The Influence of Remote Heteroatom Substituents on the Stereoselectivity of Cyclopentene Ozonolysis

William H. Bunnelle* and Terry A. Isbell

Department of Chemistry, University of Missouri—Columbia, Columbia, Missouri 65211

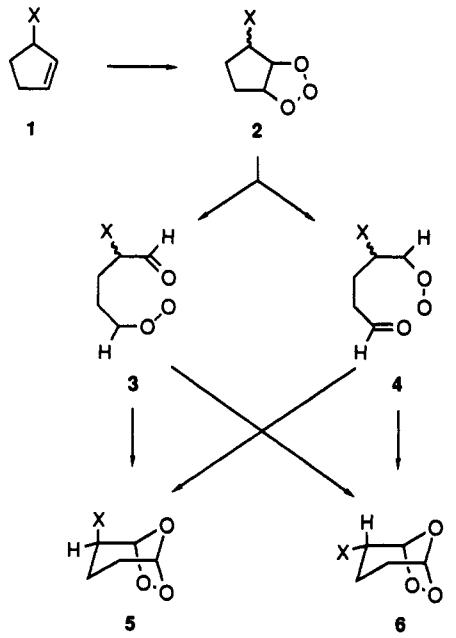
Received August 13, 1991

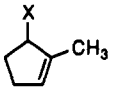
The stereoselectivity for ozonide formation from cyclopentenes with allylic heteroatom substituents has been examined. Silyl ethers give high selectivity in favor of the exo-substituted ozonide, while esters of 2-cyclopentenol form ozonide mixtures with little stereoselection. Trapping experiments establish that fragmentation of the primary ozonides is highly regioselective to give only one of the isomeric ω-oxo carbonyl oxide intermediates and that the variation in final ozonide stereochemistry results from differing interactions between the remote substituent groups and the carbonyl oxide system during cyclization of this intermediate. The effect of substituent and solvent on ozonide stereochemistry suggests a dominant role for electrostatic repulsion between carbonyl oxide and the heteroatom substituent during intramolecular cycloaddition. A chair-like transition state is proposed for this process and is in accord with the increase in exo selectivity for derivatives of 2-methyl-2-cyclopentenol.

Introduction

Extensive investigation of the mechanism of alkene ozonolysis has confirmed the essential features of the pathway originally proposed by Criegee.[1] Apart from the long-established utility of ozonolysis in synthesis and structure determination, much of the current interest in this process centers on the nature of the transient carbonyl oxide intermediate[2] formed along with a stable carbonyl compound by fragmentation of the alkene–ozone cycloadduct, the primary ozonide (1,2,3-trioxolane). The carbonyl oxide is a reactive 1,3-dipole and will, under appropriate conditions, cyclize with the carbonyl compound to produce a 1,2,4-trioxolane (final ozonide). One of the more interesting features of alkene ozonolysis is the fact that two new stereocenters are generated in the production of a final ozonide. Indeed, the (cis/trans) stereoselectivity of ozonide formation has been shown to depend, in some cases, on the starting alkene (*E*/*Z*) geometry, a result which has had a profound impact on the current understanding of the intricacies of the ozonolysis process.[3,4] Much less is known, however, about the influence of remote substituents on the stereochemistry of ozonide formation, i.e., remote stereoinduction. To our knowledge, only one systematic study has been reported. Nojima and co-workers[5] found that alkyl-substituted indenes lead to mixtures of the corresponding *exo*- and *endo*-ozonides whose proportions are largely dependent on the steric effects of the substituents, expressed both in the addition of ozone to the alkene and also during the recombination of the intermediate carbonyl oxide–carbonyl pair. Since the intermediates in alkene ozonolysis are polar, it is likely that polar substituents will exhibit electronic effects on the stereochemistry of ozonide formation, but information on this point is scarce. In connection with our work involving the chemistry of peroxides from alkene ozonolysis, we became interested in determining the way in which a remote heteroatom substituent might influence ozonide stereochemistry. In this paper, we describe our studies of the stereoselectivity in the ozonolysis of cyclopentenes 1.

Scheme I





1a X = OTBS
1b X = $OSi(iPr)_3$
1c X = $OSiMe_3$
1d X = Cl
1e X = OAc
1f X = p-anisoyloxy
1g X = benzoyloxy
1h X = 3,5-dinitrobenzoyloxy
1i X = p-nitrobenzoyloxy

7a X = OTBS
7c X = $OSiMe_3$
7e X = OAc

Substituted cyclopentenes were chosen for study because they form ozonides efficiently and because the constraints of the bicyclic ozonide system restrict the possibilities for stereoisomerism to the relative disposition of the remote substituent, as for the exo isomer **5** and the endo isomer **6**. It is not a trivial matter to sort out the factors which determine the overall stereoselectivity, since conversion of an alkene to an ozonide involves three distinct steps, each of which introduces multiple stereo- and/or regiochemical possibilities. While the ozonide stereochemistry

(1) Criegee, R.; Wenner, G. *Chem. Ber.* **1949**, *564*, 9.
(2) Reviews: (a) Sander, W. *Angew. Chem., Int. Ed. Engl.* **1989**, *29*, 344. (b) Bunnelle, W. H. *Chem. Rev.* **1991**, *91*, 335.
(3) (a) Lattimer, R. P.; Kuczkowski, R. L.; Gilles, C. W. *J. Am. Chem. Soc.* **1974**, *96*, 348. (b) Bailey, P. S.; Ferrell, T. M. *J. Am. Chem. Soc.* **1978**, *100*, 899. (c) Kuczkowski, R. L. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; pp 197–275.
(4) Cremer, D. *J. Phys. Chem.* **1979**, *70*, 1911. (b) Cremer, D. *J. Am. Chem. Soc.* **1981**, *103*, 3619. (c) Cremer, D. *J. Am. Chem. Soc.* **1981**, *103*, 3627.
(5) (a) Miura, M.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1984**, *106*, 2932. (b) Miura, M.; Fujisaka, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Org. Chem.* **1985**, *50*, 1504.
(6) Bailey, P. S. *Ozonation in Organic Chemistry*; Academic Press: New York, 1978; Vol. 1; pp 25–29.

0022-3263/92/1957-0729$03.00/0

is actually set during the final step of the Criegee mechanism, namely the intramolecular cycloaddition of carbonyl oxide with the aldehyde, it must be recognized that the ultimate stereochemical outcome can also be influenced by earlier mechanistic events. Thus, Nojima has suggested that the facial selectivity of ozone addition to the starting alkene can direct the final ozonide stereochemistry, at least in sterically congested systems.[5] Likewise, the regioselectivity of primary ozonide fragmentation may influence the overall stereoselectivity of final ozonide formation. Two modes, corresponding to cleavage of either O–O bond, are possible: each pathway leads to a different set of carbonyl oxide and carbonyl groups. For example, the substituted primary ozonide **2** can fragment to either **3** or **4**.[7] Both of these can cyclize to the *exo*- and *endo*-ozonides **5** and **6**, but it is likely that the stereoselectivities of these two cycloaddition pathways are different. To the extent that they are, the branching ratio for primary ozonide cleavage (**3**:**4**) will have a significant role in determining final ozonide stereochemistry.

Despite these potential complications, the study of stereoinduction in ozonolysis offers the possibility for learning more about the character and chemistry of the carbonyl oxide intermediate. Little is known about the way in which remote substituents influence the reactions of carbonyl oxides, but, in favorable cases, these interactions will be expressed in the ozonide stereochemistry. We have found that the stereochemistry of ozonides from 2-cyclopenten-1-ol derivatives depends markedly on the nature of the alcohol blocking group and that the mechanistic scenario can be analyzed so that the stereochemical results provide direct information about substituent effects on carbonyl oxide cyclization.

Results and Discussion

The starting materials **1a–i** were easily prepared by standard manipulations of 2-cyclopenten-1-ol,[8] or, in the case of **1d**, by addition of HCl to cyclopentadiene according to the reported procedure.[9] We have been especially interested in alcohol derivatives which lend themselves to further manipulation after ozonolysis, and so we have focused on esters and silyl ethers. The choice of substituents was limited somewhat by the tendency for some cyclopentene derivatives to suffer elimination and/or polymerization. For example, 3-chlorocyclopentene is an unpleasant and exceedingly reactive material which must be used soon after it is prepared. In contrast, the derived ozonide seems to be quite stable and can be stored in a refrigerator for many months without apparent decomposition.

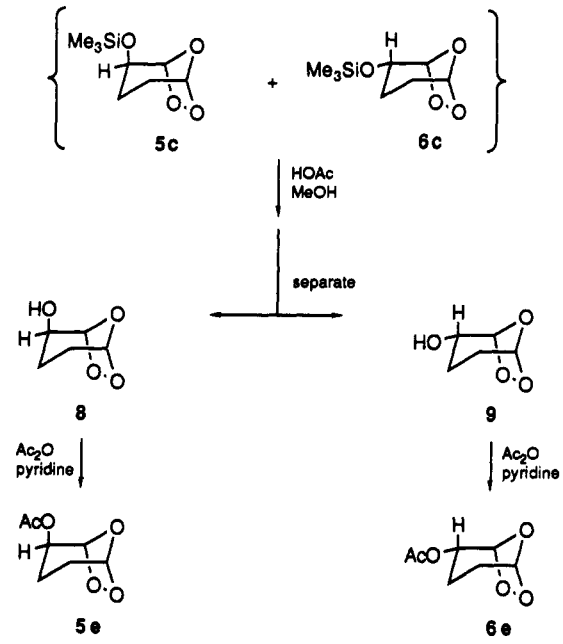
A few derivatives of 2-methyl-2-cyclopentenol (**7**) have also been included in this study. The parent alcohol was prepared by reduction of the corresponding ketone with lithium aluminum hydride and converted by standard procedures without complication to **7a**, **7c**, and **7e**.

Stereoselectivity of Ozonide Formation. Ozonation of the substituted cyclopentenes was carried out under standard conditions (0.1–0.3 M solution in dichloromethane, −78 °C). In each case, the alkene was converted to a mixture of the stereoisomeric exo and endo ozonides. The diastereomer ratios were determined from HPLC analysis of the crude reaction mixtures and are presented in Table I. The ozonides are reasonably stable, and the mixtures can be easily separated from byproducts with flash chromatography. In some cases, for example **5** and **6a,b,h,i**, the individual ozonide stereoisomers could be separated in this way. For others, however, it was not possible to separate the *endo*- and *exo* ozonides on preparative scale. Fortunately, authentic samples of the stereochemically pure ozonides could be obtained from **5** and **6c** by the synthetic manipulations outlined in Scheme II. The inseparable mixture of **5** and **6c** is readily hydrolyzed to the corresponding mixture of hydroxy ozonides **8** and **9** with a trace of acetic acid in methanol at room temperature. Under these conditions, the silyl group is removed cleanly, leaving the ozonide system intact. In contrast to the TMS ethers **5** and **6c**, the stereoisomeric hydroxy ozonides **8** and **9** are separable by careful flash chromatography. In this way, pure samples of the individual *endo*- and *exo*-hydroxy ozonides **8** and **9** are available. Further derivatization of the alcohol is straightforward. Although ozonides are known to be sensitive to acids and bases, in our experience these materials are rather robust and can be carried successfully through simple reactions like alcohol derivatization. For our purposes, the silylation or esterification of the *exo*-ozonide **8** proceeds smoothly using standard methodologies, and provides stereoisomerically pure samples of **5a**, **5c**, and **5e**. At the same time, this sequence establishes an unambig-

Table I. Stereoselectivity of Ozonide Formation from Substituted Cyclopentenes

starting material	substituent group (X)	ozonide yield (%)	stereoisomer ratio exo:endo
1a	t-Bu(Me)$_2$SiO–	81	91:9
1b	(i-Pr)$_3$SiO–	76	89:11
1c	Me$_3$SiO–	85	86:14
1d	Cl	80	75:25
1e	AcO–	64	60:40
1f	p-MeOC$_6$H$_4$CO$_2$–	79	56:44
1g	C$_6$H$_5$CO$_2$–	59	53:47
1h	3,5-(O$_2$N)$_2$C$_6$H$_3$CO$_2$–	41	45:55
1i	p-O$_2$NC$_6$H$_4$CO$_2$–	58	43:57
7a	t-Bu(Me)$_2$SiO–	61	99.4:0.6
7c	Me$_3$SiO–	62	98.5:1.5
7e	AcO–	21	91:9

Scheme II

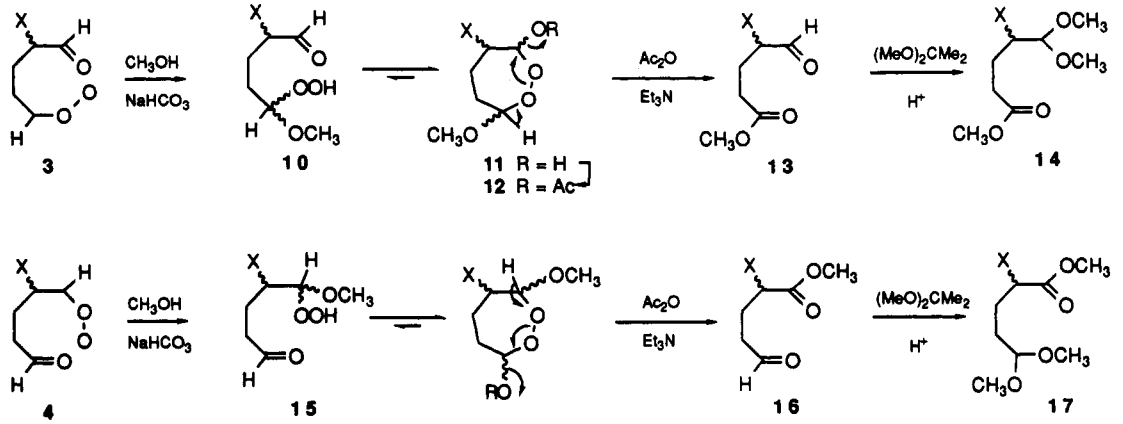


(7) Although carbonyl oxides have often been represented as zwitterionic species, most of the available evidence is consistent with a singlet diradical structure, as predicted by theoretical calculations. The representations of **3** and **4** in Scheme I, and throughout this paper, are meant to express this character. For further discussion of this point, see ref 2.

