Thiol-Olefin Cooxidation (TOCO) Reaction. 10. Phenyl Allyl Ether and *p*-Chlorothiophenol

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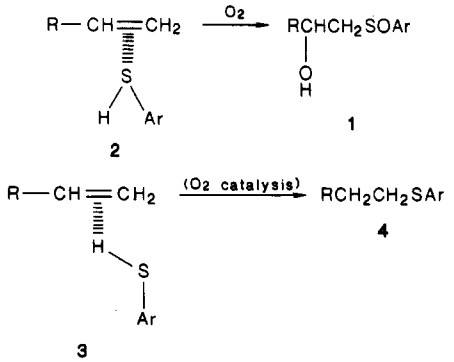
The TOCO reaction of a hexane solution of phenyl allyl ether and *p*-chlorothiophenol was investigated under photochemical and thermal activation conditions and over a temperature range of −23 to +25 °C. The formation of the desired TOCO product, the thiol–olefin anti-Markovnikov adduct, and *p*-bis(chlorophenyl) sulfide was found to vary both as a function of temperature and of the activating conditions. The equilibrium constants for the formation of the thiol–olefin complexes were determined in the case of phenyl allyl ether and the analogous 4-phenyl-1-butene as well as 1-octene, norbornene, and 1-phenylbutane in order to elucidate the nature of these associations.

Introduction

In view of our long-standing interest in the TOCO reaction, and the recently proposed reaction mechanism under nonradical-inducing conditions.[1e] it was desirable to expand the study of this fascinating reaction to an allyl ether and thus phenyl allyl ether and *p*-chlorothiophenol were chosen as the model system. The thiol–olefin cooxidation reaction can give rise to three major products: the β-hydroxy sulfoxide or TOCO products, the thiol–olefin anti-Markovnikov adduct, and the oxidation product of thiol to the corresponding disulfide. The distribution of these competitive products was determined by careful chromatographic separations and was found to vary significantly as a function of temperature (−23, 2.5, and 25 °C) and activating conditions. Since the competitive reaction paths are believed[1] to depend on the nature of thiol–olefin complexes, it was desirable to measure the association constants[1e] of the above-mentioned reactants and, for comparison, also of some related systems.

Results and Discussion

The mechanistic rationale[1a] evolved on the basis of a variety of experimental approaches, is that under nonradical-inducing and relatively high temperature conditions, the TOCO products 1 arise from a charge-transfer complex (2), formed between the olefinic π-system and the thiol acceptor, while the formation of the hydrogen-bonded complex 3 leads to the formation of thiol–olefin adduct 4.



The third major product of the TOCO reaction, namely, the disulfide derived from the thiol, is believed to be formed[1d] either very slowly, from the reaction of the "free" solvated thiol with molecular oxygen, or more rapidly, by the dissociation of a thiyl radical from a thiyl–olefin complex. Thus, since the product distribution under nonphotochemically induced thiol–olefin cooxidation reaction conditions is thought to depend heavily on the presence of the associated thiol–olefin precursors, it is advisable to discuss first the results of the NMR study (Figure 1). These shed some light on the nature and stability of the predominant complexes formed in a relatively inert

