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UNIVERSITY OF ALBERTA

(ALKOXY)ARYLDIOXIRANES FROM OZONATION OF ALKENES

BY

YU XIE

A THESIS
SUBMITTED TO THE FACULTY OF GRADUATE STUDIES
AND RESEARCH IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

EDMONTON, ALBERTA

FALL, 1994

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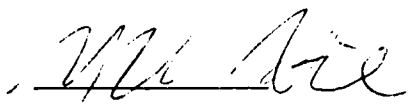

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(ALKOXY)ARYLDIOXIRANES

FROM OZONATION OF ALKENES

submitted by YU XIE in partial fulfillment of the requirements for the degree of Doctor of Philosophy in chemistry.

Supervisor
K. R. Kopecky

H. J. Liu

D. D. Tanner

M. Cowie

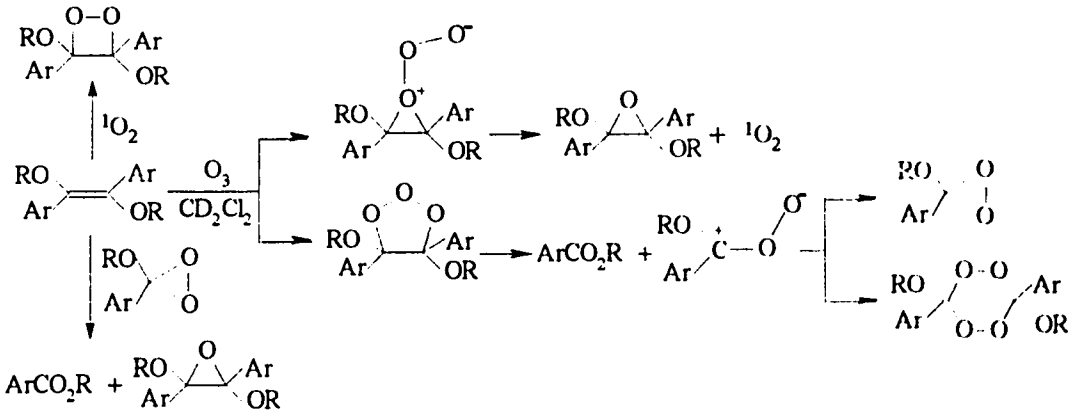
P. Sporns

A. P. Schaap

Date: September 30, 1994

Abstract

All or some of the following products are produced from ozonation of *E*- or *Z*-1,2-dialkoxy-1,2-diarylethenes under different conditions: the alkyl benzoates, 2,3-dialkoxy-2,3-diaryloxiranes, 3,4-dialkoxy-3,4-diaryldioxetanes, 3,6-dialkoxy-3,6-diaryl-1,2,4,5-tetroxanes, and (alkoxy)aryldioxiranes. The formation of the oxiranes and dioxetanes is stereospecific. Product formation and distribution vary with starting material, initial concentration of the alkene, reaction temperature, solvent, and the method of the ozonation. The initial interaction between ozone and the alkene results in the formation of two intermediates, i.e., the primary ozonide and oxygenated oxirane of the alkene. Decomposition of the oxygenated oxirane gives the oxirane and singlet oxygen which reacts with the unreacted alkene to give the dioxetane. Cleavage of the primary ozonide gives the benzoate and the (alkoxy)arylcarbonyl oxide which can either dimerize to the tetroxane or cyclize to the dioxirane. The dioxirane can either react with the unreacted alkene to give the oxirane and benzoate or remain as one of the final products. This study has shown for the first time that the dioxiranes can be produced by solution-phase ozonation of the alkenes.



Ozonation of two 1,1,2-trialkoxy-2-phenylethenes gives similar types of products as above but no evidence was obtained for the formation of dialkoxydioxiranes.

The results of ozonation of *E*-1,2-diacetoxy-1,2-diphenylethene indicate that acetoxy group is an electron-withdrawing substituent. Inverse ozonation of *E*-1-acetoxy-2-methoxy-1,2-diphenylethene yields (methoxy)phenyldioxirane in a good yield.

No evidence was found for the formation of dioxiranes from (alkoxy)alkylcarbonyl oxides, (methyl)phenylcarbonyl oxide, and diphenylcarbonyl oxide.

This study also shows that tetroxanes are a new class of chemiluminescent molecules.

Acknowledgments

I wish to express my sincere appreciation and gratitude to Professor K. R. Kopecky for his outstanding guidance throughout this research project.

I would like to thank all my teachers in Xiamen Shiyan Elementary School, Xiamen Shuangshi Middle School, Xiamen University, and University of Alberta.

I am very grateful to my wife and my family for their support.

Finally, I would like to thank the University of Alberta for providing a teaching assistantship.

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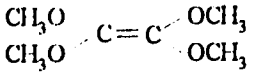

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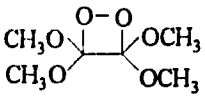

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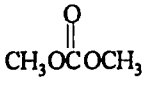

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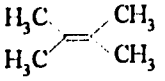

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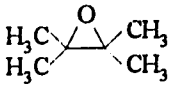

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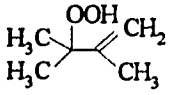

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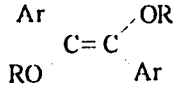

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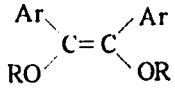

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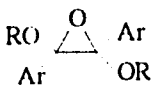

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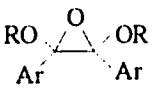

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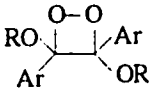

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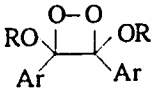

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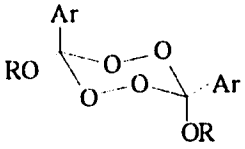

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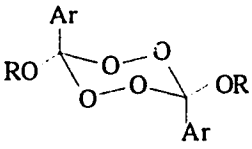

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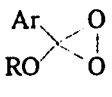

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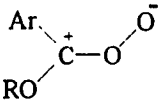
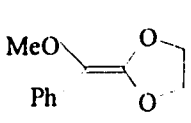


14a-e

From 8a-e to 14a-e

a: Ar = C_6H_5 , R = CH_3 **b**: Ar = C_6H_5 , R = C_2H_5 **c**: Ar = C_6H_5 , R = $CH(CH_3)_2$

d: Ar = *p*-$CH_3OC_6H_4$, R = CH_3 **e**: Ar = *p*-$O_2NC_6H_4$, R = CH_3



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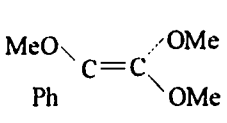

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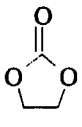

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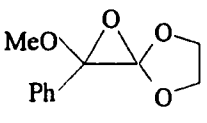

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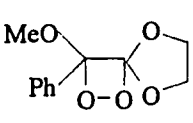

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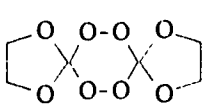

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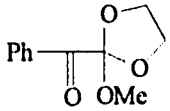

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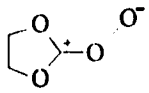

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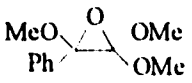

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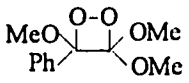

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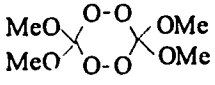

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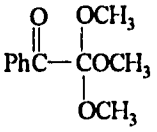

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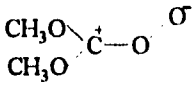

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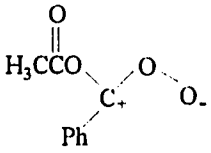

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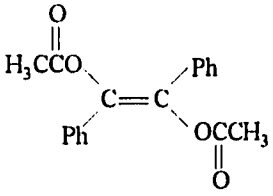

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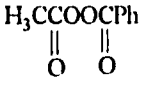

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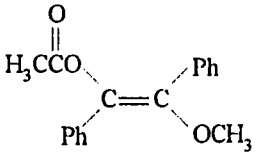

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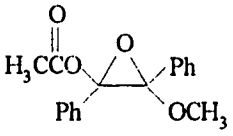

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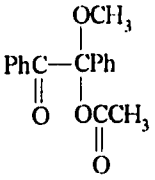

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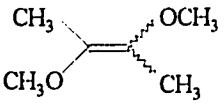

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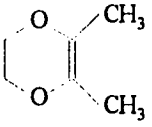

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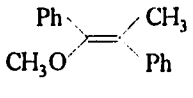

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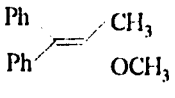

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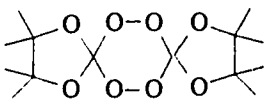

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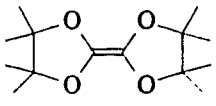

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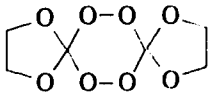

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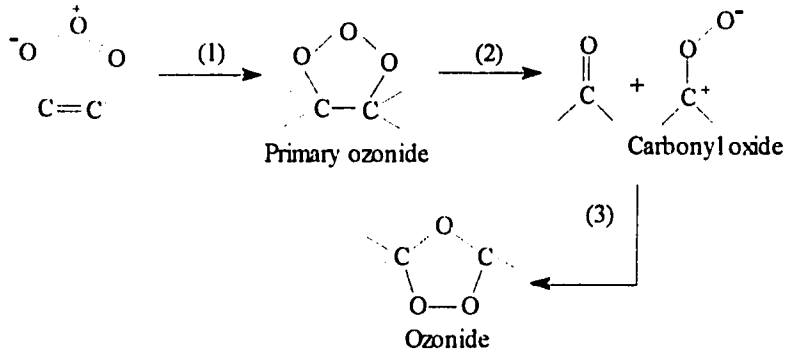
I. INTRODUCTION

Ozonolysis of alkenes to give carbonyl compounds has been a well known and widely utilized reaction in organic chemistry.[1] The basic mechanism of this reaction was established by Criegee.[2] The three-step Criegee mechanism illustrated in Scheme 1 is usually explained using 1,3-dipolar cycloaddition concepts.[3]

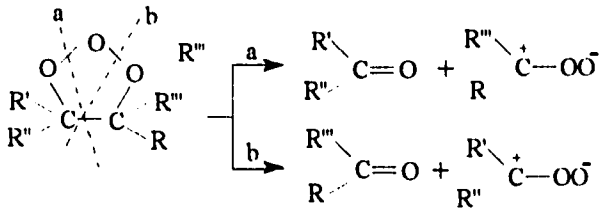


Scheme 1. The Criegee mechanism

The first step is cycloaddition of the ozone 1,3-dipole across the double bond dipolarophile to form a cyclic intermediate called a primary ozonide or 1,2,3-trioxolane. The primary ozonide is generally quite unstable and in the second step it cleaves via a cycloreversion reaction to a carbonyl compound and a carbonyl oxide or so-called Criegee intermediate. The carbonyl oxide is isoelectronic with ozone and can be considered as another 1,3-dipole. In the third step the carbonyl oxide quickly combines with the carbonyl compound to produce the final ozonide, called a 1,2,4-trioxolane, via a cycloaddition reaction which is formally analogous to the first step of the mechanism.

For an unsymmetrical alkene, there are two possible directions of the

cleavage of the primary ozonide. Each direction leads to the formation of different carbonyl oxides as shown in Scheme 2.

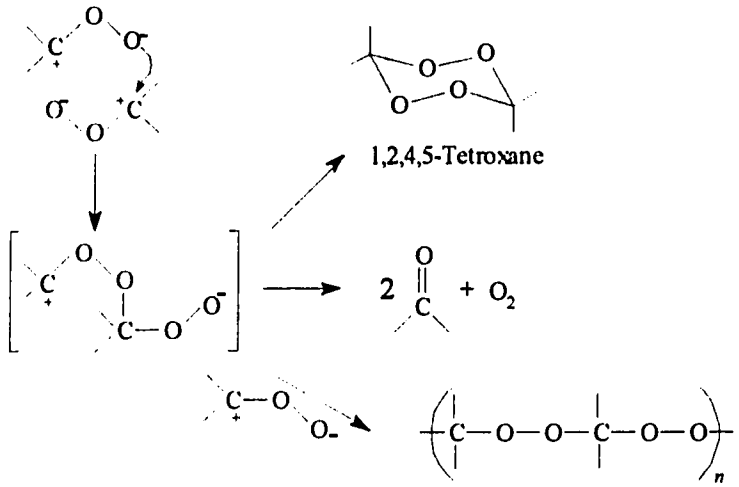


Scheme 2. Two directions of the cleavage of an unsymmetrical primary ozonide

A useful rule has been established by Fliszar[4] and Griesbaum[5]. This rule states that cleavage of the primary ozonides tends to occur in the direction which results in the placement of electron-donating substituents such as methyl on the carbonyl oxide fragment as a consequence of the stabilization of the local positive charge. Correspondingly, electron-withdrawing substituents such as acyl and halogen are incorporated in the carbonyl compound. In the ozonolysis of alkenes, which possess both an electron-donating substituent and an electron-withdrawing substituent, one of the directions of cleavage of the primary ozonide becomes dominant.

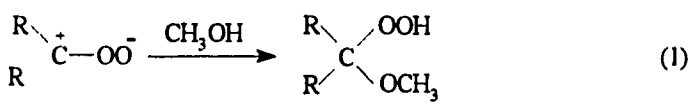
Dimerization and oligomerization of carbonyl oxides to give a 1,2,4,5-tetroxane and oligomer as minor products almost always accompany the ozonide formation, Scheme 3.[1] These generally become the major reactions when the moiety formed along with the carbonyl oxide is a ketone. The failure of the carbonyl oxide moiety to add to the carbonyl group of a ketone is generally attributed to the decreased 1,3-dipolarophilic and electrophilic character of a ketone carbonyl in comparison to that of an aldehyde carbonyl. Since a concerted 4 + 4 cycloaddition between two carbonyl oxides is thermally forbidden,[6] the formation of the tetroxanes is most likely to occur

stepwise, via a zwitterionic intermediate, giving rise to a mixture of cis and trans isomers with unsymmetrically substituted carbonyl oxides. The tetroxane ring has been shown to exist in a chair conformation.[7] The zwitterionic intermediate can, in competition with dimerization and oligomerization, decompose to two molecules of the carbonyl compound and one molecule of oxygen, as shown in Scheme 3.[8]



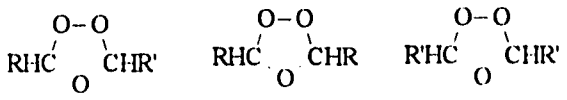
Scheme 3. Dimerization, oligomerization, and decomposition of carbonyl oxides

The transitory existence of carbonyl oxides is inferred primarily from the reaction products and from trapping reactions.[1] In protic solvents, carbonyl oxides are converted to hydroperoxides. Methanol is the most commonly used "participating" solvent in ozonolysis chemistry.[1] The reaction of carbonyl oxides with methanol forms the corresponding α-methoxyhydroperoxides, eq 1. Thus the direction of cleavage of a primary ozonide from ozonolysis of an unsymmetrical alkene can be inferred from the trapping product α-methoxyhydroperoxide.

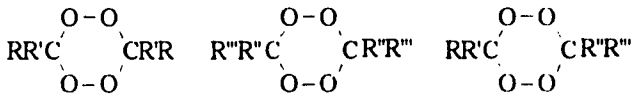


(1)

The most impressive evidence for the Criegee mechanism comes from the isolation of cross ozonides and cross 1,2,4,5-tetroxanes. According to the Criegee mechanism, the original alkene breaks into two parts which then recombine to form the ozonide. In the case of an unsymmetrical alkene RCH=CHR' or two different symmetrical alkenes RCH=CHR and R'CH=CHR' three ozonides should result:



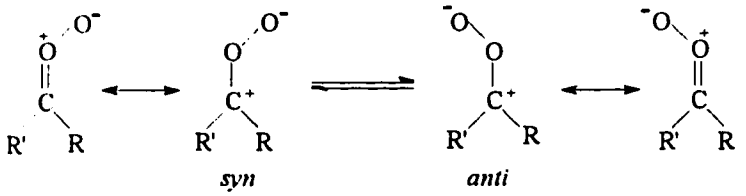
Since there are two different aldehydes and two different carbonyl oxides, they can combine in the three ways shown. Actually six ozonides, corresponding to the cis and trans forms of the above three, were isolated and characterized for methyl oleate.[9] Similarly, if the carbonyl oxides undergo the dimerization reaction, three tetroxanes (or six if the cis and trans forms are considered) can be obtained from ozonolysis of either an unsymmetrical alkene RR'C=CR"R'" or a mixture of two symmetrical alkenes RR'C=CR'R and R"R'"C=CR'"R".[10]



Additional evidence for the Criegee mechanism is that:[1] (1) ozonolysis of various alkenes in the presence of an excess of a reactive aldehyde gives a cross ozonide by interaction of the carbonyl oxide with the aldehyde rather than with the carbonyl moiety produced along with it; (2) some carbonyl oxides prepared in an entirely different manner, e.g., photooxidation of diazo compounds or oxidation of diazo compounds with singlet oxygen, react with

aldehydes to give ozonides or dimerize to give tetroxanes; and (3) cis and trans alkenes generally give the same ozonide, which can be expected if their reaction intermediates cleave first to two parts with the loss of the original geometric information of the alkenes before recombination to form the ozonide.

Subsequent to these fundamental studies, slight modifications of the basic Criegee mechanism have been made to account for geometry and formation of the reaction products. It has been observed in some cases that ozonolysis of cis alkenes gives more cis ozonide while ozonolysis of trans alkenes gives more trans ozonide.[11] This is not compatible with the Criegee mechanism. If the Criegee mechanism operated as shown above, the cis/trans ratios for the ozonides would have to be identical for the cis and trans alkenes, since in this mechanism the geometric difference of the isomers is destroyed upon the cleavage of the primary ozonides. The stereochemical results have been explained on the basis of the Criegee mechanism with the following refinements.[12] (1) The formation of primary ozonide is stereospecific, as expected from a 1,3 dipolar cycloaddition. (2) Once they are formed, the carbonyl compound and the carbonyl oxide remain attracted to each other, much like an ion pair. (3) The carbonyl oxide exists in syn and anti forms, which are produced in different amounts and can retain their configurations,



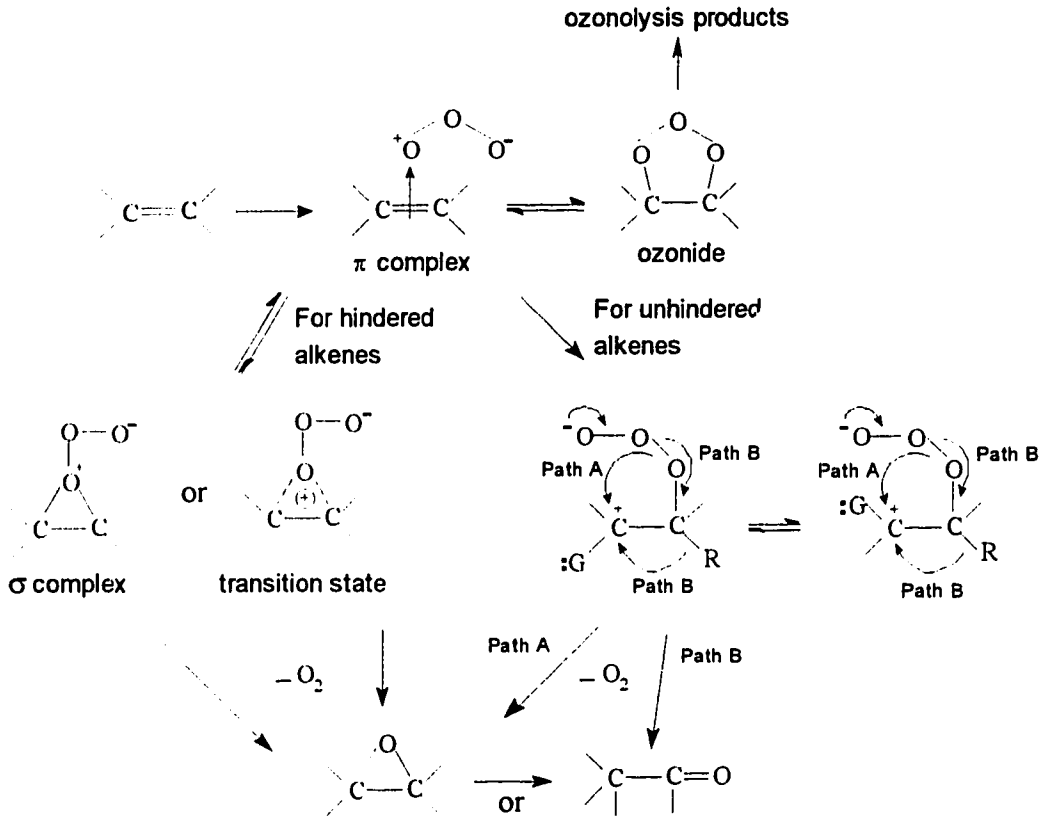
at least for a time. (4) The combination of the carbonyl compound and the

carbonyl oxide is also a 1,3-dipolar cycloaddition, therefore the configuration of the carbonyl oxide is retained in this step too.

Nowadays, the Criegee mechanism is considered as being well established and is the reference point for discussion of ozonation of alkenes.[13] However, not all alkenes undergo the ozonation reaction by the Criegee mechanism. In the Criegee mechanism, the double bond of the alkene is completely cleaved. (The term *ozonolysis* is specifically designated to the entire process involving the cleavage of the double or triple bonds by ozone, while the terms *ozonation* and *ozonization* are synonymous and refer to treatment of any substance with ozone).[1] There are many examples of ozonation leading to, in varying degrees, partial cleavage where only the π bond of the carbon-carbon double bond is broken.[14] The products, in many cases, are oxiranes; whereas in other cases they are derived from the oxirane by rearrangement, reactions with other functional groups in the molecule, or reactions with the solvent, etc. In the partial cleavage ozonation, only one atom of the ozone molecule is utilized and molecular oxygen is released, which in some cases has been shown to be singlet oxygen.[15] The various examples can roughly be divided into two categories: sterically hindered and unhindered alkenes. In the first category the degree of "partial cleavage" appears to increase with the bulk of the groups around the double bond. These reactions also appear to be stereospecific, with retention of configuration.[16] The unhindered alkenes that give oxiranes or rearrangement products usually possess electron-rich groups attached to a double-bond carbon. In the cases studied, oxirane formation is not stereospecific and there is, generally, a solvent effect. For example, ozonation of both *cis*- and *trans*-1,2-difluoroethene in methyl chloride yields only cis oxirane and formyl fluoride as the major products, whereas ozonolysis products are major

products when isobutane is used as the solvent.[17]

For these reactions the mechanism as shown in Scheme 4 was proposed.[14,16] The initial species, a π complex, was suggested to be produced



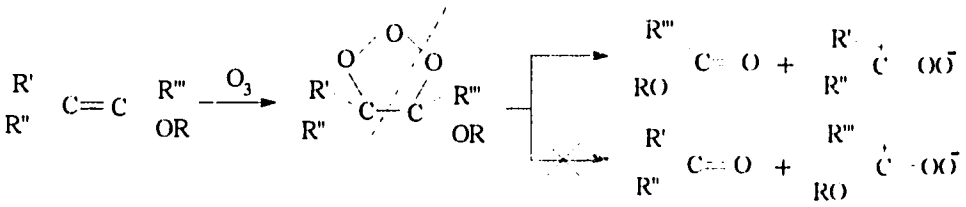
Scheme 4. Competition between ozonolysis and partial cleavage

first in any case. It, then, in general, tends to complete a 1,3-dipolar cycloaddition on the way to ozonolysis products. As the bulk of the substituents around the double bond increases, however, 1,3-dipolar cycloaddition becomes more and more hindered and loss of molecular oxygen, via a transition state or a σ complex, to yield an oxirane or other partial cleavage products becomes more and more important. For unhindered alkenes, a zwitterionic intermediate in the partial cleavage reaction was

suggested since it will be stabilized by the electron-rich substituent. Consequently, it can account for the lack of stereospecificity in the oxirane formation as well as the solvent effect.

In spite of all the previous investigations, not all the details of the mechanism of ozonation of alkenes are known. Therefore, this topic continues to attract considerable attention.[18]

The ozonation of vinyl ethers, which contain the C=C–OR moiety, has received extensive study.[19] A common feature of this reaction is that the cleavage of the primary ozonide always occurs in the direction of formation of an ester and a ketone oxide or an aldehyde oxide, Scheme 5.[20] Alkenes in

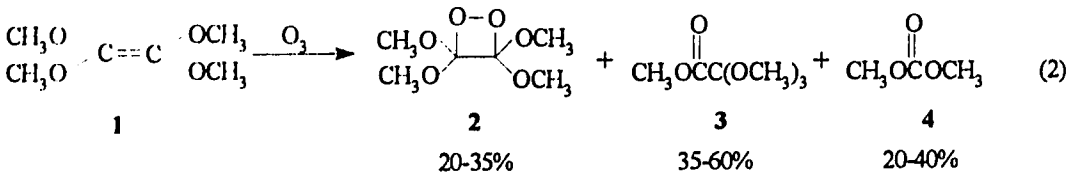


Scheme 5. Cleavage of the primary ozonides of vinyl ethers

which the double bond is connected to electron-donating groups react much faster with ozone than those in which it is connected to electron-withdrawing groups.[21] Since the –OR substituent donates electron density to the carbon-carbon double bond, vinyl ethers are categorized as electron-rich alkenes, and exhibit high reactivity toward electrophilic ozone.

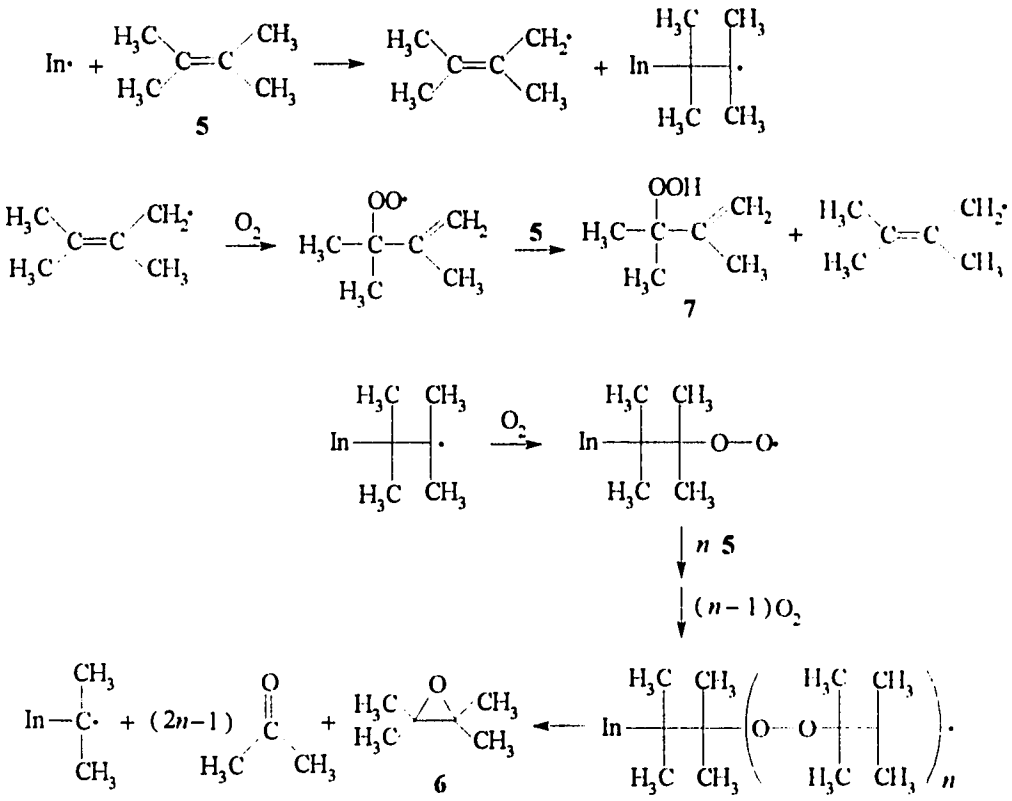
For several years the study of ozonolysis mechanism of electron-rich alkenes has been one of the research subjects in this laboratory. In the case of tetramethoxyethene **1**, it was found that ozonation of this electron-rich alkene results in the formation of mainly tetramethoxy-1,2-dioxetane (20-35%) **2** and methyl trimethoxyacetate (35-60%) **3** with relatively little cleavage product,

dimethyl carbonate (20-40%) **4**, eq 2.[22] It was observed that yields vary with



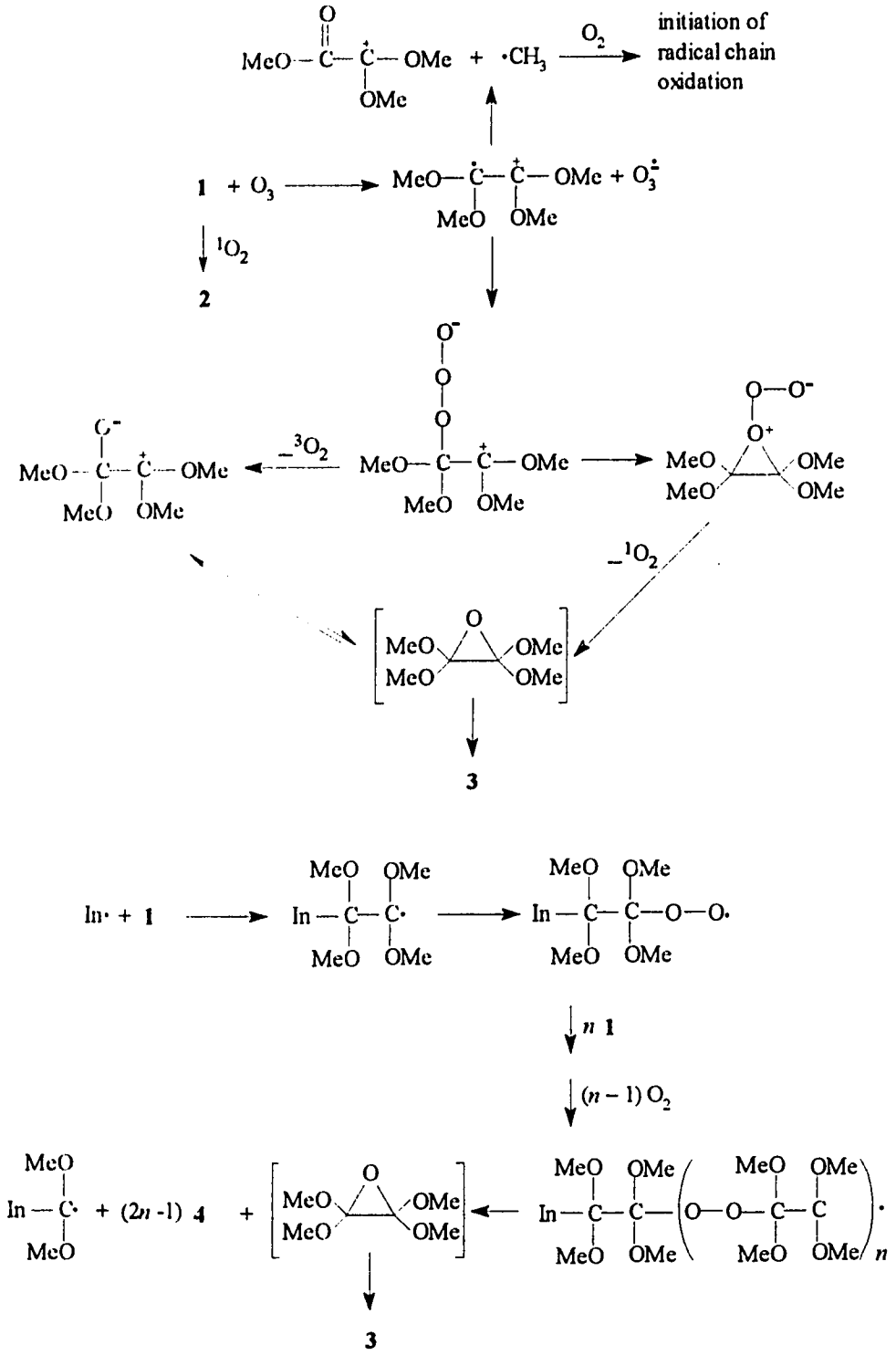
the initial concentration of **1**, temperature and the solvent. Singlet oxygen is produced in the ozonation of **1** and can be trapped with 2,5-dimethylfuran. The reaction of singlet oxygen with **1** yields the dioxetane **2**. Therefore the amount of singlet oxygen produced was considered to be the same as the amount of the dioxetane **2**. Up to 2.5 moles of **1** are consumed per mole of ozone. No evidence for the formation of any trimethoxyhydroperoxide, the adduct of dimethoxycarbonyl oxide and methanol, could be obtained by ^1H NMR when **1** was ozonized in CD_3OD. Tetramethoxy-1,2,4,5-tetroxane, the dimer of dimethoxycarbonyl oxide, was not formed either when the ozonation was carried out in an inert solvent. The absence of these two products plus the relatively a little cleavage product **4** led to the conclusion that no dimethoxycarbonyl oxide is ever formed during ozonation of **1** and, further, that the primary ozonide of **1** is not formed either. It was observed that the consumption of **1** varies with its initial concentrations and is lower when a stream of ozone in argon rather than in oxygen was used. These results suggested a possibility of a contribution from a radical chain oxidation reaction of **1** with both oxygen and ozone. Ozonation of a mixture of **1** and 2,3-dimethyl-2-butene **5** gives tetramethyloxirane **6** and 3-hydroperoxy-2,3-dimethyl-1-butene **7**. The allylic hydroperoxide **7** is well known to be a product of the reaction of singlet oxygen with **4**. However, the amount of **7**

produced was three times more than expected based on the amount of singlet oxygen produced. The formation of **6** together with excess **7** can be accounted for by a radical chain oxidation as shown in Scheme 6.[23] Since **6**



Scheme 6. Radical chain oxidation of 2,3-dimethyl-2-butene

and **7** are not formed on ozonolysis of **5** alone, the presence of **1** is required to initiate the radical chain reaction. In other words, the ozonolysis of **1** provides the initiator of the radical chain reaction. This result provides further evidence for a radical chain contribution in the ozonation of **1**. A mechanism of ozonolysis of **1** as illustrated in Scheme 7 was therefore proposed to account for the product formation and the stoichiometry of the reaction.



Scheme 7. Proposed mechanism for the ozonation of tetramethoxyethene

The initial reaction in the ozonation of **1** was proposed to be an electron transfer reaction that was calculated to be exothermic by > 35 kcal/mol. The resulting radical cation of **1** can either give a methyl radical, which serves as the initiator of the radical chain oxidation, or combine with the ozone radical anion to form the oxygenated oxirane of **1** via a zwitterionic intermediate. Loss of singlet oxygen from the oxygenated oxirane forms the oxirane **6**, which then rearranges to **3**. Reaction between the singlet oxygen and **1** gives the dioxetane **2**. The oxygenated oligomer formed from the radical chain reaction collapses to give **3** via **6** and the carbonate **4**.

It seems this is the first example in which the alkene is ozonized by such a mechanism. Obviously, the electron-donating methoxy groups play an important role here. In order to gain further insight into the action of ozone on other electron-rich alkenes, at the beginning, the ozonation of *E*- and *Z*-1,2-dimethoxy-1,2-diphenylethene (*E*- or *Z*-**8a**) was studied. In the preliminary work on *E*- and *Z*-**8a**,[22] it was found that the ozonation of *Z*-**8a** produced about 20% of the dioxetane of *Z*-**8a** and about 40% of an unidentified product, which may be the oxirane of *Z*-**8a** or its rearrangement product, in addition to methyl benzoate. These products are similar to the products formed from the ozonation of **1**. It was also found that 1.3 moles of *Z*-**8a** was consumed by each mole of ozone. These results suggested that a process similar to that in the ozonation of **1** is occurring. On the other hand, the preliminary observations on the ozonation of *E*-**8a** showed that no dioxetane was formed, one mole of *E*-**8a** was consumed by each mole of ozone and, in CD_3OD, methyl benzoate and the CD_3OD adduct of (methoxy)phenylcarbonyl oxide were the only products formed in equal amount. Hence it seems that ozonation of *E*-**8a** proceeds by the Criegee ozonolysis mechanism. If these preliminary conclusions were true, *Z*-**8a** and

E-**8a** would be ozonized by the different mechanisms.

For continuing this preliminary work, the initial object of this project is to study the ozonation of *Z*- and *E*-**8a** in depth. This includes the confirmation or identification of the products formed from *Z*- and *E*-**8a** and providing more evidence for the involvement of a radical chain oxidation reaction in the ozonation of *Z*-**8a**. However, the conclusions drawn from this detailed study are in contrast to those of the preliminary work. In order to understand the steric and electronic effects on the product formation and distribution, the ozonation of *E*- and *Z*-1,2-diethoxy-1,2-diphenylethene (*E*- and *Z*-**8b**), *E*- and *Z*-1,2-diisopropoxy-1,2-diphenylethene (*E*- and *Z*-**8c**), *E*-1,2-dimethoxy-1,2-bis(4-methoxyphenyl)ethene (*E*-**8d**), and *E*-1,2-dimethoxy-1,2-bis(4-nitrophenyl)ethene (*E*-**8e**) were also studied.

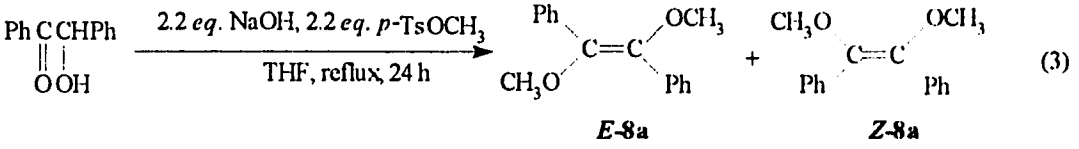
II. (ALKOXY)ARYLDIOXIRANES FROM OZONATION OF 1,2-DIALKOXY-1,2-DIARYLETHENES

At the beginning of this project, the simplest compounds of this series, *E*- and *Z*-1,2-dimethoxy-1,2-diphenylethene (*E*- and *Z*-**8a**) were synthesized and their ozonation behaviors were reinvestigated.

A. Discovery of (methoxy)phenyldioxirane from ozonation of *E*- and *Z*-1,2-dimethoxy-1,2-diphenylethene

1. Preparation of the starting alkenes

The starting alkenes *E*- and *Z*-**8a** were synthesized by methylation of benzoin dianions as described, eq 3.[24]



(3)

The two isomers were separated by flash chromatography on silica gel and their configurations were assigned on the basis of the infrared absorptions of the C=C bonds and the dipole moments.[25] The isomer with a medium absorption at 1620 to 1625 cm^{-1} and with μ = 1.71 D in benzene at 25 °C was assigned to be the *Z*-isomer; whereas the other isomer with a week absorption at 1600 cm^{-1} and with μ = 1.34 D was assigned to be the *E*-isomer. The aromatic protons of the *Z*-isomer give a singlet at δ 7.17; whereas the aromatic protons of the *E*-isomer give a multiplet at δ 7.1-7.8.[25(b)]

2. Results of normal ozonation

Small-scale reactions were carried out by delivering the ozone-oxygen mixture (the concentration of ozone was about 1×10^{-6} mole/mL) from a gas syringe through a Teflon tube into CD_2Cl_2 solutions of the alkenes in NMR tubes at various temperatures until a moistened iodine-starch test paper, which was placed on the top of the NMR tube, turned blue (hereafter, addition of the ozone-oxygen mixture to the solution of an alkene will be referred to as the normal ozonation). The reaction mixtures were analyzed by ^1H NMR spectroscopy at low temperature (usually at −20 °C) as a nondestructive method of analysis.

a) Product formation in normal ozonation

Initially, a 0.05 *M* solution of *Z*- or *E*-**8a** in CD_2Cl_2 was ozonized at −20 °C. The ^1H NMR spectrum of the reaction mixture from *Z*-**8a** showed that the OCH_3 groups of the products give only three singlets at δ (CD_2Cl_2, −20 °C): 3.87, 3.36, and 3.29 with relative intensities 1:0.4:1.7. Similarly, the ^1H NMR spectrum of the reaction mixture from *E*-**8a** also contains three singlets at δ (CD_2Cl_2, −20 °C): 3.87, 3.24, and 3.06 with relative intensities 1:1:0.04. The signal at δ 3.06 is much smaller than the other two signals and may be overlooked (as in the preliminary work). The signal at δ 3.87 was readily assigned to methyl benzoate **9a**; the signals at δ 3.29 and δ 3.24 were later assigned to *cis*- and *trans*-1,2-dimethoxy-1,2-diphenyloxirane (*cis*- and *trans*-**10a**), respectively; and the signals at δ 3.36 and δ 3.06 were assigned to *cis*- and *trans*-3,4-dimethoxy-3,4-diphenyl-1,2-dioxetanes (*cis*- and *trans*-**11a**), respectively. When the ozonation of either of the two starting alkenes was carried out at the temperatures below −20 °C, two new singlets occurring at δ (CD_2Cl_2, −20 °C) 3.59 and 3.69 appeared in the ^1H NMR spectrum of the reaction mixtures and the intensities of these signals increased with

decreasing the ozonation temperature. They were later found to be due to *trans*- and *cis*-3,6-dimethoxy-3,6-diphenyl-1,2,4,5-tetroxane (*trans*- and *cis*-**12a**).

From either isomer, only one oxirane or dioxetane is observed with the ^{1}H NMR spectrometer. At the beginning, it was reasonable to assume that the oxiranes and the dioxetanes are produced with retention of configuration, i.e., *E*-**8a** gives only the corresponding *trans*-**10a** and *trans*-**11a** whereas *Z*-**8a** gives only the corresponding *cis*-**10a** and *cis*-**11a**. In other words, the formation of the oxiranes and dioxetanes appears to be stereospecific. On the other hand, the formation of the tetroxanes is not stereospecific. Both *trans* and *cis*-**12a** are formed in approximately equal amounts by the ozonation of either *E*- or *Z*-**8a**.

Stoichiometry of a reaction can provide useful information in the study of the mechanism. The stoichiometry of an ozonolysis reaction where an alkene is ozonized by the Criegee mechanism must be 1, i.e., one mole of the alkene is consumed by each mole of ozone. If the alkene is not only consumed by ozone, the stoichiometry of that ozonation reaction will be larger than 1. For example, the stoichiometry of the ozonation of tetramethoxyethene **1** is as high as 2.5, suggesting the involvement of a radical chain oxidation reaction.[22] A method developed in this laboratory to determine the stoichiometry of an ozonation reaction is simple and accurate.[22] First, the ozone concentration is measured. A sample of the ozone-oxygen gas mixture is drawn from the effluent stream of an ozonizer into a 100-mL syringe fitted with a small diameter Teflon tube. A known volume of the ozone-oxygen mixture is delivered through the tube into a CD_3OD solution of an excess of a known amount of 2,3-dimethyl-2-butene **5** in a NMR tube at −78 °C. The ^{1}H NMR spectrum of the resulting reaction

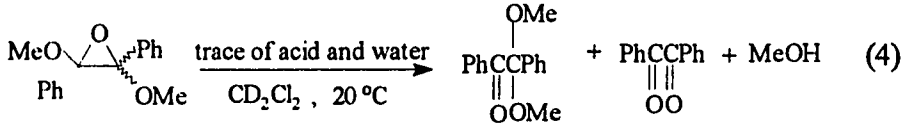
mixture contains only three singlets due to the alkene **5**, acetone, and the CD_3OD adduct of dimethylcarbonyl oxide. The integrals of the last two species are exactly the same. From the integrals of the three signals, the ozone content of the gas is calculated. Then a definite volume of the gas from the same syringe is delivered into a solution of an excess of a known amount of an alkene. The amount of the alkene consumed is calculated from the integrals of the ^1H NMR signals of the various products and the remaining alkene. The stoichiometry of the reaction is then obtained from the amount of ozone delivered and the amount of the alkene consumed. By this method, it was found that about 1.4 moles of *E*- or *Z*-**8a** were consumed by each mole of ozone at −20 °C. The stoichiometry ratio did not change significantly when the initial concentration of *E*- or *Z*-**8a** was varied from 0.04 to 0.20 *M*.

b) Identification of products

The above products were identified as follows.

(1) Identification of the oxiranes

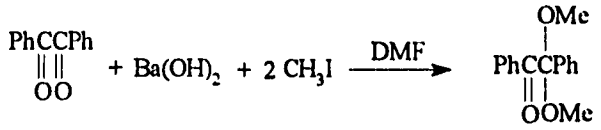
The oxiranes are unstable therefore isolating them from the reaction mixtures has not been achieved. At room temperature, some of the oxirane *trans*- or *cis*-**10a** in the reaction mixture rearranged to 2,2-dimethoxy-1,2-diphenylethanone and some hydrolyzed to benzil and methanol due to the moisture present in the solvent, eq 4. (No attempt was made to prevent the



(4)

moisture from condensing into the NMR tube when the reaction was carried out at −20 °C under atmosphere.) Thus the identifications of *trans*- and *cis*-**10a** were initially based on the separation and identification of the rearrangement product which gives the same melting point and ^1H NMR

signals as 2,2-dimethoxy-1,2-diphenylethanone independently prepared by an authentic method as shown in eq 5.[26]



(5)

Low temperature ^{13}C NMR spectroscopy is another useful tool for the identification of the oxiranes. Like the oxirane carbon atoms of **10a**, the C-2 oxirane carbon atom of 2-methoxy-3,3-dimethyl-2-phenyloxirane is also attached to one methoxy and one phenyl group. It has been reported that the chemical shift of this carbon is at δ 91.33.[27] Hence signals at δ 92.64 and δ 92.74 in the ^{13}C NMR spectra of the ozonation reaction mixtures from *E*- or *Z*-**8a** were assigned to *trans*- and *cis*-**10a**, respectively. All other ^{13}C NMR signals could be assigned to the other compounds of known structure.

(2) Identification of the dioxetanes

The dioxetanes were identified by comparison of the ^{1}H signals in the NMR spectra of the reaction mixtures with those of authentic *trans*- and *cis*-**11a** prepared by singlet oxygen oxidation of *E*- and *Z*-**8a**. The signals due to the dioxetanes disappeared immediately upon addition of a drop of a 2% CD_3OD solution of $CuCl_2$ to the ozonation reaction mixtures. Dioxetanes have been shown to be cleaved rapidly to carbonyl compounds by transition metal ions.[28] The presence of dioxetanes in the ozonation reaction mixtures was further confirmed by observation of bright chemiluminescence upon addition of the reaction mixtures to hot toluene containing 9,10-dibromo- and 9,10-bis(phenylethynyl)anthracene.[22]

(3) Isolation and identification of the tetroxanes

As the tetroxanes *trans*- and *cis*-**12a** can result from the ozonation of either *E*- or *Z*-**8a**, a mixture of the two isomeric alkenes obtained from the

preparative reaction may be used directly in the experiment aimed to isolate the tetroxanes. The ozonation reaction was carried out in a preparative scale at −78 °C in CH_2Cl_2. The two isomers of the stable tetroxanes were separated by preparative thin layer chromatography on silica gel. Since the Rf values of *cis*-**12a** and benzil happen to be identical, it was necessary first to treat the ozonation reaction mixture briefly with hot methanolic sodium hydroxide to convert the benzil to the sodium salt of benzilic acid. Both tetroxanes *trans*- and *cis*-**12a** give a ^{13}C signal at δ 117.15 for the ring carbon atoms which are substituted with three oxygen atoms and one phenyl group. The tetroxanes are decomposed to methyl benzoate radical cation and its fragmentation products upon electron impact. However, chemical ionization with NH_4^+ afforded the $(M + H^+)$ and the $(M + NH_4^+)$ ions at *m/e* 305 and 322, respectively, from each isomer. The elemental analysis of both isomers agreed with the composition of the tetroxanes.

