2SO_4 as the strong acid catalyst was the solvent. All runs were carried out at 70°.

Equilibrium Constant for the Disproportionation of 1. The disproportionation is an equilibrium, and equilibrium is reached when the concentration of 1 is about twice that of $PhCH_2SSCH_2Ph$. For each run the equilibrium constant, K_e, for the disproportionation, expressed as

$$K_e = \frac{[R'SSR'][RSSR]}{[RSSR']^2} \qquad (7)$$

was determined from measurements of the relative areas of the two peaks made 24 and 48 hr after the initiation of the reaction. There was no significant change in the relative peak areas during the second 24 hr, indicating that the reaction definitely reached equilibrium during the first 24 hr. As expected, K_e did not vary with either initial concentration of disulfide or concentration of sulfuric acid. The value of K_e was 0.27 ± 0.03.

Equilibrium constants have been determined for the disproportionation of other unsymmetrical disulfides by several groups of workers.[9-11] The value of K_e of 0.27 which we find for 1 is in good accord with the data found for other systems which indicate that K_e is normally within a factor of 2 of the statistically predicted value of 0.25.[9,10]

Kinetics of the Disproportionation of 1. Experiments at different considerations of added strong acid (H_2SO_4) showed that the disproportionation of 1 was definitely acid catalyzed under our reaction conditions. The exact nature of the dependence on acid concentration will be considered later. In all runs there was a short (5–15 min), but definitely noticeable, induction period (see Figure 1) before the disproportionation began. The length of this induction period was shorter the higher the strong acid concentration (and faster the subsequent rate of disproportionation).

Once the induction period was over the kinetic data for the disproportionation gave a reasonably good fit to what would be expected for a reversible, second-order reaction of the type

$$2A \underset{k'}{\overset{k}{\rightleftharpoons}} B + C$$

A = $PhCH_2SSC_6H_4CH_3$; B = $(PhCH_2S)_2$; C = $(CH_3C_6H_4S)_2$

Frost and Pearson[12] give the following kinetic expression for such a reaction

$$\ln\left[\frac{x(a - 2x_e) + ax_e}{a(x_e - x)}\right] = k\left[\frac{2a(a - x_e)}{x_e}\right]t \qquad (8)$$

where a = initial concentration of A (1 in this case), x = moles of A per unit volume that have disproportionated in time t, x_e = moles of A per unit volume that have disproportionated when final equilibrium is reached, and the equilibrium constant for the reaction, K_e, is defined as

$$\frac{k}{k'} = K_e = \frac{(x_e/2)^2}{(a - x_e)^2}$$

In the present case if we let λ_A = magnitude of the integral for the methylene proton peak in $PhCH_2SSC_6H_4CH_3$ and λ_B = magnitude of the integral for the methylene proton peak in $(PhCH_2S)_2$ and λ_A^∞ and λ_B^∞ represent the magnitude of these same integrals once equilibrium is reached, then

$$x = a\left[\frac{\lambda_B}{\lambda_A + \lambda_B}\right] \text{ and } x_e = a\left[\frac{\lambda_B^\infty}{\lambda_B^\infty + \lambda_A^\infty}\right]$$

If we now define two new quantities

$$y = \frac{\lambda_B}{\lambda_A + \lambda_B} \text{ and } y_e = \frac{\lambda_B^\infty}{\lambda_B^\infty + \lambda_A^\infty}$$

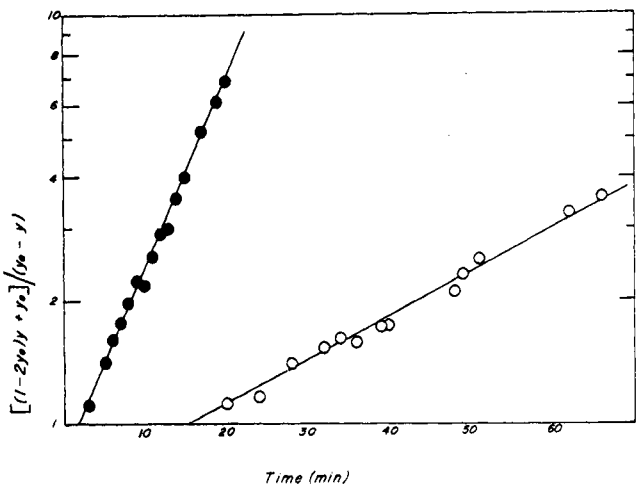


Figure 3. Effect of added *n*-butyl sulfide on the kinetics of the disproportionation of **1**. Data plotted according to eq 9. Both runs in acetic acid–0.56 *M* H_2O as solvent with 0.05 *M* H_2SO_4 and an initial concentration of **1** of 0.30 *M*. ●, 1 × 10^{-4} *M* *n*-Bu_2S added; ○, no added sulfide.

