The Base-Catalyzed Autoxidation of Sulfoxides

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The base-catalyzed autoxidation of various sulfoxides has been studied at 80° in a potassium *t*-butoxide-hexamethylphosphoramide medium. Both carboxylic and sulfonic acids as well as other fragmentation products are produced. The rates of oxygen consumption and the nature of the products varied with sulfoxide structure. Possible explanations for the observed results are offered and their implication to the oxidation of organic sulfides under these conditions is discussed.

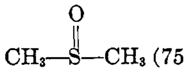
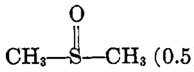
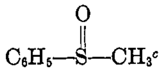
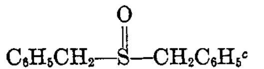
The autoxidation of organic sulfides under free-radical conditions has been the subject of several detailed studies.[1,2] Usually, alkyl and benzylic sulfides are resistant to oxidation by molecular oxygen in the absence of free-radical initiators. It has also been suggested that thiolsulfinates, sulfoxides, and α-keto sulfoxides, which are products of the free-radical autoxidation of sulfides, are responsible for the rapid decrease of sulfide autoxidation in the latter stages of reaction.[3] Previously, we have reported detailed studies on the base-catalyzed autoxidation of organic sulfides in polar solvents at low temperatures (room temperature and 80°).[4] Unlike the radical-induced reactions, the base-catalyzed oxidation of organic sulfides proceeds rapidly without any noticeable induction period. Diaralkyl ($ArCH_2$-S-CH_2Ar), aralkyl aryl ($ArCH_2$-S-Ar), aralkyl alkyl ($ArCH_2$-S-R), arylalkyl (Ar-S-R), and dialkyl (R-S-R) sulfides were converted to carboxylic acids, ketones, sulfonic acids, and olefins. Product distribution and yield were a function of the structure of the initial sulfide. In these studies, no evidence for the presence of sulfoxides as intermediate oxidation products could be obtained. Thus, it was concluded that sulfoxides were either unstable intermediates or they were not formed in these reactions. The present study was undertaken with the expectation of gaining further insight into this general area. It is specifically concerned with the base-catalyzed oxidation of sulfoxides in polar solvents.

Results and Discussion

Autoxidation studies were carried out on dimethyl sulfoxide (DMSO), phenyl methyl sulfoxide (PMSO), diphenyl sulfoxide (DPSO), and dibenzyl sulfoxide (DBSO) in the presence of excess base at 80°. Specific reaction conditions employed, product analyses, and yields are summarized in Table I. Initially, the oxidation of DMSO (neat) in the presence of KOH was studied at 80°. Methanesulfonic acid and carbon dioxide were identified as products of this reaction.[5] Reactions were next investigated in hexamethylphosphoramide (HMPA). DMSO and PMSO were oxidized in KO-*t*-Bu-HMPA at 80° to methanesulfonic acid and benzenesulfonic acid, respectively, and carbon dioxide. In these two experiments, the acid to CO_2 ratio varied from 0.92 to 1.18. Under the same conditions, DBSO was oxidized readily to benzoic acid and stilbene. DPSO, which is completely aromatic, showed no appreciable tendency to autoxidize under these conditions. In several of the experiments listed, no evidence for the presence of sulfones was observed by infrared spectroscopy. Sulfone bands at 925, 1135, and 1310 cm.$^{-1}$ were not present. In the DMSO and

TABLE I

REACTION CONDITIONS EMPLOYED AND PRODUCTS ISOLATED FROM VARIOUS SULFOXIDE OXIDATION REACTIONS AT 80°

Sulfoxide (mole)	Base (mole)	HMPA, ml.	Reaction time, hr.	Products (mole, % yield)[a]
 $CH_3-\overset{\overset{O}{\|}}{S}-CH_3$ (75 ml. neat)	KOH (0.15)	..	68	CH_3SO_3H[b] (0.001) CO_2 (0.0028)
 $CH_3-\overset{\overset{O}{\|}}{S}-CH_3$ (0.5)[c,d]	KO-*t*-Bu (0.15)	75	23	CH_3SO_3H[b,e] (0.011, 23) CO_2 (0.012, 24)
 $C_6H_5-\overset{\overset{O}{\|}}{S}-CH_3$[c]	KO-*t*-Bu (0.038)	25	69	$C_6H_5SO_3H$ (0.0103, 86.4) CO_2 (0.00882, 67)
 $C_6H_5CH_2-\overset{\overset{O}{\|}}{S}-CH_2C_6H_5$[c] (0.025)	KO-*t*-Bu (0.15)	75	20	C_6H_5COOH[f] (0.022, 88) $C_6H_5CH{=}CHC_6H_5$[f] (0.0061, 24)

