water was added and the organic layer was dried ($MgSO_4$). Evaporation of the ether and distillation of the residue at 15 Torr gave 1.5 g of material, bp 70–74°, that was further purified by preparative glpc on a QX-1 column at 110°; nmr (CCl_4) δ 0.93 (s, 6), 1.05 (s, 6), 5 9 (d, 1, J = 10 Hz), 7.4 (d, 1, J = 10 Hz).

Anal. Calcd for $C_9H_{14}O$: C, 78.12; H, 10.14. Found: C, 78.11; H, 10.30.

4,4,6,6-Tetramethylcyclohexenone (2) was prepared by the bromination-dehydrobromination of 2,2,4,4-tetramethylcyclohexanone[42] and by the methylation of 4,4-dimethylcyclohexenone.[30] The enone (5 g) was refluxed in 100 ml of ether with 3 equiv wt of $NaNH_2$ for 1 hr. Methyl iodide (3 equiv wt) was then added and the mixture refluxed for 24 hr. After cooling, 50 ml of water was added and the organic layer was dried ($MgSO_4$). Distillation at 15 Torr gave 1 g of product, bp 82–84°, which was purified by glpc on a QX-1 column at 110°; pmr (CCl_4) δ 1.17 (s, 6), 1.24 (s, 6), 1.7 (s, 2), 5.7 (d, 1, J = 10 Hz), 6.6 (d, 1, J = 10 Hz).

Anal. Calcd for $C_{10}H_{16}O$: C, 78.95; H, 10.52. Found: C, 79.13; H, 10.60.

The use of trideuteriomethyl iodide (99%, Merck Sharp and Dohme of Canada, Ltd.) gave **2** with trideuteriomethyl groups at C-6. By pmr the isotopic purity was >97%.

2,3-Benzo-5,5-dimethylcyclopentenone (1b)[43] was prepared by the methylation of 1-indanone (Eastman Organic Chemicals) by treatment with $NaNH_2$ followed by methyl iodide; pmr (CCl_4) δ 1.2 (s, 6), 2.9 (s, 2), 7.2–7.7 (m, 4).

Bicyclo[3.1.0]hex-3-en-2-one was prepared by the methylation of cyclopentenone by trimethylsulfoxonium ylide to yield bicyclo-[3.1.0]hexan-2-one in 70% yield. The bicyclic ketone (2 g) in 25 ml of ethylene glycol was treated with 3.4 g of bromine at 0°. After a few minutes the mixture was poured into a mixture of 7 g of Na_2CO_3 in 50 ml of pentane. The pentane layer was dried (Na_2SO_4) and evaporated to yield an oil which was added to 3.5 g of sodium methoxide in 45 ml of DMSO at <30°. The mixture was stirred for 20 hr at 25° before the addition of 200 ml of water. The mixture was extracted five times with 50 ml of pentane and the pentane extracts were dried (Na_2SO_4). Distillation at 28 Torr gave 2 ml of the ethylene ketal of bicyclo[3.1.0]hex-3-en-2-one, bp 89–95°. The ketal was shaken with 3 ml of 3% sulfuric acid for 10 min. The acid solution was extracted with ether and the dried ether solution evaporated to yield the enone which was purified by glpc on a 6-ft 20% DEGS on 60–80 Chromosorb W column at 140° (retention time, 8 min). The 100 mg of the enone collected had the following pmr spectral data: (CCl_4) δ 1.2 (m, 1), 1.5 (m, 1), 2.1 (m, 1), 2.5 (h, 1, J = 3 Hz), 5.5 (d, 1, J = 6 Hz), 7.6 (q, 1, J = 3 and 6 Hz). The multiplets due to the four cyclopropyl hydrogen atoms were completely separated from each other at 100 MHz.

(42) H. A. Smith, B. J. L. Huff, W. J. Powers, and D. Caine, *J. Org. Chem.*, **32**, 2851 (1967).

(43) J. H. Burckhalter and R. C. Fuson, *J. Amer. Chem. Soc.*, 70, 4184 (1948).

Organic Sulfur Chemistry. X. Selective Desulfurization of Disulfides. Scope and Mechanism[1]

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Contribution from the Department of Chemistry, McGill University, Montreal, Canada. *Received August 15, 1970*

Abstract: Organic disulfides undergo facile desulfurization to the corresponding sulfides on treatment with aminophosphines. This reaction is applicable to alkyl, aralkyl, and alicyclic disulfides and is compatible with a wide variety of common functional groups. The desulfurization process is stereospecific in that inversion of configuration occurs at one of the carbon atoms α to the disulfide group. The reaction was found to follow second-order kinetics. The rates of desulfurization are enhanced in solvents of high polarity. Activation parameters were measured and were found to be consistent with a mechanism involving nucleophilic scission of the disulfide bond in the rate-controlling step. A thermally labile phosphonium salt intermediate was observed in the desulfurization of di-2-benzothiazole disulfide (**14**).

The disulfide linkage is found in a large number of natural products[3,4] and contributes to the tertiary structure of enzymes[4] and hormones.[5] Since radiation damage to biologically important compounds may occur by scission of sulfur–sulfur bonds,[6] the cleavage of disulfides by radicals and nucleophiles has become a topic of considerable current interest.[7] In contrast to the behavior reported for a number of phosphines[8,9] and phosphites,[10,11] we have found that disulfides are

(1) For Part IX, see D. N. Harpp, J. G. Gleason, and D. K. Ash, *J. Org. Chem.*, **36**, 322 (1971).

(2) NRCC Scholarship Holder, 1968–1970.

(3) L. Young and G. A. Maw, "The Metabolism of Sulphur Compounds," Wiley, New York, N. Y., 1958.

(4) R. F. Steiner, "The Chemical Foundations of Molecular Biology," Van Nostrand, Princeton, N. J., 1965.

(5) K. G. Stern and A. White, *J. Biol. Chem.*, **117**, 95 (1937); K. Jost, V. Debabov, H. Nesvabda, and J. Rudinger, *Collect. Czech. Chem. Commun.*, **29**, 419 (1964).

(6) R. Shapira and G. Stein, *Science*, **162**, 1489 (1968); G. Stein in "Energetics and Mechanisms in Radiation Biology," G. O. Phillips, Ed., Academic Press, New York, N. Y., 1968; L. K. Mee, G. Navon, and G. Stein, *Biochim. Biophys. Acta*, 104, 151 (1965); G. Navon and G. Stein, *Israel J. Chem.*, **2**, 151 (1964); G. O. Phillips, Ed., "Energetics and Mechanisms in Radiation Biology," Academic Press, New York, N. Y., 1968; K. Dose in "Physical Processes in Radiation Biology," L. Augenstein, R. Mason, and B. Rosenberg, Ed., Academic Press, New York, N. Y., 1964; W. Snipes, Ed., "Electron Spin Resonance and the Effects of Radiation on Biological Systems," National Academy of Science, National Research Council, Washington, D. C., 1966.

(7) W. A. Pryor and K. Smith, *J. Amer. Chem. Soc.*, **92**, 2731 (1970); J. L. Kice, "Mechanism of Reactions of Sulfur Compounds," Vol. 3, Wiley, New York, N. Y., 1968, p 91; N. Kharasch and A. J. Parker, *Quart. Rep. Sulfur Chem.*, **1**, 285 (1966); N. Kharasch, "Organic Sulfur Compounds," Vol. I, Pergamon Press, Elmsford, N. Y., 1961; A. J. Parker and N. Kharasch, *Chem. Rev.*, **59**, 589 (1959).

(8) Only acyl, thioacyl, and vinylogous acyl "disulfides" desulfurize with triphenylphosphine, whereas benzyl and diethyl disulfides (among others) failed to react.[9] *p*-*N*,*N*-Dimethylamino phenyl disulfide was reported to desulfurize;[9b] however, in our hands, this substance failed to undergo desulfurization. Alkylidine alkyl disulfides have been desulfurized but undergo allylic type rearrangement *en route*.[9d]

(9) (a) A. Schönberg, *Chem. Ber.*, **68**, 163 (1935); (b) A. Schönberg and M. Barakat, *J. Chem. Soc.*, 892 (1949); (c) F. Challenger and D. Greenwood, *ibid.*, 26 (1950); (d) C. Moore and B. Trego, *Tetrahedron*, **18**, 205 (1962).

