Ozonolyses of 4,4-Dimethyl-2-cyclohexen-1-yl Acetate and 4,4-Dimethyl-2-cyclopenten-1-yl Acetate. Competition between the Steric Effects of the Allylic Methyl Groups and the Electronic Effects of the Acetoxy Group on the Direction of Cleavage of the Primary Ozonides

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In order to understand the relative directing effects of the substituent steric and electronic effects on the cleavage of the primary ozonides, ozonolyses of a series of cyclohexene and cyclopentene derivatives were conducted in methanol or in ether in the presence of trifluoroacetophenone. The ozonolysis of 4,4-dimethyl-2-cyclohexen-1-yl acetate (**1k**) in methanol provided exclusively the α-methoxyalkyl hydroperoxide **7k** derived from capture of 5-acetoxy-5-formyl-2,2-dimethylpentanal oxide by the solvent, while in the case of the relevant 4,4-dimethyl-2-cyclopenten-1-yl acetate (**1l**) the solvent-captured product **6l** derived from trapping of 2-acetoxy-5-formyl-5-methylpentanal oxide was the major product. The remarkable difference in the regiochemistry of the fragmentation between the primary ozonides, **2k** and **2l**, is rationalized in terms of the significant difference in the steric congestion.

The basic mechanism that describes the ozonolysis of an alkene to produce a 1,2,4-trioxolane (secondary ozonide) evolved during the 1950's and is known as the Criegee mechanism.[1] It consists of three steps. The first step is a [3 + 2] cycloaddition reaction of ozone with the alkene leading to formation of a primary ozonide (PO, 1,2,3-trioxolane). The second is a cycloreversion process of PO to provide the transient carbonyl oxide and a stable carbonyl compound, which may proceed in two different ways in the case of unsymmetrically substituted alkenes. Finally, recombination of the carbonyl oxide and the carbonyl compound gives the 1,2,4-trioxolane. Much of the current interest in this process centers on the factors affecting the direction of cleavage of the unsymmetrically substituted PO.[2] Three factors have been found to play an important role in determining the regiochemistry of PO cleavage, i.e., the electronic effect of the substituent attached to the C−C double bond,[3] the electronic effect of the heteroatom substituent at the allylic position,[4] and the steric effect of the allylic dialkyl substituents.[5] To predict the regiochemistry in cleavage of the PO from the given alkene, it would be required to understand the relative directive effects of these three factors. For this purpose, we have conducted ozonolyses of a series of properly-substituted cycloalkenes in the presence of trifluoroacetophenone in ether or in methanol and have determined in each case the ratios of two possible cross-ozonides or the composition of the solvent-derived products, respectively.

Table 1. Ozonolysis of Cycloalkenes 1a−n

substr	solvent	additive	products (% yield)[a]	ratio of path a:b[b]
1a	ether	$PhCOCF_3$	**8a** (67)	0:100
1b	ether	$PhCOCF_3$	**5b** (65)	100:0
1c	ether	$PhCOCF_3$	**8c** (71)	0:100
1d	ether	$PhCOCF_3$	**8d** (6)	0:100
1e	MeOH		**6e** (4), **7e** (84)	5:95[c]
1f	MeOH		**6f** (64)	100:0[d]
1g	MeOH		**10g** (72)	0:100
1h	MeOH		**6h** (28), **7h** (56)	33:67[e]
1i	MeOH		**6i** (1.5), **7i** (72)	2:98[f]
1j	MeOH		**6j** (15), **7j** (63)	19:81[f]
1k	MeOH		**10k** (68)	0:100
1l	MeOH		**12** (58), **13** (6)	90:10
1m	ether	$PhCOCF_3$	**5m** (88)	100:0
1n	ether	$PhCOCF_3$	**8n** (79)	0:100

[a] In some cases the ozonolysis product was transformed into the more stable, easily assignable compound. [b] See Schemes 1, 3, and 4 for each substrate. [c] Taken from the data in ref 3b. [d] Taken from the data in ref 5c. [e] Determined by the ^1H NMR spectra of the crude product mixture. [f] Taken from the data in ref 4a.

Results and Discussion

Ozonolysis of Alkyl-Substituted Cyclohexenes. Ozonolysis of 1-methylcyclohexene (**1a**) in the presence of trifluoroacetophenone in ether gave exclusively the crossed-ozonide **8a** (67% yield) derived from the cycloaddition of the carbonyl oxide intermediate **4a** with the additive, suggesting that the carbonyl oxide intermediate can be efficiently captured by trifluoroacetophenone, an electron-deficient ketone, and moreover, the directive effect of the electron-donating methyl group is important (Table 1 and Scheme 1). Also, the steric effect of the dialkyl groups at the allylic position was found to play an important role in determining the direction of cleavage of PO from 1,2,3,3-tetramethylcyclohexene (**1b**). Treatment of **1b** with ozone in the presence of trifluoroacetophenone resulted in exclusive formation of the crossed-ozonide **5b** (65%) derived from the reaction of the