(8) Alder, K.; Flock, F. H. *Chem. Ber.* **1956**, *89*, 1732.

(9) Moffett, R. B. *Organic Syntheses*: Wiley: New York, 1963; Collect. Vol. IV, p 238.

Scheme III



uous stereochemical correlation among these compounds. In exactly the same manner, the *endo*-hydroxy ozonide **9** can be derivatized to provide access to the isomerically pure *endo*-ozonide derivatives, although the lower yield of **9** makes this less practical for preparative purposes.

Each of the ozonides has spectroscopic properties fully in accord with the assigned structure. The endo/exo stereochemical assignments are based on analysis of the ^{1}H NMR spectra. The 6,7,8-trioxabicyclo[3.2.1]octane ring system is relatively rigid, and there is a strong preference for the six-membered ring to exist in the chair conformation.[10] Therefore, for the endo series of ozonides, the substituent is equatorial and H-2 is axial. Conversely, the *exo*-ozonides exist with the substituent in an axial orientation with H-2 equatorial. The endo–exo stereochemistry is indicated by the coupling pattern for H-2. For example, in **6e**, this proton appears as a broadened doublet of doublets (J = 10.4, 6.2 Hz) centered at 4.87 ppm, with the larger coupling characteristic of vicinal diaxial interaction. For **5e**, H-2 gives rise to a poorly resolved multiplet ($w_{1/2}$ = 9.4 Hz) at 4.75 ppm, consistent with the smaller couplings to an equatorial proton (in both isomers, vicinal coupling from H-2 to the bridgehead proton is too small to resolve, apparently due to the accumulation of electronegative substituents[11]). Similar features were observed for the other substituents, permitting the stereochemical assignments in an analogous manner.

As is evident from the data in Table I, the ozonide stereoselectivity varies considerably for the different substituents investigated. The most obvious trend is that the silyl ethers show high preference for formation of the exo-substituted ozonide **5**, while the esters exhibit little stereoselectivity. Within these groups, more subtle effects can be identified. Thus, the reaction is sensitive to steric interactions with the substituents: the bulkier trialkylsilane blocking groups show a somewhat higher degree of stereoselection. Operation of an electronic effect can be seen in the data for the benzoate esters: there is a modest increase in the proportion of *endo*-ozonide as the aryl substituent is made more electron-withdrawing. Finally, the presence of a 2-methyl group causes a marked increase in exo selectivity for both ester and silyl ether types, as exemplified by comparison of entries **7c** and **7e** with the analogues **2c** and **2e**.

Regioselectivity of PO Fragmentation. As mentioned above, the overall stereoselectivity for ozonide formation may actually represent contributions from cyclization of two different carbonyl oxides (**3** and **4**), and so the relative amounts of these intermediates should be established by appropriate trapping experiments. Earlier studies have shown that electron-withdrawing substituents can have a strong directive effect on the generation of carbonyl oxide from PO to favor the fragmentation mode which generates the carbonyl oxide at the alkene carbon most remote to the substituent.[12] In the case of cyclopentene **1**, this would lead to predominant formation of **3**, but we could not be certain at the outset of this work whether a significant amount of the other regioisomer (**4**) would also form, or how the branching ratio (**3**:**4**) might be affected by changes in the substituent from carboxylate ester to silyl ether.

The usual procedure for determining the regioselectivity of primary ozonide fragmentation involves ozonation of the alkene in a participating solvent such as methanol. Under these conditions, the intermediate carbonyl oxides are trapped by the alcohol solvent before intramolecular cyclization can occur. In principle, analysis of the resulting isomeric α-methoxyhydroperoxides (**10** vs **15**) provides the branching ratio (**3**:**4**) for fragmentation of the primary ozonide. In the present case, direct analysis of the α-methoxy hydroperoxides is not a simple matter. For example, **10** and **15** each exists as two diastereomers, corresponding to stereorandom capture of the carbonyl oxide **3** (Scheme III). Even more problematic is the fact that the aldehyde exists in equilibrium favoring the cyclic hemiperacetals (e.g., **11**), also a mixture of stereoisomers.[13] Obviously, this proliferation of isomers seriously complicates attempts at direct analysis of the α-methoxy hydroperoxides. To get around this problem, the crude ozonolyzate was treated with acetic anhydride and triethylamine, a protocol developed by Schreiber for dehydration of the α-methoxyhydroperoxide mixture to the corresponding methyl esters.[14] Thus, acetylation of the

(10) This contention is supported by MM2 calculations for the parent system as well as the exo-substituted trimethylsilyl ether, which place the chair conformers 4.4 and 3.3 kcal/mol, respectively, lower than the boat forms. Further evidence for this point comes from the X-ray crystal structure of an analogous ozonide. See: Bunnelle, W. H.; Isbell, T. A.; Barnes, C. A.; Qualls, S. *J. Am. Chem. Soc.* **1991**, *113*, 8168.

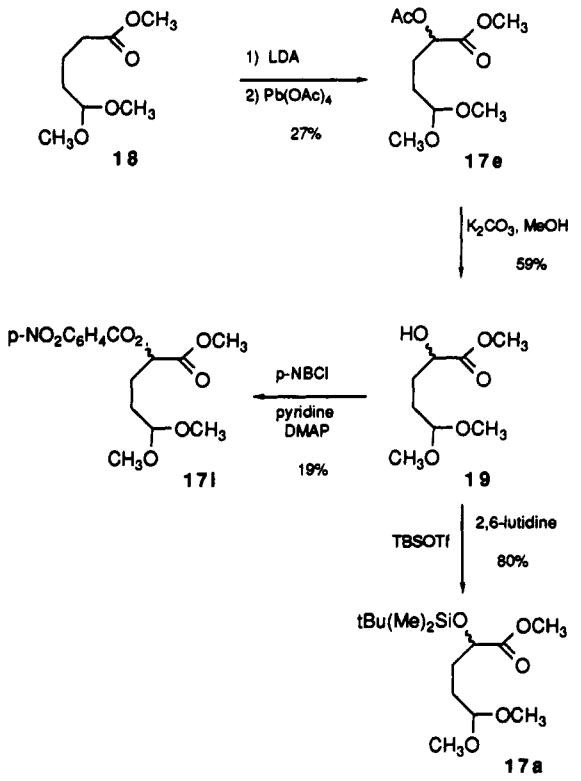
(11) Abraham, R. J.; Fisher, J.; Loftus, P. *Introduction to NMR Spectroscopy*; John Wiley and Sons: New York, 1988; pp 42–45.

(12) (a) Fliszár, S.; Renard, J. *Can. J. Chem.* **1970**, *48*, 3002. (b) Fiszár, S.; Granger, M. *J. Am. Chem. Soc.* **1970**, *92*, 3361.

(13) It has been reported that ozonation of cyclopentene in methanol leads to oligomeric peroxyhemiacetals via intermolecular reaction of **10** (X = H), and not to the intramolecular cyclization product analogous to **11**: Griesbaum, K.; Neumeister *Chem. Ber.* **1982**, *115*, 2697. Those experiments, however, were carried out at concentrations some 10 times those used by us. We do not have rigorous proof for the cyclic, monomeric peroxide structure, but the chromatographic mobility of these materials is not typical for peroxide oligomers. In addition, we do not detect diester and dialdehyde byproducts, as are found for decomposition of the oligomers.

(14) (a) Schreiber, S. L.; Claus, R. E.; Reagen, J. *Tetrahedron Lett.* **1982**, *23*, 3867. (b) Claus, R. E.; Schreiber, S. L. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VII, p 168.

Scheme IV



peroxyhemiacetal **11** direct base-induced fragmentation to give **13**, in which the carboxylate system ultimately derives from the carbonyl oxide. At the same time **15**, from trapping of the carbonyl oxide **4**, is converted to the isomeric 5-oxo ester **16**. These products proved to be rather sensitive, presumably owing to the reactivity of the free aldehyde group, and so the mixture was converted to the acetals **14** and **17** to facilitate product analysis. A representative silyl ether (**1a**) and two esters (**1e** and **1i**) were selected for this study. In each case, one dominant isomer, corresponding to **14**, was detected by NMR. The structural assignment follows from the signal for the acetal methine proton, which appears as a doublet at 4–4.5 ppm, a coupling pattern in accord with **14**, and not the isomeric α-substituted ester **17**. Signals for the minor product **17** could not be identified with confidence in the NMR spectra of the crude reaction mixtures, and so authentic samples were prepared by the route outlined in Scheme IV. Thus, methyl 5,5-dimethoxypentanoate (**18**)[15] was oxidized directly to **17e** with $Pb(OAc)_4$.[16] Methanolysis to the hydroxy ester **19** and straightforward derivatization provided access to **17a** and **17i**. With these materials in hand, it was possible to confirm the presence of small amounts of **17** in the crude ozonolysis trapping mixtures and allowed quantitation of the ratio by capillary gas chromatography (HPLC for **14**, **17i**).

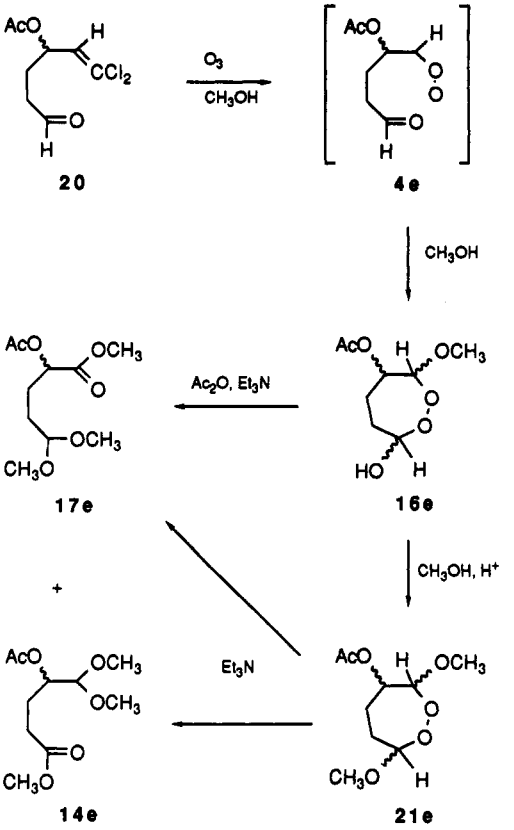
The ratios determined by this method are given in Table II. We have encountered, however, a possible source of error in this method which should be considered when determining the regioselectivity of fragmentation of primary ozonides from cyclic alkenes. We initially attempted an independent and unambiguous preparation of the less-favored carbonyl oxide **15e** by ozonolysis of the 1,1-dichloroalkene **20** in the presence of methanol. It is well-established that ozonolysis of vinyl chlorides proceeds

(15) Stevens, R. V.; Lee, A. W. M. *J. Am. Chem. Soc.* **1979**, *101*, 7032.
(16) Rubottom, G. M.; Gruber, J. M.; Marrero, R.; Juve, H. D.; Kim, C. W. *J. Org. Chem.* **1983**, *48*, 4940.

Table II. Regioselectivity of Primary Ozonide Fragmentation from Substituted Cyclopentenes

starting material	substituent group (X)	trapping products (yield, %)	carbonyl oxide branching ratio
1a	*t*-Bu(Me)$_2$SiO–	**14a** (17), **17a** (0.25)	**3a:4a** (99:1)
1e	AcO–	**14e** (72), **17e** (1.5)	**3e:4e** (98:2)
1i	*p*-$O_2NC_6H_4CO_2$–	**14i** (69), **17i** (0.7)	**3i:4i** (99:1)
7c	Me_3SiO–	**24c** (38), **25c** (27), **26c** (28)	**22c:23c** (70:30)
7e	AcO–	**24e** (32), **25e** (31), **26e** (15)	**22e:23e** (81:19)

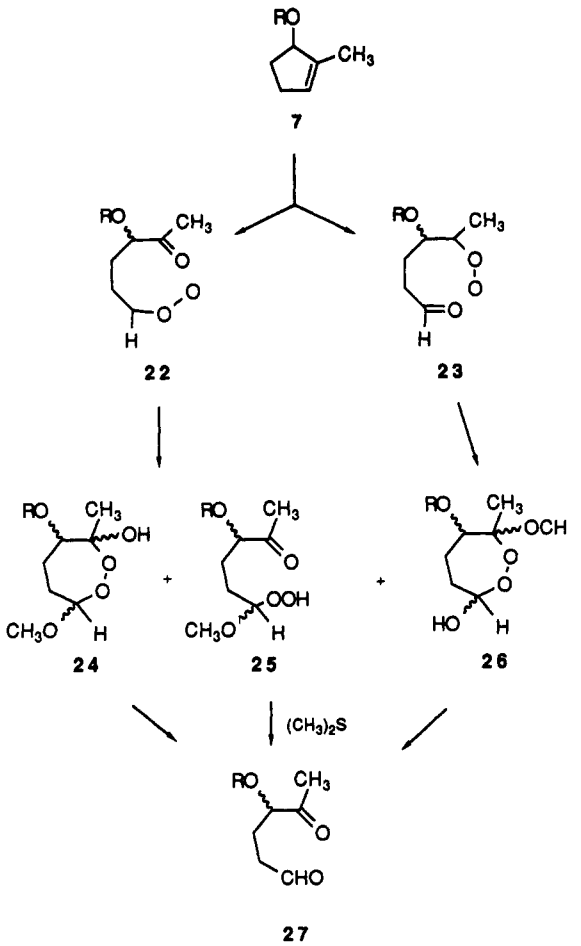
Scheme V



with reliable regioselectivity to produce the carbonyl oxide on the fragment remote to the halogen.[17] For **20**, this permits efficient access to carbonyl oxide **4e** without competing production of **3e**. To our surprise, ozonolysis of **20**, followed by the workup as described above, led to the α-substituted ester **17e**, but accompanied by 30% of ester **14e**. Since the carbonyl oxide precursor to **14e** cannot be formed from **20**, this result requires a pathway for conversion of **4e** into **14e**. One plausible route involves conversion of the cyclic methanol–carbonyl oxide adduct **16e** to the peroxydiacetal **21e** (Scheme V).[18] This material cannot be acetylated, but may be decomposed by base with loss of methoxide. Deprotonation and peroxide cleavage of this intermediate occurs with little regioselectivity and leads to both **14e** and **17e**. According to this scenario, "leakage" of the carbonyl oxide **4** to give **14** (and, equivalently, from **3** to **17**) occurs to the extent that the cyclic peroxyhemiacetal **16** (or **11**) is transformed to **21**. This

(17) (a) Keul, H.; Griesbaum, K. *Can. J. Chem.* **1980**, *58*, 2049. (b) Meister, M.; Zwick, G.; Greisbaum, K. *Can. J. Chem.* **1983**, *61*, 2385. (c) Griesbaum, K.; Bandopuadhyay, A. R. *Can. J. Chem.* **1987**, *65*, 487. (d) Griesbaum, K.; Greinert, R. *Chem. Ber.* **1989**, *123*, 391.
(18) The conversion of peroxyhemiacetals to peroxyacetals on standing in alcohol solvent has been reported previously: (a) Franz, J. E.; Knowles, W. S.; Osuch, C. *J. Org. Chem.* **1965**, *30*, 4328. (b) Bailey, P. S. *J. Org. Chem.* **1957**, *22*, 1548. See also ref 6, pp 113–115.

