J. Org. Chem. **1996,** *61,* 5939−5943

Ozonolysis of Highly Methylated 1,2-Bis(methylene)cycloalkanes. Influence of the Methyl Substituents on the Course of the Reaction

Hideyuki Yamakoshi,[†] Shin-ichi Kawamura,[†] Masatomo Nojima,*[,†] Herbert Mayr,*[,‡] and Janusz Baran[‡,§]

Department of Material Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan, and Institut fur Organische Chemie, Technische Hochschule Darmstadt, 64287 Darmstadt, Germany

Received February 27, 1996[⊗]

In the ozonolyses of highly methylated 3,3,4,4,5,5-hexamethyl-1,2-bis(methylene)cyclopentane (**1a**) and 3,3,6,6-tetramethyl-1,2-bis(methylene)cyclohexane (**1b**), the epoxidation competed with the cleavage of the C−C double bond, whereas only the latter process was observed in the case of the nonmethylated 1,2-bis(methylene)cycloalkanes **1c**,**d**. Competition experiments revealed that the reactivity of the highly methylated 1,2-bis(methylene)cycloalkanes **1a**,**b** is significantly smaller than that of the nonmethylated ones (**1c**,**d**), suggesting that the formation of the primary ozonides **2c**,**d** occurs by a concerted 1,3-dipolar cycloaddition process.

3,3,4,4,5,5-Hexamethyl-1,2-bis(methylene)cyclopentane (**1a**) incorporates a planar *s-cis*-fixed 1,3-diene system in which the nonterminal positions are sterically shielded. As a consequence, compound **1a** has been found to show a relatively great tendency to undergo 1,4-additions instead of 1,2-additions with dihalocarbenes, diphenylketene, (1,3-diphenylazaallyl)lithium, and *C,N*-diphenylnitrone.[1] We considered that the reaction of the diene **1a** with ozone would provide further insight into the mechanism of the ozonization reaction, e.g., the competition between cleavage of the C−C double bond vs epoxidation,[2] the concertedness of the 1,3-dipolar cycloaddition yielding the primary ozonide, and the direction of cleavage of the primary ozonide.[3] For this purpose, ozonolyses of the diene **1a** were conducted under several conditions, and the results were compared with those of 3,3,6,6-tetramethyl-1,2-bis(methylene)cyclohexane (**1b**) and the nonmethylated 1,2-bis(methylene)cycloalkanes **1c**,**d**.

Results and Discussion

Reaction Products. The reaction of diene **1a** with 2.5 equiv of ozone in ether led to the formation of epoxy ketone **8a** (42%) and normal ozonide **10a** (16%) (Scheme 1 and Table 1). From the reaction with 1 equiv of ozone, ozonide **10a**, vinyl epoxide **3a**, and epoxy ketone **8a** were obtained in yields of 20%, 20%, and 16%, respectively. Vinyl epoxide **3a** was labile, and during column chromatography on silica gel, it sometimes rearranged to vinyl aldehyde **12a** (Scheme 2). Pure vinyl epoxide **3a** was prepared by the reaction of diene **1a** with 3,3-dimethyl-1,2-dioxirane,[4] followed by distillation under reduced pressure (Scheme 2). Treatment of **3a** with ozone gave epoxy ketone **8a**, which was reduced by lithium aluminum hydride to give diol **13a** as a 9:1 mixture of two diastereoisomers. In contrast to the high reactivity of vinyl epoxide **3a** toward ozone, vinyl ozonide **10a** did not react with this reactive 1,3-dipole.

Scheme 1

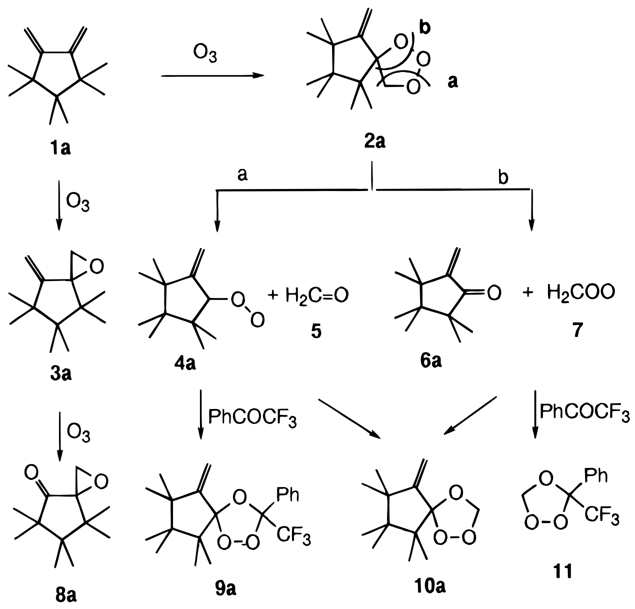


Table 1. Ozonolysis of 1,2-Bis(methylene)cycloalkanes 1a−e[a]

substr	solvent	additive[c]	products (% yield)
1a[b]	ether		**3a** (20), **8a** (16), **10a** (20)
1a	ether		**8a** (42), **10a** (16)
1a	MeOH-ether (1:2)		**8a** (24), **12a** (15)
1a	ether	$PhCOCF_3$	**8a** (42), **9a** (11), **11** (23)
1b	ether		**3b** (19), **10b** (33)
1b	MeOH−ether (1:2)		**3b** (26), **14b** (53)
1b	ether	$PhCOCF_3$	**3b** (41), **9b** (45), **11** (11)
1c	ether		**10c** (13)[d]
1c	ether	$PhCOCF_3$	**9c** (71)
1d	ether		**10d** (14)[d]
1d	ether	$PhCOCF_3$	**9d** (86)
1e	ether	$PhCOCF_3$	**9e** (71)

[a] Unless otherwise noted, substrate **1** was treated with 2.5 equiv of ozone at −70 °C. [b] Reaction with 1 equiv of ozone. [c] Reaction in the presence of 1 equiv of trifluoroacetophenone. [d] The ^{1}H NMR spectrum of the crude reaction mixture showed that the ozonide was produced almost quantitatively. However, during isolation by column chromatography on silica gel, it decomposed significantly.

