Further spectroscopic and conductivity studies are in progress to elucidate the mechanism of charge transport in these materials.

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Supplementary Material Available: Table of structure factors for 2,3-butanedione dihydrazone (9 pages). Ordering information is given on any current masthead page.

Catalytic Asymmetric Epoxidation and Kinetic Resolution: Modified Procedures Including in Situ Derivatization†

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Abstract: The use of 3A or 4A molecular sieves (zeolites) substantially increases the scope of the titanium(IV)-catalyzed asymmetric epoxidation of primary allylic alcohols. Whereas without molecular sieves epoxidations employing only 5 to 10 mol % Ti(O-*i*-Pr)$_4$ generally lead to low conversion or low enantioselectivity, in the presence of molecular sieves such reactions generally lead to high conversion (>95%) and high enantioselectivity (90–95% ee). The epoxidations of 20 primary allylic alcohols are described. Especially noteworthy are the epoxidations of cinnamyl alcohol, 2-tetradecyl-2-propen-1-ol, allyl alcohol, and crotyl alcohol—compounds which heretofore had been considered difficult substrates for asymmetric epoxidation. In the case of allyl alcohol, the use of cumene hydroperoxide substantially increases both the reaction rate and the conversion, even in the absence of molecular sieves. In general, enantioselectivities are slightly depressed (by 1–5% ee) relative to reactions employing 50–100 mol % Ti(O-*i*-Pr)$_4$. The epoxidation of low molecular weight allylic alcohols is especially facilitated and, in conjunction with in situ derivatization, provides for the synthesis of many epoxy alcohol synthons which were previously difficult to obtain. The kinetic resolution of four secondary allylic alcohols with 10 mol % Ti(O-*i*-Pr)$_4$ is also described. The role of molecular sieves in the reaction and the effects of variation in reaction stoichiometry, oxidant, and tartrate are discussed.

The reaction of an allylic alcohol with *tert*-butyl hydroperoxide (TBHP) in the presence of Ti(O-*i*-Pr)$_4$ and diethyl tartrate (DET) to form an epoxy alcohol of high enantiomeric purity was introduced in 1980 (Scheme I).[1] Since then, much has been learned about this asymmetric epoxidation process. Several reviews have been published,[2] and two theses from these laboratories have dealt with mechanistic aspects of the reaction.[3,4]

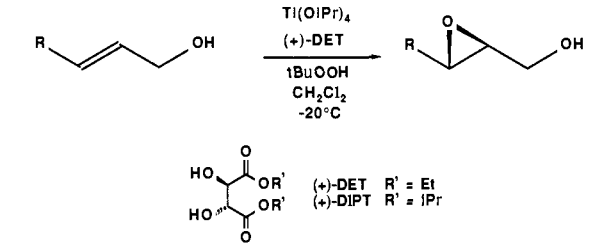
The epoxidation as initially described employs a stoichiometric amount of catalyst, even though, as noted in one of the footnotes to the original report, reactions of certain substrates can be carried out with as little as 10% catalyst with little loss of enantioselectivity and some increase in yield.

In 1981, we reported that, with slight modifications, the same procedure also effects the kinetic resolution of secondary allylic alcohols (Scheme II).[5] Again, it was noted that for certain substrates just 0.25 equiv of catalyst can be effective.

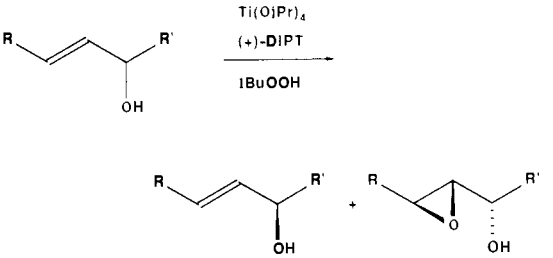
Over the next 4 years, no major modifications to the procedure were introduced. The asymmetric epoxidation reaction has proven to have wide applicability, even with use of a stoichiometric amount of catalyst, and has been the subject of an *Organic Syntheses* preparation.[6]

We recently reported a simple modification of the original procedure which allows the asymmetric epoxidation to be carried out with just 5–10% catalyst.[7] The key feature of the catalytic modification is the use of molecular sieves (zeolites). We now report in full our studies relating to this new procedure. The modifications presented here significantly expand the scope, effectiveness, convenience, and economy of the reaction. In the first part of this report, we present results relating to the synthesis of epoxy alcohols and their in situ derivatization, as well as kinetic resolutions involving catalytic amounts of the titanium–tartrate complex. In the second part we discuss factors which influence the reaction.

Scheme I



Scheme II

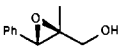
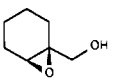
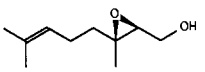
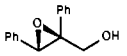
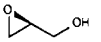
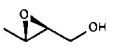


† Dedicated to Professor George Büchi on the occasion of his 65th birthday.

(1) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.
(2) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, Chapter 8, 247. Rossiter, B. E. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, Chapter 7, 193. Pfenninger, A. *Synthesis* **1986**, 89–116. The last of these reviews (Pfenninger) is somewhat out of date even for the stoichiometric reaction, especially with respect to the best experimental procedures and catalyst structure; the *Asymmetric Synthesis* reviews are more current.

0002-7863/87/1509-5765$01.50/0

Table I. Catalytic Asymmetric Epoxidations[a]

entry	product	compd no.	sieves	catalyst % Ti/% tart	tartrate	temp, °C	time, h	yield, %	ee,[f] %
	Trans Disubstituted								
1	R = C_3H_7	**1**	4A	5/6.0	(+)-DET	−20	2.5	85	94
2	R = C_7H_{15}	**2**	4A	5/7.3	(+)-DET	−23	2.5	(99)	96
3	R = C_8H_{17}	**3**	4A	5/6.0	(+)-DET	−10	1.5	78	94
4	R = phenyl	**4**	4A	5/7.5	(+)-DIPT	−20	3	89	>98[g,h]
5	R = *p*-nitrophenyl	**5**	4A	5/7.5	(+)-DIPT	−20	2	82	>98[h]
6	R = *p*-bromophenyl	**6**	4A	5/7.5	(+)-DIPT	−20	0.75	69	>98[h]
	Cis Disubstituted								
7	R = C_7H_{15}	**7**	4A	10/14	(+)-DET	−10	29	74	86
8	R = C_8H_{17}	**8**	3A	5/7.4	(+)-DIPT	−12	42	63	>80[i]
9	R = $PhCH_2OCH_2$	**9**	4A	10/14	(+)-DET	−20	43	*c*	85[j]
	Unsym-Disubstituted								
10	R = C_3H_7	**10**	3A	4.7/5.9	(+)-DET	−12	11	88	95
11	R = $C_{14}H_{29}$	**11**	3A	10/13	(+)-DET	−12	11	91	96
	Trisubstituted								
12		**12**	4A	5/7.5	(+)-DIPT	−35	2	79	>98[h]
13		**13**	4A	5/7.3	(+)-DET	−40	3	77	93
14		**14**	4A	5/7.4	(+)-DET	−20	0.75	95	91
15		**15**	3A	5/7.4	(+)-DET	−20	1.5	*d*	91
	Low Molecular Weight								
16		**16**	3A[b]	5/6.0	(+)-DIPT	0	5	65[e]	90
17		**17**	3A	5/6.0	(+)-DIPT	−20	2	70	91

[a] All reactions were carried out with TBHP except for entry 16, which employed cumene hydroperoxide (CHP). Yields reported are isolated yields except entry 2, which is for the crude product. [b] 4A molecular sieves are less effective in this reaction only. [c] The yield was not determined since, after 43 h, the reaction was far from complete. However, see ref 9. [d] This reaction was run solely for the determination of enantiomeric excess. Thus, the reaction was not worked up and no yield was obtained. [e] As a mixture containing glycidol, cumene, and small amounts of cumyl alcohol after distillation. GC and in situ trapping both indicate high conversion to glycidol (>95%). [Ko, S. Y.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 5413]. Use of TBHP leads to incomplete reaction. [f] All %ee's are reported for the crude material, unless otherwise noted. Enantioselectivity was determined by ^{1}H NMR analysis of the derived MTPA ester, except for entries 7, 8, 9, and 14, which were determined by ^{1}H NMR shift analysis of the derived acetates with Eu(hfc)$_3$ in benzene-d_6, entry 15, which was determined by HPLC on a chiral stationary phase, and entry 16, which was determined by opening by thiophenol [Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557 and see Experimental Section] followed by ^{1}H NMR shift study of the derived diacetate. [g] >98% indicates that the other enantiomer was not detectable by NMR. [h] %ee reported for recrystallized material. [i] A more accurate analysis of ee was not possible from the ^{1}H NMR spectrum because of poorly resolved peaks. [j] For an improved procedure, see ref 9.

Results

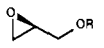
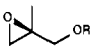
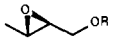
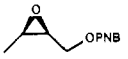
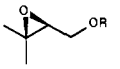
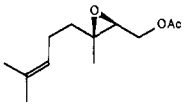
Epoxidation Involving Epoxy Alcohol Isolation. Our results for catalytic asymmetric epoxidations carried out in the presence of molecular sieves are summarized in Table I. In general, selectivity is somewhat lower than in the stoichiometric case, 1–3% more of the minor enantiomer being obtained. Fortunately, 2,3-epoxy alcohols, when crystalline, generally undergo dramatic ee improvement upon recrystallization—a felicitous circumstance!

Typical trans-disubstituted allylic alcohols (entries 1–6) can be epoxidized at −15 to −20 °C in at least 94% enantiomeric excess (ee) with just 5% Ti(O-*i*-Pr)$_4$ and 6–7.5% tartrate. The reactions are quite rapid, generally complete in 1–4 h. As in the stoichiometric procedure, cis-disubstituted allylic alcohols (entries 7–9) require longer reaction times (1–2 days). It was found that such slowly reacting substrates require more catalyst (10/12%)[8] and usually slightly higher reaction temperatures than in the case of the *trans*-allylic alcohols, in order to achieve complete reaction with minimal loss of selectivity. The monobenzyl ether of (*Z*)-2-buten-1,4-diol (entry 9) was not successfully epoxidized using the procedure described here, since after 43 h, the reaction was still far from complete. Other workers, however, have accomplished this epoxidation catalytically.[9]

(3) Finn, M. G. Ph.D. Dissertation, Massachusetts Institute of Technology, Cambridge, MA, 1985.
(4) Woodard, S. S. Ph.D. Dissertation, Stanford University, Stanford, CA, 1981.
(5) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.
(6) Hill, J. G.; Sharpless, K. B.; Exon, C. M.; Regenye, R. *Org. Synth.* **1984**, *63*, 66.
(7) Hanson, R. M.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 1922.

(8) In this report, we will use the following nomenclature to describe the catalyst system used in the reaction: *x*/*y*% catalyst refers to *x* mol % Ti(O-*i*-Pr)$_4$ and *y* mol % tartrate ester. This differs from our earlier, less specific method of description, in which "stoichiometric" implied 100% Ti(O-*i*-Pr)$_4$ and 120% tartrate ester, which we assumed to be 80% active catalyst. "Stoichiometric" is used here in reference to reactions with at least 50 mol % Ti(O-*i*-Pr)$_4$.

Table II. In Situ Derivatization of Epoxy Alcohols[a]

entry	product	compd no.	mp, °C	yield, %	$[\alpha]^{25}_D$	ee,[b] %
						
1	R = PNB	**18**	59.5–60	61	−38.7[c]	90 (92–94)
2	R = Ts	**19**	46–48.5	40	+17.5[d]	(94)
3	R = TBDPS	**20**	oil	45	−2.28	91
						
4	R = PNB	**21**	85.5–86.5	78	−5.9	92 (>98)[e]
5	R = Ts	**22**	oil	69	+4.8[d]	95
6	R = Nps	**23**	46–48	60	+5.9[d]	(92)
						
7	R = PNB	**24**	103.5–104	65	−48.5	90–92 (>98)
8	R = Ts	**25**	61.5–62	70	+34.2[d]	(>98)
9	R = TBDMS	**26**	oil	68	+13.1[d]	92
10		**27**	69–72.5	68	−28.4	(92)
						
11	R = PNB	**28**	109.5–110	70	−36.1	(>98)
12	R = Ts	**29**	oil	55	+20.1[d]	93
13	R = Nps	**30**	64.5–65	40	+22.4[d]	*f*
14		**31**	oil	98	−26.9	86

[a] Yields reported are isolated yields. For those compounds which are not oils, the melting points and rotations are reported for the recrystallized material. PNB = *p*-nitrobenzoyl, Ts = *p*-toluenesulfonyl, TBDPS = *tert*-butyldiphenylsilyl, Nps = 2-naphthalenesulfonyl, TBDMS = *tert*-butyldimethylsilyl. [b] Enantiomeric excesses in parentheses are after recrystallization. [c] $[\alpha]^{20}_D$. [d] (−)-DIPT was used in this reaction. Configuration is opposite to that depicted. [e] >98% indicates that the other enantiomer was not detectable by NMR. [f] Unable to determine.

When the reactions are carried out at −10 to −15 °C, the rather slowly reacting unsym-disubstituted allylic alcohols (entries 10 and 11) are among the best substrates, both in yield and selectivity. In contrast, use of a stoichiometric amount of catalyst leads to substantial epoxide opening both during the reaction[10] and especially when the reaction is quenched by the addition of water.[11] Epoxide opening was not observed for unsym-disubstituted allylic alcohols with use of the catalytic procedure, even in the case of 2-tetradecyl-2-propenol (entry 11), where solubility considerations mandate use of 10 mol % Ti(O-*i*-Pr)$_4$ (discussed under Concentration in the Discussion section).

Trisubstituted allylic alcohols (entries 12–15) tend to react very rapidly under these catalytic conditions. In many cases, as little as 1.1 equiv of TBHP can be used. However, compared to the stoichiometric reactions, somewhat diminished selectivities (i.e., 91–93% ee) appear to be the rule here. For example, α-phenylcinnamyl alcohol (entry 15) affords a product of 91% ee,[12] whereas under stoichiometric conditions it has always been one of our best substrates (ee >98%).

When very specific optimized conditions are used (3A molecular sieves, DIPT, cumene hydroperoxide, and reaction at 0 °C), high conversion of allyl alcohol to glycidol (entry 16) can be achieved with just 5% Ti(O-*i*-Pr)$_4$. This finding is especially significant in that use of a stoichiometric amount of Ti(O-*i*-Pr)$_4$ generally leads to decomposition of glycidol.[1] Such decomposition not only results in much lower chemical yields but also decreases the enantiomeric purity of the product.[13]

Low molecular weight allylic alcohols (entries 16 and 17) in general pose special problems with respect to product isolation and/or stability. The usual aqueous workup leads to substantial loss of the water-soluble product.[1,14,15] Alternative isolation procedures, including treatment with dimethyl sulfide and sodium fluoride,[16] triphenylphosphine,[17] sodium borohydride,[18] and anhydrous hydroxy carboxylic acids,[11,19] have been employed in the past, and use of a catalytic amount of Ti(O-*i*-Pr)$_4$ should simplify all of these methods. The isolation procedures for the two low molecular weight epoxy alcohols described here (entries 16 and 17) employ anhydrous citric acid to remove titanium. In the case of glycidol (entry 16), this quench was followed by distillation. In the epoxidation of crotyl alcohol (entry 17), it was found that the product after direct distillation was still substantially contaminated with TBHP. Hence, the excess hydroperoxide was reduced with tributylphosphine prior to distillation. This is still not an ideal workup, since the distillation is complicated by the highly viscous nature of the pot residue. In addition, polymerization of any epoxy alcohol can occur during distillation, especially if the workup has involved acid treatment. In some cases, such polymerizations can be quite exothermic, especially on a large scale.[20]

(9) D. Burdick and J. W. Scott at Hoffmann-La Roche Inc. have informed us that the asymmetric epoxidation of the monobenzyl ether of (*Z*)-2-buten-1,4-diol proceeds well under different conditions. With use of ca. 14% catalyst, epoxidation at 0 °C for 2 days gives a high yield of product of ≥95% ee. Details of this work will be reported in due course by the Hoffmann-La Roche group.

(10) Lu, L. D.-L.; Johnson, R. A.; Finn, M. G.; Sharpless, K. B. *J. Org. Chem.* **1984**, *49*, 728.

(11) Use of an anhydrous citric acid workup dramatically increases the yield of **11** in the stoichiometric Ti(O-*i*-Pr)$_4$ reaction, but it does not alleviate the problem of epoxide opening prior to workup. Hollinshead, D. M.; Sharpless, K. B., unpublished results.

(12) Product of 95% ee was obtained with (+)-dicyclododecyl tartrate and TBHP in isooctane (5/7.5% catalyst).

(13) The decomposition of epoxy alcohols by the chiral catalyst is moderately enantioselective, the major enantiomer decomposing faster than the minor. Ko, S. Y.; Sharpless, K. B., unpublished results.

(14) Dung, J. S.; Armstrong, R. W.; Anderson, O. P.; Williams, R. M. *J. Org. Chem.* **1983**, *48*, 3592.

(15) Harris, R. N.; Sundararaman, P.; Djerassi, C. *J. Am. Chem. Soc.* **1983**, *105*, 2408.

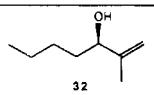
(16) Rossiter, B. E.; Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 464.

(17) Meister, C.; Scharf, H. D. *Liebigs Ann. Chem.* **1983**, 913.

(18) (a) Bessodes, M.; Abushanab, E.; Antonakis, K. *Tetrahedron Lett.* **1984**, *25*, 5899. (b) Masamune, H.; Sharpless, K. B., unpublished results.

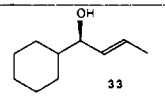
(19) Tuddenham, D.; Sharpless, K. B., unpublished results.

Table III. Kinetic Resolution with Various Tartrates[a]



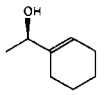
32

tartrate	yield, %	conversion, %	ee, %
(+)-DIPT	93	53	94
(+)-DCHT	92	52	97
(+)-DCDT	89	53	>98



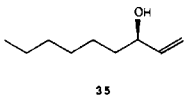
33

tartrate	yield, %	conversion, %	ee, %
(+)-DIPT	96	54	94
(+)-DCHT	92	52	95
(+)-DCDT	82	52	>98



34

tartrate	yield, %	conversion, %	ee, %
(+)-DIPT	93	63	>98
(+)-DCHT	86	63	>98
(+)-DCDT	85	66	>98



35

tartrate	yield, %	conversion, %	ee, %
(+)-DIPT	92	51	86
(+)-DCHT	91	55	>98
(+)-DCHT	80[b]	65	95
(+)-DCDT	99[c]	66	>98

[a] All reactions were carried out at −20 °C with 10% Ti(O-*i*-Pr)$_4$, 15% (+)-tartrate ester, and 0.7 equiv of TBHP/isooctane in the presence of 3A molecular sieves, except as noted. All recovered allylic alcohols had the depicted (*R*) stereochemistry. Yields are isolated yields based on percent conversion. >98% ee indicates that the other enantiomer was not detectable by NMR. [b] Employed 1.5 equiv of TBHP. [c] Trace contamination by DCDT; yield calculated from ^{1}H NMR data.

These low molecular weight epoxy alcohols are highly desirable as chiral building blocks in a wide variety of asymmetric syntheses.[14,15,21] However, the special problems associated with such compounds, namely water solubility and in certain cases a propensity for decomposition, have discouraged their widespread synthetic use. It was these problems that led us to consider an alternative to their direct isolation: in situ derivatization.