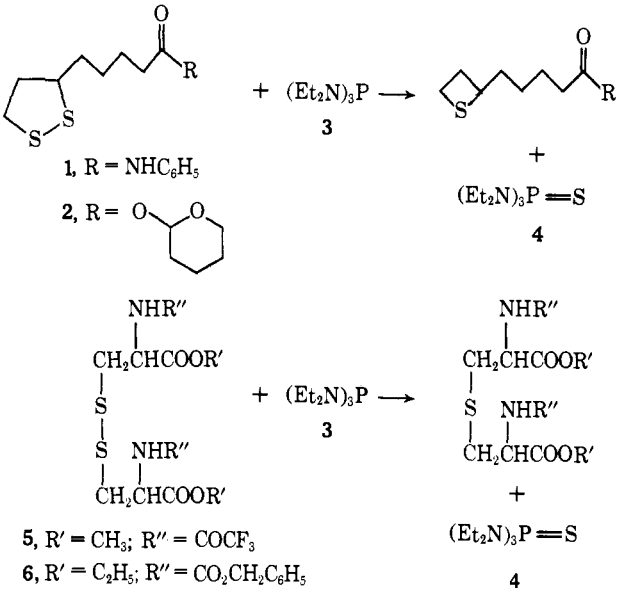
(10) When phosphites are used in this reaction, either irradiation is necessary for the reaction to take place,[11c,d,i] Arbuzov rearrangement occurs (RSSR + $(EtO)_3P \rightarrow RSEt + (EtO)_2P(O)SR$),[11a,b,d,f–h,i] or,

subject to facile desulfurization by aminophosphines.[12] Because of the synthetic and mechanistic implications of this reaction, a detailed investigation of its scope and mechanism was undertaken.

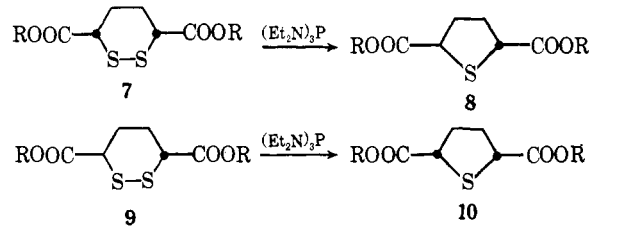
Results and Discussion

We wish to report that dialkyl, aralkyl, alicyclic, and certain diaryl disulfides undergo desulfurization under mild conditions. The results are summarized in Table I.

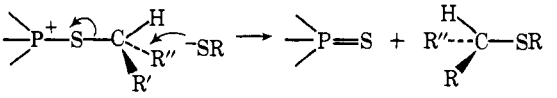
The desulfurization of several of these disulfides is worthy of special note. For example, derivatives of the naturally occurring vitamin, α-lipoic acid (**1** and **2**), and of cystine (**5** and **6**) were desulfurized in high yield to afford the corresponding thioethers.[12a,c,d]



In order to develop the synthetic scope and to delineate the mechanism of the aminophosphine–disulfide reaction, it was of crucial importance to define the stereochemical consequence of desulfurization on the carbon centers α to sulfur. The desulfurization of cyclic disulfides **7** and **9** permitted an unambiguous determination of the stereochemistry of the reaction. Desulfurization of *cis*-3,6-dicarbomethoxy-1,2-dithiane



(7) afforded a quantitative yield (vpc) of *trans*-2,5-dicarbomethoxythiolane (**8**). Similarly, *trans*-3,6-dicarbomethoxy-1,2-dithiane (**9**) afforded a quantitative yield of *cis*-2,5-dicarbomethoxythiolane (**10**). Thus, in the desulfurization of both disulfides **7** and **9**, *inversion of configuration at one of the carbon atoms α to the disulfide bridge has occurred.* Such an inversion could result from an SN2 type decomposition of an intermediate phosphonium salt (**11**) (*vide infra*).



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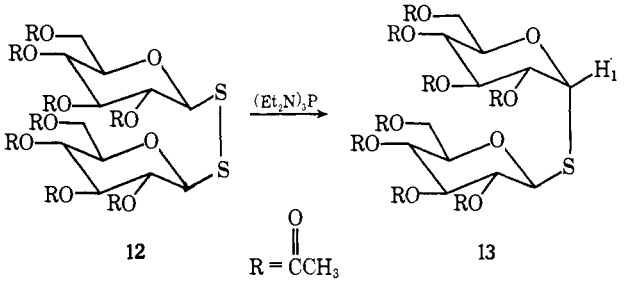
The conversion of glycosidic disulfides to their corresponding sulfides with stereochemical control at the anomeric carbon atom would provide a direct synthesis of thiotrehaloses. Such compounds are of particular interest because of their similarity to naturally occurring trehaloses and hence are attractive substrates for glycosidic enzymes.[13] Moreover, certain thio sugars are known to exhibit significant antitumor activity.[13] An appropriate disulfide for this study was β-D-glucopyranosyl disulfide octa-*O*-acetate (**12**).[14] The product of desulfurization[15] was α-D-glucopyranosyl-1-thio-β-D-glucopyranoside octa-*O*-acetate (**13**). Thus the anticipated stereochemical control is operative in this reaction.[16]



The reactions of trivalent phosphorus nucleophiles with a variety of oxygen[17] and sulfur[18] containing com-

when allylic type disulfides are employed, allylic rearrangement results.[11e,g]

(11) (a) H. Jacobson, R. Harvey, and E. V. Jensen, *J. Amer. Chem. Soc.*, 77, 6064 (1955); (b) A. Poshkus and J. Herweh, *ibid.*, 79, 4245 (1957); (c) C. Walling and R. Rabinowitz, *ibid.*, 79, 5326 (1957); (d) C. Walling and R. Rabinowitz, *ibid.*, 81, 1243 (1959); (e) C. Moore and B. Trego, *J. Chem. Soc.*, 4205 (1962); (f) H. Jacobson, R. Harvey, and E. Jensen, *J. Amer. Chem. Soc.*, 85, 1618 (1963); (g) K. Pilgram, D. Phillips, and F. Korte, *J. Org. Chem.*, 29, 1844 (1964); (h) K. Pilgram and F. Korte, *Tetrahedron*, 21, 203 (1965); (i) A. J. Kirby, *ibid.*, 22, 3001 (1966); (j) R. S. Davidson, *J. Chem. Soc.*, 2131 (1967).

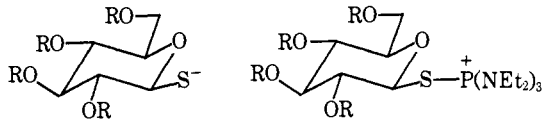
(12) (a) It should be noted that desulfurization rates for tris(dimethylamino)phosphine and tris(diethylamino)phosphine are quantitatively comparable: (b) D. N. Harpp, J. G. Gleason, and J. P. Snyder, *J. Amer. Chem. Soc.*, 90, 4181 (1968); (c) D. N. Harpp and J. G. Gleason, *J. Org. Chem.*, 35, 3259 (1970); (d) D. N. Harpp and J. G. Gleason, *ibid.*, 36, 73 (1971).

(13) M. Sakata, M. Haga, S. Tejima, and M. Akagi, *Chem. Pharm. Bull. Jap.*, 12, 652 (1964).

(14) We are grateful to Professor A. S. Perlin for suggesting this compound for our study and supplying us with its precursor.

(15) The stereochemistry of this product was determined by the observation of a single proton as a low-field doublet (τ 4.0, J = 5 Hz). This is consistent with that expected for an equatorial anomeric proton (H_1 above).