[†] Osaka University.

[‡] Technische Hochschule Darmstadt.

[§] Present address: Institute of Fundamental Chemistry, Technical University of Szczecin, Al. Piastow 42, PL-71065, Szczecin, Poland.

[⊗] Abstract published in *Advance ACS Abstracts,* July 1, 1996.

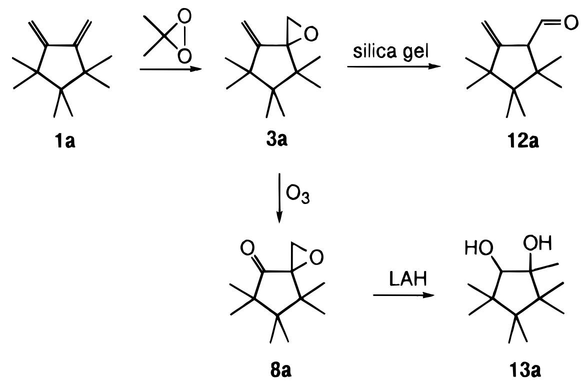
(1) Mayr, H.; Baran, J.; Heigl, U. W. *Gazz. Chim. Ital.* **1991**, *121*, 373.

(2) Bailey, P. S.; Hwang, H. H.; Chiang, C. -Y. *J. Org. Chem.* **1985**, *50*, 231.

(3) (a) Mayr, H.; Baran, J.; Will, E.; Yamakoshi, H.; Teshima, K.; Nojima, M. *J. Org. Chem.* **1994**, *59*, 5055. (b) Criegee, R. *Chem. Ber.* **1975**, *108*, 743. (c) Griesbaum, K.; Volpp, W. *Chem. Ber.* **1988**, *121*, 1795. (d) Teshima, K.; Kawamura, S.; Ushigoe, Y.; Nojima, M.; McCullough, K. J. *J. Org. Chem.* **1995**, *60*, 4755.

S0022-3263(96)00397-0 CCC: $12.00

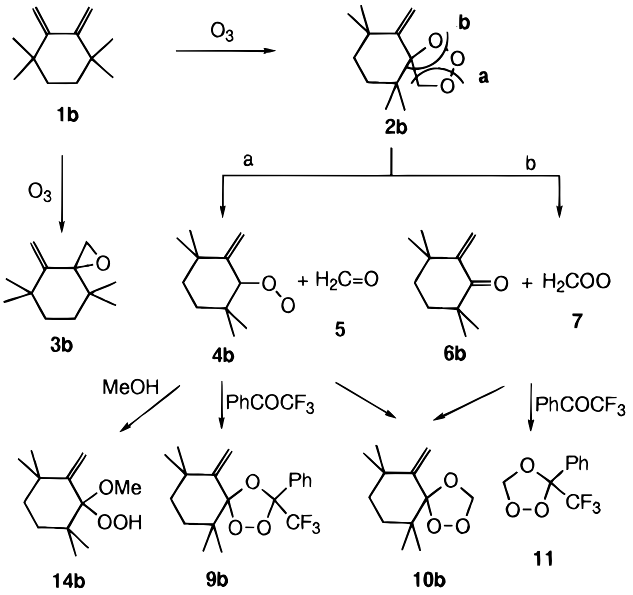
Scheme 2



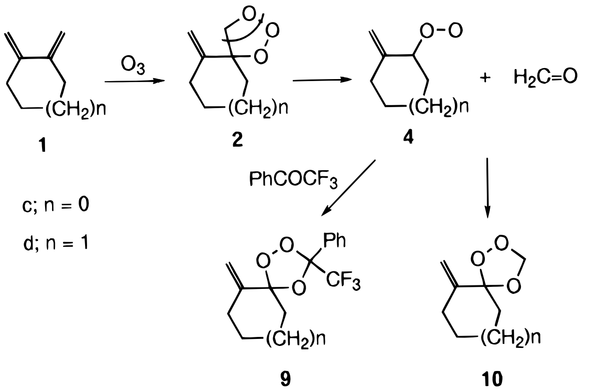
The structures of the products imply that two alternative pathways participate in the ozonization of diene **1a**: the cleavage process leading to the formation of normal ozonide **10a** and the epoxidation leading to the formation of vinyl epoxide **3a** and products **8a** and **12a** derived from it.[5] Cleavage of the double bond in **1a** proceeds *via* primary ozonide **2a** (Scheme 1). To confirm the direction of cleavage of **2a**, we first studied the reaction of diene **1a** in MeOH–ether. However, only **12a** and **8a**, derived from epoxidation, were isolated (Scheme 2). In order to capture the expected carbonyl oxides, **4a** and **7**, derived from the cycloreversion of **2a**, we conducted the reaction in ether in the presence of trifluoroacetophenone.[6] Together with epoxy ketone **8a** (42% yield), two cross-ozonides, **9a** and **11**, were obtained in yields of 11% and 23%, respectively. Though a part of the material could not be detected, the product composition **8a**/(**9a** + **11**) indicates that epoxidation and cleavage occur to a similar extent. The ratio of **9a**/**11** led us to deduce that both of the possible modes of cleavage of **2a** (paths a and b in Scheme 1) participate, the ratio being around 1:2. In other words, the formation of the less hindered formaldehyde oxide **7** predominates.

