The Intermediates in HCl-Catalyzed Cleavage and Stereomutation Reactions of Sulfoxides

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Abstract: The circumstances which produce cleavage rather than stereomutation of sulfoxides have been established by studies of the influence of solvent medium on kinetics, of added neutral salts on the cleavage product ratio, and of the differing role of water in the two reactions. On these grounds it has been inferred that tetravalent 1,1-dichloro- and acetoxy chlorosulfide intermediates (and their ion-paired equivalents), which have been previously characterized in studies of the chlorinolysis of cleavable sulfides, ArSR, also arise in the HCl-catalyzed cleavage of sulfoxides. The course of the stereomutation reaction of cleavable sulfoxides, however, is consistent also with a tetravalent 1,1-dihydroxy sulfide (and ionic species equivalent to it). A variety of effects observed to influence the extent of occurrence of a competing Pummerer rearrangement have permitted some definite conclusions with regard to the structures of intermediates in this typical acid-catalyzed reaction of sulfoxides bearing α-hydrogen.

It has been previously demonstrated[1-4] that aryl alkyl sulfides (ArSR), where R is generally capable of carbonium ion activity, undergo chlorinolysis in low dielectric protic solvents such as acetic acid with quantitative formation of RCl and ROAc. On the basis of product composition,[1-4] kinetic,[2] and stereochemical[1,2] studies of the course of this reaction, it has been deduced that the addition of chlorine to ArSR results in a multiplicity of ground-state sulfonium ion pairs in equilibrium with tetravalent sulfur[5] intermediates. Recently such intermediates have been identified[6] in a number of reactions such as

$$\mathrm{ArSR} + \mathrm{Cl_2} + \mathrm{HOAc} \rightleftharpoons \mathrm{Ar{-}\overset{Z}{\underset{X}{S}}{-}R} \overset{K_e}{\rightleftharpoons} \mathrm{Ar\overset{Z}{\underset{+}{S}}{-}R\ X^-}$$

[various ion pair relationships]

where Z = OAc or Cl and X^- may be one of several anionic species (including Cl^- and ClO_4^-), involving a divalent sulfur reaction center undergoing oxidation. In one case[6c] a diaryl dichlorosulfide was isolated and characterized by X-ray diffraction studies of its crystal structure as a trigonal bipyramid about sulfur, with the Ar group and the unshared pair occupying the basal and chlorines the apical positions.

A similar intermediate equilibrium (K_e) has been invoked by Mislow and coworkers[7] in accounting for the factors controlling the stereomutation of sulfoxides by HCl in dioxane–water media. However, a problem can be recognized since pertinent sulfide chlorination reactions proceed with rapid and complete cleavage,[1-4] whereas the corresponding sulfoxide racemizations with aqueous HCl are reported to occur without signs of cleavage for the duration necessary for racemization. Moreover, the fact that chlorinolysis of sulfides in aqueous acetic acid occurs even more rapidly than in anhydrous media is in sharp contrast to sulfoxide stereomutation where water appears to exert a rate-retarding influence.

Clearly, the two reactions could not have passed through the identical intermediate. To resolve this ambiguity, the effort was made to generate the cleavage reaction intermediate by an alternate route starting from sulfoxide, but in the solvent medium in which the sulfide chlorinolysis is usually[1-4] effected. With this objective in mind, a typical sulfoxide in acetic acid solution was allowed to react with HCl. The orange-yellow color, noted previously[1-4] to form in chlorination of the sulfide, developed almost immediately on admixture of the reagents. The products of reaction, ascertained on work-up of the reaction in the usual[1-4] manner, represented almost complete cleavage; none of the starting sulfoxide remained. (The occurrence of a small proportion of Pummerer rearrangement products[8] will be discussed in a later section of this paper.)

Results and Discussion

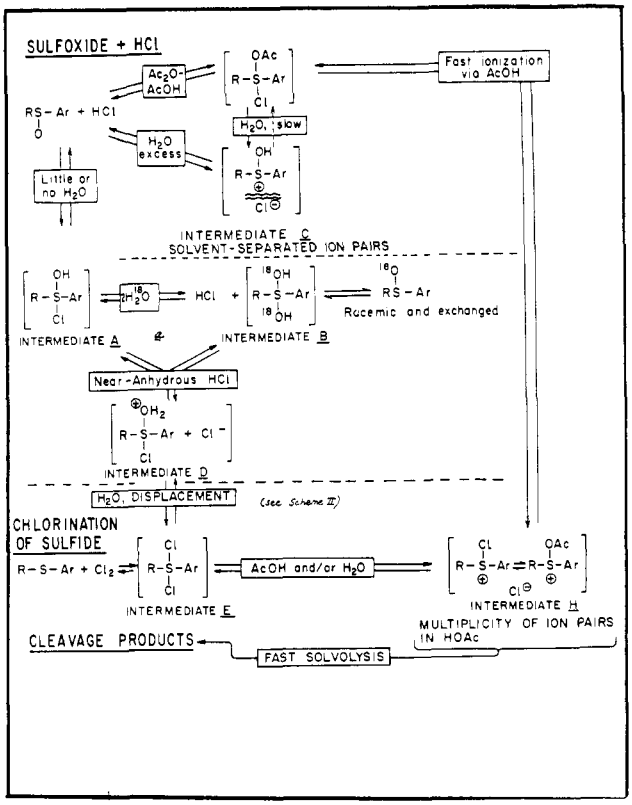
The Influence of Solvent Medium on Reaction Kinetics. The rate of formation of cleavage products was found to be first order in sulfoxide and somewhat dependent on the presence of some added acetic anhydride. Thus, in dry HOAc–HCl reaction was relatively slow, but in 80% HOAc–20% Ac_2O–0.5 *M* HCl cleavage of sulfoxide occurred nearly as rapidly as cleavage of the corresponding sulfide with Cl_2–HOAc (half-life *ca.* 6 min at 20°).

