# Mechanism of Ozonation Reactions. III. Ethers[1]

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Abstract: A study of the mechanism of the ozonation of ethers has been carried out utilizing isotope effect rate studies, competitive relative rate studies on various classes of ethers, and product analysis of ozonations using ozone–oxygen and ozone–nitrogen streams. Results are discussed in terms of both the mode of initial attack of ozone on the system and the varieties of decomposition available to the hydrotrioxide intermediate I. The over-all mechanism is a complicated one involving free radical autoxidation when oxygen is present.

The reaction of ozone with ethers has been studied sporadically over the last 100 years[2] with the work of Price and Tumolo[3] being the only thorough study carried out since the advent of modern instrumental methods of product analysis. Briefly, Price and Tumolo suggested the mechanism
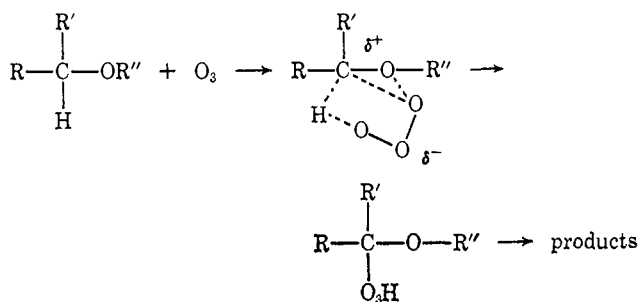
and believed that oxygen did not have a major role in the over-all mechanism.[3]

This mechanism involves as a first step an "insertion" type of reaction in the C–H bond, and is analogous to a similar insertion of ozone into the aldehydic C–H bond as proposed by White and Bailey.[4]

In our study of the aldehyde ozone reaction, we showed that isotope effects could be used effectively in distinguishing between mechanisms involving ozone as the major reagent (relatively low primary isotope effect of 2–3) and mechanisms which involved oxygen which gave much higher isotope effects.[5] In order to test Price and Tumolo's suggestion that oxygen does not have a significant role in ether ozonations, we have determined isotope effects in ether ozonations under the same general conditions as were used in our aldehyde work (*i.e.*, ozone–oxygen streams, ozone–inert gas streams, and ozonation in pyridine).[5]

A necessary adjunct to all ozone mechanistic studies is to show that all products and product ratios are the same for ozone–oxygen and ozone–inert gas reactions. Such studies have not been reported in the literature for ethers, and we present here such product studies for several structurally dissimilar ethers.

The method of studying relative rates of reactions by the competitive method is often a good one for determining mechanistic details. We, and others,[5,6] have reported such studies for ozonations of other classes of organic compounds, and this paper presents an initial study of this nature for ethers.

Interest in the general area of ozone oxidation of carbon–hydrogen single bonds has been heightened recently by reports of Batterbee and Bailey,[7] Hamilton, *et al.*,[8] and Whiting, *et al.*,[9] of various aspects of hydrocarbon and alcohol ozonations. The observation of Whiting, *et al.*, that a stable peroxidic product is formed in the ozonation of isopropyl alcohol is of particular interest to the mechanism of ether ozonations, and we have carried out several ozonation experiments with ethers relevant to Whiting's work.[9]

There is also current interest in the general topic of trioxides, the intermediate proposed by Price and Tumolo for ether ozonations, as evidenced by recent announcement of the preparation and thermal stabilities of several classes of trioxides and tetroxides.[10–13]

Experimental Section

Materials. Tetrahydropyran, tetrahydrofuran, butyl ether, benzyl methyl ether, and isopropyl ether were reagent grade materials and were distilled before use. Internal standards and products were either reagent grade chemicals or were prepared by normal procedures (*e.g.*, *t*-butyl benzoate from *t*-butyl alcohol and benzoyl chloride in pyridine).

t-Butyl ethyl ether was prepared by the method of Norris and Rigby,[14] bp 70–72° (lit. bp 73.1°), and purchased as reagent grade material. It, too, was distilled before use.

t-Butyl benzyl ether was prepared by the method of Lansbury and Pattison, bp 201–203° (760 mm) (lit.[15] bp 203–205° (760 mm)).

t-Butyl-α-d_2 ethyl ether was prepared as above from benzyl-α-d_2 chloride by the Lansbury[15] procedure. The chloride was prepared from benzyl-α-d_2 alcohol and HCl while the benzyl-α-d_2 alcohol was prepared from methyl benzoate and LiAlD$_4$.

(1) Presented in part before the Organic Chemistry Division, 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968, Abstract P-115.

(2) C. F. Schonbein, *J. Prakt. Chem.*, 66 [3], 273 (1855); F. G. Fischer, *Ann.*, 476, 233 (1929).

(3) C. C. Price and A. L. Tumolo, *J. Am. Chem. Soc.*, 86, 4691 (1964).

(4) H. M. White and P. S. Bailey, *J. Org. Chem.*, 30, 3037 (1965).

(5) R. E. Erickson, D. Bakalik, C. Richards, M. Scanlon, and G. Huddleston, *ibid.*, 31, 461 (1966).

(6) R. E. Erickson and T. Myszkiewicz, *ibid.*, 30, 4326 (1965); D. Barnard, *J. Chem. Soc.*, 4547 (1957).

(7) J. E. Batterbee and P. S. Bailey, *J. Org. Chem.*, 32, 3899 (1967).

(8) G. A. Hamilton and B. S. Ribner, International Oxidation Symposium Preprints, II-289, 1967; C. C. Schubert and R. N. Pease [*J. Am. Chem. Soc.*, 78, 2044, 5553 (1956)] have studied the kinetics of ozonations also.

(9) M. C. Whiting, A. J. N. Bolt, and J. H. Parish, International Oxidation Symposium Preprints, II-267, 1967.

(10) P. D. Bartlett and P. Günther, *J. Am. Chem. Soc.*, 88, 3288 (1966); P. D. Bartlett and G. Guaraldi, *ibid.*, 89, 4799 (1967).

(11) L. R. Anderson and W. B. Fox, *ibid.*, 89, 4313 (1967); P. G. Thompson, *ibid.*, 89, 4316 (1967).

(12) T. Mill and R. S. Stringham, *ibid.*, 90, 1062 (1968).

(13) J. A. Howard and K. U. Ingold, *ibid.*, 90, 1056 (1968).

(14) J. F. Norris and G. W. Rigby, *ibid.*, 54, 2088 (1942).

(15) P. T. Lansbury and V. A. Pattison, *J. Org. Chem.*, 27, 1933 (1962).

p-Bromobenzyl *t*-butyl ether was prepared using the Lansbury[15] procedure with *p*-bromobenzyl bromide, mp 48–50°. *Anal.*[16] Calcd for $C_{11}H_{15}BrO$: C, 54.33; H, 6.21; Br, 32.86. Found: C, 54.29; H, 6.27; Br, 32.75.

