Chemistry of Oxaziridines. 3.[1] Asymmetric Oxidation of Organosulfur Compounds Using Chiral 2-Sulfonyloxaziridines

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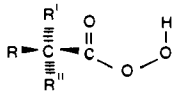
Abstract: Chiral 2-sulfonyloxaziridines, **9–12**, afford the best enantioselectivity of any chiral oxidizing reagent for the asymmetric oxidation of sulfides and disulfides to sulfoxides and thiosulfinates, respectively, 5–8 times better than chiral peracids. For asymmetric oxidations using **9–12**, the configuration of the oxaziridine three-membered ring was shown to control the configuration of the product, which could be predicted using a chiral recognition mechanism (Figure 2). The increased asymmetric bias exhibited by chiral 2-sulfonyloxaziridines was attributed to the fact that the active-site oxygen was incorporated into a rigid chiral environment. The group size difference (GSD) effect in both the oxaziridine and substrate play important roles in determining the absolute configuration of the product and the magnitude of the asymmetric bias. As the GSD increases the enantioselectivity increases.

The ultimate goal of most asymmetric syntheses is to mimic the efficiencies and stereoselectivities of enzyme-catalyzed reactions.[2] During the past several years there have been impressive achievements in the asymmetric formation of C–H and C–C bonds.[2,3] However, the fundamental processes controlling asymmetric induction that enable the achievement of high enantioselectivities are not well understood. This is particularly true of asymmetric oxidations and is best illustrated by the oxidation of unfunctionalized olefins[4–6] and sulfides[7,8] using chiral peracids and hydroperoxides. In these oxidations the asymmetric bias is very low, 0–8% ee, with the structure of the chiral peracid or hydroperoxide having little influence on the asymmetric bias. The unpredictability of the results of these asymmetric oxidations has impeded the development of theories of asymmetric induction.

Montanari et al. proposed a Cram–Prelog type steric model for predicting product configuration in the chiral peracid oxidation of sulfides.[7] However, this model failed, for example, for *n*-alkyl benzyl sulfides,[8b] and the configuration of the sulfoxide was solvent dependent.[7] Furthermore, steric requirements for these asymmetric oxidations did not parallel those of other systems using the Cram–Prelog principles.[9] In Montanari's model the effective size of *tert*-butyl is required to be larger than phenyl, whereas in most other studies the converse is true.[10] As pointed out by Mislow and co-workers, the asymmetric bias of these sulfide oxidations is very low, and quantitative comparisons are tenuous at best.[8] The difference in transition-state energies for 5% ee (52.5:47.5) at 0 °C is estimated to be only 50 cal/mol.

Enzymes are capable of carrying out the asymmetric oxidation of unfunctionalized olefins[11] and sulfides[12] very successfully. For example, the microorganisms *Mortierella isabellina* and *Helminthosporium* oxidize methyl *p*-tolyl sulfide to afford optically pure (*S*)-(−)- and (*R*)-(+)-methyl *p*-tolyl sulfoxides, respectively.[12a] Achiral oxidizing agents in the binding domain of bovine serum albumin also afford high enantioselectivity for asymmetric oxidation of sulfides to sulfoxides (81% ee max).[13]

We believe that these enzymatic systems are able to achieve this high asymmetric bias because the active site and/or substrate has been incorporated into a rigid chiral environment. Clearly, chiral peracids and hydroperoxides do not possess such features. Chiral peracids, **1**, are flexible molecules having free rotation about



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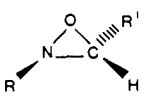

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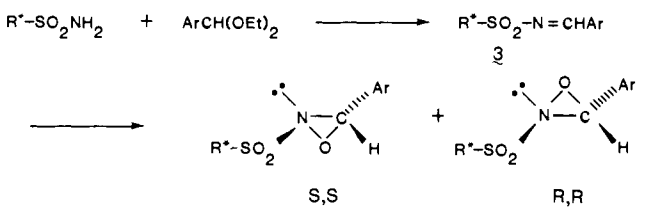
Scheme I



the bond attaching the chiral center to the active site. Furthermore, the chiral center of **1** has little influence on transition-state geometries because it is several bonds removed from the active oxygen. Compounding the problem is the fact that unfunctionalized substrates lack sites for complexing with the chiral peracid in the transition state.

If these views are correct, an efficient asymmetric oxidizing reagent for unfunctionalized substrates requires that the active site be in a rigid chiral environment and as chlose as possible to

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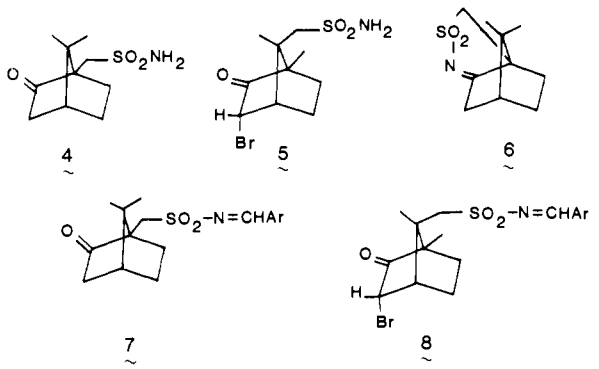
the optically active centers of that reagent. To date all attempts to prepare chiral peracids and chiral hydroperoxides with such structural features have been unsuccessful.[4,5] On the other hand, oxaziridines, 2, are a class of compounds that do have these features. In oxaziridines, **2**, the oxygen atom (active site) is in a rigid three-membered ring one bond removed from the C and N chiral centers.

During the past several years we have reported on the oxygen transfer reaction of 2-sulfonyloxaziridines (**2**, R = RSO_2, R′ = Ar).[1,14] These versatile aprotic, neutral oxidizing reagents selectivity oxidize sulfides and disulfides to sulfoxides and thiosulfinates (RS(O)SR),[15] respectively, epoxidize olefins in a syn-stereospecific manner,[16] and hydroxylate carbanions.[17,18] Recently the application of 2-sulfonyloxaziridines to the study of sulfenic acids (RSOH), a biologically important functional group, has been described.[19]

We report here the preparation of chiral 2-sulfonyloxaziridines and their application to understanding asymmetric oxidation.

Synthesis of Chiral 2-Sulfonyloxaziridines. The general synthesis of chiral 2-sulfonyloxaziridines is outlined in Scheme I.[1,14] An optically active sulfonamide ($R^*SO_2NH_2$) is condensed with the diethyl acetal of an aromatic aldehyde at 150–180 °C, affording chiral sulfonimine, **3**. Since oxidation of sulfonimines gives only (*E*)-2-sulfonyloxaziridines,[14] just two oxaziridine diastereomers having the *S,S* and *R,R* configurations at the three-membered ring are obtained on oxidation of **3**.

d-10-Camphorsulfonamide (**4**)[20] and *d*-α-bromo-π-camphor-



sulfonamide (**5**),[20] prepared from the commercially available sulfonic acids, were condensed at 150–180 °C with the appropriate aromatic aldehyde diethyl acetal to afford good yields of the corresponding sulfonimines, **7** and **8**. Care is necessary in preparing sulfonimines from sulfonamide **4**. If the temperature is too high or heating prolonged, *d*-10-camphorsulfonanhydramide (**6**)[20] is formed. Purification of products in subsequent steps becomes acutely difficult if **6** is present. In addition to heat, the formation of **6** from **4** is promoted by acids formed in the preparation of **4**. Purification of **4** to remove trace amounts of these acids greatly enhances the thermal stability of **4** toward formation of **6**.