Pure acetic anhydride is known[9] to be capable of effecting the racemization of sulfoxides. To test the possibility that the 20% acetic anhydride component of the medium may of itself be responsible for the cleavage result, the same sulfoxides were dissolved in the same medium but with the HCl reagent omitted. No re-

(1) H. Kwart and P. S. Strilko, *Chem. Commun.*, 767 (1967).
(2) H. Kwart, R. W. Body, and D. M. Hoffman, *ibid.*, 765 (1967).
(3) H. Kwart, E. N. Givens, and C. J. Collins, *J. Amer. Chem. Soc.*, **91**, 5532 (1969).
(4) H. Kwart and J. Irvine, *ibid.*, **91**, 5541 (1969).
(5) We employ the term "tetravalent sulfur" although "pentacoordinate" has also been used to describe the case where there are four covalent bonds to sulfur in addition to an unshared pair. E. L. Muetterties and R. A. Schunn (*Quart. Rev., Chem. Soc.*, **20**, 245 (1966)) and others appear to have adopted the latter nomenclature [*i.e.*, B. M. Trost, R. LaRochelle, and R. C. Atkins, *J. Amer. Chem. Soc.*, **91**, 2175 (1969), and R. Tang and K. Mislow, *ibid.*, **91**, 5644 (1969)]. However see, for another view, M. A. Sabol and K. K. Andersen, *ibid.*, **91**, 3603 (1969).
(6) (a) D. C. Owsley, G. K. Helmkamp, and M. F. Rettig, *ibid.*, **91**, 5239 (1969); (b) C. R. Johnson and J. J. Rigau, *ibid.*, **91**, 5398 (1969); (c) N. C. Baenziger, R. E. Buckles, R. J. Maner, and T. D. Simpson, *ibid.*, **91**, 5749 (1969); (d) G. Allegra, G. E. Wilson, Jr., E. Benedetti, C. Pedrone, and R. Albert, *ibid.*, **92**, 4002 (1970).
(7) K. Mislow, T. Simmons, J. T. Melillo, and A. L. Ternay, Jr., *ibid.*, **86**, 1452 (1964); see also K. Mislow, *Rec. Chem Progr.*, **28**, 217 (1967).
(8) R. Pummerer, *Ber.*, **42**, 2282 (1909); **43**, 1401 (1910). See also L. Horner and P. Kaiser, *Justus Liebigs Ann. Chem.*, **626**, 19 (1959); **631**, 198 (1960), and C. R. Johnson and W. G. Phillips, *J. Amer. Chem. Soc.*, **91**, 682 (1969).
(9) S. Oae and J. Kise, *Tetrahedron Lett.*, 1409 (1967).

action was observed even after reaction periods of three times the duration ordinarily required to give complete cleavage in the presence of HCl. One plausible inference with regard to the role of the acetic anhydride, then, holds that the formation of the tetravalent sulfur intermediate in the cleavage of sulfoxide *requires acetylation* of the hydroxysulfonium ion (C in Scheme I)

Scheme I



or the corresponding 1,1-chlorohydrin, A. Apparently, in the absence of acetylation (*i.e.*, in media containing water or in which the acetylation reaction is difficult or cannot occur), the cleavage of the reaction intermediate is either not observed or takes a different course.

The Influence of Added Neutral Salts on Product Ratio. The identity of the reaction intermediates arising on chlorination of ArSR with those produced by addition of HCl to the corresponding sulfoxide in dry acetic acid is confirmed by other lines of evidence. Thus, the effect of small amounts of added $LiClO_4$ on the proportions of the carbonium ion derived products, exhibiting (see Figure 1) the unique curvature of the plot of $[LiClO_4]$ *vs.* [ROAc]/[RCl], which has been identified[1-4] as the "special salt effect" on product composition in earlier studies on the chlorination of ArSR, is also found to be characteristic of the sulfoxide cleavage. Moreover, the induced common ion depressive effect[1-4] (by LiCl) on the [ROAc]/[RCl], where LiCl in the absence of $LiClO_4$ is almost without effect in the chlorinolysis of ArSR, is similarly observed in the HCl-catalyzed cleavage of the sulfoxide.

The most significant difference between sulfoxide cleavage by HCl and the chlorinolysis reaction of ArSR in acetic acid media lies in the fate of the ArSCl, which is the product stemming from the aryl moiety. In the case of sulfenyl chlorides which are subject to solvolysis[10] in HCl–acetic acid, the disproportionation

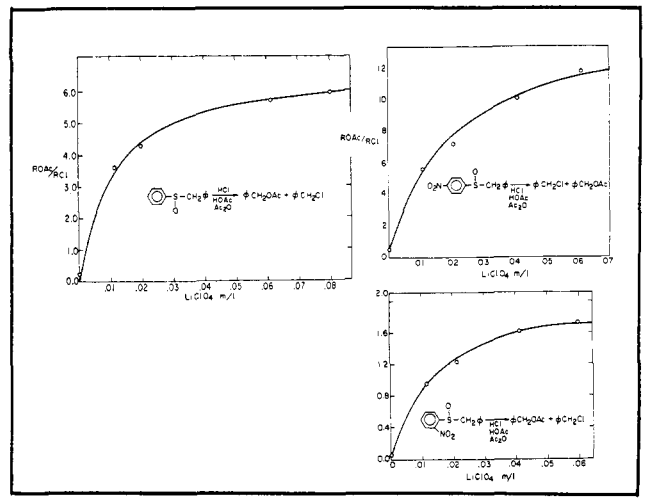


Figure 1. The "special salt effect" influence of added $LiClO_4$ on the product ratio in the HCl-catalyzed cleavage of various substituted sulfoxides.

product ArSSAr is formed. Where the primary product is a relatively unreactive sulfenyl chloride[10] (*e.g.*, Ar = *o*-nitrophenyl), it can be isolated quantitatively and, in most cases, its formation affords a convenient method of following the cleavage rate. In chlorinolysis of the sulfide, the primary product is oxidized to $ArSO_2Cl$ in acetic acid[10] in all cases before disproportionation to ArSSAr can occur.