appropriate substitution in eq 8 gives eq 9, which should govern the change in the relative intensity of the two NMR methylene peaks with time, if the disproportionation of **1** does follow reversible, second-order kinetics under our reaction conditions.

$$\ln\left[\frac{(1 - 2y_e)y + y_e}{y_e - y}\right] = k\left[\frac{a}{K_e^{1/2}}\right]t \qquad (9)$$

Figure 1 shows the kinetic data for two runs, both at 0.10 *M* H_2SO_4 but involving different initial concentrations of **1**, plotted according to eq 9. Both plots are satisfactorily linear. In accord with the requirements of eq 9 a decrease in the initial concentration of **1** does appear to lead to a proportional decrease in the slope of the plot of the data vs. time. Table I summarizes the values of the rate constant, *k*, for the various acid and disulfide concentrations, as estimated from the slopes of plots of the data according to eq 9 and the relationship, slope = $k(a/K_e^{1/2})$.

From Table I one can see that *k* increases markedly with increasing concentration of sulfuric acid. A plot of log *k* vs. $-H_0$, the Hammett acidity function for these solutions,[13] is linear with a slope of about 0.8.

Effect of Added Mercaptan. Addition of very small concentrations of either *p*-toluenethiol or α-toluenethiol to the reaction solution led to a very marked increase in the length of the induction period observed at the start of the disproportionation. This can be seen from Figure 2, which shows a plot of the rate data for two otherwise identical runs, but to one of which was added initially 3.6 × 10^{-4} *M* *p*-toluenethiol. The run with the added thiol exhibits an induction period of almost 100 min before the disproportionation of **1** starts to proceed at a significant rate. This is in contrast to the induction period of only 5 min observed in the absence of added mercaptan. However, once the induction period is over the rate of disproportionation in the run with added mercaptan is identical, within experimental error, with the rate found in the absence of added thiol. Experiments in which the concentration of added thiol was varied showed that the length of the induction period was proportional to the amount of thiol added; thus, addition of 7.2 × 10^{-4} *M* *p*-$CH_3C_6H_4SH$ under the reaction conditions of Figure 2 gave an induction period of 195 min. Other experiments showed that a given mercaptan concentration the length of the induction period was the same with added $C_6H_5CH_2SH$ as with *p*-toluenethiol.

Table I
Kinetics of the Disproportionation of Benzyl *p*-Tolyl Disulfide in Acetic Acid–1% Water at 70°

$[ArSSR]_0$, *M*	$[H_2SO_4]$, *M*	$k \times 10^3$, M^{-1} sec^{-1} [a]
0.30	0.20	2.6
0.20	0.20	2.7
0.30	0.15	2.0
	0.10	1.2
0.20	0.10	1.1
0.30	0.05	0.69

[a] Evaluated from the slope of plots of the data for each individual run according to eq 9, using the relationship k = (slope × $K_e^{1/2}$)/$[ArSSR]_0$.

Table II
Rate of Disproportionation of Benzyl *p*-Tolyl Disulfide in the Presence of Added *n*-Butyl Sulfide[a]

$[ArSSR]_0$, *M*	$[H_2SO_4]$, *M*	$[n\text{-}Bu_2S] \times 10^4$, *M*	$k \times 10^3$, M^{-1} sec^{-1} [b]
0.30	0.05	1.00	3.1
	0.15	1.00	13.0
		0.50	7.5

[a] All data for acetic acid–1% water as solvent at 70°. [b] Evaluated from the slope of plots of the data for each individual run according to eq 9, using the relationship k = (slope × $K_e^{1/2}$)/$[ArSSR]_0$.

The experiments so far discussed were all carried out without initial degassing of the reaction solution. For solutions with no added mercaptan careful degassing of the solution had no significant effect on either the length of the short induction period or on the measured rate of disproportionation. In contrast, in runs with added mercaptan initial degassing of the solution led to a pronounced increase in the length of the induction period. For example, for the run in Figure 2 the induction period was increased from 100 to 245 min. The rate of disproportionation once the induction period was over, however, was the same as in the absence of degassing.

