bromide (13.75 and −2.0 ppm) and the cyclopentadiene (133.04, 132.55, and 41.63 ppm) and appearance of the cyclopentadienide (104.9 ppm) and ethane (6.56 ppm) were monitored in ^{13}C NMR spectra of the solution. After 20 h of heating at about 45 °C, the reaction was nearly complete. Allyl bromide (12.1 g, 0.1 mol) was added; the solution warmed slightly, and precipitate gradually formed. After about 1 h, the ^{13}C NMR spectrum of the supernatant solution showed the disappearance of the cyclopentadienylmagnesium bromide and the residual ethylmagnesium bromide, the presence of the resonances of 1-pentene, and the appearance of a new set of resonances (see Table I) assigned to 1-allyl-1,3-cyclopentadiene. After 2 days at room temperature, an additional set of peaks attributed to 2-allyl-1,3-cyclopentadiene had grown to comparable size. A portion of the solution was worked up by addition of water and extraction with pentane. The pentane extract was washed with water and saturated salt solution, dried (Na_2SO_4), and distilled under vacuum (about 10 mmHg). The material distilling below 30 °C, collected on an ice bath, had a ^{13}C NMR spectrum identical with the mixture of allylcyclopentadiene isomers.[8] The remainder of the solution was treated with excess ethylmagnesium bromide. After about 2 days of gentle heating (35–40 °C), about half of the allylcyclopentadiene had reacted, and a new set of resonances assigned to allylcyclopentadienylmagnesium bromide was present (see Table I). A similar spectrum was obtained by treatment of the distilled allylcyclopentadiene mixture with ethylmagnesium bromide.

Reaction of 5-(Chloromethyl)norbornene with Sodium. In a reaction vessel with a glass stirring paddle, sodium metal (0.97 g, 42 mmol) and 4 mL of *n*-hexadecane were heated to 110 °C. Over a period of 20 min, 5-(chloromethyl)norbornene (3 mL, 20 mmol) was added dropwise. After an additional hour, the temperature was dropped to 80–90 °C, and volatile material was distilled to a cold trap under vacuum (10 mmHg). Most of the residual liquid was removed and added to water for hydrolysis. *tert*-Butyl alcohol was added to the remaining sodium, and the solvent and suspended material were again removed and hydrolyzed. The volatile products were examined by GC and ^{13}C NMR, as described above for reaction products from the Grignard reagent. Compounds **1**-H, **2**-H, **3a**-H, **3b**-H, **4**-H, and **6**-H were identified, but there was no indication of the presence of **5a**-H or **5b**-H in any of the product fractions.

Acknowledgment. We are grateful to Dr. Suzanne Wehrle and Frank Laib for assistance and advice with NMR and mass spectra, to K. Partridge for assistance in synthetic work, and to the Petroleum Research Fund, administered by the American Chemical Society, and to the Graduate School of the University of Wisconsin—Milwaukee for support of portions of this work.

Ruthenium(II)-Catalyzed Reactions of 1,4-Epiperoxides

Masaaki Suzuki,† Hiroaki Ohtake,† Yoshimi Kameya,† Nobuyuki Hamanaka,‡ and Ryoji Noyori*,†

Department of Chemistry, Nagoya University, Chikusa, Nagoya 464, Japan, and Minase Research Institute, Ono Pharmaceutical Company, Shimamoto, Osaka 618, Japan

Received May 1, 1989

The behavior of 1,4-epiperoxides in the presence of transition-metal complexes is highly dependent on the structures of the substrates and the nature of the metal catalysts. Reaction of saturated epiperoxides such as 1,3-epiperoxycyclopentane, 1,4-epiperoxycyclohexane, or dihydroascaridole catalyzed by $RuCl_2(PPh_3)_3$ in dichloromethane gives a mixture of products arising from fragmentation, rearrangement, reduction, disproportionation, etc. Prostaglandin H_2 methyl ester undergoes clean and stereospecific fragmentation to afford methyl (5*Z*,8*E*,10*E*,12*S*)-12-hydroxy-5,8,10-heptadecatrienoate and malonaldehyde. Bicyclic 2,3-didehydro 1,4-epiperoxides give the *syn*-1,2:3,4-diepoxides by the same catalyst. The monocyclic analogues are transformed to a mixture of diepoxides and furan products. The stereochemical outcome of the epoxide formation reflects unique differences in the ground-state geometry of the starting epiperoxide substrates. $FeCl_2(PPh_3)_2$ serves as a useful catalyst for the skeletal change of sterically hindered bicyclic 2,3-didehydro 1,4-epiperoxides to the *syn*-diepoxides. In addition, the Fe complex best effects the conversion of 1,4-unsubstituted 2,3-didehydro epiperoxides to furans. The Ru-catalyzed reactions are interpreted in terms of the intermediacy of inner-sphere radicals formed by atom transfer of the Ru(II) species to peroxy substrates, in contrast to the Fe-catalyzed reactions proceeding via free, outer-sphere radicals generated by an electron-transfer mechanism.

1,4-Epiperoxides (endoperoxides) have become increasingly significant as synthetic[1] and biosynthetic[2] intermediates. The diverse chemical behavior induced by the O–O bond cleavage is bewitching.[1] Mild and selective decomposition of the epiperoxides provides a synthetically useful tool for the site-specific 1,4-dioxygenation of 1,3-diene carbon frameworks.[1,3] Also, an opportunity for the interpretation of biosynthetic mechanisms may be given by chemical simulation, particularly with well-defined metallic reagents.[1g] In light of this, detailed studies have been done on the behavior of 1,4-epiperoxides in the presence of various kinds of transition-metal salts or complexes[4,5] as well as under thermal and photochemical

† Nagoya University.
‡ Ono Pharmaceutical Co.

(1) (a) Denny, R. W.; Nickon, A. *Org. Reac. (N.Y.)* **1973**, *20*, 133. (b) Nakanishi, K. In *Natural Products Chemistry*; Nakanishi, K., Goto, T., Ito, S., Natori, S., Nozoe, S., Eds.; Academic Press: New York, 1975; Vol. 2, Chapter 12. (c) Wasserman, H. H.; Murray, R. W. *Singlet Oxygen*; Academic Press: New York, 1979. (d) Balci, M. *Chem. Rev.* **1981**, *81*, 91. (e) Wasserman, H. H.; Ives, J. L. *Tetrahedron* **1981**, *37*, 1825. (f) Frimer, A. A. In *The Chemistry of Peroxides*; Patai, S., Ed.; Wiley: New York, 1983; Chapter 7. (g) Saito, I.; Nittala, S. S. In *The Chemistry of Peroxides*; Patai, S., Ed.; Wiley: New York, 1983; Chapter 11.

(2) (a) Van Dorp, D. A. In *Chemistry, Biochemistry and Pharmacological Activity of Prostanoids*; Roberts, S. M., Scheinmann, F., Eds.; Pergamon Press: Oxford, England, 1979; pp 233–242. (b) Samuelsson, B. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 805.

(3) Suzuki, M.; Oda, Y.; Noyori, R. *J. Am. Chem. Soc.* **1979**, *101*, 1623.

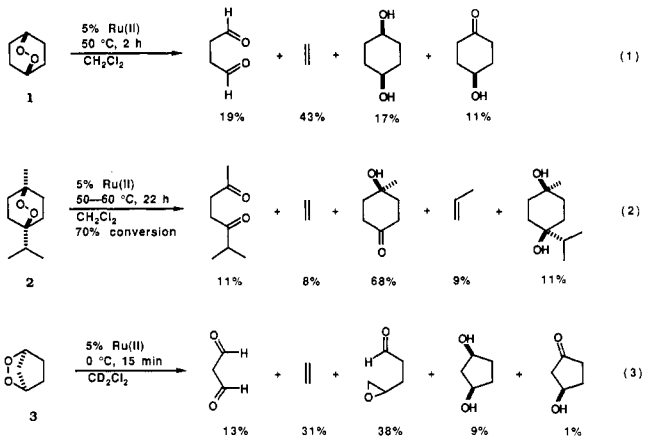
0022-3263/89/1954-5292$01.50/0 © 1989 American Chemical Society

conditions.[6] In particular, the Fe(II)-induced decomposition has been investigated extensively[1g,4e,f,8b] as a model reaction of the bioconversion of the prostaglandin (PG) endoperoxides[7,8] and other significant natural intermediates.[4e]

We have been intrigued by the use of the Ru(II)–tertiary phosphine complexes. The central metal is a member of the iron triad,[9] and such complexes are characterized by their capability to induce a reaction to occur via a one-electron-exchange mechanism[9,10] and, unlike commonly used inorganic Fe(II) salts, possess high solubility in aprotic organic solvents. We anticipated finding unique selectivities unobserved with the existing decomposition methods. In addition, some reactions with Fe(II)- or Os(II)–phosphine complexes are referenced to compare the selectivity profiles of these members of the iron triad.[11]

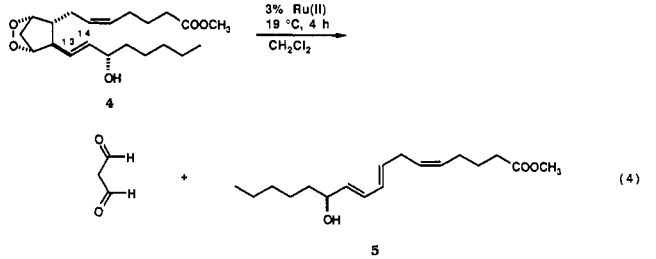
Results and Discussion

Ruthenium(II)-Catalyzed Reaction of 1,4-Epiperoxides. Tris(triphenylphosphine)ruthenium dichloride acts as an effective catalyst for decomposition of 1,4-epiperoxides under aprotic, homogeneous, and neutral conditions. When epiperoxides were treated with a catalytic amount (3–5 mol %) of $RuCl_2(PPh_3)_3$ in dichloromethane, the O–O bond was cleaved to give a mixture of products arising from fragmentation, reduction, and disproportionation. Some examples are given by eq 1–3. The reactivity is sensitive to the ring size and substitution



patterns. Simple 1,4-epiperoxycyclohexane (1) underwent smooth decomposition at 50 °C (eq 1), whereas the reaction of dihydroascaridole (2) proceeded slowly at this temperature (eq 2). The alkyl substituents at the bridgehead positions retard the reaction and also affect the product distribution. Strained 1,3-epiperoxycyclopentane (3) readily decomposed at 0 °C in the presence of the Ru(II) catalyst to afford a complicated mixture containing malonaldehyde and ethylene (eq 3). The decomposition patterns of eq 1–3 are different from those of the thermolysis or the reaction with $FeSO_4$ in protic solvents. Thermolysis of 3 in CD_2ClCD_2Cl at 73 °C is known to give a mixture of 4,5-epoxypentanal (54%), levulinaldehyde (42%), and 2,3-dioxabicyclo[2.2.1]heptane (4%).[12] Decomposition of 2 with $FeSO_4$ in aqueous ethanol affords 4-hydroxy-4-methylcyclohexanone (93%) and propane (99%).[4b]

When PGH_2 methyl ester (4) was treated in dichloromethane with 3 mol % of $RuCl_2(PPh_3)_3$ at 19 °C, smooth fragmentation took place, and methyl (5*Z*,8*E*,10*E*,12*S*)-12-hydroxy-5,8,10-hepatdecatrienoate (5, HHT methyl ester) was obtained as the sole isolable product (eq 4). The



reaction is stereospecific in nature,[13] and the trans relationship of the two side-chains in the starting material, 4, is reflected in the 8*E* product, 5. No positional or geometrical isomerization of the carbon–carbon double bond was observed under the reaction conditions.[14] Production of malonaldehyde was confirmed by the thiobarbituric acid test.[15] No methyl esters of primary PGs such as PGE_2, PGD_2, $PGF_{2\alpha}$, or thromboxane B_2 (hydrolysis product of

(4) For catalysis with Fe(II) salts, see: (a) Brown, D.; Davis, B. T.; Halsall, T. G.; Hands, A. R. *J. Chem. Soc.* **1962**, 4492. (b) Brown, D.; Davis, B. T.; Halsall, T. G. *Ibid.* **1963**, 1095. (c) Kanno, H.; Schuller, W. H.; Lawrence, R. V. *J. Org. Chem.* **1966**, *31*, 4138. (d) Hamberg, M.; Samuelsson, B. *Proc. Natl. Acad. Sci. U.S.A.* **1974**, *71*, 3400. (e) Herz, W.; Ligon, R. C.; Turner, J. A.; Blount, J. F. *J. Org. Chem.* **1977**, *42*, 1885. (f) Turner, J. A.; Herz, W. *Ibid.* **1977**, *42*, 1895. (g) *Ibid.* **1977**, *42*, 1900. (h) Porter, N. A.; Mebane, R. C. *Tetrahedron Lett.* **1982**, *23*, 2289; Herz, W.; Juo, R.-R. *J. Org. Chem.* **1985**, *50*, 618.