The behavior of 3,3,6,6-tetramethyl-1,2-bis(methylene)cyclohexane (**1b**) toward ozone in ether was similar to that of **1a** (Scheme 3 and Table 1). Treatment of the diene **1b** with ozone in ether gave vinyl ozonide **10b** (33%) and vinyl epoxide **3b** (19%). When the same reaction was repeated in MeOH–ether, however, methoxyalkyl hydroperoxide **14b**, derived from capture of ketone oxide **4b**, was isolated in 53% yield, together with vinyl epoxide **3b** (26%). The reaction of **1b** in ether in the presence of trifluoroacetophenone gave a mixture of vinyl epoxide **3b** (41%) and two cross-ozonides, **9b** and **11**. It is interesting to note that the yield of **9b** (45%) was significantly higher than that of **11** (11%). The latest reaction suggested that (i) the ratio of epoxidation vs cleavage is ca. 2:3 and (ii) for the cleavage of **2b**, path a affording the more-hindered ketone *O*-oxide **4b** is favored. It should be noticed that in the case of **2a** the alternative path b predominated.

Scheme 3



Scheme 4



To understand the methyl-substituent effects on the course of the reactions of **1a**,**b**, the ozonolyses of the nonmethylated dienes **1c**,**d** were carried out in the presence or absence of trifluoroacetophenone (Table 1 and Scheme 4). The reaction of 1,2-bis(methylene)cyclopentane (**1c**) in ether gave quantitatively the expected vinyl ozonide **10c**, which was however very labile on silica gel.[7] Therefore, the ozonide **10c** could only be isolated in a yield of 13%. Analogously, 14% of **10d** was isolated from the ozonolysis of 1,2-bis(methylene)cyclohexane (**1d**). When the reaction of the diene **1c** was conducted in the presence of trifluoroacetophenone, ketone *O*-oxide **4c** was intercepted by the additive and vinyl ozonide **9c** was isolated in 71% yield. The analogous ozonide **9d** was even obtained in 86% yield by ozonolysis of diene **1d** under the same conditions (Table 1). These results suggest that in the ozonolyses of **1c**,**d** 1,3-dipolar cycloaddition is the initial reaction and, moreover, the directions of cleavage of the primary ozonides **2c**,**d** are highly selective, yielding exclusively the corresponding ketone *O*-oxides **4c**,**d**. This is in harmony with the fact that ozonolysis of 2,3-dimethyl-1,3-butadiene (**1e**) in the presence of trifluoroacetophenone gave only the corresponding ozonide **9e** in 71% yield (eq 1). In this connection, Griesbaum and Volpp[3c] have found that ozonolysis of 2,3-di-*tert*-butyl-1,3-butadiene, a sterically more congested diene, in methanol proceeds by an alternative

---

(4) Curci, R.; Fiorentino, M.; Troisi, L.; Edwards, J. O.; Pater, R. H. *J. Org. Chem.* **1980**, *45*, 4758.

(5) (a) Bailey, P. S. *Ozonation in Organic Chemistry*; Academic Press: New York, 1978, Vol. 1; 1982, Vol. 2. (b) Bunnelle, W. H. *Chem. Rev.* **1991**, *91*, 335. (c) McCullough, K. J.; Nojima, M. In *Organic Peroxides*; Ando, W., Ed.; Wiley: New York, 1992.

(6) Fukagawa, R.; Nojima, M. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2449.

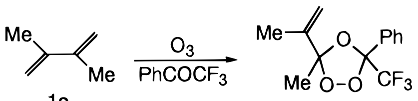
(7) Small vinyl ozonides are well-known to be labile thermally and on silica gel: Griesbaum, K.; Volpp, W.; Greinert, R.; Greunig, H.-J.; Schmid, J.; Henke, H. *J. Org. Chem.* **1989**, *54*, 383 and references therein.

Table 2. Competitive Reaction of Two Substrates with Ozone in the Presence of Trifluoroacetophenone[a]

entry	substr	products (% yield)	recovered diene (%)
1	**1a**, **1c**	**9c** (68)	**1a** (56)
2	**1a**, **15**	**16** (65)	**1a** (58)
3	**1c**, **15**	**9c** (53), **16** (35)	
4	**1b**, **1d**	**9d** (80)	**1b** (59)
5	**1b**, **15**	**16** (51)	**1b** (59)
6	**1d**, **15**	**9d** (64), **16** (33)	
7	**1c**, **1d**[b]	**10c** (43), **10d** (46)[c]	

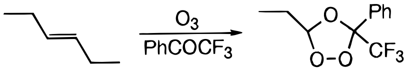
[a] Ozonolysis of a 1:1 mixture of two substrates (1 mmol of each) with ozone (1 mmol) in the presence of trifluoroacetophenone (1 mmol) in ether at −70 °C. [b] Ozonolysis in the absence of trifluoroacetophenone. [c] Yield determined by the ^{1}H NMR spectrum of the crude reaction mixture.

scission pathway, yielding formaldehyde oxide and *tert*-butyl 1-*tert*-butylvinyl ketone, together with an epoxide.



1e **9e** (1)