[a] (Moles of product/mole of reactant) × 100. [b] Russell and co-workers have observed methane sulfonic acid and dimethyl sulfone as oxidation products from KO-*t*-Bu-DMSO mixtures. See ref. 5. [c] No evidence for sulfone formation by infrared. [d] Formic acid (infrared, mass spectroscopy) and formaldehyde (2,4-DNPH, m.p. 166°) were qualitatively identified. [e] Also verified by g.c. [f] Verified by isolation in previous studies.

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(1) D. Barnard, L. Bateman, and J. I. Cunneen, "Organic Sulfur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press Inc., New York, N. Y., 1961, Chapter 21.

(2) K. U. Ingold, *Chem. Rev.*, **61**, 563 (1961).

(3) D. Barnard, L. Bateman, E. R. Cole, and J. I. Cunneen, *Chem. Ind.* (London), 918 (1958).

(4) T. J. Wallace, H. Pobiner, and A. Schriesheim, *J. Org. Chem.*, **30**, 3147 (1965).

(5) G. A. Russell, E. G. Janzen, H.-D. Becker, and F. S. Smentowski, *J. Am. Chem. Soc.*, **84**, 2652 (1962).

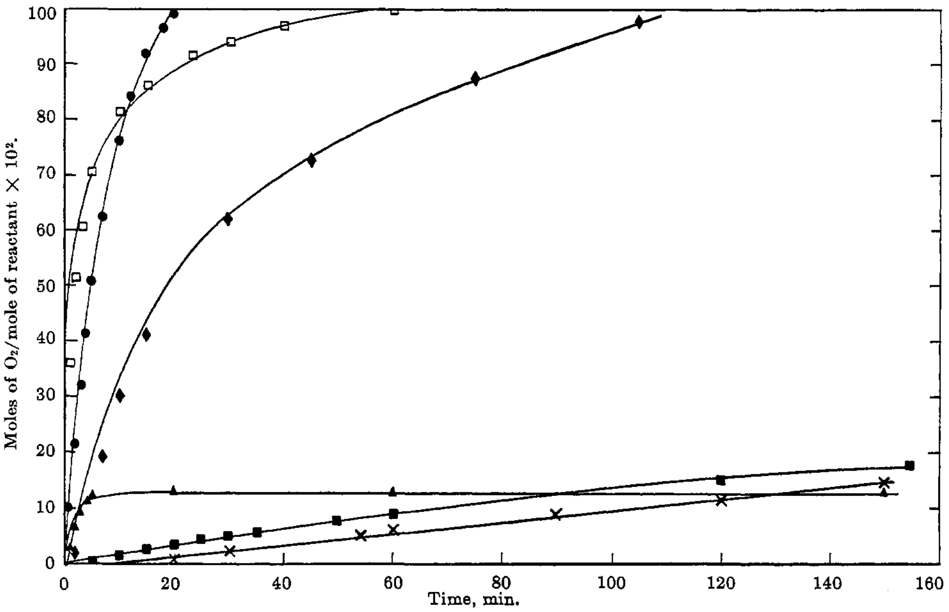


Figure 1.—Rates of oxygen consumption at 80° in HMPA: ●, dimethyl sulfoxide + KO-*t*-Bu; ◆, phenyl methyl sulfoxide + KO-*t*-Bu; ▲, dimethyl sulfone + KO-*t*-Bu; ■, dimethyl sulfoxide + KOH; ×, dimethyl sulfone + KOH; and □, dibenzyl sulfoxide + KO-*t*-Bu.