Product Analysis. A typical procedure is as follows for the ozonation of isopropyl ether. A mixture of 0.827 g of isopropyl ether and 0.784 g of *t*-amyl acetate (internal standard) was added quantitatively with 20 ml of Freon 11 and 10 ml of pyridine to an ozonation flask and cooled to −78°. An oxygen–ozone stream (4% ozone) was passed through the mixture for 1 hr with 0.1-ml samples being withdrawn at approximately 10-min intervals during the last 30 min. The samples were allowed to come to room temperature and injected into a gas chromatograph (Varian Aerograph Model 700, 10 ft × 0.25 in., 5% FFAP on 60–80 DMCS treated Chromosorb G, column at 60°, 100-ml/min flow). Sensitivities for the three products *vs.* the internal standard had previously been determined. Product ratios were determined and products were identified by comparing retention times with known samples on three to four different columns (20% Halcomid m 180 L on 60–80 Chromosorb W, 5% Carbowax 20M on 60–80 Chromosorb G, and 5% SE 30 on 60–80 Chromosorb G).

Nmr Analyses.[17] Although most product analyses were by the gas chromatographic method outlined above, several analyses were checked by nmr. Specifically several *t*-butyl formate–*t*-butyl acetate ratios were found to be the same by nmr as reported in Table V (integration of formyl proton *vs.* methyl protons of acetate) and isopropyl acetate–acetone ratios from neat isopropyl ether ozonations (with and without pyridine) were identical by the two methods. The spectrum of ozonized benzyl methyl ether was checked for the presence of methoxy benzyl hydroperoxide (lit. δ 5.63 ppm for $C_6H_5CH(OCH_3)(OOH)$ but none was found).[18] The corresponding signal for $CH_3CH(O\text{-}t\text{-Bu})(OOH)$ for the hydroperoxide from the ozonation of *t*-butyl ethyl ether was also not in evidence.

To one of the neat ozonations of isopropyl ether (0.2 mol of ether, 0.03 mol of ozone at −78°) was added 0.01 mol of pyridine. The solution was brought to room temperature and its nmr spectrum determined. Pyridine was clearly evident but no pyridine oxide was present (checked *vs.* pyridine oxide in isopropyl ether).

Relative Rate Methods. Competitive ozonations were carried out using gas chromatography with an internal standard, as has been described in previous publications.[5,6] Relative rate constants were determined from a computer program for the least-squares analysis on the slope of a log concentration *vs.* log concentration plot.

Isotope Effects. Isotope effect relative rates were determined by several methods. For *t*-butyl ethyl ether, the pseudo-first-order rate method for an oxygen–ozone stream applied successfully to aldehydes[4] gave successful results for the deuterio compound (good straight-line plot for log *c vs. t*) but was less successful for the undeuterated system (log *c vs. t* plot showed definite curvature as if the kinetics were approaching zero order in ether). The larger deviation noted in Table III can be accounted for on this basis. When pyridine was used as a solvent good pseudo-first-order rate constants were obtained for both *t*-butyl ethyl ether and its dideuterio derivative.

For ozone–nitrogen work, ozone was adsorbed on silica gel in the normal manner and a Y joint from the ozone–silica gel trap was connected to identical ozonation flasks containing internal standard, and the *t*-butyl ethyl ether and its dideuterio derivative, respectively. Helium (in some cases, nitrogen) was allowed to sweep the ozone slowly into the two ozonation flasks at 0° and samples were removed periodically and simultaneously. Data from the gas chromatograph were handled in the normal manner and a log *c vs.* log *c* plot yielded the k_H/k_D value listed in Table III.

Competitive methods were used for the determination of isotope effects for the ozonation of *t*-butyl benzyl ether. Initial results were obtained from the competition between *p*-bromobenzyl *t*-butyl ether and the corresponding protio and deuterio *t*-butyl benzyl ethers. Difficulties were encountered with both the gas chroma-

(16) Microanalyses were by Galbraith Laboratories Inc., Knoxville, Tenn.

(17) Nuclear magnetic resonance spectra were obtained with a Varian HA-60 instrument.

(18) W. P. Keaveney, M. G. Berger, and J. J. Pappas, *J. Org. Chem.*, **32**, 1537 (1967). Similar alkoxy hydroperoxides are well-known ozonation products from alkenes (P. S. Bailey, *Chem. Rev.*, **58**, 925 (1958)) and have also been prepared and studied by other methods, *e.g.*, D. B. Sharp and T. M. Patrick, Jr., *J. Org. Chem.*, **26**, 1389 (1961).

tographic analysis and the relative insolubility of the bromo derivative in Freon 11, however, and the most reliable data are those in Tables II and III using benzyl methyl ether as the competing ether.

Ozonation of Isopropyl Ether (Neat). Several experiments were carried out using ozone- (4%) oxygen streams on 15–25 ml of isopropyl ether at −78°. Absorption of ozone was not complete but the blue ozone color disappeared within 30 sec after turning off the ozone stream. After passing approximately 0.03 mol of ozone through the mixture, the solution was removed from the cold bath and allowed to come to room temperature whereupon a vigorous gas-evolving exothermic reaction was noted at about −10°. This experiment was repeated several times, adding each of reagents pyridine, lead tetraacetate, and 2,6 di-*t*-butylphenol to the solution at −78°.

Table VII shows the product analysis of one isopropyl ether ozonation in which a 1-ml sample was added to pyridine at −60° while a second 1-ml sample was allowed to warm to room temperature before product analysis.

A crude estimate of the temperature and chemical characteristics of the exothermic reaction was made by pipeting 1-ml samples of the ozonation solution into 0.2-ml solutions of pyridine, lead tetraacetate in acetic acid, and 2,6 di-*t*-butylphenol in isopropyl ether. The temperature change with time was measured and plotted to determine the temperature at which the exothermic reaction began and the chemical characteristics of the reaction were noted. Qualitative results are listed in a later section.

Similar ozonations were carried out with *t*-butyl ethyl ether and an exothermic reaction was noted for this system also. However, the compound was not investigated extensively.

Choice of Solvents. Freon-11 was used as a solvent in the majority of the reactions in this study because of its very low reactivity with ozone, the great solubility of ozone in this solvent, and favorable gas chromatographic behavior (short retention time). Other solvents such as pyridine and acetone were chosen because of hypothesized rate and product changes for polar solvents. Propyl acetate, the solvent used for the competitive experiments between tetrahydrofuran and isopropyl ether, is unreactive toward ozone and had an ideal retention time on the gas chromatograph which the other solvents did not have for this ozonation.