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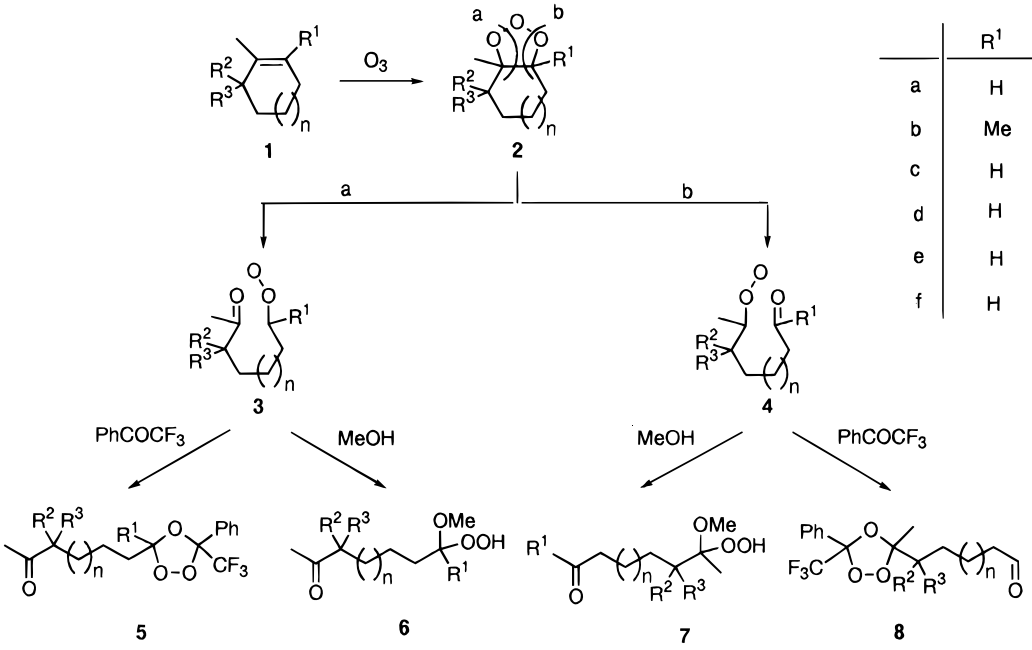
Scheme 1



	R^1	R^2	R^3	n
a	H	H	H	1
b	Me	Me	Me	1
c	H	Me	Me	1
d	H	-$(CH_2)_4$-		1
e	H	H	H	0
f	H	Me	Me	0

sterically less-congested carbonyl oxide **3b** and the additive.

To obtain information for the relative directive effect between the substituent electronic and steric effects, we then conducted the ozonolyses of 6,6-dialkyl-substituted 1-methylcyclohexenes **1c**,**d**. In each case the sole product was the crossed-ozonide **8**, derived from capture of the sterically more-congested carbonyl oxide **4** by the additive (Scheme 1 and Table 1), suggesting that in both substrates **1c**,**d** the directive effect of the electron-donating methyl substituent at C-1 is more important. This was in marked contrast to the fact that in the case of 1,5,5-trimethylcyclopentene (**1f**) the steric effect of the dimethyl groups is decisive, thereby providing exclusively the sterically less-congested carbonyl oxide intermediate **3f** (Table 1).[5c]

To understand the notable difference in behavior between two substrates, **1c** and **1f**, semiempirical calculations on the structures of POs, **2c** and **2f**, were undertaken by the PM3 method.[6] The optimized structures suggest that there exists a notable difference in the structure between **2c** and **2f** (Figure 1). In the PO **2f** the central oxygen of the 1,2,4-trioxolane ring is placed in close proximity to one of the adjacent methyl groups. In the cycloreversion process leading to the ketone oxide intermediate **4f** (path b in Scheme 1), the oxygen atom and the methyl group are likely to be brought more closely together (steric congestion), while in the alternative pathway a leading to the aldehyde oxide intermediate **3f**, the oxygen may move to come apart from the methyl substituent (strain relief).[3c] Exclusive formation of the crossed ozonide **5f** from **1f** would then imply that in path b the retarding steric effect of the allylic dimethyl groups overcomes the accelerating electronic effect of the methyl substituent at C-1, and as a result, the alternative pathway a begins to contribute predominantly. In the cycloreversion of the more extended PO **2c**, however, the steric interaction between the allylic dimethyl groups and the central oxygen of the trioxolane ring would not be important (Figure 1), and therefore, the direction of

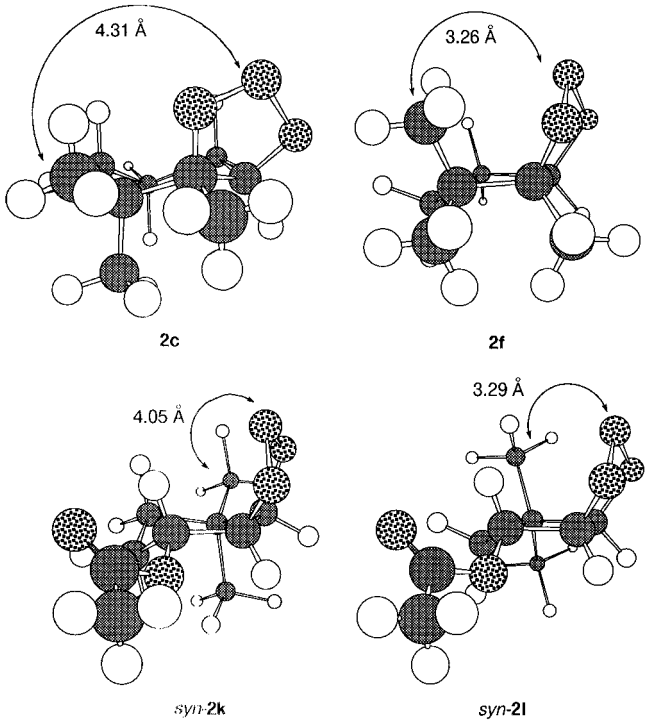


Figure 1. Structures of PO **2c**,**f**,**k**,**l** calculated by the PM3 method.

cleavage of the PO **2c** is likely to be controlled by the electronic effect of the methyl substituent at C-1. As will be seen later, a similar ring size effect has been observed between 4,4-dimethyl-2-cyclohexen-1-yl acetate (**1k**) and 4,4-dimethyl-2-cyclopenten-1-yl acetate (**1l**).