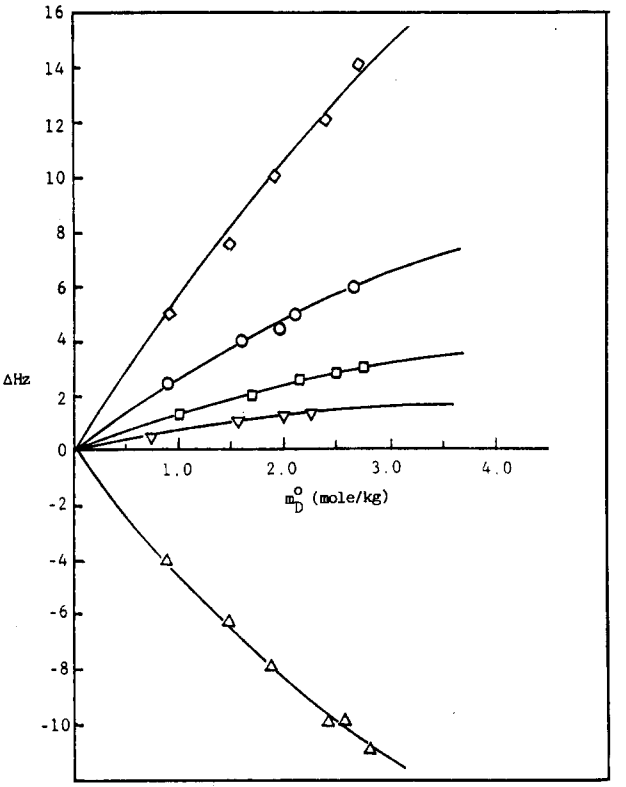


Figure 1. Plots of ΔHz vs. m^0_D (where m^0_D is the total molal concentration of the donor) for sulfhydryl proton chemical shifts in the complex of *p*-chlorothiophenol with various donors: 1-phenylbutane (◇); 4-phenyl-1-butene (○); phenyl allyl ether (□); norbornene (▽); 1-octene, (△) (see Table I).

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(1) For preceding recent papers in this series and related topics, see: (a) Szmant, H. H.; Mata, A. J.; Namis, A. J.; Panthananikal, A. M. *Tetrahedron* **1976**, *32*, 2665. (b) Szmant, H. H.; Baeza H., J. *J. Org. Chem.* **1978**, *43*, 1835. (c) D'Souza, V. T.; Nanjundiah, R.; Baeza, H., J.; Szmant, H. H. *J. Org. Chem.*, first paper in a series of four in this issue. (d) D'Souza, V. T.; Iyer, V. K.; Szmant, H. H. *J. Org. Chem.*, second paper in a series of four in this issue. (e) D'Souza, V. T.; Nanjundiah, R.; Baeza H., J.; Szmant, H. H. *J. Org. Chem.*, previous paper in this issue.

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Table I. Change in the Sulfhydryl Proton Chemical Shift (ΔHz) of *p*-Chlorothiophenol in the Presence of Various Olefins and the Equilibrium Constants ($K^{AD}_{complex}$) for the Formation of Thiol-Olefin Complexes[a,b]

no.	olefin	m^0_D[olefin][c]	ΔHz[d]	$1/m^0_D$	1/ΔHz	$K^{AD}_{complex}$, kg mol^{-1}	corr for 1/ΔHz vs. $1/m^0_D$
1	4-phenyl-1-butene	0.94	2.5	1.06	0.40		
		1.54	4.0	0.65	0.25		
		1.95	4.5	0.51	0.22	0.1349	0.9974
		2.12	5.0	0.47	0.20		
		2.67	6.0	0.37	0.17		
2	norbornene	0.75	0.5	1.33	2.00		
		1.56	1.0	0.64	1.00	0.0937	0.9993
		1.99	1.2	0.50	0.83		
		2.25	1.3	0.44	0.77		
3	phenyl allyl ether	1.03	1.3	0.97	0.78		
		1.69	2.0	0.59	0.50		
		2.15	2.5	0.46	0.40	0.0855	0.9999
		2.48	2.8	0.40	0.36		
		2.74	3.0	0.36	0.33		
4	1-octene	0.90	−4.0	1.11	−0.25		
		1.46	−6.3	0.68	−0.16		
		1.86	−8.0	0.54	−0.125	0.0606	−0.9990
		2.40	−10.0	0.42	−0.10		
		2.55	−10.0	0.39	−0.10		
		2.80	−11.0	0.36	−0.09		
5	1-phenylbutane	0.90	5.0	1.11	0.20		
		1.48	7.5	0.67	0.13		
		1.88	10.0	0.53	0.10	0.0306	0.9982
		2.40	12.0	0.42	0.08		
		2.72	14.0	0.37	0.07		
		2.84	15.5	0.35	0.065		

[a] 25 °C, in Freon-TF. [b] Initial molal concentration of *p*-chlorothiophenol in Freon-TF was 0.19 *m*. [c] m^0_D is the molal concentration of the donor (olefin). [d] Change in sulfhydryl proton chemical shift (ΔHz) of the complex relative to that of *p*-chlorothiophenol in Freon-TF at 25 °C. Upfield chemical shift is shown as +ΔHz.