Choice of Internal Standards. The internal standards used in this study were *t*-amyl acetate (all runs involving isopropyl ether, *n*-butyl ether, *t*-butyl ethyl ether, and tetrahydropyran), propyl benzoate (all runs involving benzyl *t*-butyl ether, *p*-bromobenzyl *t*-butyl ether, and benzyl methyl ether), and cyclohexane (for competitive ozonations between tetrahydrofuran and isopropyl ether). All standards were shown to be unreactive toward ozone under the reaction conditions.

Attempted Ozonation of *t*-Butyl Formate. A solution of 1.00 g of *t*-butyl formate and 1.000 g of *t*-amyl acetate (internal standard) was ozonized with an ozone–oxygen stream (5% ozone) at 0° for 1 hr. The concentration of *t*-butyl formate decreased less than 3% during this period and no new products were detectable by gas chromatography.

General Observations. In order to obtain reasonable kinetic data for *t*-butyl ethyl ether and its dideuterio derivative, the column temperature was changed from 55° (good for product analysis) to 80° and gas chromatographic peaks for *t*-butyl formate and *t*-butyl acetate overlapped so severely that quantitative analysis was not possible. However, for the dideuterio ether there was definitely more *t*-butyl formate than *t*-butyl acetate in Freon and more acetate than formate in pyridine.

Minor products (more volatile than solvents) were noted for the *t*-butyl ethyl ether and isopropyl ether ozonations.

An attempt to trap reactive radicals by ozonizing *t*-butyl ethyl ether in bromotrichloromethane was also made. Unfortunately this compound (and in fact several other alkyl bromides and bromobenzene) reacts with ozone to liberate bromine, so no meaningful product analysis could be made.

Results

Tables I–VII list the pertinent experimental results of this investigation. The data in Table II were used to calculate the k_H/k_D values for *t*-butyl benzyl ether in Freon 11. Product ratios rather than yields are listed in Tables VI and VII because both isopropyl ether and *t*-butyl ethyl ether were volatile enough that some reactant was lost during reaction. Since over-all

Table I. Relative Rates of Ozonation

Compound	Rel rate O_3-N_2, $0°$ in acetone	Rel rate O_3-N_2, $0°$ in propyl acetate	Rel rate[a] $(CH_3)_3CO\cdot$ at $0°$
Tetrahydropyran	1.0	1.0	1.0
Isopropyl ether		1.6 ± 0.1	1.02
Dibutyl ether	3.1 ± 0.1	2.9 ± 0.3[d]	1.54 $(CH_3CH_2)_2O$
Tetrahydrofuran	3.9 ± 0.4		2.2
p-Bromobenzyl t-butyl ether	4.8 ± 0.2[b]		
Benzyl t-butyl ether	8.2 ± 0.2[c]		2.9 $(C_6H_5CH_2)_2O$

[a] C. Walling and M. J. Mintz, *J. Am. Chem. Soc.*, **89**, 1515 (1967). [b] Determined *vs.* benzyl t-butyl ether at $-78°$. [c] Determined *vs.* dibutyl ether. [d] The direct determination of the relative rate of ozonation of dibutyl ether *vs.* isopropyl ether gave 1.5 ± 0.1.

changes in product ratios with changing conditions were deemed the important results, no serious attempts were made to calculate absolute yields.

Table II. Competitive Ozonations for k_H/k_D Determinations

Conditions	Solvent	Temp, °C	Rel rates[a]
	$C_6H_5CH_2O$-t-Bu/$C_6H_5CH_2OCH_3$		
O_3-O_2	Freon 11	0	2.31 ± 0.05
O_3-N_2	Freon 11	0	2.18 ± 0.10
O_3-O_2	Freon 11	-78	2.62 ± 0.16
O_3-N_2	Freon 11	-78	2.66 ± 0.10
			2.68 ± 0.12
O_3-O_2	Freon 11-pyridine[b]	-78	1.96 ± 0.04
O_3-N_2	Freon 11-pyridine	-78	1.72 ± 0.06
	$C_6H_5CH_2OCH_3$/$C_6H_5CD_2O$-t-Bu		
O_3-O_2	Freon 11	0	1.76 ± 0.10
O_3-N_2	Freon 11	0	1.69 ± 0.09
O_3-O_2	Freon 11	-78	2.39 ± 0.11
O_3-N_2	Freon 11	-78	2.53 ± 0.13
			2.49 ± 0.18
O_3-O_2	Freon 11-pyridine[b]	-78	2.13 ± 0.10
O_3-N_2	Freon 11-pyridine	-78	2.14 ± 0.08

[a] Correlation coefficient 0.98 or better for all runs. [b] 50% of each solvent by volume.

Table III. Isotope Effects on Ozonation of Ethers

Conditions	Solvent	Rate $0°$	Rate $-78°$	Method[a]
	$k(C_6H_5CH_2O$-t-Bu)/$k(C_6H_5CD_2O$-t-Bu)			
O_3-O_2	Freon 11	4.1 ± 0.2	6.3 ± 0.4	A
O_3-N_2	Freon 11	3.8 ± 0.2	6.7 ± 0.4	A
O_3-O_2	Freon 11-pyridine		4.2 ± 0.2	A
O_3-N_2	Freon 11-pyridine		3.7 ± 0.2	A
O_3-N_2	CH_2Cl_2-acetone		3.2 ± 0.2	B
O_3-N_2	Freon 11		4.8 ± 0.4[b]	B
	$k(CH_3CH_2O$-t-Bu)/$k(CH_3CD_2O$-t-Bu)			
O_3-O_2	Acetone	4.5 ± 0.4[b]		C
O_3-He	Acetone	2.4 ± 0.1		C
O_3-O_2	Pyridine	2.6 ± 0.1		C

[a] Method A, calculated from Table II; method B, from competitive experiments with p-bromobenzyl t-butyl ether; method C, see Experimental Section. [b] Correlation coefficients 0.95, all other correlation coefficients 0.98 or better.

Table IV. Relative Rates, THF *vs.* Isopropyl Ether

Conditions	Solvent	Rate $0°$[a]	Rate $-78°$
O_3-O_2	Propyl acetate	3.9 ± 0.1	9.8 ± 0.2
O_3-N_2	Propyl acetate	2.9 ± 0.1	10.2 ± 0.2
O_3-O_2	Propyl acetate-pyridine	2.9 ± 0.1	7.7 ± 0.2
O_3-N_2	Propyl acetate-pyridine	2.2 ± 0.1	9.4 ± 0.2

[a] Correlation coefficients for determinations at $0°$ were 0.98 or better while correlation coefficients for data at $-78°$ were 0.90 or better.

In addition to the quantitative results listed in the tables several qualitative observations are of mechanistic significance. The following observations were made when various reagents were added to an isopropyl ether solution which had reacted (approximately 10%) with ozone at $-78°$.