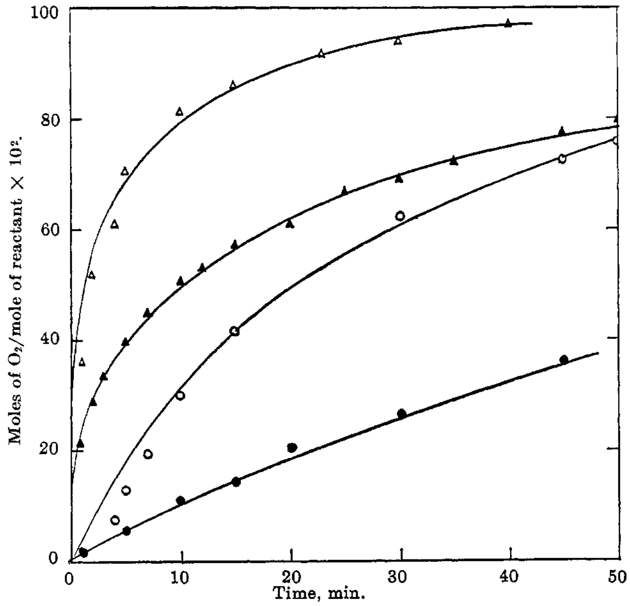


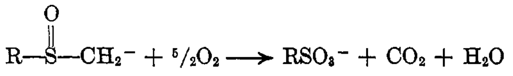
Figure 2.—Comparison of sulfide and sulfoxide reactivity in KO-*t*-Bu–HMPA at 80°: ●, $C_6H_5{-}S{-}CH_3$ + KO-*t*-Bu; ▲, $C_6H_5CH_2{-}S{-}CH_2C_6H_5$ + KO-*t*-Bu; ○, $C_6H_5{-}\overset{O}{\overset{\|}{S}}{-}CH_3$ + KO-*t*-Bu; and △, $C_6H_5CH_2{-}\overset{O}{\overset{\|}{S}}{-}CH_2C_6H_5$ + KO-*t*-Bu.

PMSO oxidations, formaldehyde and formic acid were qualitatively identified.

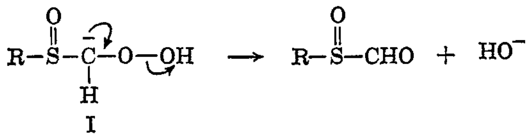
A comparison of the reactivity of the carbanions of the above sulfoxides toward molecular oxygen is shown in Figure 1 which contains a plot of moles of O_2 consumed/mole of reactant *vs.* time. Based on the initial rates of oxygen consumption, the ease of sulfoxide oxidation was DBSO > DMSO > PMSO. However, the reactivity difference between DMSO and PMSO appears to be statistical with respect to the methyl groups. Rate data for the oxidation of dimethyl sulfone in the presence of KOH and KO-*t*-Bu at 80° is also shown in Figure 1. The methyl sulfonyl carbanion ($CH_3SO_2CH_2^-$) was not oxidized readily in the presence of either base. Further, the rate of oxygen consumption by DMSO in the presence of KOH was slightly greater than that observed for dimethyl sulfone in the presence of KO-*t*-Bu.

A comparison of the reactivity of two sulfide–sulfoxide pairs is shown in Figure 2 for the KO-*t*-Bu–HMPA system at 80°. As indicated, the rates of oxygen consumption for DBSO and PMSO were much greater than those observed for their corresponding sulfides. Based on this data, it seems reasonable to conclude that sulfoxides are autoxidized more readily than sulfides in the presence of base.

The foregoing results allow certain conclusions to be made. The order of sulfoxide reactivity is consistent with initial oxidation of an α-sulfinyl carbanion. The molar ratio of sulfonic acid to carbon dioxide in the PMSO and DMSO reactions is close to unity. Thus, these two products probably arise from the same intermediate. The most probable over-all reaction is 1. Unstable peroxide derivatives are the probable intermediates. For example, intermediate I would produce an unstable aldehyde that would be an excellent source of sulfenate (RSO^-) ions. Intermediate II could yield sulfinate ions (RSO_2^-) by the path

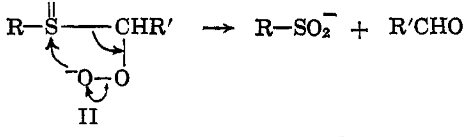


$$R{-}\overset{O}{\overset{\|}{S}}{-}CH_2^- + {}^5/_2O_2 \longrightarrow RSO_3^- + CO_2 + H_2O \qquad (1)$$



$$R{-}\overset{O}{\overset{\|}{S}}{-}\underset{H}{\underset{|}{C}}{-}O{-}OH \longrightarrow R{-}\overset{O}{\overset{\|}{S}}{-}CHO + HO^- \qquad (2)$$

I



$$R{-}\overset{O}{\overset{\|}{S}}{-}CHR'{-}O{-}O^- \longrightarrow R{-}SO_2^- + R'CHO \qquad (3)$$

