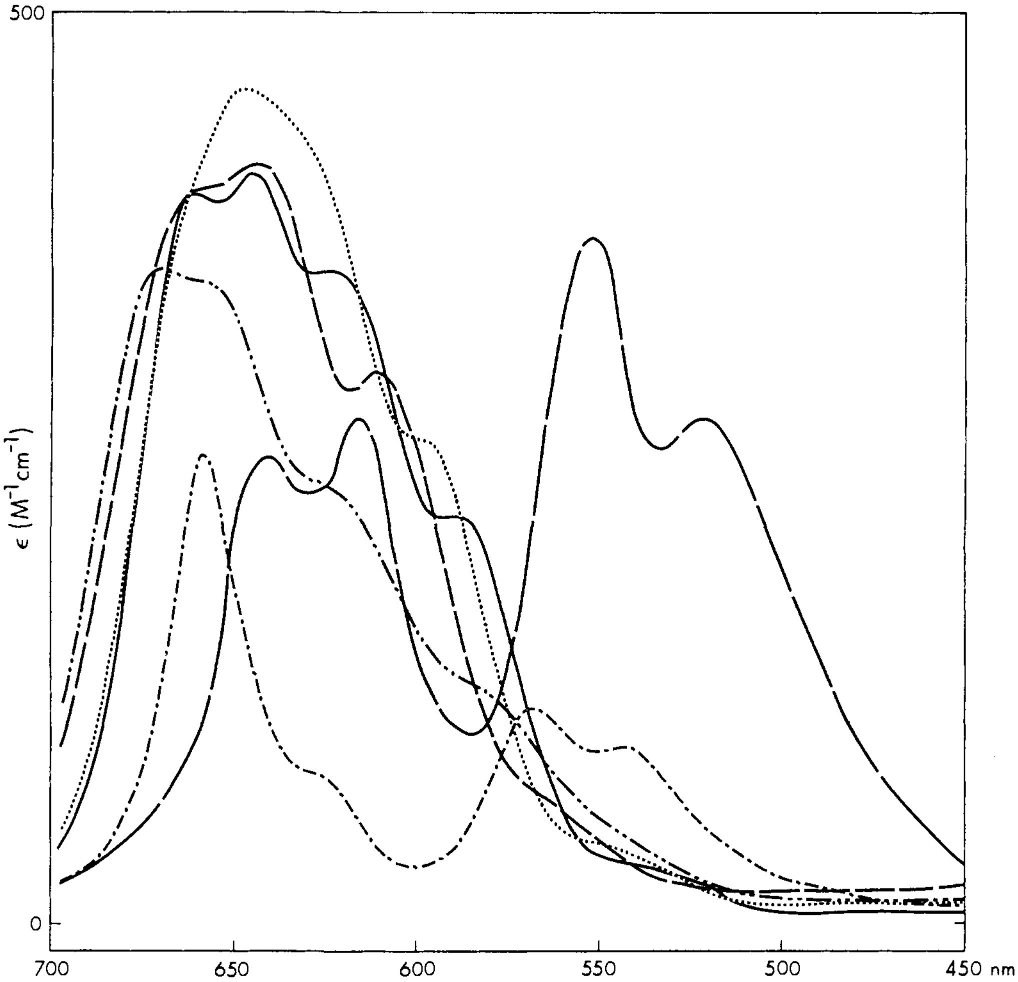


Figure 1. UV-visible spectra of 1:1 **2c**-Co(NO$_3$)$_2$ solutions saturated with different anions in 4:1 ethanol-H$_2$O; Cl$^-$ (—); Br$^-$ (- - -); I$^-$ (– – –); F$^-$ (— - — -); N$_3^-$ (— -- —). The spectrum of Co^{2+} bovine carbonic anhydrase in unbuffered solution at pH 8.8 (— —) redrawn from: Bertini, I.; Luchinat, C.; Scozzafava, A. *Inorg. Chim. Acta* **1980**, *46*, 85.

