

Kinetics of the Thiol–Disulfide Exchange. II. Oxygen-Promoted Free-Radical Exchange between Aromatic Thiols and Disulfides^{1a}

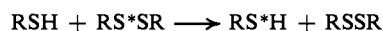
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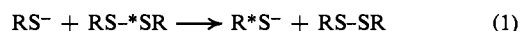
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Abstract: In nonpolar media and in the absence of bases isotopic exchange between aromatic thiols and disulfides fails to take place at an appreciable rate unless oxygen is present. The exchange reaction is accompanied by the (albeit much slower) autoxidation of the thiol. However, autoxidation inhibitors such as hydroquinone or *o*-nitrophenol are without effect on the rate. Iodine, while it moderately promotes the exchange in the absence of oxygen, effectively retards the oxygen-promoted exchange. At the same time it strongly accelerates thiol autoxidation. While an aliphatic (*n*-butyl) thiol–disulfide system does not react under conditions which lead to rapid exchange in an aromatic system, there is no appreciable rate difference between *p*-H and *p*-Cl substituents. Solvent effects on the rate are also minor. The rate equation for exchange has the form $\text{rate} = k[\text{PhSSPh}][\text{PhSH}]^{1/2}[\text{O}_2]^{1/2}$. The evidence is interpreted in terms of a radical chain mechanism with bimolecular chain termination, the rate-determining propagation step being a radical displacement at sulfur: $\text{PhS}\cdot + \text{PhS}^*\text{-SPh} \rightarrow \text{PhS}\cdot^* + \text{PhS-SPh}$. The activation energy for this step is estimated on the order of 5 kcal/mole. The initiation step is suggested to involve one oxygen and one thiol molecule ($\text{PhSH} + \text{O}_2 \rightarrow \text{PhS}\cdot + \text{HO}_2\cdot$) which is the same reaction usually assumed for thiol–olefin cooxidation. The results for exchange and cooxidation are compared and discussed and it is suggested that cooxidation may actually involve a different initiation step.

Some years ago we studied the kinetics of the isotopic exchange reaction between thiols and the corresponding disulfides under a variety of experimental conditions.² It was found that the exchange may be



catalyzed by bases and it was recognized that mercaptide ion was involved in the rate-determining nucleophilic displacement at the disulfide sulfur (eq 1).



A topic which was but briefly mentioned at that time was the possibility that aromatic disulfides may undergo exchange through a free-radical mechanism initiated by the thermal homolytic splitting of the disulfide (eq 2). Experiments conducted at 100° in



xylene disclosed a slow exchange.² No definite conclusion about the mechanism was arrived at, however, except that, if the observed exchange occurred by this mechanism, the thermal dissociation of the aromatic disulfides (eq 2) had to be extremely limited.^{3,4} When our paper² was already in print we became aware of an earlier study by Guryanova and co-workers.⁵ They had measured the rate of isotopic exchange for several thiol–disulfide systems, in nonpolar media, including a number of *para*-substituted phenyl substrates. For three systems (*n*-butyl, benzyl, and *p*-tolyl) they deter-

mined the change of rate as a function of reactant concentration. The analysis of the kinetic results led the Russian workers to conclude the reaction was *zero order* with respect to thiol and *one-half order* with respect to disulfide, which was considered to be evidence in favor of the homolytic splitting (eq 2) followed by fast hydrogen transfer (eq 3) between thiol radical and thiol



Closer scrutiny of the results obtained by the Russian workers showed, however, that their kinetic analysis was in error and the reaction orders recalculated from the data⁵ are in fact those given in Table I. Thus the

Table I

Substrate	Kinetic order in thiol	Kinetic order in disulfide
<i>p</i> -Tolyl	0.4	1.0
Benzyl	0.5	0.9
<i>n</i> -Butyl	0.25	0.85

reaction orders tend to approach one-half and unity with respect to thiol and disulfide, respectively. The larger deviations are observed for the *n*-butyl system where, however, the thiol concentration employed⁵ was far too high for a rigorous kinetic analysis (from 0.5 to 5 *M*, the latter corresponding to 450 g of butanethiol/l. Whatever significance can be attached to the results of Guryanova and co-workers,⁵ it was clear that their conclusions concerning the mechanism were wholly unsupported and the problem of the thiol–disulfide exchange in nonpolar media still open to question.