Ozonolysis of 2-Cyclohexen-1-yl Acetate and 2-Methyl-2-cyclohexen-1-yl Acetate. To investigate the electronic effect of the allylic heteroatom substituent on the regiochemistry of PO cleavage,[4] we conducted ozonolyses of 2-cyclohexen-1-yl acetate (**1g**) and 2-methyl-2-cyclohexen-1-yl acetate (**1h**) in methanol. Treatment of **1g** with ozone gave the methoxyalkyl hydroperoxide **7g** derived from capture of the carbonyl oxide intermediate **4g** by the solvent (Scheme 2 and Table 1). Since the

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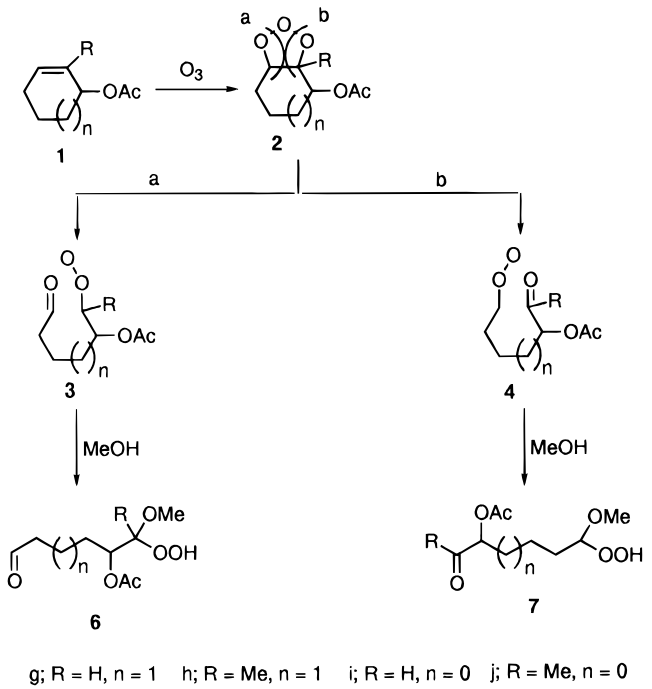
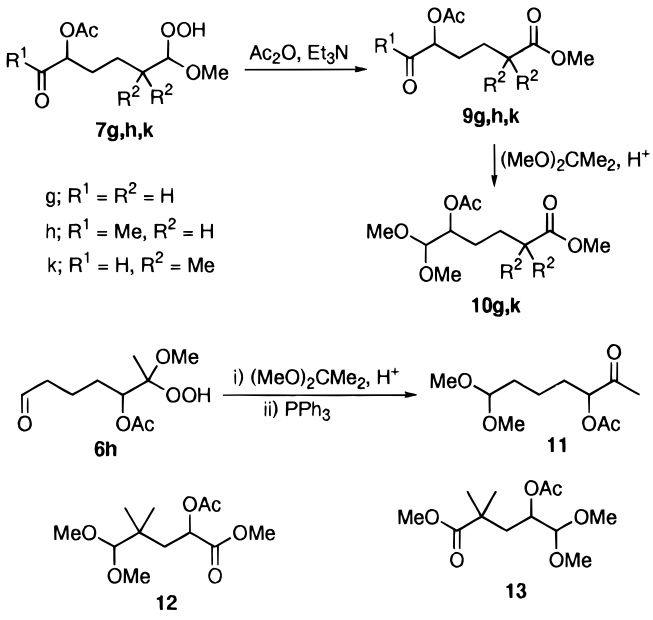
Scheme 2



g; R = H, n = 1 h; R = Me, n = 1 i; R = H, n = 0 j; R = Me, n = 0

Scheme 3



^{1}H NMR spectrum of the crude product mixture suggested that the hydroperoxide **7g** exists as a mixture with the corresponding hemiperacetal (a mixture of stereoisomers),[4a] the crude ozonolyzate was transformed into the corresponding ester by the reaction sequence illustrated in Scheme 3. From the reaction mixture, ester **10g** was isolated in a high yield of 72%. Selective contribution of the carbonyl oxide intermediate **4g** is consistent with earlier studies 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.[3a]

A somewhat different pattern of PO fragmentation was found for the methyl-substituted cyclohexene **1h**. Ozonolysis of **1h** in methanol gave a 1:2 mixture of two solvent-derived products, **6h** and **7h**. To confirm the structures, the methoxyalkyl hydroperoxide **6h** was converted into the keto acetal **11**, while the alternative solvent-derived product **7h** was transformed into the ester **9h** (Scheme 3). This implies that the presence of the methyl-substituent at C-2 leads to a larger fraction of the highly-substituted carbonyl oxide **3h** compared to ozonolysis of **1g**. Thus, while the directive effect of the heteroatom substituent still dominates in the ozonolysis of **1h**, it is partly compensated by the methyl substituent at C-2. Bunnelle and Isbell[4a] have found a similar difference in the mode of cleavage of PO between two cyclopentene derivatives, **1i** and **1j** (Scheme 2 and Table 1).