(5) For the catalysis with metals other than Fe, see: (a) [Cu(I) and Cu(II)] Porter, N. A.; Nixon, J. R.; Gilmore, D. W. *ACS Symp. Ser.* **1978**, *No. 69*, 89. (b) [Ti(III)] Paget, H. *J. Chem. Soc.* **1938**, 829. See also ref 4b. (c) [V(IV)], ref 4e. (d) [Pb(IV)] Schenck, G. O. *Angew. Chem.* **1952**, *64*, 12. (e) [Sn(II)] Natsume, H.; Muratake, H. *Tetrahedron Lett.* **1979**, 3477, and references therein. (f) [Co(II)] Boyd, J. D.; Foote, C. S.; Imagawa, D. K. *J. Am. Chem. Soc.* **1980**, *102*, 3641. Sutbeyaz, Y.; Secen, H.; Balci, M. *J. Org. Chem.* **1988**, *53*, 2312. (g) Balci, M.; Aklbulut, N. *Tetrahedron* **1985**, *41*, 1315. (h) [Rh(I)] Hagenbach, J.-P.; Vogel, P. *J. Chem. Soc., Chem. Commun.* **1980**, 1062; Hagenbach, J.-P.; Birbaum, J.-L.; Metral, J.-L.; Vogel, P. *Helv. Chim. Acta* **1982**, *65*, 887. (i) [Pd(0)] Suzuki, M.; Noyori, R.; Hamanaka, N. *J. Am. Chem. Soc.* **1981**, *103*, 5606. Suzuki, M.; Oda, Y. Noyori, R. *Tetrahedron Lett.* **1981**, *22*, 4413.

(6) Carless, H. A. J.; Atkins, R.; Fekarurhobo, G. K. *Tetrahedron Lett.* **1985**, *26*, 803, and references therein. For the acid-catalyzed cleavage, see: Yoshida, M.; Miura, M.; Kusabayashi, S. *J. Am. Chem. Soc.* **1983**, *105*, 6279; Jefford, C. W.; Jaggi, D.; Boukouvalas, J.; Kohmoto, S. *Ibid.* **1983**, *105*, 6497; Jefford, C. W.; Rossier, J.-C.; Kohmoto, S.; Boukouvalas, J. *J. Chem. Soc., Chem. Commun.* **1984**, 1496.

(7) (a) Turner, J. A.; Herz, W. *Experientia* **1977**, *33*, 1133. (b) Porter, N. A. In *Free Radicals In Biology*; Pryor, W. A., Ed.; Academic Press: New York, 1980; Vol. IV, Chapter 8. (c) Hermann, G.; Ruf, H. H.; Ullrich, V. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 487. (d) Takahashi, K.; Kishi, M. *J. Chem. Soc., Chem. Commun.* **1987**, 722. (e) *Tetrahedron Lett.* **1988**, *29*, 4595.

(8) For the chemical models other than the reaction with Fe(II) salts, see ref 5i and: Zagorski, M. G.; Salomon, R. G. *J. Am. Chem. Soc.* **1980**, *102*, 2501; *Ibid.* **1982**, *104*, 3498; *Ibid.* **1984**, *106*, 1750. Salomon, R. G.; Miller, D. B.; Zagorski, M. G.; Coughlin, D. J. *Ibid.* **1984**, *106*, 6049. Wilson, R. M.; Schnaap, K. A.; Merwin, R. K.; Ranganathan, R.; Moats, D. L.; Conrad, T. T. *J. Org. Chem.* **1986**, *51*, 4028.

(9) Ru(II)–porphyrin complexes are known to mimic heme proteins: Farrell, N.; Dolphin, D. H.; James, B. R. *J. Am. Chem. Soc.* **1978**, *100*, 324.

(10) Matsumoto, H.; Nakano, T.; Takatsu, K. Nagai, Y. *J. Org. Chem.* **1978**, *43*, 1734, and references therein. See also a review: Jardine, F. H. In *Progress in Inorganic Chemistry*; Lippard, S. J., Ed.; Wiley: New York, 1984; Vol. 31, pp 265–370.

(11) Preliminary reports: Suzuki, M.; Noyori, R.; Hamanaka, N. *J. Am. Chem. Soc.* **1982**, *104*, 2024; Noyori, R.; Suzuki, M. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 847.

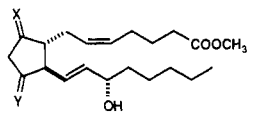
(12) Salomon, R. G.; Salomon, M. F.; Coughlin, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 660. For thermolysis of 1, see (a) Couglin, D. J.; Salomon, R. G. *J. Am. Chem. Soc.* **1979**, *101*, 2761. (b) Bloodworth, A. J.; Baker, D. S. *J. Chem. Soc., Chem. Commun.* **1981**, 547. For thermolysis of 2, see (c) Moore, C. G. *J. Chem. Soc.* **1951**, 254. For $Co^{II}TPP$-catalyzed decomposition of bicyclic saturated 1,4-epiperoxides, see ref 5g.

(13) Treatment of PGH_2 with $FeCl_2$ in aqueous solution was claimed to give (5*Z*,8*E*,10*E*,12*S*)-12-hydroxy-5,8,10-heptadecatrienoic acid in 40–50% yield without any definite stereochemical evidence.[4d]

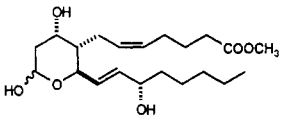
(14) Thermodynamic ratio of (*E*,*E*)-, (*E*,*Z*)-, and (*Z*,*Z*)-2,4-hexadiene is 65.5:30.7:3.8 at 20.2 °C: Doring, C. E.; Hauthal, H. G. *J. Prakt. Chem.* **1964**, *24*, 27.

(15) Waravdekar, V. S.; Saslaw, L. D. *J. Biol. Chem.* **1959**, *234*, 1945.

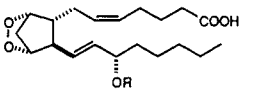
thromboxane A_2 (12)) (6–9) were detected in the reaction mixture.[16] This result should be compared with the fact that in biological systems PG endoperoxides, PGH_2 (10) or PGG_2 (11), give a mixture of thromboxane A_2 (12) and HHT by the action of thromboxane synthetase.[17]



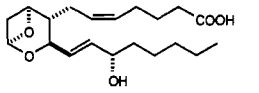
6, X = O; Y = α-OH; β-H
7, X = α-OH; β-H; Y = O
8, X = Y = α-OH; β-H



9



10, R = H
11, R = OH

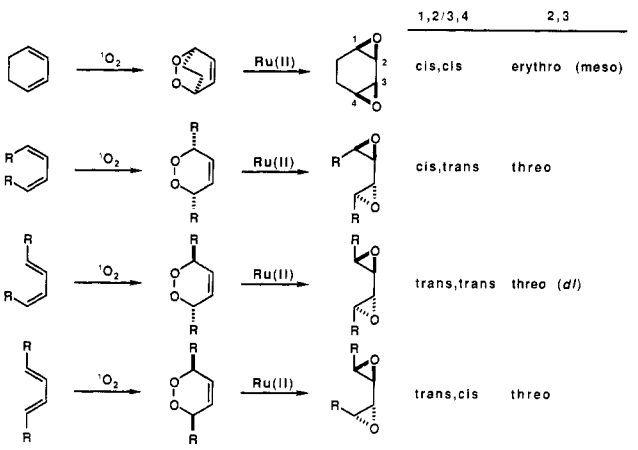


12

Ruthenium(II)-Catalyzed Reaction of 2,3-Didehydro 1,4-Epiperoxides. The reaction usually takes place near or below room temperature by using a catalytic amount of $RuCl_2(PPh_3)_3$ in dichloromethane. Solvents such as benzene, toluene, dimethoxyethane, and acetone are also usable for the reaction. The presence of the C(2)–C(3) double bond alters the reaction pathway, as exemplified in Table I. The catalyzed rearrangement of the bicyclic substrates (entries 1–4 and 9) occurs in a highly selective manner to give the corresponding *syn*-diepoxides.[5f] The reaction of ascaridole (17) proceeded rather sluggishly and gave the diepoxide together with some reduction and fragmentation products (entry 6).[18] We found that $FeCl_2(PPh_3)_2$ (soluble in dichloromethane) was a useful catalyst for conversion of this substrate to the diepoxide 45 (entry 7). The substrates having two alkyl substituents at the bridgehead positions were rather unreactive to the Ru catalysts but were efficiently converted to the diepoxides by this catalyst (see also entry 8).[19,20] Thus, a range of bicyclic 1,4-epiperoxides are convertible selectively to the *syn*-diepoxides by the adequate choice of the transition-metal phosphine complexes.[5f]

Reaction of monocyclic epiperoxides with $RuCl_2(PPh_3)_3$ gave mixtures of the diepoxide and furan products. The 1,4-unsubstituted epiperoxide gave the furan derivative predominantly (entry 20). As expected, the reactivity was decreased by increase of the bulkiness of the C(1) and C(4) substituents. Lowering the reaction temperature in the decomposition of epiperoxide **21** increased the **54**/**55** and diepoxide/furan ratios (entries 11 and 12). $[RuCl_2(PPh_3)_2]_n$ revealed similar reactivity and comparable diastereoselectivity. Other Ru(II) catalysts such as $Ru(OAc)_2(PPh_3)_2$, $RuCl_2(py)_2(PPh_3)_2$, *cis*- and *trans*-$RuCl_2(CH_3CN)_2(PPh_3)_2$, and Ru(CO)(octaethylporphine) were also employed under comparable conditions. Of these

Scheme I. Stereochemical Relationship in the Diene to Diepoxide Conversion



$RuCl_2(py)_2(PPh_2)_2$ decreased the diepoxide/furan ratio to some extent. It is worth noting that the epiperoxide to diepoxide conversion proceeded with characteristic stereochemical outcome. Thus the epiperoxides **20**–**23** gave stereoselectively the 1,2-*trans*-3,4-*cis*-2,3-*threo*-diepoxides[21] (entries 10–12, 17, and 18), whereas **24** led to the 1,2-*trans*-3,4-*trans*-2,3-*threo*-diepoxide as the major stereoisomer (entry 19). The unique stereochemical course of the Ru(II)-catalyzed reaction leading to 1,2;3,4-diepoxides can cleanly be correlated with the geometry of the starting dienes as shown in Scheme I. Cyclic (*Z*,*Z*)-1,3-dienes lead to 1,2-*cis*-3,4-*cis*-2,3-*erythro*-[21] (or *meso*-) diepoxides via bicyclic epiperoxides, whereas open-chain (*Z*,*Z*)-1,3-dienes go to 1,2-*cis*-3,4-*trans*-2,3-*threo*-diepoxides via 1,4-cis-disubstituted epiperoxides. In a like manner, open-chain (*E*,*Z*)-dienes are convertible to 1,2-*trans*-3,4-*trans*-2,3-*threo*- (or *dl*-) diepoxides and open-chain (*E*,*E*)-dienes to 1,2-*trans*-3,4-*cis*-2,3-*threo*-diepoxides as visualized in Scheme I. From these correlations, two marked differences between cyclic and open-chain substrates are recognized. First, the incorporation of two epoxy groups to the cyclic dienes proceeds with retention of the configurations of two double bonds, but the open-chain diene substrates proceed with *inversion* of the geometry of either of the two double bonds. Second, from the cyclic 1,3-dienes, the 2,3-erythro configuration is introduced in the diepoxides, whereas the 2,3-threo configurations are created from all three types of open-chain substrates.

Entries 13–16 in Table I compare thermolysis of **21** and the catalyses with the iron triad and Co(II) complexes. A similarly high stereoselectivity was observed in the reaction using Co(II)–tetraphenylporphine[5f] or $OsCl_2(PPh_3)_2$ catalyst (entries 15 and 16).[22] In contrast, such stereoselectivity diminished in thermolysis (entry 13) and, notably, in the catalysis of the Fe(II) complex, the 2,3-erythro product became dominant over the threo isomer (entry 14). $FeCl_2(PPh_3)_2$ was a good catalyst for the conversion of monocyclic 1,4-unsubstituted epiperoxides to furans (entry 21). The conversion proceeded via hydroxy enones of type **27** and their hemiacetals **28**. Indeed, the reaction of the epiperoxide **26** (see entry 21 in Table I) at −78 °C allowed ^1H NMR detection of the unstable hemiacetal intermediate **28** (a mixture of regioisomers, R, R′ = H, 3,4-epoxy-4-

(16) Reaction of **4** catalyzed by $Pd(PPh_3)_4$ gives a mixture of methyl esters of PGD_2 (17%), PGE_2 (11%), $PGF_{2\alpha}$ (41%), and HHT (4%).[5i]

(17) For biosynthetic production of HHT from PGG_2 or PGH_2, see: Nugteren, D. H.; Christ-Hazelhof, E. In *Advances in Prostaglandin and Thromboxane Research*; Samuelsson, B., Ramwell, P. W., Paoletti, R., Eds.; Raven Press: New York, 1980; pp 129–137. Haurand, M.; Ullrich, V. *J. Biol. Chem.* **1985**, *260*, 15059.

