JOC The Journal of Organic Chemistry
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pubs.acs.org/joc

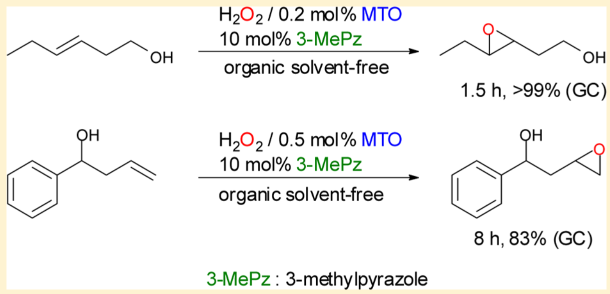
Methyltrioxorhenium-Catalyzed Epoxidation of Homoallylic Alcohols with Hydrogen Peroxide

Shigekazu Yamazaki*

Toyama Industrial Technology Center, 150 Futagami, Takaoka, Toyama 933-0981, Japan

Supporting Information

ABSTRACT: Homoallylic alcohols were efficiently converted to the corresponding 3,4-epoxy alcohols in excellent yields by methyltrioxorhenium (MTO)-catalyzed epoxidation with aqueous hydrogen peroxide as the terminal oxidant and 3-methylpyrazole (10 mol %) as an additive. The epoxidations of homoallylic alcohols proceeded under organic solvent-free conditions faster than those in dichloromethane.



Epoxidation of alkenes is an important transformation because epoxides are valuable synthetic intermediates.[1] Development of catalytic epoxidation methods using an environmentally benign oxidant such as hydrogen peroxide is currently of interest because it produces water as the only waste byproduct and has advantages of cost and atom efficiency.[2,3] Methyltrioxorhenium (MTO, CH_3ReO_3) is one of the most efficient and well-studied epoxidation catalyst using hydrogen peroxide as the oxidant. Since the original finding of the properties of MTO as an epoxidation catalyst in 1991,[4] a large number of studies related to MTO-catalyzed epoxidation have been reported.[5,6]

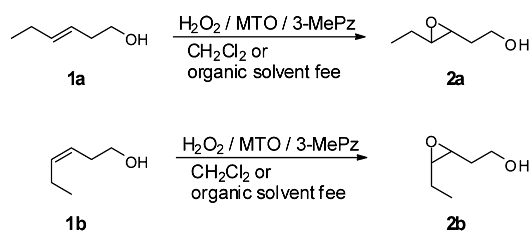
Epoxy alcohols are useful intermediates in organic synthesis.[7] The syntheses of some epoxy alcohols by MTO-catalyzed epoxidation of alkenols have been reported. MTO-catalyzed epoxidation of allylic alcohols has been explored extensively including the diastereoselectivity, kinetics, and reaction mechanism.[8] Moreover, MTO-catalyzed epoxidation of bishomoallylic alcohols has been explored, and the formation of furan compounds by intramolecular cyclization of 4,5-epoxy alcohols initially formed[9] and an isolation method of acid-sensitive 4,5-epoxy alcohols have also been reported.[6c]

On the other hand, only a few homoallylic alcohols (*cis*- and *trans*-3-hexen-1-ol, 1-nonen-4-ol) were reported on MTO-catalyzed epoxidation.[10] The 3,4-epoxy alcohols, prepared by epoxidation of homoallylic alcohols, are also known as useful synthetic intermediates.[7] Although vanadium,[11] zirconium,[12] molybdenum,[13] titanium,[14] and hafnium[12c] complexes have been reported as the catalysts for epoxidation of homoallylic alcohols, the epoxidations using these catalysts require alkyl hydroperoxides (such as *tert*-butyl hydroperoxide and cumene hydroperoxide) as the terminal oxidant. Tungstic acid has been reported to catalyze the epoxidation of homoallylic alcohols with hydrogen peroxide, but the yields of epoxides are only moderate.[15] Recently reported selenium-containing dinuclear peroxotungstate has been known as the sole effective catalyst for homoallylic alcohol epoxidation using hydrogen peroxide as the terminal oxidant.[16,17]

Here we report the results of detailed examination of MTO-catalyzed epoxidation of various homoallylic alcohols to the corresponding 3,4-epoxy alcohols with hydrogen peroxide as the terminal oxidant.

