[Chem. Pharm. Bull. 32(7)2639—2645(1984)]

Chemistry of 2-Methoxy-2,5-cyclohexadienones. II.[1] Oxidation of 2-Methoxy-4,4-dimethyl-2,5-cyclohexadienone[2]

KATSUHIDE MATOBA,* NORIO KARIBE, and TAKAO YAMAZAKI

Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, Sugitani, Toyama 930–01, Japan

(Received November 9, 1983)

2-Methoxy-4,4-dimethyl-2-cyclohexenone (II) afforded 5,6-epoxy-6-methoxy-4,4-dimethyl-6-hexanolide (III) upon reaction with *m*-chloroperbenzoic acid in 1,1,1-trichloroethane. On the other hand, the treatment of II with the same reagent in an aqueous disodium orthophosphate-methylene chloride system at 4 °C gave 2,3-epoxy-2-methoxy-4,4-dimethylcyclohexanone (V), which could be converted to methyl 2-hydroxy-1-methoxy-3,3-dimethylcyclopentanecarboxylate (VI).

2-Methoxy-4,4-dimethyl-2,5-cyclohexadienone (I) afforded 5,6-epoxy-2-methoxy-4,4-dimethyl-2-cyclohexenone (VIII) upon reaction with hydrogen peroxide in a basic medium. The reaction of I with *m*-chloroperbenzoic acid at room temperature gave 5,6-epoxy-6-methoxy-4,4-dimethyl-2-cyclohexenone (X). Neither VIII nor X gave the expected 2,3,5,6-diepoxy-2-methoxy-4,4-dimethylcyclohexanone (VII), but afforded 2,3,5,6-diepoxy-6-methoxy-4,4-dimethyl-6-hexanolide (IX).

Keywords——cyclohexadienone; 2-methoxy-2,5-cyclohexadienone; epoxidation; Baeyer–Villiger oxidation; acid-rearrangement; biogenesis

In our preceding paper,[1] the photochemical behavior of 2-methoxy-4,4-dimethyl-2,5-cyclohexadienone (I) in methanol and in benzene was reported. In this paper, we wish to report the results of epoxidation of I, carried out in order to check the feasibility of Barton's proposal[3] for the biosynthesis of acutumine (a minor alkaloid of *Sinomenium acutum* REHD, *et* WILS.), *i.e.*, that the 4-hydroxy-3-methoxy-2-cyclopentenone moiety may be generated *via* Favorskii rearrangement of the corresponding diepoxide of 2-methoxy-2,5-cyclohexadienone (Chart 1).

Prior to examination of I, the oxidation for II was carried out. Compound II was treated with hydrogen peroxide (HPO) in a basic medium[4] or with *tert*-butyl hydroperoxide (BHPO)[5] to give only unchanged starting material. This result indicates that the double bond of II is different from that of a normal α,β-unsaturated ketone and resembles an isolated double bond. Thus, II was treated wih *m*-chloroperbenzoic acid (*m*CPBA) in methylene chloride at reflux temperature to give a product with recovery of a large amount of the starting material. On the other hand, a mixture of II and *m*CPBA in 1,1,1-trichloroethane (TCE) was refluxed to give the same product as that mentioned above in good yield. This product exhibited a

Barton's proposal

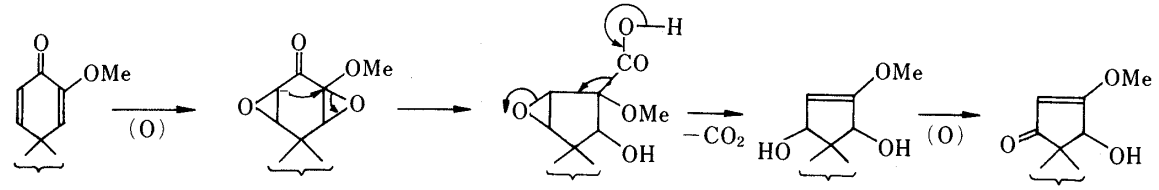
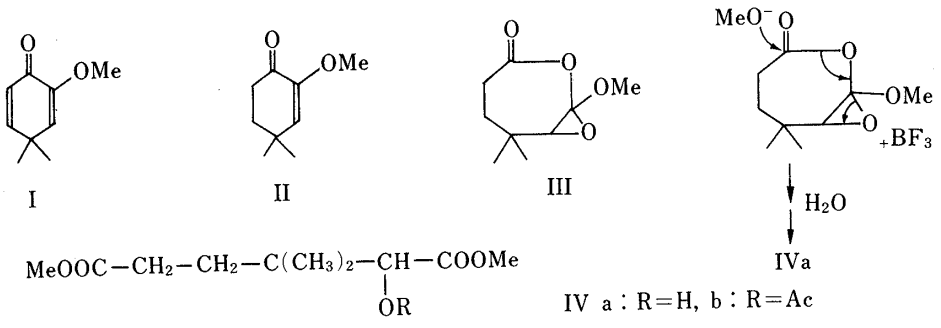
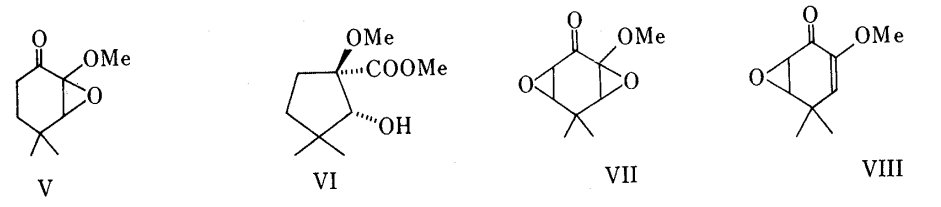