Scheme VI



process will be catalyzed by acid, and so the use of suspended $NaHCO_3$ as a buffer during ozonation has been recommended. Nevertheless, even this precaution is not completely effective in eliminating transient, high local concentrations of acid. In particular, the ozonolysis of **20** generates HCl (from reaction of the phosgene byproduct with the solvent), which apparently causes substantial conversion of **16e** to **21e** before it is scavenged. The problem should be much less serious for the ozonolysis of **1**, since only traces of acid will be produced from side reactions, and the extent of product leakage will be correspondingly lower. Nevertheless, it is risky to assume exact correspondence between the product ratios (14:17) and the regioselectivity of primary ozonide cleavage (3:4), and so the numbers in Table II should be considered as approximate values for the branching ratio. In these examples, the measured regioselectivity is high enough so that the uncertainty has little impact on the conclusions of this report, but product crossover of this type may be serious for more equally balanced systems.

A somewhat different pattern for primary ozonide fragmentation is found for the methyl-substituted cyclopentenes **7**. It is well-established that trisubstituted alkenes react with ozone to produce the more highly substituted carbonyl oxide.[12] For **7**, this should lead to a larger fraction of the α-substituted carbonyl oxide **23**, compared to ozonolysis of **1**. As described above, the respective carbonyl oxides **22** and **23** can be trapped with methanol to give the cyclic peroxyhemiacetals **24** and **26**, respectively. The methyl group in **26** interferes with application of the acetylation–decomposition sequence described above, so the mixture of peroxides has to be analyzed directly. Fortunately, this problem is simpler than for the cyclopentenes **1**—Griesbaum has shown in similar systems that the ^1H NMR signal for the hydroxy-substituted methine (**26**) is consistently downfield of that adjacent to the methoxy group (**24**), and so the relative proportions of the regioisomers can be easily determined.[19] In the event, ozonolysis of **7c** in methanol–dichloromethane (1:1) at −78 °C leads to a mixture of **24c**, **25c**, and **26c**, in relative proportion of 41:29:30, respectively (92% yield). The open chain isomer **25c** was identified by the NMR signal for the methyl ketone at 2.16 ppm; it, as well as **24c** and **26c**, exists as a mixture of diastereomers. Both **24c** and **25c** are derived from trapping of **22c**, while **23c** leads only to **26c**. The presence of significant amounts of **25c** along with **24c** is not unexpected and simply reflects the lessened propensity for cyclization of the hydroperoxide onto a ketone carbonyl, as compared to the aldehyde precursor for **26c**. In order to verify that all of the components of the mixture were peroxidic, an NMR sample was treated with excess dimethyl sulfide. After several hours at room temperature, essentially complete conversion to the ketoaldehyde **27c**, along with an equivalent amount of dimethyl sulfoxide, was observed. Taken together, these results indicate that the fragmentation of the primary ozonide from **7c** proceeds with approximately 7:3 regioselectivity in favor of **22c**. Thus, while the directing effect of the heteroatom substituent still dominates, it is partly compensated by the methyl substituent in **7c**.

Similar results were obtained for the acetate **7e**. In this case, ozonolysis in methanol–dichloromethane provides **24e**, **25e**, and **26e** in the ratio 41:40:19, respectively (77% yield), indicating 4:1 regioselectivity for production of the carbonyl oxide **22e** over **23e**.

Origin of the Stereoselectivity. The stereochemical results must be considered within the context of the Criegee mechanism for alkene ozonolysis. In principle, the overall stereoselectivity of the process can be influenced at any one (or more) of the three cycloaddition/cycloreversion steps. Therefore, each step must be taken into account in any rationalization of the substituent effect on ozonide stereoselectivity.

It is unlikely, in our view, that the stereochemistry of the final ozonides depends in any substantial way on the diastereofacial preference for addition of ozone to the alkene **1** (or **7**). The stereochemical information from ozone addition can be transferred to the final ozonide only if the intermediate carbonyl oxide–aldehyde system retains some of the conformational features of the primary ozonide. Nojima has suggested that this is the case in sterically crowded systems, and particularly that intramolecular cycloaddition takes place before significant reorientation of the carbonyl oxide can occur, so that the major ozonide product has the peroxide bridge on the face of the molecule corresponding to initial attack by ozone.[5] For the relatively unencumbered systems we have examined, single-bond rotations will be rapid, and any remnants of the primary ozonide conformation should disappear before the eventual cyclization to the ozonide, and so the facial selectivity for ozone addition will not directly influence ozonide stereochemistry.

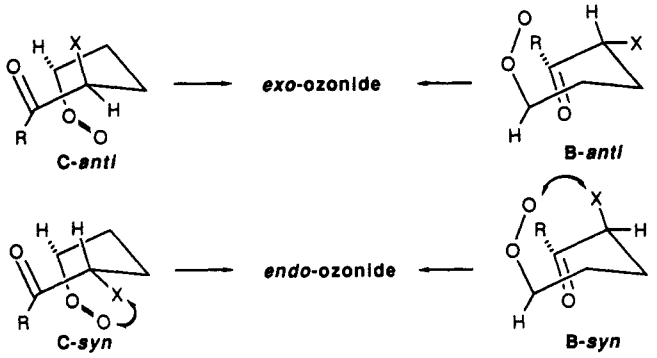
Likewise, the trapping experiments demonstrate that only one of the primary ozonide fragmentation paths contributes significantly, at least for the cyclopentenes **1**. This situation greatly simplifies analysis of the ozonolysis stereoselectivity, since it implies that the endo/exo ozonide distribution reflects the diastereoselectivity of a single step, namely the intramolecular cycloaddition of the carbonyl

(19) Griesbaum, K.; Kiesel, G. *Chem. Ber.* **1989**, *122*, 145.

oxide 3. Moreover, the cyclization process is clearly sensitive to the nature of the remote substituent, so that these experiments provide data relating to the interaction of these substituents with the carbonyl oxide.

A most striking result is the pronounced preference for production of the *exo*-ozonide when the substituent is a (trialkylsilyl)oxy group. This indicates a preferred cycloaddition mode involving approach of the carbonyl oxide to the face of the aldehyde opposite to the α-substituent. The individual ozonide stereoisomers do not interconvert under the ozonolysis conditions, and so the ozonide distribution appears to be kinetically controlled. Indeed, in the case of the silyl ethers, the diastereomer ratio is contrathermodynamic—the major *exo*-ozonide exists with the bulky substituent in the axial position on the 6,7,8-trioxabicyclo[3.2.1]octane ring system and should be significantly less stable than the *endo*-ozonide, where this group is equatorial.

What are the factors which control the orientation of carbonyl oxide–aldehyde addition in 3? It should be noted that we consider this process to be a concerted (although asynchronous), 1,3-dipolar cyclization. Stepwise mechanisms have been proposed for the carbonyl oxide addition,[20] but these have generally involved more sterically congested systems. For unencumbered systems, both theoretical and experimental studies indicate that a concerted mechanism operates.[21] For the intramolecular reactions involved here, only a few transition state geometries are possible. First, cyclization can occur only if the stereochemistry of the carbonyl oxide moiety is syn, as in 3. With that restriction, alignment of the carbonyl oxide with the aldehyde can be achieved through either a chair or a boat-like conformation, indicated C and B, respectively. When the α-substituent is present, each of these leads to two diastereotopic arrangements, labeled syn and anti to indicate the relationship between the peroxide and the substituent. In each case, it is the anti transition state geometry which leads to the *exo*-ozonide, with the syn transition state giving the *endo*-ozonide.



Initially, we felt that the preference for the anti approach of the carbonyl oxide to the aldehyde, as observed for the silyl ether and chloride substituents, might be explained by invoking a model similar to the Felkin–Anh transition state for nucleophilic attack at a carbonyl group.[22] By this reasoning, the approach of the terminal oxygen of the carbonyl oxide to the aldehyde carbon will be most favorable along a trajectory which is antiperiplanar to the substituent X, and which develops a stabilization interaction between the incipient C–O bond and the C–X σ^* orbital. It can be seen that the C, anti geometry accommodates this requirement reasonably well, and accounts for the predominant formation of the *exo*-ozonide.

This model does not, however, fit the results obtained for the ester substituents. For these compounds, a much lower proportion of *exo*-ozonide is obtained. The electron-withdrawing effect of the ester acyl group should lower the energy of the C–X σ^* orbital relative to that of the silyl ethers, and one should expect a stronger interaction with the developing C–O bond, which in turn should provide for enhanced exo selectivity. This is not observed.

Instead, we propose that electrostatic repulsion between the terminal oxygen of the carbonyl oxide and the substituent X is a critical factor in determining the ozonide stereoselectivity. The electronic structure of carbonyl oxides has been much debated, but high-level computations indicate that they are best represented as polar, singlet biradicals, where the extent of charge separation will depend on substituents and solvation.[23] In any case, the terminal oxygen atom is electron rich[24] and comes in close proximity to the heteroatom substituent X in either of the syn transition states, which destabilizes this approach relative to the alternate, anti arrangements. The extent of destabilization will depend on the nature of the substituent X, and particularly the electron density around the heteroatom. In general, one would expect that the electron density around an ester oxygen would be substantially reduced as compared to a silyl ether and the barrier to syn addition would be reduced. Therefore, the silyl ethers should exhibit a much higher selectivity for *exo*-ozonide (via anti addition) than do the esters. This is just what is found. Whereas the silyl ethers exhibit uniformly high preference for the *exo*-ozonide, the esters display little stereoselectivity. Moreover, the electronic effect is consistent with the results for the substituted benzoate esters. The electron-withdrawing nitro group causes a further, albeit modest, decrease in the proportion of *exo*-ozonide, while a *p*-methoxyl substituent has the opposite effect. Not surprisingly, the ratio from chlorocyclopentene falls in a range intermediate between the ethers and the esters—the relatively high electron density of the chlorine atom is offset somewhat by the longer C–Cl bond so that interaction with the carbonyl oxide is less pronounced.

We have observed an interesting solvent effect in the ozonolysis of the acetate **1e**. The stereoselectivity of the reaction has been found to be a gentle function of the solvent polarity, with a small but real increase in the ratio of *exo*- to *endo*-ozonide for the more polar ozonolysis solvents. In order to permit the study of a wider range of solvents, these ozonolyses were carried out at 0 °C. The results are gathered in Table III. The solvent effect can be rationalized as follows: the solvent properties are expected to influence electronic character of the carbonyl oxide, so that its polarity will increase as does that of the solvent.[25] The shift of more electron density to the terminal oxygen of the carbonyl oxide will accentuate the extent of electrostatic repulsion in the transition state

(20) (a) Su, J.-S.; Murray, R. W. *J. Org. Chem.* **1980**, *45*, 678. (b) Murray, R. W.; Su, J.-S. *J. Org. Chem.* **1983**, *48*, 817. (c) Nakamura, N.; Fujisaka, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1989**, *111*, 1799.

(21) (a) Fong, G. D.; Kuczkowski, R. L. *J. Am. Chem. Soc.* **1980**, *102*, 3763. (b) Choe, J.-I.; Kuczkowski, R. L. *J. Am. Chem. Soc.* **1983**, *105*, 4839. (c) Choe, J.-I.; Painter, M. K.; Kuczkowski, R. L. *J. Am. Chem. Soc.* **1984**, *106*, 2891. (d) Keul, H.; Kuczkowski, R. L. *J. Org. Chem.* **1985**, *50*, 3371.

(22) Anh, N. T. *Top. Curr. Chem.* **1980**, *88*, 145 and references cited therein.

(23) See, for example: Gauss, J.; Cremer, D. *Chem. Phys. Lett.* **1989**, *163*, 549. A survey of computational results is provided in ref 2b.

(24) Cremer, D.; Schmidt, T.; Sander, W.; Bischof, P. *J. Org. Chem.* **1989**, *54*, 2515.

(25) (a) Harding, L. B.; Goddard, W. A., III. *J. Am. Chem. Soc.* **1978**, *100*, 7180. (b) Steinke, T.; Hänsele, E.; Clark, T. *J. Am. Chem. Soc.* **1989**, *111*, 9107.

