Ozonolyses of 1-Alkyl-Substituted 3-Methylindenes. Remarkable Effects of the Substituent Steric Bulk and the Stereochemistry of the Carbonyl Oxide Intermediates on the Efficiency of Ozonide Formation

Shin-ichi Kawamura,[1a] Rika Takeuchi,[1a] Araki Masuyama,[1a] Masatomo Nojima,*[,1a] and Kevin J. McCullough*[,1b]

Department of Materials Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan, and Department of Chemistry, Heriot-Watt University, Edinburgh EH14 4AS, Scotland

Received March 24, 1998

Ozonolyses of 3-methyl- and 3-isopropyl-1-methylindenes (**1a**,**b**) in ether gave mainly the corresponding oligomers **3a**,**b**, while in the case of 3-phenyl- and 3-*tert*-butyl-1-methylindenes (**1c**,**d**), the corresponding exo−endo mixtures of ozonides **2c**,**d** were obtained in good yield, the exo isomer being the major one. The ozonolyses of two stereoisomeric keto vinyl ethers, (*E*)-**16** and (*Z*)-**16**, demonstrated that the stereochemistry of the derived carbonyl oxide **5c** exerts a remarkable influence on the course of the reaction. Particularly interesting is the fact that *syn*-**5c** having a proper geometry for the concerted cycloaddition provided ozonide **2c** in high yield even in the presence of trifluoroacetophenone. The high degree of similarity in the nature and distribution of the products from the ozonolyses of keto olefin (*E*)-**16** and 1-methyl-3-phenylindene (**1c**) would be consistent with their respective reactions proceeding predominantly through a common carbonyl oxide intermediate *syn*-**5c**.

Introduction

Carbonyl oxides are well-known to undergo cycloaddition with carbonyl compounds to give ozonides (1,2,4-trioxolane).[2] In the case of cycloalkenes, the efficiency is notably influenced by many factors including the ring size and the substitution pattern. As an example, ozonolysis of 1-methyl-3-phenylindene (**1c**) in an aprotic solvent such as CCl_4 has been found to give the corresponding ozonide **2c** in high yield, while in the case of 1,3-dimethylindene (**1a**), oligomeric material **3a** is the predominant product.[3] To obtain a deeper understanding for this substituent effect on the efficiency of ozonide formation, we have investigated ozonolyses of a series of 3-alkyl-substituted 1-methylindenes **1a**−**d** under several conditions. The results have been compared with those obtained from the ozonolyses of the stereoisomeric keto vinyl ethers, (*E*)-**16** and (*Z*)-**16**, which may proceed through a common carbonyl oxide intermediate **5c**.

Results and Discussion

Ozonolysis of 3-Alkyl-Substituted Indenes. Ozonolysis of 1,3-dimethylindene (**1a**) in ether gave mainly oligomeric product **3a** (92%),[4] together with ozonide **2a** (7%, exo/endo ratio = 7:3). Exactly the same trend was observed for the isopropyl-substituted indene **1b**. In the case of the phenyl-substituted indene **1c**, however, ozonide **2c** was the predominant product (66% yield; exo/endo ratio = 7:3). From the 3-*tert*-butyl-substituted one **1d** also, ozonide **2d** was obtained in a high yield of 75% (Scheme 1). These results imply that steric bulk of the alkyl substituent at C-3 plays an important role for the efficiency of the production of ozonide **2**, with the bulky substituent making the cycloaddition remarkably favorable.

In the cycloreversion of the primary ozonide (PO) **4**, two carbonyl oxide intermediates, **5** and **6**, are principally possible to be produced (Scheme 2). As a possible explanation for the observed substituent steric effect on the ozonide yield, we considered that the difference in steric bulk of the 3-alkyl substituent in **1** might affect the regiochemistry in cleavage of PO **4**, and moreover, the efficiency of the intramolecular cycloaddition is very different between the two carbonyl oxide intermediates **5** and **6**.

To understand the substituent effect on the direction of the cleavage of PO **4**, ozonolyses of indenes **1a**−**d** were conducted in the presence of trifluoroacetophenone. In this respect, we previously reported that this highly electron-deficient ketone can capture carbonyl oxides very efficiently.[5] When ozonolysis of 1,3-dimethylindene (**1a**) was undertaken in ether in the presence of 1 equiv of trifluoroacetophenone, aldehyde ozonide **7a** was obtained in 72% yield. This result demonstrates that cleavage of PO **4a** is quite selective, affording exclusively ketone

* Address correspondence to M.N. Tel. and Fax: +81-6-879-7928. E-mail: nojima@chem.eng.osaka-u.ac.jp.

(1) (a) Osaka University. (b) Heriot-Watt University.

(2) (a) Criegee, R. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 745. (b) Bailey, P. S. *Ozonation in Organic Chemistry*; Academic Press: New York, 1978; Vol. 1; 1982; Vol. 2. (c) Bunnelle, W. H. *Chem. Rev.* **1991**, *91*, 335. (d) Kuczkowski, R. L. *Advances in Oxygenated Processes*; Baumstark, A. L., Ed.; JAI Press: Greenwich, 1991; Vol. 3. (e) McCullough, K. J.; Nojima, M. In *Organic Peroxides*; Ando, W., Ed.; Wiley: New York, 1992.

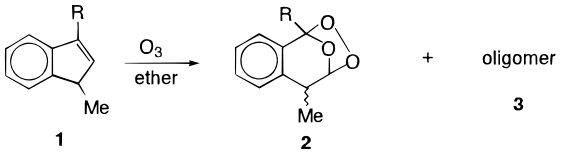
(3) Miura, M.; Ikegami, A.; Nojima, M.; Kusabayashi, S.; McCullough, K. J.; Nagase, S. *J. Am. Chem. Soc.* **1983**, *105*, 2414.