In this paper we report a number of observations and kinetic data on the isotopic exchange of thiophenol or *p*-chlorothiophenol and the corresponding disulfides in media of low polarity (cyclohexane, benzene, and acetic acid) where the base-catalyzed exchange (eq 1)

(1) (a) Supported in part by Consiglio Nazionale delle Ricerche, Rome. U. P. is indebted to Thiokol Corp., Trenton, N. J., for a fellowship. (b) To whom inquiries are to be addressed at the Istituto di Chimica Generale, Università di Pisa, Italy. (c) Istituto di Chimica Fisica, Università di Perugia.

(2) Part I: A. Fava, A. Ilceto, and A. Camera, *J. Am. Chem. Soc.*, **79**, 833 (1957).

(3) The notion that simple aromatic disulfides do not undergo extensive homolytic dissociation, much debated at the time of our earlier work,² has been more definitely established in the meantime.⁴

(4) For a review of the pertinent evidence, see U. Schmidt, *Angew. Chem. Intern. Ed. Engl.*, **3**, 602 (1964).

(5) E. N. Guryanova, V. N. Vasileva, and L. S. Kusina, *Conf. Acad. Sci., USSR Peaceful Uses At. Energy Moscow, 1955*, 163 (1956).

is likely to be negligible. It will be apparent that such exchange is promoted by molecular oxygen and, in essence, this is a report on the ability of oxygen to initiate a free-radical chain process leading to isotopic exchange between thiols and disulfides.

Experimental Section

Materials. Reagent grade commercial acetic acid was crystallized three times (discarding each time about one-half of it) and distilled, mp 16.24°. Assuming that the only significant impurity was water, a stoichiometric amount of acetic anhydride was added, refluxed for 60 hr, and distilled, mp 16.53°. Reagent grade commercial benzene was refluxed over Na-K alloy and fractionally distilled: bp 80.1°; mp 5.51°. Reagent grade commercial cyclohexane was shaken several times with a HNO₃-H₂SO₄ mixture, washed, neutralized, dried on Drierite, refluxed over Na-K alloy, and distilled, bp 80.7°. Commercial thiophenol was distilled under nitrogen before use, bp 168°. Reagent grade commercial *p*-chlorothiophenol was crystallized from absolute ethanol, mp 52°. Disulfides were prepared from the corresponding thiols by oxidation with iodine in alcoholic solutions and crystallized from absolute ethanol: diphenyl disulfide, mp 61°; *p*-chlorophenyl disulfide, mp 73°. Labeled (³⁵S) disulfides were prepared as previously reported.²

Procedure for the Exchange Experiments. The reacting solutions were made up at room temperature. Samples (2 ml) of the solutions were sealed in 5-ml dark glass ampoules under the predetermined atmosphere, *i.e.*, mixtures of nitrogen and oxygen, and put in a constant-temperature oil bath. Since reaction times were more often of the order of several hours, the time required for the solution to reach the desired temperature was usually negligible. Precautions were taken to exclude light.

Separation of the reagents was realized by precipitation. This was achieved by addition of a methanolic solution of Hg(CN)₂ which quantitatively precipitates the thiol as mercury mercaptide.⁶ This substance lends itself to the preparation of extremely good samples for radioactivity counting. To this end the precipitate was washed three times with ethanol and a "thick-layer" sample prepared by filtration on a Büchner-type filter. The cake was dried and gently pressed in order to ensure uniformity of the surface. Finally it was mounted on a support equipped with a ring cover which delimited the counting area to a definite value. Reproducibility of activity counting was within 2%.

Results

Except for a few runs in benzene and acetic acid, the reaction was carried out in cyclohexane. As soon as a systematic investigation began, it became apparent that what we had up to that point considered a purely thermal exchange was actually promoted by oxygen. This is borne out by the examination of the results plotted in Figure 1. Curve A refers to experiments carried out in an air atmosphere and curve B to experiments in which the solutions had been swept for 5 min with a stream of nitrogen (oxygen content <5 ppm) and sealed under the same atmosphere.