Table III. Solvent Effect on Ozonide Stereoselectivity

starting material	solvent	polarity[a] ϵ_r	polarity[a] μ (D)	ozonide yield (%)	stereoisomer ratio exo:endo
1e	pentane	1.84	0.0	77	49:51
1e	CCl_4	2.23	0.0	69	48:52
1e	toluene	2.38	0.30	62	62:38
1e	CH_2Cl_2	8.93	1.56	77	62:38
1e	ethyl acetate	6.02	1.83	79	67:43
1e	acetonitrile	35.94	3.54	66	66:34

[a] Solvent polarity parameters: dielectric constant (ϵ) and dipole moment (μ) taken from: Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, VCH: Weinheim, 1988; pp 408–410.

leading to the *endo*-ozonide, and so the proportion of *exo*-ozonide should increase with solvent dipolarity as is observed.

In the absence of detailed calculations, there is little information to permit a reliable distinction between the chair and boat transition states. At this point, however, we feel that the trends in ozonide stereoselectivity are best rationalized in terms of competition between the chair transition states, C,anti and C,syn. As described above, a dominant feature affecting the ozonide stereoselectivity is the electrostatic repulsion between the carbonyl oxide and the substituent group X, which favors the C, anti transition state. In this geometry, however, the substituent group is forced into a pseudoaxial orientation, while the alternate C,syn transition state places X in the more favorable pseudoequatorial position. On this basis, we might expect that as the electrostatic repulsions between the carbonyl oxide and X become less significant, an inherent preference for the *endo*-ozonide via the C,syn TS might emerge. Indeed, the predicted reversal of stereoselectivity is observed for **1g** and **1h**, a result which does not follow from consideration of the respective boat transition states.

A marked improvement in the exo selectivity is obtained for the ozonides from the 2-methylcyclopentenes **7a,c,e**, as compared to their unmethylated analogues. Thus, while 3-acetoxycyclopentene forms a 1.5:1 mixture of *exo*- and *endo*-ozonides, respectively, the ozonide mixture from 3-acetoxy-2-methylcyclopentene (**7e**) favors the exo isomer by a 10.5:1 ratio. A similar enhancement is observed for the trimethylsilyl ethers, where the predominance of the *exo*-ozonide increases from 6.5:1 (for **1c**) to better than 50:1 for **7c**. Because the 2-methylcyclopentene derivatives fragment to give appreciable amounts of both regioisomeric carbonyl oxides (70% **22c**, 30% **23c** from **7c**), the origin of the ozonide stereochemistry in these cases is less well-defined. For example, it is not clear how much of the ozonide derives from **22** and how much from **23**. Nevertheless, the data permit the deduction that cyclization of **22** occurs with higher stereoselectivity than for **3**. For example, ozonation of **7c** provides, via a 7:3 mixture of **22c** and **23c**, a 62% yield of **26c** with >50:1 exo selctivity. Even if cyclization of **23c** was 100% efficient to the *exo*-ozonide, more than half of the product must derive from **22c**, and with a minimum stereoselectivity for this carbonyl oxide of ca. 20:1. The numbers for **7e** work out less satisfactorily, because the low yield of ozonide obtained in CH_2Cl_2 (21%) does not require any contribution from cyclization of **22e**. On the other hand, we have found that ozonide formation from **7e** is considerably more efficient in pentane (70% yield); in accord with the solvent effect discussed above, the stereoselectivity in this solvent (6.6:1) is slightly lower than in dichloromethane. With the assumption that the carbonyl oxide branching ratio for **7e** is not substantially affected by the reaction solvent,[26] we may conclude that carbonyl oxide **22e** also cyclizes with substantially higher selectivity than does the unmethylated analogue **3e**.

The enhanced selectivity for the anti mode of cyclization of **22** (R = Me) compared to **3** (R = H) can be rationalized in terms of the chair-like transitions states C-anti and C-syn. As discussed above, the anti approach of the carbonyl oxide minimizes electrostatic repulsions between the carbonyl oxide and the substituent group. This preference is countered by the fact that the C-anti alignment places the substituent in a pseudoaxial orientation, instead of the less-crowded pseudo-equatorial position enforced by the C-syn transition state. When R = Me, however, its eclipsing interaction with the pseudoequatorial substituent destabilizes the C-syn transition state further relative to the C-anti arrangement, and higher selectivity is observed.

Conclusions

Cyclopentenes with a heteroatom substituent in the allylic position form ozonides with stereoselectivities which depend markedly on the nature of the pendant group. The ozonide stereochemistry results from a preferred mode of cyclization of one dominant carbonyl oxide–aldehyde pair, and the selectivity can be attributed to electrostatic interactions between the heteroatom substituent and the polar carbonyl oxide during the cyclization process. Increased stereoselectivity in favor of the *exo*-ozonide is found for 2-methyl-2-cyclopentenyl ethers and esters, which is consistent with a chair-like transition state for intramolecular cyclization to the ozonide.

Experimental Section

General. Melting points were determined on a Fisher-Johns hot stage. Boiling points are oven temperatures for bulb-to-bulb distillation at the indicated pressure. NMR spectra of solutions in $CDCl_3$ were obtained on a JEOL FX90Q (90 MHz for ^1H, 22.5 MHz for ^{13}C) or a Nicolet NT-300WB (300 MHz for ^1H, 75 MHz for ^{13}C). IR spectra of neat liquid films (or KBr pellets, as noted) were recorded on a Nicolet 20 DXB FTIR spectrometer; selected bands of interest are reported. Mass spectra of purified compounds were obtained with a Hewlett-Packard 5890 GC interfaced with a Model 5970 mass selective detector. Elemental analyses were performed by Desert Analytics, Tucson, AZ.

Thin-layer chromatography was carried out using plastic sheets precoated with silica gel $60F_{254}$, supplied by E. Merck. Detection was accomplished by visualization under UV (254 nm) or by treatment with vanillin reagent, followed by warming. Flash chromatography was performed using Merck silica gel 60 (230–400 mesh). Analytical HPLC was run on a Shimadzu LC-6 system with a 4.6 × 250 mm silica column (Alltech) using UV detection at 270 nm. Eluting solvents for all of these chromatographic methods are noted as appropriate—mixed solvents are given in volume-to-volume ratios. Capillary gas chromatography was carried out on a Shimadzu GC-9A equipped with a 0.32 mm × 30 m dimethyl silicone column.

Tetrahydrofuran and diethyl ether were distilled from Na/benzophenone just before use. Pyridine and 2,6-lutidine were purified by distillation from CaH_2. Hexanes were distilled, and reagent-grade dichloromethane and ethyl acetate were used without further purification. Solvents for HPLC were Fisher Optima grade, used without further purification. Ozone was

(26) This assumption has been shown to be valid for other alkenes. See ref 12a.

obtained in approximately 2–4% concentration in a stream of oxygen using an OREC V3-50 generator. The ozone stream was passed through a drying train consisting of a concd H_2SO_4 washing bottle followed by a dry ice cooled trap. Typically, a flow rate of 0.5–1 L/min was used.

Preparation of Starting Materials. (2-Cyclopenten-1-yloxy)dimethyl(1,1-dimethylethyl)silane (1a).[27] 2-Cyclopenten-1-ol[8] (1.0 g, 11.9 mmol) was added to a solution of *tert*-butyldimethylsilyl chloride (2.7 g, 17.9 mmol) in 10 mL of dry dimethylformamide. The solution was stirred at room temperature under N_2 for 16 h, whereupon the mixture was partioned between petroleum ether (bp 30–60, 75 mL) and water (30 mL). The organic phase was washed one more time with water then dried over Na_2SO_4 and concentrated. Bulb-to-bulb distillation (air bath 57 °C, 57 Torr) followed by flash chromatography (CH_2Cl_2) gave the pure product as a colorless oil (1.1 g, 47%): ^{1}H NMR δ 5.82 (m, 1 H), 5.70 (m, 1 H), 4.87 (m, 1 H), 2.65–1.90 (m, 3 H), 1.66 (m, 1 H), 0.88 (s, 9 H), 0.05 ppm (s, 6 H); ^{13}C NMR δ 135.5, 134.9, 78.0, 35.6, 32.4, 27.2, 27.1, -1.3, -3.0 ppm; IR ν 2956, 1255, 1071, 835, 776 cm^{-1}.

(2-Cyclopenten-1-yloxy)tris(1-methylethyl)silane (1b). A solution of 2-cyclopenten-1-ol (0.50 g, 5.9 mmol) in dry CH_2Cl_2 (5 mL) was cooled to -78 °C (dry ice 2-propanol bath temperature) under N_2. 2,6-Lutidine (1.4 mL, 11:9 mmol) was added, followed by triisopropylsilyl triflate (1.8 mL, 6.5 mmol). After 15 minutes, the cold bath was removed and the reaction mixture was allowed to stir at room temperature for 45 min. The solution was diluted with 75 mL of CH_2Cl_2 and washed with three 25-mL portions of 5% H_2SO_4 then once with 25 mL of saturated $NaHCO_3$. The organic phase was dried (Na_2SO_4) and concentrated. Purification by flash chromatography (hexane–CH_2Cl_2 (80:20)) yielded 0.82 g (58%) of **1b** as a colorless oil: bp 60 °C (0.45 Torr); ^{1}H NMR δ 5.86 (m, 1 H), 5.77 (m, 1 H), 4.98 (m, 1 H), 2.60–1.95 (m, 3 H), 1.67 (m, 1 H), 1.09 ppm (s, 21 H); ^{13}C NMR δ 134.1, 132.2, 78.0, 33.9, 30.9, 17.9, 17.6, 12.3 ppm; IR ν 2960, 2943, 2886, 1080, 1063 cm^{-1}; MS *m/z* 240 (1), 197 (36), 131 (100), 103 (62), 75 (68). Anal. Calcd for $C_{14}H_{28}OSi$: C, 69.93; H, 11.74. Found: C, 69.64; H, 11.48.

(2-Cyclopenten-1-yloxy)trimethylsilane (1c).[28] 2-Cyclopenten-1-ol (4.1 g, 48.8 mmol) was treated with a solution of *N*-(trimethylsilyl)acetamide (7.6 g, 58.0 mmol) in pyridine (20 mL), and the resulting mixture was allowed to stir at room temperature under N_2 for 27 h. The mixture was diluted with 100 mL of ether and washed repeatedly with 30-mL portions of 5% H_2SO_4 until the wash was acidic to litmus paper. The organic phase was then washed with saturated $NaHCO_3$ (50 mL) and dried over Na_2SO_4. The ether was removed by distillation through a Vigreaux column, and the residue was purified by vacuum distillation to provide a colorless liquid (89%): bp 90–95 °C, 100 Torr; ^{1}H NMR δ 6.08 (m, 1 H), 5.90 (m, 1 H), 5.05 (m, 1 H), 2.82–2.07 (m, 3 H), 1.80 (m, 1 H), 0.30 ppm (s, 9 H); ^{13}C NMR δ 133.8, 133.5, 77.5, 33.3, 30.9, 0.1 ppm; IR ν 2956, 1251, 1069, 904, 840 cm^{-1}; MS *m/e* 157 (4), 156 (28), 75 (100).

2-Cyclopenten-1-yl Acetate (1e).[29] Acetic anhydride (1.13 mL, 12.1 mmol) was added to a solution of 2-cyclopenten-1-ol (1.00 g, 11.9 mmol) in dry pyridine (5 mL), and the mixture was allowed to stir at room temperature under N_2. After 20 h, the solution was poured into 50 mL of ethyl acetate, washed successively with 5% H_2SO_4 (2 × 5 mL) and saturated $NaHCO_3$ (1 × 5 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography (CH_2Cl_2–CH_3OH, (50:1)) to yield 1.36 g (91%) of a colorless liquid: ^{1}H NMR δ 6.07 (m, 1 H), 5.73 (m, 2 H), 2.71–2.05 (m, 3 H), 1.99 (s, 3 H), 1.82 ppm (m, 1 H); ^{13}C NMR δ 170.8, 137.4, 129.1, 80.3, 30.9, 29.6, 21.1 ppm; IR ν 1732, 1238, 1025 cm^{-1}; MS *m/e* 126 (1), 84 (21), 83 (40), 67 (68), 66 (86), 43 (100).

2-Cyclopenten-1-yl 4-Methoxybenzoate (1f). *p*-Anisoyl chloride (1.12 g, 6.50 mmol) was added to a stirring solution of 2-cyclopenten-1-ol (0.50 g, 5.94 mmol) in pyridine (2 mL), resulting in an immediate exothermic reaction accompanied by precipitation of pyridinium chloride. The mixture was taken up in CH_2Cl_2 (25 mL), washed with 5% H_2SO_4 (2 × 10 mL) and saturated $NaHCO_3$ (10 mL), dried ($MgSO_4$), and concentrated. Purification by flash chromatography (hexane–EtOAc (4:1)) provided the ester as a colorless oil (1.07 g, 82%): ^{1}H NMR δ 7.98 (d, J = 9.0 Hz, 2 H), 6.88 (d, J = 9.0 Hz, 2 H), 6.13 (m, 1 H), 5.92 (m, 2 H), 3.82 (s, 3 H), 2.6–2.1 (m, 3 H), 2.00 ppm (m, 1 H); ^{13}C NMR δ 166.1, 163.1, 137.3, 131.4, 129.4, 122.9, 113.4, 80.6, 55.2, 31.1, 29.8 ppm; IR ν 1706, 1606, 1256, 1167, 1115, 1100, 1030, 772 cm^{-1}; MS *m/e* 218 (18), 152 (92), 135 (75), 67 (35), 66 (100), 65 (62). Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.15; H, 6.34.