Epoxidation Involving in Situ Derivatization. One of the greatest advantages of carrying out the asymmetric epoxidation with only a catalytic amount of Ti(O-*i*-Pr)$_4$ and tartrate ester is the potential for in situ transformations of the crude epoxy alcohol product. We had used such procedures in stoichiometric reactions, for the analytical determination of enantiomeric excess, by directly quenching an aliquot of the reaction mixture into a solution containing Et_3N, 4-(dimethylamino)pyridine (DMAP), and α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPA–Cl, Mosher chloride). However, the amount of isopropyl alcohol and chelated tartrate diester present in the stoichiometric case renders in situ esterification impractical for the preparative isolation of product.

Under catalytic conditions, on the other hand, these complications are alleviated, and preparative in situ derivatization becomes feasible. Our results are summarized in Table II. The preparation of derivatives of these low molecular weight, water-soluble epoxy alcohols is particularly significant. Not only do these derivatives possess advantages over their parent compounds in terms of ease of isolation and stability (vide supra) but they also promise to exhibit widespread synthetic utility as chiral building blocks.[22,23,25,26]

Especially noteworthy is the high crystallinity of the *p*-nitrobenzoate (PNB) ester derivatives, which simplifies product isolation and allows the ready enhancement of enantiomeric excess through recrystallization. For example, the crotyl and prenyl derivatives may be recrystallized to 100% ee. Furthermore, in many epoxide opening reactions these esters are functionally equivalent to the parent compounds, the ester group being removable in situ. Ring opening reactions can also be executed without hydrolyzing the PNB ester group, thus providing mono-protected 1,2-diols. Such reactions illustrate the broad applicability of these PNB esters in organic synthesis.[23]

In situ sulfonylation has also been successful, although several complications have been encountered in the synthesis of glycidyl sulfonates which demand comment here. Thus, while trimethyl phosphite continues to be the recommended reagent for the reduction of excess hydroperoxide, primarily because of its rapid and complete reaction at low temperature and to the volatility of both trimethyl phosphite and trimethyl phosphate, it has since been discovered that excess trimethyl phosphite present during the sulfonylation step results in the formation of the corresponding epoxy *sulfinate* as a serious side reaction.[24a] Therefore, we now recommend that the reduction be monitored very closely, using only the amount of phosphite necessary for complete reduction of the hydroperoxide. The addition of a catalytic amount of DMAP also appears to be beneficial in alleviating the problem of sulfinate production. Also isolated as a byproduct from this reaction has been the chlorohydrin resulting from epoxide opening by chloride ion. This is generally not a significant problem if the reaction mixture is kept cold, but it becomes quite serious if the reaction mixture is allowed to stand at room temperature for a long period of time.

The epoxy sulfonates possess multiple sites of potential electrophilic reactivity. Fortunately, in many cases reaction conditions can be chosen so as to selectively favor attack at only one site. For example, aryloxide nucleophiles react with glycidyl tosylate in DMF with high (97:3 to 99:1) selectivity for direct tosylate displacement. This reaction formed the basis of a recent synthesis

(20) In one instance, distillation of prenyl epoxy alcohol led to violent polymerization. In situ derivatization avoids this problem.

(21) (a) For uses of glycidol, see: Baldwin, J. J.; McClure, D. E.; Gross, D. M.; Williams, M. *J. Med. Chem.* **1982**, *25*, 931. Nakano, J.; Mimura, M.; Hayashida, M.; Kimura, K.; Nakanishi, T. *Heterocycles* **1983**, *20*, 1975. Haouet, A.; Sepulchre, M.; Spassky, N. *Eur. Polym. J.* **1983**, *19*, 1089. (b) For uses of crotyl epoxy alcohol, see: Kobayashi, Y.; Kitano, Y.; Sato, F. *J. Chem. Soc., Chem. Commun.* **1984**, 1329. Yamada, S.; Shiraishi, M.; Ohmuri, M.; Takayama, H. *Tetrahedron Lett.* **1984**, *25*, 3347. Corey, E. J.; Trybulski, E. J.; Melvin, L. S.; Nicolaou, K. C.; Secrist, J. A.; Lett, R.; Sheldrake, P. W.; Falck, J. R.; Brunelle, D. J.; Haslanger, M. F.; Kim, S.; Yoo, S. *J. Am. Chem. Soc.* **1978**, *100*, 4618.' Helbig, W. *Liebigs Ann. Chem.* **1984**, 1165. Kuroda, C.; Theramongkol, P.; Engebrecht, J. R.; White, J. D. *J. Org. Chem.* **1985**, *51*, 956. (c) For uses of prenyl epoxy alcohol, see: Dumont, R.; Pfander, H. *Helv. Chim. Acta* **1983**, *66*, 814.

(22) For uses of glycidol derivatives, see: Hardy, J. C.; Villatte, G.; Gueremy, C. *Bull. Soc. Chim. Fr. (Pt. 2)* **1982**, 304. McClure, D. E.; Arison, B. H.; Baldwin, J. J. *J. Am. Chem. Soc.* **1979**, *101*, 3666. Bouzoubaa, M.; Leclerc, G.; Rakhit, S.; Andermann, G. *J. Med. Chem.* **1985**, *28*, 896.

(23) Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Org. Chem.* **1987**, *52*, 667.

(24) (a) Klunder, J. M.; Sharpless, K. B. *J. Org. Chem.* **1987**, *52*, 2598. (b) Klunder, J. M.; Sharpless, K. B., unpublished results.

(25) Klunder, J. M.; Ko, S. Y.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 3710.

(26) Yamada, S.; Shiraishi, M.; Ohmori, M.; Takayama, H. *Tetrahedron Lett.* **1984**, *25*, 3347. Williams, David R. (Indiana University), private communication.

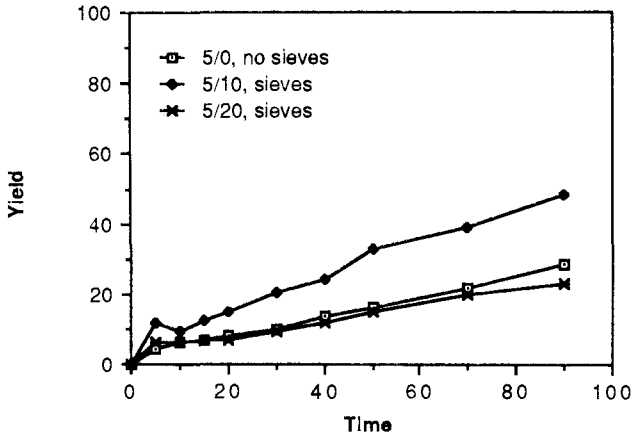


Figure 1. Effect of catalyst stoichiometry. Time (min) vs. mole fraction of epoxy alcohol as determined by GC. (*E*)-2-Hexen-1-ol, (+)-DET/TBHP/4A sieves/−30 °C. Depicted ratio is mol % Ti(O-*i*-Pr)$_4$/mol % tartrate. The 5/0 line (5% Ti(O-*i*-Pr)$_4$ with no tartrate and no molecular sieves) provides a common reference with Figure 2.

of the β-adrenergic blocking agent propranolol reported from these laboratories.[25] On the other hand, carbon nucleophiles, such as Grignard reagents under copper catalysis, lead with high selectivity to epoxide ring opening.[24b] In both types of reactions, the products still retain a reactive electrophilic center, making the epoxy sulfonates quite powerful synthetic intermediates.

Protection of the alcohol functionality after epoxidation has been important in several natural product syntheses.[26] Toward this end, in situ techniques can greatly increase the yield of silyl ether and carboxylic ester derivatives, as exemplified in Table II, entries 3, 9, and 14.

Kinetic Resolution. As mentioned in the introduction, we originally recommended use of a stoichiometric amount of catalyst for the kinetic resolution of secondary allylic alcohols.[5] However, even prior to this current study, kinetic resolutions had been carried out successfully with as little as 13–25% catalyst.[5,27] We chose for our investigation the four secondary allylic alcohols depicted in Table III. Three different tartrate esters, diisopropyl (DIPT), dicyclohexyl (DCHT), and dicyclododecyl tartrate (DCDT), were investigated.

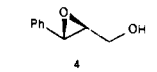
The desired conversion (51–66%) was accomplished in 3.5–29 h, except in the case of allylic alcohol **35**, which required 6–12 days. With DIPT, in the cases of **32–34** the selectivity is slightly (0–4%) lower than that found in the stoichiometric reaction. For **35**, the selectivity drops about 12%. Both DCHT and DCDT lead to higher selectivity than DIPT in these catalytic applications. Use of 1.5 equiv of TBHP and (+)-DCHT (footnote *b*) in the case of the very slowly reacting substrate **35** led to a substantially faster reaction (2.5 days), with only a slight decrease in selectivity. However, use of even more TBHP did not further increase the rate of the reaction.

Discussion

Stoichiometry. We had previously noted the importance of using at least 10% excess of tartrate ester over Ti(O-*i*-Pr)$_4$ in all asymmetric epoxidations,[5] and this recommendation holds in the catalytic mode as well: too little (<10% excess) tartrate will result in a lowering of selectivity; too much (≥100% excess) tartrate will slow the reaction unnecessarily (Figure 1).

Cinnamyl alcohol was chosen as the substrate for a study of catalyst/substrate ratios, because of the known sensitivity of the product epoxy alcohol (**4**) to the opening processes which can lead to catalyst inactivation.[2] (The titanium:tartrate ratio was held approximately constant at 1:1.2.) Previous studies in this laboratory[19] indicated that without sieves the reaction of cinnamyl alcohol proceeds to only 50% completion with the 6/7.5% catalyst. (Part of the improvement for cinnamyl alcohol in the current study is due to the use of freshly distilled cinnamyl alcohol.) As can be seen in Table IV, below the 5% level, selectivity and reaction rate drop off rapidly, even in the presence of molecular sieves and carefully purified solvent, substrate, and reagents. Thus, 5 mol % was concluded to be the minimal catalyst/substrate ratio feasible for most substrates, since measurable loss of selectivity generally occurred below this ratio.

Table IV. Dependence of Selectivity on Catalyst Stoichiometry[a]



4

product	Ti(O-*i*-Pr)$_4$, %	(+)-DIPT, %	ee, %
4	5.0	6.0	92
4	4.0	5.2	87
4	2.0	2.5	69[b]

[a] Reactions were carried out at −20 °C in the presence of 3A or 4A molecular sieves. [b] Reaction only partially complete after several hours.

It has been empirically noted that both the titanium/tartrate ratio and the temperature also have an effect on selectivity. Hence, further work is being performed in our and other[28] laboratories to determine the optimal ratio and temperature window for specific cases. The most commonly used stoichiometry is 5/6% since this works well in most cases. If the highest possible percent ee is the primary goal, then 10/12% is suggested.

Concentration. In the stoichiometric reaction, substrate concentrations must be kept low (ca. 0.1 M) in order to minimize side reactions (primarily epoxide opening) arising from the large amount of titanium–tartrate species and isopropyl alcohol in solution. However, by using a catalytic amount of the titanium–tartrate complex, the upper concentration limit can be increased to 1.0 M, although for initial studies on a substrate we recommend concentrations in the range of 0.3–0.5 M. Even with the catalytic procedure, in situ epoxide opening can become a serious problem above 0.2 M with sensitive substrates such as cinnamyl alcohol, and for these cases, we recommend concentrations near 0.1 M. On some occasions, inherent solubility in dichloromethane will determine the choice of concentration and reaction temperature. In many cases, marginally soluble substrates will be completely dissolved upon addition of Ti(O-*i*-Pr)$_4$, since titanium alkoxides have been observed to enhance the solubility of many alcohols. For some very insoluble substrates, it may therefore be necessary to employ somewhat higher catalyst/substrate ratios.

Preparation and Aging of the Catalyst. Proper preparation of the catalyst is essential for optimal rates and selectivity, although some variation in the procedure, as noted below, is tolerated by the reaction. We have never been successful with premixed stock solutions of the titanium–tartrate catalyst. The complex is not stable at room temperature, especially in the presence of molecular sieves, and optimal results are obtained only when the reagents are mixed at temperatures at or below 0 °C just prior to epoxidation.

In general, the catalyst is prepared by mixing the tartrate and Ti(O-*i*-Pr)$_4$ at −20 °C,[29] whereupon *either* TBHP *or* the allylic alcohol is added. The three components are stirred together at this temperature for 20 to 30 min prior to the addition of the fourth component. This "aging" period is critical to the success of the reaction and must not be eliminated. For example, by optimizing the aging process, chemists at Hoffmann La Roche have epoxidized (*E*)-2-hexen-1-ol with very high enantioselectivity (≥96% ee),[28] whereas in the absence of proper aging a product of only 52% ee was obtained. After the aging period the temperature is

(27) Roush, W. R.; Brown, R. J. *J. Org. Chem.* **1983**, *48*, 5093. The kinetic resolution of 2-methylenecyclohexanol is effective using 15 mol % catalyst in the presence of molecular sieves (R. C. Ronald, private communication).

(28) Burdick, D.; Scott, J. W., unpublished results.

(29) The order of addition of the first two components is unimportant.

adjusted to the appropriate level, depending on the substrate: (1) trans- and unsym-disubstituted allylic alcohols, −20 to 0 °C; (2) cis-disubstituted, −10 to 0 °C; and (3) tri- and tetrasubstituted, −40 to −20 °C.

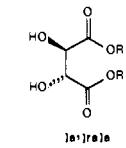
Following the aging period, the last reagent to be added may be either the allylic alcohol or the hydroperoxide. The major difference between these two methods is that in the latter case more care must be exercised in maintaining the internal temperature at the desired level, since heat is evolved more rapidly when TBHP is added last. In addition, if transesterification is a problem, then it is preferable to add the allylic alcohol last. Transesterification can be detected if the allylic alcohol appears to be completely consumed in the epoxidation step, but then reappears after the basic brine hydrolysis of the tartrate ester. If the temperature is maintained properly and transesterification is not a problem, there is no discernible difference between the two modes of addition. An advantage of adding the TBHP last, particularly on a very large scale, is that in the event of an uncontrollable exotherm during addition (albeit never yet experienced), the bulk of the oxidant would be in a separate vessel, away from the reaction mixture.

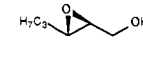
Variation of Oxidant and Oxidation Solvent. On the basis of the hypothesis that adventitious water was being introduced into the reaction primarily from the TBHP/CH_2Cl_2 solution (which must be stored refrigerated), we investigated the use of other hydroperoxides and the use of other solvents for TBHP. In one experiment involving a 5/7.5% DIPT catalyst, a freshly prepared solution of TBHP in isooctane, and carefully dried reagents, very little difference was noted in the reaction of a fast reacting substrate (geraniol) with or without sieves. Both reactions were complete within 60 min, the one with molecular sieves resulting in marginally higher selectivity (93% ee vs. 90% ee).

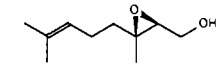
Although we have at times used solutions of TBHP in dichloroethane, dichloromethane, toluene, heptane, and isooctane, all solvents have certain disadvantages. Dichloroethane should not be used, and dichloromethane solutions must be stored refrigerated. Toluene solutions have on occasion been observed to develop a contaminant which inhibits the catalytic reaction. Except for isooctane solutions, solutions of TBHP stored at room temperature in *high density* polyethylene bottles (which are preferable to glass due to the slight chance of pressurization) are not titre-stable *due to migration of solvent through the walls of the bottle*. One will note that most of the experiments utilize TBHP in dichloromethane. This is because these procedures were performed before the efficacy of TBHP in isooctane was realized. We are now recommending TBHP in isooctane as the solvent of choice for most cases, with dichloromethane or toluene as the next choice. It should be noted that in some instances reactions utilizing TBHP in isooctane with higher substrate concentrations result in a lowering of the rate and/or % ee since too high a ratio of isooctane to dichloromethane (reaction solvent) substantially changes the solvent polarity. We generally use 0.25–0.5 M substrate concentrations for standard substrates. Solutions of TBHP in isooctane are normally stored at room temperature or at ca. 5 °C and solutions of TBHP in dichloromethane are stored at ca. 5 °C. Solutions of TBHP stored at room temperature should *not* be stored over molecular sieves, although brief treatment of the amount to be used with fresh sieves just prior to addition is recommended. One solution of TBHP in isooctane was stored at room temperature for 3 months *without sieves*, with no detectable change in titre or effectiveness. The use of 2.0 equiv of TBHP is generally suitable. Use of 3.0 equiv may be desirable for slow substrates (unsym-disubstituted and cis-disubstituted substrates), and as little as 0.6 equiv is used in kinetic resolutions.

As previously noted, the reaction of allyl alcohol to form glycidol is best accomplished with cumyl hydroperoxide (commercially available as an 80% solution in cumene). This reagent has the advantage that no azeotropic drying is necessary, the commercial solution requiring only storage overnight over molecular sieves prior to use. We have used cumyl hydroperoxide in other epoxidations and find that it leads to slightly faster reactions than TBHP. In general, however, TBHP is recommended, since product isolation is significantly easier.

Table V. Selectivity Dependence upon Tartrate Variation[a]







dialkyl tartrate	% ee of epoxy alcohol product 1	3	14
R = Et	95	94	93[b]
R = *i*-Pr	93	92	
R = $CH(CHMe_2)_2$	41[c]		41[c]

[a] Reactions were carried out at −20 °C, using a 5/6% catalyst system except as noted. All systems employed the (+)-tartrate and gave products of 2*S-trans* configuration. Reactions were carried out in the presence of 4A molecular sieves. [b] 5/7.5% catalyst system. [c] Incomplete reaction.

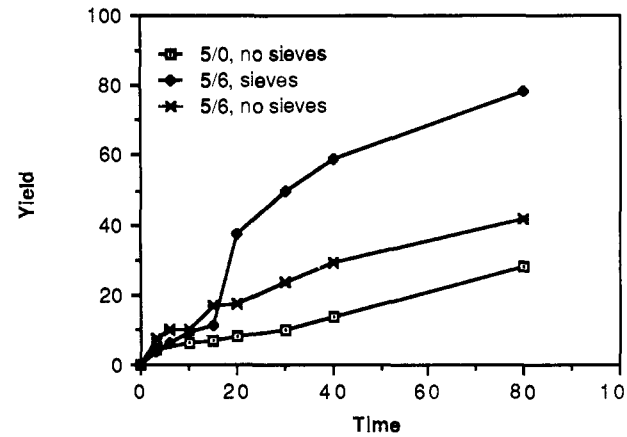


Figure 2. Comparison of reactions with and without molecular sieves. Time (min) vs. mole fraction of epoxy alcohol as determined by GC. (*E*)-2-Hexen-1-ol, (+)-DET/TBHP/4A sieves/−20 °C. Depicted ratio is mol % Ti(O-*i*-Pr)$_4$/mol % tartrate. The 5/0 line (5% Ti(O-*i*-Pr)$_4$ with no tartrate and no molecular sieves) provides a common reference with Figure 1.

Variation of Tartrate. The effect of variation of the tartrate ester upon selectivity was also examined (Table V). In general, no significant difference was observed between diethyl and diisopropyl tartrates (DET and DIPT). With simple unbranched trans-disubstituted allylic alcohols (i.e., **1**–**3**), there appears to be a slight improvement in enantioselectivity with DET. In the case of allyl alcohol, DET gave somewhat lower conversion than DIPT, but selectivity was not significantly different. Dimethyl and di-*tert*-butyl tartrates were not examined here, although dimethyl tartrate has been used successfully elsewhere for the catalytic reaction and does offer the advantage of water solubility. Use of the very bulky bis(2,4-dimethyl-3-pentyl) tartrate[31] resulted in slow reactions and very low selectivity. The variation of the tartrate ester is often a useful parameter to examine when seeking optimal conditions for a specific reaction.

