

Epoxidation of 2-Butene-1,4-diones with Hydrogen Peroxide in the Presence of a Catalytic Amount of Quaternary Ammonium Iodide

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Synopsis. The epoxidation of 1,4-disubstituted 2-butene-1,4-diones with 30% aq H_2O_2 in the presence of a catalytic amount of quaternary ammonium iodide afforded 2,3-epoxy-1,4-butanediones in high yield.

The epoxidation of α,β -unsaturated ketones was carried out with nucleophilic reagents, such as hydrogen peroxide or *t*-butyl hydroperoxide, in alkaline solution.^{1–3)} These available methods are not applicable to base-sensitive substrates.⁷⁾ There have therefore been many studies of an epoxidation reaction to overcome the problem without employing a strong base.^{4–9)} It was reported that the epoxidation reaction of α,β -unsaturated ketones using 30% aq H_2O_2 – Bu_4NF gave the corresponding epoxy ketones.⁷⁾ Also reported was a direct and stereospecific epoxidation of 2-butene-1,4-diones with $\text{MoO}_5 \cdot \text{H}_2\text{O} \cdot \text{HMPA}$, based on approaches to the synthesis of antibiotic cerulenin.^{8–10)} Although 30% aq H_2O_2 was a convenient and inexpensive reagent for the oxidation reactions, in comparison with other peroxides, the epoxidation of 1,4-disubstituted 2-butene-1,4-diones with H_2O_2 under the non-basic reaction conditions, has not been examined. We would like to report on the results of studies concerning the chemoselective epoxidation of 1,4-disubstituted 2-butene-1,4-diones with H_2O_2 in the presence of a catalytic amount of quaternary ammonium iodides.

The epoxidation of *trans*-1,4-diphenyl-2-butene-1,4-

dione (**1**), chosen as a representative 2-butene-1,4-dione for this study, with 30% aq H_2O_2 –quaternary ammonium halides in various stoichiometric ratios, was carried out. The results are summarized in Table 1. At an appropriate ratio of enedione **1**, H_2O_2 , and Bu_4NI (1:26:1, 1:28:0.5, or 1:29:0.1), *cis*-2,3-epoxy-1,4-diphenyl-1,4-butanedione (**1b**) was predominantly obtained (Entries 1–3).¹⁵⁾ The yield of *trans*- and *cis*-epoxides **1a** and **1b** was determined by the recrystallization of crude products from ethyl acetate as follows.

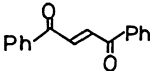
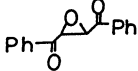
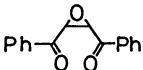
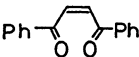
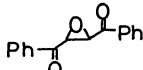
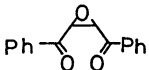
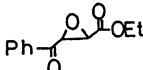
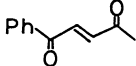
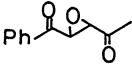
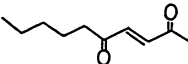
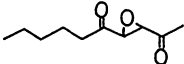
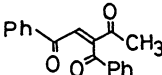
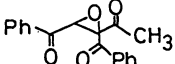
trans-2,3-Epoxy-1,4-diphenyl-1,4-butanedione (**1a**) was obtained in 10–18% yield as the first crop of crystals; *cis*-epoxide **1b** was then afforded by recrystallization of the filtrates. The stereochemistries of *trans*- and *cis*-epoxides (**1a** and **1b**) were determined by a direct comparison of the spectral data with that of *trans*-epoxide **1a**, which was alternatively prepared by the epoxidation of **1** with alkaline hydrogen peroxide. The spectral data of **1a** and **1b** were also identical with those of known compounds reported in the literature.^{8,9)} In addition, the catalytic amount of Bu_4NI (0.1 equiv) and a slight excess molar equivalent of H_2O_2 (5 equiv) gave a similar result (Entry 5). On the other hand, the epoxidation of enedione **1** with H_2O_2 and other common quaternary ammonium halides (Bu_4NF , Me_4NCl , Bu_4NBr , and $\text{PhCH}_2\text{N}(\text{Et})_3\text{Br}$) did not give *trans*- and *cis*-epoxides **1a** and **1b** in high yield (less than 15%), and a complex mixture of hydroxy derivatives was obtained