(1) When the ozonized solution was allowed to come to room temperature a vigorous gas-evolving exothermic reaction was noted at $-10°$.

(2) When pyridine was added to a portion of the ozonized solution at $-60°$ no definite exothermic reaction was noted but some gas was evolved continuously from -60 to $+18°$.

(3) When lead tetraacetate in acetic acid was added at $-78°$ a vigorous evolution of gas was noted throughout the temperature range from -78 to $-10°$ and a less severe exothermic reaction was noted at the latter temperature.

(4) When lead tetraacetate was added to an ozonized solution which had already gone through the exothermic reaction noted in (1) only a weak hydroperoxide test[19] was observed.

(5) When 2,6-di-t-butylphenol in isopropyl ether was added to a portion of the ozonized solution at $-78°$, an exothermic reaction was noted at $-10°$ whereupon the solution became bright yellow.

Other qualitative results of significance include the fact that pyridine does not react with unstable peroxidic materials to form pyridine oxide (which we believed might be the cause of its very large effects on product ratios, etc.) and the fact that nmr indicated no hydroperoxide product in ether ozonations.

Discussion

The results listed in Table I show the general correspondence between ozone reactivity and a typical free radical hydrogen-abstraction reaction.[20]

The relative rate of ozonation for $k_{p\text{-Br}}/k_0$ at $-78°$ with nitrogen carrier gas for p-bromobenzyl t-butyl ether *vs.* benzyl t-butyl ether is 0.59. This is to be compared with our similar measurements of substituted benzaldehydes[6] ($\rho = -0.94$, $k_{p\text{-Br}}/k_0 = 0.67$) at $0°$ with nitrogen carrier and the low negative ρ values found normally in free radical abstractions.[21] Thus the ozonation of ethers shows a very small polar substituent effect. Relative rates for a series of ethers seem to be more dependent on bond strengths of α-C-H bonds than any other factor. Hamilton and Ribner have compared the relative reactivity of hydrocarbon carbon-hydrogen bonds to ozonation *vs.* other types of reac-

(19) R. Criegee in "Methoden der organischen Chemie," Vol. 2, Houben-Weyl, Ed., Stuttgart, 1953, p 570.
(20) See Table I, footnote a.
(21) G. J. Gleicher, *J. Org. Chem.*, **33**, 332 (1968).

Table V. Ozonation of CH₃CH₂O-*t*-Bu

	Product ratios[a]		
Conditions	$\overset{O}{\overset{\|\|}{HCO}}$-*t*-Bu	$\overset{O}{\overset{\|\|}{CH_3CO}}$-*t*-Bu	*t*-BuOH
O₃–O₂, 0°, Freon 11	1.0	3.1	0.36–1.1[b]
O₃–N₂, 0°, Freon 11	1.0	0.9	0.65–1.45[b]
O₃–O₂, 0°, pyridine	1.0	8.0	c
O₃–O₂, −78°, neat	1.0	2.3	0.6
O₃–O₂, −78°, neat, pyridine addn[d]	1.0	5.9	0.23
O₃–N₂, −78°, neat	1.0	2.6	0.7
O₃–N₂, −78°, neat, pyridine addn[d]	1.0	3.2	0.3
O₃–O₂, −78°, Freon 11, deuterio ether[e]	1.0	0.5	

[a] Measured as mole ratios. [b] Relative amount of *t*-butyl alcohol dependent on degree of completion of ozonation. Relative percentage of *t*-butyl alcohol increases while relative percentage of *t*-butyl acetate decreases slightly during the course of the reaction. [c] Not enough formed for accurate measurement. [d] Pyridine was added to the solution at approximately −60° and allowed to remain at −60° for 15 min before being chromatographed. [e] Approximate ratio from peak heights.

Table VI. Ozonation of C₆H₅CH₂O-*t*-Bu

	Yields, %		
Conditions	$\overset{O}{\overset{\|\|}{C_6H_5CO}}$-*t*-Bu	$\overset{O}{\overset{\|\|}{C_6H_5CH}}$	(CH₃)₃COH
O₃–O₂, −78°, Freon 11[a]	62 ± 1	20 ± 1	28 ± 4
O₃–N₂, −78°, Freon 11[b]	57 ± 5	16 ± 1	20 ± 2
O₃–O₂, −78°, acetone	78	16	
O₃–O₂, −78°, pyridine–Freon 11	83	10	
O₃–O₂, −78°, Freon 11[c]	33	31	55

[a] Average of six determinations. [b] Average of five determinations. [c] Data on C₆H₅CD₂O-*t*-Bu.

Table VII. Ozonation of Isopropyl Ether

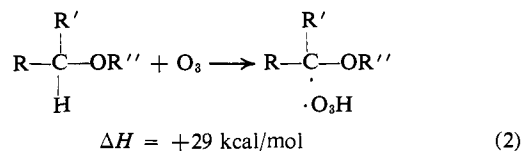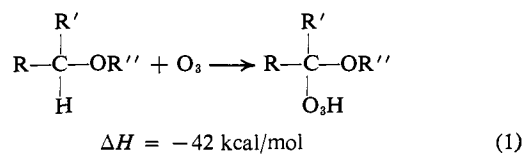| Conditions	CH₃C-OCH₃[a]	CH₃CH-OHCH₃[a]	CH₃CO₂C-H(CH₃)₂[a]
O₃–O₂, −78°, Freon 11–pyridine	1	0.9	1.8
O₃–O₂, 0°, pyridine	1	0	1.1
O₃–O₂, −78°, neat	1	1.3	2.7
O₃–O₂, −78°, pyridine added at −60°	1	1.1	1.1
O₃–N₂, −78°, neat	1	b	2.5
O₃–N₂, −78°, pyridine added at −60°	1	b	1.2

[a] Measured as mole ratios. [b] Not measured.

tions and have concluded that initial attack is also radicallike in those reactions.[8]

An over-all look at the data in Tables I–VII indicates that the mechanism of the ozonation of ethers is quite complex. The products isolated are obviously not formed directly and we will discuss the mechanism by first concentrating on the initial attack of ozone. Thus an initial mechanistic pattern will be postulated on the basis of thermochemical considerations. Then the isotope effect measurements, relative rate studies, and product distribution information will be utilized in an attempt to show that it is consistent with the mechanistic pattern suggested.