II

R′ = H, alkyl or aryl

shown. Both anions would be readily converted to sulfonate (RSO_3^-) ions. In the case of DBSO, an intermediate of type II would be most reasonable and the decomposition products would be benzaldehyde and an α-toluenesulfinate ion. The latter would oxidize readily to the α-toluenesulfonate ion which is readily oxidized to benzoic acid under these conditions.[6] The present results also explain the absence of sulfoxides in our previous autoxidation studies on sulfides. Clearly, if sulfoxides or sulfoxide derivatives are intermediates in sulfide autoxidations, their absence in the final product is due to preferential autoxidation during the reaction. As general conclusions, it is suggested that DMSO, PMSO, and other aryl methyl sulfoxides are oxidized according to eq. 2. DBSO and other diaralkyl sulfoxides and aralkyl aryl sulfoxides are most likely oxidized by eq. 3. Aralkyl methyl sulfoxides could be oxidized by both paths.

The above generalizations are limited to sulfoxides which contain only α-carbon–hydrogen bonds. If the sulfoxide contains β-carbon–hydrogen bonds the situation will be more complex. For example, the initial rates of oxygen consumption for *n*-butyl sulfoxide and sulfone in KO-*t*-Bu–HMPA at 80° are shown in Figure 3. Both compounds oxidize at essentially the same rate and these rates are comparable with that observed for DBSO and far greater than that observed for dimethyl sulfone (Figure 1). The low reactivity of dimethyl sulfone is probably due to the resonance stabilization of the methyl sulfonyl carbanion. On the other hand, the intermediates formed from the butyl compounds are unstable and rapidly β eliminate sulfenate and sulfinate ions.[7,8] The latter are probably highly unstable and readily autoxidized. Thus, the rapid and comparable rates of oxygen consumption observed for the two butyl compounds are probably due to these elimination products and not the initial sulfoxide and sulfone. As indicated in Table I, stilbene is also formed during the autoxidation of DBSO. This product most likely arises by a 1,3-rearrangement–β-elimination sequence which has previously been observed with DBSO in the absence of oxygen.[9,10]

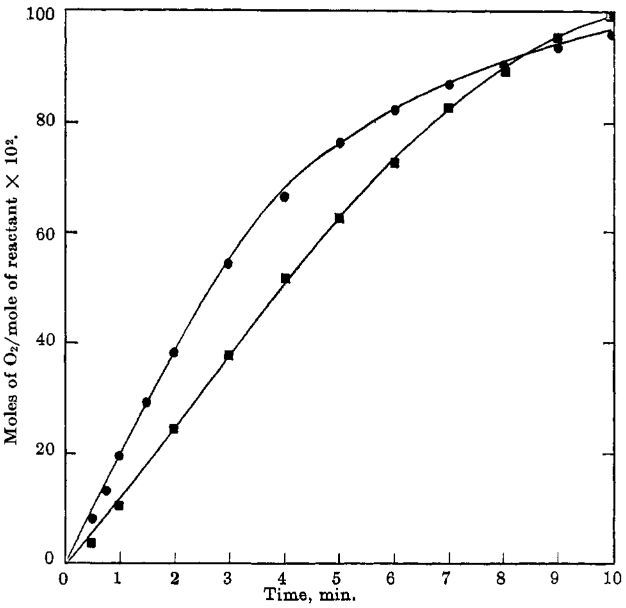


Figure 3.—Comparison of rates of oxygen consumption for *n*-butyl sulfone and *n*-butyl sulfoxide in KO-*t*-Bu–HMPA at 80°: ●, *n*-butyl sulfone; and ■, *n*-butyl sulfoxide.

Experimental Section

Reagents.—Dimethyl sulfoxide (Crown Zellerbach) and hexamethylphosphoramide (Eastman Organic Chemicals) were purified by distillation under reduced pressure over Linde 13-X Molecular Sieves to remove any adsorbed water. The sieves had previously been conditioned by calcination at 400° for 4 hr. Both reagents were stored continuously in a moisture-free drybox. Potassium *t*-butoxide was obtained from the Mine Safety Appliance Co. as the sublimed white powder and was at least 98.5% pure. Di-*n*-butyl sulfoxide, di-*n*-butyl sulfone, and dibenzyl sulfoxide were obtained from the Columbia Organic Chemicals Co. as the reagent grade materials. Diphenyl sulfoxide was obtained from the Eastman Organic Chemical Co. as the reagent grade material (m.p. 71°). Phenyl methyl sulfoxide was obtained by oxidation of the corresponding sulfide in a hydrogen peroxide–acetic acid medium.