(16) If inversion were to occur *via* a glucopyranosyl mercaptide (A)



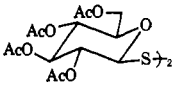
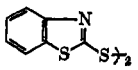
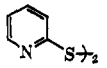
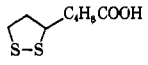
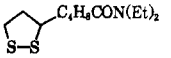
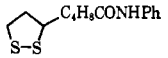
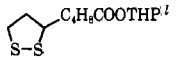
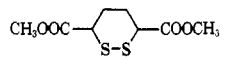
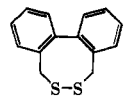
and/or a glucopyranosyl thiophosphonium cation (B) significant amounts of di-α- and di-β-glucopyranosyl octa-*O*-acetate would be formed; however, only **13** was observed.

(17) For a general review, see A. J. Kirby and S. G. Warren, "The Organic Chemistry of Phosphorus," Elsevier, New York, N. Y., 1967; R. F. Hudson, "Structure and Mechanism in Organo-Phosphorus Chemistry," Academic Press, New York, N. Y., 1965.

(18) (a) Trisulfides: D. N. Harpp and D. K. Ash, *Chem. Commun.*, 811 (1970); (b) metal dithiolate complexes: J. P. Fackler, Jr., J. A. Fetchin, and J. A. Smith, *J. Amer. Chem. Soc.*, 92, 2910 (1970); (c) desaurins: A. J. Kirby, *Tetrahedron*, 22, 3001 (1966); (d) thiocarbonates: E. J. Corey, F. A. Carey, and R. A. E. Winter, *J. Amer. Chem. Soc.*, 87, 934 (1965); (e) allyl and vinylogous allyl disulfides: ref 9d; (f) episulfides: D. B. Denny and M. J. Boskin, *J. Amer. Chem. Soc.*, 82, 4786 (1960); (g) sulfur: P. D. Bartlett and G. Meguerian, *ibid.*, 78, 3710 (1956); (h) dithioanhydrides, ref 9b.

Table I. Desulfurization of Organic Disulfides

$$R{-}S{-}S{-}R' + (Et_2N)_3P \longrightarrow R{-}S{-}R' + (Et_2N)_3P{=}S$$

Disulfide	Reaction time,[a] hr	% yield R—S—R′	% yield Other
$(C_6H_5CH_2S)_2$	4[b]	92	104[c] (**4**)
$(C_5H_{11}S)_2$	18[b]	58	
$PhSSCH_3$	0.01	86	70 (**4**)
p-$PhCH_2SSPhCH_3$	0.01	86	
$(CH_3OOCCH_2S)_2$	0.01	85	
$(C_2H_5S)_2$	48[b]	d	75[e] (**4**)
	24[f]	17[g]	
$(i\text{-}C_3H_7S)_2$	48[b]	*d*	50[c] (**4**)
$(tert\text{-}C_4H_9S)_2$	48[b,h]	1[c]	1[i] (**4**)
p-$PhCH_2SSCH_2PhNO_2$	0.5	*d*	66 $(NO_2PhCH_2)_2S$
p-$PhCH_2SSCH_2PhBr$	6[b]	38	11[i] $(PhCH_2)_2S$ 22[i] $(p\text{-}BrPhCH_2)_2S$
	0.5[b]	47 (84)[c]	
p-$CH_3PhSSPhCH_3$	24[i]	1	5 p-$(CH_3PhS)_3P{=}O$
p-$((CH_3)_2NPhS\text{-})_2$	8[b]	*d*	80 starting material recovered
	4[b]	61	
	18[b]	0	70 salt **18**
$(ZNHCH_2CH_2S\text{-})_2$[k]	4[b]	68	
$(CF_3CONHC(COOCH_3)HCH_2S\text{-})_2$	0.2	96	
$(ZNHC(COOC_2H_5)HCH_2S)_2$	1	86	99 (**4**)
ZCyOMe ZCyGlyOEt S——S	0.1		88 ZCyGlyOEt S—$)_2$
$ZNHC_2H_4SSC_2H_4COOCH_3$	1		70 $(ZNHCH_2CH_2S)_2$
	4	0	80 
	1	64	
	24	82[m]	
	432	82[n]	
	0.1	0	Polymer
	4[b]	87	
	28	101[i]	
 cis trans	0.1 0.1	102[i] 108 ± 10[i,o]	
	16[b]	38[g]	
	0.1	97	

[a] In benzene solution at room temperature, unless otherwise noted. [b] At 80°. [c] Crude yield. [d] Not isolated. [e] Vpc analysis by peak height. [f] At 90°. [g] Isolated as the sulfone. [h] In neat, excess **3** (100 mol excess). [i] Quantitative vpc analysis with internal standards. [j] At 140°. [k] Z = carbobenzoxy. [l] THP = tetrahydropyranyl. [m] Isolated as the corresponding acid. [n] Isolated as the mercuric chloride adduct. [o] Very small sample employed.

Table II

$$RSSR' + (Et_2N)_3P \longrightarrow RSR' + (Et_2N)_3P{=}S$$

Disulfide	Solvent	ϵ[a]	K_2,[b] (30°)	k_r[c]	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$[d]	pK_a[e]	Method[f]
$(C_5H_{11})_2S_2$	Benzene	2.28	$1.6 \pm 1 \times 10^{-9}$ [g]	0.00004			12.6	A
	Benzene	2.28	$1.68 \pm 0.03 \times 10^{-5}$ [h]	0.44				B
$(C_6H_5CH_2)_2S_2$	Cyclohexane	2.02	$1.5 \pm 0.1 \times 10^{-6}$		15.6	−24	11.8	A
	Benzene	2.28	$4.7 \pm 0.2 \times 10^{-5}$	1.1	13.5	−24		
	Ethyl acetate	6.02	$1.2 \pm 0.1 \times 10^{-4}$		10.2	−34		
	o-Dichlorobenzene	9.93	$2.1 \pm 0.1 \times 10^{-3}$		9.7	−28		
	Benzene	2.28	$4.5 \pm 0.2 \times 10^{-5}$	1.0	12.3	−28		A
	Ethyl acetate	6.02	$1.2 \pm 0.1 \times 10^{-4}$		8.8	−38		
	Benzene	2.28	$4.18 \pm 0.08 \times 10^{-4}$	11.0				B
$(CH_3OOCCH_2S)_2$	Benzene	2.28	$1.03 \pm 0.02 \times 10^{-1}$	2,400			9.8	B
p-$C_6H_5CH_2SSC_6H_4CH_3$	Cyclohexane	2.02	$4.46 \pm 0.03 \times 10^{-3}$				9.3	B
	Benzene	2.28	$1.20 \pm 0.03 \times 10^{-1}$	2,800	5.4	−35		
	Ethyl acetate	6.02	$6.15 \pm 0.03 \times 10^{-1}$					
$CH_3SSC_6H_5$	Cyclohexane	2.02	$1.14 \pm 0.02 \times 10^{-2}$				8.6	B
	Benzene	2.28	$4.50 \pm 0.03 \times 10^{-1}$	10,550				
	Ethyl acetate	6.02	1.51 ± 0.03					

[a] Data from NBS Circular 514, "Table of Dielectric Constants of Pure Liquids," National Bureau of Standards, 1951. [b] Average of two runs; errors are standard deviations. [c] Relative to the desulfurization (benzene, 30°) of 1,2-dithiane. [d] Measured over the temperature range 30–50°; error, ±10%. [e] pK_a of the thermodynamically most favorable mercaptide, data from D. Dmuchovsky, *et al.*, *J. Org. Chem.*, **33**, 13 (1966). [f] A = vpc analysis, B = uv analysis (see Experimental Section). [g] Measured at 80 ± 1°, extrapolated to 30°. [h] Measured at 25°.

pounds have been investigated; however, only in a few cases have detailed mechanistic studies been conducted.

