always resulted in poorer yields with starting matrial being recovered, even after stirring for several days, as an inseparable mixture with the product. Alternatively, the title compound could be prepared in 21% yield by the treatment of **10** with 1 equiv of PhSLi in THF at 0 °C.

3,7a-Dimethyl-3-hydroxy-2,3,3a,4,5,6,7,7a-octahydro-1*H*-inden-4-one (12). A mixture of methyllithium (3.15 mmol, 2.25 mL) and cuprous iodide (3.00 mmol, 570 mg) in Et_2O (10 mL) was stirred for 20 min at −40 °C and cooled to −78 °C. Boron trifluoride etherate (425 mg, 3.00 mmol) was added to the solution, and the resulting mixture was stirred for 5 min before the enedione **10** (1.00 mmol, 166 mg, in 2 mL of Et_2O) was added. The yellow-tan heterogeneous mixture was warmed to ambient temperature before being quenched with saturated NH_4Cl. Ether was added, and the organic layer was washed with saturated NH_4Cl and dried ($MgSO_4$). Analytical TLC indicated that the starting material had been completely consumed, and two new spots were observed (R_f 0.10 and 0.28, 20% EtOAc/hexanes, non-UV active, green spots with *p*-anisaldehyde spray). Flash chromatography of the crude mixture provided the product as a mixture of three isomers (58% yield). The slow moving isomer had the following spectral characteristics: IR (neat) 3411 (br, s), 2949 (s), 2870 (m), 1694 (s), 1462 (m), 1418 (m), 1375 (m), 1296 (m), 1233 (m), 1148 (m), 1117 (m); ^1H NMR δ 1.50–2.65 (m, 12 H), 1.21 (s, 3 H, Me), 1.17 (s, 3 H, Me); high-resolution mass spectrum calcd for $C_{11}H_{18}O_2$ 182.1307, obsd 182.1308. The fast moving isomers had the following spectral characteristics: IR (neat) 3414 (br, s), 2949 (s), 2868 (m), 1684 (s), 1456 (m); ^1H NMR δ 2.25–2.45 (m, 1 H), 1.2–2.6 (m, 11 H), 1.43 and 1.35 (2 s, 3 H combined, Me α to OH), 1.10 and 1.04 (2 s, 3 H combined, Me); high-resolution mass spectrum calcd for $C_{11}H_{18}O_2$ 182.1307, obsd 182.1308.

Acknowledgment. We thank the National Institutes of Health for financial support and Dr. Alvin Marcus for recording the mass spectra.

Arenesulfonate Derivatives of Homochiral Glycidol: Versatile Chiral Building Blocks for Organic Synthesis

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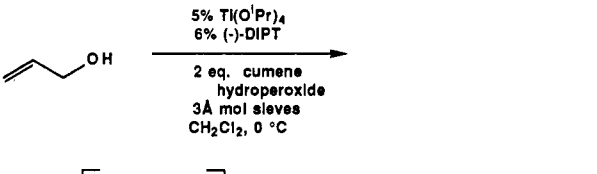
The preparation of a series of crystalline arenesulfonate derivatives of enantiomerically enriched glycidol is described. The enhancement of optical purity by recrystallization was particularly successful for two of these derivatives, glycidyl tosylate and glycidyl 3-nitrobenzenesulfonate, which were obtained in 97% ee and 99% ee, respectively. Very high regioselectivity was observed in the reactions of these compounds with a variety of nucleophiles, including aryl oxides, Et_2AlCN, organometallic reagents, and BH_3–$NaBH_4$. The application of this methodology to the synthesis of homochiral β-adrenergic blocking agents and homochiral terminal epoxides is discussed.

Homochiral glycidol (1) and related C_3-synthons have found widespread application as chiral building blocks for asymmetric synthesis.[1] Although D-mannitol has traditionally served as the ultimate precursor for many of these compounds, glycidol of high optical purity may now be more conveniently prepared by the catalytic asymmetric epoxidation of allyl alcohol.[2] However, this parent allylic alcohol is epoxidized with somewhat lower (i.e. ~90% ee) enantioselectivity than the ≥95% ee realized for most substituted allylic alcohols. This fact, in addition to special problems associated with the isolation and purification of the unstable and water-soluble product, prompted us to investigate the preparation of crystalline derivatives of glycidol, which would potentially enable the enhancement of optical purity by recrystallization. Work with two such compounds, glycidyl tosylate and glycidyl *p*-nitrobenzoate, has appeared elsewhere.[3] Here we report, in full, an investigation of the preparation and reactions of arenesulfonate derivatives of glycidol.

Preparation. Glycidyl arenesulfonates were initially prepared by treatment of glycidol with a sulfonyl chloride and triethylamine in toluene or methylene chloride at −10 °C, according to the literature procedure.[4] All derivatives were prepared in both racemic and enantiomerically enriched forms, the requisite optically active glycidol being prepared by catalytic asymmetric epoxidation of allyl alcohol.[2] Later, nonracemic glycidyl arenesulfonates were prepared more conveniently by in situ derivatization of enantiomerically enriched glycidol (eq 1),[2] a procedure that is particularly advantageous for the preparation of large quantities of a single derivative.[5]



Physical data for the glycidyl arenesulfonates that were prepared are presented in Table I. The data provided for

(1) (a) For a review see: Jurczak, J.; Pikul, S.; Bauer, T. *Tetrahedron* **1986**, *42*, 447. (b) For recent uses of glycidol, see: Burgos, C. E.; Ayer, D. E.; Johnson, R. A. *J. Org. Chem.* **1987**, *52*, 4973. 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. Baldwin, J. J.; McClure, D. E.; Gross, D. M.; Williams, M. *J. Med. Chem.* **1982**, *25*, 931. (c) For uses of glycidol derivatives, see: Takano, S.; Iwabuchi, Y.; Ogasawara, K. *J. Am. Chem. Soc.* **1987**, *109*, 5523. Bouzoubaa, M.; Leclerc, G.; Rakhit, S.; Andermann, G. *J. Med. Chem.* **1985**, *28*, 896. Lipshutz, B. H.; Kozlowski, J. A. *J. Org. Chem.* **1984**, *49*, 1147. Hardy, J.-C.; Villatte, G.; Gueremy, C. *Bull. Soc. Chem. Fr.* (*Pt. 2*) **1982**, 304.

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

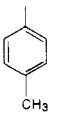
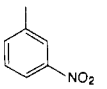
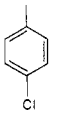
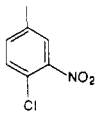
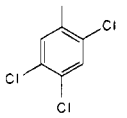
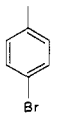
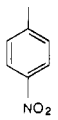
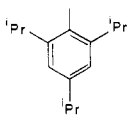
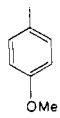
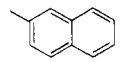
(3) (a) Klunder, J. M.; Ko, S. Y.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 3710. (b) Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Org. Chem.* **1987**, *52*, 667.

(4) (a) Nakabayashi, N.; Masuhara, E.; Iwakura, Y. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 413. (b) Chautemps, P.; Pierre, J.-L.; Arnaud, P. *C. R. Seances Acad. Sci., Ser. 3* **1968**, *266*, 622.

(5) (*R*)- and (*S*)-Glycidol of ≥88% ee have recently become commercially available (ARCO, Aldrich Chemical Co.), rendering the in situ derivatization procedure less advantageous.

0022-3263/89/1954-1295$01.50/0

Table I. Arenesulfonate Derivatives of Glycidol

compd	Ar	racemate mp, °C	optically enriched			
			mp, °C	config	$[\alpha]_D$ ($CHCl_3$)	ee, %
2a		37.5–39	47.5–48.5	*S*	+18.1	97
2b		42–50	63–64	*S*	+23.0	99
2c		52–53	61–62.5	*S*	+22.6	95
2d		50–52.5	55–55.5	*S*		94
2e		104–105	100–102	*S*	+15.5	88
2f		45.5–49.5	55–56.5	*S*	+20.1	88
2g		91–93	84–86	*S*	+26.5	82
2h		73.5–75	65–67	*S*	+11.35	86
2l		45–47	32–34	*R*	−16.6	79
2j		58–60	34–39	*S*	+14.7	

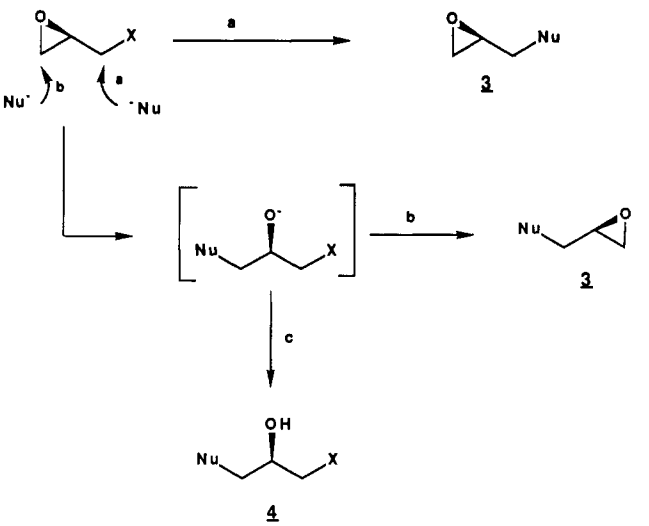
optically active compounds refer to products obtained after several recrystallizations. Although all of these derivatives are crystalline compounds, the enantiomeric excess could be enhanced for only a few, and compounds **2e–j** were never obtained in greater than 89% ee. In fact, in at least two instances (**2g**, **2j**) a decrease in optical rotation was observed upon repeated recrystallization. Glycidyl 3-nitrobenzenesulfonate (**2b**) represents a significant improvement over other derivatives, achieving 99% ee in just two to three recrystallizations.

While there appeared to be no reliable way to predict which of these compounds would recrystallize to higher enantiomeric excess, it is interesting to note that the more successful derivatives (**2a–c**) exhibit higher melting points in enantiomerically enriched form than in racemic form. The reverse is true for many glycidyl arenesulfonates.

Reactions. The termini of the arenesulfonates of glycidol offer two potential sites of electrophilic reactivity.[6]

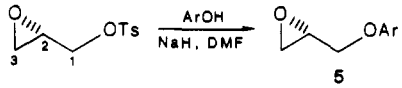
(6) Nucleophilic attack at the central carbon is also possible, of course, and attack at this position has been observed to a small extent under some acidic reaction conditions. However, this position is deactivated by both steric and electronic factors, and the contribution of C-2 attack to the product ratio is usually negligible.

