A pH Study on the Chiral Ketone Catalyzed Asymmetric Epoxidation of Hydroxyalkenes

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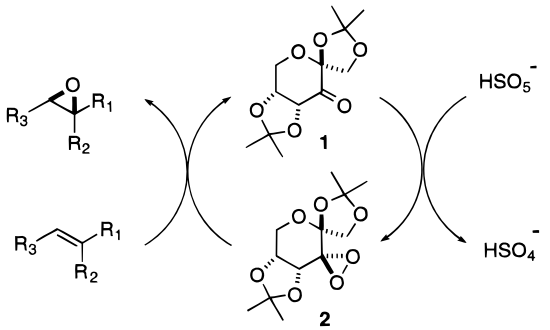
Received November 17, 1997

A detailed study shows that the chiral ketone catalyzed asymmetric epoxidations of hydroxyalkenes are highly pH dependent. The lower enantioselectivity obtained at low pH is attributed to the substantial contribution of the direct epoxidation by Oxone. At high pH the epoxidation mediated by chiral ketone out-competes the racemic epoxidation, leading to higher enantioselectivity. The effective substrates include allylic alcohol, homoallylic alcohol, and bishomoallylic alcohol. In most cases, over 90% ee was obtained.

Chiral dioxiranes have displayed remarkable potential for asymmetric epoxidation.[1−3] Recently we reported a highly enantioselective epoxidation method for trans-disubstituted and -trisubstituted unfunctionalized olefins using a fructose-derived ketone **1** as catalyst and Oxone as oxidant (Scheme 1).[4] However, under our initial reaction conditions, the enantioselectivities for hydroxy-alkenes were substantially lower.[4a] For example, the ee's for *trans*-2-hexen-1-ol and *trans*-3-hexen-1-ol were only 78% and 70%, respectively.[4a] The unusual behavior displayed by this class of olefins triggered us to carry out the investigations further. In this paper, we report our detailed studies on this subject.

Scheme 1



Results and Discussion

We were intrigued by an observation that the ee for the epoxidation of cinnamyl alcohol increased from 84%, using the initial reaction conditions (pH 7−8),[4a] to 90%, using the catalytic conditions (pH ∼10.5).[4b] We surmised that this 6% difference could result from the pH change. On the basis of this assumption, a systematic pH study on the epoxidation of hydroxyalkenes was therefore carried out.

trans-3-Hexen-1-ol and geraniol were chosen as the test substrates. The enantioselectivities were indeed dependent on the pH as shown in Figure 1. For *trans*-3-hexen-1-ol, the ee increased by 17% from pH ∼7 to ∼10.6 (Figure 1, A). In the case of geraniol, the change of the enantiomeric excesses with the pH were much more

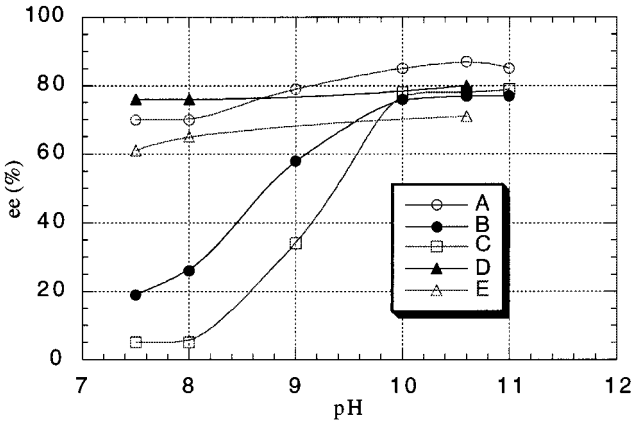


Figure 1. Plot of the enantiomeric excesses of the epoxidations of olefins against pH. The olefins presented are: *trans*-3-hexene-1-ol (A), geraniol (6,7-olefin) (B), geraniol (2,3-olefin) (C), geraniol−TBS ether (6,7-olefin) (D), and geraniol−TBS ether (2,3-olefin) (E) (for the detailed data and reaction conditions, see Tables 1−3 in Supporting Information).

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(1) For general leading references on dioxiranes, see: (a) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187−1201. (b) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205−211. (c) Curci, R.; Dinoi, A.; Rubino, M. F. *Pure Appl. Chem.* **1995**, *67*, 811−822. (d) Adam, W.; Smerz, A. K. *Bull. Soc. Chim. Belg.* **1996**, *105*, 581−599.

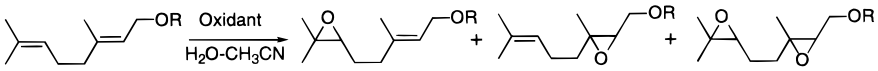
(2) For examples of in situ generation of dioxiranes, see: (a) Edwards, J. O.; Pater, R. H.; Curci, R.; Di Furia, F. *Photochem. Photobiol.* **1979**, *30*, 63−70. (b) Curci, R.; Fiorentino, M.; Troisi, L.; Edwards, J. O.; Pater, R. H. *J. Org. Chem.* **1980**, *45*, 4758−4760. (c) Gallopo, A. R.; Edwards J. O. *J. Org. Chem.* **1981**, *46*, 1684−1688. (d) Cicala, G.; Curci, R.; Fiorentino, M.; Laricchiuta, O. *J. Org. Chem.* **1982**, *47*, 2670−2673. (e) Corey, P. F.; Ward, F. E. *J. Org. Chem.* **1986**, *51*, 1925−1926. (f) Yang, D.; Wong, M. K.; Yip, Y. C. *J. Org. Chem.* **1995**, *60*, 3887−3889 and references therein. (g) Denmark, S. E.; Forbes, D. C.; Hays, D. S.; DePue, J. S.; Wilde, R. G. *J. Org. Chem.* **1995**, *60*, 1391−1407 and references therein.