The product composition data, gathered from HCl-catalyzed cleavage reactions of benzyl aryl sulfoxides, variously substituted in the aryl moiety, are compiled in Table I. In three of the cases the data are sufficient

Table I. Product Compositions Resulting from Cleavage of Benzyl Aryl Sulfoxides[d]

$$X\text{—}C_6H_4S(O)\text{—}CH_2C_6H_5 \xrightarrow[HOAc\text{–}Ac_2O\ (20\%)]{HCl\ (0.25\ M)} C_6H_5CH_2OAc + C_6H_5CH_2Cl$$

(0.05 *M*)

Medium additives, concn, *M*		Product ratio $[C_6H_5CH_2OAc]/[C_6H_5CH_2Cl]$			
$LiClO_4$	LiCl	X = H[a]	*p*-NO_2[b]	*o*-NO_2[b]	2,4-Dinitro[c]
0	0	0.23	0.44	0.05	0.12
0.01	0	3.6	5.6	0.94	
0	0.01	0.13			0.08
0	0.02	0.13			0.08
0	0.04	0.11			0.09
0	0.08	0.12			0.09
0.06	0.08				0.27
0.06	0.0	5.7	11.8	1.7	5.0
0.04	0.0	4.7	10.0	1.6	
0.02	0.0	4.3	7.2	1.2	
0.08	0.0	5.9			

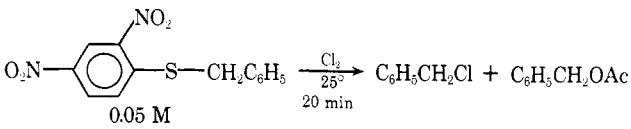
[a] Reaction was run at 77.3 ± 0.2° for 45 min. [b] Reaction was run at 77.3 ± 0.2° for 90 min. [c] Reaction was run at 50 ± 0.2° for 6 hr; [HCl] = 0.5 *M*. [d] No other products in significant amounts were formed.

to construct plots of the [ROAc]/[RCl] ratio *vs.* $[LiClO_4]$, delineating (see Figure 1) the conclusions reached in the earlier studies of sulfide chlorination, namely: (1) the chloride [RCl] product arises principally from intimate

(10) H. Kwart and E. N. Givens, *J. Amer. Chem. Soc.*, **90**, 378, 386 (1968).

ground-state sulfonium ion pairs or tetravalent sulfur intermediates; (2) the acetate [ROAc] product is formed principally from various solvent-separated ground-state sulfonium ion species; (3) the influence of lithium perchlorate on this equilibrium of ground-state sulfonium ion pairs results in the increase of product stemming from solvent-separated ion pairs. A direct comparison with the product composition results obtained by chlorination of the sulfide in the 80% AcOH–20% Ac_2O medium is seen in Table II. Although reaction

Table II. Product Compositions Resulting from Chlorinolysis of 2,4-Dinitrophenyl Benzyl Sulfide[c]



0.05 M

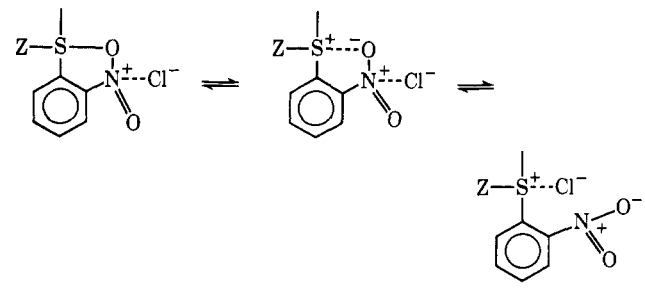
Medium additives, concn, M		Mole ratio $[C_6H_5CH_2OAc]/[C_6H_5CH_2Cl]$	
$LiClO_4$	LiCl	In HOAc–Ac_2O[a] (20%)	In AcOH[b]
0	0	0.17	0.17
0	0.07		0.12
0	0.08	0.13	
0.05	0		0.66
0.06	0	1.3	
0.05	0.07		0.24
0.06	0.08	0.26	

[a] $[Cl_2] = 0.2\ M$. [b] $[Cl_2] = 0.4\ M$. [c] No other products in significant amounts were detected.

conditions (temperature, HCl concentration, etc.) cannot be identical, the comparison appears to be valid in that 0.06 M $LiClO_4$ induces a *ca.* 25-fold increase in the acetate component of the sulfoxide cleavage product, and a *ca.* tenfold increase in the case of the sulfide chlorination product.

Of further interest is the aryl substituent influence on the product ratio. The data in Table I demonstrate that, in the absence of $LiClO_4$, a *p*-nitro subsituent increases the ROAc proportion by a factor of two, but an *o*-nitro decreases the ROAc by a factor of four. The 2,4-dinitro substitution gives results which are almost the arithmetical combination of the twofold para enhancement and the fourfold ortho inhibition of the acetate product. The occurrence of an *o*-nitro interaction with the sulfonium center generated in the chlorination of arenesulfenyl chlorides was noted earlier.[10] A similar effect appears to be operative in "stabilization" by an *o*-nitro group of the sulfonium ion intermediate in sulfoxide cleavage by HCl. While a *p*-nitro group increases the demand for solvation of the sulfonium ion (forming solvent-separated ion pairs), the *o*-nitro interaction somehow diminishes the charge deficiency on sulfur and, thus, stabilizes the intimate ion pair relationship. An attractive representation of the stabilizing interaction in the *o*-nitro sulfonium ion is the following.

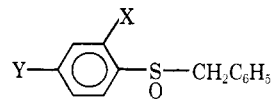
The Differing Role of Water in the Sulfoxide Cleavage and Racemization Reaction. One of the principal difficulties besetting an attempt to reconcile the two reactions (cleavage of sulfoxides and chlorination of sulfides) with a common tetravalent sulfur intermediate is the difference in response of the two reactions to water. Mislow and coworkers[7] have reported that



increasing $[H_2O]$ reduces the ease of racemization of sulfoxides by HCl; yet, the rate in $H_2{}^{18}O$ was nearly exactly equal to the rate of isotope exchange in the sulfoxide. Water is thus identified as an active reagent in the stereomutation transition state, but an excess of water would appear to be an inhibitor. On the one hand, when the cleavage intermediate is generated by chlorination of ArSR, even a large amount of water is without effect in suppressing cleavage; on the other hand, water would also seem to prevent formation of the intermediate essential to the cleavage transition state when this intermediate is developed from HCl and sulfoxide.