The Role of Molecular Sieves. The effect of molecular sieves can be quite dramatic. Figure 2 illustrates the comparison of reactions of (*E*)-2-hexen-1-ol with use of a 5/6% Ti/DET catalyst

(30) For the case of glycidol, the catalyst is aged at 0 °C. See Experimental Section, compound **16**.

(31) Ikeda, N.; Arai, I.; Yamamoto, H. *J. Am. Chem. Soc.* **1986**, *108*, 483.

with and without molecular sieves. In this case, the reaction was roughly twice as fast with sieves as without. The catalytic reactions with tartrate, with or without sieves, were both significantly faster than the control reaction involving no tartrate and no sieves (the bottom curve in Figure 2).[32]

Several experiments were designed to determine the effect of water and the role of sieves in the catalytic reaction. In one experiment, 10 mol % water was added to a solution of the 10/12% catalyst in dichloromethane at 2 °C. After being stirred for 30 min, the homogeneous solution was cooled to −10 °C and treated with TBHP and (*E*)-2-undecen-1-ol. After 20 h the reaction was only 30% complete. Product of 4% ee was obtained, indicating that just 1 equiv of water is enough to destroy the catalyst *in the absence of molecular sieves.* In an otherwise identical experiment, powdered 4A molecular sieves were added just prior to the addition of TBHP. Although slow, the reaction proceeded to greater than 90% completion after 20 h. Material of 88% ee was obtained. These results indicate that water does react with the titanium complex, but not initially in an irreversible manner. The fact that catalysis is to a great extent, although not completely, revived after addition of molecular sieves suggests both that (a) the interaction of water with the catalyst is initially reversible, molecular sieves being capable of shifting this equilibrium toward the water-free state, and (b) the reaction of water with the catalyst is eventually irreversible, molecular sieves not being capable of fully regenerating the active system. Thus, we propose that the main function of molecular sieves in these reactions is the protection of the catalyst from adventitious water in the reaction medium.

The hypothesis that molecular sieves protect the catalyst from water is also supported by the finding that 3A, 4A, and 5A molecular sieves are equally effective in the reaction (except as noted below for allyl alcohol). If such is the case, then it should be possible by careful technique to avoid exposure of the catalyst to water and thus avoid the use of molecular sieves altogether. Nevertheless, in all cases studied thus far, catalytic reactions with sieves have given higher conversions and/or higher selectivities than the same reactions carried out without molecular sieves.[33] We suspect that side reactions (such as oxidation to the aldehyde or slow titanium-catalyzed decomposition of the hydroperoxide) may generate small amounts of water *during* the reaction and that molecular sieves protect the catalyst at this stage as well.

Summary

It should be noted that we use at least a 20% excess of tartrate ester in generating the titanium–tartrate catalyst. Even with the original stoichiometric procedure it is important to use at least 10% excess tartrate for optimum results. Unfortunately, many people still follow the procedure in the original publication which called for no excess tartrate (i.e., $Ti(OiPr)_4$: tartrate ester 1:1).[1] We believe that the propagation of this less-than-optimum original recipe is responsible for many of the "substandard" asymmetric epoxidation results encountered in the literature. The failure to use excess tartrate is especially damaging to the enantiomeric excess in the case of hindered allylic alcohols. Therefore, *one should never use less than 10% excess tartrate and 20% excess is safer.* For most cases, 5% $Ti(O\text{-}i\text{-}Pr)_4$ and 6% tartrate are suitable, although a catalyst ratio of 10/12% may be necessary in cases where solubility problems arise.

In general, this new catalytic procedure for asymmetric epoxidation has several key advantages over the original stoichiometric version of the process: (1) economy due to savings on catalyst components; (2) higher yields due to less decomposition of sensitive epoxy alcohol products (e.g., **4** and **11**); (3) greatly simplified isolation procedures; (4) higher substrate concentrations; and (5) in situ derivatization.

With these improvements, the experimental simplicity of the asymmetric epoxidation now rivals that of any other epoxidation, enantioselective or otherwise. In addition, for the first time, in situ transformations are easily accomplished, making possible the synthesis of many epoxy alcohol derivatives. This is especially important for low molecular weight epoxy alcohols, since such epoxy alcohols had previously been difficult to obtain, due to the problems of decomposition and/or water solubility encountered during attempted isolation.

There are two circumstances where additional catalyst may be required. If one desires the highest possible enantiomeric purity and the crude product is not amenable to further enrichment (e.g., by recrystallization), then use of more catalyst (up to 50%) should be considered. The enantiomeric excess can be increased by a few percent (generally 1–5%) in this way. In the case of unreactive substrates, more catalyst and/or higher temperatures (up to 0 °C) may also be necessary to drive the reaction to completion.[9] In general, however, use of the minimal amount of catalyst possible for a given substrate is recommended, as use of more catalyst generally complicates the workup and lowers the yield of the epoxidation.

Experimental Section

Materials. Activation of powdered or pellet 3A molecular sieves involved heating in a vacuum oven at 160 °C and 0.05 mmHg pressure for at least 3 h. Activated crushed 3A and powdered 4A molecular sieves are similar in effect. The choice of 4A sieves for much of this work was based on convenience, as they are available from Aldrich Chemical Co. pre-activated and powdered, and thus were used as received. Upon workup, the powdered 4A sieves remain with the aqueous phase and no filtration is generally necessary. Only in the case of allyl alcohol have powdered 3A molecular sieves been observed to be more effective than 4A; it appears the allyl alcohol is small enough to be sequestered by the 4A sieves. "Chromatography" refers to flash chromatography using 230–400 mesh silica gel (EM Reagent). Cooling was accomplished through the use of one of the following baths: (1) ethylene glycol–water (2:3)/dry ice; (2) acetone/dry ice; or (3) constant temperature baths (Neslab Cryocool).

The dichloromethane (EM Reagent) used did not contain methanol and therefore was not distilled but was stored over activated 3A molecular sieve pellets. (4A sieves should not be used—we have observed pressurization of bottles of CH_2Cl_2 containing 4A sieves.) *Dichloromethane containing methanol as stabilizer should be purified before use.*[34] Diethyl tartrate (bp 80 °C, 0.5 mmHg) and diisopropyl tartrate (bp 76 °C, 0.1 mmHg) were distilled under high vacuum and stored under vacuum or under an inert atmosphere in a desiccator in round-bottomed flasks equipped with a vacuum stopcock.[35] Tartrates should not be stored over molecular sieves. We are aware that tartrate esters can be used successfully as obtained from Aldrich Chemical Co. and Fluka Chemical Corp.; however, if lower than expected yield and/or ee is obtained, the reaction should be repeated with distilled tartrate. $Ti(O\text{-}i\text{-}Pr)_4$ (bp 78–79.5 °C, 1.1 mmHg) was distilled under vacuum and stored under an inert atmosphere *in the absence of molecular sieves.* $Ti(O\text{-}i\text{-}Pr)_4$ has also been successfully used as received from Aldrich Chemical Co., but if substandard results are obtained, the purity of the titanium alkoxide, like that of the tartrate ester, should be a primary suspect. Reagents handled by syringe were measured by weight or by volume. Aqueous 70% *tert*-butyl hydroperoxide (TBHP) was obtained from the Aldrich Chemical Co.

All allylic alcohols were obtained from Aldrich Chemical Co. and used as received, except as noted below. (*E*)-3-(4-Nitrophenyl)-2-propenol was prepared from 4-nitrobenzaldehyde by base-catalyzed condensation with acetaldehyde[36] followed by reduction with sodium borohydride. (*E*)-3-(4-Bromophenyl)-2-propenol was prepared from (*E*)-3-(4-bromophenyl)-2-propenoic acid by Fischer esterification in ethanol followed by reduction with lithium aluminum hydride/aluminum trichloride.[37]

(32) The induction period observed in this particular reaction is attributed to the fact that the catalyst was not given time to form completely prior to addition of substrate and TBHP. No induction period was observed when 10–15 min was allowed for catalyst formation at −20 °C or when catalyst preparation was carried out at −10 to 0 °C.

(33) The amount of sieves used does not appear to be critical. We have used as little as 0.05 wt equiv and as much as 1 wt equiv based on substrate with no significant difference in either selectivity or reactivity. In all reactions we use molecular sieves not only in the reaction but also as a desiccant for the allylic alcohol and the TBHP solution. Both should be treated with activated sieves just prior to addition to the reaction.[54b,d] Tartrates, however, are not treated with sieves and should not be stored over sieves.

(34) Dichloromethane manufactured in Japan is often stabilized with methanol.

(35) We have distilled tartrates by vacuum distillation, Kugelrohr distillation, and wiped-film-molecular distillation.

(36) Nishimura, T. *Bull. Chem. Soc. Jpn.* **1952**, *25*, 54.

(37) Jorgenson, M. J. *Tetrahedron Lett.* **1962**, 559.

(*E*)-2-Decenol, (*E*)-2-octenol, and (*E*)-2-undecenol were prepared from the respective alkynols (Farchan Chemical Co.) by reduction with sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al).[38] (*Z*)-2-Decenol and (*Z*)-2-undecenol were prepared by reduction of the respective alkynols with hydrogen over quinoline-treated $Pd/BaSO_4$ in hexane.[39] (*Z*)-4-(Benzyloxy)-2-butenol was prepared by the monobenzylation (benzyl bromide/sodium hydride) of (*Z*)-2-buten-1,4-diol. 2-Propyl-2-propenol was prepared by reduction of the aldehyde with sodium borohydride. 2-Tetradecyl-2-propenol was prepared by reduction of the methyl ester (gift of Dr. Winston Ho of the McNeil Pharmaceutical Co.) with diisobutylaluminum hydride (DIBAL). (*E*)-2-Methyl-3-phenyl-2-propenol was prepared from the aldehyde by reduction with sodium borohydride. 1-Cyclohexenemethanol was a gift of Prof. Robert Ronald (Washington State University, Pullman, Washington). (*E*)-2,3-Diphenyl-2-propenol was prepared by reduction of the acid with lithium aluminum hydride (Et_2O/0 °C). (*E*)-2-Butenol was purchased from the Fluka Chemical Corp. (*Z*)-2-Butenol was prepared from 2-butynol by hydrogenation at atmospheric pressure with 5% quinoline-treated $Pd/BaSO_4$.[40] (±)-1-Nonen-3-ol and (±)-2-methyl-1-hepten-3-ol were obtained from Chemical Samples Co. (±)-1-Cyclohexene-1-ethanol was prepared by reduction of the ketone with diisobutylaluminum hydride. (±)-(*E*)-1-Cyclohexyl-2-buten-1-ol was prepared by the addition of cyclohexylmagnesium bromide to (*E*)-2-butenal.

Anhydrous *tert*-Butyl Hydroperoxide (TBHP). CAUTION.[41] Stock solutions of TBHP in CH_2Cl_2 were prepared as described previously,[7] and the procedure is reproduced here for convenience. Two liters of aqueous 70% TBHP and 2 L of dichloromethane are shaken in a separatory funnel.[42] The lower organic phase is transferred to a 5-L flask fitted with a heavier-than-water solvent Dean-Stark trap ("moisture test receiver, recycle type", Ace Glass Co.) with condenser. **Although we have never experienced a problem with this procedure, all heating should be done behind an adequate blast shield in a well-ventilated fume hood.** After addition of a few boiling chips, the mixture is brought to a gentle reflux with use of a heating mantle set on a low voltage. Periodically, the water is removed from the trap. After 10 h[43a] about 50–100 mL of water (the amount depends on the degree of mixing in the first step) has been recovered and no additional water is observed in the azeotrope. The TBHP solution (ca. 2.5 L) is generally divided into two batches and each is finally dried in a refrigerator for several hours (usually overnight) over 200–300 g of activated 3A sieve pellets either in an Erlenmeyer flask covered with cellophane or in a high density polyethylene bottle. The solutions (ca. 50% v/v TBHP/CH_2Cl_2, 5–6 M) are then transferred to high-density polyethylene bottles and stored over activated 3A molecular sieve pellets at 0–5 °C. When properly capped, polyethylene bottles develop negative pressure upon cooling in the refrigerator and compress. Such solutions have been stored for months without loss of effectiveness and only slight loss of titre (5–10%, possibly due to constant use, and thus warming). The titre is determined by iodometric titration (vide infra). Assay of titre by FT NMR is not recommended due to the problems of evaporation during NMR sample preparation and pulse saturation which generally lead to values ca. 5–10% above the iodometric titre.

Solutions of anhydrous TBHP in isooctane were prepared in a fashion similar to that described previously for anhydrous TBHP solutions in toluene:[43b] In a 5-L separatory funnel, 1300 mL of aqueous 70% TBHP and 700 mL of isooctane are *swirled* (not vigorously shaken, to avoid emulsions). The lower, aqueous phase (ca. 250 mL) is drawn off, and the upper, organic phase is transferred to a 3-L three-necked flask fitted with a stirbar, a thermometer, and a normal Dean-Stark trap with condenser. **Although we have never experienced a problem with this procedure, all heating should be done behind an adequate blast shield in a well-ventilated fume hood.** After addition of a few boiling chips, the mixture is brought to a gentle reflux (pot temperature 80 °C) by use of a heating mantle. Periodically during the azeotropic process, the water is drawn off. After 12 h[43a] about 150 mL of water (the amount depends on the degree of mixing in the first step) have been removed, and no more water is observed in the azeotrope (pot temperature 90 °C). The TBHP solution (ca. 1.5 L) is generally divided into two batches, and each is finally dried at room temperature for several hours (usually overnight) over 200–300 g of activated 3A sieve pellets in a high-density polyethylene bottle. The solutions (about 50% v/v TBHP/isooctane, 5–6 M) are then decanted and stored in *high-density* polyethylene bottles at *room temperature or at 5 °C in the absence of molecular sieves*. (Molecular sieves, perhaps due to traces of iron, appear to catalyze the slow decomposition of TBHP at room temperature.) Solutions prepared in this manner have remained stable (less than 5% change in titre) for several months. These anhydrous TBHP/isooctane solutions are available from Aldrich Chemical Co.

Assay by iodometric titration is effected as follows: A 0.1 N aqueous sodium thiosulfate solution is prepared (12.5 g of $Na_2S_2O_3 \cdot 5H_2O$ with enough water to make 500 mL will suffice for 15 to 20 titrations), and 50 mL of this solution is placed in a 50-mL graduated buret. A 250-mL Erlenmeyer flask is charged with 25 mL of isopropyl alcohol and 1 mL of glacial acetic acid. To this is added 10 mL of a freshly prepared, cooled solution of 20 g of sodium iodide in 100 mL of warm isopropyl alcohol. After addition of 0.25 mL of anhydrous TBHP/isooctane solution, the mixture is heated to reflux (with stirring on a hot plate or with swirling above a heat gun) and refluxed for 30–45 s. Failure to reflux the solution will result in a low titre. After dilution with 100 mL of distilled water, the warm solution is titrated rapidly with 0.1 N sodium thiosulfate (25–30 mL required) to the disappearance of the yellow iodine color. Starch indicator may be used toward the end of the titration to enhance the endpoint. The hydroperoxide concentration is calculated according to the equation [(molarity of titrant)(mL of titrant)]/[2 × (mL of TBHP solution)], i.e., 0.20 × (mL of titrant), and it should be in the range of 5–6 M. Solutions of lower molarity are obtained either by dilution with additional isooctane or by addition of less 70% TBHP at the start of the procedure.

L-(+)-Dicyclohexyl Tartrate (DCHT).[44] A mixture of 7.5 g (50 mmol) of L-(+)-tartaric acid, 12.50 g (125 mmol) of cyclohexanol, and 0.5 g of *p*-toluenesulfonic acid monohydrate in 30 mL of toluene was placed in a 100-mL flask equipped with a stirbar, a thermometer, and a Dean-Stark trap. The mixture was refluxed (pot 118 °C) for 18 h. During this time about 1.8 mL of water were removed, and the mixture became homogeneous. The solvent and excess cyclohexanol were removed by distillation under high vacuum. The resulting solid was recrystallized twice from hexane (in the first recrystallization, filtering the hot solution to remove the sulfonic acid catalyst) to give L-(+)-dicyclohexyl tartrate as a white powder (13.1 g, 84%): mp 69.5–70.5 °C; $[\alpha]^{25}_D$ +14.97° (*c* 1.71, EtOH); IR (CCl_4) 3530, 2940, 2860, 1740, 1450, 1120, 1090, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.86–5.00 (m, 2), 4.51 (s, 2), 2.83 (br s, 2), 1.18–2.00 (m, 20). Anal. Calcd for $C_{16}H_{26}O_6$: C, 61.12; H, 8.34. Found: C, 61.00; H, 8.29.

L-(+)-Dicyclododecyl Tartrate (DCDT). DCDT was prepared as described by Yamamoto.[31] A mixture of 15.0 g (100 mmol) of L-(+)-tartaric acid, 37.9 g (205 mmol) of cyclododecanol, and 60 mg of *p*-toluenesulfonic acid monohydrate in 50 mL of toluene was placed in a 250-mL three-necked flask equipped with a stirbar, a thermometer and a Dean-Stark trap. The mixture was refluxed (pot 124 °C) for 44 h. During this time about 3.6 mL of water were removed, and the mixture became homogeneous. The solvent was evaporated, and the resulting yellow solid was recrystallized twice from hexane (in the first recrystallization, filtering the hot solution to remove the sulfonic acid catalyst) to give L-(+)-dicyclododecyl tartrate as a white powder (42.3 g, 88%): mp 122–123 °C (lit.[31] mp 123 °C); $[\alpha]^{25}_D$ +8.86° (*c* 1.14, EtOH) [lit.[31] $[\alpha]^{25}_D$ +8.22 (*c* 1.17, EtOH)]; IR ($CHCl_3$) 3530, 2930, 2860, 1730, 1120, 1085 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.1–5.2 (m, 2), 4.47 (d, 2, *J* = 5.7 Hz), 3.12 (d, 2, *J* = 5.7 Hz), 1.05–1.89 (m, 44).

(38) Denmark, S. E.; Jones, T. K. *J. Org. Chem.* **1982**, *47*, 4595. Jones, T. K.; Denmark, S. E. *Org. Synth.* **1986**, *64*, 182.
(39) Cram, D. J.; Allinger, N. *J. Am. Chem. Soc.* **1956**, *78*, 2518.
(40) Moreno-Manas, M.; Trius, A. *Tetrahedron* **1981**, *37*, 3009.
(41) We have carried out this procedure many times without incident. However, solutions of oxidants and oxidizable substrates are potentially hazardous and possibly subject to violent decomposition by adventitious catalysts. When handling solutions of TBHP, the following rules should be applied: The first rule is never add a strong acid (not even a drop) to high strength TBHP solutions. The second rule is never add transition-metal salts known to be good autoxidation catalysts to high strength TBHP solutions (Mn, Fe, Ru, and Co are particularly bad). Alkyl hydroperoxides are sensitive to metal-catalyzed radical-chain decomposition. Among other things, this produces oxygen. The third rule is never work with pure TBHP and avoid using very high strength solutions of it whenever possible. We do not recommend storing TBHP solutions in glass bottles due to the slight danger of gas evolution. Instead, we recommend high-density polyethylene bottles, even though there may be some solvent migration through the walls of the bottle. Low-density polyethylene bottles should not be used as they are significantly more permeable to organic solvents, including isooctane.
(42) In cases where phase separation does not occur or there is an intractable emulsion, a brine wash has proved efficacious.[28]
(43) (a) Prolonged heating beyond this time should be avoided since gradual TBHP decomposition occurs. However, interruption of the required heating period is acceptable. (b) Hill, J. G.; Rossiter, B. E.; Sharpless, K. B. *J. Org. Chem.* **1983**, *48*, 3607.
(44) Sumitomo Patent, Jpn. Kokai Tokkyo Koho JP 82 58 632 (*Chemical Abstracts* **1982**, *97*, 144388h).

