**Registry No.**—I, 68-36-0; II, 122-52-1.

**Acknowledgments.**—The author is indebted to Mr. Claude H. Dungan for the nmr data and to Dr. Allen Kenyon for the thermogravimetric analysis.

## Desulfurization of Thietanes by Triphenylphosphine and Triethyl Phosphite

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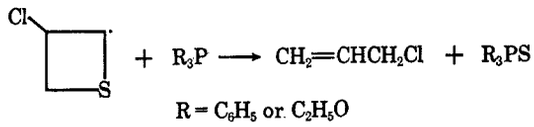
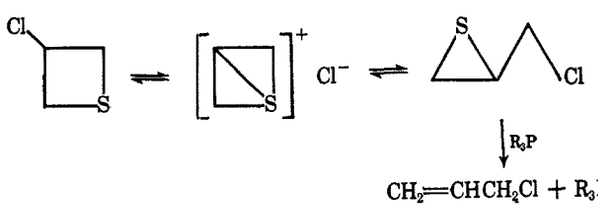
Trivalent phosphorus compounds such as triethyl phosphite or triphenylphosphine remove sulfur from episulfides (thiiranes) to give an olefin and the thionophosphate or phosphine sulfide.[2] We wish to report that certain four-membered ring sulfides (thietanes) also give up their sulfur to triphenylphosphine or triethyl phosphite, although less readily.

When 3-chlorothietane is treated with triphenylphosphine or triethyl phosphite, allyl chloride and triphenylphosphine sulfide or triethyl thionophosphate are produced. For example, in refluxing xylene (bp 137–140°) for 70 hr, a 93% yield of triphenylphosphine sulfide is obtained. 3-Hydroxythietane reacted much more slowly under the same conditions (34% of tri-



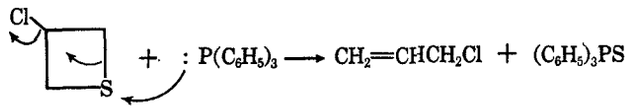

phenylphosphine sulfide after 115 hr in refluxing xylene), and thietane itself was desulfurized in low yield after a long reaction time (10% triphenylphosphine sulfide after 188 hr in refluxing xylene). Attempts to identify the organic products from the desulfurization of 3-hydroxythietane or thietane were not successful.

The desulfurization of 3-chlorothietane may proceed *via* chloromethylthiirane formed by rearrangement of 3-chlorothietane.[3] The desulfurization of chloromethylthiirane by triphenylphosphine in benzene was faster[4] than the desulfurization of 3-chlorothietane which indicates that, if the above scheme is correct, the slow




step is the rearrangement, which is not unreasonable considering the nonpolar nature of the solvent.

Alternatively, the reaction may be bimolecular.[5]




3-Hydroxythietane likewise may decompose to a cyclic ion which could rearrange to hydroxymethylthiirane which may be desulfurized to allyl alcohol. Both 3-hydroxythietane and thietane may undergo ring scission to mercaptans or mercapto radicals which can be desulfurized.[6] Possible three-carbon fragments from 3-hydroxythietane (allyl alcohol, *n*-propyl alcohol, isopropyl alcohol, acetone, propionaldehyde) were not detected by gas chromatography.

### Experimental Section

3-Hydroxythietane was prepared by a modification of the method of Sjöberg.[7] 3-Chlorothietane was prepared by the procedure of Martin and Anderson by treatment of 3-hydroxythietane with thionyl chloride in chloroform.[8]

**Reaction of Thietanes with Triphenylphosphine and Triethylphosphite.**—3-Chlorothietane (2.0 g, 0.018 mole) and triphenylphosphine (4.7 g, 0.018 mole) were dissolved in 10 ml of xylene in a 50-ml, round-bottomed flask connected to a condenser and a Dean–Stark separator which was in turn connected to a Dry Ice–acetone condenser to condense volatile materials. Benzene also can be used as a solvent but yields are lower. The mixture was refluxed for 70 hr at the end of which *ca* 0.5 g of material was obtained in the Dean–Stark trap. This material gave an immediate precipitate when treated with alcoholic silver nitrate. The liquid collected in the trap was identified as allyl chloride by comparison of its infrared spectrum with an authentic sample.

The residue in the reaction flask solidified when it was cooled. It was chromatographed on an alumina (Fischer, 80–200 mesh, activated at 110°) column with cyclohexane and benzene as eluents. A 93.5% yield of triphenylphosphine sulfide (4.96 g) was obtained. The sulfide was identified by its melting point (160–162°; lit.[9] mp 161°) and its infrared spectrum which was identical with that of an authentic sample.

The reactions with triethyl phosphite were done in the same way except that the solvent was not removed. The reaction mixtures were analyzed either by gas chromatography or fractionated under reduced pressure. Triethyl thionophosphate was obtained in yields of 40–66%.