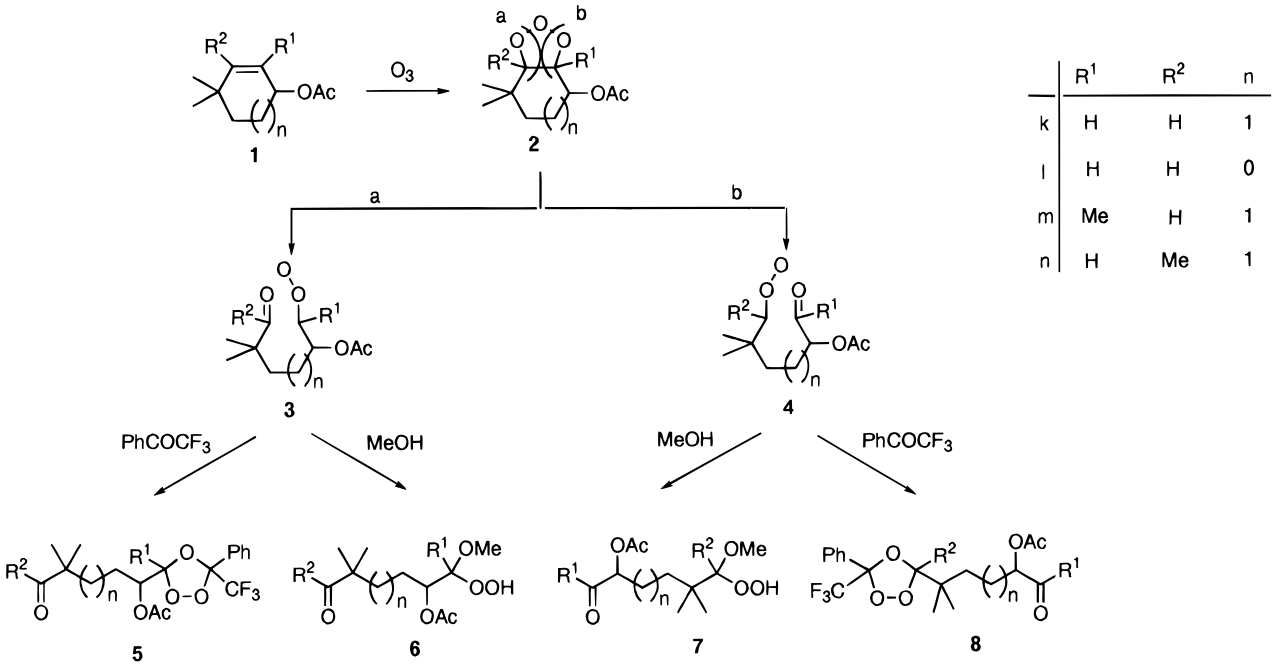
Ozonolysis of 4,4-Dimethyl-2-cyclohexen-1-yl Acetate and 4,4-Dimethyl-2-cyclopenten-1-yl Acetate. From the ozonolyses of cycloalkenes **1a-j**, it is evident that both the steric effect of the allylic dialkyl substituents and the electronic effect of the allylic heteroatom substituent play important roles in determining the direction of cleavage of PO. To know the relative strength of these two factors, we have conducted the ozonolyses of 4,4-dimethyl-2-cyclohexen-1-yl acetate (**1k**) and 4,4-dimethyl-2-cyclopenten-1-yl acetate (**1l**) (Scheme 4 and Table 1).

Treatment of **1k** with ozone in methanol gave exclusively the α-methoxyalkyl hydroperoxide **7k**, which was transformed into the ester **10k**. This clearly demonstrates that of the two directive factors the electronic effect of the allylic acetoxy group is decisive. From the reaction of **1l** with ozone in methanol, however, was obtained a 9:1 mixture of two methoxyalkyl hydroperoxides, **6l** and **7l**. The structures of two solvent-derived products, **6l** and **7l**, were confirmed by transformation into the corresponding esters, **12** and **13**, respectively (reference the sequence illustrated in Scheme 3). Thus, in the cycloreversion of PO **2l** the directive effect of the allylic methyl groups plays a more important role, thereby providing predominantly the carbonyl oxide **3l** with the geminal methyl groups most remote from the carbonyl oxide fragment. It should be noticed that this apparent difference in behavior between **2k** and **2l** is very similar to that observed between **2c** and **2f** from 1,6,6-trimethylcyclohexene (**1c**) and 1,5,5-trimethylcyclopentene (**1f**), respectively.

Since the directive effect of the allylic heteroatom substituent does not seem likely to be influenced significantly by the ring size of substrates, the notable difference in behavior between **2k** and **2l** would be due to the difference in the steric congestion. The structures of PO **2k** and PO **2l** calculated by PM 3 method seems to suggest that the difference in steric congestion between these two POs is significant (Figure 1), which in turn should reflect the difference in steric crowding between the corresponding transition states leading to the sterically-congested carbonyl oxide intermediates, **4k** and **4l**, respectively. As a result, the carbonyl oxide intermediate **4k** is predominantly produced from **2k**, while the contribution of the carbonyl oxide **3l** predominates in the case of **2l**.