Scheme I

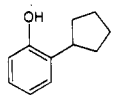
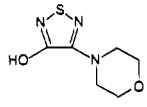


This issue of C-1 vs C-3 regioselectivity is generally a moot point when racemic materials are used. As illustrated in

Table II



5

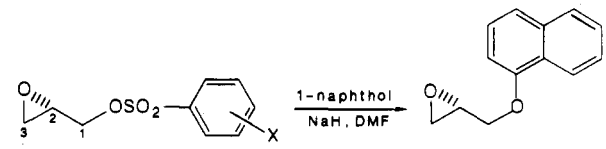
ArOH	product	yield, %	% ee (SM)	% ee (prod)	selectivity C-1:C-3
	**5a**	84	85	80	97:3
	**5b**	89	88	85	98:2
	**5c**	84	88	86	99:1
	**5d**	72	88	82	97:3

Scheme I, when initial epoxide opening (C-3 attack) is followed by displacement of the leaving group X (path b), the product is indistinguishable from that resulting from direct displacement of X by the nucleophile (path a). Only when the intermediate alkoxide is trapped before displacement of the leaving group occurs (path c) can the actual course of the reaction be determined. Even in this case, modest selectivity may often be tolerated since the products **3** and **4** are usually easily separated. In addition, **4** may be converted to the epoxide by simple treatment with base, so that the intervention of pathway c does not even represent a true loss in yield.

By contrast, when an optically enriched starting material is employed, the product resulting from path a has the opposite configuration from that produced by path b (or path c). Consequently, a poorly regioselective process results in a marked decrease in enantiomeric excess.[7] Fortunately, glycidyl arenesulfonates exhibit very high regioselectivity in reactions with a variety of nucleophiles, as detailed below.

Aryl Oxide Nucleophiles. Prior to this work, the only systematic study of regioselectivity in the reactions of glycidol derivatives was an investigation of the reactions of optically active glycidol derivatives with aryl oxide nucleophiles reported by McClure and co-workers in 1979.[8] For purposes of comparison, (2*S*)-glycidyl tosylate of 85% ee and phenol were subjected to the reaction conditions found by McClure to be the most selective for the closely related substrate, glycidyl mesylate (Table II, entry 1). The expected epoxy ether **5a** was produced in 84% yield and exhibited an enantiomeric excess of 80%, indicating a selectivity of 97:3 in favor of direct sulfonate displacement. This is a substantial improvement over the 85:15 selectivity reported by McClure for the reaction of glycidyl mesylate with the same nucleophile, and it approaches the selectivity of 98:2 those workers obtained with the highly reactive substrate, glycidyl triflate.

Table III



X	C-1:C-3	X	C-1:C-3
p-OCH_3	95.5:4.5	*m*-NO_2	≥99.8:0.02[a]
p-CH_3	97:3	*p*-NO_2	≥99.8:0.02[a]
p-Cl	99:1		

[a] None of the other enantiomer was detected.

As indicated in Table II, several other aryl oxide nucleophiles showed very similar selectivity in reactions with glycidyl tosylate. In addition, sodium or potassium hydroxide could be used in place of sodium hydride with no deterioration in regioselectivity. While the use of sodium hydride is not inconvenient on a small laboratory scale, the ability to substitute hydroxide bases offers a significant advantage for large-scale or industrial applications.

Regioselectivity was not profoundly affected by steric factors. When (2*S*)-glycidyl 2,4,6-triisopropylbenzenesulfonate (**2h**)[9] was treated with sodium phenoxide according to the reaction conditions in Table II, a greater proportion of the product resulted from C-3 attack, but the effect was minimal (C-1:C-3 = 94:6). A more dramatic shift toward C-3 attack occurred when the reaction was performed under conditions that reportedly favored epoxide opening.[8] For example, while still favoring direct displacement, the reaction of **2h** with potassium phenoxide in acetone/phenol exhibited a C-1:C-3 ratio of only 65:35.

While McClure's data provide experimental evidence for the intuitive supposition that the ratio of direct displacement to epoxide opening should increase with increasing departing ability of the leaving group, the extent to which regioselectivity was improved for glycidyl tosylate relative to glycidyl mesylate was initially surprising. The results of a systematic investigation of the effect of substituent variation in the sulfonate ester moiety are presented in Table III. Electron-deficient sulfonate esters should promote reaction at the C-1 terminus, since electron-withdrawing substituents on the leaving group are known to provide a rate-enhancing effect in nucleophilic substitution reactions.[10] The effect of electron deficiency at C-1 on reactivity at C-3 is less obvious, however.

It has been reported[11] that under neutral and basic conditions epoxide opening at the terminal position is accelerated by an adjacent electron-withdrawing group. In reactions of glycidyl arenesulfonates, if increased electron deficiency in the sulfonate ester moiety does produce a rate enhancement at both C-1 and C-3, the net effect on regioselectivity will depend on the relative degree to which each terminus is affected. It is reasonable to expect that C-1 will be more strongly affected, due to its closer proximity to the site of variation. In fact, the results of Table III do indicate increased regioselectivity with increased electron deficiency of the leaving group.

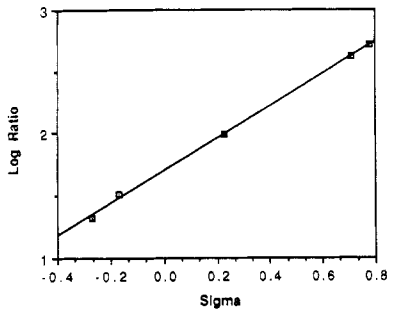
(7) Isolation of the alcohol **4** resulting from pathway c circumvents the potential problem of loss of optical purity due to poor regioselectivity. Advantage has been taken of this fact in more than one synthesis involving optically active epichlorohydrin. (a) Yo, E.; Nakagawa, K.; Hoshino, Y. *Chem. Pharm. Bull.* **1981**, *29*, 2157. (b) Kuehne, M. E.; Podhorez, D. E. *J. Org. Chem.* **1985**, *50*, 924.

(8) McClure, D. E.; Arison, B. H.; Baldwin, J. J. *J. Am. Chem. Soc.* **1979**, *101*, 3666.

(9) The pronounced steric hindrance of 2,4,6-triisopropylbenzenesulfonyl chloride has been exploited in a variety of applications, particularly in carbohydrate and nucleoside chemistry. See: *Comprehensive Organic Chemistry*; Barton, D., Ollis, W. D., Eds.; Pergamon: Oxford, 1979; Vol. 5 and references cited therein.

(10) For reviews and leading references, see: (a) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*, 2nd ed.; Plenum: New York, 1984; Part A, pp 271–274. (b) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed.; Harper & Row: New York, 1981; pp 339–342.

(11) Parker, R. E.; Isaacs, N. S. *Chem. Rev.* **1959**, *59*, 737.



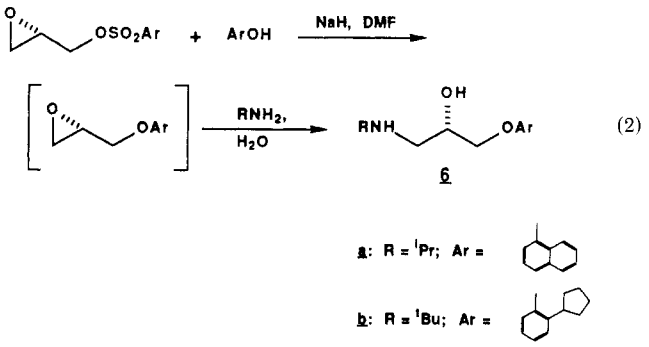
X	σ	Log Ratio
p-OCH_3	-.27	1.327
p-CH_3	-.17	1.510
p-Cl	+.23	1.996
m-NO_2	+.71	2.627*
p-NO_2	+.78	2.718*

Figure 1. log ratio vs σ. (*None of the other enantiomer was detected. These are extrapolated values.)

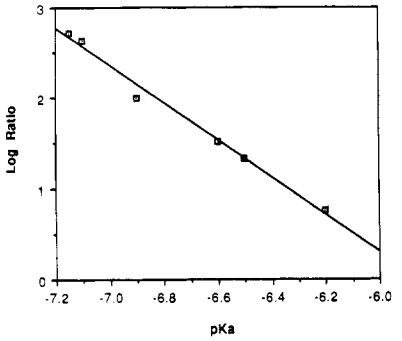
The quantitative relationship between regioselectivity and the effect of electron-withdrawing substituents on the leaving group was determined by plotting the log of the ratio vs the Hammett σ constant[12] of the substituent (Figure 1). It is interesting to note that the slope of this line (1.30) is quite similar to the ρ value of 1.37 observed for the reaction of ethyl arenesulfonates with sodium ethoxide in ethanol.[13] While the difference in solvent does not allow rigorous comparison, this similarity clearly reveals that the effect at C-1 greatly predominates over any effect at C-3.

A plot of the log of the ratio of direct displacement to epoxide opening vs pK_a of the corresponding sulfonic acid (Figure 2) allows a comparison of these results with arenesulfonates to McClure's results with alkylsulfonates. In fact, the lower regioselectivity exhibited by glycidyl mesylate correlates precisely with the lower acidity of methanesulfonic acid relative to arenesulfonic acids. The data represented in Figures 1 and 2 provide, for the first time, a quantitative correlation with predictive power between leaving group ability and regioselectivity in reactions of glycidol derivatives with aryl oxide nucleophiles.

The primary practical significance of this work, like that of the McClure study, derives from its application to the preparation of optically active β-adrenergic blocking agents. The synthesis of (2*S*)-propanolol (**6a**) from (2*S*)-glycidyl tosylate by the convenient one-pot procedure illustrated in eq 2 has been reported previously.[3a] Penbutolol (**6b**)[14] was also prepared by the same general



(2)



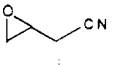
	pKa	Log Ratio
CH_3SO_3H	-6.2[a]	0.754
p-OCH_3	-6.5[b]	1.327
p-CH_3	-6.6[a]	1.510
p-Cl	-6.9[b]	1.996
m-NO_2	-7.1[c]	2.627[d]
p-NO_2	-7.15[c]	2.718[d]

Figure 2. log ratio vs pK_a. [a]Albert, A.; Serjeant, E. P. *The Determination of Ionization Constants*; Chapman and Hall: New York, 1984; p 146. [b]Estimated values based on the reported dependence of pK_a of substituted benzenesulfonic acids on σ. [Maarsen, P. K.; Bergman, R.; Cerfontain, H. *Tetrahedron* **1974**, 1211]. [c]Cumrine, D. S.; Shankweiler, J. M.; Hoffmann, R. V. *J. Org. Chem.* **1986**, *51*, 5013. [d]Extrapolated values from Figure 1.

procedure. This β-blocker synthesis is greatly improved by the use of glycidyl 3-nitrobenzenesulfonate (**2b**) in place of glycidyl tosylate (**2a**). Not only is regioselectivity markedly increased (Table III), but this compound is also easily recrystallized to an enantiomeric purity of >99% (Table I). In addition, reactions of **2b** with aryl oxide nucleophiles proceed much more rapidly than those of **2a**, generally requiring minutes rather than hours to reach completion. The rate enhancement also results in better yields, since the epoxy aryl ether product is not exposed to the aryl oxide nucleophile for more than a brief period.

