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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 $MoO_5 \cdot H_2O \cdot HMPA$, 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.

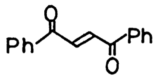
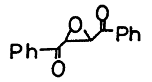
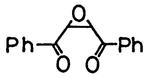
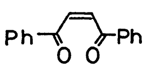
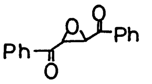
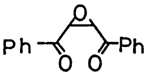
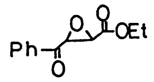
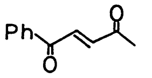
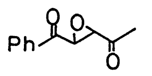
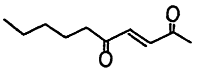
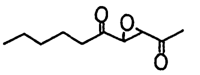
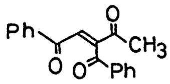
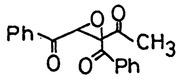
trans-2,3-Epoxy-1,4-diphenyl-1,4-butanedione (**1a**) was obtained in 10—18% yield as the first crop of crystals; *cis*-epoxide **1b** was then afforded by recrystallization of the filtrates. The stereochemistries of *trans*- and *cis*-epoxides (**1a** and **1b**) were determined by a direct comparison 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 $PhCH_2N(Et)_3Br$) 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_4NX	Products yield/%[b)]		
	Enedione **1**	H_2O_2	R_4NX		2,3-Epoxy-1,4-butanedione[c)] *trans* **1a**	*cis* **1b**	Recovered enedione **1**
1	1	26	1.0	Bu_4NI	15	73	—
2	1	28	0.5	Bu_4NI	15	71	—
3	1	29	0.1	Bu_4NI	18	70	—
4	1	28	0.5	Bu_4NI[d)]	10	75	—
5	1	5	0.1	Bu_4NI	28	63	—
6	1	32	0.1	Bu_4NI[e)]	12	38	28
7	1	—[f)]	0.1	Bu_4NI	—	—	96
8	1	29	—	—	—	—	75
9	1	28	0.6	Bu_4NF[g)]	15	15	—
10	1	28	0.8	$(CH_3)_4NCl$[g)]	—	—	66
11	1	29	0.7	Bu_4NBr[g)]	—	—	—
12	1	29	0.5	$PhCH_2N(Et)_3Br$[g)]	—	—	—
13	1	26	0.2	$PhCH_2N(Me)_3I$	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 H_2O_2–Bu_4NI in THF at 0—23 °C[a]

Substrate (S)		Molar ratio			Products		Yield/%[b]
		S	H_2O_2	Bu_4NI			
	**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 H_2O_2–$PhCH_2N(CH_3)_3I$ in THF at 0—23 °C[a]

Substrate	Molar ratio			Time	Products	
(S)	S	H_2O_2	BTMAI[c]	h		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; $PhCH_2N(CH_3)_3I$. d) Purified by recrystallization from ethyl acetate.[8,9] e) Purified by column chromatography on silica gel.

under various ratios of H_2O_2 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 H_2O_2 in the presence of another quaternary ammonium iodide ($PhCH_2N(Me)_3I$) also gave epoxides in good yield (Entry 13).

The results of the epoxidation of other 2-butene-1,4-diones with 30% aq H_2O_2–quaternary ammonium iodide (Bu_4NI or $PhCH_2N(CH_3)_3I$) 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-butenoate (**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 H_2O_2–Bu_4NI 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 H_2O_2-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 spectrometer. ^{1}H 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 $PhCH_2N(Me)_3I$ (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 $Na_2S_2O_3$ and extracted with ethyl acetate. The organic layer was washed by 0.5 M aq $Na_2S_2O_3$ 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}; ^{1}H NMR ($CDCl_3$) δ=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}; ^{1}H NMR ($CDCl_3$) δ=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}; ^{1}H NMR ($CDCl_3$) δ=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}; ^{1}H NMR ($CDCl_3$) δ=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}; ^{1}H NMR ($CDCl_3$) δ=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}; ^{1}H NMR ($CDCl_3$) δ=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 ^{1}H 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 ^{1}H 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**: $\nu_{C=O}$ 1696 cm^{-1}) after washing with CCl_4.