Thus, in the ozonolyses of cycloalkene derivatives three factors, e.g., the electronic effect of the alkyl substituent attached to the C−C double bond, the electronic effect of the allylic heteroatom substituent, and the steric effect of the allylic dialkyl substituents, affect the direction of cleavage of PO in a complicated fashion. Judged from the product contributions observed for the ozonolyses of **1b**,**c**,**h**,**k**, the order of the directive effects of these three

Scheme 4



	R^1	R^2	n
k	H	H	1
l	H	H	0
m	Me	H	1
n	H	Me	1

factors for the cyclohexene derivatives seems to follow the sequence: the electronic effect of the allylic heteroatom substituent > the electronic effect of the alkyl substituent attached to the C−C double bond > the steric effect of the allylic dialkyl substituents. In the case of cyclopentene derivatives (see results from **1f**,**j**,**l**), however, the directive effect of the allylic dimethyl groups is apparently the most important. The second is the electronic effect of the allylic heteroatom substituent, and the smallest one is the electronic effect of the alkyl substituent attached to the C−C double bond.

In the case of POs from the highly-substituted cyclohexenes **1m**,**n**, three directive effects mentioned above may compete to each other. In reality, the ozonolyses were found to be highly selective (Scheme 4 and Table 1). From the reaction of 2,4,4-trimethyl-2-cyclohexen-1-yl acetate (**1m**) with ozone in the presence of trifluoroacetophenone was obtained exclusively the crossed-ozonide **5m**, demonstrating that the sum of the directive effects of the allylic dimethyls at C-4 and the methyl substituent at C-2 exceeds the directive effect of the acetoxy substituent at C-1. Also, ozonolysis of 3,4,4-trimethyl-2-cyclohexen-1-yl acetate (**1n**) in the presence of trifluoroacetophenone gave exclusively the crossed-ozonide **8n**, derived from capture of the carbonyl oxide intermediate **4n** by the additive.

Conclusion. We have conducted ozonolyses of a series of cycloalkene derivatives in methanol or in ether in the presence of trifluoroacetophenone. On the basis of these trapping experiments of the carbonyl oxide intermediates, the factors affecting the direction of cleavage of PO and their relative importance have been elucidated. The information obtained in this study should be useful to predict the branching ratio of the given PO.

Experimental Section

General Procedures. ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ (unless otherwise noted) with $SiMe_4$ as standard. The method of ozonolysis was previously described.[7] The cycloalkenes **1a**,[8] **1b**,[9] **1c**,[10] **1d**,[11] **1g**,[12] and **1h**[13] were prepared by the reported methods.

Preparation of Acetoxy-Substituted Cycloalkenes. The acetoxy-substituted cycloalkenes **1k**−**n** were prepared from the acetylation of the corresponding 2-cycloalken-1-ols (prepared by LAH reduction of the corresponding ketones[14]). The synthesis of **1k** is representative. Acetic anhydride (4.0 g, 39.2 mmol) was added to a solution of 4,4-dimethyl-2-cyclohexen-1-ol (1.0 g, 7.9 mmol) in pyridine (8 mL), and the mixture was allowed to stir at rt. After 20 h, the solution was poured into 50 mL of ether, washed successively with 5% H_2SO_4 and saturated $NaHCO_3$, dried over $MgSO_4$, and concentrated. The residue was purified by flash column chromatography on silica gel (ether−hexane, 1:9) to yield 1.0 g (75%) of **1k**.

4,4-Dimethyl-2-cyclohexen-1-yl acetate (1k): oil; ^{1}H NMR δ 0.98 (s, 3 H), 1.03 (s, 3 H), 1.4−2.0 (m, 4 H), 2.05 (s, 3 H), 5.1−5.2 (m, 1 H), 5.54 (dd, $J = 3 \times 10$ Hz, 1 H), 5.64 (d, $J = 10$ Hz, 1 H); IR 2950, 1740 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.01; H, 10.10.

4,4-Dimethyl-2-cyclopenten-1-yl acetate (1l): oil; ^{1}H NMR δ 1.09 (s, 3 H), 1.16 (s, 3 H), 1.62 (d, $J = 4$ Hz, 1 H), 1.67 (d, $J = 4$ Hz, 1 H), 2.04 (s, 3 H), 5.6−5.7 (m, 2 H), 5.87 (d, $J = 5$ Hz, 1 H); IR 2950, 1740 cm^{-1}. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.77; H, 9.59.

2,4,4-Trimethyl-2-cyclohexen-1-yl acetate (1m): oil; ^{1}H NMR (CCl_4) δ 0.95 (s, 3 H), 1.02 (s, 3 H), 1.3−1.8 (m, 4 H), 1.63 (s, 3 H), 2.01 (s, 3 H), 5.17 (t, $J = 6$ Hz, 1 H), 5.37 (s, 1 H); IR 2950, 1740 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.29. H, 10.14.

3,4,4-Trimethyl-2-cyclohexen-1-yl acetate (1n): oil; ^{1}H NMR δ 1.00 (s, 3 H), 1.10 (s, 3 H), 1.4−2.0 (m, 4 H), 1.69 (s, 3 H), 2.04 (s, 3 H), 5.1−5.3 (m, 1 H), 5.33 (d, $J = 2$ Hz, 1 H); IR

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2950, 1740, 1240 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.19; H, 10.09.

Caution: Since organic ozonides are potentially hazardous compounds, they must be handled with due care; avoid exposure to strong heat or light, or mechanical shock, or oxidizable organic materials, or transition metal ions. No particular difficulties were experienced in handling any of the new organic ozonides synthesized in this work using the reaction scales and procedures described below together with the safeguard mentioned here.