2-Cyclopenten-1-yl Benzoate (1g).[30] The procedure for **1f** was followed, with the exception that benzoyl chloride was substituted for *p*-anisoyl chloride. An 84% yield of the product was obtained following purification by bulb-to-bulb distillation (97–99 °C, 0.8 torr; lit.[30] 91.5 °C, 0.17 torr): ^{1}H NMR δ 8.03 (dd, J = 7.7, 1.8 Hz, 2 H), 7.48 (m, 3 H), 6.15 (br d, J = 4.8 Hz, 1 H), 5.92 (m, 2 H), 2.7–2.2 (m, 3 H), 1.99 (m, 1 H); ^{13}C NMR δ 162.3, 137.6, 134.4, 132.7, 130.4, 129.4, 129.3, 128.8, 81.1, 30.9, 29.9 ppm; IR ν 3062, 1714, 1271, 1114, 1026, 711 cm^{-1}; MS *m/e* 188 (17), 105 (85), 83 (55), 77 (49), 67 (100).

2-Cyclopenten-1-yl 3,5-Dinitrobenzoate (1h).[31] This was prepared as for **1f** from 3,5-dinitrobenzoyl chloride. The crude product was crystallized from ethanol (white needles): mp 119–120 °C (lit.[31] mp 122–123 °C); ^{1}H NMR δ 9.23–9.00 (m, 3 H), 6.25 (m, 1 H), 6.00 (m, 2 H), 2.85–1.90 ppm (m, 4 H).

2-Cyclopenten-1-yl 4-Nitrobenzoate (1i).[32] The ester was synthesized from 2-cyclopenten-1-ol and *p*-nitrobenzoyl chloride according to the procedure for **1f**. Crystallization from ethanol provided white plates (80%): mp 82.5–83.5 °C (lit.[32] mp 76–78 °C); ^{1}H NMR δ 8.30 (d, J = 6.4 Hz, 2 H), 8.15 (d, J = 6.4 Hz, 2 H), 6.20 (m, 1 H), 5.90 (m, 2 H), 2.7–1.8 ppm (m, 4 H).

2-Methyl-2-cyclopenten-1-ol. A 250-mL three-neck flask equipped with a stir bar, thermocouple, and addition funnel was charged with a solution of $LiAlH_4$ (1.5 g, 39.5 mmol) in ether (60 mL). The gray mixture was cooled in an ice–water bath and stirred under N_2 as a solution of 2-methyl-2-cyclopentenone (10.0 g, 104 mmol) in ether (40 mL) was added dropwise so that the reaction temperature remained <10 °C. The excess hydride was destroyed by successive addition of water (1.5 mL), 15% NaOH (1.5 mL), and an additional 4.5 mL of water. The precipitated solids were removed by filtration and washed well with ether (40 mL). The filtrate and washings were combined and distilled, first at ambient pressure to remove the ether and finally under vacuum to obtain the pure product (7.9 g, 78%): bp 101–107 °C, 130 Torr; ^{1}H NMR δ 5.47 (m, 1 H), 4.54 (m, 1 H), 3.07 (s, 1 H), 2.4–2.0 (m, 3 H), 1.80 (m, 1 H), 1.74 ppm (br s, 3 H); ^{13}C NMR δ 141.6 (s), 127.5 (d), 79.3 (d), 33.6 (t), 29.5 (t), 13.4 ppm (q); IR ν 3330, 3035, 2941, 1050, 1025 cm^{-1}; MS *m/e* 98 (45), 97 (41), 83 (100), 55 (44).

[(2-Methyl-2-cyclopenten-1-yl)oxy]dimethyl(1,1-dimethylethyl)silane (7a). A solution of 2-methyl-2-cyclopenten-1-ol (0.50 g, 5.1 mmol) in CH_2Cl_2 (5 mL) was stirred at -78 °C under N_2 as 2,6-lutidine (1.2 mL, 10.2 mmol) and then *tert*-butyldimethylsilyl triflate (1.3 mL, 5.6 mmol) were added by syringe. The cold bath was removed after 5 min more, and the solution was allowed to come to room temperature over 30 min. CH_2Cl_2 (75 mL) was added, and the mixture was washed successively with 5% H_2SO_4 (3 × 25 mL) and saturated $NaHCO_3$ (25 mL), dried (Na_2SO_4), and concentrated. Purification by flash chromatography (hexane–EtOAc (9:1)) afforded 0.56 g (52%) of a colorless oil: bp 73 °C, 26 Torr; ^{1}H NMR δ 5.46 (s, 1 H), 4.64 (t, J = 5.9 Hz, 1 H), 2.35 (m, 1 H), 2.25 (m, 1 H), 2.15 (m, 1 H), 1.71 (s, 3 H), 1.65 (m, 1 H), 0.91 (s, 9 H), 0.94 (s, 3 H), 0.09 ppm (s, 3 H); ^{13}C NMR δ 142.0, 126.6, 80.1, 34.3, 29.6, 25.9, 18.2, 13.7, -4.5, -4.8 ppm; IR ν 2957, 1252, 1087 cm^{-1}; MS *m/e* 212 (4), 155 (13), 75 (100). Anal. Calcd for $C_{12}H_{24}OSi$: C, 67.86; H, 11.39. Found: C, 67.37; H, 11.39.

[(2-Methyl-2-cyclopenten-1-yl)oxy]trimethylsilane (7c). A solution of 2-methyl-2-cyclopenten-1-ol (737 mg, 7.52 mmol) in CH_2Cl_2 (10 mL) was stirred at -78 °C under N_2. 2,6-Lutidine (1.74 mL, 15 mmol) and trimethylsilyl trifluoromethanesulfonate

(27) Detty, M. R.; Seidler, M. O. *J. Org. Chem.* **1981**, *46*, 1283.
(28) Murata, S.; Suzuki, M.; Noyori, R. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 247.
(29) Morimoto, T.; Machida, T.; Hirano, M.; Zhung, X. *J. Chem. Soc., Perkin Trans. 1* **1988**, 909.
(30) Cocu, F. G.; Wolczunowicz, G.; Bors, L.; Posternak, T. *Helv. Chim. Acta* **1970**, *53*, 739.
(31) Friedrich, E.; Taggart, D. *J. Org. Chem.* **1978**, *43*, 805.
(32) Tufariello, J.; Bayer, A.; Spadaro, J. *J. Am. Chem. Soc.* **1979**, *101*, 3309.

(1.60 mL, 8.3 mmol) were added sequentially by syringe, and the slightly turbid solution was allowed to warm to room temperature over 30 min. The reaction mixture was washed with water (20 mL), 5% H_2SO_4 (20 mL), and saturated $NaHCO_3$ (10 mL), dried over Na_2SO_4, and concentrated. The residual oil was purified by bulb-to-bulb distillation to yield 850 mg (66%) of a mobile, colorless liquid: bp 67–69 °C, 16 Torr; ^1H NMR δ 5.47 (m, 1 H), 4.60 (m, 1 H), 2.22 (m, 3 H), 1.69 (m, 4 H), 0.13 ppm (s, 9 H); ^{13}C NMR δ 141.5 (s), 127.1 (d), 79.6 (d), 34.0 (t), 29.7 (t), 13.5 (q), 0.0 ppm (q); IR ν 2959, 1262, 1084, 897 cm^{-1}; MS m/e 170 (33), 155 (58), 75 (100), 73 (75). Anal. Calcd for $C_9H_{18}OSi$: C, 63.47; H, 10.65. Found: C, 62.33; H, 10.81.

2-Methyl-2-cyclopenten-1-yl Acetate (7e).[33] A solution of 2-methyl-2-cyclopenten-1-ol (205 mg, 2.09 mmol), pyridine (300 mg, 3.8 mmol), 4-(*N,N*-dimethylamino)pyridine (20 mg, 0.16 mmol), and acetic anhydride (300 mg, 2.94 mmol) in CH_2Cl_2 (3 mL) was stirred at room temperature for 1 h. At this time, a small amount of methanol (~0.2 mL) was added to consume the excess Ac_2O. After 10 min more, the reaction mixture was diluted with CH_2Cl_2 (5 mL) and washed sequentially with 5% H_2SO_4 (5 mL) and 10% Na_2CO_3 (5 mL), dried over $MgSO_4$, and concentrated. Bulb-to-bulb distillation provided **2d** as a colorless liquid (274 mg, 94%): bp 80–83 °C, 80 Torr; ^1H NMR δ 5.63 (m, 1 H), 5.55 (m, 1 H), 2.6–2.1 (m, 3 H), 2.05 (s, 3 H), 1.84, (m, 1 H), 1.71 ppm (br s, 3 H); ^{13}C NMR δ 171.2, 138.1, 130.8, 82.3, 31.0, 30.2, 21.3, 13.7 ppm; IR ν 1734, 1243, 1027 cm^{-1}.

Ozonide Stereoselectivities—General Procedure. *Caution: Ozonolyses should be carried out on small scale (<1 mmol) and behind a safety shield. In addition, lab personnel should be protected with a face shield and heavy gloves when handling ozonolysis products.* A stream of oxygen from the ozone generator was bubbled through a solution of the cyclopentene in CH_2Cl_2 (0.1–0.3 M) as the solution was cooled to −78 °C (dry ice 2-propanol). After ca. 5 min to allow temperature equilibration, the ozone generator was turned on, and the ozonation continued until the blue color of excess O_3 was visible. The generator was then shut off, and the stream of oxygen continued until the effluent gas was free of ozone (negative test with starch/KI paper). The flask was capped with a $CaCl_2$ drying tube, and the cold bath removed to allow the solution to warm to room temperature. A small sample was taken for analysis by HPLC. The bulk of the solution was concentrated (≤25 °C) and purified by flash chromatography. In certain cases (**5,6a**, **5,6b**, **5,6h**, **5,6i**) the stereoisomeric ozonides were separable on preparative scale, and pure samples could be obtained. For the others, pure exo diastereomers were available from derivatization of the pure exo alcohol **8**. The endo alcohol **9** was converted to some of the *endo*-ozonides, but the limited quantities of this material did not allow preparation of the entire set. The yields of the isolated ozonide fractions are given in Table I, along with the stereoisomer compositions as determined by HPLC.

Ozonides from (2-Cyclopenten-1-yloxy)dimethyl(1,1-dimethylethyl)silane (1a). From 50 mg (0.25 mmol) of silyl ether, 50 mg (80%) of the mixture of ozonides was obtained. The stereoisomers are separable by flash chromatography (hexane–EtOAc (9:1)) to provide, in order of elution.

***exo*-2-[[Dimethyl(1,1-dimethylethyl)silyl]oxy]-6,7,8-trioxabicyclo[3.2.1]octane (5a):** R_f = 0.50; ^1H NMR δ 5.72 (m, 1 H), 5.43 (m, 1 H), 3.70 (m, 1 H), 2.4–1.7 (m, 2 H), 1.7–1.3 (m, 2 H), 0.85 (s, 9 H), 0.5 ppm (s, 6 H); ^{13}C NMR δ 101.9 (d), 101.4 (d), 66.0 (d), 26.0 (t), 25.7 (q), 23.5 (t), −4.8 (q), −4.9 ppm (q); IR ν 2957, 1122, 1106 cm^{-1}. Anal. Calcd for $C_{11}H_{22}O_4Si$: C, 53.63; H, 9.00. Found: C, 53.70; H, 8.97.

***endo*-2-[[Dimethyl(1,1-dimethylethyl)silyl]oxy]-6,7,8-trioxabicyclo[3.2.1]octane (6a):** R_f = 0.40; ^1H NMR δ 5.75 (m, 1 H), 5.50 (m, 1 H), 3.80 (m, 1 H), 2.2–1.6 (m, 2 H), 1.6–1.3 (m, 2 H), 0.90 (s, 9 H), 0.10 ppm (s, 6 H); ^{13}C NMR δ 102.8, 100.6, 68.5, 29.0, 25.7, 25.2, 18.0, −4.5, −4.7 ppm; IR ν 2956, 1128, 1108, 859, 839 cm^{-1}.

Ozonides from (2-Cyclopenten-1-yloxy)tris(1-methylethyl)silane (1b). A 54-mg sample of **1b** (0.24 mmol) yields 50 mg (76%) of the ozonide mixture, which can be separated by flash chromatography (hexane–EtOAc (12:1)).

***exo*-2-[[Tris(1-methylethyl)silyl]oxy]-6,7,8-trioxabicyclo[3.2.1]octane (5b):** R_f = 0.30; ^1H NMR δ 5.78 (m, 1 H), 5.55 (m, 1 H), 3.83 (m, 1 H), 2.4–1.4 (m, 4 H), 1.05 ppm (s, 21 H); ^{13}C NMR δ 101.9, 101.4, 66.1, 26.1, 23.7, 17.9, 12.2 ppm; IR ν 2961, 1022 cm^{-1}. Anal. Calcd for $C_{14}H_{28}O_4Si$: C, 58.29; H, 9.78. Found: C, 58.39; H, 9.90.

***endo*-2-[[Tris(1-methylethyl)silyl]oxy]-6,7,8-trioxabicyclo[3.2.1]octane (6b):** R_f = 0.24; ^1H NMR δ 5.72 (m, 1 H), 5.55 (m, 1 H), 3.87 (m, 1 H), 2.1–1.4 (m, 4 H), 1.05 ppm (s, 21 H); ^{13}C NMR δ 102.9, 100.5, 68.5, 28.2, 25.0, 17.9, 12.2 ppm; IR ν 2867, 1100, 1030 cm^{-1}.

Ozonides from (2-Cyclopenten-1-yloxy)trimethylsilane (1c). Ozonolysis of 1.94 g (12.4 mmol) of **1c** provided, after purification by flash chromatography (hexane–EtOAc (9:1)), a 6.5:1 mixture of the *exo*- and *endo*-ozonides **5c** and **6c** (2.15 g, 85%). The diastereomer ratio was confirmed by HPLC analysis (hexane–CH_2Cl_2, (30:70)). The individual stereoisomers could not be separated, but were eventually prepared by silylation of the hydroxy ozonides **8** and **9**, prepared as described below.

