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Stereospecific Epoxidation of *cis*-2-Butene-1,4-diones to *cis*-2,3-Epoxybutane-1,4-diones with Oxodiperoxomolybdenum (VI), $MoO_5 \cdot H_2O \cdot HMPA$

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The epoxidation of *cis*-2-butene-1,4-diones **4** with (aqua)(hexamethylphosphoramide)oxodiperoxomolybdenum (VI), $MoO_5 \cdot H_2O \cdot HMPA$, occurred stereospecifically to give the *cis*-epoxides **5**, whose stereochemistry was assigned on the basis of chemical evidence and a comparison of their spectral data with those of the corresponding *trans*-epoxides **6**, which were prepared by the epoxidation of the *trans*-olefins **3** with alkaline hydrogen peroxide.

Keywords——stereospecific epoxidation; *cis*-epoxide; *trans*-epoxide; peroxomolybdenum complex; Wittig reaction; isomerization; paramagnetic shift; stereochemistry

The biological activities of *cis*-2,3-epoxybutane-1,4-diones, represented by the antibiotic cerulenin,[1] make them important targets for organic synthesis. Although much work has been devoted to the synthesis of *cis*-2,3-epoxybutane-1,4-dione derivatives,[1] there is no method for the synthesis of *cis*-2,3-epoxybutane-1,4-diones by a direct and stereospecific epoxidation of *cis*-2-butene-1,4-diones, because of the non-stereospecificity of the conventional epoxidation of α,β-unsaturated carbonyl compounds.[2,3] Our interest in this area, based on approaches to analogues of cerulenin, prompted us to seek a direct and stereospecific epoxidation of *cis*-2-butene-1,4-diones. We have now found that the epoxidation of *cis*-2-butene-1,4-diones **4** with (aqua) (hexamethylphosphoramide)oxodiperoxomolybdenum (VI), $MoO_5 \cdot H_2O \cdot HMPA$,[4-7] proceeded stereospecifically to give *cis*-2,3-epoxybutane-1,4-diones **5**.

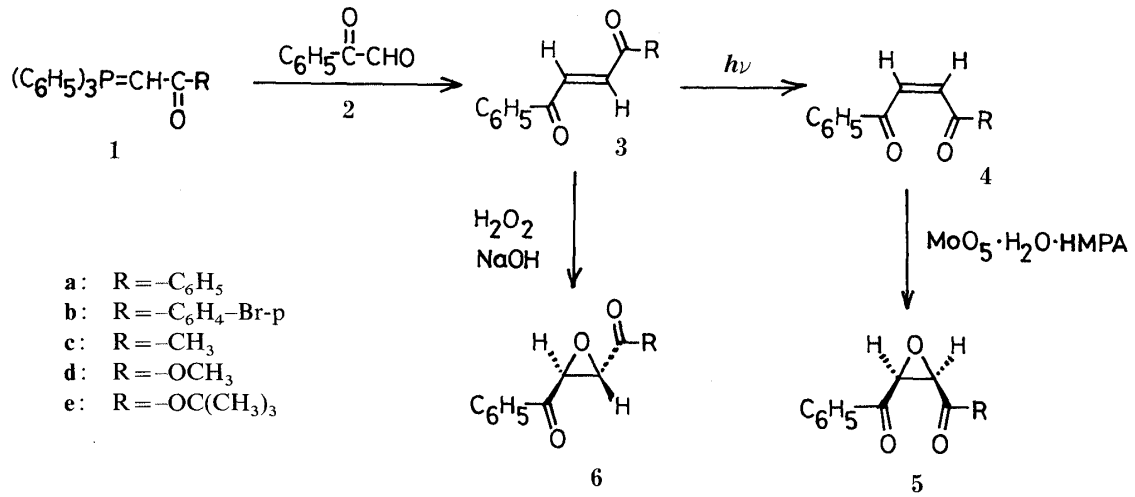


Chart 1

The preparation of the starting *cis*-2-butene-1,4-diones **4a**—**e** is illustrated in Chart 1. Thus, phosphonium ylides **1** were allowed to react with phenylglyoxal (**2**) according to the reported procedure[8] to give mixtures of *trans*- and *cis*-2-butene-1,4-diones, **3** and **4**, and then photoisomerization of the *trans*-olefins **3** was carried out under ordinary conditions[9] to give the *cis*-olefins **4**. Their structures and stereochemistries were assigned on the basis of spectral evidence. The results are summarized in Table I.