Ozonolysis of Cycloalkene Derivatives 1a−d in the Presence of Trifluoroacetophenone. Ozonolysis of 1-methylcyclohexene (**1a**) is representative. After a solution of **1a** (198 mg, 2.0 mmol) and trifluoroacetophenone (348 mg, 2.0 mmol) in ether (15 mL) was treated with ozone (O_3/O_2 stream) (1.5 equiv) at −70 °C, the crude products were separated by column chromatography on silica gel. Elution with ether−hexane (1:9) gave the crossed-ozonide **8a** (426 mg, 67%).

(3-Methyl-5-phenyl-5-trifluoromethyl-1,2,4-trioxolan-3-yl)pentanal (8a): oil; ^{1}H NMR (CCl_4) δ 1.30 (s, 3 H), 1.3−2.6 (m, 8 H), 7.2−7.6 (m, 5 H), 9.63 (t, J = 1.5 Hz, 1 H); ^{13}C NMR δ 21.86, 22.39, 23.34, 35.07, 43.46, 103.40 (q, J = 34 Hz), 113.55, 121.53 (q, J = 289 Hz), 126.54, 128.24, 128.27, 130.22, 202.02; IR 1735, 1460, 1390, 1310, 1200, 1100, 960, 720 cm^{-1}. Anal. Calcd for $C_{15}H_{17}F_3O_4$: C, 56.59; H, 5.39. Found: C, 56.59; H, 5.56.

Crossed-ozonide 5b: oil; ^{1}H NMR δ 1.148 (s, 3 H), 1.154 (s, 3 H), 1.34 (s, 3 H), 1.35−1.44 (m, 2 H), 1.55−1.61 (m, 2 H), 1.87−1.94 (m, 2 H), 2.14 (s, 3 H), 7.38−7.49 (m, 3 H), 7.54−7.56 (m, 2 H); ^{13}C NMR δ 19.27, 22.43, 24.26, 24.33, 25.11, 35.91, 39.66, 47.66, 103.37 (q, J = 32.9 Hz), 113.59, 121.50 (q, J = 289.3 Hz), 126.50, 128.27, 130.24, 131.97, 213.80; IR 2950, 1705, 1190, 1080, 955, 720 cm^{-1}. Anal. calcd for $C_{18}H_{23}F_3O_4$: C, 59.99; H, 6.43; F, 15.82. Found: C, 60.21; H, 6.35.

Crossed-ozonide 8c: oil; ^{1}H NMR (CCl_4) δ 1.10 (s, 3 H), 1.15 (s, 3 H), 1.23 (s, 3 H), 1.1−1.7 (m, 4 H), 2.38 (t, J = 6 Hz, 2 H), 7.3−7.8 (m, 5 H), 9.77 (br s, 1 H); ^{13}C NMR δ 16.89, 18.69, 22.16, 22.61, 37.75, 39.84, 44.27, 103.02 (q, J = 34 Hz), 117.12, 121.48 (q, J = 288 Hz), 126.45, 128.18, 130.04, 132.73, 202.07; IR 3000−2900, 1730, 1450, 1380, 1310, 1200, 1080, 950, 720 cm^{-1}. Anal Calcd for $C_{17}H_{21}F_3O_4$: C, 58.94; H, 6.12. Found: C, 59.24; H, 6.33.

Crossed-ozonide 8d: oil; ^{1}H NMR (CCl_4) δ 1.27 (s, 3 H), 1.3−2.5 (m, 14 H), 7.3−7.7 (m, 5 H), 9.73 (br s, 1 H); ^{13}C NMR δ 17.76, 20.24, 25.68, 25.98, 32.61, 34.43, 37.69, 44.38, 51.20, 102.75 (q, J = 33 Hz), 117.64, 121.55 (q, J = 289 Hz), 126.52, 128.22, 130.06, 132.88, 202.22; IR 1720, 1460, 1380, 1305, 1180, 1080, 950, 715 cm^{-1}.

Ozonolysis of 2-Cyclohexen-1-yl Acetates 1g,h in Methanol. Ozonolysis of **1h** is representative. To a solution of 2-methyl-2-cyclohexen-1-yl acetate **(1h)** (154 mg, 1.00 mmol) in MeOH−CH_2Cl_2 (15 mL, 1:5, v/v) was passed a slow stream of ozone (1.5 equiv) at −70 °C. After evaporation of the solvent under vacuum, the crude products were separated by column chromatography on silica gel (elution with ether) to give a mixture of two α-methoxyalkyl hydroperoxides, **6h** and **7h** (197 mg, 84%); the ratio was determined by the characteristic signal for each product in ^{1}H NMR spectrum [**6h**, δ 3.36 (s, 3 H, OMe); **7h**, δ 3.50 (s, 3 H, OMe)].

