could be located by a difference Fourier map and were refined isotropically; some hydrogen atoms were substituted by calculated H atom positions and refined in accordance to the riding model with idealized geometry (SHELX-76[40]). A total of 281 parameters were refined and a weighting scheme ($w^{-1} = \sigma^2 F_o$) was used. The final values for R and R_w were 0.039 and 0.040, respectively, with the final Fourier difference map showing a maximum of 0.14 and a minimum of -0.20 e Å^{-3}. The crystallographic figures were prepared with PLUTO[13] and ORTEP.[41]

Hydrolysis of the Silyl Enol Ether 2b with 1 N HCl. A sample of silyl enol ether **2b** (about 0.2 g) was dissolved in 30 mL of ether and shaken with 1 N HCl. The ether phase was washed twice with saturated aqueous $NaHCO_3$ and brine and dried ($MgSO_4$). Removal of the solvent by rotary evaporation yielded *cis*-**1b** as a colorless viscous oil which was pure by ^{1}H NMR analysis.

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Supplementary Material Available: Tables listing the atomic coordinates and thermal parameters, bond lengths, bond angles, and torsion angles (9 pages). Ordering information is given on any current masthead page.

(41) Johnson, C. K. ORTEP-II. Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, TN, 1976.

Stereochemical Effects on the Mechanism of the Ozonolysis of (*E*)- and (*Z*)-*o*-(2-Phenyl-3-methoxy-2-propenyl)benzophenone

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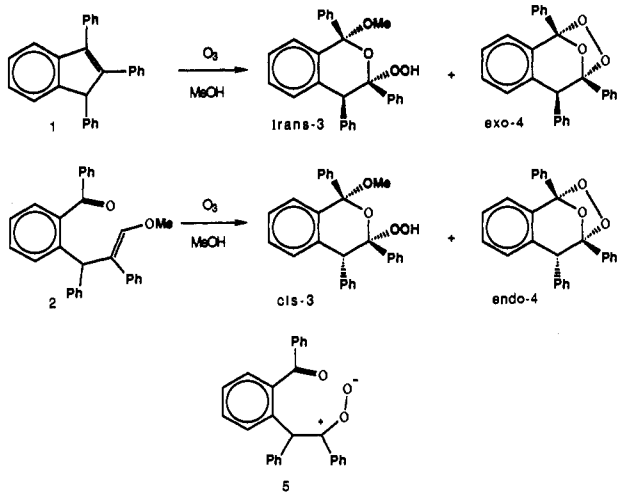
Abstract: The ozonolyses of (*E*)- and (*Z*)-*o*-(2-phenyl-3-methoxy-2-propenyl)benzophenone (**6**), which should proceed through a common carbonyl oxide intermediate **15**, afforded distinctly different reaction product mixtures, suggesting that the substrate stereochemistry exerts an influence on the overall reaction mechanism: (a) The reaction of (*E*)-**6** in carbon tetrachloride resulted in the formation of unidentified polymeric products, whereas 2,3-diphenylindene ozonide (**8**) was the major reaction product in acetic acid and methanol at 0 °C. From the ozonolysis of the isomeric keto olefin (*Z*)-**6** in both the protic and aprotic solvents, however, the ozonide **8** was obtained almost quantitatively. (b) The reaction of (*E*)-**6** in methanol–methylene chloride at -70 °C gave the methoxy hydroperoxide **9** in 81% yield, whereas the reaction of (*Z*)-**6** under similar conditions led to the formation of the hemiperacetal **10** (14% yield) together with the ozonide **8** (49% yield). Moreover, the high degree of similarity in the nature and distribution of the products from the ozonolyses of keto olefin (*Z*)-**6** and 2,3-diphenylindene (**7**) would be consistent with their respective reactions proceeding predominantly through a common carbonyl oxide intermediate.

The mechanism of the reaction of ozone with alkenes continues to attract considerable attention.[2] During our continuing study of the ozonolysis of indene derivatives,[3] it has been found that the reaction of 1,2,3-triphenylindene (**1**) with ozone in methanol–methylene chloride at -70 °C is highly stereoselective, resulting in the formation of the methanol-derived product *trans*-**3**, in which the phenyl group at the 2-position and the hydroperoxy group at the 1-position are trans-α related (Scheme I), together with the ozonide *exo*-**4**. Conversely, the stereoisomeric methanol-derived product and ozonide, *cis*-**3** and *endo*-**4**, respectively, are exclusively obtained from the related keto olefin **2** (Scheme I).[4] Since both reactions formally proceed through the carbonyl oxide intermediate

Scheme I



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

(2) (a) Bailey, P. S. *Ozonation in Organic Chemistry*; Academic Press: New York, 1978; Vol. 1, 1982; Vol. 2, (b) Kuczkowski, R. L. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 2. (c) Pryor, W. A.; Giamalva, D.; Church, D. F. *J. Am. Chem. Soc.* **1985**, *107*, 2793. (d) Griesbaum, K.; Volpp, W.; Greinert, R. *Ibid.* **1985**, *107*, 5309. (e) Nakamura, N.; Nojima, M.; Kusabayashi, S. *Ibid.* **1987**, *109*, 4969. (f) Mori, M.; Nojima, M.; Kusabayashi, S. *Ibid.* **1987**, *109*, 4407. (g) LaBarge, M. S.; Keul, H.; Kuczkowski, R. L.; Wallasch, M.; Cremer, D. *Ibid.* **1988**, *110*, 2081. (h) Gillies, J. Z.; Gillies, C. W.; Suenram, R. D.; Lovas, F. J.; Stahl, W. *Ibid.* **1989**, *111*, 3073. (i) Bunnelle, W. H.; Meyer, L. A.; Schlemper, E. O. *Ibid.* **1989**, *111*, 7612. (j) Bunnelle, W. H. *Ibid.* **1989**, *111*, 7613. (k) Sugimoto, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *Ibid.* **1990**, *112*, 3690. (l) Jaworski, K.; Smith, L. L. *J. Org. Chem.* **1988**, *53*, 545. (m) Wojciechowski, B. J.; Pearson, W. H.; Kuczkowski, R. L. *Ibid.* **1989**, *54*, 115. (n) Crandall, J. K.; Schuster, T. *Ibid.* **1990**, *55*, 1973.