Table 1. Epoxidation of *trans*-1,4-Diphenyl-2-butene-1,4-dione **1** with 30% aq H_2O_2 – R_4NI in THF at 0–23 °C^{a)}

Entry	Molar ratio			R ₄ NX	Products yield/% ^{b)}		
	Enedione 1	H ₂ O ₂	R ₄ NX		2,3-Epoxy-1,4-butanedione ^{c)}		Recovered enedione 1
					<i>trans</i> 1a	<i>cis</i> 1b	
1	1	26	1.0	Bu ₄ NI	15	73	—
2	1	28	0.5	Bu ₄ NI	15	71	—
3	1	29	0.1	Bu ₄ NI	18	70	—
4	1	28	0.5	Bu ₄ NI ^{d)}	10	75	—
5	1	5	0.1	Bu ₄ NI	28	63	—
6	1	32	0.1	Bu ₄ NI ^{e)}	12	38	28
7	1	— ^{f)}	0.1	Bu ₄ NI	—	—	96
8	1	29	—	—	—	—	75
9	1	28	0.6	Bu ₄ NF ^{g)}	15	15	—
10	1	28	0.8	(CH ₃) ₄ NCl ^{g)}	—	—	66
11	1	29	0.7	Bu ₄ NBr ^{g)}	—	—	—
12	1	29	0.5	PhCH ₂ N(Et) ₃ Br ^{g)}	—	—	—
13	1	26	0.2	PhCH ₂ N(Me) ₃ I	20	68	—

a) Enedione **1**; 0.5–1.0 mmol. THF; 10–15 ml. Reaction time; 20–78 h. b) Yield is based on enedione **1** used. c) Purified by recrystallization from ethyl acetate.^{8,9)} d) THF–DMF (4/1 v/v) was used as solvent. e) CH_2Cl_2 was used as solvent. f) H_2O (270 mol equiv) was used instead of 30% aq H_2O_2 . g) Complex mixture of hydroxy derivatives was obtained.

Table 2. Epoxidation of 2-Butene-1,4-diones with 30% aq H₂O₂-Bu₄NI in THF at 0–23 °C^{a)}

Substrate (S)	Molar ratio				Products	Yield / % ^{b)}	
	S : H ₂ O ₂ : Bu ₄ NI						
	1	1	29	0.1		1a ^{8,9)}	18 ^{c)}
						1b ^{8,9)}	70 ^{c)}
	2	1	29	0.5		1a	30 ^{c)}
						1b	54 ^{c)}
PhCOCH=CHCO ₂ Et	3	1	22	0.5		3a	60 ^{d)}
	4	1	18	0.1		4a ^{8,9)}	58 ^{d)}
	5	1	14	0.1		5a	56 ^{d)}
	6	1	30	1.0		6a ¹⁴⁾	55 ^{d)}

a) 2-Butene-1,4-dione; 0.5–1.0 mmol. THF; 10–15 ml. Reaction time; 20–45 h. b) Yield is based on 2-butene-1,4-dione used. c) Purified by recrystallization from ethyl acetate.^{8,9)} d) Purified by column chromatography on silica gel.

Table 3. Epoxidation of 2-Butene-1,4-diones with 30% aq H₂O₂-PhCH₂N(CH₃)₃I in THF at 0–23 °C^{a)}

Substrate (S)	Molar ratio			Time h	Products	
	S : H ₂ O ₂ : BTMAI ^(c)				Yield/% ^(b)	
1	1	26	0.2	48	1a ^(8,9)	20 ^(d)
					1b ^(8,9)	68 ^(d)
2	1	23	0.1	25	1a	15 ^(d)
					1b	60 ^(d)
3	1	18	0.1	96	3a	60 ^(e)
4	1	22	0.1	68	4a ^(8,9)	69 ^(e)
5	1	14	0.1	66	5a	61 ^(e)
6	1	23	0.1	47	6a ⁽¹⁴⁾	53 ^(e)

a) 2-Butene-1,4-dione; 0.5–1.0 mmol. THF; 10–15 ml. b) Yield is based on 2-butene-1,4-dione used. c) BTMAI; PhCH₂N(CH₃)₃I. d) Purified by recrystallization from ethyl acetate.^{8,9)} e) Purified by column chromatography on silica gel.

under various ratios of H₂O₂ and quaternary halides (Entries 9–12). These results suggest that the iodide ion acts as a base while promoting the conjugate addition of hydroperoxide to the carbon–carbon double bond of enedione 1.^{7,11,12)} The epoxidation of enedione 1 with H₂O₂ in the presence of another quaternary ammonium iodide (PhCH₂N(Me)₃I) also gave epoxides in good yield (Entry 13).