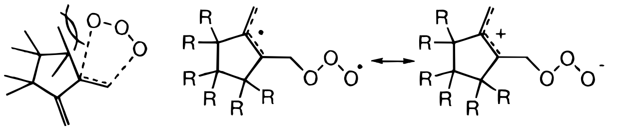
Relative Reactivities. Thus, it is clear that in the ozonolyses of bis(methylene)cycloalkanes the allylic methyls exert a significant influence on the mode of addition of ozone to the olefinic double bond and also on the direction of cleavage of the primary ozonide. To obtain information on the effect of the allylic methyls on the relative reactivity of the dienes toward ozone, we conducted a series of competitive reactions. When an equimolar mixture of the dienes **1a** and **1c** was treated with 0.5 equiv of ozone (i.e., **1a**:**1c**:O_3 = 1:1:1) in the presence of trifluoroacetophenone, the crossed-ozonide **9c** (68%) derived from capture of carbonyl oxide **4c** by trifluoroacetophenone was the sole isolable product. While 56% of unreacted diene **1a** was recovered, no evidence for the reaction of **1a** with ozone was obtained (Table 2, entry 1). The analogous experiment with a 1:1 mixture of **1b** and **1d** showed the exclusive ozonization of **1d** (Table 2, entry 4). Competition experiments with the pairs **1c**/**15** and **1d**/**15** (eq 2, Table 2, entries 3 and 6) indicated monoene **15** to be approximately half as reactive as nonmethylated dienes **1c** and **1d**. In accordance with this, the ^{1}H NMR spectrum of the reaction mixture obtained from the reaction of a 1:1 mixture of **1c** and **1d** with 0.5 equiv of ozone in ether provided a ca. 1:1 mixture of vinyl ozonides **10c** and **10d**. Yet, when equimolar mixtures of **1a** and **15** or **1b** and **15** were treated with 0.5 equiv of ozone in the presence of trifluoroacetophenone, again no evidence for the reaction of methylated dienes **1a** and **1b** was found (Table 2, entries 2 and 5). Assuming an NMR detection limit of 3%, one can derive from these experiments that methylated dienes **1a** and **1b** are at least 2 orders of magnitude less reactive than their nonmethylated counterparts **1c** and **1d**, respectively.



15 **16** (2)

Ozone is by far the most electrophilic of the common 1,3-dipoles, i.e., its reactions with C−C double bonds are controlled by the HOMO (olefin)/LUMO (O_3) interaction.[8] For electronic reasons, methylated diene **1a** (vertical ionization potential = 8.4 eV)[1] should therefore be more reactive than its nonmethylated analogue **1c** (8.73 eV) as previously reported for the relative reactivities of these two dienes toward the electrophilic diethyl acetylenedicarboxylate (k_{1a}/k_{1c} = 6.9).[9]

Scheme 5



17 **18'** (R = H, Me) **18"**

The low reactivity of **1a** (and **1b**) toward ozone, therefore, indicates that the accelerating electronic effect of the methyl groups is overcompensated by their retarding steric effect, which may be operative in the transition state of a concerted cycloaddition reaction (**17**, Scheme 5). The observed relative reactivities of the methylated and nonmethylated dienes **1** exclude a stepwise cycloaddition mechanism to account for the formation of **2**: If rate-determining attack of ozone at one of the freely accessible terminal H_2C groups of **1a** and **1c** would occur to lead to the formation of the dipolar or diradical intermediate **18** (Scheme 5), **1a** would be expected to react faster than **1c** for the electronic reasons discussed above. Reversible formation of **18** with rate-determining cyclization cannot account for the >100 fold difference in reactivity either, since all eventual intermediates **18** (R = H or CH_3) would undergo rapid cyclizations. The steric blocking which might retard the formation of primary ozonide **2a** or epoxide **3a** from **18** could be circumvented by cyclization to a seven-membered ring compound, as previously observed with other 1,3-dipoles.[1] We, therefore, have to conclude that the high rate of formation of primary ozonide **2c** compared to **2a** excludes the formation of the "ordinary" vinyl ozonide **2c** by a stepwise cycloaddition pathway. The data are consistent, however, with the formation of **2c** by a concerted 1,3-dipolar cycloaddition mechanism. Since it cannot be decided whether case c or d (Scheme 27 in ref 1) is encountered, the mechanism responsible for the formation of sterically shielded ozonides **2a** and **2b** remains open for discussion.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were taken on JEOL JNM-EX 270 MHz or JNM-PS 100 MHz spectrometer in $CDCl_3$ (unless otherwise noted) with $SiMe_4$ as standard. Dienes **1a**,[10] **1b**,[11] **1c**,[12] and **1d**[12] were prepared by the reported methods. Ozonolyses were carried out with a Nippon Ozone Model ON-1-2 ozonator; dry oxygen containing about 2% of ozone was introduced at a speed of 50 L/h in the solution of the substrate.

Reaction of 3,3,4,4,5,5-Hexamethyl-1,2-bis(methylene)cyclopentane (1a) with 2.5 Equiv of Ozone in Ether. A solution of diene **1a** (534 mg, 3.00 mmol) in ether (15 mL) was treated with 2.5 equiv of ozone at −70 °C. After evaporation of the solvent, the residue was separated by column chromatography on silica gel (column 2.0 × 60 cm; 40 g of silica gel).

---

[8] (a) Sustmann, R. *Pure Appl. Chem.* **1974**, *40*, 569. (b) Houk, K. N.; Yamaguchi, K. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. II, Chapter 13.

[9] Baran, J.; Mayr, H. *Tetrahedron* **1989**, *45*, 3347.

[10] Baran, J.; Klein, H.; Schade, C.; Will, E.; Koschinsky, R.; Bäuml, E.; Mayr, H. *Tetrahedron* **1988**, *44*, 2181.

[11] (a) Mayr, H.; Klein, H.; Sippel, E. *Chem. Ber.* **1983**, *116*, 3624. (b) Mayr, H.; Heigl, U. W.; Baran, J. *Chem. Ber.* **1993**, *126*, 1913.

[12] van Straten, J. W.; van Norden, J. J.; van Schaik, T. A. M.; Franke, G. T.; de Wolf, W. H.; Bickelhaupt, F. *Recl. Trav. Chim. Pays-Bas* **1978**, *97*, 105.

Elution with ether−hexane (3:97) gave vinyl ozonide **10a** (108 mg, 16%). Subsequent elution with ether−hexane gave keto epoxide **8a** (245 mg, 42%). Treatment of isolated ozonide **10a** (60 mg) with 1.2 equiv of ozone in ether at −70 °C, followed by column chromatography on silica gel, resulted in quantitative recovery of the ozonide **10a** (58 mg).