(18) Diepoxide **46** is obtained in 76% yield with Co(II)–*meso*-tetraphenylporphine catalyst.[5f]

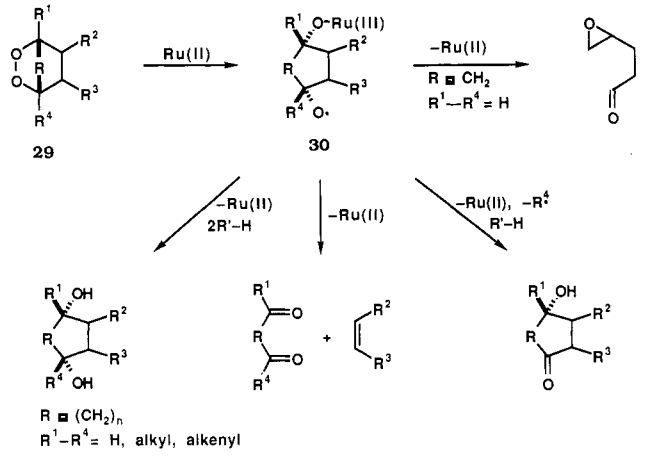
(19) Decomposition of ascaridole (**17**) with $FeSO_4$ (0.37 equiv) in a mixture of THF and water at 35 °C for 2 h gives the diol derivative (28%) via hydrolysis of the diepoxide.[4a]

(20) The reaction of **14** and **15** with the Fe(II)–phosphine catalyst gives a complex mixture.

(21) For reasonable threo/erythro nomenclature, see: Noyori, R.; Nishida, I.; Sakata, J. *J. Am. Chem. Soc.* **1981**, *103*, 2106. Noyori, R.; Nishida, I.; Sakata, J.; Nishizawa, M. *Ibid.* **1983**, *105*, 1598.

(22) $CoCl(PPh_3)_3$ or $CoCl_2(PPh_3)_3$ did not catalyze decomposition of epiperoxides at 20 °C in CH_2Cl_2. The reaction of **21** with $[CuCl(PPh_3)]_4$ at 20 °C in CH_2Cl_2 gave a complex mixture.

Scheme II



methylpentyl). These products, showing signals at δ 4.5–4.7 and 5.8, underwent dehydration at elevated temperature to give the furan product.[4g]

27 28

Mechanistic Considerations. The reaction of 1,4-epiperoxides with the Ru(II) catalyst obviously proceeds via radical pathways.[10] We consider that an inner-sphere radical species[10] is involved in the reaction. Thus all of the major products in eq 1–4 are reasonably understood in terms of the mechanism outlined in Scheme II.[23] The inner-sphere radical, depicted as **30**, resulting from the atom-transfer reaction between Ru(II) species and epiperoxide **29** serves as the key intermediate in this catalyzed decomposition. Depending on the substitution pattern, **30** undergoes various one-electron-exchange transformations. The oxy radical **30** can abstract hydrogen atoms from donors present in the reaction system to afford the 1,4-diol product. Here secondary alcohols serve as a good hydrogen donor; the Ru(II)-catalyzed reaction of **1** with added 2-propanol (10 equiv) produced acetone in 39% yield.[26] Therefore the hydroxy ketone products may be formed from the initially produced 1,4-diols.[27] The radical **30** may collapse into the corresponding dialdehyde or ketone and an olefinic residue. The ease with which the fragmentation takes place is highly dependent on the nature of R^2 and R^3. A highly selective fragmentation of this type has been demonstrated with a PG endoperoxide (eq 4), where the presence of the two side chains, particularly the ω side chain, which contains the C(13)–C(14) double

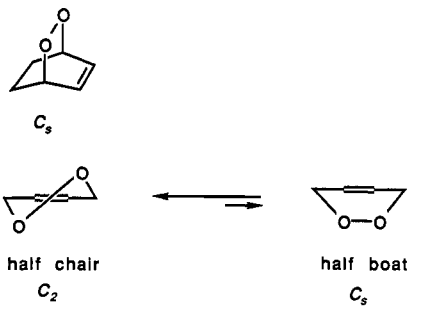
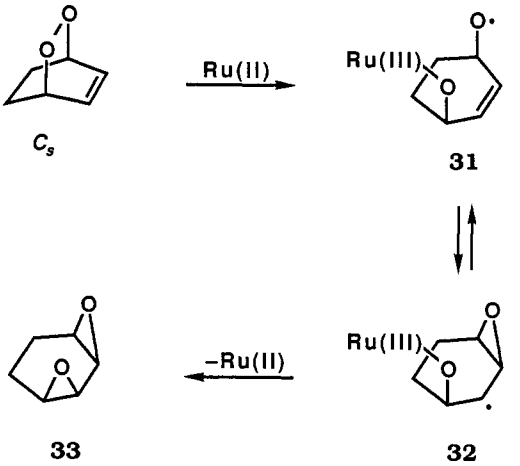
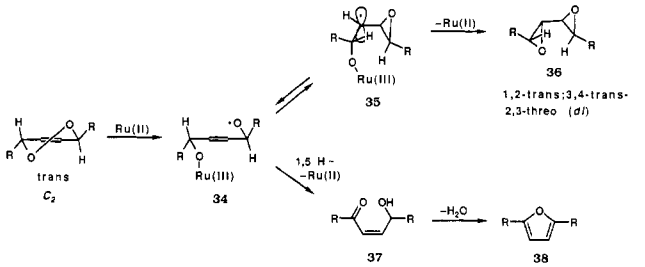


Figure 1. Geometries of bicyclic and monocyclic epiperoxides.

Scheme III. Mechanism of the Diepoxide Formation in the Bicyclic System



Scheme IV. Mechanism of the Reaction of Trans-Disubstituted Epiperoxides



bond (PG numbering), facilitates the oxy radical induced fragmentation to form the triene **5** and malonaldehyde.[28] Thus, the Ru-catalyzed fragmentation reaction of **4** is much cleaner than that of **3** (eq 3). This demonstrates a limitation on the utility of simple epiperoxides such as **3** as PGH or PGG model compounds.

The oxy radical intermediate generated from 2,3-didehydro 1,4-epiperoxide can interact with a carbon–carbon double bond present in the substrate, leading to the diepoxide products. We consider that the unique stereoselectivities obtained in Scheme I originate mainly from the differences in ground-state geometry of the epiperoxide substrates and the conformational mobility of the radical intermediates generated in the reaction. The bicyclic epiperoxides possess the structure of constrained C_s symmetry.[29] For the flexible monocyclic peroxides, however, two conformational isomers, a half-chair conformer having

(23) $RuCl_2(PPh_3)_3$ dissociates triphenylphosphine to some extent in CH_2Cl_2 to form $[RuCl_2(PPh_3)_2]_2$ and establishes an equilibrium mixture such as $2RuCl_2(PPh_3)_3 \rightleftharpoons [RuCl_2(PPh_3)_2]_2 + 2PPh_3$.[24,25]

(24) Hoffman, P. R.; Caulton, P. R. *J. Am. Chem. Soc.* **1975**, *97*, 4221.

(25) Pri-Bar, I.; Buchman, O.; Schumann, H.; Kroth, H. J.; Blum, J. *J. Org. Chem.* **1980**, *45*, 4418, and references therein.

(26) In the absence of epiperoxides, secondary alcohols are inert to the Ru(II) complex under the present reaction conditions. Treatment of 2-propanol with 5 mol % of $RuCl_2(PPh_3)_3$ (CH_2Cl_2, 25 °C/16 h and then 50 °C/2.5 h) did not produce acetone; addition of 2-cyclohexenone to this system did not afford cyclohexanone either.

(27) The phosphine does react with cyclic peroxides; reaction with saturated epiperoxides produces the diols, whereas reaction with 2,3-unsaturated 1,4-epiperoxides affords 1,3-diene 1,2-epoxides: see Clennan, E. L.; Heah, P. C. *J. Org. Chem.* **1981**, *46*, 4105. However, under the present catalytic conditions, it does not participate in the product formation to any great extent.

(28) The C(5)–C(6) double bond could also stabilize the transition state via homoallylic conjugation. See: Ingold, K. U. *ACS Symp. Ser.* **1978**, *No. 69*, 187.

(29) (a) Brown, R. S. *Can. J. Chem.* **1975**, *53*, 3439. (b) Coughlin, D. J.; Brown, R. S.; Salomon, R. G. *J. Am. Chem. Soc.* **1979**, *101*, 1533.

Table I. Catalytic Decomposition of 2,3-Didehydro 1,4-Epiperoxides with Ru(II)–phosphine and Related Complexes[a]

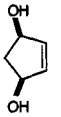
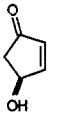
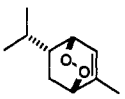
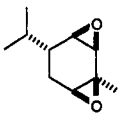
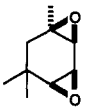
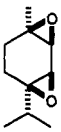
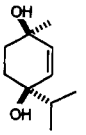
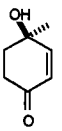
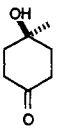
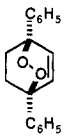
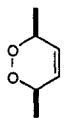
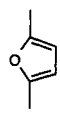
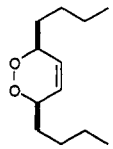
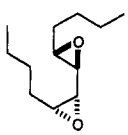
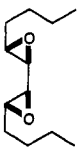
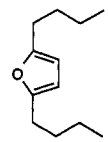
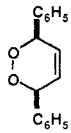
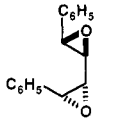
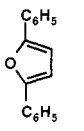
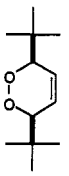
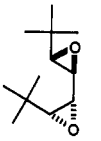
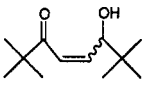
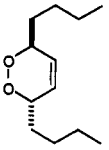
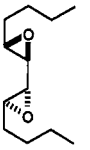
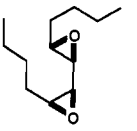
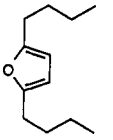
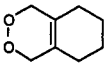
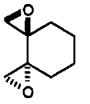
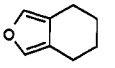
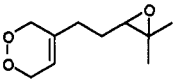
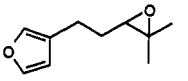
entry	epiperoxide weight, mg (mmol)	conditions: catalyst[b] (mmol)	conditions: CH_2Cl_2, mL	conditions: temp (time), °C (h)	products, % yield[c]		
							
1	**13**, 195 (2.0)	Ru (0.033)	5	−78 (1) and −25 (1)	**40**, 78,[d] 72[e]	**41**, 3[d]	**42**, 5[d]
							
2	**14**, 460 (4.1)	Ru(0.041)	5	0 (0.5) and 10 (0.5)	**43**, 91[e] (57,[d,f] 79[d,g])		
							
3	**15**, 49 (0.29)	Ru (0.011)	2	20 (3)	**44**, 85[e]		
							
4	**16**, 100 (0.65)	Ru (0.012)	2	14 (0.2)	**45**, 97, 94[e]		
5	**16**, 42 (0.27)	Fe (0.006)	2	−78 (2) and −30 (0.5)	**45**, 80[e]		
							 
6	**17**, 34 (0.2)	Ru (0.010)	1.5	25 (42)	**46**, 68[e]	**47**, 17[e]	**48**, 7[e] **49**, 7[e]
7	**17**, 148 (0.88)	Fe (0.053)	1.5	−78 (14)	**46**, 93[d]		
							
8	**18**, 21 (0.08)	Fe (0.004)	2	−78 (9)	**50**, 95[e]		
							
9	**19**, 19 (0.15)	Ru (0.002)	1.5	15 (3.5)	**51**, 98[d] (47,[d,f] 69[d,g])		
							
10	**20**, 151 (1.32)	Ru (0.053)	10	O (1)	**52**, 23	**53**, 3	**54**, 43
							
11	**21**, 25.4 (0.13)	Ru (0.006)	1.4	4 (70)	**55**, 48	**56**, 4	**57**, 38
12	**21**, 31.6 (0.16)	Ru (0.006)	1.5	18 (5)	**55**, 28	**56**, 4	**57**, 58
13	**21**, 29.9 (0.15)	none[h]	1[h]	170 (40)	**55**, 4	**56**, 2	**57**, 73
14	**21**, 24.7 (0.13)	Fe (0.005)	1	−70 (6)	**55**, 6	**56**, 12	**57**, 74
15	**21**, 20.7 (0.10)	Co (0.004)	1	0 (6)	**55**, 24	**56**, 0	**57**, 74
16	**21**, 28.5 (0.14)	Os (0.006)	1	50 (6)	**55**, 38	**56**, 2	**57**, 50
							
17	**22**, 20.6 (0.087)	Ru (0.003)	1	15 (2)	**58**, 44[e]	**59**, 34[e]	

Table I (Continued)

entry	epiperoxide weight, mg (mmol)	conditions: catalyst[b] (mmol)	conditions: CH_2Cl_2, mL	conditions: temp (time), °C (h)	products, % yield[c]		
18	 **23**, 84.3 (0.43)	Ru (0.034)	5	30 (7) and 45 (8)	 **60**, 50[e]	 **61**, 23[e]	
19	 **24**, 14.5 (0.073)	Ru (0.003)	1	30 (10)	 **62**, 30	 **63**, 6	 **57**, 40
20	 **25**, 95.2 (0.68)	Ru (0.027)	5	−78 (3)	 **64**, 1	 **65**, 76	
21	 **26**, 170 (0.92)	Fe (0.020)	2	15 (0.2)	 **66**, 78[e]		

[a] Unless otherwise stated, reaction was carried out in dichloromethane under argon atmosphere. [b] Ru = $RuCl_2(PPh_3)_3$: Fe = $FeCl_2(PPh_3)_2$; Co = Co(II)–tetraphenylporphine; Os = $OsCl_2(PPh_3)_3$. [c] Determined by GLC analysis. [d] Determined by ^1H NMR analysis. [e] Isolated yield after silica gel column chromatography. [f] Thermolysis in dichloromethane at 100–120 °C. [g] Reaction with $LiClO_4$ (9–11 mol %) in dichloromethane at 90–100 °C. [h] Thermolysis in toluene.