(3) For examples of asymmetric epoxidation mediated by chiral ketones, see: (a) Curci, R.; Fiorentino, M.; Serio, M. R. *J. Chem. Soc., Chem. Commun.* **1984**, 155−156. (b) Curci, R.; D'Accolti, L.; Fiorentino, M.; Rosa, A. *Tetrahedron Lett.* **1995**, *36*, 5831−5834. (c) See ref 2g. (d) Brown, D. S.; Marples, B. A.; Smith, P.; Walton, L *Tetrahedron* **1995**, *51*, 3587−3606. (e) Yang, D.; Yip, Y. C.; Tang, M. W.; Wong, M. K.; Zheng, J. H.; Cheung, K. K. *J. Am. Chem. Soc.* **1996**, *118*, 491−492. (f) Yang, D.; Wang, X.-C.; Wong, M.-K.; Yip, Y.-C.; Tang, M.-W. *J. Am. Chem. Soc.* **1996**, *118*, 11311−11312. (g) Song, C. E.; Kim, Y. H.; Lee, K. C.; Lee, S. G.; Jin, B. W. *Tetrahedron: Asymmetry* **1997**, *8*, 2921−2926.

(4) (a) Tu, Y.; Wang, Z.-X.; Shi, Y. *J. Am. Chem. Soc.* **1996**, *118*, 9806−9807. (b) Wang, Z.-X.; Tu, Y.; Frohn, M.; Shi, Y. *J. Org. Chem.* **1997**, *62*, 2328−2329. (c) Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224−11235.

S0022-3263(97)02106-3 CCC: $15.00
Published on Web 04/16/1998

Table 1. pH Studies on the Epoxidation of Geraniol and Its TBS Ether Using Dioxiranes and Oxone



3a R = H **4a** R = H **5a** R = H **6a** R = H
3b R = OTBS **4b** R = OTBS **5b** R = OTBS **6b** R = OTBS

entry	substrates	oxidant	pH	conv. (%)[g]	ratio (**4**/**5**)[i]
1	**3a**	DMD[a]	4.5	17	5.3
2	**3a**	DMD[a]	7.2	19	4.4
3	**3a**	DMD[a]	8.8	18	5.2
4	**3a**	DMD[a]	9.3	20	5.0
5	**3a**	DMD[a]	10.0	20	4.7
6	**3a**	DMD[a]	10.9	16	5.2
7	**3a**	Oxone[b]	7−7.5	33	2.1
8	**3a**	Oxone[c]	8.0	44	2.0
9	**3a**	Oxone[c]	9.0	38	2.3
10	**3a**	Oxone[c]	10.0	30	2.2
11	**3a**	Oxone[c]	10.7	17	2.4
12	**3a**	Oxone[c]	11.5	5	nd
13	**3b**	Oxone[b]	7−7.5	<1	nd
14	**3a** + **3b** (1/1)	Oxone[b]	7−7.5	41(<1)[h]	2.9[j]
15	**3a**	**1**/Oxone[d]	7−7.5	12.3	2.4
16	**3a**	**1**/Oxone[e]	8.0	24	3.1
17	**3a**	**1**/Oxone[e]	9.0	45	4.6
18	**3a**	**1**/Oxone[e]	10.0	58	6.1
19	**3a**	**1**/Oxone[e]	11.0	58	5.6
20	**3a**	**1**/Oxone[e]	11.5	58	5.9
21	**3a**	dioxirane **2**[f]	7.5	5	5.7
22	**3b**	**1**/Oxone[d]	7−7.5	5	4.3
23	**3b**	**1**/Oxone[e]	8.0	10	4.4
24	**3b**	**1**/Oxone[e]	10.6	41	4.5