(4) Judging from the ^{1}H NMR (the chemical shifts and the ratio of the peak areas) and IR spectra (strong ozonide bands but only a weak aldehyde band), the oligomers **3a**,**b** seem to have a normal ozonide structure: (a) ref 2a; Vol. 1, pp 33−37. (b) Murray, R. W.; Su, J.-S. *J. Org. Chem.* **1983**, *48*, 817.

(5) (a) Fukagawa, R.; Nojima, M. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2449. (b) Yamakoshi, H.; Kawamura, S.; Nojima, M.; Mayr, H.; Baran, J. *J. Org. Chem.* **1996**, *61*, 5939.

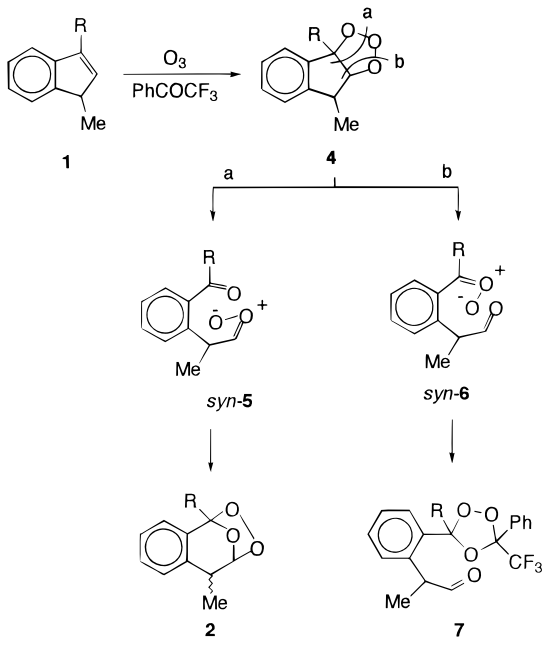
S0022-3263(98)00542-8 CCC: $15.00
Published on Web 07/23/1998

Scheme 1



R	2 % yield	2 *exo/endo* ratio	3 % yield
a; Me	7	7/3	92
b; *i*-Pr	18	4/1	80
c; Ph	66	7/3	–
d; *t*-Bu	75	4/1	–

Scheme 2

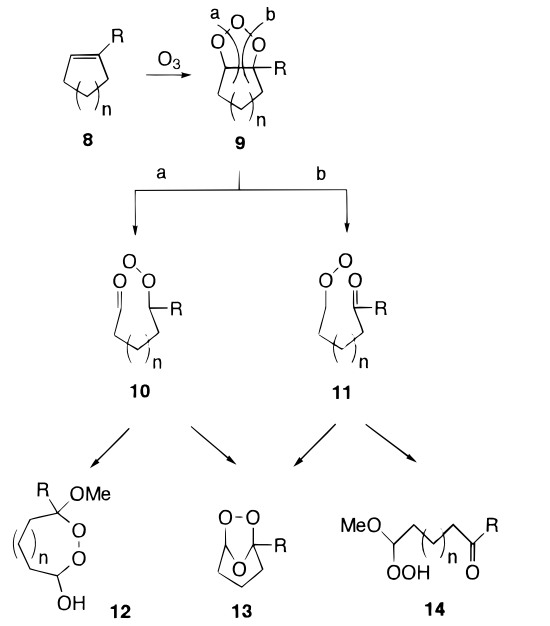


R	2 % yield	2 *exo/endo* ratio	7 % yield
a; Me	–		72
b; *i*-Pr	–		96
c; Ph	84	4/1	–
d; *t*-Bu	86	9/1	–

oxide **6a**. In the case of the indene **1b** also, aldehyde ozonide **7b** was the exclusive product. From the ozonolyses of the indenes **1c**,**d** under the same conditions, however, the expected trapping products **7c**,**d** were not obtained, and instead, ozonides **2c**,**d** were isolated almost quantitatively (Scheme 2). Thus, in the case of PO **4c**,**d**, the direction of the cleavage could not be determined by the trapping experiments. However, the following fact may suggest that steric bulk of an alkyl substituent attached directly to the C−C double bond exerts a significant influence on the regiochemistry in cleavage of PO, a bulky substituent tending to be incorporated into the carbonyl fragment.

Ozonolysis of 1-Alkyl-Substituted Cyclopentenes and Cyclohexene. As the model compounds of **1a**−**d**, we chose cyclopentenes **8a**−**c** and 1-*tert*-butylcyclohexene (**8d**) and conducted the reactions with ozone (Scheme 3). We considered that the structures of the methanol-derived ozonolysis products should provide a decisive information for the mode of cleavage of PO **9a**−**d**.[2]

Scheme 3



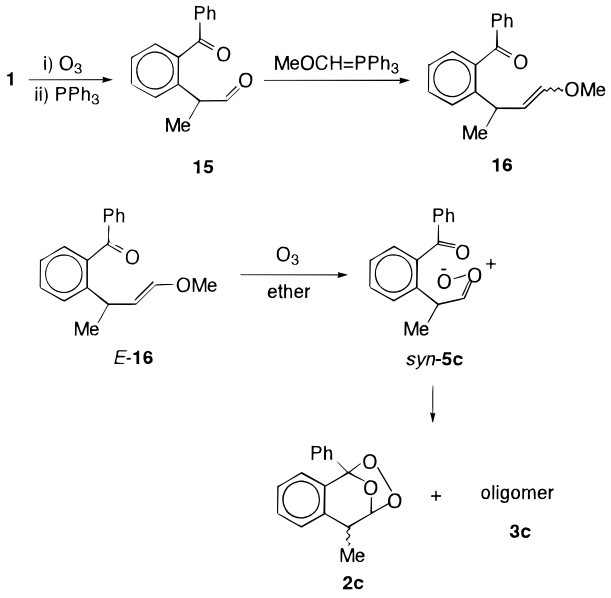
R	n	solvent	products (% yield)
a; Me	1	ether	**13a** (65)
b; Ph	1	ether	**13b** (76)
c; *t*-Bu	1	ether	**13c** (93)
a; Me	1	MeOH	**12a** (84), **14a** (4)[a]
b; Ph	1	MeOH	**12b** (25), **13b** (10), **14b** (35)
c; *t*-Bu	1	MeOH	**13c** (82), **14c** (10)
d; *t*-Bu	2	MeOH	**14d** (65)