To confirm the structure, the hydroperoxide **7h** was transformed into the ester **9h**. After the ozonolysis as above, the residue (a 1:2 mixture of **6h** and **7h** from 1.56 mmol of **1h**) was taken up in CH_2Cl_2 (4 mL) and cooled to 0 °C. Acetic anhydride (795 mg, 5 equiv) and triethylamine (236 mg, 1.5 equiv) were added, and the solution was stirred at rt for 20 h. This was treated with methanol (1 mL) for 15 min and then diluted with ether (50 mL). The solution was washed with 5% H_2SO_4 and saturated $NaHCO_3$, dried over $MgSO_4$, and concentrated. The crude products were separated by column chromatography on silica gel. From the fraction eluted by ether−hexane (1:1) was obtained methyl 5-acetoxy-6-oxoheptanoate **(9h)** (167 mg, 50%): oil; ^{1}H NMR δ 1.6−1.9 (m, 4 H), 2.16 (s, 3 H), 2.17 (s, 3 H), 2.36 (t, J = 7 Hz, 2 H), 3.68 (s, 3 H), 5.00 (dd, J = 8 × 4 Hz, 1 H); ^{13}C NMR δ 20.59, 20.66, 26.13, 29.47, 33.30, 51.66, 78.22, 170.55, 173.40, 204.99; IR 2950, 1740, 1450, 1380, 1250 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.59; H 7.61.

The hydroperoxide **6h** was transformed into the ketone **11** as follows. A 1:2 mixture of **6h** and **7h** (197 mg) was dissolved in 2,2-dimethoxypropane (2 mL), treated with a few crystals of *p*-toluenesulfonic acid, and stirred at rt. After 2 h, the reaction mixture was diluted with ether (50 mL). The solution was washed with saturated $NaHCO_3$ and saturated brine, dried over $MgSO_4$, and concentrated. The ^{1}H NMR spectrum of the residue suggested that **6h** was converted into the corresponding dimethoxy-substituted ketone, while the hydroperoxide **7h** was remained intact. The crude products were separated by column chromatography on silica gel. The fraction containing the corresponding dimethoxy-substituted ketone (elution by ether−hexane, 1:5), after concentration (180 mg), was dissolved in benzene (5 mL) and treated with triphenylphosphine (262 mg, 1.00 mmol) for 20 h. After evaporation of the solvent, the crude products were separated by column chromatography on silica gel. Elution with ether−hexane (1:1) gave 3-acetoxy-7,7-dimethoxyheptan-2-one **(11)** (48 mg, 21%): oil; ^{1}H NMR δ 1.4−1.8 (m, 6 H), 2.15 (s, 3 H), 2.16 (s, 3 H), 3.32 (s, 6 H), 4.35 (t, J = 6 Hz, 1 H), 4.99 (dd, J = 8 × 5, Hz, 1 H); ^{13}C NMR δ 20.40, 20.66, 26.11, 30.01, 32.08, 52.83, 52.90, 78.54, 104.19, 170.56, 205.21; IR 2950, 1740, 1380, 1240 cm^{-1}. Anal. Calcd for $C_{11}H_{20}O_5$: C, 56.88; H, 8.68. Found: C, 57.08; H, 8.77.

Methyl 5-acetoxy-6,6-dimethoxyhexanoate (10g): oil; ^{1}H NMR (CCl_4) δ 1.4−1.8 (m, 4 H), 2.08 (s, 3 H), 3.38 (s, 3 H), 3.42 (s, 3 H), 3.68 (s, 3 H), 4.30 (d, J = 5 Hz, 1 H), 4.9−5.1 (m, 1 H); ^{13}C NMR δ 20.66, 21.04, 28.55, 33.73, 51.54, 54.54, 55.44, 72.16, 104.42, 170.51, 173.71; IR 2950, 1740, 1440, 1370, 1240, 1080 cm^{-1}. Anal. Calcd for $C_{11}H_{20}O_6$: C, 53.22; H, 8.12. Found: C, 52.97; H, 8.23.

Ozonolysis of 4,4-Dimethyl-2-cycloalken-1-yl Acetates 1k,l in Methanol. Ozonolysis of **1k** is representative. 4,4-Dimethyl-2-cyclohexen-1-yl acetate (**1k**) (240 mg, 1.43 mmol) was dissolved in MeOH−CH_2Cl_2 (15 mL, 1:5), and solid $NaHCO_3$ (0.5 g) was added. To the mixture cooled in a dry ice−methanol bath (−70 °C), was passed a slow stream of ozone (1.5 equiv). After the reaction, ether (30 mL) was added, the solid $NaHCO_3$ was removed by filtration, and the filtrate was concentrated at aspirator pressure, taking care to keep the reaction mixture below 40 °C. The residue was taken up in CH_2Cl_2 (4 mL). Then, acetic anhydride (729 mg, 5 equiv) and triethylamine (216 mg, 1.5 equiv) were added, and the solution was stirred at rt for 20 h. This was treated with methanol (1 mL) for 15 min. After concentration, the crude products were separated by column chromatography on silica gel. Elution with ether−hexane (1:1) gave methyl 2,2-dimethyl-5-acetoxy-5-formylpentanoate **(9k)** (243 mg, 74%): oil; ^{1}H NMR δ 1.19 (s, 6 H), 1.4−1.8 (m, 4 H), 2.19 (s, 3 H), 3.68 (s, 3 H), 4.9−5.0 (m, 1 H), 9.51 (s, 1 H).

The ester **9k** was then dissolved in 2,2-dimethoxypropane (2 mL), treated with a few crystals of *p*-toluenesulfonic acid, and stirred at rt for 2 h. After conventional workup, the crude products were separated by column chromatography on silica gel. Elution with ether−hexane (1:1) gave **10k** (269 mg, 68%).