Effect of Added *n*-Butyl Sulfide. The addition of very small amounts (10^{-4} *M*) of *n*-butyl sulfide led to a very marked increase in the rate of disproportionation of **1**. This is evident from Figure 3, which shows the rate data for two runs, both at 0.05 *M* H_2SO_4 and 0.3 *M* **1**, one without added sulfide and the other containing 1 × 10^{-4} *M* *n*-butyl sulfide. From Figure 3 it appears that the rate data for the sulfide-catalyzed reaction give a satisfactorily linear plot vs. time when plotted according to eq 9, suggesting that the sulfide-catalyzed reaction is apparently also second order in disulfide. Experimental second-order rate constants for the different runs with added sulfide are shown in Table II. It is evident that this reaction, like the simple disproportionation, is subject to acid catalysis. From the very limited data it also appears that the rate increases with increasing sulfide concentration in an essentially linear manner.

Initial addition of mercaptan also leads to an induction period with the sulfide-catalyzed disproportionation, although the length of this induction period is much shorter than that caused by addition of the same amount of mercaptan to the ordinary disproportionation. Thus addition of either 3.6 × 10^{-4} *M* *p*-toluenethiol or $C_6H_5CH_2SH$ to an undegassed solution containing 1 × 10^{-4} *M* *n*-Bu_2S, 0.3 *M* **1**, and 0.15 *M* H_2SO_4 led to an induction period of about 10 min before disproportionation commenced instead of the

100-min period observed (Figure 2) under these conditions in the absence of sulfide. As in the other cases the rate after the induction period was over was identical with that observed in the corresponding run without added mercaptan.

Discussion

The important experimental observations regarding the disproportionation of 1 under the present reaction conditions are as follows. First, the kinetics of the approach to equilibrium show a quite good fit to what would be expected for a reversible reaction which is second order in disulfide. Second, the reaction is subject to marked acid catalysis. Third, the reaction can also be strongly catalyzed by the addition of small amounts of an *n*-alkyl sulfide. (This sulfide-catalyzed disproportionation is also acid catalyzed.) Finally, the disproportionation can be effectively completely inhibited for significant periods of time by the addition of very small amounts of either *p*-toluenethiol or benzyl mercaptan.

The inhibition by added mercaptans (Figure 2) is reminiscent of what one observes[14] for the inhibition of a free-radical chain reaction where the inhibitor suppresses the chain reaction by intercepting the chain-carrying radicals and is thereby slowly consumed in the process, so that after a certain period when the inhibitor has been completely used up the reaction commences at its normal uninhibited rate. However, when one examines this particular reaction system, it is not possible to propose any reasonable free-radical chain sequence for the disproportionation where added mercaptan could act as an inhibitor. Specifically, the only likely reactions of either thiol with a free radical are the hydrogen-atom transfers shown in eq 10, and any thiol

$$R\cdot' + RSH \longrightarrow R'H + RS\cdot \quad (10a)$$

$$R\cdot' + ArSH \longrightarrow R'H + ArS\cdot \quad (10b)$$

radicals formed in this fashion should promote, not inhibit, the disproportionation of 1 via the following reactions.

$$RS\cdot + RSSAr \longrightarrow RSSR + ArS\cdot \quad (11a)$$

$$ArS\cdot + RSSAr \longrightarrow ArSSAr + RS\cdot \quad (11b)$$

Although the inhibition by mercaptans can thus not be explained by a free-radical mechanism for the disproportionation, it could be explained by invoking a chain-type mechanism involving *ionic* intermediates where added thiol concentrations in excess of a certain value are sufficient to suppress the chain reaction almost completely. Furthermore, such a mechanism seems both a reasonable and a realistic possibility for the disproportionation of 1 under our reaction conditions. The particular mechanism that would seem to fit the data best is shown in Chart I. In this mechanism the chain-propagation steps are eq 15 and 16, which involve nucleophilic displacements by 1 on ions 2 and 3. The steady-state concentration of 2 and 3 will be governed by the equilibria shown as eq 13 and 14. Under normal circumstances, i.e., no added mercaptan, ArSH and RSH will be present only at the *same very low* equilibrium concentration as 2 and 3. Addition of mercaptan to a level much higher than this very low, normal, equilibrium concentration will, of course, drastically decrease the concentration of 2 (or 3) present at equilibrium and will correspondingly reduce the rate of chain propagation, thereby leading to marked inhibition of the disproportionation.