(3) (a) Miura, M.; Ikegami, A.; Nojima, M.; Kusabayashi, S.; McCullough, K. J.; Nagase, S. *J. Am. Chem. Soc.* **1983**, *105*, 2414. (b) McCullough, K. J.; Nojima, M.; Miura, M.; Fujisaka, T.; Kusabayashi, S. *J. Chem. Soc., Chem. Commun.* **1984**, 35. (c) Miura, M.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1984**, *106*, 2932. (d) Miura, M.; Fujisaka, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Org. Chem.* **1985**, *50*, 1504.

(4) Nakamura, N.; Fujisaka, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1989**, *111*, 1799.

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Table I. Ozonolyses of Keto Olefins (*E*)-**6** and (*Z*)-**6** and 2,3-Diphenylindene (**7**)

starting material	solvent	reaction temp (°C)	products (% yield)
(*E*)-**6**	CCl_4	0	**11** (5)[b]
(*E*)-**6**	MeOH-CH_2Cl_2[a]	0	**8** (20), **9** (44), **11** (19)
(*E*)-**6**	MeOH-CH_2Cl_2[a]	−70	**9** (81), **11** (6)
(*E*)-**6**	AcOH-CH_2Cl_2[a]	0	**8** (54)[b]
(*Z*)-**6**	CCl_4	0	**8** (84), **11** (6)
(*Z*)-**6**	MeOH-CH_2Cl_2[a]	0	**8** (73), **11** (4)
(*Z*)-**6**	MeOH-CH_2Cl_2[a]	−70	**8** (49), **10** (14), **11** (6)
(*Z*)-**6**	AcOH-CH_2Cl_2[a]	0	**8** (93), **11** (6)
7	CCl_4	0	**8** (86), **11** (2)
7	MeOH-CH_2Cl_2[a]	0	**8** (81), **10** (5)
7	MeOH-CH_2Cl_2[a]	−70	**8** (65), **10** (15), **11** (3)
7	AcOH-CH_2Cl_2[a]	0	**8** (68), **11** (1)

[a] In the mixed-solvent system, 50 vol % of CH_2Cl_2 was used. [b] Unidentified polymeric products were also produced in a significant amount.

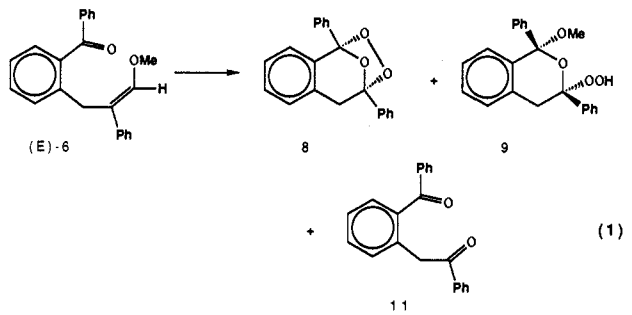
5, the significant differences between the stereochemistries of corresponding products were not anticipated at the outset.

To obtain deeper understanding of the complex, but interesting, ozonolysis mechanism of indenes and related substrates, ozonolyses of the geometrical isomers of *o*-(2-phenyl-3-methoxy-2-propenyl)benzophenone, (*E*)-**6** and (*Z*)-**6**, respectively, have been carried out under a variety of reaction conditions. The results have been compared with those obtained from ozonolyses of 2,3-diphenylindene (**7**) under corresponding conditions. Surprisingly, the ozonolysis reactions of the isomeric substrates, (*E*)- and (*Z*)-**6**, proceed by quite different pathways, whereas (*Z*)-**6** and 2,3-diphenylindene (**7**) give rise to similar ozonolysis products.

Results and Discussion

The ozonolysis of keto olefin (*E*)-**6** in carbon tetrachloride resulted in the formation of unidentified polymeric products together with a small amount of diketone **11**. When the reaction was undertaken in acetic acid–methylene chloride, however, the expected 2,3-diphenylindene ozonide (**8**) was obtained in 54% yield.[5] These results would imply that ozonide formation is favored in participating solvent rather than in nonpolar, nonparticipating solvent.[2f] A similar trend had been noted previously in the ozonolysis of the keto olefin **2**.[4] In the case of the isomeric keto olefin (**Z**)-*6*, however, the ozonide **8** was the predominant product irrespective of the solvent (Table I).

When the ozonolysis of the keto olefin (*E*)-**6** was undertaken in methanol–methylene chloride solution at −70 °C, a solid, methanol-derived product was obtained as a single isomer in 81% yield (eq 1) The usual analytical and spectroscopic properties



of this product indicated that it had incorporated one molecule of methanol and contained a hydroperoxide group. An X-ray crystallographic analysis unambiguously identified this compound as the isochroman derivative depicted in structural formula **9** and Figure 1. A selection of the more important bond lengths and angles is given in Table II. Although the general features of the molecular geometry of **9** are not markedly different from those of other isochromans isolated previously from the ozonolyses of indenes or related acyclic keto olefins,[3b,4,7] the syn relationship

(5) Bailey, P. S. *Chem. Ber.* **1954**, *87*, 993.

Table II. Derived Geometrical Parameters for Isochroman (**9**)

(a) Bond Lengths (Å) with Standard Deviations

O(1)-C(1)	1.418 (3)	C(2)-H(2B)	0.921 (4)
O(1)-C(9)	1.424 (3)	C(2)-C(3)	1.502 (4)
O(2)-O(3)	1.464 (3)	C(3)-C(4)	1.397 (4)
O(2)-C(1)	1.418 (3)	C(3)-C(8)	1.393 (3)
O(3)-H(3)	0.95 (4)	C(4)-C(5)	1.379 (4)
O(4)-C(9)	1.424 (3)	C(5)-C(6)	1.377 (4)
O(4)-C(10)	1.443 (3)	C(6)-C(7)	1.380 (4)
C(1)-C(2)	1.521 (4)	C(7)-C(8)	1.395 (4)
C(1)-C(17)	1.512 (3)	C(8)-C(9)	1.524 (3)
C(2)-H(2A)	0.937 (4)	C(9)-C(11)	1.529 (3)