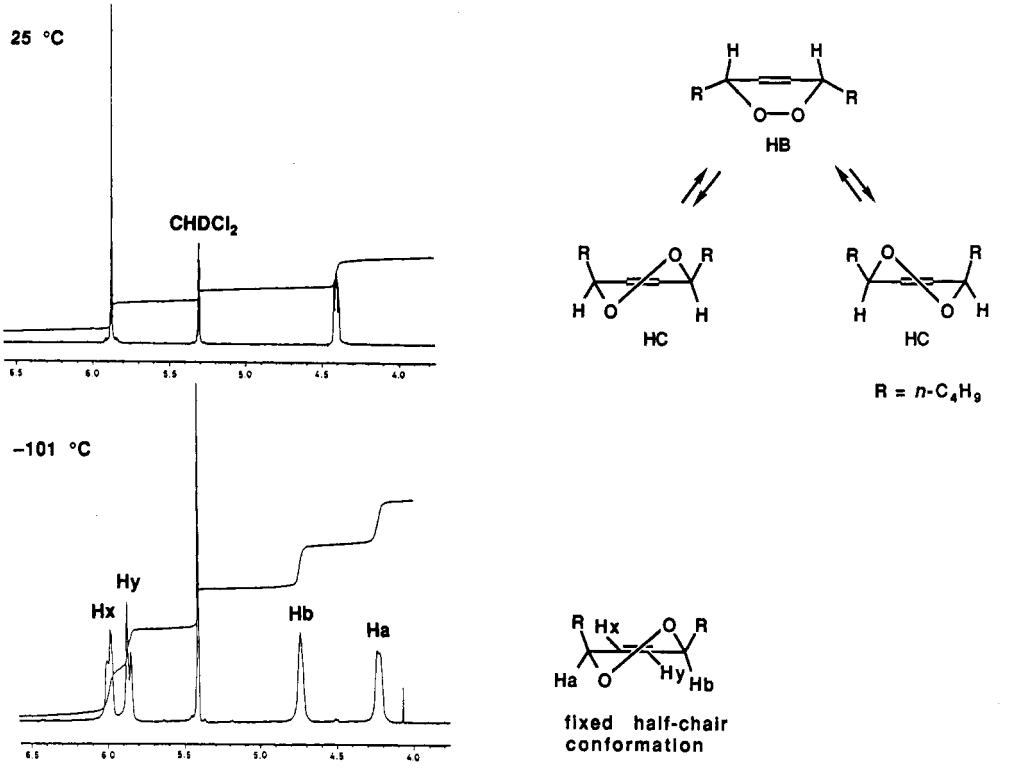


Figure 2. ^1H NMR spectra of *cis*-5,8-epiperoxy-6-dodecene (**21**) (400 MHz, 13:27:60 $CCl_4/CDCl_3/CD_2Cl_2$).

C_2 chirality and a half-boat structure characterized by C_s symmetry, are possible (Figure 1), where the former is evidently preferable.[30,33] The ^1H NMR spectrum of *cis*-5,8-epiperoxy-6-dodecene (**21**), as illustrated in Figure 2, gives two signals due to allylic and vinyl protons at δ 4.40

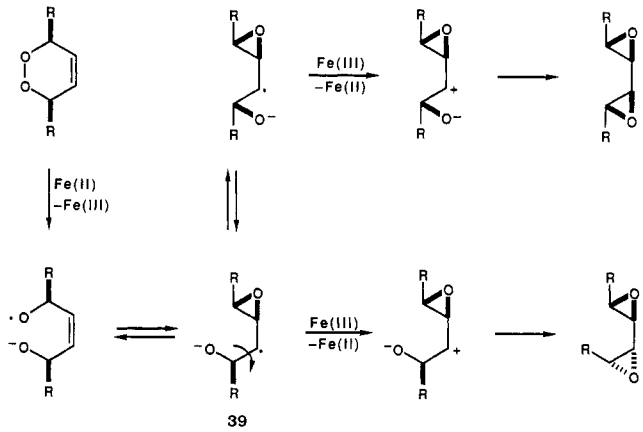
(30) (a) Kondo, T.; Matsumoto, M.; Tanimoto, M. *Tetrahedron Lett.* **1978**, 3819. (b) Kondo, T.; Tanimoto, M.; Matsumoto, M. *Ibid.* **1980**, *21*, 1649.

(31) The same conclusion was obtained for the epiperoxides **20** (−110 °C, CD_2Cl_2), **22** (−126 °C, CD_2Cl_2), **23** (−124 °C, CD_2Cl_2), and **25** (−100 °C, CD_2Cl_2), respectively (see Experimental Section).

and 5.88, respectively, at 25 °C. When the system is cooled to −101 °C, these signals are separated into two sets of two peks at δ 4.23, 4.74 and 5.85, 6.00 with the same integrals. This clearly indicates that the fixation of the conformation takes place at this temperature and only the half-chair conformer exists.[31] In a like manner half-chair conformers are exclusive in the trans-disubstituted epiperoxide **24**, where the conformer having two substituents occupying pseudoequatorial positions is predominant over the diaxial form (5.8:1 ratio judged from signal intensities of the allylic protons at −101 °C).[32] The bicyclic epiperoxides which possess a basic skeleton of constrained C_s symmetry, as seen in Scheme III, generate the reactive radical species **31**, which is forced to cyclize to diepoxide **33**, having the 2,3-erythro or meso structure. Here involvement of the inner-sphere radical intermediates, **31** ⇌ **32**,[5f,11,35] conceivably supresses the side reactions,[36,39] resulting in the selective diepoxide formation. The weak, covalent nature of the Ru(III)–O bond may contribute to the smooth epoxy-ring closure of **32**. On the other hand, monocyclic substrates having the dissymmetric C_2 structure produce the intermediate **34** (Scheme IV). The oxy radical tends to interact reversibly[35] with the carbon–carbon double bond through the least conformational change (least motion pathway) to form the carbon radical species, **35**. Ultimately, **35** undergoes the second, facile epoxy-ring formation to give **36**. The diepoxide has a 1,2-trans-3,4-trans-2,3-threo structure. Alternatively, the flexible structure **34** can undergo the 1,5-hydrogen shift, resulting in the transformation to furan **38** via hydroxy enone **37**. The half-chair conformer of the corresponding 1,4-cis-disubstituted epiperoxide has two diastereotopic oxygens. Its behavior in the presence of Ru catalyst, however, is basically identical with that of the 1,4-trans compounds described above.

In summary, the Ru(II)-catalyzed reactions of 1,4-epiperoxides may involve radical intermediates, but such radical species behave differently from the free radicals formed by photolysis or thermolysis.[6] The Ru atom profoundly affects the stability and reactivity of the radicals through interactions with the oxygen atom, allowing selective transformations under mild conditions. The reactivity is sensitive to steric factors. In thermal and Fe(II) complex catalyzed reactions it has been observed that

Scheme V. Fe(II)-Induced Diepoxide Formation



39

furan is the predominant product. The Fe(II)-induced decomposition, as has been frequently suggested, would involve an outer-sphere, one-electron-transfer mechanism.[4f,5f] Easy decomposition of the sterically hindered substrates with Fe(II) complexes (entries 7 and 8 in Table I) is also consistent with such consideration. Since, as depicted in Scheme V, diepoxide formation requires oxidation of carbon radical **39** to its carbocation,[40] competing stereomutation at the stage of **39** results in nonstereoselective transformation (entry 14 in Table I).

Experimental Section

General Remarks. IR spectra were obtained with a JASCO IRA-1 spectrometer. ^1H NMR spectra were obtained with a JEOL FX-90Q spectrometer at Nagoya University or a JEOL GX-400 spectrometer at the Institute for Molecular Science, with TMS as internal standard. ^{13}C NMR spectra were measured on a JEOL FX-90Q spectrometer with TMS or $CDCl_3$ as internal standards. Mass spectra (MS) were recorded with an Hitachi RMU-6C or JEOL JMSD-10 mass spectrometer with an ionization energy of 75 eV. High-resolution mass spectra (HRMS) were recorded with a JEOL MMS-DX-300 spectrometer. Elemental analyses were performed by the faculty of Departments of Engineering or Agriculture of Nagoya University. Bulb-to-bulb distillation was performed by using a Büchi Kugerrohrofen. The cited temperature of distillation refers to the oven temperature and therefore not true boiling points. R_f values on TLC were recorded on E. Merck precoated (0.25 mm) silica gel 60 F_{254} plates. The plates were sprayed with a solution of 2% *p*-anisaldehyde in 5% ethanolic sulfuric acid or $Cu(OAc)_2/H_3PO_4/H_2O$ (3:29:80) and then heated until the spots became clearly visible. Column chromatography was conducted using silica gel 60 (E. Merck, 7734, 70–230 mesh) or silica gel BW-80 (Fuji Devison, 80–200 mesh). Medium-pressure column chromatography was conducted using silica gel 60 (E. Merck, 230–400 mesh) with equipment of a Kiriyama ILC-PB column system (a glass column and a pump). GLC analysis was conducted on an Hitachi 063 or 163 gas chromatograph instrument.

Catalysts. $RuCl_2(PPh_3)_3$[41] was donated by Professor J. Tsuji at Tokyo Institute of Technology or purchased from Strem Chemicals. $Ru(OAc)_2(PPh_3)_2$, $RuCl_2(Py)_2(PPh_3)_2$, *cis*-$RuCl_2(CH_3CN)_2(PPh_3)_2$, and *trans*-$RuCl_2(CH_3CN)_2(PPh_3)_2$ were prepared by the reported methods.[41] Ru(CO)(OEP) (OEP: octaethylporphine)[43] was donated by Professor H. Ogoshi at Kyoto University. $[RuCl_2(PPh_3)_2]_n$,[25] $OsCl_2(PPh_3)_3$,[25] and $FeCl_2(PPh_3)_2$[44]

(32) The structural assignment was made on the basis of the Vogel's argument that the pseudoaxial proton resonates at the lower field (δ 4.64–4.90) than does the pseudoequatorial one (δ 4.04–4.35).[33] The 5.8:1 ratio corresponds to $\Delta G°$ = 1.0 kcal/mol (25 °C).[34] The MO calculation of **20** by using the MONSTER GAUSSION 81 STO-3G basis set under BFGS optimization suggests that the two conformers in gas phase are very close in energy, however.

(33) Hagenbach, J.-P.; Vogel, P. *Tetrahedron Lett.* **1979**, 561.

(34) Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; Wiley: New York, 1972; p 158.

(35) Surzur, J.-M. In *Reactive Intermediates*; Abramovitch, R. A. Ed.; Plenum Press: New York, 1982; Vol. 2, Chapter 3. Nussbaum, A. L.; Wayne, R.; Yuan, E.; Sarre, O. Z.; Oliveto, E. P. *J. Am. Chem. Soc.* **1965**, *87*, 2451. Suzuki, A.; Miyaura, N.; Itoh, M.; Brown, H. C.; Holland, G. W.; Negishi, E. *Ibid.* **1971**, *93*, 2792.

(36) Thermolysis of **13** in ethanol produces (*Z*)-4,5-epoxy-2-pentenal (58%) and the *syn*-diepoxide **40** (7%).[37] Heating of **14** and **19** in dichloromethane gave the diepoxides **43** and **51** in 57 and 47% yields, respectively. Addition of $LiClO_4$ improved the yields of the diepoxides to 79 and 67%, respectively (see Experimental Section). Photolysis of **14** in cyclohexane gave the *syn*-diepoxide **43** (27%) and 3,4-epoxycyclohexanone (22%).[38]

(37) Schülte-Elte, K. H.; Willhalm, B.; Ohloff, G. *Angew. Chem.* **1969**, *81*, 1045.

