

Oxygenation of Hydrocarbons. 6.¹

Electrophilic Oxygenation of Aliphatic Alcohols, Ketones, and Aldehydes with Ozone in Superacids. Preparation of Bifunctional Derivatives

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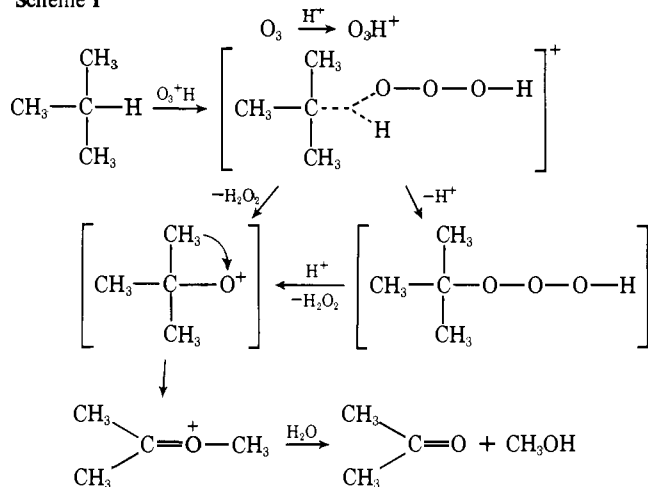
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Abstract: The reaction of ozone with aliphatic alcohols, ketones, and aldehydes in magic acid-SO₂ClF or FSO₃H solution has been investigated. Experimental results indicate the reactions proceed via electrophilic insertion of protonated ozone into the C-H σ bonds of the substrates at positions γ - or further removed from the oxonium centers present in the superacidic media. No oxidation products of the protonated (and thus protected) carbinol or carbonyl groups were observed. The reactions allow the preparation of bifunctional oxygenated derivatives.

Introduction

We reported previously the electrophilic nature of protonated ozone in superacidic media in its insertion reactions into the C-H or C-C σ bonds in alkanes.² For example, isobutane in superacids (1:1 FSO₃H-SbF₅ (magic acid), FSO₃H, HF-BF₃), or in HF and H₂SO₄ readily reacted with ozone, giving, via the intermediate dimethylmethoxycarbenium ion, acetone and methyl alcohol (Scheme I).

Scheme I



Despite the high reactivity of protonated ozone with alkanes in superacids, methyl alcohol, acetone, or acetaldehyde were not further oxidized by ozone in magic acid-SO₂ClF solution under our reaction conditions employed. In this superacidic system, these substrates are present as completely protonated species,³ i.e., CH₃OH₂⁺, (CH₃)₂C=O-H⁺, and CH₃(H)C=O-H⁺. Hence, it is reasonable to assume that protonated ozone will not readily react further with σ bonds in the proximity of the oxonium center in protonated substrates. On the other hand, σ bonds which are located sufficiently far from the charged oxonium center may be attacked by protonated ozone.

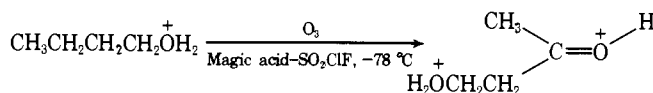
In order to clarify the behavior of oxygenated compounds in ozone-superacid systems, we now wish to report the results of our studies of the reaction of aliphatic alcohols, ketones, and aldehydes in magic acid-SO₂ClF or FSO₃H solution with ozone.

Results and Discussion

Alcohols. The results of the reaction of aliphatic alcohols

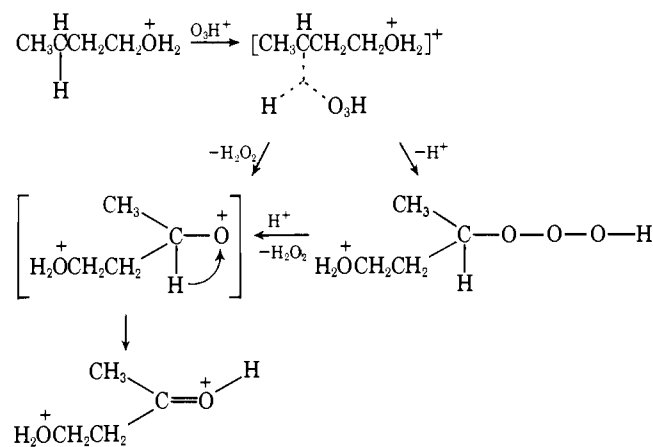
with ozone in magic acid-SO₂ClF or FSO₃H solution are summarized in Table I.