Initial attack of ozone on carbon–hydrogen bonds has been rationalized in the literature by two different reactions. Reaction 1 (or its modified form involving a prior ozone–ether complex) has been suggested for ethers by Price and Tumolo[3] and Bailey, *et al.*,[4,7] for aldehydes and anthrone-type derivatives and will be referred to in this paper as an insertion reaction. In reaction 2, a tight radical pair forms which then can undergo various reactions including coupling to give I. This mechanism has been suggested by Hamilton and

Ribner[8] for hydrocarbon ozonations and by Whiting, Bolt, and Parish[9] for hydrocarbon and alcohol ozonations. Reaction 1 would probably require a rather large negative entropy of activation while reac-
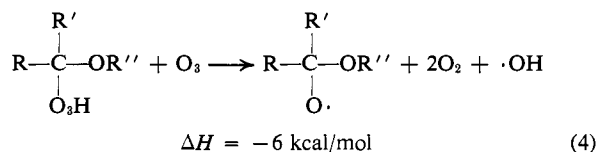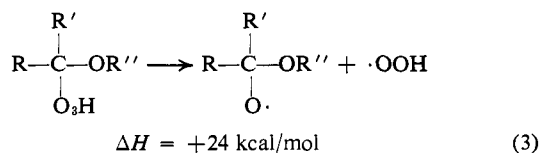
$$R-\underset{\underset{H}{\|}}{\overset{\overset{R'}{\|}}{C}}-OR'' + O_3 \longrightarrow R-\underset{\underset{O_3H}{\|}}{\overset{\overset{R'}{\|}}{C}}-OR''$$

$$\Delta H = -42 \text{ kcal/mol} \tag{1}$$

$$R-\underset{\underset{H}{\|}}{\overset{\overset{R'}{\|}}{C}}-OR'' + O_3 \longrightarrow R-\underset{\underset{\cdot O_3H}{\|}}{\overset{\overset{R'}{\|}}{C}}-OR''$$

$$\Delta H = +29 \text{ kcal/mol} \tag{2}$$

tion 2 would obviously require a high energy of activation.[22] We suggest that the relatively high reactivity of ethers (benzyl *t*-butyl ether reacts very rapidly with ozone in Freon at −78°) in nonpolar solvents argues against reaction 2 as a significant contributor to the total reaction pathway. The possibility of such a reaction occurring for alcohol ozonations where the hydrotrioxide radical can be solvated is not discounted.[23]

The over-all results of the investigation suggest that at least at higher temperatures there may be a significant
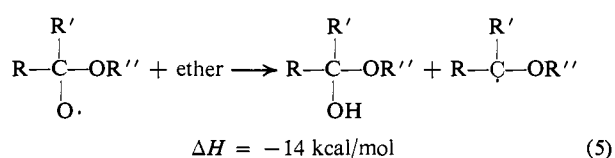
(22) The ΔH values in this paper have been calculated using isobutane as a model and thermochemical data from Benson (S. W. Benson, *J. Am. Chem. Soc.*, **86**, 3922 (1964); S. W. Benson, *J. Chem. Educ.*, **42**, 502 (1965); S. W. Benson and R. Shaw, International Oxidation Symposium Preprints, I-565, 1967). It would have been preferable to use a technique such as the Benson and Buss method [*J. Chem. Phys.*, **29**, 546 (1968)] for calculating these enthalpies but the proper data are unavailable. Isobutane is a reasonable model in that some ether α-carbon–hydrogen bonds are weaker and some are stronger. The relative energy differences are the important quantities.

(23) Professor Whiting (private communication) suggests that a solvation enthalpy for HO₃· of 13 + 7 kcal/mol will make the alcohol ozonation endothermic by only 15 ± 13 kcal/mol.
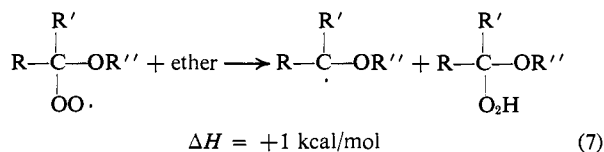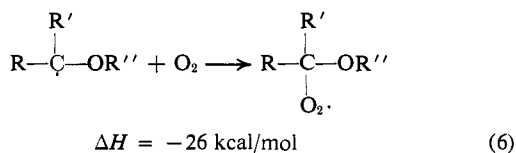
contribution from a free radical chain mechanism. Two of the most reasonable initiating steps for such a reaction are represented by eq 3 and 4.

$$R-\underset{\underset{O_3H}{|}}{\overset{\overset{R'}{|}}{C}}-OR'' \longrightarrow R-\underset{\underset{O\cdot}{|}}{\overset{\overset{R'}{|}}{C}}-OR'' + \cdot OOH$$

$$\Delta H = +24 \text{ kcal/mol} \qquad (3)$$

$$R-\underset{\underset{O_3H}{|}}{\overset{\overset{R'}{|}}{C}}-OR'' + O_3 \longrightarrow R-\underset{\underset{O\cdot}{|}}{\overset{\overset{R'}{|}}{C}}-OR'' + 2O_2 + \cdot OH$$

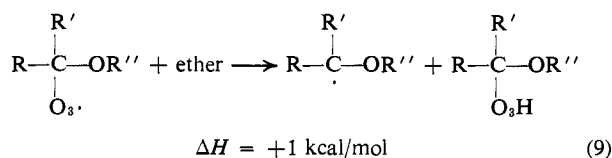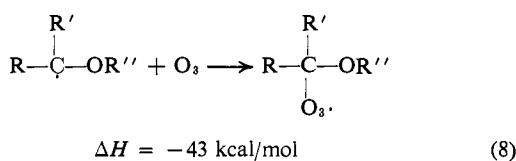$$\Delta H = -6 \text{ kcal/mol} \qquad (4)$$

Reaction 3 is rather endothermic, but, as an initiation reaction for a long chain radical chain process, is conceivable (as would be eq 2). Reaction 4 is analogous to the known reaction of hydroperoxides with ozone.[24] The most reasonable continuation for a chain reaction would be

$$R-\underset{\underset{O\cdot}{|}}{\overset{\overset{R'}{|}}{C}}-OR'' + \text{ether} \longrightarrow R-\underset{\underset{OH}{|}}{\overset{\overset{R'}{|}}{C}}-OR'' + R-\underset{}{\overset{\overset{R'}{|}}{C}}-OR''$$

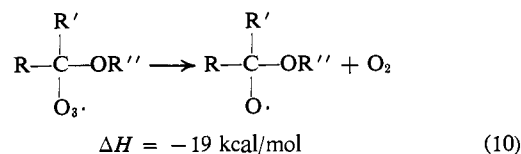$$\Delta H = -14 \text{ kcal/mol} \qquad (5)$$