[a] Griesbaum, K.; Kiesel, G. *Chem. Ber.* **1989**, *122*, 145

In ether, the cyclopentene derivatives **8a**−**c** gave in each case the corresponding ozonides **13a**−**c** in high yield. For the ozonolysis of **8a** in methanol, Griesbaum and Kiesel[6] conducted an elaborate analysis of the solvent-derived ozonolysis products and confirmed that the ratio of the contribution of ketone oxide **10a** and aldehyde oxide **11a** is 20:1. It should be noticed that this trend is very similar to the predominant formation of ketone oxide **6a** from PO **4a**. Ozonolysis of 1-phenylcyclopentene (**8b**) in methanol gave hemiperacetal **12b** (25%) and hydroperoxide **14b** (35%), together with the corresponding ozonide **13b** (10%), suggesting that aldehyde oxide **11b** is the major intermediate. From the ozonolysis of 1-*tert*-butylcyclopentene (**8c**) under the same conditions, ozonide **13c** was obtained in a high yield of 82%, together with hydroperoxide **14c** (10%). In the case of 1-*tert*-butylcyclohexene (**8d**), however, production of the corresponding ozonide was completely suppressed, and instead, only hydroperoxide **14d** was obtained in 65% yield. These results imply that the nature of the alkyl substituent at C-1 affects the regiochemistry of the cleavage of PO **9a**−**d** remarkably; in the case of the relatively small methyl substituent, the substituent electronic effect determines the direction, giving predominantly the more hindered ketone oxide **10a**,[7] while in the case of the phenyl- and *tert*-butyl-substituted ones,

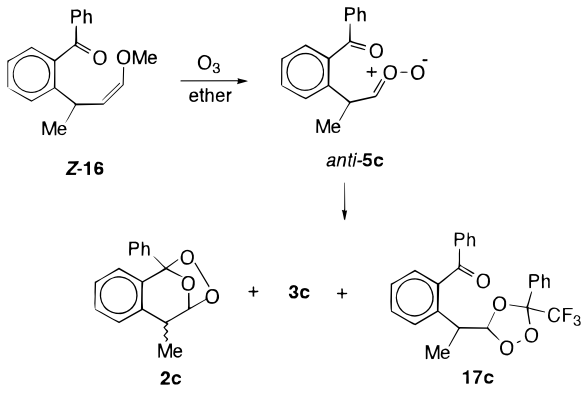
(6) Griesbaum, K.; Kiesel, G. *Chem. Ber.* **1989**, *122*, 145.
(7) Fliszar, S.; Belzecki, C.; Chylinska, J. B. *Can. J. Chem.* **1967**, *45*, 221.

Scheme 4



additive	2c % yield	2c *exo/endo* ratio	3c % yield
None	52	3/2	13
$PhCOCF_3$	90	7/3	–

Scheme 5



additive	2c % yield	2c *exo/endo* ratio	3c % yield	17c % yield
None	8	0/100	55	
$PhCOCF_3$			33	52
CF_3CH_2OH	77	7/3		

relief of strain in PO **9b**,**d** is important, thereby providing mainly the sterically less-congested aldehyde oxide **11b**−**e**.[8] It may be, therefore, reasonable to expect that in the case of bulky PO **4c**,**d** also, contribution of the less-hindered aldehyde oxides **5c**,**d** is important.[9]

Ozonolysis of the Stereoisomeric Keto Vinyl Ethers. An important question is the quantitative formation of ozonide **2c** from the ozonolysis of **1c** in the presence of trifluoroacetophenone. A possible explanation is that even in the presence of this efficient carbonyl oxide trapping agent, carbonyl oxide **5c**, if it has a proper geometry, may undergo intramolecular cycloaddition very rapidly. To generate the desired isomeric carbonyl oxides, *syn*- and *anti*-**5c**, selectively and independently, we considered that ozonolyses of the regioisomeric keto vinyl ethers, (*E*)- and (*Z*)-**16**, seem to be most promising, since Kuczkowski and co-workers[10] had elegantly demonstrated that in the ozonolyses of stereolabeled ethyl vinyl ethers the ethoxy substituent steers formation of the carbonyl oxide to the remote alkene position, with a geometry opposite to that of the precursor vinyl tether.

Vinyl ethers, (*E*)- and (*Z*)-**16**, were prepared as shown in Scheme 4. The isomers were separated by flash column chromatography on $AgNO_3$-treated silica gel.[11a] Ozonolysis of vinyl ether (*E*)-**16** was carried out in ether at −70 °C, and the crude product mixture was separated by column chromatography on silica gel. Thus, the corresponding ozonide **2c** was obtained in 52% yield (the exo/endo ratio = 3:2), together with a small amount of oligomeric material **3c** (Scheme 4). In the case of the isomeric vinyl ether (*Z*)-**16**, however, the oligomeric material **3c** (55%) was the major product (Scheme 5). A remarkable difference in behavior between (*E*)-**16** and (*Z*)-**16** was observed in the reaction in the presence of trifluoroacetophenone, too. From (*Z*)-**16**, only keto ozonide **17c**, derived from capture of carbonyl oxide **5c** by the additive, was obtained in 52% yield. In contrast, the reaction of (*E*)-**16** under the same conditions resulted in the quantitative formation of ozonide **2c**[12] (exo/endo ratio = 3:2) (Schemes 4 and 5).

