filtered, and the Et_2O distilled off through a 21 × 1 cm spiral column. The residue was directly analyzed by GC. Example (run 11): 15.4 mg of *R*-**1** (ec 99.6%, 15.3 mg of *R*-**1**, 0.1 of mg *S*-**1**), 46.0 mg of *S*-**1** (ec 98.3%, 45.2 mg of *S*-**1**, 0.8 mg of *S*-**1**), totalling 16.1 mg of *R*-**1** + 45.3 mg of *S*-**1** = 61.4 mg (0.40 mmol), ec 26.2% (Table I; $X_{R\text{-}1} = 0.262$), 14.8 mg of K (0.38 mmol, 0.95 equiv), which dissolved within 49 s. After workup, the crude mixture was analyzed once on the Supelcowax column, (*R*-**1** + *S*-**1**) = 61.48%, (*R*-**2** + *S*-**2**) = 29.21%, (*R*-**3** + *S*-**3**) = 9.31%, conversion about 77% [100 - (61.48 - (29.21 + 9.31)) = 77.04], (*R*-**2** + *S*-**2**)/(*R*-**3** + *S*-**3**) = 75.8/24.2 (Table I; $Y_{(R\text{-}3+S\text{-}3)} = 0.242$), and once on the nickel heptafluorobutyrylcamphorate column, *R*-**2**/*S*-**2** = 31/69 (Table I; $Y'_{R\text{-}2} = 0.310$), *R*-**3**/*S*-**3** = 3/97 (Table I; $Y'_{R\text{-}3} = 0.030$).

The low-conversion procedure was essentially the same, except that somewhat less K was used and the volumes and amounts of substrate were correspondingly much larger. Example (run 21): A solution of 800.6 mg of *RS*-**1** (400.3 mg of *R*-**1**, 400.3 mg of *S*-**1**) and 200.9 mg of *R*-**1** (ec 99.6%, 200.1 mg of *R*-**1**, 0.8 mg of *S*-**1**), totalling 600.4 mg of *R*-**1** + 401.1 mg of *S*-**1** = 1001.5 mg (6.6 mmol), ec 60.0% (Table I; $X_{R\text{-}1} = 0.600$), in 39 mL of THF was syringed via septum into 230 mL of NH_3 in a three-necked flask maintained in a CO_2/acetone bath under Ar. To the resulting, stirred (Teflon-coated magnetic stirring bar) solution was added 2.3 mg of K (0.06 mmol, 0.009 equiv), which dissolved within 15 s. After workup, the crude mixture was analyzed three times on the Supelcowax column, (*R*-**1** + *S*-**1**) = 99.587, 99.585, 99.591%, mean 99.588%, (*R*-**2** + *S*-**2**) = 0.353, 0.358, 0.356%, mean 0.356%, (*R*-**3** + *S*-**3**) = 0.057, 0.057, 0.053%, mean 0.056%, conversion about 0.8%, (*R*-**2** + *S*-**2**)/(*R*-**3** + *S*-**3**) = 86.1/13.9, 86.3/13.7, 87.0/13.0, mean 86.4/13.6 (Table I; $Y_{(R\text{-}3+S\text{-}3)} = 0.136$). Part of the (*R*-**1** + *S*-**1**) was removed by small-scale preparative GC, and two ~1-mg samples were collected in glass capillaries. Each was dissolved in hexane and each analyzed once on the Supelcowax column. Sample I: (*R*-**1** + *S*-**1**) = 77.68%, (*R*-**2** + *S*-**2**) = 19.04%, (*R*-**3** + *S*-**3**) = 3.28%, (*R*-**2** + *S*-**2**)/(*R*-**3** + *S*-**3**) = 85.3/14.7. Sample II: (*R*-**1** + *S*-**1**) = 83.19%, (*R*-**2** + *S*-**2**) = 14.39%, (*R*-**3** + *S*-**3**) = 2.42%, (*R*-**2** + *S*-**2**)/(*R*-**3** + *S*-**3**) = 85.6/14.4. Sample I was analyzed four times on the nickel heptafluorobutyrylcamphorate column, *R*-**2**/*S*-**2** = 52/48, 52/48, 53.5/46.5 (no integration in one analysis), *R*-**3**/*S*-**3** = 86/14, 84/16, 85/15, 87.5/12.5, and sample II once, *R*-**2**/*S*-**2** = 54/46, *R*-**3**/*S*-**3** = 86/14, mean *R*-**2**/*S*-**2** = 52.9/47.1 (Table I; $Y'_{R\text{-}2} = 0.529$), mean *R*-**3**/*S*-**3** = 85.7/14.3 (Table I; $Y'_{R\text{-}3} = 0.857$).

The runs and the results of the gas chromatographic analyses [except the proportions of (*R*-**1** + *S*-**1**) on the Supelcowax column] are listed in Table I.

Acknowledgment. V.R. is greatly indebted to H. B. Kagan for discussions and lessons in kinetic resolution. Discussions with J. R. Bourne, H. Fischer, J. W. Huffman, P. Müller, E. Oliveros, W. R. Roth, D. Seebach, B. Sharpless, I. Ugi, and G. Whitesides are gratefully acknowledged, but V.R. is solely responsible for any deficiencies of this paper. Thanks are also due to M. Lindström at Firmenich for determining the ec's of *R*-**1**, *S*-**1**, and *RS*-**1** on the cyclodextrin column.

Chemistry of Oxaziridines. 17.[1] *N*-(Phenylsulfonyl)(3,3-dichlorocamphoryl)oxaziridine: A Highly Efficient Reagent for the Asymmetric Oxidation of Sulfides to Sulfoxides

Franklin A. Davis,* R. Thimma Reddy,[†] Wei Han,[†] and Patrick J. Carroll[‡]

Contribution from the Department of Chemistry, Drexel University, Philadelphia, Pennsylvania 19104, and Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104. *Received July 10, 1991*

Abstract: The synthesis, structure, and enantioselective oxidations of a new chiral *N*-sulfonyloxaziridine **12c** [3,3-dichloro-1,7,7-trimethyl-2′-(phenylsulfonyl)spiro[bicyclo[2.2.1]heptane-2,3′-oxaziridine]] are reported. This oxidant, which exhibits remarkably high and predictable ee's for the enantioselective oxidation of prochiral sulfides to sulfoxides, is prepared in three steps from (+)- or (−)-camphor in 50% overall yield. Steric effects are primarily responsible for the molecular recognition and are predictable using a simple active-site model where the nonbonded interactions between the R_L and R_S groups of the sulfide (R_L-S-R_S) and the active-site surface are minimized in a planar transition-state structure. The fact that alkyl aryl sulfides give high ee's in nonpolar solvents suggests that there is also a stereoelectronic component to the molecular recognition. High ee's (>90%) are anticipated for those sulfides where the difference in size of the groups directly bonded to the sulfur atom is large, i.e., aryl, *tert*-butyl vs CH_2R (R = H, alkyl, benzyl, etc). The X-ray structure and studies with the dihydro, difluoro, and dibromo oxaziridines **12a**, **12b**, and **12d** reveal that the exceptional enantioselectivities displayed by **12c** are a consequence of a molecular cleft or groove, defined by the oxaziridine chlorine atoms and phenylsulfonyl group, on the active-site surface.

Enantiomerically pure sulfoxides are widely used intermediates for the synthesis of optically active materials.[2] The reaction of an organometallic reagent with a diastereomerically pure menthyl *p*-toluenesulfinate, the Andersen procedure, is the method most often employed for the synthesis of chiral nonracemic sulfoxides.[3,4] However, this procedure is limited in the synthesis of highly functionalized sulfoxides and for certain dialkyl sulfoxides.[5] The asymmetric oxidation of a prochiral sulfide with an enantiopure oxidizing reagent, at least in principle, is an attractive alternative because (i) the sulfoxide would be available in one step and (ii) those sulfoxides not readily accessible by the Andersen procedure could be realized.

(1) Davis, F. A.; Kumar, A.; Chen, B.-C. *J. Org. Chem.* **1991**, *56*, 1143.

(2) For excellent reviews on the synthesis and application of chiral sulfoxides, see: (a) Posner, G. H. In *The Chemistry of Sulphones and Sulphoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; John Wiley & Sons Ltd.: Chichester, England, 1988; Chapter 16, pp 823-849. (b) Posner, G. H. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, Chapter 8, pp 225-240. (c) Barbachyn, M. R.; Johnson, C. R. In *Asymmetric Synthesis*; Morrison, J. D., Scott, J. W., Eds.; Academic Press: New York, 1983; Vol. 4, Chapter 2, pp 227-256. (d) Solladie', G. *Synthesis* **1981**, 185.

(3) Andersen, K. K. In *The Chemistry of Sulphones and Sulphoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; John Wiley & Sons Ltd.: Chichester, England, 1988; Chapter 3, pp 55-94.

(4) Mikolajczyk, M.; Drabowicz, J. *Top. Stereochem.* **1982**, *13*, 333.

(5) Rebiere, F.; Kagan, H. B. *Tetrahedron Lett.* **1989**, *30*, 3659.

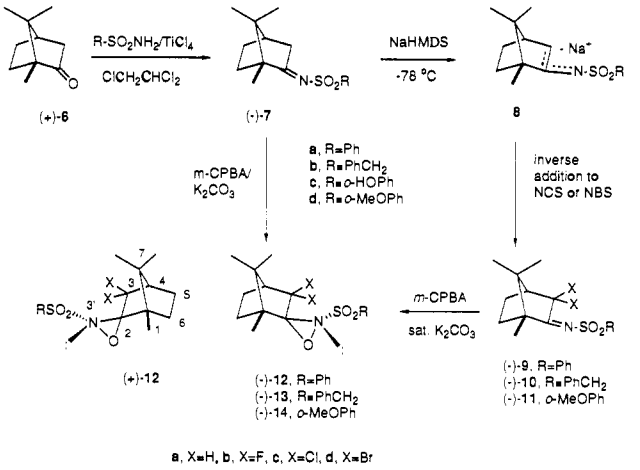
0002-7863/92/1514-1428$03.00/0

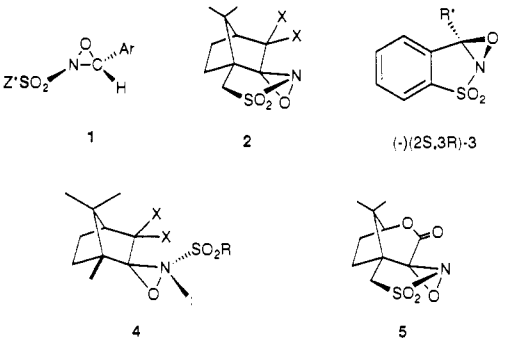
All of the chiral oxidizing systems developed to date exhibit highly variable and unpredictable stereoselectivities, being both substrate- and reagent-dependent.[3,4,6] This is to be expected because sulfides are examples of *nonfunctionalized* substrates.[7] Lacking functional groups, these compounds are unable to coordinate with the oxidant to form the highly ordered, rigid transition-state geometries which are a prerequisite for most enantioselective transformations that occur with high stereoselectivity.[2,6] In nonfunctionalized substrates, steric and stereoelectronic noncovalent forces must be relied upon to control the molecular recognition.[8] Unfortunately, the influence of stereoelectronic noncovalent forces on molecular recognition is poorly understood because of the difficulty in separating these effects from those due to steric forces.[8,9] For this reason, the development of reagents for the asymmetric oxidation of structurally diverse, nonfunctionalized substrates (i.e., chiral sulfoxide) that afford high and predictable stereoselectivities is a formidable synthetic challenge.

For the oxidation of sulfides to sulfoxides, chiral peracids give poor results (0–10% ee),[10] although oxidation in chiral media is, in a few cases, better (up to 80% ee).[10d] Asymmetric oxidations using chiral Fe(III) porphyrins give ee's in the range 14–48%.[10e] Kagan and co-workers demonstrated that the Sharpless reagent, modified with water, is a highly efficient system for the asymmetric oxidation of methyl aryl sulfides (Ar–S–Me) to sulfoxides with ee's ≥90.[11] However, with other sulfides this reagent system is unpredictable, giving lower ee's; for example, *n*-butyl and isopropyl *p*-tolyl sulfides result in 20% and 63% ee, respectively. While the mechanism of molecular recognition appears to be largely steric in origin, it is not fully understood primarily because the structure of the active site is unknown.