The fact that the presence of oxygen changes relative rates, isotope effects, and product distribution strongly suggests that it enters into the reaction. The obvious reaction sequence would be

$$R-\underset{}{\overset{\overset{R'}{|}}{C}}-OR'' + O_2 \longrightarrow R-\underset{\underset{O_2\cdot}{|}}{\overset{\overset{R'}{|}}{C}}-OR''$$

$$\Delta H = -26 \text{ kcal/mol} \qquad (6)$$

$$R-\underset{\underset{OO\cdot}{|}}{\overset{\overset{R'}{|}}{C}}-OR'' + \text{ether} \longrightarrow R-\underset{}{\overset{\overset{R'}{|}}{C}}-OR'' + R-\underset{\underset{O_2H}{|}}{\overset{\overset{R'}{|}}{C}}-OR''$$

$$\Delta H = +1 \text{ kcal/mol} \qquad (7)$$

Ozone is consumed in the reaction even when oxygen is present and, as noted above, since thermochemical data and kinetic considerations suggest that neither direct insertion nor direct hydrogen abstraction are favorable, ozone reactions which are part of a free radical chain reaction offer reasonable alternatives. Either
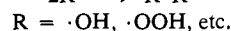
$$R-\underset{}{\overset{\overset{R'}{|}}{C}}-OR'' + O_3 \longrightarrow R-\underset{\underset{O_3\cdot}{|}}{\overset{\overset{R'}{|}}{C}}-OR''$$

$$\Delta H = -43 \text{ kcal/mol} \qquad (8)$$

$$R-\underset{\underset{O_3\cdot}{|}}{\overset{\overset{R'}{|}}{C}}-OR'' + \text{ether} \longrightarrow R-\underset{}{\overset{\overset{R'}{|}}{C}}-OR'' + R-\underset{\underset{O_3H}{|}}{\overset{\overset{R'}{|}}{C}}-OR''$$

$$\Delta H = +1 \text{ kcal/mol} \qquad (9)$$

$$R-\underset{\underset{O_3\cdot}{|}}{\overset{\overset{R'}{|}}{C}}-OR'' \longrightarrow R-\underset{\underset{O\cdot}{|}}{\overset{\overset{R'}{|}}{C}}-OR'' + O_2$$

$$\Delta H = -19 \text{ kcal/mol} \qquad (10)$$

the chain propagating steps 8, 9 or 8, 10, 5 are feasible on thermochemical grounds.

The termination steps for chain processes such as those in eq 5–10 have received a great deal of attention in recent years. Equations 11–14 are based on obvious literature analogies.

$$2R-\underset{\underset{O\cdot}{|}}{\overset{\overset{R'}{|}}{C}}-O-R'' \longrightarrow \left\{ R-\underset{\underset{OR''}{|}}{\overset{\overset{R'}{|}}{C}}-O- \right\}_2 \qquad (11)$$

$$R-\underset{\underset{O\cdot}{|}}{\overset{\overset{R'}{|}}{C}}-OR'' + R-\underset{\underset{O_2\cdot}{|}}{\overset{\overset{R'}{|}}{C}}-OR'' \underset{-30°}{\overset{}{\rightleftarrows}} \left\{ R-\underset{\underset{OR''}{|}}{\overset{\overset{R'}{|}}{C}}-O- \right\}_2 O \qquad (12)$$

$$2R-\underset{\underset{OR''}{|}}{\overset{\overset{R'}{|}}{C}}-O_2\cdot \underset{-85°}{\overset{}{\rightleftarrows}} \left\{ R-\underset{\underset{OR''}{|}}{\overset{\overset{R'}{|}}{C}}-O-O- \right\}_2 \longrightarrow 2R-\underset{\underset{OR''}{|}}{\overset{\overset{R'}{|}}{C}}-O\cdot + O_2$$

$$\qquad (13)$$

$$2R\cdot \longrightarrow R-R \qquad (14)$$
$$R = \cdot OH, \cdot OOH, \text{ etc.}$$

The -30 and $-85°$ temperatures suggested above are those shown to be limiting values for the stabilities of trioxides and tetroxides, respectively, by Bartlett and coworkers,[10] and are probably not too much different for these systems.

The competitive method of determining relative rates, always a somewhat risky procedure,[25] can lead to particular frustrations in reactions which turn out to be radical abstractions, as we believe these to be. For example, the data listed in Table IV for 0° with oxygen as a carrier for $k_{THF}/k_{isopropyl}$ involve a measurement of relative decreases in concentrations of two ethers. Our mechanism suggests a *minimum* of three reactions (1, 7, and 9) by which ether can disappear, and reactions 7 and 9 would each involve two different radicals. Since these radicals would all be expected to have different selectivities,[26] cross-checks of relative rates with different ethers should not be expected to be successful. As a particular case in point the competitive method of determining isotope effects (see Table III) would not necessarily lead to identical results when two different ethers (in this case *p*-bromobenzyl *t*-butyl ether and benzyl methyl ether) are used as competing reagents.

Nonetheless, the data in Tables II–IV make two points quite clear: (1) isotope effects and relative rates are greatly changed by changes in conditions, and (2) nitrogen as a carrier leads to lower isotope effects and relative rates at 0°.

We suggest that the latter point may be due to the increased selectivity of RR'(OR'')COO· (reaction 7) vs. RR'(OR'')CO· (reaction sequence 8, 10, 5). Both of these radicals are probably present under all ozonation conditions but the former would clearly be present in in-
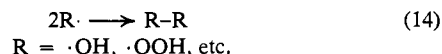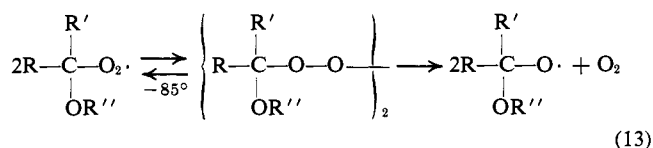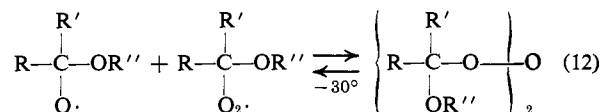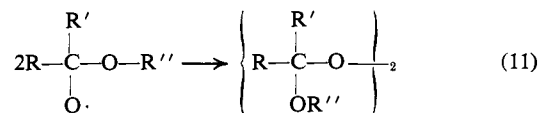
(24) D. Barnard, G. P. McSweeney, and J. F. Smith, *Tetrahedron Letters*, No. **14**, 1 (1960). Although the exact mechanism of the hydroperoxide ozonation is unknown, a simple calculation for $R_3CO_2H + O_3 \rightarrow R_3CO_2\cdot + O_2 + \cdot OH$ leads to a value of $\Delta H = +13$ kcal/mol. That is, the hydrotrioxide is considerably more susceptible to ozone attack on a thermochemical basis.

(25) P. S. D. De La Mare and R. Bolton, "Electrophilic Additions to Unsaturated Systems," Elsevier Publishing Co., Amsterdam, The Netherlands, 1966, p 115.