2c-Co^{2+} spectra are not indicative of tetrahedral coordination but are more consistent with predominant 5- and/or 6-coordinate Co^{2+}.[9,10] Thus the metal binding site of **2c** is flexible enough to allow access of one or more additional ligands other than the three from the phosphine. This feature may be important if the transition state for CO$_2$ hydration by **2c**-Zn^{2+} involves 5-coordinate Zn^{2+}.[1d]

Catalytically, the **2a-c**-Zn^{2+} complexes are interesting. While **2a,b-Zn^{2+}** show negligible catalysis toward CO$_2$ hydration, **2c**-Zn^{2+} appears to be active (Table I). No catalysis by **2a**, **2b**, or **2c** is observed in the absence of Zn^{2+}. The observation that catalysis by **2c**-Zn^{2+} is reduced at pH 6.5 relative to what is observed at 7.0 may indicate that some basic form of this complex is catalytically viable.[11]

Ligand **2c** shows other features in common with CA. Small ligands such as bipyridyl and terpyridine characteristically bind to Zn^{2+} very rapidly (10^6 M^{-1} s^{-1})[12] with slightly positive E_a's and slightly negative $\Delta S^\ddagger$ values (8.4 kcal/mol and -5 eu, respectively).[12] Apo-CA binds Zn^{2+} somewhat slower (2 × 10^4 M^{-1} s^{-1}, pH 7.5),[13] with a high E_a and large positive $\Delta S^\ddagger$ (20.8 kcal/mol and +30 eu).[13] Between pH 5 and 7, **2c** also binds Zn^{2+} slowly (3 × 10^4 M^{-1} s^{-1}), in agreement with its being a reasonable model for the CA metal site; however, its activation parameters (9.9 kcal/mol and -4 eu, respectively) are more indicative of those for a smaller ligand.

Although the catalysis afforded by **2c**-Zn^{2+} is encouraging, it is modest when compared to that exhibited by the enzyme. Further study of this and related ligands is clearly warranted to delineate the minimum features responsible for activity.

Acknowledgment. We thank the University of Alberta and NSERCC for financial support of this work, Professor R. B. Jordan for assistance in determining CO$_2$ hydration rates by stopped flow kinetics, and Dr. A. Khalaj for preliminary synthetic efforts directed toward the phosphines.

J. Huguet, R. S. Brown*
Department of Chemistry, University of Alberta
Edmonton, Alberta, Canada T6G 2G2
Received June 26, 1980

---

[11] Titration experiments on **2c**-Zn^{2+} show an ionization of some associated group which we tentatively assign as **2c**-Zn^{2+}-OH$_2$. However, the titration curve is not easily analyzed as having arisen from a single well-defined event. **Note Added in Proof.** More recent experiments with **2c**-Zn^{2+} indicate that its catalysis toward CO$_2$ hydration drops at pH 7.5 to ~60 M^{-1} s^{-1}. This may indicate that **2c**-Zn^{2+} suffers some complex hydrolysis at increased pH as does **1**-**Zn^{2+}**. Experiments performed under slightly different conditions indicate that the k_{cat} terms for both CO$_2$ hydration and HCO$_3^-$ dehydration may be substantially larger than reported in Table I.

[12] Hoyler, R. H.; Hubbard, C. D.; Kettle, S. F. A.; Wilkins, R. G. *Inorg. Chem.* **1965**, *4*, 929; **1966**, *5*, 622.

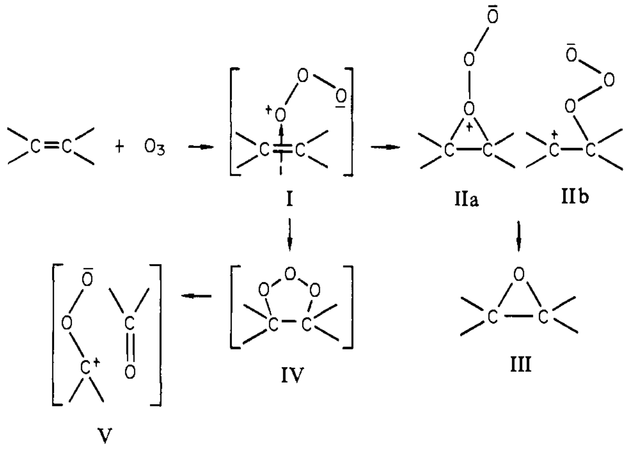
[13] Henkens, R. W.; Sturtevant, J. M. *J. Am. Chem. Soc.* **1968**, *90*, 2669.