Since inhibition of the disproportionation by added thiols in the fashion shown in Chart I would not result in any significant net consumption of the added thiol, to explain the observed (Figure 2) cessation of that inhibition after a certain time period one must assume that under our reaction conditions there are one or more side reactions that consume mercaptan irreversibly. Reasonable possibilities for such reactions exist and will be discussed later. However, let us first see if the mechanism shown in Chart I is consistent with the kinetics observed for the disproportionation in the absence of added mercaptan.

Chart I
Mechanism of the Acid-Catalyzed Disproportionation of an Unsymmetrical Disulfide

$$ArSSR + H^+ \rightleftharpoons ArS\overset{+}{S}(H)R \rightleftharpoons Ar\overset{+}{S}(H)SR \quad (12)$$

$$ArSSR + Ar\overset{+}{S}(H)SR \rightleftharpoons Ar\overset{+}{S}(R)SSR\ (\mathbf{2}) + ArSH \quad (13)$$

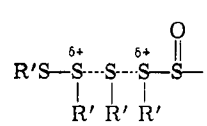
$$ArSSR + ArS\overset{+}{S}(H)R \rightleftharpoons RS\overset{+}{S}(Ar)SAr\ (\mathbf{3}) + RSH \quad (14)$$

chain-propagating steps:

$$ArSSR + RS\overset{+}{S}(Ar)SAr\ (\mathbf{3}) \rightleftharpoons Ar\overset{+}{S}(R)SSR\ (\mathbf{2}) + ArSSAr \quad (15)$$

$$ArSSR + Ar\overset{+}{S}(R)SSR\ (\mathbf{2}) \rightleftharpoons Ar\overset{+}{S}(Ar)SSR\ (\mathbf{3}) + RSSR \quad (16)$$

Besides eq 15 and 16 there are 22 additional possible reactions involving disulfides (ArSSR, RSSR, and ArSSAr) and the different possible dithiosulfonium ions (2, 3, and four other –S–S$^+$–S– cations). Some of these do not lead to conversion of one disulfide to another; others do. Unless some simplification is made the complete array of reactions is too complex to analyze kinetically in a straightforward manner. Fortunately, for this particular system, one significant simplification appears justified based on certain earlier results. *p*-Tolyl disulfide and benzyl disulfide have been found[8] to exhibit closely similar reactivity in the disulfide–sulfinic acid reaction. This fact and the fact that the rate-determining transition state in that reaction has the structure



suggest that for all of the different possible displacements by disulfides on dithiosulfonium ions in the disproportionation of 1, i.e.

$$-S-S + S-\overset{+}{S}-S- \longrightarrow -S-\overset{+}{S}-S + S-S- \quad (17)$$

the rate constants may be about the same, regardless of which particular sulfurs in eq 17 bear a *p*-tolyl group and which a benzyl group.

If we also assume that the equilibrium constants for the formation of the various dithiosulfonium ions from disulfides (eq 12–14 and analogous equations) are about the same for all the possible cations, then, to a reasonable first approximation, the mechanism in Chart I can be simplified for kinetic purposes to the following (eq 18–20)

$$D + H^+ \overset{K_1}{\rightleftharpoons} DH^+ \quad (18)$$

$$D + DH^+ \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} I^+ + T\text{–}SH \quad (19)$$

$$D + I^+ \xrightarrow{k_3} D' + I^+ \quad (20)$$

where D = disulfide (ArSSR, RSSR, or ArSSAr), DH^+ = protonated disulfide, I^+ = **2**, **3**, and the other dithiosulfonium ions, and TSH = thiol.

