increase in the yields of cis adducts as the complex-forming ability of the substituted thiols[6] increases.

Experimental Section

Materials. *p*-Chlorothiophenol (Aldrich Chemical Co.) was recrystallized from aqueous ethanol, mp 51–52 °C. Styrene (Eastman Organic Chemicals) was freshly vacuum distilled, bp 38–39 °C (10 Torr). Substituted styrenes (obtained from Dow Chemical Co. by courtesy of Dr. R. Dolinski) were freshly vacuum-distilled before use. Indene (Eastman Organic Chemicals) was freshly vacuum-distilled before use, bp 60–61 °C (12 Torr). All the other solvents reported in Table I were reagent grade and were used without further purification. The thiophenols reported in Tables III and IV were freshly vacuum-distilled before use. Benzo-1,2-cyclohexene and benzo-1,2-cycloheptene (obtained from the University of Puerto Rico by courtesy of Professor Oswaldo Cox) were found to be sufficiently pure to be used without further purification.

^{1}H NMR. The chemical shifts reported in Tables I, III, and IV were determined by means of a Varian A 60 spectrometer calibrated by side band techniques using a Hewlett Packard Model 4204 A oscillator and a Model 5216 A electronic counter. Samples were contained in a 5-mm o.d. NMR tube.

Determination of Thiol–Olefin Complex Formation. A Freon 113 solution of *p*-chlorothiophenol of known concentration was placed in a 5-mm o.d. NMR tube. The tube was fitted with a rubber septum and flushed with nitrogen, and 0.01 mL of tetramethylsilane was injected. The ^{1}H NMR spectra were recorded by means of a Varian EM 360 A spectrometer. Known volumes of the olefin of interest were injected into the NMR tubes and the spectra were recorded after each injection. The addition of olefin were continued until no change in the chemical shift of the S*H* signal was observed. The error in chemical shift measurements was ±0.1 Hz. The association constants ($K^{AD}{}_{complex}$) were calculated from the slope and the intercept of the plot of reciprocal change in chemical shift ($1/\Delta$Hz vs. reciprocal molality ($1/m^0{}_D$) as described in ref 9, 142.

Acknowledgment. We thank Professor Oswaldo Cox, University of Puerto Rico, Rio Piedras, for a generous gift of the benzo-1,2-cycloalkenes and Dr. Richard Dolinski of the Dow Chemical Company for the generous gift of the substituted styrenes.

Supplementary Material Available: Figures 3 and 7–9 (4 pages). Ordering information is given on any current masthead page.

Thiol–Olefin Cooxidation (TOCO) Reaction. 8. Solvent Effects in the Oxidation of Some Thiols with Molecular Oxygen

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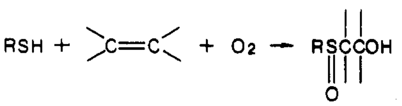
The rates of the noncatalytic oxidation of various thiols by molecular oxygen are a function of the chemical environment of the thiol. A relationship between the chemical shifts of the sulfhydryl proton and the rate of oxidation of the given thiol is demonstrated and discussed.

Introduction

In our search for a self-consistent mechanism of thiol–olefin cooxidation (TOCO) reaction[1–6] under conditions



that avoid the intentional formation of free radicals, we were led to question the suggested[7] initiation of the reaction through thiyl radicals generated by the interaction of thiols with molecular oxygen:

$$RSH + O_2 \rightarrow RS^{\bullet} + HOO^{\bullet}$$

This initiation of a free-radical chain reaction may indeed be valid when the TOCO reaction is catalyzed photochemically or by means of chemical radical initiators. Also, it may be valid during the later stages of a TOCO reaction in which the accumulation of hydroperoxides eventually can lead to a self-catalyzed, rapid, homolytic reaction.[8] However, at the early stage of the TOCO reaction carried out under conditions that avoid the intentional formation of thiyl radicals, the latter would have to arise from the reaction of thiols and molecular oxygen. Hence, it was of interest to investigate this reaction per se.