(b) Angles (deg) with Standard Deviations

C(1)-O(1)-C(9)	119.18 (18)	C(2)-C(3)-C(4)	120.05 (23)
O(3)-O(2)-C(1)	109.53 (16)	C(2)-C(3)-C(8)	120.25 (22)
O(2)-O(3)-H(3)	99.0 (25)	C(4)-C(3)-C(8)	119.68 (23)
C(9)-O(4)-C(10)	114.56 (18)	C(3)-C(4)-C(5)	120.6 (3)
O(1)-C(1)-O(2)	113.07 (19)	C(4)-C(5)-C(6)	119.7 (3)
O(1)-C(1)-C(2)	109.69 (19)	C(5)-C(6)-C(7)	120.4 (3)
O(1)-C(1)-C(17)	107.36 (18)	C(6)-C(7)-C(8)	120.63 (24)
O(2)-C(1)-C(2)	102.60 (19)	C(3)-C(8)-C(7)	118.92 (22)
O(2)-C(1)-C(17)	112.43 (18)	C(3)-C(8)-C(9)	120.83 (21)
C(2)-C(1)-C(17)	111.70 (19)	C(7)-C(8)-C(9)	120.20 (21)
C(1)-C(2)-H(2A)	104.2 (3)	O(1)-C(9)-O(4)	108.87 (18)
C(1)-C(2)-H(2B)	103.4 (3)	O(1)-C(9)-C(8)	113.33 (19)
C(1)-C(2)-C(3)	110.70 (21)	O(1)-C(9)-C(11)	106.32 (17)
H(2A)-C(2)-H(2B)	114.9 (4)	O(4)-C(9)-C(8)	106.81 (19)
H(2A)-C(2)-C(3)	113.4 (3)	O(4)-C(9)-C(11)	110.86 (18)
H(2B)-C(2)-C(3)	109.5 (3)	C(8)-C(9)-C(11)	110.70 (18)

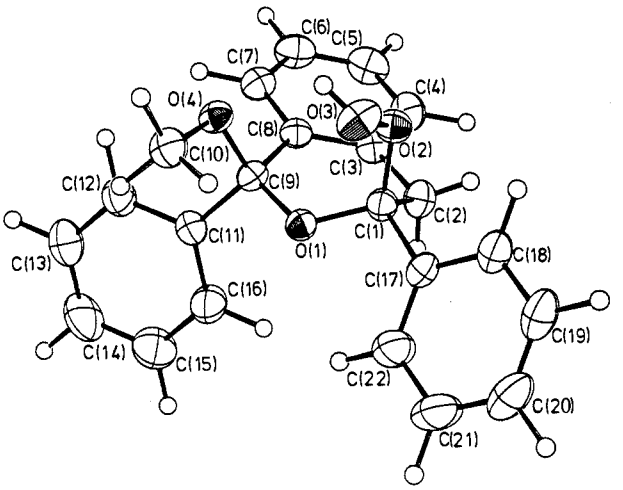
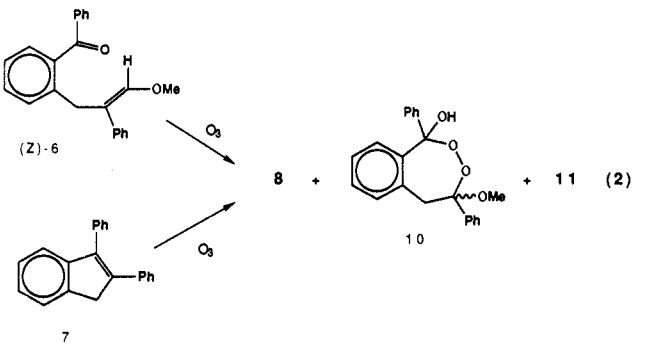


Figure 1. X-ray crystal structure of the solvent-derived product **9**.

between the hydroperoxy group at C(1) and the methoxy group at C(9) is retained even though **9** is less sterically crowded than the other related systems.

On the other hand, ozonolysis of the isomeric keto olefin (*Z*)-**6** under identical conditions afforded in 14% yield a different methanol-derived product, which has been assigned the hemiperacetal structure **10**, together with the ozonide **8** (49% yield) (eq 2). Treatment of **9** and **10** with catalytic quantities of



trifluoroacetic acid in methanol–methylene chloride solution gave

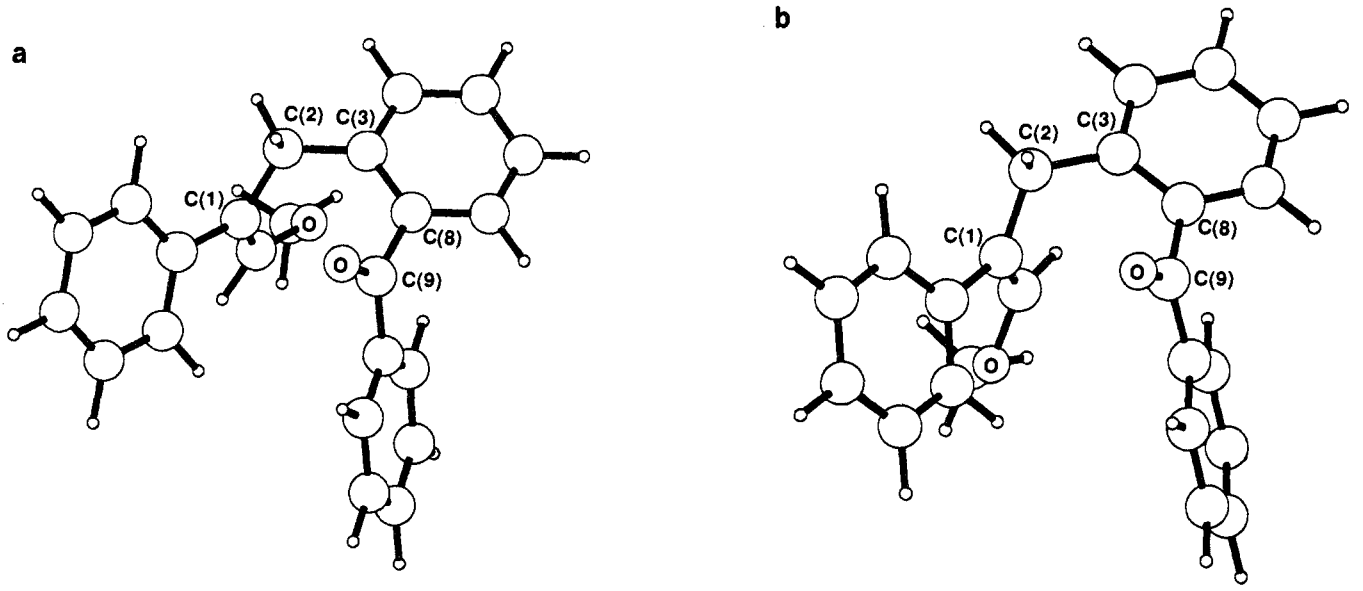
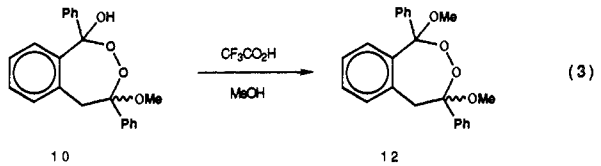