General Preparation and Analysis of Mosher Esters.[45] This method was suitable for the enantiomeric excess (ee) determination of nearly all trans-disubstituted epoxy alcohols, some trisubstituted epoxy alcohols, and most secondary allylic alcohols. The reactions were generally run on a 0.15-mmol scale. A mixture of 18 mg (0.15 mmol, 1.0 equiv) of 4-(dimethylamino)pyridine (DMAP) and 100 μL of triethylamine in 0.5 mL of CH_2Cl_2 was treated with the substrate (either neat or as an aliquot of a crude epoxidation reaction mixture). Immediately, 30 μL of neat (+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPA chloride) was added. The solution became warm and turned orange. Reactions were generally complete in a few minutes. It is important to monitor the reaction by TLC to ensure complete reaction; kinetic resolution in an incomplete reaction may significantly alter ee measurements. Reactions were quenched by addition of 3-(dimethylamino)propylamine (40–60 μL) and concentrated, and the residue was passed through a short plug of silica gel in order to remove polar impurities (20% EtOAc/hexane). ^1H NMR analysis in C_6D_6 at 250 or 300 MHz focused on the terminal methylene protons (in the case of a primary epoxy alcohol) or on the allylic methine proton (in the case of a secondary allylic alcohol obtained by kinetic resolution). In the former case, these protons typically were observed as a diastereomeric pair of AB doublets (or doublets of doublets) around δ 4.8. The downfield pair was compared by integration to determine the enantiomeric excess. The Mosher esters of trans epoxy alcohols can also be analyzed by GC (Supelco fused silica capillary column, SP-2330).

General Preparation and Shift Study Analysis of Acetates. This method was suitable for all cis-disubstituted epoxy alcohols and for 2,3-epoxygeraniol (**14**). Acetates were prepared as described above for Mosher esters, using acetyl chloride, or by reaction with acetic anhydride in pyridine. The reactions were generally complete after 2 h at room temperature. ^1H NMR analysis involved sequential treatment of a solution of about 10 mg of an acetate in 0.5 mL of C_6D_6 with 10–20 μL portions of a filtered solution of 30–40 mg of europium(III) tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorate], $Eu(hfc)_3$, in 0.5 mL of C_6D_6 and observation of the acetate CH_3.

General Analysis by HPLC on a Chiral Stationary Phase. This method was suitable for the analysis of *trans*-2,3-diphenyloxiranemethanol (**15**), the bis-Mosher ester of the thiophenyl diol arising from thiophenol opening of glycidol (**16**), as well as the Mosher ester of the iodohydrin derived from glycidyl tosylate (**19**). In the Experimental Section, chiral HPLC analysis refers to chiral stationary phase high performance liquid chromatography which was performed on a Pirkle Type 1-A 250 × 10 mm ID preparative column (Regis). In the case of **16** and **19**, one is only separating diastereomers, but we found the Pirkle column to be superior to achiral columns.

Absolute configurations were determined either by direct comparison of the observed rotation with the literature value or by spectroscopic (shift reagent) and polarimetric analogy based on previous work in these laboratories. One error was found; the sign of the literature rotation is incorrect for allylic alcohol **34**.[5]

General Notes for Workup Procedures. All of the asymmetric epoxidation procedures in which the epoxy alcohol was isolated employed one of the following workup methods (A–D). The appropriate choice of workup procedure is substrate dependent, but each procedure is most applicable for a general class of compounds, as indicated. For any given workup, actual examples are listed in parentheses after the title. The procedures are all described for reactions utilizing 0.1 mol of substrate, 3.0 g of sieves, 5 mmol of $Ti(O\text{-}i\text{-}Pr)_4$, 6 mmol of tartrate, and 0.2 mol of TBHP. For any given reaction, the amounts should be scaled appropriately.

A. Ferrous Sulfate/Tartaric Acid Workup (Epoxy Alcohols I, 1, and 3). (For scale considerations see General Notes for Workup Procedures. For structure I see Scheme I, R = C_5H_{11}.) This procedure works well for most hydrophobic epoxy alcohols and is a simplified version of the workup described in ref 6. The key advantage is that it is the only one described which removes tartrate, $Ti(O\text{-}i\text{-}Pr)_4$, and TBHP. Hence, it is especially useful for those compounds which are not easily separated from TBHP through either distillation or recrystallization.

A freshly prepared solution of 33 g (0.12 mol) of ferrous sulfate heptahydrate and 10 g (0.06 mol) of tartaric acid [or 11 g (0.06 mol) of citric acid monohydrate instead of tartaric acid] in a total volume of 100 mL of deionized water is cooled to ca. 0 °C, by means of an ice water bath. The epoxidation reaction mixture is allowed to warm to ca. 0 °C and then is slowly poured into a beaker containing the precooled stirring ferrous sulfate solution (external cooling is not essential during or after this addition).[46a] The two-phase mixture is stirred for 5–10 min and then transferred to a separatory funnel. The phases are separated[46b] and the aqueous phase is extracted with two 30-mL portions of ether. The combined organic layers are treated with 10 mL of a precooled (0 °C) solution of 30% NaOH (w/v) in saturated brine.[47] The two-phase mixture is stirred vigorously for 1 h at 0 °C. Following transfer to a separatory funnel and dilution with 50 mL of water, the phases are separated and the aqueous layer is extracted with ether (2 × 50 mL). The combined organic layers are dried over sodium sulfate, filtered, and concentrated.[48]

B. Simplified Aqueous Workup (Epoxy Alcohols 2, 7–15). (For scale considerations, see General Notes for Workup Procedures.) This procedure works well for most hydrophobic epoxy alcohols. It removes tartrate and $Ti(O\text{-}i\text{-}Pr)_4$, but it does not reduce the excess hydroperoxide. In most cases, this is not a problem, since the oxidant can usually be easily removed by azeotropic distillation with toluene, by fractional distillation, by chromatography, or by product recrystallization. Chemists have a justifiable fear of peroxides, and they are often reluctant to employ a workup procedure which does not involve initial reduction of the excess peroxide. However, it is important to stress that TBHP is one of the most stable members of the peroxide family, and the dilute TBHP solutions employed in these reactions are thermally very stable and pose essentially no danger, particularly since there are no autooxidation catalysts or strong acids present.[41]

After the reaction mixture is warmed to 0 °C, the catalyst is quenched with water (30 mL; ca. 20 times the weight of $Ti(O\text{-}i\text{-}Pr)_4$ used in the reaction) and the mixture is stirred for 30–60 min, while allowing it to warm to room temperature. Hydrolysis of the tartrate is then effected by adding 6.0 mL of a 30% aqueous solu n of NaOH saturated with sodium chloride[47] and stirring vigorously. ıfter 10–20 min of stirring, a sudden, dramatic phase separation may occur (case I). If it does, there will be a small, milky, sieves-containing aqueous phase on top and a slightly translucent organic phase on the bottom. The lower organic phase is removed and combined with two 30-mL dichloromethane extractions of the aqueous phase.[49] If this phase separation does not occur (case II), then after an additional 30–60 min of vigorous stirring, the reaction mixture is transferred to a separatory funnel. A small amount (ca. 5% v/v) of methanol is added to the mixture, followed by very brief shaking. Immediate phase separation often occurs, allowing for the simple removal of the lower organic phase. If emulsion is still a problem, then the mixture is filtered through a small plug of glass wool. The organic phase is separated and combined with two 30-mL CH_2Cl_2 extractions of the aqueous phase.

In case I, there may be insufficient time for complete ester hydrolysis to occur. Nevertheless, one should take advantage of the phase separation since removal of the emulsive titanium salts greatly facilitates the subsequent purification. In any event, the combined organic extracts from either case I or case II should be checked at this point for the presence of tartrate.[50] Incomplete hydrolysis is seldom a problem for

(45) (a) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. (b) *R*-(+)-α-Methoxy-α-(trifluoromethyl)phenylacetyl chloride (Mosher chloride) was prepared from 5 g of *R*-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid, using 3 molar equiv of oxalyl chloride and a catalytic amount of DMF (1 drop) in 1 mL of hexane. After stirring at room temperature for 0.5 h, the mixture was heated for ca. 3 h. The volatiles were removed at reduced pressure, and the product was distilled under vacuum (50 °C, 0.6 mmHg). [Bosshard, H. H.; Mory, R.; Schmid, M.; Zollinger, H. *Helv. Chim. Acta* **1959**, *42*, 1653. Egawa, Y.; Suzuki, M.; Okuda, T. *Chem. Pharm. Bull.* **1963**, *11*, 589.] In our experience, the commercially available (+)- and (−)-Mosher acids have not been of consistently high optical purity. In such a case, the acid should be further resolved with α-methylbenzylamine (S. Mosamune and R. M. Kennedy, unpublished results).

(46) (a) In the case of these particular compounds (I, **1** and **3**), the reaction was quenched by adding 100 mL of the ferrous sulfate solution to the reaction vessel at −10 °C and then stirring at room temperature until two phases formed. Although there is nothing wrong with this approach on a small scale, it is not recommended for large-scale epoxidations, since with this order of addition there is the potential for the iron salts to catalyze radical chain decomposition of the TBHP. (b) Dr. Joseph Timko (the Upjohn Company) has informed us that in a case where phase separation failed to occur, filtration of the emulsive mixture through Celite was easily accomplished and gave two clear phases. This workup was performed on a 147-mol scale!

(47) 100 mL of a 30% solution are prepared by adding 5 g of sodium chloride to a solution of 30 g of sodium hydroxide in 90 mL of water.

(48) On occasion, DIPT proves difficult to hydrolyze completely. In such a situation, the crude oil should be dissolved in 50 mL of ethyl ether and cooled to 0 °C. A solution of 30% NaOH in brine (10 mL) is then added and the two-phase mixture stirred *vigorously* for 1 h at 0 °C. The phases are separated, the aqueous layer is extracted with ether, and the combined organics are dried over sodium sulfate.

(49) If emulsions result, especially after the first extraction, the addition of a small amount (ca. 5% v/v) of methanol followed by very brief shaking is generally advisable. Petroleum ether may also be used for the secondary extractions.

DET but sometimes occurs with DIPT. If there is a substantial amount of tartrate, this may make the subsequent distillation or crystallization difficult, in which case, the procedure in ref 48 should be followed. If there is little or no DIPT remaining, then the organic phase is dried over sodium sulfate. Filtration and concentration yields a crude product containing TBHP.

C. **Nonacidic Aqueous Workup (Epoxy Alcohols 4–6).** (For scale considerations, see General Notes for Workup Procedures.) This is a slight modification of workup B, and it also does not remove excess hydroperoxide. In some cases it may be important to add base rather than water initially, to avoid epoxide opening under the slightly acidic conditions of a direct water quench. A limiting feature of this workup is the large quantities of $MgSO_4$ and Celite required.

The cold (−20 °C) reaction mixture is quenched with 8 mL of a 10% aqueous solution of sodium hydroxide saturated with sodium chloride.[51] After ether (10% v/v) is added, the cold bath is removed and the stirred mixture is allowed to warm to 10 °C. Stirring is maintained for an additional 10 min at 10 °C, whereupon $MgSO_4$ (8 g) and Celite (1 g) are added. After a final 15 min of stirring, the mixture is allowed to settle and the clear solution is filtered through a pad of Celite, washing with ethyl ether. Concentration yields the crude product containing TBHP, which can be removed as discussed in workup B.

D. **Nonaqueous Workup (Epoxy Alcohols 16 and 17).** (For scale considerations, see General Notes for Workup Procedures.) This procedure may be employed in those cases where the product is water soluble. It serves only to remove the titanium as its insoluble citrate complex.

After the reaction is complete, 1.05 g (5 mmol)[52] of citric acid monohydrate dissolved in 150 mL of 10% acetone in ethyl ether or 0.96 g (5 mmol)[52] of anhydrous citric acid in 150 mL of ethyl ether is added.[53] The cooling bath is removed, and the mixture is stirred for 20–30 min. After filtration through a pad of Celite, the filtrate is concentrated to yield the crude epoxy alcohol containing tartrate and TBHP.

General Notes for the Catalytic Asymmetric Epoxidation. All reactions were carried out under an inert atmosphere (dry nitrogen or argon). In general, the reactions were run in three-necked round-bottomed flasks equipped with a thermometer to monitor the internal temperature of the solution. For large-scale reactions, overhead stirrers were preferred. Solutions of TBHP were treated just before addition as detailed in ref 54b. For compounds **2** and **4–15** the allylic alcohols were dissolved in a small amount of CH_2Cl_2 and treated with activated 3A or 4A sieves, 10–15 min prior to addition. What is currently believed to be the *optimal general procedure* is described below for epoxy alcohol I. However, the experimentals which follow (**1–17**) display some variation in procedure. The process can tolerate these variations, as noted in the Discussion section. For additional comments on alternate procedures or suggestions for optimization, please refer to the Discussion section and the preceding Materials section. In some cases, the reaction was performed only a few times and may not represent optimal conditions. For simplicity's sake, the procedures are described in detail for only a few substrates. Hence, the experimentals for **1**, **3**, and **5–15** are brief and refer back to an earlier procedure. In these cases, the aging process should be carried out as described in the relevant detailed procedure, using the appropriate amounts of reagents. The actual epoxidation times and temperature are as noted in the abbreviated procedure.

General Procedure for the Catalytic Asymmetric Epoxidation. (2*S*-*trans*)-3-Pentyloxiranemethanol (I, **Scheme I**, **R** = C_5H_{11}). An oven-dried 1-L three-necked round-bottomed flask equipped with a magnetic stirbar, pressure equalizing addition funnel, thermometer, nitrogen inlet, and bubbler was charged with 3.0 g of 4A powdered, activated molecular sieves[33] and 350 mL of dry CH_2Cl_2. The flask was cooled to −20 °C. L-(+)-Diethyl tartrate[54a] (1.24 g, 6.0 mmol) and Ti(O-*i*-Pr)$_4$ (1.49 mL, 1.42 g, 5.0 mmol, via syringe) were added sequentially with stirring. The reaction mixture was stirred at −20 °C as TBHP[54b] (39 mL, 200 mmol, 5.17 M in isooctane) was added through the addition funnel at a moderate rate (over ca. 5 min). The resulting mixture was stirred at −20 °C for 30 min. (*E*)-2-Octenol (12.82 g, 100 mmol, freshly distilled), dissolved in 50 mL of CH_2Cl_2, was then added dropwise through the same addition funnel over a period of 20 min, being careful to maintain the reaction temperature between −20 and −15 °C. The mixture was stirred for an additional 3.5 h at −20 to −15 °C. Workup A was then performed,[54c] yielding a white solid (12.6 g, 88% crude yield, 92.3% ee by GC analysis of the Mosher ester). After two recrystallizations from petroleum ether (bp 40–60 °C) at −20 °C, a white solid was obtained (10.5 g, 73% yield, >98% ee by GC analysis of the Mosher ester): mp 38–39.5 °C; $[\alpha]^{25}_D$ −42.7° (*c* 4.7, $CHCl_3$); IR (Nujol) 3100, 2920, 2860, 1460, 1375, 1040, 880 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.92 (ddd, 1, J = 3.8, 5.6, 13.2 Hz), 3.64 (ddd, 1, J = 4.5, 7.5, 13.2 Hz), 2.90–3.00 (m, 2), 1.90 (br s, 1), 1.21–1.60 (m, 8), 0.90 (t, 3, J = 7.5 Hz). Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.19. Found: C, 66.53; H, 11.05.

(2*S*-*trans*)-3-Propyloxiranemethanol (1).[6] The epoxidation was performed as described for I, in this case in 150 mL of CH_2Cl_2 with 3.0 g of powdered, activated 4A molecular sieves, 1.49 mL (1.42 g, 5.0 mmol) of Ti(O-*i*-Pr)$_4$, 1.24 g (6.0 mmol) of L-(+)-diethyl tartrate,[54a] 39 mL of a 5.17 M solution of TBHP[54b] in isooctane (200 mmol), and 10.0 g (100 mmol, 97% purity, stored over 3A sieves) of (*E*)-2-hexenol (dissolved in 50 mL CH_2Cl_2) at −20 to −15 °C for 2.5 h. Workup A was then performed,[54c] yielding a colorless oil (11.1 g, 96% crude yield). Purification by Kugelrohr distillation (17 mmHg, 100 °C) gave a colorless oil (9.9 g, 85% yield, 94% purity, 94.1% ee by GC analysis of the Mosher ester): $[\alpha]^{25}_D$ −46.3° (*c* 3.87, $CHCl_3$); (lit.[6] $[\alpha]^{25}_D$ −46.6° [*c* 1.0 $CHCl_3$]); IR (film) 3400, 2960, 2930, 2870, 1460, 1380, 1100, 1065, 1045, 1010, 980, 945, 915, 900, 855 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.92 (ddd, 1, J = 2, 6, 12 Hz), 3.63 (ddd, 1, J = 4, 7, 12 Hz), 2.9–3.0 (m, 2), 2.1–2.2 (m, 1), 1.4–1.6 (m, 4), 0.97 (t, 3, J = 8 Hz).

(2*S*-*trans*)-3-Heptyloxiranemethanol (2). A mixture of powdered, commercially activated 4A molecular sieves (300 mg)[33] and 30 mL of CH_2Cl_2 was cooled to 0 °C. L-(+)-Diethyl tartrate[54a] (97 mg, 0.47 mmol) and Ti(O-*i*-Pr)$_4$ (91 mg, 0.32 mmol) were added sequentially. After the mixture was cooled to −20 °C, TBHP[54b] (2.2 mL, 12.8 mmol, 5.8 M in CH_2Cl_2) was added and the resulting mixture was stirred for 20 min, whereupon (*E*)-2-decen-1-ol (1.00 g, 6.4 mmol)[54d] was added. Stirring was maintained at ca. −23 °C for 2.5 h. After workup B, evaporation of volatiles provided a white, free-flowing solid, weight 1.10 g (100%), mp 43.5–48.5 °C. Analysis of the ester derived from (+)-MTPA chloride indicated 96% ee. Recrystallization from petroleum ether (bp 60–90 °C) gave crystals of mp 49.5–50.0 °C; $[\alpha]^{25}_D$ −36.5° (*c* 2.8, $CHCl_3$); IR ($CHCl_3$) 3600, 2980, 2950, 2925, 2858, 1460, 1080, 1020, 880 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.92 (br d, 1, J = 13 Hz), 3.58–3.70 (m, 1), 2.9–3.0 (m, 2), 1.8–1.9 (m, 1), 1.2–1.6 (m, 12), 0.90 (t, 3, J = 7 Hz).