To gain insight into the reaction pathway, a kinetic study of the desulfurization of a variety of disulfide types was undertaken. The reaction of dibenzyl disulfide with tris(diethylamino)phosphine (**3**) was carried out in benzene solution with several initial concentrations of disulfide and phosphine.[19] From a plot of

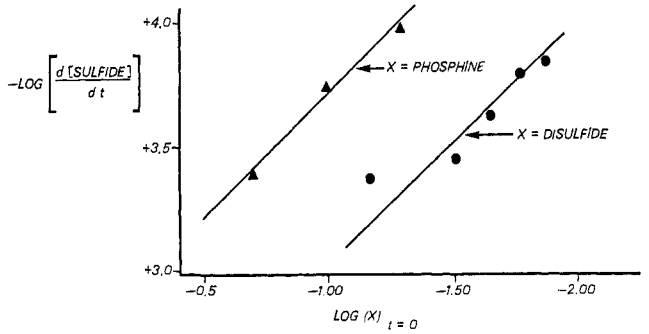


Figure 1. A plot of −log [initial velocity] *vs.* log [initial concentration] for the desulfurization of dibenzyl disulfide.

log initial velocity *vs.* log initial concentration (Figure 1), partial reaction orders of 0.96 (phosphine) and 1.01 (disulfide) were obtained. Thus the desulfurization of benzyl disulfide by tris(diethylamino)phosphine (**3**) is a second-order reaction, first order each in phosphine and disulfide. It was similarly demonstrated that all desulfurization reactions studied followed second-order kinetics.

The rates of desulfurization of a number of disulfides in selected solvents were measured by vpc and uv techniques.[20] These results are summarized in Table II. Experimental rates were found to vary over a range of 10^9. A striking feature of these observations is the marked dependence of the rate constant on the polarity

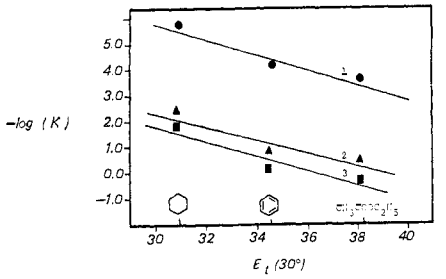


Figure 2. Correlation of rates with solvent polarity parameter E_t(30°): 1, dibenzyl disulfide; 2, benzyl tolyl disulfide; 3, methyl phenyl disulfide.

of the reaction medium. A plot of log (*K*) *vs.* the solvent polarity parameter E_t(30°)[21] illustrates this point (Figure 2). The acceleration in rate with increasing solvent polarity is of the same order of magnitude as that observed for the reaction of triphenylphosphine with sulfur[18g] and the quaternization of tertiary amines with alkyl halides[22] (Table III), reactions in which charged intermediates have been implicated.

The effect of solvent on the enthalpy and entropy of activation (Table II) provides some insight into the nature of the transition state. The high negative $\Delta S^{\ddagger}$ is in accord with that observed in bimolecular reactions[23] and is suggestive of considerable ordering in the

(19) Experimentally, it was found that consistent vpc analyses were obtained if an aliquot of the reaction mixture was quenched with sulfur before vpc analysis. The reaction of **3** with S_8 is much faster than any of these desulfurizations.[18g] In this way, analyses were reproducible to ±2%.

(20) These techniques are mutually compatable for rate comparisons; see, for example, M. K. Knecht, *J. Amer. Chem. Soc.*, **91**, 7667 (1969).

(21) K. Dimroth, C. Reichardt, T. Siepmann, and F. Bohlmann, *Justus Liebigs Ann. Chem.*, **661**, 1 (1963); for a general review of solvent polarity parameters, see C. Reichardt, *Angew. Chem., Int. Ed. Engl.*, **4**, 29 (1965).

(22) H. G. Grimm and H. Ruf, *Z. Phys. Chem., Abt. B*, **13**, 301 (1931).

(23) K. B. Wiberg, "Physical Organic Chemistry," Wiley, New York, N. Y., 1964, pp 379–381.

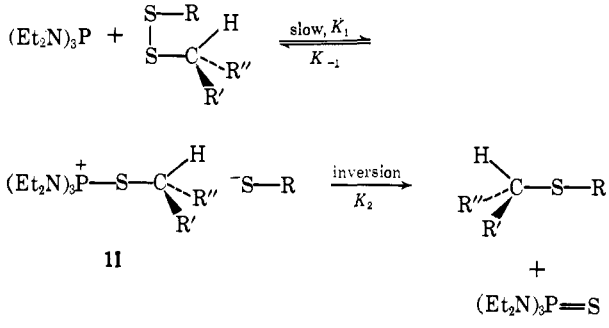
Table III. Comparison of Solvent Effects of Selected Reactions

Solvent	$\epsilon_{25°}$	Relative rate of reaction (benzene = 1.0) Benzyl disulfide +3	Benzyl tolyl disulfide +3	Phenyl methyl disulfide +3	Ph_3P^a $+S_8$	Menschutkin reaction[b] $R_3N + R'Br$
Hexane	1.89					0.01
Cyclohexane	2.02	0.03	0.03	0.04	0.01	
Benzene	2.28	1.0	1.0	1.0	1.0	1.0
Chlorobenzene	5.62				2.6	3.5
Ethyl acetate	6.02	2.6	3.3	5.1		
o-Dichlorobenzene	9.93	43				
Benzonitrile	25.2					28

[a] Data from ref 18g. [b] Data from ref 22.

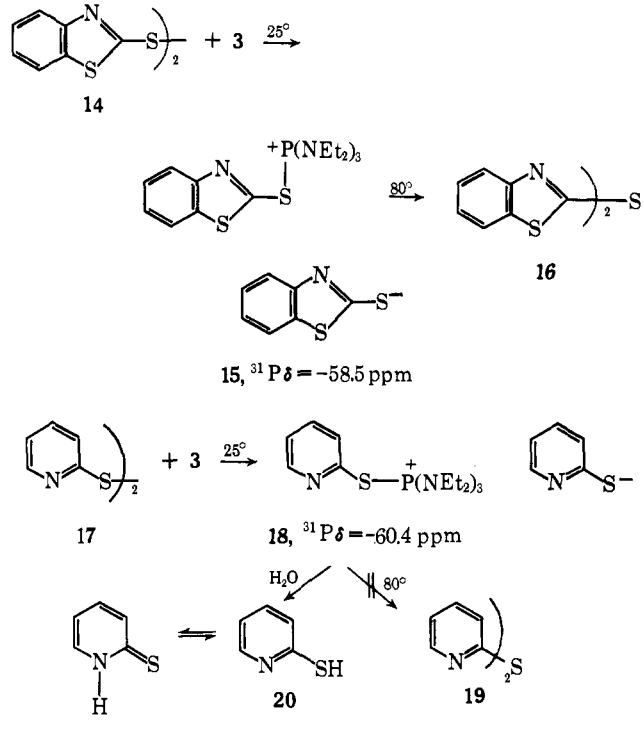
activated complex. Solvation of a transition state in which charge separation has occurred should cause a lowering of $\Delta H^{\pm}$ as the solvent polarity is increased. This was observed for the desulfurization of both dibenzyl disulfide and 1,2-dithiane (Table II). Thus the occurrence of a charged intermediate in the rate-determining step of the desulfurization reaction is strongly indicated. An intermediate, **11**, consistent with the above data, is depicted in Scheme I. This salt may

Scheme I



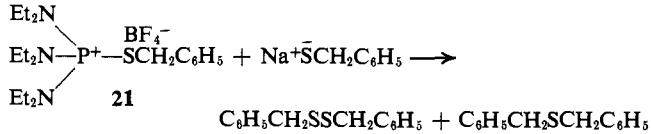
arise by nucleophilic cleavage of the disulfide bond by phosphine. The intermediacy of this phosphonium salt is in accord with the stereochemical results since the decomposition of salt **11** would be expected to proceed with inversion of configuration. If this mechanism is operative, and the anion is being displaced in the rate-controlling step, the overall rate of desulfurization should be some function of the mercaptide stability. That is, the smaller the pK_a of the mercaptide the better its ability to act as a leaving group and hence the faster the reaction. Table II shows that as the pK_a of the displaced mercaptide decreases by 4 pK_a units, the rate of desulfurization increases by a factor of over 10^8. The linear correlation of log k *vs.* pK_a is shown in Figure 3.