[a] All reactions were carried out at room temperature with dimethyldioxirane (DMD) (0.25 eq) (for details see the Experimental Section). [b] The reaction was carried out with substrate (1 eq) in CH_3CN−aqueous Na_2(EDTA) (4×10^{-4} M) (1.5:1 v/v) by adding a mixture powder of Oxone (0.5 eq) and $NaHCO_3$ (1.55 eq) over 1 h at 0 °C, followed by additional 1 h stirring at 0 °C. [c] Oxone (0.5 eq) was added as an aqueous Na_2(EDTA) (4×10^{-4} M) solution through a syringe pump at 0 °C over 1.5 h (for the detail control of the pH, see the Experimental Section). [d] The reactions were carried out with substrate (1 eq) and ketone **1** (1 eq) in CH_3CN−aqueous Na_2(EDTA) (4×10^{-4} M) (1.5:1 v/v) by adding a mixture powder of Oxone (0.5 eq) and $NaHCO_3$ (1.55 eq) over 1 h at 0 °C, followed by additional 1 h of stirring at 0 °C. [e] The reactions were carried out with substrate (1 eq) and ketone **1** (0.3 eq). Oxone (0.5 eq) was added as an aqueous Na_2(EDTA) (4×10^{-4} M) solution through a syringe pump at 0 °C over 1.5 h (for the detail control of the pH, see the Experimental Section). [f] For details, see the Experimental Section. [g] Determined by the ^{1}H NMR. The conversion of geraniol was kept low to minimize the formation of the bisepoxide. [h] The conversion for **3a** is 41%, and the conversion for **3b** is <1%. [i] Determined by the ^{1}H NMR analysis of the crude reaction mixtures. For the DMD mediated epoxidation of **3a**, no bisepoxide **6a** was observed. For others, small amounts of bisepoxides **6a** or **6b** were formed in some cases, and the ^{1}H NMR signals of the bisepoxides partially overlapped with the signals of the monoepoxides. Therefore, the presented ratio is actually the ratio of (**4** + **6**)/(**5** + **6**). [j] This ratio is for substrate **3a**.

drastic. For the epoxide distal to the OH group, the ee increased from 19% to 77% when the pH was changed from ∼7 to ∼11 (Figure 1, B). For the epoxide proximal to the OH group, the ee change was even greater, from <5% to 79% when the pH was changed from ∼7 to ∼11 (Figure 1, C). The effect of pH on the epoxidation of the geraniol TBS ether was studied for comparison. As shown in Figure 1 (D and E), the ee change with the pH was much smaller for the TBS ether than for that of geraniol. The slightly lower enantioselectivity at lower pH could be due to the epoxidation catalyzed by the acetone, resulting from the decomposition of ketone **1** since the ketone catalyst decomposes faster at lower pH.[4b] These results strongly suggested that the variation of the enantioselectivity with pH was directly related to the OH group.

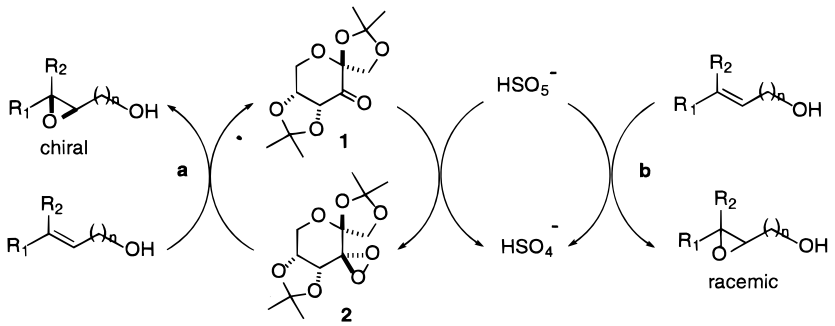
It has been established that the hydroxyl group can hydrogen bond with the dioxirane to affect the regio- and diastereoselectivities of the epoxidations.[5] To explore the possibility of this hydrogen-bonding effect on the enantioselectivity, the following experiment was carried out. An excess of ketone **1** was treated with Oxone in H_2O−CH_3CN at pH 7−7.5 to preform dioxirane **2**. After a short time, the bulk of the aqueous layer was removed by a cold pipet, and geraniol was added to the remaining solution.[6] Enough epoxides were obtained to determine the ee's, although a low conversion (5%) was observed. The ee's for both epoxides (70% ee for 6,7-epoxide **4a**, 50% ee for 2,3-epoxide **5a**) were substantially higher than the ee's obtained by usual in situ epoxidation (Figure 1, B and C), even though the pH was the same in both cases (7−7.5). The results suggested that the hydrogen bonding between the OH group of the olefin and the dioxirane was not the major factor for the lower ee obtained at low pH, since the hydrogen bonding in both cases was expected to be very similar.

Furthermore, the pH is expected to have little effect on the hydrogen bonding over the currently tested range (pH 7−11.5), since the pK_a for the alcohol is usually greater than 14. To further support this notion, the epoxidation of geraniol with dimethyldioxirane (DMD) at

(5) For the leading references on the epoxidation of hydroxyalkenes by dioxiranes, see: (a) Cicala, G.; Curci, R.; Fiorentino, M.; Laricchiuta, O. *J. Org. Chem.* **1982**, *47*, 2670−2673. (b) Murray, R. W.; Singh, M.; Williams, B. L.; Moncrieff, H. M. *Tetrahedron Lett.* **1995**, *36*, 2437−2440. (c) Adam, W.; Smerz, A. K. *Tetrahedron* **1995**, *51*, 13039−13044. (d) Adam, W.; Smerz, A. K. *J. Org. Chem.* **1995**, *61*, 3506−3510. (e) Murray, R. W.; Singh, M.; Williams, B. L.; Moncrieff, H. M. *J. Org. Chem.* **1996**, *61*, 1830−1841. (f) See ref 1d. (g) Adam, W.; Mitchell, C. M.; Paredes, R.; Smerz, A. K. Veloza, A. *Liebigs Ann./Rec.* **1997**, 1365−1369.