The assignments of the stereochemistry of *trans*- and *cis*-**12a** were accomplished by variable temperature ^1H NMR. The ^1H NMR signal of the OCH_3 groups of the isomer melting at 145-146 °C broadened on cooling and was split into two peaks, from δ 3.69 at −20 °C to δ 3.70 and δ 3.53 at −80 °C, Figure 1; whereas the OCH_3 signal of the isomer melting at 113-114 °C only shifted from δ 3.59 at −20 °C to δ 3.65 at −80 °C but remained a singlet. These isomers were thus assigned to *cis*- and *trans*-**12a**, respectively. These assignments were based on the fact that the two methoxy groups of the *cis*-**12a** are in different chemical enviroments. When temperature is low enough, the rate of interconversion of the two equivalent chair conformations becomes slow enough for a NMR spectrometer to show the chemical shift difference between the equatorial and axial methoxy groups. Both of the two methoxy groups of *trans*-**12a** are expected to be in the axial positions due to

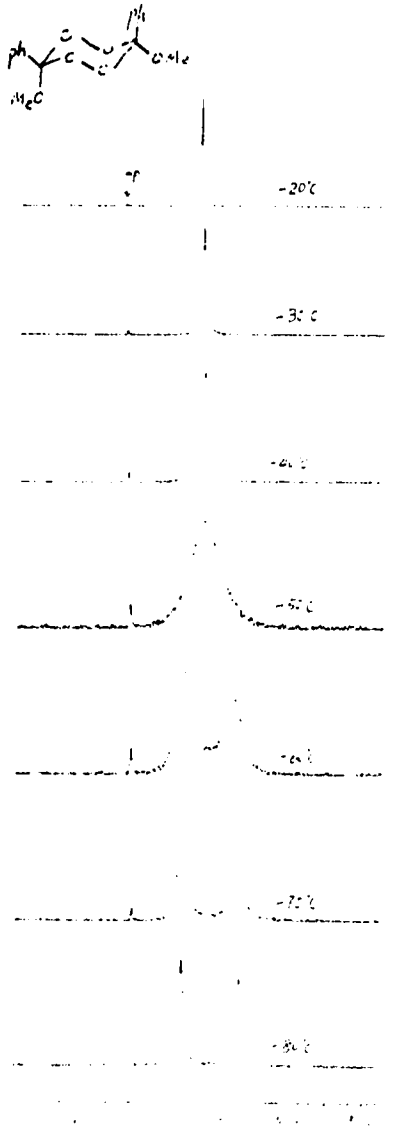
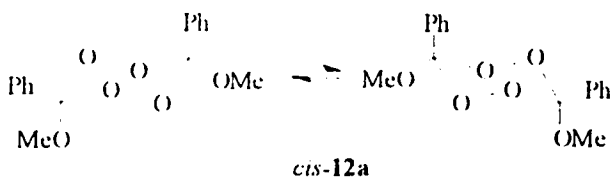
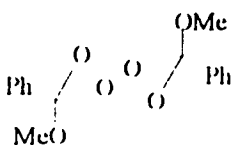


Figure 1. The proton NMR signals of the methoxy groups of *cis*-3,6-dimethoxy-3,6-diphenyltetroxane at various temperatures.

the anomeric effect. This effect refers to the preference of an electronegative substituent located on a carbon α to a hetero atom in heterocyclic rings to adopt an axial rather than the sterically favored equatorial orientation.[29]



cis-**12a**



trans-**12a**

3. Inverse ozonation and discovery of (methoxy)phenyldioxirane

In the study of the concentration effect on the product distribution, it was noticed that when the initial concentrations of the starting alkene *E*- or *Z*-**8a** are below 0.05 *M*, in addition to the products mentioned above, the ozonation reaction mixtures contain a new product as indicated by a new ^{1}H NMR signal at δ 3.50. The lower the initial concentrations of *E*- or *Z*-**8a**, the more intense is this new signal. This observation can be well explained if the new product is able to compete with ozone to react with the unreacted alkenes. If the ozone delivery rate is kept the same, the lower the initial concentrations of the alkene, the more alkene will be consumed by ozone and therefore the more new product generated will remain unreacted. To prove this postulate, a small amount of *E*- or *Z*-**8a** was added into the ozonation mixtures containing this new product. The ^{1}H NMR spectrum of the resulting mixture showed that the new signal disappeared and the intensities of the signals due to the oxiranes and methyl benzoate increased correspondingly, indicating that the new product indeed reacts with the alkenes and the products of this reaction are the oxiranes and methyl benzoate. To avoid the secondary reaction between *E*- or *Z*-**8a** and the new product, a small amount of a dilute solution of *E*- or *Z*-**8a** was added into a CD_2Cl_2 solution saturated with ozone at −78 °C. The rapid reaction between the excess ozone and the small amount of *E*- or *Z*-**8a** should greatly deplete the amount of *E*- or *Z*-**8a** available to react with the new product. As expected, the new product was produced under these conditions. A large amount of the tetroxanes *trans*- and *cis*-**12a**, however, was also produced at this temperature. Furthermore, by this method only a very small amount of the alkenes can be used and thus a very dilute solution of the new product can be obtained. In order to increase the concentration as well as the yield of the new product, 100 mL of the

ozone-oxygen mixture (containing about 1×10^{-4} moles of ozone) and 0.5 mL of a CD_2Cl_2 solution of *E*- or *Z*-**8a** (containing about 2×10^{-5} moles of the alkene) are delivered simultaneously through two Teflon tubes to the bottom of a NMR tube at –20 °C (this will be simply referred to as inverse ozonation hereafter). In this way, ozone is in excess of the alkene during the entire process. The inverse ozonation of a 0.05 *M* solution of *E*-**8a** at –20 °C results in the formation of three major products: methyl benzoate **9a**, the new product, and the oxirane *trans*-**10a** with relative intensities 1:0.8:0.5. As expected, the yield of the new product increases at the expense of that of the oxirane *trans*-**10a**. It was also observed that the normal ozonation reaction mixtures are colorless whereas the reaction mixtures of the inverse ozonation are light-yellow. Addition of *E*- or *Z*-2-butene or other alkenes to the reaction mixture leads to the consumption of the new product and the stereospecific conversion of the added alkenes to the corresponding oxiranes. Coincident with the consumption of the new product by the alkenes is an equivalent increase in the amount of methyl benzoate and a loss of the yellow color. These observations were reminiscent of dioxiranes that are stereospecific epoxidizing agents.[30] Solutions of dioxiranes have been shown to be yellow; the color is attributed to a long wavelength tail (to *ca* 450 nm) of a weak (ε = 9 - 13) n-σ^* absorption at 320-350 nm.[31] Thus, it was very likely that the new product is a dioxirane. The ^{13}C NMR spectra of the reaction mixtures from the inverse ozonation of either *E*- or *Z*-**8a** show the presence of a new signal at δ 109.07. The chemical shift of this signal is in the region expected for a carbon atom attached to three oxygen atoms and a phenyl group. Based on these results, we concluded that the new product is (methoxy)phenyldioxirane **13a**. This is the first example of the formation of dioxirane from ozonation of alkenes in solution. A preliminary report of this discovery was published.[32]

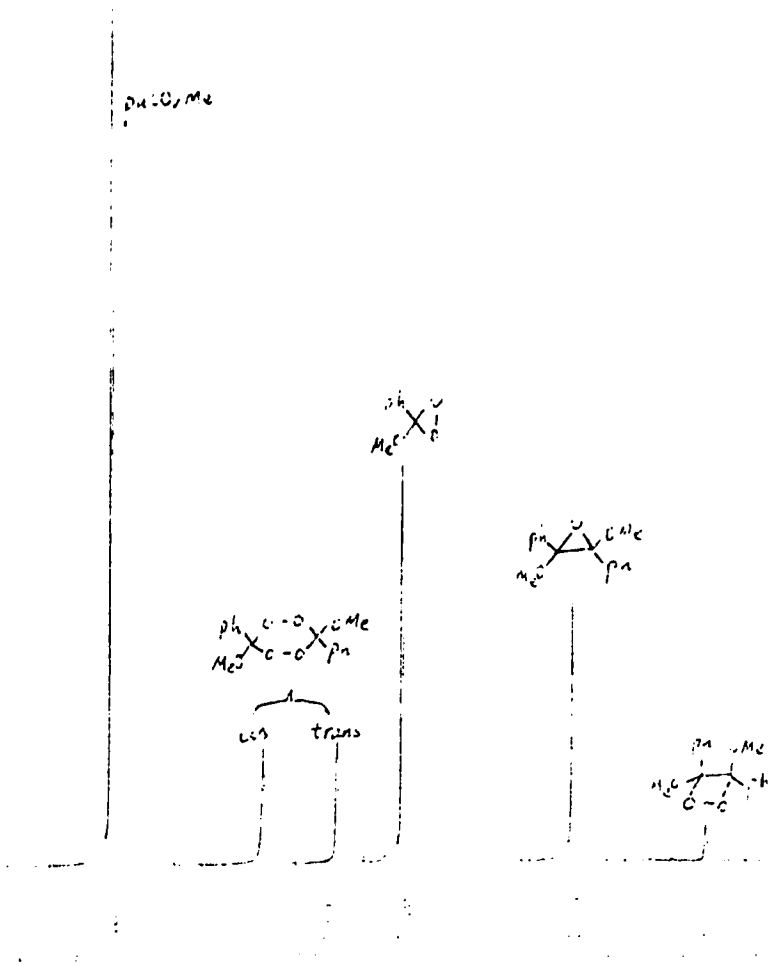


Figure 2. The ^{1}H NMR spectrum of the methoxy groups of ozonation products of *E*-1,2-dimethoxy-1,2-diphenylethene.

The above experiments show that epoxidation of the starting alkenes by the reaction intermediate (methoxy)phenyldioxirane **13a** contributes to the formation of the oxiranes *trans*- and *cis*-**10a** in the ozonation of *E*- and *Z*-**8a**. This was further confirmed by the ozonation of mixtures of *E*- or *Z*-**8a** and other alkenes, such as 2,3-dimethyl-2-butene, *cis*- and *trans*-2-butene, etc. The corresponding oxiranes of these alkenes are produced while the yields of the oxirane *trans*- or *cis*-**10a** are lowered. Control experiments showed that

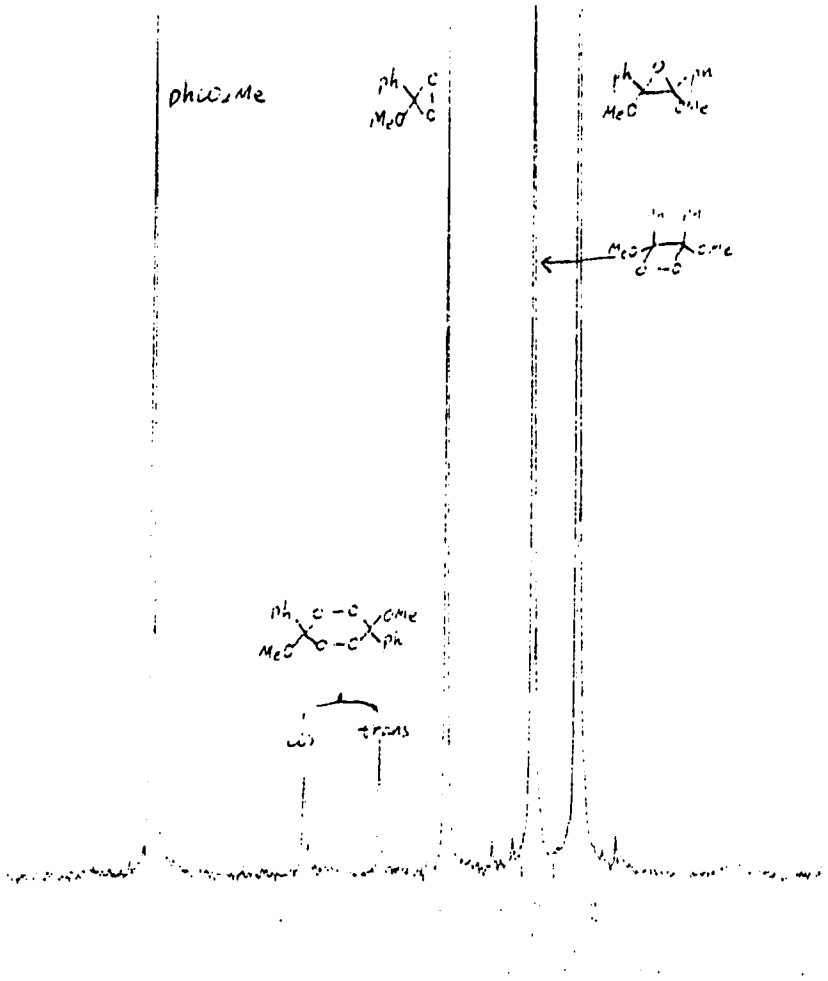


Figure 3. The ^{1}H NMR spectrum of the methoxy groups of ozonation products of *Z*-1,2-dimethoxy-1,2-diphenylethene.

the ozonolysis of these alkenes alone does not produce any oxiranes. This observation can be accounted for by the competition between *E*- or *Z*-**8a** and the alkenes toward **13a**. The formations of *cis*- and *trans*-2-butene oxides are stereospecific, indicating the dioxirane **13a**, like other dioxiranes, is a stereospecific epoxidation agent. The oxiranes of *cis*- and *trans*-2-butene were identified by comparing the chemical shifts and multiplicities of their ^{1}H NMR signals with ^{1}H NMR spectra of the authentic samples prepared by

epoxidation of the alkenes with *m*-chloroperbenzoic acid.

Like other dioxiranes, the dioxirane **13a** is not a stable compound at room temperature. A CD_2Cl_2 solution of the inverse ozonation reaction mixture can be stored at –20 °C for a few days without significant change in the concentration of **13a**. However, at room temperature the intensity of the ^1H NMR signal due to the methoxy group of **13a** decreases slowly as the intensity of the signal due to the methoxy group of **9a** increases correspondingly, indicating that **13a** decomposes to **9a**. The half-life of **13a** in CD_2Cl_2 at 25 °C is about six hours. Along with the decomposition of **13a** the yellow color also disappears.

The product formation from the ozonation of *E*- and *Z*-**8a** is represented by the ozonation of *E*-**8a** as shown in eq 6 and the product distribution under various conditions is summarized in Table 1. (All the data in this table and the following tables, except otherwise stated, are the average of at least three experiments. The errors are within ±0.02). The ^1H NMR spectra of the methoxy groups of ozonation products of *E*- and *Z*-**8a** are shown in Figure 2 and Figure 3, respectively. Since the ^1H NMR signals of the OCH_3 groups of the various products are well separated, determinations of the product distributions were based on the integrals of the OCH_3 signals.

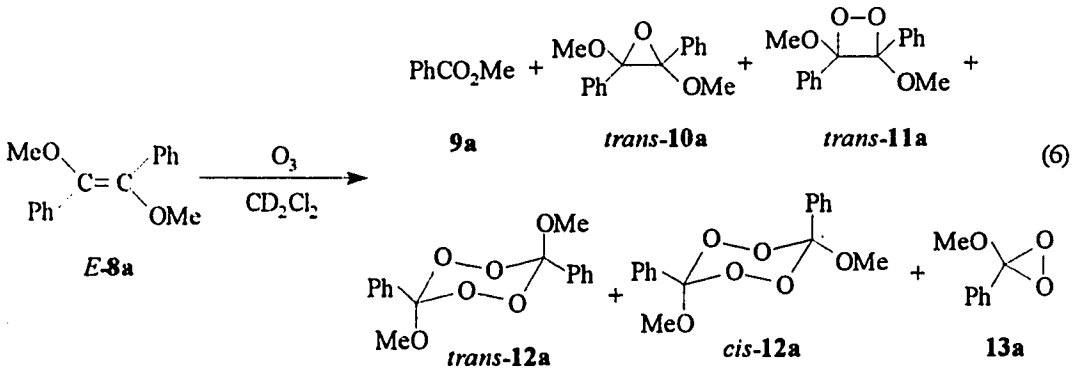


Table 1. Product distribution from the ozonation of *E*- and *Z*-1,2-dimethoxy-1,2-diphenylethene **8a** in CD_2Cl_2

Alkene	Conc.	Method	Temp.	Products, moles per mole of **8a**				
	M		°C	**9a**	**10a**[a]	**11a**[a]	**12a**[b]	**13a**
E-**8a**	0.005	normal	–20	0.94	0.29	0.01	<0.01	0.44
	0.01			0.88	0.41	0.01	0.01	0.26
	0.05			0.92	0.50	0.02	0.02	0.00
	0.1			0.90	0.51	0.02	0.02	0.00
	0.2			0.88	0.51	0.02	0.03	0.00
	0.08	normal	0	0.90	0.53	0.01	0.01	0.00
			–20	0.94	0.50	0.02	0.01	0.00
			–40	0.94	0.44	0.02	0.07	0.00
			–60	1.00	0.28	0.02	0.20	0.00
			–78	1.06	0.20	0.02	0.25	0.00
	0.005	inverse[c]	–20	0.86	0.16	0.01	0.00	0.80
	0.025			0.84	0.20	0.02	0.00	0.72
	0.05			0.86	0.21	0.02	0.00	0.68
			–78	1.01	0.12	0.02	0.21	0.29
Z-**8a**	0.005	normal	–20	0.66	0.44	0.12	0.01	0.20
	0.01			0.64	0.49	0.11	0.02	0.12
	0.05			0.65	0.52	0.12	0.03	0.01
	0.1			0.64	0.53	0.12	0.03	0.00
	0.2			0.62	0.53	0.12	0.04	0.00
	0.08	normal	0	0.62	0.58	0.08	0.03	0.00
			–20	0.64	0.56	0.10	0.02	0.00
			–40	0.58	0.53	0.13	0.05	0.00
			–60	0.56	0.50	0.17	0.05	0.00

Table 1 Continued

			−78	0.52	0.47	0.20	0.07	0.00
Z-**8a**	0.005	inverse[c]	−20	0.60	0.32	0.14	0.00	0.48
	0.025			0.52	0.37	0.15	0.00	0.44
	0.05			0.56	0.42	0.12	0.00	0.36
			−78	0.52	0.36	0.19	0.07	0.24

[a] Only *trans* from *E*-**8a** and only *cis* from *Z*-**8a**.

[b] About equal amounts of *cis* and *trans*.

[c] Simultaneous slow addition of the ozone-oxygen mixture (100 mL) and a solution of **8a** (0.5 mL) into the bottom of a NMR tube through two fine tubes.

4. Discussion of the ozonation mechanism

a) Evidence against a radical chain oxidation

At the beginning of this project, it was suspected that a radical chain oxidation reaction was involved in the ozonation of *E*- or *Z*-**8a**. However, the following experiments provided evidence against this suspicion.

As mentioned in the introduction, evidence for a radical chain contribution in the ozonation of tetramethoxyethene **1** was obtained from the ozonation of a mixture of **1** and 2,3-dimethyl-2-butene **5**, where a large amount of the allylic hydroperoxide **7** was formed. Applying the same methodology, a 1:2 mixture of *E*- or *Z*-**8a** and **5** was treated with a limited amount of ozone, which resulted in the formation of methyl benzoate **9a**, the oxirane **10a**, tetramethyloxirane **6** and the allylic hydroperoxide **7**, as shown in eq 7 and Table 2. Determinations of the yields of **6** and **7** are based on the

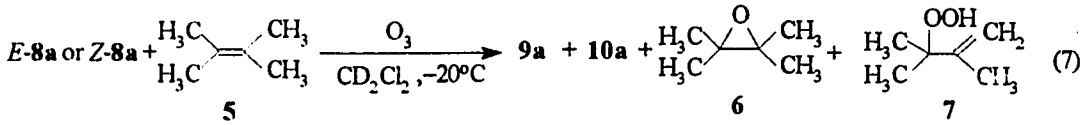


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Table 2. Product distribution from the ozonation of mixtures of 0.04 *M* 1,2-dimethoxy-1,2-diphenylethene **8a** and 0.08 *M* 2,3-dimethyl-2-butene **5** in CD_2Cl_2

	Temp.	Percent alkene consumed		Products, moles per mole of **8a**			
Alkene	°C	**8a**	**5**	**9a**	**10a**	**6**[b]	**7**[b]
Z-**8a**[a]	–20	48	55	1.04	0.43	0.58	0.35
	–78	40	49	0.79	0.53	0.35	0.48
E-**8a**	–20	38	74	1.61	0.19	0.81	0.31
	–78[c]	35	66	1.39	0.14	0.43	0.17

[a] From the integrals of the ^{1}H NMR signals of the products from *Z*-**8a** the ozonation reaction mixtures contained approximately 8% of unidentified products which gave ^{1}H NMR signals at δ 3.40-3.48.

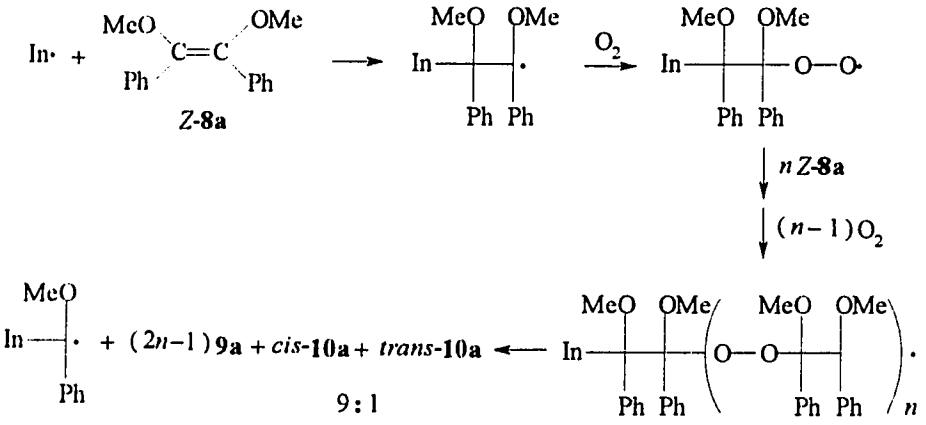
[b] Based on the amount of **10a** produced.

[c] The ozonation reaction also produced 0.16 moles of the tetroxanes *cis*- and *trans*-**12a** from each mole of *E*-**8a**.

relative integrals of the ^{1}H NMR signals of the oxirane **10a** and those of **6** and **7**. No dioxetanes **11a** were detected. The formation of **6** and **7** was similar to the ozonation of **1** with **5**. Control experiments showed that **6** and **7** were not formed in ozonolysis of **5** alone under the same conditions. The formation of the oxirane **6** can be well explained by epoxidation of the alkene **5** by the dioxirane **13a**. The yields of **7** are less than those of *cis*-**10a** and a little more than those of *trans*-**10a**. As discussed in the introduction[22] a radical chain oxidation of **5** would also result in the formation of **7**. If **7** were produced in this way, much higher yield of **7** than actually formed would be expected as in the ozonation of **1** with **5**. Thus, the possible radical chain oxidation is unlikely to occur. Even if it occurred, it did not contribute much to the formation of **7**. The allylic hydroperoxide **7** is well-known to be a product of the reaction of **5** and singlet oxygen. Since no dioxetanes **11a** were detected, the formation of **7** could be the result of trapping singlet oxygen by

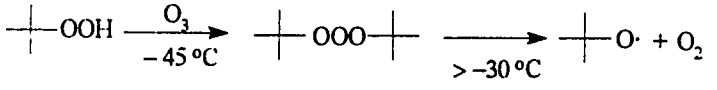
5. Competitive photooxidation experiments showed that **5** is 2.3 times as reactive as *Z*-**8a** (44.8% of *Z*-**8a** and 74.8% of **5** were consumed by a limited amount of singlet oxygen) and 8.4 times as reactive as *E*-**8a** toward singlet oxygen (22.1% of *E*-**8a** and 87.7% of **5** were consumed by a limited amount of singlet oxygen). The relative activities were calculated as described[33] (also see Scheme 13).

The formation of the oxiranes *trans*- and *cis*-**10a** in the ozonation of *Z*- or *E*-**8a** can also be accounted for by a radical chain oxidation as illustrated in Scheme 8,[22] but the following experiments showed that this is not true. A



Scheme 8. Formation of the oxiranes by a radical chain oxidation reaction

radical chain oxidation of *Z*- or *E*-**8a** in the presence of oxygen was initiated at −20 °C by decomposition of di-*tert*-butyl trioxide prepared by ozonation of *tert*-butyl hydroperoxide at −45 °C, eq 8.[34] The first-order rate constant for the decomposition of this trioxide at −24.8 °C was reported to be 4.6×10^{-4} s^{-1}. The results showed that the radical chain oxidation results in the



(8)

formation of many products, some of them never appear in the ozonation reaction mixtures. From *E*-**8a**, along with other products, only the *trans*-**10a** was detected in the reaction mixture by the ^{1}H NMR. However, both *cis*- and *trans*-**10a** are formed from *Z*-**8a** and the ratio of *cis*- to *trans*-**11a** is 9:1, Scheme 8. In other words the formation of the oxiranes from the radical chain oxidation of *Z*-**8a** was stereoselective instead of stereospecific. The stereospecificity in the formation of 2-butene oxides in the ozonation of mixtures of *E*- or *Z*-**8a** and *E*- or *Z*-2-butene also could not be explained by a radical chain reaction. It has been reported that in auto-oxidation of *E*- and *Z*-2-butene the ratio of trans oxirane to cis oxirane was 2.3 from *E*-2-butene and 2.2 from *Z*-2-butene at 120 °C in benzene.[35] Considering that the conditions used in the literature were quite different from ozonation conditions used in this study, we attempted to initiate a radical chain oxidation of *Z*- and *E*-2-butene in the presence of oxygen at –20 °C by decomposition of di-*tert*-butyl trioxide. Unfortunately, under these conditions no oxiranes were detected in several tries.

Moreover, if the radical chain oxidation reaction occurred, similar to the ozonation of tetramethoxyethene **1**,[22] the amount of the alkene consumed by each mole of ozone would increase if the initial concentration of the alkene was increased and would decrease if ozone in argon instead of ozone in oxygen was used. However, it was found that the amount of the alkene consumed by each mole of ozone in the ozonation of *E*- and *Z*-**8a** did not vary significantly when the initial concentration of the alkene was changed from 0.04 to 0.2 *M* or in the absence of oxygen during the ozonation.

Based on the results of these experiments, we concluded that under the ozonation conditions employed the possibility of the radical chain reaction can be ruled out or at least it cannot compete appreciably with the other

reactions.

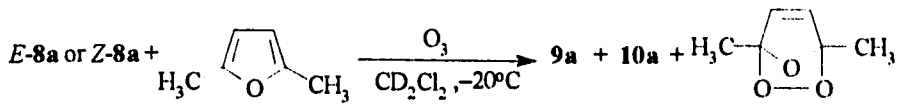
b) Possible ozonation mechanism

There is no doubt that the tetroxanes *trans*- and *cis*-**12a** arise from dimerization of (methoxy)phenylcarbonyl oxide **14a** which in turn should result from the cleavage of the primary ozonides of *E*- and *Z*-**8a**. Therefore the formation of the tetroxanes provides strong evidence that at least some *E*- and *Z*-**8a** are ozonized by the Criegee ozonolysis mechanism.

In competition with the dimerization, the cyclization of **14a** gives the dioxirane **13a**. As seen from Table 1, the yields of *trans*- and *cis*-**12a** increase as the reaction temperature is lowered. This is also observed in the ozonolysis of other alkenes.[36] On the contrary, higher yields of **13a** are obtained at higher temperatures. It has been reported that cyclization of carbonyl oxides to dioxiranes should overcome an energy barrier.[37]

The discovery that the dioxirane **13a** is produced in the ozonation reaction and is a stereospecific epoxidizing agent makes the possibility that the oxiranes *trans*- and *cis*-**10a** are formed by transfer of an oxygen atom from (methoxy)phenylcarbonyl oxide **14a** to *E*- or *Z*-**8a** unlikely. Murray and co-workers observed that singlet oxygen oxidation of diazodiphenylmethane in the presence of alkenes leads to the formation of oxiranes.[38] The epoxidizing species were presumed to be carbonyl oxides. However, unlike the epoxidation of alkenes by dioxiranes, the epoxidation is much less efficient and is not stereospecific: *E* alkenes give *trans*-oxiranes while *Z* alkenes give predominantly *cis*-oxiranes.

Evidence supporting the formation of **11a** by reaction of **8a** with singlet oxygen was obtained by conducting the ozonation of **8a** in the presence of 2,5-dimethylfuran, an efficient singlet oxygen scavenger.[39] No dioxetane was formed when a 1:6 mixture of *E*- or *Z*-**8a**:2,5-dimethylfuran



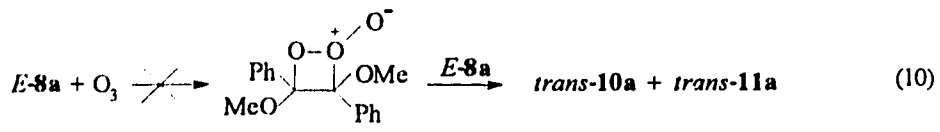
(9)

was incompletely ozonized although the benzoate **9a** and the oxirane **10a** were still formed, eq 9. 2,5-Dimethylfuran is 20 and 6 times as reactive as *E*-**8a** and *Z*-**8a**, respectively, toward singlet oxygen as determined by competitive singlet oxygen oxidation of *E*- or *Z*-**8a** and 2,5-dimethylfuran at 0 °C. Thus complete scavenging of singlet oxygen by 2,5-dimethylfuran under the ozonation conditions would be expected. The endoperoxide of 2,5-dimethylfuran was identified by its ^{1}H NMR spectrum which shows two singlets at δ 1.8 and 6.3.[39] Control experiments showed that the endoperoxide is not formed in the ozonolysis of 2,5-dimethylfuran alone under the same conditions. The dimethylfuran is much less reactive toward ozone than **8a**. When a 1:1 mixture of *Z*-**8a** and 2,5-dimethylfuran was partially ozonized to 40% conversion of *Z*-**8a**, only weak signals were present in the ^{1}H NMR spectrum of the reaction mixture that could be attributed to ozonolysis products of 2,5-dimethylfuran.

As presented in Table 2, incomplete ozonation of a mixture of **8a** and **5**, which led to the formation of the allylic hydroperoxide **7** instead of the dioxetane **11a**, also indicates that singlet oxygen is generated in the ozonation of **8a**.

Competitive singlet oxygen oxidation of *Z*- and *E*-**8a** showed that *Z*-**8a** is four times as reactive as *E*-**8a** toward singlet oxygen. This can partially account for the higher yield of the dioxetane obtained from the ozonation of *Z*-**8a** than from *E*-**8a**.

The evidence that the dioxetanes **11a** are formed by the reaction between *E*- or Z-**8a** and singlet oxygen rules out another conceivable route to

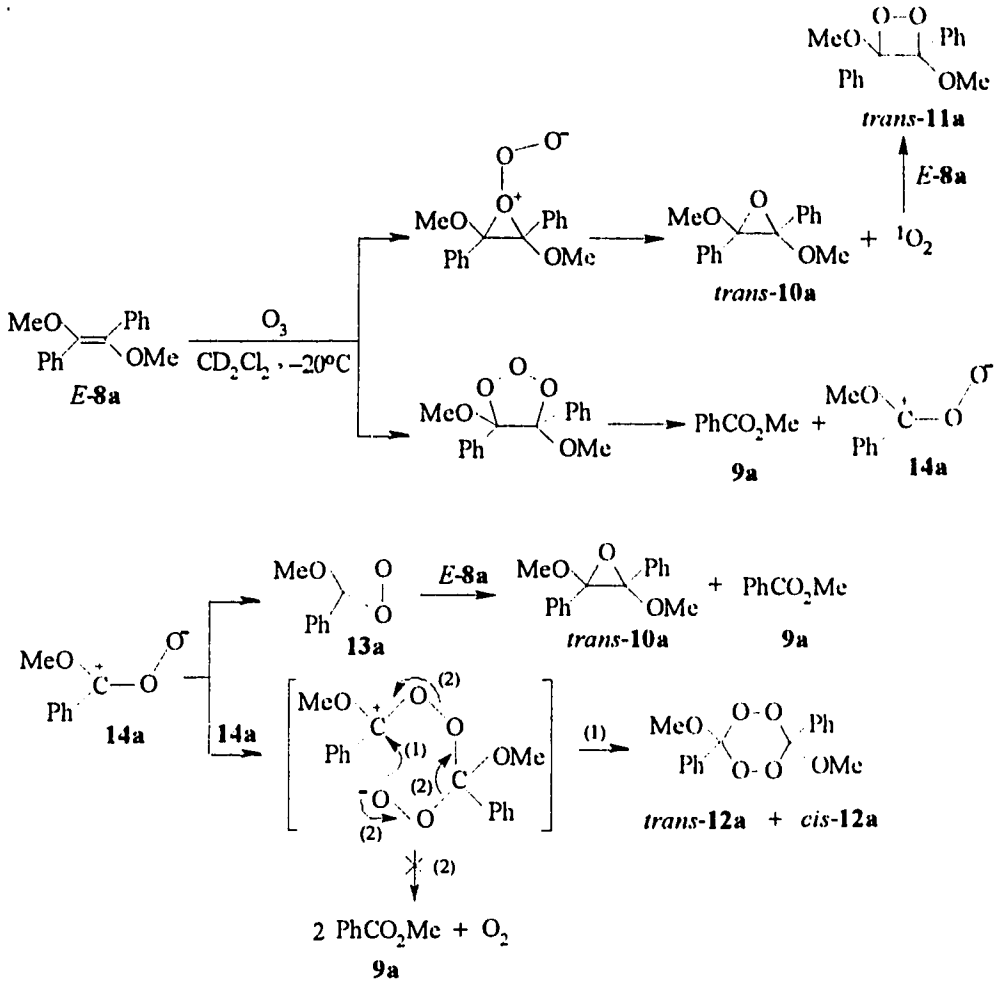


(10)

the oxiranes **10a** and the dioxitanes **11a** as illustrated in eq 10 for *E*-**8a**. The peroxydioxetane produced by interaction of the alkene and ozone would transfer an oxygen atom to **8a** and lead to the formation of the oxirane **10a** and the dioxetane **11a**. Such a route of dioxetane formation in the ozonolysis of alkene had been proposed[40] but was soon shown to be incorrect.[41] Furthermore, it is unlikely that such a route to the dioxetanes **11a** and oxiranes **10a** would be affected by the presence of 2,5-dimethylfuran. Thus, **10a** and **11a** are not produced in such a route.

Based on the product formation and the discovery of the dioxirane **13a**, a proposed mechanism, which combines the ozonolysis and partial cleavage pathways, for the ozonation of *E*- and *Z*-1,2-dimethoxy-1,2-diphenylethene **8a** is illustrated in Scheme 9 for *E*-**8a**.

Two initial pathways are present in the ozonation of **8a**. In one of these pathways, the oxygenated oxirane of **8a** is proposed as a reaction intermediate. The fragmentation of this intermediate gives the oxirane **10a** and a molecule of singlet oxygen. The singlet oxygen reacts with a second molecule of **8a** to form **11a**. In the other pathway, the primary ozonide is the reaction intermediate. The cleavage of the primary ozonide gives methyl benzoate **9a** and (methoxy)phenylcarbonyl oxide **14a**. The carbonyl oxide **14a** either isomerizes to the dioxirane **13a** or dimerizes with another molecule of **14a** to form the tetroxanes *cis*- and *trans*-**12a** via a zwitterionic intermediate. A possible reaction of the zwitterion is the decomposition to form two molecules of **9a** and one molecule of oxygen which could be singlet oxygen.[8] However, the later study in Chapter IV shows that this reaction

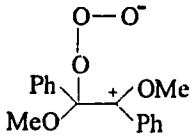


Scheme 9. Ozonation mechanism of *E*-1,2-dimethoxy-1,2-diphenylethene

does not occur. In the inverse ozonation, **13a** becomes a final ozonation product. In the normal ozonation, however, **13a** transfers an oxygen atom to unreacted **8a** to give **9a** and **10a**. According to this mechanism, each mole of ozone can consume more than one mole of the alkene. The stoichiometry obtained shows that actually about 1.4 moles of the alkene is consumed by one mole of ozone. This is consistent with the proposed mechanism.

Stereospecific formation of oxiranes and liberation of singlet oxygen in ozonolysis of some sterically hindered alkenes have been observed.[16] To

rationalize oxirane and molecular oxygen formation oxygenated oxiranes have been proposed as the reaction intermediates.[16] Although *E*- and *Z*-**8a** are not highly hindered alkenes, one of the intermediates in the ozonation of *E*- or *Z*-**8a** is suggested to be an oxygenated oxirane because the alternative zwitterionic intermediate in which the positive charge could be stabilized by the electron-rich methoxy group can be ruled out. Similar zwitterion forms



have been postulated as intermediates in the ozonation of *E*- and *Z*-1,2-difluoroethene where the formation of oxirane is stereoselective.[17] In the case of the ozonation of *E*- and *Z*-**8a**, if the ring closure were faster than the C—C bond rotation the formation of oxiranes would be stereospecific. However, there is no evidence for formation of any oxirane or dioxetane from reactions between ozone and the following alkenes which could form zwitterions

$CH_2=C(OCH_3)_2$ $CH_3CH=C(OCH_3)_2$ $(CH_3)_2C=C(OCH_3)_2$

where the positive charge is similarly stabilized.[22] Therefore it is unlikely that the zwitterion in the ozonation of *E*- or *Z*-**8a** is an intermediate.

Initially, the proposed ozonation mechanism was mainly based on the consideration of the reaction products. According to this mechanism, the oxirane **10a** is produced through two reaction pathways, i.e., the direct ozone epoxidation via the oxygenated oxirane and the indirect dioxirane epoxidation. The above discussion has already provided strong evidence for the presence of the dioxirane epoxidation pathway. However, because the oxygenated oxirane has never been directly observed, it was necessary to search for more evidence to prove the presence of the direct ozone epoxidation pathway.

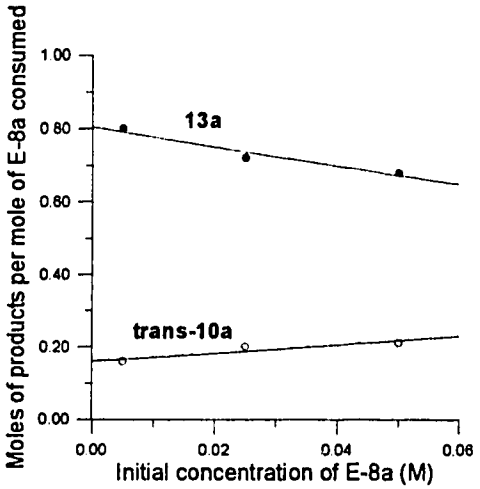


Figure 4. Concentration effect on the yields of product in the inverse ozonation of *E*-**8a** in CD_2Cl_2 at −20 °C.

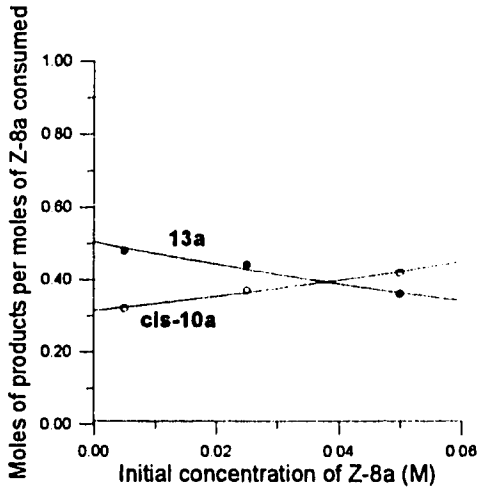


Figure 5. Concentration effect on the yields of product in the inverse ozonation of *Z*-**8a** in CD_2Cl_2 at −20 °C.

At first, it was considered to choose the reaction conditions that would only allow *E*- or *Z*-**8a** to react with ozone but not with the dioxirane **13a**. If the oxirane *trans*- or *cis*-**10a** would still form under such conditions, it would have to result from the direct ozone epoxidation of *E*- or *Z*-**8a**. Actually, the reaction conditions in the inverse ozonation were designed toward such ideal conditions. From the inverse ozonation data in the Table 1, the yields of *trans*- or *cis*-**10a** and **13a** are plotted against the initial concentrations of *E*- and *Z*-**8a** in Figure 4 and Figure 5, respectively. It can be seen that the yield of **13a** increases and the yields of *trans*- and *cis*-**10a** decrease with the decrease of the initial concentration of *E*- or *Z*-**8a**, suggesting that a small amount of **13a** still reacts with the alkenes even in the presence of an excess amount of ozone. Extrapolating the yield curves of **10a** and **13a** to zero concentration of *E*- or *Z*-**8a** gives the yields of *trans*- or *cis*-**10a** and **13a**. The plots show that at the zero concentration of the alkenes the ozonation of one mole of *E*-**8a** would produce 0.15 moles of *trans*-**10a** and 0.82 moles of **13a**; the ozonation of one mole of *Z*-**8a** would produce 0.32 moles of *trans*-

10a and 0.51 moles of **13a**. The oxiranes **10a** produced under such conditions must completely result from the direct ozone epoxidation of the alkenes because the alkene can only be consumed by ozone.

Since the competitive tetroxane formation almost does not occur at –20 °C, it is reasonable to assume that the cleavage of each molecule of the primary ozonide results in the formation of one molecule of the dioxirane **13a**. Therefore, it can be roughly estimated from the above data that the reaction between *E*-**8a** and ozone at –20 °C initially results in an oxygenated oxirane:primary ozonide ratio of about 15:85, and that from *Z*-**8a** is about 39:61. (An example of the calculations of these data is as follows: the percentage of the oxygenated oxirane formed from *Z*-**8a** = 0.32 / (0.32 + 0.51) ≈ 39%). These ratios show that more oxygenated oxirane is formed from *Z*-**8a** than from *E*-**8a**, implying more singlet oxygen will be produced from *Z*-**8a**, and, hence, more dioxetane *cis*-**11a** will be produced. As mentioned above, *Z*-**8a** is four times as reactive as *E*-**8a** toward singlet oxygen. The combination of these two factors can qualitatively account for the higher yields of the dioxetane *cis*-**11a** obtained from the ozonation of *Z*-**8a**.

It was observed that the partial ozonation of *E*- or *Z*-**8a** in the presence of excess 2,3-dimethyl-2-butene **5** resulted in lower yields of the oxiranes *trans*- or *cis*-**10a**, but to different extents. Upon ozonation of a 1:20 mixture of *E*- or *Z*-**8a** to **5** at –78 °C with a limited amount of ozone, the relative ratio of *cis*-**10a**:**9a** dropped from about 0.8:1 to about 0.5:1 while the ratio of *trans*-**10a**:**9a** dropped from about 0.5:1 to as little as 0.1:1. 2,3-Dimethyl-2-butene **5** shows high reactivity toward the dioxirane **13a** as determined by the competitive epoxidation experiments to be described later. In the presence of a large amount of such a reactive foreign alkene, the formation of **10a** from

the indirect dioxirane epoxidation pathway would be greatly suppressed since **13a** would mainly epoxidize the foreign alkene instead of *E*- or *Z*-**8a**. The formation of the oxiranes from the direct ozone epoxidation pathway, however, should not be affected. The fact that the yield of *cis*-**10a** was reduced much less than that of *trans*-**10a** confirms the above estimation that more oxygenated oxirane is formed from *Z*-**8a** than from *E*-**8a**.

For several entries in Table 1 the yields of *trans*- and *cis*-**10a** exceed 0.5 moles per mole of the alkene consumed. This could only occur in cases where the oxiranes are not just formed by the indirect dioxirane epoxidation. If the oxiranes were solely formed by dioxirane epoxidation, the oxirane yield would be no more than 0.5 moles per mole of the alkene consumed since equal amounts of the alkene and the dioxirane, an ozonation intermediate, would be required.

It was noted that in the inverse ozonation reactions the yields of the oxiranes *trans*- and *cis*-**10a** are significantly reduced but the yields of the dioxetanes *trans*- and *cis*-**11a** are almost not changed from those of the normal ozonation. This was contradictory to our expectation. If nearly all of the alkene molecules were consumed by ozone in the inverse ozonation, there should be no more alkene left for singlet oxygen to react with, so the yields of the dioxetanes should be much lower. This experimental result even made us consider the possibility that the dioxetanes were produced from the direct interaction between *E*- or *Z*-**8a** and ozone. However this possibility had been ruled out by the ozonation of mixtures of *E*- or *Z*-**8a** and 2,5-dimethylfuran experiments in which no dioxetanes were formed. After further consideration of the reaction conditions, we reasoned that between the outer solution of ozone and the fresh alkene drop around the outlet of the alkene addition tube there is a reaction zone where the alkene and ozone encounter and react.

Some singlet oxygen and the dioxirane **13a** produced in this zone will diffuse into the fresh alkene drop to react with the new coming alkene. The diffusion rate of singlet oxygen is apparently higher than that of the bulkier dioxirane. Thus, the yields of the dioxetanes in the inverse ozonation is almost the same as in the normal ozonation. This analysis can also explain the observation that a small amount of the dioxirane **13a** still reacts with *E*- or *Z*-**8a** even under the inverse ozonation conditions.

5. Attempts to trap (methoxy)phenylcarbonyl oxide

a) With methanol and methoxide ion

One of the methods of preventing the formation of the dioxirane **13a** is by trapping its precursor, (methoxy)phenylcarbonyl oxide **14a**. If the carbonyl oxide were trapped completely before it cyclized to the dioxirane, the formation of the oxirane would provide strong evidence for the presence of the direct ozone epoxidation pathway. Usually, carbonyl oxides can be trapped very easily by methanol which serves as a participating solvent to form α-methoxy hydroperoxides.[1,42] The product distribution from the ozonation of *E*- or *Z*-**8a** in a 4:1 mixture of CD_3OD and CD_2Cl_2 is summarized in Table 3. It was surprising to find, from the ^1H NMR spectrum, that *trans*- and *cis*-**12a**, the dimers of the carbonyl oxide **14a**, were still formed in the ozonation of *E*- or *Z*-**8a** at –60 °C and there was no new signal for the expected α-methoxy hydroperoxide. When the ozonation of *E*- or *Z*-**8a** was carried out at –20 °C, although no signals of *trans*- and *cis*-**12a** were detected, no new signal formed either. This means **14a** can not be trapped by methanol. The reason why **14a** does not react with methanol is unclear. Later, a stronger nucleophile, methoxide ion, was used to trap **14a**. Ozonation was carried out in a 4:1 mixture of a 0.5 *M* solution of sodium methoxide-D_3 and

Table 3. Product distribution from the ozonation of *E*- and *Z*-1,2-dimethoxy-1,2-diphenylethene **8a** in CD_3OD/CD_2Cl_2[a]

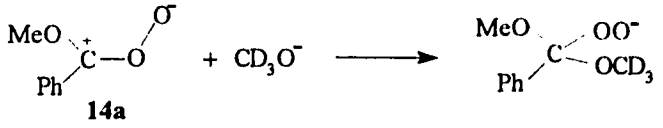
Alkene	Conc.	Method	Temp.	Products, moles per mole of **8a**			
	M		°C	**9a**	**10a**[b]	**11a**[b]	**12a**[c]
E-**8a**	0.05	normal	–20	0.96	0.52	<0.01	0.00
			–60	0.98	0.46	0.02	0.03
Z-**8a**	0.05	normal	–20	0.75	0.55	0.07	0.00
			–60	0.74	0.52	0.09	0.02

[a] The alkene was firstly dissolved in 0.1 mL of CD_2Cl_2 and then 0.4 mL of CD_3OD was added.

[b] Only *trans* from *E*-**8a** and only *cis* from *Z*-**8a**.

[c] About equal amounts of *cis* and *trans*.

CD_2Cl_2 at –78 °C. About 3.5 times of the amount of ozone was required in this basic solution than that required in the normal neutral solutions to complete the reaction. This could be because much of the ozone was destroyed in the basic solution.[43] The tetroxanes **12a** were not detected and a new product that gave a singlet at δ 3.10 in the ^1H NMR spectrum was found. Although the product that gives this signal has not been isolated, a signal at δ 116.73 in the ^{13}C NMR spectrum of the reaction mixture indicates that it has a carbon atom attached to three oxygen atoms and one phenyl group, consistent with the structure of the expected adduct of **14a** and methoxide ion, suggesting that methoxide ion trapped the carbonyl oxide **14a**, eq 11.



14a (11)

It was found that even in the presence of the methoxide ions, the ozonation of *Z*-**8a** still produced the oxirane *cis*-**10a** and the dioxetane *cis*-**11a**, and the ozonation of *E*-**8a** still produced *trans*-**10a**, Table 4. Compared

Table 4. Product distribution from the ozonation of *E*- and *Z*-1,2-dimethoxy-1,2-diphenylethene **8a** in the presence of CD_3ONa[a] in CD_3OD/CD_2Cl_2

Alkene	Temp.	Products, moles per mole of **8a**				
	°C	**9a**[b]	**10a**[c]	**11a**[c]	**12a**	Adduct
E-**8a**	−20	1.21	0.17	0	0	0.45
	−40	1.24	0.14	0	0	0.48
	−60	1.16	0.12	0	0	0.60
Z-**8a**	−20	0.91	0.33	0.03	0	0.37
	−40	0.88	0.35	0.04	0	0.34
	−60	0.81	0.32	0.08	0	0.39

[a] The concentration of *E*- or *Z*-**8a** was 0.05 *M* and the concentration of CD_3ONa was 0.5 *M*. The ratio of CD_3OD to CD_2Cl_2 was 4:1.