7,7,8,8,9,9-Hexamethyl-6-methylene-1,2,4-trioxaspiro[4.4]nonane (10a): oil; ^{1}H NMR (CCl_4) δ 0.88 (br s, 12 H), 1.08 (s, 3 H), 1.12 (s, 3 H), 5.07 (s, 1 H), 5.10 (s, 1 H), 5.18 (s, 1 H), 5.38 (s, 1 H); ^{13}C NMR δ 18.86, 21.03, 22.23, 23.19, 29.22, 29.69, 42.90, 44.34, 47.78, 94.09, 110.89, 115.11, 158.73. Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.17; H, 9.78.

4-Oxo-5,5,6,6,7,7-hexamethyl-1-oxaspiro[2.4]heptane (8a): oil; ^{1}H NMR (CCl_4) δ 0.90 (br s, 12 H), 1.08 (s, 3 H), 1.27 (s, 3 H), 2.74 (d, J = 7 Hz, 1 H), 2.90 (d, J = 7 Hz, 1 H); ^{13}C NMR δ 20.13, 21.32, 21.79, 23.20, 23.68, 24.75, 39.56, 42.87, 49.32, 51.87, 66.22, 220.66; IR 2900−3000, 1740, 1380 cm^{-1}. Reduction of **8a** with lithium aluminum hydride in ether led to the quantitative formation of 2,3,3,4,4,5,5-heptamethyl-1,2-cyclopentanediol (**13a**) as a 9:1 mixture of two stereoisomers, from which only the major isomer was isolated in a pure state by crystallization from hexane: mp 123−128 °C; ^{1}H NMR δ 0.80 (s, 3 H), 0.84 (s, 3 H), 0.90 (s, 3 H), 0.91 (s, 3 H), 0.98 (s, 3 H), 1.00 (s, 3 H), 1.18 (s, 3 H), 3.56 (s, 1 H); IR 3500−3100, 3000−2900, 1460, 1380, 1100, 1050 cm^{-1}. Anal. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08. Found: C, 71.77; H, 12.18.

Reaction of Diene 1a with 1 Equiv of Ozone in Ether. A solution of diene **1a** (303 mg, 1.70 mmol) in ether (15 mL) was treated with 1 equiv of ozone at −70 °C. After evaporation of the solvent, the residue was separated by column chromatography on silica gel. Elution with ether−hexane (3:97) gave a mixture of vinyl ozonide **10a** and 4-methylene-5,5,6,6,7,7-hexamethyl-1-oxaspiro[2.4]heptane (**3a**) (the **10a**/**3a** ratio = 1:1; 143 mg, 40%), which could not be separated. Subsequent elution with ether−hexane (8:92) gave keto epoxide **8a** (53 mg, 16%).

Treatment of 1a with 3,3-Dimethyl-1,2-dioxirane. To a solution of diene **1a** (615 mg, 3.45 mmol) in benzene was added a solution of $2KHSO_5-KHSO_4-K_2SO_4$ (Oxone) (2.9 g), $NaHCO_3$ (2.0 g), and 18-crown-6 (123 mg) in acetone (2.3 mL)/H_2O (25 mL), and the mixture was kept at room temperature for 4 h. After ether (50 mL) was added, the organic layer was washed with aqueous $NaHCO_3$ and then with saturated brine, and the solvent was evaporated (room temperature, 15 mmHg). Then the residue was distilled under reduced pressure to give epoxide **3a** (400 mg, 60%).

4-Methylene-5,5,6,6,7,7-hexamethyl-1-oxaspiro[2.4]heptane (3a): bp 80 °C/3 mmHg; ^{1}H NMR (CCl_4) δ 0.88 (br s, 12 H), 1.07 (s, 3 H), 1.17 (s, 3 H), 2.58 (d, J = 6 Hz, 1 H), 2.88 (d, J = 6 Hz, 1 H), 4.85 (s, 1 H), 4.88 (s, 1 H); ^{13}C NMR δ 20.58, 21.58, 21.91, 22.54, 28.72, 29.08, 42.66, 44.37, 45.16, 54.49, 67.80, 104.89, 159.84.

Reaction of Vinyl Epoxide 3a with Ozone. A slow stream of ozone (1 equiv) was passed into an ether solution (15 mL) of **3a** (270 mg, 1.39 mmol) at −70 °C. After evaporation of the solvent, the residue was separated by column chromatography on silica gel. Elution with ether−hexane (8:92) gave epoxy ketone **8a** (192 mg, 70%).

Ozonolysis of Diene 1a in MeOH−Ether. A MeOH−ether solution (15 mL, 1:2 v/v) of compound **1a** (250 mg, 1.40 mmol) was treated with ozone (3.50 mmol, 2.5 equiv) at −70 °C. After ether (50 mL) was added, the organic layer was washed with aqueous $NaHCO_3$ and then with saturated brine, and the solvent was evaporated (room temperature, 15 mmHg). The ^{1}H NMR spectra of the crude products showed the formation of vinyl epoxide **3a** and epoxy ketone **8a**. Column chromatography of the residue on silica gel (ether−hexane, 5:95) resulted in the elution of vinyl aldehyde **12a** (41 mg, 15%) and then epoxy ketone **8a** (66 mg, 24%).

2-Formyl-3,3,4,4,5,5-hexamethyl-1-methylenecyclopentane (12a): oil; ^{1}H NMR (CCl_4) δ 0.88 (s, 6 H), 1.05 (s, 6 H), 1.08 (s, 3 H), 1.20 (s, 3 H), 3.05 (q, J = 3 Hz, 1 H), 4.88 (d, J = 3 Hz, 1 H), 5.10 (d, J = 3 Hz, 1 H), 9.60 (d, J = 3 Hz, 1 H); ^{13}C NMR δ 19.39, 21.95, 23.24, 26.01, 28.42, 29.59, 47.40, 47.43, 47.76, 64.94, 108.28, 158.38, 204.32; IR 2900−3000, 1715, 1450, 1380, 1140, 1070, 880 cm^{-1}.