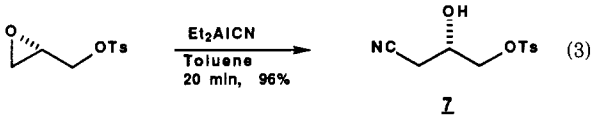
Carbon Nucleophiles. In addition to the β-adrenergic blocking agents, other compounds for which glycidyl tosylate could serve as a suitable precursor include the biologically and synthetically important β-hydroxybutyric acids.[15] Access to these compounds from glycidyl tosylate requires homologation by one carbon atom, a transformation most readily accomplished by addition of cyanide ion. In this case it was necessary to effect selective epoxide opening without subsequent ring closure.[16] All reactions

(12) Ritchie, C. D.; Sager, W. F. *Prog. Phys. Org. Chem.* **1964**, *2*, 323.
(13) Morgan, M. S.; Cretcher, L. H. *J. Am. Chem. Soc.* **1948**, *70*, 375.
(14) Härtgelder, V. G.; Lessenich, H.; Schmitt, K. *Arzneim-Forsch.* **1972**, *22*, 930.
(15) (a) For syntheses of γ-amino-β-hydroxybutyric acid (GABOB) and carnitine, see: Bianchi, D.; Cabri, W.; Cesti, P.; Francalanci, F.; Ricci, M. *J. Org. Chem.* **1988**, *53*, 104. Takano, S.; Yanase, M.; Sekiguchi, Y.; Ogasawara, K. *Tetrahedron Lett.* **1987**, *28*, 1783. Renaud, P.; Seebach, D. *Synthesis* **1986**, 424. Rajashekhar, B.; Kaiser, E. T. *J. Org. Chem.* **1985**, *50*, 5480. Pellegata, R.; Dosi, I.; Villa, M.; Lesma, G.; Palmisano, G. *Tetrahedron* **1985**, *41*, 5607. Rossiter, B. E.; Sharpless, K. B. *J. Org. Chem.* **1984**, *49*, 3707. Zhou, B.; Gopalan, A. S.; VanMiddlesworth, F.; Shieh, W.-R.; Sih, C. J. *J. Am. Chem. Soc.* **1983**, *105*, 5925. (b) For synthetic applications of optically active 3,4-dihydroxy butyrates and related compounds, see: Walkup, R. D.; Cunningham, R. T. *Tetrahedron Lett.* **1987**, *28*, 4019. Saito, S.; Matsumoto, S.; Sato, S.; Inaba, M.; Moriwake, T. *Heterocycles* **1986**, *24*, 2785.
(16) The epoxy nitrile i, obtainable from glycidyl tosylate either by direct sulfonate displacement or by epoxide opening and displacement, is not a useful synthetic intermediate due to its extreme sensitivity toward elimination, with concomitant loss of stereochemistry. See ref 42.



i

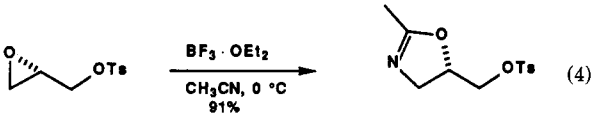
employing cyanide salts proved unsuccessful, even those performed under conditions of acid catalysis.[17] The desired product **7** was obtained upon treatment of glycidyl tosylate with acetone cyanohydrin and catalytic potassium cyanide, but in only 20% yield.



(3)

7

Successful results were finally obtained with Nagata's[18] reagent, Et_2AlCN (eq 3). Apparently, coordination of the epoxide oxygen to aluminum activates the ring-opening process and prevents subsequent ring closure. This success prompted an attempt to effect epoxide opening with potassium cyanide in the presence of a Lewis acid. These efforts were not successful, but in the process it was discovered that $BF_3{\cdot}OEt_2$ catalyzes the reaction of glycidyl tosylate with acetonitrile to afford cleanly the oxazoline **8** (eq 4).[19]



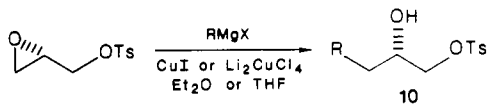
(4)

8

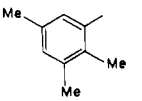
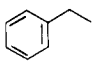
While the application of glycidyl tosylate to the synthesis of β-adrenergic blocking agents and β-hydroxybutyric acids was readily apparent based on the skeletal similarity of these molecules, we felt that the utility of homochiral glycidyl tosylate would extend beyond the synthesis of molecules bearing a close relationship to the glycerol substructure. An illustration of this fact required the development of procedures for the selective introduction of more complex carbon nucleophiles. Reported reactions of epichlorohydrin with organometallic reagents have proceeded primarily by way of epoxide opening.[20] However, these results might well be a reflection of the poor leaving group ability of Cl^-, and one might expect tosylate displacement to be more competitive with ring opening.

Not surprisingly, simple Grignard and lithium reagents provided unsatisfactory results. Epoxide opening has been more effectively accomplished with a wide variety of organocopper compounds,[21] and the side reactions, such as epoxide rearrangement, that result from the Lewis acidity of other organometallic reagents are not generally observed. Lipshutz[22] has found that the higher order mixed cuprates $R_2Cu(CN)Li_2$ are particularly useful for effecting epoxide opening under mild conditions. Treatment of (2*R*)-glycidyl tosylate of 88% ee with $Ph_2Cu(CN)Li_2$ according to the published procedure afforded the epoxide (*R*)-**9** in 64% yield, as well as varying amounts of 1,3-diphenylpropan-2-ol (eq 5).

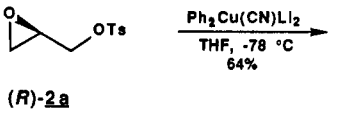
Table IV



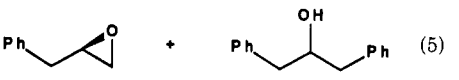
10

R	product	% yield[a]
	**10a**	79
	**10b**	69
	**10c**	90
	**10d**	56 (84)
n-C_6H_{13}	**10e**	74 (93)
	**10f**	49 (90)

[a] Yield in parentheses is based on recovered starting material.



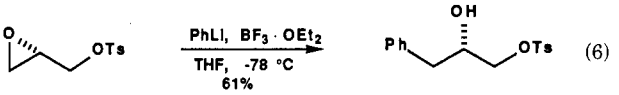
(*R*)-**2a**
88% ee



(5)

(*R*)-**9**
$[\alpha]_D$ +17.5° (EtOH)

Addition of organometallic species to epoxides has also been effected by treatment of the epoxide with an organolithium reagent and $BF_3{\cdot}OEt_2$.[23] (2*S*)-Glycidyl tosylate of 88% ee was treated with $PhLi{-}BF_3{\cdot}OEt_2$ to afford the hydroxy tosylate **10a** in 61% yield (eq 6). Although a significant amount of starting material (38%) was recovered from this reaction, no products resulting from tosylate displacement could be detected.



(6)

(*S*)-**2a**
88% ee

10a

The addition of an organometallic reagent to glycidyl tosylate was most conveniently accomplished by a copper-catalyzed Grignard reaction. Under these conditions as well, tosylate displacement by the intermediate alkoxide did not generally occur, and the hydroxy tosylate products were isolated in moderate to good yield (Table IV). A persistent side reaction was epoxide opening by the halide ion of the Grignard reagent. When copper iodide was employed as the copper source, the iodohydrin was also observed. Halohydrin formation appeared to be significantly reduced, although not eliminated, when the source of copper was Li_2CuCl_4.[24]

(17) For example, epoxide opening has been previously accomplished by treatment with 30% aqueous NaCN and 30% aqueous HOAc in ethanol. Kuwamura, T.; Takahashi, H. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 1345. In the case of glycidyl tosylate, however, the result was only a poor recovery of starting material.

(18) Nagata, W.; Yoshioka, M.; Okamura, T. *J. Chem. Soc. C* **1970**, 2365.

(19) The preparation of oxazolines from epoxides by treatment with a nitrile and $BF_3{\cdot}OEt_2$ has been reported previously: Lindsay Smith, J. R.; Norman, R. O. C.; Stillings, M. R. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1200.

(20) (a) Schuda, A. D. C.; Mazzocchi, P. H.; Fritz, G.; Morgan, T. *Synthesis* **1986**, 309. (b) Yamaguchi, M.; Hirao, I. *Tetrahedron Lett.* **1983**, *24*, 391. (c) South, M. S.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1984**, *106*, 4181. (d) Russell, S. W. *Recl. Trav. Chim. Pays-Bas.* **1975**, *94*, 43. (e) Russell, S. W.; Pabon, H. J. J. *J. Chem. Soc., Perkin Trans. 1* **1982**, 545.

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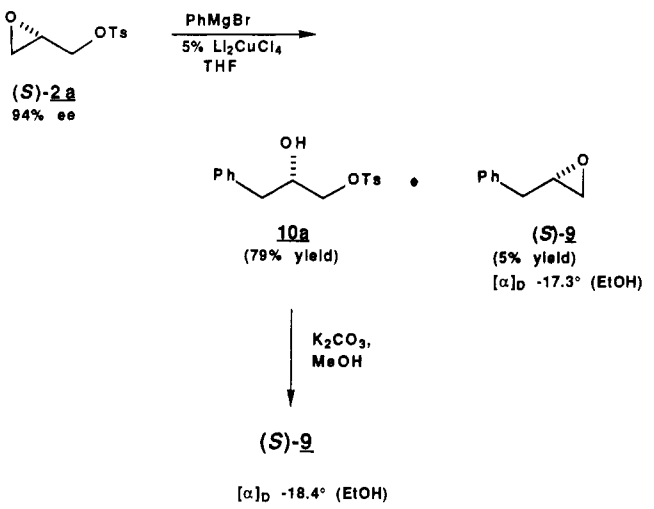
(22) Lipshutz, B. H.; Kozlowski, J.; Wilhelm, R. S. *J. Am. Chem. Soc.* **1982**, *104*, 2305. See also ref 21a and references cited therein.

(23) Eis, M. J.; Wrobel, J. E.; Ganem, B. *J. Am. Chem. Soc.* **1984**, *106*, 3693.