[b] The ^1H NMR spectra were recorded at −20 °C soon after the ozonation reaction was finished to avoid the methoxy group of methyl benzoate being exchanged by the methoxy-D_3 group of the base.

[c] Only *trans* from *E*-**8a** and only *cis* from *Z*-**8a**.

with those from *Z*-**8a**, however, higher yields of the adduct and lower yields of the oxirane were obtained from *E*-**8a**. This is consistent with the previous conclusion, which was based on the results of the inverse ozonation, that more carbonyl oxide is generated from the ozonation of *E*-**8a** and less oxirane *trans*-**10a** is formed from the direct epoxidation pathway in the proposed ozonation mechanism.

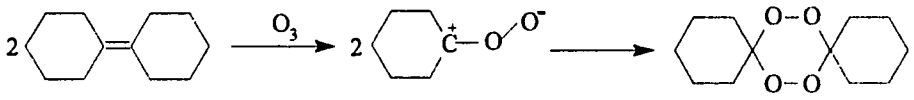
b) With acetaldehyde

In step three of the Criegee mechanism, the carbonyl oxide recombines with the internally generated carbonyl compound to produce an ozonide. If there is an external carbonyl compound present in the solution, a cross ozonide will be produced.[1] This provides another method to trap carbonyl oxides.

The carbonyl compound formed during ozonation of *E*- or *Z*-**8a** is methyl benzoate **9a**. Esters usually have low reactivity toward carbonyl oxides,[1,42] so it is not surprising that there is no ozonide produced from the ozonation of *E*- or *Z*-**8a**. Aldehydes have been shown to be much more reactive than ketone or ester toward carbonyl oxides to form ozonides.[1] Ozonation of *E*- or *Z*-**8a** in the presence of excess acetaldehyde, however, caused no change in the product formation and distribution, as seen by inspection of the ^{1}H NMR spectra. No new signal could be assigned to the expected cross ozonide. This experiment indicates that **14a** does not react with aldehydes either.

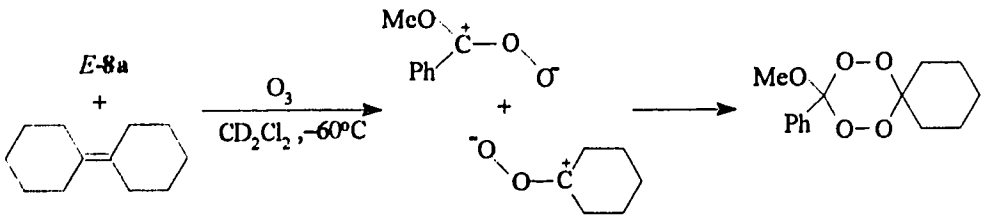
c) With cyclohexanone oxide

Ozonolysis of cyclohexylidenecyclohexane in nonparticipating solvents produces the corresponding tetroxane in good yield, eq 12.[44] The reactivities



(12)

of **8a** and cyclohexylidenecyclohexane are similar as indicated by the observation that both alkenes were consumed upon treatment of a 1:1 mixture of the two alkenes with a limited amount of ozone. Thus, ozonation of a mixture of *E*- or *Z*-**8a** and cyclohexylidenecyclohexane should produce (methoxy)phenylcarbonyl oxide **14a** and cyclohexanone oxide at the same time. It was expected that most of **14a** would react with the coexistent cyclohexanone oxide if the concentration of latter was much higher than that of **14a**. The expected cross tetroxane, 3-methoxy-3-phenyl-1,2,4,5-tetraoxaspiro[5.5]undecane, was indeed produced in the ozonation of a 2:1 mixture of cyclohexylidenecyclohexane and *E*- or *Z*-**8a** in CD_2Cl_2 at −60 °C, eq 13. The OCH_3 group of the cross tetroxane gave a signal at δ 3.48. The ^{1}H



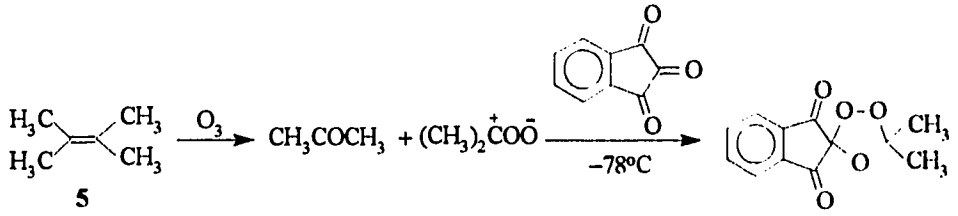
(13)

NMR spectrum also showed that *cis*- and *trans*-**12a** were still produced under these conditions, indicating that the trapping of **14a** was not complete. Further increase in the ratio of cyclohexylidenecyclohexane to **8a** was restricted by the poor solubility of cyclohexylidenecyclohexane. The solid cross tetroxane was isolated from the ozonation reaction mixture in the same way as the isolation of the tetroxanes **12a**. Chemical ionization with NH_4^+ afforded the $(M + NH_4^+)$ ion at *m/e* 284.

d) With indanetrione

Since methanol cannot trap (methoxy)phenylcarbonyl oxide **14a**, other types of the carbonyl oxide trap that can be used under neutral conditions were sought. It has been reported that α-dicarbonyl compounds, such as diketones or diesters, are more dipolarophilic than monoketones or monoesters toward carbonyl oxides, probably due to mutual activation of the two carbonyl groups.[19b,45] It was felt that the central carbonyl group of 1,2,3-triones might be more reactive toward carbonyl oxides. Therefore, the readily available indanetrione was chosen to trap carbonyl oxides. In the trial tests, ozonolysis of 2,3-dimethyl-2-butene **5** was carried out in the presence of the trione. Ozonolysis of 2,3-dimethyl-2-butene **5** in aprotic solvents always yields some complex oligomer.[44] In the presence of the trione, however, the complex ^1H NMR signals due to the oligomer completely disappear and a singlet at δ 1.7 appears. The integral of this signal is equal to that of acetone. These exploratory experiments showed that the trione scavenges dimethylcarbonyl oxide quantitatively and the product is 2,2-dimethyl-1,3,4-

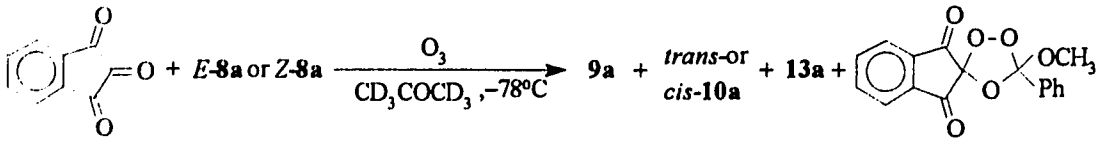
trioxaspiro[4.4]-7,8-benzononane-6,9-dione, eq 14.[46]



(14)

Inspired by this result, we attempted to use the trione to capture (methoxy)phenylcarbonyl oxide **14a**. A new singlet at δ 3.77 appeared in the ^{1}H NMR spectra of the reaction mixtures obtained by the inverse ozonation of either *E*- or *Z*-**8a** in the presence of excess trione at −78 °C in acetone-D_6. No tetroxanes **12a** were detected, suggesting the carbonyl oxide **14a** was trapped by the trione. Therefore, the new signal is tentatively assigned to the reaction product of the carbonyl oxide **14a** and the trione. In the presence of the trione the oxirane *trans*- or *cis*-**10a** is still produced. No dioxirane **13a** is formed from *E*-**8a**, while **13a** is still formed from *Z*-**8a**. For unknown reasons the yield of **13a** obtained from *Z*-**8a** in the presence of the trione is even higher than that in the absence of the trione. This could be because either the trione affects the dioxirane formation or the proton signal is due to an unknown product which gives a signal that happens to have the same chemil shift as the dioxirane. The product formation and distribution of the inverse ozonation of *E*- or *Z*-**8a** in the presence of excess trione are shown in Scheme 10.

In the absence of the trione, under the identical conditions, 0.32 and 0.23 moles per mole of the alkene of the dioxirane **13a** are produced from the inverse ozonation of *E*-**8a** and *Z*-**8a**, respectively. If the disappearance of **13a** in the ozonation of *E*-**8a** in the presence of the trione is due to **14a** being captured by the trione, then **14a** from *Z*-**8a** should be captured by the trione as well. It is not clear why **13a** is still formed from *Z*-**8a** under such

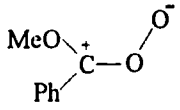


From *E*-**8a**[a]	yield[b]	1.56	0.10	0	0.24
Z-**8a**[a]		0.82	0.31	0.38(?)	0.17

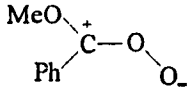
[a]. 4 mg of the alkene dissolved in 0.5 ml of acetone saturated with the trione.
[b]. moles, per mole of the alkene.

Scheme 10. Inverse ozonation of *E*- or *Z*-1,2-dimethoxy-1,2-diphenylethene in the presence of excess indanetrione

conditions. It has been suggested that the ozonolysis of *E*- and *Z*-1-ethoxypropene produces different amounts of syn and anti carbonyl oxides ($CH_3HC^+OO^-$), which combine at different rates with dipolarophiles and thus lead to variation in the dioxolane stereoisomer ratios.[47] It is therefore possible that the carbonyl oxides generated from *Z*-**8a** and from *E*-**8a** have different reactivities because they have different geometric conformations, one is syn and the other is anti, as shown below:



syn-**14a**



anti-**14a**

The isomer generated from *E*-**8a** has higher reactivity toward the trione; while the other isomer from *Z*-**8a**, has lower reactivity toward the trione or cyclizes more rapidly and consequently is only partially trapped.

B. Steric effects on ozonation of *E*- and *Z*-1,2-diethoxy-1,2-diphenylethene and *E*- and *Z*-1,2-diisopropoxy-1,2-diphenylethene

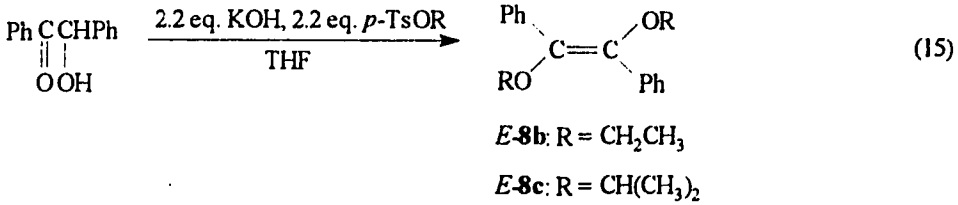
In order to further explore the ozonation of 1,2-dialkoxy-1,2-diphenylethenes and to study the steric effects involved in the reaction, the ozonation of *E*- and *Z*-1,2-diethoxy-1,2-diphenylethene (*E*- and *Z*-**8b**) and *E*- and *Z*-1,2-diisopropoxy-1,2-diphenylethene (*E*- and *Z*-**8c**) was studied.

As already mentioned, oxygenated oxiranes have been suggested as reaction intermediates in the ozonation of some sterically hindered alkenes.[16] It was therefore predicted that if the bulk of the alkoxy groups in the starting alkenes was increased, the alkenes would prefer to form more oxygenated oxiranes rather than primary ozonides. Hence more oxiranes would be produced from the direct ozone epoxidation pathway and more singlet oxygen would be generated. Consequently higher yields of the dioxetanes and under the inverse ozonation conditions higher yields of the oxiranes could be anticipated. Since the isopropoxy group is bulkier than the methoxy group, the ozonation of *E*- and *Z*-**8c** would be a good model to test this prediction. The proof of this prediction would provide more evidence for the proposed mechanism for the ozonation of *E*- and *Z*-**8a**.

It was expected that the ozonation behavior of **8b** should be between those of **8a** and **8c**. Therefore, the ozonation of *E*- and *Z*-**8b** was also studied.

1. Preparation of the starting alkenes

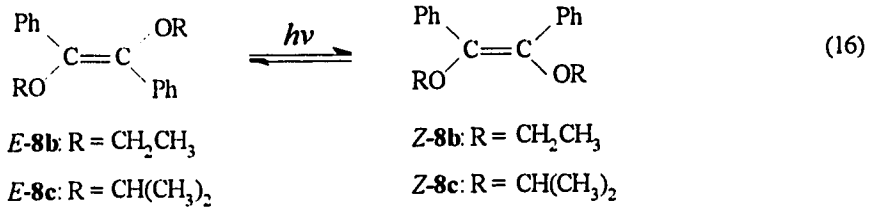
The starting alkenes *E*-**8b** and *E*-**8c** were similarly prepared as *E*- and *Z*-**8a**, eq 15. The yields of *E*-**8b** and *E*-**8c**, however, were much lower (only



(15)

20% for *E*-**8b** and 16% for *E*-**8c**) than those of *E*- and *Z*-**8a** (total yields 50%). Lower yields of *E*-**8b** and *E*-**8c** are probably because ethyl and isopropyl groups are bulkier than the methyl group. The increased steric hindrance reduces the rates of the S_N2 reactions between the *p*-toluenesulfonates and the benzoin dianions. Hence other competing reactions become predominant in the syntheses of *E*-**8b** and *E*-**8c**.

It was reported,[24] and confirmed in this study, that both isomers of **8a** can be obtained with the use of either potassium hydroxide or sodium hydroxide as base in the synthesis of **8a** and the use of potassium hydroxide results in a higher *E*-**8a**:Z-**8a** ratio. However, with the use of potassium hydroxide as base in the synthesis of **8b** or **8c**, only the *E*-isomer of **8b** or **8c** was obtained. When sodium hydroxide was used, none of the desired products was obtained. The *Z*-isomers of **8b** and **8c** were obtained by photoisomerization of the corresponding *E*-isomers followed by chromatographic separation, eq 16.



E-**8b**: R = CH_2CH_3 *Z*-**8b**: R = CH_2CH_3

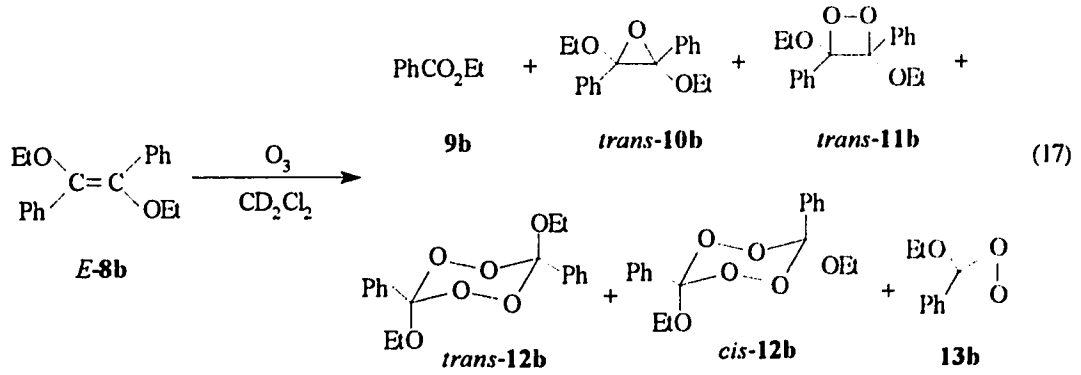
E-**8c**: R = $CH(CH_3)_2$ *Z*-**8c**: R = $CH(CH_3)_2$ (16)

The geometrical assignments of *E*- and *Z*-**8b** and *E*- and *Z*-**8c** were based on their ^1H NMR spectra. In the study of the structural assignments of the geometrical isomers of some nuclear-substituted 1,2-dimethyl-1,2-diphenylethenes by means of ^1H NMR, Inamoto et al observed that the methyl groups of the *E*-isomers absorb at higher fields than those of the *Z*-isomers.[49] The same phenomenon was also observed for 1,2-dimethoxy-1,2-diphenylethenes **8a**. The chemical shifts of the methoxy groups of *E*-**8a** and *Z*-**8a** are at δ 3.38 and 3.59, respectively. Applying this rule to **8b**, we

assigned the isomers that give the methylene proton signals centered at δ 3.53 and 3.73 to be *E*-**8b** and *Z*-**8b**, respectively. Similarly, for **8c**, the isomers that give the methine proton signals centered at δ 3.70 and 3.92 are assigned to be *E*-**8c** and *Z*-**8c**, respectively. According to these assignments, it was noticed that in **8a-c**, compared with those of the *E*-isomers, the phenyl groups of the *Z*-isomers give simpler signals in the ^{1}H NMR spectra. This can be taken as another useful rule for distinguishing *Z* and *E* isomers of 1,2-diphenyl substituted ethenes. For example, the phenyl groups of *Z*-**8a** or *Z*-**8b** give a sharp singlet while those of *E*-**8a** or *E*-**8b** give complex multiplets. Although the phenyl groups of *Z*-**8c** do not give a singlet, the range of the signals (δ 7.08-7.20) they give is narrower than that of *E*-**8c** (δ 7.20-7.83). It has been reported that the multiplicity of aromatic protons of a phenyl group adjacent to a double bond depends on the rotational angle of the phenyl group.[49] The rotational angles of the same geometric isomers must be very similar, but quite different from those of the other geometric isomers.

2. Results of normal and inverse ozonation

The results of ozonation of *E*- or *Z*-**8b**, as illustrated in eq 17 for *E*-**8b**, are very similar to those of *E*- or *Z*-**8a** and therefore did not provide useful new information in the study of the ozonation mechanism. The products



(17)

obtained from the ozonation of *E*- or *Z*-**8b** are ethyl benzoate **9b**; *trans*- or *cis*-1,2-diethoxy-1,2-diphenyloxiranes (*trans*- or *cis*-**10b**); *trans*- or *cis*-3,4-diethoxy-3,4-diphenyl-1,2-dioxetanes (*trans*- or *cis*-**11b**); and *trans*- and *cis*-3,6-diethoxy-3,6-diphenyl-1,2,4,5-tetroxanes (*trans*- and *cis*-**12b**). Inverse ozonation of either *E*- or *Z*-**8b** results in the formation of (ethoxy)phenyldioxirane **13b** along with the above products. The product distribution from the ozonation of *E*- or *Z*-**8b** is summarized in Table 5.

The identifications of the oxiranes *trans*- and *cis*-**10b** were accomplished by taking advantage of the fact that (methoxy)phenyldioxirane **13a** is a powerful stereospecific epoxidizing agent. The ^{1}H NMR spectra of the ozonation reaction mixtures of *E*- and *Z*-**8b** were compared with those of the authentic samples of the oxiranes prepared by epoxidation of the respective alkenes with **13a**. As observed from the TLC and ^{1}H NMR spectra, at room temperature the oxiranes **10b** were hydrolyzed to benzil and ethanol by the moisture and a trace of acids in the solvent.

The oxiranes can also be identified by comparing the difference of the ^{1}H NMR spectra obtained before and after addition of a starting alkene to its inverse ozonation reaction mixtures. In this experiment, it was always observed that the signals of the dioxiranes disappeared and the intensities of the signals of the oxiranes and the benzoates increased by an equivalent amount. In this way the dioxiranes and the oxiranes can be identified in the same experiment.

Because the oxirane carbons of **10b** are stereogenic atoms, the protons of the methylene groups in **10b** are not chemical shift equivalent although they are three bonds removed from the stereogenic atom. Each proton of the methylene is split by the other (J_{gem} = ~ 8.9 Hz) and by the neighboring methyl protons (J_{vic} = ~ 7.6 Hz), giving rise to a doublet of quartets. For

Table 5. Product distribution from the ozonation of *E*- and *Z*-1,2-diethoxy-1,2-diphenylethene **8b** in CD_2Cl_2

Alkene	Conc.	Method	Temp.	Products, moles per mole of **8b**				
	M		°C	**9b**	**10b**[a]	**11b**[a]	**12b**[b]	**13b**
E-**8b**	0.01	normal	–20	0.84	0.32	0.00	0.00	0.48
	0.05			0.87	0.42	0.01	0.02	0.10
	0.10			0.92	0.46	0.01	0.03	0.08
	0.20			0.91	0.46	0.02	0.04	0.06
	0.05	normal	0	0.87	0.39	0.14	0.00	0.08
			–40	0.94	0.37	0.08	0.02	0.10
			–60	0.88	0.36	0.01	0.09	0.21
			–80	1.05	0.20	0.01	0.13	0.27
	0.05	inverse[c]	–20	0.80	0.29	0.00	0.00	0.54
Z-**8b**	0.05	normal	–20	0.60	0.56	0.11	0.03	0.00
	0.05	inverse[c]	–20	0.48	0.42	0.13	0.00	0.42

[a] Only *trans* from *E*-**8b** and only *cis* from *Z*-**8b**.

[b] About equal amounts of *cis* and *trans*.

[c] Simultaneous slow addition of the ozone-oxygen mixture (100 mL) and a solution of **8b** (0.5 mL) into the bottom of a NMR tube through two fine tubes.

trans-**10b**, the shifts are δ 3.48 and δ 3.61. Since the shift difference between them is small, the two doublets of quartets are somewhat overlapping and the AB pattern from the geminal coupling is quite complex. For *cis*-**10b**, the shifts are δ 3.42 and δ 3.61. The shift difference is a little larger, so the two doublets of quartets could be observed.

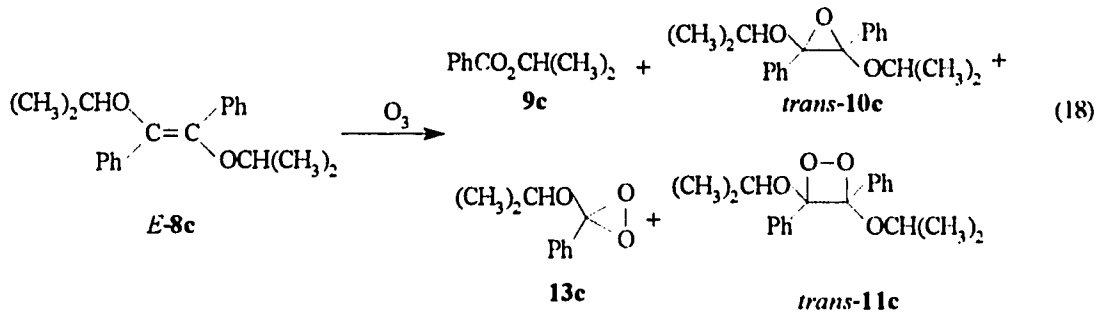
The dioxetanes *trans*- and *cis*-**11b** were identified by the same means as the dioxetanes **11a**. The ring carbons of the dioxetanes **11b** are stereogenic atoms, so protons the methylene protons in **11b** are not chemical shift equivalent either and have the same splitting pattern as those of **10b**. The shifts of the doublets of quartets of **11b** are well separated from each other (δ 3.58 and 3.83 for *cis*-**11b**; δ 3.17 and 3.47 for *trans*-**11b**).

The tetroxanes *trans*- and *cis*-**12b** directly crystallized from the ozonation mixtures of *E*-**8b** after the solvent was evaporated. Separations and identifications of the two isomers were similar to that of *trans*- and *cis*-**12a**. On cooling from 20 to −20 °C the sharp quartet of the methylene protons of the isomer melting at 140-141 °C was broadened and that of the isomer melting at 145-147 °C remained sharp. These isomers were thus assigned to be *cis*- and *trans*-**12b**, respectively. Chemical ionization with NH_4^+ afforded the ($M + NH_4^+$) ions at *m/e* 350 from each isomer.

Determination of the product distribution from the ozonation of *E*- and *Z*-**8b** becomes complex due to the overlapping of some ^1H NMR signals. The doublet of quartets of the two OCH_2 groups of *trans*-**10b** at δ 3.38-3.70 overlaps half of the doublet of quartets of the two OCH_2 groups of *trans*-**11b** at δ 3.39-3.55. Because the other half of the signals of the two OCH_2 groups of *trans*-**11b** at δ 3.08-3.26 is well separated from the other signals, the total integral of the two OCH_2 groups of *trans*-**10b** can be calculated by subtracting the integral of the signals at δ 3.08-3.26 from the integral of the signals at δ 3.38-3.70. Half of the ^1H NMR signals of the two OCH_2 groups of *cis*-**10b** at δ 3.34-3.50 are well separated from the other signals and the other half of it at δ 3.51-3.71 overlap half of the signals of the two OCH_2 groups of *cis*-**11b** at δ 3.48-3.68. The other half of the signals of the two OCH_2 groups of *cis*-**11b** at δ 3.73-3.92 overlap the quartet of the OCH_2 group of **13b** at δ 3.79. Determination of the signal integrals of *cis*-**10b**, *cis*-**11b** and **13b** is therefore based on the integrals of the well separated half of the signals of the two OCH_2 groups of *cis*-**10b**.

Ozonation of *E*- or *Z*-**8c** yielded isopropyl benzoate **9c**, *trans*- or *cis*-1,2-diisopropoxy-1,2-diphenyloxiranes (*trans*- or *cis*-**10c**), *trans*- or *cis*-3,4-diisopropoxy-3,4-diphenyl-1,2-dioxetanes (*trans*- or *cis*-**11c**), and

(isopropoxy)phenyldioxirane **13c**, eq 18. Unlike the ozonation of **8a** and **8c**, no tetroxane was detected by ^{1}H NMR. The product distribution from the ozonation of *E*- and *Z*-**8c** is summarized in Table 6.



(18)

The ozonation products of *E*- and *Z*-**8c** were identified in the same ways as those of *E*- or *Z*-**8b**. In the presence of moisture and a trace of acids, the oxiranes **10c** were hydrolyzed to benzil and isopropyl alcohol as observed from the ^{1}H NMR spectra. The authentic sample of the dioxetane *trans*-**11c** was isolated from the reaction mixture obtained by singlet oxygen oxidation of *E*-**8c**. This dioxetane appears to be much more stable than its homologues **11a** and **11b**, presumably because it is more sterically crowded. Usually, sterically crowded dioxetanes, such as dioxetanes of biadamantylidene[50] and binorbornylidene,[51] are much more stable than sterically uncrowded dioxetanes. In the dark, the half-life of *trans*-**11c** determined by ^{1}H NMR is about sixteen hours at 40 °C in acetone-D_6.

The ring carbon atoms of the oxiranes *trans*- and *cis*-**10c** and the dioxetanes *trans*- and *cis*-**11c** are also stereogenic atoms. The protons of the methyl groups in **10c** and **11c** are not chemical shift equivalent even though they are four bonds removed from the stereogenic atoms. Thus, absorptions of the two methyl groups are split by the neighboring methine protons (Jvic =

Table 6. Product distribution from the ozonation of *E*- and *Z*-1,2-diisopropoxy-1,2-diphenylethene **8c**

Alkene	Solvent	Conc. *M*	Method	Temp. °C	Products, moles per mole of 8c[b]			
					9c	**10c**	**11c**	**13c**
E-**8c**	CD_2Cl_2	0.01	normal	–20	0.53	0.36	0.13	0.50
		0.05			0.53	0.41	0.12	0.41
		0.10			0.57	0.47	0.11	0.27
		0.20			0.62	0.54	0.10	0.11
		0.05	normal	0	0.58	0.43	0.12	0.31
				–40	0.50	0.41	0.12	0.41
				–60	0.54	0.43	0.15	0.31
				–78	0.51	0.50	0.16	0.16
		0.05	inverse[c]	–20	0.53	0.38	0.08	0.51
	acetone-D_6	0.05	normal	0	0.64	0.38	0.02	0.56
				–20	0 62	0.41	0.02	0.51
				–78	0.69	0.44	0.02	0.38
		0.10	normal	–20	0.63	0.42	0.03	0.47
		0.05	inverse[c]	–20	0.65	0.40	<0.01	0.55
	CD_3OD	0.02[d]	normal	–20	0.82	0.40	0.01	0.36
		0.01[d]		–78	0.61	0.59	<0.01	0.21
Z-**8c**	CD_2Cl_2	0.05	normal	–20	0.49	0.48	0.11	0.34
				–78	0.50	0.54	0.15	0.11
		0.05	inverse[c]	–20	0.55	0.45	0.08	0.39

[a] Only *trans* from *E*-**8c** and only *cis* from *Z*-**8c**.

[b] No corresponding tetroxanes **12c** were found.

[c] Simultaneous slow addition of the ozone-oxygen mixture (100 mL) and a solution of **8c** (0.5 mL) into the bottom of a NMR tube through two fine tubes.

[d] The concentration of the solution was limited by the solubility of *E*-**8c**.

~6 Hz), giving rise to two doublets.

In the ^1H NMR spectra the septets of the OCH groups of the various products from the ozonation of *E*- and *Z*-**8c** are well separated and occur at δ (CD_2Cl_2, –20 °C): 5.18, **9c**; 3.87, *trans*-**10c**; 3.84, *cis*-**10c**; 3.70, *trans*-**11c**;

4.47, *cis*-**11c**; 4.33, **13c**. However, if the ozonation of *E*-**8c** is not complete as in the case of determination of the stoichiometry of the reaction, the signals of the OCH groups of the starting material *E*-**8c** at δ 3.70 completely overlap those of *trans*-**11c**. Fortunately, the doublet of the CH_3 groups of *E*-**8c** at δ 0.98 and one of the two doublets of the CH_3 groups of *trans*-**11c** at δ 0.82 are well separated from other signals. Thus, the peak areas of OCH groups of *E*-**8c** and *trans*-**11c** can be calculated.

Competitive ozonation of a mixture containing equivalent amounts of *E*-**8a** and *E*-**8c** at −78 °C showed that 54% of *E*-**8a** and only 9% of *E*-**8c** were consumed by a limited amount of ozone. Hence, *E*-**8a** is 8.2 times more reactive than *E*-**8c** toward ozone. Similarly, competitive epoxidation experiments showed that *E*-**8a** is 8.1 times as reactive as *E*-**8c** toward the dioxirane **13a** (61% of *E*-**8a** and 11% of *E*-**8c** were consumed by a limited amount of **13a**) and 22.1 times as reactive as *E*-**8c** toward the dioxirane **13c** (36% of *E*-**8a** and 2% of *E*-**8c** were consumed by a limited amount of **13c**). Competitive singlet oxygen oxygenation showed that *E*-**8a** is 2.6 times more reactive than *E*-**8c** toward singlet oxygen (40% of *E*-**8a** and 18% of *E*-**8c** were consumed by a limited amount of singlet oxygen). All of these experiments showed that *E*-**8c** is less reactive than *E*-**8a**. The lower reactivity of *E*-**8c** must originate from its sterically hindered nature.

The stoichiometry of ozonation of *E*-**8c** was determined by delivery of a less than an equivalent amount of ozone to a 0.05 *M* solution of *E*-**8c** at −20 °C. The result turned out to be that 1.1 moles of *E*-**8c** is consumed by each mole of ozone. Determination of the stoichiometry of ozonation of *E*-**8b** is impossible from the ^1H NMR spectra since the signals of the unreacted *E*-**8b** overlap those of the other products.

3. Steric effects on the product formation

The most distinct difference between the ozonation of **8c** and **8a** or **8b** is that (isopropoxy)phenyldioxirane **13c** is always present in the reaction mixtures regardless of whether the reactions are carried out under the normal ozonation conditions or under the inverse ozonation conditions, although the yields of **13c** are slightly higher in the inverse ozonation than those in the normal ozonation. Upon addition of *E*- or *Z*-**8c** to the solution containing **13c**, the corresponding oxirane *trans*- or *cis*-**10c** is produced and **13c** is converted to isopropyl benzoate **9c**, but about a half hour is needed to finish this epoxidation reaction at −20 °C. Under the same conditions, however, the epoxidation of *E*-**8b** by **13b** can be finished within a few minutes and the epoxidation of *E*- or *Z*-**8a** by **13a** is almost instantaneous. Even at −80 °C, it is still impossible to monitor the process of the epoxidation of *E*-**8a** by **13a** with ^{1}H NMR spectroscopy. Such a great difference in the reaction rates can only be attributed to the steric effects. Apparently, the reaction between **13c** and **8c** suffers much more steric hindrance than that between **13a** and **8a**. For this reason the epoxidation of **8c** by **13c** is too slow to compete with the reaction of ozone and **8c**. Therefore, **8c** is almost only consumed by ozone in either the normal or the inverse ozonation and **13c** produced will not be involved in further reaction. This result confirms the previous conclusion from an opposite point that the dioxirane **13a** is produced in the ozonation of **8a** but it reacts very fast with the unreacted starting alkene **8a**, so it is not an observed product in most of the normal ozonation reaction mixtures.

The rate constants for the reaction between the alkene *E*-**8c** and the dioxirane **13c** were determined by ^{1}H NMR to be 0.125 and 0.019 M^{-1} s^{-1} at −20 and −40 °C, respectively. The activation energy of this reaction was therefore estimated to be 11.1 kcal/mole.

As expected, the yield of the dioxetane *trans*-**11c** is about five times of that of the dioxetane *trans*-**11a** and the yield of *cis*-**11c** is about one and half times of that of *cis*-**11a**. Higher yields of the dioxetanes **11c** indicate that more singlet oxygen is produced in the ozonation of **8c** than in the ozonation of **8a**, which in turn means more oxygenated oxiranes are formed. This confirms the initial prediction.

Because the epoxidation of **8c** by **13c** can not compete with the reaction of **8c** with ozone, it is reasonable to assume that the oxirane **10c** produced under the inverse ozonation conditions at −20 °C is exclusively formed from the oxygenated oxirane pathway and **13c** which is formed from the primary ozonide pathway does not undergo further reaction. From Table 6, initially 0.38 moles of the oxygenated oxirane and 0.51 moles of the primary ozonide are formed from *E*-**8c**; 0.45 moles of the oxygenated oxirane and 0.39 moles of the primary ozonide are formed from *Z*-**8c**. On these bases the reaction between ozone and *E*-**8c** at −20 °C results initially in an oxygenated oxirane:primary ozonide ratio of about 43:57 and that from *Z*-**8c** is about 54:46. In the previous section, it was estimated that the initial reaction between ozone and *E*-**8a** at −20 °C results in an oxygenated oxirane:primary ozonide ratio of about 15:85 and that from *Z*-**8a** is about 37:63. Indeed, more oxygenated oxirane is formed from **8c** than from **8a**.

Because about 0.1 moles of the dioxetane *trans*-**11c** are produced from each mole of *E*-**8c** and the dioxirane **13c** almost does not contribute to the formation of **10c**, on the basis of the proposed mechanism it can be estimated that each mole of ozone will consume about 1.1 moles of *E*-**8c**, which was the observed value.

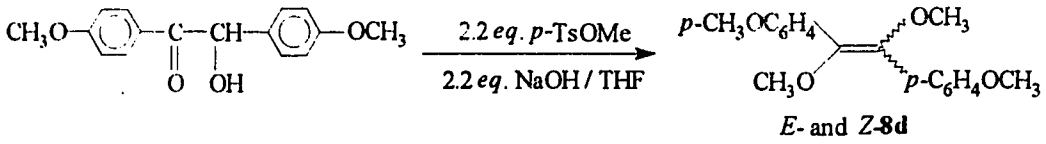
In summary, the results of ozonation of **8c** further confirm the proposed ozonation mechanism.

C. Electronic effects on ozonation of *E*-1,2-dimethoxy-1,2-bis(4-methoxyphenyl)ethene and *E*-1,2-dimethoxy-1,2-bis(4-nitrophenyl)ethene

In order to study electronic effects in the ozonation of electron-rich alkenes, two pairs of derivatives of *E*- and *Z*-**8a** were synthesized and their *E*-isomers were subjected to ozonation. In *E*- and *Z*-1,2-dimethoxy-1,2-bis(4-methoxyphenyl)ethene (*E*- and *Z*-**8d**) the *p*-hydrogen of each phenyl ring is substituted with a strong electron-donating methoxy group; whereas in *E*- and *Z*-1,2-dimethoxy-1,2-bis(4-nitrophenyl)ethene (*E*- and *Z*-**8e**) the *p*-hydrogen of each phenyl ring is substituted with a strong electron-withdrawing nitro group. The substituents provide opposite electronic effects on the starting alkenes as well as on the ozonation reaction intermediates, such as the carbonyl oxides. It was hoped that by the investigation of ozonation behaviors of these two derivatives, better understanding of the ozonation mechanism of the electron-rich alkenes could be achieved.

1. Preparation of the starting alkenes

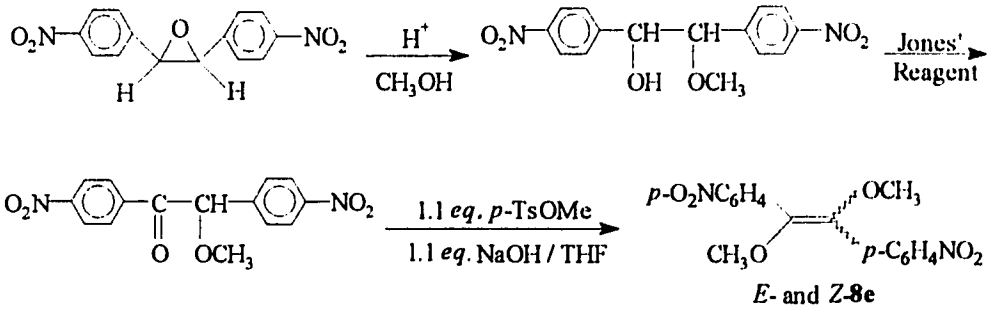
The alkenes *Z*- and *E*-**8d** were prepared by the method used to prepare *Z*- and *E*-**8a**, i.e., alkylation of the dianions of 4,4'-dimethoxybenzoin with methyl *p*-toluenesulfonate, eq 19. The two isomers were separated by fractional crystallization from methanol.



E- and *Z*-**8d** (19)

The stereochemical assignments of *E*- and *Z*-**8d** were based on their ^{1}H NMR spectra. Applying the rule discussed in the assignments of *E*- and *Z*-**8b-c**, we assign the isomers with the signal of the vinyl methoxy groups at δ 3.35 and 3.55 to be *E*- and *Z*-**8d**, respectively. Irradiation of either isomer with a mercury lamp leads to formation of a mixture of both isomers.

Because 4-nitrobenzoin cannot be readily prepared by the classical benzoin condensation of 4-nitrobenzaldehyde,[52] the synthesis of *E*- and *Z*-1,2-dimethoxy-1,2-bis(4-nitrophenyl)ethene **8e** was accomplished by the route shown in Scheme 11. The starting material used here was *cis*-4,4'-dinitrostilbene oxide. After opening the oxirane ring in acidic methanol and oxidation of the resulting α-methoxy alcohol with Jones' reagent, the obtained methoxy ketone was alkylated with methyl *p*-toluenesulfonate in the presence of base to give *E*- and *Z*-**8e** in 52% total yield. The two isomers were separated and identified by the same methods as *E*- and *Z*-**8d**. The isomer with the ^{1}H NMR signal of the methoxy groups at δ 3.42 was assigned to be *E*-**8e** and the other isomer with that at δ 3.69 was assigned to be *Z*-**8e**.



Scheme 11. Synthesis of *E*- and *Z*-1,2-dimethoxy-1,2-bis(4-nitrophenyl)ethene

2. The results of normal and inverse ozonation

As expected, the results of ozonation of *E*-**8d** and *E*-**8e** were similar to

those of *E*-**8a**. Like those of *E*-**8a**, the product distributions of ozonation of *E*-**8d** and *E*-**8e** are also dependent on the reaction temperature, the initial concentration of starting materials, and the ozonation method, Table 7. No

Table 7. Product distribution from the ozonation of *E*-1,2-dimethoxy-1,2-bis(4-methoxyphenyl)ethene *E*-**8d** and *E*-1,2-dimethoxy-1,2-bis(4-nitrophenyl)ethene *E*-**8e** in CD_2Cl_2

				Products, moles per mole of alkene				
Alkene	Conc.	Method	Temp.	benzoate	oxirane	dioxetane	tetroxane	dioxirane
	M		°C	**9**	**10**	**11**	**12**[a]	**13**
E-**8d**	0.01	normal	–20	0.76	0.45	0.01	0.00	0.32
	0.05			0.86	0.53	0.01	0.00	0.06
			–78	0.88	0.46	0.02	0.06[b]	0.04
		inverse	–20	1.20	0.17	0.02	0.00	0.40
E-**8e**	0.01	normal	–20	1.04	0.14	0.00	0.00	0.68
	0.05			1.05	0.18	0.00	0.00	0.58
			–40	1.03	0.16	0.00	0.12	0.53
	0.01		–78	1.01	0.13	0.00	0.21	0.31
	0.05	inverse	–20	1.06	0.07	0.00	0.00	0.76

[a] About equal amounts of *cis* and *trans*.

[b] Estimated based on the integrals of the weak signals in the methoxy region. See explanation in the text.

dioxetane of *E*-**8e**, *trans*-**11e**, was observed under any reaction conditions. When the reactions were carried out at –20 °C, the formation of tetroxanes *cis*- and *trans*-**12e** and *cis*- and *trans*- **12d** was negligible (less than 2%). The intensities of two signals at δ 3.63 and 3.55 in the ozonation mixture of *E*-**8e** increased as the reaction temperature was lowered. The similar change in the intensities of the signals of the tetroxanes *cis*- and *trans*-**12a** was also

observed in the ozonation of *E*- and *Z*-**8a**. Furthermore the chemical shifts of these two signals are very close to those of *cis*- and *trans*-**12a**. Thus these two signals are tentatively assigned to the tetroxanes *cis*- and *trans*-**12e**, respectively. The ozonation of *E*-**8d** at −78 °C yields some minor products as observed from the ^{1}H NMR spectrum of the reaction mixture. It was impossible, however, to tell the signals of the tetroxanes *cis*- and *trans*-**12d** from many weak signals of methoxy groups in the expected region. The dioxirane **13d** was observed when the initial concentration of **8d** was low enough or when **8d** was ozonized under the inverse ozonation conditions. Most importantly, the dioxirane **13e**, like **13c**, was observed in all cases although the yield of **13e** was higher under the inverse ozonation conditions.

The oxiranes, *trans*-2,3-dimethoxy-2,3-di(4-methoxyphenyl)oxirane (*trans*-**10d**) and *trans*-2,3-dimethoxy-2,3-di(4-nitrophenyl)oxirane (*trans*-**10e**), were identified by comparing the ^{1}H NMR spectra of the ozonation reaction mixtures with those of the standard samples prepared by epoxidation of *E*-**8d** or *E*-**8e** with the dioxirane **13a**. Signals at δ 3.22 and δ 3.29 were assigned to the oxirane ring methoxy groups of *trans*-**10d** and *trans*-**10e**, respectively. The dioxetane, *trans*-2,3-dimethoxy-2,3-di(4-methoxyphenyl)dioxetane (*trans*-**11d**) was identified by comparing the ^{1}H NMR spectrum of the ozonation reaction mixture with that of an authentic sample prepared by singlet oxygen oxidation of *E*-**8d**. A signal at δ 3.06 was assigned to the dioxetane ring methoxy groups of **11d**. Methoxy(4-methoxyphenyl)dioxirane **13d** was identified by adding cyclohexene to the reaction mixture prepared by the inverse ozonation of *E*-**8d**. Cyclohexene was epoxidized and a ^{1}H NMR signal of the original reaction mixture at δ 3.44 disappeared. This signal was then assigned to the dioxirane ring methoxy group of **13d**. Methoxy(4-nitrophenyl)dioxirane **13e** was identified

in the same way. The methoxy group of **13e** gives a singlet at δ 3.52.

3. Electronic effects on the product formation

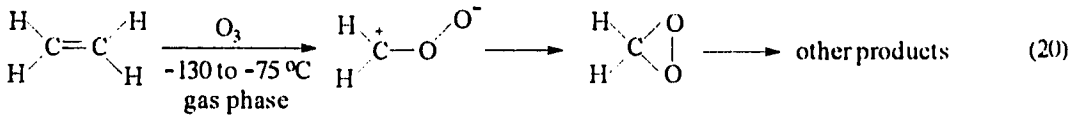
The results in Table 7 show that relatively higher yields of the dioxirane **13e** are obtained from the ozonation of *E*-**8e** under both the normal and inverse ozonation conditions. Compared with *E*-**8a**, *E*-**8e** is a less electron-rich alkene because of the presence of the electron-withdrawing nitro groups in the phenyl rings. Therefore *E*-**8e** must be less reactive toward dioxiranes than *E*-**8a** since dioxiranes are electrophilic agents.[30] Thus the presence of **13e** in the reaction mixtures of the normal ozonation of *E*-**8e** can be attributed to the slow reaction of *E*-**8e** with **13e** due to the electronic effects. In the ozonation mechanism proposed for *E*-**8a**, the oxirane *trans*-**10a** is produced from two pathways, i.e., direct ozone epoxidation pathway and the indirect dioxirane epoxidation pathway. The fact that the yield of the oxirane *trans*-**10e** is lower than those of *trans*-**10a** or *trans*-**10d** is consistent with this mechanism as the reaction between the dioxirane **13e** and the alkene *E*-**8e** does not occur readily. The presence of the nitro groups in the benzene rings of *E*-**8e** can also account for the absence of dioxetane **11e**. The electron-withdrawing nitro groups reduce the reactivity of *E*-**8e** toward singlet oxygen.

Due to different reactivities of the three alkenes investigated and probably different amounts of the three corresponding carbonyl oxides generated during the ozonation, it is hard to discuss the electronic effects of the substituents on the cyclization tendency of the (methoxy)arylcarbonyl oxides from the yields of the corresponding dioxiranes. Nevertheless, like the ozonation of *E*-**8c**, the ozonation of *E*-**8e** also provides strong support for the proposed mechanism.

D. More discussion of (alkoxy)aryldioxiranes

1. Formation of dioxiranes

Dioxiranes are cyclic isomers of carbonyl oxides.[30] The possibility of isomerization of carbonyl oxides to dioxiranes has been an interesting topic for a long time. As early as in 1905, dioxiranes have been considered as possible intermediates in the ozonolysis of alkenes.[53] In 1977, Lovas and Suenram rigorously established that the simplest parent dioxirane is an intermediate in the low temperature (−130 to −75 °C), gas-phase ozonolysis of ethene, eq 20.[54]



(20)

In solution-phase ozonolysis reactions, however, before the discovery in this study, no conclusive evidence had been obtained for the intermediacy of dioxiranes in the ozonolysis of alkenes. In some cases, dioxiranes have been proposed as intermediates in the ozonation of certain alkynes and alkenes,[55] but there was no strong support.

(In a recent publication Murray and co-workers claimed that ozonolysis of 2,3-dimethyl-2-butene **5** produced tetramethyloxirane **6** and the allylic hydroperoxide **7**.[18(a)] To account for the formation of these products, these authors suggested that dimethyldioxirane and singlet oxygen are the reaction intermediates. However, these authors were not able to provide convincing evidence to support their suggestions. A more detailed discussion

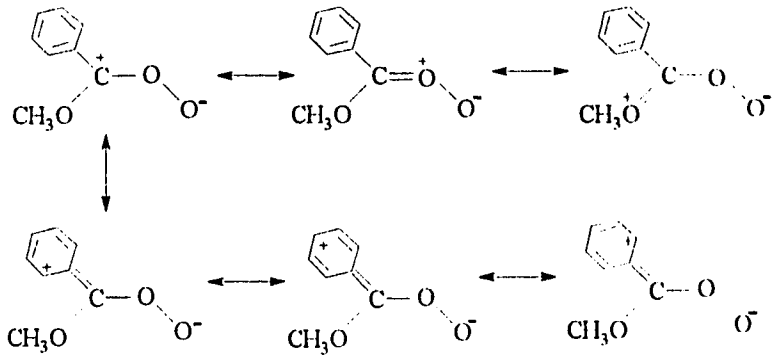
of this subject is included in the appendix of this dissertation.)

A preliminary publication of this study[32] reported for the first time that (methoxy)phenyldioxirane **13a** can be obtained as one of the reaction products from the ozonation of 1,2-dimethoxy-1,2-diphenylethene **8a**. Further studies revealed that all of the (alkoxy)arylcarbonyl oxides studied are able to cyclize to the corresponding dioxiranes. Since only ordinary ozonation conditions are employed in this study, the (alkoxy)arylcarbonyl oxides **14a-e** must have some intrinsic properties. As already mentioned, unlike other carbonyl oxides, **14a** could not be trapped by methanol. Moreover, no oligomer of **14a** is formed although the dimers of **14a** can be formed in significant amounts in the ozonation of **8a**. Unveiling these mysterious properties would be very interesting in both ozonation and dioxirane chemistry.

