such as the $H_2O$ molecule of present concern. We believe this classification also has the utility that the encumbrance of the carbonium ion (bonding to it) may be more completely specified if known. Thus, for example, the Doering–Zeiss intermediate[37] is classified as having front and back-side encumbrances.

The encumbered carbonium ion intermediate $R \ldots OH_2^+$ has been previously invoked (in somewhat different forms) to explain the results of stereochemical investigations of the mechanism of the $O^{18}$ exchange reaction of *sec*-butyl alcohol[32,38] and 1-phenyl ethanol.[7]

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[37] W. von E. Doering and H. H. Zeiss, THIS JOURNAL, **75**, 4733 (1953); *cf.* Also A. Streitwieser, Jr., *Chem. Revs.*, **56**, 573 (1956).

[38] C. A. Bunton, A. Konasiewicz and D. R. Llewellyn, *J. Chem. Soc.*, 607 (1955).

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY]

# Concerning the Mechanism of the Reaction of Trisubstituted Phosphines with Episulfides[1]

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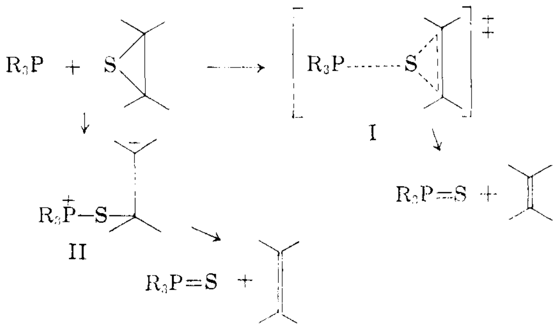
Triphenylphosphine and tributylphosphine react with *cis*-2-butene episulfide and *trans*-2-butene episulfide to give *cis*-2-butene and *trans*-2-butene, respectively. The kinetics of the reaction of triphenylphosphine with these two episulfides and 1-butene episulfide have been measured in several solvents of different dielectric constants. The rates of the reactions are relatively insensitive to large changes in dielectric constant of the medium. These data indicate that the desulfurization reaction proceeds by a nucleophilic attack by the phosphine on the sulfur to give the phosphine sulfide and olefin in one step. This process is envisioned as a smooth displacement on sulfur with little or no charge separation in the transition state.

The reactions of episulfides with many nucleophilic reagents such as lithium diethylamide,[2] primary and secondary amines[3] and mercaptide ions[3,4] proceed with ring opening and formation of a mercaptide ion or a mercaptan. With organolithium compounds,[5] triphenylphosphine[6] and triethyl phosphite,[6–8] the respective products are the alkyl or aryl lithium mercaptides, triphenylphosphine sulfide, triethyl thiophosphonate and in each case the olefin resulting from desulfurization of the episulfide.

Quite recently Neureiter and Bordwell[8] have shown that the desulfurization reaction is stereospecific. They treated *cis*-2-butene episulfide and *trans*-2-butene episulfide with phenyllithium and triethyl phosphite. In every case the *cis*-episulfide gave essentially pure *cis*-olefin, and the *trans*-episulfide gave essentially pure *trans*-olefin. These results have been confirmed by work in this Laboratory. It has been found that triphenylphosphine and tributylphosphine react with *cis*-2-butene episulfide to give *cis*-2-butene, and with *trans*-2-butene episulfide to give *trans*-2-butene.

As Neureiter and Bordwell[8] pointed out, these results are most easily explained by a mechanism which involves direct attack by the nucleophile on the sulfur atom of the episulfide ring. Such an attack could give rise to the products by proceeding through a transition state, I, which yields the olefin and the phosphine sulfide in one step. Another less likely possibility involves displacement on sulfur to give the intermediate II. If II is formed it must decompose to the products faster than rotation about the central carbon–carbon bond can occur. Rotation would ultimately lead to a mixture of olefins.



Since these reactions are rather novel, it seemed of interest to investigate in more detail the exact nature of the desulfurization process. In order to do this a kinetic study was initiated. The general kinetic procedure was modeled closely after that employed by Bartlett and Meguerian[9] in their study of the reaction of sulfur with triarylphosphines.

The rates of the reactions of *cis*-2-butene episulfide and *trans*-2-butene episulfide with triphenylphosphine were measured in several solvents. The rate data are summarized in Table I. The reaction is bimolecular, first order in each reactant. It can easily be seen that varying the dielectric constant of the solvent by a factor of *ca.* 16 has only a small effect on the rate of the reaction. Bartlett and Meguerian[9] have found that the rate of the reaction of triphenylphosphine with sulfur is markedly affected by small changes in the dielectric

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[1] Some of this work has been presented in preliminary form, *Chemistry & Industry*, 330 (1959).