(2*S*-*trans*)-3-Octyloxiranemethanol (3).[7] The epoxidation was performed as described for I, in this case in 35 mL of CH_2Cl_2 with 300 mg of powdered, activated 4A molecular sieves, 150 μL (143 mg, 0.5 mmol) of Ti(O-*i*-Pr)$_4$, 124 mg (0.6 mmol) of L-(+)-diethyl tartrate,[54a] 4.0 mL of a 5.1 M solution of TBHP[54b] in isooctane (20 mmol), and 1.70 g (10 mmol, dissolved in 5 mL CH_2Cl_2) of (*E*)-2-undecenol at −15 to −10 °C for 1.5 h. After workup A was performed, a white solid was obtained (1.80 g, 94% ee by GC analysis of the Mosher ester). Recrystallization twice from petroleum ether (bp 40–60 °C) at −15 °C yielded a white solid (1.45 g, 78% yield, >98% ee by GC analysis of the Mosher ester): mp 58.5–60 °C; $[\alpha]^{25}_D$ −35.5° (*c* 2.59, $CHCl_3$); IR ($CHCl_3$) 3600, 2920, 2860, 1460, 1080, 1010, 890 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.95 (ddd, 1, *J*

(50) DIPT is sometimes difficult to visualize with the usual phosphomolybdic acid spray. A much better visualizing agent for DIPT is ammonium molybdate and cerric sulfate in H_2SO_4/H_2O [ammonium molybdate 6.25 g, cerric sulfate 2.5 g, concentrated H_2SO_4 25 mL, H_2O 125 mL]. The R_f of DIPT in 40% EtOAc/hexane on silica TLC is ca. 0.30.

(51) 100 mL of a 10% solution are prepared by adding 10 g of sodium chloride to a solution of 10 g of sodium hydroxide in 95 mL of water. Our early experiments (**4–6**) were performed with a 10% NaOH solution in brine.[6] However, we have since found that a 30% solution[47] is just as effective and somewhat more convenient because of the smaller volume. Hence, we believe that a 30% solution would be very effective in this workup procedure and would probably reduce the amount of $MgSO_4$ required.

(52) It is important that the molar amount of citric acid used be exactly or slightly less than that of Ti(O-*i*-Pr)$_4$ to avoid the problems caused by excess acid remaining in solution.

(53) A small amount of acetone is utilized to help dissolve the monohydrate. Anhydrous citric acid will dissolve in neat ether.

(54) (a) Tartrates are extremely viscous. They should be weighed into a flask, dissolved in a minimum amount of CH_2Cl_2, and transferred via cannula or syringe, or weighed using a syringe equipped with a 15 gauge needle. (b) Somewhat more than the required amount of TBHP solution should be dispensed into a small flask or graduated cylinder containing activated 3A or 4A sieve pellets. The flask is stoppered and after a few minutes, the desired volume of solution is transfered to the reaction flask, either by syringe, addition funnel, or direct addition. Syringe needles should never be inserted into any stock solution of TBHP which is to be stored. Cold stock solutions of TBHP in dichloromethane should be warmed to room temperature prior to opening (warm water baths are convenient) in order to minimize exposure to moisture. (c) Any yellow color from the $FeSO_4$ workup can usually be removed by filtration of the dried solution through a pad of Celite (10 g) and silica gel (20 g). (d) The allylic alcohol was dissolved in a small (ca. 0.5 mL/g substrate) amount of CH_2Cl_2 and dried with 3A molecular sieves 10–15 min prior to addition. Following addition, the sieves should be rinsed with CH_2Cl_2 to ensure complete transfer. (e) Other things being equal, constant stirring is optimal, but this should not be sustained at the expense of maintaining the correct temperature. Hence, if a constant temperature bath is not available for the extended reaction times, it is acceptable to store the reaction mixture in the freezer unstirred. For kinetic resolutions, it has been noted that stirring improves both reaction rate and enantiomeric excess.

= 3, 6, 13 Hz), 3.65 (ddd, 1, J = 5, 7, 12 Hz), 2.9–3.0 (m, 2), 1.8–1.9 (m, 1), 1.2–1.75 (m, 14), 0.91 (t, 3, J = 7 Hz). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.91. Found: C, 70.91; H, 11.61.

(2*S*-*trans*)-3-Phenyloxiranemethanol (Epoxycinnamyl Alcohol, 4). A flame-dried 5-L three-necked flask was fitted with an overhead mechanical stirrer, thermometer, and dropping funnel, flushed with nitrogen, and charged with 6.55 g (0.028 mol) of L-(+)-diisopropyl tartrate[54a] and 3.5 L of CH_2Cl_2. After the mixture was cooled to −20 °C, 20 g of activated, powdered 4A molecular sieves, 5.55 mL (5.30 g, 0.019 mol) of Ti(O-*i*-Pr)$_4$, and 96.9 mL of a 7.7 M solution of TBHP[54b] in CH_2Cl_2 (0.746 mol) were added sequentially. The mixture was allowed to stir at −20 °C for 1 h and then treated with a solution of 50.0 g (0.373 mol) of freshly distilled (*E*)-3-phenyl-2-propenol (cinnamyl alcohol) in 70 mL of CH_2Cl_2, added dropwise over 1 h. After 3 h at −20 °C, the reaction was quenched via workup C. Azeotropic removal of the TBHP with toluene at reduced pressure and finally subjection to high vacuum (0.2 mmHg) gave a yellow oil. Recrystallization from petroleum ether/ethyl ether at −20 °C gave slightly yellow crystals (50.0 g, 89%, >98% ee by analysis of the ester derived from (+)-MTPA chloride): mp 51.5–53 °C (lit.[55] oil); $[\alpha]^{25}_D$ −49.6° (*c* 2.4, $CHCl_3$) (lit.[55] for 2*R* $[\alpha]^{20}_D$ +45.9° [*c* 1.5, EtOH]); IR ($CHCl_3$) 3580, 3450, 2980, 2920, 2870, 1600, 1450, 1380, 1100, 1070, 1020, 880, 860, 845 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.2–7.5 (m, 5), 4.18 (dd, 1, J = 3, 13 Hz), 3.95 (d, 1, J = 3 Hz), 3.81 (dd, 1, J = 5, 13 Hz), 3.25–3.3 (m, 1), 2.2 (br s, 1, $w_{1/2}$ = 40 Hz).

(2*S*-*trans*)-3-(4-Nitrophenyl)oxiranemethanol (5). A flame dried 5-L three-necked flask was fitted as for **4** and charged with a mixture of 45 g of powdered, activated 4A molecular sieves and 3 L of dry CH_2Cl_2. After cooling to −5 °C, L-(+)-diisopropyl tartrate (10.54 g, 0.045 mol)[54a] and 8.93 mL (8.52 g, 0.030 mol) of Ti(O-*i*-Pr)$_4$ were added sequentially. After the mixture was cooled to −20 °C, 107.4 g (0.60 mol)[54d] of (*E*)-3-(4-nitrophenyl)-2-propenol was added and the mixture stirred for 10 min. A 7.0 M solution of TBHP[54b] in CH_2Cl_2 (172 mL, 1.20 mol) was added, taking care to maintain the temperature near −20 °C. After the mixture was stirred at −20 °C for 2 h, workup C (workup B should also be suitable, since this compound is not acid sensitive) yielded a yellow solid, which was washed with petroleum ether. The crude product was dissolved in a minimum amount of ethyl acetate, filtered through a small pad of silica gel (to remove traces of titanium dioxide), and recrystallized from hexane/ethyl acetate to give a yellow solid (96 g, 82%, >98% ee by analysis of the ester derived from (+)-MTPA chloride): mp 97–98 °C; $[\alpha]^{25}_D$ −37.4° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3600, 1600, 1515, 1350, 1105, 1070, 865, 845, 820 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.22 (d, 2, J = 8 Hz), 7.48 (d, 2, J = 8 Hz), 4.05–4.2 (m, 2), 3.8–3.95 (m, 1), 3.2–3.3 (m, 1), 2.15 (m, 1). Anal. Calcd for $C_9H_9NO_4$: C, 55.38; H, 4.65; N, 7.18. Found: C, 55.25; H, 4.64; N, 7.09.

(2*S*-*trans*)-3-(4-Bromophenyl)oxiranemethanol (6). Epoxidation as described for **4** was performed in this case in 1.5 L of CH_2Cl_2 with 33 g of powdered, activated 4A molecular sieves, 5.76 mL (5.50 g, 0.019 mol) of Ti(O-*i*-Pr)$_4$, 6.80 g (0.029 mol) of L-(+)-diisopropyl tartrate,[54a] 110 mL of a 7.0 M solution of TBHP[54b] in CH_2Cl_2 (0.77 mol), and 82.4 g (0.387 mol) of (*E*)-3-(4-bromophenyl)-2-propenol[54d] at −20 °C for 45 min. After workup C, a white solid was obtained, which was dissolved in a minimum amount of ethyl acetate, filtered through a small pad of silica gel with ethyl acetate (to remove traces of titanium dioxide), and recrystallized from hexane/ethyl acetate to give a white solid (61.1 g, 69%, >98% ee by analysis of the ester derived from (+)-MTPA chloride): mp 67–68 °C; $[\alpha]^{25}_D$ −35.2° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3600, 2990, 2920, 2865, 1595, 1485, 1445, 1390, 1070, 1010, 890, 870, 840, 810 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.48 (d, 2, J = 8 Hz), 7.18 (d, 2, J = 8 Hz), 4.08 (br d, 1, J = 13 Hz), 3.92 (d, 1, J = 3 Hz), 3.83 (br d, 1, J = 13 Hz), 3.15–3.25 (m, 1), 1.8 (br s, 1, $w_{1/2}$ = 20 Hz). Anal. Calcd for $C_9H_9BrO_2$: C, 47.19; H, 3.96. Found: C, 47.19; H, 3.98.

(2*S*-*cis*)-3-Heptyloxiranemethanol (7). Epoxidation as described for **2** was performed in this case in 30 mL of CH_2Cl_2 with 500 mg of powdered, activated 4A molecular sieves, 182 mg (0.64 mmol, 10 mol %) of Ti(O-*i*-Pr)$_4$, 190 mg (0.92 mmol, 14 mol %) of L-(+)-diethyl tartrate,[54a] 2.2 mL of a 5.8 M solution of TBHP[54b] in CH_2Cl_2 (12.8 mmol), and 1.0 g (6.4 mmol) of (*Z*)-2-decen-1-ol[54d] at −20 °C. After an initial 0.5-h period of stirring at −20 °C, the reaction mixture was refrigerated (ca. −10 °C) unstirred[54e] for 29 h. Following workup B, evaporation of volatiles provided a colorless solid, which was Kugelrohr distilled to give a white solid (0.81 g, 74%, 86% ee by analysis of the ester derived from (−)-MTPA chloride) of mp 39.5–42.5 °C. Recrystallization from petroleum ether provided a white solid: mp 43.0–43.5 °C; $[\alpha]^{25}_D$ −4.8° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3600, 2950, 2920, 2850, 1455, 1028 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.8–3.95 (m, 1), 3.6–3.75 (m, 1), 3.1–3.2 (m, 1), 3.0–3.1 (m, 1), 1.8–1.9 (br s, 1, $w_{1/2}$ = 16 Hz), 1.2–1.7 (m, 12), 0.91 (t, 3, J = 7 Hz). Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.57; H, 11.60.

(2*S*-*cis*)-3-Octyloxiranemethanol (8). This reaction, using only 5/7.5% catalyst, is not recommended as a general procedure for this substrate, since *cis* olefins are normally more successfully epoxidized with higher catalyst ratios (10/12–14%, see **7**). This reaction is described solely to demonstrate the use of this ratio of catalyst on this type of substrate. Epoxidation as described for **2** was performed in 9 mL of CH_2Cl_2 with 170 mg of powdered, activated 4A molecular sieves, 71 mg (0.25 mmol) of Ti(O-*i*-Pr)$_4$, 86 mg (0.37 mmol) of L-(+)-diisopropyl tartrate,[54a] 1.3 mL of a 7.5 M solution of TBHP[54b] in isooctane (9.8 mmol), and 0.85 g (5.0 mmol) of (*Z*)-2-undecen-1-ol[54d] at −12 °C (refrigerated, unstirred[54e]) for 42 h. After workup B, evaporation of volatiles provided a colorless solid (>80% ee by analysis of the ester derived from (+)-MTPA chloride; a more accurate ee determination was not possible from the ^{1}H nmr spectrum, since the peaks were poorly resolved). Recrystallization from pentane gave a white solid (0.584 g, 63%): mp 50–51 °C (lit.[56] mp 49 °C); $[\alpha]^{25}_D$ −3.5° (*c* 1.3, $CHCl_3$) [lit.[56] $[\alpha]^{25}_D$ −4.2° (*c* 1, $CHCl_3$)]; IR ($CHCl_3$) 3600, 2950, 2930, 2860, 1460, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.88 (m, 1), 3.68 (m, 1), 3.1–3.2 (m, 1), 3.0–3.1 (m, 1), 1.2–1.8 (m, 15), 0.9 (t, 3, J = 7 Hz). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.91. Found: C, 70.62; H, 11.59.

(2*S*-*cis*)-3-(Benzyloxymethyl)oxiranemethanol (9). This procedure is not recommended as a general procedure for the synthesis of this compound. However, other workers have successfully epoxidized this substrate under catalytic conditions.[9] Epoxidation as described for **2** was performed, in this case, in 50 mL of CH_2Cl_2 with 1.0 g of powdered, activated 4A molecular sieves, 218 mg (0.77 mmol) of Ti(O-*i*-Pr)$_4$, 220 mg (1.07 mmol) of L-(+)-diethyl tartrate,[54a] 4.0 mL of a 4.0 M solution of TBHP[54b] in toluene (16.0 mmol), and 1.33 g (7.5 mmol) of (*Z*)-4-(benzyloxy)-2-buten-1-ol[54d] at −20 °C. After 43 h, the reaction was still far from complete. Quenching of an aliquot with acetic anhydride/triethylamine gave the acetate. Analysis by ^{1}H NMR with Eu(hfc)$_3$ indicated a selectivity of 85% ee.

(*S*)-2-Propyloxiranemethanol (10). Epoxidation as described for **2** was performed in this case in 10 mL of CH_2Cl_2 with 150 mg of activated, powdered 3A molecular sieves, 69 mg (0.24 mmol) of Ti(O-*i*-Pr)$_4$, 63 mg (0.30 mmol) of L-(+)-diethyl tartrate,[54a] 2.5 mL of a 5.1 M solution of TBHP[54b] in CH_2Cl_2 (12.8 mmol), and 0.51 g (5.1 mmol) of 2-propyl-2-propenol[54d] at an initial temperature of −23 °C. After stirring for 2 h at −23 °C, the reaction mixture was refrigerated at −12 °C for 11 h (unstirred).[54e] After workup B, evaporation of volatiles provided a colorless oil, which was chromatographed by MPLC (ethyl ether), followed by solvent removal at 90 mmHg to give a colorless oil (0.52 g, 88%, 95% ee by analysis of the ester derived from (+)-MTPA chloride): $[\alpha]^{25}_D$ −25.9° (*c* 1.2, $CHCl_3$); IR (film) 3400, 2950, 2880, 1460, 1380, 1180, 1040, 945, 810 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.72 (d, 1, J = 12 Hz), 3.55 (d, 1, J = 12 Hz), 2.84 (d, 1, J = 6 Hz), 2.60 (d, 1, J = 6 Hz), 1.6–1.8 (m, 2), 1.0–1.5 (m, 3), 0.86 (t, 3, J = 7 Hz). Anal. (of the derived 4-nitrobenzoate, an oil) Calcd for $C_{13}H_{15}NO_5$: C, 58.86; H, 5.70; N, 5.28. Found: C, 58.92; H, 5.95; N, 5.23.

(*S*)-2-Tetradecyloxiranemethanol (11).[10] Epoxidation as described for **2** was performed in this case in 10 mL of CH_2Cl_2 with 300 mg of activated, powdered 3A molecular sieves, 110 mg (0.39 mmol) of Ti(O-*i*-Pr)$_4$, 105 mg (0.51 mmol) of L-(+)-diethyl tartrate,[54a] 2.0 mL of a 5.1 M solution of TBHP[54b] in CH_2Cl_2 (10.2 mmol), and 1.0 g (3.93 mmol) of 2-tetradecyl-2-propenol[54d] at an initial temperature of −23 °C. After stirring for 2 h at −23 °C, the reaction mixture was refrigerated at −12 °C for 11 h (unstirred).[54e] Workup B with 2.0 mL of water and 0.5 mL of basic brine gave clean phase separation. After drying, the slightly translucent suspension was filtered through a small pad of silica gel (ethyl acetate as eluent) and concentrated to an oil. Chromatography (MPLC, petroleum ether/ethyl ether (1/1) initially, then neat ethyl ether eluent) and solvent removal gave a crystalline solid (0.97 g, 91%, 96% ee by analysis of the ester derived from (+)-MTPA chloride): mp 41.5–42.6 °C; $[\alpha]^{25}_D$ −10.9° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3600, 2920, 2850, 1460, 1060 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.80 (dd, 1, J = 4, 12 Hz), 3.65 (dd, 1, J = 8, 12 Hz), 2.90 (d, 1, J = 5 Hz), 2.68 (d, 1, J = 5 Hz), 1.1–1.9 (m, 27), 0.90 (t, 3, J = 7 Hz).

(2*S*-*trans*)-2-Methyl-3-phenyloxiranemethanol (12). After catalyst preparation and aging at −23 °C, the epoxidation was performed as described for **4**, in this case in 1.5 L of CH_2Cl_2 with 40 g of powdered, activated 4A molecular sieves, 10.1 mL (9.61 g, 0.0338 mol) of Ti(O-*i*-Pr)$_4$, 11.9 g (0.0507 mol) of L-(+)-diisopropyl tartrate,[54a] 193 mL of a 7.0 M solution of TBHP[54b] in CH_2Cl_2 (1.35 mol), and 100.0 g (0.676

(55) Melloni, P.; Della Torre, A.; Lazzari, E.; Mazzini, G.; Meroni, M. *Tetrahedron* **1985**, *41*, 1393.

(56) Spur, B.; Crea, A.; Peters, W.; Koenig, W. *Arch. Pharm.* **1985**, *318*, 225.

mol) of (*E*)-2-methyl-3-phenyl-2-propenol[54d] at −35 °C for 2 h. After workup B, evaporation gave a crude yellow oil, which was diluted with 70 mL of petroleum ether and allowed to crystallize in a freezer overnight (−20 °C). Filtration gave white crystals (87 g, 79%, >98% ee by ^{1}H NMR analysis of the ester derived from (+)-MTPA chloride): mp 57.5–58.5 °C; $[\alpha]^{25}_D$ −16.9° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3450, 2995, 2980, 2965, 2885, 1700, 1600, 1490, 1450, 1380, 1090, 1055, 980, 960, 915, 900, 850 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.2–7.4 (m, 5), 4.22 (s, 1), 3.7–3.9 (m, 2), 2.1–2.2 (m, 1), 1.12 (s, 3). Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.05; H, 7.38.

(1*S*)-7-Oxabicyclo[4.1.0]heptane-1-methanol (13). After catalyst preparation and aging at −23 °C, the epoxidation was performed as described for **2**, in this case in 30 mL of CH_2Cl_2 with 300 mg of powdered, activated 4A molecular sieves, 91 mg (0.32 mmol) of Ti(O-*i*-Pr)$_4$, 97 mg (0.47 mmol) of L-(+)-diethyl tartrate,[54a] 2.2 mL of a 5.8 M solution of TBHP[54b] in CH_2Cl_2 (12.8 mmol), and 0.72 g (6.4 mmol) of 1-cyclohexenylmethanol[54d] at −40 °C for 3 h. After workup B, chromatography on 15 g of silica gel (30–60 petroleum ether/ethyl ether 4/1 initially, then 1/1, then 2/3) and solvent removal at 10 mmHg gave a clear, colorless oil (0.63 g, 77%, 93% ee by analysis of the ester derived from (+)-MTPA chloride): $[\alpha]^{25}_D$ −22.8° (*c* 2.6, $CHCl_3$); IR ($CHCl_3$) 3500, 2995, 2970, 2860, 1450, 1430, 1400, 1360, 1105, 1075, 1040, 1020, 1000, 915, 895, 870, 860, 830 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.5–3.8 (m, 2), 3.28 (d, 1, *J* = 5 Hz), 1.2–2.1 (m, 9). Anal. Calcd (of the derived *p*-nitrobenzoate, mp 92–93 °C) for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.46; H, 5.91; N, 4.68.