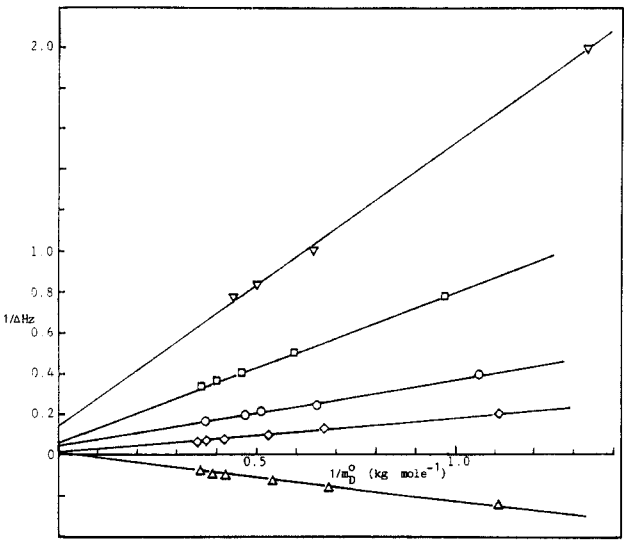
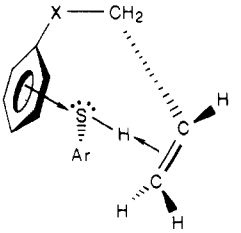


Figure 2. Plots of $1/\Delta Hz$ vs. $1/m^0_D$ for the formation of complexes between *p*-chlorothiophenol and various donors: norbornene (▽); phenyl allyl ether (□); 4-phenyl-1-butene (○); 1-phenylbutane (◇); 1-octene (△) (see Figure 1).

1,1,2-trichloro-1,2,2-trifluoroethane (Freon TF) solvent (Figure 2).

The results summarized in Table I show that, of the five electron donors investigated here, only 1-octene causes downfield chemical shifts of the thiyl proton of *p*-chlorothiophenol used throughout this study. This result is in line with the hydrogen bonding (3) expected of such a simple olefin, its reluctance to give a TOCO reaction (under nonphotochemically induced reaction conditions), and the formation of the anti-Markovnikov adduct when the reaction is catalyzed by means of oxygen or radiation. Also, the formation of a weak charge-transfer complex analogous to **2** between the π-system of 1-phenylbutane and the thiol is not unexpected in view of the similar ^{1}H NMR results reported elsewhere.[1c] The π electrons of the strained norbornene ring system can be seen to give rise to a stronger charge-transfer complex than those of 1-octene, and this, too, is not surprising because of the preferential TOCO reactivity[2] of the more strained double bond in either *exo*- or *endo*-dicyclopentadiene. Of special relevance to our primary interest in the TOCO reaction of phenyl allyl ether is the observation that 4-phenyl-1-butene forms a stronger charge-transfer complex with *p*-chlorothiophenol than the allyl ether ($K^{AD}_{complex}$, 13.5×10^{-2} vs. 8.5×10^{-2} kg mol^{-1}) and also that the former causes larger upfield chemical shift of the thiyl proton than the latter. These results suggest that while 4-phenyl-1-butene may engage the thiol in doubly associated complex **5a**, the replacement of the α-methylene group by an oxygen function creates a weakening of the association most likely due to repulsions between the nonbonded electrons of the oxygen and sulfur moieties in **5b**.