The conversion of dioxymethyl ($H_2C^+OO^-$) to the parent dioxirane has received extensive computational studies.[42] According to Cremer's ab initio calculations,[56] this conversion is exothermic by 31.3 kcal/mol, and has an activation barrier of 22.8 kcal/mol. This means that isomerization of carbonyl oxides to dioxiranes is thermodynamically favorable, but involves a substantial activation barrier. Ozonolysis of alkenes produces carbonyl oxides with considerable excess energy. If this internal energy is not dissipated efficiently, such as in the gas phase and at low temperature, a vibrationally excited carbonyl oxide may isomerize to the dioxirane. Generally, in solution this internal energy is efficiently dissipated through collisional deactivation between the carbonyl oxide and the solvent. Therefore for thermally equilibrated dioxymethyl in solution, the activation barrier of the isomerization to dioxirane seems to prevent this isomerization to be competitive with other bimolecular processes.[42]

Since the cyclization of the (alkoxy)arylcarbonyl oxides **14a-e** do occur, it means that the activation barriers of isomerization of **14a-e** to **13a-e** would be lower than that of dioxymethyl. Unfortunately, at present the activation barriers are not available.

It is worth noting that compared with other carbonyl oxides, **14a-e** have



Scheme 12. Resonance forms of (methoxy)phenylcarbonyl oxide

more resonance forms and the positive charge is highly delocalized as shown in Scheme 12 for **14a**. It is therefore possible that the aryl and alkoxy substitutes stabilize the carbonyl oxides and provide more chance for them to cyclize to the dioxiranes.

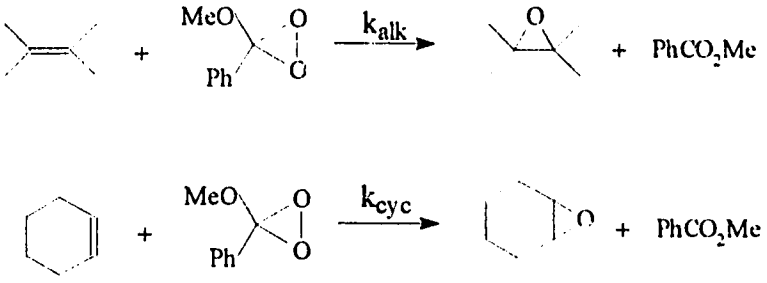
Although carbonyl oxides are usually represented as zwitterions, high-level computational methods consistently demonstrate that the carbonyl oxides are more properly represented by a singlet diradical ground state.[42] It has been realized that a singlet diradical can have a spectrum of character ranging from a pure diradical to a zwitterion[42,57] and, thus, react in the form best suited for the experimental conditions. The current view of the carbonyl oxide favors that the electronic structure of the carbonyl oxide is best represented as a superposition of diradical and zwitterionic states,

presumably the former dominates.[42] It is therefore possible that the electronic configurations of the carbonyl oxides with alkoxy and aryl substituents are more complex than the simple zwitterionic forms. Probably the special properties of **14a-e** are because they have special electronic configurations. To give a satisfactory answer to these questions, more studies, such as computational studies, are needed. But it is not within the scope of this investigation.

2. Rate studies on epoxidation by the dioxiranes

a) Relative rate studies

Until now all of the dioxiranes discovered in this study have not been isolated from the reaction mixtures, therefore a comprehensive study of the chemistry of these interesting oxidants is largely restricted. Even so, with the use of ^{1}H NMR spectroscopy rate studies on the epoxidation by **13a** or **13c** still can be achieved. The relative reactivities of various alkenes to **13a** at –78 °C were determined by competitive epoxidation between an alkene and cyclohexene. The experiments were carried out by addition of a CD_2Cl_2 solution containing equimolar amounts of cyclohexene and an alkene to a vigorously stirred CD_2Cl_2 solution containing less than the stoichiometric amount of **13a** in a small round-bottom flask which was immersed in a dry ice-acetone bath. After about 30 minutes, the reaction mixtures were analyzed with ^{1}H NMR spectroscopy at room temperature. The reaction was finished within a few minutes as indicated by the disappearance of the yellow color of the dioxirane. By a simple analysis, the relative rate constants (k_{alk}/k_{cyc}) were determined from the percentages of the remaining alkenes as shown in Scheme 13.



$$-\frac{d[\text{alkene}]}{dt} = k_{alk}[\text{alkene}][\text{dioxirane}]$$

$$-\frac{d[\text{cyclohexene}]}{dt} = k_{cyc}[\text{cyclohexene}][\text{dioxirane}]$$

$$\frac{k_{alk}}{k_{cyc}} = \frac{\ln \frac{[\text{alkene}]_f}{[\text{alkene}]_i}}{\ln \frac{[\text{cyclohexene}]_f}{[\text{cyclohexene}]_i}} = \frac{\ln(\%\text{ of unreacted alkene} / 100)}{\ln(\%\text{ of unreacted cyclohexene} / 100)}$$

Scheme 13. Determination of relative rate constants

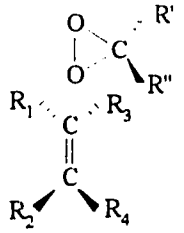
The results (Table 8) indicate that (methoxy)phenyldioxirane **13a**, like dimethyldioxirane,[58] is an electrophilic reagent. The lower reactivity of the crotonate or cinnamate and complete lack of reactivities of the fumarate and maleate toward **13a** are consistent with the electron-deficient characters of these alkenes. It was observed that *Z*-**8a** is more reactive than *E*-**8a** toward **13a**. This could be one of the reasons that the yield of the dioxirane **13a** is lower from the inverse ozonation of *Z*-**8a** than from *E*-**8a**. *Z*-2-Butene is also more reactive than *E*-2-butene. It has been shown that *Z*-alkenes are more reactive than their *E*-counterparts toward dimethyldioxirane.[59] For example, *Z*-3-methyl-3-hexene is 1.5 times as reactive as its *E*-isomer. A spiro

Table 8. Relative reactivities of competitive epoxidation of various alkenes and cyclohexene with (methoxy)phenyldioxirane **13a** in CD_2Cl_2[a]

Alkene	% of unreacted		k_{alk} / k_{cyc}
	alkene	cyclohexene	
2,3-dimethyl-2-butene	21	83	8.4
***Z*-8a**	17	78	7.1
***E*-8a**	28	76	4.6
1-methylcyclohexene	43	70	2.4
Z-2-butene	38	51	1.4
E-2-butene	42	46	1.1
cyclohexene	—	—	1.0
methyl *E*-cinnamate	92	25	0.06
methyl *E*-crotonate	96	23	0.03
diethyl fumarate	100	43	0.00
dimethyl maleate	100	65	0.00

[a]. Reaction Temp. −78 °C, time 30 minutes. Single experiment for each alkene.

transition state has been proposed to explain these rate differences. Such a transition state would permit a less hindered approach of dioxiranes to *Z*-alkenes. Epoxidation by the dioxirane **13a** might also proceed via such a spiro transition state.



b) Absolute rate studies

The absolute rate of epoxidation of methyl *E*-cinnamate by **13a** was determined. A CD_2Cl_2 solution containing **13a** in a NMR tube was prepared by the inverse ozonation of 5 mg of ***E*-8a** at −20 °C. The concentration of

13a was determined by using a known amount of toluene as an internal standard. Approximately an equivalent amount of methyl *E*-cinnamate was injected into the NMR tube at −78 °C. The resulting solution was shaken vigorously at −78 °C and immediately placed into a NMR probe which was precooled to the desired temperature. The consumption of the alkene and **13a** and the formation of the corresponding oxirane and methyl benzoate with time were monitored by ^{1}H NMR. Treatment of the data obtained gave the second-order rate constants k_2. The k_2 determined for the epoxidation of methyl *E*-cinnamate by **13a** at −20 and at −40 °C were 2.82×10^{-2} (Table 9 and Figure 6) and 0.59×10^{-2} M^{-1}sec^{-1} (Table 10 and Figure 7), respectively. Accordingly, the Arrhenius activation energy was calculated, E_a = 9.2 kcal mol^{-1}. Murray and co-workers had earlier determined the activation energy for the epoxidation of ethyl *E*-cinnamate by dimethyldioxirane, E_a = 14.1 kcal mol^{-1}.[58] Epoxidation of methyl *E*-cinnamate was expected to be similar to that of ethyl *E*-cinnamate. Therefore, (methoxy)phenyldioxirane **13a** is a more reactive dioxirane than dimethyldioxirane.

The epoxidation of *E*- or *Z*-**8a** by **13a** is a very rapid reaction. Even at −78 °C it was still impossible to monitor the reaction process with ^{1}H NMR. The epoxidation of *E*-**8c** by **13c**, on the other hand, is much slower and can be easily monitored with ^{1}H NMR. In the same way as above, the second-order rate constants for the epoxidation of *E*-**8c** by **13c** at −20 and −40 °C in CD_2Cl_2 were found to be 12.27×10^{-2} (Table 11 and Figure 8) and 1.86×10^{-2} M^{-1}sec^{-1} (Table 12 and Figure 9), respectively. The Arrhenius activation energy was therefore determined, E_a = 11.0 kcal mol^{-1}.

The second-order rate constants for the epoxidation of methyl *E*-crotonate by (methoxy)phenyldioxirane **13a**, methoxy(4-methoxy)phenyldioxirane **13d**, and methoxy(4-nitrophenyl)dioxirane **13e** at

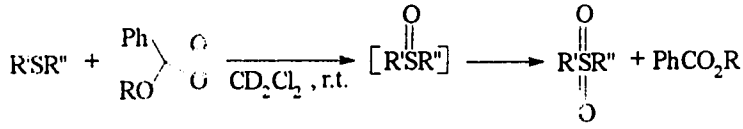
–20 °C were determined to be 0.82×10^{-2} (Table 13 and Figure 10), 0.72×10^{-2} (Table 14 and Figure 11), and 5.38×10^{-2} $M^{-1}sec^{-1}$ (Table 15 and Figure 12), respectively. The electron-withdrawing substituent NO_2 accelerates the reaction while the electron-donating substituent OCH_3 decelerates the reaction. This result is consistent with the report that dioxiranes are electrophilic oxidizing agents.[30] The electron-withdrawing substituents enhance the electrophilicity of the dioxirane; and the electron-donating substituents have the opposite effect.

3. Other reactions of the dioxiranes

Like other dioxiranes, the (alkoxy)aryldioxiranes can effectively perform other oxygen transfer reactions besides the epoxidation reaction. Two of these reactions observed are listed below. The reaction products were identified by comparison of the ^1H NMR spectra of the reaction mixtures with those of authentic samples.

a) Oxidation of sulfur compounds

Dioxiranes are strong oxidation agents toward sulfur compounds.[30] It was observed that the dioxiranes **13a** and **13c** rapidly oxidize dimethyl sulfide and methyl phenyl sulfide to the corresponding sulfones probably via the sulfoxides, eq 21.



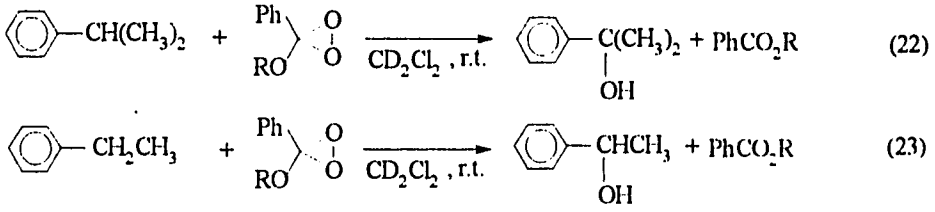
(21)

R', R"= CH_3 , Ph R= CH_3 , $CH(CH_3)_2$

b) Reaction with saturated hydrocarbons

The dioxiranes **13a** and **13c** are able to oxidize cumene to 2-phenyl-2-propanol and ethylbenzene to α-methylbenzyl alcohol at room temperature,

eq 22 and eq 23, but toluene is inert to **13a** or **13c**. In both cases an O atom only inserts into the benzilic C—H bond. At room temperature, the reaction between **13a** and cumene needed about half an hour to accomplish, much longer than the epoxidation reactions described above. It took several hours for the reaction between **13a** and ethylbenzene and during that period some of **13a** decomposed. Similar relative reactivities of insertion by dimethyldioxirane of these three hydrocarbons have been observed.[60]



E. Conclusion

This study has shown for the first time that carbonyl oxides with alkoxy and aryl substituents generated from the ozonation of 1,2-dialkoxy-1,2-diarylethenes **8a-e** in solution are able to cyclize to the corresponding dioxiranes. Depending on reaction conditions and the starting alkenes, the dioxiranes produced can undergo further reaction with the alkenes or exist as one of the final products.

Unlike in the ozonation of tetramethoxyethene **1**, no evidence was found for the presence of a radical chain reaction in the ozonation of 1,2-dialkoxy-1,2-diarylethenes studied. A mechanism combining two initial reaction pathways between ozone and the alkenes was suggested to account for the product formation and the stoichiometries of the ozonation reactions.

According to this mechanism, the oxiranes arise from the reaction of the alkenes with ozone as well as from the reaction of the alkenes with the ozonation reaction intermediate dioxiranes.

The reactions between the alkenes and the dioxiranes are controlled by steric effects as well as electronic effects of the substituents on the alkenes. Both the bulky vinyl alkoxy group and the electron-withdrawing substituent of the phenyl ring can reduce the reaction rates between the alkenes and the dioxiranes.

(Methoxy)phenyldioxirane **13a** shows higher reactivity than dimethyldioxirane and therefore has a potential to be a useful oxidizing agent.

F. Experimental

Melting points were determined using an Electrohome apparatus. NMR spectra were recorded on Brucker WH-200 and Brucker WH-300 spectrometers. High resolution electron impact ionization mass spectra (EIMS) were recorded on an Associated Electrical Industries (AEI) MS-50 spectrometer. Chemical ionization mass spectra (CIMS) were recorded on an Associated Electrical Industries (AEI) MS-12 spectrometer using ammonia as the carrier gas. IR spectra were recorded on a NICOLET 750 MAGNA FTIR spectrophotometer as KBr pellets or thin films. Analytical thin layer chromatography was performed on silica-coated plastic plates (Silica gel 60 F-254, Merck) and visualized under ultraviolet light. Preparative separations were performed by preparative thin layer chromatography or flash chromatography on silica gel[61] (Merck, 230-400 mesh). Tetrahydrofuran was dried by distillation from sodium-benzophenone ketyl. 2,3-Dimethyl-2-butene

5 was purified by preparative GLC. (Column 10% SE-30 on 60/80 chromosorb W, injector 170 °C, detector 120 °C, column 80 °C, retention time 20 min.) before use. ^{1}H NMR analysis of purified **5** indicated that no tetramethyloxirane **6** or allylic hydroperoxide **7** was present. All other solvents were reagent grade and were used as received. In the following preparations, no attempt was made to optimize the yields.

1. Synthesis of the starting alkenes

*a) Synthesis of E- and Z-1,2-dimethoxy-1,2-diphenylethene (E- and Z-**8a**)*

The procedure of the synthesis was similar to that described.[24] To a solution of benzoin (4.24 g, 20 mmol) and methyl *p*-toluenesulfonate (7.5 g, 40 mmol) in THF (150 mL) was added with stirring finely ground sodium hydroxide (2.0 g, 50 mmol) under argon. The reaction mixture was heated under reflux for 10 hours. When the ground sodium hydroxide was poured into the solution, the reaction mixture turned viscous and dull green immediately and then gradually pale yellow during reflux. Most of the solvent was removed with a rotary evaporator and the viscous residue was poured into water (300 mL) and extracted with benzene (100 mL × 3). The combined benzene layer was washed with water, saturated sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and a pale yellow solid was obtained. Recrystallization from methanol afforded a mixture (2.4 g, 50.0% total yield) of *E*- and *Z*-**8a**. The isomers were separated by flash column chromatography on silica gel with 5% ethyl acetate in hexane as eluent. Recrystallization from methanol gave 1.0 g of *E*-**8a** (20.8%) and 1.2 g of Z-**8a** (25.0%).

***E*-1,2-Dimethoxy-1,2-diphenylethene (*E*-8a)**: mp 95.5-96.5 °C (methanol) (Lit.[62] mp 97-98 °C); ^{1}H NMR ($CDCl_3$, TMS): δ 3.38 (s, 6 H,

OCH_3), 7.25-7.48 (m, 6 H, Ar), 7.60-7.70 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$): δ 58.74 128.09, 128.49, 128.67, 134.60, 145.51; FTIR: 1596 cm^{-1} (weak intensity, C=C); Exact mass calcd for $C_{16}H_{16}O_2$: 240.1150. EIMS *m/e*: 240.1146 (M^+).

Z-1,2-Dimethoxy-1,2-diphenylethene (Z-8a): mp 124.5-125.5 °C (methanol) (Lit.[62] mp 125.5-126.5 °C); ^1H NMR ($CDCl_3$, TMS): δ 3.59 (s, 6 H, OCH_3), 7.17 (s, 10 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 58.60 127.86, 128.26, 130.25, 135.46, 143.74; FTIR: 1633 cm^{-1} (medium intensity, C=C); Exact mass calcd for $C_{16}H_{16}O_2$: 240.1150. EIMS *m/e*: 240.1152 (M^+).

*b) Synthesis of E- and Z-1,2-diethoxy-1,2-diphenylethene (E- and Z-**8b**) and E- and Z-1,2-diisopropoxy-1,2-diphenylethene (E- and Z-**8c**)*

Ethyl *p*-toluenesulfonate is commercially available and isopropyl *p*-toluenesulfonate was prepared according to the procedure described.[63]

Pyridine (100 mL) was added dropwise to a mixture of *p*-toluenesulfonyl chloride (70 g, 0.37 mol) and 2-propanol (24 g, 0.40 mol) in an ice-water bath. The reaction mixture was kept stirring at 0–5 °C for two hours. Crushed ice (200 g) was added to the mixture followed by cold dilute HCl until the aqueous layer became strongly acidic. The mixture was then extracted with ether (150 mL × 3) and the combined ethereal layer was washed with water, 5 % sodium bicarbonate, water, brine and dried over anhydrous sodium sulfate. After evaporation of the solvent, the crude product (75 g, 95 %) was obtained which was directly used in the next step without further purification.

Isopropyl *p*-toluenesulfonate ^1H NMR ($CDCl_3$, TMS): δ 1.65 (d, J = 6.1 Hz, 6 H, CH_3), 2.45 (s, 3 H, CH_3), 4.73 (septet, J = 6.1 Hz, 1 H, CH), 7.33 (pseudo d, J = 7.9 Hz, 2 H, Ar), 7.79 (pseudo d, J = 7.9 Hz, 2 H, Ar).

The procedure for synthesis of **8b** and **8c** was the same as that of **8a**

except that the base used was potassium hydroxide. Recrystallization from methanol afforded only the *E*-isomers. The yield of *E*-**8b** was 20% and the yield of *E*-**8c** was 16%.

***E*-1,2-Diethoxy-1,2-diphenylethene (*E*-8b):** mp 57.0-58.0 °C (methanol); ^{1}H NMR ($CDCl_3$, TMS): δ 1.13 (t, J = 6.9 Hz, 6 H, CH_3), 3.53 (q, J = 6.9 Hz, 4 H, CH_2), 7.21-7.46 (m, 6 H, Ar), 7.48-7.70 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 15.22, 66.36, 127.47, 127.92, 128.33, 134.75, 144.20; FTIR ($CHCl_3$): 1600 cm^{-1} (medium intensity, C=C); Exact mass calcd for $C_{18}H_{20}O_2$: 268.1463. EIMS *m/e*: 268.1454 (M^+); Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H 7.51. Found: C, 80.64; H, 7.51.

***E*-1,2-Diisopropoxy-1,2-diphenylethene (*E*-8c):** mp 100.5-101.5 °C (methanol); ^{1}H NMR ($CDCl_3$, TMS): δ 0.98 (d, J = 6.0 Hz, 12 H, CH_3), 3.70 (septet, J = 6.0 Hz, 2 H,), 7.20-7.42 (m, 6 H), 7.76-7.83 (m, 4 H); ^{13}C NMR ($CDCl_3$, TMS): δ 22.22, 71.92, 127.11, 127.55, 129.09, 135.20, 143.10; FTIR ($CHCl_3$): 1598.5 cm^{-1} (medium intensity, C=C); Exact mass calcd for $C_{20}H_{24}O_2$: 296.1776. EIMS *m/e*: 296.1778 (M^+); Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.03; H 8.17. Found: C, 81.10; H, 8.30.

The two *Z*-isomers were obtained by photoisomerization of the corresponding *E*-isomers. The procedure is illustrated by the preparation of *Z*-**8b** below.

A 10 mL CH_2Cl_2 solution of *E*-**8b** (0.5 g) in a large size NMR tube was irradiated with a HANOVIA medium pressure mercury lamp at room temperature for two hours. The solvent was evaporated and the residue was dissolved in methanol. Part of the *E*-isomer crystallized upon cooling the mixture in an ice-water bath and the crystal was removed by filtration. Therefore the content of the *Z*-isomer which remained in the filtrate was enriched. The *Z*-**8b** (0.07 g, 14%) was isolated from the filtrate by flash

column chromatography on silica gel with 5% ethyl acetate in hexane as eluent and recrystallized from methanol.

In the same way, *Z*-**8c** (0.11 g, 22%) was obtained from *E*-**8c** (0.5 g).

In both cases the elemental analyses was not determined due to lack of enough sample.

***Z*-1,2-Diethoxy-1,2-diphenylethene (*Z*-8b):** mp 38.0-39.0 °C (methanol); ^{1}H NMR ($CDCl_3$, TMS): δ 1.27 (t, J = 7.0 Hz, 6 H, CH_3), 3.73 (q, J = 7.0 Hz, 4 H, CH_2), 7.14 (s, 10 H, Ar); ^{13}C NMR (CD_2Cl_2): δ 15.79, 66.32, 128.16, 136.16, 142.94. Exact mass calcd for $C_{18}H_{20}O_2$: 268.1463. EIMS *m/e*: 268.1453 (M^+).

***Z*-1,2-Diisopropoxy-1,2-diphenylethene (*Z*-8c):** mp 74.5-75.0 °C (methanol); ^{1}H NMR ($CDCl_3$, TMS): δ 1.21 (d, J = 6.0 Hz, 12 H, CH_3), 3.92 (septet, J = 6.0 Hz, 2 H, CH), 7.08-7.15 (m, 6 H, Ar). 7.15-7.20 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 22.70, 71.03, 127.11, 127.79, 129.98, 136.33, 142.24. Exact mass calcd for $C_{20}H_{24}O_2$: 296.1776. EIMS *m/e*: 296.1776 (M^+).

c) Synthesis of E- and Z-1,2-dimethoxy-1,2-bis(4-methoxyphenyl)ethene (E- and Z-8d)

A mixture of 4,4'-dimethoxybenzoin (2.72 g, 10 mmol), methyl *p*-toluenesulfonate (3.8 g, 40 mmol) and finely ground sodium hydroxide (1.0 g, 25 mmol) in 150 mL of THF was heated under reflux with stirring for 15 hours under nitrogen. The mixture was poured into water and extracted with benzene (3 × 50 mL). The combined extracts were washed with water, brine and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the oily residue was crystallized from methanol. Recrystallization from methanol afforded 0.8 g (26.7%) of *E*-**8d** as light yellow needles. The solvent of the mother liquor was evaporated and the

residue which contained mainly *Z*-**8d** was chromatographed on silica gel with 10% ethyl acetate in hexane as eluent to give *Z*-**8d** (0.4 g, 13%) as light yellow needles.

***E*-1,2-Dimethoxy-1,2-bis(4-methoxyphenyl)ethene (*E*-8d):** mp 118.0-119.0 °C (methanol); ^{1}H NMR (CD_2Cl_2): δ 3.35 (s, 6 H, OCH_3), 3.83 (s, 6 H, OCH_3), 7.30 (m, 4 H, Ar), 7.58 (m, 4 H, Ar); ^{13}C NMR (CD_2Cl_2): δ 55.63, 58.55, 113.89, 127.16, 129.85, 144.54, 159.50; FTIR ($CHCl_3$): 1609 cm^{-1} (medium intensity, C=C); Exact mass calcd for $C_{18}H_{20}O_4$: 300.1362. EIMS *m/e*: 300.1361 (M^+); Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.97; H, 6.72. Found: C, 71.60; H, 6.74.

***Z*-1,2-Dimethoxy-1,2-bis(4-methoxyphenyl)ethene (*Z*-8d):** mp 43.0-44.0 °C (methanol); ^{1}H NMR (CD_2Cl_2): δ 3.55 (s, 6 H, OCH_3), 3.75 (s, 6 H, OCH_3), 6.72 (m, 4 H, Ar), 7.09 (m, 4 H, Ar); Exact mass calcd for $C_{18}H_{20}O_4$: 300.1362. EIMS *m/e*: 300.1361 (M^+); Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.97; H, 6.72. Found: C, 71.68; H, 6.83.

*d) Synthesis of E- and Z-1,2-dimethoxy-1,2-bis(4-nitrophenyl)ethene (E- and Z-**8e**)*

2-Methoxy-1,2-bis(4-nitrophenyl)ethanol A few drops of concentrated sulfuric acid were added to a suspension of *cis*-4,4'-dinitrostilbene oxide[64] (2.89 g, 10 mmol) in anhydrous methanol (150 mL) and the mixture was stirred and heated under reflux for 30 hours. During this time, the reaction mixture became a clear yellow solution. The methanol was removed under reduced pressure and an orange solid was obtained. Recrystallization of the solid from ethanol gave a yellow powder (3.0 g, 94%), mp 124-136 °C. The broad range of the melting point indicated that it was a mixture of *threo* and *erythro* α-methoxy alcohols. (Lit.[65] mp *threo* 182 °C, *erythro* 154 °C). ^{1}H NMR ($CDCl_3$, TMS): δ 3.01 (b, 1 H, OH), 3.35 (s,

3 H, OCH_3), 4.25 (d, J = 7.8 Hz, 1 H, CHO), 4.79 (d, J = 7.8 Hz, 1 H, CHO), 7.16-7.28 (m, 4 H, Ar), 8.02-8.14 (m, 4 H, Ar).

2-Methoxy-1,2-bis(4-nitrophenyl)ethanone Jones' reagent was added dropwise to 50 mL of a vigorously stirred acetone solution of the α-methoxy alcohol (3.0 g, 9.4 mmol) in an ice-water bath until the brown color of the oxidizing agent no longer disappeared. After stirring at room temperature for another three hours, the excess oxidizing agent was destroyed by sodium sulfite. The top acetone layer of the resulting reaction mixture was decanted into water and the aqueous mixture was extracted with ether (100 mL × 3). The combined extract was washed with water, brine, and dried over anhydrous sodium sulfate. The ether was evaporated and the yellow residue was crystallized from methanol to give the α-methoxy ketone (2.2 g, 74%) as a yellow solid, mp 130-132 °C (Lit.[65] mp 136 °C); ^{1}H NMR ($CDCl_3$, TMS): δ 3.54 (s, 3 H, OCH_3), 5.45 (s, 1 H, HCO), 7.66 (m, 2 H, Ar), 8.12-8.32 (m, 6 H, Ar).

***E*- and *Z*-1,2-Dimethoxy-1,2-bis(4-nitrophenyl)ethene (*E*- and *Z*-8e)** Sodium hydride (0.24 g, 10 mmol) was added to a stirring solution of the above prepared α-methoxy ketone (2.2 g, 7 mmol) and methyl *p*-toluenesulfonate (1.86 g, 10 mmol) in THF (100 mL) under nitrogen at room temperature. The mixture was stirred and heated under reflux overnight. After work-up as in the preparation of **8a**, a dark oily residue with some brown powder was obtained. Fractional crystallization from methanol gave two fractions. The first one was purified by recrystallization from methanol to give *E*-**8e** (0.7 g, 30%) as a yellow powder. The second fraction which contained mainly the *Z*-isomer was purified by chromatography on silica gel with 10% ethyl acetate in hexane as eluent to give *Z*-**8e** (0.5 g, 22%) as a yellow powder.

***E*-1,2-Dimethoxy-1,2-bis(4-nitrophenyl)ethene (*E*-8e)**: mp 220.5-222.0 °C (methanol); ^{1}H NMR (CD_2Cl_2): δ 3.42 (s, 6 H, OCH_3), 7.92(d, J = 9.2 Hz, 4 H, Ar), 8.27 (d, J = 9.2 Hz, 4 H, Ar). ^{13}C NMR (CD_2Cl_2): δ 59.40, 123.84, 129.55, 140.43, 146.38, 147.64; FTIR ($CHCl_3$): 1589 cm^{-1} (medium intensity, C=C); Exact mass calcd for $C_{16}H_{14}N_2O_6$: 330.0851. EIMS *m/e*: 330.0846 (M^+); Anal. Calcd for $C_{16}H_{14}N_2O_6$: C, 58.18; H, 4.27; N, 8.48. Found: C, 58.11; H, 4.29; N, 8.42.

***Z*-1,2-Dimethoxy-1,2-bis(4-nitrophenyl)ethene (*Z*-8e)**: mp 201-204 °C (methanol); ^{1}H NMR (CD_2Cl_2): δ 3.69 (s, 6 H, OCH_3), 7.34 (d, J = 9.2 Hz, 4 H, Ar), 8.04 (d, J = 9.2 Hz, 4 H, Ar); Exact mass calcd for $C_{16}H_{14}N_2O_6$: 330.0851. EIMS *m/e*: 330.0844 (M^+); Anal. Calcd for $C_{16}H_{14}N_2O_6$: C, 58.18; H, 4.27; N, 8.48. Found: C, 58.10; H, 4.32; N, 8.40.

2. Ozonation of the alkenes

Ozone (approximately 2% v/v or 1 × 10^{-6} mol/mL) in oxygen was generated in a WELSBACH laboratory ozonizer and was taken up from the effluent stream of the ozonizer into a 100-mL gas syringe. The ozone-oxygen mixture can be stored in the syringe for several hours at room temperature with no loss in ozone content.[22] Small scale ozonation reactions were carried out in NMR tubes at various temperatures, from 0 to −78 °C, in an acetone bath. The reaction temperature given was that of the bath. All the NMR tubes used were freed of acid by soaking in ammonia solution overnight, draining, and drying at 140 °C. Syringes used to deliver solvent or ozone were similarly treated except that they were dried in the air. The reaction mixtures were analyzed by ^{1}H NMR spectroscopy at low temperature, in most cases at −20 °C. The NMR solvents were passed through a plug of powdered potassium carbonate and stored in a bottle which contained some powdered

potassium carbonate. A 0.5 *M* solution of sodium methoxide-D_3 was prepared by dissolving sodium metal in CD_3OD.

a) Normal ozonation

Typical conditions were as follows. The ozone-oxygen mixture stored in the syringe was delivered into a solution of the alkenes through a 1-mm Teflon tube that reached to the bottom of the NMR tube. The flow rate was approximately 20 mL/min. A piece of moistened potassium iodide starch test paper placed at the open end of the NMR tube was used as an indicator. In the cases of complete ozonation, the ozone was delivered into the solution of an alkene until the test paper became dark blue.

b) Inverse ozonation

Typical conditions were as follows. The ozone-oxygen mixture (100 mL, ~0.1 mmol) contained in a 100-mL syringe and 0.5 mL of solution of an alkene (about 5 mg of the alkene, ~0.02 mmol) contained in a 1-mL syringe were slowly injected at the same time through two fine Teflon tubes to the bottom of a NMR tube which was placed in a cooling bath. By this way, the concentration of ozone in the NMR tube was kept in excess over that of the alkene during the entire process. After finishing the injection, argon (40 mL) was slowly bubbled through the solution to expel the excess ozone while the NMR tube remained in the cooling bath. The samples prepared in this way are always light-yellow indicating the presence of dioxiranes.

c) Competitive ozonation of a mixture of two alkenes

A mixture of two alkenes, each approximately 0.05 *M*, in CD_2Cl_2 in a NMR tube was ozonized under the normal ozonation conditions at –78 °C with a limited amount of ozone. The resulting reaction mixture was analyzed by ^1H NMR spectroscopy at –20 °C and the relative reactivity of the alkenes toward ozone was calculated by the method described in Scheme 13.

d) Determination of product distributions from ^1H NMR spectra of the reaction mixtures

A typical example of calculation of product distribution from the integrals of ^1H NMR signals of each product is illustrated below. In one of the experiments, inverse ozonation of 5 mg of *E*-**8a** at −20 °C in CD_2Cl_2 gave four products. The ^1H NMR signals of CH_3O of these products are well separated and in this example the integrals are 84.98 (**9a**, one CH_3O), 68.64 (**13a**, one CH_3O), 40.44 (*trans*-**10a**, two CH_3O), and 3.23 (*trans*-**11a**, two CH_3O). The sum of the integrals is 197.27. All of these CH_3O groups are out of the CH_3O groups of the starting material *E*-**8a** which has two CH_3O groups. Therefore ozonation of each mole of *E*-**8a** produced 0.86 moles (84.98 × 2 / 197.27) of **9a**; 0.70 moles (68.64 × 2 / 197.27) of **13a**; 0.20 moles (40.44 / 197.27) of *trans*-**10a**; and 0.02 moles (3.23 / 197.27) of **11a**.

e) Determination of the stoichiometry of an ozonation reaction

The stoichiometry of an ozonation reaction was measured as follows. A known volume (usually 20.0 mL) of the ozone-oxygen mixture contained in a 100-mL syringe was delivered into excess 2,3-dimethyl-2-butene (2.5 μl) in 0.5 mL of CD_3OD at −78 °C. The reaction mixture was analyzed by ^1H NMR, measuring the integrals of the signals due to remaining 2,3-dimethyl-2-butene, acetone, and the dimethylcarbonyl oxide-CD_3OD adduct. A solution containing a known amount of an alkene (measured on a balance and transferred carefully into a NMR tube) was then treated with a limited amount of the calibrated ozone-oxygen mixture. The ozonation reaction mixture was then analyzed by ^1H NMR. The amount of the alkene consumed by the known amount of ozone was calculated from the integrals of the OCH_3 groups (for *E*- and *Z*-**8a**) or OCH groups (for *E*-**8c**) of the remaining alkenes and the products.

3. Singlet oxygen oxygenation of the alkenes

The authentic dioxetanes were prepared by photooxygenation of the corresponding alkenes.

*a) Preparation of trans- and cis-3,4-dimethoxy-3,4-diphenyl-1,2-dioxetane (trans- and cis-**11a**)*

A methanol/ether solution (5 mL, 1:1 mixture of the solvents) of *E*- or *Z*-**8a** (24 mg, 0.1 mmol) and 1 mg of Rose Bengal in a large size NMR tube was irradiated with a 200-W incandescent bulb while kept in an ice-water bath. A slow stream of oxygen was delivered into the solution through a fine Teflon tube that reached to the bottom of the NMR tube. The reaction was monitored with TLC until the spot due to the starting material disappeared. The solvent was evaporated under reduced pressure and the residue was subjected to preparative TLC with 10% ethyl acetate in hexane as eluent. The TLC plate was pretreated with 20% methanolic ammonia solution. The bands that contained the dioxetanes were cut off and the dioxetanes were extracted with 10 mL of CH_2Cl_2. The solvent was evaporated under reduced pressure and the residues were recrystallized from methanol to give the dioxetanes as white powders. The isolated yields of the dioxetanes *trans*- and *cis*-**11a** were 22% and 18%, respectively.

***trans*-3,4-Dimethoxy-3,4-diphenyl-1,2-dioxetane (*trans*-11a):** mp 58.0-60.5 °C (methanol) (Lit.[63] mp 59-61); ^{1}H NMR ($CDCl_3$, TMS): δ 3.06 (s, 6 H, OCH_3), 7.40-7.50 (m, 6 H, Ar), 7.54-7.60 (m, 4 H, Ar).

***cis*-3,4-Dimethoxy-3,4-diphenyl-1,2-dioxetane (*cis*-11a):** mp 66.5-68.0 °C (methanol) (Lit.[63] mp 67-68); ^{1}H NMR ($CDCl_3$, TMS): δ 3.36 (s, 6 H, OCH_3), 7.12-7.18 (m, 6 H, Ar), 7.30-7.36 (m, 4 H, Ar).

*b) Preparation of trans-3,4-diisopropoxy-3,4-diphenyl-1,2-dioxetane (trans-**11c**)*

A solution of (0.9 g, 3 mmol) *E*-**8c** in 50 mL CH_2Cl_2 that contained some Rose Bengal adsorbed on silica gel was vigorously stirred and irradiated with a 200-W incandescent bulb while kept in an ice-water bath. A slow stream of oxygen was bubbled through the mixtures. After 2 hours of irradiation the sensitizer was removed by filtration and the solvent was evaporated under reduced pressure. Recrystallization of the residue from methanol gave 0.5 g of *trans*-**11c** (50%) as white cubes.

***trans*-3,4-Diisopropoxy-3,4-diphenyl-1,2-dioxetane (*trans*-11c):** mp 81.0-82.0 °C (methanol); ^{1}H NMR (CD_2Cl_2): δ 0.82 (d, J = 6.1 Hz, 6 H, CH_3), 1.02 (d, J = 6.1 Hz, 6 H, CH_3), 3.70 (septet, J = 6.1 Hz, 2 H, OCH), 7.40-7.49 (m, 6 H, Ar), 7.55-7.64 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 23.59, 24.14, 68.50, 114.03, 128.13, 128.28, 129.30, 136.20. FTIR ($CHCl_3$): 1035 cm^{-1}; Exact mass calcd for $C_{20}H_{24}O_4$: 328.1674; CIMS *m/e*: 346 ($M + NH_4^+$).

c) Preparation of authentic samples of other dioxetanes

Small scale preparations of the other dioxetanes were carried out in NMR tubes and CD_2Cl_2 was used as the solvent. The procedure was similar to that of **11a**. No attempt was made to isolate the dioxetanes. After the reaction, the reaction mixture was filtered through a cotton plug into another NMR tube and analyzed with ^{1}H NMR at –20 °C.

The presence of the dioxetanes in the above reaction mixtures as well as in the ozonation reaction mixtures was evidenced by the observation of the luminescence of the hot reaction mixture containing 9,10-dibromo- and 9,10-bis(phenylethynyl)anthracene as fluorescers. The ^{1}H NMR signals that rapidly disappeared after addition of a trace of $CuCl_2$ dissolved in CD_3OD to the reaction mixtures were assigned to the dioxetanes. The signals of the aromatic protons could not be specified because they were superimposed

upon those of other compounds.

***cis*-3,4-Diethoxy-3,4-diphenyl-1,2-dioxetane (*cis*-11b):** ^{1}H NMR (CD_2Cl_2, –20 °C): δ 1.25 (t, J = 7.0 Hz, 6 H, CH_3), 3.58 (dq, 2 H, J = 9 and 7.5 Hz, OCH_2), 3.83 (dq, 2 H, J = 9 and 7.5 Hz, OCH_2), and signals of aromatic protons.

***trans*-3,4-Diethoxy-3,4-diphenyl-1,2-dioxetane (*trans*-11b):** ^{1}H NMR (CD_2Cl_2, –20 °C): δ 1.05 (t, J = 7.1 Hz, 6 H, CH_3), 3.17 (dq, 2 H, J = 9 and 7.5 Hz, OCH_2), 3.47 (dq, 2 H, J = 9 and 7.5 Hz, OCH_2), and signals of aromatic protons.

***cis*-3,4-Diisopropoxy-3,4-diphenyl-1,2-dioxetane (*cis*-11c):** ^{1}H NMR (CD_2Cl_2, –20 °C): δ 0.94 (d, J = 6.1 Hz, 6 H, CH_3), 1.19 (d, J = 6.1 Hz, 6 H, CH_3), 4.47 (septet, J = 6.1 Hz, 2 H, OCH), and signals of aromatic protons.

***trans*-3,4-Dimethoxy-3,4-bis(4-methoxyphenyl)-1,2-dioxetane (*trans*-11d):** ^{1}H NMR (CD_2Cl_2, –20 °C): δ 3.06 (s, 6 H, OCH_3), 3.84 (s, 6 H, $ArOCH_3$), and signals of aromatic protons.

d) Competitive singlet oxygen oxygenation of a mixture of two alkenes

A mixtures of two alkenes in a NMR tube, each approximately 0.02 *M*, in CD_2Cl_2 that contained some Rose Bengal adsorbed on silica gel was irradiated with a 200-W incandescent bulb while kept in an ice-water bath. A slow stream of oxygen was bubbled through the mixture. After approximately 0.5 hours of irradiation the sensitizer was removed by filtration. The resulting reaction mixture was analyzed by ^{1}H NMR and the relative reactivity of the alkenes toward singlet oxygen was calculated by the method described in Scheme 13.

4. Products isolated from the ozonation reaction mixtures

a) Benzoates

Ozonation of **8a-e** under any conditions always produced the corresponding benzoates which were isolated from the reaction mixtures by chromatography on silica gel with 10% ethyl acetate in hexane as eluent.

Methyl benzoate (9a): ^{1}H NMR ($CDCl_3$, TMS): δ 3.88 (s, 3 H, OCH_3), 7.38-7.62 (m, 3 H, Ar), 7.95-8.06 (m, 2 H, Ar).

Ethyl benzoate (9b): ^{1}H NMR ($CDCl_3$, TMS): δ 1.40 (t, J = 7.0 Hz, 3 H, CH_3), 4.31 (q, J = 7.0 Hz, 2 H, CH_2) 7.20-7.70 (m, 3 H, Ar), 7.90-8.10 (m, 2 H, Ar).

Isopropyl benzoate (9c): ^{1}H NMR ($CDCl_3$, TMS): δ 1.33 (d, J = 6.2 Hz, 6 H, CH_3), 5.18 (septet, J = 6.2 Hz, 1 H, CH), 7.40-7.70 (m, 3 H, Ar), 7.95-8.10 (m, 2 H, Ar); ^{13}C NMR (CD_2Cl_2): δ 22.08, 68.69, 128.66, 129.75, 131.53, 133.03, 166.24.

Methyl 4-methoxybenzoate (9d): mp 48-51 °C; ^{1}H NMR ($CDCl_3$, TMS): δ 3.82 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 6.91 (d, J = 8.8 Hz, 2 H, Ar), 7.95 (d, J = 8.8 Hz, 2 H, Ar).

Methyl 4-nitrobenzoate (9e): mp 94-96 °C; ^{1}H NMR ($CDCl_3$, TMS): δ 3.93 (s, 3 H, OCH_3), 8.14 (s, 4 H, Ar).

b) Isolation and preparation of 2,2-dimethoxy-1,2-diphenylethanone:

The title compound is the rearrangement product of *cis*- or *trans*-**10a**. Several small scale reaction mixtures of the normal ozonation of *E*-**8a** in CD_2Cl_2 at −20 °C were combined and the combined mixture was allowed to stand at room temperature overnight. The solvent was evaporated and the residue was chromatographed on silica gel with 20% ethyl acetate in hexane as eluent. The isolated product showed the same melting point and ^{1}H NMR absorptions as a sample prepared according to the authentic method[26] shown below.

To a mixture of benzil (4 g, 0.02 mol) and $Ba(OH)_2$ (20 g, 0.12 mol) in

60 mL of DMF was added CH_3I (10 mL, 0.16 mol). The reaction mixture was stirred for six hours at room temperature and was poured into 300 mL of water. The resulting mixture was extracted with ether (50 mL × 3). The combined extract was washed with water, brine, and dried over anhydrous sodium sulfate. The ether was evaporated and the yellow residue was crystallized from methanol to give the product (4.54 g, 93%) as a white solid.

2,2-Dimethoxy-1,2-diphenylethanone mp 67-70 °C (methanol) (Lit.[26] mp 68 °C); ^1H NMR ($CDCl_3$, TMS): δ 3.26 (s, 6 H, OCH_3), 7.20-7.92 (m, 8 H, Ar), 8.10-8.30 (m, 2 H, Ar).

c) Tetroxanes

(1) Isolation of *trans*- and *cis*-3,6-dimethoxy-3,6-diphenyl-1,2,4,5-tetroxane (*trans*- and *cis*-**12a**)

A mixture of *E*- and *Z*-**8a** (1.2 g) in 20 mL of CH_2Cl_2 was completely ozonized at −78 °C. The reaction mixture was allowed to stand at room temperature overnight and then the solvent was evaporated. The residue was dissolved in 20 mL of methanol and 20 mL of 1 *M* aqueous solution of KOH was added. The mixture was heated under reflux for 15 minutes and poured into 100 mL of water. The resulting mixture was extracted with CH_2Cl_2 (4 × 50 mL) and the combined CH_2Cl_2 solution was concentrated. Preparative thin layer chromatography of the residue (10 developments with 2% ethyl acetate in hexane) gave enough amounts of the tetroxanes *trans*- and *cis*-**12a** for characterization experiments (isolated yields were undetermined).

***cis*-3,6-Dimethoxy-3,6-diphenyl-1,2,4,5-tetroxane (*cis*-12a):** mp 113.0-114.0 °C (methanol); ^1H NMR ($CDCl_3$, TMS): δ 3.69 (s, 6 H, OCH_3), 7.28-7.40 (m, 6 H, Ar), 7.45-7.55 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 53.36, 117.15, 127.50, 128.69, 130.45, 132.60; Exact mass calcd for $C_{16}H_{16}O_6$: 304.0947. CIMS *m/e*: 305 ($M + H^+$), 322 ($M + NH_4^+$); Anal.

Calcd for $C_{16}H_{16}O_6$: C, 63.15; H 5.30. Found: C, 62.90; H, 5.37.

***trans*-3,6-Dimethoxy-3,6-diphenyl-1,2,4,5-tetroxane (*trans*-12a):** mp 145.0-146.0 °C (methanol); ^{1}H NMR ($CDCl_3$, TMS): δ 3.59 (s, 6 H, OCH_3), 7.40-7.52 (m, 6 H, Ar), 7.68-7.78 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 53.56, 117.15, 127.66, 128.76, 131.48, 131.57; IR (KBr): 1103, 1280 cm^{-1}; Exact mass calcd for $C_{16}H_{16}O_6$: 304.0947. CIMS *m/e*: 305 (M + H^+), 322 (M + NH_4^+); Anal. Calcd for $C_{16}H_{16}O_6$: C, 63.15; H 5.30. Found: C, 62.82; H, 5.39.

(2) Isolation of *trans*- and *cis*-3,6-diethoxy-3,6-diphenyl-1,2,4,5-tetroxane (*trans*- and *cis*-**12b**)

Similarly, a mixture of *E*- and *Z*-**8b** (1.5 g) in 20 mL of CH_2Cl_2 was completely ozonized at −78 °C. The reaction mixture was allowed to stand at room temperature in an unstoppered flask to let the solvent slowly evaporate. After about two days, the tetroxanes (*trans*- and *cis*-**12b**) were crystallized from the ozonation reaction mixture. The sticky residue was diluted with 5 mL of cold methanol and filtered to give the crystals of the tetroxanes. Recrystallization from methanol provided 0.06 g of a mixture of cis- and trans-tetroxanes. The separation of the cis and trans isomers was achieved by preparative TLC (six developments with 2% ethyl acetate in hexane).

***cis*-3,6-Diethoxy-3,6-diphenyl-1,2,4,5-tetroxane (*cis*-12b):** mp 140.0-141.0 °C (methanol); ^{1}H NMR ($CDCl_3$, TMS): δ 1.34 (t, J = 7.0 Hz, 6 H), 3.97 (q, J = 7.0 Hz, 4 H), 7.32-7.55 (m, 10 H, Ar); Exact mass calcd for $C_{18}H_{20}O_6$: 332.1260. CIMS *m/e*: 350 (M + NH_4^+). Anal. Calcd for $C_{18}H_{20}O_6$: C, 65.05; H, 6.07. Found: C, 65.10; H, 6.03.

***trans*-3,6-Diethoxy-3,6-diphenyl-1,2,4,5-tetroxane (*trans*-12b):** mp 145.0-147.0 °C (methanol); ^{1}H NMR ($CDCl_3$, TMS): δ 1.40 (t, J = 7.0 Hz, 6 H), 3.79 (q, J = 7.0 Hz, 4 H), 7.42-7.76 (m, 6 H, Ar), 7.65-7.75 (m, 4 H, Ar);

^{13}C NMR (CD_2Cl_2): δ 15.03, 61.76, 116.75, 127.75, 128.66, 131.29, 132.34. Exact mass calcd for $C_{18}H_{20}O_6$: 332.1260. CIMS *m/e*: 350 (M + NH_4^+). Anal. Calcd for $C_{18}H_{20}O_6$: C, 65.05; H, 6.07. Found: C, 65.03; H, 6.01.

(3) Isolation and identification of the cross tetroxane

A mixture of *E*-**8a** (0.24 g, 1 mmol) and cyclohexylidenecyclohexane (0.33 g, 2 mmol) dissolved in 50 mL of CH_2Cl_2 was completely ozonized at −60 °C. The reaction mixture was allowed to stand at room temperature overnight and then the solvent was evaporated. The residue was dissolved in 20 mL of methanol and 20 mL of 1 *M* aqueous solution of KOH was added. The mixture was heated to reflux for 20 min., poured into 200 mL of water, and extracted with CH_2Cl_2 (50 mL × 3). The cross tetroxane in the CH_2Cl_2 layer was isolated by preparative thin layer chromatography on SiO_2 (ten developments with 2% ethyl acetate in hexane). After recrystallization from methanol, 2 mg of the cross tetroxane was obtained.