At first, the epoxidation of *trans*- and *cis*-3-hexen-1-ol was examined (Scheme 1 and Table 1). The epoxidation of *trans*-3-hexen-1-ol **1a** with 1.2 equiv of 35% hydrogen peroxide as an oxidant, 0.2 mol % of MTO as the catalyst, and 10 mol % of 3-methylpyrazole (3-MePz) as the additive[6a−c] in dichloromethane resulted in the formation of corresponding *trans*-epoxide **2a** in 95% yield by 8 h reaction at 20 °C (entry 1). Dichloromethane is the most commonly used solvent for MTO-catalyzed epoxidation because fast rate, high yield, and high selectivity are obtained by using this solvent.[5b] In a similar manner, the epoxidation of *cis*-3-hexen-1-ol **1b** with 0.1 mol % of MTO in dichloromethane afforded 98% yield of *cis*-epoxide **2b** at 20 °C within a 5 h reaction (entry 3). The epoxidation proceeded with retention of the stereochemistry around the olefinic bonds of the substrates. The reaction times can be

Scheme 1. Epoxidation of *trans*- and *cis*-3-Hexen-1-ol



Received: August 27, 2012
Published: October 5, 2012

Table 1. MTO-Catalyzed Epoxidation of *trans*-3-Hexen-1-ol, *cis*-3-Hexen-1-ol, and Cyclohexene[a]

entry	substrate	solvent	MTO (mol %)	temp (°C)	time (h)	% epoxide[b]
1	*trans*-3-hexen-1-ol (**1a**)	CH_2Cl_2	0.2	20	8	95
2	*trans*-3-hexen-1-ol (**1a**)	*c*	0.2	10	1.5	>99
3	*cis*-3-hexen-1-ol (**1b**)	CH_2Cl_2	0.1	20	5	98
4	*cis*-3-hexen-1-ol (**1b**)	*c*	0.1	10	1	>99
5	cyclohexene (**1c**)	CH_2Cl_2	0.2	20	2	>99
6	cyclohexene (**1c**)	*c*	0.2	20	2	>99

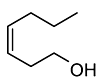
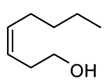
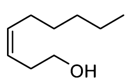
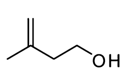
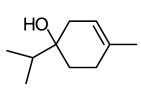
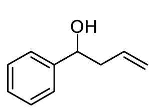
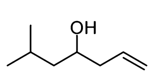
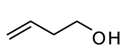
[a]Alkene (10 mmol), 35% H_2O_2 (12 mmol), 3-methylpyrazole (1 mmol), in CH_2Cl_2 (5 mL) or without organic solvent. [b]Analysis by GC. [c]Reaction without organic solvent.

reduced drastically by performing the reactions under organic solvent-free conditions even at lower temperature (10 °C).[6b] The alkenols **1a** and **1b** were converted to the corresponding 3,4-epoxy alcohols **2a** and **2b** quantitatively within 1.5 and 1 h, respectively (entries 2 and 4). On the other hand, the rates of epoxidation of cyclohexene **1c**, which does not have a hydroxyl group, using dichloromethane as the solvent and without organic solvent were comparable (entries 5 and 6).

The concentration of hydrogen peroxide in organic phase (substrate 3-hexen-1-ol) during the epoxidations of **1a** and **1b** under organic solvent-free conditions must be higher than that in dichloromethane because the substrate alkenols have a hydroxyl group. The higher concentration of hydrogen peroxide enhances the rate of the formation of the catalytically active peroxo species.[6b] This must be the reason for faster rates of epoxidation of **1a** and **1b** under organic solvent-free conditions than for those in dichloromethane.

Similarly, the epoxidations of *cis*-3-hepten-1-ol **1d**, *cis*-3-octen-1-ol **1e**, and *cis*-3-nonen-1-ol **1f** were examined. These homoallylic alcohols afforded over 90% yield of corresponding 3,4-epoxy alcohols **2d−f** both in dichloromethane and without organic solvent conditions (Table 2, entries 1−6). Again, faster rates of epoxidation under organic solvent-free conditions than in dichloromethane were observed. However, the differences of the rates of epoxidations that use and do not use organic solvent become small by increasing molecular size of the substrates. This might be because increasing molecular size of the homoallylic alcohols causes increasing hydrophobicity that leads to lower concentration of hydrogen peroxide in organic