5a, X = CH_2
b, X = O

Another reason for the observed spectral difference between 4-phenyl-1-butene and phenyl allyl ether could be the competitive hydrogen bonding between the thiol and the oxygen function in the case of the ether. Thus, on the basis of these observations it appears that phenyl allyl ether forms a relatively weak charge-transfer complex

(2) Szmant, H. H.; Veas, C. T. manuscript in preparation.

Table II. Summary of Product Distribution for the TOCO Reaction in the Presence of an Excess of Oxygen[a,b]

expt no.	reactants: $XYCH_2CH=CH_2$ X	Y	thiol or disulfide	reactn temp,[e] °C	$h\nu$	reactn time	% convn[c]	product distribution,[d] %: TOCO product	addn product	disulfide
1	C_6H_5	O	*p*-ClC_6H_4SH	rt	no	5 days	83 ± 4	60	31	9
2	C_6H_5	O	*p*-ClC_6H_4SH	−23	no	5 days	7 ± 2	27	59	14
3	C_6H_5	O	*p*-ClC_6H_4SH	rt	yes	5 h	92 ± 2	55	12	33
4	C_6H_5	O	*p*-ClC_6H_4SH	2.5	yes	5 h	68 ± 2	85	13	2
5	C_6H_5	O	*p*-ClC_6H_4SH	−23	yes	5 h	20 ± 2	45	51	4
6	C_6H_5	$-CH_2-$	*p*-ClC_6H_4SH	rt	no	5 days	50 ± 2	17	67	16
7	C_6H_5	O	$(p\text{-}ClC_6H_4S)_2$	rt	yes	5 h	61 ± 3	2	57	41
8	C_6H_5	O	$(p\text{-}ClC_6H_4S)_2$	rt	yes	15 h	68 ± 2	9	59	32
9	C_6H_5	O	$(p\text{-}ClC_6H_4S)_2$	rt	yes	24 h	83 ± 2	26	57	17

[a] Equimolar concentrations (0.01 *m*) of olefin and thiol (or disulfide) in hexane. [b] Results reported are averages of two to four experiments. [c] Based on the conversion of initial thiol to the isolated products, i.e., 0.01 mol of thiol − (mol TOCO + mol adduct + 2 mol disulfide). [d] Percentage distribution of the three major isolated products. [e] rt = room temperature.

with the thiol in competition with hydrogen-bonded complexes involving either the ethereal and/or the olefinic functions.

The last mentioned conclusion explains the product distribution obtained in the cooxidation of phenyl allyl ether at room temperature in the absence of photochemical activation (expt 1 in Table II). We note that there is produced an approximately 2:1 ratio of TOCO product to anti-Markovnikov adduct, presumably reflecting the presence, in solution, of an excess of the charge-transfer complex precursor.

As the temperature is lowered to −23 °C, we observed an inversion in the TOCO products/anti-Markovnikov adducts ratio (expt 2 in Table II) in accord with the previously arrived[1a,c] general conclusion that lower temperatures favor the thiol–olefin adduct formation. Under identical experimental conditions, the reaction of 4-phenyl-1-butene gives a significantly higher yield of the anti-Markovnikov adduct than phenyl allyl ether (expt 1 and 6 in Table II). This difference in product distribution suggests that the doubly associated complex **5a** promotes the pathway dependent on hydrogen bonding that is not favored normally at room temperature. The lower extent of reaction of **5a** as compared to **5b** can be related to a higher activation energy requirement in the stronger, doubly associated complex.

The use of black light to catalyze the TOCO reaction accelerates it by generating thiyl radicals through the direct scission of the thiyl function. Thus, understandably, the reaction at room temperature (expt 3) produces a relatively high yield of diaryl disulfide and this yield decreases markedly as the reaction temperature is lowered to 2.5 or to −23 °C (expt 4 and 5). However, the distribution of the remaining products at these lower temperatures suggests that the thiyl radical is not generated by photolysis of "free" thiol but rather by photolysis of a complexed thiol. As the reaction temperature is lowered to 2.5 °C, the more stable charge-transfer complex **2** is photolyzed to give an increased yield of TOCO product with a correspondingly smaller yield of disulfide. However, as the reaction temperature is further lowered to −23 °C, the photolysis seems to occur in the hydrogen-bonded complex, the stability of which, as stated above, is favored at lower temperatures. This explains the increased yield of the thiol–olefin adduct at the expense of the yield of TOCO products.