3-Methoxy-3-phenyl-1,2,4,5-tetraoxaspiro[5.5]undecane ^1H NMR ($CDCl_3$, TMS): δ 1.4-1.9 (m, 6 H, CH_2), 2.32 (t, J = 7.8 Hz, 4 H, CH_2), 3.48 (s, 3 H, OCH_3), 7.42-7.49 (m, 3 H, Ar), 7.60-7.64 (m, 2 H, Ar); Exact mass calcd for $C_{14}H_{18}O_5$: 266.1154. CIMS *m/e*: 284 (M + NH_4^+).

5. Products present in the ozonation reaction mixtures at low temperature

The following products were unstable at room temperature and were not isolated from the ozonation reaction mixtures. Their identification was discussed in the discussion part. The signals of the aromatic protons of these products could not be assigned because they overlapped those of other products. The ^{13}C NMR signals of the dioxiranes and oxiranes were obtained

as follows. Inverse ozonation of a desired alkene in CD_2Cl_2 at –20 °C gave a mixture containing mainly corresponding benzoate, oxirane and dioxirane (from ^1H NMR). Several such prepared mixtures were combined and the combined mixture was concentrated by blowing nitrogen into the mixture at –40 °C to give a concentrated sample suitable for ^{13}C NMR spectroscopy. After a ^{13}C NMR spectrum was recorded, a suitable amount of the starting alkene was added to the above sample at –20 °C. A reaction between the dioxirane and the alkene gave the benzoate and the oxirane. The second ^{13}C NMR spectrum of this sample which now contained mainly the benzoate and the oxirane in a greater amount (from ^1H NMR) was recorded. The ^{13}C NMR spectrum of the benzoate was obtained independently. The signals that disappeared after the addition of the alkene were assigned to the dioxirane. The signals that increased in intensity (not these due to the benzoate) after the addition of the alkene were assigned to the oxirane. The ^1H NMR signals of the dioxiranes and the oxiranes were obtained in the same way except that the sample did not need to be concentrated.

***trans*-2,3-Dimethoxy-2,3-diphenyloxirane (*trans*-10a):** ^1H NMR (CD_2Cl_2, –20 °C): δ 3.24 (s, 3 H, OCH_3), and signals of aromatic protons; ^{13}C NMR (CD_2Cl_2, –20 °C): δ 52.73, 92.64, 128.11, 128.30, 128.96, 132.62.

***cis*-2,3-Dimethoxy-2,3-diphenyloxirane (*cis*-10a):** ^1H NMR (CD_2Cl_2, –20 °C): δ 3.29 (s, 3 H, OCH_3), and signals of aromatic protons; ^{13}C NMR (CD_2Cl_2, –20 °C): δ 53.36, 92.73, 127.99,128.48, 128.92, 132.30.

***trans*-2,3-Diethoxy-2,3-diphenyloxirane (*trans*-10b):** ^1H NMR (CD_2Cl_2, –20 °C): δ 1.08 (t, J = 6.2 Hz, 6 H, OCH_3), 3.48 (dq, 2 H, J = 8.9 and 7.6 Hz, OCH_2), 3.61 (dq, 2 H, J = 8.9 and 7.6 Hz, OCH_2), and signals of aromatic protons.

***cis*-2,3-Diethoxy-2,3-diphenyloxirane (*cis*-10b):** ^1H NMR (CD_2Cl_2, –20

°C): δ 1.18 (t, J = 7.0 Hz, 6 H, CH_3), 3.42 (dq, 2 H, J = 8.9 and 7.6 Hz, OCH_2), 3.61 (dq, 2 H, J = 8.9 and 7.6 Hz, OCH_2), and signals of aromatic protons.

***trans*-2,3-Diisopropoxy-2,3-diphenyloxirane (*trans*-10c):** ^1H NMR (CD_2Cl_2, –20 °C): δ 0.95 (d, J = 6.0 Hz, 6 H, CH_3), 1.16 (d, J = 6.0 Hz, 6 H, CH_3), 3.87 (septet, J = 6.0 Hz, 2 H, OCH), and signals of aromatic protons; ^{13}C NMR (CD_2Cl_2, –20 °C): δ 22.66, 23.05, 66.46, 91.06, 128.59,129.40, 130.63, 143.68.

***cis*-2,3-Diisopropoxy-2,3-diphenyloxirane (*cis*-10c):** ^1H NMR (CD_2Cl_2, –20 °C): δ 1.07 (d, J = 6.2 Hz, 6 H, CH_3), 1.24 (d, J = 6.2 Hz, 6 H, CH_3), 3.84 (septet, J = 6.2 Hz, 2 H, OCH) and signals of aromatic protons.

***trans*-2,3-Dimethoxy-2,3-bis(4-methoxyphenyl)oxirane (*trans*-10d):** ^1H NMR (CD_2Cl_2, –20 °C): δ 3.23 (s, 6 H, OCH_3), 3.82 (s, 6 H, OCH_3), 6.91 (d, J = 8.76 Hz, 4 H, Ar), 7.40 (d, J = 8.76 Hz, 4 H, Ar).

***trans*-2,3-Dinitro-2,3-bis(4-nitrophenyl)oxirane (*trans*-10e):** ^1H NMR (CD_2Cl_2, –20 °C): δ 3.32 (s, 6 H, OCH_3), and signals of aromatic protons.

(Methoxy)phenyldioxirane (13a): ^1H NMR (CD_2Cl_2, –20 °C): δ 3.50 (s, 3 H, OCH_3) and signals of aromatic protons. ^{13}C NMR (CD_2Cl_2, –20 °C): δ 50.11, 109.07, 127.21, 129.03, 130.84, 131.43.

(Ethoxy)phenyldioxirane (13b): ^1H NMR (CD_2Cl_2, –20 °C): δ 1.27 (t, J = 7.0 Hz, 3 H, CH_3), 3.79 (q, J = 7.0 Hz, 2 H, OCH_2) and signals of aromatic protons.

(Isopropoxy)phenyldioxirane (13c): ^1H NMR (CD_2Cl_2, –20 °C): δ 1.23 (d, J = 6.1 Hz, 6 H, CH_3), 4.33 (septet, J = 6.1 Hz, 1 H, OCH), and signals of aromatic protons. ^{13}C NMR (CD_2Cl_2, –20 °C): δ 22.86, 66.29, 108.34,126.87, 129.11, 130.82, 132.50.

Methoxy(4-methoxyphenyl)dioxirane (13d): ^1H NMR (CD_2Cl_2, –20 °C): δ

3.44 (s, 3 H, OCH_3), 3.81 (s, 3H, OCH_3), 6.91 (d, J = 8.7 Hz, 2 H, Ar), 7.55 (d, J = 8.7 Hz, 2 H, Ar).

Methoxy(4-nitrophenyl)dioxirane (13e): ^{1}H NMR (CD_2Cl_2, −20 °C): δ 3.52 (s, 3 H, OCH_3), and signals of aromatic protons.

6. Radical chain oxidation of *E*- or *Z*-1,2-dimethoxy-1,2-diphenylethene at low temperature

An ozone-oxygen mixture was bubbled into *tert*-butyl hydroperoxide (5 μl) in 0.5 mL of CD_2Cl_2 in a NMR tube at −45 °C until the blue color of ozone persisted for ten minutes. Oxygen was bubbled through for another five minutes to expel the excess ozone left in the solution. A solution of *trans*- or *cis*-**8a** (4 mg) in 0.2 mL of CD_2Cl_2 was added to the above solution while oxygen was kept bubbling through at −20 °C for another four hours. The reaction mixture was analyzed by ^{1}H NMR at −20 °C.

7. Dioxirane epoxidation rate study

a) Relative rate study

A CD_2Cl_2 solution (0.5 mL) of the reaction mixture (containing approximately 2×10^{-5} moles of **13a**) prepared by the inverse ozonation of 6 mg of *E*-**8a** at −20 °C in a NMR tube was poured into a 0.5 mL of vigorously stirring CD_2Cl_2 solution of equivalent amounts of cyclohexene and an alkene (approximately 2×10^{-5} moles each) in a 5 mL-flask which was placed in a dry ice-acetone bath. The NMR tube and the flask had been freed of acid as described previously. The reaction mixture was stirred at −78 °C for 30 minutes and then analyzed by ^{1}H NMR at room temperature.

b) Absolute Rate Study

Typical conditions were as follows. A solution of the dioxirane **13a** in

a NMR tube was prepared by the inverse ozonation of 5.5 mg of *E*-**8a** dissolved in 0.5 mL of CD_2Cl_2 at −20 °C. The amount of dioxirane **13a** was measured by comparison of the ^1H NMR integral of the methoxy group of **13a** with the integral of the methyl group of a known amount of toluene (2.0 μl) which was added as an internal standard. An approximately equivalent amount of methyl *E*-cinnamate (~2.6 mg) in 0.2 mL of CD_2Cl_2 was injected into the NMR tube which was placed in a dry ice-acetone bath and the solution was shaken vigorously while kept inside the bath. The NMR tube was then put as soon as possible into a NMR probe which was precooled to the desired temperature. The integrals of the reactants and products was recorded by ^1H NMR every five or ten minutes and compared with that of the internal standard until most of **13a** was consumed. The values of the second-order rate constant, k_2, were calculated from the usual expression,

$$k_2 = \frac{1}{a-b} \ln \frac{b(a-x)}{a(b-x)} \frac{1}{t}$$

where a = the initial concentration of the alkene, b = the initial concentration of the dioxirane, x = the concentration of the oxirane produced, and t = the reaction time. The Arrhenius activation energy was calculated from the equation

$$E_a = 1.987 \frac{T_2 T_1}{T_2 - T_1} \ln \frac{k_2}{k_1}$$

The results of the absolute rate studies are summarized in Table 9-15 and Figure 6-12 which are created by a computer program.

Table 9. Epoxidation of methyl *E*-cinnamate by (methoxy)phenyldioxirane **13a** in CD_2Cl_2 at –20 °C

Initial concentration of methyl *E*-cinnamate = $2.81 \times 10^{-2}\,M$

Initial concentration of (methoxy)phenyldioxirane **13a** = $2.22 \times 10^{-2}\,M$

Internal standard: Toluene

Time (sec)	Conc.of the oxirane ($10^{-2}M$)	$\frac{1}{a-b}\ln\frac{b(a-x)}{a(b-x)}$	k_2 ($10^{-2}M^{-1}sec^{-1}$)
0	0		
300	0.45	8.81	2.97
600	0.73	16.59	2.77
900	0.98	26.02	2.88
1200	1.15	34.49	2.87
1500	1.30	44.04	2.93
1800	1.39	51.07	2.83
2400	1.55	67.10	2.80

Average $k_2 = 2.86 \times 10^{-2}\,M^{-1}sec^{-1}$

From Figure 3, $k_2 = 2.82 \times 10^{-2}\,M^{-1}sec^{-1}$

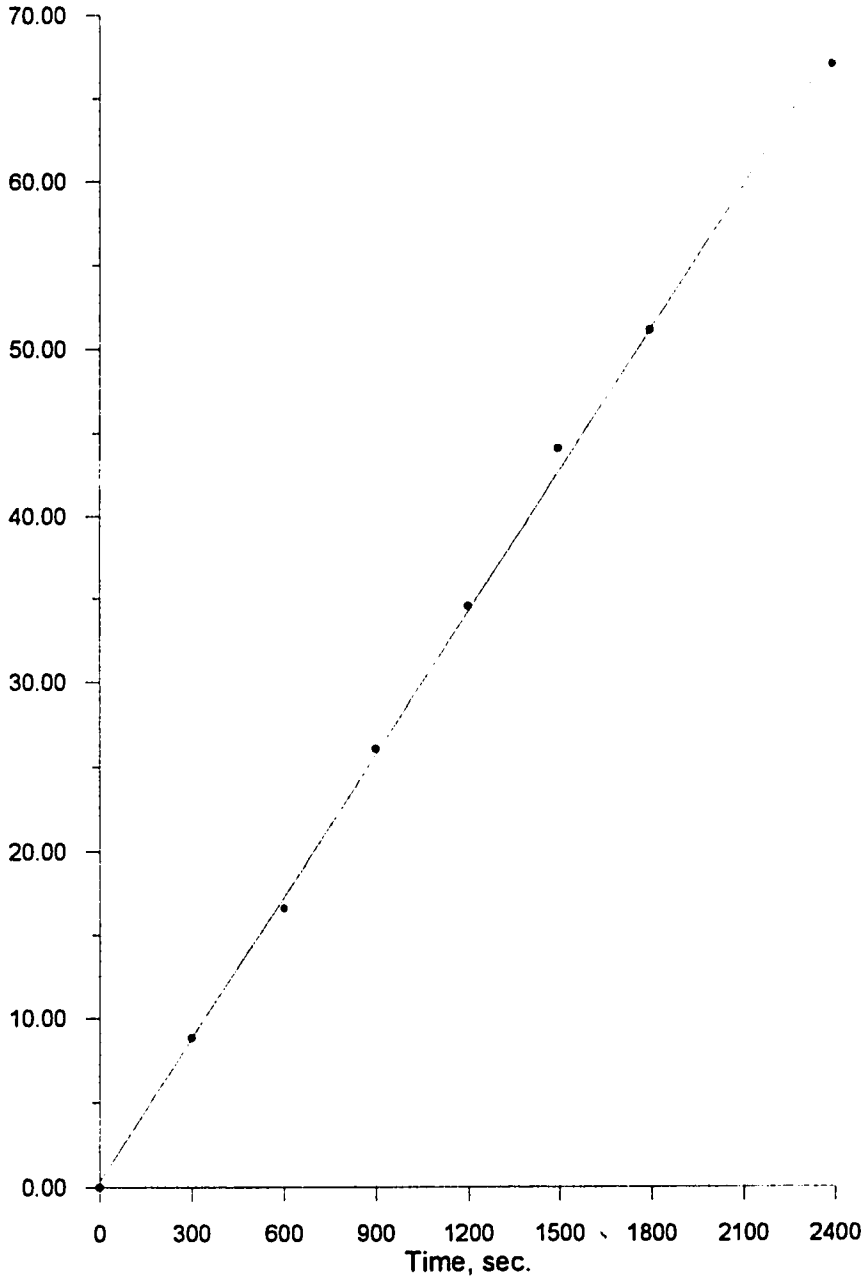


Figure 6. Epoxidation of methyl *E*-cinnamate by (methoxy)phenyldioxirane **13a** in CD_2Cl_2 at −20 °C.

Table 10. Epoxidation of methyl *E*-cinnamate by (methoxy)phenyldioxirane **13a** in CD_2Cl_2 at −40 °C

Initial concentration of methyl *E*-cinnamate = $2.72 \times 10^{-2}\ M$

Initial concentration of (methoxy)phenyldioxirane **13a** = $2.05 \times 10^{-2}\ M$

Internal standard: Toluene

Time (sec)	Conc. of the oxirane ($10^{-2} M$)	$\frac{1}{a-b}\ln\frac{b(a-x)}{a(b-x)}$	k_2 ($10^{-2} M^{-1}\text{sec}^{-1}$)
0	0		
300	0.09	1.68	0.57
600	0.19	3.71	0.62
900	0.28	5.71	0.63
1200	0.35	7.38	0.62
1800	0.47	10.55	0.58
2400	0.59	14.16	0.58

Average $k_2 = 0.60 \times 10^{-2} M^{-1}\text{sec}^{-1}$

From Figure 4, $k_2 = 0.59 \times 10^{-2} M^{-1}\text{sec}^{-1}$

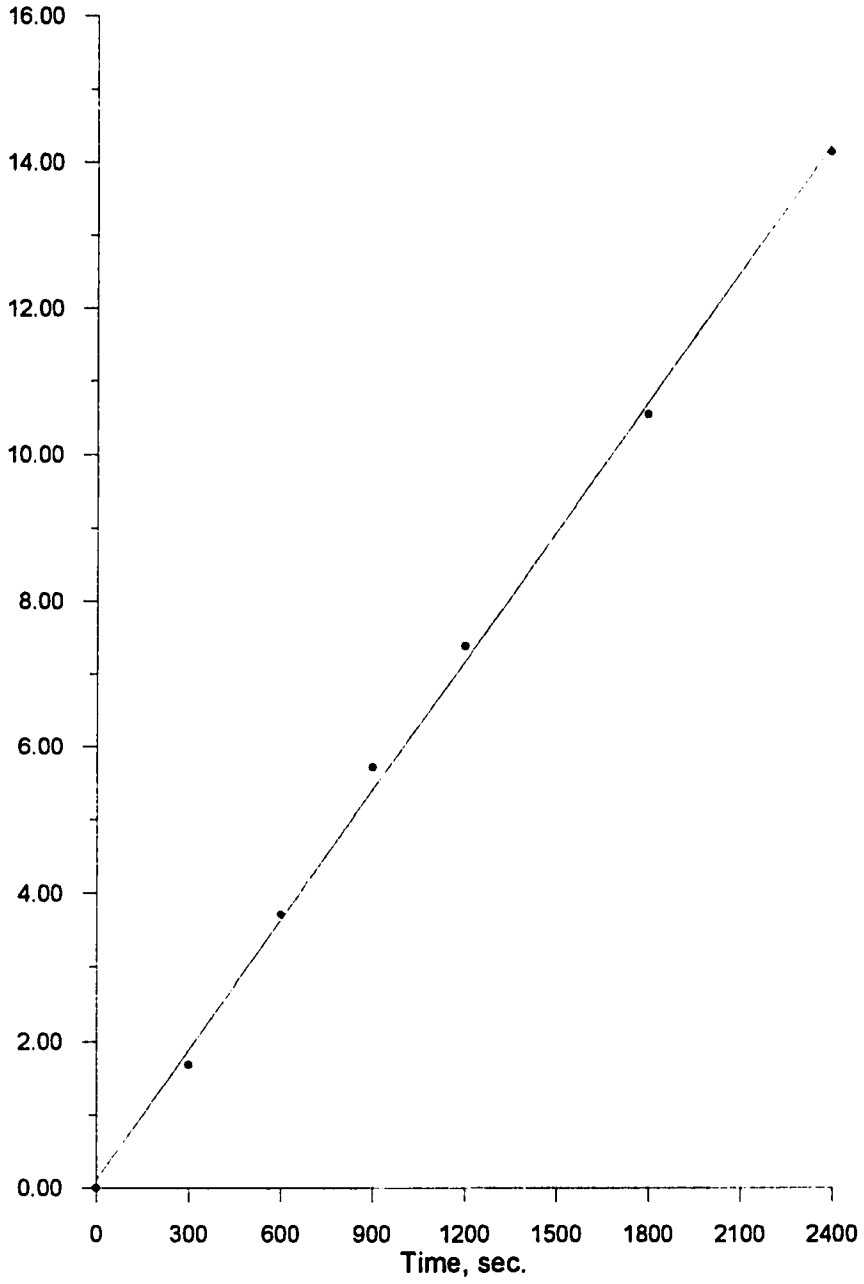


Figure 7. Epoxidation of methyl *E*-cinnamate by (methoxy)phenyldioxirane **13a** in CD_2Cl_2 at –40 °C.

Table 11. Epoxidation of *E*-1,2-diisopropoxy-1,2-diphenylethene *E*-**8c** by (isopropoxy)phenyldioxirane **13c** in CD_2Cl_2 at –20 °C

Initial concentration of *E*-1,2-diisopropoxy-1,2-diphenylethene *E*-**8c** = 1.89×10^{-2} *M*

Initial concentration of (isopropoxy)phenyldioxirane **13c** = 1.38×10^{-2} *M*

Internal standard: Toluene

Time (sec)	Conc. of the oxirane ($10^{-2}M$)	$\frac{1}{a-b}\ln\frac{b(a-x)}{a(b-x)}$	k_2 ($10^{-2}M^{-1}sec^{-1}$)
0	0	0	
300	0.60	36.98	12.32
600	0.87	74.25	12.37
900	1.02	112.36	12.48
1200	1.11	146.35	12.20

Average $k_2 = 12.34 \times 10^{-2} M^{-1}sec^{-1}$

From Figure 5, $k_2 = 12.27 \times 10^{-2} M^{-1}sec^{-1}$

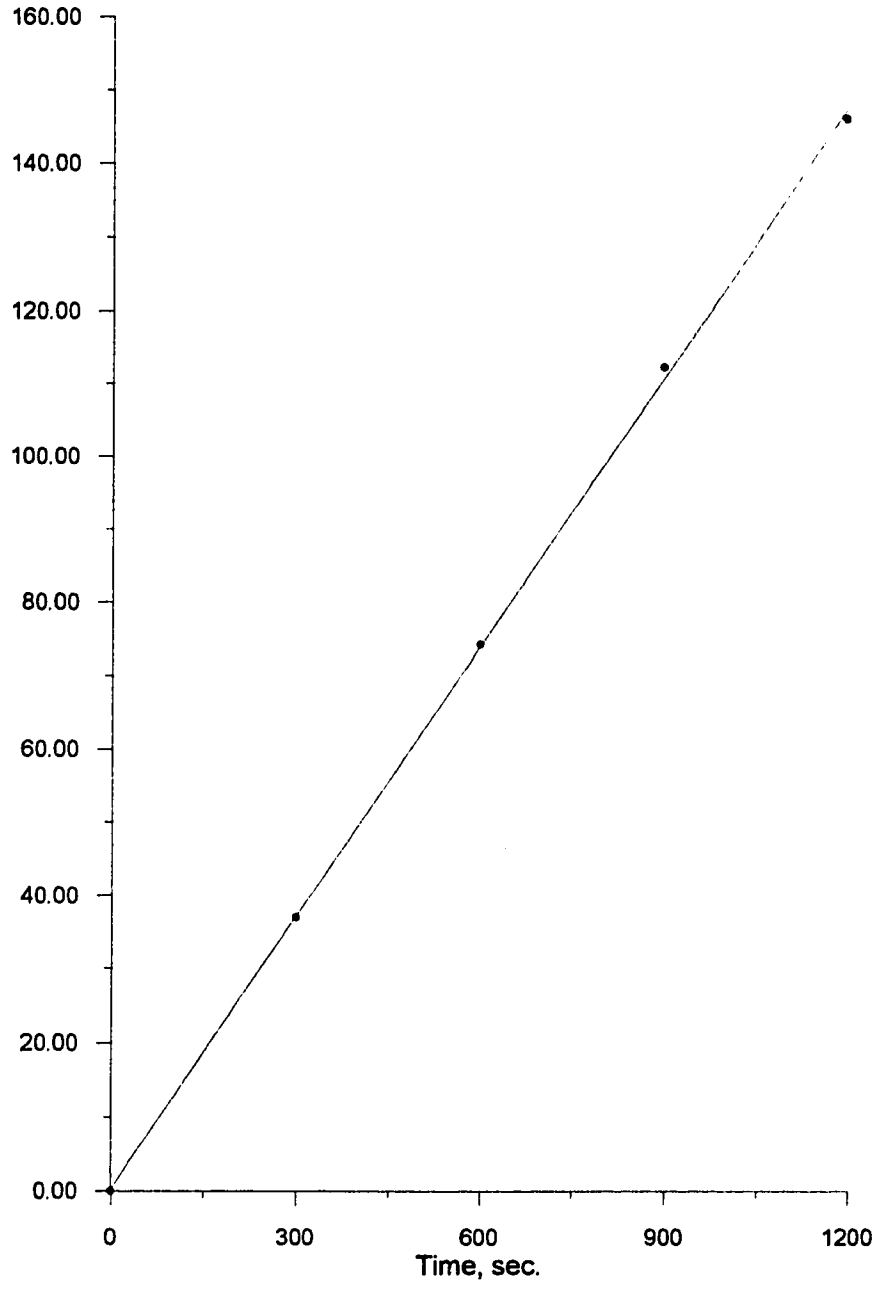


Figure 8. Epoxidation of *E*-1,2-diisopropoxy-1,2-diphenylethene *E*-**8c** by (isopropoxy)phenyldioxirane **13c** in CD_2Cl_2 at –20 °C.

Table 12. Epoxidation of *E*-1,2-diisopropoxy-1,2-diphenylethene *E*-**8c** by (isopropoxy)phenyldioxirane **13c** in CD_2Cl_2 at –40 °C

Initial concentration of *E*-1,2-diisopropoxy-1,2-diphenylethene *E*-**8c** = $1.23 \times 10^{-2} M$

Initial concentration of (isopropoxy)phenyldioxirane **13c** = $1.15 \times 10^{-2} M$

Internal standard: Toluene

Time (sec)	Conc.of the oxirane ($10^{-2}M$)	$\frac{1}{a-b}\ln\frac{b(a-x)}{a(b-x)}$	k_2 ($10^{-2} M^{-1}sec^{-1}$)
0	0		
600	0.14	11.22	1.87
1200	0.26	23.64	1.97
1800	0.34	33.39	1.85
2400	0.41	43.43	1.82
3000	0.45	51.94	1.73
3600	0.54	70.21	1.95

Average $k_2 = 1.87 \times 10^{-2} M^{-1}sec^{-1}$

From Figure 6, $k_2 = 1.86 \times 10^{-2} M^{-1}sec^{-1}$

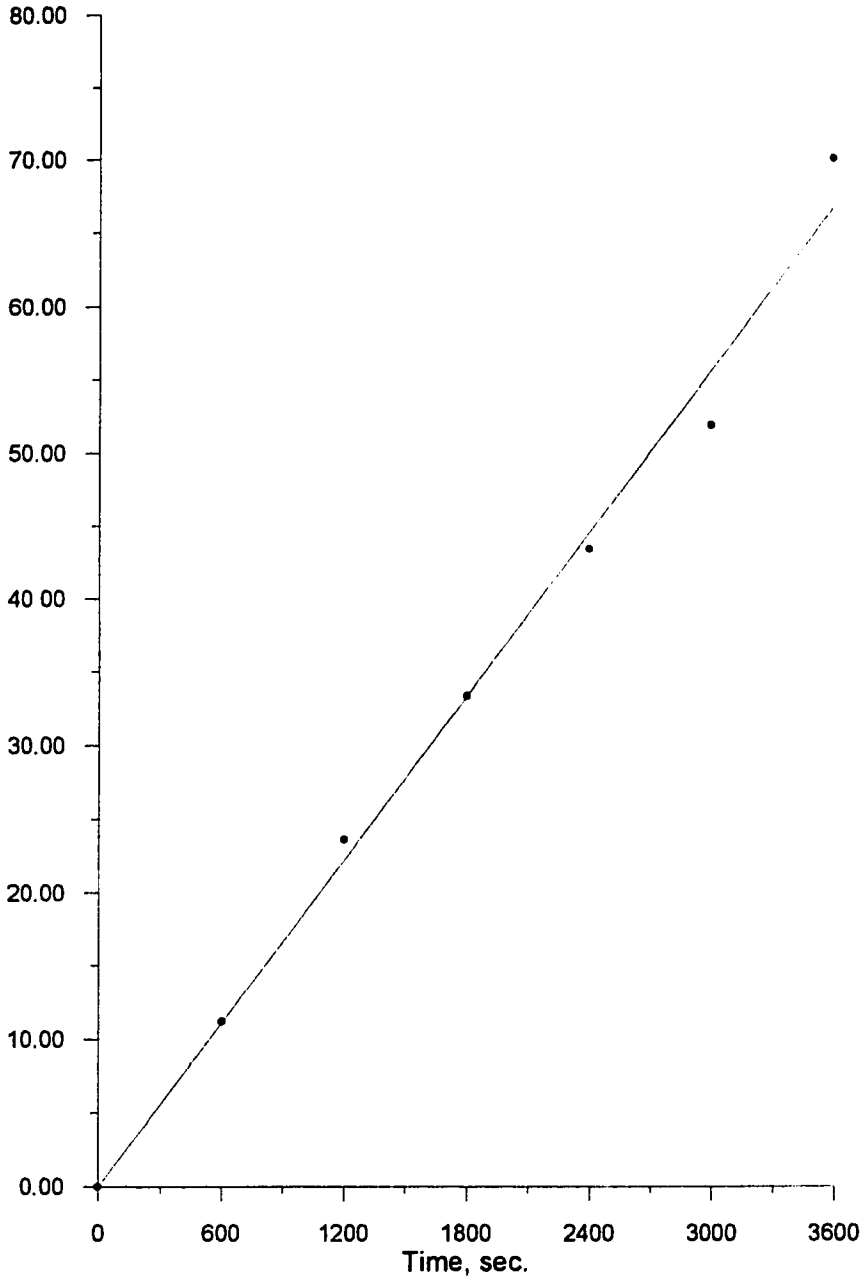


Figure 9. Epoxidation of *E*-1,2-diisopropoxy-1,2-diphenylethene ***E*-8c** by (isopropoxy)phenyldioxirane **13c** in CD_2Cl_2 at −40 °C.

Table 13. Epoxidation of methyl *E*-crotonate by (methoxy)phenyldioxirane **13a** in CD_2Cl_2 at −20 °C

Initial concentration of methyl *E*-crotonate = $2.86 \times 10^{-2} M$

Initial concentration of (methoxy)phenyldioxirane **13a** = $2.64 \times 10^{-2} M$

Internal standard: Toluene

Time (sec)	Conc. of the oxirane ($10^{-2} M$)	$\frac{1}{a-b} \ln \frac{b(a-x)}{a(b-x)}$	k_2 ($10^{-2} M^{-1} sec^{-1}$)
0	0	0	
600	0.33	4.97	0.83
1200	0.58	9.74	0.81
1800	0.82	15.48	0.86
2400	0.98	20.19	0.84
3600	1.22	29.23	0.81

Average $k_2 = 0.83 \times 10^{-2} M^{-1} sec^{-1}$

From Figure 7, $k_2 = 0.82 \times 10^{-2} M^{-1} sec^{-1}$

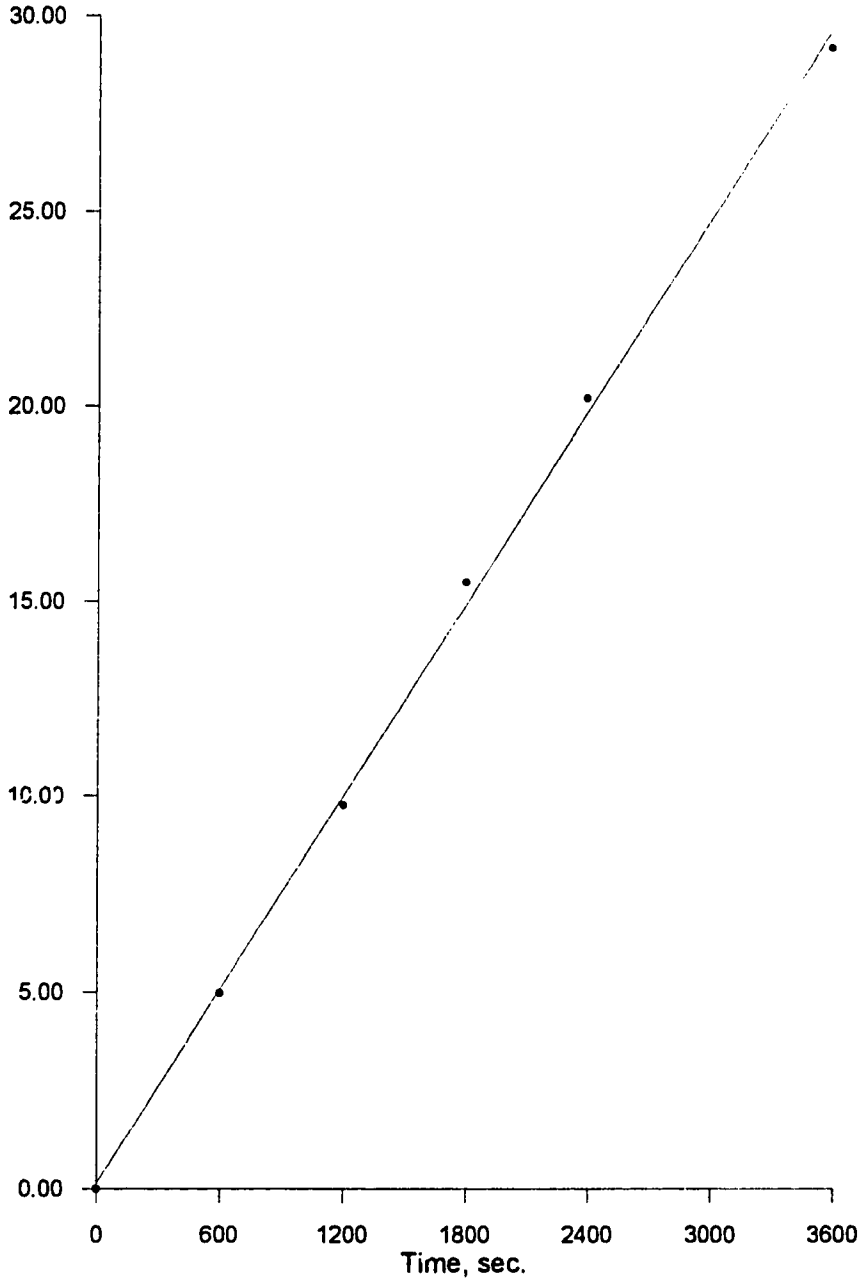


Figure 10. Epoxidation of methyl *E*-crotonate by (methoxy)dioxirane **13a** in CD_2Cl_2 at –20 °C.

Table 14. Epoxidation of methyl *E*-crotonate by methoxy(4-methoxyphenyl)dioxirane **13d** in CD_2Cl_2 at −20 °C

Initial concentration of methyl *E*-crotonate = $1.13 \times 10^{-2}\,M$

Initial concentration of methoxy(4-methoxyphenyl)dioxirane **13d** = $1.35 \times 10^{-2}\,M$

Internal standard: Toluene

Time (sec)	Conc. of the oxirane ($10^{-2}M$)	$\frac{1}{a-b}\ln\frac{b(a-x)}{a(b-x)}$	k_2 ($10^{-2}M^{-1}sec^{-1}$)
0	0	0	
600	0.063	4.35	0.73
1200	0.126	9.20	0.77
1800	0.164	12.41	0.69
2400	0.220	17.56	0.73

Average $k_2 = 0.73 \times 10^{-2}M^{-1}sec^{-1}$

From Figure 8, $k_2 = 0.72 \times 10^{-2}M^{-1}sec^{-1}$

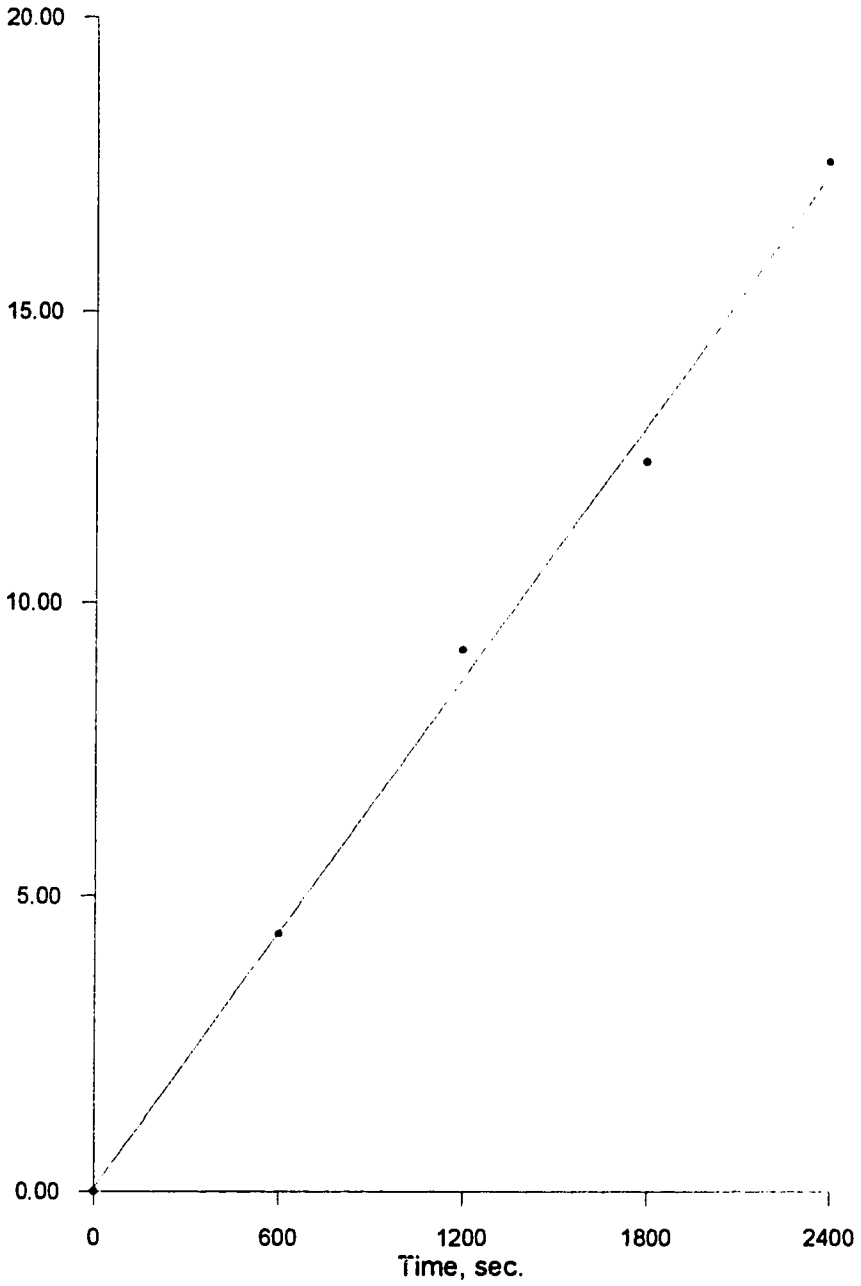


Figure 11. Epoxidation of methyl *E*-crotonate by methoxy(4-methoxyphenyl)dioxirane **13d** in CD_2Cl_2 at –20 °C.

Table 15. Epoxidation of methyl *E*-crotonate by methoxy(4-nitrophenyl)dioxirane **13e** in CD_2Cl_2 at −20 °C

Initial concentration of methyl *E*-crotonate = $1.39 \times 10^{-2}\,M$

Initial concentration of methoxy(4-nitrophenyl)dioxirane **13e** = $1.20 \times 10^{-2}\,M$

Internal standard: Toluene

Time (sec)	Conc. of the oxirane ($10^{-2}M$)	$\frac{1}{a-b}\ln\frac{b(a-x)}{a(b-x)}$	k_2 ($10^{-2}M^{-1}sec^{-1}$)
0	0	0	
300	0.22	15.91	5.30
600	0.40	34.80	5.80
900	0.51	50.66	5.63
1200	0.60	67.43	5.62
1500	0.65	78.82	5.25

Average $k_2 = 5.52 \times 10^{-2}\,M^{-1}sec^{-1}$

From Figure 9, $k_2 = 5.38 \times 10^{-2}\,M^{-1}sec^{-1}$

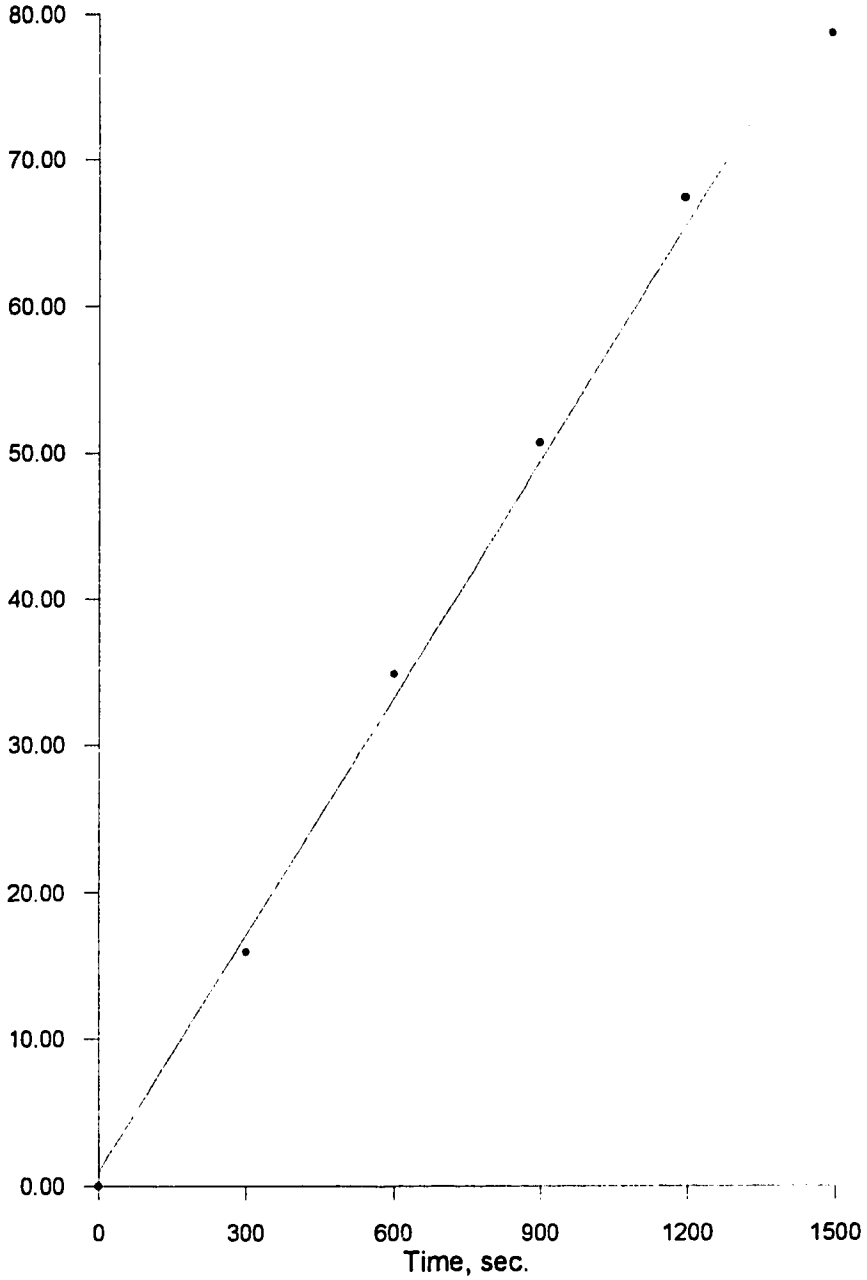
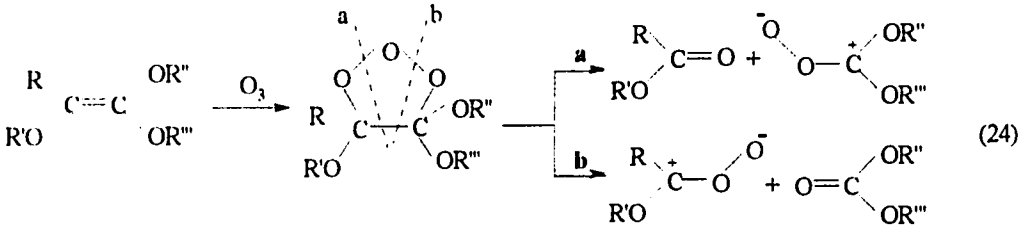


Figure 12. Epoxidation of methyl *E*-crotonate by methoxy(4-nitrophenyl)dioxirane **13e** in CD_2Cl_2 at –20 °C.

III. SYNTHESIS AND OZONATION OF 2-[(METHOXY)PHENYL]METHYLENE-1,3-DIOXOLANE AND 1,1,2-TRIMETHOXY-2-PHENYLETHENE

Dioxiranes are efficient oxygen transfer agents.[30] After the discovery that (methoxy)phenyldioxirane **13a** is one of the reaction products of the ozonation of *E*- or *Z*-1,2-dimethoxy-1,2-diphenylethene (*E*- or *Z*-**8a**), it was hoped that **13a** could be prepared in better yield and with fewer side products by ozonation of other alkenes.

The ozonation of 1,1,2-trialkoxy-2-phenylethenes was first considered. To the best of our knowledge, 1,1,2-trialkoxy substituted alkenes had never been synthesized. There are two possible directions for cleavage of the primary ozonide of a trialkoxy substituted alkene, eq 24. In direction *a* only



(24)

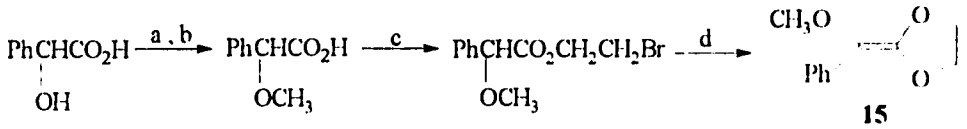
one alkoxy substituent is incorporated in the carbonyl product formed, whereas in direction *b* two alkoxy substituents are incorporated in the carbonyl product formed. It is well known that primary ozonides of vinyl ethers always cleave in the direction to give an ester and a carbonyl oxide, i.e., the alkoxy substituent is incorporated in the carbonyl product formed.[19,20] Hence, direction *b* may be more favorable over direction *a* because in direction *b* one more alkoxy substituent is incorporated in the carbonyl product. If the primary ozonide of 1,1,2-trialkoxy-2-phenylethene

cleaved in the expected direction, a carbonate and an (alkoxy)phenylcarbonyl oxide would be produced and the latter would be able to cyclize to a dioxirane. To study this possibility, 2-[(methoxy)phenyl]methylene-1,3-dioxolane **15** and 1,1,2-trimethoxy-2-phenylethene **16** were synthesized and subjected to ozonation.

Results and Discussion

1. Synthesis of the starting alkenes

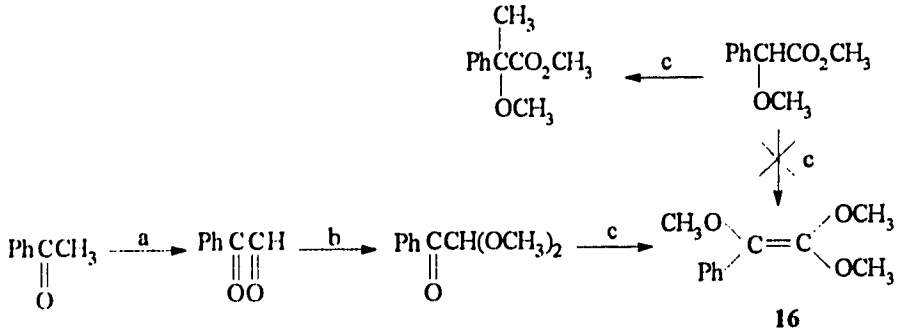
No precedent was found for the synthesis of trialkoxy substituted alkenes. It was reported that some ketene acetals could be prepared by intramolecular cyclization of 2-bromoethyl esters.[66] This method was extended to synthesize 2-[(methoxy)phenyl]methylene-1,3-dioxolane **15** from 2-bromoethyl (methoxy)phenylacetate as shown in Scheme 14.



Reaction Conditions: a. 10 *eq.* $(MeO)_2SO_2$, 20 *eq.* NaOH/ H_2O b. H_2SO_4
c. 1.5 *eq.* $HOCH_2CH_2Br$, Cat. TsOH/Benzene d. 1.1 *eq.* NaH/ DMSO

Scheme 14. Synthesis of 2-[(methoxy)phenyl]methylene-1,3-dioxolane

Preparation of 1,1,2-trimethoxy-2-phenylethene **16** from the corresponding methyl α-methoxyphenylacetate was unsuccessful. Even with the use of polar aprotic solvents, such as DMSO or HMPA-THF, only the C-alkylated product was obtained. The alkene **16** was prepared by O-alkylation of 2,2-dimethoxy-1-phenylethanone as shown in Scheme 15.



Reaction Conditions: a. ScO_2 / Dioxane; b. cat. H_2SO_4 / CH_3OH / Benzene; c. 1.2 *eq.* NaH / DMSO then 1.1 *eq.* *p*-$TsOCH_3$

Scheme 15. Synthesis of 1,1,2-trimethoxy-2-phenylethene

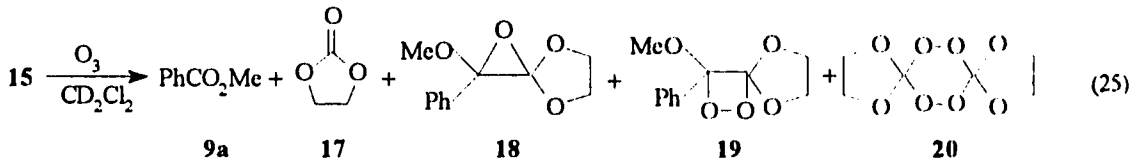
The α-keto acetal (94% pure) obtained from phenylglyoxal was contaminated with 1,1,2,2-tetramethoxyethylbenzene and other minor impurities. The contaminants were hard to remove completely and had to be carried over to the next step. Thus, the purity of the final product **16** was only ~95% even after several recrystallizations. Fortunately, the impurities are inert to ozone.