Table 2. MTO-Catalyzed Epoxidation of Homoallylic Alcohols[a]

entry	substrate	solvent	MTO (mol%)	temp (°C)	time (h)	conv[b] (%)	epoxide[b,c] (%)
1	 **1d**	CH_2Cl_2	0.1	15	4	>99	99
2		-[d]	0.1	10	2	>99	98
3	 **1e**	CH_2Cl_2	0.1	10	5	>99	95
4		-[d]	0.1	10	2	>99	93 (85)[e]
5	 **1f**	CH_2Cl_2	0.2	10	3	>99	>99
6		-[d]	0.2	10	2	>99	>99
7	 **1g**	CH_2Cl_2	0.1	20	8	95	94
8		-[d]	0.1	10	1.5	>99	>99
9[f]	 **1h**	CH_2Cl_2	0.1	10	1	>99	96[g]
10[h]	 **1i**	CH_2Cl_2	0.5	20	8	79	76
11[h]		-[d]	0.5	10	8	90	83
12[h]	 **1j**	CH_2Cl_2	1	20	8	98	98 (77)[i]
13[h]		-[d]	1	10	8	99	97
14[h]	 **1k**	CH_2Cl_2	0.5	20	8	87	87
15[h]		-[d]	0.5	10	3	92	92

[a]Alkenol (10 mmol), 35% H_2O_2 (12 mmol), 3-methylpyrazole (1 mmol), in CH_2Cl_2 (5 mL) or without organic solvent. [b]Analysis by GC. [c]Yields based on alkenols used. [d]Reaction without organic solvent. [e]Isolated yield of 10 g scale reaction. See Experimental Section for detail. [f]3-Methylpyrazole (1 mmol) and 1-methylimidazole (0.1 mmol) were used as additives. [g]Isolated yield. [h]H_2O_2 (15 mmol). [i]Isolated yield of 15 mmol scale reaction by Kugelrohr distillation. See Experimental Section for detail.

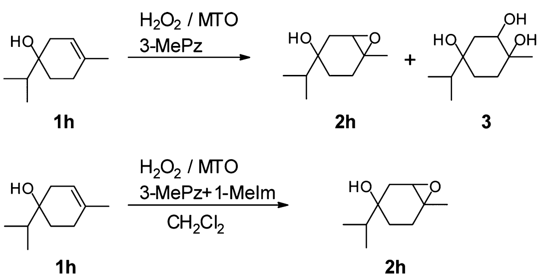
dx.doi.org/10.1021/jo301825j | J. Org. Chem. 2012, 77, 9884−9888

phase (homoallylic alcohols under organic solvent-free conditions). The lower hydrogen peroxide concentration in the organic phase resulted in a slower rate of epoxidation.

Epoxidation of 3-methyl-3-buten-1-ol **1g** gave corresponding 3,4-epoxy alcohol **2g** in high yield (entries 7 and 8). The reaction times required for these epoxidations were 8 h at 20 °C in dichloromethane and 1.5 h at 10 °C under organic solvent-free conditions. The difference of the rates of epoxidation of this five-carbon substrate in dichloromethane and without organic solvent is comparable to that of *trans*-3-hexen-1-ol **1a**, a six-carbon substrate. In the case of the epoxidation of **1g** without organic solvent, the phase of the reaction mixture that was separated to an organic (**1g**) and aqueous layer at the beginning of the reaction became homogeneous gradually as the reaction proceeded.

Epoxidation of (±)-terpinen-4-ol **1h** produced a small amount of triol **3** as byproduct which was a hydrolysis product of the initially formed epoxide **2h** under the reaction conditions (Scheme 2). The ratio of triol **3** increased gradually on standing

Scheme 2. Epoxidation of (±)-Terpinen-4-ol 1h



the reaction mixture at ambient temperature. When the epoxidation of **1h** was performed with the addition of 1 mol % of 1-methylimidazole (1-MeIm) that strongly inhibits the hydrolysis of epoxides,[6c] 96% yield of epoxide was obtained by 1 h reaction at 10 °C in dichloromethane (entry 9). No hydrolysis product **3** was detected under the conditions. The *cis*/*trans* ratio of **2h** was 88/12, which was higher than that of CH_3CO_3H/NaOAc epoxidation (*cis*/*trans* ratio, 79:21) and was lower than those of the epoxidations using $H_2O_2/NaWO_4$ (93:7), TBHP/$VO(acac)_2$ (>90:1), and $H_2O_2/CH_3CN/K_2CO_3$ (>90:1).[17] The epoxidation of **1h** under similar conditions without organic solvent resulted in creamy form within 1 h, and the progress of the reaction stopped.