Ozonolysis of Trifluoroethylene, 1,1-Difluoroethylene, and Perfluoroethylene. Epoxide and Ozonide Formation

Sir:

Ozone and trifluoroethylene were mixed in 1,1,2-trichloro-1,2,2-trifluoroethane at 0 °C. The major volatile products have been identified as formyl fluoride, carbonyl fluoride, trifluoroethylene ozonide, and trifluoroethylene oxide. Obtained in lower yield was *trans*-1,2-difluoroethylene ozonide. Also studied by using the same conditions as above were the reactions of ozone with 1,1-difluoroethylene and perfluoroethylene. Carbonyl fluoride and 1,1-difluoroethylene ozonide are the major volatile products of the ozonolysis of 1,1-difluoroethylene. This result is consistent with that found at -75 °C in CH_3Cl.[1,2] Carbonyl fluoride and perfluoroethylene oxide have been identified as the major volatile products of the ozonolysis of perfluoroethylene. Gozzo and Camaggi have found the same products under similar reaction conditions. They also found minor amounts of perfluorocyclopropane and a trace amount of perfluoroethylene ozonide.[3]

Epoxides are formed in the ozonolysis of sterically hindered 1-olefins[4] as well as *cis*- and *trans*-1,2-difluoroethylenes[5] and perfluoroethylene.[3] Bailey and Lane proposed a mechanism which consists of a competition leading to ozonide through molozonide IV and carbonyl oxide V and electrophilic attack of ozone to give epoxide III via a π complex (I)[6] or a σ complex (IIa or IIb).[7-9]



In the case of perfluoroethylene it was postulated difluorocarbonyl oxide and carbonyl fluoride form from the reaction of ozone with perfluoroethylene. Epoxide comes from difluorocarbonyl oxide reacting with perfluoroethylene. Ozonolyses of deuterium-labeled *cis*- and *trans*-1,2-difluoroethylenes[5] have shown there is no carbon scrambling in epoxide formation, and the results could be rationalized by both the complete[3] and partial cleavage mechanisms[4] outlined.

The results of this work combined with previous investigations[3,5] show that fluorinated epoxides are major ozonolysis products from fluorinated ethylenes when fluorines are substituted on both sides of the double bond. In contrast, vinyl fluoride[10] and 1,1-difluoroethylene[1] ozonolyses produce solely ozonide and aldehyde as major products. Present studies show that for the series 1,1-difluoroethylene, trifluoroethylene, and perfluoroethylene, ozonide yields are 20% for 1,1-difluoroethylene ozonide, 13% for trifluoroethylene ozonide, and none detected for perfluoroethylene ozonide.

It is likely that the initial attack of ozone on the olefin is governed by the electron-withdrawing effects of the fluorine atoms. Huisgen has mentioned that the electrophilic attack of ozone as in I can be treated as a 1,3-dipolar cycloaddition.[11] Hence, he reasoned that chlorinated and fluorinated alkenes are poor 1,3-dipolarophiles due to a decrease in electron density of the double bond. The present results are consistent with this trend. Perfluoroethylene will not react with ozone at -95 °C whereas vinyl fluoride and *cis*-1,2-difluoroethylene react readily.[10] Even though the overall rate may decrease with increased fluorination, it is possible the partial cleavage route to epoxide via II is favored over 1,3-dipolar cycloaddition when fluorines are substituted on both sides of the double bond.

The trend noted in ozonide yields for 1,1-difluoroethylene, trifluoroethylene, and perfluoroethylene does not necessarily indicate poorer 1,3-dipolarophilic reactivity toward ozone. The appearance of carbonyl fluoride as a major product in the ozonolysis of perfluoroethylene shows a complete cleavage pathway is contributing to the reaction mechanism. It is possible the observed trend in ozonide yield in part reflects differences in reactivity of the carbonyl oxide intermediate (V) and aldehyde.[12] If increasing fluorination of V and/or aldehyde lowers reactivity of these species toward each other, then the observed low yield of perfluoroethylene ozonide[3] (none detected in the present study) is reasonable. Aldehyde trapping experiments are currently under investigation to determine carbonyl oxide reactivity and whether these species are involved in epoxide formation.

