Volume of Activation in the Racemization of Optically Active Sulfoxides and Sulfonium Salts

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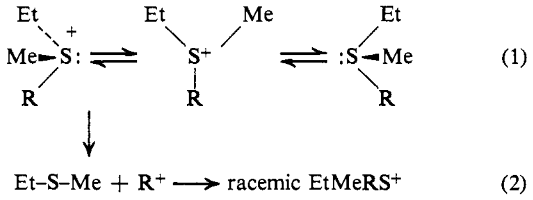
Abstract: Activation volumes have been determined for a number of racemizations of pyramidal sulfur compounds in order to help discriminate between bond distortion and bond breakage as rate-determining steps. Phenacylethylmethylsulfonium ion and the diaryl sulfoxides have ΔV^* near zero, which suggests racemization by pyramidal inversion. *t*-Butylethylmethylsulfonium ion and benzyl *p*-tolyl sulfoxide have ΔV^* values of +6.4 and +26 ml/mol, respectively; thus the transition state of the former would appear to be partly dissociated, the latter completely dissociated. A unique mechanism involving a cyclic transition state has been proposed for allyl *p*-tolyl sulfoxide and the measured values of ΔV^* (+1.0, +1.4) indicate loose bonding in comparison to the transition states for other allylic shifts.

In the last 4 years there has been a revival of interest in the optical stability of pyramidal sulfur compounds, and we have been provided with a variety of clues to the mechanisms of racemization of sulfonium salts,[1-3] sulfoxides,[4-6] and sulfinate esters.[7] At the outset one might have hoped for a unitary mechanism, but the facts now available seem to require a surprising number and variety of mechanistic hypotheses. Fortunately, most of them are well suited to testing by determination of activation volume since they do not involve an ambiguous interplay between effects of solvent electrostriction and changes of bond lengths, nor do they have equilibria preceding the rate-determining step. Exceptions are the sulfonium ylide[8] and the sulfinate ester,[7] which we have left out of consideration. At present the interpretation of activation volumes has a secure empirical foundation, and a number of recent reviews are available.[9-12]

For the racemization of sulfonium salts two mechanisms have been proposed and tested experimentally. They may be described as pyramidal inversion without bond breakage (1) and temporary dissociation into carbonium ion and sulfide (2). Examples of R groups which have been used in kinetic studies are *t*-butyl and substituted *t*-butyl,[1] benzyl and substituted benzyl,[2] phenacyl,[2] and adamantyl.[3] Both Darwish and Mislow generally favor the pyramidal inversion mechanism on the grounds that the rate is not very sensitive either to substitution or the nature of R. Darwish does, however, advocate the dissociative mechanism for *p*-methoxybenzylethylmethylsulfonium ion on the basis of a thousandfold rate enhancement and other less compelling evidence. As shown in Table I, the volumes of activation for the racemization of *t*-butylethylmethylsulfonium ion and phenacylethylmethylsulfonium ion are +6.4 ± 1.0 ml/mol and 0 ± 2 ml/mol, respectively. These values may be interpreted in a rough way on the basis of reaction type alone. Molecular scission and fusion usually result in volume changes near +10 and −10 ml/mol, respectively, and ionization causes a contraction of 25 ml/mol in water. Neither of the proposed mechanisms involves the production or destruction of ions, and thus the electrostrictive volume change may be neglected. For mechanism 1 we should expect a zero volume change and for mechanism 2 a value of +10 ml/mol. Fortunately, we also have empirical results for model reactions. For examples of racemization by bond distortion in 6-nitrodiphenic acid[13] and various N-benzenesulfonyl-N-carboxymethylarylamines[14] the activation volumes are clustered around zero with a maximum value of 2 ml/mol. For mechanism 2 a



$$\text{Et–S–Me} + R^+ \longrightarrow \text{racemic EtMeRS}^+ \qquad (2)$$

Table I. Activation Volumes for Racemization

Substance	Solvent	Temp, °C	ΔV^*
t-BuEtMeS$^+$	Water	40.0	6.4 ± 1.0
PhCOCH$_2$EtMeS$^+$	Water	60.5	0 ± 2
PhCOCH$_2$EtMeS$^+$	EtOH	60.5	0 ± 2
PhCOCH$_2$EtMeS$^+$	MeOH	60.5	0 ± 2
Ph-SO-*p*-tolyl	Toluene	192.0	−2 ± 2
α-Naph-SO-*p*-tolyl	Toluene	187.0	0 ± 2
PhCH$_2$-SO-*p*-tolyl	Toluene	141.3	26 ± 2
Allyl-SO-*p*-tolyl	Toluene	43.0	1.0 ± 1.0
Allyl-SO-*p*-tolyl	EtOH	60.0	1.4 ± 1.0