In view of the formation of bis(*p*-chlorophenyl) disulfide and the possibility that the latter is dissociated photochemically to thiyl radicals, it was of interest to examine the product distribution when a mixture of phenyl allyl ether and disulfide was irradiated in the presence of oxygen over an extended period of time (expt 7–9). The rather constant yield (58 ± 1%) of the anti-Markovnikov adduct suggests that the formation and photochemical dissociation of the adduct reach an equilibrium. On the other hand, the TOCO products are apparently immune to photochemical dissociation under the conditions employed in this work. Hence, we observe a gradual accumulation of TOCO products as the disulfide is consumed. The formation of the anti-Markovnikov adduct apparently involves the abstraction of hydrogen atoms from the allyl ether and/or the solvent.

In conclusion, the TOCO behavior of phenyl allyl ether and that of the analogous 4-phenyl-1-butene are consistent with those of the olefins studied previously.

Experimental Section

Materials. *p*-Chlorothiophenol (Aldrich Chemical Co.) was recrystallized from aqueous ethanol, mp 51–52 °C. Bis(*p*-chlorophenyl) sulfide was an authentic sample prepared previously[1a,b] in this laboratory. All the other materials used were reagent grade and used without further purification unless mentioned otherwise. Norbornene (99%, mp 44–46 °C), 1-octene (97%, bp 122–123 °C), 4-phenyl-1-butene (bp 177–178 °C), 1-phenylbutane (99+%, bp 183 °C), and phenyl allyl ether (96%, bp 192 °C) were purchased from Aldrich Chemical Company. Freon TF (1,1,2-trichloro-1,2,2-trifluoroethane) was purchased from E. I. du Pont de Nemours & Company.

Visualization Methods of TLC Spots. The most commonly used visualization reagent was 1% (w/v) ceric sulfate [$Ce(SO_4)_4$] solution in a dilute sulfuric acid. TLC plates were sprayed by this reagent and heated for 3–5 min at 150–160 °C. All TLC spots, in our studies, were visualized by this method unless mentioned otherwise. The procedure for the preparation of this reagent is as follows: 8 g of ceric sulfate was dissolved in the mixture of 190 mL of concentrated sulfuric acid and 650 mL of water.

Cooxidation of Equimolar Amounts of *p*-Chlorothiophenol and Olefin in the Presence of Excess Oxygen. The TOCO reactions were studied at several temperatures under thermal and photochemical activation conditions. The general procedures are described as follows.

(a) Under Nonphotochemical Activation. The desired olefin (0.01 mol), phenyl allyl ether or 4-phenyl-1-butene, and 0.01 mol (1.45 g) of *p*-chlorothiophenol were dissolved in separate 100-mL portions of hexane. The two solutions were mixed and maintained at room temperature. The reaction at −23 °C was done by using a refrigerated reactor equipped with automatic temperature control. Oxygen was bubbled continuously through the reaction mixture. The thiol content monitored by TLC nearly disappeared after 5 days and the reaction mixture was warmed for 5 min at 50–60 °C and then cooled to room temperature. After the reaction mixture was cooled, the white precipitate was filtered, crystallized from a mixture of hexane/toluene (1:1), mp 86–87 °C, 1.4149 g (4.55×10^{-3} mol, 60% of isolated products), gave a single spot in TLC [R_f 0.06, toluene/ethyl acetate (75:25)] and was identified as a thiol–olefin cooxidation product by IR (Figure 3),[3] NMR

(Figure 4),[3] and elemental analysis. The IR spectra taken in Nujol showed stretching frequencies at 3320 cm^{-1} (OH), 1055 (S=O), 1095 (CO), and 1600 for aromatic C=C.