These results would suggest that the intramolecular cyclization to form ozonide **2c** in ether can proceed for *syn*-**5c**. In contrast, the isomeric carbonyl oxide *anti*-**5c** cannot achieve a conformation for the concerted intramolecular cycloaddition and ultimately engages in the intermolecular reaction to form oligomeric material **3c**. Probably, for a concerted, intramolecular cycloaddition of a carbonyl oxide with an aldehyde or ketone, the possible transition-state geometries are limited by the length of the tether connecting the reactive groups. In the case of a carbonyl oxide such as **5** having a short tether, cyclization is possible only if the carbonyl oxide has the geometry syn with respect to the trapping group. It should be noticed that there are some precedents that support this rationalization.[11]

In this respect, it is worth noting that in the ozonolyses in both the presence and absence of trifluoroacetophenone vinyl ether (*E*)-**16** and 1-methyl-3-phenylindene (**1c**) give rise to high yields of ozonide **2c** with similar exo/endo ratios. This leads us to deduce that ozonolysis of indene **1c** also proceeds by carbonyl oxide *syn*-**5c**. The most

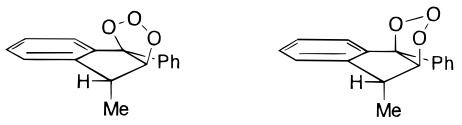
(8) (a) Criegee, R. *Chem. Ber.* **1975**, *108*, 743. (b) Griesbaum, K.; Volpp, W. *Chem. Ber.* **1988**, *121*, 1795. (c) Mayr, H.; Baran, J.; Will, E.; Yamakoshi, H.; Teshima, K.; Nojima, M. *J. Org. Chem.* **1994**, *59*, 5055.

(9) Nojima, T.; Ishiguro, K.; Sawaki, Y. *J. Org. Chem.* **1997**, *62*, 6911.

(10) (a) Keul, H.; Kuczkowski, R. L. *J. Org. Chem.* **1985**, *50*, 3371. (b) Wojciechowski, B. J.; Pearson, W. H.; Kuczkowski, R. L. *J. Org. Chem.* **1989**, *54*, 115.

(11) Ozonolyses of the regioisomers of keto vinyl ethers; (a) Bunnelle, W. H.; Lee, S.-G. *Tetrahedron Lett.* **1994**, *35*, 8141. (b) McCullough, K. J.; Nakamura, N.; T. Fujisaka, T.; Nojima, M.; Kusabayashi, S. *J. Am. Chem. Soc.* **1991**, *113*, 1786. Ozonolysis of tethered cycloalkenes: Bunnelle, W. H.; Lee, S.-G. *J. Am. Chem. Soc.* **1992**, *114*, 7577.

(12) The increased formation of ozonide **2c** in the reaction in the presence of trifluoroacetophenone (90%) as compared with the reaction in the absence of the additive (52%) would be interpreted as that this polar additive would stabilize the carbonyl oxide moiety by coordination, thereby suppressing the oligomerization quite significantly. A similar assistance by a polar nitrone in ozonide formation has been observed for the ozonolysis of acenaphthylene: Satake, S.; Ushigoe, Y.; Nojima, M.; McCullough, K. J. *J. Chem. Soc., Chem. Commun.* **1995**, 1469.



endo-**4c**; 47.86 *exo*-**4c**; 49.23

Figure 1. Heat of formation of primary ozonides **4c** (kcal/mol).

stable structure of PO **4c** determined by semiempirical calculations[13,14] seems to support this. As shown in Figure 1, the lowest-energy conformation for PO **4c** has the 1,2,3-trioxolane ring in an endo-folded envelop. A least-motion fragmentation from *endo*-**4c** would lead to the syn-oriented carbonyl oxide *syn*-**5c**.[15]

Although it seems to be difficult extended *anti*-carbonyl oxide *anti*-**5c** to undergo intramolecular cycloaddition in ether (8% yield), ozonolysis of *Z*-**16c** in trifluoroethanol gives ozonide **2c** in a high yield of 77% (exo/endo = 3:2) (Scheme 5). This may suggest that ozonide formation occurs efficiently, if we choose reaction conditions in which stepwise intramolecular cyclization can overcome intermolecular oligomerization.[16] In this protic solvent with a poor nucleophilicity, solvation of the carbonyl oxide moiety should enhance the electrophilicity of carbon atom C-1 in **5c**, facilitating its partial capture by the oxygen atom of the adjacent carbonyl group to give the pivotal cyclic intermediate **18** (Scheme 6). Subsequent cyclization yields ozonide **2c**.

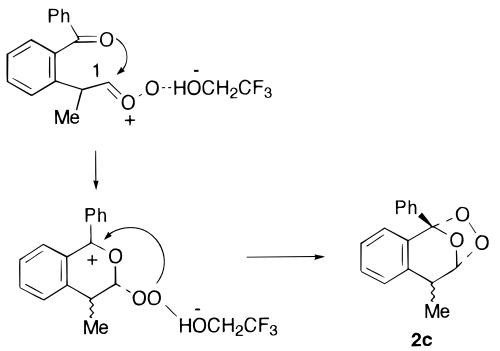
Conclusion

We have conducted ozonolyses of 3-alkyl-substituted 1-methylindenes **1a**−**d** and of the relevant keto vinyl ethers, (*E*)- and (*Z*)-**16**, under several conditions. The results thus obtained imply that (i) formation of ozonide **2** from **1** in ether is remarkably influenced by the steric bulk of the 3-alkyl-substituent, the yield increasing with the increase in steric bulk of the substituent at C-3, (ii) the origin would be the substituent-dependent regioselectivity in cleavage of PO **4**, and (iii) stereochemistry of carbonyl oxide **5** is also important, formation of ozonide **2** in aprotic solvent occurring very easily, if carbonyl oxide **5** has the geometry syn with respect to the trapping group.