Aliphatic alcohols with short alkyl chains such as methyl, ethyl, and *n*-propyl failed to react under the reaction conditions with ozone. However, oxidation of *n*-butyl or higher homologue primary alcohols, which have secondary C-H bonds γ to the oxonium center, can take place at these bonds, giving keto al-



cohols as products. Products obtained, together with their ¹³C NMR and ¹H NMR parameters, are given in Table II.

Scheme II



These results are in sharp contrast to those observed in the absence of magic acid. In trichlorofluoromethane solution, ozonation of alcohols was reported to give exclusively products of α oxidation, i.e., carboxylic acids and ketones.⁴ It is thus reasonable to assume that presently studied reactions proceed via electrophilic oxygenation of the involved C-H bonds of the alcohols with protonated ozone, in analogy with previously studied alkanes, as shown in Scheme II, with the superacid protecting the fully protonated carbinol groups from oxidation.

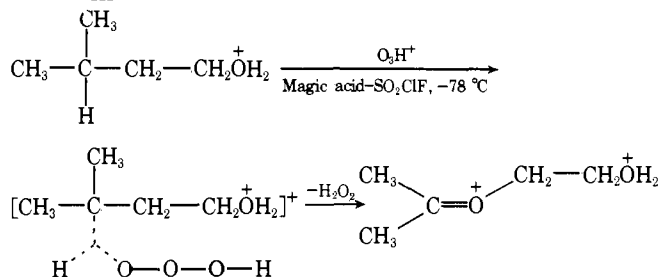
As reported in our preceding work,² the relative reactivity of σ bonds in alkanes with protonated ozone was generally found to be R₃C-H > R₂(H)C-H > R(H₂)C-H > C-C. This order of reactivity is again found in the present study. 3-Methyl-1-butanol (with a tertiary C-H bond at the γ position) undergoes reaction more readily than *n*-butyl alcohol (with a

Table I. Reaction Products of Aliphatic Alcohols with Ozone in Superacids^a

Alcohol	Superacid system	Reaction temp, °C	Conversion ^b %	Products
CH ₃ OH	MA ^c	-10	NR ^d	
CH ₃ CH ₂ OH	MA	-10	NR	
CH ₃ CH ₂ CH ₂ OH	MA	-20	NR	
	MA	-40	Low	
Same	FSO ₃ H	-20	NR	
CH ₃ CH ₂ CH ₂ CH ₂ OH	MA	-78	Tr	
Same	MA	-40	30	Same
Same	FSO ₃ H	-30	NR	
	MA	-78	NR	
Same	MA	-40	100	
Same	FSO ₃ H	-40	NR	
	MA	-78	NR	
Same	MA	-50	Low	
Same	MA	-40	30	
	MA	-78	100	
Same	FSO ₃ H	-78	70	
	MA	-78	Low	
Same	MA	-40	60	Same ^j
Same	FSO ₃ H	-40	NR	
CH ₃ CH ₂ CH ₂ CH ₂ CH ₂ OH	MA	-78	100	
Same	FSO ₃ H	-40	Tr	Same
	MA	-78	100	
Same	FSO ₃ H	-40	Low	Same
	MA	-78	100	
Same	FSO ₃ H	-78	Low	Same

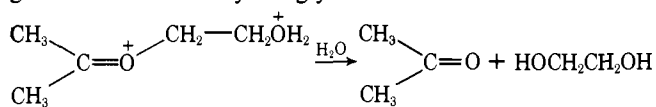
^a All experiments were carried out using magic acid (2.0 ml) -SO₂ClF (2.0 ml) - 10 mmol of alcohol or FSO₃H (3 ml) - 10 mmol of alcohol with 40 mmol of ozone (5% in oxygen). ^b Based on substrate. Analyzed by ¹H NMR spectroscopy. ^c Magic acid (FSO₃H - SbF₅, 1:1) - SO₂ClF solution. ^d No reaction takes place. ^e Chemical shifts of this compound were reported in our previous work; see G. A. Olah, D. G. Parker, N. Yoneda, and F. Pelizza, *J. Am. Chem. Soc.*, 98, 2245 (1976). ^f See ref 6. ^g Major product. ^h Almost 100%. ⁱ Traces of unidentified products were also observed. ^j Some CO₂ (δ¹³C 125.1) was also observed.