Chart 1

carbonyl band at 1750 cm^{-1} in the infrared (IR) spectrum and a doublet (J = 1.8 Hz) peak at δ 4.42 ppm in the nuclear magnetic resonance (NMR) spectrum. From these data and the elemental analysis, the structure 5,6-epoxy-6-methoxy-4,4-dimethyl-6-hexanolide (III) was assigned to the product. The doublet signal in the NMR spectrum may be attributable to the C_5-proton coupling through four σ bonds with one of the C_3-protons (W rule). From the examination of a molecular model, the C_5-proton must be quasi-equatorial. An alternative orientation of the Baeyer–Villiger oxidation was excluded by the NMR spectral data and by mechanistic considerations (the effect of an electron-donating methoxy group and the migrating aptitude in this oxidation). To confirm the structure of III, it was treated with boron trifluoride etherate (BF_3–Et_2O) in methanol to give an oily compound, which gave only one peak in high performance liquid chromatography (HPLC), two singlet signals at δ 2.7 (1H) and 3.65 (3H) ppm due to hydroxy and methoxy groups and a singlet signal at δ 3.82 (4H) ppm due to methoxy and C_2-protons in the NMR spectrum, and absorption bands at 3545, 1740, and 1720 cm^{-1} in the IR spectrum due to hydroxy and two ester groups, respectively. The elemental analysis was consistent with $C_{10}H_{18}O_5$. Thus, the product in the solvolysis was suggested to be dimethyl 2-hydroxy-3,3-dimethyladipate (IVa), and the mechanism of formation of IVa from III is proposed to be as shown in Chart 2. Compound IVa was derived to its acetate (IVb) by treatment with acetic anhydride in pyridine. Compound IVb exhibited three singlet peaks at δ 3.67, 3.77, and 4.59 ppm due to two methoxy groups and the C_2-proton, respectively, in the NMR spectrum.

Although the epoxidation of II could be performed by *m*CPBA, unexpected over-oxidation was observed. Thus, milder conditions (reaction temperature and acidity of the reaction medium) were investigated for this *m*CPBA oxidation. The expected 2,3-epoxy-2-