It was desirable to obtain direct experimental evidence for the phosphonium salt intermediate. Application of various analytical techniques (^1H and ^{31}P nmr, uv, vpc) provided no information concerning possible short-lived species in the desulfurization of aralkyl and dialkyl disulfides. However, a thermally labile phosphonium salt intermediate was observed in the reaction of di-2-benzothiazole disulfide **14** with aminophosphine **3**. This heterocyclic disulfide, on treatment with **3**, gave an oil **15**, which showed a ^{31}P resonance signal at −58.5 ppm relative to H_3PO_4. Phosphoniun salts have been shown to exhibit similar ^{31}P chemical shifts.[1,24] When heated, the oil dissolved and a 61% yield of sulfide **16** was obtained. Although di-2-pyridyl disulfide (**17**) likewise gave a phosphonium salt (**18**, ^{31}P −60.4 ppm) the corresponding sulfide **19** was



not formed on prolonged heating. Addition of water to **18** provided 2-mercaptopyridine (**20**).

The reversibility of the formation of the intermediate phosphonium salt was demonstrated in that salt **21**, on



reaction with sodium benzylmercaptide, furnished dibenzyl disulfide and dibenzyl sulfide as products. Thus a mechanism consistent with solvent effects on rate, pK_a, and stereochemical data may be formulated (Scheme I): a highly polarizable sulfur–sulfur bond is cleaved by nucleophilic attack of a phosphine on one of the sulfur atoms in a slow, reversible step with a concomitant displacement of a relatively stable mercaptide anion. The phosphonium salt which is thereby gen-

(24) J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High-Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 2, Pergamon Press, London, 1966; M. M. Crutchfield, C. H. Dungan, J. H. Letcher, V. Mark, and J. R. Van Wazer, "Topics in Phosphorus Chemistry, Volume 5," M. Grayson and E. J. Griffith, Ed., Interscience, New York, N. Y., 1967.

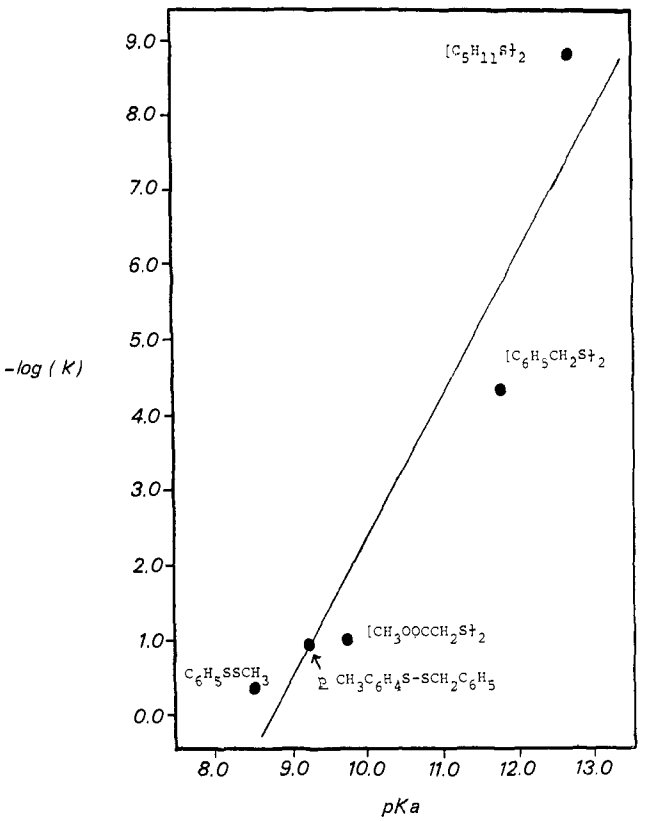
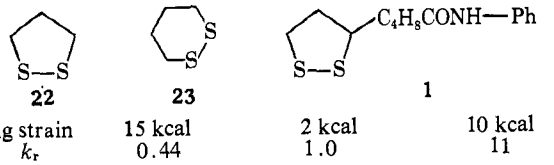


Figure 3. Correlation of rates with the pK_a of the displaced mercaptide.

erated rapidly decomposes to products *via* an SN2-type displacement of phosphine sulfide by this anion.

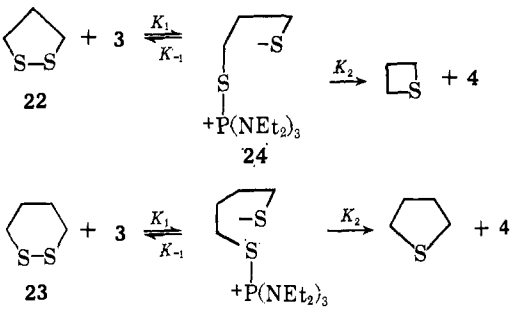
Factors which promote the formation of a phosphonium salt should have a considerable effect on the rate of desulfurization. The effects of solvent and mercaptide basicity have been discussed. Other influences affecting the rate are sulfur–sulfur bond strength[25] and degree and direction of polarization of the disulfide bond.

The former effect is readily detected in the ionic scission of cyclic disulfides by tris(diethylamino)phosphine (**3**). The reaction of **3** with 1,2-dithiolane (**22**) proceeds 10,000 times faster than that with the open chain analog, amyl disulfide, even though the pK_a of the displaced mercaptides would be comparable (Table II). The acceleration clearly results from the release of ring strain.[26] The most stable conformation for disulfides is that in which the dihedral angle (CSS–SSC) is near 90°.[27] In six-membered disulfides the dihedral angle is reduced to 70°.[28] Distortion of the dihedral angle results in ring strain of about 2 kcal/mol.[29] In five-membered disulfides, this angle is reduced to 26° and the ring strain increases to 10–14 kcal/mol.[29] As would be expected, the tendency for cyclic disulfides to undergo nucleophilic scission of the sulfur–sulfur bond increases with decreasing ring size.[29] In view of this, it is surprising to find that the most highly strained disulfide,



	22	23	1	
Ring strain	15 kcal		2 kcal	10 kcal
k_r	0.44		1.0	11

1,2-dithiolane (**22**), reacts the slowest while 1,2-dithiane (**23**), the least strained, reacts about twice as fast. This difference likely results from the relative magnitudes of K_1, K_{-1}, and K_2 (eq 1).[30] The five-membered disulfide is highly strained; hence, ionic scission (k_1) is very rapid. Recyclization of the phosphonium salt **24** to form sulfide (K_2) requires reclosure to a four-membered ring, a process which would be expected to be slow.[31] In contrast, disulfide **23** is not highly strained and therefore ionic scission (K_1) would be slower than for disulfide **22**.



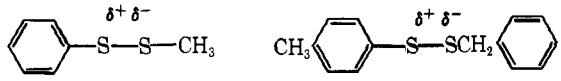
$$-\frac{d[RSSR]}{dt} = K_1\frac{K_2}{K_{-1}+K_2}[RSSR][(Et_2N)_3P] \quad (1)$$

The reverse process (K_{-1}) will proceed at a rate comparable to that of **22**. However, recyclization to afford products (K_2) requires a five-membered transition state as compared to the four-membered transition state of disulfide **22**. Cyclization reactions leading to the formation of five-membered rings occur 10^3–10^5 times faster than the analogous processes involving four-membered rings.[32] Thus for **22** the overall acceleration due to ring strain is partially counteracted by a decrease in K_2 due to the strain effects of a four-membered transition state. Disulfide **23**, however, does not encounter the latter decelerating effect and hence the full effect of ring strain is observed. The increased reactivity of α-lipoic acid anilide **1** may be the result of a substituent effect on the recyclization of the intermediate phosphonium salt. It has been observed that the presence of alkyl substituents aids in cyclization reactions which lead to the formation of three- and four-membered rings.[31] The origin of this effect, however, is not fully understood.[31,33]