Scheme II

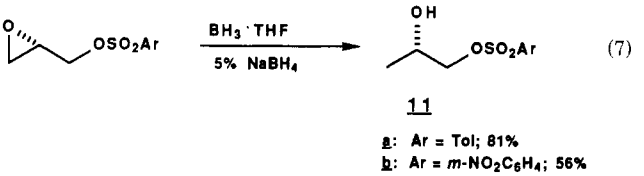


Ether and THF were both examined as solvents for the reaction. Solubility considerations often mandated the use of THF, particularly when Li_2CuCl_4 was used. The results were not consistent, however, with each nucleophile requiring individually optimized conditions. The reaction temperature also appeared to have a critical effect on the yield in some cases. Similar observations have been reported for copper-catalyzed Grignard reactions of racemic epichlorohydrin and epibromohydrin.[20a]

The isolation of hydroxy tosylate **10** as the major product from these reactions is proof that the epoxide terminus was the primary site of reaction. However, some reactions also afforded small quantities of the corresponding epoxide, which could have resulted either from ring closure of the intermediate hydroxy tosylate or from direct tosylate displacement. Ring closure of the major product **10a**, obtained from the reaction of (2*S*)-glycidyl tosylate (94% ee) with $PhMgBr/Li_2CuCl_4$, was effected by treatment with K_2CO_3/MeOH to provide (*S*)-**9**[25] (Scheme II). A comparison of the optical rotation of this epoxide with that of the minor product from the copper-catalyzed Grignard reaction indicated that the latter material resulted almost exclusively from ring closure rather than by direct displacement. Similarly, the optical rotation of the product resulting from the reaction of glycidyl tosylate with $Ph_2Cu(CN)Li_2$ (eq 5) indicated high regioselectivity for initial epoxide opening in that reaction as well.

The hydroxytosylates produced by the copper-catalyzed Grignard reactions of glycidyl tosylate provide a valuable route to terminal epoxides of high optical purity. In contrast to the high enantioselectivities attainable in asymmetric epoxidations of allylic alcohols, attempted asymmetric epoxidations of nonfunctionalized olefins have been only moderately successful.[26] This has necessitated indirect routes to these epoxides, and a number of chiral building blocks have been used for this purpose.[27] Since ring closure of hydroxytosylates may be simply and quantitatively accomplished, the synthesis of optically active terminal epoxides from glycidyl tosylate is a convenient two-step procedure, as illustrated in Scheme II.

Extension of this methodology to allow access to homochiral propylene oxide appeared desirable in light of the considerable attention it has recently received.[28,29] This purpose required the chemospecific reduction of the epoxide in the presence of the tosylate moiety. An initial attempt employing sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al, Aldrich) was unsuccessful, affording only a poor recovery of unchanged starting material. It has been reported[30] that carbohydrate epoxides bearing adjacent tosyloxy substituents may be selectively reduced with diborane in the presence of a catalytic amount of sodium borohydride. In fact, the known hydroxytosylate **11a**[27c] was produced in 81% yield upon subjection of (2*S*)-glycidyl tosylate to the reported reaction conditions (eq 7). The reaction of (2*S*)-glycidyl 3-nitrobenzenesulfonate was somewhat less successful but still provided **11b** in 56% yield, along with recovered starting material (23%).



(7)

Conclusion

We have established that very high regioselectivity can be attained in the reactions of glycidyl arenesulfonates with a variety of nucleophiles. The glycidyl arenesulfonates described here are stable, crystalline compounds, which are now readily available in high optical purity and in either enantiomeric form.[31] As such, we anticipate that they will find rapid acceptance as versatile chiral building blocks, suitable for a wide variety of synthetic purposes. In particular, glycidyl 3-nitrobenzenesulfonate (**2b**) will generally be the substrate of choice for reactions requiring direct displacement of the arenesulfonate moiety, while glycidyl tosylate (**2a**) may be preferred when selective epoxide opening is desired.

(24) Tamura, M.; Kochi, J. *Synthesis* **1971**, 303.

(25) Hirano, T.; Inoue, S.; Tsuruta, T. *Makromol. Chem.* **1976**, *177*, 3245.

(26) (a) Sinigalia, R.; Michelin, R. A.; Pinna, F.; Strukul, G. *Organometallics* **1987**, *6*, 728. (b) Hopkins, R. B.; Hamilton, A. D. *J. Chem. Soc., Chem. Commun.* **1987**, 171. (c) Davis, F. A.; Chattopadhyay, S. *Tetrahedron Lett.* **1986**, *27*, 5079. (d) Davis, F. A.; Harakal, M. E.; Awad, S. B. *J. Am. Chem. Soc.* **1983**, *105*, 3123. (e) Mansuy, D.; Battioni, P.; Renaud, J.-P.; Guerin, P. *J. Chem. Soc., Chem. Commun.* **1985**, 155. (f) Broser, E.; Krohn, K.; Hintzer, K.; Schurig, V. *Tetrahedron Lett.* **1984**, *25*, 2463. (g) Groves, J. T.; Myers, R. S. *J. Am. Chem. Soc.* **1983**, *105*, 5791. (h) Kagan, H. B.; Mimoun, H.; Mark, C.; Schurig, V. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 485.

(27) (a) D-Mannitol: Schmidt, U.; Talbiersky, J.; Bartkowiak, F.; Wild, J. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 198. (b) Amino acids: Castedo, L.; Castro, J. L.; Riguera, R. *Tetrahedron Lett.* **1984**, *25*, 1205. See also ref 25. (c) Hydroxy acids: Kim, M.-J.; Whitesides, G. M. *J. Am. Chem. Soc.* **1988**, *110*, 2959. Chenault, H. K.; Kim, M.-J.; Akiyama, A.; Miyazawa, T.; Simon, E. S.; Whitesides, G. M. *J. Org. Chem.* **1987**, *52*, 2608. Hirano, T.; Inoue, S.; Tsuruta, T. *Makromol. Chem.* **1976**, *177*, 3237. Seuring, B.; Seebach, D. *Helv. Chim. Acta* **1977**, *60*, 1175. (d) (*S*)-3-(Phenylthio)-1,2-propanediol: Fujisawa, T.; Itoh, T.; Nakai, M.; Sato, T. *Tetrahedron Lett.* **1985**, *26*, 771.

(28) For alternative syntheses, see: (a) Koppenhoefer, B.; Schurig, V. *Org. Synth.* **1988**, *66*, 160. (b) Simon, E. S.; Whitesides, G. M.; Cameron, D. C.; Weitz, D. J.; Cooney, C. L. *J. Org. Chem.* **1987**, *52*, 4042. (c) Yura, T.; Iwasawa, N.; Clark, R.; Mukaiyama, T. *Chem. Lett.* **1986**, 1809. (d) Ellis, M. K.; Golding, B. T. *Org. Synth.* **1985**, *63*, 140. (e) Oppolzer, W.; Dudfield, P. *Tetrahedron Lett.* **1985**, *26*, 5037.

(29) Recent examples of synthetic applications include: (a) Quinkert, G.; Heim, N.; Glenneberg, J.; Billhardt, U.-M.; Autze, V.; Bats, J. W.; Dürner, G. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 362. (b) Manna, S.; Viala, J.; Yadagiri, P.; Falck, J. R. *Tetrahedron Lett.* **1986**, *27*, 2679. (c) White, J. D.; Somers, T. C.; Reddy, G. N. *J. Am. Chem. Soc.* **1986**, *108*, 5352. (d) Mori, K.; Senda, S. *Tetrahedron* **1985**, 541. (e) Hillis, L. R.; Ronald, R. C. *J. Org. Chem.* **1985**, *50*, 470. (f) Nicolaou, K. C.; Randall, J. L.; Furst, G. T. *J. Am. Chem. Soc.* **1985**, *107*, 5556.

(30) Fu, Y.-L.; Bobek, M. *J. Org. Chem.* **1980**, *45*, 3836.

(31) Both enantiomers of glycidyl tosylate and glycidyl 3-nitrobenzenesulfonate are now commercially available from Aldrich Chemical Co., Milwaukee, WI.

Experimental Section[32]

General Procedure for the Determination of Enantiomeric Excess of Glycidol Derivatives: Mosher Ester Analysis. A small sample (30–50 mg) of epoxy ether or glycidyl arenesulfonate was converted to the iodohydrin by Cornforth's procedure.[33] After being dried under high vacuum, a portion (ca. 0.01 mmol) of this product was dissolved in CH_2Cl_2 (2 mL) with triethylamine (3–4 drops), and stoichiometric amounts of DMAP and (+)-MTPA-Cl (25–30 μL) were added. The reaction was monitored by TLC, ensuring complete reaction before quenching with 3-(dimethylamino)propylamine (3–4 drops).

After several minutes, silica gel was added and the solvent was evaporated. The residue was loaded onto a short plug of silica gel, and the product was eluted with 20% ethyl acetate–hexane, making sure that no separation of diastereomers occurred. Solvent evaporation afforded the Mosher ester[34] as a mixture of diastereomers. The diastereomeric ratio was determined by ^1H NMR (250 MHz, C_6D_6 or $CDCl_3$) or by HPLC on a chiral stationary phase (Pirkle Type 1-A 250 × 10 mm ID preparative column (Regis), elution with *i*-PrOH–hexane mixtures). In all cases, comparison was made to the product derived from racemic material.

General Procedure for the Synthesis of Glycidyl Arenesulfonates. The arenesulfonyl chloride (5.0–5.1 mmol) was added to a solution of racemic or homochiral glycidol (5.0 mmol) and triethylamine (5.5 mmol) in 10–20 mL of toluene or dichloromethane at −10 °C.[35] After being allowed to stand at this temperature for 10–20 h, the reaction mixture was either filtered to remove precipitated ammonium salts or washed with 5% H_2SO_4, saturated $NaHCO_3$, and brine. Concentration afforded the crude product, which was purified by flash chromatography and/or recrystallization. Isolated yields ranged from 50% to 90% and were probably dependent upon the age and purity of the glycidol used. Melting point data for the racemic compounds are provided in Table I.

(2*S*)-Glycidyl 4-Toluenesulfonate [(2*S*)-2a].[36] The preparation of (2*S*)-**2a** by in situ sulfonylation has been described in detail elsewhere.[2,3a] After workup, filtration through silica gel, and concentration, the crude product was obtained as an orange oil (260 g), which was dissolved in ether (100 mL) and crystallized by addition of petroleum ether (150 mL) with cooling. An off-white solid was collected and recrystallized from 5:1 ether–petroleum ether (120 mL) to afford 89.0 g (39%) of (2*S*)-**2a**: mp 46–48 °C; $[\alpha]^{25}_D$ +17.6° (*c* 2.13, $CHCl_3$). A portion of this material (15 g) was recrystallized twice more to provide 8.6 g of white crystals: mp 47.5–48.5 °C; $[\alpha]^{25}_D$ +18.1° (*c* 2.1, $CHCl_3$); ≥97% ee; IR (KBr) 3075, 3000, 2935, 1598, 1362, 1195, 1180, 965, 915, 815, 775, 666, 558 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8 Hz, 2 H), 7.36 (d, *J* = 8 Hz, 2 H), 4.26 (dd, *J* = 3, 11.4 Hz, 1 H), 3.95 (dd, *J* = 6, 11.4 Hz, 1 H), 3.16–3.23 (m, 1 H), 2.82 (apparent t, *J* = 5 Hz, 1 H), 2.60 (dd, *J* = 3, 5 Hz, 1 H), 2.46 (s, 3 H). Anal. Calcd for $C_{10}H_{12}O_4S$: C, 52.62; H, 5.30. Found: C, 52.75; H, 5.29.