The rate of the epoxidation of 1-phenyl-3-buten-1-ol **1i**, a terminal alkene, was slower than those of disubstituted and trisubstituted alkenols examined above (**1a**−**h**). The conversion at 8 h with a larger amount of MTO (0.5 mol %) is 79% in dichloromethane and 90% without organic solvent (entries 10 and 11). Similarly, a larger amount of MTO was required for good conversion of other terminal alkenes, 6-methyl-1-hepten-4-ol **1j** and 3-buten-1-ol **1k** (entries 12−15). No stereoselectivity was observed for MTO-catalyzed epoxidation of **1i** and **1j** (both of *cis*/*trans* ratios of **2i** and **2j** were 50/50),[10b] while some homoallylic alcohol epoxidation systems show *cis*-selectivity (e.g., $VO(acac)_2$/TBHP[11d] and $H_2O_2/CH_3CN/K_2CO_3$;[17] epoxidation of **1i** and **1j** with $H_2O_2/CH_3CN/K_2CO_3$ afforded epoxides with *cis*/*trans* ratio of 64/36 and 68/32, respectively).

In summary, we found that 3,4-epoxy alcohols can be effectively prepared by MTO-catalyzed epoxidation of homoallylic alcohols with hydrogen peroxide as the terminal oxidant. Homoallylic alcohols that have disubstituted and trisubstituted alkene moieties afforded over 90% yield of epoxides with 0.1−0.2 mol % of MTO, and those with terminal alkene also afforded high yield of epoxides with 0.5−1 mol % of MTO with prolonged reaction time. We also found that in the case of small homoallylic alcohols (that have 4−10 carbons), the rates of epoxidations without organic solvent are faster than those in dichloromethane. Unfortunately, the MTO-catalyzed oxidation of acyclic secondary homoallylic alcohols afforded epoxides without stereoselectivity.

EXPERIMENTAL SECTION

General. Methyltrioxorhenium was prepared according to the reported procedure.[18] 1-Phenyl-3-buten-1-ol **1i** and 6-methyl-1-hepten-4-ol **1j** were prepared according to the reported procedure.[19] The concentration of H_2O_2 was determined by iodometric titration before use. The progress of the reaction was monitored by GC analysis (FID detector). The conversion of alkenols and yield of epoxides were determined by GC internal standard technique. GC analyses were performed using GL Sciences InertCap 1 column (30 m length × 0.25 mm i.d., 0.25 μm polydimethylsiloxane film thickness).

General Procedure of Homoallylic Alcohol Epoxidation (Table 1, entry 3). A 50 mL flask equipped with a stirbar was charged with CH_2Cl_2 (5 mL), *cis*-3-hexen-1-ol **1b** (1.18 mL, 10 mmol), 3-methylpyrazole (81 μL, 1.0 mmol, 10 mol %), and MTO (2.5 mg, 0.010 mmol, 0.1 mol %). The mixture was maintained at 20 °C by immersing in a temperature-controlled water bath. H_2O_2 (35%, 1.01 mL, 12 mmol) was added all at once to the stirring solution. The resulting two-phase mixture was stirred vigorously at 20 °C. The progress of the reaction was monitored at appropriate intervals by GC analysis of small aliquots of the organic phase. The conversion of **1b** and yield of epoxide **2b** were determined by a GC internal standard method. The GC internal standard material (*n*-undecane) was added just before the first analysis. The epoxide was isolated and identified in a separate experiment as follows. The reaction mixture was poured into brine and extracted with CH_2Cl_2. The organic layer was washed successively with brine and aqueous $Na_2S_2O_3$. Then the organic layer was washed with aqueous solution of tartaric acid to remove 3-methylpyrazole, followed with aqueous solution of $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4, and CH_2Cl_2 was distilled out by an evaporator. The oily residue obtained was dried under vacuum. The crude epoxide was purified by Kugelrohr distillation under reduced pressure.

***trans*-3,4-Epoxy-1-hexanol (2a).**[11b,12b,c,16] ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.00 (t, *J* = 7.6 Hz, 3H), 1.50−1.65 (m, 2H), 1.65−1.76 (m, 1H), 1.92−2.02 (m, 1H), 2.29 (br, 1H), 2.76−2.81 (m, 1H), 2.86−2.91 (m, 1H), 3.75−3.82 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.8, 24.9, 34.2, 56.6, 59.4, 59.9.