(2*S*-*trans*)-3-Methyl-3-(4-methyl-3-pentenyl)oxiranemethanol (2,3-Epoxygeraniol) (14). Epoxidation as described for **2** was performed in this case in 50 mL of CH_2Cl_2 with 1.8 g of powdered, activated 4A molecular sieves, 0.91 g (3.2 mmol) of Ti(O-*i*-Pr)$_4$, 1.0 g (4.8 mmol) of L-(+)-diethyl tartrate,[54a] 15.6 mL of a 6.2 M solution of TBHP[54b] in CH_2Cl_2 (97 mmol), and 10.0 g (65 mmol) of freshly distilled (*E*)-3,7-dimethyl-2,6-octadien-1-ol[54d] at −20 °C for 45 min. After workup B, evaporation of volatiles provided a colorless oil. This compound decomposes under normal vacuum distillation so it was Kugelrohr distilled (0.4 mmHg, 80 °C) to give a colorless oil (10.95 g, 99%, chemical purity ca. 95% by ^{1}H NMR,[57] 91% ee by ^{1}H NMR shift analysis of the derived acetate with Eu(hfc)$_3$): $[\alpha]^{25}_D$ −5.3° (*c* 3.0, $CHCl_3$) (lit.[58] $[\alpha]_D$ −5.89° [$CHCl_3$]); IR (film) 3400, 2980, 2920, 2850, 1450, 1360, 1250, 1220, 1200, 1120, 1060, 870 cm^{-1}; ^{1}H NMR (C_6D_6) δ 5.1 (br t, 1, *J* = 9 Hz), 3.4–3.6 (m, 2), 2.8 (dd, 1, *J* = 6, 7 Hz), 2.05 (q, 2, *J* = 7 Hz), 1.62 (s, 3), 1.48 (s, 3), 1.3–1.7 (m, 3), 1.06 (s, 3).

(2*S*-*trans*)-2,3-Diphenyloxiranemethanol (15). This reaction was performed simply to determine the enantioselectivity, without any attempt at product isolation. Epoxidation as described for **2** was performed in this case in 15 mL of CH_2Cl_2 with 0.10 g of activated, powdered 3A molecular sieves, 25 mg (0.088 mmol) of Ti(O-*i*-Pr)$_4$, 27 mg (0.131 mmol) of L-(+)-diethyl tartrate,[54a] 1.0 mL of a 5.1 M solution of TBHP[54b] in CH_2Cl_2 (5.1 mmol), and 0.40 g (1.77 mmol) of (*E*)-2,3-diphenyl-2-propenol[54d] at −20 °C for 90 min. After workup B, a portion of the organic layer (0.5 mL) was concentrated, dissolved in 1 mL of ethyl ether, subjected to chiral HPLC analysis (2 μL, 3% isopropyl alcohol/hexane, 5.0 mL/min, 254 nm UV detection), and found to be of 91% ee. For example, about 2 μL of a solution of 10 mg of the epoxy alcohol **15** in 1 mL of ethyl ether was injected, and elution with 3% isopropyl alcohol in hexane, at a flow rate of 5.0 mL/min, gave retention times of 14 min (starting allylic alcohol), 21 min ((2*R*-*trans*)-**15**), and 23 min ((2*S*-*trans*)-**15**).

(*S*)-Oxiranemethanol (Glycidol, 16). An oven-dried 500-mL round-bottomed flask fitted with a septum and a stirbar was charged with 3.5 g of 3A powdered, activated molecular sieves[33] and 190 mL of CH_2Cl_2. Then 1.39 g (1.25 mL, 5.95 mmol) of L-(+)-diisopropyl tartrate[54a] and 5.81 g (6.8 mL, 0.10 mol) of allyl alcohol (stored over 3A sieves) were added, and the solution was cooled to −5 °C. Ti(O-*i*-Pr)$_4$ (1.4 g, 1.5 mL, 5.0 mmol) was added, and the mixture was stirred at −5 ± 2 °C for 10–30 min. Commercial grade 80% cumene hydroperoxide (36 mL, ca. 0.2 mol, dried over 3A molecular sieves prior to use) was added slowly over a period of 30 min. The mixture was stirred at −5 ± 2 °C for 5 h, at which time GC analysis of the reaction mixture indicated >95% reaction (20–30-m fused silica carbowax capillary, 70 °C). The reaction was quenched by using workup D. Distillation at reduced pressure (50 °C, 5 mmHg) afforded 9.83 g of a mixture containing cumene, 2-phenyl-2-propanol, a small amount of cumene hydroperoxide, and 49% glycidol[59] (as determined by NMR, 0.065 mol, 65% of theoretical yield). A 1.0 mol scale reaction using the same procedure afforded 48% of the theoretical yield of glycidol. Determination of enantiomeric excess was carried out by derivatization: A small amount of the isolated glycidol/cumene mixture was treated with thiophenol and Ti(O-*i*-Pr)$_4$ in CH_2Cl_2.[60] The opening product, 3-thiophenyl-1,2-propanediol, isolated after acidification with 10% H_2SO_4, was peracetylated with acetic anhydride in pyridine. Analysis of the diacetate by ^{1}H NMR (C_6D_6) in the presence of the chiral shift reagent Eu(hfc)$_3$ indicated a selectivity of 90% ee. Enantiomeric purity could also be determined by chiral HPLC analysis of the derived bis-Mosher ester.

(2*S*-*trans*)-3-Methyloxiranemethanol (Epoxy Crotyl Alcohol, 17). Crushed, activated 3A molecular sieves (3.0 g)[33] were introduced into a flame-dried 1-L flask under nitrogen. After the flask was flushed for several minutes with N_2, 200 mL of CH_2Cl_2 were added and the flask was cooled to −20 °C. L-(+)-Diisopropyl tartrate[54a] (1.42 g, 6.0 mmol), (*E*)-2-buten-1-ol (7.21 g, 100 mmol, stored over sieves), and Ti(O-*i*-Pr)$_4$ (1.42 g, 5.0 mmol) were added sequentially. Stirring was maintained for 15 min at −20 °C, whereupon 26.0 mL of a 7.7 M solution of TBHP[54b] in CH_2Cl_2 (200 mmol) was added via cannula. The reaction mixture was stirred at −20 °C for 2 h. Careful quenching of the excess TBHP was accomplished by the slow addition of tributylphosphine (20.2 g, 100 mmol) at −20 °C. After the mixture was checked to ensure that all of the hydroperoxide had been reduced,[65] workup D was performed. The resulting viscous oil was distilled (18 mmHg, 81–82 °C) to give **17** as a clear, colorless oil (6.17 g, 70%, chemical purity 93% by ^{1}H NMR, 90–92% ee by analysis of the ester derived from (+)-MTPA chloride): $[\alpha]^{25}_D$ −50.1° (*c* 4.54, C_6H_6) [(lit.[16] $[\alpha]^{24}_D$ −55° (*c* 0.22, C_6H_6)]; IR ($CHCl_3$) 3400, 2988, 2940, 2880, 1445, 1383, 1103, 1040, 991, 859, 810 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.89 (dd, 1, *J* = 3.0, 13.0 Hz), 3.61 (dd, 1, *J* = 3.7, 13.0 Hz), 3.04 (dq, 1, *J* = 2.9, 5.6 Hz), 2.91 (ddd, 1, *J* = 2.9, 3.0, 3.7 Hz), 1.34 (d, 3, *J* = 5.6 Hz).

General Notes for the in Situ Derivatization. Most of the comments mentioned in the general notes for the catalytic asymmetric epoxidation are germane here as well. Each experimental describes an epoxidation and derivatization. All of the epoxidation procedures are abbreviated, referring back to the detailed procedures for **16** or **17**. The following experimentals (**18–30**) contain only details of the scale, appropriate tartrate, reaction time and temperature, and if necessary, change in substrate (**21–23, 27–30**). The aging process should be performed as described in the earlier detailed procedure. The quenching of excess TBHP as well as the in situ esterification, sulfonylation, and silylation are described in detail for **18, 22** (**23**), and **20**, respectively. Subsequent preparations refer to these procedures, using the appropriate amounts of reagents and the noted reaction times.

General Procedure for the Catalytic Asymmetric Epoxidation Employing in Situ Derivatization: (*R*)-Oxiranemethanol 4-Nitrobenzoate (18).[61] Epoxidation of allyl alcohol was carried out as described above (**16**) on a 1.0-mol scale with L-(+)-DIPT. After 6 h at −5 ± 2 °C, the mixture was cooled to −20 °C and carefully treated with 180 mL (189 g, 1.5 mol) of trimethyl phosphite, P(OMe)$_3$, added over a period of 1 h, taking care that the temperature did not rise above −20 °C. The mixture was then treated with 170 mL (123 g, 1.2 mol) of triethylamine and a solution of 185.6 g (1 mol) of *p*-nitrobenzoyl chloride in 250 mL of CH_2Cl_2 and stirred for 1 h at 0 °C. After filtration through a pad of Celite, the filtrate was washed with 10% aqueous tartaric acid (2 × 250 mL), saturated $NaHCO_3$ (3 × 250 mL), and brine (2 × 250 mL). The organic phase was dried over Na_2SO_4, filtered through a small pad of silica gel, and concentrated to an oil (first at 12 mmHg, then under high vacuum (0.2 mmHg) at 60 °C) to remove any remaining cumene, 2-phenyl-2-propanol, trimethyl phosphite, and trimethyl phosphate. The oil solidified on standing and was recrystallized twice from ether to give 135.7 g of **18** (61%, 92–94% ee by analysis of the bis-Mosher ester of the derived thiophenyl diol in a manner similar[23] to that described for glycidol (**16**)). **18**: mp 59.5–60.0 °C (lit.[62] mp 59–60 °C); $[\alpha]^{20}_D$ −38.7° (*c* 3.02, $CHCl_3$) [lit.[62] $[\alpha]^{20}_D$ +37.9° (*c* 3.38, $CHCl_3$)]; IR (Nujol) 3120, 2970, 2920, 2860, 1730, 1610, 1520, 1460 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.21–8.37 (m, 4), 4.76 (dd, 1, *J* = 3, 13 Hz), 4.21 (dd, 1, *J* = 7, 13 Hz), 3.37 (m, 1), 2.96 (t, 1, *J* = 5 Hz), 2.77 (dd, 1, *J* = 3, 5 Hz). Anal. Calcd for $C_{10}H_9NO_5$: C, 53.81; H, 4.06; N, 6.28. Found: C, 53.68; H, 4.20; N, 6.23.

(*S*)-Oxiranemethanol 4-Methylbenzenesulfonate (Glycidyl Tosylate, 19).[63,64] This compound was prepared as previously described,[25] with

(57) The ca. 5% impurity seen in the NMR spectrum is related to an impurity in the geraniol, possibly a double-bond isomer.

(58) Nozoe, S.; Koike, Y.; Kusano, G. *Tetrahedron Lett.* **1984**, *25*, 1371.

(59) The ^{1}H NMR spectrum of **16** was identical with that of racemic glycidol obtained from Aldrich.

(60) Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557.

(61) Although having the *R* designation, this compound is homochiral with (*S*)-glycidol.

(62) Sowden, J. C.; Fischer, H. O. L. *J. Am. Chem. Soc.* **1942**, *64*, 1291. Data are for the (*S*)-enantiomer.

(63) Although having the *S* designation, the configuration of this compound is opposite to that of (*S*)-glycidol.

the following exception: the cold reaction mixture was worked up directly without prior warming to room temperature, in order to avoid substantial epoxide opening by chloride ion. The procedure is repeated here for convenience. Epoxidation of allyl alcohol was carried out as described above for glycidol (**16**) on a 1.0-mol scale with D-(−)-DIPT. After 6 h at −5 ± 2 °C, the mixture was cooled to −20 °C and carefully treated with 141 mL (148.9 g, 1.2 mol) of trimethyl phosphite, $P(OMe)_3$, added over a period of 1 h, taking care that the temperature did not rise above −20 °C. The reduction of hydroperoxide was carefully monitored.[65] Triethylamine (175 mL, 127 g, 1.26 mol) was then added, followed by addition of *p*-toluenesulfonyl chloride (200.4 g, 1.05 mol) as a solution in 250 mL of dichloromethane. The flask was stoppered and transferred to a freezer at −20 °C. After 10 h, the reaction mixture was filtered through a pad of Celite, washing with additional dichloromethane. The resultant yellow solution was washed with 10% aqueous tartaric acid, followed by saturated brine, dried over $MgSO_4$, and concentrated to afford an oil, from which volatile components (e.g., cumene, 2-phenyl-2-propanol, $P(OMe)_3$, $OP(OMe)_3$, etc.) were removed at 65 °C on a rotary evaporator equipped with a dry ice condenser.[66] The residue was filtered through a short pad of silica gel (ca. 1 g per g of crude oil), eluting with dichloromethane. Concentration gave a lemon yellow oil (193.5 g), which was dissolved in ca. 175 mL of warm Et_2O and crystallized by addition of petroleum ether (20 mL) and cooling, seeding with pure material.[67] The resulting off-white solid was recrystallized twice (Et_2O–petroleum ether), seeding, before refrigeration, each time with pure material. The tosylate (**19**) was obtained as large white prisms (91.7 g, 40%, 94% ee). Attempts to measure the ee directly, via ^1H NMR in the presence of chiral shift reagents, or by HPLC on a chiral stationary phase, proved unsuccessful. Therefore, tosylate **19** was converted to the corresponding iodohydrin, following the published procedure.[68] The crude iodohydrin was then directly esterified with (+)-MTPA chloride. The methoxy peaks of the two diastereomers exhibit nearly base line separation in the ^1H NMR (250 MHz) spectrum in C_6D_6. Alternatively, ee measurements have been made by chiral HPLC analysis of the Mosher ester (5% *i*-PrOH/hexane). **19**: mp 46–48.5 C; $[\alpha]^{25}_D$ +17.5° (*c* 2.13, $CHCl_3$); IR (KBr) 3075, 3000, 2935, 1598, 1362, 1195, 1180, 965, 915, 815, 775, 666, 558 cm^{-1}; NMR ($CDCl_3$) δ 7.81 (d, 2, J = 8 Hz), 7.36 (d, 2, J = 8 Hz), 4.26 (dd, 1, J = 3, 11.4 Hz), 3.95 (dd, 1, J = 6.0, 11.4 Hz), 3.16–3.23 (m, 1), 2.82 (t, 1, J = 5 Hz), 2.60 (dd, 1, J = 3, 5 Hz), 2.46 (s, 3). Anal. Calcd for $C_{10}H_{12}O_4S$: C, 52.62; H, 5.30. Found: C, 52.75; H, 5.29.

(*S*)-Oxiranemethanol *tert*-Butyldiphenylsilyl Ether (20).[63] The epoxidation of allyl alcohol was performed as described above for **16** on a 0.1-mol scale, in this case with D-(−)-DIPT. After 6 h at −5 ± 2 °C, the mixture was cooled to −20 °C and carefully treated with 18.0 mL (18.9 g, 0.15 mol) of trimethyl phosphite, $P(OMe)_3$, added over a period of 1 h, taking care that the temperature did not rise above −20 °C. The mixture was then treated with 16.7 mL (12.1 g, 0.12 mol) of triethylamine and a solution of 0.51 g (0.005 mol) of DMAP and 27.49 g (0.1 mol) of *tert*-butyldiphenylsilyl chloride in 200 mL of CH_2Cl_2. The flask was stoppered and transferred to a freezer at −20 °C. After 10 h, the reaction mixture was allowed to warm to room temperature and then filtered through a pad of Celite, washing with additional CH_2Cl_2. The resulting yellow solution was washed with saturated NH_4Cl solution, followed by saturated brine, dried over $MgSO_4$, and concentrated to afford an oil. The volatile components were removed under high vacuum (0.2 mmHg) at 65 °C by use of a Kugelrohr apparatus. The residue was then dissolved in 50 mL of Et_2O and treated with 10% NaOH in saturated brine.[51] The resulting biphasic solution was stirred vigorously at room temperature for 30 min. After the layers were separated, the organic phase was washed with saturated brine and dried over $MgSO_4$. Solvent was removed by rotary evaporator, and the resulting oil was distilled (0.1 mmHg, 138–140 °C) to give **20** as a clear, colorless viscous oil (14.1 g, 45%, 91% ee by Mosher ester analysis of the derived iodohydrin as described above for **19**). **20**: $[\alpha]^{25}_D$ −2.28° (*c* 9.07, $CHCl_3$); IR ($CHCl_3$) 2962, 2940, 2968, 1365, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.67–7.71 (m, 5), 7.35–7.45 (m, 5), 3.86 (dd, 1, J = 2.9, 12.5 Hz), 3.70 (dd, 1, J = 4.4, 12.5 Hz), 3.10–3.13 (m, 1), 2.73 (dd, 1, J = 3.3, 5.8 Hz), 2.60 (dd, 1, J = 3.3, 5.1 Hz), 1.06 (s, 9). Anal. Calcd for $C_{19}H_{24}O_2Si$: C, 73.03; H, 7.74. Found: C, 73.13; H, 7.88.

(*R*)-2-Methyloxiranemethanol 4-Nitrobenzoate (21).[61] The epoxidation of 2-methallyl alcohol was performed with L-(+)-DIPT as described above for **16**, except in this case, the reaction was maintained at −20 °C for 4.5 h and the scale was 1.0 mol. Quenching and esterification as described for **18**, followed by recrystallization first from ethyl ether and then from isopropyl ether, gave 184.8 g of **21** (78%, >98% ee by Mosher ester analysis of the thiophenyl diol as described above for **18**): mp 85.5–86.5 °C; $[\alpha]^{25}_D$ −5.87° (*c* 2.98, $CHCl_3$); IR (Nujol) 3120, 2960, 2930, 2860, 1720, 1610, 1530, 1465 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.2–8.4 (m, 4), 4.60 (d, 1, J = 11 Hz), 4.25 (d, 1, J = 11 Hz), 2.89 (d, 1, J = 4 Hz), 2.78 (d, 1, J = 4 Hz), 1.49 (s, 3). Anal. Calcd for $C_{11}H_{11}NO_5$: C, 55.69; H, 4.67; N, 5.91. Found: C, 55.70; H, 4.81; N, 5.81.

(*S*)-2-Methyloxiranemethanol 4-Methylbenzenesulfonate (22).[63] The epoxidation of 2-methallyl alcohol was performed as described above for **16**, except in this case at −20 °C and on a 10.0-mmol scale with D-(−)-DIPT. After 4.5 h, trimethyl phosphite (1.9 mL, 2.0 g, 16.0 mmol) was added carefully,[65,69] so as not to allow the reaction temperature to rise above −20 °C. Triethylamine (2.1 mL, 1.5 g, 14.8 mmol), DMAP[69] (150 mg, 1.2 mmol), and *p*-toluenesulfonyl chloride (1.91 g, 10.0 mmol, as a solution in 50 mL of CH_2Cl_2) were then added.