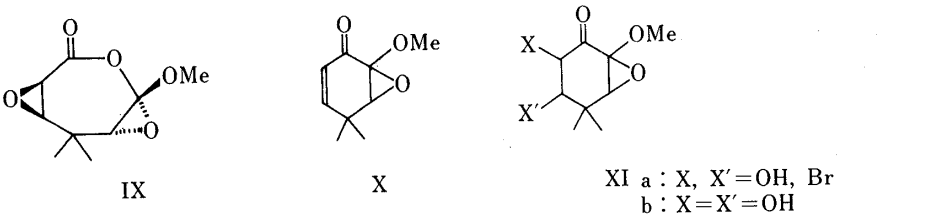


Chart 2

methoxy-4,4-dimethylcyclohexanone (V) was obtained in 18.8% yield when *m*CPBA oxidation was carried out at 4 °C for a few days in a bilayer system of methylene chloride-aqueous disodium orthophosphate. In this case, II was recovered in 24.3% yield. Compound V exhibited a carbonyl absorption at 1720 cm^{-1} in the IR spectrum and two singlet signals at δ 3.59 and 3.14 ppm due to the methoxy and C_3 protons, respectively, in the NMR spectrum. To examine the feasibility of Barton's proposal mentioned above, V was treated with BF_3–Et_2O in methanol to give an oily compound, which exhibited absorption maxima at 3540 and 1742 cm^{-1} in the IR spectrum, a parent peak at *m/e* 202 in the mass spectrum (MS), and signals at δ 3.55 (1H), 3.41 (3H), 3.29 (3H) ppm in the NMR spectrum. These data suggest that the product may be methyl 2-hydroxy-1-methoxy-3,3-dimethylcyclopentanecarboxylate (VI), as expected. The yield of VI from V was 69.0%. The doublet signals (J=1.6 Hz) at δ 3.55 ppm due to the C_2-proton in the NMR spectrum suggested that this proton must be fixed in a quasi-equatorial position (W rule). Further, mechanistic considerations indicate that the methoxy and hydroxy groups are *trans* to each other. As V gave the expected rearrangement product, the preparation of the diepoxide of I (VII) was then tried. At first, I was treated with HPO in a basic medium to give an oily product, which exhibited a carbonyl band at 1690 cm^{-1} in the IR spectrum, a parent peak at *m/e* 168 in the MS, and signals at δ 3.39, 3.56 and 5.27 ppm due to the two protons at the epoxy carbon and the vinylic proton, respectively, in the NMR spectrum. The product was suggested from the spectral data to be 5,6-epoxy-2-methoxy-4,4-dimethyl-2-cyclohexenone (VIII), and the elemental analysis was consistent with $C_9H_{12}O$. The yield of VIII from I was 35.8%, and the recovery of the starting material was 21.5%. Attempts to increase the yield of VIII were unsuccessful. The doublet signal (J=2.8 Hz) at δ 5.27 ppm revealed that the C_5-proton must be quasi-equatorial. To obtain VII, VIII was treated with *m*CPBA under conditions similar to those used in the preparation of V. However, the starting material was recovered unchanged. When a solution of VIII in TCE was refluxed in the presence of this reagent, the product consisted of colorless needles, which exhibited a carbonyl band at 1755 cm^{-1} in the IR spectrum, a parent peak at *m/e* 200 in the MS, and two doublet signals at δ 3.30 and 3.36 ppm and a singlet peak at δ 4.86 ppm due to three protons attached to the epoxy carbons in the NMR spectrum. From these physical data and the fact that III was obtained from II, this crystalline product was considered to be 2,3,5,6-diepoxy-6-methoxy-4,4-dimethyl-6-hexanolide (IX). The peak at δ 4.86 ppm in the NMR spectrum is attributable to the C_5-proton and is at about 1 ppm lower field than the peaks due to the C_3-proton in V, but at similar field to that in III. Furthermore, the relative configuration of the two epoxy rings in IX was determined to be as shown in Chart 2 from the shape of the signal at δ 4.86 ppm, that is, the singlet signal excluded the alternative configuration in which W-coupling between the C_3- and C_5-protons should be observed.

As it was impossible to convert I into VII *via* VIII as mentioned above, another route from I to VII was tried. Compound I was treated with *m*CPBA under conditions similar to those used in the preparation of V from II to give the unchanged starting material. Next, the reaction was carried out at room temperature to give an oily product, which exhibited a conjugated carbonyl band at 1698 cm^{-1} in the IR spectrum, and signals at δ 3.35, 5.73, and 6.18 ppm due to the proton attached to the epoxy carbon and two olefinic protons, respectively, in the NMR spectrum. From these physical data, this oily product was considered to be the expected product, 5,6-epoxy-6-methoxy-4,4-dimethyl-2-cyclohexenone (X). The chemical shift of the C_5-proton in X was similar to that in V and was about 1 ppm higher than that in III. Furthermore, since the NMR signal of the C_5-proton was a doublet, the proton must be fixed in the quasi-equatorial position. Next, repeated attempts were made to obtain VII from X using HPO in basic media. When X was treated with this reagent at room temperature in methanol, IX was obtained as the sole product in a yield of 6.4% instead of the expected product, VII. To obtain the suspected decomposition product (acid and/or