(38) Maheshwari, K. K.; de Mayo, P.; Wiegand, D. *Can. J. Chem.* **1970**, *48*, 3266.

(39) Application of this Ru(II)-catalyzed reaction: (synthesis of chorismic acid): Hoare, J. H.; Policastro, P. P.; Berchtold, G. A. *J. Am. Chem. Soc.* **1983**, *105*, 6264. Decomposition of trioxides: Ito, Y.; Matsuura, A.; Otani, R.; Matsuura, T. *Ibid.* **1983**, *105*, 5699. Matsuura, A.; Nishinaga, A.; Ito, Y.; Matsuura, T. *Chem. Lett.* **1985**, 993.

(40) Kochi, J. K. In *Organometallic Mechanisms and Catalysis*; Academic Press: New York, 1978; Chapters 2 and 6.

(41) Hallman, P. S.; Stephenson, T. A.; Wilkinson, G. *Inorg. Synth.* **1972**, *12*, 238.

(42) Gilbert, J. D.; Wilkinson, G. *J. Chem. Soc.* **1969**, 1749.

(43) Bonnet, J. J.; Eaton, S. S.; Eaton, G. R.; Holm, R. H.; Ibers, J. A. *J. Am. Chem. Soc.* **1973**, *95*, 2141.

(44) Pignolet, L. H.; Forster, D.; Horrocks, W. de W., Jr. *Inorg. Chem.* **1968**, *7*, 828.

were prepared by the reported methods. $Co^{II}TPP$[45] was donated by Dr. K. Yasufuku at the Institute of Physical and Chemical Research (RIKEN). $[CuCl(PPh_3)]_4$,[46] $CoCl_2(PPh_3)_2$[47] and $CoCl(PPh_3)_3$[48] were prepared by the reported methods.

Solvents and Materials. CH_2Cl_2 and acetone were freshly distilled from P_4O_{10} under argon atmosphere. Benzene, toluene, and dimethoxyethane (DME) were freshly distilled from sodium benzophenone ketyl or CaH_2 under argon atmosphere. Solvents were degassed by freeze/thaw cycles under high vacuum before use. (2*E*,4*E*)-Hexadiene, 1,3-cyclohexadiene, 1,3-cycloheptadiene, α-terpinene, and 1,4-diphenyl-1,3-butadiene were purchased from Aldrich. 1,3-Butadiene, α-phellandrene, and β-myrcene were purchased from Tokyo Kasei. Cyclopentadiene was prepared by pyrolysis[49] of dicyclopentadiene (Aldrich). (5*E*,7*E*)-Dodecadiene,[50] (5*E*,7*Z*)-dodecadiene,[51] (5*E*,7*E*)-2,2,7,7-tetramethyloctadiene,[50] 1,2-dimethylenecyclohexane,[52] 1,5,5-trimethyl-1,3-cyclohexadiene,[53] and 1,4-diphenyl-1,3-cyclohexadiene[54] were prepared by the reported methods. Rose bengal was purchased from Chroma. *meso*-Tetraphenylporphine was purchased from Aldrich. The methyl esters of PGE_2, PGD_2, $PGF_{2\alpha}$, and thromboxane B_2 are products of Ono Pharmaceutical Co.

Epiperoxides. 1,4-Epiperoxycyclohexane (**1**), dihydroascaridole (**2**), and 1,3-epiperoxycyclopentane (**3**) were prepared by diimide reduction[55] of the corresponding 2,3-didehydro-1,4-epiperoxides **14**, **17**, and **13**, respectively. PGH_2 methyl ester (**4**) was prepared from $PGF_{2\alpha}$ methyl ester by the procedures reported by Porter.[56] 3,5-Epiperoxycyclopentene (**13**) was prepared by the reported method.[57] 3,6-Epiperoxycyclohexene (**14**),[58] the epiperoxide **15**,[4f] ascaridole (**17**),[4a] 3,7-epiperoxycycloheptene (**19**),[59] *cis*-3,6-dimethyl-1,2-dioxa-4-cyclohexene (**20**),[60] *cis*-3,6-diphenyl-1,2-dioxa-4-cyclohexene (**22**),[60,61] and the epiperoxide **26**[4f] were prepared by the photosensitized oxygenation of the corresponding 1,3-dienes using a 500-W iodine lamp for several hours at 0 °C in the presence of rose bengal or *meso*-tetraphenylporphine while bubbling the solution with oxygen.[60] The new epiperoxides **16**, **18**, **21**, **23**, **24**, and **25** were prepared from the corresponding 1,3-dienes by a similar photooxygenation technique.[60]

3,6-Epiperoxy-3,5,5-trimethylcyclohexene (16): ^1H NMR (CCl_4) δ 0.83 (s, 3, CH_3), 1.20 (d, 1, J = 12 Hz, a porton of CH_2), 1.25 (s, 6, 2 CH_3), 1.62 (d, 1, J = 12 Hz, a proton of CH_2), 3.90 (dd, 1, J = 6 and 1.5 Hz, CHO), 6.20 (dd, 1, J = 7 and 1.5 Hz, vinyl), 6.55 (dd, 1, J = 7 and 6 Hz, vinyl); MS, m/z 154 (M^+), 139, 125, 123, 122, 111, 108, 107. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69,82; H, 9.44.

3,6-Diphenyl-3,6-epiperoxycyclohexene (18): mp 131–132 °C; TLC R_f 0.57 (1:1 ether/hexane); ^1H NMR ($CDCl_3$) δ 1.9–2.8 (m, 4, 2 CH_2), 6.88 (s, 2, vinyl), 7.4–7.7 (m, 10, phenyls); ^{13}C NMR ($CDCl_3$) δ 29.8, 78.5, 126.1, 128.4, 128.6, 136.6, 139.7; MS, m/z 264 (M^+). Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.90; H, 6.07.

***cis*-3,6-Dibutyl-1,2-dioxa-4-cyclohexene (21)**: ^1H NMR ($CDCl_3$) δ 0.89 (t, 6, J = 6 Hz, 2 CH_3), 1.1–1.8 (m, 12, 6 CH_2), 4.44 (br t, 2, J = 6 Hz, 2 CHO), 5.86 (s, 2, vinyl); MS, m/z 198 (M^+), 180, 167, 166, 138, 137, 123, 110, 109. Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.38; H, 11.48.

***cis*-3,6-Di-*tert*-butyl-1,2-dioxa-4-cyclohexene (23)**: IR (neat) 1475, 1360 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (br s, 18, 6 CH_3), 4.08 (br s, 2, 2 CHO), 6.07 (br s, 2, vinyls); ^{13}C NMR (CD_2Cl_2) δ 26.1, 34.6, 85.3, 126.2. Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.69; H, 11.18.

***trans*-3,6-Dibutyl-1,2-dioxa-4-cyclohexene (24).** A mixture of (5*E*,7*Z*)-dodecadiene (3.0 g, 18 mmol) and *meso*-tetraphenylporphine (300 mg) in CH_2Cl_2 (250 mL) was bubbled by introducing oxygen during irradiation with a 500-W iodine lamp at 0 °C for 2 h. After the solvent was evaporated under reduced pressure (aspirator), the residual material was subjected to column chromatography on silica gel (200 g) by using a 20:1 mixture of hexane and ether as eluant to give a 9:1 mixture[62] of the stereoisomers **21** and the desired **24**. The pure **24** (240 mg, 6.7%) was isolated by repeating the medium-pressure column chromatography on silica gel (40-mm-o.d. × 30 cm; the flow rate, 20 mL/min) using a 100:1 to 50:1 (gradient) mixture of hexane and ether as eluant: IR ($CHCl_3$) 1462 cm^{-1}; ^1H NMR (400 MHz, $CCl_4/CDCl_3/CD_2Cl_2$ (13:27:60), 25 °C) δ 0.90 (t, 6, J = 6 Hz, 2 CH_3), 1.3–1.6 (m, 12, 6 CH_2), 4.55 (br t, 2, 2 CHO), 5.85 (br s, 2, vinyl); ^{13}C NMR ($CDCl_3$, 25 °C) δ 14.0, 22.7, 27.4, 32.3, 78.1, 128.2; MS, m/z 198 (M^+), 180, 167, 166, 151, 141, 138, 137, 123, 113, 110, 109. Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.67; H, 10.93. The photosensitized oxygenation of the corresponding (*Z*,*Z*)-diene under similar conditions gave a 9:1 mixture of **21** and **24**. The relative configuration of the two butyl substituents at the C(3) and C(6) positions of **24** was determined by ^1H NMR analysis in the presence of the chiral shift reagent. Thus two peaks at δ 4.64 at C(3) (or C(6)) and 5.74 at C(4) (or C(5)) were separated into two sets of two peaks at 5.40 and 5.55 and at 6.00 and 6.08, respectively, in the presence of $Eu(hfc)_3$ (11 mol %) in C_6H_6. In contrast, no separation of the peaks was observed with the isomer **21** in the presence of the same chiral shift reagent.

3,4-Dioxabicyclo[4.4.0]dec-1(6)-ene (25): IR (neat) 1435, 1347, 1005, 770 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.5–1.8 (m, 4, 2 CH_2), 1.8–2.1 (m, 4, 2 CH_2C=), 4.3–4.5 (m, 4, 2 CH_2O); ^{13}C NMR ($CDCl_3$) δ 22.2, 24.7, 72.5, 125.8. Anal. Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.67; H, 8.30.

NMR Spectral Data of Some 1,4-Epiperoxides at Ambient and Low Temperatures. 20: ^1H NMR (CD_2Cl_2, 25 °C) δ 1.25 (d, 6, J = 6.8 Hz, 2 CH_3), 4.56 (dq, 2, J = 6.6 and 0.9 Hz, 2 CHO), 5.85 (d, 2, J = 0.7 Hz, vinyls); ^1H NMR (CD_2Cl_2, −110 °C) δ 1.18 (br d, 1, J = 6.2 Hz, CH_3), 1.40 (br d, 1, J = 5.5 Hz, CH_3), 4.50 (br, 1, CHO), 4.79 (br, 1, CHO), 5.93 (br d, 2, vinyls). **21**: ^1H NMR (400 MHz, $CCl_4/CDCl_3/CD_2Cl_2$ (13:27:60), 25 °C) δ 0.91 (t, 6, J = 7.0 Hz, 2 CH_3), 1.3–1.7 (m, 12, 6 CH_2), 4.40 (t, 2, J = 6.0 Hz, 2 CHO), 5.88 (s, 2, vinyls); ^1H NMR (400 MHz, $CCl_4/CDCl_3/CD_2Cl_2$ (13:27:60), −101 °C) δ 0.91 (br t, 6, 2 CH_3), 1.2–1.9 (br m, 12, 6 CH_2), 4.23 (br d, 1, J = 7.1 Hz, CHO), 4.74 (br s, 1, CHO), 5.85 (br d, 1, J = 9.6 Hz, vinyl), 6.00 (br d, 1, J = 9.6 Hz, vinyl). **22**: ^1H NMR (CD_2Cl_2, 25 °C) δ 5.68 (d, 2, J = 1 Hz, 2 CHO), 6.38 (d, 2, J = 1 Hz, vinyls), 7.48 (m, 10, phenyls); ^1H NMR (CD_2Cl_2, −126 °C) δ 5.54 (br s, 1, CHO), 5.91 (br s, 1, CHO), 6.42 (br s, 2, vinyls), 7.54 (br s, 10 phenyls). **23**: ^1H NMR (CD_2Cl_2, 25 °C) δ 0.96 (s, 18, 6 CH_3), 4.05 (d, 2, J = 0.5 Hz, 2 CHO), 6.09 (d, 2, J = 0.5 Hz, vinyls); ^1H NMR (CD_2Cl_2, −128 °C) δ 0.96 (br s, 18, 6 CH_3), 3.85 (br s, 1, CHO), 4.27 (br s, 1, CHO), 6.12 (br s, 2, vinyls); ^{13}C NMR (CD_2Cl_2, 25 °C) δ 26.1, 34.6, 85.3, 126.2; ^{13}C NMR (CD_2Cl_2, −124 °C) δ 26.0 27.0, 34.2, 36.2, 84.2, 86.1, 125.3, 127.0. **24**: ^1H NMR (400 MHz, $CCl_4/CDCl_3/CD_2Cl_2$ (13:27:60), 25 °C) δ 0.89 (t, 6, J = 7.0 Hz, 2 CH_3), 1.3–1.6 (m, 12, 6 CH_2), 4.55 (t, 2, J = 6.0 Hz, 2 CHO), 5.85 (s, 2, vinyls); ^1H NMR (400 MHz, $CCl_4/CDCl_3/CD_2Cl_2$ (13:27:60), −101 °C) δ 0.89 (t, 6, J = 7.0 Hz, 2 CH_3), 1.3–1.6 (m, 12, 6 CH_2), 4.17 (d, 0.29, j = 9.8 Hz, 0.29 CHO), 4.71 (br s, 1.70, 1.7 CHO), 5.89 (s, 1.70, 1.7 vinyl), 5.97 (s, 0.29, 0.29 vinyl). **25**: ^1H NMR (CD_2Cl_2, 30 °C) δ 1.5–2.0 (m, 8, 4 CH_2), 4.33 (m, 4, 2 CH_2O); ^1H NMR (CD_2Cl_2, −100 °C) δ 1.4–2.0 (br, 8, 4 CH_2), 4.11 (br d, 2, J = 14.3 Hz, 2 CHO), 4.65 (br d, 2, J = 15.2 Hz, 2 CHO).