When oxygen is present, the McKay plot⁸ is linear up to at least three half-lives. When the solutions are swept with nitrogen, the rate is very much slower and a McKay plot concave upward is obtained, the rate becoming negligible after some exchange (40–50%) has occurred. The exchange, occurring under a nitrogen atmosphere, was not investigated further.

(6) It is interesting to remark that while most divalent mercury salts (HgX₂) precipitate mixtures of Hg(SC₆H₅)₂ and C₆H₅S-Hg-X of variable composition according to the ratio of thiophenol to HgX₂,⁷ we have found that with Hg(CN)₂ (a saturated methanolic solution was used) the precipitate consists exclusively of Hg(SC₆H₅)₂ irrespective of the ratio of thiophenol to Hg(CN)₂. This circumstance permits one to use the precipitate obtained with Hg(CN)₂ directly for activity counting purposes, thereby eliminating the tedious oxidation to BaSO₄.

(7) H. Lecher, *Ber.*, **48**, 1429 (1915); **53**, 575 (1920).

(8) A. C. Wahl and N. A. Bonner, Eds., "Radioactivity Applied to Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1951, p 11.

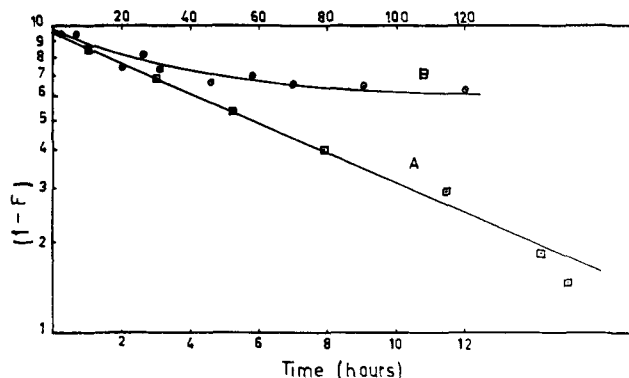


Figure 1. Curve A, conditions of run 4, Table II, lower time scale; curve B, same as A, but without oxygen, upper time scale.

The finding that oxygen was required for the exchange to proceed suggested that the exchanging system was unstable, isotopic exchange being the side effect of some net chemical reaction simultaneously occurring in the system, possibly the autoxidation of the thiol. Actually the linearity of the $\log(1-F)$ vs. time plot gave no guarantee that the exchanging system is a stable one since, if the net reaction is the oxidation of thiol to disulfide, the same exchange-rate law would be applicable as for a stable system, independent of the actual mechanism of the oxidation.⁹

An independent check of the stability of the system was therefore necessary and this was achieved by following the loss of thiol (iodine titer) during exchange.¹⁰ It was found that oxidation of thiol is very much slower than exchange. For example, under the conditions of the experiments plotted in Figure 1, curve A, after 150 hr, corresponding to about 25 half-lives for exchange, only 4% of thiophenol had been consumed. This result, if it established that for all practical purposes the exchanging system was a stable one, did not disprove the idea that isotopic exchange resulted as a side effect of the (albeit much slower) autoxidation of the thiol (Table II). That this

Table II. Comparison between Rate of Autoxidation and Rate of Exchange of *p*-Chlorothiophenol and *p*-ChlorodiphenylDisulfide under Various Conditions^a

Solvent	$R \times 10^6$, equiv $l^{-1} \text{ sec}^{-1}$	Thiol oxidized after 20 hr, %
Cyclohexane	1.6	0.5
Acetic acid	3.8	4.8
Acetic acid + Co(II) acetate $10^{-3} M$	9.6	9.1

^a ArSH, 0.1 M; ArSSAr, 0.05 M; temperature, 110°; air atmosphere.

may be actually so is sustained by the observation that conditions which favor the autoxidation also favor the exchange. Some pertinent results are reported in Table II whose major feature is the effect that a well-

(9) C. P. Luehr, G. E. Challenger, and B. I. Master, *J. Am. Chem. Soc.*, **78**, 1314 (1956).