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[1] D. Darwish and G. Tourigny, *J. Amer. Chem. Soc.*, 88, 4303 (1966).
[2] D. Darwish, S. H. Hui, and R. Tomilson, *ibid.*, 90, 5631 (1968).
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[6] P. Bickart, F. Carson, J. Jacobus, E. Miller, and K. Mislow, *ibid.*, 90, 4869 (1968); R. Tang and K. Mislow, private communication.
[7] E. Ciuffarin, M. Isola, and A. Fava, *ibid.*, **90**, 3594 (1968).
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[10] W. J. le Noble, *Progr. Phys. Org. Chem.*, **5**, 207 (1967).
[11] K. E. Weale, "Chemical Reactions at High Pressures," E. and F. Spon, Ltd., London, 1967.
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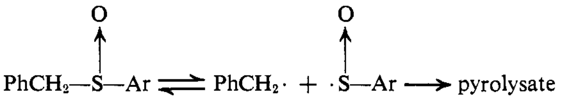
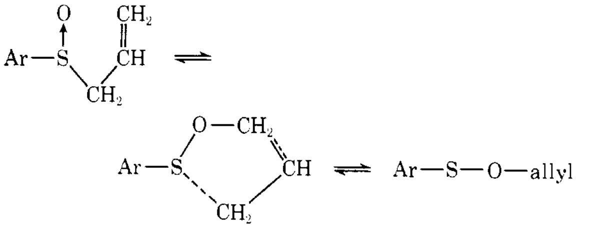
very suitable model is the solvolysis of *t*-butyldimethylsulfonium ion,[15] for which the activation volume is 9 ml/mol, but even better is the value of 8 ml/mol obtained for hydrolysis of *t*-butylethylmethylsulfonium ion by increasing the temperature above that required for racemization. In the light of these data we propose mechanism 1 for the phenacylsulfonium salt and mechanism 2 for the *t*-butyl derivative with due regard to the possibility that dissociation of *t*-butyl cation and sulfide may be not quite complete. These conclusions also harmonize with the great difference in SN1 reactivity between phenacyl and *t*-butyl substrates.

Most of the racemizations of sulfoxides investigated by Mislow[4-6] have half-lives of a few hours at temperatures near 200°, and the mechanism of pyramidal inversion has been ascribed to them. The benzyl and allyl sulfoxides, however, racemize at much greater rates, and the evidence suggests that their mechanisms are not only abnormal, but even different from each other. Concurrently with its racemization, benzyl *p*-tolyl sulfoxide produces dibenzl, *p*-tolyl *p*-toluenethiolsulfonate, benzyl *p*-tolyl sulfide, and benzaldehyde. It seems likely therefore that the sulfoxide undergoes reversible homolysis with loss of optical activity accompanying the recombination process.



$$PhCH_2-\overset{\overset{O}{\uparrow}}{S}-Ar \rightleftharpoons PhCH_2\cdot + \cdot\overset{\overset{O}{\uparrow}}{S}-Ar \longrightarrow \text{pyrolysate} \quad (3)$$

The allyl sulfoxide racemizes by far the most rapidly of all, and it produces no free-radical products. The mechanism below has been postulated, and the accessibility of the pathway has been unequivocally demonstrated.[6]



(4)

For mechanism 3 we should expect an activation volume near +10 ml/mol, since one bond is broken and no ions are produced. As a model we might adopt the homolytic iodinolysis of pentaphenylethane, which has an activation volume of +13 ml/mole.[16] The experimental value is +26 ml/mol, which indicates that bond breaking is essentially complete in the transition state. The total volume change for reactions of the type A → B + C rarely exceeds 20 ml/mol. Lest it be thought that a part of the expansion is due to release of solvent by depolarization of the S–O bond, it should be pointed out that the change of volume on mixing dimethyl sulfoxide with either polar or nonpolar solvents is so small that detection is difficult.[15] We conclude from this that electrostriction by sulfoxides is negligible. We can suggest no other special explanation for the large magnitude of the activation volume, but a survey of the literature makes us suspect a general tendency toward exaggerated activation volumes in reactions which are carried out at high temperature (140° in the present case) in order to obtain reasonable rates of reaction across high energy barriers.