The two 1,1,2-trialkoxy-2-phenylethenes slowly decomposed to complex products during the storage at room temperature but can be stored in acid-free containers at −5 °C for several months without significant decomposition.

2. Ozonation of 2-[(methoxy)phenyl]methylene-1,3-dioxolane

The ozonation and other related reactions were carried out in a similar manner as those described previously. The major products (up to 80% of the total products) from the ozonation of **15** in CD_2Cl_2 were methyl benzoate **9a**, ethylene carbonate **17**, 2-methoxy-2-phenyl-1,4,7-trioxaspiro[2.4]heptane **18** (the oxirane of **15**), 1-methoxy-1-phenyl-2,3,5,8-tetraoxaspiro[3.4]octane **19**

(the 1,2-dioxetane of **15**) and 1,4,6,7,9,12,13,14-octaoxadispiro[4.2.4.2]tetradecane **20** (the dimer of the ethylene carbonate oxide), eq 25. The total amount of unidentified products which gave a cluster of small signals between δ 3.0 and δ 4.5 in the ^{1}H NMR spectrum accounted for approximately 20% of all the products.



(25)

The ^{1}H NMR signals of the CH_3O groups of the oxirane **18**, the dioxetane **19** and methyl benzoate **9a** are well separated from other signals, and occur at δ 3.44, 3.57, and 3.89, respectively. The OCH_2CH_2O group of ethylene carbonate **17** gives an isolated singlet at δ 4.50. The ^{1}H NMR signals of the OCH_2CH_2O group of **18** and **19** overlap and give two multiplets at δ 4.00-4.15 and δ 4.15-4.30. The OCH_2CH_2O group of the tetroxane **20** gives a singlet at δ 4.24, overlapping one of the two multiplets of **18** and **19**. Therefore, the integral due to **20** is the difference of the integrals of the signals between δ 4.15-4.30 and δ 4.00-4.15.

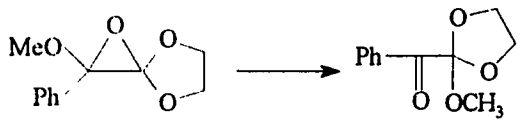
Unlike in the ozonation of *E*- and *Z*-1,2-dimethoxy-1,2-diphenylethene (*E*- and *Z*-**8a**), it was found that the product distribution was not dependent on the initial concentrations of **15** and furthermore there was no difference in the product formations and distributions between the normal and inverse ozonation of **15**. As seen from Table 16, the product distribution was slightly dependent on the reaction temperatures.

Ethylene carbonate **17** and methyl benzoate **9a** were readily identified by their ^{1}H NMR signals.

Table 16. Product distribution from the ozonation of 2-[(methoxy)phenyl]methylene-1,3-dioxolane[a]

Solvent	Conc. *M*	Method	Temp. °C	Products, moles per mole of alkene				
				benzoate **9a**	carbonate **17**	oxirane **18**	dioxetane **19**	tetroxane **20**
CD_2Cl_2	0.01	normal	–20	0.67	0.24	0.15	0.10	0.02
	0.05		20	0.89	0.25	0.14	0.08	0.02
			–20	0.68	0.23	0.16	0.11	0.03
			–78	0.55	0.22	0.20	0.14	0.05
	0.20		–20	0.69	0.26	0.17	0.11	0.02
		inverse	–20	0.69	0.24	0.15	0.11	0.03
$(CD_3)_2CO$	0.05	normal	–78	0.58	0.30	0.23	0.07	0.07

The oxirane **18** was identified by comparison of the ^1H NMR spectrum of the ozonation reaction mixture with that of an authentic sample prepared by epoxidation of **15** with the dioxirane **13a**. A singlet at δ 3.44 and two multiplets at δ 4.05-4.12 and δ 4.22-4.29 are assigned to the OCH_3 and OCH_2CH_2O groups of **18**, respectively. At room temperature, **18** soon rearranged to 2-benzoyl-2-methoxy-1,3-dioxolane **21** that gives a singlet at δ 3.42 for the methoxy group and an easily identified doublet at δ 8.10 for the two ortho protons of the phenyl ring, eq 26. The rearrangement product **21**



18 **21** (26)

was isolated from the reaction mixture by chromatography and was identified by ^1H, ^{13}C NMR, and mass spectrometries. Two signals at δ 190.04 and 118.22 in the ^{13}C NMR spectrum of **21** were assigned to the carbonyl carbon atom and the carbon atom attached to three oxygen atoms, respectively. The electron impact ionization mass spectrum gave the exact masses of the (M –

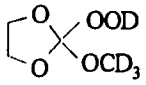
$OCH_3)^+$ and $C_6H_5CO^+$ ions, while the chemical ionization with NH_4^+ afforded the $(M + NH_4^+)$ ion at *m/e* 226.

The dioxetane **19** was identified by comparison of the ^1H NMR spectrum of the ozonation reaction mixture with that of an authentic sample prepared by singlet oxygen oxidation of **15**. A singlet at δ 3.57 disappeared when the reaction mixture was shaken with a drop of a deuterated methanol solution of $CuCl_2$, indicating the decomposition of the dioxetane by the transition metal ion.[28] Consequently, this signal was assigned to the methoxy group of **19**. Other signals of **19** overlap signals of the other products. The formation of the dioxetane **19** was further confirmed by the observation of luminescence upon addition of the reaction mixture to hot toluene containing 9,10-dibromo- and 9,10-bis(phenylethynyl)anthracene. Evidence that **19** was formed by the reaction of **15** with singlet oxygen was obtained by ozonation of a 1:4 mixture of **15**:2,5-dimethylfuran. The result of this competitive reaction showed that no the dioxetane **19** was detected by ^1H NMR and the endoperoxide of 2,5-dimethylfuran was produced instead. As discussed previously, this result indicates that **19** was produced by singlet oxygen oxidation of **15**.

The dimer of the ethylene carbonate oxide **20** was isolated directly as a white powder from the reaction mixture after the solvent was evaporated. It can be recrystallized from methanol and stored at room temperature without decomposition. The structure and composition of this oxygen-rich compound was determined by ^1H and ^{13}C NMR spectroscopies, chemical ionization mass spectrometry, and elemental analysis. It gives only one singlet at δ 4.24 in the ^1H NMR spectrum. The ^{13}C NMR spectrum shows two signals at δ 66.52 and 143.11. The low field signal indicates the presence of a carbon atom attached to four oxygen atoms. Chemical ionization with NH_4^+ afforded

the ($M + NH_4^+$) ion at *m/e* 226. The result of the elemental analysis is consistent with the composition of this molecule.

When deuterated methanol was used as the solvent, the major products were methyl benzoate **9a**, ethylene carbonate **17**, the oxirane **18** (or its rearrangement product), and the dioxetane **19**. Because there are many unidentified signals between δ 3.0 and δ 4.5 in the ^1H NMR spectra of the reaction mixtures, the precise determination of the yields of the identified products from the ^1H NMR spectra is impossible. The signal of the tetroxane **20** was not detected with ^1H NMR because the presence of the unidentified signals. It was not clear whether **20** was produced, but even if it were produced its yield was largely diminished compared with that when CD_2Cl_2 was used as the reaction solvent. A strong singlet at δ 3.10 was found in the ^1H NMR spectra of the reaction mixtures. This signal was initially attributed to the possible deuterated methanol and ethylene carbonate oxide adduct.



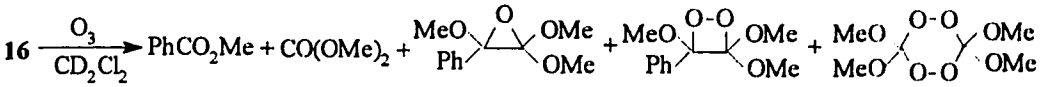
However, the chemical shift of the OCH_2CH_2O group of this compound is impossible to be at such a high field. The identity of the species that gives this signal is still unknown.

Vinyl ethers have been shown to be more reactive toward ozone than alkenes which have no oxygen atom attached to the double bond carbon atoms.[21] It was expected that 2-[(methoxy)phenyl]methylene-1,3-dioxolane **15** would be more reactive than 1,2-dimethoxy-1,2-diphenylethene **8a** because **15** has one more alkoxy substituent attached to the double bond carbon atoms. This prediction was proved to be right by the competitive ozonation of a 1:1 mixture of **15** and *E*-**8a** at −78 °C. It turned out that **15** was about six times as reactive as *E*-**8a**.

Determination of the stoichiometry of the ozonation of **15** was carried out by delivering a limited amount of a calibrated ozone-oxygen mixture to a 0.05 *M* CD_2Cl_2 solution of **15** at –20 °C. The amount of **15** consumed was obtained from the integrals of the signals of the remaining **15** and the sum of integrals of the signals of all the products. It turned out that 1.7-1.9 moles of **15** was consumed by each mole of ozone.

3. Ozonation of 1,2,2-trimethoxy-2-phenylethene

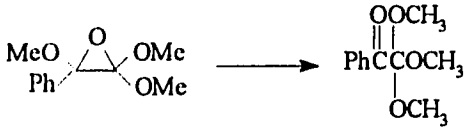
The ^1H NMR spectra of the reaction mixtures showed that the ozonation of 1,2,2-trimethoxy-2-phenylethene **16** in CD_2Cl_2 resulted in the same types of products as those in the ozonation of 2-[(methoxy)phenyl]methylene-1,3-dioxolane **15**. The major products are methyl benzoate **9a** and dimethyl carbonate **4**. Other identified products are 1,1,2-trimethoxy-2-phenyl oxirane **23**, 1,1,2-trimethoxy-2-phenyldioxetane **24** and (presumably) tetramethoxytetroxane **25**. However, perhaps due to the formation of oligomer of the carbonyl oxide, there are many unidentified signals with small to medium intensities between δ 3.0 and δ 4.0. Because of the presence of these unidentified signals, the determination of product yields is impossible from the ^1H NMR spectra of the reaction mixtures. The relative intensities of the ^1H NMR signals of the methoxy groups of the identified products are given in eq 27.



(27)

	9a	**4**	**23**	**24**	**25** (?)
- 20°C	1	1.11	0.33	0.28	0.17
- 78°C	1	0.67	0.21	0.03	0.43

The dioxetane **24** and the oxirane **23** were identified by comparison of the ^{1}H NMR spectrum of the ozonation reaction mixture with those of authentic samples prepared by singlet oxygen oxidation of **15** and epoxidation of **15** with the dioxirane **13a**. The three methoxy groups of **24** give three singlets at δ 3.18, 3.33, and 3.52. The three methoxy groups of **23** give three singlets at δ 3.20, 3.35, and 3.66. However, this oxirane is very unstable. In the most cases, it rearranged to 2,2,2-trimethoxy-1-phenylethanone **26**, a trimethyl orthoester, before the ^{1}H NMR spectra were recorded, eq 28. The



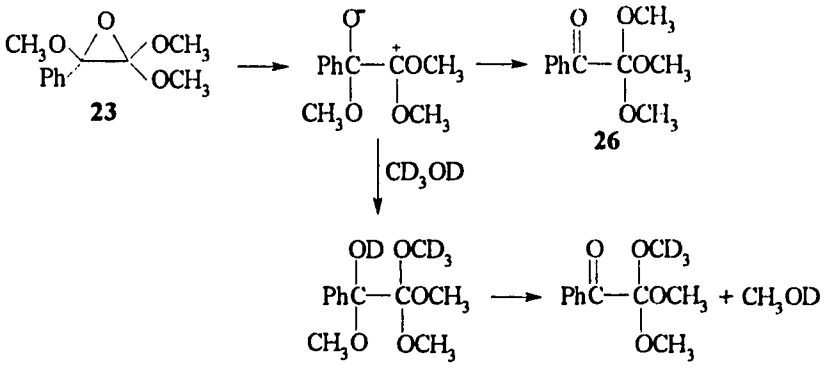
26 (28)

three methoxy groups of **26** give only one singlet at δ 3.26, indicating that they are all equivalent. A well separated doublet at δ 8.20, indicating the presence of a benzoyl moiety, was conveniently used to recognize this rearrangement product from the reaction mixture because the signal of its methoxy groups overlaps other signals. A small amount of this rearrangement product was isolated from the reaction mixture with preparative TLC. It is readily hydrolyzed by moisture to methyl benzoylformate which gives a singlet at δ 3.98. This further confirms that the precursor of the ester is an orthoester.

It is commonly observed that in the ozonation of alkenes the yields of tetroxanes increase as the reaction temperature is lowered,[67] e.g., the yields of *cis*- and *trans*-3,6-dimethoxy-3,6-diphenyltetroxane **12a** and the yield of the dimer of ethylene carbonate oxide **20** are all higher at −78 °C than at −20 °C as discussed previously. In the ozonation of **16**, it was found that the intensity of a singlet at δ 3.57 significantly increased as the ozonation

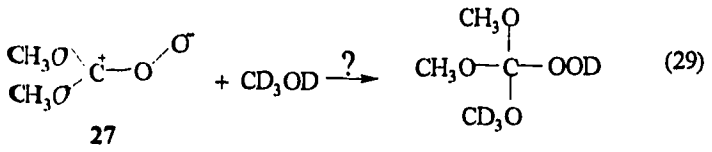
temperature was lowered. Therefore this signal was tentatively assigned to the expected 3,3,6,6-tetramethoxy-1,2,4,5-tetroxane **25**. Although the isolation of this oxygen-rich compound has not been achieved, the chemical ionization mass spectrum of the concentrated reaction mixture contains a signal at *m/e* 236, suggesting the presence of the (**25** + NH_4^+) ion.

When the reactions were carried out in CD_3OD at −20 °C, three additional signals appeared between δ 3.20 and δ 3.40 in the ^1H NMR spectra of the reaction mixtures. One of these signals (δ 3.34, −20 °C) is due to CH_3OD. The other two signals (δ 3.32 and 3.28, −20 °C) disappeared simultaneously in a few minutes upon warming the reaction mixture to room temperature. Those due to CH_3OD and **26**, the rearrangement product of the oxirane, increased in intensity while the signals due to methyl benzoate **9a** and dimethyl carbonate **4** did not change in intensity. These observations indicate that a precursor of **26** is trapped by CD_3OD in a reaction that is competitive with the rearrangement of the precursor to **26** at −20 °C, as shown in Scheme 16. An analogous mechanism was proposed to account for the rather similar observations made in the ozonation of tetramethoxyethene in CD_3OD below −50 °C.[22]



Scheme 16. Trapping the rearrangement intermediate of 1,1,2-trimethoxy-2-phenyloxirane in CD_3OD

Another new signal appeared at δ 3.03 as a singlet in the ^{1}H NMR spectra of the reaction mixtures when the reactions were carried out in CD_3OD at −20 °C. After the reaction mixture was allowed to stand at room temperature for two hours, this signal disappeared. It was also observed that the ^{1}H NMR spectra of the reaction mixtures in which CD_3OD was used as the solvent were simpler than those in which CD_2Cl_2 was used as the solvent. These observations could be explained if the species that gives this new signal were the dimethylcarbonate oxide-CD_3OD adduct, eq 29. However, a



27 (29)

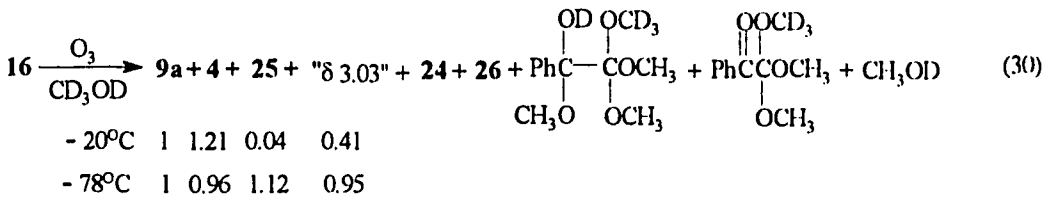
rather similar signal at δ 3.10 was observed in the ozonation of **15** in methanol. As discussed in the last section, it is not due to the ethylene carbonate oxide-CD_3OD adduct. If this parallelism is true, it may well indicate that the new signal at δ 3.03 is not due to the dimethylcarbonate oxide-CD_3OD adduct. Because the chemical shift alone provides little help in the identification of this signal, the identity of the species that gives this signal is still unknown.

When the reaction was carried out in CD_3OD at −78 °C, the signal at δ 3.57, which was tentatively assigned to the tetroxane **25**, still appeared in the ^{1}H NMR spectra of the reaction mixtures. Its intensity was as strong as those of methyl benzoate **9a** or dimethyl carbonate **4**, indicating a significant amount of **25** was produced. This observation suggests that dimethylcarbonate oxide cannot be trapped by methanol or at least the trapping reaction is inefficient.

Although the intensities of the signals of the dioxetane **24** were too small to be distinguished from other small signals on the base line of the ^1H NMR spectra, the observation of luminescence upon mixing the reaction mixtures with hot toluene containing the fluorescers indicates that a small amount of **24** was formed from the ozonation of **16** in CD_3OD.

Because the ^1H NMR signals of CD_3OD overlapped the signals of CH_3OD and the oxirane rearrangement product **26**, it is difficult to measure the exact integrals of the signals of CH_3OD and **26**. Therefore the product distribution in the ozonation of **15** in CD_3OD is unavailable. In eq 30, the products formed and the relative intensities of the signals due to the methoxy groups of the benzoate **9a**, the carbonate **4**, the tetroxane **25**, and the unknown compound which gives the signal at 3.03 are given in order to give a rough idea of the results of the ozonation of **15** in CD_3OD.

The determination of the stoichiometry of the ozonation of **16** was



(30)

carried out by delivering a limited amount of a calibrated ozone-oxygen mixture to a 0.05 *M* CD_2Cl_2 solution of **16** at −20 °C using toluene as an internal standard. It turned out that 1.2 moles of **16** was consumed by each mole of ozone.

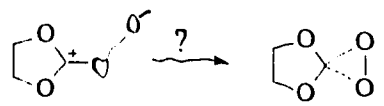
4. Discussion of the ozonation mechanism

Both **15** and **16** are 1,1,2-trialkoxy-2-phenylethenes and the ozonation

of **15** and **16** results in the same types of products, therefore they are expected to have similar ozonation mechanisms. Because more information was obtained from the ozonation of **15**, the following discussion is based on the results of the ozonation of **15**. The conclusion of this discussion should also apply to the ozonation of **16**.

(Methoxy)phenyldioxirane **13a** was not observed in the ozonation of **15** in methylene chloride at various temperatures. The tetroxanes *cis*- and *trans*-**12a** were not found either even when the reaction was carried out at −78 °C. It has been shown in Chapter II that significant amounts of *cis*- and *trans*-**12a** were formed in the ozonation of *E*- and *Z*-**8a** at this temperature. Instead, the formation of the tetroxane **20**, the dimer of the ethylene carbonate oxide, indicates that the cleavage of the primary ozonide of **15** proceeds in the direction to give methyl benzoate **9a** and ethylene carbonate oxide **22**. This cleavage direction is in contrast to what was expected.

It is uncertain whether ethylene carbonate oxide **22** can cyclize to the corresponding dioxirane, eq 31. If the dioxirane is a reaction intermediate, like in the ozonation of 1,2-dimethoxy-1,2-diphenylethene **8a**, some

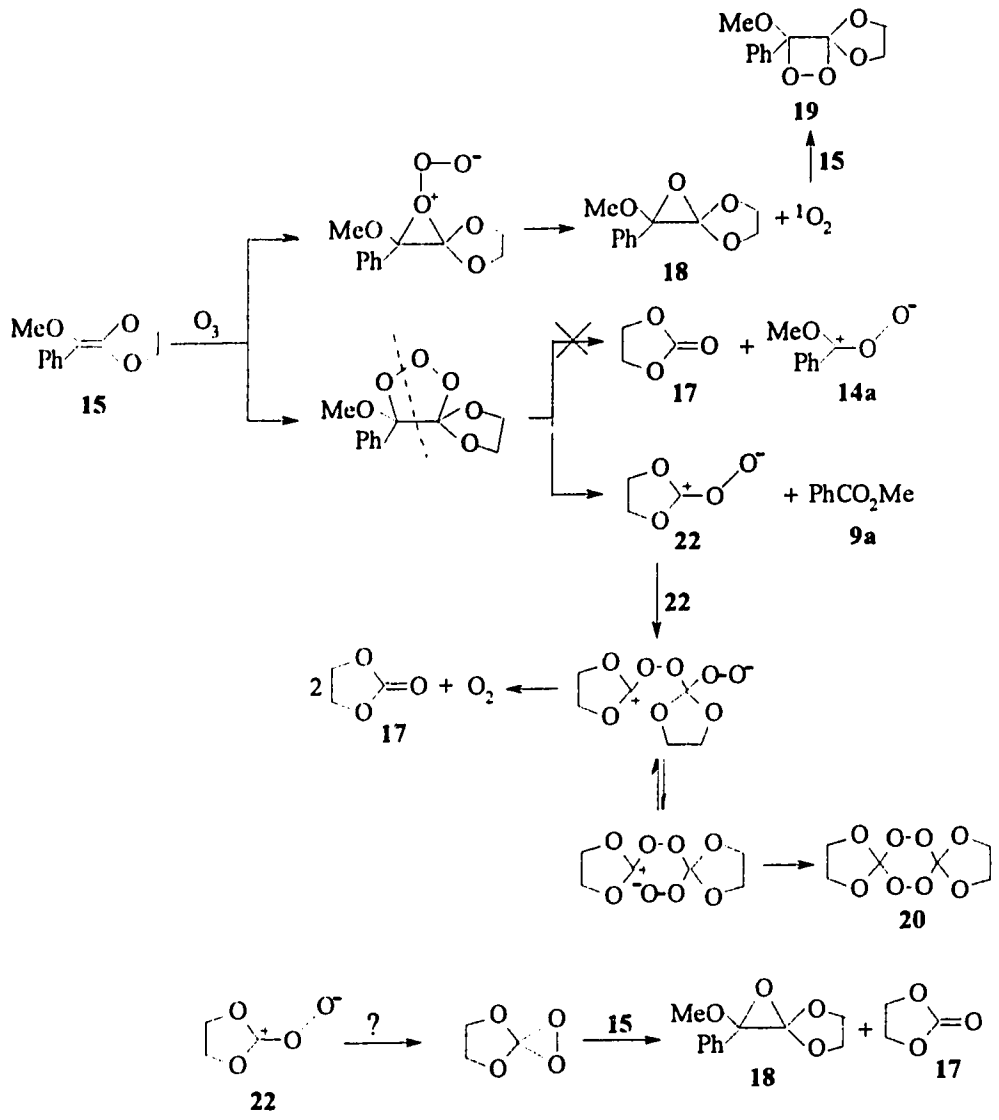


22 (31)

differences in the product formation and distribution would be expected between the inverse and normal ozonation of **15**. Actually, no difference was found. Furthermore, unlike in the ozonation of a mixture of **8a** and 2,3-dimethyl-2-butene **5** where a significant amount of tetramethyloxirane **6** was produced, no **6** was found in ozonation of a 1:5 mixture of **15** and **5**. These

observations seem to indicate that the cyclization of ethylene carbonate oxide to the corresponding dioxirane never occurred. However, considering that **15** has three oxygen atoms attached to the double bond carbons and is more electron-rich than **8a**, it is possible that the reaction between **15** and the dioxirane is much faster than the reaction between **15** and ozone. If this is true, even under the inverse ozonation conditions, the dioxirane would compete effectively with ozone to react with **15**. If the reaction between **15** and the dioxirane is much faster than the reaction between 2,3-dimethyl-2-butene **5** and the dioxirane, even in the presence of an excess amount of **5**, the dioxirane would selectively epoxidize **15** instead of **5**. Thus, the possibility of the formation of the dialkoxydioxirane in the ozonation of 1,1,2-trialkoxy-2-phenylethene still cannot be ruled out. To solve this problem, it is necessary to seek an alkene that can produce a dialkoxycarbonyl oxide but reacts slowly with dioxiranes.

The formation of the oxirane **18** and the dioxetane **19** suggests that, similar to the oxygenated oxirane of **8a**, the oxygenated oxirane of **15** could be one of the reaction intermediates. On the other hand, the formation of the tetroxane **20** implies the presence of the carbonyl oxide **22** which must result from the cleavage of the primary ozonide of **15**. Therefore, the proposed ozonation mechanism of **15** as shown in Scheme 17 is analogous to the one proposed for the ozonation of **8a**, although the uncertainty of the cyclization of ethylene carbonate oxide **22** to the corresponding dioxirane remains. Dimerization of the ethylene carbonate oxide **22** may not be concerted but proceed via a dimeric zwitterion, which can also decompose to two molecules of ethylene carbonate **17** and one molecule of oxygen. This could be another route to singlet oxygen. Because the other direction of the cleavage of the primary ozonide that can lead to the formation of **17** and **14a** has been ruled



Scheme 17. Possible ozonation mechanism of 2-[(methoxy)phenyl]methylene-1,3-dioxolane

out, the carbonate **17** must mainly arise from the decomposition of the dimeric zwitterion.

No evidence was found for the formation of the ethylene carbonate oxide-CD_3OD adduct. Also, a large amount of ethylene carbonate **17** was still produced when the ozonation was carried out in CD_3OD. These observations indicate that ethylene carbonate oxide **22** cannot be trapped by

methanol. This is possible because the alkoxy substituted carbonyl oxides would be less electrophilic than alkyl substituted carbonyl oxides. It was shown in the previous chapter that (methoxy)phenylcarbonyl oxide **14a** cannot be trapped by methanol.

Since the carbonyl oxide **22** cannot be trapped by methanol, the dimerization of the carbonyl oxide to the tetroxane **20** should easily occur. However, **20** was not found when the ozonation of **15** was carried out in CD_3OD. A plausible explanation for the absence of **20** in methanol is suggested. It is reasonable to assume that the intramolecular cyclization of the dimeric zwitterion of the carbonyl oxide **22** needs a suitable geometry. In aprotic solvents of low polarity, such as CD_2Cl_2, the zwitterion would adopt a cyclic conformation in which the positive and negative ends of the zwitterion are close to each other like an intramolecular ion pair. Thus, the intramolecular cyclization can easily take place to give the tetroxane **20**. In polar protic solvents, such as CD_3OD, both charged ends would be stabilized by the solvent molecules through extensive solvation and the zwitterion would adopt a linear conformation which would be unsuitable for the cyclization to take place.

Difficulty was encountered in accounting for the stoichiometry of the ozonation of **15** with the proposed ozonation mechanism in Scheme 17. Although the formation of the oxirane **18** and the dioxetane **19** implies each mole of ozone will consume more than one mole of **15**, it was found that 1.7-1.9 moles of **15** were consumed per mole of ozone. Such a high stoichiometric ratio suggests that a radical chain reaction may be involved in the ozonation of **15**. However, the possibility of a radical chain reaction was ruled out based on the following experiment. In contrast to the ozonation of a mixture of tetramethoxyethene **1** and 2,3-dimethyl-2-butene **5**, where the

amount of 3-hydroperoxy-2,3-dimethyl-1-butene **7** produced was much more than expected,[22] ozonation of a 1:5 mixture of **15** and **5** gave only a minute amount of the allylic hydroperoxide **7**. If a radical chain reaction were involved, the yield of **7** should be much higher. It was found that no dioxetane **19** was produced in the presence of **5**. Similar to the ozonation of a mixture of **8a** and **5** discussed in Chapter II, this result suggested that **7** was produced from the reaction of singlet oxygen with **5** instead from the radical chain oxidation. The higher than expected stoichiometric ratio obtained could be due to a technical problem. As mentioned, the ^{1}H NMR spectrum of the ozonation mixture of **15** contained many small unidentified signals, therefore a large error can be expected in the integrals of these small signals. If the NMR spectrometer used had higher resolution, this problem probably could be averted.

Determination of the stoichiometry of the ozonation of **16** was carried out in a similar manner described previously except a known amount of toluene was used as an internal standard. The amount of **16** consumed by a limited amount of ozone was obtained from the integrals of the signals of the remaining **16** and toluene. As both the remaining **16** and toluene have strong signals, their integrals are fairly accurate. The stoichiometry of the ozonation of **16** was determined to be 1.2 moles of **16** per mole of ozone. This is consistent with the proposed mechanism.

Conclusion

Similar to 1,2-dialkoxy-1,2-diphenylethenes, 1,1,2-trialkoxy-2-phenylethenes are ozonized by a mechanism that combines the ozonolysis and partial cleavage reactions.

The primary ozonides of 1,1,2-trialkoxy-2-phenylethenes cleaves exclusively in the direction to give benzoates and dialkoxycarbonate oxide. Therefore, (alkoxy)phenyldioxiranes cannot be prepared by the ozonation of 1,1,2-trialkoxy-2-phenylethenes.

No evidence was found in this study that dialkoxycarbonyl oxides can cyclize to the corresponding dioxiranes, but the possibility of this cyclization still cannot be ruled out.

Dialkoxycarbonate oxides have poor reactivity toward the participating solvent methanol.

Experimental

The ozonation, singlet oxygen oxidation and other related experiments were carried out in a similar manner as that described previously. The authentic samples of the oxiranes **18** and **23** and the dioxetanes **19** and **24** were also prepared in the same ways as those described previously.

1. Synthesis of 2-[(methoxy)phenyl]methylene-1,3-dioxolane (15)

(±)-α-Methoxyphenylacetic acid [68] Dimethyl sulfate (630 g, 5 mol) was added to an aqueous solution (1 L) of DL-mandelic acid (76 g, 0.5 mol) and sodium hydroxide (400 g, 10 mol) at room temperature. The mixture was stirred overnight and a white precipitate was collected which was then suspended in 500 mL of water. Concentrated sulfuric acid was added dropwise while the suspension was cooled with an ice water bath until the mixture became strongly acidic. The solid dissolved and formed an organic layer that was then extracted with ether (200 mL × 3). The combined ethereal layer was washed with saturated brine, dried, and the solvent was evaporated. Distillation of the residue under reduced pressure gave 33.2 g (40%) of the

product: bp_{12} 150-155 °C, (Lit.[69] bp_{18} 165 °C); ^1H NMR: ($CDCl_3$, TMS): δ 3.45 (s, 3 H, OCH_3), 4.86 (s, 1 H, CH), 7.50 (s, 5 H, Ar), 11.3 (s, 1 H, CO_2H).

2-Bromoethyl α-methoxyphenylacetate A mixture of α-methoxyphenylacetic acid (16.6 g, 0.1 mol), 2-bromoethanol (18.8 g, 0.15 mol), and *p*-toluenesulfonic acid (0.2 g) was heated under reflux in 200 mL of benzene. The water formed was separated by azeotropic distillation until the distillate appeared as one phase. The solvent was evaporated and the residue was distilled under reduced pressure to give the bromo ester (25.1 g, 92%): $bp_{0.9}$ 136-139 °C; ^1H NMR ($CDCl_3$, TMS): δ 3.42 (s, 3 H, OCH_3), 3.38-3.50 (m, 2 H, CH_2Br), 4.35-4.48 (m, 2 H, OCH_2), 4.82 (s, 1 H, CH), 7.30-7.40 (m, 3 H, Ar), 7.40-7.48 (m, 2 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 28.12, 57.35, 64.21, 82.31, 127.16, 128.61, 128.80, 135.81, 170.20; FTIR: 698, 731, 1074, 1107, 1454, 1753, 2937 cm^{-1}; Exact mass calcd for $C_{11}H_{13}BrO_3$: 273.1335. EIMS *m/e*: 273.1331 (M^+); Anal. Calcd for $C_{11}H_{13}BrO_3$: C, 48.37; H, 4.80; Br, 29.26. Found: C, 48.39; H, 4.77; Br, 29.12.

2-[(Methoxy)phenyl]methylene-1,3-dioxolane (15): The bromo ester (1.35 g, 5.0 mmol) was injected slowly to a stirring suspension of sodium hydride (0.13 g, 0.55 mmol) in anhydrous DMSO (10 mL) under argon. The brown reaction mixture was stirred for two hours at room temperature and then was poured into ice-water (50 mL). The resulting mixture was extracted with petroleum ether (20 mL × 3). The combined organic layer was dried over anhydrous sodium sulfate and the solvent was evaporated. Crystallization of the residue from methanol gave the ketene acetal (0.58 g, 61%): mp 58.0-59.5 °C; ^1H NMR ($CDCl_3$, TMS): δ 3.57 (s, 3 H, OCH_3), 4.31-4.50 (m, 4 H, OCH_2CH_2O), 7.05 (t, J = 7.5 Hz, 1 H, Ar), 7.28 (t, J = 7.5 Hz, 2 H, Ar), 7.52(d, J = 8.0 Hz, 2 H, Ar); ^{13}C NMR ($CDCl_3$,

TMS): δ 59.55, 65.43, 67.06, 114.98, 123.45, 124.18, 127.97, 134.47, 155.81; FTIR: 697, 763, 1046, 1140, 1445, 1491, 1594, 1673 cm^{-1}; Exact mass calcd for $C_{11}H_{12}O_3$: 192.07864. EIMS *m/e*: 192.0788 (M^+); Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.30. Found: C, 68.56; H, 6.34.

2. Synthesis of 1,1,2-trimethoxy-2-phenylethene

Phenylglyoxal: The glyoxal was synthesized according to the standard procedure.[70] To a solution of selenium dioxide (59 g, 0.53 mol) in dioxane (300 mL) and water (10 mL) at 55 °C, acetophenone (60 g, 0.5 mol) was slowly introduced. The reaction mixture was stirred at 100°C for four hours. The hot solution was decanted from precipitated selenium and the dioxane and water were removed by distillation through a short column. The residue was distilled under reduced pressure to give the phenylglyoxal (52 g, 77.6%) as a yellow oil: bp_{100}160-165 °C (Lit.[70] bp_{125}142°C); ^1H NMR ($CDCl_3$, TMS): δ 7.40-7.70 (m, 3 H, Ar), 8.14-8.40 (m, 2 H, Ar), 9.75 (s, 1 H, CHO).

2,2-Dimethoxy-1-phenylethanone: Phenylglyoxal (52 g, 0.39 mol), dry methanol (200 mL), and a few drops of concentrated sulfuric acid were heated under reflux overnight in 100 mL of benzene. A small amount of sodium methoxide was added to the cooled mixture to neutralize the acid. Methanol was evaporated and the residue was distilled under reduced pressure. The fraction with bp_{16}133-134 °C (Lit.[71] $bp_{0.25}$85-86 °C) was collected. The product (20 g, 28%) was obtained as a light-yellow oil with 94% purity. The major impurities were 2,2-dimethoxy-2-phenylacetaldehyde and 1,1,2,2-tetramethoxyethylbenzene. These impurities were very difficult to remove even after redistillation. ^1H NMR ($CDCl_3$, TMS): δ 3.46 (s, 6 H, OCH_3), 5.23 (s, 1 H, CH), 7.38-7.62 (m, 3 H, Ar), 8.05-8.18 (m, 2 H, Ar);

^{13}C NMR ($CDCl_3$, TMS): δ 54.42, 103.38, 128.17, 129.45, 133.43, 133.74, 193.25.

1,1,2,2-Tetramethoxyethylbenzene: A by-product of the synthesis of 2,2-dimethoxy-1-phenylethanone. This compound was also prepared in high yield (98%) by heating a mixture of phenylglyoxal and an excess amount of trimethyl orthoformate in methanol with a catalytic amount of sulfuric acid: bp_{20}145-150 °C; ^1H NMR ($CDCl_3$, TMS): δ 3.31 (s, 6 H, OCH_3), 3.43 (s, 6 H, OCH_3), 4.22 (s, 1 H, CH), 7.22-7.40 (m, 3 H, Ar), 7.44-7.56 (m, 2 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 49.68, 57.35, 102.44, 107.05, 127.49, 128.03, 128.30, 137.54.

1,1,2-Trimethoxy-2-phenylethene (16): To a slurry of sodium hydride (1.2 g, 0.05 mol) in dry DMSO (10 mL), 2,2-dimethoxy-1-phenylethanone (7.2 g, 0.04 mol) was added under nitrogen. The reaction mixture was stirred at room temperature for 40 minutes and methyl *p*-toluenesulfonate (8.0 g, 0.043 mol) in dry DMSO (4 mL) was added. The reaction mixture was stirred at room temperature for another two hours and then quenched with methanol (0.5 mL). Cold water (50 mL) was added and the product was extracted with ether (20 mL × 3). The combined ethereal layer was washed with water (20 mL), brine and dried over anhydrous sodium carbonate. The solvent was evaporated and the residue was distilled under reduced pressure. The light-yellow distillate was redistilled to give the product as a colorless oil (4.3 g, 55%). Several recrystallizations from methanol at −78 °C were unsuccessful in removing a small amount of impurities (5%) from the product: bp_{14}125-126 °C; ^1H NMR ($CDCl_3$, TMS): δ 3.56 (s, 3 H, OCH_3), 3.64 (s, 3 H, OCH_3), 3.70 (s, 3 H, OCH_3), 7.30-7.42 (m, 3 H, Ar), 7.55-7.66 (m, 2 H, Ar); ^{13}C NMR (CD_2Cl_2, TMS): δ 56.87,

58.08, 59.66, 126.53, 126.57, 127.71, 128.44, 134.78, 154.33. Exact mass calcd for $C_{11}H_{14}O_3$: 194.0943. EIMS *m/e*: 194.0940 (M^+).

3. Products isolated from the ozonation reaction mixtures

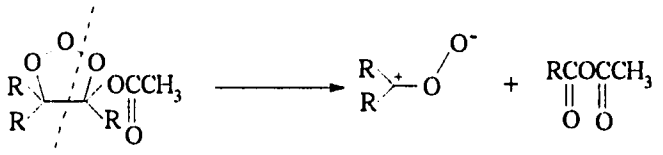
2-Benzoyl-2-methoxy-1,3-dioxolane (21): The ozonation reaction mixture of 0.48 g (2.5 mmol) of **15** in 10 mL of CH_2Cl_2 at −20 °C was allowed to stand overnight at room temperature. The solvent was evaporated under reduced pressure and the rearrangement product was isolated as an oil (0.06 g, 11.5%) from the residue by flash column chromatography on silica gel with 15% ethyl acetate in hexane as eluent. ^{1}H NMR ($CDCl_3$, TMS): δ 3.42 (s, 3 H, OCH_3), 4.08-4.14 (m, 2 H, CH_2), 4.22-4.28 (m, 2 H, CH_2), 7.35-7.58 (m, 3 H, Ar), 8.10-8.18 (m, 2 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 49.31, 65.98, 118.22, 128.19, 130.63, 133.09, 133.40, 190.04; Exact mass calcd for $C_{11}H_{12}O_4$: 208.0736. EIMS *m/e*: 177.0549 $(M - OCH_3)^+$, 105.0344 ($C_6H_5C{=}O^+$); CIMS *m/e*: 226 ($M + NH_4^+$), 177 $(M - OCH_3)^+$, 105 ($C_6H_5C{=}O^+$).

1,4,6,7,9,12,13,14-Octaoxadispiro[4.2.4.2]tetradecane (20): A solution of **15** (1.92 g, 0.01 mol) in CH_2Cl_2 (40 mL) was completely ozonized at −78 °C. The reaction mixture was allowed to stand at room temperature in an unstoppered flask to let the solvent slowly evaporate away. After two days, the tetroxane was crystallized from the ozonation reaction mixture. The sticky residue was triturated with 10 mL of cold methanol and the solid was collected by filtration. Recrystallization from methanol afforded 0.03 g (0.13 mmol, 1.3%) of the tetroxane as a white powder: mp 195.0-197.0 °C dec; ^{1}H NMR ($CDCl_3$, TMS): δ 4.24(s, CH_2); ^{13}C NMR ($CDCl_3$, TMS): δ 66.52, 143.11; Exact mass calcd for $C_6H_8O_8$: 208.0219. EIMS *m/e*:

226 ($M + NH_4^+$); Anal. Calcd for $C_6H_8O_8$: C, 34.625; H, 3.87. Found: C, 34.35; H, 3.72.

IV. OZONATION OF *E*-1,2-DIACETOXY-1,2-DIPHENYLETHENE AND *E*-1-ACETOXY-2-METHOXY-1,2-DIPHENYLETHENE

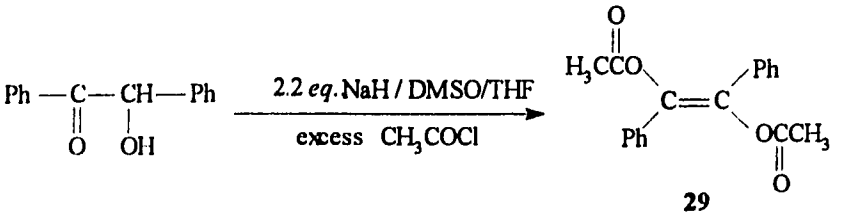
The initial purpose of this part of the study was to investigate whether (acetoxy)phenylcarbonyl oxide **28** generated from ozonation of an alkene can isomerize to the corresponding dioxirane. Earlier reports on the ozonolysis of vinyl acetates[72] indicated that the acetoxy substituted carbonyl oxides cannot be prepared in this way because the cleavage of the primary ozonide of a vinyl acetate occurs in the direction to give an anhydride and a dialkylcarbonyl oxide. No acetoxy substituted carbonyl oxides were formed, eq 32.



(32)

If 1,2-diacetoxy substituted alkenes are ozonized by Criegee mechanism, acetoxy substituted carbonyl oxides will be generated. Therefore (acetoxy)phenylcarbonyl oxide **28** should be generated from the ozonolysis of 1,2-diacetoxy-1,2-diphenylethene **29**. This alkene was synthesized by diacetylation of the benzoin dianions as shown in eq 33 although the yield was only 10%. Only one of the two possible isomers was obtained from the diacetylation, but irradiation of a solution of this isomer with a medium pressure mercury lamp resulted in the formation of a mixture of the two isomers.

The first isomer isolated from the diacetylation reaction was tentatively assigned to be the *E* isomer, and the new isomer produced by the irradiation



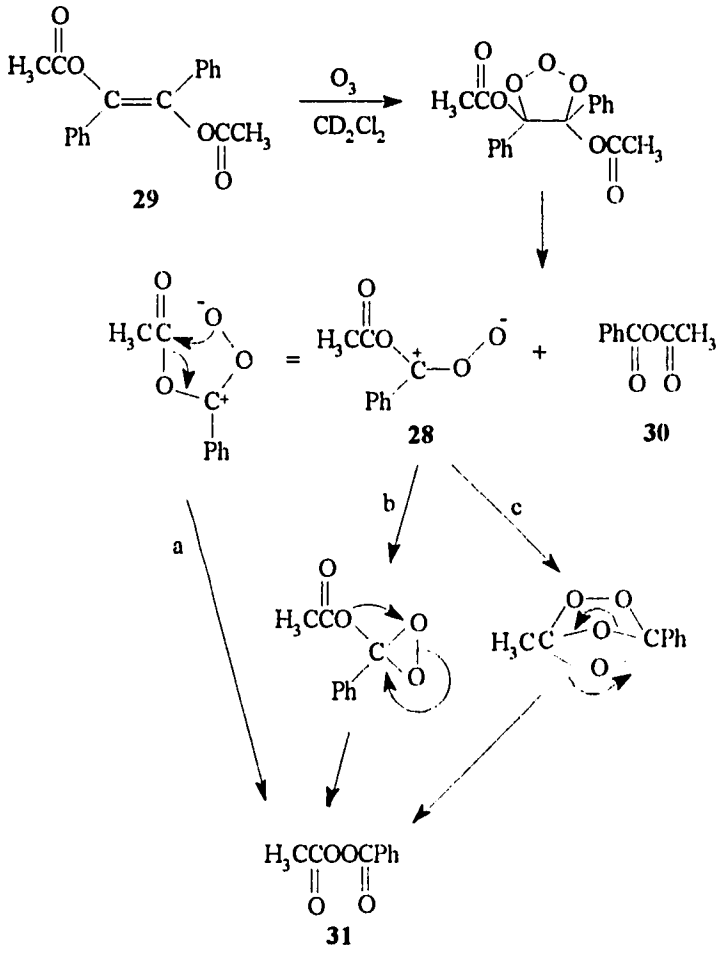
(33)

29

of the first isomer was assigned to be the *Z* isomer. These assignments were based on the chemical shifts and the multiplicities of the ^{1}H NMR signals of the phenyl groups. As discussed in Chapter II, the ^{1}H NMR signals of the phenyl groups of the *Z* isomers of 1,2-dialkoxy-1,2-diphenylethenes *Z*-**8a-c** are much simpler and occur at higher fields than those of their counterparts. For example, the phenyl groups of *Z*-**8a** give a singlet at δ 7.17 while the phenyl groups of *E*-**8a** give two multiplets at δ 7.25-7.48 and δ 7.60-7.70. Applying this rule to *E*- and *Z*-1,2-diacetoxy-1,2-diphenylethene, we assigned the first isomer to be the *E* isomer because its phenyl groups give two multiplets at δ 7.30-7.42 and δ 7.50-7.58 and the new isomer to be the *Z* isomer because its phenyl groups give a singlet at δ 7.30. In agreement with these assignments, the first isomer has a larger Rf value on the TLC plate, indicating it is less polar.

Delivering a mixture of ozone and oxygen into a CD_2Cl_2 solution of **29** at various temperatures results in the formation of only two products, acetic benzoic anhydride **30** and acetyl benzoyl peroxide **31**, in equal amounts. These two products were identified by comparison of the ^{1}H NMR spectra of the reaction mixtures with those of authentic samples. The authentic sample of **30** was prepared by the reaction of sodium benzoate with acetyl chloride in ether.[73] The authentic sample of **31** was prepared by atmospheric oxidation of a mixture of benzaldehyde and acetic anhydride in the presence of a trace of dibenzoyl peroxide.[74] Acetic benzoic anhydride **30** gives a singlet at δ 2.37

and acetyl benzoyl peroxide **31** gives a singlet at δ 2.26. No signals that could be assigned to other products were found in the ^{1}H NMR spectra of the reaction mixtures. The formation of these two products can be accounted for by the mechanisms as illustrated in Scheme 18.



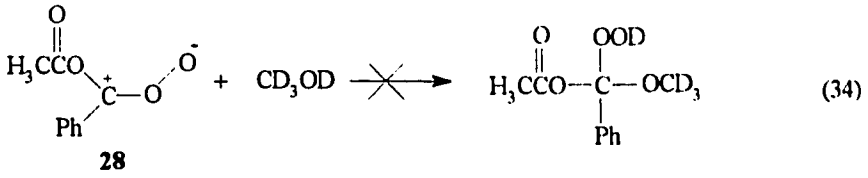
Scheme 18. Proposed mechanisms for ozonation of *E*-1,2-diacetoxy-1,2-diphenylethene

The initial reaction of ozone and **29** gives the primary ozonide which then decomposes to the anhydride **30** and the carbonyl oxide **28**. Three alternative reaction pathways can account for the formation of **31** from **28** as shown in Scheme 18. The intramolecular nucleophilic substitution to give the

peroxyanhydride **31** directly (pathway *a*) is most likely to occur because the negatively charged oxygen is a good nucleophile, the OC^+ moiety is a good leaving group,[75] and a five-membered transition state is involved. The other two indirect pathways are analogous to those proposed to account for the anhydride formation in the ozonation of certain alkynes.[76] In pathway *b*, cyclization of the carbonyl oxide gives the corresponding dioxirane which then rearranges to the peroxyanhydride **32**. Since dioxiranes are known to be stable at low temperature for several days,[59] the rearrangement of the dioxirane to give the peroxyanhydride **32** as shown in pathway *b* under the reaction conditions is not likely to occur. If this argument is correct, the implication is that (acetoxy)phenylcarbonyl oxide cannot isomerize to the corresponding dioxirane. In pathway *c*, intramolecular cycloaddition of the nascent carbonyl oxide with the adjacent ester group gives a bicyclic intermediate.[77] Such a bicyclic intermediate, however, can be expected to be a very strained molecule and will not be easily formed. Therefore, the peroxyanhydride **32** is not produced from pathway *c* either.

Ozonation of **29** in CD_3OD at various temperatures also gives equal amounts of the anhydride **30** and the peroxide **31** as observed from the ^1H NMR spectra of the reaction mixtures. The chemical shifts of the acetyl groups of **30** and **31** in CD_3OD are at δ 2.36 and 2.24, respectively. The presence of these two products is further confirmed by two doublets at around δ 8.0, which are due to the ortho protons of the benzoyl groups of **30** and **31**. The (acetoxy)phenylcarbonyl oxide-CD_3OD adduct should not give these signals. The possibility that **31** was produced from the decomposition of the (acetoxy)phenylcarbonyl oxide-CD_3OD adduct can be ruled out since only **30** and **31** were found even when **29** was ozonized at −78 °C in CD_3OD and the reaction mixture was rapidly analyzed by ^1H NMR at −70 °C. Therefore, like

(methoxy)phenylcarbonyl oxide **14a**, (acetoxy)phenylcarbonyl oxide **28** is another carbonyl oxide that cannot be captured by methanol, eq 34.