(10) Under the conditions of these experiments, which were identical with those for exchange, the amount of oxygen present was enough to oxidize 60% of the thiol.

known autoxidation catalyst, Co(II),¹¹ has on both exchange and oxidation of thiol.

Reaction Orders. More detailed information concerning the nature of the exchange reaction and the catalysis by oxygen can be obtained from the rate expression for the exchange. The fact established above, that the exchange has proceeded very extensively before any appreciable modification of the reactant concentration has occurred, may be utilized to determine the form of the rate expression, by treating the exchange as if it occurred in a stable system. This was obtained by determining the rate of exchange as a function of reactants and oxygen concentrations, as reported in Table III.

Table III. Rate of Exchange between Thiophenol and Diphenyl Disulfide in Cyclohexane

Run	PhSH, equiv/l.	PhSSPh, equiv/l.	p_{O_2} , ^a torr	Temp, °C	$R_{ex} \times 10^7$, equiv l. ⁻¹ sec ⁻¹
1	0.1	0.1	15	110	5.5
2	0.1	0.1	30	110	7.4
3	0.1	0.1	76	110	11.8
4	0.1	0.1	152	110	15.9
5	0.1	0.01	152	110	1.56
6	0.1	0.001	152	110	0.13
7	0.25	0.1	152	110	23.6
8	0.03	0.1	152	110	8.5
9	0.1	0.1	152	100	8.0
10	0.1	0.1	152	120	30.4
11	0.1	0.1	152	130	55.0
12 ^b	0.1	0.1	152	110	15.9
13 ^c	0.1	0.1	152	110	15.9
14 ^d	0.1	0.1	152	110	16.0
15 ^{d,e}	0.1	0.1	0	110	3.2
16 ^{d,e}	0.1	0.1	152	110	4.2
17 ^{d,f}	0.1	0.1	152	110	1.4
18 ^g	0.1	0.1	152	110	17
19 ^h	0.1	0.1	152	110	14.8
20 ^h	0.1	0.1	152	80	1.8
21 ⁱ	0.1	0.1	152	110	40.0

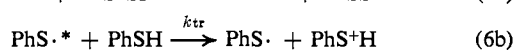
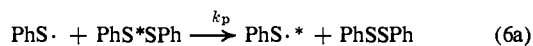
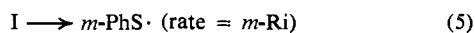
^a Oxygen partial pressure in the gas phase at 20°. ^b Hydroquinone, 10^{-3} M. ^c *o*-Nitrophenol, 5×10^{-3} M. ^d *p*-ClC₆H₄SH and (*p*-ClC₆H₄S). ^e Iodine, 5×10^{-4} M. ^f Iodine, 1×10^{-4} M. ^g *m*-Dinitrobenzene, 1.9×10^{-2} M. ^h Benzene solvent. ⁱ Acetic acid solvent.

Orders of reaction were obtained from the slope of the log-log plots of rate *vs.* concentration (runs 1–8). This analysis has shown that the reaction is one-half order both in oxygen and in thiophenol and first order in disulfide. Consequently the rate expression for the oxygen-catalyzed exchange in cyclohexane is

$$\text{rate} = k[O_2]^{1/2}[\text{PhSH}]^{1/2}[\text{PhSSPh}] \quad (4)$$

Discussion

The form of the rate expression suggests a radical-chain mechanism with second-order chain termination. Equations 5–7 give a reasonable reaction sequence



(11) C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p 427 ff.

which, as will be shown below, agrees with the rate expression. It comprises an initiation step (5) (not detailed at this stage), a propagation step which involves a radical displacement at sulfur and a hydrogen transfer between a thiyl radical and a thiol molecule (6a and 6b, respectively) and a bimolecular termination step (7) involving two thiyl radicals. In this mechanism the thiyl radical is supposed to be the only chain carrier; in other words, any radical produced in the initiation step is assumed to undergo rapid hydrogen transfer with thiol.