[2] H. Gilman and L. A. Woods, THIS JOURNAL, **67**, 1843 (1945).

[3] H. R. Snyder, J. M. Stewart and J. B. Ziegler, *ibid.*, **69**, 2672 (1947).

[4] C. C. J. Culvenor, W. Davis and N. S. Heath, *J. Chem. Soc.*, 282 (1949).

[5] F. G. Bordwell, H. M. Anderson and B. M. Pitt, THIS JOURNAL, **76**, 1082 (1954).

[6] R. E. Davis, *J. Org. Chem.*, **23**, 1767 (1958).

[7] R. D. Schuetz and R. L. Jacobs, *ibid.*, **23**, 1799 (1958).

[8] N. P. Neureiter and F. G. Bordwell, THIS JOURNAL, **81**, 578 (1959).

[9] P. D. Bartlett and G. Meguerian, *ibid.*, **78**, 3710 (1956).

TABLE I

REACTION RATES FOR EPISULFIDES AND TRIPHENYLPHOSPHINE

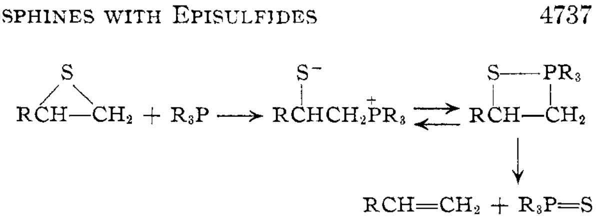
| Episulfide, butene | Solvent | $k_2 \times 10$,[3] l./mole min. at 40° |
|---|---|---|
| *cis*-2- | *m*-Xylene[a] | 1.24, 1.26 |
| *cis*-2- | Cyclohexanone[a] | 1.61, 1.58 |
| *cis*-2- | N,N-Dimethylformamide[a] | 1.77, 1.86 |
| *trans*-2- | *m*-Xylene | 0.58, 0.55 |
| *trans*-2- | N,N-Dimethylformamide | .64, 0.85[b] |
| 1- | *m*-Xylene | .54 |
| 1- | Cyclohexanone | 1.13 |

[a] The dielectric constants of these solvents at 20° are *m*-xylene 2.4, cyclohexanone 18.2, and N,N-dimethylformamide 37.6. [b] The relatively poor reproducibility in these two rate constants is probably due to impurities in the solvent.

constant of the solvent. Rate increases of several hundred fold were found with small increases in the dielectric constant of the medium. They have very reasonably attributed this effect to a separation of charge in the rate-controlling step. Their results establish fairly conclusively that the rate of an ionic displacement by a phosphine on a sulfur atom is affected by the dielectric constant of the medium. The results found in this study are therefore most consistent with a transition state which has little or no charge separation. Such a transition state is best represented by I. On the other hand, the transition state which precedes II would be expected to have a fairly large degree of ionic character and its rate of formation should be markedly affected by the dielectric constant of the medium. In order for II to be formed without passing through a transition state which has considerable charge separation, it would be necessary for the transition state to resemble quite closely the starting materials. Since in II a negative charge is localized on carbon, a process which is generally energetically unfavorable, it would seem that the transition state would reflect, to a considerable degree, this requirement. For this reason I appears to be the more satisfactory transition state.

It is interesting to note that the *trans*-episulfide reacted somewhat slower than the *cis*-episulfide by *ca.* a factor of two. This difference in rate is probably due to greater relief of steric interactions in the transition state for the *cis*-episulfide. In the case of the *cis*-episulfide any non-bonded interactions between the two methyl groups are lessened in the transition state since there is a broadening in the bond angles toward 120°. In the *trans*-episulfide case there is a reduction in methyl–hydrogen interactions which are undoubtedly smaller than the methyl–methyl interaction. This argument is strengthened by the observation that 1-butene episulfide reacts at a rate very similar to that found for the *trans*-episulfide.

It is known that the two methyl groups in the 2-butene episulfides hinder nucleophilic attack on the secondary carbon atoms. It seemed necessary therefore to investigate the reactions of an episulfide which had a primary carbon atom as part of the thiirane ring. Such an episulfide might undergo reaction at the primary carbon atom rather than on sulfur.[10] Such a process could give rise ultimately to the olefin and phosphine sulfide.



The kinetics of the reaction of 1-butene episulfide were measured in two solvents of different dielectric constants. The rate constants found corresponded closely to those obtained for the *trans*- and *cis*-episulfides. These findings indicate that there has been no mechanistic change.