The results of the epoxidation of other 2-butene-1,4-diones with 30% aq H₂O₂-quaternary ammonium iodide (Bu₄NI or PhCH₂N(CH₃)₃I) are shown in Tables 2 and 3. *cis*-1,4-Diphenyl-2-butene-1,4-dione (2) also afforded

cis-epoxide 1b predominantly as well as *trans*-enedione 1. *trans*-1-Phenyl-2-pentene-1,4-dione (4), *trans*-3-decene-2,5-dione (5), and ethyl 4-oxo-4-phenyl-2-butenate (3) afforded the corresponding *trans*-2,3-epoxy derivatives (3a, 4a, and 5a). The stereochemistries of *trans*-epoxides of 3a, 4a, and 5a were assigned based on the ¹H NMR spin–spin coupling constants between the epoxy ring protons; 3a–5a showed coupling constants of 2 Hz. This coupling constant was in good agreement with the reported value for *trans*-vicinal coupling in epoxides.^{8,9)} 3-Benzoyl-1-phenyl-2-pentene-1,4-dione (6) also afforded the corresponding epoxide (6a)¹⁴⁾ in good yield.

On the other hand, the epoxidation of α,β -unsaturated ketones such as 5-isopropenyl-2-methyl-2-cyclohexen-1-one, 4-(2,6,6-trimethyl-2-cyclohexen-1-yl)-3-buten-2-one, 3-methyl-2-cyclohexen-1-one, 4,4-dimethyl-2-cyclohexen-1-one, and chalcone with H₂O₂-Bu₄NI did not give corresponding epoxides in high yield (less than 10%). α,β -Unsaturated ketones were recovered unchanged in 61–98% yield.

Thus, the reagent 30% aq H₂O₂-quaternary ammonium iodides provides a new convenient method for mild and chemoselective epoxidation of 2-butene-1,4-diones without using a strong base. Further application of epoxidation with this method to *cis*-2-butene-1,4-diones and other functional unsaturated compounds is now in progress.

Experimental

IR spectra were recorded on a JASCO FT-IR 5000 spec-

trometer. ^1H NMR spectra were taken on a Hitachi R-24B spectrometer with TMS as an internal standard. MS spectra were taken on a JEOL-HX 110 spectrometer at 70 eV. The products were identified by spectroscopic data.

General Procedure. To a solution of 2-butene-1,4-dione (1 mmol) and Bu_4NI or $\text{PhCH}_2\text{N}(\text{Me})_3\text{I}$ (0.1 mmol) in THF (10 ml) at 0°C was added dropwise 30% aq H_2O_2 (5–30 mmol) dissolved in THF (3 ml). After stirring for 20–96 h at 0 – 23°C , the reaction mixture was poured into 0.5 M aq KI. The resulting mixture was treated with 0.5 M aq $\text{Na}_2\text{S}_2\text{O}_3$ and extracted with ethyl acetate. The organic layer was washed by 0.5 M aq $\text{Na}_2\text{S}_2\text{O}_3$ and successively saturated aq NaCl and dried by MgSO_4 . After removal of solvent in vacuo, the residue was purified by recrystallization or column chromatography on silica gel (Wakogel C-200) with CCl_4 and CHCl_3 (1:1, v/v). Epoxy diketones **1a**–**6a** were obtained in 53–91% yield.

2-Butene-1,4-diones were prepared according to the literature procedure.¹³⁾

trans-1,4-Diphenyl-2-butene-1,4-dione (**1**) was prepared by Friedel–Crafts acylation of benzene with fumaroyl dichloride. *cis*-1,4-Diphenyl-2-butene-1,4-dione (**2**) and 3-benzoyl-1-phenyl-2-pentene-1,4-dione (**6**) were prepared by oxidation of corresponding furan derivatives with HNO_3 in acetic acid.

trans-1-Phenyl-2-pentene-1,4-dione (**4**) and *trans*-3-decene-2,5-dione (**5**) were prepared by pyridinium chlorochromate (PCC) oxidation of corresponding 2,5-dialkylfuran derivatives.