The enantiopure *N*-sulfonyloxaziridines have proven to be useful reagents for the enantioselective oxidation of a variety of substrates with high and predictable stereoselectivities.[12] In our laboratory four types of enantiopure *N*-sulfonyloxaziridines **1–4** have been prepared and evaluated. In their oxidations these reagents exhibit different stereoselectivities reflecting their dissimilar active-site structures. Oxaziridines of type **1** epoxidize nonfunctionalized *trans*-alkenes with stereoselectivities up to 94% ee.[13] The (camphorylsulfonyl)oxaziridines **2** are much better than types **1**, **3**,[14] or **4** for the oxidation of prochiral metal enolates to α-hydroxy carbonyl compounds, with ee's often better than 95%.[15] While **1–3**, (3-oxocamphorylsulfonyl)oxaziridine (**2**, X = O),[16a] and the actone **5**,[16b] developed by Herrmann et al., all oxidize sulfides to sulfoxides, the ee's are at best only modest (3–72%).

Scheme I





The most effective and general *N*-sulfonyloxaziridines developed to date for the asymmetric oxidation of sulfides (selenides) to sulfoxides (selenoxides) are type **4**, a new class of these reagents.[17] In this paper, details of the synthesis of **4**, its structure, its stereoselective oxidations, and a mechanistic rationale for the molecular recognition are presented.

Results

Synthesis of *N*-Sulfonylcamphorimines. (−)-*N*-Sulfonylcamphorimine **7** is prepared by treating an equivalent amount of the appropriate sulfonamide (RSO_2NH_2) with (1*R*)-(+)-camphor (**6**) and 0.65 equiv of $TiCl_4$ in 1,1,2-trichloroethane and refluxing for 24 h (Scheme I). Following the addition of a second 0.65 equiv of $TiCl_4$, heating was continued (24 h) and the sulfonylimines were isolated by flash chromatography in >80% isolated yield. The use of other solvents (THF, toluene) or the addition of triethylamine resulted in reduced yields (40–65%). Condensation of *o*-methoxybenzenesulfonamide with (+)-**6** and 1.0 equiv of $TiCl_4$ gave, in addition to (−)-**7d**, the demethylated derivative (−)-**7c** in 41% yield. The use of 2 equiv of $TiCl_4$ increased the yield of (−)-**7c** to 57%. The hydroxy derivative was readily converted into **7d** by treatment with MeI/K_2CO_3 in 93% yield.

The dichloro and dibromo imines **9–11** were prepared by the addition of aza enolate **8**, generated by treatment of **7** with 2.5–3 equiv of sodium bis(trimethylsilyl)amide (NaHMDS), to a −78

(6) For leading references on the asymmetric oxidation of sulfides to sulfoxides, see: Davis, F. A.; McCauley, J. P., Jr.; Chattopadhyay, S.; Harakal, M. E.; Towson, J. C.; Watson, W. H.; Tavanaiepour, I. *J. Am. Chem. Soc.* **1987**, *109*, 3370.

(7) For examples of the asymmetric dihydroxylation and epoxidation of nonfunctionalized alkenes, see: (dihydroxylation) Kwong, H.; Sorato, C.; Ogino, Y.; Chen, H.; Sharpless, K. B. *Tetrahedron Lett.* **1990**, *31*, 2999 and references cited therein. Epoxidation: Shang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801.

(8) (a) For general discussions of noncovalent forces, see: Kollman, P. In *The Chemistry of Enzyme Action*; Page, I. M., Ed.; Elsevier: New York, 1984; Vol. 6, Chapter 2. (b) *Chemical Approaches to Understanding Enzyme Catalysis*; Green, B. S., Ashani, Y., Chipman, D., Eds.; Wiley Elsevier: Amsterdam, New York, 1982. (c) Jorgensen, W. L.; Severance, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 4768 and references cited therein.

(9) Polar noncovalent forces: (π-stacking) (a) Trost, B. M.; O'Krongly, D.; Belletire, J. L. *J. Am. Chem. Soc.* **1980**, *102*, 7595. Dipole–dipole, van der Waals attraction: (b) Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238.

(10) (a) Folli, U.; Iarossi, D.; Montanari, F.; Torre, G.; Simmons, T. *J. Chem. Soc. C* **1968**, 1317. (b) Mislow, K.; Green, M. M.; Laur, P.; Melillo, J. T.; Simmons, T.; Ternay, A. L., Jr. *J. Am. Chem. Soc.* **1965**, *87*, 1958. (c) Pirkle, W. H.; Rinaldi, P. L. *J. Org. Chem.* **1977**, *42*, 2080. (d) Also see ref 6. (e) Groves, J. T.; Viski, P. *J. Org. Chem.* **1990**, *55*, 3628. In this study the stereoselectivity is difficult to evaluate because, in addition to sulfoxides, sulfones are also produced, suggesting the possibility that kinetic resolution is influencing the degree of enantioinduction.

(11) (a) Pitchen, P.; Dunach, E.; Deshmukh, M. N.; Kagan, H. B. *J. Am. Chem. Soc.* **1984**, *106*, 8188. (b) Dunach, E.; Kagan, H. B. *Nouv. J. Chim.* **1985**, *9*, 1. (c) Kagan, H. B.; Dunach, E.; Nemecck, C.; Pitchen, P.; Samuel, O.; Zhao, S.-H. *Pure Appl. Chem.* **1985**, *57*, 1911. (d) Kagan, H. B. *Stereochem. Org. Bioorg. Transform. Proc. Workshop Conf. Hoechst, 17th 1986*; Bartmann, W., Sharpless, K. B., Eds.; VCH: Weinheim, Germany, 1987; pp 31–48. (e) Zhao, S. H.; Kagan, H. B. *Tetrahedron* **1987**, *43*, 5135.

(12) For a review on the asymmetric oxidations of *N*-sulfonyloxaziridines, see: Davis, F. A.; Sheppard, A. C. *Tetrahedron* **1989**, *45*, 5703.

(13) Davis, F. A.; Przeslawski, R. M.; Chattopadhyay, S. Unpublished results.

(14) Davis, F. A.; Thimma Reddy, R.; McCauley, J. P., Jr.; Przeslawski, R. M.; Harakal, M. E.; Carroll, P. J. *J. Org. Chem.* **1991**, *56*, 809.

(15) (a) Davis, F. A.; Sheppard, A. C.; Chen, B.-C.; Haque, M. S. *J. Am. Chem. Soc.* **1990**, *112*, 6679. (b) Davis, F. A.; Chen, B.-C. *Tetrahedron Lett.* **1990**, *31*, 6823. (c) Davis, F. A.; Weismiller, M. C. *J. Org. Chem.* **1990**, *55*, 3715. (d) Davis, F. A.; Kumar, A.; Chen, B.-C. *Tetrahedron Lett.* **1991**, *32*, 867.

(16) (a) Glahsl, G.; Herrmann, R. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1753. (b) Meladinis, W.; Verfurth, U.; Herrmann, R. *Z. Naturforsch.* **1989**, *44b*, 1453.

(17) Davis, F. A.; Thimma Reddy, R.; Weismiller, M. C. *J. Am. Chem. Soc.* **1989**, *111*, 5964.

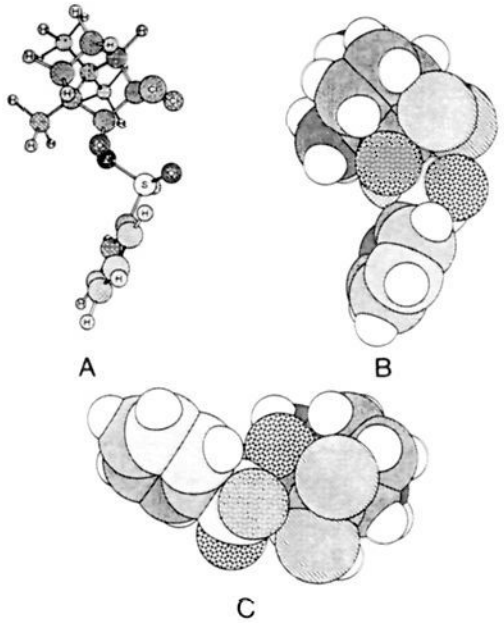
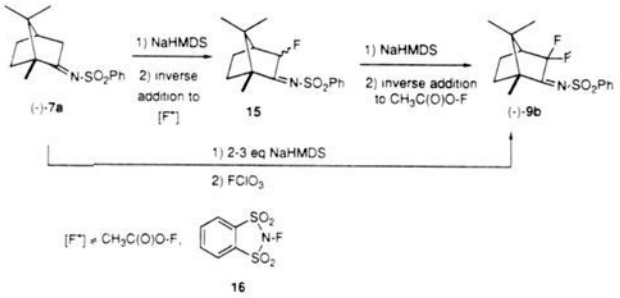


Figure 1. Computer-generated X-ray structure of (3′*R*,2*S*)-(+)-**12c**.

°C solution of 3.0 equiv of *N*-chloro- or *N*-bromosuccinimide. The dichloro and dibromo sulfonylimines **9** and **10** were generated in greater than 80% yield and purified by crystallization or flash chromatography. Sulfonylimines **9–11** gave satisfactory elemental analyses and exhibited characteristic infrared absorptions at 1590–1680 cm^{-1} due to the C=N double bond of the sulfonylimine. The ^{13}C NMR absorption at δ 175–200 ppm for the imino carbon atom is particularly diagnostic for these compounds.

Attempts to prepare the difluoro sulfonylimine **9b** by treatment of aza enolate **8a** with *N*-fluoro-*N*-alkylsulfonamides or with *N*-fluoropyridinium triflate failed, resulting in recovery of the starting material. Addition of aza enolate **8a** to a 0 °C solution of acyl hypofluorite ($CH_3C(O)OF$)[18] gave only the monofluoro sulfonylimine **15** in less than 30% yield. Addition of **8a** (R = Ph) to 2.0 equiv of *N*-fluoro-*o*-benzenedisulfonimide [N-FOBS] (**16**),[19] a stable, easily prepared source of "electrophilic" fluorine, improved the yield of **15** to 65%. However, none of the desired difluoro compound (−)-**9b** was detected. Compound **9b** was prepared in 40% yield by treatment of the sodium aza enolate of **15** with acetyl hypofluorite.

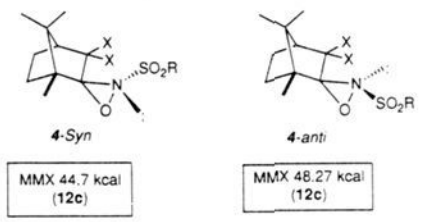


The most expeditious route to **9b** is treatment of aza enolate **8a** with perchloryl fluoride ($FClO_3$) at 0 °C to give a 40:60 mixture of **15**/**9b**, from which **9b** was isolated in 43% yield by chromatography. The difluoride **9b** gave a satisfactory elemental analysis, and the two fluorine atoms appear as an AB quartet centered at −100.3 ppm in the ^{19}F NMR. While we experienced no difficulties in using perchloryl fluoride, explosions with this reagent have been reported.[20]

(Camphorylsulfonyl)oxaziridines. Biphasic oxidation of *N*-sulfonylcamphorimines **7** and **9–11** with >95% *m*-chloroperbenzoic acid (*m*-CPBA) saturated with potassium carbonate (K_2CO_3) afforded the corresponding (camphorylsulfonyl)oxaziridines **12–14** in poor to excellent yields (23–87%). While oxidation of the unsubstituted sulfonylimines **7a–d** were complete within 3–4 h, the substituted derivatives **9–11** required 4–7 days. In each of these examples it was necessary to add *m*-CPBA/K_2CO_3 each day to drive the oxidation to completion. The best results were obtained, particularly with large-scale oxidations (>20 g), when the sulfonylimine was dissolved in a minimum amount of CH_2Cl_2. Lower yields and longer reaction times resulted on dilution with the only exception being difluoro sulfonylimine **9b**, which gave oxaziridine **12b** in greater than 88% isolated yield within 3 h. Undoubtedly, the slow rate of oxidation of **9–11** can be attributed to the bulky X-substituents adjacent to the C–N double bond, which inhibits the Bayer–Villiger type oxidation. Compounds **12–14** gave satisfactory elemental analyses and exhibit, in their ^{13}C NMR spectra, a characteristic absorption at δ 95–101 ppm for the oxaziridine carbon atom.

Oxaziridine (+)-**12c**, the antipode of (−)-**12c**, was prepared in a similar manner starting from (1*S*)-(−)-camphor (**6**).