The reactions of 3-hydroxythietane and thietane with triphenylphosphine and triethyl phosphite were done in the same way as the reaction of 3-chlorothietane. 3-Hydroxythietane and triphenylphosphine in refluxing benzene for 110 hr gave 4% triphenylphosphine sulfide; in refluxing xylene for 115 hr a 34% yield of the phosphine sulfide was obtained. Yields of 11 and 13% of triethyl thionophosphate were obtained when 3-hydroxythietane was refluxed in xylene for 66 and 90 hr, respectively. No triphenylphosphine sulfide was obtained when the phosphine and thietane itself were refluxed in benzene for 110 hr. In refluxing xylene for 188 hr a 10% yield of triphenylphosphine

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(2) C. C. J. Culvenor, W. Davies, and N. S. Heath, *J. Chem. Soc.*, 282 (1949); R. E. Davis, *J. Org. Chem.*, **23**, 1767 (1958); N. P. Neureiter and F. G. Bordwell, *J. Am. Chem. Soc.*, **81**, 578 (1959); D. B. Denney and M. J. Boskin, *ibid.*, **82**, 4736 (1960); R. D. Schuetz and R. L. Jacobs, *J. Org. Chem.*, **26**, 3467 (1961).

(3) J. C. Martin and D. J. Anderson, 139th National Meeting of the American Chemical Society, St. Louis, Mo., March 1961, Abstracts, p 31-O. The reverse rearrangement, probably through the bridged sulfonium ion, has been reported to occur in the alkaline hydrolysis of chloromethylthiirane to 3-hydroxythietane: E. P. Adams, K. N. Ayad, F. P. Doyle, D. O. Holland, W. H. Hunter, J. H. C. Nayler, and A. Queen, *J. Chem. Soc.*, 2665 (1960).

(4) After 9.5 hr a 77% yield of triphenylphosphine sulfide was obtained from chloromethylthiirane, whereas after 163.5 hr a 72% yield of the phosphine sulfide was obtained from 3-chlorothietane. Desulfurization of chloromethylthiirane by triethyl phosphite has been reported previously: R. D. Schuetz and R. L. Jacobs, *J. Org. Chem.*, **23**, 1799 (1958).

(5) We wish to thank the referee who suggested that the data in Table I are more in accord with second-order kinetics.

(6) F. W. Hoffman, R. J. Ess, T. C. Simmons, and R. S. Hanzel, *J. Am. Chem. Soc.*, **78**, 6414 (1956); C. Walling and R. Rabinowitz, *ibid.*, **81**, 1243 (1959); C. Walling, O. H. Basedow, and E. S. Savas, *ibid.*, **82**, 2181 (1960).

(7) B. Sjöberg, *Svensk Kem. Tidskr.*, **50**, 250 (1938); B. Sjöberg, *Ber.*, **75**, 15 (1942); D. C. Dittmer and M. E. Christy, *J. Org. Chem.*, **26**, 1324 (1961).

(8) We are indebted to Professor J. C. Martin for communicating the details of this procedure to us. Further details may be found in M. E. Christy, Ph.D. Thesis, University of Pennsylvania, 1961; S. M. Kotin, Ph.D. Thesis, University of Pennsylvania, 1962.

(9) W. Strecker and C. Grossmann, *Ber.*, **49**, 74 (1916).

sulfide was obtained from thietane and a reflux time of 185 hr with triethyl phosphite yielded 10% of triethyl thionophosphate.

**Comparison of Reactivity of Chloromethylthiirane and 3-Chlorothietane.**—A solution of chloromethylthiirane (4.0 g, 0.036 mole) and triphenylphosphine (9.5 g, 0.036 mole) in 100 ml of benzene was refluxed. Aliquots of 10 ml were taken at various times, the solvent was removed under vacuum, and the residue was chromatographed on an alumina column with cyclohexane and benzene. The weight of triphenylphosphine sulfide eluted from the column was converted into per cent yield. The same procedure was followed with 3-chlorothietane. The results are shown in Table I.

TABLE I

COMPARISON OF REACTIVITY OF 3-CHLOROTHIETANE AND CHLOROMETHYLTHIIRANE WITH TRIPHENYLPHOSPHINE IN REFLUXING BENZENE

| 3-Chlorothietane | | Chloromethylthiirane | |
|---|---|---|---|
| Time, hr | % $(C_6H_5)_3PS$ | Time, hr | % $(C_6H_5)_3PS$ |
| 8.5 | 19 | 9.5 | 77 |
| 22.5 | 26 | 22.25 | 82 |
| 46.5 | 40 | 46.25 | 84 |
| 60.5 | 49 | 70.25 | 81 |
| 84.5 | 58 | 94.25 | 85 |
| 163.5 | 72 | 162.25 | 85 |

**Registry No.**—Triphenylphosphine, 603-35-0; triethyl phosphite, 122-52-1; 3-chlorothietane, 6013-95-2; 3-hydroxythietane, 10304-16-2; chloromethylthiirane, 3221-15-6.