***trans*-2,3-Epoxy-1,4-diphenyl-1,4-butanedione (1a):** Mp 130 – 131°C (from ethyl acetate) (lit.^{8,9)} Mp 129 – 130°C ; IR (KBr) 1686 cm^{-1} ; ^1H NMR (CDCl_3) $\delta=4.48$ (2H, s), 7.30 – 7.76 (6H, m), 7.95 – 8.21 (4H, m); MS m/z (rel intensity) 252 (M^+ 0.3), 147 (64), 105 (100), and 77 (34).

***cis*-2,3-Epoxy-1,4-diphenyl-1,4-butanedione (1b):** Mp 129 – 130°C (from ethyl acetate) (lit.^{8,9)} Mp 127.5 – 128.5°C ; IR (KBr) 1696 cm^{-1} ; ^1H NMR (CDCl_3) $\delta=4.48$ (2H, s), 7.33 – 7.78 (6H, m), 7.91 – 8.28 (4H, m); MS m/z (rel intensity) 252 (M^+ 0.3), 147 (66), 105 (100), and 77 (35).

Ethyl *trans*-2,3-Epoxy-4-oxo-4-phenylbutanoate (3a): IR (neat) 1748 and 1694 cm^{-1} ; ^1H NMR (CDCl_3) $\delta=1.31$ (3H, t, $J=7.0$), 3.68 (1H, d, $J=2.0$), 4.30 (2H, q, $J=7.0$), 4.41 (1H, d, $J=2.0$), 7.31 – 7.70 (3H, m), 7.90 – 8.16 (2H, m); MS m/z (rel intensity) 220 (M^+ 1), 147 (29), 105 (100), and 77 (25).

***trans*-2,3-Epoxy-1-phenyl-1,4-pentanedione (4a):** Mp 50 – 51°C (from ether) (lit.^{8,9)} Mp 48 – 49°C ; IR (KBr) 1723 and 1692 cm^{-1} ; ^1H NMR (CDCl_3) $\delta=2.18$ (3H, s), 3.61 (1H, d, $J=2.0$), 4.30 (1H, d, $J=2.0$), 7.25 – 7.68 (3H, m), 7.81 – 8.08 (2H, m); MS m/z (rel intensity) 147 (99), 105 (100), 85 (19), and 77 (78).

***trans*-3,4-Epoxy-2,5-decanedione (5a):** Mp 60 – 61°C (from pentane); IR (KBr) 1707 cm^{-1} ; ^1H NMR (CDCl_3) $\delta=0.86$ (3H, t, $J=6.0$), 2.08 (3H, s), 1.06 – 1.83 (6H, m), 2.23 – 2.56 (2H, m), 3.51 (2H, m); MS m/z (rel intensity) 184 (M^+ 9), 141 (23), 128 (18), 99 (100), 85 (28), and 71 (61).

3-Benzoyl-2,3-epoxy-1-phenyl-1,4-pentanedione (6a):¹⁴⁾ IR (neat) 1715 and 1688 cm^{-1} ; ^1H NMR (CDCl_3) $\delta=2.26$ (3H, s),

4.64 (1H, s), 7.30 – 7.76 (6H, m), 7.93 – 8.26 (4H, m); MS m/z (rel intensity) 294 (M^+ 0.8), 251 (9), 189 (28), 147 (100), 105 (95), and 77 (39).

We wish to express our thanks to Professor Masanori Sakamoto for the information concerning NMR and IR data of *trans*- and *cis*-2,3-epoxy-1,4-butanediones. We also thank Professors Masaaki Yoshifuji and Masafumi Yasunami for their help in the measurements of ^1H NMR spectra. We wish to thank Mr. Toshio Sato of Instrumental Analysis Center for Chemistry Faculty of Science of Tohoku University for the measurements of MS spectra.

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- 14) Though the stereochemistry of **6a** was proposed as shown the figure in Table 2 on the basis of the reaction manners of enediones **1** and **4**, it could not be exactly determined by the assignment of ^1H NMR and IR spectral data of **6a**.
- 15) The structure of crude products was determined as *cis*-epoxide by its FT-IR spectral data (KBr; *cis*-epoxide **1b**: $\nu_{\text{C=O}}$ 1696 cm^{-1}) after washing with CCl_4 .