$\lambda_{max}^{dilute\ NaOH}$ 393; λ_{max}^{Nujol} 3.22, 6.04, 6.30, 7.78, 8.08, 8.58–8.80, 9.85, 10.7, 11.35, 12.18, 12.95, 13.6–13.9 μ.

Antimicrobial Assay.—These were carried out as previously described[8a] using a representative selection of bacteria, fungi, and actinomycetes. Compounds **8** and **9** were inactive at 50 μg/ml. The minimum inhibitory concentrations of **4** and **3** in μg/ml are given in parentheses after the microorganisms; a dash means inactive at 50 μg/ml, an asterisk indicates static activity: *Trichophyton mentagrophytes* 171 (25*) (25*), *Sarcina lutea* 14 (–) (20), *Corynebacterium fimi* 22 (–) (20), *Mycobacterium smegmatis* 607 (25*) (50), *M. rhodochrous* 271 (5*) (50), *Norcardia asteroides* 3409 (5*) (40), *N. coeliaca* 3520 (20*) (50*), *Actinoplanes* sp. W13 (25*) (50), *Microellobosporia cinerea* 3855 (–) (50*).

Acknowledgments.—The author wishes to thank Mrs. M. P. Lechevalier for invaluable guidance in fermentation procedures and for testing the pure substances against microorganisms. The excellent technical assistance of Mrs. Eva M. Fekete is acknowledged. The author is grateful to Dr. Y. Okami for an authentic sample of griseolutic acid, to Dr. R. Brown for compound **8**, to Dr. W. D. Celmer for aureothricin, and, especially, to Dr. B. C. Das and Dr. E. Lederer for the mass spectrum of compound **7**.

Synthesis and Selected Reactions of 3-Methyl-2,5-dihydrothiophene 1-Oxide[1]

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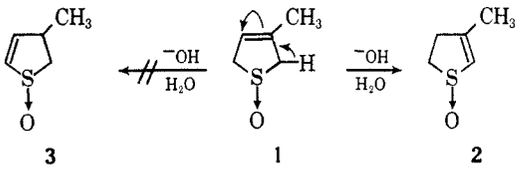
As an extension of the studies with the dihydrothiophene 1-oxides,[3] we have prepared the previously unknown 3-methyl-2,5-dihydrothiophene 1-oxide (**1**) and have investigated some selected reactions of this compound.

Sulfoxide **1** was obtained by the hydrogen peroxide oxidation of the corresponding sulfide which had been prepared by a known method[4] and purified using the aqueous sulfuric acid technique developed in our laboratory.[3] The structure of **1** was supported by elemental analysis, spectral data, and by chemical conversion to the well-characterized sulfone.[5]

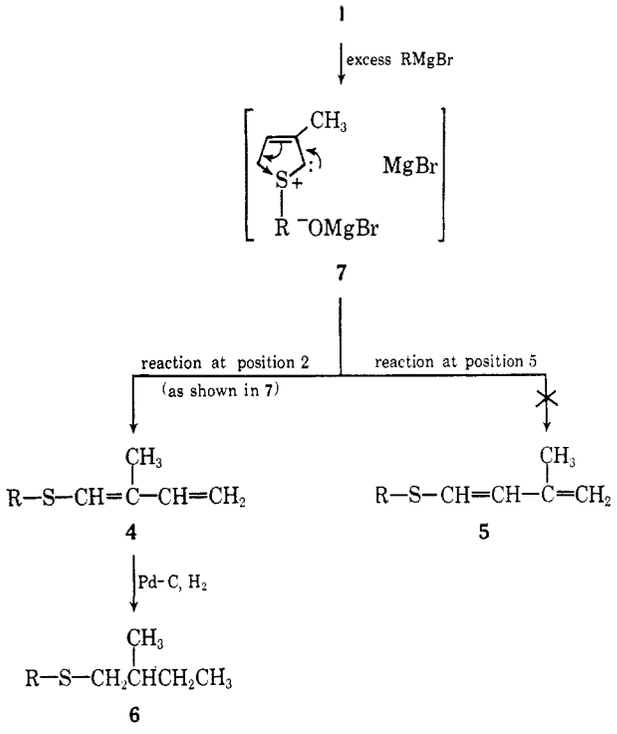
The behavior of **1** under alkaline conditions was studied to determine if isomerization of the olefinic bond would occur as was observed with the corresponding sulfone.[6] On treatment with 0.5 *N* sodium hydroxide, **1** underwent partial isomerization to give 3-methyl-4,5-dihydrothiophene 1-oxide (**2**). Sulfoxide **2** was not isolated; however, it was detected in-