Scheme III



secondary C-H bond at the γ position) with protonated ozone giving oxidation-rearrangement products as shown in Scheme III.

The hydrolysis of the dimethyl- β -oxyethoxycarbenium ion gives acetone and ethylene glycol:⁵



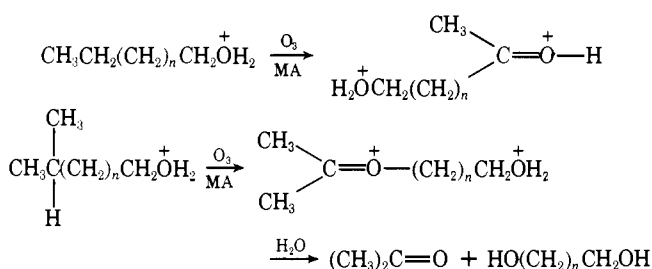
The data of Table I show that tertiary or secondary C-H bonds of primary alcohols located γ - or further away from the

Table II. NMR Chemical Shifts for Reaction Products Listed in Table I

Compound ^a	¹³ C NMR chemical shifts ^b							¹ H NMR chemical shifts ^c							
	¹ C	² C	³ C	⁴ C	⁵ C	⁶ C	⁷ C	1	3	4	5	6	7	C=O ⁺ H ⁺ OH ₂ ⁺	
	30.6	244.1	42.0	67.3				3.4	4.3	5.2				14.8	10.1
	30.3	246.4	39.5	20.8	75.6			3.2	3.8	2.7	4.9			13.9	9.3
	30.2	247.6	33.3	17.4	26.4	78.2		3.2	3.7	2.2	2.3	5.0		13.0	9.0
	32.8	248.0	28.2	78.3	70.7			3.2	3.2	5.3	5.0				10.5
	32.6	246.5	27.8	78.5	26.7	73.5		3.2	3.2	5.2	2.8	5.1			9.5
	32.3	244.7	27.3	83.3	23.1	24.5	78.1	3.2	3.2	5.1	2.5	2.5	5.0		9.1

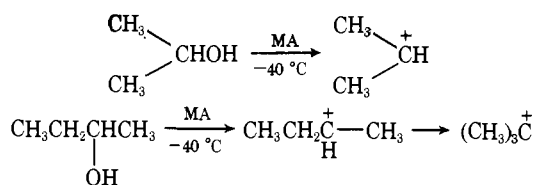
^a Magic acid -SO₂ClF solution. ^b δ¹³C external Me₄Si -60 °C. ^c δ¹H external Me₄Si -60 °C.

oxonium center undergo insertion reaction with protonated ozone, giving oxidation products⁶ in good yield. In general, straight chain primary alcohols produce keto alcohols (in their protonated form), and branched chain primary alcohols give dimethoxyalkoxycarbenium ions. The latter, upon hydrolysis, give acetone and the corresponding glycol.

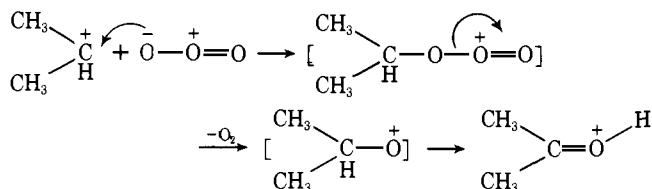


Similar reactions also take place in FSO₃H in the case of aliphatic alcohols in which *n* in the above formulae is larger than 4, at -40 °C. However, the yield of products is lower than that of magic acid-SO₂ClF solution. Obviously, ozone in the presence of FSO₃H is a weaker reagent as protonated ozone than in the presence of magic acid.