For mechanism 4 we expected an activation volume near −10 ml/mol, since a new bond is formed and no ions are produced. Model processes available from the literature include various Claisen rearrangements[17] (−8 to −18 ml/mol) and the rearrangement of methallyl azide[18] (−9 ml/mol). Because the above involve migration from oxygen or nitrogen, we have also measured the activation volume for the rearrangement of allyl thiocyanate to allyl isothiocyanate which provides a closer analogy. The measured value is −8 ml/mol. To our surprise the value for racemization of allyl *p*-tolyl sulfoxide is +1.0 with toluene as solvent and +1.4 in ethanol. The invariance with solvent indicates the absence of electrostrictive effects, and reinforces a conclusion drawn earlier because the rate is insensitive to solvent. We can reconcile the results to mechanism 4 only by adopting the hypothesis that the bonding in the transition state is loose in comparison to that of other cyclic allylic rearrangements. Table II shows the magnitude of the anomaly and also shows that the entropy of activation is atypical. The fact that the entropy is markedly less negative also points to a loosely bound transition state.

Table II. Activation Volumes and Entropies for Allylic Shifts

Rearranging substrate	ΔV,* ml	ΔS*, eu
Allyl *p*-cresyl ether[a]	−14 to −18	−8 to −20
α,α-Dimethylallyl azide[b]	−9	−10
γ,γ-Dimethyl azide[b]	−8	−11
Allyl thiocyanate[c]	−8	−9
1-Cyclohexenylallylmalonitrile[d]		−12
1-Ethylpropenylallylmalonitrile[d]		−11
Ethyl(1,3-dimethyl-1-butenyl)-allyl cyanoacetate[d]		−14
Allyl *p*-tolyl sulfoxide[e]	+1	−0.7, −4.9

[a] See ref 17. [b] See ref 18. [c] A. Gagneux, S. Winstein, and W. G. Young, *J. Amer. Chem. Soc.*, **82**, 5956 (1960). [d] E. G. Foster, A. C. Cope, and F. Daniels, *ibid.*, **69**, 1893 (1947). [e] See ref 6.

Experimental Section

Resolution of Sulfonium Salts. Phenacylethylmethylsulfonium perchlorate and *t*-butylethylmethylsulfonium iodide were resolved by conversion to the hydrogen (−)-dibenzoyltartrate salts according to reports by Darwish.[1,2] In our experiments, however, the *t*-butyl derivative gave a salt which crystallized with 1 mol of additional (−)-dibenzoyltartaric acid to give $C_{43}H_{44}O_{16}S$, mp 132 dec $[\alpha]^{24}D$ −92.5° (ethanol). The neutralization equivalent was 283 ± 1 (calcd 283) and it contained 3.85% S (calcd 3.78). To prepare the substance, a mixture of 1.30 g of *t*-butylethylmethylsulfonium iodide, 5 ml of 1.0 *N* sodium hydroxide solution, and 3.00 g of (−)-dibenzoyltartaric acid in aqueous alcohol was crystallized by addition of water and recrystallized from aqueous alcohol, yielding 2.0 g.

Racemization of Sulfonium Salts. A portion of sulfonium hydrogen dibenzoyltartrate sufficient to give a sulfonium sulfate solution having a rotation of 1–2° in 1.6 dm was placed in a separatory funnel and shaken with 10 ml of water, 10 ml of ether, and a twofold excess of sulfuric acid. The aqueous layer was allowed to evaporate slightly to remove ether, and its optical rotation was measured before and after the heating period.

Preparation of Sulfoxides. The methods of Mislow, *et al.*,[4-6] were used without modification. The physical constants agreed well with those reported.

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Racemization of Sulfoxides. A portion of sulfoxide sufficient to give approximately 2° rotation in a 1.6-dm cell was weighed out and dissolved in 10 ml of solvent. The allyl *p*-tolyl sulfoxide, however, received special treatment because of its optical instability. The substance was prepared in the form of an ether solution which was rapidly fanned almost to dryness under a powerful air stream and then taken up in alcohol or toluene. Sufficient solution for ten measurements was prepared at once and preserved in a freezer at −15°. The phenyl, naphthyl, and benzyl sulfoxides require such a high temperature that the high-pressure cell could not be preheated. Reaction times of about 10 hr were used in order to reduce the effect of the 4-min characteristic time in thermal equilibration.

Hydrolysis of *t*-Butylethylmethylsulfonium Ion. Solutions were made up as for racemization, but the excess acid was exactly neutralized before heating. Progress of the reaction was determined by titration with standard alkali.