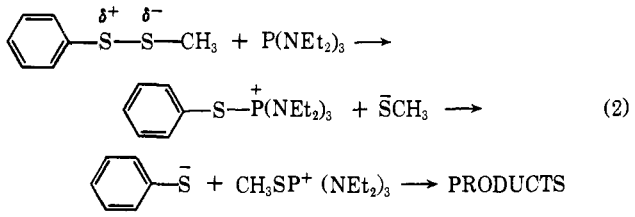
The polarization of the sulfur–sulfur bond in an unsymmetrical disulfide is a consequence of the relative electronegativities of the substituents bound to sulfur.[11a]

(25) R. E. Davis, J. B. Louis, and A. Cohen, *J. Amer. Chem. Soc.*, **88**, 1 (1966).
(26) Differences in $\Delta S^{\pm}$ would be expected to be minor (*cf.* Table II).
(27) L. Pauling, *Proc. Nat. Acad. Sci. U. S.*, **35**, 495 (1949).
(28) J. G. Affleck and G. Dougherty, *J. Org. Chem.*, **15**, 865 (1950).
(29) A. Schöberl and H. Gräfje, *Justus Liebigs Ann. Chem.*, **614**, 66 (1958).
(30) The proposed kinetic expression is based upon a steady-state approximation which appears to be justified since no intermediates were detected (nmr, vpc, uv, ir) during the reaction. The solvent effect and mercaptide pK_a dependence would require that k_1 be rate limiting. However, if K_2 is not very much greater than K_{-1} (*i.e.*, $(K_{-1} + K_2) \cong K_2$), it may not be neglected in considering the overall rate of reaction.
(31) E. L. Eliel, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, pp 61–163.
(32) H. Freundlich and G. Salomon, *Z. Phys. Chem.*, **166**, 161 (1933); L. Smith and B. Platon, *Ber.*, **55**, 3143 (1922); H. Nilsson and L. Smith, *Z. Phys. Chem., Abt. A*, **166**, 136 (1933); R. G. Kelso, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *J. Amer. Chem. Soc.*, 77, 1751 (1955).
(33) C. K. Ingold, *J. Chem. Soc.*, **119**, 305, 951 (1921); R. M. Beesley, C. K. Ingold, and J. F. Thorpe, *ibid.*, 107, 1080 (1915).

For benzyl tolyl and phenyl methyl disulfides, charge is most likely distributed as follows. Such a polarization is consistent with attack of electrophilic agents on the

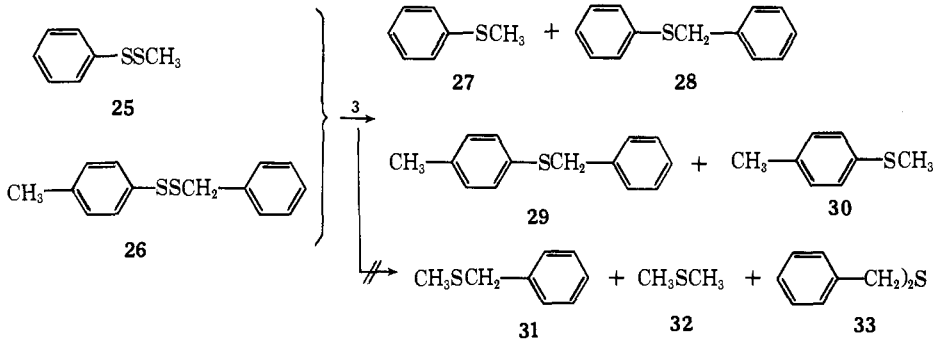


more negative sulfur atom.[34] This polarization should serve as well to direct the incoming phosphine toward the more positive sulfur atom; however, this would result in the displacement of the least stable mercaptide[35] (eq 2).



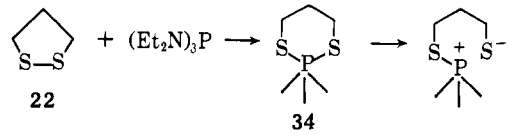
(2)

Evidence against this event was obtained in the following way. When disulfides **25** and **26** were mixed with phosphine **3**, only sulfides **27–30** were formed. If CH_3S^- and/or $C_6H_5CH_2S^-$ were generated during the



reaction, sulfides **31–33** should have appeared as products as well.[36] Since none of these compounds was detected, we conclude that attack does not occur at the more positively polarized sulfur atom of the disulfide (eq 2).

An alternative to phosphine displacement at positive sulfur involves rapid insertion of phosphorus into the sulfur–sulfur bond affording a pentacovalent intermediate prior to a slow ionization step.[37] Such a possibility can, however, be eliminated. The ionization of phosphorane **34** to a phosphonium salt should proceed at a rate comparable to that of the



analogous pentavalent phosphorus intermediate from an aliphatic disulfide. In fact, dithiolane **22** desulfurizes over 10,000 times faster than the open chain disulfide (Table II). An acceleration of this magnitude is consistent only with direct ionic scission of the sulfur–sulfur bond of **22**. Thus attack by phosphine does not appear to occur at either the more positive sulfur or at both sulfur atoms simultaneously. Attack must consequently take place at the more negatively charged sulfur atom with displacement of the more stable mercaptide. Since formation of a phosphonium salt is endothermic,[38] a high degree of P–S bond formation is indicated for the corresponding transition state.[39] Polarization effects thus are secondary to mercaptide basicity. The observed solvent polarity–rate dependence (Table II) supports this concept.

The mechanism proposed in Scheme I suggests that other sulfenyl compounds possessing a highly polarizable S–X bond and a good potential anion (X^-) might be subject to such a desulfurization reaction. Thus, this reaction may be generalized

We have demonstrated that thiolsulfonates (X = SO_2),[1,40] trisulfides (X = SS),[18a] sulfenimides (X = NR_2''),[41] and sulfenate esters (X = O)[42] undergo desulfurization by aminophosphines. Further investigations to extend the scope and generality of this reaction are in progress.

Experimental Section[43]

Melting points were taken on a Gallenkamp apparatus and are corrected. Boiling points are uncorrected. Proton nmr were measured on a Varian A60 or T60 spectrophotometer. ^{31}P nmr spectra were measured on a Varian DP 60 spectrophotometer at 19.3 MHz. Mass spectra were recorded on an AEI-MS 902 mass spectrometer and are reported in order of decreasing intensity. An F & M 5750 research chromatograph was used for vpc analyses. Uv measurements were performed on a Coleman 124 spectrophotometer equipped with a Coleman 165 recorder.

Desulfurization of Disulfides. The following example is illustrative for the desulfurization of alkyl, aralkyl, alicylic, and aryl disulfides. Precise reaction times, temperatures, and solvents are summarized in Table I. The crude reaction mixture was distilled, crystallized, or chromatographed as required. A solution of 3.69 g (15 mmol) of benzyl disulfide and 4.40 g (18 mmol) of tris(diethylamino)phosphine (**3**)[12a] in 20 ml of dry benzene was refluxed for 4 hr; the solvent was removed under vacuum and the residue chromatographed over a silica gel column. Elution with an 8:2

(34) C. G. Moore and M. Porter, *J. Chem. Soc.*, 2890 (1958); G. Leandri and A. Tundo, *Ann. Chim. (Rome)*, **44**, 74 (1954).

(35) There is literature precedent for such a process; see R. G. Hiskey and D. N. Harpp, *J. Amer. Chem. Soc.*, **86**, 2014 (1964).

(36) When salt **21** was treated with $CH_3CH_2S^-$, benzyl ethyl sulfide was formed. Thus, crossover products are possible.

(37) That slow ionization occurs after rapid insertion follows from the observed kinetics.

(38) Disulfide interchange occurs when ditolyl and diphenyl disulfides are mixed with phosphine **3**. Diphenyl disulfide must therefore be cleaved by **3**. The concentration of the salt is negligible (^{31}P measurement); its formation must therefore be endothermic.

(39) G. S. Hammond, *J. Amer. Chem. Soc.*, 77, 334 (1955).

(40) D. N. Harpp and J. G. Gleason, *Tetrahedron Lett.*, 1447 (1969).