Figure 2. Minimum energy conformations of keto olefins (a) (*E*)- and (b) (*Z*)-**6** as determined by molecular mechanics calculations.

the ozonide **8** and the dimethoxy hemiperacetal **12** in quantitative yield, respectively, consistent with the previous structural assignment (eq 3).[6,7] When (*E*)-**6** was ozonized at higher tem-



10 12 (3)

perature (0 °C), the yield of the ozonide increased significantly with a concomitant decrease in the yield of the methanol-derived product **9** (Figure 1). Similar changes in the product composition with temperature were also noted in the case of (*Z*)-**6** (Table I). In addition, the ozonolyses of (*Z*)-**6** and 2,3-diphenylindene (**7**) show similar variations in product composition with solvent and temperature; e.g., ozonolysis of indene **7** in carbon tetrachloride and acetic acid gave the ozonide **8** as the major product, and, in methanol, the hemiperacetal **10**, rather than the isochroman **9**, was obtained as the sole methanol-derived product (Table I and eq 2).

Although the formation of each of the monomeric ozonolysis products, viz., the ozonide **8** and the solvent-participated products **9** and **10**, derived from the isomeric keto olefins (**E**)- and (*Z*)-**6** and indene **7** can be understood in terms of an overall mechanism involving conventional ozonolysis intermediates,[8] the compositions of the respective product mixtures are less readily rationalized, particularly in the cases of the isomeric substrates (*E*)- and (*Z*)-**6**, which are formally precursors of the same carbonyl oxide intermediate. The observed variations in chemical behavior of the carbonyl oxide intermediates derived from different substrates could be related to a number of factors, including (a) conformational preferences of the olefinic substrate, (b) the modes of formation and cycloreversion of the corresponding primary ozonides, and (c) solvent effects.

Molecular mechanics calculations (MMP2[9a]) carried out on the substrates (*E*)- and (*Z*)-**6** suggest that their respective minimum energy conformations, although different in energy, show similar structural features (Figure 2). In particular, the 3-methoxy-2-phenyl-2-propenyl and benzoyl groups are found to be stacked roughly parallel with respect to each other and substantially rotated (ca. 60–70°) out of coplanarity with the central benzo ring. Both systems appear to favor an antiparallel arrangement for the carbonyl and the olefinic groups, though the barrier to interconversion between the two parallel conformations by rotation about the C(8)–C(9) bond[9b] is estimated to be ~7 kcal mol^{-1}. In addition, since there are no substituents on C(2) in (*E*)- and (*Z*)-**6**, rotation of the propenyl side chain about bond C(1)–C(2) by ±10° from the minimum position can be accommodated without incurring severe increases in steric energy. In conclusion, the molecular mechanics calculations suggest that the comparatively minor, if any, differences in substrate conformations would not account for the substantial discrepancies in the overall reaction pathways of (*E*)- and (*Z*)-**6**.

Keul and Kuczkowski have shown that ozonolyses of deuterium-labeled *E*,*Z* pairs of simple olefins and vinyl ethers give rise to a consistent degree of stereoselectivity in the resulting 1,2,4-trioxolane and 1,2-dioxolane products.[10] The observed stereoselectivity has been rationalized in terms of the formation of a preponderance of either the syn or anti isomer of the intermediate carbonyl oxide HDCOO, depending on the olefinic substrate configuration. Similarly, the marked variations in the stereochemistry of 1,2-dioxolanes, but not that of the corresponding 1,2,4-trioxolane products, from the ozonolysis of (*E*)- and (*Z*)-1-ethoxypropene suggest that the configurational isomers of the carbonyl oxide CH_3CHOO had been produced in different relative amounts from each alkene.[2m] If analogous stereochemical effects are more generally operative in ozonolysis reactions, they may provide a more satisfactory rationale for the observed variations in the nature and distribution of the products derived from the keto olefins (*E*)- and (*Z*)-**6**.

As a consequence of the sterically congested nature of keto olefins (*E*)- and (*Z*)-**6**, the approach of ozone should be restricted to the least hindered face of the olefinic double bond in each case. Concerted cycloaddition of ozone with retention of olefin con-

(6) In contrast to the hydroperoxy proton of the methoxy hydroperoxide **9** (^{1}H NMR δ 8.60), the hydroxy proton of the hemiperacetal **10** appeared at δ 4.19 in the ^{1}H NMR spectra, as expected.[7a] The large difference of chemical shift in ^{1}H NMR spectra between the vicinal protons at the 6-position seems to be characteristic of the hemiperacetal derived from ozonolysis of indene derivatives in methanol. In the cases of **10** and **12**, the differences are as large as 1.32 and 1.33 ppm, respectively. The similar large difference is observed for 3,7-dimethoxy-3-phenyl-4,5-benzo-1,2-dioxacycloheptane (0.9 ppm) and 3,7-dimethoxy-4,5-benzo-1,2-dioxacycloheptane (0.97 ppm).[7b] In the case of the isochroman derivative **9**, however, the difference in chemical shift between the vicinal protons at the 4-position is 0.24 ppm. This value is in good agreement with the difference (0.3 ppm) between the corresponding protons in 2,3-diphenylindene ozonide (**8**).