Structure of N-Substituted (Camphorylsulfonyl)oxaziridines. In principle, oxidation of *N*-sulfonylcamphorimines **9–11** could lead to mixtures of the *syn*-**4** and *anti*-**4** oxaziridines. Jennings



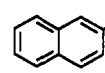
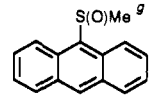
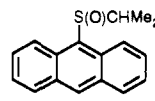
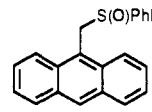
et al. established that the nitrogen atom in certain *N*-sulfonyloxaziridines is not configurationally stable at ambient temperatures ($\Delta G^{\ddagger}$ = 19.8–20.6 kcal/mol) with the equilibrium preference dependent on the substituents.[21] However, inspection of both the ^1H and ^{13}C NMR spectra of **12** and **13** suggest that only a single oxaziridine isomer was formed.

The computer-generated X-ray crystal structure of (+)-**12c** is shown in Figure 1 and establishes that the phenylsulfonyl group is syn to the two chlorine atoms. An unfavorable interaction between the camphor methyl and bulky phenylsulfonyl group is most likely responsible for this syn orientation. Indeed the MMX calculated steric energies indicate that there is a 3.57 kcal difference between the syn and anti forms.[22] The oxaziridine three-membered ring in (+)-**12c** has the 3′*R*,2*S* configuration. It is reasonable to assume that oxaziridines **12–14** have a similar preference for the syn orientation.

The structure of the oxaziridine three-membered ring in **12c** is not statistically different from those in **1–3**. The π-orbital of the phenyl CSO_2 carbon in (+)-**12c** and other oxaziridines is gauche with respect to the sulfonyl oxygens.[23] Similar gauche orientations of the lone pair of electrons are observed for α-sulfonyl carbanions[24] and the isoelectronic sulfonamides[25] in both solution and the solid state. Ab initio calculations by Bors and Streitwieser on [(methylsulfonyl)methyl]lithium predicted this minimum energy conformation and ascribed it to an $n_C-\sigma^*_{SR}$ interaction.[26]

(18) Rozen, S.; Brand, M. *Synthesis* **1985**, 665.
(19) Davis, F. A.; Han, W. *Tetrahedron Lett.* **1991**, *32*, 1631.
(20) Rozen, S.; Filler, R. *Tetrahedron* **1985**, *41*, 1111.
(21) Jennings, W. B.; Watson, S. P.; Boyd, D. R. *J. Chem. Soc., Chem. Commun.* **1988**, 931. Jennings, W. B.; Watson, S. P.; Tolley, M. S. *J. Am. Chem. Soc.* **1987**, *109*, 8099.
(22) *PCMODEL (MMX)*; Gilbert, K. E.; Gajewski, J. J., Serena Software, P. O. Box 3076, Bloomington, IN 47402-3076.
(23) Chen, J. S.; Watson, W. H.; Davis, F. A.; Lamendola, J. F., Jr.; Nadir, U. K. *Acta Crystallogr.* **1978**, *B34*, 261. Kimura, M.; Watson, W. H.; Davis, F. A.; Lamendola, J. F., Jr.; Nadir, U. K. *Acta Crystallogr.* **1979**, *B35*, 234.
(24) Gais, H.-J.; Vollhardt, J.; Lindner, H. J. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 939.
(25) Jordan, T.; Smith, W. H.; Lohr, L. L.; Lipscomb, W. N. *J. Am. Chem. Soc.* **1963**, *85*, 846. Vikov, L. V.; Khargittai, I. Y. *Dokl. Akad. Nauk SSSR* **1966**, *168*, 1065. Jennings, W. B.; Spratt, R. *J. Chem. Soc., Chem. Commun.* **1970**, 1418.
(26) Bors, D. A.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 1397.

Table I. Asymmetric Oxidation of Aryl Alkyl Sulfides to Sulfoxides Using (Camphorylsulfonyl)oxaziridines (−)-**12a** and (−)-**12c** at 20 °C

entry	sulfoxide	solvent	% ee (configuration) [time (h)] % yield[a] **12a** (X = H)	**12c** (X = Cl)	$[\alpha]^{20}_D$, deg (acetone)	modified Sharpless[b]
1	*p*-tol-S(O)-Me[c,d]	CH_2Cl_2	28 (*S*) [1] 80	62 (*S*) [1] 60		96 (*R*)[e]
2		CCl_4	26 (*S*) [40] 22	>95 (*S*) [4] 95	−139.0 (*c* 1.6)	
3	*p*-MeOPh-S(O)-Me[c]	CH_2Cl_2		72 (*S*)[f] [2] 62		86
4		CH_2Cl_2 (−78 °C)		83 (*S*) [5] 73	−113.8 (*c* 3.09, $CHCl_3$)	
5		CCl_4		80 (*S*) [2] 74		
6	*p*-tol-S(O)-*n*-Bu[g]	CH_2Cl_2	11 (*S*) [1] 70	61 (*S*) [1] 90		20 (*R*)[b]
7		CCl_4	8 (*S*) [18] 90	91 (*S*) [3] 90	−162.3 (*c* 3.2)	
8		CCl_4		91 (*R*)[h] [3] 90	+157.6 (*c* 1.1)	
9	*p*-tol-S(O)-*i*-Pr[g]	CH_2Cl_2		54 (*S*) [1] 95	−119.0 (*c* 3.0)	
10		CCl_4		66 (*S*) [6] 95		
11	*p*-MeOPh-S(O)-*i*-Pr[c]	CH_2Cl_2		68 (*S*)[f] [4] 95	−113.8 (*c* 0.37, $CHCl_3$)	63 (*R*)
12		CCl_4		64 (*S*) [6] 95		
13	*p*-tol-S(O)-CH_2Ph[c]	CH_2Cl_2		82 (*S*) [3] 86		7 (*R*)
14		CCl_4		94 (*S*) [3] 88	−179.1 (*c* 1.3)	
15	PhS(O)-[d]	CCl_4	23 (*S*) [40] 23	92 (*S*) [18] 90	−131.6 (*c* 1.1)	95 (*R*)[i]
16	PhS(O)CMe_3	CH_2Cl_2		6 (*S*) [48] 34		
17		CCl_4		26 (*S*) [48] 50	+13.3 (*c* 0.7)	
18	 [c]	CH_2Cl_2		86 (*S*) [8] 91		90[i]
19		CCl_4		94 (*S*) [8] 84	−125.5 (*c* 1.0, $CHCl_3$)	
20	 [g]	CH_2Cl_2	64 (*S*) [1] 70	95 (*S*) [1] 90	−138.8 (*c* 1.2)	86 (*R*)[i]
21		CCl_4	73 (*S*) [1] 80	95 (*S*) [48] 60		
22		CCl_4 (65 °C)		86 (*S*) [5] 62		
23		CCl_4		95 (*R*)[h] [48] 70	+136.2 (*c* 1.4)	
24	 [g]	CH_2Cl_2	68 (*S*) [1] 74	86 (*S*) [2] 70		
25		CCl_4		94 (*S*) [48] 60		
26	 [c]	CH_2Cl_2		70 (*S*)[f] [18] 66		
27		CCl_4		85 (*S*) [48] 60	+63.5 (*c* 0.45, $CHCl_3$)	

[a] Isolated yields. [b] Oxidation at −20 °C for 4–22 h. See ref 12. [c] ee's determined using Eu(hfc)$_3$. [d] Determined by comparison of the rotation to literature values. [e] Reference 11e. [f] Proposed configuration based on active-site model. [g] The sulfoxide enantiomers were separated on a Regis Pirkle covalent phenylglycine HPLC column eluting with 95:5 hexane/isopropyl alcohol. The *S*-sulfoxides were the first to be eluted. See ref 6. [h] Oxidation using (+)-**12c**. [i] Reference 11a.

Table II. Asymmetric Oxidation of Dialkyl Sulfides to Sulfoxides Using (Camphorylsulfonyl)oxaziridine (−)-**12c** at 20 °C

entry	sulfoxide	solvent	% ee (config) [time (h)] % yield[a]	$[\alpha]^{20}_D$, deg ($CHCl_3$)	modified Sharpless[b]
1	$PhCH_2$-S(O)-CMe_3[c,d]	CH_2Cl_2	94 (*S*) [48] 80	−220.0 (*c* 1.7)	
2		$CHCl_3$	90 (*S*) [48] 80		
3		CCl_4	91 (*S*) [48] 80		
4		CCl_4 (65 °C)	85 (*S*) [1] 80		
5	Me-S(O)-CMe_3[c,d]	CH_2Cl_2	93 (*S*) [6] 90		
6		CCl_4	94 (*S*) [18] 84	+7.1 (*c* 1.0)	53 (*R*)
7		CCl_4	94 (*R*)[e] [12] 84		
8	$PhCH_2$-S(O)-Me	CH_2Cl_2	14 (*S*) [2] 90		58 (*S*)
9		CH_2Cl_2 (−78 °C)	19 (*S*) [3] 90	+19.5 (*c* 4.6, EtOH)	
10		CCl_4	13 (*S*) [2] 94		
9	Me-S(O)-$(CH_2)_7CH_3$[c,d]	CH_2Cl_2	15 (*S*) [0.5] 61		80 (*R*)[f]
10		$CHCl_3$	14 (*S*) [0.5] 60		
11		$CHCl_3$ (−15 °C)	45 (*S*) [0.5] 60		
12		$CHCl_3$ (−60 °C)	58 (*S*) [4] 57	+43.0 (*c* 1.1, acetone)	
13		CCl_4	15 (*S*) [0.5] 60		

[a] Isolated yields. [b] Oxidations at −30 °C for 4–22 h. See ref 11a. [c] Determined by comparison of the rotation to literature values. [d] ee's determined using Eu(hfc)$_3$. [e] Oxidation using (+)-**12c**. [f] Reference 11e.

While solution and solid-state structures often differ significantly, we believe that **12** has a relatively fixed conformation in solution which approximates the solid-state structure (Figure 1). In support of this hypothesis are the similar gauche orientations for sulfonyl compounds in both solution and the solid state, discussed above, and the fact that a temperature-dependent ^{1}H NMR study of **12** failed to detect any significant changes in its spectra. Furthermore, the high ee's observed for **12c** (Tables I–IV) would seem to be incompatible with a conformationally mobile reagent because the stereoselectivity of such a reagent would be dependent

Table III. Asymmetric Oxidation of Functionalized Sulfides to Sulfoxides Using (Camphorylsulfonyl)oxaziridines **12a** and **12c** at 20 °C

entry	sulfoxide	solvent	% ee (config) [time (h)] % yield[a] **12a** (X = H)	% ee (config) [time (h)] % yield[a] **12b** (X = Cl)	$[\alpha]^{20}_D$, deg (acetone)	modified Sharpless[b]
1	Ph-S(O)-CH=CH_2[c]	CCl_4	21 (*S*) [40] 25	85 (*S*) [48] 60	−262.4 (*c* 1.7)	70 (*R*)[d]
2	Ph-S(O)-$CH_2CO_2CH_3$[c,e]	CCl_4	23 (*S*) [40] 18	94 (*S*) [48] 65	−174.0 (*c* 1.5)[g]	64 (*R*)[d]
3		CCl_4		94 (*R*)[f] [17] 47	+178.9 (*c* 1.86)	
4	Ph-S(O)-$CH_2C(O)CH_3$[c,e]	CCl_4	no rxn	84 (*S*) [48] 52	−183.2 (*c* 1.1)	60 (*R*)[d]
5						
6	Ph-S(O)-CH_2CN[e]	CCl_4	no rxn	>95 (*S*) [48] 45	−170.1 (*c* 1.0)	34 (*R*)[d]
7	*n*-BuC≡C-S(O)-Me	CH_2Cl_2		66 (*R*)[f] [48] 55	−56.7 (*c* 2.1)	75 (*R*)[b]
8		CCl_4		75 (*R*)[f] [48] 53	−67.3 (*c* 1.9)	
9		CCl_4		76 (*S*) [48] 55	+69.1 (*c* 1.5)	
10		CCl_4		80 (*S*)[h] [3] 60	−57.4 (*c* 0.6)[i]	

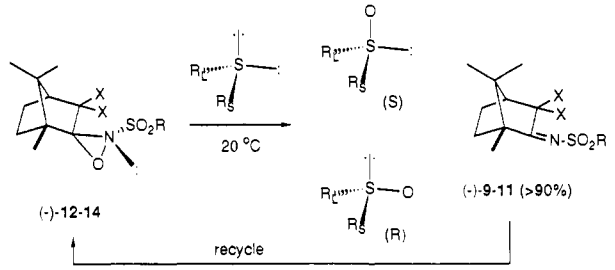
[a] Isolated yields. [b] Oxidations at −30 °C for 4–22 h. See ref 11. [c] Determined by comparison of the rotation to literature values. [d] Reference 11b. [e] ee's determined using $Eu(hfc)_3$. [f] Oxidation using (+)-**12c**. [g] Ethanol solvent. [h] Proposed configuration based on active-site model. [i] $CHCl_3$ solvent.