***cis*-3,4-Epoxy-1-hexanol (2b).**[11b,12b,16] ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (t, *J* = 7.6 Hz, 3H), 1.47−1.74 (m, 3H), 1.83−1.92 (m, 1H), 2.92 (br, 1H), 2.90−2.96 (m, 1H), 3.08−3.14 (m, 1H), 3.77−3.89 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.3, 21.1, 30.4, 55.0, 57.9, 60.2.

***cis*-3,4-Epoxy-1-heptanol (2d).**[11b] ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.95−1.02 (m, 3H), 1.43−1.59 (m, 4H), 1.64−1.74 (m, 1H), 1.84−1.93 (m, 1H), 2.38 (br, 1H, OH), 2.94−2.99 (m, 1H), 3.07−3.13 (m, 1H), 3.79−3.91 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 19.7, 29.8, 30.5, 54.9, 56.6, 60.5.

***cis*-3,4-Epoxy-1-octanol (2e).**[11b,12c,16] ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (t, *J* = 7.1 Hz, 3H), 1.33−1.60 (m, 6H), 1.61−1.75 (m, 1H), 1.84−1.93 (m, 1H), 2.21 (m, 1H, OH), 2.92−2.99 (m, 1H), 3.07−3.13 (m, 1H), 3.75−3.92 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 22.5, 27.6, 28.5, 30.5, 55.0, 56.8, 60.6.

***cis*-3,4-Epoxy-1-nonanol (2f).**[11b,16] ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (t, *J* = 7.1 Hz, 3H), 1.27−1.60 (m, 8H), 1.64−1.76 (m, 1H), 1.82−1.94 (m, 1H), 2.05 (br, 1H, OH), 2.92−3.00 (m, 1H), 3.07−3.14 (m, 1H), 3.79−3.94 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 22.5, 26.1, 27.8, 30.5, 31.6, 55.0, 56.8, 60.7.

dx.doi.org/10.1021/jo301825j | J. Org. Chem. 2012, 77, 9884−9888

3-Methyl-3,4-epoxy-1-butanol (2g).[12b,c,16] ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38 (s, 3H), 1.82−1.99 (m, 2H), 2.45 (br, 1H, OH), 2.64 (d, *J* = 4.6 Hz, 1H), 2.81 (d, *J* = 4.6 Hz, 1H), 3.66−3.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 37.7, 53.0, 56.4, 59.1.

1,2-Epoxy-*p*-menthan-4-ol (2h).[20] A 50 mL flask equipped with a stirbar was charged with CH_2Cl_2 (5 mL), (±)-terpinen-4-ol **1h** (1.54g, 10 mmol), 3-methylpyrazole (81 μL, 1.0 mmol, 10 mol %), 1-methylimidazole (8 μL, 0.1 mmol, 1 mol %), and MTO (2.5 mg, 0.010 mmol, 0.1 mol %). The mixture was cooled to 10 °C by immersing in a temperature-controlled water bath. H_2O_2 (35%, 1.01 mL, 12 mmol) was added all at once to the stirring solution. The resulting two-phase mixture was stirred vigorously at 10 °C. The disappearance of **1h** was confirmed by GC analysis of small aliquots of the organic phase after 1 h. The reaction mixture was poured into brine and extracted with CH_2Cl_2. The organic layer was washed successively with brine and aqueous $Na_2S_2O_3$, and then dried over anhydrous Na_2SO_4. The solvent of the organic layer was removed out using an evaporator, and the oily residue obtained was dried under vacuum. 1,2-Epoxy-*p*-menthan-4-ol **2h** (1.63g, 96% yield, 95% purity by GC) was obtained as colorless oil. The *cis*/*trans* ratio was 88/12, which was determined by GC. The NMR signals of *cis*- and *trans*-isomers were identified using the *cis*-isomer prepared according to the literature method.[17] Most of the signals of *cis*- and *trans*-isomers in ^{1}H NMR overlapped. ^{1}H NMR (400 MHz, $CDCl_3$): (*cis*/*trans* mixture) δ 0.86−0.95 (m, 6H), 1.30−1.42 (m, 1H), 1.36 (s, 1H), 1.49−1.66 (m, 2H), 1.79−1.93 (m, 2H), 2.00−2.09 (m, 1H), 2.12−2.24 (m, 1H), 2.98 (*trans*-C2, d, *J* = 5.0 Hz), 3.20−3.23 (*cis*-C2, m, 1H total of *cis* and *trans*), 3.53 (s, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$): (*cis*) δ 16.5, 16.7, 23.8, 25.7, 29.3, 31.8, 36.8, 58.6, 62.0, 71.8; (*trans*) δ 16.6, 16.7, 22.8, 25.3, 27.4, 33.1, 38.3, 57.7, 57.7, 70.6.