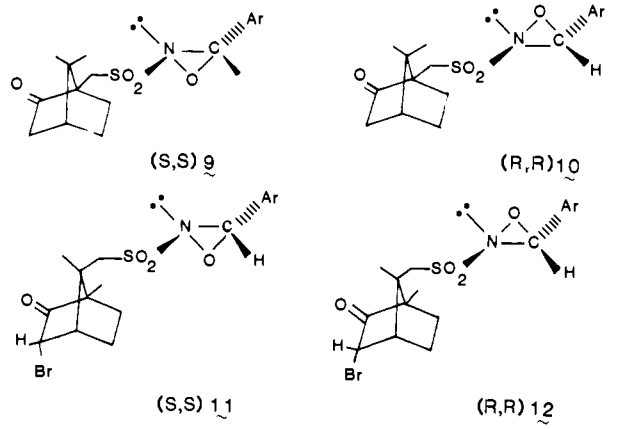
Table I. Oxidation of Sulfonimines 7 and 8 to Oxaziridines 9/10 and 11/12

sulfonimine	conditions, °C	% yield[a]	ratio of oxaziridine diastereomers[b]
7a	0–5	90	65:35
7b	0–5	78	65:35
7c	0–5	87	66:34
7d	0–5	90	65:35
	−5	90	65:35
	25	90	65:35
	0–5[c]	85	50:50
8d	0–5	90	50:50
	−10	90	55:45
	0–5[c]	80	54:46

[a] Isolated yields. [b] Determined by NMR see text. [c] 10% benzyltriethylammonium chloride (BTEAC) added.

In most cases satisfactory elemental analyses were obtained for chiral sulfonimines **7** and **8**. The ^1H NMR spectra of **7** and **8** display characteristic absorptions at 8.9–9.6 ppm for the sulfonimine protons and AB quartets in the region 3.1–3.8 ppm for the diastereotropic methylenesulfonyl protons.

Oxidation of sulfonimines **7** and **8** with *m*-chloroperbenzoic acid (*m*-CPBA) utilizing biphasic conditions affords good yields, 85–90%, of the corresponding mixtures of oxaziridine diasteromers, **9/10** and **11/12**. The ratios of **9/10** (60-MHz NMR) and **11/12**



(250-MHz NMR) in these mixtures were determined by integration of the methylenesulfonyl protons appearing as two overlapping AB quartets in the region 3.3–4.0 ppm. In some mixtures of **9/10** the oxaziridine ring protons are separated by 1–2 Hz. In both **9/10** and **11/12** the camphor methyl groups of each diastereomer can be discerned in the mixtures and used to estimate the diastereomer ratios (Table I).

Several attempts were made to alter the ratios of the oxaziridine diastereomers by varying the sulfonimine oxidation conditions. Lowering the temperature of oxidation has no influence on the ratio of **9/10** and only a slight effect on the ratio of **11/12** (Table I). A phase-transfer catalyst, benzyltriethylammonium chloride (BTEAC), decreases the ratio of **9/10** from 65:35 to 50:50 but slightly improves the ratio for **11/12**. Note that the best ratio of oxaziridine diastereomers, 65:35, is observed for sulfonimines **7**. Apparently the camphor carbonyl group is playing some role in directing the peracid to a particular face of the sulfonimine. These results are summarized in Table I.

Attempts to separate the diastereomeric mixtures of oxaziridines by fractional sublimation or chromatography were unsuccessful owing to the instability of 2-sulfonyloxaziridines under these conditions. The procedure that proved to be most successful for separating the mixtures was fractional crystallization. The best solvent for the *d*-(10-camphorsulfonyl)oxaziridines, **9/10**, was ethyl ether/chloroform and for the *d*-α-bromo-π-camphorsulfonyl oxaziridines, **11/12**, methanol.

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Table II. Asymmetric Oxidations of Sulfides Using Chiral 2-Sulfonyloxaziridines in $CHCl_3$

entry	oxaziridine[a,b]	temp, °C	sulfoxides, % ee (configuration) PhS(O)Me (14a)	PhS(O)CMe$_3$ (14b)	p-TolS(O)Me (14c)	p-TolS(O)CMe$_3$ (14e)
1	(+)-9a/10a (62:38)	25			1.26 (S)	
2		−50			4.08 (S)	
3	(−)-9b/10b (63:37)	25			1.50 (R)	
4		−50			3.74 (R)	
5	(−)-9c/10c (67:33)	25	1.6 (R)	2.0 (R)	1.3 (R)	2.0 (R)
6		−50	2.8 (R)	1.6 (R)	5.25 (R)	1.6 (R)
7	(S,S)-(−)-9d	25			17.0 (S)	11.0 (S)
8		−50			31.0 (S)	9.2 (S)
9	(R,R)-(+)-10d	25			21.3 (R)	
10	(S,S)-(−)-11d	25			10.3 (S)	11.0 (S)
11		−50			21.4 (S)	12.5 (S)
12	(R,R)-(+)-12d	25			16.6 (R)	19.1 (R)
13		−50			26.0 (R)	15.1 (R)

[a] Oxaziridine considered to be optically pure unless otherwise noted. [b] Configuration of (S,S)-9d and (R,R)-10d determined by chiral recognition mechanism; configuration of (S,S)-11d and (R,R)-12d determined by X-ray.

Table III. Effect of Solvent on the Asymmetric Oxidation of Sulfides to Sulfoxides Using Chiral 2-Sulfonyl Oxaziridines at 25 °C

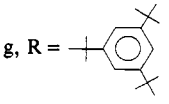
entry	oxaziridine	solvent	sulfoxide, % ee (configuration) p-TolS(O)Me (14c)	p-TolS(O)CMe$_3$ (14e)	PhCH$_2$S(O)Me (14f)
1	(S,S)-(−)-9d	CCl_4	12.9 (S)		
2		$CHCl_3$	17.0 (S)	11.0 (S)	1.1 (S)
3		Et_2O	15.4 (S)	10.5 (S)	
4		PhH	22.7 (S)	9.6 (S)	2.2 (R)
5		PhH[a]	26.0 (S)		
6		Ph-Me[b]	35.1 (S)		
7		Me_2CO	14.3 (S)		
8		DMF	13.8 (S)		
9		$CHCl_3 \cdot BF_3OEt_2$[c]	12.4 (S)		
10		EtOH	16.3 (S)		
11	(S,S)-(−)-11d	$CHCl_3$	10.3 (S)	11.9 (S)	
12		PhH		9.9 (S)	
13	(R,R)-(+)-12d	$CHCl_3$	16.6 (R)	19.1 (R)	1.1 (S)
14		PhH			2.5 (R)

[a] 0–5 °C. [b] −78 °C. [c] 10 mol %.

Although the ratio of the oxaziridine diastereomers derived from monosubstituted aromatic aldehydes **9a–c/10a–c** was improved by crystallization, all attempts to obtain at least one of them optically pure were unsuccessful. For oxaziridines **9d/10d** and **11d/12d** prepared from the 2-chloro-5-nitrobenzaldehyde, it was possible to obtain the individual diastereomeric oxaziridines optically pure. Thus, several crystallizations of **9d/10d** from ether gave (−)-**9d** in 50% yield optically pure and (+)-**10d** in 20% yield optically pure. Similar crystallizations of **11d/12d** from methanol afforded (−)-**11d** in 30% yield and (+)-**12d** in 35% yield optically pure. Optical purity was determined by 250-MHz ^{1}H NMR spectroscopy and by the optical rotation.