Results

The oxygen consumption in the noncatalyzed oxidation of *p*-chlorothiophenol to the disulfide by means of molecular oxygen in various solvents was observed to follow a pseudo-first-order rate law. The first-order rate constants obtained and corrected for solubility of oxygen in the given solvent are reported in Table I. Two distinct linear relationships could be obtained when these corrected rate constants were plotted against the reciprocal dielectric constants of the solvents (Figure 1). The pronounced effect of the dielectric constants on the rate of oxidation seen in slope A is produced by dipolar aprotic solvents and amines. The oxidation rates were relatively insensitive to the changes of the dielectric constants of the less polar solvents.

This relationship bears a remarkable similarity with the relationship of the chemical shift of a sulfhydryl proton with the reciprocal dielectric constant of the solvent.[9] The

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Table I. The Effect of Solvents on the Rate of Oxygen Consumption by *p*-Chlorothiophenol at 26 °C

no.		DC[a]	oxygen[b] solubility, M	$t_{1/2}$, h	10^5k_{exp}, s^{-1}	rel rate	10^4k_{corr}, s^{-1}	k_{rel}[c]
1	hexane	1.89	0.0261	18	1.06	2.0	4.1	1.0
2	CCl_4	2.24	0.0161	15	1.28	2.4	8.0	2.0
3	benzene	2.28	0.0146	22	0.87	1.6	5.6	1.4
4	toluene	2.38	0.0090	14	1.37	2.6	15.2	3.7
5	*o*-xylene	2.57	0.0124	11	1.75	3.3	14.1	3.4
6	ethyl ether	4.34	0.0130	14	1.38	2.6	10.6	2.6
7	chloroform	4.81	0.0144	15	1.28	2.4	8.9	2.2
8	chlorobenzene	5.62	0.0130	18	1.06	2.0	8.2	2.0
9	ethyl acetate	6.02	0.0114	16	1.20	2.3	10.5	2.6
10	pyridine	12.40	0.0074	1.4	13.60	25.7	183.8	44.8
11	isoamyl alcohol	14.70	0.0114	27	0.71	1.3	6.2	1.5
12	acetone	20.70	0.0149	10.5	1.83	3.5	12.2	3.0
13	ethanol	24.55	0.0100	23.0	0.84	1.6	8.4	2.0
14	methanol	32.70	0.0165	24.5	0.78	1.5	4.7	1.1
15	nitrobenzene	34.82	0.0053	36.0	0.53	1.0	10.0	2.4
16	Me_2SO	46.68	0.0024	4.0	4.81	9.1	200.4	48.9
17	paraffin oil		0.0080	60	0.32	0.6	7.5	1.8
18	tetralin	2.77	0.0066	42.0	0.46		7.0	1.7
19	*n*-BuOH	17.51	0.0024	40	0.80	1.5	33.3	6.1

no.		DC[a]	estimated[b] O_2 solubility M	$t_{1/2}$, h	10^5k_{exp}, s^{-1}	rel rate	10^4k_{corr}, s^{-1}	k_{rel}[c]
21	dioxane	2.21	0.0512	30.0	0.64	1.2	5.13	1.25
22	Et_3N	2.42	0.0595	1.67	11.60	21.9	79.95	19.5
23	mesitylene	2.57	0.0640	20.0	0.96	1.8	6.15	1.50
24	CS_2	2.64	0.0920	14.0	1.38	2.6	6.15	1.50
25	anisole	4.33	0.0800	16.0	1.20	2.3	8.20	2.00
26	THF	7.58	0.0660	13.0	1.48	2.8	9.23	2.25
27	CH_2Cl_2	8.93	0.0520	17.0	1.13	2.1	9.23	2.25
28	2,6-lutidine	12.40	0.0173	2.5	7.70	14.5	182.45	44.5
29	HMPA	30.00	0.0011	36.0	0.53	1.0	194.75	47.5
30	CH_3NO_2	35.87	0.0292	27.0	0.73	1.4	10.25	2.5
31	DMF	36.71	0.0038	10.5	1.83	3.5	196.80	48
32	CH_3CN	38.40	0.0020	20.0	0.96	1.8	198.03	48.3

[a] From the Eastman Organic Chemical Bulletin, 1975, Vol. 47, 1. [b] Estimated by assuming the 1/DC values fit the graph on the basis of compounds of known oxygen solubility listed in Table I. [c] Relative to the rate in hexane.