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ with $SiMe_4$ as standard. Indenes **1a**−**d**[3] and cycloalkenes **8a**−**d**[17] were prepared by the reported methods. 1-Methyl-3-isopropylindene (**1b**): bp 110 °C (3 mmHg); ^{1}H NMR δ 1.25 (d, J = 7.6 Hz, 3 H), 1.27 (d, J = 6.9 Hz, 6 H), 2.8−2.9 (m, 1 H), 3.40 (q, J = 7.6 Hz, 1 H), 6.10 (s, 1 H), 7.2−7.4 (m, 4 H); ^{13}C NMR δ 16.37, 21.52, 26.74, 43.36, 119.37, 122.64, 124.37, 126.08, 132.58, 144.12, 149.15, 150.26. Anal. Calcd for $C_{13}H_{16}$: C, 90.64; H, 9.36. Found: C, 90.36; H, 9.45. 1-Methyl-3-*tert*-butylindene (**1d**): bp 110 °C (0.1 mmHg); ^{1}H NMR δ 1.27 (d, J = 7.6 Hz, 3 H), 1.36 (s, 9 H), 3.36 (q, J = 5.6 Hz, 1 H), 6.10 (s, 1 H), 7.2−7.6 (m, 4 H); ^{13}C NMR δ 16.46, 29.42, 32.87, 42.75, 122.14, 122.82, 124.10, 125.71, 133.30, 143.13, 151.12, 151.39. Anal. Calcd for $C_{14}H_{18}$: C, 90.32; H, 9.68. Found: C, 89.90; H, 9.80. The method of ozonolysis[11b] and the physical properties of ozonides **2a**,**c**[3] and of keto aldehyde **15c**[3] were previously described.

Scheme 6



Caution: Since organic ozonides and peroxides 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 or peroxides synthesized in this work using the reaction scales and procedures described below together with the safegard mentioned above.

Preparation of Vinyl Ethers. The preparation of vinyl ethers (*E*)- and (*Z*)-**16** is representative. A solution of phenyllithium (prepared from 2.9 g of bromobenzene and 268 mg of lithium) and methoxymethyltriphenylphosphonium chloride (5.8 g) in ether (70 mL) was stirred at room temperature for 3 min. Then, an ether solution of keto aldehyde **15c** (4.0 g, 16.8 mmol) was added dropwise to it, and the mixture was stirred at 30 °C for 15 h. The solution was diluted with ice-cold water and ether, and the separated organic layer was washed with saturated brine, dried ($MgSO_4$), and concentrated. Column chromatography on silica gel of the residue gave a mixture of (*E*)- and (*Z*)-**16** (1.5 g, 43%). The mixture was separated by flash column chromatography on $AgNO_3$-treated silica gel. Elution with hexanes−ethyl acetate (98:2) gave (*E*)-**16** (479 mg, 11%). Subsequent elution with hexanes−ethyl acetate (97:3) gave (*Z*)-**16** (561 mg, 13%).

(*E*)-[2-(1-Methyl-3-methoxy-2-propenyl)phenyl]phenylmethanone (***E*)-16:** oil; ^{1}H NMR δ 1.29 (d, J = 7.0 Hz, 3 H), 3.37 (s, 3 H), 3.6−3.8 (m, 1 H), 4.84 (dd, J = 13.0 and 8.0 Hz, 1 H), 6.13 (d, J = 13.0 Hz, 1 H), 7.2−7.9 (m, 9 H); ^{13}C NMR δ 22.64, 34.34, 55.67, 107.67, 125.19, 127.01, 127.69, 128.32, 130.08, 130.15, 133.24, 137.63, 138.10, 145.57, 147.17, 198.85; IR 2980, 1670, 1600, 1460, 930, 700 cm^{-1}. Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.58; H, 6.69.

Keto vinyl ether (*Z*)-16: oil; ^{1}H NMR δ 1.29 (d, J = 7.0 Hz, 3 H), 3.26 (s, 3 H), 4.0−4.1 (m, 1 H), 4.49 (dd, J = 8.0 and 6.0 Hz, 1 H), 5.67 (d, J = 6.0 Hz, 1 H), 7.2−7.9 (m, 9 H); ^{13}C NMR δ 22.63, 31.05, 59.00, 111.34, 124.92, 126.79, 127.46, 128.03, 129.94, 130.15, 132.88, 137.68, 138.40, 145.19, 147.75, 198.72; IR 2980, 1680, 1610, 1460, 1010, 940, 720 cm^{-1}. Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.42; H, 6.66.

Ozonolysis of 3-Alkyl-Substituted 1-Methylindenes 1a−d in Ether. The reaction of indene **1b** is representative. Over a solution of 1-methyl-3-isopropylindene **1b** (345 mg, 2.0 mmol) in ether (20 mL) was passed a slow stream of ozone (1.5 equiv) at −70 °C. After evaporation of the solvent, the crude products were separated by column chromatography on silica gel. Elution with ether−hexane (1:9, v/v) gave ozonide **2b**. Subsequent elution with ether−hexane (1:1, v/v) gave oligoozonide **3b**: viscous oil; ^{1}H NMR δ 0.6−1.8 (br s), 2.8−3.4 (br s), 5.0−6.0 (br s), 7.0−7.7 (br s), the ratio of the peak areas being 9:2:1:4; IR 1730 (weak), 1140, 1060, 980 cm^{-1};