1H NMR ($CDCl_3/Me_4Si$) (ppm): 3.10 (SCH_2, d, 2, J = 6.0 Hz), 3.83 (OCH_2, d, 2, J = 4.0 Hz), 4.17 (OH, s, 1), 4.50 (OCH, quintet, 1, J = 3.0 Hz), 7.18 (aromatic H, complex multiplet, 9).

Anal. Calcd for $C_{15}H_{15}O_3SCl$: C, 57.97; H, 4.86; S, 10.32; Cl, 11.41. Found: C, 58.01; H, 4.72; S, 10.46; Cl, 11.26.

After filtering the cooxidation product, the unreacted thiol was removed from the reaction mixture by washing first with 10% aqueous sodium hydroxide solution and then with water. The hexane layer was separated and dried over anhydrous sodium sulfate. Solvent and unreacted olefin were removed under reduced pressure by means of a rotatory evaporator leaving 0.8640 g of yellowish oily mixture. This oily mixture gave two spots in TLC [R_f values, 0.85 and 0.46, toluene/ethyl acetate (75:25)] corresponding to the disulfide and thiol–olefin addition product, respectively. The mixture was separated by column chromatography. Silica gel (J. T. Baker's, 60–200 mesh) was activated overnight at 110 °C and 100 g was packed in a 1 in. × 5 ft column. A homogeneous mixture of 0.8640 g of the product mixture was introduced into the column. The column was first eluted with 1 L of hexane followed by 1 L of toluene then with 750 mL of ethyl acetate. The eleven fractions of approximately 250 mL were collected without interruptions. The fractions were evaporated and individually analyzed by TLC, and the residues of the appropriate beakers were combined and weighed. Typical separations and TLC analyses are given in Table III[3] (expt 1 in Table II), Table IV[3] (expt 2 in Table II), and Table V[3] (expt 6 in Table II). As shown in Table III[3], fractions 1–3 gave 0.2000 g (0.69×10^{-3} mol, 9% of isolated products) of disulfide identified by comparison of its NMR spectrum (Figure 5)[3] with that of an authentic sample. Fractions 6–9 gave 0.6551 g (31% of isolated products) of yellow oil identified by NMR spectra (Figure 6)[3] as the thiol–olefin addition product.

^1H NMR ($CDCl_3/Me_4Si$) (ppm): 1.22 (CCH_2C, quintet, 2, J = 2.0 Hz), 3.20 (SCH_2, t, 2, J = 3.0 Hz), 4.03 (OCH_2, t, 2, J = 2.0 Hz), 7.20 (aromatic H, m, 9).

For the reaction at −23 °C, the reaction mixture was quenched by addition of 100 mL of 10% solution of sodium thiosulfate in order to convert the hydroperoxides to the corresponding alcohols. The hexane layer was separated from the thiosulfate solution and worked up as described above to give 0.1820 g of yellowish oily product mixture that was separated by column chromatography (see Table IV[3] for details).

The distribution of the three major products of the TOCO reaction is summarized in Table II.

(b) Under Photochemical Activation. The desired sulfur compound (0.01 mol), *p*-chlorothiophenol or *p*-chlorophenyl disulfide, and 0.01 mol (1.34 g) of phenyl allyl ether were dissolved in separate 100-mL portions of hexane. The two solutions were mixed and maintained at room temperature. The reactions at 2.5 °C and at −23 °C were carried out in a refrigerated reactor equipped with automatic temperature control. The reaction mixture was introduced into a 2.5 × 12 in. glass tube equipped with a thermometer and an oxygen inlet. The glass tube was irradiated with black light from four individually controlled cylindrical PCQ-X1 lamps while oxygen was bubbled continuously through the reaction mixture. The thiol content of the reaction mixture was monitored by TLC and was found to be nearly totally consumed after 5 h. The reaction mixture was warmed for 5 min at 50–60 °C and then cooled to room temperature. The unreacted thiol was removed from the reaction mixture by washing first with 10% aqueous sodium hydroxide solution and then with water. The hexane layer was dried over anhydrous sodium sulfate. Solvent and unreacted olefin were removed under reduced pressure by means of a rotatory evaporator, leaving 2.10 g of yellowish oil. The oily mixture was dissolved in hot toluene and crystallization was induced by cooling and scratching the wall of the beaker in an ice bath. The crystals were filtered, recrystallized from toluene, and dried to give 1.19 g (3.83×10^{-3} mol, 55% of the thiol–olefin cooxidation product): mp 86.0–87.0 °C; the same NMR spectrum as Figure 4;[3] a single spot in TLC [R_f 0.06, toluene/ethyl acetate (75/25)].