The following inferences can be perceived from the data (see Table III). Aryl benzyl sulfoxides react rapidly, forming benzyl chloride and ArSCl in 4 N HCl–dioxane solution where the $[H_2O]$ is $\leq 2\%$ by volume. The orange-yellow coloration, which is not to be seen in the more aqueous medium, is immediately apparent, and, after a relatively short reaction period, only cleavage products can be isolated. As the water content of the medium is increased, however, the cleavage reaction becomes vanishingly slow. The stereomutation reaction, on the contrary, is readily observable[7] with 4 N HCl in 67% dioxane–33% water.

Table III. Product Distributions (Mol %) Derived from the Reactions of Substituted Phenyl Benzyl Sulfoxides in Dioxane[e] and in Ac_2O (20%)–AcOH (80%)



Substituent		Solvent				
		—Dioxane—		—Ac_2O–AcOH[d]—		
X	Y	C_6H_5-CH_2Cl	C_6H_5-CHO	C_6H_5-CH_2Cl	C_6H_5-CHO	C_6H_5-CH_2OAc
NO_2	H	100[a]	0	95	0	5
NO_2	NO_2	100[a]	0	88	0	12
H	H	33[b]	77	70	14	16
H	NO_2	75[a]	25	68	2	30
H	H	45[c]	55			

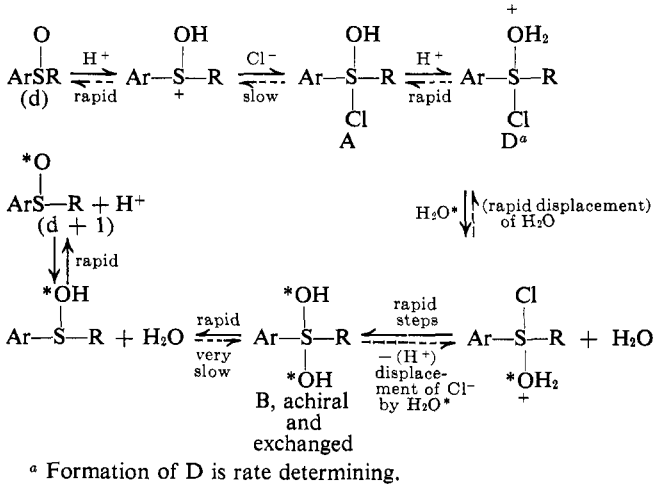
[a] At room temperature for 90 min with 4 N HCl (dry). [b] At room temperature for 20 min with 4 N HCl (dry). [c] At room temperature for 180 min with 4 N HCl (2% H_2O by volume). [d] See Table I. [e] 67% dioxane; 33% H_2O.

The obviously differing roles of water in the two reactions can readily be reconciled with a multiplicity of reaction intermediates, as seen with the aid of Scheme I which diagrams the various cleavage and stereomutation relationships. (i) Since water strongly retards and acetic anhydride accelerates in acetic acid solution, a very plausible cleavage intermediate is the acetoxysulfonium ion formed by acetylation of a hydroxysul-

fonium C or a 1,1-chlorohydrin precursor A. (ii) In essentially dry dioxane solution, the conjugate acid of the initially formed 1,1-chlorohydrin (D) experiences rapid displacement by chloride ion to form a symmetrical 1,1-dichloride (E) in equilibrium with its chlorosulfonium chloride ion pair, H. This rapid displacement can be correlated with the high nucleophilic activity of chloride ion in nonhydroxylic media.[11] The same intermediate E is also formed in the reaction of chlorine with ArSR in nonhydroxylic solvents like chloroform and dioxane, and readily undergoes a cleavage course responsive to the same medium influences (special salt effect, etc.), but this is not the only reaction that could occur in nonhydroxylic media. (iii) In aqueous dioxane–HCl solutions, the initially formed 1,1-chlorohydrin, A, cannot experience the displacement reaction leading to the symmetrical dichloride because water strongly suppresses the nucleophilic activity of chloride ion.[11] In fact, excessive amounts of water may even prevent formation of the 1,1-chlorohydrin, which is also dependent on the nucleophilic properties of chloride ion in reaction with the conjugate acid of sulfoxide.[12] However, as demanded by the isotopic tracer results,[7] the necessarily symmetrical intermediate in stereomutation must be formed with the participation of water.

Scheme II presents an attractive alternative to the

Scheme II



[a] Formation of D is rate determining.

presently accepted view[13] that the stereomutation of sulfoxides brought about by HX in hydroxylic media must involve a halosulfonium ion (or its equivalent 1:1 dichloride). This proposal accounts for the observed dependence of the racemization and exchange rates on the square of the hydrogen ion concentration.[13] It is also fully in accord with the requirement that racemization and exchange occur with equal rates. Finally, it allows for all these observations without invoking a chlorosulfonium ion, an intermediate which, on the basis of the data and reasoning discussed above, would demand a cleavage reaction course that is not observed.

The most significant point of departure in Scheme II from the previously proposed[13] stereomutation mechanism in dilute aqueous solution lies in the steps following the rate-determining formation of the chlorohydrin A. While chloride is the more nucleophilic agent toward the hydroxysulfonium ion in the step forming A, the data identify H_2O as the stronger nucleophile in displacement reactions of tetracovalent intermediates like D. Such variation among reagents in nucleophilic properties and order of nucleophilic reactivity with change in valence state of the sulfur seat of displacement is not surprising in view of similar observations reviewed by Kice.[14] There is no difficulty also in accepting the premise (depicted in Scheme II) that D submits to displacement and exchange of its H_2O ligand at a rate which is even faster than the displacement of the chloride ligand. The rapid succession of such steps ultimately results in formation of the 1,1-diol B which is both achiral and completely exchanged.