(2*S*)-Glycidyl 3-Nitrobenzenesulfonate [(2*S*)-2b]. Compound (2*S*)-**2b** was prepared by in situ sulfonylation[2] in 57% yield (mp 54–60 °C, 96% ee) after crystallization from ether–hexane. A portion of this material (2.635 g) was recrystallized twice from ethanol to afford 1.745 g of pure crystals: mp 63–64 °C; $[\alpha]^{25}_D$ +23.0° (*c* 2.14, $CHCl_3$); 99% ee; IR (KBr) 3114, 3090, 1611, 1532, 1469, 1451, 1428, 1354, 1280, 1257, 1188, 1132, 1086, 1076, 1004, 981, 963, 919, 913, 889, 867, 842, 820, 758, 739, 674, 667, 596, 585, 549, 524, 447, 430, 405 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.79 (t, *J* = 1.5 Hz, 1 H), 8.54 (m, 1 H), 8.28 (m, 1 H), 7.82 (t, *J* = 8 Hz, 1 H), 4.50 (dd, *J* = 3.4, 11.4 Hz, 1 H), 4.04 (dd, *J* = 6.0, 11.4 Hz, 1 H), 3.23 (m, 1 H), 2.86 (t, *J* = 4.5 Hz, 1 H), 2.64 (dd, *J* = 2.5, 4.75 Hz, 1 H). Anal. Calcd for $C_9H_9NO_6S$: C, 41.70; H, 3.50; N, 5.40. Found: C, 41.78; H, 3.57; N, 5.40.

(2*S*)-Glycidyl 4-Chlorobenzenesulfonate [(2*S*)-2c]. In situ sulfonylation[2] of (2*R*)-glycidol afforded (2*S*)-**2c** in 38% yield (mp 60.7–62.3 °C, 94% ee) after crystallization from ether–hexane. Recrystallization from ethanol–hexane produced a 34% yield of pure crystals: mp 61–62.5 °C; $[\alpha]^{25}_D$ +22.6° (*c* 2.02, $CHCl_3$); 95.2% ee; IR (KBr) 3100, 1572, 1478, 1452, 1399, 1360, 1281, 1180, 1136, 1089, 1019, 960, 917, 868, 826, 770, 754, 709, 628, 576, 531, 489, 448 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8 Hz, 2 H), 7.55 (d, *J* = 8 Hz, 2 H), 4.34 (dd, *J* = 3.4, 11.4 Hz, 1 H), 3.97 (dd, *J* = 6, 11.4 Hz, 1 H), 3.21 (m, 1 H), 2.84 (t, *J* = 4.5 Hz, 1 H), 2.62 (dd, *J* = 2.5, 4.8 Hz, 1 H). Anal. Calcd for $C_9H_9ClO_4S$: C, 43.47; H, 3.65. Found: C, 43.50; H, 3.74.

(2*S*)-Glycidyl 4-Chloro-3-nitrobenzenesulfonate [(2*S*)-2d]. Crystallization of the crude oil from ether–petroleum ether provided a 41% yield of (2*S*)-**2d**: mp 49–54 °C. Recrystallization from ethanol–ethyl acetate then gave pure crystals: mp 54.7–55.2 °C; 94% ee; IR (KBr) 3105, 3015, 1605, 1573, 1541, 1454, 1400, 1385, 1363, 1339, 1252, 1197, 1190, 1170, 1159, 1107, 1056, 995, 979, 963, 945, 922, 914, 899, 868, 842, 779, 767, 759, 670, 647, 591, 576, 533, 494, 452 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.43 (d, *J* = 2 Hz, 1 H) 8.05 (dd, *J* = 2.1, 8.5 Hz, 1 H), 7.79 (d, *J* = 8.5 Hz, 1 H), 4.51 (dd, *J* = 2.8, 11.6 Hz, 1 H), 4.04 (dd, *J* = 6.5, 11.6 Hz, 1 H), 3.23 (m, 1 H), 2.87 (apparent t, *J* = 4.5 Hz, 1 H), 2.6 (dd, *J* = 2.5, 4.4 Hz, 1 H). Anal. Calcd for $C_9H_8O_6ClNS$: C, 36.81; H, 2.75; N, 4.77. Found: C, 36.98; H, 2.81; N, 4.75.

(2*S*)-Glycidyl 2,4,5-Trichlorobenzenesulfonate [(2*S*)-2e]. The crude product was recrystallized from toluene–petroleum ether to provide 0.59 g (53%) of (2*S*)-**2e**: mp 98–100.5 °C; $[\alpha]^{25}_D$ +14.6° (*c* 1.59, $CHCl_3$). A second recrystallization afforded 0.40 g (36%) of pure crystals: mp 100–102 °C; $[\alpha]^{25}_D$ +15.5° (*c* 2.68, $CHCl_3$); 88% ee; IR (KBr) 3100, 3000, 1443, 1372, 1185, 1070, 948, 885, 820, 600 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.16 (s, 1 H), 7.70 (s, 1 H), 4.47 (dd, *J* = 3, 11.6 Hz, 1 H), 4.09 (dd, *J* = 6.3, 11.6 Hz, 1 H), 3.25–3.29 (m, 1 H), 2.86 (apparent t, *J* = 4.5 Hz, 1 H), 2.66 (dd, *J* = 3, 4.5 Hz, 1 H). Anal. Calcd for $C_9H_7Cl_3O_4S$: C, 34.04; H, 2.22. Found: C, 34.10; H, 2.21.

(2*S*)-Glycidyl 4-Bromobenzenesulfonate [(2*S*)-2f].[37] Trituration of the crude oil with petroleum ether afforded a white solid, which was recrystallized from ether–petroleum ether to give a 56% yield (1.12 g) of (2*S*)-**2f**: mp 54–56 °C; $[\alpha]^{25}_D$ +19.0° (*c* 2.70, $CHCl_3$). A second recrystallization gave 0.84 g (42%) of pure white needles: mp 55–56 °C; $[\alpha]^{25}_D$ +20.1° (*c* 1.88, $CHCl_3$); 88% ee; IR (KBr) 3100, 1575, 1365, 1182, 960, 828, 612 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.69–7.82 (m, 4 H), 4.34 (dd, *J* = 3, 11.4 Hz, 1 H), 3.97 (dd, *J* = 6.2, 11.4 Hz, 1 H), 3.17 (m, 1 H), 2.84 (apparent t, *J* = 4.5 Hz, 1 H), 2.61 (dd, *J* = 3, 4.5 Hz, 1 H). Anal. Calcd for $C_9H_9BrO_4S$: C, 36.87; H, 3.09. Found: C, 36.96; H, 3.11.

(2*S*)-Glycidyl 4-Nitrobenzenesulfonate [(2*S*)-2g]. Crystallization from ethyl acetate–petroleum ether afforded as a first crop 0.84 g (48%) of (2*S*)-**2g**: mp 84–86 °C; $[\alpha]^{25}_D$ +28.7° (*c* 2.45, $CHCl_3$). A second recrystallization gave 0.62 g (35%) of material with mp 85–87 °C and $[\alpha]^{25}_D$ +26.5° (*c* 2.19, $CHCl_3$). Mosher ester analysis of the derived iodohydrin indicated an enantiomeric excess of 82% for the product of the second recrystallization: IR (KBr) 3110, 3080, 1610, 1540, 1370, 1350, 1193, 957, 830, 615 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.37–8.45 (m, 2 H), 8.11–8.24 (m, 2 H), 4.48 (dd, *J* = 3, 11.6 Hz, 1 H), 4.03 (dd, *J* = 6.7, 11.6 Hz, 1 H), 3.19–3.25 (m, 1 H), 2.85 (apparent t, *J* = 4.5 Hz, 1 H), 2.63 (dd, *J* = 3, 4.5 Hz, 1 H). Anal. Calcd for $C_9H_9NO_6S$: C, 41.70; H, 3.50. Found: C, 41.72; H, 3.44.

(2*S*)-Glycidyl 2,4,6-Triisopropylbenzenesulfonate [(2*S*)-2h]. The crude product was purified by recrystallization from petroleum ether to provide 1.32 g (59%) of (2*S*)-**2h**: mp 65–67 °C; $[\alpha]^{25}_D$ +11.35° (*c* 2.44, $CHCl_3$); 86% ee; IR (KBr) 2965,

(32) Melting points are uncorrected. Flash chromatography was performed on Merck silica gel 60 (230–400 mesh) as described by Still [Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923]. All commercial reagents were used as received unless otherwise noted. (±)-Glycidol (Aldrich) was distilled under reduced pressure and stored at −20 °C. (2*R*)- and (2*S*)-glycidol were prepared as previously described.[2] Copper(I) iodide (99.999%) was used as received from Cerac.

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

(34) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(35) If the homochiral glycidol used contained cumene hydroperoxide, this was reduced with $(MeO)_3P$ prior to addition of triethylamine and sulfonyl chloride. See ref 2.

(36) Racemic **2a** has been reported previously: (a) Pierre, J.-L.; Arnaud, P. *Bull. Soc. Chim. Fr.* **1969**, 2868. (b) Ichikawa, K. *Yuki Gosei Kagaku Kyokaishi* **1964**, *22*, 553. See also ref 4a.

(37) This compound has been reported as the racemate: Whalen, D. L. *Tetrahedron Lett.* **1978**, 4973.

2880, 1600, 1345, 1182, 965, 815, 670, 570 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.19 (s, 2 H), 4.27 (dd, J = 3, 11.2 Hz, 1 H), 4.14 (heptet, J = 6.7 Hz, 2 H), 3.94 (dd, J = 6.1, 11.2 Hz, 1 H), 3.24 (m, 1 H), 2.91 (heptet, J = 7 Hz, 1 H), 2.84 (apparent t, J = 4.5 Hz, 1 H), 2.62 (dd, J = 3, 4.5 Hz, 1 H), 1.27 (d, J = 6.7 Hz, 12 H), 1.26 (d, J = 7 Hz, 6 H). Anal. Calcd for $C_{18}H_{28}O_4S$: C, 63.49; H, 8.29. Found: C, 63.47; H, 8.48.