Oxidation Experiments.—All base–solvent systems were made up to the appropriate molarity under nitrogen in a heavy-walled Pyrex flask equipped with a side arm. The reactant was added to the reaction flask, and the flask was sealed under nitrogen, removed from the drybox, and transferred to the oxidation apparatus. Oxygen was stored in a polyethylene balloon under 1-atm. pressure and passed through a wet-test meter and into a calcium chloride drying tower and finally through a water-cooled Friedrichs condenser and into the reaction flask containing the reaction mixture. The system was flushed with oxygen through the flask side arm, the side arm was sealed, and an equilibrium pressure was established. The reaction was initiated by stirring at 1300 r.p.m. The volume of oxygen consumed as a function of time was determined from the wet-test meter which allows an estimation of the volume of gas consumed within ±1 cc. With this method, a constant oxygen pressure of 1 atm. was maintained above the system. All reactions were allowed to proceed until no apparent oxygen consumption was observed. This oxidation technique was recently described in greater detail.[11]

Quantitative Determination of Products.—Quantitative analysis of all products and starting materials was carried out according to the method of Pobiner, Wallace, and Hofmann.[12] Two procedures were employed. One involves an extraction–ion exchange–infrared procedure and the other an extraction–ultraviolet procedure. Both methods rely on initial homogenization with water and subsequent extraction with cyclohexane to remove the starting material. The latter removes any spectral interference during the determination of acidic products. The acidic products remain as their acid salts in the aqueous–HMPA phase and are subsequently liberated by acidification with hydrochloric acid. If the acid is aromatic it can be quantitatively determined directly by ultraviolet spectroscopy from standard curves. If the acidic material is aliphatic or presents a weak ultraviolet absorption, it is determined by the ion exchange–infrared method. This involves treating the aqueous phase with Amberlite LA-2 anion-exchange resin. The free acid is extracted with CCl_4 and quantitatively determined by infrared spectroscopy. These methods were accurate to within 95–99% for all products isolated and identified.

Identification of Products.—The structure of the products reported have been confirmed by various methods following isolation by conventional methods. These methods are summarized below for each product. (a) Benzoic acid was identified by its characteristic infrared and ultraviolet spectra and its melting point (122–123°). (b) Stilbene was confirmed by its characteristic ultraviolet and infrared spectra and its melting point (124°). (c) Benzenesulfonic acid was confirmed by its characteristic ultraviolet and infrared spectra and the preparation of its

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[6] T. J. Wallace, H. Pobiner, and A. Schriesheim, *J. Org. Chem.*, **29**, 888 (1964).

[7] T. J. Wallace, J. E. Hofmann, and A. Schriesheim, *J. Am. Chem. Soc.*, **85**, 2739 (1963).

[8] J. E. Hofmann, T. J. Wallace, and A. Schriesheim, *ibid.*, **86**, 1561 (1964).

[9] T. J. Wallace, *et al.*, *Proc. Chem. Soc.*, 137 (1963).

[10] T. J. Wallace, *et al.*, *J. Chem. Soc.*, 1271 (1965).

[11] T. J. Wallace, W. Bartok, and A. Schriesheim, *J. Chem. Educ.*, **40**, 39 (1963).

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phenylhydrazinium salt (m.p. 178–180°, lit.[13] m.p. 170°). (d) Carbon dioxide was determined by the infrared technique of Pobiner[14] which is both qualitative and quantitative. (e) Methanesulfonic acid was identified by its infrared spectrum and by g.c. comparison of retention times using an authentic sample (2-ft. silicone rubber column, 30 wt. % on Chromosorb W, 0.25-in. stainless steel tubing, temperature programmed at 9°/min. on an F & M Model 609 flame-ionization gas chromatograph). (f) Formic Acid was identified by g.c. comparison with an authentic sample.

Acknowledgment.—The author wishes to acknowledge the technical assistance of Mr. H. Pobiner on several of the analytical techniques employed.