For reasons that are not fully documented at present, the tetracovalent sulfide D must replace its ligands very much faster than it is formed. The possibility of pseudorotation in such systems has been discussed.[15] Moreover, the assumption of an intermediate like B in the racemization of noncleavable sulfoxides in strong (75% H_2SO_4) acid solutions[16] cannot be construed as inconsistent with this possibility.

Our studies have also established that, in acetic acid, chlorination of diphenyl sulfide leads only to the corresponding sulfoxide without any evidence of cleavage. Similarly, diphenyl sulfoxide both in acetic acid–hydrochloric acid and in dry dioxane–HCl *also* produces the orange-yellow color of intermediate E and its ionization products[8] (as is observed in chlorination of the same sulfide), but, again, affords no cleavage. Intermediate E can, therefore, intervene in the anhydrous HCl-catalyzed stereomutation of *noncleavable sulfoxides*,[17] being formed reversibly from intermediate D as shown in Scheme I.

The Competing Pummerer Reaction. In some cases it was observed that a part of the product originated from a competing side reaction under the usual conditions leading to cleavage of sulfoxides with HCl. It is well known that a sulfoxide which has a HC α to the sulfinyl group experiences Pummerer rearrangement[8] in acid solution, when the α hydrogen is activated by acidifying substituents. Benzaldehyde and benzenethiol, which in the present work are frequently observed to accompany sulfoxide cleavage, may be regarded as Pummerer products.[18]

(11) See, for examples, A. J. Parker, *J. Chem. Soc.*, 1328 (1961); W. M. Weaver and J. D. Hutchison, *J. Amer. Chem. Soc.*, **86**, 261 (1964); S. Winstein, L. G. Savedoff, S. Smith, I. D. R. Stevens, and J. S. Gall, *Tetrahedron Lett.*, 24 (1960).

(12) It is possible that intermediate A could suffer racemization *via* pseudorotation. This route for sulfoxide stereocomputation by HCl is rendered somewhat doubtful, however, by the experimental fact that the rate of racemization in the presence of $H_2{}^{18}O$ is equal to the rate of isotope exchange. The racemization mechanism represented in Scheme II calling for the exchange reaction to occur in a displacement of chloride ion that produces a symmetrical intermediate, which has been very rapidly equilibrated with water in the medium, is consistent with this fact.

(13) D. Landini, F. Montanari, G. Modena, and G. Scorrano, *J. Amer. Chem. Soc.*, **92**, 7168 (1970); J. H. Krueger, *Inorg. Chem.*, **5**, 132 (1966).

(14) J. L. Kice, *Accounts Chem. Res.*, **1**, 58 (1968).

(15) Private communication, Professor I. Ugi, University of Southern California.

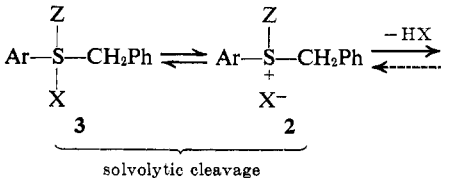
(16) N. Kunieda and S. Oae, *Bull. Chem. Soc. Jap.*, **41**, 696 (1968); *ibid.*, **42**, 1324 (1969).

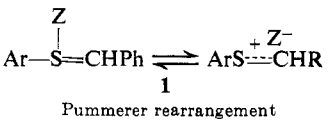
(17) We define a cleavable sulfoxide as one which can form a carbonium ion by ionization of the intermediate E. For example, this definition applies to sulfoxides (RSOAr), where R = isopropyl or *tert*-butyl, but not to methyl, ethyl, or phenyl.

(18) For examples of Pummerer products and other aspects of their rearrangement, see J. A. Smythe, *J. Chem. Soc.*, 349 (1909); K. Fries and W. Vogt, *Justus Liebigs Ann. Chem.*, **381**, 312 (1911); T. Zincke and P. Jorg, *Ber.*, **42**, 3362 (1909); H. Page and S. Smiles, *J. Chem. Soc.*, 1112 (1910); H. Gilman and J. Eisch, *J. Amer. Chem. Soc.*, **77**, 3862 (1955); H. J. Shine and C. F. Dais, *J. Org. Chem.*, **30**, 2145 (1965).

The relative amounts of benzaldehyde and benzyl chloride products formed under the specified reaction conditions are summarized in Table III. The circumstances which appear to depress or completely eliminate the formation of Pummerer rearrangement products can be summarized as follows: (a) When the sulfoxide structure possesses no hydrogen on the α carbon, as in aryl *tert*-butyl sulfoxides, only normal cleavage products are obtained. (b) The presence of *ca.* 2% water in the dioxane–HCl solution depresses the extent of benzaldehyde(s) formation. (c) When the cleavage reaction is accelerated, as in the cases exhibiting the "special salt effect" accompanying [$LiClO_4$] additions, the Pummerer is correspondingly diminished. (d) A *p*-nitroaryl substituent strongly inhibits benzaldehyde(s); an *o*-nitro eliminates this kind of product entirely.

It is now generally accepted[19] that the Pummerer and Pummerer-like rearrangements involve an intermediate oxy or halosulfonium ylide, as represented by **1** for the aryl benzyl substrates. It is evident, also, that this ylide is equilibrated with the corresponding oxy- or halosulfonium ion pair, **2**, and its tetravalent sulfur equivalent, **3**. Thus, the competition of solvolytic cleavage and Pummerer rearrangement processes controls the product composition. Except for the nitroaryl substituent effect, the important factors which



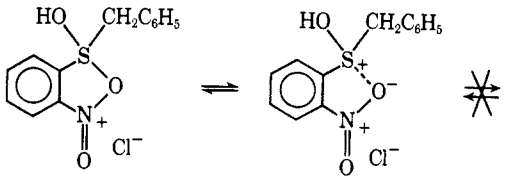


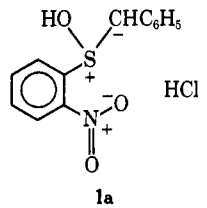
Z = OH, OAc, Cl, etc.

govern this equilibrium in acetic acid or in dioxane–HCl solution can be perceived in conjunction with the observations a–d summarized above. It might have been expected that the nitro substituent would promote ylide **1** formation (and, therefore, the Pummerer) as it does when substituted on or near the α carbon.