Ozonolysis of Diene 1a in the Presence of Trifluoroacetophenone in Ether. Ozonolysis of **1a** (214 mg, 1.20 mmol) was conducted in the presence of 1 equiv of trifluoroacetophenone (209 mg, 1.20 mmol) in ether (15 mL). After evaporation of the solvent, the residue was separated by column chromatography on silica gel. The first fraction (elution with ether−hexane, 2:98) gave ozonide **9a** (50 mg, 11%) as a 9:1 mixture of two stereoisomers (major isomer, δ 4.68, 4.78; minor isomer, δ 5.35, 5.87) (vinyl protons). By repeated column chromatography on silica gel, the major isomer of **9a** was isolated in a pure state. From the second fraction, ozonide **11** (60 mg, 23%) was obtained. The third fraction (elution with ether−hexane, 8:92) contained epoxy ketone **8a** (100 mg, 42%).

3-Phenyl-3-(trifluoromethyl)-6-methylene-7,7,8,8,9,9-hexamethyl-1,2,4-trioxaspiro[4.4]nonane (9a): oil; ^{1}H NMR (CCl_4) δ 0.93 (s, 6 H), 1.03 (s, 6 H), 1.07 (s, 3 H), 1.15 (s, 3 H), 4.68 (s, 1 H), 4.78 (s, 1 H), 7.3−7.7 (m, 5 H); ^{13}C NMR δ 18.34, 21.51, 22.52, 23.47, 29.16, 29.71, 42.81, 44.43, 47.70, 102.63 (q, J = 33 Hz), 111.58, 119.00, 121.61 (q, J = 288 Hz), 126.90, 128.14, 128.18, 130.13, 157.52; Anal. Calcd for $C_{20}H_{25}F_3O_3$: C, 64.85; H, 6.80. Found: C, 64.58; H, 6.94.

3-Phenyl-3-(trifluoromethyl)-1,2,4-trioxolane (11): oil; ^{1}H NMR (CCl_4) δ 5.13 (s, 1 H), 5.45 (s, 1 H), 7.3−7.7 (m, 5 H); ^{13}C NMR δ 95.56, 103.03 (q, J = 34 Hz), 121.49 (q, J = 289 Hz), 126.77, 128.73, 130.58, further signals not detectable. Anal. Calcd for $C_9H_7F_3O_3$: C, 49.10; H, 3.21. Found: C, 49.00; H, 3.03.

Ozonolysis of 3,3,6,6-Tetramethyl-1,2-bis(methylene)cyclohexane (1b) in Ether. A slow stream of ozone (2.5 equiv) was passed into an ether solution (15 mL) of **1b** (197 mg, 1.20 mmol) at −70 °C. After evaporation of the solvent, the residue was separated by column chromatography on silica gel. Elution with ether−hexane (2:98) gave first ozonide **10b** (84 mg, 33%) and then epoxide **3b** (40 mg, 19%).

6-Methylene-7,7,10,10-tetramethyl-1,2,4-trioxaspiro[4.5]decane (10b): oil; ^{1}H NMR (CCl_4) δ 0.93 (s, 6 H), 1.13 (s, 6 H), 1.3−1.6 (m, 4 H), 5.00 (s, 1 H), 5.02 (d, J = 2 Hz, 1 H), 5.10 (s, 1 H), 5.28 (d, J = 2 Hz, 1 H); ^{13}C NMR δ 23.10, 28.66, 29.78, 34.13, 35.68, 37.26, 38.23, 94.25, 110.70, 111.83, 150.42. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.78; H, 9.75.

4-Methylene-5,5,8,8-tetramethyl-1-oxaspiro[2.5]octane (3b): oil; ^{1}H NMR (CCl_4) δ 0.78 (s, 3 H), 0.88 (s, 3 H) 1.05 (s, 3 H), 1.13 (s, 3 H), 1.2−1.8 (m, 4 H), 2.22 (d, J = 6 Hz, 1 H), 2.87 (d, J = 6 Hz, 1 H), 4.74 (d, J = 2 Hz, 1 H), 4.98 (d, J = 2 Hz, 1 H); ^{13}C NMR δ 22.54, 24.43, 26.99, 28.60, 34.63, 35.39, 36.14, 37.97, 53.59, 63.87, 104.97, 153.80.

Ozonolysis of 1b in the Presence of Trifluoroacetophenone in Ether. A slow stream of ozone (2.5 equiv) was passed into an ether solution (15 mL) of **1b** (246 mg, 1.50 mmol) and trifluoroacetophenone (251 mg, 1.50 mmol) at −70 °C. After evaporation of the solvent, the residue was separated by column chromatography on silica gel. Elution with ether−hexane (2:98) gave ozonide **9b** (240 mg, 45%) as a 4:1 mixture of two isomers (on the basis of the signals of the vinyl protons in the ^{1}H NMR spectrum). Subsequent elution with ether−hexane (5:95) gave ozonide **11** (37 mg, 11%) and then vinyl epoxide **3b** (110 mg, 41%). Repeated column chromatography of a 4:1 mixture of two isomeric ozonides of **9b** resulted in the isolation of the major isomer in a pure state.

3-Phenyl-3-(trifluoromethyl)-6-methylene-7,7,10,10-tetramethyl-1,2,4-trioxaspiro[4.5]decane (9b) (major isomer): oil; ^{1}H NMR (CCl_4) δ 0.7−2.0 (m, 16 H), 4.81 (s, 1 H), 5.00 (s, 1 H), 7.3−7.7 (m, 5 H); ^{13}C NMR δ 22.85, 23.68, 28.64, 29.49, 34.73, 35.81, 37.45, 38.11, 103.35 (q, J = 33 Hz), 112.86, 116.04, 121.58 (q, J = 290 Hz), 126.65, 127.90, 129.72, 131.88, 148.35. Anal. Calcd for $C_{19}H_{23}F_3O_3$: C, 64.03; H, 6.51. Found: C, 64.12; H, 6.55. The minor isomer was obtained as an admixture with 75% of the major one; oil, the following additional signals were assigned to this isomer: ^{1}H NMR (CCl_4) δ 0.7−2.0 (m, 16 H), 5.16 (s, 1 H), 5.53 (s, 1 H), 7.3−7.7 (m, 5 H); ^{13}C NMR δ 23.42, 23.70, 27.64, 28.18, 34.43, 34.86, 35.87, 37.58, 103.40 (q, J = 33 Hz), 111.61, 117.29, 121.64 (q, J = 290 Hz), 126.95, 127.92, 128.14, 129.94, 147.57.