(2*R*)-Glycidyl 4-Methoxybenzenesulfonate [(2*R*)-2i]. Purification of the crude product afforded 1.04 g (85%) of (2*R*)-**2i** as colorless oil: $[\alpha]^{25}_D$ −16.6° (*c* 1.34, $CHCl_3$); 79% ee. Repeated triturations with petroleum ether at −78 °C induced this material to crystallize, giving an oily white solid, mp 32–34 °C, which melted upon attempted high vacuum drying: IR (thin film) 3110, 3070, 3010, 2955, 2850, 1598, 1362, 1265, 1195, 1170, 970, 838, 570 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.83–7.89 (m, 2 H), 6.99–7.04 (m, 2 H), 4.25 (dd, J = 3, 11 Hz, 1 H), 3.94 (dd, J = 6, 11 Hz, 1 H), 3.89 (s, 3 H), 3.16–3.23 (m, 1 H), 2.82 (apparent t, J = 5 Hz, 1 H), 2.60 (dd, J = 3, 5 Hz, 1 H). Anal. Calcd for $C_{10}H_{12}O_5S$: C, 49.17; H, 4.95. Found: C, 49.17; H, 5.17.

(2*S*)-Glycidyl 2-Naphthalenesulfonate [(2*S*)-2j]. Purification by flash chromatography (elution with ethyl acetate–hexane) and trituration with petroleum ether produced (2*S*)-**2j** as a white solid: mp 34–39 °C; $[\alpha]^{25}_D$ +14.7° (*c* 2.49, $CHCl_3$). Recrystallization from ether–petroleum ether provided 0.98 g (37%) of (2*S*)-**2j**: mp 38–45 °C; $[\alpha]^{25}_D$ +13.5° (*c* 2.60, $CHCl_3$). Due to the unfavorable physical properties of this compound (i.e. decreasing optical rotation with recrystallization), no effort was made to measure the enantiomeric excess: IR (thin film) 3060, 3010, 2940, 1360, 1180, 965, 866, 820, 665, 560 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.51 (s, 1 H), 7.86–8.03 (m, 4 H), 7.61–7.73 (m, 2 H), 4.32 (dd, J = 3, 11 Hz, 1 H), 4.00 (dd, J = 6.1, 11 Hz, 1 H), 3.17–3.24 (m, 1 H), 2.81 (apparent t, J = 4.8 Hz, 1 H), 2.59 (dd, J = 3, 5 Hz, 1 H).

Reactions of Glycidyl Arenesulfonates with Aryl Oxide Nucleophiles. Calculation of Regioselectivity. Regioselectivity (*a*:*b*) was calculated according to the formula: $a = 1/2[\%$ ee (SM) + % ee (prod)]/% ee (SM); $b = 1 - a$.

General Procedure. A solution of the aryl alcohol (1.0–1.1 equiv) in dry DMF was added by cannula to a suspension of sodium hydride (1.1–1.5 equiv) in DMF at room temperature under a nitrogen atmosphere. After 30 min, the glycidyl arenesulfonate (1.0 equiv) was added by cannula as a solution in DMF. The resulting mixture (ca. 0.1–0.2 M) was stirred at room temperature, and the progress of the reaction was monitored by TLC (ethyl acetate–hexane).

When complete, the reaction was quenched with saturated NH_4Cl, and the mixture was diluted with water and extracted with portions of ether. The combined organic extracts were washed (saturated $NaHCO_3$ or 10% NaOH and brine), dried ($MgSO_4$), and concentrated to give an oil. Purification by flash chromatography afforded the epoxy ether.

(*S*)-(+)-3-(Phenyloxy)-1,2-epoxypropane [(*S*)-5a]. Reaction of (2*S*)-glycidyl tosylate [(2*S*)-**2a**] (85% ee, 79.1 mg, 0.35 mmol) with phenol (39.2 mg, 0.42 mmol) and NaH (10.4 mg, 0.43 mmol) was performed according to the general procedure. Workup after 7 h, and purification by flash chromatography (elution with ethyl acetate–hexane), afforded 0.44 g (84%) of (*S*)-**5a**[8] as a colorless oil, $[\alpha]^{25}_D$ +14.1° (*c* 2.36, MeOH) [lit.[38] $[\alpha]^{25}_D$ +14.8° (*c* 2 or 3, MeOH)]. The spectral properties of this compound matched the reported[8] data. Mosher ester analysis (^1H NMR, $CDCl_3$) of the derived iodohydrin indicated an enantiomeric excess of 80%. The regioselectivity for direct tosylate displacement was 97:3.

(*S*)-(+)-3-(Naphthyloxy)-1,2-epoxypropane [(*S*)-5b]. (2*S*)-Glycidyl 3-nitrobenzenesulfonate [(2*S*)-**2b**] (98.8% ee, 0.207 g, 1.0 mmol) was treated with 1-naphthol (0.121 g, 0.84 mmol) and NaH (oil-free, 0.024 g, 1.0 mmol) according to the general procedure. Workup after 30 min afforded crude crystalline (*S*)-**5b**. Mosher ester analysis (^1H NMR, $CDCl_3$) of the derived iodohydrin indicated an enantiomeric excess of 98.8%. The reaction selectivity was ≥99.8:0.2. Similarly, (2*S*)-glycidyl 4-methoxybenzenesulfonate, (2*S*)-glycidyl tosylate, (2*S*)-glycidyl 4-chlorobenzenesulfonate, and (2*S*)-glycidyl 4-nitrobenzenesulfonate were treated with 1-naphthol and sodium hydride according to the general procedure to give the reaction selectivities of 95.5:4.5, 98:2, 99:1, and ≥99.8:0.2, respectively: IR (thin film) 3060, 3005, 2930, 1582, 1400, 1275, 1245, 1100, 795, 775 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.28–8.31 (m, 1 H), 7.78–7.82 (m, 1 H), 7.32–7.52 (m, 4 H), 6.80 (d, J = 7.6 Hz, 1 H), 4.40 (dd, J = 3.1, 11.0 Hz, 1 H), 4.14 (dd, J = 5.5, 11.0 Hz, 1 H), 3.46–3.51 (m, 1 H), 2.97 (t, J = 5 Hz, 1 H), 2.85 (dd, J = 2.6, 5 Hz, 1 H).

(*S*)-1,2-Epoxy-3-(2′-cyclopentylphenoxy)propane [(*S*)-5c]. (2*S*)-Glycidyl tosylate [(2*S*)-**2a**] (88% ee, 0.125 g, 0.55 mmol) was treated with 2-cyclopentylphenol (0.092 g, 0.57 mmol) and NaH (16.3 mg, 0.68 mmol) according to the general procedure. After stirring overnight, workup and purification (flash chromatography, elution with CH_2Cl_2–hexane) afforded 0.102 g (84%) of (*S*)-**5c**[39] as a colorless oil. Multiple chromatographies were necessary in order to achieve complete separation from 2-cyclopentylphenol: IR (thin film) 3060, 3040, 2960, 2875, 1490, 1450, 1240, 755 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.08–7.26 (m, 4 H), 4.23 (dd, J = 3, 11 Hz, 1 H), 3.98 (dd, J = 5, 11 Hz, 1 H), 3.28–3.42 (m, 1 H), 2.91 (apparent t, J = 5 Hz, 1 H), 2.77 (dd, J = 3, 5 Hz, 1 H), 1.48–2.09 (m, 9 H). Mosher ester analysis (^1H NMR, C_6D_6) of the derived iodohydrin indicated an enantiomeric excess of 86%. The reaction selectivity was 99:1.

(*S*)-3-(2,3-Epoxypropoxy)-4-(*N*-morpholino)-1,2,5-thiadiazole [(*S*)-5d]. Reaction of (2*S*)-glycidyl tosylate [(2*S*)-**2a**] (88% ee, 0.113 g, 0.049 mmol) with 3-hydroxy-4-(*N*-morpholino)-1,2,5-thiadiazole[40] (0.103 g, 0.55 mmol) and NaH (15.1 mg, 0.63 mmol) according to the general procedure afforded after workup and purification (flash chromatography, elution with ethyl acetate–methylene chloride) 0.086 g (72%) of (*S*)-**5d**[41] as a white solid: mp 113.5–114.5 °C (lit.[41] mp 113–114 °C). The spectral properties of this compound matched the reported data. Mosher ester analysis (^1H NMR, $CDCl_3$) of the derived iodohydrin indicated an enantiomeric excess of 82%. The reaction selectivity was 97:3.

Similarly, reaction of (2*S*)-glycidyl 3-nitrobenzenesulfonate [(2*S*)-**2b**] (≥99% ee) with 3-hydroxy-4-(*N*-morpholino)-1,2,5-thiadiazole and NaH according to the general procedure (reaction time of 14 h) afforded (2*S*)-**5d** in 86% yield and ≥99% ee.

Synthesis of β-Adrenergic Blocking Agents. (2*S*)-(−)-Penbutolol [(2*S*)-6b]. Sodium hydride (washed with hexane, 84 mg, 2.1 mmol) was suspended in DMF (4 mL) in a 10-mL, round-bottomed flask equipped with a rubber septum. 2-Cyclopentylphenol (324 mg, 2.0 mmol) was added dropwise with a hypodermic syringe. After the mixture was stirred for 15 min, a clear, light-brown solution was obtained. Stirring was continued for an additional 15 min; the reaction mixture was then cooled in an ice bath, and (2*S*)-glycidyl 3-nitrobenzenesulfonate [(2*S*)-**2b**] (≥99% ee, 467 mg, 1.8 mmol) was added. After the mixture was stirred for 10 min, the ice bath was removed, and stirring was continued for an additional 20 min at room temperature. In order to determine the optical purity of the product, a 0.25-mL aliquot of the reaction mixture was removed, and (2*S*)-*o*-cyclopentylphenyl glycidyl ether was isolated by extraction with ether in the usual way. Mosher ester analysis (300 MHz, ^1H NMR, C_6D_6) of the derived iodohydrin indicated an enantiomeric excss of ≥99%.

To the remainder of the reaction mixture, water (0.18 mL) and *tert*-butylamine (1.89 mL, 18 mmol) were added successively, and the resulting mixture was heated at reflux for 4.5 h under a nitrogen atmosphere. The reaction mixture was then cooled to room temperature, water (25 mL) was added, and the mixture was extracted twice with ether (40 mL, 10 mL). The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to afford 524 mg of crude crystals, which were recrystallized from *n*-heptane to give 423 mg (86%) of (2*S*)-**6b**,[14] mp 68–72 °C [lit.[14] mp 68–72 °C; $[\alpha]^{20}_D$ −11.5° (*c* 1.0, MeOH)].

Reactions of Glycidyl Tosylate with Carbon Nucleophiles. Reaction of Glycidyl Tosylate with Et_2AlCN [(*S*)-7]. This reaction was performed in a manner similar to the procedure described by Nagata, et al.[18] A solution of Et_2AlCN (1.5 M in toluene, 0.34 mL, 0.51 mmol) was added to (2*S*)-glycidyl tosylate

(38) McClure, D. E. Private communication.