(41) D. N. Harpp and B. A. Orwig, *ibid.*, 2691 (1970).

(42) D. N. Harpp and B. A. Orwig, unpublished results. Certain alkyl sulfenate esters have been shown to desulfurize: D. H. R. Barton, G. Page, and D. A. Widdowson, *Chem. Commun.*, 1466 (1970).

(43) Detailed experimental procedures have already been published, see ref 12c, d.

hexane–chloroform mixture afforded a colorless oil which crystallized on standing to yield 2.95 g (92%) of benzyl sulfide as colorless crystals, mp 50° (lit.[44] mp 50°), which did not depress the melting point of an authentic sample and was identical in all respects (ir, nmr, vpc (three columns), tlc) with authentic sulfide. Further elution of the column with chloroform afforded 4.3 g (104%) of crude aminophosphine sulfide **4** which was identical (vpc, ir) with an authentic sample prepared by the procedure of Stuebe and Lankelma.[45]

Preparation and Desulfurization of *cis*- and *trans*-3,6-Dicarbomethoxy-1,2-dithiane. ***cis*-3,6-Dicarbomethoxy-1,2-dithiane (7).** To a solution of 400 mg (2.3 mmol) of *cis*-1,2-dithiane-3,6-dicarboxylic acid[46] in 5 ml of methanol was added 3 drops of thionyl chloride. After standing 24 hr, the solvent was removed under vacuum and the residue crystallized from cyclohexane to afford 300 mg (65%) of colorless needles: mp 72–76°; ir (KBr) 1720 cm^{-1} (COO); mass spectrum, parent ion at *m/e* 236.0145 (calcd for $C_8H_{12}O_4S_2$: 236.0177).

***trans*-3,6-Dicarbomethoxy-1,2-dithiane (9).** In a similar manner, 50 mg (0.28 mmol) of *trans*-1,2-dithiane-3,6-dicarboxylic acid[46] was esterified in methanol to yield 50 mg of crude oil which could not be crystallized but which was judged to be greater than 98% pure by vpc: ir (film) 1730 cm^{-1} (COO); mass spectrum, parent ion at *m/e* 236.0143 (calcd for $C_8H_{12}O_4S_2$: 236.0177).

Desulfurization of *cis*-3,6-Dicarbomethoxy-1,2-dithiane (7). A solution of 0.149 mmol of the *cis*-diester **7**, 0.0715 mmol of tris(dimethylamino)phosphine oxide (internal standard for vpc analysis), and 0.230 mmol of tris(diethylamino)phosphine (**3**) in 1 ml of dry benzene was shaken for 10 min. Sulfur was added to destroy the excess phosphine, and the resulting mixture analyzed by vpc. The reaction products consisted of a mixture of 0.005 mmol of unreacted disulfide **7** and 0.147 mmol of *trans*-2,5-dicarbomethoxythiophane (**8**). Thus, the yield of *trans*-diester was 101.8% (based on recovered **7**). No *cis*-2,5-dicarbomethoxythiophane (**10**) was detected in the product mixture.

Desulfurization of *trans*-3,6-Dicarbomethoxy-1,2-dithiane (9). The desulfurization of *trans*-3,6-dicarbomethoxy-1,2-dithiane (**9**) was performed as described for the cis isomer **7** above. Thus, from 0.0146 mmol of **9** was obtained 0.0158 mmol (108 ± 10%) of *cis*-2,5-dicarbomethoxythiophane (**10**). No trans isomer was detected in the product mixture.

For both of the above desulfurizations, vpc standards were prepared by esterification (methanol, thionyl chloride) of the appropriate acids. Neither of these esters was crystalline, but both were judged to be greater than 98% pure (vpc–tlc): mass spectrum, for ester **8**, parent ion at *m/e* 204.0437 (calcd for $C_8H_{12}O_4S$: 204.0456); for ester **10**, parent ion at *m/e* 204.0426 (calcd for $C_8H_{12}O_4S$: 204.0456).

Desulfurization of Di-2-benzothiazole Disulfide (14). A solution of 3.32 g (10 mmol) of di-2-benzothiazole disulfide (**14**) and 3.0 g (12 mmol) of tris(diethylamino)phosphine (**3**) in 25 ml of benzene was stirred at room temperature. A red oil formed immediately on mixing **14** with **3**. After refluxing 4 hr, this red oil redissolved and phosphine sulfide **4** was detected on tlc. The solvent was removed under vacuum and the residue chromatographed over silica gel. Elution with 9:1 ethyl acetate–hexane afforded an oil which on stirring with hexane deposited 1.83 g (61%) of di-2-benzothiazole sulfide **16** as colorless crystals, mp 96–98°. Crystallization from ethanol afforded colorless needles: mp 97–98° (lit.[47] mp 99°); ir (KBr) 1450 cm^{-1} (C=N), 760 (aromatic), 700 (C–S); nmr ($CDCl_3$) 1.9–2.8 (m); mass spectrum, parent ion *m/e* 300, fragments at 167, 108, 242, 69.

In a similar experiment, di-2-benzothiazole disulfide (**14**) (372 mg, 1.0 mmol), tris(diethylamino)phosphine (**3**) (250 mg, 1.0 mmol), and 0.5 ml of benzene were mixed in an nmr tube. The ^{31}P nmr spectrum exhibited a single resonance at −58.5 ppm (relative to H_3PO_4). The mixture was transferred to a 5-ml flask and refluxed under nitrogen for 3 hr. Analysis (tlc) of the reaction mixture indicated the presence of di-2-benzothiazole sulfide **16** and tris(diethylamino)phosphine sulfide (**4**).

Reaction of Di-2-pyridyl Disulfide (17) with Phosphine 3. A solution of 0.222 g (1.0 mmol) of di-2-pyridyl disulfide (**17**) and 0.30 g (1.2 mmol) of tris(diethylamino)phosphine (**3**) in 5 ml of dry benzene was refluxed for 18 hr in a nitrogen atmosphere. A yellow oil which formed immediately upon mixing **17** and **3** did not redissolve. This oil reacted exothermically with water; 2-mercaptopyridine (**20**) was detected (tlc) as one of the hydrolysis products.

To characterize this yellow oil, the reaction was repeated. Thus, 220 mg (1.0 mmol) of disulfide **17** and 0.25 g (1.0 mmol) of **3** were mixed with 0.5 ml of benzene in an nmr tube. A yellow oil formed immediately. The ^{31}P nmr spectrum of this oil exhibited a strong signal at −60.4 ppm relative to phosphoric acid.

Preparation of Tris(diethylamino)benzylthiophosphonium Fluoroborate (21). A suspension of 1.95 g (10 mmol) of silver tetrafluoroborate and 2.78 g (10 mmol) of tris(diethylamino)phosphine sulfide (**4**) in 50 ml of dry dichloromethane was stirred in a nitrogen atmosphere at −78° while 1.71 g (10 mmol) of benzyl bromide in 10 ml of dry dichloromethane was added dropwise. The resulting mixture was allowed to warm up to room temperature. After stirring the mixture for 0.5 hr, the silver bromide was removed by filtration and the crude salt precipitated as an oil by dilution with hexane. The oil was separated and washed ten times with hexane, precipitated from dichloromethane with hexane, and washed as before. The oil was dried under vacuum in the dark to yield 4.0 g (83%) of a viscous hydroscopic oil. When prepared in this manner, the salt contained 5–15% (nmr) occluded phosphine sulfide **4**. The nmr spectrum of this salt showed aromatic protons as a singlet at τ 2.55, benzylic protons as a doublet (J_{PH} = 8.0 Hz) at τ 5.77, methylene protons as a multiplet at 6.7, and methyl protons as a triplet (J_{HH} = 7.5 Hz) at τ 8.75; ir (film) 1460 cm^{-1}, 1400, 1015 (broad), 800.