(7) (a) McCullough, K. J.; Fujisaka, T.; Nojima, M.; Kusabayashi, S. *Tetrahedron Lett.* **1988**, *29*, 3375. (b) Miura, M.; Nojima, M.; Kusabayashi, S. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2909.

(8) The ozonolysis of enol ethers has been shown to proceed via carbonyl oxide intermediates. See: Ref 2m. Wojciechowski, B. J.; Chiang, C.-Y.; Kuczkowski, R. L., *J. Org. Chem.* **1990**, *55*, 1120.

(9) (a) Allinger, N. L. MMP2 (85), QCPE, University of Indiana, Bloomington, IN 47401. (b) Numbering of the model structures corresponds to that adopted in the X-ray structure of the solvent-derived product **9** (see Figure 1).

(10) Keul, H.; Kuczkowski, R. L. *J. Org. Chem.* **1985**, *50*, 3371.

figuration would give the corresponding isomeric primary ozonides **13** and **14**, each of which on subsequent selective cycloreversion[11] would be expected to provide the key carbonyl oxide intermediate in either syn or anti configurations, **15a** and **15b**, respectively. A number of schemes to predict the stereochemical outcome of the cycloreversion of primary ozonides derived from acyclic olefins have been proposed, including those devised by Bauld and Bailey and Kuczkowski (see ref 2a,b and references therein).

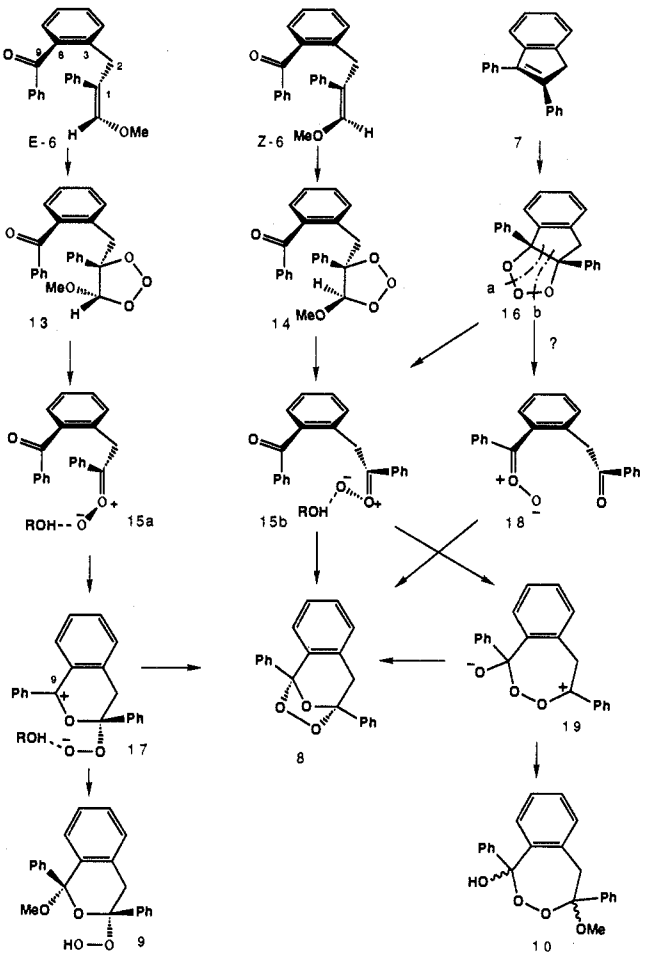
Consistent with the aforementioned predictions, if the phenyl and methoxy groups in **13** are both in axial positions,[12] cycloreversion should result in formation of the syn isomer **15a**. Conversely, if the phenyl and methoxy groups in **14** are in equatorial and axial positions, respectively, then breakdown of the primary ozonide should yield the anti isomer **15b**. Although the formation and cycloreversion of the respective primary ozonides **13** and **14** could be considered to be concerted processes, the subsequent intramolecular recombination reactions between the carbonyl oxide and the carbonyl groups in the above sterically congested systems are more likely to proceed in a stepwise fashion under kinetic control.

The more extended arrangement in the syn isomer **15a** should favor intermolecular coupling reactions to give oligomeric peroxides, particularly in a nonparticipating solvent like carbon tetrachloride. In methanol–methylene chloride, solvation of the carbonyl oxide moiety should enhance the electrophilicity of carbon atom C(1), facilitating its partial capture by the oxygen atom of the adjacent carbonyl group to give the pivotal cyclic intermediate **17**. Subsequent competition between the pendent peroxy group and methanol for capture of the carbocationic center at C(9) in **17** would yield either the ozonide **8** or the methoxy hydroperoxide **9**, respectively. At lower temperatures, when solvent cage effects are more pronounced, solvent capture appears to be very highly favored at the expense of cyclization. As the temperature is increased, however, the latter process becomes increasingly important. The absence of solvent-derived products from ozonolyses of (*E*)-**6** in acetic acid is consistent with acetic acid being a comparatively poor nucleophile. Thus, although the intermediate is probably solvated in an extended conformation, there are only two significant reactions occurring, the stepwise formation of the ozonide **8** competing with intermolecular oligomerization.