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The Reaction of Trialkyl Phosphites with Maleate Esters

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The reaction of trialkyl phosphites with monomethyl maleate at temperatures below 100° has been investigated and a mechanism has been suggested to account for the products of the reaction. Tetraalkylphosphonosuccinates were the main reaction product. Dialkyl maleates and/or fumarates, carbon dioxide, and trialkylphosphonopropionates were found in equivalent amounts as major by-products. Changes in the nature of the alkyl group of the phosphorous ester has been shown to affect the rate of the reaction but not to change the nature of the products appreciably. The suggested mechanism involves a simultaneous 1,4 nucleophilic substitution by the tertiary phosphite at both electrophilic carbon atoms of the α,β-unsaturated maleate system followed by an Arbuzov-like rearrangement of the intermediate adduct. Substitution β to the carboxylic acid group is suggested to result in the formation of the tetraalkylphosphonosuccinate while the by-products result from alternate substitution β to the carbomethoxy group with simultaneous esterification of the monomethyl maleate and decarboxylation of the resulting intermediate β-dialkylphosphono-β-carboxypropionic ester. Experimental evidence is presented to support the suggested mechanism.

The first report of the reaction of trialkyl phosphites with acrylic and methacrylic acids, by Kamai and Kukhtin,[2] was subsequently followed by the disclosure of similar reactions with other α,β-unsaturated systems.[3] Attempts to extend the reaction to maleic acid and to monoalkyl maleates were unsuccessful, however.[4] During this period, the mechanism for the reaction has been the subject of discussion.[5]

An investigation of the reaction of trialkyl phosphites with monoalkyl maleates was subsequently undertaken in these laboratories during the preparation of phosphorus-containing unsaturated polyesters.[6] These initial investigations have now been extended with the objective of studying the mechanism of the reaction. Although this report deals primarily with the reaction of trimethyl phosphite (I) and monomethyl maleate (II), the effect of various phosphite substituents on the reaction has also been investigated.

TABLE I

G.C. ANALYSIS OF THE REACTION MIXTURE FROM MONOMETHYL MALEATE AND TRIMETHYL PHOSPHITE

	%
Trimethyl phosphite	0.7
Dimethyl phosphonate	1.6
Dimethyl methylphosphonate	7.4
Dimethyl fumarate and/or maleate[a]	16.5
Trimethyl phosphonopropionate	18.7
Tetramethyl phosphonosuccinate	64.0
Unknown	0.7
Carbon dioxide[b]	17.8

[a] This method does not distinguish between fumarate or maleate since both compounds appear at the same place in the chromatogram. [b] The carbon dioxide was determined by absorption in aqueous sodium hydroxide during the reaction followed by back titration with acid.

Reaction of Trimethyl Phosphite with Monomethyl Maleate.—The identification of trimethyl phosphonopropionate (III) as a by-product of this reaction by gas chromatography has already been reported.[6] The detailed analysis of the crude reaction mixture using a recently reported gas chromatographic procedure[7] is now summarized in Table I. It can be seen from these data that tetramethyl phosphonosuccinate (IV) is confirmed as the main reaction product, while the phosphonopropionate III composes 18.7% of the crude reaction mixture. Dimethyl fumarate (V), and/or maleate (VI), and carbon dioxide (VII) were also products of the reaction as previously reported,[6] in yields almost equivalent to that of III. It is interesting to note that three reaction products, III, IV, and V, quantitatively account for all the maleate II originally charged to the reaction mixture.

The presence of the phosphonopropionate III in the chromatogram was determined by the usual technique of adding known amounts of authentic III to a previously analyzed crude reaction mixture and noting a corresponding increase in the g.c. peak. The yield of the fumarate V was found to be in good agreement with the yield reported[6] by simple distillation of the reaction mixture. The reaction and reaction products are summarized in Chart I.

Isomerization of Dimethyl Maleate.—Initial attempts to suggest a mechanism to account for the experimental facts were centered around a logical explanation for the formation of dimethyl fumarate.

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[1] To whom inquiries should be directed.

[2] G. Kamai and V. A. Kukhtin, *J. Gen. Chem. USSR*, **27**, 2431 (1957).

[3] (a) G. Kamai and V. A. Kukhtin, *ibid.*, **27**, 2436 (1957); (b) V. A. Kukhtin and K. M. Orekhova, *ibid.*, **30**, 1539 (1960); (c) B. A. Arbuzov and V. M. Zorostrava, *Bull. Acad. Sci. USSR*, 962 (1960); (d) V. A. Ginsberg and A. Ya. Yakubovich, *J. Gen. Chem. USSR*, **30**, 3936 (1960).

[4] G. Kamai and V. A. Kukhtin, *Tr. Kazansk. Khim.-Tekhnol. Inst.*, **23**, 133 (1957); *Chem. Abstr.*, **52**, 9948 (1958).

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