(6) It should be noted that dioxirane **2** was very short-lived. It has been extremely difficult to isolate this species. In this case, it was hoped that some dioxirane would remain within a short time.

Scheme 2



different pH values was then carried out (Table 1, entries 1−6). It has been known that the ratio of the two epoxides (**4a**/**5a**) will vary if the hydrogen bonding between the dioxirane and the hydroxyl group is affected by changing the reaction conditions (e.g., changing the solvent).[5] As shown in Table 1, the ratios (**4a**/**5a**) indeed remained similar over the tested range (4.5−10.9), which clearly demonstrated that the pH change did not affect the hydrogen bonding, if such hydrogen bonding existed in this case. Therefore, the variation of the enantioselectivity with the pH is highly unlikely to be due to the alteration of any hydrogen bonding between the hydroxyl group and dioxirane **2**.

A more likely explanation is that the observed low enantioselectivity at low pH could be due to a substantial amount of the racemic epoxidation produced by Oxone itself (pathway **b** in Scheme 2).[7] To further illustrate this possibility, the epoxidations of geraniol and its TBS ether were carried out in the absence of ketone **1** (Table 1). A substantial amount of the geraniol was epoxidized in the absence of the ketone catalyst (Table 1, entries 7−12). In contrast, the epoxidation of the TBS ether was negligible under the current reaction conditions (Table 1, entry 13). When both the alcohol and the TBS ether were present in the reaction mixture, only the alcohol was epoxidized (Table 1, entry 14). This result strongly suggested that the epoxidation by Oxone was facilitated by the hydroxyl group in the substrate. The hydroxyl group could form a hydrogen bond with Oxone to achieve epoxidation in an intramolecular fashion,[8] and/or the hydroxyl group could enhance the water solubility of the substrate, consequently facilitating the reaction between the olefin and Oxone.

Studies showed that the epoxidation efficiency by Oxone was slightly affected by the pH but not substantially (Table 1, entries 7−12). The higher enantioselectivity obtained at high pH could largely be due to an enhanced nucleophilicity of Oxone toward ketone catalyst **1**, increasing the formation of dioxirane **2**, which outcompetes the direct epoxidation by Oxone. The competition between the two pathways (**a** and **b**) was also clearly reflected by the ratio of the two epoxides (**4a**/**5a**) (distal epoxide vs proximal epoxide). The ratio of two epoxides (**4a**/**5a**) was around 2 for the direct epoxidation by Oxone (Table 1, entries 7−11). However, this ratio was higher (5−6) when the olefins were epoxidized by dioxiranes (Table 1, entries 1−6, 21). When the epoxidation was carried out in an in situ fashion using ketone **1** as catalyst, the ratio (**4a**/**5a**) increased from 2.4 to around 6 when the pH was changed from about 7 to >10 (Table 1, entries 15−20), indicating that the epoxidation by Oxone (pathway **b**) dominated at low pH and the epoxidation by the dioxirane dominated at high pH (pathway **a**).

The enantioselectivities obtained for both test substrates (*trans*-3-hexene-1-ol and geraniol) at high pH (about 10.5) were quite high. The ee's were further improved by changing solvents (for details, see Supporting Information) and lowering the reaction temperature. Encouraged by these results, we investigated the asymmetric epoxidation of a variety of hydroxyalkenes under the optimized conditions. The olefins included allylic alcohols, homoallylic alcohols, and bishomoallylic alcohols.[9] As shown in Table 2, high enantiomeric excesses were obtained in many cases.

In summary, we found that the asymmetric epoxidation of hydroxyalkenes is highly pH dependent. At low pH, the hydroxyl group facilitated epoxidation by Oxone is dominant, resulting in lower enantiomeric excesses. As the pH is increased, it appears the Oxone is more likely to react with the chiral ketone to form the corresponding dioxirane which subsequently reacts with the olefin, yielding a higher enantioselectivity. The effective substrates include allylic alcohols, homoallylic alcohols, and bishomoallylic alcohols. The resulting chiral epoxides should be synthetically useful. The current study allows us to further understand the factors involved in the dioxirane mediated epoxidation and to further expand the synthetic scope of the current asymmetric epoxidation method.

Experimental Section

For detailed information regarding general methods, see ref 4c. For detailed GC and HPLC conditions, see Supporting Information.