Table II. Solvent Effect of Substituted Benzenes on the Rate of Oxygen Consumption by Different Thiophenols at 26 ± 2 °C in Hexane

thiol (0.057 M)	cosolvent (0.104 M)	$t_{1/2}$, h	10^5k, s^{-1}	10^4k_{corr},[a] s^{-1}
p-ClC_6H_4SH	none	18	1.06	4.1
	toluene	30	0.64	2.5
	mesitylene	56	0.34	1.3
m-MeC_6H_4SH	none	22.5	0.85	3.3
	toluene	30.0	0.64	2.5
	mesitylene	32.0	0.60	2.3
C_6H_5SH	none	24.5	0.78	3.0
	toluene	27.0	0.71	2.7
	mesitylene	31.0	0.62	2.3
p-$MeOC_6H_4SH$	none	24.0	0.80	3.1
	toluene	30.0	0.64	2.5
	mesitylene	33.0	0.58	2.2
p-$O_2NC_6H_4SH$	none[b]	37.0	0.52	2.0

[a] Corrected for the solubility of oxygen in the solvent. [b] Mixture of ethyl acetate and hexane (1:6) by volume.

Table III. Effect of Thiol Structure on the Rate of Oxygen Consumption at 26 ± 2 °C in Pyridine

no.	thiol (0.057 M)	$t_{1/2}$, min	10^5k, s^{-1}	10^4k_{corr},[b] s^{-1}
1	*p*-$O_2NC_6H_4SH$	60	19.3	260.8
2	*m*-$CF_3C_6H_4SH$	240	4.8	64.9
3	*p*-ClC_6H_4SH	85	13.6	183.8
4	*p*-$MeOC_6H_4SH$	165	7.0	94.6
5	*p*-FC_6H_4SH	85	13.6	183.6
6	*p*-*t*-BuC_6H_4SH	97	11.9	160.8
7	*m*-MeC_6H_4SH	75	15.4	208.1
8	C_6H_5SH	120	9.6	130.2
9	*p*-$H_2NC_6H_4SH$	280	4.1	55.7
10	*p*-$MeOC_6H_4SH$[a]	45[a]	25.7[a]	347.3[a]
11	*m*-$CF_3C_6H_4SH$[a]	64[a]	18.1[a]	243.0[a]
12	*p*-$O_2NC_6H_4SH$[a]	65[a]	17.8[a]	240.5[a]
13	*t*-BuC_6H_4SH[a]	47[a]	24.6[a]	332.4[a]
14	*m*-MeC_6H_4SH[a]	48[a]	24.1[a]	325.1[a]
15	C_6H_5SH[a]	60[a]	19.3[a]	260.8[a]
16	*p*-FC_6H_4SH[a]	50[a]	23.1[a]	312.2[a]
17	*p*-ClC_6H_4SH[a]	50[a]	23.1[a]	312.2[a]

[a] In the presence of 2 equiv of water the basis of the thiol. [b] Corrected for solubility of oxygen in pyridine.

Table IV. Effect of Thiol Concentration on the Rate of Oxygen Consumption in the Conversion of *p*-Chlorothiophenol to the Corresponding Disulfide in Hexane at 26 °C

no.	thiol, M	$t_{1/2}$, h	10^5k, s^{-1}	10^4k_{corr},[a] s^{-1}
1	0.057	18.0	1.06	4.1
2	0.057[b]	25.0	0.78	3.0
3	0.570	15.5	1.24	4.8
4	0.114	13.5	1.44	5.5

[a] Corrected for the solubility of oxygen in hexane. [b] In the presence of 1 equiv of 30% hydrogen peroxide.

coincidence of these two relationships is demonstrated by the plot of the log of the corrected rate constants of the oxidation of *p*-chlorothiophenol against the chemical shift of the sulfhydryl proton in the same solvent (Figure 2).