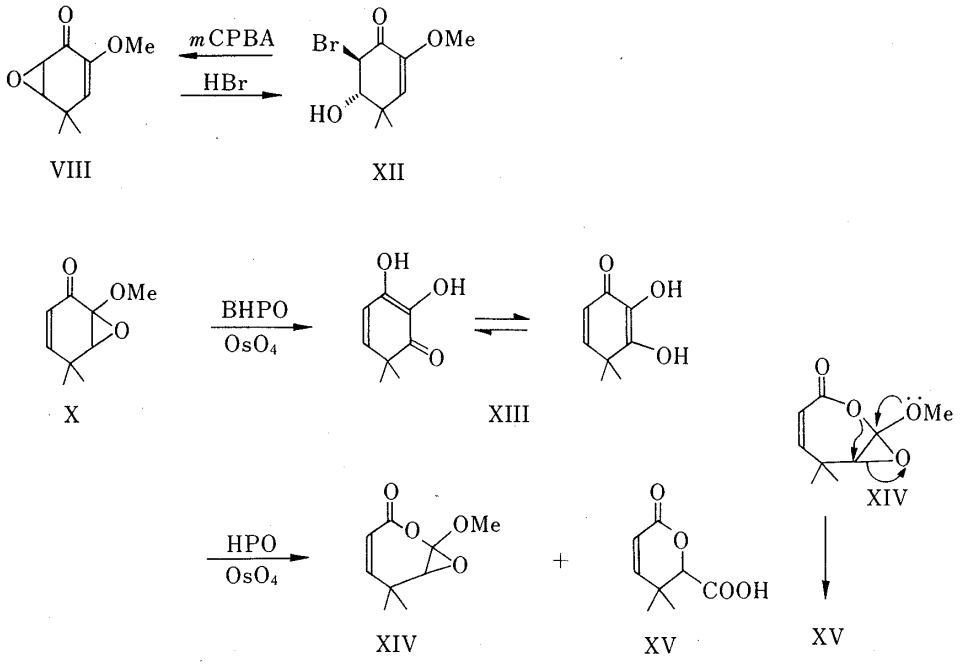


Chart 3

alcohol), the aqueous layer was acidified, salted-out and extracted with ethyl acetate. However, the residue could not be purified. Further, in the reaction of X with BHPO, only IX was obtained as a product.

As the expected diepoxide, VII, was not obtained, we turned our attention to the synthesis of the analogous compound, XI.

First, hydrobromination of VIII was examined. Compound VIII was treated with hydrobromic acid to give colorless needles, which exhibited absorptions at 3600 and 1703 cm^{-1} due to the hydroxy group and the carbonyl group, respectively, in the IR spectrum, and two doublet signals ($J=12$ Hz) at δ 3.77 and 4.81 ppm in the NMR spectrum. The IR, NMR, and MS and the elemental analysis indicated the crystalline compound to be *trans*-6-bromo-5-hydroxy-2-methoxy-4,4-dimethyl-2-cyclohexenone (XII). The coupling constant revealed that the substituents on the C_5- and C_6-positions were both equatorial. The yield of XII from VIII was 70.0%. When XII was treated with *m*CPBA in the bilayer system as mentioned for the preparation of X, XIa was not formed, but XII was re-epoxidized to VIII in a yield of 61.5%.

Next, to synthesize the α-glycol XIb, X was treated with BHPO or HPO in the presence of a catalytic amount of osmium tetroxide. When BHPO was used the product was dimethyldihydroxycyclohexadienone (XIII), which gave a positive ferric chloride test and exhibited three peaks at δ 1.37, 6.14, and 6.53 ppm due to the geminal methyl, and two vinylic protons, respectively, in the NMR spectrum. Compound XIII also showed a bathochromic shift with methanolic base in the ultraviolet (UV) spectrum. On the other hand, in the case of HPO, two products were isolated. One was an oily compound, and its physical data and the elemental analysis were consistent with the structure 5,6-epoxy-6-methoxy-4,4-dimethyl-2-hexen-6-olide (XIV). The other product was an unstable crystalline compound, which could not be recrystallized; the IR and MS showed the existence of a carboxyl group, and the structure was considered to be 5-carboxyl-4,4-dimethyl-2-penten-5-olide (XV). The mechanism of formation may be as shown in Chart 3.

As mentioned above, all attempts to obtain the diepoxide, VII, were unsuccessful, and therefore, Barton's proposal could not be examined. However, the oxidation behavior of I

and II and the acid rearrangement of V obtained from II were elucidated.

Experimental

All melting points were taken on a Kofler block, and the boiling points are uncorrected. IR spectra were determined by using a JASCO A 102 or a JASCO IRA 1 diffraction grating spectrophotometer; absorption data are given in cm^{-1}. NMR spectra were recorded on a Varian EM-360, JEOL PMX-60, Varian EM-390, or Varian XL-200 spectrometer with tetramethylsilane (TMS) as an internal standard. The chemical shifts and coupling constants (J) are given in δ and Hz, respectively. MS were measured with a JEOL D-200 (70 eV, direct inlet system) spectrometer. UV spectra were obtained in MeOH with a Hitachi 200-10 spectrophotometer, and absorption maxima are given in nm. HPLC was carried out using a Waters ALC 244 instrument equipped with a Radial Pak A LC Cartridge (8 m/m × 10 cm) as a column. The flow rate of the solvent used in HPLC was 2 ml/min. All solvents were removed by evaporation under reduced pressure.