3 **1** **2**

directly in two ways. First, half of a chloroform extract of the aqueous reaction mixture was treated with 30% hydrogen peroxide and the sulfones corresponding to **1** and **2** were identified by gas–liquid partition chromatography (glpc). The other half of the organic extract was treated with 48% hydriodic acid, and the sulfides corresponding to **1** and **2** were identified by glpc analysis. Results using this technique indicated that after 96 hr or longer, **1** and **2** were present in the original reaction mixture in a ratio of 1.8:1. No evidence for formation of the isomeric 3-methyl-2,3-dihydrothiophene 1-oxide (**3**) was obtained.

The behavior of **1** in the presence of Grignard reagents was especially interesting since reaction at the nonequivalent α-carbon atoms could yield the two isomeric butadienyl sulfides **4** and **5** *via* ring cleavage. When **1** was treated with excess phenyl- and *n*-propylmagnesium bromide, 1-phenylthio- and 1-*n*-propyl-



4a and **6a**, R = C_6H_5
4b and **6b**, R = *n*-C_3H_7

thio-2-methyl-1,3-butadiene (**4a** and **4b**) were obtained in 70 and 49% yield, respectively. These dienyl sulfides readily polymerized on standing at room temperature but were stable for extended periods when stored in the dark at 0°. No by-products were detected in either reaction.

The general dienyl sulfide structure of these compounds was supported by analytical data and by ultraviolet absorption at 288 mμ (ϵ 21,700) for **4a** and at 281 (17,300) for **4b**. Strong absorption at 6.19 and 6.31 μ in the infrared spectrum of **4a** and at 6.18 in the

(1) Presented at the Southeastern Regional Meeting of the American Chemical Society, Louisville, Ky., Oct 1966.

(2) (a) Abstracted in part from the Ph.D. dissertation of D. W. Kreh, Virginia Polytechnic Institute, 1966; (b) to whom any correspondence should be addressed: Building 231, Tennessee Eastman Co., Kingsport, Tenn., 37662; (c) George Mason College, Fairfax, Va. 22030.

(3) (a) R. C. Krug and D. E. Boswell, *J. Heterocyclic Chem.*, **4**, 309 (1967); (b) D. E. Boswell, Ph.D. Dissertation, Virginia Polytechnic Institute, Blacksburg, Va., 1963.

(4) (a) S. F. Birch and D. T. McAllan, *J. Chem. Soc.*, 3411 (1951). (b) In our laboratory, a ternary mixture of unrefined neutral sulfides present in the ratio of 1:3:16 was obtained. The major component was the desired 3-methyl-2,5-dihydrothiophene. The middle component was the 4,5-dihydro isomer while the minor component was most probably the theoretically possible, but as yet uncharacterized, 2,3-dihydro isomer.

(5) R. L. Frank and R. P. Seven, *Org. Syn.*, **3**, 499 (1955).

(6) J. Böesken and E. de Roy van Zuydewijn, *Proc. Acad. Sci.* (Amsterdam), **40**, 23 (1937).

spectrum of **4b** further substantiated this structure. A terminal —CH=CH_2 group was indicated by strong absorptions at 10.11 and 11.05 μ in the spectrum of **4a** and at 10.10 and 11.11 μ in that of **4b**. Interpretation of the nmr data also supported this general structure and suggested the presence of a methyl group at C-2 of the diene moiety.

Conclusive proof of structure was obtained by identification of the corresponding saturated sulfides obtained on catalytic reduction of the butadienyl sulfides. The saturated sulfides were shown to be 1-phenylthio- and 1-*n*-propythio-2-methylbutane (**6a** and **6b**) by comparison of their physical and spectral properties with those of authentic samples of **6a** and the previously unreported **6b**. Spectral properties of authentic samples of the saturated sulfides corresponding to dienyl sulfide structure **5** were markedly different from those of **6a** and **6b**.