Table IV. Influence of Oxaziridine Structure on the Asymmetric Oxidation of Sulfides to Sulfoxides at 20 °C

entry	oxaziridine	solvent	% ee (config) [time (h)] % yield[a] *p*-tol-S(O)-Me	*p*-tol-S-Bu-*n*	9-anthryl-S-Me
1	(−)-**12a** (X = H)	CH_2Cl_2	28 (*S*) [1] 80	11 (*S*) [1] 70	64 (*S*) [1] 70
2		CCl_4	26 (*S*) [40] 22	8 (*S*) [3] 90	73 (*S*) [1] 80
3	(−)-**12b** (X = F)	CH_2Cl_2	52 (*S*) [0.5] 82	60 (*S*) [0.5] 88	96 (*S*) [1] 75
4		CCl_4	80 (*S*) [2] 85	75 (*S*) [2] 86	95 (*S*) [12] 70
5	(−)-**12c** (X = Cl)	CH_2Cl_2	62 (*S*) [1] 60	61 (*S*) [1] 90	95 (*S*) [1] 90
6		CCl_4	>95 (*S*) [4] 95	91 (*S*) [3] 90	95 (*S*) [48] 60
7	(−)-**12d** (X = Br)	CH_2Cl_2	64 (*S*) [2] 70	66 (*S*) [2] 88	88 (*S*) [48] 82
8		CCl_4	66 (*S*) [4] 76	68 (*S*) [4] 84	
9	(−)-**13c** (X = Cl)	CH_2Cl_2	55 (*S*) [4] 85	66 (*S*) [4] 90	69 (*S*) [48] 80
10		CCl_4	64 (*S*) [4] 77	73 (*S*) [4] 80	75 (*S*) [48] 83
11	(−)-**14c** (X = Cl)	CCl_4	72 (*S*) [6] 85	78 (*S*) [6] 82	82 (*S*) [48] 81

[a] Isolated yields.

Scheme II



on the concentration, the molecular recognition, and the reactivity of *each* species involved.

Enantioselective Oxidation of Sulfides to Sulfoxides. The oxidations of sulfides to sulfoxides by **12a** (X = H) and **12c** (X = Cl) are summarized in Tables I–III. These oxidations were carried out by treating the sulfide with an equivalent amount of the oxaziridine in the appropriate solvent at 20 °C (Scheme II). The reaction progress was monitored by TLC, and the sulfoxides were separated from the sulfonylimines by preparative TLC in 60–95% isolated yields. The corresponding sulfonylimines **9a** and **9c** were isolated in >90% yield and recycled. The enantiomeric purity of the sulfoxides was determined using the chiral shift reagent Eu(hfc) and/or by HPLC using a chiral Pirkle HPLC column. The absolute configurations were established by comparison with authentic samples, with literature values, and by application of the active-site model (see below).

For all asymmetric oxidations studied, *N*-(phenylsulfonyl)-(3,3-dichlorocamphoryl)oxaziridine (**12c**) [3,3-dichloro-1,7,7-trimethyl-2′-(phenylsulfonyl)spiro[bicyclo[2.2.1]heptane-2,3′-oxaziridine]] gave much better ee's than the dihydro reagent **12a** (Tables I–III). The highest ee's, >90%, were observed for those sulfides in which the groups attached to the sulfide (R_L-S-R_S) were sterically much different (Table I and II). For example, methyl *p*-tolyl sulfoxide (Table I, entry 2) and methyl *tert*-butyl sulfoxide (Table II, entries 5 and 6) were both obtained in >94% ee. On the other hand, the ee's for *tert*-butyl phenyl sulfoxide (Table I, entries 16 and 17) and methyl benzyl sulfoxide (Table II, entries 8 and 10) were considerably lower, i.e., 6–26% and 14% ee, respectively. Indeed, a regular decrease in the stereoselectivity is seen as the steric bulk of the alkyl group in Ar-S-R increases (Table I, entries 1–12, 16, and 17). This phenomenon, known as the Group Size Difference (GSD) effect,[6,27] is observed for many stereoselective transformations, including Kagan's modified Sharpless reagent (MSR). Notably **12c** gave *n*-butyl *p*-tolyl sulfoxide in 91% vs 20% ee for the MSR (Table I, entries 6 and 7). Although **12c** and Kagan's reagent generally gave similar results for the aryl alkyl sulfides (Table I), the dialkyl sulfides (Table II) were much less predictable.

For the asymmetric oxidation of the functionalized sulfoxides listed in Table III, oxaziridine **12c** gave much better ee's than the modified Sharpless reagent. Most of these sulfoxides are chiral synthons frequently used in EPC synthesis and are usually prepared by the Andersen procedure.[2] Even in those examples where the ee's were <90%, e.g., phenyl vinyl sulfoxide and (phenylsulfinyl)acetone, a single crystallization improved the enantiopurity to better than 95%.

Oxidations of alkyl aryl sulfides carried out in low dielectric solvents, such as CCl_4, gave the highest ee's (Table I). For example, oxidation of methyl *p*-tolyl sulfide with **12c** in CH_2Cl_2 afforded the sulfoxide in 62% ee, whereas in CCl_4 the enantiopurity was better than 95% (Table I, entries 1 and 2). Similar solvent effects were not observed with the dihydro reagent **12a** or for oxidations of dialkyl sulfides by **12c** (Table II).

The rates of oxidation, which varied from 1 to 48 h, were influenced by the solvent, the substrate, and the oxaziridine. In general the rates for sulfide oxidations were faster with **12c** (X = Cl) versus **12a** (X = H), consistent with the fact that oxygen transfer is accelerated by electron-attracting groups attached to the oxaziridine carbon.[27] Oxidations in CCl_4 were generally slower

(27) Davis, F. A.; Billmers, J. M.; Gosciniak, D. J.; Towson, J. C.; Bach, R. D. *J. Org. Chem.* **1986**, *51*, 4240.

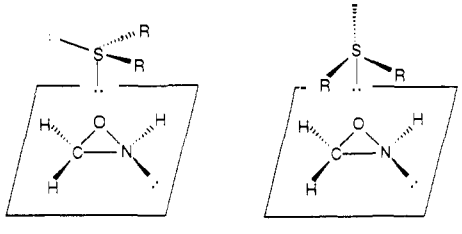
than those carried out in a more polar solvent such as CH_2Cl_2. This may be due in part to the low solubility of the oxidizing reagent in the less polar solvents and/or a stereoelectronic effect (see below). The rates of oxidation for hindered sulfides (Table I, entries 21–27; Table II, entries 1–3) or those having electron-attracting groups adjacent to the sulfur atom were also slower (Table III) and consistent with the S_N2 mechanism.[28] In these cases the rates can be increased, without significant loss of stereoselectivity, by oxidation at higher temperatures. For example the rate of oxidation of methyl 9-anthryl sulfide and *tert*-butyl benzyl sulfide was increased from 48 h at 20 °C to 1–5 h at 65 °C with a decrease in the ee from 91–95 to 85% (Table I, entries 21 and 22, and Table II, entries 3 and 4). Reducing the temperature of oxidation of methyl *n*-octyl sulfide from 20 to −60 °C improved the stereoselectivity from 14 to 58% ee (Table II, entries 9–12).

As observed for other asymmetric oxidations using enantiopure *N*-sulfonyloxaziridines **1–5**, the configuration of the oxaziridine three-membered ring controls the stereochemistry of the product.[6,12–15] Thus (3′*R*,2*S*)-(+)-**12c** afforded in every case the (*R*)-sulfoxides while (3′*S*,2*R*)-(−)-**12c** gave the (*S*)-sulfoxides (Table I, entries 8 and 23; Table II, entry 7; and Table III, entries 3 and 9).

Discussion

The mechanism of oxygen transfer for *N*-sulfonyloxaziridines involves an S_N2 type displacement of the sulfonylimine by the nucleophile which is facilitated by a relatively weak oxygen–nitrogen bond and the enthalpy of the carbon–nitrogen π-bond (Scheme II).[27] The "electrophilic" nature of oxaziridines is attributed to the fact that these compounds possess a relatively weak σ-bond whose σ^* component can readily decrease in energy very early along the reaction coordinate.[28,29] For the oxidation of sulfoxides to sulfones by oxaziridines, 50% of the net charge transferred to the oxaziridine fragment resides on oxygen in the transition state.[29]

In an earlier study, empirically based on structure–reactivity trends, a planar transition-state geometry **17** was established for the asymmetric oxidation of sulfides to sulfoxides by enantiopure *N*-sulfamyloxaziridines **1**.[6] However, ab initio calculations indicated that there are no stereoelectronic influences on the transition structures, and the energies of the planar-**17** and spiro-**18** structures are essentially the same.[29] The apparent electronic



indifference of these model transition states to the orientation of approach of the reactants was attributed to the relatively long distances between the "electrophilic" oxygen and substrate. It was concluded that the molecular recognition or transition-state orientation is steric in origin, governed by the structures of the substrate and the active-site microenvironment of the oxaziridine. Thus, experiment and theory support our recent suggestion that complementary topological disymmetry near the active-site oxygen in *N*-sulfonyloxaziridines is a fundamental requirement for achieving high stereoinduction with these reagents.[14]

For the asymmetric oxidation of sulfides to sulfoxides by (3′*R*,2*S*)-(+)-*N*-(phenylsulfonyl)(3,3-dichlorocamphoryl)oxaziridine (**12c**), "Newman"-like transition-state structures I–IV are analyzed for their nonbonded interactions (Figure 2). Initial

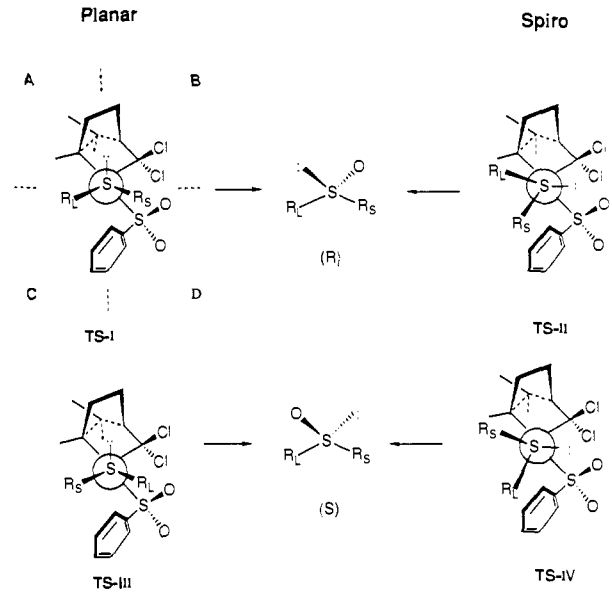


Figure 2. Transition-state structures for oxygen transfer from (3′*R*,2*S*)-(+)-**12c** to a sulfide.

inspection of these structures, however, suggests that quadrants A, B, and D are occupied by large groups while quadrant C is vacant. This analysis suggests that (+)-**12c** should exhibit low stereoselectivities for the oxidation of sulfides (R_L–S–R_S) because there is no way to minimize the nonbonded interactions between the R_S group of the sulfide and the oxaziridine; e.g., structures TS-I–TS-IV have similar energies. The fact is, however, (+)-**12c** strongly favors the (*R*)-sulfoxide; this means that structures TS-I and TS-II are of lower energy than TS-III and TS-IV.

Closer inspection of (+)-**12c** reveals that there is a groove or molecular cleft in the active-site surface which is defined by a chlorine atom and the phenylsulfonyl group (Figure 1). This molecular cleft and vacant quadrant C are primarily responsible for the high molecular recognition observed for oxaziridines of this type.[30] Apparently this cleft, which is 4.6 Å wide, is able to accommodate a small methyl or methylene group (R_S) of the sulfide while rejecting the larger (R_L) groups. Thus, planar TS-I (Figure 2) is of lower energy than TS-III and TS-IV. As noted above, as the size of the sulfide R_S group increases from methyl to isopropyl to *tert*-butyl, the ee's decrease from better than 95 to 26%, i.e., the GSD effect.