Preparation and Characterization of the Olefin Substrates. *trans*-4-Phenyl-2-buten-1-ol (Table 2, Entry 2). Treatment of (carbethoxymethylene) triphenylphosphorane with phenylacetaldehyde in dry benzene at room temperature gave a mixture of *trans*- and *cis*-olefins which were separated by flash chromatography (hexanes−ether, 10:1 v/v): ethyl *trans*-4-phenyl-2-butenoate (89% yield) as a colorless oil, R_f = 0.31 (hexanes−ether, 10:1 v/v). DIBAL-H reduction of ethyl

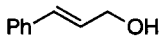
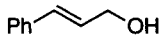
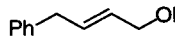
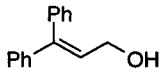
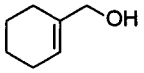
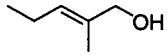
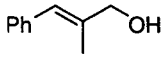
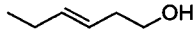
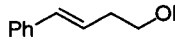
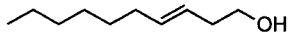
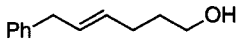
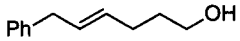
(7) For the leading references on the epoxidation of olefins by Oxone, see: (a) Bloch, R.; Abecassis, J.; Hassan, D. *J. Org. Chem.* **1985**, *50*, 1544−1545. (b) Zhu, W.; Ford, W. T. *J. Org. Chem.* **1991**, *56*, 7022−7026. (c) See ref 5g.

(8) Such hydrogen bonding is likely to enhance the epoxidation reactivity of Oxone by dispersing the negative charge of Oxone (see ref 5g).

(9) For highly enantioselective epoxidation of allylic alcohols, see: (a) Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; Chapter 4.1. (b) Katsuki, T.; Martin, V. S. *Org. React.* **1996**, *48*, 1−299.

(10) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765−5780.

Table 2. Asymmetric Epoxidation of Representative Hydroxyalkenes Catalyzed by Ketone 1 and ent-1[a]

Entry	Olefins	T (°C)	t (h)	Yield[c] (%)	ee (%)	Config.[h]
1		-10	3	85	94 (98[g])[d]	(R,R)[10]
	 **(ent-1)**	-10	3	82	94[d]	(S,S)[10]
2		-10	2	45	91[d]	(R,R)[11]
		-15[b]	7	43	92[d]	
3		-10	3	68	91[e]	(R,R)[10]
4		0	2	87	94[d]	(R)[i]
5		-10	3	92	92[f]	(R,R)[10,12]
		-15[b]	5	93	94[f]	
6		-10	3	83	91[f]	(R,R)[13]
		-15[b]	5	85	92[f]	
7		-15[b]	5	75	74[d]	(R,R)[10]
8		-10	3	82	90[e]	(R,R)[14]
9		0	2	90	91[d]	(R,R)[i]
10		-10	2	86	90[e]	(R,R)[i]
		-15[b]	5	83	91[e]	
11		0	2	87	91[d]	(R,R)[i]
	 **(ent-1)**	0	2	88	91[d]	(S,S)[i]

[a] All reactions were carried out with substrate (1 eq), ketone **1** (0.3 eq), Oxone (1.38 eq), and K_2CO_3 (5.8 eq) in DMM−CH_3CN−aqueous K_2CO_3/AcOH (prepared by adding 0.5 mL of AcOH to 100 mL of 0.1 M aqueous K_2CO_3, pH 9.3) (2:1:2 v/v) unless otherwise noted. [b] DME was used instead of DMM−CH_3CN as solvent. [c] Isolated yield. [d] Enantioselectivity was determined by chiral HPLC (Chiralcel OD column). [e] Enantioselectivity was determined by the ^1H NMR shift analysis of derived acetate with $Eu(hfc)_3$. [f] Enantioselectivity was determined by chiral GC (Chiraldex B-TA column). [g] After recrystallization. [h] The absolute configuration was determined by comparing the measured optical rotations with the reported ones. [i] The absolute configuration was tentatively assumed by analogy based on the spiro reaction mode.

trans-4-phenyl-2-butenoate in dry ether afforded *trans*-4-phenyl-2-buten-1-ol (96% yield) as a lightly yellow oil.[11b]

3,3-Diphenyl-2-propen-1-ol (Table 2, entry 4): prepared by the DIBAL-H reduction (90% yield) of the corresponding ester obtained by the Wittig reaction (93% yield) of triethyl phosphonoacetate and benzophenone;[15] white crystals, mp 55−57 °C (recrystallized from hexanes−ether); IR (KBr) 3327, 1628 cm^{-1}; ^1H NMR δ 7.45−7.1 (m, 10H), 6.26 (t, J = 6.6 Hz, 1H), 4.23 (d, J = 6.6 Hz, 2H), 1.6 (s, 1H); ^{13}C NMR δ 144.4, 142.0, 139.2, 129.9, 128.4, 128.37, 127.82, 127.8, 127.77, 127.7, 60.89.

1-Cyclohexenylmethanol[10] (Table 2, entry 5): prepared by the DIBAL-H reduction of the corresponding methyl cyclohexene-1-carbonate obtained by esterification of cyclohexene-1-carbonic acid (72% yield for two steps).

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***trans*-2-Methyl-2-penten-1-ol**[13a] **(Table 2, entry 6):** prepared by the DIBAL-H reduction of *trans*-2-methyl-2-penten-1-al in THF with 90% yield.

***trans*-4-Phenyl-3-buten-1-ol (Table 2, entry 9):** prepared by the $LiAlH_4$ reduction of *trans*-styrylacetic acid in THF with 86% yield; IR (KBr) 3357, 1657 cm^{-1}; ^1H NMR δ 7.4−7.1 (m, 5H), 6.48 (d, J = 15.9 Hz, 1H), 6.19 (dt, J = 15.9, 7.2 Hz, 1H), 3.72 (t, J = 6.3 Hz, 2H), 2.46 (dt, J = 7.2, 6.3 Hz, 2H), 2.0 (br s, 1H); ^{13}C NMR δ 137.4, 132.8, 128.7, 127.4, 126.6, 126.2, 62.13, 36.52.