Results of the Grignard reactions can be explained by considering formation of the sulfonium salt **7** which undergoes proton abstraction at position 2 followed by cleavage of the carbon–sulfur bond at position 5. The formation of vinyl methyl sulfide and ethylene on treatment of S-methyltetramethylenesulfonium iodide with phenyllithium has been explained in a like manner.[7] Exclusive proton loss at the more sterically hindered position 2 in both the Grignard and isomerization reactions can be rationalized in terms of the electronic effect of the methyl group on the olefinic bond of **1** and the resulting increased acidity of the hydrogen atoms at position 2 over those at position 5.[8] Similar reasoning has been used to explain stereospecific reactions of the corresponding sulfone.[9]

Experimental Section[10]

3-Methyl-2,5-dihydrothiophene 1-Oxide (1).—3-Methyl-2,5-dihydrothiophene was prepared in 13% yield by the reduction of 3-methylthiophene with sodium and methyl alcohol in liquid ammonia. The unrefined reaction products were treated with 50% sulfuric acid in isopentane and the desired 2,5-dihydro isomer was distilled at 144° (718 mm), n^{20}D 1.5192 (lit.[4a] bp 147.5° (760 mm), n^{20}D 1.5196). The mercuri chloride derivative from this sulfide was obtained in 84% yield, mp 125–127° (lit.[4a] mp 127.5–128°).

A well-stirred solution of 10.0 g (0.10 mole) of 3-methyl-2,5-dihydrothiophene in 40 ml of redistilled acetone was cooled to 0° in an ice bath and was treated with 14.7 g of 30% hydrogen peroxide (4.42 g, 0.13 mole hydrogen peroxide) while maintaining the reaction temperature below 8°. The resulting solution was allowed to warm to room temperature and to stand for 60 hr. The solution was concentrated by flash evaporation and the residue was extracted with two 35-ml portions of chloroform. The organic extracts were combined, dried, and concentrated. Vacuum distillation of the residue yielded 8.2 g of colorless distillate, bp 60–62.5° (0.12 mm). Two redistillations afforded 6.6 g (57%) of colorless **1**: bp 94–96° (0.95 mm); n^{25}D 1.5296. Redistillation of this material from powdered calcium hydride gave an analytical sample: bp 123° (4.7 mm); n^{25}D 1.5298; d^{25}_4 1.159; infrared $\lambda_{max}^{CCl_4}$ 3.28, 3.44, 6.02, 6.95, 7.15, 7.24, 7.67, 8.17, 8.83, 9.50, 9.82, 11.25, and 11.65 μ; nmr signals (neat), broad absorption at τ 4.54 (1 H), quartet at 6.62 (J = 17 cps, 4 H), and broad absorption at 8.29 (3 H).

Anal. Calcd for C_5H_8OS: C, 51.69; H, 6.94; S, 27.60. Found: C, 51.37; H, 7.19; S, 27.83.

A similar experiment carried out on a preparative scale using 73.4 g (0.73 mole) of 3-methyl-2,5-dihydrothiophene and 99.0 g of 30% hydrogen peroxide afforded **1** in 64% yield.

A 3.1-g (0.027 mole) sample of **1** in 25 ml of glacial acetic acid was treated with 3.98 g of 30% hydrogen peroxide, and the resulting solution was heated to reflux for 1.5 hr. Volatile material was removed on a steam bath at *ca.* 25 mm and the residue was dissolved in benzene. The solution was dried, filtered, and warmed on a hot plate, and petroleum ether (bp 30–60°) was added until the solution became turbid. Filtration of the chilled solution afforded 2.4 g (68%) of crude 3-methyl-2,5-dihydrothiophene 1,1-dioxide. A single recrystallization from methyl alcohol gave white flaky crystals, mp and mmp 62–63° (lit.[5] 63.5–64°).

A solution of 0.579 g (5 mmoles) of **1** in 10 ml of water was treated slowly with 2.66 g of 48% hydriodic acid (1.27 g, 0.01 mole of hydrogen iodide). This solution was stirred for 0.5 hr, cooled, and extracted with a single 30-ml portion of petroleum ether. The gas chromatogram (15% tricresyl phosphate, 75°) of this extract showed the presence of only 3-methyl-2,5-dihydrothiophene.