Asymmetric Oxidations Using Chiral 2-Sulfonyloxaziridines. Asymmetric oxidations were accomplished by dropwise addition of the chiral 2-sulfonyloxaziridines to the sulfide, **13**, or disulfide,

$RS(O)_nR'$ $RS(O)_nSR$

13, $n = 0$ **15**, $n = 0$
14, $n = 1$ **16**, $n = 1$
a, R = Ph; R′ = Me a, R = p-Tol
b, R = Ph; R′ = CMe_3 b, R = t-Bu
c, R = p-Tol; R′ = Me
d, R = p-Tol; R′ = i-Pr
e, R = p-Tol; R′ = CMe_3
f, R = $PhCH_2$; R′ = Me
g, R = 

15, in the desired solvent at the appropriate temperature. At 25 °C oxidation of sulfides was complete in less than a minute with no detectable sulfone formation.[8] Chiral sulfoxides and thiosulfinates **14** and **16** were isolated by sublimination and/or preparative TLC in 75–85% yield. The corresponding chiral sulfonimines, **7** and **8**, were isolated in greater than 90% yield and recycled. The percent enantiomeric excess (% ee.) was determined by dividing the observed optical rotation of the product by the rotation of the pure enantiomer reported in the literature and by use of a chiral shift reagent. Agreement was within ±1.0% ee. Chiral oxidations were performed at least twice and the results averaged. These results are summarized in Table II.

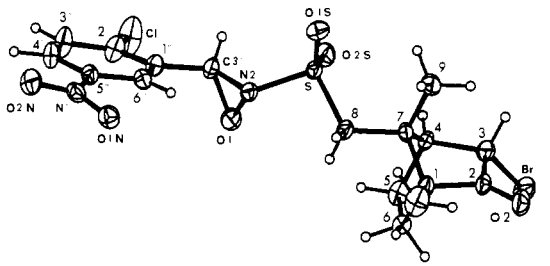


Figure 1. ORTEP drawing of compound (−)-**11d**. Thermal ellipsoids are drawn at the 35% probability level. Hydrogen atoms are represented by spheres of arbitary size.

Significantly, the enantioselectivity (% ee) for oxidation of sulfides to sulfoxides using chiral oxaziridines **9d**, **10d**, **11d**, and **12d** was 5–8 times better than similar oxidations using chiral peracids (Table I).[7] Furthermore, there was no effect of solvent on the product absolute configuration (Table III), in contrast to oxidation with chiral peracids.[7]

Oxaziridine Absolute Configuration (Chiral Recognition Mechanism). Figure 1 is an ORTEP drawing of (−)-**11d** and establishes the absolute configuration of the oxaziridine three-

Table IV. Valence Angles (Deg) for (−)-11d

C(1Me)-C(1)-C(2)	113.6 (7)	C(8)-S-N(2')	96.8 (3)
C(1Me)-C(1)-C(6)	115.9 (8)	O(1S)-S-O(2S'	119.7 (4)
C(1Me)-C(1)-C(7)	119.6 (7)	O(1S)-S-N(2')	101.9 (3)
C(2)-C(1)-C(6)	102.5 (6)	O(2S)-S-N(2')	111.9 (4)
C(2)-C(1)-C(7)	101.6 (6)	S-N(2')-O(1')	110.2 (4)
C(6)-C(1)-C(7)	101.2 (6)	S-N(2')-C(3')	115.0 (5)
C(1)-C(2)-O(2)	128.2 (7)	O(1')-N(2')-C(3')	58.2 (5)
C(1)-C(2)-C(3)	105.7 (6)	N(2')-O(1')-C(3')	58.8 (5)
O(2)-C(2)-C(3)	126.1 (7)	N(2')-C(3')-O(1')	63.1 (5)
Br-C(3)-C(2)	109.5 (5)	N(2')-C(3')-C(1'')	115.7 (6)
Br-C(3)-C(4)	115.1 (5)	O(1')-C(3')-C(1'')	116.4 (6)
C(2)-C(3)-C(4)	103.0 (6)	C(3')-C(1'')-C(2'')	119.4 (6)
C(3)-C(4)-C(5)	109.6 (6)	C(3')-C(1'')-C(6'')	120.6 (6)
C(3)-C(4)-C(7)	99.0 (6)	C(2'')-C(1'')-C(6'')	119.9 (6)
C(5)-C(4)-C(7)	101.3 (6)	Cl-C(2'')-C(1'')	119.5 (6)
C(4)-C(5)-C(6)	103.2 (7)	Cl-C(2'')-C(3'')	119.8 (6)
C(1)-C(6)-C(5)	105.4 (7)	C(1'')-C(2'')-C(3'')	120.7 (7)
C(1)-C(7)-C(4)	94.8 (5)	C(2'')-C(3'')-C(4'')	119.8 (8)
C(1)-C(7)-C(8)	109.2 (6)	C(3'')-C(4'')-C(5'')	119.7 (7)
C(1)-C(7)-C(9)	112.9 (7)	C(4'')-C(5'')-C(6'')	121.3 (7)
C(4)-C(7)-C(8)	114.7 (6)	C(4'')-C(5'')-N('')	120.0 (6)
C(4)-C(7)-C(9)	114.5 (6)	C(6'')-C(5'')-N('')	118.7 (6)
C(8)-C(7)-C(9)	109.8 (6)	C(1'')-C(6'')-C(5'')	118.3 (7)
C(7)-C(8)-S	116.7 (5)	C(5'')-N('')-O(1N)	118.9 (6)
C(8)-S-O(1S)	111.3 (4)	C(5'')-N('')-O(2N)	116.9 (7)
C(8)-S-O(2S)	112.3 (3)	O(1N)-N('')-O(2N)	124.2 (7)

Table V. Interatomic Distances (Å) for (−)-11d

Br-C(3)	1.961 (7)	S-O(2S)	1.417 (6)
C(1)-C(1Me)	1.53 (1)	S-N(2')	1.735 (6)
C(1)-C(2)	1.50 (1)	N(2')-O(1')	1.48 (1)
C(1)-C(6)	1.57 (1)	N(2')-C(3')	1.42 (1)
C(1)-C(7)	1.55 (1)	O(1')-C(3')	1.409 (9)
C(2)-O(2)	1.182 (9)	C(3')-C(1'')	1.501 (9)
C(2)-C(3)	1.54 (1)	Cl-C(2'')	1.729 (8)
C(3)-C(4)	1.55 (1)	C(1'')-C(2'')	1.39 (1)
C(4)-C(5)	1.54 (1)	C(1'')-C(6'')	1.36 (1)
C(4)-C(7)	1.57 (1)	C(2'')-C(3'')	1.39 (1)
C(5)-C(6)	1.52 (1)	C(3'')-C(4'')	1.34 (1)
C(7)-C(8)	1.543 (9)	C(4'')-C(5'')	1.39 (1)
C(7)-C(9)	1.54 (1)	C(5'')-C(6'')	1.41 (1)
C(8)-S	1.766 (7)	C(5'')-N('')	1.45 (1)
S-O(1S)	1.422 (6)	N('')-O(1N)	1.222 (9)
		N('')-O(2N)	1.237 (8)

membered ring as *S,S* (Figure 1).[21] Consequently the configuration of the oxaziridine three-membered ring in (+)-**12d** is *R,R*.

The X-ray structure of (*S,S*)-(−)-**11d** indicates that phenyl and oxaziridine rings make an angle of 66.5 (9)°. C(3'), N(2'), and the electron pair on N(2) are coplanar with the phenyl ring. The H(6'')···N(2')distance is 2.46 (1) Å, which brings the lone pair of N(2') in close proximity to H(6''). In the solid state H(8a) is within 2 Å of one of the lone pairs on O(1'). The oxygen electron pair on the phenyl side of the oxaziridine molecule is not sterically hindered. While solution conformation may differ significantly from those in the solid state, the H(6'')···N lone pair and H(8a)···O electron pair interactions may lead to a slightly longer lifetime of the solid-state conformation in solution. This would indicate that higher product chirality would be favored by low temperatures and nonpolar solvents, as observed (Tables II and III). Models indicate that the bulky groups on the sulfone side of the oxaziridine ring exhibit more conformations sterically hindering the oxygen lone pair.