The rate of oxygen consumption by various thiophenols was lower in the presence of small amounts of substituted benzenes as compared to the rate in pure hexane (Table II). The first-order rate constants gave a linear Hammett relationship (Figure 3) with a positive ρ value in hexane, they were independent of substituents in the presence of 2 equiv of toluene, and they gave a positive ρ value in the presence of 2 equiv of mesitylene. Surprisingly, the oxidation of various substituted thiophenols in pyridine gave a nonlinear Hammett relationship (Figure 3). However,

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(9) D'Souza, V. T.; Nanjundiah, R., Baeza, H. J.; Szmant, H. H. *J. Org.* Chem., following paper in this issue.

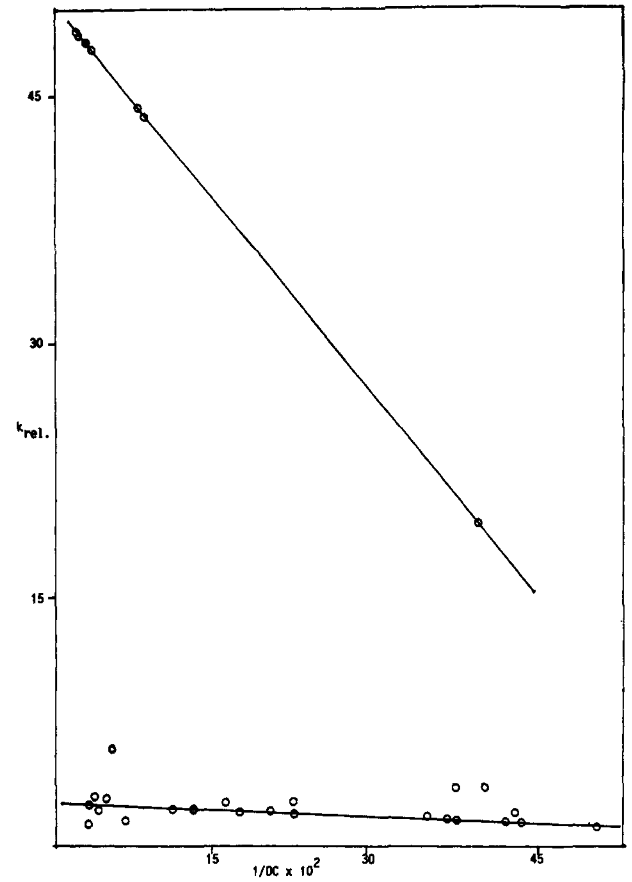

Figure 1. Solvent effects on the relative rates of oxidation of *p*-chlorothiophenol by molecular oxygen at 25 °C.

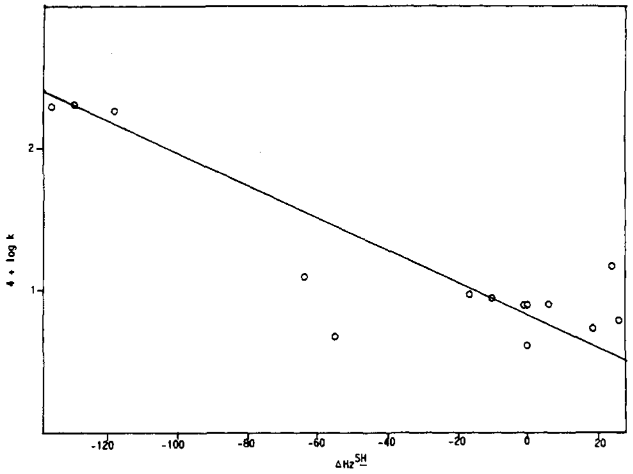

Figure 2. Plot of ΔHz^{SH} vs. log *k* of oxidation of *p*-chlorothiophenol by molecular oxygen in various solvents.

a linear Hammett relationship (E in Figure 3) was obtained when 2 equiv of water were added to the pyridine solutions of the thiols (Table III).