Base-Catalyzed Isomerization of 1.—A solution of 2.2 g (0.02 mole) of **1** in 100 ml of 0.5 *N* sodium hydroxide was stirred periodically and maintained at 25°. After 72 hr, a 25-ml portion of the alkaline solution was withdrawn and extracted with three 25-ml portions of chloroform. The combined extracts were divided into two equal portions and each was concentrated by flash evaporation. One residue was dissolved in 10 ml of acetone and treated with 0.40 g of 30% hydrogen peroxide (0.12 g, 3.5 mmoles of hydrogen peroxide). After a 4-hr reflux period, glpc analysis (6.3% Carbowax 1500, 135°) of this solution showed the presence of 3-methyl-2,5- and 3-methyl-4,5-dihydrothiophene 1,1-dioxide in a 3.0:1 ratio. The second residue was dissolved in 10 ml of water and treated with 1.34 g of 48% hydriodic acid (0.64 g, 5 mmoles of hydrogen iodide). This solution was stirred for 0.5 hr, cooled, and extracted with 10 ml of petroleum ether. Glpc analysis (15% tricresyl phosphate, 75°) showed the presence of 3-methyl-2,5- and 3-methyl-4,5-dihydrothiophene in a 2.8:1 ratio.

Another 25-ml portion of the original reaction mixture was withdrawn after 96 hr and worked up and reduced in the previous manner. Glpc analysis of the reduction products showed the presence of the 2,5- and 4,5-dihydro sulfide isomers in a 1.8:1 ratio. Similar work-up after 120 hr showed the ratio of reduction products to be unchanged.

1-Phenylthio-2-methyl-1,3-butadiene (4a).—To a well-stirred Grignard reagent prepared from 62.8 g (0.40 mole) of bromobenzene and 9.7 g (0.40 g-atom) of magnesium turnings in 325 ml of tetrahydrofuran was slowly added 11.6 g (0.10 mole) of **1** in 75 ml of tetrahydrofuran. The reaction mixture was stirred at 0° for 1 hr, and after warming to 25° was stirred for 20 hr at room temperature. The mixture was cooled to 0° and carefully hydrolyzed with 19.6 g of concentrated sulfuric acid in 325 ml of ice water. The aqueous layer was extracted with two 100-ml portions of ethyl ether. The combined organic layers were washed with 50 ml of water, dried, and concentrated. Distillation of the residual oil yielded 13.4 g of pale yellow liquid: bp 77–79° (0.15 mm). Redistillation of this material afforded 12.3 g (70%) of colorless **4a**: bp 77° (0.15 mm); n^{25}D 1.6192; d^{25}_4 1.0329; ultraviolet λ_{max}^{EtOH} 288 mμ (ϵ 21,700); infrared $\lambda_{max}^{CCl_4}$ 3.26, 3.32, 3.43, 5.56, 6.19, 6.31, 6.76, 6.94, 7.25, 7.54, 7.70, 8.37, 9.17, 9.46, 9.72, 10.11, 11.05, 11.75, 12.20, 13.71, 14.29, and 14.50 μ; nmr signals (neat), multiplet between τ 3.00–3.43 (6 H), multiplet between 4.09–4.40 (1 H), multiplet between 5.06–5.60 (2 H), doublet at 8.58 (J = 1.0 cps, 1.5 H), and doublet at 8.62 (J = 1.0 cps, 1.5 H). Glpc analysis (15% Dow 550, 100–225° at 10°/min) showed only one peak.

Anal. Calcd for $C_{11}H_{12}S$: C, 74.94; H, 6.88; S, 18.19. Found: C, 74.90; H, 6.97; S, 17.97.

1-*n*-Propylthio-2-methyl-1,3-butadiene (4b).—This material

(7) F. Weygand and H. Daniel, *Chem. Ber.*, **94**, 3145 (1961).

(8) Alternatively, sulfoxide **3** and dienyl sulfides of structure **5** may have been formed yet not survived the reaction, isolation, or detection conditions. In the isomerization reaction for example, **3** may have gone undetected if it were linked in an equilibrium process with the undoubtedly more thermodynamically stable **1** and **2**.

(9) R. C. Krug, J. A. Rigney, and G. R. Tichelaar, *J. Org. Chem.*, **27**, 1305 (1962); (b) F. E. Didot, M. S. Thesis, Virginia Polytechnic Institute, Blacksburg, Va., 1957.