Treatment of *cis*-1,4-diphenyl-2-butene-1,4-dione (**4a**) with 2 mol eq of $MoO_5 \cdot H_2O \cdot$ HMPA in methylene chloride at room temperature for a week gave *cis*-2,3-epoxy-1,4-diphenylbutane-1,4-dione (**5a**) in 92% yield. When the epoxidation of **4a** was carried out with 1 mol eq of $MoO_5 \cdot H_2O \cdot$HMPA, the yield of **5a** decreased (36%). The structure and stereochemistry were confirmed by direct comparison of the spectral data and chemical behavior with those of the corresponding *trans*-epoxide **6a**, which was alternatively prepared by the epoxidation of the *trans*-olefin **3a** with alkaline hydrogen peroxide.[3] Since the mass, infrared (IR), ^{1}H- and ^{13}C-nuclear magnetic resonance (NMR) spectra of **5a** were strikingly similar to those of **6a**, **5a** is isomeric with **6a**. The ^{1}H-NMR spectrum obtained in the presence of a shift reagent, $Eu(DPM)_3$,[10] showed a significant difference between **5a** and **6a**; the

Table I. Product Distributions of the Wittig Reaction of **1** with **2** and the Photoisomerization of **3**

	The Wittig reaction of **1** with **2**		The photoisomerization of **3**	
	Yield (%)[a]	Ratio (**3**:**4**)[c]	Yield (%)[a]	Ratio (**3**:**4**)[c]
a	Quant. (80)[b]	20:1	Quant. (82)[d]	1:9
b	81 (78)	26:1	Quant. (51)	1:4.3
c	Quant. (87)	6.7:1	Quant. (47)	1:5.3
d	Quant. (85)	5.7:1	Quant. (48)	1:5.3
e	84 (70)	5:1	Quant. (42)	1:4.4

a) Isolated yields of a mixture of **3** and **4**. *b*) Isolated yield (%) of the *trans*-olefin **3** in parenthesis. *c*) The ratios were determined by area measurement of characteristic peaks in the ^{1}H-NMR spectra of the total product mixtures. *d*) Isolated yield (%) of the *cis*-olefin **4** in parenthesis.

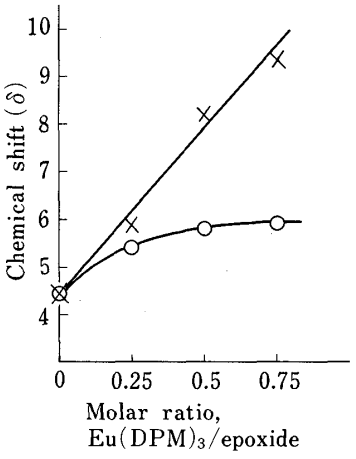


Fig. 1. Chemical Shift Changes Induced by $Eu(DPM)_3$ in the 60 MHz ^{1}H-NMR Spectra of the *cis*-Epoxide **5a** and the *trans*-Epoxide **6a** (each 25 mg, 0.12 mmol) in $CDCl_3$ (0.5 ml)

○: methine protons of **5a**, ×: methine protons of **6a**.

Table II. The Epoxidation of *cis*-2-Butene-1,4-diones **4** with $MoO_5 \cdot H_2O \cdot$HMPA

Product **5**	Yield (%)[a] of **5**	Recovered yield (%)[a] of **4**	**3**
a	92 (92)[b]	Trace	Trace
b	62 (86)	22	6
c	43 (60)	19	9
d	21 (68)	28	41
e	44 (98)	55	

a) Isolated yields. *b*) Yields in parenthesis were based on consumed starting olefins.

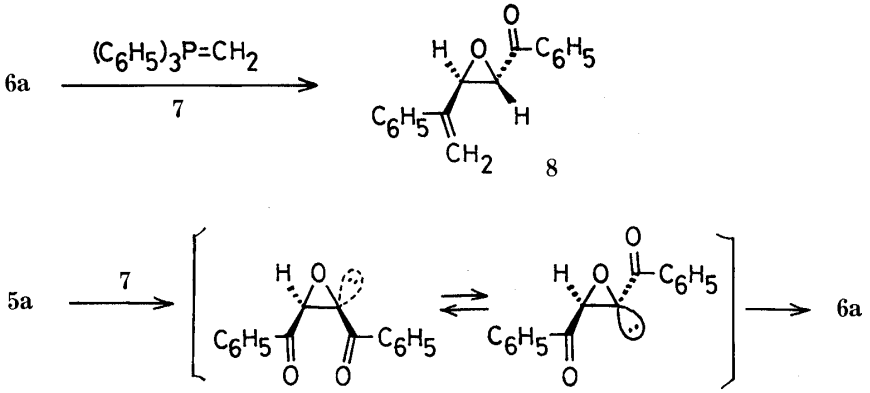


Chart 2

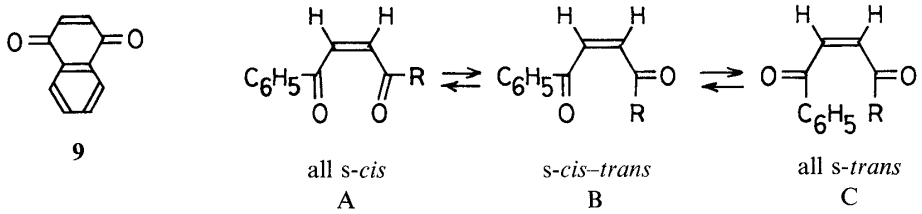
TABLE III. Physical Data for *cis*- and *trans*-2,3-Epoxybutane-1,4-diones, **5** and **6**