(13) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209, 221.
(14) Toyoda, J. *JCPE News Lett.* **1990**, *2*, 37.
(15) (a) Bailey, P. S.; Ferrell, T. M. *J. Am. Chem. Soc.* **1978**, *100*, 899. (b) Lattimer, R. P.; Kuczkowski, R. L.; Gillies, C. L. *J. Am. Chem. Soc.* **1974**, *96*, 348. (d) Cremer, D. *J. Am. Chem. Soc.* **1981**, *103*, 3619.
(16) (a) Sugimoto, T.; Nojima, M.; Kusabayashi, S. *J. Org. Chem.* **1990**, *55*, 3816. (b) Nakamura, N.; Fujisaka, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1989**, *111*, 1799.
(17) (a) Starkis, M.; Orfanopouplos, M. *Synth. Commun.* **1993**, *23*, 425. (b) Fadel, A.; Salaun, J. *Tetrahedron* **1985**, *41*, 1267. (c) Herbert, C. B.; Cary, J. L. *J. Org. Chem.* **1979**, *44*, 1913.

molecular weight (vapor-pressure osmometry; CH_2Cl_2) 684.98. Anal. Calcd for $(C_{13}H_{16}O_3)_n$: C, 70.89; H, 7.32. Found: C, 69.82; H, 6.87. Treatment of either **2b** or **3b** with 1 equiv of triphenylphosphine in benzene gave the corresponding keto aldehyde **15b** quantitatively.

***exo*-1-Isopropyl-5-methyl-4,5-dihydro-1,4-epoxy-1*H*-2,3-benzodioxepin (1-methyl-3-isopropylindene ozonide, *exo*-2b)**: mp 78−79 °C (from methanol); ^{1}H NMR δ 1.15 (d, J = 6.9 Hz, 3 H), 1.22 (d, J = 6.6 Hz, 3 H), 1.35 (d, J = 7.3 Hz, 3 H), 2.8−2.9 (m, 1 H), 2.96 (q, J = 7.3 Hz, 1 H), 5.78 (s, 1 H), 7.2−7.3 (m, 4 H); ^{13}C NMR δ 15.17, 18.28, 19.07, 26.97, 39.19, 105.23, 107.87, 123.34, 126.38, 128.86, 129.00, 133.68, 137.18. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.28; H, 7.52.

***endo*-2b** (in admixture with 60% of *exo*-**2b**; characteristic signals in NMR spectra are shown): oil; ^{1}H NMR δ 1.13 (d, J = 6.9 Hz, 3 H), 1.21 (d, J = 6.6 Hz, 3 H), 1.35 (d, J = 7.3 Hz, 3 H), 2.8−2.9 (m, 1 H), 3.34 (qd, J = 7.3, 2.0 Hz, 1 H), 5.77 (d, J = 2.0 Hz 1 H), 7.2−7.4 (m, 4 H); ^{13}C NMR δ 14.74, 15.22, 19.01, 27.32, 38.17, 104.22, 108.19.

***exo*-1-*tert*-Butyl-5-methyl-4,5-Dihydro-1,4-epoxy-1*H*-2,3-benzodioxepin (*exo*-2d)**: mp 119−120 °C; ^{1}H NMR δ 1.19 (d, J = 7.3 Hz, 3 H), 1.27 (s, 9 H), 2.83 (q, J = 7.3 Hz, 1 H), 5.64 (s, 1 H), 7.0−7.2 (m, 3 H), 7.58 (d, J = 7.9 Hz, 1 H); ^{13}C NMR δ 18.60, 27.14, 36.50, 39.23, 105.82, 108.84, 124.76, 125.55, 128.45, 129.31, 134.32, 138.13. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.81; H, 7.86.

***endo*-2d** (in admixture with 60% of *exo*-**2d**): oil; ^{1}H NMR δ 1.23 (d, J = 7.3 Hz, 3 H), 1.27 (s, 9 H), 3.22 (qd, J = 7.3 and 1.0 Hz, 1 H), 5.66 (d, J = 1.0 Hz, 1 H), 7.0−7.6 (m, 4 H); ^{13}C NMR (only characteristic signals are shown) δ 15.10, 26.96, 36.79, 38.26, 104.28, 109.15.

Oligomer 3a: viscous oil; ^{1}H NMR δ 1.0−2.0 (br s), 2.8−3.1 (br s), 5.3−5.7 (br s), 6.9−7.8 (br s), the ratio of the peak areas being 6:1:1:4; IR 1720 (weak), 1120, 1180, 960 cm^{-1}; molecular weight (vapor-pressure osmometry; CH_2Cl_2) 828.55. Anal. Calcd for $(C_{11}H_{12}O_3)_n$: C, 68.74; H, 6.29. Found: C, 67.16; H, 6.58.

Ozonolysis of Indenes 1a−d in Ether in the Presence of Trifluoroacetophenone. Ozonolysis of **1a** is representative. Over a solution of indene **1a** (298 mg, 2.07 mmol) and trifluoroacetophenone (358 mg, 2.06 mmol) in ether (20 mL) was passed a slow stream of ozone (1.5 equiv) at −70 °C. Then, the reaction mixture was poured into ice-cold aqueous $NaHCO_3$ and was extracted with ether. After the mixture was dried and concentrated, the products were separated by column chromatography on silica gel (column, 2 × 50 cm; 20 g of silica gel). Elution with ether−hexane (7:93, v/v) gave **7a** (619 mg, 82%).

1-[2-[1-Methyl-4-phenyl-4-(trifluoromethyl)-2,3,5-trioxanyl]phenyl]propionaldehyde (7a): oil (a mixture of two isomers); ^{1}H NMR δ 1.42 (d, J = 6.6 Hz) + 1.48 (d, J = 6.9 Hz) (3 H), 1.74 (s) + 1.75 (s) (3 H), 4.2−4.4 (m, 1 H), 7.0−7.8 (m, 9 H), 9.72 (s) + 9.74 (s) (1 H); ^{13}C NMR δ 15.47, 16.21, 26.49, 26.70, 49.11, 49.38, 103.76 (q, J = 34 Hz), 104.26 (q, J = 34 Hz, 1 H), 112.65, 113.05, 119.07 (q, J = 284 Hz), 123.07 (q, J = 288 Hz), 200.57, 200.68. Anal. Calcd for $C_{19}H_{17}F_3O_4$: C, 62.30; H, 4.68. Found: C, 62.50; H,4.76.