It will be recalled that Pummerer rearrangement is not observed in the chlorination of cleavable sulfides[17] in acetic acid solution. Consequently, it can be surmised that under these circumstances the intermediate acetoxy- or chlorosulfonium ion pair **2** (and the covalent species **3**) undergoes solvolytic cleavage much faster than conversion to the ylide **1**. We can now also assume that this cleavage taking place in the sulfoxide–HCl-Ac_2O–AcOH reaction (medium) passes through the identical intermediate. Thus, we must also conclude that, where Pummerer rearrangement is occurring in competition with cleavage, the required sulfonium ylide is *not* derived from the cleavable sulfonium ion **2** (Z = OAc or Cl), but from the noncleavable hydroxysulfonium ion (Z = OH). This same hydroxysulfonium ion and its tetravalent equivalent A, while directly implicated in the stereomutation reaction, are also the precursors of the solvolytic cleavage intermediate H (*via* a rate-determining acetylation step), and the precursors of the intermediate E (*via* a displacement on the intermediate D under anhydrous HCl conditions) (see Scheme I).

On this basis, the nitroaryl substituent effect diminishing or eliminating the competing Pummerer rearrangement is readily understandable. Thus, the steady-state concentration of the necessary hydroxysulfonium ion pair **2** (Z = OH) is strongly diminished by the inductive effect of both the *p*- and *o*-nitro substituents; that is, nitro is acting to reduce the basicity of the sulfoxide oxygen and to increase the nucleophilic susceptibility of **2a**, its conjugate acid, with the formation of the covalent intermediate **3a**. The *o*-nitro group, by virtue of a bridging interaction previously identified[10]





in the reactions of similar *o*-nitrosulfinyl structures and noted above as a factor in the cleavage reaction, displaces the equilibrium away from the ylide **1a**. It therefore enhances the concentration of those components of the equilibrium which undergo acetylation or displacement of OH and subsequent fast solvolytic cleavage.

Experimental Section

Preparative Methods. Substituted phenyl benzyl sulfoxides studied in the present work are summarized in Table IV. All the sulfoxides were prepared from the corresponding sulfides by oxidation with hydrogen peroxide or sodium metaperiodate. Two typical examples are the following.

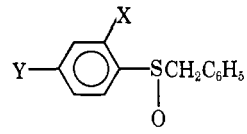
(1) *p*-Nitrophenyl Benzyl Sulfoxide. Method A. A solution of 3.1 g of 50% hydrogen peroxide was added to 8.5 g of *p*-nitrophenyl benzyl sulfide in 350 ml of acetic acid at room temperature. The resulting solution was stirred for 48 hr at room temperature, and then poured into approximately 1 l. of water. The precipitate was filtered and purified by recrystallization from acetone; yield, 5.0 g (55%); mp 174–175.5°.

(2) Benzyl Phenyl Sulfoxide. Method B. To benzyl phenyl sulfide (88 g) dissolved in 700 ml of methanol was added 1 l. of 0.5 *M* aqueous sodium metaperiodate while maintaining the temperature near 5°. The mixture was stirred overnight at temperatures below 10°. The benzyl phenyl sulfoxide which precipitated from solution in this period was filtered and purified by recrystallization from ethanol; 72.9 g (70%); mp 122–123°.

General Preparations of Sulfides (See Table V for Methods and Properties). In most cases, this was carried out in either of the following ways. (a) When aryl halides were activated by highly electron-withdrawing substituents, the sulfides were prepared *via* the reaction of the aryl halide with sodium α-toluenethiolate. (b) When the aryl halides were not activated, the sulfides were obtained from the reaction of the appropriate sodium thiophenolate and benzyl chloride.

(19) See for more extensive discussion: W. E. Parham and M. D. Bhavsar, *J. Org. Chem.*, **28**, 2686 (1963); D. Walker, and J. Leib, *Can. J. Chem.*, **40**, 1242 (1963); W. J. Kenney, J. A. Walsh, and D. A. Davenport, *J. Amer. Chem. Soc.*, **83**, 4019 (1961); although for an alternative viewpoint, see G. E. Wilson, Jr., and H. G. Huang, *J. Org. Chem.*, **35**, 3002 (1970).

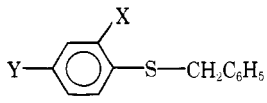
Table IV. Physical Constants and Preparative Methods Summarized for



Substituent X	Substituent Y	Oxidation method[c]	Mp (lit. mp), °C	Elemental anal. Calcd, % C	H	N	S	Obsd, % C	H	N	S
NO_2	H	A	162–164	59.8	4.24	5.37		60.0	4.12	5.41	
NO_2	NO_2	A	140° dec	51.0	3.29	9.15		51.2	3.16	9.22	
H	NO_2	A	174–175.5 (168–169)[a]	59.8	4.24	5.37		59.8	4.25	5.35	
CF_3	H	A	55–57	59.2	3.92	20.5	11.8	59.2	4.03	20.0	11.2
CH_3	H	B	70–72[e]								
CN	H	A	113–115	69.8	4.58		13.3	69.0	4.59		13.1
NH_2	H	A	94–96	67.5	5.70	6.0		67.4	5.59	6.01	
tert-Bu	H	B	56–57.5	75.0	7.36		11.8	75.1	7.44		11.8
CO_2Me	H	A	118–120	65.6	5.15			65.0	5.3		
NO_2NO_2[f]	H	A	107 dec	51.0	3.29	9.15		51.1	3.16	9.17	
H	H	B	122–123 (123)[b]								

[a] Reference 20. [b] Reference 21. [c] Method A, 50% H_2O_2 in AcOH; method B, 0.5, 0.4 *M* aqueous $NaIO_4$ (G. Leandri, A. Mangini, and R. Passerini, *J. Chem. Soc.*, 1386 (1957)). [d] Confirmed by high-resolution mass spectroscopy. [e] Reference 22. [f] 2,6-Dinitro.