For this reaction scheme the rate of interconversion of disulfides is

$$\text{Rate} = k_3[I^+][D]$$

From the stoichiometry of the scheme, unless mercaptan is deliberately added, $[I^+]$ = [TSH]. If we assume a steady state in $[I^+]$, this leads to

$$[I^+] = \left[\frac{K_1k_2}{k_{-2}}\right]^{1/2}[D]^{1/2}[DH^+]^{1/2} = \left[\frac{K_1k_2}{k_{-2}}\right]^{1/2} h_0^{1/2}[D]$$

and to the following predicted rate expression.

$$\text{Rate} = k_3\left[\frac{K_1k_2}{k_{-2}}\right]^{1/2} h_0^{1/2}[D]^2 \quad (21)$$

Thus, provided our assumptions are reasonably valid, the disproportionation of **1** should follow kinetics which are second order in disulfide concentration, as indeed observed. The dependence of rate on acidity is predicted to follow $h_0^{1/2}$. Because of the difficulty in defining h_0 accurately for different types of substrates in strongly acid media, one cannot really say whether the observed dependence of rate on acidity is consistent with such a half-power dependence. However, it does appear that the observed increase in rate with acid concentration is somewhat less pronounced than that found[15] for certain other acid-catalyzed reactions involving sulfur substrates in this same medium where the reaction rate would be expected to show a first-order dependence on h_0. Therefore the experimental data are certainly not inconsistent with the predicted dependence of rate on acidity.

The inhibition of the disproportionation by added thiols is, of course, explained by their effect on the equilibrium shown as eq 19.

In the experiments with added thiol the marked increase in the length of the induction period upon degassing suggests that air oxidation of mercaptan to disulfide is one of the important side reactions normally leading to consumption of added thiol and eventual termination of the induction period. Another likely route for consumption of mercaptan would be via its reaction with the solvent, acetic acid, to give a thiol ester. While we are not certain what is the origin of the short induction periods that are observed in the absence of added thiol, the high concentrations of **1** employed (0.2–0.3 *M*), the very low concentrations of thiol ($\sim 3 \times 10^{-4}$ *M*) sufficient to give quite prolonged inhibition, and the short length of those induction periods, all make it attractive to suggest that they are due to the presence of very small amounts of a thiol impurity in the starting disulfide.

The catalysis of the disproportionation of **1** by added *n*-butyl sulfide and a suggested mechanism for that catalysis remain to be discussed.

The mechanism shown in Chart II represents an explanation for the catalysis by added *n*-Bu_2S that seems plausible based on other experience.[8,15,16] From previous studies[8] we know that *n*-Bu_2S should be a much better nucleophile toward sulfur than is **1**. From the work of Smallcombe and Caserio[16] we know that the equilibrium constant for the reaction

$$MeS\overset{+}{S}(Me)\text{–}SMe + Me_2S \rightleftharpoons Me_2\overset{+}{S}SMe + MeSSMe$$

is greater than 10^3. As a consequence the equilibrium constants for eq 22 and 23 should be much more favorable than those for eq 13 and 14. Because of this the steady-state concentration of **4** and **5**, and therefore of mercaptans RSH and ArSH, should be considerably larger than the steady-state concentration of mercaptans in the mechanism in Chart I. As a result the length of the induction period caused by a given concentration of added mercaptan should be considerably shorter for the sulfide-catalyzed reaction than it is for the ordinary disproportionation, as is indeed observed. The di-*n*-butylthioalkylsulfonium ions **4** and **5** should be able to give rise to an ionic chain-type disproportionation of **1** in the manner shown in eq 24 and 25.

What sort of kinetic behavior would be expected for the mechanism in Chart II? If, as in the earlier treatment of the ordinary disproportionation, we assume that the reactivity of various species is effectively independent of whether one has a tolyl or a benzyl group attached to sulfur, then, for kinetic purposes, we can approximate the mechanism in Chart II by the following

$$D + H^+ \overset{K_1}{\rightleftharpoons} DH^+$$

$$Bu_2S + DH^+ \underset{k_{-a}}{\overset{k_a}{\rightleftharpoons}} Z^+ + TSH$$

$$Z^+ + D \underset{k_{-b}}{\overset{k_b}{\rightleftharpoons}} I^+ + Bu_2S \xrightarrow{k_c} Z^+ + D'$$

where Z^+ = **4** or **5**, and the other symbols have the same meaning as in eq 18–20. If we assume a steady state in $[Z^+]$ and $[I^+]$, and that, unless mercaptan is deliberately added, $[Z^+] \simeq$ [TSH], this leads to the following predicted rate expression.

$$\text{Rate} = k_b\left[\frac{k_c}{k_c + k_{-b}}\right]\left[\frac{k_a}{k_{-a}}\right]^{1/2} K_1^{1/2} h_0^{1/2}[Bu_2S]^{1/2}[D]^{3/2} \quad (26)$$