Aldehyde ozonide 7b: oil (a mixture of two isomers); ^{1}H NMR δ 0.78 (d, J = 6.9 Hz) + 0.79 (d, J = 6.9 Hz) + 0.84 (d, J = 6.9 Hz) (6 H), 1.45 (d, J = 6.6 Hz) + 1.48 (d, J = 6.6 Hz) (3 H), 2.2−2.4 (m, 1 H), 4.2−4.4 (m, 1 H), 7.1−7.7 (m, 4 H), 9.73 (s, 1 H); ^{13}C NMR δ 15.20, 15.44, 16.39, 17.00, 17.11, 17.20, 36.19, 36.61, 49.22, 49.29, 104.33 (q, J = 30 Hz), 105.23 (q, J = 30 Hz), 117.16, 117.23, 121.06 (q, J = 288 z), 121.13 (J = 288 Hz), 126.61, 126.85, 127.96, 128.30, 129.18, 129.27, 129.38, 130.26, 132.20, 135.76, 136.59, 136.69, 200.97. Anal. Calcd for $C_{21}H_{21}F_3O_4$: C, 63.96; H, 5.37. Found: C, 63.97; H, 5.37.

Ozonolysis of 1-Alkyl-Substituted Cyclopentenes 8a−d in MeOH-Ether. Ozonolysis of **8b** is representative. Over a solution of 1-phenylcyclopentene (**8b**) (288 mg, 2.00 mmol) in MeOH-ether (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−hexane 7:93) to give phenylcyclopentene ozonide (**13b**):[18] oil; ^{1}H NMR δ 1.8−2.4 (m, 6 H), 6.0 (s, 1 H), 7.3−7.6 (m, 5 H); ^{13}C NMR δ 15.92, 28.84, 32.94, 103.50, 107.80, 125.64, 128.19, 129.25, 135.72. Subsequent elution with ether−hexane (7:3) gave hemiperacetal **12b** (116 mg, 25%). Elution with ether−hexane (1:1) gave hydroperoxide **14b** (155 mg, 35%).

3-Methoxy-3-phenyl-7-hydroxy-1,2-dioxepane (12b): oil, a mixture of two isomers; ^{1}H NMR δ 1.5−2.4 (m, 6 H), 3.14 (s, 1.8 H) + 3.20 (s, 1.2 H), 3.70 (d, J = 5.0 Hz, 0.4 H, H−D exchange in D_2O) + 4.03 (d, J = 5.6 Hz, 0.6 H, H−D exchange in D_2O), 5.46 (q, J = 5.6 Hz, 0.6 H, triplet in D_2O), 5.58 (ddd, J = 3.0, 5.0, 6.3 Hz, 0.4 H, d × d in D_2O), 7.3−7.5 (m, 5 H); ^{13}C NMR δ 17.15, 17.18, 36.50, 36.88, 40.47, 42.21, 49.94, 50.46, 101.19, 103.30, 108.41, 109.24, 125.86, 126.54, 128.23, 128.36, 138.51, 139.55. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.37; H, 7.48.

5-Hydroxy-5-methoxyvalerophenone (14b): oil; ^{1}H NMR δ 1.7−1.9 (m, 4 H), 3.02 (t, J = 6.9 Hz, 2 H), 3.52 (s, 3 H), 4.79 (t, J = 5.3 Hz, 1 H), 7.4−8.0 (m, 5 H), 9.64 (br s, 1 H); ^{13}C NMR δ 19.01, 30.64, 37.77, 55.85, 108.86, 125.86, 126.49, 128.03, 133.12, 136.75, 200.27. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.03; H, 7.23.

1-*tert*-Butylcyclopentene ozonide (13c): oil; ^{1}H NMR δ 1.03 (s, 9 H), 1.7−2.3 (m, 6 H), 5.76 (s, 1 H); ^{13}C NMR δ 16.09, 25.12, 27.12, 29.42, 36.19, 103.15, 112.35. Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.72; H, 9.15.

***tert*-Butyl 4-hydroperoxy-4-methoxybutyl ketone (14c):** oil; ^{1}H NMR δ 1.14 (s, 9 H), 1.6−1.7 (m, 4 H), 2.5−2.6 (m, 2 H), 3.50 (s, 3 H), 4.72 (t, J = 4.9 Hz, 1 H), 8.81 (s,1 H); ^{13}C NMR δ 18.60, 26.38, 30.59, 35.74, 44.08, 55.80, 108.23, 216.37. Anal. Calcd for $C_{10}H_{20}O_4$: C, 58.80; H, 9.87. Found: C, 59.01; H, 9.66.

***tert*-Butyl 5-hydroperoxy-5-methoxypentyl ketone (14d):** oil; ^{1}H NMR δ 1.13 (s, 9 H), 1.3−1.8 (m, 6 H), 2.51 (t, J = 7.3 Hz, 2 H), 3.51 (s, 3 H), 4.74 (t, J = 2.6 Hz, 1 H), 9.25 (br s, 1 H); ^{13}C NMR δ 23.43, 24.15, 26.29, 31.13, 36.12, 44.05, 55.83, 108.43, 216.40. Anal. Calcd for $C_{11}H_{22}O_4$: C, 60.81; H, 9.74. Found: C, 61.03; H, 9.87.