Epoxide	IR $\nu_{max}^{CHCl_3}$ cm^{-1}	^{1}H-NMR ($CDCl_3$) δ
5a	1685 (C=O)	4.48 (2H, s, –CH–), 7.2—7.6 (6H, m, Ar-H), 7.8—8.1 (4H, m, Ar-H)
6a	1685 (C=O)	4.48 (2H, s, –CH–), 7.2—7.6 (6H, m, Ar-H), 7.9—8.2 (4H, m, Ar-H)
5b	1685 (C=O)	4.30 (1H, d, J=5 Hz, –CH–), 4.42 (1H, d, J=5 Hz, –CH–), 7.2—7.5 (5H, m, Ar-H), 7.6—8.1 (4H, m, Ar-H)
6b	1685 (C=O)	4.38 (1H, d, J=2 Hz, –CH–), 4.43 (1H, d, J=2 Hz, –CH–), 7.3—8.2 (9H, m, Ar-H)
5c	1710 (–COMe)	2.15 (3H, s, $-CH_3$), 3.78 (1H, d, J=5 Hz, –CH–COMe),
	1685 (–COPh)	4.33 (1H, d, J=5 Hz, –CH–COPh), 7.2—7.7 (3H, m, Ar-H), 7.8—8.1 (2H, m, Ar-H)
6c	1705 (–COMe)	2.25 (3H, s, $-CH_3$), 3.65 (1H, d, J=2 Hz, –CH–COMe),
	1685 (–COPh)	4.30 (1H, d, J=2 Hz, –CH–COPh), 7.2—7.7 (3H, m, Ar-H), 7.8—8.1 (2H, m, Ar-H)
5d	1750 ($-CO_2Me$)	3.63 (3H, s, $-OCH_3$), 3.86 (1H, d, J=5 Hz, –CH–CO_2Me),
	1680 (–COPh)	4.21 (1H, d, J=5 Hz, –CH–COPh), 7.3—7.7 (3H, m, Ar-H), 7.8—8.1 (2H, m, Ar-H)
6d	1750 ($-CO_2Me$)	3.68 (1H, d, J=2 Hz, –CH–CO_2Me), 3.86 (3H, s, $-OCH_3$),
	1685 (–COPh)	4.43 (1H, d, J=2 Hz, –CH–COPh), 7.4—7.7 (3H, m, Ar-H), 7.9—8.2 (2H, m, Ar-H)
5e	1745 ($-CO_2Bu$)	1.25 (9H, s, $-C(CH_3)_3$), 3.73 (1H, d, J=5 Hz, –CH–CO_2Bu),
	1700 (–COPh)	4.10 (1H, d, J=5 Hz, –CH–COPh), 7.3—7.7 (3H, m, Ar-H), 7.9—8.2 (2H, m, Ar-H)
6e	1740 ($-CO_2Bu$)	1.53 (9H, s, $-C(CH_3)_3$), 3.67 (1H, d, J=2 Hz, –CH–CO_2Bu),
	1690 (–COPh)	4.33 (1H, d, J=2 Hz, –CH–COPh), 7.2—7.7 (3H, m, Ar-H), 7.8—8.1 (2H, m, Ar-H)

paramagnetic shift of the epoxy ring protons of **5a** was smaller than that of **6a**, and decreased at a molar ratio $Eu(DPM)_3$/**5a** of approximately 0.5 (Fig. 1). The results can be attributed to the complexation of the shift reagent with the two carbonyl oxygen atoms of **5a**. Reaction of **6a** with the phosphonium ylide **7** gave an olefinic product **8**, while that of **5a** with **7** resulted not in a Wittig reaction but in isomerization of **6a**.

Similarly, *cis*-1-(*p*-bromophenyl)-4-phenyl-2-butene-1,4-dione (**4b**), *cis*-1-phenyl-2-pentene-1,4-dione (**4c**), methyl *cis*-4-oxo-4-phenyl-2-butenoate (**4d**), and *tert*-butyl *cis*-4-oxo-4-phenyl-2-butenoate (**4e**) were converted to the corresponding *cis*-epoxides **5b—e**, together with recovered **3b—d** and **4b—e**[11] (Table II). The structures and stereochemistries were assigned on the basis of direct comparison of the spectral data with those of the corresponding *trans*-epoxides **6b—e** prepared by epoxidation of the *trans*-olefins **3b—e** with alkaline hydrogen peroxide (Table III). Assignments of the spatial relationships of the two carbonyl groups in **5b—e** and **6b—e** were based on a comparison of the spin–spin coupling constants between the epoxy ring protons; **5b—e** showed coupling constants of 4—5 Hz, while **6b—e** showed coupling constants of 2 Hz. These coupling constants were in good agreement with the reported values for *cis*- and *trans*-vicinal coupling in epoxides.[12] The epoxidation of

4 proceeded stereospecifically to give **5** free of the *trans* isomer **6** (checked by thin layer chromatography (TLC)). In contrast, the *trans*-olefins **3** and naphthoquinone (**9**) did not react with $MoO_5 \cdot H_2O \cdot HMPA$.