(26) C. Walling and E. A. McElhill, *J. Am. Chem. Soc.*, **73**, 2927 (1951).

creased amounts when oxygen is used as the ozone carrier.

The selectivity measurements at $-78°$ are also of interest. Other information indicates that profound differences in the total mechanism are to be expected between reactions carried out at these two temperatures. Two general points are obvious: decreasing the temperature not only decreases the likelihood of reaction 3 but greatly increases the relative rate of reaction 1 over *all* reactions because it would be expected to have a smaller activation energy than any other reaction.

There are some differences between ozone–oxygen and ozone–nitrogen streams evident in Tables II–IV. All measurements at $-78°$ in Table IV were subject to greater experimental error due to the fact that large relative rates require greater accuracy in measuring small changes in concentration of the least reactive compound and/or small total concentrations of the most reactive compound. Data at $-78°$ in Tables II and III show isotope effects to be only slightly decreased for ozone–oxygen *vs.* ozone–nitrogen streams. Reasonable postulations for relative rates of eq 1–10 can be used to rationalize these results.

Products.[27] Some of the processes for product formation from ether ozonations are reasonably obvious. For example, *t*-butyl formate is most likely formed from homolytic cleavage of $CH_3CH(O$-*t*-$Bu)O\cdot$ in the *t*-butyl ethyl ether ozonation while the *t*-butyl alcohol from this ozonation and the benzyl ether are easily obtainable from the corresponding hemiacetals. Equation 15 shows the general homolytic reaction

$$R-\underset{\underset{O\cdot}{|}}{\overset{\overset{R'}{|}}{C}}-OR'' \longrightarrow R-\overset{\overset{O}{\|}}{C}-OR'' + R' \qquad (15)$$
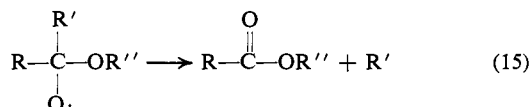
The fact that no *t*-butyl formate is formed in the ozonation of *t*-butyl benzyl ether is accounted for by the difference in bond energies (C–C *vs.* C–phenyl) in the ethers in question. In fact, C–H homolytic cleavage becomes feasible when the CH bond is particularly weak as is the case when R is phenyl and R′ is H in eq 15. The isopropyl acetate formed in the ozonation of isopropyl ether can also be accounted for by eq 15.
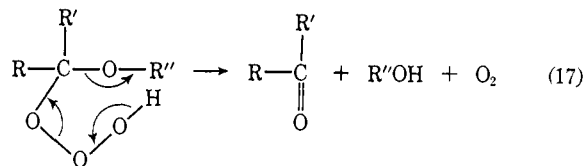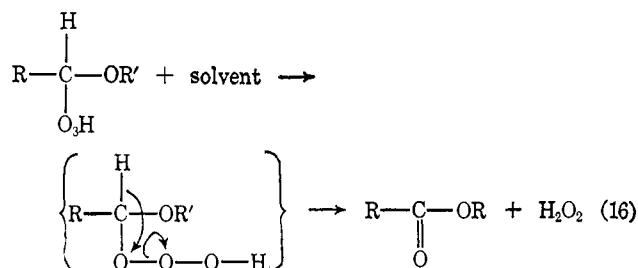
Heterolytic solvent-induced pathways can account for a portion of the major products as shown in eq 16.[28] All of the trioxides and tetroxides which are possible ozonation intermediates offer reasonable cyclic mechanistic pathways to products. Equation 17 shows one possible concerted decomposition.

Differences in product ratios can be accounted for in general terms by the proposed mechanism. Changes in the amount of *t*-butyl formate from *t*-butyl ethyl ether (and in the ratio of isopropyl acetate to cleavage prod-

$$R-\underset{\underset{O_3H}{|}}{\overset{\overset{H}{|}}{C}}-OR' + \text{solvent} \longrightarrow$$

$$\left\{ R-\underset{\underset{O-O-O-H}{|}}{\overset{\overset{H}{|}}{C}}-OR' \right\} \longrightarrow R-\overset{\overset{O}{\|}}{C}-OR + H_2O_2 \quad (16)$$

$$R-\underset{O}{\overset{\overset{R'}{|}}{C}}-O-R'' \longrightarrow R-\underset{\underset{O}{\|}}{\overset{\overset{R'}{|}}{C}} + R''OH + O_2 \quad (17)$$

ucts in isopropyl ether ozonations) can be rationalized as follows.

(a) Increasing solvent polarity should increase the rate of reaction 16 and decrease the amount of *t*-butyl formate (or isopropyl acetate) formed.

(b) Increasing the amount of oxygen present should increase the rate of reaction 6, decrease the amount of $RR'C(OR'')O\cdot$ present, and therefore decrease products formed by homolytic cleavage.

(c) An isotope effect on product ratios should be evident (increased amount of homolytic cleavage and/or increased amounts of hemiacetal products for deuterated products). All of the above points are observable in Tables V–VII.

Product ratios at -78 *vs.* $0°$ are not strictly accounted for by the above scheme. Several other reactions could be hypothesized but the 17 reactions already suggested seem to be as reasonable as current data allow.[29,30] Our mechanism also does not adequately describe the retention of configuration found for several ozonations of hydrocarbons.[8,9]

The product data from the neat ozonations of *t*-butyl ethyl ether (Table V) show (a) an intermediate is formed which can interact with pyridine to yield new product ratios and (b) this intermediate is not the only product present at low temperature because product ratios would be identical for both pyridine addition experiments if it were.

The qualitative observations on the effects of the addition of various reagents to ozonized isopropyl ether at $-78°$ would suggest that an unstable hydroperoxidic intermediate decomposes into radical products at about

(27) Most product ratios do not appear to be affected by further ozonation of any of the products. We have shown that *t*-butyl formate does not react significantly with ozone, and Walling and Mintz[20] have shown that formates react considerably slower than ethers in *t*-butoxide radical abstractions. Benzaldehyde and isopropyl alcohol yields do depend on conditions employed since both are further ozonized.

Also products do not appear to be formed through gas chromatographic pyrolysis of peroxidic intermediates as we have shown in several cases that product ratios obtained by gas chromatographic methods are identical with those obtained by nmr.

(28) The large acetate–formate ratios found when pyridine is present can be accounted for by eq 16. The effect of pyridine on other ozonation reactions has been under active investigation (K. Griesbaum, *Chem. Commun.*, 920 (1966); K. Griesbaum and G. W. Burton, *Preprints, Div. Petrol. Chem.*, 13, 216 (1968).