Ozonolysis of Vinyl Ether (*E*)-16 in Ether. Over a solution of (*E*)-**16** (105 mg, 0.39 mmol) in ether (15 mL) was passed a slow stream of ozone (1 equiv) at −70 °C. After evaporation of the solvent, the crude products were separated by column chromatography on silica gel. Elution with ether−hexane (1:20, v/v) gave a 3:2 mixture of *exo*- and *endo*-ozonide **2c** (52 mg, 52%). The exo/endo ratio was determined by comparing the peak areas of the two characteristic methine signals, δ 3.14 (q, J = 7.3 Hz) and δ 3.53 (qd, J = 4.9, 2.3 Hz), in the ^{1}H NMR spectrum. Subsequent elution with ether−hexane (1:1, v/v) gave oligoozonide **3c** (13 mg, 13%).

Oligomer 3c: viscous oil; ^{1}H NMR δ 1.2−1.4 (br s), 3.0−3.6 (br s), 5.3−5.7 (br s), 6.9−7.8 (br s), the ratio of the peak areas being 3:1:1:9; IR 3400, 2940, 2870, 1750, 1670, 1460, 1270, 1080, 1030, 760, 710 cm^{-1}; molecular weight (vapor-pressure osmometry; CH_2Cl_2) 531.19. Anal. Calcd for $(C_{16}H_{14}O_3)_n$: C, 74.58; H, 5.55. Found: C, 74.68; H, 6.02.

Ozonolysis of Vinyl Ether (*E*)-16 in Ether in the Presence of Trifluoroacetophenone. Over a solution of (*E*)-**16** (13 mg, 0.052 mmol) and trifluoroacetophenone (8.9 mg, 0.052 mmol) in ether (20 mL) was passed a slow stream of ozone (1.5 equiv) at −70 °C. After workup as above, the products were separated by column chromatography on silica gel. Elution with ether−hexane (1:20,v/v) gave ozonide **2c** (12 mg, 90%; exo/endo ratio = 7:3).

Ozonolysis of Vinyl Ether (*Z*)-16 in Ether. Over a solution of (*Z*)-**16** (157 mg, 0.59 mol) in ether (15 mL) was passed a slow stream of ozone (1 equiv) at −70 °C. After evaporation of the solvent, the crude products were separated by column chromatography on silica gel. Elution with ether−hexane (1:20, v/v) gave ozonide *endo*-**2c** (12 mg, 8%). Subse-

(18) Castonguay, J.; Bertrand, M.; Carles, J.; Fliszar, S.; Rousseau, Y. *Can. J. Chem.* **1969**, *47*, 919.

quent elution with ether−hexane (1:1, v/v) gave oligoozonide **3c** (82 mg, 55%).

Ozonolysis of Vinyl Ether (*Z*)-16 in Ether in the Presence of Trifluoroacetophenone. To a solution of (*Z*)-**16** (90 mg, 0.36 mmol) and trifluoroacetophenone (63 mg, 0.36 mmol) in ether (20 mL) was passed a slow stream of ozone (1.5 equiv) at −70 °C. After workup as above, the products were separated by column chromatography on silica gel. Elution with ether−hexane (1:9, v/v) gave keto ozonide **17c** (80 mg, 52%). Treatment of **17c** with 1 equiv of triphenylphosphine in benzene gave a mixture of keto aldehyde **15c** and trifluoroacetophenone quantitatively.

2-[1-[4-Phenyl-4-(trifluoromethyl)-2,3,5-trioxanyl]ethyl]benzophenone (17c): oil (a mixture of four isomers); ^{1}H NMR δ 1.26 (d, J = 7.3 Hz) + 1.27 (d, J = 7.3 Hz) + 1.43 (d, J = 6.9 Hz), 1.45 (d, J = 5.9 Hz) (3 H), 3.3−3.4 (m) + 3.6−3.7 (m) + 3.7−3.8 (m) + 4.0−4.1 (m) (1 H), 5.38 (d, J = 4.9 Hz) + 5.41 (d, J = 4.6 Hz) + 5.73 (d, J = 5.0 Hz) + 5.76 (d, J = 5.6 Hz) (1 H), 5.97 (s) + 5.98 (s) (1 H), 7.2−8.2 (m, 14 H); ^{13}C NMR (only characteristic signals are shown) δ 14.07, 15.40, 15.76, 15.92, 35.44, 35.76, 36.89, 37.09, 107.48, 107.53, 108.91, 109.04, 117.76 (J = 288 Hz), 117.74 (J = 288 Hz), 117.85 (J = 288 Hz), 120.17 (J = 288 Hz), 197.84, 198.06, 198.09, 198.15; IR 1670 cm^{-1}. Anal. Calcd for $C_{24}H_{19}F_3O_4$: C, 67.29 H, 4.47. Found: C, 67.53; H, 4.35.

Ozonolysis of Vinyl Ether (*Z*)−16 in CF_3CH_2OH−Ether. A solution of (*Z*)-**16** (78 mg, 0.308 mmol) in CF_3CH_2-OH-ether (20 mL, 1:2, v/v) was treated with 1.5 equiv of ozone at 0 °C. After workup as above, the crude products were separated by column chromatography on silica gel. The first fraction (elution with ether−hexane 1:15) contained ozonide **2c** (60 mg, 76%; exo/endo ratio = 3:2).

Theoretical Calculations. The theoretical studies were performed by PM3 molecular orbital method.[9] The MOPAC program (QCPE No. 455), which was revised as OS/2 Version 5.01 to adapt for the use of a NECPC computer, was obtained through the Japan Chemistry Program Exchange (JCPE).[10] Final geometries and energetics were obtained by optimizing the total molecular energy with respect to all structural variables.

Acknowledgment. This work was supported in part by a Grant-in Aid for Scientific Research on Priority Areas (10153238 and 10166211) from the Ministry of Education, Science, Culture and Sports of Japan. We thank British Council (Tokyo) for the award of travel grants to M.N. and K.J.Mc.

JO980542N