9

all s-*cis* A | s-*cis*–*trans* B | all s-*trans* C

Chart 3

The epoxidation is specific to *cis*-olefins **4**, which can exist as the all s-*cis* conformer A, and might occur initially by the formation of an intermediate cyclic complex involving **4** and the MoO_5 reagent. In *cis*-olefins **4**, a conformational equilibrium among all s-*cis* A, s-*cis*–*trans* B, and all s-*trans* conformations C can be attained. The equilibrium distribution of the conformations depends on the bulkiness of the substituents (R).[13] A bulky substituent destabilizes B and C relative to A, and the equilibrium favors the all s-*cis* form A. Thus, the epoxidation of **4e** (R=–OBu-*tert*) occurs smoothly compared to that of **4d** (R=–OMe) (Table II). On the other hand, naphthoquinone (**9**), which is held in the form of all s-*trans* C, did not react with $MoO_5 \cdot H_2O \cdot HMPA$.

For comparison, we also investigated the reaction of the *cis*-olefin **4a** with several conventional epoxidizing agents. Treatment of **4a** with alkaline hydrogen peroxide gave the *trans*-epoxide **6a** in 86% yield, without formation of the *cis*-isomer **5a**. Reaction of **4a** with hydrogen peroxide by using sodium tungstate catalyst[14] did not yield the desired **5a**. Reaction of **4a** with *m*-chroloperbenzoic acid (*m*-CPBA) resulted not in epoxidation but in isomerization into the *trans*-olefin **3a**.

In conclusion, the stereospecific epoxidation of *cis*-olefin **4** has been achieved for the first time by using $MoO_5 \cdot H_2O \cdot HMPA$ to give the *cis*-epoxides **5**. This result is a unique example of epoxidation of electron-deficient olefins with MoO_5 complex; the MoO_5 complexes are well known as reagents for the epoxidation of electron-rich olefins,[5] but do not react with electron-deficient olefins such as α,β-unsaturated carbonyl compounds.[6] Further mechanistic studies and examination of the scope of this epoxidation are in progress.

Experimental

All melting and boiling points are uncorrected. IR spectra were recorded on a Hitachi 260-10 spectrophotometer. ^1H- and ^{13}C-NMR spectra were measured with JEOL JNM-PMX 60 and JEOL FX-60 spectrometers, respectively, using tetramethylsilane as an internal standard. Ultraviolet (UV) absorption spectra were recorded on a Hitachi 124 spectrometer. Mass spectra (MS) were obtained with a JEOL D-300 spectrometer operating at 70 eV. Column chromatography was carried out on silica gel (80—100 mesh, Kanto Chemical Co., Inc.). Silica gel 60 PF_{254} (Merck) was used for preparative TLC.

General Procedure for Preparation of *trans*-2-Butene-1,4-diones 3a—e——A solution of a phosphonium ylide (**1a—e**) and phenylglyoxal (**2**) in CH_2Cl_2 was stirred at room temperature for 24 h. Afrer removal of the solvent *in vacuo*, the residue was purified by column chromatography on silica gel with CH_2Cl_2 (for **3a**, **b**), $CHCl_3$ (for **3c**, **d**), and C_6H_6 (for **3e**) as an eluent to give the corresponding *trans*-olefin (**3a—e**), together with the *cis*-isomer (**4a—e**). The yields of the products are listed in Table I.

trans-1,4-Diphenyl-2-butene-1,4-dione (**3a**): This was prepared from benzoylmethylenetriphenylphosphorane[8] (**1a**) (1.9 g, 5 mmol) and phenylglyoxal (**2**) (836 mg, 5.5 mmol) in CH_2Cl_2 (25 ml). Recrystallization from EtOH gave **3a**, mp 111—112 °C (lit.[8] mp 110—112 °C). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1690 (C=O). ^1H-NMR ($CDCl_3$) δ: 7.2—7.7 (6H, m, Ar-H), 7.92 (2H, s, =CH–), 7.8—8.15 (4H, m, Ar-H).

trans-1-(*p*-Bromophenyl)-4-phenyl-2-butene-1,4-dione (**3b**): This was prepared from *p*-bromobenzoyl-

methylenetriphenylphosphorane[8] (**1b**) (4.59 g, 10 mmol) and **2** (1.47 g, 9.7 mmol) in CH_2Cl_2 (30 ml). Recrystallization from ethyl acetate gave **3b**, mp 119—121 °C (lit.[15] mp 127 °C). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1650 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 7.2—8.15 (11H, m, Ar-H and =CH–). MS *m/e*: 316 (M^++2), 314 (M^+).

trans-1-Phenyl-2-pentene-1,4-dione (**3c**): This was prepared from acetylmethylenetriphenylphosphorane[16] (**1c**) (5.09 g, 16 mmol) and **2** (2.35 g, 17.6 mmol) in CH_2Cl_2 (40 ml). Recrystallization from ligroin gave **3c**, mp 38.5—39.5 °C (lit.[17] mp 46 °C). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1705 (–COMe), 1665 (–COPh). ^{1}H-NMR ($CDCl_3$) δ: 2.37 (3H, s, $-COCH_3$), 6.90 (1H, d, J=15 Hz, =CH–COMe), 7.2—7.9 (6H, m, Ar-H and =CH–). MS *m/e*: 174 (M^+).