Since the ozonolyses of (*Z*)-**6** in methanol did not yield the solvent-derived product **9** in isolable quantities (<5%), it is presumed that these reactions had proceeded primarily through the isomeric carbonyl oxide intermediate **15b**. Not only is the nature of the solvent-derived product different, but the yields of **10** are considerably lower than those of **9** under corresponding reaction conditions (Table I). Although the solvent-derived product **10** was isolated as a single isomer, its relative stereochemistry could not be determined unambiguously from the available spectroscopic data. Since the carbonyl oxide moiety **15b** is generated in close proximity to the benzoyl group within the solvent cage and the formation of 7-membered ring peroxides is more favored than in the corresponding carbocyclic systems because of a reduction in Pitzer strain in the former, it is considered that **10** is formed under kinetic control by a nucleophilic attack of the terminal oxygen of the carbonyl oxide group on the carbonyl carbon of the benzoyl group to give the cyclic intermediate **19**. Subsequent intramolecular ring closure would produce the ozonide **8**, whereas intermolecular capture of methanol would give **10**. The predominance of the ozonide **8** over the cyclic hemiperacetal **10** as the major ozonolysis product from (*Z*)-**6**, even in methanol at low temperature, suggests that intramolecular ring closure is the more rapid process.[13]

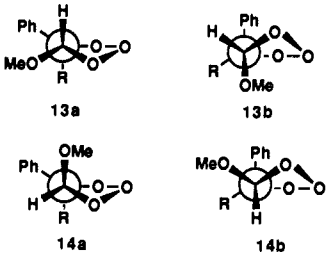
The primary ozonide derived from 2,3-diphenylindene (**7**) should give, via the scission pathways a and b (Scheme II), both possible intermediate carbonyl oxide–carbonyl pairs, **15** and **18**, respectively, with the latter being more favored on account of the possibility of extended charge delocalization into two aromatic systems. In the ozonolyses of several trisubstituted indenes, it has been found, however, that the primary ozonides in most cases tended to decompose selectively by mechanisms analogous to cleavage pathway a.[14] Since no products unambiguously related

Scheme II



(11) In accord with the ozonolysis results from 1-methyl-2-methoxystyrene, the primary ozonides **13** and **14** would be expected to give selectively the carbonyl oxides **15a** and **15b** and methyl formate (see ref 2e). The small quantities of diketone **11** observed in several product mixtures arise from the alternative scission pathway.

(12) The primary ozonides **13** and **14** would be expected to adopt conformations that minimize gauche-type repulsive interactions between the methoxy group and the phenyl and R (representing the remainder of the molecule) groups on the respective adjacent carbon centers. Thus, inspection of molecular models of **13** and **14** suggests that conformations **13b** and **14a** would be favored, respectively, on steric grounds. As a consequence of the



axial methoxy groups, there is the possibility of additional stabilization of **13b** and **14a** by anomeric effects though such effects are not widely reported for five-membered ring systems. See: Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag, New York, 1983; pp 61, 62.

(13) The solvent-derived product could be formed by solvent capture of the carbonyl oxide moiety to yield an intermediate methoxy hydroperoxide followed by an intramolecular cyclization reaction between the hydroperoxy and benzoyl groups. This alternative mechanism is less favored for the following reasons: (i) Following decomposition of the primary ozonide from (*Z*)-**6**, intramolecular cyclizations appear to be significantly faster in this system than intermolecular solvent capture; otherwise, the solvent-derived product **10** would be expected to represent a greater proportion of the product mixture. (ii) If solvent capture had occurred first, the product **10** would probably have been obtained as a mixture of isomers.

to intermediate **18** were isolated, it is inferred that if **18** is formed, it must undergo rapid recombination to ozonide **8**.

The strong similarities in the compositions of the ozonolysis product mixtures derived from keto olefin (*Z*)-**6** and indene **7** under corresponding conditions would be consistent with the notion that they share a common key intermediate, viz., the anti isomer **15b**. This would require that the cycloreversion of the primary ozonide **16** follows scission pathway a in a highly stereoselective fashion. The formation of the anti isomer **15b** could be favored on the grounds that this would minimize steric interactions between the middle oxygen of **16**, which will ultimately become the terminal oxygen of the carbonyl oxide moiety and the neighboring phenyl group in the transition state of the cycloreversion process. Thus, following reorientation of the carbonyl group in **15b**, the system is set up for intramolecular cyclization to the ozonide **8** via either stepwise or concerted processes. The hemiperacetal **10** would be expected to arise in a stepwise fashion as described above. It is unlikely that the isomeric carbonyl oxide intermediate **15a** had been formed to any significant extent since **9** was not isolated from any of the ozonolyses of **7** in methanol. From the available data, it is not possible to determine unequivocably if the ozonide **8** has been formed exclusively by concerted processes, though a preponderance of ozonide **8**, even in methanol at −70 °C, strongly suggests that intramolecular recombination processes in intermediate **15b** if stepwise must be rapid.

In summary, the results of the ozonolysis of keto olefins (*E*)- and (*Z*)-**6** and indene **7** are consistent in general with a conventional Criegee mechanism. The major differences between the product compositions from the isomeric keto olefins (*E*)- and (*Z*)-**6** suggest that (a) the respective carbonyl oxide intermediates are formed predominantly as either the syn or the anti isomer, depending on the configuration of the substrate and (b) syn/anti isomerism of the carbonyl oxide moieties is significantly slower, particularly at low temperatures, than the rates of the various competing intra- and intermolecular processes. The ozonolysis of indene **7** proceeds through a selective scission pathway leading to a carbonyl oxide intermediate that behaves in a chemical fashion similar to that derived from (*Z*)-**6**.

Experimental Section

General Data. ^1H and ^{13}C NMR spectra were obtained in $CDCl_3$ with JNM-PS-100 and JNM-GSX-400 spectrometers (Faculty of Engineering, Osaka University), respectively. Mass data were obtained with a Hitachi RMU-6H spectrometer and infrared spectra with a Hitachi 215 spectrometer.

Ozonolysis Procedure. An alkene, **6** or **7** (1 mmol), dissolved in an appropriate solvent (30 mL), was ozonized by passing a slow stream of ozone (20 mmol of ozone and 50 mL of oxygen/h) through the mixture. The excess ozone was removed by flushing the solution with a slow stream of nitrogen for several minutes.

Preparation of Vinyl Ethers 6. To a 200-mL flask equipped with a mechanical stirrer and maintained under nitrogen was added (methoxymethyl)triphenylphosphonium chloride[11] (6 mmol) and then ether (100 mL). To the mixture was syringed an ether solution of phenyllithium (6 mmol) at −10 °C during 2 min. Subsequently, an ether solution of (2-benzoylmethyl)benzophenone (**11**) (6 mmol) was syringed in 1 min, and the mixture was kept at 20 °C for 20 h. After workup, the crude products were triturated with ether–hexane to remove triphenylphosphine oxide. Then, the organic layer was concentrated, and the products were separated by column chromatography on silica gel.