(45) Rothemund, P.; Menotti, A. R. *J. Am. Chem. Soc.* **1948**, *70*, 1808.
(46) Churchill, M. R.; Berman, S. A.; Osborn, J. A.; Wormald, J. *Inorg. Chem.* **1972k**, *11*, 1818.
(47) Chatt, J.; Shaw, B. L. *J. Chem. Soc.* **1961**, 285.
(48) Aresta, M.; Rossi, M.; Sacco, A. *Inorg. Chem. Acta* **1969**, *3*, 227.
(49) Moffett, R. B. *Org. Synth. Coll. Vol.* **1963**, *4*, 238.
(50) Zweifel, G.; Miller, R. L. *J. Am. Chem. Soc.* **1970**, *92*, 6678.
(51) Zweifel, G.; Polston, N. L.; Whitney, C. C. *J. Am. Chem. Soc.* **1968**, *90*, 6243.
(52) Blomquist, A. T. *J. Am. Chem. Soc.* **1957**, *79*, 3916.
(53) Dauben, W. G.; Lorber, M. E.; Vietmeyer, N. D.; Shapiro, R. H.; Duncan, J. H.; Tomer, K. *J. Am. Chem. Soc.* **1968**, *90*, 4762.
(54) Dale, J.; Kristinsen, P. O. *Acta Chem. Scand.* **1971**, *25*, 359.
(55) Coughlin, D. J.; Brown, R. S.; Salomon, R. C. *J. Am. Chem. Soc.* **1979**, *101*, 1533, and references therein.
(56) Porter, N. A.; Byers, J. D.; Mebane, R. C.; Gilmore, D. W.; Nixon, J. R. *J. Org. Chem.* **1978**, *43*, 2088. See also: Porter, N. A.; Byers, J. D.; Ali, A. E.; Eling, T. E. *J. Am. Chem. Soc.* **1980**, *102*, 1183.
(57) Schenck, G. O.; Dunlap, D. E. *Angew. Chem.* **1956**, *68*, 248.
(58) Kanako, C.; Sugimoto, A.; Tanaka, S. *Synthesis* **1974**, 876.
(59) Cope, A. C.; Liss, T. A.; Wood, G. W. *J. Am. Chem. Soc.* **1957**, *79*, 6287.
(60) Kondo, K.; Matsumoto, M. *J. Chem. Soc., Chem. Commun.* **1972**, 1332. Matsumoto, M.; Dobashi, S.; Kuroda, K.; Kondo, K. *Tetrahedron* **1985**, *41*, 2147.
(61) Rio, G.; Berthlet, J. *Bul. Soc. Chim. Fr.* **1969**, 1664.
(62) Similar phenomena were observed in photooxygenation of (*E*,*Z*)-2,4-hexadiene. See: Gollnick, K.; Griesbeck, A. *Tetrahedron Lett.* **1983**, *24*, 3303.

Thermolysis of 2,3-Didehydro 1,4-Epiperoxides (Entry 13 in Table I). A solution of **21** (29.9 mg, 0.15 mmol) in toluene was heated at 170 °C for 40 h under argon atmosphere in a sealed glass tube. After the mixture was cooled to room temperature, the glass tube was opened in air. GLC analysis (see the conditions described in entry 11 in Table I) indicated the formation of **55** (4%), **56** (2%), and **57** (73%).

A similar operation using **14** (28.3 mg, 0.25 mmol) in CH_2Cl_2 (3 mL) at 100 °C for 20 h gave **43** in 57% yield (^1H NMR analysis using cyclododecane as internal standard); **19** (19.6 mg, 0.16 mmol) in CH_2Cl_2 (3 mL) at 120 °C for 20 h gave **51** in 47% yield. Heating a mixture of **14** (22.7 mg, 0.2 mmol) and $LiClO_4$ (2 mg, 0.019 mmol) in CH_2Cl_2 (3 mL) at 90 °C for 40 h gave **43** in 79% yield; **19** (15.8 mg, 0.13 mmol) with $LiClO_4$ (1.5 mg, 0.014 mmol) in CH_2Cl_2 (3 mL) at 100 °C for 20 h gave **51** in 67% yield.

Transition-Metal-Catalyzed Reaction of 1,4-Epiperoxides. Unless otherwise stated, the reaction was conducted under argon atmosphere. Prior to introduction of solvents or materials, the reaction vessel (glass tube or ampule) was dried in vacuo under heating with a heat gun and then filled with argon.

Ru(II)-Catalyzed Decomposition of 1 (Eq 1). $RuCl_2(PPh_3)_3$ (8.8 mg, 0.0092 mmol) was placed in a glass tube, and the atmosphere was replaced with argon. Then a solution of **1** (21 mg, 0.18 mmol) and 1,1,2,2-tetrachloroethane (15.5 mg, 0.092 mmol, internal standard for ^1H NMR analysis) in CD_2Cl_2 (0.6 mL) was added and a glass tube was sealed. The mixture was heated at 50 °C for 2 h. After the mixture was cooled, the glass tube was opened in air. The ^1H NMR spectrum indicated the formation of succinaldehyde[63] [19.2%, δ 2.80 (s, 4, 2 CH_2CO), 9.75 (s, 2, CHO)]. To this mixutre was added methyl caprate (11.4 mg, 0.061 mmol, internal standard), and the mixture was subjected to GLC analysis (10% silicon XE-60 on Uniport UP, 3-mm-o.d. × 2 m, 1 kg/cm^2, 135 °C), indicating the formationof *cis*-1,4-dihydroxycyclohexane[64] (17%, t_r 4.57 min) and 4-hydroxycyclohexanone[65] (11%, t_r 6.07 min). Analysis of the ethylene product was conducted as follows. After the reaction was carried out under the same conditions described above, the glass tube was opened while being cooled with liquid nitrogen. Bromine (5 equiv) was added quickly to the mixture at this temperature, the tube was capped with a rubber septum, and the resulting mixture was warmed to room temperature. GLC analysis (3% OV-1 on Chromosorb W, 3-mm-o.d. × 2 m, 1.3 kg/cm^2, 25 °C) using 1-bromobutane as internal standard indicated the formation of 1,2-dibromoethane (43%, t_r 2.71 min). The decomposition reaction was also conducted in the presence of 2-propanol (10 equiv) under the same conditions to indicate the formation of acetone (39%). Succinaldehyde was not detected under such reaction conditions.

Ru(II)-Catalyzed Decomposition of 2 (Eq 2). $RuCl_2(PPh_3)_3$ (9.6 mg, 0.01 mmol) and a solution of **2** (34 mg, 0.2 mmol) in CH_2Cl_2 (1 mL) was placed in a glass tube under argon. The tube was sealed, and the mixture was heated at 50–60 °C for 22 h. The mixture was cooled and opened in air. Toluene (9.2 mg, 0.1 mmol) was added as an internal standard, and the mixture was submitted to ^1H NMR analysis, which indicated the formation of 6-methyl-2,4-heptanedione[66a] (8%), 4-hydroxy-4-methylcyclohexanone[4b,66b] (48%), and *cis*-1,4-dihydroxy-1-isopropyl-4-methylcyclohexane[66a] (8%), together with the unreacted **2** (30%). These structures were confirmed by ^1H NMR after purification by silica gel column chromatography using a 1:1 mixture of hexane and ether and then a 1:2 to 1:1 mixture of ethyl acetate and benzene as eluants. The formation of ethylene and propylene was confirmed by GLC analysis[13a] (3% OV-1 on Chromosorb W, 3 mm-o.d. × 2 m, 1.3 kg/cm^2, 25 °C) after treatment with bromine using the same procedure described in the decomposition of **1**. The formation of 1,2-dibromoethane (8%, t_r 3.01 min) and 1,2-dibromopropane (9%, t_r 4.54 min) was indicated.

Ru(II)-Catalyzed Decomposition of 3 (Eq 3). $RuCl_2(PPh_3)_3$ (11 mg, 0.012 mmol) was placed in a glass tube and the system was flushed with argon. To this a cold (0 °C) solution of **3** (23 mg, 0.23 mmol) in CD_2Cl_2 (0.6 mL) was added. After 15 min, tetrachloroethane was added as an internal standard, and the mixture was submitted to ^1H NMR analysis, which indicated the formation of 4,5-epoxypentanal[12] (38%, δ 1.6–2.2 (m, 2, CH_2), 2.4–3.0 (m, 5, 3 CHO and CH_2CO), 9.74 (t, 1, J = 1 Hz, CHO)). This mixture with added methyl caprate (14.3 mg, 0.077 mmol) as an internal standard was submitted to GLC analysis (10% silicon XE-60 on Uniport HP, 3 mm-o.d. × 2 m, 1 kg/cm^2, 135 °C), which indicated the formation of 4,5-epoxypentanal (38%, t_r 1 min), *cis*-1,3-dihydroxycyclopentane[67] (9%, t_r 2.37 min), and 4-hydroxycyclopentanone[68] (1%, t_r 3.72 min). The formation of ethylene (31%) was confirmed by GLC analysis after converting the dibromo derivative using the same treatment[13a] described in the decomposition of **1**. Determination of the yield of malonaldehyde: After the reaction was conducted using **3** (12 mg, 0.12 mmol) and $RuCl_2(PPh_3)_3$ (5.7 mg, 0.06 mmol) under the same conditions, the reaction mixture was extracted twice with H_2O (2 mL each). The aqueous extracts were diluted with H_2O to 100 mL. Then 1 mL of this solution was mixed with an aqueous solution (1 mL) of sodium thiobarbiturate (4.9×10^{-2} M) and acidified with 1 N HCl to pH 2. The mixture was heated for 20 min,[15] and then the pink solution was diluted with H_2O to 40 mL and subjected to colorimetry with an optical density of 0.59 at 532 nm. The total quantity of malonaldehyde (1.12 mg, 13%) formed in this reaction was determined from the reported authentic values of the optical density (0.66 for 0.3127×10^{-6} g/mL).[15]

Ru(II)-Catalyzed Reaction of PGH_2 Methyl Ester (4, Eq 4). PGH_2 methyl ester (**4**) was stable in CH_2Cl_2 at room temperature (19 °C) for 24 h. To a solution of **4** (1 mg, 0.0027 mmol) in CH_2Cl_2 (0.5 mL) a solution of $RuCl_2(PPh_3)_3$ (0.07 mg, 0.000073 mmol) in CH_2Cl_2 (0.1 mL) was added at 0 °C, and the mixture was stirred at 19 °C for 4 h under argon atmosphere. The reaction mixture showed a single spot on TLC. The product was separated by preparative TLC using a 6:3:1 mixture of ethyl acetate, cyclohexane, and THF as solvent to give the pure **5**: TLC R_f 0.75 (6:3:1 ethyl acetate/cyclohexane/THF); IR (neat) 3400, 1740, 1650 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.88 (t, 3, J = 7.3 Hz, C(17)H_3), 1.23–1.35 (m, 8, C(13–16)H_2), 1.42 (br, 1, OH), 1.70 (tt, 2, J = 7.3 and 7.3 Hz, C(3)H_2), 2.08 (dt, 2, J = 5.5 and 7.4 Hz, C(4)H_2), 2.32 (t, 2, J = 7.3 Hz, C(2)H_2), 2.82 (t, 2, J = 6.3 Hz, C(7)H_2), 3.68 (s, 3, OCH_3), 4.10 (br, 1, C(12)H), 5.43 (t, 2, J = 5.5 Hz, =C(5,6)H), 5.59 (dd, 1, J = 14.7 and 7.4 Hz, =C(11)H), 5.66 (dt, 1, J = 14.7 and 6.6 Hz, =C(8)H), 6.04 (dd, 1, J = 14.7 and 11 Hz, =C(9 or 10)H), 6.17 (dd, 1, J = 14.7 and 11 Hz, =C(10 or 9)H); MS, m/z 294 (M^+), 276, 263, 255, 223, 180, 99.

Analysis of malonaldehyde: The reaction was conducted using **4** (2 mg, 0.0055 mmol) and $RuCl_2(PPh_3)_3$ (0.26 mg, 0.00028 mmol) in CH_2Cl_2 (1.5 mL) at 19 °C for 3 h under argon. Malonaldehyde was extracted into water by shaking with a mixture of H_2O (10 mL) and benzene (20 mL). After extraction twice with water (10 mL each), the combined aqueous solutions were subjected to the thiobarbituric acid test,[15] which indicated the formation of malonaldehyde in 41% yield (0.163 mg).