Methyl *trans*-4-Oxo-4-phenyl-2-butenoate (**3d**): This was prepared from methoxycarbonylmethylenetriphenylphosphorane[18] (**1d**) (3.54 g, 9.6 mmol) and **2** (1.41 g, 10.5 mmol) in CH_2Cl_2 (30 ml). Distillation under reduced pressure gave **3d**, bp 120—130 °C/1 mmHg (bath temperature) (lit.[19] bp 75—80 °C/0.1 mmHg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 ($-CO_2Me$), 1670 (–COPh). ^{1}H-NMR ($CDCl_3$) δ: 3.78 (3H, s, $-OCH_3$), 6.73 (1H, d, J=15 Hz, =CH–CO_2Me), 7.3—7.5 (3H, m, Ar-H), 7.75—7.9 (3H, m, Ar-H and =CH–). MS *m/e*: 190 (M^+).

tert-Butyl *trans*-4-Oxo-4-phenyl-2-butenoate (**3e**): This was prepared from *tert*-butoxycarbonylmethylenetriphenylphosphorane (**1e**) (2.5 g, 9.04 mmol) and **2** (1.38 g, 9.04 mmol) in CH_2Cl_2 (20 ml). Distillation under reduced pressure gave **3e**, bp 179—184 °C (bath temperature). *Anal.* Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.47; H, 6.97. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1710 ($-CO_2Bu$), 1670 (–COPh). ^{1}H-NMR ($CDCl_3$) δ: 1.53 (9H, s, $-C(CH_3)_3$), 6.77 (1H, d, J=16 Hz, =CH–CO_2Bu), 7.78 (1H, d, J=16 Hz, =CH–COPh), 7.2—8.2 (5H, m, Ar-H).

General Procedure for Preparation of *cis*-2-Butene-1,4-diones 4a—e——A solution of a *trans*-olefin (**3a—e**) in degassed ether was irradiated with a 200 W high pressure mercury lamp in a Pyrex vessel at 5—10 °C for 1—2 h. After removal of the solvent *in vacuo*, the residue was purified by recrystallization or column chromatography on silica gel to give the corresponding *cis*-olefin (**4a—e**). The yields of the products are listed in Table I.

cis-1,4-Diphenyl-2-butene-1,4-dione (**4a**): This was prepared from the *trans*-olefin **3a** (2.70 g, 11 mmol) in degassed ether (240 ml). Recrystallization from ether gave **4a**, mp 133.5—134.5 °C (lit.[20] mp 136—137 °C). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1665 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 7.12 (2H, s, =CH–), 7.2—7.65 (6H, m, Ar-H), 7.8—8.1 (4H, m, Ar-H). MS *m/e*: 236 (M^+).

cis-1-(*p*-Bromophenyl)-4-phenyl-2-butene-1,4-dione (**4b**): This was prepared from the *trans*-olefin **3b** (1.58 g, 5 mmol) in degassed ether (250 ml). Column chromatography on silica gel with CH_2Cl_2 as an eluent followed by recrystallization from ethyl acetate gave **4b**, mp 94—95 °C (lit.[15] mp 103.5 °C). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1670 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 6.95 (1H, d, J=11 Hz, =CH–), 7.07 (1H, d, J=11 Hz, =CH–), 7.25—8.4 (9H, m, Ar-H). MS *m/e*: 316 (M^++2), 314 (M^+).

cis-1-Phenyl-2-pentene-1,4-dione (**4c**): This was prepared from the *trans*-olefin **3c** (750 mg, 4.3 mmol) in degassed ether (120 ml). Column chromatography on silica gel with CH_2Cl_2 as an eluent gave **4c** as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700 (–COMe), 1665 (–COPh). ^{1}H-NMR ($CDCl_3$) δ: 2.27 (3H, s, $-COCH_3$), 6.56 (1H, d, J=12 Hz, =CH–COMe), 6.81 (1H, d, J=12 Hz, =CH–COPh), 7.35—7.7 (3H, m, Ar-H), 7.8—8.1 (2H, m, Ar-H). MS *m/e*: 174 (M^+).

Methyl *cis*-4-Oxo-4-phenyl-2-butenoate (**4d**): This was prepared from the *trans*-olefin **3d** (3.50 g, 18.4 mmol) in degassed ether (140 ml). Column chromatography on silica gel with $CHCl_3$ as an eluent followed by recrystallization from ether–*n*-hexane gave **4d**, mp 65—66 °C. *Anal.* Calcd for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.25; H, 5.29. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725 ($-CO_2Me$), 1680 (–COPh). ^{1}H-NMR ($CDCl_3$) δ: 3.53 (3H, s, $-OCH_3$), 6.16 (1H, d, J=12 Hz, =CH–CO_2Me), 6.76 (1H, d, J=12 Hz, =CH–COPh), 7.25—7.5 (3H, m, Ar-H), 7.6—7.9 (2H, m, Ar-H). MS *m/e*: 190 (M^+).

tert-Butyl *cis*-4-Oxo-4-phenyl-2-butenoate (**4e**): This was prepared from the *trans*-olefin **3e** (830 mg, 3.58 mmol) in degassed ether (250 ml). Recrystallization from ethyl acetate gave **4e**, mp 59—61 °C. *Anal.* Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.13; H, 6.94. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735 ($-CO_2Bu$), 1695 (–COPh). ^{1}H-NMR ($CDCl_3$) δ: 1.25 (9H, s, $-OC(CH_3)_3$), 6.17 (1H, d, J=12 Hz, =CH–CO_2Bu), 6.76 (1H, d, J=12 Hz, =CH–COPh), 7.3—7.6 (3H, m, Ar-H), 7.8—8.1 (2H, m, Ar-H).