The bond distances and valence angles are within the normal range.[21] Although the standard deviations of the structural parameters are large, the 4° bending of the carbonyl oxygen atom O(2) out of the C(1)C(2)C(3)C(4) plane and away from the methylene bridge C(3) is consistent with observations of π-system

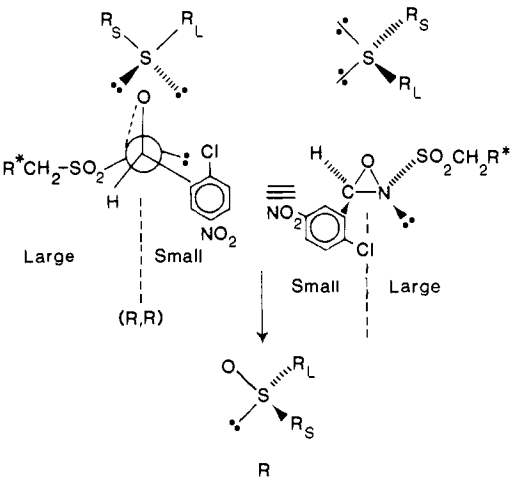


Figure 2. Chiral recognition model.

distortions in norbornene systems.[23] The nitro group is twisted slightly away from coplanarity with the phenyl ring, as indicated by torsion angles C(4'')C(5'')N''O(1N) and C(6'')C(5'')N''O(2N) of −11.1 (9) and 9.5 (9)°. Tables IV and V summarize the interatomic distances and valence angles for (−)-**11d**.

Attempts to obtain suitable crystals of (−)-**9d** or (+)-**10d** for X-ray analysis were unsuccessful. The assignments of the *S,S* and *R,R* configurations to the oxaziridine three-membered rings of (−)-**9d** and (+)-**10d**, respectively, are based on the chiral recognition model discussed below.

Inspection of Dreiding and space-filling CPK models of (*S,S*)-(−)-**11d** (Figure 1) suggests that the 2-chloro-5-nitrophenyl group behaves as if it were smaller than the camphorsulfonyl group in the region of the oxaziridine three-membered ring. Thus the oxaziridine three-membered ring can be divided into large and small regions in the vicinity of the active-site oxygen (Figure 2). Models support similar conclusions for **9d**/**10d**.

The mechanism for oxygen transfer by 2-sulfonyloxaziridines is believed to be similar to that for peracids, namely a nucleophilic attack by the substrate on the electrophilic oxaziridine oxygen atom.[15,24] Therefore, the preferred diastereomeric transition state for sulfide oxidation by chiral 2-sulfonyl oxaziridines should be the one in which the enantiotopic electron pair on sulfur attacks the electrophilic oxaziridine oxygen atom in such a way that the large (R_L) and small (R_S) groups of the substrate (R_L–S–R_S) face the small and large regions of the oxaziridine three-membered ring (Figure 2). That is where the R_L group is as far away as possible from the bulky camphorsulfonyl group. Thus (*S,S*)-(−)-**11d** and (*R,R*)-(+)-**12d** will afford sulfoxides of the *S* and *R* configurations, respectively. Conversely, if sulfoxides of the *S* and *R* configurations are obtained, then the configuration of the oxaziridine three-membered rings must be *S,S* and *R,R*, respectively.

This model, Figure 2, ignoring electronic and solvent effects, is supported by the results summarized in Tables II and III. for oxidations using (*S,S*)-(−)-**11d** and (*R,R*)-(+)-**12d**, only sulfoxides of the *S* and *R* configurations, respectively, were obtained (Table II, entries 9–13). This means that the absolute configuration of the oxaziridine three-membered ring controls the configuration of the product as required by the model (Figure 2). Similar results are observed for oxidations using (*S,S*)-(−)-**9d** and (*R,R*)-(+)-**10d**, in each case giving the predicted product (Table II, entries 7–9).

As already mentioned, oxidation using chiral 2-sulfonyloxaziridines do not display a dependency of the product absolute configuration on the solvent (Table III). Even the presence of BF_3OEt_2 has no effect on the product configuration and little effect on the enantioselectivity (Table III, entry 9). the unimportance of electronic effects on these oxidations is further supported by

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Table VI. Group Size Difference (GSD) Effect on the Oxidation of Sulfides (Disulfides) to Sulfoxides (Thiosulfinates) by (*S,S*)-(−)-9d in $CHCl_3$ at 25 °C

entry	sulfide (disulfide)	sulfoxide (thiosulfinate) % ee (configuration)
1	$PhCH_2$-S-Me	1.1 (*S*)
2	*p*-Tol-S-CMe_3	11.1 (*S*)
3	*p*-Tol-S-Me	17.0 (*S*)
4	*p*-Tol-S-$CHMe_2$	20.8 (*S*)
5	2,4,6-*t*-$Bu_3C_6H_2$SMe	46.0 (*S*)
6	*p*-Tol-S-S-Tol-*p*	2.1 (*S*)
7	Me_3C-S-S-CMe_3	13.8 (*S*)[a]

[a] Proposed configuration based on the model.

the similar enantioselectivity obtained with **9d/10d** and **11d/12d**. In **9d/10d** and **11d/12d** the relationship of the polar camphor carbonyl group to the active site in each of them is quite different. Significantly, steric effects for our model (Figure 2) are the same as those observed for other systems where the Cram–Prelog principles have been evoked, i.e., the effective size of phenyl being larger than *tert*-butyl.[9,10]

The only exceptions to these generalizations are in those cases where the asymmetric induction is very low, i.e., methyl benzyl sulfide (1–2% ee). In such examples predictions are difficult.

The model outlined in Figure 2 suggests that configurations of the oxaziridine three-membered ring in the major diastereomers of (+)-**9a/10a**, (−)-**9b/10b**, and (−)-**9c/10c** are *S,S*, *R,R*, and *R,R*, respectively. However, such assignments are risky because of the low optical yields and the strong possibility that the asymmetric bias for the *S,S* and *R,R* oxaziridine diastereomers will be different. In this regard, it is significant that the (*R,R*)-(+)-**10d** and (*R,R*)-(+)-**12d** give greater enantioselectivity than do the corresponding (*S,S*)-(−)-**9d** and (*S,S*)-(−)-**11d**, diastereomers, respectively (Table II; compare entries 7 and 10 with 9 and 12).

Group Size Difference (GSD) Effect. The results summarized in Tables II and III establish that the effective size of the groups attached to the oxaziridine three-membered ring controlled the absolute configuration of the product. For asymmetric oxidations using chiral 2-sulfonyloxaziridines, we believe that this difference in size, *g*roup *s*ize *d*ifference (GSD), in both the oxaziridine and substrate plays an important role in determining the magnitude of the asymmetric bias as well.

The model, figure 2, suggests that as the GSD increases the asymmetric bias should also increase. This view is supported by the results for sulfide oxidations using oxaziridine (*S,S*)-(−)-**9d** and summarized in Table VI. As the difference in size of the groups attached to the sulfur atom (R_L–S–R_S) increases the asymmetric induction increases. Methyl benzyl sulfide (**13f**) has the smallest GSD, and the optical purity of the corresponding sulfoxide is only 1.1% ee. On the other hand, methyl 2,4,6-tri-*tert*-butylphenyl sulfide (**14g**) has the maximum GSD and gives the highest enantioselectivity on oxidation, 46.0% ee. Observe that the latter sulfoxide, **14g**, has the *S* configuration, determined using (*R*)-(−)-phenyl(trifluoromethyl)carbonyl (Pirkle solvent),[25] as predicted by the model (Figure 2).