28 (34)

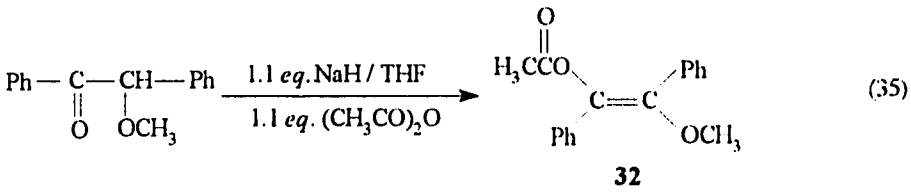
An unexpected discovery in the ozonation of 1,2-diacetoxy-1,2-diphenylethene **29** is that **29** reacts very slowly with ozone. It was found that during the process of ozonation ozone kept escaping from the reaction mixture even though most of **29** was still unconsumed. This phenomenon is in contrast to the ozonation of electron-rich alkenes, such as **8a**, or even simple alkenes but is also observed in the ozonation of electron-deficient alkenes, such as fumarates. It was reported that the relative reactivity of diethyl fumarate to styrene toward ozone at 0 °C was 0.26.[78] Competitive ozonation of equivalent amounts of **29** and diethyl fumarate showed that **29** is only 0.34 times as reactive as diethyl fumarate toward ozone in $CDCl_3$ at room temperature (11% of **29** and 29% of diethyl fumarate were consumed by a limited amount of ozone). Like electron-deficient alkenes, **29** is also difficult to be epoxidized by dioxiranes. No reaction was observed between **29** and (methoxy)phenyldioxirane **13a** at −20 °C. However, at the same temperature a smooth reaction was observed between methyl *E*-cinnamate and **13a** as shown in Chapter II. A slow reaction between **29** and **13a** occurred when the reaction mixture was warmed to room temperature. It took about 0.5 hours to finish the reaction and a singlet at δ 1.89 was found in the ^1H NMR spectrum of the reaction mixture. This signal was tentatively assigned to the methyl groups of the corresponding oxirane of **29**. Since electron-withdrawing

substituents reduce the reactivity of an alkene toward electrophilic reagents, these experiments indicate that the two acetoxy groups are strong electron-withdrawing substituents instead of electron-donating substituents and **29** is an electron-deficient alkene. This conclusion is in contrast to that of a reference[79] in which vinyl acetate was classified as an electron-rich alkene. In this reference, electron-rich alkenes and electron-deficient alkenes were classified according to their experimental ionization potentials. The ionization potential of ethene is 10.51 eV. The alkenes which have lower ionization potentials than ethene were classified as electron-rich alkenes, e.g., 2-butene (9.13 eV) and methyl vinyl ether (9.08 eV). The alkenes which have higher ionization potentials than ethene were classified as electron-deficient alkenes, e.g., methyl acrylate (10.72 eV). The ionization potential of vinyl acetate was given by these authors to be 10.76 eV, which is higher than that of ethene and even higher than that of the electron-deficient methyl acrylate. However, vinyl acetate was still classified as an electron-rich alkene by the authors without any explanation.

In the ozonation of *E*-1,2-dimethoxy-1,2-diphenylethene *E*-**8a**, it was found that the epoxidation of *E*-**8a** by the reaction intermediate (methoxy)phenyldioxirane **13a** is very difficult to avoid because the electron-rich *E*-**8a** has high reactivity toward the electrophilic dioxirane **13a**. In the ozonation of *E*-1,2-dimethoxy-1,2-bis(*p*-nitrophenyl)ethene *E*-**8e**, it was found that the reactivity of this alkene is greatly reduced due to introducing the electron-withdrawing nitro groups at the para position of the benzene rings. Because the acetoxy group is an electron-withdrawing substituent, the alkene 1-acetoxy-2-methoxy-1,2-diphenylethene **32** would be expected to be less reactive toward dioxiranes than *E*-**8a**. If the ozonation of **32** can produce the dioxirane **13a**, **32** should react slower with **13a** than *E*-**8a**. Hence, this

may be a good method for generating the dioxirane **13a** with less interference from the byproducts. But it was unknown whether the primary ozonide of **32** will cleave in the desired direction to give the anhydride **30** and (methoxy)phenylcarbonyl oxide **14a** or in the alternative direction to give methyl benzoate and (acetoxy)phenylcarbonyl oxide. This was also worth studying.

The alkene **32** was synthesized by O-acetylation of the benzoin methyl ether anion in 15% yield, eq 35.



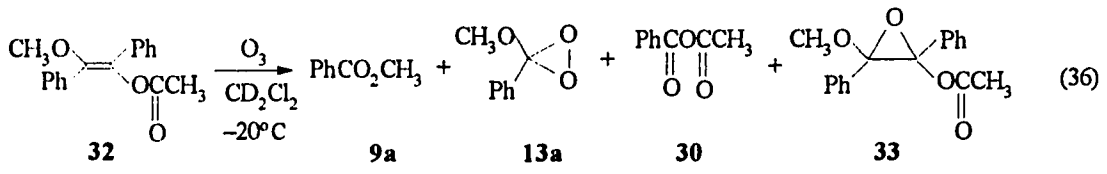
32 (35)

Again, only one isomer was isolated from the reaction mixture. The ^{1}H NMR signals of the methoxy and acetyl groups of this isomer are at δ 3.48 and 1.98, respectively. It was expected that irradiation of a CD_2Cl_2 solution of this isomer should give a mixture of two isomers. Indeed, the ^{1}H NMR spectrum of the irradiated reaction mixture contained two sets of signals. One was due to the original isomer, the other was assumed to be due to the new isomer. The ^{1}H NMR signals of the methoxy and acetyl groups of the new isomer are at δ 3.42 and 2.26, respectively. The ^{1}H NMR spectrum of the new isomer has a sharp singlet at δ 7.30 for one of the two phenyl groups. Based on the same reasons for the assignments of *E*- and *Z*-1,2-diacetoxy-1,2-diphenylethene, the original isomer was tentatively assigned to be the *E* isomer and the new isomer to be the *Z* isomer. According to these assignments, the signal of the methoxy group of the *Z* isomer is at a higher

field (δ 3.42) than that of the *E* isomer (δ 3.48) because the methoxy group of *Z*-1-acetoxy-2-methoxy-1,2-diphenylethene is located in the shielding zone of the nearby carbonyl group. This is in contrast to those of *E*- and *Z*-1,2-dimethoxy-1,2-diphenylethene **8a** where the signal of the methoxy groups of *Z*-**8a** is at a lower field (δ 3.59) than that of *E*-**8a** (δ 3.38).

Competitive ozonation and dioxirane epoxidation of 1:1 mixtures of **32** and *E*-**8a** at −78 °C in CD_2Cl_2 showed that **32** is only 0.09 times as reactive as *E*-**8a** toward ozone (12.7% of **32** and 77.3% of *E*-**8a** were consumed by a limited amount of ozone) and 0.23 times as reactive as *E*-**8a** toward the dioxirane **13a** (10.1% of **32** and 36.8% of *E*-**8a** were consumed by a limited amount of the dioxirane). Competitive singlet oxygen oxidation of *E*-**8a** and **32** at 0 °C showed that **32** is only 0.08 times as reactive as *E*-**8a** toward singlet oxygen (7.0% of **32** and 61.9% of *E*-**8a** were consumed). As expected, **32** is indeed much less reactive than *E*-**8a** toward electrophilic agents.

The ozonation of **32** in CD_2Cl_2 at −20 °C yields four products: methyl benzoate **9a**, the dioxirane **13a**, the anhydride **30**, and 1-acetoxy-2-methoxy-1,2-diphenyloxirane **33** as shown in eq 36. When the reaction temperatures



32 **9a** **13a** **30** **33** (36)

are below −20 °C, *cis*- and *trans*-3,6-dimethoxy-3,6-diphenyl-1,2,4,5-tetroxane **12a** begin to appear. Acetyl benzoyl peroxide **31** and the corresponding dioxetane of **32** were never detected from the reaction mixtures by ^1H NMR. The product distributions in the ozonation of **32** under various conditions are summarized in Table 17.

Table 17. Product distribution from the ozonation of *E*-1-acetoxy-2-methoxy-1,2-diphenylethene in CD_2Cl_2

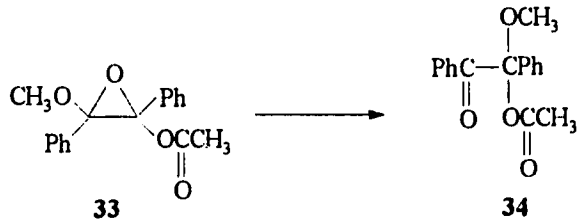
Conc.	Method	Temp.	Products, moles per mole of **32**				
M		°C	**9a**	**13a**	**30**	**33**[a]	**12a**[b]
0.005	normal	–20	0.22	0.56	0.78	0.22	0.00
0.05			0.45	0.11	0.56	0.44	0.00
0.10			0.47	0.06	0.52	0.47	0.00
0.20			0.50	0.00	0.50	0.50	0.00
0.05		–50	0.41	0.13	0.58	0.41	0.02
0.02[c]		–78	0.28	0.12	0.72	0.28	0.16
0.005	inverse	–20	0.10	0.81	0.91	0.09	0.00
0.05			0.21	0.59	0.80	0.20	0.00

a. The sum of the yields of the oxirane **33** and its rearrangement product, 2-acetoxy-2-methoxy-1,2-diphenylethanone **34**.

b. About equal amounts of *cis* and *trans*.

c. The concentration is restricted by the solubility of the alkene at this temperature.

The oxirane **33** was identified by comparison of the ^1H NMR spectrum of the reaction mixture with that of an authentic sample prepared by the epoxidation of **32** with the dioxirane **13a**. The signals at δ 3.31 and 1.83 were assigned to the methoxy and acetyl groups of **33**, respectively. In many cases, the formation of the oxirane **33** was represented by the presence of the oxirane **33** itself and its rearrangement product, 2-acetoxy-2-methoxy-1,2-diphenylethanone **34**, eq 37. The rearrangement product **34** was isolated from



33 **34** (37)

the reaction mixture by flash chromatography on silica gel and its structure was determined by NMR, IR, and mass spectroscopies. It gives two singlets at δ 3.22 and 2.16 for the methoxy and acetyl groups and a doublet-like signal at δ 7.92-7.95 for the ortho protons of the benzoyl group in the ^{1}H NMR spectrum. The signals at δ 103.75 and 192.83 in the ^{13}C NMR spectrum indicate the presence of a carbon atom attached to two oxygen atoms and a ketone carbonyl carbon atom, respectively. Electron impact ionization mass spectroscopy gave the exact masses of the $(M - OCOCH_3)^+$ and $C_6H_5CO^+$ ions, while the chemical ionization with NH_4^+ afforded the $(M + NH_4^+)$ ion at *m/e* 302.

As seen from Table 17, normal ozonation of a 0.2 *M* solution of **32** at −20 °C in CD_2Cl_2 produces only three products: methyl benzoate **9a**, the anhydride **30**, and the oxirane **33**. The yields of these three products are exactly the same, i.e., 0.5 moles each from each mole of **32**. The yield of the dioxirane **13a** increases as the initial concentration of **32** is lowered. In the inverse ozonation of **32** at −20 °C, the yield of **13a** can be as high as 0.81 moles per mole of **32** consumed (i.e., 81% yield). Methyl benzoate **9a** (10%) and the oxirane **33** (9%) are minor products here. The yield of **13a** is higher and the amounts of the byproducts are smaller than those in the inverse ozonation of *E*-**8a**. At this point, the inverse ozonation of **32** is a better way to produce the dioxirane **13a**. Although the yield of **32** obtained (15%) by acetylation of the benzoin methyl ether anion is not satisfactory, it is possible to obtain a higher yield by changing reaction conditions because no attempt was made to optimize the yield at this stage.

It is worth noting that methyl benzoate **9a** and the oxirane **33** are always produced in equal amounts. This observation implies that methyl benzoate **9a** and the oxirane **33** are exclusively produced from the

epoxidation of the starting alkene **32** by the dioxirane **13a**. Unlike the previous cases studied, no direct ozone epoxidation is involved.

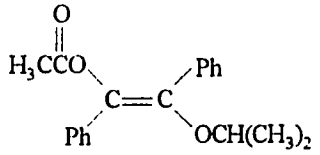
The formation of the tetroxanes **12a** at lower reaction temperatures could be via the zwitterionic intermediate of the dimer of (methoxy)phenylcarbonyl oxide. In Chapter II, it was suggested that the zwitterionic intermediate might decompose to two molecules of methyl benzoate and one molecule of singlet oxygen. This hypothesis could not be examined in the study of the ozonation of *E*- and *Z*-1,2-dimethoxy-1,2-diphenylethene (*E*- and *Z*-**8a**), but the results of the ozonation of **32** provide strong evidence against it. If this decomposition did occur, it would provide another source for the formation of methyl benzoate and therefore the yields the benzoate would be higher than those of the oxirane when **32** is ozonized at low temperatures. However, the results of the ozonation of **32** showed that even when the tetroxanes **12a** are produced the yields of methyl benzoate are still the same as those of the oxirane. Thus, the decomposition of the zwitterionic intermediate does not occur.

In those ozonation reactions carried out at –20 °C, the yields of the anhydride **30** are equal to the sum of the yields of methyl benzoate **9a** and the dioxirane **13a**; while in those reactions carried out below –20 °C, the yields of the anhydride **30** are equal to the yields of the benzoate **9a** plus the yields of the dioxirane **13a** plus two times of the yields of the tetroxanes **12a**. This indicates that the cleavage of the primary ozonide of **32** must exclusively occur in such a direction to give the anhydride **30** and (methoxy)phenylcarbonyl oxide **14a**, which is the common precursor of the dioxirane **13a** and the tetroxanes **12a**. This is the direction that was hoped for at the beginning. If the primary ozonide cleaved in the alternative direction, (acetoxy)phenylcarbonyl oxide **28** produced would lead to the formation of

the peroxide **31** and the amount of methyl benzoate **9a** would not be equal to that of the oxirane **33**. This was not observed.

The product formation and the relative amounts of the products can be well accounted for by the mechanism as illustrated in Scheme 19. Cleavage of the primary ozonide of **32** gives the anhydride **30** and (methoxy)phenylcarbonyl oxide **14a**. The carbonyl oxide **14a** then cyclizes to the dioxirane **13a** or reacts with another molecule of **14a** to form the tetroxanes *cis*- and *trans*-**12a** when the temperature is lower than –20 °C. In the normal ozonation, the reaction of the dioxirane **13a** with the unreacted starting alkene **32** gives the oxirane **33** and the benzoate **9a**. In the inverse ozonation, most of the dioxirane **13a** remains unreacted.

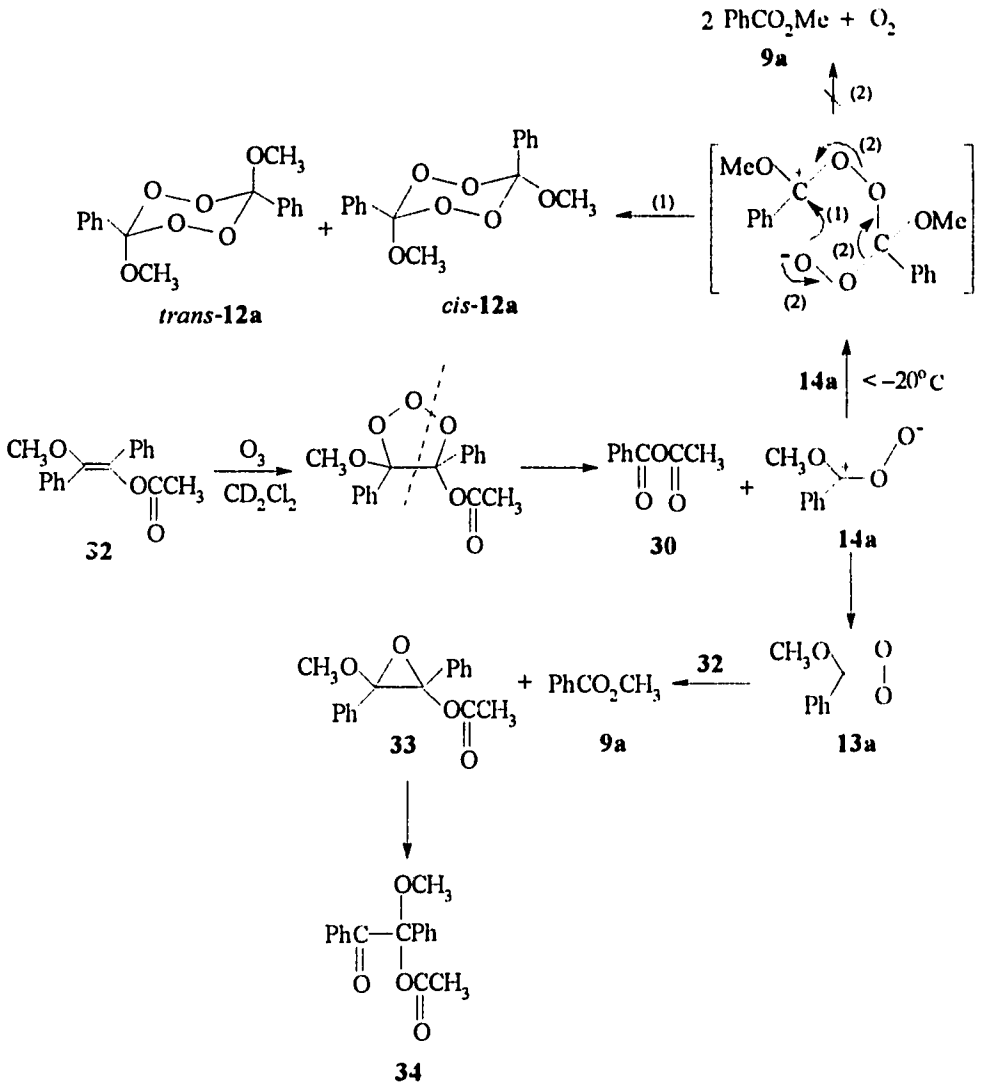
Based on the knowledge accumulated from the above study, we designed an alkene, *E*-1-acetoxy-2-isopropoxy-1,2-diphenylethene,



which combines both the electron-withdrawing and sterically bulky substituents. This alkene can be prepared by acetylation of the benzoin isopropyl ether anion. It was expected that just by simple normal ozonation of this alkene a high yield of (isopropoxy)phenyldioxirane **13c** can be obtained. A preliminary experiment gave a very promising result but no detailed study has been carried out on this alkene yet.

The conclusions of this part of the study are as follows.

1. No evidence was found that (acetoxy)phenylcarbonyl oxide can cyclize to the corresponding dioxirane.
2. (Acetoxy)phenylcarbonyl oxide is another carbonyl oxide that cannot be captured by methanol.



Scheme 19. Ozonation mechanism of *E*-1-acetoxy-2-methoxy-1,2-diphenylethene

3. Because the acetoxy groups serve as electron-withdrawing substituents, 1,2-diacetoxy-1,2-diphenylethene **29** is an electron-deficient alkene.

4. Substitution of one of the methoxy groups of *E*-1,2-dimethoxy-1,2-diphenylethene *E*-**8a** with an electron-withdrawing acetoxy group gives *E*-1-acetoxy-2-methoxy-1,2-diphenylethene **32** which has greatly reduced reactivity toward ozone and dioxiranes.

5. The primary ozonide of 1-acetoxy-2-methoxy-1,2-diphenylethene exclusively cleaves in the direction to give acetic benzoic anhydride **30** and (methoxy)phenylcarbonyl oxide **14a**. The latter can cyclize to the dioxirane **13a** or dimerize to the tetroxanes **12a**.

6. The zwitterionic intermediate of the dimer of (methoxy)phenylcarbonyl oxide cannot decompose to methyl benzoate and singlet oxygen.

7. The inverse ozonation of 1-acetoxy-2-methoxy-1,2-diphenylethene **32** is a better way to produce (methoxy)phenyldioxirane **13a** than the inverse ozonation of 1,2-dimethoxy-1,2-diphenylethene **8a**.

Experimental

The ozonation, singlet oxygen oxidation, and other related reactions were carried out in the same manner described previously.

***E*-1,2-Diacetoxy-1,2-diphenylethene (29)** Benzoin (4.24 g, 20 mmol) dissolved in 50 mL of THF was added to a suspension of sodium hydride (1.1 g, 44 mmol) in 5 mL of DMSO at room temperature under nitrogen. The reaction mixture was stirred at room temperature for 30 minutes, then an excess amount of acetyl chloride (5 mL, 88 mmol) was injected. The dark-blue color of the benzoin dianion disappeared immediately and a white NaCl precipitate formed. After ten minutes, THF and the excess acetyl chloride were evaporated under reduced pressure. The residue was poured into water (100 mL) and extracted with ether (40 mL × 3). The combined ethereal layer was washed with water, brine and dried over anhydrous sodium sulfate. The ether was evaporated and the residue was crystallized from methanol. The crude product was purified by

recrystallization from methanol to give the product as a white granular solid (0.6 g, 10%): mp 143-144 °C; ^{1}H NMR ($CDCl_3$, TMS): δ 2.06 (s, 6 H, $COCH_3$), 7.30-7.42 (m, 6 H, Ar), 7.50-7.58 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 20.90, 127.45, 128.36, 128.58,133.48, 139.67, 168.73; FTIR: 1112, 1200, 1211, 1752 cm^{-1}; Exact mass calcd for $C_{18}H_{16}O_4$: 296.1049. EIMS *m/e*: 296.1047 (M^+); Anal. Calcd for $C_{18}H_{16}O_4$: C, 72.95; H, 5.45. Found: C, 72.94; H, 5.43.

Z-1,2-Diacetoxy-1,2-diphenylethene This compound was not isolated. Irradiation of a CD_2Cl_2 solution of the *E* isomer (10 mg) in a NMR tube with a medium pressure mercury lamp at room temperature for one hour gave a mixture of the *E* and *Z* isomers. Since the ^{1}H NMR signals of the *E* and *Z* isomers do not overlap, the ^{1}H NMR signals of the *Z* isomer were drawn from the spectrum of the reaction mixture.

^{1}H NMR (CD_2Cl_2): δ 2.10 (s, 6 H, $COCH_3$), 7.30(s, 10 H, Ar).

Acetic benzoic anhydride (30)[73] The authentic sample of the mixed anhydride was prepared by the slow addition of an excess amount of acetyl chloride (10 mL, 0.18 mol) to sodium benzoate (1.44 g, 0.01 mol) in 100 mL of ether at room temperature. Sodium chloride was filtered off. Evaporation of the solvent and the excess acetyl chloride under reduced pressure gave the product as a colorless liquid (1.49 g, 91%). ^{1}H NMR ($CDCl_3$, TMS): δ 2.37 (s, 3 H, $COCH_3$), 7.40-7.65 (m, 3 H, Ar), 8.00-8.10 (m, 2 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 22.34, 128.34, 128.79, 130.41, 134.41, 162.91, 166.46; Exact mass calcd for $C_9H_8O_3$: 164.0473. EIMS *m/e*: 164.0474 (M^+).

Acetyl benzoyl peroxide (31)[74] A mixture of benzaldehyde (5.3 g, 0.05 mol), acetic anhydride (10.2 g. 0.1 mol) and a trace of benzoyl peroxide was stirred vigorously for two days at room temperature while exposed to air. The reaction mixture was poured into 100 mL of cold water. A yellow oil

separated and soon crystallized. The solid was isolated by filtration and purified by recrystallization from benzene-pentane to give the peroxide (0.9 g, 10%): mp 35-36 °C (Lit.[80] mp 37-38 °C); ^{1}H NMR ($CDCl_3$, TMS): δ 2.26 (s, 3 H, OCH_3), 7.40-7.65 (m, 3 H, Ar), 7.94-8.00 (m, 2 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 16.59, 128.73, 129.65, 134.23, 162.23, 166.16.

***E*-1-Acetoxy-2-methoxy-1,2-diphenylethene (32)** Benzoin methyl ether (4.52 g, 20 mmol) dissolved in 50 mL of THF was added to a suspension of sodium hydride (0.53 g, 22 mmol) in 10 mL of THF at room temperature under nitrogen. After 30 minutes, acetic anhydride (2.24 g, 22 mmol) was added. The reaction mixture was stirred at room temperature overnight. The solvent was evaporated under reduced pressure and 100 mL of water was added to the residue. The mixture was extracted with ether (60 mL × 3). The combined ethereal layer was washed with water, brine and dried over anhydrous sodium sulfate. The ether was evaporated and the residue was crystallized from methanol to afford the crude product. Recrystallization from methanol gave the product as a white granular solid (0.80 g, 15%): mp 99.5-100.0 °C; ^{1}H NMR ($CDCl_3$, TMS): δ 1.98 (s, 3 H, $COCH_3$), 3.48 (s, 3 H, OCH_3), 7.30-7.50 (m, 8 H, Ar), 7.62-7.70 (m, 2 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 20.78, 57.98, 126.57, 127.70, 128.19, 128.33, 128.60, 128.76, 132.98, 133.92, 134.62, 148.72, 169.68; FTIR: 1126, 1210, 1756 cm^{-1}; Exact mass calcd for $C_{17}H_{16}O_3$: 268.1099. EIMS *m/e*: 268.1100 (M^+); Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.09; H, 6.01. Found: C, 76.09; H, 6.00.

***Z*-1-Acetoxy-2-methoxy-1,2-diphenylethene** This compound was not isolated from the reaction mixture of irradiation of a CD_2Cl_2 solution of the *E*-isomer. The ^{1}H NMR signals of this compound were obtained in the same way as those of *Z*-1,2-diacetoxy-1,2-diphenylethene. ^{1}H NMR

(CD_2Cl_2): δ 2.26 (s, 3 H, $COCH_3$), 3.42 (s, 3 H, OCH_3), 7.04-7.20 (m, 5 H, Ar), 7.30 (s, 5 H, Ar).

2-Acetoxy-2-methoxy-1,2-diphenylethanone (34) A stream of ozone was introduced to a solution of *E*-1-acetoxy-2-methoxy-1,2-diphenylethene **32** (0.27 g, 1 mmol) in 5 mL of CH_2Cl_2 at room temperature until the alkene was completely consumed. The solvent was evaporated and the residue was separated by flash chromatography (silica gel, 10% ethyl acetate in hexane) to give the product (0.12 g, 42%) as a colorless oil. ^1H NMR ($CDCl_3$, TMS): δ 2.18 (s, 3 H, $COCH_3$), 3.22 (s, 3 H, OCH_3), 7.30-7.55 (m, 6 H, Ar), 7.55-7.70 (m, 2 H, Ar), 7.89-8.00 (m, 2 H, Ar); ^{13}C NMR ($CDCl_3$, TMS): δ 21.14, 51.31, 104.19, 127.27, 128.43, 129.13, 129.80, 129.93, 132.80, 135.26, 135.32, 168.89, 193.13; FTIR: 1228, 1700, 1758 cm^{-1}; Exact mass calcd for $C_{17}H_{16}O_4$: 284.1049. EIMS *m/e*: 241.0866 ($M - OCOCH_3)^+$, 105.0344 ($C_6H_5CO^+$); CIMS *m/e*: 302 ($M + NH_4^+$).

V. INVESTIGATION OF OTHER CARBONYL OXIDES

A. Ozonation of 1,2-dialkyl-1,2-dialkoxy alkenes and 1,2-dialkyl-1,2-diaryl alkenes

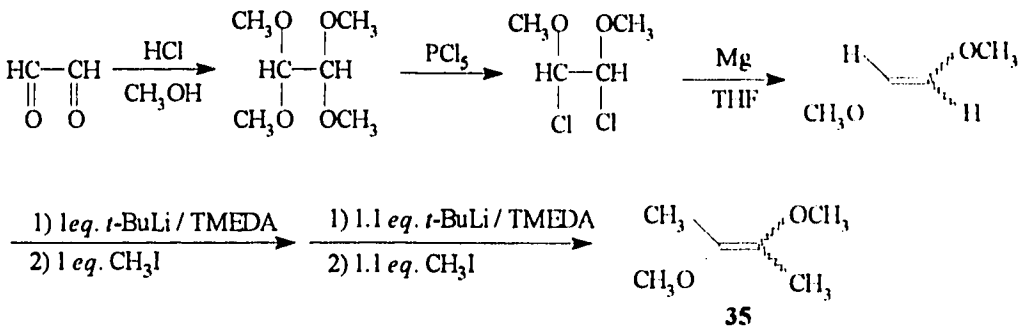
The previous studies showed that the (alkoxy)arylcarbonyl oxides generated from the ozonation of suitable alkenes have two special properties. First, they cannot be trapped by methanol. Second, they can cyclize to the corresponding (alkoxy)aryldioxiranes. Obviously, these special properties must result from either the existence of the two substituents, i.e., aromatic aryl group and alkoxy group, or only one of them. It is then very natural to ask whether (alkoxy)alkylcarbonyl oxides or (alkyl)arylcarbonyl oxides generated under the same conditions can cyclize to their corresponding dioxiranes. Each of the carbonyl oxides has one substituent which is the same as one of the substituents of (alkoxy)arylcarbonyl oxides. To find the answer to this question, the following investigations were carried out.

Results and Discussion

1. Ozonation of two 1,2-dialkyl-1,2-dialkoxy alkenes

The ozonation of 1,2-dialkyl-1,2-dialkoxy alkenes was expected to generate (alkoxy)alkylcarbonyl oxides. Therefore, the ozonation of 2,3-dimethoxy-2-butene **35** and 2,3-dimethyl-1,4-dioxene **36** were examined.

It was reported that vinyl ether derivatives could be prepared by alkylation of vinyl ether anions.[81] By this method, a mixture of *E*- and *Z*-**35** was synthesized by successive methylation of a mixture of *E*- and *Z*-1,2-dimethoxyethene as illustrated in Scheme 20. After purification with



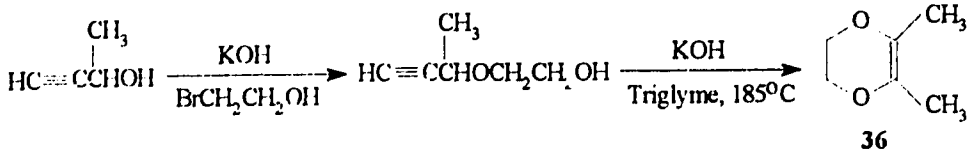
TMEDA: tetramethylethylenediamine

Scheme 20. Synthesis of *E*- and *Z*-2,3-dimethoxy-2-butene

preparative GLC, the combined yield of the two isomers was 37.9%. Separation of the two isomers was not achieved. The ^{1}H NMR spectrum of **35** obtained showed that the major product gives two singlets with identical intensities at δ 1.77 and 3.42 in CD_2Cl_2 and the minor one gives those at δ 1.71 and 3.50. It has been reported[82] that the ^{1}H NMR spectrum of a mixture of *Z*- and *E*-**35** contains two sets of signals: one at δ 1.74 and 3.51 and the other at δ 1.82 and 3.42 in acetone-D_6. According to the ^{1}H NMR spectrum, the final products obtained still contained some unidentified impurities. The total integrals of the signals of these impurities accounted for 13.3% of the total integrals of all signals.

Following the procedure described in the literature,[83] 2,3-dimethyl-1,4-dioxene **36** was synthesized in 48 % yield by isomerization and cyclization of 2-(3-butyn-2-yloxy)ethanol in the presence of base at high temperature as shown in Scheme 21. The crude product was purified by preparative GLC. The purified **36** gives two singlets at δ 1.68 and 3.95 in the ^{1}H NMR spectrum.

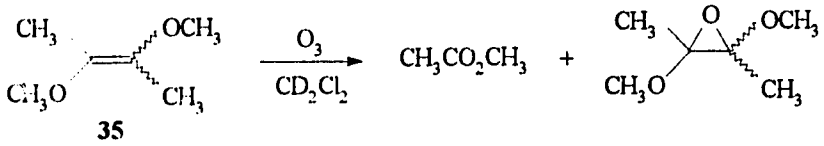
The ozonation reactions were carried out in the same way as those described previously. Because the impurities also reacted with ozone,



36

Scheme 21. Synthesis of 2,3-dimethyl-1,4-dioxene

complete ozonation of **35** afforded a complex reaction mixture. Fortunately, it was observed that if **35** was partially ozonized to about 50% conversion the intensities of the signals of the impurities almost did not decrease, indicating that the impurities were less reactive than **35** toward ozone. The major products identified from the reaction mixtures of the partial ozonation of **35** in CD_2Cl_2 at −20 °C were methyl acetate and *cis*- and *trans*-1,2-dimethyl-1,2-dimethoxyoxirane, eq 38. The integrals of the signals of the methyl groups of

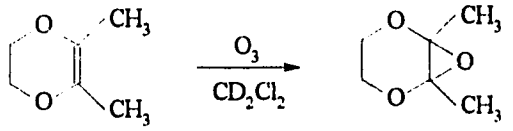


35 (38)

methyl acetate account for approximately 38% of the total integrals of the signals of the total products and those of the oxiranes are approximately 27%. The other products that were represented by many weak to medium ^1H NMR signals were unidentified. Methyl acetate was the expected cleavage product and was readily identified from the ^1H NMR spectra of the reaction mixtures. The oxiranes were identified by comparison of ^1H signals in the NMR spectra of the reaction mixtures with those of an authentic sample prepared by epoxidation of **35** with (methoxy)phenyldioxirane **13a**. One of the oxiranes gives two singlets at δ 3.32 and 1.51 and the other gives those at δ 3.38 and 1.46.

Ozonation of **36** in CD_2Cl_2 at −20 °C yields mainly the oxirane of **36** which gives one singlet at δ 1.46 for the methyl group and a multiplet at

δ 3.60-3.90 for the OCH_2CH_2O group, eq 39. The integrals of the signals of



36 60% (39)

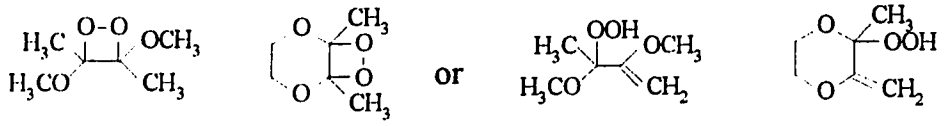
the oxirane account for approximately 60% of the total integrals of the signals of all products. This oxirane was identified in the same way as above. Other products were unidentified. Two singlets with medium intensities at around δ 2.1 in the ^1H NMR spectra of the reaction mixtures could be due to acetyl groups. This would mean that some cleavage products are produced.

Further study of the ozonation of these two 1,2-dialkoxy-1,2-dialkylethenes revealed the following common features.

First, although many signals in the ^1H NMR spectra of the ozonation mixtures were not assigned, the product distributions were identical under both the normal and inverse ozonation conditions and were independent of the concentrations of the starting materials (from 0.01 to 0.1 *M*) or the reaction temperatures (from 0 to −78 °C).

Second, cyclohexene oxide was never produced when a mixture of cyclohexene and **35** or **36** was ozonized or by adding cyclohexene to the reaction mixtures prepared by the inverse ozonation of **35** or **36**. A small ^1H NMR signal at the position of tetramethyloxirane was observed in the reaction mixtures of partial ozonation of a mixture of **35** or **36** and 2,3-dimethyl-2-butene **5**. However, the intensity of this signal, unlike those of other signals, did not increase when the amount of ozone delivered was increased, indicating that tetramethyloxirane is not produced in the ozonation either.

Third, the ^1H NMR spectra of the reaction mixtures showed that ozonation of a mixture of 2,3-dimethyl-2-butene **5** and **35** or **36** resulted in the formation of 2,3-dimethyl-3-hydroperoxy-1-butene **7**. The amount of **7** was approximately only one fifth of that of the oxirane of **35** or one third of that of the oxirane of **36**. As discussed in Chapter II, this observation suggests that the radical chain oxidation is unlikely to occur and singlet oxygen is produced in the ozonation of the two alkenes. If this is true, in the absence of 2,3-dimethyl-2-butene **5**, the singlet oxygen generated from the ozonation of **35** or **36** should react with **35** or **36** to yield either dioxetanes or allylic hydroperoxides:



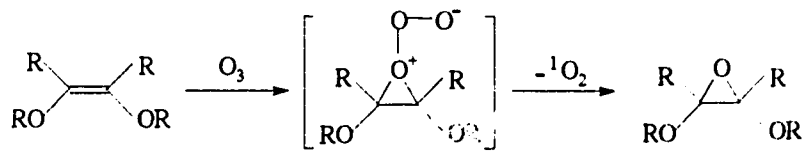
However, no luminescence was observed upon addition of the reaction mixtures to hot toluene containing 9,10-dibromo- and 9,10-bis(phenylethynyl)anthracene, indicating no dioxetanes are produced; and there are no signals at the vinyl proton absorption region in the ^1H NMR spectra of the reaction mixtures, indicating the allylic hydroperoxides are not produced either. The fate of singlet oxygen is unknown.

Last, when the ozonation reactions were carried out in CD_3OD, very complex spectra were obtained from either alkene. Unfortunately, only methyl acetate could be identified from the reaction mixtures of **35** and none of the products was identified from **36**. It is not clear whether the possible reaction of the carbonyl oxides with CD_3OD occurred. The oxiranes were not detected even when the reactions were carried out at –78 °C and the resulting reaction mixtures were immediately analyzed by ^1H NMR at the same temperature. Addition of CD_3OD to the ozonation reaction mixtures of **35** or

36 in CD_2Cl_2 at −78 °C resulted in the rapid disappearance of the signals of the oxiranes at the same temperature, indicating the oxiranes were decomposed in the presence of CD_3OD.[84] It was noted that the NMR spectra of the reaction mixtures after addition of CD_3OD were very similar to those from the ozonation of **35** or **36** in CD_3OD.

The first two features are in contrast to those of the ozonation of 1,2-dimethoxy-1,2-diphenylethene *E*- and *Z*-**8a**. If the carbonyl oxides are generated along with other cleavage products, the contrast may suggest that the (alkoxy)alkylcarbonyl oxides generated under the ozonation conditions do not cyclize to the corresponding dioxiranes. However, no evidence was found that (alkoxy)alkylcarbonyl oxides are ever generated from the ozonation of either alkene. In the ozonation of **35**, the formation of the cleavage product methyl acetate could mean that the carbonyl oxide is also generated. In the ozonation of **36**, we even don't really know whether the cleavage products are produced. Therefore, at present it is still doubtful whether (alkoxy)alkylcarbonyl oxides cannot cyclize to the corresponding dioxiranes.

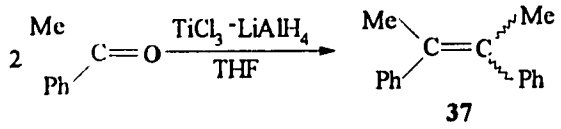
Since only a few products were identified in the ozonation of **35** or **36**, no enough information needed to discuss the ozonation mechanisms has been collected. Nevertheless, the formation of the oxiranes of **35** and **36** and the evidence for the involvement of singlet oxygen imply that the oxiranes could be produced from the direct interaction of the electron-rich alkenes with ozone via the oxygenated oxiranes or similar intermediates, eq 40.



(40)

2. Ozonation of *E*- and *Z*-2,3-diphenyl-2-butene

The simplest (alkyl)arylcarbonyl oxide, (methyl)phenylcarbonyl oxide, can be generated by the ozonation of *E*- and *Z*-2,3-diphenyl-2-butene **37** which were synthesized by the McMurry reaction as shown in eq 41.[85]

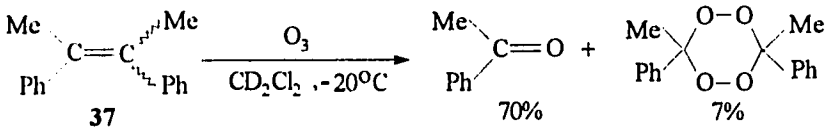


(41)

37

It has been reported[86] that the ozonolysis of **37** on polyethylene gave the corresponding ozonide, which could not be obtained by the ozonolysis in solution. However, to my knowledge, the product formation of the ozonolysis of **37** in solution has not yet been reported.

The ^{1}H NMR spectra of the reaction mixtures showed that ozonation of *E*- or *Z*-**37** in CD_2Cl_2 yields acetophenone as the major product and 3,6-dimethyl-3,6-diphenyl-1,2,4,5-tetroxane, the dimer of (methyl)phenylcarbonyl oxide, as a miner product, eq 42. The other minor products that are



(42)

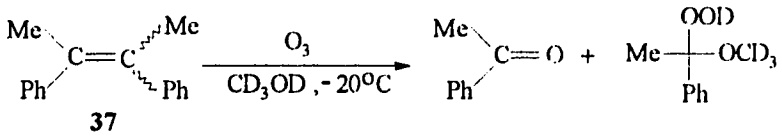
37 70% 7%

represented by small complex ^{1}H NMR signals between δ 1 and δ 6 were unstable and were not identified. The methyl group of acetophenone gives a singlet at δ 2.56. The methyl groups of the tetroxane give a singlet at δ 1.28. The integral of the signal of the methyl group of acetophenone accounts for 70% of the total integrals of the signals between δ 1 and δ 6 and that of the tetroxane is approximately 7%.

The tetroxane was isolated as a white crystal by chromatography on

silica gel. The observed sharp melting point (187.5-188.5 °C) and only one singlet at δ 1.28 even at −50 °C for the methyl groups indicated that only the trans isomer of the tetroxane was formed. Similar observations were also found in literature.[87] Dimerization of carbonyl oxides should yield both cis and trans tetroxanes. It is not clear why the cis isomer was not observed.

The ozonation of **37** in CD_3OD gives only two products in equal amounts. One of them is acetophenone and the other, which gives a singlet at δ 1.56, is presumably the adduct of (methyl)phenylcarbonyl oxide with CD_3OD, eq 43.[87(a)] This observation demonstrates that *E*- and *Z*-**37** are ozonized by the Criegee ozonolysis mechanism.



(43)

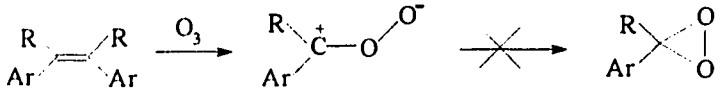
The following observations provided evidence that (methyl)phenyldioxirane was not produced from the ozonation of *E*- and *Z*-**37**.

The product distributions of the ozonation of *E*- and *Z*-**37** are independent of the initial concentrations (from 0.01 to 0.2 *M*) and the method of ozonation, i.e., the normal or inverse ozonation.

No signal of the methyl groups of oxirane of *E*-**37** (at δ 1.26) was detected in the ozonation reaction mixtures from *E*-**37**. The ^1H NMR spectra of the reaction mixtures of *Z*-**37** contained a singlet at δ 1.79. The intensity of this signal was increased by addition of some authentic sample of the oxirane of *Z*-**37** prepared by epoxidation of *Z*-**37** with *m*-chloroperbenzoic acid or with dioxirane **13a** to the reaction mixture. However, this signal disappeared

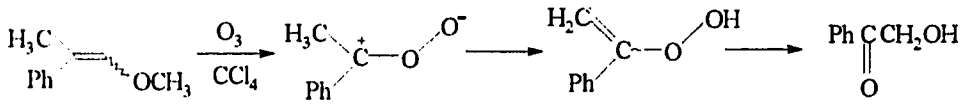
after the ozonation mixtures of *Z*-**37** were allowed to stand at room temperature overnight. As the authentic sample was quite stable under the same conditions, this signal was not due to the oxirane of *Z*-**37**. Thus no oxiranes are produced from ozonation of *E*- and *Z*-**37**.

Based on the above observations, it is concluded that (alkyl)arylcarbonyl oxides generated under the ozonation conditions do not cyclize to the corresponding dioxiranes, eq 44.



(44)

Nakamura et al[87(a)] reported that α-hydroxyacetophenone was isolated from the ozonation reaction mixture of 1-methoxy-2-phenyl-2-propene by column chromatography on silica gel. The formation of this product was accounted for by the rearrangement of (methyl)phenylcarbonyl oxide as shown in eq 45.



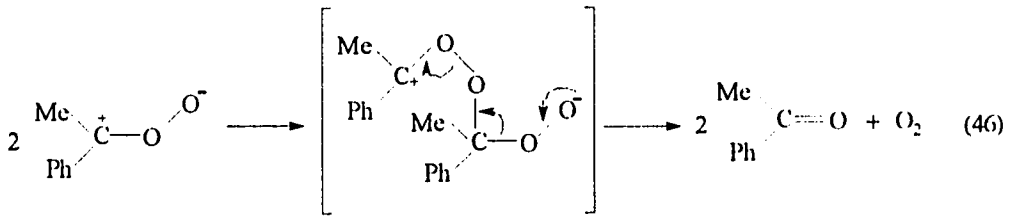
(45)

The ^{1}H NMR spectra of the ozonation of **37** showed a singlet at δ 4.90 which was the same as that reported by Nakamura et al for α-hydroxyacetophenone. However, this signal appeared only after the ozonation mixtures were allowed to stand at room temperature for some time. The "fresh" ozonation mixtures did not have such a signal. If α-hydroxyacetophenone were really produced from the rearrangement of the carbonyl oxide as suggested by Nakamura, it should be in the "fresh" ozonation mixtures as well because the rearrangement of the carbonyl oxide must be very rapid. The observation in this study suggests that α-

hydroxyacetophenone is produced by some slow process, such as decomposition of some unstable primary ozonolysis products.

B. Ozonation of *Z*-1-methoxy-1,2-diphenylpropene and 2-methoxy-1,1-diphenylpropene

It was observed in the last section that the yield of acetophenone in the ozonation of *E*- and *Z*-**37** in the non-participating solvent accounts for up to 70% of all the products. If acetophenone only arose from the cleavage of the primary ozonides of *E*- and *Z*-**37**, the maximum yield of acetophenone would be 50%. The reaction as shown in eq 46 is suggested to account for the



(46)

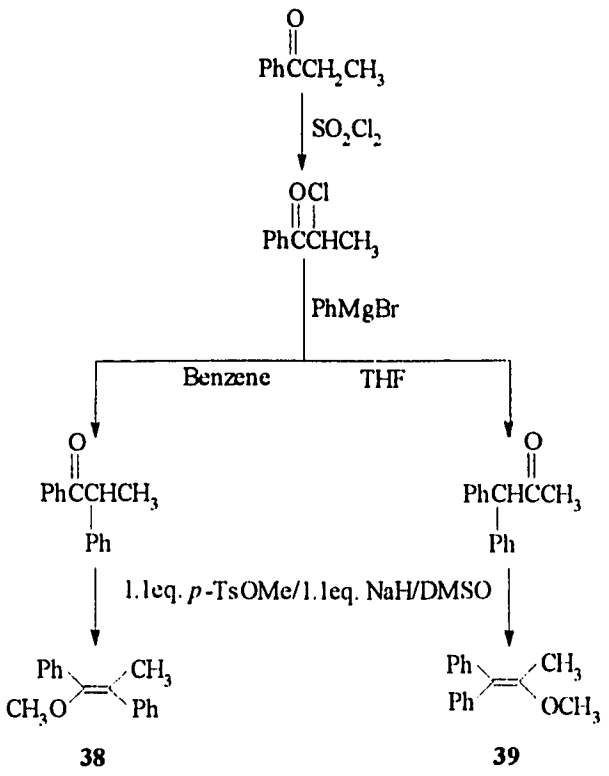
excess yield of acetophenone. Similar reactions have been suggested in ozonolysis of other alkenes.[8] The oxygen evolved in this reaction may be singlet oxygen. However, the method used to detect singlet oxygen in the ozonation of **8a** and other electron-rich alkenes failed here because *E*- and *Z*-**37** are much less reactive toward ozone than the probe 2,3-dimethyl-2-butene **5**. During ozonation of a mixture of *E*- or *Z*-**37** and **5**, ozone did not react with *E*- and *Z*-**37** until **5** was completely consumed. In order to confirm the presence of this reaction and furthermore to test the property of the oxygen evolved, the study of the ozonolysis of an alkene other than **37** is needed. This alkene should satisfy two requirements. First, it should be more reactive than *E*- and *Z*-**37** and its reactivity toward ozone should be comparable with that of 2,3-dimethyl-2-butene **5**. Second, the cleavage of its primary ozonide

can unambiguously give (methyl)phenylcarbonyl oxide but not acetophenone. So any acetophenone found in the reaction mixture must arise from the decomposition of (methyl)phenylcarbonyl oxide. The vinyl ether 1-methoxy-1,2-diphenylpropene **38** could be a suitable alkene for this study because it must be more reactive than **37** and the cleavage of the primary ozonide of **38** should give only methyl benzoate and the desired (methyl)phenylcarbonyl oxide.