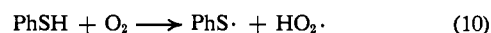
If the hydrogen transfer (6b) is fast compared to the radical displacement (6a), the rate of exchange is simply the rate of step 6a, $R_{ex} = k_p [\text{PhS}\cdot][\text{PhSSPh}]$, which, in the steady-state approximation, becomes

$$R_{ex} = k_p [\text{PhSSPh}] \left(\frac{mR_i}{2k_t} \right)^{1/2} \quad (8)$$

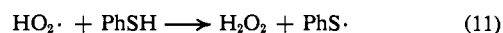
Equation 8 is equivalent to the rate expression (eq 4) if the rate expression for initiation is

$$R_i = k_i [\text{PhSH}][O_2] \quad (9)$$

According to 9, the initiation step involves one oxygen and one thiol molecule. A likely process is reaction 10, where one thiol and one oxygen molecule react to give one thiyl and one hydroperoxy radical.



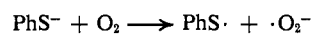
The hydroperoxy radical can further react with thiol in a fast step to give a second thiyl radical



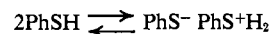
so that two thiyl radicals would be formed in each initiation act. Therefore k of eq 4 becomes

$$k = k_p k_i^{1/2} k_t^{-1/2} \quad (12)$$

Another possible initiation reaction may involve the thiol conjugate base attacking the oxygen molecule



This would lead to the same kinetics for initiation if it is assumed that the thiophenoxide anion is formed in an autoprotolytic equilibrium



If the thiophenoxide ion was involved, however, an electron-transfer agent would be expected to greatly enhance the rate.¹² This appears not to be the case; *m*-dinitrobenzene in high concentration does not increase the rate appreciably (Table III, run 19). Therefore we favor reaction 10 as the initiation step.

Effect of Structure and Solvent. A structural change from phenyl to *p*-chlorophenyl (runs 4 and 14) does not affect the rate of thiol–disulfide exchange appreciably. On the other hand an aliphatic thiol–disulfide system does not undergo isotopic exchange at any appreciable rate under the same temperature and oxygen pressure.¹³ This is consistent with the proposal (eq 10) that initiation involves breaking an RS–H bond, the S–H bond dissociation energy for an aliphatic thiol being some 14 kcal/mole greater than for an aromatic one.¹⁴ For the two aromatic thiols, the S–H bond dissociation energy

(12) G. A. Russell, E. G. Janzen, and E. T. Storm, *J. Am. Chem. Soc.*, **86**, 1807 (1964).

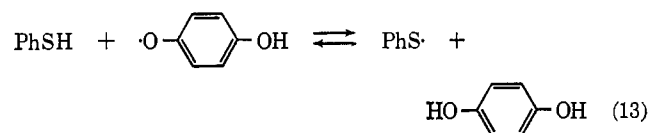
(13) G. Reichenbach, unpublished results.

(14) J. A. Kerr, *Chem. Rev.*, **66**, 465 (1966).

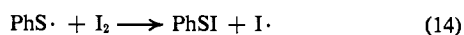
could be expected to be lower, and the initiation rate correspondingly greater, for *p*-chlorothiophenol than for thiophenol. The observed lack of structural effect may arise from a balance of an increase of initiation rate and a comparable decrease of propagation rate.

Changing the solvent produces little effect on the exchange rate; the rates in benzene (run 20) and cyclohexane appear to be about equal; while acetic acid is about 2.5 times faster than cyclohexane (runs 21 and 4). However, these rate factors have little meaning since the over-all rate depends on the solubility of oxygen, which may well vary from solvent to solvent. Thus the only reasonable conclusion is that both the structure and the solvent effect are small, which is further indication of the radical nature of the oxygen-promoted exchange.

Inhibition by Iodine. As shown in Table III, the effect of addition of several substances to the reacting system was tested. Common autoxidation inhibitors such as hydroquinone and *o*-nitrophenol¹⁵ appear to have no effect (runs 12 and 13). We tend to explain this observation by assuming that in the presence of an active hydrogen transfer agent such as thiophenol¹⁶ the phenols cannot compete effectively for free-radical species. In other words, equilibrium 13 would lie far to the right.