Inspection of Table VI, would suggest that the results for oxidation of isopropyl *p*-tolyl sulfide (**13d**) are not in accord with the GSD principals proposed above because asymmetric oxidation of sulfides **13c** and **13d** gives sulfoxides with similar asymmetric bias, 17.0 vs. 20.8% ee. allinger et al. have reported, however, that the conformational size of isopropyl is comparable, to that of a methyl group.[26]

The asymmetric bias for oxidation of di-*tert*-butyl disulfide (**15b**) to thiosulfinate **16b** is greater than for oxidation of *p*-tolyl disulfide (**15a**) (13.8% ee vs. 2.1% ee). The opposite trend might have been anticipated on the basis of a consideration of the effective sizes of aryl and *tert*-butyl. However, the possibility of racemization of *p*-tolyl *p*-toluenethiosulfinate (**16a**) during isolation cannot be ruled out. Facile racemization of chiral arene arylthiosulfinates by heat, acids, and bases has been described.[27]

Solvent and temperature effects on the asymmetric bias can also be seen in terms of the GSD principle. when the temperature of oxidation is lowered from 25 to −50 °C the enantioselectivity for oxidation of methyl *p*-tolyl sulfide (**13c**) to sulfoxide **14c** increases 2-fold. A comparable increase is not observed for oxidation of *tert*-butyl *p*-tolyl sulfide (**13e**) (Table II, entries 7–13). With the exceptions of benzene and toluene most of the solvents listed in Table III have little influence on the sulfoxide enantioselectivity. Whereas an increase in the asymmetric bias was observed in benzene for oxidation of methyl *p*-tolyl sulfide (**14c**), a similar effect was not observed for **14e** (Table III, entries 4–6). How the GSD influences these solvent and temperature effects is unclear at this time.

Conclusions

The enantioselectivity for asymmetric oxidations of unfunctionalized substrates such as sulfides and disulfides can be increased by incorporating the active site of the oxidizing reagent into a rigid chiral environment, such as in 2-sulfonyloxaziridines. From studies of asymmetric oxidations using these chiral oxidizing reagents, factors important in controlling product absolute configuration appear to be largely steric in nature. The group size difference (GSD) effect in the oxaziridine and substrate play important roles in determining both the absolute configuration of the product and the magnitude of the asymmetric bias. As the GSD increases, the enantioselectivity increases.

The method of choice for preparing chiral sulfoxides in high optical purity remains the "Andersen" synthesis, the reaction of an organometallic reagent with an optically active sulfinate ester.[8,28] When this procedure cannot be used, as in the preparation of chiral thiosulfinates, or proves to be problematical,[29] oxidations using chiral 2-sulfonyloxaziridines are indicated. Another potentially important area of application of these chiral reagents is asymmetric hydroxylations, recently demonstrated by the chiral synthesis of (+)-kjellmanianone.[18]

The real value of chiral 2-sulfonyloxaziridines is expected to be in elucidating the fundamental factors controlling asymmetric oxidations. The reason for this is that 2-sulfonyloxaziridines are stable, have a well-defined active site, and can be manipulated in a systematic manner.[1,14] Chiral 2-sulfonyloxaziridines are also important in assigning the absolute configuration of oxidation products, difficult to do in other ways. For example, Mikolajczk and Drabowicz report the resolution of *tert*-butyl 2-methyl-2-propanethiosulfinate (**16b**) via the β-cyclodextrin inclusion complex.[30] They obtain **16b** with $[\alpha]_D$ +21.1° (13.6% ee) but are unable to assign the configuration. It is likely that the absolute configuration of (+)-**16b** is *R*, because oxidation of di-*tert*-butyl disulfide (**15b**) with (*S,S*)-(−)-**9d** affords (−)-**16b**, predicted by the model (Figure 2) to have the *S* configuration.

Experimental Section

Melting points were determined on a Mel-Temp apparatus and are uncorrected. ^1H NMR spectra were measured on Varian A-60A (60 MHz) and Varian HR-250 (250 MHz) NMR spectrometers. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. *m*-Chloroperbenzoic acid (*m*-CPBA), *d*-10-camphorsulfonic acid monohydrate, and *d*-α-bromocamphor-π-sulfonic acid ammonium salt were purchased from Aldrich Chemical Co. and used without additional purification. Aromatic aldehyde diethyl acetals were prepared as previously described[14] unless otherwise noted. Sulfides were prepared by standard methods.

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***d*-10-Camphorsulfonamide (4).** In a 100-mL round-bottom flask equipped with a magnetic stir bar and reflux condenser was placed thionyl chloride, 18 g (11 mL, 0.152 mol). *d*-10-Camphorsulfonic acid monohydrate (10 g, 0.0431 mol) was added portionwise, and stirring for 10 min at room temperature was followed by heating at reflux for 1.5 h. The unreacted thionyl chloride was removed on the rotory evaporator, the last traces being removed by azeotropic distillation with 2 × 30 mL portions of benzene. The crude, solid *d*-10-camphorsulfonyl chloride was dissolved in 150 mL of chloroform in a 250-mL three-necked flask equipped with magnetic stir bar and ammonia gas inlet. The reaction mixture was cooled in an ice bath, and ammonia gas was slowly allowed to pass over the solution for 30–40 min. The reaction mixture was poured through a bed of 30–40 g of dry silica gel G in a 150-mL Büchner funnel. The bed was washed with 600 mL of 10% ether in chloroform, and the combined filtrates were evaporated under vacuum to afford 8.2 g (82%) of white solid **4**: mp 128–30 °C (lit.[20] mp 127 °C); $[\alpha]_D$ + 22.8° (*c* 1.0, methanol).

***d*-α-Bromocamphor-π-sulfonamide (5).** In a 250-mL round-bottom flask equipped with condenser and mechanical stirrer was placed 25 g (0.076 mol) of *d*-α-bromocamphor-π-sulfonic ammonium salt and 47.0 g (0.23 mol) of phosphorus pentachloride. After the mixture was mixed well, the reaction was stirred for 15 min at room temperature and then at 70 °C for 15 min. Toluene (200 mL) was added and the reaction mixture heated for 20 min at 70–80 °C. After cooling, the reaction mixture was poured over ice, and toluene solvent was separated from the aqueous phase and dried over anhydrous $MgSO_4$. The toluene solvent was transferred to a 500-mL three-necked flask and cooled in an ice bath, and ammonia was passed slowly through the solution for 2 h. After addition of 200 mL of *n*-pentane, the white solid was collected by filtration and extracted with warm chloroform, 3 × 150 mL. Evaporation of the chloroform solvent gave 19.8 g (84%) of white crystals of **5**: mp 139–141 °C (lit.[20] mp 144–145 °C); $[\alpha]_D$ +112.6° (*c* 2, acetone).

Preparation of Chiral Sulfonimines 7 and 8. The general preparation of sulfonimines **7** and **8** is illustrated for the synthesis of **7d**.