***trans*-3-Decen-1-ol (Table 2, entry 10):** prepared by the $LiAlH_4$ reduction of *trans*-3-decenoic acid in THF with 90% yield; colorless oil; IR (KBr) 3329, 1653 cm^{-1}; ^1H NMR δ 5.56 (dt, J = 15.3, 6.6 Hz, 1H), 5.37 (dtt, J = 15.3, 6.6, 1.2 Hz, 1H), 3.63 (t, J = 6.3 Hz, 2H), 2.27 (dt, J = 6.6, 6.3 Hz, 2H), 2.02 (q, J = 6.6 Hz, 2H), 1.45 (br s, 1H), 1.4−1.2 (m, 8H), 0.89 (t, J = 6.6 Hz, 3H); ^{13}C NMR δ 134.7, 125.9, 62.22, 36.19, 32.89, 31.92, 29.63, 29.07, 22.83, 14.3.

***trans*-6-Phenyl-4-hexen-1-ol (Table 2, entry 11):** prepared by the DIBAL-H reduction of methyl *trans*-6-phenyl-4-hexenoate[4b] with 92% yield; colorless oil; IR (KBr) 3350, 1660 cm^{-1}; ^1H NMR δ 7.4−7.15 (m, 5H), 5.66 (dt, J = 15.3, 6.6, 1H), 5.54 (dt, 15.3, 6.3 Hz, 1H), 3.66 (t, J = 6.6 Hz, 2H), 3.37 (d, J = 6.3 Hz, 2H), 2.15 (dt, J = 7.5, 6.6 Hz, 2H), 1.85 (br s, 1H), 1.68 (tt, J = 7.5, 6.6 Hz, 2H); ^{13}C NMR δ 141, 131.2, 129.7, 128.6, 128.5, 126.1, 62.51, 39.16, 32.46, 28.93.

General Procedure for pH Study. To a mixture of geraniol (0.154 g, 1 mmol) and tetrabutylammonium hydrogen sulfate (0.015 g, 0.04 mmol) in acetonitrile (10 mL) and aqueous K_2CO_3/AcOH (7 mL) (prepared by adding 0.5 mL of glacial AcOH to 100 mL of 0.1 M aqueous K_2CO_3) (the pH of the reaction solution was adjusted with 1 M aqueous AcOH for 8−10, and with 1 M aqueous K_2CO_3 for 10−11.5) was added ketone **1** (0.0774 g, 0.3 mmol). After the reaction mixture was cooled with an ice bath, a solution of Oxone (0.31 g, 0.5 mmol) in aqueous Na_2(EDTA) (4×10^{-4} M) (5 mL) was added through a syringe pump over 1.5 h. The reaction pH was monitored with a Corning 320 pH meter with a Corning "3 in 1" pH combination electrode and was maintained by adding aqueous K_2CO_3. After completion of the addition of Oxone, the reaction was immediately quenched with CH_2Cl_2 (20 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were washed with brine and dried (Na_2SO_4). Upon the removal of the solvent, the conversion and ratio were determined by the ^1H NMR analysis of the crude products. Separation by flash chromatography [the silica gel was buffered with 1% triethylamine solution in hexanes−ether (2:1 v/v); hexanes−ether (2:1 to 1:1 v/v) was used as the eluent] gave 2,3-epoxygeraniol and 6,7-epoxygeraniol.

2,3-Epoxygeraniol: colorless oil; R_f = 0.13 (hexanes−ether, 1:1 v/v); $[\alpha]_D^{23}$ = +4.6° (*c* 0.7, $CHCl_3$) (79% ee, determined by chiral GC, G-TA column) (Figure 1, pH 11) [lit.[10] $[\alpha]_D^{25}$ = −5.3° (*c* 3.0, $CHCl_3$) for (*S*,*S*)-form (91% ee)].

6,7-Epoxygeraniol:[5a] colorless oil; R_f = 0.08 (hexanes−ether, 1:1 v/v); $[\alpha]_D^{23}$ = +9.7° (*c* 1.1, $CHCl_3$) (77% ee, determined by chiral GC, B-TA column) (Figure 1, pH 11).