Influence of Structure. That the size of the molecular cleft in **12** is largely responsible for the molecular recognition is supported by the fact that altering its dimensions strongly influences the stereoselectivity (Table IV). For example, changing X in **12a–c** from H to F to Cl results in an increase in the ee from 26 to >95% (CCl_4 solvent) for the oxidation of the aryl alkyl sulfides listed in Table IV. Replacement of X by a bulky bromine atom results in a reagent, **12d**, which gives lower ee's in these oxidations (Table IV, entries 7 and 8). The fact that there is little relationship between the stereoselectivity and the electronegativity of X appears to rule out any significant stereoelectronic contribution to the molecular recognition by the halogen. A similar decrease in the stereoselectivity is observed for **13c** and **14c** where phenyl has been changed to benzyl and *o*-methoxyphenyl (Table IV, entries 9–11). From these studies we concluded that nonbonded steric interactions in the transition state are largely responsible for the molecular recognition.

Influence of Solvent. The fact that nonbonded steric interactions are controlling the molecular recognition is supported by the lack of solvent effects for the enantioselective oxidation of dialkyl sulfides to sulfoxides **12c** (Table II). However, oxidations of aryl alkyl sulfides in low dielectric solvents such as CCl_4 with **12b** (X = F) and **12c** (X = Cl) gave higher ee's than oxidations carried

(28) Bach, R. D.; Wolber, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 1410.
(29) Bach, R. D.; Coddens, B. A.; McDouall, J. J. W.; Schlegel, H. B.; Davis, F. A. *J. Org. Chem.* **1990**, *55*, 3325.

(30) The importance of molecular clefts in molecular recognition has been discussed. See Rebek, J., Jr. *Science* **1987**, *235*, 1478.

Table V. Influence of Solvent Polarity on the Asymmetric Oxidation of *n*-Butyl *p*-Tolyl Sulfide by (−)-**12c** at 20 °C

entry	solvent	dielectric constant[a] (ϵ)	*p*-tol-S(O)-*n*-Bu % ee (config)[b]
1	*n*-hexane	2.02	90 (*S*)
2	CCl_4	2.24	91 (*S*)
3	toluene	2.35	80 (*S*)
4	$CHCl_3$	4.18	79 (*S*)
5	Et_2O	4.34	78 (*S*)
6	CH_2Cl_2	9.08	76 (*S*)
7	pyridine	12.3	76 (*S*)
8	CH_3CN	35.1	75 (*S*)

[a] Gordon, A. J.; Ford, R. A. In *The Chemist's Companion*, John Wiley & Sons: New York, 1972. [b] The sulfoxide enantiomers were separated on a Regis Pirkle covalent phenylglycine HPLC column eluting with 95:5 hexane/isopropyl alcohol.

out in more polar solvents (Tables I and IV). As illustrated in Table V for the asymmetric oxidation of *n*-butyl *p*-tolyl sulfide, solvent polarity has little effect on the ee after $CHCl_3$ (ϵ = 4.18) and acetonitrile (ϵ = 35.1) gave comparable results. These results suggest that for the oxidation of alkyl aryl sulfides steric and, to a lesser extent, polar factors are responsible for the molecular recognition.

Although the energies of these solvent-induced stereoselective effects are quite small, 0.3–0.4 kcal/mol, they signify the difference between a reaction of synthetic utility and one that is not, i.e., >95 and 62% ee for methyl *p*-tolyl sulfoxide in CCl_4 and CH_2Cl_2, respectively (Table I, entries 1 and 2). While speculations on the origins of these effects are problematic because of the small energies involved, we believe that a discussion of these phenomena is particularly relevant in light of their significance.

Qualitatively polar solvents increase the rates for the oxidation of sulfides to sulfoxides by **12** (Table I). Faster rates are generally associated with earlier transition states (Hammond postulate) and would be expected to result in lower ee's because of nonbonded interactions in the transition state which become less important. Consistent with this explanation is the fact that methyl *p*-methoxyphenyl sulfide is oxidized by **12b** within 2 h and gives the sulfoxide in 80% ee, whereas methyl *p*-tolyl sulfide requires twice as long and affords the sulfoxide in >95% ee (Table I, entries 2 and 5). Rate acceleration by the polar solvents is also consistent with the fact that ab initio calculations indicated that the transition state is more polar than the ground state.[29]

Another explanation for the solvent-induced stereoselectivity effects is that the association of polar solvent molecules with the C–X bond or sulfonyl group in **12b** and **12c** alters the size of the molecular cleft. Note that **12a** (X = H) and **12d** (X = Br), which lack the polar C–X bond, do not show the solvent effects.[31] Solvents are known to stereospecifically associate with polar functional groups in molecules, such as carbon–halogen bonds, sulfonyl groups, and aromatic π-systems.[33] A change in the solution conformation of **12** and/or of the substrate induced by the solvent may also influence the molecular recognition. The fact that similar solvent-induced effects are not observed for the oxidation of dialkyl sulfides (Table II) may simply mean that in these examples steric forces overwhelmingly predominate.

Influence of the Aromatic Group. Good to excellent ee's are observed for the oxidation of sulfides to sulfoxides when an aromatic ring is directly attached to the sulfur atom. Since (−)-**12c** always affords the (*R*)-sulfoxide, in our model (Figure 2) the aryl substituent acts as the largest (R_L), most sterically demanding group. In these examples phenyl is observed to be somewhat larger than a *tert*-butyl group (Table I, entries 16 and 17). Following

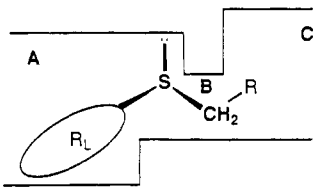
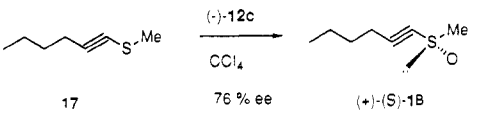


Figure 3. Active-site model for (+)-**12** (top view).

the lead of Kagan,[11e] we carried out the asymmetric oxidation of methyl *n*-1-hexynyl sulfide (**17**) with (−)-**12c** in order to evaluate the relative importance of steric and electronic effects of the π-system. Sulfoxide (*S*)-(−)-**18** was obtained in 76% ee, establishing that the alkynyl group acted as a large group. Similar trends were observed for the modified Sharpless reagent. Thus, as noted by others, an aromatic ring in an asymmetric transformation is able to influence the molecular recognition by a mixture of polar and steric effects.[11e,34]



The origin of the polar effects induced by unsaturated groups on chiral recognition is not well-understood and at times is rationalized in terms of nonbonding π-interactions and/or π-stacking arrangements.[9,34] The possibility of a similar attractive π-stacking arrangement between the basic aryl group of the sulfide and the acidic phenylsulfonyl group in **12** stabilizing TS-I can be disregarded in our case. Enantioselective oxidation of methyl and isopropyl *p*-methoxyphenyl sulfides, good π-bases, actually resulted in lower ee's relative to the corresponding *p*-tolyl derivatives (Table I, compare entries 3–5, 11, and 12 with 1, 2, 9, and 10).

The most likely cause of the solvent-induced stereoselectivity effects observed in the oxidation of the alkyl aryl sulfides is the rate acceleration caused by association of the polar solvent molecules with the aromatic π-system of the sulfide and/or stabilization of the polar transition state. This results in an earlier transition state where the nonbonded steric interactions become less important. Other explanations that cannot be ruled out at this time are changes in the solution conformations and the effective group sizes of the oxidant and substrate caused by the polar solvent.

Active-Site Model. The active-site model, illustrated in Figure 3, is proposed for the asymmetric oxidation of sulfides to sulfoxides by (3′*R*,2*S*)-(+)-**12c** and is based on analysis of its crystal structure (Figure 1) and the substrate structure–reactivity trends summarized in Tables I–IV. The model consists of three pockets, A–C, which distinguish the active site. Pocket B, defined by the chlorine atoms and the phenylsulfonyl group, is responsible for the high enantioselectivities exhibited by this reagent for the oxidation of sulfides (R_L–S–R_S) to sulfoxides. The proviso is that R_L is a large aromatic or *tert*-butyl group and R_S is a smaller methyl, methylene, cyclopropyl, or vinyl group. Pocket A is large enough in volume such that it is able to accommodate the bulky 9-anthryl group; i.e., all of the alkyl 9-anthryl sulfides give uniformly high ee's, >90%. Pocket C must also be large in size because high ee's (>90%) are also realized when R (Figure 3) is a bulky phenyl group (Tables I and II: see entries 13 and 14 and 1–3, respectively). However, pocket C is apparently not as large as pocket A because the ee drops from 94 to 85% on changing R from phenyl to 9-anthryl (Table I: compare entries 14 and 27). Additional support for this model is the fact that our reagent is unable to distinguish a methyl group from an *n*-butyl, *n*-octyl, or benzyl group. Thus, substrate molecular recognition is largely

(31) No detectable change in the ^1H NMR spectra of **12c** was noted on addition of incremental amounts of Eu(fod)$_3$ in an attempt to locate sites of Lewis basicity.[32]

(32) Davis, F. A.; Towson, J. C.; Weismiller, M. C.; Lal, S.; Carroll, P. J. *J. Am. Chem. Soc.* **1988**, *110*, 8477.

(33) Suarez, A.; Brinon, M. C.; de Bertorello, M. M.; Sierra, M. G.; Joseph-Nathan, P. *J. Chem. Soc., Perkin Trans. 2* **1990**, 2071 and references cited therein.

(34) (a) Guette, J. P.; Capillon, J.; Perlat, M.; Guette, M. *Tetrahedron Lett.* **1974**, *28*, 2409. (b) Hopkins, P. B.; Fuchs, P. L. *J. Org. Chem.* **1978**, *43*, 1208. (c) Middland, M. M. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, Part A, p 57. (d) Noyori, R.; Tomino, I.; Tanimoto, Y.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6709. (e) Falorni, M.; Lardicci, L.; Rosini, C.; Giamcomelli, G. *J. Org. Chem.* **1986**, *51*, 2030.

determined by the nonbonded interactions of the two groups *directly* bonded to the sulfur atom in the sulfide and the active-site surface of the oxaziridine.

Summary and Conclusions

N-(Phenylsulfonyl)(3,3-dichlorocamphoryl)oxaziridine (**12c**) represents a highly efficient reagent for the enantioselective oxidation of aryl alkyl, dialkyl, and functionalized sulfides to sulfoxides with high and predictable stereoselectivities. Since the configuration of the oxaziridine three-membered ring controls the stereochemistry of the sulfoxide, both enantiomers are readily available by choice of (+)- or (−)-**12c**. The absolute stereochemistry of the products is predicted in terms of a simple steric model, which involves minimization of nonbonded interactions between the R_L and R_S groups of the sulfide (R_L–S–R_S) and the active-site surface of the oxaziridine in a planar transition-state orientation. High ee's are predicted for those sulfides where the group size difference (GSD) of the substituents directly bonded to the sulfur atom is large, i.e., aryl, *tert*-butyl vs CH_2R (R = H, alkyl, benzyl, etc). The molecular cleft, defined by the chlorine atoms and phenylsulfonyl group, is primarily responsible for the high molecular recognition exhibited by **12c**. While the origin of the molecular recognition is predominantly steric, the solvent-induced stereoselectivity effects suggest that there is a polar component as well. Our new reagent is generally superior to Kagan's modified Sharpless reagent, which gives synthetically useful ee's only for methyl aryl sulfides and is much less predictable.

Experimental Section

IR spectra were recorded on a Perkin-Elmer 467 grating spectrometer using sodium chloride plates for liquids and potassium bromide disks for solids. NMR spectra were recorded on a JEOL FX90Q (90, 89.5 MHz) or on a Bruker 250 (250 MHz) instrument. Proton and carbon chemical shifts are reported relative to tetramethylsilane (TMS). Fluorine chemical shifts were relative to fluorotrichloromethane ($CFCl_3$). Analytical HPLC separations were carried out on a Varian 9010 liquid chromatograph using a Varian 9050 UV detector (254 nm). Gas–liquid partition chromatography (GLC) was performed on a Varian 3700 GC and on a Perkin-Elmer 8310 instrument. Perkin-Elmer 8500 capillary GLC % OV-17 (6 ft × $^1/_8$ in., 80/100 Supelcoport) and SPB-35 (60 m × 0.75 mm, 1 μm film thickness, borosilicate glass) columns were used for the GLC analyses. *meta*-Chloroperbenzoic acid (*m*-CPBA) was purified using a monophosphate buffer on pH 7.5.[35] Melting points were recorded on a Mel-Temp apparatus and were uncorrected. Organic reagents were purchased primarily from Aldrich Chemical Co. and used as obtained unless stated otherwise. THF and ether were distilled from sodium and benzophenone prior to use. *N*-chloro- and *N*-bromosuccinimide were crystallized from water and dried under vacuum overnight prior to use. Elemental analyses were performed by Micro-Analysis, Inc. of Wilmington, DE.