Methyl 2,2-dimethyl-5-acetoxy-6,6-dimethoxyhexanoate (10k): oil; ^{1}H NMR (CCl_4) δ 1.13 (s, 6 H), 1.4−1.7 (m, 4 H), 2.00 (s, 3 H), 3.27 (s, 3 H), 3.33, (s, 3 H), 3.62 (s, 3 H), 4.18 (d, J = 6 Hz, 1 H), 4.93 (td, J = 6 × 3 Hz, 1 H); ^{13}C NMR δ 20.81, 24.46, 24.78, 24.89, 35.69, 41.75, 51.50, 54.20, 55.11, 72.27, 104.12, 170.24, 177.79; IR 2950, 1740, 1380, 1240, 1080 cm^{-1}. Anal. Calcd for $C_{13}H_{24}O_6$: C, 56.51; H, 8.75. Found: C, 57.04; H, 8.62.

Methyl 2-acetoxy-4,4-dimethyl-5,5-dimethoxypentanoate (12): oil; ^{1}H NMR δ 0.93 (s, 3 H), 0.96 (s, 3 H), 1.7−1.8 (m, 2 H), 2.14 (s, 3 H), 3.51 (s, 6 H), 3.37 (s, 3 H), 3.85 (s, 1 H), 5.13 (dd, J = 8 × 4 Hz, 1 H); ^{13}C NMR δ 20.60, 21.78, 22.86, 37.54, 39.05, 52.08, 58.31, 58.38, 70.12, 113.23, 170.21, 171.27; IR 2950, 1750, 1380, 1240, 1080 cm^{-1}. Anal. Calcd for $C_{12}H_{22}O_6$: C, 54.95; H, 8.45. Found: C, 54.91; H, 8.53.

Methyl 2,2-dimethyl-4-acetoxy-5,5-dimethoxylpentanoate (13) (in admixture with 80% **12**): oil; ^{1}H NMR δ 1.18 (s, 3 H), 1.21 (s, 3 H), 1.7−1.8 (m, 2 H), 2.02 (s, 3 H), 3.39 (s, 3 H), 3.41 (s, 3 H), 3.66 (s, 3 H), 4.22 (d, J = 5 Hz, 1 H), 5.0−

5.1 (m, 1 H); ^{13}C NMR δ 20.83, 23.72, 26.81, 38.55, 40.13, 51.56, 54.66, 55.49, 69.40, 104.69, 170.08, 177.75.

Ozonolysis of Highly-Substituted Cyclohexen-2-yl Acetates 1m,n in the Presence of Trifluoroacetophenone. Ozonolysis of **1m** is representative. After treating a solution of 2,4,4-trimethyl-2-cyclohexen-1-yl acetate (**1m**) (192 mg, 1.05 mmol) and trifluoroacetophenone (184 mg, 1.05 mmol) in ether (15 mL) with ozone (1.5 equiv) at −70 °C, the crude products were separated by column chromatography on silica gel. Elution with ether−hexane (1:4) gave the crossed-ozonide **5m** (373 mg, 88%).

2,2-Dimethyl-5-acetoxy-6-[3-methyl-5-phenyl-5-(trifluoromethyl)-1,2,4-trioxolan-3-yl]pentanal (5m): oil (a 1:1 mixture of two isomers); ^{1}H NMR δ 1.08 (s, 3 H), 1.09 (s, 1.5 H), 1.10 (s, 1.5 H), 1.36 (s, 1.5 H), 1.5−1.7 (m, 4 H), 2.16 (s, 1.5 H), 2.11 (s, 3 H), 5.24 (t, J = 6 Hz, 0.5 H), 5.29 (t, J = 6 Hz, 1 H), 7.4−7.6 (m, 5 H), 9.45 (s, 0.5 H), 9.46 (s, 0.5 H); ^{13}C NMR δ 17.21, 19.08, 20.77, 20.81, 21.17, 21.24, 21.37, 21.40, 24.64, 25.00, 32.69, 33.06, 45.48, 72.40, 72.76, 104.10 (q, J = 34 Hz), 104.48 (q, J = 34 Hz), 112.42, 112.54, 121.01 (q, J = 287 Hz), 121.13 (q, J = 288 Hz), 126.68, 126.77, 128.30, 128.41, 128.41, 128.59, 130.49, 131.95, 132.38, 169.95, 170.02, 205.55, 205.60; IR 2950, 1760, 1460, 1220, 1090, 760 cm^{-1}. Anal. Calcd for $C_{19}H_{23}F_3O_6$: C, 56.43; H, 5.73. Found: C, 56.66; H, 6.01.

2-(Acyloxy)-5-methyl-5-[3-methyl-5-phenyl-5-(trifluoromethyl)-1,2,4-trioxolan-4-yl]hexanal (8n): oil; ^{1}H NMR δ 1.11 (s, 3 H), 1.21 (s, 3 H), 1.26 (s, 3 H), 1.5−2.0 (m, 4 H), 2.20 (s, 3 H), 4.9−5.0 (m, 1 H), 7.3−7.6 (m, 5 H), 9.54 (s, 1 H); ^{13}C NMR δ 18.86, 20.56, 23.22, 23.97, 31.63, 33.40, 39.48, 103.18 (q, J = 34 Hz), 117.01, 121.44 (q, J = 289 Hz), 126.57, 128.34, 130.24, 132.67, 170.64, 198.25; IR 3000, 1750, 1380, 1090, 960, 720 cm^{-1}. Anal. Calcd for $C_{19}H_{23}F_3O_6$: C, 56.43; H, 5.73. Found: C, 55.87; H, 6.00.

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