Epoxidation of Geraniol by Preformed Dioxirane 2 (Table 1, Entry 21). To a cold (0 to −5 °C, ice−salt bath) mixture of ketone **1** (0.52 g, 2 mmol) and $NaHCO_3$ (0.24 g, 2.9 mmol) in acetonitrile (10 mL) and aqueous Na_2(EDTA) (4×10^{-4} M) (7 mL) was added a solution of Oxone (0.55 g, 0.9 mmol) in aqueous Na_2(EDTA) (4×10^{-4} M) (3 mL) over 5 min. After the mixture was stirred at this temperature for another 5 min, most of the aqueous layer (about two-thirds) was removed by a cold pipet, and a cold solution of geraniol (0.154 g, 1 mmol) in acetonitrile (3 mL) was added. Upon being stirred at −5 °C for 15 min, the reaction was quenched with CH_2Cl_2 (20 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), washed with brine, and dried over Na_2SO_4. The conversion and ratio were determined by the ^1H NMR analysis of the crude products. Separation via flash chromatography [the silica gel was buffered with 1% triethylamine solution in hexanes−ether (2:1 v/v); hexanes−ether (2:1 to 1:1 v/v) was used as the eluent] gave 2,3-epoxygeraniol (50% ee) and 6,7-epoxygeraniol (70% ee).

pH Study on the Epoxidation of Geraniol by DMD. The dimethyldioxirane (DMD) acetone solution (0.05 M) was freshly prepared by Murray's method,[16] and DMD solution (0.05 M in acetone, 2.5 mL, 0.125 mmol) was added at room temperature to a mixture of geraniol (0.077 g, 0.5 mmol) in acetonitrile (7 mL) and aqueous K_2CO_3/AcOH (5 mL) (prepared by adding 0.5 mL of AcOH to 100 mL of 0.1 M aqueous K_2CO_3). (The pH of the reaction solution was adjusted with 1 M aqueous AcOH.) After the addition of the DMD solution the pH was monitored with a Corning 320 pH meter with a Corning "3 in 1" pH combination electrode. Having been stirred at room temperature for 30 min, the reaction mixture was extracted with CH_2Cl_2 (3 × 20 mL), washed with brine, dried (Na_2SO_4), and concentrated. The conversion and ratio were determined by the ^1H NMR analysis of the crude products.

General Epoxidation Procedure for Table 2. *trans*-Cinnamyl alcohol (0.136 g, 1 mmol), ketone **1** (0.0774 g, 0.3 mmol), and tetrabutylammonium hydrogen sulfate (0.015 g, 0.016 mmol) were dissolved in DMM/CH_3CN (2:1 v/v) (10 mL). An aqueous K_2CO_3/HOAc solution (7 mL) (prepared by mixing 100 mL of 0.1 M aqueous K_2CO_3 with 0.5 mL of acetic acid (pH 9.3)) was added with stirring, and the mixture was cooled to about −10 °C (inside; outside is about −10 °C to −15 °C) via a NaCl−ice bath. A solution of Oxone (0.85 g, 1.38 mmol) in aqueous Na_2(EDTA) (4×10^{-4} M) (5 mL) and a solution of K_2CO_3 (0.8 g, 5.8 mmol) in water (5 mL) were added dropwise separately via a syringe pump over a period of 3 h. The reaction was immediately quenched with CH_2Cl_2 (20 mL) and water. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), washed with brine, dried over Na_2SO_4, concentrated, and purified by flash chromatography [the silica gel was buffered with 1% Et_3N in hexanes−ether (2:1 v/v); hexanes−ether (2:1 to 1:1 v/v) was used as eluent] to afford (*R*,*R*)-3-phenyloxiranemethanol as white crystals (0.128 g, 85%; 94% ee).

***trans*-3-Phenyloxiranemethanol (Table 2, entry 1):** white crystals, mp 47−49 °C (recrystallized from hexanes−ether); $[\alpha]_D^{25}$ = +50.0° (*c* 1.2, $CHCl_3$) (recrystallized from hexanes−ether); $[\alpha]_D^{23}$ = −48.6° (*c* 1.11, $CHCl_3$) (**ent-1**) [Lit.[10] mp 51.5−53 °C; $[\alpha]_D^{25}$ = −49.6° (*c* 2.4, $CHCl_3$) for (*S*,*S*)-form].

(*R*,*R*)-3-(Phenylmethyl)oxiranemethanol (Table 2, entry 2): colorless oil; $[\alpha]_D^{23}$ = +34.1° (*c* 1.27, $CHCl_3$) [lit.[11a] $[\alpha]_D^{26}$ = −34.4° (*c* 0.99, $CHCl_3$) for (*S*,*S*)-form.]

(*R*,*R*)-3-Propyloxiranemethanol (Table 2, entry 3): colorless oil; $[\alpha]_D^{23}$ = +45.4° (*c* 1.07, $CHCl_3$) [lit.[10] $[\alpha]_D^{25}$ = −46.3° (*c* 3.87, $CHCl_3$) for (*S*,*S*)-form].

(*R*)-3,3-Diphenyloxiranemethanol (Table 2, entry 4): colorless oil; $[\alpha]_D^{25}$ = +33.8° (*c* 0.42, $CHCl_3$); IR (KBr) 3392, 3060, 3029, 1602, 1496, 1448, 1273, 1077, 1035, 764, 754, 699 cm^{-1}; ^1H NMR δ 7.45−7.25 (m, 10H), 3.73−3.62 (m, 2H), 3.45 (m, 1H), 1.9 (br s, 1H); ^{13}C NMR δ 140.3, 137.0, 128.6, 128.55, 128.2, 128.2, 128.0, 127.0, 66.39, 65.92, 62.3. Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.48; H, 6.13.