Ozonolysis of Diene 1b in MeOH−Ether. A MeOH−ether solution (15 mL, 1:2 v/v) of compound **1b** (197 mg, 1.20 mmol) was treated with ozone (3.00 mmol, 2.5 equiv) at −70 °C. After ether (50 mL) was added, the organic layer was washed with aqueous $NaHCO_3$ and then with saturated brine, and the solvent was evaporated (room temperature, 15 mmHg). Column chromatography of the residue on silica gel (ether−hexane, 2:98) resulted in the elution of vinyl epoxide **3b** (56 mg, 26%). Elution with ether−hexane (8:92) gave methoxyalkyl hydroperoxide **14b** (137 mg, 53%).

1-Methoxy-2-methylene-3,3,6,6-tetramethylcyclohexyl hydroperoxide (14b): oil; ^{1}H NMR δ 1.01 (s, 3 H), 1.15 (s, 9 H), 1.2−1.7 (m, 4 H), 3.33 (s, 3 H), 5.33 (d, J = 2 Hz, 1 H), 5.43 (d, J = 2 Hz, 1 H), 7.20 (br s, 1 H); ^{13}C NMR δ 22.83, 23.40, 29.89, 35.33, 36.18, 37.08, 40.66, 50.72, 106.91, 114.81, 148.66. Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.29; H, 10.28. Found: C, 67.40; H, 10.25.

Ozonolysis of 1,2-Bis(methylene)cycloalkanes 1c,d in Ether. Ozonolysis of **1c** is representative. A solution of diene **1c** (198 mg, 2.10 mmol) in ether (15 mL) was treated with 1 equiv of ozone at −70 °C. After evaporation of the solvent, the ^{1}H NMR spectrum of the crude product mixture was measured, which indicated exclusive formation of vinyl ozonide **10c**. Column chromatography on silica gel (elution with ether−hexane, 3:97) gave vinyl ozonide **10c** (40 mg, 13%). Subsequent elution with ether−hexane (1:1) gave a complex mixture of unidentified products (180 mg).

6-Methylene-1,2,4-trioxaspiro[4.4]nonane (10c): oil; ^{1}H NMR δ 1.5−2.1 (m, 4 H), 2.2−2.7 (m, 2 H), 5.10 (s, 1 H), 5.18 (s, 1 H), 5.20 (t, J = 2 Hz, 1 H), 5.38 (t, J = 2 Hz, 1 H); ^{13}C NMR δ 21.12, 30.06, 35.90, 94.61, 112.57, 115.64, 146.28.

6-Methylene-1,2,4-trioxaspiro[4.5]decane (10d): oil; ^{1}H NMR δ 1.4−2.4 (m, 8 H), 4.91 (t, J = 1 Hz, 1 H), 5.15 (s, 1 H), 5.20 (t, J = 1 Hz, 1 H), 5.21 (s, 1 H); ^{13}C NMR δ 24.01, 26.76, 33.68, 35.31, 94.09, 107.71, 109.67, 144.85.

Ozonolysis of 1,2-Bis(methylene)cycloalkanes 1c,d and 2,3-Dimethyl-1,3-butadiene (1e) in the Presence of Trifluoroacetophenone in Ether. Ozonolysis of 1,2-dimethylenecyclohexane (**1d**) is representative. Ozonolysis of **1d** (203 mg, 1.88 mmol) was conducted in the presence of 1 equiv of trifluoroacetophenone (327 mg, 1.88 mmol) in ether (15 mL). After evaporation of the solvent, the residue was separated by column chromatography on silica gel. Elution with ether−hexane (3:97) gave ozonide **9d** (484 mg, 86%).

3-Phenyl-3-(trifluoromethyl)-6-methylene-1,2,4-trioxaspiro[4.4]nonane (9c): oil (one stereoisomer); ^{1}H NMR δ (CCl_4) 1.5−2.2 (m, 4 H), 2.2−2.7 (m, 2 H), 5.45 (t, J = 2 Hz, 1 H), 5.83 (t, J = 2 Hz, 1 H), 7.3−7.7(m, 5 H); ^{13}C NMR δ 21.50, 30.18, 36.88, 103.51 (q, J = 33 Hz), 116.13, 116.24, 121.81 (q, J = 289 Hz), 126.54, 128.27, 128.31, 130.30, 141.56; IR 3000−2900, 1460, 1310, 1190, 1080, 1060, 715 cm^{-1}. Anal. Calcd for $C_{14}H_{13}F_3O_3$: C, 58.73; H, 4.59. Found: C, 58.43; H, 4.66.

3-Phenyl-3-(trifluoromethyl)-7-methylene-1,2,4-trioxaspiro[4.5]nonane (9d): oil (a 85:15 mixture of two isomers); ^{1}H NMR δ 1.3−2.6 (m, 8 H), 4.73 (s, 0.15 H), 4.89 (s, 0.15 H), 5.02 (t, J = 1 Hz, 0.85 H), 5.47 (t, J = 1 Hz, 0.85 H), 7.3−7.8 (m, 5 H); ^{13}C NMR (major isomer) δ 23.56, 26.62, 34.32, 35.82, 103.67 (q, J = 34 Hz), 111.34, 111.97, 121.61 (q, J = 289 Hz), 126.63, 128.23, 128.28, 130.28, 140.99; the following additional signals were assigned to the minor isomer in the ^{13}C NMR spectrum; δ 24.08, 26.92, 33.48, 33.98, 103.97 (q, J = 34 Hz), 110.85, 111.90, 130.15, 144.17; IR 2950, 1460, 1310, 1190, 1090, 960, 720 cm^{-1}. Anal. Calcd for $C_{15}H_{15}F_3O_3$: C, 60.00: H, 5.04. Found: C, 59.80: H, 4.99.