The results in Table IV show that the rate of oxygen consumption in the conversion of *p*-chlorothiophenol to

$$2\ RSH + {}^1/_2\ O_2 \rightarrow RSSR + H_2O$$

the corresponding disulfide is essentially independent of the initial concentration of the thiol, and, interestingly enough, it is not aided by the presence of hydrogen peroxide.

Discussion

The oxidation of thiols are known to have first-power dependence in oxygen and for the initial 20–30% of the reaction first-power dependence in thiols.[10] Thus, the rate of oxygen consumption in the oxidation of thiols to disulfide by molecular oxygen can be expected to follow the rate law

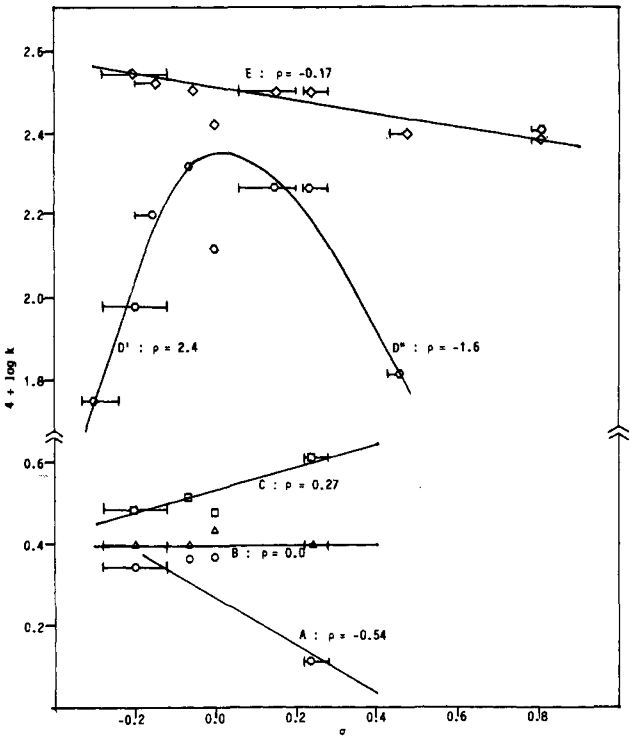

Figure 3. Hammett plots for the oxidation of substituted thiophenols at 25 °C under various solvation conditions: (A) hexane + mesitylene, (B) hexane + toluene, (C) hexane, (D) pyridine, (E) pyridine + H_2O.

$$R = \frac{-dO_2}{dt} = k[O_2][RSH]$$

In the presence of an excess of oxygen, and assuming a sufficiently high rate of diffusion, it follows that

$$R = \frac{-dO_2}{dt} = k_{exp}[RSH]$$

where $k_{exp} = k[O_2]$. Thus, the experimental rate constants must be corrected for the oxygen solubility in the given solvent in order to obtain a better correlation with the reciprocal of dielectric constant of the series of solvents.

The remarkable similarity between the solvent effects in the oxidation of *p*-chlorothiophenol under discussion and the response of the chemical shift of its sulfhydryl proton[9] to the same series of solvents (Figure 2) reveals that analogous solvation phenomena are involved in both cases. Thus, a scheme of solute–solvent interactions similar to the one proposed previously[9] can also be invoked for the oxidation of thiols.

Nonspecific solute–solvent interactions represented by A are expected to occur in the case of such inert solvents as hexane, but the small, positive *ρ* (C in Figure 3) indicates

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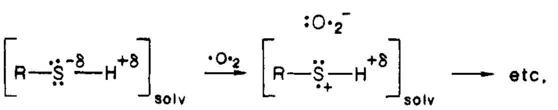
[10] Capozzi, G.; Modena, G. *The Chemistry of Thiol Group*; *Patai, S., Ed.*; John Wiley and Sons: New York, 1974; p 806.

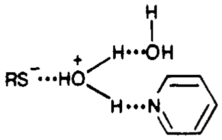
that the substituent-induced polarization of the thiol favors oxidation.