5,6-Epoxy-6-methoxy-4,4-dimethyl-6-hexanolide (III)——A solution of 2-methoxy-4,4-dimethyl-2-cyclohexenone (II) (0.2 g, 1.3 mmol) and *m*CPBA (purity 70%, 0.91 g, 3.9 mmol) in TCE was refluxed for 33 h, then washed with sat. $NaHCO_3$ and brine, dried and evaporated to give an oily compound, 0.28 g, which was purified on an SiO_2 column with 5% AcOEt–benzene as the eluant to give III (176 mg, 73.1%). bp < 140 °C (5 mmHg). IR (CCl_4): $\nu_{C=O}$ 1750, δ 1203, 1159, 1081. NMR (CCl_4): 1.01 and 1.20 (each 3H, s, geminal Me), 1.3—2.1 (2H, m, C_3–H), 2.4—2.7 (2H, m, C_2–H), 3.80 (3H, s, MeO–), 4.42 (1H, d, J=1.8, C_5–H). MS *m/e* (%): 188 (M^++2, 80.6), 187 (M^++1, base peak), 169 (72.6), 155 (77.7). *Anal.* Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.55; H, 7.33. *Cf*; Calcd for $C_9H_{14}O_4+1/12\ H_2O$: C, 57.59; H, 7.61.

Dimethyl 2-Hydroxy-3,3-dimethyladipate (IVa)——A methanolic mixture of III (23.5 mg) and BF_3–Et_2O (1 ml) was refluxed for 30 min. The solution was neutralized with $NaHCO_3$, diluted with water and extracted with Et_2O. The organic layer was washed with brine, dried and concentrated to give IVa (26.9 mg, 92%). HPLC (MeOH : H_2O = 3 : 1): t_R 1.63 min. (MeOH : H_2O = 1 : 1): t_R 7.17 min. IR (film): ν_{OH} 3545, $\nu_{C=O}$ 1740, 1720. NMR (CCl_4): 0.91 (6H, s, geminal Me), 1.4—1.9 and 2.1—2.5 (each 2H, m, 2 × CH_2<), 2.7 (1H, br s, OH), 3.65 (3H, s, OMe), 3.82 (4H, s, MeO– and >CH–O). MS, *m/e* (%): 219 (M^++1, 0.2), 129 (94.3), 127 (82.4). *Anal.* Calcd for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 55.24; H, 8.30. Acetate (IVb): IVa was acetylated with Ac_2O and pyridine to give IVb in a quantitative yield. bp < 153 °C (10 mmHg). IR (film): $\nu_{C=O}$ 1750. NMR (CCl_4): 1.00 (6H, s, geminal CH_3), 1.4—1.9 (2H, m, >CH_2), 2.0—2.5 (2H, m, >CH_2), 2.16 (3H, s, Ac), 3.67 and 3.77 (each 3H, s, OMe), 4.59 (1H, s, >CH–O). MS, *m/e* (%): 261 (M^++1, 0.1), 201 (M^+ − OAc, 15.7). *Anal.* Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.75. Found: C, 55.30; H, 7.61.

2,3-Epoxy-2-methoxy-4,4-dimethylcyclohexanone (V)——Na_2HPO_4 12 H_2O (6.5 g) in H_2O (80 ml) and *m*CPBA (70%, 919 mg, 3.73 mmol) were added to a solution of II (0.5 g, 3.25 mmol) in CH_2Cl_2 (100 ml). The mixture was stirred vigorously at 4 °C for 65.4 h, then the organic layer was separated, washed with 10% aq. NaOH solution and brine, dried, and evaporated to give an oily compound (468 mg), which was fractionated through an SiO_2 column. V (104 mg, 18.8%), III (114 mg, 18.8%), and II (122 mg, 24.3%) were successively eluted with 5% AcOEt–benzene and 10% AcOEt–benzene. V: IR ($CHCl_3$): $\nu_{C=O}$ 1720. NMR (CCl_4): 1.14 and 1.20 (each 3H, s, geminal Me), 1.4—2.5 (4H, m, 2 × CH_2<), 3.14 (1H, s, C_3–H), 3.59 (3H, s, MeO–). MS *m/e* (%): 171 (M^++1, 28.2), 156 (34), 139 (M^+ − OMe, base peak). High resolution MS, Calcd for $C_9H_{14}O_3$: *m/e* 170.0794. Found: *m/e* 170.0955.