(10) Infrared spectra were recorded on a Beckman IR-5 spectrophotometer. Ultraviolet spectra were recorded on a Beckman DK-2A ratio recording spectrophotometer. The nmr spectra were recorded on a Varian A-60 spectrometer using TMS as an external standard. Glpc analyses were carried out with a Wilkens Aerograph Model 204 instrument equipped with a Sargent Model SR 1-mv full scale recorder. Gas Chrom Z was used as the solid support for all columns. Organic extracts were dried using anhydrous magnesium sulfate and solutions were concentrated *in vacuo*. Melting points are corrected. Boiling points are uncorrected. Elemental analyses were carried out by Galbraith Laboratories, Inc., Knoxville, Tenn.

was prepared from 1-bromopropane, magnesium turnings, and **1** as described in the previous experiment. The exit line from the reaction flask was connected to a vessel containing 25 ml of bromine in 100 ml of chloroform to trap any by-product propene. After stirring for 15 hr at 25°, the mixture was cooled to 0° and hydrolyzed with an ice-cold solution of 10.7 g of ammonium chloride in 15 ml of water. The mixture was allowed to warm to room temperature, and the aqueous layer was extracted with two 100-ml portions of ethyl ether. The combined organic layers were washed with 50 ml of water, dried, and concentrated. Vacuum distillation of the residue yielded 8.2 g of liquid, bp 75–78° (18 mm). Redistillation afforded 6.9 g (49%) of colorless **4b**: bp 85° (20 mm); $n^{25}D$ 1.5233; d^{25}_4 0.8993; ultraviolet λ_{max}^{EtOH} 281 mμ (ε 17300); infrared $\lambda_{max}^{CCl_4}$ 3.25, 3.40, 5.54, 6.18, 6.88, 7.03, 7.25, 7.74, 8.06, 8.36, 9.47, 10.10, 11.11, and 11.60 μ; nmr signals (neat), multiplet between τ 3.13–3.64 (1 H), broad singlet at 4.37 (1 H), multiplet between 4.91–5.33 (2 H), triplet at 7.65 (J = 8.0 cps, 2 H), doublet at 8.44 (J = 1.0 cps, 3 H), multiplet between 8.54–8.94 (2 H), and triplet at 9.30 (J = 8.0 cps, 3 H). Glpc analysis (15% Dow 550, 50–175° at 10°/min) showed only one peak.

Anal. Calcd for $C_8H_{14}S$: C, 67.55; H, 9.91; S, 22.54. Found: C, 67.70; H, 9.80; S, 22.30.

Reduction of the excess bromine in the trapping solution with sodium bisulfite and subsequent glpc analysis showed the absence of 1,2-dibromopropane.

Reduction of Butadienyl Sulfide 4a.—A mixture of 32.0 g of 10% palladium-on-carbon catalyst in 100 ml of 95% ethyl alcohol was placed in a Parr hydrogenation apparatus and shaken at 39 psig until no further sorption of hydrogen was detected. A solution of 7.0 g (0.18 mole) of **4a** in 100 ml of ethyl alcohol was then carefully added to the activated catalyst. This mixture was shaken at 47 psig for 4 hr (final pressure 42.5 psig). The solution was filtered through Celite and the collected catalyst was washed with 100 ml of boiling ethyl alcohol. The filtrate was concentrated to *ca.* 60 ml and diluted with 60 ml of ethyl ether. The ether solution was washed with 10% sodium hydroxide and water, dried, and concentrated. Distillation of the residue afforded 4.2 g (13%) of colorless **1-phenylthio-2-methylbutane** (**6a**): bp 125° (17 mm); $n^{25}D$ 1.5362 (lit.[11] bp 99–101° (4.5 mm), $n^{20}D$ 1.5408). Glpc analysis (15% Dow 550, 100–225° at 10°/min) showed only one peak. The infrared and nmr spectra of this material were in excellent agreement with those of an authentic sample of **6a** having $n^{25}D$ 1.5369 which was prepared in this laboratory using the procedure described in footnote 11. Treatment of the spent catalyst with mineral acid resulted in the evolution of hydrogen sulfide. Thus, the low yield of **6a** could be attributed to desulfurization which accompanied reduction.

Reduction of Butadienyl Sulfide 4b.—A 5.4-g (0.038 mole) sample of **4b** was reduced as described in the previous experiment. Work-up and distillation yielded 1.3 g (23%) of colorless **1-*n*-propylthio-2-methylbutane** (**6b**): bp 170° (710 mm); $n^{25}D$ 1.4490. Glpc analysis (15% Dow 550, 120°) showed only one peak. The infrared and nmr spectra were in excellent agreement with those of an authentic sample of the previously unreported **6b**.