3-Methyl-3-(1-methylethenyl)-5-phenyl-5-(trifluoromethyl)-1,2,4-trioxolane (9e): oil (one stereoisomer); ^{1}H NMR (CCl_4) δ 1.43 (s, 3 H), 1.90 (d, J = 0.6 Hz, 3 H), 5.10 (q, J = 0.6 Hz, 1 H), 5.38 (s, 1 H), 7.2−7.8 (m, 5 H). Anal. Calcd for $C_{13}H_{13}F_3O_3$: C, 56.93; H, 4.79. Found: C, 56.59; H, 4.68.

Competitive Ozonolysis of Dienes 1a and 1c in the Presence of Trifluoroacetophenone. A mixture of **1a** (178 mg, 1.00 mmol), **1c** (94 mg, 1.00 mmol), and trifluoroacetophenone (174 mg, 1.00 mmol) in ether (15 mL) was treated with ozone (1.00 mmol) at −70 °C. After evaporation of the solvent, the residue was separated by column chromatography on silica gel. The first fraction (elution with hexane) contained starting diene **1a** (99 mg, 56%). The second fraction (elution with ether−hexane, 2:98) gave ozonide **9c** (195 mg, 68%).

Competitive Ozonolysis of Diene 1a and 3-Hexene (15) in the Presence of Trifluoroacetophenone. A mixture of diene **1a** (178 mg, 1.00 mmol), 3-hexene (**15**) (84 mg, 1.00 mmol), and trifluoroacetophenone (174 mg, 1.00 mmol) in ether (15 mL) was treated with ozone (1.00 mmol) at −70 °C. After evaporation of the solvent, the residue was separated by column chromatography on silica gel. The first fraction (elution with hexane) contained starting diene **1a** (103 mg, 58%). The second fraction (elution with ether−hexane, 2:98) gave 3-ethyl-5-phenyl-5-(trifluoromethyl)-1,2,4-trioxolane (**16**) (161 mg, 65%) as a 2:1 mixture of two stereoisomers.

3-Ethyl-5-phenyl-5-(trifluoromethyl)-1,2,4-trioxolane (16): oil; ^{1}H NMR δ 0.97 (t, J = 8 Hz, 2.1 H), 1.10 (t, J = 8 Hz, 0.9 H), 1.7−1.8 (m, 2 H), 5.23 (t, J = 5 Hz, 0.33 H), 5.56 (t, J = 5 Hz, 0.67 H), 7.4−7.6 (m, 5 H); ^{13}C NMR (major isomer) δ 7.71, 23.97, 103.69 (q, J = 33 Hz), 107.91, 121.68 (q, J = 287 Hz), 126.79, 128.27, 130.26, 132.51; the following additional signals were assigned to the minor isomer in the ^{13}C NMR spectrum; δ 7.74, 22.36, 103.30 (q, J = 33 Hz), 106.74, 121.67 (q, J = 287 Hz), 126.67, 128.39, 130.56. Anal. Calcd for $C_{11}H_{11}F_3O_3$: C, 53.23; H, 4.47. Found: C, 53.29; H, 4.66.

Competitive Ozonolysis of Diene 1c and 3-Hexene (15) in the Presence of Trifluoroacetophenone. A mixture of diene **1c** (94 mg, 1.00 mmol), 3-hexene (**15**) (84 mg, 1.00 mmol) and trifluoroacetophenone (174 mg, 1.00 mmol) in ether (15 mL) was treated with ozone (1.00 mmol) at −70 °C. After evaporation of the solvent, the residue was separated by column chromatography on silica gel. Elution with ether−hexane (2:98) gave a mixture of ozonide **9c** and 3-ethyl-5-phenyl-5-(trifluoromethyl)-1,2,4-trioxolane (**16**) (239 mg). On the basis of the characteristic signals of ozonide **9c** (δ 5.83) and ozonide **16** (δ 5.23, 5.56) in the ^{1}H NMR spectrum, the ratio was determined to be ca. 3:2.

Competitive Ozonolysis of Dienes 1b and 1d in the Presence of Trifluoroacetophenone. A mixture of **1b** (164 mg, 1.00 mmol), **1d** (108 mg, 1.00 mmol), and trifluoroacetophenone (174 mg, 1.00 mmol) in ether (15 mL) was treated with ozone (1.00 mmol) at −70 °C. After evaporation of the solvent, the residue was separated by column chromatography on silica gel. The first fraction (elution with hexane) contained starting diene **1b** (96 mg, 59%). The second fraction (elution with ether−hexane, 2:98) gave ozonide **9d** (240 mg, 80%).

Competitive Ozonolysis of Dienes 1c and 1d in Ether. A mixture of **1c** (94 mg, 1 mmol) and **1d** (108 mg, 1 mmol) in ether (15 mL) was treated with ozone (1 mmol) at −70 °C. After evaporation of the solvent, the ^{1}H NMR spectrum of the residue indicated the formation of a ca. 1:1 mixture of the ozonides **10c** (40%, δ 5.38) and **10d** (43%, δ 4.91). By column chromatography on silica gel (elution with hexane), a 1:1 mixture of two ozonides, **10c** and **10d** (16 mg), was obtained.

Acknowledgment. J.B. thanks the Deutsche Akademische Austauschdienst for a stipend.

JO960397I