Methyl 2-Hydroxy-1-methoxy-3,3-dimethylcyclopentanecarboxylate (VI)——A methanolic mixture of V (50 mg, 0.29 mmol) and BF_3–Et_2O (1 ml) was stirred at room temperature for about 30 min. The resulting solution was poured into cold water, followed by neutralization with sat. $NaHCO_3$. The aq. solution was extracted with Et_2O. The Et_2O layer was washed with brine, then dried and concentrated to give an oily compound (47.3 mg), which was purified by SiO_2 column chromatography. VI (40 mg, 69%) was eluted with 5% AcOEt–benzene. bp < 123 °C (7.5 mmHg). IR (film): ν_{OH} 3540, $\nu_{C=O}$ 1742. NMR (CCl_4): 1.10 and 1.24 (each 3H, s, geminal Me), 3.29 and 3.41 (each 3H, s, OMe), 3.55 (1H, d, J=1.6, C_2–H). MS, *m/e* (%): 202 (M^+, 67.7%), 174 (M^+ − CO, 55.9), 171 (M^+ − MeO, 60.4). *Anal.* Calcd for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 58.30; H, 9.14. *Cf*; Calcd for $C_{10}H_{18}O_4+1/5H_2O$: C, 58.35; H, 9.01.

5,6-Epoxy-2-methoxy-4,4-dimethyl-2-cyclohexanone (VIII)——HPO (30%, 0.95 ml, 9.3 mmol) and 6 N NaOH solution (0.27 ml) were added to a methanolic solution of I (0.5 g, 3.3 mmol) at 15 °C. After 5 min, the reaction mixture was stirred at 20—30 °C for 3 h and then diluted with water. The extracted Et_2O layer was washed with brine, dried and concentrated to give an oily compound (329 mg), which was purified through an SiO_2 column. VIII (198 mg, 35.8%) and I (108 mg, 21.5%) were successively obtained from the 5% AcOEt–benzene eluate. bp < 130 °C (7.5 mmHg) IR (film): $\nu_{C=O}$ 1690, $\nu_{C=C}$ 1628. NMR ($CDCl_3$): 1.26 and 1.37 (each 3H, s, geminal Me), 3.39 (1H, dd, J=3.8 and 2.8, C_5–H), 3.56 (1H, d, J=3.8, C_6–H), 3.56 (3H, s, OMe), 5.27 (1H, d, J=2.8, C_3–H). MS, *m/e* (%): 168 (M^+, 22), 153 (M^+ − Me, 19.6), 137 (3.1), 125 (base peak). *Anal.* Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 63.89; H, 6.98.

5,6-Epoxy-6-methoxy-4,4-dimethyl-2-cyclohexenone (X)——$Na_2HPO_4 12H_2O$ (13 g) in H_2O (140 ml) and

*m*CPBA (70%, 2.16 g, 8.76 mmol) were added to a CH_2Cl_2 solution of I (1 g, 6.58 mmol), and the mixture was stirred vigorously for 63 h at room temperature. The organic layer was separated, washed with 10% aq. NaOH and brine, dried and evaporated. The oily residue was separated by SiO_2 column chromatography. X (811 mg, 73.4%) and I (75 mg, 7.4%) were eluted with 5% and 50% AcOEt–benzene, respectively. bp <120 °C (9.5 mmHg). NMR (CCl_4): 1.31 (6H, s, Me), 3.35 (1H, d, $J=2.6$, C_5–H), 3.66 (3H, s, OMe), 5.73 (1H, d, $J=11$, C_2–H), 6.18 (1H, dd, $J=11$ and 2.8, C_3–H). MS, *m/e* (%): 169 ($M^+ +1$, 4.4), 168 (M^+, 6.2), 153 ($M^+ -$Me, 21), 141 (*m/e* 169 − CO, 34.2), 139 (base peak), 109 (62.8). *Anal.* Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 63.78; H, 7.25. *Cf*; Calcd for $C_9H_{12}O_3+1/10H_2O$: C, 63.59; H, 7.23. IR (film): $\nu_{C=O}$ 1698.

2,3,5,6-Diepoxy-6-methoxy-4,4-dimethyl-6-hexanolide (IX)——1) Using *m*CPBA: A mixture of VIII (35 mg, 0.21 mmol), *m*CPBA (108.5 mg, 0.63 mmol), and TCE (20 ml) was refluxed for 4 h. The reaction mixture was washed with sat. $NaHCO_3$ and brine, then dried to give an oily compound, which was fractionated through an SiO_2 column to give crystalline IX (21 mg, 52.4%). This product was recrystallized from hexane–benzene to give colorless needles, mp 102—103.5 °C. IR ($CHCl_3$): $\nu_{C=O}$ 1775. NMR ($CDCl_3$): 1.03 and 1.38 (each 3H, s, geminal Me), 3.20 (1H, d, $J=4$, C_3–H), 3.36 (1H, d, $J=4$, C_2–H), 3.86 (3H, s, OMe), 4.84 (1H, s, C_5–H). MS, *m/e* (%): 200 (M^+, 1.5), 168 ($M^+ - O_2$, 1.8), 141 ($M^+ -$CO−OMe, base peak). High resolution MS, Calcd for $C_9H_{12}O_5$: *m/e* 200.0684. Found: *m/e* 200.0570. *Anal.* Calcd for $C_9H_{12}O_5$: C, 53.99; H, 6.04. Found: C, 54.11; H, 6.12.