2-Propanol and 2-butanol in magic acid-SO₂ClF do not react with ozone at -78 °C, but give protonated acetone and dimethylmethoxycarbenium ion at -40 °C, respectively. In these systems, protolytic ionization of the alcohols is taking place at a reaction temperature of -40 °C, giving rise to the corresponding alkylcarbenium ion:



The formed alkylcarbenium ions can then react readily with ozone, giving oxidation products as reported previously.²

Table III. Reaction Products of Aliphatic Ketones and Aldehydes with Ozone^a in Magic Acid

Substrate	Reaction temp, °C	Conversion ^b %	Products
	-10	NR	
	-40	NR	
	-40	NR	
	-78	100	
	-78	100	
	-78	100	
	-50	NR	
	-40	Low	
	-78	60	
CH ₃ CHO	-10	NR	
CH ₃ CH ₂ CHO	-30	NR	
CH ₃ CH ₂ CH ₂ CHO	-78	80	

^a All experiments were carried out using magic acid (2.0 ml) -SO₂ClF or SO₂ (2.0 ml)-10 mmol of substrate with 40 mmol of ozone (5% in oxygen). ^b Based on substrate. ^c Magic acid-SO₂ solution. ^d Some CO₂ and traces of unidentified products were also observed.

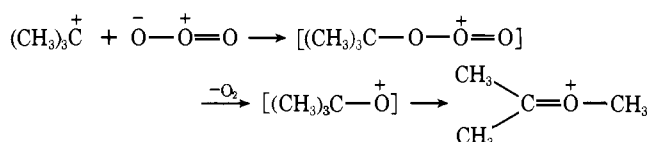


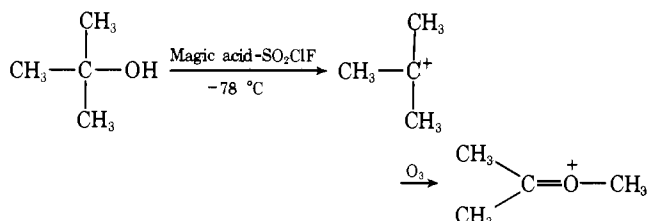
Table IV. NMR Chemical Shifts for Reaction Products Listed in Table III

Compound	¹³ C NMR chemical shifts ^c							¹ H NMR chemical shifts ^f								
	¹ C	² C	³ C	⁴ C	⁵ C	⁶ C	⁷ C	1	2	3	4	5	6	7	g	h
	30.4	245.0	36.7	36.7	245.0	30.4		3.5	4.4	4.4		3.5		15.6		
	30.3	247.4	41.9	14.5	41.9	247.4	30.3	3.1	3.6	2.5	3.6			3.1	13.4	
	7.1	34.9	245.1	36.7	38.3	248.4	30.4	1.9	3.9		4.1	4.1		3.1	13.7 and 14.1	
	246.3	35.6	35.0 ^d	246.3					4.4	4.4	4.4	4.4			16.0	
	248.4	35.6	17.3	36.8 ^e	248.4	42.8	41.9 ^e	3.6	2.2	3.6		4.0	4.0	15.2		
	30.5	244.9	46.4	36.3	232.9			3.2	4.2	4.0	9.5			14.7	13.8	

^a Magic acid-SO₂ClF solution. ^b Magic acid-SO₂ solution. ^c δ_{13C} external Me₄Si -60 °C. ^d Chemical shift difference between ²C and ³C comes from syn and anti form. ^e Chemical shift difference between C₂ and C₄, and C₆ and C₇ comes from syn and anti form. ^f δ_{1H} external

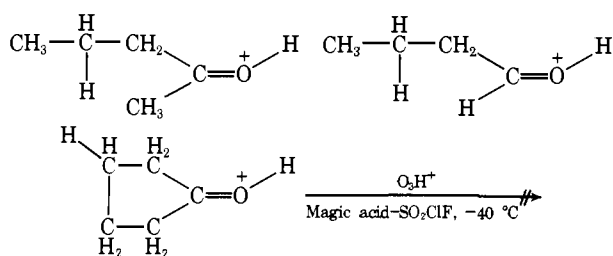
Me₄Si -60 °C. ^g ^h

This tendency is increased when the reaction is carried out using *tert*-butyl alcohol. *tert*-Butyl alcohol itself in magic acid-SO₂ClF solution gives very readily and quantitatively the trimethylcarbenium ion even at -78 °C. In the presence of ozone under the same conditions it thus gives the dimethylmethoxycarbenium ion:



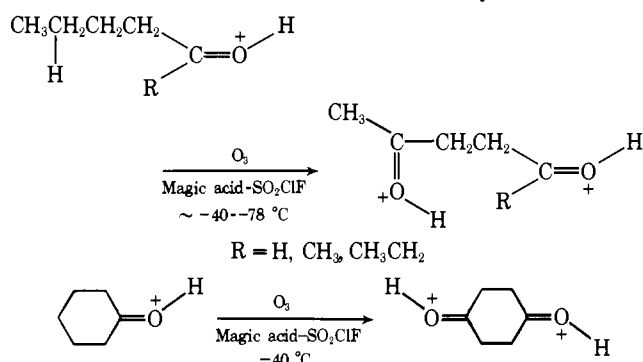
Ketones and Aldehydes. The results of the reactions of aliphatic ketones and aldehydes studied are summarized in Table III. The ¹H NMR and ¹³C NMR chemical shifts of products are given in Table IV.