Table V. Physical Properties and Preparation Methods for



Substituent X	Substituent Y	Method	Mp or bp (lit.), °C
NO_2	H	C	83–84 (83)[a]
NO_2	NO_2	C	132–133 (130)[b]
H	NO_2	C	123–124 (123)[c]
CF_3	H	C	47–48.5[h]
CH_3	H	D	110.5–111.5 (0.15 mm)[i]
CN	H	C	*g*
NH_2	H	D	162–163 (0.4 mm) (43–44)[d]
tert-Bu	H	D	155–157 (0.5 mm)[i]
H	CH_3	D	42–43 (44)[e]
CO_2Me	H	D	61–62[i]
NO_2, NO_2	H	C	92[i]
H	H	D	41–42 (42)[f]

[a] A. Sieglitz and H. Koch, *Chem. Ber.*, **58**, 78 (1925). [b] R. W. Bost, K. R. Starnes, and E. L. Wood, *J. Amer. Chem. Soc.*, **64**, 1165 (1942). [c] W. R. Waldon and E. E. Reid, *ibid.*, **45**, 2399 (1923). [d] A. Buraway, C. Turner, W. I. Hyslop, and P. Raymerks, *J. Chem. Soc.*, 82 (1954). [e] E. Fromm, *Ann.*, **396**, 75 (1913). [f] E. Fromm, *Ber.*, **41**, 3397 (1908). [g] Not isolated, characterized as sulfoxide. [h] *Anal.* Calcd for $C_{14}H_{11}F_3S$: C, 62.6; H, 4.13; F, 21.2. Found: C, 62.6; H, 4.20; F, 21.2. [i] *Anal.* Calcd for $C_{15}H_{14}SO_2$: C, 69.8; H, 5.50; S, 12.40. Found: C, 69.8; H, 5.47; S, 12.48. [j] Characterized as sulfoxide.

(3) Preparation of *o-tert*-Butylthiophenol. (i) Preparation of *o-tert*-Butylphenyl *N,N*-Diethylthiocarbamate (4). A solution of 44 g (0.55 mol) of pyridine, 75.1 g (0.5 mol) of *o-tert*-butylphenol, and 75.6 g (0.5 mol) of *N,N*-diethylthiocarbamyl chloride in 400 ml of xylene (bp 139–140°) was refluxed for 6 hr. The solution was washed with H_2O after it cooled to room temperature and was then distilled under reduced pressure: bp 162–163.5° (0.4 mm); yield 0.78 g; ir (C=S) 1510 cm^{-1}.

(ii) Preparation of *o-tert*-Butylphenyl *N,N*-Diethylthiocarbamate (5). Using a procedure similar to one developed earlier[23] in these laboratories, the thiocarbamate **4** (prepared above) was rearranged to the corresponding thiocarbamate. A solution of 67 g (0.25 mol) of **4** in 300 ml of toluene was pyrolyzed at 425°. The crude product **5** (ir (C=O) 1665 cm^{-1}) obtained by stripping off toluene on a rotary evaporator was used for the next reaction without further purification.

(iii) Isolation of *o-tert*-Butylthiophenol. This compound was obtained by hydrolysis of the crude product **5** with refluxing EtOH–NaOEt in the presence of a small amount of β-naphthylbenzylamine (antioxidant) under nitrogen for 24 hr. The cooled solution was diluted with water and extracted with methylene chloride to remove the disulfide (impurity). The aqueous solution was then acidified with 20% HCl and extracted with methylene chloride, the solvent was flashed off, and the residue was distilled under vacuum: bp 103–104° (0.8 mm); yield, 28.2 g 65% overall including step i and iii; ir (S–H) 2560 cm^{-1}.

Product Studies. In Acetic Acid–Acetic Anhydride. All the reactions between the sulfoxides and HCl were carried out in the manner described below using phenyl benzyl sulfoxide as the example.

A 5.0-ml quantity of 0.81 *N* HCl in dry acetic acid[24] was added as rapidly as possible to 10.0 ml of an Ac_2O–AcOH (3:7 by volume) solution that was 0.075 *M* in phenyl benzyl sulfoxide. (When required by the design of the experiment, $LiClO_4$ was added in the appropriate quantity with the substrate.) This solution was transferred to an ampoule, which was sealed and kept for 45 min at 77.3 ± 0.2° in an oil bath. After the ampoule was rapidly cooled by immersion in an ice–water bath, the solution was poured into approximately 200 ml of water and vigorously extracted four times with 50-ml portions of pentane. The combined extracts were washed with 5% sodium bicarbonate solution and then with water, and finally dried over $MgSO_4$. The volume of the pentane solution was reduced to about 3 ml on a flash evaporator prior to analysis by glc methods. The ratio of benzyl chloride to benzyl acetate was determined at least twice on the glc and the average value recorded if the correspondence was close (as it usually was).

In Dioxane. All the reactions between sulfoxides and HCl in this medium were carried out as in the following example of phenyl benzyl sulfoxide. To 1.0 ml of dry dioxane (dried over molecular sieve, type 4A) solution containing 0.200 g of phenyl benzyl sulfoxide was added as rapidly as possible 9.0 ml of dioxane which was 4.4 *N* in HCl. The yellow color appeared almost instantly and disappeared after about 20 min at room temperature. This solution was then quenched in the same way as described in the Ac_2O–AcOH medium experiments except that diethyl ether was used for extraction. The sample was submitted to glc for estimation of the relative amounts of benzyl chloride and benzaldehyde.

In Dioxane–H_2O. Phenyl benzyl sulfoxide (0.197 g) was dissolved in 10.0 ml of 4 *N* HCl in dioxane–H_2O (2:1 by volume). This solution was kept at room temperature (about 20°) for 24 hr. No yellow color was detected in this reaction. After neutralizing with aqueous sodium hydroxide, it was extracted with diethyl ether

(20) G. Leandri, A. Mangini, and R. Passerini, *J. Chem. Soc.*, 1386 (1957).

(21) R. L. Shriner, H. C. Struck, and W. J. Jorison, *J. Amer. Chem. Soc.*, **52**, 2060 (1930).