The identification of the cross ozonide, *trans*-1,2-difluoroethylene ozonide, in the ozonolysis of trifluoroethylene is consistent with the complete cleavage route. In terms of the Criegee mechanism it is likely IV cleaves to give both monofluoro- and difluorocarbonyl oxide. *cis*-1,2-Difluoroethylene ozonide has not been isolated in sufficient yield to characterize. It is likely that a small shoulder on the *trans*-ozonide peak in the gas chromatogram is the *cis*-ozonide because it has the same retention time known for authentic *cis*-ozonide.[5] This places an upper limit of 10/90 upon the *cis*-/*trans*-ozonide ratio which is in agreement with the stereochemical predictions contained in an earlier investigation of *cis*- and *trans*-1,2-difluoroethylenes.[5]

In a typical reaction, 2.5 mmol of ozone and 3.0 mmol of olefin are allowed to flow separately into 30 mL of $CF_2ClCFCl_2$ at atmospheric pressure and 0 °C. The ozone is adsorbed on silica gel and then purged with helium to remove oxygen from the system.[13] Flow rates for ozone (in He) and olefin are approximately 0.12 mmol/min.[14] Products are collected by two methods: low-temperature fractional distillation of the solvent and collection of material bubbled out of the solvent. Further purification is done by gas chromatography using a 17-ft Teflon column packed with 10% halocarbon oil on 40–60 mesh Chromosorb T at 22 °C.[15]

1,1-Difluoroethylene ozonide, perfluoroethylene oxide, formyl fluoride, and carbonyl fluoride were identified by their known gas-phase infrared spectra.[1,16-18] Trifluoroethylene oxide was characterized by IR, NMR, and mass spectral means. It has been mentioned as a known compound; however, no spectral data were given.[19,20] A prominent feature of the gas-phase infrared spectrum

---

(1) Gillies, C. W.; Sponseller, S. P.; Kuczkowski, R. L. *J. Phys. Chem.* **1979**, *83*, 1545–1549.

(2) The carbonyl fluoride and formaldehyde reported in ref 1 were from ozonide decomposition; lower boiling fractions containing solvent were not analyzed in that work. A solid white peroxidic material is found left in the reactor after the distillation of the volatile materials. This material was subsequently reduced by a 0.1 M KI solution. However, a residue was not found in the perfluoroethylene and trifluoroethylene reactions.

(3) Gozzo, F.; Camaggi, G. *Chim. Ind. (Milan)* **1968**, *50*, 197–199.

(4) Bailey, P. S.; Lane, A. G. *J. Am. Chem. Soc.* **1967**, *89*, 4473–4478.

(5) Gillies, C. W. *J. Am. Chem. Soc.* **1977**, *99*, 7239–7245.

(6) Bailey, P. S.; Ward, J. W.; Carter, T. P.; Nieh, E.; Fischer, C. M.; Khashab, A. Y. *J. Am. Chem. Soc.* **1974**, *96*, 6136–6140.

(7) Criegee, R. *Rec. Chem. Prog.* **1957**, *18*, 111–120. Criegee, R. *Adv. Chem. Ser.* **1959**, *No. 21*, 133–135.

(8) Bailey, P. S.; Mainthia, S. B.; Abshire, C. J. *J. Am. Chem. Soc.* **1960**, *82*, 6136–6142.

(9) Story, P. R.; Murray, R. W.; Youssefyeh, R. D. *J. Am. Chem. Soc.* **1966**, *88*, 3144–3146.

(10) Mazur, U.; Lattimer, R. P.; Lopata, A.; Kuczkowski, R. L. *J. Org. Chem.* **1979**, *44*, 3181–3185. Mazur, U.; Kuczkowski, R. L. *Ibid.* **1979**, *44*, 3185–3188.

(11) Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 565–632; 633–796.

(12) In ref 10 results indicate that formaldehyde traps carbonyl oxide more effectively than formyl fluoride.

(13) Bailey, P. S.; Reader, A. M. *Chem. Ind. (London)* **1961**, 1063–1064.

(14) Higher flow rates of perfluoroethylene with ozone resulted in explosions. A blast shield was used in the ozonolyses to protect the operator.

(15) In the case of perfluoroethylene, contents of the low boiling trap consist of carbonyl fluoride, perfluoroethylene oxide, and unreacted olefin. These are separated by chemical means. Carbonyl fluoride reacts rapidly with H_2O to give hydrogen fluoride and carbon dioxide. The hydrogen fluoride is removed by a low-temperature fractional distillation and carbon dioxide by passing it over Ascarite. Unreacted olefin is removed by bromine addition.

(16) Craig, N. C. *Spectrochim. Acta, Part A* **1972**, *28A*, 1195–1201.

(17) Morgan, H. W.; Staats, P. A.; Goldstein, J. H. *J. Chem. Phys.* **1956**, *25*, 337–342.

(18) Nielsen, A. A.; Burke, T. G.; Woltz, P. J. H.; Jones, E. A. *J. Chem. Phys.* **1952**, *20*, 596–604.