As shown in Scheme 22, treatment of α-chloropropiophenone with phenylmagnesium bromide in benzene according to the procedure described in literature[88] yielded 1,2-diphenyl-1-propanone. It was accidentally found that if the solvent used was tetrahydrofuran instead of benzene a completely different product 1,1-diphenyl-2-propanone was obtained. Alkylation of the anion of 1,2-diphenyl-1-propanone yielded *Z*-1-methoxy-1,2-diphenylpropene **38**. The structure of **38** was identified by comparison the ^1H signals observed (two singlets at δ 1.96 and 3.25 in $CDCl_3$) with those reported (δ 1.93 and 3.21 in CCl_4). Alkylation of the anion of 1,1-diphenyl-2-propanone yielded 2-methoxy-1,1-diphenylpropene **39** which gave two singlets at δ 1.95 and 3.58 for the methyl and methoxy groups. The reported ^1H signals of **39** are at δ 1.91 and 3.51 in CCl_4.[89] Since ozonolysis of the vinyl ether **39** would provide an authentic method to generate diphenylcarbonyl oxide, this alkene was used to study the cyclization and oxidation properties of diphenylcarbonyl oxide.

Ozonation of these two alkenes was carried out in the manner described previously. The major reaction products are consistent with the Criegee reaction process and indicate that the cleavage of the primary ozonide of the vinyl ethers is in the same direction usually observed.

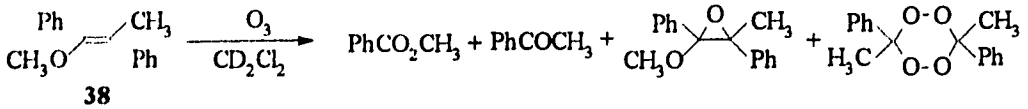
The main product from the ozonation of **38** in CD_2Cl_2 at −78°C is methyl benzoate **9a**. Other identified minor products are 1-methoxy-2-methyl-



Scheme 22. Synthesis of *Z*-1-methoxy-1,2-diphenylpropene **38** and 2-methoxy-1,1-diphenylpropene **39**

1,2-diphenyloxirane, 3,6-dimethyl-3,6-diphenyl-1,2,4,5-tetroxane, and acetophenone. The ^{1}H signals of unidentified products are the same as those of ozonolysis of 1,2-diphenyl-2-butene **37**, indicating they result from the reactions of (methyl)phenylcarbonyl oxide. α-Hydroxyacetophenone was not observed in the "fresh" reaction mixture either but was observed later. The oxirane of **38** was identified by comparison of ^{1}H signals (at δ 1.32, 3.11) in the NMR spectra of the reaction mixture with those of an authentic sample prepared by epoxidation of **38** with (methoxy)phenyldioxirane **13a**. The relative intensities of the proton signals of the identified products are indicated in eq 47.

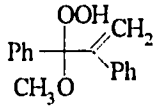
The formation of a significant amount of acetophenone provides evidence for the reaction as shown in eq 46. It seems, however, that the



38 (47)

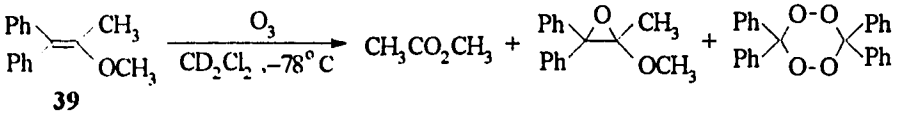
Relative intensities	(−20°C)	100	19	8	4
of proton signals:	(−78°C)	100	4	8	8

molecular oxygen produced from this reaction is not singlet oxygen because no signal was observed in the vinyl proton region in the ^{1}H NMR spectrum of the reaction mixture of partial ozonolysis of **38** to 32% consumption. The control experiment showed that singlet oxygen oxidation of **38** produced one major product which gives two doublets with identical intensities at δ 5.58 and 5.87 and one singlet at δ 3.28. These signals are presumably due to the allylic hydroperoxide



The fact that no singlet oxygen is produced in the ozonolysis of **38** is further confirmed by the partial ozonolysis of a 1:2 mixture of **38** and 2,3-dimethyl-2-butene **5** since the expected allylic hydroperoxide of **5** is not observed.

Only the signals of two products, methyl acetate and 1-methoxy-1-methyl-2,2-diphenyloxirane, were found in the non-aromatic proton region of the ^{1}H NMR spectrum of the reaction mixture of ozonation of **39** in CD_2Cl_2 at −78°C. The amount of the oxirane was about one tenth of that of the acetate. After the solvent was evaporated, another product 3,3,6,6-tetraphenyl-1,2,4,5-tetroxane was isolated as a cubic crystal, eq 48. The



39 (48)

oxirane of **39** which gives two singlets at δ 1.42 and 3.56 was identified by

oxirane of **39** which gives two singlets at δ 1.42 and 3.56 was identified by the same method as above. The tetroxane melts at 210-212 °C, which is identical to the melting point reported.[90] When the reaction was carried out in CD_3OD, the acetate and oxirane are also produced in the similar relative amount as in CD_2Cl_2 but some ^1H NMR signals of tetroxane was not observed, suggesting diphenylcarbonyl oxide is captured by methanol. No tetramethyloxirane **6** or cyclohexene oxide was detected from the ozonation reaction mixture of **39** and 2,3-dimethyl-2-butene **5** or cyclohexene.

For the formation of the oxirane, two alternative reactions would be postulated, i.e., direct ozone epoxidation via an oxygenated oxirane (or its analogous) and epoxidation by a reaction intermediate which could be either diphenylcarbonyl oxide or its cyclic isomer diphenyldioxirane. Of the two mechanistic alternatives, however, the latter reaction can be ruled out, since the formation of the expected oxiranes of other alkene is not observed. The same conclusion was obtained from ozonolysis of other similar vinyl ethers.[89] This means that (1) diphenylcarbonyl oxide generated by ozonolysis of alkene cannot cyclize to the corresponding dioxirane and (2) diphenylcarbonyl oxide cannot transfer an oxygen atom to other alkenes. The latter conclusion is in contrast to Murray and co-workers' report.[38] These authors claimed that singlet oxygen oxidation of diazodiphenylmethane produced diphenylcarbonyl oxide which is able to epoxidize alkenes.

Conclusion

Because no evidence for formation of the (alkoxy)alkylcarbonyl oxides from the ozonation of 2,3-dimethoxy-2-butene **35** and 2,3-dimethyl-1,4-

dioxene **36** was obtained, it remains a question that whether the (alkoxy)alkylcarbonyl oxides can cyclize to the dioxiranes.

(Alkyl)arylcarbonyl oxides and diphenylcarbonyl oxide generated by the ozonation of suitable alkenes cannot cyclize to the corresponding dioxiranes.

The molecular oxygen produced by decomposition of (methyl)phenylcarbonyl oxide via a dimeric zwitterion is not singlet oxygen.

Diphenylcarbonyl oxide generated by ozonolysis of alkenes cannot transfer oxygen atom to alkenes.

Experimental

The ozonation reactions were carried out in the same manner as described previously.

1. Synthesis of *E*- and *Z*-2,3-dimethoxy-2-butene (*E*- and *Z*-35)

1,1,2,2-Tetramethoxyethane was prepared according to the procedure described in the literature.[91] A mixture of a 40% aqueous solution of glyoxal (80 g, 0.55 mol) and methanol (200 mL) was saturated with dry hydrogen chloride. The methanol was removed by distillation and the residue was distilled under reduced pressure to give 1,1,2,2-tetramethoxyethane (44 g, 53%): bp_{10}48 °C (Lit.[91] bp_{12}53 °C); ^{1}H NMR ($CDCl_3$, TMS): δ 3.42 (s, 12 H, OCH_3), 4.24 (s, 2 H, OCHO).

1,2-Dichloro-1,2-dimethoxyethane was prepared according to the procedure described in the literature.[92] 1,1,2,2-Tetramethoxyethane (43 g, 0.21 mol) was added dropwise with stirring to phosphorus pentachloride (120

g, 0.58 mol) in a water bath. Stirring was continued for 1.5 hours at room temperature until all the solid phosphorus pentachloride disappeared. Direct distillation of the reaction mixture under reduced pressure gave a 3.6:1 mixture of *meso* and *rac*. 1,2-dichloro-1,2-dimethoxyethane (33.6 g, 75%): bp_{12}60-63 °C; ^{1}H NMR ($CDCl_3$, TMS): *meso* δ 3.61 (s, 6 H, OCH_3), 5.50 (s, 2 H, CHCl), *rac*. δ 3.63 (s, 6 H, OCH_3), 5.57 (s, 2 H, CHCl) (Lit.[92] ^{1}H NMR (CCl_4): δ 3.52 (s, 6 H *rac*. + 6 H *meso*), *meso* δ 5.42 (s, 2 H), and *rac*. δ 5.50 (s, 2 H)).

***E*- and *Z*-1,2-Dimethoxyethene** were prepared according to the procedure described in the literature.[93] A few drops of 1,2-dibromoethane were added to a flask containing magnesium (5.1 g, 0.21 mol) and dry THF (50 mL) to initiate the reaction. Once the reaction started, a solution of 1,2-dichloro-1,2-dimethoxyethane (33.6 g, 0.21 mol) in THF (20 mL) was added dropwise to the flask at a rate to keep the reaction temperature at around 40 °C. At the end of the addition, the mixture was boiled for ten minutes, cooled to room temperature, and filtered. The filtrate was poured into a fresh aqueous ammonium chloride solution (200 mL) and the resulting mixture was extracted with ether. The extract was washed with brine and dried over anhydrous sodium sulfate. Fractional distillation gave an approximately 1:1 mixture of *E*- and *Z*-1,2-dimethoxyethene (12.0 g, 65%): bp_{710}80-90 °C; ^{1}H NMR ($CDCl_3$, TMS): *E*-isomer δ 3.41 (s, 6 H, OCH_3), 6.26 (s, 2 H, HC=C), *Z*-isomer δ 3.58 (s, 6 H, OCH_3), 5.30 (s, 2 H, HC=C). (Lit.[93] ^{1}H NMR (acetone-D_6): *E*-isomer δ 3.40, 6.28, *Z*-isomer δ 3.49, 5.25).

***E*- and *Z*-2,3-Dimethoxy-2-butene (*E*- and *Z*-35):** A 1.7 *M* pentane solution (24 mL, 0.041 mol) of *tert*-butyllithium was added to a stirring solution of a mixture of *E*- and *Z*-1,2-dimethoxyethene (3.6 g, 0.041 mol) in 40 mL of tetramethylethylenediamine at –40 °C under argon, and the mixture

was stirred at this temperature for two hours. Methyl iodide (2.55 mL, 0.041 mol) was added dropwise and the mixture was permitted to warm to room temperature in the course of three hours. The mixture was cooled to −40 °C again and the second portion of *tert*-butyllithium (27 mL, 0.045 mol) was added. After the mixture was stirred at this temperature for two hours, the second portion of methyl iodide (2.8 mL, 0.045 mol) was added and the mixture was permitted to slowly warm to room temperature. A fresh aqueous ammonium chloride solution (100 mL) was added and the mixture was extracted with ether. The extract was washed with brine, dried over anhydrous sodium sulfate, and rapidly passed through a short column of silica gel and eluted with ether. Evaporation of the solvent gave a sticky light brown liquid. Purification by preparative GLC (Column 10% SE-30 on 60/80 chromosorb W, injector 170 °C, detector 120 °C, column 80 °C, retention time 30 min.) gave a mixture (2.08 g) of the two isomers and some unidentified impurities according to the ^{1}H NMR spectrum. The integrals of the signals of the major isomer which gave two singlets at δ 1.71 and 3.50, the miner isomer which gave two singlets at δ 1.77 and 3.42, and the impurities accounted for 56.4%, 30.3%, and 13.3% of the total integrals of the all signals, respectively. The combined yield of the two isomers was 37.9%. The reported chemical shifts of the ^{1}H NMR signals of a mixture of *Z*- and *E*-**35** in acetone-D_6 were at δ 1.74 and 3.51 for one isomer and δ 1.82 and 3.42 for the other isomer.[82]

2. Synthesis of 2,3-dimethyl-1,4-dioxene (36)

3-Butyn-2-ol was prepared according to the procedure described in the literature.[92] Acetylene was introduced into a liquid ammonia (approximately

200 mL) solution of sodium amide (39 g, 1.0 mol) at −40 to −50 °C until the gray color of the mixture turned black. Acetaldehyde (56 mL, 1.0 mol) dissolved in 60 mL of dry ether was added dropwise to the ammonia solution. The reaction mixture was stirred at room temperature overnight. During this period the ammonia was allowed to evaporate. Ether (200 mL) and a saturated aqueous solution of ammonium chloride (100 mL) were added into the black sticky residue. The ether layer was separated and the aqueous layer was extracted with ether. The combined extracts were washed with water, brine, dried over anhydrous magnesium sulfate. The solvent was evaporated and the residue was distilled to give the product (34.5 g, 50%): bp_{705}100-105 °C, (Lit.[94] bp_{150}66-67 °C); ^1H NMR ($CDCl_3$, TMS): δ 1.48 (d, J = 6.7 Hz, 3 H, CH_3), 2.47 (d, J = 2.1 Hz, 1 H, HC≡C), 2.50 (b, 1 H, OH), 4.54 (dq, J = 6.7 and 2.1 Hz, 1 H, CH).

2-(3-Butyn-2-yloxy) ethanol was prepared according to the procedure described in the literature.[85] 2-Bromoethanol (35 g, 0.28 mol) was added dropwise to a rapidly stirring suspension of finely powdered potassium hydroxide (16 g, 0.28 mol) in 3-butyn-2-ol (20 g, 0.28 mol) at 0 °C. During the addition, potassium bromide precipitated. The reaction mixture was stirred at room temperature overnight and then poured into water and the resulting mixture was extracted with ether. The extract was washed with water, brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated and the sticky residue was distilled under reduced pressure to give 2-(3-butyn-2-yloxy) ethanol (13 g, 41%): bp_{12}70-74 °C, (Lit.[83] bp_{12}72-73 °C); ^1H NMR ($CDCl_3$, TMS): δ 1.47 (d, J = 6.7 Hz, 3 H, CH_3), 2.07 (b, 1 H, OH), 2.45 (d, J = 2.1 Hz, 1 H, HC≡C), 3.42-3.95 (m, 4 H, OCH_2CH_2O), 4.24 (dq, J = 6.7 and 2.1 Hz, 1 H, HCO).

2,3-Dimethyl-1,4-dioxene (36) was prepared according to the procedure described in the literature.[83] A slurry of finely powdered potassium hydroxide (4.0 g, 0.07 mol) in 75 mL of redistilled triethylene glycol dimethyl ether was placed in a 100 mL flask equipped with a magnetic stirrer, a dropping funnel, and a distillation apparatus. The mixture was stirred vigorously and heated to 180 ± 5 °C in an oil bath. 2-(3-Butyn-2-yloxy)ethanol (8.0 g, 0.07 mol) was added dropwise in 15 minutes. During the addition, the volatile products (bp_{710} 82-85 °C) distilled from the reaction mixture. When the distillation slowed, the temperature of the oil bath was raised to 195 °C and remained at that temperature for ten minutes. The ^1H NMR spectrum showed that the distillate contained approximately 70% of the desired product. The crude product was purified by preparative GLC. (Column 10% SE-30 on 60/80 chromosorb W, injector 170 °C, detector 120°C, column 100 °C, retention time 27 min.) to give 3.8 g (48%) of the product. ^1H NMR ($CDCl_3$, TMS): δ 1.68 (s, 6 H, $CH_3C{=}CCH_3$), 3.95 (s, 4 H, OCH_2CH_2O). (Lit.[83] ^1H NMR (CCl_4, TMS): δ 1.67, 3.92).

3. Synthesis of *E*- and *Z*-2,3-diphenyl-2-butene (37)

This synthesis followed the procedure described in the literature.[85] To 200 mL of THF at −70 °C was added 32 g of McMurry reagent (a 4:1 mixture of $TiCl_3$ and $LiAlH_4$, purchased from Aldrich) with stirring. The mixture was allowed to warm to room temperature and 6.0 g (0.05 mol) of acetophenone was added dropwise. The reaction mixture was stirred under reflux for six hours and then at room temperature overnight. Water was added and the mixture was extracted with ether. The extract was washed with water, brine, and dried over anhydrous magnesium sulfate. Evaporation of the

extract gave an oily residue. Fractional recrystallization from methanol yielded first *E*-**37** (1.0 g, 20%) as white needles and then *Z*-**37** (1.6 g, 30%) as a white powder.

***E*-2,3-diphenyl-2-butene**: mp 95.0-97.0 °C, (Lit.[85] 94-100 °C); ^{1}H NMR ($CDCl_3$, TMS). δ 1.88 (s, 6 H, C=CCH_3), 7.18-7.43 (m, 10 H, Ar).

***Z*-2,3-diphenyl-2-butene**: mp 52.0-54.0 °C, (Lit.[85] 53-63 °C); ^{1}H NMR ($CDCl_3$, TMS): δ 2.17 (s, 6 H, C=CCH_3), 6.90-7.15 (m, 10 H, Ar).

4. Synthesis of 1-methoxy-1,2-diphenylpropene (38)

α-Chloropropiophenone Sulfuryl chloride (28.3 g, 0.21 mol) was slowly added dropwise with stirring to propiophenone (26.8 g, 0.20 mol) contained in a flask equipped with a drying-tube at room temperature. The reaction mixture was kept stirring overnight. Distillation under reduced pressure offered the product (32.4 g, 95.0%) as a light yellow oil. bp_{15}115-120 °C, (Lit.[88] bp_{18}126-128°C); ^{1}H NMR ($CDCl_3$, TMS): δ 1.75 (d, J = 6.5 Hz, 3 H, CH_3), 5.25 (q, J = 6.5 Hz, 1 H, CH), 7.42-7.65 (m, 3 H, Ar), 7.96-8.08 (m, 2 H, Ar).

1,2-Diphenyl-1-propanone Bromobenzene (18.8 g, 0.12 mol) was added to magnesium (3.65 g, 0.15 mol) in dry ether (50 mL) at such a rate to keep a gentle reflux. After finishing the addition the reaction mixture was heated to reflux for 0.5 hours. The phenylmagnesium bromide in ether was transferred to a dropping funnel and was added dropwise with stirring into the ice cooled α-chloropropiophenone (20.4 g, 0.12 mol) in benzene (100 mL). The reaction mixture was refluxed for two hours. The precipitate was removed by filtration and washed with ether. The combined filtrate was washed with ammonium chloride aqueous solution, water, brine, and dried

over anhydrous magnesium sulfate. The solvent was evaporated and the crude product was obtained by distillation under reduced pressure. Recrystallization from methanol gave the purified product (13 g, 52%). $bp_{2.0}$125-140 °C, (Lit.[88] $bp_{2.5}$130-145°C); ^{1}H NMR ($CDCl_3$, TMS): δ 1.58 (d, J = 6.5 Hz, 3 H, CH_3), 4.80 (q, J = 6.5 Hz, 1 H, CH), 7.30-7.70 (m, 8 H, Ar), 8.01-8.21 (m, 2 H, Ar); Exact mass calcd for $C_{15}H_{14}O$: 210.1045. EIMS *m/e*: 210.1043 (M^+).

***Z*-1-Methoxy-1,2-diphenyl-1-propene (38):** 1,2-Diphenyl-1-propanone (2.1 g, 0.01 mol) was added to a suspension of sodium hydride (0.3 g, 0.013 mol) in DMSO (20 mL). The reaction mixture turned to yellow cloudy. After stirring for 15 minutes, *p*-TsOMe (2.05 g, 0.011 mol) was added dropwise. The reaction mixture was kept stirring for three hours at room temperature. A little amount of methanol was added to the mixture to destroy the excess base. The mixture was poured to cold water (200 mL) and extract with ether (50 mL × 3). The combined extract was washed with water, brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated and the residue was crystallized from methanol to give the product (0.92 g, 41%) which was assigned to be the *Z* isomer of the two possible isomers according to the literature.[89] mp 52.5-54.0 °C; ^{1}H NMR ($CDCl_3$, TMS): δ 1.96 (s, 3 H, CH_3), 3.25 (s, 3 H, OCH_3), 7.15-7.50 (m, 10 H, ArH), (Lit.[89] ^{1}H NMR (CCl_4): δ 1.93, 3.21); ^{13}C NMR ($CDCl_3$, TMS): δ 19.59, 57.61, 118.15, 126.27, 127.97, 128.01, 128.23, 129.75, 135.59, 141.32,150.78; FTIR: 1071, 1491cm^{-1}; Exact mass calcd for $C_{16}H_{16}O$: 224.1201. EIMS *m/e*: 224.1200 (M^+); Anal. Calcd for $C_{16}H_{16}O$: C, 85.67; H 7.19. Found: C, 85.56; H, 7.30.

5. Synthesis of 1-methoxy-1,2-diphenylpropene (39)

1,1-Diphenyl-2-propanone The preparation procedure of this

compound was exactly the same as that of 1,2-diphenyl-1-propanone except the solvent used was THF instead of benzene. Recrystallization of the crude product from methanol gave the product (11.5 g, 45.6%). $bp_{1.8}$130-145 °C, (Lit.[95] $bp_{1.5}$135-138 °C); mp 59.0-60.0 °C (Lit.[96] mp 62-63 °C); ^1H NMR ($CDCl_3$, TMS): δ 2.20 (s, 3 H, CH_3), 5.10 (s, 1 H, CH), 7.18-7.35 (m, 10 H); ^{13}C NMR ($CDCl_3$, TMS): δ 29.93, 64.91, 127.15, 128.63, 128.90, 138.28, 206.27; FTIR: 1715 cm^{-1}; Exact mass calcd for $C_{15}H_{14}O$: 210.1045. EIMS *m/e*: 210.1050 (M^+).

2-Methoxy-1,1-diphenyl-1-propene (39): 1,1-Diphenyl-2-propanone (2.1 g, 0.01 mol) was added to a suspension of sodium hydride (0.3 g, 0.013 mol) in DMSO (20 mL). The reaction mixture turned to yellow cloudy. After stirring for 15 min., *p*-TsOMe (2.05 g, 0.011 mol) was added dropwise. The reaction mixture was kept stirring for three hours at room temperature. A little amount of methanol was added to the mixture to destroy the excess base. The mixture was poured to cold water (200 mL) and extract with ether (50 mL × 3). The combined extract was washed with water, brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated and the residue was crystallized from methanol to give the product (1.3 g, 58%). mp 53.0-54.0 °C; ^1H NMR ($CDCl_3$, TMS): δ 1.95 (s, 3 H, CH_3), 3.58 (s, 1 H, CH), 7.10-7.35 (m, 10 H, Ar); (Lit.[89] ^1H NMR (CCl_4): δ 1.91, 3.51); ^{13}C NMR ($CDCl_3$, TMS): δ 15.84, 55.94, 121.91, 125.75, 126.23, 127.63, 128.10, 129.85, 130.67, 140.41, 142.12, 150.53; FTIR: 1050, 1236, 1616 cm^{-1}; Exact mass calcd for $C_{16}H_{16}O$: 224.1201. EIMS *m/e*: 224.1207 (M^+); Anal. Calcd for $C_{16}H_{16}O$: C, 85.67; H 7.19. Found: C, 85.69; H, 7.24.

6. Isolation of the ozonation products

The ozonation of a mixture of *E*- and *Z*-2,3-diphenyl-2-butene **37** (0.5 g) in CH_2Cl_2 (20 mL) was carried out at 0 °C. The solvent was evaporated and the products were isolated by column chromatography on silica gel with 15% of ethyl acetate in hexane as eluent. The first fraction contained the tetroxane and the second fraction contained acetophenone.

3,6-Dimethyl-3,6-diphenyl-1,2,4,5-tetroxane: mp 187.5-188.5 °C; ^{1}H NMR ($CDCl_3$, TMS): δ 1.28 (s, 6 H, CH_3), 7.30-7.65 (m, 10 H, Ar).(Lit.[89] mp 188-190 °C; ^{1}H NMR: δ 1.32 (s, 6 H), 6.78-7.95 (m, 10 H)). Exact mass calcd for $C_{16}H_{16}O_4$: 272.1049. CIMS: *m/e* = 290 ($M + NH_4^+$).

Acetophenone: δ 2.58 (s, 3 H, CH_3), 7.40-7.65 (m, 4 H, Ar), 7.90-8.05 (m, 2 H, Ar).

3,3,6,6-Tetraphenyl-1,2,4,5-tetroxane: The ozonation of 2-Methoxy-1,1-diphenyl-1-propene **39** (0.7 g, 3 mmol) in CH_2Cl_2 (20 mL) was carried out at −40 °C. The solvent was evaporated and the tetroxane was crystallized from the residue. Recrystallization from methanol afforded the tetroxane (0.33 g, 28%) as a cubic crystal. mp 210-212 °C (Lit.[90] mp 214-215 °C); ^{1}H NMR ($CDCl_3$, TMS): δ 6.70-7.90 (m, 20 H, Ar). ^{13}C NMR ($CDCl_3$): δ 111.45, 128.21,128.33, 128.69, 128.77, 130.11, 130.83, 136.50, 137.55. Exact mass calcd for $C_{26}H_{20}O_4$: 396.1362. CIMS: *m/e* = 414 ($M + NH_4^+$).

7. The chemical shifts of oxiranes

The following oxiranes were not isolated. The ^{1}H NMR chemical shifts of them were obtained from the spectra of the authentic samples. The procedure of preparation of authentic samples of the oxiranes are as follows. Inverse ozonation of *E*-1,2-dimethoxy-1,2-diphenylethene *E*-**8** (0.4 mg) in CD_2Cl_2 (0.5 mL) at −20 °C gave a reaction mixture containing

(methoxy)phenyldioxirane **13a**. To this mixture a small amount of the interested alkene was added and the ^1H NMR spectrum of the resulting reaction mixture was then recorded at –20 °C. The signals that were not due to the materials of known structures were assigned to the newly produced oxirane.

***trans*- and *cis*-2,3-dimethoxy-2,3-dimethyloxirane:** ^1H NMR (CD_2Cl_2, –20 °C): δ 1.51 (s, 6 H, CH_3), 3.32 (s, 6 H, OCH_3), and δ 1.46 (s, 6 H, CH_3), 3.38 (s, 6 H, OCH_3).

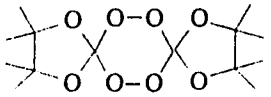
2,3-dimethyl-1,4-dioxene oxide: ^1H NMR (CD_2Cl_2, –20 °C): δ 1.46 (s, 6 H, CH_3), 3.60-3.90 (m, 4 H, OCH_2CH_2O).

trans-1-Methoxy-2-methyl-1,2-diphenyloxirane ^1H NMR (CD_2Cl_2, –20 °C): δ 1.32 (s, 3 H, CH_3), 3.11 (s, 3 H, OCH_3), and signals of the aromatic protons.

1-Methoxy-1-methyl-2,2-diphenyloxirane ^1H NMR (CD_2Cl_2, –20 °C): δ 1.42 (s, 3 H, CH_3), 3.56 (s, 3 H, OCH_3), and signals of the aromatic protons.

VI. DISCOVERY OF TETROXANES AS A NEW CLASS OF CHEMILUMINESCENT MOLECULES

Searching for potentially luminescent molecules that are not 1,2-dioxetanes is one of the research subjects in this laboratory. Among several structures that were considered was octamethyl-1,4,6,7,9,12,13,14-octaoxadispiro[4.2.4.2.]tetradecane **40** which might undergo decomposition to four molecules of acetone and two of carbon dioxide, eq 45. The reaction



40

$$\xrightarrow[\Delta H_f = -109\ \text{kcal/mole}]{} 4\ (CH_3)_2CO + 2\ CO_2 \qquad (45)$$

is calculated to be exothermic by 108.9 kcal/mole using the data in Table 18.[97]

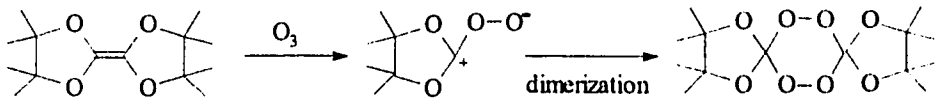
Table 18. Enthalpies of formation (kcal/mol) used in thermochemical calculations[a]

Group	ΔH^0_f (kcal/mol)	Group	ΔH^0_f (kcal/mol)
$C-(H)_3(C)$	−10.08	$O-(C)_2$	−23.2
$C-(O)(C)_3$	−6.6	O-(C)(O)	−4.5
$C-(O)(C)(H)_2$	−8.5	$(CH_3)_2CO$	−51.7
$C-(O)_4$	−43.1	H_2CO	−26.0
CO_2	−94.05		
Strain Corrections			
ring correction (1,3-dioxolane)	6.0		
alkane gauche correction	0.8		
ether oxygen gauche correction	0.3		

Since **40** would quite likely be kinetically stable and may require an activation energy for decomposition of upwards of 30 kcal/mole,[98] the

difference in the heats of formation of the transition state for decomposition of **40** and the products should be 130 kcal/mole or more. This is more than enough to form an electronically excited acetone molecule and is greater than that, 90 kcal/mole, available in the thermolysis of tetramethyl-1,2-dioxetane.[99]

An obvious reaction that might lead to **40** is the dimerization of the corresponding carbonyl oxide which might be generated from ozonolysis of alkene **41**, eq 46. Since there was no straightforward method to prepare **41**,

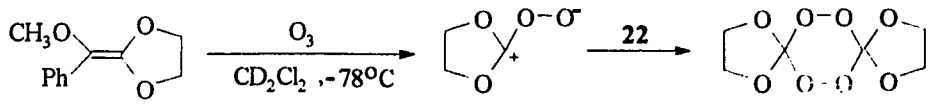


(46)

41 **40**

the ozonolysis of the readily available model compound tetramethoxyethene **1** was reexamined.[22] However, as mentioned in Chapter I, the results of the ozonolysis of **1** showed that the major products are dimethyl carbonate, methyl trimethoxyacetate and the dioxetane. Only a small amount of cleavage product is formed. No evidence could be obtained for the formation of dimethoxycarbonyl oxide during the reaction. It therefore seems that the tetroxane **40** can not be prepared by ozonolysis of the tetraalkoxy substituted ethene **41**.

It was found that 1,4,6,7,9,12,13,14-octaoxadispiro[4.2.4.2]tetradecane **20** (the dimer of the ethylene carbonate oxide) is produced from ozonation of 2-[(methoxy)phenyl]methylene-1,3-dioxolane **15** (see Chapter III), eq 47. The

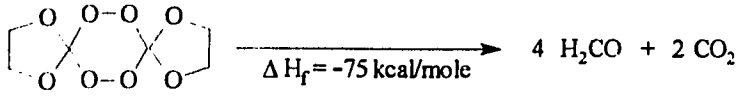


(47)

15 **22** **20**

structure of **20** is very similar to that of **40**. This molecule is calculated to

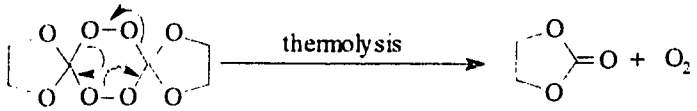
release 74.7 kcal/mole of heat if it decomposed to four molecules of formaldehyde and two of carbon dioxide, eq 48.



(48)

20

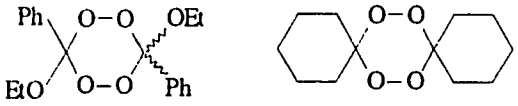
Indeed, a flash of luminescence was observed upon thermolysis of **20** in the presence of the fluorescent 9,10-bis(phenylethynyl)anthracene at 180 ° C in a melting point tube. In the absence of the fluorescer, no light was observed. Surprizingly, only ethylene carbonate **17** was detected by ^{1}H NMR and the expected formaldehyde was not found, indicating that the thermolysis of **20** gives ethylene carbonate **17** and (presumably) oxygen instead of formaldehyde and carbon dioxide, eq 49.



(49)

20 **17**

For this mode of decomposition, no special structural feature is needed for tetroxanes. To confirm this, the luminescent property of two other types of tetroxanes, 7,8,15,16-tetraoxadispiro[5.2.5.2]tetradodecane **42** and a mixture of *cis*- and *trans*-3,6-diethoxy-3,6-diphenyl-1,2,4,5-tetroxane **12b**,



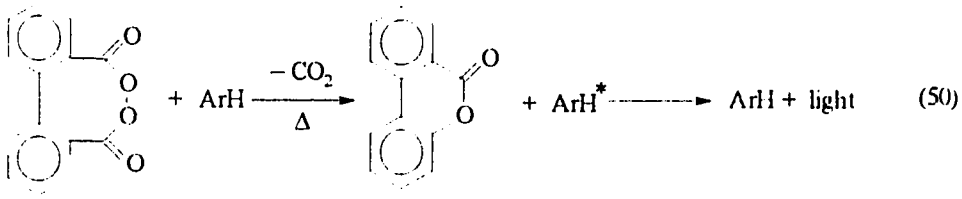
12b **42**

were investigated. Thermolysis of the tetroxanes **12b** or **42** in the presence of 9,10-bis(phenylethynyl)anthracene at 180 °C in a melting point tube also

results in a flash luminescence. These are the first examples of tetroxanes as a new class of luminescent molecules.

The lowest temperature at which a methyl benzoate solution of a tetroxane and a fluorescer (0.1 *M* each) gives visible light was investigated. Due to the availability, only two tetroxanes, **12b** and **42**, and two fluorescers, 9,10-bis(phenylethynyl)anthracene and 1,4-dimethoxy-9,10-diphenylanthracene, were used in this study. It was found that the lowest temperature was independent of the tetroxanes but dependent on the fluorescers. When 9,10-bis(phenylethynyl)anthracene was used, at about 190 °C the mixture began giving a dim light which could be last for a few minutes; when 1,4-dimethoxy-9,10-diphenylanthracene was used, the lowest temperature was 180 °C.

It was reported by Schuster[100] that thermolysis of diphenoyl peroxide (DPP) in a variety of solvents in the presence of any of several easily oxidized fluorescent hydrocarbons (ArH) generates carbon dioxide, benzocoumarin and light, eq 50. Schuster and co-workers also showed that the ArH is a catalyst for the reaction, and that its catalytic effectiveness depends inversely on its oxidation potential. The mechanism advanced to

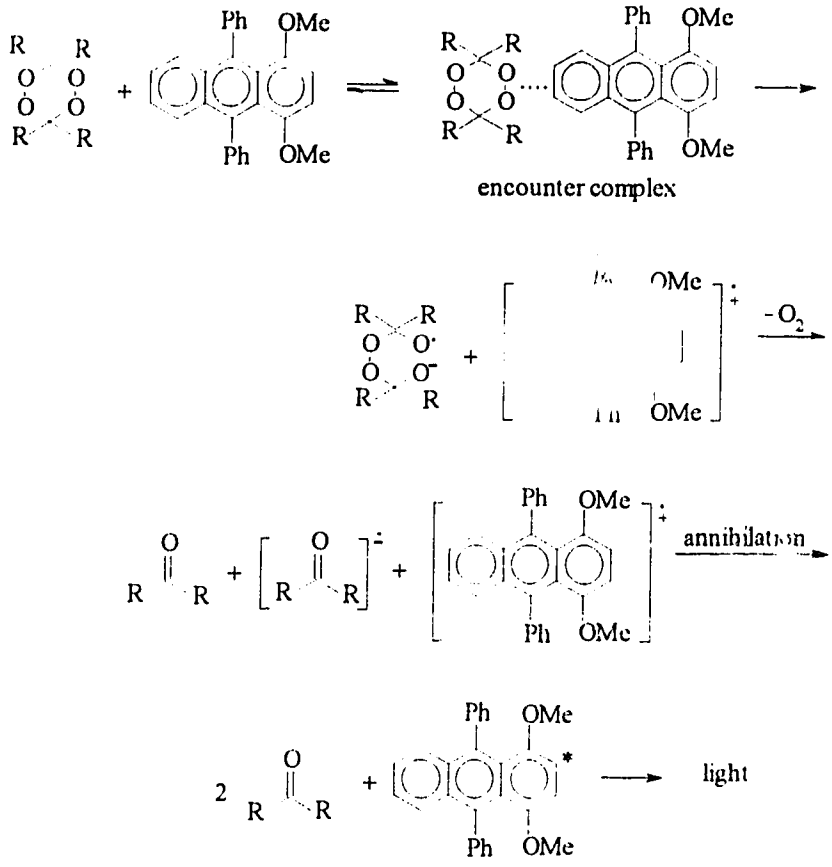


(50)

explain these, among other, observations is called as chemically initiated electron-exchange luminescence (CIEEL) mechanism.

We suspect that the mechanism of thermolysis of tetroxanes in the

presence of the fluorescers is similar to that of thermolysis of diphenoyl peroxide (DPP), i.e., a CIEEL mechanism as shown in Scheme 23. The first



Scheme 23. ...ally initiated electron-exchange luminescence (CIEEL) mechanism proposed for the thermolysis of a tetroxane in the presence of a fluorescer

step is the diffusion together of a tetroxane molecule and a fluorescer molecule (e.g., 1,4-dimethoxy-9,10-diphenylanthracene) to form an encounter complex. Thermal activation of the encounter complex results in transfer of an electron from the fluorescer to the tetroxane. Molecular oxygen is released from the resulting radical anion of the tetroxane and a carbonyl compound and a radical anion of this carbonyl compound are produced. Back-electron

transfer from the radical anion of the carbonyl compound to the radical cation of the fluorescer results in the annihilation of these oppositely charged radical ions and the formation of the electronically excited fluorescer which then emits light in the process of degradation to its ground state.

The above observed lowest fluorescence temperatures of the two fluorescers are consistent with this mechanism. Because of the presence of the two electron-donating methoxy substituents in 1,4-dimethoxy-9,10-diphenylanthracene, it is expected that the one-electron oxidation potential of it would be lower than that of 9,10-bis(phenylethynyl)anthracene. (The oxidation potential of 1,4-dimethoxy-9,10-diphenylanthracene is 0.79 V.[101] The oxidation potential of 9,10-bis(phenylethynyl)anthracene is unavailable but is expected to be similar to that of 9,10-diphenylanthracene which is 1.35 V.[102]) This means the electron transfer will take place more easily between a tetroxane and 1,4-dimethoxy-9,10-diphenylanthracene and thus the fluorescence temperature is lower.

Experimental

1. Identification of the thermolysis product of the tetroxane 20

A small amount of **20** was placed in a NMR tube which was then sealed under vacuum. Upon heating to 180 °C the solid tetroxane **20** was decomposed to a liquid. The seal was opened while the NMR tube was placed in a dry ice-acetone bath and 0.5 mL of CD_2Cl_2 was added. The ^1H NMR spectrum of the reaction mixture was then recorded at room temperature.

2. Study of the lowest luminescence temperatures

Methyl benzoate solutions (0.1 *M*) of 3,6-diethoxy-3,6-diphenyl-

1,2,4,5-tetroxane **12b**, 7,8,15,16-tetraoxadispiro[5.2.5.2]tetradodecane **42**, 9,10-bis(phenylethynyl)anthracene, and 1,4-dimethoxy-9,10-diphenylanthracene were prepared. A mixture of 0.5 mL of the solution of a fluorescer and the same volume of the solution of a tetroxane in a test tube was put into a preheated oil bath in a dark room. The temperature of the oil bath at which the mixture began giving visible light was recorded.

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Appendix

The Question of Dioxirane Formation in the Ozonolysis of Tetramethylethylene

Recently Murray and co-workers published a paper entitled "The Ozonolysis of Tetramethylethylene. Concentration and Temperature Effects".[18(a)] The following summarizing statements were made by these authors. "The products of the ozonolysis of tetramethylethylene in hexane or methylene chloride are remarkably dependent on the concentration of tetramethylethylene. Ozonolysis in neat tetramethylethylene gives mostly tetramethylethylene epoxide as product. As the concentration of tetramethylethylene is reduced, more acetone diperoxide is formed until it becomes the major product. The reaction also produces 3-hydroperoxy-2,3-dimethyl-1-butene. The product distribution is also quite dependent on reaction temperature. At a given concentration of the alkene the epoxide yield decreases as the temperature is lowered. Simultaneously the acetone diperoxide yield increases with lower temperature. The results are explained by postulating that energy-rich acetone oxide can be partially converted to dimethyldioxirane which is primarily responsible for the epoxidation."

It is necessary to reconsider these authors' conclusion.

First of all, there are many obvious inconsistencies in the paper. For example, these authors claimed: "The major reaction products were tetramethylethylene epoxide, **8**, the hydroperoxide **9**, and acetone diperoxide, **5**." However, according to Table I of the paper, even in the best case the total yield of these three products was just 16.29%. Actually, the major reaction product of ozonolysis of TME must be acetone. But these authors did not even mention it.

Second, all the discussions of these authors were based on the results of ozonolysis of TME to only *2%* conversion. These authors stated: "When higher conversions are used it is more difficult to obtain precision in the data since the ozone/oxygen stream tends to carry away products even when a dry ice/acetone condenser is used." This statement implies that at higher conversions the yields of the above three products were lowered due to the loss of the products. No control experiment was carried out to support this statement. It is sure that the ozone/oxygen stream will carry away some products, but the amounts of the products lost will be very low especially at low temperature (the temperature was varied from 0 °C to −80 °C by these authors). The boiling points of the starting alkene and the solvents are TME 73 °C, methylene chloride 39.8-40.0 °C, and hexane 68-69 °C. The boiling point of the product TME oxide is 90.2-91.4 °C (753 mmHg),[103] higher than those of TME and either solvent. The boiling point of the hydroperoxide under atmospheric pressure is unavailable, but the reported bp is 54 °C (9 mmHg).[104] Acetone diperoxide is a solid and the reported melting point is 132-132.5°C.[105] The vapor pressures of the three products are lower than those of the starting alkene or the solvents. Furthermore these three products just account for very small fractions of the whole reaction mixtures even if the conversion of TME were raised to higher than 2% or neat TME was used. Actually, in most cases the concentrations of TME were 10, 30 and 50%. Most importantly, there is no question that the main component of the gas stream is oxygen. Considering all these factors, one can easily conclude that the partial pressures of these three products in the outlet gas stream are extremely low. Thus, if the gas stream carries away something from the reaction mixture, it will carry away mainly the solvent or TME instead of the products. Therefore, it is not likely that higher conversion will affect the

precision of the data collected. Experimentally, whether the gas stream will carry away enough products to make the data collected inaccurate can be easily examined by carrying out a control experiment, such as passing a stream of oxygen through a solution of TME oxide for a certain time under the ozonolysis conditions and analyzing how much of TME oxide was lost.

Third, in the discussion part, these authors stated: "Thus at high concentrations of **4** (i.e., TME) higher yields of epoxide are formed since dioxirane **13** (or carbonyl oxide **12**) has a greater opportunity to react with **4**. Concurrently there is a decrease in the formation of the diperoxide **5** as the concentration of **4** is increased since the carbonyl oxide precursor is removed by conversion to **13** and subsequent reaction with **4** to give epoxide."

The first sentence implies that at the lower concentrations of TME, the dioxirane formed has less opportunity to react with TME, so the lower yields of epoxide are obtained. In the another paper, Murray has reported that solutions of dimethyldioxirane can be stored at low temperature for several days.[59] Therefore, at the temperatures these authors employed dimethyldioxirane should not decompose in a short time. The time needed to finish the reaction between TME and dimethyldioxirane under the ozonolysis conditions these authors employed can be estimated as follows. Since only 2% of TME were converted to products, the concentration of TME is almost unchanged and is much larger than the concentrations of the dioxirane and the epoxide. Therefore, the second-order kinetic equation

$$t = \frac{1}{a-b} \ln \frac{b(a-x)}{a(b-x)} \frac{1}{k_2}$$

can be simplified to

$$t = \frac{1}{a} \ln \frac{b}{b-x} \frac{1}{k_2}$$

where *a* is the initial concentration of TME, b is the initial concentration of the dioxirane, and *x* is the concentration of the epoxide. The half-time (when $x = 1/2b$) for this reaction is

$$t_{v2} = \frac{\ln 2}{a \cdot k_2}$$

The second-rate constant for this epoxidation reaction at 25 °C was reported to be 7.1 ± 0.6 $M^{-1}S^{-1}$.[60] The lowest concentration of TME these authors employed is 1% (v/v), that is 0.11 *M* (the density of TME is 0.875 g/mL, the molecular weight is 84.16. So, $1 \times 0.875/84.16/0.1 \approx 0.10$). Thus,

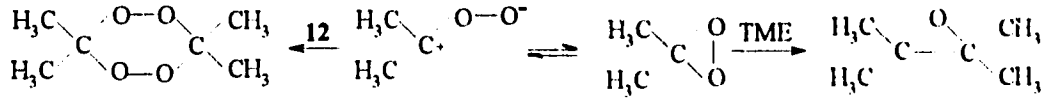
$$t_{v2} = \frac{\ln 2}{0.10 \cdot 7.1} = 0.98 \text{ second}$$

In neat TME, the concentration of TME is 10.4 *M* ($100 \times 0.875/84.16/0.1$). Thus,

$$t_{v2} = \frac{\ln 2}{10.4 \cdot 7.1} = 0.01 \text{ second}$$

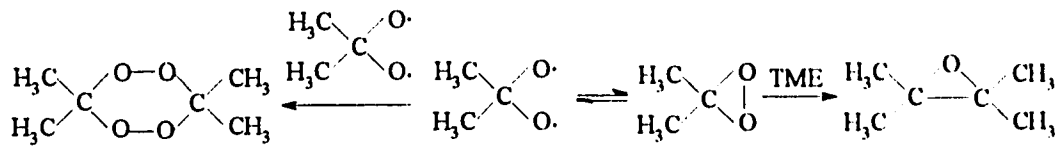
These data mean that as long as the dioxirane is produced, even at the lowest concentration of TME the epoxidation reaction can be completely finished in a few seconds. In other words, the opportunities of the reaction of dioxirane with TME are actually the same at different concentrations of TME and so the yields of epoxide should be independent of the initial concentrations of TME.

The second sentence implies that the conversion of the carbonyl oxide to either the dioxirane or the diperoxide is dependent on the initial concentration of TME. This can only happen if the following two alternative equilibria were present in the reaction system even though the authors did not clearly say so.



12

or



Thus, at higher concentrations of TME, the equilibria were shifted to the right so higher yields of the epoxide and lower yields of the diperoxide were obtained. However, to the best of our knowledge, there is no evidence or precedent of the equilibrium between the dioxirane and the corresponding carbonyl oxide or the diradical intermediate.[30(a)] Because such kinds of equilibria do not exist, the conversion of the common precursor carbonyl oxide to either dioxirane or diperoxide should not depend on the initial concentrations of TME. The competition between the formation of dioxirane and the formation of diperoxide from the common precursor carbonyl oxide should be dependent on the temperature because the two reactions have different reaction activation energies, as found in our study and also agreed by the authors. The other factors that may affect this competition would be the concentration of the carbonyl oxide and the polarity of the solvent.

Last, without considering the possible autooxidation of TME, these authors attributed the formation of TME epoxide and the hydroperoxide to the reactions of TME with dioxirane and singlet oxygen. In my opinion, the epoxide and the hydroperoxide are most likely formed from a radical chain oxidation reaction as discussed in Chapter I of this thesis. TME is such a material that it is very easy to undergo autooxidation. As described by the

authors, a trace of epoxide could be detected by just storing a purified sample of TME at room temperature for 3 hours and 20 minutes and after 24 hours both epoxide and hydroperoxide could be detected. It can be expected that if a stream of oxygen is passed through the sample (as in the ozonolysis), a much shorter time will be needed to form the two products. Unfortunately, this simple control experiment was not carried out by the authors. Furthermore, the hydroperoxide, once it is produced, will react with ozone. It has been shown that the reaction between hydroperoxide and ozone will result in the formation of various radicals.[34] If this reaction does occur here, the resulting radicals will serve as initiators and the radical chain reaction will be largely accelerated. Thus, the formation of the epoxide and the hydroperoxide in less than 10% yield can be well accounted for by the radical chain oxidation reaction and the involvement of dioxirane epoxidation and singlet oxygen oxygenation is unnecessary.

On the basis of the above discussion, personally I believe these authors did not provide convincing evidence to support their conclusion that the dimethyldioxirane is involved in the ozonolysis of TME.