(29) P. S. Bailey [P. S. Bailey, J. E. Keller, D. A. Mitchard, and H. M. White, paper presented at the International Oxidation Symposium, San Francisco, Calif., Aug 1967; P. S. Bailey, D. A. Mitchard, and A. Y. Khashab, *J. Org. Chem.*, 33, 2675 (1968); we thank Professor Bailey for preprints of these publications] has proposed that the mechanism of the ozonation of amines takes place at least partially through an ozonate anion radical. Although we have no proof that such a process

$$R_3N^+OOO^- \rightleftharpoons R_3N\cdot^+ + \cdot O_3^-$$
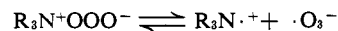
does not take place for ethers or alcohols, the considerably higher ionization potentials of the latter compounds *vs.* the amines [D. W. Turner, *Advan. Phys. Org. Chem.* 4, 31 (1966)] makes such a mechanism less likely.

(30) Another interesting reaction from the thermodynamic viewpoint is $RR'C(OR'')OO\cdot + O_3 \rightarrow RR'C(OR'')O\cdot + 2O_2$, $\Delta H = -36$ kcal/mol. Reaction 7 would be less likely to compete with this at low temperatures and the over-all result would be that eq 5, 6, and the latter would add up to give the same result as 5, 8, and 10. That is, the presence of oxygen would not change product ratios, isotope effects, or ozone stoichiometry even though it would be a reactant. Calculations for both this equation and eq 10 assume ground-state oxygen to be produced, which may not occur.

−10°. The temperature of decomposition, the strong hydroperoxide test before decomposition (and weak test after the exothermic reaction), and the fact that no hydroperoxide is present in the nmr spectra of several of the ethers studied would suggest that this intermediate is the hydrotrioxide, I.

The exothermic decomposition at −10° found for this system checks qualitatively with Bartlett and Guaraldi's observation[10] of a sharp irreversible decrease in the esr signal from di-t-butyl trioxide at about −12°.

Even if I is this thermally unstable intermediate, the amount formed directly by reaction 1 $vs.$ the amount formed in reaction 9 cannot be ascertained by the data presented in this paper. It is certain that reaction 1 cannot be the only one operating, even at −78°, since product ratios, relative rates, etc., vary with oxygen $vs.$ nitrogen as the ozone carrier.[31]

(31) Although this investigation leaves many questions unanswered as to the exact mechanism of the ozonation of ethers, isotope effect measurements and relative rate determinations appear to be of limited

In summary, the mechanism of the ozonation of ethers is a complicated one involving a free radical chain process and an unstable intermediate tentatively assigned structure I. Varying conditions (solvent polarity, temperature, and ozone carrier gas) could lead to more synthetic utility for the ozonation of ethers.

further usefulness. The identity of the temperature-sensitive intermediate and the exact product distribution are amenable to study by low-temperature nmr spectroscopy, and we have begun such a study. It has been suggested by a referee that since an unstable intermediate (presumably I) is present, a reaction sequence 1, 3, 5, 6, 7 and termination reactions 11–14 can account for the reaction mechanism more simply than the sequence outlined. Analogy and thermochemical reasoning led us to consider reactions such as (4) and (8) to go along with reaction 1 as ozone-consuming reactions. Until both the amount (we believe it to be present in small yield) and the exact structure of the unknown intermediate are established, we prefer the mechanism hypothesized here.

α-Halo Sulfones. X. Kinetics and Mechanism of the Rearrangement of Acyclic α-Halo Sulfones with Hydroxide Ion[1]

Leo A. Paquette and Lawrence S. Wittenbrook

Contribution from the Department of Chemistry, The Ohio State University, Columbus, Ohio 43210. Received June 5, 1968

Abstract: Kinetic and product studies of the reactions of $CH_3CH_2SO_2CHClR$ and $CH_3CHClSO_2CH_2R$ with hydroxide ion in aqueous dioxane have been performed. As the size of the R group increases from methyl to isopropyl, the proportion of *cis* olefin in the product mixture is seen to decrease. Parallel results were obtained when these α-chloro sulfones were rearranged with phenyllithium in xylene. The *cis* isomer did predominate in all cases and was seen to be formed consistently in greater relative yield when the leaving group was attached to the more bulky of the alkyl groups within a given isomeric pair. Although the rates of rearrangement did not vary excessively within the series examined, slightly faster displacements of chloride ion were noted when the halogen was attached to the less bulky alkyl substituent. A mechanistic interpretation is advanced to reconcile the available data.

The reaction by which α-halo sulfones (**1**) are converted to olefins upon treatment with base has developed into a transformation of considerable theoretical interest.[2] Because the double bond in the product (**2**) cleanly and unequivocally supplants the sulfonyl group of the starting halo sulfone, the rearrangement has also proven synthetically useful.[3] However utilitarian the process may be, it is the mecha-

$$RCH_2SO_2CHR' \xrightarrow{\text{base}} RCH{=}CHR'$$
$$\underset{\displaystyle Cl}{|}$$
$$\mathbf{1} \qquad\qquad \mathbf{2}$$
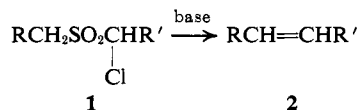
(1) For previous paper in this series, see L. A. Paquette, L. S. Wittenbrook, and K. Schreiber, *J. Org. Chem.*, **33**, 1080 (1968).

(2) For recent reviews of this subject, see (a) L. A. Paquette, *Accounts Chem. Res.*, **1**, 209 (1968); (b) L. A. Paquette in "Mechanisms of Molecular Migrations," Vol. I, B. S. Thyagarajan, Ed., Interscience Publishers, New York, N. Y., 1968, in press; (c) F. G. Bordwell, *Organosulfur Chem., Org. Sulfur Symp., 2nd Groningen, Neth.*, 311 (1966).

(3) (a) L. A. Paquette, *J. Am. Chem. Soc.*, **86**, 4383 (1964); (b) N. P. Neureiter, *J. Org. Chem.*, **30**, 1313 (1965); (c) L. A. Paquette and J. C. Philips, *Tetrahedron Letters*, 4645 (1967).

nistic detail of this rearrangement which continues to be the prime concern of several research groups principally because the Ramberg–Bäcklund reaction has supplied a number of uniquely varied and subtle problems which appear to be resolvable by physical-organic techniques.

At the present time, the gross mechanistic features of the title reaction are quite well understood.[2] Thus, evidence from a number of sources clearly indicates the existence of a rapid preequilibrium between the α-halo sulfone and all of its possible carbanions. Further, the rate of release of halide ion in aqueous base has been shown to be first order in halo sulfone and first order in hydroxide ion. Although the alkaline conditions required for rearrangement are sufficiently strenuous to preclude isolation of intermediate episulfones, the availability of both symmetrical and unsymmetrical episulfones by alternate syntheses has made it possible to establish that the decomposition of these three-membered sulfones under customary rearrangement conditions is markedly stereospecific.[4] There-