(39) For a report of the racemate see ref 14.

(40) We thank Merck Sharp & Dohme Research Laboratories for a sample of this compound.

(41) McClure, D. E.; Engelhardt, E. L.; Mensler, K.; King, S.; Saari, W. S.; Huff, J. R.; Baldwin, J. J. *J. Org. Chem.* **1979**, *44*, 1826.

[(2*S*)-**2a**] (0.115 g, 0.50 mmol) in 5 mL of toluene at room temperature under a nitrogen atmosphere. After 20 min, the reaction mixture was diluted with ether and cooled in an ice bath. A 5% aqueous solution of H_2SO_4 was added, the layers were separated, and the organic layer was washed (saturated $NaHCO_3$, brine), dried (Na_2SO_4), concentrated, and dried under high vacuum to give (*S*)-**7** as a clear, colorless oil (0.124 g, 96%): $[\alpha]^{25}_D$ −14.2° (*c* 1.72, EtOH). The spectral characteristics of this compound were identical with those reported for the racemate.[42]

Reaction of Glycidyl Tosylate with CH_3CN–$BF_3{\cdot}OEt_2$ [(*S*)-8]. $BF_3{\cdot}OEt_2$ (0.25 mmol) was added to a solution of (2*S*)-glycidyl tosylate (94% ee, 0.456 g, 2.0 mmol) in 20 mL of CH_3CN at −15 °C. The reaction mixture was allowed to warm gradually to 0 °C. After 7 h, additional $BF_3{\cdot}OEt_2$ (0.25 mL) was added, and within minutes all remaining starting material had been consumed. The reaction was quenched with saturated $NaHCO_3$, and the aqueous layer was extracted with portions of ether. The combined organic extracts were washed (saturated $NaHCO_3$, brine), dried ($MgSO_4$), and concentrated to give (*S*)-**8** as a colorless oil, which solidified to a waxy solid upon standing (0.489 g, 91%). The product was unstable at room temperature. An analytically pure sample was obtained by flash chromatography (elution with ethyl acetate–hexane): mp 110–113 °C; $[\alpha]^{25}_D$ +44.6° (*c* 2.10, $CHCl_3$); IR ($CHCl_3$) 2970, 2890, 1678, 1370, 1190, 1178, 995, 960, 830, 815, 555 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8 Hz, 2 H), 7.37 (d, *J* = 8 Hz, 2 H), 4.62–4.73 (m, 1 H), 4.10 (dd, *J* = 3.8, 10.9 Hz, 1 H), 4.02 (dd, *J* = 6, 10.9 Hz, 1 H), 3.86 (ddq, *J* = 10, 15, 1 Hz, 1 H), 3.51 (ddq, *J* = 7, 15, 1 Hz, 1 H), 2.46 (s, 3 H), 1.90 (t, *J* = 1 Hz, 3 H). Anal. Calcd for $C_{12}H_{15}NO_4S$: C, 53.51; H, 5.61; N, 5.20. Found: C, 53.26; H, 5.68; N, 5.14.

Reaction of Glycidyl Tosylate with $Ph_2Cu(CN)Li_2$ [(*R*)-9]. Copper cyanide (0.100 g, 1.1 mmol) was placed in a 25-mL, two-necked, pear-shaped flask and successively dried azetotropically with two 2-mL portions of toluene. After all of the solvent had been removed under high vacuum, the salt was suspended in 3 mL of THF, and the mixture was cooled to −78 °C under a nitrogen atmosphere. Phenyllithium (1.66 M in cyclohexane–ether, 1.2 mL, 2.0 mmol) was added by syringe, and the resulting tan-colored solution was stirred for 5 min, warmed to −30 °C, and stirred for an additional 5 min. (2*R*)-Glycidyl tosylate [(2*R*)-**2a**] (88% ee, 0.229 g, 1.0 mmol) was then added by cannula, as a precooled solution in 2 mL of THF.

After 2 h the reaction was quenched with pH 8 NH_4Cl, and the mixture was stirred at room temperature for 1–2 h. The aqueous layer was extracted with portions of ether, and the combined organic extracts were washed with water and brine, dried ($MgSO_4$), and concentrated. Purification of the resulting oil by flash chromatography (elution with ethyl acetate–hexane) afforded 0.086 g (64%) of (*R*)-**9** as a light yellow liquid: $[\alpha]^{25}_D$ +17.5° (*c* 1.94, EtOH) [lit.[25] for (*S*)-**9** $[\alpha]^{27}_D$ −10.0° (neat)]; IR (thin film) 3095, 3065, 3035, 2995, 2920, 1497, 1454, 1405, 850, 740, 705, 700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.13–7.53 (m, 5 H), 3.13–3.20 (m, 1 H), 2.93 (dd, *J* = 6, 14.5 Hz, 1 H), 2.78–2.88 (m, 2 H), 2.56 (dd, *J* = 4, 6 Hz, 1 H).

Also isolated from this reaction was 0.043 g (20%) of 1,3-diphenylpropan-2-ol.

Reaction of Glycidyl Tosylate with PhLi–$BF_3{\cdot}OEt_2$ [(*S*)-10a]. To a solution of $BF_3{\cdot}OEt_2$ (0.13 mL, 1.0 mmol) in 7 mL of THF at −78 °C was added dropwise phenyllithium (1.66 M in cyclohexane–ether, 0.60 mL, 1.0 mmol), followed by a precooled THF solution of (2*S*)-glycidyl tosylate [(2*S*)-**2a**] (88% ee, 0.228 g, 1.0 mmol). After 45 min, the reaction mixture was quenched with saturated $NaHCO_3$, allowed to warm to room temperature, and concentrated under reduced pressure. The aqueous residue was extracted with portions of ether, and the combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated to give an oil. Purification by flash chromatography (elution with ethyl acetate–hexane) afforded 0.185 g (61%) of (*S*)-**10a**, along with 0.087 g (38%) of recovered starting material. For (*S*)-**10a**: $[\alpha]^{25}_D$ +4.6° (*c* 1.68, EtOH); IR (thin film) 3540, 3070, 3040, 2960, 2930, 1360, 1192, 1180, 1100, 980, 840, 670 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8 Hz, 2 H), 7.12–7.38 (m, 7 H), 3.90–4.13 (m, 3 H), 2.64 (apparent d, *J* = 7 Hz, 2 H), 2.45 (s, 3 H), 2.10 (d, *J* = 4.7 Hz, 1 H, O*H*).

Reaction of Glycidyl Tosylate with PhMgBr–Li_2CuCl_4 [(*S*)-10a]. Phenylmagnesium bromide (3.0 M in ether, 3.4 mL, 10.2 mmol) was added to a solution of Li_2CuCl_4[24] (0.1 M in THF, 5.1 mL, 0.51 mmol) in THF (40 mL) at −30 °C. The resulting yellow-brown solution was stirred at that temperature for 30 min and then was added slowly dropwise to a precooled (−30 °C) THF solution (60 mL) of (2*S*)-glycidyl tosylate [(2*S*)-**2a**] (94% ee, 2.280 g, 10.0 mmol) in a 250-mL, three-necked, round-bottomed flask equipped with a low-temperature thermometer, rubber septum, and nitrogen inlet.

After 2 h the reaction was quenched by addition of saturated NH_4Cl (10 mL) at low temperature. Addition of 5 mL of water and 25 mL of ether produced a clean separation of layers. The aqueous layer was extracted with 25 mL of fresh ether, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated to give an oil. Purification by flash chromatography (elution with ethyl acetate–hexane) afforded (*S*)-**10a** (2.564 g, 84%), 1,3-diphenylpropan-2-ol (0.187 g, 9%), and (*S*)-**9** (0.062 g, 5%): $[\alpha]^{25}_D$ −17.3° (*c* 2.07, EtOH).

Hydroxytosylate (*S*)-**10a** (0.167 g, 0.55 mmol) was treated with K_2CO_3/MeOH for 2 h to afford epoxide (*S*)-**9** (0.048 g, 65%): $[\alpha]^{25}_D$ −18.42° (*c* 2.4, EtOH).

Reaction of Glycidyl Tosylate with Cyclohexylmagnesium Chloride–CuI [(*S*)-10b]. A dry, 25-mL, pear-shaped flask was charged with CuI (19.3 mg, 0.10 mmol) under a nitrogen atmosphere. Ethyl ether (4 mL) was added, the suspension was cooled to −40 °C, and cyclohexylmagnesium chloride (2.0 M in ether, 0.50 mL, 1.0 mmol) was added to give a greenish-brown inhomogeneous mixture. After 10 min, (±)-glycidyl tosylate [(±)-**2a**] (0.228 g, 1.0 mmol) was added as a solution in 6 mL of ether. The reaction mixture was stirred for 3 h, quenched with saturated NH_4Cl, and diluted with additional ether. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated to give an oil, which was purified by flash chromatography (elution with ethyl acetate–hexane) to provide **10b** (0.214 g, 69%): IR (thin film) 3540, 2925, 2855, 1360, 1192, 1180, 978, 957, 834, 817, 670, 560 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8 Hz, 2 H), 7.36 (d, *J* = 8 Hz, 2 H), 4.02 (dd, *J* = 2.5, 9.3 Hz, 1 H), 3.90–3.98 (m, 1 H), 3.85 (dd, *J* = 6.8, 9.3 Hz, 1 H), 2.46 (s, 3 H), 2.13 (d, *J* = 4.4 Hz, 1 H, O*H*), 0.78–1.73 (m, 13 H).

Reaction of Glycidyl Tosylate with Mesitylmagnesium Bromide–CuI [(*S*)-10c]. Reaction of (2*S*)-glycidyl tosylates [(2*S*)-**2a**] (94% ee, 0.187 g, 0.82 mmol) with mesitylmagnesium bromide (1.0 M in THF, 0.82 mL, 0.82 mmol) and CuI (0.016 g, 0.08 mmol) was performed as described above, this time in ether at −25 °C for 30 min. Workup and chromatographic purification (elution with ethyl acetate–hexane) afforded 0.257 g (90%) of (*S*)-**10c** as a colorless oil: $[\alpha]^{25}_D$ +10.4° (*c* 2.48, EtOH); IR (thin film) 3540, 2960, 2920, 1360, 1192, 1180, 1100, 980, 835, 815, 670, 560 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, as the acetate) δ 7.76 (d, *J* = 8.2 Hz, 2 H), 7.33 (d, *J* = 8.2 Hz, 2 H), 6.79 (s, 2 H), 5.08–5.17 (m, 1 H), 4.05–4.15 (m, 2 H), 2.96 (dd, *J* = 8.5, 14.3 Hz, 1 H), 2.79 (dd, *J* = 6.5, 14.3 Hz, 1 H), 2.45 (s, 3 H), 2.24 (s, 6 H), 2.23 (s, 3 H), 1.88 (s, 3 H). Anal. Calcd for $C_{19}H_{24}O_4S$: C, 65.49; H, 6.94. Found: C, 65.19; H, 7.01.