***N*-(2-Chloro-5-nitrobenzylidene)-*d*-10-camphorsulfonamide (7d).** A mixture of 5 g (0.022 mol) of sulfonamide **4** and 6.18 g (0.0238 mol) of 2-chloro-5-nitrobenzaldehyde diethyl acetal[31] was placed in a 25-mL round-bottom flask equipped with magnetic stir bar and a short-path distillation head. The reaction mixture became homogeneous when immersed in an oil bath preheated to 165 °C. Heating was continued until evolution of ethanol had ceased (no more than 20 min), after which the hot reaction mixture was placed under vacuum to remove the last traces of ethanol. The viscous sulfonimine on washing with ethyl ether crystallized. The solid was collected and dissolved in benzene, and *n*-pentane was added to afford 6.1 g (70%) of crude **7d**: mp 167–170 °C; $[\alpha]_D$ +128° (*c* 1.0, $CHCl_3$). An analytical sample of **7d** was obtained by crystallization from toluene: mp 179–180 °C; IR (KBR) 1755 (C=O), 1620 (C=N), 1350, 1140 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 0.95 (s, 3 H, Me), 1.15 (s, 3 H, Me), 1.4–2.7 (m, 7 H), 3.2 (d, 1 H, CH_2, *J* = 15 Hz), 3.8 (d, 1 H, CH_2, *J* = 15 Hz), 7.6–8.1 (m, 4 H, Ar), 9.6 (s, 1 H, N=CH); $[\alpha]_D$ +128.0° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{17}H_{19}ClN_2O_5S$: C, 51.26; H, 4.77. Found: C, 51.13; H, 4.95.

***N*-(2-Nitrobenzylidene)-*d*-10-camphorsulfonamide (7a)**: 60% (ether); mp 121–122 °C; IR (KBR) 1750 (C=O), 1610 (C=N), 1140 and 1160 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 0.9 (s, 3 H, Me), 1.2 (s, 3 H, Me), 1.4–2.7 (m, 7 H), 3.2 (d, 1 H, CH_2, *J* = 15 Hz), 3.8 (d, 1 H, CH_2, *J* = 15 Hz), 7.7–8.4 (m, 4 H, Ar), 9.4 (s, 1 H, N=CH); $[\alpha]_D$ +21.8 (*c* 1.0, $CHCl_3$). A satisfactory elemental analysis could not be obtained.

***N*-(3-Nitrobenzylidene)-*d*-10-camphorsulfonamide (7b)**: 80% (ether); mp 107–108 °C; IR (KBR) 1750 (C=O), 1610 (C=N), 1340 and 1160 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 0.9 (s, 3 H, Me), 1.1 (s, 3 H, Me), 1.3–2.7 (m, 7 H), 3.1 (d, 1 H, CH_2, *J* = 15 Hz), 3.65 (d, 1 H, CH_2 *J* = 15 Hz), 7.4–8.7 (m, 4 H, Ar), 8.9 (s, 1 H, N=CH); $[\alpha]_D$ +10.91° (*c* 14.4, $CHCl_3$). Anal. Calcd for $C_{17}H_{20}N_2O_5S$: C, 56.04; H, 5.49. Found: C, 55.90; H, 5.56.

***N*-(4-Nitrobenzylidene)-*d*-10-camphorsulfonamide (7c)**: 78% (ether); mp 156–157 °C; IR (KBr) 1750 (C=O), 1610 (C=N), 1350 and 1160 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 0.95 (s, 3 H, Me), 1.25 (s, 3 H, Me), 1.4–2.6 (m, 7 H), 3.2 (d, 1 H, CH_2, *J* = 15 Hz), 3.8 (d, 1 H, CH_2, *J* = 15 Hz), 8.0–8.5 (m, 4 H, Ar), 9.1 (s, 1 H, N=CH); $[\alpha]_D$ +21.47° (*c* 0.81, $CHCl_3$). Anal. Calcd for $C_{17}H_{20}N_2O_5S$: C, 56.04; H, 5.49. Found: C, 55.85; H, 5.56.

***N*-(2-Chloro-5-nitrobenzylidene)-*d*-α-bromocamphor-π-sulfonamide (8)**: 82% (chloroform/*n*-pentane); mp 152–154 °C; IR (KBr) 1740 (C=O), 1640 nC=N), 1360 and 1155 (SO_2) cm^{-1}; NMR 1.06 (s, 3 H, Me), 1.38 (s, 3 H, Me), 1.5–2.5 (m, 5 H), 3.25 (m, 1 H), 3.23 (s, 1 H, CH_2, *J* = 14 Hz), 3.65 (s, 1 H, CH_2, *J* = 14 Hz), 4.7 (d, 1 H, *J* = 4 Hz), 7.7–9.1 (m, 3 H, Ar), 9.35 (s, 1 H, N=CH); $[\alpha]_d$ +92.70° (*c* 2.0, acetone). Anal. Calcd for $C_{17}H_{18}ClBrN_2O_5S$: C, 42.74; H, 3.79. Found: C, 42.66; H, 3.81.

General Synthesis of Chiral 2-Sulfonyl Oxaziridines. In a 500-mL Morton flask equipped with mechanical stirrer and an addition funnel was placed 100 mL of saturated aqeuous $NaHCO_3$ and 0.0075 mol of the appropriate sulfonimine **7** or **8** in 100 mL of chloroform. the reaction mixture was cooled to 0–5 °C in an ice bath and stirred vigorously. A solution of 2.9 g (0.014 mol) of 85% *m*-CPBA in 60 mL of chloroform was added dropwise over 30 min. after the mixture was stirred at room temperature for 3.5 h, the chloroform layer was separated and washed successively with 100 mL of 5% Na_2SO_3, 100 mL of saturated aqueous $NaHCO_3$, 2 × 100 mL of water, and 25 mL of saturated NaCl solution. The chloroform solution was dried over anhydrous K_2CO_3 and evaporated in vacuo below 40 °C. the crude oxaziridine diastereomers were triturated with ether/*n*-pentane until solid.

The diastereomeric oxaziridines mixtures were analyzed by NMR spectroscopy and purified as described below.

2-(*d*-10-Camphorsulfonyl)-3-(2-nitrophenyl)oxaziridine (9a/10a): 90% (ether); mp 111–115 °C; (62:38) $[\alpha]_D$ +17.00° (*c* 5, $CHCl_3$); IR (KBr) 1750 (C=O), 1160 and 1390 (SO_2) cm^{-1}; NMR ($CDCl_3$) (major diastereomer) δ 1.0 (s, 3 H, Me), 1.2 (s, 3 H, Me), 1.4–2.7 (m, 7 H), 3.35 (d, 1 H, CH_2 *J* = 15 Hz), 3.85 (d, 1 H, CH_2, *J* = 15 Hz), 6.2 (s, 1 H, CH), 7.6–8.5 (m, 4 H, Ar); (minor diastereomer) δ 1.2 (s, 3 H, Me), 1.2 (s, 3 H, Me), 1.4–2.7 (m, 7 H), 3.25 (d, 1 H, CH_2, *J* = 15 Hz), 3.95 (d, 1 H, CH_2, *J* = 15 Hz), 6.2 (s, 1 H, CH)8 7.7–8.4 (m, 4 H, Ar). A satisfactory elemental analysis could not be obtained.

2-(*d*-10-Camphorsulfonyl)-3-(3-nitrophenyl)oxaziridine (9/10b): 78% (ether); mp 117–118 °C; (67:37) $[\alpha]_D$ - 94.7° (4.44 $CHCl_3$); IR (KBr) 1750 (C=O), 1160 and 1350 (SO_2) cm^{-1}; NMR ($CDCl_3$) (major diastereomer) δ 1.0 (s, 3 H, Me), 1.2 (s, 3 H, Me), 1.4–2.8 (m, 7 H), 3.35 (d, 1 H, CH_2, *J* = 15 Hz), 3.85 (d, 1 H, CH_2, *J* = 15 Hz)8 5.65 (s, 1 H, CH) 7.6–8.5 (m, 4 H, Ar); (minor diastereomer) δ 1.2 (s, 3 H, Me), 1.2 (s, 3 H, Me), 1.4–2.8 (m, 7 H), 3.25 (d, 1 H, CH_2, *J* = 15 Hz), 3.95 (d, 1 H, CH_2, *J* = 15 Hz), 5.65 (s, 1 H, CH), 7.7–8.4 (m, 4 H, Ar). Anal. Calcd for $C_{17}H_{20}N_2O_6S$: C, 53.68; H, 5.25. Found: C, 53.62; H, 5.18.