The more interesting results are provided by the experiments carried out in the presence of iodine, which appears to be an effective inhibitor.¹⁷ However, the behavior is peculiar insofar as iodine at low concentration depresses the rate more than at higher concentration (Table III, runs 16 and 17). Experiments conducted *in the absence of oxygen* actually showed that iodine can act as an initiator of thiol-disulfide exchange.¹³ For example, under the conditions of run 16, but in the absence of oxygen (run 15), the rate of exchange was found to be $10^7 \times R_{\text{ex}} = 3.2 \text{ equiv l.}^{-1} \text{ sec}^{-1}$. Assuming as a first approximation that initiation by oxygen and by iodine occur independently, one can subtract the rate of run 15 from that of run 16 to give the iodine-inhibited rate, $10^7 \times R_{\text{ex}} = 1.0 \text{ equiv l.}^{-1} \text{ sec}^{-1}$. This value, when compared with the uninhibited rate, $10^7 \times R_{\text{ex}} = 16.0$ (run 14), clearly indicates that iodine is an effective inhibitor of the oxygen-promoted exchange. The inhibitory effect can be explained in terms of reaction of phenylthiyl radicals with molecular iodine to form sulfenyl iodide (PhSI)



which could further act as a scavenger of thiyl radicals.



(15) K. U. Ingold, *Chem. Rev.*, **61**, 563 (1961).

(16) For the ability of thiols to act as hydrogen transfer agents, see, for instance, S. G. Cohen and S. Aktipis, *J. Am. Chem. Soc.*, **88**, 3587 (1966), and previous papers by S. G. Cohen.

(17) It is to be remarked that in anhydrous hydrocarbon solvent the common oxidation of thiols by iodine fails to take place. This is not surprising on energetic grounds since the gas-phase enthalpy change is unfavorable by 1 kcal/mole.¹⁴ Only when water or some other polar solvent is present can solvation of H^+ and I^- ions drive the reaction to completion.

Both reactions can effectively reduce the steady-state concentration of the chain carrier, $\text{PhS}\cdot$.

There are no data in the literature which can support reactions 14 and 15 on energetic grounds. In fact there are no reported examples of compounds even containing the S-I bond. This, however, cannot be assumed as evidence that the S-I bond is very weak, weaker in fact than the I-I bond. Dr. E. Ciuffarin of this laboratory has been able to isolate a sulfenic iodide, triphenylmethanesulfenyl iodide, as a solid whose solutions in hydrocarbon solvents can be kept indefinitely at room temperature, provision being taken for the exclusion of light.¹⁸ It is then conceivable that reaction 14 may be important in iodine inhibition.

It is interesting to remark that while thiols are not appreciably oxidized by iodine,¹⁷ the presence of iodine very markedly accelerates thiol autoxidation. Under the conditions of run 15, 10% was oxidized in 5 hr while in the absence of iodine the oxidation occurred to an extent no greater than 0.2% (as estimated from data obtained for much longer time intervals, see Table I).

Clearly reactions 14 and 15 account for inhibition of isotopic exchange as well as the acceleration of thiol autoxidation, the mechanism being very plausible if the PhS-I bond energy is intermediate between I-I (35.5 kcal) and PhS-SPh (45 kcal).^{19,20} This is very reasonable in view of the negligible electronegativity difference between sulfur and iodine.

The results of the iodine experiments are in apparent contradiction with those of Table II, where conditions fostering autoxidation were shown to foster exchange as well. Clearly in the cases considered in Table II the increase in autoxidation rate must be linked to an increase in the rate of initiation.

Activation Energy. Runs 4 and 9-11 allow the determination of an "apparent" activation energy of 19.2 kcal/mole. This value is not the temperature coefficient for the rate constant, k of eq 4, because of two facts: (i) the oxygen partial pressure was not constant throughout runs 4 and 9-11 but was permitted to change with temperature and (ii) the solubility of oxygen in cyclohexane varies with temperature. By assuming ideal behavior, the first factor can be easily computed to add about 0.6 kcal/mole to the apparent activation energy.