Epoxidation of *cis*-2-Butene-1,4-diones 4a—e with $MoO_5 \cdot H_2O \cdot$HMPA——General Procedure: A solution of a *cis*-2-butene-1,4-dione (**4a—e**) and $MoO_5 \cdot H_2O \cdot$HMPA in CH_2Cl_2 was stirred at room temperature for a week. After removal of the solvent *in vacuo*, the residue was purified by column chromatography on silica gel with $CHCl_3$ (for **4a, c**), CH_2Cl_2 (for **4b, d**), or C_6H_6 (for **4e**) as an eluent. The yields, IR, and ^{1}H-NMR spectral data of the products **5a—e** are illustrated in Tables II and III.

cis-2,3-Epoxy-1,4-diphenylbutane-1,4-dione (**5a**): i) With 2 mol eq of $MoO_5 \cdot H_2O \cdot$HMPA: This was prepared from **4a** (314 mg, 1.3 mmol) and $MoO_5 \cdot H_2O \cdot$HMPA (1044 mg, 2.8 mmol) in CH_2Cl_2 (40 ml) in 92% yield (300 mg). An analytical sample was obtained by recrystallization from ethyl acetate, mp 127.5—128.5 °C. *Anal.* Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.80. Found: C, 76.11; H, 4.81. ^{13}C-NMR ($CDCl_3$) δ: 57.66 (d, epoxy ring carbons), 128.69, 133.89 (each d, Ar-C), 135.46 (s, Ar-C), and 191.80 (s, carbonyl carbons). UV λ_{max}^{EtOH} nm (log ε): 252.0 (4.36). MS *m/e*: 252 (M^+).

ii) With 1 mol eq of $MoO_5 \cdot H_2O \cdot$HMPA: This was prepared from **4a** (118 mg, 0.5 mmol) and $MoO_5 \cdot H_2O \cdot$HMPA (187 mg, 0.5 mmol) in CH_2Cl_2 (7 ml) in 36% yield (45 mg).

cis-1-(*p*-Bromophenyl)-2,3-epoxy-4-phenylbutane-1,4-dione (**5b**): This was prepared from **4b** (377 mg, 1.2 mmol)

and $MoO_5 \cdot H_2O \cdot HMPA$ (895 mg, 2.4 mmol) in CH_2Cl_2 (30 ml) in 62% yield (245 mg). An analytical sample was obtained by recrystallization from ethyl acetate, mp 138—140 °C. *Anal.* Calcd for $C_{16}H_{11}BrO_3$ C, 58.02; H, 3.33. Found: C, 57.93; H, 3.33. MS *m/e*: 332 ($M^+ + 2$), 330 (M^+).

cis-2,3-Epoxy-1-phenylpentane-1,4-dione (**5c**): This was prepared from **4c** (309 mg, 1.78 mmol) and $MoO_5 \cdot H_2O \cdot HMPA$ (1330 mg, 3.56 mmol) in CH_2Cl_2 (18 ml) in 43% yield (144 mg). An analytical sample was obtained by distillation under reduced pressure, bp 110—120 °C/2 mmHg (bath temperature). *Anal.* Calcd for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.45; H, 5.29. MS *m/e*: 190 (M^+).

Methyl *cis*-2,3-Epoxy-4-oxo-4-phenylbutanoate (**5d**): This was prepared from **4d** (570 mg, 3 mmol) and $MoO_5 \cdot H_2O \cdot HMPA$ (2240 mg, 6 mmol) in CH_2Cl_2 (30 ml) in 21% yield (130 mg). An analytical sample was obtained by recrystallization from C_6H_6, mp 99—101 °C. *Anal.* Calcd for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89. Found: C, 64.05; H, 4.91. MS *m/e*: 206 (M^+).

tert-Butyl *cis*-2,3-Epoxy-4-oxo-4-phenylbutanoate (**5e**): This was prepared from **4e** (241 mg, 1.04 mmol) and $MoO_5 \cdot H_2O \cdot HMPA$ (569 mg, 1.77 mmol) in CH_2Cl_2 (10 ml) in 44% yield (115 mg). An analytical sample was obtained by recrystallization from ether–*n*-hexane, mp 49.5—51 °C. *Anal.* Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.79; H, 6.53.

General Procedure for Preparation of *trans*-2,3-Epoxybutane-1,4-diones 6a—e——A NaOH solution was added dropwise to a solution of one of **3a—e** or **4a** and 30% H_2O_2 in MeOH at 0—10 °C. The reaction mixture was stirred for 0.5—2 h at the same temperature and partitioned between water and CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by recrystallization or, in some cases, by column chromatography on silica gel to give the corresponding *trans*-epoxides **6a—e**.