Reaction of Tris(diethylamino)benzylthiophosphonium Fluoroborate (21) with Sodium Benzyl Mercaptide. A suspension of 0.073 g (0.5 mmol) of sodium benzyl mercaptide in 2 ml of dry benzene was shown by vpc to be free of benzyl disulfide and benzyl sulfide. To this suspension was added 0.244 g (0.5 mmol) of the phosphonium salt **21** in 2 ml of dry benzene. A reaction occurred immediately, a brown solid precipitated, and the solution turned black. After allowing the mixture to settle for 1 min, the supernatant liquid was analyzed by vpc; both benzyl disulfide and benzyl sulfide were observed as products. A large amount of phosphine sulfide **4** was also present in the mixture. On standing 18 hr, the product ratio was unchanged. No phosphine **3** was detected by vpc.[48]

When silver tetrafluoroborate (0.1 g) was mixed in benzene solution with the aminophosphine **3**, the colorless solution turned black and a fine black solid deposited. A tlc chromatogram of this solution showed several spots on development with iodine.

The Reaction of Disulfides 25 and 26 with Phosphine 3. Equimolar quantities of disulfides **25** and **26** and phosphine **3** were mixed in dry benzene at room temperature for 5 min and the reaction mixture analyzed by vpc. Only sulfides **27–30** and phosphine sulfide **4** were detected.

Kinetics of Desulfurization. Method A. Gas Chromatography. All materials were recrystallized or redistilled prior to use in these kinetic experiments. An F & M 5750 research chromatograph equipped with a Perkin-Elmer Model 194B printing integrator and a flame ionization detector was employed to monitor the reactions. The gas chromatographic analyses were reproducible to better than ±2%. For all experiments, a 6 ft × 1/8 in. stainless steel column packed with 10% diethylene glycol succinate on Chromosorb W/AW-MCDS maintained at an oven temperature of 220° (injection port temperature, 330°; detector port temperature, 350°) was employed. Helium was used as a carrier gas at a flow rate of 50 ml/min. The solutions of disulfide and phosphine were equilibrated for 15 min in a constant-temperature bath (Bronwill Thermomix constant temperature circulator employed for temperature control) at the desired temperature before each run.

The requisite amounts of reactants were volumetrically transferred to a flask, stoppered, shaken quickly, and immersed in a constant-temperature bath. After appropriate time intervals (at least four per run), aliquots of the reaction mixture were removed, the reaction was quenched with excess sulfur, and the resulting mixture was analyzed by vpc. All experiments were performed in duplicate.

In those experiments in which stoichiometric amounts of phosphine and disulfide were used, the areas of the disulfide and sulfide peaks in the gas chromatogram were used in the calculation of rate

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(48) The reaction did not proceed to completion since the displaced phosphine (reverse reaction) was complexed by BF_3. See E. Fluck, "Topics in Phosphorus Chemistry," Vol. 4, M. Grayson and E. J. Griffith, Ed., Interscience, New York, N. Y., 1967, p 304.

constants

$$k = \frac{f(\text{sulfide area})}{tD_0(\text{disulfide area})}$$

where k = second-order rate constant ($1\ M^{-1}\ \text{sec}^{-1}$), t = time (sec), f = vpc calibration factor, and D_0 = initial disulfide concentration. All calculations were performed on an IBM 360/50 computer using a least-squares program. Rate constants were calculated for the initial portion (10–50%) of the reaction for which second-order kinetics were observed to be valid.

For those experiments in which nonstoichiometric amounts of reactants were employed, sulfide and/or disulfide concentrations were calculated. This equation is valid if the conversion of phosphine to phosphine sulfide by the sulfur quench is quantitative.

$$[\text{sulfide}] = \frac{f(\text{sulfide area})[\text{phosphine}]}{(\text{phosphine sulfide area})}$$

This was demonstrated in that 0.247 g (1.00 mmol) of tris(diethylamino)phosphine (3) reacted with excess sulfur to afford 0.275 g (0.99 mmol, 99%) of tris(diethylamino)phosphine sulfide (4). These concentrations of phosphine and phosphine sulfide were measured by vpc against diphenyl sulfide as a primary standard. From the disulfide concentration thus calculated, the second-order rate constant (k) was calculated by the method of least squares.

Method B. Ultraviolet Spectrophotometry. A Coleman 124 spectrophotometer equipped with a Coleman 165 recorder and a Neslab constant-temperature regulator (±0.2°) was employed at constant wavelength to monitor the disappearance of disulfide with time. The solutions of disulfide and phosphine were equilibrated for 15–30 min at a given temperature before each run.

The requisite volumes of disulfide and phosphine stock solutions were transferred to the uv cell and allowed to equilibrate further in the cell holder for 3–5 min prior to measurement of absorbance as a function of time. Pseudo-first-order conditions were employed with an excess (at least tenfold stoichiometrically) of phosphine. All runs were performed in duplicate. The value of the pseudo-first-order rate constants (k') were calculated from plots of $\ln((A_0 - A_\infty)/(A_t - A_\infty))$ *vs.* time by the least-squares method. All calculations were performed by an IBM 360/50 computer. The rate constants were calculated from the initial portion of the reaction for which first-order kinetics were seen to be valid; all reactions were allowed to continue for at least six half-lives before A_∞ was recorded.

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Kinetics and Stereochemistry of the Hydrochlorination of 1,2-Dimethylcyclohexene[1a]

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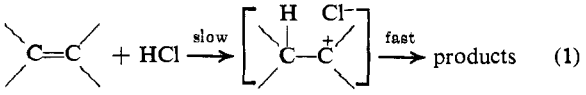
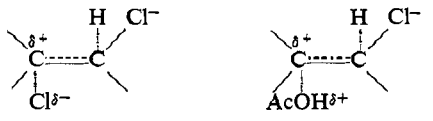
Abstract: Reaction of 1,2-dimethylcyclohexene with HCl in HOAc leads to the formation of *trans*-1-chloro- (TC), *cis*-1-chloro- (CC), *trans*-1-acetoxy- (TA), and *cis*-1-acetoxy-1,2-dimethylcyclohexane (CA), as well as 1,6-dimethylcyclohexene. While TC and CC are relatively stable to the reaction conditions, TA, CA, and 1,6-dimethylcyclohexene are not stable and react to yield mixtures of the other compounds. The kinetically controlled product distributions and the initial rate of addition were measured at less than 10% conversion. It was found that the fraction of TC formed increases markedly with HCl concentration and with the added chloride salt concentration, the dependence indicating that dissociated chloride ion intervenes in the formation of TC. The effect of chloride salt on the rate of reaction establishes that this intervention occurs in the rate-limiting step. These results are interpreted in terms of a carbonium chloride ion pair reaction (AdE2 mechanism) competing with a termolecular anti addition process (AdE3 mechanism), the latter dominating in the presence of large chloride salt concentrations. The products of addition were also studied in several other solvents. Addition of HCl in methanol gives primarily TC, the fraction of TC increasing with [HCl]. In contrast, addition in acetyl chloride gives ~73% CC and the product composition varies little with [HCl]. Addition in methylene chloride also gave ~74% CC while addition in pentane yielded 92% TC under conditions of kinetic control.

In an earlier series of papers, evidence was presented supporting the view that the hydrochlorination of *tert*-butylethylene and styrene in acetic acid occurs *via* a carbonium chloride ion pair mechanism (eq 1)[2]



(1)

whereas the hydrochlorination of cyclohexene occurs predominantly by a termolecular (AdE3) anti addition mechanism.[3,4] The latter process occurs *via* a transition state resembling **1** for formation of cyclohexyl chloride and **2** for formation of cyclohexyl acetate.



1 **2**

The earlier observations of anti addition of HBr to 1,2-dimethylcyclohexene by Hammond and Nevitt[5] and of HCl to 1,2-dimethylcyclopentene by Hammond

(1) (a) We gratefully acknowledge support of this research by the National Science Foundation and by The Research Corporation; taken in part from the Thesis of C. Allen McPherson, University of California, San Diego, Calif., 1969; (b) Alfred P. Sloan Foundation Fellow, 1966–1968; (c) National Defense Education Act Predoctoral Fellow.

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