Reaction of Glycidyl Tosylate with Benzylmagnesium Chloride–Li_2CuCl_4 [(*S*)-10d]. A 25-mL, two-necked, pear-shaped flask was charged with Li_2CuCl_4 (0.10 M in THF, 0.5 mL, 0.05 mmol) and dry THF (6 mL) under a nitrogen atmosphere, and the solution was cooled to −35 °C. Benzylmagnesium chloride (2.0 M in THF, 0.5 mL, 1.0 mmol) was added dropwise to produce a yellow-green solution. After 40 min, a precooled solution of (2*S*)-glycidyl tosylate [(2*S*)-**2a**] (94% ee, 0.228 g, 1.0 mmol) in 3 mL of THF was added via cannula. Within several minutes the color of the reaction mixture changed to tan. After 3 h, TLC still showed remaining starting material, but the reaction did not appear to be progressing any further. Workup as described above and purification by flash chromatography (elution with ethyl acetate–methylene chloride) afforded, in addition to 0.064 g (28%) of recovered starting material, 0.179 g (56%) of (*S*)-**10d**: mp 65–68.5 °C; $[\alpha]_D^{25}$ −4.7° (*c* 1.5, EtOH); IR (KBr) 3575, 3000, 2960, 1355, 1176, 952, 850, 673, 562 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8 Hz, 2 H), 7.35 (d, *J* = 8 Hz, 2 H), 7.13–7.31 (m, 5 H), 3.79–4.05 (m, 3 H), 2.59–2.83 (m, 2 H), 2.45 (s, 3 H), 1.11

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(d, J = 5 Hz, 1 H, OH), 1.63–1.84 (m, 2 H). Anal. Calcd for $C_{17}H_{20}O_4S$: C, 63.72; H, 6.29. Found: C, 63.43; H, 6.33.

Reaction of Glycidyl Tosylate with *n*-Hexylmagnesium Bromide–Li_2CuCl_4 [(*S*)-10e]. (2*S*)-Glycidyl tosylate [(2*S*)-**2a**] (94% ee, 0.227 g, 0.99 mmol) was treated with *n*-hexylmagnesium bromide (2.0 M in ether, 0.50 mL, 1.0 mmol) and Li_2CuCl_4 (0.1 M in THF, 0.50 mL, 0.05 mmol) as described above for **10d**, except in this case the reaction was performed at −50 °C. Workup after 1 h and purification (flash chromatography, elution with ethyl acetate–hexane) afforded 0.229 g (74%) of (*S*)-**10e** as a white solid: mp 50–52 °C; $[\alpha]_D^{25}$ −2.6° (*c* 2.56, EtOH). Also isolated was 0.043 g (19%) of unchanged glycidyl tosylate. For (*S*)-**10e**: IR (KBr) 3560, 2960, 2930, 2860, 1350, 1175, 958, 846, 820, 678, 532 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.80 (d, J = 8.2 Hz, 2 H), 7.36 (d, J = 8.2 Hz, 2 H), 4.02–4.07 (m, 1 H), 3.84–3.91 (m, 2 H), 2.46 (s, 3 H), 2.03 (d, J = 4.7 Hz, 1 H), 1.25–1.60 (m, 12 H), 0.87 (t, J = 6.6 Hz, 3 H). Anal. Calcd for $C_{16}H_{26}O_4S$: C, 61.31; H, 8.36. Found: C, 61.22; H, 8.23.

Reaction of Glycidyl Tosylate with Vinylmagnesium Bromide–Li_2CuCl_4 [(*S*)-10f]. Reaction of (2*S*)-glycidyl tosylate [(2*S*)-**2a**] (94% ee, 0.227 g, 1.0 mmol) with vinylmagnesium bromide (1.0 M in THF, 1.0 mL, 1.0 mmol) and Li_2CuCl_4 (0.1 M in THF, 0.5 mL, 0.05 mmol) was performed as described above, in this case in THF at −35 °C. Workup after 3 h and purification by flash chromatography (elution with ethyl acetate–methylene chloride) afforded, in addition to 0.093 g (41%) of recovered starting material, 0.125 g (49%) of (*S*)-**10f**: $[\alpha]_D^{25}$ +3.2° (*c* 1.95, EtOH); IR (thin film) 3530, 3080, 2985, 2950, 2930, 1645, 1360, 1192, 1180, 980, 925, 830, 815, 670, 560 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.80 (d, J = 8 Hz, 2 H), 7.36 (d, J = 8 Hz, 2 H), 5.66–5.85 (m, 1 H), 5.07–5.14 (m, 2 H), 3.45–4.14 (m, 3 H), 2.46 (s, 3 H), 2.23–2.28 (m, 2 H), 2.19 (d, J = 3 Hz, 1 H, OH).

Reaction of Glycidyl Tosylate with BH_3·THF/$NaBH_4$ [(*S*)-11a]. To a solution of (2*S*)-glycidyl tosylate [(2*S*)-**2a**] (94% ee, 0.229 g, 1.0 mmol) and $NaBH_4$ (2 mg, 0.05 mmol) in THF (10 mL) at 0 °C under a nitrogen atmosphere was added 1.0 mL (1.0 mmol) of BH_3·THF (1.0 M in THF). The reaction was allowed to warm gradually to room temperature. After 4 h starting material was still visible by TLC, but the reaction did not appear to be progressing. The reaction was quenched by the addition of 2 mL of 5% H_2SO_4–THF (1:1) and extracted with ether. The combined organic extracts were washed (brine), dried ($MgSO_4$), and concentrated to afford a colorless oil in which a small amount of a white precipitate was suspended. Purification by flash chromatography (elution with ethyl acetate–methylene chloride) afforded 0.187 g (81%) of (*S*)-**11a**[27c,29a] as a colorless oil, which solidified upon standing at room temperature: mp 32–34 °C; $[\alpha]_D^{25}$ +11.0° (*c* 1.57, $CHCl_3$) [lit.[29a] mp 31–32 °C; $[\alpha]_D^{25}$ +12.2° (*c* 1.06, $CHCl_3$)]; IR (KBr) 3470, 2990, 1600, 1355, 1180, 980, 935, 816, 640, 560 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.81 (d, J = 8 Hz, 2 H), 7.37 (d, J = 8 Hz, 2 H), 4.00–4.12 (m, 1 H), 4.00 (dd, J = 3, 10 Hz, 1 H), 3.85 (dd, J = 7, 10 Hz, 1 H), 2.46 (s, 3 H), 2.14 (d, J = 4 Hz, 1 H, OH), 1.17 (d, J = 3 H).

Reaction of Glycidyl 3-Nitrobenzenesulfonate with BH_3·THF/$NaBH_4$ [(*S*)-11b]. (2*S*)-Glycidyl 3-nitrobenzenesulfonate [(2*S*)-**2b**] (≥99% ee, 0.258 g, 1.0 mmol) was treated with BH_3·THF (1.0 M in THF, 1.0 mL, 1.0 mmol) and $NaBH_4$ (3.5 mg) in 10 mL of THF at 0 °C as described for **2a** above. After 4 h, additional BH_3·THF (0.1 mL, 0.1 mmol) was added, but TLC continued to show remaining starting material. After 5 h additional $NaBH_4$ (2 mg) was added, and the reaction mixture was allowed to warm to room temperature. Starting material still remained, but the reaction was quenched as described above, and the product was purified by flash chromatography (elution with ethyl acetate–methylene chloride) to afford 0.059 g (23%) of recovered starting material and 0.146 g (56%) of **11b** as a pale yellow solid: mp 61.5–63.5 °C; $[\alpha]_D^{25}$ +8.8° (*c* 2.43, $CHCl_3$); IR (KBr) 3440, 3120, 2990, 2930, 1615, 1538, 1360, 1195, 970, 930, 895, 740, 675, 668, 600 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.78 (t, J = 2 Hz, 1 H), 8.51–8.55 (m, 1 H), 8.25–8.29 (m, 1 H), 7.82 (t, J = 8 Hz, 1 H), 3.95–4.17 (m, 3 H), 2.03 (d, J = 4 Hz, 1 H, OH), 1.21 (d, J = 6.5 Hz, 3 H).

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Registry No. (±)-**1**, 61915-27-3; (*S*)-**1**, 60456-23-7; (±)-**2a**, 118712-54-2; (*S*)-**2a**, 70987-78-9; (*R*)-**2a**, 113826-06-5; (±)-**2b**, 118712-55-3; (*S*)-**2b**, 115314-14-2; (±)-**2c**, 118712-56-4; (*S*)-**2c**, 115314-15-3; (±)-**2d**, 118712-57-5; (*S*)-**2d**, 115314-16-4; (±)-**2e**, 118629-62-2; (*S*)-**2e**, 118712-58-6; (±)-**2f**, 118629-63-3; (*S*)-**2f**, 118712-59-7; (±)-**2g**, 118629-64-4; (*S*)-**2g**, 118712-60-0; (±)-**2h**, 118629-65-5; (*S*)-**2h**, 118712-61-1; (±)-**2i**, 118629-66-6; (*R*)-**2i**, 118712-62-2; (±)-**2j**, 118629-67-7; (*S*)-**2j**, 118712-63-3; **5a**, 71031-03-3; **5b**, 61249-00-1; **5c**, 118629-68-8; **5d**, 69500-53-4; **6b**, 38363-40-5; **7**, 118712-64-4; **8**, 118629-69-9; (*R*)-**9**, 91420-74-5; (*S*)-**9**, 61393-94-0; (*S*)-**10a**, 118629-70-2; (±)-**10b**, 118629-71-3; (*S*)-**10c**, 118629-72-4; (*S*)-**10d**, 118629-73-5; (*S*)-**10e**, 118629-74-6; (*S*)-**10f**, 118629-75-7; **11a**, 32464-98-5; **11b**, 118629-76-8; phenol, 108-95-2; 1-naphthol, 90-15-3; 2-cyclohexylphenol, 1518-84-9; 4-morpholino-3-hydroxy-1,2,5-thiadiazole, 30165-97-0; tosyl chloride, 98-59-9; *m*-nitrobenzenesulfonyl chloride, 121-51-7; *p*-chlorobenzenesulfonyl chloride, 98-60-2; 4-chloro-3-nitrobenzenesulfonyl chloride, 97-08-5; 2,4,5-trichlorobenzenesulfonyl chloride, 15945-07-0; *p*-bromobenzenesulfonyl chloride, 98-58-8; 2,4,6-triisopropylbenzenesulfonyl chloride, 6553-46-4; *p*-methoxybenzenesulfonyl chloride, 98-68-0; naphthalenesulfonyl chloride, 93-11-8.