trans-2,3-Epoxy-1,4-diphenylbutane-1,4-dione (**6a**): i) From **3a**: **6a** was prepared from **3a** (3.78 g, 16 mmol), 30% H_2O_2 (4.8 ml), and 6 N NaOH (0.4 ml) in MeOH (150 ml). The curd product was recrystallized from ethyl acetate to obtain a pure sample in 90% yield (3.62 g), mp 129—130 °C (lit.[3] mp 128—129 °C). ^{13}C-NMR ($CDCl_3$) δ: 56.47 (d, epoxy ring carbons), 128.60, 128.94, 134.36 (each d, Ar-C), 135.12 (s, Ar-C), and 192.04 (s, carbonyl carbons). UV λ_{max}^{EtOH} nm ($\log \varepsilon$): 252.3 (4.42). MS *m/e*: 252 (M^+).

ii) From **4a**: **6a** was prepared from **4a** (237 mg, 1 mmol), 30% H_2O_2 (0.3 ml), and 6 N NaOH (0.025 ml) in MeOH (9 ml) in 86% yield (217 mg). This material was identical with an authentic specimen obtained from **3a**.

trans-1-(*p*-Bromophenyl)-2,3-epoxy-4-phenylbutane-1,4-dione (**6b**): This was prepared from **3b** (377 mg, 1.2 mmol), 30% H_2O_2 (0.4 ml), and 2 N NaOH (0.1 ml) in MeOH (12 ml) in 88% yield (317 mg). An analytical sample was obtained by recrystallization from ethyl acetate, mp 117—119 °C. *Anal.* Calcd for $C_{16}H_{11}BrO_3$: C, 58.02; H, 3.33. Found: C, 57.63; H, 3.18. MS *m/e*: 332 ($M^+ + 2$), 330 (M^+).

trans-2,3-Epoxy-1-phenylpentane-1,4-dione (**6c**): This was prepared from **3c** (870 mg, 5 mmol), 30% H_2O_2 (1.5 ml), and 6 N NaOH (0.13 ml) in MeOH (45 ml) in 82% yield (780 mg). An analytical sample was obtained by recrystallization from ether, mp 48—49 °C. *Anal.* Calcd for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.26; H, 5.16. MS *m/e*: 190 (M^+).

Methyl *trans*-2,3-Epoxy-4-oxo-4-phenylbutanoate (**6d**): This was prepared from **3d** (1.14 g, 6 mmol), 30% H_2O_2 (1.8 ml), and 6 N NaOH (0.15 ml) in MeOH (54 ml) in 51% yield (625 mg). An analytical sample was obtained by column chromatography on silica gel ($CH_2Cl_2 : C_6H_6 = 10 : 1$ as an eluent), followed by recrystallization from C_6H_6, mp 43—45 °C. *Anal.* Calcd for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89. Found: C, 64.05; H, 4.91. MS *m/e*: 206 (M^+).

tert-Butyl *trans*-2,3-Epoxy-4-oxo-4-phenylbutanoate (**6e**): This was prepared from **3e** (372 mg, 1.6 mmol), 30% H_2O_2 (5 ml), and 6 N NaOH (0.04 ml) in MeOH (15 ml) in 79% yield (314 mg). An analytical sample was obtained by column chromatography on silica gel ($CHCl_3$ as an eluent), followed by recrystallization from ether–*n*-hexane, mp 47.5—49 °C. *Anal.* Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.83; H, 6.65. MS *m/e*: 248 (M^+).

Reaction of the *trans*-Epoxide 6a with the Phosphonium Ylide 7——The phosphonium ylide **7** was generated by a modification of the reported methods.[21] A 35% NaOH solution (70 ml) was added to a vigorously stirred solution of the *trans*-epoxide **6a** (3.0 g, 11.9 mmol), methyltriphenylphosphonium iodide (11.55 g, 28.6 mmol), and triethylbenzylammonium chloride (30 mg) in CH_2Cl_2 (98 ml) at room temperature. The mixture was stirred at the same temperature for 2 d. The aqueous layer was separated and extracted with CH_2Cl_2, and the combined organic layer was washed with brine. The extract was dried over Na_2SO_4, then concentrated *in vacuo* to give a residue. The residue was purified by column chromatography on silica gel with C_6H_6 as an eluent to give *trans*-2,3-epoxy-1,4-diphenyl-4-pentene-1-one (**8**) (2.16 g, 72%). An analytical sample was obtained by recrystallization from EtOH, mp 54.5—56.5 °C. *Anal.* Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.36; H, 5.55. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1680 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 3.95 (1H, m, –CH–C=CH_2), 5.58 (1H, d, J=2 Hz, –CH–COPh), 5.56, 5.60 (2H, each br s, =CH_2), 7.2—7.7 (8H, m, Ar-H), 7.9—8.2 (2H, m, Ar-H).

Reaction of the *cis*-Epoxide 5a with the Phosphonium Ylide 7——By using a procedure similar to that described above for the reaction of **6a** with **7**, the *cis*-epoxide **5a** (252 mg, 1 mmol) was treated with methyltriphenylphosphonium iodide (515 mg, 1.27 mmol), triethylbenzylammonium chloride (5 mg), and 35% NaOH (6 ml) in CH_2Cl_2 (8 ml) for 3 d. The *trans*-epoxide **6a** was obtained in 47% yield (118 mg). This material was identical with an authentic specimen obtained from **3a**.