Fluorination was carried out in the apparatus recommended by Matheson Gas Products for the handling of dilute concentrations of F_2/N_2. For a related apparatus, see ref 36. *Caution*: *Fluorine is a poisonous, corrosive gas which is a powerful oxidant.*

Typical Procedure for the Synthesis of N-Substituted Camphorimines 7. In a dry two-necked, 1-L round-bottom flask equipped with a magnetic stirring bar, argon inlet, reflux condenser, and a rubber septum were placed 15.2 g (100 mmol) of camphor and 15.7 g (100 mmol) benzenesulfonamide (or the appropriate sulfonamide) in 500 mL of dry 1,1,2-trichloroethane. The contents were cooled to 0 °C, and 50 mL of titanium tetrachloride (0.65 equiv, 1 M in CH_2Cl_2) solution was added via syringe over a period of 45 min. The reaction mixture was slowly brought to room temperature and refluxed for 24 h (GLC analysis of reaction mixtures indicated 60% imine). At this time an additional 50 mL of titanium tetrachloride was added at 0 °C, and the reaction mixture was refluxed for an additional 24 h. After cooling to room temperature, the contents were washed with 500 mL of 5% K_2CO_3 solution and brine and dried. Removal of the solvent under vacuum afforded the crude sulfonylimine, which was purified by flash chromatography eluting with 20% ether/pentane and crystallized from ethanol.

(−)-***N*-(Phenylsulfonyl)camphorimine (7a)**: yield 80%; mp 92–93 °C (lit. mp 92–95 °C); $[\alpha]^{20}_D$ −35.8° (*c* 3.0, $CHCl_3$); IR (KBr) 1600 (C=N), 1300 and 1140 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 1.2–1.5 (m, 2 H, CH_2), 1.7–1.9 (m, 2 H, CH_2), 2.0–2.1 (m, 1 H, CH), 2.5 (d, 1 H, *J* = 16 Hz), 2.9–3.1 (m, 1 H, CH), 7.4–7.6 (m, 3 H, ArH), 7.9–8.0 (m, 2 H, ArH); ^{13}C NMR ($CDCl_3$) δ 10.45, 18.63, 19.2, 26.3, 31.12, 39.8, 43.57, 47.62, 57.47, 126.60, 128.38, 132.36, 140.37, 201.31 (C=N). Anal. Calcd for $C_{16}H_{21}NO_2S$: C, 65.98; H, 7.22. Found: C, 65.97; H, 7.08.

(+)-*N*-(Phenylsulfonyl)camphorimine (7a): yield 72%; mp 93–94 °C; $[\alpha]^{20}_D$ +36.1° (*c* 4.1, $CHCl_3$); IR (KBr), 1615 (C=N), 1305 and 1135 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3), 1.21–1.6 (m, 2 H, CH), 1.71–190 (m, 2 H, CH_2), 2.05–211 (m, 1 H, CH), 2.51 (d, 1 H, *J* = 15.8 Hz), 2.9–3.1 (m, 1 H, CH), 7.4–7.6 (m, 3 H, CH), 7.9–8.05 (m, 2 H, Ar); ^{13}C NMR ($CDCl_3$) δ 10.46, 18.65, 19.0, 26.5, 31.2, 39.5, 43.61, 47.60, 57.50, 126.61, 128.50, 132.40, 140.40, 201.51 (C=N). Anal. Calcd for $C_{16}H_{21}NO_2S$: C, 65.98; H, 7.22. Found: C, 65.69; H, 7.09.

***N*-(Benzylsulfonyl)camphorimine (7b)**: yield 70%; mp 65–6 °C; $[\alpha]^{20}_D$ −34.6° (*c* 1.4, $CHCl_3$); IR (KBr) 1631 (C=N), 1311 and 1155 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.6 (s, 3 H, CH_3), 0.89 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 1.1–1.32 (m, 2 H, CH_2), 1.63–1.85 (m, 2 H, CH_2), 1.9 (m, 1 H, CH_2), 2.28 (d, 1 H, *J* = 19 Hz), 2.8–2.9 (m, 1 H, CH), 4.39 (s, 2 H, CH_2), 7.3–7.4 (m, 3 H, ArH), 7.4–7.5 (m, 2 H, ArH); ^{13}C NMR ($CDCl_3$) δ 10.8, 18.9, 19.4, 26.5, 31.5, 40.2, 43.8, 47.8, 57.8, 59.7, 128.4, 128.9, 130.9, 202.5 (C=N). Anal. Calcd for $C_{17}H_{23}NO_2S$: C, 66.85; H, 7.54. Found: C, 66.62; H, 7.14.

***N*-[(*o*-Methoxyphenyl)sulfonyl]camphorimine (7d)**. In a dry 500-mL, two-necked round-bottom flask equipped with a magnetic stirring bar, argon inlet, reflux condenser, and a rubber septum were placed 1.52 g (10 mmol) of camphor and 1.87 g (10 mmol) *o*-methoxybenzenesulfonamide[37] in 100 mL of dry 1,1,2-trichloroethane. The reaction mixture was cooled to 0 °C in an ice bath, and 10 mL (1 equiv, 1 M in CH_2Cl_2) of titanium tetrachloride was added via syringe over a period of 20 min. The reaction mixture was refluxed for 12 h, cooled to room temperature, and washed with 500 mL of 5% K_2CO_3 solution and brine and dried. Solvent removal afforded the crude imines **7c** and **7d** in a ratio of 40:60 (by NMR). Imine **7d** was isolated in 57% yield by flash chromatography eluting with 15% ethyl acetate/*n*-hexane followed by the slower moving demethylated imine **7c** in 41% yield.

Imine 7d: mp 113–114 °C; $[\alpha]^{20}_D$ −32.1° (*c* 1.6, $CHCl_3$); IR (KBr) 1637 (C=N), 1307 and 1155 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 1.03 (s, 3 H, CH_3), 1.2–1.5 (m, 2 H, CH_2), 1.7–2.0 (m, 2 H, CH_2), 2.05 (t, 1 H, *J* = 8 Hz), 2.6 (d, 1 H, *J* = 1.8 Hz), 2.9–3.2 (m, 1 H, CH), 3.9 (s, 3 H, OCH_3), 6.9–7.2 (m, 2 H, ArH), 7.4–7.6 (m, 1 H, ArH), 8.08 (d, 2 H, *J* = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 10.9, 19, 19.5, 26.8, 40.3, 44, 47.7, 56, 57.7, 77.2, 112.1, 120.2, 128.4, 129.4, 134.6, 157.1, 201.1 (C=N). Anal. Calcd for $C_{17}H_{23}NO_3S$: C, 63.55; H, 7.16. Found: C, 63.47; H, 6.89.

Demethylated imine 7c: mp 109–111 °C; $[\alpha]^{20}_D$ −40.8° (*c* 1.0, $CHCl_3$); IR (KBr) 3415 (OH), 1630 (C=N), 1300 and 1150 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75 (s, 3 H, CH3), 0.98 (s, 6 H, CH3), 1.2–1.5 (m, 2 H), 1.5–1.6 (m, 2 H), 1.85 (t, 1 H, *J* = 8 Hz), 2.65 (d, 1 H, *J* = 18 Hz), 2.5–2.7 (m, 1 H), 6.9–7.1 (m, 2 H), 7.4–7.5 (m, 1 H, ArH), 7.7–7.8 (m, 1 H, ArH), 8.9 (s, 1 H, ArH); ^{13}C NMR ($CDCl_3$) δ 10.7, 19.0, 19.6, 26.6, 31.5, 40.5, 44.0, 48.3, 58.2, 118.7, 120.0, 128.1, 135.4, 154.7, 203.1 (C=N). Anal. Calcd for $C_{16}H_{21}NO_3S$: C, 62.54; H, 6.84. Found: C. 62.6; H, 6.81.

Conversion of 7c into 7d. In a 500-mL dry, single-necked, round-bottom flask equipped with a magnetic stirring bar, argon inlet, and reflux condenser were placed 2.8 g (9 mmol) of *N*-[(*o*-hydroxyphenyl)-sulfonyl]camphorimine (**7c**), 1.3 g (9 mmol) K_2CO_3 and 1.2 mL (2 equiv) of MeI in 150 mL of dry acetone, and the solution was refluxed for 2 h. The reaction mixture was filtered, the solvent removed, the solid material dissolved in 100 mL of CH_2Cl_2, and the organic layer washed with 2 N H_2SO_4, water, and brine and dried. Removal of the solvent afforded the crude imine, which was purified by flash chromatography eluting with 20% ether/pentane to give 2.72 g (93%) of **7d**.

Typical Procedure for the Synthesis of *N*-(Arylsulfonyl)-3,3-dihalocamphorimines (9–11). In a dry 1-L, three-necked round-bottom flask equipped with a magnetic stirring bar, argon inlet, and rubber septum was placed 5.8 g (20 mmol) of the appropriate imine in 250 mL of THF. The contents were cooled to −78 °C, and 60 mL of NaHMDS (1 M solution, 3 equiv) was added via syringe over a period of 30 min. The solution was stirred for 45 min and then added via a cannula tube to a separate 1-L two-necked flask equipped with an argon inlet and rubber septum containing 8.0 g (60 mmol) *N*-chlorosuccinimide or 10.7 g (60 mmol) of *N*-bromosuccinimide in 300 mL of THF cooled to −78 °C. *Caution*: *NCS and NBS can react vigorously with THF.* This is avoided by rapidly cooling the mixture to −78 °C. After the addition was com-

(35) Schwartz, N. N.; Blumbergs, J. H. *J. Org. Chem.* **1964**, *29*, 1976.
(36) Purrington, S. T.; Woodard, D. L. *J. Org. Chem.* **1991**, *56*, 142.
(37) Graham, S. L.; Scholz, T. H. *Synthesis* **1986**, 1031.

plete, the reaction mixture was stirred for 4 h (NMR showed almost 90% conversion to the dihalo compound) and quenched by adding 20 mL of saturated NH_4Cl solution. The solution was warmed to room temperature and diluted with 200 mL of ether, and the organic layer was washed with water and brine and dried. Following removal of the solvent, the crude product was purified by crystallization from absolute ethanol.

(−)-*N*-(Phenylsulfonyl)-3,3-dichlorocamphorimine (9c): yield 80%; mp 141–2 °C; $[\alpha]^{20}_D$ −28.7° (*c* 2.9, $CHCl_3$); IR (KBr) 1635 (C=N), 1310 and 1150 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.70–1.87 (m, 2 H CH_2), 1.9–2.1 (m, 1 H, CH), 2.22–2.38 (m, 1 H, CH), 2.64–2.72 (m, 1 H, CH), 7.53–7.6 (m, 3 H, ArH), 8.01 (m, 2 H, ArH); ^{13}C NMR ($CDCl_3$) δ 12.82, 21.64, 23.48, 25.45, 30.30, 48.19, 59.66, 60.99, 128.16, 128.38, 131.07, 192 (C=N). Anal. Calcd for $C_{16}H_{19}Cl_2NO_2S$: C, 53.34; H, 5.27. Found: C, 53.50; H, 5.34.

(+)-*N*-(Phenylsulfonyl)-3,3-dichloroamphorimine (9c): yield 77%; mp 142–143 °C; $[\alpha]^{20}_D$ +28.20° (*c* 1.7, $CHCl_3$); IR (KBr) 1635 (C=N) 1320 and 1155 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (s, 3 H, CH_3), 1.21 (s, 3 H CH_3), 1.33 (s, 3 H, CH_3), 1.71–188 (m, 2 H, CH_2), 1.92–2.10 (m, 1 H, CH), 2.23–2.38 (m, 1 H, CH), 2.65–2.70 (m, 1 H, CH), 7.53–7.6 (m, 3 H, Ar), 8.02 (m, 2 H, Ar); ^{13}C NMR ($CDCl_3$) δ 12.81, 21.65, 23.48, 25.46, 30.35, 48.21, 59.80, 60.11, 128.20, 128.40, 131.06, 191.9 (C=N). Anal. Calcd for $C_{16}H_{19}Cl_2NO_2S$: C, 53.34; H, 5.27. Found: C, 53.58; H, 5.34.