***exo*-2-[(Trimethylsilyl)oxy]-6,7,8-trioxabicyclo[3.2.1]octane (5c):** ^1H NMR δ 5.78 (m, 1 H), 5.48 (m, 1 H), 3.72 (m, 1 H), 2.5–1.75 (m, 2 H), 1.75–1.48 (m, 2 H), 0.15 ppm (s, 9 H); ^{13}C NMR δ 101.7, 101.3, 65.7, 25.9, 23.3, −0.1 ppm; IR ν 2958, 2928, 1105, 1021 cm^{-1}. Anal. Calcd for $C_8H_{16}O_4Si$: C, 47.03; H, 7.89. Found: C, 46.75; H, 7.98.

***endo*-2-[(Trimethylsilyl)oxy]-6,7,8-trioxabicyclo[3.2.1]octane (6c):** ^1H NMR δ 5.75 (m, 1 H), 5.62 (m, 1 H), 3.76 (m, $w_{1/2}$ = 17 Hz, 1 H), 2.54–1.94 (m, 4 H), 0.16 ppm (s, 9 H); ^{13}C NMR δ 102.7, 100.6, 68.2, 29.0, 25.1, 0.1 ppm; IR ν 2959, 1103 cm^{-1}.

***exo*- and *endo*-6,7,8-Trioxabicyclo[3.2.1]octan-2-ol (8 and 9).** A solution of 1.1 g (5.2 mmol) of **5b** and **6b** (6.5:1 ratio) in methanol (25 mL) was treated with one drop of acetic acid and allowed to stir at room temperature for 8 h. The solution was concentrated, and the residue was subjected to flash chromatography (hexane–EtOAc (1:1)), which results in separation of the individual stereoisomers (254 mg of **8** and 21 mg of **9**; total yield of 40%):

***exo*-6,7,8-Trioxabicyclo[3.2.1]octan-2-ol (8):** R_f = 0.19; ^1H NMR δ 5.72 (m, 1 H), 5.67 (m, 1 H), 3.77 (m, 1 H), 3.32 (m, 1 H), 2.5–1.4 ppm (m 4 H); ^{13}C NMR δ 101.1, 101.0, 64.9, 25.3, 22.2 ppm; IR ν 3427, 2960 cm^{-1}. Anal. Calcd for $C_5H_8O_4$: C, 45.46; H, 6.10. Found: C, 45.12; H, 6.14.

***endo*-6,7,8-Trioxabicyclo[3.2.1]octan-2-ol (9):** R_f = 0.21; ^1H NMR δ 5.82 (m, 1 H), 5.67 (m, 1 H), 3.50 (m, 1 H), 3.32 (s, 1 H), 2.3–1.4 ppm (m 4 H); ^{13}C NMR δ 102.5, 100.6, 67.4, 29.0, 25.8 ppm; IR ν 3427, 2960 cm^{-1}.

Ozonides from 3-Chlorocyclopentene (1d). Ozonolysis of 10.0 g (97.6 mmol) of **1d** gave, after purification by flash chromatography (CH_2Cl_2), an inseparable mixture of ozonides **5d** and **6d** (3:1 ratio by HPLC) as a pale yellow liquid (11.7 g, 80%): ^1H NMR δ 5.84 (br s, 1 H), 5.71 (br s, 1 H), 4.03 and 4.00 (m, endo and exo isomer, respectively, total 1 H), 2.63 (m, 1 H), 2.38 and 2.19 (m, endo and exo isomer, respectively, total 1 H), 1.90 (m, 1 H), 1.73 ppm (m, 1 H); ^{13}C NMR (exo isomer) δ 101.4, 100.6, 52.8, 25.2, 23.6 ppm; (endo isomer) δ 101.4, 100.4, 54.8, 29.2, 25.7 ppm; IR ν 1118, 1099, 1049, 1012, 942, 929, 898, 645 cm^{-1}. Anal. Calcd for $C_5H_7O_3Cl$: C, 39.89; H, 4.69. Found: C, 39.80; H, 4.74.

Ozonides from 2-Cyclopenten-1-yl Acetate (1e). The crude ozonolysate from 60 mg (0.47 mmol) of **1e** was purified by flash chromatography (hexane–EtOAc (2:1)) to give a mixture of ozonides **5e** and **6e** (51 mg, 62% yield, 1.57:1 diastereomer ratio by HPLC). Authentic samples of the pure exo and endo stereoisomers were prepared by acetylation of the corresponding alcohols **8** and **9**.

***exo*-2-Acetoxy-6,7,8-trioxabicyclo[3.2.1]octane (5e).** Acetic anhydride (52 μL, 0.55 mmol) and a few crystals of 4-(dimethylamino)pyridine were added to a cooled (0 °C) solution of **8** (61 mg, 0.46 mmol) in CH_2Cl_2 (2 mL), and the mixture was stirred under N_2 for 15 min at 0 °C, then for 6 h at room temperature. The reaction was diluted with CH_2Cl_2 (10 mL), washed successively with 5% H_2SO_4 (2 × 5 mL) and saturated $NaHCO_3$ (5 mL), dried over Na_2SO_4, and concentrated to leave pure **5e** (47%): ^1H NMR δ 5.80 (m, 2 H), 4.75 (m, 1 H), 2.6–1.9 (m, 2 H), 2.15 (s, 3 H), 1.80 ppm (m, 2 H); ^{13}C NMR δ 170.4, 101.4, 98.7, 66.9, 26.1, 21.0, 20.2 ppm; IR ν 2964, 2936, 1745 cm^{-1}. Anal. Calcd for $C_7H_{10}O_5$: C, 48.28; H, 5.79. Found: C, 48.21; H, 5.84.

(33) Curran, D. P.; Rakiewicz, D. M. *Tetrahedron* **1985**, *41*, 3943.

***endo*-2-Acetoxy-6,7,8-trioxabicyclo[3.2.1]octane (6e).** The endo acetate was prepared similarly from **9**, to provide **6e**: ^{1}H NMR δ 5.80 (s, 1 H), 5.70 (s, 1 H), 4.85 (ddd, J = 10.5, 6.3, 1.4 Hz, 1 H), 2.2–1.8 (m, 4 H), 2.09 ppm (s, 3 H); ^{13}C NMR δ 170.9, 100.5, 99.5, 69.1, 28.6, 20.8, 20.7 ppm; IR ν 1738, 1235, 1039, 910 cm^{-1}.

Ozonides from 2-Cyclopenten-1-yl 4-Methoxybenzoate (1f): The crude ozonolysate from 137 mg of **1f** (0.52 mmol) was purified by flash chromatography (CH_2Cl_2) to yield a 1.23:1 mixture of stereoisomers (HPLC: t_R = 42.2 and 35.6 min for the exo and endo isomers, respectively, CH_2Cl_2–hexane (85:15)) in 80% yield. A small sample of each stereoisomer for ^{1}H NMR could be obtained by HPLC; the other data reported is for the ozonide mixture.

***exo*- and *endo*-2-[(4-Methoxybenzoyl)oxy]-6,7,8-trioxabicyclo[3.2.1]octane (5f and 6f):** ^{1}H NMR (exo stereoisomer, **5f**): δ 8.00 (d, J = 8.7 Hz, 2 H), 6.91 (d, J = 8.7 Hz, 2 H), 5.88 (br s, 2 H), 5.00 (m, $w_{1/2}$ = 8 Hz, 1 H), 3.88 (s, 3 H), 2.6–1.7 ppm (m, 4 H); (endo stereoisomer, **6f**) δ 8.02 (d, J = 8.7 Hz, 2 H), 6.92 (d, J = 8.7 Hz, 2 H), 5.83 (br s, 2 H), 5.09 (dd, J = 9.5, 7.0 Hz, 1 H), 3.87 (s, 3 H), 2.3–1.8 ppm (m, 4 H); ^{13}C NMR δ 165.3, 165.2, 163.6, 131.7, 121.8, 121.5, 113.6, 101.3, 100.7, 99.9, 98.9, 69.3, 66.9, 55.3, 28.8, 26.2, 21.1, 20.3 ppm; IR ν 2964, 1713, 1607, 1260, 1169, 1102, 1028 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_6$: C, 58.65; H, 5.30. Found: C, 57.88; H, 5.15.

Ozonides from 2-Cyclopenten-1-yl Benzoate (1g). A 60-mg sample of **1g** provided 45 mg (59%) of a mixture of **5g** and **6g** (1.14:1 by HPLC, hexane–CH_2Cl_2 (15:85)). The isomers could be separated by flash chromatography (hexane–EtOAc (9:1)).

***exo*-2-(Benzoyloxy)-6,7,8-trioxabicyclo[3.2.1]octane (5g):** R_f = 0.29; ^{1}H NMR δ 8.09 (dd, J = 7.7, 2.0 Hz, 2 H), 7.54 (m, 3 H), 5.89 (br s, 2 H), 5.00 (m, $w_{1/2}$ = 7.9 Hz, 1 H), 2.43 (m, 1 H), 2.2–1.7 ppm (m, 3 H); ^{13}C NMR δ 165.7, 133.3, 129.7, 128.4, 101.4, 98.9, 67.2, 26.3, 10.4 ppm (one aromatic signal not resolved); IR ν 1718, 1271, 1112, 958, 712 cm^{-1}. Anal. Calcd for $C_{12}H_{12}O_5$: C, 61.02; H, 5.12. Found: C, 61.06; H, 4.96.

***endo*-2-(Benzoyloxy)-6,7,8-trioxabicyclo[3.2.1]octane (6g):** R_f = 0.23; ^{1}H NMR δ 8.06 (dd, J = 7.8, 2.0 Hz, 2 H), 7.52 (m, 3 H), 5.84 (br s, 1 H), 5.10 (ddd, J = 9.9, 6.7, 1.1 Hz, 1 H), 2.4–1.8 ppm (m, 4 H); ^{13}C NMR δ 165.6, 133.4, 129.8, 129.3, 128.4, 100.7, 11.1, 69.7, 29.7, 28.9 ppm; IR ν 1718, 1267, 1090, 1027, 902, 709 cm^{-1}.

Ozonides from 2-Cyclopenten-1-yl 3,5-Dinitrobenzoate (1h). Ozonolysis of a 129-mg sample of **1h** (0.46 mmol) gave a mixture of **5h** and **6h** (0.83:1 by HPLC with hexane–EtOAc (65:35)), which could be separated by flash chromatography (hexane–EtOAc (4:1)).

***exo*-2-[(3,5-Dinitrobenzoyl)oxy]-6,7,8-trioxabicyclo-[3.2.1]octane (5h):** R_f = 0.54; ^{1}H NMR δ 9.29 (t, J = 2.1 Hz, 1 H), 9.18 (d, J = 2.1 Hz, 2 H), 5.94 (s, 2 H), 5.09 (m, 1 H), 2.58 (m, 1 H), 2.18 (m, 1 H), 1.98 ppm (m, 2 H); ^{13}C NMR δ 161.9, 148.7, 133.2, 129.8, 122.8, 101.5, 98.1, 69.4, 26.2, 20.3 ppm; IR (KBr) ν 1727, 1533, 1340, 1275, 720 cm^{-1}. Anal. Calcd for $C_{12}H_{10}N_2O_9$: C, 44.18; H, 3.09. Found: C, 44.97; H, 3.03.

***endo*-2-[(3,5-Dinitrobenzoyl)oxy]-6,7,8-trioxabicyclo-[3.2.1]octane (6h):** R_f = 0.45; ^{1}H NMR δ 9.26 (t, J = 2.1 Hz, 1 H), 9.16 (d, J = 2.1 Hz, 2 H), 5.89 (s, 1 H), 5.87 (s, 1 H), 5.20 (ddd, J = 10.6, 6.2, 1.2 Hz, 1 H), 2.36 (m, 1 H), 2.22 (m, 1 H), 2.05 ppm (m, 2 H); ^{13}C NMR δ 161.8, 148.7, 133.0, 129.6, 122.8, 100.8, 99.1, 71.7, 29.0, 21.0 ppm; IR ν 1733, 1630, 1541, 1347, 1275, 1169, 1038, 1025, 918 cm^{-1}.

Ozonides from 2-Cyclopenten-1-yl 4-Nitrobenzoate (1i). Ozonolysis of **1i** (1.78 g, 7.6 mmol) yields a mixture of **5i** and **6i** (1.18 g, 58% yield, 0.77:1 by HPLC using hexane–EtOAc (1:1)). Small samples of the pure stereoisomers could be obtained by flash chromatography:

***exo*-2-[(4-Nitrobenzoyl)oxy]-6,7,8-trioxabicyclo[3.2.1]octane (5i):** ^{1}H NMR δ 8.33 (d, J = 9.0 Hz, 2 H), 8.25 (d, J = 9.0 Hz, 2 H), 5.90 (m, 2H), 5.03 (m, 1 H), 2.55 (m, 1 H), 2.07 (m, 1 H), 1.95–1.75 ppm (m, 2 H); ^{13}C NMR δ 163.6, 150.7, 134.8, 130.9, 123.6, 101.4, 98.5, 68.3, 26.2, 20.3 ppm; IR (KBr) ν 1726, 1528, 1348, 1273, 1103 cm^{-1}. Anal. Calcd for $C_{12}H_{11}NO_7$: C, 51.25; H, 3.94. Found: C, 51.13; H, 3.93.

***endo*-2-[(4-Nitrobenzoyl)oxy]-6,7,8-trioxabicyclo[3.2.1]-octane (6i):** ^{1}H NMR δ 8.31 (d, J = 9.0 Hz, 2 H), 8.23 (d, J = 9.0 Hz, 2 H), 5.87 (m, 1 H), 5.83 (m, 1 H), 5.14 (ddd, J = 10.6, 6.3, 1.3 Hz, 1 H), 2.31 (m, 1 H), 2.12 (m, 1 H), 2.0–1.8 ppm (m, 2 H); ^{13}C NMR δ 163.8, 150.8, 134.6, 130.9, 123.6, 100.8, 99.5, 70.6, 28.9, 21.1 ppm; IR (CCl_4) ν 1728 cm^{-1}.