**Acknowledgment.**—This work was supported by the National Science Foundation.

## Experimental[11]

***cis*-and *trans*-2-Butene Episulfides.**—The two episulfides were synthesized by the method of Price and Kirk.[12] The physical constants of these materials were in accord with those reported in the literature.[8,12]

**1-Butene episulfide** was prepared from 1-butene epoxide and potassium thiocyanate. Its physical properties agreed with those in the literature.[13]

**Reaction of the 2-Butene Episulfides with Triphenylphosphine.**—To a solution of triphenylphosphine (6.0 g., 0.0225 mole) in 10 ml. of chloroform was added a solution of the 2-butene episulfide (1.89 g., 0.0215 mole) in 6 ml. of chloroform. The reaction mixture was refluxed for 1 hour. The butene was distilled from the reaction mixture and analyzed. Evaporation of the chloroform afforded triphenylphosphine sulfide which was crystallized from ethanol, m.p. 158° (lit.[14] 158°).

**Reaction of the 2-Butene Episulfides with Tributylphosphine.**—A mixture of tributylphosphine (8.0 g., 0.04 mole), the 2-butene episulfide (2.0 g., 0.023 mole) and 15 ml. of di-*n*-butyl ether was heated to 120–130°. The butene was distilled from the reaction mixture.

**Analysis of 2-Butenes.**—The butenes were analyzed by gas-phase chromatography. The instrument used was a K and M gas chromatograph, model 17A. A 2-foot silver nitrate–polyethylene glycol column was used at a temperature of 25°. Helium was used as the carrier gas at a flow rate of 30 ml./min. Under these conditions, the retention time was 2 minutes for the *trans*-2-butene and 8 minutes for the *cis* isomer. By analyzing known mixtures it was estimated that amounts greater than 1% of either 2-butene could be detected.

| Time, min. | $I_2$, ml. | $(C_6H_5)_3P$, ml. | $C$, m./l. | $k \times 10^3$ |
|---|---|---|---|---|
| | 40.00 | 7.65 | 0.308 = $C_0$ | |
| | 40.01 | 7.51 | | |
| 300 | 40.01 | 12.51 | .264 | 1.80 |
| 360 | 40.00 | 13.29 | .256 | 1.78 |
| 905 | 40.00 | 19.17 | .206 | 1.77 |
| 1080 | 40.00 | 20.43 | .194 | 1.76 |
| 1320 | 40.00 | 22.22 | .179 | 1.77 |
| 1480 | 40.02 | 23.18 | .170 | 1.78 |
| 1620 | 40.00 | 24.01 | .163 | 1.78 |
| 1830 | 40.01 | 25.10 | .154 | 1.77 |
| 2575 | 40.03 | 28.05 | .128 | 1.77 |
| 2946 | 40.00 | 29.00 | .119 | 1.75 |
| | | | | 1.77 |

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(10) It is well known that monosubstituted epoxides undergo nucleophilic ring opening reactions almost exclusively at the primary carbon atom thus indicating that the unsubstituted carbon is much more susceptible to nucleophilic attack. Further discussion can be found in M. S. Newman, "Steric Effects in Organic Chemistry," J. Wiley and Sons, New York, N. Y., 1950, pp. 106–114.

(11) Melting points and boiling points are uncorrected.

(12) C. C. Price and P. F. Kirk, THIS JOURNAL, **75**, 2396 (1953).

(13) M. Delepine and P. Jaffeux, *Compt. rend.*, **172**, 158 (1921).

(14) G. M. Kosolapoff, "Organophosphorus Compounds," J. Wiley and Sons, New York, N. Y., 1950, p. 32.

**Kinetic Procedure.**—Solutions of the episulfide and triphenylphosphine of identical concentration were prepared and thermostated at 40 ± 0.1°. After thermal equilibrium had been reached the solutions were mixed. The progress of the reaction was followed by pipetting 1-ml. aliquots into a known excess of standard iodine solution (*ca.* 0.01 *N*) and rapidly back-titrating the excess iodine with standard triphenylphosphine solution (*ca* 0.01 *N*). Both standard solutions used a mixture of 75% benzene and 25% ethanol as the solvent. Two aliquots taken within the first 3 minutes were used to establish the initial concentration. The second-order rate constants were calculated from the equation $k = \left(\frac{1}{c} - \frac{1}{c_0}\right)\frac{1}{t}$. The data for a representative run on *cis*-2-butene episulfide are compiled below. The solvent used was N,N-dimethylformamide. The iodine concentration was 0.00935*N* and the iodine/triphenylphosphine titer was 0.91.