1-Phenyl-3,4-epoxy-1-butanol (2i). Colorless oil. The *cis*/*trans* ratio was approximately 50/50, which was determined by ^{1}H NMR integration of protons at C1. The NMR signals of *cis*- and *trans*-isomers were determined using *cis*-rich mixture (*cis*/*trans* = 64/36) that was prepared according to the literature method.[17] ^{1}H NMR (400 MHz, $CDCl_3$): (*cis*/*trans* mixture) δ 1.72−2.15 (m, 2H), 2.45−2.49 (*cis*-C1, m), 2.55−2.59 (*trans*-C1, m, 1H total of *cis* and *trans*), 2.70−2.82 (*cis*- and *trans*-C2, m, 2H, overlap OH proton), 2.94−3.00 (*cis*-C1, m), 3.11−3.17 (*trans*-C1, m, 1H total of *cis* and *trans*), 4.87−4.93 (m, 1H), 7.24−7.40 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): (*cis*) δ 41.7, 46.7, 50.2, 72.6, 125.7, 127.6, 128.4, 143.7; (*trans*) δ 41.3, 47.1, 49.9, 71.6, 125.5, 127.5, 128.4, 144.0. Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 72.94; H, 7.35.

1,2-Epoxy-6-methyl-4-heptanol (2j). Colorless oil. The *cis*/*trans* ratio was 50/50, which was determined by GC by using GL Sciences InertCap WAX column (30 m length × 0.25 mm i.d., 0.25 μm film thickness). The NMR signals of *cis*- and *trans*-isomers were determined using a *cis*-rich mixture (*cis*/*trans* = 68/32) that was prepared according to the literature method.[17] ^{1}H NMR (400 MHz, $CDCl_3$): (*cis*/*trans* mixture) δ 0.88−0.97 (m, 6H), 1.21−1.31 (m, 1H), 1.43−1.62 (m, 2H), 1.72−1.87 (m, 2H), 2.14 (br, 1H, OH), 2.49−2.53 (*cis*-C1, m), 2.59−2.64 (*trans*-C1, m, 1H total of *cis* and *trans*), 2.77−2.81 (*cis*-C2, m), 2.81−2.86 (*trans*-C2, m, 1H total of *cis* and *trans*), 3.07−3.13 (*cis*-C1, m), 3.13−3.19 (*trans*-C1, m, 1H total of *cis* and *trans*), 3.86−4.02 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): (*cis*) δ 21.9, 23.2, 24.3, 40.2, 46.5, 46.5, 50.4, 68.1; (*trans*) δ21.9, 23.2, 24.3, 39.7, 46.6, 46.9, 50.1, 67.0. Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.23; H, 10.90.

3,4-Epoxy-1-butanol (2k).[12b,c] ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.64−1.74 (m, 1H), 1.88−1.98 (m, 1H), 2.56−2.60 (m, 1H), 2.81 (t, *J* = 4.3 Hz, 1H), 3.07−3.12 (m, 1H), 3.59 (s, 1H, OH), 3.74−3.81 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 34.7, 46.6, 50.2, 59.2.