Ozonolysis of [(2-Methyl-2-cyclopenten-1-yl)oxy]dimethyl(1,1-dimethylethyl)silane (7a). Ozonation of **7a** (106 mg, 0.50 mmol) followed by flash chromatography afforded 51 mg of the ozonide **25a** (>99:1 diastereoselectivity) as a colorless oil (51 mg, 39% yield): ^{1}H NMR δ 5.77 (s, 1 H), 3.62 (m, 1 H), 2.4–1.6 (m, 4 H), 1.52 (s, 3 H), 0.97 (s, 9 H), 0.11 ppm (s, 6 H); ^{13}C NMR δ 108.2, 102.8, 68.7, 25.7, 25.4, 24.6, 21.1, 17.9, –4.5, –5.0 ppm; IR ν 2957, 1101, 1019, 850, 837 cm^{-1}. Anal. Calcd for $C_{12}H_{24}O_4Si$: C, 55.35; H, 9.29. Found: C, 55.75; H, 9.39.

Ozonolysis of [(2-Methyl-2-cyclopenten-1-yl)oxy]trimethylsilane (7c). Ozonolysis of **7c** (492 mg, 2.9 mmol) leads to a 98.5:1.5 mixture of *exo*- and *endo*-ozonides, as determined by HPLC (hexane–CH_2Cl_2 (40:60)). The ozonide yield, after flash chromatography (hexane–EtOAc (4:1)), was 394 mg (62%) of >98% *exo*-ozonide **25c**: ^{1}H NMR δ 5.76 (br s, 1 H), 3.61 (m, $w_{1/2}$ = 7 Hz, 1 H), 2.32 (m, 1 H), 2.00 (m, 1 H), 1.68–1.50 (m, 2 H), 1.49 (s, 3 H), 0.16 ppm (s, 9 H); ^{13}C NMR δ 108.0, 102.7, 68.6, 25.3, 24.4, 17.7, 0.1 ppm; IR ν 2959, 1251, 1088, 827 cm^{-1}.

Ozonolysis of (2-Methyl-2-cyclopenten-1-yl) Acetate (7e). Ozonolysis of **7e** (115 mg, 0.82 mmol) leads to a 10.5:1 mixture of *exo*- and *endo*-ozonides, as determined by HPLC (hexane–EtOAc (9:1)). Flash chromatography (hexane–EtOAc (4:1)) provides 32 mg (21%) of the *exo*-ozonide **25e**, admixed with ca. 9% of the endo isomer. A pure sample was obtained by crystallization from pentane: mp 48–49 °C; ^{1}H NMR δ 5.81 (br s, 1 H), 4.78 (br d, J = 3.9 Hz, 1 H), 2.40 (m, 1 H), 2.14 (s, 3 H), 2.0–1.6 (m, 3 H), 1.49 ppm (s, 3 H); ^{13}C NMR (exo) δ 170.0, 106.3, 102.6, 69.0, 25.6, 21.5, 21.0, 17.6 ppm; (endo) δ 170.0 (assumed), 107.0, 102.0, 71.8, 29.5, 22.1, 20.9, 17.1 ppm; IR ν 1734, 1378, 1255, 912 cm^{-1}. Anal. Calcd for $C_8H_{12}O_5$: C, 51.06; H, 6.43. Found: C, 50.90; H, 6.62.

Carbonyl Oxide Trapping Studies: Ozonolyses in Methanol–Dichloromethane. General procedure: the alkene (ca. 1.6 mmol) was dissolved in CH_3OH–CH_2Cl_2 (1:5, 15 mL), and solid $NaHCO_3$ (40 mg, 0.48 mmol) was added. The mixture was cooled in a dry ice–2-propanol bath (–78 °C) under a stream of dry O_2. After ca. 5 min to assure temperature equilibration, the ozone generator was turned on, and ozonation continued until the solution turned blue. The excess ozone was purged with O_2 until no residual O_3 remained as indicated by KI/starch paper. A $CaCl_2$ drying tube was placed on the flask and the solution allowed to warm to room temperature. The solid $NaHCO_3$ was removed by filtration through a plug of glass wool, and the filtrate was diluted with an equal volume of benzene and concentrated at aspirator pressure, taking care to keep the reaction mixture at or below room temperature (the benzene aids in removing traces of methanol). The residue was taken up in CH_2Cl_2 (5 mL) and cooled to 0 °C under N_2 (ice–water bath). Acetic anhydride (490 mg, 4.8 mmol) and triethylamine (210 mg, 2.1 mmol) were added, and the solution was stirred for 15 min at 0 °C then for 2 h at room temperature. This was treated with methanol (1 mL) for 15 min in order to destroy the excess acetic anhydride and then diluted with CH_2Cl_2 (50 mL). The solution was washed successively with 5% H_2SO_4 (3 × 20 mL) and saturated $NaHCO_3$ (20 mL), dried over Na_2SO_4, and concentrated. The crude 5-oxo esters were dissolved in 2,2-dimethoxypropane (2 mL), treated with a few crystals of *p*-toluenesulfonic acid, and stirred at room temperature. After 2 h, the reaction mixture was diluted with CH_2Cl_2 (20 mL). The solution was washed with saturated $NaHCO_3$ (2 × 20 mL), dried over Na_2SO_4, and concentrated. This reaction mixture was analyzed by capillary GC (dimethylsilicone 0.25 μm on 0.32 mm × 30 m fused silica column, 120 °C for 15 min, increase at 3 °C/min to 140 °C, then at 10 °C/min to 200 °C).

Methyl 5,5-Dimethoxy-4-[[dimethyl(1,1-dimethylethyl)-silyl]oxy]pentanoate (14a). Treatment of **1a** (200 mg, 110 mmol) under the conditions described above gave a crude mixture which contained **14a** and **17a** in a 98.5:1.5 ratio by GC. A pure sample of **14a** was obtained by flash chromatography (CH_2Cl_2–MeOH (20:1)): ^{1}H NMR δ 4.10 (d, J = 7.8 Hz, 1 H), 3.75 (m, 1 H), 3.70 (s, 3 H), 3.40 (s, 6 H), 2.45 (t, J = 7.9 Hz, 2 H), 1.75 (m, 2 H), 0.90 (s, 9 H), 0.10 ppm (s, 6 H); ^{13}C NMR δ 174.2, 107.4, 71.9, 55.9, 55.0, 51.4, 29.5, 27.5, 25.8, 18.1, –4.4, –4.9 ppm; IR ν 2954, 1742, 1256, 1111, 1095, 837, 777 cm^{-1}; MS *m/e* 275 (M

– OMe, 3), 217 (34), 185 (15), 89 (38), 75 (100). Anal. Calcd for $C_{14}H_{30}O_5Si$: C, 54.87; H, 9.87. Found: C, 54.91; H, 9.89.

Methyl 5,5-Dimethoxy-4-(acetyloxy)pentanoate (14e). Assay of the product mixture from **1e** indicates that **14e** and **17e** are present in a 96.7:3.3 ratio. Purification by flash chromatography (CH_2Cl_2–MeOH (20:1)) provides the title compound in 74% yield: ^1H NMR δ 5.00 (m, 1 H), 4.30 (d, J = 5.6 Hz, 1 H), 3.70 (s, 3 H), 3.45 (s, 3 H), 3.40 (s, 3 H), 2.35 (m, 2 H), 2.10 (s, 3 H), 1.90 ppm (m, 2 H); ^{13}C NMR δ 173.4, 104.2, 71.3, 55.3, 51.6, 29.9, 24.6, 20.9 ppm; IR ν 2954, 1741, 1240, 1074 cm^{-1}; MS m/e 203 (M – MeO, 2), 129 (19), 75 (100), 43 (27). Anal. Calcd for $C_{10}H_{18}O_6$: C, 51.27; H, 7.75. Found: C, 51.03; H, 7.76.

Methyl 5,5-Dimethoxy-4-[(4-nitrobenzoyl)oxy]pentanoate (14i). Ozonation of 100 mg (0.43 mmol) of **1i** according to the procedure described above, yields a 98.4:1.6 distribution of esters **14i** and **17i**, as determined by HPLC (hexane–EtOAc (80:20)). After flash chromatography (CH_2Cl_2), **14i** was isolated in 70% yield (93 mg): ^1H NMR δ 8.25 (AB quartet, 4 H), 5.30 (m, 1 H), 4.45 (d, J = 5.6 Hz, 1 H), 3.62 (s, 3 H), 3.48 (s, 3 H), 3.41 (s, 3 H), 2.40 (m, 2 H), 2.15 ppm (m, 2 H); ^{13}C NMR δ 173.1, 163.9, 150.5, 148.0, 135.2, 130.8, 104.1, 73.1, 55.4, 55.3, 51.6, 29.8, 24.6 ppm; IR ν 2953, 1730, 1118, 1103, 1017 cm^{-1}; MS m/e 275 (M – OMe, 3), 217 (34), 185 (15), 89 (38), 75 (100). Anal. Calcd for $C_{15}H_{19}NO_8$: C, 52.79; H, 5.61. Found: C, 52.50; H, 5.56.

Methyl 5,5-Dimethoxy-2-(acetyloxy)pentanoate (17e). The oxidation procedure of Rubottom et al.[16] was used. Diisopropylamine (1.2 mL, 8.4 mmol) was dissolved in dry THF (20 mL) in a flame-dried flask with a magnetic stir bar under N_2. The solution was cooled to 0 °C, and n-BuLi (2.0 M in hexane, 4.2 mL, 8.4 mmol) was added by syringe. The solution was stirred for 5 min at –78 °C, then allowed to warm to 0 °C for 15 min. The LDA solution was recooled to –78 °C and stirred as a solution of **18**[15] (1.0 g, 5.6 mmol) in dry THF (7 mL) was added dropwise over 5 min. After 15 min, the yellow solution was treated with chlorotrimethylsilane (1.2 mL, 9.5 mmol). The cold bath was removed and the mixture allowed to stir at room temperature for 3 h. The solvents were removed under vacuum (20 Torr) and the residue redissolved in CH_2Cl_2 (10 mL). This solution was added dropwise to a stirring, cooled (0 °C) mixture of $Pb(OAc)_4$ (2.9 g, 7.2 mol) in CH_2Cl_2 (15 mL). After the addition was complete, the brownish mixture was allowed to stir at room temperature for 30 min and then treated with $(nBu)_4N^+F^-$ (1 M in THF, 8.0 mL, 8 mmol). After 20 min more, the mixture was filtered through Celite, and the solids were washed well with CH_2Cl_2 (50 mL). The combined filtrates were washed successively with 5% H_2SO_4 (30 mL) and 10% Na_2CO_3 (30 mL), dried ($MgSO_4$), and concentrated. Purification by medium-pressure chromatography (EM Sciences Lobar column eluting with hexane–EtOAc (9:1)) provided 365 mg (27%) of **17e**: bp 79 °C, 1.7 Torr; ^1H NMR δ 5.03 (dd, J = 7.4, 5.0 Hz, 1 H), 4.38 (t, J = 5.6 Hz, 1 H), 3.75 (s, 3 H), 3.33 (s, 3 H), 3.32 (s, 3 H), 2.14 (s, 3 H), 2.1–1.8 (m, 2 H), 1.72 ppm (m, 2 H); ^{13}C NMR δ 170.51, 170.46, 103.7, 71.8, 53.1, 52.8, 52.3, 28.1, 26.2, 20.6 ppm; IR ν 2958, 1745, 1223 cm^{-1}; MS m/e 203 (M – MeO, 1), 129 (24), 101 (34), 75 (100), 43 (37). Anal. Calcd for $C_{10}H_{18}O_6$: C, 51.27; H, 7.75. Found: C, 51.32; H, 7.44.

Methyl 5,5-Dimethoxy-2-hydroxypentanoate (19). Diester **17e** (51 mg, 0.22 mmol) was stirred with potassium carbonate (72 mg, 0.44 mmol) in methanol (4 mL) at 0 °C for 20 min. Ether (50 mL) was added, and the mixture washed with saturated NaCl (3 × 25 mL), dried over Na_2SO_4, and concentrated. The alcohol was purified by flash chromatography (hexane–EtOAc (2:1), gradient to 1:1), which provided 25 mg (59%) of **19** as a colorless oil: ^1H NMR δ 4.40 (t, J = 5.6 Hz, 1 H), 3.80 (s, 3 H), 3.30 (s, 3 H), 3.05 (s, 1 H), 1.9–1.6 ppm (m, 4 H); ^{13}C NMR δ 175.2 (s), 104.0 (d), 70.0 (d), 52.8 (q), 52.6 (q), 52.3 (q), 29.1 (t), 27.8 (t); IR ν 3456, 2954, 1741, 1129 cm^{-1}; MS m/e 161 (M – MeO, 2), 129 (25), 101 (82), 75 (100), 69 (47).

Methyl 5,5-Dimethoxy-2-[[dimethyl(1,1-dimethylethyl)-silyl]oxy]pentanoate (17a). A solution of **19** (81 mg, 0.42 mmol) in CH_2Cl_2 (2 mL) was cooled to –78 °C under N_2 and treated sequentially with 2,6-lutidine (147 μL, 1.26 mmol) and *tert*-butyldimethylsilyl triflate (194 μL, 0.84 mmol). The solution was allowed to warm to room temperature over 30 min, at which time it was diluted with CH_2Cl_2 (50 mL) and washed with 5% H_2SO_4 (3 × 15 mL) and saturated $NaHCO_3$ (15 mL). The organic phase was dried (Na_2SO_4) and concentrated to a residue which was purified by flash chromatography (hexane–EtOAc (9:1)) to yield pure **17a** (102 mg, 80%): ^1H NMR δ 4.37 (t, J = 5.5 Hz, 1 H), 4.22 (m, 1 H), 3.72 (s, 3 H), 3.31 (s, 3 H), 3.30 (s, 3 H), 1.8–1.7 (m, 4 H), 0.91 (s, 9 H), 0.08 (s, 3 H), 0.06 ppm (s, 3 H); ^{13}C NMR δ 174.0, 104.1, 71.8, 52.8, 52.5, 51.8, 30.1, 28.0, 18.2, 5.0, –5.4 ppm (t); IR ν 2953, 1758, 1733, 1128 cm^{-1}; MS m/e 275 (M – MeO, 5), 217 (100), 89 (50), 75 (84), 73 (38), 59 (36). Anal. Calcd for $C_{14}H_{30}O_5Si$: C, 54.87; H, 9.87. Found: C, 55.14; H, 9.96.