Anal. Calcd for $C_{15}H_{15}O_3SCl$: C, 57.97; H, 4.86; S, 10.32; Cl, 11.41. Found: C, 57.75; H, 4.78; S, 10.27; Cl, 11.56.

The filtrate from the isolation of the TOCO product was concentrated under reduced pressure by means of a rotatory evaporator to give 0.8928 g of yellow oil. This mixture gave two spots [R_f values, 0.85 and 0.46, toluene/ethyl acetate (75:25)] in TLC that correspond to the disulfide and thiol–olefin addition product. The mixture, 0.8928 g, was separated by column chromatography using 100 g of silica gel, 1 in. × 3 ft column, by means of the same separation procedure as described for the reaction under nonphotochemical activation. Typical results and TLC analyses are shown in Table VI[3] (expt 3 in Table II), Table VII[3] (expt 5 in Table II), and Table VIII[3] (expt 7 in Table II). As shown in Table VI[3], fractions 1–4 gave 0.6580 g (2.29×10^{-3} mol, 33% of isolated products) of disulfide and fractions 6–10 gave 0.2311 g (8.29×10^{-4} mol, 12% of isolated products) of thiol–olefin addition product.

In the case of reactions carried out at 2.5 °C and −23 °C the reaction mixture was quenched by addition of 100 mL of a 10% solution of sodium thiosulfate and the rest of the workup procedure was the same as that described above.

The summary of the distribution of the three major products in the TOCO reaction is presented in Table II.

Determination of Thiol–Olefin Complex Formation by Means of ^1H NMR. The chemical shifts reported in Table I were determined by means of a Varian EM 360 spectrometer. A dilute solution (0.19 m or 0.3 M) of *p*-chlorothiophenol was used in order to avoid self-association. A solution of *p*-chlorothiophenol (0.19 m) in Freon TF was placed in a 5-mm o.d. NMR tube. The tube was flushed with nitrogen and fitted with a rubber stopper, 0.01 mL of tetramethyl silane was injected followed by known volumes of olefin, and the spectra were recorded as soon as possible after each injection. The addition of olefin was continued until no change in the chemical shift of the sulfhydryl proton was observed. The chemical shifts as a function of olefin concentration (Figure 1) are summarized in Table I together with the manipulation of the data in order to arrive at the association constants as described in the literature.[4,5] The corresponding plot of the reciprocals of chemical shifts as a function of the reciprocals of donor concentrations is shown in Figure 2. The error limit in $K^{AD}_{complex}$ is ±1%.

Acknowledgment. We thank M-H-W Laboratories, Phoenix, AZ, for microanalyses reported in this work.

Registry No. Phenyl allyl ether, 1746-13-0; *p*-chlorothiophenol, 106-54-7; 4-phenyl-1-butene, 768-56-9; norbornene, 498-66-8; 1-octene, 111-66-0; 1-phenylbutane, 104-51-8; *p*-chlorophenyl disulfide, 1142-19-4.

Supplementary Material Available: Figures 3–6 and Tables III–VIII (10 pages). Ordering information is given on any current masthead page.

(3) See paragraph at the end of paper about supplementary material.

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