The second factor is the heat of solution of oxygen. In view of the lack of solubility data for oxygen in cyclohexane the heat of solution may be approximated by that in a similar hydrocarbon solvent, 2-methylheptane, for which solubility data are reported,²¹ allowing an estimate of $\Delta H_s = -0.5 \text{ kcal/mole}$.

Applying these two corrections, the over-all activation energy for the exchange process can be calculated to be $E_a = 19.1 \text{ kcal/mole}$. From eq 12 it can be deduced that $E_a = E_p + (1/2E_i - 1/2E_t) \approx E_p + 1/2E_i$, if E_t is assumed to be negligible.

Assuming the reverse of reaction 10 to be negligibly activated, E_i can be set equal to the enthalpy change

(18) E. Ciuffarin and G. Tentori, unpublished results.

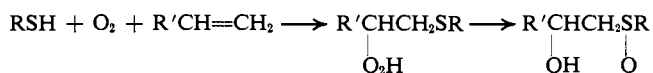
(19) The disulfide link in alkyl compounds is characterized by $D = 73 \text{ kcal}$.²⁰ For diaryl disulfides it is probably reduced by roughly 28 kcal/mole. This estimate is based on the bond dissociation energies of $\text{CH}_3\text{S}-\text{H}$ (89 kcal) and $\text{PhS}-\text{H}$ (75 kcal).¹⁴

(20) T. L. Cottrell, "The Strength of Chemical Bonds," Academic Press Inc., New York, N. Y., 1954, p 284.

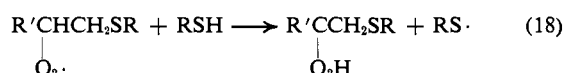
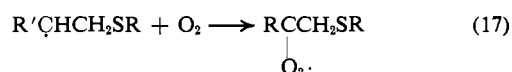
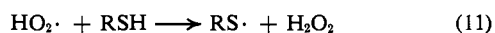
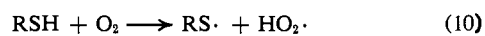
(21) H. Stephen and T. Stephen, "Solubilities of Inorganic and Organic Compounds," Vol. I, Part 1, Pergamon Press, Ltd., London, 1963, p 573.

for reaction 10 which, computed from the appropriate bond dissociation energies,¹⁴ turns out to be about 28 kcal/mole. Thus the activation energy for the rate-determining propagation step (reaction 6a) results: $E_p = 5$ kcal/mole. This value, although quite reasonable, should be taken with great caution and considered as an approximation at best. The uncertainty arises in the first place because the bond dissociation energies used to make the calculation were given without an estimate of their limits of accuracy.¹⁴ Second, gas-phase rather than solution bond dissociation energies were used.

The Cooxidation of Thiols with Olefins. It is interesting to compare our results on the oxygen-promoted exchange with those on the cooxidation of thiols with olefins to give 2-sulfinylethanol through the intermediacy of the corresponding 2-mercaptoethyl hydroperoxides.



This reaction type was first studied by Kharash and co-workers²² and subsequently by Ford, Pitkethly, and Young, who established its *trans* stereochemical course,²³ and by Oswald, who was able to isolate the intermediate hydroperoxide.²⁴ Since then the reaction has been extensively investigated, especially by Oswald, who has recently reviewed the subject.²⁵ In spite of the numerous investigations, however, the reaction has never been subject to kinetic analysis and the accepted mechanism is that proposed by Kharash in 1951.²²



This sequence and ours (eq 6a, 6b, 7, 10, and 11) have a common initiation mechanism (reaction 10) which seems difficult to reconcile with the vastly different rates at which exchange and autoxidation occur; exchange occurs at manageable rates at elevated temperatures (100° or higher) while cooxidation may take place readily at 0° and below.²⁵ A lower limit of the activation energy for reaction 10 has been estimated above to be on the order of 28 kcal/mole from bond dissociation energies.¹⁴ On this basis a 100° temperature interval involves a rate factor of 10⁶. This in turn implies that if the two processes have the same initiation reaction (and both have bimolecular chain termination), the cooxidation chain must be at least 10³ times longer than the exchange chain (this result

(22) M. S. Kharash, W. Nudenberg, and G. I. Mantell, *J. Org. Chem.*, **16**, 524 (1951).