Reaction of the *cis*-Olefin 4a with H_2O_2 by Using Na_2WO_4 Catalyst——A 30% H_2O_2 solution (0.2 ml, 1.7 mmol)

was added to a suspension of **4a** (118 mg, 0.5 mmol) and $Na_2WO_4 \cdot 2H_2O$ (50 mg, 0.15 mmol) in MeOH (5 ml) at room temperature. The mixture was stirred at the same temperature for 20 h, and partitioned between water and $CHCl_3$. The organic layer was washed with brine, dried over $MgSO_4$, and concentrared *in vacuo*. The residue was purified by preparative TLC with $CHCl_3$ as a developing solvent to gave the *trans*-epoxide **6a** (37 mg, 29%), together with recovered **4a** (40 mg, 34%).

Reaction of the *cis*-Olefin 4a with *m*-CPBA——A solution of **4a** (24 mg, 0.1 mmol) and *m*-CPBA (70% contained, 25 mg, 0.1 mmol) in dry CH_2Cl_2 (3 ml) was stirred at room temperature for a week. After removal of the solvent *in vacuo*, the residue was purified by preparative TLC with C_6H_6 as a developing solvent to give the *trans*-olefin **3a** (13 mg, 52%). This material was identical with an authentic specimen obtained from **1a** and **2**.

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References and Notes

1) For a recent synthesis and biological properties of cerulenin, see: A. A. Jakubowski, F. S. Guziec, Jr., M. Sugiura, C. C. Tam, M. Tishler, and S. Ōmura, *J. Org. Chem.*, **47**, 1221 (1982); H. Funabashi, S. Iwasaki, and S. Okuda, *Tetrahedron Lett.*, **1983**, 2673.
2) H. O. House, "Modern Synthetic Reactions," 2nd ed., W. A. Benjamin Inc., California, 1972, p. 292.
3) Epoxidation of the *trans*- and *cis*-olefins, **3a** and **4a**, with alkaline hydrogen peroxide gave only the *trans*-epoxide **6a**: R. E. Lutz and F. N. Wilder, *J. Am. Chem. Soc.*, **56**, 1987 (1934).
4) The reagent is readily prepared from MoO_3, 30% hydrogen peroxide, and HMPA: H. Mimoun, I. S. Roch, and L. Sajus, *Bull. Soc. Chim. Fr.*, **1969**, 1481.
5) For a review, see: H. Mimoun, *Angew. Chem. Int. Ed. Engl.*, **21**, 734 (1982); *idem*, "The Chemistry of Peroxides," ed. by S. Patai, John Wiley and Sons, New York, 1983, Chapter 15, p. 463.
6) H. Mimoun, I. S. Roch, and L. Sajus, *Tetrahedron*, **26**, 37 (1970).
7) C.-S. Chien, T. Suzuki, T. Kawasaki, and M. Sakamoto, *Chem. Pharm. Bull.*, **32**, 3945 (1984); C.-S. Chien, T. Takanami, T. Kawasaki, and M. Sakamoto, *ibid.*, **33**, 1843 (1985).
8) D. B. Denney, L. C. Smith, J. Song, C. J. Rossi, and C. D. Hall, *J. Org. Chem.*, **28**, 778 (1963).
9) H. E. Zimmerman, H. G. Dürr, R. S. Givens, and R. G. Lewis, *J. Am. Chem. Soc.*, **89**, 1863 (1967).
10) A. F. Cockerill, G. L. O. Davies, and D. M. Rackham, *Chem. Rev.*, **73**, 553 (1973); K. A. Kime and R. E. Sievers, *Aldrichimica Acta*, **10**, 54 (1977).
11) Most of the *cis*-olefins **4** were unstable to heat, being isomerized to the *trans*-olefins **3**: R. D'Ascoli, M. D'Auria, A. De Mico, G. Piancatelli, and A. Scettri, *J. Org. Chem.*, **45**, 4500 (1980).
12) T. J. Batterham, "NMR Spectra of Heterocycles," John Wiley and Sons, New York, 1978, p. 365.
13) A similar dependence is observed in the conformational equilibrium of α,β-unsaturated carbonyl compounds; G. Montaudo, V. Librando, S. Caccamese, and P. Maravigna, *J. Am. Chem. Soc.*, **95**, 6365 (1973).
14) The reagent system is used in the epoxidation of α,β-unsaturated acids, *e.g.*, maleic acid to *cis*-epoxysuccinic acid: G. B. Payne and P. H. Williams, *J. Org. Chem.*, **24**, 54 (1958).
15) W. Heffe and F. Kröhnke, *Chem. Ber.*, **89**, 822 (1956).
16) F. Ramirez and S. Dershowitz, *J. Org. Chem.*, **22**, 41 (1957).
17) T. Severin and D. König, *Chem. Ber.*, **107**, 1499 (1974).
18) H.-J. Bestmann and O. Kratzer, *Chem. Ber.*, **95**, 1894 (1962).
19) H.-J. Bestmann, G. Graf, and H. Hartung, *Justus Liebigs Ann. Chem.*, **706**, 68 (1967).
20) M. Takebayashi, T. Ibata, and K. Ueda, *Bull. Chem. Soc. Jpn.*, **43**, 1500 (1970).
21) S. D. Clarke, C. R. Harrison, and P. Hodge, *Tetrahedron Lett.*, **1980**, 1375.