(22) N. J. Leonard and C. R. Johnson, *ibid.*, **84**, 3701 (1962).

(23) H. Kwart and E. R. Evans, *J. Org. Chem.*, **31**, 413 (1966); E. R. Evans, Ph.D. Dissertation, University of Delaware 1964.

(24) This was prepared according to the method discussed by S. Winstein, E. Greenwald, and L. L. Ingraham, *J. Amer. Chem. Soc.*, **70**, 821 (1948).

(three 50-ml portions) and dried over $MgSO_4$. The solvent was then stripped off on a rotary evaporator, keeping the water bath temperature below 25°. In this fashion 0.200 g of solid was recovered. This solid was identified as nearly pure starting material by its nmr spectrum.

Chlorinolysis of 2,4-Dinitrophenyl Benzyl Sulfide in Ac_2O–AcOH and in AcOH. A typical experiment can be described as follows: to 7.5 ml of Ac_2O–AcOH (40:60 by volume) containing 0.2195 g of 2,4-dinitrophenyl benzyl sulfide, 0.0964 g of $LiClO_4$ and 0.0530 g of LiCl were added as rapidly as possible 7.5 ml of dry acetic acid which was 0.4 *M* in chlorine, while maintaining total darkness. This solution was kept at 25° for 20 min, and then poured into water. It was then worked up in the same fashion as the sulfoxides in the Ac_2O–AcOH medium. The concentrated sample was submitted (as described earlier) to glc determination of the ratio of benzyl chloride and benzyl acetate.

Chlorinolysis of Phenyl Benzyl Sulfide in Dioxane–H_2O (2:1 by volume). (a) In the Presence of 4 *N* HCl. Dry chlorine was passed for 5 min into 50 ml of 4 *N* HCl in dioxane–H_2O solution containing 0.530 g of phenyl benzyl sulfide (in the dark). The yellow solution obtained was kept for 1 hr at room temperature. This was then poured into 300 ml of water and extracted with diethyl ether (three 50-ml portions). The combined extracts were washed with aqueous $NaHSO_3$ and aqueous $NaHCO_3$ and H_2O, and finally dried over $MgSO_4$. Residual liquid obtained after evaporation of solvent showed strong sulfonyl group absorptions (1190 and 1380 cm^{-1}). This was treated with concentrated aqueous NH_4OH which yielded benzenesulfonamide, mp 153° (uncorr) (lit.[25] 156°).

(b) In the Absence of HCl. The formation of benzenesulfonyl chloride was again indicated by its ir absorption and its conversion to the amide.

Color Observations and Reaction Kinetics. (a) When phenyl benzyl sulfoxide or phenyl *tert*-butyl sulfoxide was treated with HCl (0.3 *N*) in Ac_2O (20%)–AcOH at 20°, a yellow solution was obtained within a very short period of time. This color disappeared after several hours. The uv spectrum of this yellow solution showed λ_{max} 392 mμ, which was exactly the same wavelength observed for the yellow solution obtained on chlorinolysis of benzyl phenyl sulfide.

(b) Identification of the ArSCl Product of Sulfoxide Cleavage. A large excess of cyclohexene was added to the solution obtained from the reaction of 2,4-dinitrophenyl benzyl sulfoxide with HCl (1.2 *N*) for 14 hr in Ac_2O (20%)–AcOH at room temperature. This solution was kept at room temperature for 36 hr and then poured into water. The solid which precipitated was washed with water and dried. This solid was identified by its ir, nmr, and mp of 115–117° (lit.[26] 117–118°) to be 2-chlorocyclohexyl 2,4-dinitrophenyl sulfide (after recrystallization from ethanol).

(c) Kinetics. (i) Titration Method. For 2,4-dinitrophenyl benzyl sulfoxide in Ac_2O (20%)–AcOH, 2,4-dinitrophenyl benzyl sulfoxide (0.3864 g) was dissolved in 8.3 ml of acetic acid and kept at 20 ± 0.5°. To this solution was added 16.7 ml of 0.77 *M* HCl in 30% Ac_2O– 70% AcOH at 20 ± 0.5°. A 5-ml sample was taken up at the end of a specified time period and quickly quenched in a large excess of aqueous potassium iodide solution. The mixture was stirred for 5 min at room temperature. The solid which precipitated was filtered and washed thoroughly. The combined filtrate was then titrated with a standard solution of sodium thiosulfate (0.01 *N*) using starch as an indicator. Some typical data obtained in this manner are shown in Table VI. A plot of the data conformed to a first-order rate law according to which the specific rate constant was readily computed as $k = 1.1 \times 10^{-1}$ min^{-1} and $t_{1/2} = 6.3$ min.

Table VI

Time, min	$Na_2S_2O_3$, ml
2.0	0.55
5.5	0.94
10.5	1.37
20.0	1.68
45.0	1.86

(ii) Pursuing the Formation of Benzyl Chloride (for *o*-Nitrophenyl Sulfide) in AcOH Medium Containing 0.05 *M* *o*-Nitrophenyl Benzyl Sulfoxide. In this kinetic study, formation of benzyl chloride was followed by quenching aliquot amounts at specified time intervals. Analysis was carried out by means of glc procedures with 1,2,3-trichlorobenzene as an internal standard. The plots of this ratio *vs.* time (see Table VII) showed good first-order characteristics; in the example above, the specific pseudo-first-order rate constant was computed to be $k = 3.6 \times 10^{-3}$ min^{-1} and $t_{1/2} = 190$ min.

Table VII

Time, min	Ratio of $[C_6H_5CH_2Cl]$/[standard]
0	0
30	0.271
60	0.508
120	0.927
210	1.410
360	1.930

Acknowledgment. We are grateful for the support given by the donors of the American Chemical Society Petroleum Research Fund for the work reported here under PRF 4288-AC4.

(25) Handbook of Chemistry and Physics, 41st ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1960, p 842.

(26) N. Kharasch, H. L. Wehmeister, and H. Tigerman, *J. Amer. Chem. Soc.*, **69**, 1612 (1947).