As contrasted with the reaction of previously discussed aliphatic alcohols, secondary C-H bonds of aliphatic ketones and aldehydes located even γ- to the carbonyl oxygen do not react with protonated ozone in the presence of magic acid-SO₂ClF solution at -40 °C, e.g.

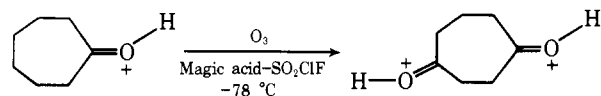


The strong electron-withdrawing effect of the protonated carbonyl oxygen is sufficiently strong to inhibit reaction at

these C-H bonds. Reactions of higher homologue ketones and aldehydes, however, do take place with ozone in magic acid, giving oxygenated products which arise from oxygen insertion into σ bonds located further from the carbonyl function.



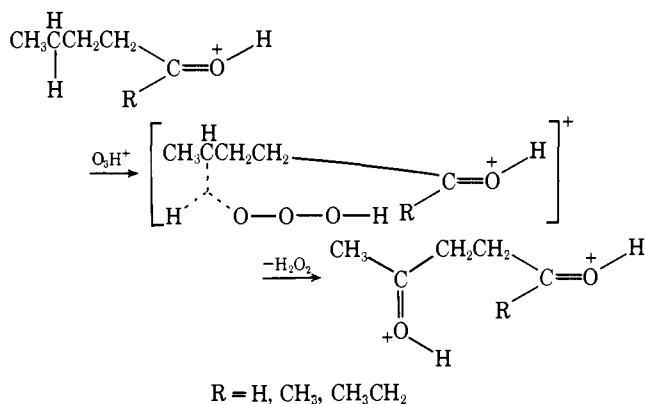
In case of cyclohexanone, the yield of 1,4-cyclohexanedione is low, even at a reaction temperature of -40 °C. However, the reaction of cycloheptanone, having two methylene groups γ- to the carbonyl carbon, produces 1,4-cycloheptanedione in 60% yield at -78 °C.



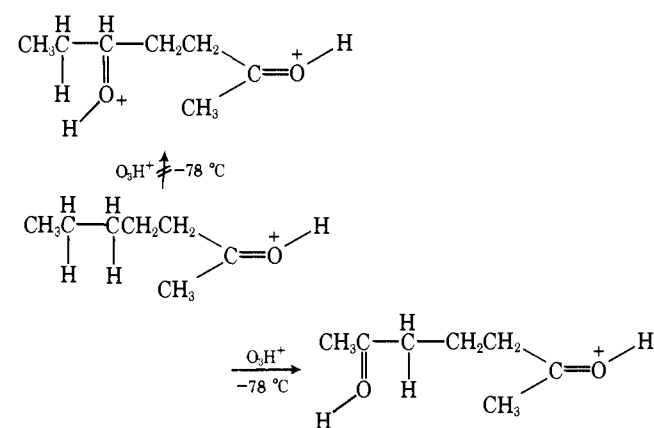
In previously studied ozonolysis reactions of aldehydes with neutral ozone, White and Bailey⁷ and Erickson et al.⁸ suggested that the ozone's attack on the carbonyl carbon is a concerted 1,3-dipolar insertion, having electrophilic character. There was, however, no other attack observed than on the carbonyl carbon. Reactions of ketones with neutral ozone also yielded only products due to attack on the carbonyl carbon.⁹

In contrast, presently studied systems using superacidic

conditions in reactions with 5% ozone containing oxygen give no products (judging from their NMR spectroscopic analysis) arising from carbonyl-carbon oxidation. Hence, the reaction path can be described as involving electrophilic oxygenation of C-H σ bonds by protonated ozone:



Although protonated ozone can, as shown, undergo insertion into secondary γ -C-H bonds, in the case of 2-heptanone the secondary δ -C-H bonds react exclusively:



Thus the position of electrophilic attack by O_3H^+ seems to show considerable selectivity due to the effect of the carboxonium center present in the substrate.