***p*-Menthane-1,2,4-triol (3). Isolation of Byproduct on (±)-Terpinen-4-ol (1h) Epoxidation.** A 50 mL flask equipped with a stirbar was charged with (±)-terpinen-4-ol **1h** (3.09 g, 20 mmol), 3-methylpyrazole (161 μL, 2.0 mmol, 10 mol %), and MTO (10 mg, 0.040 mmol, 0.2 mol %). The mixture was cooled to 10 °C by immersing in a temperature-controlled water bath. H_2O_2 (35%, 2.02 mL, 24 mmol) was added all at once to the stirring solution. The resulted mixture was stirred at 10 °C. The disappearance of **1h** was confirmed by GC analysis after 2 h. The ratio of epoxide **2h**/triol **3** was 96.5/3.5 by a GC peak area ratio at this stage. The reaction mixture solidified after standing the mixture at room temperature for one night. Dichloromethane was added to the mixture, and insoluble white product was collected by filtration and then washed with ethyl acetate. The obtained white solid was recrystallized from ethyl acetate to give *p*-menthane-1,2,4-triol **3** (1.57g, 42%) as white prisms, mp 171−172 °C (lit.[21] mp 173 °C). ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.81 (d, *J* = 6.9 Hz, 6H), 1.10 (s, 3H), 1.19−1.31 (m, 2H), 1.35−1.52 (m, 2H), 1.59−1.81 (m, 3H), 3.32−3.37 (m, 1H), 4.22 (s, 1H, OH), 4.60 (s, 1H, OH), 5.17 (d, *J* = 6.9 Hz, 1H, OH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 16.9, 17.0, 27.1, 29.3, 29.6, 34.0, 37.4, 70.0, 73.3, 73.9.

Procedure for Epoxidation of 6-Methyl-1-hepten-4-ol (1j) (Table 2, entry 12, Isolated Yield). A 50 mL flask equipped with a stirbar was charged with CH_2Cl_2, 6-methyl-1-hepten-4-ol **1j** (1.92 g, 15.0 mmol, >99% purity by GC), and 3-methylpyrazole (0.121 mL, 1.5 mmol, 10 mol %). The temperature of the flask was adjusted to 20 °C by applying an external water bath. MTO (37.4 mg, 0.15 mmol, 1 mol %) was added to the solution, and then H_2O_2 (35%, 1.9 mL, 23 mmol) was added all at once to the stirring solution. The resulting two-phase mixture was stirred vigorously at 20 °C. After 8 h, the reaction mixture was poured into brine, and the organic layer was washed successively with brine (2 times) and an aqueous solution of $Na_2S_2O_3$. Then the organic layer was washed with an aqueous solution of tartaric acid (0.5 g in 20 mL of H_2O) to remove 3-methylpyrazole, followed with an aqueous solution of $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4, and CH_2Cl_2 was distilled out by an evaporator. The residual orange oil was dried under vacuum to give crude 1,2-epoxy-6-methyl-4-heptanol **2j** (1.91 g). Kugelrohr distillation of the crude product under reduced pressure (5 Torr, 100−105 °C) afforded pure 1,2-epoxy-6-methyl-4-heptanol **2j** as colorless oil (1.67 g, 77% yield, >99% purity by GC).

Procedure for 10 g Scale Epoxidation of *cis*-3-Octen-1-ol (1e) (Table 2, entry 4). A 100 mL flask equipped with a stirbar and thermometer was charged with *cis*-3-octen-1-ol **1e** (10 g, 78.0 mmol, >97% purity by GC) and 3-methylpyrazole (0.63 mL, 7.8 mmol, 10 mol %). The flask was cooled to 10 °C by applying an external cooling bath. MTO (19.4 mg, 0.078 mmol, 0.1 mol %) was added to the solution, and then H_2O_2 (35%, 7.9 mL, 94 mmol) was added dropwise to the stirring solution from a dropping funnel (ca. 20 min). During the H_2O_2 addition, the temperature of the solution was kept below 27 °C. The resulting two-phase mixture was stirred vigorously at 10 °C. The reaction was completed after 2 h, and CH_2Cl_2 was added to the reaction mixture. The organic layer of the reaction mixture was washed successively with brine (2 times) and with an aqueous solution of $Na_2S_2O_3$. Then the organic layer was washed with an aqueous solution of tartaric acid (2.5 g in 25 mL of H_2O) to remove 3-methylpyrazole completely, followed with an aqueous solution of $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4, and CH_2Cl_2 was distilled out by an evaporator. The residual yellow oil was dried under vacuum to give crude *cis*-3,4-epoxy-1-octanol **2e** (11.2 g). Distillation of the crude product under reduced pressure (4 Torr, 106−107 °C) afforded *cis*-3,4-epoxy-1-octanol **2e** as colorless oil (9.6 g, 85% yield, >97% purity by GC).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Determination of *cis*/*trans* ratio of epoxides, **2h**, **2i**, and **2j**, and ^{1}H and ^{13}C NMR spectra of **2a**, **2b**, **2d−k**, and **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: s-yamazk@itc.pref.toyama.jp.

Notes

The authors declare no competing financial interest.

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