2) Using HPO: An aq. solution (0.5 ml) of NaOH (95%, 66 mg, 1.57 mmol) was added over 5 min to a methanolic solution (2 ml) of X (264 mg, 1.57 mmol) and HPO (30%, 0.9 ml, 8.8 mmol). The mixture was stirred for 3 h at room temperature, diluted with H_2O (50 ml) and extracted with Et_2O. The Et_2O layer was washed with brine and dried. X (79 mg, 30%) was recovered from this Et_2O solution. The mother liquor was acidified with 5% HCl, salted-out and extracted with AcOEt. The organic layer was dried and concentrated to give an oily substance (153 mg), which was purified through an SiO_2 column. IX (20 mg, 6.4%) was eluted with 10% AcOEt–benzene. An oily compound eluted with AcOEt was treated with an excess of CH_2N_2 to give an unidentifiable mixture.

3) Using BHPO: A methanolic solution (3 ml) of X (0.1 g, 0.6 mmol) and BHPO (70%, 85.4 mg, 0.72 mmol) was treated with 1 N NaOH solution at 30—40 °C to adjust the pH to 8.5. The mixture was stirred for 1 h, diluted with H_2O (30 ml) and extracted with Et_2O. In the same manner as described in 2), X (60.2 mg, 50%) was recovered from the Et_2O layer and an oily material (51.4 mg) consisting mainly of IX was obtained from the AcOEt layer.

***trans*-6-Bromo-5-hydroxy-2-methoxy-4,4-dimethyl-2-cyclohexenone (XII)**——A solution of VIII (0.1 g, 0.6 mmol) in CCl_4 (2 ml) was added over 0.5 h to a CCl_4 solution of HBr (47%, 0.13 ml) under ice-cooling. The mixture was stirred for 1.5 h at this temperature, then the organic layer was separated and the aq. solution was extracted with CCl_4. The combined CCl_4 layer was dried and evaporated to give recovered VIII (8.8 mg, 8.3%). The aq. solution was basified with 10% Na_2CO_3 and extracted with Et_2O. The Et_2O layer was washed with brine and dried. The oily residue obtained after removal of the solvent crystallized to give 104 mg (70.0%) of product, mp 87—89 °C (recrystallized from CCl_4). IR (film): ν_{OH} 3600, $\nu_{C=O}$ 1703, ν 1619. NMR ($CDCl_3$): 1.21 and 1.35 (each 3H, s, geminal Me), 2.5—3.0 (1H, br s, OH), 3.65 (3H, s, OMe), 3.77 (1H, br d, $J=12$, C_5–H), 4.81 (1H, d, $J=12$, C_6–H), 5.67 (1H, d, $J=1$, C_3–H). MS, *m/e* (%): 250 ($M^+ +2$, 0.9), 240 ($M^+ +1$, 3.4), 248 (M^+, 1), 169 ($M^+ -$Br, base peak), 137 ($M^+ -$Br−MeOH, 75.5), 109 (*m/e* 137 − CO, 47.1). *Anal.* Calcd for $C_9H_{13}BrO_3$: C, 43.39; H, 5.26. Found: C, 43.13; H, 5.20.

Reaction of XII and *m*CPBA——Na_2HPO_4 $12H_2O$ (280 mg) in H_2O (10 ml) and *m*CPBA (70%, 96 mg, 0.39 mmol) were added to a CH_2Cl_2 solution of XII (64.7 mg, 0.26 mmol) under ice-cooling. The mixture was stirred for 16 h at 4 °C, and for 5 h at room temperature, then washed with 10% NaOH and brine, and evaporated to give VIII (27 mg, 61.5%). The identity of VIII was confirmed by NMR comparison with an authentic sample.