The chemical shift[9] results caused by aromatic solvents suggest that the predominant solvation is best represented by a donor–acceptor complex shown as B, and this is borne out by the decreased rates of oxidation when 2 equiv of an aromatic solvent are added to the hexane solution of the different thiols. In this interaction the thiol acts as an acceptor and the effect is more noticeable in the case of mesitylene as compared to toluene because of the greater donor ability of the former. The solvation by mesitylene seems to decrease the intrinsic polarity of the thiol function while the toluene causes merely a leveling effect in the acidity of all thiols involved in these comparisons.

Weakly hydrogen-bonding solvents of relatively low dielectric constants (chloroform, carbon tetrachloride, etc.) are expected to give rise to complexes represented by C, and here too, the rates of oxidation should be a function of the relative, substituent-induced polarization, i.e., the relative acidity of the thiol function. However, in the case of strongly hydrogen-bonding solvents of relatively high dielectric constants such as those that follow slope A in Figure 1 (DMF, Me_2SO, etc.), the hydrogen-bonded complex D must be in equilibrium with the solvent-separated, or even further ionized, complex E. The thiolate anion, of course, is subject to facile electron loss to the incoming oxygen molecule. This continuum of hydrogen-bonded interactions represented by C, D, and E is nicely illustrated with the case of pyridine.

The low dielectric constant of pyridine causes little dissociation of its hydrogen-bonded complex with thiol and the nonlinear Hammett plot (D in Figure 3) can be thought to result from an interplay of an increasing polarization of the hydrogen-bonded thiol function, on one hand ($\rho = +2.4$ in the D′ portion of the graph), and the increasing delocalization of the electron density away from the sulfur moiety ($\rho = -1.6$ in the D″ portion of the graph), on the other hand. The presence of 2 equiv of water caused a remarkable linearity (E in Figure 3) of the Hammett plot and the negative ρ value (−0.17) indicates that the unfavorable delocalization of the electron density away from the sulfur moiety still dominates the electron transfer to oxygen in the complex. It is noteworthy that the oxidation of *p*-nitrothiophenol is not subject to the effect of the presence of water in the pyridine solution: apparently the strong electron-withdrawing nature of the nitro group is sufficient to give the delocalized *p*-nitrothiophenolate ion without the cooperation of water.



The results reported in Table IV suggest either an absence of an intermolecular association of *p*-chlorothiophenol molecules or an insignificant effect of such association on the rate of oxidation.

Experimental Section

Materials. *p*-Chlorothiophenol (Aldrich Chemical Co.) was recrystallized from aqueous ethanol, mp 51–52 °C. *m*-Thiocresol, *p*-methoxythiophenol, thiophenol, and *p*-*tert*-butylthiophenol (Aldrich Chemical Co.) were purified by vacuum distillation. *p*-Fluorothiophenol (Pfaltz and Bauer) and *p*-nitrothiophenol (Aldrich Chemical Co.) were used without further purification. *m*-(Trifluoromethyl)thiophenol was synthesized by means of the reaction of the diazonium salt of *m*-(trifluoromethyl)aniline with ethyl xanthate. The latter was freshly prepared by heating ethanol and KOH with CS_2. The product was characterized by ^1H NMR and refractive index ($n^{22}_D = 1.4871$, lit.[11], $n^{25}_D = 1.4872$).

Kinetic Experiments. The thiophenol of interest was dissolved in 35 mL of hexane and the reaction flask was thermostated at 26 ± 2 °C. The reaction flask was also connected to a gas buret filled with oxygen as described elsewhere.[8] The rates of oxygen consumption in the oxidation of the thiols followed the pseudo-first-order rate law and the rate constants were determined from the observed half-lives ($t_{1/2} = \ln 2/k$). The solvents were removed under diminished pressure, and the resulting oil was dissolved in dichloromethane, washed first with 10% sodium hydroxide and then with water, and finally dried over anhydrous sodium sulfate. The product obtained on evaporation of dichloromethane was found to be identical with the authentic samples of the corresponding disulfides. No other products were detected by TLC.

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[11] Stacy, C. N.; Berson, C. R. *J. Org. Chem.* **1959**, *24*, 1892.