(−)-*N*-(Phenylsulfonyl)-3,3-dibromocamphorimine (9d): yield 87%; mp 145–146 °C; $[\alpha]^{20}_D$ −47.36° (*c* 4.7, $CHCl_3$); IR (KBr) 1645 (C=N), 1320 and 1150 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.11 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 1.67–2.46 (m, 4 H, CH_2), 2.81 (d, 1 H, *J* = 3.8 Hz, CH), 7.53–7.6 (m, 3 H, ArH), 8.02–8.04 (m, 2 H, ArH); ^{13}C NMR ($CDCl_3$) δ 13.43, 22.89, 24.61, 29.07, 30.01, 48.62, 59.73, 60.43, 77.2, 126.80, 128.69, 132.58, 141.55, 191.63 (C=N). Anal. Calcd for $C_{16}H_{19}Br_2NO_2S$: C, 42.78; H, 4.23. Found: C, 42.76; H, 4.24.

(−)-*N*-(Benzylsulfonyl)-3,3-dichlorocamphorimine (10c): yield 72%; mp 99.5–101 °C; $[\alpha]^{20}_D$ −92.3° (*c* 1.3, $CHCl_3$); IR (KBr) 1666 (C=N), 1325 and 1145 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (s, 3 H, CH_3), 1.17 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 1.72 (m, 2 H, CH_2), 2.03 (m, 1 H, CH), 2.23 (m, 1 H, CH), 2.65 (d, 1 H, *J* = 4.2 Hz), 4.54 (s, 2 H, CH_2), 7.38 (m, 3 H, ArH), 7.54 (m, 2 H, ArH); ^{13}C NMR ($CDCl_3$) δ 12.8, 21.6, 23.5, 25.5, 30.3, 48.2, 59.6, 59.8, 60.1, 128.2, 128.4, 131.1, 191.1 (C=N). Anal. Calcd for $C_{17}H_{21}Cl_2NO_2S$: C, 54.54; H, 5.65. Found: C, 54.15; H, 5.61.

(−)-*N*-[(*o*-Methoxyphenyl)sulfonyl]-3,3-dichlorocamphorimine (11c): yield 73%; mp 145–146 °C; $[\alpha]^{20}_D$ −41.9° (*c* = 1.1, $CHCl_3$); IR (KBr) 1660 (C=N), 1319 and 1155 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (s, 3 H, CH_3), 1.25 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.65–1.85 (m, 2 H, CH_2), 1.89–2.12 (m, 1 H, CH), 1.18–1.41 (m, 1 H, CH), 2.65 (d, 1 H, *J* = 4.2 Hz), 3.92 (s, 3 H, OCH_3), 6.93–7.13 (m, 2 H, ArH), 7.5–7.63 (m, 1 H, ArH), 7.98 (dd, 1 H, J_1 = 8 Hz, J_2 = 2.3 Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 13.2, 21.9, 23.8, 25.8, 30.6, 48.3, 56.2, 59.9, 60.2, 105.9, 112.3, 119.8, 128.7, 134.6, 157.2, 203.4 (C=N). Anal. Calcd for $C_{17}H_{21}Cl_2NO_3S$: C, 52.30; H, 5.38. Found: C, 51.85; H, 5.17.

***exo*/*endo*-(−)-*N*-(Phenylsulfonyl)-3-fluorocamphorimine (15). From *N*-Fluoro-*o*-benzenedisulfonimide (16).** In an oven-dried 50-mL two-necked round-bottom flask equipped with a magnetic stirring bar, argon inlet, and rubber septum was placed 0.2 g (0.7 mmol) of (−)-*N*-(phenylsulfonyl)camphorimine (**7a**) in 40 mL of THF. The solution was cooled to −78 °C, and 0.75 mL of (1.1 equiv) NaHMDS was added via syringe. After the reaction mixture was stirred for 30 min, 0.18 g (0.76 mmol) of **16**[19] dissolved in 5 mL of THF was added, and the reaction was warmed to 20 °C, stirred for 4 h, and quenched by addition of 1 mL of saturated NH_4Cl solution. The solution was washed with brine and dried, and the solvent was removed to afford crude **15** as a 10:90 exo/endo mixture (by NMR), which was purified by flash chromatography using 5% ethyl acetate/*n*-pentane: yield 65%; IR (KBr) 1635 (C=N), 1310 and 1150 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.99–1.02 (m, 9 H, CH_3), 1.2–1.4 (m, 2 H, CH_2), 1.61–1.8 (m, 1 H, CH_2), 1.9–2.1 (m, 1 H, CH), 2.2–2.4 (m, 1 H, CH), 5.5 (d, 1 H, *J* = 50 Hz, CHF, exo), 5.85 (dd, J_1 = 50 Hz, J_2 = 4.5 Hz, CHF, endo),[38] 7.5–7.62 (m, 3 H, ArH), 7.9–8.1 (m, 2 H, ArH); ^{19}F NMR ($CFCl_3$ in $CDCl_3$) δ −169.1 (d, *J* = 52.9 Hz, endo), −189.2 (d, *J* = 52.9 Hz, exo); ^{13}C NMR ($CDCl_3$) δ 10.6, 19.4, 21.1, 21.2, 22.4, 22.6, 30.8, 47.6, 49.0, 57.2, 89.6, 92.8 (*J* = 199.7 Hz), 127.6, 128.7, 133.0, 139.9, 194.0 (C=N). Anal. Calcd for $C_{16}H_{20}FNO_2S$: C, 62.14; H, 6.47. Found: C, 61.81; H, 6.28.

From Acetyl Hypofluorite. In an oven-dried 100-mL two-necked round-bottom flask equipped with a magnetic stirring bar, argon inlet, and rubber septum and fitted with a distillation head and condenser attached to a 50-mL collecting flask was placed 2.91 g of (−)-*N*-(phenylsulfonyl)camphorimine (**7a**). The reaction flask was cooled to 0 °C, 12 mL of NaHMDS (1.2 equiv) was added under argon, and the solution was stirred for 15 min to generate the aza enolate. The collection flask was cooled to −78 °C, the THF solvent was evaporated to dryness under vacuum, and 30 mL of dry THF was added to the resulting solid sodium aza enolate **8**.

Acetyl hypofluorite was prepared using a modification of the procedure reported by Rosen.[18] In a separate oven-dried 500-mL two-necked round-bottom flask fitted with an S/T Teflon adapter with Teflon inlet and outlet tubes, the latter attached to a soda lime tower, was placed 8.2 g (0.1 mol) NaOAc in 400 mL of Freon ($CFCl_3$). The reaction flask was cooled to −78 °C, and a 10% F_2 (balance N_2) gas mixture (Matheson) was bubbled through the reaction mixture for approximately 3–4 h until a concentration of 7–8 equiv of acetyl hypofluorite was obtained. The concentration of the acetyl hypofluorite was determined by removal of a 4-mL aliquot of the reaction mixture, addition of 25 mL of a 3 N H_2SO_4/0.5 g KI solution, and titration of the liberated iodine with a standard 0.1 N sodium thiosulfate solution. The aza enolate **8** prepared above was then added to the −78 °C solution of acetyl hypofluorite via a cannula tube with stirring. After 30 min, the reaction mixture was allowed to warm to room temperature, transferred to a 1-L separatory funnel containing 100 mL of a 5% $Na_2S_2O_3$ solution, washed with aqueous $NaHCO_3$, water, and brine, and dried. Removal of the solvent gave a mixture **7/15** in a ratio of 35:65.

(−)-*N*-(Phenylsulfonyl)-3,3-difluorocamphorimine (9b). The crude mixture **7/15** was treated as described above with 10 mL of NaHMDS. The solvent was removed by distillation, 30 mL of THF was added, and then the mixture was added via a cannula tube to 7–10 equiv of a solution of acetyl hypofluorite to give the difluoro imine **9b**, which was isolated by flash chromatography eluting with 20% ether/*n*-pentane to give 1.3 g (40%): mp 79 °C; $[\alpha]^{20}_D$ −12° (*c* 2.0, $CHCl_3$); IR (KBr) 1635 (C=N), 1310 and 1150 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.99 (s, 3 H, CH_3), 1.03 (s, 6 H, CH_3), 1.67–2.0 (m, 4 H, CH_2), 2.3–2.36 (m, 1 H, CH), 7.5–7.62 (m, 3 H, ArH), 8.0–8.04 (m, 2 H, ArH); ^{19}F NMR ($CFCl_3$ in $CDCl_3$) δ −100 ppm. Anal. Calcd for $C_{16}H_{19}F_2NO_2S$: C, 58.75; H, 5.81. Found: C, 58.97; H, 5.86.

From Perchloryl Fluoride (FO_3Cl). In a dry 250-mL three-necked round-bottom flask equipped with a inlet tube, magnetic stirring bar, argon inlet, rubber septum, and thermometer was placed 2.91 g (10 mmol) of *N*-(phenylsulfonyl)camphorimine (**7a**) in 100 mL of freshly distilled THF and cooled to 0 °C. NaHMDS (30 mL, 3 equiv) was added via a syringe to the reaction mixture over a period of 20 min. After the reaction was stirred for 20 min, perchloryl fluoride (Pennwalt)[40] was bubbled slowly through the reaction mixture for 30 min while the reaction temperature was carefully maintained at 0 °C in an ice bath. At this time argon was bubbled through the reaction mixture for 15 min; the reaction was quenched by addition of 20 mL of saturated NH_4Cl and diluted with ether, and the organic portion was washed with water and brine and dried. Removal of the solvent gave a mixture **15/9b** (40:60), which was purified by flash chromatography eluting with 20% ether/*n*-pentane to yield 1.4 g (43%) of **9b**.

Typical Procedure for the Synthesis of Enantiomerically Pure (Camphorylsulfonyl)oxaziridine: (3′*S*,2*R*)-(−)-*N*-(Phenylsulfonyl)(3,3-dichlorocamphoryl)oxaziridine (12c). In a 2-L Morton three-necked round-bottom flask equipped with a mechanical stirrer and 150-mL addition funnel was placed 12.6 g (35 mmol) of *N*-(phenylsulfonyl)-3,3-dichlorocamphorimine (**9c**) dissolved in 100 mL CH_2Cl_2 and 75 mL of a saturated K_2CO_3 solution. The reaction mixture was vigorously stirred, and 9.2 g (52.5 mmol) of *m*-CPBA >95% pure dissolved in 75 mL of CH_2Cl_2 was added dropwise. The reaction progress was monitored by TLC (80% CH_2Cl_2/*n*-pentane), and after 24 h an additional 9.2 g of *m*-CPBA in 75 mL of CH_2Cl_2 and 75 mL of saturated K_2CO_3 were added each day until the reaction went to completion (approximately 5 days in the case of dichloro and dibromo imines **9–11**). For the other imines oxidation was complete within 3–5 h. The reaction was quenched by addition of 200 mL of saturated sodium sulfite, the organic layer was separated, and the aqueous layer was extracted with 2 × 150 mL of CH_2Cl_2. The combined organic portions were washed with saturated $NaHCO_3$, water, and brine and dried. Removal of the solvent afforded the crude oxaziridine. The dichloro and dibromo oxaziridines required purification by flash chromatography, eluting with 30% CH_2Cl_2/*n*-pentane to remove the faster moving dimer of *m*-CPBA, bis(*m*-chloro-

(38) The exo/endo ratios were assigned based on the fact that *exo*-bromocamphor gives a singlet while the *endo*-bromocamphor gives a doublet.[39]

(39) Beque, J.; Charpentier-Morize, M.; Pardo, C.; Sansulet, J. *Tetrahedron* **1978**, *34*, 293.

(40) Perchloryl fluoride is a reactive, toxic gas which should be handled with caution. We experienced no adverse reactions in its application. For a discussion of its use and leading references, see: Peet, N. P.; McCarthy, J. R.; Sunder, S.; McCowan, J. *Synth. Commun.* **1986**, *16*, 1551.

benzoyl) peroxide.[41] The other oxaziridines were purified by crystallization from absolute ethanol.

(−)-***N*-(Phenylsulfonyl)camphoryloxaziridine (12a)**: yield 87%; mp 133–135 °C; $[\alpha]^{20}_D$ −198° (*c* 3.0, $CHCl_3$); IR (KBr) 1340 and 1175 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.61 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 1.1 (s, 3 H, CH_3), 1.47–2.0 (m, 6 H, CH_2), 2.90–2.99 (m, 1 H, CH_2), 7.56 (t, 2 H, *J* = 8.23 Hz, ArH), 7.69 (m, 1 H, ArH), 7.95 (d, 2 H, *J* = 8.23 Hz); ^{13}C NMR ($CDCl_3$) δ 9.3, 19, 20.2, 26.73, 29.2, 35.7, 44.75, 48.2, 50.45, 98.6 (oxaziridine carbon), 128.32, 129.06, 134.11, 136.2. Anal. Calcd for $C_{16}H_{21}NO_3S$: C, 62.54; H, 6.54. Found: C, 62.35; H, 6.76.