(19) Tarrant, P.; Allison, C. G.; Barthold, K. P. "Fluorine Chemistry Reviews"; Marcel Dekker: New York, 1971; pp 77–113.

is a strong band at 1536 cm^{-1} which is consistent with the ring breathing mode found in other fluorinated epoxides.[5,16] The ^{1}H NMR spectrum consists of eight peaks located centrosymmetrically at 35.3, 38.0, 40.4, and 43.1 Hz from the center. The chemical shift in CDCl$_3$ is 5.85 ppm (Me$_4$Si internal reference). Analysis of the spectrum gives the following coupling constants: J_{HF}(gem) = 78.6 Hz, J_{HF}(cis or trans) = 5.1 Hz, and J_{HF}(cis or trans) = 2.7 Hz. The chemical shift and coupling constants correlate well with those reported for *cis*-1,2-difluoroethylene oxide.[5,21] The mass spectral fragmentation patterns are similar to those found in other fluorinated epoxides.[5,22] Trifluoroethylene ozonide was characterized by IR, NMR, and mass spectrometry. The gas-phase infrared spectrum consists of strong absorptions in the 1350–1050-cm^{-1} region which is very reasonable as compared to other similar ozonides.[1,3,5,10] The ^{1}H NMR spectrum consists of four peaks located centrosymmetrically at 39.1 and 36.7 Hz from the center. The chemical shift in (CD$_3$)$_2$CO is 7.63 ppm (Me$_4$Si internal reference). This compares well with the chemical shift of 7.60 ppm found in *trans*-1,2-difluoroethylene ozonide in the same solvent.[23] Analysis of the spectrum gives the following coupling constants: J_{HF}(gem) = 75.8 Hz, J_{HF}(trans) = 2.4 Hz, and J_{HF}(cis) = 0 Hz. These values compare well with those found in vinyl fluoride ozonide and *trans*-1,2-difluoroethylene ozonide.[5,10] The mass spectral fragmentation patterns are similar to other fluorinated ozonides.[1,3,5,10] *trans*-1,2-Difluoroethylene ozonide was identified by its known gas-phase infrared spectrum.[5]

Acknowledgment is made to Philip Ralli for help in obtaining NMR spectra and Karl Moschner for help with the mass spectrometer. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

---

(20) Ginsburg, V. A.; Vlasova, E. S.; Vasil'eva, M. N.; Mirzabekova, N. S.; Makarov, S. P.; Shchekotiskin, A. I.; Yakubovich, A. Ya. *Dokl. Akad. Nauk SSSR.* **1963**, *149*, 97–99.

(21) The chemical shift of *cis*-1,2-difluoroethylene oxide in CDCl$_3$ is 5.45 ppm (Me$_4$Si internal reference): C. W. Gillies, unpublished results.

(22) Prager, J. H. *J. Org. Chem.* **1966**, *31*, 392–394.

(23) R. L. Kuczkowski, private communication.

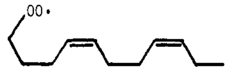
John W. Agopovich, Charles W. Gillies*
Cogswell Laboratory, Rensselaer Polytechnic Institute
Troy, New York 12181

Received June 30, 1980

Serial Cyclization of Peroxy Free Radicals: Models for Polyolefin Oxidation

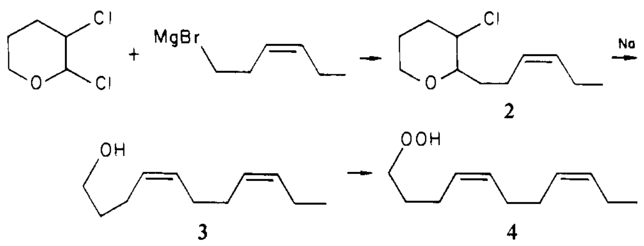
Sir:

The fate of peroxy radicals formed in autoxidation is dependent on several factors involving both the conditions of oxidation and molecular structure. In polyunsaturated materials, intramolecular addition of peroxy radicals to double bonds to form cyclic peroxides has been demonstrated,[1-4] and cyclic peroxides may well be primary products in the oxidative degradation of polyolefins such as diene polymers as well as in the autoxidation of isoprenoid and lipid natural products.[5] We chose peroxy radical **1** as a model for polybutadiene autoxidation, and we report here the isolation and characterization of novel polycyclic polyperoxides resulting from the serial cyclization of radical **1**. This study establishes the validity of the concept of serial cyclization in polymer and natural-product oxidation and provides information about factors important in the stereochemical control of free-radical cyclization.