Conclusions

From the results obtained, it is reasonable to conclude that the observed oxygenation reactions are due to electrophilic insertion by protonated ozone into the involved C-H δ bonds of the aliphatic alcohols, ketones, or aldehydes via two-electron three-center bonded carbonium ions. The reactivity of C-H bonds toward protonated ozone is effected by the electron-withdrawing nature of the carboxonium centers present in the superacidic media and thus shows significant selectivity.

Experimental Section

Materials. All substrates (alcohols, ketones, and aldehydes) were commercially available and of highest purity. They were used without further purification. SbF_5 and FSO_3H were used after distillation. Ozone was generated with a Welsbach T-816 generator.

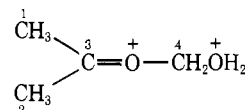
Oxygenation Procedures. The appropriate substrate (10 mmol; alcohol, aldehyde, ketone) in 1.5 ml of SO_2ClF solution cooled to $-78^\circ C$ was added to magic acid (2.0 ml) $-SO_2ClF$ (0.5 ml) solutions at $-78^\circ C$ in a 15-ml glass reaction vessel, equipped with gas inlet and outlet. The reaction mixture was then reacted with 30–50 mmol of ozone (5% in oxygen) being bubbled through the solution at a flow rate of 0.3 l./min at the temperature (generally $-78^\circ C$) indicated, with sufficient external cooling. Upon ozonolysis the colorless solutions usually turned brown.

After introduction of the desired amount of ozone an aliquot of the resultant solution, without isolation of products, was subjected to analysis by 1H and ^{13}C NMR spectroscopy (being transferred into a precooled NMR tube for direct analysis). The experimental conditions were similar to those described in our preceding papers.^{1,2} Another aliquot was hydrolyzed with excess of crushed ice. After neutralization with Na_2CO_3 the products [i.e., corresponding diols (alcohols), keto alcohols, and dicarbonyl (carbonyl) compounds] were extracted with the ether and analyzed by gas-liquid chromatography.

Acknowledgment. Partial support of our work by the National Science Foundation is gratefully acknowledged.

References and Notes

- (1) Part 5: G. A. Olah, D. G. Parker, and N. Yoneda, *J. Org. Chem.* in press.
- (2) G. A. Olah, N. Yoneda, and D. G. Parker, *J. Am. Chem. Soc.*, **98**, 5261 (1976).
- (3) For a summary, see G. A. Olah, A. M. White, and D. H. O'Brien, *Chem. Rev.*, **70**, 561 (1970), and references given therein.
- (4) M. C. Whiting, A. J. N. Bolt, and Y. H. Parish, *Adv. Chem. Ser.*, No. **77**, 4 (1968).
- (5) As isolated products after quenching the magic acid solution of 3-methyl-1-butanol.
- (6) Attempts were also made to compare the relative reactivity between secondary C-H and tertiary C-H bonds at β position with ozone in magic acid- SO_2ClF solution using propyl alcohol and 2-methylpropanol, respectively. The former did not react, even at temperature of $-20^\circ C$, but the latter undergoes reaction at $-50^\circ C$, giving as dimethylloxymethoxycarbonium ion, i.e.,



- which arises from oxygen insertion into the tertiary C-H bond in 2-methylpropanol. $\delta^{13}C$ (Me₄Si) 32.9 (C₁), 248.4 (C₂), 28.4 (C₃), 182.6 (C₄); δ^1H (Me₄Si) 3.1 (CH₃) (the acidic $^+OH_2$ protons could not be clearly observed). The system, however, based on the complexity of the NMR spectra, contains other by-products and is not sufficiently clear to allow conclusions to be reached. When the reaction was carried out at $-40^\circ C$ or above, dimethylmethoxycarbonium ion formation was predominant. This arises from direct ionization of the precursor alcohol which gives trimethylcarbonium ion.
- (7) H. M. White and P. S. Balley, *J. Org. Chem.*, **30**, 3037 (1965).
 - (8) E. Erickson, D. Bakalk, C. Richards, M. Scanlon, and G. Huddleston *J. Org. Chem.*, **31**, 461 (1966).
 - (9) J. E. Leffler, *Chem. Rev.*, **45**, 385 (1949).