Elution with benzene gave first the keto olefin (*E*)-**6**: an oil; ^1H NMR δ 3.54 (s, 3 H), 3.84 (s, 2 H), 6.27 (s, 1 H), 6.8–7.8 (m, 14 H); IR 1660, 1600 cm^{-1}; MS *m/e* 328 (M^+). Anal. Calcd for $C_{23}H_{20}O_2$: C, 84.04; H, 6.09. Found: C, 83.67; H, 6.02.

From the second fraction was obtained (*Z*)-**6**: an oil; ^1H NMR δ 3.42 (s, 3 H), 3.66 (s, 2 H), 5.85 (s, 1 H), 6.8–7.9 (m, 14 **H**): IR 1660, 1600 cm^{-1}; MS *m/e* 328 (M^+). Anal. Calcd for $C_{23}H_{20}O_2$: C, 84.04; H, 6.09. Found: C, 83.80; H, 6.00.

The assignment of the stereochemistry of the keto olefin **6** was based on the difference in chemical shift of the vinyl proton between the two isomers. In the ^1H NMR spectra of the very relevant (*E*)- and (*Z*)-1-methyl-2-bromostyrene, the vinyl proton of the *E* isomer appears at a lower field compared with that of the *Z* isomer.[12] The same relation held for (*E*)- and (*Z*)-2-methoxystyrene.

***E* isomer**: ^1H NMR δ 3.60 (s, 3 H), 5.68 (d, J = 13 **Hz**, 1 H), 6.93 (d, J = 13 Hz, 1 H), 6.9–7.2 (m, 5 H).

***Z* isomer**: ^1H NMR δ 3.70 (s, 3 H), 5.10 (d, J = 7 Hz, 1 H), 5.98 (d, J = 7 Hz, 1 H), 6.8–7.5 (m, 5 H).

Ozonolysis of Keto Olefin (*E*)-6 in Acetic Acid–Methylene Chloride. The reaction of keto olefin (*E*)-**6** (1 mmol) with 1.5 equiv of ozone in acetic acid–methylene chloride (30 mL; 1:1, v/v) was undertaken at 0 °C. After ether was added (50 mL), the organic layer was washed with aqueous $NaHCO_3$ and then with saturated brine. The crude products were separated by column chromatography on silica gel.

The first fraction (elution with benzene–hexane (1:1)) contained 2,3-diphenylindene ozonide (**8**): mp 119 °C (from methanol); ^1H NMR δ 3.60 (d, J = 17 Hz, 1 H), 3.83 (d, J = 17 Hz, 1 H), 6.8–7.9 (m, 14 H).[5]

From the second fraction (elution with benzene) was obtained a mixture of polymeric products: a glassy material; ^1H NMR δ 3.3–3.6 (m), 6.6–8.0 (m), the ratio of the peak areas being ~1:7; IR 1660, 1600 cm^{-1}. Anal. Calcd for $(C_{21}H_{16}O_3)_n$: C, 79.74; H, 5.06. Found: C, 80.00; H, 4.90.

Ozonolysis of Keto Olefin (*E*)-6 in Methanol–Methylene Chloride at −70 °C. To a methanol–methylene chloride solution (30 mL; 1:1, v/v) of keto olefin (*E*)-**6** (1 mmol) was passed a slow stream of ozone (1.5 equiv) at 0 °C. After ether was added (50 mL), the organic layer was washed with potassium dihydrogen phosphate and then with saturated brine. The crude products were triturated with ether–hexane to afford 1,3-diphenyl-1-methoxy-3-hydroperoxyisochroman (**9**): mp 145–148 °C (from ethyl acetate–hexane); ^1H NMR δ 3.19 (d, J = 16.5 Hz, 1 H), 3.43 (d, J = 16.5 Hz, 1 H), 3.50 (s, 3 H), 6.9–7.7 (m, 14 H), 8.60 s, 1 H; H–D exchange in D_2O); ^{13}C NMR δ 38.911 (1 C), 51.749 (1 C), 101.999 (1 C), 104.553 (1 C), 125.878–141.802 (18 C); IR 3375 cm^{-1}. Anal. Calcd for $C_{22}H_{20}O_4$: C, 75.84; H, 5.79. Found: C, 75.65; H, 5.78.

Treatment of the isochroman derivative **9** with catalytic amounts of trifluoroacetic acid in methylene chloride or methanol–methylene chloride at 20 °C for 1 h yielded predominantly the ozonide **8**.

The residue was chromatographed on silica gel (elution with benzene) to give the diketone **11**: mp 67–68 °C (from methanol); ^1H NMR δ 4.56 (s, 2 H), 6.7–8.0 (m, 14 H); IR 1690, 1660 cm^{-1}.[5]

Ozonolysis of Keto Olefin (*Z*)-6 in Methanol–Methylene Chloride at −70 °C. The reaction of keto olefin (*Z*)-**6** (1 mmol) and 1.5 equiv of ozone in methanol–methylene chloride (30 mL; 1:1, v/v) was undertaken at −70 °C. The crude products were column chromatographed on silica gel. The first fraction (elution with benzene–hexane (1:1)) contained the ozonide **8**. From the second fraction (elution with benzene) was obtained the diketone **11**. The final fraction (elution with ether–benzene (1:50)) contained 3,7-diphenyl-3-hydroxy-7-methoxy-4,5-benzo-1,2-dioxacycloheptane (**10**): mp 118–119 °C (from ethyl acetate–hexane); ^1H NMR δ 2.91 (d, J = 14 Hz, 1 H), 3.26 (s, 3 H), 4.19 (s, 1 H; H–D exchange in D_2O), 4.23 (d, J = 14 Hz, 1 H), 7,0–7.6 (m, 14 H); ^{13}C NMR δ 46.265 (1 C), 50.564 (1 C), 108.354 (1 C), 110.661 (1 C), 126.532–140–946 (18 C); IR 3400, 1490, 1450, 1140, 1050 cm^{-1}. Anal. Calcd for $C_{22}H_{20}H_{20}O_4$: C, 75.86; H, 5.75. Found: C, 75.42; H, 5.85.