1

Scheme I



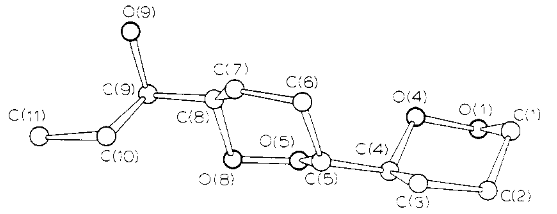
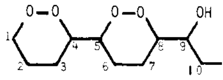


Figure 1. Structure and solid-state conformation of **5a**.

Hydroperoxide **4**, prepared according to Scheme I, served as a precursor to **1**.[6] Thus, 0.2 M **4** in benzene under oxygen was treated with 0.1 to 1.0 radical equiv of di-*tert*-butyl hyponitrite (DTBN)[7] initiator at 30 °C. After approximately 50% consumption of **4** (48–72 h), the reaction was terminated by cooling to 0 °C, followed by addition of an amount of triphenylphosphine equal to the initial number of moles of **4**. Thin-layer chromatography showed two peroxide-positive products (R_f 0.39 and 0.29)[8] in addition to alcohol **3** and Ph$_3$PO. High-performance LC[9] provided four major crystalline peroxide products (**5a–d**) with retention volumes and percentage of peroxide mixture as follows: **5a**, 69 mL, 30%; **5b**, 78 mL, 33%; **5c**, 120 mL, 15%; **5d**, 132 mL, 22%. Product accountability approached 70%, and **5a–d** were far and away the dominant products of the reaction as judged by high-performance LC and TLC. Although compound **5** has four chiral centers and thus eight diastereomers are possible, it is highly significant that only four major racemic products having this polycyclic structure were found.

The four peroxide products **5a–d** gave similar ^{1}H and ^{13}C NMR spectra which notably lacked any vinylic proton or carbon signals. ^{1}H NMR spectra generally displayed a triplet [δ 1.0 (3 H, CH$_3$)], a broad multiplet [δ 1.2–2.2 (10 H)], a multiplet [δ 3.5 (1 H α to OH)], and another broad multiplet [δ 4.2, 5 H α to -O-O-]. In addition to having a single signal between 9.5 and 10.1 ppm, the ^{13}C NMR spectra contained a group of five signals from 22 to 26 ppm, two signals in the 73-ppm region, and three more



5

---

(1) Porter, N. A.; Funk, M. O.; Gilmore, D.; Isaac, R.; Nixon, J. *J. Am. Chem. Soc.* **1976**, *98*, 6000.

(2) Roza, M.; Francke, A. *Biochim. Biophys. Acta* **1978**, *528*, 119.

(3) Chan, H. W. S.; Matthew, J. A.; Coxon, D. T. *J. Chem. Soc., Chem. Commun.* **1980**, 235.

(4) Golub, M. A.; Hsu, M. S.; Wilson, L. A. *Rubber Chem. Technol.* **1975**, *48*, 953.

(5) Porter, N. A. *Free Radicals Biol.*, **1980**, *4*, 261.

(6) (a) Hydroperoxide **4** is a mixture of *E* and *Z* isomers at Δ_4 while the stereochemistry about Δ_8 is only *Z*. The Δ_4 *E* and *Z* isomers may be separated by high-performance LC. The synthesis of **4** follows literature procedures directly. See ref 1 and also: Ansell, L.; Selleck, K. *J. Chem. Soc.* **1956**, 1238. (b) Wawzorek, S.; Klimstra, P. D.; Kallio, R. E. *J. Org. Chem.* **1960**, *25*, 621. This procedure was used for synthesis of the hydroperoxide from the mesylate.

(7) (a) Mendenhall, G. D. *J. Am. Chem. Soc.* **1974**, *96*, 5000. (b) Kiefer, H.; Traylor, T. G. *Tetrahedron Lett.* **1966**, 6163.

(8) TLC was carried out on silica plates (Merck Co.) with ether solvent.

(9) High-performance LC was carried out on a Whatman Magnum 9 10-μm silica column with refractive index detection. Solvent used in the chromatography was 5% isopropyl alcohol/hexane.

0002-7863/80/1502-7574$01.00/0