Chart II
Possible Mechanism for *n*-Butyl Sulfide Catalysis of the Disproportionation of 1

$$ArSSR + H^+ \rightleftharpoons ArS\overset{+}{S}(H)R \rightleftharpoons Ar\overset{+}{S}(H)SR \quad (12)$$

$$n\text{-}Bu_2S + ArS\overset{+}{S}(H)R \rightleftharpoons n\text{-}Bu_2\overset{+}{S}SAr + RSH \quad (22)$$

4

$$n\text{-}Bu_2S + Ar\overset{+}{S}(H)SR \rightleftharpoons n\text{-}Bu_2\overset{+}{S}SR + ArSH \quad (23)$$

5

chain-propagation steps

$$4 + ArSSR \rightleftharpoons n\text{-}Bu_2S + ArS\overset{+}{S}(Ar)SR \rightleftharpoons ArSSAr + 5 \quad (24)$$

$$5 + ArSSR \rightleftharpoons n\text{-}Bu_2S + RS\overset{+}{S}(R)SAr \rightleftharpoons RSSR + 4 \quad (25)$$

Equation 26 predicts that the rate should depend on the ½ power of disulfide concentration rather than the second power as in the simple disproportionation. However, the experimental data (Figure 3) still seem to plot just as well in accord with eq 9 as did those for the simple disproportionation. We do not know, though, whether an actual ½ power dependence on disulfide concentration would result in enough deviation from linearity in a plot of the data according to eq 9 for the deviation to be readily apparent. While we had time in the present study to make only a very limited investigation of the dependence of the rate on the concentration of added sulfide, this seems to be more pronounced than the half-power dependence required by eq 26.

Although the fit of the experimental data to the predictions of eq 26 does not therefore seem as good as one would like, no plausible alternative mechanism to explain the catalysis by the added sulfide is readily apparent. One possible source of part of the difficulty may simply be that the simplifying assumptions made in order to reduce the kinetic scheme to one of manageable complexity may not be entirely valid for the sulfide-catalyzed reaction. In any event we feel that the mechanism in Chart II still offers at present the best working hypothesis to explain the catalysis observed with added *n*-butyl sulfide.

Experimental Section

Preparation of Benzyl *p*-Tolyl Disulfide. The method of Harpp et al.[17] was employed. A solution of 3.80 g (0.014 mol) of *N*-(*p*-tolylthio)phthalimide and 1.74 g (0.014 mol) of distilled α-toluenethiol in 70 ml of dry benzene was refluxed under nitrogen for 72 hr. The solution was filtered to remove crystalline phthalimide and the benzene solvent was removed under reduced pressure. The residue of crude benzyl *p*-tolyl disulfide was recrystallized twice at low temperature from a small amount of ethanol and then once from ligroin. The purified disulfide melted at 33° (lit.[8] mp 33–34°), yield 3.35 g (97%).

Purification of Solvents and Other Reagents. Glacial acetic acid was purified by refluxing 1 l. of commercial glacial acetic acid with 100 g of acetyl borate for 36 hr. The acetic acid was then slowly distilled off, and the fraction boiling at 117–117.5° was collected and retained. *p*-Toluenethiol was purified by recrystallization from ethanol, mp 44°. α-Toluenethiol was purified by distillation under reduced pressure, bp 144.5° (105 mmHg). *n*-Butyl sulfide was fractionally distilled before use.

Procedure for Kinetic Runs. The required amount of benzyl *p*-tolyl disulfide (1) was weighed directly into a small volumetric flask and then dissolved in a small amount of acetic acid–1% H_2O. The proper amount of a stock solution of sulfuric acid in the same solvent was then added by pipet. In those runs containing added thiol or *n*-butyl sulfide the desired amounts of stock solutions of these reagents in acetic acid–1% water were also added at this point. The entire solution was then made up to volume with additional acetic acid–1% water, and a portion of the final solution was placed in an nmr tube which was then tightly capped. The NMR tube was then placed in the thermostatted (70°) probe of a Jeol Minimar 100 NMR spectrometer. Two or three minutes were allowed for the tube to come to thermal equilibrium and for the phase and position adjustment of the spectrum. The region where the methylene protons of 1 (δ 3.83 ppm) and benzyl disulfide (δ 3.48 ppm) absorb was integrated rapidly two to four times (this required a maximum of 30 sec) at given time intervals. The relative areas of the two methylene proton singlets were used to determine the relative concentrations of 1 and benzyl disulfide at any given time. To determine the equilibrium concentration of the two disulfides the tube was removed from the probe and allowed to stand in a 70° constant-temperature bath for an additional 2 days. Measurements of the relative areas of the two NMR peaks were then made at 24 and 48 hr after the initiation of the reaction. There was no significant change in the relative peak areas during the second 24 hr.