Ru(II)-Catalyzed Reaction of 2,3-Didehydro 1,4-Epiperoxides. The standard reaction procedure used is illustrated by the conversion of 3,6-epiperoxycyclohexene (**14**) to *syn*-1,2;3,4-diepoxycyclohexane (**43**, entry 2 in Table I). $RuCl_2(PPh_3)_3$ (39 mg, 0.041 mmol) and CH_2Cl_2 (5 mL) were placed in an ampule under argon atmosphere. To this a solution of **14** (460 mg, 4.1 mmol) in CH_2Cl_2 (5 mL) was added to 0 °C with stirring through a stainless steel cannula under slight argon stream. The mixture was stirred at this temperature for 0.5 h and at 10 °C for 0.5 h. The reaction mixture was directly subjected to column chromatography on silica gel (15 g) using a 3:1 mixture of ether and hexane as eluant to give the diepoxide **43** (417.1 mg, 91%):[39] ^1H NMR ($CDCl_3$) δ 1.83 and 1.85 (s, each, 4, 2 CH_2), 3.0–3.2 (br, 2, 2 CHO), 3.3–3.4 (dd, 2, J = 2 and 3 Hz, 2 CHO).

Table I lists experimental details for other cases. Unless otherwise stated, the reaction was carried out by a similar procedure.

Conversion of 13 to 40, 41, and 42 (Entry 1). To a solution of $RuCl_2(PPh_3)_3$ (31.2 mg, 0.033 mmol) in CH_2Cl_2 (10 mL), a cold

(63) Haga, T.; Mori, H.; Nakanome, T. *Japanese* Patent 71-19929, 1968; *Chem. Abstr.* **1971**, *75*, 98168g.
(64) Grob, C. A.; Baumann, W. *Helv. Chim. Acta* **1955**, *38*, 594.
(65) Haslanger, M.; Lawton, G. *Synth. Commun.* **1974**, *4*, 155.
(66) (a) Moore, C. G. *J. Chem. Soc.* **1951**, 234. (b) Corey, E. J.; Barza, S.; Klotmann, G. *J. Am. Chem. Soc.* **1969**, *91*, 4782.
(67) Salomon, R. G.; Salomon, M. F. *J. Am. Chem. Soc.* **1977**, *99*, 3501.
(68) McIntosh, J. M.; Beaumier, P. *J. Org. Chem.* **1972**, *37*, 2905.

(−78 °C) solution of **13** (195 mg, 1.99 mmol) in CH_2Cl_2 (5 mL) was added quickly at −78 °C through a cannula under an argon stream. The mixture was stirred at −78 °C for 1 h, −40 °C for 0.5 h, and then −25 °C for 1 h. After the reaction mixture was evaporated, toluene (103.7 mg, 1.13 mmol, internal standard) was added to the residue. The mixture was submitted to ^1H NMR analysis, which indicated the formation of **40** (78%), **41** (3.2%), and **42** (4.8%). The mixture was then chromatographed on a column of silica gel (6 g) using a 1:1 mixture of hexane and ether as eluant to give **40** (140.2 mg, 71.8%),[69] **41** (5.1 mg, 2.6%),[38] and **42** (6.8 mg, 3.5%)[58] as oils. **40**: ^1H NMR ($CDCl_3$) δ 1.62 (dt, 1, J = 16 and 3 Hz, a proton of CH_2), 2.10 (d, 1, J = 16 Hz, a proton of CH_2), 3.50 (br d, 2, 2 CHO), 3.70 (br q, 2, 2 CHO). **41**: ^1H NMR ($CDCl_3$) δ 2.26 (dd, 1, J = 18 and 2.5 Hz, a proton of CH_2CO), 2.1–2.5 (br, 1, OH), 2.80 (dd, 1, J = 18 and 6 Hz, a proton of CH_2CO), 5.05 (m, 1, CHO), 6.20 (dd, 1, J = 6 and 1 Hz, vinyl), 7.55 (dd, 1, J = 6 and 3 Hz, vinyl).

Conversion of 15 to the Diepoxide 44 (Entry 3). Liquid chromatography (LC) with a SiO_2 (3 g) column, hexane/ether (5:1) as eluant yielded **44**: R_f 0.28 (1:1 hexane/ether); ^1H NMR ($CDCl_3$) δ 0.94 and 0.99 (d each, 6, J = 6 Hz, $C(CH_3)_2$), 1.52 (s, 3, CH_3), 1.4–2.0 (m, 4, 2 CH and CH_2), 2.8–3.0 (m, 2, 2 CHO), 3.13 (d, 1, J = 4.0 Hz, CHO).[4f]

Conversion of 16 to the Diepoxide 45 (Entry 4). LC: SiO_2 (5 g), petroleum ether/ether (3:1) as eluant. **45**: ^1H NMR ($CDCl_3$) δ 1.00 (s, 3, CH_3), 1.06 (s, 3, CH_3), 1.31 (d, 1, J = 15 Hz, a proton of CH_2), 1.34 (s, 3, CH_3), 1.68 (d, 1, J = 15 Hz, a proton of CH_2), 2.77 (d, 1, J = 4 Hz, CHO), 3.11 (d, 1, J = 3 Hz, CHO), 3.39 (dd, 1, J = 4 and 3 Hz, CHO); MS, m/z 154 (M^+), 139, 125, 121, 112, 111. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.07; H, 9.21.

Conversion of 17 to 46, 47, 48, and 49 (Entry 6). LC: SiO_2 (1.5 g), ethyl acetate/benzene (2:1 to 1:1, gradient) as eluant. **48** and **49** were obtained as a 1:1 mixture. **46**: ^1H NMR ($CDCl_3$) δ 0.97 and 1.03 (d each, 6, J = 6 Hz, $C(CH_3)_2$), 1.40 (s, 3, CH_3), 1.5–2.0 (m, 5, CH and CH_2), 3.16 (s, 2, 2 CHO).[70] **47**: ^1H NMR ($CDCl_3$) δ 0.90 and 0.96 (d each, 6, J = 6 Hz, $C(CH_3)_2$), 1.25 (s, 3, CH_3), 1.6–2.0 (m, 5, CH and CH_2), 2.0–2.4 (br, 2, 2 OH), 5.55 (d, 1, J = 10 Hz, vinyl), 5.73 (d, 1, J = 10 Hz, vinyl).[71] **48**: IR (neat) 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (s, 3, CH_3), 2.0–2.6 (m, 5, 2 CH_2 and OH), 5.90 (d, 1, J = 10 Hz, vinyl), 6.79 (d, 1, J = 10 Hz, vinyl); MS, m/z 126 (M^+). This compound was converted to **49** by catalytic hydrogenation on Pd/C. **49**: IR (neat) 3600–3200, 1708 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38 (s, 3, CH_3), 1.8–2.4 (m, 7, 3 CH_2 and OH), 2.6–2.9 (m, 2, CH_2); MS, m/z 128 (M^+), 113, 110.[66]

Conversion of 19 to the Diepoxide 51 (Entry 9). **51**: ^1H NMR ($CDCl_3$) δ 1.2–2.5 (m, 6, 3 CH_2), 3.1–3.3 (br, 4, 4 CHO).[72]

Conversion of 20 to the Diepoxides 52 and 53 and the Furan 54 (Entry 10). GLC: **52**, t_r 6.99 min (21%); **53**, t_r 5.27 min (3%) (5% PEG-HT on Uniport HP, 3-mm-o.d. × 3 m, 0.95 kg/cm^2, 100 °C, undecane as internal standard); **54**, t_r 1.95 min (43%) (5% PEG-HT on Uniport HP, 3-mm-o.d. × 6 m, 1.1 kg/cm^2, 50 °C). **52**: ^1H NMR ($CDCl_3$) δ 1.35 (d, 3, J = 4.5 Hz, CH_3), 1.41 (d, 3, J = 4.5 Hz, CH_3), 2.5–2.8 (m, 2, 2 CHO), 2.8–3.3 (m, 2, 2 CHO); ^{13}C NMR ($CDCl_3$) δ 13.9, 17.2, 51.5, 52.1, 56.0, 56.3. **53**: ^1H NMR ($CDCl_3$) δ 1.23 (d, 6, J = 6 Hz, 2 CH_3), 2.48 (d, 2, J = 1.5 Hz, 2 CHO), 2.87 (dq, 2, J = 6 and 1.5 Hz, 2 CHO). The stereostructures of **52** and **53** were confirmed by comparison of these GLC retention times with those of authentic diepoxides prepared from (*Z,E*)- and (*E,E*)-2,4-hexadienes, respectively, with *m*-chloroperbenzoic acid.[73] **54** was identical with the commercial sample (Aldrich).

Conversion of 21 to the Diepoxides 55 and 56 and the Furan 57 (Entry 11). GLC: **55**, t_r 17.76 min (48%); **56**, t_r 15.53 min (4%); **57**, t_r 2.92 min (38%) (5% PEG-HT on Uniport HP, 3-mm-o.d. × 3 m, 1.0 kg/cm^2, 145 °C; methyl laurate as internal standard). **55**: ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 and 0.93 (t each, 6, J = 7 Hz, 2 CH_3), 1.2–1.8 (m, 12, 6 CH_2), 2.66 (dd, 1, J = 6.4 and 2.1, CHO), 2.71 (dd, 1, J = 6.4 and 4.3 Hz, CHO), 2.90 (dt, 1, J = 5.5 and 2.1 Hz, CHO), 2.99 (dt, 1, J = 5.8 and 4.3 Hz, CHO); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.5, 28.0, 28.3, 28.9, 31.3, 55.5, 55.7, 56.3, 56.5. Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.81; H, 11.16. **56**: ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, 6, J = 7.1 Hz, 2 CH_3), 1.3–1.5 (m, 8, 4 CH_2), 1.5–1.6 (m, 4, 2 CH_2), 2.62 (br s, 2, 2 CHO), 2.88 (br t, 2, J = 5.6 Hz, 2 CHO); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.4, 27.9, 31.2, 56.8, 57.1. **57**: ^1H NMR ($CDCl_3$) δ 0.92 (t, 6, J = 6.4 Hz, 2 CH_3), 1.1–1.8 (m, 8, 4 CH_2), 2.57 (t, 4, J = 6.8 Hz, 2 CH_2), 5.83 (s, 2, vinyl); MS, m/z 180 (M^+).[74] The stereostructures of **55** and **56** were confirmed by comparison of their GLC retention times with those of authentic diepoxides prepared from (*Z,E*)- and (*Z,Z*)-5,7-dodecadienes, respectively, with *m*-chloroperoxybenzoic acid.[73] Four stereoisomeric diepoxides were derived from (*Z,E*)-5,7-dodecadiene, and two stereoisomeric diepoxides were derived from (*Z,Z*)-5,7-dodecadiene. GLC analysis clearly demonstrated that stereoisomeric diepoxides other than **55** and **56** were not involved in the present Ru(II)-catalyzed reaction. Retention times (t_r) of other stereoisomers are as follows: 6,7-*erythro*-5,6-*cis*-7,8-*trans*-diepoxydodecane, t_r 13.95 min; 6,7-*threo*-5,6-*trans*-7,8-*trans*-diepoxydodecane, t_r 17.56 min; a mixture of 6,7-*threo*- and 6,7-*erythro*-5,6-*cis*-7,8-*cis*-diepoxydodecanes, t_r 14.46 and 18.23 min, respectively. These stereoisomers can be isolated by preparative GLC (5% PEG-HT on Uniport HP, 12 mm-o.d. × 3 m, 1,3 kg/cm^2, 160 °C).