(*R*,*R*)-7-Oxabicyclo[4.1.0]heptane-1-methanol (Table 2, entry 5): colorless oil; $[\alpha]_D^{25}$ = +22.7° (*c* 0.55, $CHCl_3$) (−10 °C); $[\alpha]_D^{23}$ = +23.7° (*c* 1.0, $CHCl_3$) (−15 °C) [lit.[10] $[\alpha]_D^{25}$ = −22.8° (c 2.6, $CHCl_3$) for (*S*,*S*)-form (93% ee)].

(*R*,*R*)-2-Methyl-3-ethyloxiranemethanol (Table 2, entry 6): colorless oil; $[\alpha]_D^{23}$ = +18.0° (*c* 0.85, $CHCl_3$) (−10 °C), $[\alpha]_D^{23}$ = +18.4° (*c* 0.9, $CHCl_3$) (−15 °C) [lit.[13b] $[\alpha]_D^{24}$ = −21.3° (*c* 1.78, $CHCl_3$) for (*S*,*S*)-form].

(*R*,*R*)-2-Methyl-3-phenyloxiranemethanol (Table 2, entry 7): colorless oil; $[\alpha]_D^{23}$ = +13.0° (*c* 0.87, $CHCl_3$) [lit.[10] $[\alpha]_D^{25}$ = −16.9° (*c* 2.0, $CHCl_3$) for (*S*,*S*)-form (>98% ee)].

(*R*,*R*)-3-Ethyloxiraneethanol (Table 2, entry 8): colorless oil; $[\alpha]_D^{23}$ = +45.2° (*c* 1.07, EtOH) [lit.[14] $[\alpha]_D^{25}$ = +17.69° (*c* 1.73, EtOH) (41% ee)].

(*R*,*R*)-3-Phenyloxiraneethanol (Table 2, entry 9): colorless oil; $[\alpha]_D^{25}$ = +48.2° (*c* 0.42, $CHCl_3$); IR (KBr) 3416, 2947, 1604, 1497, 1460, 1052, 1027, 878, 762, 749, 698 cm^{-1}; ^1H NMR δ 7.4−7.2 (m, 5H), 3.86 (t, J = 6.0 Hz, 2H), 3.73 (d, J = 2.1

(16) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847−2853.

Hz, 1H), 3.15 (ddd, J = 6.3, 4.2, 2.1 Hz, 1H), 2.1 (dtd, J = 14.7, 6.0, 4.2 Hz, 1H), 1.99 (br s, 1H), 1.86 (ddt, J = 14.7, 6.3, 6.0 Hz, 1H); ^{13}C NMR δ 137.5, 128.7, 128.4, 125.8, 61.16, 60.0, 58.3, 34.79. Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.12; H, 7.31.

(*R*,*R*)-3-Hexyloxiraneethanol (Table 2, entry 10): colorless oil; $[\alpha]_D^{23} = +39.0°$ (*c* 0.82, $CHCl_3$) (−10 °C); IR (KBr) 3434, 2929, 1468, 1378, 1053, 893, 724 cm^{-1}; ^{1}H NMR δ 3.78 (dd, J = 6.0, 5.7 Hz, 2H), 2.86 (ddd, J = 6.6, 4.2, 2.4 Hz, 1H), 2.79 (td, J = 5.4, 2.4 Hz, 1H), 2.04 (br s, 1H), 1.97 (dddd, J = 14.7, 6.9, 6.0, 4.2 Hz, 1H), 1.69 (dddd, J = 14.7, 6.6, 5.7, 5.4 Hz, 1H), 1.6−1.2 (m, 10H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR δ 60.25, 58.51, 57.08, 34.39, 32.15, 31.93, 29.28, 26.1, 22.74, 14.25. Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.59; H, 11.58.

***trans*-3-(Phenylmethyl)oxiranepropanol (Table 2, entry 11):** colorless oil; $[\alpha]_D^{25} = +23.4°$ (*c* 0.72, $CHCl_3$); $[\alpha]_D^{25} = -22.4°$ (*c* 0.68, $CHCl_3$) (**ent-1**); IR (KBr) 3414, 2939, 1600, 1496, 1454, 1186, 1058, 934, 747, 700 cm^{-1}; ^{1}H NMR δ 7.35−7.15 (m, 5H), 3.62 (t, J = 5.9 Hz, 2H), 2.97−2.75 (m, 4H), 1.87 (br s, 1H), 1.8−1.6 (m, 3H), 1.57−1.45 (m, 1H); ^{13}C NMR δ 137.4, 129.1, 128.7, 126.8, 62.43, 59.16, 58.73, 38.56, 29.18, 28.64. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.60, H, 8.28.

Acknowledgment. We are grateful for the generous financial support from Colorado State University, the General Medical Sciences of the National Institutes of Health (GM55704-01), the Beckman Young Investigator Award Program, the Camille and Henry Dreyfus New Faculty Awards Program, and Hoechst Celanese. We would like to thank Michael Frohn, Jon Lorenz, Yong Tu, and Yuanming Zhu for their helpful discussions.

Supporting Information Available: The NMR spectral, GC and HPLC data for the determination of the enantiomeric excess of the formed epoxides along with the detailed data of the pH and solvent studies (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO972106R