After 5 h at −10 °C, the sulfonylation reaction mixture was filtered through Celite and rinsed with additional CH_2Cl_2. The filtrate was washed with 10% tartaric acid, saturated $NaHCO_3$, and saturated NaCl, dried over $MgSO_4$, and concentrated to a yellow-orange oil. Cumyl alcohol (2-phenyl-2-propanol) and other volatiles were removed by Kugelrohr distillation (65–70 °C, 0.2 mmHg). The crude epoxy tosylate was chromatographed (EtOAc/hexane: 10% EtOAc, then 20% EtOAc) to afford **22** as a colorless oil (1.56 g, 69%, 95% ee by ^1H NMR shift analysis, and containing ca. 2% of the sulfinate byproduct). In 5% ethyl acetate/dichloromethane on silica TLC, the sulfonate derivative has an R_f of 0.54, while the sulfinate derivative has an R_f of 0.32. The sulfinate byproduct was removed by chromatography (1% EtOAc/CH_2Cl_2). The pure epoxy tosylate was obtained as a colorless oil: $[\alpha]^{25}_D$ +4.84° (*c* 4.19, $CHCl_3$); IR (film) 3060, 2990, 2930, 1600, 1362, 1192, 1180, 975, 820, 670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.80 (d, 2, J = 8 Hz), 7.36 (d, 2, J = 8 Hz), 4.05 (d, 1, J = 11 Hz), 3.93 (d, 1, J = 11 Hz), 2.70 (d, 1, J = 4.6 Hz), 2.64 (d, 1, J = 4.6 Hz), 2.46 (s, 3), 1.36 (s, 3). Anal. Calcd for $C_{11}H_{14}O_4S$: C, 54.53; H, 5.82. Found: C, 54.37; H, 5.89.

Also isolated (as a 1:1 mixture of diastereomers) from the reaction to form **22** was (*S*)-2-methyloxiranemethanol 4-methylbenzenesulfinate:[53] IR (film) 3060, 2980, 2935, 2880, 1600, 1495, 1450, 1400, 1135, 1083, 970, 815, 755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.61 (d, 2, J = 8 Hz), 7.60 (d, 2, J = 8 Hz), 7.35 (d, 2, J = 8 Hz), 7.34 (d, 2, J = 8 Hz), 4.07 (A of AB, 1, J = 11 Hz), 3.98 (A' of A'B', 1, J = 11 Hz), 3.54 (B' of A'B', 1 J = 11 Hz), 3.43 (B of AB, 1, J = 11 Hz), 2.62–2.72 (m, 4), 2.43 (s, 6), 1.38 (s, 3), 1.34 (s, 3). Anal. Calcd for $C_{11}H_{14}O_3S$: C, 58.40; H, 6.25. Found: C, 58.14; H, 6.18.

(*S*)-2-Methyloxiranemethanol 2-Naphthalenesulfonate (23).[63] The epoxidation of 2-methallyl alcohol was performed as described above for **16**, except in this case at −20 °C on a 50.0-mmol scale with D-(−)-DIPT. After 5 h the reaction was quenched by addition of trimethyl phosphite (7.3 mL, 7.68 g, 62 mmol) over a period of 1.5 h, being careful not to allow the reaction temperature to rise above −20 °C. Triethylamine (8.4 mL, 6.10 g, 60 mmol) and a solution of 2-naphthalenesulfonyl chloride (11.33 g, 50 mmol, purified by Soxhlet extraction with petroleum ether) in 30 mL of CH_2Cl_2 were then added.

After 10 h at −10 °C (refrigerated, unstirred), the reaction was worked up as described above for **22**, concentration giving 38.1 g of an orange-brown oil. Cumyl alcohol and other volatiles were removed by rotary evaporation under high vacuum (0.2 mmHg) at 65 °C, and the residue was passed through a short column of silica gel, eluting with CH_2Cl_2. Concentration and recrystallization twice from ether/petroleum ether gave **23** as a white solid (8.43 g, 60%; 92% ee by ^1H NMR shift analysis): mp 46–48 °C; $[\alpha]^{25}_D$ +5.9° (*c* 2.9, $CHCl_3$); IR (KBr) 3065, 3000, 2935, 1355, 1180, 975, 815, 665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.50 (br s, 1), 7.63–8.04 (m, 6), 4.11 (d, 1, J = 10.7 Hz), 3.99 (d, 1, J = 10.7

(64) This compound has previously been reported as the racemate. (a) Pierre, J.-L.; Arnaud, P. *Bull. Soc. Chim. Fr.* **1969**, 2868. (b) Chautemps, P.; Pierre, J.-L.; Arnaud, P. *C. R. Seances Acad. Sci., Ser. 3* **1968**, *266*, 622. This publication also describes the preparation of racemic epoxy crotyl tosylate. (c) Nakabayashi, N.; Masuhara, E.; Iwakara, Y. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 413. (d) Ichikawa, K. *Yuki Gosei Kagaku Kyokaishi* **1964**, *22*, 553.

(65) The use of an excessive amount of trimethyl phosphite is now strongly discouraged, as excess trimethyl phosphite present in the reaction mixture during tosylation results in formation of the sulfinate as a serious byproduct. It is now recommended that after addition of 1.0 equiv of $(MeO)_3P$, additional $(MeO)_3P$ should be added in portions of 0.05 equiv, carefully monitoring reduction of the hydroperoxide [TLC in 40% EtOAc/hexane; tetramethylphenylenediamine spray indicator (1.5 g in MeOH:H_2O:HOAc 128:25:1 mL)].

(66) On a smaller scale, removal of the volatile components by Kugelrohr distillation is preferred.

(67) Seeding greatly facilitates crystallization in this case. Seed crystals may be obtained by purifying a small portion of the crude oil by column chromatography (silica gel, EtOAc/hexane, 5–20% gradient elution).

(68) Cornforth, J. W.; Cornforth, R. H.; Mathew, K. K. *J. Chem. Soc.* **1959**, 112.

(69) The presence of DMAP reduces the amount of sulfinate formed. Its use is less critical if trimethyl phosphite addition is controlled carefully.

Hz), 2.70 (d, 1, J = 4.6 Hz), 2.64 (d, 1, J = 4.6 Hz), 1.37 (s, 3). Anal. Calcd for $C_{14}H_{14}O_4S$: C, 60.41; H, 5.07. Found: C, 60.21; H, 5.01.

(2*S*-*trans*)-3-Methyloxiranemethanol 4-Nitrobenzoate (24). The epoxidation was performed with L-(+)-DIPT as described above for **17**, in this case on a 1.0-mol scale at −20 °C. After 2 h, quenching and esterification (including workup and recrystallization) as described for **18** yielded **24** as brittle yellow needles (154 g, 65%, >98% ee by ^{1}H NMR shift analysis): mp 103.5–104 °C; $[\alpha]^{25}_D$ −48.5° (c 3.77, $CHCl_3$); IR ($CHCl_3$) 2980, 2935, 1734, 1611, 1350, 1275, 1100 cm^{-1}; ^{1}H NMR (C_6D_6) δ 7.68–7.76 (m, 4), 4.33 (dd, 1, J = 3.0, 12.3 Hz), 3.76 (dd, 1, J = 7.0, 12.3 Hz), 2.62 (ddd, 1, J = 1.9, 3.0, 7.0 Hz), 2.46 (dq, 1, J = 1.9, 5.6 Hz), 0.96 (d, 3, J = 5.6 Hz). Anal. Calcd for $C_{11}H_{11}NO_5$: C, 55.69; H, 4.67. Found: C, 55.54; H, 4.68.

An 85% yield of **24** was obtained when the reaction was performed at 1.0 M concentration on a 0.1-mol scale.

(2*R*-*trans*)-3-Methyloxiranemethanol 4-Methylbenzenesulfonate (25). The epoxidation was performed as described above for **17** on a 0.1-mol scale, in this case with D-(−)-DIPT. Quenching, esterification at −10 °C for 10 h, and workup as described for **22** were performed. Recrystallization twice of the crude oil (ether-petroleum ether) yielded **25** as white needles (17 g, 70%, 98% ee by ^{1}H NMR shift analysis): mp 61.5–62 °C; $[\alpha]^{25}_D$ +34.22° (c 3.29, $CHCl_3$); IR ($CHCl_3$) 2980, 2935, 1601, 1356, 1175, 1150 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.75 (d, 2, J = 8 Hz), 7.31 (d, 2, J = 8 Hz), 4.15 (dd, 1, J = 3.6, 11.8 Hz), 3.92 (dd, 1, J = 5.8, 11.8 Hz), 2.81–2.89 (m, 2), 2.40 (s, 3), 1.24 (d, 3, J = 4.6 Hz). Anal. Calcd for $C_{11}H_{14}O_4S$: C, 54.53; H, 5.82. Found: C, 54.68; H, 5.91.

(2*R*-*trans*)-3-Methyloxiranemethanol *tert*-Butyldimethylsilyl Ether (26). The epoxidation was performed as described above for **17** on a 0.1-mol scale, in this case with D-(−)-DIPT. Quenching and silylation were performed as described for **26** with 15.1 g (0.1 mol) of *tert*-butyldimethylsilyl chloride. After workup as described for **26** and removal of the solvent, the resulting oil was distilled (0.25 mmHg, 41–42 °C) to yield a clear, colorless liquid (11.6 g, 68%, 92% ee by Mosher ester analysis of the derived iodohydrin as described above for **19**): $[\alpha]^{25}_D$ +13.12° (c 7.53, $CHCl_3$); IR ($CHCl_3$) 2938, 2865, 1450, 1390, 1125, 1083 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.79 (dd, 1, J = 3.7, 12.5 Hz), 3.68 (dd, 1, J = 5.0, 12.5 Hz), 2.92 (dq, 1, J = 2.7, 4.6 Hz), 2.79–2.83 (m, 1), 1.32 (d, 3, J = 4.6 Hz), 0.90 (s, 9), 0.076 (s, 3), 0.069 (s, 3). Anal. Calcd for $C_{10}H_{22}O_2Si$: C, 59.35; H, 10.96. Found: C, 59.60; H, 11.30.

(2*S*-*cis*)-3-Methyloxiranemethanol 4-Nitrobenzoate (27). The epoxidation of *cis*-2-butenol was performed with L-(+)-DIPT as described above for **17**, except in this case on a 22.6-mmol (1.63 g) scale at −20 °C for 20 h. Quenching and esterification as described for **18** followed by recrystallization twice from ethyl ether gave **27** as a crystalline solid (4.64 g, 68%, 92% ee by ^{1}H NMR shift analysis): mp 69–72.5 °C; $[\alpha]^{25}_D$ −28.4° (c 1.76, $CHCl_3$); IR (Nujol) 2960, 2930, 2860, 1730, 1530, 1465, 1380 cm^{-1}; ^{1}H NMR (C_6D_6) δ 7.59–7.73 (m, 4), 4.27 (dd, 1, J = 4, 13 Hz), 3.96 (dd, 1, J = 8, 12 Hz), 2.87 (m, 1), 2.63 (m, 1), 0.88 (d, 3, J = 5 Hz). Anal. Calcd for $C_{11}H_{11}NO_5$: C, 55.69; H, 4.67; N, 5.91. Found: C, 55.68; H, 4.59; N, 5.78.

(*S*)-3,3-Dimethyloxiranemethanol 4-Nitrobenzoate (28). The epoxidation of 3-methyl-2-butenol was performed with L-(+)-DIPT as described above for **17**, except in this case on a 1.0-mol scale at −40 °C for 2 h, using 1.1 equiv of TBHP[54b] (260 mL of a 4.2 M CH_2Cl_2 solution). Quenching and esterification were performed as described for **18**, care being taken not to allow the reaction temperature to rise above room temperature. After workup as described for **18** and removal of solvent, one cold recrystallization[70] (−30 °C) gave **28** as fine, pale yellow needles, which were indefinitely stable at room temperature (175 g, 70%, >98% ee by analysis as described above for **18**): mp 109.5–110 °C; $[\alpha]^{25}_D$ −36.09° (c 4.94, $CHCl_3$); IR ($CHCl_3$) 2967, 2940, 1735, 1611, 1383, 1345, 1280, 1101 cm^{-1}; ^{1}H NMR (C_6D_6) δ 7.69–7.77 (m, 4), 4.39 (dd, 1, J = 3.7, 11.9 Hz), 4.03 (dd, 1, J = 7.3, 11.9 Hz), 2.83 (dd, 1, J = 3.7, 7.3 Hz), 1.05 (s, 3), 1.0 (s, 3). Anal. Calcd for $C_{12}H_{13}NO_5$: C, 57.36; H, 5.21; N, 5.58. Found: C, 57.54; H, 5.53; N, 5.53.

(*R*)-3,3-Dimethyloxiranemethanol 4-Methylbenzenesulfonate (29). The epoxidation of 3-methyl-2-butenol was performed as described above for **28**, in this case on a 0.01-mol scale with D-(−)-DIPT. Quenching, sulfonylation at −10 °C for 10 h, and workup as described for **22** gave **29** as a clear colorless liquid[71] (1.32 g, 55%, 93% ee by Mosher ester analysis of the derived iodohydrin as described above for **19**): $[\alpha]^{25}_D$ +20.15° (c 7.48, $CHCl_3$); IR ($CHCl_3$) 2975, 2940, 1735, 1603, 1450, 1355, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.82 (d, 2, J = 8.8 Hz), 7.37 (d, 2, J = 8.8 Hz), 4.06–4.17 (m, 2), 2.98 (t, 1, J = 5.3 Hz), 2.43 (s, 3), 1.27 (s, 3), 1.20 (s, 3). Anal. Calcd for $C_{12}H_{16}O_4S$: C, 56.23; H, 6.29. Found: C, 55.99; H, 6.37.

(*R*)-3,3-Dimethyloxiranemethanol 2-Naphthalenesulfonate (30). The epoxidation of 3-methyl-2-butenol was performed as described above for **28**, in this case on a 0.035-mol scale with D-(−)-DIPT. Quenching and sulfonylation were performed as described for **22**, taking care not to allow the reaction temperature to rise above room temperature. After workup as described above for **22** and removal of solvent, one cold recrystallization[70] (−30 °C) gave **30** as white needles, which were found to be unstable at room temperature[71] (4.1 g, 40%, analysis of enantiomeric purity was not successful): mp 64.5–65 °C; $[\alpha]^{25}_D$ +22.43° (c 3.57, $CHCl_3$); IR ($CHCl_3$) 2985, 2938, 1620, 1595, 1453, 1355, 1133 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.51 (d, 1, J = 3.1 Hz), 7.87–8.04 (m, 4), 7.26–7.73 (m, 2), 4.21 (dd, 1, J = 5.6, 10.9 Hz), 4.15 (dd, 1, J = 5.6, 10.9 Hz), 3.00 (t, 1, J = 5.6 Hz), 1.28 (s, 3), 1.21 (s, 3). Anal. Calcd for $C_{15}H_{16}O_4S$: C, 61.62; H, 5.52. Found: C, 61.80; H, 5.50.

(2*S*-*trans*)-3-Methyl-3-(4-methyl-3-pentenyl)oxiranemethanol Acetate (2,3-Epoxygeraniol Acetate, 31). The epoxidation was performed as described above for **14**, although here care was not taken to reduce the exotherm upon addition of the substrate, leading to slightly lower than optimal selectivity. In this case, the reaction was performed on 1.0 g (6.4 mmol) of geraniol at −20 to −10 °C for 15 min. Then, triethylamine (2 mL, 11.5 mmol), acetic anhydride (1.2 mL, 12 mmol), and DMAP (50 mg, 0.40 mmol) were added, and the reaction mixture was allowed to warm to room temperature. After 15 min, TLC showed no epoxy alcohol. Filtration through Celite, evaporation of solvent, dilution with 40 mL of ether, and washing first with 5% H_2SO_4 (3 × 5 mL) and then with 3 M pH 7 buffer (Na/K phosphate, 5 mL[72]) gave a clear, colorless solution. Drying of the organic phase over $MgSO_4$ and concentration gave an oil, which was Kugelrohr distilled (100 °C, 0.15 mmHg) to give epoxy acetate **31** as a colorless oil (1.36 g, 99%, chemical purity >95% by ^{1}H NMR, 86% ee by ^{1}H NMR shift analysis): $[\alpha]^{25}_D$ −26.9° (c 10, $CHCl_3$) (lit.[73] $[\alpha]^{25}_D$ −24.8° [c 1.5, $CHCl_3$]); IR (film) 2960, 2920, 2860, 1735, 1430, 1370, 1230, 1070, 1030, 980, 880, 835 cm^{-1}; ^{1}H NMR (C_6D_6) δ 5.1 (br t, 1, J = 8 Hz), 4.17 (dd, 1, J = 4, 11 Hz), 3.95 (dd, 1, J = 5, 11 Hz), 2.88 (dd, 1, J = 4, 5 Hz), 2.0 (br q, 2, J = 8 Hz) 1.65 (s, 3), 1.63 (br s, 3), 1.48 (br s, 3), 1.2–1.6 (m, 2), 1.04 (s, 3).

General Procedure for the Kinetic Resolution of Secondary Allylic Alcohols. To a room temperature solution of the allylic alcohol (1.0 equiv) and the tartrate ester (0.15 equiv) in CH_2Cl_2 (0.25 M in substrate) were added powdered and activated 3A sieves (20–30 wt % based on allylic alcohol) and a saturated hydrocarbon internal standard, (*n*-decane, 40 μL/1.0 mmol of substrate) for GC monitoring of percent conversion. The stirred mixture, maintained under an inert atmosphere, was cooled to −10 to −20 °C, treated with Ti(O-*i*-Pr)$_4$ (0.10 equiv) and allowed to stir for about 20 to 30 min at −20 °C. During this time, a small aliquot (ca. 100 μL) was removed, diluted with 100 μL of ether, and quenched into an aqueous solution of $FeSO_4$ and citric acid prepared as described in general workup A, to provide a T_0 GC sample. The reaction was then treated with a solution of TBHP in isooctane (0.7 equiv, 4.5 M, dried with freshly activated 3A pellets for 30 min prior to addition) added by gastight syringe. The reaction was stirred at −20 ± 2 °C (maintained by constant temperature bath (NesLab Cryocool)) and monitored by GC. It has been noted[54e] that stirring improved both the reaction rate and percent ee. After more than 50% conversion, the reaction was quenched (Workup A) with an aqueous solution of $FeSO_4$ and citric acid at −20 °C and stirred vigorously without cooling for 30 min until two clear phases appeared. The phases were separated and the aqueous phase was extracted twice with dichloromethane.

If diisopropyl tartrate (DIPT) was used, the combined organic phases were concentrated to approximately the original volume and then stirred for 30 min with 30% NaOH in brine (1.0 mL/1.0 mmol of substrate) to hydrolyze the DIPT.[47] After phase separation and extraction, the combined organic phases were washed with saturated brine and dried ($MgSO_4$). The crude product was then purified by flash chromatography on silica gel (20% EtOAc/hexane). Removal of dicyclohexyl tartrate or dicyclododecyl tartrate can be effected either by distillation if the product is more volatile than the tartrate or by flash chromatography (20% EtOAc/hexane). NMR analysis (C_6D_6) of the ester derived from (+)-MTPA chloride indicated the given selectivity.

Kinetic Resolution of 2-Methyl-1-hepten-3-ol (32) with (+)-DIPT.

(70) A cold recrystallization was performed because the solution of this epoxy prenyl derivative in ether appears unstable when heated above room temperature. The crude material is simply dissolved in ether and placed in the freezer.