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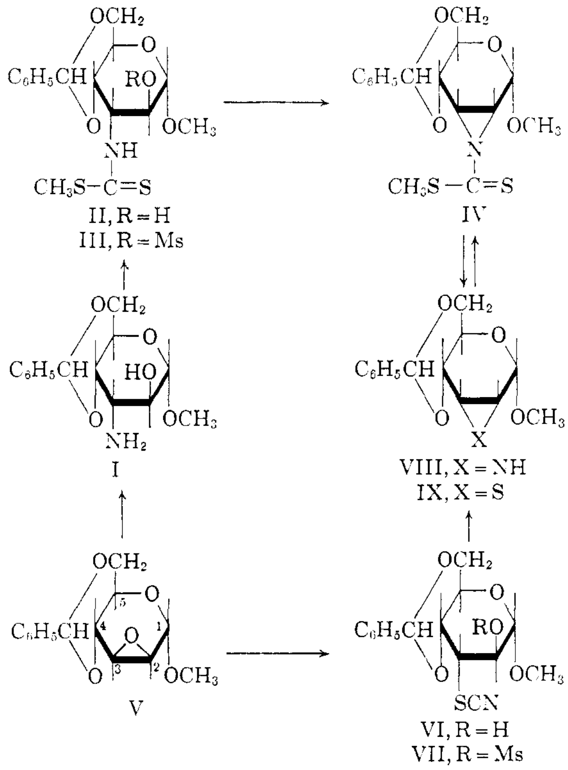
# COMMUNICATIONS TO THE EDITOR

## POTENTIAL ANTIRADIATION DRUGS. I. SUGAR ETHYLENIMINES AND EPISULFIDES.[1]

*Sir:*

Epoxides are among the most versatile intermediates in rare sugar synthesis.[2] In particular, those epoxides that are fused to sugar rings of either the pyranose or furanose form provide pathways for certain transformations that would otherwise be hindered or prevented by the very low $S_N2$ reactivity of the secondary sulfonate esters or secondary halides in sugar rings. The ethylenimines and episulfides that correspond to these fused epoxides ought to be equally interesting intermediates in sugar synthesis but have not been described previously.[3] In work directed toward the synthesis of sugars containing a β-mercaptoethylamine moiety, methods that should have general utility have been developed for the preparation of these unique sugar derivatives containing both types of three-membered rings, and are the subject of this Communication.

The 3-aminoaltroside I[4] with carbon disulfide and iodomethane in pyridine which contained triethylamine[5] gave a quantitative yield of the crude crystalline dithiocarbamate II, m.p.[6] 187–190° (Found: C, 52.2; H, 5.57; S, 17.2). Conventional sulfonylation in pyridine afforded 89% of the crystalline mesylate (III), m.p. 168–170° (Found: C, 46.0; H, 5.38; S, 20.7), which, when heated at 60° for 4–5 minutes with 1.10 equivalents of sodium methoxide in methanol–2-methoxyethanol, gave 65% of the thioacylated ethylenimine IV, m.p. 198–212° (Found: C, 54.4; H, 5.42; S, 18.4). Compound IV showed no infrared C═N absorption near 6.2 μ which would be expected for the isomeric thiazoline that would result from sulfur participation in the displacement.[7] The "complex neighboring group"[8] participation, then, went by predominant, if not exclusive, nitrogen attack in this instance to form a three-membered ring, although a pathway to the isomeric and less-strained five-membered thiazoline would seem to have been available. Reduction of IV with sodium borohydride–aluminum chloride in diglyme[9] gave an unstable solid which showed a positive nitroprusside reaction and SH infrared absorption at 3.9 μ and was evidently the result of reduction of the thiocarbonyl group. When this compound was



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[1] This work was carried out under the joint auspices of the Office of the Surgeon General, Medical Research and Development Command, under Contract No. DA49-193-MD-268 and of the Cancer Chemotherapy National Service Center, National Cancer Institute, under Contract No. SA43-ph-1892. The opinions expressed in this manuscript are those of the authors and not necessarily those of either sponsoring agency.

[2] For a recent review, see F. H. Newth, *Quart Revs.* (*London*), **13**, 30 (1959).

[3] A. M. Creighton and L. N. Owen, *J. Chem. Soc.*, 1024 (1960), recently have described the preparation of 5,6-dideoxy-5,6-epithio-1,2-O-isopropylidene-α-L-idose. The episulfide ring of this compound, however, is situated in the sugar ring side-chain, and would be expected to have a reactivity comparable to that of simple aliphatic episulfides.

[4] W. H. Myers and G. J. Robertson, This Journal, **65**, 8 (1943).

[5] J. C. Crawhall and D. F. Elliott, *J. Chem. Soc.*, 2071 (1951).

[6] Melting points given are for the analytical samples.

[7] The thioacylethylenimide IV could be rearranged to the isomeric thiazoline, which showed strong infrared absorption at 6.25–6.4μ (work to be published).

[8] S. Winstein and R. Boschan, This Journal, **72**, 4669 (1950).

[9] H. C. Brown and B. C. Subba Rao, *ibid.*, **77**, 3164 (1955).