Conversion of 22 to the Diepoxide 58 and the Furan 59 (Entry 17). LC: SiO_2 (2.5 g), hexane/ether (10:1) as eluant. **58**: ^1H NMR ($CDCl_3$) δ 2.76 (dd, 1, J = 2.6 Hz, CHO), 3.18 (dd, 1, J = 6 and 4 Hz, CHO), 3.68 (d, 1, J = 2 Hz, CHO), 4.20 (d, 1, J = 4 Hz, CHO), 6.9–7.5 (m, 10, Ar); MS, m/z 238 (M^+), 220, 180, 179. Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.64; H, 5.92. Found: C, 80.59; H, 5.99. **59**: ^1H NMR ($CDCl_3$) δ 6.76 (s, 2, vinyl), 7.2–7.9 (m, 10, aromatic); MS, m/z 220 (M^+).[61]

Conversion of 23 to the Diepoxide 60 and the Enones 61 (Entry 18). LC: SiO_2 (12 g), pentane/ether (10:1 to 1:1, gradient) as eluant. **60**: TLC R_f 0.76 (1:1 hexane/ether); IR (neat) 1360, 895 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (s, 9, $C(CH_3)_3$), 1.05 (s, 9, $C(CH_3)_3$), 2.57 (dd, 1, J = 6.8 and 4.4 Hz, CHO), 2.69 (d, 1, J = 2.6 Hz, CHO), 2.75 (d, 1, J = 4.4 Hz, CHO), 3.03 (dd, 1, J = 6.8 and 2.6 Hz, CHO); ^{13}C NMR ($CDCl_3$) δ 25.8, 27.5, 30.6, 31.5, 52.8, 59.6, 63.0, 65.0. Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.65; H, 11.19. **61**: a mixture of stereoisomers isolated by column chromatography on silica gel (4 g) using a 5:1 mixture of hexane and ether as eluant. Less polar *E* isomer: mp 52–53 °C; IR ($CHCl_3$) 1687, 1624, 1362, 1067 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (s, 9, $C(CH_3)_3$), 1.20 (s, 9, $C(CH_3)_3$), 1.65 (d, 1, J = 5.0 Hz, OH), 3.98 (ddd, 1, J = 5.0, 4.6, and 0.9 Hz, CHO), 6.71 (dd, 1, J = 15.2 and 0.9 Hz, vinyl), 7.02 (dd, 1, J = 15.2 and 4.6 Hz, vinyl); HRMS calcd for $C_{12}H_{20}O$ ($M^+ - H_2O$) 180.1514, found 180.1519. More polar *Z* isomer: ^1H NMR ($CDCl_3$) δ 1.00 (s, 18, 2 $C(CH_3)_3$), 4.72 (dd, 1, J = 2.2 and 1.3 Hz, CHO), 6.16 (dd, 1, J = 5.7 and 2.2 Hz, vinyl), 7.46 (dd, 1, J = 5.7 and 1.3 Hz, vinyl); HRMS calcd for $C_{12}H_{20}O$ ($M^+ - H_2O$) 180.1514, found 180.1534. This *Z* isomer is unstable and gradually decomposes in chloroform. The *Z* structure was assigned by comparison of the coupling constants of its vinyl protons with those of the *E* isomer.

Conversion of 24 to the Diepoxides 62 and 63 and the Furan 57 (Entry 19). GLC: **62**, t_r 17.56 min (30%); **63**, t_r 13.95 min (6%); **57**, t_r 2.92 min (40%; 5% PEG-HT on Uniport HP, 3-mm-o.d. × 3 m, 1.0 kg/cm^2, 145 °C; methyl laurate as internal standard). **62**: ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, 6, J = 7.1 Hz, 2 CH_3), 1.3–1.5 (m, 8, 2 CH_2), 1.5–1.6 (m, 4, 2 CH_2), 2.67 (br s, 2, 2 CHO), 2.91 (br t, 2, J = 5.6 Hz, 2 CHO); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.5, 28.0, 31.3, 55.9, 56.7. No impurities were detected by these NMR assays. HRMS calcd for $C_8H_{13}O$ ($M^+ - C_4H_9$) 141.0916, found 141.0886. **63**: ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, 3, 7 Hz, CH_3), 0.94 (t, 3, J = 7 Hz, CH_3), 1.1–1.8 (m, 12, 6CH_2), 2.66 (dd, 1, J = 6.4 and 2.1 Hz, CHO), 2.75 (dd, 1, J = 6.4 and 4.0 Hz, CHO), 2.98 (dt, 1, J = 6.1 and 2.1 Hz, CHO), 3.02 (dt, 1, J = 6.1 and 4.0 Hz, CHO); ^{13}C NMR ($CDCl_3$) δ 13.8, 22.5, 27.8, 28.0, 28.6, 31.2, 54.7, 55.3, 56.8, 57.5. No impurities were detected

(69) Tolbert, B.; Steyn, R.; Franks, J. A. Jr.; Sable, H. Z. *Carbohydr. Res.* **1967**, *5*, 62.
(70) Boche, I.; Runquist, O. *J. Org. Chem.* **1968**, *33*, 4285.
(71) Schenck, G. O.; Kinkel, K. G.; Martens, H.-J. *Justus Liebigs Ann. Chem.* **1953**, *584*, 125.
(72) Floyd, D. M.; Cimarusti, C. M. *Tetrahedron Lett.* **1979**, 4129, and references therein.
(73) Heasley, G. H.; Hodges, R. V.; Heasley, V. L. *J. Org. Chem.* **1974**, *39*, 1769.
(74) Hillers, S.; Berzins, A. *Latvijas PSR Zinatnu Acad. Vestis, Kim. Ser.* **1962**, 113; *Chem. Abstr.* **1963**, *59*, 1565a.

by these NMR assays. HRMS calcd for $C_8H_{13}O_2$ ($M^+ - C_4H_9$) 141.0915, found 141.0888. The stereostructures **62** and **63** were confirmed by comparison of their GLC retention times with those of authentic diepoxides prepared from (*E,E*)- and (*E,Z*)-5,7-dodecadienes, respectively, with *m*-chloroperbenzoic acid.

Conversion of 25 to the Diepoxide 64 and the Furan 65 (Entry 20). GLC: **64**, t_r 15.29 min (1%); **65**, t_r 5.11 min (76%; 5% PEG-HT on Uniport HP, 3-mm-o.d. × 3 m, 1.0 kg/cm², 110 °C; pentadecane as internal standard). **64**: ^{1}H NMR ($CDCl_3$) δ 1.2–2.2 (br, 8, 4 CH_2), 2.59 (d, 2, J = 5.3 Hz, 2 CHO), 2.85 (dd, 2, J = 5.3 and 1.3 Hz, 2 CHO); HRMS calcd for $C_8H_{12}O_2$ (M^+) 140.0837, found 140.0820. The 2,3-threo structure of **64** was confirmed by ^{1}H NMR analysis in the presence of the chiral shift reagent. Thus the peak at δ 2.59 (d) was separated into two peaks at δ 3.12 (d) and 3.14 (d) in the presence of Eu(hfc)$_3$ (a chiral shift reagent; 7.1 mol %) in $CDCl_3$. A 7:93 mixture of **64** and 2,3-erythro diepoxide (stereoisomer of **64**) was prepared by the diepoxidation of 1,2-dimethylenecyclohexane with *m*-chloroperoxybenzoic acid in CH_2Cl_2. Each of these two stereoisomers was isolated by preparative GLC (5% PEG-HT on Uniport HP, 12-mm-o.d. × 3 m). The 2,3-erythro isomer: ^{1}H NMR ($CDCl_3$) δ 1.6–1.9 (br, 8, 4 CH_2), 2.57 (d, 2, J = 5.3 Hz, 2 CHO), 2.72 (d, 2, J = 5.3 Hz, 2 CHO). This stereoisomer did not indicate any separation of peaks in the presence of the same chiral shift reagent, reconfirming the 2,3-threo structure of **64**. **65**: ^{1}H NMR ($CDCl_3$) δ 1.6–1.8 (m, 4, 2 CH_2), 2.4–2.7 (br, 4, 2 CH_2), 7.1 (s, 2, aromatic); ^{13}C NMR ($CDCl_3$) δ 20.1, 23.5, 121.5, 137.3.[75]

A Catalytic Decomposition of 2,3-Didehydro 1,4-Epiperoxides with $FeCl_2(PPh_3)_2$. The standard procedure for the reaction is illustrated by the conversion of 3,6-diphenyl-3,6-epiperoxycyclohexene (**18**) to the *syn*-diepoxide **50** (entry 8 in Table I).

To a solution of **18** (20.7 mg, 0.078 mmol) in CH_2Cl_2 (2 mL) $FeCl_2(PPh_3)_2$ (2.7 mg, 0.004 mmol) was added at −78 °C while being stirred under argon. After being stirred at this temperature for 9 h, the mixture was directly subjected to column chromatography on silica gel (2 g) using a 10:1 mixture of hexane and ether as eluant to give **50** (19.6 mg, 95%): TLC R_f 0.57 (1:1 ether/hexane); ^{1}H NMR ($CDCl_3$) δ 2.0–2.7 (m, 4, 2 CH_2), 3.32 (s, 2, 2 CHO), 7.2–7.7 (m, 10, Ar); ^{13}C NMR ($CDCl_3$) δ 26.3, 57.2, 57.9, 125.1, 127.7, 128.5, 140.5; MS, m/z 264 (M^+). Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.79; H, 6.14.

Table I lists experimental details for other cases (see entries 5, 7, 14, and 21). Unless otherwise stated, the reaction was conducted by a similar procedure.

Conversion of 16 to the Diepoxide 45 (Entry 5). LC: SiO_2 (5 g), ether/hexane (1:4 to 2:1, gradient) as eluant.

Conversion of Ascaridole (17) to the Diepoxide 46 (Entry 7). ^{1}H NMR analysis was conducted using methyl laurate as an internal standard.

Conversion of 26 to the Furan 66 (Entry 21). LC: SiO_2 (5 g), hexane/ether (5:1) as the eluant. **66**: ^{1}H NMR ($CDCl_3$) δ 1.23 (s, 3, CH_3), 1.30 (s, 3, CH_3), 1.6–1.9 (m, 2, CH_2), 2.4-2.9 (m, 3, CHO and CH_2), 6.30 (br s, 1, Ar), 7.2–7.4 (m, 2, Ar).[4f]

Decomposition of 21 with $Co^{II}TPP$ (Entry 15). GLC was conducted using methyl laurate as the internal standard under such conditions as described in entry 11 in Table I.

Decomposition of 21 with $OsCl_2(PPh_3)_3$ (Entry 16). The reaction was conducted in a sealed glass tube under argon. GLC was conducted using methyl laurate as the internal standard under such conditions as described in entry 11 in Table I.

Acknowledgment. We thank Drs. Y. Naya and H. Naoki of Suntory Institute for Bioorganic Research and Professor H. Takaya of Institute of Molecular Science for the 360- and 400-MHz ^{1}H NMR measurement, respectively. We are grateful to Professors J. Tsuji of Tokyo Institute of Technology and H. Ogoshi of Kyoto University and Dr. K. Yasufuku of the Institute of Physical and Chemical Research (RIKEN) for donation of ruthenium catalysts. We are also indebted to Professor S. Suzuki of our department for the suggestion for the malonaldehyde assay. We also thank Professor K. Hirao of our University for his helpful guidance in conducting MO calculations. This work was partly supported by Grant-in-Aid for Specially Promoted Research No. 62065005 from the Ministry of Education, Science, and Culture of Japan.

Supplementary Material Available: ^{1}H and ^{13}C NMR spectra of the diepoxides **62** and **63** (4 pages). Ordering information is given on any current masthead page.

(75) Okazaki, R.; Negishi, Y.; Inamoto, N. *J. Org. Chem.* **1984**, *49*, 3819.

Catalysis by Cucurbituril. The Significance of Bound-Substrate Destabilization for Induced Triazole Formation[1]

William L. Mock,* Ted A. Irra, James P. Wepsiec, and Mita Adhya

Department of Chemistry, University of Illinois at Chicago, Chicago, Illinois 60680

Received May 30, 1989

A mechanistic investigation is described for the cycloaddition induced between $RNH_2^+CH_2C{\equiv}CH$ and $RNH_2^+CH_2CH_2N_3$ (R = H, *t*-Bu) consequent to encapsulation by the polycyclic molecular receptor cucurbituril ($C_{36}H_{36}N_{24}O_{12}$). The reaction is shown to be substantially accelerated (ca. 10^5-fold), and the kinetic characteristics of catalytic saturation behavior, substrate inhibition, and slow product release are documented. For substrates with R = *t*-Bu a rotaxane product results, and inhibition kinetics with $NH_3^+CH_2CH_2C(CH_3)_3$ are also examined. A rate enhancement attributed to bound-substrate destabilization is detected. The significance of this effect and its connection with the phenomenon of nonproductive binding in catalytic systems are discussed.

Understanding enzymic catalysis represents perhaps the most severe challenge of mechanistic organic chemistry. Because of the complexity of proteins, analogues which mimic aspects of biochemical catalysis are desirable. Excellent progress has been made in devising synthetic molecular receptors, and much is being learned about *specificity* in molecular recognition from imaginatively engineered models of this nature.[2] Even more arduous is

(1) Taken in part from the Ph.D. Thesis of M. Adhya, University of Illinois, Chicago, 1986; *Diss. Abstr. Int. B* **1986**, *47*, 1056.

(2) Recent reviews: Breslow, R. *Adv. Enzymol. Relat. Areas Mol. Biol.* **1986**, *58*, 1. Franke, J.; Vogtle, T. *Top. Curr. Chem.* **1986**, *132*, 135. Sutherland, I. O. *Chem. Soc. Rev.* **1986**, *15*, 63. Cram, D. J. *Angew, Chem., Int. Ed. Engl.* **1988**, *27*, 1009. Diederich, F. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 362. Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 90. Rebek, J. *Top. Curr. Chem.* **1988**, *149*, 189. Stoddart, F. *Chem. Brit.* **1988**, *24*, 1203.

0022-3263/89/1954-5302$01.50/0 © 1989 American Chemical Society