2-(*d*-10-Camphorsulfonyl)-3-(2-chloro-5-nitrophenyl)oxaziridine (9d/10d). The oxaziridine diasteromers were separated as follows: approximately 3.0 g of crude **9d/10d** (65:35 mixture) obtained as described above was triturated with 2 × 15 mL protions of *n*-pentane. After each *n*-pentane wash was decanted the residue was further triturated with 10–15 mL of ether. The oily residue gradually solidified into white crystals and a pale green ether solution. The mixture was filtered and the residue washed with 10 mL of ether. The solid was then recrystallized from ether, seeding with a crystal of pure (−)-**9d** obtained by repeated crystallization of **9d**. (−)-**9d** was obtained in 60% yield and determined to be 90% optically pure. On cooling of the ether filtrate, the minor diastereomer, (+)-10d, slowly crystallized from solution and was determined to be 90% optically pure by NMR spectroscopy.

The minor diasteromer, (+)-**10d**, was more conveniently obtained as follows: 5 g of a 50:50 diastereomeric mixture of **9d/10d** obtained by using 10% BTEAC (Table I) was dissolved in 5–7 mL of chloroform followed by addition of 5 mL of ether. The solution was cooled and seeded with a crystal of pure (+)-**10d**. Approximately 2.0 g of (+)-**10d** was obtained 80% optically pure. Crystallization from ether gave (+)-**10d** optically pure. (−)-**9d** can be obtained from the filtrate by adding 5 mL of ether and seeding with a crystal of pure (−)-**9d**. Anal. Calcd for $C_{1719}ClN_2O_6S$: C, 49.21; H, 4.62. Found: C, 49.09; H, 4.62.

(***S*,*S***)-(−)-**9d**: 50% yield; mp 140–141 °C dec; $[\alpha]_D$ -77.60° (*c* 1.0, $CHCl_3$) IR (KBr) 1750 (C=O), 1175 and 1350 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 1.0 (s, 3 H, Me), 1.25 (s, 3 H, Me), 1.4–2.8 (m, 7 H), 3.50 (d, 1 H, CH_2, *J* = 15 Hz), 3.90 (d, 1 H, CH_2, *J* = 15 Hz), 5.95 (s, 1 H, CH), 7.6–8.5 (m, 3 H, Ar).

(***R*,*R***)-(+)-**10d**: 40% yield; mp 121–122 °C dec; $[\alpha]_D$ +120.0° (*c* 1.0, $CHCl_3$); IR (KBr) 1750 (C=O), 1175 and 1350 (SO_2) cm^{-1}; NMR ($CDCl_3$) 1.0 (s, 3 H, Me), 1.20 (s, 3 H, Me), 1.4–2.8 (m, 7 H), 3.25 (d, 1 H, CH_2, *J* = 15 Hz), 3.95 (d, 1 H, CH_2, *J* = 15 Hz), 5.90 (s, 1 H, CH), 7.6–8.5 (m, 3 H, Ar).

2-(*d*-α-Bromo-π-camphorsulfonyl)-3-(2-chloro-5-nitrophenyl)oxaziridine (11d/12d). Anal. Calcd for $C_{17}H_{18}BrClN_2O_6S$: C, 41.35; H, 3.67. Found: C, 41.08; H, 3.55. The oxaziridine diastereomers were separated as follows:

A 10-g portion of the crude mixture of **11d/12d** (50:50) was triturated under four separated 50-mL portions of boiling methanol. The residue was crystallized from chloroform/ether to yield 2.5 g of pure (>90%) (*R*,*R*)-(+)-12d. The combined triturated fractions were cooled in an ice/methanol bath and the crystallized oxaziridines collected by filtration. The material, approximately 6 g, consisted of a 50:50 mixture of **11d/12d**. this material was dissolved in approximately 20 mL of chloroform and cooled, and 10–15 mL of diethyl ether was added. On allowing the

(31) Bordwell, F. G.; Strange, H. *J. Am. Chem. Soc.* **1955**, *77*, 5939.

solution to come to room temperature, 1.5 g of (*S,S*)-(−)-**11d**, 94% optically pure was produced. successive dilution of the mother liquor with portions of ether produced further fractions of varying composition. Additional crystallizations of these fractions from methanol gave (*S,S*)-(−)-**11d** and (*R,R*)-(+)-**12d**, optically pure.

(***S,S***)-(−)-**11d**: 30% yield; mp 154–156 °C dec; $[\alpha]_D$ −6.2° (*c* 2.0, acetone) IR (KBr) 1760 (C=O), 1160 and 1350 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 1.1 (s, 3 H, Me), 1.40 (s, 3 H, Me), 1.5–3.3 (m, 6 H), 3.50 (d, 2 H, CH_2, *J* = 6 Hz), 4.6 (d, 1 H, *J* = 5 Hz), 6.0 (s, 1 H, CH), 7.2–8.4 (m, 3 H, Ar).

(***R,R***)-(+)-**12d**: 35% yield; mp 166–168 °C dec; $[\alpha]_D$ +164.5° (*c* 2.0, acetone) IR (KBr) 1760 (C=O), 1160 and 1350 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 1.1 (s, 3 H, Me), 1.40 (s, 3 H, Me), 1.5–3.2 (m, 6 H), 3.50 (d, 2 H, CH_2, *J* = 6 Hz), 4.6 (d, 1 H, *J* = 5 Hz), 6.0 (s, 1 H, CH), 7.2–8.4 (m, 3 H, Ar).

General Procedure for Asymmetric Oxidations. In a 25-mL round-bottom flask equipped with magnetic stirring bar and dropping funnel was placed the appropriate sulfide or disulfide (typically 0.1–0.2 g) in 3–4 mL of the appropriate solvent. One equivalent of the chosen chiral 2-sulfonyl oxaziridine was dissolved in 5 mL of the appropriate solvent and added dropwise with stirring to the reaction mixture. at 25 °C the reaction mixture was allowed to stir for 15 min after addition was complete. For oxidations carried out at −50 to −78 °C, the oxaziridine was added by using a special low-temperature jacketed addition funnel and was stirred for 1 h after addition was complete. The solvent was removed under vacuum and the residue treated according to one of the following procedures.

Sulfoxides **14a** and **14c** were isolated by fractional sublimation at a bath temperature of 80 °C and a pressure of 1.0 torr. Sulfoxides **14b**, **14d**, **14e**, **14f**, **14g** and thiosulfinates **16a,b** were isolated by washing the reaction mixture with *n*-pentane to selectively solubilized the sulfinyl compound. Evaporation of the pentane solution gave the crude sulfinyl compounds, which were further purified by preparative TLC (silica gel G, 1000 μ, ether solvent).