Independent experiments showed that the presence of added α-toluenethiol, *p*-toluenethiol, and *n*-butyl sulfide in the concentrations used did not result in any signal in the NMR region being integrated that would interfere with the accurate determination of the disulfide rates by the NMR procedure. The NMR spectra of 1, benzyl disulfide, and *p*-tolyl disulfide were measured independently in acetic acid–1% H_2O and found to agree with those previously reported.[8]

The procedures so far described applied to those runs in which no special precautions were taken to exclude oxygen from the reaction solution. The procedure for those runs in which oxygen was excluded differed from this in the following way. First, small portions of all the necessary stock solutions were independently degassed and after the final degassing pure nitrogen was admitted to the flask containing the degassed solution, the stopcock connecting it to the vacuum system was closed, and the closed flask was transferred to a nitrogen-filled drybox. Deaerated solvent was also prepared in the same way and a solution of the disulfide and the various other reagents was prepared under nitrogen in the drybox. A portion of this solution was transferred to an NMR tube in the drybox, and the tube was tightly capped before being removed from the drybox.

Measurements showed that no appreciable disproportionation of 1 took place in any of the reaction solutions at room temperature before they were placed in the NMR probe at 70°. An experiment at 70° in which 0.3 *M* 1 was dissolved in acetic acid–1% H_2O containing only 0.005 *M* sulfuric acid showed that in the absence of a significant amount of added strong acid the rate of disproportionation of 1 in this solvent at that temperature is extremely slow. Therefore all of the measured rate of disproportionation under our reaction conditions is due to the acid-catalyzed reaction.

Registry No.—1, 16601-19-7; *n*-butyl sulfide, 544-40-1.

References and Notes

(1) This research supported by the National Science Foundation, GP-25799.
(2) M. Calvin, "Mercaptans and Disulfides," Oak Ridge, Tenn., 1954 (U.S. Atomic Energy Report UCRL-2438).
(3) A. P. Ryle and F. Sanger, *Biochem. J.*, **60**, 535 (1955).
(4) R. E. Benesch and R. Benesch, *J. Am. Chem. Soc.*, **80**, 1666 (1958).
(5) G. K. Helmkamp and D. C. Owsley, *J. Am. Chem. Soc.*, **89**, 4558 (1967); Ibid., **90**, 1635 (1968).
(6) Unpublished results of A. Fava and G. Reichenbach quoted on p 90 of ref 7.
(7) E. Culffarin and A. Fava, *Progr. Phys. Org. Chem.*, **6**, 81–109 (1968).
(8) J. L. Kice and E. H. Morkved, *J. Am. Chem. Soc.*, **86**, 2270 (1964).
(9) G. Dalman, J. McDermed, and G. Gorin, *J. Org. Chem.*, **29**, 1480 (1964).
(10) B. Haraldson et al., *Acta Chem. Scand.*, **14**, 1509 (1953).
(11) S. F. Birch, T. V. Cullum, and R. A. Dean, *J. Inst. Pet., London*, **39**, 206 (1953).
(12) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism", 2nd ed, Wiley, New York, N.Y., 1961, pp 187–188.
(13) J. Rocek, *Collect. Czech. Chem. Commun.*, **22**, 1 (1957).
(14) P. D. Bartlett and H. Kwart, *J. Am. Chem. Soc.*, **72**, 1051 (1950).
(15) J. L. Kice and G. B. Large, *J. Org. Chem.*, **33**, 1940 (1968); J. L. Kice, C. G. Venier, G. B. Large, and L. Heasley, *J. Am. Chem. Soc.*, **91**, 2028 (1969).
(16) S. H. Smallcombe and M. C. Caserio, *J. Am. Chem. Soc.*, **93**, 5826 (1971).
(17) D. N. Harpp, D. K. Ash, T. G. Bach, J. G. Gleason, B. A. Orwing, and W. F. Van Horn, *Tetrahedron Lett.*, 3551 (1970).