1-*n*-Propylthio-2-methylbutane (**6b**).—To a solution of 4.0 g (0.10 mole) of sodium hydroxide in 75 ml of water was slowly added 7.62 g (0.10 mole) of *n*-propyl mercaptan. The resulting solution was warmed to 50° and carefully treated with 15.1 g (0.10 mole) of optically active 1-bromo-2-methylbutane.[12] The mixture was vigorously stirred for 6 hr at 80–90°. The cooled mixture was diluted with water, and the organic layer was washed with 40 ml of 10% sodium hydroxide and two 50-ml portions of water. Distillation of the dried organic layer yielded 6.1 g (42%) of colorless **6b**: bp 174° (712 mm). Redistillation yielded an analytical sample: bp 178° (713 mm); $n^{25}D$ 1.4512; d^{25}_4 0.8422; infrared $\lambda_{max}^{CCl_4}$ 3.44, 6.85, 7.25, 7.48, 7.74, 7.82, and 8.11 μ; nmr signals (neat), multiplet between τ 7.50–7.87 (4 H), multiplet between 8.33–8.90 (major peaks separated by 7 cps, 8 H), and multiplet between 9.06–9.34 (6 H).

Anal. Calcd for $C_8H_{18}S$: C, 65.69; H, 12.39; S, 21.92. Found: C, 65.62; H, 12.16; S, 22.15.

(11) V. N. Ipatieff, H. Pines, and B. S. Friedman, *J. Am. Chem. Soc.*, **60**, 2731 (1938).

(12) This alkyl halide was prepared in moderate yield from active amyl alcohol: H. O. Jones, *J. Chem. Soc.*, 138 (1905).

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A Radical-Induced ε Elimination[1]

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We recently reported a radical-induced 1,3 elimination from a three-carbon acyclic skeleton and pointed out that all of the mechanisms we could envision for this reaction involved processes or intermediate species which are unprecedented in free-radical chemistry.[2] The determination of whether this reaction can yield larger rings is naturally of interest for both mechanistic and synthetic reasons.[3] We wish to report that cyclopentane can be produced by reaction of 1,5-diiodopentane with a peroxide.[4] Results are summarized in Table I.

TABLE I

REACTION OF 1,5-DIIODOPENTANE WITH *t*-BUTYL AND BENZOYL PEROXIDES

	Reactn conditions[a]		
	168°, 1 hr		115°, 70 min
Reactants, mmole			
$I(CH_2)_5I$	0.428	0.266	0.271
$(PhCO_2)_2$[b]			0.407
$(t\text{-}BuO)_2$[b]	0.439	0.440	
Products, mmole[c]			
Cyclopentane	0.023	0.024	0.012
Pentene	*d*	*d*	0.008
$CH_3(CH_2)_4I$	0.071	0.041	0.023
$CH_2{=}CH(CH_2)_3I$	Trace	Trace	0.003
$Ph(CH_2)_5I$	0.005		0.007
$Ph(CH_2)_4CH_3$	0.004	0.006	0.013
$I(CH_2)_5I$	0.10		
PhI	0.007	0.008	0.45
CH_3I	0.46	0.57	
$PhCH_3$	0.034	0.013	
CH_3COCH_3	0.54	0.57	
$(CH_3)_3COH$[e]	0.35	0.27	
$(CH_3)_2{=}CH_2$[e]	0.013	0.007	

[a] No significance should be attached to the reaction time with the exception that it is long enough so that no detectable reaction occurred on further heating. [b] No reaction occurred in the absence of peroxide. [c] In addition, we observed in the 115° run trace amounts of materials which had the same vpc retention times as (4-pentenyl)benzoate and (5-iodopentyl)-benzoate. [d] Undetermined. [e] The effect of reaction time on the isobutylene:*t*-butyl alcohol ratio was not studied.

All of the mechanisms mentioned in connection with our 1,3-diiodopropane → cyclopropane conversion,[2] in particular a carbon radical displacement on carbon, should be considered as possibilities for the present

(1) This work was supported by a Frederick Gardner Cottrell grant from the Research Corporation and a Biomedical Sciences Support grant from the National Institutes of Health.

(2) L. Kaplan, *J. Am. Chem. Soc.*, **89**, 1753 (1967).

(3) See W. S. Trahanovsky and M. P. Doyle, *J. Org. Chem.*, **32**, 146 (1967), for a recent unsuccessful attempt to observe an ε elimination.

(4) This reaction was mentioned in passing in footnote 9 of our earlier communication.[2]