(23) J. F. Ford, R. C. Pitkethly, and V. O. Young, *Tetrahedron*, **4**, 325 (1958).

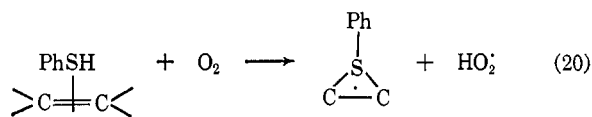
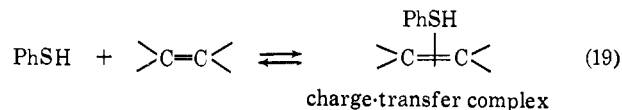
(24) A. A. Oswald, *J. Org. Chem.*, **24**, 443 (1959); **26**, 842 (1961).

(25) A. A. Oswald and T. J. Wallace in "Organic Sulfur Compounds," Vol. II, Pergamon Press, Ltd., London, 1966, Chapter 8, p 205.

arises from eq 8 whereby the exchange rate is related to the square root of the initiation rate).

We have carried out an experiment designed to test the plausibility of this factor. Thiophenol and styrene, both 0.1 *M*, were cooxidized in cyclohexane solvent in the presence of radioactive diphenyl disulfide. After 3 hr of air bubbling at room temperature, 67% of the thiol had reacted. The residual thiol, precipitated out and counted, appeared to have incorporated no radioactivity to any appreciable extent (<1%, *i.e.*, within the limits of the separation method). This experiment proved that *if thiyl radicals are produced* they have no appreciable chance to compete for disulfide but rather add to styrene. Thus the specific rate of reaction 16 must be at least several hundreds of times greater than that of reaction 5.

Although the result of this experiment is consistent with the idea that the chain length for cooxidation is much greater than for exchange, it does by no means rule out the possibility that the two reactions may actually involve different initiation. This view is suggested by the observation that the cooxidation rate is strongly dependent on the unsaturated compound; it is much greater for styrene than for 2-octene²² and for phenylacetylene it is so fast that autoxidation takes place readily even at -75°.²⁶ These findings are difficult to reconcile simply on the basis of different propagation rates for different olefins, but they suggest that the unsaturated compound is actually involved in the initiation step. While we believe that elucidation of this point requires a kinetic study, a suggestive hypothesis is that the species involved in initiation may be a thiol-olefin charge-transfer complex from which the abstraction of a hydrogen atom by molecular oxygen results in the formation of a radical species much more stable than thiyl, thus effectively reducing the activation free energy for initiation.



(In reaction 20 the radical species is formulated as a bridged radical²⁷ in agreement with the observed exclusive *trans* addition.^{23,25}) In view both of the donor properties of dicoordinate sulfur compounds, which are well documented,²⁸ and of the dramatic effect that olefinic or acetylenic substances may have in inducing homolysis,²⁹ we think that reactions 19 and 20 may be a reasonable starting point for a reexamination of the thiol-olefin cooxidation.

(26) K. Griesbaum, A. A. Oswald, and B. E. Hudson, Jr., *J. Am. Chem. Soc.*, **85**, 1969 (1963).

(27) P. S. Skell and P. D. Readio, *J. Am. Chem. Soc.*, **86**, 3334 (1964); P. S. Skell and R. R. Pavlis, *ibid.*, **86**, 2956 (1964).

(28) See, for instance, R. J. Niedzielski, R. S. Drago, and R. L. Middaugh, *ibid.*, **86**, 1694 (1964).

(29) G. Fraenkel and P. D. Bartlett, *ibid.*, **81**, 5582 (1959); C. Walling, J. Heaton, and D. D. Tanner, *ibid.*, **87**, 1715 (1965); For a discussion on molecule-induced homolysis, see W. A. Pryor, "Free Radicals," McGraw-Hill Book Co., Inc., New York, N. Y., 1966, p 119ff.