## Equilibration and Acid Hydrolysis of Biotin Sulfoxides[1a,b]

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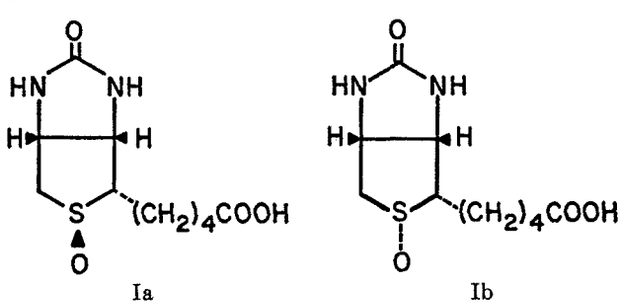
*Received November 2, 1966*

Biotin sulfoxides (Ia and b) have been considered to be intermediates in the microbiological degradation of biotin.[2] To supplement an understanding of the metabolism of these compounds, studies on the acid hydrolysis of biotin sulfoxides were carried out.




Ia Ib

biotin sulfoxide isomers

Whereas treatment with 1 *N* formic acid and 0.1 *N* hydrochloric acid did not affect biotin *d*-sulfoxide, partial epimerization of the sulfoxide grouping of the compound was obtained in 1 *N* hydrochloric acid (Figure 1). Acid-catalyzed racemization of other sulfoxides in 97% sulfuric acid[3] and in 12 *M* aqueous HCl–dioxane (1:2)[4] has been reported previously. Analogous results have been obtained by treatment of the *l*-sulfoxide under the same conditions. Equilibration of the *d*-sulfoxide follows clean pseudo-first-order kinetics in the beginning, with deviations starting after about 16 hr, mainly resulting from competition of hydrolysis reactions with the inversion. Under the conditions used the initial rate constants were $k_d = 1.38 \times 10^{-5}$ sec$^{-1}$ for inversion of the *d*-sulfoxide and $k_l = 0.47 \times 10^{-5}$ sec$^{-1}$ for the *l*-sulfoxide. The products formed showed $R_f$ values which were in agreement with those found for biotin *l*-sulfoxide or biotin *d*-sulfoxide, respectively, in both solvent systems used (see Table I). The ratio of *l*-sulfoxide to *d*-sulfoxide was determined to be 3:1 after a reaction time of 66 hr, which is in good agreement with the value for the equilibrium ratio calculated from initial rate constants $k_d$ and $k_l$. The reaction showed a remarkable specificity for catalysis by hydrogen chloride since both 1 *N* formic acid and 1 *N* sulfuric acid did not invert the configuration of biotin *d*-sulfoxide. This specificity is in agreement with similar results obtained by Mislow, *et al.*[4] These investigators postulated a mechanism for the HCl-catalyzed inversion of configuration of sulfoxides involving a symmetrical sulfur dichloride intermediate or transition state: $R_2SO + 2HCl \rightarrow R_2SCl_2 +$

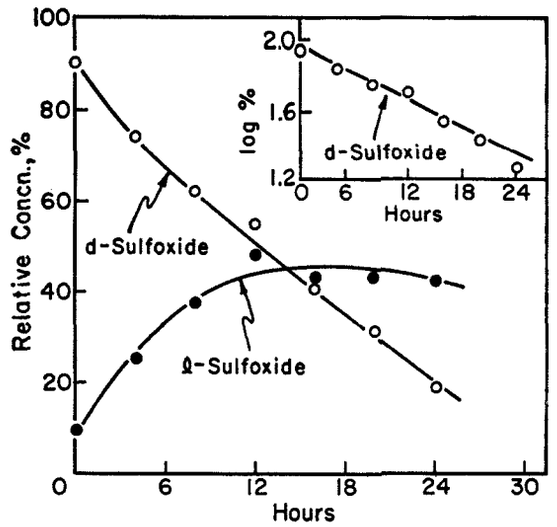



Figure 1.—Partial inversion of configuration of biotin *d*-sulfoxide ($c_0$ = 2 mg/ml of 1 *N* HCl, 100°, concentration given as % of radioactive material present).

TABLE I

PAPER CHROMATOGRAPHY OF BIOTIN ANALOGS

| Compd | $R_f$ values A[a] | B[b] |
|---|---|---|
| Biotin | 0.67 | 0.68 |
| Biotin sulfone | 0.28 | 0.20 |
| Biotin *d*-sulfoxide | 0.40 | 0.45 |
| Biotin *l*-sulfoxide | 0.25 | 0.38 |
| Diaminocarboxylic acid sulfate of biotin | 0.13 | 0.51 |

[a] Water-saturated 1-butanol. [b] 1-Butanol–methanol–benzene–water (2:1:1:1).

(1) (a) Presented, in part, at the 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1966; (b) supported, in part, by Research Grant AM-08721 from the National Institute of Arthritis and Metabolic Diseases, U. S. Public Health Service; (c) recipient of a Fulbright Travel Scholarship.

(2) R. N. Brady, H. Ruis, D. N. McCormick, and L. D. Wright, *J. Biol. Chem.*, **241**, 4717 (1966).

(3) S. Oae, T. Kitao, and Y. Kitaoka, *Chem. Ind.* (London), 291 (1961).

(4) K. Mislow, T. Simmons, J. T. Melillo, and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, **86**, 1452 (1964).