(−)-***N*-(Phenylsulfonyl)(3,3-difluorocamphoryl)oxaziridine (12b)**: yield 88%; mp 153 °C; $[\alpha]^{20}_D$ −145.3° (*c* 2.9, $CHCl_3$); IR (KBr) 1340 and 1170 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.69 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 1.23 (d, 3 H, *J* = 4.74 Hz, CH_3), 1.5–2.0 (m, 4 H, CH_2), 7.6–7.84 (m, 3 H, ArH), 8.12 (d, 2 H, *J* = 7.4 Hz, ArH); ^{19}F NMR ($CFCl_3$ in $CDCl_3$) δ −88.6 (d, 1 H, *J* = 247 Hz), −108.7 (d, 1 H, *J* = 247 Hz). Anal. Calcd for $C_{16}H_{19}F_2NO_3S$: C, 56.00; H, 5.54. Found: C, 55.99; H, 5.51.

(3′*S*,2*R*)-(−)-*N*-(Phenylsulfonyl)(3,3-dichlorocamphoryl)oxaziridine (12c): yield 75%; mp 121–122 °C; $[\alpha]^{20}_D$ −159° (*c* 4.2, $CHCl_3$); IR (KBr) 1340 and 1170 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.67 (s, 3 H, CH_3), 1.07 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.43–1.55 (m, 2 H, CH_2), 1.79–1.98 (m, 1 H, CH_2), 2.2–2.35 (m, 1 H, CH), 2.65–2.77 (m, 1 H, CH), 7.58–7.69 (m, 3 H, ArH), 8.08 (d, 2 H, *J* = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 10.59, 21.87, 22.81, 25.29, 28.50, 46.02, 54.12, 63.79, 88.23, 104.66 (oxaziridine carbon), 128.56, 129.04, 134.15, 138.18, 174.39. Anal. Calcd for $C_{16}H_{19}Cl_2NO_3S$: C, 51.07; H, 5.05. Found: C, 50.95; H, 5.08.

(3′*R*,2*S*)-(+)-*N*-(Phenylsulfonyl)(3,3-dichlorocamphoryl)oxaziridine (12c): yield 73%; mp 122–123 °C; $[\alpha]^{20}_D$ +157.0° (*c* 4.1, $CHCl_3$); IR (KBr) 1335 and 1175 (SO_2) cm^{-1}; ^1H NMR δ 0.68 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.44–1.55 (m, 2 H, CH_2), 1.80–1.98 (m, 1 H, CH), 1.15–2.32 (m, 1 H, CH), 2.65–2.74 (m, 1 H, CH), 7.58–7.71 (m, 3 H, Ar), 8.05 (d, 2 H, *J* = 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 10.63, 21.91, 22.84, 25.30, 28.52, 46.11, 54.17, 63.82, 88.20, 104.59 (oxaziridine carbon), 128.55, 129.04, 134.17, 138.20, 174.42. Anal. Calcd for $C_{16}H_{19}Cl_2NO_3S$: C, 51.07; H, 5.05. Found: C, 50.98; H, 5.16.

(−)-***N*-(Phenylsulfonyl)(3,3-dibromocamphoryl)oxaziridine (12d)**: yield 23%; mp 124–127 °C; $[\alpha]^{20}_D$ −121° (*c* 2.8, $CHCl_3$); IR (KBr) 1340 and 1170 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.66 (s, 3 H, CH_3), 1.09 (s, 3 H, CH_3), 1.45 (s, 3 H, CH_3), 1.24–2.35 (m, 4 H, CH_2), 2.93 (s, 1 H, CH), 7.55–7.73 (m, 3 H, ArH), 8.08 (d, 2 H, *J* = 8.4 Hz). Anal. Calcd for $C_{16}H_{19}Br_2NO_3S$: C, 41.30; H, 4.08. Found: C, 41.20; H, 4.07.

(−)-***N*-(Benzylsulfonyl)(3,3-dichlorocamphoryl)oxaziridine (13c)**: yield 30%; mp 90–91 °C; $[\alpha]^{20}_D$ −112° (*c* 0.8, $CHCl_3$); IR (KBr) 1354 and 1137 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.61 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 1.25 (s, 3 H, CH_3), 1.4–1.63 (m, 2 H, CH_2), 1.7–1.9 (m, 1 H, CH), 2.03–2.28 (m, 1 H, CH), 2.4–2.67 (m, 1 H, CH), 4.3–4.6 (m, 2 H, CH_2), 7.18–7.5 (m, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 10.6, 21.9, 22.7, 25.3, 28.5, 46.1, 54.1, 60.1, 63.7, 77.2, 102.1 (oxaziridine carbon), 126.8, 128.7, 129.1, 131.1. Anal. Calcd for $C_{17}H_{23}NO_3S$: C, 52.31; H, 5.42. Found: C, 52.24; H, 5.59.

(−)-***N*-[(*o*-Methoxyphenyl)sulfonyl](3,3-dichlorocamphoryl)oxaziridine (14c)**: yield 35%; mp 143–144 °C; $[\alpha]^{20}_D$ −136.1° (*c* 1.14, $CHCl_3$); IR (KBr) 1354 and 1161 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.72 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 1.53 (s, 3 H, CH_3), 1.19–1.52 (m, 2 H), 1.76–2.02 (m, 1 H, CH_2), 2.10–2.39 (m, 1 H, CH_2), 2.56–2.77 (m, 1 H, CH), 3.95 (s, 3 H, OCH_3), 7.02–7.15 (m, 2 H, ArH), 7.71–7.56 (m, 1 H, ArH), 7.85–8.14 (m, 1 H, ArH); ^{13}C NMR ($CDCl_3$) δ 10.7, 13.9, 22.0, 23.1, 25.4, 28.4, 46.5, 54.6, 56.8, 64.5, 90.2 (oxaziridine carbon), 112.8, 120.1, 131.6, 132.8, 136.2, 158.2. Anal. Calcd for $C_{17}H_{21}NO_3S$: C, 50.24; H, 5.17. Found: C, 49.86; H, 4.83.

Preparation of *p*-Tolyl (9-Anthrylmethyl) Sulfide. In a dry three-necked flask equipped with a magnetic stirrer, condenser, addition funnel, and argon bubbler was placed 0.096 g (4 mmol) of a 50% mineral oil dispersion of sodium hydride. The dispersion was washed with *n*-pentane, 20 mL of dry THF was added, and the reaction mixture was cooled to 0 °C. Di-*p*-tolyl disulfide (0.49 g, 2 mmol) in 20 mL of THF was added dropwise over 10 min. After the reaction mixture was refluxed for 0.5 h, it was cooled to 0 °C, and 0.49 g (2.2 mmol) of 9-(chloromethyl)-anthrancene (Aldrich) in 10 mL of THF was added. After stirring at room temperature for 18 h, the reaction mixture was cooled to 0 °C and cautiously quenched by addition of 10 mL of water. The solution was diluted with ether, washed with water and brine, and dried, and the solvent was removed to give the crude *p*-tolyl (9-anthrylmethyl) sulfide, which was purified by flash chromatography (eluting with *n*-pentane) to give 0.46 g (75%): mp 119–121 °C; ^1H NMR ($CDCl_3$) δ 2.35 (s, 3 H, $ArCH_3$), 5.06 (s, 2 H, CH_2), 7.13 (d, 2 H, *J* = 7.79 Hz, ArH), 7.36–7.50 (m, 6 H, ArH), 8.0 (d, 2 H, *J* = 7.79 Hz, ArH), 8.24 (d, 2 H, *J* = 8.62, ArH), 8.4 (s, 1 H, ArH); MS (70 eV) *m/z* (relative intensity) 314 (M^+, 24.6), 191 (base peak, 100).

General Procedure for Oxidation of Sulfides to Sulfoxides. In a 5-mL round-bottom flask equipped with a magnetic stirring bar and argon inlet was placed (0.25 mmol) of the appropriate oxaziridine in 5 mL of CH_2Cl_2 or 10 mL of CCl_4, followed by the addition of 1.1 equiv of the sulfide in 5 mL of solvent. The progress of the reaction was monitored by TLC (80% CH_2Cl_2/pentane), and the sulfoxide was isolated by preparative TLC (silica gel G) by eluting with ether. The sulfoxide had the lowest R_f value.

General Procedure for Determining the Enantiomeric Purity of the Sulfoxides. The optical purities and absolute configurations of the sulfoxides were determined using the Regis Pirkle covalent phenylglycine HPLC column. The *n*-butyl and *p*-tolyl sulfoxides were separated by eluting with 90% *n*-hexane/10%-isopropyl alcohol at a flow rate of 1.0 mL/min. The methyl 9-anthryl sulfoxide was separated by eluting with 80% *n*-hexane/20% isopropyl alcohol at a flow rate of 1.0 mL/min. Each analysis was run at least twice and the results averaged. As previously reported the (*S*)-sulfoxides were the first to be eluted.[6] The enantiomeric purity of the other sulfoxides was determined by optical rotation and/or by chiral shift reagent experiments. Good correlation of the enantiomeric purity was observed using either method.

Procedure for ^1H NMR Chiral Shift Reagent Experiments. In an NMR tube was placed approximately 10 mg of the appropriate sulfoxide in 0.3 mL of $CDCl_3$. The solvent was filtered through dried 4-Å molecular sieves prior to use to minimize the water content. An NMR spectrum was taken to establish the initial chemical shifts of the protons and the purity of the sulfoxide. Tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III) [Eu(hfc)$_3$] derivative was added to the NMR tube in successive increments until base line separation of the absorption for the enantiomers was obtained. The enantiomeric purity (% ee) was obtained by subtracting the percentage calculated for each enantiomer from the integration data. NMR shift experiments using Eu(hfc)$_3$ were performed on racemic samples of the sulfoxides to identify the absorptions. Separation of the enantiomeric absorption for the methyl groups or the aromatic protons adjacent to the sulfoxide moiety was observed for most of the sulfoxides.

X-ray Analysis of (3′*R*,2*S*)-(+)-(Phenylsulfonyl)(3,3-dichlorocamphoryl)oxaziridine (12c). $C_{16}H_{19}NSO_3Cl_2$ crystallizes in the monoclinic space group $P2_1$ (systematic absences *h*00, *h* = odd; 0*k*0, *k* = odd; and 00*l*, *l* = odd), with *a* = 9.783 (1), *b* = 14.838 (2), *c* = 12.592 (2) Å, β = 102.75 (1)°, *V* = 1782.7 (8) Å^3, *Z* = 4, and d_{calcd} = 1.402 g/cm^3. The cell constants were determined from a least-squares fit of the setting angles for 25 accurately centered reflections. X-ray intensity data were collected on an Enraf-Nonius CAD4 diffractometer employing graphite-monochromated Cu K_α radiation (λ = 1.541 84 Å) and using the ω–2θ scan technique. A total of 3356 reflections were measured over the ranges: $4 \le 2\theta \le 2.0$–$65.0°$, $0 \le h \le 11$, $-17 \le k \le 0$, $-14 \le l \le 14$. Three standard reflections measured every 3500 s of X-ray exposure showed no intensity decay over the course of data collection.

The intensity data were corrected for Lorentz and polarization effects but not for absorption. Of the reflections measured, a total of 2928 unique reflections with $F^2 > 3\sigma(F^2)$ were used during subsequent structure refinement.

The structure was solved by direct methods (MULTAN11/82). Refinement was by full-matrix least-squares techniques based on *F* to minimize the quantity $\sum w(|F_o| - |F_c|)^2$ with $w = 1/\sigma^2(F)$. Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were included as constant contributions to the structure factors and were not refined. Refinement converged to R_1 = 0.077 and R_2 = 0.099.

Acknowledgment. This work was supported by a grant from the National Science Foundation (CHE 9143917). We thank Robert M. Przeslawski for performing the low-temperature NMR studies and Prof. David R. Dalton, Temple University, for helpful discussions.

Supplementary Material Available: Tables of atomic positional parameters, thermal parameters, bond distances, and bond angles of (3′*R*,2*S*)-(+)-*N*-(phenylsulfonyl)(3,3-dichlorocamphoryl)oxaziridine (**12c**) from the X-ray experiments (11 pages). Ordering information is given on any current masthead page.

(41) Davis, F. A.; Towson, J. C.; Vashi, D. B.; Thimma Reddy, R.; McCauley, J. P., Jr.; Harakal, M. E.; Gosciniak, D. *J. Org. Chem.* **1990**, *55*, 1254.