General Procedure for Determining Optical Purities of Sulfoxides and Thiosulfinates. Optical yields were ascertained by comparing the optical rotations of the sulfinyl compounds obtained via asymmetric oxidation using chiral 2-sulfonyloxaziridine with those reported in the literature.[32] The optical yields determined in this manner were verified by a series of 60-MHz ^1H NMR spectra ($CDCl_3$ at increasing concentration of the chiral shift reagent tris[3-(((heptafluoropropyl)hydroxymethylene)-*d*-camphorato]europium(III) derivative [Eu(hfc)$_3$]. When the shift difference of the appropriate absorption was at least 9 Hz, the peak areas were determined by integration. Agreement between the two methods was approximately ±1.0% ee.

All asymmetric oxidations were carried out at least twice and the results averaged (Table II–III and VI).

Methyl 2,4,6-Tri-*tert*-butylphenyl Sulfide (13g). In a 25-mL three-necked flask equipped with magnetic stirring bar, condenser, syringe, and nitrogen inlets was placed 0.5 g (0.37 mol of 57%) of sodium hydride. After the sodium hydride was washed several times with *n*-pentane, 0.4 g (0.0014 mol) of 2,4,6-tri-*tert*-butylbenzenethiol[33] dissolved in 5 mL of dry THF was added. After the mixture was stirred at room temperature for 30 min 2 mL of iodomethane was added and the reaction mixture allowed to stir overnight under an atmosphere of dry nitrogen. After cautious addition of water, the solution was extracted with ethyl ether, 2 × 50 mL portions. After drying over anhydrous $MgSO_4$, the ether solution was evaporated under vacuum to give the oily sulfide, which was chromatographed (silica gel G, *n*-pentane) to give 0.38 g (93%) of white crystals, mp 48–50 °C, judged to be greater than 95% pure by NMR spectroscopy: NMR ($CDCl_3$) δ 1.3 (s, 13 H), 1.65 (s, 14 H), 2.2 (s, 3 H, S-Me), 7.4 (S, 2 H, Ar).

(*S*)-(−)-Methyl 2,4,6-Tri-*tert*-butylphenyl Sulfoxide (14g). The oxidation of **13g** by (*S,S*)-(−)-**9d** was carried out as described above in chloroform solvent at 25 °C except that the reaction time was 2 h. Sulfoxide **14g** was isolated in 35% yield after isolation by *n*-pentane extraction and preparative TLC on silica gel G (2:1 *n*-pentane/ether): mp 131–133 °C; $[\alpha]_D$ −54.9 (*c* 4.17, $CHCl_3$); IR (KBr) 1082 (S=O) cm^{-1}; NMR ($CDCl_3$) δ 1.25 (s, 9 H, CMe_3), 1.6 (s, 18 H, CMe_3), 2.6 (s, 3 H, S(*O*)Me), 7.3 (s, 2 H, Ar). Anal. Calcd for $C_{19}H_{32}OS$: C, 74.02; H, 10.38. Found: C, 74.30; H, 10.36.

The configuration and optical purity of **14g** were determined by using (*R*)-(−)-phenyl(trifluoromethyl)carbinol as described by Pirkle et al.[25] Increasing concentrations of this chiral solvent when added to (−)-**14g** in $CDCl_3$ resulted in splitting of the Me group into a doublet (maximum 5 Hz) along with an upfield shift in its absorption position.

X-ray Analysis of (−)-11d. A small single crystal of dimensions 0.47 × 0.10 × 0.05 mm was used for all X-ray measurements. The unit cell was found to be orthorhombic, and systematic absences were consistent with space group $P2_12_12$. Room-temperature lattice parameters were refined by a least-squares procedure using 15 reflections whose angles were measured by a centering routine associated with the diffractometer.

Crystal Data: $C_{17}H_{18}BrClN_2O_6S$, M_r 493.77, *a* = 8.109 (2) Å, *b* = 33.395 (6) Å, *c* = 7.368 (2) Å, *V* = 1995.3 (8) Å, *Z* = 4, d_c = 1.64 g cm^{-3}, μ = 56.03 cm^{-1} (Cu Kα, λ = 1.54178 Å).

All data were collected on a Syntex $P2_1$ diffractometer system by the θ–2θ scanning technique using a variable scan speed and a graphite monochromator. Of the 1967 reflections measured, 1544 had intensities greater than 3σ(*I*). Periodically monitored reflections showed no sifnigicant changes in intensity. The direct methods program QTAN[34] was used to solve the structure. Full-matrix least-squares refinement with anisotropic thermal parameters led to an *R* factor of 0.052 and a ω*R* of 0.067 where $R = \sum||F_o| - |F_c||/\sum|F_o|$ and $\omega R = (\sum\omega(|F_o| - |F_c|)^2/\sum\omega|F_o|^2)^{1/2}$. Hydrogen atom positions were calculated but not included in the structure factor calculations. The function minimized in the refinement was $\sum\omega(|F_o| - |F_c|)^2$ where $\omega = 1/\sigma(F_o)^2$. Although the absolute configurations can be ascertained from the known stereochemistry of the endo form of 3-bromo-*d*-camphor, refinement of both enantimers indicate the configuration shown in Figure 1 can be accepted at the 99.9% confidence level.[35]

Final difference maps were checked for residual electron density. Atomic scattering factors were calculated by the XRAY76 program,[36] and the real and imaginary components of the anomalous dispersion were taken from International Tables for X-ray Crystallography.[37] Interatomic distances and valence angles are presented in Tables IV and V.

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Registry No. 4, 60933-63-3; **5**, 60886-78-4; **7a**, 82679-81-0; **7b**, 72538-29-5; **7c**, 72538-28-4; **7d**, 82679-82-1; **8**, 82679-83-2; **9a**, 82679-84-3; **9b**, 72581-75-0; **9c**, 72581-74-9; **9d**, 81310-08-9; **10a**, 82730-20-9; **10b**, 72538-31-9; **10c**, 72538-30-8; (***R,R***)(+)-**10d**, 81369-89-3; (***S,S***)-(−)-**11d**, 82446-77-7; (***R,R***)(+)-**12d**, 81422-07-3; **13a**, 100-68-5; **13b**, 3019-19-0; **13c**, 623-13-2; **13d**, 14905-81-8; **13e**, 7439-10-3; **13f**, 766-92-7; **13g**, 22693-44-3; (**R**)-**14a**, 4850-71-9; (**R**)-**14b**, 4850-72-0; (**R**)-**14c**, 1519-39-7; (**R**)-**14d**, 5056-07-5; **14d**, 50337-53-6; (**R**)-**14e**, 1693-83-0; (**S**)-**14e**, 67501-10-4; (**R**)-**14f**, 2843-91-6; (**S**)-**14f**, 14090-81-4; (**S**)-**14g**, 82679-85-4; **15a**, 103-19-5; **15b**, 110-06-5; (***R***)-(+)-**16b**, 67734-35-4; (***S***)-(−)-**16b**, 60011-16-7; camphorsulfonic-*10-d* acid, 3144-19-9; bromocamphor-π-sulfonic-α-*d* ammonium salt, 14575-84-9; 2-chloro-5-nitrobenzaldehyde diethyl acetal, 20423-20-5.

Supplementary Material Available: Tables of atomic positional parameters, thermal parameters, and calculated and observed structure factors, including fractional coordinates, bond distances, and bond angles of **11d** from the X-ray experiments (14 pages). Ordering information is given on any current masthead page.

(32) Reference 7: (*R*)-sulfoxides: **14a**, $[\alpha]_D$ +178.3° (*c* 2.1, chloroform); **14b**, $[\alpha]_D$ +174.6° (*c* 2.0, chloroform). Reference 6a: (*R*)-sulfoxides: **14c** $[\alpha]_D$ +141.0° (ethanol); **14d**, $[\alpha]_D$ +180.0° (ethanol); **14c**, $[\alpha]_D$ +190.0° (ethanol). Thiosulfinate **16**: see ref 25a.

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