Dimethyldihydroxycyclohexadienone (XIII)——A *tert*-butanolic solution (2 ml) of X (75 mg, 0.45 mmol), Triton B (40% methanolic, 0.02 ml), H_2O (0.07 ml), BHPO (70%, 0.1 ml, 0.72 mmol) and a 0.5% *tert*-butanolic solution (0.045 ml) of OsO_4 were mixed and stirred overnight at 4 °C. Then 5% $NaHSO_3$ aq. solution (1 ml) was added. An oily residue obtained after concentration of this mixture was extracted with Et_2O. The Et_2O layer was washed with brine, dried over anhyd. $MgSO_4$, and concentrated to give an oily substance (36 mg). The aq. solution was extracted with AcOEt after salting-out. As the residue (26.5 mg) obtained from the AcOEt layer was similar to that from the Et_2O layer in thin-layer chromatography (TLC), the combined material was purified through an SiO_2 column. From the 30% AcOEt–benzene eluate, crystalline XIII (35.8 mg, 51%) was obtained. mp 102—112 °C (sublim., recrystallized from benzene). $FeCl_3$-test: blue. IR ($CHCl_3$): ν_{OH} 3390, $\nu_{C=O}$ 1672, ν 1637, 1579. UV (MeOH), λ_{max} (ε): 213 (25900), 340 (5030). (MeOH–OH^-): 220 (33500), 378 (6970). NMR ($CDCl_3$): 1.37 (6H, s, geminal Me), 6.14 (1H, d, $J=9$, C_6–H), 6.53 (1H, d, $J=9$, C_5–H). MS, *m/e* (%): 155 ($M^+ +1$, 19.2), 154 (M^+, 97.4), 139 ($M^+ -$Me, 29.5), 126 ($M^+ -$CO, 38.3), 111 (*m/e* 126 − Me, 70.6), 93 (*m/e* 111 − H_2O, 38.7). *Anal.* Calcd for $C_8H_{10}O_3$: C, 62.32; H, 6.54. Found: C, 62.04; H, 6.28.

5,6-Epoxy-6-methoxy-4,4-dimethyl-2-hexen-6-olide (XIV) and 5-Carboxy-4,4-dimethyl-2-penten-5-olide (XV)——An ether solution (0.1 ml) of OsO_4 (4.6 mg) was added to an ether solution (3 ml) of X (0.1 g, 0.6 mmol) and HPO (30%, 0.3 ml, 2.9 mmol) at 0—2 °C. The mixture was vigorously stirred for 30 min at this temperature and then overnight at room temperature. The reaction mixture was washed with water, dried, and concentrated to give an oily material (48.3 mg). The aq. layer was acidified with 5% HCl and extracted with AcOEt. The oily residue (53.9 mg)

from AcOEt and that from Et_2O were combined and purified by SiO_2 column chromatography. XIV (13.7 mg, 11.7%) and XV (26.2 mg, 25.0%) were obtained from the 10 and 20% AcOEt–benzene eluates as an oily material and an unstable crystalline compound, respectively. XIV: bp <168 °C (17 mmHg). IR ($CHCl_3$): $\nu_{C=O}$ 1730. NMR ($CDCl_3$): 1.16 and 1.35 (each 3H, s, geminal Me), 3.87 (3H, s, OMe), 4.80 (1H, s, C_5–H), 6.00 (1H, d, $J=10$, C_2–H), 6.65 (1H, d, $J=10$, C_3–H). MS, *m/e* (%): 184 (M^+, 0.8), 166 (M^+-H_2O, 0.7), 125 ($M^+-CO-OMe$, 48.4). *Anal.* Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.46; H, 6.59. XV: mp 46—51 °C (crude). IR ($CHCl_3$): ν_{OH} 3600—2400, $\nu_{C=O}$ 1733. NMR ($CDCl_3$): 1.21 and 1.38 (each 3H, s, geminal Me), 4.97 (1H, s, C_5–H), 5.8—6.2 (1H, br s, OH), 5.94 (1H, d, $J=10$, C_2–H), 6.64 (1H, d, $J=10$, C_3–H). MS, *m/e* (%): 171 ($M^+ +1$, 0.6), 170 (M^+, 0.7), 125 (M^+-COOH, base peak).

Acknowledgements The authors thank Mr. M. Morikoshi and Mr. M. Ogawa for the high resolution mass spectral measurements and the elemental analyses, respectively.

References and Notes

1) Part I: K. Matoba, K. Karibe, and T. Yamazaki, *Chem. Pharm. Bull.*, **30**, 3906 (1982).
2) A part of this work was presented at the 103rd Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, April 1983.
3) D. H. R. Barton, A. J. Kirby, and G. W. Kirby, *J. Chem. Soc.* (*C*), **1968**, 929.
4) R. L. Wasson and H. O. House, "Organic Synthesis," Coll. Vol. IV, ed. by N. Rabjohn, John Wiley and Sons, Inc., New York, 1963, p. 552.
5) N. C. Yang and R. A. Finnegan, *J. Am. Chem. Soc.*, **80**, 5845 (1958).