(71) The aryl sulfonate derivatives of epoxy prenyl alcohol demonstrate marked instability, the tosyl derivative decomposing at room temperature within 1 week and the naphthalenesulfonate derivative decomposing within 12 h at room temperature. However, the authors believe that both these compounds can be used successfully in a synthetic sequence if the compounds are either stored cold or used immediately.

(72) The 3 M pH 7 phosphate buffer was prepared by mixing 1.5 mol of Na_2HPO_4, 1.5 mol of KH_2PO_4, and sufficient water to make up one liter of solution.

(73) Hanson, R. M. *Tetrahedron Lett.* **1984**, *25*, 3783.

The reaction was performed on a 3.0 mmol scale (384 mg). After 27 h, GC analysis indicated that 53% of the allylic alcohol had been consumed. Ferrous sulfate workup followed by basic brine treatment as described above (General Procedure) provided (*R*)-(+)-2-methyl-1-hepten-3-ol (168 mg after chromatography, 93% yield based on percent conversion, 93.7% ee). $[\alpha]^{25}_D$ +3.64° (*c* 2.06, EtOH) (lit.[5] $[\alpha]^{23}_D$ +3.24° [*c* 4.07, EtOH]).

Kinetic Resolution of 2-Methyl-1-hepten-3-ol (32) with (+)-DCHT. The reaction was performed on a 3.0 mmol scale. After 29 h (52% conversion), ferrous sulfate workup as described above (General Procedure) provided (*R*)-allylic alcohol **32** (170 mg after chromatography, 92% yield based on percent conversion, 96.8% ee). $[\alpha]^{25}_D$ +3.84° (*c* 2.24, EtOH).

Kinetic Resolution of 2-Methyl-1-hepten-3-ol (32) with (+)-DCDT. The reaction was performed on a 3.0 mmol scale. After 24 h (53% conversion), ferrous sulfate workup as described above (General Procedure) provided (*R*)-allylic alcohol **32** (160 mg after chromatography and 89% yield based on percent conversion, >98% ee). $[\alpha]^{25}_D$ +4.19° (*c* 2.36, EtOH).

Kinetic Resolution of (*E*)-1-Cyclohexyl-2-buten-1-ol (33) with (+)-DIPT. The reaction was performed on a 2.0 mmol scale (308 mg). After 15 h (54% conversion), ferrous sulfate workup followed by basic brine treatment as described above (General Procedure) provided (*R*)-allylic alcohol **33** (136 mg after chromatography, 96% yield based on percent conversion, 94% ee). $[\alpha]^{25}_D$ −13.33° (*c* 2.76, EtOH) (lit.[5] $[\alpha]^{23}_D$ −14.6° [*c* 4.38, EtOH]).

Kinetic Resolution of (*E*)-1-Cyclohexyl-2-buten-1-ol (33) with (+)-DCHT. The reaction was performed on a 2.0 mmol scale. After 16 h (52% conversion), ferrous sulfate workup as described above (General Procedure) provided (*R*)-allylic alcohol **33** (136 mg after chromatography, 92% yield based on percent conversion, 95% ee). $[\alpha]^{25}_D$ −13.24° (*c* 2.62, EtOH).

Kinetic Resolution of (*E*)-1-Cyclohexyl-2-buten-1-ol (33) with (+)-DCDT. The reaction was performed on a 2.0 mmol scale. After 16 h (52% conversion), ferrous sulfate workup as described above (General Procedure) provided (*R*)-allylic alcohol **33** (122 mg after chromatography, 82% yield based on percent conversion, >98% ee). $[\alpha]^{25}_D$ −13.62° (*c* 3.15, EtOH).

Kinetic Resolution of 1-Cyclohexene-1-ethanol (34) with (+)-DIPT. The reaction was performed on a 3.0 mmol scale (378 mg). After 3.5 h (63% conversion), ferrous sulfate workup followed by basic brine treatment as described above (General Procedure) provided (*R*)-allylic alcohol **34** (130 mg after chromatography, 93% yield based on percent conversion, >98% ee). $[\alpha]^{20}_D$ +3.29° (*c* 2.49, EtOH) (lit.[5] $[\alpha]^{23}_D$ "−2.88°" should read "+2.88°" [*c* 3.33, EtOH]).

Kinetic Resolution of 1-Cyclohexene-1-ethanol (34) with (+)-DCHT. The reaction was performed on a 3.0-mmol scale. After 3.5 h (63% conversion), ferrous sulfate workup as described above (General Procedure) provided (*R*)-allylic alcohol **34** (120 mg after chromatography and Kugelrohr distillation, 86% yield based on percent conversion, >98% ee). $[\alpha]^{23}_D$ +3.57° (*c* 1.40, EtOH).

Kinetic Resolution of 1-Cyclohexene-1-ethanol (34) with (+)-DCDT. The reaction was performed on a 3.0 mmol scale. After 4 h (66% conversion), ferrous sulfate workup as described above (General Procedure) provided (*R*)-allylic alcohol **34** (110 mg after chromatography and Kugelrohr distillation, 85% yield based on percent conversion, >98% ee). $[\alpha]^{23}_D$ +3.16° (*c* 1.96, EtOH).

Kinetic Resolution of 1-Nonen-3-ol (35) with (+)-DIPT. The reaction was performed at −22 ± 2 °C on a 2.0-mmol scale (284 mg), using 60 μL (0.2 mmol) of Ti(O-*i*-Pr)$_4$ and 190 μL (1.1 mmol) of TBHP/isooctane[54b] in 8 mL of CH_2Cl_2. After 13 days (51% conversion), ferrous sulfate workup followed by basic brine treatment as described above (General Procedure) provided (*R*)-allylic alcohol **35** (128 mg after chromatography, 92% yield based on percent conversion, 86% ee). $[\alpha]^{25}_D$ −14.9° (*c* 1.13, EtOH) [lit.[5] $[\alpha]^{25}_D$ −19.1° (*c* 6.7, EtOH)].

Kinetic Resolution of 1-Nonen-3-ol (35) with (+)-DCHT. The reaction was performed on a 2.0-mmol scale. After 7.5 days (55% conversion), ferrous sulfate workup as described above (General Procedure) provided (*R*)-allylic alcohol **34** (117 mg after chromatography, 91% yield based on percent conversion, >98% ee). $[\alpha]^{25}_D$ −17.0° (*c* 0.96, EtOH). The reaction using 1.5 equiv of TBHP was performed analogously. After 63 h (65% conversion), ferrous sulfate workup as described above (General Procedure) gave an 80% yield of material of 95% ee.

Kinetic Resolution of 1-Nonen-3-ol (35) with (+)-DCDT. The reaction was performed on a 2.0-mmol scale. After 11 days (66% conversion), ferrous sulfate workup as described above (General Procedure) provided (*R*)-allylic alcohol **34** (95 mg after chromatography and precipitation of most of the crystalline DCDT impurity with hexane, 99% yield based on percent conversion, contaminated by a small amount of DCDT, >98% ee).

Reaction Using a Large Excess of Tartrate. Three reactions were carried out simultaneously in the same cooling bath, performed as described above for **2**, differing only in the amount of L-(+)-diethyl tartrate employed. In each reaction, 0.40 g (4.0 mmol) of (*E*)-2-hexen-1-ol, 57 mg (0.20 mmol) of Ti(O-*i*-Pr)$_4$, 2.0 mL of TBHP (8.0 mmol, 4.0 M, toluene), and 0.5 g of powdered 4A molecular sieves were used. The amount of L-(+)-diethyl tartrate used in each reaction was as follows: (A) 168 mg (0.80 mmol), (B) 82 mg (0.40 mmol), (C) none. In addition, 70 mg of dodecane was added to each reaction as a GC internal standard. The reactions were carried out at −30 °C for 2 h and then allowed to warm to −24 °C. Monitoring of the reactions by GC (100-μL aliquots were removed and quenched with saturated aqueous Na_2SO_4 and Et_2O; 20–30 m fused silica SE-30 capillary column) gave the results presented in Figure 1.

Effect of Molecular Sieves on the Catalytic Asymmetric Epoxidation. Three reactions were carried out simultaneously in the same cooling bath, performed as described above for **2**, differing only in the amount of L-(+)-diethyl tartrate and molecular sieves employed. In each reaction, 0.40 g (4.0 mmol) of (*E*)-2-hexen-1-ol, 57 mg (0.20 mmol) of Ti(O-*i*-Pr)$_4$, and 0.79 mL of TBHP (4.4 mmol, 5.6 M, CH_2Cl_2) were used. The amount of L-(+)-diethyl tartrate used in each reaction was as follows: (A) 50 mg (0.24 mmol), (B) 50 mg (0.24 mmol), (C) none. The amount of powdered 4A molecular sieves used in each reaction was as follows: (A) 0.5 g, (B) none, (C) none. In addition, 70 mg of dodecane was added to each reaction as a GC internal standard. The reactions were carried out at −20 °C. Monitoring of the reactions by GC (100-μL aliquots were removed and quenched with saturated aqueous Na_2SO_4 and Et_2O; 20–30 m fused silica SE-30 capillary column) gave the results presented in Figure 2.

Effect of Water on the Catalytic Asymmetric Epoxidation. Two reactions were carried out simultaneously in the same cooling bath as follows: To 15 mL of CH_2Cl_2 in a 25-mL flask at −2 °C were added 124 mg (0.60 mmol) of L-(+)-diethyl tartrate and 142 mg (0.50 mmol) of Ti(O-*i*-Pr)$_4$. After 10 min at 0 °C, 9.0 μL (0.50 mmol) of water was added via a glass capillary. The mixture was stirred vigorously at 0 °C until the mixture was homogeneous (30 min). At this point, half of the solution, "B", was transferred to a second flask (also at 0 °C) containing 100 mg of 4A molecular sieves, leaving solution "A" with no sieves. Both solutions were stirred a further 45 min at 0 °C, and then each was cooled to −10 °C and treated with 0.88 mL of TBHP (5.0 mmol, 5.7 M in CH_2Cl_2). After the mixture stood for 40 min at −10 °C, 0.42 g (2.5 mmol) of (*E*)-2-undecen-1-ol was added to each flask. After 20 h at −10 °C the reactions were quenched as described for **2**. ^{1}H NMR indicated that reaction "A", without sieves, was only 30% complete (4% ee), while reaction "B" was >90% complete (88% ee).

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Registry No. **1**, 89321-71-1; **2**, 99745-00-3; **3**, 101976-99-2; **4**, 104196-23-8; **5**, 1885-07-0; **6**, 106948-05-4; **7**, 107033-43-2; **8**, 96249-61-5; **9**, 78513-07-2; **10**, 106948-06-5; **11**, 88424-62-8; **12**, 107033-44-3; **13**, 107033-45-4; **13** (*p*-nitrobenzoate), 106948-11-2; **14**, 82188-73-6; **15** (isomer 1), 74963-01-2; **15** (isomer 2), 88424-61-7; **16**, 60456-23-7; **17**, 50468-21-8; **18**, 106268-95-5; **19**, 70987-78-9; **20**, 107033-46-5; **21**, 106268-96-6; **22**, 106948-07-6; **23**, 106948-08-7; **24**, 106268-97-7; **25**, 107033-47-6; **26**, 107078-95-5; **27**, 107033-48-7; **28**, 106268-98-8; **29**, 106948-09-8; **30**, 106948-10-1; **31**, 91048-16-7; (±)-**32**, 79605-66-6; (*R*)-**32**, 79646-47-2; (±)-**33**, 79605-62-2; (*R*)-**33**, 79646-42-7; (±)-**34**, 79646-40-5; (*R*)-**34**, 79605-68-8; (±)-**35**, 79605-61-1; (*R*)-**35**, 79646-41-6; DCHT, 83071-79-8; DCDT, 99686-57-4; TBHP, 75-91-2; D-(−)-DIPT, 62961-64-2; Ti(O-*i*-Pr)$_4$, 546-68-9; $CH_3(CH_2)_{13}C(=CH_2)COOCH_3$, 73472-08-9; (*E*)-PhCH=C(CH_3)CHO, 15174-47-7; (*E*)-PhCH=C(Ph)CH_2OH, 22835-64-9; (*E*)-PhCH=C(Ph)CO_2H, 91-48-5; (*Z*)-4-(benzyloxymethyl)-2-butenol, 81028-03-7; (*Z*)-2-buten-1,4-diol, 6117-80-2; 2-propyl-2-propenol, 4364-51-6; 2-propyl-2-propenal, 1070-13-9; 2-tetradecyl-2-propenol, 88393-66-2; (*E*)-2-methyl-3-phenyl-2-propenal, 55131-20-9; 1-acetyl-1-cyclohexene, 932-66-1; (±)-(*E*)-1-cyclohexyl-2-buten-1-ol, 79605-62-2; (*E*)-2-butenal, 123-73-9; (*E*)-2-undecenol, 75039-84-8; (*E*)-2-decen-1-ol, 18409-18-2; L-(+)-diisopropyl tartrate, 2217-15-4; (*E*)-3-phenyl-2-propenol, 4407-36-7; (*E*)-3-(4-nitrophenyl)-2-propenol, 35271-56-8; (*E*)-3-(4-bromophenyl)-2-propenol, 105515-33-1; (*Z*)-2-methyl-3-phenyl-2-propenol, 39924-63-5; 1-cyclohexenylmethanol, 4845-04-9; (*E*)-3,7-dimethyl-2,6-octadien-1-ol, 106-

24-1; allyl alcohol, 107-18-6; (s)-2-methyloxiranemethanol 4-methylbenzenesulfinate (isomer 1), 106948-12-3; (s)-2-methyloxiranemethanol 4-methylbenzenesulfinate (isomer 2), 106948-13-4; cyclohexyl bromide, 108-85-0; cyclododecanol, 1724-39-6; L-(+)-diethyl tartrate, 87-91-2; (E)-2-hexen-1-ol, 928-95-0; (Z)-2-decen-1-ol, 4194-71-2; (Z)-2-undecen-1-ol, 75039-83-7; cumene hydroperoxide, 80-15-9; (E)-2-buten-1-ol, 504-61-0; p-nitrobenzoyl chloride, 122-04-3; tert-butyldiphenylsilyl chloride, 58479-61-1; 2-methyl-2-propen-1-ol, 513-42-8; 2-naphthalenesulfonyl chloride, 93-11-8; 3-methyl-2-buten-1-ol, 556-82-1; geraniol, 106-24-1.

Mechanism of the Gas-Phase Thermolysis of Monomethylsilane

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Abstract: The thermolysis of monomethylsilane (MMS) has been studied as a function of pressure (33–400 Torr), temperature (340–440 °C), and conversion. Under conditions of very low (typically, 0.5%) conversion and in a carefully seasoned vessel the major products are H_2 and dimethyldisilane (DMDS). Dimethylsilane (DMS) comprises ~5% of the major products. MMS-d_3 generates D_2 exclusively. In the presence of ~10% C_2H_4 the yields of H_2 and DMDS are considerably reduced and both products follow first-order kinetics in their formation. Also, the formation of DMS is completely suppressed, and the Arrhenius parameters for the molecular process $CH_3SiH_3 \rightarrow CH_3\ddot{S}iH + H_2$ (1a) when determined from the rate of H_2 production and from ($CH_3\ddot{S}iH + CH_3SiH_3 \rightarrow$ DMDS) production are $\log k_{1a} = (15.02 \pm 0.10) - (63270 \pm 310)/2.3RT$ and $(14.87 \pm 0.12) - (63150 \pm 350)/2.3RT$, respectively. The "molecular" rate constant for H_2, however, includes a small contribution from radical processes that cannot be completely suppressed. When the latter expression for k_{1a} is used, the rate data for H_2 in the unscavenged reaction can be fitted to a mechanism incorporating a second primary step, a slow, surface-catalyzed reaction generating H• and CH_3SiH_2• radicals, which then set up a short chain:

$$CH_3SiH_2^\bullet + CH_3SiH_3 \rightarrow DMDS + H$$

$$H + CH_3SiH_3 \rightarrow H_2 + CH_3SiH_2^\bullet$$

On the basis of kinetic analysis of the data it is concluded that the chain is terminated linearly by CH_3SiH_2• radicals at the surface, with $\log A\ (s^{-1}) = 11.7$ and $E_a \approx 32.3$ kcal mol^{-1}. The derived rate expression for the surface-catalyzed radical initiation step $CH_3SiH_3 \rightarrow CH_3SiH_2^\bullet + H$ (1b) is $\log k_{1b} = 12.7 - 57900/2.3RT$. From the measured kinetic data the following thermochemical values were derived: $D(CH_3\dot{S}iH\text{–}H) = 73.5$ kcal mol^{-1} and $\Delta H_f(CH_3\ddot{S}iH) = 51.9$ kcal mol^{-1}.

Several studies on the kinetics and mechanism of the thermal unimolecular decomposition of monomethylsilane (MMS) are documented in the literature; yet, to date, the reader is confronted by a number of puzzling discrepancies in the reported data and conclusions. This can be readily visualized from the following chronological summary of findings.

Kohanek, Estacio, and Ring (KER)[1] carried out the flow thermolysis of MMS at 520 °C and found the products to be H_2, 1,2-dimethyldisilane (DMDS), and dimethylsilane (DMS) along with a small amount of CH_4, in relative ratios of 1.0, 0.6, 0.2, and ~0.02, respectively. One year later, in 1970, Ring, Puentes, and O'Neal (RPO)[2] reported that the hydrogen fraction from the flow thermolysis of a mixture of MMS and MMS-d_3 at 510–515 °C and 10–15 Torr consisted of 28.32% D_2, 16.21% HD, and 51–52% H_2. From these and similar results using SiH_4/SiD_4 mixtures they concluded that the two primary processes initiating the decomposition of MMS are

$$CH_3SiH_3 \rightarrow CH_3\ddot{S}iH + H_2 \qquad (1a)$$

$$CH_3SiH_3 \rightarrow CH_3SiH_2^\bullet + H^\bullet \qquad (1b)$$

At the same time, Davidson[3] carried out some experiments in a static system at 527–627 °C and suggested that Si–C cleavage was also taking place:

$$CH_3SiH_3 \rightarrow CH_3^\bullet + SiH_3^\bullet \qquad (1c)$$

As part of our ongoing research program on the thermal and photochemical behavior of silicon hydrides we have examined the static-system thermolysis of MMS in detail and we (NS) reported our preliminary findings in 1978.[4] In brief, the thermolysis of MMS at 40–400 Torr and 340–440 °C generated H_2 and DMDS in approximately equal yields and DMS as a minor (~5%) product under strict conditions of low (<1%) conversion and inert (seasoned) reaction surfaces. CH_4 was not a product. Using C_2H_4 as a radical scavenger, we determined from measurements of H_2 the following Arrhenius parameters for step 1a:

$$\log k_{1a}\ (s^{-1}) = (14.95 \pm 0.11) - (63200 \pm 330)/2.3RT$$

The same coefficients were obtained from the measurement of the DMDS product arising via the reaction

$$CH_3\ddot{S}iH + CH_3SiH_3 \rightarrow (CH_3SiH_2)_2 \qquad (2)$$

The radical reaction 1b is probably surface catalyzed and initiates a moderately long chain reaction wherein, in the absence of C_2H_4, large amounts of additional H_2 and DMDS are generated. Thermolysis of MMS-d_3 generated D_2 exclusively.

Subsequently, Davidson and Ring (DR)[5] studied the very low pressure (10^{-1}–10^{-2} Torr) static thermolysis of MMS at 569 and 727 °C using mass spectrometric detection for H_2 and CH_4. The Arrhenius parameters obtained for the decomposition of MMS in the range 625–727 °C

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