Methyl 5,5-Dimethoxy-2-[(4-nitrobenzoyl)oxy]pentanoate (17i). To a solution of **19** (24 mg, 0.12 mmol) in CH_2Cl_2 (2 mL) was added *p*-nitrobenzoyl chloride (25 mg, 0.14 mmol), pyridine (10 μL, 0.12 mmol), and a few crystals of 4-(dimethylamino)-pyridine. After 18 h, the reaction was worked up as for **17a** and the crude product purified by flash chromatography (hexane–EtOAc (1:1)), yielding 7 mg (19%) of the nitrobenzoate **17i**: ^1H NMR δ 8.28 (br s, 4 H), 5.32 (t, J = 5.9 Hz, 1 H), 4.44 (t, J = 5.5 Hz, 1 H), 3.79 (s, 3 H), 3.35 (s, 6 H), 2.14–2.04 (m, 2 H), 1.99–1.26 ppm (m, 2 H); ^{13}C NMR δ 169.8, 164.1, 150.7, 134.7, 130.9, 123.5, 103.7, 73.0, 53.2, 52.9, 52.5, 28.2, 26.3 ppm (t); IR ν 2956, 1751, 1732, 1531, 1278, 1120, 721 cm^{-1}. Anal. Calcd for $C_{15}H_{19}NO_8$: C, 52.79; H, 5.61. Found: C, 52.53; H, 5.50.

Independent Access to the Carbonyl Oxide (17d). Preparation of 6,6-Dichloro-4-(acetyloxy)-5-hexenal (20). A solution of the Grignard reagent prepared from 4-bromo-1-butene (4.9 mmol) and Mg turnings (5.4 mmol) in dry ether (17 mL) was cooled to 0 °C under N_2. β,β-dichloroacrolein[34] (500 mg, 4.48 mmol) was added by syringe, and the mixture was stirred for 15 min. Ether (75 mL) was added, and the solution was washed with 5% H_2SO_4 (25 mL) and saturated $NaHCO_3$ (25 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography (hexanes–EtOAc (4:1)) to provide 500 mg (77%) of 1,1-dichloro-1,6-heptadien-3-ol: ^1H NMR δ 5.95 (d, J = 9.3 Hz, 1 H), 5.75 (m, 1 H), 5.05 (m, 2 H), 4.40 (m, 1 H), 2.15 (m, 3 H), 1.65 ppm (m, 2 H); ^{13}C NMR δ 137.5 (d), 132.2 (d), 122.4 (s), 115.2 (t), 69.1 (d), 35.2 (t), 29.1 ppm (t); IR ν 3328, 2930, 1620 cm^{-1}; MS m/e 145 (M^+ – Cl, 5), 129 (15), 127 (77), 125 (100), 91 (13), 89 (10), 61 (21). Anal. Calcd for $C_7Hl_{30}Cl_2O$: C, 46.44; H, 5.57. Found: C, 46.54; H, 5.78.

A solution of the alcohol (395 mg, 2.70 mmol) in CH_2Cl_2 (4 mL) was treated with acetic anhydride (380 μL, 4.1 mmol) and pyridine (440 μL, 5.4 mmol). After 19 h, the reaction was diluted with CH_2Cl_2, washed with 5% H_2SO_4 (3 × 15 mL) and saturated $NaHCO_3$ (15 mL), dried over Na_2SO_4, and concentrated to give 1,1-dichloro-3-(acetyloxy)-1,6-heptadiene: ^1H NMR δ 5.82 (m, 1 H), 5.65 (m, 1 H), 5.10 (m, 2 H), 4.92 (s, 1 H), 2.2–1.5 (m, 4 H), 2.05 ppm (s, 3 H); ^{13}C NMR δ 169.7 (s), 136.9 (d), 128.4 (d), 124.3 (s), 115.4 (t), 71.0 (d), 32.8 (t), 28.9 (t), 20.8 ppm (q); IR ν 1745, 1627, 1230 cm^{-1}; MS m/e 180 (M^+ – Ac) 162 (4), 127 (18), 91 (16), 66 (6), 43 (100). Anal. Calcd for $C_9H_{12}Cl_2O_2$: C, 48.45; H, 5.42. Found: C, 48.12; H, 5.50.

A solution of 1,1-dichloro-3-(acetyloxy)-1,6-heptadiene (926 mg, 4.2 mmol) in CH_2Cl_2–MeOH (5:1, 15 mL) was cooled to –78 °C under a purging stream of O_2. Ozone was passed through the solution until a faint blue color developed, at which point the excess O_3 was removed in the O_2 stream (negative KI/starch test). Dimethyl sulfide (1 mL) was added to decompose the peroxides, and the reaction was allowed to warm to room temperature for 4 h. Purification by flash chromatography (hexane–EtOAc (4:1)) yielded 635 mg of the aldehyde **20** (68%): ^1H NMR δ 9.78 (t, J = 0.6, 1 H), 5.86 (d, J = 8.7 Hz, 1 H), 5.52 (m, 1 H), 2.55 (m, 2 H), 2.02 (s, 3 H), 2.00 ppm (m, 2 H).

Ozonolysis of **20** was carried out under the trapping/rearrangement conditions as described for **1e**, except that ozonation of the vinylidene dichloride was considerably slower, requiring 1 h for complete reaction. Analysis of the crude reaction product by capillary GC indicates the presence of **14e** and **17e** in a ratio of 27.2:72.8.

Trapping of Carbonyl Oxides from 2-Methylcyclopenten-1-ol Derivatives. A mixture of **7** (0.3 mmol) in methanol–CH_2Cl_2 (1:1, v/v, ca. 0.08 M) containing $NaHCO_3$ (1 equiv) was cooled to –78 °C and ozonized as before. After removal of the excess ozone, the mixture was allowed to warm to room temperature and concentrated. The residue was taken up in

(34) Hanack, M.; Korhummel, C. *Synthesis* **1987**, 944.

EtOAc (1 mL), filtered, and rinsed through a short (1-in.) column of silica gel with EtOAc. The solvent was removed and the peroxide mixture analyzed by NMR.

Peroxides from 7c. Ozonation of **7c** (72 mg) provided 97 mg (92%) of a mixture of **24c**, **25c**, and **26c** in a 41:29:30 ratio by NMR: ^{1}H NMR (in $CDCl_3$, after shake with D_2O to remove interfering OH signal) δ 5.20 (m, **26c**, 0.30 H), 4.69 (m, **24c** and **25c**, 0.70 H), 4.1–3.5 (m, 1 H), 3.48–3.39 (5 s, 3 H), 2.16 (s, **25c**, 0.88 H), 2.1–1.6 (m, 4 H), 1.45–1.15 (5 s, **24c** and **26c**, 2.10 H), 0.19–0.09 ppm (3 s, 9 H). Treatment of this mixture with excess $(CH_3)_2S$ caused conversion to **27c** over a 20-h period: ^{1}H δ 9.77 (t, J = 1.3 Hz, 1 H), 4.05 (t, J = 6.5 Hz, 1 H), 2.52 (t, J = 7.6 Hz, 2 H), 2.18 (s, 3 H), 2.00 (m, 2 H), 0.14 ppm (s, 9 H).

Peroxides from 7e. Ozonation of 44 mg (0.32 mmol) of **7e** provided 54 mg (77%) of a peroxide mixture containing **24e**, **25e**, and **26e** in a 41:40:19 ratio by NMR: ^{1}H δ 5.28 (m, **26e**, 0.19 H), 5.03 (m, **24e** and **25e**, 0.81 H), 4.9–4.7 (m, 1 H), 3.5–3.3 (6 s, 3 H), 2.21–2.05 (6 s, OAc for all and CH_3 for **25e**, 4.2 H), 2.1–1.7 (m, 4 H), 1.5–1.2 ppm (6 s, **24e** and **26e**, 1.8 H). Exposure of this mixture to excess $(CH_3)_2S$ overnight led to ketoaldehyde **27e**: ^{1}H δ 9.78 (br s, 1 H), 5.02 (dd, J = 7.5, 5.1 Hz, 1 H), 3.46 (s, 3 H), 2.61 (t, J = 7.3 Hz, 2 H), 2.20 (s, 3 H), 2.14 (s, 3 H), 2.13 ppm (m, 2 H).

Acknowledgment. We are grateful to the National Science Foundation for financial support of this research (CHE-8806198). The NMR instrumentation used in this work was also supported, in part, by the NSF. T.I. thanks donors to the Chemistry Department at the University of Missouri for support in the form of Bent and Nightingale Summer Fellowships.

Notes

Rare Phenazine L-Quinovose Esters from a Marine Actinomycete

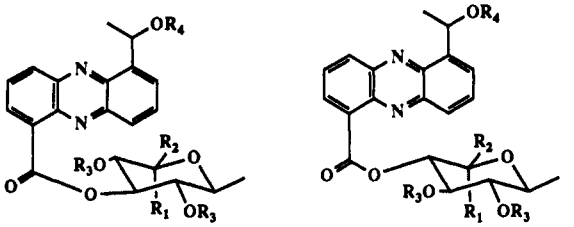
Charles Pathirana, Paul R. Jensen, Ryan Dwight, and Willian Fenical*

Scripps Institution of Oceanography, University of California, San Diego, La Jolla, California 92093-0236

Received July 29, 1991

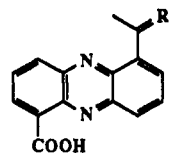
Although soil-derived bacteria have proven to be the major source for commercial antibiotics and related bioactive metabolites, similar microorganisms found in marine habitats have been almost totally ignored.[1] This has been due, in part, to the diversity of unique bacteria in marine habitats and the fact that many of these microorganisms are not readily brought into culture. As part of a continuing program to explore the nutritional requirements, distributions, and secondary metabolites produced by marine bacteria,[2] we have initiated several studies of bacteria from bay and estuarine environments. A study of the shallow sediments in Bodega Bay, CA, resulted in the isolation of a filamentous bacterium (isolate CNB-253, an unknown *Streptomyces* sp.) which was found to produce compounds with broad-screen antibacterial activity. Subsequent fermentation in saltwater-based media, followed by EtOAc extraction of the whole broth, vacuum flash chromatographic purification of the extract, and HPLC purification led to the isolation of four new alkaloid esters of the rare phenazine class (**1**–**4**, Chart I).[3] In addition, minor quantities of the known compounds

Chart I

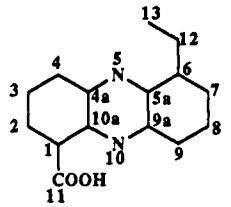


1. R_1=OH, R_2=R_3=R_4=H
4. R_1=R_3=R_4=H, R_2=OH
5. R_1=OAc, R_2=H, R_3=R_4=Ac

2. R_1=OH, R_2=R_3=R_4=H
3. R_1=R_3=R_4=H, R_2=OH
6. R_1=OAc, R_2=H, R_3=R_4=Ac



7. R= =O
8. R=H, OH



6-acetylphenazine-1-carboxylic acid (**7**) and saphenic acid (**8**) were also isolated.[4]

Revealing their isomeric relationships, all four phenazine alkaloid esters (**1**–**4**) showed identical molecular ions at m/z 414 amu (LREIMS), which was analyzed by high-resolution methods for $C_{21}H_{22}N_2O_7$. The ^{1}H NMR spectra for all four compounds (Table I) showed six aromatic protons and those from a hexose sugar pyranose functionality. The ^{1}H NMR spectrum of the major compound, **2**, resolved the aromatic resonances, and decoupling experiments revealed that they belonged to two isolated spin systems each involving three contiguous protons. All four compounds also showed a methyl group at δ 1.8 ppm (d, J = 6.5 Hz) that was coupled to a deshielded methine proton at δ 5.8 ppm (dq, J = 2.0, 6.5 Hz) which simplified to a quartet upon changing the NMR solvent from pure

(1) (a) Faulkner, D. J. *Nat. Prod. Rep.* **1991**, *8*(2), 97 and earlier reviews in the same journal. (b) Fenical, W.; Jensen, P. R. In *Advances in Marine Biotechnology*, Zaborsky, O. K., Attaway, D. A., Eds.; Plenum Press: New York, Vol. 1, in press.

(2) (a) Gil-Turnes, M. S.; Hay, M. E.; Fenical, W. *Science* **1989**, *246*, 116. (b) Gustafson, K.; Roman, M.; Fenical, W. *J. Am. Chem. Soc.* **1989**, *111*, 7519. (c) Pathirana, C.; Tapiolas, D. M.; Jensen, P. R.; Dwight, R.; Fenical, W. *Tetrahedron Lett.* **1991**, *32*(21), 2323. (d) Tapiolas, D. M.; Roman, M.; Fenical, W.; Stout, T. J.; Clardy, J. *J. Am. Chem. Soc.* **1991**, *113*, 4682.

(3) (a) Berger, J. In *Encyclopedia of Chemical Technology*, Mark, H. E., Othmer, D. F., Overberger, C. G., Seaborg, G. T., Eds.; Wiley Interscience: New York, 1978; Vol. 3, pp 1–21. (b) Gerber, N. N. *J. Heterocycl. Chem.* **1969**, *6*, 297.

(4) Geiger, A.; Keller-Schierlein, W.; Brandl, M.; Zahner, H. *J. Antibiotics* **1988**, *41*, 1542.

0022-3263/92/1957-0740$03.00/0