Rearrangement of Allyl Thiocyanate. Allyl thiocyanate was prepared from allyl chloride and ammonium thiocyanate.[19] Reaction mixtures were prepared by dissolving 0.30 g in 10 ml of carbon tetrachloride, and rearranged to the isothiocyanate by heating for several hours at 54.2°. The progress of the reaction was followed by ir analysis. The spectra were scanned very slowly by hand in the 2000–2200- and 1200–1500-cm^{-1} regions using a Perkin-Elmer Model 421 spectrometer, and the composition was determined by comparison with the spectra of known synthetic mixtures covering the range of 23–31% reaction, where the method was most sensitive.

High-Pressure Apparatus. The apparatus has been described previously,[20] but the oil-filled thermostat has been replaced by a 200-lb aluminum ingot which has been bored to receive the high-pressure vessel. An oil film is used to improve the thermal contact.

Calculation of Activation Volumes. The logarithm of the ratio of the rate constant at pressure to the rate constant at 1 atm (k_p/k_1) was plotted against pressure, and the best straight line was drawn through the origin and the other points. The slope was used to evaluate the activation volume according to the equation

$$RT(\partial \ln k/\partial P)_T = -\Delta V^*$$

In all cases where comparison was possible, either directly or by calculation using activation parameters, our values of k_1 agreed satisfactory with those previously reported.

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Photolysis of Dibenzoyl Peroxide[1]

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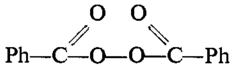
Abstract: The dissociation of dibenzoyl peroxide by radiation from a high-pressure mercury lamp was observed by electron spin resonance spectroscopy. Measurements were made on single crystals of dibenzoyl peroxide irradiated at 4.2°K. From the magnitude of the dipole–dipole interaction between the pairs of radicals formed by each dissociation it is concluded that phenyl radicals are produced, *i.e.*, Ph—C(=O)—O—O—C(=O)—Ph → 2CO$_2$ + 2Ph.

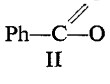
Perhaps the most familiar of organic peroxides is dibenzoyl peroxide (I), which is used extensively



$$\mathrm{Ph{-}C({=}O){-}O{-}O{-}C({=}O){-}Ph}$$

I

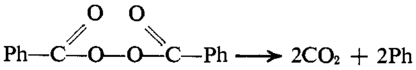
in the plastics industry to initiate polymerization. Thermal dissociation of the weak peroxide bond yields benzoyloxy radicals (II) which initiate the polymerization process.



$$\mathrm{Ph{-}C({=}O){-}O}$$

II

The process can be accelerated by using ultraviolet light to promote dissociation. Phenyl radicals, which also initiate polymerization, and CO$_2$ can also be formed in the decomposition of peroxide, *i.e.*



$$\mathrm{Ph{-}C({=}O){-}O{-}O{-}C({=}O){-}Ph} \longrightarrow 2\mathrm{CO_2} + 2\mathrm{Ph}$$

Using electron spin resonance (esr) spectroscopy, Symons and Townsend[2] attempted to detect the formation of radicals in ultraviolet-irradiated glasses containing dibenzoyl peroxide. However, they were unable to detect any esr absorption. In this report, we give an account of the dissociation of dibenzoyl peroxide in single crystals of dibenzoyl peroxide exposed to ultraviolet irradiation at 4.2°K, as observed by esr spectroscopy.

Experimental Section

Single crystals of dibenzoyl peroxide were grown by slow evaporation from benzene solutions. The crystals are orthorhombic, belonging to the space group P2$_1$2$_1$2$_1$, with four molecules per unit cell. The crystal structure of dibenzoyl peroxide has been determined from X-ray diffraction measurements by Sax and McMullan.[3]

The esr measurements were made using a K-band spectrometer (24.0 Gc/sec) utilizing superheterodyne detection. A crystal was mounted on a copper wire and suspended at the center of the cylindrical sample cavity which resonated in the TE011 mode. The cavity was immersed in liquid helium (4.2°K) in a dewar provided with sapphire windows. The crystal was exposed to light from an Osram high-pressure Hg lamp (HBO, 100 W). The light was focused on the crystal by quartz lenses.

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(1) Supported by Public Health Grant No. RH 00450 and AEC Contract No. AT(30-1)3558.

(2) M. C. R. Symons and M. G. Townsend, *J. Chem. Soc.*, 263 (1959).

(3) M. Sax and R. K. McMullan, *Acta Crystallogr.*, **22**, 281 (1967).