Treatment of the hemiperacetal **10** with catalytic amounts of trifluoroacetic acid in methylene chloride gave quantitatively the ozonide **8**, while the reaction in methanol–methylene chloride resulted in the formation of 3,7-dimethoxy-3,7-diphenyl-4,5-benzo-1,2-dioxacycloheptane (**12**): an oil; ^1H NMR δ 2.63 (d, J = 15 Hz, 1 H), 3.21 (s, 3 H), 3.51 (s, 3 H), 4.05 (d, J = 15 Hz, 1 H), 6.42 (d, J = 6 Hz, 1 H), 6.8–8.1 (m, 13 H); IR 1450, 1120, 1070, 970, 740, 700 cm^{-1}; MS *m/e* 362 (M^+). Anal. Calcd for $C_{23}H_{22}O_4$: C, 76.24; H, 6.08. Found: C, 75.95; H, 6.30.

Ozonolysis of 2,3-Diphenylindene (7) in Carbon Tetrachloride. A solution of **7** (1 mmol) in carbon tetrachloride (30 mL) was treated with 1.5 mmol of ozone. After evaporation of the solvent, the crude products

(14) Ozonolyses of 1-methyl-, 1-phenyl-, and 1-chloro-2,3-diphenylindenes in methanol afforded solvent-derived products that are derived unambiguously from cycloreversion of the respective primary ozonides via scission pathways analogous to a (Scheme II) (see refs 3b, 4, and 7). On the other hand, the corresponding 1-acetoxy derivative gives a solvent-derived product that arises selectively from the alternative cleavage pathway.[7] From the revised structures of the solvent-derived products obtained quantitatively from the ozonolysis of cholesterol derivatives in methanol, it has been concluded that the corresponding intermediate primary ozonides must decompose in a highly selective manner.[15] In all of the above examples there is no unequivocable explanation for the high degree of selectivity observed for the cycloreversion of the each of the corresponding primary ozonides.

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were separated by column chromatography on silica gel. The first fraction (elution with benzene-hexane (1:1)) contained the ozonide **8** (86% yield). From the second fraction (elution with benzene) was isolated the diketone **11** (2% yield).

Crystal data for solvent-participated product 9: $C_{22}H_{20}O_4$, colorless needles, M_r = 348.4, triclinic, a = 8.5201 (9) Å, b = 9.3045 (13) Å, c = 12.0403 (12) Å, α = 71.817 (9)°, β = 88.336 (8)°, γ = 83.044 (10)°, V = 900.1 Å^3, Z = 2, D_c = 1.285 g cm^{-3}, space group $P\bar{1}$ (No. 2) from successful structure solution and refinement, λ = 0.710693 Å, μ(Mo Kα) = 0.82 cm^{-1}, F(000) = 368, data crystal ~0.45 × 0.35 × 0.20 mm.

Structure Solution and Refinement. The intensity data were collected on an Enraf-Nonius CAD-4 diffractometer with use of ω-2θ scanning and graphite-monochromated Mo Kα X-radiation over the region $1.5 < \theta < 23°$. The 1897 observed intensities with $I \geq 3\sigma(I)$ were corrected for Lorentz and polarization, but not for absorption or crystal decay. The structure was solved by direct methods (SHELXS86[13]) and refined by use of full-matrix least-squares techniques (SHELX76[13]) with anisotropic temperature factors for the non-hydrogen atoms. All the hydrogen atoms were located on a difference Fourier map and included in the refinement process on idealized positions (C-H = 0.95 Å). The phenyl and methyl groups were treated as idealized rigid groups. At convergence, the conventional and weighted R factors ($w^{-1} = [\sigma^2(F) + 0.000386(F^2)]$) were 0.040 and 0.052, respectively. The final difference Fourier map contained no features greater than ±0.15 e Å^{-3}.

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Registry No. *E*-**6**, 131618-93-4; *Z*-**6**, 131618-94-5; **7**, 5324-00-5; **8**, 131618-95-6; **9**, 131618-96-7; **10**, 131618-97-8; **11**, 53067-91-7; **12**, 131618-98-9.

Supplementary Material Available: Tables of atomic fractional coordinates, anisotropic vibration parameters, and torsion angles (3 pages); listing of observed and calculated structure factors (12 pages). Ordering information is given on any current masthead page.

Stereoselective Intermolecular Radical Additions to Amide-Substituted Alkenes

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Abstract: The free-radical addition of carbon radicals to two alkenes substituted with chiral pyrrolidine amides has been studied. The two alkenes studied were both amides of 2,5-dimethylpyrrolidine, available as either the *R,R* or *S,S* enantiomer from D- or L-alanine. One alkene studied was the unsymmetrical monoamide derived from 4-oxo-2-pentenoic acid (**1**), while the other substrate examined was the diamide of fumaric acid, **2**. Hexyl, cyclohexyl, and *tert*-butyl radical addition to the amide of 4-oxo-2-pentenoic acid (**1**) gave approximately equal amounts of addition at the carbonyl and amide ends of the alkene. The two stereoisomeric products formed from addition at the carbonyl end were formed in nearly 1:1 product ratio while the products formed by addition at the amide end were formed in ratios as high as 40:1 (*tert*-butyl addition at 0 °C). Addition of cyclohexyl or *tert*-butyl radical to the fumaric diamide gives essentially only one stereoisomer, (diastereomeric ratio 50:1 and 80:1 at room temperature). This approach provides the highest reported stereoselectivity for radical addition to an acyclic chiral alkene. Furthermore, a rationale for the diastereoselectivity is presented that suggests that the amide selectivity is steric in origin and will be general.

Recent advances in the understanding of effects that influence chemo- and regioselectivities of radical reactions have dramatically increased the use of free-radical chemistry in organic synthesis.[1] The formation of C-C bonds by radical additions to alkenes is one of the most synthetically useful reactions that free radicals undergo and new radical chain sequences involving the formation of C-C bonds have greatly expanded the utility of this process.[2-7] Steric and polar effects (and to a lesser extent, radical stabilization) play important roles in addition reactions, and chemo- and regioselectivities of radical additions can be predicted and understood on the basis of these effects.[8-11] Unfortunately, the factors controlling stereochemistry in radical addition for acyclic radicals and for acyclic alkenes are poorly understood.[12] This limitation restricts the use of radicals in C-C bond forming reactions when compared to concerted reactions and reactions utilizing other

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